STRUCTURE & REACTIVITY V: REACTIVITY IN ORGANIC, BIOLOGICAL AND INORGANIC CHEMISTRY 3

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CHAPTER OVERVIEW

1: Reduction and Oxidation Reactions

1.1: Oxidation State

Electron transfer is one of the most basic processes that can happen in chemistry. It simply involves the movement of an electron from one atom to another. Many important biological processes rely on electron transfer, as do key industrial transformations used to make valuable products. In biology, for example, electron transfer plays a central role in respiration and the harvesting of energy from glucose, as well as the storage of energy during photosynthesis. In society, electron transfer has been used to obtain metals from ores since the dawn of civilization.

Oxidation state is a useful tool for keeping track of electron transfers. It is most commonly used in dealing with metals and especially with transition metals. Unlike metals from the first two columns of the periodic table, such as sodium or magnesium, transition metals can often transfer different numbers of electrons, leading to different metal ions. Sodium is generally found as Na^+ and magnesium is almost always Mg^{2+}, but manganese could be Mn^{2+}, Mn^{3+}, and so on, as far as Mn^{7+}.

At first glance, "oxidation state" is often synonymous with "charge on the metal". However, there is a subtle difference between the two terms. For example, in a coordination complex, a metal atom that is ostensibly an ion with a charge of +2 may have very little charge on it at all. Instead, the positive charge may be delocalized onto the ligands that are donating their own electrons to the metal. Oxidation state is used instead to describe what the charge on the metal ion would be if the coordinated ligands were removed and the metal ion left by itself.

Oxidation state is commonly denoted by Roman numerals after the symbol for the metal atom. This designation can be shown either as a superscript, as in Mn^{II}, or in parentheses, as in Mn(II); both of these descriptions refer to a Mn^{2+} ion, or what might have been a Mn^{2+} ion before it got into a bonding situation.

Exercise 1.1.1

Translate the following oxidation state descriptions into charges on the metal.

a) Ag^{I} b) Ni(II) c) Mn^{VII} d) Cr(VI) e) Cu(III) f) Fe^{IV} g) Os^{VIII} h) Re(V)

Answer a

a) Ag^+

Answer b

b) Ni^{2+}

Answer c

c) Mn^{7+}

Answer d

d) Cr^{6+}

Answer e

e) Cu^{3+}

Answer f

f) Fe^{4+}

Answer g

g) Os^{8+}

Answer h

h) Re^{5+}

Exercise 1.1.2

a. Provide the valence shell electron configuration for each metal species in the previous question (e.g. oxygen's is $2s^2 2p_x{}^2 2p_y{}^1 2p_z{}^1$).

b. Draw an energy level diagram showing the occupation of valence s, p and d levels for each metal species in the previous question.

The oxidation state of a metal within a compound can be determined only after the other components of the compound have been conceptually removed. For example, metals are frequently found in nature as oxides. An oxide anion is O^{2-}, so every oxygen in a compound will correspond to an additional 2- charge. In order to balance charge, the metal must have a corresponding plus charge.

For example, sodium oxide has the formula Na_2O. If the oxygen ion is considered to have a 2- charge, and there is no charge overall, there must be a corresponding charge of +2. That means each sodium ion has a charge of +1.

? Exercise 1.1.3

Determine the charge on the metal in each of the following commercially valuable ores. Note that sulfur, in the same column of the periodic table as oxygen, also has a 2- charge as an anion.

a) galena, PbS b) cassiterite, SnO_2 c) cinnabar, HgS d) pyrite, FeS_2 e) haematite, Fe_2O_3 f) magnetite, Fe_3O_4

Answer a

a) Pb^{2+} & S^{2-}

Answer b

b) Sn^{4+} & 2 O^{2-}

Answer c

c) Hg^{2+} & S^{2-}

Answer d

d) Fe^{4+} & 2 S^{2-}

Answer e

e) 2 Fe^{3+} & 3 O^{2-}

Answer f

f) 2 Fe^{3+} & 1 Fe^{2+} & 4 O^{2-}

? Exercise 1.1.4

Sphalerite is a common zinc ore, ZnS. However, sphalerite always has small, variable fractions of iron in place of some of the zinc in its structure. What is the likely oxidation state of the iron?

Answer

Probably Fe^{2+}, to replace Zn^{2+} ions.

? Exercise 1.1.5

Sometimes non-metals such as carbon are thought of in different oxidations states, too. For example, the coke used in smelting metal ores is roughly C, in oxidation state 0. Determine the oxidation state of carbon in each case, assuming oxygen is always 2- and hydrogen is always 1+.

a) carbon monoxide, CO b) carbon dioxide, CO_2 c) methane, CH_4 d) formaldehyde, H_2CO e) oxalate, $C_2O_4^{2-}$

Answer a

a) C^{2+}

Answer b

b) C^{4+}

Answer c

c) C^{4-}

Answer d

d) C^0

Answer e

e) C^{3+}

Exercise 1.1.6

Sometimes it is useful to know the charges and structures of some of the earth's most common anions. Draw Lewis structures for the following anions:

a) hydroxide, HO^- b) carbonate, CO_3^{2-} c) sulfate, SO_4^{2-} d) nitrate, NO_3^-

e) phosphate, PO_4^{3-} f) silicate, SiO_4^{4-} g) inosilicate, SiO_3^{2-}

Exercise 1.1.7

Use your knowledge of common anions to determine the oxidation states on the metals in the following ores.

a) dolomite, $MgCO_3$ b) malachite, $Cu_2CO_3(OH)_2$ c) manganite, MnO(OH)

d) gypsum, $CaSO_4$ e) rhodochrosite, $MnCO_3$ f) rhodonite, $MnSiO_3$

Answer a

a) Mg^{2+}

Answer b

b) Cu^{2+}

Answer c

c) Mn^{3+}

Answer d

d) Ca^{2+}

Answer e

e) Mn^{2+}

Answer f

f) Mn^{2+}

Exercise 1.1.8

In mixed-metal species, the presence of two different metals may make it difficult to assign oxidation states to each. For the following ores, propose one solution for the oxidation states of the metals.

a) chalcopyrite, $CuFeS_2$ b) franklinite, $ZnFe_2O_4$ c) beryl, $Be_3Al_2(SiO_3)_6$ d) bornite or peacock ore, Cu_5FeS_4

e) turquoise, $CuAl_6(PO_4)_4(OH)_8$

Answer a

a) Cu(II), Fe(II)

Answer b

b) Zn(II), Fe(III)

Answer c

c) Be(II), Al(III)

Answer d

d) Cu(I), Fe(III)

Answer e

e) Cu(II), Al(III)

? Exercise 1.1.9

Feldspars are believed to make up about 60% of the earth's crust. The alkali, alkaline earth and aluminum metals in these tectosilicates are typically found in their highest possible oxidation states. What are the charges on the silicates in the following examples?

a) orthoclase, $KAlSi_3O_8$ b) anorthite, $CaAl_2Si_2O_8$ c) celsian, $BaAl_2Si_2O_8$ d) albite, $NaAlSi_3O_8$

? Exercise 1.1.10

Frequently, minerals are solid solutions in which repeating units of different compositions are mixed together homogeneously. For example, labradorite is a variation of anorthite in which about 50% of the aluminum ions are replaced by silicon ions and about 50% of the calcium ions are replaced by sodium ions. Show that this composition would still be charge neutral overall.

1.2: Redox Reactions

"Oxidation state" implies a description that can change: a metal can go from one oxidation state to another. For example, a Cu(I) can become a Cu(0). It does so by an electron transfer from one place to another. In the case of Cu(I)/Cu(0), an electron would have to be donated by some other species.

A loss of electrons is called an "oxidation", whereas a gain of electrons is called a "reduction" (as immortalized in the mnemonic: LEO the lion goes GER). Since an electron always goes from somewhere to somewhere else, one thing is always oxidized when something else is reduced. (Note that this is a little like proton transfer reactions: a proton is always transferred from one basic site to another, and is never really by itself.) These paired processes are called "reduction-oxidation" reactions, or "redox" for short.

So the reduction of Cu(I) to Cu(0) is just a "half-reaction"; it needs a corresponding oxidation to make it happen. Li could donate an electron, for example, to become Li^+. In a biological setting, a Fe(III) in an important protein may need an extra electron to become Fe(II) in order to do its job (your life may be at stake here). It could get the electron from a nearby Cu(I), which becomes Cu(II).

Exercise 1.2.1

Balance the following half reactions by adding the right number of electrons to one side or the other.

a) Cu → Cu(I) b) Fe(III) → Fe

c) Mn → Mn^{3+} d) Zn^{2+} → Zn

e) F^- → F_2 f) H_2 → H^+

Answer a

a) $Cu \rightarrow Cu^+ + e^-$

Answer b

b) $Fe^{3+} + 3\ e^- \rightarrow Fe$

Answer c

c) $Mn \rightarrow Mn^{3+} + 3\ e^-$

Answer d

d) $Zn^{2+} + 2\ e^- \rightarrow Zn$

Answer e

e) $2\ F^- \rightarrow F_2 + 2\ e^-$

Answer f

f) $H_2 \rightarrow 2\ H^+ + 2\ e^-$

Sometimes, redox reactions work out very neatly: one participant needs an electron or two, and the other participant has one or two electrons to give. For example, a Cu^{2+} ion in need of two electrons to become a Cu atom might get them from a Zn atom, which would become a Zn^{2+} ion.

In other words (or other symbols):

$$\mathrm{Cu^{2+} + 2\,e^- \longrightarrow Cu}$$

$$\mathrm{Zn^{2+} \longrightarrow Zn + 2\,e^-}$$

Adding those together:

$$\mathrm{Cu^{2+} + Zn \longrightarrow Cu + Zn^{2+}}$$

Note that the electrons on each side just cancel each other, much like adding the same thing to both sides of an equals sign.

So, overall, a copper ion could get a couple of electrons from a zinc atom, leaving a copper atom and a zinc ion. Wouldn't the opposite reaction also be possible?

$$\mathrm{Cu} + \mathrm{Zn}^{2+} \longrightarrow \mathrm{Cu}^{2+} + \mathrm{Zn}$$

On paper, yes. In reality, it doesn't work as well in this direction. In order to help keep track of what redox reactions are actually able to occur, chemists have compiled something called the activity series of metals. The activity series just lists metals in the order in which they are most likely to give up an electron. Metals appearing at the top of the series give up an electron most easily. Metals at the bottom don't give up electrons so readily.

Metal	Ion Formed	Reactivity with Acids
Cs	Cs^+	reacts with water
Rb	Rb^+	
K	K^+	
Li	Li^+	
Ba	Ba^+	
Sr	Sr^+	
Ca	Ca^{2+}	
Mg	Mg^{2+}	reacts with HCl
Al	Al^{3+}	
Mn	Mn^{2+}	
Zn	Zn^{2+}	
Cr	Cr^{2+}	
Fe	Fe^{2+}	
Cd	Cd^{2+}	
Co	Co^{2+}	
Ni	Ni^{2+}	
Sn	Sn^{2+}	
Pb	Pb^{2+}	
H_2	H^+	
Sb	Sb^{2+}	reacts with oxidizing acids
Bi	Bi^{3+}	(HNO_3, etc)
Cu	Cu^{3+}	
Hg	Hg^{2+}	
Ag	Ag^+	
Au	Au^{3+}	
Pt	Pt^{2+}	

The activity series was put together using a variety of information about redox reactions. Sometimes, maybe one metal was simply placed with another metal ion to see whether the reaction occurred. Often other reactions were studied in order to infer how easily a particular metal would give up its electrons. Some of the trends in the activity series have simple explanations and others do not. We will see later that there are many different factors that govern redox reactions.

We have seen a few reactions in which one metal atom simply transfers an electron or two to another metal ion. Other times, things may be slightly more complicated. There may be an issue of conserving matter, for instance. For example, hydrogen gas, H_2, can be oxidised to give proton, H^+. We can't have more hydrogen atoms before the reaction than afterwards; matter can't just be created or destroyed. To solve that problem, the oxidation of hydrogen gas, H_2, produces two protons, not just one, and so two electrons are involved as well.

Alternatively, two half-reactions may actually involve different numbers of electrons, and so proportions of each half reaction need to be adjusted in order to match the number of electrons properly.

? Exercise 1.2.2

Put the following pairs of half reactions together to make a full reaction in each case. Make sure you have balanced the half reactions first.

a) Cu(I) → Cu(II) and Fe(III) → Fe(II) b) Cu(I) → Cu(0) and Ag(0) → Ag(I)

c) F_2 → F^- and Fe → Fe^{3+} d) Mo^{3+} → Mo and Mn → Mn^{2+}

Answer a

a) Cu(I) + Fe(III) → Cu(II) + Fe(II)

Answer b

b) Cu(I) + Ag(0) → Cu(0) + Ag(I)

Answer c

c) 3 F_2 + 2 Fe → 6 F^- + 2 Fe(III)

Answer d

d) 2 Mo^{3+} + 3 Mn → 2 Mo + 3 Mn^{2+}

In many cases, redox reactions do not just involve simple metal ions or atoms. Often, the metal atom is found within a compound or a complex ion. For example, one of the most common oxidizing agents in common use is permanganate ion, MnO_4^-, which is usually converted to manganese dioxide, MnO_2 during a reaction.

That means the half reaction here is:

$$\mathrm{MnO_4^-} \longrightarrow \mathrm{MnO_2}$$

In order to sort out how many electrons are being traded, we need to know the oxidation state of manganese before and after the reaction. That turns out to be Mn(VII) before and Mn(IV) afterwards. That means 3 electrons are added to permanganate to produce manganese dioxide.

Now we have:

$$\mathrm{MnO_4^-} + 3\,\mathrm{e^-} \longrightarrow \mathrm{MnO_2}$$

But now we just have a mass balance problem again. There are oxygen atoms before the reaction that have just disappeared after the reaction. Where could those oxygen atoms have gotten to? On this planet, the simplest answer to that question is always water. So maybe 2 waters were produced as part of the reaction.

That gives us:

$$\mathrm{MnO_4^-} + 3\,\mathrm{e^-} \longrightarrow \mathrm{MnO_2} + 2\,\mathrm{H_2O}$$

Only now we have more problems. First of all, now we have some hydrogen atoms on the right that we didn't have on the left. Where did these things come from? Also, there is this niggling problem of negative charges that we had before the reaction that we don't have after the reaction. Charge, like matter, doesn't just appear or disappear. It has to go someplace, and we have to explain where.

We'll kill two birds with one stone. Maybe some protons were added to the reaction at the beginning, giving us those hydrogen atoms for the water and balancing out the charge.

We are left with:

$$MnO_4^- + 3\,e^- + 4\,H^+ \longrightarrow MnO_2 + 2\,H_2O$$

It all works out. There are four negative charges on the left, and four plus charges, so no charge overall. There are no charges on the right. There is one manganese on the left and on the right. There are four oxygens on the left and on the right. There are four hydrogens on the left and on the right.

An Alternative Situation is Possible

Now let's take a little detour. We're going to go back in time, to the point where we realized we had a problem with our oxygen atoms.

Now we have:

$$MnO_4^- + 3\,e^- \longrightarrow MnO_2$$

But now we just have a mass balance problem again. There are oxygen atoms before the reaction that have just disappeared after the reaction. Where could those oxygen atoms have gotten to? And while we're at it, there are four negative charges on the left and none on the right. Charge doesn't just appear or disappear during a reaction. It has to be balanced.

One solution for this problem involves the production of hydroxide ions, HO^-, during the reaction. Hydroxide ions are pretty common; there are a few in every glass of water. The charge in the reaction would be balanced if four hydroxide ions were produced, and it would explain where those oxygen atoms went.

That gives us:

$$MnO_4^- + 3\,e^- \longrightarrow MnO_2 + 4\,OH^-$$

Now the charge is balanced! But the oxygen atoms aren't. And where did those hydrogen atoms come from?

Well, on this planet, a good source of hydrogen and oxygen atoms is water. Maybe the reaction needs water.

That means:

$$MnO_4^- + 3\,e^- + 2\,H_2O \longrightarrow MnO_2 + 4\,OH^-$$

One manganese on each side. Four hydrogens on each side. Six oxygens on each side. Four negative charges on each side. Nothing has appeared or disappeared during the reaction. We know where everything went.

There is actually a shortcut to get to this solution. If we already know how to balance the reaction in acididc media, we just add enough hydroxides to neutralize the acid ($H^+ + {}^-OH = H_2O$). But we have to add those hydroxides *to both sides*. Some of the waters will then cancel out to leave the balanced reaction.

Start with acid

$$MnO_4^- + 3\,e^- + 4\,H^+ \longrightarrow MnO_2 + 2\,H_2O$$

Add base to both sides

$$MnO_4^- + 3\,e^- + 4\,H^+ + 4\,OH^- \longrightarrow MnO_2 + 2\,H_2O + 4\,OH^-$$

Neutralize

$$MnO_4^- + 3\,e^- + 4\,H_2O \longrightarrow MnO_2 + 2\,H_2O + 4\,OH^-$$

Cancel the extra waters

$$MnO_4 + 3\,e^- + 2\,H_2O \longrightarrow MnO_2 + 4\,OH^-$$

Now we're back. We have seen two different outcomes to this problem. The moral of the story is that sometimes there is more than one right answer. In the case of redox reactions, sometimes things happen a little differently depending on whether things are occurring under acidic conditions (meaning, in this context, that there are lots of protons around) or in basic conditions (meaning there aren't many protons around but there is hydroxide ion).

Apart from helping us to keep track of things, the presence of acids (protons) and bases (hydroxide ions) in redox reactions are common in reality. For example, batteries rely on redox reactions to produce electricity; the electricity is just a current of electrons trying to get from one site to another to carry out a redox reaction. Many batteries, such as car batteries, contain acid. Other batteries, like "alkaline" batteries, for example, contain hydroxide ion.

? Exercise 1.2.3

Balance the following half reactions. Assume the reactions are in acidic conditions.

a)$MnO_2 \rightarrow Mn(OH)_2$ b) $NO \rightarrow N_2O$

c)$HPO_3^{2-} \rightarrow H_2PO_2^-$ d) $Sn(OH)_6^{2-} \rightarrow HSnO_2^-$

Answer a

a) $MnO_2 + 2\ H^+ + 2\ e^- \rightarrow Mn(OH)_2$

Answer b

b) $2\ NO + 2\ e^- + 2\ H^+ \rightarrow N_2O + H_2O$

Answer c

c) $HPO_3^{2-} + 2\ e^- + 3\ H^+ \rightarrow H_2PO_2^- + H_2O$

Answer d

d) $Sn(OH)_6^{2-} + 2\ e^- + 3\ H^+ \rightarrow HSnO_2^- + 4\ H_2O$

? Exercise 1.2.4

State whether or not a reaction would occur in the following situations.

a. Copper wire is covered in nitric acid.
b. Copper wire is covered in zinc chloride.
c. An aluminum sheet is covered in lead chloride.
d. A silver coin is submerged in hydrochloric acid.
e. calcium metal is dropped in water.
f. an iron bar is dipped in hydrochloric acid.
g. a manganese(II) complex is treated with sodium amalgam
h. chromium metal is covered in water

Answer a

a) yes

Answer b

b) no

Answer c

c) yes

Answer d

d) no

Answer e

e) yes

Answer f

f) yes

Answer g

g) yes

Answer h

h) no

Exercise 1.2.5

a) Given the standard reduction potentials below (vs. NHE), determine the cell potential for the reduction of O_2 to O_2^- by Cu(I) ion.

$$\mathrm{Cu^{2+} + e^- \longrightarrow Cu^+} \backslash)\backslash(E^\circ = +0.153V$$

$\mathrm{Cu^+ + e^- \longrightarrow Cu}\ \ E^\circ = +0.521V$
$\mathrm{O_2 + e^- \longrightarrow O_2^-}\ \ E^\circ = -0.33V$

b) Is the reaction favored under these conditions?

c) Reactions in the presence of metals often involve substrate binding. Show, with arrows and structures, the substrate binding step that would be involved in this case.

d) Explain how this factor may influence the reduction potential of the oxygen.

e) Explain how the following observation supports your answer.

$$\mathrm{O_2 + H^+ e^- \longrightarrow HO_2} \backslash)\backslash(E^\circ = -0.13V$$

f) Metal ions in biology are usually coordinated by amino acid residues. Show a Cu(I) ion coordinated to two aspartic acid residues and two histidine residues.

g) Explain how this factor may influence the reduction potential of the copper.

Answer a

a) E_{rxn} = - 0.153 V - 0.33 V = - 0.483 V

Answer b

b) No.

Answer c

c)

Answer d

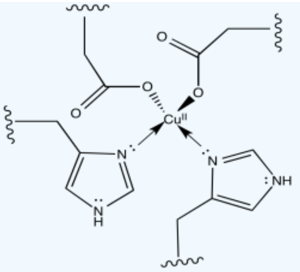
d) The O_2 is activated as an electrophile. Addition of an electron may become easier.

Answer e

e) The reduction potential is 0.2 V more positive when the resulting superoxide ion is stabilised by binding a proton. A similar shift could occur when coordinated to copper.

Answer f

f)



Answer g

The two aspartate ions would make the copper complex less cationic. That may make it easier to remove an electron from the copper complex.

? Exercise 1.2.6

The use of Cl_2 in water treatment has been linked to production of harmful chlorinated species in waterways. ClO_2 has been proposed as an alternative, so researchers at Purdue decided to investigate its potential reactivity with common aqueous ions such as iron. (Margerum, *Inorg. Chem.* **2004**, *43*, 7545-7551.)

$$\mathrm{ClO_2} + \mathrm{e^-} \longrightarrow \mathrm{ClO_2^-} \backslash)\backslash(E^\circ = 0.95V$$

$$\mathrm{Fe^{3+}} \mathrm{e^-} \longrightarrow \mathrm{Fe^{2+}} \backslash)\backslash(E^\circ = 0.77V$$

a. Provide an overall reaction from these half-reactions.
b. Calculate the potential for the overall reaction.
c. Is the reaction favored?
d. Provide a Lewis structure for ClO_2 (connectivity O-Cl-O).
e. Propose a reason for the overall thermodynamics (i.e. favored or disfavored) of the reaction.
f. Does the mechanism seem more likely to proceed by an inner sphere mechanism or by an outer sphere mechanism? Explain why.
g. The addition of ClO_2^- to Fe^{3+} (aq) is known to produce the complex $(H_2O)_5Fe(ClO_2)^{2+}$. This complex has a broad absorption band between 480 and 540 nm in the UV-Visible spectrum. Upon mixing ClO_2 and Fe^{2+} (aq), a broad absorbance appears at 500 nm within 20 ms. Explain this observation.

Answer a

a) $Fe^{2+} + ClO_2 \rightarrow Fe^{3+} + ClO_2^-$

Answer b

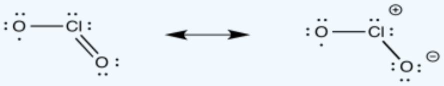
b) $E_{rxn} = 0.95\ V - 0.77\ V = 0.18\ V$

Answer c

c) yes.

Answer d

d)



Answer e

e) ClO_2 has an unpaired electron. ClO_2^- has electrons paired.

Answer f

f) It could be inner sphere: the oxygen in the ClO_2 could coordinate to the iron.

Answer g

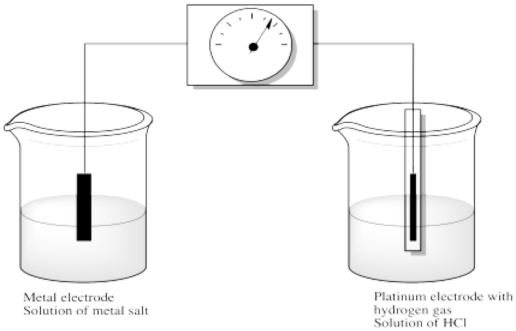
g) The mixture quickly forms $(H_2O)_5Fe(ClO_2)^{2+}$ via inner sphere electron transfer.

1.3: Reduction Potential

Iron and copper are two common metals in biology, and they are both involved in electron relays in which electrons are passed from one metal to another to carry out transformations on substrates in cells. But which one passes the electron to which? Or can it go either way?

How easily one metal can pass an electron to another, or how easily one metal can reduce another, is a pretty well-studied question. There are some preferences, some of which can be easily understood.

In order to look at this question, electrochemists typically measure the voltage produced when a circuit is set up that includes an electron made of the metal in question and an electrode made of a "standard hydrogen electrode". In a standard hydrogen electrode, hydrogen gas (H_2) reacts on a platinum surface to produce two electrons and two protons. The electrons travel along a wire to the other electrode. The other electrode sits in an aqueous solution containing a salt of the metal in question. How easily is the metal ion reduced by accepting the electrons from the standard hydrogen electrode? The more downhill energetically this process is, the more positive is the voltage measured in the circuit.



For example, we might put some copper(II) salts, such as $CuSO_4$, into the solution together with a copper electrode. Then we would see whether the copper in solution is spontaneously reduced to copper metal. That would happen, essentially, if the copper ion is more easily reduced than a proton. Thus, an electron released by hydrogen flows from the platinum electrode to the copper electrode and is picked up by copper ions waiting in solution.

Otherwise, what would happen if the reaction were not spontaneous? If no reaction occurred at all, maybe there would be no voltage. However, if the opposite reaction were to occur -- if copper were able to provide an electron to convert protons into molecular hydrogen -- then current would flow through the circuit in the opposite direction. A voltage would register, but it would be negative.

As it happens, the reaction is spontaneous, the hydrogen does send electrons through the wire, turning into protons in the process, and at the other end of the wire, the copper ion is converted into copper metal, putting another layer on the surface of the electrode. The voltage is about 0.34V.

This is a comparative, rather than absolute, measurement. We are measuring the intrinsic potential of an electron to be transferred from one species, a hydrogen molecule, to another, a Cu(II) ion.

It is also an intensive, rather than extensive, property. It does not matter how much copper we have, or how much hydrogen; the electron still has the same natural tendency to flow from the hydrogen to the copper.

The results of many such studies, carefully measured under specific conditions for maximum reproducibility, are gathered in a table of reduction potentials. The reactions are referred to as "half-reactions" because they each provide only half the picture of what is going on. The electron in each reaction doesn't come from nowhere; every reaction in the table would involve transfer of an electron from elemental hydrogen to form a proton.

Half Reaction (species are aqueous unless noted otherwise)	Potential, Volts
$\mathrm{Li^+ + e^- \longrightarrow Li(s)}$	- 3.04

$\mathrm{Al(OH)_3(s) + 3\,e^- \longrightarrow Al(s) + 3\,OH^-}$	- 2.31
$\mathrm{Al^{3+} + 3\,e^- \longrightarrow Al(s)}$	- 1.662
$\mathrm{Zn^{2+} + 2\,e^- \longrightarrow Zn(s)}$	- 0.762
$\mathrm{Fe^{2+} + 2\,e^- \longrightarrow Fe(s)}$	- 0.44
$\mathrm{CO_2(g) + 2\,H^+ 2\,e^- \longrightarrow CO(g) H_2O}$	- 0.11
$\mathrm{SnO(s) 2\,H^+ + 2\,e^- \longrightarrow Sn(s) + H_2O}$	- 0.10
$\mathrm{2\,H^+ + 2\,e^- \longrightarrow H_2(g)}$	0.00
$\mathrm{Fe_3O_4(s) + 8\,H^+ + 8\,e^- \longrightarrow 3\,Fe(s) + 4\,H_2O}$	+ 0.085
$\mathrm{Cu^{2+} + 2\,e^- \longrightarrow Cu^0}$	+ 0.34
$\mathrm{Ag_2O(S) + H_2O + 2\,e^- \longrightarrow 2\,Ag(s) + 2\,OH^- aq}$	+ 0.342
$\mathrm{O_2(g) + 2\,H_2O + 4\,e^- \longrightarrow 4\,OH^-}$	+ 0.40
$\mathrm{CO(g) + 2\,H^+ + 2\,e^- \longrightarrow C(s) + H_2O}$	+ 0.52
$\mathrm{Cu^+ + e^- \longrightarrow Cu(s)}$	+ 0.52
$\mathrm{MnO_4^- + 2\,H_2O + 3\,e^- \longrightarrow MnO_2(s) + 4\,OH^-}$	+ 0.59
$\mathrm{Fe^{3+} + e^- \longrightarrow Fe^{2+}(aq)}$	+ 0.77
$\mathrm{Ag^+ + e^- \longrightarrow Ag(s)}$	+ 0.796
$\mathrm{MnO_2 + 4\,H^+ + 2\,e^- \longrightarrow Mn^{2+} + 2\,H_2O}$	+ 1.23
$\mathrm{MnO_4^- + 4\,H^+ + 3\,e^- \longrightarrow MnO_2(s) + 2\,H_2O}$	+ 1.70
$\mathrm{Au^+ + e^- \longrightarrow Au(s)}$	+ 1.83
$\mathrm{F_2(g) + e^- \longrightarrow 2\,F^-}$	+ 2.87

Much more extensive tables of reduction potentials can be found; for example, see the following Wikipedia data page.

A positive reduction potential indicates a spontaneous reaction. That makes sense, for instance, in the reaction of fluorine to give fluoride ion. For that reaction, E^0 = 2.87 V. Of course, fluorine is a very electronegative element, and it will spontaneously accept an electron to obtain a noble gas configuration.

A negative reduction potential, on the other hand, indicates a reaction that would not occur spontaneously. For example, we would not expect lithium cation to accept an electron. We are used to thinking about alkali metals easily giving up their electrons to become cations. The reduction of lithium ion has a reduction potential E^0 = -3.04 V. This reaction would only occur if it were driven by an expenditure of energy.

The opposite reaction, on the other hand, would be the oxidation of lithium metal to give a lithium cation. That reaction would occur spontaneously, and would have a spontaneous "oxidation potential". In fact, that value is + 3.04 V. The oxidation potential is always the same magnitude of the reduction potential for the reverse reaction, but with the opposite sign.

These signs may seem counter-intuitive if you are used to thinking of free energy changes. A negative free energy change means energy is lost in a reaction. A positive free energy change means energy must be put into a reaction to drive it forward. In fact, reduction potential and free energy are closely linked by the following expression:

$$\Delta G = -nFE^0$$

in which n = number of electrons transferred in the reaction; F = Faraday's constant, 96 500 Coulombs/mol.

So, a positive reduction potential translates into a negative free energy change.

Note that reduction potentials are pretty sensitive to changes in the environment. Factors that may stabilize one particular metal ion may not have the exact same effect on another, and so the preference for one state versus another will be altered slightly under different conditions.

For example, permanganate ion (MnO_4^-) has a more positive reduction potential under "acidic conditions" (with excess protons in solution) compared to "basic conditions" (with a paucity of protons in solution and instead an excess of hydroxide ion). The reduction potential under acidic conditions is +1.23V, compared to +0.59 V under basic conditions.

Tables of reduction potentials are also useful in assessing the opposite reaction. For example, lithium metal spontaneously reduces protons to produce hydrogen gas, becoming lithium ion in turn. The potential for that reaction is simply the opposite of the reduction potential of lithium ion; this is called the oxidation potential of lithium metal. The more positive a metal's oxidation potential, the more easily it is oxidized. However, we don't need a separate table of those values; they are just the opposite of the reduction potentials. Reactions with negative reduction potentials easily go backwards, reducing the proton to hydrogen gas by taking an electron from the reducing agent.

However, the most important use of standard reduction potentials is combining them to find out the potential of new reactions.

For example, when it says in the table that

$$\mathrm{Cu^+ + e^- \longrightarrow Cu(s)}\backslash)\backslash(E^0 = 0.53V$$

It really means that is the potential produced for a specific reaction involving electron transfer between hydrogen and copper ion:

$$\mathrm{H_2(g) + 2\,Cu^+ \longrightarrow 2\,Cu(s) + 2\,H^+}\backslash)\backslash(E^0 = 0.53V$$

And when it says that

$$\mathrm{Fe^{2\,+} + 2\,e^- \longrightarrow Fe(s)}\backslash)\backslash(E^0 = -0.44V$$

It really means that

$$\mathrm{H_2(g) + Fe^{2\,+} \longrightarrow Fe(s) + 2\,H^+}\backslash)\backslash(E^0 = -0.44V$$

But now we know that reaction is endergonic, with a negative reduction potential and a positive free energy change. However, the reverse reaction

$$\mathrm{Fe(s) + 2\,H^+ \longrightarrow H_2(g) + Fe^{2\,+}}\backslash)\backslash(E^0 = 0.44V$$

has a positive reduction potential and would proceed easily.

Now, if we combine those previous reactions, simply by adding them together

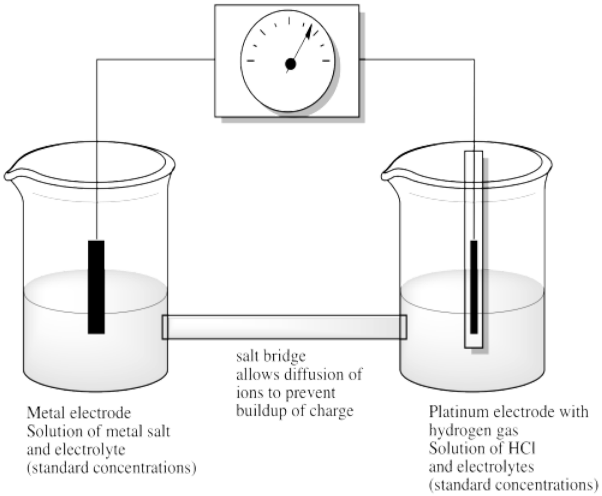
$$\mathrm{H_2(g) + 2\,Cu^+ + Fe(s) + 2\,H^+ \longrightarrow H_2(g) + Fe^{2\,+} + 2\,Cu(s) + 2\,H^+}\backslash)\backslash(E^0 = 0.44 + 0.53V$$

and simplifying

$$2\,\mathrm{Cu}^{+} + \mathrm{Fe(s)} \longrightarrow \mathrm{Fe}^{2+} + 2\,\mathrm{Cu(s)}\backslash)\backslash(E^0 = 0.97V$$

That means the hydrogen reaction doesn't need to be involved at all. It's just a common reference point for all the other reactions. If we know how far uphill (or downhill) any two reactions are compared to that one, then we know how they compare to each other, too.

We should note that electrochemistry is a business that demands great care. There are a number of factors that can cause variations in the potential that is measured, and so we need to be very careful to control for those factors. For example, if there is a buildup of charge in one solution or another (because we are taking cations out of solution in one case and putting them into solution in the other), the ability to remove more electrons at one electrode and deliver them at another may be hindered. For that reason, a "salt bridge" is incorporated into the design of the system; this bridge allows ions to diffuse from one cell to the other in order to keep charge balanced. Also, the solutions are maintained at a standard concentration to make sure measurements are always made in comparable circumstances. Finally, non-reactive electrolytes (salts) are added to solution to aid in conductivity and maintain a constant ionic strength.



Exercise 1.3.1

Calculate oxidation states to confirm that the manganese ion is being reduced in the following reaction:

$$\mathrm{MnO_4^-} + 2\,\mathrm{H_2O} + 3\,\mathrm{e^-} \longrightarrow \mathrm{MnO_2(s)} + 4\,\mathrm{OH^-}$$

Answer

MnO_4^- : 4 x O^{2-} (= 8^-) + Mn^{7+} = 1^- overall

MnO_2 : 2 x O^{2-} (= 4^-) + Mn^{4+} = neutral overall

difference = 3 e^-

Exercise 1.3.2

Balance the following half reactions by adding the right number of electrons to one side or the other, based on oxidation state. Then add water molecules and protons to help balance oxygens and overall charge.

a. $S_2O_8^{2-}$ → 2 SO_4^{2-}
b. HPO_3^{2-} → P
c. Ti_2O_3 → 2 TiO
d. N_2 → 2 NH_2OH

Answer a

a) SO_4^{2-} : 4 x O^{2-} (= 8^-) + S^{6+} = 2^- overall

$S_2O_8^{2-}$: 8 x O^{2-} (= 16^-) + 2 x S^{7+} (= 14^+) = 2^- overall

difference = 1 e^- per S, or 2 e^- overall

$S_2O_8^{2-} + 2\ e^- \rightarrow 2\ SO_4^{2-}$

Answer b

b) HPO_3^{2-} : 3 x O^{2-} (= 6^-) + H^+ + P^{3+} = 2^- overall

P : P(0)

difference = 3 e^-

$HPO_3^{2-} + 3\ e^- + 5\ H^+ \rightarrow P + 3\ H_2O$

Answer c

c) Ti_2O_3 : 3 x O^{2-} (= 6^-) + 2 x Ti^{3+} (= 6^+) = neutral overall

TiO : O^{2-} + Ti^{2+} = neutral overall

difference = 1 e^- per Ti, or 2 e^- overall

$Ti_2O_3 + 2\ e^- + 2\ H^+ \rightarrow 2\ TiO + H_2O$

Answer d

d) N_2 : N(0)

NH_2OH : O^{2-} + 3 x H^+ (= 3^+) + N^- = neutral overall

difference = 1 e^- per N, or 2 e^- overall

$N_2 + 2\ e^- + 2\ H^+ + 2\ H_2O \rightarrow 2\ NH_2OH$

? Exercise 1.3.3

Why is the reduction potential of Li^+ so negative?

Answer

Lithium is an alkali metal, in the first column of the periodic table. It has a relatively low ionization energy because it has a noble gas configuration as a cation. That noble gas configuration is stable because of the relatively large number of nuclear protons and a relatively short distance between the nucleus and the outermost shell of electrons. In lithium metal, the outermost electron is relatively far from the nucleus and so it is at a relatively high energy, and easily lost.

? Exercise 1.3.4

Why is the reduction potential of F_2 so positive?

Answer

Fluorine is a halogen, with a relatively high electron affinity. It easily gains an electron to get to a noble gas configuration as a fluoride anion. That noble gas configuration is stable because of the relatively large number of nuclear protons and a relatively short distance between the nucleus and the outermost shell of electrons.

? Exercise 1.3.5

Rank the following metals from most easily oxidized to least easily oxidized: gold, iron, aluminum, copper, lithium.

Answer

From most easily oxidized to least easily oxidized: Li > Al > Fe > Cu > Au

Exercise 1.3.6

Calculate reduction potentials for the following reactions:

a. $\mathrm{Au + Ag^{+} \longrightarrow Au^{+} + Ag}$
b. $\mathrm{Zn + Fe^{2+} \longrightarrow Zn^{2+} + Fe}$
c. $\mathrm{Li + Cu^{+} \longrightarrow Li^{+} + Cu}$
d. $\mathrm{Ag + Fe^{3+} \longrightarrow Ag^{+} + Fe^{2+}}$

Answer a

a) E^0 = + 0.796 (Ag^+/Ag) - 1.83 (Au/Au^+) = -1.034 V (no forward reaction)

Answer b

b) E^0 = - 0.44 (Fe^{2+}/Fe) + 0.762 (Zn/Zn^{2+}) = + 0.0322 V (forward reaction)

Answer c

c) E^0 = + 0.52 (Cu^+/Cu) + 3.04 (Li/Li^+) = + 3.56 V (forward reaction)

Answer d

d) E^0 = + 0.77 (Fe^{3+}/Fe^{2+}) - 0.796 (Ag/Ag^+) = - 0.026 V (no forward reaction)

Exercise 1.3.7

In general, if one reaction is combined with the reverse of a reaction above it in the table, will the overall reaction be spontaneous? What about if a reaction is combined with the reverse of a reaction below it?

Answer

When the table of standard reduction potentials is displayed with the most negative value at the top and the most positive value at the bottom, any given half-reaction will go forward if it is coupled with the reverse of a half-reaction that lies above it in the table. The opposite is not the case; no half reaction will go forward if it is coupled with the reverse of a half-reaction below it in the table.

1.4: Reduction Potential and Energy Levels

Reduction potentials are relative. Standard reduction potentials are reported relative to the reduction of protons in a standard hydrogen electrode (SHE). But what would we see if we used some other sort of electrode for comparison?

For example, instead of a hydrogen electrode, we might use a fluorine electrode, in which we have fluoride salts and fluorine gas in solution with a platinum electrode. (Maybe we just don't think working with hydrogen is dangerous enough.)

The "reduction potentials" we measure would all be relative to this reaction now. They would tell us: how much more motivated is this ion to gain an electron than fluorine?

The resulting table would look something like this:

Half Reaction (species are aqueous unless noted otherwise)	Potential, Volts, Relative to Fluorine Reduction
$Li^+ + e^- \rightarrow Li(s)$	- 5.91
$Al(OH)_3(s) + 3e^- \rightarrow Al(s) + 3OH^-$	- 5.18
$Sc^{3+} + 3e^- \rightarrow Sc(s)$	- 4.95
$Al^{3+} + 3e^- \rightarrow Al(s)$	- 4.53
$V^{2+} + 2e^- \rightarrow V(s)$	- 4.00
$Zn^{2+} + 2e^- \rightarrow Zn(s)$	- 3.632
$Fe^{2+} + 2e^- \rightarrow Fe(s)$	- 3.31
$CO_2(g) + 2H^+ + 2e^- \rightarrow CO(g) + H_2O$	- 2.98
$Cu^+ + e^- \rightarrow Cu(s)$	- 2.98
$2H^+ + 2e^- \rightarrow H_2(g)$	- 2.87
$Fe_3O_4(s) + 8H^+ + 8e^- \rightarrow 3Fe(s) + 4H_2O$	- 2.79
$Cu^{2+} + 2e^- \rightarrow Cu^0$	- 2.53
$CO(g) + 2H^+ + 2e^- \rightarrow C(s) + H_2O$	- 2.35
$MnO_4^- + 2H_2O + 3e^- \rightarrow MnO_2(s) + 4OH^-$	- 2.28
$Fe^{3+} + e^- \rightarrow Fe^{2+}$	- 2.10
$Ag^+ + e^- \rightarrow Ag(s)$	- 2.074
$MnO_2 + 4H^+ + 2e^- \rightarrow Mn^{2+} + 2H_2O$	- 1.64
$MnO_4^- + 4H^+ + 3e^- \rightarrow MnO_2(s) + 2H_2O$	- 1.17
$Au^+ + e^- \rightarrow Au(s)$	- 1.04
$F_2(g) + 2e^- \rightarrow 2F^-$	0.00

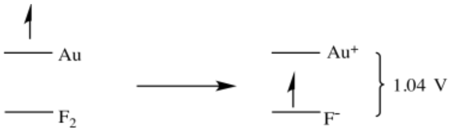
The trouble is, there isn't much out there that would be more motivated than fluorine to gain an electron. All of the potentials in the table are negative because none of the species on the left could take an electron away from fluoride ion. However, if we turned each of these reactions around, the potentials would all become positive. That means gold, for instance, could give an electron to fluorine to become Au(I). This electron transfer would be spontaneous, and a voltmeter in the circuit between the gold electrode and the fluorine electrode would measure a voltage of 1.04 V.

That potential is generated by the reaction:

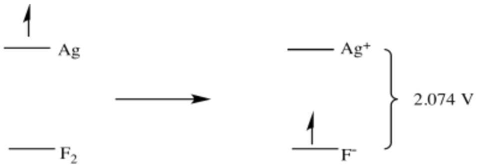
$$2\,Au(s) + F_2(g) \longrightarrow 2\,Au^+ + 2\,F^-$$

Notice that, because 2 electrons are needed to reduce the fluorine to fluoride, and because gold only supplies one electron, two atoms of gold would be needed to supply enough electrons.

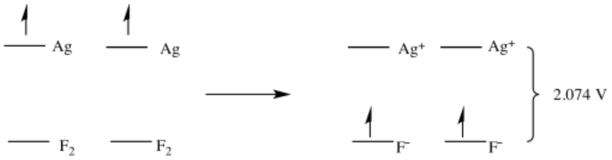
The reduction potentials in the table are, indirectly, an index of differences in electronic energy levels. The electron on gold is at a higher energy level than if it were on fluoride. It is thus motivated to spontaneously transfer to the fluorine atom, generating a potential in the circuit of 1.04V.



Silver metal is even more motivated to donate an electron to fluorine. An electron from silver can "fall" even further than an electron from gold, to a lower energy level on fluoride. The potential in that case would be 2.074 V.



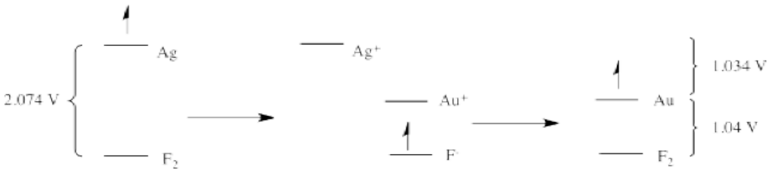
There are a couple of things to note here. The first is that, if potential is an index of the relative energy level of an electron, it doesn't matter whether one electron or two is transferred. They are transferred from the same, first energy level to the same, second energy level. The distance that the electron falls is the same regardless of the number of electrons that fall. A reduction potential reflects an inherent property of the material and does not depend on how many electrons are being transferred.



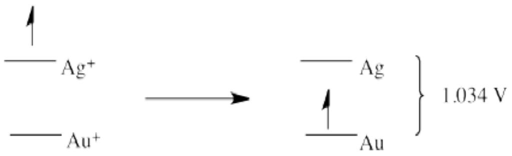
- Reduction potentials reflect the energy difference between two states
- The difference between those two states involves an exchange of one or more electrons
- Frequently, the reduction potential simply reflects the energy level of the electron in one state versus the other (although we will see other factors later)
- The number of electrons transferred *does not* affect the energy difference between the two states, and so does not affect the reduction potential
- The number of electrons *would* affect the overall energy gained / released during the electron transfer reaction (because $\Delta G = -nFE$)

Another important note is that, if reduction potentials provide a glimpse of electronic energy levels, we may be able to deduce new relationships from previous information. For example, if an electron on gold is 1.04 V above an electron on fluoride, and an electron on silver is 2.074 V above an electron on fluoride, what can we deduce about the relative energy levels of an electron on silver vs. gold?

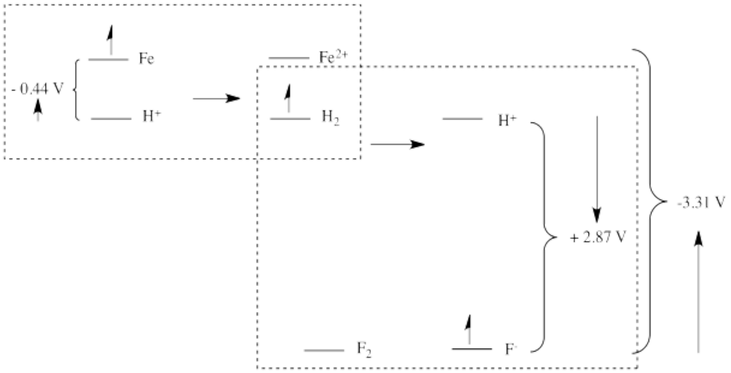
The answer is that the electron on silver is 1.034 V above the electron on gold. We know this because reduction potentials are "state functions", reflecting an intrinsic property of a material. It doesn't matter how we get from one place to another; the answer will always be the same. That means that if we transfer an electron from silver to gold indirectly, via fluorine, the overall potential will be the same as if we transfer the electron directly from silver to gold. So, the electron drops from silver to fluorine (a drop of 2.074 V). The electron then hops (under duress) up to gold (a climb of 1.04 V). The net drop is only 1.034 V.



That's the same value we would expect to measure if we took a standard solution of gold salts and a gold electrode and connected it, via a circuit, to a standard solution of silver salts and a silver electrode.



In fact, the table above doesn't reflect any experimental measurements; it's simply the table of standard reduction potentials from the previous page, with the reduction potential of fluorine subtracted from all the other values.

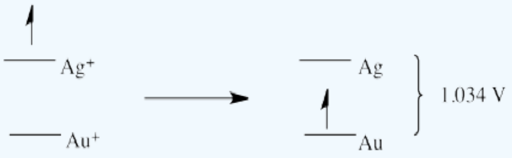


In other words, mapping out the distance from iron to SHE (in terms of the reduction potential for Fe^{2+} + 2 e$^-$ → Fe(s)), together with the distance from SHE to fluorine gives the potential relative to IFE (imaginary fluorine electrode).

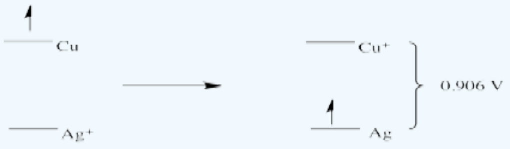
? Exercise 1.4.1

a. Show an energy diagram showing the relative energy levels when an electron is transferred from silver to gold(I) ion. What is the potential for this reaction?
b. Show an energy diagram showing the relative energy levels when an electron is transferred from copper to silver(I) ion. What is the potential for this reaction?
c. Show how the results of (a) and (b) can be used to determine the potential for the transfer of an electron from copper to gold(I) ion.

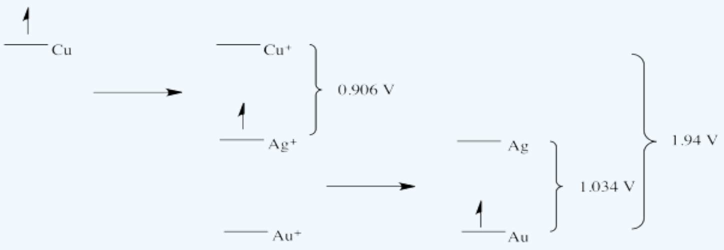
Answer a



Answer b



Answer c



? Exercise 1.4.2

Frequently in biology, electron transfers are made more efficient through a series of smaller drops rather than one big jump. To think about this, consider the transfer of an electron from lithium to fluorine. (Neither of these species is likely to be found in an organism, but this transfer is a good illustration of a big energy difference.)

a. Write an equation for this reaction.
b. What would be the potential for this reaction?
c. This is a highly exothermic reaction; however, our imaginary organism that attempts to harness this reaction as an energy source is likely to burst into flames every time the reaction occurs. Comment on the organism's Darwinian fate.
d. Propose, instead, a series of reactions that the organism could use to slow down the release of energy. Suppose the organism, apart from fluorine and lithium, also harbors reserves of scandium(III), silver(I), copper(I), vanadium(II) and gold(I).
e. Show an energy diagram for this series of reactions and label the potential for each step. Explain why this approach would more efficiently harness the energy of lithium's electron.

Answer a

a) $2\ Li + F_2 \rightarrow 2\ Li^+ + 2\ F^-$

Answer b

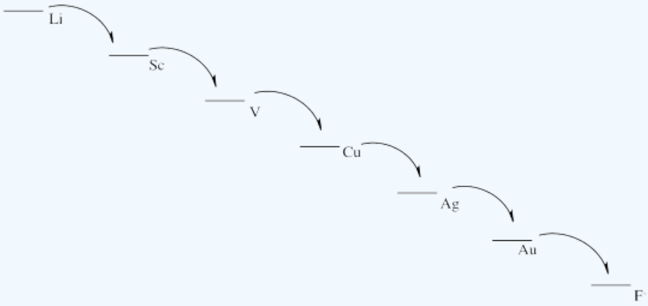
b) $E^o = +5.91\ V$

Answer c

c) Things look pretty grim.

Answer d

d)



Answer e

e) This scheme would result in the release of a small amount of energy at each stage. Each step could be harnessed to perform a task more efficiently, with less heat loss.

? Exercise 1.4.3

An "activity series" is a ranking of elements in terms of their "activity" or their ability to provide electrons. The series is normally written in a column, with the strongest reducing metals at the top. Beside these elements, we write the ion produced when the metal loses its electron(s). Looking at the table of reduction potentials relative to fluorine on this page, construct an activity series for the available elements.

Answer

Li

Sc

Al

V

Zn

Fe

Cu

H_2

Ag

Au

Exercise 1.4.4

Construct an activity series for the alkali metals using the following standard reduction potentials (relative to SHE): Fr, -2.9 V; Cs, -3.026 V; Rb, -2.98 V; K, -2.931 V; Na, -2.71 V; Li, -3.04 V.

Answer

Li

Cs

Rb

K

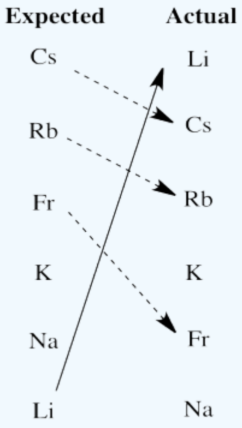
Fr

Na

Exercise 1.4.5

In reality, the energy gap that leads to a reduction potential is sometimes more complicated than following an electron as it moves from one level to another. Use the activity series you have constructed for the alkali metals to compare and contrast the redox potential with your expectations of energy level / ease of electron donation based on standard periodic trends.

Answer



There are really two significant departures from expectation here. Lithium is much more active than expected based on electronegativity. The larger alkali metals, cesium, rubidium and francium, are all less active than expected on that basis.

We will see that another factor the influences activity in redox is the stability of ions in aqueous solution. Lithium cation is a small ion; water molecules bind very strongly to the ion because the electrons get relatively close to lithium's nucleus. That strong binding stabilizes this ion especially, tipping the malance of the reaction more strongly towards oxidation of lithium. The larger alkali metal ions are not nearly as stabilized by water ligands in aqueous solution, so the balance of their reactions does not tilt as strongly towards aqueous ions.

1.5: Factors Influencing Redox Potential

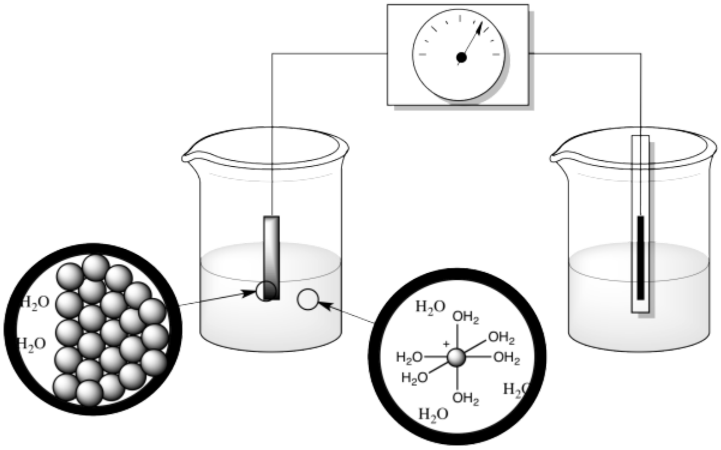
In general, the ions of very late transition metals -- those towards the right-hand end of the transition metal block, such as copper, silver and gold -- have high reduction potentials. In other words, their ions are easily reduced. Alkali metal ions -- on the very left edge of the periodic table, such as potassium or cesium -- have very negative reduction potentials. These ions are very difficult to reduce. These trends are not surprising, because alkali metals are generally at the lower end of the electronegativity scale and are typically found as cations, not as neutral atoms. Late transition metals are *comparatively* electronegative in this case, and so we would expect their ions to attract electrons more easily than alkali metal ions.

The nice thing about redox is you can always look at it from either direction. Oxidation is simply the opposite of reduction. How easily does an alkali metal lose an electron? If the standard reduction potential of lithium is very negative, then the oxidation potential of lithium ion is very positive. If it is uphill to transfer an electron from hydrogen to lithium cation, it must be downhill to transfer an electron from a lithium atom to a proton. After all, hydrogen is more electronegative than any of the alkalis. Of course, since a late transition metal is generally more electronegative than an alkali metal, copper or silver or gold ought to be more difficult to oxidize than sodium or potassium.

The large trends in redox chemistry are not surprising, then. It's simply a matter of the electron moving to a lower energy level on another atom.

If we look a little more closely, though, there are plenty of exceptions to the general trend. For example, in the coinage triad, gold has the most positive reduction potential, followed by silver, then copper. That's exactly the opposite of expectations; copper, at the top of the column, should be the most electronegative and have the most positive reduction potential, not the least. What's going on in those cases?

Well, there's more going on than just moving an electron. Remember, in the measurement of a reduction potential, we are generally working with a metal electrode in an aqueous solution of ions.

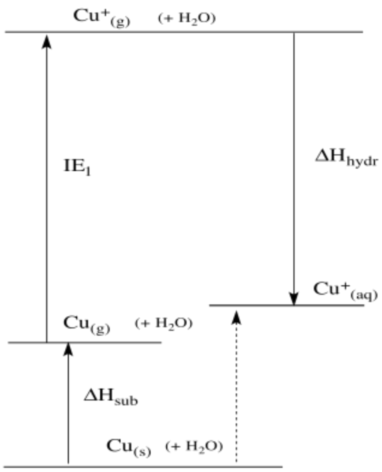


What else is going on in this reaction? Well, the atom that gets reduced starts out as an ion in water, but an ion in water doesn't sit around on its own. It's a Lewis acid, an electrophile. Water is a nucleophile, a potential ligand. So the ion in solution is actually a coordination complex. It swims around for a while, then bumps into the cathode, where it picks up the electron. But the resulting ion doesn't stay in solution; it gets deposited at the electrode, along with others of its kind. It becomes part of a metal solid.

So there are three different things happening here: ligand dissociation, electron transfer and solid formation. If we could get some physical data on each of those events, we might be able to explain why these reduction potentials are contrary to expectations.

The kinds of data we have available for these individual steps may actually fit the opposite reaction better. We can estimate the energy involved in the removal of a metal atom from the solid, the loss of an electron from the metal, and the binding of water to the resulting ion. These data come from measurement of the heat of vaporization of the metal, the ionization energy of the metal, and the enthalpy of hydration of the metal.

We can use these data to construct a thermodynamic cycle. The cycle describes an alternate pathway from copper metal to aqueous Cu(I) ion. The alternative pathway, if we've chosen it correctly, ought to give us a pretty good idea of the enthalpy change involved in the reduction of copper.



The trouble is, these data all involve the gas phase. If they really applied to this situation, it would be as if metal atoms sprayed out into the air above the electrode, shot their electrons back, grabbed some water molecules that drifted by, and then dropped down into the solution. Of course that doesn't happen; we don't see a little, sparkly, metallic mist appear when we connect the circuit, or little lightning bolts from the cloud of metal atoms to the electrode, and we don't see a splash or a fizz or little tendrils of steam as the resulting ions drop into the water.

That doesn't matter. The data we have here are still very useful. That's because what we are looking at -- the energy difference between two states -- is a state function. That means it doesn't matter how we get from one state to the other; the overall difference will always be the same. So if the reaction did happen via the gas phase, the energy change would be exactly as it is when it happens directly at the electrode - solution interface. We can do a sort of thought experiment using the data we know, and even though those steps don't really happen the way they do in the experiments that gave rise to the data, they will eventually lead to the right place. This sort of imaginary path to mimic a reaction we want to know more about employs an idea called "Hess's Law". It is frequently used to gain insight into reactions throughout chemistry.

- Hess' Law states that the enthalpy of a chemical process is the same, whether the process takes place in one step or several steps.
- In other words, enthalpy is a state function.

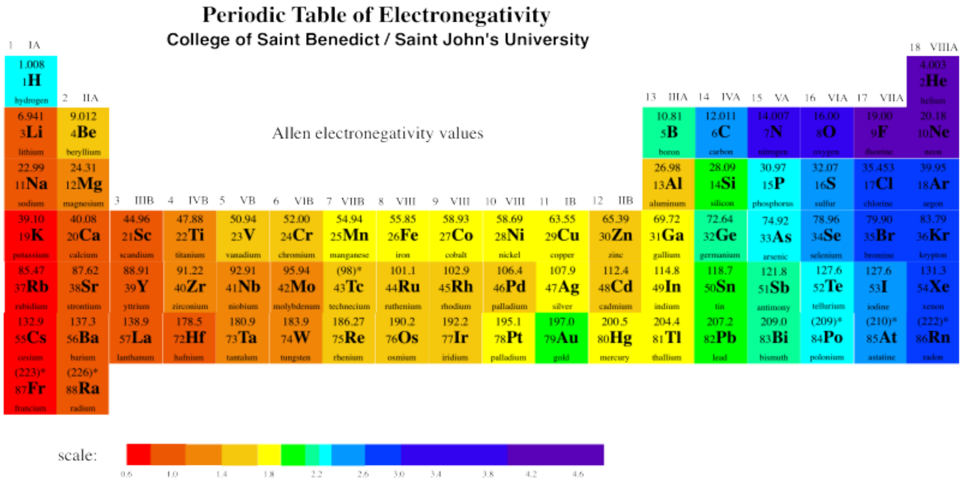
Here are the data for copper, silver, and gold

element	copper	silver	gold
reduction potential, E^o, V	+0.520	+0.7996	+1.83
1st ionization energy, kJ/mol	745.5	731	890
heat of sublimation, kJ/mol	313	265	355
enthalpy of hydration, kJ/mol	-593	-473	-615
covalent radius, Angstroms	1.32	1.45	1.36

Taking all of these data together, we can get a better picture of the overall energy changes that would occur during a reduction or, more directly, an oxidation.

The first thing to note is that copper has a higher ionization energy than silver. As expected, Cu^+ really is harder to form than Ag^+, because copper is more electronegative than silver. But wait a minute -- Au^+ appears to be the hardest to form of all three. It's as if gold were the most electronegative of these three elements -- but it's at the bottom of this column.

Gold really is more electronegative than copper or silver. Take a look at the electronegativity chart below.



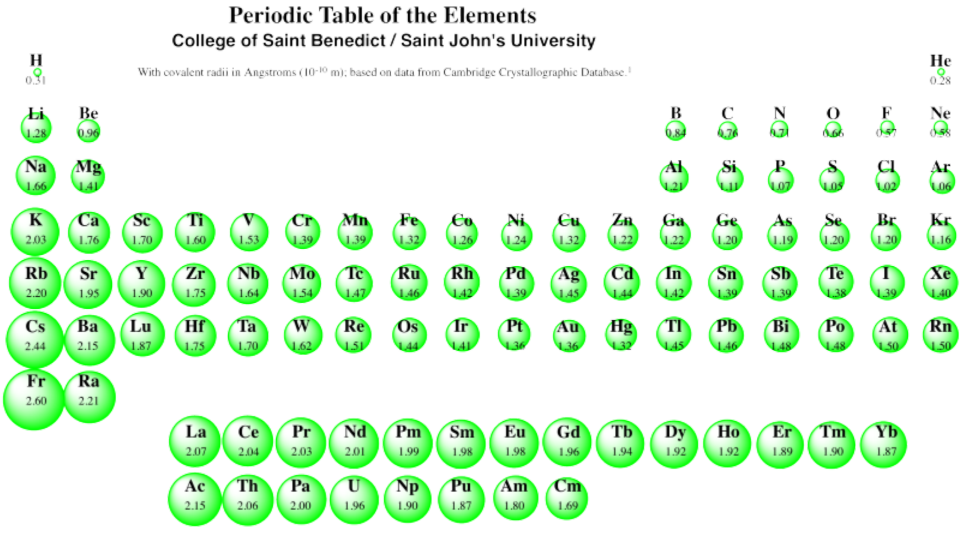
Periodic Table of Electronegativity

College of Saint Benedict / Saint John's University

Allen electronegativity values

1 IA	2 IIA	3 IIIB	4 IVB	5 VB	6 VIB	7 VIIB	8 VIII	9 VIII	10 VIII	11 IB	12 IIB	13 IIIA	14 IVA	15 VA	16 VIA	17 VIIA	18 VIIIA
1.008 1 H hydrogen																	4.003 2 He helium
6.941 3 Li lithium	9.012 4 Be beryllium											10.81 5 B boron	12.011 6 C carbon	14.007 7 N nitrogen	16.00 8 O oxygen	19.00 9 F fluorine	20.18 10 Ne neon
22.99 11 Na sodium	24.31 12 Mg magnesium											26.98 13 Al aluminum	28.09 14 Si silicon	30.97 15 P phosphorus	32.07 16 S sulfur	35.453 17 Cl chlorine	39.95 18 Ar argon
39.10 19 K potassium	40.08 20 Ca calcium	44.96 21 Sc scandium	47.88 22 Ti titanium	50.94 23 V vanadium	52.00 24 Cr chromium	54.94 25 Mn manganese	55.85 26 Fe iron	58.93 27 Co cobalt	58.69 28 Ni nickel	63.55 29 Cu copper	65.39 30 Zn zinc	69.72 31 Ga gallium	72.64 32 Ge germanium	74.92 33 As arsenic	78.96 34 Se selenium	79.90 35 Br bromine	83.79 36 Kr krypton
85.47 37 Rb rubidium	87.62 38 Sr strontium	88.91 39 Y yttrium	91.22 40 Zr zirconium	92.91 41 Nb niobium	95.94 42 Mo molybdenum	(98)* 43 Tc technecium	101.1 44 Ru ruthenium	102.9 45 Rh rhodium	106.4 46 Pd palladium	107.9 47 Ag silver	112.4 48 Cd cadmium	114.8 49 In indium	118.7 50 Sn tin	121.8 51 Sb antimony	127.6 52 Te tellurium	127.6 53 I iodine	131.3 54 Xe xenon
132.9 55 Cs cesium	137.3 56 Ba barium	138.9 57 La lanthanum	178.5 72 Hf hafnium	180.9 73 Ta tantalum	183.9 74 W tungsten	186.27 75 Re rhenium	190.2 76 Os osmium	192.2 77 Ir iridium	195.1 78 Pt palladium	197.0 79 Au gold	200.5 80 Hg mercury	204.4 81 Tl thallium	207.2 82 Pb lead	209.0 83 Bi bismuth	(209)* 84 Po polonium	(210)* 85 At astatine	(222)* 86 Rn radon
(223)* 87 Fr francium	(226)* 88 Ra radium																

There are a few deviations from expectation in periodic trends, but this one is probably attributable to a phenomenon called "the lanthanide contraction". Notice the covalent radii of gold and silver in the table above. Normally, we expect atoms to get bigger row by row, as additional layers of electrons are filled in. Not so for the third row of transition metals. To see the probable reason for that, you have to look at the whole periodic table, and remember for the first time ever that the lanthanides and actinides -- the two orphaned rows at the bottom -- actually fit in the middle of the periodic table. The lanthanides, in particular (lanthanum, La, to ytterbium, Yb), go in between lutetium (Lu) and Hafnium (Hf).



Periodic Table of the Elements

College of Saint Benedict / Saint John's University

With covalent radii in Angstroms (10^{-10} m); based on data from Cambridge Crystallographic Database.[1]

H 0.31																	He 0.28
Li 1.28	Be 0.96											B 0.84	C 0.76	N 0.71	O 0.66	F 0.57	Ne 0.58
Na 1.66	Mg 1.41											Al 1.21	Si 1.11	P 1.07	S 1.05	Cl 1.02	Ar 1.06
K 2.03	Ca 1.76	Sc 1.70	Ti 1.60	V 1.53	Cr 1.39	Mn 1.39	Fe 1.32	Co 1.26	Ni 1.24	Cu 1.32	Zn 1.22	Ga 1.22	Ge 1.20	As 1.19	Se 1.20	Br 1.20	Kr 1.16
Rb 2.20	Sr 1.95	Y 1.90	Zr 1.75	Nb 1.64	Mo 1.54	Tc 1.47	Ru 1.46	Rh 1.42	Pd 1.39	Ag 1.45	Cd 1.44	In 1.42	Sn 1.39	Sb 1.39	Te 1.38	I 1.39	Xe 1.40
Cs 2.44	Ba 2.15	Lu 1.87	Hf 1.75	Ta 1.70	W 1.62	Re 1.51	Os 1.44	Ir 1.41	Pt 1.36	Au 1.36	Hg 1.32	Tl 1.45	Pb 1.46	Bi 1.48	Po 1.48	At 1.50	Rn 1.50
Fr 2.60	Ra 2.21																

La 2.07	Ce 2.04	Pr 2.03	Nd 2.01	Pm 1.99	Sm 1.98	Eu 1.98	Gd 1.96	Tb 1.94	Dy 1.92	Ho 1.92	Er 1.89	Tm 1.90	Yb 1.87
Ac 2.15	Th 2.06	Pa 2.00	U 1.96	Np 1.90	Pu 1.87	Am 1.80	Cm 1.69						

1. Beatriz Cordero et al. *Dalton Trans*. **2008**, *21*,:2832–2838.

As a result, the third row of transition metals contain many more protons in their nuclei, compared to the second row transition metals of the same column. Silver has ten more protons in its nucleus than rubidium, the first atom in the same row as silver, but gold has twenty four more than cesium. The third row "contracts" because of these additional protons.

So the exceptionally positive reduction potential of Au^+ (and, by relation, the exceptionally negative oxidation potential of gold metal)may be a result of the lanthanide contraction.

What about copper versus silver? Copper still has a higher electronegativity than silver, but copper metal is more easily oxidized. It's not that copper is more easily pulled away from the metallic bonds holding it in the solid state; copper's heat of vaporization is a little higher than silver's. That leaves hydration. In fact, copper ion does have a higher enthalpy of hydration than silver; more energy is released when water binds to copper than when water binds to silver. The difference between these two appears to be all about the solvation of the copper ion, which is more stable with respect to the metal than is silver ion.

Why would that be? Well, copper is smaller than silver. A simple look at Coulomb's law reminds us that the closer the electrons of the donor ligand are to the cation, the more tightly bound they will be. Looking at it a slightly different way, copper is smaller and "harder" than silver, and forms a stronger bond with water, which is a "hard" ligand.

Taking a look at a Hess's Law cycle for a redox reaction is a useful approach to get some additional insight into the reaction. It lets us use data to assess the influence of various aspects of the reaction that we can't evaluate directly from the reduction potential, because in the redox reaction all of these factors are conflated into one number.

? Exercise 1.5.1

Compare the reduction potentials of lithium, sodium and potassium ions. Can you use data on heat of vaporization, ionization energy and enthalpy of solvation to determine what factors are responsible for the order of ease of oxidation of these metals?

Answer

Li^+/Li: $E^0 = -3.04$ V; $\Delta H_{vap} = 147$ kJ/mol; IE = 520 kJ/mol; $\Delta H_h = -520$ kJ/mol

Na^+/Na: $E^0 = -2.71$ V; $\Delta H_{vap} = 97$ kJ/mol; IE = 495 kJ/mol; $\Delta H_h = -406$ kJ/mol

K^+/K: $E^0 = -2.931$ V; $\Delta H_{vap} = 77$ kJ/mol; IE = 419 kJ/mol; $\Delta H_h = -320$ kJ/mol

Potassium should be the easiest of the three to oxidize. It is easier to oxidize than sodium. However, lithium's high heat of hydration reverses the trend and tips the balance of reaction in favour of ion formation.

? Exercise 1.5.2

Compare the reduction potentials of copper, nickel and zinc ions. Can you use data on heat of vaporization, ionization energy and enthalpy of solvation to determine what factors are responsible for the order of ease of oxidation of these metals?

Answer

Cu^{2+}/Cu: $E^0 = +0.340$ V; $\Delta H_{vap} = 300$ kJ/mol; IE = 745 kJ/mol & 1958 kJ/mol; $\Delta H_h = -2099$ kJ/mol

Ni^{2+}/Ni: $E^0 = -0.25$ V; $\Delta H_{vap} = 377$ kJ/mol; IE = 737 kJ/mol & 1753 kJ/mol; $\Delta H_h = -2096$ kJ/mol

Zn^{2+}/Zn: $E^0 = -0.7618$ V; $\Delta H_{vap} = 123$ kJ/mol; IE = 906 kJ/mol & 1733 kJ/mol; $\Delta H_h = -2047$ kJ/mol

In this case, zinc may be considered the outlier. Copper should be easier to reduce than nickel based solely on electronegativity. However, zinc's very low heat of vaporization suggests that formation of the solid metal is less favoured in that case, helping to tilt the balance toward zinc ion instead.

? Exercise 1.5.3

Born Haber cycles are another example of thermodynamic cycles based on Hess' Law. These particular constructions are used to calculate the lattice energy of an ionic solid: the amount of energy released when ions in the gas phase condense to form an ionic lattice. This quantity is not easily measured directly.

The alternative pathway taken in the Born Haber cycle imagines that the separate ions in the lattice are first formed from the individual elements. The heat of formation of the ionic solid from the elements is usually known (or easily found on the internet, Herr Born and Herr Haber's favorite tool for evening relaxation), as are other physical parameters such as enthalpy of sublimation, ionization energies, electron affinities and so on.

Construct diagrams for the Born Haber cycle and estimate the lattice energy in each of the following cases.

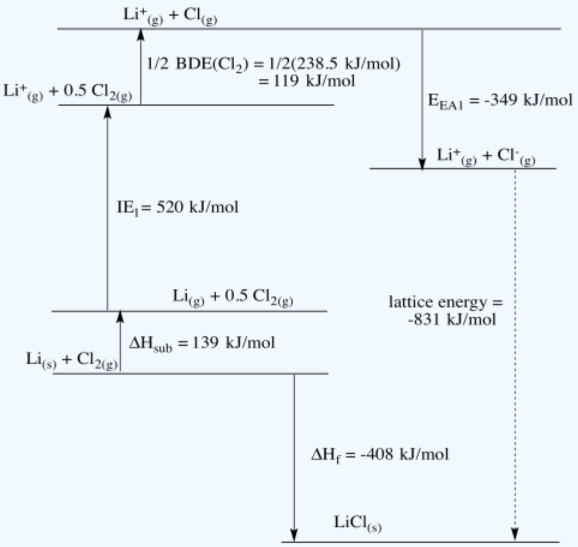
a) LiCl b) CaF_2 c) HgO d) ZnS

Some useful data can be found below. Note that enthalpy is a state function, so enthalpy of sublimation is roughly equal to enthalpy of fusion plus enthalpy of vaporization.

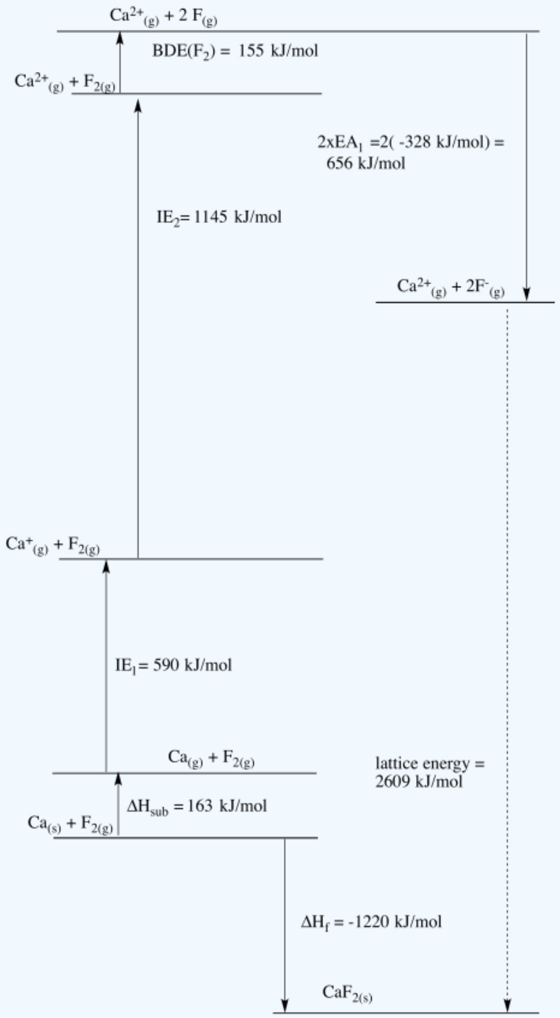
	mp (°C)	bp (°C)	ΔH_{fus} (kJ/mol)	ΔH_{vap} (kJ/mol)	IE_1 (kJ/mol)	IE_2 (kJ/mol)	E_{ea1} (kJ/mol)	E_{ea2} (kJ/mol)
lithium	180	1330	3	136	520	7298	-50	-
calcium	842	1484	9	155	590	1155	-	-

zinc	419	907	7	115	906	1733	-	-
mercury	-39	356	2	59	1007	1810	85	-
oxygen	-218	-183	0.4	7	1314	3388	-226	879
fluorine	-219	-188	-	7	1681	3374	-347	-
sulfur	115	444	2	45	1000	2252	-100	435
chlorine	-101	-34	6	20	1250	2298	-368	-

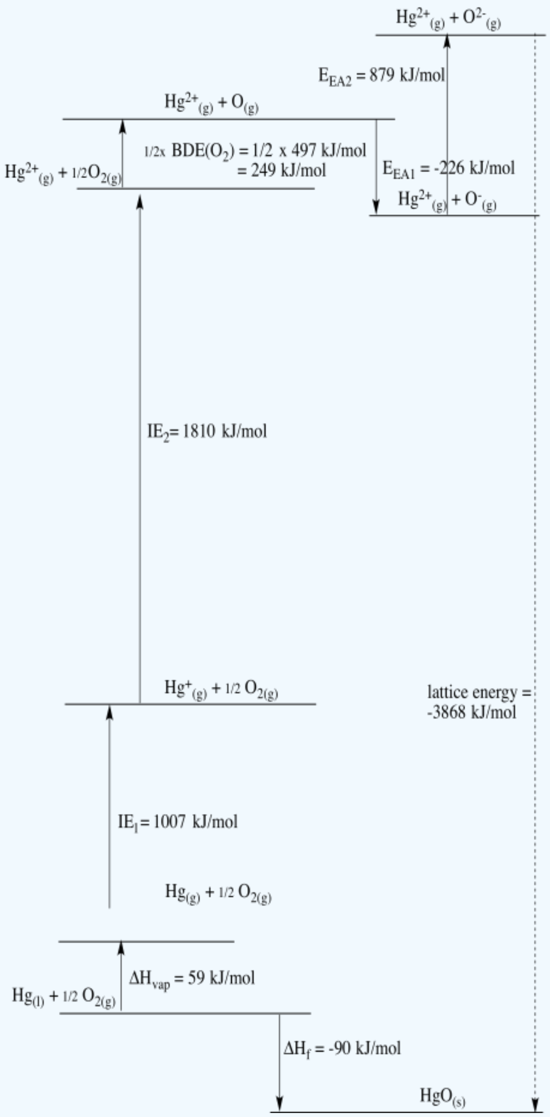
Answer a



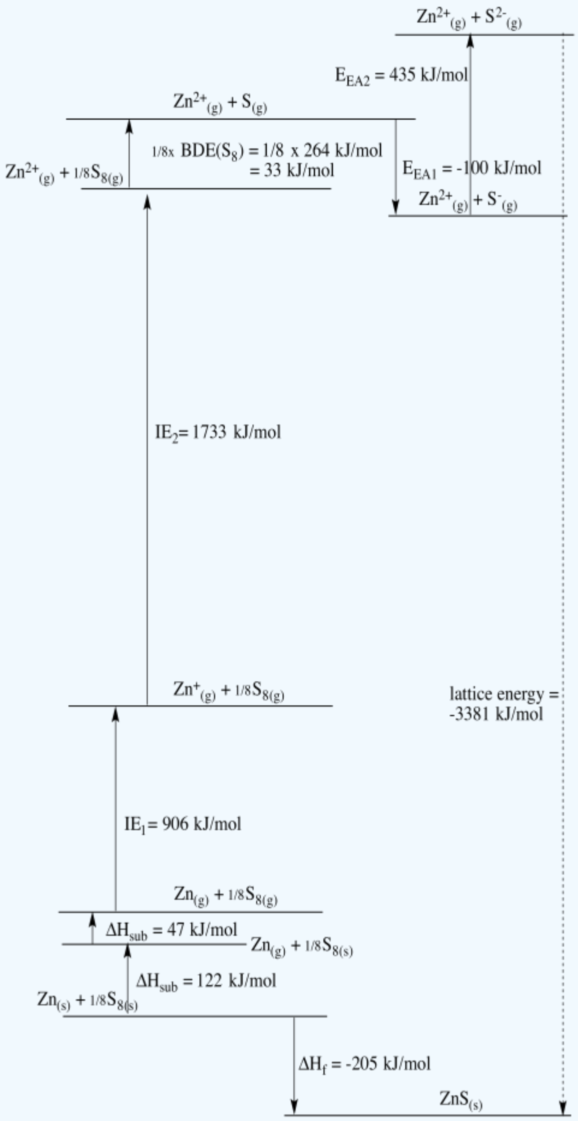
Answer b


$Ca^{2+}_{(g)} + 2\ F_{(g)}$
$BDE(F_2) = 155$ kJ/mol
$Ca^{2+}_{(g)} + F_{2(g)}$
$2xEA_1 = 2(-328$ kJ/mol$) =$ 656 kJ/mol
$IE_2 = 1145$ kJ/mol
$Ca^{2+}_{(g)} + 2F^-_{(g)}$
$Ca^+_{(g)} + F_{2(g)}$
$IE_1 = 590$ kJ/mol
$Ca_{(g)} + F_{2(g)}$
lattice energy = 2609 kJ/mol
$\Delta H_{sub} = 163$ kJ/mol
$Ca_{(s)} + F_{2(g)}$
$\Delta H_f = -1220$ kJ/mol
$CaF_{2(s)}$

Answer c


$Hg^{2+}_{(g)} + O^{2-}_{(g)}$
E_{EA2} = 879 kJ/mol
$Hg^{2+}_{(g)} + O_{(g)}$
1/2x BDE(O_2) = 1/2 x 497 kJ/mol
= 249 kJ/mol
$Hg^{2+}_{(g)} + 1/2O_{2(g)}$
E_{EA1} = -226 kJ/mol
$Hg^{2+}_{(g)} + O^{-}_{(g)}$
IE_2= 1810 kJ/mol
$Hg^{+}_{(g)} + 1/2\ O_{2(g)}$
lattice energy =
-3868 kJ/mol
IE_1 = 1007 kJ/mol
$Hg_{(g)} + 1/2\ O_{2(g)}$
ΔH_{vap} = 59 kJ/mol
$Hg_{(l)} + 1/2\ O_{2(g)}$
ΔH_f = -90 kJ/mol
$HgO_{(s)}$

Answer d


Zn2+(g) + S2-(g)
EEA2 = 435 kJ/mol
Zn2+(g) + S(g)
1/8x BDE(S8) = 1/8 x 264 kJ/mol
= 33 kJ/mol
Zn2+(g) + 1/8S8(g)
EEA1 = -100 kJ/mol
Zn2+(g) + S-(g)
IE2= 1733 kJ/mol
Zn+(g) + 1/8S8(g)
lattice energy =
-3381 kJ/mol
IE1= 906 kJ/mol
Zn(g) + 1/8S8(g)
ΔHsub = 47 kJ/mol
Zn(g) + 1/8S8(s)
ΔHsub = 122 kJ/mol
Zn(s) + 1/8S8(s)
ΔHf = -205 kJ/mol
ZnS(s)

1.6: Reduction of Ores

Metal ores are typically salts, such as oxides, carbonates or sulfides Conversion of these ores into metals requires oxidation/reduction reactions.

That's not always the case. Some early forays into metallurgy involved native gold (native meaning the metal is found in its elemental state in nature). Gold is relatively soft. It could be easily worked and shaped by heating it. Occasionally, native silver and copper can also be found.

? Exercise 1.6.1

Explain, with the help of a table of standard reduction potentials, why silver and gold can sometimes be found as elements rather than salts.

Answer

Both reduction potentials are very positive.

$Ag^+ + e^- \rightarrow Ag (s)\ E^0 = + 0.796$ V

$Au^+ + e^- \rightarrow Au (s)\ E^0 = + 1.83$ V

That means both metals are likely to be found in the reduced state.

However, a major leap forward came when people learned to make alloys, mixing in small amounts of other metals to make harder, sturdier materials. For example, the addition of tin to copper ushered in "the bronze age". Tin itself had to be made from its ore via smelting; the earliest evidence for this process comes from what is now Turkey, where it was performed over eight thousand years ago. However, alloys were apparently not discovered until several thousand years later.

In smelting, ore is heated to a high temperature in the presence of carbon sources, such as charcoal or coke. The partial combustion of the carbon source produces carbon monoxide which acts as a reducing agent.

? Exercise 1.6.2

Show the half-reactions involved in the reduction of tin oxide with carbon monoxide. Use them to come up with a balanced reaction for the process, and calculate the standard potential for the reaction.

Answer

$SnO (s) + 2H^+ + 2 e^- \rightarrow Sn (s) + H_2O\ E^0 = -0.10$ V

$CO(g) + H_2O \rightarrow CO_2(g) + 2H^+ + 2 e\text{-}\ E^0 = - (-0.11$ V)

$SnO (s) + CO (g) \rightarrow Sn (s) + CO_2 (g)\ \Delta E^0 = + 0.01$ V

Another major advance in metallurgy involved the conversion of iron ores into iron and steel. There is evidence that iron smelting in sub-Saharan Africa and Sri Lanka about three thousand years ago. Archaeological evidence in Sri Lanka shows that smelters were located on mountainsides facing the ocean, where constant winds provided ample oxygen to produce fires hot enough for smelting.

In the United States, the discovery of iron ores in the states along the Great Lakes, the use of the Great Lakes as a transportation network, and the availability of anthracite coal in Pennsylvania fueled the development of an American steel industry and the rise of a major industrial power. The fact that the great lakes states are still referred to as the "rust belt" is a testament to the manufacturing prowess of the region throughout the twentieth century, which proceeded from having all the necessary features for an iron-based economy in close geographic proximity.

Exercise 1.6.3

Show the half-reactions involved in the reduction of iron oxide with carbon monoxide. Assume the iron oxide is prsent as magnetite, Fe_3O_4. Use them to come up with a balanced reaction for the process, and calculate the standard potential for the reaction.

Answer

$Fe_3O_4(s) + 8\ H^+ + 8\ e^- \rightarrow 3Fe(s) + 4\ H_2O\ E^0 = +0.085\ V$

$CO(g) + H_2O \rightarrow CO_2(g) + 2H^+ + 2\ e\text{-}\ E^0 = -\ (-0.11\ V)$

$Fe_3O_4(s) + 4CO\ (g) \rightarrow 3Fe(s) + 4CO_2\ (g)\ \Delta E^0 = +\ 0.195\ V$

Exercise 1.6.4

Show the half-reactions involved in the reduction of aluminum oxide with carbon monoxide. Assume the aluminum is present as an ion in Al_2O_3. Use the half-reactions to come up with a balanced reaction for the process, and calculate the standard potential for the reaction.

Answer

$Al^{3+}_{(aq)} + 3e^- \rightarrow Al\ (s)\ E^0 = -1.662\ V$

$CO(g) + H_2O \rightarrow CO_2(g) + 2H^+ + 2\ e\text{-}\ E^0 = -\ (-0.11\ V)$

$2\ Al^{3+}(aq) + 3CO\ (g) + 3H_2O \rightarrow 2Al(s) + 3CO_2\ (g)\ \Delta E^0 = -\ 1.772\ V$

Aluminum is a very important material in our economy. It is lightweight, strong, and forms a very hard oxide coating when exposed to the elements, rather than the rust that results from weathering steel. In contrast to the steel industry, the aluminum industry is a far-flung operation in which ore mined on one continent may be shipped to another for processing. However, aluminum metal isn't accessible via smelting. So how is it done?

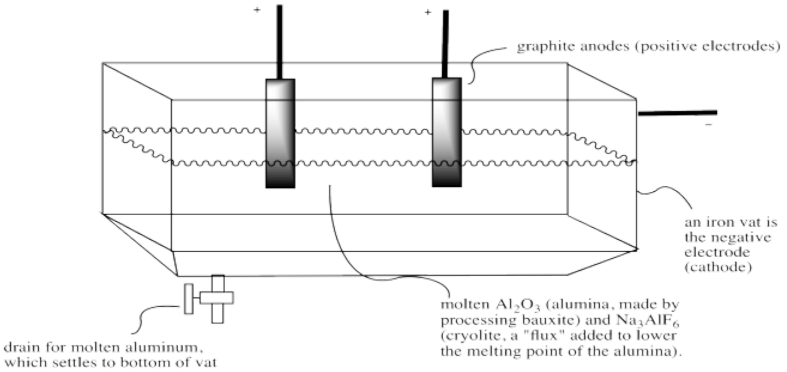
Just as a thermodynamically favored redox reaction can produce a voltage in a circuit, if we already have a voltage produced by another source, we can drive an unfavorable redox reaction to completion. We can drive the reaction backwards.

Quebec is a major producer of aluminum, despite being endowed with virtually no aluminum ore. Bauxite, the major aluminum-containing ore, is a mixture of minerals of formulae $Al(OH)_3$ or $AlO(OH)$ found amalgamated with other clays and minerals. It is found near the earth's surface in tropical and sub-tropical areas, left behind after of millenia of erosion and drainage of more soluble materials from underlying bedrock. The major producers of bauxite are Vietnam, Australia and Guinea, as well as a number of countries in South America.

Why ship bauxite all the way to the taiga to make aluminum? Aluminum production requires a lot of electrons, and those electrons can't be provided by coal or coke. Instead, they usually come from massive hydroelectric generating stations, such as the 16,000 megawatt James Bay Project in northern Quebec. To make aluminum, you go where electricity is cheap and plentiful.

The bauxite is first processed to help remove all those other materials that come mixed with the aluminum ore. It is dissolved in base, filtered and re-precipitated with acid. The residue is heated to drive off water, leaving pure alumina (Al_2O_3).

Instead of performing this redox reaction in aqueous solution, it is done in the molten state. Alumina has a melting point around 2,000 ^oC, but that temperature drops to a much more manageable 1,000 ^oC if a "flux" is added. To avoid contaminating the aluminum ions, cryolite has often been used as the flux, because it is also an aluminum salt (Na_3AlF_6).



The alumina is melted in an iron vat, which conveniently functions as one of the electrodes in the redox reaction. It is the cathode, supplying electrons. Graphite anodes draw electrons out of the bath to complete a circuit. Two reactions occur: aluminum ions are reduced to aluminum at the cathode, which drops to the bottom of the vat and is drained away periodically. Oxide ions are oxidized to molecular oxygen at the anodes. However, at these temperatures, the oxygen quickly reacts with the carbon anodes to produce carbon dioxide -- that is, the anodes actually disappear as the reaction proceeds.

? Exercise 1.6.5

Take a look at the redox reaction happening in the vat.

a. Provide a half reaction for reduction of aluminum ion.
b. Provide a half reaction for oxidation of the oxide anion.
c. Provide an overall, balanced reaction.
d. Calculate the standard potential for this reaction. (Don't worry about the lack of an aqueous solution; we'll just get an estimate of the real potential. Also, you can use the value of the reduction potential of oxygen to yield hydroxide as an approximation)

Answer

$Al^{3+} + 3e^- \rightarrow Al\ (s)\ E^0 = -1.662\ V$

$2\ O^{2-} \rightarrow O_2(g) + 4e^-\ E^0 = -\ (.40\ V,\ \text{estimated})$

$4\ Al^{3+}(aq) + 6\ O^{2-}\ (aq) \rightarrow 4\ Al\ (s) + 3O_2\ (g)\ \Delta E^0 = -\ 2.062\ V$

? Exercise 1.6.6

Cryolite (Na_3AlF_6) is added to get alumina to melt at a lower temperature. Unlike bauxite, it's a somewhat rare mineral found in Greenland and Quebec. Presumably, the aluminum ions in the cryolite also get reduced. Wouldn't the rare cryolite quickly get used up? Explain why this isn't a problem.

Answer

Even if the aluminum ions from the cryolite are reduced to Al^0, they will be replenished by new aluminum ions from the bauxite ore.

1.7: Reduction in Batteries

A measurement of a reduction potential involves connection of a circuit between two half-cells. Electrons produced by an oxidation reaction in one half-cell must flow to the other half-cell, where a reduction reaction takes place. If that flow of electrons is used to do work, we are using a chemical reaction to produce and harness electricity. We have a battery.

1.8: Balancing Redox Reactions

In any reaction, it is useful to quantify things. How much product will there be? How much of each reactant do we need to add? What ratios do we need? There are an awful lot of reactions for which this process is straightforward, but sometimes it can be tricky. Redox reactions are sometimes on the tricky side (although certainly not always). For that reason, it's good to have a reliable method for balancing redox reactions: determining the ratios of reactants needed to give the products in the proper amounts.

Suppose, for example, we have a reaction in which silver oxide (Ag_2O) reacts with manganese ion (Mn^{3+}) to produce manganese dioxide and silver. That's:

$$\mathrm{Mn^{3\,+} + Ag_2O \longrightarrow MnO_2 + Ag}$$

What would the balanced reaction look like?

The first thing to do is make sure you are working with one **half-reaction** at a time. So that's:

$$\mathrm{Mn^{3\,+} \longrightarrow MnO_2}$$

and

$$\mathrm{Ag_2O \longrightarrow Ag}$$

We start out by balancing the **atoms** involved, one at a time. First we look at the atoms other than hydrogen or oxygen, and we just balance those by adding the right coefficient.

$$\mathrm{Mn^{3\,+} \longrightarrow MnO_2}$$

and

$$\mathrm{Ag_2O \longrightarrow Ag}$$

Second, we balance the **oxygen** atoms by adding water to one side or the other.

$$\mathrm{Mn^{3\,+} + 2\,H_2O \longrightarrow MnO_2}$$

and

$$\mathrm{Ag_2O \longrightarrow 2\,Ag + H_2O}$$

Third, we balance any **hydrogens** by adding protons.

$$\mathrm{Mn^{3\,+} + 2\,H_2O \longrightarrow 4\,H^{+} + MnO_2}$$

and

$$\mathrm{Ag_2O + 2\,H^{+} \longrightarrow 2\,Ag + H_2O}$$

Fourth, we balance the **charge** by adding electrons.

$$\mathrm{Mn^{3\,+} + 2\,H_2O \longrightarrow 4\,H^{+} + MnO_2 + e^{-}}$$

and

$$\mathrm{Ag_2O + 2\,H^{+} + 2\,e^{-} \longrightarrow 2\,Ag^{+}H_2O}$$

Fifth, we **multiply** so that the number of electrons is the same in both reactions.

$$\mathrm{2 \times (Mn^{3\,+} + 2\,H_2O \longrightarrow 4\,H^{+} + MnO_2 + e^{-})}$$

or

$$\mathrm{2\,Mn^{3\,+} + 4\,H_2O \longrightarrow 8\,H^{+} + 2\,MnO_2 + 2\,e^{-}}$$

and

$$\mathrm{Ag_2O + 2\,H^{+} + 2\,e^{-} \longrightarrow 2\,Ag + H_2O}$$

Sixth, we simply **add** these two reactions together. The reaction arrow functions like an equals sign. The left side adds to the left side, and the right side adds to the right.

$$2\,Mn^{3+} + 4\,H_2O + Ag_2O + 2\,H^+ + 2\,e^- \longrightarrow 8\,H^+ + 2\,MnO_2 + 2\,e^- + 2\,Ag + H_2O$$

At that point, gratifyingly, the equation simplifies. Notice that we have added the same number of electrons to each side; they cancel out. That's perfect, because it means we have supplied just the right number of electrons from one half reaction to satisfy the other half reaction.

$$2\,Mn^{3+} + 4\,H_2O + Ag_2O + 2\,H^+ \longrightarrow 8\,H^+ + 2\,MnO_2 + 2\,Ag + H_2O$$

Also if we subtract one water from each side, things get slightly simpler.

$$2\,Mn^{3+} + 3\,H_2O + Ag_2O + 2\,H^+ \longrightarrow 8\,H^+ + 2\,MnO_2 + 2\,Ag$$

Subtracting two protons from each side makes it simpler still.

$$2\,Mn^{3+} + 3\,H_2O + Ag_2O \longrightarrow 6\,H^+ + 2\,MnO_2 + 2\,Ag$$

This method works for any redox reaction, no matter how complicated.

? Exercise 1.8.1

Balance the following reactions.

a. $Cu + MoO_2 \longrightarrow Cu_2O + Mo$
b. $NH_2OH + Ag_2O \longrightarrow N_2 + Ag$
c. $Fe_3O_4 + CO \longrightarrow Fe + CO_2$
d. $I_2 + MnO_4^- \longrightarrow IO_3^- + MnO_2$
e. $H_3Mo_7O_{24} + S_2O_3^{2-} \longrightarrow Mo + So_3^{2-}$

Answer a

a) Cu --> Cu_2O MoO_2 --> Mo

2 Cu --> Cu_2O MoO_2 --> Mo

2 Cu + H_2O --> Cu_2O MoO_2 --> Mo + 2 H_2O

2 Cu + H_2O --> Cu_2O + 2 H^+ $4H^+$ + MoO_2 --> Mo + 2 H_2O

2 Cu + H_2O --> Cu_2O + 2 H^+ + $2e^-$ $4e^-$ + $4H^+$ + MoO_2 --> Mo + 2 H_2O

2x (2 Cu + H_2O --> Cu_2O + 2 H^+ + $2e^-$) $4e^-$ + $4H^+$ + MoO_2 --> Mo + 2 H_2O

adding:

4 Cu + 2 H_2O --> 2 Cu_2O + 4 H^+ + $4e^-$

$4e^-$ + $4H^+$ + MoO_2 --> Mo + 2 H_2O

equals

4 Cu + MoO_2 --> 2 Cu_2O + Mo

Answer b

b) NH_2OH --> N_2 Ag_2O --> Ag

2 NH_2OH --> N_2 Ag_2O --> 2 Ag

2 NH_2OH --> N_2 + 2 H_2O Ag_2O --> 2 Ag + H_2O

2 NH_2OH --> N_2 + 2 H_2O + 2 H^+ 2 H^+ + Ag_2O --> 2 Ag + H_2O

2 NH_2OH --> N_2 + 2 H_2O + 2 H^+ + 2 e- 2 H^+ + Ag_2O + 2 e- --> 2 Ag + H_2O

adding:

2 NH_2OH --> N_2 + 2 H_2O + 2 H^+ + 2 e-

2 H^+ + Ag_2O + 2 e- --> 2 Ag + H_2O

equals

2 NH_2OH + Ag_2O --> N_2 + 2 Ag + 3 H_2O

Answer c

c) Fe_3O_4 --> Fe CO --> CO_2

Fe_3O_4 --> 3 Fe CO --> CO_2

Fe_3O_4 --> 3 Fe + 4 H_2O H_2O + CO --> CO_2

8 H^+ + Fe_3O_4 --> 3 Fe + 4 H_2O H_2O + CO --> CO_2 + 2 H^+

8 e^- + 8 H^+ + Fe_3O_4 --> 3 Fe + 4 H_2O H_2O + CO --> CO_2 + 2 H^+ + 2 e^-

8 e^- + 8 H^+ + Fe_3O_4 --> 3 Fe + 4 H_2O 4x (H_2O + CO --> CO_2 + 2 H^+ + 2 e^-)

adding:

8 e^- + 8 H^+ + Fe_3O_4 --> 3 Fe + 4 H_2O

4 H_2O + 4 CO --> 4 CO_2 + 8 H^+ + 8 e^-

equals

Fe_3O_4 + 4 CO --> 3 Fe + 4 CO_2

Answer d

d) I_2 --> IO_3^- MnO_4^- --> MnO_2

I_2 --> 2 IO_3^- MnO_4^- --> MnO_2

6 H_2O + I_2 --> 2 IO_3^- MnO_4^- --> MnO_2 + 2 H_2O

6 H_2O + I_2 --> 2 IO_3^- + 12 H^+ 4H^+ + MnO_4^- --> MnO_2 + 2 H_2O

6 H_2O + I_2 --> 2 IO_3^- + 12 H^+ + 10 e^- 3 e^- + 4H^+ + MnO_4^- --> MnO_2 + 2 H_2O

3x (6 H_2O + I_2 --> 2 IO_3^- + 12 H^+ + 10 e^-) 10x (3 e^- + 4H^+ + MnO_4^- --> MnO_2 + 2 H_2O)

adding

18 H_2O + 3 I_2 --> 6 IO_3^- + 36 H^+ + 30 e^-

30 e^- + 40 H^+ + 10 MnO_4^- --> 10 MnO_2 + 20 H_2O

equals

3 I_2 + 4 H^+ + 10 MnO_4^- --> 6 IO_3^- + 10 MnO_2 + 2 H_2O

Answer e

e) $H_3Mo_7O_{24}$ --> Mo $S_2O_3^{2-}$ --> SO_3^{2-}

$H_3Mo_7O_{24}$ --> 7 Mo $S_2O_3^{2-}$ --> 2 SO_3^{2-}

$H_3Mo_7O_{24}$ --> 7 Mo + 24 H_2O 3H_2O + $S_2O_3^{2-}$ --> 2 SO_3^{2-}

45 H^+ + $H_3Mo_7O_{24}$ --> 7 Mo + 24 H_2O 3H_2O + $S_2O_3^{2-}$ --> 2 SO_3^{2-} + 6 H^+

45 e^- + 45 H^+ + $H_3Mo_7O_{24}$ --> 7 Mo + 24 H_2O 3H_2O + $S_2O_3^{2-}$ --> 2 SO_3^{2-} + 6 H^+ + 4 e^-

4 x (45 e^- + 21 H^+ + $H_3Mo_7O_{24}$ --> 7 Mo + 24 H_2O) 45 x (3H_2O + $S_2O_3^{2-}$ --> 2 SO_3^{2-} + 6 H^+ + 4 e^-)

adding:

180 e^- + 180 H^+ + 4 $H_3Mo_7O_{24}$ --> 28 Mo + 96 H_2O

135 H_2O + 45 $S_2O_3^{2-}$ --> 90 SO_3^{2-} + 270 H^+ + 180 e^-

equals

$4\ H_3Mo_7O_{24} + 45\ S_2O_3^{2-} + 39\ H_2O$ --> $28\ Mo + 90\ SO_3^{2-} + 90\ H^+$

checking:

28 Mo --> 28 Mo; 90 S --> 90 S; 90 H --> 90 H; 270 O --> 270 O

In the event that the reaction is described as occuring under basic conditions, we can simply "neutralize" our protons at the end, by adding hydroxide to both sides.

$$2\,\mathrm{Mn^{3+}} + 3\,\mathrm{H_2O} + \mathrm{Ag_2O} + 6\,\mathrm{OH^-} \longrightarrow 6\,\mathrm{H^+} + 6\,\mathrm{OH^-} + 2\,\mathrm{MnO_2} + 2\,\mathrm{Ag}$$

Which of course means

$$2\,\mathrm{Mn^{3+}} + 3\,\mathrm{H_2O} + \mathrm{Ag_2O} + 6\,\mathrm{OH^-} \longrightarrow 6\,\mathrm{H_2O} + 2\,\mathrm{MnO_2} + 2\,\mathrm{Ag}$$

Simplifying to

$$2\,\mathrm{Mn^{3+}} + \mathrm{Ag_2O} + 6\,\mathrm{OH^-} \longrightarrow 3\,\mathrm{H_2O} + 2\,\mathrm{MnO_2} + 2\,\mathrm{Ag}$$

? Exercise 1.8.2

Balance the following reactions under basic conditions.

a. $\mathrm{Fe(OH)_2} + \mathrm{N_2H_4} \longrightarrow \mathrm{Fe_2O_3} + \mathrm{NH_4^+}$
b. $\mathrm{MnO_4^-} + \mathrm{V^{3+}} \longrightarrow \mathrm{HMnO_4^-} + \mathrm{VO_2^+}$

Answer a

a) $Fe(OH)_2$ --> Fe_2O_3 N_2H_4 --> NH_4^+

2 $Fe(OH)_2$ --> Fe_2O_3 N_2H_4 --> 2 NH_4^+

2 $Fe(OH)_2$ --> Fe_2O_3 + H_2O N_2H_4 --> 2 NH_4^+

2 $Fe(OH)_2$ --> Fe_2O_3 + H_2O + 2 H^+ 4 H^+ + N_2H_4 --> 2 NH_4^+

2 $Fe(OH)_2$ --> Fe_2O_3 + H_2O + 2 H^+ + 2 e^- 2 e^- + 4 H^+ + N_2H_4 --> 2 NH_4^+

adding:

2 $Fe(OH)_2$ --> Fe_2O_3 + H_2O + 2 H^+ + 2 e^-

2 e^- + 4 H^+ + N_2H_4 --> 2 NH_4^+

equals:

2 $Fe(OH)_2$ + 2 H^+ + N_2H_4 --> Fe_2O_3 + H_2O + 2 NH_4^+

in basic conditions:

2 $Fe(OH)_2$ + 2 H^+ + 2 ^-OH + N_2H_4 --> Fe_2O_3 + H_2O + 2 NH_4^+ + 2 ^-OH

2 $Fe(OH)_2$ + 2 H_2O + N_2H_4 --> Fe_2O_3 + H_2O + 2 NH_4^+ + 2 ^-OH

2 $Fe(OH)_2$ + H_2O + N_2H_4 --> Fe_2O_3 + 2 NH_4^+ + 2 ^-OH

Answer b

b) MnO_4^- --> $HMnO_4^-$ V^{3+} --> VO^{2+}

MnO_4^- --> $HMnO_4^-$ V^{3+} + H_2O --> VO^{2+}

H^+ + MnO_4^- --> $HMnO_4^-$ V^{3+} + H_2O --> VO^{2+} + 2 H^+

e^- + H^+ + MnO_4^- --> $HMnO_4^-$ V^{3+} + H_2O --> VO^{2+} + 2 H^+ + e^-

adding:

e^- + H^+ + MnO_4^- --> $HMnO_4^-$

$V^{3+} + H_2O \text{ --> } VO^{2+} + 2\ H^+ + e^-$

equals:

$MnO_4^- + V^{3+} + H_2O \text{ --> } HMnO_4^- + VO^{2+} + H^+$

under basic conditions:

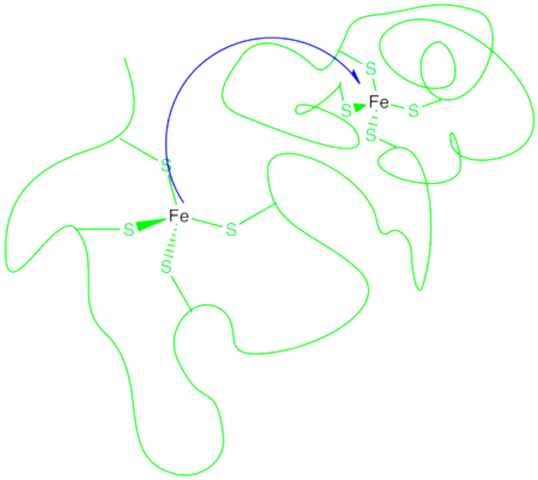
$MnO_4^- + V^{3+} + H_2O + {}^-OH \text{ --> } HMnO_4^- + VO^{2+} + H^+ + {}^-OH$

$MnO_4^- + V^{3+} + H_2O + {}^-OH \text{ --> } HMnO_4^- + VO^{2+} + H_2O$

$MnO_4^- + V^{3+} + {}^-OH \text{ --> } HMnO_4^- + VO^{2+}$

1.9: Outer Sphere Electron Transfer

How does an electron get from one metal to another? This might be a more difficult task than it seems. In biochemistry, an electron may need to be transfered a considerable distance. Often, when the transfer occurs between two metals, the metal ions may be constrained in particular binding sites within a protein, or even in two different proteins.



That means the electron must travel through space to reach its destination. Its ability to do so is generally limited to just a few Angstroms (remember, an Angstrom is roughly the distance of a bond). Still, it can react with something a few bond lengths away. Most things need to actually bump into a partner before they can react with it.

This long distance hop is called an outer sphere electron transfer. The two metals react without ever contacting each other, without getting into each others' coordination spheres. Of course, there are limitations to the distance involved, and the further away the metals, the less likely the reaction. But an outer sphere electron transfer seems a little magical.

Barrier to Reaction: A Qualitative Picture of Marcus Theory

So, what holds the electron back? What is the barrier to the reaction? Rudy Marcus at Caltech has developed a mathematical approach to understanding the kinetics of electron transfer, in work he did beginning in the late 1950's. We will take a very qualitative look at some of the ideas in what is referred to as "Marcus Theory". An electron is small and very fast. All those big, heavy atoms involved in the picture are lumbering and slow. The barrier to the reaction has little to do with the electron's ability to whiz around, although even that is limited by distance. Instead, it has everything to do with all of those things that are barely moving compared to the electron.

Imagine an iron(II) ion is passing an electron to an iron(III) ion. After the electron transfer, they have switched identities; the first has become an iron(III) and the second has become an iron(II) ion.

Nothing could be simpler. The trouble is, there are big differences between an iron(II) ion and an iron(III) ion. For example, in a coordination complex, they have very different bond distances. Why is that a problem? Because when the electron hops, the two iron atoms find themselves in sub-optimal coordination environments.

? Exercise 1.9.1

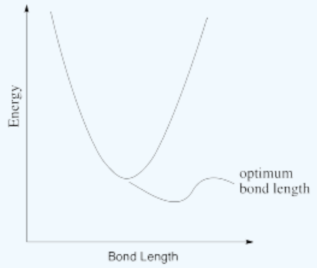
Suppose an electron is transferred from an Fe(II) to a Cu(II) ion. Describe how the bond lengths might change in each case, and why. Don't worry about what the specific ligands are.

Answer

The bonds to iron would contract because the increased charge on the iron would attract the ligand donor electrons more strongly. The bonds to copper would lengthen because of the lower charge on the copper.

Exercise 1.9.2

In reality, a bond length is not static. If there is a little energy around, the bond can lengthen and shorten a little bit, or vibrate. A typical graph of molecular energy vs. bond length is shown below.



a. Why do you think energy increases when the bond gets shorter than optimal?
b. Why do you think energy increases when the bond gets longer than optimal?
c. In the following drawings, energy is being added as we go from left to right. Describe what is happening to the bond length as available energy increases.

Answer a

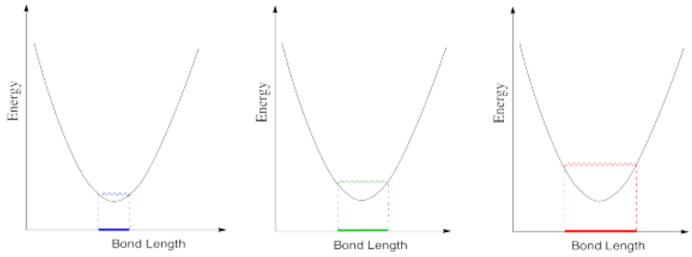
a) Most likely there are repulsive forces between ligands if the bonds get too short.

Answer b

b) Insufficient overlap between metal and ligand orbitals would weaken the bond and raise the energy.

Answer c

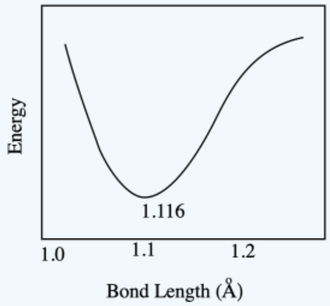
c) The range of possible bond lengths gets broader as energy is increased. The bond has more latitude, with both longer and shorter bonds allowed at higher energy.



Exercise 1.9.3

The optimum C-O bond length in a carbon dioxide molecule is 1.116 Å. Draw a graph of what happens to internal energy when this bond length varies between 1.10 Å and 1.20 Å. Don't worry about quantitative labels on the energy axis.

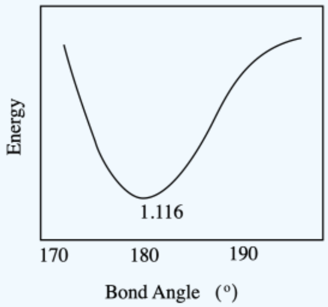
Answer



Exercise 1.9.4

The optimum O-C-O bond angle in a carbon dioxide molecule is 180 °. Draw a graph of what happens to internal energy when this bond angle varies between 170 ° and 190 °. Don't worry about quantitative labels on the energy axis.

Answer



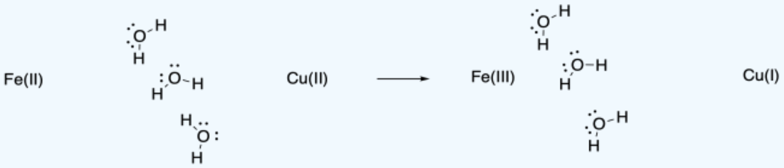
The barrier to electron transfer has to do with reorganizations of all those big atoms before the electron makes the jump. In terms of the coordination sphere, those reorganizations involve bond vibrations, and bond vibrations cost energy. Outside the coordination sphere, solvent molecules have to reorganize, too. Remember, ion stability is highly influenced by the surrounding medium.

Exercise 1.9.5

Draw a Fe(II) ion and a Cu(II) ion with three water molecules located somewhere in between them. Don't worry about the ligands on the iron or copper. Show how the water molecules might change position or orientation if an electron is transferred from iron to copper.

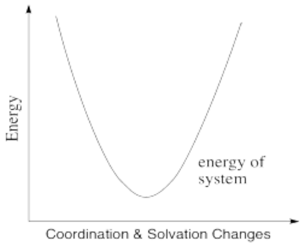
Answer

The water molecules may pivot toward the more highly charged Fe(III), or they may shift closer to it because of the attraction between the ion and the dipole of the water molecule.



Keep in mind that such adjustments would happen in non-polar solvents, too, although they would involve weaker IMFs such as ion - induced dipole interactions.

Thus, the energetic changes needed before electron transfer can occur involve a variety of changes, including bond lengths of several ligands, bond angles, solvent molecules, and so on. The whole system, involving both metals, has some optimum set of positions of minimum energy. Any deviations from those positions requires added energy. In the following energy diagram, the x axis no longer defines one particular parameter. Now it lumps all changes in the system onto one axis. This picture is a little more abstract than when we are just looking at one bond length or one bond angle, but the concept is similar: there is an optimum set of positions for the atoms in this system, and it would require an input of energy in order to move any of them move away from their optimum position.

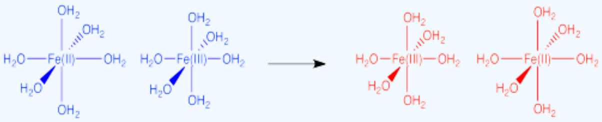


It is thought that these kinds of reorganizations -- involving solvent molecules, bond lengths, coordination geometry and so on -- actually occur prior to electron transfer. They happen via random motions of the molecules involved. However, once they have happened, there is nothing to hold the electron back. Its motion is so rapid that it can immediately find itself on the other atom before anything has a chance to move again.

Consequently, the barrier to electron transfer is just the amount of energy needed for all of those heavy atoms to get to some set of coordinates that would be accessible in the first state, before the electron is transferred, but that would also be accessible in the second state, after the electron is transfered.

Exercise 1.9.6

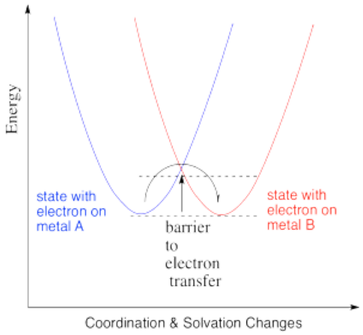
Describe some of the changes that contribute to the barrier to electron transfer in the following case.



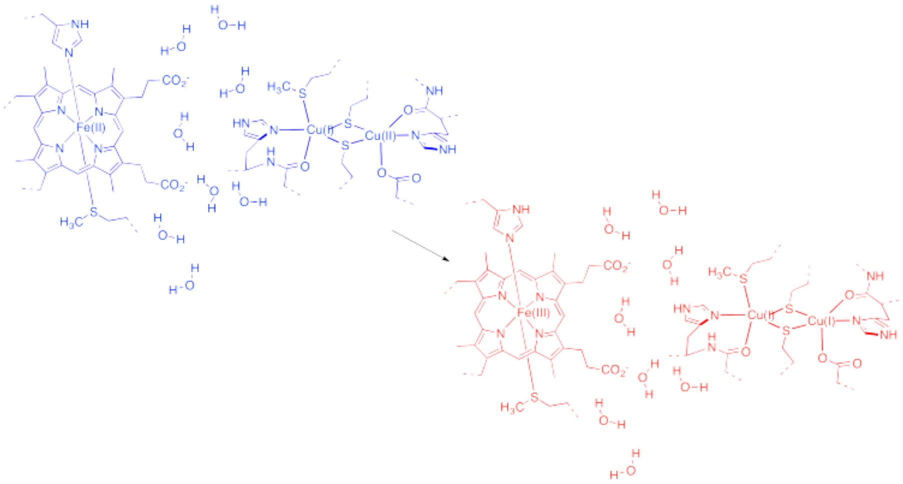
Answer

The reactants and products are very similar in this case. However, the Fe(III) complex has shorter bonds than the Fe(II) complex because of greater electrostatic interaction between the metal ion and the ligands. These changes in bond length needed in order to get ready to change from Fe(III) to Fe(II) (or the reverse) pose a major barrier to the reaction.

In the drawing below, an electron is transferred from one metal to another metal of the same kind, so the two are just switching oxidation states. For example, it could be an iron(II) and an iron(III), as pictured in the problem above. In the blue state, one iron has the extra electron, and in the red state it is the other iron that has the extra electron. The energy of the two states are the same, and the reduction potential involved in this transfer is zero. However, there would be some atomic reorganizations needed to get the coordination and solvation environments adjusted to the electron transfer. The ligand atoms and solvent molecules have shifted in the change from one state to another, and so our energy surfaces have shifted along the x axis to reflect that reorganization.



That example isn't very interesting, because we don't form anything new on the product side. Instead, let's picture an electron transfer from one metal to a very different one. For example, maybe the electron is transferred from cytochrome c to the "copper A" center in cytochrome c oxidase, an important protein involved in respiratory electron transfer.



Exercise 1.9.7

In the drawing above, some water molecules are included between the two metal centres.

a. Explain what happens to the water molecules in order to allow electron transfer to occur, and why.
b. Suppose there were a different solvent, other than water, between the complexes. How might that affect the barrier to the reaction?

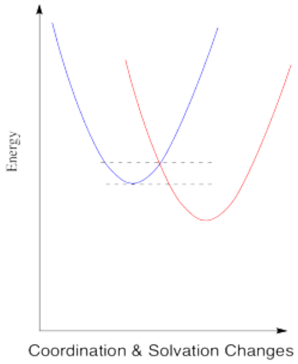
Answer a

a) The drawing is an oversimplification, but in general the water molecules are shown reorienting after the electron transfer because of ion-dipole interactions. In this case, the waters are shown orienting to present their negative ends to the more positive iron atom after the electron transfer. In reality, in a protein there are lots of other charges (including charges on the ligand) that may take part in additional ion-dipole interactions.

Answer b

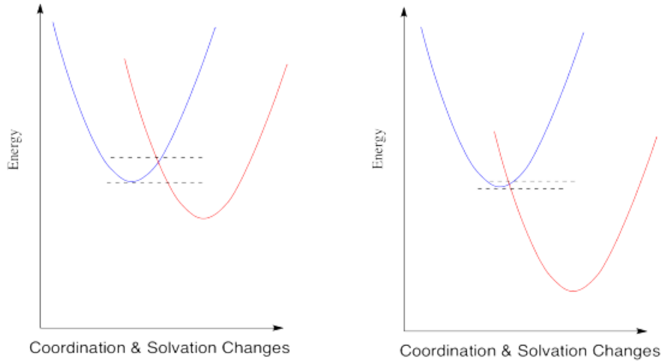
b) Because electron transfer is so fast, atomic and molecular reorganisations are actually thought to happen before the electron transfer. The water molecules would happen to shift into a position that would provide the greatest possible stabilisation for the ions and then the electron would be transferred. A less polar solvent than water would be less able to stabilize ions and the electron would be slower to transfer as a result. In addition, a less polar solvent than water would be a poor medium to transmit an electron, which is charged and therefore stabilized by interactions with polar solvents.

The energy diagram for the case involving two different metals is very similar, except that now there is a difference in energy between the two states. The reduction potential is no longer zero. We'll assume the reduction potential is positive, and so the free energy change is negative. Energy goes down upon electron transfer.



Compare this picture to the one for the degenerate case, when the electron is just transferred to a new metal of the same type. A positive reduction potential (or a negative free energy change) has the effect of sliding the energy surface for the red state downwards. As a result, the intersection point between the two surfaces also slides downwards. Since that is the point at which the electron can slide from one state to the other, the barrier to the reaction decreases.

What would happen if the reduction potential were even more positive? Let's see in the picture below.



The trend continues. According to this interpretation of the kinetics of electron transfer, the more exothermic the reaction, the lower its barrier will be. It isn't always the case that kinetics tracks along with thermodynamics, but this might be one of them.

But is all of this really true? We should take a look at some experimental data and see whether it truly works this way.

Oxidant	E°	*k* ($M^{-1}s^{-1}$) (margin of error shown in parentheses)
Co(diene)$(NH_3)_2^{3+}$	0.12	3.0(4)
Co(diene)H_2O)NCS^{2+}	0.38	11(1)
Co(diene)$(H_2O)_2^{3+}$	0.53	800(100)
Co(EDTA)	0.60	6000(1000)

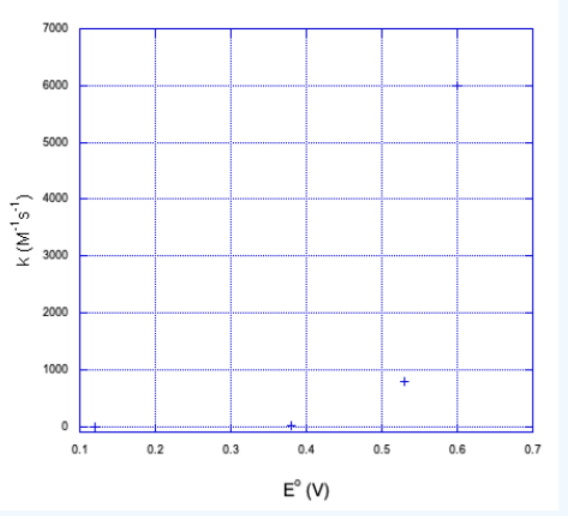
As the reduction potential becomes more positive, free energy gets more negative, and the rate of the reaction dramatically increases. So far, Marcus theory seems to get things right.

? Exercise 1.9.8

a. Plot the data in the above table.
b. How would you describe the relationship? Is it linear? Is it exponential? Is it direct? Is it inverse?
c. Plot rate constant versus free energy change. How does this graph compare to the first one?

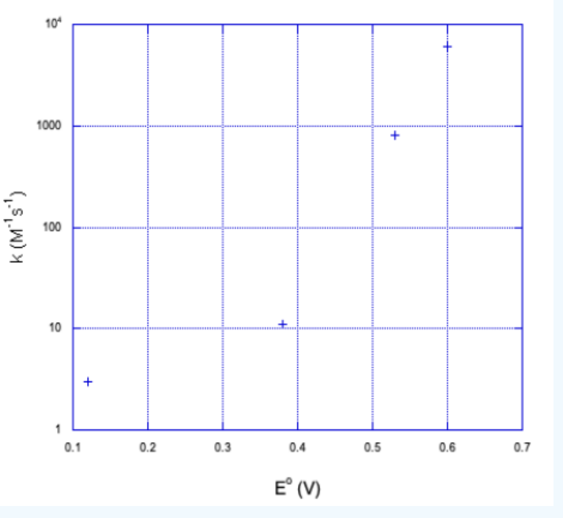
Answer a

a) Here is a plot of the data.



Answer b

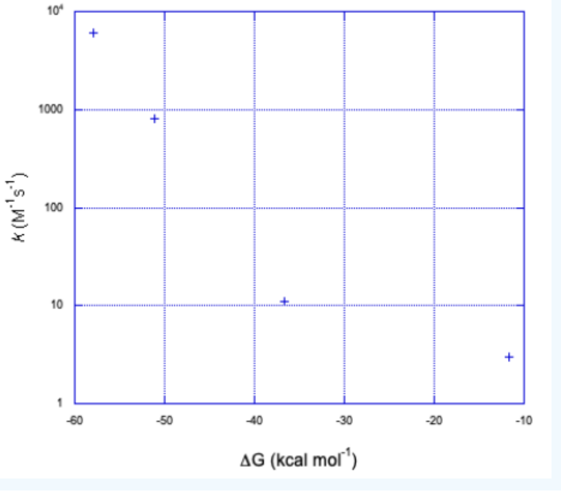
b) It doesn't look linear. If we plot the y axis on a log scale, things become a little more linear.



It looks closer to a logarithmic relationship than a linear one.

Answer c

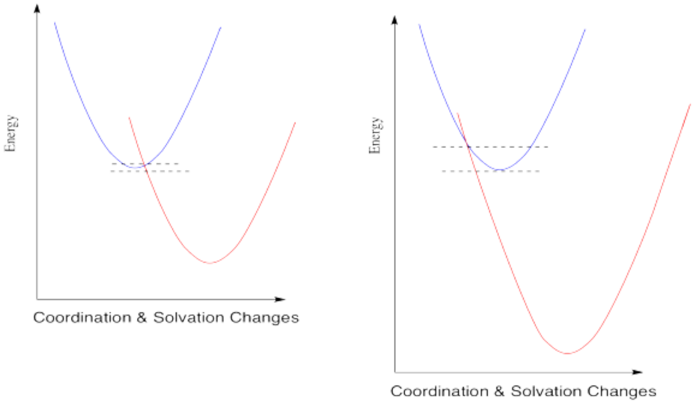
c) Assuming one electron transfer:



The graph takes the same form but in the opposite direction along the x axis.

Marcus Inverted Region

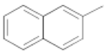
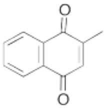
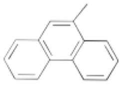
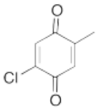
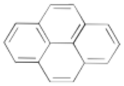
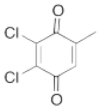
When you look a little closer at Marcus theory, though, things get a little strange. Suppose we make one more change and see what happens when the reduction potential becomes *even more* positive.



So, if Marcus is correct, at some point as the reduction potential continues to get more positive, reactions start to slow down again. They don't just reach a maximum rate and hold steady at that plateau; the barrier gets higher and higher and the reactions get slower and slower. If you feel a little skeptical about that, you're in good company.

Marcus always maintained that this phenomenon was a valid aspect of the theory, and not just some aberration that should be ignored. The fact that nobody had ever actually observed such a trend didn't bother him. The reason we didn't see this kind of thing, he said, was that we just hadn't developed technology that was good enough to measure these kind of rates accurately.

But technology did catch up. Just take a look at the following data (from Miller, *J. Am.Chem. Soc.* **1984**, *3047*).

Acceptor	ΔG	*k*	Acceptor	ΔG	*k*
	-0.05	2×10^6		-1.9	6×10^8
	-0.2	2×10^7		-2.2	1×10^8
	-0.5	1×10^9		-2.4	6×10^7

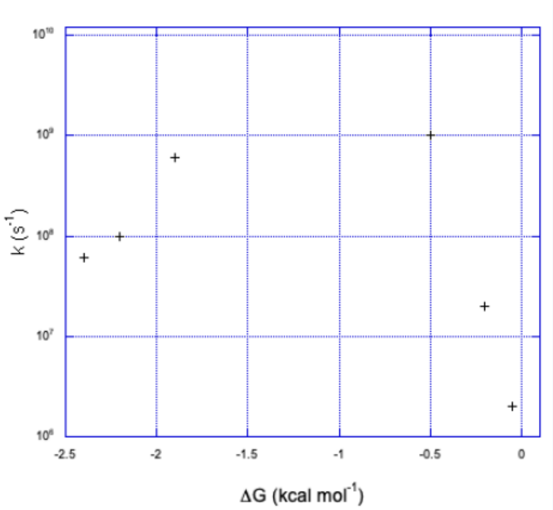
Don't worry that there are no metals involved anymore. An electron transfer is an electron transfer. Here, an electron is sent from the aromatic substructure on the right to the substructure on the left. By varying the part on the left, we can adjust the reduction potential (or the free energy change, as reported here.

Exercise 1.9.9

a. Plot the data in the above table.
b. How would you describe the relationship?

Answer a

a)



Answer b

b) We can see two sides of an inverted curve. The reaction gets much faster as the free energy becomes more negative, but at some point the rate begins to decrease again.

As the reaction becomes more exergonic, the rate increases, but then it hits a maximum and decreases again. Data like this means that the "Marcus Inverted Region" is a real phenomenon. Are you convinced? So were other people. In 1992, Marcus was awarded the Nobel Prize in Chemistry for this work.

? Exercise 1.9.10

Take a look at the donor/acceptor molecule used in Williams' study, above. a) Why do you suppose the free energy change is pretty small for the first three compounds in the table? b) Why does the free energy change continue to get bigger over the last three compounds in the table?

Answer

The acceptor compound becomes an anion when it accepts an electron. The first three compounds do not appear to be strongly electrophilic; they can accept electrons simply because of resonance stability of the resulting anion. The last three have electron withdrawing groups (chlorines and oxygens) that would stabilize the anion even further.

? Exercise 1.9.11

The rates of electron transfer between cobalt complexes of the bidentate bipyridyl ligand, $Co(bipy)_3^{n+}$, are strongly dependent upon oxidation state in the redox pair. Electron transfer between Co(I)/Co(II) occurs with a rate constant of about 10^9 $M^{-1}s^{-1}$, whereas the reaction between Co(II)/Co(III) species proceeds with $k = 18$ $M^{-1}s^{-1}$.

a. What geometry is adopted by these complexes?
b. Are these species high spin or low spin?
c. Draw d orbital splitting diagrams for each complex.
d. Explain why electron transfer is so much more facile for the Co(I)/Co(II) pair than for the Co(II)/Co(III) pair.

Answer a

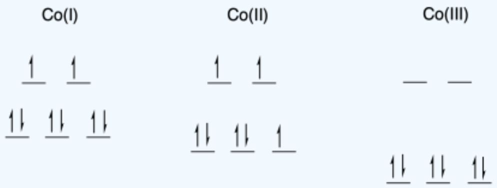
a) octahedral; bpy is a bidentate ligand.

Answer b

b) Co is first row; Co(I) and Co(II) have relatively low charge. Usually we would expect them to be high spin. Co(III) is at a cut-off point in the first row; it is just electronegative enough that it is usually low spin.

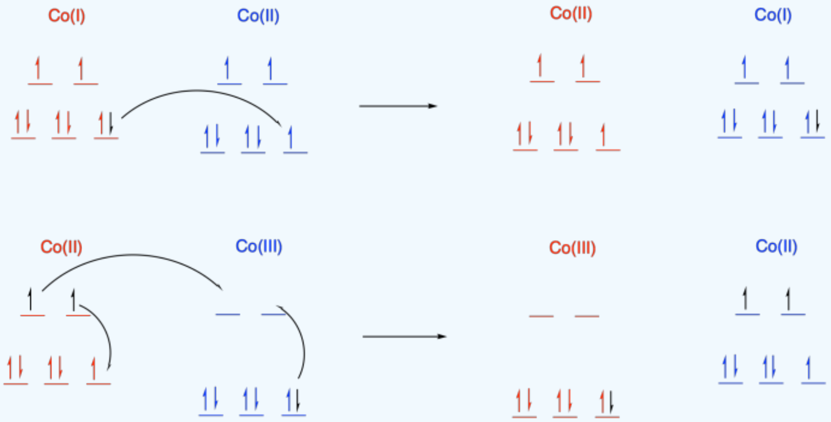
Answer c

c)



Answer d

d) In a transfer from Co(II) to Co(III), there is additional reorganization needed because the metal changes between high and low spin. Not only does one electron have to move from one metal to another metal, but additional electrons have to shuffle from one orbital to another on the same metal to accommodate the change. These reorganizations have a barrier, slowing the reaction.



1.10: Inner Sphere Electron Transfer

In some cases, electron transfers occur much more quickly in the presence of certain ligands. For example, compare the rate constants for the following two electron transfer reactions, involving almost exactly the same complexes:

$$\mathrm{Co(NH_3)_6^{3+} + Cr^{2+} \longrightarrow Co^{2+} + Cr^{3+} + 6\,NH_3} \quad k = 10^{-4} M^{-1} s^{-1}$$

$$\mathrm{Co(NH_3)_5Cl^{2+} + Cr^{2+} \longrightarrow Co^{2+} + CrCl^{2+} + 6\,NH_3} \quad k = 6 \times 10^{5} M^{-1} s^{-1}$$

(Note: aqua ligands are omitted for simplicity. Ions, unless noted otherwise, are aqua complexes.)

Notice two things: first, when there is a chloride ligand involved, the reaction is much faster. Second, after the reaction, the chloride ligand has been transferred to the chromium ion. Possibly, those two events are part of the same phenomenon.

Similar rate enhancements have been reported for reactions in which other halide ligands are involved in the coordination sphere of one of the metals.

In the 1960’s, Henry Taube of Stanford University proposed that halides (and other ligands) may promote electron transfer via bridging effects. What he meant was that the chloride ion could use one of its additional lone pairs to bind to the chromium ion. It would then be bound to both metals at the same time, forming a bridge between them. Perhaps the chloride could act as a conduit for electron transfer. The chloride might then remain attached to the chromium, to which it had already formed a bond, leaving the cobalt behind.

Electron transfers that occur via ligands shared by the two metals undergoing oxidation and reduction are termed "inner sphere" electron transfers. Taube was awarded the Nobel Prize in chemistry in 1983; the award was based on his work on the mechanism of electron transfer reactions.

Exercise 1.10.1

Take another look at the two electron transfer reactions involving the cobalt and chromium ion, above.

a. What geometry is adopted by these complexes?
b. Are these species high spin or low spin?
c. Draw d orbital splitting diagrams for each complex.
d. Explain why electron transfer is accompanied by loss of the ammonia ligands from the cobalt complex.
e. The chloride is lost from the cobalt complex after electron transfer. Why does it remain on the chromium?

Answer a

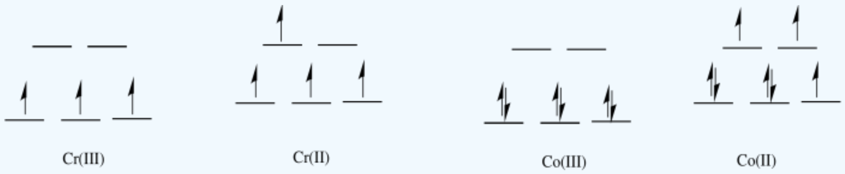
a) octahedral

Answer b

b) In the first row, 2^+ complexes are almost always high spin. However, 3^+ complexes are sometimes low spin.

Answer c

c)



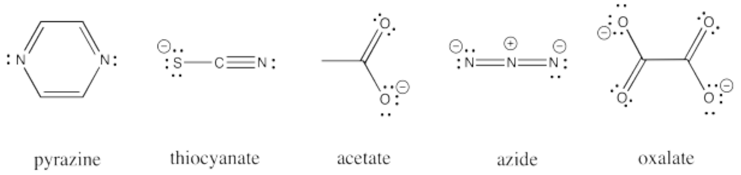
Answer d

d) The Co(II) complex is high spin and labile. The ligands are easily replaced by water.

Answer e

e) The Cr(III) complex is only d^3; it is inert.

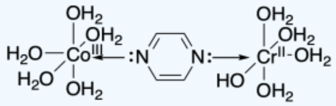
Other ligands can be involved in inner sphere electron transfers. These ligands include carboxylates, oxalate, azide, thiocyanate, and pyrazine ligands. All of these ligands have additional lone pairs with which to bind a second metal ion.

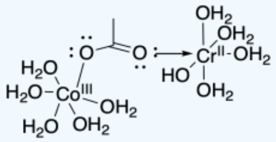


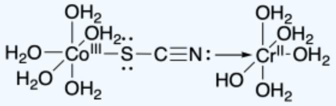
Exercise 1.10.2

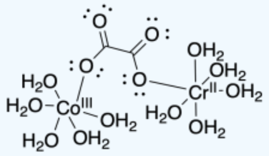
Draw an example of each of the ligands listed above bridging between a cobalt(III) and chromium(II) aqua complex.

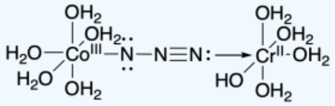
Answer









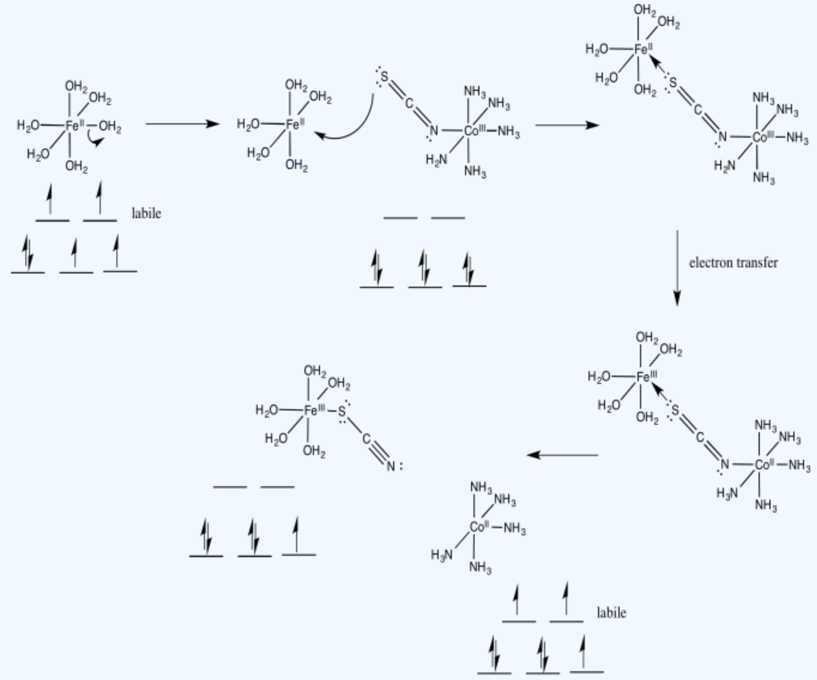


Exercise 1.10.3

Explain, with structures and d orbital splitting diagrams, how the products are formed in the following reaction, in aqueous solution.

$$\mathrm{Fe(OH_2)_6^{2+} + (SCN)Co(NH_3)_5^{2+} \longrightarrow (NCS)Fe(OH_2)_5^{2+} + Co(OH_2)_6^{2+} + 5\,NH_3}$$

Answer

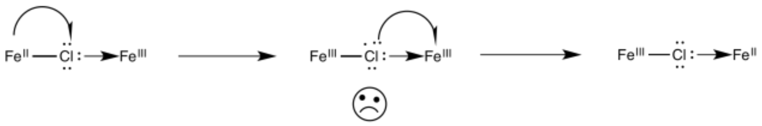


How does the electron travel over the bridge?

Once the bridge is in place, the electron transfer may take place via either of two mechanisms. Suppose the bridging ligand is a chloride. The first step might actually involve an electron transfer from chlorine to the metal; that is, the chloride could donate one electron from one of its idle lone pairs. This electron could subsequently be replaced by an electron transfer from metal to chlorine.

Sometimes, we talk about the place where an electron *used to be*, describing it as a "hole". In this mechanism, the electron donated from the bridging chloride ligand leaves behind a hole. The hole is then filled with an electron donated from the other metal.

Alternatively, an electron might first be transferred from metal to chlorine, which subsequently passes an electron along to the other metal. In the case of chlorine, this idea may be unsatisfactory, because chlorine already has a full octet. Nevertheless, some of the other bridging ligands may have low-lying unoccupied molecular orbitals that could be populated by this extra electron, temporarily.

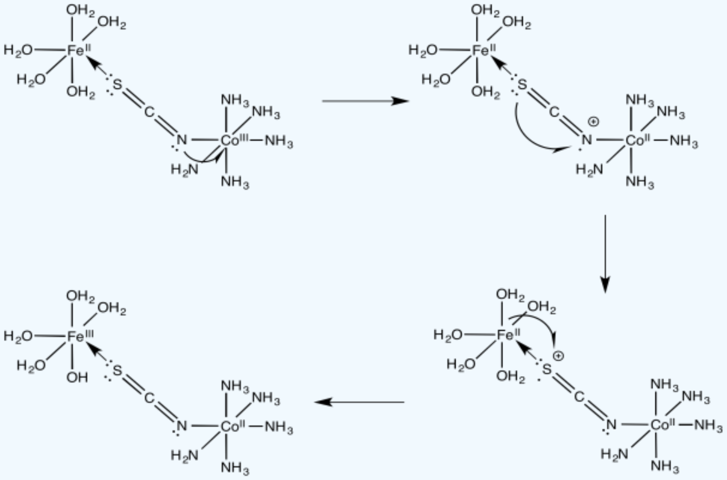


Exercise 1.10.4

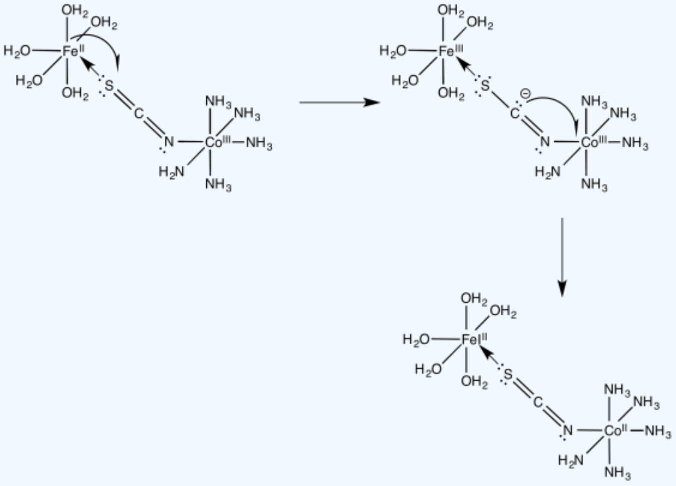
For the iron / cobalt electron transfer in problem Exercise 1.10.3(RO9.3.), show

a. an electron transfer mechanism via a hole migration along the bridge
b. an electron transfer mechanism via an electron migration along the bridge

Answer a



Answer b



Exercise 1.10.5

One of the many contributions to the barrier for electron transfer between metal ions is internal electronic reorganization.

a) Draw d orbital splitting diagrams for each of the following metal ions in an octahedral environment.

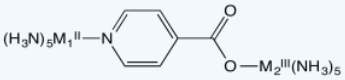
Ru(II) or Os(II)

Ru(III) or Os(III)

Co(II)

Co(III)

Flash photolysis is a method in which an electron can be moved instantly “uphill” from one metal to another (e.g. from M_2^{II} to M_1^{III}, below); the electron transfer rate can then be measured as the electron “drops” back from M_1^{II} to M_2^{III}.



b) Explain the relative rates of electron transfer reaction in this system, as measured by flash photolysis in the table below.

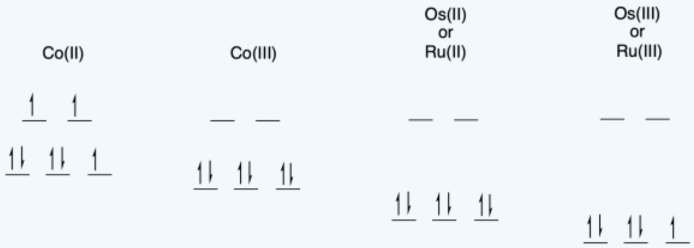
M_1^{II}	M_2^{III}	k_{obs} s^{-1}
Os	Ru	> 5 x 10^9

Os	Co	1.9 x 10^5

c) Does the reaction above probably occur via an inner sphere or by an outer sphere pathway? Why?

Answer a

a)



Answer b

b) The electron transfer between Os(II) and Ru(III) will not involve any electron reorganization because both are low spin to begin with. However, the electron transfer between Os(II) and Co(III) will result in cobalt changing from low spin to high spin. The need to move electrons between different d orbitals on the cobalt will add to the barrier, slowing down the reaction.

Answer c

c) The pathway is probably inner sphere because of the bridging ligand. Furthermore, the conjugation in the bridging ligand would help in conducting an electron from one end of the ligand to the other, either through an electron mechanism or a hole mechanism.

Exercise 1.10.6

Outer sphere electron transfer rates depend on the free energy change of the reaction (ΔG°) and the distance between oxidant and reductant (d) according to the relation

Rate constant = $k = Ae^{(-\Delta G)}e^{-d}$

a) What happens to the rate of the reaction as distance increases between reactants?

One potential problem in measuring rates of intramolecular electron transfer (i.e. *within* a molecule) is competition from intermolecular electron transfer (*between* molecules).

b) What would you do in the flash photolysis experiment above to discourage intermolecular electron transfer?

c) How could you confirm whether you were successful in discouraging intermolecular reaction?

Answer a

a) The rate decreases exponentially as distance increases.

Answer b

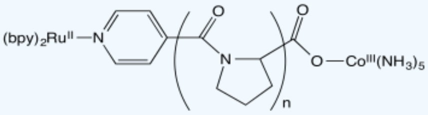
b) You might keep the concentration low in order to increase the distance between molecules, reducing the likely hood of an outer-sphere electron transfer.

Answer c

c) If you ran the experiment at a series of dilutions, intramolecular electron transfer would be unaffected but outer sphere electron transfer would not. If the rates were the same across a number of different concentrations, the reaction would probably be intramolecular.

Exercise 1.10.7

Stephan Isied and coworkers at Rutgers measured the following electron transfer rates between metal centers separated by a peptide. (*Chem Rev* **1992**, *92*, 381-394)



a. The proline repeating unit is crucial in ensuring a steady increase in distance between metal centers with increased repeat units, n. Why?
b. An inner sphere pathway in this case is expected to be somewhat slow because of the lack of conjugation in the polyproline bridge. Explain why.
c. Plot the data below, with log*k* on the y axis (range from 4-9) and d on the x axis (12-24 Angstroms).

n	d (Å)	k_{obs} (s^{-1})
1	12.2	5×10^8
2	14.8	1.6×10^7
3	18.1	2.3×10^5
4	21.3	5.1×10^4
5	24.1	1.8×10^4

d) A linear relationship is in agreement with Marcus theory; log*k* = - c x d. Is your plot linear?

Isied offers a number of possible explanations for the data, all of which involve two competing reaction pathways.

e) Suggest one explanation for the data.

Answer a

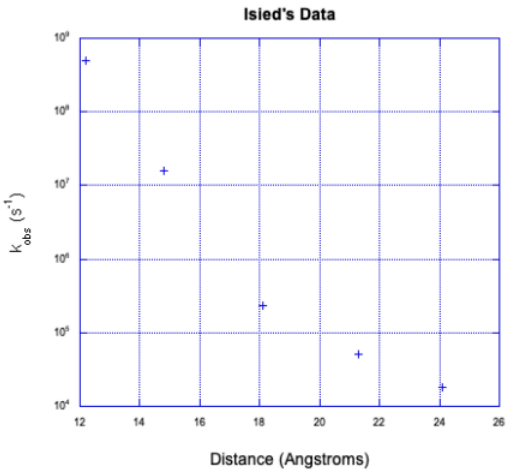
a) Rings are frequently used to introduce conformational rigidity (or decrease conformational flexibility), limiting the range of potential shapes a molecule could adopt. If the molecule can't wiggle around as much, then the distance between the ends of the molecule should be more constant.

Answer b

b) Although the ligand is bridging, it would be difficult to picture either an electron or hole mechanism of inner sphere electron transfer. There are few pi bonds or lone pairs to use as places to put electrons or temporarily remove electrons from, shuttling the electrons from place to place along the ligand. A conjugated system would be much more likely to carry out inner sphere electron transfer.

Answer c

c)



Answer d

d) The data is not linear.

Answer e

e) The data appear to show two lines that cross. That's a classic symptom of two competing mechanisms. The faster mechanism, to the left, is probably an intramolecular electron transfer. The slower mechanism, to the right, may be an intermolecular electron transfer.

1.11: Cyclic Voltammetry

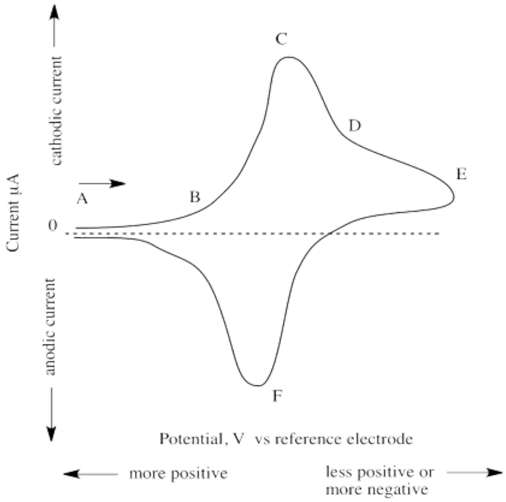
Cyclic voltammetry is a commonly used method of measuring the reduction potential of a species in solution. The species may be a coordination complex or a redox-active organic compound, for example. Cyclic voltammetry provides additional data that can be interpreted to make conclusions about the reduction / oxidation reaction and the stability of the species resulting from the electron transfer.

In cyclic voltammetry, rather than measuring the voltage produced by a reaction as we discussed before, a voltage is instead applied to the solution. The voltage is changed over time and current through a circuit is monitored. When the voltage reaches a point at which a reduction/oxidation is induced, current begins to flow. A cyclic voltammogram is a plot of current versus applied voltage.

In the experiment, the species of interest is dissolved along with some electrolyte, which promotes conductivity in the solution. Three electrodes are inserted into the solution. The working electrode, where the reduction / oxidation reaction takes place, is mostly covered with an insulator, but has a small disc of electrode exposed so the reaction can take place in a carefully controlled area. The counter electrode completes the circuit. A reference electrode with a known potential is also used in order to measure the potential applied to the cell. Unusually, the solution must not be stirred.

To begin the experiment, a potential is applied that is much more positive than the potential of the reference electrode. This step ensures that the species of interest is completely oxidized to begin with. The voltage is then swept in the negative direction at a constant rate. That is, the potential at the working electrode gets lower and lower, possibly until it becomes negative compared to the reference electrode. At some point, the voltage sweep is reversed, and it becomes more and more positive until it returns to the initial setting.

The (simulated) results of such an experiment are shown below.



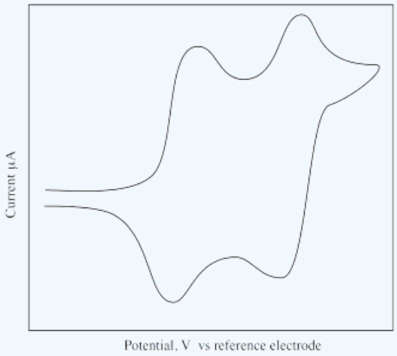
At point A, the potential is very positive but is then swept to lower and lower values. At point B, current begins to flow as the voltage reaches a point that allows reduction to occur. Current keeps increasing until, at point C, all of the species in the vicinity of the working electrode has already been reduced. This point is called "cathodic peak potential". Current then begins to decrease, although some still keeps flowing as more of the species slowly diffuses over to the working electrode (point D).

The reasons for two of the features of the experimental design are now apparent. The reason for the very small exposed surface of the working electrode (usuallyan exposed disc about 1 mm wide) is to limit the area in which reaction takes place, so that we can observe when a controlled population of species has been reduced. The reason for not stirring the solution is similar; if we stirred the solution, more species would be continually and quickly fed to the working electrode and we would never observe a point at which the reaction was "finished".

At some point, the potential is increased again (point E). Current keeps decreasing; that trend is reversed as the previously reduced species is again oxidized. This time, current flows in the opposite direction, and a negative peak is observed. At point F, all of the species in the vicinity of the working electrrode has been oxidized, and current begins to "drop" again. This point is called "anodic peak potential". The "formal potential" is the mean of anodic and cathodic peak potential.

Exercise 1.11.1

What is different about the following cyclic voltammogram compared to the previous one? Explain what is happening in this sample.

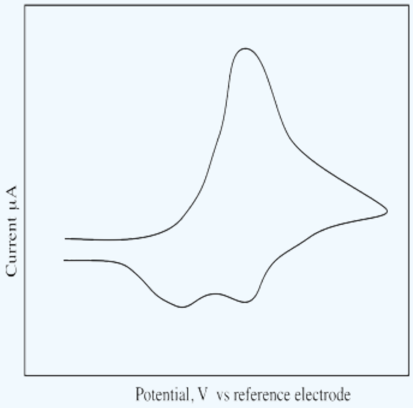


Answer

The compound undergoes a two-electron oxidation. The oxidized species then undergoes a two-electron reduction.

Exercise 1.11.2

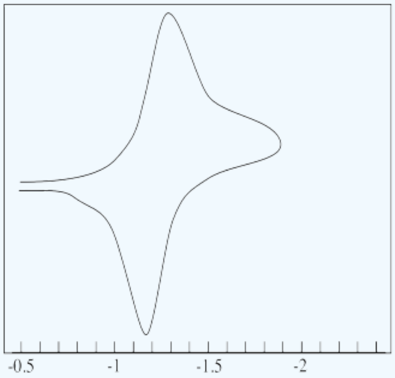
What is different about the following cyclic voltammogram? Explain what is happening in this sample.



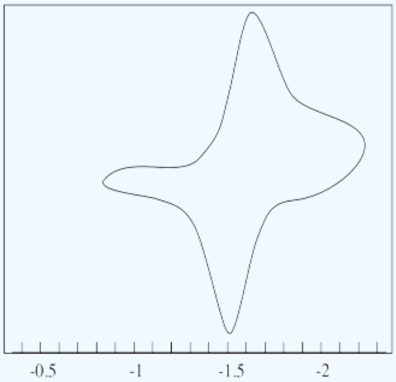
Exercise 1.11.3

Estimate the reduction potentials in the following cyclic voltamograms.

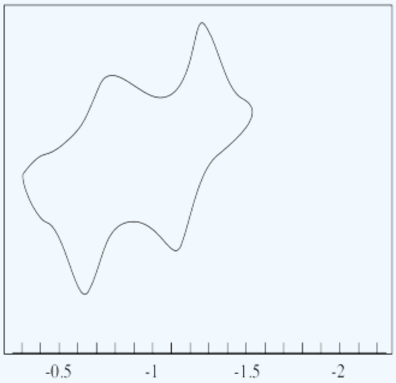
a)



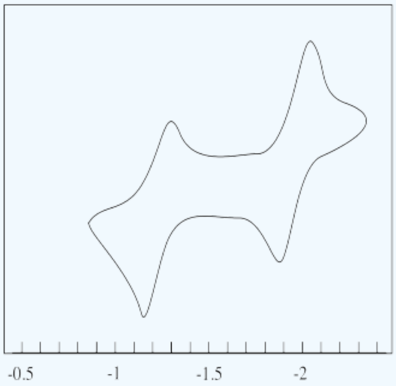
b)



c)



d)



1.12: Organic Redox

The idea of oxidation states is not normally applied to organic compounds, but it can be useful to do so. When we do, we can gain some insight into certain reactions of organic molecules.

For example, carbon dioxide, CO_2, can be thought of as having carbon in an oxidized state. If we apply the usual oxidation state rule, carbon dioxide is overall neutral and contains two oxygens, each with 2- charge. To counter that charge, carbon must be in oxidation state 4+.

On the other hand, methane, CH_4, can be thought of as having carbon in a reduced state. If we apply the usual oxidation state rule here, methane is overall neutral but contains four protons. That means the carbon must be in a 4- oxidation state. Of course, the carbon does not behave as if it has a minus four charge. But we will see that this sort of exercise can be useful for book-keeping purposes.

? Exercise 1.12.1

Assign the formal oxidation state to carbon in the following molecules.

a) methanol, CH_3OH b) formaldehyde or methanal, CH_2O c) carbonate, CO_3^{2-} d) hydrogen cyanide, HCN

e) ethane, CH_3CH_3 f) ethene, CH_2CH_2 g) ethyne, CHCH

The general trend here is that the more bonds there are to oxygen, the more oxidized is carbon. The more bonds there are to hydrogen, the more reduced is carbon.

Oxidation Levels in Organic Compounds

Before we look at redox reactions in organic compounds, we should take a look at a slightly different convention for assessing oxidation states in organic molecules. This convention is the use of oxidation levels rather than oxidation states. An oxidation state refers to an individual atom. An oxidation level refers to a molecule; it reflects the overall sum of the oxidation states of the atoms in that molecule.

Why would we look at things that way? Clearly, we lose some of the detail. Given an oxidation level, you don't immediately know what atom would have what charge. But because these compounds are covalent, rather than ionic, the oxidation state isn't a completely reliable measure of charge, anyway. It is useful for relative comparisons (which carbon would have more buildup of positive charge?) but not absolute measurement (exactly how much charge is on this carbon?). Oxidation level drops that detail but instead gives us a quick comparison between two molecules, such as the reactant and the product of a redox reaction, and that allows us to quickly assess what has happened over the course of the reaction: is this an oxidation, or a reduction?

How does it work? Instead of a focus on atoms, there is a focus on bonds. Look at the number of C-H bonds in a molecule and assign a value of -1 for each bond. Add those numbers into a total. Next, look at the number of C-X bonds in the molecule, in which X is a heteroatom (something other than carbon or hydrogen); that is most often oxygen, but sometimes nitrogen, a halogen, or some other electronegative element. Each of these bonds counts as +1. Add those into the running total. The result is the oxidation level.

- Each C-H bond counts as -1
- Each C-X bond (such as C-O, C-N etc) counts as +1

For example, look at methanol, CH_3OH.

C-H bonds	3-
C-X bonds	1+
Oxidation Level	2-

Note that we don't worry about O-H bonds. We are just looking at carbon, which is the redox-active atom in organic molecules.

Compare that result to methanal, CH_2O.

C-H bonds	2-
C-X bonds	2+
Oxidation Level	0

Also compare it to formate ion, HCO_2^-.

C-H bonds	1-
C-X bonds	3+
Oxidation Level	2+

In these cases, the oxidation level is the same as the oxidation state on the carbon atom. That's because there is only one carbon atom in the molecule. If we have additional carbons, oxidation level becomes a much more efficient way of comparing compounds.

Exercise 1.12.2

Compare oxidation levels in the following pairs of compounds.

a. CH_2CHCH_3 and $CH_3CH_2CH_3$
b. CH_3CH_2CHO and $CH_3CH_2CH_2OH$
c. $CH_3CH(OH)CH_2CH_2OH$ and CH_3COCH_2CHO

Answer a

a) CH_2CHCH_3

C-H bonds	6-
C-X bonds	0
Oxidation Level	6-

$CH_3CH_2CH_3$

C-H bonds	8-
C-X bonds	0
Oxidation Level	8-

Propane results from a two-electron reduction of propene.

Answer b

b) CH_3CH_2CHO

C-H bonds	6-
C-X bonds	2+
Oxidation Level	4-

$CH_3CH_2CH_2OH$

C-H bonds	7-
C-X bonds	1_
Oxidation Level	6-

Propanol results from a two-electron reduction of propanal.

Answer c

c) $CH_3CH(OH)CH_2CH_2OH$

C-H bonds	8-
C-X bonds	2+
Oxidation Level	6-

CH_3COCH_2CHO

C-H bonds	6-
C-X bonds	4+
Oxidation Level	2-

3-oxobutanal results from a four-electron oxidation of 1,3-butanediol.

Mechanism of Organic Redox

Adding a hydrogen nucleophile to a carbonyl electrophile is routinely referred to as a reduction. For example, adding sodium borohydride to methanal would result in reduction to form methanol. Of course, a hydride is really a proton plus two electrons. We could write an equation for the reduction of methanal that looks a lot like the redox reactions we see in a table of standard reduction potentials.

$$CH_2O + H^- + H^+ \longrightarrow CH_3OH \tag{1.12.1}$$

or

$$CH_2O + 2\,e^- + 2\,H^+ \longrightarrow CH_3OH \tag{1.12.2}$$

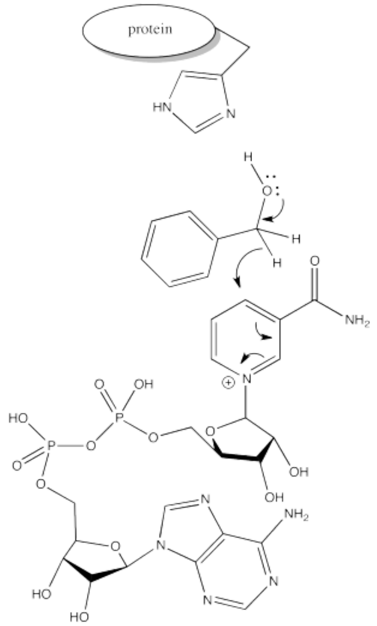
It stands to reason that the opposite reaction, the conversion of methanol to methanal, is a two electron oxidation.

$$CH_3OH \longrightarrow CH_2O + 2\,e^- + 2\,H^+ \tag{1.12.3}$$

We know how to accomplish the reduction of methanal, at least on paper. We just add a complex metal hydride, such as lithium aluminum hydride or sodium borohydride, to the carbonyl compound. After an acidic aqueous workup to remove all the lithium and aluminum compounds, we get methanol. For practical reasons, methanol may be difficult to isolate this way, but that's the general idea of the reaction.

How do we accomplish the reverse reaction: the conversion of an alcohol into a carbonyl?

One way would be to provide a hydride acceptor in the reaction, so that we could catch hydride as it comes off the methanol. The most well-known such entity is NAD+, of course. There are biological oxidations that employ NAD+ for this reason.

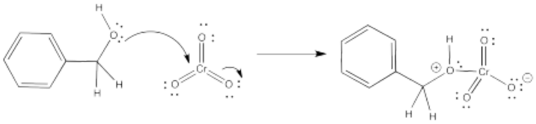


More generally, the reaction can be accomplished in a number of ways, on paper, by separating out the two tasks involved. We need something to accept the two protons: that's a base. We need something to accept the two electrons: that's an oxidizing agent.

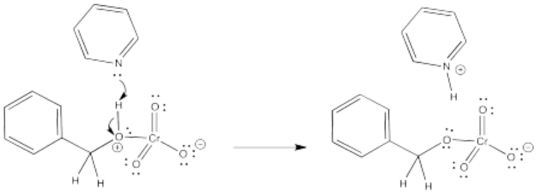
For the latter task, there are a number of high oxidation state transition metal compounds that are quite willing to accept two electrons. One of the most widely employed is Cr(VI), which accepts two electrons to become Cr(IV). A number of other methods are available, having been developed partly to avoid the toxicity of chromium salts, but let's look at the chromium case as an example.

A simple chromium(VI) compound is chromium trioxide. A simple base is pyridine. If we took these two reagents together with benzyl alcohol in a solvent such as dichloromethane, what would happen? OK, you might not want to try this, because chromium trioxide has an alarming capacity to cause spontaneous combustion in organic compounds, but we can do it on paper.

Is chromium trioxide a nucleophile or an electrophile? That Cr(VI) is pretty electrophilic, surely. So what part of the benzyl alcohol is nucleophilic? The oxygen atom. When we mix these things, the oxygen atom would likely coordinate to the chromium.



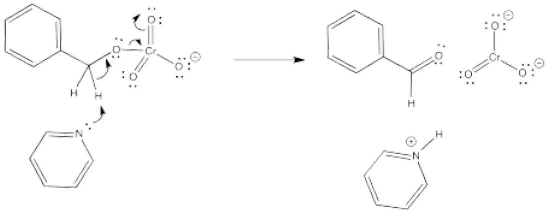
When the oxygen atom coordinates to the chromium, the oxygen gets a positive formal charge. It is now motivated to lose a proton. That's what the pyridine is for.



Now we have accomplished one of the goals of the reaction. We have removed a proton from benzyl alcohol. We have one more proton and two electrons left. The second proton will have to come from the carbon attached to the oxygen; that's the place where we need to form a carbonyl.

But wait a minute. You can't take two protons off the same molecule, can you? And certainly not from two atoms that are right next to each other. Doesn't that generate an unstable dianion?

Not this time. The chromium is there to accept two electrons. We won't generate an anion at all, as far as the benzyl alcohol is concerned. It is oxidized to benzaldehyde.



Exercise 1.12.3

A completely different outcome to this reaction would be obtained in aqueous solution because of the equilibrium that exists between a carbonyl and the geminal diol (or hydrate) in water. Instead of obtaining an aldehyde, a carboxylic acid would be obtained via a second reduction. Provide a mechanism for this reaction.

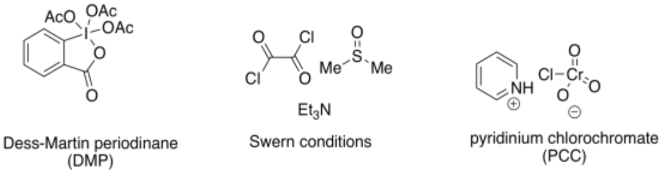
Oxidation of alcohols is strongly dependent on conditions. In general, there needs to be a hydrogen on the alcoholic carbon (H-C-O-H). If there is no hydrogen on that carbon, the alcohol is pretty difficult to oxidise to a ketone. If there is one hydrogen on that carbon -- that is, if the alcohol is secondary -- then the alcohol becomes a ketone.

If there are two hydrogens on that alcoholic carbon (H_2C-OH), i.e. if the alcohol is a primary one, then two different products may result. Removal of just one hydrogen from the alcoholic carbon, and replacement with an additional bond to oxygen, results in formation of an aldehyde. On the other hand, replacement of the second hydrogen from the alcoholic carbon, and replacement with another oxygen, would lead to formation of a carboxylic acid.

That second case -- replacement of the second hydrogen with an oxygen -- only happens in aqueous media. The aldehyde that forms after the first oxidation (H-C=O) must become hydrated (H-C(OH)$_2$) in order for the second oxidation to occur, making the carboxylic acid (HO-C=O). As a result, if a primary alcohol is oxidised via a reagent that requires water as a solvent, the carboxylic acid results. If an organic-soluble reagent is used, the reaction stops at the aldehyde.

- Oxidation of secondary alcohols results in formation of ketones.
- Oxidation of primary acohols results in aldehydes if mild oxidants are used in organic solvents.
- Oxidation of primary alcohols results in carboxylic acids under aqueous conditions.

The most common methods for mildly converting primary alcohols to aldehydes are Swern oxidations and Dess-Martin oxidations. Dess-Martin oxidations employ a high-oxidation state iodine compound -- that's I(V), compared to the more commonly encountered I^- ion. The reduction product is an I(III) compound. Swern oxidations employ sulfur in a moderately high oxidation state of zero; the sulfur is reduced to S^{2-} in the Me_2S side product.



In both cases, the oxidation mechanism is similar to the one illustrated with chromium oxide and pyridine. The oxygen donates to the oxidizing atom (the chromium, the sulfur, or the iodine). Deprotonation of the carbon leads to formation of the C=O bond and reduction of the oxidising agent by two electrons.

With Swern oxidations, the mechanism has an added "priming" step, because the thionyl oxidant (S=O) must first be activated; the thionyl oxygen donates to the carbonyl of the oxalyl chloride, $(COCl)_2$. The sulfur is then ready to accept an alcohol donor. Once the alcohol undergoes oxidation, the oxygen from the thionyl group is completley transferred to the oxalyl group, forming both carbon dioxide and carbon monoxide in a subsequent disproportionation reaction.

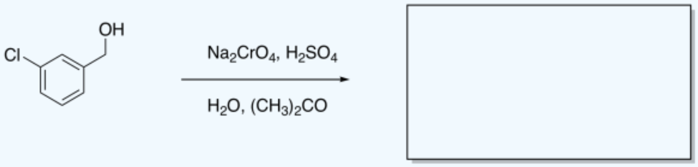
Oddly enough, although PCC looks like a good candidate for aqueous oxidation (it is ionic, after all), it is frequently absorbed onto a solid surface (usually alumina, Al_2O_3) and used as a heterogeneous catalyst in organic solvent. Like most heterogeneous catalysts, it works rather slowly, but it is pretty selective for aldehyde formation.

Most "ionic" oxidants really are used in the presence of water, and they do convert primary alcohols into carboxylic acids. Examples include sodium chromate, Na_2CrO_4, dichromate, $Na_2Cr_2O_7$, and potassium permanganate, $KMnO_4$. These reagents are much harsher than Swern conditions or DMP, however, and they can lead to extensive decomposition of the reactant. Chromates are sometimes prepared as a solution called Jones reagent, in which the oxidant is pre-mixed with sulfuric and and water; the reagent also contains some acetone, to help solubilise the organic compound to be oxidised.

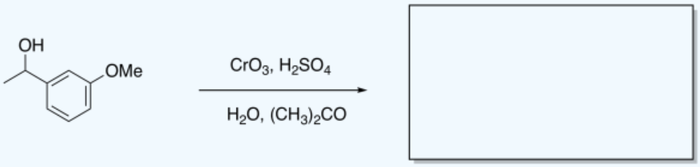
Exercise 1.12.4

Fill in the missing products.

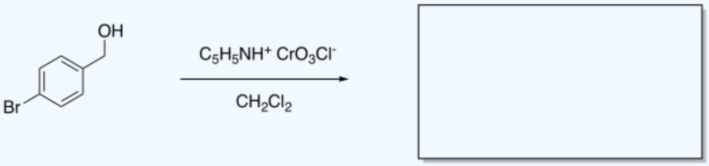
a)



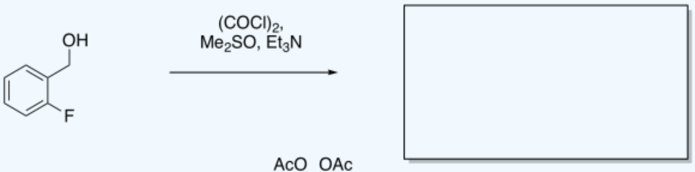
b)



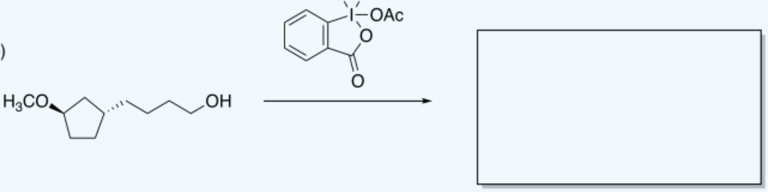
c)



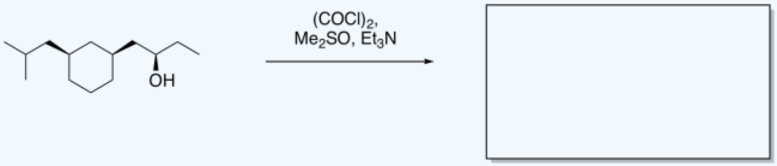
d)



e)

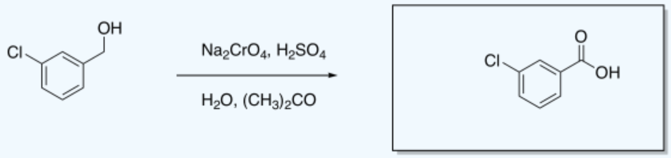


f)



Answer

a)



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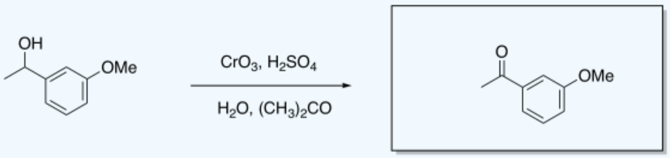
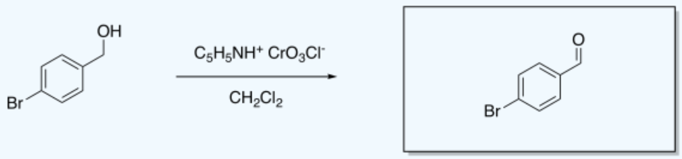
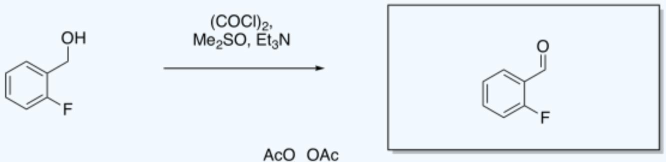


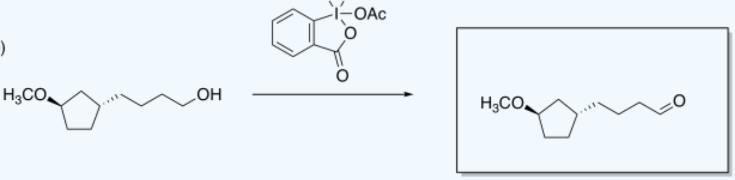
c)



d)



e)



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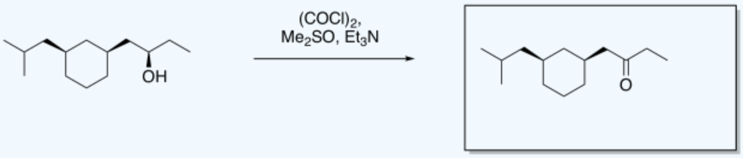
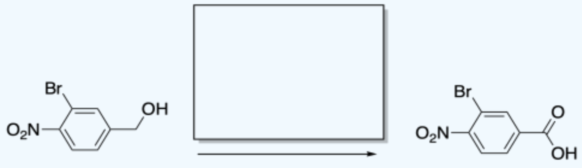


? Exercise 1.12.5

Fill in the missing reagents.

a)



b)

c)

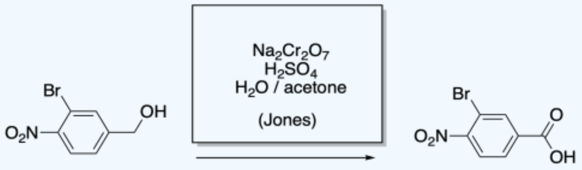
d)

e)

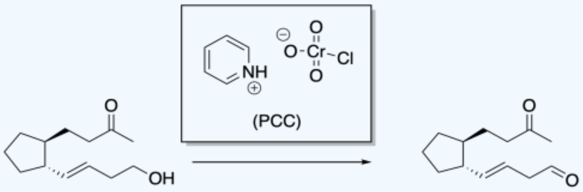
Answer

Multiple answers may be possible. However, (a) and (e) require aqueous oxidizing conditions whereas (b) excludes aqueous oxidizing conditions.

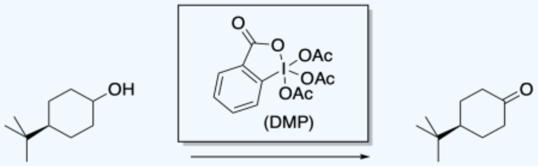
a)



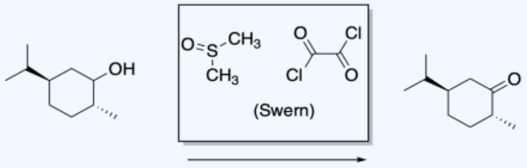
b)



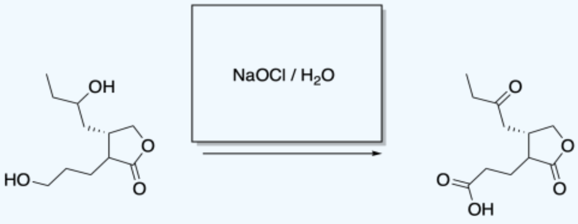
c)



d)

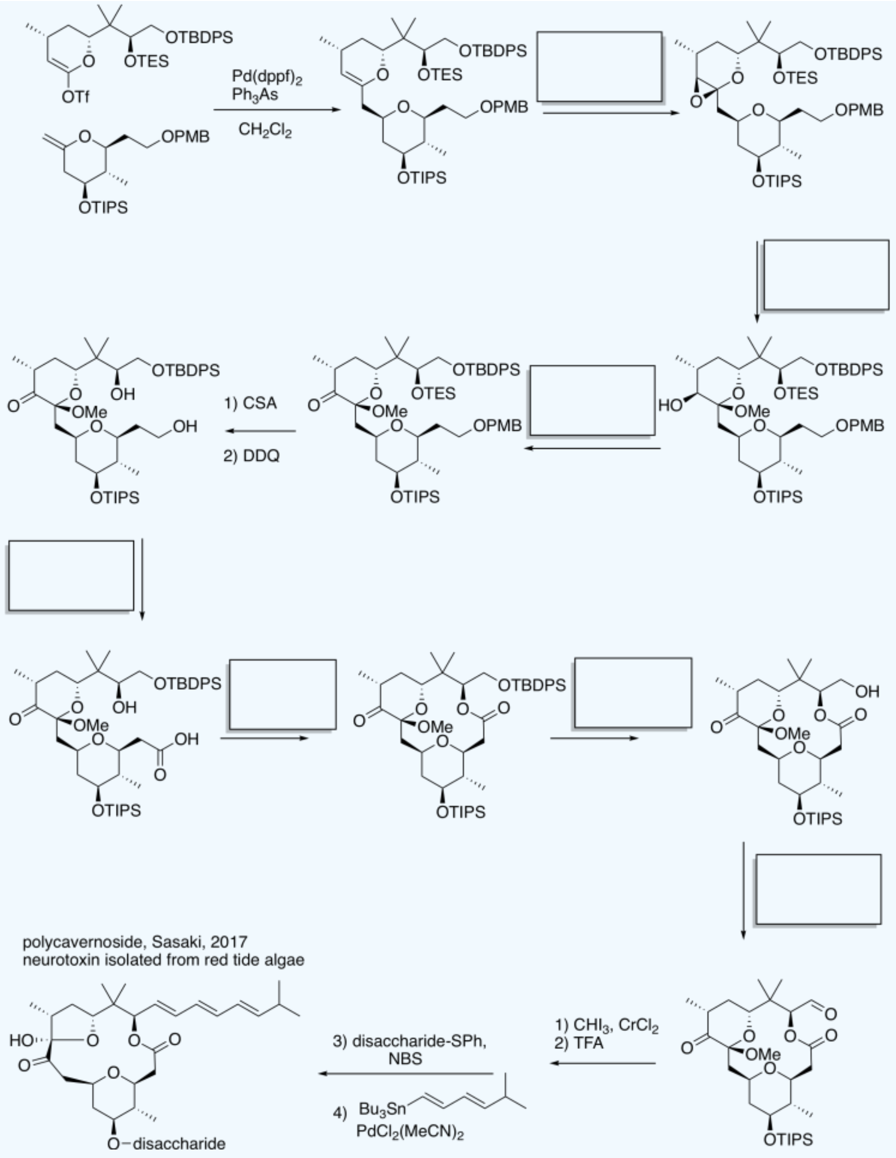


e)



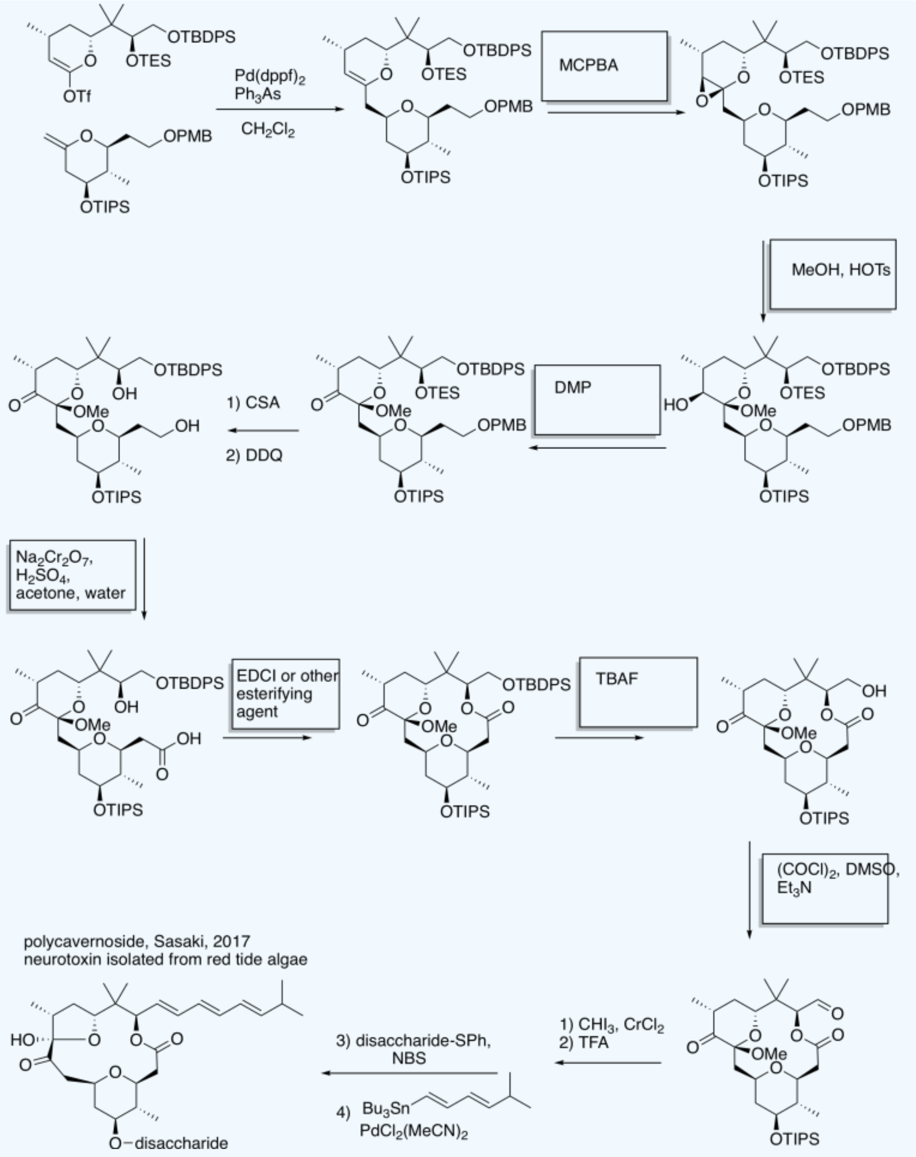
Exercise 1.12.6

Fill in the blanks in the following synthesis.



polycavernoside, Sasaki, 2017
neurotoxin isolated from red tide algae

Answer


OTBDPS
OTES
OTf
OPMB
OTIPS
Pd(dppf)$_2$
Ph$_3$As
CH$_2$Cl$_2$
MCPBA
MeOH, HOTs
DMP
1) CSA
2) DDQ
HO
OMe
OH
Na$_2$Cr$_2$O$_7$,
H$_2$SO$_4$,
acetone, water
EDCI or other esterifying agent
TBAF
(COCl)$_2$, DMSO,
Et$_3$N
polycavernoside, Sasaki, 2017
neurotoxin isolated from red tide algae
1) CHI$_3$, CrCl$_2$
2) TFA
3) disaccharide-SPh,
NBS
4) Bu$_3$Sn
PdCl$_2$(MeCN)$_2$
O–disaccharide

1.13: Potential and Concentrations

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1.14: Solutions to Selected Problems

Exercise 1.1.1:

a) Ag^+ b) Ni^{2+} c) Mn^{7+} d) Cr^{6+} e) Cu^{3+} f) Fe^{3+} g)Os^{8+} h) Re^{5+}

Exercise 1.1.3:

a) Pb^{2+} & S^{2-} b) Sn^{4+} & 2 O^{2-} c) Hg^{2+} & S^{2-} d) Fe^{4+} & 2 S^{2-} e) 2 Fe^{3+} & 3 O^{2-} f) 2 Fe^{3+} & 1 Fe^{2+} & 4 O^{2-}

Exercise 1.1.4:

Probably Fe^{2+}, to replace Zn^{2+} ions.

Exercise 1.1.5:

a) C $^{2+}$ b) C^{4+} c) $^{4-}$ d) C^0 e) C^{3+}

Exercise 1.1.7:

a) Mg^{2+} b) Cu^{2+} c) Mn^{3+} d) Ca^{2+} e) Mn^{2+} f) Mn^{2+}

Exercise 1.1.8:

a) Cu(II), Fe(II) b) Zn(II), Fe(III) c) Be(II), Al(III) d) Cu(I), Fe(III) e) Cu(II), Al(III)

Exercise 1.2.1:

a. $\mathrm{Cu} \longrightarrow \mathrm{Cu}^+ + \mathrm{e}^-$
b. $\mathrm{Fe}^{3+} + 3\,\mathrm{e}^- \longrightarrow \mathrm{Fe}$
c. $\mathrm{Mn} \longrightarrow \mathrm{Mn}^{3+} + 3\,\mathrm{e}^-$
d. $\mathrm{Zn}^{2+} + 2\,\mathrm{e}^- \longrightarrow \mathrm{Zn}$
e. $2\,\mathrm{F}^- \longrightarrow \mathrm{F}_2 + 2\,\mathrm{e}^-$
f. $\mathrm{H}_2 + 2\,\mathrm{H}^+ + 2\,\mathrm{e}^-$

Exercise 1.2.2:

a. $\mathrm{Cu(I)} + \mathrm{Fe(III)} \longrightarrow \mathrm{Cu(II)} + \mathrm{Fe(II)}$
b. $\mathrm{Cu(I)} + \mathrm{Ag(0\,)} \longrightarrow \mathrm{Cu(0\,)} + \mathrm{Ag(I)}$
c. $3\,\mathrm{F}_2 + 2\,\mathrm{Fe} \longrightarrow 6\,\mathrm{F}^- + 2\,\mathrm{Fe(III)}$
d. $2\,\mathrm{Mo}^{3+} + 3\,\mathrm{Mn} \longrightarrow 2\,\mathrm{Mo} + 3\,\mathrm{Mn}^{2+}$

Exercise 1.2.3:

a. $\mathrm{MnO}_2 + 2\,\mathrm{H}^+ + 2\,\mathrm{e}^- \longrightarrow \mathrm{Mn(OH)}_2$
b. $2\,\mathrm{NO} + 2\,\mathrm{e}^- + 2\,\mathrm{H}^+ \longrightarrow \mathrm{N}_2\mathrm{O} + \mathrm{H}_2\mathrm{O}$
c. $\mathrm{HPO}_3^{2-} + 2\,\mathrm{e}^- + 3\,\mathrm{H}^+ \longrightarrow \mathrm{H}_2\mathrm{PO}_2^- + \mathrm{H}_2\mathrm{O}$
d. $\mathrm{Sn(OH)}_6^{2-} + 2\,\mathrm{e}^- + 3\,\mathrm{H}^+ \longrightarrow \mathrm{HSnO}_2^- + 4\,\mathrm{H}_2\mathrm{O}$

Exercise 1.2.4:

a) yes b) no c) yes d) no e) yes f) yes g) yes h) no

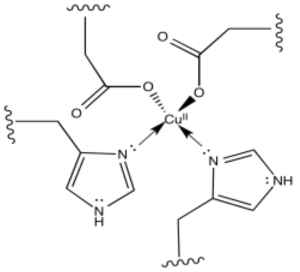
Exercise 1.2.5:

a. $E_{rxn} = -0.153V - 0.33V = -0.483V$
b. No.
c.

d) The O_2 is activated as an electrophile. Addition of an electron may become easier.

e) The reduction potential is 0.2 V more positive when the resulting superoxide ion is stabilised by binding a proton. A similar shift could occur when coordinated to copper.

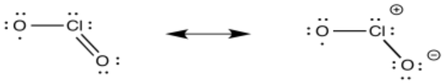
f)



g) The two aspartate ions would make the copper complex less cationic. That may make it easier to remove an electron from the copper complex.

Exercise 1.2.6:

a. $\mathrm{Fe^{2+} + ClO_2 \longrightarrow Fe^{3+} + ClO_2^-}$
b. $E_{rxn} = 0.95V - 0.77V = 0.18V$
c. yes.
d.



e) ClO_2 has an unpaired electron. ClO_2^- has electrons paired

f) It could be inner sphere: the oxygen in the ClO_2 could coordinate to the iron.

g) The mixture quickly forms $(H_2O)_5Fe(ClO_2)^{2+}$ via inner sphere electron transfer.

Exercise 1.3.1:

MnO_4^- : $4 \times O^{2-}\ (=8^-) + Mn^{7+} = 1^-$ overall

MnO_2 : $2 \times O^{2-}\ (=4^-) + Mn^{4+} =$ neutral overall

difference = 3 e^-

Exercise 1.3.2:

a) SO_4^{2-} : $4 \times O^{2-}\ (=8^-) + S^{6+} = 2^-$ overall

$S_2O_8^{2-}$: $8 \times O^{2-}\ (=16^-) + 2 \times S^{7+}\ (=14^+) = 2^-$ overall

difference = 1 e^- per S, or 2 e^- overall

$$\mathrm{S_2O_8^{2-} + 2\,e^- \longrightarrow 2\,SO_4^{2-}}$$

b) HPO_3^{2-} : $3 \times O^{2-}\ (=6^-) + H^+ + P^{3+} = 2^-$ overall

P : P(0)

difference = 3 e^-

$$\mathrm{HPO_3^{2-} + 3\,e^- + 5\,H^+ \longrightarrow P + 3\,H_2O}$$

c) Ti_2O_3 : $3 \times O^{2-}\ (=6^-) + 2 \times Ti^{3+}\ (=6^+)$ = neutral overall

TiO : O^{2-} + Ti^{2+} = neutral overall

difference = 1 e^- per Ti, or 2 e^- overall

$$\mathrm{Ti_2O_3 + 2\,e^- + 2\,H^+ \longrightarrow 2\,TiO + H_2O}$$

d) N_2 : N(0)

NH$_2$OH : $O^{2-} + 3 \times H^+ \ (= 3^+) + N^-$ = neutral overall

difference = 1 e$^-$ per N, or 2 e$^-$ overall

$$\mathrm{N_2 + 2\,e^- + 2\,H^+ + 2\,H_2O \longrightarrow 2\,NH_2OH}$$

Exercise 1.3.3:

Lithium is an alkali metal, in the first column of the periodic table. It has a relatively low ionization energy because it has a noble gas configuration as a cation. That noble gas configuration is stable because of the relatively large number of nuclear protons and a relatively short distance between the nucleus and the outermost shell of electrons. In lithium metal, the outermost electron is relatively far from the nucleus and so it is at a relatively high energy, and easily lost.

Exercise 1.3.4

Fluorine is a halogen, with a relatively high electron affinity. It easily gains an electron to get to a noble gas configuration as a fluoride anion. That noble gas configuration is stable because of the relatively large number of nuclear protons and a relatively short distance between the nucleus and the outermost shell of electrons.

Exercise 1.3.5:

From most easily oxidized to least easily oxidized: Li > Al > Fe > Cu > Au

Exercise 1.3.6:

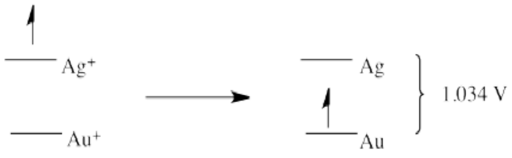
a. $E^0 = +0.796(\frac{Ag^+}{Ag}) - 1.83(\frac{Au}{Au^+}) = -1.034V$ (no forward reaction)
b. $E^0 = -0.44(\frac{Fe^{2+}}{Fe}) + 0.762(\frac{Zn}{Zn^{2+}}) = +0.0322V$ (forward reaction)
c. $E^0 = +0.52(\frac{Cu^+}{Cu}) + 3.04(\frac{Li}{Li^+}) = +3.56V$ (forward reaction)
d. $E^0 = +0.77(\frac{Fe^{3+}}{Fe^{3+}}) - 0.796(\frac{Ag}{Ag^+}) = -0.026V$ (no forward reaction)

Exercise 1.3.7:

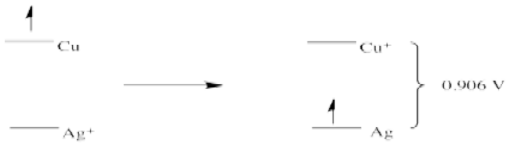
When the table of standard reduction potentials is displayed with the most negative value at the top and the most positive value at the bottom, any given half-reaction will go forward if it is coupled with the reverse of a half-reaction that lies above it in the table. The opposite is not the case; no half reaction will go forward if it is coupled with the reverse of a half-reaction below it in the table.

Exercise 1.4.1:

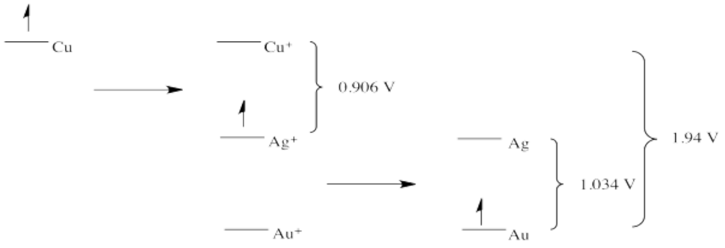
a)



b)

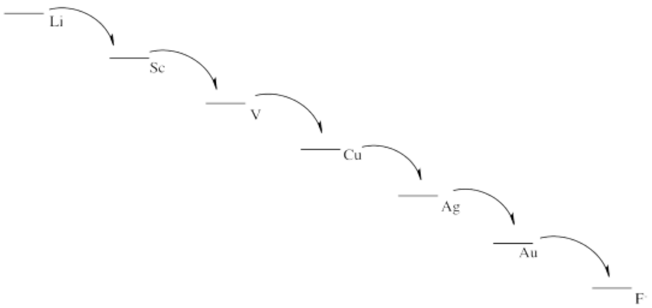


c)



Exercise 1.4.2:

a. $2\,Li + F_2 \longrightarrow 2\,Li^+ + 2\,F^-$
b. E° = +5.91 V
c. Things look pretty grim.
d.

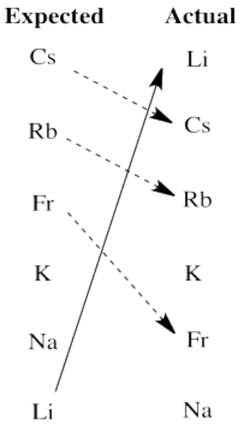


e) This scheme would result in the release of a small amount of energy at each stage. Each step could be harnessed to perform a task more efficiently, with less heat loss.

Exercise 1.4.3:

Exercise 1.4.4:

Exercise 1.4.5:



There are really two significant departures from expectation here. Lithium is much more active than expected based on electronegativity. The larger alkali metals, cesium, rubidium and francium, are all less active than expected on that basis.

We will see that another factor the influences activity in redox is the stability of ions in aqueous solution. Lithium cation is a small ion; water molecules bind very strongly to the ion because the electrons get relatively close to lithium's nucleus. That strong binding stabilizes this ion especially, tipping the malance of the reaction more strongly towards oxidation of lithium. The larger alkali metal ions are not nearly as stabilized by water ligands in aqueous solution, so the balance of their reactions does not tilt as strongly towards aqueous ions.

Exercise 1.5.1:

Li^+/Li: $E^0 = -3.04V$; $\Delta H_{vap} = 147\frac{kJ}{mol}$; $IE = 520\frac{kJ}{mol}$; $\Delta H_h = -520\frac{kJ}{mol}$

Na^+/Na: $E^0 = -2.71V$; $\Delta H_{vap} = 97\frac{kJ}{mol}$; $IE = 495\frac{kJ}{mol}$; $\Delta H_h = -406\frac{kJ}{mol}$

K^+/K: $E^0 = -2.931V$; $\Delta H_{vap} = 77\frac{kJ}{mol}$; $IE = 419\frac{kJ}{mol}$; $\Delta H_h = -320\frac{kJ}{mol}$

Potassium should be the easiest of the three to oxidize. It is easier to oxidize than sodium. However, lithium's high heat of hydration reverses the trend and tips the balance of reaction in favor of ion formation.

Exercise 1.5.2:

Cu^{2+}/Cu: $E^0 = +0.340V$; $\Delta H_{vap} = 300\frac{kJ}{mol}$; $IE = 745\frac{kJ}{mol} \& 1958\frac{kJ}{mol}$; $\Delta H_h = -2099\frac{kJ}{mol}$

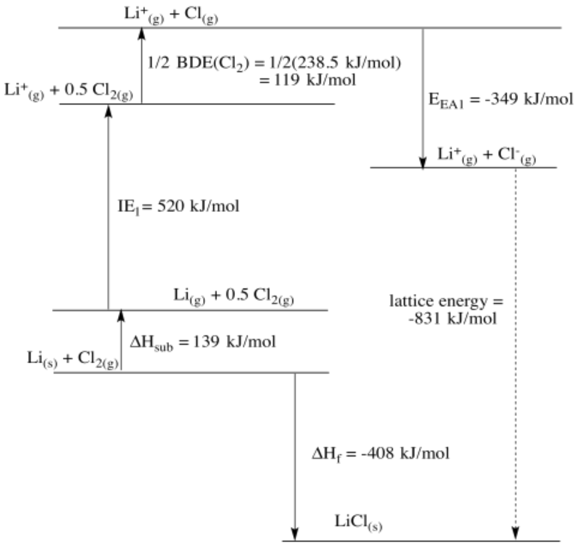
Ni^{2+}/Ni: $E^0 = -0.25V$; $\Delta H_{vap} = 377\frac{kJ}{mol}$; $IE = 737\frac{kJ}{mol} \& 1753\frac{kJ}{mol}$; $\Delta H_h = -2096\frac{kJ}{mol}$

Zn^{2+}/Zn: $E^0 = -0.7618V$; $\Delta H_{vap} = 123\frac{kJ}{mol}$; $IE = 906\frac{kJ}{mol} \& 1733\frac{kJ}{mol}$; $\Delta H_h = -2047\frac{kJ}{mol}$

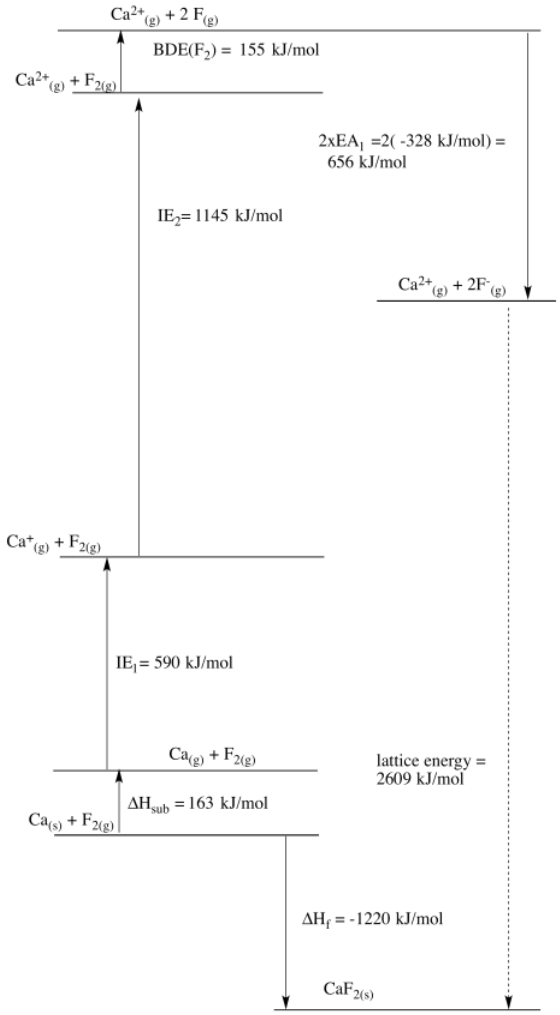
In this case, zinc may be considered the outlier. Copper should be easier to reduce than nickel based solely on electronegativity. However, zinc's very low heat of vaporization suggests that formation of the solid metal is less favored in that case, helping to tilt the balance toward zinc ion instead.

Exercise 1.5.3:

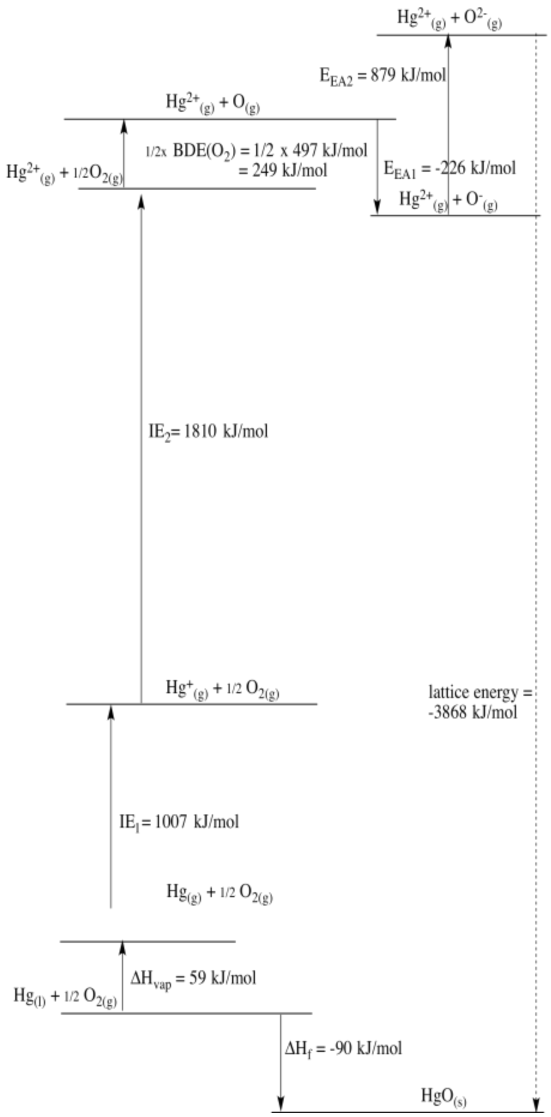
a)


$Li^+_{(g)} + Cl_{(g)}$
1/2 BDE(Cl_2) = 1/2(238.5 kJ/mol)
= 119 kJ/mol
$Li^+_{(g)} + 0.5\ Cl_{2(g)}$
E_{EA1} = -349 kJ/mol
$Li^+_{(g)} + Cl^-_{(g)}$
IE_1 = 520 kJ/mol
$Li_{(g)} + 0.5\ Cl_{2(g)}$
lattice energy =
-831 kJ/mol
ΔH_{sub} = 139 kJ/mol
$Li_{(s)} + Cl_{2(g)}$
ΔH_f = -408 kJ/mol
$LiCl_{(s)}$

b)

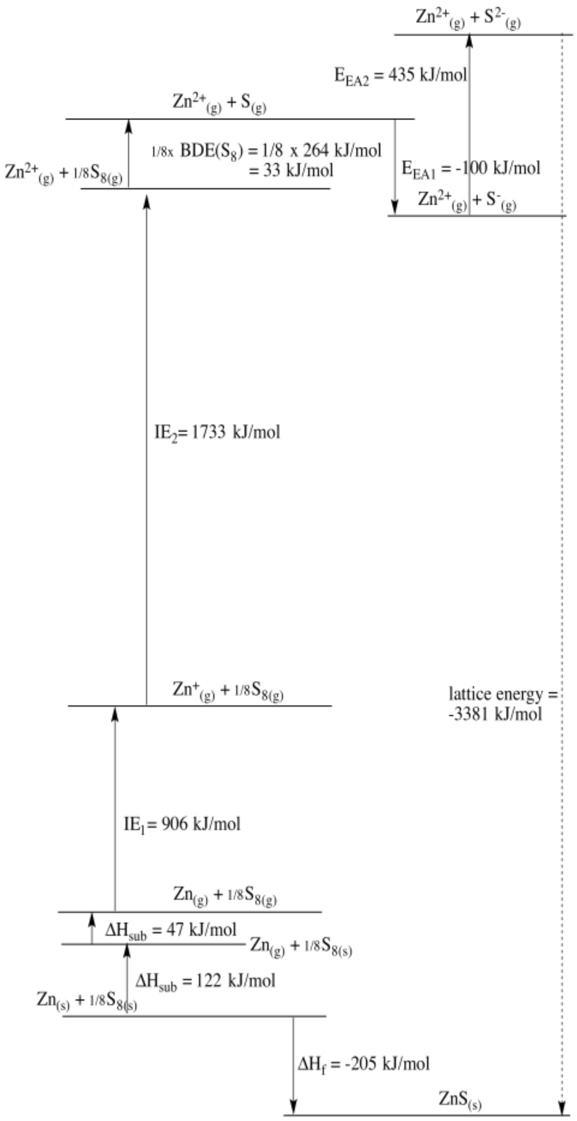

$Ca^{2+}_{(g)} + 2\ F_{(g)}$
BDE(F_2) = 155 kJ/mol
$Ca^{2+}_{(g)} + F_{2(g)}$
$2xEA_1$ =2(-328 kJ/mol) =
656 kJ/mol
IE_2= 1145 kJ/mol
$Ca^{2+}_{(g)} + 2F^-_{(g)}$
$Ca^+_{(g)} + F_{2(g)}$
IE_1= 590 kJ/mol
$Ca_{(g)} + F_{2(g)}$
lattice energy =
2609 kJ/mol
ΔH_{sub} = 163 kJ/mol
$Ca_{(s)} + F_{2(g)}$
ΔH_f = -1220 kJ/mol
$CaF_{2(s)}$

c)



$Hg^{2+}_{(g)} + O^{2-}_{(g)}$
E_{EA2} = 879 kJ/mol
$Hg^{2+}_{(g)} + O_{(g)}$
1/2x BDE(O_2) = 1/2 x 497 kJ/mol = 249 kJ/mol
$Hg^{2+}_{(g)} + 1/2 O_{2(g)}$
E_{EA1} = -226 kJ/mol
$Hg^{2+}_{(g)} + O^{-}_{(g)}$
IE_2= 1810 kJ/mol
$Hg^{+}_{(g)} + 1/2\ O_{2(g)}$
lattice energy = -3868 kJ/mol
IE_1 = 1007 kJ/mol
$Hg_{(g)} + 1/2\ O_{2(g)}$
ΔH_{vap} = 59 kJ/mol
$Hg_{(l)} + 1/2\ O_{2(g)}$
ΔH_f = -90 kJ/mol
$HgO_{(s)}$

d)



Exercise 1.6.1:

Both reduction potentials are very positive.

$$\mathrm{Ag^+} + \mathrm{e^-} \longrightarrow \mathrm{Ag(s)}\ E^0 = +0.796V$$

$$\mathrm{Au^+} + \mathrm{e^-} \longrightarrow \mathrm{Au(s)}\ E^0 = +1.83V$$

That means both metals are likely to be found in the reduced state.

Exercise 1.6.2:

$$\mathrm{SnO(s)} + 2\,\mathrm{H^+} + 2\,\mathrm{e^-} \longrightarrow \mathrm{Sn(s)} + \mathrm{H_2O}\ E^0 = -0.10V$$

$$\mathrm{CO(g)} + \mathrm{H_2O} \longrightarrow \mathrm{CO_2(g)} + 2\,\mathrm{H^+} + 2\,\mathrm{e^-}\ E^0 = -(-0.11V)$$

$$\mathrm{SnO(s)} + \mathrm{CO(g)} \longrightarrow \mathrm{Sn(s)} + \mathrm{CO_2(g)}\ \Delta E^0 = +0.01V$$

Exercise 1.6.3:

$$\mathrm{Fe_3O_4(s)} + 8\,\mathrm{H^+} + 8\,\mathrm{e^-} \longrightarrow 3\,\mathrm{Fe(s)} + 4\,\mathrm{H_2O}\ E^0 = +0.085V$$

$$\mathrm{CO(g)} + \mathrm{H_2O} \longrightarrow \mathrm{CO_2(g)} + 2\,\mathrm{H^+} + 2\,\mathrm{e^-}\ E^0 = -(-0.11V)$$

$$\mathrm{Fe_3O_4(s)} + 4\,\mathrm{CO(g)} \longrightarrow 3\,\mathrm{Fe(s)} + 4\,\mathrm{CO_2(g)}\ \Delta E^0 = 0.195V$$

Exercise 1.6.4:

$$\mathrm{Al^{3+}_{(aq)}} + 3\,\mathrm{e^-} \longrightarrow \mathrm{Al(s)}\ E^0 = -1.662V$$

$$\mathrm{CO(g)} + \mathrm{H_2O} \longrightarrow \mathrm{CO_2(g)} + 2\,\mathrm{H^+} + 2\,\mathrm{e^-}\ E^0 = -(-0.11V)$$

$$2\,\mathrm{Al^{3+}(aq)} + 3\,\mathrm{CO(g)} + 3\,\mathrm{H_2O} \longrightarrow 2\,\mathrm{Al(s)} + 3\,\mathrm{CO_2(g)}\ \Delta E^0 = -1.772V$$

Exercise 1.6.5:

$$\mathrm{Al^{3+}} + 3\,\mathrm{e^-} \longrightarrow \mathrm{Al(s)}\ E^0 = -1.662V$$

$$2\,\mathrm{O^{2-}} \longrightarrow \mathrm{O_2(g)} + 4\,\mathrm{e^-}\ E^0 = -(.40V,\ estimated)$$

$$4\,\mathrm{Al^{3+}(aq)} + 6\,\mathrm{O^{2-}(aq)} \longrightarrow 4\,\mathrm{Al(s)} + 3\,\mathrm{O_2(g)}\ \Delta E^0 = -2.062V$$

Even if the aluminum ions from the cryolite are reduced to $\mathrm{Al^0}$, they will be replenished by new aluminum ions from the bauxite ore.

Exercise 1.7.1:

$$\Delta G = -nFE^0_{cell}$$

$$\Delta G = -2 \times 96485 \frac{J}{V\ mol} \times 1.43V$$

$$\Delta G = -275947 \frac{J}{mol} = -276 \frac{kJ}{mol}$$

Exercise 1.7.2:

$$\Delta G = -nFE^0_{cell}$$

$$\Delta G = -2 \times 96485 \frac{J}{V\ mol} \times 1.3V$$

$$\Delta G = -250861 \frac{J}{mol} = -251 \frac{kJ}{mol}$$

Exercise 1.7.3:

$$\mathrm{Ag_2O(s)} + \mathrm{H_2O} + 2\,\mathrm{e^-} \longrightarrow 2\,\mathrm{Ag(s)} + 2\,\mathrm{OH^-(aq)} E^0 = +0.342V$$

$$\mathrm{Zn(s)} \longrightarrow \mathrm{Zn^{2+}(aq)} + 2\,\mathrm{e^-}\ E^0 = -(-0.762V)$$

$$\mathrm{Ag_2O(s)} + \mathrm{H_2O} + \mathrm{Zn(s)} \longrightarrow 2\,\mathrm{Ag(s)} + 2\,\mathrm{OH^-(aq)} + \mathrm{Zn^{2+}(aq)}\ \Delta E^0 = +1.104V$$

Exercise 1.7.4:

a) Charge on complex calculated as follows:

charge on metal: 3+

charge on ligand donors (4 neutral N, 2 anionic N donors): 2-

other charges on ligand (carboxylate arm): 1-

overall: 0

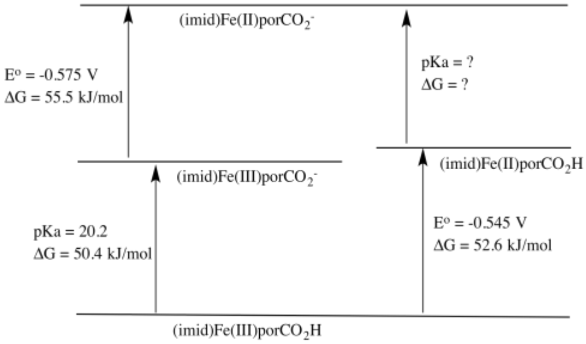
b) $\Delta GG = RTlogK = RT(-pK_a) = -8.314 \frac{J}{K\ mol} \times 300K \times (-20.2) = 50382 \frac{J}{mol} = 50.4 \frac{kJ}{mol}$

c) It is more difficult to add the electron to the more negatively charged anion, so the reduction potential is more negative in that case.

d) $\Delta G = -nFE^o = -1 \times 96485 \frac{J}{V\ mol} \times (-0.545V) = 52583 \frac{J}{mol} = 52.6 \frac{kJ}{mol}$

e) $\Delta G = -nFE^o = -1 \times 96485 \frac{J}{V\ mol} \times (-0.575V) = 55479 \frac{J}{mol} = 55.5 \frac{kJ}{mol}$

f)



$$\Delta G_{Fe(II)CO_2H/CO_2^-} = 50.4 + 55.5 - 52.6\frac{kJ}{mol} = 53.3\frac{kJ}{mol}$$

$$\Delta G = -RT logK_a$$

$$K_a = e^{(\frac{-\Delta G}{RT})} = e^{(\frac{-53300}{8.314J/Kmol \times 300K})} = e^{-21.4}$$

pKa = 21.4

g) The Fe(III) complex is easier to deprotonate because it yields an anionic species, whereas the Fe(II) complex yields a dianionic species. The greater charge buildup in the latter would cost more energy.

Exercise 1.8.1:

a) $Cu \longrightarrow Cu_2O$ $MoO_2 \longrightarrow Mo$

$$2\,Cu \longrightarrow Cu_2O\)\(MoO_2 \longrightarrow Mo$$

$$2\,Cu + H_2O \longrightarrow Cu_2O\)\(MoO_2 \longrightarrow Mo + 2\,H_2O$$

$$2\,Cu + H_2O \longrightarrow Cu_2O + 2\,H^+\)\(4\,H^+ + MoO_2 \longrightarrow Mo + 2\,H_2O$$

$$2\,Cu + H_2O \longrightarrow Cu_2O + 2\,H^+ + 2\,e^-\)\(4\,e^- + 4\,H^+ + MoO_2 \longrightarrow Mo + 2\,H_2O$$

$$2 \times (2\,Cu + H_2O \longrightarrow Cu_2O + 2\,H^+ + 2\,e^-)\)\(4\,e^- + 4\,H^+ + MoO_2 \longrightarrow Mo + 2\,H_2O$$

adding:

$$4\,Cu + 2\,H_2O \longrightarrow 2\,Cu_2O + 4\,H^+ + 4\,e^-$$

$$4\,e^- + 4\,H^+ + MoO_2 \longrightarrow Mo + 2\,H_2O$$

equals

$$4\,Cu + MoO_2 \longrightarrow 2\,Cu_2O + Mo$$

b) $NH_2OH \longrightarrow N_2$ $Ag_2O \longrightarrow Ag$

$$2\,NH_2OH \longrightarrow N_2\)\(Ag_2O \longrightarrow 2\,Ag$$

$$2\,NH_2OH \longrightarrow N_2 + 2\,H_2O\)\(Ag_2O \longrightarrow 2\,Ag + H_2O$$

$$2\,NH_2OH \longrightarrow N_2 + 2\,H_2O + 2\,H^+\)\(2\,H^+ + Ag_2O \longrightarrow 2\,Ag + H_2O$$

$$2\,NH_2OH \longrightarrow N_2 + 2\,H_2O + 2\,H^+ + 2\,e^-\)\(2\,H^+ + Ag_2O + 2\,e^- \longrightarrow 2\,Ag + H_2O$$

adding:

$$2\,NH_2OH \longrightarrow N_2 + 2\,H_2O + 2\,H^+ + 2\,e^-$$

$$2\,H^+ + Ag_2O + 2\,e^- \longrightarrow 2\,Ag + H_2O$$

equals

$$2\,NH_2OH + Ag_2O \longrightarrow N_2 + 2\,Ag + 3\,H_2O$$

c) $Fe_3O_4 \longrightarrow Fe\ CO \longrightarrow CO_2$

$$Fe_3O_4 \longrightarrow 3\,Fe\backslash)\backslash(CO \longrightarrow CO_2$$

$$Fe_3O_4 \longrightarrow 3\,Fe + 4\,H_2O\backslash)\backslash(H_2O + CO \longrightarrow CO_2$$

$$8\,H^+ + Fe_3O_4 \longrightarrow 3\,Fe + 4\,H_2O\backslash)\backslash(H_2O + CO \longrightarrow CO_2 + 2\,H^+$$

$$8\,e^- + 8\,H^+ + Fe_3O_4 \longrightarrow 3\,Fe + 4\,H_2O\backslash)\backslash(H_2O + CO \longrightarrow CO_2 + 2\,H^+ + 2\,e^-$$

$$8\,e^- + 8\,H^+ + Fe_3O_4 \longrightarrow 3\,Fe + 4\,H_2O\backslash)\backslash(4 \times (H_2O + CO \longrightarrow CO_2 + 2\,H^+ + 2\,e^-)$$

adding:

$$8\,e^- + 8\,H^+ + Fe_3O_4 \longrightarrow 3\,Fe + 4\,H_2O$$

$$4\,H_2O + 4\,CO \longrightarrow 4\,CO_2 + 8\,H^+ + 8\,e^-$$

equals

$$Fe_3O_4 + 4\,CO \longrightarrow 3\,Fe + 4\,CO_2$$

d) $I_2 \longrightarrow IO_3^-\ \ MnO_4^- \longrightarrow MnO_2$

$$I_2 \longrightarrow 2\,IO_3^-\backslash)\backslash(MnO_4^- \longrightarrow MnO_2$$

$$6\,H_2O + I_2 \longrightarrow 2\,IO_3^-\backslash)\backslash(MnO_4^- \longrightarrow MnO_2 + 2\,H_2O$$

$$6\,H_2O + I_2 \longrightarrow 2\,IO_3^- + 12\,H^+\backslash)\backslash(4\,H^+ + MnO_4^- \longrightarrow MnO_2 + 2\,H_2O$$

$$6\,H_2O + I_2 \longrightarrow 2\,IO_3^- + 12\,H^+ + 10\,e^-\backslash)\backslash(3\,e^- + 4\,H^+ + MnO_4^- \longrightarrow MnO_2 + 2\,H_2O$$

$$3 \times (6\,H_2O + I_2 \longrightarrow 2\,IO_3^- + 12\,H^+ + 10\,e^-)\backslash)\backslash(10 \times (3\,e^- + 4\,H^+ + MnO_4^- \longrightarrow MnO_2 + 2\,H_2O)$$

adding

$$18\,H_2O + 3\,I_2 \longrightarrow 6\,IO_3^- + 36\,H^+ + 30\,e^-$$

$$30\,e^- + 40\,H^+ + 10\,MnO_4^- \longrightarrow 10\,MnO_2 + 20\,H_2O$$

equals

$$3\,I_2 + 4\,H^+ + 10\,MnO_4^- \longrightarrow 6\,IO_3^- + 10\,MnO_2 + 2\,H_2O$$

e) $H_3Mo_7O_{24} \longrightarrow Mo\ \ S_2O_3^{2-} \longrightarrow SO_3^{2-}$

$$H_3Mo_7O_{24} \longrightarrow 7\,Mo\backslash)\backslash(S_2Oe^{2-} \longrightarrow 2\,SO_3^{2-}$$

$$H_3Mo_7O_{24} \longrightarrow 7\,Mo + 24\,H_2O\backslash)\backslash(3\,H_2O + S_2O_3^{2-} \longrightarrow 2\,So_3^{2-}$$

$$45\,H^+ + H_3Mo_7O_{24} \longrightarrow 7\,MO + 24\,H_2O\backslash)\backslash(3\,H_2O + S_2O_3^{2-} \longrightarrow 2\,SO_3^{2-} + 6\,H^+$$

$$45\,e^- + 45\,H^+ + H_3Mo_7O_{24} \longrightarrow 7\,Mo + 24\,H_2O\backslash)\backslash(3\,H_2O + S_2O_3^{2-} \longrightarrow 2\,SO_3^{2-} + 6\,H^+ + 4\,e^-$$

$$4 \times (45\,e^- + 21\,H^+ + H_3Mo_7O_{24} \longrightarrow 7\,Mo + 24\,H_2O)\backslash)\backslash(45 \times (3\,H_2O + S_2O_3^{2-} \longrightarrow 2\,SO_3^{2-} + 6\,H^+ + 4\,e^-)$$

adding:

$$180\,e^- + 180\,H^+ + 4\,H_3Mo_7O_{24} \longrightarrow 28\,Mo + 96\,H_2O$$

$$135\,H_2O + 45\,S_2O_3^{2-} \longrightarrow 90\,SO_3^{2-} + 270\,H^+ + 180\,e^-$$

equals

$$4\,H_3Mo_7O_{24} + 45\,S_2O_3^{2-} + 39\,H_2O \longrightarrow 28\,Mo + 90\,SO_3^{2-} + 90\,H^+$$

checking:

$$28\,\mathrm{Mo} \longrightarrow 28\,\mathrm{Mo};\ 90\,\mathrm{S} \longrightarrow 90\,\mathrm{S};\ 90\,\mathrm{H} \longrightarrow 90\,\mathrm{H};\ 270\,\mathrm{O} \longrightarrow 270\,\mathrm{O}$$

Exercise 1.8.2:

a) $\mathrm{Fe(OH)_2} \longrightarrow \mathrm{Fe_2O_3}$ $\mathrm{N_2H_4} \longrightarrow \mathrm{NH_4^+}$

$$2\,\mathrm{Fe(OH)_2} \longrightarrow \mathrm{Fe_2O_3}{\color{red}\backslash)\backslash(}\mathrm{N_2H_4} \longrightarrow 2\,\mathrm{NH_4^+}$$

$$2\,\mathrm{Fe(OH)_2} \longrightarrow \mathrm{Fe_2O_3} + \mathrm{H_2O}{\color{red}\backslash)\backslash(}\mathrm{N_2H_4} \longrightarrow 2\,\mathrm{NH_4^+}$$

$$2\,\mathrm{Fe(OH)_2} \longrightarrow \mathrm{Fe_2O_3} + \mathrm{H_2O} + 2\,\mathrm{H^+}{\color{red}\backslash)\backslash(}4\,\mathrm{H^+} + \mathrm{N_2H_4} \longrightarrow 2\,\mathrm{NH_4^+}$$

$$2\,\mathrm{Fe(OH)_2} \longrightarrow \mathrm{Fe_2O_3} + \mathrm{H_2O} + 2\,\mathrm{H^+} + 2\,\mathrm{e^-}{\color{red}\backslash)\backslash(}2\,\mathrm{e^-} + 4\,\mathrm{H^+} + \mathrm{N_2H_4} \longrightarrow 2\,\mathrm{NH_4^+}$$

adding:

$$2\,\mathrm{Fe(OH)_2} \longrightarrow \mathrm{Fe_2O_3} + \mathrm{H_2O} + 2\,\mathrm{H^+} + 2\,\mathrm{e^-}$$

$$2\,\mathrm{e^-} + 4\,\mathrm{H^+} + \mathrm{N_2H_4} \longrightarrow 2\,\mathrm{NH_4^+}$$

equals:

$$2\,\mathrm{Fe(OH)_2} + 2\,\mathrm{H^+} + \mathrm{N_2H_4} \longrightarrow \mathrm{Fe_2O_3} + \mathrm{H_2O} + 2\,\mathrm{NH_4^+}$$

in basic conditions:

$$2\,\mathrm{Fe(OH)_2} + 2\,\mathrm{H^+} + 2\,\mathrm{OH^-} + \mathrm{N_2H_4} \longrightarrow \mathrm{Fe_2O_3} + \mathrm{H_2O} + 2\,\mathrm{NH_4^+} + 2\,\mathrm{OH^-}$$

$$2\,\mathrm{Fe(OH)_2} + 2\,\mathrm{H_2O} + \mathrm{N_2H_4} \longrightarrow \mathrm{Fe_2O_3} + \mathrm{H_2O} + 2\,\mathrm{NH_4^+} + 2\,\mathrm{OH^-}$$

$$2\,\mathrm{Fe(OH)_2} + \mathrm{H_2O} + \mathrm{N_2H_4} \longrightarrow \mathrm{Fe_2O_3} + 2\,\mathrm{NH_4^+} + 2\,\mathrm{OH^-}$$

b) $\mathrm{MnO_4^-} \longrightarrow \mathrm{HMnO_4^-}$ $\mathrm{V^{3+}} \longrightarrow \mathrm{VO^{2+}}$

$$\mathrm{MnO_4^-} \longrightarrow \mathrm{HMnO_4^-}{\color{red}\backslash)\backslash(}\mathrm{V^{3+}} + \mathrm{H_2O} \longrightarrow \mathrm{VO^{2+}}$$

$$\mathrm{H^+} + \mathrm{MnO_4^-} \longrightarrow \mathrm{HMnO_4^-}{\color{red}\backslash)\backslash(}\mathrm{V^{3+}} + \mathrm{H_2O} \longrightarrow \mathrm{VO^{2+}} + 2\,\mathrm{H^+}$$

$$\mathrm{e^-} + \mathrm{H^+} + \mathrm{MnO_4^-} \longrightarrow \mathrm{HMnO_4^-}{\color{red}\backslash)\backslash(}\mathrm{V^{3+}} + \mathrm{H_2O} \longrightarrow \mathrm{VO^{2+}} + 2\,\mathrm{H^+} + \mathrm{e^-}$$

adding:

$$\mathrm{e^-} + \mathrm{H^+} + \mathrm{MnO_4^-} \longrightarrow \mathrm{HMnO_4^-}$$

$$\mathrm{V^{3+}} + \mathrm{H_2O} \longrightarrow \mathrm{VO^{2+}} + 2\,\mathrm{H^+} + \mathrm{e^-}$$

equals:

$$\mathrm{MnO_4^-} + \mathrm{V^{3+}} + \mathrm{H_2O} \longrightarrow \mathrm{HmnO_4^-} + \mathrm{VO^{2+}} + \mathrm{H^+}$$

under basic conditions:

$$\mathrm{MnO_4^-} + \mathrm{V^{3+}} + \mathrm{H_2O} + \mathrm{OH^-} \longrightarrow \mathrm{HMnO_4^-} + \mathrm{VO^{2+}} + \mathrm{H^+} + \mathrm{OH^-}$$

$$\mathrm{MnO_4^-} + \mathrm{V^{3+}} + \mathrm{H_2OOH^-} \longrightarrow \mathrm{HMNO_4^-} + \mathrm{VO^{2+}} + \mathrm{H_2O}$$

$$\mathrm{MnO_4^-} + \mathrm{V^{3+}} + \mathrm{OH^-} \longrightarrow \mathrm{HMnO_4^-} + \mathrm{VO^{2+}}$$

Exercise 1.9.1:

The bonds to iron would contract because the increased charge on the iron would attract the ligand donor electrons more strongly. The bonds to copper would lengthen because of the lower charge on the copper.

Exercise 1.9.2:

a. Most likely there are repulsive forces between ligands if the bonds get too short.

b. Insufficient overlap between metal and ligand orbitals would weaken the bond and raise the energy.
c. The range of possible bond lengths gets broader as energy is increased. The bond has more latitude, with both longer and shorter bonds allowed at higher energy.

Exercise 1.9.6:

The reactants and products are very similar in this case. However, the Fe(III) complex has shorter bonds than the Fe(II) complex because of greater electrostatic interaction between the metal ion and the ligands. These changes in bond length needed in order to get ready to change from Fe(III) to Fe(II) (or the reverse) pose a major barrier to the reaction.

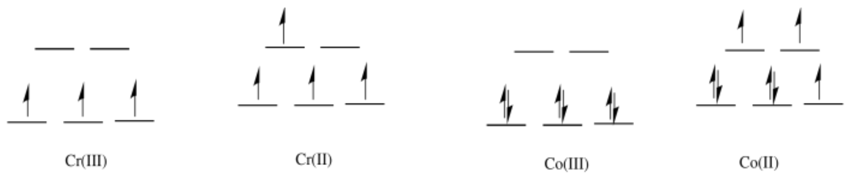
Exercise 1.9.7:

a. The drawing is an oversimplification, but in general the water molecules are shown reorienting after the electron transfer because of ion-dipole interactions. In this case, the waters are shown orienting to present their negative ends to the more positive iron atom after the electron transfer. In reality, in a protein there are lots of other charges (including charges on the ligand) that may take part in additional ion-dipole interactions.
b. Because electron transfer is so fast, atomic and molecular reorganisations are actually thought to happen before the electron transfer. The water molecules would happen to shift into a position that would provide the greatest possible stabilisation for the ions and then the electron would be transferred. A less polar solvent than water would be less able to stabilize ions and the electron would be slower to transfer as a result.

Exercise 1.10.1:

a. octahedral
b. In the first row, 2^+ complexes are almost always high spin. However, 3^+ complexes are sometimes low spin.

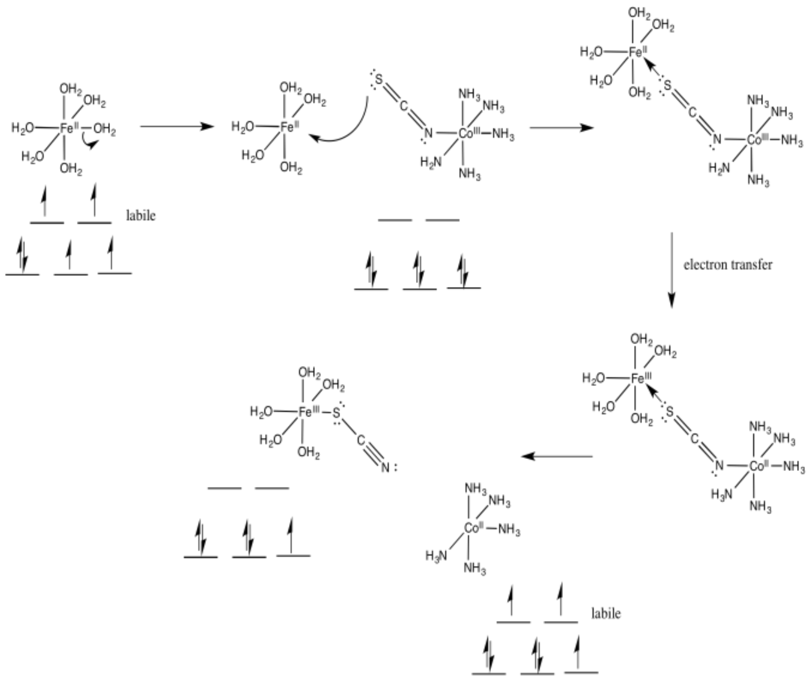
c)



d) The Co(II) complex is high spin and labile. The ligands are easily replaced by water.

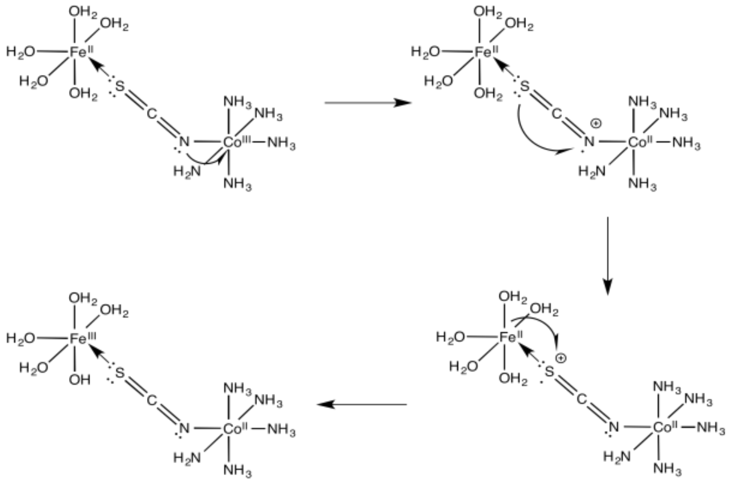
e) The Cr(III) complex is only d^3; it is inert.

Exercise 1.10.3



Exercise 1.10.4:

a)



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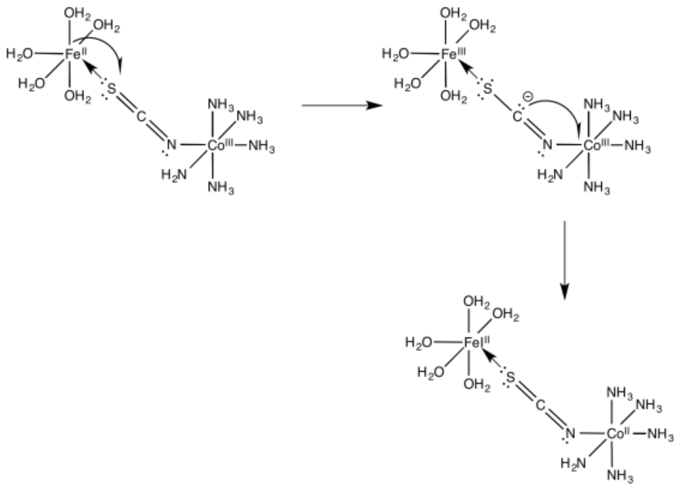


Exercise 1.11.1:

The compound undergoes a two-electron oxidation. The oxidized species then undergoes a two-electron reduction.

Exercise 1.12.2:

a) CH_2CHCH_3

C-H bonds	6-
C-X bonds	0
Oxidation Level	6-

$CH_3CH_2CH_3$

C-H bonds	8-
C-X bonds	0
Oxidation Level	8-

Propane results from a two-electron reduction of propene.

b) CH_3CH_2CHO

C-H bonds	6-
C-X bonds	2+
Oxidation Level	4-

$CH_3CH_2CH_2OH$

C-H bonds	7-
C-X bonds	1_
Oxidation Level	6-

Propanol results from a two-electron reduction of propanal.

c) $CH_3CH(OH)CH_2CH_2OH$

C-H bonds	8-
C-X bonds	2+
Oxidation Level	6-

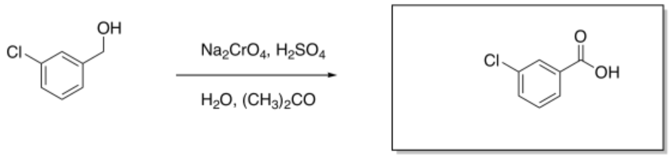
CH_3COCH_2CHO

C-H bonds	6-
C-X bonds	4+
Oxidation Level	2-

3-oxobutanal results from a four-electron oxidation of 1,3-butanediol.

Exercise 1.12.3:

a)



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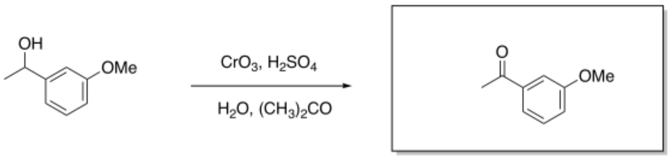

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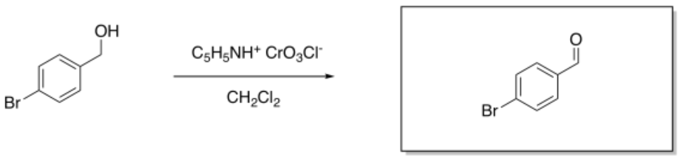
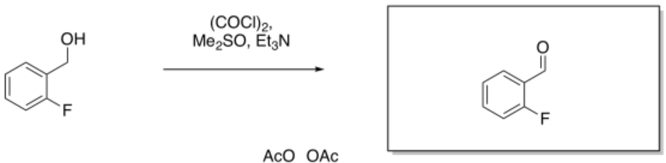
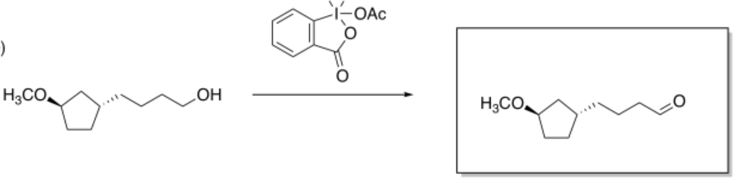


d)



e)



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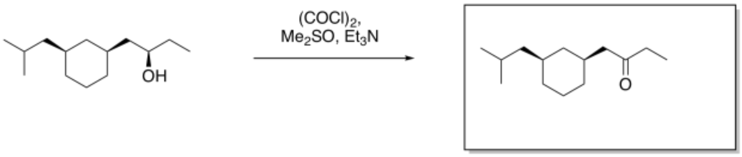
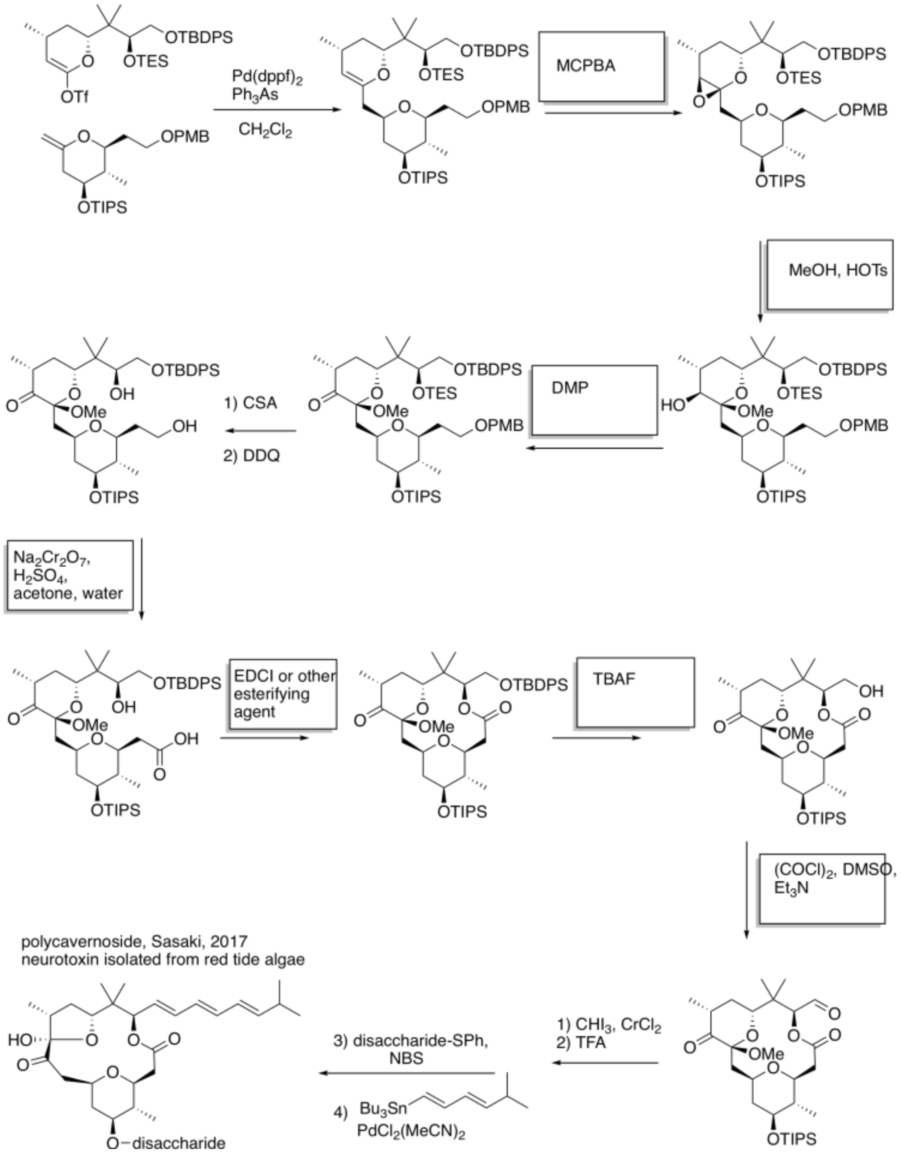


Exercise 1.12.4:


OTBDPS
OTES
OTf
OPMB
OTIPS
Pd(dppf)$_2$
Ph$_3$As
CH$_2$Cl$_2$
MCPBA
MeOH, HOTs
HO
OMe
DMP
1) CSA
2) DDQ
OH
Na$_2$Cr$_2$O$_7$,
H$_2$SO$_4$,
acetone, water
EDCI or other esterifying agent
TBAF
(COCl)$_2$, DMSO,
Et$_3$N
1) CHI$_3$, CrCl$_2$
2) TFA
3) disaccharide-SPh,
NBS
4) Bu$_3$Sn
PdCl$_2$(MeCN)$_2$
polycavernoside, Sasaki, 2017
neurotoxin isolated from red tide algae
O−disaccharide

CHAPTER OVERVIEW

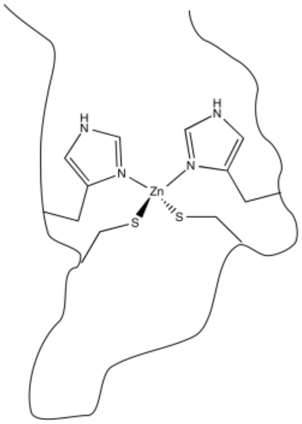
2: Reduction Potentials of Metal Ions in Biology

2.1: Introduction

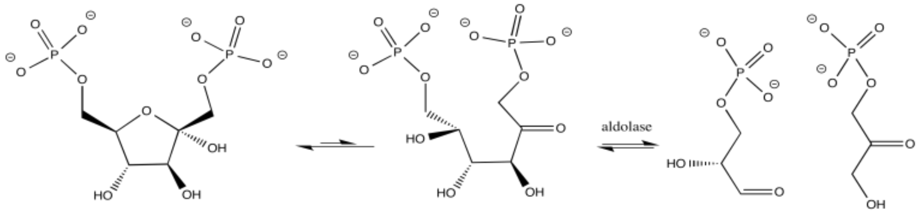
Metal ions play many important roles in biology. Sometimes these roles are structural: a metal ion may simply coordinate to an atom in a biomolecule that acts as a ligand, holding the biomolecule in a particular shape. Zinc finger proteins are a widely studied example. In these cases, a zinc ion binds to the protein in such a way the the protein is held in a particular shape. Generally, this shape serves an important purpose, such as being able to more tightly bind to a DNA molecule or even a small molecule.

- Metal ions can hold proteins and other biomolecules in particular shapes.

In order to bind to the zinc ion, the protein must possess atoms that are able to act as ligands. Lots of atoms in proteins can potentially do so, including, fir instance, the carbonyl oxygen along the protein backbone. However, it is very common for specific amino acid residues to act as ligands. These residues have to be located at just the right position along the protein chain. In the case of zinc finger proteins, one common set of ligands is a pair of histidine residues and a pair of cysteine residues.



In other cases, the metal ion may play the role of a Lewis acid. A substrate that binds to the metal is electrophilically activated; it becomes more able to accept electron donation from a nucleophile. Examples include alcohol dehydrogenases and aldolases, which often contain zinc ions that coordinate carbonyls in the substrate. The activated carbonyl compound undergoes reaction more easily.

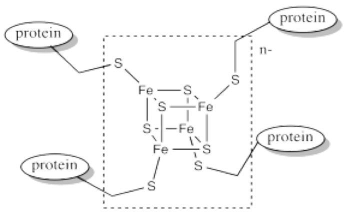


- Metal ions can act as Lewis acid catalysts.

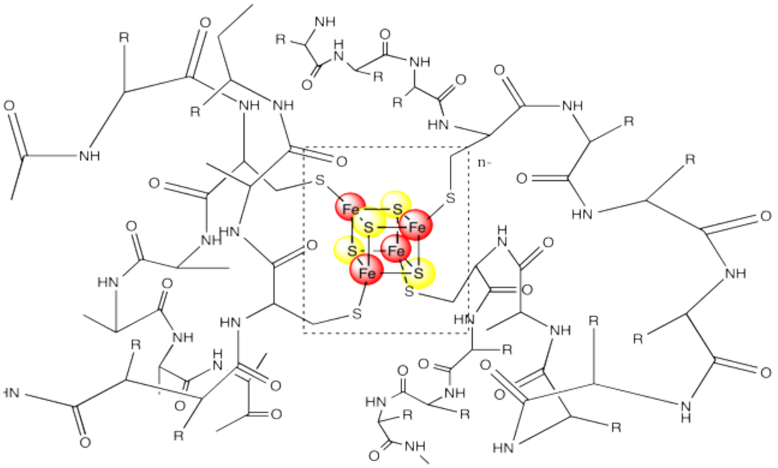
In many cases, metal ions are redox-active. They may donate or accept an electron from a substrate. Alternatively, they may take part in an electron relay, passing electrons from one to another in order to accomplish electron transport over a long distance.

- Metal ions can transfer electrons, one at a time, as needed.

Ferredoxins are examples of such redox-active sites in biology. Ferredoxins often have a cubic core structure. The corners of the cubes are composed of alternating iron and sulfur atoms. Ferredoxins and related structures are often called iron sulfur clusters.



Notice that the iron atoms are held in place via coordination to a surrounding protein. In this case, the irons atoms are bound to cysteine residues. The metal centre is often found buried inside the protein, so that it is completely surrounded by the other amino acid residues. These other resdiues can have a significant impact on the properties of the metal centre, even though they are not directly bound to any metal.



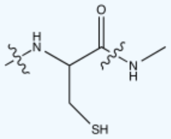
? Exercise 2.1.1

The following amino acid residues are the most commonly observed ligands for metal ions in biology. Draw each one at pH 7.

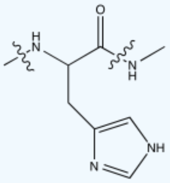
a) cysteine b) histidine c) aspartic acid

Answer

a)



b)



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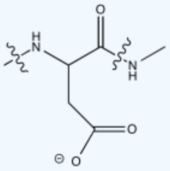


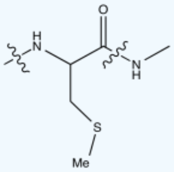
? Exercise 2.1.2

Although the following amino acid residues are not as commonly observed as ligands for metal ions, they are sometimes found in that role. Draw each one at pH 7.

a) methionine b) tyrosine c) glutamic acid d) serine e) threonine

Answer

a)



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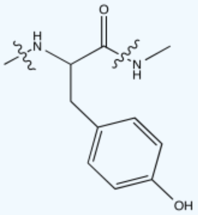
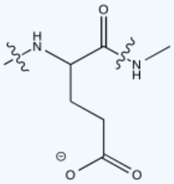
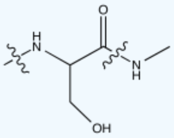


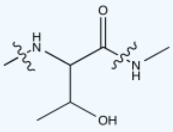
c)



d)



e)

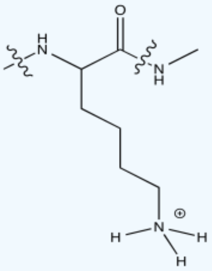


? Exercise 2.1.3

Lysine is not generally observed to coordinate to metal ions in biology (although there may be exceptions). Explain why, using its structure at pH 7.

Answer

At neutral pH, lysine would normally be protonated. It would not have a lone pair on the nitrogen to coordinate a metal ion.

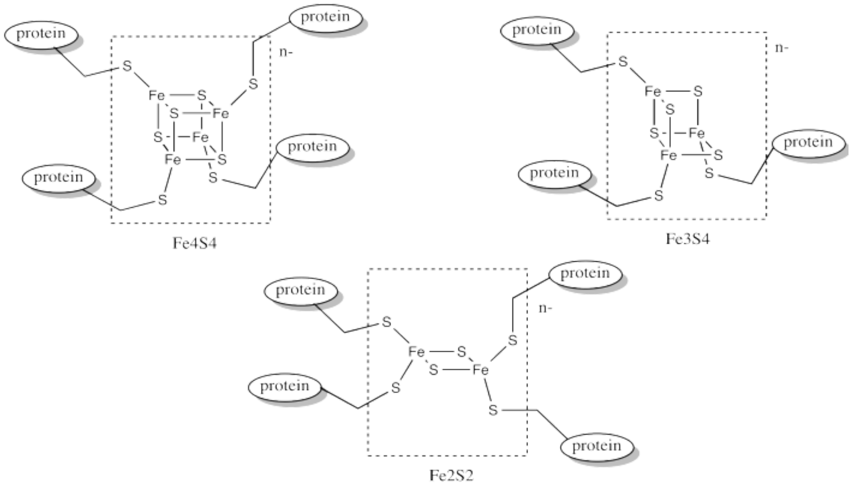


The redox potential of the metal ion is vitally important. Reduction potentials must be matched so that the electron transfer will occur easily. The electron transfer may be from the metal to the substrate; in that case, the reduction potential of the substrate must be greater (more positive) than that of the metal ion. Transfer of electron from the metal to the substrate will be favored.

Of course, if an electron is transferred from the substrate to the metal ion, the opposite would have to be true. The reduction potential of the metal ion would have to be a little more positive than that of the substrate.

In an electron relay, we would need a series of different metal ions, each one with a slightly more positive reduction potential than the last. That way, electrons would keep getting passed from one carrier to the next, and they would travel in the right direction, rather than getting scatterred around randomly.

In order to maintain subtle differences between reduction potentials of metal centres, Nature has developed a wide array of these complexes. Often, the differences between these species involve subtle variations in the coordination environment. For example, a wide variety of iron sulfur clusters are known in biology; a few of them are shown below.



- Subtle differences in metalloprotein structure can lead to subtle differences in redox properties.

There is a more subtle aspect to these reduction potentials, however. In most cases, there shouldn't be a very large difference between reduction potentials of one species and another.

Why does it matter? Doesn't it seem like a big difference in reduction potentials means the electron transfer is more exothermic? Shouldn't a more exothermic reaction happen even more easily? Isn't that what we want?

Not, really, and there are a couple of reasons why. One reason involves thermodynamic efficiency and heat loss. If a reaction is too exothermic, the energy given off by the reaction is lost as heat energy to the surroundings. Because organisms spend a lot of their time trying to gather energy in order to live, wasting energy isn't a good idea.

The other reason involves the catalytic or cyclic nature of many systems in biology. We can and do re-make lots of chemical species needed for biological activity on a regular basis, but if we can re-use things we don't have to spend as much of our energy re-making and using up reactants over and over again. Lots of species are simply reset to their original state so that they can do their job once more. The easier it is to reset that species, the more often it can keep participating in a cycle, doing the same job over and over again.

In terms of electron transfer, we would like the reduction potential of an electron acceptor to be positive enough so that it easily accepts an electron from its donor. However, we want it to be able to pass its electron along, and get ready to accept another one. That means its reduction potential can't be too positive. It has to be just right.

For reasons like these ones, reduction potentials in biology have to be finely regulated. This problem is as enormously complicated as it is important. In this section, we are going to take a look at a few of the factors that can come into play in modulating reduction potentials in biology. We are certainly not going to gain a great deal of predictive ability, because too many factors can be involved and it will be hard to decide which factor is most important. However, we will be able to understand some of the ways in which different situations influence reduction potentials.

2.2: The Effect of Charge (Local Effects)

Electron transfer reactions result in changes in charge. Issues of charge stability are therefore crucial in determining whether or not a reaction is favored. If the donation of an electron will result in increasing negative charge on a complex, then donation may be inhibited. That's because the buildup of charge is energetically unfavorable. On the other hand, if donation of an electron would result in decrease of charge on the complex, then donation may occur more easily.

- Local charge (including the metal atom and its ligands) can influence the reduction potential.
- Often, the more positively charged the central coordination complex in the metalloprotein (or the less negatively charged), the higher its reduction potential.

Remember: this is just one of several factors that could influence the behaviour of a coordination complex. Strict rules do not apply here.

? Exercise 2.2.1

Calculate the overall charges on the following metal complexes, given the indicated oxidation state on the metal.

a. $Ag^{I}(NH_3)_2$
b. $Fe^{II}(H_2O)_6$
c. $Cu^{II}(NH_3)_4$
d. $Ag^{I}Cl_2$
e. $Co^{III}(NH_3)_4Cl_2$
f. $Hg^{II}I_4$
g. $Fe^{II}(CN)_6$
h. $Co^{II}(SCN)_4$
i. $Cr^{VI}O_4$
j. $Co^{III}(NO_2)_3(NH_3)_3$
k. $Co^{III}(NH_2CH_2CH_2NH_2)_2Br_2$
l. $Re^{I}(CH_3)(CO)_5$

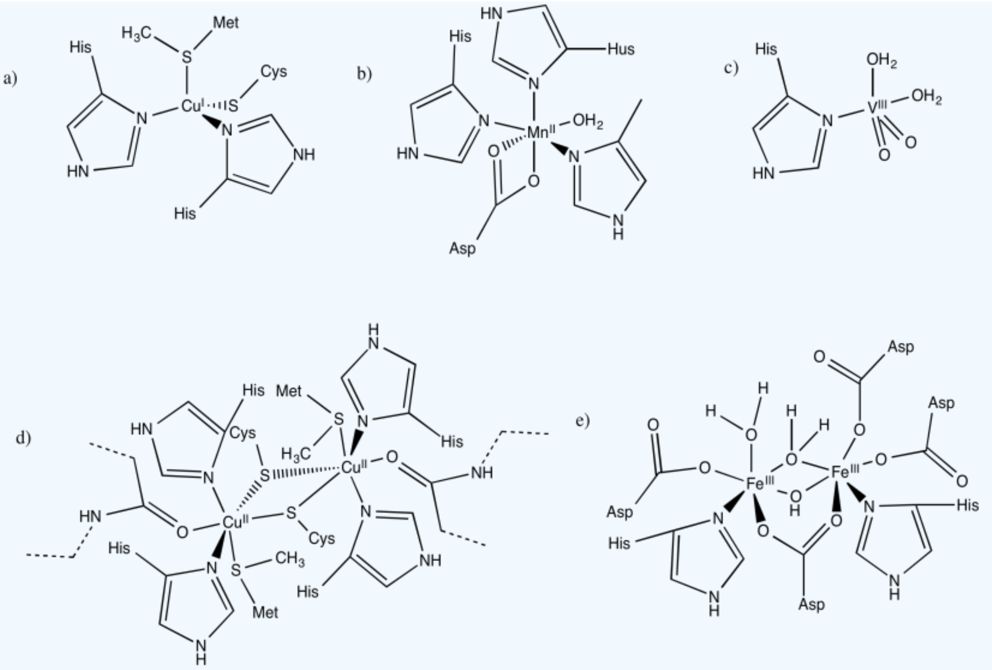
? Exercise 2.2.2

Given the overall charges on the following coordination complexes, calculate the oxidation state of the metal.

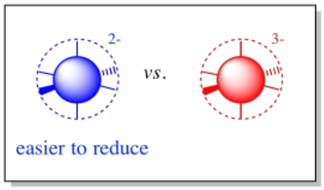
a. $[CuCl_4]^{2-}$
b. $[Pt(NH_3)_4]^{2+}$
c. $[Au(CN)_2]^{-}$
d. $[CrF_4]^{2+}$
e. $[PtCl_6]^{2-}$
f. $[FeCl(CN)_5]^{3-}$
g. $[Pt(NH_2CH_2CH_2NH_2)_2Cl_2]^{2+}$
h. $[Cu(CF_3)_4]^{-}$
i. $[Ni(C_2O_4)_2(H_2O)_2]^{2-}$
j. $[CoCl(NO_2)(NH_3)_4]^{+}$
k. $[Co(NH_3)_4SO_4]^{-}$
l. $[Ag(S_2O_3)_2]^{3-}$

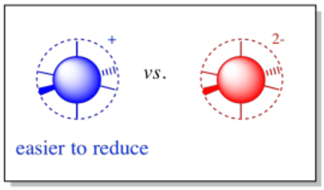
? Exercise 2.2.3

Indicate the charges on the central complex in the following biological sites. (The entire protein would have a charge, depending on amino acid residues; we are just interested in the local charge that we can see here.)

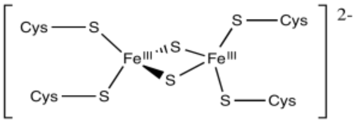


Upon reduction, the complex will become more negatively charged, because it is accepting an electron. Alternatively, it may become less positively charged. In any case, the electron will be more easily accepted into a complex with a lower negative charge to begin with. Build up of charge costs energy.



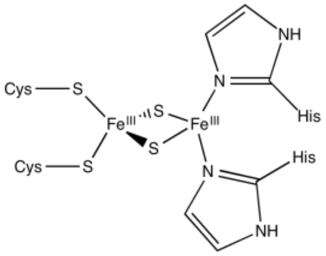


A good example of this charge effect can be seen among iron-sulfur clusters. Iron-sulfur clusters frequently participate in electron transfer pathways in biology. The range of reduction potentials among these proteins is quite wide, ranging from -700 to +400 mV.



Typically these clusters contain multiple iron and sulfur atoms and are held in place by cysteine residues from a surrounding protein. The sulfur atoms are present as sulfide anions (S^{2-}); there are usually two or four of them in the cluster. The cysteine residues are typically deprotonated, so they act as thiolate anions (RS^-). The number of cysteine residues attached to the cluster varies. Usually there is a sufficient number to give the iron a tetrahedral geometry. The iron atoms can be present as Fe(II) or Fe(III), so charges can vary. There might be two, three or four iron ions in the cluster. The most common combinations are two iron and two sulfur atoms or else four iron and four sulfur atoms.

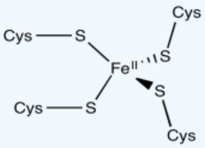
Rieske iron centres are "high-potential iron proteins", meaning they have especially positive reduction potentials. They have histidines in place of cysteines in some positions. As a result, the central coordination complex is more positively charged, or at least less negatively charged. Because the central complex is less negatively charged, it can more easily accept an electron than other iron sulfur proteins.



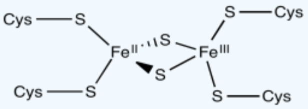
Exercise 2.2.4

Calculate the charges on the following iron-sulfur complexes.

a)



b)



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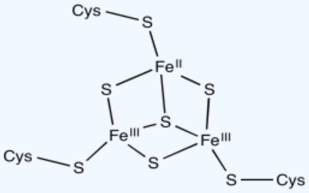

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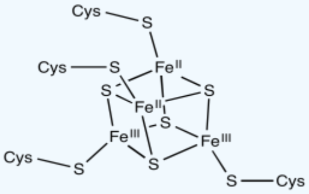

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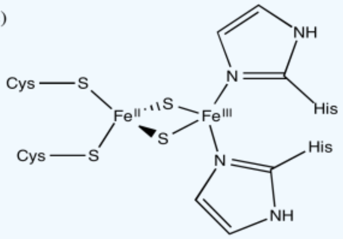

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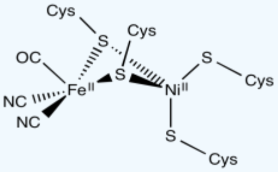
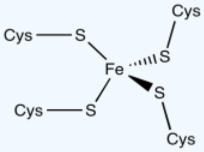


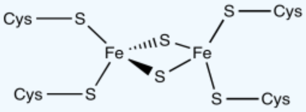
Exercise 2.2.5

The following iron complexes have multiple possible oxidation states. What is the range of possible charges on each complex, assuming each iron atom could be Fe(II) or Fe(III)?

a)



b)



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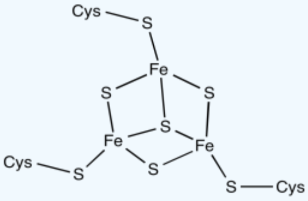

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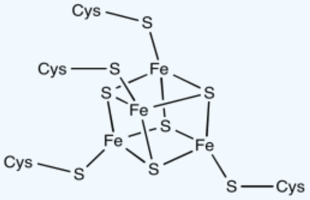


Exercise 2.2.7

In order to build a better understanding of the properties of metalloproteins, the Pecoraro lab at University of Michigan has studied the binding of synthetic peptides to copper (*J. Am. Chem. Soc.* **2013**, *135*, 18096-18107.) Some of the synthetic peptides are shown below, along with the reduction potentials for the bound copper species:

$$(\text{peptide})_3\text{Cu}^{\text{II}} + \text{e}^- \longrightarrow (\text{peptide})_3\text{Cu}^{\text{I}}$$

Peptide	Sequence	E°
A	Ac-G WKALEEK LKALEE LKALEEE **H**KAL**K**EK G-NH_2	504 mV
B	Ac-G WKALEEK LKALEE LKALEEE **H**KAL**Q**EK G-NH_2	474 mV
C	Ac-G WKALEEK LKALEE LKALEEE **H**KAL**E**EK G-NH_2	440 mV

a. The copper binds to the histidine. Draw the structure of the binding site.
b. Calculate the local charge at the binding site when bound to (i) Cu^{I} and (ii) Cu^{II}.
c. If the overall charge on the peptide complex A_3Cu^{II} is zero, what are the charges on (i) B_3Cu^{II} and (ii) C_3Cu^{II}?
d. Suggest a reason for the change in the reduction potentials between the three complexes.
e. By comparison, the reduction potential of aqueous Cu^{II} is 159 mV. Suggest a reason for the difference bteween the reduction potential of aqeous copper and the peptide complexes.

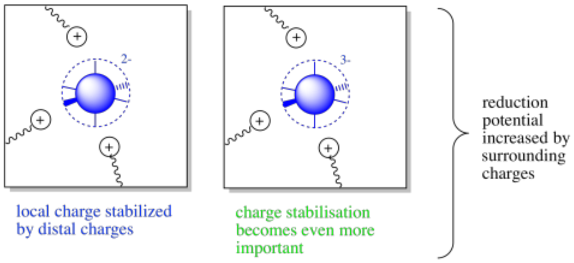
2.3: Effect of Charge- Distal Effects, or Effects of the Medium

The charge on a coordination complex, found within a metalloprotein, has a strong influence on the reduction potential of the metal centre. Other factors in the surrounding medium can either stabilise or destabilise that charge. Consequently, we need to consider the interaction of the metal centre with its surroundings.

Consider a metal centre in which the local charge -- that is, the sum of the charges on the metal ion and its coordinated ligands -- is -2. The addition of an electron would result in a local charge of -3.

But why are we talking about this "local charge"? Isn't -3 the charge on the whole molecule? Well, no. Remember, we are talking about a protein. It is a very large molecule. What's more, it has lots of other charges associated with it. Many amino acid residues may be neutral, but some have negative charges and others have positive charges.

Those charges are bound to interact with the charge on the metal centre. There would be coulombic interactions between the charges. Think about a case in which there are a number of nearby, positively charged amino acid residues.

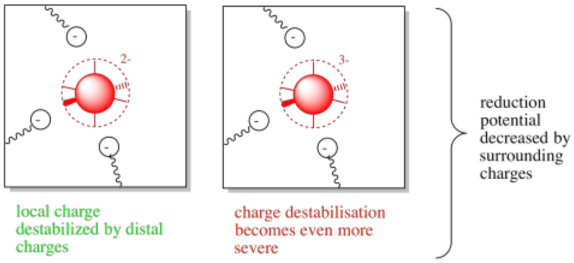


Those positively charged residues would have an attractive interaction with the metal centre. The overall energy would be lowered by this interaction. If another electron were added to the metal centre, and it became more negative, the interaction with the neighbouring positive charges would be even greater. As a result, a balance is tipped within this protein. The positively charged residues stabilize both the oxidized and the reduced state of the metal centre, but they stabilize the reduced state even more. Reduction potential increases in this case.

? Exercise 2.3.1

Which amino acid residues are generally found with positive charges at neutral pH?

Now let's think about the opposite case. We'll take the same metal centre, but surround it with some negatively charged amino acid residues.



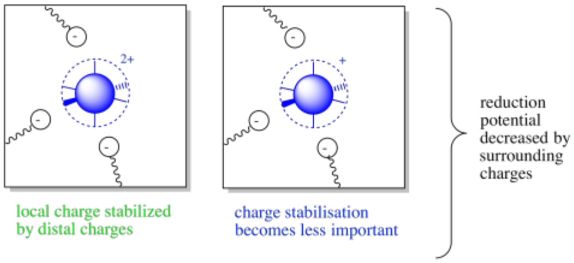
In this case, the neighbouring amino acid residues would destabilise the charge on the metal centre. However, if the metal became reduced, the situation would become even worse. The buildup of negative charge would lead to increasing repulsive and destabilising forces. The reduction potential would be lowered.

? Exercise 2.3.2

What amino acid residues are generally found with negative charges at neutral pH?

Of course, not all protein-metal complexes have a negative charge around the metal ion. If the coordinating donors are neutral rather than anionic, the complex may have an overall positive charge. How will that change things?

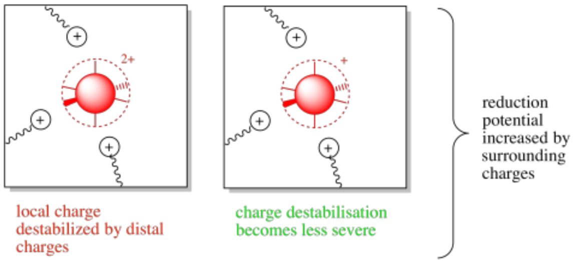
Well, the details do change, but the overall idea remains the same. This time, surrounding amino acid residues will stabilize the complex only if they are negatively charged. Of course, the more positively charged the complex, the more important that interaction. This situation may result in a decreased reduction potential.



local charge stabilized by distal charges

charge stabilisation becomes less important

That situation would be reversed in the presence of nearby amino acid residues with positive charges. In that case, the destabilization of the more positive oxidized state may motivate the complex toward accepting an electron. The reduction potential may be increased in this case.

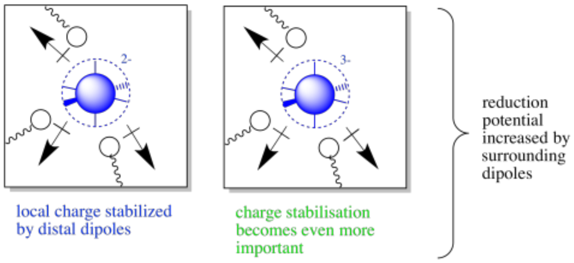


local charge destabilized by distal charges

charge destabilisation becomes less severe

All of these examples involve just a few amino acid residues that are actually charged at neutral pH or thereabouts. Does that mean that these factors are rare, only to be considered when there happen to be such residues close enough to actually make a difference?

Not really. Remember, a protein has lots of polar aspects. Even in the absence of charges, there are a number of amino acid residues that would have dipole moments. These dipole moments would have ion-dipole interactions with charged metal centres. In general, neighbouring dipoles would be able to stabilise charges, provided the amino acid residues were conformationally flexible enough to interact with the charge in a stabilising way.



local charge stabilized by distal dipoles

charge stabilisation becomes even more important

? Exercise 2.3.3

Of the following pairs of amino acids, which one is more polar?

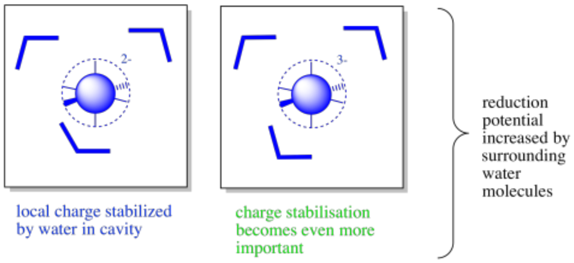
a) lysine or leucine b) alanine or glutamine c) histidine or valine

d) Ile or Asp e) Pro or Thr f) Asn or Ala

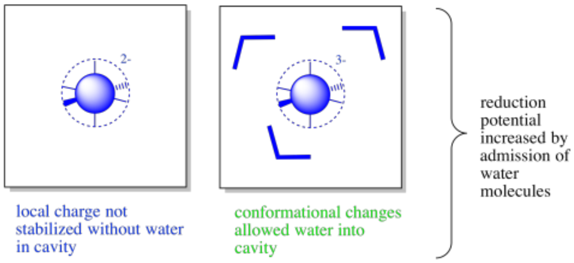
g) K or M h) Y or F i) R or E

Of course, it doesn't have to be an amino acid residue that interacts with the charged metal centre. The backbone of the protein itself has some very polar carbonyls. Remember, these carbonyls are especially polar because of π-donation from the amide nitrogens. One of these moieties could be oriented in such a way as to interact with a metal centre, influencing its reduction potential.

There may also be water molecules present in the interior of the protein. The coordination complex may be found in a large enough fold or cavity along the protein that water molecules are allowed to enter, stabilising any charges.



Furthermore, conformational changes upon oxidation or reduction may lead to the opening or closing of channels into the protein. Conformational changes could be linked to the redox activity because metal-ligand bond may lengthen or contract as a result of oxidation-reduction reactions. Consequently, it is possible that waters would be present in one state but not in another. From a predictive point of view, this makes for an extremely complicated situation. However, from the point of view of nature, it provides for an enhanced level of control over the properties of the metalloprotein.



2.4: The Effect of pH

Hydrogen ions, or protons, are crucial supplies in various chemical and biological processes. The available level of these supplies, essentially, is what we mean by pH.

"Low pH" corresponds to a very high concentration of protons. "High pH" corresponds to a very low concentration of protons.

Mathematically, $pH = -log[H^+]$. A chemically more correct statement in water is pH = -log[H_3O^+], since in water there will be no free protons; the protons will be bound to water molecules, forming hydronium ions. However, in some of our discussions we will simplify and refer to it as [H^+]. The use of pH rather than [H_3O^+] allows for comparison of concentrations over a much larger range, since we are using a logarithmic scale.

[H_3O^+] (mol L^{-1})	pH
0.1	1
0.01	2
0.001	3
0.0001	4
0.00001	5
0.000001	6
0.0000001	7

The log scale just highlights the number of decimal places in the number.

The concept of pH goes further than that, however. Water contains polar bonds that are able to ionize, forming a hydroxide ion and a proton. An individual water moleule does not ionize very easily, but given a very, very large number of water molecules, a few of them would be found in this ionized state. Water will contain a few hydroxide ions and a few protons.

Regular, garden-variety water typically has pH close to 7. It might range a little lower or higher depending on what minerals are dissolved in it. A very low pH, maybe 1 to 3, would be considered very acidic. A very high pH, maybe 12 to 14, is very basic. At low pH, water contains lots of protons and very, very few hydroxide ions, if any. That's because the equilibrium between ionized and non-ionized water gets pushed to the non-ionized side by the extra protons. That's le Chatelier's principle. At high pH, there is actually an overabundance of hydroxide ions and essentially no free protons. That's because any free protons react with the hydroxide ions to re-form water. That's le Chatelier's principle, again.

The pH has an influence on the redox potential of a metalloprotein because free protons or hydroxide ions alter the protonations state of the protein. Free protons can add to basic nitrogen sites, increasing the positive charge on the protein (or lowering negative charge). Hydroxide can remove protons from acidic sites, increasing negative charge (or lowering positive charge) on the protein.

Let's take a look at what happens to an amino acid when it undergoes a drastic change in pH. We'll use alanine as an example. Starting at pH 1, alanine actually has a plus charge. The amino end of the compound is protonated. As pH increases, the concentration of free protons drops further and further. Physically, we would carry out this change by adding a base such as hydroxide ion to consume the free protons. Eventually, the equilibrium shifts and the carboxylic acid goup, the most acidic position in the molecule, releases its proton to replace the ones that were removed from solution. At that point, the charge on the alanine is overall neutral.

Going even further, eventually the protonated amino group loses its proton, too. At that point, the alanine has an overall negative charge.

Alanine has two pK_a values over the common pH range of 1-14. It has an acidic carboxylic acid group and a potentially acidic quaternary ammonium group.

Exercise 2.4.1

Define the following equilibrium constants of alanine, in terms of concentrations of species.

a) K_{a1} b) K_{a2}

Exercise 2.4.2

Define pK_a in terms of K_a.

Exercise 2.4.3

Show that, for an amino acid such as alanine, pKa1 is equal to the pH at which the acidic group is 50% ionised; i.e. there are equal amounts of ionised and non-ionised molecules.

Several amino acids have acidic or basic side chains. In that case, there would be an additional protonation state. As a result, many amino acids have three different pK_a values. Examples are shown in the table below.

amino acid	pK_{a1}	pK_{a2}	pK_{a3}
arginine	2.03	9.00	12.10
aspartic acid	1.95	3.71	9.66
cysteine	1.91	8.14	10.28
glutamic acid	2.16	4.15	9.58
histidine	1.70	6.04	9.09
lysine	2.15	9.15	10.67

Exercise 2.4.4

For each entry in the table of amino acids above, assign the pKa value to the acidic/basic site in the structure

Exercise 2.4.5

Draw the structure of each of the amino acids in the above table at neutral pH (pH 7).

Exercise 2.4.6

Amino acids have an α-position, next to the carbonyl. Why doesn't that position have a pK_a value in the table above?

Answer

> The pK_a of an α-position is typically about 20, although it can vary depending on what other groups are nearby. That is too high to build up a significant amount of the deprotonated species in water, which has a pK_a (in water) of 14.

As a result of these structural changes at different pH, proteins can change protonation states when the pH changes. Such a change would have a dramatic impact on the properties of the protein. One of these properties is reduction potential. As we have already seen, charge is one of the factors that has a strong influence on the reduction potential of a metalloprotein.

Because a protein might have lots of acidic or basic amino acids in the vicinity of the metal center, the effects of pH change could be very complicated. Some sites might become protonated during a change in the environment, whereas others might become deprotonated.

? Exercise 2.4.7

Predict whether the reduction potential of an Fe^{3+} center would increase or decrease in the following situations.

a. There is a nearby histidine; pH changes from 7 to 5.
b. There is a nearby aspartic acid; pH changes from 4 to 3.
c. There is a nearby glutamic acid; pH changes from 4 to 5.

Answer a

a) The pK_a of the side chain of histidine is about 6.0; upon changing from pH 7 to pH 5, this group would become protonated and positively charged. The positive charge would be more stabilising (or less destabilising) toward Fe^{2+} than Fe^{3+}; the reduction potential would increase.

Answer b

b) The pK_a of the side chain of histidine is about 3.7; upon changing from pH 4 to pH 3, this group would become protonated and positively charged. The positive charge would be more stabilising (or less destabilising) toward Fe^{2+} than Fe^{3+}; the reduction potential would increase.

Answer c

c) The pK_a of the side chain of histidine is about 4.2; upon changing from pH 4 to pH 5, this group would become deprotonated and negatively charged. The negative charge would be more stabilising (or less destabilising) toward Fe^{3+} than Fe^{2+}; the reduction potential would decrease.

2.5: Hard and Soft Acid and Base Considerations

There are a number of amino acid residues that commonly bind to metal ions in biology. Do certain metal ions have a preference for certain donor atoms? And do those donor atoms have an influence on the properties of the metal complexes that are formed?

The principle of hard and soft acids and bases (HSAB) is useful here. Remember, this is a classification system that is based on the amount of charge density on acids and bases. Small ions with tightly held charges are called "hard". Larger, more polarizable ions are called "soft". Typically, hard cations (hard acids) combine more readily with hard anions (hard bases). Soft bases combine readily with soft acids.

? Exercise 2.5.1

Which of the following cations would be considered hard?

a) Hg^+ b) Ti^{4+} c) Ca^{2+} d) Cu^+

Answer

Ti^{4+} and Ca^{2+}

? Exercise 2.5.2

Which of the following anions would be considered hard?

a) F^- b) I^- c) CH_3S^- d) HO^-

Answer

F^- and HO^-

Remember that in the case of cations, increasing positive charge makes the cation smaller, because the increasing positive charge draws the remaining electrons closer to the nucleus. That means that some metals could conceivably be thought of as soft in one oxidation state but hard in another. A more highly charged cation would be harder.

A few ions are placed in the following table for reference, with extra attention to cases that occur on biology.

	hard	borderline	soft
acids	H^+, Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Co^{3+}, Fe^{3+}	Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}	Cu^+, Ag^+, Au^+, Hg^+, Cd^{2+}, Hg^{2+}
bases	F^-, HO^-, H_2O, Cl^-, RO^-, O_2^-, $CH_3CO_2^-$, RNH_2, CO_3^{2-}, NO_3^-	NO_2^-, Br^-, N_2, pyridine, imidazole	RSH, RS^-, S^{2-}, CN^-, CO, I^-, C_2H_4, H^-, CH_3^-

Notice that some ions are in between the hard and soft categories. These borderline acids bond most readily with borderline bases.

? Exercise 2.5.3

Choose the best match for the following ions.

a. Co^{2+} with CO_3^{2-}, NO_2^- or S^{2-}
b. Mg^{2+} with imidazole, CN^- or $CH_3CO_2^-$
c. Cu^+ with RS^-, pyridine or H_2O
d. Fe^{2+} with N_2, I^- or HO^-
e. Zn^{2+} with O_2^-, imidazole or RSH

Answer a

a) Co^{2+} with NO_2^-

Answer b

b) Mg^{2+} with $CH_3CO_2^-$

Answer c

c) Cu^+ with RS^-

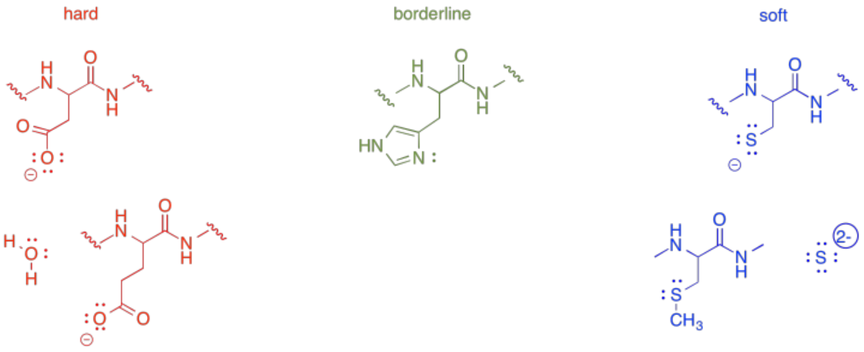
Answer d

d) Fe^{2+} with N_2

Answer e

e) Zn^{2+} with imidazole

Many of the metal ions in the table above are biologically useful. From the information in the table, it shouldn't be too surprising that Fe^{2+} ions are often bound to histidine, which coordinates to the metal through an imidazole group. On the other hand, sometimes the same metals in different oxidation states may be coordinated by other amino acid residues. For example, higher oxidation state Fe^{3+} may more commonly have aspartate or glutamate donors.



Exercise 2.5.4

Choose the best match for the following metal ions.

a. Fe^{3+} with asp, his or cys
b. Cu^+ with glu, asp or met
c. Zn^{2+} with glu, his or cys
d. Cu^{2+} with his, H_2O or S^{2-}
e. Co^{3+} with glu, cys or met

Answer a

a) Fe^{3+} with asp

Answer b

b) Cu^+ with met

Answer c

c) Zn^{2+} with his

Answer d

d) Cu^{2+} with his

Answer e

e) Co^{3+} with glu

It's important to get familiar with these relationships. However, metal ions are rarely coordinated only to one type of ligand in biology. There may be three or four different kinds of amino acids bound to the same metal ion in one complex. We don't just find the same metal ion bound to the same amino acid all the time.

Why is that? If Fe^{2+} forms the most stable complexes with histidine, why doesn't it just bind to histidine and nothing else? The answer is complicated, but has something to do with the fact that the metal ion will make do with the amino acids that are available at a specific site in the protein. Sometimes the match may not be ideal. That's to our advantage, though. After all, metal ions do not just play structural roles in biology. They are also supposed to do something.

Very often, a coordinated ligand can tune the reactivity of a metal ion. It does so not by stabilising the metal ion in its current state but by stabilising an alternative state, if only the metal ion would undergo a reaction to get there. A combination of amino acid residues and other ligands may act together to hold the metal ion in a fine balance between two oxidation states. After all, once a metal ion has reacted, it needs to get back to the way it was before. The cell can't afford to keep importing more trace elements just to keep going. It needs to recycle its reagents through catalysis.

? Exercise 2.5.5

Choose the amino acid residue that would have the effect on the metal ion as described, based on HSAB principles.

a. Increase the reduction potential of Cu^{2+}: asp, his or met.
b. Decrease the reduction potential of Fe^{3+}: glu, his or cys.
c. Make Cu^{+} easier to oxidise: his, cys or met.
d. Make Fe^{2+} easier to oxidise: asp, his or cys.
e. Make Fe^{3+} easier to reduce: asp, glu or cys.

Answer a

a) Increase the reduction potential of Cu^{2+}: met.

Answer b

b) Decrease the reduction potential of Fe^{3+}: glu.

Answer c

c) Make Cu^{+} easier to oxidise: his.

Answer d

d) Make Fe^{2+} easier to oxidise: asp.

Answer e

e) Make Fe^{3+} easier to reduce: cys.

2.6: Effect of Geometry

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2.7: Magnetic Measurements

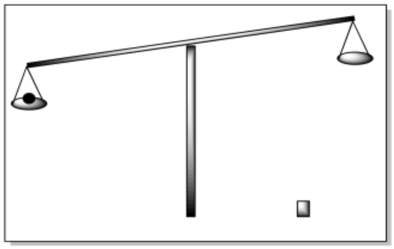
There are a number of physical methods used to study the properties of metal ions in biology. These studies may be performed on simple model compounds. Model compounds are coordination compounds that are designed to mimic the coordination environment of a metal ion in biology. For example, if a metal ion appears to be coordinated by three histidines, then an appropriate model complex might have three ligands with nitrogen donors. The hope is that the simpler coordination complex might still provide some insight into the properties of the metal centre in the much more complicated metalloprotein.

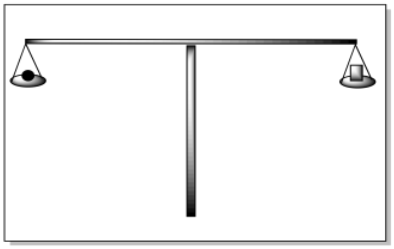
Frequently, measurements can also be perfomed on the metalloprotein itself. Obviously this provides much more useful information, at least potentially, because the results describe the system of interest, rather than some simplified model. However, sometimes obtaining the data reliably can be more troublesome with the metalloprotein.

Physical methods used in the study of metalloproteins include cyclic voltammetry and other electrochemical studies. These methods tell us directly about the reduction potential of the material. In addition, electron paramagnetic resonance spectroscopy (EPR) can provide information about the environment of unpaired electrons in the sample. That information can give us some insight into the structure of a metal complex.

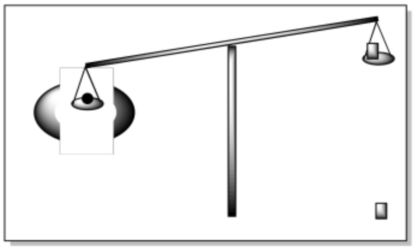
Like EPR, magnetic measurements can provide some information about the presence of unpaired electrons in a sample. That's because unpaired electrons have an attraction for magnetic fields. We can actually measure that attraction to a magnetic field to get some idea about how many unpaired electrons are present. In principle, the more unpaired electrons, the stronger the attraction to the magnetic field. That means magnetic measurements can tell us about the oxidation state of a material.

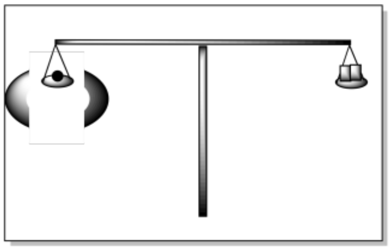
In principle, a magnetic measurement can be done very simply. All it takes is a balance and a magnetic field. We all know how a balance works. In a simple model from an earlier time, we place the sample in one pan. The balance tips over. We find the appropriate weight - a little piece of carefully prepared metal, certified by some bureau of standards. The balance balances. The masses in the two pans must be equal.





With a Gouy balance, the same idea applies, but we throw in a magnetic field, too. Even when it should be balanced, the balance tips, because of an attraction to the magnetic field. We need to find another weight that will get the balance even again. The weight needed to balance the scale is proportional to the attraction of the material to the magnetic field.





All sorts of calculations ensue. We know the mass of the original material, and we presumably know its molecular weight, so we know the number of moles of material in the balance. That leads us to a value called the molar magnetic susceptibility, X_M. The magnetic moment actually changes with temperature, so we need to take that into account to report "the effective magnetic moment."

$$\mu_{eff} = 2.83\sqrt{XMT}\beta$$

n which T is the temperature and β is a constant, the Bohr magneton. Usually the value is just left in units of β so we don't have to plug that value in.

In a very simple world, that effective magnetic moment is simply caused by the unpaired electrons in the sample. The predicted value is called μ_{so}, the "spin only" magnetic moment. That value is related to the unpaired spins by:

$$\mu_{so} = \sqrt{n(n+2)}\,\beta$$

in which n is the number of unpaired electrons.

Ideally, the effective magnetic moment is just caused by those unpaired electrons, so it is the same as the spin only effective moment.

$$\mu_{so} = \mu_{eff}$$

That makes it fairly easy to estimate the number of unpaired electrons in the sample, given the effective magnetic moment.

? Exercise 2.7.1

Estimate μ_{eff} for each of the following numbers of unpaired electrons.

a) n = 0 b) n = 1 c) n = 2 d) n = 3 e) n = 4 f) n = 5

Answer a

a) 0 β

Answer b

b) 1.73 β

Answer c

c) 2.83 β

Answer d

d) 3.87 β

Answer e

e) 4.89 β

Answer f

f) 5.92 β

Overall, the relationship is simpler than it initially appears. The effective magnetic moment, in Bohr magneton units, is always approximately one more than the number of unpaired electrons.

$$n = \mu_{eff} - 1$$

? Exercise 2.7.2

Estimate μ_{eff} for each of the following metals.

a) octahedral Co^{2+} (high spin) b) octahedral V^{2+} c) tetrahedral Mn^{4+} (low spin) d) tetrahedral Mo^{4+}

e) octahedral Cr^{2+} (high spin) f) octahedral Co^{3+} (low spin) g) octahedral Mn^{2+} (high spin)

Answer a

a) approx. 4 β

Answer b

b) approx. 4 β

Answer c

c) approx. 2 β

Answer d

d) approx. 3 β

Answer e

e) approx. 5 β

Answer f

f) approx. 0 β

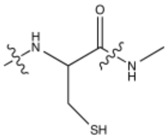
Answer g

g) approx. 6 β

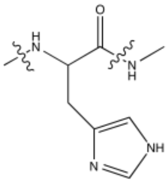
2.8: Solutions for Selected Problems

Exercise 2.1.1:

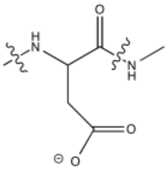
a)



b)

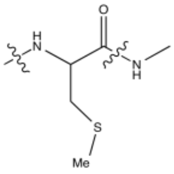


c)

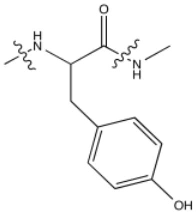


Exercise 2.1.2:

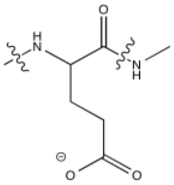
a)



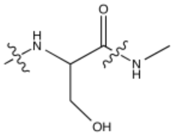
b)



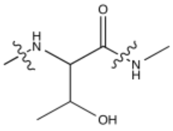
c)



d)

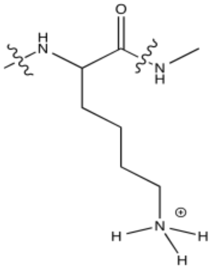


e)



Exercise 2.1.3:

At neutral pH, lysine would normally be protonated. It would noy have a lone pair on the nitrogen to coordinate a metal ion.



Exercise 2.4.6:

The pK_a of an α-position is typically about 20, although it can vary depending on what other groups are nearby. That is too high to build up a significant amount of the deprotonated species in water, which has a pK_a (in water) of 14.

Exercise 2.4.7:

a. The pK_a of the side chain of histidine is about 6.0; upon changing from pH 7 to pH 5, this group would become protonated and positively charged. The positive charge would be more stabilising (or less destabilising) toward Fe^{2+} than Fe^{3+}; the reduction potential would increase.
b. The pK_a of the side chain of histidine is about 3.7; upon changing from pH 4 to pH 3, this group would become protonated and positively charged. The positive charge would be more stabilising (or less destabilising) toward Fe^{2+} than Fe^{3+}; the reduction potential would increase.
c. The pK_a of the side chain of histidine is about 4.2; upon changing from pH 4 to pH 5, this group would become deprotonated and negatively charged. The negative charge would be more stabilising (or less destabilising) toward Fe^{3+} than Fe^{2+}; the reduction potential would decrease.

Exercise 2.5.1:

Ti^{4+} and Ca^{2+}

Exercise 2.5.2:

F^- and HO^-

Exercise 2.5.3:

a. Co^{2+} with NO_2^-
b. Mg^{2+} with $CH_3CO_2^-$
c. Cu^+ with RS^-
d. Fe^{2+} with N_2
e. Zn^{2+} with imidazole

Exercise 2.5.4:

Choose the best match for the following metal ions.

a. Fe^{3+} with asp
b. Cu^+ with met
c. Zn^{2+} with his
d. Cu^{2+} with his
e. Co^{3+} with glu

Exercise 2.5.5:

Choose the amino acid residue that would have the effect on the metal ion as described, based on HSAB principles.

a. Increase the reduction potential of Cu^{2+}: met.
b. Decrease the reduction potential of Fe^{3+}: glu.
c. Make Cu^+ easier to oxidise: his.
d. Make Fe^{2+} easier to oxidise: asp.
e. Make Fe^{3+} easier to reduce: cys.

Exercise 2.7.1:

a) 0 β b) 1.73 β c) 2.83 β d) 3.87 β e) 4.89 β f) 5.92 β

Exercise 2.7.2:

a) approx. 4 β b) approx. 4 β c) approx. 2 β d) approx. 3 β

e) approx. 5 β f) approx. 0 β g) approx. 6 β

CHAPTER OVERVIEW

3: Understanding Mechanism

3.1: Intermediates

By now you are familiar with a range of reaction types in organic, inorganic, and biochemistry. The purpose of this chapter is to help you review some of the tools that we use in communicating how reactions happen.

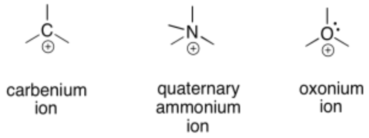
First and foremeost, a mechanism is a sequence of intermediates. What happens to the structure of the compound as it undergoes chemical change? Does that change happen all at once, or does it happen in stages? If it happens in stages, what kinds of intermediates are involved?

Let's review some different kinds of reactive intermediates that may occur along a reaction pathway. These intermediates are not particularly stable, and so they go on to react further until they form more stable products.

Cations

Cations and anions can be unstable for the simple reason that charge separation costs energy. There are a few cases in which these ions are really quite stable -- alkali cations such as Na^+ and halide anions such as Cl^- come to mind -- but here we are interested in exploring the less stable, more temporary examples of ions.

Unlike sodium ions, cations of carbon, nitrogen, or oxygen are reactive. These relatively electronegative atoms are not very stable with a positive charge.



Carbocations, or carbenium ions, in which the positive charge is on a carbon atom, are generally unstable. Carbon is in the upper right part of the periodic table, so it is not particularly electropositive like sodium. A positive charge on carbon frequently makes a molecule reactive. Nevertheless, this intermediate is frequently encountered during organic reactions.

Are all carbocations equally unstable? No. In general, there are two main factors that stabilize carbocations. The first, and most important, is the degree of substitution. A tertiary carbocation, in which the carbon with the positive charge is attached to three other carbon atoms, is fairly stable. A primary carbocation, in which the carbon bearing the positive charge is attached to only one other carbon and two hydrogen atoms, is not so stable. A secondary carbocation, with the positive carbon attached to two other carbons and a hydrogen atom, is intermediate in stability. Of course, a methyl cation, in which a positive carbon is attached to three hydrogen atoms, is not very stable at all.

The reasons for these differences are sometimes explained in terms of hyperconjugation. According to this idea, weak interactions between the unoccupied p orbital on the positive carbon and the occupied sigma bonds on the neighbouring carbons can stabilize the cation somewhat. Very loosely, imagine these bonds, which are made of pairs of electrons, can allow a little bit of negative charge to overlap with the cation, lowering its overall positive charge just a tad. More correctly, the empty p orbital can interact with the sigma bonds to produce two molecular orbital combinations; one of these is an in-phase combination and is lower in energy than either of the original orbitals, whereas the other, out-of-phase combination is a little higher in energy. Because only two electrons are involved, from the sigma bond, both can get to a lower energy level this way. They both drop into the lower energy combination. In that sense, the cation is stable not just because the positive charge is any less but because the neighbouring bonds can drop lower in energy.

The second factor that stabilizes positive charge is resonance delocalization. If a double bond is adjacent to a cation, conjugation between filled and empty p orbitals allows the positive charge to be distributed across multiple carbon atoms. This effect lowers the amount of positive charge borne by an one carbon atom. this kind of delocalizing effect is very common in stabilizing reactive intermediates. For this reason, allylic ($CH_2{=}CH{-}CH_2^+$) and benzylic cations ($C_6H_5CH_2^+$) are particularly stable. They are about as stable as a secondary cation along a regular carbon chain, even if they would otherwise be only primary cations.

Of course, other atoms can be cations, too. As seen above, oxygens and nitrogens are very commonly encountered as cations. That is partly because they are very good at donating electrons to neighbouring atoms in need.

? Exercise 3.1.1

Identify the positive atom in each of the following molecules.

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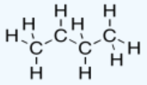

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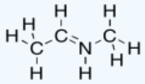

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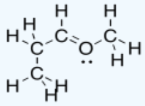

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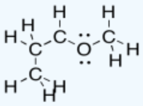

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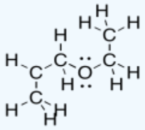

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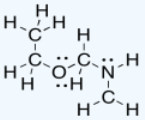

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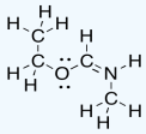

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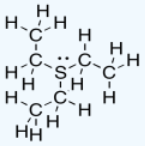

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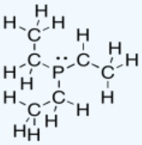

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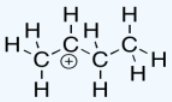

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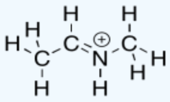

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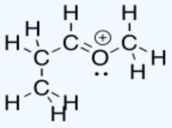

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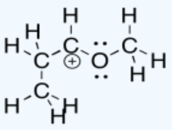

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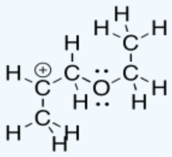

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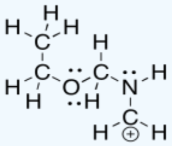

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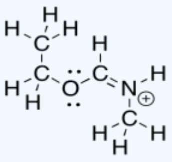

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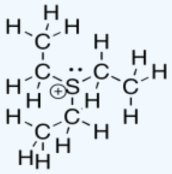

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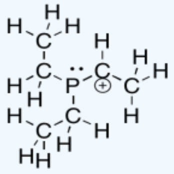

? Exercise 3.1.2

Within each group, rank the cations from most stable to least stable.

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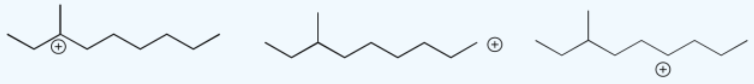

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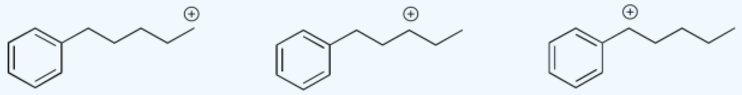

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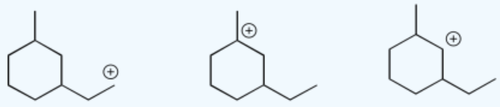

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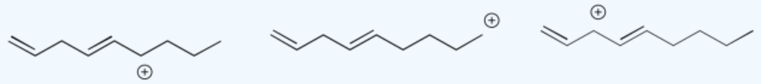

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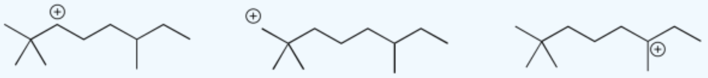

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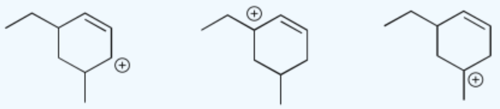

Answer

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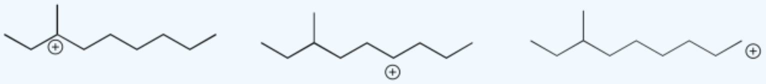

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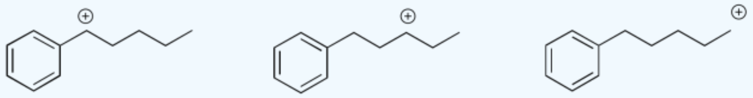

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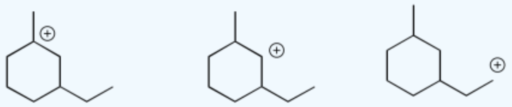

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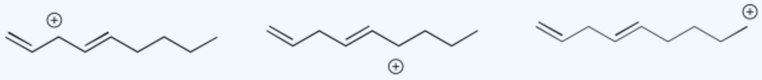

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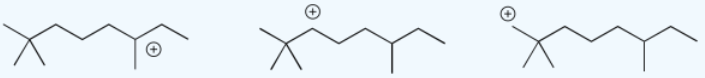

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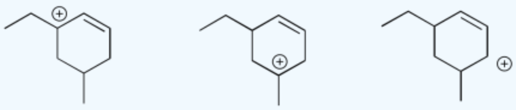
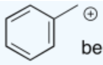


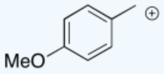
Exercise 3.1.3

Sometimes, remote groups provide additional stabilization for a cation. Indicate whether each of the following cations would be more stable or less stable than a benzyl cation, and explain why.



benzyl cation

a)



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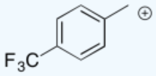

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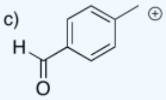

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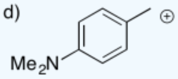

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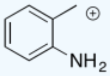

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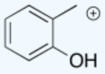

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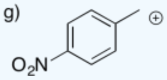

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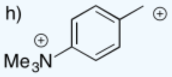

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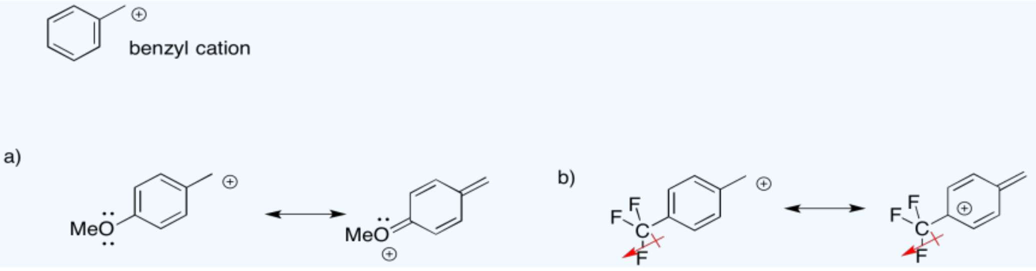
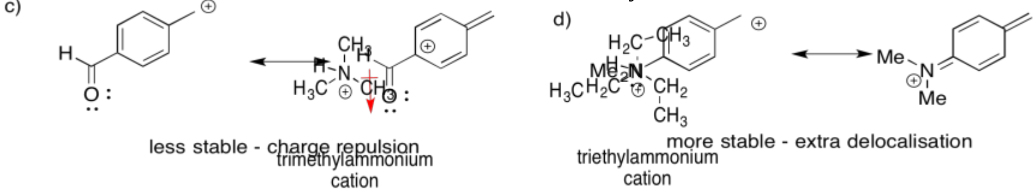
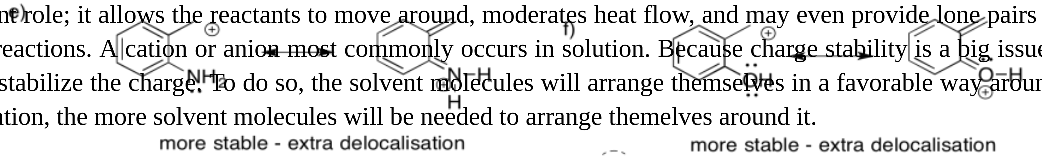
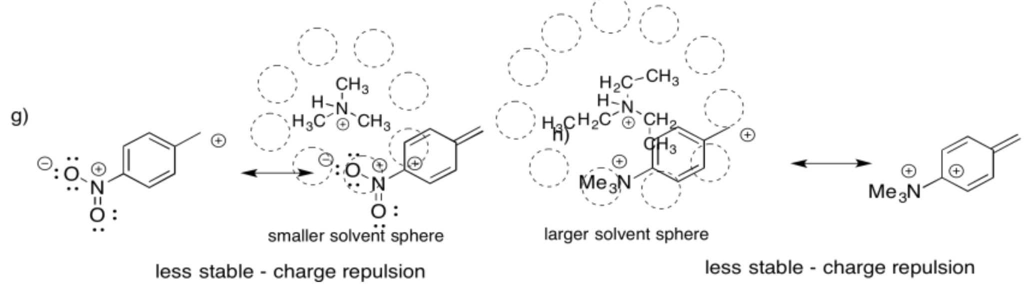


There are other, more subtle factors that can influence the stability of cations. Charge stability is affected by the structure further away from the atom bearing the charge. For example, a triethylammonium cation and a trimethylammonium cation look pretty similar. However, a triethlammonium cation is a little less stable than a trimethylammonium cation.



The difference in these cations is related to the size of the overall molecule. Reactions usually take place in a solvent. The solvent plays an important role; it allows the reactants to move around, moderates heat flow, and may even provide lone pairs or protons to aid in acid/base reactions. A cation or anion most commonly occurs in solution. Because charge stability is a big issue, the solvent will also help to stabilize the charge. To do so, the solvent molecules will arrange themselves in a favorable way around the cation. The bigger the cation, the more solvent molecules will be needed to arrange themelves around it.

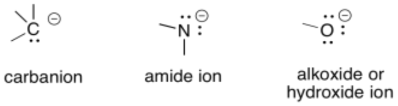




Anions

Negatively charged ions are also common intermediates in reactions. Like cations, anions are frequently unstable species. These species are stabilized by a number of different factors, not unlike cation stability.

Carbanions, amide ions and alkoxide ions are examples of anionic intermediates.



Remember, there are just a few key factors that explain a great deal of questions about anion stability.

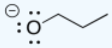
Within a column of the periodic table, when comparing two atoms with negative charge, the stability of the anions principally depends on polarizability of the atom. Polarizability refers to how easily distorted the electrons are around the atom. The larger the atom, and the further the electrons from the nucleus, the more polarizable it is. The more polarizable the atom, the more stable the anion.

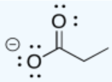
Within a row of the periodic table, the more electronegative an atom, the more stable the anion.

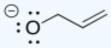
? Exercise 3.1.4

Within each group, rank the anions from most stable to least stable.

a)







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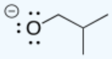

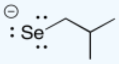

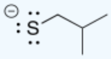

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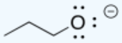

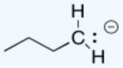

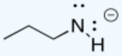

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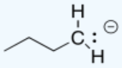
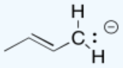
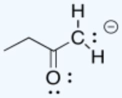
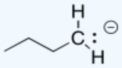
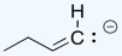


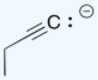




e)







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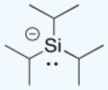

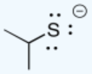

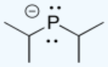

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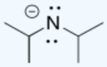

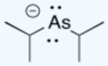

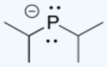

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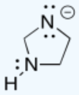

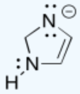

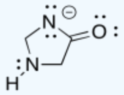

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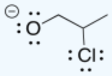
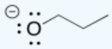
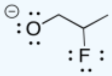
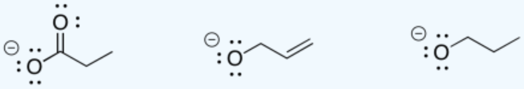






Answer

a)



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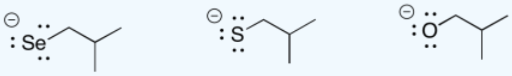

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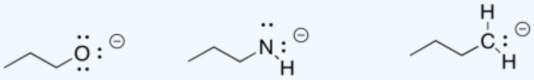
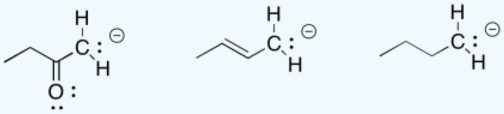


d)



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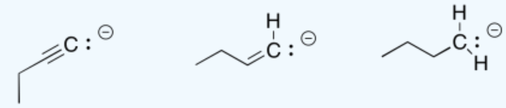

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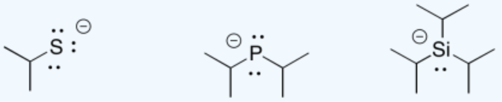

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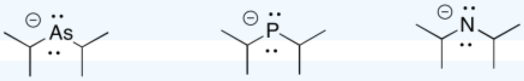
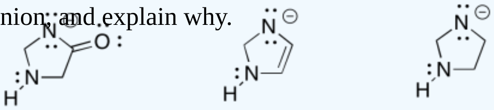


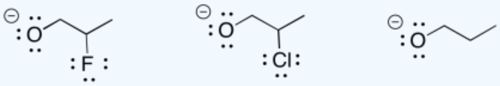
? Exercise 3.1.5

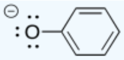
Sometimes, remote groups provide additional stabilization for a cation. Indicate whether each of the following anions would be more stable or less stable than a phenoxide anion, and explain why.

h)



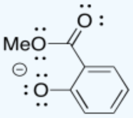
i)



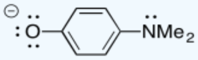


phenoxide or phenolate anion

a)



b)



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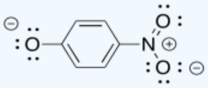

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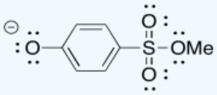

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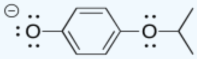

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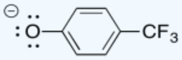

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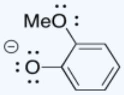

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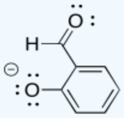
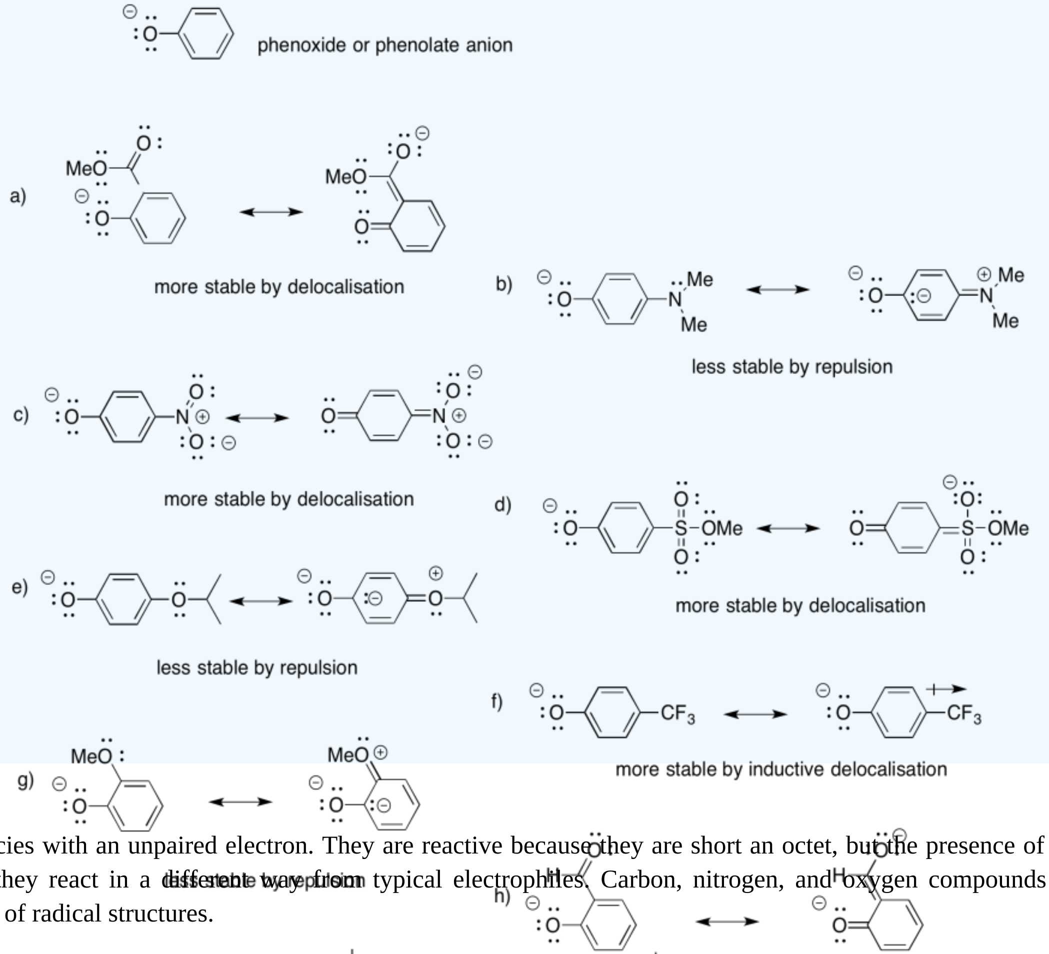


Answer



more stable by delocalisation

less stable by repulsion

more stable by delocalisation

more stable by delocalisation

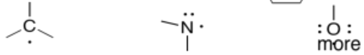
less stable by repulsion

more stable by inductive delocalisation

more stable by delocalisation

Radicals

Radicals are species with an unpaired electron. They are reactive because they are short an octet, but the presence of an unpaired electron means they react in a different way from typical electrophiles. Carbon, nitrogen, and oxygen compounds show some typical examples of radical structures.



Note that these radicals do not necessarily have charges. That is because they are bonding to one atom fewer than normal, but they are retaining just one of the electrons from the missing bond. In fact, radicals are often formed by breaking a bond within a normal, "closed-shell" compound, such that each atom involved in the bond takes one of the electrons with it. This is called "bond homolysis" and implies the bond is split evenly between the atoms. In contrast, "bond heterolysis" means the bond is broken unevenly, with one atom taing both of the electrons.

? Exercise 3.1.6

Confirm that there is no formal charge in each of the species shown above.

Answer a

a) formal charge = # e$^-$ in periodic table - # e$^-$ nonbonding - (# e$^-$ in bonds)/2

formal charge = 4 - 1 - 6/2 = 0

Answer b

b) formal charge = # e$^-$ in periodic table - # e$^-$ nonbonding - (# e$^-$ in bonds)/2

formal charge = 5 - 3 - 4/2 = 0

Answer c

c) formal charge = # e$^-$ in periodic table - # e$^-$ nonbonding - (# e$^-$ in bonds)/2

formal charge = 6 - 5 - 2/2 = 0

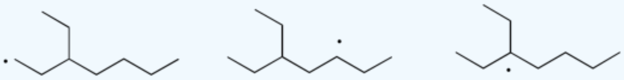
Radical ions are also possible. Radical anions can result from the addition of an extra electron to a normal, closed-shell compound. Radical cations can result through the removal of an electron from a normal, closed-shell compound.

Because radicals are electron-deficient species, in the sense that they lack an octet, they are often stabilized by the same factors that would stabilize a cation. In particular, they are stabilized by resonance delocalization, and carbon radicals are more stable on more-substituted carbons than on less-substituted carbons, just like cations. However, they are generally less sensitive that cations to these factors, because they do not actually have a positive charge.

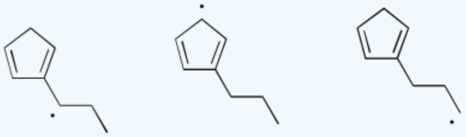
? Exercise 3.1.7

Within each group, rank the radicals from most stable to least stable.

a)



b)



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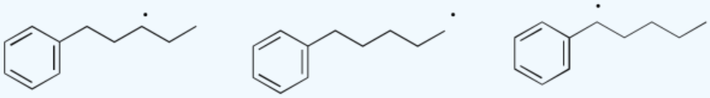
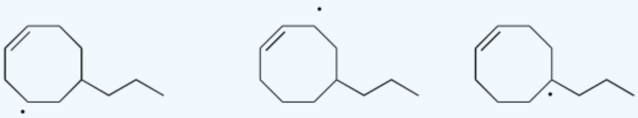


d)



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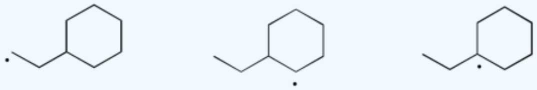
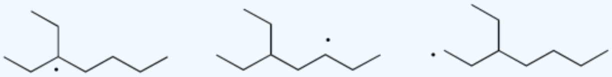


Answer

a)



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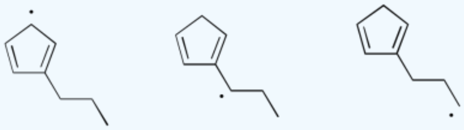

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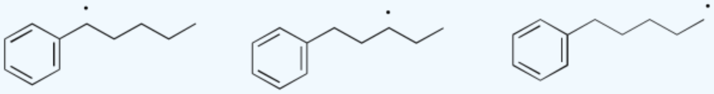

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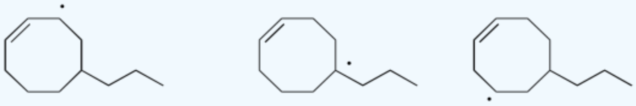

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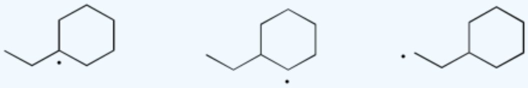
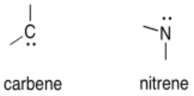
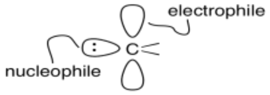


Carbenes and Nitrenes

We don't often see carbenes and the related nitrenes, but they are important intermediates in synthetic processes involving electrophilic addition to alkenes. Carbenes and nitrenes are two electrons short of an octet, but do not have a formal charge.



Carbenes are unusual because they can be thought of as both electrophiles or nucleophiles. The have lone pairs -- the usual requirement for a nucleophile. They also have an empty orbital, which would typically make them electrophiles.

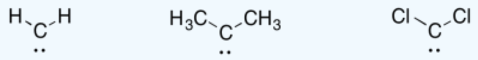


Because they lack an octet, carbenes and nitrenes can be stabilized through pi-donatin.

Exercise 3.1.8

Arrange the following carbenes in order from most stable to least stable.

a)



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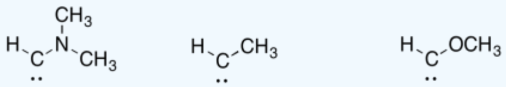

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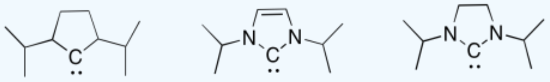

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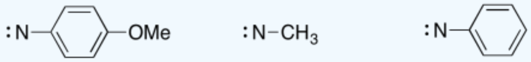
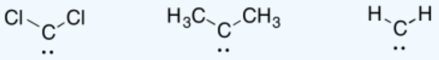


Answer

a)



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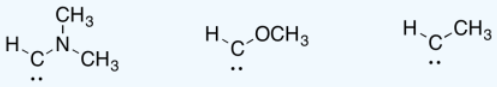

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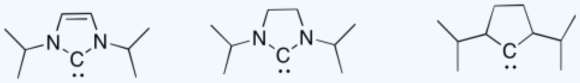

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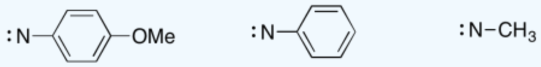
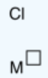
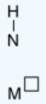


Coordination Complexes

Exercise 3.1.8

In the following pictures, decide whether the ligand is an anionic or neutral donor. Use the correct symbol (a line or an arrow) to stand for the ligand-metal bond. Assign the oxidation state to the metal to satisfy the overall charge.

a)

b)

c)

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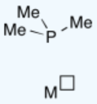
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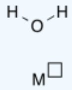

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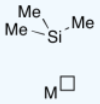
g)

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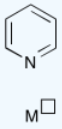
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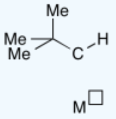
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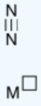

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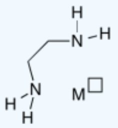
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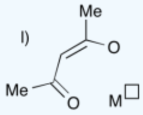
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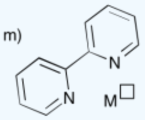
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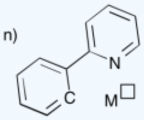
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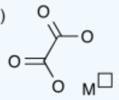

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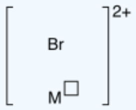
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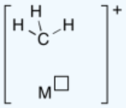
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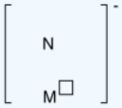
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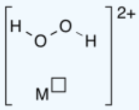
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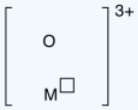

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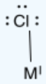
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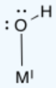
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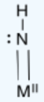
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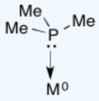
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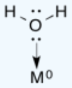

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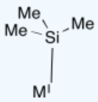
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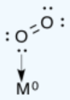
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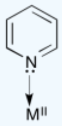
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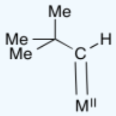
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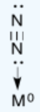

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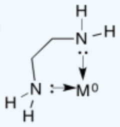
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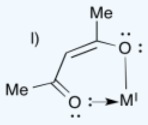
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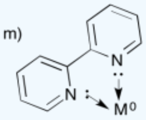
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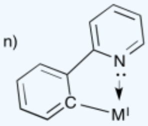
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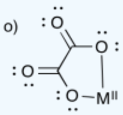

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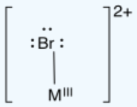
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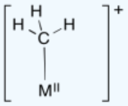
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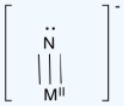
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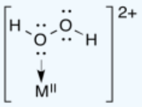
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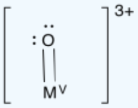

3.2: Energetics

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3.3: Arrow Conventions

Symbolic Notation

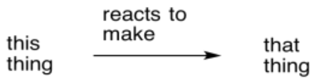
Sometimes in mathematics and science we need to convey an idea based on concepts we have learned previously. In mathematics, we use a plus sign (+) to indicate that we are putting these things together; we use a minus sign (-) to indicate we are taking some of these things away. Alternatively, we could use that plus sign to indicate that we have a surplus (a positive number) or that minus sign to show that we have a deficit or a debt (a negative number).

We don't even need to think about what these signs mean because we learned about them in elementary school. We have used them so often that we instantly get the idea of what is going on. In fact, symbolic notation is really how all of mathematics works; when we see the number three, we immediately associate it with a trio of objects (***).

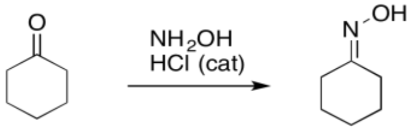
In chemistry, we start using this symbolic notation early on, as well. The most important symbols may be those used for the elements themselves, such as C for carbon or Fe for iron. We also use arrows, lots of different kinds of them, to convey a number of different ideas. You probably already know a little about some of these symbols, but now that you have encountered them a few times, we should review.

Conveying Relationships Between Structures

Chances are, the first arrow you encountered in a chemistry class was a reaction arrow. A reaction arrow just tells you that a change has taken place, and one thing has turned into another. The arrow points from the old thing (the thing that reacted) to the new thing (the thing that forme



The reaction arrow is used in an "equation of reaction". The thing that reacted is called the reactant. The thing that formed is called the product. Normally the reaction is written from left to right, with the reactant on the left and the product on the right, but that isn't always necessary. The important thing is that the arrow points from reactant to product.

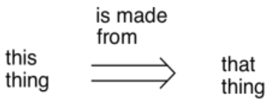


The reactants and products themselves are usually drawn using symbolic structures. These structures might be complete Lewis or Kekule structures, or they might be abbreviated line structures in organic compounds. Sometimes we leave out the structure and just use the formulae of the compounds, although we are losing some information that way. Sometimes in biochemistry a simple acronym is used to stand for the compound, such as NADH or AcSCoA, because the structures are relatively complicated. Nevertheless, the idea implied by the reaction arrow is always the same.

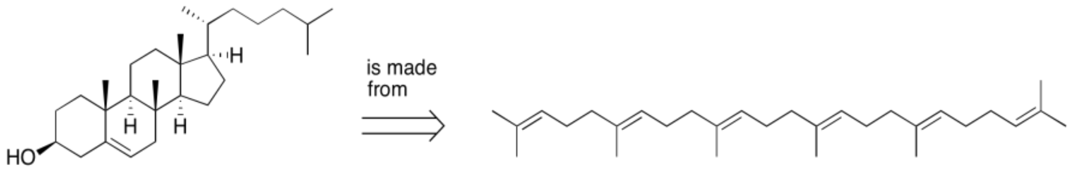
Sometimes, you may see a whole series of compounds linked from one to the next by reaction arrows. That means we are dealing with a series of reactions. We might be looking at a synthesis, in which an initial reactant forms a first product, which becomes the reactant for the next reaction, in a slow, building-up process that eventually produces a desired target compound.

The reaction arrow seems pretty simple to draw, although you do have to be careful not to draw the wrong kind of arrow. This one is just a straight line with an arrowhead at one end. Sometimes, the line can have a slight curve to it. That's usually because a series of reactions are connected in a cycle, and the series of reactions must lead back to the beginning. That's how we might show a catalytic cycle, for example.

Just to see how we can sometimes convey the wrong idea by drawing the wrong kind of arrow, consider something called a "retrosynthetic arrow". A retrosynthetic arrow differs from a reaction arrow because a retrosynthetic arrow shows what a compound is made from. In other words, it points from the product of a reaction (or series of reactions) to the reactant. Retrosynthetic arrows are used to illustrate possible sources of a compound of interest, whether the compounds are made in nature, industrially, or in a lab.

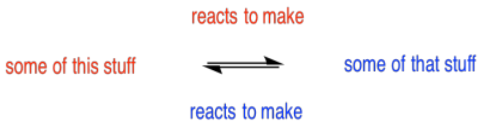


That sounds like it could be confusing, but fortunately a retrosynthetic arrow looks very different from a reaction arrow. It is an outline of an arrow, rather than a simple line and arrowhead. By choosing the right kind of arrow, you can clearly convey whether you are considering a reaction that you could do with a compound or wondering where the compound came from originally.



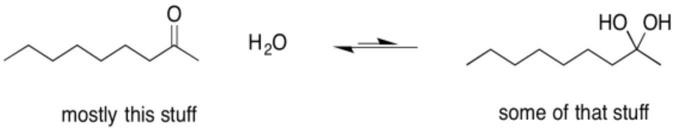
Biosynthetically, cholesterol is made from squalene, a polyunsaturated hydrocarbon. Squalene is an example of a class of compounds called terpenes, recognizable by their five-carbon monomer units.

Reaction arrows can be more subtle in the case of reversible reactions, or equilibrium processes. An equilibrium between two different compounds or groups of compounds can be illustrated using a combination of two arrows: one pointing from left to right and one pointing from right to left. Drawing the arrow that way implies that the reaction could proceed in either direction.



Usually, the individual arrows within that double, equilibrium arrow are drawn with only half an arrowhead.

Sometimes, one of the individual arrows in the equilibrium arrow is drawn a little longer than the other one. This symbol is meant to imply that, although the reaction is reversible, it proceeds more readily in one direction than the other. The left-to-right arrow may be the longer one, indicating that the reaction favors products; presumably it is exothermic (or exergonic, anyway). The right-to-left-arrow might be the longer one, indicating that the reaction mostly stays on the reactant side; it must be endothermic (or at least endergonic).



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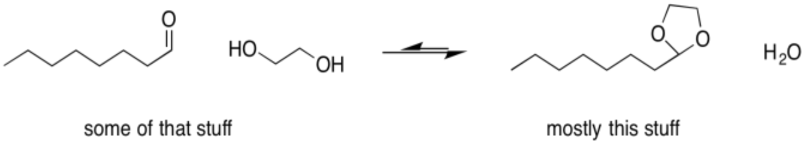
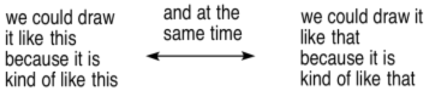
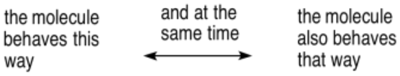


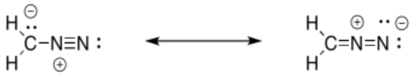
There is another symbol that people sometimes confuse with an equilibrium arrow. It is a resonance arrow. In a resonance arrow, one straight line has an arrowhead on each end, so that it points in two different directions. It is similar in appearance to an equilibrium arrow, but it has only one stem, whereas an equilibrium arrow has two separate ones.



The resonance arrow indicates that the molecule behaves like both structures at the same time. This situation is termed a "superposition of states" in quantum mechanics.



For example, in a diazomethane molecule, the resonance structures convey that there is a buildup of negative charge on two separate atoms: both the carbon and the terminal nitrogen. In a given situation, the diazomethane may behave one way or the other.



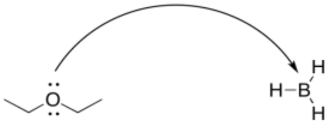
A resonance arrow does not imply that two compounds can change back and forth. It doesn't even mean that they can switch back and forth extremely rapidly. It means that there are two different structures that we can draw for the compound, but that neither one describes the compound satisfactorily. In general, that's because of delocalisation. At least one electron in the compound is not restricted to one position as indicated in the structural drawing; instead, it spreads out to be in two positions at once. Remember, electrons are very small and they enjoy particle-wave duality. They don't have to behave like little objects that have to be moved. They can behave like waves that extend through space.

Curved Arrows: Bond-Making and -Breaking Events

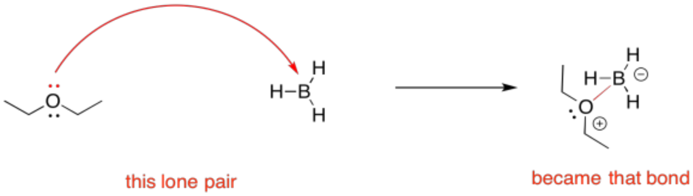
Among the unlearned, curved arrow conventions are just a curly fluorish on a drawing of a reaction. Used properly, these symbols convey meaning to the reader and enhance our understanding of a mechanism.

A curved arrow illustrates the path taken by a pair of electrons during a reaction. The stem of the arrow starts at the electron pair in question; it's usually a lone pair, but it could also be a pi bond in some cases. The arrowhead points to the position that attracts the electrons; that might be a cation or some other electron-deficient site.

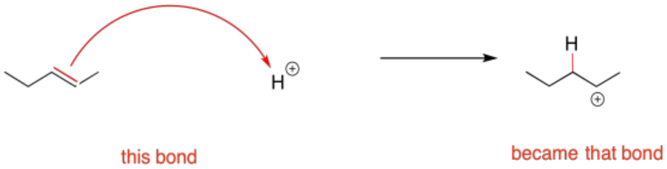
For example, in a Lewis acid-base reaction, the arrow would curve from the lone pair on the Lewis base to the electron-deficient atom in the Lewis acid. It might curve from a lone pair on an oxygen atom to a boron atom.



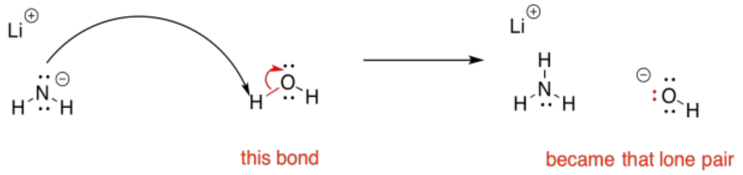
If we follow through to show the product of the reaction, we would find that a new bond is formed. The new bond used to be a lone pair, but now it is shared between the Lewis base and the Lewis acid. The curved arrow shows the direction of electron flow. The curved arrow also highlights the transformation of that lone pair into a bond.



Something similar happens when the Lewis base is really an alkene nucleophile. The pi bond in the alkene is transformed into a new sigma bond.



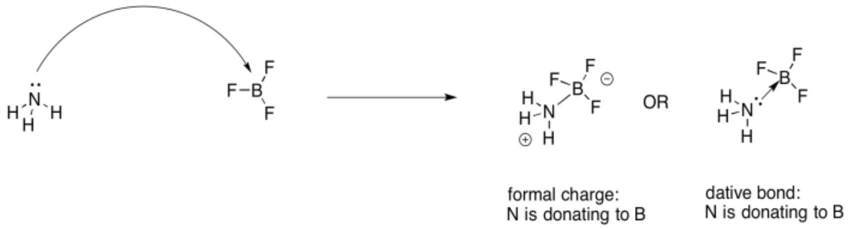
Curved arrows don't just illustrate bond formation. They can also illustrate bond breaking. In a proton transfer, a sigma bond might be converted into a lone pair. That's the opposite of what we saw in the Lewis acid-base reaction.



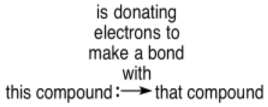
Because curved arrows illustrate transformations between non-bonding and bonding electrons, it's important to show the electrons in a mechanism. That means showing lone pairs on heteroatoms such as oxygen and nitrogen. When we do so, it underscores the changes that are occurring in that step. It makes the reaction pathway more clear on paper, and it also reinforces the physical changes in the structure of the molecule over the course of the reaction.

Working with Dative Bonds

A Lewis acid-base reaction results in a Lewis adduct. In the Lewis adduct, one partner has donated a lone pair to the other partner, forming a bond. If the Lewis acid and the Lewis base are both neutral (uncharged), then there will be formal charges on the Lewis acid-base adduct. The Lewis base has shared an entire pair of electrons to form a bond, rather than just contributing one electron to form a regular covalent bond. It will have a formal positive charge. The Lewis acid will contribute no electrons of its own, but will still gain a bond. It will have a formal negative charge. The adduct is a zwitterion: neutral overall, but containing both a positive and a negative formal charge on different atoms.

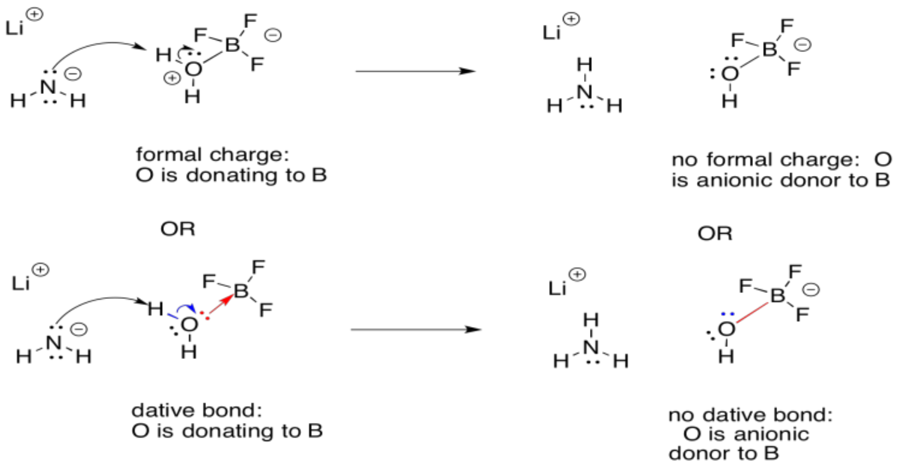


Formal charges tell us something real about the structure, because there really has been a net transfer of electron density from the Lewis base towards the Lewis acid. However, there is an alternative way of showing this arrangement, using a dative bond formalism. That requires another arrow. This one is short and straight, and points from the lone pair on the neutral donor attom toward the acceptor atom.



The dative bond arrow has something in common with the curved arrow. It illustrates the transfer of electron density from a lone pair toward an electrophile. However, it is meant to be read as static, rather than dynamic. It is structural, rather than reactive.

The advantage of the dative bond formalism is simply that it obviates the use of formal charge. That can be useful in more complicated molecules that would otherwise have lots of formal charges on different atoms. In addition, it reminds us of the transient nature of a dative bond, which usually form reversibly.

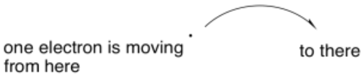


There's one more fine point about dative bond formalisms. Usually, the short arrow is only used to illustrate electron donation from a neutral donor. The bond from an anionic donor to an electrophile is generally drawn as a simple straight line, like any other bond. That distinction is sometimes helpful in underscoring the different types of ligands in a more complicated coordination complex.

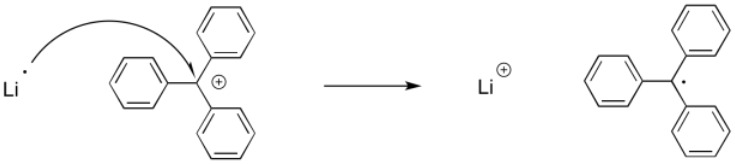
As a result, if we were to illustrate a proton transfer involving an activated, neutral molecule, the short arrow in the neutral donor would shift to a straight line in the anionic donor.

Radicals and Single-Electron Transfers

Some reactions do not involve the movement of an electron pair, and so we need a symbol that conveys the idea of a single electron participating in a chemical change. Instead of the refular curved arrow that suggests the movement of two electrons, we use a similar arrow having only half an arrowhead. It's more like a fish hook.

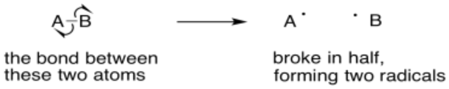


In a single electron transfer, one electron is exchanged from a position on one atom or molecule to a position on another. We can show that using the single-electron arrow.

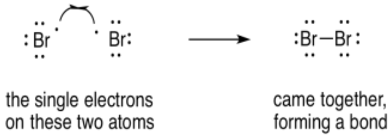


Note that there is a different consequence here than in a two-electron process. A two electron process typically results in the transformation of a lone pair into a bond, or vice versa. A single electron process does not. A bond requires two electrons, so when a single electron moves from one place to another, we are not forming or breaking bonds.

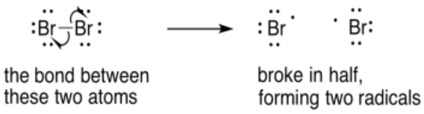
However, there are some one-electron processes that do entail bond formation or bond cleavage. Radical reactions involve unpaired electrons that pair up to make a bond. They might also involve bonds that break to produce unpaired electrons.



Radical reactions are often very different from the typical polar reactions such as acid-base reactions. Rather than being driven by electrostatic attractions, they are motivated by electron pairing and relative bond strengths. So, we might do something that would seem counter-intuitive if we are used to dealing with polar processes. In forming a bond, we would show two of those fish hook arrows coming together; the electrons are not repelling each other because they are becoming spin-paired.



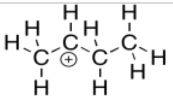
In breaking a bond, we would show two arrows diverging in opposite directions. The electrons that were spin-paired in the bond are retreating, each to a different side of the original bond.



In polar reactions, we never really have arrows moving in opposite directions like that. They are drawn towards a positive position, so they move in the same direction. In radical reactions, to fish hooks meeting together signals bond formation, whereas two fish hooks leading away from each other signals bond breaking.

3.4: Solutions to Selected Problems

a)



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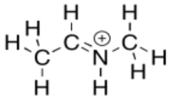

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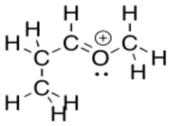

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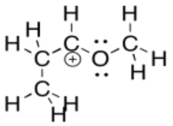

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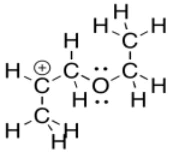

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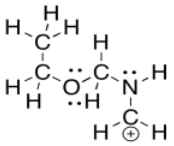

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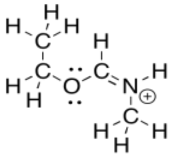

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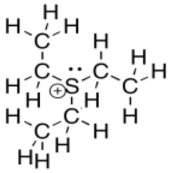

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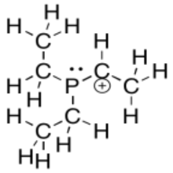

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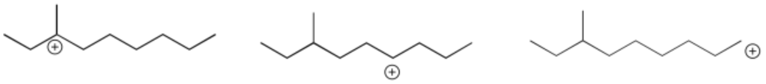

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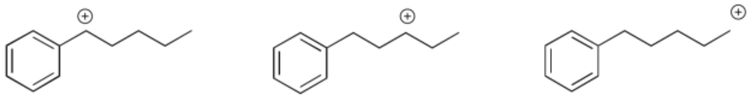

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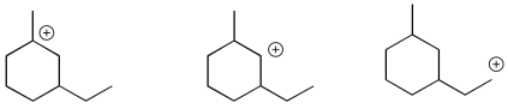

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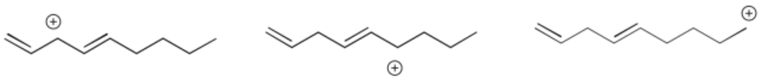

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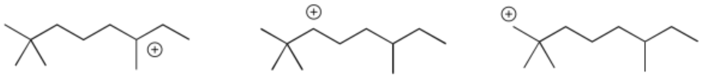

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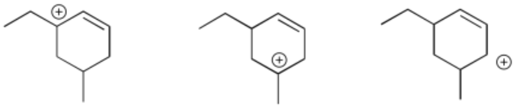
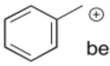
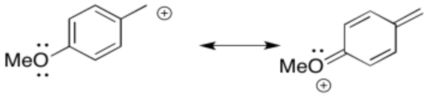




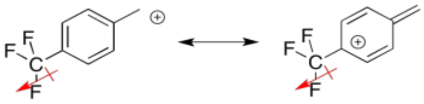
benzyl cation

a)



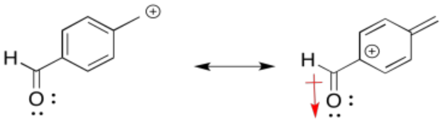
more stable - extra delocalisation

b)



less stable - charge repulsion

c)



less stable - charge repulsion

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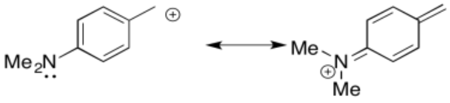
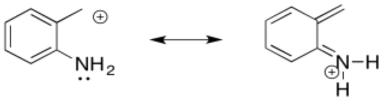


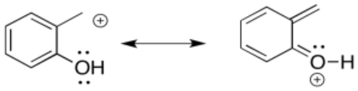
more stable - extra delocalisation

e)



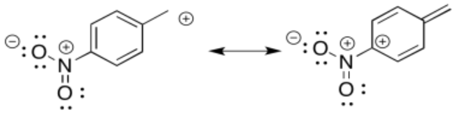
more stable - extra delocalisation

f)



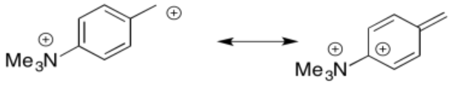
more stable - extra delocalisation

g)

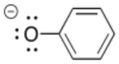


less stable - charge repulsion

h)

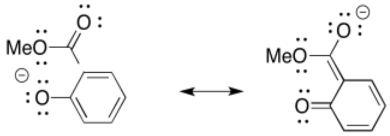


less stable - charge repulsion



phenoxide or phenolate anion

a)

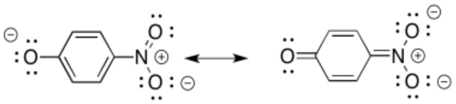


more stable by delocalisation

b)

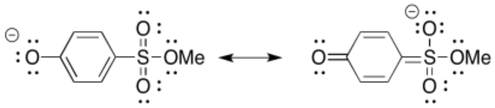
less stable by repulsion

c)



more stable by delocalisation

d)



more stable by delocalisation

e)

less stable by repulsion

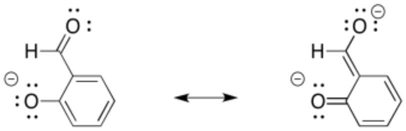
f)

more stable by inductive delocalisation

g)

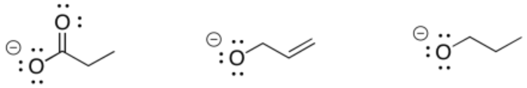
less stable by repulsion

h)



more stable by delocalisation

a)



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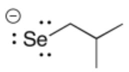
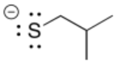
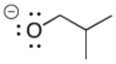

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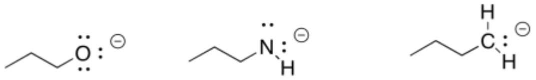

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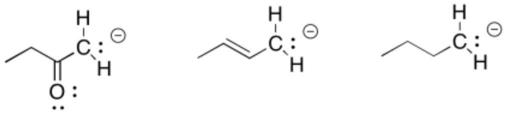

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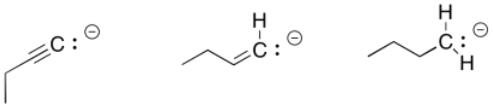

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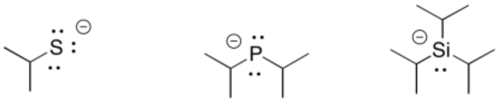

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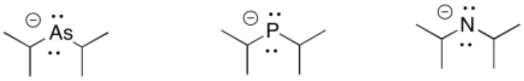

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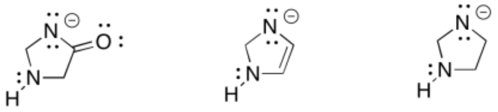

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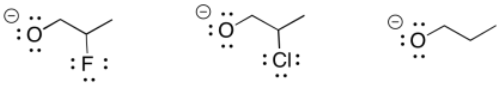


$$\text{a) formal charge} = \#e^- \text{ in periodic table} - \#e^- \text{nonbonding} - \frac{\#e^- \text{in bonds}}{2}$$

$$\text{formal charge} = 4 - 1 - \frac{6}{2} = 0$$

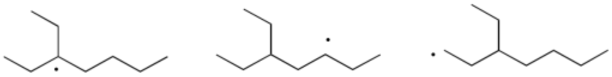
$$\text{b) formal charge} = \#e^- \text{ in periodic table} - \#e^- \text{nonbonding} - \frac{\#e^- \text{in bonds}}{2}$$

$$\text{formal charge} = 5 - 3 - \frac{4}{2} = 0$$

$$\text{c) formal charge} = \#e^- \text{ in periodic table} - \#e^- \text{nonbonding} - \frac{\#e^- \text{in bonds}}{2}$$

$$\text{formal charge} = 6 - 5 - \frac{2}{2} = 0$$

a)



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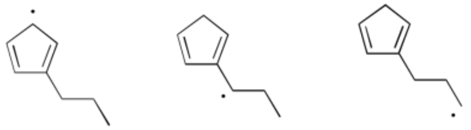

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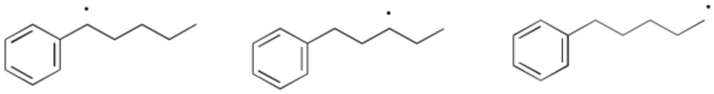

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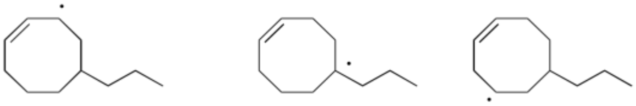

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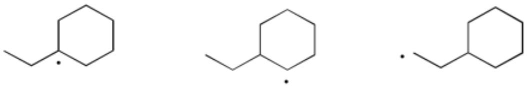

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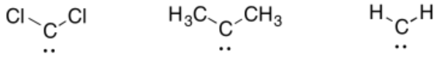

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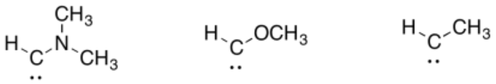

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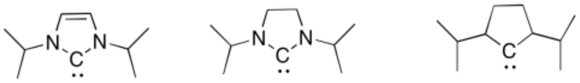

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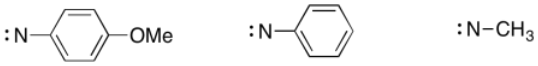

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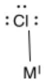

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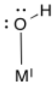

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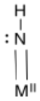

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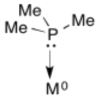

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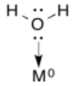

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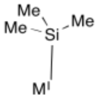

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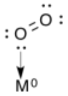

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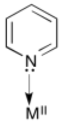
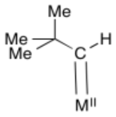


i)



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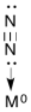

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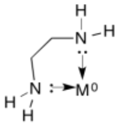

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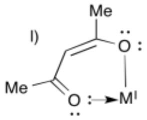

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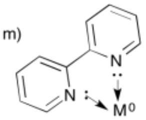

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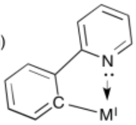

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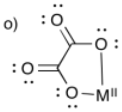

p)

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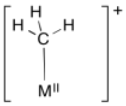

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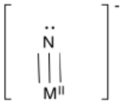
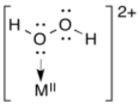


s)



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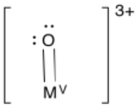


CHAPTER OVERVIEW

4: Oxygen Binding and Reduction

4.1: Introduction

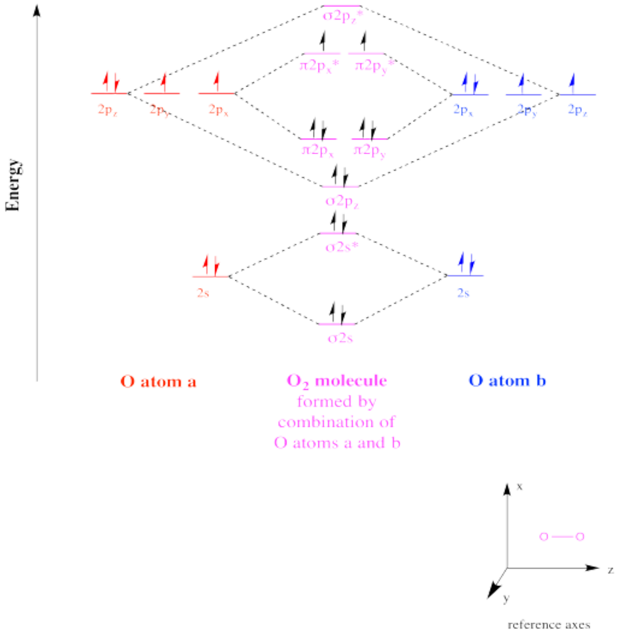
The earth is an oxygen-rich place. Elemental oxygen, O_2, makes up about 20% of the earth's atmosphere by weight. Oxygen atoms, bound in water, make up about 85% of the hydrosphere (the earth's oceans, rivers and lakes). Oxygen atoms also comprise about 45% of the lithosphere (the earth's crust), mostly bound in the form of silicates, aluminosilicates and carbonates.

In this chapter, we will focus on elemental oxygen and the ways nature has evolved to make use of O_2 as a reactant. Dioxygen has a double nature, like Dr. Jeckyll and Mr. Hyde. It is necessary for life, providing a driving force for basic metabolic processes. That driving force ultimately comes from the exergonic conversion of O_2 into water. However, nature has also had to evolve mechanisms to protect itself against reactive oxygen species, which would otherwise cause permanent damage to biomolecules. Those reactive oxygen species arise from the reduction of atmospheric oxygen. They also have dual roles, acting as important cell signalling molecules as well as dangers to the cell, and so their regulation is crucial in biochemistry.

Although da Vinci noted in the 1400's that air contained several components, one of which could support combustion, in a sense oxygen was not "discovered" until the turbulent 1770's. It was first isolated from air in experiments performed by Carl Wilhelm Scheele, a German pharmaceutical chemist (although his homeland of Pomerania was at that time part of Sweden, which extended to the south shores of the Baltic sea). This discovery was soon followed by an independent one by the English scientist and fire-and-brimstone preacher, Joseph Priestley. However, early research on oxygen is often associated with Antoine Lavoisier, whose experiments built upon those of Scheele and Priestley and are generally considered to mark the beginnings of modern chemistry.

These men did not lead long, peaceful lives. Priestley was forced to emigrate to Pennsylvania because of his troublemaking ways, Lavoisier was unfortunately executed during the reign of terror following the French Revolution, and Scheele's habit of tasting his experiments led to an early death from kidney failure. In contrast, a fourth scientist who is closely associated with oxygen, Henry Cavendish, died a wealthy (but remarkably reclusive) man of nearly eighty, having achieved some fame in England for his discoveries. Cavendish established the exact proportion of oxygen and nitrogen in the air, demonstrated in an impressively explosive way how oxygen and his other discovery, hydrogen, could be combined to make water, and even found time to accurately weigh the planet Earth.

Oxygen, present at the birth of modern chemistry, continued to make appearances in the development of the field. In the 1840's, Michael Faraday, the great English chemist and physicist, first demonstrated the O_2 is paramagnetic, meaning it is attracted to a magnetic field. Sixty years later, American chemist and physicist Robert Mulliken explained this property through "molecular orbital theory" (sometimes called Hund-Mulliken theory after its developers). This explanation should be familiar to college-level chemistry students.



The molecular orbital interaction diagram for O_2 shows how two oxygen atoms would combine under symmetry constraints to produce new orbitals in an O_2 molecule. The net four electrons in bonding levels (i.e. at lower energy than they were in the atoms, as opposed to antibonding levels, which are at higher energy than they were in the separate atoms) suggests two bonds, since a bond between two atoms generally has two electrons. This prediction is also predicted by simple Lewis theory (i.e. that's what you would draw in a Lewis structure).

However, in contrast to the Lewis structure, in which all of the electrons in O_2 are paired, Mulliken's MO picture suggests that there are two unpaired electrons. Because species with unpaired electrons are attracted to magnetic fields, this picture provides a compelling explanation for the paramagnetic behaviour of elemental oxygen.

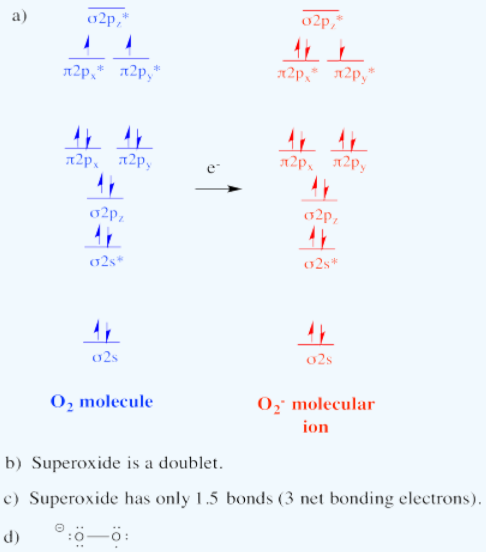
This species is called a triplet state. A triplet is a state in which there are two net spins in the molecule, which has consequences in spectroscopy. If there were no net spins (i.e. they are all paired), the state would be described as a singlet. If there were one net spin (all other spins paired), it would be called a doublet.

Exercise 4.1.1

If O_2 accepts one electron, it forms a species called "superoxide" ion.

a. Draw the MO diagram for the species formed when O_2 accepts one electron.
b. Is this new species a singlet, doublet or triplet?
c. How would you describe the net number of bonds (the bond order) in this species?
d. Draw a Lewis structure for this species.

Answer



b) Superoxide is a doublet.

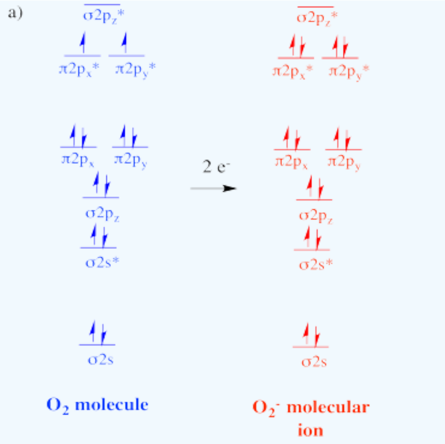
c) Superoxide has only 1.5 bonds (3 net bonding electrons).

Exercise 4.1.2

If O_2 accepts two electrons, it forms a species called "peroxide" ion.

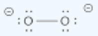
a. Draw the MO diagram for the species formed when O_2 accepts two electrons.
b. Is this new species a singlet, doublet or triplet?
c. How would you describe the net number of bonds (the bond order) in this species?
d. Draw a Lewis structure for this species.

Answer

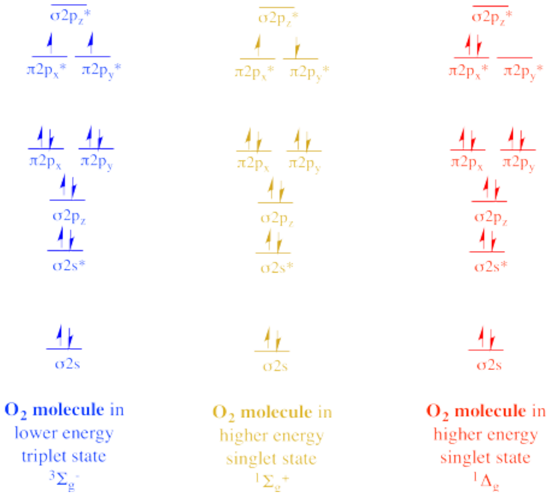


b) Peroxide is a singlet.

c) Peroxide has only 1 bond (2 net bonding electrons).

d) 

In the 1930's, other forms of O_2 were discovered by spectroscopists. By monitoring the interaction of light with oxygen, they detected evidence for different electronic states, meaning different arrangements of electrons. W. H. J. Childs and R. Mecke observed a singlet state in which two electrons appeared to be unpaired but with opposite spins. According to Hund's rule, this a higher energy state, because the electrons in singly-occupied orbitals should have the same spin. This state is described by spectroscopists as the ${}^1\Sigma_g^+$ state. The usual form of O_2 is described as the ${}^3\Sigma_g^-$ state. The ${}^1\Sigma_g^+$ excited state is about 25 kcal/mol higher in energy than the ${}^3\Sigma_g^-$ ground state.



Gerhard Herzberg, the German-Canadian Nobel Laureate, observed a second singlet state. In this case, the electrons are spin-paired within the same orbital, also in violation of Hund's rule, since an empty orbital exists at the same energy level. This form of O_2 is described as the ${}^1\Delta_g$ state. It is about 35 kcal/mol higher in energy than the ground state.

Although they are clearly higher in energy than the usual ground state, these two singlet states can arise when an oxygen molecule absorbs extra energy. Singlet oxygen undergoes reactions that are different from the usual triplet oxygen and it is considered a reactive oxygen species; it is linked to LDL cholesterol oxidation and cardiovascular damage, for example.

There is one last historical development in oxygen chemistry that we'll look at here. In the 1960's, Estonian-American chemist Lauri Vaska demonstrated the reversible binding of O_2 to a coordination complex, *trans*-[Ir(CO)Cl(PPh$_3$)$_2$]. This observation was made when Vaska was a research scientist at the Mellon Insitute, now part of Carnegie-Mellon University in Pittsburgh.

? Exercise 4.1.3

Show a mechanism, with arrows, for the binding of oxygen to Vaska's complex.

This last example is particularly important in this chapter. The binding of oxygen by a transition metal is, of course, an essential step for the survival of every vertebrate. However, haemoglobin is a very complicated molecule. At the time that Vaska made his discovery, there was a need to demonstrate things like how an oxygen molecule could bind to a metal. How did it attach? Did it bind though a lone pair or a pi bond? In what geometry did it bind? Was the Fe-O-O bond linear? Was it angular or bent?

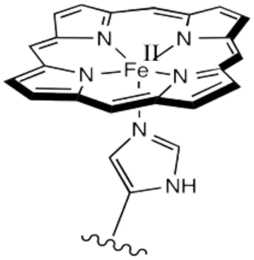
Frequently in the field of bioinorganic chemistry, simple coordination complexes serve as models for the complicated tasks carried out by transition metals in biology. "Model compounds", as they are called, provide the kind of precedent upon which researchers start to build a picture of what is happenning within the complex environment of the cell. That kind of precedent may take the form of structural studies, in which particular coordination environments and geometries may indicate what may be possible in a metalloenzyme. It may also involve reactivity studies, in which a small complex believed to resemble the active site of a metalloprotein is shown to undergo reactions that may be relevant to biological processes.

Visit an overview of oxygen from a biochemical perspective at Henry Jakubowski's Biochemistry Online.

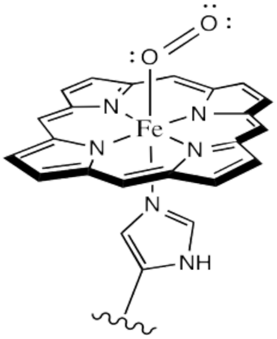
4.2: Oxygen Binding

Oxygen is vital to life. Very small organisms can get enough oxygen passively from their surroundings, but larger, more complicated organisms need to have better mechanisms for getting oxygen to the cells. Medium-sized organisms such as insects can manage to pump air to their tissues via a system of tubes leading in from pores along their bodies. Organisms bigger than that need a more complicated circulation system involving arteries and veins. Oxygen dissolves pretty well in water, but we can get even more oxygen into our system by binding it to carrier molecules.

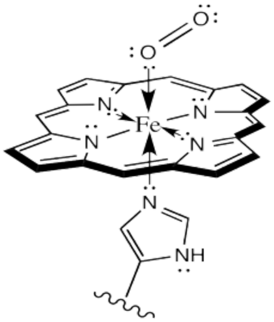
The most common carrier molecule for oxygen, used by vertebrates like us, is hemoglobin. Hemoglobin contains a five-coordinate Fe(II) centre in a heme or porphyrin ligand. In the picture, only the coordination complex is shown, stripped of the surrounding protein. Also, there are other groups attached to the porphyrin (the nitrogen-containing ring) but they are left out of the picture for simplicity.



Oxygen binds to the iron in the heme, forming an octahedral iron complex. This form is called oxyhemoglobin; the form without the bound oxygen is called deoxyhemoglobin. Lots of interesting things happen as a result of oxygen binding, structurally speaking. First of all, the heme changes shape. In order to accommodate the change from a pseudo-square planar geometry to an octahedral one, the shape of the heme changes from a distorted bowl to a plane.



Sometimes, keeping track of oxidation states in coordination complexes is easier if using dative bond formalisms. In particular, if a donor arom is neutral, the bond to the metal is shown using a dative bond symbol. That's a short, straight arrow from the donor electron pair to the metal. Bonds between anionic donor atoms and the metal are shown as regular short lines, as we typically draw other bonds.



Looking at the complex that way, it is easier to see that the iron atom is depicted as Fe(II); it has two anionic nitrogen donors from the heme ring. We'll look into the situation more closely later.

? Exercise 4.2.1

Draw d orbital splitting diagrams for the iron porphyrin centre in deoxyhemoglobin and in oxyhemoglobin.

Hemoglobin is exceptionally good at transporting oxygen to the tissues not only because it can bind iron tightly under the right conditions, but because it can also let go under the right conditions, releasing oxygen to the tissues. Because hemoglobin is such a complex protein, it has been very difficult to study, although researchers have made impressive strides in undertsanding proteins in recent years.

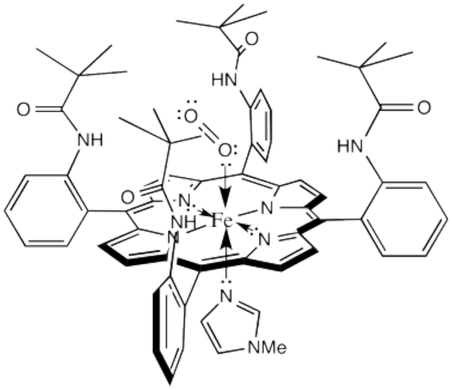
Instead, bioinorganic chemists have developed model compounds to gain insight into hemoglobin and other important biological compounds. Model compounds are relatively simple compounds that possess a number of characteristics of their more complicated cousins. For example, simple porphyrins are relatively easy to make; if you wanted to study oxygen binding with a simple example, an iron-porphyrin complex would be a great model complex.

The trouble is, that doesn't work very well. Such a complex binds oxygen irreversibly; it never lets go. Part of the problem is that the oxygen "bridges" to other iron-porphyrin complexes, which wouldn't happen in hemoglobin. In hemoglobin, the heme is buried and protected within the protein.

? Exercise 4.2.2

Show the complex that would result if an oxygen molecule bridged between two iron porphyrin complexes.

The laboratory of James Collman at Stanford University has been involved in modelling hemoglobin for decades. They succeeded in demonstrating reversible oxygen binding to the "picket fence" porphyrin complex shown below. The bulky tert-butyl groups serve to keep the bound oxygen from bridging to another complex.



That alone is an interesting result. It demonstrates that one of the many roles for the protein in this system is to sterically protect the iron heme complex, modifying its reactivity.

There is just one small problem. It's called the *M* value. The *M* value is an index of the discrimination between oxygen binding and carbon monoxide binding. It's actually the ratio of the partial pressures of the two gases needed to half-saturate the hemoglobin (i.e. so that 50% of iron atoms have bound O_2 or CO).

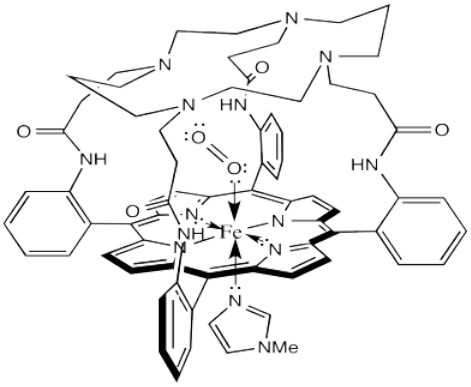
$$M - \frac{P^{CO}_{1/2}}{P^{O_2}_{1/2}}$$

The lower the *M* value, the greater the favorability for O_2 binding compared to CO binding. In hemoglobin, this value is about 100, although it will vary from one organism to another. That means hemoglobin binds CO about 100 times better than it binds O_2. However, the picket fence heme has an *M* value over 25,000. That means it is much poorer at binding O_2, relatively, than hemoglobin.

Why worry about CO binding in these studies? Of course, carbon monoxide poisoning is a serious and potentially fatal condition. There is a deeply problematic consequence of CO poisoning, however, that could be much worse if the *M* value in an organism was as high as in the picket fence porphyrin. CO is actually a product of the normal breakdown of heme molecules over time in the cell.

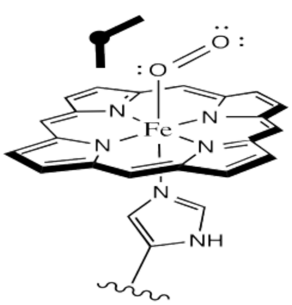
If our hemoglobin had an *M* value like that of the picket fence porphyrin, we would all be dead, poisoned by our own metabolic processes.

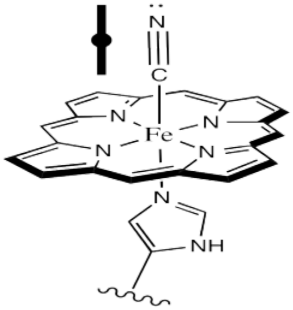
Not content to rest on their laurels, the Collman lab went back to the drawing board and developed lots of other model complexes. For example, the one shown below has an *M* value closer to 0.005.



What does that tell us about hemoglobin? It may be nothing, but it could be indicating another role for the surrounding protein in the hemoglobin molecule. The domed or vaulted model compound suggests a protective covering for the oxygen binding site. Is it possible that O_2 can fit inside but CO cannot?

It is pretty well-established via other model studies, as well as direct study of oxyhemoglobin, that when oxygen binds to a metal such as iron, the Fe-O-O forms an angle of somewhere around 120 °. The complex has a bent geometry. However, when CO binds to a metal, it does so in a linear fashion. It may be that in a vaulted model complex, the CO simply can't stand up straight, so the complex is destabilized. Presumably, the protein could contribute to a similar destabilization of CO-bound hemoglobin.



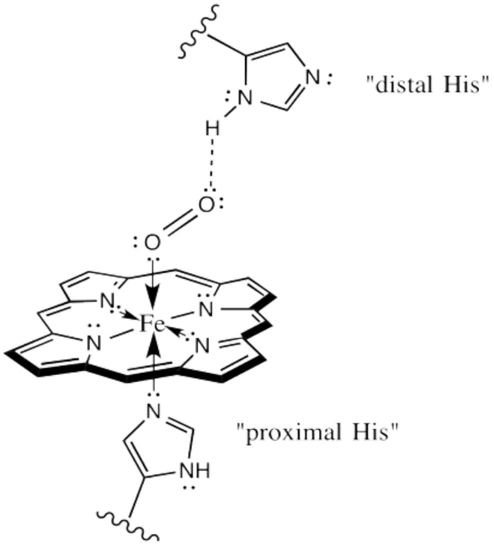


Exercise 4.2.3

Why might O_2 bind in a bent fashion whereas CO bounds in a linear mode?

This idea has been somewhat controversial. Results from quantum mechanical calculations, for instance, suggest that the Fe-C-O bond actually has a fair amount of leeway. These results suggest that the CO can be "tipped over" and still remain strongly bound. Nevertheless, Collman's results provided a useful starting point for further investigations.

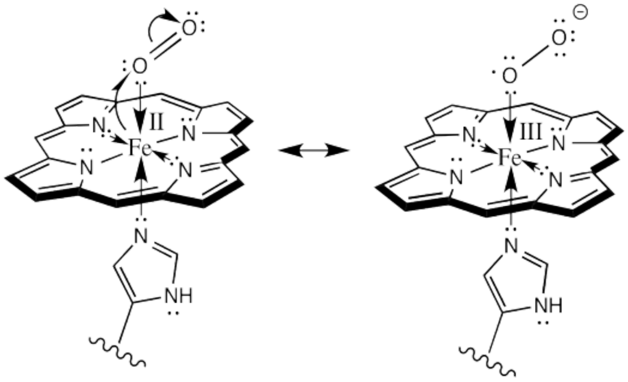
The protein may play other roles in enhancing oxygen selectivity. X-ray crystallographic studies suggest a role for hydrogen bonding between the "distal histidine" site and bound oxygen. The distal site simply refers to a second nearby histidine, other than the one that is bound to the iron (the "proximal histidine"), and a little further away. That histidine could be ideally situated to hydrogen bond with bound oxygen, but out of place for optimal interaction with a bound CO.



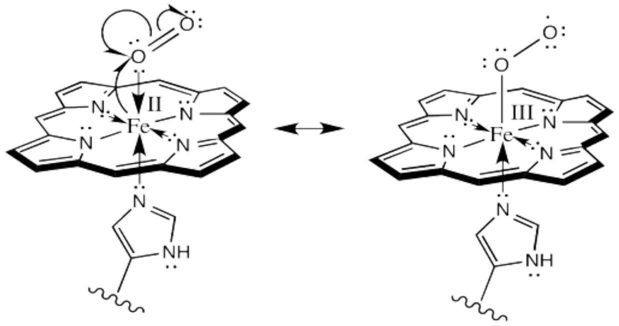
There is one more important event to look at in oxygen binding. Evidence indicates that oxyhemoglobin is actually an Fe(III) species, rather than Fe(II). The iron is oxidized by the bound oxygen.

As always, it is useful to map out the movement of electrons, schematically, in this event. Because this event would be a one electron oxidation, we need a different kind of arrow to show where the electrons go. Most of our previous mechanisms have involved electron pairs rather than single electrons. For single electrons, we show a single-headed arrow, rather than a double-headed one.

Here is one way we could show the oxidation of the iron (and the reduction of the oxygen):



Or alternatively, we could show it like this:



Remember, in the structure on the right, the oxygen bound to iron is considered an anionic donor, shown with a regular line bond instead of a dative arrow.

There is something really amazing about that last event. Hemoglobin doesn't form an oxygen complex at all. It forms a complex with superoxide ion, O_2^-, which it has manufactured itself. When it is ready for delivery to the cells, the superoxide gives back the electron to the iron, and turns back into an everyday oxygen molecule.

Exercise 4.2.4

Describe in words what the curved arrows are showing in the above two schemes.

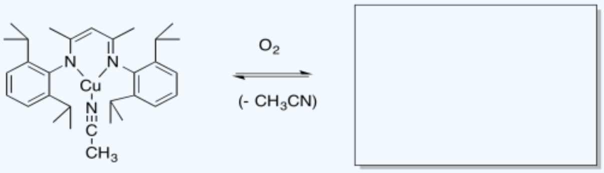
Exercise 4.2.5

Explain why the oxidation of iron would lead to tighter binding of the oxygen.

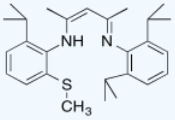
Exercise 4.2.6

Modeling studies of Cu(I) complexes like the one below reveal that exposure to O_2 results in a square planar Cu(III) peroxide complex (Tolman et al, *J. Am. Chem. Soc*. **2006**, *128*, 3445-3458 and references therein).

a) Draw the product of the reaction.



b) A similar copper complex prepared with the following ligand also binds O_2, but with a much lower equilibrium binding constant. Draw the copper complex and the O_2 adduct and explain the difference in O_2 binding constants.



c) DBM (dopamine β-monooxygenase) and a similar copper monooxygenase, PHM (peptidylglycine α-hydroxylating monooxygenase), both contain copper atoms bound to two histidines, a cysteine and a water. Explain the researchers' choice of model compounds above in this context.

d) Explain how the cysteine in these active sites might help to control OH radical levels in the cell.

4.3: Oxygen Reduction

Molecular oxygen is exploited in a variety of ways in biology. Apart from its central role in metabolism, it also plays a crucial part in the modification of many compounds through the incorporation of oxygen atoms into the structure.

For example, the cytochromes P450 form an important class of enzymes involved in the oxidation of substrates, chiefly in the liver. One atom of oxygen from an O_2 molecule is incorporated into the substrate molecule; the remaining oxygen atom is converted to water. This type of enzyme is called a "monooxygenase" because of the addition of one oxygen atom from O_2 into the substrate.

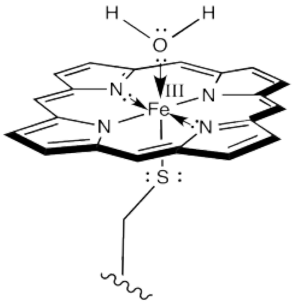
The addition of oxygen atoms to molecules, typically in the form of hydroxyl groups, is vitally important. The reaction may have evolved for a number of reasons. A key reason is to increase the water-solubility of small organic molecules, which are then more easily excreted via the urine or broken down via subsequent reactions. Hydroxylation lets us get rid of foreign substances. Otherwise, these hydrophobic molecules would build up in the tissues.

The cytochrome P450 pathway is a major avenue for the breakdown and excretion of pharmaceuticals, for instance. We can get rid of these substances after they have done their job. In other cases, pharmaceuticals are not active until they are hydroxylated; the reaction acts as an "on" switch. In still other cases, hydroxylation is a dangerous complication, converting a helpful pharmaceutical into a toxin.

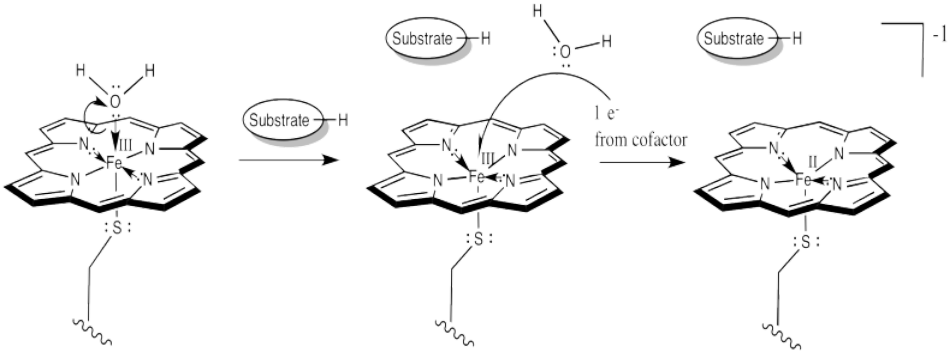
Exactly how does the O_2 get broken into pieces suitable for incorporation into other molecules? It's a very complicated problem. There is an entire field of chemists who study "small molecule activation", which refers to the breakdown of things like O_2, N_2, CO or methane for their subsequent conversion into other compounds. In fact, there is an entire field of chemists and biochemists who just focus on cytochrome P450, trying to learn more about how it works. They do so both to understand more about a biological system that is related to human health and to gain insight into how to improve industrial processes involving oxidation of substrates.

Some things are pretty well understood. We'll take a general look, leaving out some important details so things aren't too overwhelming.

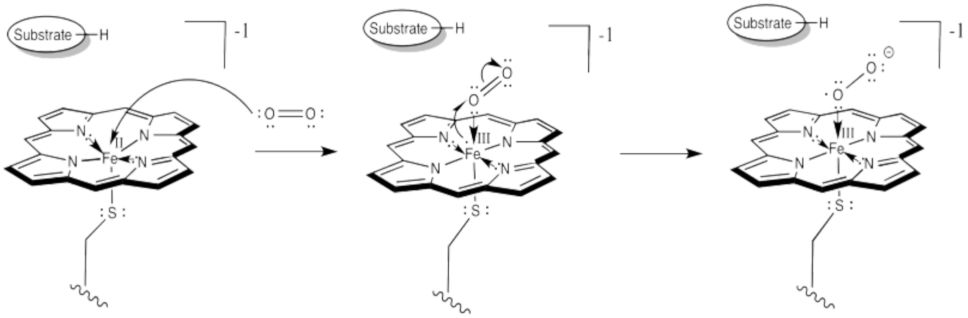
The first step is just the binding of dioxygen to a metal. In cytochrome P450, that iron atom looks very much like the one in hemoglobin. In its resting state, it is formally an Fe(III) ion in a porphyrin ring, but with an axial cysteine donor instead of a histidine. In addition, a water molecule is coordinated to form an octahedral complex.



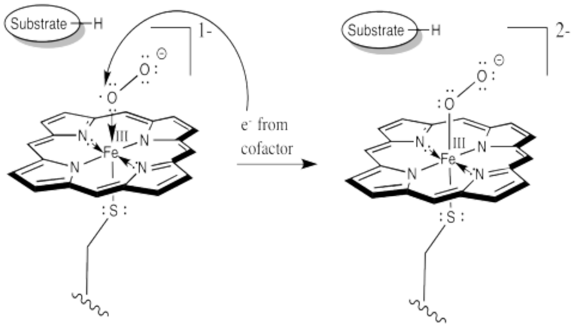
That leaves no place for the dioxygen to bind. However, once the substrate enters the enzyme, a conformational change results in loss of the water molecule. After that, an electron is delivered from a cofactor, leading to an Fe(II) complex.



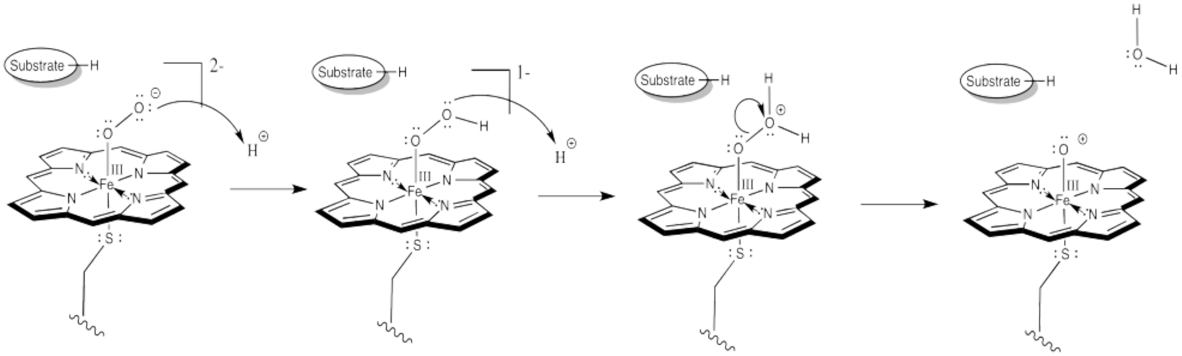
At this point, things are looking a little more like hemoglobin. Just as in hemoglobin, the O_2 binds to the iron, which immediately transfers an electron to the bound dioxygen, forming an Fe(III) superoxide complex.



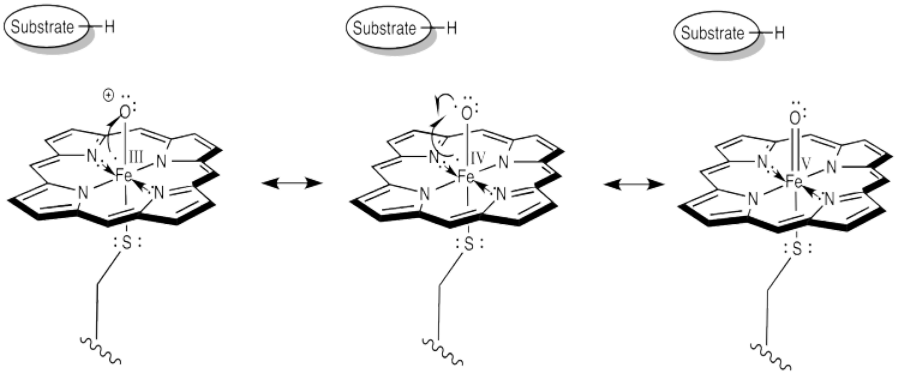
The difference is that things do not stop there. The addition of a second electron from a cofactor tips things a little further. One more electron turns the superoxide ion into a peroxide ion.



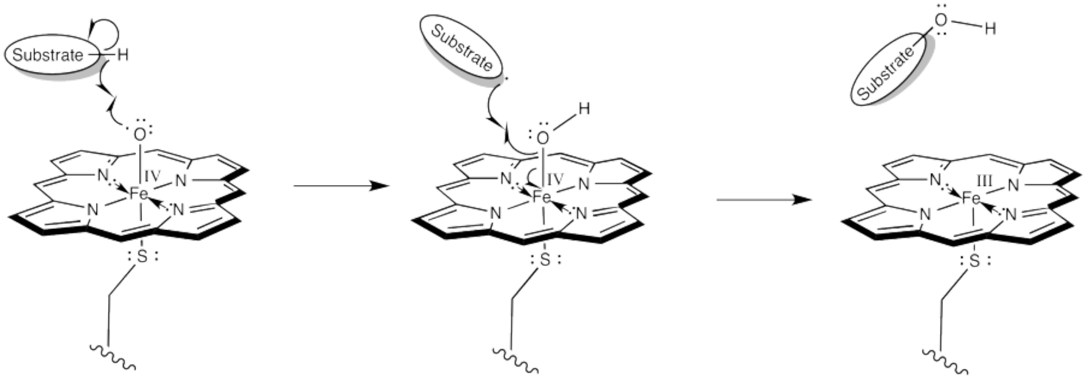
At this point, we have completely severed the first of the two O=O bonds. We are almost there. The subsequent addition of two protons leads to the formation of a water molecule. Now we have one oxygen atom bound to iron.



How do we think about that species? We can think about several resonance structures. The electron-deficient oxygen is attached to an iron atom. The iron possesses a reservoir of electrons. It can donate one to the oxygen atom. It might even donate two electrons, making an iron (V) oxide complex, but that might be going too far.



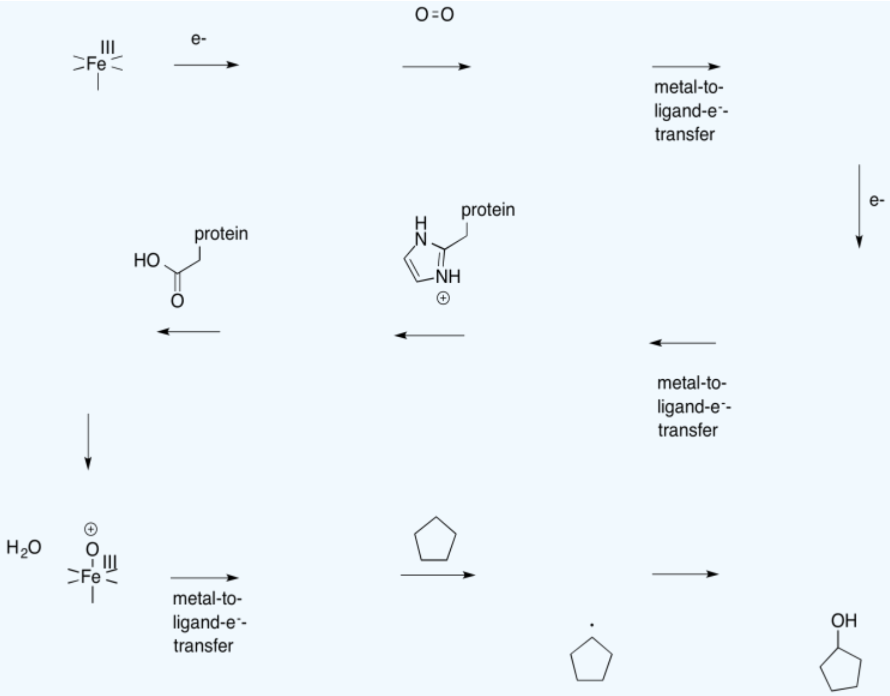
In the resonance structure with iron (IV), we see an oxygen atom with a single, unpaired electron. This species is called a radical. Radicals are notorious for ripping hydrogen atoms from other molecules. That just makes a new radical. This is the trouble with radicals; they are hard to get rid of, because they are always making more. It also makes an iron hydroxy complex, which can combine with the radical in a "rebound" step to form the hydroxylated compound.



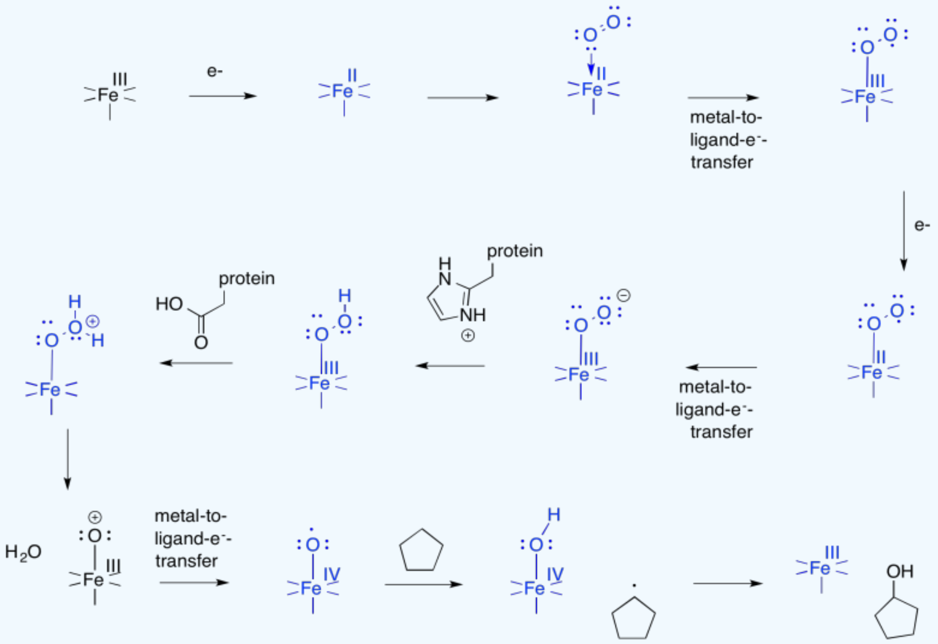
We will see more of this kind of event in the chapter on radicals.

Exercise 4.3.1

Fill in the missing intermediates in the following scheme.

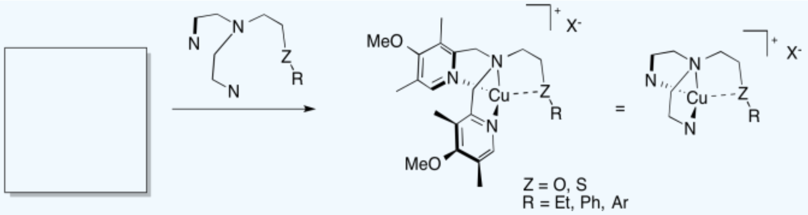


Answer



? Exercise 4.3.2

The Karlin lab (Johns Hopkins) has developed a series of model compounds for copper-containing monooxygenases (*J. Am. Chem. Soc.* **2014**, *136*, 8063-71).



a) Fill in a reasonable starting material that you might find in the chemistry stockroom.

b) Reaction with O_2 gives dimeric copper complexes (L_nCu_2) of two types: with one bridging peroxide anion or with two bridging oxide anions. Draw both dimers.

c) O_2 is reduced / oxidized (select one) by _____ (number of) electrons to make peroxide anion.

d) O_2 is reduced / oxidized (select one) by _____ (number of) electrons to make oxide anion.

e) Identify the oxidation states of the copper ions in the two dimers.

f) In the ligand, if the group ZR = SEt, the reaction forms the peroxide bridge. If ZR = OEt, it forms the oxide bridge. Suggest a reason why.

g) With Z = S, the group R both influences which dimer forms and affects the Cu-S bond. Predict the combination of features found in each product and provide an explanation.

R = Et peroxide / oxide Cu-S bond / no Cu-S bond

R = Ph peroxide / oxide Cu-S bond / no Cu-S bond

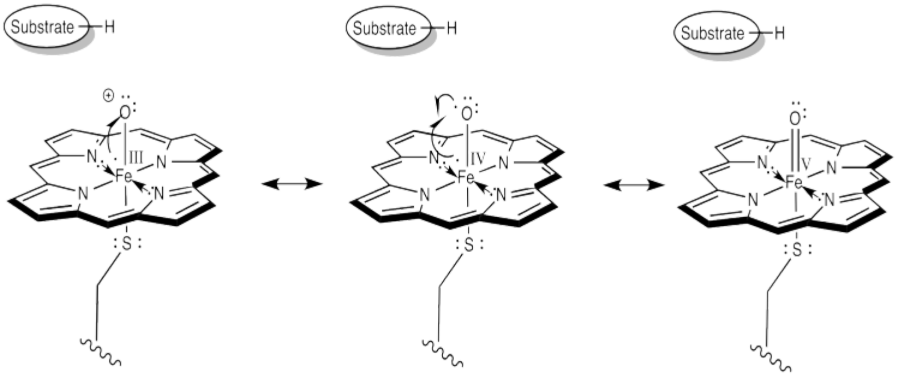
4.4: Metal Oxos

In the previous section, we saw the Fe(IV) oxo group of Cytochrome P450 do something unusual. It grabbed a hydrogen atom from a substrate molecule. It did not take a proton. It took the hydrogen atom complete with its electron.

This type of reactivity is characteristic of radicals. Radicals are species that have unpaired electrons. Generally, but not always, they have odd numbers of electrons in their valence shells, leaving one electron without a spin partner. Having an odd number of electrons also leaves these compounds short of a full octet. From that point of view, it is easy to see the driving force for a reaction, from the point of view of the radical species.

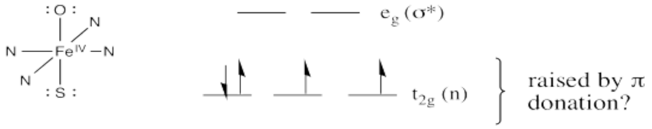
However, this reaction is unusual. There are lots of metal oxo compounds on earth, but only some of them engage in this kind of radical behaviour. What makes some oxos different, in particular some biologically important iron oxos?

Let's take another look at that active form of the iron oxo complex in Cytochrome P450.

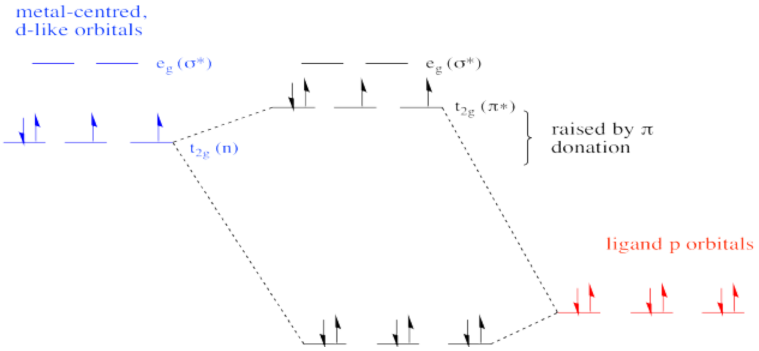


Earlier, we decided to think about this complex using the Fe(IV) structure. That would be a d^4 iron complex. The coordination geometry appears to be octahedral. Chances are that in such a high oxidation state we would have a low-spin iron. Overall, that should give the frontier orbital diagram shown below.

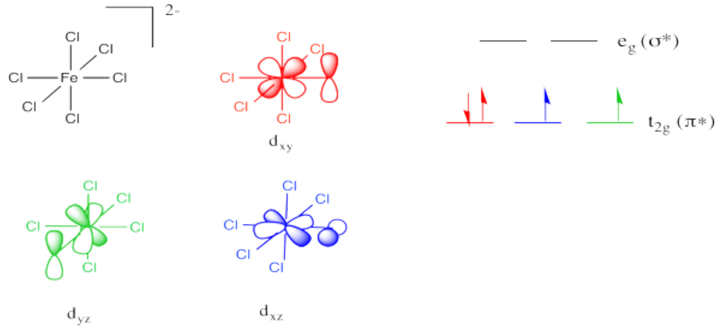
The oxo donor would have lone pairs. It would be a π donor. The same is true of the cysteine ligand trans to the oxo. We should probably modify our d orbital splitting diagram accordingly.



Remember, a π donor brings a pair of electrons from a relatively low-lying ligand orbital. The donor orbital interacts with one of the metal d orbitals that were previously non bonding. In-phase and out-of-phase combinations result. The in-phase combination is lower in energy and the out-of-phase combination is higher in energy than the levels we started with. Because the π donor is donating a lone pair, that lone pair drops in energy. It becomes a π bond. The electrons in the metal orbital involved in the interaction become anti bonding. Overall, the gap between the lower and upper d levels gets smaller.

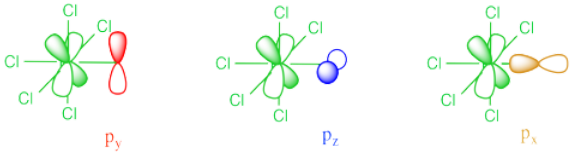


At least, that's how it would work in a normal case. In a simple example of a coordination complex, all six ligands might be the same. For example, if we had an octahedral Fe(IV) chloride complex such as $FeCl_6^{2-}$, all six chloride ligands would be potential π donors. Different p orbitals on the chlorines would be able to interact with each of the three non bonding d orbitals, raising them all in energy via a π bonding interaction.

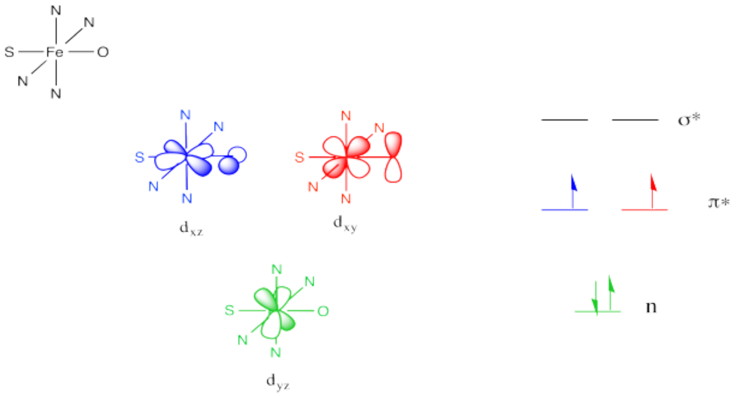


Note the choice of different orbitals to illustrate pi dontaion along different axes. In two cases, the orientation of the oxygen p orbital may have changes, or the metal d orbital may have changes, or both. There is a need for symmetry matching in these interactions.

Look at a chlorine attached to the right of the metal (along the x axis, at least as defined by the orbital labels above). It would not be able to form π overlap with the d_{yz} orbital. The symmetry isn't right.

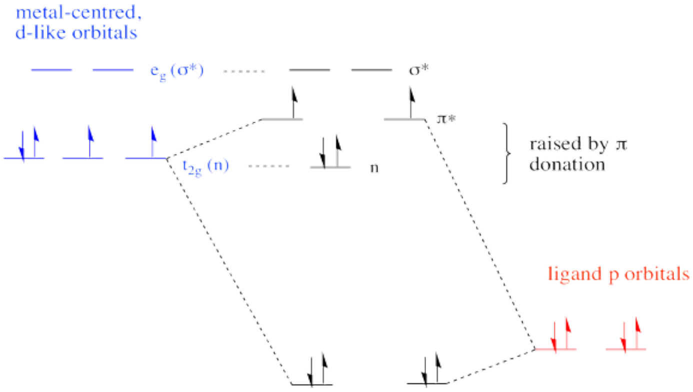


In our example of Cytochrome P450, things are different from the example in which all of the ligands were the same. In Cytochrome P450, only the oxygen and the sulfur can donate. As a result, one of the non bonding d orbitals is not participating in π bonding. That's because the π donors are unable to interact with one of the d orbitals. It is too far away and it has the wrong symmetry to overlap with either of the oxygen p orbitals that can participate in the π bond.



The same would be true for the sulfur atom, since it is located along the same axis as the oxo ligand.

The net result is different from the π donor picture we have seen before. Because the π donation is restricted along one axis, not all of the non bonding d orbitals are elevated to π* levels. Only two of them form this interaction. The third remains unchanged.

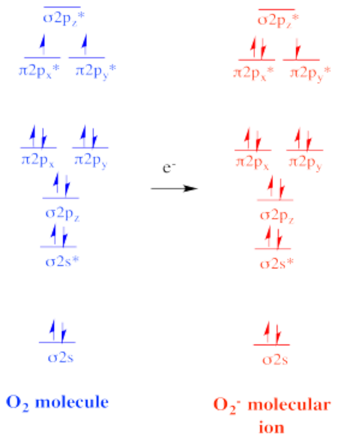


The overall frontier picture of an Fe(IV) oxo reveals two unpaired electrons in the π antibonding level. As a result, the pi bond may be considered relatively weak compared to some other metal oxo complexes. That may result in increased reactivity. In contrast, a d^0 or d^2 oxo is usually much more inert than a d^4 oxo.

4.5: Solutions to Selected Problems

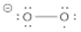
Exercise 4.1.1:

a)



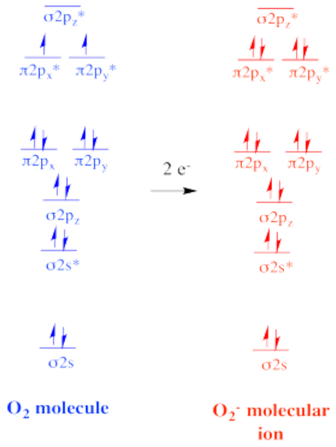
b) Superoxide is a doublet.

c) Superoxide has only 1.5 bonds (3 net bonding electrons).

d) 

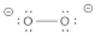
Exercise 4.1.2:

a)

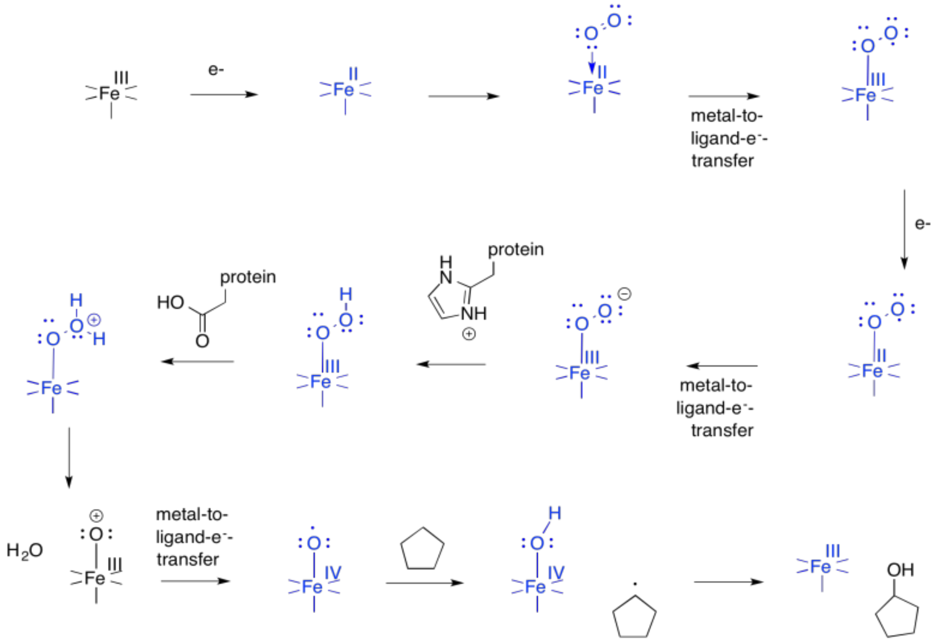


b) Peroxide is a singlet.

c) Peroxide has only 1 bond (2 net bonding electrons).

d) 

Exercise 4.3.1:


Fe III
e-
Fe II
Fe II
metal-to-ligand-e⁻-transfer
Fe III
e-
Fe II
metal-to-ligand-e⁻-transfer
Fe III
H N NH protein
Fe III
HO O protein
Fe
H2O
Fe III
metal-to-ligand-e⁻-transfer
Fe IV
Fe IV
H
Fe III
OH

CHAPTER OVERVIEW

5: Nitrogen Reduction

5.1: Introduction to Nitrogen Reduction

Nitrogen is the most abundant element in earth's atmosphere. It makes up about 80% of the air around us. It is also a key component of biomolecules. Nitrogen contributes a crucial part of amino acids, which in turn make up proteins, which are the cell's machinery. Nitrogen also provides a crucial part of DNA, which transmits our genetic code and governs the expression of those proteins. Although less well known, many nitrogen-containing natural products such as alkaloids play important roles in biology.

Getting that nitrogen out of the air and into the cell is a Herculean task. Nitrogen in the air is present in its elemental form, which is diatomic nitrogen or dinitrogen, N_2. The nitrogen in biomolecules is always found individually; it is always bound to other atoms, especially carbon and hydrogen, but never to other nitrogens. That means the two nitrogen atoms in dinitrogen atom have to be cleaved apart so that they can be combined with other atoms in these useful molecules. That's a problem. N_2 is exceptionally stable. Breaking the bond between the two nitrogen atoms costs about 225 kcal/mol. Most of the other bonds in the universe are not nearly so strong.

So how do we break that incredibly strong bond and combine it with other atoms to make molecules? For most of our history, we didn't (we being people). Neither could other animals. Neither could plants. Microbes could do it all along, though.

Certain bacteria, called diazotrophs, contain an enzyme called nitrogenase that can catalytically convert dinitrogen to ammonia. Some diazotrophs, called rhizobacteria, have a symbiotic relationship with specific kinds of plant roots. They provide ammonia or amino acids to the plant and the plant provides them with organic compounds such as malate that can be metabolised to obtain energy.

$$\mathrm{N_2 + 6\,H^+ + 6\,e^- \longrightarrow 2\,NH_3}$$

All plants need nitrogen to grow, but by evolving to have this symbiotic relationship with rhizobacteria, legume plants have found a distinct advantage over others.

Other bacteria actually live on ammonia. They use it for metabolism the way other organisms use carbohydrates. In doing so, they oxidise the ammonia to nitrites the way other organisms oxidise carbohydrates to carbon dioxide.

$$\mathrm{NH_3 + O_2 \longrightarrow NO_2^- + 3\,H^+ + 2\,e^-}$$

There are even bacteria that oxidise the nitrites.

$$\mathrm{2\,No_2^- + O_2 \longrightarrow 2\,NO_3^-}$$

Exercise 5.1.1

Calculate the oxidation state of nitrogen in each of the following compounds.

a) N_2 b) NH_3 c) NH_4^+ d) NO_2^- e) NO_3^-

Answer a

a) 0

Answer b

b) 3-

Answer c

c) 3-

Answer d

d) 3+

Answer e

e) 5+

Exercise 5.1.2

The oxidation of nitrite must involve electron transfer. Identify:

a. the oxidant
b. the reductant
c. the number of electrons transferred from reductant to oxidant

Answer a

a) O_2

Answer b

b) NO_2^-

Answer c

c) 2 e^-

All of these compounds -- ammonia, nitrites, and nitrates -- can be used by plants as sources of nitrogen. People, who have been farming for thousands of years, have developed a number of methods of making sure their crops had plenty of these nutrients available. There are familiar stories of different Native American groups planting corn and squash along with rhizobacter-nurturing beans. In South America, Andean farmers collected guano for their fields.

At the turn of the twentieth century, a great leap forward came with the discovery that ammonia could be manufactured directly from nitrogen on a massive scale. This technology, called the Haber-Bosch process, is responsible for a significant portion of the nitrogen found in food.

The focus of this chapter is on the processes that have allowed the cleavage of the nitrogen bond, by both biological and industrial means.

See the section on nitrogenase at Henry Jakubowski's Biochemistry Online.

5.2: The Haber-Bosch Process

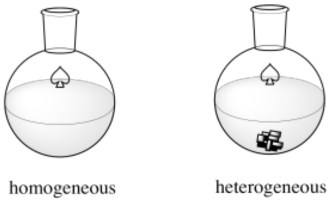
The Haber-Bosch Process is one of the world's most important industrial reactions. It provides for the synthesis of ammonia directly from elemental nitrogen, N_2, and hydrogen, H_2. Since its development in the early twentieth century, it has led to the production of an enormous quantity of fertilizer, vastly increasing global food production. As a result, it is estimated that a significant fraction of the nitrogen content in the typical human body is ultimately derived from this process.

At the time of its development, the Haber-Bosch Process supplanted a growing dependence on guano, seabird droppings, harvested in order to enrich farmland. Although this method had been practiced by the Inca for centuries, European demand in the late 1800's placed growing pressure on resources in Peru and the Caribbean. Because nitrogen is a limiting factor for plant growth, treatment of soil with nitrogen- and phosphorus-rich guano led to remarkable improvement in crop yields.

In the late 1700's, Henry Cavendish had been able to produce nitrates with an electric arc in air. A Norwegian development, the Birkland-Eyde Process, harnessed the hydroelectric power available in that country in order to scale Cavendish's feat to industrial production, but the reaction was still terribly inefficient. Fritz Haber was able to develop a much more successful procedure for ammonia production (the reduced state, rather than the oxidized nitrates), which was adopted by BASF. Originally the local Baden Aniline and Soda Factory, this German company is now the world's biggest chemical producer.

Haber himself was a fascinating and controversial figure who hoped to improve the human condition through industrial contributions to agriculture; he also developed pesticides. However, he was roundly condemned for developing and implementing chlorine gas against Allied troops during World War I. Although Haber, who was Jewish, died before the Holocaust, many members of his extended family were murdered in concentration camps; in some of these camps, internees were executed by poison derived from Haber's pesticides.

The Haber-Bosch Process is an example of heterogeneous catalysis. Many catalysts operate via homogeneous catalysis, in which the reaction occurs in one phase (in solution). In heterogeneous catalysis, the reaction occurs at the interface between two phases. In this case, the two phases are the gas phase and the solid phase. The reactants, hydrogen and nitrogen, are both gases. They are both introduced into a vessel under enromous pressure and high temperature. The catalyst is a carefully prepared iron oxide supported on a mixture of other metal oxides, although ruthenium and osmium variations have also been used and offer some advantages.



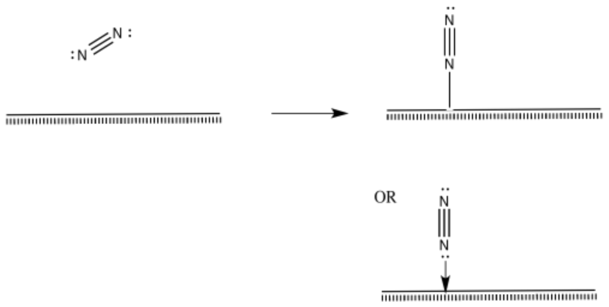
In this case, the reaction involves gas phase reactants and a solid catalyst. The reaction takes place on the surface of the catalyst. We might depict such a surface as a row of atoms. The reaction takes place only on the surface of the atoms (for example, along the top of the picture below). Rows of atoms beneath the surface would not necessarily contribute to the reaction. In the picture below, the second row of atoms might play no role at all in the reaction, other than to provide a place for the top row of atoms to sit.

It might be more convenient to just think of the reaction happening on a flat surface of metal, ignoring its makeup of atoms.

So, molecules come along and they react on that surface. The mechanisms by which molecules react at the surface may be familiar to us. We might find parallels in organometallic chemistry. The surface is, after all, made of metal atoms.

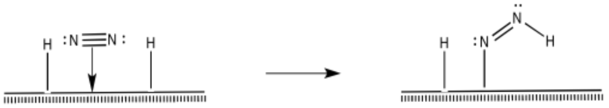
Hydrogen molecules probably become activated through oxidatve addition.

Nitrogen molecules must bind at the surface, too.

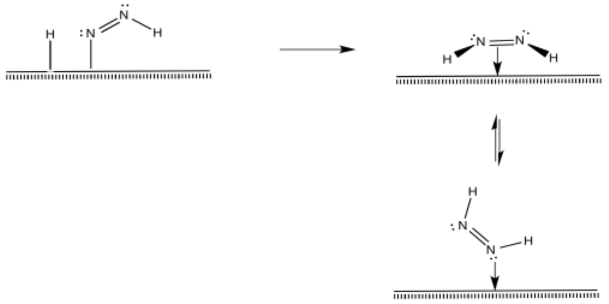


The nitrogen is depicted as "end-bound" above, using its lone pair to attach to the metal. It is also possible that the molecule leans over and becomes "side-bound".

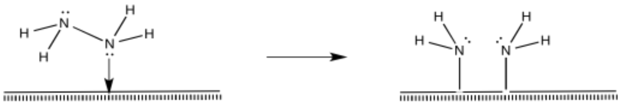
How do the nitrogen and hydrogens react further to make ammonia? There are different possibilities. For instance, a 1,2-insertion reaction seems possible.



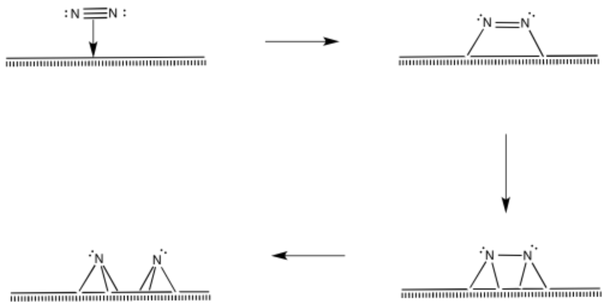
After that, a reductive elimination would result in formation of a second N-H bond.



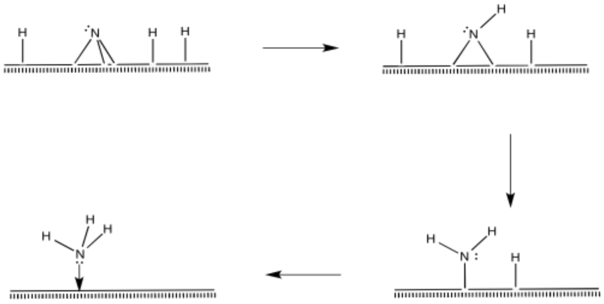
That process, so far, results in the conversion of dinitrogen to diazene, N_2H_2. The diazene could react further to make hydrazine (N_2H_4) and, ultimately, ammonia.



Of course, the reaction could happen in other ways, too. There are surface studies that suggest the presence of nitrides, imides and amides (M≡N, M=NH, M-NH_2). The presence of nitrides suggests a series of oxidative additions starting with dinitrogen, proceeding all the way to nitride, N^{3-}.



Once the nitride is in place, N-H bonds could form via reductive eliminations. The first reductive amination would result in an imide, the second would produce an amide, and the third would produce ammonia.


H
N
H
H
H
N
H
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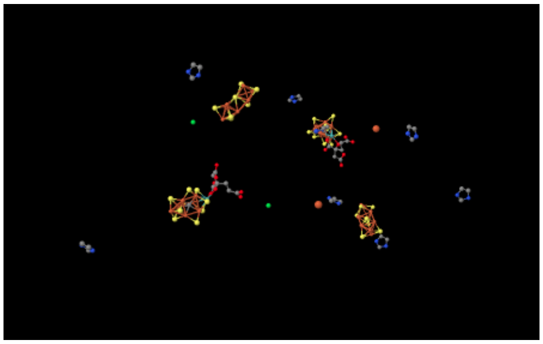
N
H

5.3: Nitrogenase

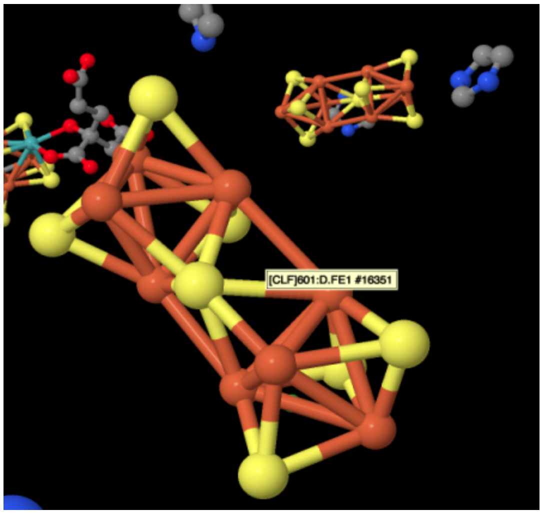
A number of organisms take part in the nitrogen cycle, but from the point of view of chemistry, the diazotrophs have received the most attention. That's partly because their conversion of atmospheric nitrogen to ammonia mirrors the twentieth century marvel of the Haber-Bosch Process, which has been responsible for a tremendous increase in global food production over the last century.

The ammonia-manufacturing center of the diazotroph is nitrogenase. The picture below is taken from an X-ray crystal structure of the enzyme (reference cited at the bottom of the page). Rather than showing the individual atoms, as X-ray structures normally do (except hydrogens, which are too small to detect), the structure is depicted in cartoon form. The cartoon image of a protein is meant to convey key substructures: the pink parts are α-helices, the yellow ribbons are β-sheets, and the white threads are loops.

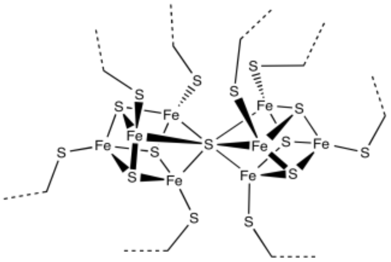
If we delete all of the protein from the image -- that is, the chain of amino acids that make up nitrigenase -- then we are left with a few "ligands". Ligands in this context are simply other molecules or ions found within the protein; often the ligands are bound to amino acid side chains. Looking at the ligands below, we can see that nitrogenase is actually a dimer. The group of molecules in the left half of the picture are the same as the group of molecules in the right half of the picture, although they are rotated upside down with respect to the others.



A couple of the structures in the picture above are metal ions; they look like little balls. To get a better view of the other structures, let's zoom in a little closer.



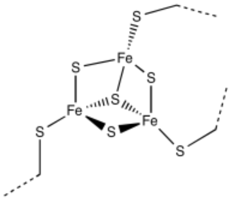
That's an iron sulfur cluster photobombing the picture. The red spheres are colour-coded for iron, whereas the yellow sphered are colour coded for sulfur. The bars between the atoms may or may not represent bonds; X-ray diffraction doesn't really detect bonds, just the highly electron-dense atoms, but the software inserts bonds when it detects atoms that are close together. The iron-sulfur bonds are certainly real. The red bonds shown between the iron atoms probably are not real, although there is a possibility of magnetic coupling between the iron atoms within the cluster. A drawing of the cluster is provided below. The drawing also includes additional sulfur donors on the iron atoms, but those are from cysteine residues in the protein, which has been rendered invisible in the picture above.



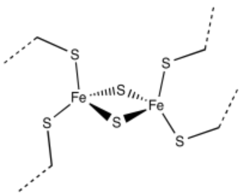
[8Fe7S]
("P cluster")

This particular cluster contains 8 iron atoms and 7 sulfide ions (S^{2-}); it's referred to as an [8Fe7S] cluster for short. Iron sulfur clusters are actually pretty common in biology. Probably the most common is a [4Fe4S] cluster, although [3Fe4S] and [2Fe2S] clusters are often seen, too. Iron sulfur clusters are usually charged. The amount of charge on the overall clusters depends on the oxidation states of the iron atoms. The oxidation states can change because these clusters function as electron relays. They can accept an electron from elsewhere in the protein and send it on to where it is needed.

[4Fe4S]



[3Fe4S]



[2Fe2S]

Exercise 5.3.1

Indicate the charges on the following clusters.

a. [4Fe4S], with two Fe^{2+} and two Fe^{3+}
b. [3Fe4S], with two Fe^{3+} and an Fe^{2+}
c. [2Fe2S], with one Fe^{2+} and one Fe^{3+}

Answer a

a) S: 4 x 2^- = 8^- ; CysS: 4 x 1^- = 4^- ; Fe: 2 x 2^+ + 2 x 3^+ = 10^+ ; total = 2^-

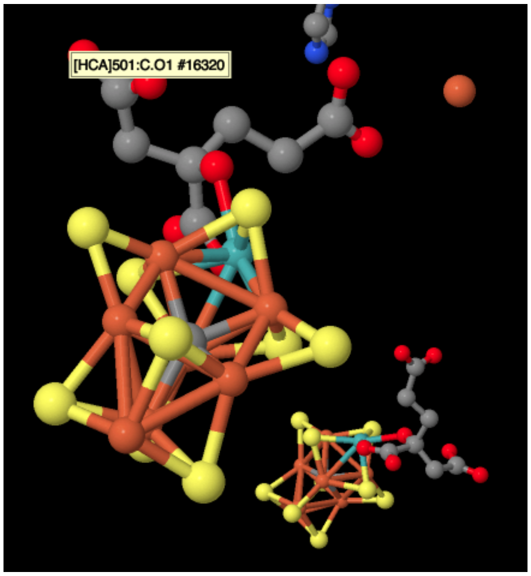
Answer b

b) S: 4 x 2^- = 8^- ; CysS: 3 x 1^- = 3^- ; Fe: 1 x 2^+ + 2 x 3^+ = 8^+ ; total = 3^-

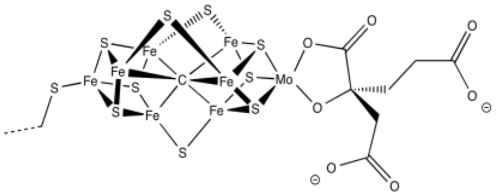
Answer c

c) S: 2 x 2^- = 4^- ; CysS: 4 x 1^- = 4^- ; Fe: 2^+ + 3^+ = 5^+ ; total = 3^-

There are also a couple of histidines visible in the picture above. They were probably introduced when the researchers were growing the crystals. A far more interesting structure is barely visible on the left. That's actually the iron-molbdenum or Fe-Mo cofactor, also called the M cluster. It's the site of nitrogen reduction in the enzyme. A much clearer view of this structure is provided below. Because we are looking at a dimer, we can see a second M cluster behind.

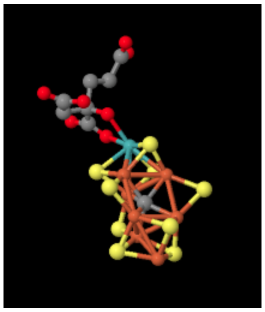


A drawing of the M cluster is shown below. It bears some resemblance to [8Fe7S]. This time, the atom in the center is believed to be a carbon. A trio of additional sulfides bridge between the two cubes, and in one corner an iron atom has been replaced by a molybdenum.



FeMo cluster
("M cluster")

Here is a picture of the M cluster from a different angle. The molybdenum with its attached ligand is in the upper left, coordinated by yellow sulfides. The gray atom in the middle is probably a carbon atom.

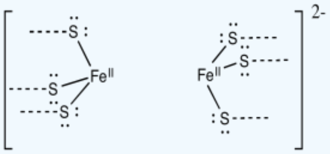


The mechanism by which nitrogenase reduces nitorgen to ammonia is likely somewhat different from the mechanism in the Born-Haber Process. Rather than treatment with hydrogen gas, under biological conditions the mechanism is likely to involve reduction via individual electrons and protons. Exactly how the electrons and protons arrive at their destination is an interesting question.

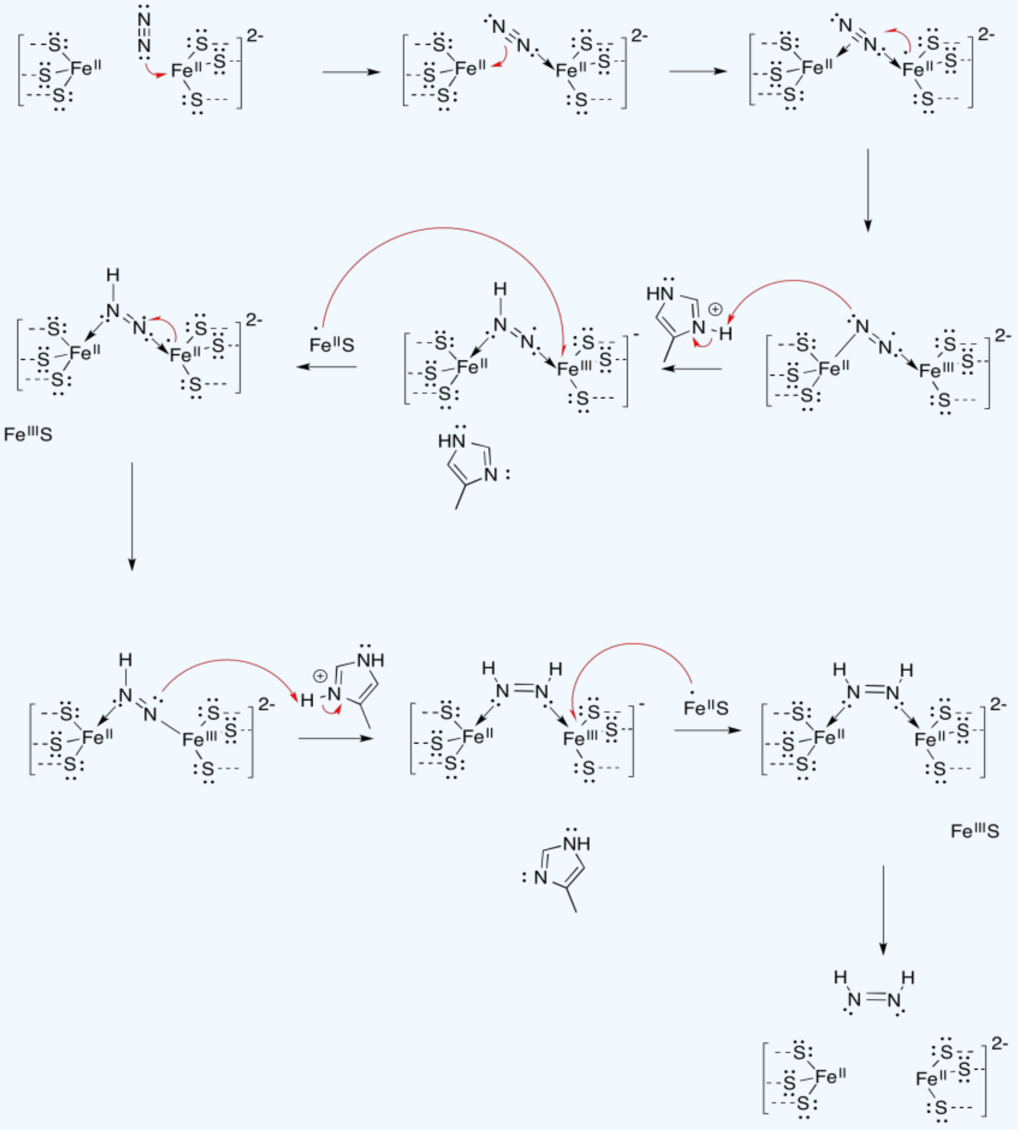
One possibility is that the dinitrogen is reduced one electron and one proton at a time. The FeS clusters would be able to deliver electrons via an electron relay running through the cell. Amino acid residues in the protein would be able to shuttle protons in as needed.

Exercise 5.3.2

Provide a mechanism for the reduction of dinitrogen, N_2, to diazene, HN=NH, via alternating additions of electrons and protons. Assume the following model is the site of the reaction, with appropriate electron and proton donors nearby.



Answer

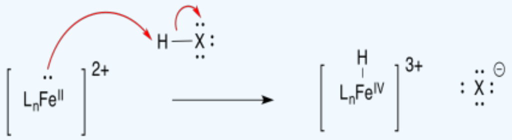


Alternatively, the process could more closely resemble the Haber-Bosch Process, using classic "organometallic" reaction mechanism such as oxidative addition, insertion and reductive elimination. In fact, recent evidence suggests H2 may be produced by some nitrogenases under biological conditions. That observation is consistent with the operation of this type of mechanism.

Exercise 5.3.3

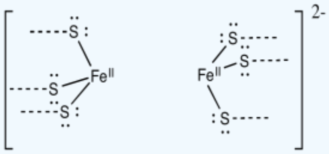
Show how protonation of an iron atom is equivalent to an oxidative addition.

Answer

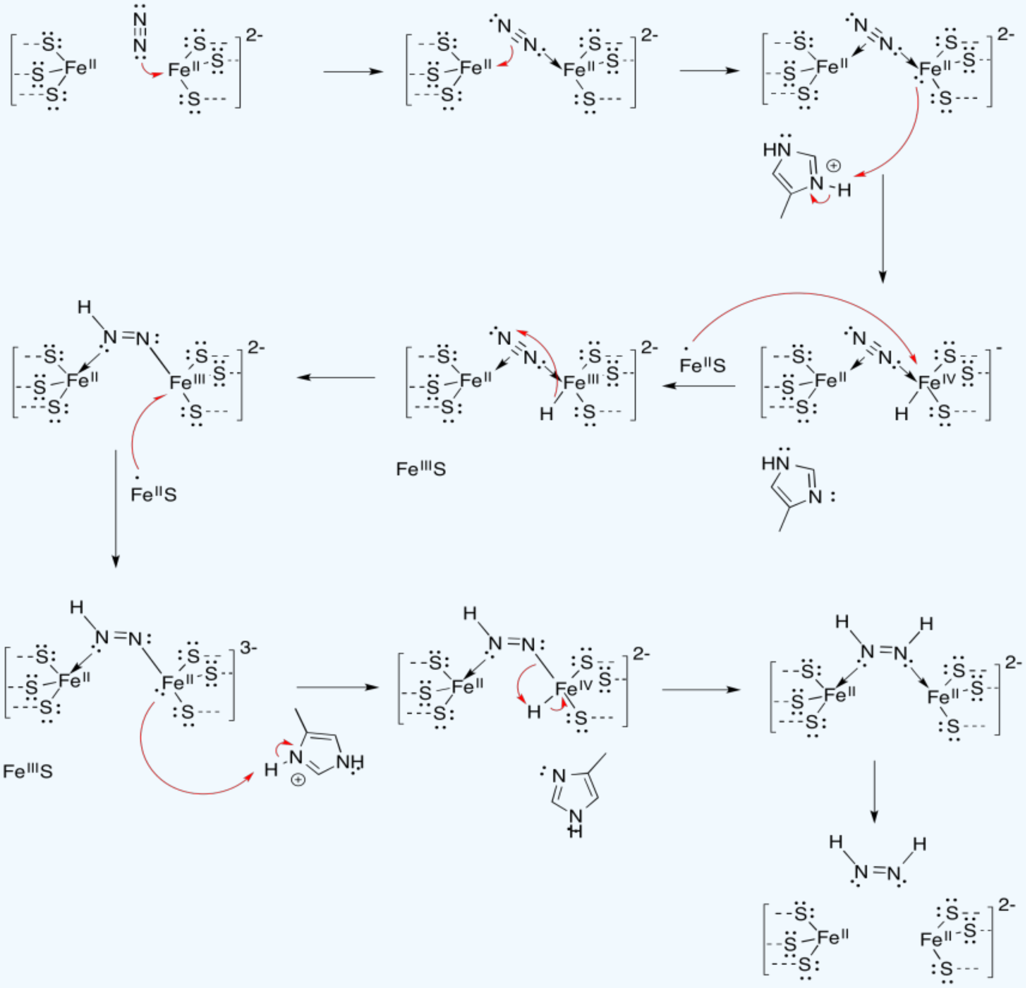


Exercise 5.3.4

Provide a mechanism for the reduction of dinitrogen, N_2, to diazene, HN=NH, via a series of organometallic steps (association/dissociation, oxidative addition/reductive elimination, insertion/elimination).



Answer

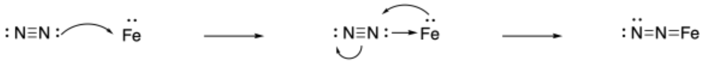


5.4: Model Studies for Nitrogen Binding

If nitrogen is to be reduced, it first has to be bound. However, nitrogen is remarkably inert. Chemists routinely run reactions under an atmosphere of pure nitrogen because of its lack of reactivity. Fine chemical companies bottle compounds under nitrogen to ensure that the contents remain in pristine condition while sitting on the shelf. If nitrogen doesn't react with anything, how does it react with an iron atom in nitrogenase?

What is the weakness of the dinitrogen molecule? That turns out to be related to its strength. The enormously strong nitrogen-nitrogen triple bond is composed of a sigma bond and two pi bonds. The corresponding antibonding orbital allows nitrogen to act as a pi acceptor.

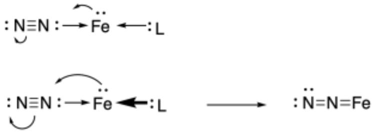
That means there is a good chance of getting the very unreactive nitrogen molecule to bind to a transition metal. An occupied d orbital on an iron atom could back-donate into that nitrogen orbital, holding the dinitrogen more securely on the iron. The nitrogen can be bound.



Just to make that scenario more likely, the metal could be tuned in order to maximise its ability to backbond with the nitrogen. That means it needs a lot of electron density. An electron-rich metal atom would readily donate electron density into nitrogen's pi acceptor orbital. Then the nitrogen would bind more tightly.

One factor that would help is a low oxidation state. A low oxidation state on the metal would leave it with more electron density to donate to the nitroge pi acceptor orbital.

A secondary factor is strongly donating ancillary ligands. These other ligands would play a supporting role by lending additional electron density to the transition metal so that it could bind to the nitrogen even more tightly.



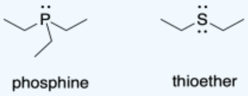
As with other metalloproteins, researchers have spent a great deal of effort studying nitrogenase. They have also expended a tremendous amount of effort studying model compounds. Model compounds are simpler molecules that incorporate selected aspects of the metalloprotein. By intentionally designing a model compound to include certain features of the metal centre in the protein, researchers can evaluate what role those features play in the reactivity of the metalloprotein.

It's pretty obvious that we might want a model compound for nitrogenase to contain iron atoms. After all, nitrogenase contains a number of iron atoms at its active site. Of course, it also contains molybdenum, or in some cases vanadium. A model compound might contain those atoms, instead. Alternatively, it could contain atoms other than the ones found in the native enzyme. That would be a sort of pushing-the-envelope approach. If an electron-rich metal is important, how electron rich can we go? Or how electron-poor can we get and still be able to bind nitrogen? By exploring things that aren't part of the natural system, we might better see the importance of those things that are.

The same is true with the ancillary ligands, those that support the metal but that may not be directly involved in catalysis. The electron-rich sulfides in nitrogenase may be an important part of a model compound. So could phosphines, whose phosphorus donor atoms are of a similar size to sulfur. Phosphines are commonly used industrially in organometallic catalysis and might make good mimics of the sulfur ligands in nitrogenase.

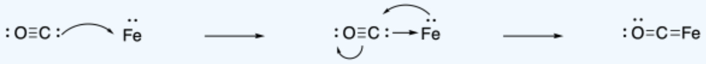
Exercise 5.4.1

Consider the ligand type presented by a phosphine compared to a thioether. What might be the disadvantage of using a phosphine as a stand-in for a sulfur donor?



Answer

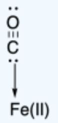
Having said all of that, it is worth emphasizing that binding nitrogen is still not easy. Sometimes, researchers who want to study the potential for nitrogen binding in a given complex start with binding carbon monoxide instead. Why carbon monoxide? First of all, it is much easier to bind than dinitrogen. It is a much stronger pi acceptor, because the pi antibonding orbital is much more heavily located on the carbon that sigma donates to the metal. Of course, you may already know that there are some important transition metal reactions that involve binding and reducing carbon monoxide.

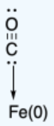


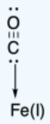
Furthermore, carbon monoxide studies can be useful because carbon monoxide acts as a "reporter ligand". It is easily monitored by IR spectroscopy, for instance. Dinitrogen is a poor candidate for IR study because of the non-polar N-N bond. (It can be observed via Raman spectroscopy, which gives similar information but is slightly more complicated to run.) The CO bond is easily detected in the IR spectrum, it is in a region that isn't usually cluttered with other peaks from other bonds, and it is quite sensitive to the oxidation state of the metal. That's because of the strong back-bonding from a filled metal d orbital into the pi antibonding orbital of carbon monoxide. The more back-donation from the metal, the weaker the CO bond, resulting in a drop in the frequency in the IR spectrum.

Exercise 5.4.2

Rank the following species in terms of their CO stretching frequency in the IR spectrum.







Exercise 5.4.3

Nitrogen can bind to metals in a number of ways. Draw structures that illustrate the following binding modes:

a) an end-bound, terminal nitrogen ligand bound via a lone pair

b) a side-bound, terminal nitrogen ligand bound via donation from a pi bond

c) an end-bound, bridging nitrogen ligand bound via a lone pair

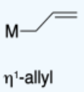
d) a side-bound, bridging nitrogen ligand bound via donation from a pi bond

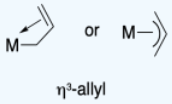
e) a bridging nitrogen ligand bound via donation from a pi bond and a lone pair

Exercise 5.4.4

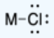
In naming coordination compounds, the prefixes eta (η) and mu (μ) are sometimes used to indicate ligand binding modes such as the ones described above.

Eta describes the number of ligand atoms bound to a single metal atom, and is generally used when there are pi bonds that could donate, bringing two or more donor atoms close to the metal.

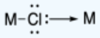




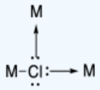
Mu is used to indicate a bridging ligand, and if followed by a number it can describe the number of metal atoms bridged by one ligand.



chloro



μ2-chloro



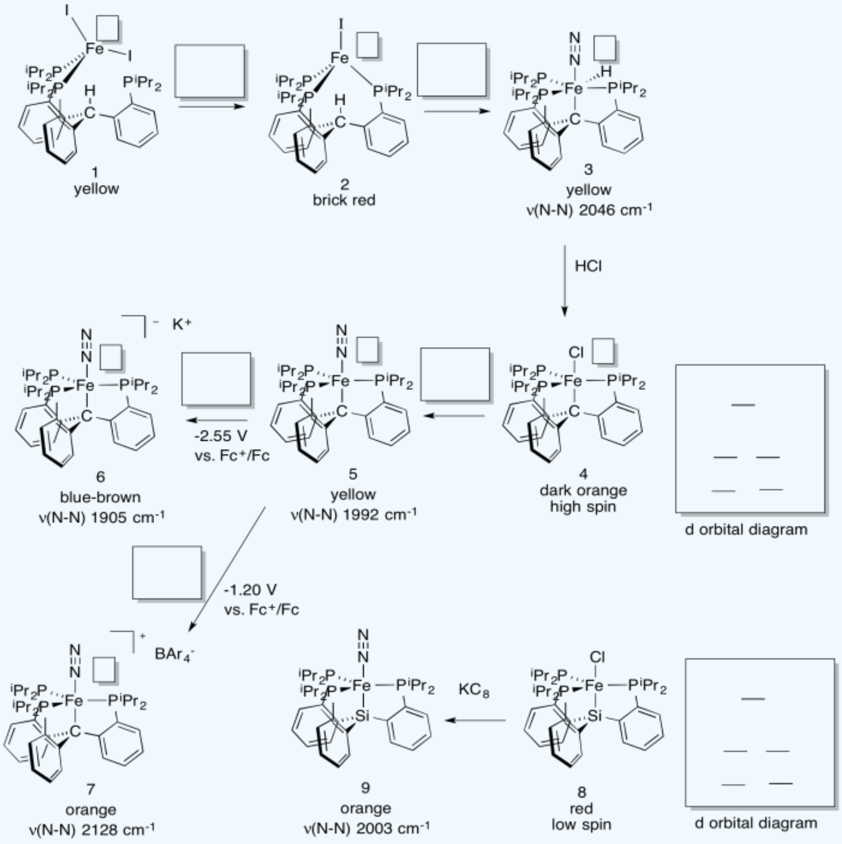
μ3-chloro

Use these notations to describe the nitrogen binding modes in the previous question.

Exercise 5.4.5

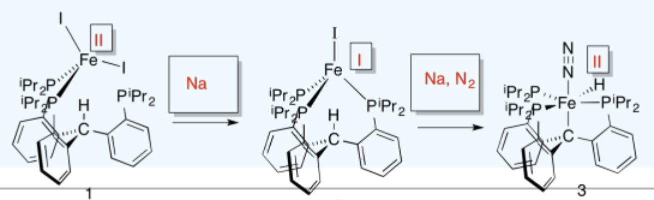
Jonas Peters' lab (Caltech) has developed a new system in an attempt to model the effect of a reported carbon atom in the structure of Fe/Mo cofactor of nitrogenase (*J. Am. Chem. Soc.* **2014**, *136*, 1105-1115). The system catalytically produces ammonia in the presence of N_2, acid and Na.

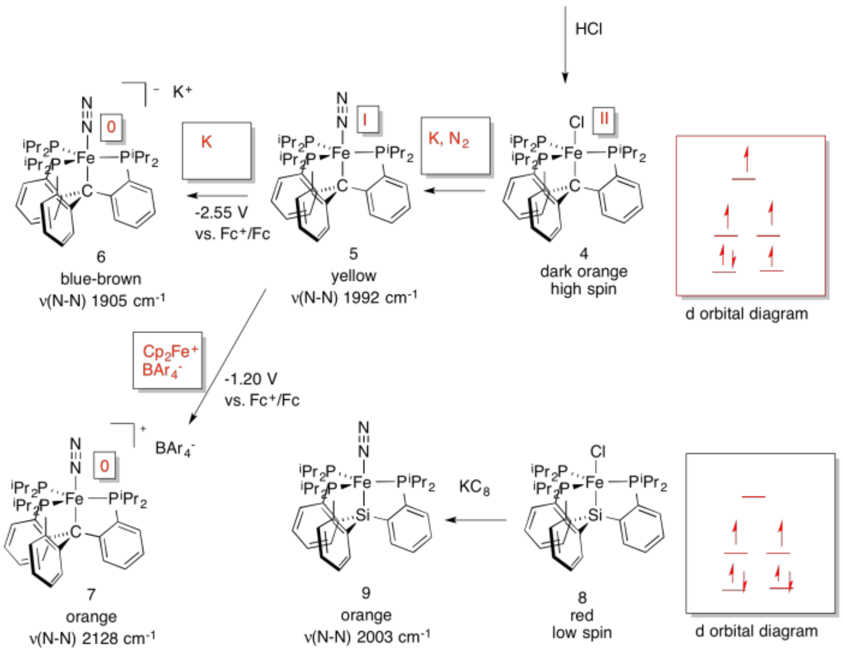
a) Fill in the oxidation states.
b) Fill in missing reagents.
c) Fill in d orbital splitting diagrams.
d) Explain the differences in the N-N stretching frequencies.


1
yellow
2
brick red
3
yellow
ν(N-N) 2046 cm-1
HCl
4
dark orange
high spin
d orbital diagram
5
yellow
ν(N-N) 1992 cm-1
-2.55 V
vs. Fc+/Fc
6
blue-brown
ν(N-N) 1905 cm-1
K+
-1.20 V
vs. Fc+/Fc
BAr4-
7
orange
ν(N-N) 2128 cm-1
9
orange
ν(N-N) 2003 cm-1
KC8
8
red
low spin
d orbital diagram

Answer

Answers don't reflect the true reagents, but show what a student might think of.





d) As the Fe becomes more reduced, the N-N stretching frequency decreases. That's because the more electron density there is on the Fe, the more it is able to backbond to the N_2 (N_2 is a π acceptor).

5.5: Model Studies for Nitrogen Reduction

Model studies for nitrogen reduction seek to develop coordination compounds that can mimic the activity of nitrogenase, which converts atmospheric dinitrogen into ammonia or ammonium ion. Over the past few decades, there have been more and more reports of dinitrogen complexes, so researchers have clearly figured out some of the factors to accomplish that part of the reaction.

It's one thing to be able to bind a dinitrogen ligand to a metal center, but it's quite another thing to be able to conert that dinitrogen into ammonia. That strong N-N triple bond costs about 200 kcal/mol to break; that's a very high cost to pay and it isn't easy to do. The other part of nitrogen fixation involves formation of the N-H bond; this part of the process could actually be exothermic, and so it might be an easier problem to solve.Most studies aiming to make progress towards ammonia production start with reduction of a metal center so that it in turn will have sufficient reducing power to bind dinitrogen. Acids are then added to supply the protons needed to form N-H bonds. Proposed mechanisms of nitrogen fixation in nature involve a series of electron transfer and proton transfer steps, so the addition of acid seems like a reasonable way to model the process.

? Exercise 5.5.1

Assign the oxidation state on nitrogen in the following molecules:

a) dinitrogen b) diazene, N_2H_2 c) hydrazine, N_2H_4 d) ammonia, NH_3

? Exercise 5.5.2

Draw a mechanism with curved arrows and intermediates showing:

i) sodium metal reducing Fe(II) to Fe(0)

ii) binding molecular nitrogen

iii) protonation to form a diazene complex, containing an H_2N_2 ligand.

? Exercise 5.5.3

Draw the following possible intermediates of nitrogen reduction:

a) a diazene complex b) a hydrazine complex

c) a diazenyl anion complex d) a hydrazinyl anion complex

e) a bridging hydrazine complex f) a bridging diazene complex (two structures)

g) a bridging hydrazinyl anion complex h) a bridging diazenyl anion complex (three structures)

i) a bridging hydrazinyl dianion complex (two structures) j) a bridging diazenyl dianion complex

---

5.6: Solutions for Selected Problems

Exercise 5.1.1:

a) 0 b) 3- c) 3- d) 3+ e) 5+

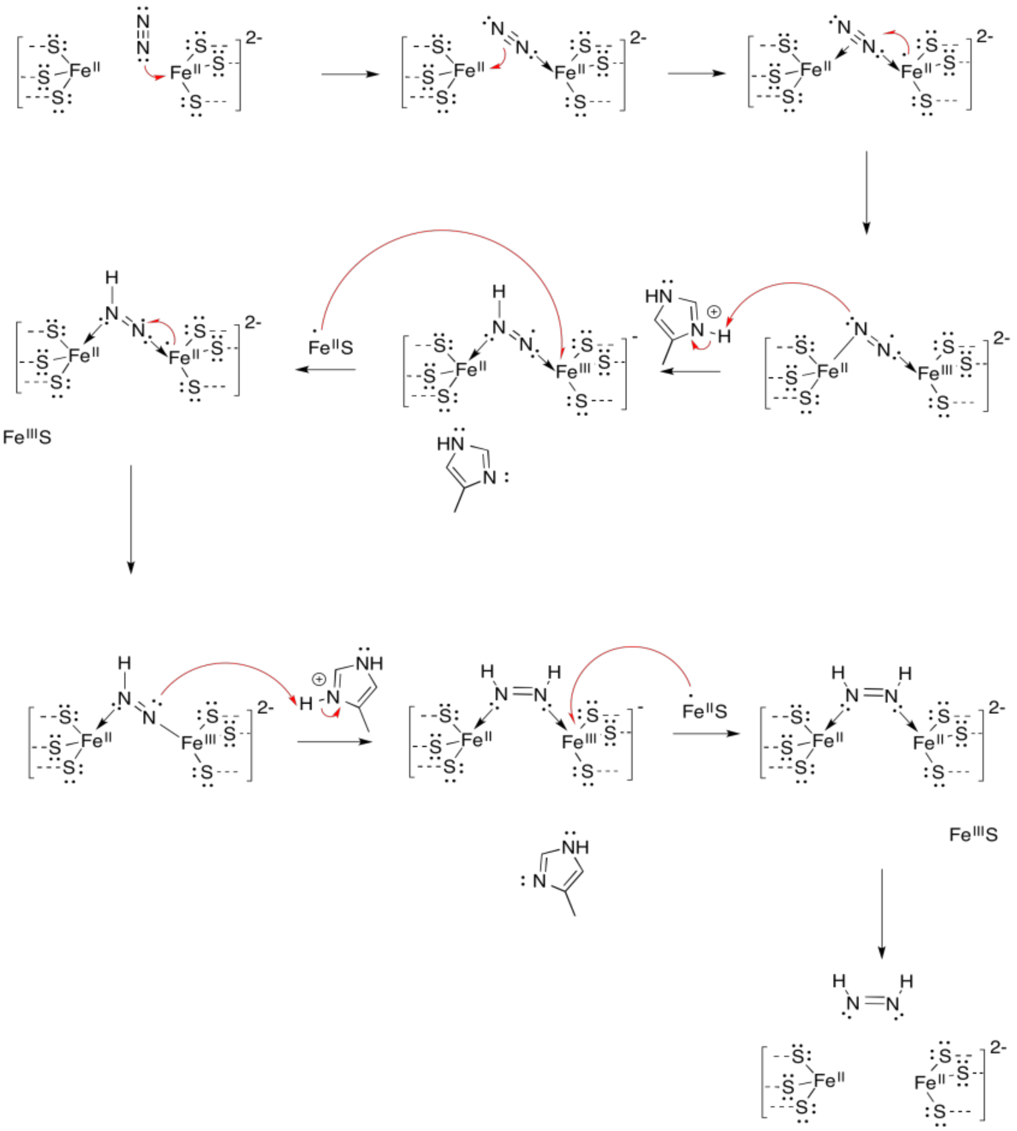
Exercise 5.1.2:

a) O_2 b) NO_2^- c) 2 e^-

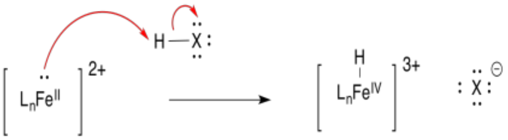
Exercise 5.3.1:

a. S: $4 \times 2^- = 8^-$; Fe: $2 \times 2^+ + 2 \times 3^+ = 10^+$; total $= 2^+$
b. S: $4 \times 2^- = 8^-$; Fe: $1 \times 2^+ + 2 \times 3^+ = 8^+$; total $= 0$
c. S: $2 \times 2^- = 4^-$; Fe: $2^+ + 2^+ = 5^+$; total $= 1^+$

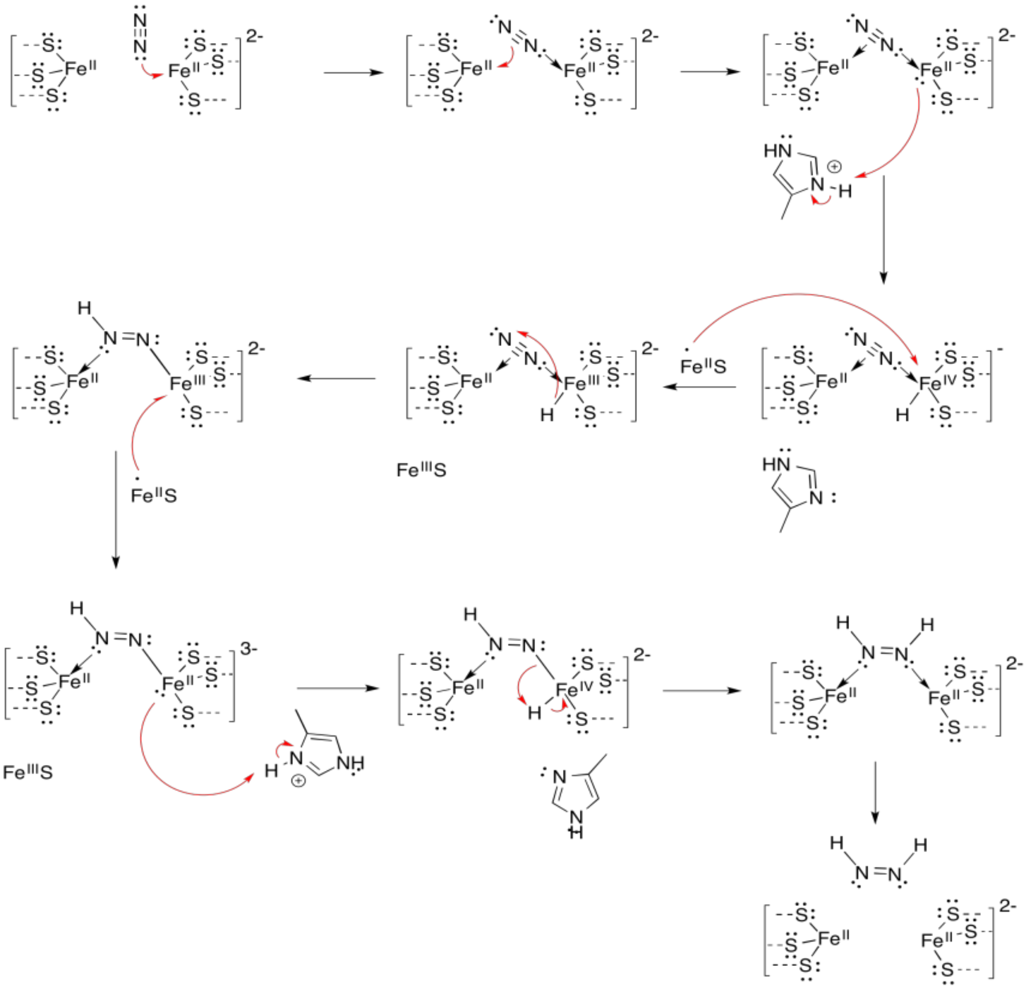
Exercise 5.3.2:



Exercise 5.3.3:

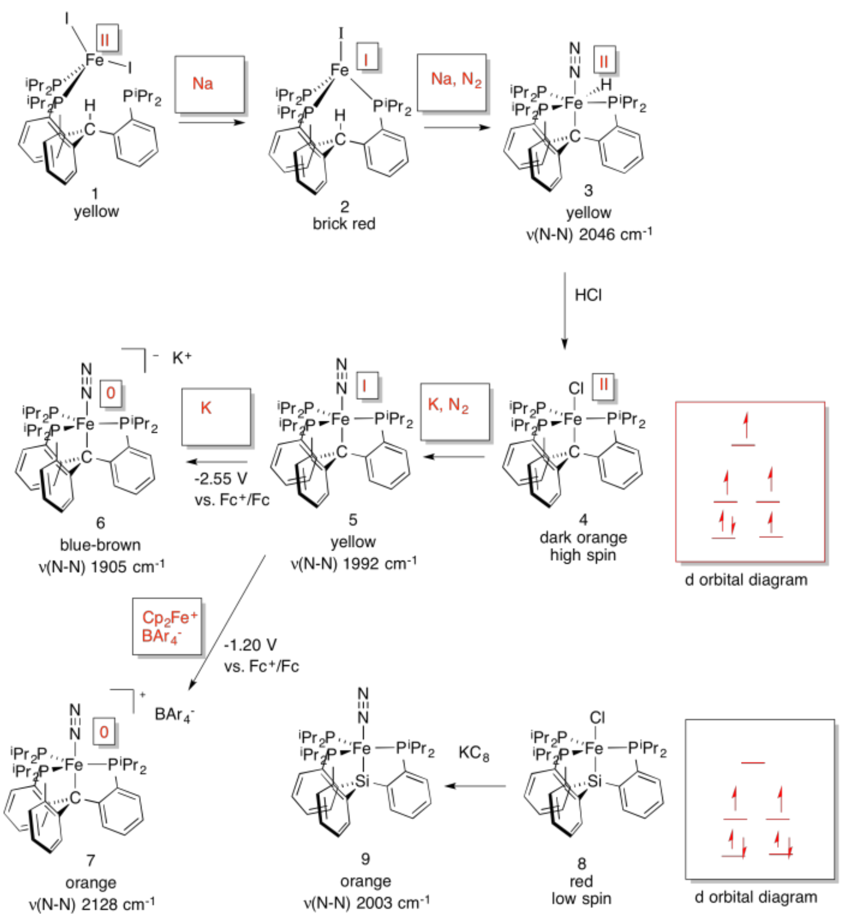


Exercise 5.3.4:



Exercise 5.4.1:

Answers don't reflect the true reagents, but show what a student might think of.



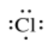
d) As the Fe becomes more reduced, the N-N stretching frequency decreases. That's because the more electron density there is on the Fe, the more it is able to backbond to the N_2 (N_2 is a π acceptor).

CHAPTER OVERVIEW

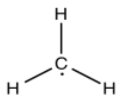
6: Radical Reactions

6.1: Introduction to Radicals

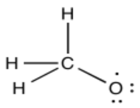
Radicals are species that have unpaired electrons. They can be atoms or molecules and they can be neutral species or ions. Frequently, radicals are very reactive. However, their mode of reactivity does not fall neatly within the normal patterns of Lewis acids and bases, or nucleophiles and electrophiles.



a chlorine radical



a methyl radical



a methoxy radical

Radicals play common roles in atmospheric chemistry, including equilibration of the ozone layer. They are also found in a variety of biochemical pathways. In addition, radicals are employed in a number of useful processes, such as the polymerization of methyl methacrylate or vinyl chloride, commonly used to make shatter-resistant "glass" and pipes for plumbing, respectively.

Compounds of p-block elements form radicals if one of the atoms has seven electrons in its valence shell rather than the usual eight.

? Exercise 6.1.1

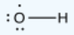
Draw structures for the following neutral radicals, making sure to fill in the correct number of electrons.

a) Br b) OH c) CH_3CH_2 d) CH_3CH_2S e) CH_2CHCH_2 f) NO g) $(CH_3)_2NO$ h) NO_2

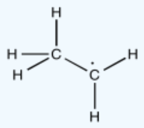
Answer

a)

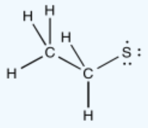
b)



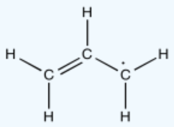
c)



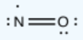
d)



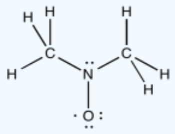
e)



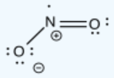
f)



g)



h)



A molecule could become a radical in a number of different ways. A bond may break in half via the addition of energy, in the form of either heat or light. Otherwise, it may simply transfer one of its electrons elsewhere. Again, this event may be precipitated by the addition of heat or light energy. Of course, a molecule that receives an additional electron from elsewhere may also become a radical.

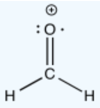
? Exercise 6.1.2

Draw structures for the following cationic radicals, making sure to fill in the correct number of electrons and the formal charge.

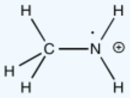
a) $H_2C=O$ b) CH_3NH_2 c) CH_3OCH_3 d) $CH_3CH_2CH_2Br$ e) $CH_3CH_2CHCH_2$

Answer

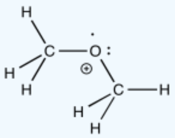
a)



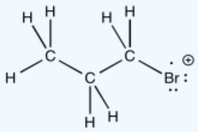
b)



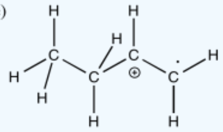
c)



d)



e)



Exercise 6.1.3

Draw structures for the following anionic radicals, making sure to fill in the correct number of electrons.

a) O_2 b) H_2CO c) CH_3CCCH_3 d) cyclo-C_6H_6

The compounds above are all simple radicals, containing one unpaired electron. Compounds may also have more than one unpaired electron.

Elemental oxygen, O_2, is a diradical. Although its Lewis structure does not suggest anything unusual, its molecular orbital diagram reveals that oxygen actually has two unpaired electrons.

Exercise 6.1.4

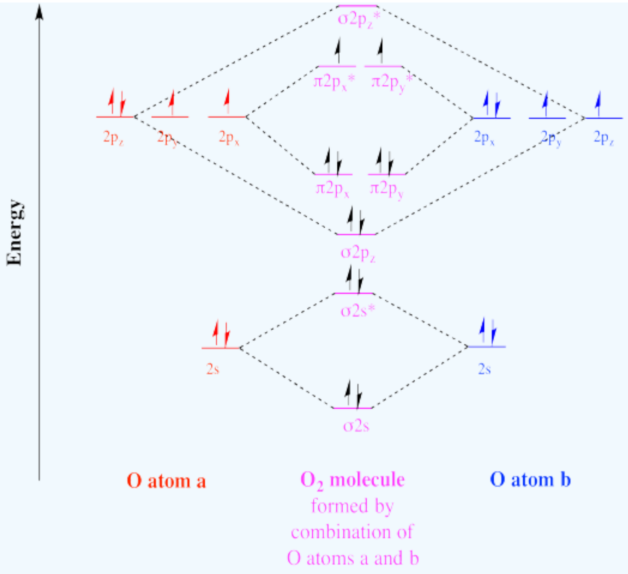
Show two Lewis structures for O_2: one illustrating its double bond, and the other illustrating its diradical character.

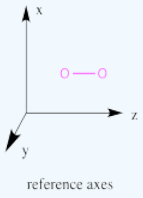
Answer

Exercise 6.1.5

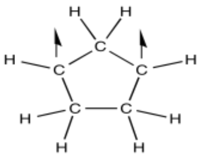
Show, with a molecular orbital interaction diagram, the diradical character of dioxygen.

Answer

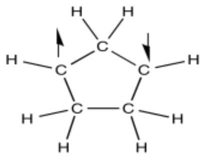




A diradical could take two different forms. For example, molecular oxygen has two singly-occupied molecular orbitals. The single electron in each of those orbitals could adopt one of two different spin states. Both could adopt the same spin state (designated with arrow "up", for example), or they could be "spin-paired" (one "up", one "down"). The former situation is called a "triplet state", whereas the latter case is termed a "singlet state". These two situations result in some physical differences, such as different interactions with a magnetic field.



triplet diradical
spins unpaired



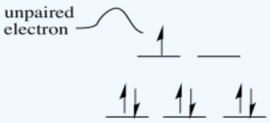
singlet diradical
spins paired

Subsequent pages will focus on the reactivity of radicals, with an emphasis on the stages of radical chain reactions.

? Exercise 6.1.6

Some transition metal compounds have radical characteristics. Show why, using a low spin Co(II) complex in an octahedral environment as an example.

Answer



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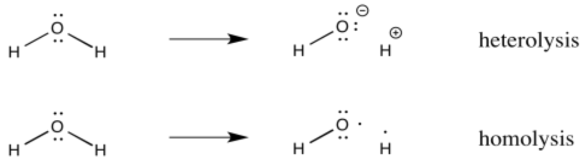
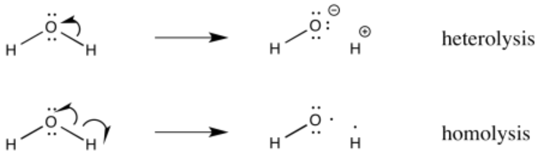
6.2: Radical Initiation- Bond Homolysis

Sometimes, radicals form because a covalent bond simply splits in half. Two atoms that used to be bonded to each other go their separate ways. Each atom takes with it one electron from the former bond. This process is called homolysis, meaning the bond is breaking evenly. In contrast, heterolysis is the term for a bond that breaks via ionization, with one atom getting both electrons from the bond.



- Homolysis describes breaking a bond in half, with one electron going to each side of the former bond.

In pictures, we show this process using curved arrows, but the arrows we use are slightly different from the ones you may be used to seeing in polar reaction chemistry. Instead of a regular arrowhead, we use a half arrowhead. This kind of arrow looks a little more like a fish hook. It is easy to remember the roles of the two kinds of arrows, because a full arrowhead describes the movement of an electron pair, whereas a half arrowhead describes the movement of only one electron.



Why would a covalent bond simply break apart? There are really a number of factors and a number of events that may result in this situation. The simple part of the story is that the bond must have been weak in the first place. There was enough energy available in the form of heat transferred from the surroundings (or sometimes in the form of light) to overcome the stabilization energy of the bond.

What makes a bond weak or strong? That is a complicated question. Many factors influence bond strength. However, two of the main factors responsible for covalent bond strength are the degree of electron sharing because of "overlap" and the degree of bond polarity resulting from "exchange". Most strong covalent bonds rely on a mixture of these two factors.

One fairly common feature in homolysis is a bond between two atoms of the same kind. For example, elemental halogens often undergo homolysis pretty easily. The ease with which these bonds can be split in half is illustrated by their low bond dissociation energies. Not much energy needs to be added in order to overcome the bonds between these atoms.

Bond	Bond Dissociation Energy (kcal/mol)
H-H	105
C-C	85
N-N	65
O-O	47
F-F	37
S-S	45
Cl-Cl	57
Br-Br	45
Sn-Sn	45
I-I	35

This propensity for radical formation can be understood in terms of the lack of a polar component in these bonds. These atoms rely solely on atomic overlap to share electrons with each other.

There is a notable exception to the rule that homoatomic bonds are inherently weak, and that is a carbon-carbon bond. Its bond dissociation energy is listed in the table for comparison with the halogens. The relative strength of carbon-carbon bonds gives rise to a multitude of carbon-based "organic" compounds in nature. The formation of bonds between like atoms is called "catenation"; carbon is the world champion.

? Exercise 6.2.1

Draw structures for the following reagents and show curved arrows to illustrate the initiation of radicals in each case.

a) Br_2 b) H_2O_2 c) $(CH_3)_3CO_2H$ d) $(CH_3)_2SbSb(CH_3)_2$ e) $CH_3CH_2CH_2CH_2SSCH_2CH_2CH_2CH_3$

Silicon ($BDE_{Si\text{-}Si}$ = 53 kcal/mol) and sulfur ($BDE_{S\text{-}S}$ = 54 kcal/mol) are also capable of catenation, but the bonds that these atoms form between themselves are much weaker than C-C bonds. It seems to be generally true that larger atoms form weaker bonds, at least in the main group of the periodic table. After all, I-I bonds are weaker than Br-Br bonds, which are weaker than Cl-Cl bonds.

It is sometimes argued that this trend is a result of poor spatial overlap between the more diffuse p orbitals nearer the bottom of the periodic table. However, the other side of the equation must not be ignored. Once these bonds break, two new radicals form. Just as ions are more stable on larger, more polarizable atoms, so are radicals.

- Radicals are more stable on larger, more polarizable atoms.
- For example, sulfur radicals are more stable than oxygen radicals.

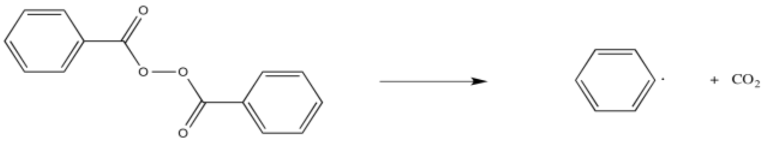
These trends show up in a comparison of carbon-halogen bond strengths. The average carbon-iodine bond is much weaker than the average carbon-fluorine bond.

Bond	BDE (kcal/mol)
C-F	116
C-Cl	78
C-Br	68
C-I	51

Other factors that stabilize radicals can also tilt events in favor of bond homolysis. For example, during catalytic hydrogenations, ether linkages at benzylic positions are often cleaved. A C-O bond is not inherently weak, but a benzylic radical is quite stable. It is the stability of the resulting radical that weakens this particular C-O bond and allows it to be broken so easily.

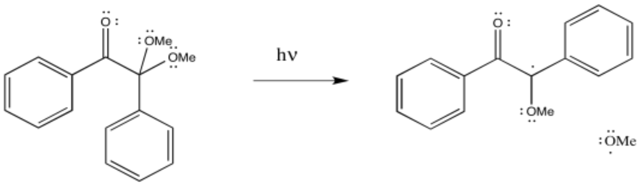
- Particularly stable radicals form relatively easily.
- For example, benzylic radicals form very easily.

Some compounds are commonly used as radical initiators. For example, peroxides contain weak O-O bonds that can cleave to form radicals. That's the initial event in the formation of a radical from benzoyl peroxide, but the resulting carboxyl radical quickly decomposes in favor for carbon dioxide formation.



AIBN, on the other hand, can cleave to produce a very strong dinitrogen triple bond, leaving behind two radicals.

DMPA is a photoinitiator; it is cleaved by the addition of light.



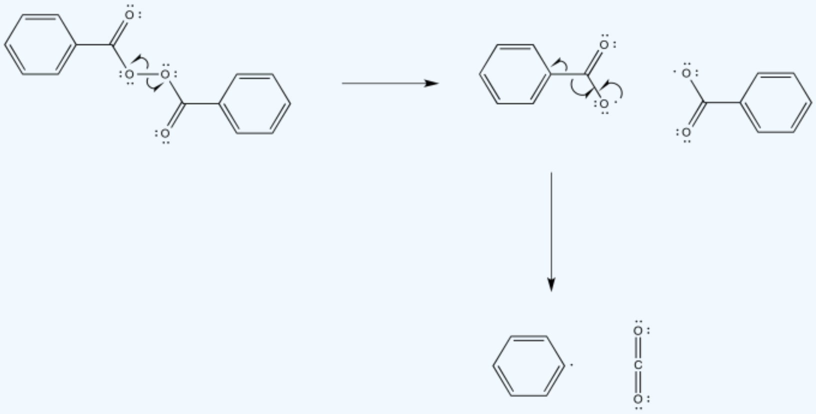
Exercise 6.2.2

Provide mechanisms for radical formation from

a) benzoyl peroxide b) AIBN c) DMPA

Answer a

a)

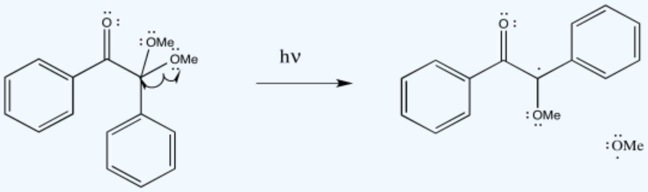


Answer b

b)

Answer c

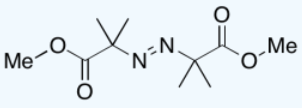
c)



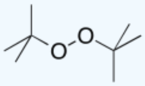
Exercise 6.2.3

The following initiators form radicals relatively easily. Provide mechanisms for radical formation in each case.

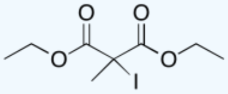
a)



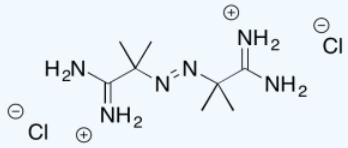
b)



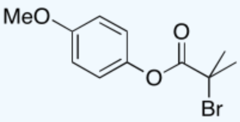
c)



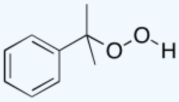
d)



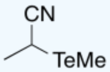
e)



f)



g)



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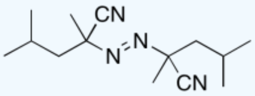
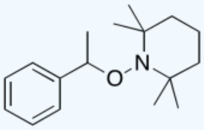
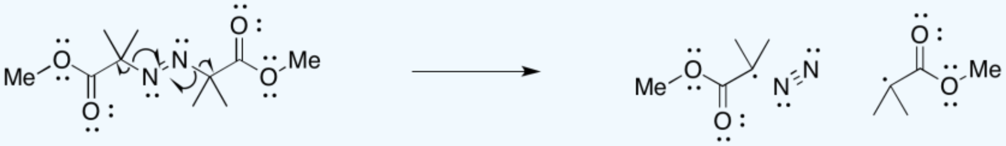


i)

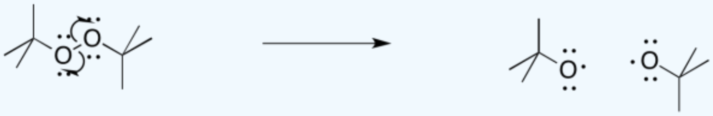


Answer

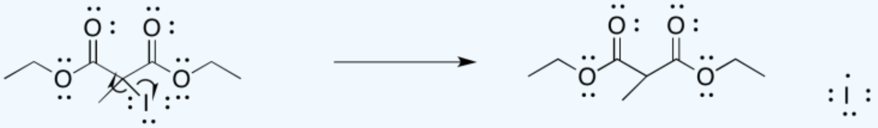
a)



b)

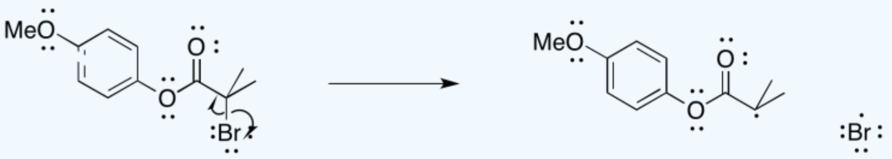


c)



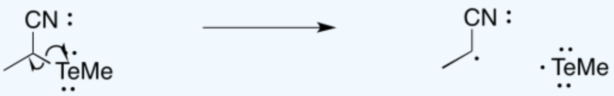
d)

e)

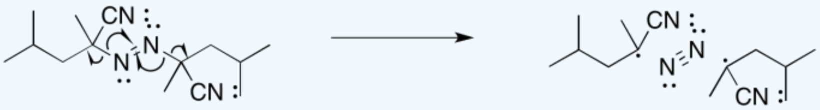


f)

g)



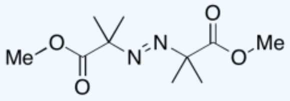
h)



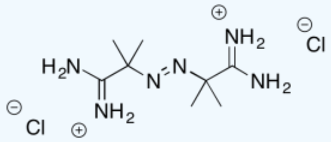
i)

? Exercise 6.2.4

Chemists have a wide range of initiators available. The following two examples are similar in some ways, but may be useful under different conditions. For what conditions might each initiator best be suited?



vs.



6.3: Radical Initiation- Radical Stability

Bond strength isn't just about the interaction of the two fragments bonded together. It is also influenced by the stability of those two species on their own. When the bond is broken, what pieces are left over?

The formation of radicals may be driven by the weakness of a particular bond. In terms of radical formation via bond homolysis, the reaction is more product-favored if the bond being broken is weak. In other words, the bond is not very low in energy, so the overall reaction may become more downhill (or at least less uphill). In that case, forward reaction is favored because of reactant destabilization.

However, a downhill reaction could also occur through product stabilization. For example, we have already seen that larger, more polarizable atoms form more stable radicals. Iodine radicals are more stable than bromine radicals, and sulfur radicals are more stable than oxygen radicals.

There are other factors, too. One of the most important factors is resonance. We have seen that the stability of anions and cations is strongly influenced by delocalization. Factors that spread the excess charge onto multiple atoms, rather than allowing charge to concentrate on one atom, make charged species much more stable.

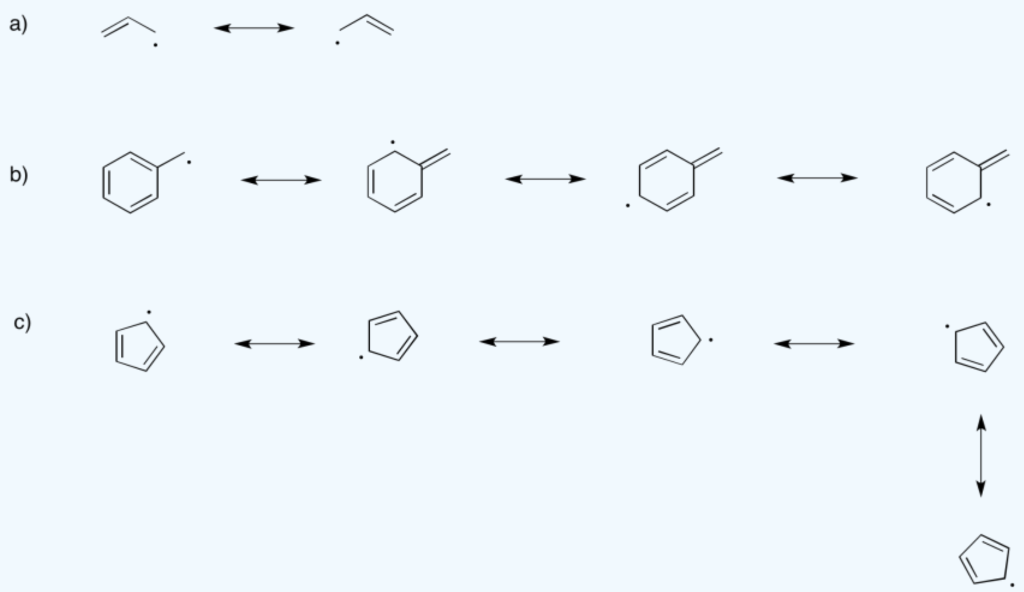
For example, carbon-based anions are relatively unstable, but a delocalized carbanion is within the realm of possibility. Enolate ions are particularly easy to obtain because negative charge is partially delocalized onto a more electronegative oxygen atom. Delocalization also strongly stabilizes radicals. It is one of the most important factors in the stability of carbon-based radicals.

? Exercise 6.3.1

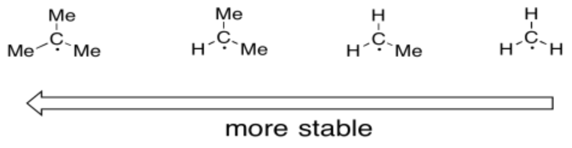
Illustrate the resonance stabilization in the following radicals

a) allyl, CH_2CHCH_2 b) benzyl, $CH_2C_6H_5$ c) cyclopentadienyl, C_5H_5

Answer



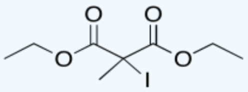
Radicals on carbon atoms are also stabilized when they are in more substituted positions. just as carbocations are more stable if they are on more substituted positions, carbon radicals are also more stable in these positions. A tertiary radical is more stable than a secondary one. A secondary radical is more stable than a primary one.



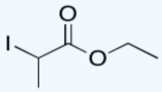
Exercise 6.3.2

Rate constants for the dissociation of the following initiators to form an iodine atom and a radical were measured under a specific set of conditions. For each pair, explain why one compound undergoes homolysis more quickly.

a)

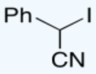


160 $M^{-1}s^{-1}$

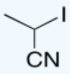


4 $M^{-1}s^{-1}$

b)

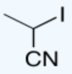


2500 $M^{-1}s^{-1}$

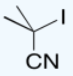


40 $M^{-1}s^{-1}$

c)

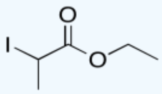


40 $M^{-1}s^{-1}$

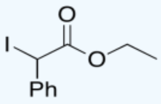


58 $M^{-1}s^{-1}$

d)

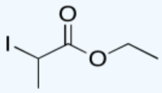


4 $M^{-1}s^{-1}$

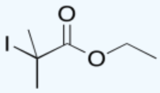


130 $M^{-1}s^{-1}$

e)



4 $M^{-1}s^{-1}$



23 $M^{-1}s^{-1}$

Answer

a)

more delocalized
forms more easily

b)

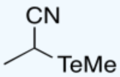
more delocalized
forms more easily

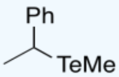
c)

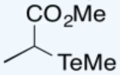
Exercise 6.3.3

Predict the relative order of bond dissociation rates for the following initiators, which would each form a tellerium radical and a carbon radical.

more substituted
forms more easily

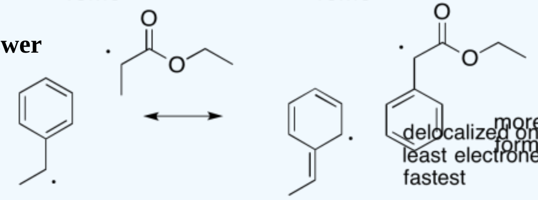






Answer

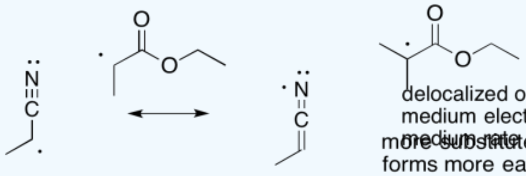
d)



more delocalized
forms more easily

delocalized onto carbon
least electronegative
fastest

e)



delocalized onto nitrogen
medium electronegative
medium rate

more substituted
forms more easily

delocalized onto oxygen
mostt electronegative
slowest

6.4: Radical Initiation- Single Electron Transfer

We saw in the section on redox reactions that single electrons can be transferred from one species to another. Because one electron is transferred at a time, radicals can be initiated this way.

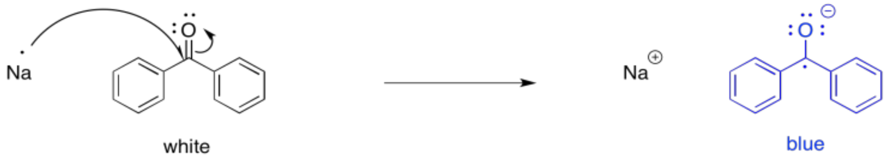
Metals that are high in the activity series, such as lithium or sodium, can easily donate their valence electrons to organic compounds. As a result, those organic compounds become radicals.

$$\mathrm{Li} \longrightarrow \mathrm{Li}^{+} + \mathrm{e}^{-}$$

$$\mathrm{Na} + \mathrm{Na}^{+} + \mathrm{e}^{-}$$

The possibility for this reaction is most easily illustrated with an example from carbonyl chemistry. Carbonyls are electrophiles. The electrophilic carbon normally accepts a pair of electrons from a nucleophilic donor. However, a single electron could be thought of as a nucleophile, too.

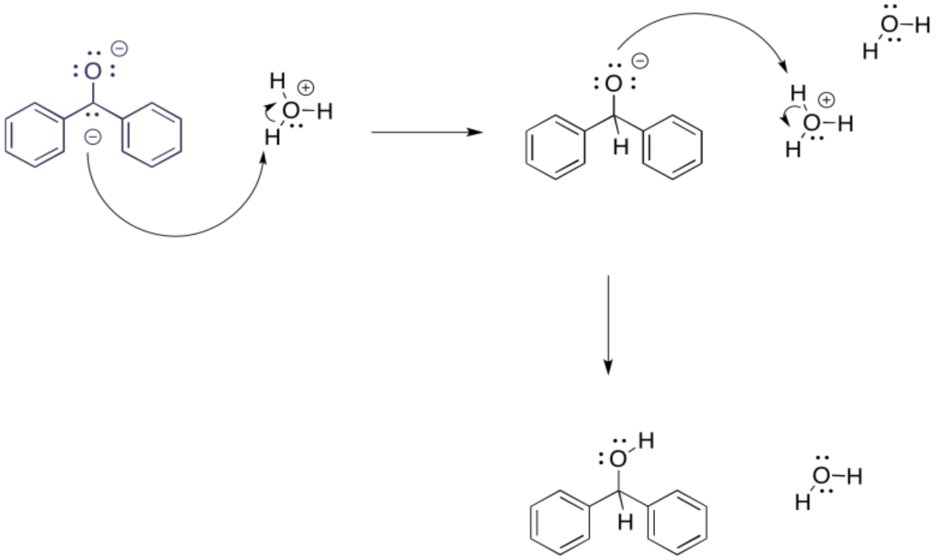
For example, if benzophenone is dissolved in an unreactive solvent, such as ether, over a few pieces of sodium, the sodium can transfer an electron to the carbonyl. The interesting thing about this reaction is that, although benzophenone is a white (or colourless) compound and ether is a colourless liquid, the ether solution turns deep blue after a couple of hours. Benzophenone radical anion is a deep blue colour.



Benzophenone radical has long played an important role in research labs. For many years, sodium has been used as a drying agent for organic solvents. Because of the well-known propensity of sodium to react with water, any traces of water in a flask of ether are destroyed. They are converted to sodium hydroxide and hydrogen gas. However, in the absence of water -- that is, if the sodium has already done its job -- the sodium can transfer electrons to benzophenone in solution, producing a blue colour. Benzophenone thus works as an indicator to let researchers know that the solvent is dry.

After a few more hours, the colour changes once more to a deep purple. That's because a second electron gets transferred to the benzophenone radical, forming benzophenone dianion. That's when you know the solvent is really, really dry. However, all of this has to be done under a nitrogen atmosphere, or else the benzophenone radical anion undergoes additional reaction with oxygen, producing yellow schmutz all over the flask instead of the beautiful purple colour. This drying method also works with benzene or toluene, or with a little modification, saturated hydrocarbons such as pentane. It doesn't work with many other solvents, which might instead react directly with the sodium.

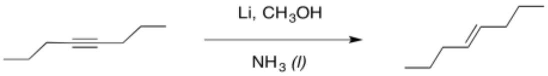
But what would happen if, at this point, we carefully introduced some protons? Maybe it is in the form of an acid, either strong (HCl) or very weak (NH_4Cl). The benzophenone dianion would surely get protonated, and since it is a dianion it would get protonated twice.



The overall result is a reduction of the benzophenone to the corresponding alcohol, 1,1-diphenylmethanol. It would be just like we had added sodium borohydride, a source of nucleophilic hydride (that's a proton plus two electrons) and then did an acid workup (adding a second proton). In this case, we have just added the components (two electrons, two protons) in a different order.

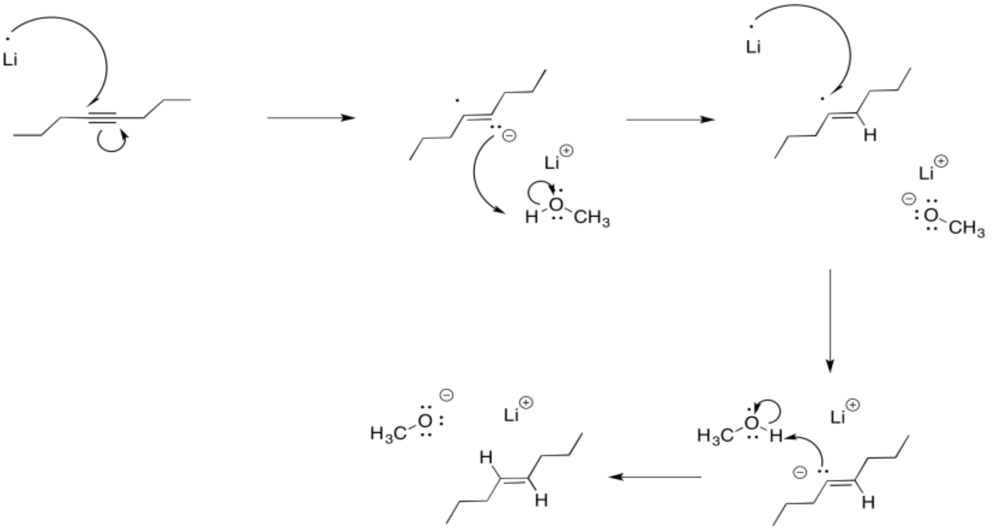
Furthermore, this method of reducing things isn't really limited to carbonyls. Alkynes and aromatics are also susceptible to reduction to the radical anion or dianion, although the reaction is more commonly performed using lithium.

We can imagine a similar process of protonation occurring to get an alkene. It looks a little like an alkyne reduction, but instead of using H_2 as the source of hydrogen atoms, we have used an alkali metal as the source of the electrons and an alcohol as the source of protons.

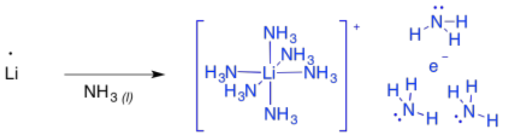


Interestingly, these latter reactions are stereospecific. The sites of the anions (and subsequent protonations) are as far apart as possible. That means that the anions are found *trans*- to each other in the alkenyl anion. As a result, the *trans* alkene always results from lithium reduction. This reaction is complementary to hydrogenation with Lindlar's catalyst, which always results is *cis* alkenes.

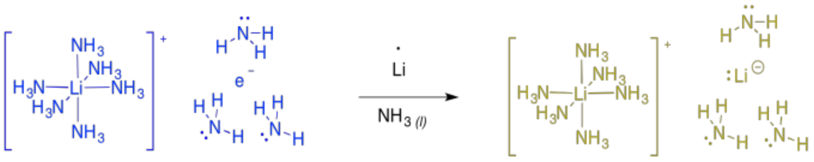
It may be surprising that the dianion is not required in order to get this "keep-the-negative-charges-far-apart" selectivity. Normally, these reductions are conducted in liquid ammonia, often with a little bit of alcohol added. Under those conditions, the initial radical anion is protonated before the second electron donation. The dianion never actually forms, yet the selectivity is still the same. Repulsion between the lone pair and the radical are enough to account for the stereoselectivity.



These reactions are sometimes called "dissolving metal reductions" because the lithium metal dissolves in the liquid ammonia. In ammonia and some amines, the metal actually undergoes ionization to produce Li^+ and e^-. This "salt" is called "lithium electride" and it produces a bright blue colour. It is really a coordination complex, with a hexaammine lithium cation and an ammonia-solvated electron. Furthermore, the solution is paramegnetic and highly conducting, because of all of those unpaired electrons floating around on their own.

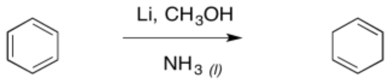


If you keep adding more and more lithium to the ammonia, at some point the solution becomes diamagnetic and turns gold in colour. At this point, the evidence suggests formation of "lithium lithide", or Li^+ Li^-. The same thing happens with other alkali metals, such as sodium or potassium, producing bronze-coloured sodium sodide or potassium potasside.

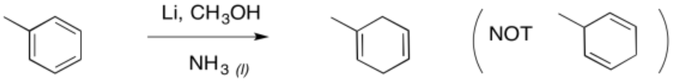


Similar reactions occur with aromatic systems. These reactions are called "Birch reductions". Because of the same electron-electron repulsion problem encountered in alkyne reduction, Birch reductions always result in the radical / anions positioning themselves at the 1,4-positions in the benzene ring.

The result is a cyclohexa-1,4-diene. Just like with the alkyne reduction, the Birch reduction is usually performed with a small amount of alcohol in solution.



Furthermore, the remaining double bonds from a Birch reduction are in the more substituted positions; that's understandable in terms of the trend of alkene stability, in which more substituted double bonds are more stable.



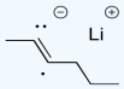
Exercise 6.4.1

Illustrate the products of single electron transfer from lithium to the following compounds

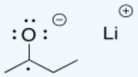
a) 2-hexyne, $CH_3CC(CH_2)_2CH_3$ b) 2-butanone, $CH_3COC_2H_5$ c) allyl bromide, CH_2CHCH_2Br

Answer

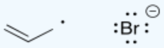
a)



b)



c)



Exercise 6.4.2

Single electron transfer is much more difficult to a carboxylate anion than to an aldehyde or ketone. Explain why.

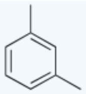
Answer

> The reduction potential of the negatively charged carboxylate anion would be much less positive than the reduction potential for the neutral aldehyde or ketone. We think of a carboxylate anion as much less electrophilic than aldehydes and ketones for the same reason.

Exercise 6.4.3

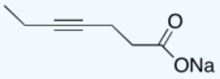
Show the products of dissolving metal or Birch reductions in the following cases.

a)

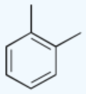


b)

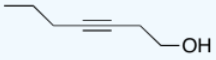
c)



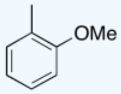
d)



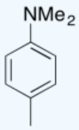
e)



f)

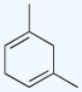


g)

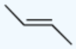


Answer

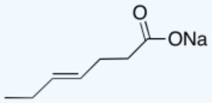
a)



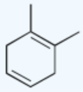
b)



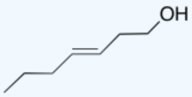
c)



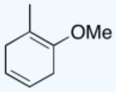
d)



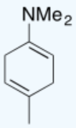
e)



f)



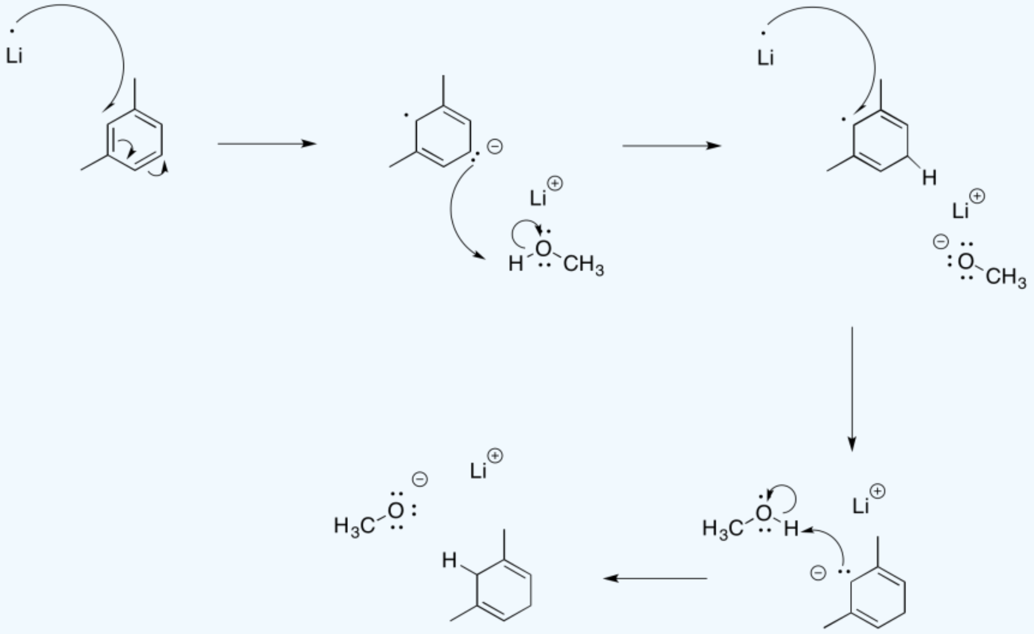
g)



? Exercise 6.4.4

Show the mechanism for the Birch reduction of *m*-xylene (*m*-dimethylbenzene) with lithium and methanol in liquid ammonia.

Answer

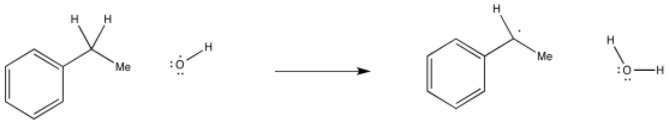

Li
Li
H
O
CH3
Li
H
Li
O
CH3
H3C
O
H
Li
H3C
O
Li
H

6.5: Radical Propagation

Radicals are known for engaging in "chain reactions". In a chain reaction, a reactive intermediate is generated. When it reacts, it leaves another reactive intermediate, much like the first. This event is called "propagation".

There are a couple of common ways that propagation occurs. The radical might achieve its stable electron count by snatching another atom, especially a hydrogen atom. That event is called hydrogen atom abstraction. Alternatively, a radical may bond with one of the electrons in a pi bond.

In the abstraction of an atom, the radical forms a bond with that atom. That bond gives the radical an even number of electrons again.



Exercise 6.5.1

Show, with arrows, the mechanism for abstraction of a hydrogen atom from ethylbenzene by a hydroxyl radical.

Answer

It's important to note that in a hydrogen atom abstraction, the radical is reacting not just with the proton, but with the entire hydrogen atom. It is taking the electron, too.

Exactly which atom gets abstracted has a lot to do with bond strengths. For example, O-H bonds are quite strong (up to 120 kcal/mol, in water, for example). Thus, an OH radical will frequently abstract hydrogen atoms, because there is an energetic payoff when that happens.

Of course, a bond also has to get broken during an abstraction. That costs some energy. C-H bonds are also pretty strong, so they may be hard to break. However, some C-H bonds in particular are weaker than others. For example, in order to break a benzylic C-H bond, the cost is only about 88 kcal/mol. In the case of hydrogen atom abstraction from ethylbenzene by hydroxyl radical, the trade-off is worth it.

Exercise 6.5.2

Draw a reaction progress diagram for the abstraction of a hydrogen atom from ethylbenzene by a hydroxyl radical.

It is not always the case that a reaction is purely determined by the thermochemistry of the bonds involved. Sometimes, there are kinetic factors that block the path to the more stable product, or that lower the path to the less stable product. However, in many atom abstractions, because the old bond is being broken at the same time that the new bond is being formed, both factors matter in the rate determining step. By the time the transition state is reached, the stability of the complex is influenced both by the bond that is being broken and the bond that is being made. As a result, the thermodynamics of the reaction can have a strong influence on the pathway to products.

Bond	Dissociation Energy (kcal/mol)	Bond	Dissociation Energy (kcal/mol)
F-H	136	Br-H	88
Cl-H	103	I-H	71
EtO-H	105	O_2N-OMe	42
CH_3S-H	87	Cl-OMe	48

PhO-H	87	H_3C-OMe	85
Me_2N-H	91	H_3C-NH_2	85
Et_3Si-H	96	H_3C-F	115
Bu_3Ge-H	88	CH_3-H_2C-Cl	85
Bu_3Sn-H	78	CH_3-H_2C-Br	72
Me_3Sn-Cl	100	CH_3-H_2C-I	57

Exercise 6.5.3

Indicate whether a dimethylamine radical is likely to carry out hydrogen atom abstraction from each of the following molecules.

a) Et_3SiH b) PhOH c) EtOH d) Bu_3SnH e) HF f) HI

Answer a

a) no; a stronger bond would have to be broken and replaced with a weaker bond.

Answer b

b) yes; a weaker bond would be broken and replaced with a stronger one.

Answer c

c) no

Answer d

d) yes

Answer e

e) no

Answer f

f) yes

Exercise 6.5.4

Indicate whether a chlorine atom abstraction would be likely to occur in each of the following cases.

a. Chloroethane is exposed to methoxy radical.
b. Chloroethane is exposed to trimethyltin radical.
c. Trimethyltin chloride is exposed to methoxy radical.

Answer a

a) no

Answer b

b) yes

Answer c

c) no

Sometimes, the identity of the two atoms that form a bond does not tell the entire story about bond strengths. In the case of C-H bonds of hydrocarbons, for example, a range of bond strengths have been experimentally determined. There is a 40 kcal/mol difference between the weakest C-H bond in a simple hydrocarbon and the strongest (that's about 175 kJ/mol, for the metricoriented). These bond strengths are remarkably senstive to subtle structural differences, largely because of relative stabilities of the resulting radicals when the bond is broken.

Bond	Bond dissociation energy (approximate; kcal/mol)
HCC-H (aryl)	130
Ph-H (aryl)	110
CH_2=CH-H (vinyl)	106
H_3C-H	105
CH_3CH_2-H	98
$(CH_3)_2CH$-H	95
$(CH_3)_3C$-H	92
$PhCH_2$-H (benzyl)	88
CH_2=CH-CH_2-H (allyl)	88

? Exercise 6.5.5

Propose reasons for the trends in bond strengths among the following groups.

a. H_3C-H , CH_3CH_2-H , $(CH_3)_2CH$-H, $(CH_3)_3C$-H
b. $(CH_3)_2CH$-H, $PhCH_2$-H, CH_2=CH-CH_2-H
c. HCC-H, CH_2=CH-H, CH_3CH_2-H

Answer a

a) The effect is similar to the stability of carbocations. The more substituted radical is more stable. Thus, the trend from most to least stable is tertiary > secondary > primary > methyl radical. The trend likely originates from a hyperconjugation effect, as in carbocations.

Answer b

b) The trend here is that if the radical is delocalized by resonance, it is more stable. The allyl and benzyl radicals are more stable than the isopropyl radical. This trend is also seen in cations.

Answer c

c) The trend here has to do with "hybridization effects" or the atomic orbitals that contribute to the formation of molecular orbitals involved in the relevant bond. In a linear alkyne, the C-H bond can be formed only from some combination involving a hydrogen 1s orbital, carbon 2s orbital and one of the carbon 2p orbitals. This combination is called a "sp" hybrid and the orbital that combines with the hydrogen can be considered 50% 2s, 50% 2p in character.

In a planar alkene, the C-H bond can be formed only from some combination involving a hydrogen 1s orbital, carbon 2s orbital and two of the carbon 2p orbitals (since two of them could lie in this plane). This combination is called a "sp^2" hybrid and the orbital that combines with the hydrogen can be considered 33% 2s, 66% 2p in character.

In a tetrahedral alkane, the C-H bond can be formed from some combination involving a hydrogen 1s orbital, carbon 2s orbital and all three of the carbon 2p orbitals. This combination is called a "sp^3" hybrid and the orbital that combines with the hydrogen can be considered 25% 2s, 75% 2p in character.

Because a 2s orbital is lower in energy than a 2p orbital, a bond that has greater 2s character is lower in energy than a bond with less 2s character. That means that a bond with greater 2s character is harder to break than a bond with less 2s character. Hence, the alkane C-H bond is weaker than the alkene C-H bond, which is weaker than the alkyne C-H bond.

? Exercise 6.5.6

Explain why a trialkyltin radical (R_3Sn) would not be able to remove a hydrogen atom from propane, but could abstract a chlorine atom from chloroethane.

Answer

The Sn-H bond has a dissociation energy of about 78 kcal/mol, compared to about 98 kcal/mol for the C-H bond in ethane. The formation of the Sn-H bond would not compensate for the energy needed to break the C-H bond. On the other hand, the 100 kcal/mol released upon formation of a Sn-Cl bond would more than make up for the 85 kcal/mol required to breal a C-Cl bond.

We could try to rationalise those differences, although bond strengths are always very complicated issues and we will not be able to explain things satisfactorily without quantum mechanical calculations. Let's start with two basic factors, though: the amount of covalency and the amount of polarity.

The difference between the covalent radii of tin and hydrogen (1.39 vs. 0.31 Å) is much greater than the difference between tin and chlorine (1.39 vs 1.02 Å), so there may be less overlap and less covalency between tin and hydrogen than between tin and chlorine. By comparison, the covalent radius of carbon is about 0.76, which puts it somewhere in between hydrogen and chlorine.

In addition, as measured on the Pauling scale, the electronegativity values of these atoms are: chlorine, 3.16; carbon, 2.55; hydrogen, 2.2; tin, 1.96. The tin-chlorine bond would have a large ionic component; this additional component of bonding would strengthen the Sn-Cl bond.

Addition to an alkene is another common propagation pathway in radical reactions. In this case, a π (pi) bond is broken in the alkene to form a new bond to the radical species. That leaves the second electron from the π bond to form a new radical species.

Π bonds are often weaker than σ bonds, making this pathway energetically accessible in many cases. Perhaps more importantly, the electrons in π bonds are found above and below a flat part of the molecule, leaving them open and accessible for reaction with radicals.

Bond	Bond dissociation energy (kcal/mol)	Bond	Bond dissociation energy (kcal/mol)
H_3C-CH_3	90	$H_2C=CH_2$	174
H_3C-NH_2	85	$H_2C=NH$	?
H_3C-OH	92	$H_2C=O$	179

? Exercise 6.5.7

Show a mechanism, with curved arrows, for the reaction of pentene with bromine atom.

Answer

? Exercise 6.5.8

Calculate the strengths of the following pi bonds.

a. In ethene.
b. In methanal.

Answer a

a) 174 - 90 kcal/mol = 84 kcal/mol for the π contribution only

Answer b

b) 179 - 92 kcal/mol = 87 kcal/mol for the π contribution only

? Exercise 6.5.9

The pi bond in PhCH=NPh has been calculated to have a dissociation energy of 77 kcal/mol.

a. Estimate the missing imine C=N bond dissociation energy in the above table.
b. Explain why your estimate may be unreliable.

Answer a

a) 85 + 77 kcal/mol = 162 kcal/mol for the combined σ + π contribution

Answer b

b) There may be significant differences between the π bond in methanal imine (CH_2=NH) and the imine for which we have bond strength data. For example, breaking the bond would result in radicals next to phenyl groups, which may be significantly stabilized. On the other hand, the π bond itself may be significantly stabilized by conjugation. Thus, our estimate is probably not correct, but it is difficult to say whether it is too high or too low.

6.6: Radical Termination

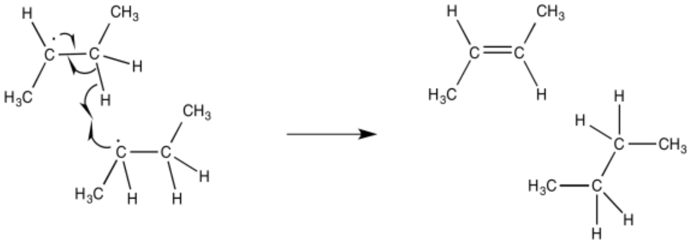
If propagation steps lead to chain reactions, continually leading to the formation of new radicals that engage in further propagation reactions, then where does it end? That self-perpetuating cycle can be part of the beauty of radical reactions, allowing a very small amount of initiator to efficiently start a process that then sustains itself. However, it is important that the reaction has an end point, so that it does not continue to run out of control.

There are a couple of different ways that radical reactions commonly come to an end. These elementary reactions are called terminations steps. The simplest event that could occur is a radical recombination step. In that case, two radicals approach each other and bond together, sharing their previously unpaired electrons.

- In termination steps, two radicals come together to make no radicals.

Energetically, termination steps like this one should be pretty favorable, because they involve formation of a new bond. These steps are mostly limited by the low concentration of radicals in solution. If two radicals don't happen to bump into each other, then they won't react together.

A second event leading to termination also involves the collision of two radicals. However, the trajectory of the two radicals is slightly different, so that the unpaired electrons do not connect with each other. Instead, the unpaired electron on one radical molecule encounters a hydrogen on the other molecule. If the hydrogen is alpha to the radical, it is easily abstracted, forming a double bond.



Researchers are actually able to measure the bond strength of such a hydrogen alpha to a radical. They find that the bond is considerably weakened compared to a similar hydrogen atom in a molecule that does not contain a radical in the same position.

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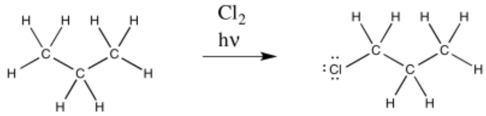
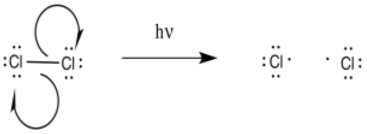
6.7: Radical Substitution

There are a couple of classic reactions based on radical chemistry that are often used to illustrate different consequences of the mechanism. One of these reactions is the radical substitution of a halogen atom for a hydrogen atom.



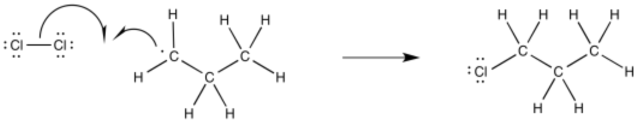
This reaction is commonly observed with chlorine and bromine. Multiple products are possible; only one of these products is shown above.

As a radical reaction, the first step would have to be an initiation step. If the reaction proceeds as written, via the addition of molecular chlorine and light, then initiation would involve direct homolysis of the chlorine-chlorine bond.



Once the chlorine radicals are present, propagation steps would occur. Given the ultimate replacement of a hydrogen by a chlorine atom, radical abstraction of a hydrogen atom seems likely. That event would lead to the formation of an alkyl radical.

The newly-formed alkyl radical would be able to engage in propagation reactions as well. For example, it could react with another chlorine molecule. It would produce a new chlorine radical and the reaction product, chloroproane.

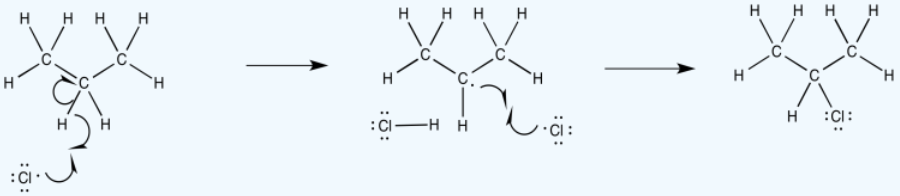


Alternatively, if we wanted to imagine the full range of elementary steps in radical reactions, we could picture a termination step, with another chlorine combining with that alkyl radical to form a chloroalkane product.

? Exercise 6.7.1

Propose a mechanism, with curved arrows, for the formation of 2-chloropropane via radical chlorination.

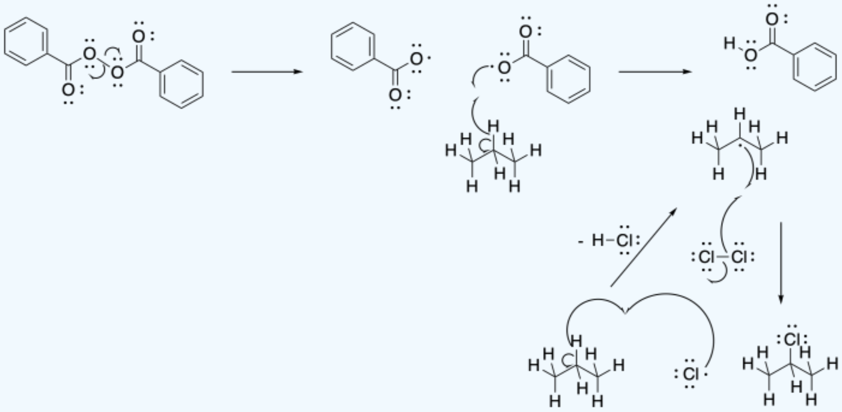
Answer



Exercise 6.7.2

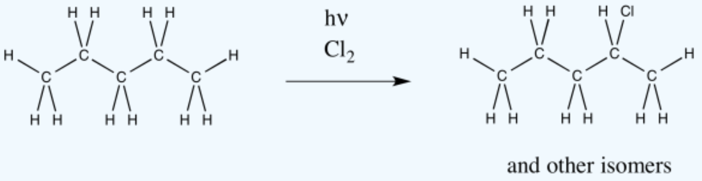
Propose a mechanism, with curved arrows, for the following variation on radical chlorination.

Answer



Exercise 6.7.3

Radical chlorination of pentane also results in multiple products. One of them is shown below. What other isomers are formed?



Answer

2-chloropentane is shown; 1-chloropentane and 3-chloropentane would form, too.

Exercise 6.7.4

Which product would be the major one in radical chlorination of propane? Why?

Answer

2-bromopropane.

Clearly, radical halogenation could result in a mixture of products. That's because there are different hydrogen atoms that could be extracted in the first propagation step. Abstracting a hydrogen atom from the middle carbon of propane would lead ultimately to 2-chloropropane. Abstracting a hydrogen atom from either of the end carbons of propane would lead to formation of 1-chloropropane.

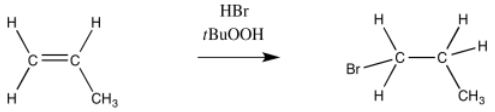
6.8: Radical Addition

Radical addition to alkenes is another classic example of a radical reaction. Like radical substitution, it illustrates some important elements of radical reactivity.

The most common example of radical addition to alkenes seen in college chemistry textbooks is radical addition of hydrogen bromide, HBr. That's because it complements the usual addition of HBr to an alkene.

In the usual addition, HBr adds in a Markovnikov fashion to place the bromine at the more-substituted end of the alkene and the hydrogen on the less substituted end (remember the adage, "the rich get richer and the poor get poorer").

In contrast, addition of HBr under radical conditions leads to the bromine attaching at the least-substituted position, whereas the hydrogen bonds to the most-substituted position. This is a Robin Hood reaction.

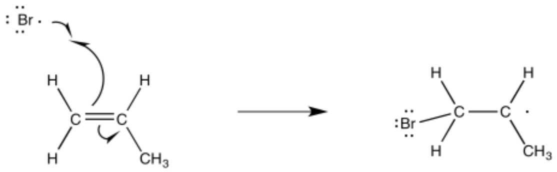


How does that reversal in regiochemistry come about? Consider the mechanism of the reaction.

Radical addition of HBr is almost always done in the presence of peroxides. The peroxide acts as an initiator for the reaction. The O-O bond may break through the simple action of thermal energy (maybe even at room temperature).

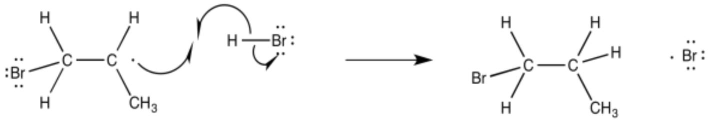
The alkoxy or hydroxy radicals that result from this initiation step are left to induce radical propagation. Certainly one of the easiest available targets is the relatively weak H-Br bond. Abstraction of a hydrogen atom from HBr produces a bromine radical.

One of the things that the bromine radical could do is add to the double bond of an alkene. When it does so, it will bind to one end or the other of the former double bond. To which end will it go?



Like cations, radicals are considered to be somewhat electron-deficient. They are stabilized by electron-donating factors. That means that, like a cation, the radical will be more favorable on the most-substituted carbon of the formal double bond.

Notice that this step is actually governed by almost the exact same factor that governs the polar addition of HBr. The regiochemistry is governed by the stability of the intermediate. Once that event has transpired, the regiochemistry of the product is fixed. It only remains for the alkyl radical to pluck a hydrogen atom from another HBr molecule, forming the final product and generating another bromine radical.



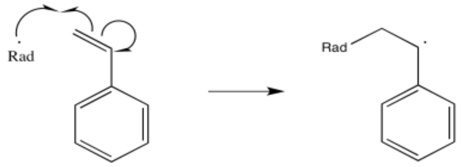
more stable   less stable

6.9: Radical Polymerization

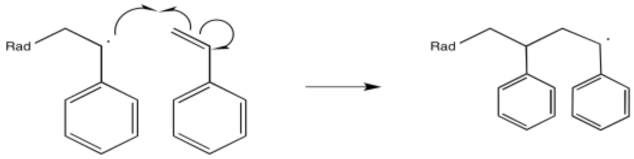
Radical addition to alkenes can be applied to the production of macromolecules. Like other polymerisation reactions involving alkenes, it involves the formation of a reactive intermediate by the action of an initiator on an alkene. A chain reaction results in which other alkenes are enchained into a polymer.

The term "initiator" here is used in a slightly different way than we have used it with other radical reactions. The radical initiator has already undergone its reaction to form a radical. That radical then initiates chain growth. This step is really a propagation step in terms of types of radical elementary reactions, because one radical leads to a new radical.

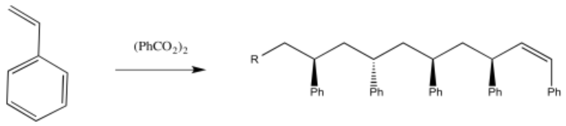
Polystyrene is one example of a material that is frequently prepared via radical conditions. During the reaction, a radical adds to the double bond of the alkene.



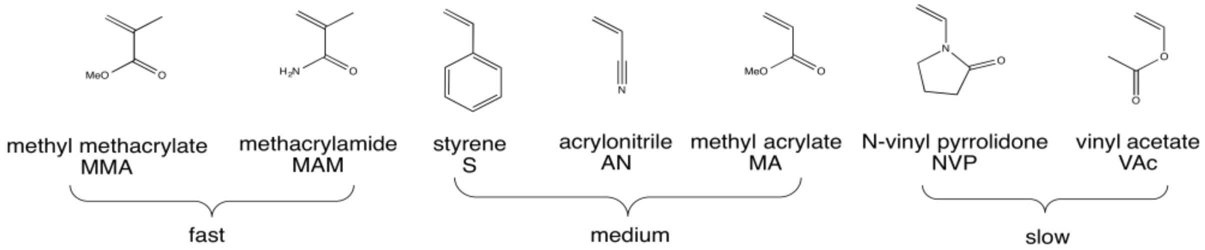
The newly-formed radical, in regular alkene addition, would then react with something to abstract an atom and achieve stable, closed-shell configuration. However, in a polymerisation reaction, alkene molecules are intentionally packed closely together. Either they are very concentrated in solution or else they are neat (with no solvent at all). As a result, the newly-formed radical just gobbles up another alkene.



There are lots of ways to carry out this reaction. One way would be to take some styrene, heat it up until it melts, and add some benzoyl peroxide.



Radical polymerisation is a critical method of preparing polymers. The figure below shows a number of monomers that are commonly polymerised under radical conditions.



? Exercise 6.9.1

Look at the monomers listed above.

a. For each of the three groups (fast, medium and slow), identify what structural features the members of the group have in common that distinguishes them from the other groups.
b. Propose a reason why the fast group undergoes more rapid polymerisation than the other groups.
c. Propose a reason why the medium group undergoes more rapid polymerisation than the slow group.

Answer a

a) Fast: disubstituted, conjugated alkenes

Medium: monosubstituted, conjugated alkenes

Slow: alkenes monosubstituted with a heteroatom

Answer b

b) Fast: the radical formed would be both tertiary and conjugated. This stable radical forms very quickly.

Medium: the radical formed would be conjugated, but not tertiary. The radical does not form quite as quickly as in the above group.

Answer c

c) Medium: the radical formed would be both conjugated. This stable radical forms quickly.

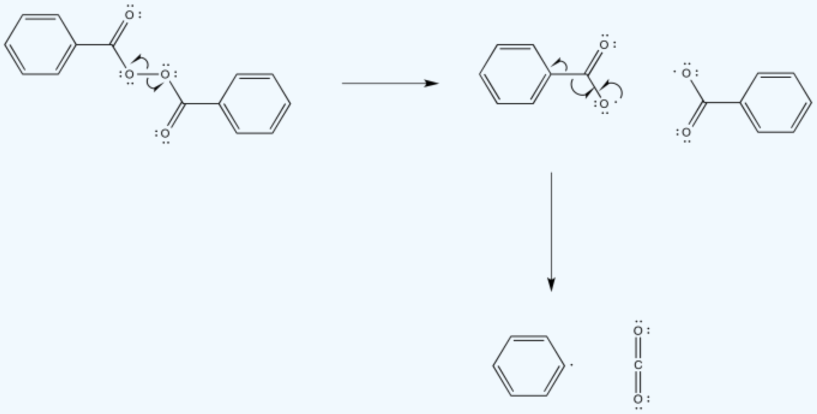
Slow: the radical formed would not be conjugated in the usual sense (although heteroatoms next to radicals do provide some stability). The radical does not form very quickly compared to radicals next to double bonds.

? Exercise 6.9.2

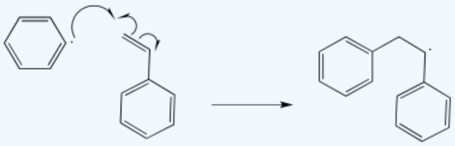
Provide a mechanism for the polymerisation of styrene in the presence of benzoyl peroxide, up through the first couple of propagation steps.

Answer

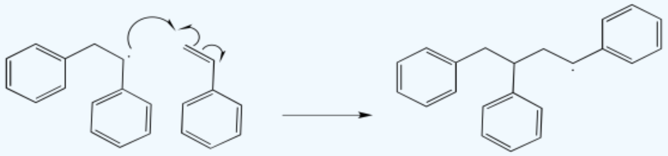
The mechanism would begin with initiation of the benzoyl peroxide.



The resulting phenyl radical acts as the initiator for polymerisation.

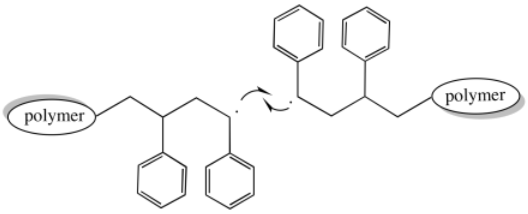


Additional propagation steps follow.



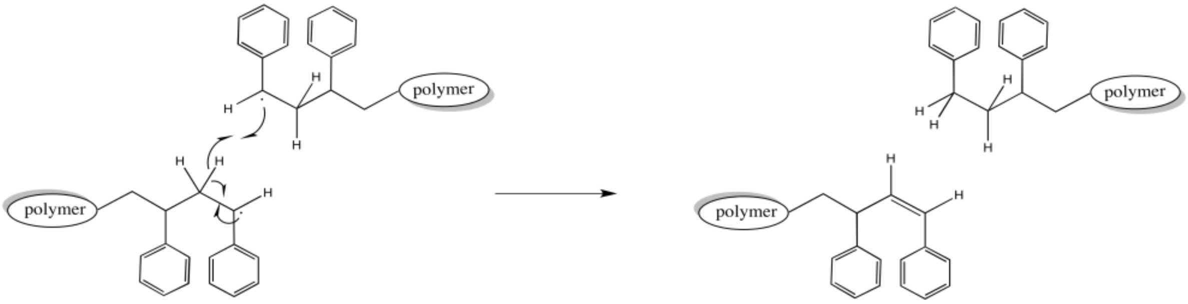
A radical polymerisation, after the initiator gets going, is just a series of propagation steps in a row. How does it all stop? There must be a termination reaction. That can happen in a couple of different ways.

For example, two growing chains might encounter each other, head-to-head. A collision could bring the unpaired electrons together to form a new bond. Two growing polymer chains would come to an end at once. At the same time, the chain length and molecular weight doubles as two chains combine into one.

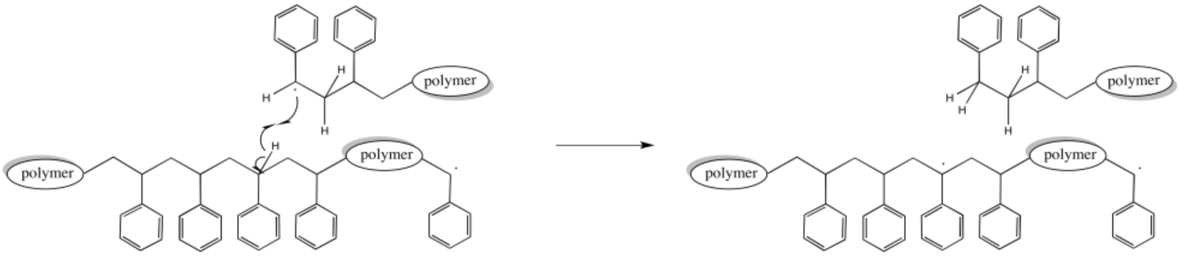


Of course, most of the other chains in the polymerisation continue growing normally. As a result, the distribution of molecular weights broadens dramatically. Some chains are twice as long as the others.

Alternatively, when two growing chains collide, one might carry out a hydrogen atom abstraction on the other. The hydrogen abstracted might come from the head of the chain, alpha to the active radical. That C-H bond is a little bit weaker, as bonds alpha to radicals typically are. The chain that picks up the hydrogen is no longer a radical. The chain that loses a hydrogen is no longer a radical, either. Both chains stop growing. Because other chains around them continue to grow, these one lag behind, resulting in a wider distribution of chain lengths.

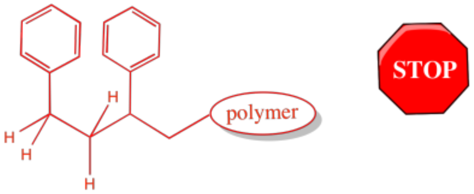


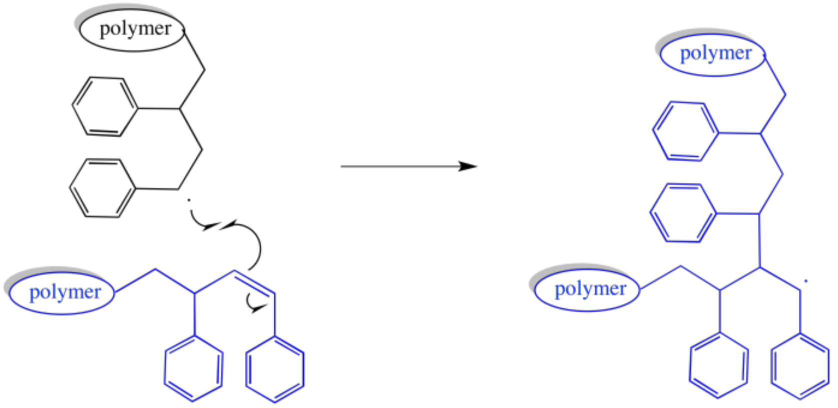
Of course, a hydrogen atom abstraction could happen elsewhere along the chain. In that case, the chain that abstracted the hydrogen stops growing, as before. However, the chain that lost the hydrogen now has two radicals. That makes two sites of chain growth. This chain starts growing twice as fast as the others. Eventually, that's going to lead to a big difference in molecular weights.



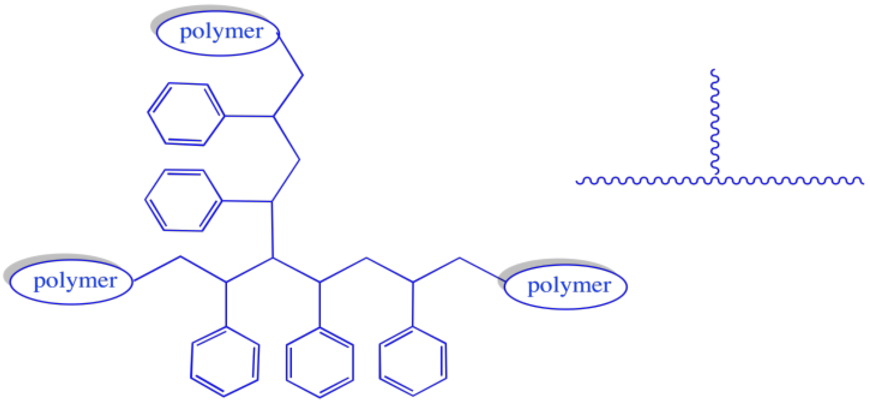
These termination events, all of which are possible and which occur more or less randomly, have profound consequences on the material produced.

There is an effect on chain length and molecular weight. Chains that have abstracted a hydrogen atoms come to a complete halt. They stop growing altogether. On the other hand, chains that have had a hydrogen stolen from them may grow again. Either they have an additional radical introduced, or else they form a π bond, which can react with another radical and start growing again. When they do, it will again be a case of two chains coming together -- an active one and a macromonomer -- leading to a trmendous jump in molecular weight.





The morphology of the polymer is clearly altered by these events. Most growing chains are simply linear: they consist of a series of enchained monomers, all in one row. However, in either of the cases in which a growing chain has lost a hydrogen atom, then continued to grow, the shape will be branched.



These two architectures have very different properties. For example, we would expect a very different T_g in a branched polymer than a linear one, with chains flowing more freely at lower temperatures in the linear one.

? Exercise 6.9.3

It has been found that radical polymerisation of styrene with a benzoyl peroxide initiator follows the rate law:

$$Rate = k[styrene][peroxide]^{1/2}$$

Explain why this rate law occurs, based on the mechanism.

Answer

The monomer dependence is straightforward: the more monomer there is present, the faster it can be enchained by the growing radical chain.

The initiator dependence is slightly more complicated, but not much. The more growing radical chains there are, the faster the monomers can be enchained. The more phenyl radical is formed, each initiating a new radical chain, then the more growing radical chains there will be.

$\text{Rate} = k\,[\text{monomer}][\text{Ph}\cdot]$

The more benzoyl peroxide there is, the more phenyl radical there will be, but the relationship is not linear, as explained below.

Benzoyl peroxide cleaves in two, ultimately producing two phenyl radicals:

$K_{eq} = [\text{Ph}\cdot]^2/[\text{BP}]$

so $[\text{Ph}\cdot]^2 = K_{eq}\,[\text{BP}]$

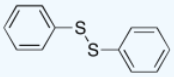
and $[\text{Ph}\cdot] = K_{eq}^{1/2}\,[\text{BP}]^{1/2}$

therefore $\text{Rate} = k\,[\text{monomer}][\text{Ph}\cdot]^{1/2}$

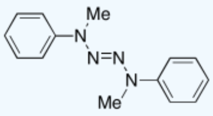
Exercise 6.9.4

Provide mechanisms for radical formation from the following initiators:

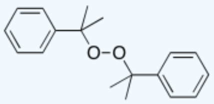
a)



b)

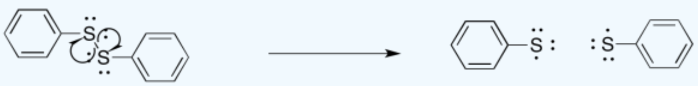


c)

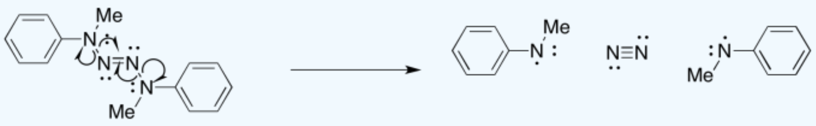


Answer

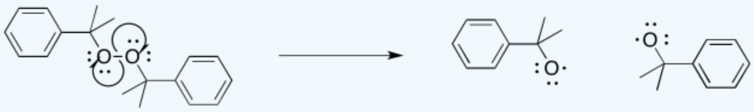
a)



b)



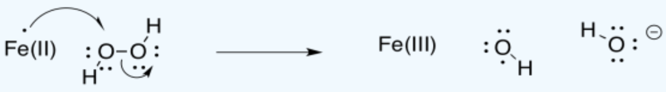
c)



Exercise 6.9.5

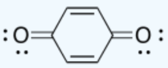
There is a great deal of interest in aqueous polymerisations for environmental reasons. Hydrogen peroxide is an obvious water-soluble initiator; however, it is slow to initiate polymerisation. Show how initiation can be accelerated in the presence of Fe(II) ions.

Answer

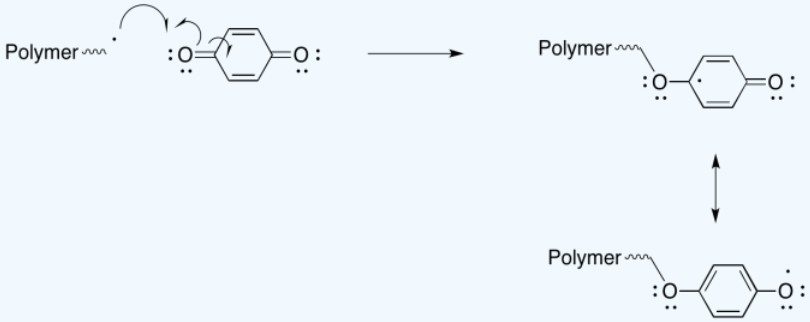


Exercise 6.9.6

A number of compounds can be used as inhibitors of radical polymerisation. For example, benzoquinone will stop radical chains from growing. Show a mechanism for its reaction with a growing polymer chain and explain why the product of the reaction is a relatively stable radical.



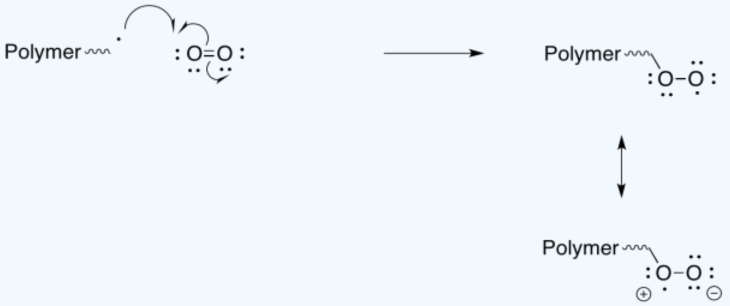
Answer



Exercise 6.9.7

It may be surprising that one of the most effective inhibitors of radical polymerisation is molecular oxygen; it can slow the polymerisation rate by a factor of tens of thousands. The radical that results from the addition of O_2 to a growing chain is considered to be resonance-stabilised. Show the mechanism of O_2 addition and demonstrate resonance stability in the product.

Answer



Peroxy radicals are relatively stable and react slowly. However, when they do react, they also undergo reactions other than radical polymerisation, so that they are even more effective as inhibitors of polymerisation.

6.10: Living Radical Polymerisation

Chain polymerisation reactions result in the efficient conversion of monomers into high molecular weight polymers. However, chain termination events result in a broadening of the polydispersity index of the material. In other words, instead of producing a material composed of molecules that are all about the same molecular weight, a wide range of sizes of molecules result. Some of the chains are very short and others are very long. That's a problem, because the chain length (and the associated property, molecular weight) strongly influence the properties of the material. If the size of the molecules is not controlled, neither are the properties. If the properties are not controlled, the material won't perform reliably in its intended application.

Exercise 6.10.1

The degree of polymerisation of a polymer is simply the average number of monomers incorporated in each polymer chain. Given the following "feed ratios" (ratios of monomer to initiator), what is the *expected* degree of polymerisation in each case?

a. methyl methacrylate : AIBN 500 : 1
b. styrene : benzoyl peroxide 1000 : 1
c. acrylonitrile : tert-butyl peroxide 600 : 3

Answer a

Because each initiator breaks in half, forming two radicals, one initiator starts two growing chains. Every initiator will, on average, consume half the monomers, assuming no unexpected chain termination events.

a) DP = 500 monomers / 2 growing chains = 250

Answer b

Because each initiator breaks in half, forming two radicals, one initiator starts two growing chains. Every initiator will, on average, consume half the monomers, assuming no unexpected chain termination events.

b) DP = 1000 monomers / 2 growing chains = 500

Answer c

Because each initiator breaks in half, forming two radicals, one initiator starts two growing chains. Every initiator will, on average, consume half the monomers, assuming no unexpected chain termination events.

c) DP = 600 monomers / 3 growing chains = 200

Exercise 6.10.2

The measured degree of polymerisation indicates the number average molecular weight of the polymer (M_n). Calculate M_n in each of the following cases.

a. polystyrene, with DP = 1250
b. polymethacrylamide, with DP = 725
c. poly(methyl acrylate), with DP = 1420

Answer a

M_0 = molecular weight of monomer in each case. 1 D (Dalton) = 1 amu

a) $M_n = DP \times M_0 = 1250 \times 104$ D = 130,000 D = 130 kD

Note that end groups were neglected in these calculations; they may contribute a significant percentage of total molecular weight at lower DP. A more accurate calculation would account for the identity of both end groups.

Answer b

M_0 = molecular weight of monomer in each case. 1 D (Dalton) = 1 amu

b) $M_n = DP \times M_0 = 725 \times 85$ D = 61,625 D = approximately 62 kD

Note that end groups were neglected in these calculations; they may contribute a significant percentage of total molecular weight at lower DP. A more accurate calculation would account for the identity of both end groups.

Answer c

M_0 = molecular weight of monomer in each case. 1 D (Dalton) = 1 amu

c) $M_n = DP \times M_0 = 1420 \times 86$ D = 122,120 D = approximately 122 kD

Note that end groups were neglected in these calculations; they may contribute a significant percentage of total molecular weight at lower DP. A more accurate calculation would account for the identity of both end groups.

? Exercise 6.10.3

Alternatively, if the number average molecular weight of the polymer is measured, that result can be used to establish the degree of polymerisation. What is DP in each of the following cases?

a. polyacrylonitrile, with M_n = 11,450 D
b. poly(vinyl acetate), with M_n = 24,760 D
c. polystyrene, with M_n = 927,000 D

Answer a

a) $DP = M_n / M_0$ = 11,450 D / 53 D = 216

Answer b

b) $DP = M_n / M_0$ = 24,760 D / 86 D = 288

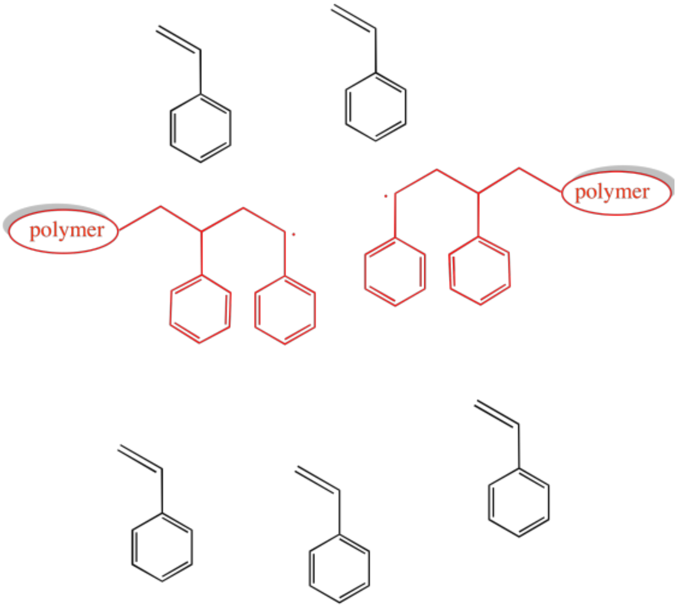
Answer c

c) $DP = M_n / M_0$ = 927,000 D / 104 D = 8,914

Living polymerisation refers to processes in which unexpected chain termination does not occur. The chain keeps growing and growing as long as more monomer is supplied. In extremely hardy cases, the term "immortal" polymerisation is sometimes used.

Typically, strategies for living polymerisation involve controlling the reactivity of the intermediates. Frequently, the concentration of the growing chains is kept low. If the concentration of growing chains is kept low, then unexpected side reactions involving the reactive growing chain will be kept to a minimum.

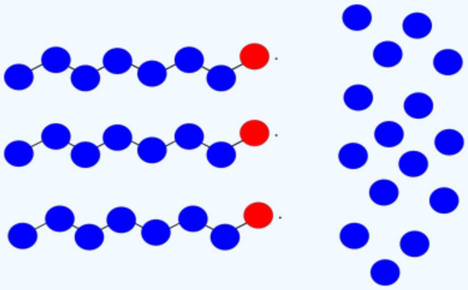
In radical polymerisation, growing chains with radicals at their growing ends will be surrounded by monomers. The radicals devour and enchain the monomers as they move through the reaction medium.



Typical chain-terminating events in radical polymerisation involve the collision of two growing chains. That event could result in head-to-head radical recombination, formation of a double bond via hydrogen abstraction at the head of a chain ("head biting") or formation of a new radical along the backbone of the polymer ("backbiting").

? Exercise 6.10.4

Suppose you have three growing polymer chains. The monomers have molecular weight = 100 D. Each chain is currently 8 repeat units long.



a. What is the current molecular weight of each chain?
b. If 15 monomers remain in solution, what is the expected degree of polymerisation of each chain, assuming they all grow at the same rate?
c. What is the expected average molecular weight?
d. What is the expected PDI?
e. Suppose two of the chains join together in a termination step. What will be the molecular weight of the new chain?
f. If the third chain keeps growing, what molecular weight will it reach?
g. What will be the average molecular weight?
h. What will be the PDI (assume it's just the ratio of largest to smallest molecular weight)?

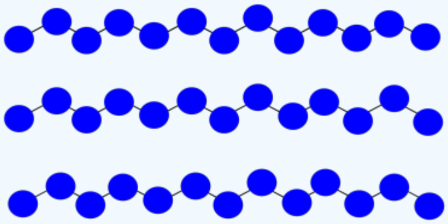
Answer a

a) MW = 8 x 100 D = 800 D

Answer b

b) 15 monomers / 3 chains = 5 new monomers / chain

DP = 8 + 5 = 13



Answer c

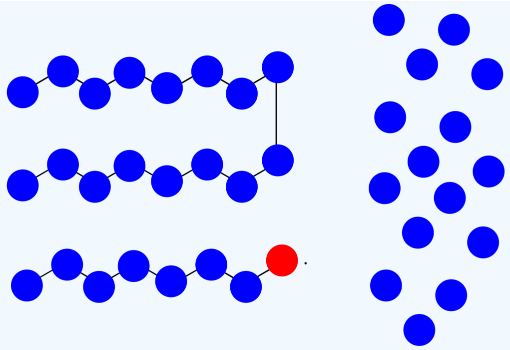
c) MW = 13 x 100 D = 1,300 D

Answer d

d) All chains are the same length; PDI = 1.0

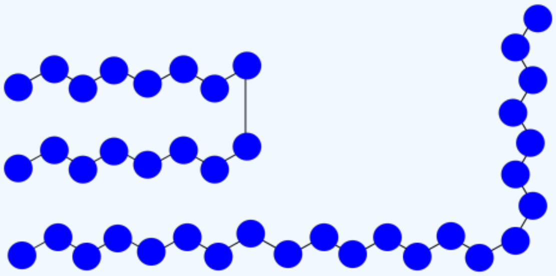
Answer e

e) MW = 16 x 100 D = 1,600 D



Answer f

f) MW = (8 + 15) x 100 D = 2,300 D



Answer g

g) M_n = (2,300 + 1,600 D) / 2 = 1,950 D

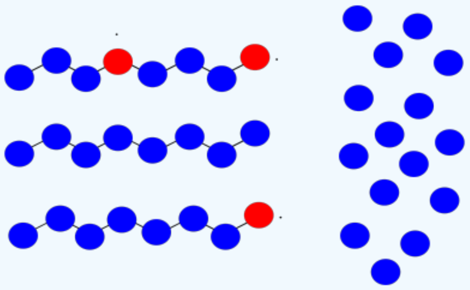
Answer h

h) PDI = 2,300 D / 1,600 D = 1.44

? Exercise 6.10.5

Suppose once again you have three growing polymer chains. The monomers have molecular weight = 100 D. Each chain is currently 8 repeat units long.

This time, one chain abstracts a hydrogen atom from the backbone of another. The first chain is terminated; the second now has two sites of growth. All three sites continue to grow at the same rate.



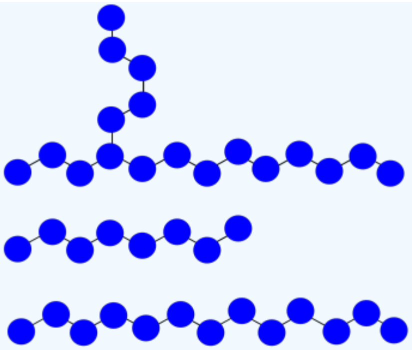
a. What will be the molecular weight of each chain?
b. What will be the average molecular weight?
c. What will be the PDI (assume it's just the ratio of largest to smallest molecular weight)?

Answer a

a) The chain that abstracted the hydrogen: MW = 8 x 100 D = 800 D

The branched chain: MW = 18 x 100 D = 1,800 D

The normal chain: MW = 13 x 100 D = 1,300 D



Answer b

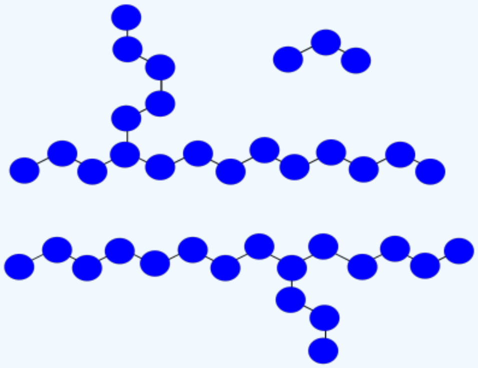
b) M_n = (1,800 + 1,300 + 800 D) / 3 = 1,300 D

Answer c

c) PDI = 1,800 / 800 D = 2.25

? Exercise 6.10.6

Practically, polymers are purified by precipitation and washing after they are prepared. That means very short oligomers are washed away.



a. What is the average molecular weight of the impure mixture shown above, assuming each monomer has molecular weight = 100 D?
b. After precipitation and washing, if small oligomers are washed away, what is the avergae molecular weight of the isolated polymer?

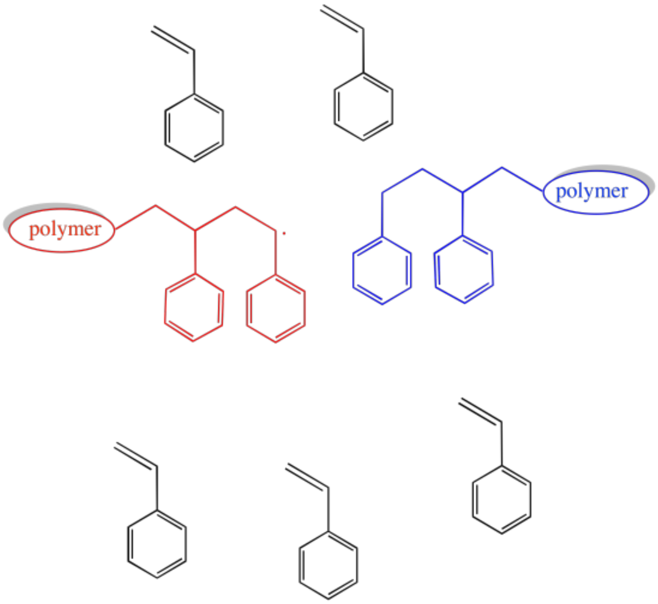
Answer a

a) M_n = (1,700 + 1,800 + 300 D) / 3 = 3,800 D / 3 = 1,267 D

Answer b

b) M_n = (1,700 + 1,800 D) / 2 = 3,500 D / 2 = 1,750 D

If the concentration of growing chains is limited, then the probability that any of these events will occur is also limited.

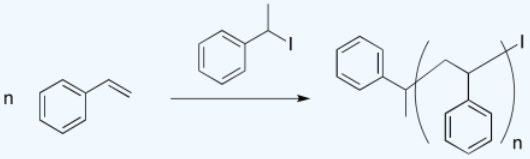


Certainly, the rate of chain growth also slows when the concentration of growing chains is lowered. That is the price to pay for a smooth operation.

The key to living radical polymerisation is to reversibly stop chain growth, sending a polymer chain from an active state into a dormant state. While in the dormant state, the polymer chain is less likely to undergo random chain-termination events. It can't grow, either, until it is brought back into an active state.

Exercise 6.10.7

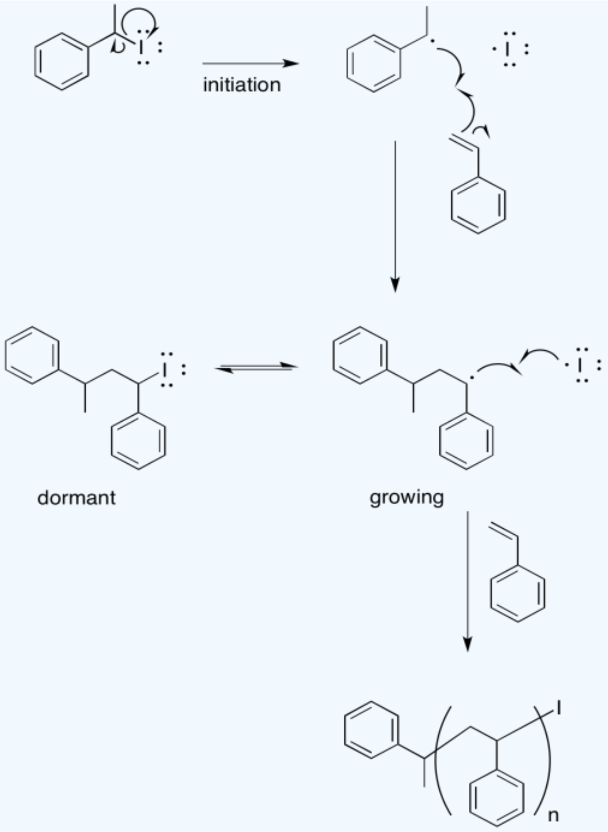
An early attempt at living polymerisation employed an alkyl iodide initiator. Thermal initiation (initiation by heating) resulted in a reactive alkyl radical and an iodine atom.



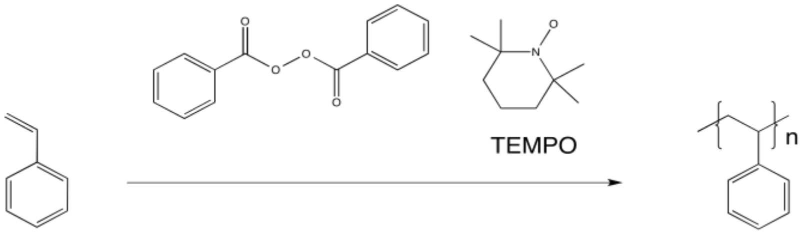
Provide a mechanism for styrene polymerisation, making sure to show the following points:

a. initiation
b. propagation
c. recombination with iodine atom
d. a growing chain
e. a "dormant" chain that could re-initiate and start growing again, but which is currently safe from random termination

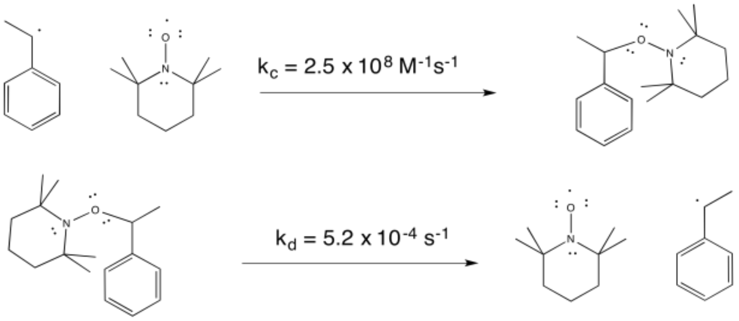
Answer



Researchers at IBM found that polystyrene polymerisation proceeded much more smoothly when TEMPO, a relatively stable radical, was added to the reaction. The reaction also proceeded more slowly, resulting in overall lower molecular weight of the polymer. However, the distribution of molecular weight was much more uniform. All of the chains were of similar sizes, relatively speaking. As a result, the properties of the material were much more controlled.



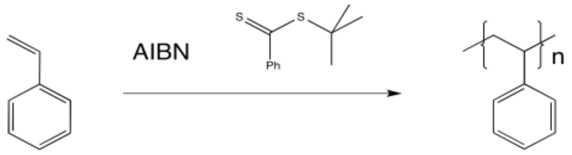
TEMPO helps to control the polymerisation by forming a reversible bond with the growing end of the polymer chain. The radical on TEMPO combines with the radical on the head of the polymer to form a C-O bond. The bond can break again (unusually, for a C-O bond), allowing the polymer chain to resume growing periodically.



Two of the most common methods of inducing living radical polymerisation are RAFT and ATRP. RAFT stands for radical atom fragmentation polymerisation. Like the TEMPO reaction, it involves a reversible radical recombination to form a covalent bond.

RAFT was developed by a group of Australian chemists in the late 1990's, including Enzio Rizzardo, Graeme Moad and San Thang of Australia's national science agency, CSIRO. ATRP stands for atom-transfer radical polymerisation. It was developed in the mid 1990's by Krysztof Matyjaszewski at Carnegie Mellon in Pittsburgh and his post-doctoral associate, Jin-Shan Wang, now at Shanghai Jiao Tong University. An independent discovery of the method was made by Mitsuo Sawamoto at Kyoto University in Japan.

RAFT most commonly employs a thioester (or similar compound) as a chain transfer agent. The chain transfer agent intercepts a growing polymer chain, but does so reversibly.



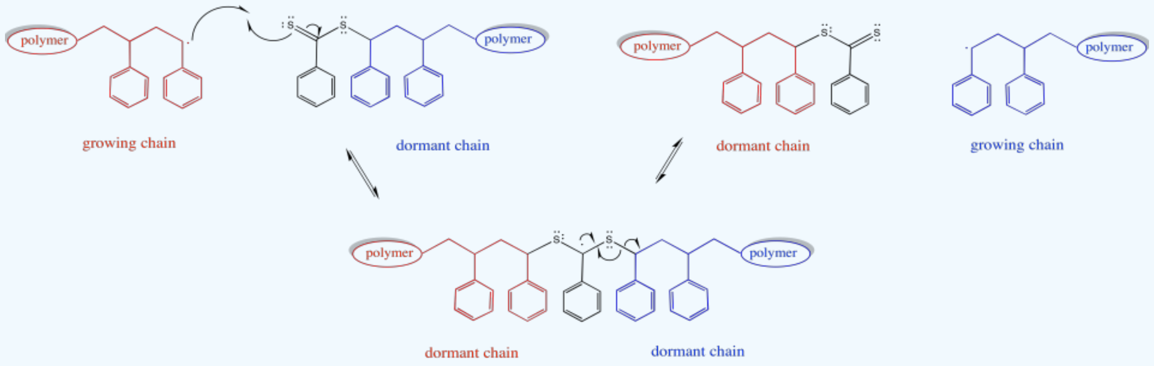
The thioester can react with a radical, placing the growing chain in a dormant state. It can also release a new radical, which can then initiate polymerisation. Eventually, it will regulate the growth of two polymer chains.

In addition, a third species present in equilibrium holds both chains dormant. The chain transfer agent can reversibly release one of these dormant chains at a time.

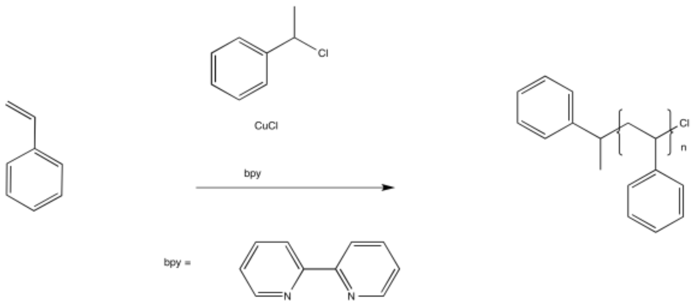
Exercise 6.10.8

Provide a mechanism for conversion of a growing chain into a dormant chain via RAFT.

Answer



In ATRP, a similar process works to keep a fraction of the chains in a dormant state. A key component of this method is a copper(I) complex.



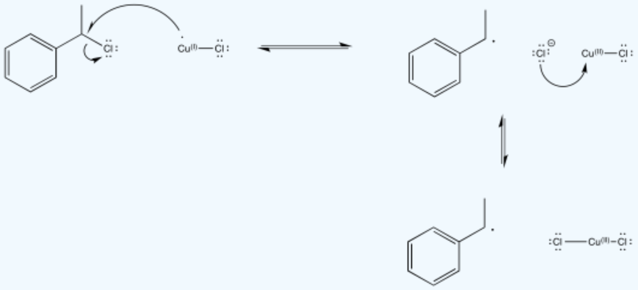
The role of the copper(I) complex is to transfer an electron to an inactive species, producing a copper(II) species and a radical. For example, in initiation of the reaction above, the Cu(I) transfers an electron to the alkyl halide to become Cu(II). In turn, the chlorine atom on the alkyl halide becomes chloride anion, Cl^-, and the alkyl portion is left as an initiating radical.

One of the reasons ATRP is so important is that it provides a very reliable and inexpensive way to control polymerisation. In addition, it can be adapted to a wide range of useful processes. For example, Matyjaszeki has developed methods of electrochemically controlling the reaction; polymerisation can literally be turned on and off with a switch. Yusuf Yagci and coworkers at Istanbul Technical University developed a photoinduced ATRP process, in which polymerisation begins when the lights come on and stops when it gets dark. Other researchers, including the Hawker lab at UCSB, have also promoted the utility of this approach.

? Exercise 6.10.9

Provide a mechanism for initiation using ATRP.

Answer



? Exercise 6.10.10

Provide a mechanism for conversion of a growing chain to a dormant chain using ATRP.

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6.11: Detection of Unpaired Electrons

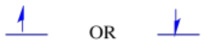
There are experimental methods for the detection of unpaired electrons. One of the hallmarks of unpaired electrons in materials is interaction with a magnetic field. That interaction can be used to provide information about compounds containing unpaired electrons.

Electron Paramagnetic Resonance

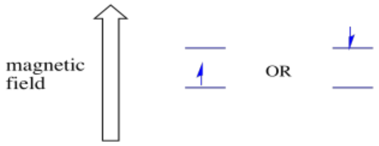
Electron paramagnetic resonance (EPR) or electron spin resonance (ESR) is a spectroscopic method. It depends upon the energetic separation of two spin states that exists only in the presence of a magnetic field.

EPR is very closely related to another common type of spin resonance spectroscopy, NMR.

Spin is a quantum property that has no real analogy that would make sense to us on a macroscopic level. However, we do know that spin has associated with it magnetic properties. An electron can have either of two values for these magnetic properties. There are various labels given to these values: sometimes "up" and "down", sometimes, +1/2 and -1/2. However, whichever value of spin an electron possesses makes no difference energetically.



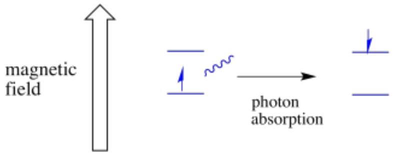
The two possible spin states are the same energetically -- unless a magnetic field is present. Once that situation arises, there is an energetic separation between the two states.



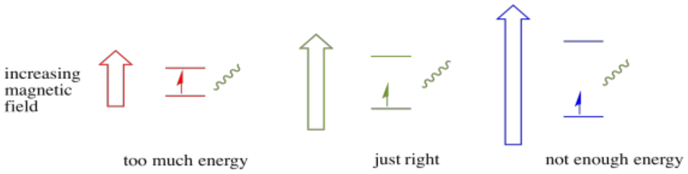
In the presence of a magnetic field, the two spin states separate into two different energy levels. The amount of separation between the energy levels depends on the magnitude of the magnetic field. The stronger the magnetic field, the greater the separation.

This case is only true for unpaired spins. Remember, unpaired spins interact with a magnetic field. If everything is spin-paired, nothing happens. That's very useful, because it gives us a way to detect those unpaired electrons.

An electron in one spin state can still be excited to the other by the absorbance of a photon. Alternatively, an electron in the higher state can drop down to the lower one if it releases a photon.



In order for any of this to happen, the energy of the photon must exactly match the energy difference between states. This Goldilocks rule is called the resonance condition. The amount of energy supplied to jump from one energy level to the next has to be just right. Too little energy and the electron won't make it. Too much energy and the electron won't make it either. It's waiting for just the right photon.



Just how much energy does a photon have? Remember your Planck-Einstein relationship. It described the energy of a photon:

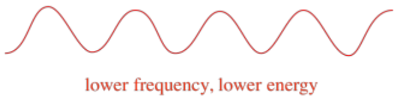
$$E = h\nu$$

E is the energy of the photon, *h* is Planck's constant (6.625 x 10^{-34} Js) and ν is the frequency of the photon (it looks like a Roman vee, but it's the Greek letter, nu).

Alternatively, because of the relationship between wavelength and frequency:

$$E = \frac{hc}{\lambda}$$

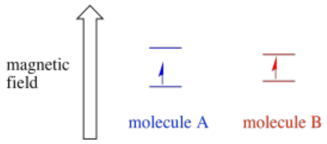
The new quantities are c, the speed of light (3.0 x 10^8 m s^{-1}) and λ, the wavelength of the photon.



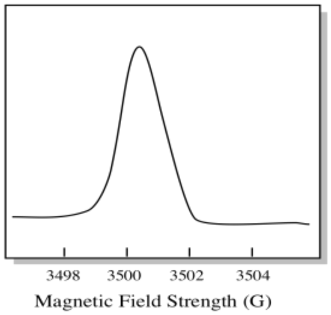
So, in general, different wavelengths of light deliver different amounts of energy. Blue light, with a wavelength close to 475 nm, has more energy than red light, with a wavelength close to 700 nm.

In EPR, the general range of electromagnetic radiation, or the general kind of photon, is microwave radiation. The frequency of these photons is about 9 or 10 GHz. (Another type of spectroscopy, rotational spectroscopy, also measures the absorbance of microwaves. It typically uses somewhat higher frequencies of microwaves. Rotational spectroscopy gives structural or bonding information about molecules in the gas phase.)

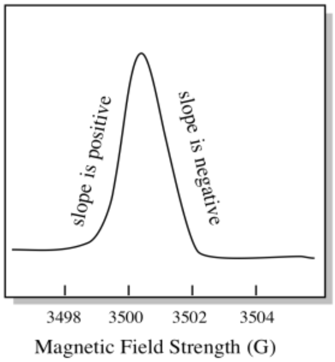
Depending on the environment of the unpaired electron, it may be more susceptible or less susceptible to the influence of the external magnetic field. That means the energy splitting between the two spin states will vary from one molecule to another. As a result, different molecules in the same magnetic field would absorb different wavelengths of microwave radiation.



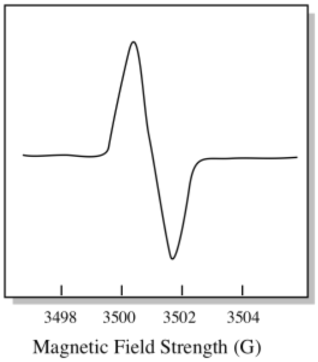
Usually, an EPR spectrometer is designed so that it supplies a fixed wavelength of microwave radiation to the sample. The magnetic field is adjusted and the instrument measures what field strength was required for absorption of the photons. An EPR spectrum shows absorbance as a function of magnetic field strength.



There is something a little different about how EPR spectra are usually displayed. It is displayed as a derivative of the plot shown above. That's because of the way that the instrument measures the change in absorbance as it changes the magnetic field; i.e. it measures d(absorbance)/d(magnetic field). That's the slope of the previous plot.



As a result, an EPR spectrum really looks more like this. The part above the baseline reflects the positive slope in the previous plot. The part below the baseline reflects the negative slope in the previous plot.



The magnetic field strength is not typically the value that is reported for the peak position. Instead, something called the g-value is reported. The g-value arises from the equation for the Zeeman effect (the effect of the magnetic field on the splitting between spin energy levels). That relationship is:

$$\Delta E = g\beta B$$

in which ΔE is the energy difference between spin states, g is the g-value, a proportionality constant that depends on how susceptible the electron is to the influence of the magnetic field, β is the Bohr magneton (9.274×10^{-24} J T^{-1}) and B is the applied magnetic field.

That means that, for photon absorption,

$$h\nu = g\beta B$$

and so

$$g = \frac{h\nu}{\beta B}$$

Remember, *h* and β are just constants. That means g is a measure of the ratio of the photon absorbed to the magnetic field used. It's a standardisation step. If people have instruments that use slightly different wavelengths of microwave radiation, then the magnetic fields they measure for the same samples would not agree. If everyone just measures the ratio of wavelength to field strength, it should all even out. The g-value is a reproducible measure of the environment of an electron that should be the same from one laboratory to another.

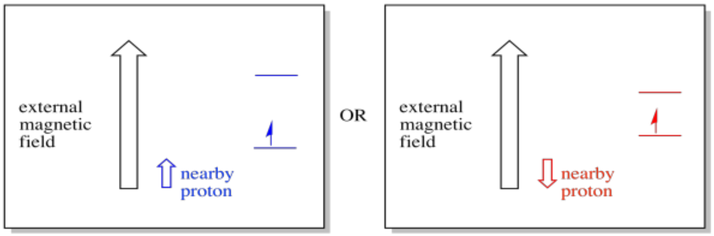
A similar practice is used in NMR spectroscopy, for similar reasons. When we report a chemical shift in ppm instead of Hz, we are correcting for the strength of the magnetic field in the instrument we are using. Otherwise the same sample would give two different shifts on two different instruments.

Coupling in EPR

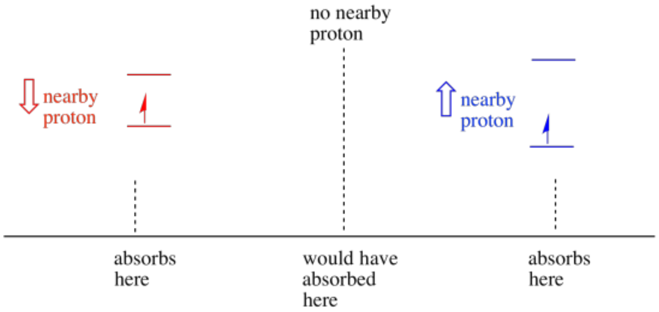
Coupling is a phenomenon in which magnetic fields interact with each other. In EPR, coupling comes about because of the influence of nearby nuclei on the electron that is being observed.

For example, you may already know that a hydrogen atom's nucleus has an unpaired spin. That's the basis of ^{1}H NMR spectroscopy. If that nucleus has an unpaired spin, it has an associated magnetic field. Because the hydrogen nucleus could have either spin value, +1/2 or -1/2, then it has two possible magnetic fields associated with it.

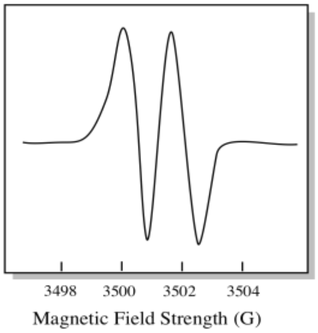
A nearby electron, placed in an external magnetic field, could now be in either of two different situations. Either the neighbouring proton adds a little bit to the magnetic field, or it subtracts a little bit from the external field.



As a result, the electron can experience two different fields. Remember, we are not dealing with a single molecule in spectroscopy. We are dealing with huge numbers of molecules. Some of the molecules will be in one situation. Some of the molecules will be in the other situation. We will see both situations. There will be absorbance at two different magnetic field strengths.

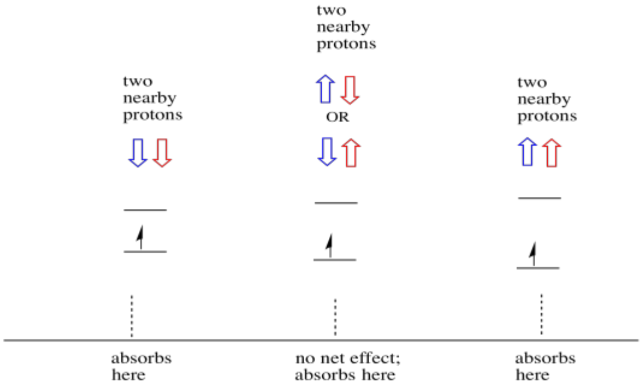


As a result, the EPR spectrum shows two peaks, like this:

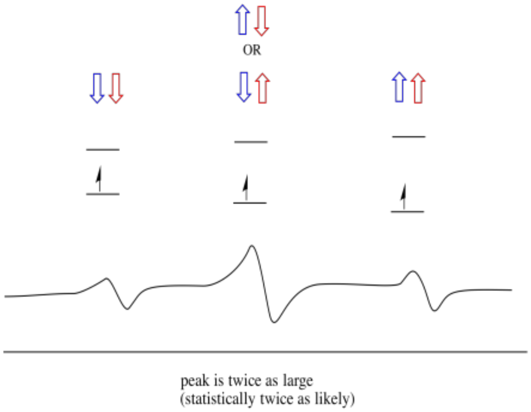


This type of peak in the spectrum is called a doublet, because of the double absorbance. This characteristic of an EPR peak is called its multiplicity. How many lines is the peak split into? Two. It is a doublet.

Things are even more interesting if there are two nearby protons. In that case, both neighbouring protons have spin. Either spin could have value +1/2 or -1/2. Maybe they are both +1/2. Maybe they are both -1/2. Maybe there is one of each. These three possible combinations will have three different effects on the magnetic field experienced by the electron.



As a result, there are three peaks in the spectrum. The spectrum is called a triplet. This triplet is shown below, underneath the diagram that illustrates the spin combinations of the neighbouring hydrogens.



Notice that, because either hydrogen could be up or down in the mixed combination, there are two ways of arriving at that middle state. That combination is twice as likely as the other two, because there is only one way of getting those combination: both hydrogens' spins are up, in one case. Both hydrogens are down in the other. As a result, the middle peak in a triplet is twice as large as the peaks on the edges.

? Exercise 6.11.1

Show that, with three neighbouring hydrogens, a quartet would result, in which the ratios of the peaks are 1:3:3:1.

Answer

The combinations are:

a) all spins down (and there is only one way to do that)

b) two of the spins are down, but one is up (and each of the three protons could be up, so there are three ways of doing that)

c) two of the spins are up, but one is down (and each of the three protons could be down, so there are three ways of doing that)

d) all spins up (and there is just one way to do that).

The result is a 1:3:3:1 quartet.

? Exercise 6.11.2

Predict the multiplicity in the EPR spectrum for each of the following alkoxy radicals (note that oxygen and carbon have no unpaired spins; assume the same is true for X):

a) $X_3C\text{-}O^\cdot$ b) $X_2CH\text{-}O^\cdot$ c) $XCH_2\text{-}O^\cdot$ d) $CH_3\text{-}O^\cdot$

Answer a

a) singlet

Answer b

b) doublet

Answer c

c) triplet

Answer d

d) quartet

? Exercise 6.11.3

Suppose benzene were reduced by one electron to obtain the benzene radical anion. What would be the multiplicity in the EPR spectrum?

Answer

A septet (in a 1:3:5:7:5:3:1 ratio).

Coupling to Metal Ions

Lots of nuclei other than hydrogen have a net spin. If the unpaired electron happens to be found on a metal, the EPR spectrum may provide confirmation of that structural information. This confirmation may come from both the magnetic field information (similar to chemical shift in NMR) and from the multiplicity.

Nuclear spins of selected metals are shown below.

Metal	Spin
V	7/2
Mn	5/2
Fe	0
Co	7/2
Cu	3/2

In each of these metals, the nucleus has different possible magnetic fields. Note that their effects are slightly more complicated than that of a hydrogen atom. For example, copper, with spin 3/2, acts a little like three different hydrogen nuclei (each with spin +/- 1/2) in terms of its effect on a nearby electrom's EPR spectrum. The multiplicity of an unpaired electron on a copper ion should be pretty distinctive.

? Exercise 6.11.4

Predict the multiplicity of a peak in the EPR spectrum for an unpaired electron on each of the following metals:

a) vanadium b) manganese c) iron d) cobalt e) copper

Answer a

a) an octet (in a 1:3:5:7:7:5:3:1 ratio)

Answer b

b) a sextet (in a 1:3:5:5:3:1 ratio)

Answer c

c) a singlet

Answer d

d) an octet

Answer e

e) a quartet (in a 1:3:3:1 ratio)

Sometimes things are more complicated, because different isotopes of the same element may have different possible spin values. In fact, that is true with hydrogen and carbon, but the great majority of hydrogen is found as ^{1}H, so in general we can think of it as having spin = 1/2; the great majority of carbon is ^{12}C, with spin = 0.

The natural isotopes of iron, and their nuclear spins, are shown in the table below.

Isotope	Spin	% Abundance
^{54}Fe	0	5.9
^{56}Fe	0	91.8
^{57}Fe	1/2	2.1
^{58}Fe	0	0.2

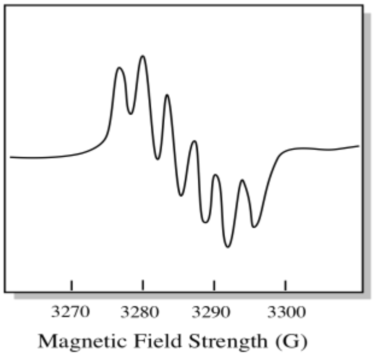
The EPR spectrum of an unpaired electron on iron may be slightly more complicated than we first thought. Within the sample, some of the electrons would be situated on iron ions with spin = 1/2, although most would not. This complication may be enough to introduce a slight variation in the appearance of the spectrum, but overall it would still look pretty much like a singlet.

However, in many cases things do get much more complex. Molybdenum provides a good example.

Isotope	Spin	% Abundance
^{92}Mo	0	14.8
^{94}Mo	0	9.3
^{95}Mo	5/2	15.9
^{96}Mo	0	16.7
^{97}Mo	5/2	9.6
^{98}Mo	0	24.1
^{100}Mo	0	9.6

There are seven naturally occurring isotopes of molybdenum. Five of them have spin = 0, so an unpaired electron on those isotopes would give rise to a simple singlet in the EPR spectrum. The other two isotopes, comprising 25% of the total, have spin = 5/2. Most unpaired electrons on molybdenum would show up as a singlet. However, a significant fraction would show up as a sextet. That means that, in an ideal case, an unpaired electron on molybdenum would give rise to a singlet with a sextet superimposed on it (about a quarter as strong as the singlet).

This situation might look something like the drawing below.



In reality, EPR spectra are enormously complicated in many cases. They often look like fuzzy blobs. There are so many things coupling to so many other things that it becomes almost impossible to decipher by eye. In most cases, computer simulations are run and the experimental data is compared to the computer simulations to obtain structural insight.

? Exercise 6.11.5

Vanadium is present in some nitrogenases and so there has been interest in model complexes (e.g. Sandro Gambarotta *et al*, *J. Am. Chem. Soc.* **1994**, *116*, 6927-6928). Gambarotta used the following synthesis, in THF solvent:

$$VCl_3 + [(Me_3Si)_2N]K \longrightarrow [(Me_3Si)_2N]_3V(THF)$$

a. Draw the structure of the product of the reaction.
b. Draw a d orbital splitting diagram for this complex.
c. An EPR spectrum was recorded for this compound. Sketch the spectrum, given that vanadium has nuclear spin I = 7/2.
d. Estimate μ_{eff} for this compound.

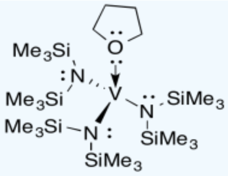
The compound reacts with N_2, forming a N_2-bridged dimer.

e) Draw the structure of this product.

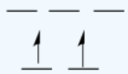
f) This compound produces no EPR spectrum. Provide a resonance structure of (e) that explains this observation.

Answer

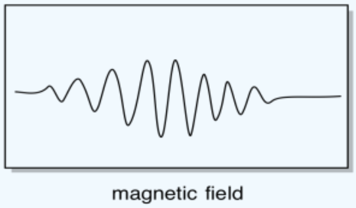
a)



b)

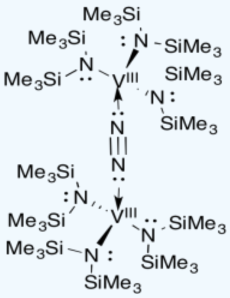


c)

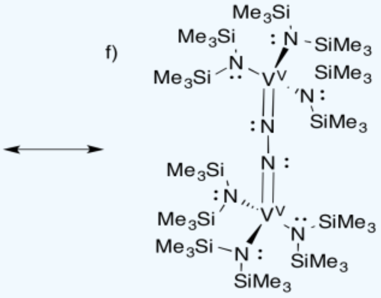


d) $\mu = 2.8$

e)



f)



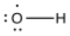
EPR spectra provided courtesy of Virtual Imagination / Slapdash Chemistry Creations.

6.12: Solutions for Selected Problems

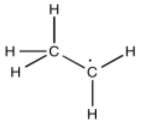
Exercise 6.1.1:

a)

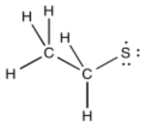
b)



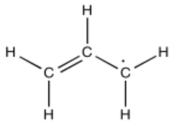
c)



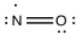
d)



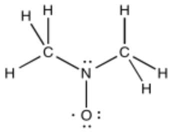
e)



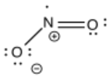
f)



g)

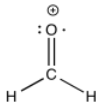


h)



Exercise 6.1.2:

a)



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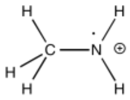

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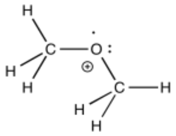

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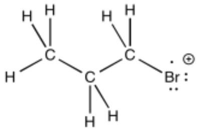
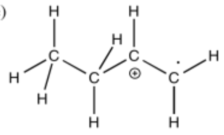
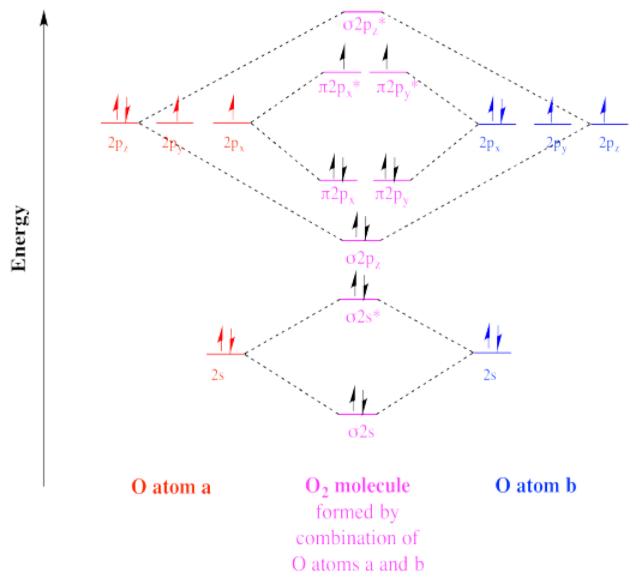


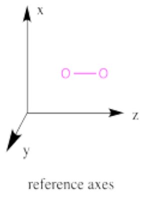
e)



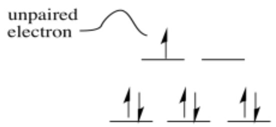
Exercise 6.1.4:

Exercise 6.1.5:



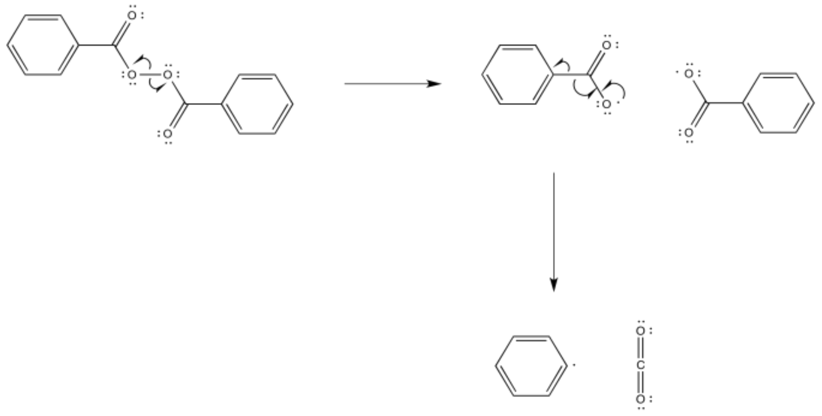


Exercise 6.1.6:



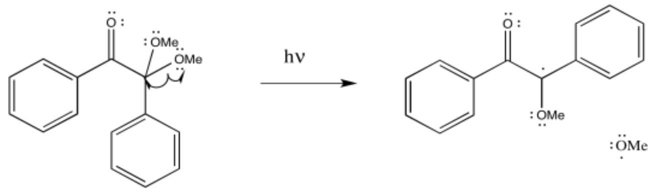
Exercise 6.2.2:

a)



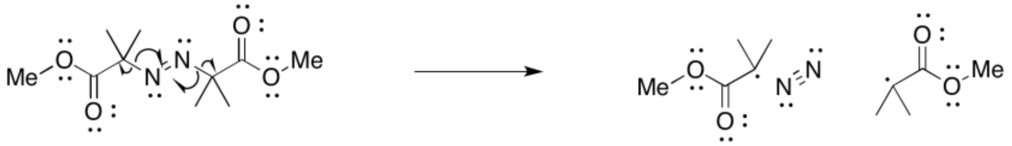
b)

c)

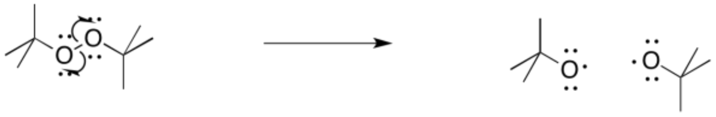


Exercise 6.2.3:

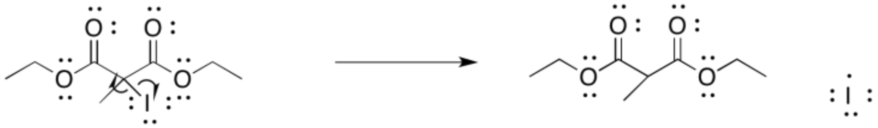
a)



b)



c)



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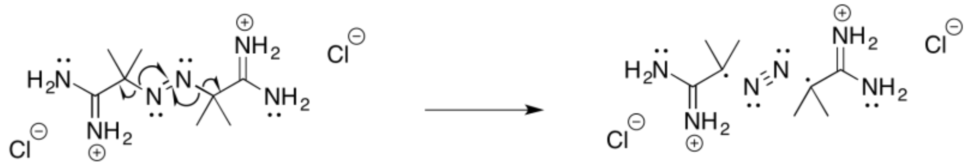

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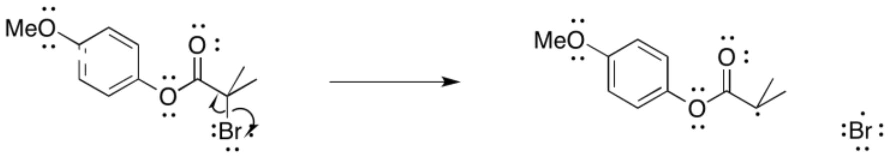

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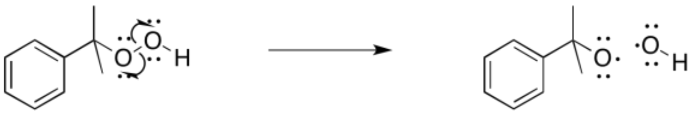

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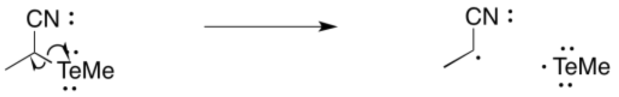

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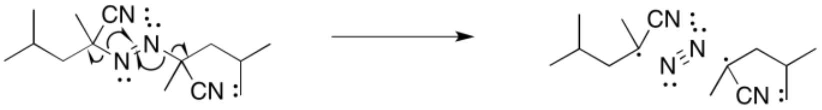

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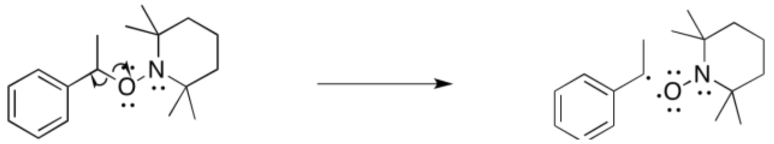
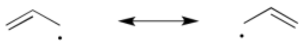


Exercise 6.3.1:

a)



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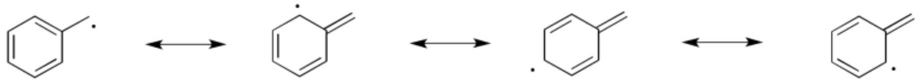
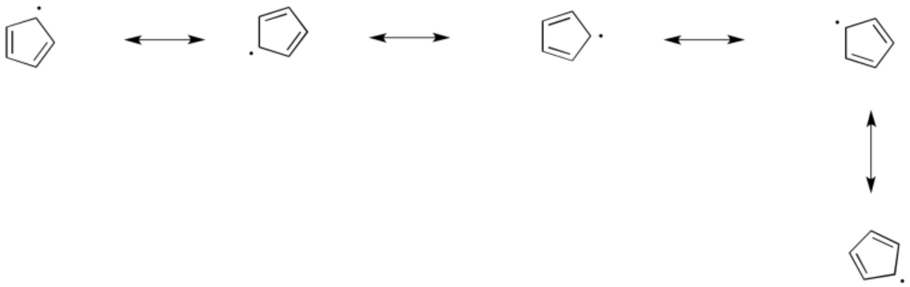
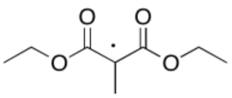


c)

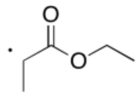


Exercise 6.3.2:

a)



more delocalized
forms more easily



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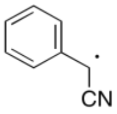
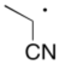


more delocalized
forms more easily



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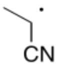
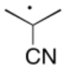
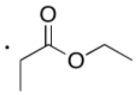
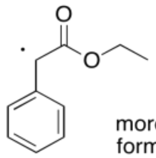




more substituted
forms more easily

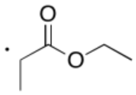
d)

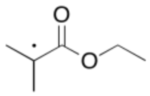




more delocalized
forms more easily

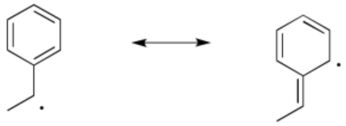
e)



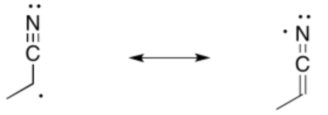


more substituted
forms more easily

Exercise 6.3.3:



delocalized onto carbon
least electronegative
fastest

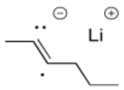


delocalized onto nitrogen
medium electronegative
medium rate

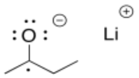
delocalized onto oxygen
mostt electronegative
slowest

Exercise 6.4.1:

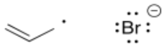
a)



b)



c)

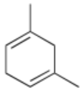


Exercise 6.4.2:

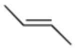
The reduction potential of the negatively charged carboxylate anion would be much less positive than the reduction potential for the neutral aldehyde or ketone. We think of a carboxylate anion as much less electrophilic than aldehydes and ketones for the same reason.

Exercise 6.4.3:

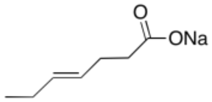
a)



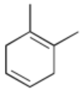
b)



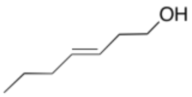
c)



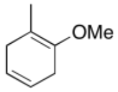
d)



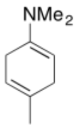
e)



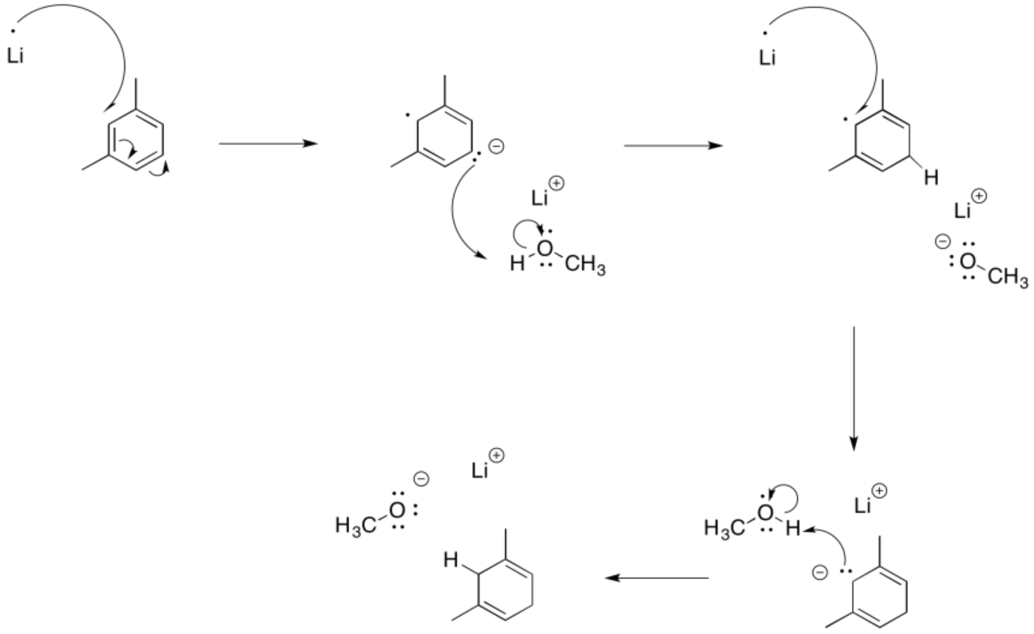
f)



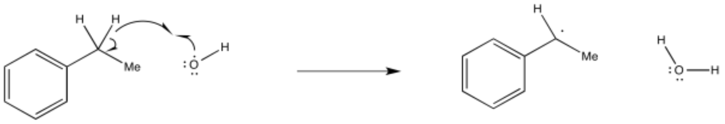
g)



Exercise 6.4.4:



Exercise 6.5.1:



Exercise 6.5.3:

a) no; a stronger bond would have to be broken and replaced with a weaker bond.

b) yes; a weaker bond would be broken and replaced with a stronger one.

c) no

d) yes

e) no

f) yes

Exercise 6.5.4:

a) no b) yes c) no

Exercise 6.5.5:

a. The effect is similar to the stability of carbocations. The more substituted radical is more stable. Thus, the trend from most to least stable is tertiary > secondary > primary > methyl radical. The trend likely originates from a hyperconjugation effect, as in carbocations.
b. The trend here is that if the radical is delocalized by resonance, it is more stable. The allyl and benzyl radicals are more stable than the isopropyl radical. This trend is also seen in cations.
c. The trend here has to do with "hybridization effects" or the atomic orbitals that contribute to the formation of molecular orbitals involved in the relevant bond. In a linear alkyne, the C-H bond can be formed only from some combination involving a hydrogen 1s orbital, carbon 2s orbital and one of the carbon 2p orbitals. This combination is called a "sp" hybrid and the orbital that combines with the hydrogen can be considered 50% 2s, 50% 2p in character.

In a planar alkene, the C-H bond can be formed only from some combination involving a hydrogen 1s orbital, carbon 2s orbital and two of the carbon 2p orbitals (since two of them could lie in this plane). This combination is called a "sp^2" hybrid and the orbital that combines with the hydrogen can be considered 33% 2s, 66% 2p in character.

In a tetrahedral alkane, the C-H bond can be formed from some combination involving a hydrogen 1s orbital, carbon 2s orbital and all three of the carbon 2p orbitals. This combination is called a "sp^3" hybrid and the orbital that combines with the hydrogen can be considered 25% 2s, 75% 2p in character.

Because a 2s orbital is lower in energy than a 2p orbital, a bond that has greater 2s character is lower in energy than a bond with less 2s character. That means that a bond with greater 2s character is harder to break than a bond with less 2s character. Hence, the alkane C-H bond is weaker than the alkene C-H bond, which is weaker than the alkyne C-H bond.

Exercise 6.5.6:

The Sn-H bond has a dissociation energy of about 78 kcal/mol, compared to about 98 kcal/mol for the C-H bond in ethane. The formation of the Sn-H bond would not compensate for the energy needed to break the C-H bond. On the other hand, the 100 kcal/mol released upon formation of a Sn-Cl bond would more than make up for the 85 kcal/mol required to breal a C-Cl bond.

We could try to rationalise those differences, although bond strengths are always very complicated issues and we will not be able to explain things satisfactorily without quantum mechanical calculations. Let's start with two basic factors, though: the amount of covalency and the amount of polarity.

The difference between the covalent radii of tin and hydrogen (1.39 vs. 0.31 Å) is much greater than the difference between tin and chlorine (1.39 vs 1.02 Å), so there may be less overlap and less covalency between tin and hydrogen than between tin and chlorine. By comparison, the covalent radius of carbon is about 0.76, which puts it somewhere in between hydrogen and chlorine.

In addition, as measured on the Pauling scale, the electronegativity values of these atoms are: chlorine, 3.16; carbon, 2.55; hydrogen, 2.2; tin, 1.96. The tin-chlorine bond would have a large ionic component; this additional component of bonding would strengthen the Sn-Cl bond.

Exercise 6.5.7:

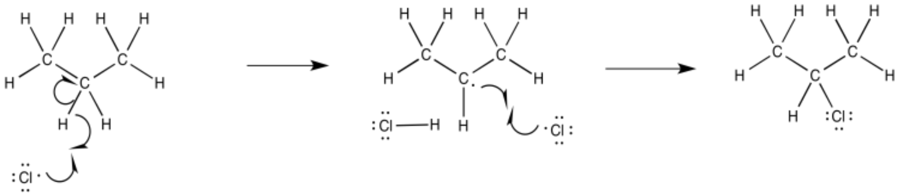
Exercise 6.5.8:

a. 174 - 90 kcal/mol = 84 kcal/mol for the π contribution only
b. 179 - 92 kcal/mol = 87 kcal/mol for the π contribution only

Exercise 6.5.9:

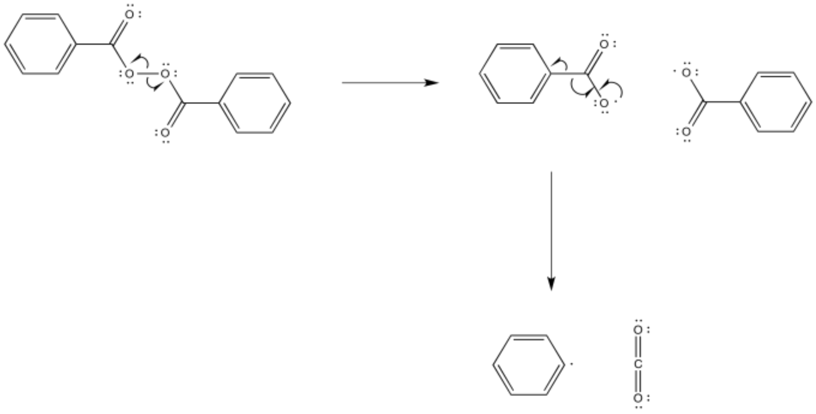
a. 85 + 77 kcal/mol = 162 kcal/mol for the combined σ + π contribution
b. There may be significant differences between the π bond in methanal imine (CH_2=NH) and the imine for which we have bond strength data. For example, breaking the bond would result in radicals next to phenyl groups, which may be significantly stabilized. On the other hand, the π bond itself may be significantly stabilized by conjugation. Thus, our estimate is probably not correct, but it is difficult to say whether it is too high or too low.

Exercise 6.7.1:

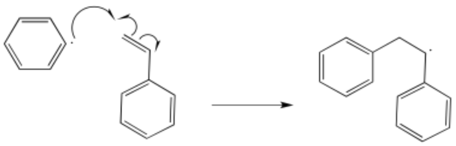


Exercise 6.9.2:

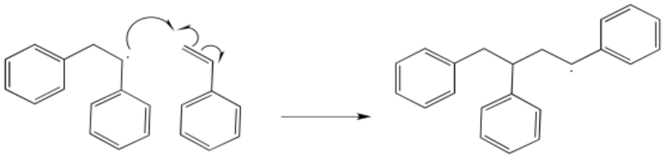
The mechanism would begin with initiation of the benzoyl peroxide.



The resulting phenyl radical acts as the initiator for polymerisation.



Additional propagation steps follow.



Exercise 6.9.3:

The monomer dependence is straightforward: the more monomer there is present, the faster it can be enchained by the growing radical chain.

The initiator dependence is slightly more complicated, but not much. The more growing radical chains there are, the faster the monomers can be enchained. The more phenyl radical is formed, each initiating a new radical chain, then the more growing radical chains there will be.

$$Rate = k[monomer][Ph\cdot]$$

The more benzoyl peroxide there is, the more phenyl radical there will be, but the relationship is not linear, as explained below.

Benzoyl peroxide cleaves in two, ultimately producing two phenyl radicals:

$$K_{eq} = \frac{[Ph\cdot]^2}{[BP]}$$

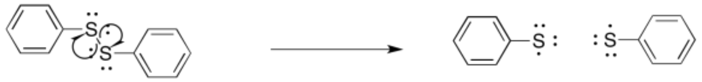
so $[Ph\cdot]^2 = K_{eq}[BP]$

and $[Ph\cdot] = K_{eq}^{1/2}[BP]^{1/2}$

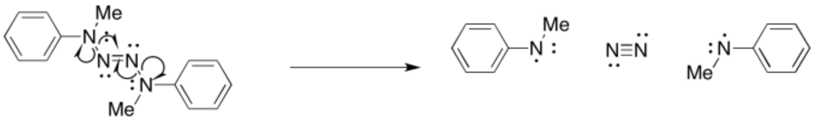
therefore $Rate = k[monomer][Ph\cdot]^{1/2}$

Exercise 6.9.4:

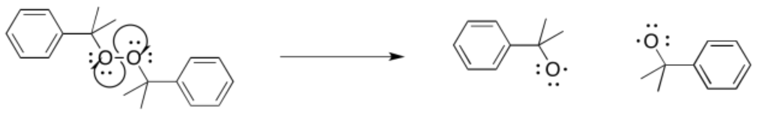
a)



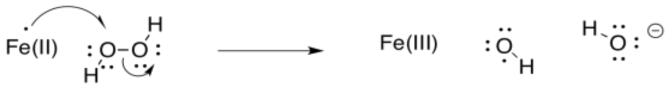
b)



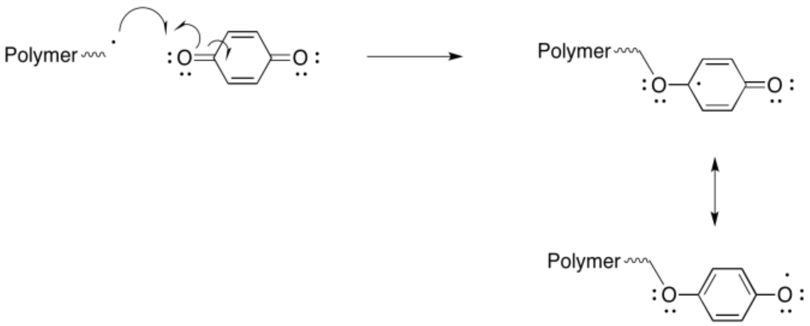
c)



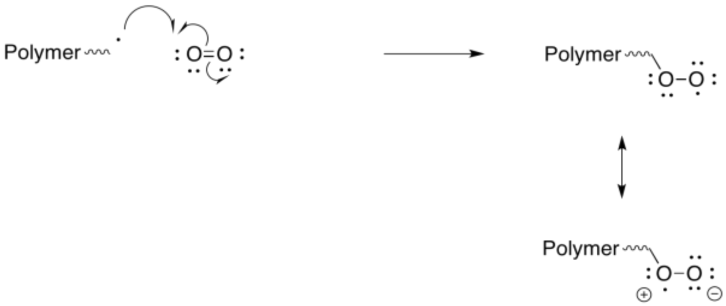
Exercise 6.9.5:



Exercise 6.9.6:



Exercise 6.9.7:



Peroxy radicals are relatively stable and react slowly. However, when they do react, they also undergo reactions other than radical polymerisation, so that they are even more effective as inhibitors of polymerisation.

Exercise 6.10.1:

Because each initiator breaks in half, forming two radicals, one initiator starts two growing chains. Every initiator will, on average, consume half the monomers, assuming no unexpected chain termination events.

a. DP = 500 monomers / 2 growing chains = 250
b. DP = 1000 monomers / 2 growing chains = 500
c. DP = 600 monomers / 3 growing chains = 200

Exercise 6.10.2:

M_0 = molecular weight of monomer in each case. 1 D (Dalton) = 1 amu

a) M_{n} = DP \times M_{0} = 1250 \times 104 D = 130000D = 130 kD}

b) M_{n} = DP \times M_{0} = 725 \times 85 D = 61625D = approximately \: 62 kD}

c) M_{n} = DP \times M_{0} = 1420 \times 86 D = 122120 D = approximately \: 122 kD}

Note that end groups were neglected in these calculations; they may contribute a significant percentage of total molecular weight at lower DP. A more accurate calculation would account for the identity of both end groups.

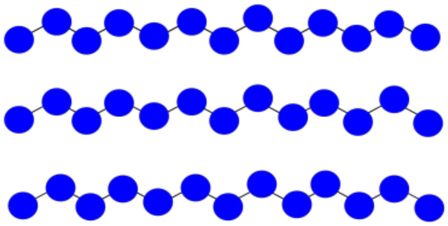
Exercise 6.10.3:

a. DP = \frac{M_{n}}{M_{0}} = \frac{11450D}{53D} = 216}
b. (DP = \frac{M_{n}}{M_{0}} = \frac{24760D}{86D} = 288}\)
c. (DP = \frac{M_{n}}{M_{0}} = \frac{927000D}{104D} = 8914}\)

Exercise 6.10.4:

a. $MW = 8 \times 100D = 800D$
b. 15 monomers / 3 chains = 5 new monomers / chain

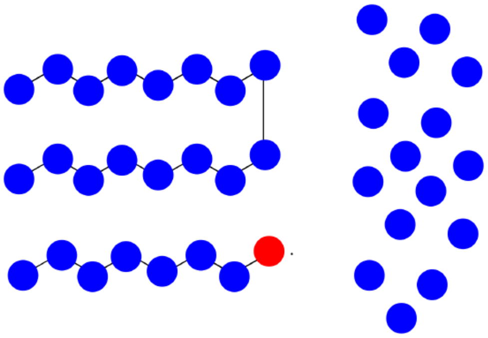
$$DP = 8 + 5 = 13$$



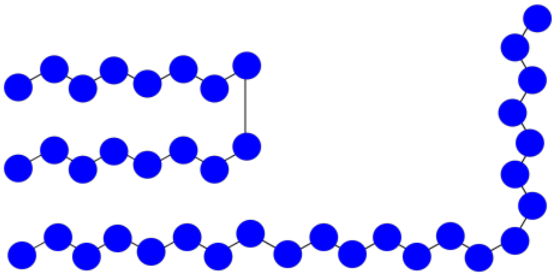
c) $MW = 13 \times 100D = 1300D$

d) All chains are the same length; PDI = 1.0

e) $MW = 16 \times 100D = 1600D$



f) $MW = (8+15) \times 100D = 2300D$



g) $M_n = \frac{2300+1600D}{2} = 1950D$

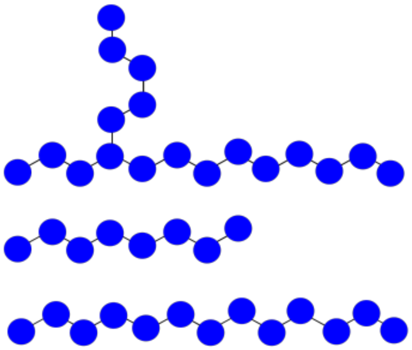
h) $PDI = \frac{2300D}{1600D} = 1.44$

Exercise 6.10.5:

a) The chain that abstracted the hydrogen: $MW = 8 \times 100D = 800D$

The branched chain: $MW = 18 \times 100D = 1800D$

The normal chain: $MW = 13 \times 100D = 1300D$



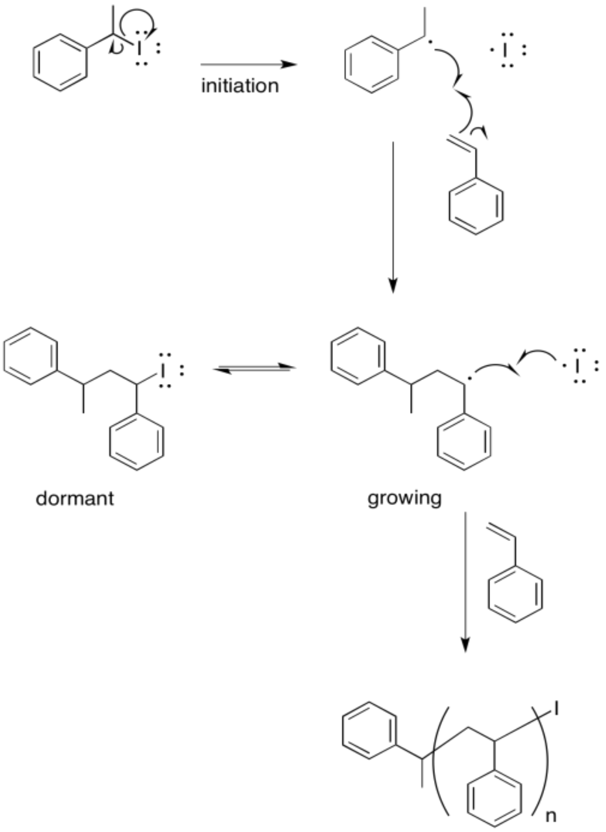
b) $M_n = \frac{1800+1300+800D}{3} = 1300D$

c) $PDI = \frac{1800}{800D} = 2.25$

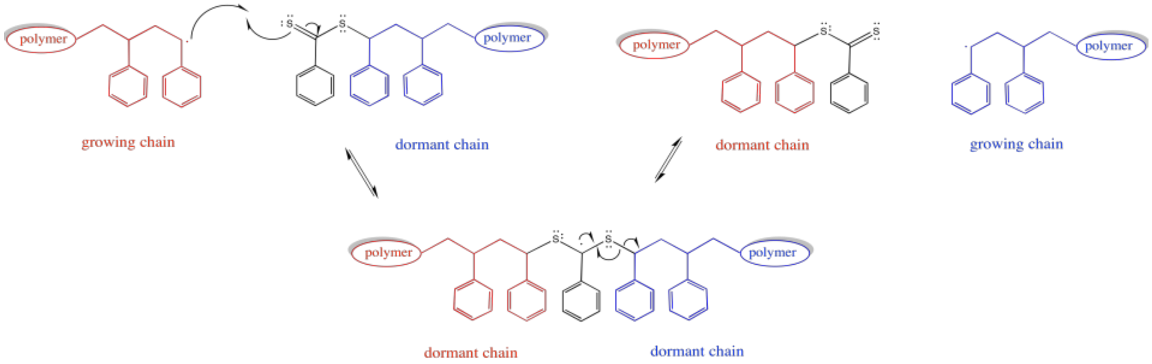
Exercise 6.10.6:

a. $M_n = \frac{17000+1800+300D}{3} = \frac{3800D}{3} = 1267$
b. $M_n = \frac{1700+1800}{2} = \frac{3500D}{2} = 1750D$

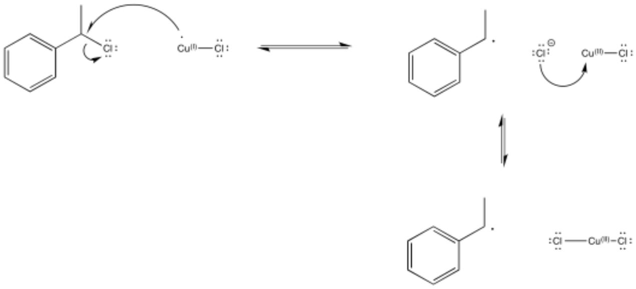
Exercise 6.10.7:



Exercise 6.10.8:



Exercise 6.10.9:



Exercise 6.11.1:

The combinations are:

a. all spins down (and there is only one way to do that)

b. two of the spins are down, but one is up (and each of the three protons could be up, so there are three ways of doing that)

c. two of the spins are up, but one is down (and each of the three protons could be down, so there are three ways of doing that)
d. all spins up (and there is just one way to do that).

The result is a 1:3:3:1 quartet.

Exercise 6.11.2:

a) singlet b) doublet c) triplet d) quartet

Exercise 6.11.3:

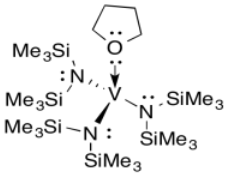
A septet (in a 1:3:5:7:5:3:1 ratio).

Exercise 6.11.4:

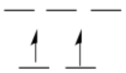
a. an octet (in a 1:3:5:7:7:5:3:1 ratio)
b. a sextet (in a 1:3:5:5:3:1 ratio)
c. a singlet
d. an octet
e. a quartet (in a 1:3:3:1 ratio)

Exercise 6.11.5:

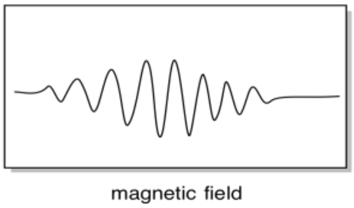
a)



b)

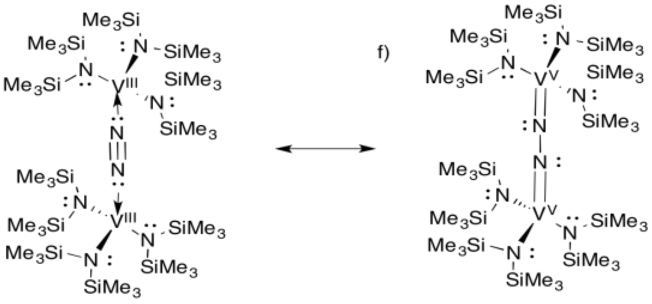


c)



d) $\mu = 2.8$

e)



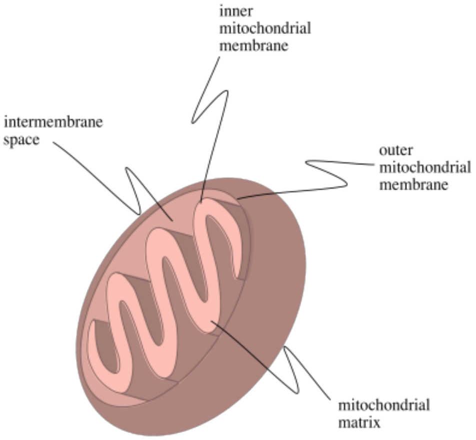
CHAPTER OVERVIEW

7: Oxidative Phosphorylation

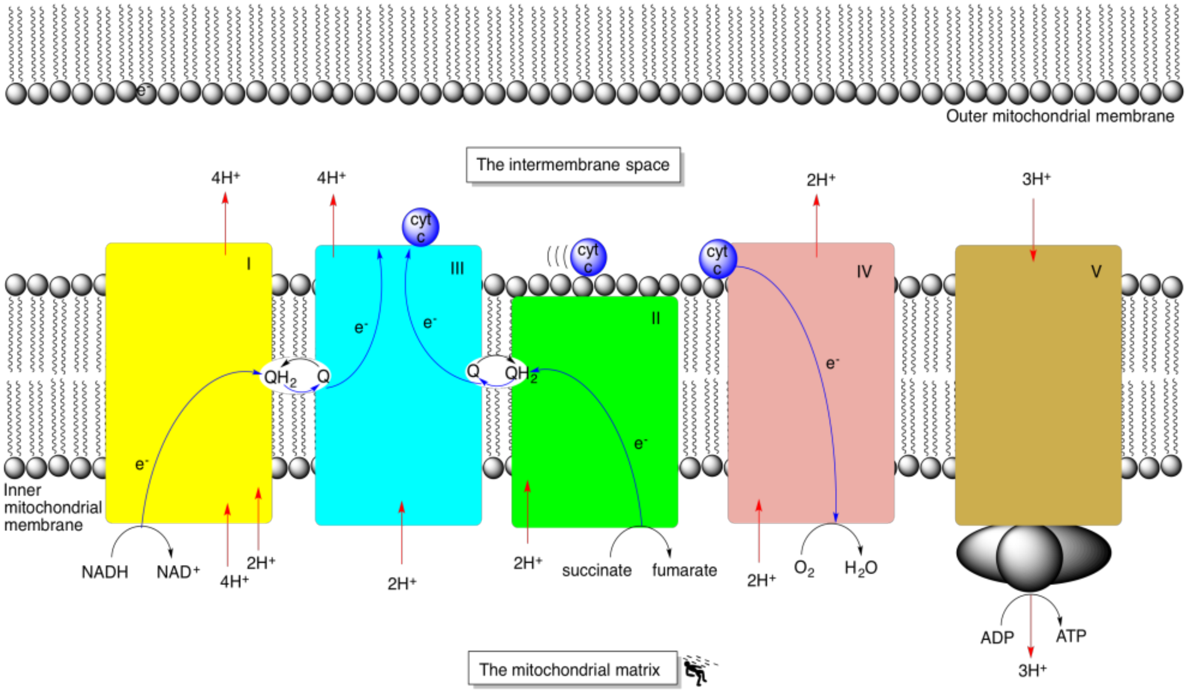
7.1: Introduction to Oxidative Phosphorylation

Oxidative phosphorylation is a metabolic process in which energy is harnessed for the production of ATP. The process occurs in the mitochondria. Electrons released through the oxidation of glucose are shuttled into the oxidative phosphorylation supercomplex via FMNH2. The electrons are passed through a remarkable electron transport chain along and across the mitochondrial membrane. The electron transport chain releases minute amounts of energy with each electron transfer, and the transport is coupled to the pumping of protons across the mitochondrial membrane. Eventually, the electrons are delivered to molecular oxygen, which is reduced to water. Finally, the protons that have gathered on the edge of the mitochondrial membrane cascade back across, turning a molecular millwheel that drives the manufacture of ATP. The ATP is used to power processes throughout the cell.

The mitochondria are the site of metabolic activity in the eukaryotic cell. The citric acid cycle occurs within the mitochondrial matrix, catalysed by a range of metabolic enzymes. For this reason, mitochondria are sometimes called "the power plants of the cell". Oxidative phosphorylation plays a central role in this production, harvesting electrons from NADH and succinate to manufacture ATP.



The complexes involved in oxidative phosphorylation are embedded in the inner mitochondrial membrane. In the picture below, the lower portion of the outer mitochondrial membrane is visible at the top. The inner mitochondiral membrane stretches across the middle of the picture. Both membranes are formed by lipid bilayers. In contrast, both the intermembrane space and the mitochondrial matrix are aqueous environments. The complexes that take part in oxidative phosphorylation are labelled I-V in the picture.



Each complex is actually a collection of different proteins; Complex I alone is composed of over 40 protein subunits, but in the picture above each complex has been simplified to one monolithic block. Each complex has its own specialised role. Both Complex I and Complex II serve as entry points for electrons into the respiratory electron transport chain. Complex I accepts electrons from NADH, produced in glycolysis and the citric acid cycle. Complex II accepts electrons from succinate, which is one of the intermediates in the citric acid cycle. In fact, Complex II is an integral part of the citric acid cycle, since it carries out a key step in that process.

- Complex I and II are the entry points for electrons into the electron transport chain.

Both Complex I and Complex II release small amounts of energy as electrons roll energetically downhill to sites of higher and higher reduction potential. The electrons are then shuttled to the same acceptor, Complex III, via a lipid-soluble electron carrier molecule. The electron transport chain continues, releasing some more energy before the electrons are passed to the final destination in Complex IV. This time, the trip from Complex III to Complex IV is conducted via a hydrophilic protein, cyctochrome c. Electrons travel through Complex IV, back towards the matrix, and are accepted by molecular oxygen, resulting in its reduction to water.

- Small amounts of energy are released as electrons move to sites of higher reduction potential.
- Complex IV is the final destination of the electron transport chain.
- In Complex IV, electrons are used to convert O_2 to H_2O.

Complex I, III and IV all use the energy released from the electron transport chain to pump protons from the matrix into the intermembrane space. The proton gradient that results across the inner mitochondrial membrane is used to power ATP production in complex V. In addition, a couple of protons are consumed by Complex I and Complex II as they package electrons into the lipid-soluble carrier, ubiquinone/ubiquinol. However, Complex II does not transport any electrons all the way across the inner mitochondrial membrane.

- Complex I, III and IV all use the energy released from the electron transport chain to pump protons across the inner mitochondrial membrane.
- The proton gradient across the membrane drive a nano-millwheel used to manufacture ATP from ADP and inorganic phosphate.

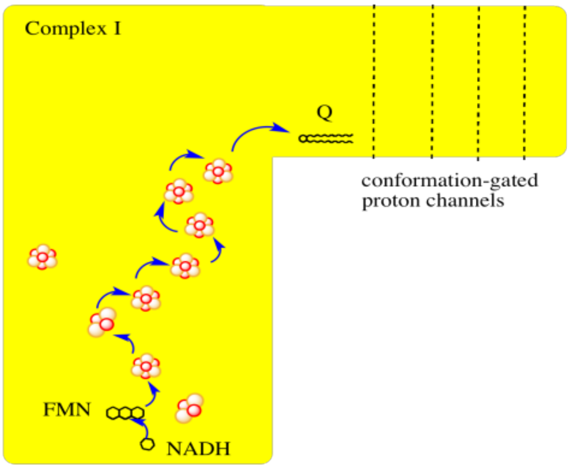
In the following pages we will take a closer look at each of the complexes that take part in this process.

Visit an overview of oxidative phosphorylation at Henry Jakubowski's Biochemistry Online.

7.2: Complex I

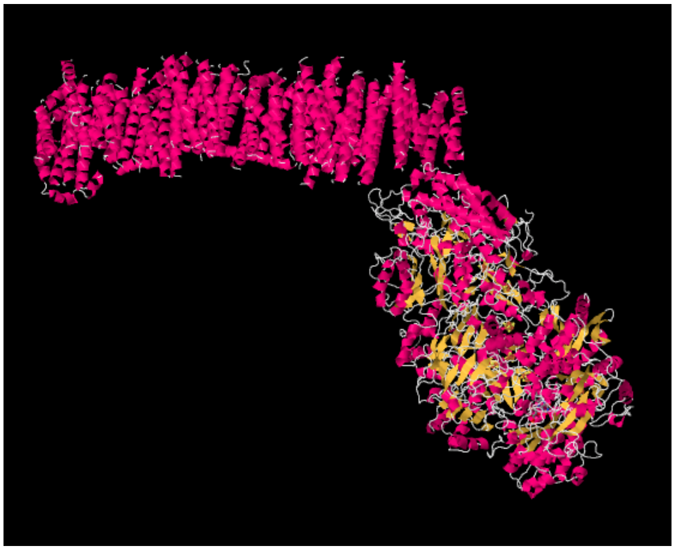
Complex I is a collection of proteins that serves as one of two entry points into oxidative phosphorylation; the other is complex II. Both of these complexes accept electrons from molecules produced in the catabolism of glucose. By shuttling these electrons from one electron acceptor to another, generally moving to higher potential (remember, in redox terminology, that means lower energy) the assembly of proteins that take part in oxidative phosphorylation are able to produce ATP. ATP, in turn, is used to power other metabolic processes.

The main events in Complex I are summarised in the cartoon below. You can see the electrons entering from the matrix at the bottom of the picture (the pathway is shown by the blue arrows). They are delivered by NADH and handed off to FMN; this step will be discussed below. The electrons are transferred via outer sphere electron transfer through a series of iron sulfur clusters and are eventually delivered to the lipid-soluble ubiquinone (Q).



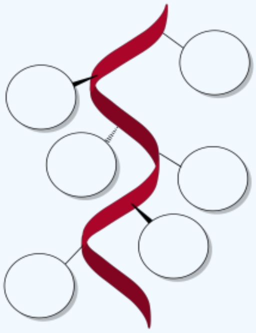
- Complex I marks the beginning of the electron transport chain.
- Electrons are delivered from NADH, pass through Complex I, and finally reach a ubiquinone.
- The energy released during electron transport helps pump protons across the complex.

The picture below is from an X-ray crystal structure of Complex I (the source of the data is cited at the end of this page). Rather than showing every atom, which is the usual result of a crystal structure, the data are displayed in a "cartoon" form, so that you can get a better sense of the overall structure. The picture is also colour-coded to help you see structures more clearly. The pink helices (spirals) along the top are the portion of the complex that is bound in the inner mitochondrial membrane. The membrane, too, would extend acorss the top of the picture from left to right. It is easy to imagine the parallel bundle of α-helices fitting nicely in the midst of the parallel array of phospholipids that form the membrane. The egg-shaped, yellow and pink form to the lower right is the part of the complex that extends out into the mitochondrial matrix. The yellow portions indicate β-sheets, whereas the white threads indicate loops.

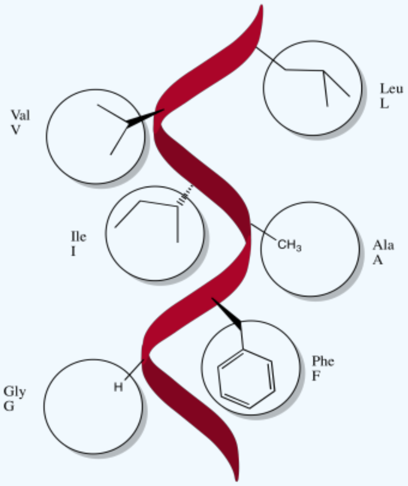


Exercise 7.2.1

Specific amino acids are likely to be found along the α-helices that bind in the membrane. Indicate different possibilities below.

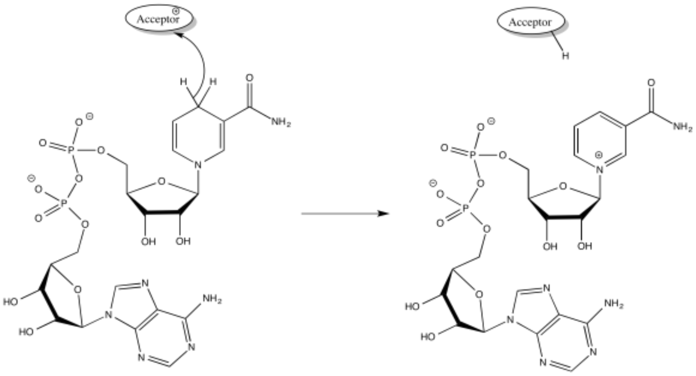


Answer



In the case of Complex I, the electrons are introduced in the form of NADH. Electrons travel through Complex I and eventually are delivered to ubiquinone; ubiquinone carries the electrons to the next stage of the oxidative phosphorylation supercomplex, which is Complex III. Because Complex I takes electrons from NADH and delivers them to ubiquinone, Complex I is also referred to as "NADH:ubiquinone oxidoreductase".

NADH is produced during glycolysis and the TCA cycle. Remember, NADH is a two-electron donor: it donates a hydride ion to a substrate, becoming NAD$^+$. A hydride ion, of course, is just a proton and two electrons.



- NADH produced in glycolsis and the TCA cycle delivers a pair of electrons to Complex I.
- The NADH is delivered to complex I from the mitochondrial matrix (in the interior of the mitochondrion).

By far the most common electron acceptor in the oxidative phosphorylation supercomplex is an iron atom. Of course, the most common oxidation states for iron ions are Fe^{2+} and Fe^{3+}. An iron in the 3+ oxidation state is able to accept an electron, becoming Fe^{2+}. In contrast, an iron in the 2+ oxidation state could pass an electron on, becoming Fe^{3+} in the process.

Picture a bucket brigade, in which people passing buckets of water from one to another all act together to put out a fire. The iron atoms act in much the same way, each passing an electron to the next in order to complete the electron transport chain.

- Electron transport is accomplished via many small steps rather than a few large ones.

If we strip away the proteins from Complex I, we can get a picture of some of the other pieces inside. Looking at the X-ray crystal structure data, we can simply ignore every atom in the protein, until we are left with the "ligands". In biochemistry, ligands means the stuff attached to the proteins (as opposed to in inorganic chemistry, where it means the stuff attached to the metals). That's what we see below. The red and yellow shapes that you see are iron sulfide complexes, strung along so that they can pass electrons along through Complex I. The pieces that we see here are found within the hydrophilic part of Complex I; that is, they are found within the yellow and pink egg-shaped part seen in the structure above. This picture is oriented in the same direction as the one above; the iron complexes extend from the lower part of the hydrophilic domain all the way up to the edge of the hydrophobic, membrane-bound portion of the complex.

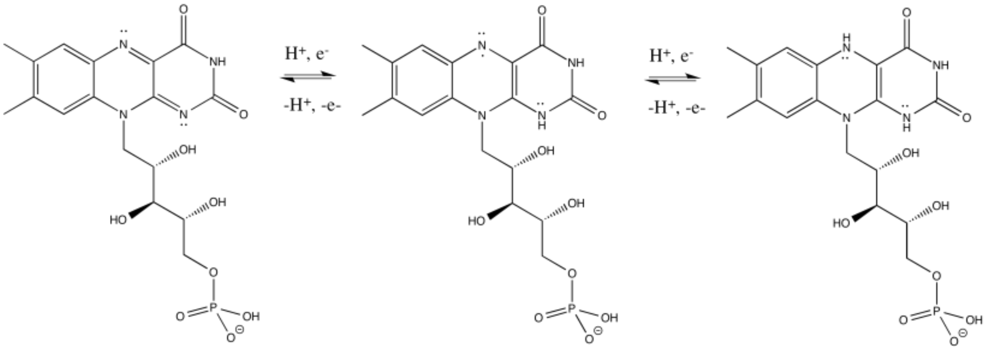
So, we have a "wire" to carry the electrons through the complex after they are delivered by NADH. We have a mismatch problem, however. NADH is a two electron donor. An Fe^{3+} ion is a one-electron acceptor. We need an adapter for this electrical connection. The adapter comes in the form of FMN. FMN is the structure with some atoms coloured in blue and red near the bottom right corner of the picture.

- NADH only donates two electrons at a time.
- The iron ions in the electron transport chain can toggle between Fe(III) and Fe(II); they can accept only one electron at a time.
- An adapter is needed to convert two-electron transfer into one-electron transfer.

FMNH2 is a little bit like NADH. Its oxidized form, FMN, can accept two electrons and a proton in the form of a hydride ion, as well as an additional proton. In other words, FMN accepts H$^-$ and H$^+$ to become FMNH2. However, a slightly different route is available to FMN. It can also undergo reduction one electron at a time. In reality, the addition of an electron would be shortly preceded by or shortly followed by addition of a proton, in order to keep the overall charge the same. This state, FMNH, is called the semiquinone form.

What's the difference between NAD and FMN? Why is one able to accept only a pair of electrons, whereas the other can accept one at a time? When FMN accepts one electron, it becomes a radical. Radicals are unstable, reactive species. They can be stabilised chiefly by delocalisation. The additional conjugation in FMN compared to NAD allows the odd electron to be delocalised more extensively in FMN. That radical stability is the key difference.

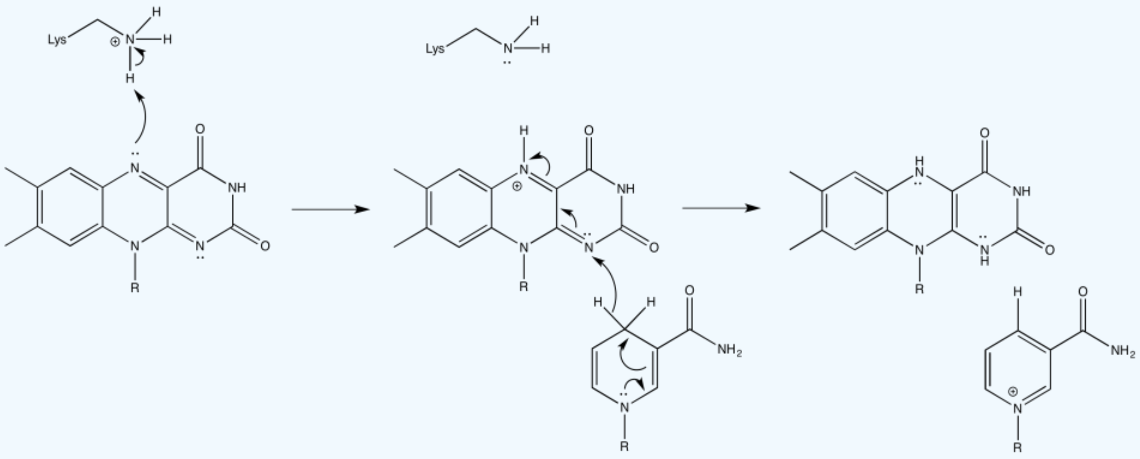
- The presence of extended conjugation stabilises a radical on FMNH.
- The stability of this radical allows FMN to accept one electron at a time.



Exercise 7.2.2

Provide a mechanism for the conversion of FMN to FMNH2 in the presence of NADH and a lysine side chain, at pH 7.

Answer



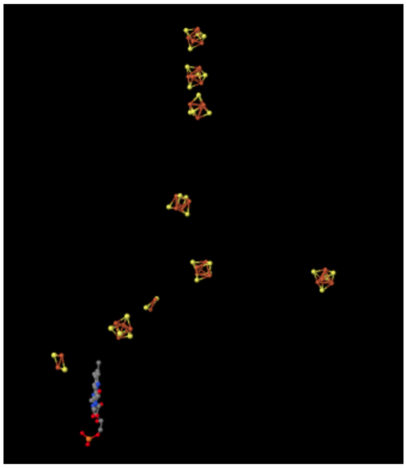
Once FMNH2 has formed, the reverse is true, of course. It can give up one electron at a time. As a result, FMN can take a pair of electrons coming in from NADH and send them out one at a time into the electron transport chain.

The rest of the electron transport chain through Complex I is a series of iron-sulfur clusters. As the name suggests, these clusters consist of iron and sulfur atoms. The most common variety contains four iron atoms and four sulfur atoms arranged at the corners of a cube. These clusters are often referred to as 4Fe4S clusters for obvious reasons: there are 4 iron atoms and 4 sulfur atoms. The sulfur atoms at the corners are really sulfide ions, S^{2-}. In addition to the three sulfur ions, each of the iron atoms is also bound to an anionic cysteine residue, so that the iron has tetrahedral coordination geometry. The iron atoms are present as a combination of Fe^{2+} and Fe^{3+} ions.

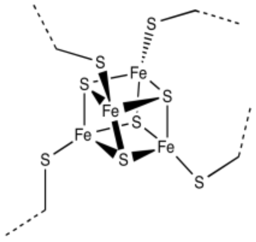
- Iron sulfur clusters are very common in biological electron transport.
- The iron ions can be Fe(II) or Fe(III).
- The ligands for the iron ions include sulfide ions, S^{2-}.

- The iron sulfide clusters are usually held in place in the protein by cysteine ligands ($CysS^-$).

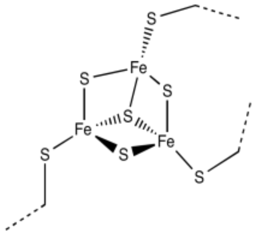
Here is another view of the ligands, seen from a different point of view this time. See whether you can find a group of four iron atoms (coloured red) bound with four sulfur atoms (coloured yellow).



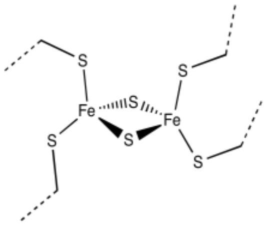
There are other variations of FeS clusters. A very common one is a 2Fe2S cluster, which of course consists of two iron atoms and two sulfide ions at alternating corners of a diamond. There are a couple of these clusters visible in the picture above. Again, the iron atoms could be Fe^{2+} or Fe^{3+} ions, or one of each. Also, each iron is usually bound to two additional cysteine anions to complete a tetrahedral geometry. Those groups aren't shown here, though, because we have left the protein out of the picture. (We will see eventually that other amino acids occasionally bind iron sulfur clusters in place of cysteine.)



[4Fe4S]



[3Fe4S]



[2Fe2S]

Another possibility is a 3Fe4S cluster, a lop-sided affair in which one of the iron atoms is essentially left out of the FeS cube.

Exercise 7.2.3

Assuming one iron is present as Fe(III) and the rest as Fe(II), calculate the overall charges on:

a) 2Fe2S b) 3Fe4S c) 4Fe4S

Answer a

a) Iron charges: Fe(II) + Fe(III) = 5^+

Ligand charges: 2 sulfides = 2 x 2^- = 4^- ; 4 cysteines = 4 x 1^- = 4^- ; total = 8^-

Overall: 3^-

Answer b

b) Iron charges: 2 x Fe(II) + Fe(III) = 4^+ + 3^+ = 7^+

Ligand charges: 4 sulfides = 4 x 2^- = 8^- ; 3 cysteines = 3 x 1^- = 3^- ; total = 11^-

Overall: 4^-

Answer c

c) Iron charges: 3 x Fe(II) + Fe(III) = 6^+ + 3^+ = 9^+

Ligand charges: 4 sulfides = 4 x 2^- = 8^- ; 4 cysteines = 4 x 1^- = 4^- ; total = 12^-

Overall: 3^-

Exercise 7.2.4

Environment plays a role in modulating reduction potentials in proteins. Suppose a 2Fe2S cluster was in a mixed Fe(II)/(III) oxidation state. How would its reduction potential when surrounded by nonpolar amino acid residues compare to its reduction potential when surrounded by polar amino acid residues?

Answer

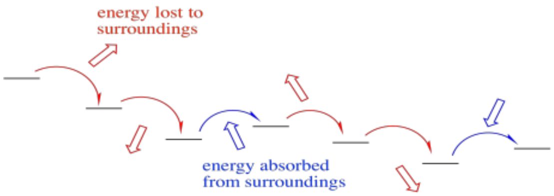
Upon reduction, the charge on a 2Fe2S cluster will increase from 3^- to 4^-, assuming it starts in a mixed Fe(II)/(III) state (whereas if it starts in a Fe(III)/(III) state, the overall charge will increase from 2^- to 3^-). These anions would be stabilised by strong intermolecular interactions such as ion-dipole forces. Both states (oxidised and reduced) will be stabilised by a polar environment, but the more highly charged reduced state will depend even more strongly on stabilisation by the environment. As a result, we might expect the reduction potential to be lower when surrounded by nonpolar amino acid residues, and higher if surrounded by polar residues.

There is a whole series of these clusters in Complex I. The electrons delivered from NADH are sent from one to the next and then to the next. There are a couple of reasons for this arrangement.

Because these clusters are all bound in place by the protein -- completely immobilised -- the electron transfer has to occur via an outer sphere mechanism. Why are there so many clusters? Remember, outer sphere electron transfers have a limited range. The electron, under most circumstances, can only hop so far. By providing a series of conducting FeS clusters, the electron can hop from one to the next, arranged like stepping stones across a river.

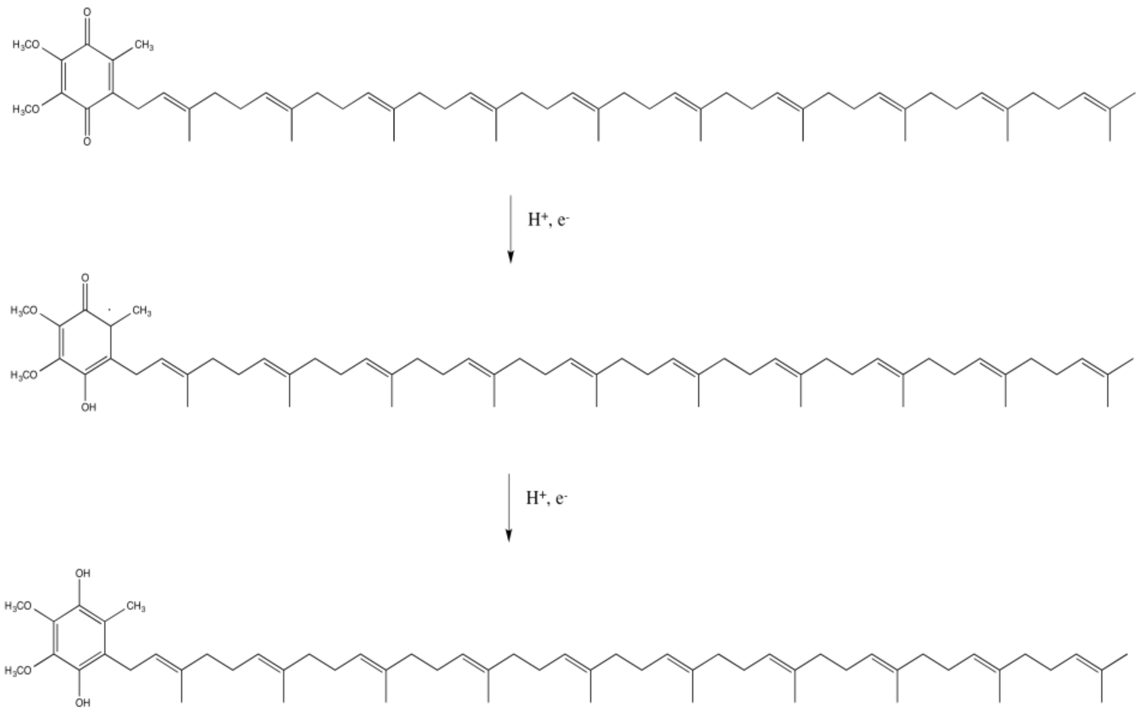
Not only that, but the electron transport chain takes electrons from NADH and delivers them, ultimately, to molecular oxygen in Complex IV. The molecular oxygen is converted to water. That transfer from NADH to water is very exothermic. The reaction is very much downhill in energy. In order to make this transfer practically feasible, and in order to harness the enormous amount of energy involved, the electrons are allowed to step downhill just a little at a time.

Occasionally, electrons may even hop back uphill slightly, recapturing energy that has been lost to the surroundings in previous transfers. This damping effect may make the whole process more efficient. Still, the electrons are overall rolling downhill energetically. An electron may jump uphill a few times, but eventually those uphill jumps will be followed by a downhill drop, so that overall the electron has moved to lower energy.



- An occasional uphill electron transfer absorbs energy.
- Re-absorption boosts efficiency by preventing heat loss.

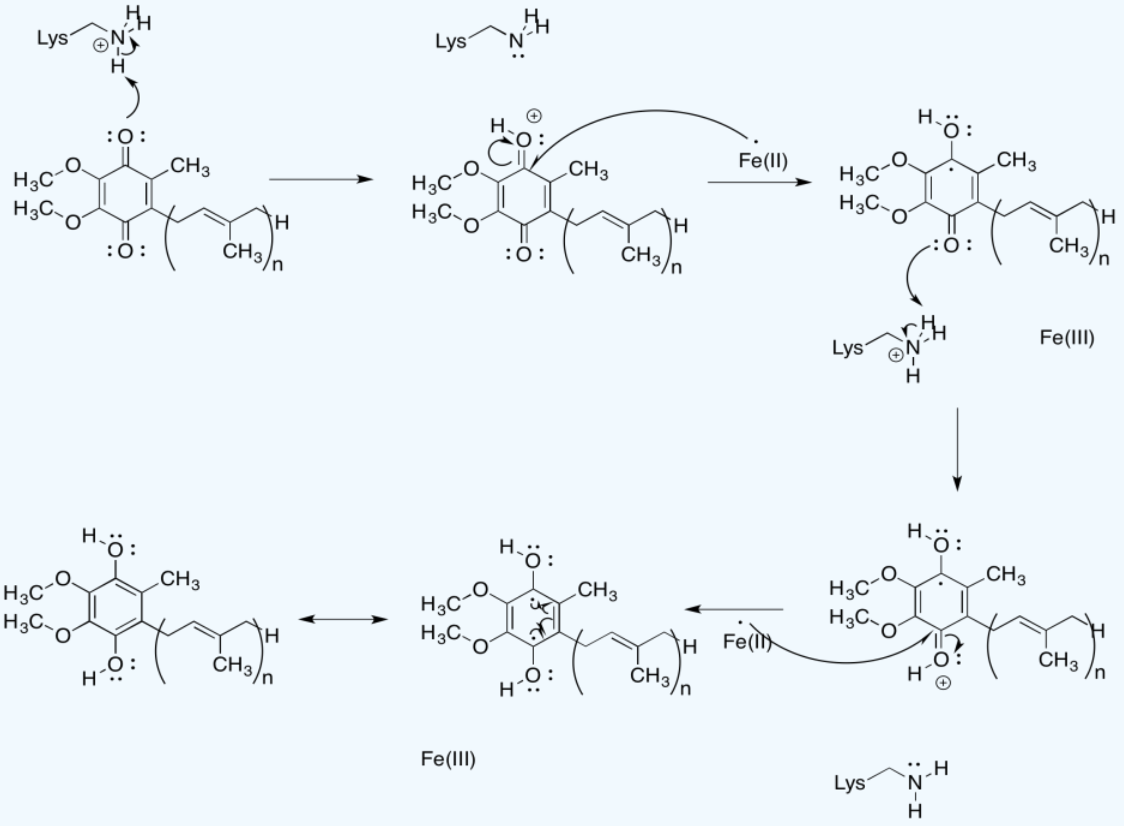
In Complex I, the final destination for the electron transport chain is a ubiquinone, sometimes abbreviated as Q or UQ. Like FMN, UQ is a two electron, two proton acceptor, to become UQH2. Also like FMN, UQ can accept one proton and one electron at a time, to form the semiquinone form, UQH. Once again, this is a radical species.



Exercise 7.2.5

Provide a mechanism for the conversion of UQ to UQH2 in the presence of Fe^{2+} ions and lysine side chains, at pH 7.

Answer



UQ is very different from the FeS clusters or the FMN because it isn't attached to a protein. It isn't tied down. It can move around. That makes it a mobile electron carrier. In addition to being a relatively high-potential electron acceptor (at least compared to other things in Complex I), the role of UQH2 is to deliver electrons to Complex III so that the electron transport chain can continue.

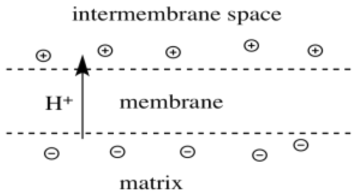
The trouble is, if UQH2 is mobile, what's to keep it from wandering away? How is its pathway limited so that it is more likely to reach its destination? Remember that the oxidative phosphorylation supercomplex is a group of membrane-bound proteins. They are held in a lipid-rich environment. The structure of UQH2, with its long tail, is very lipophilic. If it stays in the membrane, its movements are limited to two dimensions, rather than three, and it is much more likely to reach its destination of Complex III.

- Ubiquinone is a lipid-soluble, mobile electron carrier.
- Its movement is restricted to the mitochondrial membrane.

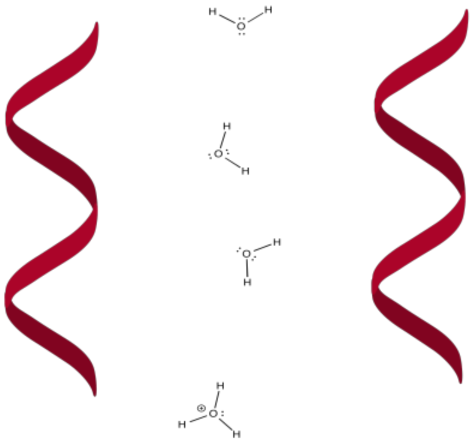
There is one more important feature of Complex I. Like some of the other complexes involved in oxidative phosphorylation (Complexes III and IV), Complex I pumps protons across the inner mitochondrial membrane. Ultimately, the protons that have gathered on the edge of the inner mitochondrial membrane cascade back across, turning a molecular millwheel that drives the manufacture of ATP. The ATP is used to power processes throughout the cell.

- Protons are actively pumped across the mitochondrial membrane.
- As a result, a charge develops across the membrane.
- The mitochondrial matrix becomes "n-doped" or negatively charged.
- The intermembrane space becomes "p-doped" or positively charged.

This proton pump is an example of active transport. Energy is expended to transport protons across the membrane, despite a buildup of positive charge in the intermembrane space (and a corresponding buildup of negative charge in the matrix). The energy released by the electron transport chain may be responsible for conformational changes in the protein that help this transport occur.

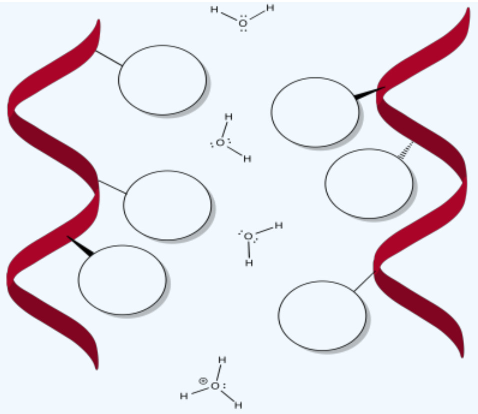


There still seems to be some discussion going on about how, exactly, the proton pump works in this system. However, some things are clear. The transport of proteins across a hydrophobic membrane is likely facilitated by the presence of hydrophilic portions of the protein. There are believed to be channels that open up in the protein, allowing water molecules to move through the protein. Because the protein is embedded in the membrane, these protons are also crossing the membrane at the same time.

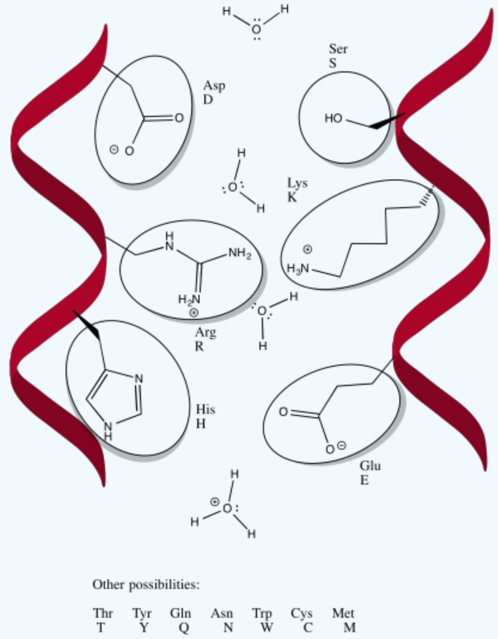


Exercise 7.2.6

Frequently, specific amino acids can play a role in assisting the transport of protons (or other ions). Fill in some different possibilities for these amino acids.

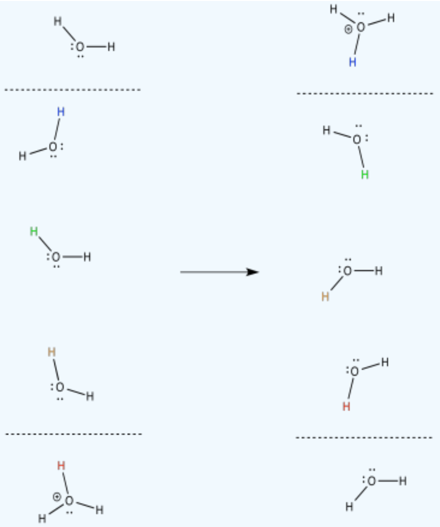


Answer

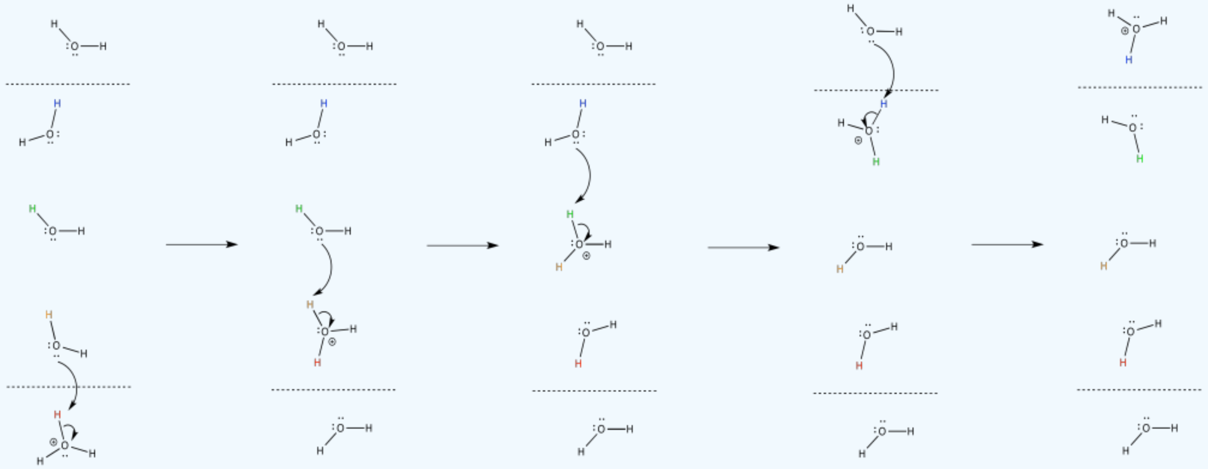


Exercise 7.2.7

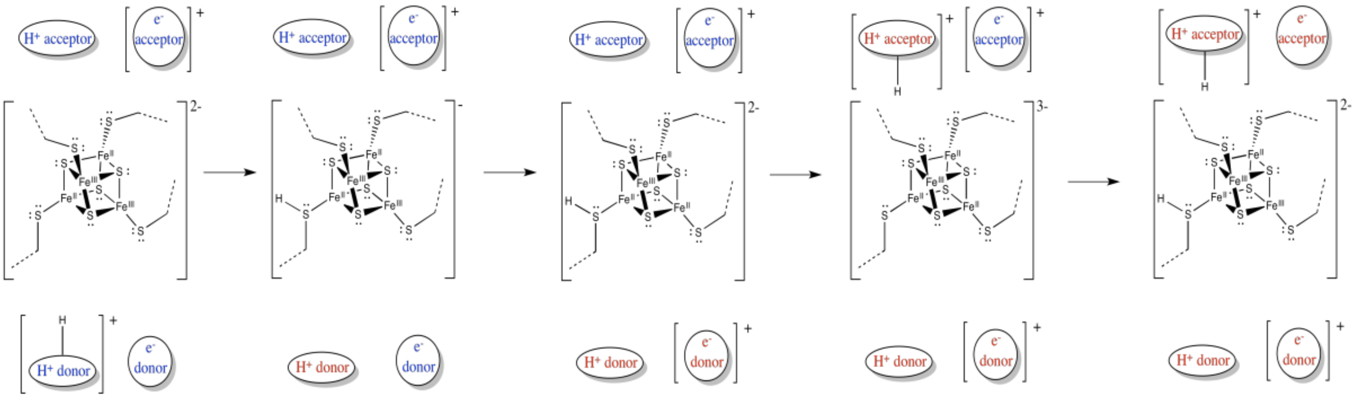
In general, the proton that enters the complex on one side of the membrane is probably not the same proton that emerges on the other side. Provide a mechanism with arrows to illustrate this process.



Answer



The release of energy over the electron transport chain drives the transport of protons across the membrane. There is another factor that helps, too. Like the electrons, the protons travel from the matrix toward the intermembrane space. Both positive and negative chages are traveling in the same direction. That raises the possibility of coupled transport, in which the flow of electrons through the protein makes it easier for protons to follow along (or vice versa).



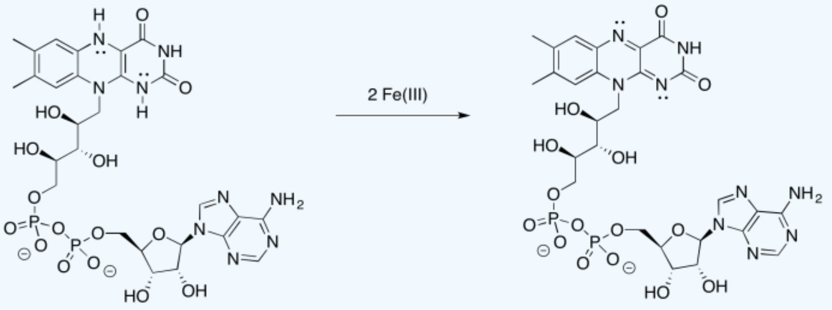
In coupled transport, the movement of an proton is quickly followed by the transfer of an electron (or vice versa).

- Electrons and protons are travelling in the same direction through complex I: from the matrix toward the intermembrane space.
- Their opposite charges may lead to a coupled mechanism in which the movement of one makes it easier for the other to follow.

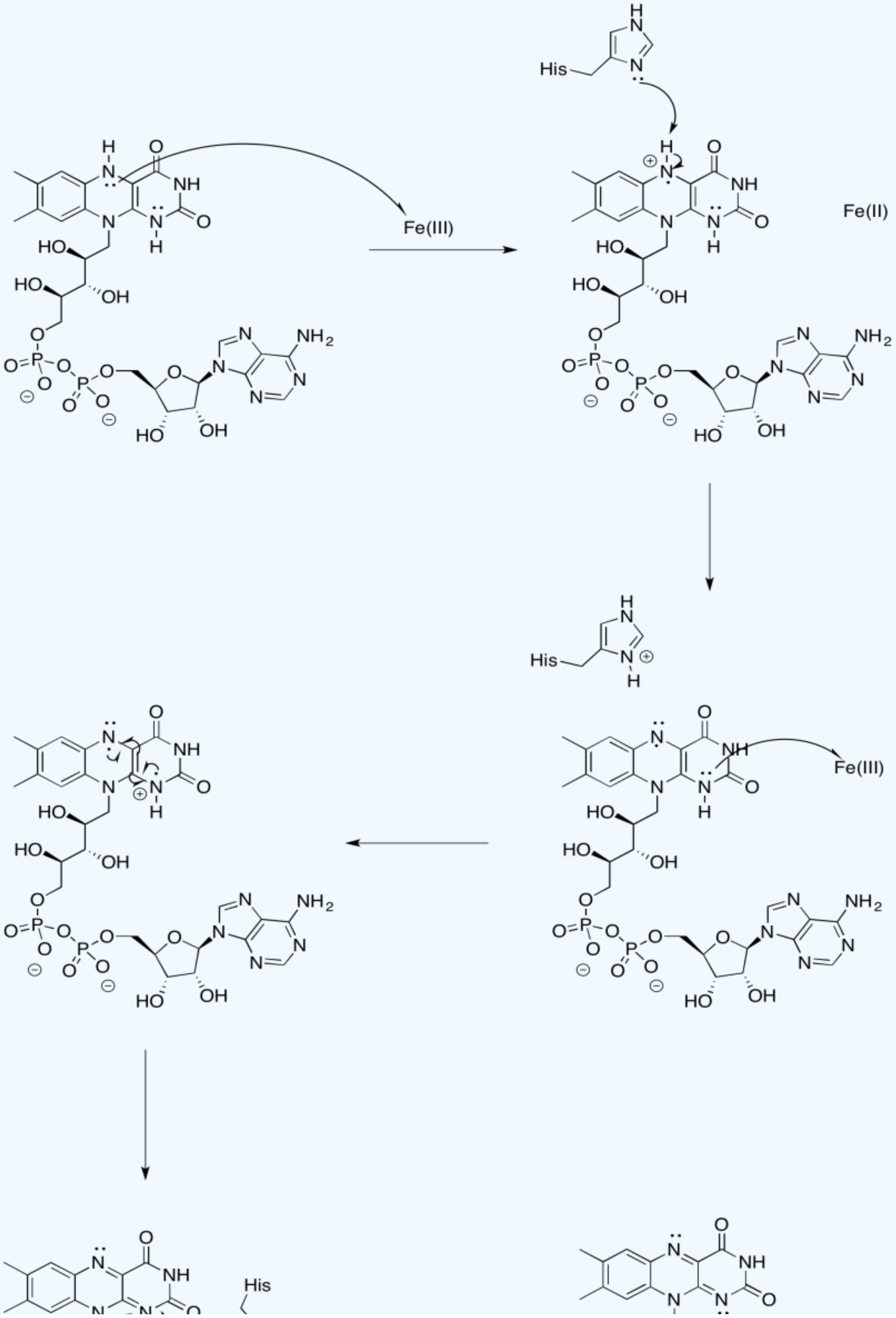
Complex I is not the only entry point for electrons into the electron transport chain. Complex II plays a similar role. Together, they harvest energy from the electron transport chain; that energy is ultimately used to make ATP, which can move through the cell to release energy elsewhere.

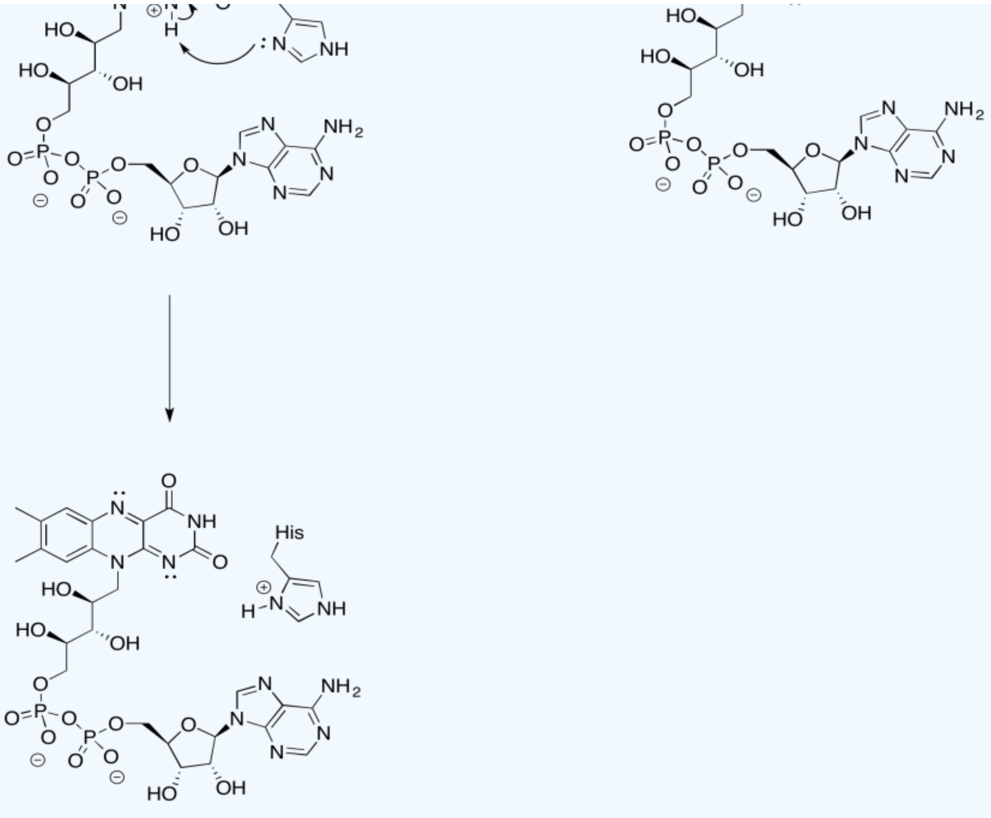
Exercise 7.2.8

Provide a mechanism for the oxidation of FMNH2 by iron(III).



Answer

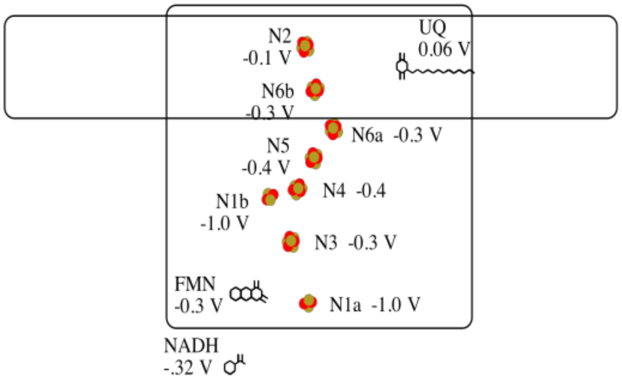




Exercise 7.2.9

It's difficult to measure the reduction potential of an individual site within a protein. However, researchers have been able to estimate these values by measuring EPR spectra under various conditions. For example, here is an approximate picture of potentials in Complex I.

a. Two of the N clusters are probably not directly involved in the electron transport chain. Which ones?
b. Use the data in the diagram to construct a potential energy diagram for the transfer of the electron along the pathway.

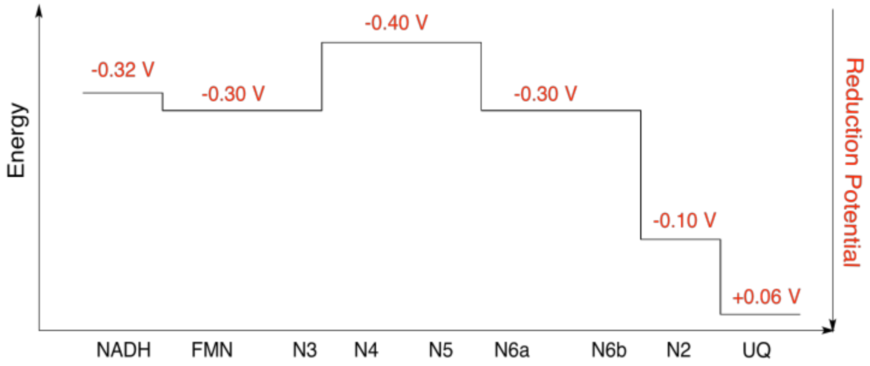


Answer a

a) N1a and N1b are most likely not involved, because their reduction potentials are too negative.

Answer b

b)



Exercise 7.2.10

Using the values in the figure above, calculate the energy change when an electron is transferred from the N5 cluster to the N6a cluster.

Answer

Assuming the reduction potentials are:

N5(ox) + e^- → N5(red) E^o_{red} = -0.40 V

N6a(ox) + e^- → N6a(red) E^o_{red} = -0.30 V

Then the potential difference for the reaction, ΔE^o = -0.30 - (-0.40) V = 0.10 V.

The Faraday relation $\Delta G = -nF\Delta E^o$ gives

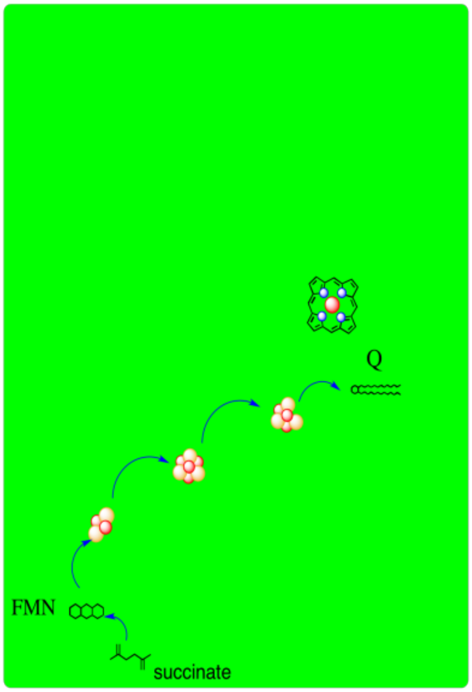
$\Delta G = -1 \times 96{,}485\ J\ V^{-1}\ mol^{-1} \times 0.10\ V = 9{,}649\ J\ mol^{-1} = 9.7\ kJ\ mol^{-1}$

7.3: Complex II

Complex II is another group of proteins that serves as a second entry point into the electron transport chain, which is involved in the additional production of ATP to power cellular processes. The electron transport chain releases minute amounts of energy with each electron transfer, and the transport is coupled to the pumping of protons across the mitochondrial membrane. Eventually, the electrons are delivered to molecular oxygen, which is reduced to water, in Complex IV.

A schematic of Complex II is provided below. It shows electrons provided by succinate traveling first to FAD and then along a series of iron sulfur clusters to a ubiquinone acceptor.

- Complex II, like Complex I, is an entry point into the electron transport chain.
- In Complex II, two electrons are delivered from succinate.

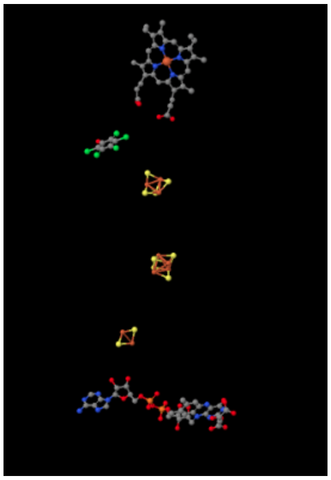


The X-ray crystal structure of Complex II is shown below. It is depicted in cartoon form to highlight the structure, with pink helices, yellow sheets and white loops. Just as in the structure of Complex I, the structure here is shown oriented so that the inner mitochondrial membrane would stretch across the top of the picture; if it were shown, we would see it in cross section, from side to side. Once again, there is a hydrophobic domain in the upper part of the complex that would be embedded in that membrane. Below that lies a much larger hydrophilic domain, which would extend into the mitochondrial matirx.

Complex II actually plays a part in another biochemical process, the citric acid cycle. One of the steps of the citric acid cycle is the oxidation of succinate to fumarate. It is during this oxidation that additional electrons are introduced into the electron transport chain via Complex II. At the same time, two protons are delivered from succinate as well. The loss of two protons and two electrons from succinate corresponds to a formal loss of H_2 (formal, meaning a molecule of H_2 is not actually formed, but the pieces are equivalent to a full H2 molecule). A double bond forms in the new fumarate molecule, which is said to be "dehydrogenated" with respect to the original succinate. Complex II is the enzyme that carries out this transformation in the citric acid cycle, and so the complex is also called "succinate dehydrogenase".

- Complex II is actually an integral part of the TCA cycle, which takes place in the mitochondrial matrix.
- Conversion of succinate to fumarate is a two-electron, two-proton process.

Shown below, the proteins are stripped out of the picture to reveal some of the working parts inside. Having already seen Complex I, you will probably recognize a few iron sulfur clusters, shown again in red and yellow. At the bottom of the picture, close to the matrix, you can see a flavenoid structure, a little like the FMN you saw in Complex I. At the top, actually buried within the hydrophobic portion (you can just see the edge of it if you look between two of the pink helices in the picture above), is an iron heme complex; it's a little like the active site of hemoglobin. You can see the iron atom, coded in red, and the four nitrogen atoms around it, coloured blue. However, it is not clear what role this heme actually plays in electron transport through Complex II.



In between the highest iron sulfur cluster and the iron heme is a molecule of pentafluorophenol. That's not supposed to be there in the cell. It's an inhibitor; the researchers added it to hold the place of a ubiquinone while they were growing the crystal that they would analyse to get this structure. There is actually a second inhibitor in the structure, an oxaloacetate, which holds the place of the succinate molecule that would deliver electrons to the complex. However, the oxaloacetate is not clearly visible because it's partly obscured by the flavenoid at the bottom of the picture.

- Like in Complex I, electrons eventually arrive at ubiquinone in Complex II.
- Ubiquinone is a mobile, lipid-soluble, two-electron carrier.

Complex II is unique in a another important way. Unlike Complexes I, III, and IV, it takes part in the electron transport chain but does not actively pump protons across the inner mitochondrial membrane. Instead, the electrons that it harvests contribute to building the proton gradient once they arrive at Complex III (and later at Complex IV).

- Complex II does not pump protons directly.
- Complex II does send two protons on to Complex III in the form of the reduced ubiquinol.

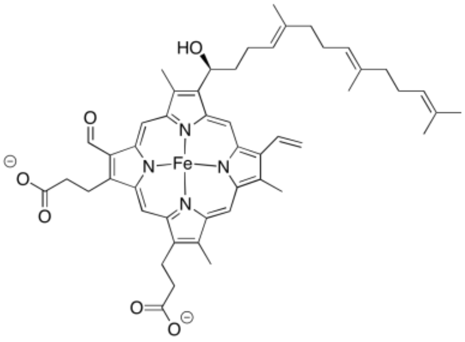
In terms of how those electrons make their arrival, the picture is somewhat similar to Complex I. Succinate is a hydride donor in this reaction, so it is donating two electrons. As in Complex I, a series of FeS clusters will eventually relay the electrons, so we have a matching problem. To step down from a two-electron process to a one-electron process, another flavenoid, FAD, acts as an intermediary. Like the related FMN, FAD can accept either one or two electrons at a time, and its reduced form, FADH2, can donate either one or two electrons at a time.

- Just like in Complex I, an adapter is needed to convert the two-electron process of succinate oxidation to the one-electron process of iron reduction.
- The adapter is another flavenoid structure, FAD, which is very similar to the FMN used in Complex I.

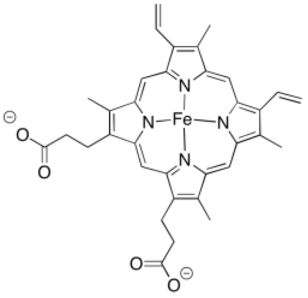
After the electrons have arrived and are stored in the form of FADH2, they are passed along, one at a time, through a series of three FeS clusters. Just as in Complex I, these carriers are all bound to the proteins, so they are held in one place and do not move. The outer sphere mechanism by which the electrons are transferred can only operate over a short distance, from one electron carrier to the next.

Complex II also contains a structure we did not see in Complex I: a cytochrome. A cytochromes is a protein that contains a heme complex of iron. They look a little bit like hemoglobin, with which you are undoubtedly familiar by now. As in the FeS clusters, the cytochrome can access either the Fe(II) or the Fe(III) state. Like the FeS clusters, they just accept one electron at a time. We will find out that some cytochromes are mobile, but this one is not. It stays where it is and waits for a ubiquinone to bind nearby.

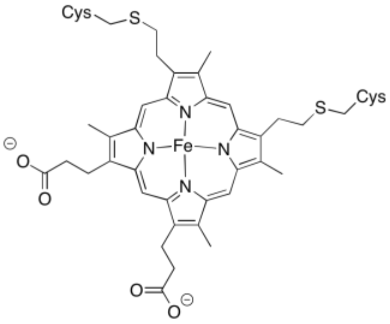
There are few different variations in the heme family that are commonly encountered in biology. Heme b is a common one and has the simplest structure. Heme a contains a hydrocarbon tail as well as a formyl group (-HC=O) attached to its central porphyrin ring. Heme c is covalently bound to the surrounding protein via cysteine residues.



heme a



heme b



heme c

Exercise 7.3.1

Look again at the X-ray crystal structure of the ligand in Complex II. Which type of heme is present?

Answer

Heme b.

Exercise 7.3.2

The basic porphyrin structure at the centre of all the hemes is a macrocycle with the formula $(C_4H_2NCH)_4$. Draw this structure.

Answer

A porphyrin contains four pyrrole rings (five-membered, aromatic ring containing a nitrogen) arranged to form a 16-membered macrocycle.

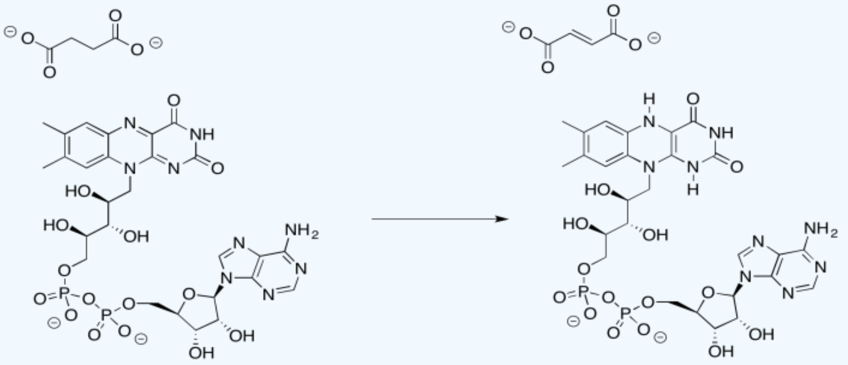
The exact role of the cytochrome in Complex II is unclear. Although cytochromes form part of the electron transport chain in Complexes III and IV, it might not do so in Complex II. Another possible role is storage of an electron (which does arrive through the electron transport chain). When the ubiquinone binds nearby, the cytochrome may release its electron to the ubiquinone. A second electron would arrive directly from the nearby FeS cluster. That mechanism may allow for more rapid reduction of ubiquinone to ubiquinol, so that it spends less time in the semiquinone stage. As a result, the radical species would be less likely to move away before being fully reduced. Radical species can cause damage, so limiting the movement of radical species through the cell is important.

- The role of the heme group in Complex I is not clear.
- It has been suggested that the heme group may act like a capacitor. It may store one of the two electrons needed to reduce ubiquinone to ubiquinol.
- Storage of an extra electron could result in more rapid reduction of ubiquinone to ubiquinol.
- Rapid, two-electron reduction limits the lifetime of potentially damaging radical intermediates in the cell.

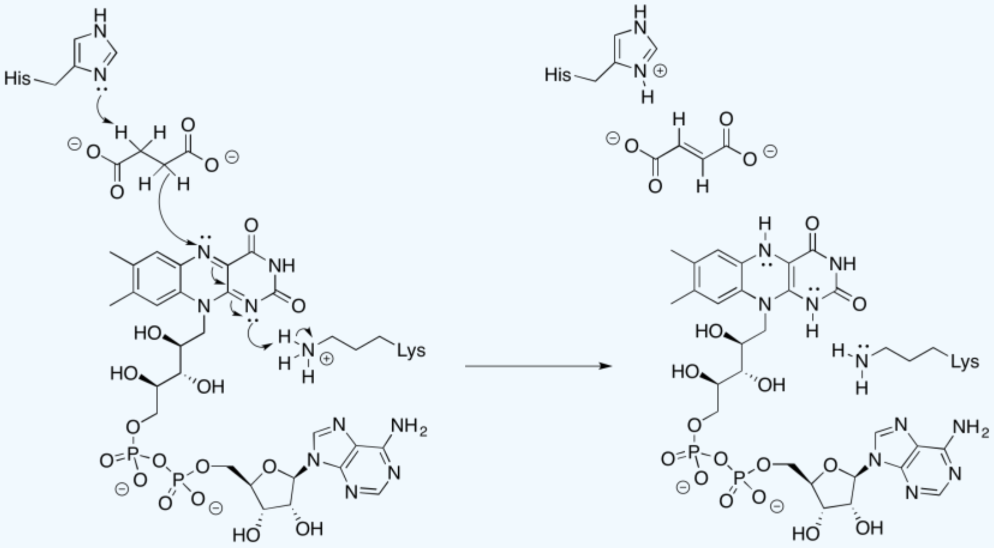
Once two protons and two electrons are delivered to ubiquinone, the resulting ubiquinol travels on to Complex III for the next step in oxidative phosphorylation.

Exercise 7.3.3

Provide a mechanism for the reduction of FAD by succinate.

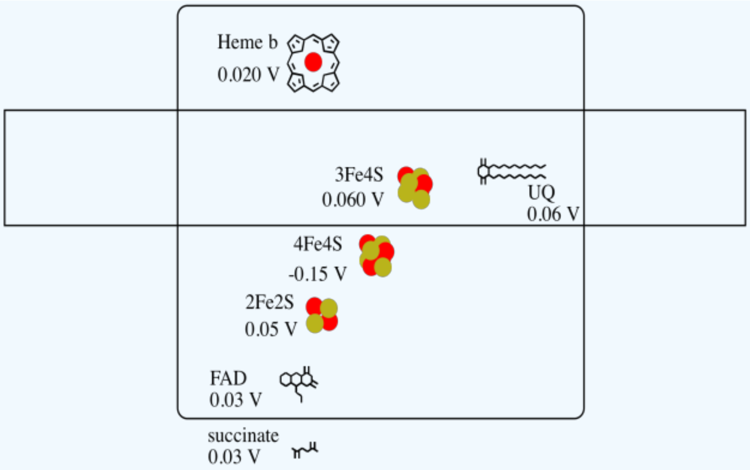


Answer

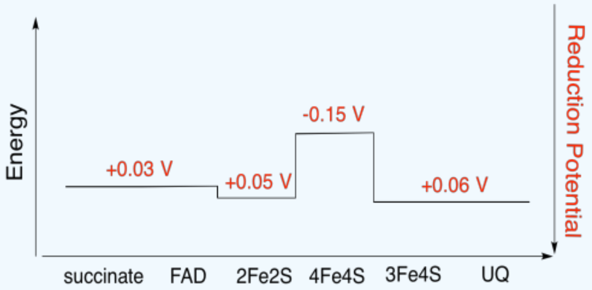


Exercise 7.3.4

It's difficult to measure the reduction potential of an individual site within a protein. However, researchers have been able to estimate these values by measuring EPR spectra under various conditions. Assuming the reduction potentials below, draw a reaction progress diagram for transport of an electron all the way from succinate to ubiquinone.



Answer



Exercise 7.3.5

Using the values in the figure above, calculate the energy change when an electron is transferred from the 4Fe4S cluster to the 3Fe4S cluster.

Answer

Assuming the reduction potentials are:

4Fe4S(ox) + e^- → 4Fe4S(red) E^o_{red} = -0.15 V

3Fe4S(ox) + e^- → 3Fe4S(red) E^o_{red} = 0.06 V

Then the potential difference for the reaction, ΔE^o = 0.06 - (-0.15) V = 0.21 V.

The Faraday relation $\Delta G = - n\,F\,\Delta E^o$ gives

ΔG = - 1 x 96,485 J V^{-1} mol^{-1} x 0.21 V = 20,262 J mol^{-1} = 20 kJ mol^{-1}

Exercise 7.3.6

Assuming all iron is present as Fe(III), calculate the overall charges on:

a) 2Fe2S b) 3Fe4S c) 4Fe4S

Answer a

a) Iron charges: 2 x Fe(III) = 6^+

Ligand charges: 2 sulfides = 2 x 2^- = 4^- ; 4 cysteines = 4 x 1^- = 4^- ; total = 8^-

Overall: 2^-

Answer b

b) Iron charges: 3 x Fe(III) = 9^+

Ligand charges: 4 sulfides = 4 x 2^- = 8^- ; 3 cysteines = 3 x 1^- = 3^- ; total = 11^-

Overall: 2^-

Answer c

c) Iron charges: 4 x Fe(III) = 12^+

Ligand charges: 4 sulfides = 4 x 2^- = 8^- ; 4 cysteines = 4 x 1^- = 4^- ; total = 12^-

Overall: 0

X-ray crystal structures: Zhou, Q., Zhai, Y., Lou, J., Liu, M., Pang, X., Sun, F. Thiabendazole inhibits ubiquinone reduction activity of mitochondrial respiratory complex II via a water molecule mediated binding feature. *Protein Cell* **2011**, *2*, 531-542. Images obtained via RCSB Protein Data Bank (3SFD).

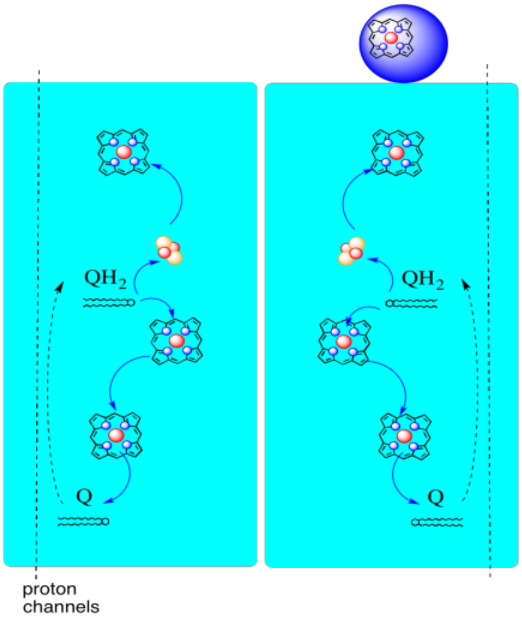
7.4: Complex III

Complex III accepts electrons from both Complex I and Complex II. The electrons arrive in the form of ubiquinol, UQH2, which delivers two electrons and two protons and is converted back to ubiquinone, UQ. The ubiquinone then shuttles back to Complex I or Complex II to collect more electrons.

- Complex III is the destination for electrons arriving from both Complex I and Complex II.
- Complex III uses energy released in downhill electron transfers to pump more protons across the inner mitochondrial membrane.
- The proton gradient across the membrane is used to drive ATP formation at Complex V.
- Complex III then sends its electrons on to Complex IV.

The path of electrons through Complex III is shown below. Note that the complex is a dimeric structure, with two equivalent paths: one shown on the left and the other on the right. Electrons are delivered from UQH2, ubiquinol, in the middle of the picture, traveling upward to the mobile cytochrome c at the top. A second electron pathway allows travel downward in the picture, toward another molecule of ubiquinone, which recycles the electrons in a loop.

- Complex III features an unusual, diverging electron pathway.
- One electron travels on toward cytochrome c.
- The second electron is eventually recycled into another ubiquinol.

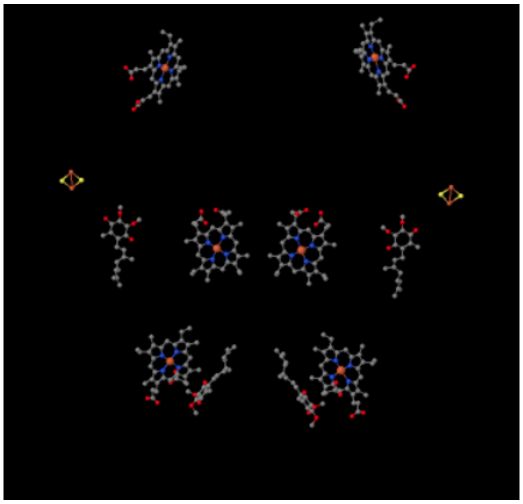


The X-ray structure of Complex III is shown in cartoon form below. The inner mitochondrial membrane would intersect the upper middle portion of the complex. The majority of the complex projects below, into the matrix (the bottom of the picture, in this orientation) although a significant amount also protrudes into the intermembrane space.

Complex III continues the electron transport chain, sending electrons to higher reduction potential (and lower free energy) and towards a meeting with molecular oxygen in Complex IV. Protons are also pumped from the mitochondrial matrix, across the inner mitochondrial membrane and into the intermembrane space. At the same time, a second electron route results in an effective recycling of half the electrons that come into the complex, increasing the number of protons pumped per electron arriving at Complex III.

- It has been suggested that the electron-recycling loop provides a mechanism for drawing more protons up from the matrix.

We can see this unusual arrangement if we ignore the proteins to reveal the ligands, below. The complex can more clearly be seen as a dimer; the left half of the picture is exactly the same as the right, although reflected the opposite way. Electrons enter the complex via the mobile carrier, ubiquinol, visible on the right and left side of the picture about halfway down; you can see the ringand a chain hanging from it.



When UQH2 binds to Complex III, one electron is sent on to an FeS cluster, whereas the second is sent to an iron heme center, called heme B_L. The FeS cluster is visible just above the ubiquinol and to the edge of the picture. The heme B_L is toward the center of the picture.

Although it isn't apparent in the X-ray picture shown, this FeS cluster is different than the ones that you saw earlier. This one is held in place with different amino acid side chains. You can't see that in the picture because the entire protein has been left out, along with those amino acids that are binding to the cluster. Whereas most FeS clusters are held in place exclusively by cysteines, this cluster is held in place by two cysteiens on one side but by two histidines on the other. This peculiar FeS cluster is called a Rieske cluster.

Rieske clusters are important because they are "high potential FeS clusters". That means that they have exceptionally positive reduction potentials compared to other FeS clusters. The reduction potential of any ligand in a protein is highly dependent on its environment, and so there is a wide range of values in most cases. That's true for iron sulfur clusters; normal ones have reduction potentials that range from -1.0 V to about +0.05 V. Rieske clusters have potentials that range from about 0V to about 0.4 V.

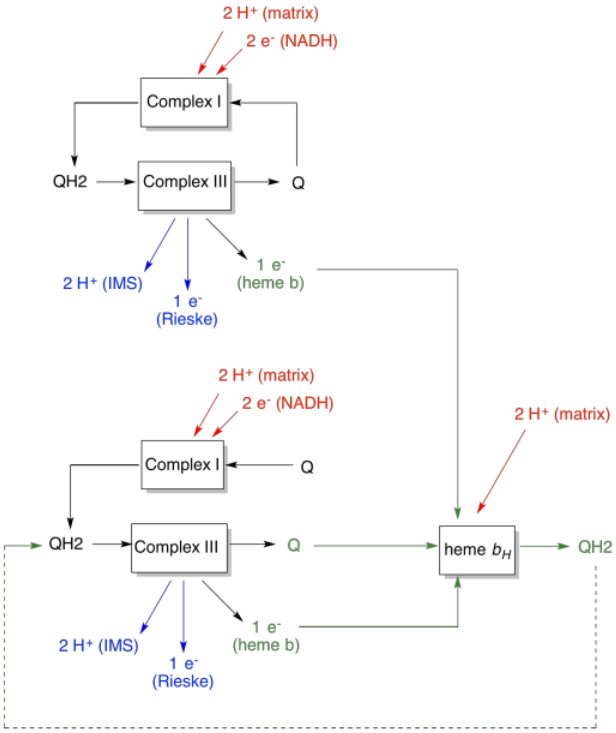
From the FeS cluster, the electron is sent on to another iron heme center in a membrane-bound unit called cytochrome c1. Cytochrome c1 can be seen at the top of the picture. Because this picture is oriented in the same way as the other X-ray structures of the respiratory complex, we can see that this electron is getting transported up toward the intermembrane space. Finally, this electron is transferred to another heme, but this heme is bound in a small, mobile protein, called cytochrome c. Cytochrome c is another mobile electron carrier. It carries the electron on to complex IV. We'll get back to the cytochrome c a little later.

Before we get to that, where does the other electron go? From heme B_L, the second electron is passed to another iron porphyrin complex, heme BH. That's toward the bottom of the picture, so this electron is actually getting sent back toward the matrix. Waiting by the heme B_L, however, there is another ubiquinone, UQ. It's waiting for the electron. It will actually wait for two, then leave its dock and go back around to the ubiquinol (UQH2) binding site to deliver the electrons again.

Why bother? Why not just send the electrons on their way properly the first time around? It seems they are getting recycled for some reason. It's believed that this diversion allows for additional protons to be pumped across the mitochondrial membrane. When the second ubiquinone gets reduced to ubiquinol via the acceptance of two electrons, it also picks up two more protons from the matrix below. Those protons will eventually get passed along toward the intermembrane space when the ubiquinol gets oxidized again. This recycling, and squeezing out a couple of extra protons to increase the proton gradient, is called the Q loop.

The advantage of the Q-loop is explained in the following diagram. In the diagram, inputs to complex III are shown in red, outputs are shown in blue, and recycled elements are in green. If one ubiquinol simply delivered its electrons and protons and was done, there would be two protons delivered per ubiquinol. That's one proton output per electron that was input.

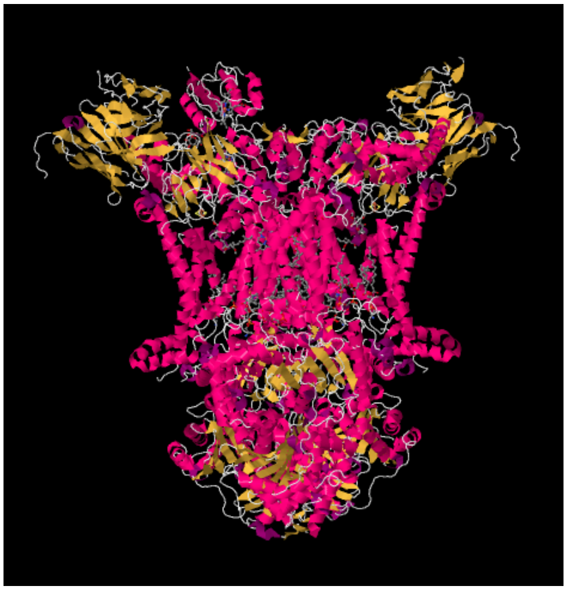
A second ubiquinol would do exactly the same thing. There would be four protons output for four electrons initially input. That's still one proton output per electron that was input.



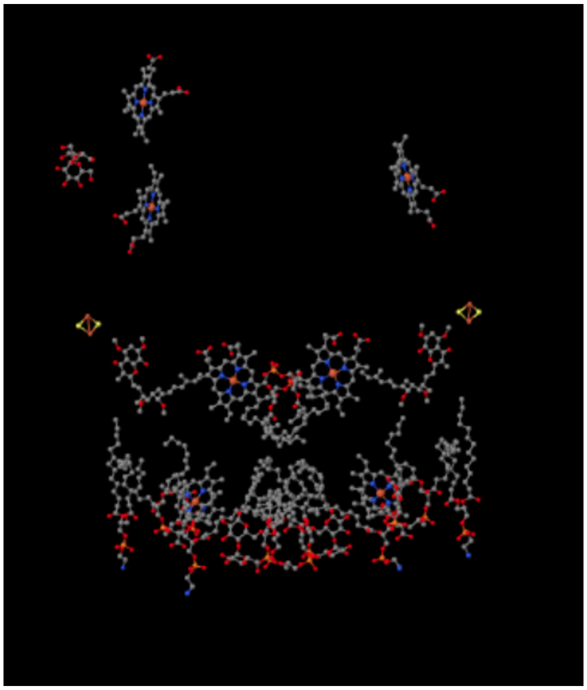
If, instead, one electron is recycled each time, then every second ubiquinol leads to the delivery of an extra pair of protons. That's because in picking up the recycled electrons, a ubiquinone has had to travel back to the matrix side of the membrane and pick up two more protons. Overall, that means six protons are delivered for four electrons input, or 1.5 protons output per electron input. Since the proton gradient is what is generating the ATP, then by increasing the number of protons pumped per electron coming in, efficiency is increased.

- The Q-loop increases the number of protons pumped per electron input into the system.

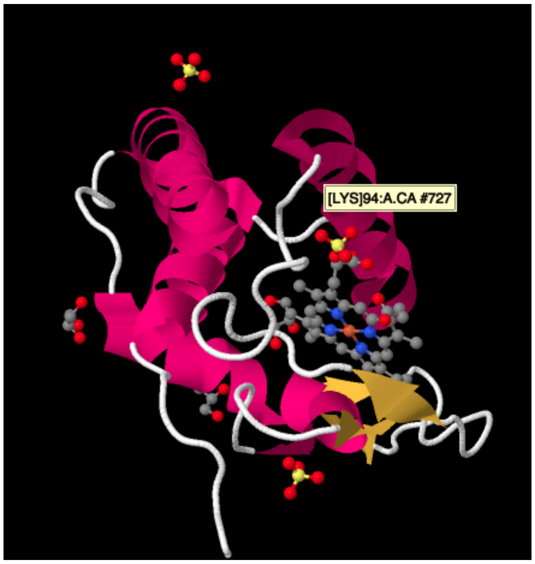
Now let's get back to the outgoing electron carrier, cytochrome c, which will ferry the electrons on to Complex IV. In the picture below, from a different X-ray crystal structure, the Complex has been found with a cyctochrome c docking at the binding site. Cytochrome c is a pink globular protein attached at the top of the picture, on the left half of the dimer as we look at it here. It's sitting at the edge of the intermembrane space, which is aqueous media. Unlike the ubiquinone, which slips along through the lipid bilayer of the membrane, cytochrome c rolls or slides or swims over the top to its destination.



The same view is shown below without the protein. The bottom part of the picture is pretty cluttered with lipids, and there is a sugar hanging around to the upper left, but right at the very top you can see the iron porphyrin that is nestled inside the cytochrome c.



A closer look at an X-ray structure of a cyctochrome c, below, shows a relatively simple picture compared to the complexes we have been looking at. There are a couple of helices, a couple of sheets, some loops, and that iron porphyrin or heme again. A few sulfate ions are floating around nearby, as well as a couple of glycerol molecules, probably introduced during purification or crystallisation of the protein. Note that the heme is found at the edge of the protein. That location may make it easier for electron transfer from Complex III, or to Complex IV.



- Cytochrome c is the final destination of electrons moving through Complex III.
- Cytochrome c is a mobile, one-electron carrier.
- Cytochrome c is actually a small, hydrophilic protein.
- Cytochrome c is found above the mitochondrial membrane, at the edge of the intermembrane space.

What keeps cyctochrome c from wandering off into the intermembrane space? If it did so, it would interrupt the efficient flow of electrons. It is possible that cytochrome c moves back and forth between Complex III and Complex IV via a mechanism called "steering". In steering, the carrier is guided along a pathway via complementary charges. For example, if the membrane is negatively charged because of polar groups on the membrane surface, then positive charges on the surface of the cytochrome c may restrict its movement to the membrane surface. That alone would reduce its mobility from three dimensions (anywhere in the intermembrane space) to two dimensions (anywhere on the membrane surface). It is possible that additional interactions reduce its mobility even further to a one-dimensional track between the two complexes.

- Steering, based on complementary charges, keeps the cytochrome c from being lost in the intermembrane space.

Exercise 7.4.1

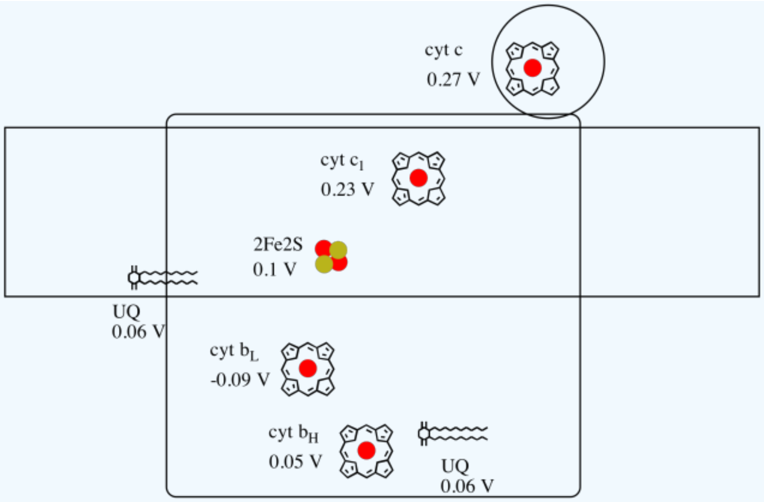
Suggest possible amino acid residues at the surface of cytochrome c that may help it stay on a negatively charged membrane surface.

Answer

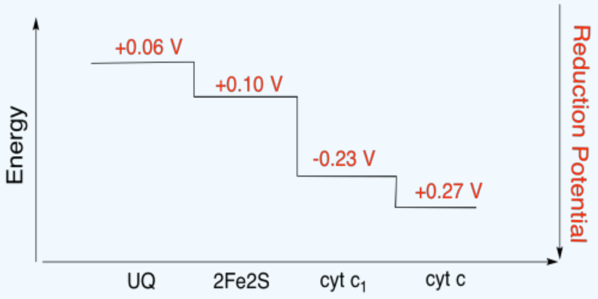
Arginine and lysine are positively charged at neutral pH.

Exercise 7.4.2

It's difficult to measure the reduction potential of an individual site within a protein. However, researchers have been able to estimate these values by measuring EPR spectra under various conditions. Assuming the reduction potentials below, draw a reaction progress diagram for transport of an electron all the way from the initial ubiquinone donor all the way to cytochrome c.



Answer



Exercise 7.4.3

Using the values in the figure above, calculate the energy change when an electron is transferred from the 2Fe2S cluster to the cytochrome c_1.

Answer

Assuming the reduction potentials are:

2Fe2S(ox) + e^- → 2Fe2S(red) $E^o_{red} = 0.10$ V

cyt c_1(ox) + e^- → cyt c_1(red) $E^o_{red} = 0.230$ V

Then the potential difference for the reaction, $\Delta E^o = 0.23 - (0.10)$ V = 0.13 V.

The Faraday relation $\Delta G = -\, n\, F\, \Delta E^o$ gives

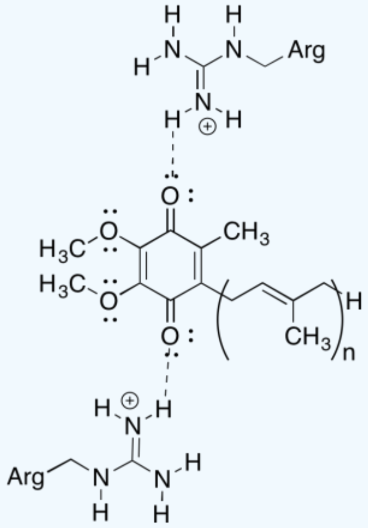
$\Delta G = -\ 1 \times 96{,}485\ J\ V^{-1}\ mol^{-1} \times 0.13\ V = 12{,}543\ J\ mol^{-1} = 12.5\ kJ\ mol^{-1}$

Exercise 7.4.4

One of the perplexing things about this complex is that, in the electron recycling loop, electron transfer appears to go from an initial ubiquinone to a final ubiquinone, with no overall driving force. However, reduction potentials are very sensitive to environment. Show how nearby arginine residues might make the reduction potential of a ubiquinone more positive.

Answer

The positive arginine residues would confer partial positive charge on the ubiquinone via hydrogen bonding; the ubiquinone would have a more positive reduction potential as a result.



See the focus page on the structure of Complex III at Biochemistry Online.

X-ray crystal structure of Complex III from: Gao, X., Wen, X., Esser, L., Quinn, B., Yu, L., Yu, C.-A., Xia, D. Structural basis for the quinone reduction in the bc1 complex: a comparative analysis of crystal structures of mitochondrial cytochrome bc1 with bound substrate and inhibitors at the Qi site. *Biochemistry* **2003**, *4*, 9067-9080. (1NTZ)

X-ray crystal structure of Complex III with bound cytochrome c from: Solmaz, S.R., Hunte, C. Structure of complex III with bound cytochrome c in reduced state and definition of a minimal core interface for electrontransfer. *J. Biol. Chem.* **2008**, *283*, 17542-17549. (3CXH)

X-ray crystal structure of cytochrome c from: Enguita, F.J., Pohl, E., Turner, D.L., Santos, H., Carrondo, M.A. Structural evidence for a proton transfer pathway coupled with haem reduction of cytochrome c" from Methylophilus methylotrophus. *J. Biol. Inorg. Chem.* **2006** *11*, 189. (1OAE)

7.5: Complex IV

Complex IV is the final destination in the electron transport chain. Here, the electrons that have been travelling through the other members of the respiratory supercomplex are finally delivered to O_2, reducing it to water. That's an impressive feat, because a number of reactive oxygen species must be formed between the initial addition of an electron and the final release of water, but the reaction is controlled in such a way that the possibility of cell damage is minimised. At the same time, more protons are pumped across the inner mitochondrial membrane.

- In Complex IV, electrons are delivered to their final destination, a molecule of O_2.
- The O_2 is reduced to water.

Exercise 7.5.1

Write a balanced redox half-reaction to show how many electrons are needed to reduce an oxygen molecule to water.

Answer

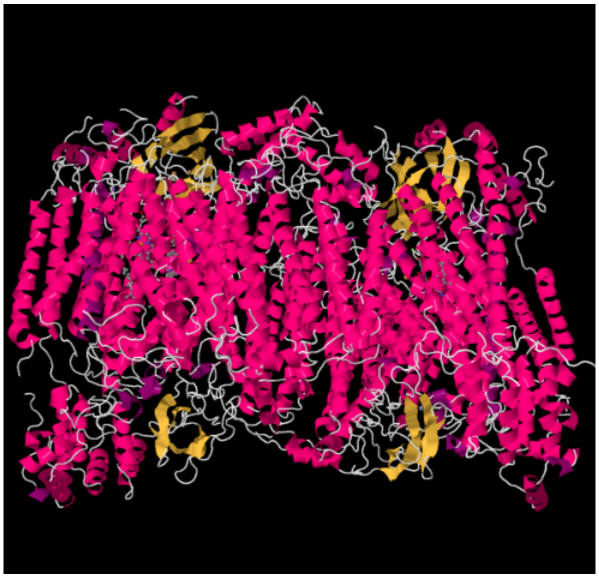
$O_2 \rightarrow H_2O$

$O_2 \rightarrow 2\ H_2O$ (O balanced)

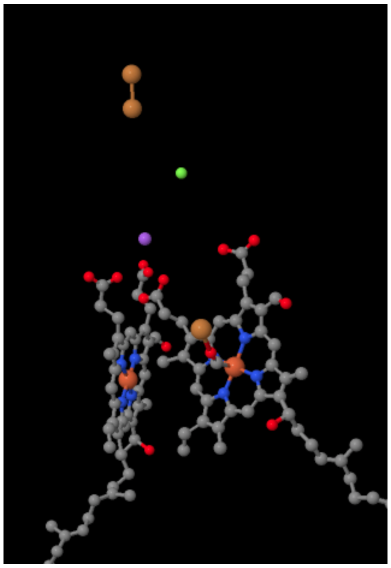
$O_2 + 4H^+ \rightarrow 2\ H_2O$ (H balanced)

$O_2 + 4e^- + 4H^+ \rightarrow 2\ H_2O$ (charge balanced)

The X-ray structure of Complex IV is shown below. Again, the matrix is at the lower end of the picture and the intermembrane space is at the top. That's where the cytochrome c docks, at the top.



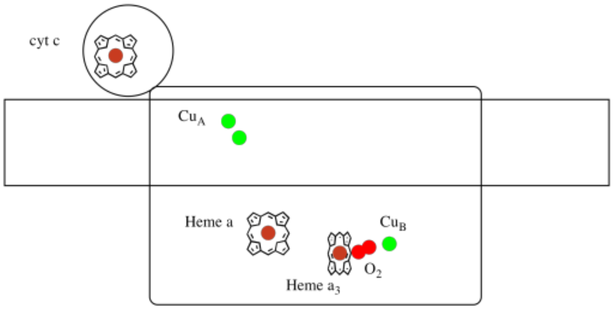
The mobile electron carrier, cytochrome c, binds at Complex IV and delivers an electron to a binuclear copper site called Cu_A. We can see that binuclear copper site when we look inside the protein, below. It is bound just to the protein and nothing else, so we just see the two copper ions on their own at the top of the picture. This pair of copper atoms sends the electron on to a heme, cytochrome a, which you can see below and to the left. From there, the electron proceeds to another binuclear cluster, this time consisting of a heme-bound iron (cytochrome a3) and a nearby copper (Cu_B). This binuclear site carries out the reduction of dioxygen to water. In the structure, there is a carbon monoxide molecule bound in the active site between cytochrome a3 and Cu_B. The carbon atoms is attached to the iron and the oxygen is attached to the copper. That's where the oxygen molecule would bind, waiting to be reduced to water.



If you think about that, it means that electrons are traveling in the opposite direction from what we saw in the first three complexes. In Complexes I and II, electrons were delivered from the mitochondrial matrix and traveled up toward the intermembrane space, stopping at a ubiquinone in the mitochondrial membrane. In Complex III, electrons continued in that "upward" direction, from the mitochondrial membrane to the cytochrome c in the intermembrane space. In Complex IV, electrons are reversing course, traveling back toward the mitochondrial matrix. Remember, the mitochondrial matrix is n-doped because of proton pumping, so these electrons are traveling from the positive side of the membrane to the negative side. That must be difficult.

- In Complex IV, electron transport is in the opposite direction from the other complexes.
- Electrons travel from the intermembrane space side to the mitochondrial matrix side, against the charge gradient.

Let's take another look at the important ligands for the complex. A cartoon is shown below. In the cartoon, the O_2 molecule is shown binding in that position between the heme a_3 and the Cu_B. That dinuclear metal site is where the oxygen molecule is reduced to water.

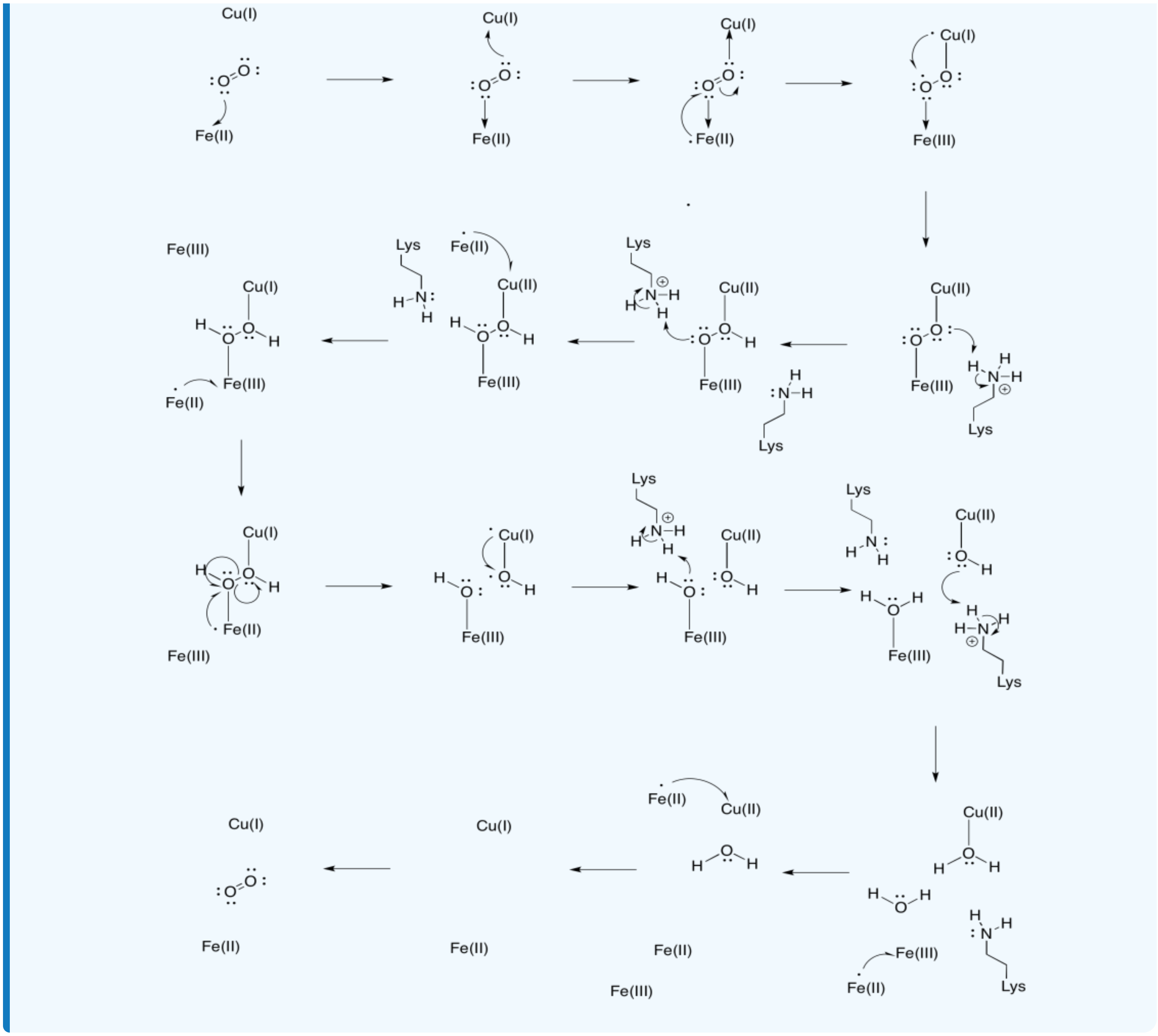


Because four electrons are needed to reduce O_2 to H_2O, four cytochrome c molecules must bind at Complex IV before that reduction can proceed. It is likely that the coordination environment of the oxygen molecule -- between two metals, rather than just bound to one -- allows it be be more rapidly reduced all the way to water rather than forming reactive oxygen species that persist in the cell, such as peroxides.

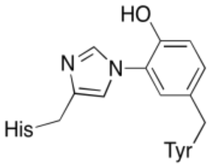
Exercise 7.5.2

Assume the iron in heme a3 starts in a reduced Fe(II) state and the CuB starts in a reduced Cu(I) state. Provide a mechanism for the reduction of oxygen to water, with the addition of four electrons and four protons. Use Fe(II) as the electron donor and lysine as the proton donor.

Answer



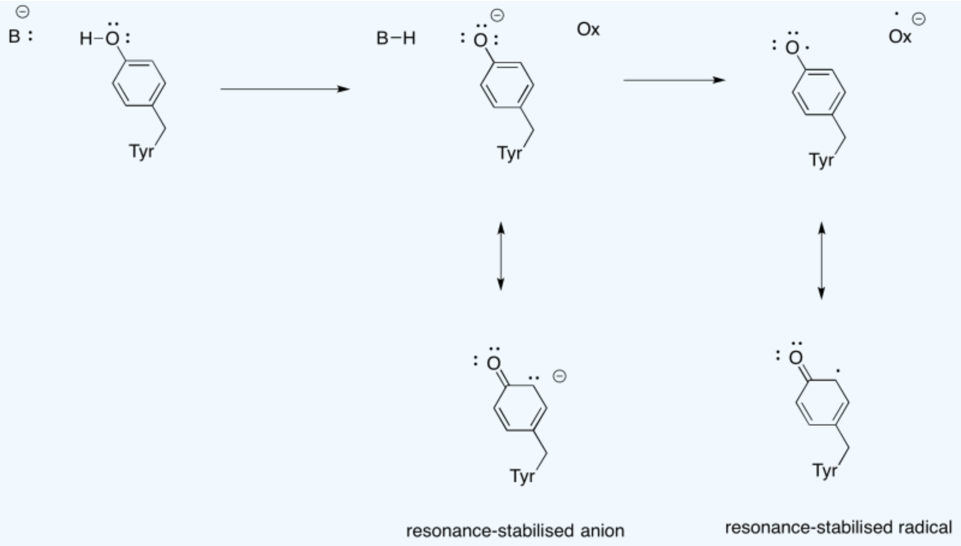
In addition to those two metals, there is also a modified histidine-tyrosine conjugate bound to CuB. It has been suggested that this tyrosine provides another source of immediate electrons that may be used in reduction.



Exercise 7.5.3

Show why a tyrosine can be a source of both a proton and an electron in biochemical processes.

Answer



In addition to the need to reduce oxygen to water, Complex IV also contributes to the proton gradient, pumping additional protons across the mitochondrial membrane. That task presents additional challenges. A simple coupling mechanism is not possible, because the electrons are moving in the opposite direction. It is though that the mechanism involves conformational changes in the protein that occur as the metals change oxidation states. Subtle changes in coordination environment may result in displacement of amino acid residues nearby. It is easy to imagine that if a particular amino acid shifts upward toward the intermembrane space, it may pull a proton with it.

- Proton pumping and electron transport run in opposite directions in Complex IV and must be uncoupled.
- Proton pumping in Complex IV must rely on conformational changes.

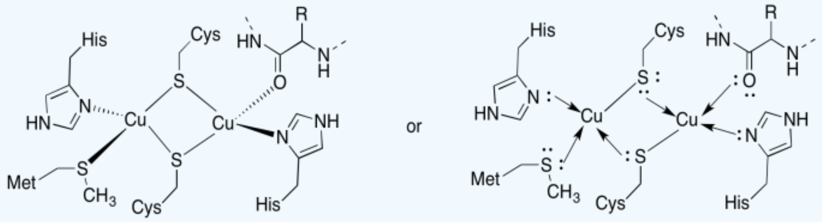
Exercise 7.5.4

The Cu_A site contains two coppers, boound by two bridging cysteines. Both are bound by terminal histidines. In addition, one copper is bound by an additional methionine, whereas the other is bound by a carbonyl from the protein backbone.

a. Draw the coppers in their binding sites.
b. Describe the geometry of each copper.
c. If each copper is Cu(I), what is the coordinated electron count on each copper in the complex?
d. If each copper is Cu(I), what is the overall charge on the complex?

Answer a

a)



Answer b

b) tetrahedral

Answer c

c) Cu(I) = d^{10}

4 donors = 8 e^-

total = 18e$^-$

Answer d

d) 2 x Cu(I) = 2^+

2 x Cys-S$^-$ = 2^-

All others neutral

Total = 0

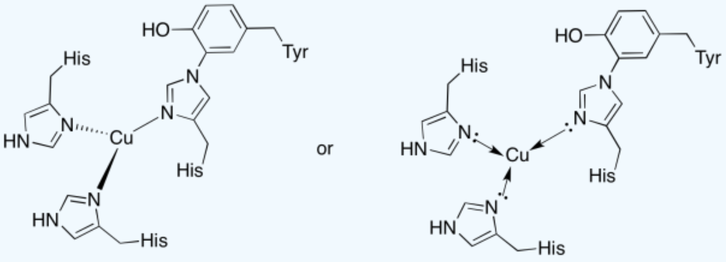
Exercise 7.5.5

The copper in the Cu$_B$ site is bound by two histidines and the histidine-tyrosine conjugate.

a. Draw the copper in the binding site.
b. Describe the geometry of the copper.
c. If copper is Cu(I), what is the coordinated electron count in the complex?
d. If copper is Cu(I), what is the overall charge on the complex?

Answer a

a)



Answer b

b) trigonal planar

Answer c

c) Cu(I) = d^{10}

3 donors = 6 e$^-$

total = 16 e$^-$

Answer d

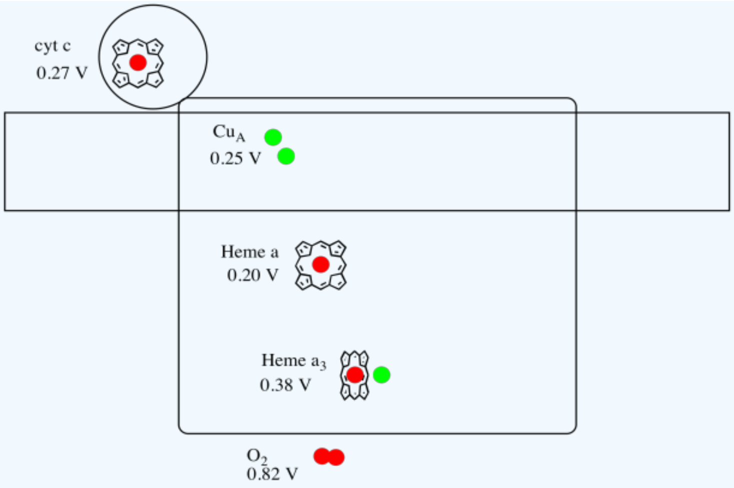
d) Cu(I) = 1^+

histidines neutral

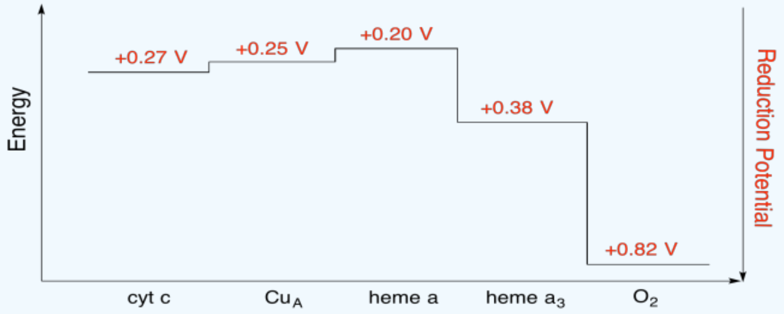
Total = 1^+

Exercise 7.5.6

It's difficult to measure the reduction potential of an individual site within a protein. However, researchers have been able to estimate these values by measuring EPR spectra under various conditions. Assuming the reduction potentials below, draw a reaction progress diagram for transport of an electron all the way from cytochrome c to molecular oxygen.



Answer



Exercise 7.5.7

Using the values in the figure above, calculate the energy change when an electron is transferred from heme a to heme a_3.

Answer

Assuming the reduction potentials are:

heme a(ox) + e^- → heme a(red) $E^o_{red} = 0.20$ V

heme a_3(ox) + e^- → heme a_3(red) $E^o_{red} = 0.38$ V

Then the potential difference for the reaction, $\Delta E^o = 0.38 - (0.20)$ V = 0.18 V.

The Faraday relation $\Delta G = - n\, F\, \Delta E^o$ gives

$\Delta G = - 1 \times 96{,}485\ \mathrm{J\ V^{-1}\ mol^{-1}} \times 0.13\ \mathrm{V} = 17{,}367\ \mathrm{J\ mol^{-1}} = 17.4\ \mathrm{kJ\ mol^{-1}}$

7.6: Complex V

Oxidative phosphorylation is a metabolic process in which energy is harnessed for the production of ATP. So far we have looked at the electrons transport chain,which is reponsible for the establishment of a proton gradient across the inner mitochondrial membrane. The actual synthesis of ATP occurs in complex V.

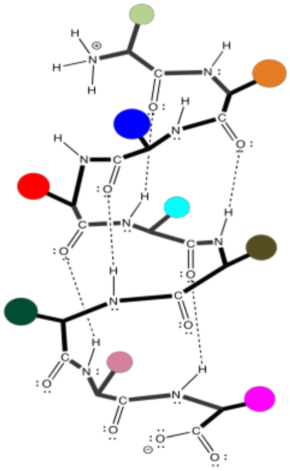
Complex V is very large and contains many different proteins. However, we will simplify the picture here. Schematically, Complex V consists of a proton channel leading from the intermembrane space into the matrix. As protons rush back through the membrane after having been pumped out along the electron transport chain, they cause rotation of a nanoscale millwheel. This millwheel helps bind ADP to phosphate, forming ATP.

- Rotation of a molecular rotor in Complex V helps bring an ADP and a phosphate together to form ATP.
- Rotation of the rotor is powered by protons dropping back through Complex V and into the mitochondiral matrix below.
- The intermembrane space is p-doped (excess positive charge) whereas the mitochondrial matrix is n-doped (excess negative charge), driving the flow of protons toward the mitochondrial matrix.
- For every three protons that drop through the complex, one ATP molecule is formed.

An X-ray crystal structure of Complex V is shown below. At the top of the picture, you can see the membrane-bound portion. Those α-helices run parallel to the fatty acid chains in the lipid layer, so that the protein fits snugly into the membrane. The lower part of the structure is the portion that extends into the matrix.

Exercise 7.6.1

Recall that in an α-helix, the amino acid residues project outward around the helix. Suggest some residues that are likely to be found along the membrane-bound portion of the complex.



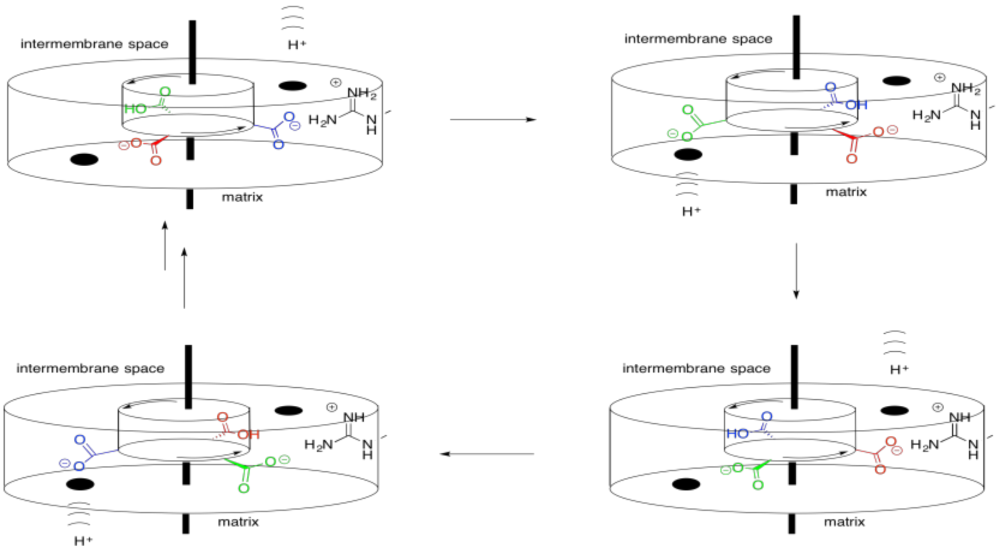
Answer

These amino acids would probably be non-polar: alanine, glycine, methionine, isoleucine, leucine, methionine, phenylalanine, tryptophan, valine.

Looking at the structure from underneath -- that is, from the vantage point of the matrix -- we can see the rotational symmetry of Complex V. Complex V contains a molecular rotor that is used in the manufacture of ATP. This rotor is made from a group of proteins that are able to move past another group of proteins as protons pass through the complex.

The mechanism of the rotor works something like an electric motor. The molecular engine contains two parts: a stationary part, or stator, and a rotating part, or rotor. The two parts have complementary charges. The stationary part has a positively charged arginine residue. The rotating part has a negatively charged aspartate residue. The aspartate residue is attracted to the arginine residue, causing the rotor to begin to rotate.

- The stator is the stationary part of a motor.
- The rotor is the revolving part of a motor.
- A temporary attraction draws a site on the rotor toward the stator.
- When that attraction is turned off, momentum carries that site on the rotor past the stator.



Of course, if that were the entire story, the aspartate (and the rotor) would stop moving when it got as close as possible to the arginine. That would be the end of the story. Instead, a proton arrives as it moves from the intermembrane space toward the matrix. It binds to the aspartate, rendering it neutral. No longer charged, the aspartate continues to move past the arginine.

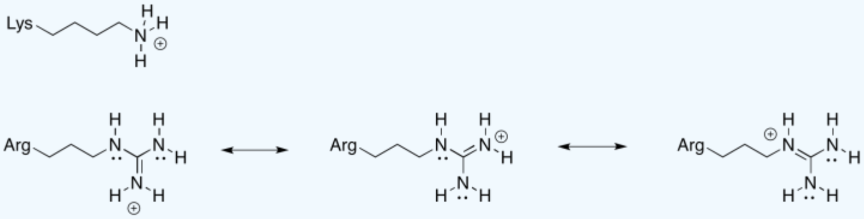
Meanwhile, another aspartate residue encounters the continuation of the proton channel that leads onward to the matrix. It releases its proton, becoming charged. It is then attracted to the arginine in the stator, continuing the rotation of the rotor.

Exercise 7.6.2

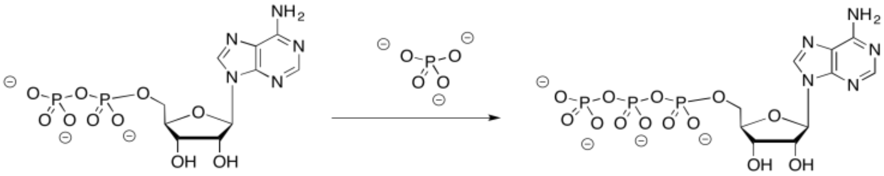
You could also imagine a lysine residue at the stator rather than the arginine shown above. Why is an arginine a more reliable positive stator than lysine?

Answer

There is always an equilibrium between the protonated state and the deprotonated state in a charged amino acid residue. For this position, an amino acid is needed that is more reliably in the protonated state; that is, the equilibrium lies more heavily to the protonated side of the equation. Because of the resonance-stabilised cation that results from protonation, arginine is much more likely to remain in a protonated state than lysine. That will make for a more efficient millwheel.



ADP and phosphate bind at the interface of two proteins along this assembly. The rotation apparently is involved in an approximation mechanism. During the conformational changes that result from the molecular rotation, the ADP and phosphate are brought close enough together that they are more likely to bind to each other, forming ATP.



Exercise 7.6.3

Why might it be difficult to bring ADP and phosphate together without this mechanism?

Answer

ADP and phosphate are both anions; they would repel normally each other. When bound in the active site, their charges are likely neutralized by complementary charges in the active site.

Exercise 7.6.4

Formation of an ATP from ADP costs about 30 kJ/mol. Assuming you could capture all of the energy released by transferring two electrons from NADH to O_2, how many units of ATP could be made?

Answer

Assuming the reduction potentials are:

$NAD^+ + 2e^- + 2\ H^+ \rightarrow NADH\ E^o_{red} = -0.32\ V$

$0.5\ O_2 + 2e- + 2\ H+ \rightarrow H_2O\ E^o_{red} = 0.816\ V$

Then the potential difference for the reaction, $\Delta E^o = 0.816 - (-0.32)\ V = 1.136\ V$.

The Faraday relation $\Delta G = -\ n\ F\ \Delta E^o$ gives

$\Delta G = -\ 2 \times 96{,}485\ J\ V^{-1}\ mol^{-1} \times 1.136\ V = 219{,}213\ J\ mol^{-1} = 219\ kJ\ mol^{-1}$

so $219\ kJ\ mol^{-1} / 30\ kJ\ mol^{-1} = 7.3$

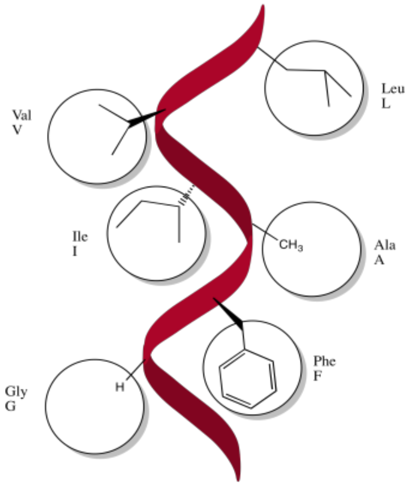
With 100% efficiency, 7 moles of ATP could be produced per mole of NADH. In reality, about half that amount is produced (closer to 3 moles ATP per mole NADH).

See the focus page on the structure of Complex V at Biochemistry Online.

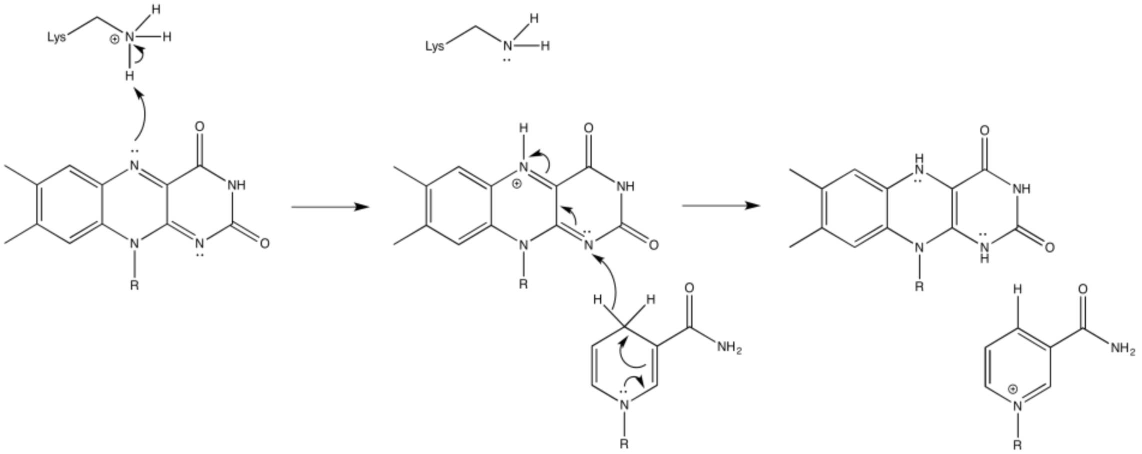
X-ray structures from: Watt, I.N., Montgomery, M.G., Runswick, M.J., Leslie, A.G.W., Walker, J.E. Bioenergetic cost of making an adenosine triphosphate molecule in animal mitochondria. *Proc.Natl.Acad.Sci.USA* **2010**, *107*, 16823. Images from RCSB Protein Data Bank (2XND).

7.7: Solutions for Selected Problems

Exercise 7.2.1:



Exercise 7.2.2:



Exercise 6.2.3:

a) Iron charges: $Fe(II) + Fe(III) = 5^{+}$

Ligand charges: $2\ sulfides\ = 2 \times 2^{-} = 4^{-}; 4\ cysteines\ = 4 \times 1^{-} = 4^{-};\ total\ = 8^{-}$

Overall: 3^{-}

b) Iron charges: $2 \times Fe(II) + Fe(III) = 4^{+} + 3^{+} = 7^{+}$

Ligand charges: $4\ sulfides\ = 4 \times 2^{-} = 8^{-}; 3\ cysteines\ = 3 \times 1^{-} = 3^{-};\ total\ = 11^{-}$

Overall: 4^{-}

c) Iron charges: $3 \times Fe(II) + Fe(III) = 6^{+} + 3^{+} = 9^{+}$

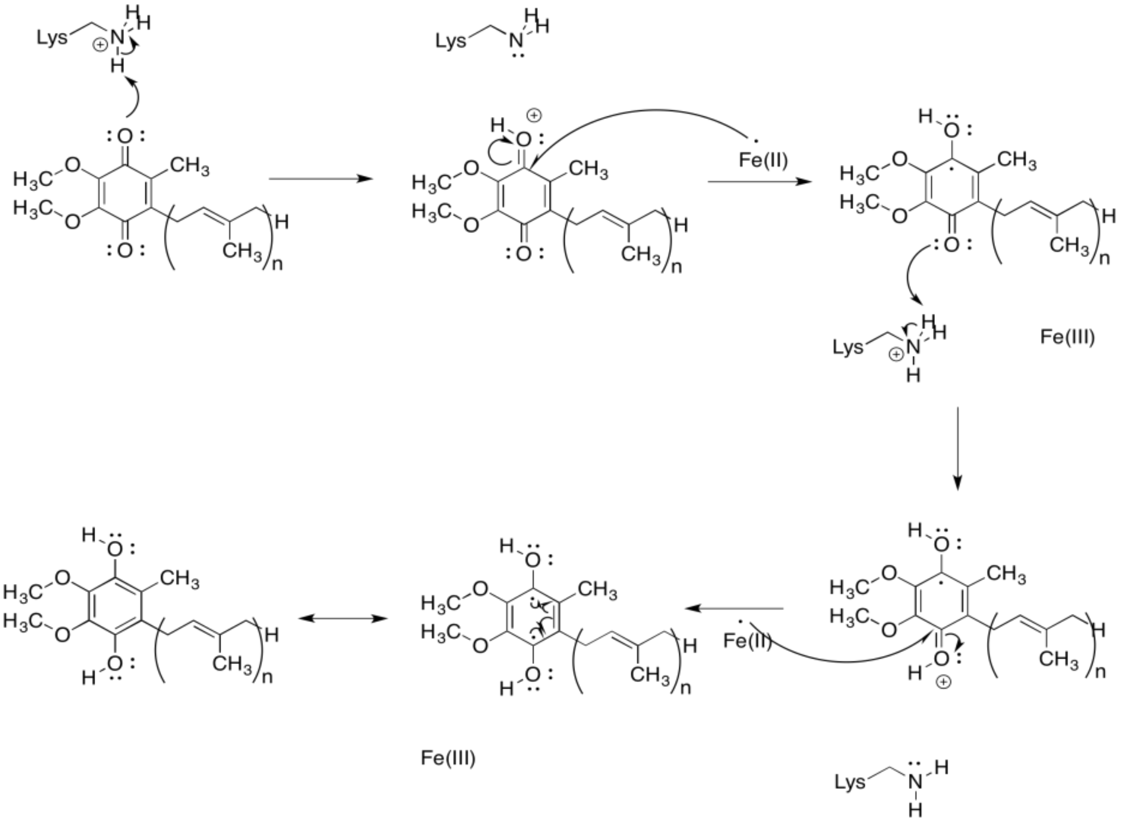
Ligand charges: $4\ sulfides\ = 4 \times 2^{-} = 8^{-}; 4\ cysteines\ = 4 \times 1^{-} = 4^{-};\ total\ = 12^{-}$

Overall: 3^{-}

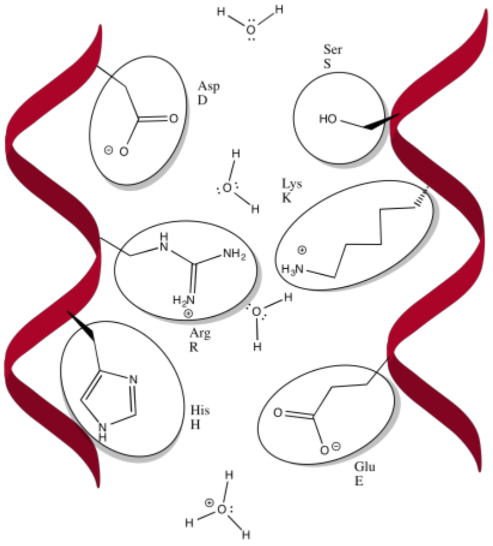
Exercise 7.2.4:

Upon reduction, the charge on a 2Fe2S cluster will increase from 3^{-} to 4^{-}, assuming it starts in a mixed Fe(II)/(III) state (whereas if it starts in a Fe(III)/(III) state, the overall charge will increase from 2^{-} to 3^{-}). These anions would be stabilised by strong intermolecular interactions such as ion-dipole forces. Both states (oxidised and reduced) will be stabilised by a polar environment, but the more highly charged reduced state will depend even more strongly on stabilisation by the environment. As a result, we might expect the reduction potential to be lower when surrounded by nonpolar amino acid residues, and higher if surrounded by polar residues.

Exercise 7.2.5:



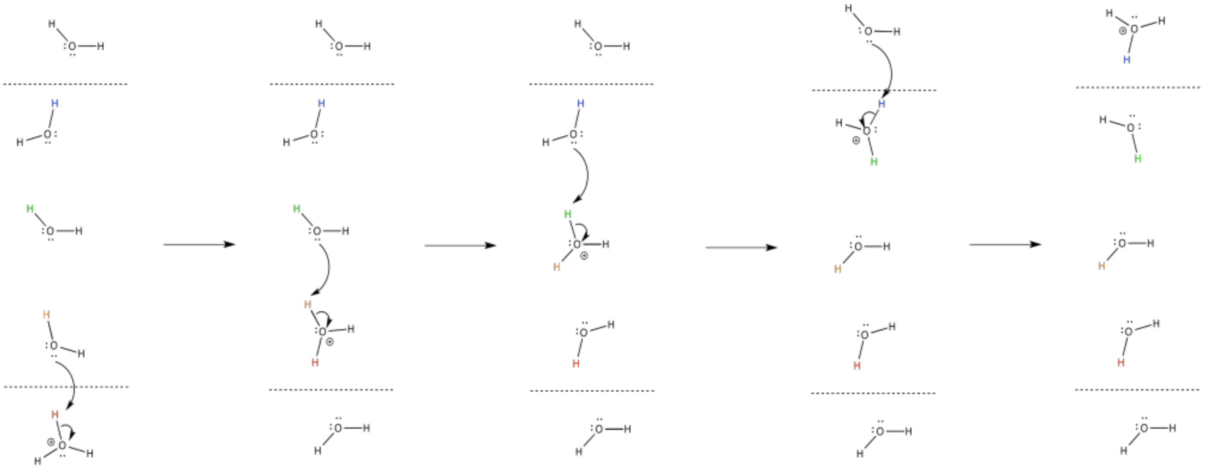
Exercise 7.2.6:



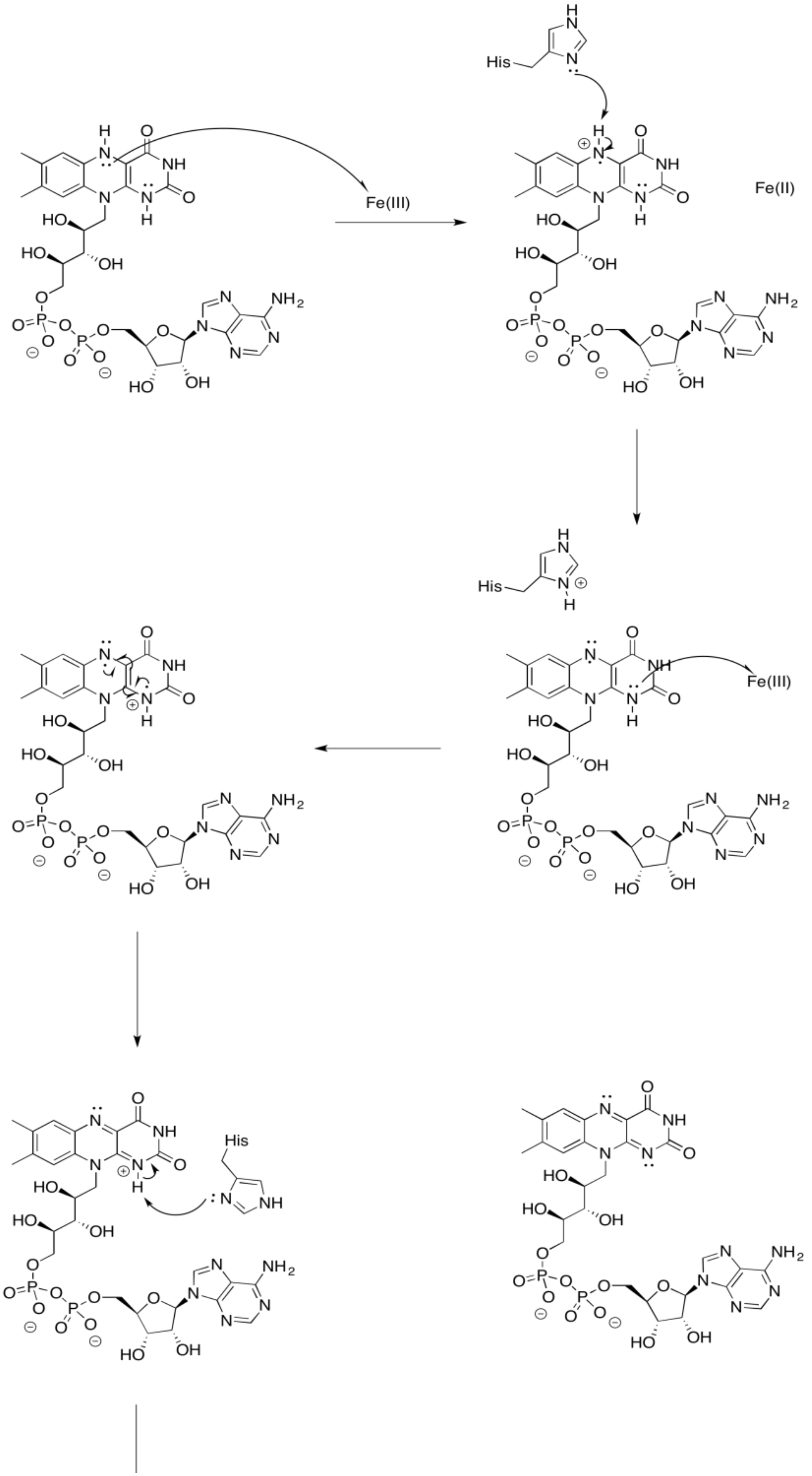
Other possibilities:

Thr T
Tyr Y
Gln Q
Asn N
Trp W
Cys C
Met M

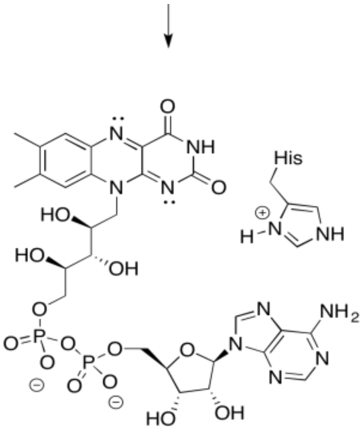
Exercise 7.2.7:



Exercise 7.2.8:



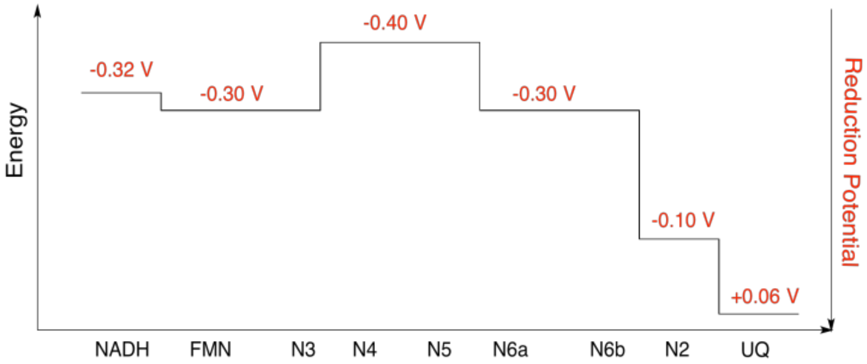
Fe(III)
His
Fe(II)
His
Fe(III)
His



<u>Exercise 7.2.9:</u>

a) N1a and N1b are most likely not involved, because their reduction potentials are too negative.

b)



<u>Exercise 7.2.10:</u>

Assuming the reduction potentials are:

$$N5(ox) + e^- \rightarrow N5(red) \backslash)\backslash(E^o_{red} = -0.40V$$

$$N6a(ox) + e^- \rightarrow N6a(red) \backslash)\backslash(E^o_{red} = -0.30V$$

Then the potential difference for the reaction, $\Delta E^o = -0.30 - (-0.40)V = 0.10V$

The Faraday relation $\Delta G = -nF\Delta E^o$ gives

$$\Delta G = -1 \times 96485 \frac{J}{V\ mol} \times 0.10V = 9649 \frac{J}{mol} = 9.7 \frac{kJ}{mol}$$

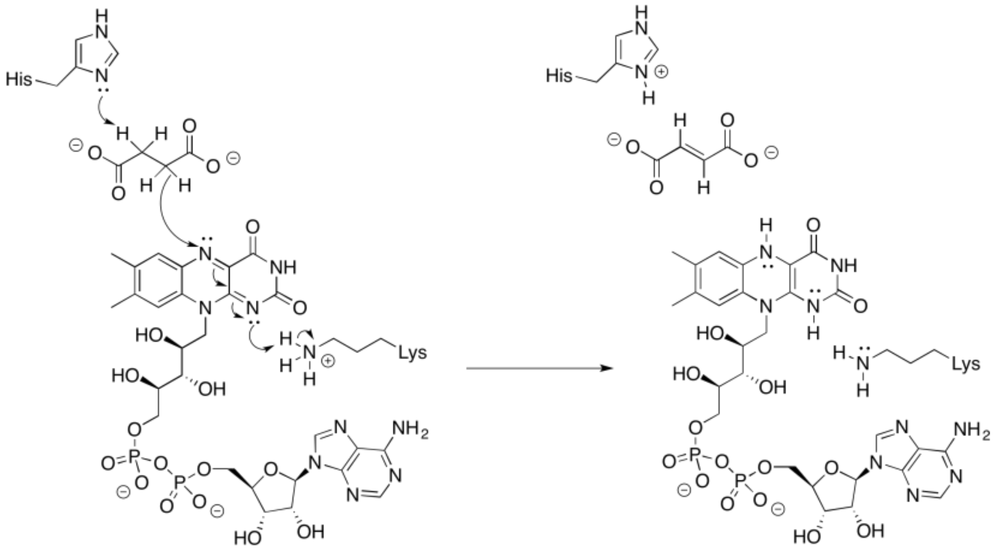
<u>Exercise 7.3.1:</u>

Heme b.

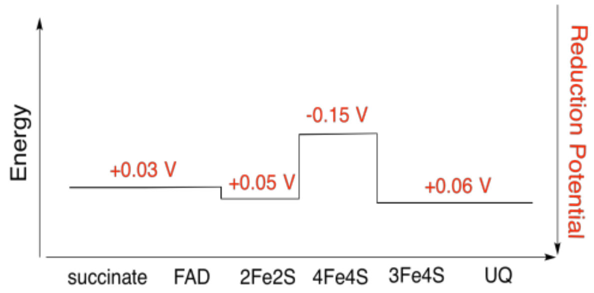
<u>Exercise 7.3.2:</u>

A porphyrin contains four pyrrole rings (five-membered, aromatic ring containing a nitrogen) arranged to form a 16-membered macrocycle.

<u>Exercise 7.3.3:</u>



Exercise 7.3.4:



Exercise 7.3.5:

Assuming the reduction potentials are:

$$4Fe4s(ox)+e^{-}\rightarrow 4Fe4S(red)\backslash)\backslash(E^{o}_{red}=-0.15V$$

$$3Fe4S(ox)+e^{-}\rightarrow 3Fe4S(red)\backslash)\backslash(E^{o}_{red}=0.06V$$

Then the potential difference for the reaction, $\Delta E^{o}=0.06-(-0.15)V=0.21V$

The Faraday relation $\Delta G=-nF\backslash\mathrm{Dleta}E^{o}$ gives

$$\Delta G=-1\times 96485\frac{J}{V\ mol}\times 0.21V=20262\frac{J}{mol}=20\frac{kJ}{mol}$$

Exercise 7.3.6:

a) Iron charges: $2\times Fe(III)=6^{+}$

Ligand charges: 2 $sulfides\ =2\times 2^{-}=4^{-};4\ cysteines\ =4\times 1^{-}=4^{-};\ total\ =8^{-}$

Overall: 2^{-}

b) Iron charges: $3\times Fe(III)=9^{+}$

Ligand charges: 4 $sulfides\ 4\times 2^{-}=8^{-};3\ cysteines\ =3\times 1^{-}=3^{-};\ total\ =11^{-}$

Overall: 2^{-}

c) Iron charges: $4\times Fe(III)=12^{+}$

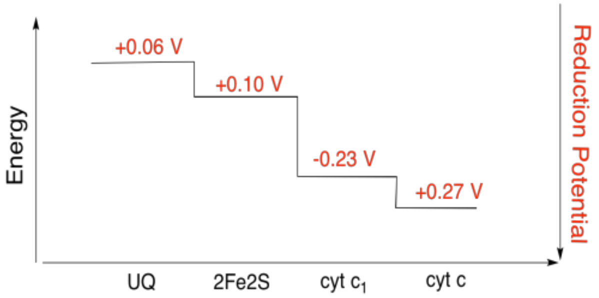
Ligand charges: 4 $sulfides=4\times 2^{-}=8^{-};4\ cysteines\ =4\times 1^{-}=4^{-};\ total\ =12^{-}$

Overall: 0

Exercise 7.4.1:

Arninine and lysine are positively charged at neutral pH.

Exercise 7.4.2:



Exercise 7.4.3:

Assuming the reduction potentials are:

$$2Fe2S(ox) + e^- \rightarrow 2Fe2S(red)\backslash)\backslash(E^o_{red} = 0.10V$$

$$cyt\ c_1(ox) + 3^- \rightarrow cyt\ c_1(red)\backslash)\backslash(E^o_{red} = 0.230V$$

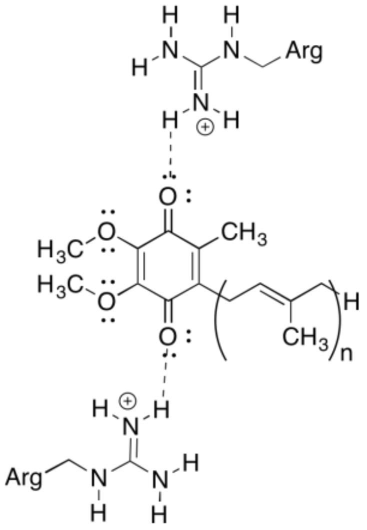
Then the potential difference for the reaction, $\Delta E^o = 0.23 - (0.10)V = 0.13V$

The Faraday relation $\Delta G = -nF\Delta E^o$ gives

$$\Delta G = -1 \times 96485 \frac{J}{V\ mol} \times 0.13V = 12543 \frac{J}{mol} = 12.5 \frac{kJ}{mol}$$

Exercise 7.4.4:

The positive arginine residues would confer partial positive charge on the ubiquinone via hydrogen bonding; the ubiquinone would have a more positive reduction potential as a result.



Exercise 7.5.1:

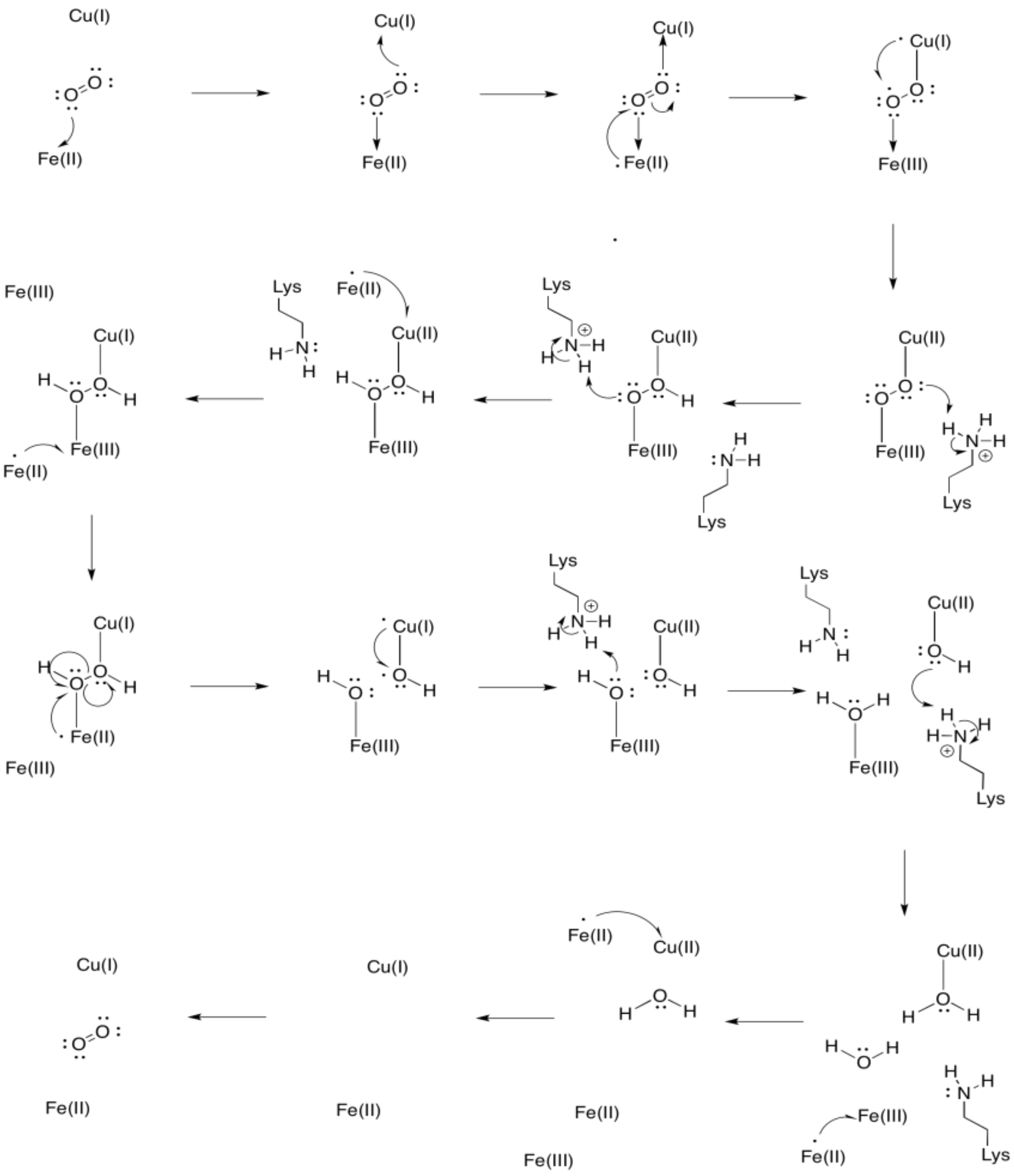
$$O_2 \longrightarrow H_2O$$

$O_2 \longrightarrow 2\,H_2O$ (O balanced)

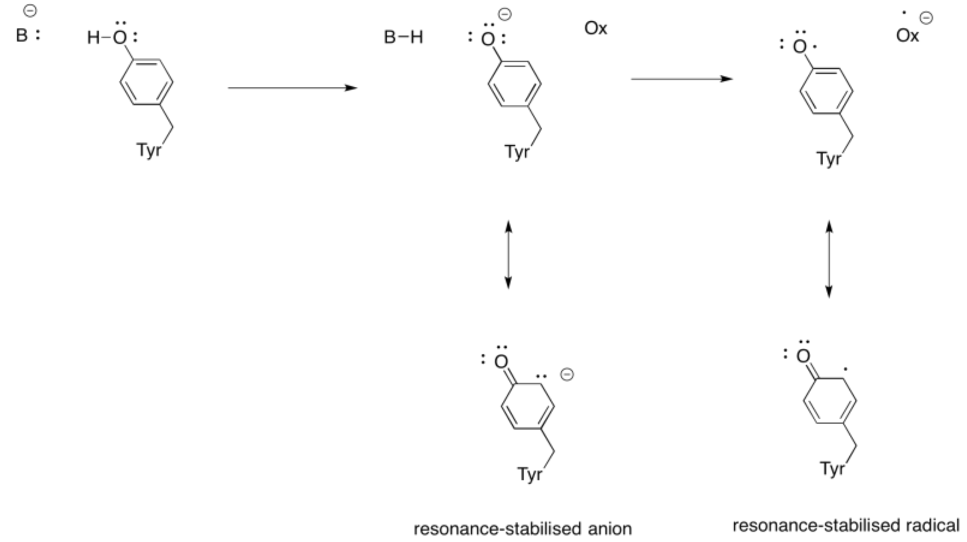
$O_2 + 4\,H^+ \longrightarrow 2\,H_2O$ (H balanced)

$O_2 + 4\,e^- + 4\,H^+ \longrightarrow 2\,H_2O$ (charge balanced)

Exercise 7.5.2:

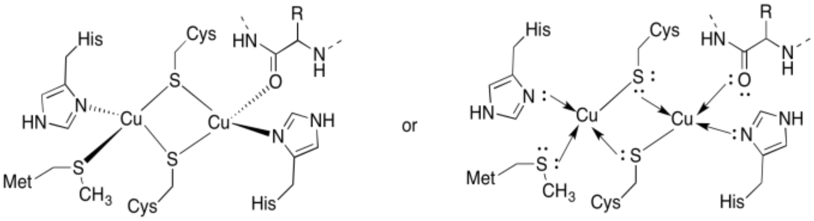


Exercise 7.5.3:



Exercise 7.5.4:

a)



b) tetrahedral

c) Cu(I) = d^{10}

4 donors = 8 e^-

total = $18e^-$

d) 2 x Cu(I) = 2^+

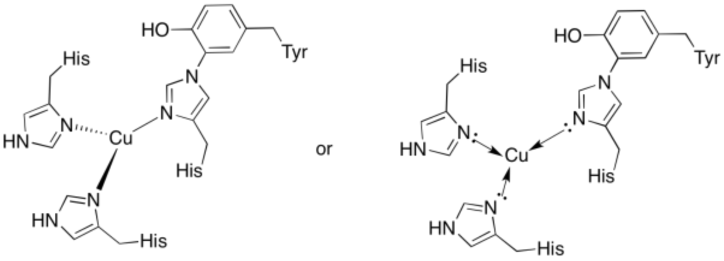
2 x Cys-S^- = 2^-

All others neutral

Total = 0

Exercise 7.5.5:

a)



) trigonal planar

c) Cu(I) = d^{10}

3 donors = 6 e^-

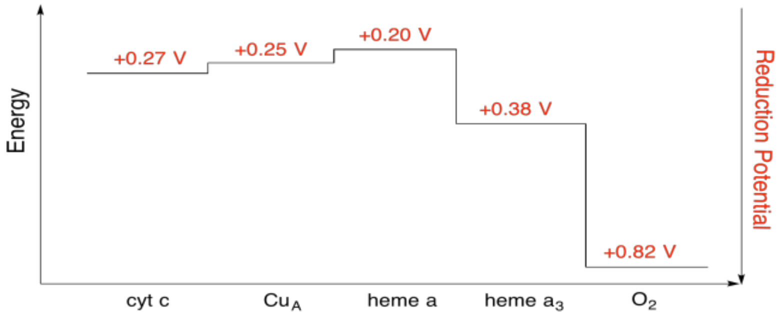
total = 16 e^-

d) Cu(I) = 1^+

histidines neutral

Total = 1^+

Exercise 7.5.6:



Exercise 7.5.7:

Assuming the reduction potentials are:

$$heme\ a(ox) + e^- \rightarrow heme\ a(red)\backslash)\backslash(E^o_{red} = 0.20V$$

$$heme\ a_3(ox) + e^- \rightarrow heme\ a_3(red)\backslash)\backslash(E^o_{red} = 0.38V$$

Then the potential difference for the reaction, $\Delta E^o = 0.38 - (0.20)V = 0.18V$

The Faraday relation $\Delta G = -nF\Delta E^o$ gives

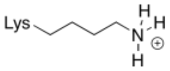
$$\Delta G = -1 \times 96485 \frac{J}{V\ mol} \times 0.13V = 17367 \frac{J}{mol} = 17.4 \frac{kJ}{mol}$$

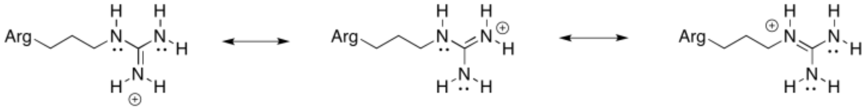
Exercise 7.6.1:

These amino acids would probably be non-polar: alanine, glycine, methionine, isoleucine, leucine, methionine, phenylalanine, tryptophan, valine.

Exercise 7.6.2:

There is always an equilibrium between the protonated state and the deprotonated state in a charged amino acid residue. For this position, an amino acid is needed that is more reliably in the protonated state; that is, the equilibrium lies more heavily to the protonated side of the equation. Because of the resonance-stabilised cation that results from protonation, arginine is much more likely to remain in a protonated state than lysine. That will make for a more efficient millwheel.





Exercise 7.6.3:

ADP and phosphate are both anions; they would repel normally each other. When bound in the active site, their charges are likely neutralized by complementary charges in the active site.

Exercise 7.6.4:

Assuming the reduction potentials are:

$$\mathrm{NAD^+} + 2\,\mathrm{e^-} + 2\,\mathrm{H^+} \longrightarrow \mathrm{NADH}\backslash)\backslash(E^o_{red} = -0.32V$$

$$0 \cdot 5\,\mathrm{O_2} + 2\,\mathrm{e^-} + 2\,\mathrm{H^+} \longrightarrow \mathrm{H_2O}\backslash)\backslash(E^o_{red} = 0.816V$$

Then the potential difference for the reaction, $\Delta E^o = 0.816 - (-0.32)V = 1.136V$

The Faraday relation $\Delta G = -NF\Delta E^o$ gives

$$\Delta G = -2 \times 96475 \frac{J}{V\ mol} \times 1.136V = 219213 \frac{J}{mol} = 219 \frac{kJ}{mol}$$

so $\frac{219 \frac{kJ}{mol}}{30 \frac{kJ}{mol}} = 7.3$

With 100% efficiency, 7 moles of ATP could be produced per mole of NADH. In reality, about half that amount is produced (closer to 3 moles ATP per mole NADH).

CHAPTER OVERVIEW

8: Photochemical Reactions

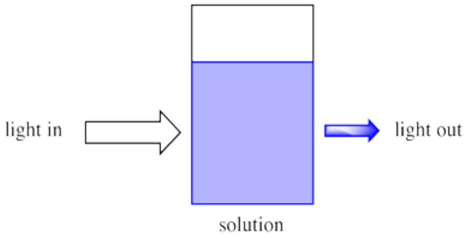
8.1: Absorbance

Let's think first about the interaction of light with matter.

We have all seen light shine on different objects. Some objects are shiny and some are matte or dull. Some objects are different colours. Light interacts with these objects in different ways. Sometimes, light goes straight through an object, such as a window or a piece of glass.

Because chemical reactions are frequently conducted in solution, we will think about light entering a solution.

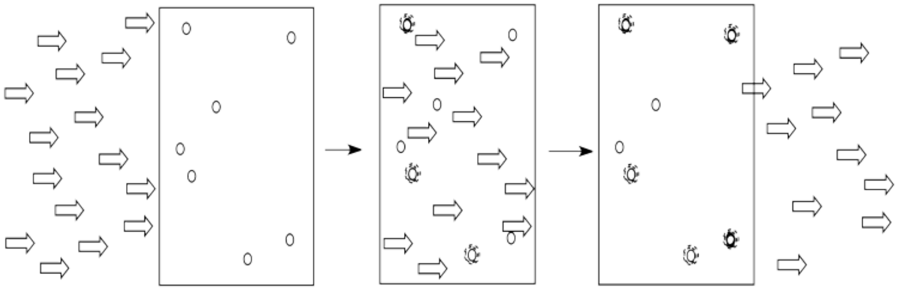
Imagine sunlight shining through a glass of soda. Maybe it is orange or grape soda; it is definitely coloured. We can see that as sunlight shines through the glass, coloured light comes out the other side. Also, less light comes out than goes in.



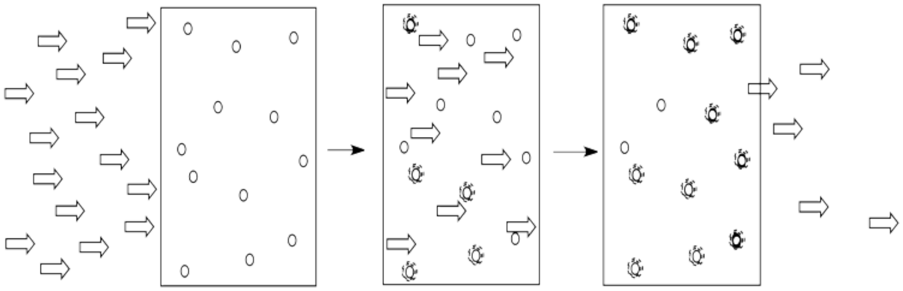
Maybe some of the light just bounces off the glass, but some of it is definitely absorbed by the soda.

So, what is the soda made of? Molecules. Some of these molecules are principally responsible for the colour of the soda. There are others, such as the ones responsible for the flavour or the fizziness of the drink, as well as plain old water molecules. The soda is a solution; it has lots of molecules (the solute) dissolved in a solvent (the water).

Light is composed of photons. As photons shine through the solution, some of the molecules catch the photons. They absorb the light. Generally, something in the molecule changes as a result. The molecule absorbs energy from the photon and is left in an excited state.

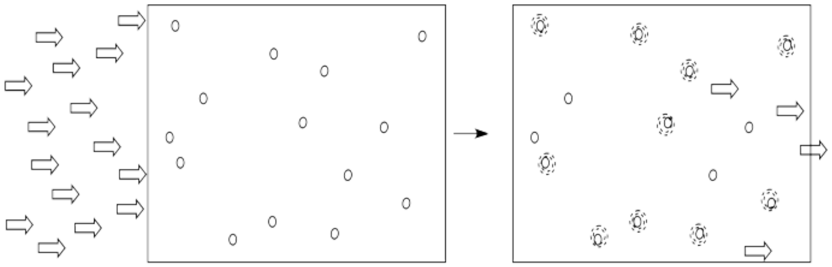


The more of these molecules there are in the solution, the more photons will be absorbed. If there are twice as many molecules in the path of the light, twice as many photons will be absorbed. If we double the concentration, we double the absorbance.



- The amount of light absorbed depends on the concentration of the solution.

Alternatively, if we kept the concentration of molecules the same, but doubled the length of the vessel through which the light traveled, it would have the same effect as doubling the concentration. Twice as much light would be absorbed.



- The absorbance depends on the length of cell holding the solution.

These two factors together make up part of a mathematical relationship, called Beer's Law, describing the absorption of light by a material:

$$A = \varepsilon c l$$

in which A = Absorbance, the percent of light absorbed; c = the concentration; l = the length of the light's path through the solution; ε = the "absorptivity" or "extinction coeficient" of the material, which is a measure of how easily it absorbs a photon that it encounters.

That last factor, ε, suggests that not all photons are absorbed easily, or that not all materials are able to absorb photons equally well. There are a couple of reasons for these differences.

Exercise 8.1.1

Calculate the absorbance in the following cases.

a. A sample with a molar absorptivity ε = 60 L $mol^{-1}cm^{-1}$ is diluted to a 0.01 mol L^{-1} solution in water and placed in a 1 cm cell.
b. A sample with a molar absorptivity ε = 3,000 L $mol^{-1}cm^{-1}$ is diluted to a 3.5 x 10^{-5} mol L^{-1} solution in water and placed in a 1 cm cell.
c. A sample with a molar absorptivity ε = 1.4 L $mol^{-1}cm^{-1}$ is diluted to a 0.25 mol L^{-1} solution in water and placed in a 0.5 cm cell.
d. A sample with a molar absorptivity ε = 23,000 L $mol^{-1}cm^{-1}$ is diluted to a 2.5 x 10^{-6} mol L^{-1} solution in water and placed in a 1 cm cell.
e. A sample with a molar absorptivity ε = 14,000 L $mol^{-1}cm^{-1}$ is diluted to a 0.015 mmol L^{-1} solution in water and placed in a 1 cm cell.

Answer a

a) A = ε c l = 60 L mol^{-1} cm^{-1} x 0.01 mol L^{-1} x 1 cm = 0.60 = 60 %

Answer b

b) A = ε c l = 3,000 L mol^{-1} cm^{-1} x 3.5 x 10^{-5} mol L^{-1} x 1 cm = 0.105 = 10.5 %

Answer c

c) A = ε c l = 1.4 L mol^{-1} cm^{-1} x 0.25 mol L^{-1} x 0.5 cm = 0.175 = 17.5 %

Answer d

d) A = ε c l = 23,000 L mol^{-1} cm^{-1} x 2.5 x 10^{-6} mol L^{-1} x 1 cm = 0.0575 = 5.75 %

Answer e

e) A = ε c l = 14,000 L mol^{-1} cm^{-1} x 0.015 mmol L^{-1} x 1 cm = 14,000 L mol^{-1} cm^{-1} x 0.015 x 10^{-3} mol L^{-1} x 1 cm = 0.21 = 21 %

Exercise 8.1.2

Calculate the extinction coefficient in the following cases.

a. 30% absorbance is observed with a 0.01 mol L^{-1} solution in a 1 cm cell.
b. 25% absorbance is observed with a 0.025 mol L^{-1} solution in a 1 cm cell.
c. 95% absorbance is observed with a 0.00175 mol L^{-1} solution in a 0.5 cm cell.
d. 66% absorbance is observed with a 0.025 mmol L^{-1} solution in a 1 cm cell.

Answer a

a) $\varepsilon = A / c\, l = 0.30 / (0.01 \text{ mol L}^{-1} \text{ x } 1 \text{ cm}) = 30 \text{ L mol}^{-1} \text{ cm}^{-1}$

Answer b

b) $\varepsilon = A / c\, l = 0.25 / (0.025 \text{ mol L}^{-1} \text{ x } 1 \text{ cm}) = 10 \text{ L mol}^{-1} \text{ cm}^{-1}$

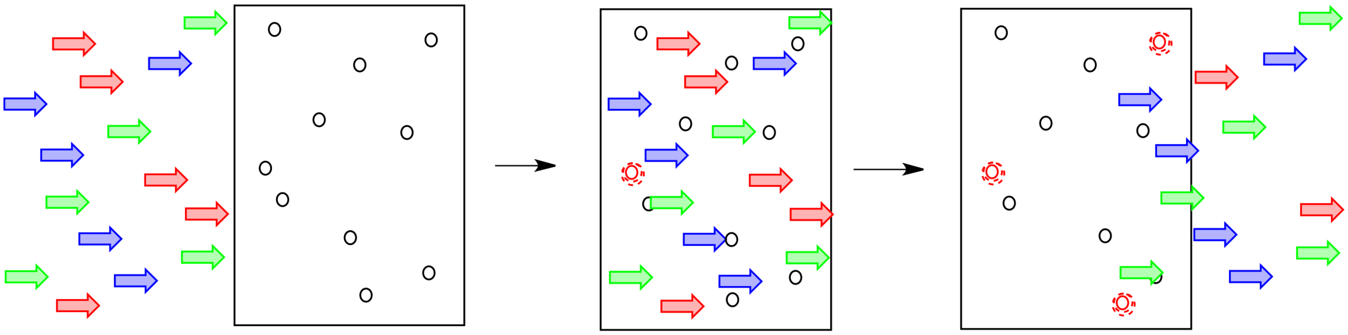
Answer c

c) $\varepsilon = A / c\, l = 0.30 / (0.01 \text{ mol L}^{-1} \text{ x } 1 \text{ cm}) = 543 \text{ L mol}^{-1} \text{ cm}^{-1}$

Answer d

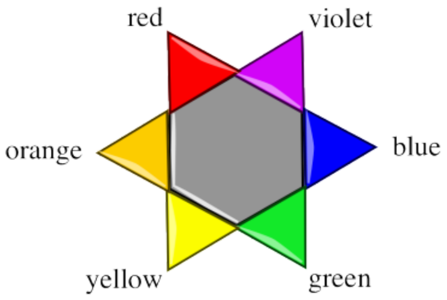
d) $\varepsilon = A / c\, l = 0.66 / (0.025 \text{ m mol L}^{-1} \text{ x } 1 \text{ cm}) = 0.66 / (0.025 \text{ x } 10^{-3} \text{ mol L}^{-1} \text{ x } 1 \text{ cm}) = 26{,}400 \text{ L mol}^{-1} \text{ cm}^{-1}$

Often a particular soda will absorb light of a particular colour. That means, only certain photons corresponding to a particular colour of light are absorbed by that particular soda.



How does that affect what we see? If the red light is being absorbed by the material, it isn't coming back out again. The blue and yellow light still are, though. That means the light coming out is less red, and more yellowy-blue. We see green light emerging from the glass.

A "colour wheel" or "colour star" can help us keep track of the idea of complementary colours. When a colour is absorbed on one side of the star, we see mostly the colour on the opposite side of the star.



Exercise 8.1.3

a. What colour of photon is probably most strongly absorbed by a glass of orange soda?
b. What colour of photon is most strongly absorbed by a glass of lime soda?
c. What colour of photon is most strongly absorbed by a glass of blue raspberry kool-aid?

d. What colour of photon is most strongly absorbed by a glass of pineapple soda?
e. What colour of photon is most strongly absorbed by a glass of cherry soda?

Answer a

a) blue

Answer b

b) red

Answer c

c) orange

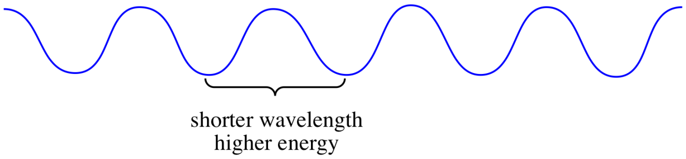
Answer d

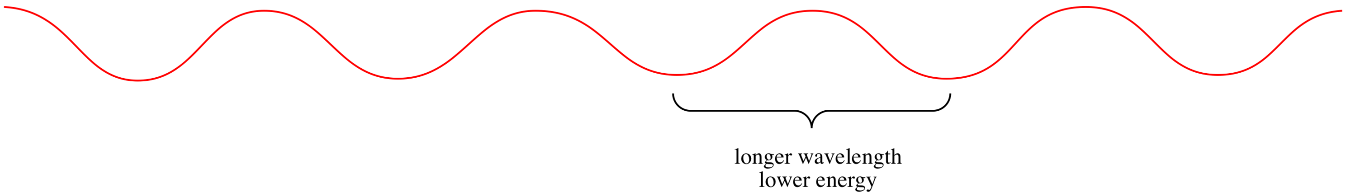
d) violet

Answer e

e) green

Why do certain materials absorb only certain colours of light? That has to do with the properties of photons. Photons have particle-wave duality, just like electrons. They have wave properties, including a wavelength.





That wavelength corresponds to the energy of a photon, according to the Planck-Einstein equation:

$$E = \frac{hc}{\lambda}$$

in which E = energy of the photon, h = Planck's constant (6.625 x 10^{-34} J s^{-1}), c = speed of light (3.0 x 10^{8} m s^{-1}), λ = wavelength of light in m.

Alternatively, the Planck-Einstien equation can be thought of in terms of frequency of thr photon: as a photon passes through an object, how frequently does one of its "crests" or "troughs" encounter the object? How frequently does one full wavelength of the photon pass an object? That parameter is inversely proportional to the wavelength. The equation becomes:

$$E = H\nu$$

in which ν = the frequency of the photon, in s^{-1}.

Exercise 8.1.4

a. Calculate the energy of a photon with a wavelength of 1 x 10^{-5} m.
b. Calculate the energy of a photon with a wavelength of 125 nm.
c. Calculate the energy of a photon with a wavelength of 1025 nm.
d. Calculate the energy of a photon with a wavelength of 450 μm.
e. Calculate the energy of a photon with a wavelength of 850 Å.

Answer a

a) $E = hc/\lambda = (6.625 \times 10^{-34}\ \text{Js mol}^{-1} \times 3.0 \times 10^{8}\ \text{m s}^{-1})/1 \times 10^{-5}\ \text{m} = 1.98 \times 10^{-20}\ \text{J}$

Answer b

b) $E = hc/\lambda = (6.625 \times 10^{-34}\ \text{Js mol}^{-1} \times 3.0 \times 10^{8}\ \text{m s}^{-1})/125 \times 10^{-9}\ \text{m} = 1.59 \times 10^{-18}\ \text{J}$

Answer c

c) $E = hc/\lambda = (6.625 \times 10^{-34}\ \text{Js mol}^{-1} \times 3.0 \times 10^{8}\ \text{m s}^{-1})/1025 \times 10^{-9}\ \text{m} = 1.94 \times 10^{-19}\ \text{J}$

Answer d

d) $E = hc/\lambda = (6.625 \times 10^{-34}\ \text{Js mol}^{-1} \times 3.0 \times 10^{8}\ \text{m s}^{-1})/450 \times 10^{-6}\ \text{m} = 4.42 \times 10^{-22}\ \text{J}$

Answer e

e) $E = hc/\lambda = (6.625 \times 10^{-34}\ \text{Js mol}^{-1} \times 3.0 \times 10^{8}\ \text{m s}^{-1})/850 \times 10^{--10}\ \text{m} = 2.3 \times 10^{-18}\ \text{J}$

Exercise 8.1.5

a. Calculate the wavelength of a 1.36×10^{-17} J photon.
b. Calculate the wavelength of a 4.72×10^{-24} J photon.
c. Calculate the wavelength of a 9.26×10^{-7} J photon.

Answer a

a) $\lambda = hc/E = (6.625 \times 10^{-34}\ \text{Js mol}^{-1} \times 3.0 \times 10^{8}\ \text{m s}^{-1})/1.46 \times 10^{--17}\ \text{J} = 1.36 \times 10^{-8}\ \text{m}$

Answer b

b) $\lambda = hc/E = (6.625 \times 10^{-34}\ \text{Js mol}^{-1} \times 3.0 \times 10^{8}\ \text{m s}^{-1})/4.72 \times 10^{--24}\ \text{J} = 4.21 \times 10^{-2}\ \text{m}$

Answer c

c) $\lambda = hc/E = (6.625 \times 10^{-34}\ \text{Js mol}^{-1} \times 3.0 \times 10^{8}\ \text{m s}^{-1})/9.26 \times 10^{--17}\ \text{J} = 2.15 \times 10^{-19}\ \text{m}$

Exercise 8.1.6

a. Calculate the wavelength of a photon with a frequency of $6.7 \times 10^{10}\ \text{s}^{-1}$.
b. Calculate the wavelength of a photon with a frequency of 1500 MHz.
c. Calculate the frequency of a photon with a wavelength of 9.8×10^{-10} m.
d. Calculate the frequency of a photon with a wavelength of 4.3×10^{-12} m.

Answer a

a) $E = h\nu = hc/\lambda$; so $\nu = c/\lambda$; or $\lambda = c/\nu = 3.0 \times 10^{8}\ \text{m s}^{-1}/6.7 \times 10^{10}\ \text{s}^{-1} = 4.48 \times 10^{-3}\ \text{m}$

Answer b

b) $\lambda = c/\nu = 3.0 \times 10^{8}\ \text{m s}^{-1}/1500 \times 10^{6}\ \text{s}^{-1} = 0.2\ \text{m}$

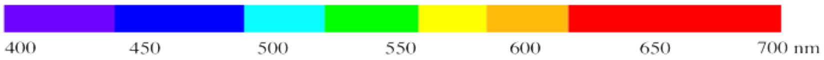
Answer c

c) $\nu = c/\lambda = 3.0 \times 10^{8}\ \text{m s}^{-1}/9.8 \times 10^{-10}\ \text{m} = 3.06 \times 10^{15}\ \text{s}^{-1}$

Answer d

d) $\nu = c/\lambda = 3.0 \times 10^{8}\ \text{m s}^{-1}/4.3 \times 10^{-12}\ \text{m} = 7.0 \times 10^{19}\ \text{s}^{-1}$

The visible spectrum, shown below, contains a very limited range of photon wavelengths, between about 400 and 700 nm.



The higher the frequency, the higher the energy of the photon. The longer the wavelength, the lower the energy of the photon.

As a result of this relationship, different photons have different amounts of energy, because different photons have different wavelengths.

Exercise 8.1.7

Different portions of the electromagnetic spectrum interact with matter in different ways. Because of that, we can use different wavelengths of light to gain different kinds of information about a material. Calculate the amount of energy involved in the following kinds of interactions, in units of kJ/mol.

a. Molecular bond rotations, measured by microwave spectroscopy. Suppose the microwave has a wavelength 1 mm long.
b. Bond stretching and bending, measured by infrared spectroscopy. Suppose the IR wavelength is 1,000 nm long.
c. Nuclear magnetic moments, measured by radio waves in NMR. Assume the radio wave is 1 m long.
d. The excitation of an electron from one energy level to another, measured by ultraviolet and visible spectroscopy. Assume the visible light's wavelength is 500 nm long.

Answer a

a) $E = h\,c / \lambda$

$E = (6.625 \text{ x } 10^{-34}\text{ J s mol}^{-1} \text{ x } 3.0 \text{ x } 10^{8}\text{ m s}^{-1})/ (1 \text{ mm x } 10^{-}3 \text{ m mm}^{-1}) = 1.99 \text{ x } 10^{-22}\text{ J}$

That's for one molecule. On a per mole basis, $E = 1.99 \text{ x } 10^{-22}\text{ J x } 6.02 \text{ x } 10^{23}\text{ mol}^{-1} = 120\text{ J mol}^{-1} = 0.12\text{ kJ mol}^{-1}$.

Answer b

b) $E = h\,c / \lambda$

$E = (6.625 \text{ x } 10^{-34}\text{ J s mol}^{-1} \text{ x } 3.0 \text{ x } 10^{8}\text{ m s}^{-1})/ (1000 \text{ nm x } 10^{-9}\text{ m nm}^{-1}) = 1.99 \text{ x } 10^{-19}\text{ J}$

That's for one molecule. On a per mole basis, $E = 1.99 \text{ x } 10^{-19}\text{ J x } 6.02 \text{ x } 10^{23}\text{ mol}^{-1} = 120{,}000\text{ J mol}^{-1} = 120\text{ kJ mol}^{-1}$.

Answer c

c) $E = h\,c / \lambda$

$E = (6.625 \text{ x } 10^{-34}\text{ J s mol}^{-1} \text{ x } 3.0 \text{ x } 10^{8}\text{ m s}^{-1})/ (1\text{ m}) = 1.99 \text{ x } 10^{-25}\text{ J}$

That's for one molecule. On a per mole basis, $E = 1.99 \text{ x } 10^{-25}\text{ J x } 6.02 \text{ x } 10^{23}\text{ mol}^{-1} = 0.120\text{ J mol}^{-1} = 1.2 \text{ x } 10^{-4}\text{ kJ mol}^{-1}$.

Answer d

d) $E = h\,c / \lambda$

$E = (6.625 \text{ x } 10^{-34}\text{ J s mol}^{-1} \text{ x } 3.0 \text{ x } 10^{8}\text{ m s}^{-1})/ (500 \text{ nm x } 10^{-9}\text{ m nm}^{-1}) = 3.98 \text{ x } 10^{-19}\text{ J}$

That's for one molecule. On a per mole basis, $E = 3.98 \text{ x } 10^{-19}\text{ J x } 6.02 \text{ x } 10^{23}\text{ mol}^{-1} = 239{,}000\text{ J mol}^{-1} = 239\text{ kJ mol}^{-1}$.

Exercise 8.1.8

The visible spectrum ranges from photons having wavelengths from about 400 nm to 700 nm. The former is the wavelength of violet light and the latter is the wavlength of red light. Which one has higher energy: a photon of blue light or a photon of red light?

Answer

Blue.

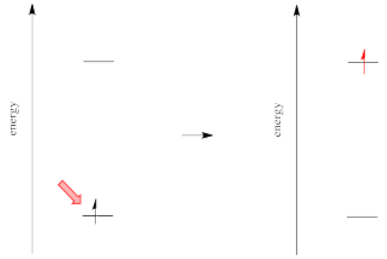
Exercise 8.1.9

Ultraviolet light -- invisible to humans and with wavelengths beyond that of violet light -- is associated with damage to skin; these are the cancer-causing rays from the sun. Explain their danger in terms of their relative energy.

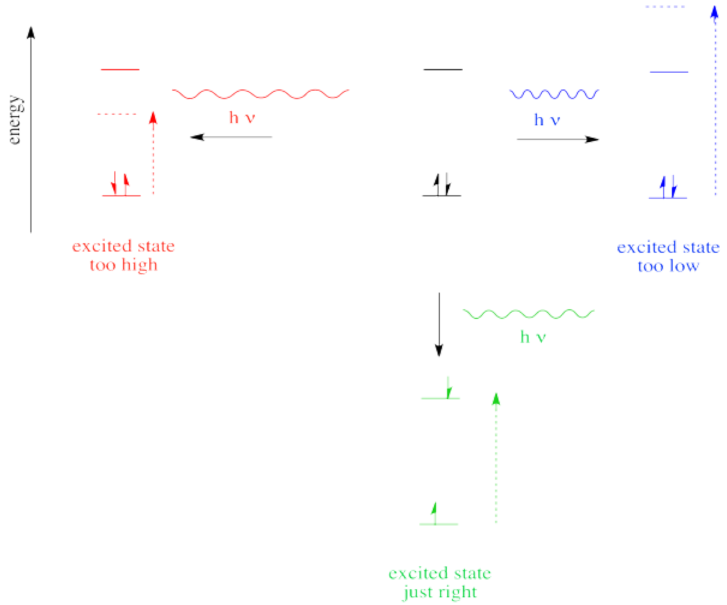
Answer

Ultraviolet light, with a shorter wavelength than visible light, is much higher in energy and potentially more damaging.

Different materials absorb photons of different wavelengths because absorption of a photon is an absorption of energy. Something must be done with that energy. In the case of ultraviolet and visible light, the energy is of the right general magnitude to excite an electron to a higher energy level.

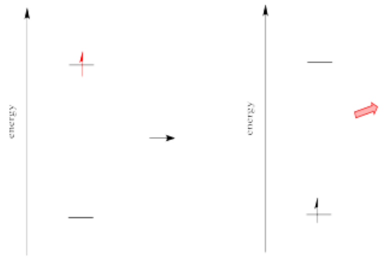


However, we know that energy is quantized. That means photons will be absorbed only if they have exactly the right amount of energy to promote an electron from its starting energy level to a higher one (producing an "excited state"). Just like Goldilocks, a photon with too much energy won't do the trick. Neither will a photon with too little. It has to be just right.



If the absorption of a UV-visible photon is coupled to the excitation of an electron, what happens when the electron falls back down to the ground state? You might expect a photon to be released.

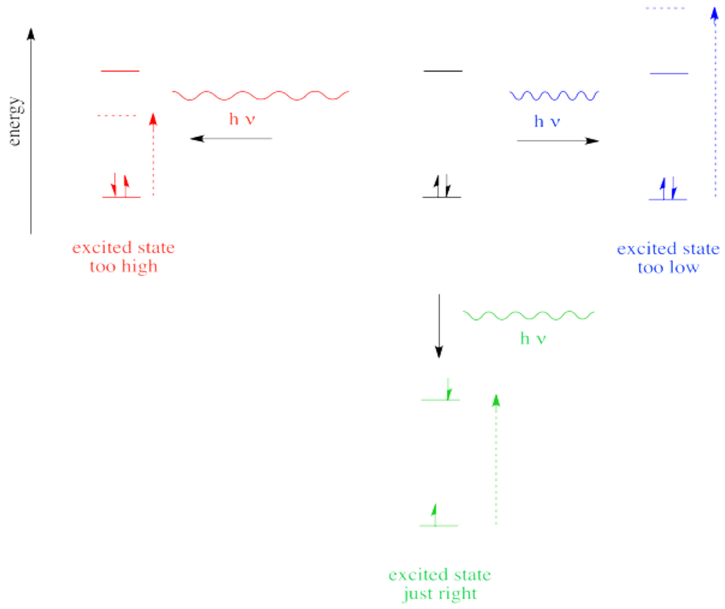
This phenomenon was observed during the late nineteenth century, when scientists studied the "emission spectra" of metal ions. In these studies, the metal ions would be heated in a flame, producing characteristic colours. In that event, the electron would be thermally promoted to a higher energy level, and when it relaxed, a photon would be emitted corresponding to the energy of relaxation.



By passing this light through a prism or grating, scientists could separate the observed colour into separate lines of different wavelengths. This evidence led directly to the idea of Niels Bohr and others that atoms had electrons in different energy levels, which is part of our view of electronic structure today.

8.2: Rules of Absorbance

So far, we have come across one big rule of photon absorbance. In order to be absorbed, a photon's energy has to match an energy difference within the compound that is absorbing it.



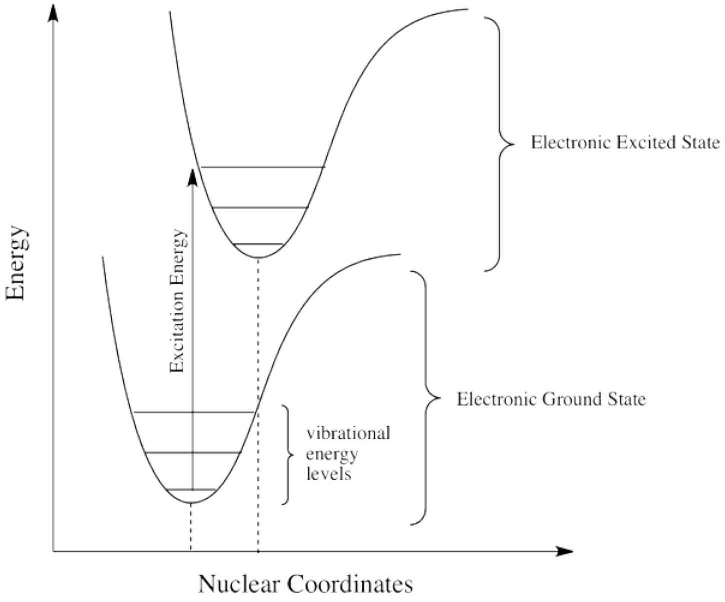
In the case of visible or ultraviolet light, the energy of a photon is roughly in the region that would be appropriate to promote an electron to a higher energy level. Different wavelengths would be able to promote different electrons, depending on the energy difference between an occupied electronic energy level and an unoccupied one.

Other types of electromagnetic radiation would not be able to promote an electron, but they would be coupled to other events. For example, absorption of infrared light is tied to vibrational energy levels. Microwave radiation is tied to rotational energy levels in molecules.

Thus, one reason a photon may or may not be absorbed has to do with whether its energy corresponds to the available energy differences within the molecule or ion that it encounters.

Franck-Condon: Electronic and Vibrational Coupling

Photons face other limitations. One of these is a moderate variation on our main rule. It is called the Frank Condon Principle. According to this idea, when an electron is excited from its normal position, the ground state, to a higher energy level, the optimal positions of atoms in the molecule may need to shift. Because electronic motion is much faster than nuclear motion, however, any shifting of atoms needed to optimize positions as they should be in the excited state will have to wait until after the electron gets excited. In that case, when the electron lands and the atoms aren't yet in their lowest energy positions for the excited state, the molecule will find itself in an excited vibrational state as well as an excited electronic state.



That means the required energy for excitation doesn't just correspond to the difference in electronic energy levels; it is fine-tuned to reach a vibrational energy level, which is quantized as well.

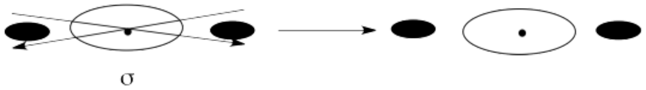
- The Franck Condon Principle states that electronic transitions are vertical.
- A vertical transition is one in which non of the nuclei move while the electron journeys from one state to another.
- A vertical transition may begin in a vibrational ground state of an electronic ground state and end in a vibrational excited state of an electronic excited state.

LaPorte: Orbital Symmetry

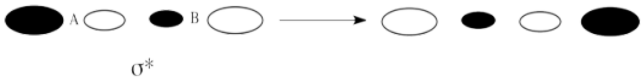
There are other restrictions on electronic excitation. Symmetry selection rules, for instance, state that the donor orbital (from which the electron comes) and the acceptor orbital (to which the electron is promoted) must have different symmetry. The reasons for this rule are based in the mathematics of quantum mechanics.

What constitutes the same symmetry vs. different symmetry is a little more complicated than we will get into here. Briefly, let's just look at one "symmetry element" and compare how two orbitals might differ with respect to that element.

If an orbital is centrosymmetric, one can imagine each point on the orbital reflecting through the very centre of the orbital to a point on the other side. At the end of the operation, the orbital appears unchanged. That means the orbital is symmetric with respect to a centre of inversion..



If we do the same thing with a sigma antibonding orbital, things turn out differently.



In the drawing, the locations of the atoms are labelled A and B, but the symmetry of the orbital itself doesn't depend on that. If we imagine sending each point on this orbital through the very centre to the other side, we arrive at a picture that looks exactly the opposite of what we started with.

These two orbitals have different symmetry. A transition from one to the other is allowed by symmetry.

Exercise 8.2.1

Decide whether each of the following orbitals is centrosymmetric.

a) an s orbital b) a p orbital c) a d orbital d) a π orbital e) a π* orbital

Exercise 8.2.2

Decide whether each of the following transitions would be allowed by symmetry.

a) π → π* b) p → π* c) p → σ* d) d → d

Symmetry selection rules are in reality more like "strong suggestions". They depend on the symmetry of the molecule remaining strictly static, but all kinds of distortions occur through molecular vibrations. Nevertheless, these rules influence the likelihood of a given transition. The likelihood of a transition, similarly, has an influence upon the extinction coefficient, ε.

transition	ε, extinction coefficient
π → π*	3,000 - 25,000 M^{-1} cm^{-1}
p → π*	20 - 150 M^{-1} cm^{-1}
p → σ*	100 - 7,000
d → π* (MLCT)	10,000 - 50,000 M^{-1} cm^{-1}
d → d	5 - 400 M^{-1} cm^{-1}

Exercise 8.2.1

Suggest the type of transition that is probably occurring in each case.

a. A Ti(III) complex absorbs at 377 nm with ε = 95 M^{-1} cm^{-1}.
b. A terpenoid ketone absorbs at 538 nm with ε = 11,500 M^{-1} cm^{-1}.
c. A Ru(II) compound absorbs at 444 nm with ε = 36,000 M^{-1} cm^{-1}.

Answer a

a) d → d

Answer b

b) π → π*

Answer c

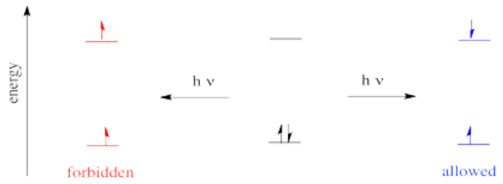
c) MLCT

Spin State

Let's take a quick look at one last rule about electronic emissions. This rule concerns the spin of the excited electron, or more correctly, the "spin state" of the excited species. The spin state describes the number of unpaired electrons in the molecule or ion.

number of unpaired electrons	spin state
0	singlet
1	doublet
2	triplet
3	quartet

The rule says that in an electronic transition, the spin state of the molecule must be preserved. That means if there are no unpaired electrons before the transition, then the excited species must also have no unpaired electrons. If there are two unpaired electrons before the transition, the excited state must also have two unpaired electrons.



That allowed diagram should looks strange to you. We are used to filling in electrons with spin paired for a good reason: we are following Hund's rule, that says the lowest energy state has any unpaired spins parallel, not opposite. In fact, the state on the left really is lower in energy than the state on the right; it's just that the electrons can't get from the middle state (the ground state) to the left state easily via absorption of a photon. However, they can get from the ground state to the state on the right pretty easily via photon absorption.

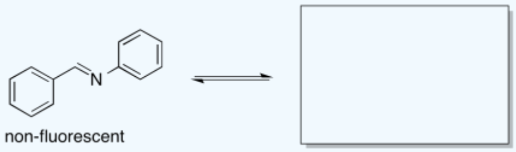
The state on the left is called a triplet state (the "multipicity" of the state is the number of parallel spins plus one). The state on the right is called the singlet state. The ground state is also a singlet state. Overall, we have a ground singlet state, an excited singlet state and an excited triplet state.

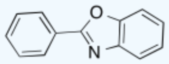
As it happens, because the excited triplet state is a little lower in energy than the excited singlet state, the electron can eventually relax into the excited triplet state. It can flip, without absorbing or releasing a photon. This even is called intersystem crossing. It is related to fluorescence and phosphorescence phenomena that we will look at next.

Exercise 8.2.4

Cis-trans isomerism of C=N bonds provides a path for rapid vibrational relaxation from excited states. Compounds containing this bond do not fluoresce because they are able to relax back to the ground state by transferring energy into rotational and vibrational states.

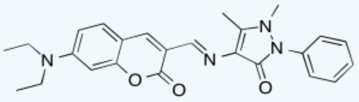
a) Illustrate this type of isomerism in the example below left.


non-fluorescent


fluorescent

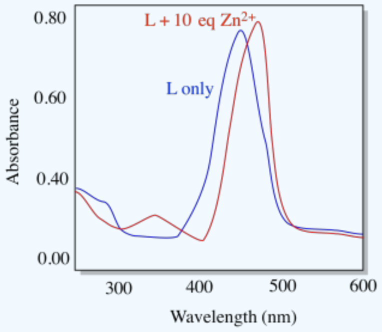
b) Some imines (above right) are strongly fluorescent. Explain the difference.

c) Would you predict the following compound, Compound L, to absorb UV-Vis light?


Compound **L**

d) Would you predict Compound L to be fluorescent?

Compound L shows the absorption spectrum below (conditions: [L] = 10^{-6} M; cell length = 1 cm).

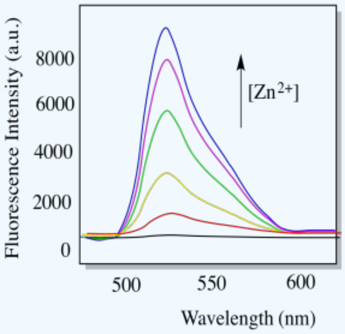


e) What is its approximate molar absorptivity at its λ_{max} (ϵ, M^{-1} cm^{-1})

f) Is this transition allowed or forbidden?

g) Identify the type of transition that is likely involved.

h) In the presence of zinc ion, compound L becomes strongly fluorescent (below). Explain why with a structure. (P.-F. Wang, Org. Lett. 2007, 9, 33-36)



i) Propose a practical application for compound L.

Answer b

b) The one on the left can relax by channelling some energy into molecular vibration, especially its *cis-trans* isomerisation. The one on the right can't do that because its rotation is restricted by the presence of the ring.

Answer c

c) Of course! It's crawling with pi bonds. A strong pi-pi* transition in the visible region seems likely.

Answer d

d) Probably not. It does not have restricted rotation, so the *cis-trans* isomerisation route is available for relaxation.

Answer e

e) $A = \varepsilon b c$, so $\varepsilon = A / b c = 0.77 / (1 \text{ cm} \times 10^{-6} \text{ M}) = 7.7 \times 10^{5} \text{ M}^{-1} \text{ cm}^{-1}$

Answer f

f) That's a large molar absorptivity constant. It's allowed.

Answer g

g) Undoubtedly this is that pi-pi* transition we were thinking about earlier.

Answer h

h) If the compound binds to zinc, it probably does so via bidentate coordination. The resulting ring restricts the degrees of freedom in the compound so it can't undergo cis-trans isomerisation, closing off a route to rapid relaxation.

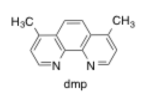
Answer i

i) A compound like this could be used to detect metal ions such as Zn^{2+}. Because the amount of fluorescence depends strongly on the Zn^{2+} concentration, it could be used to measure the amount of the ion present.

Exercise 8.2.5

Electron transfer between metal ions is a crucial event in a number of biochemical processes, such as oxidative phosphorylation and photosynthesis. It is thought that amino acid residues may help conduct electrons over the long distances between metals.

Harry Gray and co-workers have conducted studies of electron transfer in blue copper (azurin) proteins (J. Am. Chem. Soc. 2013, 135, 15515-15525). In the study, the protein is first tagged with [(dmp)Re(CO)3]+, which binds to a histidine residue.



a. Draw the Re complex bound to histidine. It forms the fac isomer. Make sure you draw the ligand structures.
b. This complex is orange. What colour does it absorb?

c. If you wanted to use a laser to get the complex into an excited state, what wavelength would you choose?

d. When pulsed with a laser, the compound undergoes metal-to-ligand charge transfer (MLCT).

i) Draw the d orbital splitting diagram for this complex in the ground state.

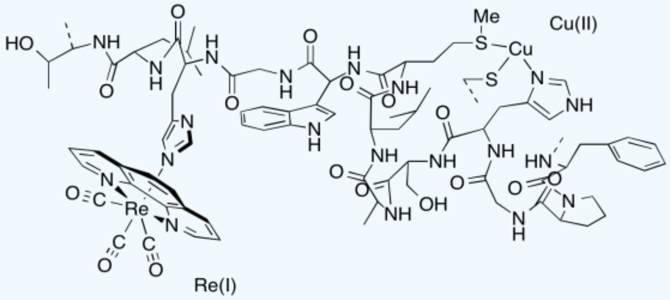
ii) Add to your diagram a ligand orbital for MLCT at an appropriate energy level. Label it (σ, π, n etc).

iii) Show the corresponding orbital diagram for the excited state.

iv) The complex now contains a "hole" (where an electron used to be). Circle it.

e) The complex undergoes intersystem crossing to the triplet state within a picosecond (10^{-12} s). Show this change.

Electron transfer ensues involving the Cu(I)/(II) site ($E^0 = 0.3$ V) and the Re complex ($E^0 = 1.4$ V). This reaction occurs within several nanoseconds (10^{-9} s).



f) A portion of the X-ray crystal structure of the Cu(II) form of the protein is shown above; the structure is assumed to be similar when Cu(I) is present. Draw an arrow showing the direction of electron transfer on the structure.

g) This ET reaction is conveniently monitored by IR spectroscopy, observing the carbonyl ligands on the Re complex.

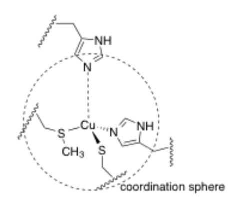
i) In what region of the IR spectrum would you observe these ligands?

ii) When electron transfer occurs, would the IR frequency shift to higher cm^{-1} or to lower cm^{-1}? Explain why.

iii) The Cu-Re distance is approximately 20 Angstroms. Does electron transfer probably occur via an outer sphere mechanism or an inner sphere one?

h) In site-directed mutagenesis studies, electron transfer did not occur in a W122F mutant; i.e. with W122 ($E^0 = 1.37$ V) replaced by F ($E^0 = 1.6$ V). Draw a mechanism for electron transfer in the native, tagged protein that incorporates this information.

i) The reduction potential of the blue copper (II / I) site varies among different forms of the protein, from about 200 mV to 1000 mV. It has been suggested that this value is influenced mostly by amino acid residues beyond the coordination sphere. Draw in two amino acid residues that would decrease the reduction potential, and briefly state how they would do so.



Afterword: In the Re experiment, the electron eventually goes back to where it came from, but not until several microseconds (10^{-6} s) have passed.

Answer b

b) An orange complex would absorb blue light, its complementary colour.

Answer c

c) A blue laser would work. Maybe somewhere around 476 nm.

Answer d

d) Notice a Re(II) site results, because it has transferred an electron to the ligand.

Answer f

f) The reduction potentials (1.4 V > 0.3 V) suggest transfer from copper (I) to rhenium (II).

Answer g

g) i) The carbonyl stretches would be observed somewhere around 2000 cm^{-1}.

ii) The electron transfer from the Cu(I) to the Re(II) site would result in a Re(I) site. The carbonyl stretch would shift to a lower wavenumber. That is because the lower oxidation state on the metal results in increased backbonding to the π-accepting carbonyls.

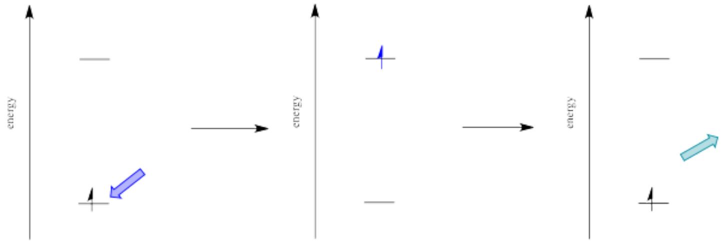
iii) At that distance, an outer sphere mechanism seems likely; it isn't clear how something could bridge that distance, other than the peptide chain itself, which probably lacks sufficient conjugation to conduct electrons.

Answer h

h) Tryptophan acts as a stepping stone between copper and rhenium. Phenylalanine, with a higher reduction potential than rhenium, does not.

8.3: Fluorescence and Phosphorescence

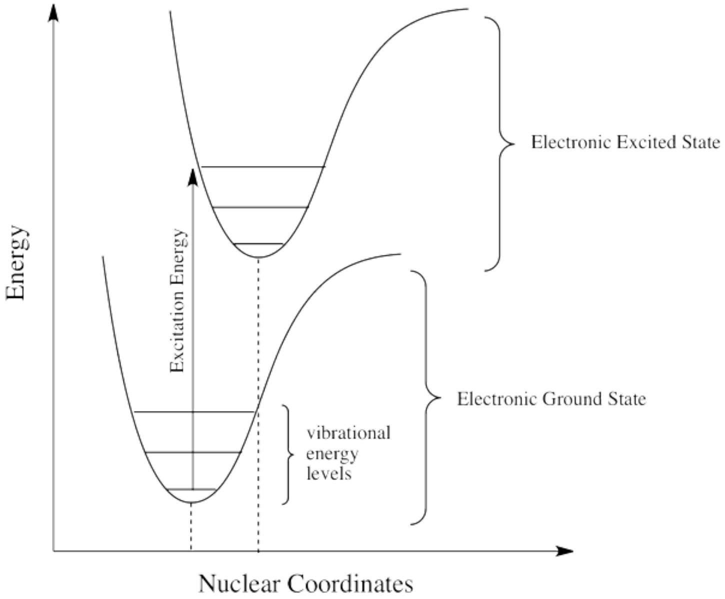
Sometimes, when an excited state species relaxes, giving off a photon, the wavelength of the photon is different from the one that initially led to excitation. When this happens, the photon is invariably red-shifted; its wavelength is longer than the initial one. This situation is called "fluorescence".



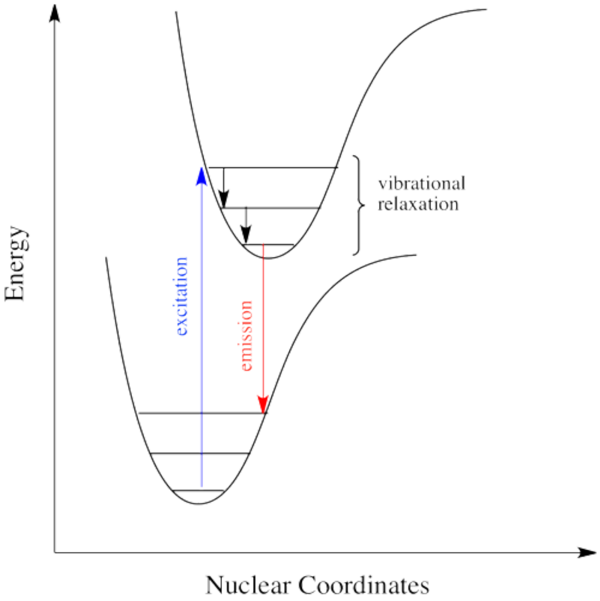
How can that be? Isn't energy quantized? How is the molecule suddenly taking a commission out of the energy the original photon brought with it?

Relaxation and Fluorescence

This discrepancy is related to the Franck-Condon principle from the previous page. When an electron is promoted to an electronic excited state, it often ends up in an excited vibrational state as well. Thus, some of the energy put into electronic excitation is immediately passed into vibrational energy. Vibrational energy, however, doesn't just travel in photons. It can be gained or lost through molecular collisions and heat transfer.



The electron might simply drop down again immediately; a photon would be emitted of exactly the same wavelength as the one that was previously absorbed. On the other hand, if the molecule relaxes into a lower vibrational state, some of that initial energy will have been lost as heat. When the electron relaxes, the distance back to the ground state is a little shorter. The photon that is emitted will have lower energy and longer wavelength than the initial one.



Just how does a molecule undergo vibrational relaxation? Vibrational energy is the energy used to lengthen or shorten bonds, or to widen or squeeze bond angles. Given a big enough molecule, some of this vibrational energy could be transferred into bond lengths and angles further away from the electronic transition. Otherwise, if the molecule is small, it may transfer some of its energy in collisions with other molecules.

There are lots of examples of energy being transferred this way in everyday life. In a game of pool, one billiard ball can transfer its energy to another, sending it toward the pocket. Barry Bonds can transfer a considerable amount of energy through his bat into a baseball, sending it out of the park, just as Serena Williams can send a whole lot of energy whizzing back at her sister. In curling, one stone can transfer its energy to another, sending it out of the house and giving Canada the gold over Sweden.

Exercise 8.3.1

How does the energy of an electronic absorption compare to other processes? To find out, you might consider the excitation of an entire mole of molecules, rather than a sinle molecule absorbing a single photon. Calculate the energy in kJ/mol for the following transitions.

a. absorbance at 180 nm (ultraviolet)
b. absorbance at 476 nm (blue)
c. absorbance at 645 nm (red)

Answer a

a) E = h c / λ

E = (6.625 x 10^{-34} J s mol^{-1} x 3.0 x 10^{8} m s^{-1})/ (180 nm x 10^{-9} m nm^{-1}) = 1.10 x 10^{-18} J

That's for one molecule. On a per mole basis, E = 1.10 x 10^{-18} J x 6.02 x 10^{23} mol^{-1} = 665,000 J mol^{-1} = 665 kJ mol^{-1}.

For comparison, the relatively strong and unreactive C-H bond in methane has a bond dissociation energy of only 440 kJ mol^{-1}. (That's a thermodynamic value; to actually break the bond would cost more input of energy, to get over the kinetic energy barrier for bond cleavage.)

Answer b

b) E = h c / λ

E = (6.625 x 10^{-34} J s mol^{-1} x 3.0 x 10^{8} m s^{-1})/ (476 nm x 10^{-9} m nm^{-1}) = 4.17 x 10^{-19} J

That's for one molecule. On a per mole basis, E = 4.42 x 10^{-19} J x 6.02 x 10^{23} mol^{-1} = 251,000 J mol^{-1} = 251 kJ mol^{-1}.

Answer c

c) E = h c / λ

E = (6.625 x 10^{-34} J s mol^{-1} x 3.0 x 10^{8} m s^{-1})/ (645 nm x 10^{-9} m nm^{-1}) = 3.08 x 10^{-19} J

That's for one molecule. On a per mole basis, E = 3.08 x 10^{-19} J x 6.02 x 10^{23} mol^{-1} = 138,000 J mol^{-1} = 138 kJ mol^{-1}.

Exercise 8.3.2

How does the energy of an excitation between vibrational states compare to that of an electronic excitation? Typically, infrared absorptions are reported in cm-1, which is simply what it looks like: the reciprocal of the wavelength in cm. Because wavelength and frequency are inversely related, wavenumbers are considered a frequency unit. Calculate the energy in kJ/mol for the following transitions.

a. absorbance at 3105 cm^{-1}
b. absorbance at 1695 cm^{-1}
c. absorbance at 963 cm^{-1}

Answer a

a) λ = 1 / wavenumber = 1 / 3105 cm^{-1} = 3.22 x 10^{-4} cm x 0.01 m cm^{-1} = 3.22 x 10^{-6} m

E = *h* c / λ

E = (6.625 x 10^{-34} J s mol^{-1} x 3.0 x 10^{8} m s^{-1})/ (3.22 x 10^{-6} m) = 6.17 x 10^{-20} J

That's for one molecule. On a per mole basis, E = 6.17 x 10^{-20} J x 6.02 x 10^{23} mol^{-1} = 37,000 J mol^{-1} = 37 kJ mol^{-1}.

Answer b

b) λ = 1 / wavenumber = 1 / 1695 cm^{-1} = 5.90 x 10^{-4} cm x 0.01 m cm^{-1} = 5.90 x 10^{-6} m

E = *h* c / λ

E = (6.625 x 10^{-34} J s mol^{-1} x 3.0 x 10^{8} m s^{-1})/ (3.22 x 10^{-6} m) = 3.37 x 10^{-20} J

That's for one molecule. On a per mole basis, E = 3.37 x 10^{-20} J x 6.02 x 10^{23} mol^{-1} = 20,000 J mol^{-1} = 20 kJ mol^{-1}.

Answer c

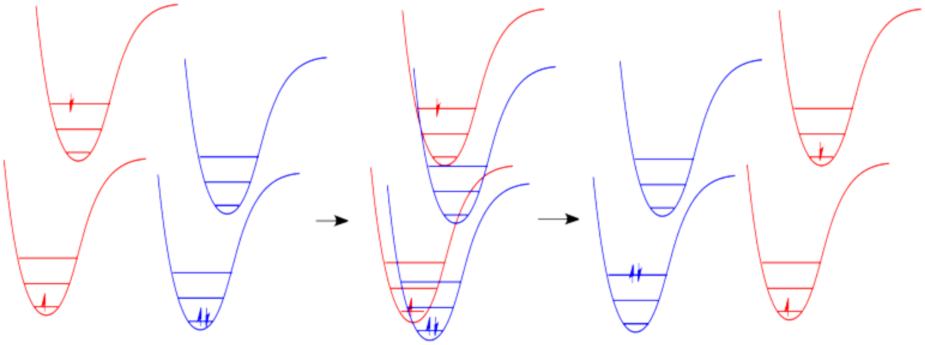
c) λ = 1 / wavenumber = 1 / 963 cm^{-1} = 1.04 x 10^{-3} cm x 0.01 m cm^{-1} = 1.04 x 10^{-5} m

E = *h* c / λ

E = (6.625 x 10^{-34} J s mol^{-1} x 3.0 x 10^{8} m s^{-1})/ (1.04 x 10^{-5} m) = 1.91 x 10^{-20} J

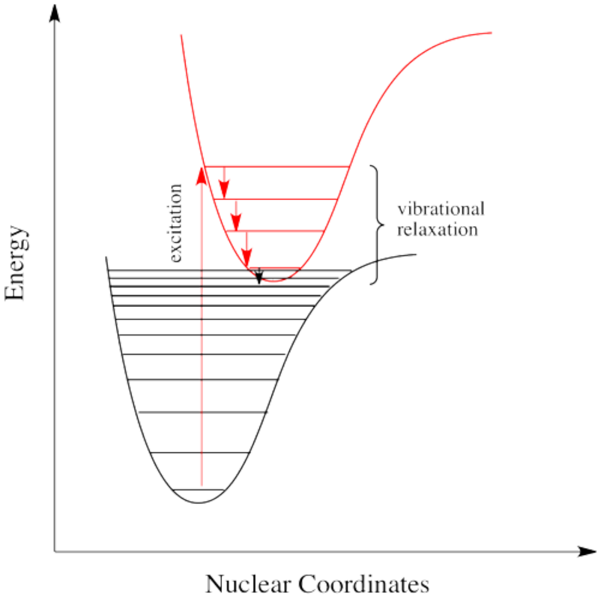
That's for one molecule. On a per mole basis, E = 1.91 x 10^{-20} J x 6.02 x 10^{23} mol^{-1} = 11,500 J mol^{-1} = 11.5 kJ mol^{-1}.

In molecules, as one molecule drops to a lower vibrational state, the other will hop up to a higher vibrational state with the energy it gains. In the drawing below, the red molecule is in an electronic excited and vibrational state. In a collision, it transfers some of its vibrational energy to the blue molecule.



Radiationless Transitions: Internal Conversion

If electrons can get to a lower energy state, and give off a little energy at a time, by hopping down to lower and lower vibrational levels, do they need to give off a giant photon at all? Maybe they can relax all the way down to the ground state via vibrational relaxation. That is certainly the case. Given lots of vibrational energy levels, and an excited state that is low enough in energy so that some of its lower vibrational levels overlap with some of the higher vibrational levels of the ground state, the electron can hop over from one state to the other, without releasing a photon.



This event is called a "radiationless transition", because it occurs without release of a photon. The electron simply slides over from a low vibrational state of the excited electronic state to a high vibrational state of the electronic ground state. We will see a couple of iinds of radiationless transitions. Specifically, if the electron simply keeps dropping a vibrational level at a time back to the ground state, the process is called "internal conversion".

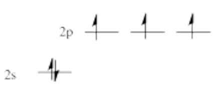
Internal conversion has an important consequence. Because the absorption of UV and visible light can result in energy transfer into vibrational states, much of the energy that is absorbed from these sources is converted into heat. That can be a good thing if you happen to be a marine iguana trying to warm up in the sun after a plunge in the icy Pacific. It can also be a tricky thing if you are a process chemist trying to scale up a photochemical reaction for commercial production of a pharmaceutical, because you have to make sure the system has adequate cooling available.

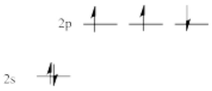
Radiationless Transitions: Intersystem Crossing

There is a very similar event, called "intersystem crossing", that leads to the electron getting caught between the excited state and the ground state. Just as, little by little, vibrational relaxation can lead the electron back onto the ground state energy surface, it can also lead the electron into states that are intermediate in energy.

For example, suppose an organic molecule undergoes electronic excitation. Generally, organic molecules have no unpaired electrons. Their ground states are singlet states. According to one of our selection rules for electronic excitation, the excited state must also have no unpaired electrons. In other words, the spin on the electron that gets excited is the same after excitation as it was before excitation.

However, that's not the lowest possible energy state for that electron. When we think about atomic orbital filling, there is a rule that governs the spin on the electrons in degenerate orbitals: in the lowest energy state, spin is maximized. In other words, when we draw a picture of the valence electron configuration of nitrogen, we show nitrogen's three p electrons each in its own orbital, with their spins parallel.

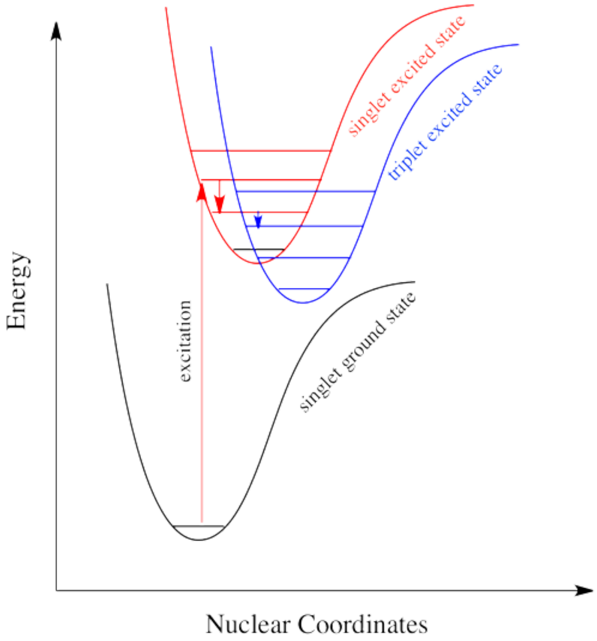




The picture with three unpaired electrons, all with parallel spins, shows a nitrogen in the quartet spin state. Having one of those spins point the other way would result in a different spin state. One pair of electrons in the p level would be spin-paired, one up and one down, even though they are in different p orbitals. That would leave one electron without an opposite partner. The nitrogen would be in a doublet spin state.

That isn't what happens. The quartet spin state is lower in energy than the doublet state. That's just one of the rules of quantum mechanics: maximize spin when orbitals are singly occupied.

It's the same in a molecule. The triplet state is lower in energy than the singlet state. Why didn't the electron get excited to the triplet state in the first place? That's against the rules. But sliding down vibrationally onto the triplet state from the singlet excited state isn't, because it doesn't involve absorption of a photon.

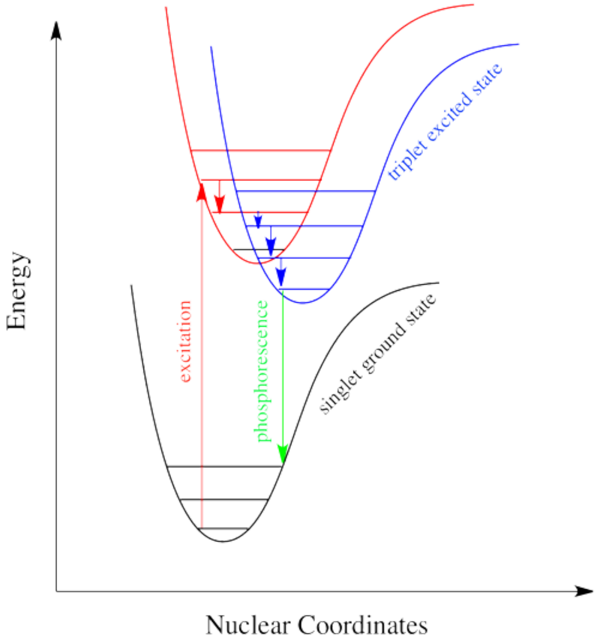


Intersystem crossing can have important consequences in reaction chemistry because it allows access to triplet states that are not normally avaiable in many molecules. Because triplet states feature unpaired electrons, their reactivity is often typified by radical processes. That means an added suite of reactions can be accessed via this process.

Phosphorescence: A Radiationless Transition Followed by Emission

Intersystem crossing is one way a system can end up in a triplet excited state. Even though this state is lower in energy than a singlet excited state, it can't be accessed directly via electronic excitation because that would violate the spin selection rule.

That's where the electron gets stuck, though. The quick way back down to the bottom is by emitting a photon, but because that would involve a change in spin state, it isn't allowed. Realistically speaking, that means it takes a long time. By "a long time", we might mean a few seconds, several minutes, or possibly even hours. Eventually, the electron can drop back down, accompanied by the emission of a photon. This situation is called "phosphorescence".

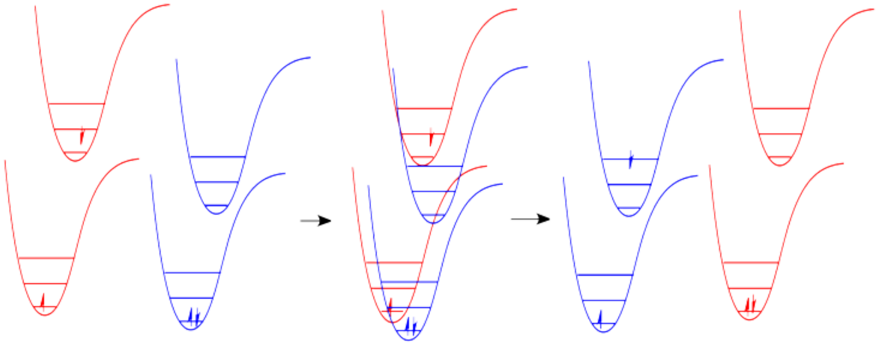


Molecules that display phosphorescence are often incorporated into toys and shirts so that they will glow in the dark.

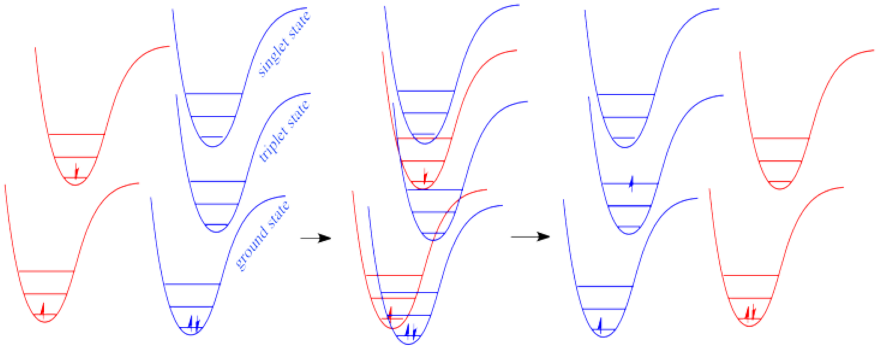
Photosensitization

We have already seen that an excited state molecule can transfer some vibrational energy to another molecule via a collision. What about the energy of the electroic excited state? Can a molecule transfer a large quantum of energy to another -- essentially a photon's worth, but without the photon? The answer is yes.

In a collision, one molecule in an electronic excited state can transfer its energy to another. In the process, the first molecule returns to the ground state and the second is excited. This process is called "photosensitization".



Photosensitization can occur in a couple of different ways. Because photosensitization does not involve absorption or emission of a photon, it can also lead to formation of a triplet excited state.



The significance of photosensitization is that compounds that do not have strong chromophores can still access electronic excited states if they come into contact with other molecules that do have strong chromophores. There are a number of compounds that are routinely used to induce excitation in other molecules; these photochemical enablers are referred to as photosensitizers.

Exercise 8.3.1

Photoredox processes have experienced a great deal of attention from researchers. (For a nice overview, see Stephenson, *J. Org. Chem*. **2012**, *77*, 1617-1622).

a. Photochemically excited species are often good reducing agents (or photoredox agents). Show why with the help of a generic energy diagram showing a HOMO → LUMO excitation.
b. Ru(II) complexes such as $\mathrm{Ru(bpy)_3}^{2+}$ are good photoredox agents. Comment on the usefulness of $\mathrm{Ru(bpy)_3}^{2+}$ as a regular reducing agent (in its ground state), based on the following equation.

$$\mathrm{Ru(bpy)}_3^{3+} + \mathrm{e}^- \longrightarrow \mathrm{Ru(bpy)}_3^{2+}\backslash)\backslash(E^0 = 1.26V$$

c) Calculate the energy difference between states suggested by this standard reduction potential.

d) $\mathrm{Ru(bpy)_3}^{2+}$ absorbs very strongly in the visible spectrum (450 nm). What colour is it?

e) What type of transition do you think this is?

f) Calculate the energy difference from the ground state to the initially formed excited state $\mathrm{Ru(bpy)_3}^{2+}$*.

g) What is the multiplicity of this initially formed excited state (e.g. a singlet or a triplet etc)? Show why.

h) The initially formed excited state $\mathrm{Ru(bpy)_3}^{2+}$* undergoes internal conversion (radiationless relaxation) and intersystem crossing to form triplet $\mathrm{Ru(bpy)_3}^{2+}$* before phosphorescence occurs at 615 nm. What colour is observed upon phosphorescence?

i) Calculate the energy difference from the triplet $\mathrm{Ru(bpy)_3}^{2+}$* to the ground state.

j) The difference between the wavelength absorbed and the wavelength emitted during fluorescence or phosphorescence is called the *Stokes shift*. What is the Stokes shift in this case?

k) Calculate the amount of energy transferred to vibrational states during the internal conversion.

l) Calculate the potential for the following reaction:

$$\mathrm{Ru(bpy)}_3^{3+} + \mathrm{e}^- \longrightarrow \mathrm{Ru(bpy)}_3^{2+\cdot} \;\text{(triplet state)}\; E^0 = ?V$$

m) Compare the usefulness of $\mathrm{Ru(bpy)_3}^{2+}$ +vs. $\mathrm{Ru(bpy)_3}^{2+}$*as a reducing agent.

Answer b

b) $\mathrm{Ru(bpy)_3}^{2+}$ would be a terrible reducing agent. The reduction potential of $\mathrm{Ru(bpy)_3}^{3+}$ is very high. That means $\mathrm{Ru(bpy)_3}^{2+}$ would not give up an electron very easily.

Answer c

c) $\Delta G = - n F E^0$

$\Delta G = - 1 \times 97{,}485 \text{ J V}^{-1} \text{ mol}^{-1} \times 1.26 \text{ V} = -123,000 \text{ J mol}^{-1} = -123 \text{ kJ mol}^{-1}$

Answer d

d) It absorbs in the blue part of the spectrum and appears orange.

Answer e

e) It absorbs very strongly, so probably not d-d. It is probably MLCT, from the ruthenium to the π* in the bpy ligand.

Answer f

f) $E = h c / \lambda$

$E = (6.625 \times 10^{-34} \text{ J s mol}^{-1} \times 3.0 \times 10^{8} \text{ m s}^{-1}) / (450 \text{ nm} \times 10^{-9} \text{ m nm}^{-1}) = 4.42 \times 10^{-19} \text{ J}$

That's for one molecule. On a per mole basis, $E = 4.42 \times 10^{-19}$ J x 6.02×10^{23} mol^{-1} = 266,000 J mol^{-1} = 266 kJ mol^{-1}.

Answer g

g) Ru^{2+} would be low spin d^6, a singlet ground state. The excited state will also be a singlet state.

Answer h

h) 615 nm is in the orange region of the spectrum. This is light given off by the complex as it relaxes, so it is the colour we see.

Answer i

i) $E = h\, c / \lambda$

$E = (6.625 \times 10^{-34}$ J s mol^{-1} x 3.0×10^8 m s^{-1})/ (615 nm x 10^{-9} m nm^{-1}) = 3.23×10^{-19} J

That's for one molecule. On a per mole basis, $E = 3.23 \times 10^{-19}$ J x 6.02×10^{23} mol^{-1} = 195,000 J mol^{-1} = 195 kJ mol^{-1}.

Answer j

j) Stokes shift = 615 nm - 450 nm = 165 nm

Answer k

k) $\Delta E = E_1 - E_2$ = 266 - 195 kJ mol^{-1} = 71 kJ mol^{-1}

However, it would not be lost all at once, but in small increments equivalent to the differences between vibrational states.

Answer l

l) If we were to reduce $Ru(bpy)_3{}^{3+}$ directly into an excited state, we would arrive at a state much higher in energy than the ground state. That reduction would be harder to accomplish. In this case, the ending state would be 195 kJ mol^{-1} higher than $Ru(bpy)_3{}^{2+}$.

ΔG = 195 - 123 kJ mol^{-1} = 72 kJ mol^{-1}

$E^0 = - \Delta G / n F$ = - (72 kJ mol-1 x 1000 kJ J^{-1}) / (1 x 96,485 J V^{-1} mol^{-1}) = -0.75 V

Answer m

m) The oxidation of $Ru(bpy)_3{}^{2+*}$ would be very favourable compared to the oxidation of $Ru(bpy)_3{}^{2+}$. The former is a much better reducing agent.

8.4: Photolysis

We have seen that the absorption of photons (especially in the ultraviolet-visible spectrum) is connected to the excitation of electrons. After excitation, a number of different relaxation pathways lead back to the ground state. Sometimes, absorption of a photon leads to a vastly different outcome. Instead of just relaxing again, the molecules may undergo bond-breaking reactions, instead.

An example of this phenomenon is observed in the complex ion $[Co(NH_3)]_6^{3+}$. Addition of UV light to this complex results in loss of ammonia. In the absence of UV light, however, the complex ion is quite stable.

In many cases, loss of a ligand is followed by replacement by a new one. For example, if an aqueous solution of $[Co(NH_3)]_6^{3+}$ is photolysed, an ammonia ligand is easily replaced by water.

Exercise 8.4.1

Draw a d orbital splitting diagram for $[Co(NH_3)]_6^{3+}$. Explain why this complex is normally inert toward substitution.

Exercise 8.4.2

Use the d orbital splitting diagram for $[Co(NH_3)]_6^{3+}$ to explain why this complex undergoes substitution upon irradiation with UV light

Photolysis is the term used to describe the use of light to initiate bon-breaking events. Photolysis frequently involves the use of high-intensity ultraviolet lamps. The high intensity light is needed in order to provide enough photons to get higher conversion of reactant into a desired product.

Two very different things could happen as a result of photon absorption. In one case, the molecule absorbs the photon, then somehow relaxes again, remaining unchanged overall. In the other case, the absorption of the photon results in bond cleavage and the formation of a new product. As a result, for every photon absorbed, there is a certain chance that the molecule will actually undergo a reaction, and a certain chance that the molecule will just relax again.

"Quantum yield" is an expression used to define the efficiency of a photolytic reaction. The quantum yield is just the number of molecules of reactant formed per photon absorbed. On a macroscopic level, we might say it is the number of moles of reactant formed per mole of photons absorbed.

Quantum yield = number of molecules of product formed / number of photons absorbed

The higher the quantum yield, the more efficient the reaction, because it requires less light in order to successfully form the product.

Exercise 8.4.3

Calculate the quantum yield in the following cases.

a. 6 mmoles of product results from absorption of 24 mmoles of photons.
b. 54 mmoles of photons are required to produce 3 mmoles of product.
c. 1.2×10^{-6} moles of product are formed after absorption of 4.2×10^{-5} moles of photons.

In practice, determination of quantum yield is complicated because of the need to calculate exactly how many photons have been absorbed, in addition to how much product has been formed.

8.5: Atmospheric Photochemistry- Ozone

There are lots of ways that light plays an important role in the world. Life on earth is heavily dependent on photosynthesis. Energy from the sun can be harvested and used to make ATP, which can then be used for carbohydrate synthesis. The energy found in light, however, can also be very damaging. In fact, ultraviolet light would make life impossible on earth were it not for the intercession of the high-atmosphere ozone layer. By undergoing reactions that absorb UV light, the molecules involved in the ozone cycle block much of the most harmful sunlight from reaching the earth's surface.

The ozone cycle is a series of reactions involving allotropes of oxygen. Oxygen can be present as oxygen atom, O; as oxygen molecule, O_2; or as ozone, O_3. Of course, dioxygen, or molecular oxygen, is by far the most common of these forms, constituting about 20% of our atmosphere.

That's where we will start. There is plenty of dioxygen in our atmosphere, and so photons from the sun encounter these molecules pretty frequently. If the photons have sufficient energy, they can break the O-O bond, forming oxygen atoms.

$$\mathrm{O_2 + energy \longrightarrow 2\,O}$$

That photolysis reaction (meaning, "broken by light") leads to a buildup of oxygen atoms in the upper atmosphere. Of course, these oxygen atoms are likely to encounter oxygen molecules, which are very abundant. When they do, they can undergo a bond-forming reaction, to make ozone. This reaction is purely bond-forming, and it is exothermic.

$$\mathrm{O + O_2 \longrightarrow O_3 + energy}$$

There are also a couple of reactions that cause removal of ozone from the atmosphere. The first is the reaction of ozone with ultraviolet light. The energy from the sunlight can break the O-O bond in ozone, converting it back into dioxygen and oxygen atom.

$$\mathrm{O_3 + energy \longrightarrow O + O_2}$$

In addition, as ozone and oxygen atom build up, collisions between these two species becomes increasingly likely. If that happens, an oxygen atom abstraction is an obvious outcome, in which two dioxygen molecules are the products. This reaction involves both bond-breaking and bond-making, but the reaction is overall exothermic.

$$\mathrm{O_3 + O \longrightarrow 2\,O_2 + energy}$$

Notice those two energy-consuming reactions. One of them occurs in the ozone creation phase and one in the ozone removal phase. Together, these reactions contribute to the consumption of ultraviolet light as it passes through the stratosphere, so that less ultraviolet light reaches the earth's surface below. However, the two reactions are on opposing sides of a cycle. Consumption of some sunlight leads to ozone formation, but consumption of sunlight also leads to ozone destruction.

The thermodynamics of the ozone cycle are illustrated below. Again, two of the reactions are endothermic, whereas two others are endothermic.

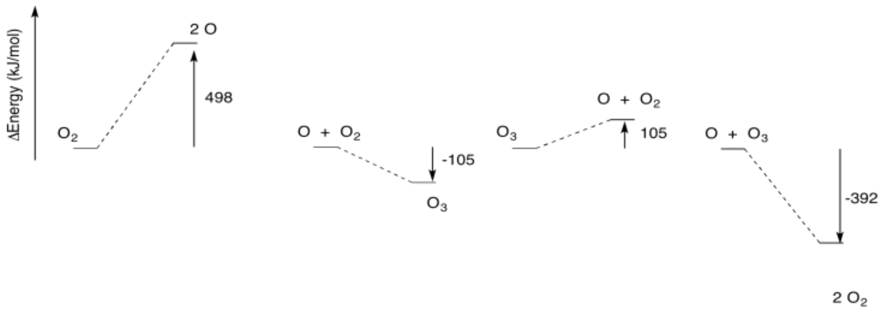


Figure 8.5.1: Thermodynamics of steps involved in the natural ozone cycle.

The endothermic steps actually require more energy than is implied in the picture above. As in any reaction, it usually isn't sufficient to supply enough energy to get from one side of the reaction to the other. There is also an energy barrier to overcome. That's part of the reason these reactions need ultraviolet light.

The first reaction requires light of wavelengths shorter than about 240 nm.

$$\mathrm{O_2} \xrightarrow{h\nu,\ \lambda < 220\ \mathrm{nm}} \mathrm{2\,O}$$

The second reaction requires light of wavelengths shorter than about 325 nm.

$$O_3 \xrightarrow{h\nu,\ \lambda < 325\text{ nm}} O + O_2$$

Exercise 8.5.1

Why is there an upper limit to the wavelength of light capable of inducing these reactions?

Answer

The longer the wavelength, the lower the energy. Photons of wavelength longer than 240 nm would not have enough energy to overcome the barrier for the dioxygen-cleaving reaction.

Exercise 8.5.2

Calculate the energy, in J, of the following photons:

a. 220 nm
b. 325 nm

Answer a

According to the Planck-Einstein relation:

E = hv

or, since v = c / λ

E = hc / λ

in which h = Planck's constant = 6.625 x 10^{-34} Js,

c = speed of light = 3.0 x 10^{8} m/s,

v = frequency,

λ = wavelength.

a) E = hc / λ

E = (6.525 x 10^{-34} Js)(3.0 x 10^{8} m/s) / (220 nm)(10^{-9} m/nm)

E = 9.03 x 10^{-19} J

Answer b

b) E = hc / λ

E = (6.525 x 10^{-34} Js)(3.0 x 10^{8} m/s) / (325 nm)(10^{-9} m/nm)

E = 6.12 x 10^{-19} J

Exercise 8.5.3

a. Given the wavelength of light needed for the photolysis of O_2, calculate the barrier to the reaction, in kJ/mol.
b. Sketch a reaction progress diagram for the reaction.

Answer a

Remember, the mole is the conversion unit from the molecular scale to the macroscopic scale.

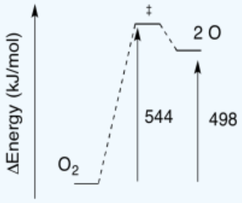
a) E = (8.28 x 10^{-19} J / photon)(6.02 x 10^{23} photons/mol)

E = 543,770 J/mol

E = 544 kJ/mol

Answer b

b)



Exercise 8.5.4

a. Given the wavelength of light needed for the photolysis of O_3, calculate the barrier to the reaction, in kJ/mol.
b. Sketch a reaction progress diagram for the reaction.

Answer a

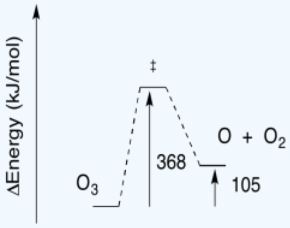
a) E = (6.12 x 10^{-19} J / photon)(6.02 x 10^{23} photons/mol)

E = 368,146 J/mol

E = 368 kJ/mol

Answer b

b)



Exercise 8.5.5

Given the principle of microscopic reversibility, calculate the barrier to the following reactions, in kJ/mol.

a. $2\,O \longrightarrow O_2$
b. $O + O_2 \longrightarrow O_3$

Answer a

The reactions must take the same pathway, and go over the same barrier, forward and back.

a) The reverse barrier: E = 544 - 498 kJ/mol

E = 46 kJ/mol

Answer b

b) The reverse barrier: E = 368 - 105 kJ/mol

E = 263 kJ/mol

Ozone is clearly at a higher energy than dioxygen. The fact that appreciable amounts exist in the upper atmosphere can be attributed to the constant input of energy from the sun. This is an example of an environmental steady state. The ratio of ozone to oxygen, although still pretty low even in the stratosphere, is elevated above its natural equilibrium value because energy is constantly being added, pushing the system uphill in energy.

The Problem with Chlorine

In 1974, Sherwood Rowland, a professor of chemistry at the University of California, Irvine, and Mario Molina, a Mexican post-doctoral associate in his laboratory, authored a paper in the journal *Nature* outlining how chlorofluorocarbons (CFCs) could play a role in interfering with the ozone cycle. CFCs at that time were an economically important compound because they were a non-toxic, highly effective refrigerant used in millions of homes and businesses worldwide. Rowland and Molina shared the 1995 Nobel Prize in Chemistry with Paul Crutzen, a Dutch citizen working at the Max Planck Institute in Germany, who similarly reported the effects of nitrogen oxides on the ozone cycle.

The problem with CFCs is really the fact that, in the upper atmosphere, they can break down to form chlorine atoms. For example, freon-12, or CF_2Cl_2, can absorb ultraviolet light, resulting in cleavage of the C-Cl bond.

Chlorine atom in the stratosphere interferes with the ozone cycle by consuming both ozone and, indirectly, a key intermediate in ozone formation, oxygen atom.

$$\mathrm{O_3 + Cl \longrightarrow ClO + O_2}$$

$$\mathrm{ClO + O \longrightarrow O_2 + Cl}$$

What makes the role of chlorine particularly problematic is that, in addition to wiping out ozone and an intermediate needed to replace it, the chlorine is regenerated at the end, so it is able to go back into the system and do it all over again. It is destructive to ozone, and with catalytic efficiency.

After environmental regulations were introduced mandating an eventual industry-wide phase-out of CFCs, industry was able to respond with the development of chlorine-free substitutes that were still non-toxic and non-flammable (both important for household use). Hydrofluorocarbons are the major type of replacement that has been developed for use today. There are other compounds commonly used as refrigerants, but they have significant drawbacks. Ammonia is toxic, and hydrocarbons are very flammable.

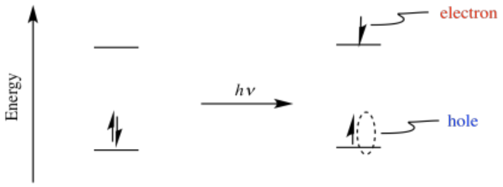
There is an additional consideration that researchers must take into account in looking for CFC replacements, however: lifetime. If a molecule lasts too long in the atmosphere, there is the risk of a long-term buildup that may result in additional environmental consequences. The fact that chlorocarbons and fluorocarbons contain polar C-Cl and C-F bonds means that they will absorb infrared radiation strongly, so they will act as greenhouse gases. That's part of the reason hydrofluorocarbons are used. The C-H bond in a hydrofluorocarbon is easily broken by atmospheric hydroxy radical, because of the strength of the new O-H bond that is formed. That event provides for a decomposition pathway that removes the molecule from the atmosphere more quickly.

8.6: Applications of Photochemistry- Photoredox Catalysis

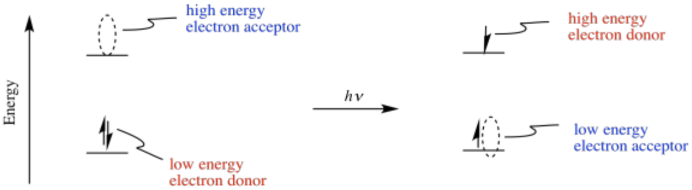
There are lots of ways that photochemistry can be harnessed to do useful things. Solar power is an obvious example: sunlight is used to excite an electron in a solar panel, leading to generation of electricity. That kind of power can potentially have a broad impact on other aspects of the energy industry. For example, a number of researchers have been trying to use sunlight as an energy source to make hydrogen from water.

Photoredox catalysis is the application of photochemistry to carry out redox reactions catalytically. For example, if sunlight were absorbed by a material such as a semiconductor, resulting in excitation of an electron, the resulting species may have the energy to reduce the protons in water to dihydrogen. If the semiconductor could be regenerated with a reducing agent, the process would be catalytic.

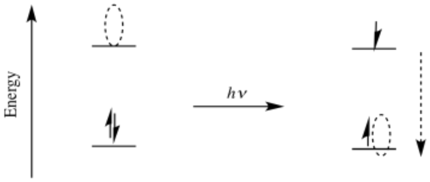
Perhaps the most powerful aspect of photoexcitation is that it results in both a powerful oxidant and a powerful reductant. Excitation of an electron results in electron/hole pair separation. After excitation, the electron is in a higher energy level, and it leaves behind a "hole", where the electron used to be.



Because the electron is at a higher energy level than it used to be, donation to an acceptor is more favorable than it was before. The compound has become a better reducing agent through photoexcitation. Also, because the hole is lower in energy than the LUMO of the ground state, it will more easily accept and electron from a donor. That means the compound has also become a better oxidising agent through photoexcitation.



We can estimate how much the reducing or oxidizing power of a compound changes upon excitation by a photon. For example, the reduction potential depends upon the relative energy level of the orbital into which an electron would be donated. Upon photoexcitation, that energy level changes. It goes from the ground state LUMO to the level of the hole introduced where an electron used to be. The difference in energy between those two levels is the same as the energy of the photon that was absorbed.



We can calculate the energy of the absorbed photon. That quantity is given by the Planck-Einstein relation:

$$E = h\nu \text{ or } E = \frac{hc}{\lambda}$$

in which E is energy, *h* is Planck's constant, ν is the frequency of the photon, c is the speed of light, and λ is the wavelngth of the photon.

That energy is the same as the distance between the ground state LUMO and the excited state hole. Now, that is a quantum-scale energy difference, found within a single molecule. When we talk about reduction potentials, we are discussing a macroscopic phenomenon. Reduction potentials are measured on the scale of human experience, the scale of the very large, the scale that we can easily observe. Macroscopic measurements involve vast numbers of atoms, and the convenient unit of a vast number of atoms is a mole. Remember, that's just the conversion factor between an easily measurable quantity of mass (a gram) and a quantum-scale quantity of mass (an atomic mass unit, also called an amu or a Dalton).

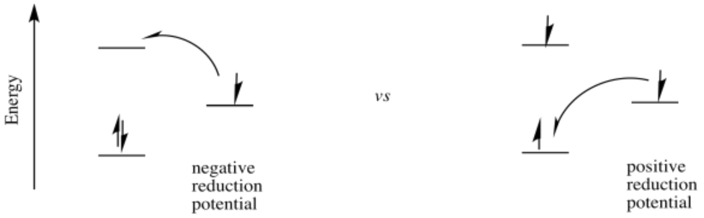
So we might think about how much energy it would take to get an entire mole of molecules into the excited state, which would simply require the use of Avogadro's number. Clearly this will be a much bigger amount of energy than it takes to excite a single molecule, and we would get there by multiplying by Avogadro's number.

$$E = (h\nu)N_A \; or \; E = (\frac{hc}{\lambda})N_A$$

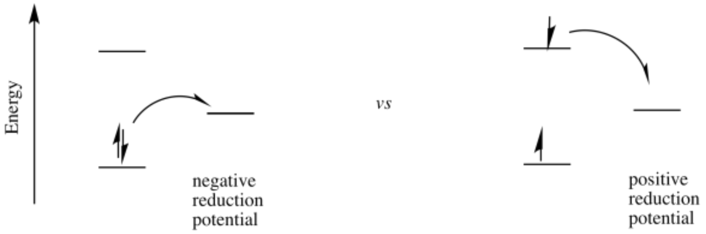
in which N_A = Avogadro's number.

(We could equally well be dealing with an individual atom or some other kind of compound rather than a molecule, but the argument would be the same.)

Because the excited state hole is that much lower in energy than the original LUMO, an electron falling into that hole would release that much more energy than an electron falling into the ground state LUMO. On the macroscopic scale, a mole of electrons falling into the excited state hole would release so much more energy than a mole of electrons falling into the ground state LUMO; that energy difference is the quantity that we have just calculated using Avogadro's number.



Of course, a similar argument holds for the excited state electron. It is much more likely to be donated to an acceptor after first having been excited.



We know that the free energy released when an electron falls to a lower level is related to the reduction potential. That difference is given by the relation

$$\Delta G = -nF\Delta E^o$$

in which ΔG is the free energy change, n is the number of electrons transferred, *F* is the Faraday constant, and ΔEº is the cell reduction potential, or the difference in reduction potential between the donor and the acceptor.

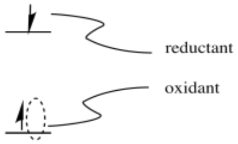
Here we will make a slight approximation. The energy of the photon is roughly the difference in free energy upon electron transfer from a donor to the excited state hole compared to the ground state LUMO (although the energy calculated in the Planck-Einstein relation doesn't say anything about entropy, which is an implicit part of the free energy change).

$$E_{excitation} \sim \Delta G_{reduction}$$

From there, it is a short step to figure out the change in reduction potential when the electron is excited.

$$\Delta E^o_{new} = \Delta E^o_{original} + \Delta E^o_{photo}$$

The possibility for tremendous utility of an excited state species in catalysis arises from the fact that the excited state can be both a better reductant and a better oxidant than the ground state species. As a better oxidant, it can easily oxidize another compound; as a better reductant, it can then be reduced again, forming the original, ground state species and completing a catalytic cycle. Alternatively, it could act as a reductant first and complete the cycle by becoming reduced again; the order of the two steps does not really matter.



Let's think about the example of hydrogen production. Hydrogen is very appealling as a fuel because, when it burns, it provides a large amount of energy through the formation of strong O-H bonds. In addition, the product of its combustion is water, which does not pose any obvious problems as a pollutant. An economy based on hydrogen consumption is potentially more sustainable in environmental terms.

Where could we get hydrogen to drive this economy? Currently, we obtain hydrogen from coal and natural gas. In a process called steam reforming, hydrocarbon gases such as methane can be passed over a catalyst in the presence of steam, producing H_2 and carbon oxygenates, mostly CO but also some CO_2. A similar process can be carried out using coal instead of natural gas. The carbon monoxide is usually captured for other industrial processes, but it can also be used to make even more hydrogen via the water gas shift reaction. In the water gas shift reaction, the carbon monoxide is again treated with steam over a different catalyst, producing H_2 and carbon dioxide.

Although the water gas shift reaction is exothermic, steam reforming is overall endothermic, so energy must be expended in order to produce hydrogen. That situation isn't optimal, because we end up having to spend a lot of energy in order to produce an energy source. In addition, we produce carbon dioxide, which is a greenhouse gas, the human production of which has been convincingly linked to global warming and climate change. Furthermore, coal and natural gas reserves may be plentiful right now, but the same was also once true of petroleum reserves, and although petroleum companies continue to locate and extract new deposits of petroleum, the extraction process becomes more difficult and expensive as these deposits become more and more remote or inaccessible.

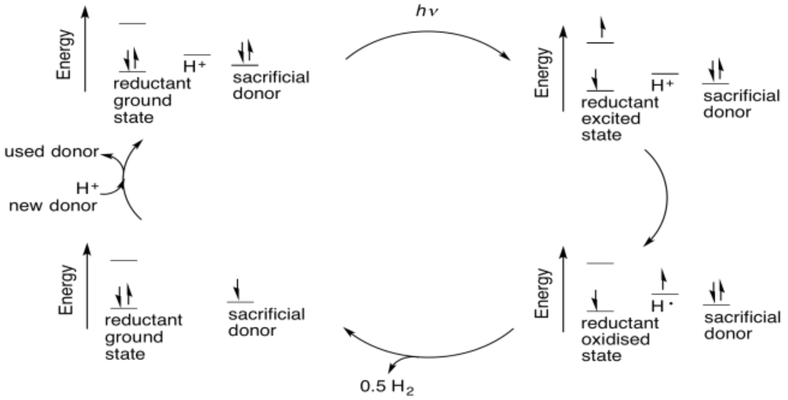
Water is the most abundant source of hydrogen on earth. It would be much easier to produce hydrogen from water. People have been doing that for about 200 years, just by placing electrodes in water and applying a voltage. This is called electrolysis of water. The trouble is, the electrolysis of water requires massive amounts of electricity. Electricity production requires energy consumption. In the United States, electricity production still depends heavily on consumption of coal and natural gas, so instead of replacing our need for these commodities, we have simply removed them from sight.

Photoredox catalysis may offer a solution. By producing hydrogen from water catalytically, we take a roundabout approach that requires less energy than direct electrolysis of water. By driving the reaction photochemically, we can harness sunlight to provide that energy.

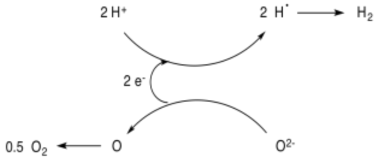
There are different possible routes that can convert protons to dihydrogen catalytically. One example occurs with coordination compounds. Some coordination compounds in low oxidation states can be protonated at the metal centre by water. Protonation of a metal centre is formally an oxidative addition. Once the proton is bound to the metal centre, it is considered a hydride ligand, so it has formally changed from H^+ to H^-. The two electrons to convert it to a hydride came from the metal.

Catalytic turnover results after the metal centre has been protonated twice, resulting in a pair of hydride ligands on the metal. Reductive elimination of dihydrogen returns two of the electrons to the metal centre; the other two leave with the dihydrogen. The metal still needs two more electrons from another source, because in undergoing two oxidative additions it has donated a total of four electrons to the protons.

One of the problems with this approach is that in order to make the process catalytic, the two electrons that were sent to the protons in water to make hydrogen must be replaced. Many researchers in this area have used sacrificial electron donors, compounds that can donate electrons to the catalyst to replace the ones given to the protons. Sacrificial donors could be biological cofactors such as ascorbate or succinate, or they could be simple amines.



Because these donors are consumed in this process, they represent a potential inefficiency in the form of a waste side product. Some researchers hope to circumvent this problem by tying in an additional catalytic cycle that regenerates the electron donors. Others hope to bypass this problem by using the oxygen atom in water as the sacrificial donor, producing dioxygen, but doing so with a low energy cost is a challenge.

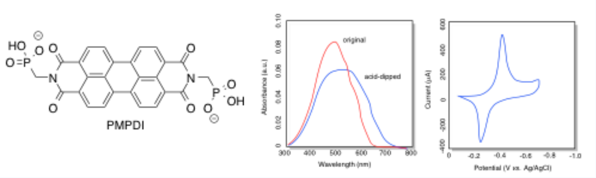


Another problem is how to drive the system photochemically. A common approach in current research efforts involves the use of semiconducting materials that can absorb sunlight (that's what solar panels are, after all). The excited state electron is passed to the catalytic component of the system, and the hole is filled by the sacrificial electron donor.

Exercise 8.6.1

Researchers at Colorado State have developed a new system for photolysis of water (Finke, ACS Appl. Mater. Interfaces, 2014, ASAP).

PDI (below), a type of dye used in automobile paint, was coated onto an indium tin oxide plate. The UV-Vis spectrum was obtained and the reduction potential was measured.



a. What colour is the original PDI-coated plate?
b. What is the longest wavelength absorbed?
c. Translate this wavelength into energy, in kJ/mol.
d. Translate this energy into a potential, in Volts.
e. Show a diagram of photon absorbance to explain why this energy is a more accurate reflection of the band gap in PDI than that of other wavelengths that are absorbed.
f. What type of transition is probably involved, given the structure of PDI?

$$MLCT\ d-d\ n\rightarrow\pi*\pi\rightarrow\pi*$$

g) What happens to the energy of the transition after dipping the plate in acid?

It is thought that this transition can be intermolecular in this case:

$$2PDI+h\nu\rightarrow PDI+\ PDI-$$

h) Most molecules don't undergo intermolecular photonic excitation. What makes it easier in this case?

i) How is the idea of intermolecular photonic excitation consistent with the acid-dipped experiment?

j) Use the cyclic voltamogram to estimate the reduction potential of PDI vs Ag/AgCl.

Cobalt oxide was photodeposited on the PDI surface by dipping the plate in phosphate buffered (KH_2PO_4/ K_2HPO_4) cobalt nitrate solution ($Co(NO_3)_2$) and irradiating with a xenon arc lamp.

k) Show a d orbital splitting diagram for the octahedral aqueous cobalt ion before and after photon absorption.

l) Provide a mechanism for the formation of $Co(IV)_2O$ in that solution.

The following reduction potentials have been reported in the literature:

indium tin oxide: -0.10 V vs NHE

cobalt oxide: 1.23 V vs NHE

water: 0.83 V vs NHE

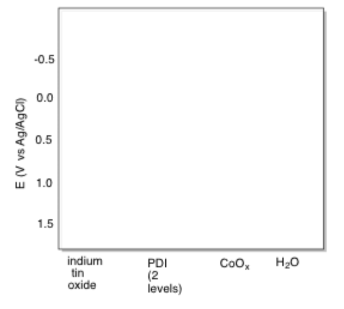
Now we have a problem, because some of our reduction potentials are compared to NHE; they tell us how easy it is to reduce something compared to reducing H^+. Some are compared to Ag/AgCl; they tell us how easy it is to reduce something compared to reducing Ag^+.

m) If the reduction potential of Ag^+ is +0.20 V vs NHE, then what are the following potentials vs. Ag/AgCl?

i) indium tin oxide ii) cobalt oxide iii) water

n) Calculate the reduction potential of the excited state PDI*.

o) Fill in the appropriate energy levels for the species indicated.



p) Add curved arrows to indicate electron flow through the system during photolytic oxygen generation.

q) Studies indicate that the system does not work if the PDI does not have phosphates attached to it. Explain why.

Answer a

a) The original PDI has an absorption maximum at just under 500 nm. It absorbs blue-green, so it would be expected to appear red-orange.

Answer b

b) The longest wavelength absorbed is approximately 625 nm.

Answer c

c) $E = hc/\lambda = (6.625 \times 10^{-34}\ \text{Js mol}^{-1} \times 3.0 \times 10^{8}\ \text{m s}^{-1})/625 \times 10^{-9}\ \text{m} = 3.18 \times 10^{-19}\ \text{J}$

That's the energy of a photon. A mole of photons would have energy multiplied by Avogadro's number, N_A.

$E = 3.18 \times 10^{-19}\ \text{J} \times NA = 3.18 \times 10^{-19} \times 6.02 \times 10^{23}\ \text{mol}^{-1} = 1.91 \times 10^{5}\ \text{J mol}^{-1} = 191\ \text{kJ mol}^{-1}$

Answer d

d) If we approximate $E = \Delta G$, and given that $\Delta G = - nFE^0$

Then for this single-electron excitation, $E^0 = - \Delta G / n F = - 1.91 \times 10^{5}\ \text{J mol}^{-1} / (1 \times 96{,}485\ \text{J V}^{-1}\ \text{mol}^{-1}) = -1.97\ \text{V}$

Answer f

f) Given the structure of PDI, the transition is probably π --> π*.

Answer g

g) The longest wavelength absorbed shifts toward the red, to about 700 nm, after dipping in acid. The energy of the transition is lowered to

$E = hc/\lambda = (6.625 \times 10^{-34}$ Js mol$^{-1} \times 3.0 \times 10^{8}$ m s$^{-1})/700 \times 10^{-9}$ m $= 2.84 \times 10^{-19}$ J

$E = 2.84 \times 10^{-19}$ J x NA $= 3.18 \times 10^{-19} \times 6.02 \times 10^{23}$ mol$^{-1} = 1.71 \times 10^{5}$ J mol^{-1} = 171 kJ mol^{-1}

Answer h

h) These very flat molecules can probably stack very tightly together. The distance between the π electrons on one molecule and the π* orbital on a neighbouring molecule is very small. An intermolecular transition is possible.

Answer i

i) What happens when the film is dipped in acid? It gets protonated. The anionic phosphate groups would become neutralized. The molecules would be able to stack even more closely together, lowering the energy required to excite an electron from one molecule to the other.

Answer j

j) The onset of the reduction wave appears to be about -0.40 V, as shown by the peak in the cyclic voltamogram.

Answer m

m) $E^{0}_{(vs\ Ag+/AgCl)} = E^{0}_{(vs\ NHE)} + 0.20$ V (i.e. the positive reduction potential of Ag+ vs. NHE indicates an electron is

i) $E^{0}_{(vs\ Ag+/AgCl)} = -\ 0.10\ V + 0.20\ V = +\ 0.10\ V$

ii) $E^{0}_{(vs\ Ag+/AgCl)} = +\ 1.23\ V + 0.20\ V = +\ 1.43\ V$

iii) $E^{0}_{(vs\ Ag+/AgCl)} = +\ 0.83\ V + 0.20\ V = +\ 1.03\ V$

Answer n

n) The excited state can be reduced by placing an electron in the hole vacated by the excited electron. This level is 1.97 V below the conductance band in energy, which has a reduction potential of -0.40 V (its potential is 1.97 V more positive than the conductance band).

Thus, -0.40 V + 1.97 V = + 1.57 V.

Answer q

q) The phosphates probably coordinate to the cobalt oxide, forming a bridge for electron transfer.

Exercise 8.6.2

Researchers in China have developed Ag-AgBr nanoparticles capable of catalysing the photochemical degradation of pollutants in sunlight. (*Langmuir* **2010**, *26*, 18723-18727)

a. The AgBr nanoparticles are first formed by autoclaving $AgNO_3$ and tetraalkylammonium bromide. Show an equation for this reaction.
b. The AgBr nanoparticles absorb strongly between 250-450 nm. What colour are they?
c. The structure of AgBr can be described as face centered cubic bromide with silver in the octahedral holes. Draw a unit cell.

The AgBr nanoparticles are suspended in water and exposed to sunlight for several hours until Ag picoparticles form on the surfaces of the nanoparticles.

d) Compare the size of nanoparticles to picoparticles.

e) Photoreduction of silver is believed to involve electron transfer from solvent. Show a mechanism for Ag(0) formation.

f) The Ag-AgBr nanoparticles absorb strongly from 250-850 nm. What colour are they?

In remediation assays, methyl orange is used as a stand-in for water-borne pollutants. The authors speculate that photon absorption causes electron / hole pairs that lead to reduction of O_2 and oxidation of water, respectively, generating reactive oxygen species.

h) Draw an MO or band gap picture to help illustrate these two processes (water oxidation and O_2 reduction).

i) Show a mechanism for radical propagation using a reactive oxygen species and methyl orange.

Answer a

a) $Ag^+_{(aq)} + NO_3^-{}_{(aq)} + Bu_4N^+{}_{(aq)} + Br^-{}_{(aq)} \rightarrow AgBr_{(s)} + Bu_4N^+{}_{(aq)} + NO_3^-{}_{(aq)}$

Answer b

b) They absorb in the violet-blue range and would appear yellow-orange.

Answer d

d) A nanometer is 10^{-9} m, whereas a picometer is 10^{-12} m. A picoparticle is 1,000 times smaller than a nanoparticle.

Answer f

f) They absorb across the visible spectrum and appear black.

8.7: Photoredox Catalysis in Organic Chemistry

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8.8: Solutions to Selected Problems

Exercise 8.1.1:

a. $A = \varepsilon cl = 6 \frac{L}{mol\ cm} \times 0.01 \frac{mol}{L} \times 1cm = 0.60 = 60\%$
b. $A = \varepsilon cl = 3000 \frac{L}{mol\ cm} \times 3.5 \times 10^{-5} \frac{mol}{L} \times 1cm = 0.105 = 10.5\%$
c. $A = \varepsilon cl = 1.4 \frac{L}{mol\ cm} \times 0.25 \frac{mol}{L} \times 0.5cm = 0.175 = 17.5\%$
d. $A = \varepsilon cl = 23000 \frac{L}{mol\ cm} \times 2.5 \times 10^{-6} \frac{mol}{L} \times 1cm = 0.0575 = 5.75\%$
e. $A = \varepsilon cl = 14000 \frac{L}{mol\ cm} \times 0.015 \frac{mmol}{L} \times 1cm = 14000 \frac{L}{mol\ cm} 0.015 \times 10^{3-} \frac{mol}{L} \times 1cm = 0.21 = 21\%$

Exercise 8.1.2:

a. $\varepsilon = \frac{A}{cl} = \frac{0.30}{(0.01 mol\ L^{1-} \times 1cm)} = 30 \frac{L}{mol\ cm}$
b. $\varepsilon = \frac{A}{cl} = \frac{0.25}{(0.025 mol\ L^{-1} \times 1cm)} = 10 \frac{L}{mol\ cm}$
c. $\varepsilon = \frac{A}{cl} = \frac{0.30}{(0.01 mol\ L^{-1} \times 1cm)} = 543 \frac{L}{mol\ cm}$
d. $\varepsilon = \frac{A}{cl} = \frac{0.66}{(0.025 mmol\ L^{-1} \times 1cm)} = 26400 \frac{L}{mol\ cm}$

Exercise 8.1.3:

a. blue
b. red
c. orange
d. violet
e. green

Exercise 8.1.4:

a. $E = \frac{hc}{\lambda} = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{8} m\ s^{-1})}{1 \times 10^{-5} m} = 1.98 \times 10^{-20} J$
b. $E = \frac{hc}{\lambda} = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{-8} m\ s^{-1})}{125 \times 10^{-9} m} = 1.59 \times 10^{-18} J$
c. $E = \frac{hc}{\lambda} = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{-8} m\ s^{-1})}{1025 \times 10^{-9} m} = 1.94 \times 10^{-19} J$
d. $E = \frac{hc}{\lambda} = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{8} m\ s^{-1})}{450 \times 10^{-6} m} = 4.42 \times 10^{-22} J$
e. $E = \frac{hc}{\lambda} = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{-8} m\ s^{-1})}{850 \times 10^{-10} m} = 2.3 \times 10^{-18} J$

Exercise 8.1.5:

a. $\lambda = \frac{hc}{E} = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{-8} m\ s^{-1})}{1.46 \times 10^{-17} J} = 1.36 \times 10^{-8} m$
b. $\lambda = \frac{hc}{E} = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{-8} m\ s^{-1})}{4.72 \times 10^{-24} J} = 4.21 \times 10^{-2} m$
c. $\lambda = \frac{hc}{E} = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{-8} m\ s^{-1})}{9.26 \times 10^{-17} J} = 2.15 \times 10^{-19} m$

Exercise 8.1.6:

a. $E = h\nu = \frac{hc}{\lambda}$; so $v = \frac{c}{\lambda}$; or $\lambda = \frac{c}{v} = \frac{3.0 \times 10^{8} m\ s^{-1}}{6.7 \times 10^{10} s^{-1}} = 4.48 \times 10^{-3} m$
b. $\lambda = \frac{c}{v} = \frac{3.0 \times 10^{8} m\ s^{-1}}{1500 \times 10^{6} s^{-1}} = 0.2m$
c. $v = \frac{c}{\lambda} = \frac{3.0 \times 10^{8} m\ s^{-1}}{9.8 \times 10^{-10} m} = 3.06 \times 10^{15} s^{-1}$
d. $v \frac{c}{\lambda} = \frac{3.0 \times 10^{8} m\ s^{-1}}{4.3 \times 10^{-12} m} = 7.0 \times 10^{19} s^{-1}$

Exercise 8.1.7:

a) $E = \frac{hc}{\lambda}$

$$E = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{8} m\ s^{-1})}{(1mm \times 10^{-3} m\ mm^{-1})} = 1.99 \times 10^{-22} J$$

That's for one molecule. On a per mole basis, $E = 1.99 \times 10^{-22} J \times 6.02 \times 10^{23} mol^{-1} = 120 J mol^{-1} = 0.12 kJ\ mol^{-1}$

b) $E = \frac{hc}{lambda}$

$$E = \frac{(6.625 \times 10^{-34} Js\, mol^{-1} \times 3.0 times 10^{8} m\, s^{-1})}{(1000nm \times 10^{-9} m\, nm^{-1})} = 1.99 \times 10^{-19} J$$

That's for one molecule. On a per mole basis, $E = 1.99 \times 10^{-19} J \times 6.02 \times 10^{23} mol^{-1} = 120000 J\, mol^{-1} = 120 kJ\, mol^{-1}$

c) $E = \frac{hc}{\lambda}$

$$E = \frac{(6.625 \times 10^{-34} Js\, mol^{-1} \times 3.0 \times 10^{8} m\, s^{-1})}{(1m)} = 1.99 \times 10^{-25} J$$

That's for one molecule. On a per mole basis, $E = 1.99 \times 10^{-25} J \times 6.02 \times 10^{23} mol^{-1} = 0.120 J\, mol^{-1} = 1.2 \times 10^{-4} kJ\, mol^{-1}$

d) $E = \frac{hc}{\lambda}$

$$E = \frac{(6.625 \times 10^{-34} Jsmol^{-1} \times 3.0 \times 10^{8} ms^{-1})}{=} (500nm \times 10^{-9} m\, nm^{-1}) = 3.98 \times 10^{-19} J$$

That's for one molecule. On a per mole basis, $E = 3.98 \times 10^{-19} J \times 6.02 \times 10^{23} mol^{-1} = 239000 Jmol^{-1} = 239 kJ\, mol^{-1}$

Exercise 8.1.8:

Blue.

Exercise 8.1.9:

Ultraviolet light, with a shorter wavelength than visible light, is much higher in energy and potentially more damaging.

Exercise 8.2.3:

a. $d \rightarrow d$
b. $\pi \rightarrow \pi*$
c. MLCT

Exercise 8.2.4:

a.
b. The one on the left can relax by channelling some energy into molecular vibration, especially its *cis-trans* isomerisation. The one on the right can't do that because its rotation is restricted by the presence of the ring.
c. Of course! It's crawling with pi bonds. A strong pi-pi* transition in the visible region seems likely.
d. Probably not. It does not have restricted rotation, so the *cis-trans* isomerisation route is available for relaxation.
e. $A = \varepsilon bc$; so $\varepsilon = \frac{A}{bc} = \frac{0.77}{1cm \times 10^{-6} M} = 7.7 \times 10^{5} M^{-1} cm^{-1}$
f. That's a large molar absorptivity constant. It's allowed.
g. Undoubtedly this is that pi-pi* transition we were thinking about earlier.
h. If the compound binds to zinc, it probably does so via bidentate coordination. The resulting ring restricts the degrees of freedom in the compound so it can't undergo cis-trans isomerisation, closing off a route to rapid relaxation.

i) A compound like this could be used to detect metal ions such as Zn^{2+}. Because the amount of fluorescence depends strongly on the Zn^{2+} concentration, it could be used to measure the amount of the ion present.

Exercise 8.2.5:

a)

b) An orange complex would absorb blue light, its complementary colour.

c) A blue laser would work. Maybe somewhere around 476 nm.

d) Notice a Re(II) site results, because it has transferred an electron to the ligand.

e)

f) The reduction potentials (1.4 V > 0.3 V) suggest transfer from copper (I) to rhenium (II).

g) i) The carbonyl stretches would be observed somewhere around 2000 cm^{-1}.

iii) The electron transfer from the Cu(I) to the Re(II) site would result in a Re(I) site. The carbonyl stretch would shift to a lower wavenumber. That is because the lower oxidation state on the metal results in increased backbonding to the π-accepting carbonyls.

iii) At that distance, an outer sphere mechanism seems likely; it isn't clear how something could bridge that distance, other than the peptide chain itself, which probably lacks sufficient conjugation to conduct electrons.

h) Tryptophan acts as a stepping stone between copper and rhenium. Phenylalanine, with a higher reduction potential than rhenium, does not.

i)

Exercise 8.3.1:

a) $E = \frac{hc}{\lambda}$

$$E = \frac{(6.625 \times 10^{-34} Jsmol^{-1} \times 3.0 \times 10^{8} ms^{-1})}{(180nm \times 10^{-9} m\ nm^{-1})} = 1.10 \times 10^{-18} J$$

That's for one molecule. On a per mole basis, $E = 1.10 \times 10^{-18} J \times 6.02 \times 10^{23} mol^{-1} = 665000 Jmol^{-1} = 665 kJ\ mol^{-1}$

For comparison, the relatively strong and unreactive C-H bond in methane has a bond dissociation energy of only 440 kJ mol^{-1}. (That's a thermodynamic value; to actually break the bond would cost more input of energy, to get over the kinetic energy barrier for bond cleavage.)

b) $E = \frac{hc}{\lambda}$

$$E = \frac{(6.625 \times 10^{-34} J\ s\ mol^{-1} \times 3.0 \times 10^{8} m\ s^{-1})}{(476nm \times 10^{-9} m\ nm^{-1})} = 4.17 \times 10^{-19} J$$

That's for one molecule. On a per mole basis, $E = 4.42 \times 10^{-19} J \times 6.02 \times 10^{23} mol^{-1} = 251000 J\ mol^{-1} = 251 kJ\ mol^{-1}$

c) $E = \frac{hc}{\lambda}$

$$E = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{8} ms^{-1})}{(645nm \times 10^{-9} m\ nm^{-1})} = 3.08 \times 10^{-19} J$$

That's for one molecule. On a per mole basis, $E = 3.08 \times 10^{-19} J \times 6.02 \times 10^{23} mol^{-1} = 138000 Jmol^{-1} = 138 kJmol^{-1}$

Exercise 8.3.2:

a) $\lambda = \frac{1}{wavenumber} = \frac{1}{3105cm^{-1}} = 3.22 \times 10^{-4} cm \times 0.01m\ cm^{-1} = 3.22 \times 10^{-6} m$

$$E = \frac{hc}{\lambda}$$

$$E = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{8} ms^{-1})}{(3.22 \times 10^{-6} m)} = 6.17 \times 10^{-20} J$$

That's for one molecule. On a per mole basis, $E = 6.17 \times 10^{-20} J \times 6.02 \times 10^{23} mol^{-1} = 37000 J\ mol^{-1} = 37 kJmol^{-1}$

b) $\lambda = \frac{1}{wavenumber} = \frac{1}{1695cm^{-1}} = 5.90 \times 10^{-4} cm \times 0.01mcm^{-1} = 5.90 \times 10^{-6} m$

$$E = \frac{hc}{\lambda}$$

$$E = \frac{(6.625 \times 10^{-34} J\ s\ mol^{-1} \times 3.0 \times 10^{8} ms^{-1})}{(3.22 \times 10^{6} m)} = 3.37 \times 10^{-20} J$$

That's for one molecule. On a per mole basis, $E = 3.37 \times 10^{-20} J \times 6.02 \times 10^{23} mol^{-1} = 20000 Jmol^{-1} = 20 kJmol^{-1}$

c) $\lambda = \frac{1}{wavenumber} = \frac{1}{963cm^{-1}} = 1.04 \times 10^{-3} cm \times 0.01m\ cm^{-1} = 1.04 \times 10^{-5}$

$$E = \frac{hc}{\lambda}$$

$$E = \frac{(6.625\times 10^{-34} Jsmol^{-1}\times 3.0\times 10^{8}ms^{-1})}{(1.04\times 10^{-5}m)} = 1.91\times 10^{-20}J$$

That's for one molecule. On a per mole basis, $E = 1.91\times 10^{-20}J\times 6.02\times 10^{23}mol^{-1} = 11500Jmol^{-1} = 11.5kJmol^{-1}$

Exercise 8.3.3:

a)

b) Ru(bpy)$_3^{2+}$ would be a terrible reducing agent. The reduction potential of Ru(bpy)$_3^{3+}$ is very high. That means Ru(bpy)$_3^{2+}$ would not give up an electron very easily.

c) $\Delta G = -nFE^0$

$$\Delta G = -1\times 97485JV^{-1}mol^{-1}\times 1.26V = -123kJmol^{-1}$$

d) It absorbs in the blue part of the spectrum and appears orange.

e) It absorbs very strongly, so probably not d-d. It is probably MLCT, from the ruthenium to the π* in the bpy ligand

f) $E = \frac{hc}{\lambda}$

$$E = \frac{(6.625\times 10^{-34}Js\,mol^{-1}\times 3.0\times 3.0\times 10^{8}ms^{-1})}{(450nm\times 10^{-9}m\,nm^{-1})} = 4.42\times 10^{-19}J$$

That's for one molecule. On a per mole basis, $E = 4.42\times 10^{-19}J\times 6.02\times 10^{23}mol^{-1} = 266000Jmol^{-1} = 266kJmol^{-1}$

g) Ru^{2+} would be low spin d^6, a singlet ground state. The excited state will also be a singlet state.

h) 615 nm is in the orange region of the spectrum. This is light given off by the complex as it relaxes, so it is the colour we see.

i) $E = \frac{hc}{\lambda}$

$$E = \frac{(6.625\times 10^{-34}Jsmol^{-1}\times 3.0\times 10^{8}m\,s^{-1})}{(615nm\times 10^{-9}m\,nm^{-1})} = 3.23\times 10^{-19}J$$

That's for one molecule. On a per mole basis, $E = 3.23\times 10^{-19}J\times 6.02\times 10^{23}mol^{-1} = 195000J\,mol^{-1} = 195kJ\,mol^{-1}$

j) Stokes shift $= 615nm - 450nm = 165nm$

k) $\Delta E = E_1 - E_2 = 266 - 195kJ\,mol^{-1} = 71kJ\,mol^{-1}$

However, it would not be lost all at once, but in small increments equivalent to the differences between vibrational states.

l) If we were to reduce Ru(bpy)$_3^{3+}$ directly into an excited state, we would arrive at a state much higher in energy than the ground state. That reduction would be harder to accomplish. In this case, the ending state would be 195 kJ mol^{-1} higher than Ru(bpy)$_3^{2+}$.

$$\Delta G = 195 - 123kJ\,mol^{-1} = 72kJ\,mol^{-1}$$

$$E^0 = \frac{-\Delta G}{nF} = -\frac{(72kJ\,mol^{-1}\times 1000kJ\,J^{-1})}{(1\times 96485J:V^{-1}mol^{-1})} = -0.75V$$

m) The oxidation of Ru(bpy)$_3^{2+*}$ would be very favorable compared to the oxidation of Ru(bpy)$_3^{2+}$. The former is a much better reducing agent.

Exercise 8.5.1:

The longer the wavelength, the lower the energy. Photons of wavelength longer than 240 nm would not have enough energy to overcome the barrier for the dioxygen-cleaving reaction.

Exercise 8.5.2:

According to the Planck-Einstein relation:

$$E = h\nu$$

or, since $V = \frac{c}{\lambda}$

$$E = \frac{hc}{\lambda}$$

in which h = Planck's constant = 6.625 x 10^{-34} Js,

c = speed of light = 3.0 x 10^{8} m/s,

ν = frequency,

λ = wavelength.

a) $E = \frac{hc}{\lambda}$

$$E = \frac{(6.525 \times 10^{-34} Js)(3.0 \times 10^8 m/s)}{(200nm)(10^{-9} m/nm)}$$

$$E = 9.03 \times 10^{-19} J$$

b) $E = \frac{hc}{\lambda}$

$$E = \frac{(6.525 \times 10^{-34} Js)(3.0 \times 10^8 m/s)}{(325nm)(10^{-9} m/nm)}$$

$$E = 6.12 \times 10^{-19} J$$

Exercise 8.5.3:

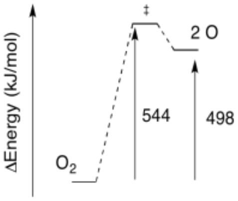
Remember, the mole is the conversion unit from the molecular scale to the macroscopic scale.

a) $E = (8.28 \times 10^{-19} J/photon)(6.02 \times 10^{23} photons/mol)$

$$E = 543770 \frac{J}{mol}$$

$$E = 544 \frac{kJ}{mol}$$

b)



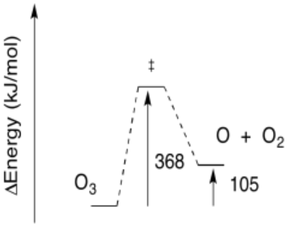
Exercise 8.5.4:

a) $E = (6.12 \times 10^{-19} J/photon)(6.02 \times 10^{23} photons/mol)$

$$E = 368146 \frac{J}{mol}$$

$$E = 368 \frac{kJ}{mol}$$

b)



Exercise 8.5.5:

The reactions must take the same pathway, and go over the same barrier, forward and back.

a) The reverse barrier: $E = 544 - 498\,\frac{kJ}{mol}$

$$E = 46\frac{kJ}{mol}$$

b) The reverse barrier: $E = 368 - 105\,\frac{kJ}{mol}$

$$E = 263\frac{kJ}{mol}$$

Exercise 8.6.1:

a. The original PDI has an absorption maximum at just under 500 nm. It absorbs blue-green, so it would be expected to appear red-orange.
b. The longest wavelength absorbed is approximately 625 nm.
c. $E = \frac{hc}{\lambda} = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{8} ms^{-1})}{625 \times 10^{-9} m} = 3.18 \times 10^{-19} J$

That's the energy of a photon. A mole of photons would have energy multiplied by Avogadro's number, N_A.

$$E = 3.18 \times 10^{-19} J \times NA = 3.18 \times 10^{-19} \times 6.02 \times 10^{23} mol^{-1} = 1.91 \times 10^{5} J\ mol^{-1} = 191 kJ mol^{-1}$$

d) If we approximate $E = \Delta G$, and given that $\Delta G = -NFE^0$

Then for this single-electron excitation, $E^0 = \frac{-\Delta G}{nF} = \frac{-1.91 \times 10^{5} J\ mol^{-1}}{(1 \times 96485 J\ V^{-1} mol^{-1})} = -1.97V$

e)

f) Given the structure of PDI, the transition is probably π --> π*.

g) The longest wavelength absorbed shifts toward the red, to about 700 nm, after dipping in acid. The energy of the transition is lowered to

$$E = \frac{hc}{\lambda} = \frac{(6.625 \times 10^{-34} Js\ mol^{-1} \times 3.0 \times 10^{8} m\ s^{-1})}{300 \times 10^{-9} m} = 2.84 \times 10^{-19} J$$

$$E = 2.84 \times 10^{-19} J \times NA = 3.18 \times 10^{-19} \times 6.02 \times 10^{23} mol^{-1} = 1.71 \times 10^{5} J\ mol^{-1} = 171 kJ\ mol^{-1}$$

h) These very flat molecules can probably stack very tightly together. The distance between the π electrons on one molecule and the π* orbital on a neighbouring molecule is very small. An intermolecular transition is possible.

i) What happens when the film is dipped in acid? It gets protonated. The anionic phosphate groups would become neutralized. The molecules would be able to stack even more closely together, lowering the energy required to excite an electron from one molecule to the other.

j) The onset of the reduction wave appears to be about -0.40 V, as shown by the peak in the cyclic voltamogram.

k)

l)

m) $E^0_{({}_{vs} Ag+/AgCl)} = E^0_{({}_{vs} NHE)} + 0.20V$ (i.e. the positive reduction potential of Ag+ vs. NHE indicates an electron is

i) $E^0_{({}_{vs} Ag+/AgCl)} = -0.10V + 0.20V = +0.10V$

ii) $E^0_{({}_{vs} Ag+/AgCl)} = +1.23V + 0.20V = +1.43V$

iii) $E^0_{({}_{vs} Ag+/AgCl)} = +0.83V + 0.20V = +1.03V$

n) The excited state can be reduced by placing an electron in the hole vacated by the excited electron. This level is 1.97 V below the conductance band in energy, which has a reduction potential of -0.40 V (its potential is 1.97 V more positive than the conductance band).

Thus, $-0.40V + 1.97V = +1.57V$.

o)

p)

q) The phosphates probably coordinate to the cobalt oxide, forming a bridge for electron transfer.

Exercise 8.6.2:

a. $\mathrm{Ag^+_{(aq)} + NO^-_{3(aq)} + Bu_4N^+_{(aq)} + Br^-_{(aq)} \longrightarrow AgBr_{(s)} + Bu_4N^+_{(aq)} + NO^-_{3(aq)}}$
b. They absorb in the violet-blue range and would appear yellow-orange.
c.
d. A nanometer is 10^{-9} m, whereas a picometer is 10^{-12} m. A picoparticle is 1,000 times smaller than a nanoparticle.
e.
f. They absorb across the visible spectrum and appear black.
g.

CHAPTER OVERVIEW

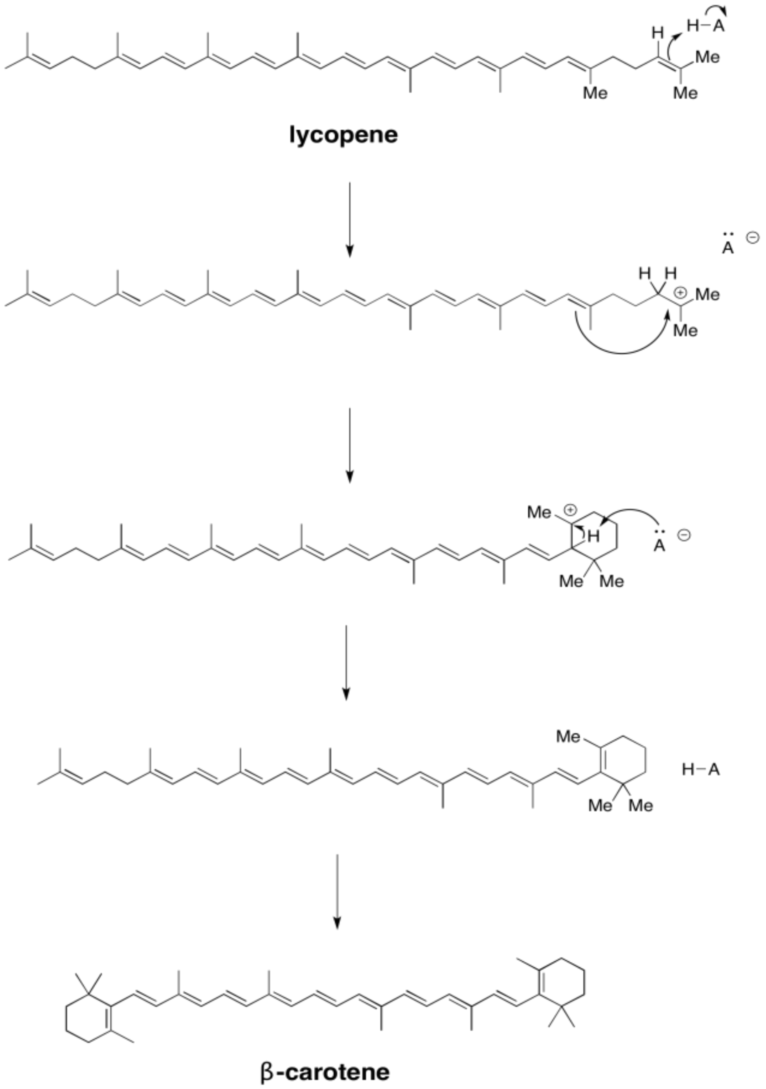
9: Photosynthesis

9.1: Solutions to Selected Problems

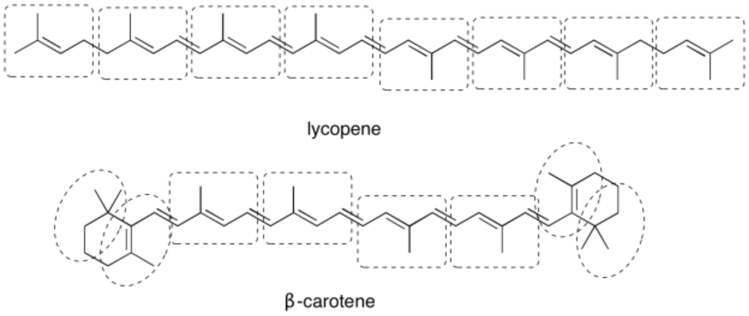
Exercise 9.2.1:

a. blue and red; green
b. green; red
c. blue; orange
d. violet

Exercise 9.2.2:

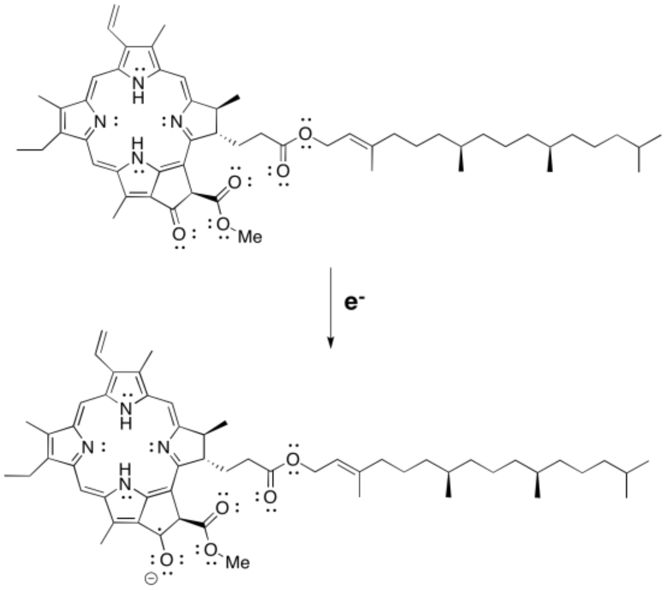


Exercise 9.2.3:



Exercise 9.3.1:

a)

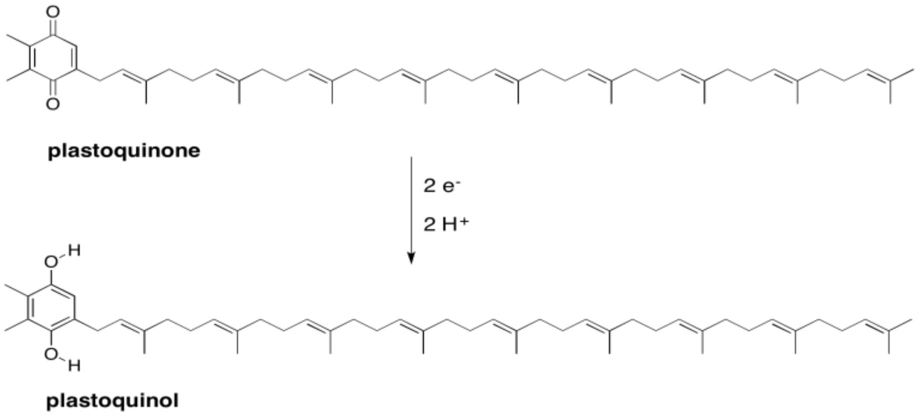


b)

Exercise 9.3.2:

Pheophytin b is probably more electrophilic because of the extra formyl (-HC=O) group. At first glance, it would be expected to have a more positive reduction potential.

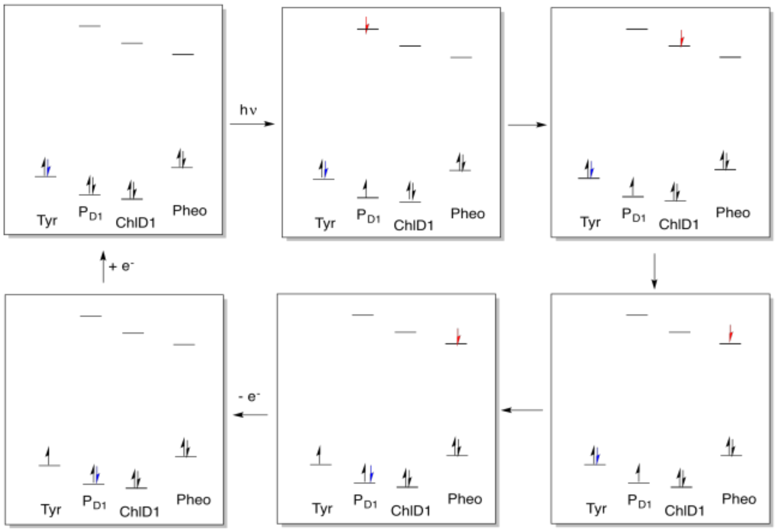
Exercise 9.3.3:



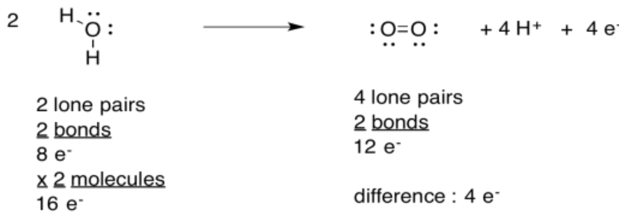
Exercise 9.3.4:

$$\Delta E = E^o(red) - E^o(ox) = 1.3 - 1.229V = 0.07V$$

Exercise 9.3.5:



Exercise 9.4.1:



Exercise 9.4.2:

a) Fe(II, III) active b) Mg(II) inactive c) Cu(I, II) active d) Li(I) inactive

e) Zn(II) inactive f) Sc(III) inactive g) Co(II, III) active h) Cr(II, III) active

Exercise 9.5.1:

The first pair of plastoquinols recycle two electrons between them, pumping two additional protons via a recycled quinol. The proton output is 1.5 times what it would be without the Q-loop (from 1 proton/electron + 0.5 proton/electron). Now remember that this recycled quinol also delivers two electrons, one of which is recycled. To get a second electron to generate a new recycled quinol, we would have to go through the entire, two-new-plastoquinol cycle again. We would get another two protons but it would have required eight electrons to get there, or 0.25 protons output per electron input. The proton output would rise to 1.75 times what it would be without the Q-loop (from 1 proton/electron + 0.5 proton/electron + 0.25 proton/electron). A series will result if we keep going. The series is 1 + 1/2 + 1/4 + 1/8 + 1/16 + ... + $1/2^n$, and it will converge to 2. Therefore, the Q-loop doubles the number of protons pumped across the membrane.

Exercise 9.5.2:

The major factor appears to be charge stabilisation. Suppose both iron atoms start as Fe(III). They have an overall 6^+ charge. The two sulfides are each 2^-, for an overall Fe_2S_2 core charge of 2^+. If ligated by four cysteines (Cys-S^-), then the overall charge of the coordination compound is 2^-. Addition of an electron will result in an increase in negative charge, to 3^-. Now, that was starting from the fully oxidised state. If instead we start in a mixed Fe(II/III) oxidation state, then addition of an electron results in a 4^- charge on the coordination complex. That charge buildup will be energetically difficult.

If ligated by two cysteines (Cys-S^-) and two neutral histidines, then the overall charge of the coordination compound is 0. Addition of an electron will result in a negative charge, 1^-. If instead we start in a mixed Fe(II/III) oxidation state, then addition of an electron results in a 2^- charge on the coordination complex. That lower charge buildup required in this case will be energetically less difficult.

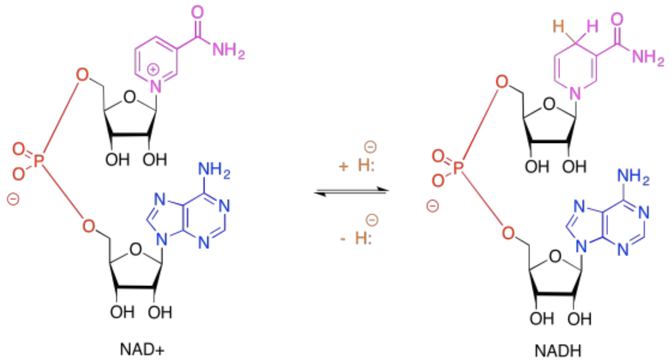
Exercise 9.5.3:

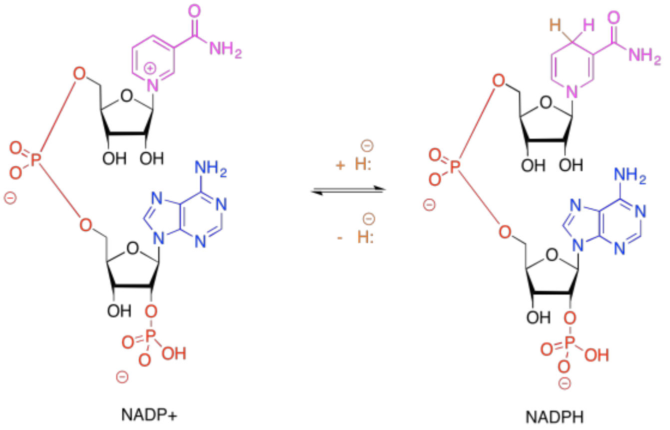
Copper is further to the right in the periodic table and is consequently more electronegative than iron. That is the major reason that copper is below iron in the activity series or metals. On that basis alone (and ignoring any differences in the coordination environment), we might expect a more positive reduction potential on a copper ion than an iron ion. Copper would therefore be a better electron acceptor, and would be useful in creating a greater driving force for electron transfer later in the electron transport chain.

Exercise 9.5.4:

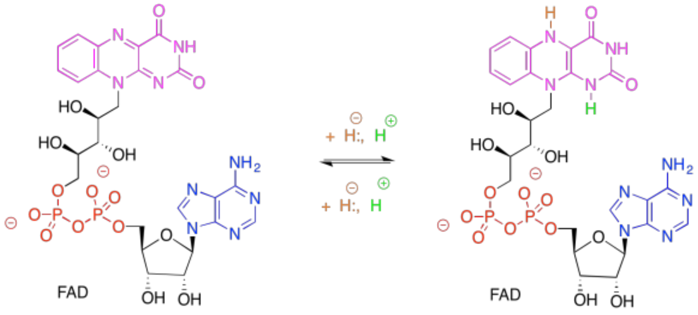
a. With only one anionic donor, the charge of the complex that contains Cu(II) would be 1^+.
b. With one anionic donor, the charge of the complex that contains Cu(I) would be 0.
c. Reduction of plastocyanin results in a decrease of charge, whereas reduction of the FeS cluster results in an increase of charge. That factor alone could make plastocyanin easier to reduce, with a more positive reduction potential.

Exercise 9.6.1:





Exercise 9.6.2:



Exercise 9.6.3:

Remember, NADP+, like NAD+, is solely a 2-electron oxidising agent. It can only receive a pair of electrons associated with a hydride. Ferredoxin, via an FeS cluster, can only give one electron at a time. An adapter is needed between these two carriers. FAD can accept either 1 or 2 electrons, proceeding to either FADH· radical (stabilised via extensive resonance delocalisation) or to FADH2.

Exercise 9.6.4:

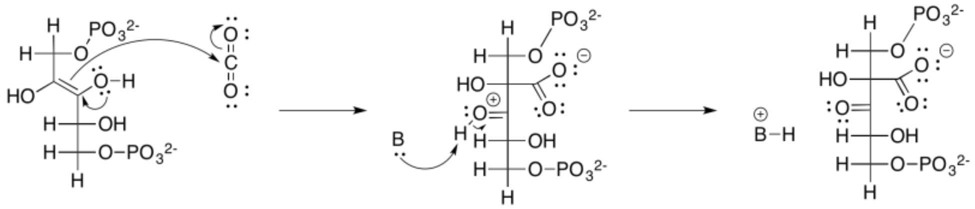
a. Releasing antennae molecules from the light harvesting complex in photosystem II would decrease both the number of photons captured and the number of electrons sent into the electron transport chain. Conversely, in a "chromophore pool" model, releasing these molecules from photosystem II would make them more available for uptake by photosystem I, resulting in greater absorption of photons there, and greater capacity to accept incoming electrons. If regulated, these two systems should be able to level out at an identical rate of photon absorption.
b. Kinases phosphorylate the hydroxy side chains in serine residues (and sometimes threonines and tyrosines). That covalent modification results in a change in the charge of the side chain from neutral to anionic. Significant conformational changes in the protein can be expected to result. It is likely that this conformational change results in looser binding of the antennae molecules in the light harvesting complex of photosystem II.

Furthermore, kinase appears to promote tighter binding of antennae molecules at photosystem I, presumable through a conformational change there. The result is a shift of these molecules from the available pool, such that additional chromophores become available in photosystem I and fewer are retained in photosystem II, until photon absorption at the two sites is equal.

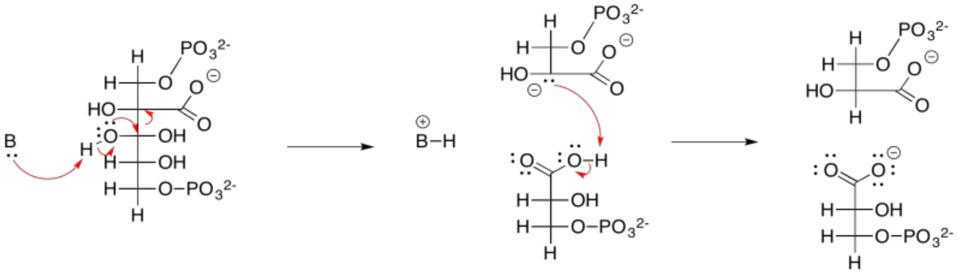
c) In fact, phosphatase, which is the complementary enzyme to kinase, is activated when photosystem I has high activity compared to photosystem I. Phosphatases remove phosphate groups from serines and related residues. The result would be tighter binding of antennae molecules at photosystem I and looser binding of antennae molecules at photosystem II, so that light absorption could be evened out between the two sites.

The use of phosphatases and kinases to effect opposite objectives in regulation is common in a number of biochemical systems.

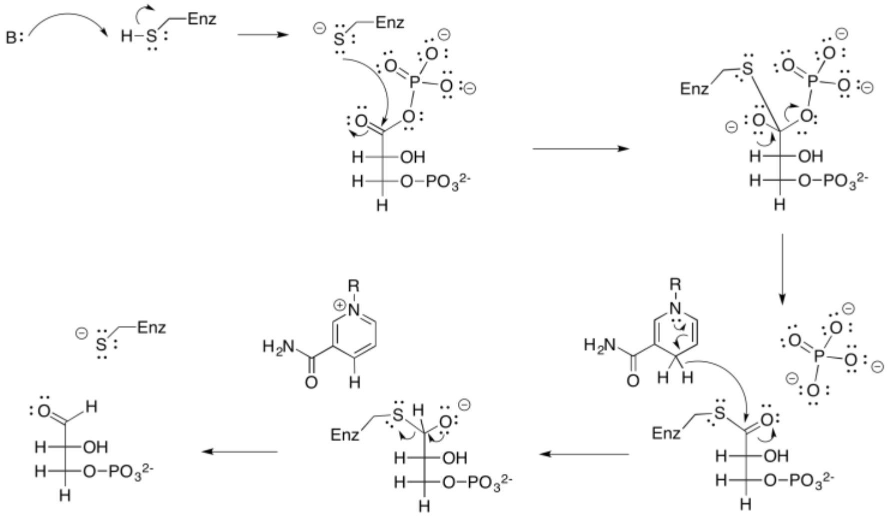
Exercise 9.8.1:



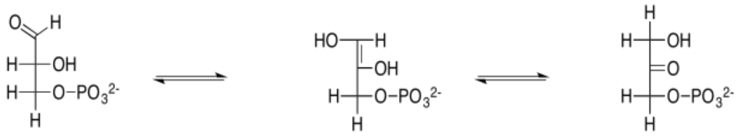
Exercise 9.8.2:



Exercise 9.8.3:



Exercise 9.8.4:



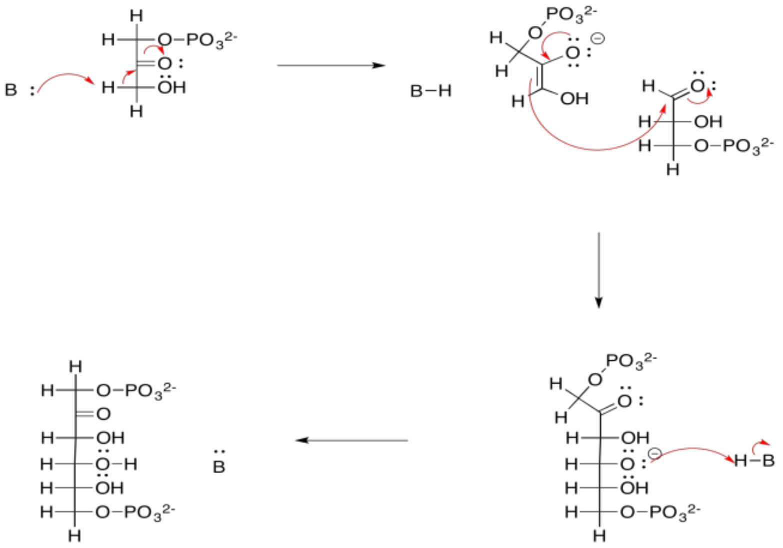
glyceraldehyde-3-phosphate

enol intermediate

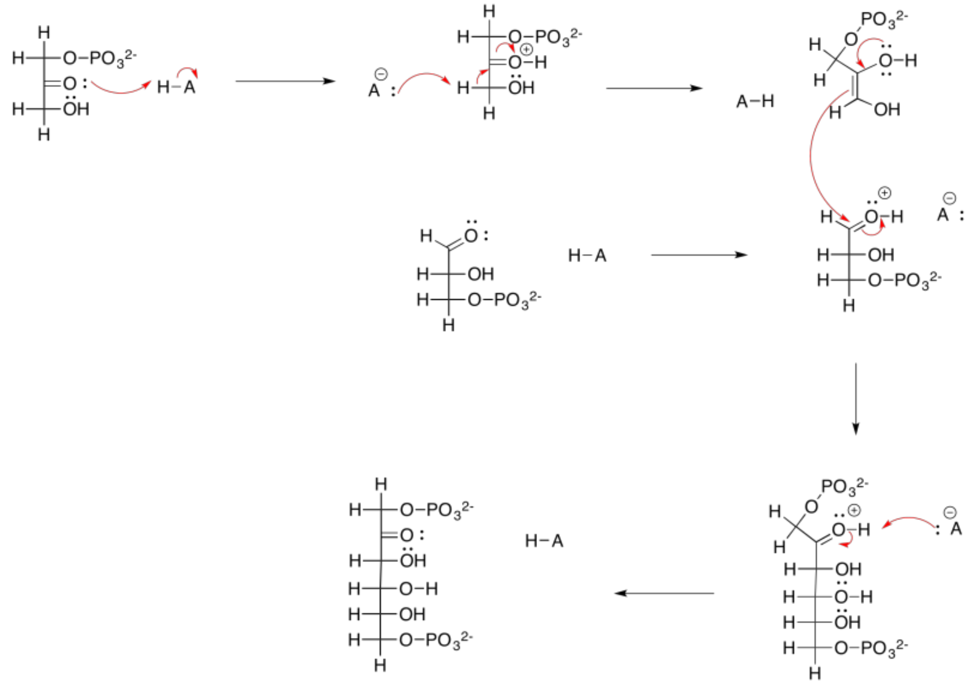
dihydroxyacetone phosphate

Exercise 9.8.5:

a)

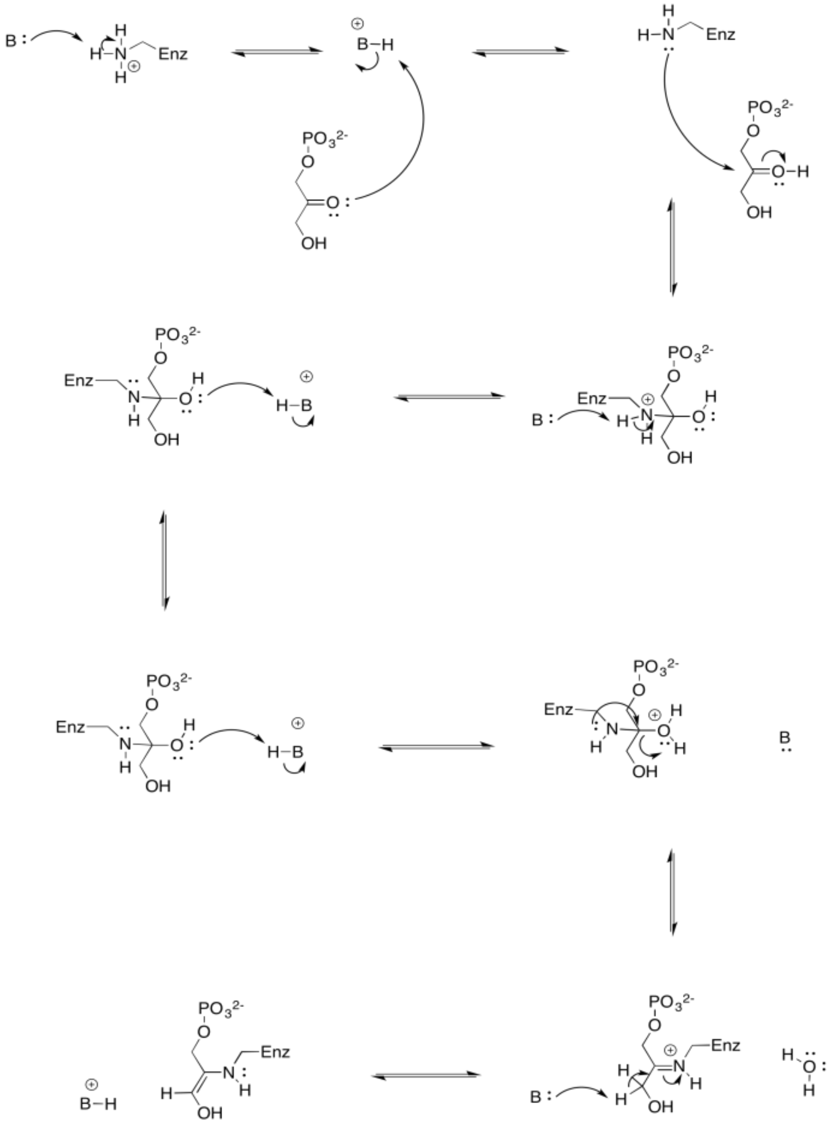


b)



Exercise 9.8.6:

a)



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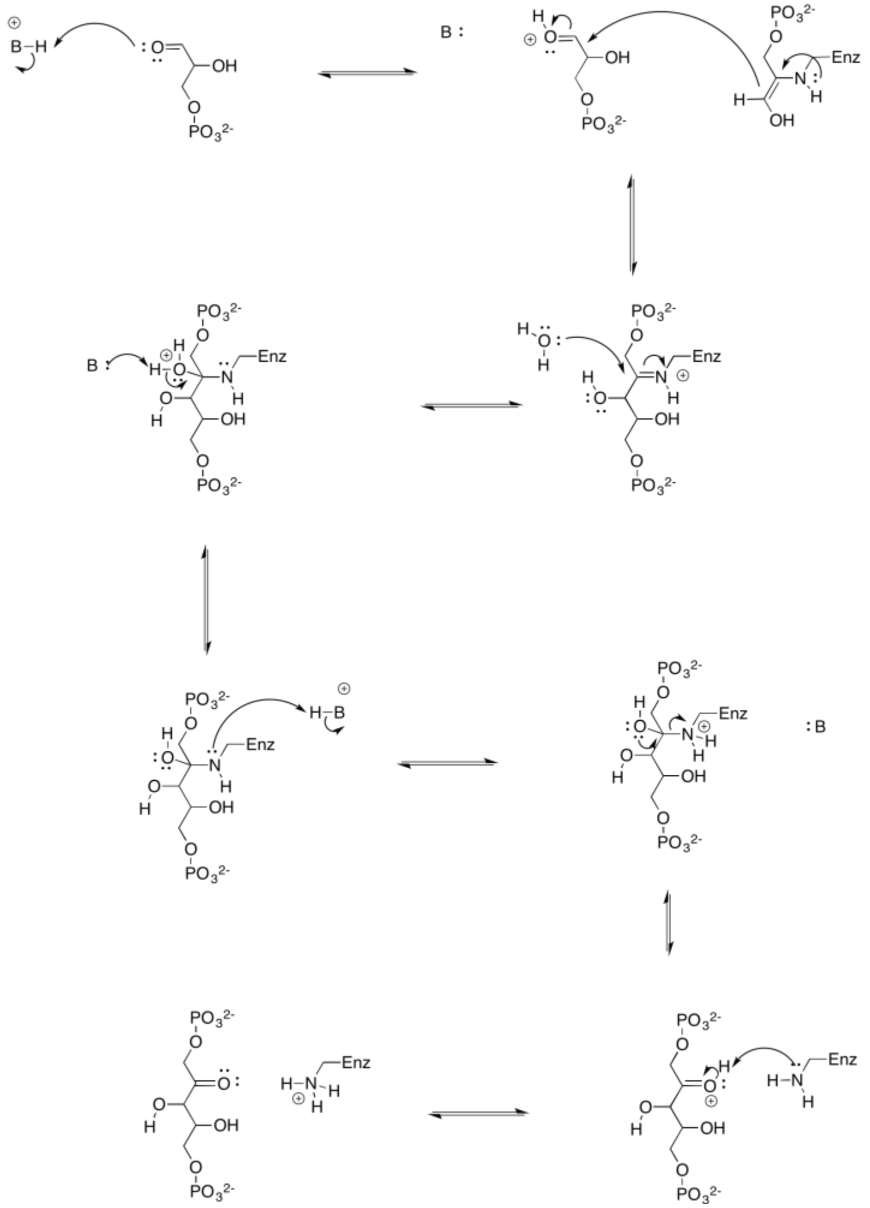
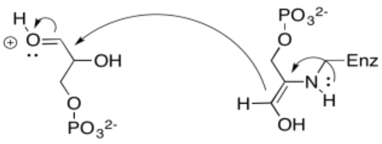
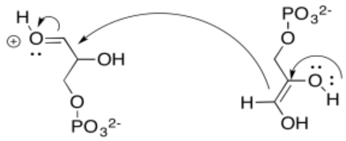


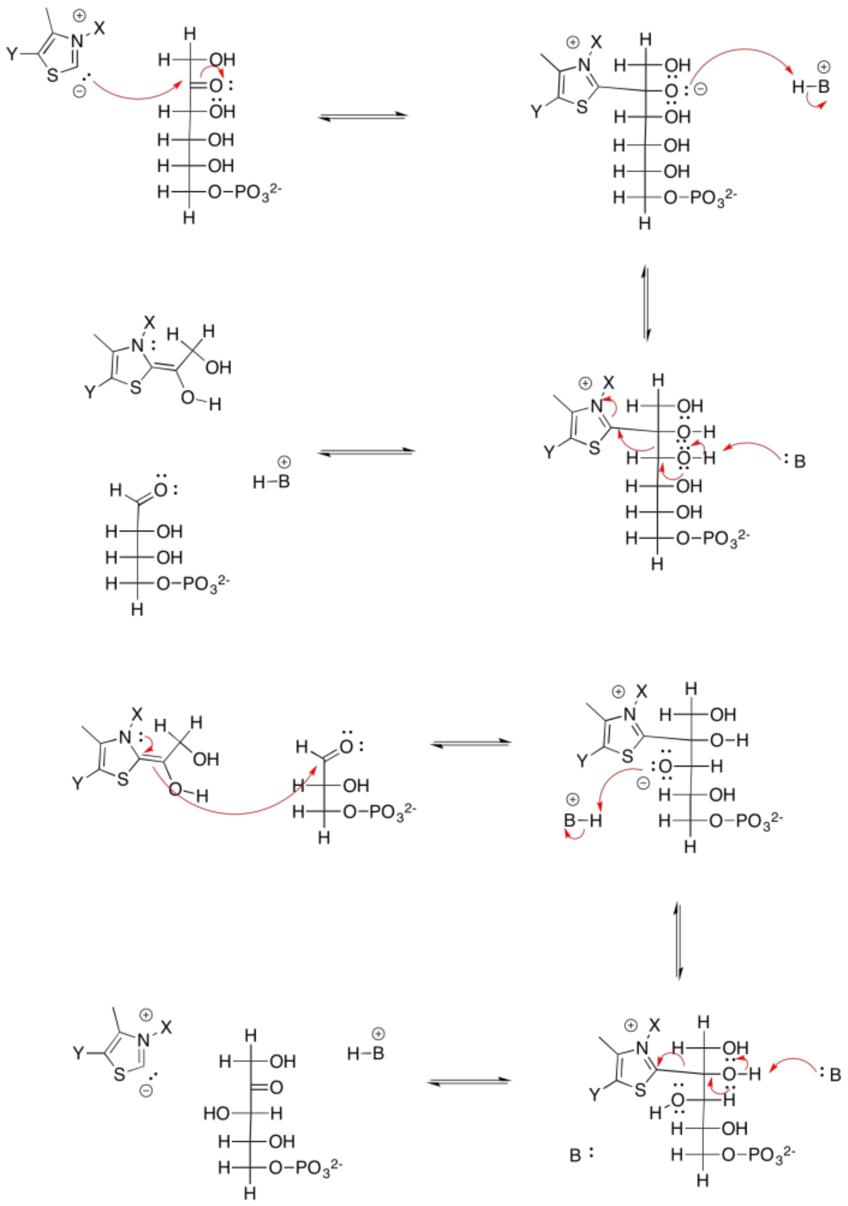
Exercise 9.8.7:

The regular enol pathway is driven by pi-donation from an oxygen atom. The enamine pathway is driven by pi-donation from a nitrogen. Nitrogen is less electronegative and a better pi-donor than oxygen, so the enamine pathway is faster.

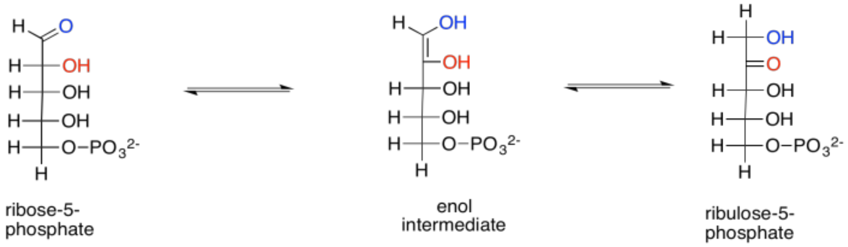




Exercise 9.8.8:



Exercise 9.8.9:

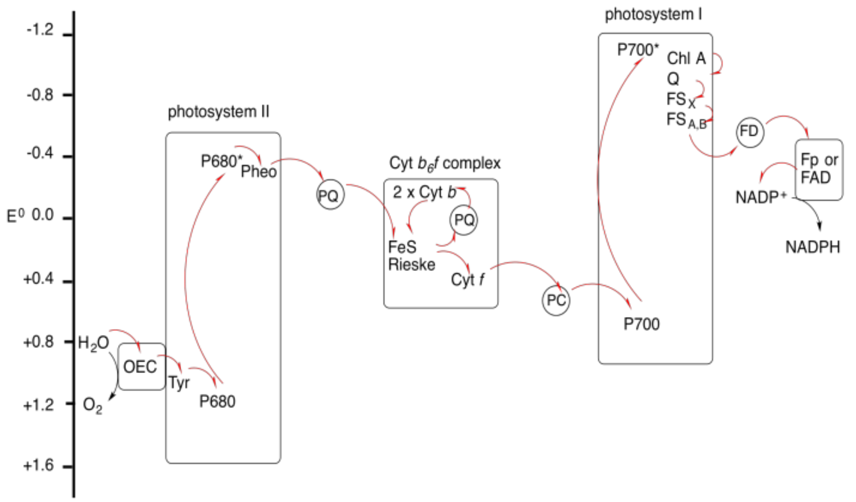


Exercise 9.8.10:

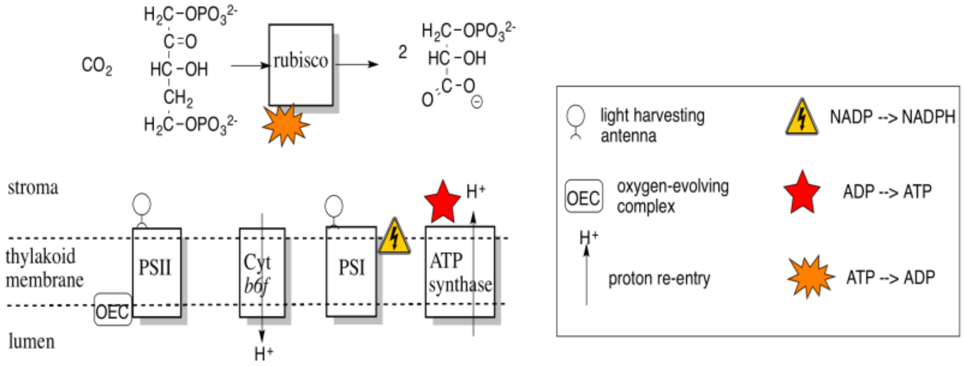
Reaction that are in equilibrium are often under substrate control. Because the enzyme can catalyse the reaction in both directions, the direction of the reaction driven by the enzyme is controlled by the relative amount of reactants on either side of the reaction. For example, if the xylulose concentration greatly increased, then the amount of xylulose bound by the enzyme would also increase, so the enzyme would shift xylulose into ribulose and thereby maintain equilibrium. If the ribulose concentration greatly increased, then more ribulose would be bound by the enzyme, and the ribulose would be converted into xylulose.

Exercise 9.9.1:

a)



Exercise 9.9.2:



9.2: Introduction to Photosynthesis

In biology, energy is needed in order to drive all sorts of biochemical processes. Energy is needed to stay alive. There are plenty of energy sources on earth. Tectonic forces release massive amounts of heat and drive the conversion of some minerals into gaseous products; for example, metal sulfides such as zincblende can be converted to gaseous hydrogen sulfide, H_2S. Sometimes, all that heat and gas finds its way to the earth's surface in the form of volcanoes. In the oceans, some marine organisms get their energy from gases released from volcanic vents, such as methane and hydrogen sulfide. However, sunlight is an even more abundant source of energy over most of the earth's surface. In photosynthesis, light energy is absorbed and used to make ATP. Remember, ATP is like a portable battery pack in biology; it can travel to different parts of a cell where it can be used to power uphill steps in biochemical reactions.

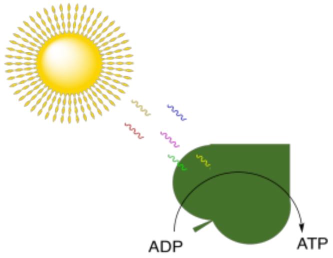


Figure 9.2.1: Absorption of photons from the sun is coupled to production of ATP, the biological battery pack.

Plants, algae, and some bacteria are capable of carrying out photosynthesis. They could get the immediate benefit of portable ATP molecules to drive biochemical reactions. However, the production of ATP in photosynthesis is also connected to carbon capture. Carbon dioxide from the air is incorporated into carbohydrate molecules. This conversion happens in a series of reactions called "dark reactions", because they keep happening even without sunlight. The carbohydrates can be stored, long-term, and later they can be used as energy sources via glycolysis and the citric acid cycle.

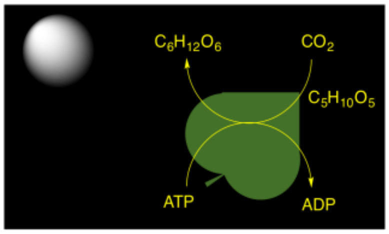


Figure 9.2.2: In photosynthesis, the ATP is diverted to carbohydrate production for long-term energy storage.

Animals, of course, benefit from this process indirectly because they can also use carbohydrates as a source of energy. The breakdown of carbohydrates releases energy through the usual trade-off: slightly weaker C-H and C-C bonds are broken and slightly stronger O-H and C-O bonds are made, meaning there is an overall release of energy. By eating plants, we can immediately access these carbohydrates without all the fuss of standing in the sun all day making them ourselves.

If you remember some basic plant biology, you may be familar with another aspect of photosynthesis. The "balanced reaction" for photosynthesis also involves the conversion of water to molecular oxygen, as follows:

$$6\,CO_{2\ (g)} + 6\,H_2O_{(l)} \longrightarrow C_6H_{12}O_{6(s)} + 6\,O_{2(g)}$$

Oxygen is a key player in oxidative phosphorylation, in which glycolysis and the TCA cycle are made even more efficient by boosting the amount of ATP produced for every glucose molecule broken down. Most organisms (including us) just can't survive without that extra ATP; we depend on plants for our survival in more ways than one.

But in contrast to what is suggested by the balanced reaction, the production of oxygen by plants is actually carried out separately from carbohydrate synthesis. Production of oxygen is actually part of the "light reaction", along with ATP synthesis.

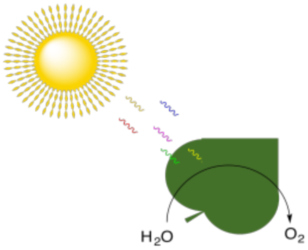


Figure 9.2.3: Photosynthesis is also associated with the production of molecular oxygen.

In photosynthesis, water is oxidised to produce molecular oxygen. Plants take the electrons that they have stripped from the water molecules and divert them into an electron transport chain. Energy harnessed by that electron transport chain is used to convert ADP to ATP. In oxidative phosphorylation, organisms (including plants) take electrons from NADH and succinate and divert them into an electron transport chain, eventually depositing them onto an oxygen molecule to make water. Energy harnessed by that electron transport chain is used to convert ADP to ATP.

That means we have two opposite processes that both are harnessed to produce ATP. In one process, the electrons run downhill energetically and are deposited on dioxygen to make water. That's oxidative phosphorylation. Photosynthesis is really oxidative phosphorylation running in reverse: the electrons start on water and proceed through an electron chain from there. But if oxidative phosphorylation runs downhill, then photosynthesis must run uphill.

That's where the light comes in. The light absorbed in photosynthesis is used to lift the electrons uphill in energy; from there, they can start rolling downhill through the electron transport chain, releasing energy along the way that can be harnessed for ATP formation.

All of these events take place in a special organelle in the plant called the chloroplast. Chloroplasts are a little bit like mitochondria, where the important metabolic processes such the TCA cycle and oxidative phosphorylation take place. Like mitochondria, chloroplasts contain their own DNA and ribosomes for protein production and they are passed on directly from mother cell to daughter cell. Chloroplasts have a double membrane and are filled with an aqueous medium called the stroma.

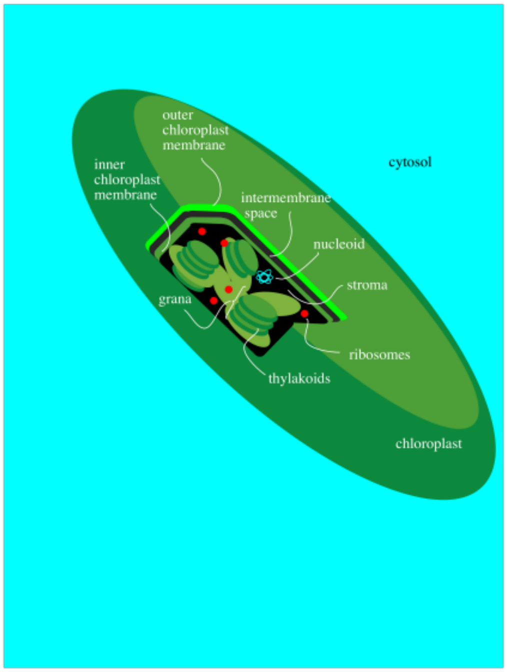


Figure 9.2.4: Simplified diagram of a chloroplast.

Within the chloroplast there are structures called thylakoids. A thylakoid is like a complex water balloon; it has a membrane and is filled with an aqueous medium called the lumen. Unlike a simple water balloon, though, the thylakoid has portions that are deeply folded, so that they look like discs stacked in layers. These portions of the thylakoid are called the grana. The regular, non-folded portions are called the lamellae.

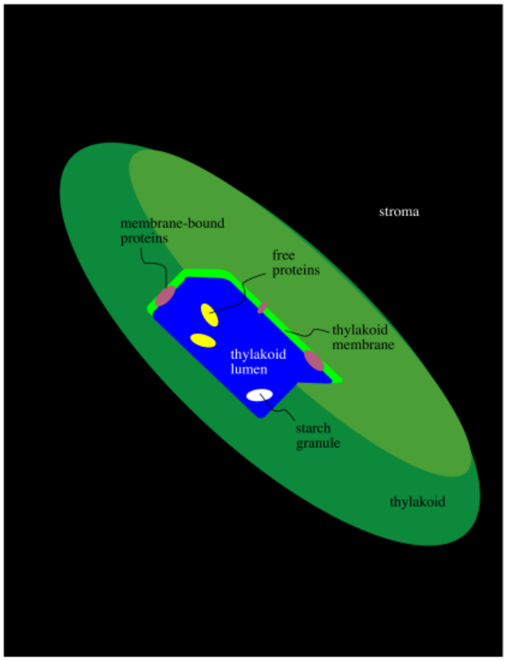


Figure 9.2.5: Simplified diagram of thylakoid structure.

The thylakoid plays a very important role in phtosynthesis. A group of protein complexes bound to the thylakoid membrane carry out the absorption of light energy, the conversion of water to dioxygen, and the production of ATP, as well as an electron carrier, NADPH. The ATP and NADPH are released into the surrounding stroma. A soluble protein in the stroma, called ribulose bisphosphate carboxylase (RuBisCo) captures carbon dioxide and covalently attaches it to a carbohydrate molecule. Other proteins then use the ATP and NADPH to reduce the carboxylate group (from the CO_2) into a regular part of the carbohydrate chain. In this way, rather than trying to knit six carbon dioxide molecules together into a glucose, the problem is simplified into just taking up one carbon dioxide at a time, adding it into a pre-existing sugar.

The ATP is produced by an ATP synthase, which is very similar to the complex used for the same purpose during oxidative phosphorylation. Just like the ATP synthase in the mitochondria, this one is driven by a proton gradient. The proton gradient is created through an electron transport pathway, just like the one in the mitochondria. In fact, many of the features of photosynthesis are pretty similar to oxidative phosphorylation. A crucial difference is that the electron transport chain in oxidative phosphorylation starts with NADH and ends with water, whereas in photosynthesis it is the reverse: the chain starts with water and ends with NADPH. The electron transport chain in oxidative phosphorylation is exothermic, running downhill in energy. The electron transport chain in photosynthesis would be endothermic, but can be sustained by the input of energy in the form of light.

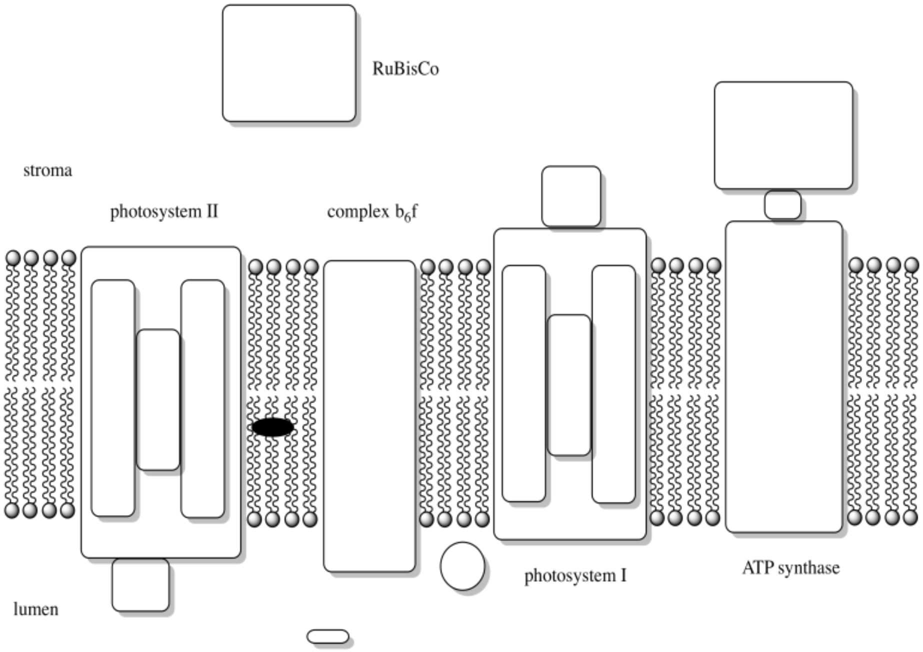


Figure 9.2.6: Simplified diagram of the major participants in photosynthesis.

See the section on photosynthesis at Henry Jakubowski's Biochemistry Online.

9.3: Photosystem II- Harvesting the Photons

It all starts with Photosystem II. Photosystem I comes later; the two complexes are named that way because Photosystem I was discovered before Photosystem II.

The picture below is a "cartoon rendering" of an X-ray crystal structure of photosystem II. So, researchers first took a solution of protein and somehow coaxed the protein molecules out of solution in the form of a crystal. In a crystal, the molecules are oriented in an organised array, so they are all lined up in a regular way. The researchers took the crystal and placed it in a beam of X-rays, then measured how the X-rays scattered when they hit the crystal. That scattering pattern was used to construct a three-dimensional map of the atomic positions in the protein. Because that is an awful lot of atoms, biochemists often present the map in different ways that are less complicated.

The cartoon rendering doesn't show where the individual atoms are, but it shows the locations of any alpha helices (pink) and beta sheets (yellow) as well as the chain formed by the rest of the protein that isn't organized in either of those ways (white). The parallel helices are typical of a membrane-bound protein; the top part of the structure can easily fit in among the parallel tails of the lipid bilayer that forms the thylakoid membrane.

Figure 9.3.1: Results from an X-ray crystal structure of photosystem II in the marine cyanobacterium *Thermosynechococcus elongatus*.[1]

The structure below is shown from the same point of view, but with the protein removed. You can see that the protein is holding lots of smaller molecules in place; it is packed full of them. That's in sharp contrast to the complexes of the oxidative phosphorylation pathway, where there were at most a half-dozen metal clusters, which were directly attached to the protein, and a couple of ubiquinones, which were free.

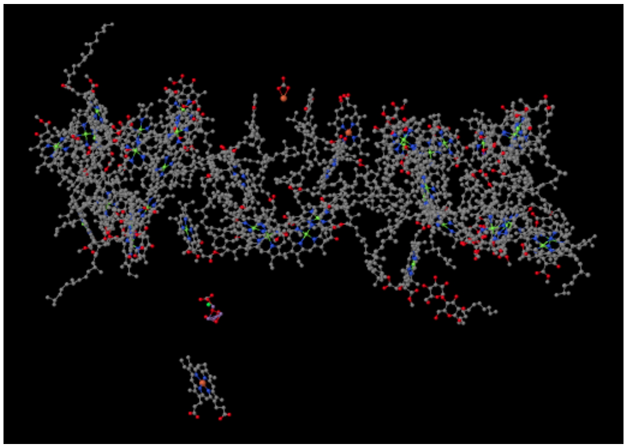


Figure 9.3.2: Results from an X-ray crystal structure of photosystem II showing ligands only (the non-protein part of the structure).[1]

We're going to take just a moment and focus on something interesting in the lower left part of that picture. The whole thing is interesting, of course, but this is something extraordinarily important to us as humans. Halfway between the big, tangled mass of molecules at the top and the single molecule at the bottom (a heme, in case you were wondering) there is a small blob of atoms. Some of the atoms are red (oxygen, in this case) and some are purple (manganese); there is also a grey one (calcium) and even a green one (probably a stray chloride ion that photobombed the structure). This is the oxygen-evolving complex. It's responsible for producing all of the molecular oxygen, O_2, on earth. Your life depends on it.

We'll get back to the oxygen-evolving complex in a later unit. Right now let's figure out what all those other molecules are doing in that scrum at the top of the picture, and why they are important. This is the light harvesting complex. Its job is to collect energy from sunlight and convert that energy into forms that the plant can use. Of course, somewhere along the line you learned in biology class that chlorophyll is what makes photosynthesis possible, and there are several chlorophyll molecules in the light harvesting complex. There are many different members of this family of molecules in nature, found in different organisms that can survive on sunlight: plants, algae, some plankton, a few bacteria. The chlorophylls commonly found in plants are chlorophyll a and chlorophyll b, shown below.

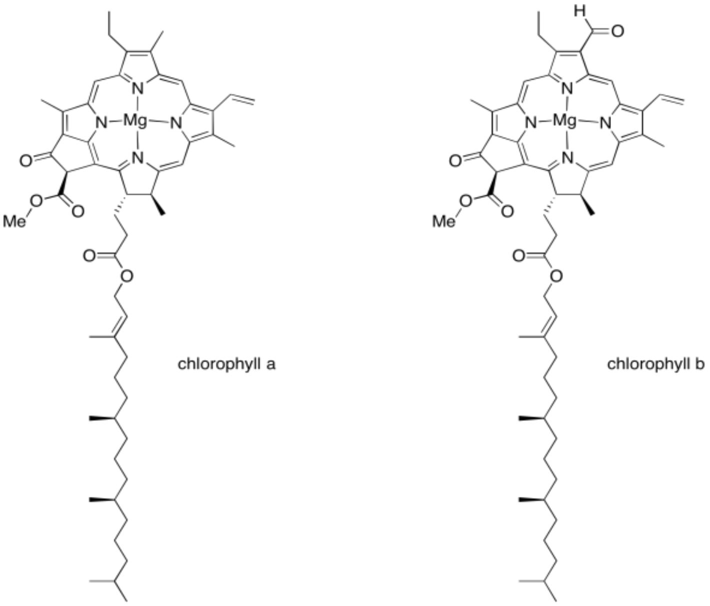


Figure 9.3.3: The two common types of chlorophyll found in plants.

A chlorophyll is an example of a porphyrin, like the one that forms the heme unit in hemoglobin. It has a flat, polycyclic structure composed of four nitrogen-containing pyrole rings. Those nitrogen atoms can bind metal ions such as iron (in hemoglobin, myoglobin, and various cytochromes) or, in this case, magnesium.

Why are there two different chlorophylls, though? There are even more if you count the variations that are common in organisms other than plants. It takes a great deal of energy for a cell to manufacture different molecules; wouldn't it be more efficient to just make one kind of chlorophyll?

The advantage of chlorophyll diversity can be seen in UV-Vis spectra of the different compounds. Chlorophyll a has a couple of absorption maxima around 430 and 660 nm; there are also some smaller absorption features near 410 and 600 nm.

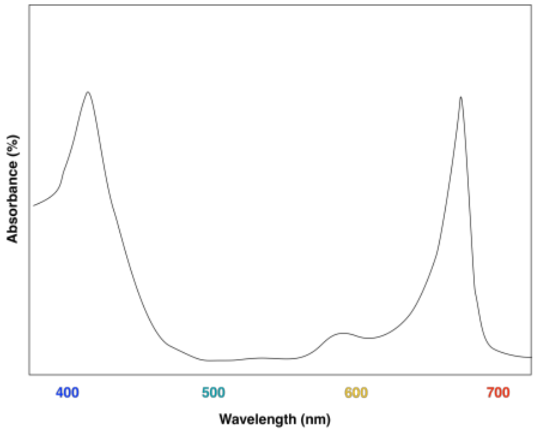


Figure 9.3.4: Artist's simulation of the visible light portion of a typical UV-Vis spectrum seen for chlorophyll a.

A look at the UV-Vis spectrum of chlorophyll b shows some strong similarities. There are still two major absorption maxima, near those for chlorophyll a, but they have shifted to about 450 and 640 nm.

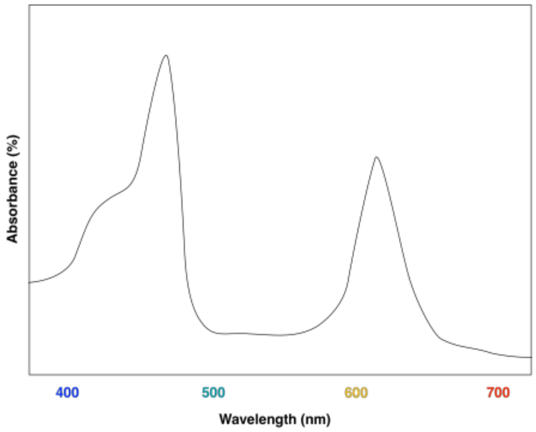


Figure 9.3.5: Artist's simulation of the visible light portion of a typical UV-Vis spectrum seen for chlorophyll b.

It probably isn't surprising that the two molecules have roughly similar UV-Vis spectra, since they have similar structures. Minor differences in the structures are responsible for subtle variations in energy levels of the donor and acceptor orbitals involved in the electronic transition, resulting in slightly different absorption maxima.

The combination of the two different chlorophylls would lead to a UV-Vis spectrum that looks a little like this one:

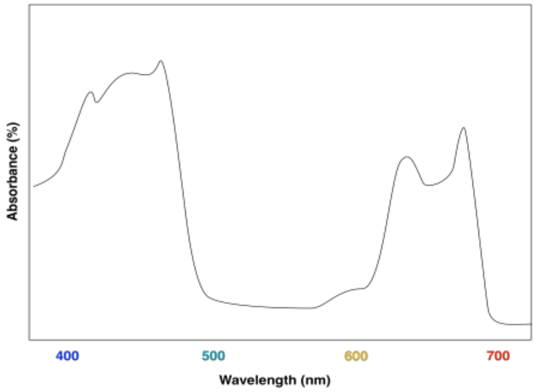


Figure 9.3.6: Artist's simulation of the visible light portion of a UV-Vis spectrum for a sample containing both chlorophyll a and chlorophyll b.

The effect is to harvest light from a slightly broader range of the visible spectrum. That makes for a more efficient process. Because sunlight contains wavelengths that range all across the visible spectrum (and beyond), the more of these wavelengths that can be captured, the more efficient photosynthesis can be.

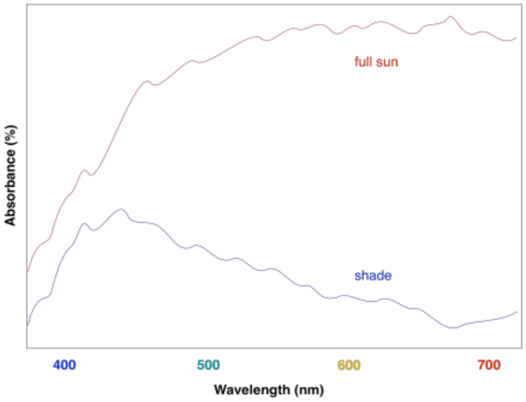


Figure 9.3.7: Artist's simulation of the UV-Vis spectrum of sunlight reaching the surface of the earth.

For this reason, the light harvesting complex contains more than one kind of chlorophyll, but it also contains other molecules. The most important class of these non-chlorophyll molecules includes the carotenoids. Compounds such as lycopene, β-carotene, and zeaxanthin are examples of carotenoids.

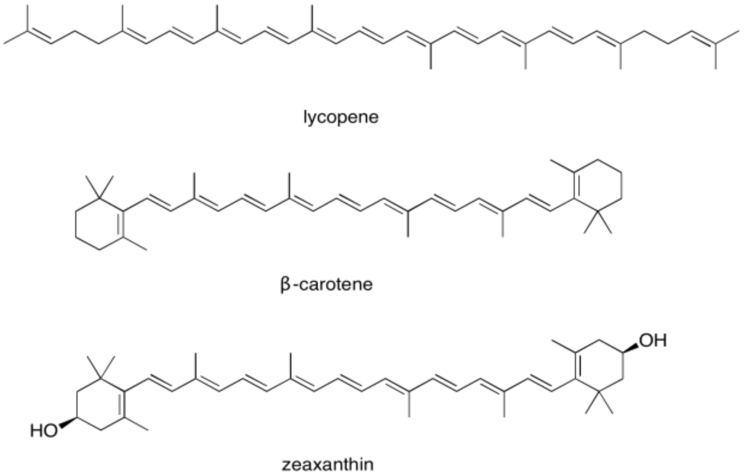


Figure 9.3.8: Some examples of carotenoids

These compounds help to further broaden absorption by the light harvesting complex. We can see how they might start to fill in the gap in the previous spectrum that was based only on chlorophyll content.

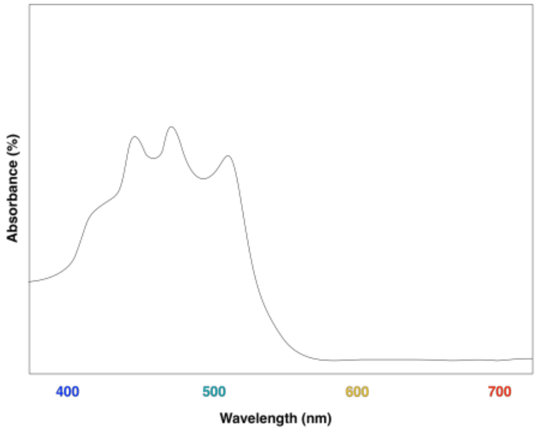


Figure 9.3.9: Artist's simulation of the visible light portion of a UV-Vis spectrum of lycopene.

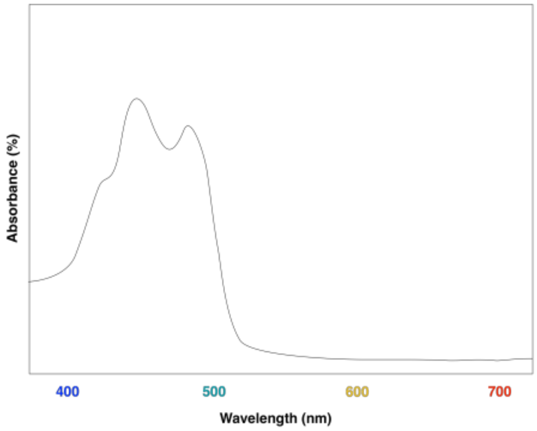


Figure 9.3.10: Artist's simulation of the visible light portion of a UV-Vis spectrum of β-carotene.

Overall, the result is a collection of molecules that can capture photons from across much of the visible spectrum, although not all. That's important, because solar radiation reaching the surface of the earth covers a broad range of wavelengths. Capturing as much light as possible increases the efficiency of the process. The fact that plants do reflect some visible light results in their green colour.

What next? All of that captured light energy needs to be converted into a different form; that's the whole point of photosynthesis. We aren't quite ready for that, though. The light harvesting complex just collects the light; the nearby reaction center is where the conversion process begins. You can think of the light harvesting complex as an antenna or as a funnel that sends energy to the reaction center, where the process of converting the energy into ATP (and, later, carbohydrates) will begin.

How does the energy get to the reaction center? It happens through a process of radiationless energy transfer. Once it absorbs the right amount of energy, the reaction centre will initiate an electron transport chain, much like the one that operated in oxidative phosphorylation. A photon doesn't need to strike the reaction centre itself, however, because it can strike any of the surrounding chromophores in the light harvesting complex. These molecules are all in close contact with each other, so it is relatively easy for molecules to collide and to transfer that entire amount of energy from one molecule to the next. During that transfer, the first molecule relaxes back to the ground state and the next molecule is excited into the excited state.

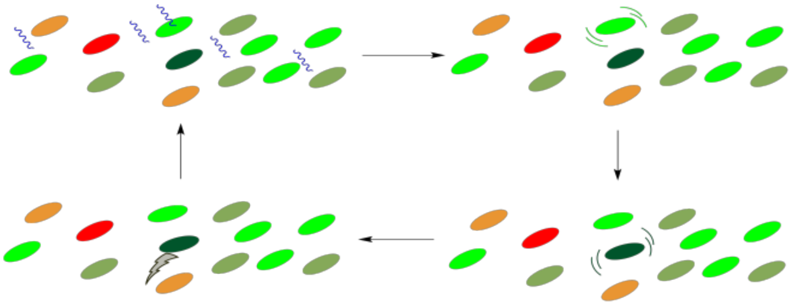


Figure 9.3.11: Cartoon showing photon collection and energy transfer to the reaction centre (dark green), where an electron transport chain begins

This process is very similar to photosensitization. In photosensitization, a molecule containing a chromophore, which can absorb a photon, transfers its energy to a second molecule, which has no chromophore and can't absorb light by itself. In the light harvesting complex, all of the molecules contain chromophores and could potentially absorb a photon. The point is that it doesn't matter which of them absorbs the photon; any of these absorptions will result in a cascade of radiationless transfers until the energy arrives at the right place. Once the energy reaches the reaction center, an electron transport chain will begin, and the energy released along this chain will be captured for the manufacture of ATP.

Conversely, it has been suggested that this array of molecules also affords protection to the cell. Under conditions in which the light intensity is too great, the reaction centre may become excited without an available outlet, as downstream participants in the pathway may not be ready to receive electrons. If that happens, a retro-mechanism may allow the reaction centre to relax once again, with energy dissipated to the surroundings through internal conversion.

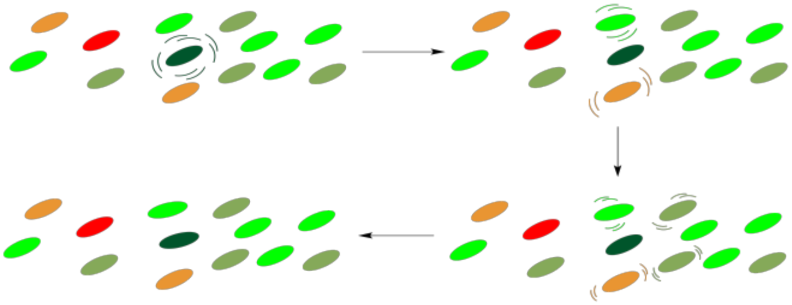


Figure 9.3.12: Cartoon showing energy dissipation through the light harvesting complex.

? Exercise 9.3.1

In general, if a compound has one main absorption in the visible spectrum, we see the complementary colour. If a compound has two main absorptions in different parts of the spectrum, we generally see the colour of the "trough" or dip in the spectrum between these absorption maxima.

a. What colour(s) correspond to the UV-Vis absorption maxima of chlorophyll a? What colour do we see when we look at chlorophyll a?
b. What colour(s) correspond to the UV-Vis absorption maxima of lycopene? What colour do we see when we look at lycopene?
c. What colour(s) correspond to the UV-Vis absorption maxima of β-carotene? What colour do we see when we look at β-carotene?
d. Zeaxanthin is an example of a xanthophyll; xanthophylls get their name from the Greek roots "phyllon" (leaf) and "xanthos" (yellow). What colour probably corresponds to the UV-Vis absorption maximum of zeaxanthin?

Answer a

a) blue and red; green

Answer b

b) green; red

Answer c

c) blue; orange

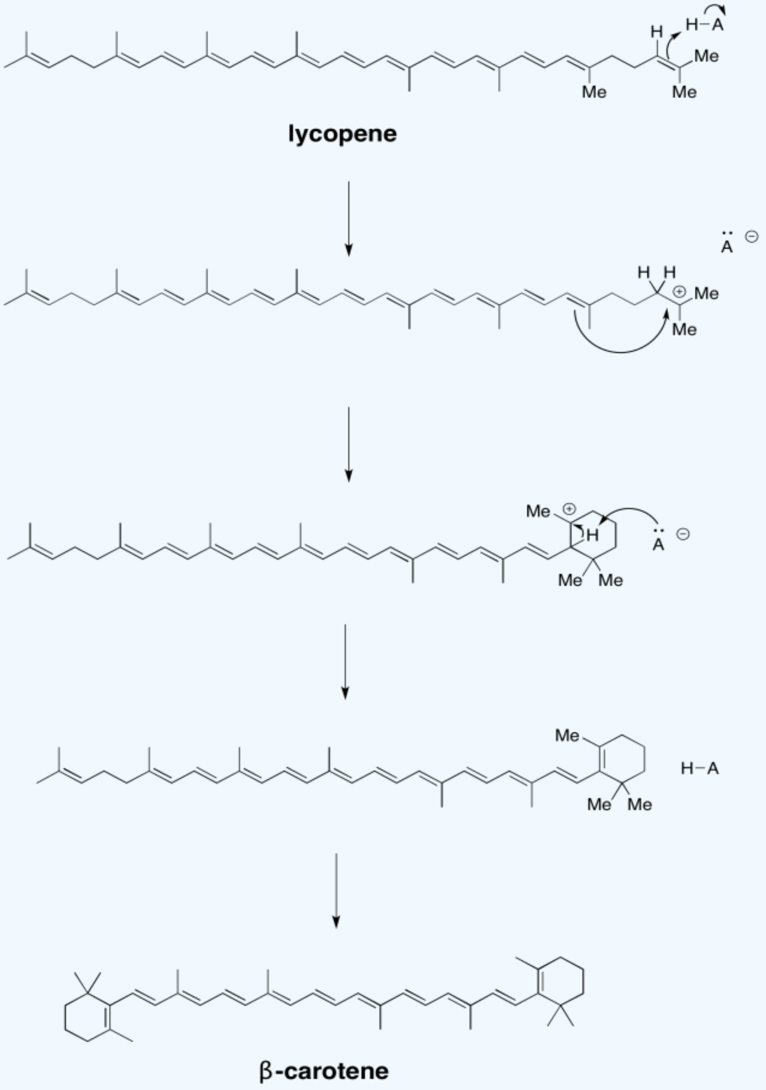
Answer d

d) violet

Exercise 9.3.2

The carotenoids are biosynthetically related to each other. Show how, in principle, lycopene could be converted to β-carotene via simple acid/base catalysis.

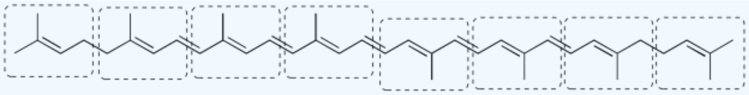
Answer



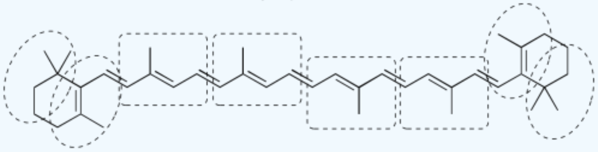
Exercise 9.3.3

The carotenoids are examples of an enormous class of natural products called terpenes. Terpenes can be thought of as oligomers formed from 5-carbon isoprene units. Show the location of the five-carbon units in lycopene and β-carotene.

Answer



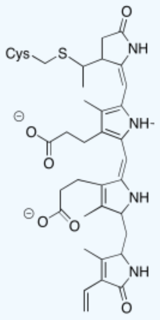
lycopene



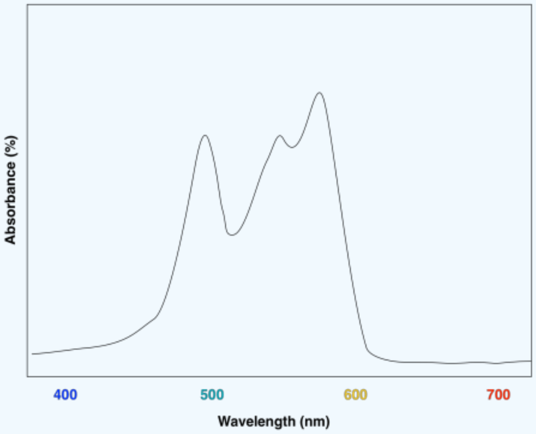
β-carotene

Exercise 9.3.4

Some marine algae contain phycoerythrin, a protein that is covalently linked to a unique chromophore. The chromophore structure and an artist's rendering of the UV spectrum are shown below.



phycoerythrin



a. What colours are absorbed by the chromophore?
b. What colour does the chromophore appear?
c. What is the evolutionary advantage that drives the algae to make this chromophore?

1. X-ray crystal structures: Ferreira, K.N.; Iverson, T.M.; Maghlaoui, K.; Barber, J.; Iwata, S. Architecture of the photosynthetic oxygen-evolving center. *Science* **2004**, *303*, 1831-1838. Images obtained via RCSB Protein Data Bank (1S5L).

9.4: Photosystem II- Electron Transfer

The goal of photosynthesis is to capture light energy from the sun and convert it into forms that are useful to the plant. The process begins in Photosystem II, where the light harvesting complex absorbs photons and relays that energy to the reaction centre, which can refer to a specific protein within photosystem II or, more specifically, to a pair of chlorophylls within that protein. What happens there?

The first goal of photosynthesis is the production of ATP. As in oxidative phosphorylation, that task is accomplished by releasing energy through an electron transport chain. In general, electrons need to be transferred from a position of high energy (or low potential) to low energy (or high potential). Photoexcitation helps that process because it leads to the formation of a low-energy hole as well as a high-energy electron.

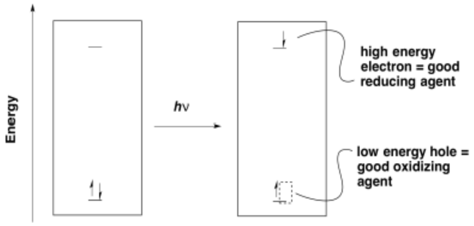


Figure 9.4.1: Electron hole-pair separation in photoredox processes.

Once an electron has been excited, it finds itself at a much higher energy level. It can easily slide downhill to a lower energy acceptor orbital. Note that the energy level of the acceptor orbital could be anywhere below the higher electronic level in the excited state. It could even be above the original electronic level in the ground state. That means that an electron transfer that would have been uphill if it occurred from the ground state would now be downhill from the excited state.

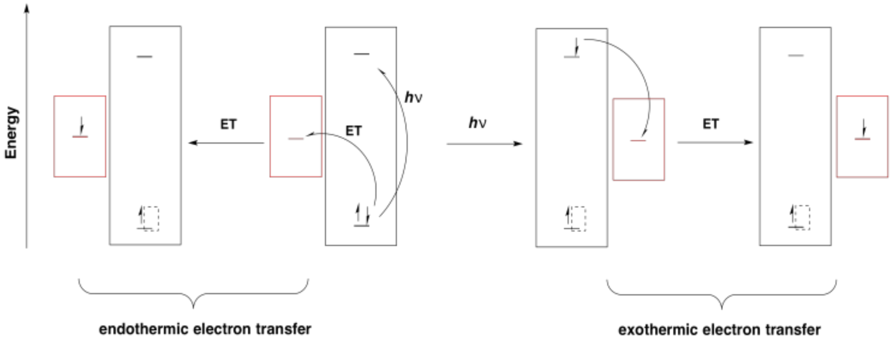


Figure 9.4.2: A ground state vs. excited state reductant.

Furthermore, any donor that is above the original electronic level in energy could drop an electron into the new hole. Without photoexcitation, electron donation would be much more endothermic.

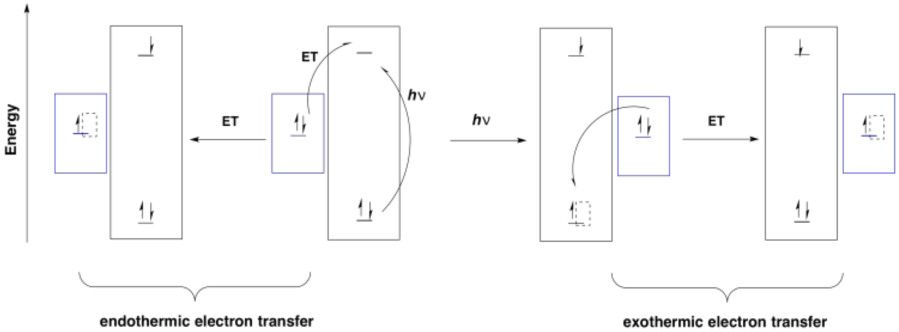


Figure 9.4.3: A ground state vs. excited state oxidant.

The reaction centre is sometimes referred to as P680, for pigment 680, so called because it has a UV-Vis absorbance maximum at 680 nm. It could absorb visible light directly, but more likely it is excited by transfer of energy from the surrounding antennae molecules in the light-harvesting complex. The reaction centre is actually composed of two pairs of chlorophylls. One of these pairs sits very near together; they are parallel to each other and overlapping so closely that they are practically touching. This special pair is called the chlorophyll dimer, and each individual chlorphyll within the pair is sometimes given the abbreviation P_{D1} or P_{D2}.

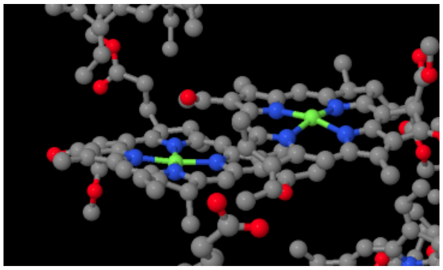


Figure 9.4.4: X-ray structure showing the chlorophyll dimer in the reaction centre.[1]

These two special chlorophylls form an excitonic dimer. That means that the two molecules behave as if they were only one molecule during a photochemical event. When a photon is absorbed, or the equivalent amount of energy transferred from another molecule, the excitonic dimer enters into an excited state in which an electron has been passed from one chlorophyll to the other.

$$P680 \rightarrow P680*$$

or

$$P_{D1}P_{D2} \rightarrow P_{D1}^{+}P_{D2}^{-}*$$

Why would that happen, from a biological perspective? Maybe the electronic separation simply makes one half a better reducing agent (it is negative) and the other half a better oxidizing agent (it is positive). Alternatively, that separation of the electron and the hole between two different molecules could lead to a more efficient photoredox process by making relaxation a little more difficult. Certainly the excited electron could recombine with the hole via the same pathway by which it was formed, with transfer of energy back to a surrounding molecule. Other relaxation pathways are less likely, however. It would be unlikely for the $P680^{-}*$ half to relax via a simple cascade through vibrational states since the electron would find no hole to drop into on that molecule.

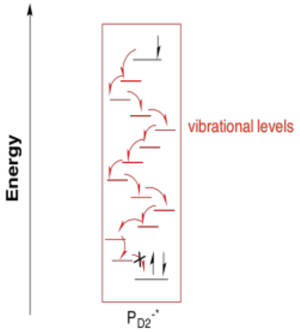


Figure 9.4.5: The pathway to relaxation of $P_{D1}^{-}*$ via internal conversion is blocked by lack of a hole.

Instead, the excited electron enters into an electron transport pathway. The electron is first transferred to a nearby chlorophyll a (ChlD1). From there, an immediate, rapid transfer to a pheophytin molecule follows. A pheophytin is really just a chlorophyll without a magnesium ion in the middle.

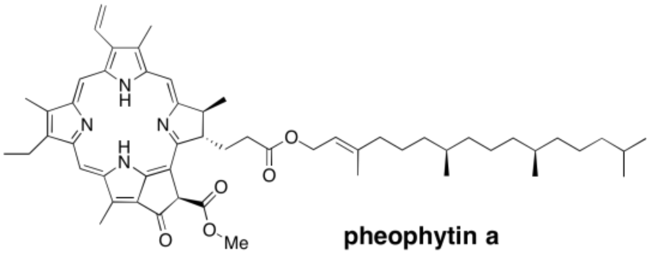


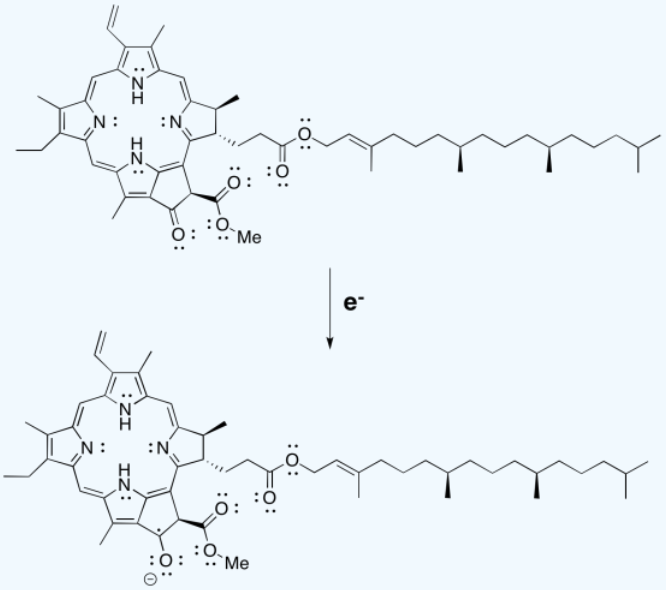
Figure 9.4.6: A pheophytin.

Exercise 9.4.1

Reduction of pheophytin results in a resonance-delocalised anion. Show one resonance structure of the radical anion:

a. with an oxygen-centred anion.
b. with a nitrogen-centred anion.

Answer a



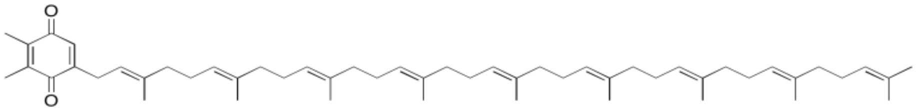
Exercise 9.4.2

Based on the structures of the analogous chlorophyll a and chlorophyll b, which would be expected to have a more positive reduction potential: pheophytin a or pheophytin b?

Answer

Pheophytin b is probably more electrophilic because of the extra formyl (-HC=O) group. At first glance, it would be expected to have a more positive reduction potential.

The subsequent destination in the electron transport chain is a plastoquinone. Like the related ubiquinones found in oxidative phosphorylation, plastoquinones are mobile, two-electron carriers. Mobile electron carriers are needed in order to transport electrons from one complex to another. The plastoquinones are also quite lipophilic, so their range of motion is restricted to the thylakoid membrane. That restriction boosts the efficiency of photosynthesis by making it unlikely for the transported electrons to be lost elsewhere in the cell.



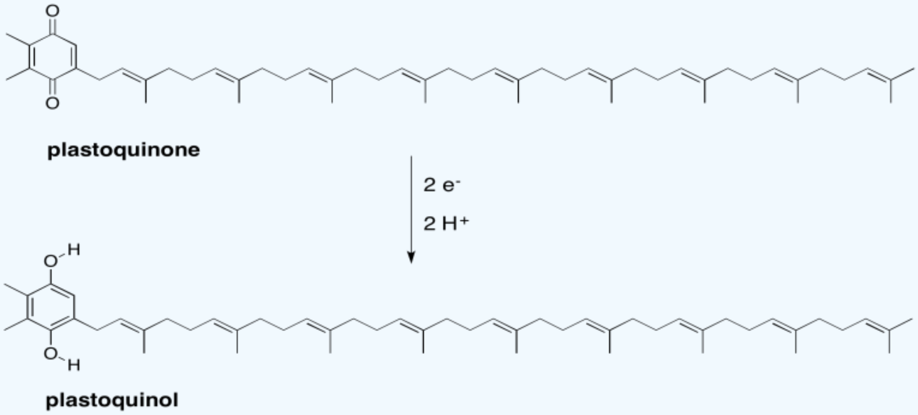
plastoquinone

Figure 9.4.7: Plastoquinone.

Exercise 9.4.3

Show the product of the two-electron, two-proton reduction of plastoquinone (plastoquinol).

Answer



There are actually two plastoquinones in the electron transport chain, however, and only the second one is mobile. The first one is covalently bound to the protein. The two plastoquinones have different reduction potentials, probably because of their environments, and so the first plastoquinone not only acts as a stepping stone to the second, but also allows for a more gradual loss of energy as the electrons rolls downhill. At this point, the second plastoquinol leaves photosystem II behind and travels to complex b6f, which will play an important role in ATP production via proton pumping.

We are not quite finished with Photosystem II, though. What happened to that hole that was left behind in the excitonic dimer? $P_{D2}{}^{+}*$ is pretty significant; it has been described as nature's most powerful oxidising agent. It needs to be: its job is ultimately to oxidise water to dioxygen. Remember, the opposite reaction, reduction of dioxygen to water, served as the final destination for electrons during oxidative phosphorylation. That exothermic half-reaction served as part of the driving force for the electron transport chain, the associated proton pumping, and ATP formation. To drive that reaction backward by stripping electrons from water will require a very strong oxidising agent.

In fact, the reduction potential of $P_{D2}{}^{+}*$ has been estimated at +1.3 V (vs SHE); that is quite positive. For comparison, the reduction potential of dioxygen under acidic conditions is +1.229 V (vs SHE).

Exercise 9.4.4

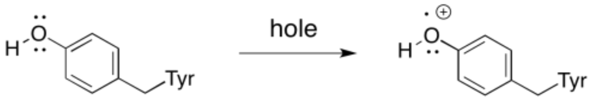
What is the reaction potential for the oxidation of water by $P_{D2}{}^{+}*$?

Answer

$\Delta E = E^o \text{ (red)} - E^o \text{ (ox)} = 1.3 - 1.229 \text{ V} = 0.07 \text{ V}$

In a sense, the reaction centre does not stand at the start of the electron transport chain at all. It is partway along; the real start of the electron transport chain is water. Electrons from water drop into the hole on $P_{D2}{}^{+}*$, forming a complete P680. The P680 absorbs a photon, sending the electron all the way up into $P_{D1}{}^{-}*$, and down they fall from there along the rest of the pathway. The reaction centre is like the engine on a ski lift or roller coaster, pulling in electrons and then sending them past to their next destination.

There are actually a couple of intermediaries between $P_{D2}{}^{+}*$ and the water, however. The nearest one is a tyrosine residue. It provides the electron that immediately replaces that which has been sent out of the reaction centre.



Scheme 9.4.1: Oxidation of tyrosine.

The next intermediary is the oxygen-evolving complex. The oxygen evolving complex is a manganese oxo cluster that strips electrons from water while, at the same time, combining them to make dioxygen.

We can summarise the events of photosystem II in a couple of ways. One way is to try to picture, roughly, how the different players involved so far are arranged in the protein complex. We can imagine how a photon is absorbed, and how that energy is passed along to the reaction centre. We can imagine a pathway for the electron through this system, too.

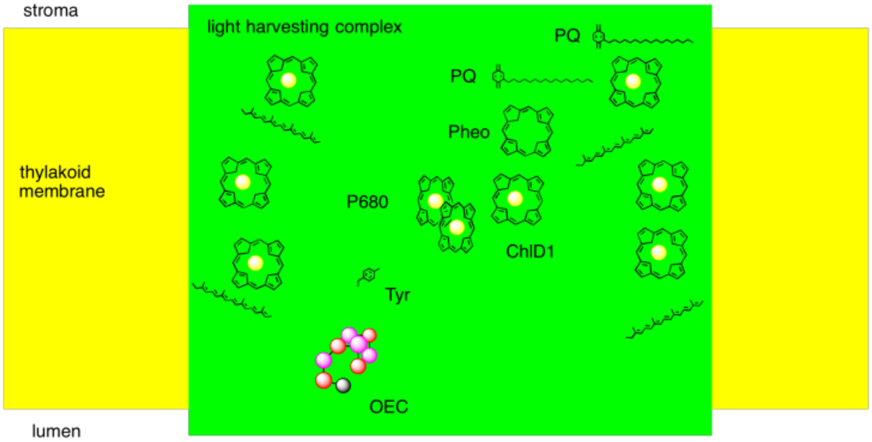


Figure 9.4.8: Simple diagram of some important elements of photosystem II.

Alternatively, it is useful to display these components not in physical space, but in energy or potential space. By looking at the reduction potentials of the species, we can start to imagine how the electron transport chain works, and we can see more clearly the role played by light absorption. The absorbed photon lifts the electron up from a low energy level (corresponding roughly to the reduction potential of $P_{D2}{}^{+}*$) to a much higher one (corresponding to the reduction potential of $P_{D1}{}^{-}*$). Furthermore, we can understand another reason why the electron does not simply relax back to the ground state after the reaction centre becomes excited: the electron is quickly carried downhill through another pathway, involving transfer to other molecules.

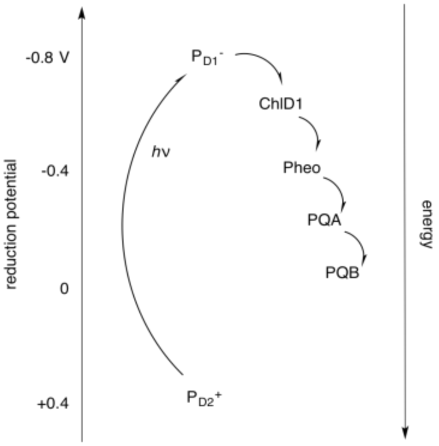
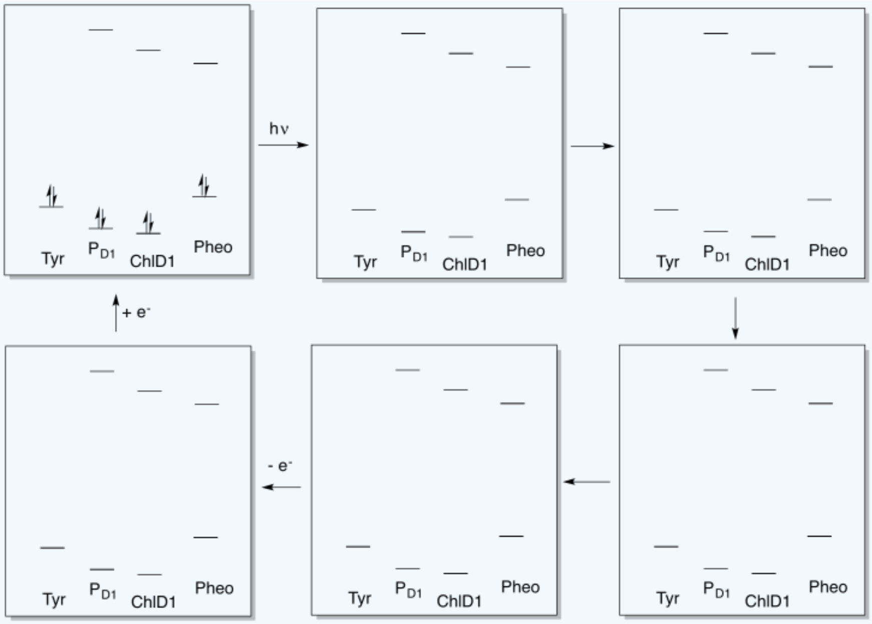


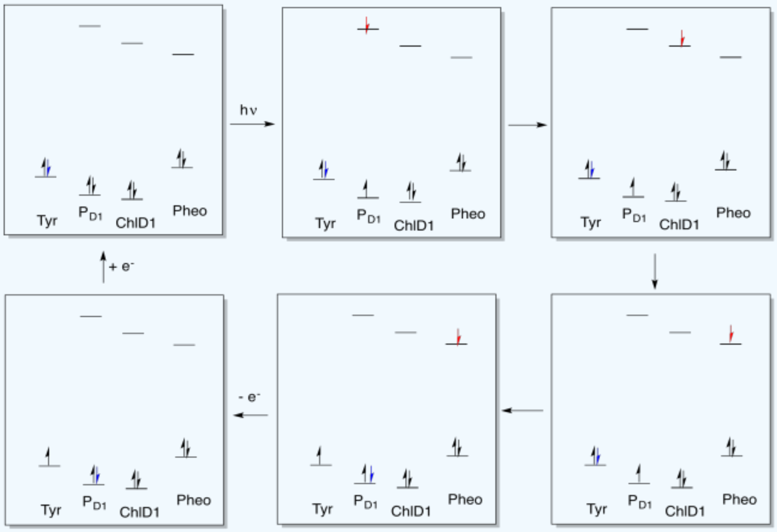
Figure 9.4.9: Diagram of some important elements of photosystem II and their reduction potentials.

? Exercise 9.4.5

The activity within photosystem II can be thought of as a catalytic cycle. Draw out the changes in electronic populations of the species below as a result of the sequence of events that starts with photon absorption.



Answer



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1. X-ray crystal structures: Deisenhofer, J., Epp, O., Sinning, I., Michel, H. Crystallographic refinement at 2.3 A resolution and refined model of the photosynthetic reaction centre from *Rhodopseudomonas viridis. J. Mol. Biol*. **1995**, *246*, 429-457. Images obtained via RCSB Protein Data Bank (1PRC).

9.5: Photosystem II - The Oxygen-Evolving Complex

You may recall that the oxygen-evolving complex is found deep in Photosystem II. It's found near that yellow-coded bundle of beta-sheets in the lower left of the picture below; that part of the complex is called the manganese-stabilizing protein. Remember, Photosystem II is embedded in the thylakoid membrane. The membrane surrounds the pink portion of alpha-helices in the top half of the picture. The stroma, the aqueous medium that surrounds the thylakoid, is at the very top of the picture. In the lower part of the picture, the protein is dipping its toes into the lumen; that's the watery medium inside the thylakoid.

Figure 9.5.1: X-ray crystallographic structure of photosystem II in the marine cyanobacterium *Thermosynechococcus elongatus*.[1]

When we strip away all of the proteins, we are left with a number of ligands that were embedded inside. That includes the light-harvesting complex that we have already looked at, as well as the small clutch of atoms called the oxygen-evolving complex (OEC). The OEC is found a little further down in the picture, at the edge of the lumen. You can see its manganese atoms, coloured purple in this picture, as well as red oxygens and grey calcium, mid-way down and a little to the left.

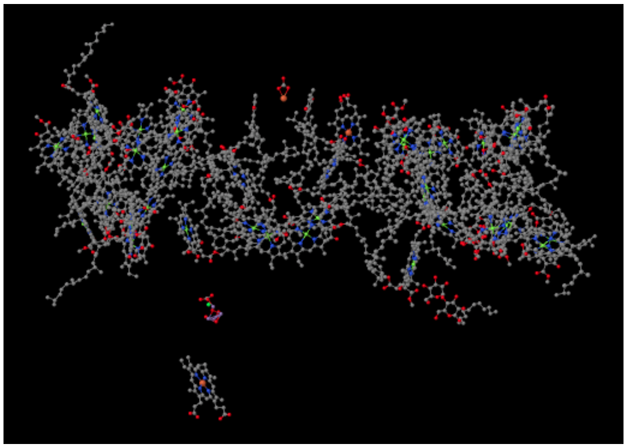


Figure 9.5.2: X-ray crystallographic structure of photosystem II, showing only the ligands.[1]

Let's zoom in for a closer look. A couple of stray atoms are visible in the picture, but focus on the atoms that are connected together. The "spokes" mean that the X-ray crystallography software has decided these atoms are close enough together that they are bonded to each other. The purple manganese atoms might not really be bonded to each other in terms of sharing a pair of electrons between the atoms, but they are magnetically coupled, sharing electrons in a different sense. We can see that the atoms almost form a cube, although it has one corner torn open. It's not unlike an FeS cluster, only with manganese and oxygen instead of iron and sulfur.

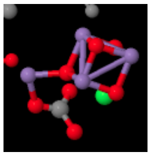
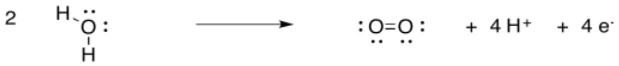


Figure 9.5.3: X-ray crystallographic structure of photosystem II: a close-up of the oxygen-evolving complex (in a different orientation from the figure above).[1]

The task of this little cube is to carry out a reaction that is indispensible for our existence on earth. It needs to convert water into oxygen. From an evolutionary point of view, there is a distinct advantage to the use of water as a source of electrons. There is an almost endless supply: we have oceans full of it on this planet. The trouble is, removing an electron from water results in an oxygen radical; in biochemistry, this is called a reactive oxygen species. Reactive oxygen species can be chaotic, evil characters inside a cell, reacting indiscriminately with any other structures that they contact. For that reason, it would be safer to oxidise the water all the way to dioxygen.

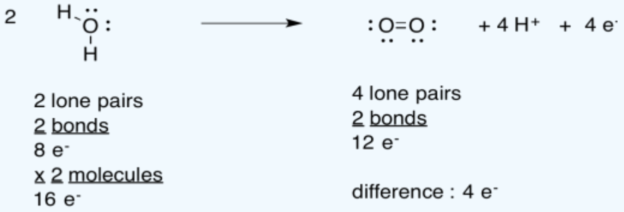


Scheme 9.5.1: The oxidation of water to dioxygen.

? Exercise 9.5.1

Use the Lewis structures to confirm the number of electrons involved in the oxidation of water.

Answer



That four-electron oxidation of water is a pretty challenging task. The opposite event, the four-electron reduction of dioxygen to water, served as the thermodynamic sink for the electron transport chain in oxidative phosphorylation. Nevertheless, it was also pretty challenging, because it required the rapid introduction of four electrons into the system in order to fully reduce the dioxygen to water, without the formation of free reactive oxygen species that might wreak havoc in the cell.

In that case, the problem was solved through a large number of iron and copper atoms within Complex IV, serving as a reservoir of electrons for rapid reduction. Furthermore, the actual site of reduction was a close-set iron and copper pair, allowing the dioxygen to bridge between two metals to aid in that rapid reduction.

The oxygen-evolving complex uses a similar strategy, but with a reverse bias. The cluster of manganes ions provides a reservoir of holes rather than electrons, allowing for the rapid oxidation of water to dioxygen. The role of the calcium ion is not clear, since calcium is not redox-active; it is always Ca^{2+}. Remember, metals in the first few columns of the periodic table are always found in their maximum oxidations states, corresponding to a noble gas configuration. However, it may play another role in binding water or stabilizing the cluster.

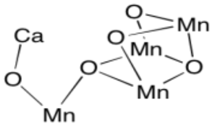


Figure 9.5.4: The oxygen-evolving complex (cluster only; coordinating amino acid residues neglected).

? Exercise 9.5.2

It can be useful to know which metal ions are typically redox-active and which are not (i.e. those metals that are always found in the same oxidation state). For the following metals, indicate whether the metal is redox-active and provide its most common oxidation state(s).

a) Fe b) Mg c) Cu d) Li

e) Zn f) Sc g) Co h) Cr

Answer a

a) Fe(II, III) active

Answer b

b) Mg(II) inactive

Answer c

c) Cu(I, II) active

Answer d

d) Li(I) inactive

Answer e

e) Zn(II) inactive

Answer f

f) Sc(III) inactive

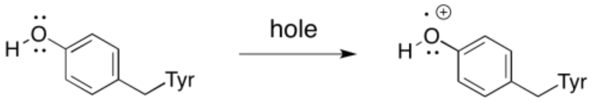
Answer g

g) Co(II, III) active

Answer h

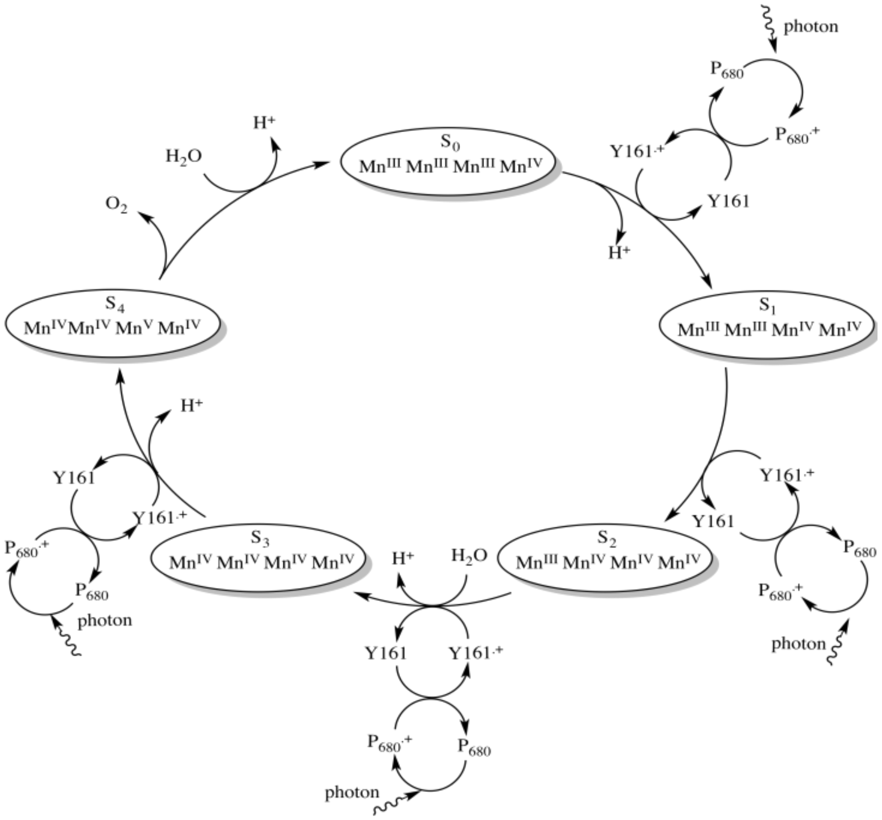
h) Cr(II, III) active

Remember that there is an intermediary between P680^{+}* and the oxygen-evolving complex. There is a tyrosine residue, called Tyr161 because of its position in the primary structure of the protein, situated between the oxygen-evolving complex and P680^{+}*. It conducts the electron from manganese to the chlorophyll in the reaction centre. An electron is first transferred from Tyr161 to P680^{+}*. An electron from manganese then replaces the missing electron on Tyr161.



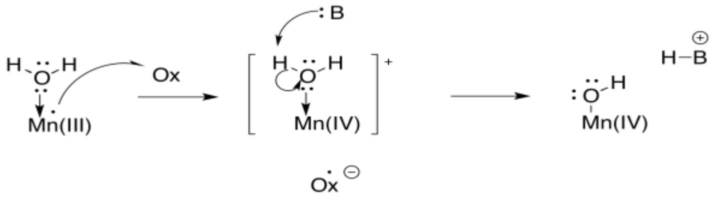
Scheme 9.5.2: Oxidation of tyrosine 161.

It takes the removal of four electrons to oxidise water to oxygen, so all of that has to happen four times. Four photons must be absorbed, exciting P680 four times. Each time, an electron from Tyr161 replaces the electron that was excited from the ground state in P680, leaving behind a hole. The electron in Tyr161 is replaced by an electron from manganese. These events are illustrated in an overall mechanism called the Kok cycle (pronounced "coke" cycle).



Scheme 9.5.3: The Kok cycle, relating photon absorption, manganese oxidation, and water oxidation.

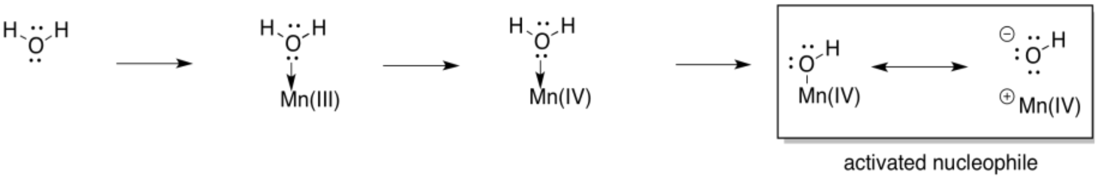
The Kok cycle illustrates the storage of holes on the manganese atoms. The holes are just the places where electrons used to be. We can think of them as a buildup of positive charge. The cycle also shows one of the steps in water oxidation that is evident in the equation for the reaction: the loss of four protons. The loss of protons is probably linked directly to the oxidation of the manganese ions. Any time an atom or molecule becomes more positively charged, it becomes more highly acidic.



Scheme 9.5.4: Deprotonation of a water molecule linked to manganese oxidation.

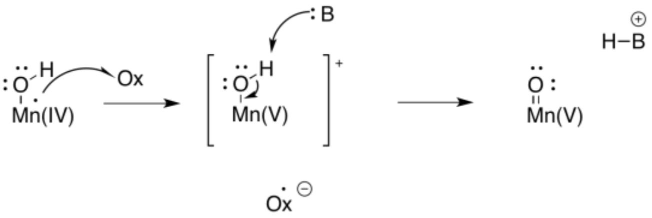
From the point of view of the water molecule, just binding to a manganese makes it more likely to lose a proton, because it is donating electrons to another atom and thereby taking on a formal positive charge on oxygen. So, a water molecule becomes much more acidic when it binds to a metal atom. That's a common event in biochemistry. The buildup of additional positive charge on manganese makes this deprotonation even more likely.

In terms of how the O-O bond is formed, different pathways are conceivable, but the simplest possibility involves activation of the water as a nucleophile. Deprotonation results in a hydroxide ion. Although the hydroxide is bound to the metal atom, the polarity of the bond allows the hydroxide to behave as a nucleophile.



Scheme 9.5.5: Metal binding and deprotonation activates water as a nucleophile.

At this point, you have also seen water become activated as a nucleophilic hydroxide ion in other biochemical pathways, so this development should not be a big surprise. What about an electrophile? Well, one way to provide an electrophile is to deprotonate the hydroxide to make a metal oxo. That deprotonation could be linked to another oxidation at manganese.

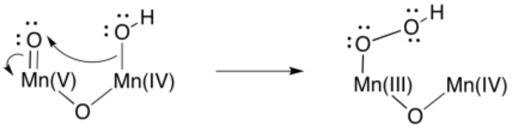


Scheme 9.5.6: Deprotonation of a hydroxy ligand, forming a metal oxo complex, linked to manganese oxidation.

Metal oxo compounds can develop electrophilic character at oxygen because of π-donation from oxygen to a metal ion in a high oxidation state. The donation of a lone pair to the metal would give oxygen a formal positive charge. The oxygen would be activated as an electrophile.

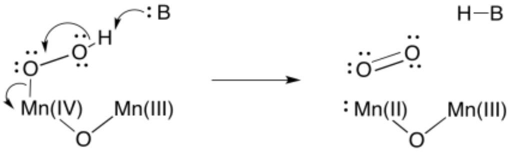
Scheme 9.5.7: π-Donation from oxygen in a metal oxo complex, showing electrophilic character on oxyge

At that point, it is easy to imagine how one oxygen (a hydroxy ligand) could act as a nucleophile while a second (an oxo ligand) acts as an electrophile. An O-O bond would form, accompanied by a two-electron reduction at manganese.



Scheme 9.5.8: A possible O-O bond-forming event, accompanied by manganese reduction.

Formation of a second O=O bond would result in a second two-electron reduction at manganese. In two easy steps, the entire four-electron reduction of manganese -- and four-electron oxidation of water -- has been accomplished. Because there are four manganese ions within the cluster, it is a simple matter to redistribute electrons so that the manganese ions have similar oxidation states.



Scheme 9.5.9: possible O=O bond-forming event, accompanied by manganese reduction

Of course, because we are dealing with a manganese oxo cluster rather than an individual manganese ion, electrons can be reshuffled at any time. Oxidation states in clusters are complicated, because of the ease of transferring or even delocalising electrons within the system.

Scheme 9.5.10: Electronic resorganisation within the manganese oxo cluster.

Again, there are other possible mechanisms, and you know enough chemistry at this point that you should be able to propose some alternatives.

? Exercise 9.5.3

a. Propose an alternative mechanism for oxygen evolution using classic organometallic mechanistic steps (oxidative addition, reductive elimination, insertion, beta-elimination).
b. What side products might be detected if this mechanism operated?

Exercise 9.5.4

a. Propose an alternative mechanism for oxygen evolution using radical mechanistic steps.
b. What side products might be detected if this mechanism operated?

One last point about the oxygen-evolving complex. The goal of photosynthesis is to make ATP; that ATP will be used to convert CO_2 to carbohydrates. The way to make ATP in this case is to use an electron transport chain to release enough energy to generate a proton gradient. The water is the starting point for that electron transport chain. But wait, there is a bonus: just by oxidising the water, we have released protons into the lumen. That's a head start on setting up a proton gradient.

1. X-ray crystal structures: Ferreira, K.N.; Iverson, T.M.; Maghlaoui, K.; Barber, J.; Iwata, S. Architecture of the photosynthetic oxygen-evolving center. *Science* **2004**, *303*, 1831-1838. Images obtained via RCSB Protein Data Bank (1S5L).

9.6: Adding a Proton Pump- Cytochrome b6f Complex

The goal of photosynthesis is to produce ATP, which is in turn used to produce carbohydrates through carbon capture. ATP is generated via a proton gradient, which in turn is maintained through an electron transport chain. The cytochrome b_6f complex is closely analogous to complex III in oxidative phosphorylation. It plays a major role in generating a protein gradient during photosynthesis.

An X-ray crystal structure of cytochrome b_6f is shown below. Once again, it is a membrane-bound protein. The stroma lies at the top of the picture and the lumen at the bottom.

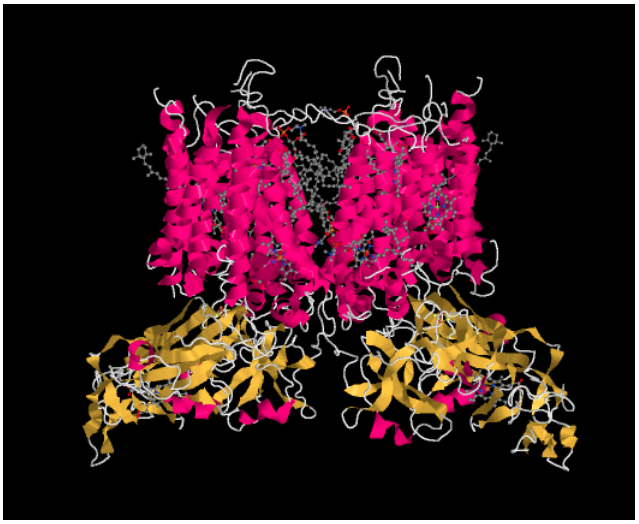


Figure 9.6.1: X-Ray crystallographic structure of cytochrome b_6f from the cyanobacteria, *Mastigocladus laminosus*.[1]

The ligand-only view of the structure is provided below. We can see a dimeric structure here, with the left half mirroring the right half. Near the bottom of each dimer, there is a heme. Just above that, we can see an FeS cluster; it is actually a 2Fe2S cluster, and specifically a Rieske cluster. That is just like the FeS cluster in complex III. Rieske clusters have very positive reduction potentials because of their unique coordination environment.

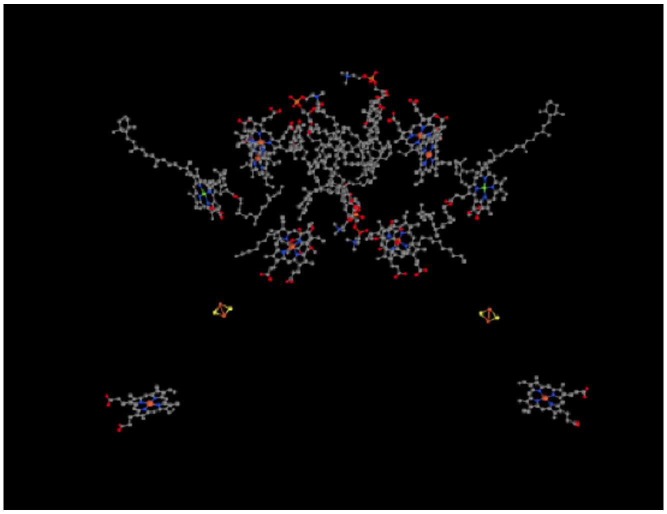


Figure 9.6.2: Ligand-only view of the X-Ray crystallographic structure of cytochrome b6f from the cyanobacteria, *Mastigocladus laminosus*.[1]

Above the Rieske clusters, things get a little more cluttered. There are a couple of more hemes on each side with their red iron atoms, as well as a chlorophyll with its magnesium shown in yellow. In addition, there are lots of terpenoid structures, such as carotenoids. Not all of these ligands have roles that are clearly understood, and we will focus on the bare essentials.

Cytochrome b_6f is shown in a simplified form in a diagram below. Onle one of the two units in the dimer is shown. Each unit is itself a relatively small complex, containing only four proteins: cyctchrome b_6, cytochrome f, a Rieske protein, and "subunit IV", whose role is not well understood.

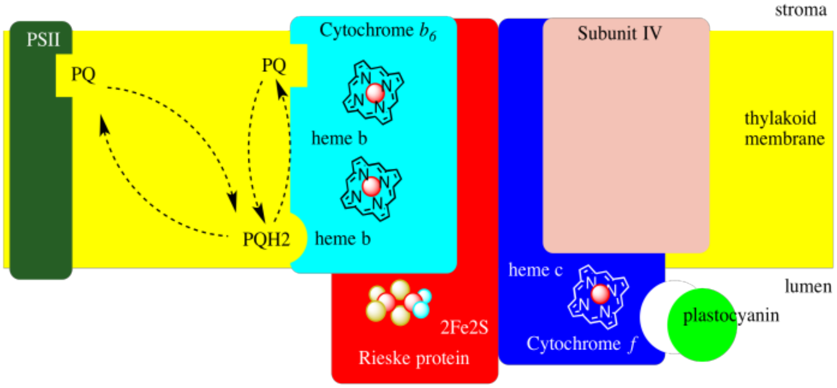


Figure 9.6.3: Simplified picture of some main features of cytochrome b6f. The picture shows a monomer only.

Photosystem II eventually produces a mobile plastoquinol which travels through the thylakoid membrane to cytochrome b_6f, binding near the lumen side of the membrane. The plastoquinone releases its two electrons and its two protons and can return to photosystem II for more. Alternatively, the plastoquinone might just travel across to the stroma side of the mebrane, where it can pick up two new protons from the stroma as well as two more electrons.

Where do the two electrons come from? They are recycled in the "Q-loop". When it arrives at cyctochrome b_6f, instead of sending both electrons along the electron transport chain, the plastoquinone only sends one electron in that direction. That first electron travels to the Rieske FeS cluster, then to a cytochrome f (that's a cytochrome b found in plants), and finally to a soluble, mobile electron carrier, plastocyanin.

The other electron travels in the other direction, back toward the stroma, via a pair of hemes. After two plastoquinols have delivered their electrons to cytochrome b_6f, a waiting plastoquinone can be reduced again to plastoquinol, picking up two more protons from the stroma. That plastoquinol can then travel back across the membrane to deliver its two protons to the lumen. One of its electrons gets sent down the electron transport chain, and the other electron gets recycled (again).

The advantage of the Q-loop is explained in the following diagram. In the diagram, inputs to cytochrome b_6f are shown in red, outputs are shown in blue, and recycled elements are in green. If one plastoquinol simply delivered its electrons and protons and was done, there would be two protons delivered per plastoquinol. That's one proton output per electron that was input.

A second plastoquinol would do exactly the same thing. There would be four protons output for four electrons initially input. That's still one proton output per electron that was input.

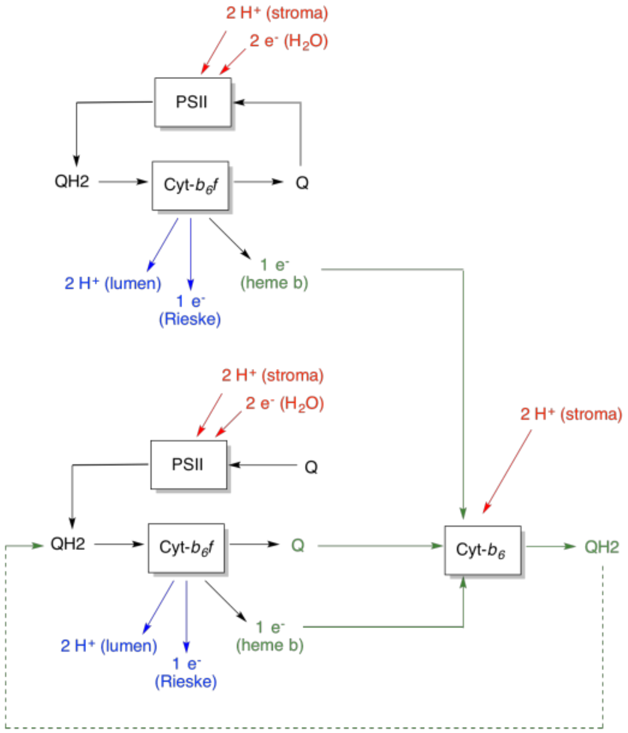


Figure 9.6.4: Diagram showing protons pumped per electron consumed, with the addition of the Q-loop. Inputs are shown in red and outputs in blue. Recycled elements are provided in green.

If, instead, one electron is recycled each time, then every second plastoquinol leads to the delivery of an extra pair of protons. That's because in picking up the recycled electrons, a plastoquinone has had to travel back to the stroma side of the membrane and pick up two more protons. Overall, that means six protons are delivered for four electron input, or 1.5 protons output per electron input. Since the proton gradient is what is generating the ATP, then by increasing the number of protons pumped per electron coming in, efficiency is increased.

? Exercise 9.6.1

The efficiency advantage is even greater than that described above. The Q-loop is thought to *double* the amount of protons pumped by cytochrome b6f. Explain why.

Answer

The first pair of plastoquinols recycle two electrons between them, pumping two additional protons via a recycled quinol. The proton output is 1.5 times what it would be without the Q-loop (from 1 proton/electron + 0.5 proton/electron). Now remember that this recycled quinol also delivers two electrons, one of which is recycled. To get a second electron to generate a new recycled quinol, we would have to go through the entire, two-new-plastoquinol cycle again. We would get another two protons but it would have required eight electrons to get there, or 0.25 protons output per electron input. The proton output would rise to 1.75 times what it would be without the Q-loop (from 1 proton/electron + 0.5 proton/electron + 0.25 proton/electron). A series will result if we keep going. The series is $1 + 1/2 + 1/4 + 1/8 + 1/16 + ... + 1/2^n$, and it will converge to 2. Therefore, the Q-loop doubles the number of protons pumped across the membrane.

The electron transport chain through cytochrome b6f is rather short. The electron is first passed to a "high-potential FeS cluster", or Rieske cluster. It differs from most FeS clusters in that two of the amino acid residues that bind it in the protein are histidines, rather than the usual cysteines. Rieske clusters usually have higher reduction potentials than other FeS clusters. They were one of the last in a series of FeS clusters encountered in the electron transport chain in oxidative phosphorylation, and their more positive reduction potential was needed to keep the electron transport chain moving in the right direction.

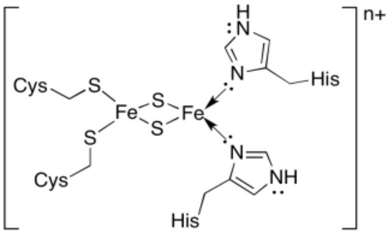


Figure 9.6.5: Coordination environment of the iron atoms in a Rieske FeS cluster.

Exercise 9.6.2

The reduction potential of a Rieske FeS cluster is generally more positive than that of a regular FeS cluster, in which the Fe_2S_2 core is held in place by four cysteines. Explain why.

Answer

The major factor appears to be charge stabilisation. Suppose both iron atoms start as Fe(III). They have an overall 6^+ charge. The two sulfides are each 2^-, for an overall Fe_2S_2 core charge of 2^+. If ligated by four cysteines (Cys-S^-), then the overall charge of the coordination compound is 2^-. Addition of an electron will result in an increase in negative charge, to 3^-. Now, that was starting from the fully oxidised state. If instead we start in a mixed Fe(II/III) oxidation state, then addition of an electron results in a 4^- charge on the coordination complex. That charge buildup will be energetically difficult.

If ligated by two cysteines (Cys-S^-) and two neutral histidines, then the overall charge of the coordination compound is 0. Addition of an electron will result in a negative charge, 1^-. If instead we start in a mixed Fe(II/III) oxidation state, then addition of an electron results in a 2^- charge on the coordination complex. That lower charge buildup required in this case will be energetically less difficult.

The final stop for the electron is a small, soluble protein, plastocyanin. The electron carrier in plastocyanin is not an iron, but rather a copper atom. The copper ion, which can toggle between Cu^+ and Cu^{2+}, is held in place by two histidines, a methionine, and a cysteine. The plastocyanin transports the electron through the lumen to the next complex, photosystem I.

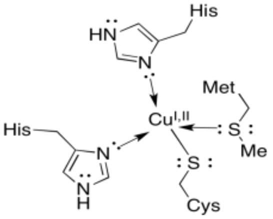


Figure 9.6.6: Coordination environment of the copper ion in plastocyanin.

Exercise 9.6.3

Use periodic trends to suggest a reason why a copper atom appears later in the electron transport chain, whereas several iron atoms appeared earlier in the chain.

Answer

Copper is further to the right in the periodic table and is consequently more electronegative than iron. That is the major reason that copper is below iron in the activity series or metals. On that basis alone (and ignoring any differences in the coordination environment), we might expect a more positive reduction potential on a copper ion than an iron ion. Copper would therefore be a better electron acceptor, and would be useful in creating a greater driving force for electron transfer later in the electron transport chain.

Exercise 9.6.4

a. What would be the overall charge on the coordination complex in plastocyanin, assuming the Cu(II) state?
b. What would be the overall charge on the coordination complex in plastocyanin, assuming the Cu(I) state?
c. Based on charge considerations alone, how would you expect the reduction potential of plastocyanin to compare to the Rieske FeS cluster?

Answer a

a) With only one anionic donor, the charge of the complex that contains Cu(II) would be 1^+.

Answer b

b) With one anionic donor, the charge of the complex that contains Cu(I) would be 0.

Answer c

c) Reduction of plastocyanin results in a decrease of charge, whereas reduction of the FeS cluster results in an increase of charge. That factor alone could make plastocyanin easier to reduce, with a more positive reduction potential.

1. X-ray crystal structures: Kurisu, G.; Zhang, H.; Smith, J.L.; Cramer, W.A. Structure of the cytochrome b6f complex of oxygenic photosynthesis: tuning the cavity. *Science* **200**3, *302*, 1009-1014. Images obtained via RCSB Protein Data Bank (1VF5).

9.7: Harvesting the Photons- Photosystem I

Having already generated the proton gradient used for ATP generation, what is there left to do?

Remember back to that high school biology class when you first saw the equation for photosynthesis.

$$6\,CO_{2(g)} + 6\,H_2O_{(l)} \longrightarrow C_6H_{12}O_{6(s)} + 6\,O_{2(g)}$$

We can break that into two half reactions. The first is the oxidation of water.

$$2\,H_2O_{(l)} \longrightarrow O_{2(g)} + 4\,H^+_{(aq)} + 4\,e^-_{(aq)}$$

The other half is the reduction of carbon dioxide.

$$6\,CO_{2(g)} + 24\,H^+_{(aq)} \longrightarrow 24\,e^-_{(aq)} \longrightarrow C_6H_{12}O_{6(s)} + 6\,H_2O_{(l)}$$

Although these two half-reactions are physically separated from each other, the electrons must still get from one to the other in order to complete the full reaction. We have already accomplished the first reaction and now have electrons in hand to carry out the second. We are going to need a biological reducing agent, like NADH, to carry out the second. In this case, we will use a closely-related compound, NADPH.

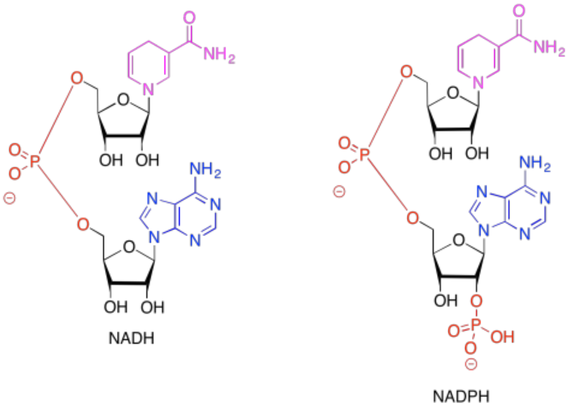


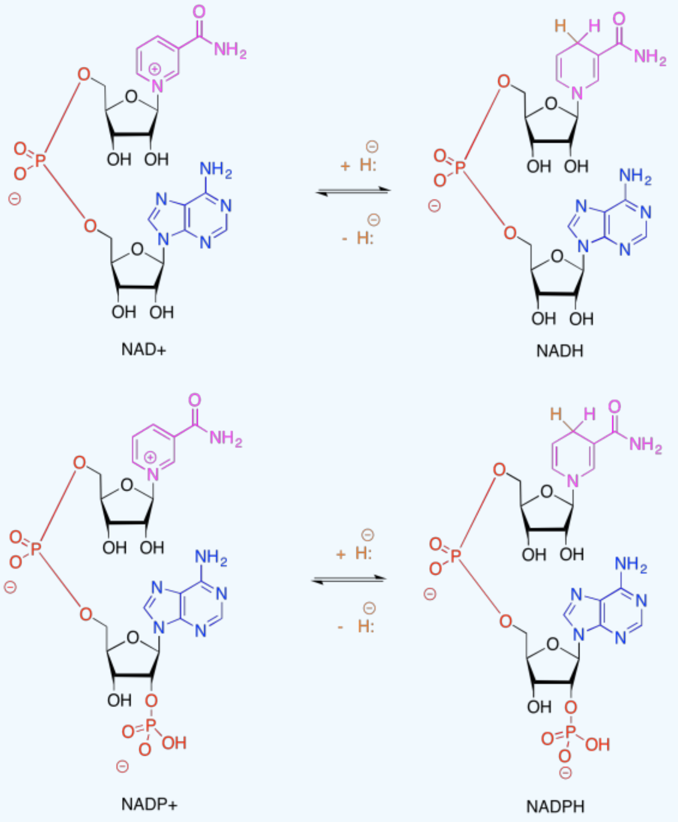
Figure 9.7.1: Comparative structures of two related electron carriers: NADH and NADPH.

In both of the drawings above, the purple portion of the compound is where the electrons are accepted. The black portion is sugar, the blue is a purine base, and the red is the phosphate part.

Exercise 9.7.1

Because NADH and NADPH are electron carriers, it is important to recognise both reduced and oxidised forms. Given the reduced forms of NADH and NADPH shown above, draw the oxidised forms, and show where the :H$^-$ is incorporated in the molecule in the reduced form.

Answer



The problem is, NADPH is a relatively high-energy electron carrier -- remember, NADH was at the uphill end of the electron transport chain in oxidative phosphorylation -- and our electrons have just ridden their sled to the bottom of the hill. If we are going to make NADPH, we will need to tug the electrons back uphill again. That's essentially the job of photosystem I, shown below.

Figure 9.7.2: Results from an X-ray crystal structure of photosystem I in the marine cyanobacterium *Synechococcus elongatus*.[1]

The ligand-only view of the crystal structure reveals a picture that should be somewhat familar now: a host of antennae molecules forming a light-harvesting complex. Once again, the antennae molecules include mostly chlorophylls, as well as carotenoids such as carotene and lycopene, plus a few xanthins like violaxanthin; the exact molecules vary depending on whether we are looking at plants, algae, or bacteria.

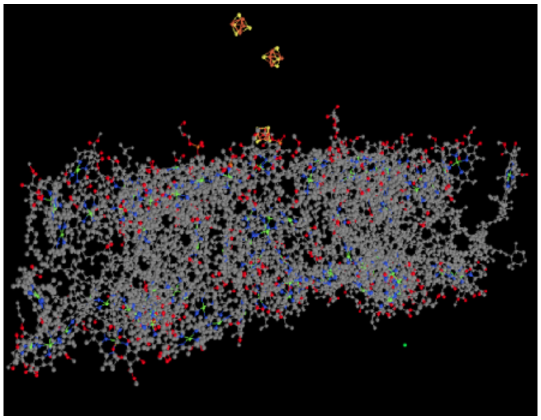


Figure 9.7.3: Ligand-only view of an X-ray crystal structure of photosystem I.

Also visible in the ligand-only view is a group of FeS clusters. These clusters play a role in the electron-transport chain of photosystem I, conducting the electron toward the stroma, where they will be used to reduce NADP+ to NADPH. That biological reducing agent, closely related to NADH, will be used to help reduce carbon dioxide.

Let's pause for a moment. Most of the X-ray crystal structures we have seen have come from bacteria. Of course, we are much more familiar with the idea of photosynthesis in plants. Are the proteins and processes involved in photosynthesis in one anything like the other? For comparison, here is photosystem I from a spinach plant.

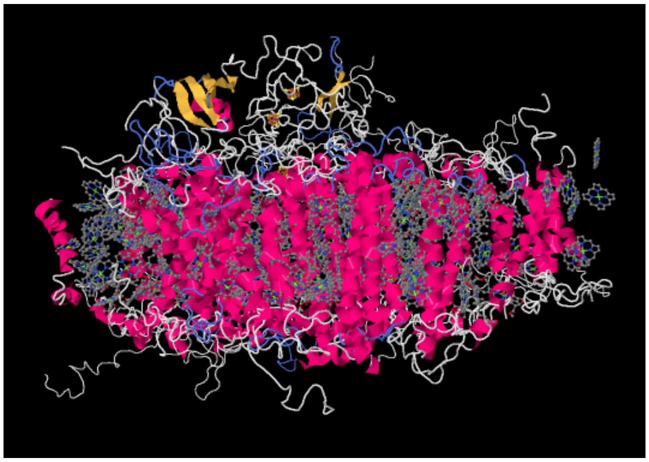


Figure 9.7.4: Results from an X-ray crystal structure of photosystem I in spinach.[2]

It is roughly similar, although not identical, to the one from the bacterium. There is a broad swath of alpha helices through the middle, topped with a bundle of beta sheets. If anything, the protein from the spinach looks superficially a little simpler than the one from the bacterium. The ligand-only view, below, is strikingly similar, showing a spray of chromophores and a series of iron-sulfur clusters.

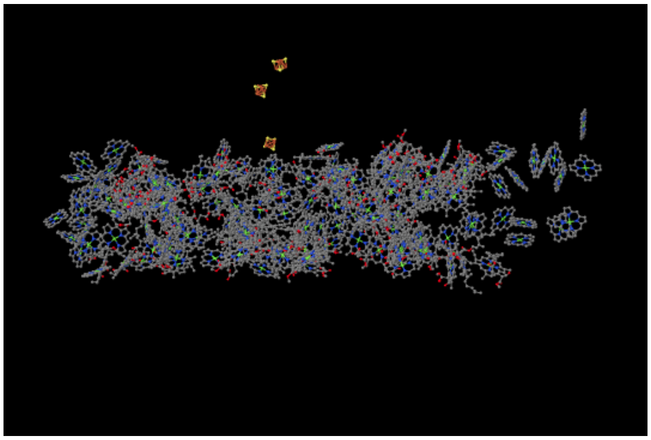


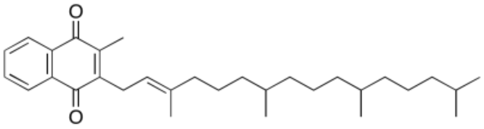
Figure 9.7.5: Ligands-only view from an X-ray crystal structure of photosystem I in spinach.

Let's pick up the story where we left off when we were discussing cytochrome b_6f. A single electron was being transported by the soluble, mobile electron carrier, plastocyanin. That single electron is delivered directly to the reaction centre of photosystem I. That reaction centre is quite similar to the one in photosystem II, although it absorbs photons of a slightly longer wavelength, 700 nm. The P700 centre contains an excitonic dimer, a closely-spaced pair of chlorophyll molecules that absorb the photon and undergo electron / hole separation on the two different molecules.

Just as in P680, the P700* excited state can accept an electron onto the chlorphyll partner that has the hole, $P_{D2}{}^{+}*$. That's where the plastocyanin delivers its electron.

Meanwhile, the part of the dimer with the extra electron, $P_{D1}{}^{-}*$, passes the electron on to another station on the electron transport chain. Part of the goal here is to get the electrons back to the stroma where the NADP+ is waiting. If you think about it, the electrons started out in the lumen, on a water molecule. They traveled across the thylakoid membrane in photosystem II until they joined a plastoquinone and picked up a couple of protons; those protons came from the stroma. The plastoquinones travelled back across the membrane, a stealth migration of polar H^+ in the form on nonpolar PQH2, and delivered their protons to the lumen. The side-kick electrons skipped along the edge of the lumen in a plastocyanin carrier, and are now traveling back toward the stroma to that waiting NADP+. The NADPH will be produced in the stroma because that's where it will be needed for CO_2 capture.

Again, just as in P680, the first electron acceptor after P700 is a single chlorophyll. This chlorophyll anion that forms is slightly downhill in energy from the one in the dimer, $P_{D1}{}^{-}*$. From there, the electron passes to a phylloquinone, which is just another variation on the familar quinone family.



phylloquinone

Figure 9.7.6: The structure of phylloquinone

The phylloquinone sends the electron into that series of three FeS clusters visible in the crystal structure. From there, the electron leaves photosystem I and is deposited on a ferredoxin, a small protein that binds another iron sulfur cluster. The ferredoxin is located in the stroma, where it can bind with an enzyme called ferredoxin NADP+ reductase. Like most enzymes, the name says exactly what it does: it catalyses the reaction in which ferredoxin reduces NADP+, resulting in NADPH.

The crystal structure of a ferredoxin is shown below. This particular one is not from photosystem I (it is found in a nitrogen-fixing bacterium), but it gives you the idea. The protein is simple enough that you can see that it is a dimer; the top half is the same as the bottom half, flipped over. You can also clearly see a 2Fe2S cluster at the edge of each subunit. The location of that FeS cluster near the edge of the protein is probably important in facilitating electron transfer with another protein.

Figure 9.7.7: X-ray crystal structure of a ferredoxin, a small protein containing a FeS cluster, from *Azotobacter vinelandii*.[3]

The ferredoxin is an electron carrier protein. Its job is to deliver electrons to the ferredoxin NADP+ reductase in the stroma, which will then use the electrons to make NADPH. NADPH is a biological source of hydride ion (formally, H-, or a proton plus two electrons) that in this context will be used to help reduce carbon dioxide into carbohydrate. Below, we can see an example. This is another dimeric protein with rotational symmetry: the left side is the same as the right, but turned over.

Figure 9.7.8: X-ray crystal structure of a ferredoxin NADP+ reductase from *Bacillus subtilis*.[4]

If we look inside, we can see the NADP+ molecules waiting at either end of the structure, at both the far left and the far right. In addition, there is a pair of molecules that look vaguely related to NADP+ toward the middle of the picture. Those are two FAD molecules. The FAD molecules are there to conduct electrons from the ferredoxin t the NADP+.

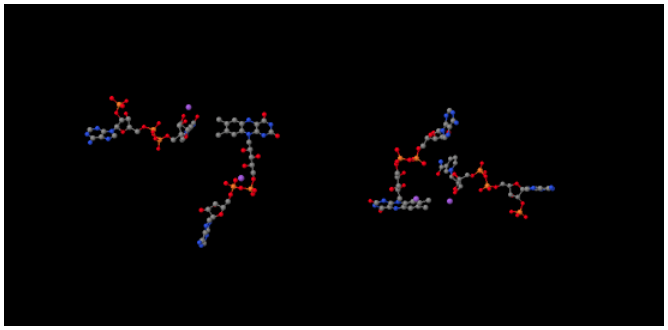


Figure 9.7.9: Ligand-only view of the X-ray crystal structure of a ferredoxin NADP+ reductase.

In the picture below, the purple part of the molecule is the redox-active region. It is able to accept electrons. The black part is sugar, the blue is a purine base, and the red is phosphate.

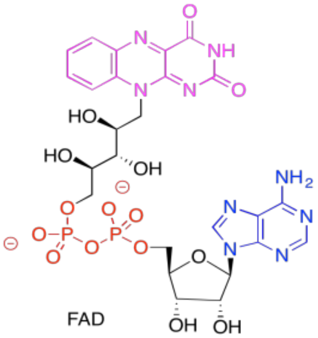
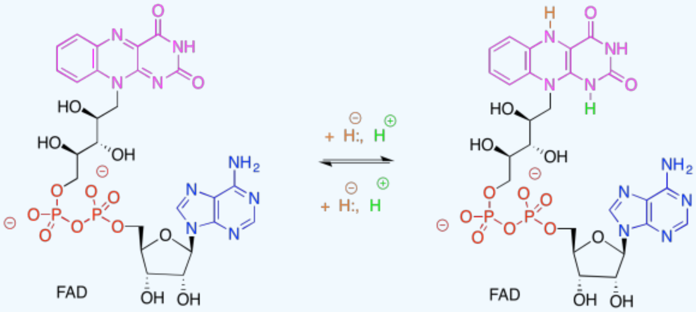


Figure 9.7.10: The structure of the electron carrier, FAD.

? Exercise 9.7.2

Show the reduced form of FAD. Remember, the reduced form is called FADH2.

Answer



? Exercise 9.7.3

What role do you think the FAD plays in ferredoxin NADP+ reductase? Why doesn't the ferredoxin reduce the NADP+ directly?

Answer

Remember, NADP+, like NAD+, is solely a 2-electron oxidising agent. It can only receive a pair of electrons associated with a hydride. Ferredoxin, via an FeS cluster, can only give one electron at a time. An adapter is needed between these two carriers. FAD can accept either 1 or 2 electrons, proceeding to either FADH$^{\cdot}$ radical (stabilised via extensive resonance delocalisation) or to FADH2.

? Exercise 9.7.4

Because photosystem II and photosystem I are part of the same electron transport chain, it is important that the reaction centre in one is getting excited just as often as the reaction centre in the other. Regulation is partly accomplished via covalent modification. For example, insufficient activity at photosystem I results in activation of a kinase, which results in release of some of the antennae molecules from the light harvesting complex in photosystem II.

a. How would this situation help to remedy the lack of parity in activity between photosystem I and photosystem II?
b. Explain how the kinase would achieve this result.
c. Suppose the opposite situation occurred: insufficient activity at photosystem II. What enzyme would probably be activated to remedy the situation?

Answer a

a) Releasing antennae molecules from the light harvesting complex in photosystem II would decrease both the number of photons captured and the number of electrons sent into the electron transport chain. Conversely, in a "chromophore pool" model, releasing these molecules from photosystem II would make them more available for uptake by photosystem I, resulting in greater absorption of photons there, and greater capacity to accept incoming electrons. If regulated, these two systems should be able to level out at an identical rate of photon absorption.

Answer b

b) Kinases phosphorylate the hydroxy side chains in serine residues (and sometimes threonines and tyrosines). That covalent modification results in a change in the charge of the side chain from neutral to anionic. Significant conformational changes in the protein can be expected to result. It is likely that this conformational change results in looser binding of the antennae molecules in the light harvesting complex of photosystem II.

Furthermore, kinase appears to promote tighter binding of antennae molecules at photosystem I, presumable through a conformational change there. The result is a shift of these molecules from the available pool, such that additional chromophores become available in photosystem I and fewer are retained in photosystem II, until photon absorption at the two sites is equal.

Answer c

c) In fact, phosphatase, which is the complementary enzyme to kinase, is activated when photosystem I has high activity compared to photosystem I. Phosphatases remove phosphate groups from serines and related residues. The result would be tighter binding of antennae molecules at photosystem I and looser binding of antennae molecules at photosystem II, so that light absorption could be evened out between the two sites.

The use of phosphatases and kinases to effect opposite objectives in regulation is common in a number of biochemical systems.

We can summarize with a sketch of photosystem I:

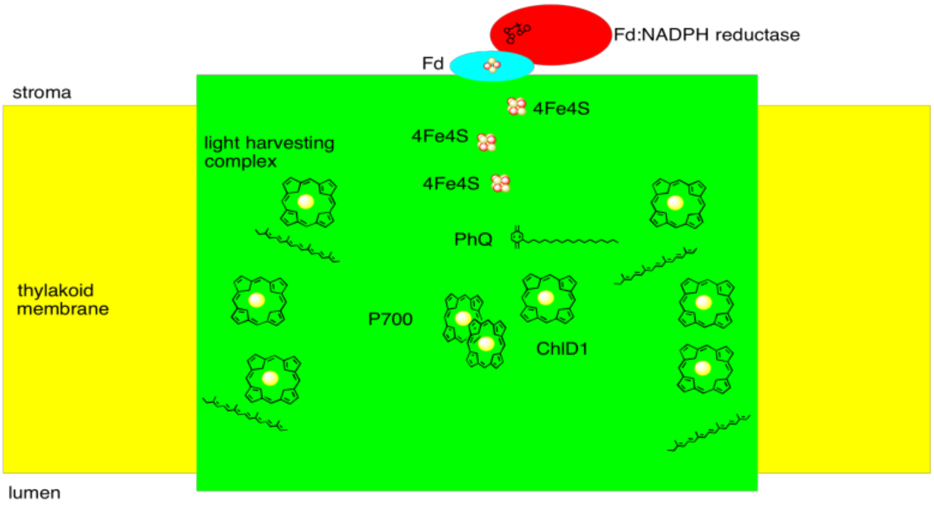


Figure 9.7.11: Sketch of photosystem I.

1. X-ray crystal structures: Jordan, P.; Fromme, P.; Witt, H.T.; Klukas, O.; Saenger, W.; Krauss, N. Three-dimensional structure of cyanobacterial photosystem I at 2.5 A resolution. *Nature* **2001**, *411*, 909-917. Images obtained via RCSB Protein Data Bank (1JB0).

2. X-ray crystal structures: Amunts, A., Drory, O., Nelson, N. The structure of a plant photosystem I supercomplex at 3.4 A resolution. *Nature* **2007**, *447*, 58-63. Images obtained via RCSB Protein Data Bank (2o01).

3. X-ray crystal structures: Schlesier, J., Rohde, M., Gerhardt, S., Einsle, O. A Conformational Switch Triggers Nitrogenase Protection from Oxygen Damage by Shethna Protein II (FeSII). *J. Am. Chem. Soc.* **2016**, *138*, 239-247. Images obtained via RCSB Protein Data Bank (5ffi).

4. X-ray crystal structures: Komori, H., Seo, D., Sakurai, T., Higuchi, Y. Crystal structure analysis of Bacillus subtilis ferredoxin-NADP(+) oxidoreductase and the structural basis for its substrate selectivity. *Protein Sci.* **2010**, *19*, 2279-2290. Images obtained via RCSB Protein Data Bank (3Lzw).

9.8: ATP Synthase

One of the goals of photosynthesis is to make ATP. ATP is frequently employed in biology to drive uphill reactions. The hydrolysis of ATP to give ADP is a downhill reaction, so it releases energy.

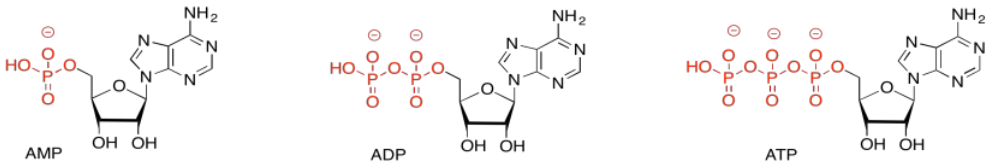


Figure 9.8.1: The adenosine phosphate family.

Formation of ATP from ADP requires addition of phosphate. It's an uphill reaction, so the cell has to expend energy to produce ATP. ATP synthase harnesses a proton gradient to drive a molecular rotor, much like a millwheel, in order to bring ADP and phosphate in close proximity so that they can form ATP. You may already be familiar with ATP synthase from oxidative phosphorylation, where it works exactly the same way.

ATP synthase is thought of as having three states. In the "loose" state, ADP and phosphate (P*i*) can enter the binding site easily. Once these two substrates are in the binding site, the enzyme enters the "tight" state, in which ADP and phosphate are constricted and form ATP. At that point, the enzyme goes through an "open" phase in which ATP can leave easily.

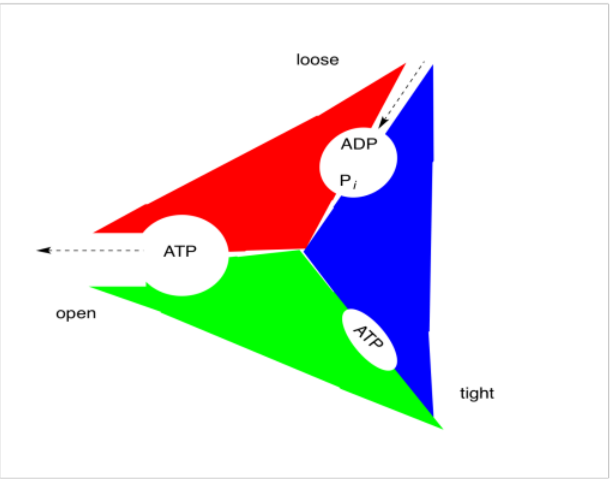


Figure 9.8.2: The three states of ATP synthase.

As in oxidative phosphorylation, the changes in states are coupled to rotation of one part of the multiprotein complex (the rotor) with respect to another (the stator). The principle is similar to that of an electric motor. If the stator is positively charged and certain positions of the rotor are negatively charged, then the opposite charges will attract and the rotor will begin to turn. Once the negatively charged part of the rotor reaches the positively charged part of the stator, however, everything should come to a stop. The reason it doesn't is because a proton drops into the the anionic position of the rotor just as it is approaching the stator. Now neutralized, this position is no longer attracted to the stator, and it just sails past. Meanwhile, another anionic position is approaching the stator, keeping the rotor turning. As soon as it is a safe distance away from the stator, a hole opens up below the rotor and the protons falls away, regenerating an anionic position that is once again attracted to the next stator.

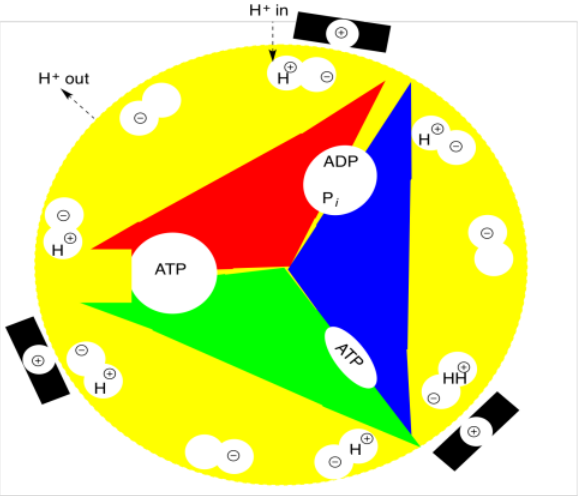


Figure 9.8.3: The proton pump and ATP synthase.

In the case of photosynthesis, the proton is "dropping in" from the lumen and later "falling down" into the stroma; its motion in that direction is driven by the proton gradient. So that proton gradient in turn drives the motion of the rotor. The motion of the rotor, in turn, drives conformational changes within (and between) the protein subunits of ATP synthase. Those conformational changes promote ATP formation through an approximation effect.

9.9: Carbon Capture and Carbohydrate Pool

One of the main goals of photosynthesis is to take the ATP and NADPH produced through the electron transport chain and use them to store energy in the form of carbohydrates. The key event in carbohydrate storage is the capture of carbon dioxide from the atmosphere. That task is carried out by ribulose-1,5-bisphosphate carboxylase (usually abbreviated as rubisco). Rubisco is found inside the chloroplasts, in the stroma.

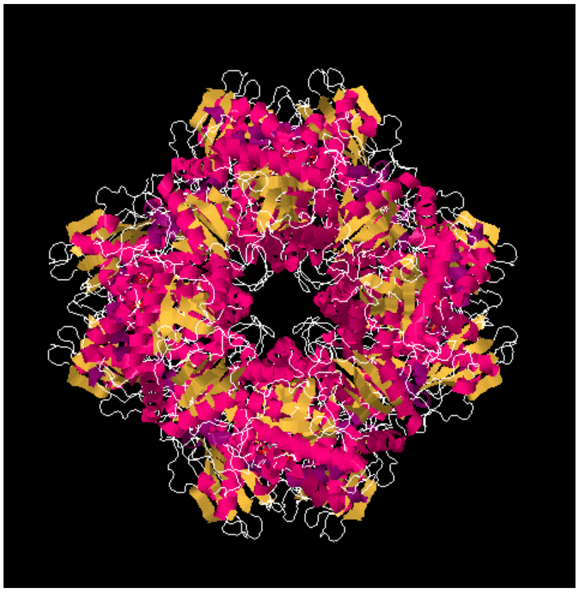


Figure 9.9.1: X-ray structure of ribulose bisphosphate carboxylase from spinach, shown in a cartoon view.

Rubisco is an aggregate of sixteen proteins, but it contains only two different kinds of proteins; it is composed of eight molecules of one protein plus eight molecules of the other. It is a huge protein, with a molecular weight of 50 or 60 kDa. Its primary function is to use a five-carbon sugar, ribulose, as a scaffold on which to attach a carbon dioxide molecule. The result, after reduction with NADH, is a six-carbon sugar.

In the picture below, you can see the ribulose-1,5-bisphosphate molecules awaiting their carbon dioxide. There are actually eight of them, but they are arranged in four stacks when viewed from this angle, with four molecules in the front and four behind them.

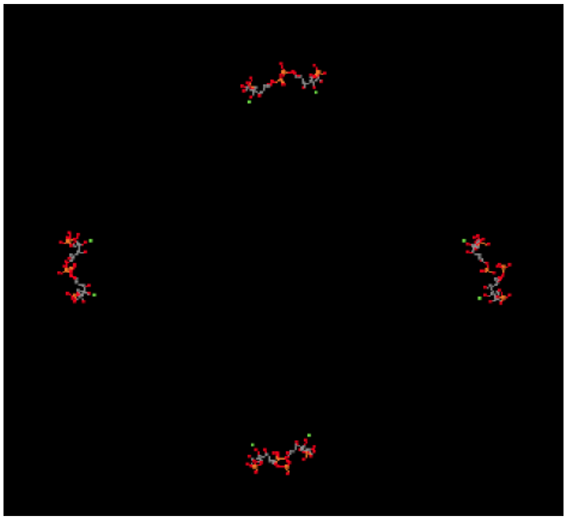
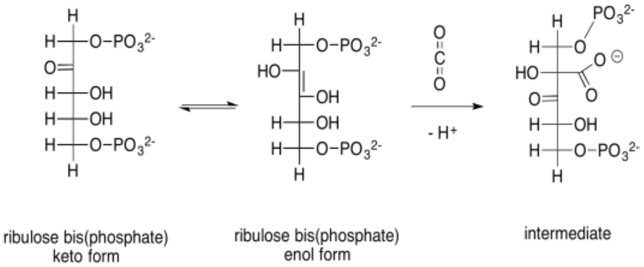


Figure 9.9.2: X-ray structure of ribulose bisphosphate carboxylase from spinach, shown from the same angle as the previous picture but in a ligand-only view to reveal eight bound ribulose-1,5-bisphosphate molecules.

The capture of the carbon dioxide is accomplished through a simple aldol reaction. Under biological conditions, this reaction happens via the neutral, enol form of ribulose-1,5-bisphosphate, rather than the anionic enolate ion, because there is not a strong enough base to produce appreciable quantities of the enolate ion. To get to the enol form, a proton must be transferred from an alpha position to the oxygen of the ketone.

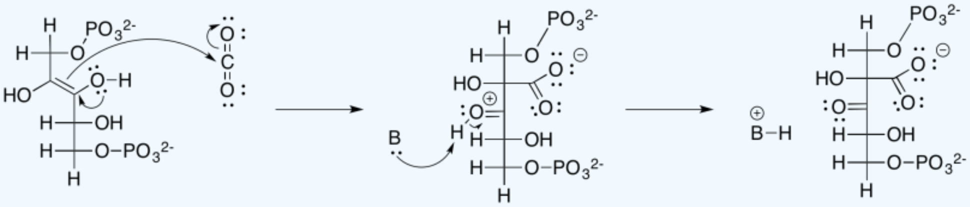


Scheme 9.9.1: Aldol reaction between the enol form of ribulose-1,5-bisphosphate and carbon dioxide.

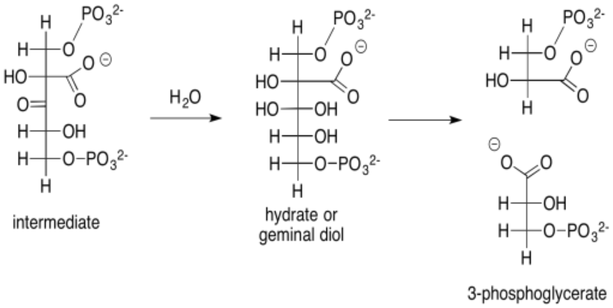
Exercise 9.9.1

Provide a mechanism, with curved arrows, for the capture of the carbon dioxide by the enol of ribulose bisphosphate.

Answer



That intermediate, resulting from the aldol reaction of ribulose bisphosphate and carbon dioxide, does not last very long. It is quickly hydrated to form a geminal diol (twin OH groups on one carbon), and the geminal diol decomposes via a retro-aldol reaction. Remember, a retro-aldol reaction is an aldol reaction in reverse. Instead of an enolate nucleophile adding to a carbonyl electrophile, an alcoholic oxygen pi-donates to form a new carbonyl, and as a result an enolate is produced as a leaving group.

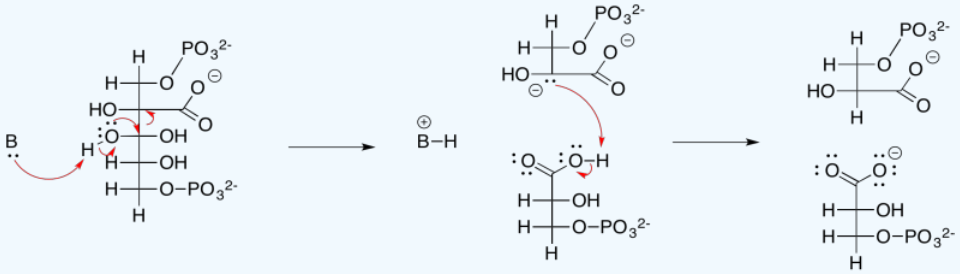


Scheme 9.9.2: The rapid decomposition of the carbon-captured intermediate to 3-phosphoglycerate.

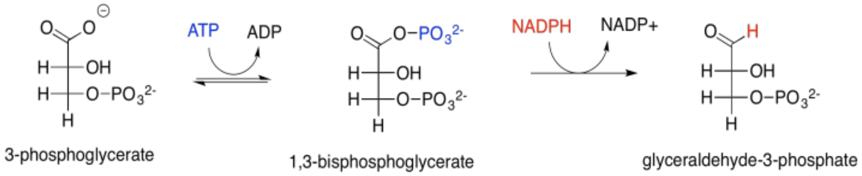
Exercise 9.9.2

Provide a mechanism, with curved arrows, for the cleavage of the geminal diol into two 3-phosphoglycerate molecules.

Answer



At this point, the ATP and NADPH produced in the electron transport chain come into the picture. The NADPH converts the carboxylate group into an aldehyde; at that point, the CO_2 has become fully incorporated into a normal sugar, albeit the smallest one there is. The ATP is first used in order to activate the 3-phosphoglycerate. The NADPH can't displace the oxide (O^{2-}) from 3-phosphoglycerate; oxide is a terrible leaving group, and the carboxylate group isn't particularly electrophilic with that negative charge hanging around. The 3-phosphoglycerate would be a much better nucleophile. Well, instead of reacting directly with the NADPH, it reacts with the ATP forst. Phosphoglycerate kinase activates the ATP, which is then ready to behave as an electrophile. The negatively charged 3-phosphoglycerate donates to the terminal phosphate group on the ATP, displacing ADP. The kinase has done its job, forming a phosphoanhydride.



Scheme 9.9.3: The conversion of 3-phosphoglycerat to glyceraldehyde-3-phosphate.

Let's think about phosphoanhydrides for a minute. They are a little like acid anhydrides in structure. An acid anhydride has an oxygen atom between two carbonyls. Normally, the excellent pi-donating ability of an oxygen atom "protects" an attached carbonyl from approaching nucleophiles; in a sense, the electrophilic site on the carbonyl is already filled by the lone pair from the oxygen. In an anhydride, however, that lone pair is in a dither. It is divided between two carbonyls and so it can only donate half as well to either one of them. Since it isn't doing much good as a pi-donor, the other half of oxygen's behaviour emerges: it is also an excellent sigma-acceptor, because it is a very electronegative atom. That leaves the acid anhydride as a very good electrophile.

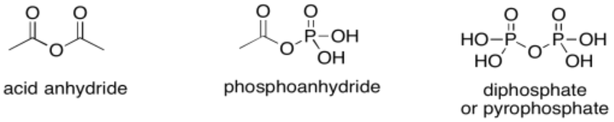


Figure 9.9.3: Three analogous electrophilic structures.

Of course, phosphoanhydrides behave in exactly the same way, but the ostensibly pi-donating oxygen is stuck between one carbonyl and one phosphoryl group. It is unable to pi-donate effectively to the carbonyl, and so its electron-withdrawing ability takes over instead. A phosphoanhydride is an excellent electrophile, just like a regular anhydride. Both are "high on the ski hill", if you remember the analogy for carboxyloid reactivity.

Incidentally, polyphosphates tend to be pretty electrophilic, too, which is one of the factors driving the high reactivity of ATP.

The result is that the rather nucleophilic 3-phosphoglycerate has been transformed in one step into the highly electrophilic 1,3-bisphosphoglycerate, an example of a phosphoanhydride. That makes it much easier for the NADPH to donate a nucleophilic hydride to the carbonyl, forming an aldehyde. The exact mechanism, catalysed by glyceraldehyde phosphate dehydrogenase, involves a group transfer step. The carbonyl is transferred from the phosphate group to a cysteine residue in the enzyme. The advantage of group transfer is chiefly entropic: instead of the NADPH and the phosphoanhydride both binding in the enzyme and reacting together, at this point the NADPH must simply bind with the enzyme and react with the enzyme itself, because the glycerate group has become covalently bound to the enzyme.

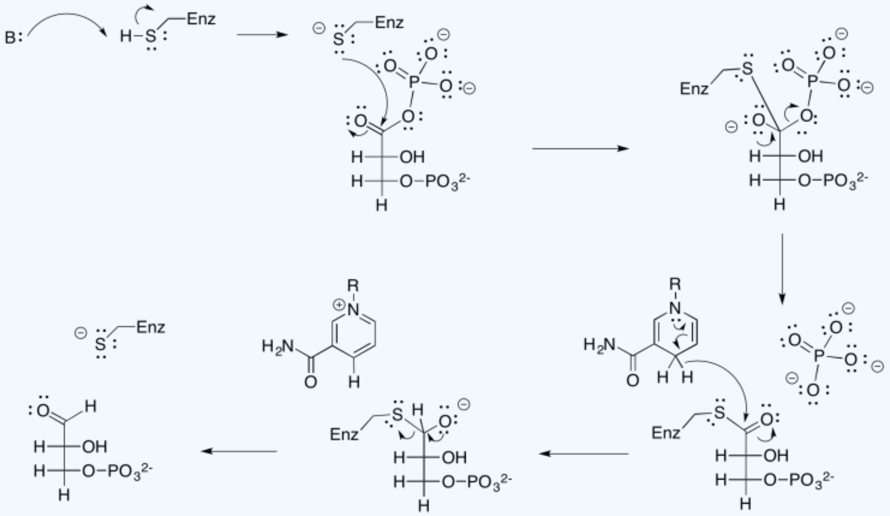
Moreover, the new functional group formed during group transfer is a thioester. Thioesters, like phosphoanhydrides, are excellent electrophiles. Although the second-row pi-donors, oxygen and nitrogen, are exceptionally good at donating to carbonyls, the third-row pi-donors, such as chlorine and sulfur, are not. Instead, their relatively high electronegativity activates the carbonyl. That means group transfer occurs without any loss of reactivity, which is essential for catalysis.

Figure 9.9.4: Two high-energy electrophilic structures; both have weak, third-row pi-donors.

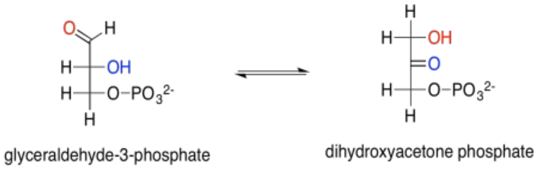
Exercise 9.9.3

Provide a mechanism for the NADPH reduction of 1,3-bisphosphoglycerate.

Answer



The glyceraldehyde formed via reduction by NADPH is the simplest of the carbohydrates; you can think of it as the grandmother of all sugars, which can be thought of as forming through extension of glyceraldehyde's carbon chain. In this case, we really have the phosphorylated form of the sugar, rather than the sugar itself. Glyceraldehyde, or glyceraldehyde-3-phosphate, can be transformed easily into another molecule via tautomerism. That is the movement of one proton from one position to another, and in this example it leads to dihydroxyacetonephosphate.

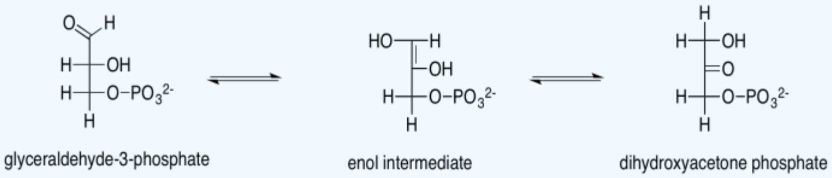


Scheme 9.9.4: Tautomerism between glyceraldehyde and dihydroxyacetone (phosphorylated version).

Exercise 9.9.4

Show the enol intermediate between glyceraldehyde-3-phosphate and dihydroxyacetone phosphate.

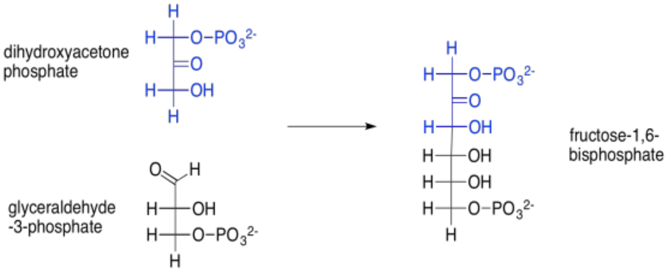
Answer



Glyceraldehyde is, of course, an aldose, with its carbonyl at the end of the three-carbon chain, forming an aldehyde functional group. The other carbons have hydroxyl groups; that's what makes it a carbohydrate (a polyhydroxylated aldehyde or ketone). Dihydroxyacetone is a ketose, with its carbonyl in the middle of the chain, forming a ketone functional group. That group is flanked by two alcohols. The fact that glyceraldehyde can turn into dihydroxyacetone is partly significant because the biosynthetic potential of this small building block is opened up by allowing it to form twice as many structures.

There are a number of ensuing reactions that have the effect of quickly interconverting these sugars into different carbohydrates in a sort of carbon pool. The plant can draw on this carbon pool for various purposes, whether it is to send sugars elsewhere in the plant or to regenerate some more ribulose in order to grab more carbon dioxide. By grabbing more carbon dioxide, that carbon pool gets bigger and bigger. The series of reactions governing this carbon pool is called the Calvin cycle. It is really more of a network than a cycle, with molecules able to hop back and forth between various parts of the cycle, rather than everything following monotonously in lockstep.

For example, the aldol reaction of those two triose phosphate molecules -- dihydroxyacetone phosphate and glyceraldehyde-3-phosphate -- leads to fructose-1,6-bisphosphate. This reaction is accomplished through the help of an enzyme, aldolase. Fructose, or fruit sugar, is one of the few sugars that are readily absorbed through our digestive system.



Scheme 9.9.5: Aldol reaction of two trioses to make the hexoketose, fructose (again, a phosphorylated version).

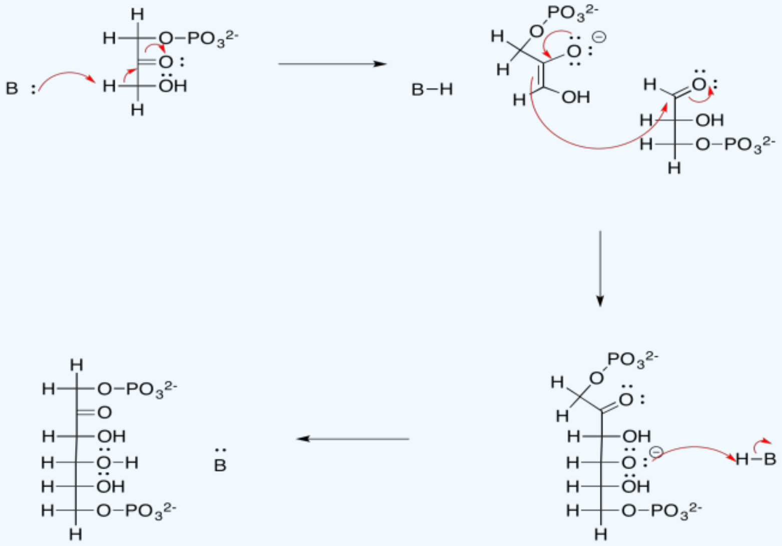
Exercise 9.9.5

Provide a mechanism for the formation of fructose-1,6-bisphosphate, above

a. under basic conditions
b. under acidic conditions

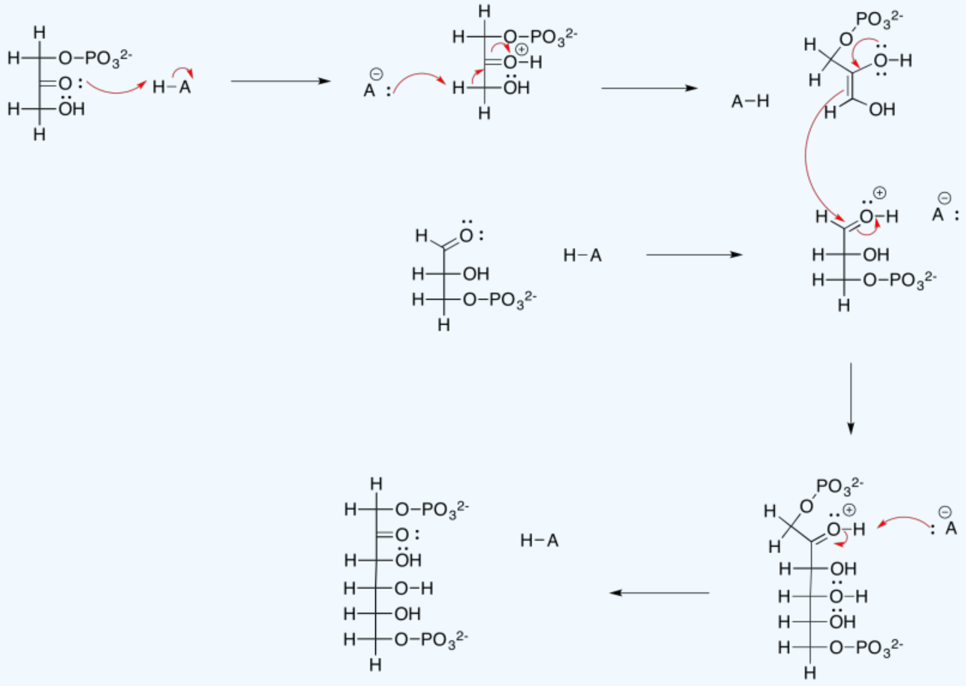
Answer a

a)



Answer b

b)



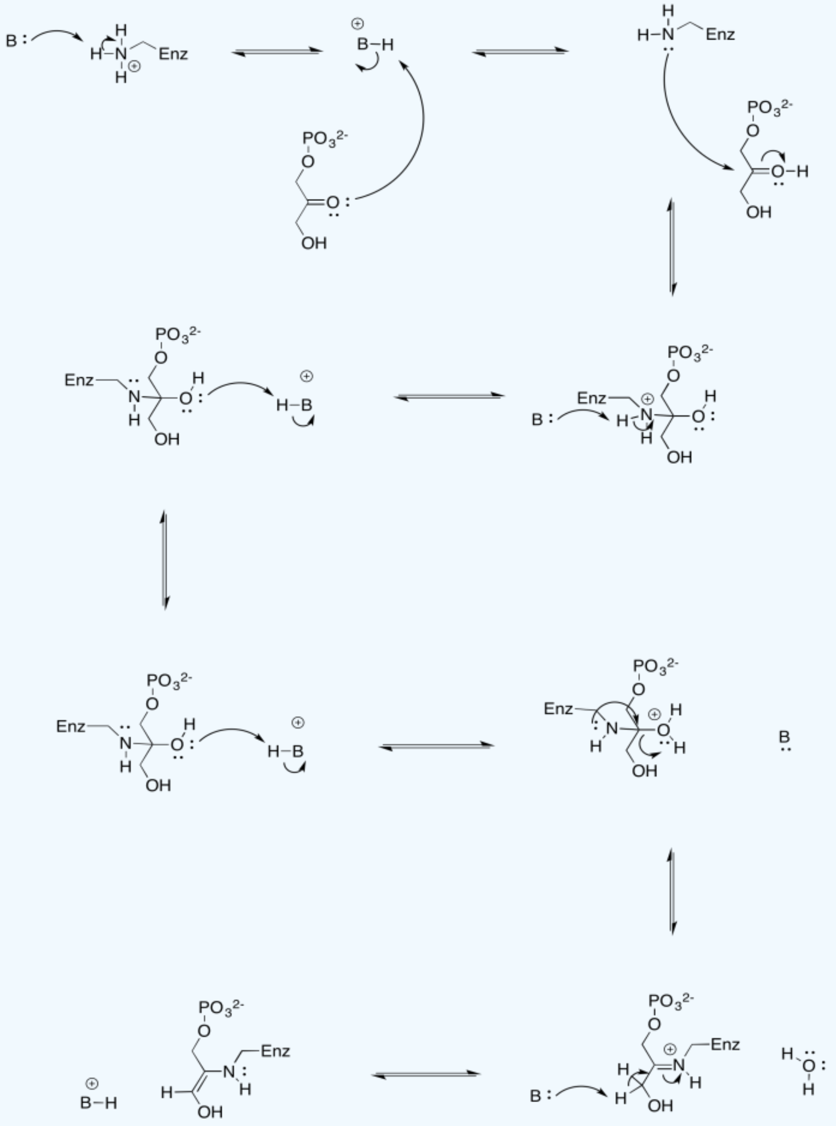
Exercise 9.9.6

Many biological aldol reactions actually occur via an enamine intermediate.

a. Provide a mechanism for the formation of an enamine from dihydroxyacetone phosphate.
b. Provide a mechanism for formation of fructose-1,6-bisphosphate via the enamine of dihydroxyacetone phosphate.

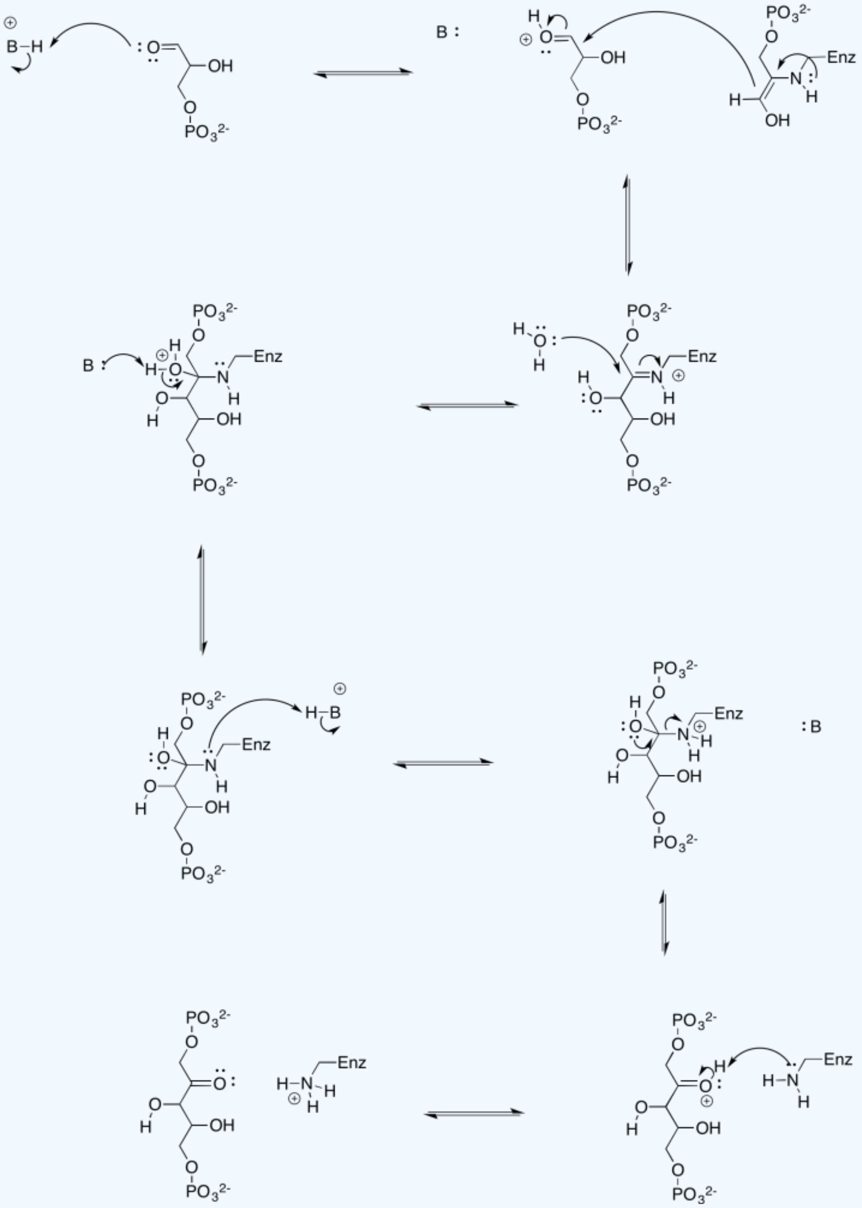
Answer a

a)



Answer b

b)

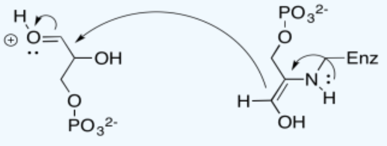


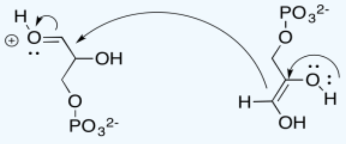
? Exercise 9.9.7

Why is enamine catalysis used in biochemical pathways? What makes it faster than a regular enol pathway?

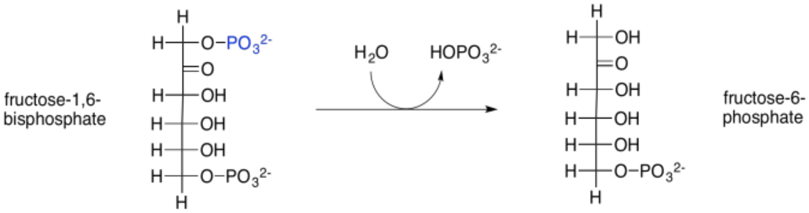
Answer

The regular enol pathway is driven by pi-donation from an oxygen atom. The enamine pathway is driven by pi-donation from a nitrogen. Nitrogen is less electronegative and a better pi-donor than oxygen, so the enamine pathway is faster.



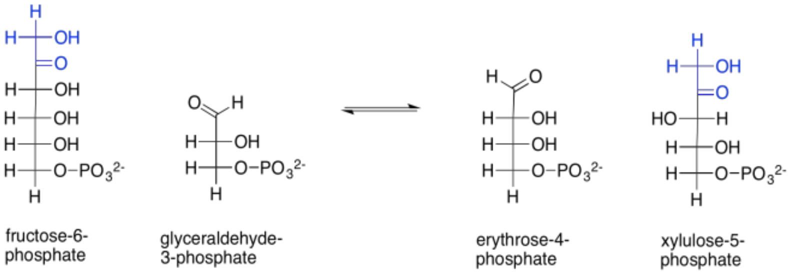


The next step in the Calvin cycle is just a dephosphorylation, carried out with the help of a phosphatase. In this case, the enzyme is called fructose-1,6-bisphosphatase. Phosphorylations and dephosphorylations of substrates, like phosphorylation and dephosphorylation of enzymes, are often key regulatory steps, required to promote a reaction involving an enzyme.



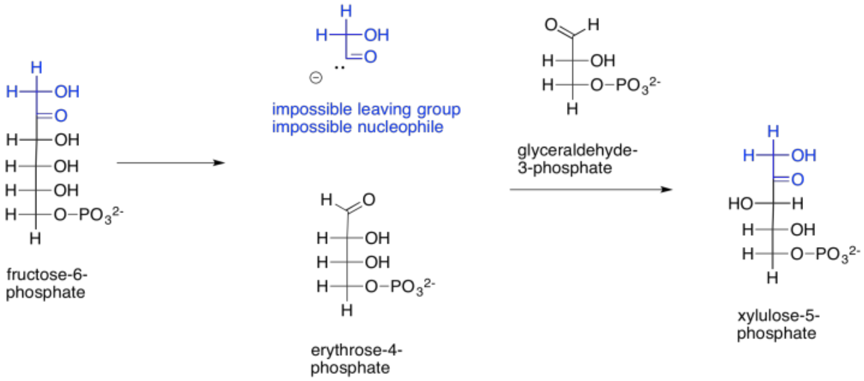
Scheme 9.9.6: Transformation of fructose-1,6-bisphosphate via a phosphatase.

On to the next step. This is when things get a little bit funky. Two carbohydrate molecules undergo a sort of metathesis together. In a metathesis reaction, compounds are split up and recombined in a new way. In this reaction, fructose-6-phosphate combines with another glyceraldehyde-3-phosphate. After the reaction, the two old sugars have been changed into two new ones: erythrose-4-phosphate and xylulose-5-phosphate. It appears as though the fructose has been split and two of its carbons have connected with the glyceraldehyde chain.



Scheme 9.9.7: The reorganisation of fructose-6-phosphate and glyceraldehyde-3-phosphate into two new sugars.

How does that happen? The main part of the fructose-6-phosphate molecule turns into erythrose-4-phosphate. You can imagine that much happening if the number three carbon's hydroxy group performs a pi donation to form the new aldehyde group. That's the topmost OH group, in black, in fructose-6-phosphate. That explains the erythrose-4-phosphate formation. The trouble is, that pi donation would require that something leaves carbon three. The leaving group would be an anionic carbonyl. You probably haven't seen such a leaving group before, for good reason.



Scheme 9.9.8: A mechanistic quandary: conversion of fructose-6-phosphate to erythrose-4-phosphate formally appears to involve an unprecedented leaving group.

Let's not abandon this idea, just yet. If that leaving group did form (and it doesn't), that would explain the formation of xylulose-5-phosphate, too. The carbonyl-based anion, if it were to act as a nucleophile, would form a new carbon-carbon bond, opening up the carbonyl of glyceraldehyde-3-phosphate to form the hydroxy group on what is now carbon three of xylulose-5-phosphate (uppermost on the left, in black).

There is more to this reaction than just one step. The problem is, we need to form a better leaving group. That will take some extra effort. The addition of the ylide of thiamine pyrophosphate (TPP) will help. By adding temporarily to the carbonyl of fructose-6-phosphate, we can get around the problem of having an anion form on the carbonyl carbon.

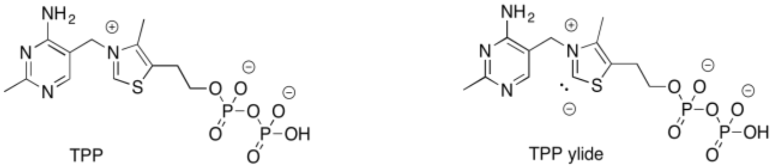


Figure 9.9.5: Thiamine pyrophosphate. The corresponding ylide is able to stabilise "carbonyl" leaving groups.

This same strategy comes up during the citric acid cycle (or TCA cycle), where you may have seen the TPP ylide before. In that cycle, the decarboxylation of pyruvate is impossible because there is no alpha carbon on which to stabilise the anion that forms via decarboxylation. The negative charge on the carbonyl carbon may seem like a good idea, because it is near the electronegative oxygen. Unlike an alpha position, though, the lone pair cannot fully delocalise onto the oxygen. That's because the lone pair associated with the anion -- the lone pair that forms from the broken bond -- must be orthogonal to the pi bond.

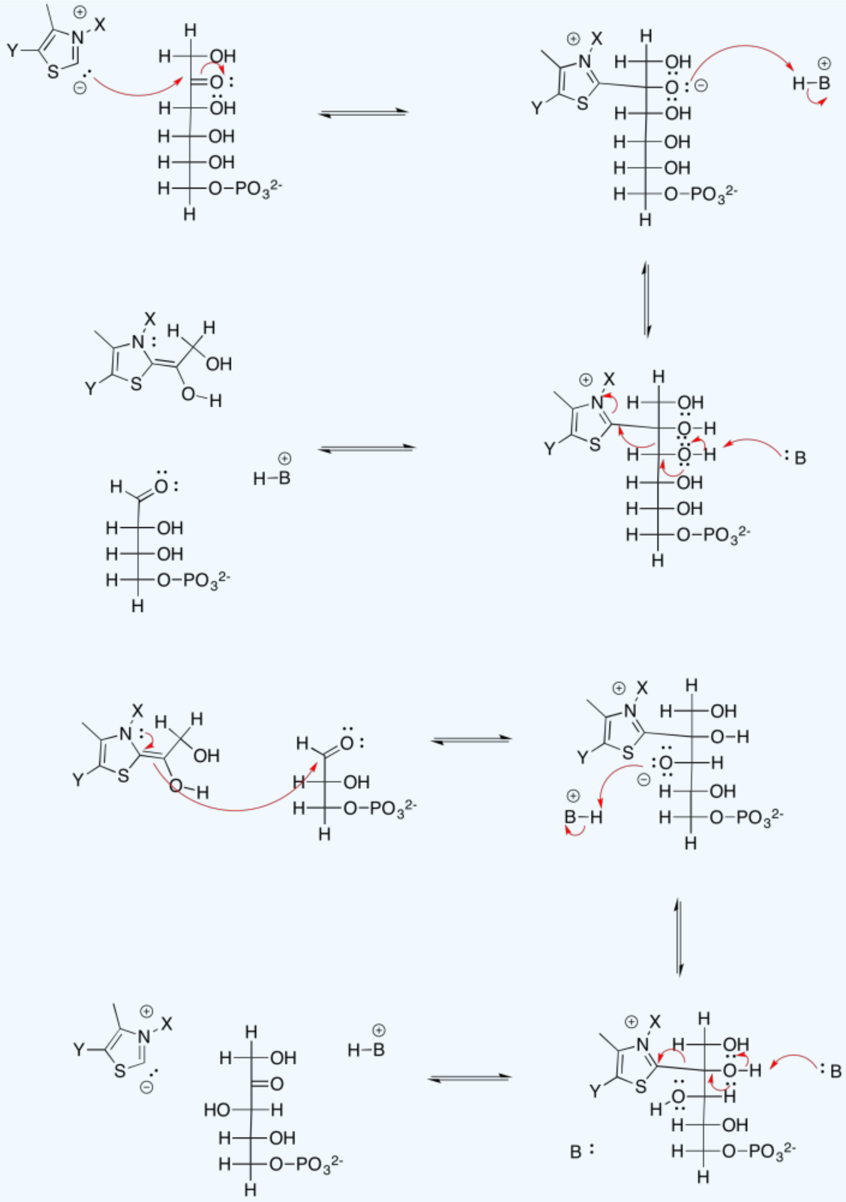
TPP comes to the rescue. Addition of TPP ylide to the ketone installs an iminium ion, turning the former carbonyl carbon into an alpha position (it is alpha to an imine instead of a carbonyl, but it works the same way). The required anion is now fully stabilised by resonance.

In the transketolase reaction, the anion also needs to be stabilised at the carbonyl position. The TPP ylide can add to the carbonyl of the sugar, installing an imine next to the former carbonyl carbon. After the reaction is done, the TPP can be displaced again to form a new carbonyl on xylulose-5-phosphate. All of this process is catalysed by an enzyme, transketolase.

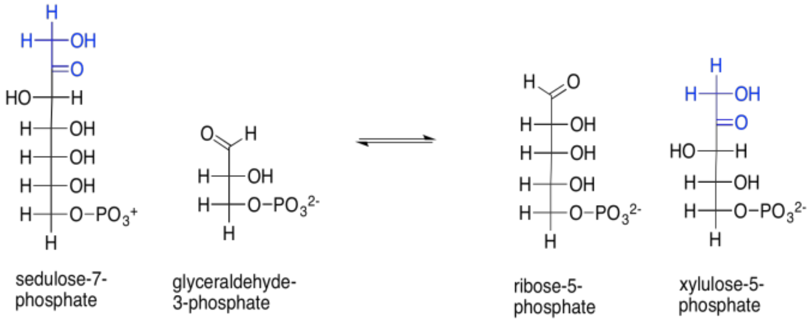
Exercise 9.9.8

Provide a mechanism for the TPP-mediated conversion of fructose-6-phosphate and 3-glyceraldehyde phosphate into erythrose-4-phosphate and xylylose-4-phosphate.

Answer

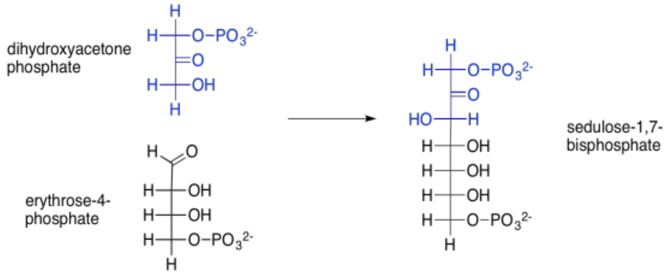


That isn't the only reaction catalysed by transketolase. Sedulose-7-phosphate also reacts with glyceraldehyde-3-phosphate, in this case forming ribulose-5-phosphate and xylulose-5-phosphate. Note that first product: ribose. Ribose is the ketose form of the aldose sugar, ribulose. Ribulose was the sugar we started with; its bisphosphate form was taken up by rubisco to trap CO_2. We are very close to completing a cycle, and are almost ready to capture another carbon dioxide molecule, adding more stock to the carbon pool.



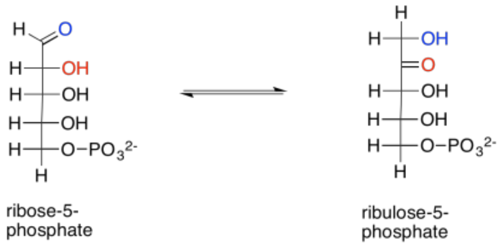
Scheme 9.9.9: The similar reaction of sedulose-7-phosphate with glyceraldehyde-3-phosphate is also catalysed by transketolase.

But where does that sedulose come from, anyway? That's the product of another aldol reaction, this time between dihydroxyacetone phosphate and erythrose-4-phosphate. Erythrose-4-phosphate was the other product of our first transketolase reaction.



Scheme 9.9.10: Sedulose-1,7-bisphosphate is formed via and aldol reaction, catalysed by aldolase.

We are almost finished the complete Calvin cycle. First, ribose-5-phosphate just needs to be converted to ribulose-5-phosphate. That entails a keto-enol mechanism, in which an alpha proton is transferred to the carbonyl oxygen. The reaction is accelerated in the presence of the enzyme, ribose phosphate isomerase.

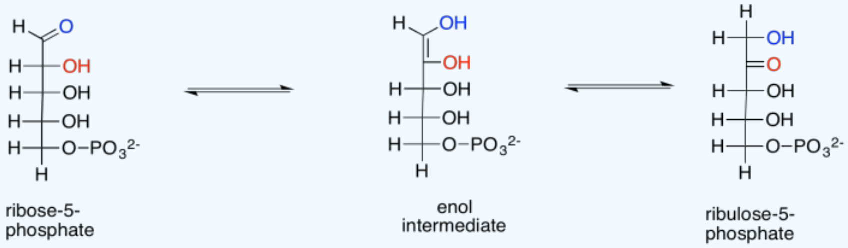


Scheme 9.9.11: Ribulose-5-phosphate is also formed via tautomerism of ribose-5-phosphate.

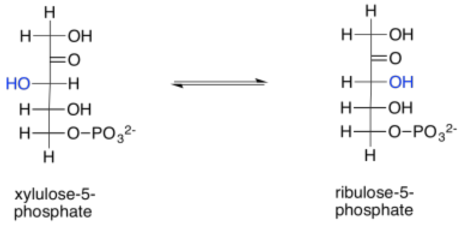
Exercise 9.9.9

Show the enol intermediate between ribose-5-phosphate and ribulose-5-phosphate.

Answer



Ribulose is produced in another reaction within the Calvin cycle, too. Ribulose-5-phosphate is just the epimer of xylulose-5-phosphate. In other words, it is the stereoisomer formed by removing a proton from the chiral alpha position of xylulose-5-phosphate and putting it back on the wrong side. The configuration at that position is changed from *(S)* to *(R)*, producing the diastereomeric ribulose-5-phosphate instead. This reversible reaction is undertaken by the enzyme, ribulose phosphate epimerase.



Scheme 9.9.12: Ribulose-5-phosphate is also formed via epimerisation of xylulose-5-phosphate.

Xylulose-5-phosphate was one of the products of both transketolase-catalysed reactions; one of those reactions also produced ribose-5-phosphate. That means the same reaction provides two precursors to ribulose-5-phosphate (xylulose-5-phosphate and ribose-5-phosphate) and another reaction, catalysed by the same enzyme, produces a third (another molecule of xylulose-5-phosphate).

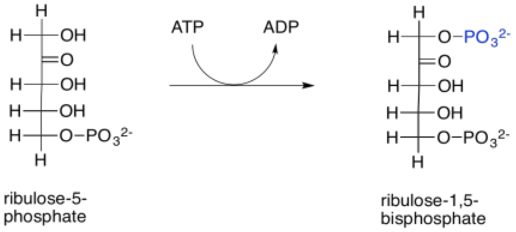
? Exercise 9.9.10

The name, ribulose phosphate epimerase, suggests that the same enzyme actually carries out the reverse reaction: the conversion of ribulose-5-phosphate to xylulose-5-phosphate. How might such a reversible reaction be regulated?

Answer

> Reaction that are in equilibrium are often under substrate control. Because the enzyme can catalyse the reaction in both directions, the direction of the reaction driven by the enzyme is controlled by the relative amount of reactants on either side of the reaction. For example, if the xylulose concentration greatly increased, then the amount of xylulose bound by the enzyme would also increase, so the enzyme would shift xylulose into ribulose and thereby maintain equilibrium. If the ribulose concentration greatly increased, then more ribulose would be bound by the enzyme, and the ribulose would be converted into xylulose.

The ribulose-5-phosphate will be ready to bind rubisco and take up a carbon dioxide molecule as soon as it is phosphorylated by ribulose phosphate kinase. This reaction is largely irreversible as written because of the expenditure of ATP.



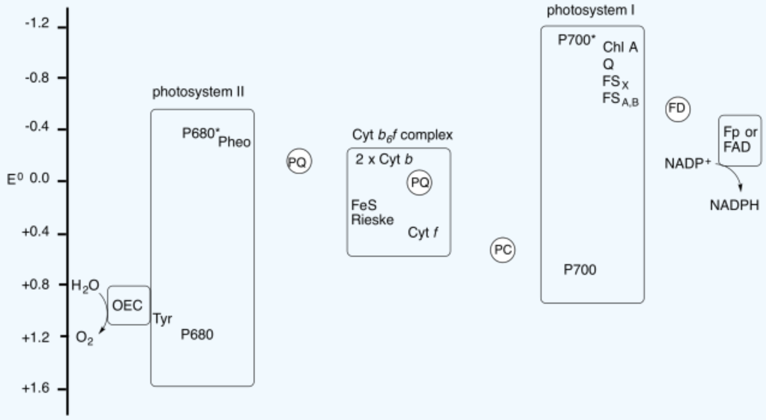
Scheme 9.9.13: Readying the ribulose-5-phosphate for incorporation of another CO_2 molecule in rubisco.

X-ray crystal structures: Taylor, T.C.; Andersson, I. The structure of the complex between rubisco and its natural substrate ribulose 1,5-bisphosphate. *J. Mol. Biol.* **1997** *265*: 432-444. Images obtained via RCSB Protein Data Bank (1RCX).

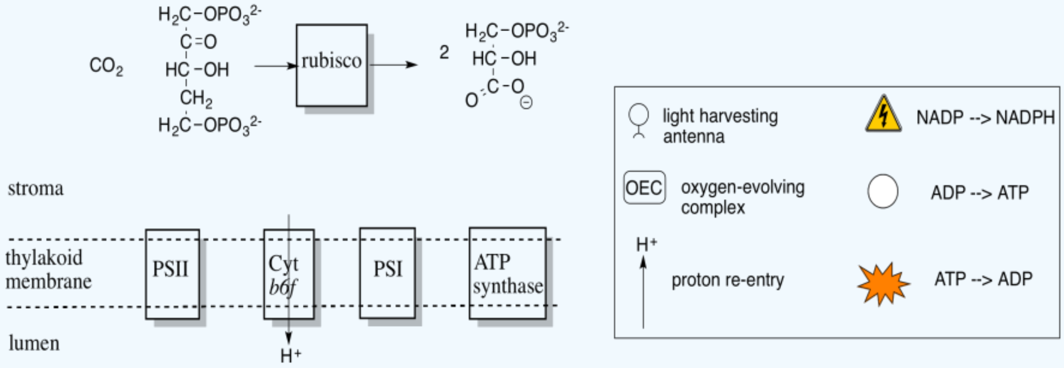
9.10: Additional Problems

Exercise 9.10.1

Provide arrows to illustrate the electron transport chain in the following scheme.



Exercise 9.10.2



CHAPTER OVERVIEW

10: Reactions Under Orbital Control

10.1: Introduction

Pericyclic reactions differ from the ones we have looked at so far because they are not easily understood in Lewis acid- Lewis base terms. There is not always a clear nucleophile and electrophile in these reactions. In fact, they may appear to involve completely non-polar reactants.

The classic example of a pericyclic reaction is a Cope rearrangement. In a Cope rearrangement, a molecule reorganizes itself, trading in some sigma bonds for pi bonds, so that by the end of the reaction the atoms are connected in a slightly different way. At first, it doesn't seem like much has happened in this reaction, but if you look closely, you can see how specific bonds have changed places.

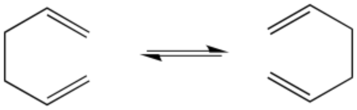


Figure 10.1.1: A very simple Cope rearrangement in 1,5-hexadiene.

Highlighting specific bonds with colour is helpful here. Keeping track of electrons with arrows usually helps, too.

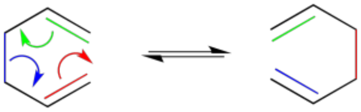


Figure 10.1.2: The Cope rearrangement highlighted with colour.

Cycloadditions are very closely related to pericyclic reactions. The most common example of a cycloaddition reaction is a Diels Alder reaction. A Diels Alder reaction takes place between two alkenes. Below, you can see a Diels Alder reaction between ethene and 1,3-butadiene.

Figure 10.1.3: Diels Alder reaction between ethene and 1,3-butadiene.

Once again, keeping track of electrons can help us to establish what is going on here.

Figure 10.1.4: Diels Alder reactionwith electron movement highlighted.

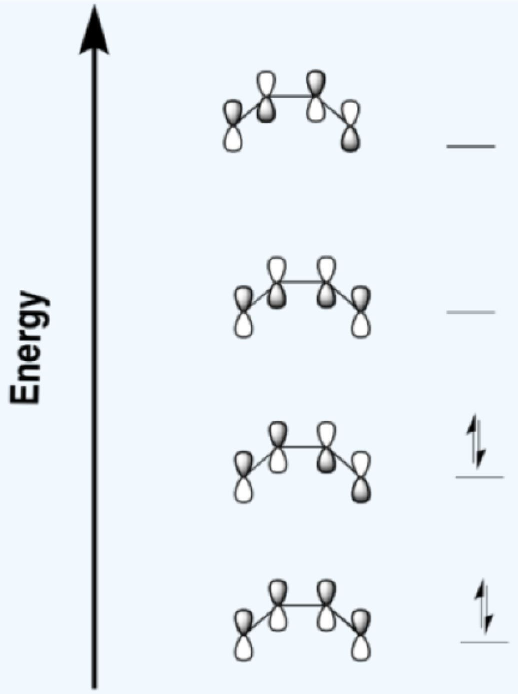
Normally, we think of both of these compounds as nucleophiles. It isn't easy to see why one would react with the other. It isn't easy to see how electrons would be attracted from one molecule to the other.

Instead, pericyclic reactions rely on weak attractions between (or within) molecules that can lead to electronic interactions that result in new bond formation. Normally, pericyclic reactions are studied using molecular orbital calculations to map out these electronic interactions. That analysis makes use of group theory, the mathematics of symmetry. However, they are also explained qualitatively using simplified molecular orbital pictures; that's the approach we'll take here.

? Exercise 10.1.1

Pericylic reactions depend on molecular orbital interactions. Draw the π-bonding molecular orbitals for butadiene, ranked in energy. In other words, draw a Huckel molecular orbital diagram for butadiene.

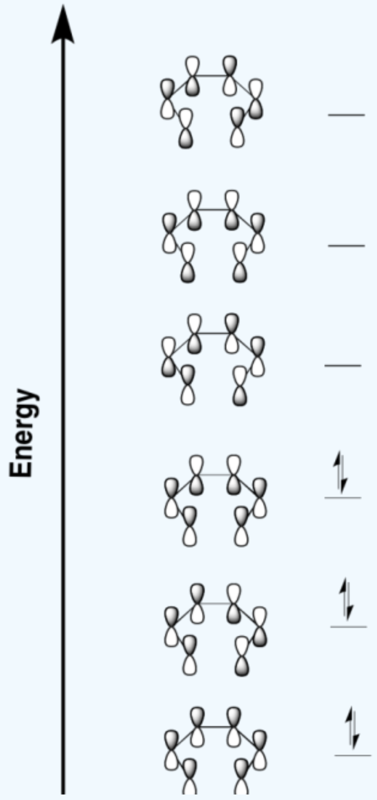
Answer



Exercise 10.1.2

Draw a Huckel molecular orbital diagram for hexatriene.

Answer



10.2: Cope and Claisen Rearrangements

A rearrangement is a reaction in which one molecule undergoes bonding changes, with the transfer of one atom or group from one position in the molecule to another.

Proton tautomerism is a kind of rearrangement. A proton is removed from one site in the molecule and put back in a different site nearby. Tautomerism generally requires a couple of proton transfer steps in a row. A proton is removed from one site and then a proton is placed on the new site. (In another variation, a proton is added at one site and then a proton is removed from the old site.)

However, rearrangements often involve the concerted transfer of a group from one site to another within the molecule. The group loses its bond to one site and gains its bond to the other site at the same time.

A Cope rearrangement happens that way.

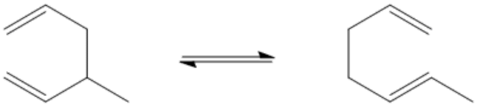


Figure 10.2.1: A Cope rearrangement

At first it may not seem like much has happened in this reaction. The two pi bonds have changed position, however, and so has one of the sigma bonds. That means a total of six electrons have moved (two electrons per bond).

Figure 10.2.2: A diagram of electron movement in a Cope rearrangement.

It does not matter which directions you draw the arrows moving in figure PR2.2. They could be shown going clockwise or counterclockwise. There is no electrophile or nucleophile. However, the arrows help with "electron book-keeping". The number of electrons is significant, however.

- Six electrons move in a circle of six atoms.

That patterns is reminiscent of benzene. This reaction may be related to the unusual stability of benzene. The transition state for this reaction is considered to be somewhat like benzene. Halfway between one structure and the other, the electrons are delocalized around the ring of atoms.

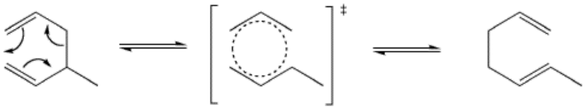


Figure 10.2.3: The transition state in a Cope rearrangement.

A Cope rearrangement can be considered to occur via a rearrangement of overlap between a group of orbitals around this ring. Two orbitals forming a sigma bond tilt away from each other while two orbitals that are pi bonding tilt toward each other.

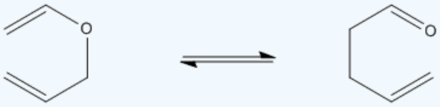
Figure 10.2.4: Orbital rearrangement in a Cope rearrangement

Now there are p orbitals parallel to each other on the left, able to form new pi bonds.

Many concerted rearrangements can be thought of in terms of these orbital reorganizations.

? Exercise 10.2.1

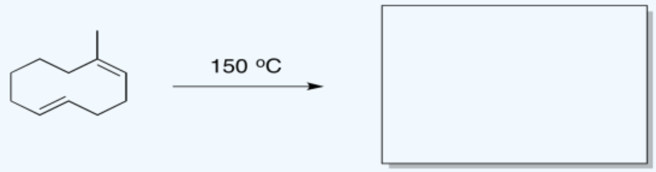
A Claisen rearrangement is very similar to a Cope rearrangement, but oxygen is involved.

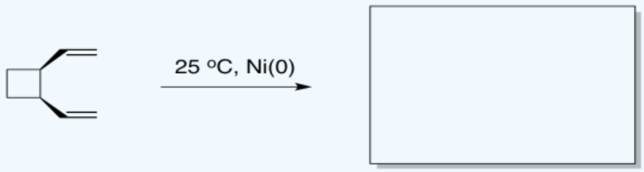


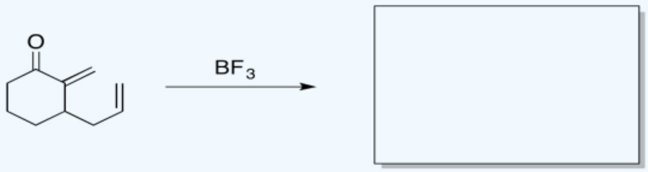
a. Draw curved arrows to keep track of electrons in this Claisen rearrangement.
b. Draw the aromatic transition state of the Claisen rearrangement.
c. Draw the orbital reorganization in the Claisen rearrangement.

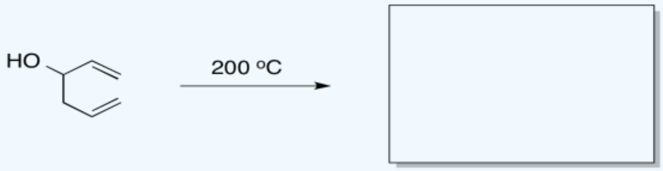
? Exercise 10.2.2

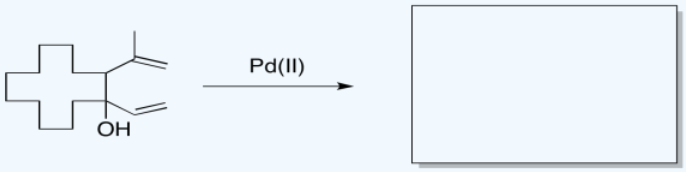
Provide products for the following Cope rearrangements.











Answer

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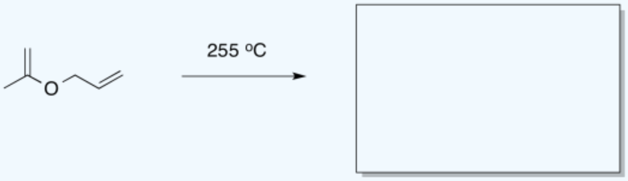
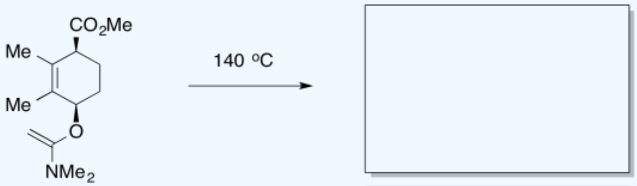
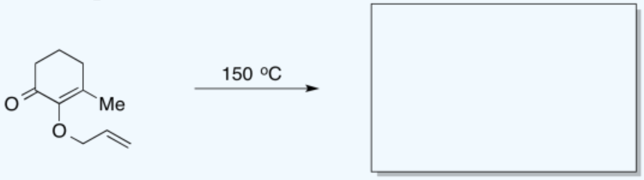
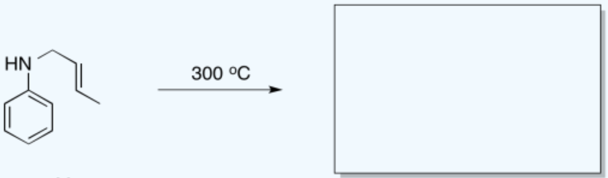
Exercise 10.2.3

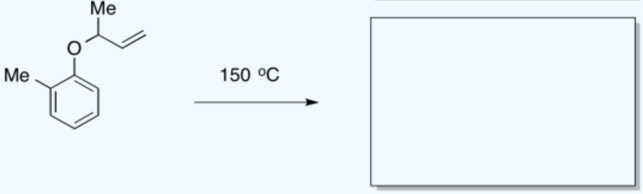
Provide products for the following Claisen rearrangements.


255 °C


CO$_2$Me
Me
Me
O
NMe$_2$
140 °C


O
Me
O
150 °C

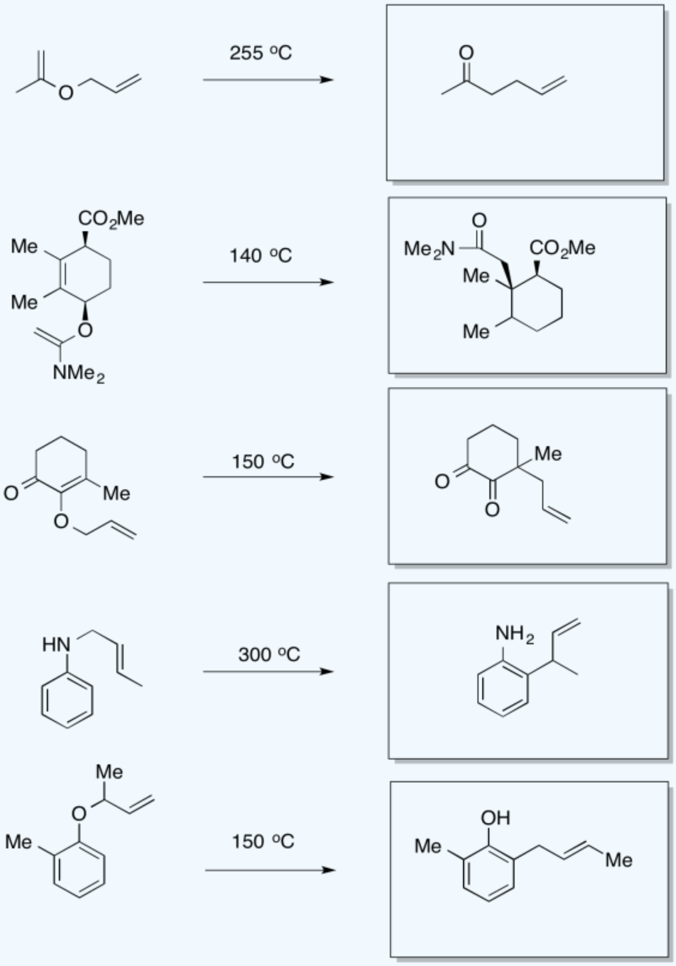

HN
300 °C

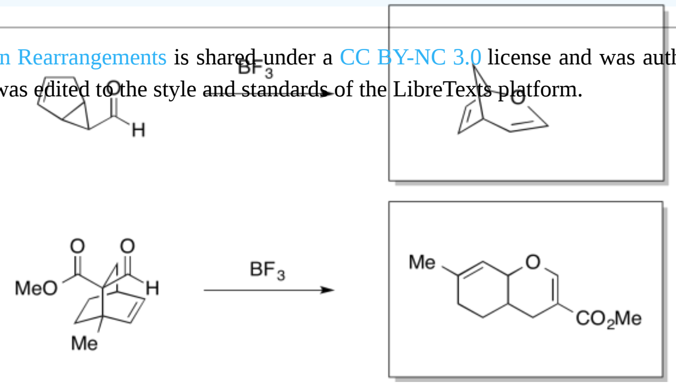

Me
O
Me
150 °C


O
H
BF$_3$


O
O
MeO
H
Me
BF$_3$

Answer


255 °C
O
CO$_2$Me
Me
Me
O
NMe$_2$
140 °C
Me$_2$N
O
CO$_2$Me
Me
Me
O
Me
O
150 °C
O
O
Me
HN
300 °C
NH$_2$
Me
O
Me
150 °C
OH
Me
Me


O
H
BF$_3$
O
O
O
MeO
H
Me
BF$_3$
Me
O
CO$_2$Me

10.3: The Diels Alder Reaction

As noted previously, the Diels Alder reaction is a classic example of a cycloaddition reaction. A cycloaddition reaction has a lot in common with a pericyclic reaction like a Cope rearrangement.

Figure 10.3.1: The Diels Alder reaction.

Unlike the Cope and Claisen rearrangements, this reaction often occurs intermolecularly (between two molecules). It requires an alkene on one molecule and a conjugated diene on the other molecule. The alkene is referred to as a "dienophile"; it reacts with the conjugated pair of double bonds. In the drawing below, the ethene and the 1,3-butadiene are labelled as diene and dienophile, respectively.

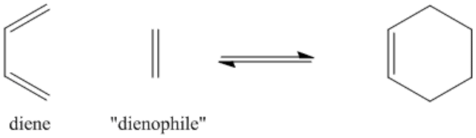
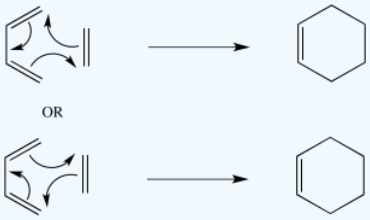


Figure 10.3.2: The diene and dienophile in the Diels Alder reaction.

Exercise 10.3.1

Draw curved arrows to keep track of electrons in the Diels Alder reaction.

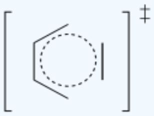
Answer



Exercise 10.3.2

Draw the aromatic transition state of the Diels Alder reaction.

Answer

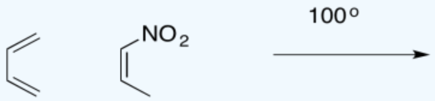


Exercise 10.3.3

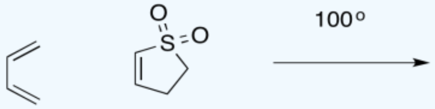
Provide products for the Diels Alder reactions below.

a)

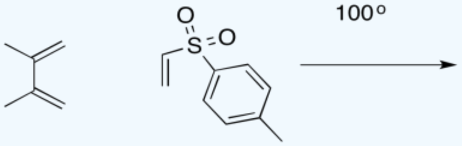
b)



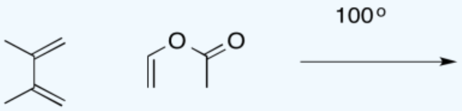
c)



d)



e)



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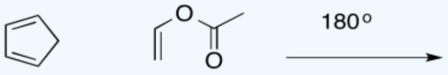
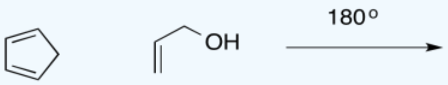
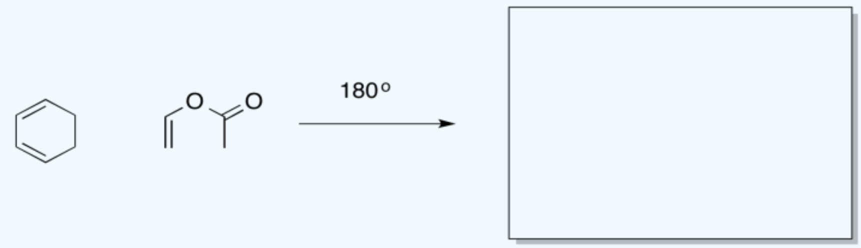


g)



h)



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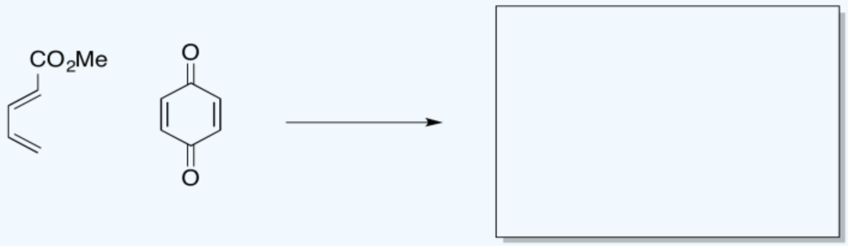
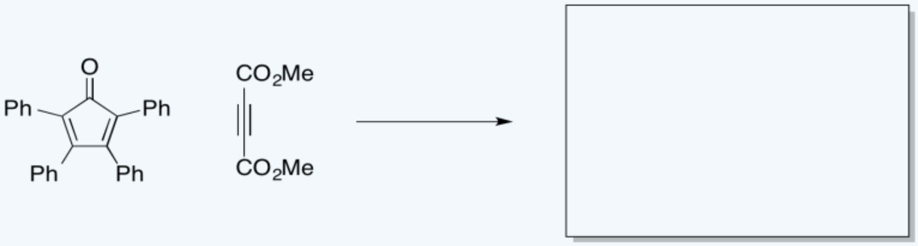
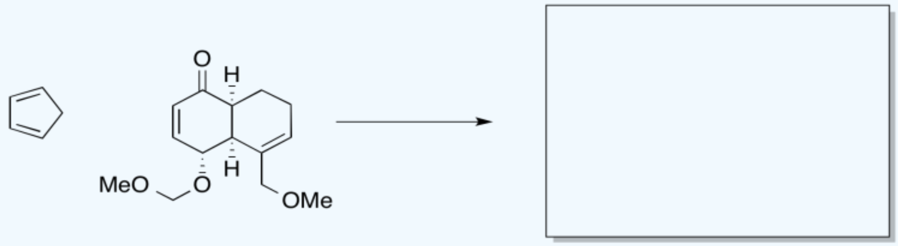


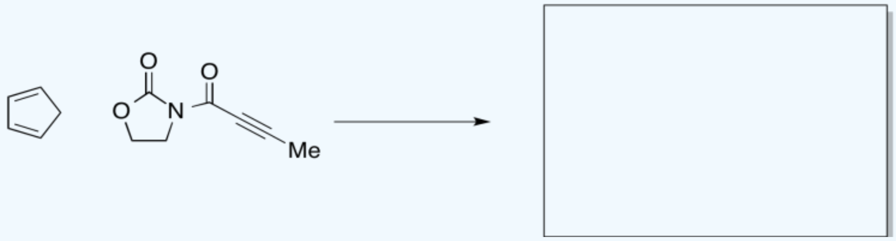
j)



k)

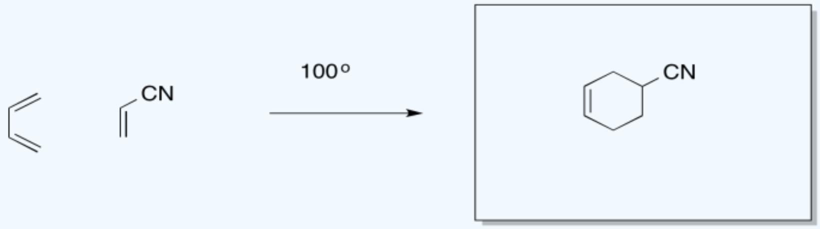


l)

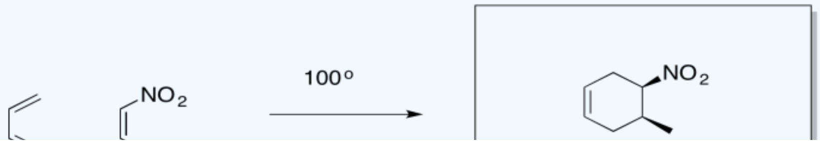


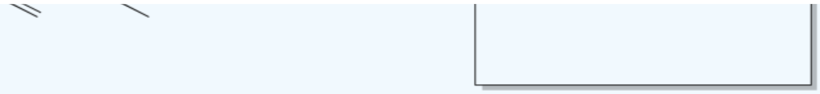
Answer

a)



b)





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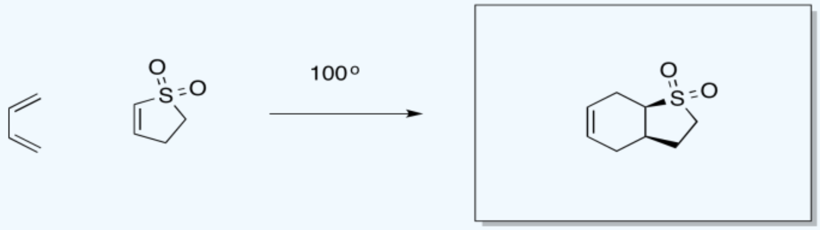

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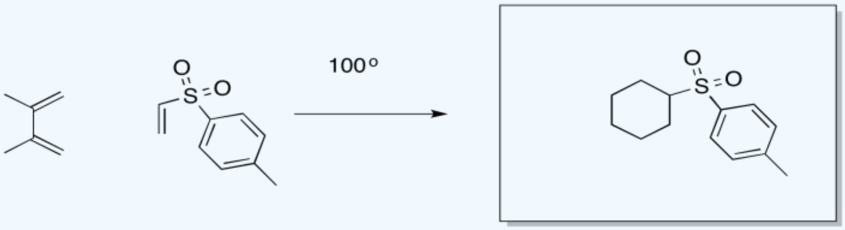

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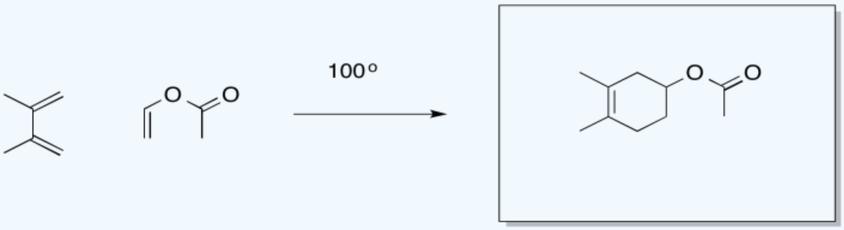

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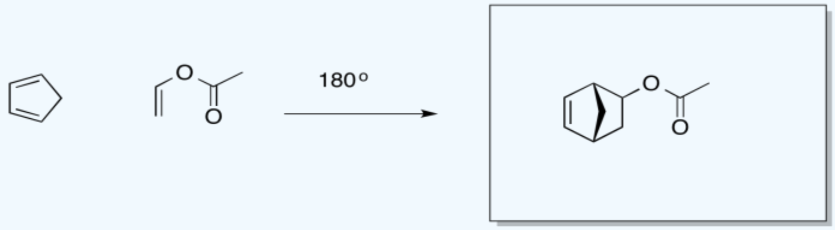

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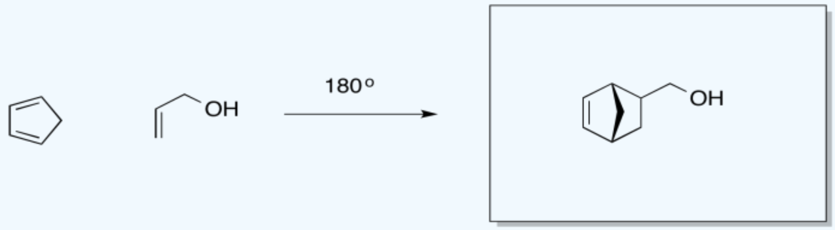

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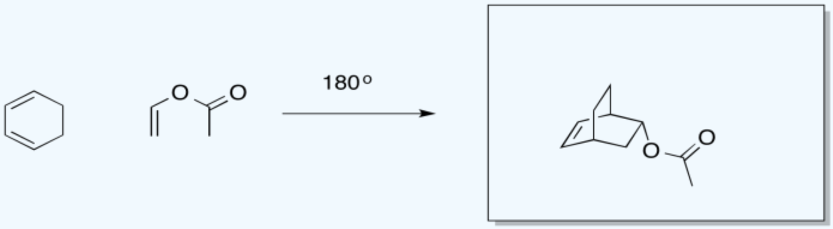
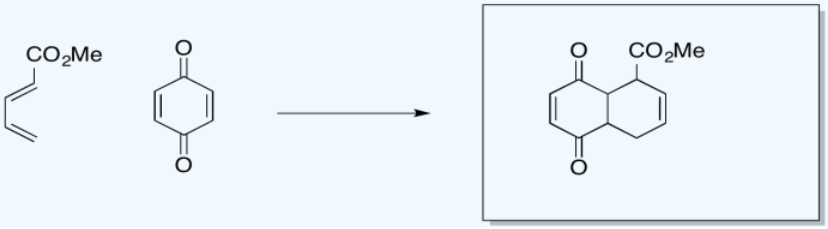
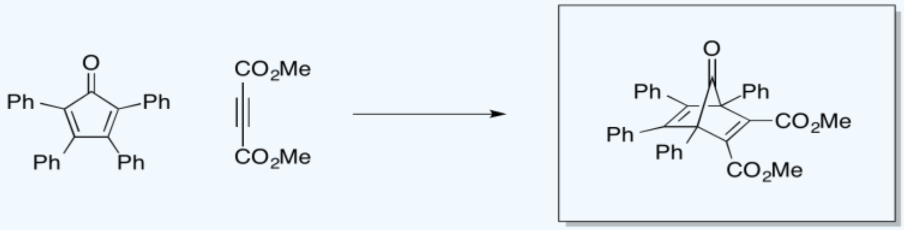


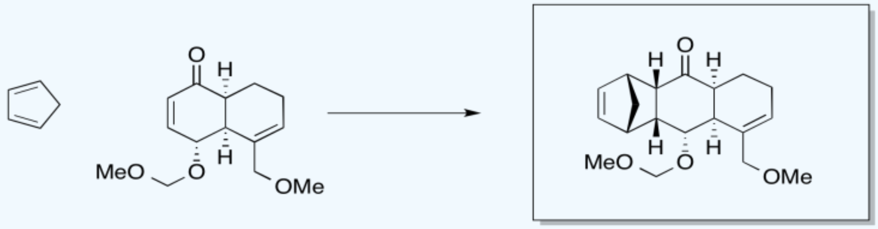
i)



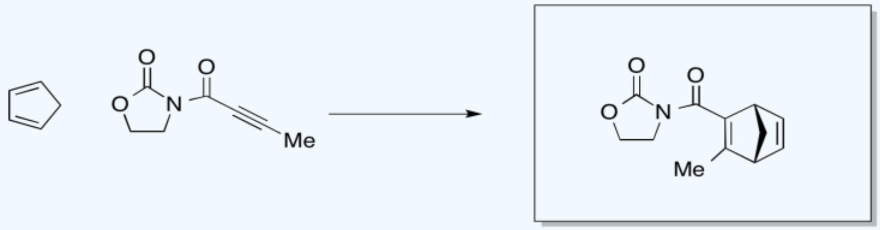
j)



k)



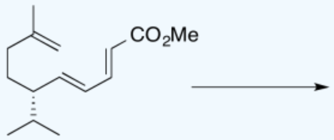
l)



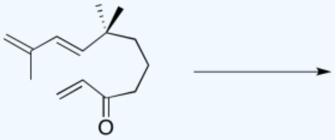
Although Diels Alder reactions frequently occur between two molecules, they can happen intramolecularly as well. In these cases, there must be an alkene in one part of the molecule that is able to reach over and interact with a conjugated diene on another part. In some ways, intramolecular Diels Alder reactions can be easier than their intermolecular counterparts for reasons of internal entropy. Rather than bringing two molecules together and combining them into one, the intramolecular Diels Alder starts with one molecule to begin with.

? Exercise 10.3.4

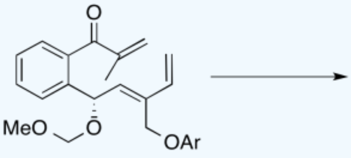
a)



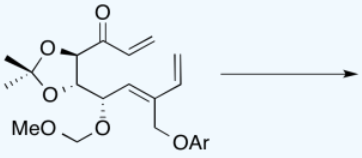
b)



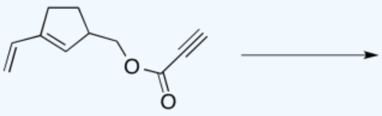
c)



d)



e)



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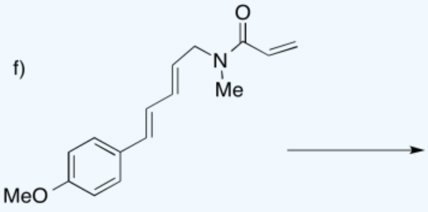
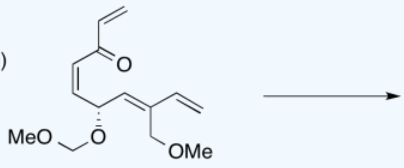


g)



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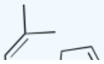
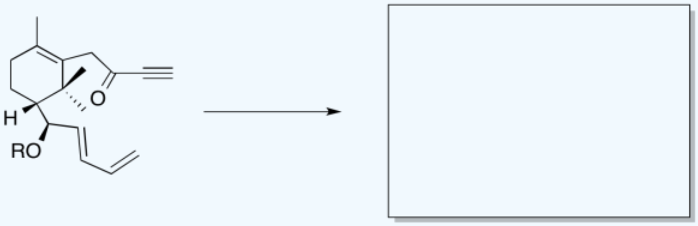
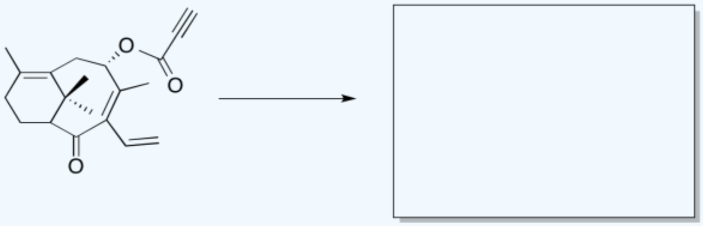


i)

j)



k)



Answer

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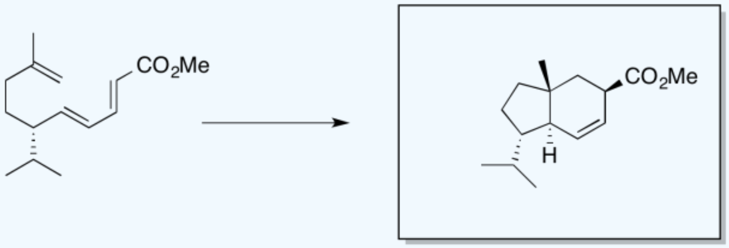

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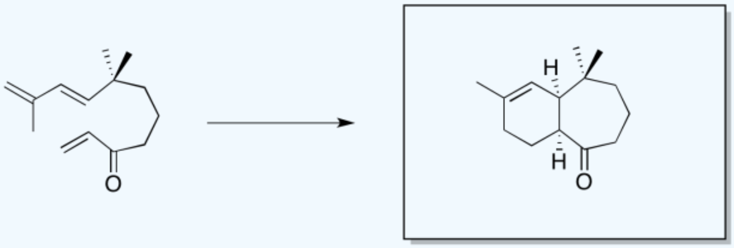

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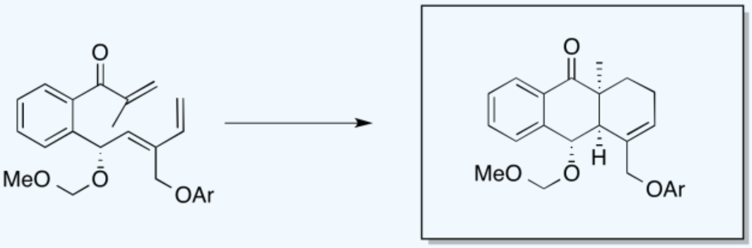

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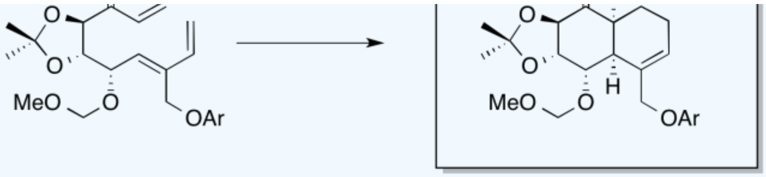
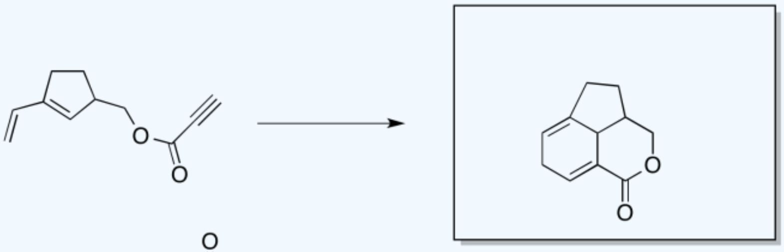
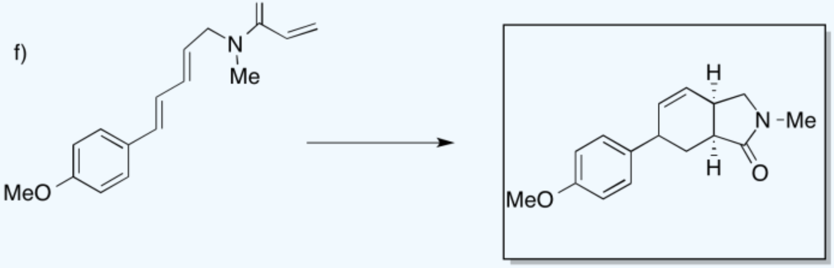

O
O
MeO
O
OAr
O
O
MeO
O
H
OAr

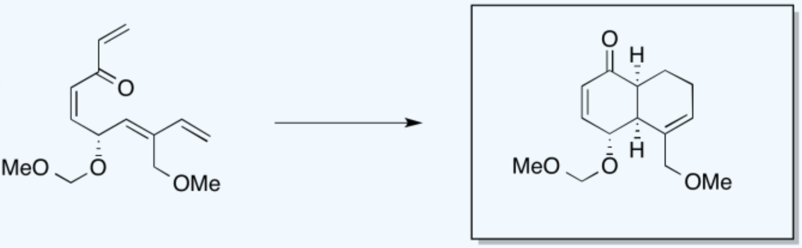
e)


O
O
O
O

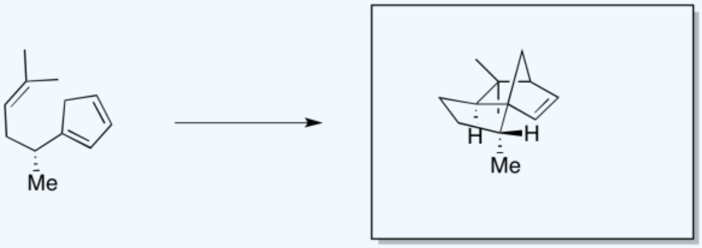
f)


O
N
Me
MeO
H
N -Me
H
O
MeO

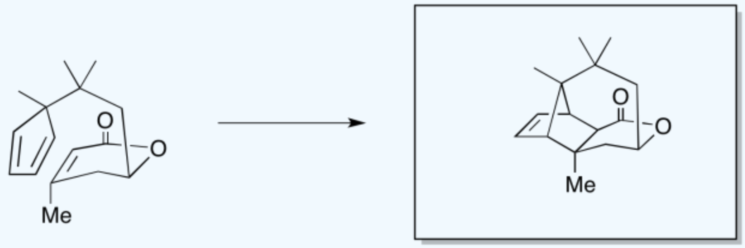
g)


O
MeO
O
OMe
O
H
MeO
O
H
OMe

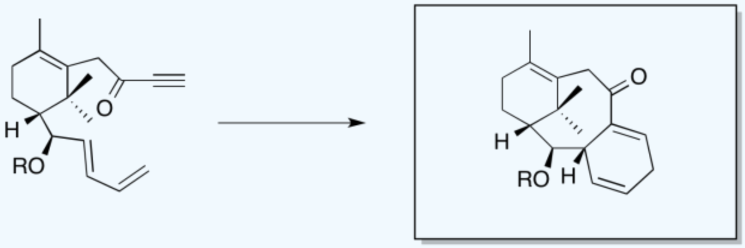
h)

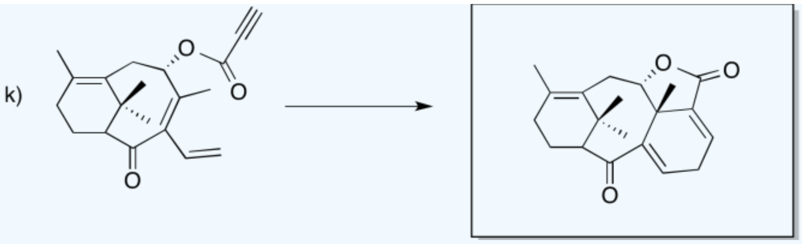

Me
H
H
Me

i)


O
O
Me
O
O
Me

j)


O
H
RO
O
H
RO
H



Many pericyclic reactions are reversible. The reversible process is usually named the same way as the forward reaction, but with the prefix "retro". For example, a Diels Alder reaction and the corresponding retro-Diels Alder reaction are shown together below.

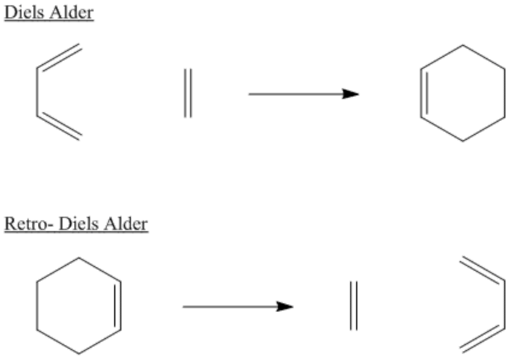


Figure 10.3.3: A Diels Alder reaction and its reverse.

Typically, Diels Alder reactions occur at low or moderate temperatures (between 25 °C and 100 °C is a common range). In comparison, retro Diels Alder reactions require more elevated temperatures, often above 200 °C. The forward reaction is favored at low temperature, whereas the retro reaction is favored at high temperature.

? Exercise 10.3.5

Draw curved arrows for the retro-Diels Alder reaction to form ethene and 1,3-butadiene.

? Exercise 10.3.6

Explain why higher temperatures promote the retro-Diels Alder reaction using the expression for free energy of a reaction, $\Delta G = \Delta H - T\Delta S$

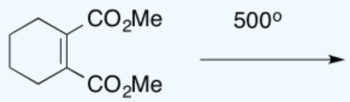
Answer

> The retro-Diels Alder reaction is entropically favoured, because two molecules are made from one molecule. As a result, energy becomes partitioned into additional states because the degrees of freedom are increasing. Internal entropy increases during this reaction. Mathematically, the entropy term is negative in the expression for free energy, so as entropy increases the free energy becomes lower. Because that term is actually a product of entropy and temperature, an increase in temperature has the effect of amplifying the influence of entropy on the free energy of the reaction. Hence, this reaction is favoured by internal entropy factors, which come to dominate at elevated temperature.

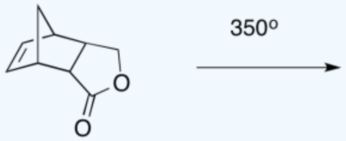
? Exercise 10.3.7

Provide products for the following retro-Diels Alder reactions.

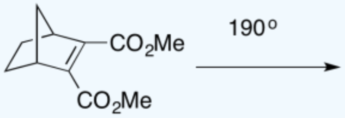
a)


CO2Me
CO2Me
500o

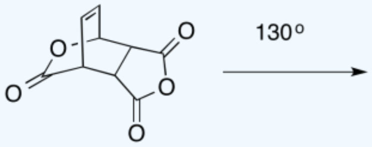
b)


O
O
350o

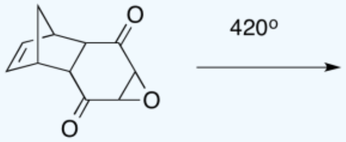
c)


CO2Me
CO2Me
190o

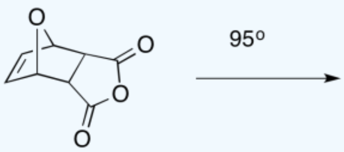
d)


O
O
O
O
O
O
130o

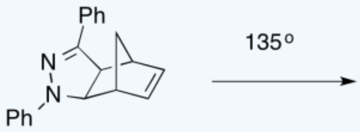
e)


O
O
O
420o

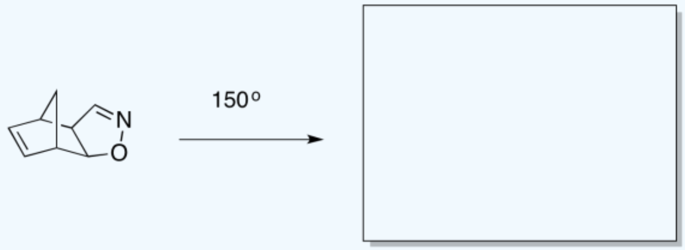
f)


O
O
O
O
95o

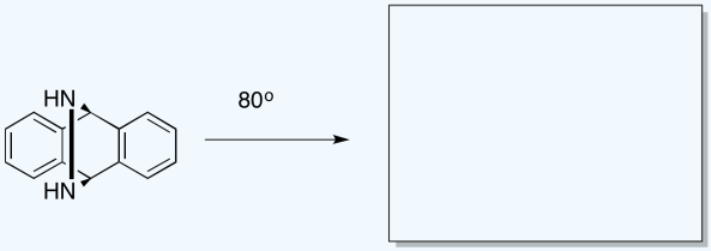
g)


Ph
N
N
Ph
135o

h)



i)



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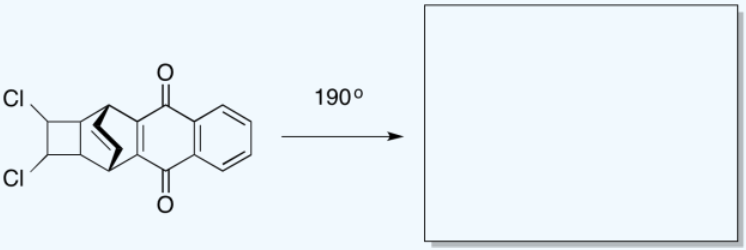
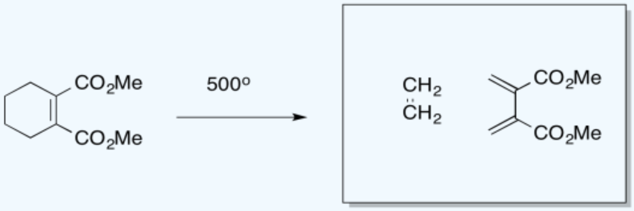


Answer

a)



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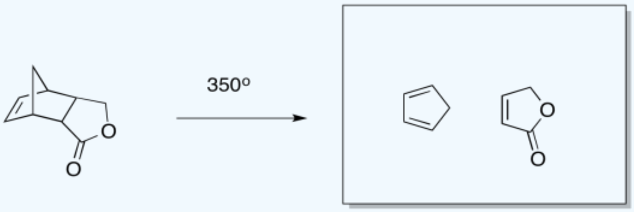
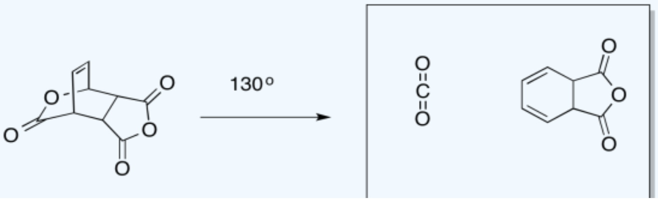
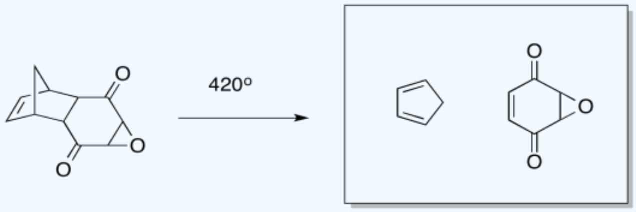


c)

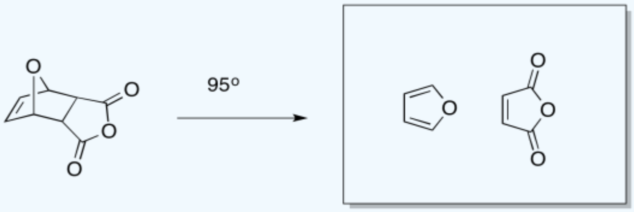
d)



e)



f)



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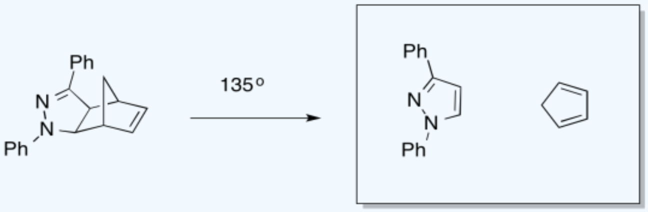

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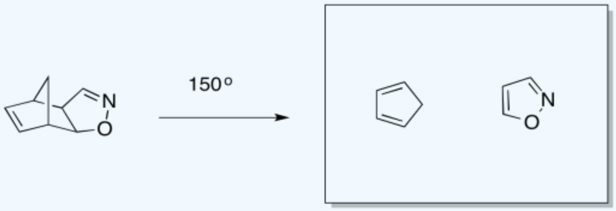

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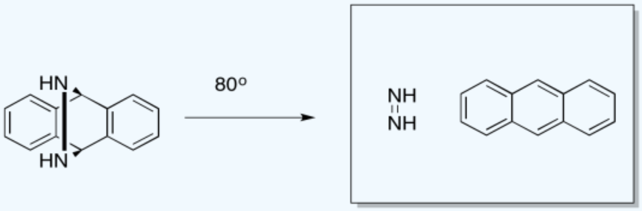

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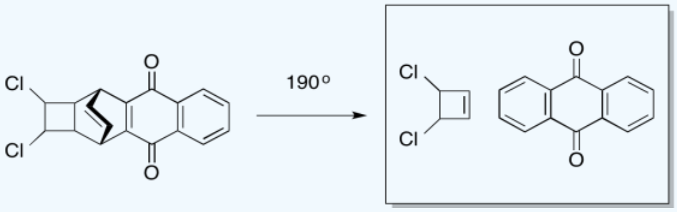
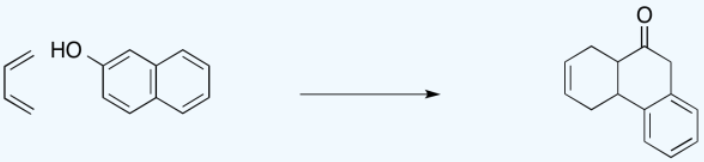
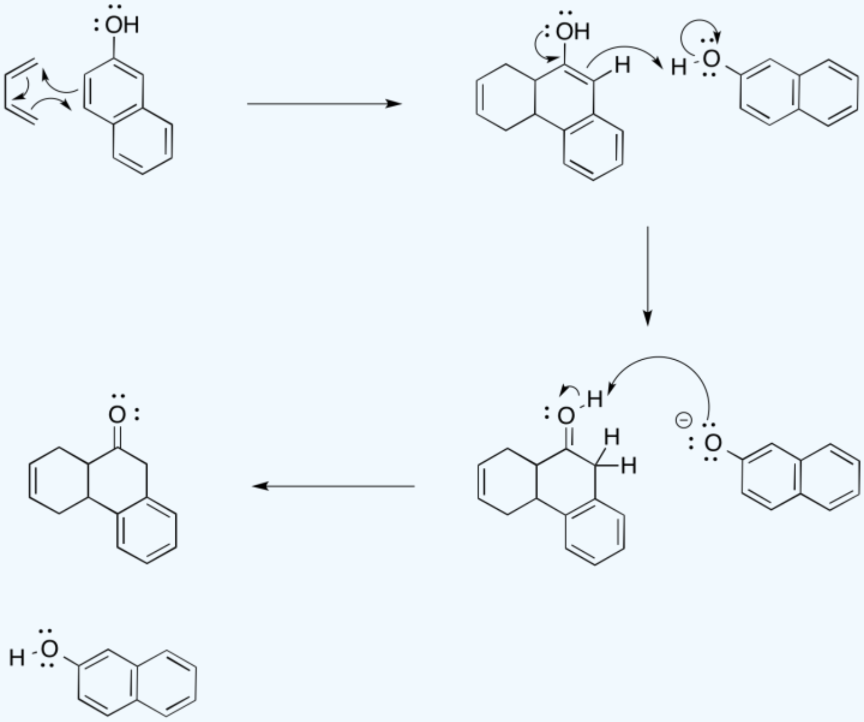


? Exercise 10.3.8

Sometimes, there are subsequent steps that occur after a cycloaddition reaction. For example, the following Diels Alder reaction involving naphthol produces a tautomerised product. Show the mechanism for the reaction sequence.



Answer



The reaction can be thought of in terms of a reorganization of electrons between these two molecules. In the Diels Alder reaction, we can think of an interaction between the LUMO on one molecule and the HOMO on the other. As it happens, the LUMO on one molecule has the correct symmetry such that it can overlap and form a bonding interaction with the HOMO on the other molecule.

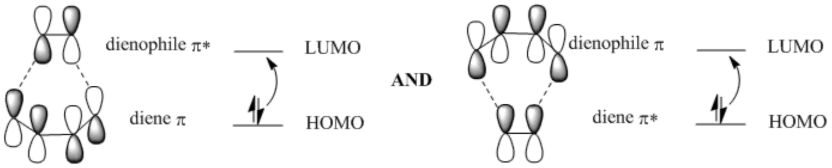


Figure 10.3.3: Qualitative molecular orbital picture of the Diels Alder reaction.

Pay attention to the p orbital drawings on the carbons that will bond to each other to form the six-membered ring. It is important that those orbitals are able to overlap with each other to form an in-phase interaction. In that way, these carbon atoms at the ends of the diene and dienophile are able to bond with each other.

A Diels Alder reaction is sometimes called a [2+4] addition reaction. A 2-carbon unit on one molecule interacts with a 4-carbon unit on another molecule.

In contrast, the addition of one regular alkene to another regular alkene would be called a [2+2] addition reaction. If this reaction occurred, two alkenes would come together to form a four-membered ring.

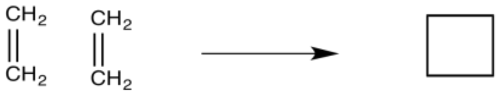


Figure 10.3.4: A [2+2] addition reaction.

However, [2+2] addition reactions don't occur without special circumstances. We will look at the requirements for that reaction later.

10.4: Regiochemistry in Diels Alder Reactions

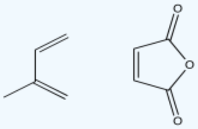
The Diels Alder reaction is the most common cycloaddition reaction. It allows the construction of six-membered rings, These rings are very common in biological small molecules. These compounds are often of interest in medicinal chemistry and other areas of chemical biology. As a result, they are frequently targeted in synthetic studies. Being able to make these compounds, as well as compounds that are structurally related, is a key part of carrying out studies that will help us understand how they work in nature.

When two compounds combine in a Diels Alder reaction, a new ring is formed. Each reactant has two ends: there are two ends on the double bond in the dienophiles, and two ends on the diene, as well. Which end of the diene connects to which end of the dienophile? That is a question of regiochemistry, because we are asking where the reaction happens, or where the new bonds form.

We have thought about pericyclic reactions as being very different from polar reactions involving electrophiles and nucleophiles. That isn't always the case. In fact, there can be a pronounced polar component to these reactions. The cycloaddition of polar molecules is often much faster than nonpolar ones, and can be accelerated in the presence of Lewis acids. The Lewis acids can act as catalysts that activate the reactants, making them even more polar so that the attraction between the two components is greater.

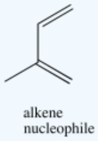
? Exercise 10.4.1

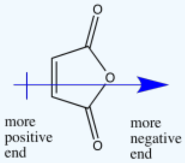
Maleic anhydride is frequently used as a dienophile in Diels Alder reactions. Explain how this component would enhance the interaction between the diene and the dienophile in the following case.



Answer

The maleic anhydride is polarized, with electron density drawn toward the anhydride functional group on one side of the ring. As a result, the other side of the ring is left more positive, and will attract the polarizable electron density from the diene.



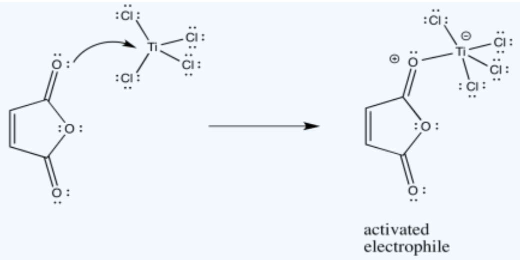


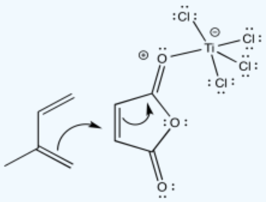
? Exercise 10.4.2

Show how, in the previous question, the interaction between the molecules would be enhanced through the addition of a Lewis acid, such as titanium tetrahloride, $TiCl_4$.

Answer

Lewis acids frequently activate carbonyl compounds towards interaction with nucleophiles. They do so by binding to the lone pairs on the carbonyl oxygen, drawing electron density away from the oxygen and, inductively, away from the neighbouring portion of the molecule.





enhanced pull on electrons from diene

If the reactants are polar, they may not be very symmetric. There may be a polar group attached to a double bond, causing the double bond to become more reactive but also making the molecule more complicated.

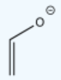
As a result, regiochemistry matters. If each component, the diene and the dienophile, have two very distinctive ends, then it matters which end connects to which, because we could potentially have two different products with completely different properties.

Generally, an understanding of resonance structures can help us to predict how two compounds are going to combine in a Diels Alder reaction.

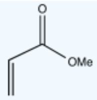
? Exercise 10.4.3

Identify each of the following compounds as electrophilic or nucleophilic at carbon. In each case, include an additional resonance structure to justify your choice.

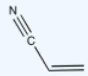
a)



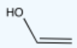
b)



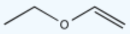
c)



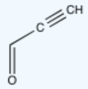
d)



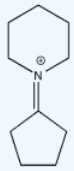
e)



f)



g)



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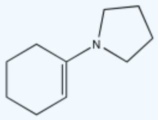
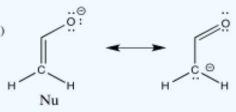


Answer

a)



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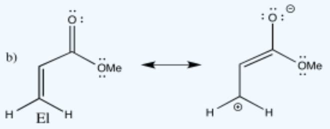

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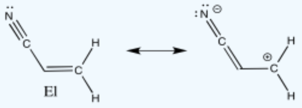

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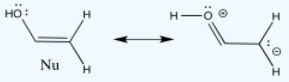

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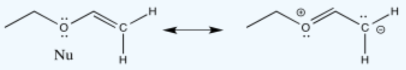

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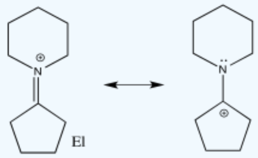
g)



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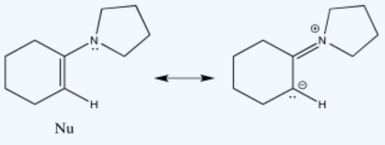
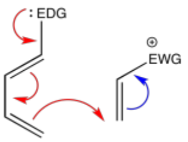


If a diene and a dienophile are to react together, their interaction can be enhanced if one of the reactants is an electrophile and one is a nucleophile. Typically, in these cases the diene is designed to act as a nucleophile and the dienophile is chosen to act as an electrophile. However, there is no particular reason it has to be that way, other than the idea that the two double bonds of the diene already appear to be more electron-rich than the single double bond of the dienophile, and so it seems we only need to give them a little nudge in that direction.

In general, an electron-withdrawing group is installed on the dienophile. Remember, an electron-withdrawing group typically contains a multiple bond to an electronegative atom. If you think of electrophilic substitutions, these were the groups that typically acted as deactivating groups and meta-directors in that situation. Carbonyls, nitriles, and nitro groups are all examples of electron-withdrawing groups.

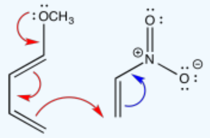


In a complementary manner, an electron-donating group is installed on the diene. Remember, π-donors are good examples of electron-donating groups. In electrophilic aromatic substitutions, electron-donating groups typically acted as ortho-para directors, and were usually activating groups in that situation. Alkoxyl groups and amines are good examples.

? Exercise 10.4.4

Illustrate this electrophile/nucleophile interaction using the diene, $CH_3OCH{=}CHCH{=}CH_2$ and the dienophile, $CH_2{=}CHNO_2$.

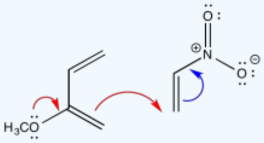
Answer



? Exercise 10.4.5

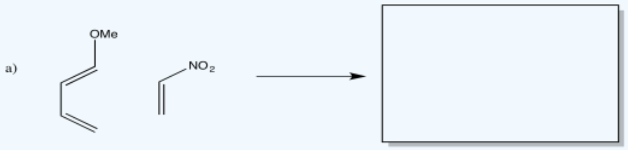
A similar interaction is possible using an isomer of the diene in the previous question, $CH_2{=}C(OCH_3)CH{=}CH_2$. Illustrate the electrophile/nucleophile interaction between this diene and the dienophile, $CH_2{=}CHNO_2$.

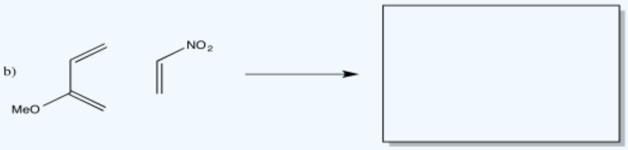
Answer



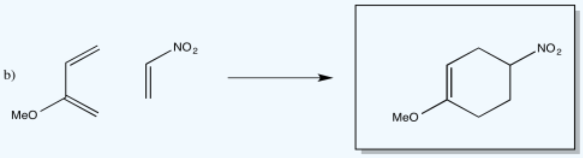
? Exercise 10.4.6

Provide the products of Diels Alder reactions between the reactants below.

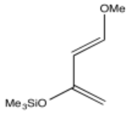




Answer



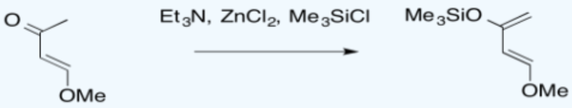
Perhaps the most widely used polar diene is Danishefsky's diene, developed in the laboratory of Samuel Danishefsky of Columbia University and Memorial Sloan-Kettering Cancer Center. Columbia University is a world leader in research in the field of organic chemistry. Danishefsky's lab specializes in the synthesis of complex molecules that may be of medicinal interest.



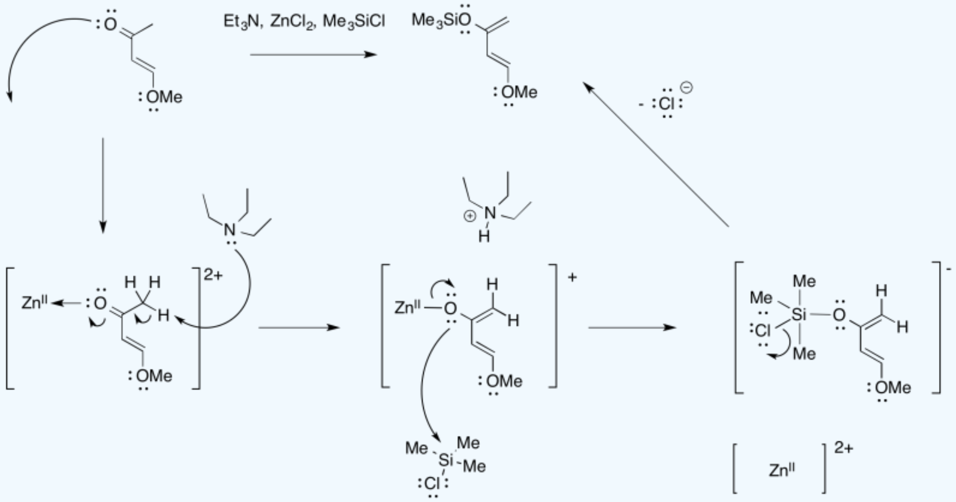
Danishefsky's diene, and others like it, allow for controlled regiochemistry in Diels Alder reactions because π-donation from the alkoxy and siloxy groups both push electron density toward the same location on the diene. It is then able to react more easily with a dienophile. If the dienophile is asymmetric, which in this case means one end is more positive than the other, then the reaction occurs in a predictable way.

Exercise 10.4.7

Provide a mechanism for the formation of Danishefsky's diene under the following conditions.

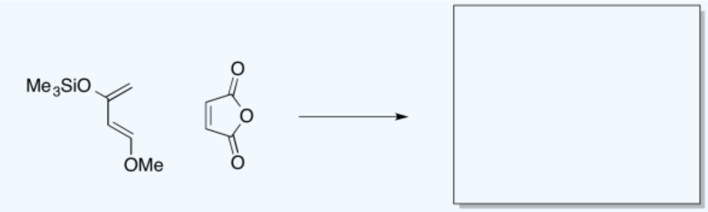


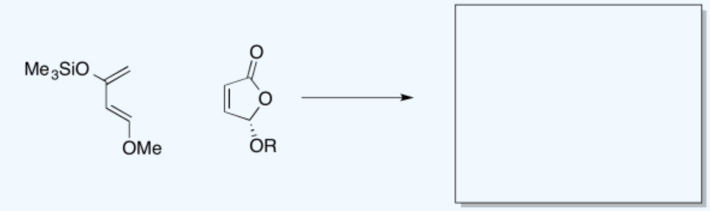
Answer

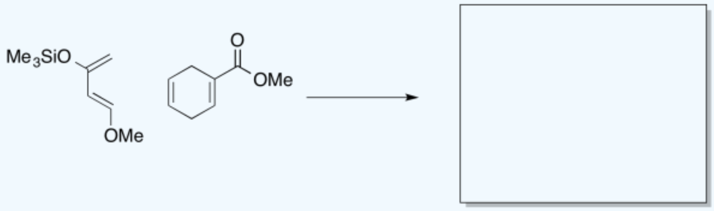


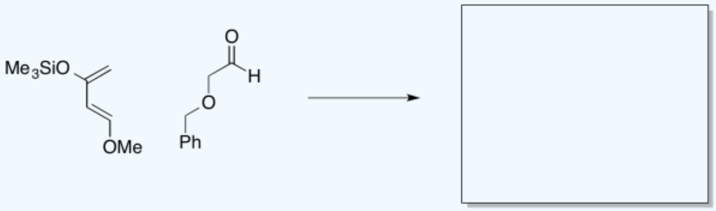
Exercise 10.4.8

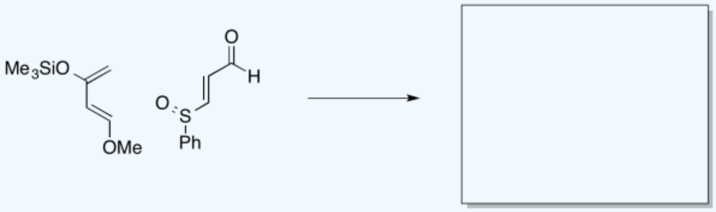
Show the products of the following reactions, including preferred regiochemistry.


Me3SiO
OMe
O
O
O

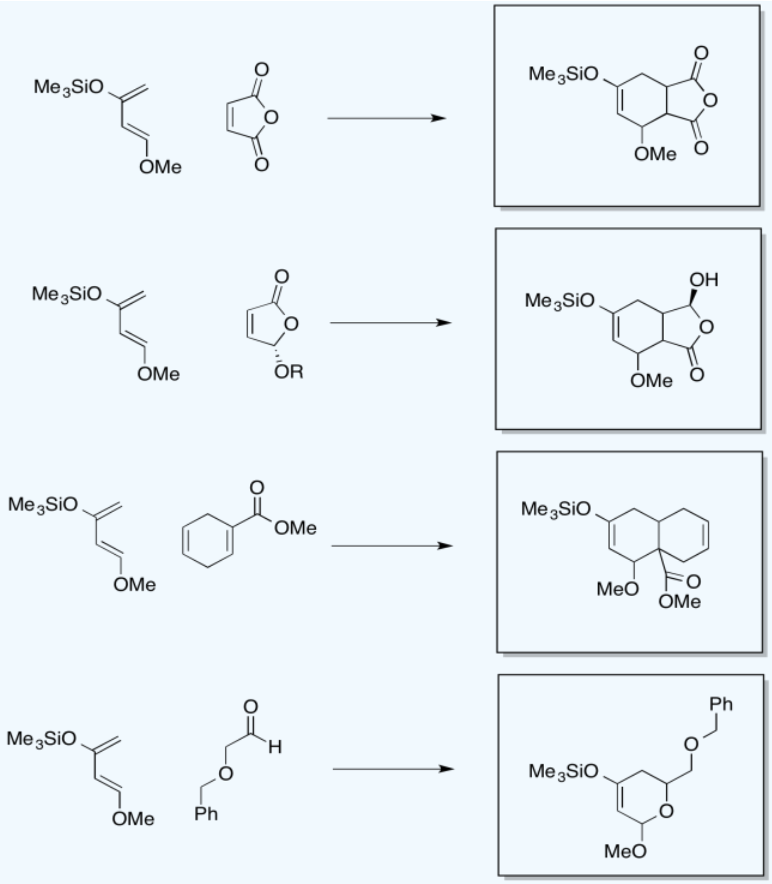

Me3SiO
OMe
O
O
OR

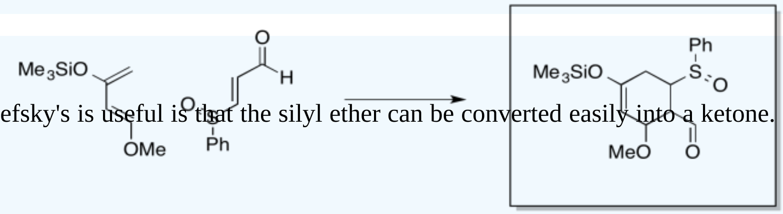

Me3SiO
OMe
O
OMe


Me3SiO
OMe
O
H
O
Ph


Me3SiO
OMe
O
H
O
S
Ph

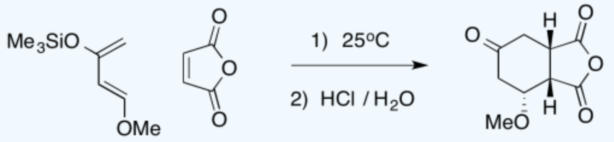
Answer



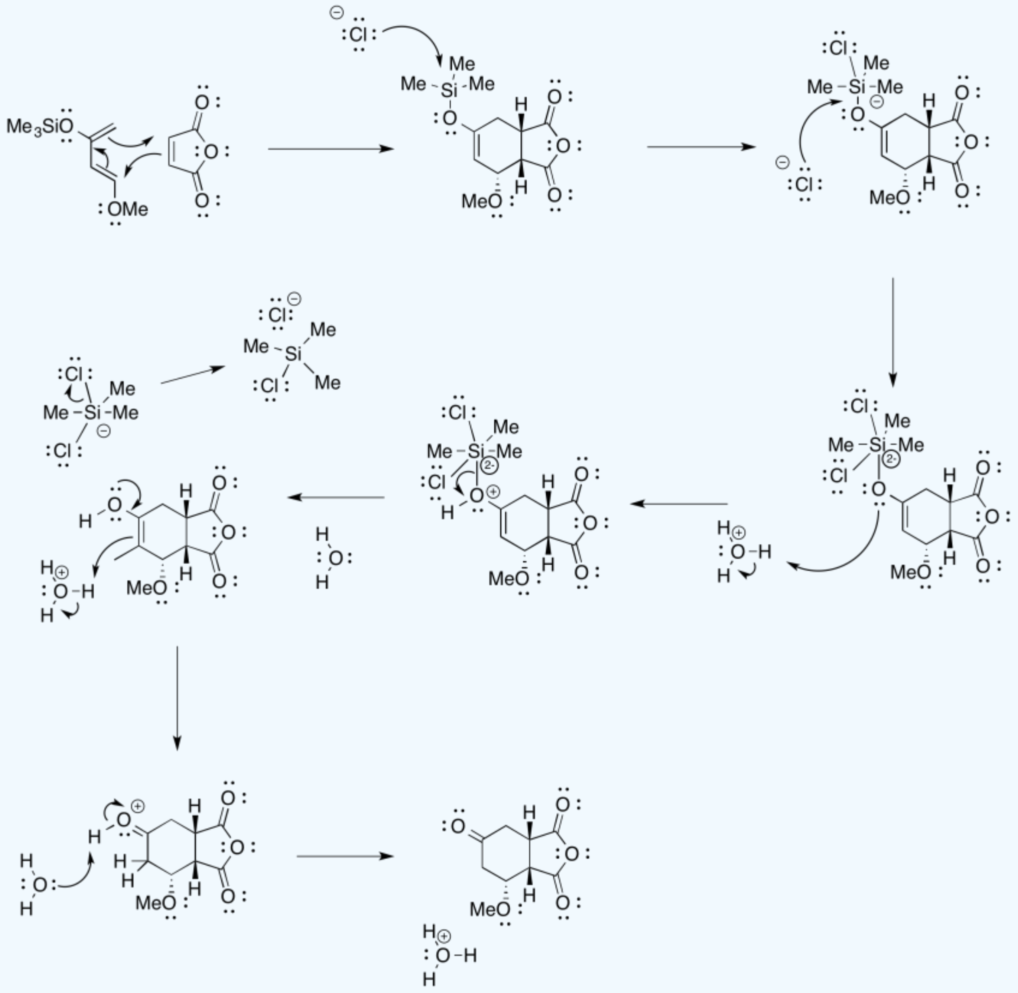


Exercise 10.4.9

One of the reasons Danishefsky's is useful is that the silyl ether can be converted easily into a ketone. Provide mechanisms for the sequence below.


Me3SiO
OMe
O
1) 25ºC
2) HCl / H2O
H
MeO

Answer

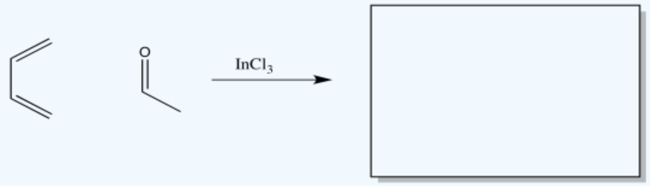

Me3SiO
OMe
Cl
Me
Me - Si - Me
O
H
MeO
2-
H - O - H

Sometimes, the Diels Alder reaction can work equally well with compounds other than alkenes. Of course, they work with alkynes instead of alkenes in the dienophile; the only difference in that case is that an extra double bond remains in the product. Sometimes, alkynes can react in the presence of alkenes, probably because the alkyne is less sterically hindered.

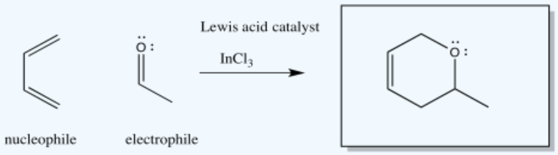
Carbonyls and imines also have double bonds. As such, they can also react sometimes. Because they are electrophilic by nature, they will react better with a more nucleophilic partner. They may also need to be activated.

? Exercise 10.4.10

Show the product of the following reaction.



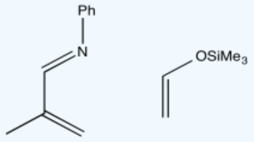
Answer



Note that, so far, we have looked at polarity-assisted Diels Alder reactions in which the diene takes the role of nucleophile (it is more electron-rich to begin with) and the dienophile takes the role of eletrophile. It doesn't have to be that way. By placing an electron-withdrawing group on the diene and an electron-donating group on the dienophile, we would still get complementary reactivity. This type of approach is called an "inverse electron demand" DIels Alder reaction, because it is the opposite of the usual method.

? Exercise 10.4.11

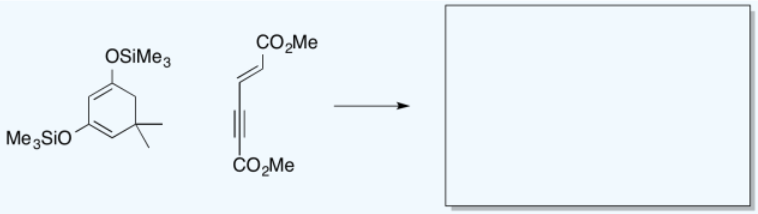
Show a mechanism with curved arrows to make a prediction about regiochemistry in the following reaction.

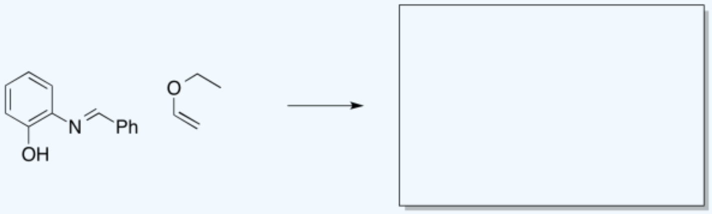


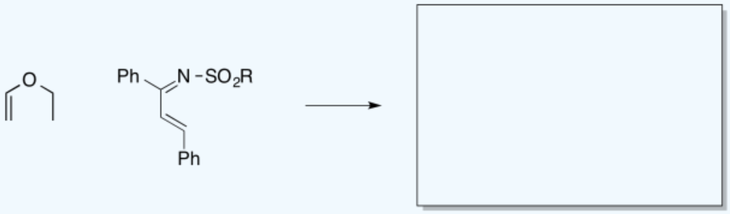
Answer

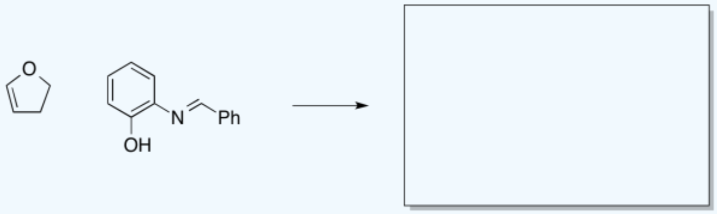
Exercise 10.4.12

Show the products of the following reactions, including preferred regiochemistry.

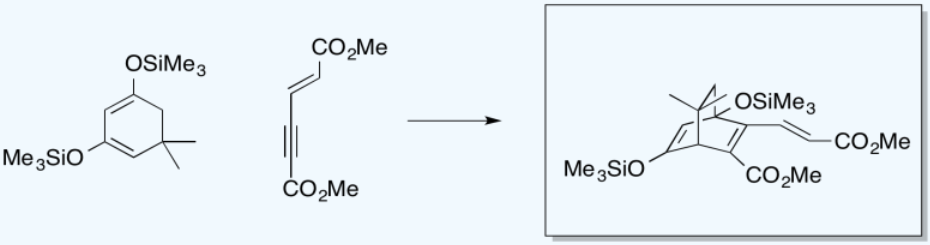






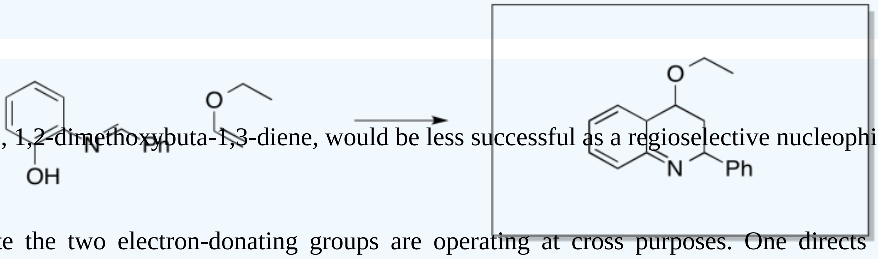


Answer



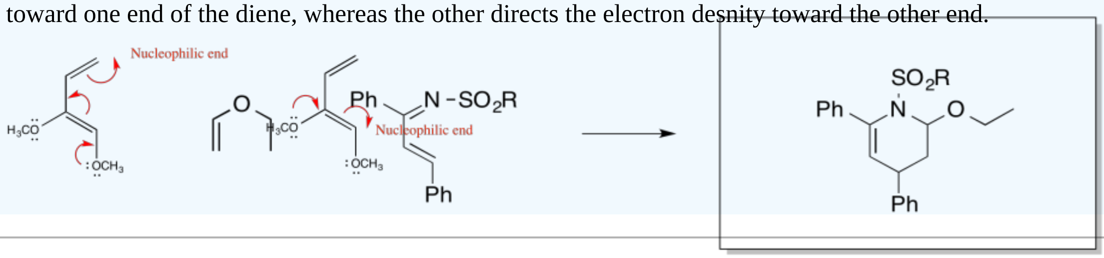
Exercise 10.4.13

Show why the dienophile, 1,2-dimethoxybuta-1,3-diene, would be less successful as a regioselective nucleophile.



Answer

The drawings indicate the two electron-donating groups are operating at cross purposes. One directs electron density toward one end of the diene, whereas the other directs the electron desnity toward the other end.



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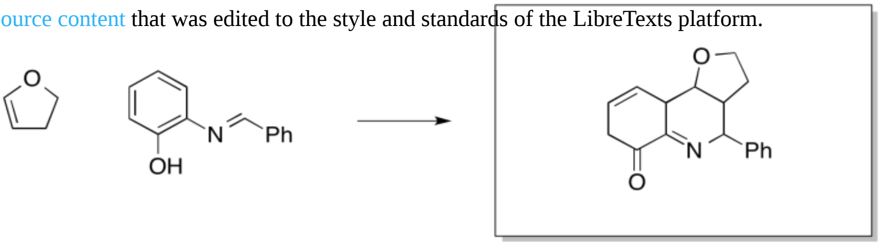
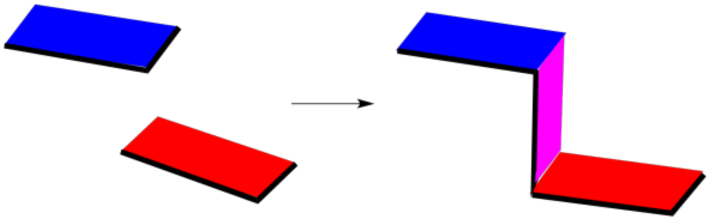


10.5: Endo and Exo Products

The Diels Alder reaction is probably the most common cycloaddition. It allows the construction of six-membered rings, which are very common in biological small molecules which are frequently synthetic targets.

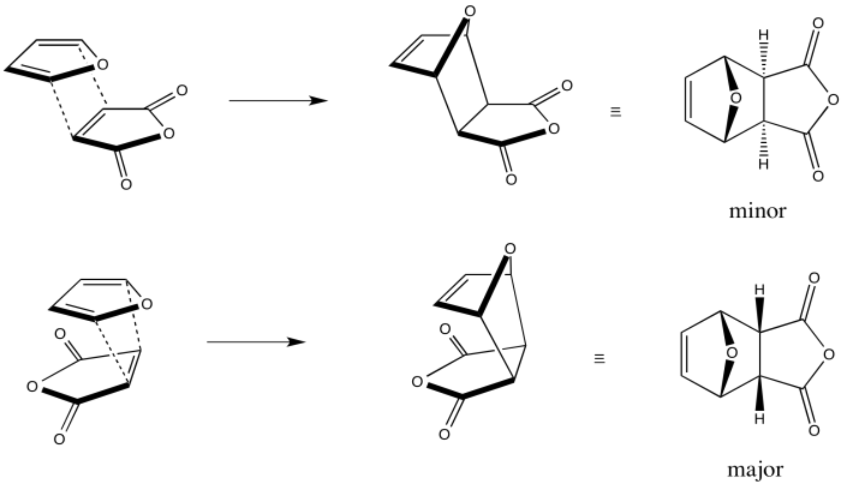
Often, there are already rings in the molecules undergoing reaction, and a new one is being added. When two *cyclic* structures combine in a Diels Alder reaction, a third ring is formed in between the original ones. There are different ways the two original rings can combine, leading to different stereochemical outcomes. These two outcomes are called "exo" and "endo" addition.

An exo addition looks something like this, schematically. The two molecules approach with minimal overal between their faces; they combine edge-on. The exo product that results has a sort of Z-shape.



An endo addition looks more like this, schematically. Two cyclic molecules approach each other so that there is maximum overlap between their faces. The endo product that results has a kind of C-shape.

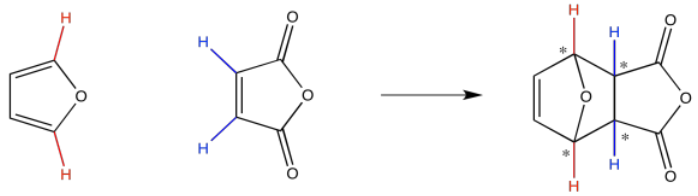
Let's look at these two modes of addition with real molecules. Here we are adding furan, the diene, to maleic anhydride, the dienophile. The two reactants can approach each other such that one appears to be trailing behind the other, and in this case they appear to be facing the same direction, as far as the orientation of the oxygen atoms goes. This approach leads to the zig-zag exo product. In the other case, the two molecules can be directly on top of each other; one molecule appears to be folded underneath the other. This approach leads to the curled-up endo product.



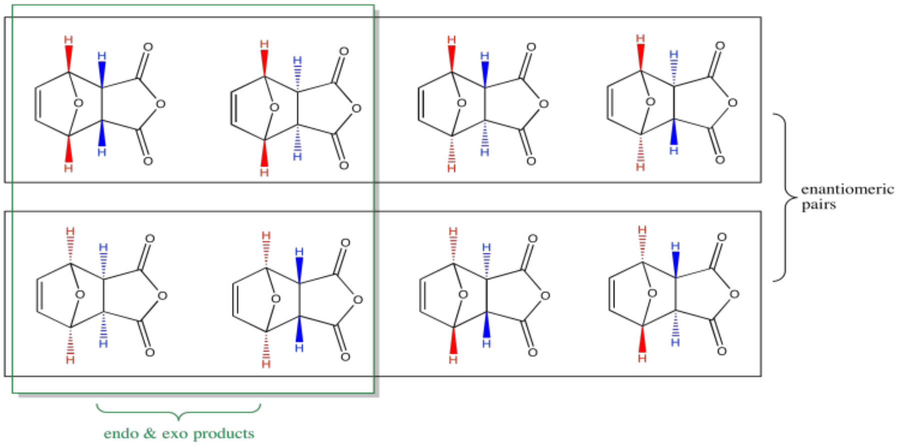
In fact, as the diagram shows, the endo product is usually the favored one. Often, the margin is substantial; one might see 90% endo product or greater in some cases, although the ratio is sometimes much lower.

The reason for this difference has something to do with an interaction between the delocalised π-system of the diene and the substituent groups attached to the dienophile. A number of researchers attribute the prefernece to a "secondary molecular orbital interaction" between the diene and the dienophile, whereas others describe the interaction as a London dispersion interaction, in which the weak intermolecular attractions stabilise the transition state in one geometry.

The endo and exo products are really two different diastereomers. If you think about it, you can see that when two rings fuse together to make a third, four new stereocenters can be created.



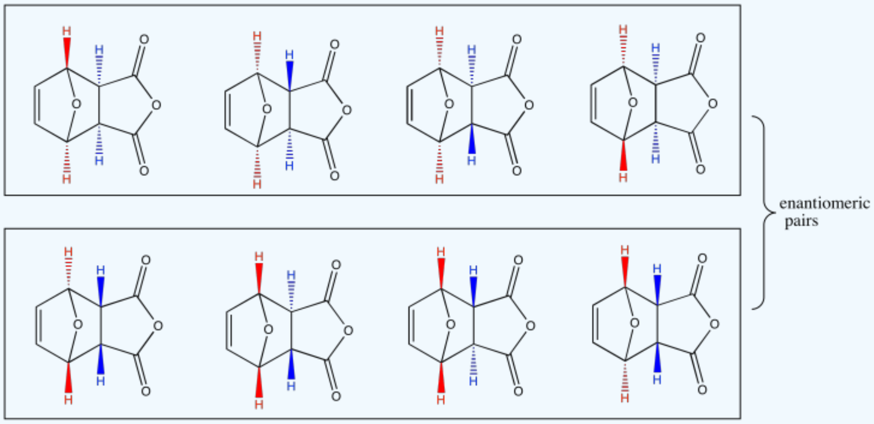
Since each chiral centre could have two possible configurations, there are sixteen possible stereoisomers that could result in the reaction shown above. That's a lot of structures. Just eight of them are shown below. Note that they occur in pairs of enantiomers. However, most of those diastereomers don't really occur.



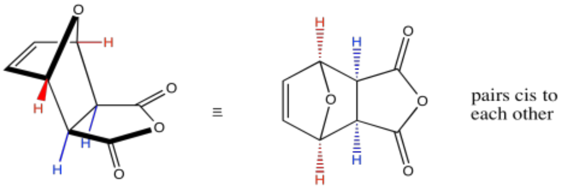
Exercise 10.5.1

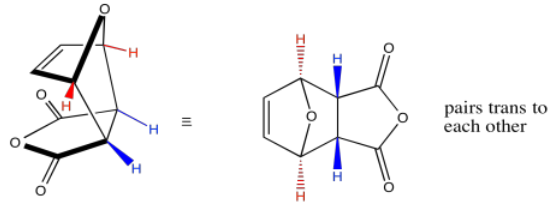
Draw the other stereisomers of the product formed from the reaction between furan and maleic anhydride.

Answer

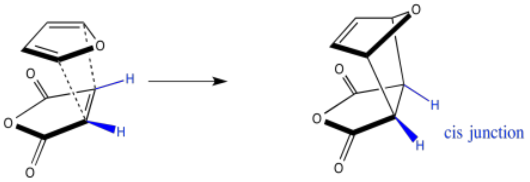


If we look at the molecule in this way, with the hydrogens highlighted on the ends of the diene and the dienophile, it may be easier to see the stereochmical relationships in the exo and endo products. In the exo product, the pair of hydrogens on the diene ends up *cis* to the pair of hydrogens on the dienophile when the rings become fused. In the endo product, the opposite is true: the pair of hydrogens on the diene come out *trans* to the pair of hydrogens on the dienophile when the rings fuse together.

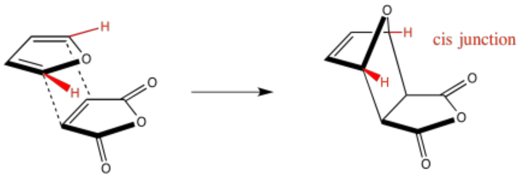




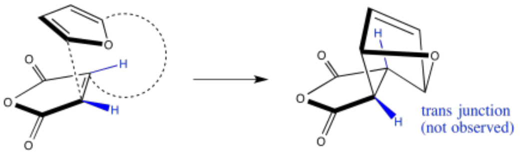
Note that the hydrogens on the ends of the diene come out *cis* to each other, as well. They would be *cis* to each other in the ring, and that relationship does not change over the course of the reaction.



The same thing is true with the hydrogens on the dienophile.



It would be very difficult for the two *cis* hydrogens on one ring to become *trans* in the product, because it would require that one ring react via two different faces at the same time. It would be difficult to get one ring twisted around to do that. As a result, we can ignore most of the diastereoisomers that could result from a Diels Alder reaction on paper, and focus on the endo and exo products.

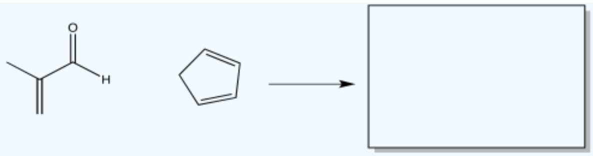


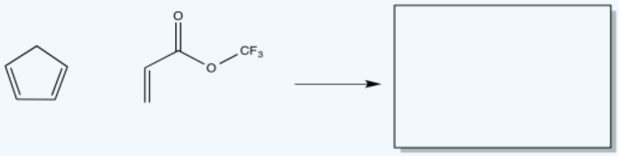
Of course, Diels Alder reactions between rings like these always have the potential to produce pairs of enantiomers. Because two enantiomers are equal in energy to each other, there is no inherent preference for forming one over the other. In other words, there would actually be two endo products, and they would be enantiomers of each other. There would also be two exo products, and those would be anantiomers of each other, too.

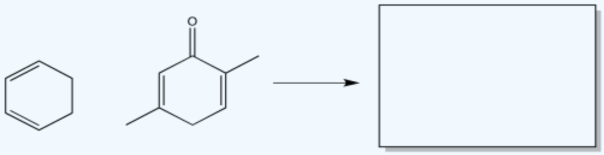
Methods are available for influencing the formation of one enantiomer exclusively. These methods involve the use of chiral catalysts. These catalysts may contain Lewis acidic metals or they may contain some combination of hydrogen bond donors and acceptors. In either case, the role of the catalyst is to tether the reactants close together so that they will undergo the reaction. If the catalyst is itself chiral, the reactants will often fit together one way more easily than another, so that the formation of one enantiomer is preferred.

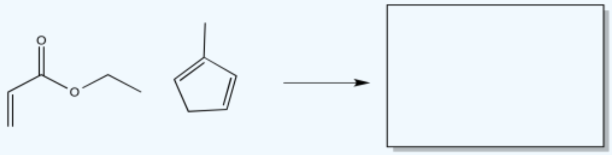
? Exercise 10.5.2

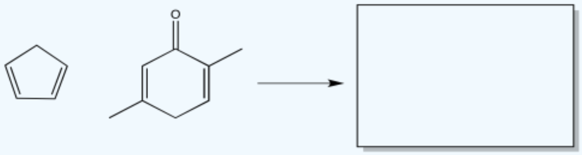
Show the products of the following reactions, including preferred stereochemistry.

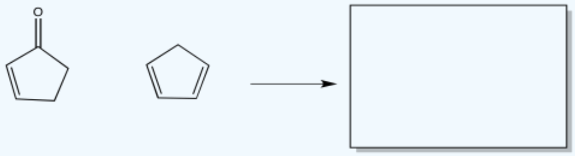

O
H


O
O
CF₃


O


O
O


O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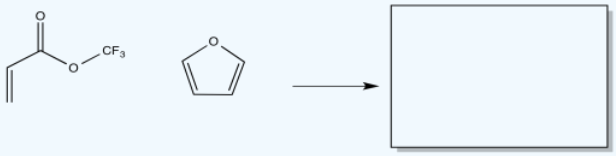
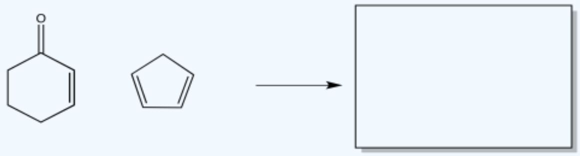
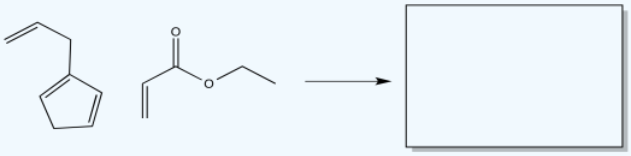

O
O
CF₃
O


O


O
O

10.6: Photochemical Cycloaddition

As noted previously, the Diels Alder reaction is a classic example of a pericyclic reaction.

Figure 10.6.1: The Diels Alder reaction

A Diels Alder reaction is sometimes called a [2+4] addition reaction. A 2-carbon unit on one molecule interacts with a 4-carbon unit on another molecule.

In contrast, the addition of one regular alkene to another regular alkene would be called a [2+2] addition reaction. If this reaction occurred, two alkenes would come together to form a four-membered ring.

However, [2+2] addition reactions don't occur without special circumstances. There are a couple of reasons why, and you may be able to suggest some at this point.

You might say that the four-membered ring would be much more strained than the six-membered ring formed by the Diels Alder reaction. That is true, but it may not be reason enough to prevent the reaction from happening. Four-membered rings do occur in nature despite their strain energy.

You might also say that the benzene-like transition state that stabilizes the pathway through a Cope or Diels Alder reaction isn't possible in a [2+2] addition. In fact, the transition state would be more like antiaromatic cyclobutadiene. The transition state would be very high in energy.

Another problem shows up if we look at the orbital interactions in a [2+2] addition reaction. The HOMO on one alkene and LUMO on the other alkene do not overlap so that bonds can form between the two ends. If the p orbitals on one end are in phase, the p orbitals on the other end must be out of phase. The concerted reorganization of bonding possible for the Diels Alder reaction can't happen here.

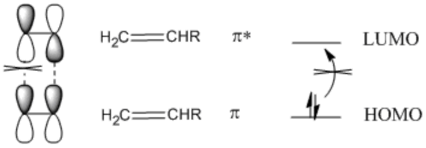


Figure 10.6.3: Qualitative molecular orbital picture of [2+2] addition reaction.

In fact, there is a way around that problem. Irradiating an alkene with UV light leads to promotion of an electron from the HOMO to the LUMO. The alkene is now in an "excited state".

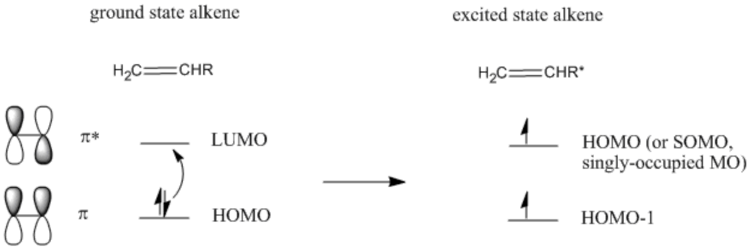


Figure 10.6.4: Excitation of an electron in an alkene.

This does not happen with 100% efficiency, so only some of the alkenes will become excited. In the excited state alkene, the LUMO now resembles the HOMO of the ground state alkene. Because of the matching symmetry between these orbitals, the addition reaction can proceed.

Figure 10.6.5: HOMO-LUMO interaction between a ground-state alkene and an excited-state alkene.

A [4+2] reaction is sometimes referred to as "thermally-allowed", whereas a [2+2] addition is sometimes referred to as "photolytically-allowed." This distinction refers to the need for electronic excitation to accomplish the latter type of reaction.

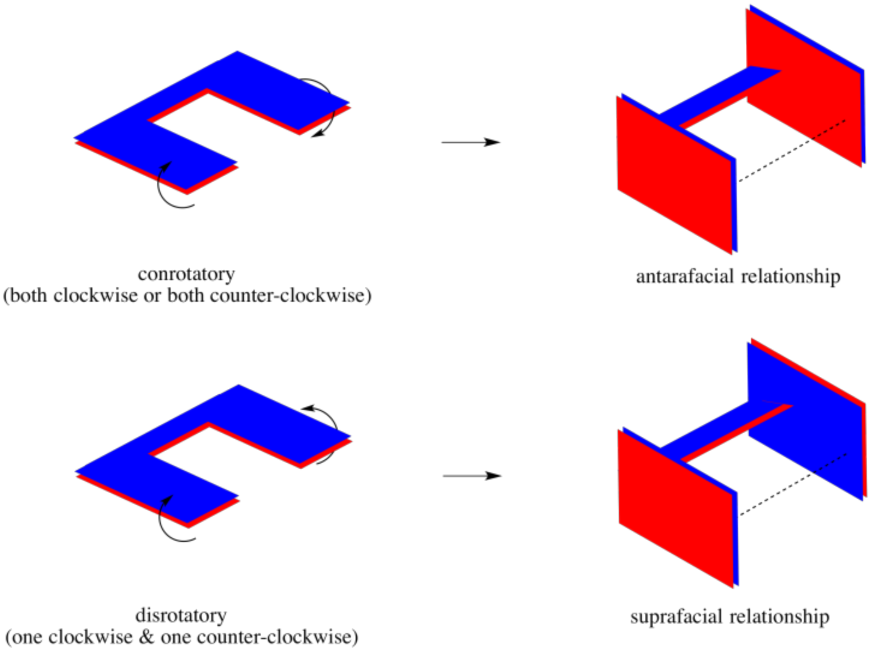
10.7: Facial Selectivity

In addition to the consequences of endo- vs. exo- additions in the Diels Alder reaction, pericyclic reactions are subject to additional stereochemical constraints. In this section we will look at more issues of topology, or how the surfaces of the molecules fit together. Although this topic applies to both cycloadditions and true pericyclic rearrangements, we will start by looking at cycloadditions.

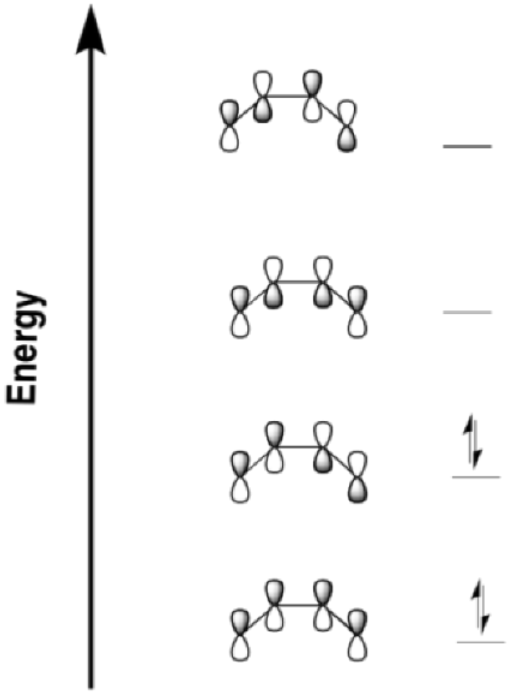
So far, we have made the simple assumption that two molecules in a Diels Alder reaction would simply come together in a face-to-face fashion. It is easy to imagine that one molecule would sit above the other as they approach, and form bonds from one face of one molecule to one face of the other molecule. In fact, it often happens that way, and this relationship is called a suprafacial addition.

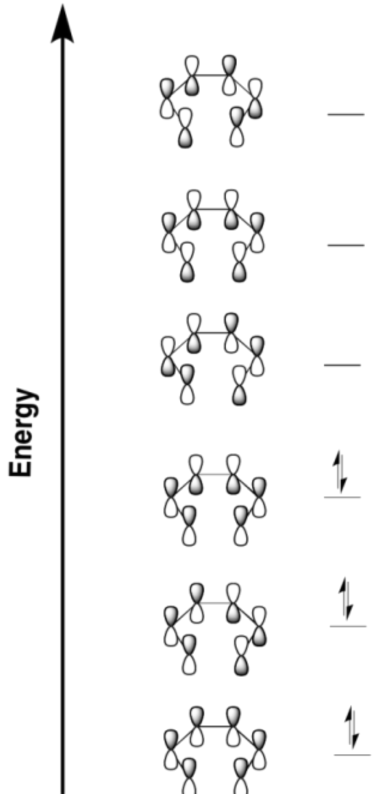
However, sometimes something else happens. Imagine one molecule is able to approach the other at a slight angle, such that it is able to slip in between the ends of the other molecule. A molecule would be interacting with its neighbour not just along one face, but along two. It would form bonds via both its top and its bottom face. This type of addition is called antarafacial. It's not exactly like the cartoon shown above, but to get additional detail we will need to look at molecular orbital pictures.

In a true pericyclic reaarrangement such as a Cope or Claisen rearrangement, similar things can happen. When two ends of a molecule fold in to bond with each other, you can imagine doing so in either of two ways. Maybe the two ends roll towards each other, so that the top face on one end of the molecule connects with the top face on the other. Maybe the top face on one end connects with the lower face on the other end.



Sometimes, the motions that the molecule would undergo to put these interactions in place are called "conrotatory" (rotating together) and "disrotatory" (rotating opposite ways). The interactions they produce, however, are just like the interactions in cycloadditions, with either an antarafacial or a suprafacial relationship, respectively.



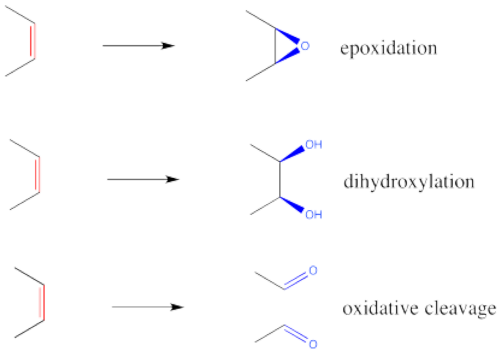


Number of electron pairs	suprafacial / disrotatory	antarafacial / conrotatory
even	photochemical	thermal
odd	thermal	photochemical

10.8: Alkene Oxidations

There are a number of additions to alkenes that occur via concerted mechanisms. Alkene oxidations are among the most synthetically useful of these reactions because they are able to convert simple hydrocarbon starting materials into oxygen-containing compounds. The resulting heteroatomic functional groups may open up new avenues of synthetic utility or they may reflect aspects of a target natural product.

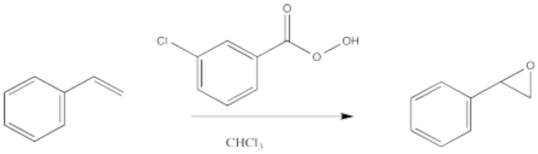
The three most common alkene oxidations are epoxidation, dihydroxylation and oxidative cleavage.



Epoxidation

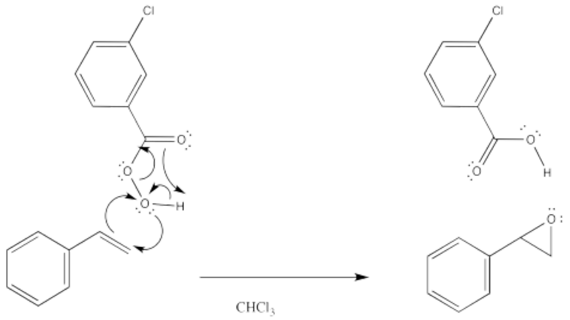
Epoxidation is a method for converting an alkene into an epoxide. The reagent required is always a peroxo species. A peroxo species looks very much like a normal oxygen-containing compound, but with an extra oxygen in it. Historically, the most common such reagent was *m*-chloroperbenzoic acid (*m*CPBA).

However, other reagents can also be used, such as hydrogen peroxide (H_2O_2) or potassium hydrogen persulfate ($KHSO_5$), marketed under the trade name Oxone. The latter methods are considered "greener" or more environmentally friendly, because the side poducts (water or sulfate, respectively) are pretty innocuous. These methods are generally slower and are often used with a catalyst. Catalysts used with hydrogen peroxide include Lewis acidic species such as sodium tungstate (Na_2WO_4) needed to activate the peroxide. A similar reaction using titanium (IV) and chiral ligands leads to an enantiomerically pure epoxide; this reaction is called "Sharpless epoxidation". With oxone, ketones are used as oxygen transfer catalysts in a method referred to as "Shi oxidation".



The electrophilicity of peroxy compounds continues a theme seen in halogens such as chlorine and bromine. When two oxygen atoms are connected to each other, one of the can act as an electrophile, just as when two halogens are connected together.

During the epoxidation, the peroxy compound simply delivers its extra oxygen to the double bond. The oxygen atom both accepts a pair of electrons from the double bond and donates an electron pair to the double bond at the same time.



The reaction has something in common with pericyclic reactions. In pericyclic reactions and other reactions that take place under control of orbital symmetry, it is common to see six electrons circulating in a ring as a central feature of the mechanism. This picture is reminiscent of the aromatic structure of benzene. In fact, that aromatic stabilization is thought to play a role in stabilizing the transition states of various reactions. In this case, the three electron pairs involve delivery of the oxygen, proton transfer and π donation to the carbonyl in mCPBA. However, a similar set of arrows might not be found in the reaction of hydrogen peroxide.

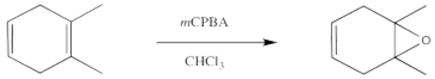
Exercise 10.8.1

Show how the carbonyl in *m*CPBA may help activate the donor oxygen toward reaction with the alkene.

Exercise 10.8.2

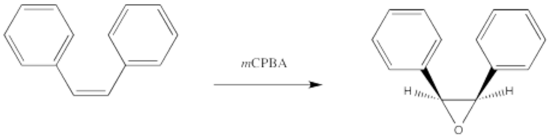
Show how a titanium (IV) ion may help activate the donor oxygen in hydrogen peroxide toward reaction with the alkene.

The electrophilic nature of the peroxy compound is seen in the selectivity of the epoxidation reaction. Alkenes that are more electron rich tend to react much more quickly than other ones. For example, more substituted alkenes, often regarded as being electron-rich, can be selectively epoxidized in the presence of other alkenes.



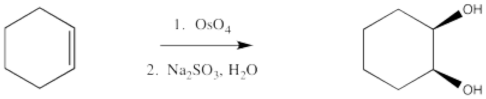
Furthermore, although enones can sometimes be epoxidized, the reaction is generally slower than with regular alkenes. Of course, the carbonyl attached to the alkene in an enone makes the alkene very electron-poor.

Part of the evidence for a concerted mechanism for epoxidation comes from the stereochemistry of the reaction. In general, if a *cis*-alkene is epoxidized, the two groups that were *cis* to each other in the alkene remain *cis* to each other in the epoxide. If the groups start out *trans* to each other, they remain *trans* in the epoxide. Just as in hydroboration, there is no opportunity for these stereochemical relationships to change.

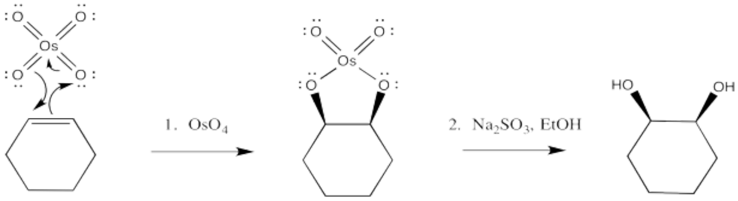


Dihydroxylation

Dihydroxylation is the addition of an OH group to both sides of an alkene. Typically, when reagents such as osmium tetroxide are used, the hydroxyl groups are added to the same face of the double bond. This reaction is therefore called a *syn*-dihydroxylation.

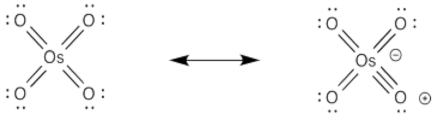


Osmate esters can be isolated from this reaction, resulting from the concerted addition of osmium tetroxide to the alkene. Once again, this step can be compared to a pericyclic reaction. However, the osmate ester is usually decomposed *in situ* through the addition of a "reducing agent" such as sodium sulfite.



Once again, the concerted nature of the reaction is seen in the stereochemistry of the product. The fact that both oxygens, which come from the osmium, are delivered to the same face of the alkene suggests that they are added at the same time.

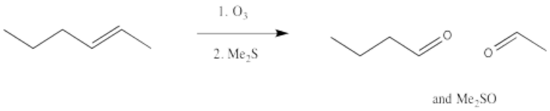
It isn't uncommon for oxygen atoms to form additional π bonds to transition metals such as osmium. In this case, we could think of the osmium as forming an 18 electron complex as a result. Whether or not that resonance contributor is an important representation of osmium tetroxide, it is a helpful device to think of how the oxygen might form an initial attraction to the alkene.



Because of osmium tetroxide's high cost, potent toxicity and alarming propensity to rapidly sublime, other reagents are preferred. It is quite common to still use a catalytic amount of osmium tetroxide, though, along with a co-oxidant. Co-oxidants can be things like Fe(III) salts and air, although hydrogen peroxide is often used.

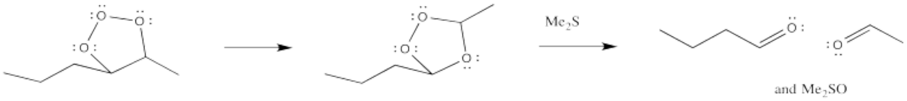
Oxidative Cleavage: Ozonolysis

Ozonolysis results in the complete cleavage of a double bond into two parts. The resulting fragments are each capped by an oxygen atom.



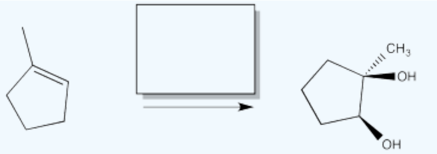
Once again, this reaction starts out with a concerted addition of the ozone to the alkene.

However, the first-formed adduct, termed a molozonide, quickly rearranges to a second product, termed an ozonide. Both of these species can be isolated. However, in practice this is rarely done because of the appalling tendency of molozonides and ozonides to explode unexpectedly. The ozonide is instead decomposed through the addition of a reducing agent, such as dimethylsulfide or zinc, leaving two oxygen-containing fragments behind.

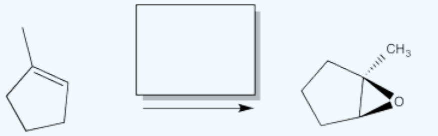


? Exercise 10.8.3

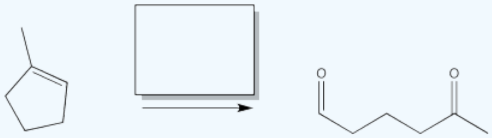
Fill in the reagents for the following alkene oxidations.

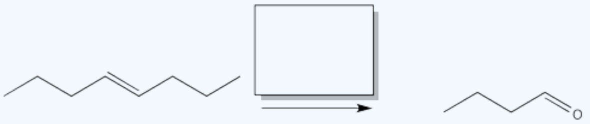


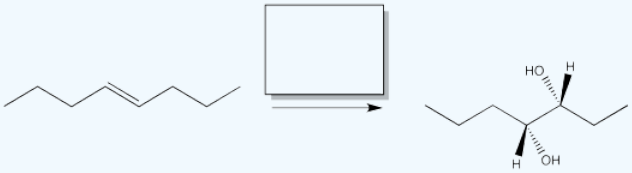
& enantiomer



& enantiomer







Answer a

a) OsO_4, H_2O

Answer b

b) mCPBA

Answer c

c) 1. O_3; 2. Me_2S or Zn

Answer d

d) 1. O_3; 2. Me_2S or Zn

Answer e

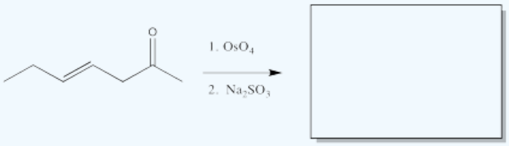
e) OsO_4, H_2O

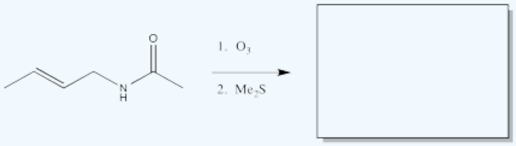
Answer f

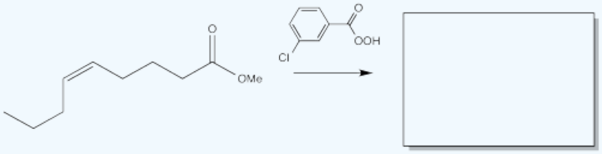
f) mCPBA

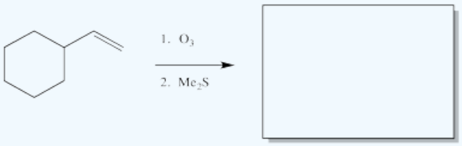
Exercise 10.8.4

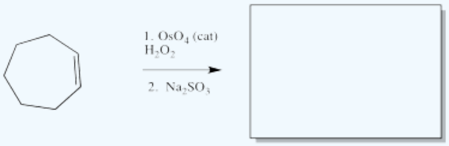
Fill in the products of the following alkene oxidations.

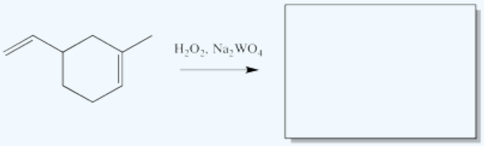


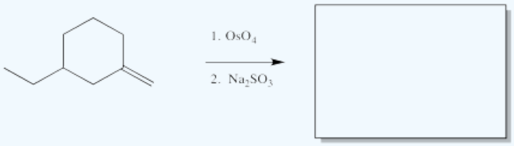


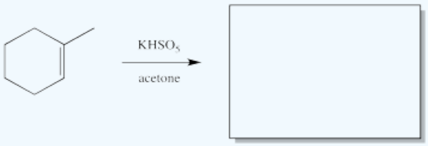










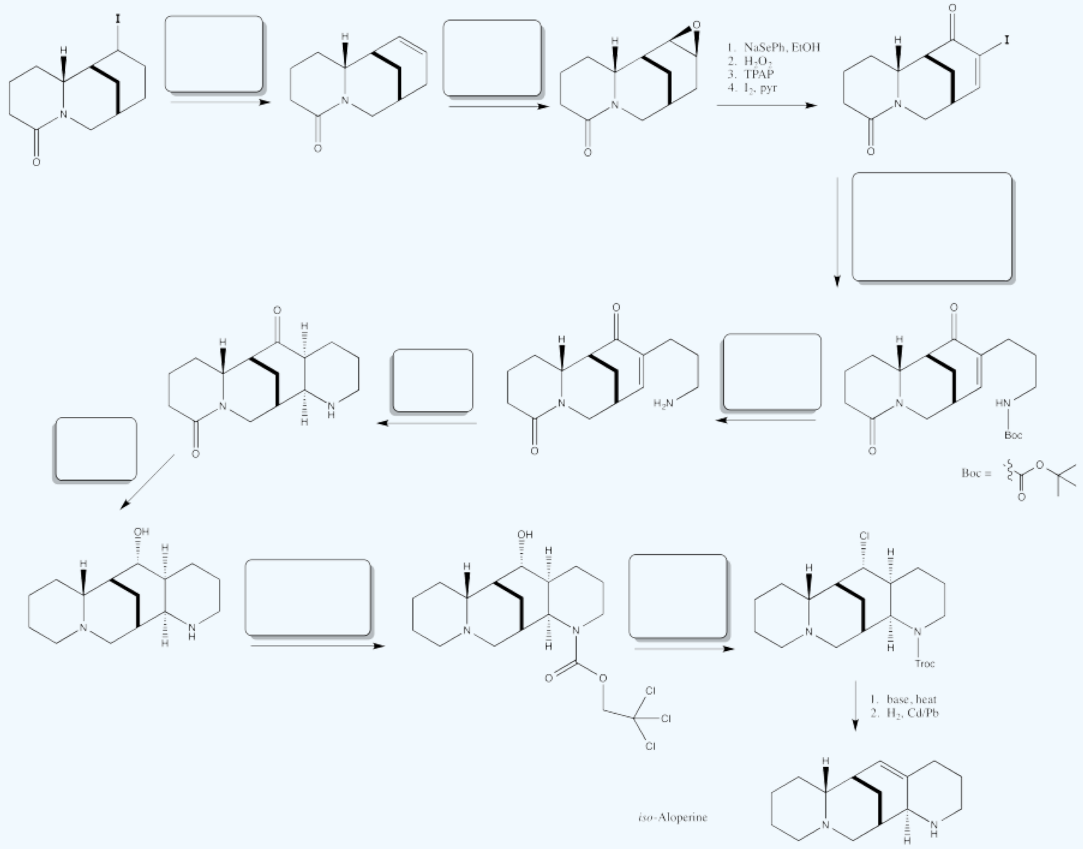


Exercise 10.8.5

Fill in the blanks in the following synthesis.

iso-Aloperine

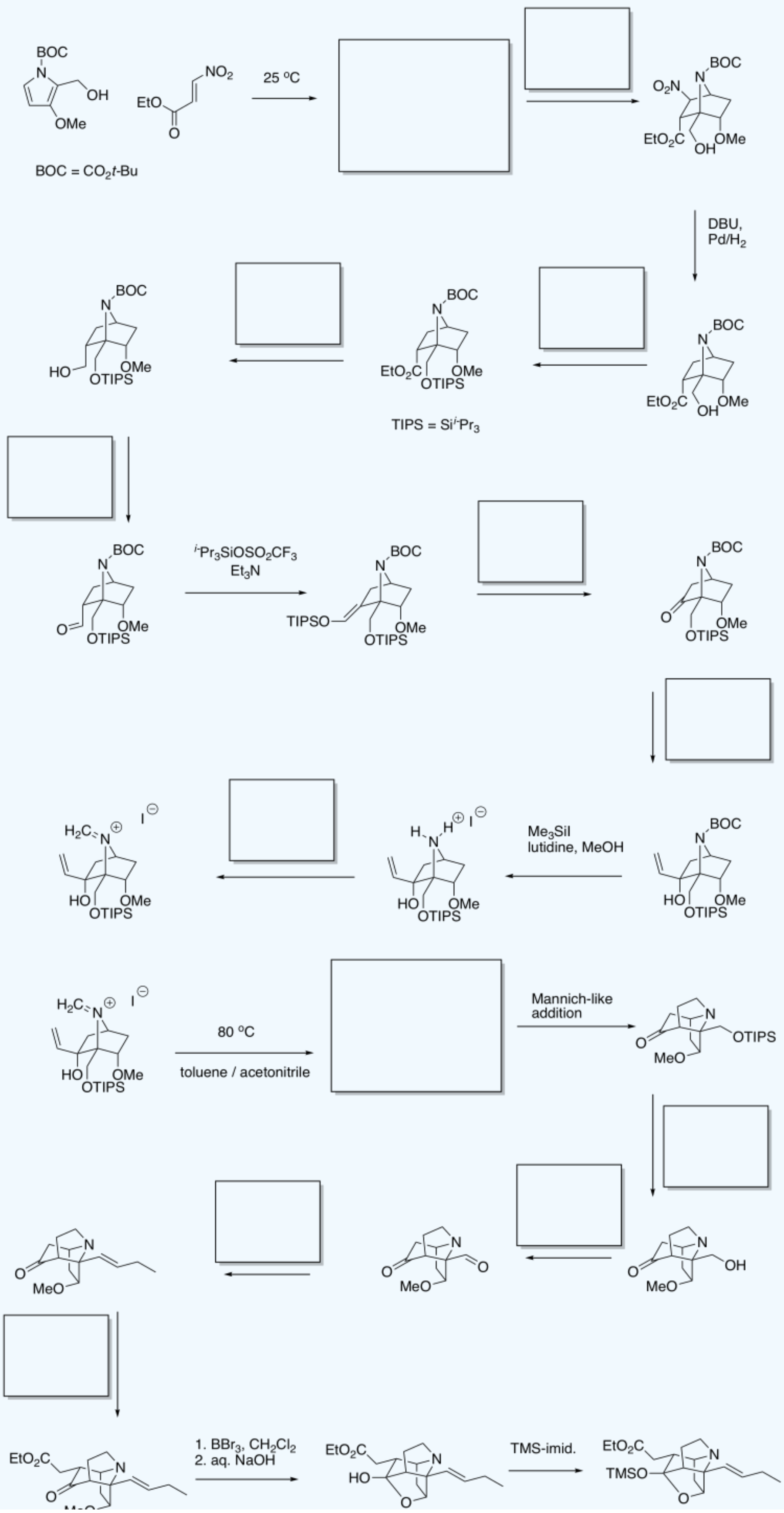
Brosius, Overman, *J. Org. Chem.* **1997**, *62*, 440.

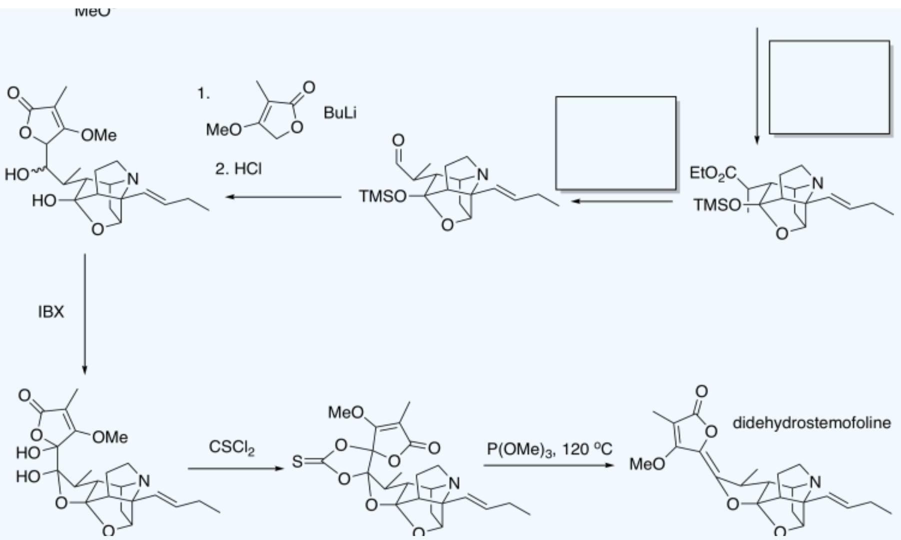


? Exercise 10.8.6

Fill in the blanks in the following synthesis.

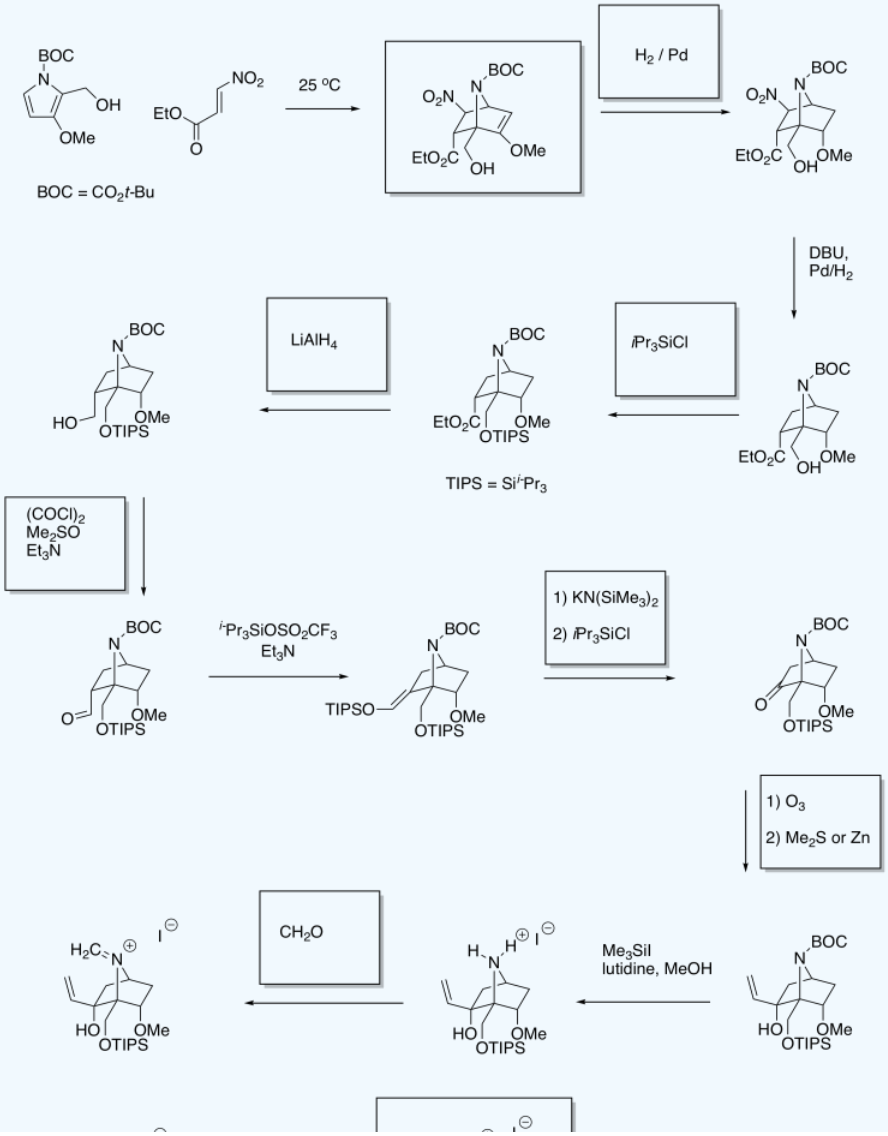
Synthesis of Didehydrostemofoline (Overman, 2003)
Isolated from a family of East Asian plants; deters insect feeding.

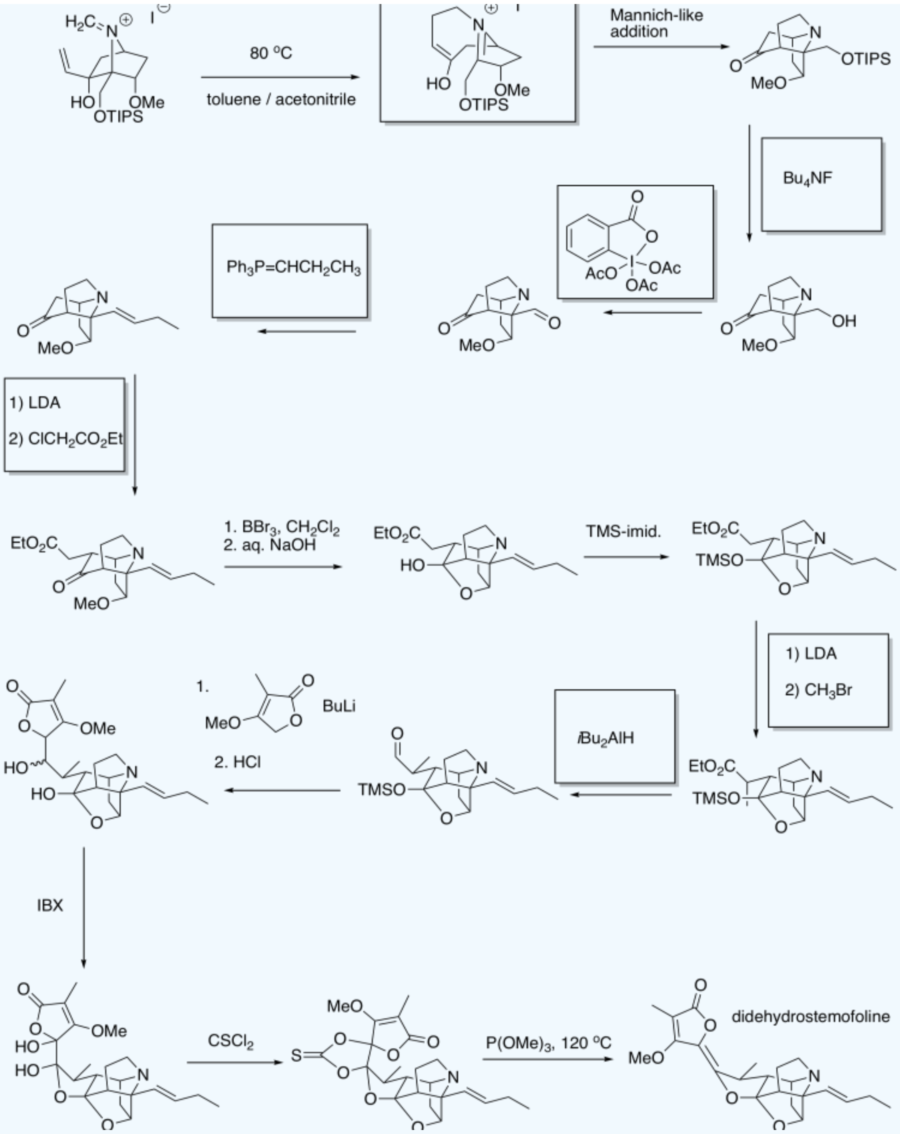




Answer

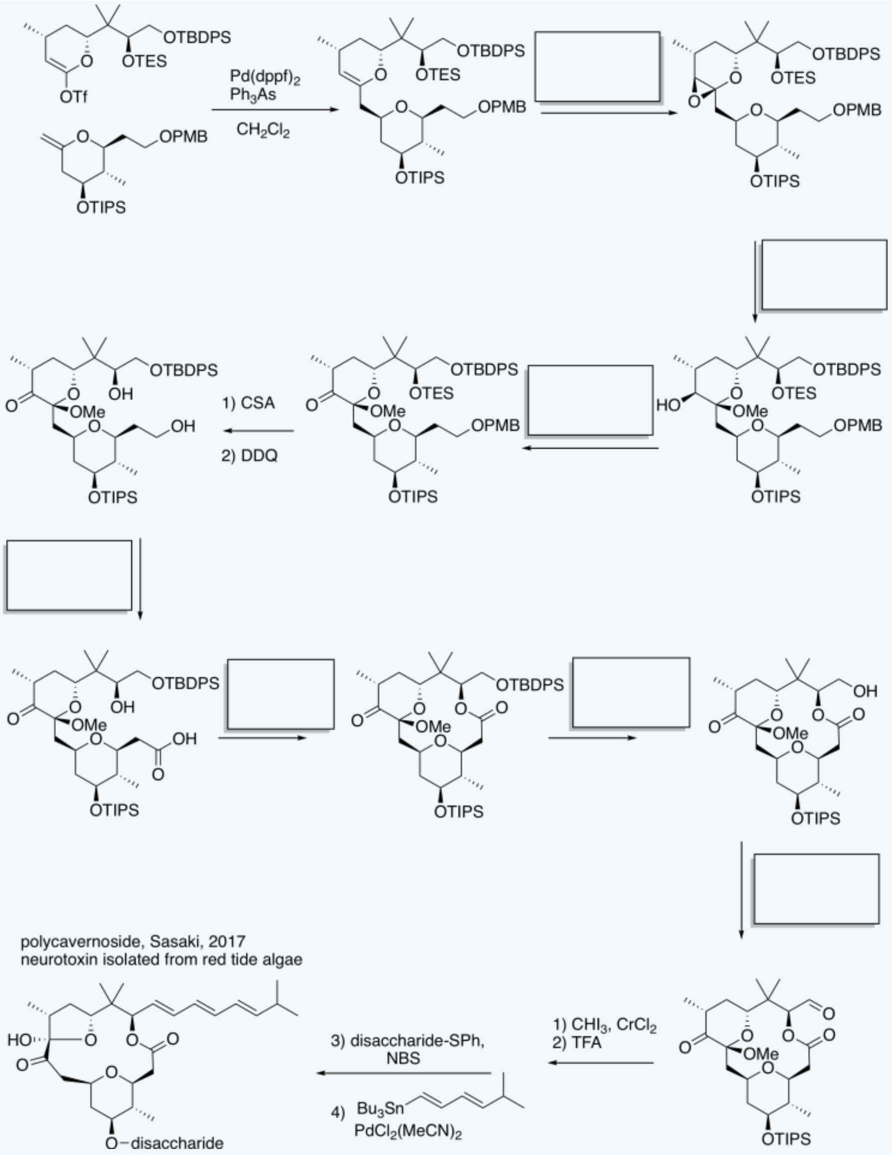
Synthesis of Didehydrostemofoline (Overman, 2003)
Isolated from a family of East Asian plants; deters insect feeding.





? Exercise 10.8.7

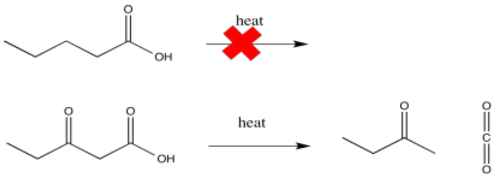
Fill in the blanks in the following synthesis.



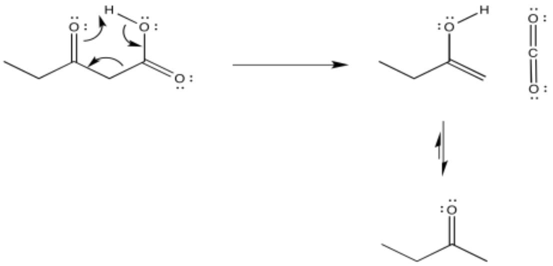
OTBDPS
OTES
OTf
OPMB
OTIPS
Pd(dppf)$_2$
Ph$_3$As
CH$_2$Cl$_2$
HO
OMe
OH
1) CSA
2) DDQ
polycavernoside, Sasaki, 2017
neurotoxin isolated from red tide algae
O–disaccharide
3) disaccharide-SPh, NBS
4) Bu$_3$Sn
PdCl$_2$(MeCN)$_2$
1) CHI$_3$, CrCl$_2$
2) TFA

10.9: Decarboxylations

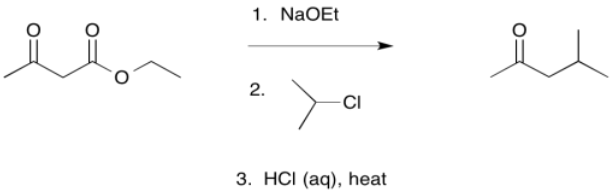
Decarboxylation refers to the loss of carbon dioxide from a molecule. This event generally happens upon heating certain carboxylic acids. It can't be just any compound; most commonly, there must be a carbonyl group β- to the carboxylic acid functional group.



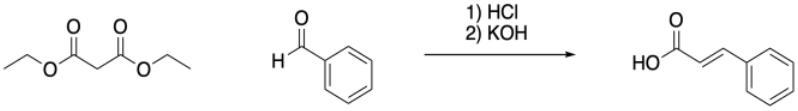
The presence of the second carbonyl in that position is crucial in stabilizing the transition state of the reaction. If we try to follow the reaction using curved arrows, we can see something similar to what we have already observed in pericyclic reactions such as the Cope rearrangement. Three pairs of electrons in a six-membered ring are responsible for the reaction.



The loss of carbon dioxide from β-keto acids and esters is a key event in some important processes. Some typical synthetic methods include the acetoacetic ester synthesis and the malonic ester synthesis. These are two methods of α-alkylation. In these approaches, the presence of a carbonyl β- to a second carbonyl makes it much easier to remove the α-proton in between. That means simple bases such as sodium ethoxide are good enough to remove the proton efficiently and allow an alkylation reaction. However, once it is no longer needed for this activating effect, one of the ester groups can then be removed via decarboxylation.



The Knoevenagel reaction is a third, related example of a synthetic transformation that relies on decarboxylation. It differs from the other two in that it involves a carbonyl condensation rather than an alylation. Once again, the reaction is followed by decarboxylation.

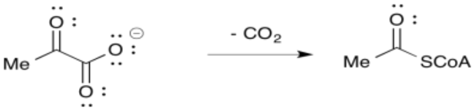


Decarboxylations are also common in biochemistry. For example, loss of CO_2 from isocitrate provides α-ketoglutarate. This step is one of several exergonic events in the citric acid cycle.

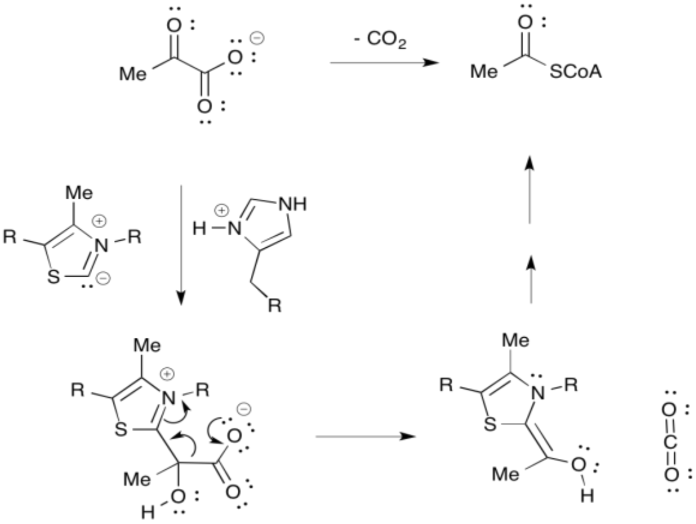
Exercise 10.9.1

Provide a mechanism for the conversion of isocitrate to α-ketoglutarate.

Many reactions in biochemistry involve decarboxylations, even without a stabilizing group in the β-position. For example, in the entry point to the citric acid cycle, pyruvate is decarboxylated during the formation of acetyl coenzyme A.



However, a closer look at the mechanistic pathways of these reactions reveals there is something more going on. Intermediate steps involve the introduction of these stabilizing groups, which are later removed again. In the case of pyruvate decarboxylation, the compound must be activated by the addition of a thiamine ylide. The iminium group in the resulting intermediate plays the same role as that of the β -keto group in the decarboxylations we have already seen.

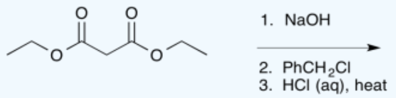


Subsequent steps result in the loss of the thiamine group and its replacement with a thioester linkage.

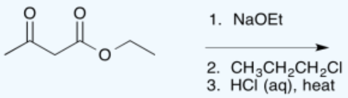
? Exercise 10.9.2

Provide products for each of the following reactions.

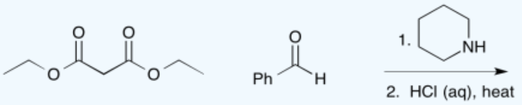
a)



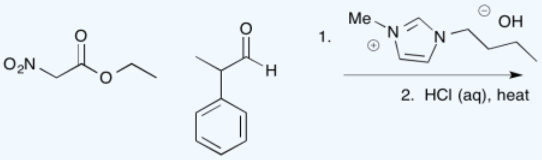
b)



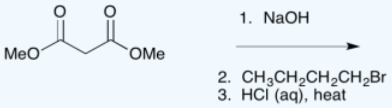
c)



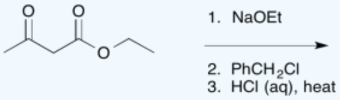
d)



e)

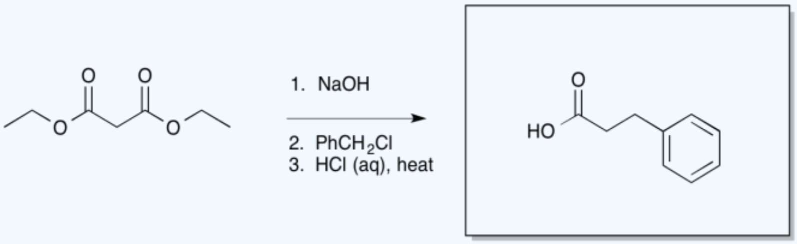


f)

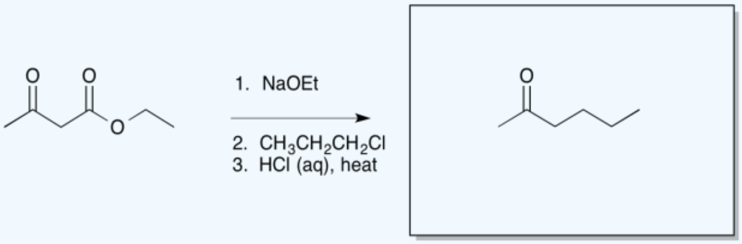


Answer

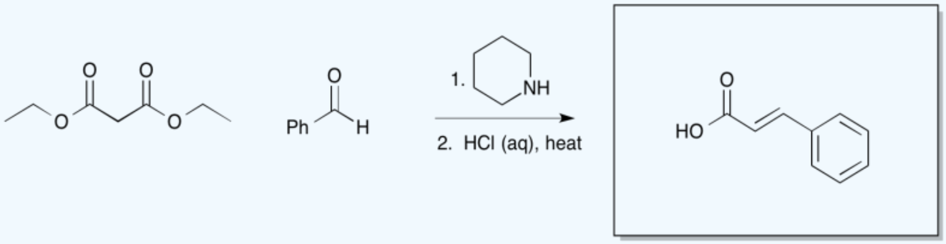
a)


O
O
O
O
1. NaOH
2. $PhCH_2Cl$
3. HCl (aq), heat
O
HO

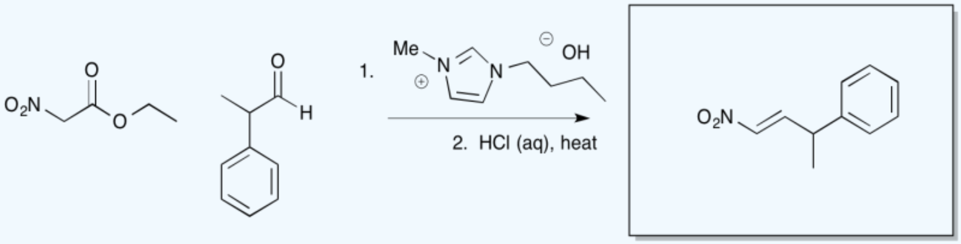
b)


O
O
O
1. NaOEt
2. $CH_3CH_2CH_2Cl$
3. HCl (aq), heat
O

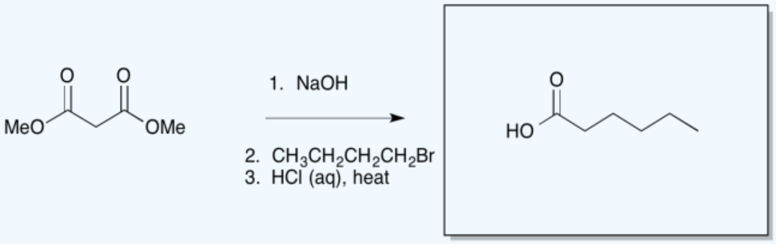
c)


O
O
O
O
O
Ph
H
1.
NH
2. HCl (aq), heat
O
HO

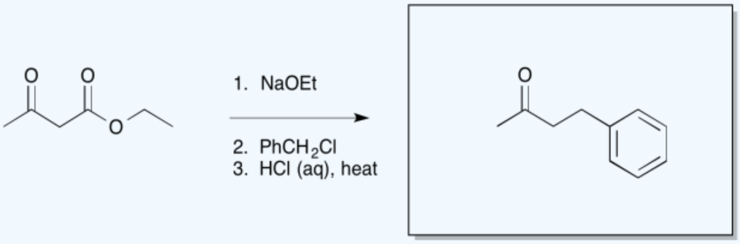
d)


O_2N
O
O
O
H
1.
Me
N
N
OH
2. HCl (aq), heat
O_2N

e)


O
O
MeO
OMe
1. NaOH
2. $CH_3CH_2CH_2CH_2Br$
3. HCl (aq), heat
O
HO

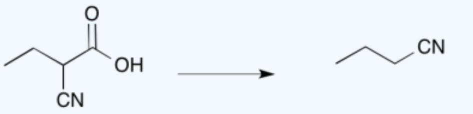
f)


O
O
O
1. NaOEt
2. $PhCH_2Cl$
3. HCl (aq), heat
O

Exercise 10.9.3

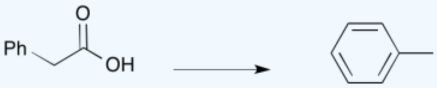
Carbonyls are not the only groups that can promote decarboxylation. Provide a mechanism for each of the following reactions.

a)



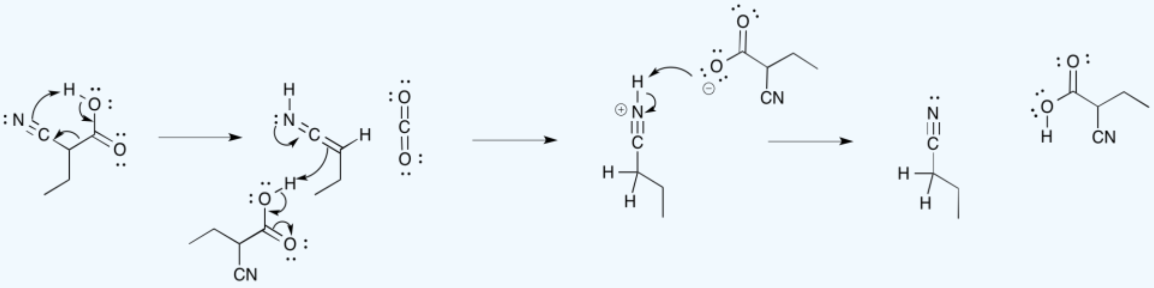
b)

c)

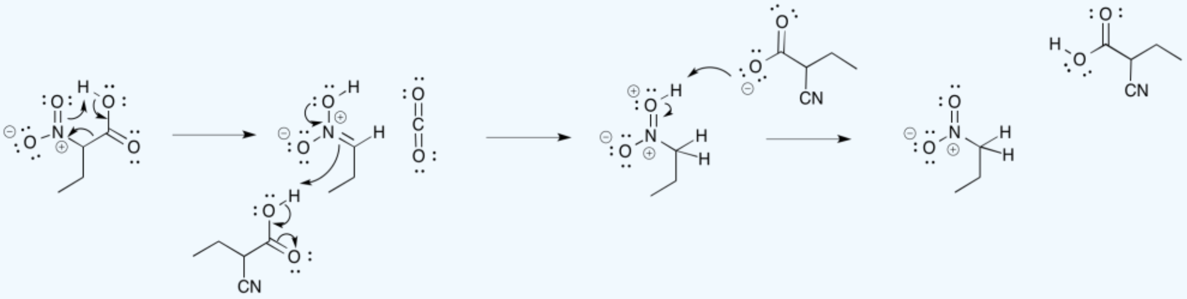


Answer

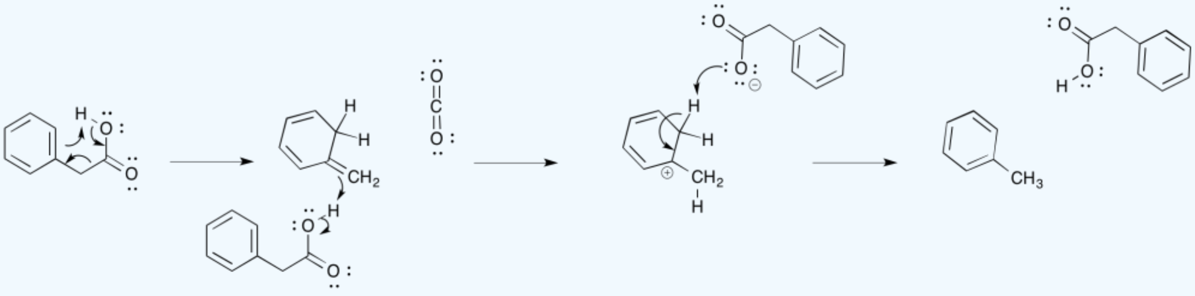
a)



b)

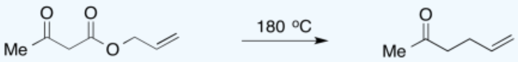


c)

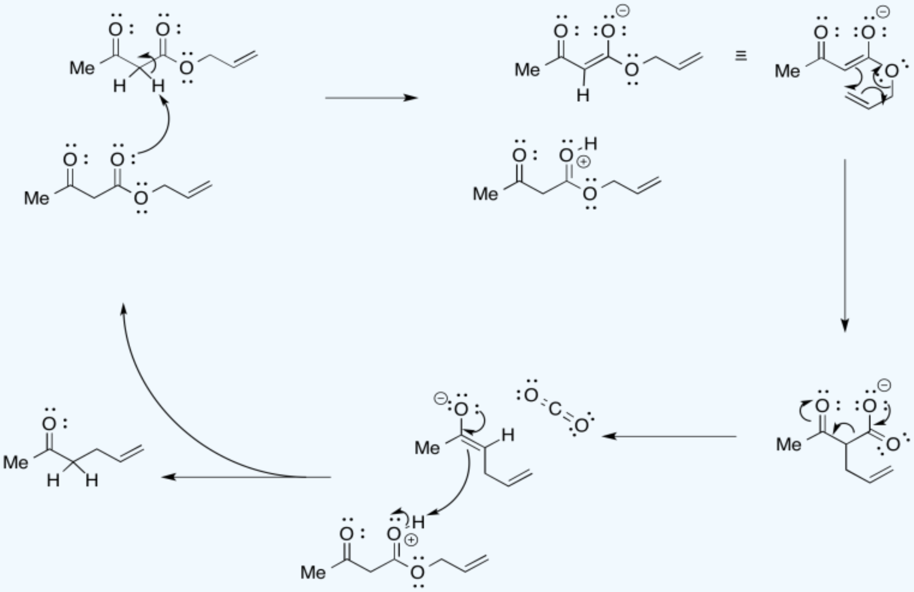


Exercise 10.9.4

Provide a mechanism for the Carroll Reaction, which involves the initial formation of an enol intermediate.



Answer



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10.10: Olefin Metathesis

Olefin metathesis, or alkene metathesis, is an important process in petroleum refining and in the synthesis of important compounds such as pharmaceuticals. The mechanism of olefin metathesis is related to pericyclic reactions like Diels Alder and [2+2] reactions. In other words, it occurs through the concerted interaction of one molecule with another.

In petroleum refining, heating alkenes over metal oxide surfaces results in the formation of longer-chain alkenes. In particular, terminal olefins (with the double bond at the end of the chain) are converted into internal olefins (with the double bond somewhere in the middle of the chain).

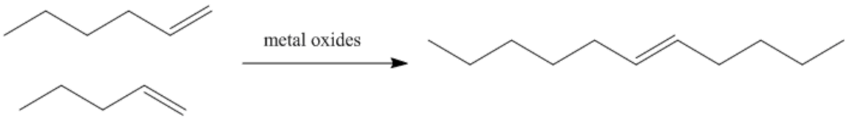

Figure 10.10.1: Olefin metathesis produces longer-chain "internal olefins" from shorter chain "terminal olefins".

What does that reaction have to do with addition reactions involving double bonds?

Clearly, the alkenes have double bonds. In addition, so do the metal oxides. Metal atoms inside the metal oxides are bridged together by oxygen atoms. The surface of the metal oxides may be covered with a mixture of hydroxyl groups as well as terminal oxides (M=O groups). The terminal oxides on the surface are the important part of the catalyst.

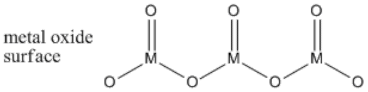

Figure 10.10.2: A simplified structure of a chunk of metal oxide surface.

When metal alkylidene complexes were developed in the 1970's, it was found that they, too, could catalyze this reaction.

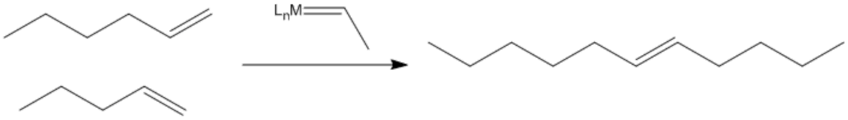

Figure 10.10.3: In olefin metathesis, the active species is a metal carbene.

In fact, scientists working in petroleum chemistry soon came to believe that metal oxides on the catalyst surface were converted to alkylidenes, which then carried out the work of olefin metathesis.

The reaction, it turns out, involves a [2+2] cycloaddition of an alkene to a metal alkylidene (to the metal-carbon double bond). This reaction results in a four-membered ring, called a metallacyclobutane.

The [2+2] cycloaddition is quickly followed by the reverse reaction, a retro-[2+2]. The metallacyclobutane pops open to form two new double bonds.

This mechanism is called the Chauvin mechanism, after its first proponent, Yves Chauvin of the French Petroleum Institute. Chauvin's proposal of this mechanism shortly after the discovery of metal alkylidenes by Dick Schrock at DuPont earned him a Nobel Prize in 2005. Chauvin and Schrock shared the prize with Bob Grubbs, who made it possible for the reaction to be adapted easily to the synthesis of complex molecules such as pharmaceuticals.

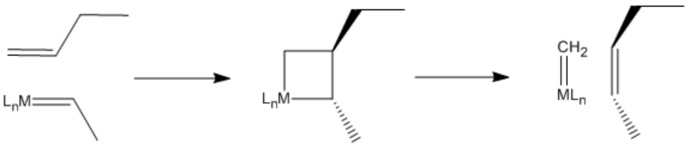

Figure 10.10.4: The Chauvin mechanism for olefin metathesis.

Why does olefin metathesis lead to the formation of internal alkenes? The [2+2] addition and retro-[2+2] reactions occur in equilibrium with each other. Each time the metallacyclobutane forms, it can form two different pairs of double bonds through the retro reaction. In the presence of terminal alkenes, one of those pairs of alkenes will eventually include ethene. Since ethene is a gas, it is easily lost from the system, and equilibrium shifts to the right in the equation below.

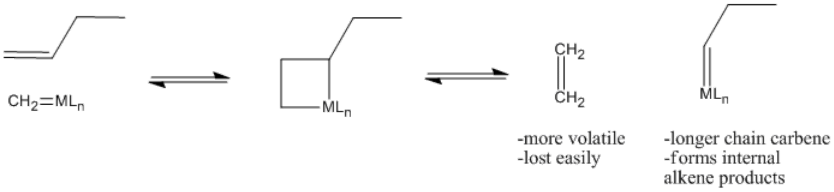

Figure 10.10.5: Olefin metathesis proceeds via cycloaddition to produce metallocylcobutanes.

That leaves a longer-chain alkylidene on the metal, ready to be attached to another long chain through subsequent [2+2] addition and reversion reactions.

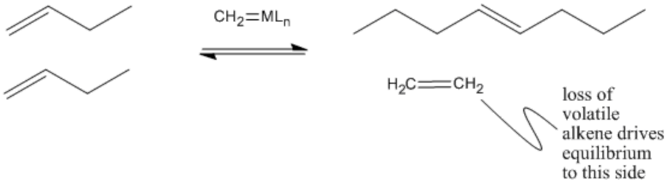

Figure 10.10.6: Olefin metathesis produces longer-chain "internal olefins" from shorter chain "terminal olefins" because volatile, short chain products are lost, shifting equilibrium.

In most cases, a [2+2] addition won't work unless photochemistry is involved, but it does work with metal alkylidenes. The reason for this exception is thought to involve the nature of the metal-carbon double bond. In contrast to an orbital picture for an alkene, an orbital picture for an alkylidene pi bond suggests orbital symmetry that can easily interact with the LUMO on an alkene. That's because a metal-carbon pi bond likely involves a d orbital on the metal, and the d orbital has lobes alternating in phase like a pi antibonding orbital.

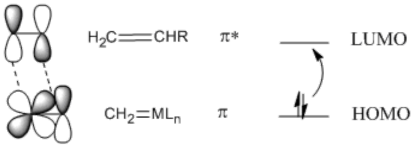

Figure 10.10.7: Olefin metathesis produces longer-chain "internal olefins" from shorter chain "terminal olefins".

A variety of catalysts have been developed for olefin metathesis. The laboratories of Bob Grubbs at CalTech and Dick Schrock at MIT have been particularly important in this area, although other labs have contributed significantly, including that of Amir Hoveyda at Boston College. The Schrock catalysts are based on tungsten or, more commonly, molybdenum. These catalysts are among the most efficient available, operating at very high turnover frequencies.

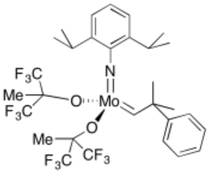

Figure 10.10.8: A Schrock catalyst for olefin metathesis.

There are other variations, including some designed for alkyne metathesis rather than alkene metathesis. There is also a commercially-available Schrock-Hoveyda catalyst; that one is chiral, and can be used to carry out olefin metathesis enantioselectively. When presented with a racemic mixture of substrates, this catalysts will select one substrate preferentially over the other. However, the Schrock catalysts can be intolerant of heteroatom functional groups. Molybdenum and tungsten are highly electrophilic, so lone pairs on atoms such as halogens or nitrogens can sometimes inhibit these metals. These compounds are also highly intolerant of air and moisture, for similar reasons.

Grubbs catalysts are more tolerant than Schrock catalysts, although they do not operate at nearly the speed that the molybdenum and tungsten ones can achieve. Because they are less sensitive to air and moisture, they are more commonly used for small-scale, benchtop reactions. In larger scale, industrial reactions, air- and moisture-sensitivity is usually a less compelling factor than speed.

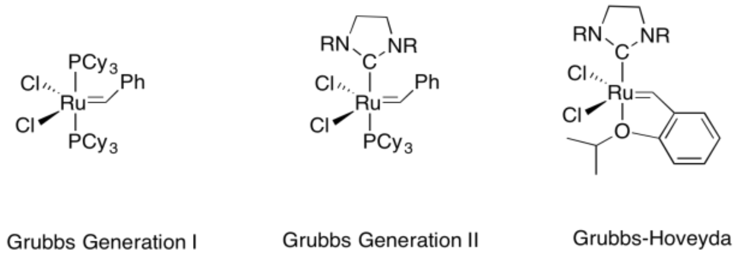

Figure 10.10.9: A series of Grubbs catalysts for olefin metathesis.

There are several "generations" of Grubbs catalysts that are commercially available, but a range of others have also been developed. New generations tend to offer a much higher reaction rate.

In addition to the simple "partner-swapping" of olefin metathesis, which is very important to the petroelum industry, there are other useful variations on the reaction. For example, a cyclic alkene that undergoes olefin metathesis forms two new double bonds, but these parts of the molecule are still connected to each other. Thus, an olefin metathesis between a cyclic alkene a chain alkene might produce a diene.

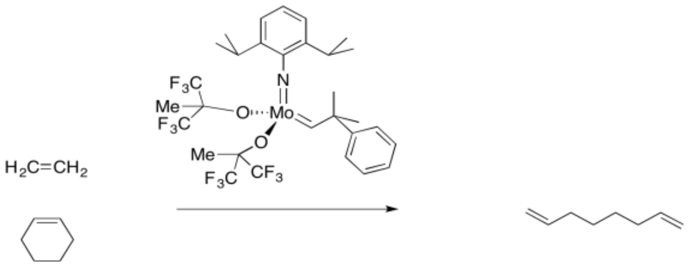

Figure 10.10.10: An example of ring opening metathesis. Usually, the rings are more strained than this one.

But remember, these reactions occur in equilibrium. If a cyclic alkene can be converted into a diene, then under the right conditions, a diene can be converted to a cyclic alkene. This reaction has become very important in the synthesis of organic compounds by the agricultural and pharmaceutical industries. RIngs of many different sizes, even very large ones, can be made in this way.

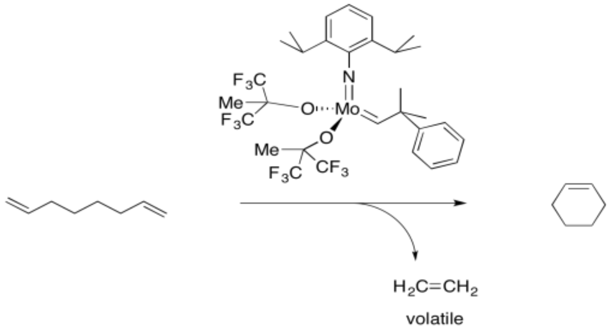

Figure 10.10.11: An example of ring-closing metathesis.

On the other hand, if the cyclic alkene by itself is treated with an olefin metathesis catalyst, it may link to other cyclic alkenes. That's because each cyclic alkene forms two new double bonds, one on each end. If each molecule forms two double bonds, a long chain of dienes will form. The result would be a polymer.

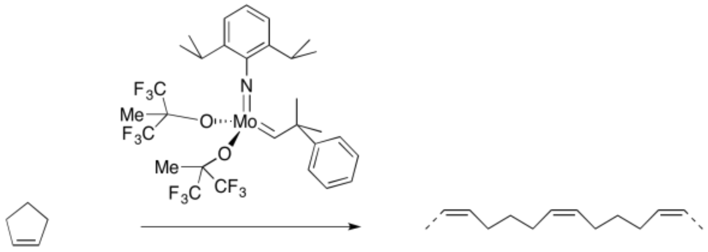

Figure 10.10.12: An example of ring-opening metathesis polymerisation (ROMP).

Exercise 10.10.1

Show the products of the following reaction.

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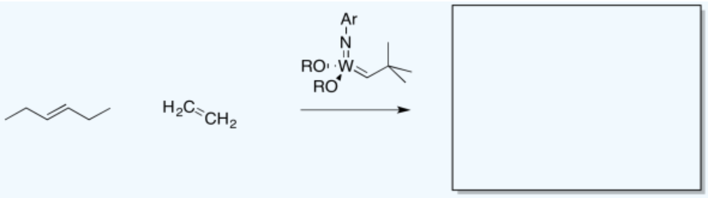

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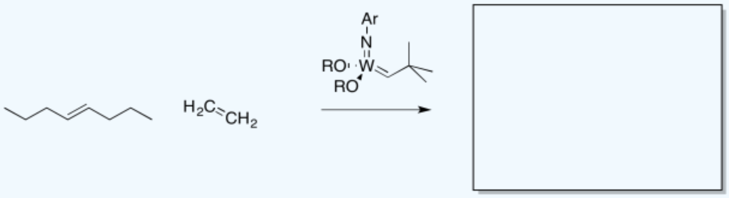

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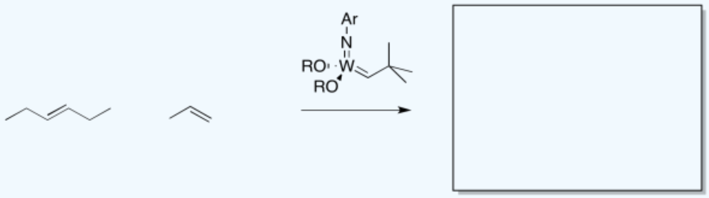

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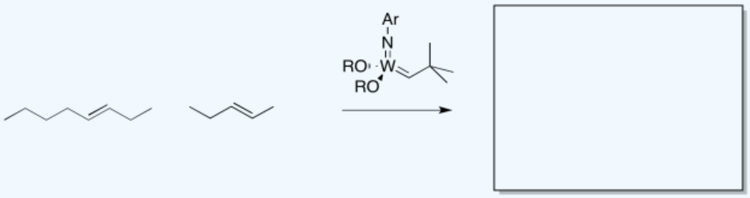

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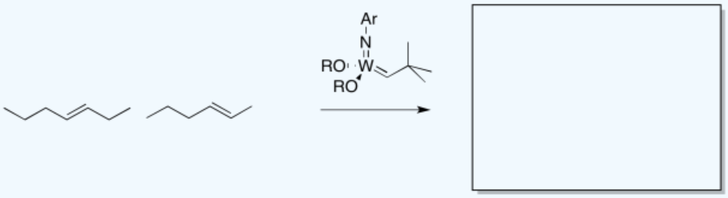

Answer

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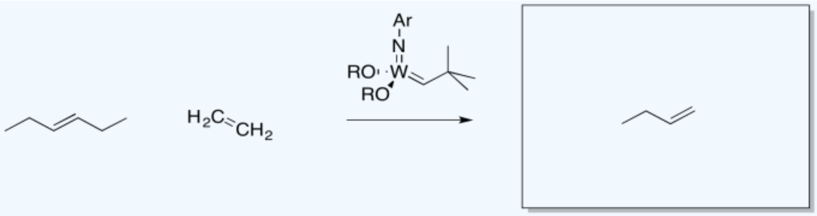

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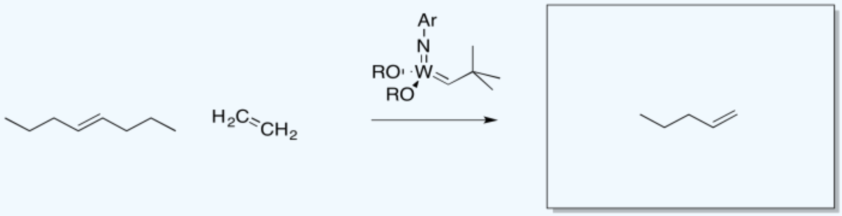

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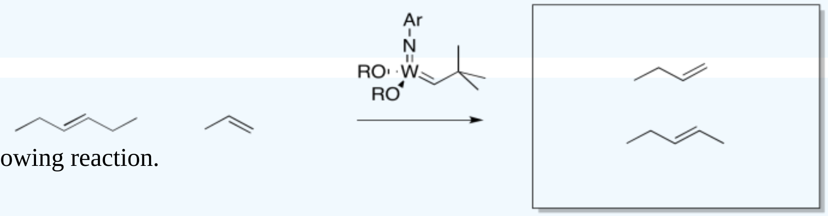
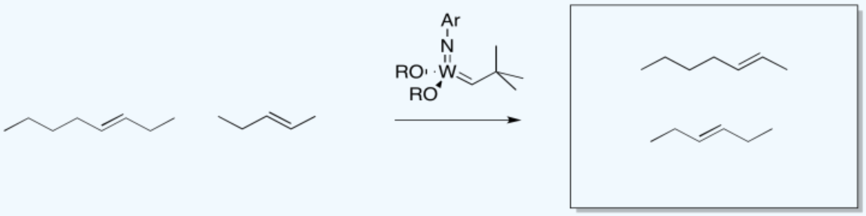


? Exercise 10.10.2

Show the products of the following reaction.

d)



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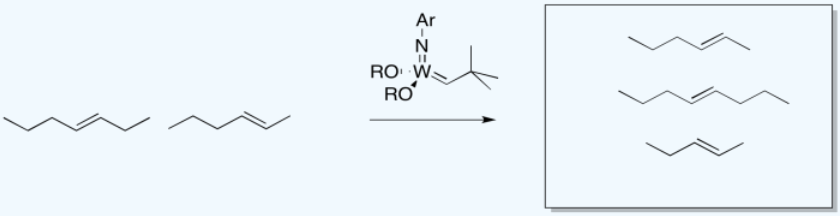

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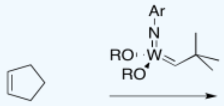

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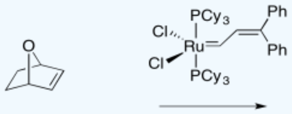

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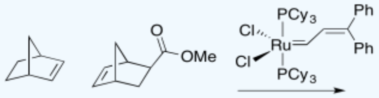

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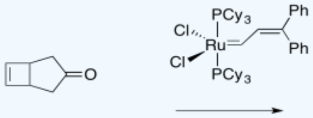

Answer

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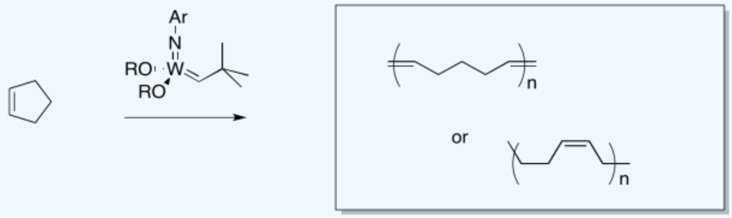
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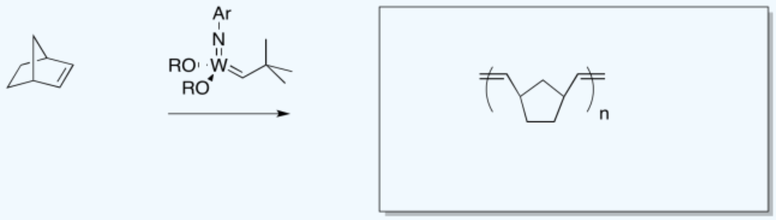
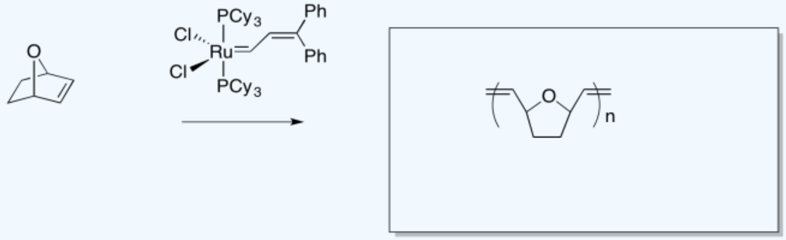
N
RO
W
RO
n
or
n

b)


Ar
N
RO
W
RO
n

c)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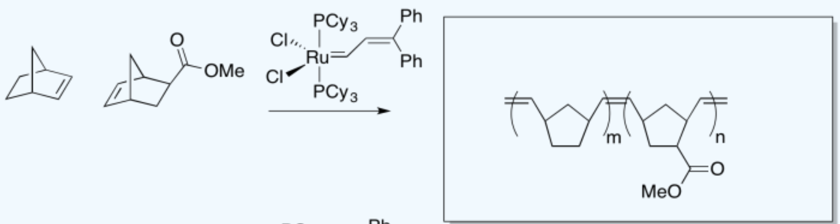
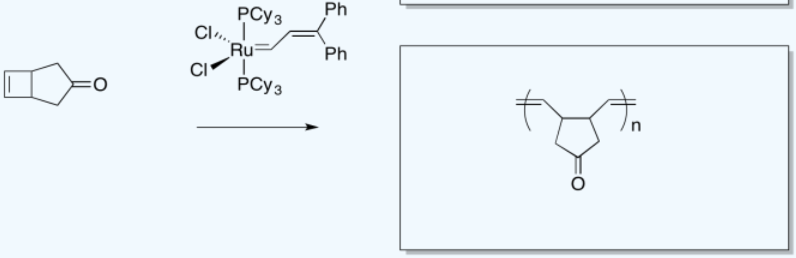
PCy3
Ph
Cl
Ru
Cl
Ph
PCy3
O
n

d)


O
OMe
PCy3
Ph
Cl
Ru
Cl
Ph
PCy3
m
n
O
MeO

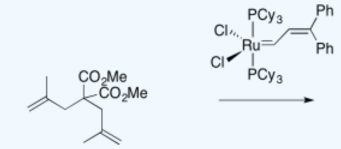
e)


O
PCy3
Ph
Cl
Ru
Cl
Ph
PCy3
n
O

Exercise 10.10.3

Show the products of the following reaction.

a)



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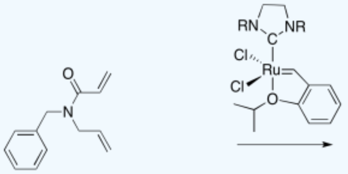

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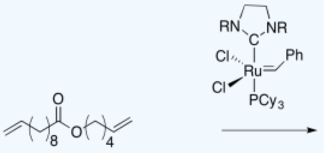

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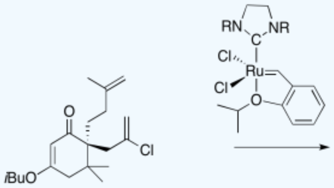

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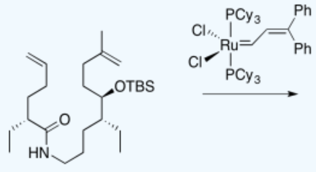
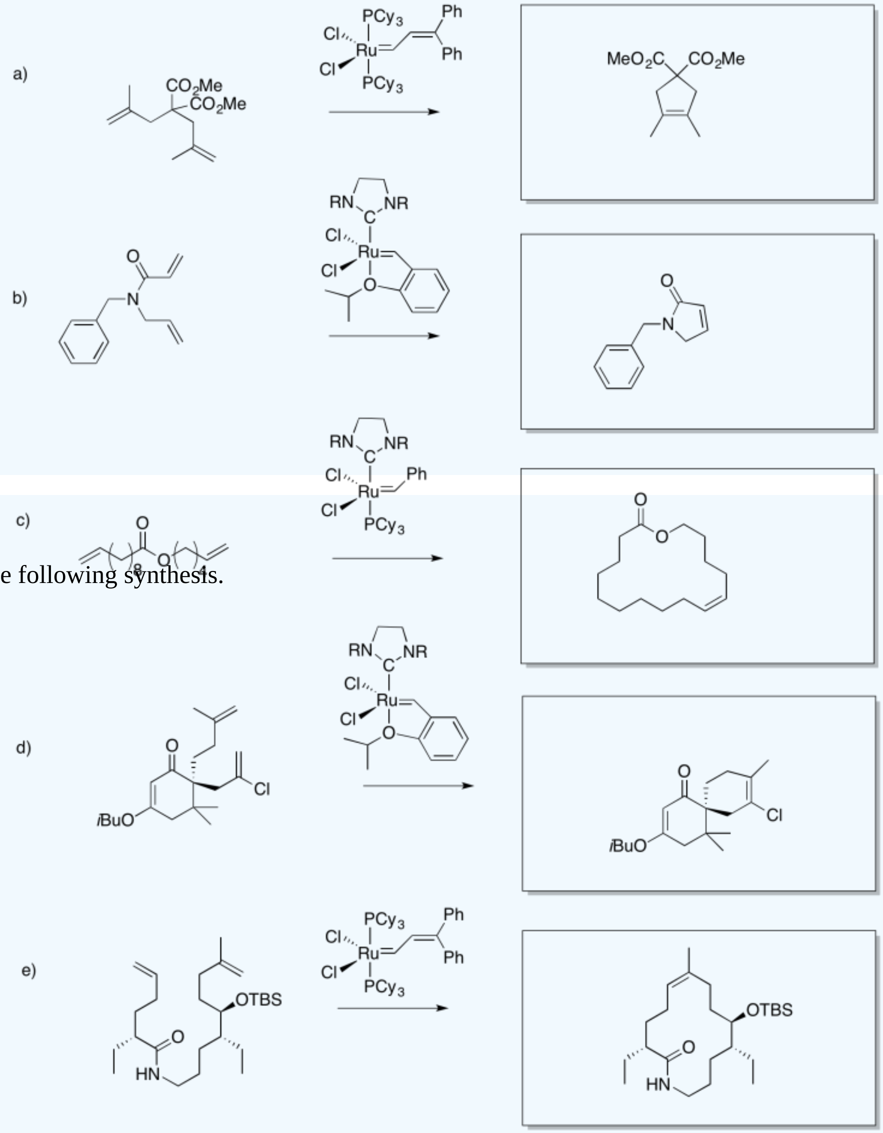


Answer

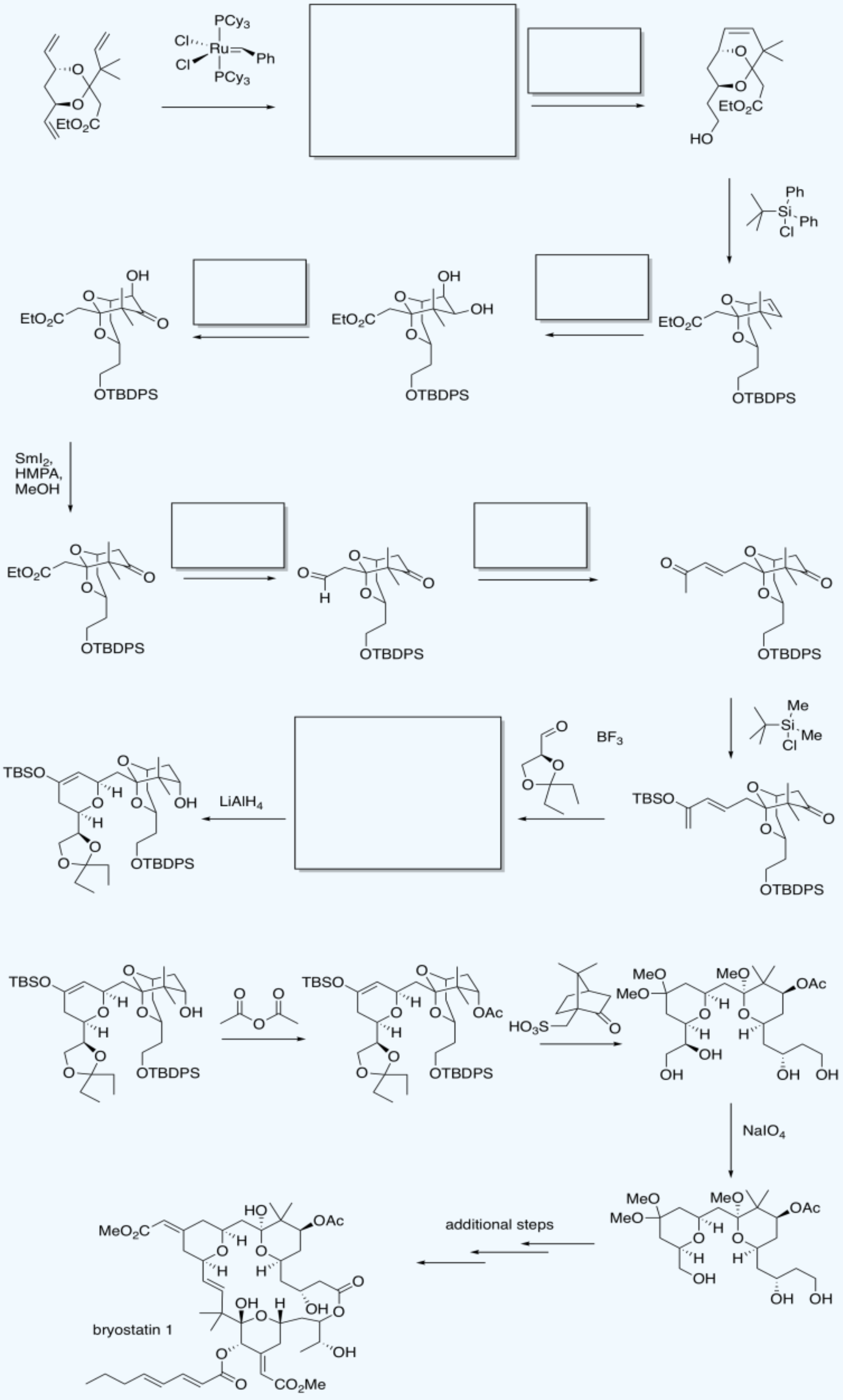


? Exercise 10.10.4

Fill in the blanks in the following synthesis.

Bryostatin Partial Synthesis (Burke, UW-Madison, 2004)

One of a family of natural products isolated from the nudibranch, Bugula neritina. Bryostatin 1 was unsuccessful as an anticancer agent but shows promise in trials against Alzheimer's.

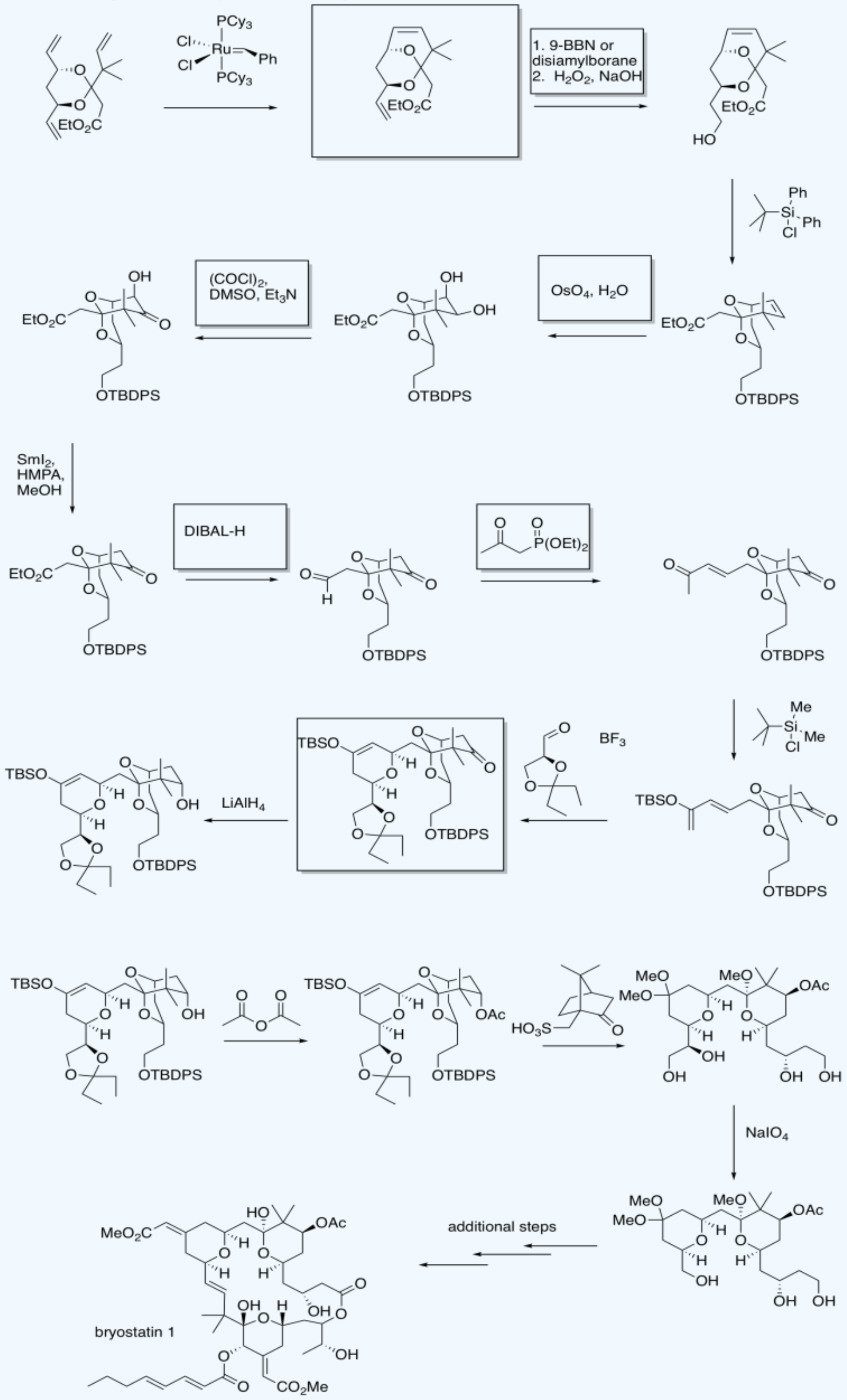


bryostatin 1

Answer

Bryostatin Partial Synthesis (Burke, UW-Madison, 2004)

One of a family of natural products isolated from the nudibranch, Bugula neritina. Bryostatin 1 was unsuccessful as an anticancer agent but shows promise in trials against Alzheimer's.



10.11: Sigma Bond Metathesis

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10.12: Solutions to Selected Problems

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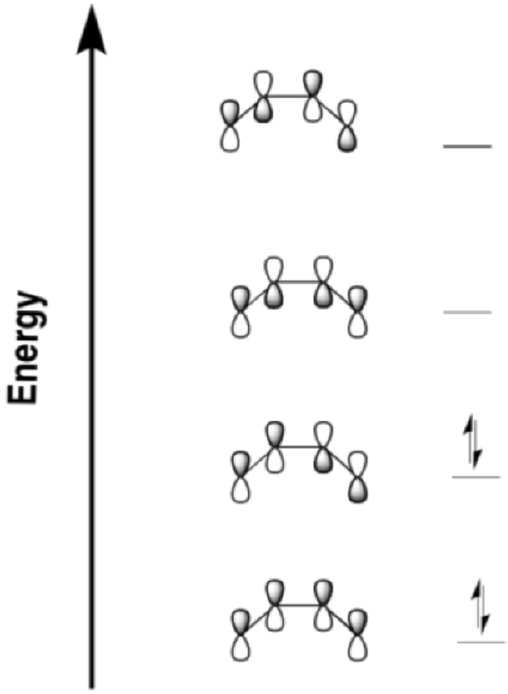

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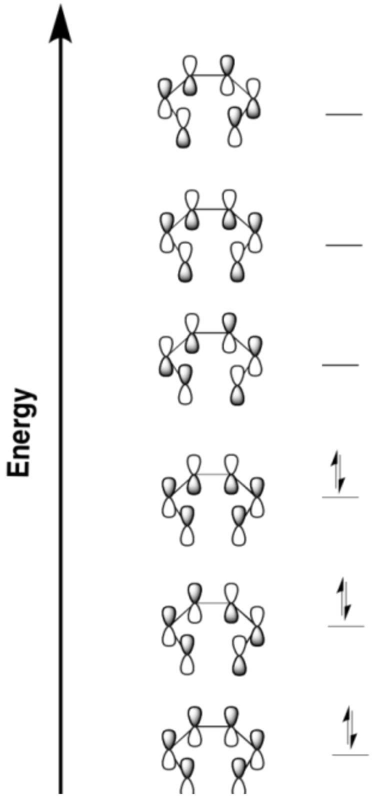

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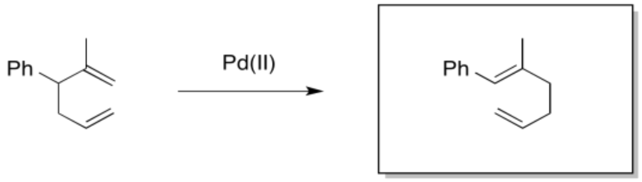

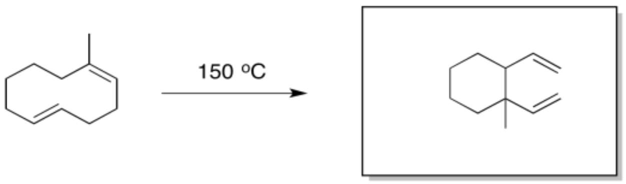

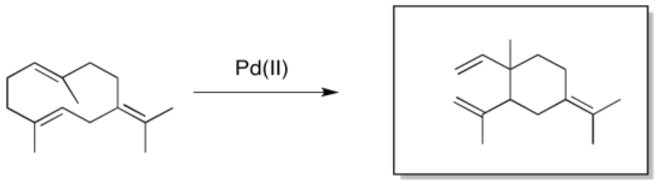

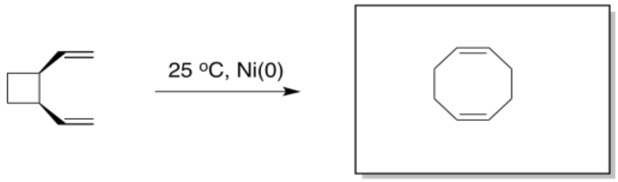

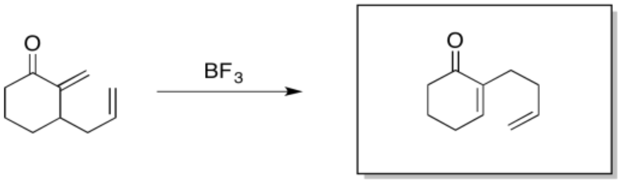

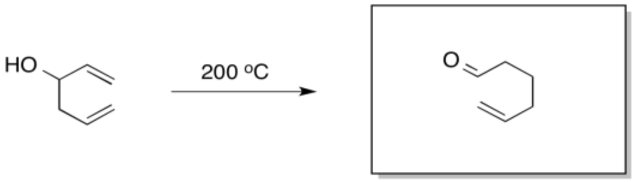

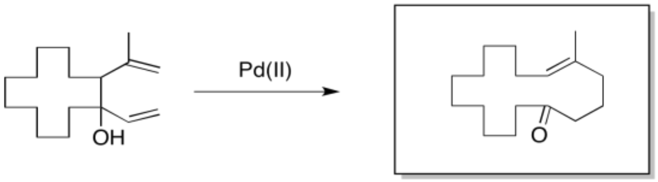

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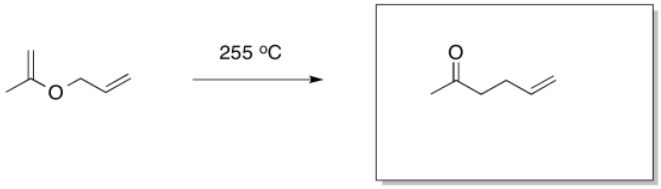

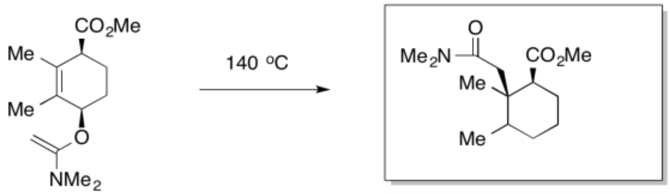

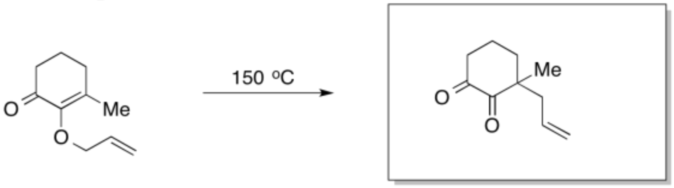

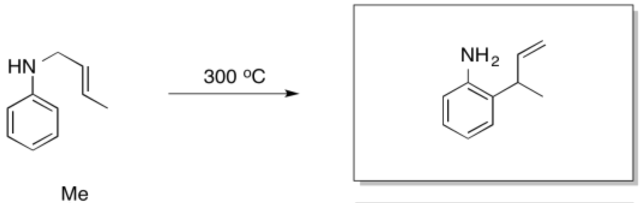

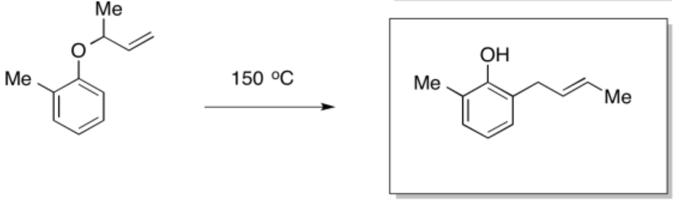

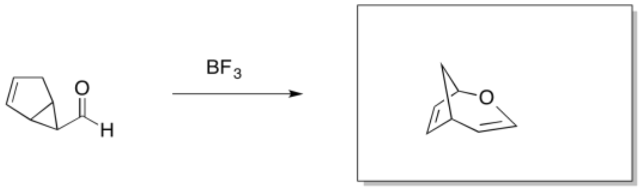

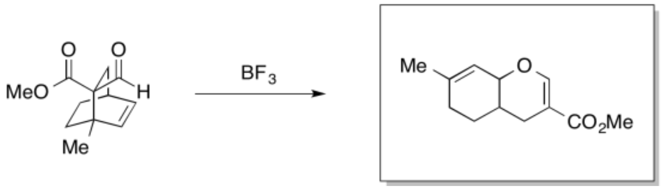

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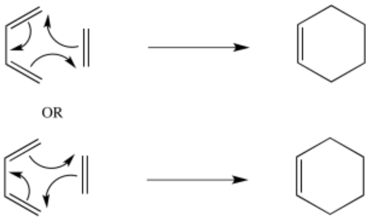

Exercise 10.3.2:

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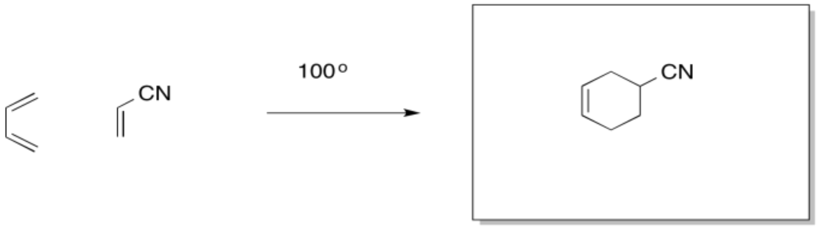

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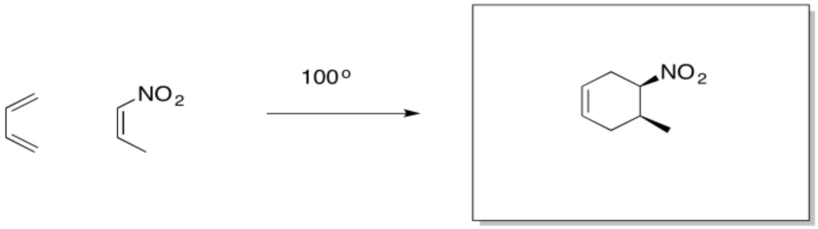

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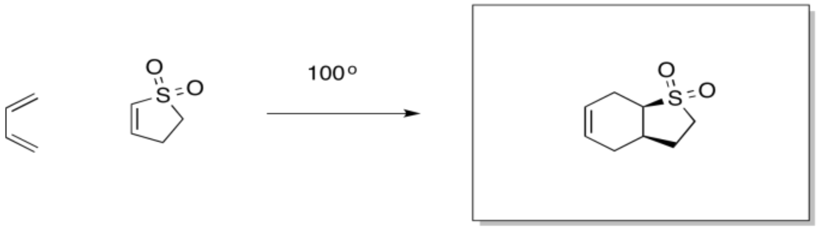

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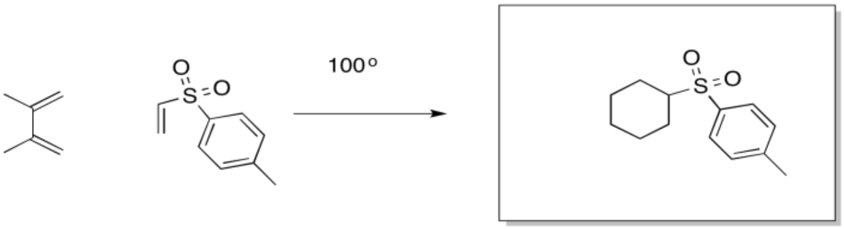

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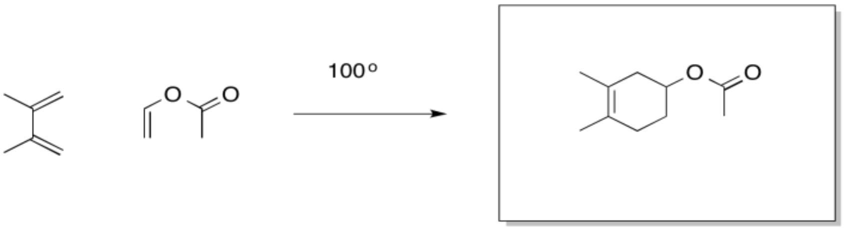

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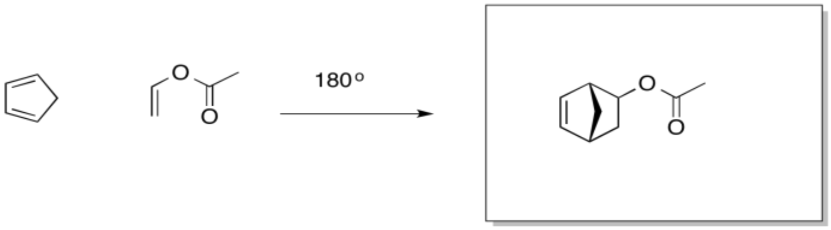

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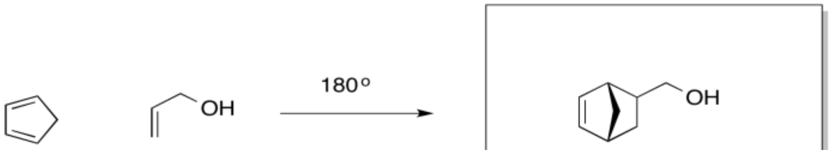

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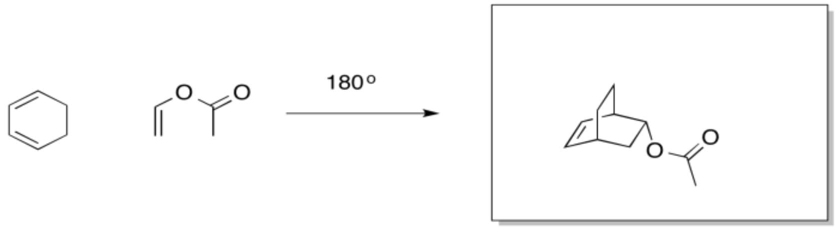

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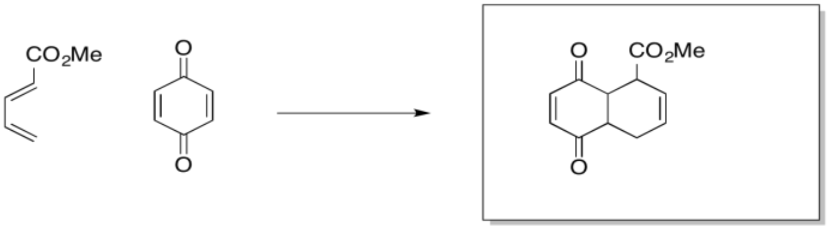

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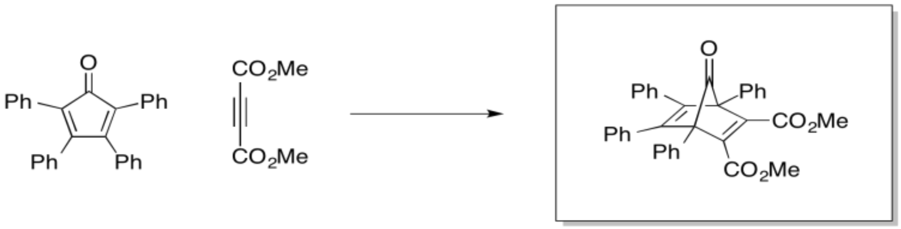
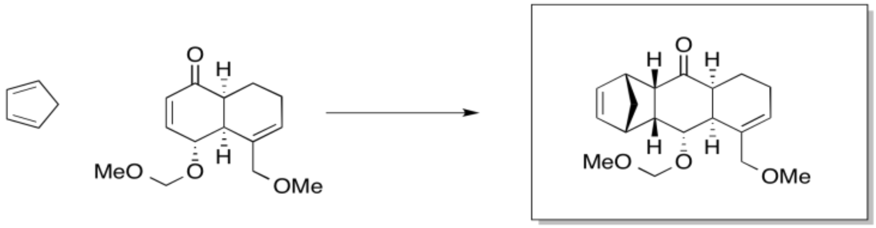
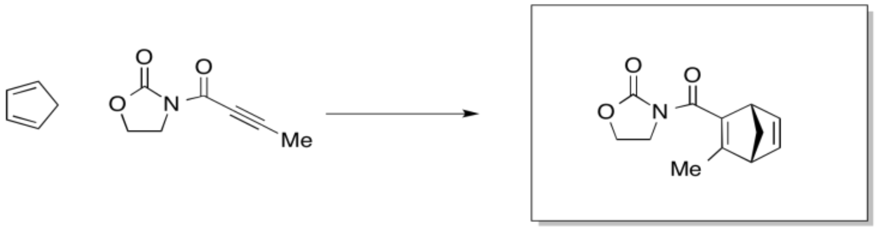


k)

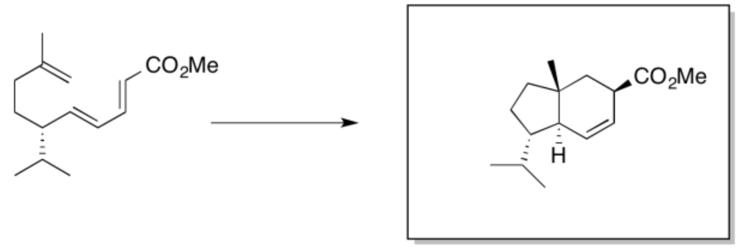


l)

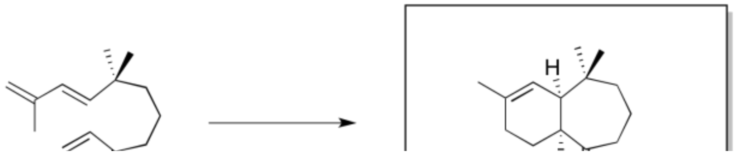


Exercise 10.3.4:

a)

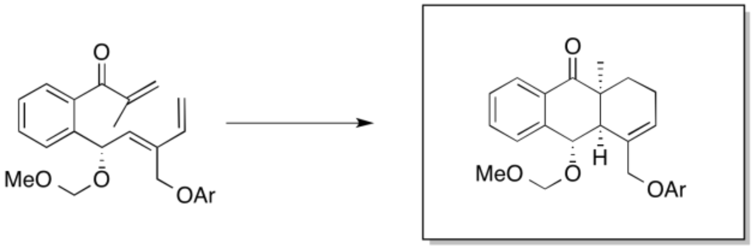


b)

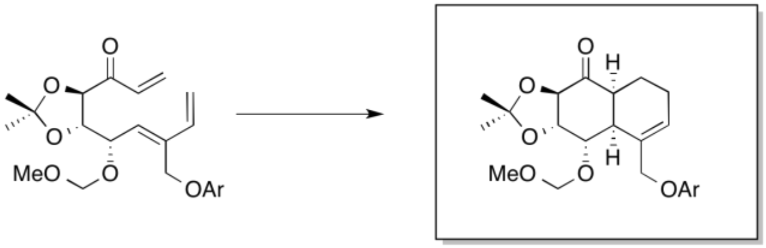



O
H
O

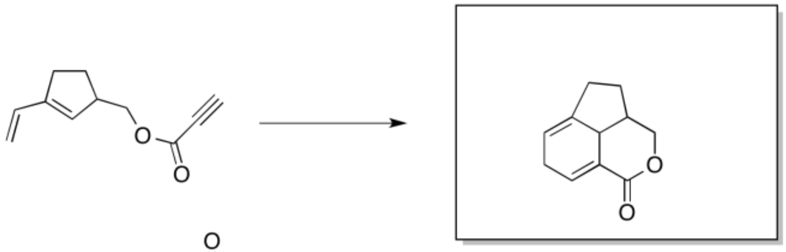
c)


O
MeO
O
OAr
O
MeO
O
H
OAr

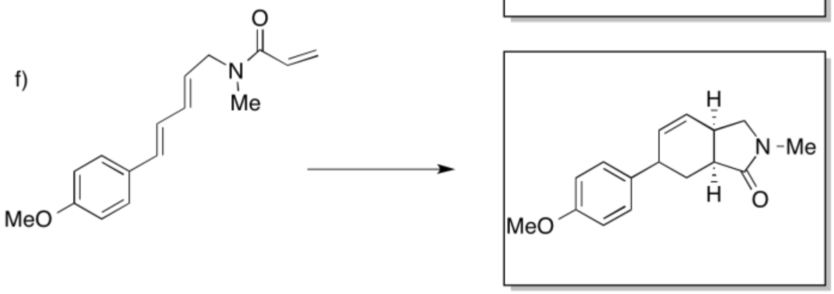
d)


O
O
O
MeO
O
OAr
O
H
O
O
MeO
O
H
OAr

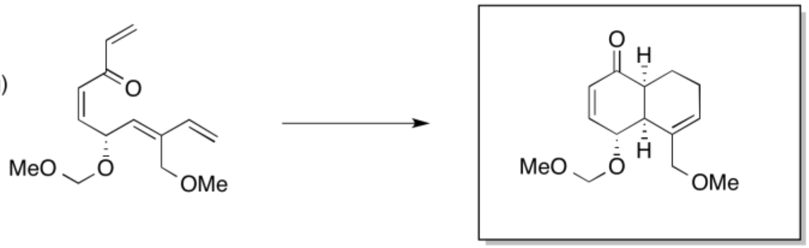
e)


O
O
O
O

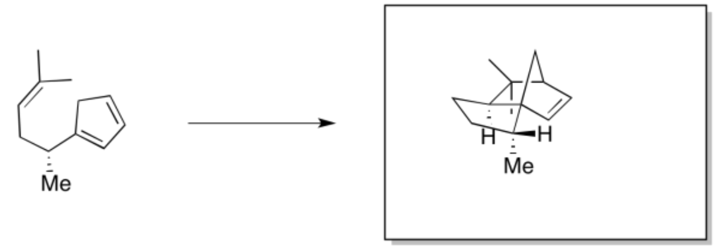
f)


O
N
Me
MeO
H
N -Me
H
O
MeO

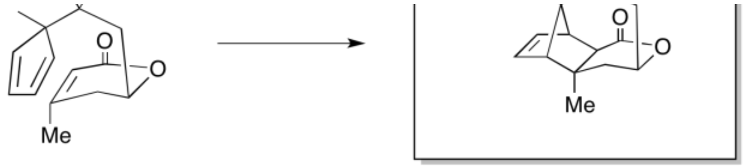
g)


O
MeO
O
OMe
O
H
MeO
O
H
OMe

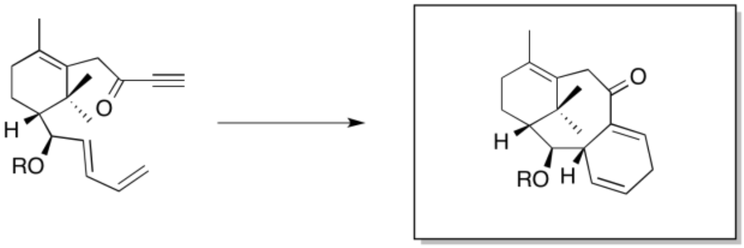
h)


Me
H
H
Me

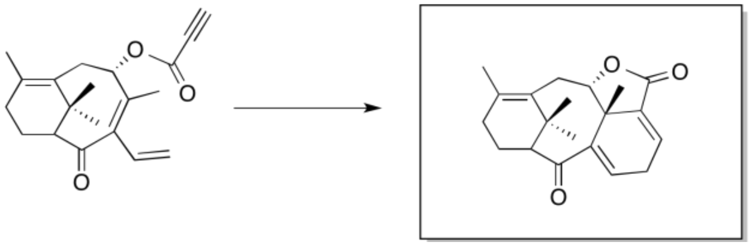
i)



j)



k)

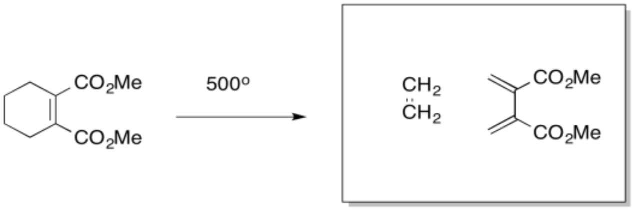


Exercise 10.3.6

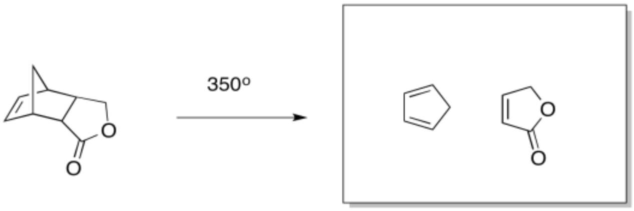
The retro-Diels Alder reaction is entropically favored, because two molecules are made from one molecule. As a result, energy becomes partitioned into additional states because the degrees of freedom are increasing. Internal entropy increases during this reaction. Mathematically, the entropy term is negative in the expression for free energy, so as entropy increases the free energy becomes lower. Because that term is actually a product of entropy and temperature, an increase in temperature has the effect of amplifying the influence of entropy on the free energy of the reaction. Hence, this reaction is favored by internal entropy factors, which come to dominate at elevated temperature.

Exercise 10.3.7:

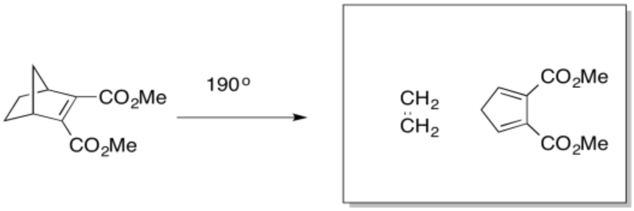
a)



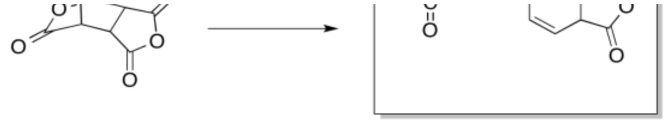
b)



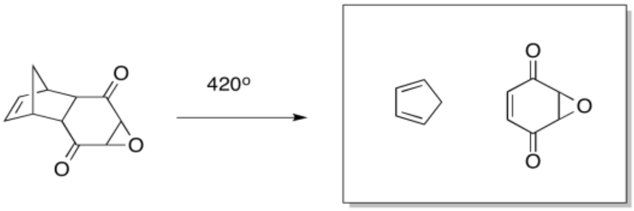
c)



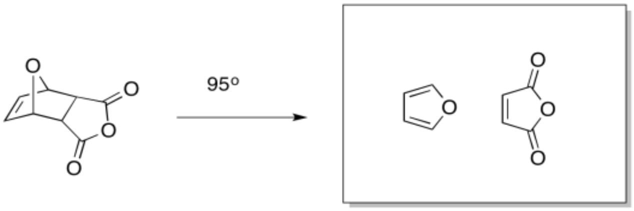
d)



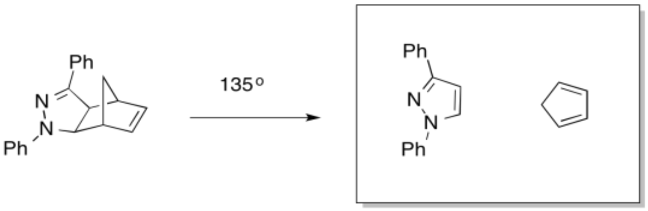
e)



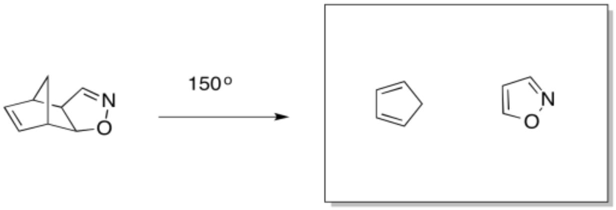
f)



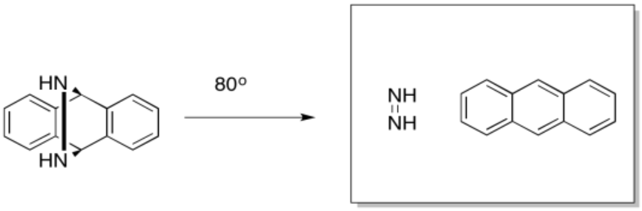
g)



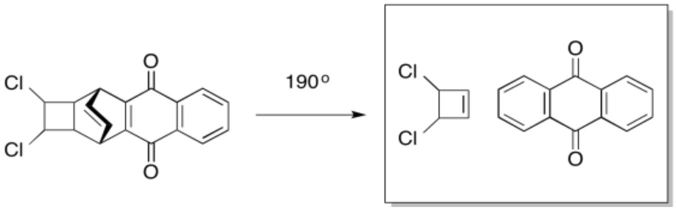
h)



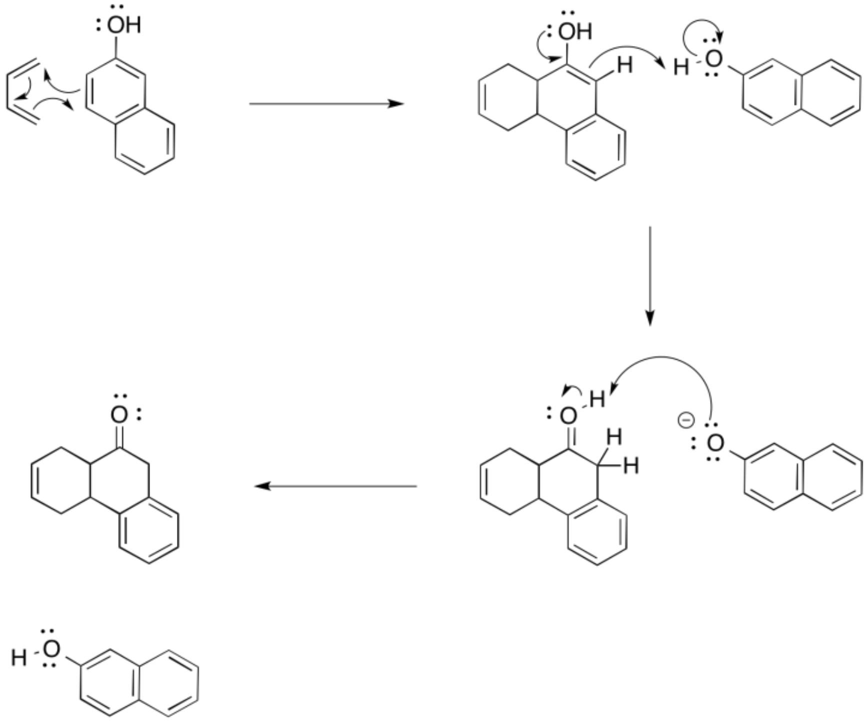
i)



j)

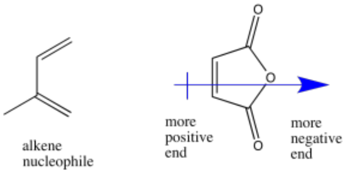


Exercise 10.3.8:



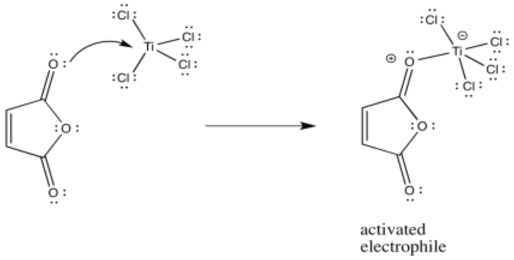
Exercise 10.4.1:

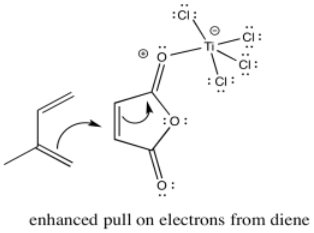
The maleic anhydride is polarized, with electron density drawn toward the anhydride functional group on one side of the ring. As a result, the other side of the ring is left more positive, and will attract the polarizable electron density from the diene.



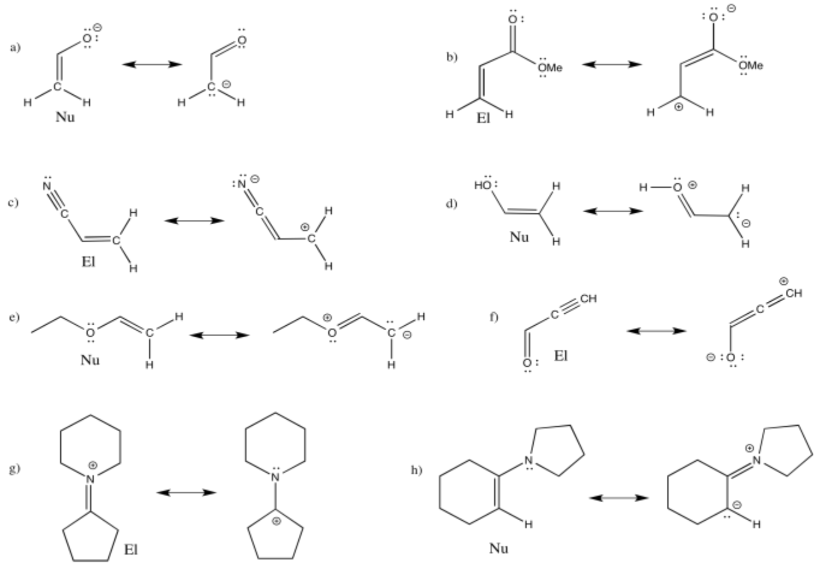
Exercise 10.4.2:

Lewis acids frequently activate carbonyl compounds towards interaction with nucleophiles. They do so by binding to the lone pairs on the carbonyl oxygen, drawing electron density away from the oxygen and, inductively, away from the neighbouring portion of the molecule.

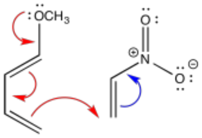




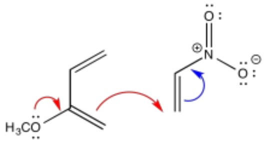
Exercise 10.4.3:



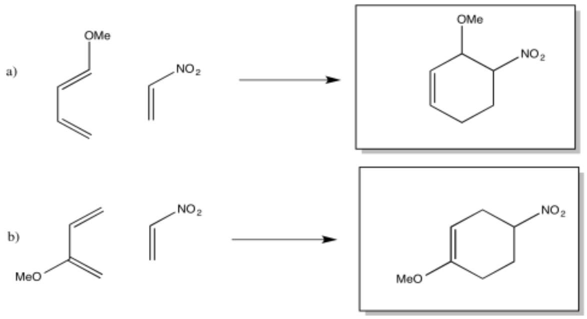
Exercise 10.4.4:



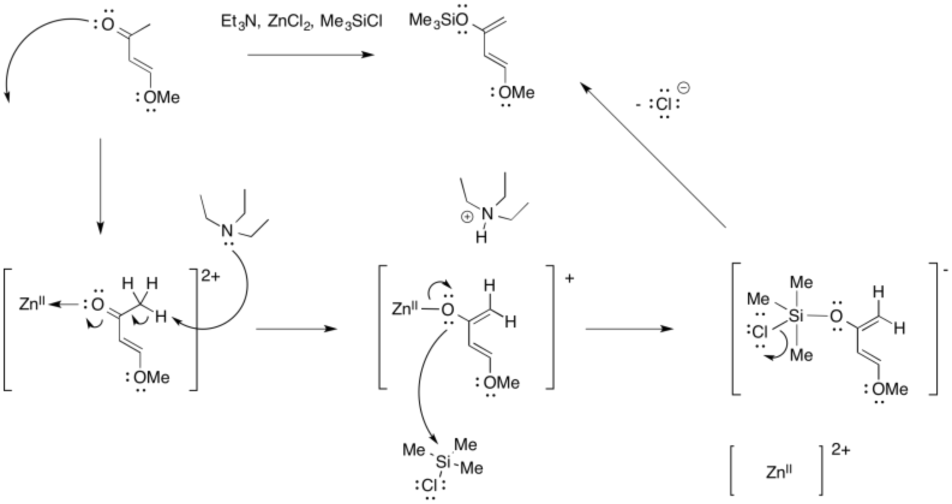
Exercise 10.4.5:



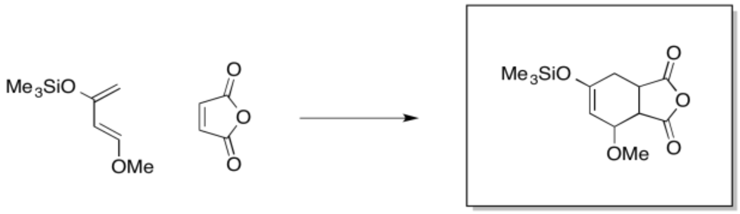
Exercise 10.4.6:

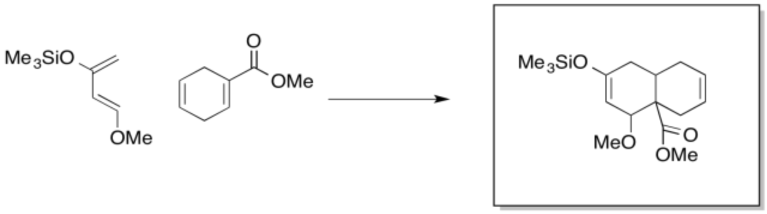


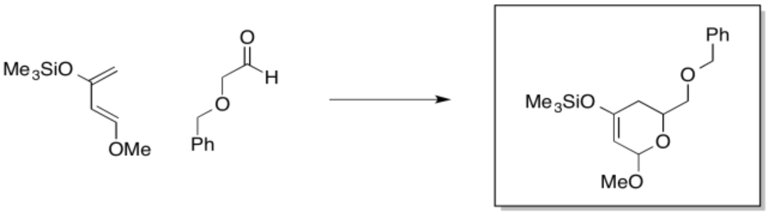
Exercise 10.4.7:

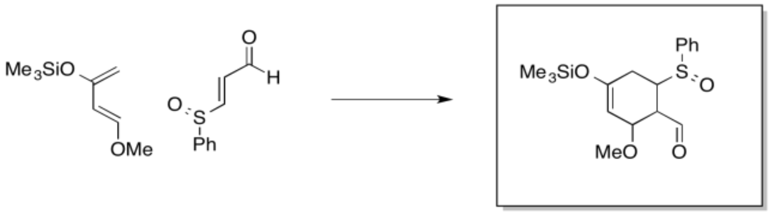


Exercise 10.4.8:

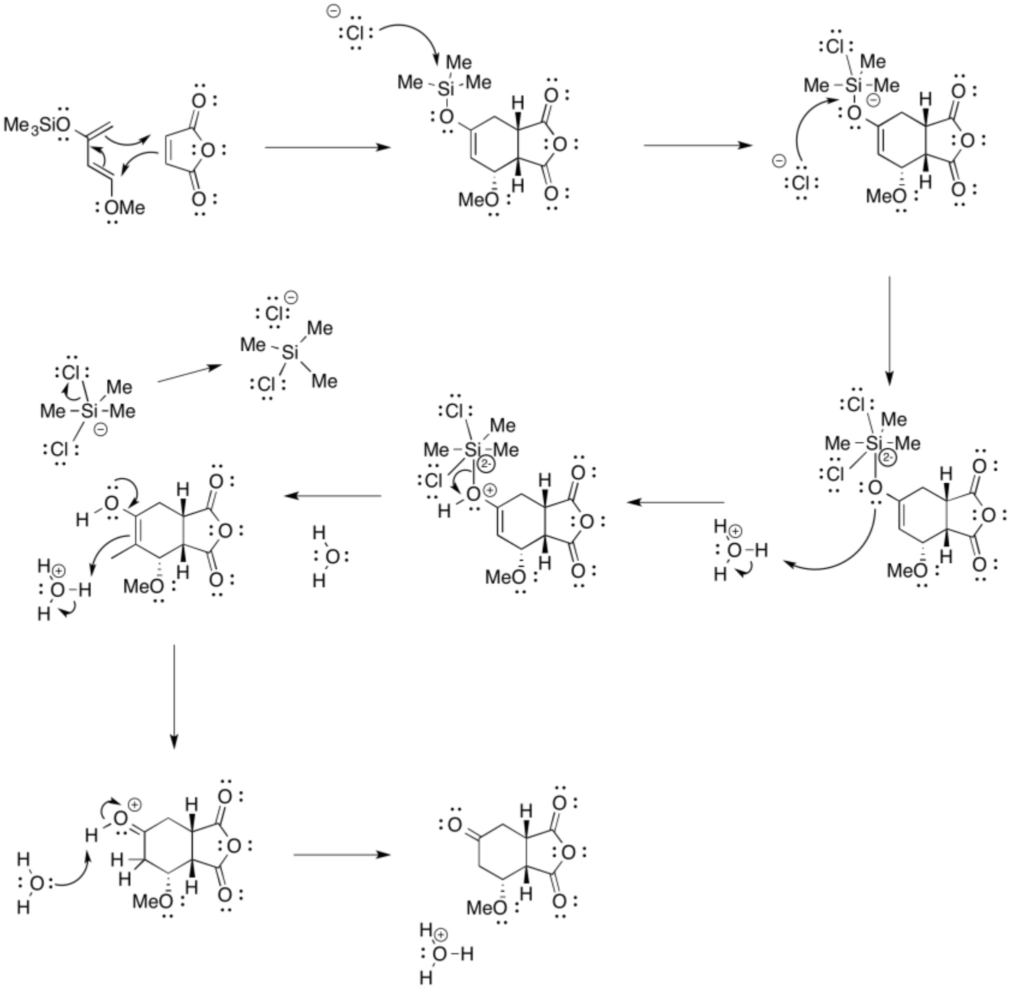




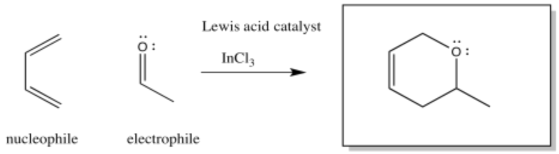




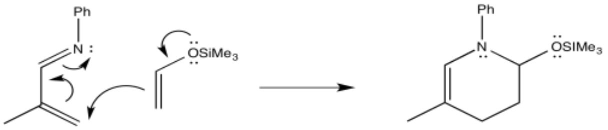
Exercise 10.4.9:



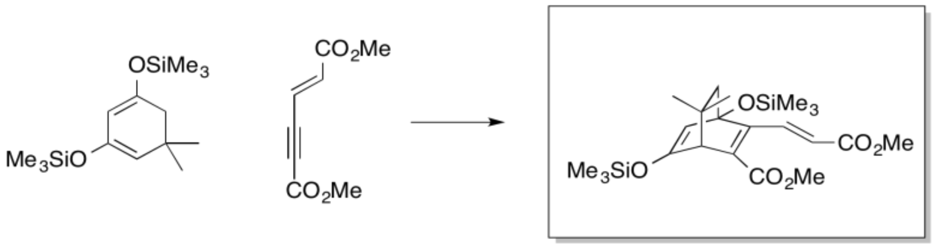
Exercise 10.4.10:

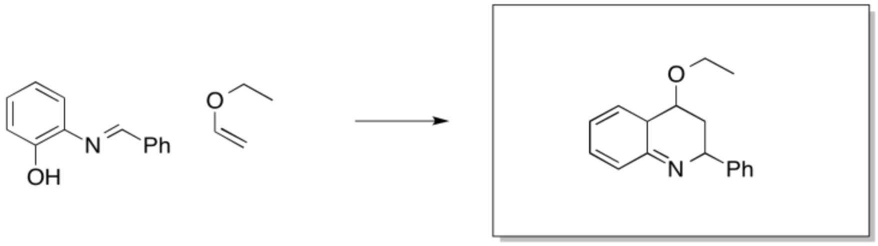


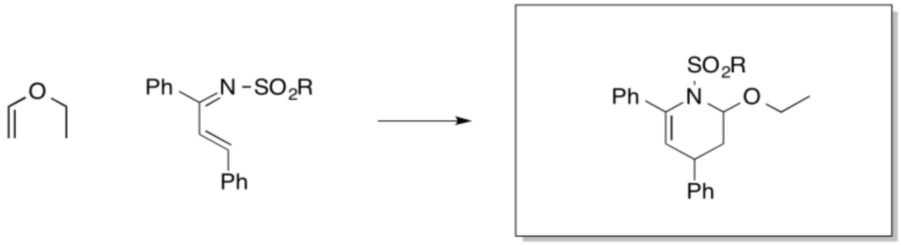
Exercise 10.4.11:

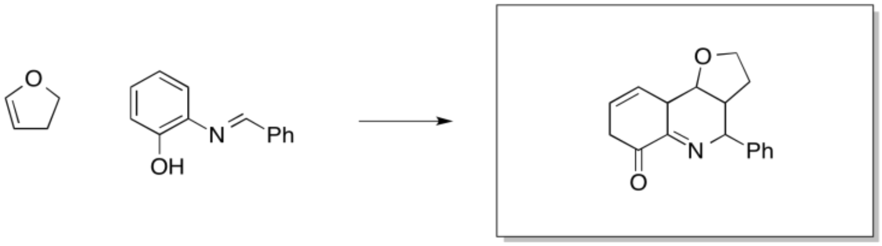


Exercise 10.4.12:



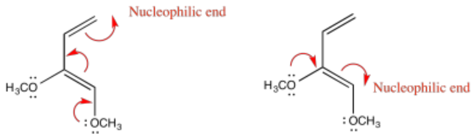




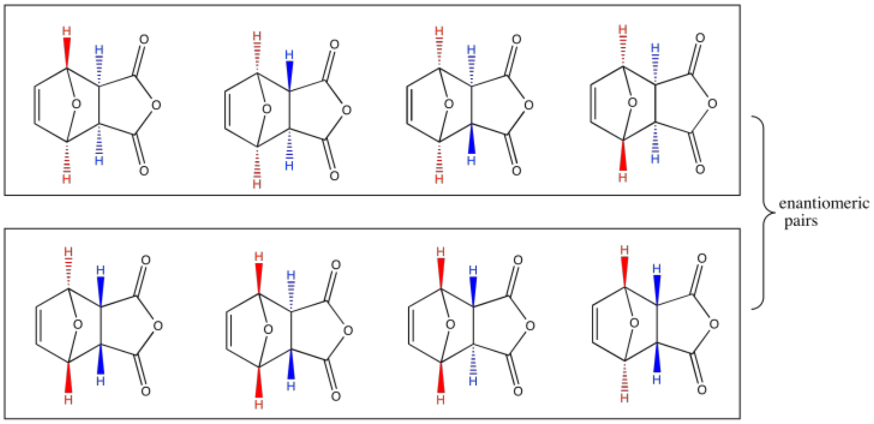


Exercise 10.4.13:

The drawings indicate the two electron-donating groups are operating at cross purposes. One directs electron density toward one end of the diene, whereas the other directs the electron desnity toward the other end.



Exercise 10.5.1:



Exercise 10.8.3:

a) OsO_4, H_2O

b) mCPBA

c) 1. O_3; 2. Me_2S or Zn

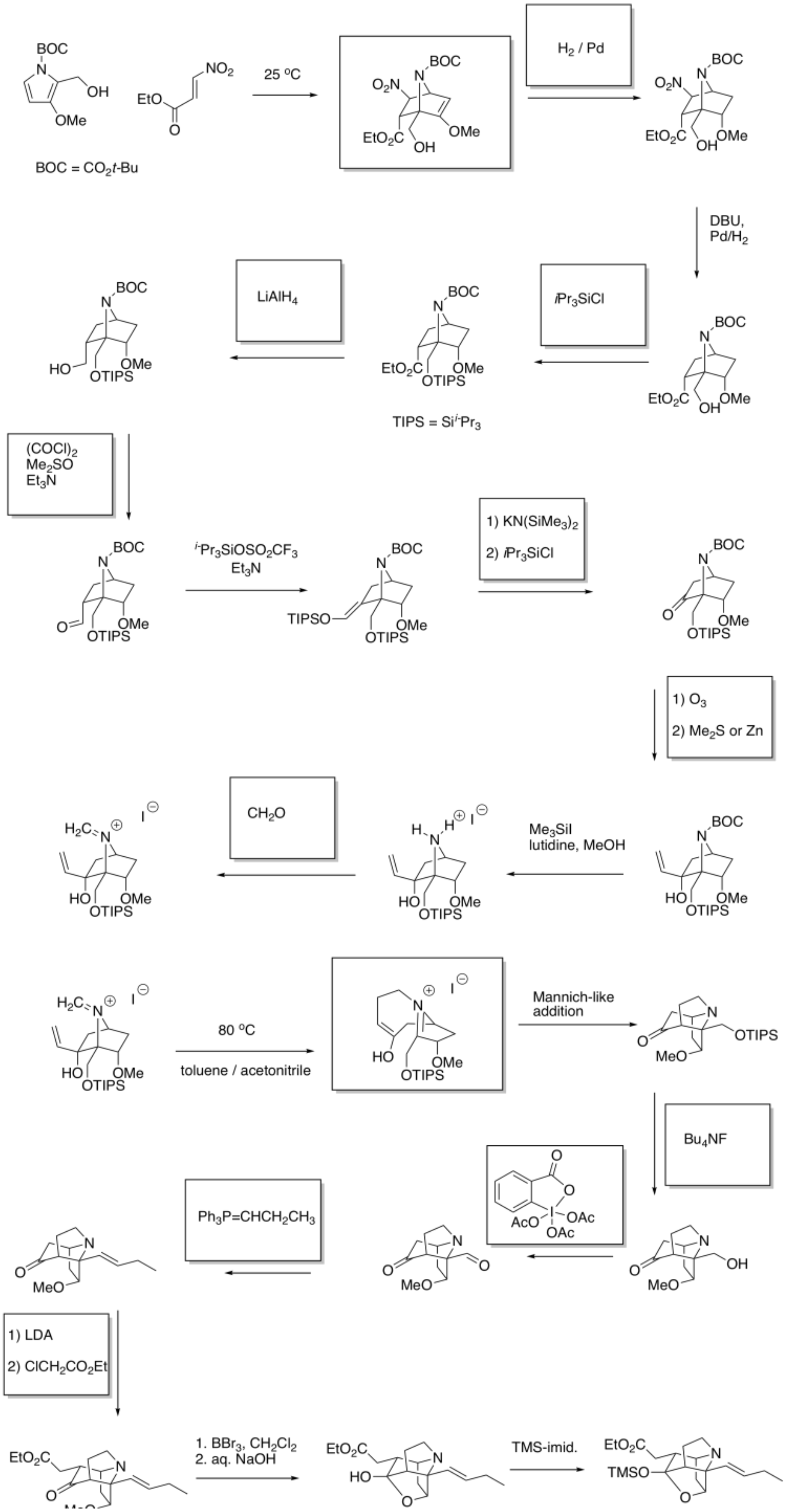
d) 1. O_3; 2. Me_2S or Zn

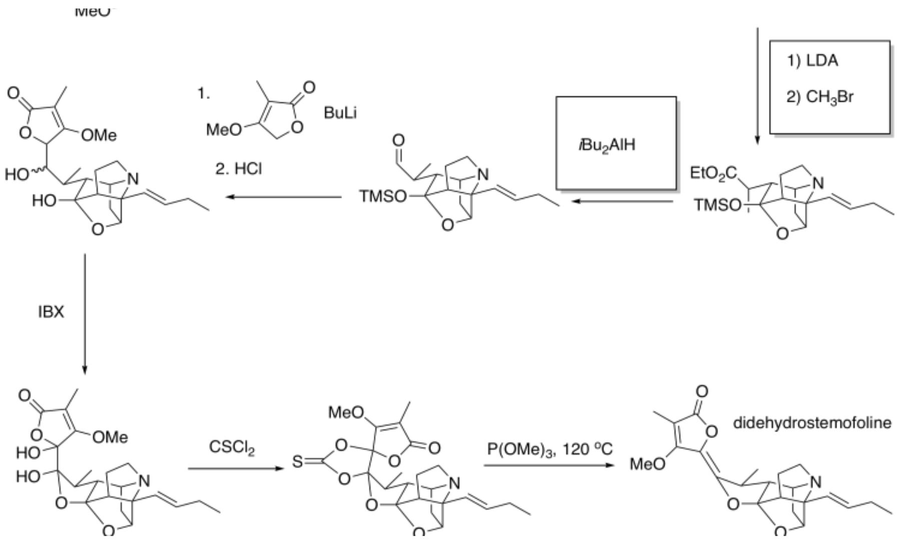
e) OsO_4, H_2O

f) mCPBA

Exercise 10.8.6:

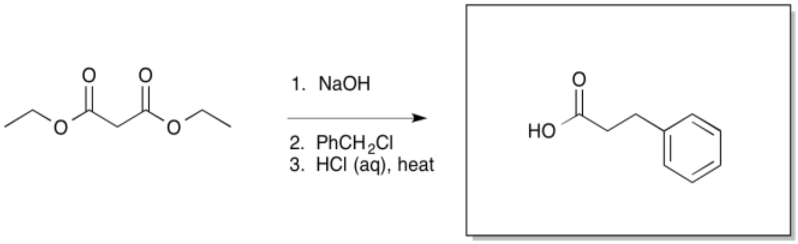
Synthesis of Didehydrostemofoline (Overman, 2003)
Isolated from a family of East Asian plants; deters insect feeding.



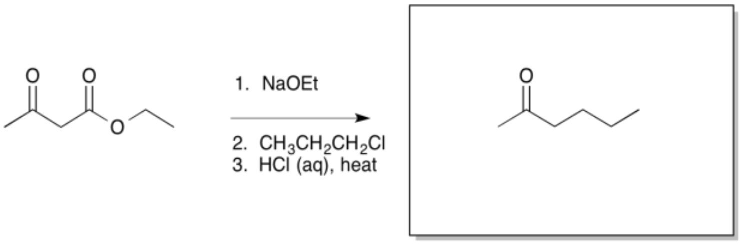


Exercise 10.9.2:

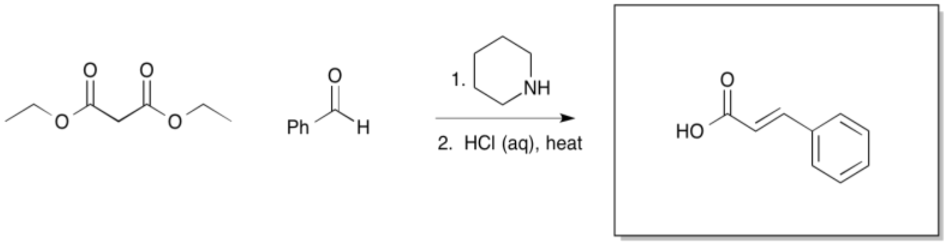
a)



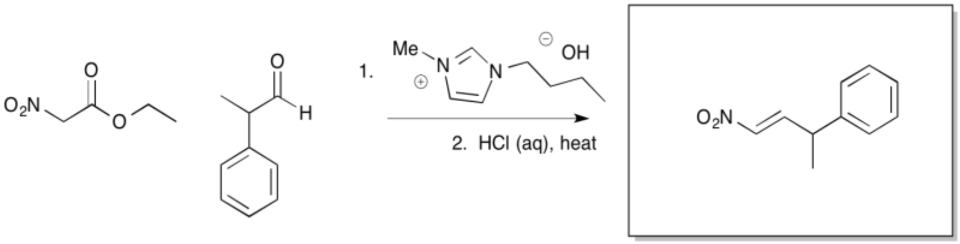
b)



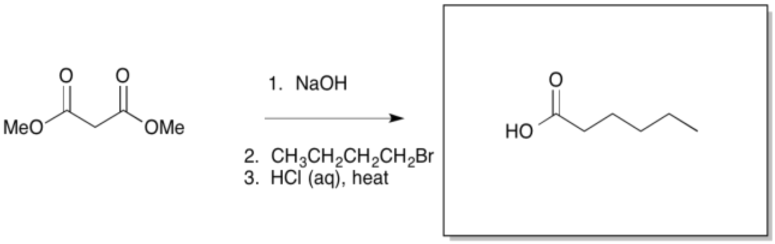
c)



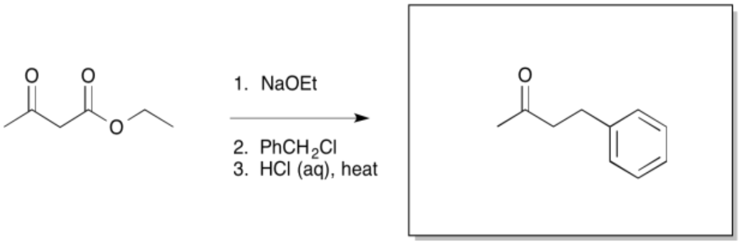
d)



e)

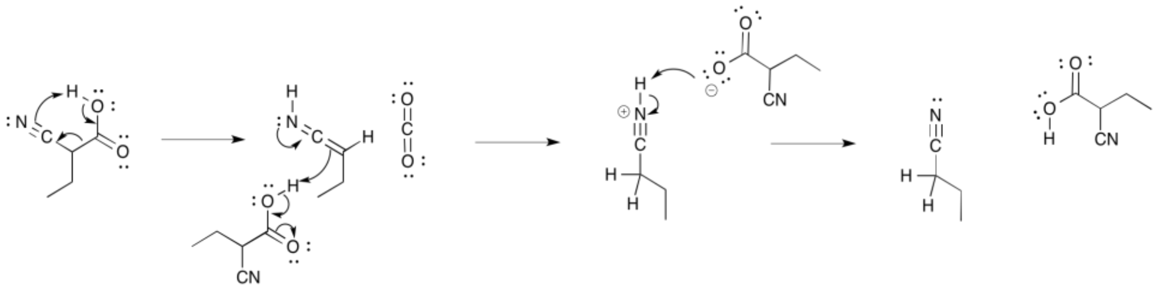


f)



Exercise 10.9.3:

a)



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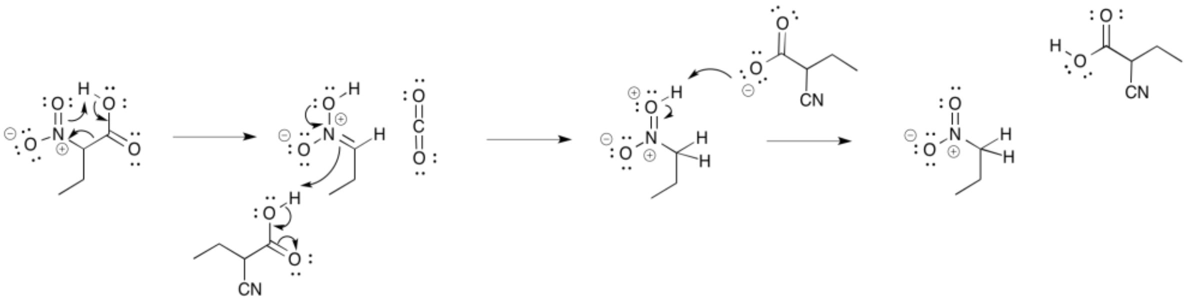

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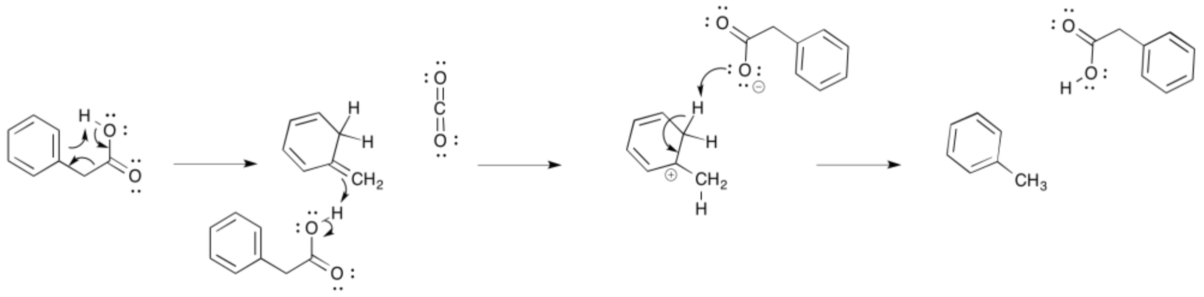
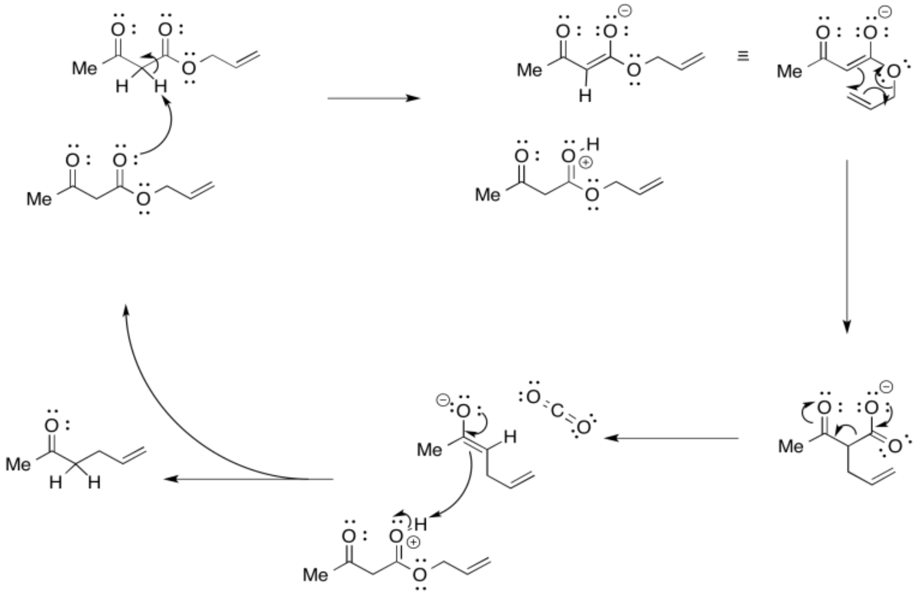
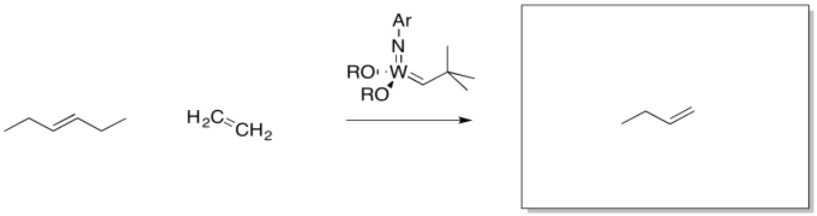


Exercise 10.9.4:



Exercise 10.10.1:

a)



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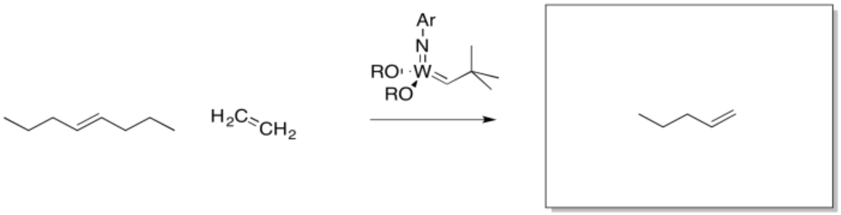
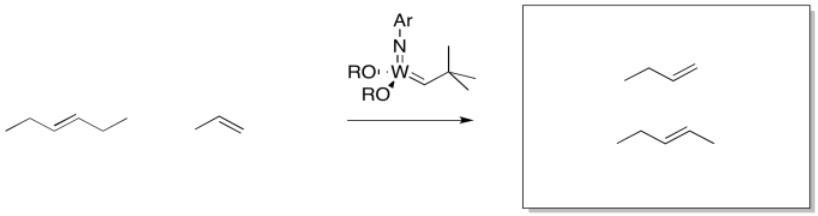


c)



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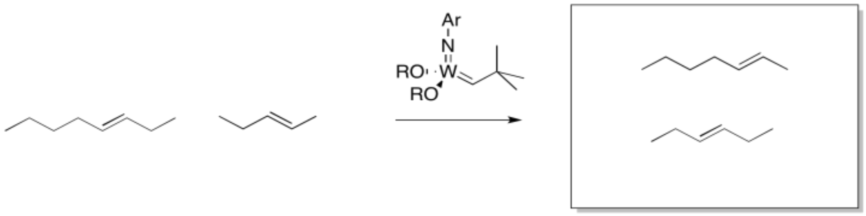

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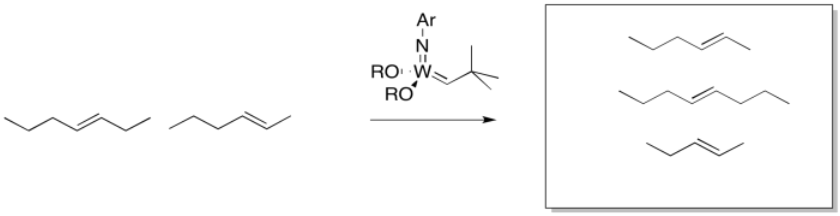
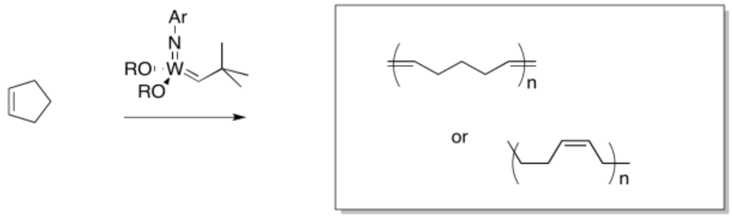


Exercise 10.10.2:

a)



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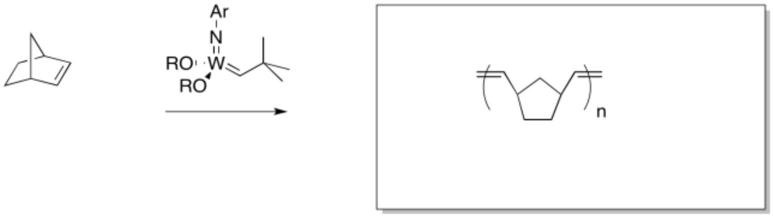

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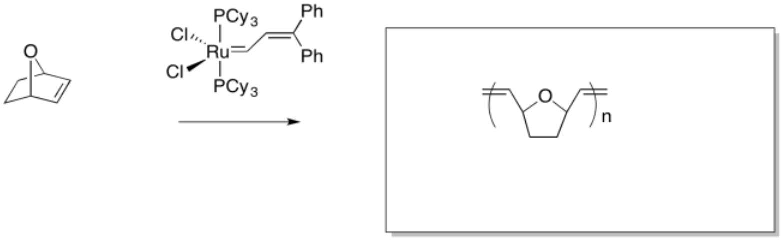

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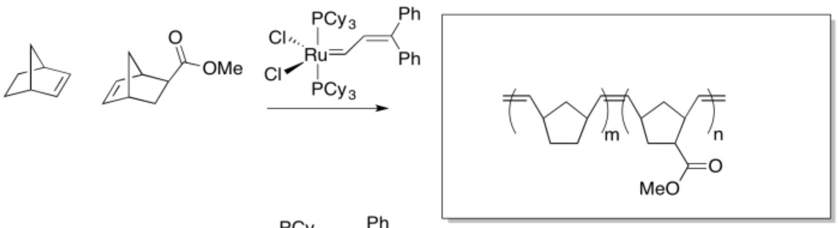
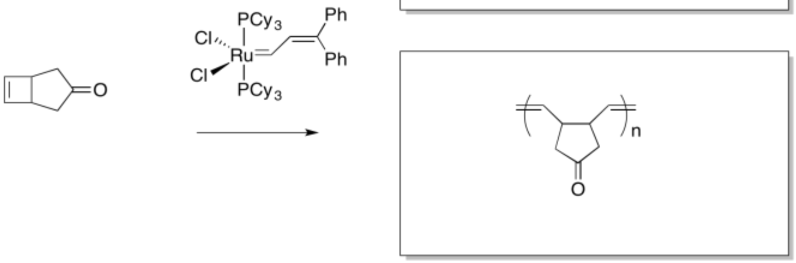
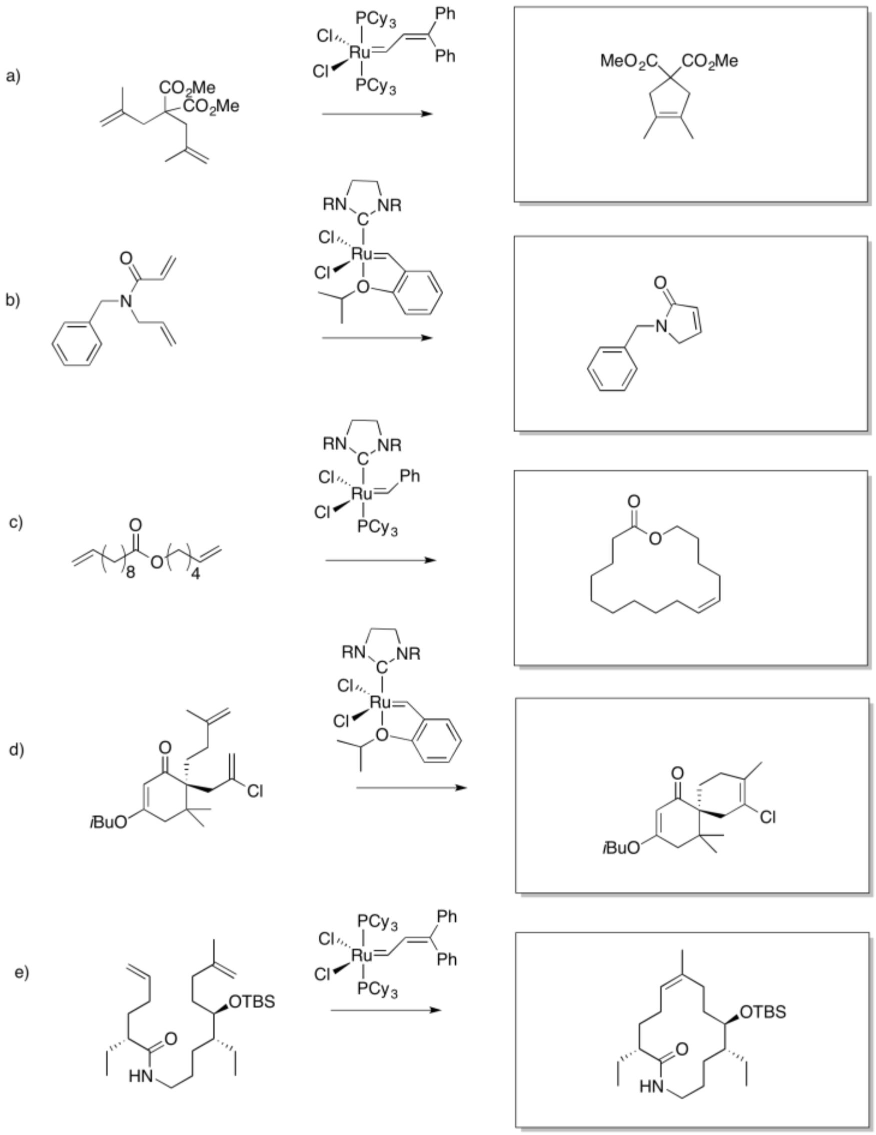


e)



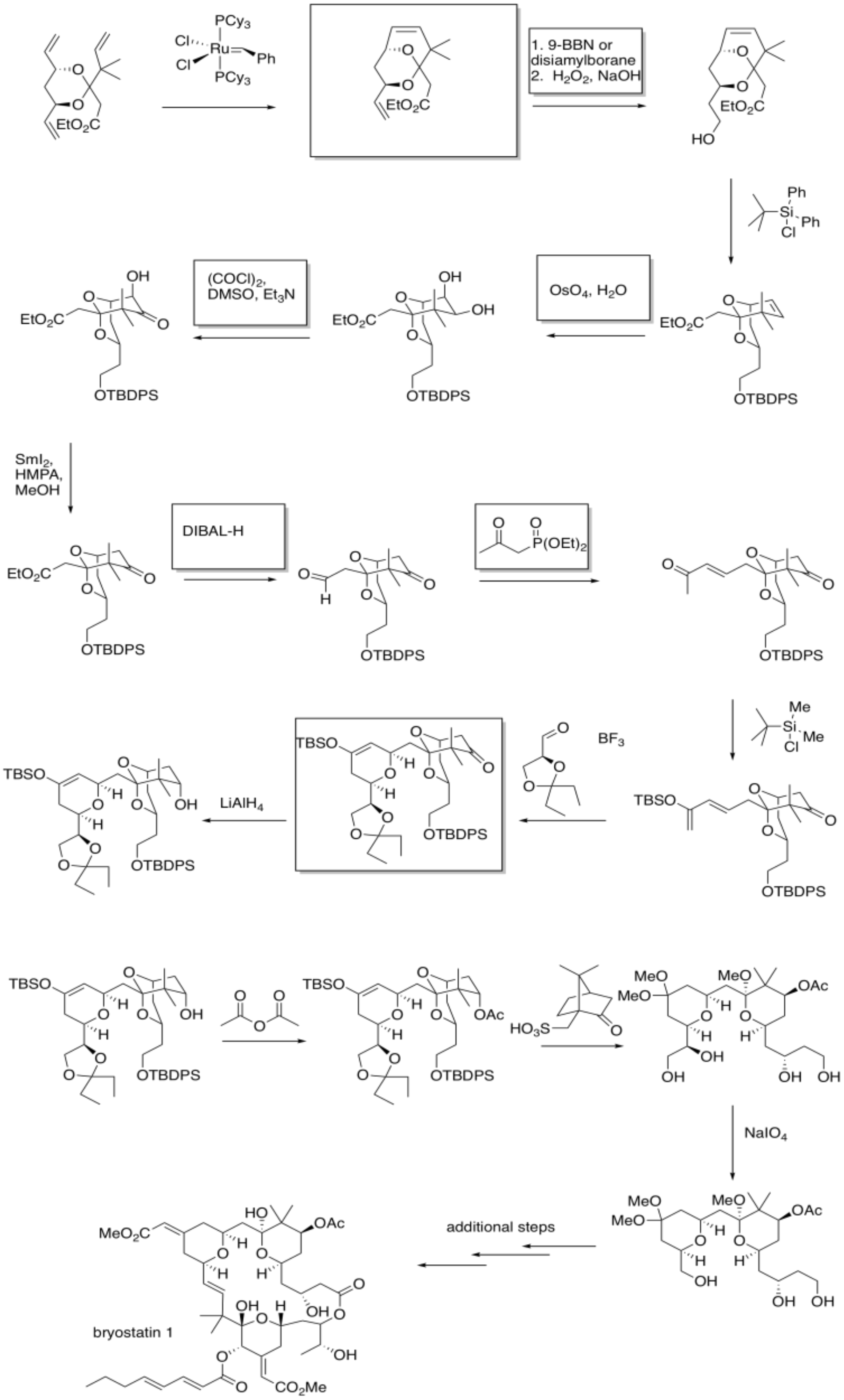
Exercise 10.10.3:



Exercise 10.10.4:

Bryostatin Partial Synthesis (Burke, UW-Madison, 2004)

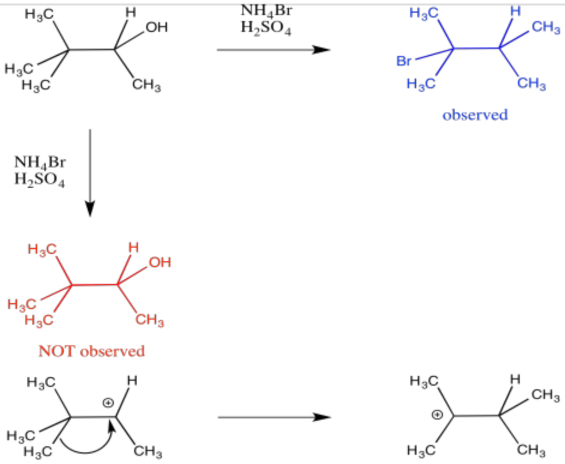
One of a family of natural products isolated from the nudibranch, Bugula neritina. Bryostatin 1 was unsuccessful as an anticancer agent but shows promise in trials against Alzheimer's.



CHAPTER OVERVIEW

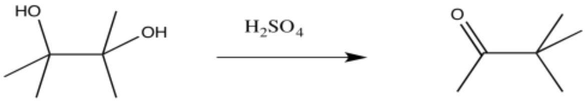
11: Electrophilic Rearrangement

11.1: Introduction



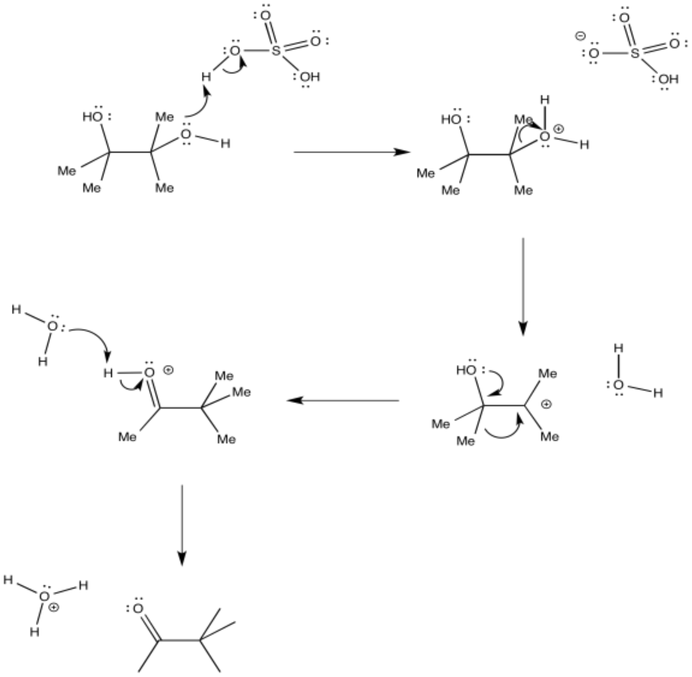
11.2: Pinacol Rearrangement

The pinacol rearrangement is a reaction of 1,2-diols. It takes place under the influence of strong acids, including mineral acids like sulfuric acid. It can also be brought about via the use of Lewis acids. The reaction overall involves the loss of one of the hydroxyl groups, the conversion of the other hydroxyl group into a carbonyl, and the shift of an alkyl group.



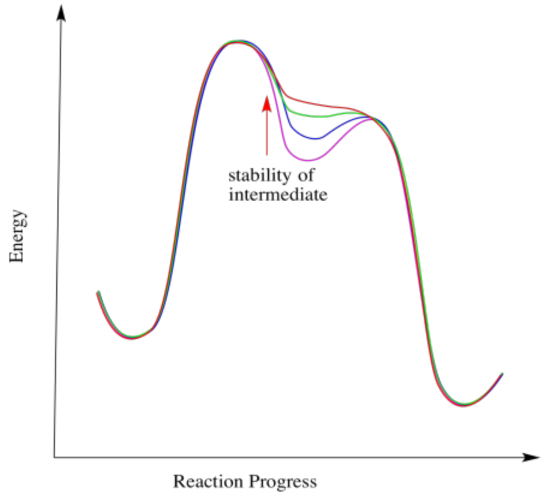
The heart of the rearraction is the 1,2-shift of an alkyl group. This shift is assisted by π-donation from the oxygen, converting the C-O bond into a carbonyl at the same time.

The entire mechanism would look like this:



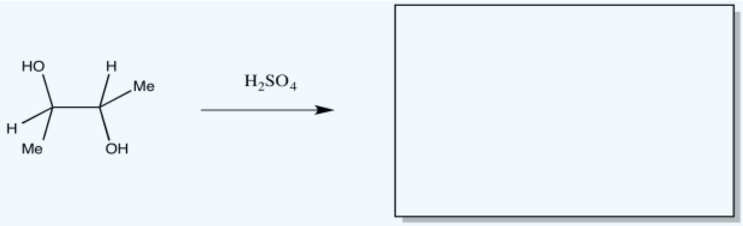
In many rearrangements, formation of the actual cation is not necessarily involved. The 1,2-shift could occur as the water molecule leaves. The protonated oxygen may draw enough electron density toward itself to induce the shift.

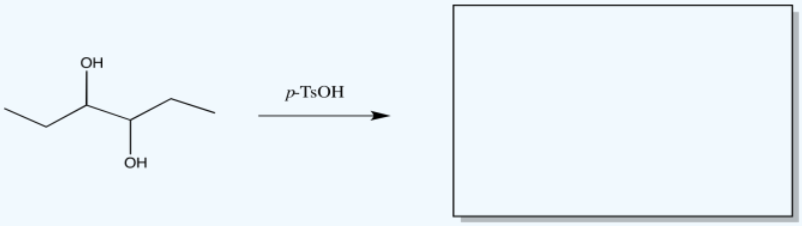
Frequently there is a fine line between alternative reaction pathways. In many cases, the stability of an intermediate determines whether a reaction happens in stages or in one step. If the intermediate is relatively stable, the reaction will happen in steps. The less stable the intermediate, the more likely the reaction will proceed in a concerted manner.

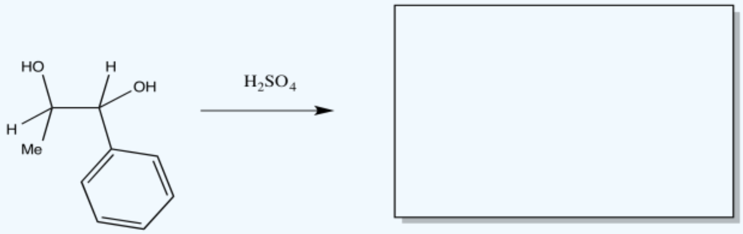


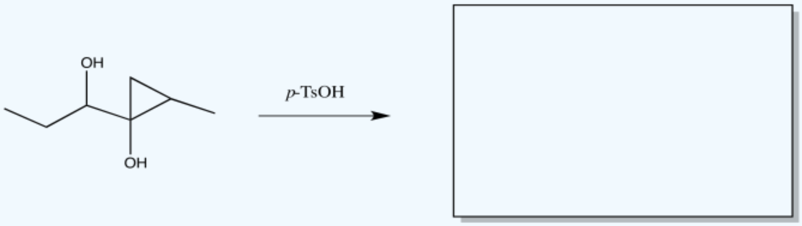
Exercise 11.2.1

Fill in the products of the following pinacol rearrangements.

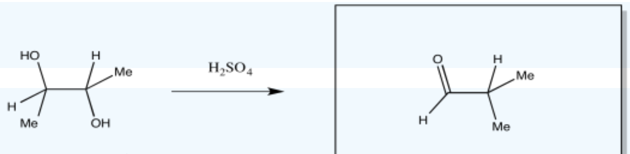






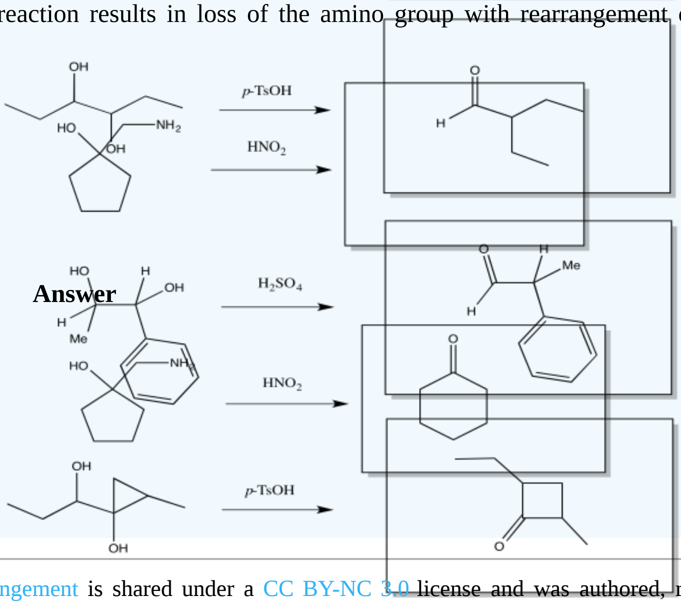


Answer



Exercise 11.2.2

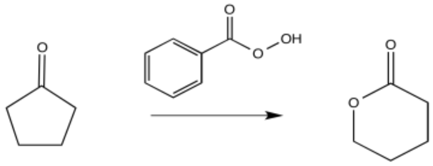
The Tiffeneau Demjanov rearrangement is superficially similar to a pinacol rearrangement. It occurs when a β-amino alcohol is treated with nitrous acid. The reaction results in loss of the amino group with rearrangement of the molecule. Predict the product of the reaction.



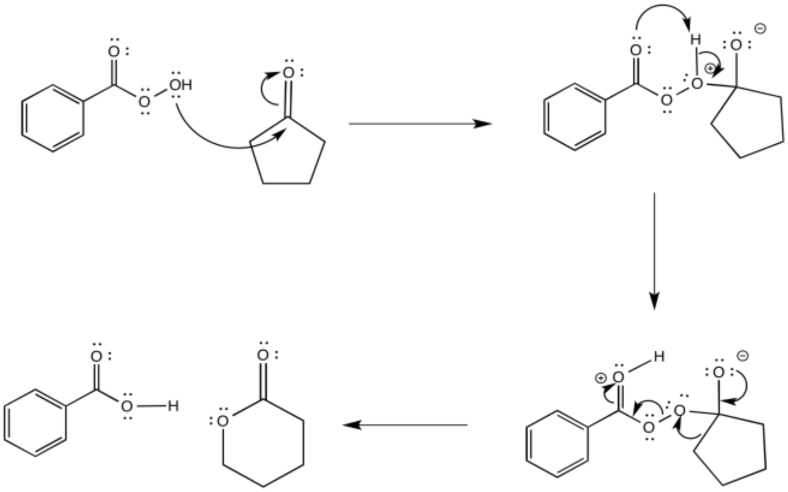
Answer

11.3: Baeyer-Villiger Rearrangement

The Baeyer-Villiger rearrangement is the conversion of a ketone to an ester via the insertion of an oxygen atom next to the carbonyl.

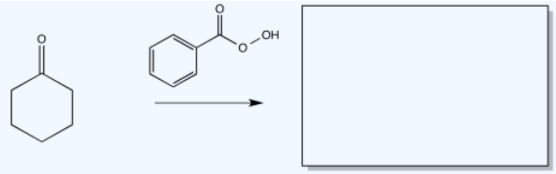


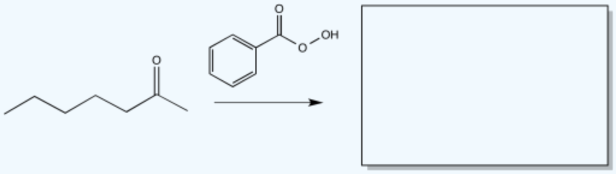
The reaction involves initial addition of a peroxide to the carbonyl carbon. The resulting adduct undergoes rearrangement to form the ester.

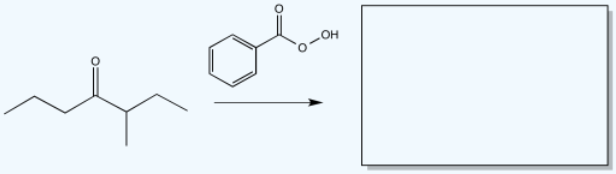


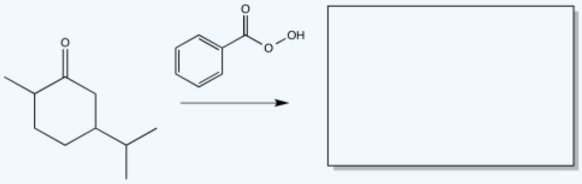
Exercise 11.3.1

Predict the products of the following Baeyer-Villiger reactions.

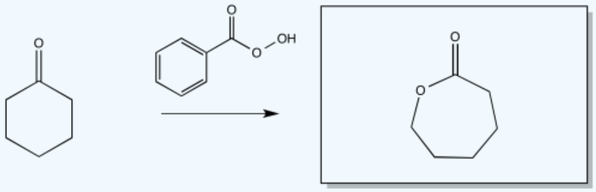


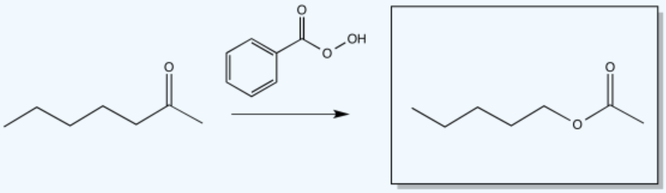


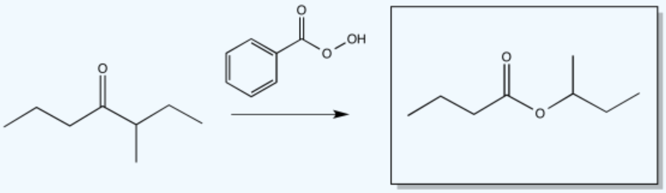


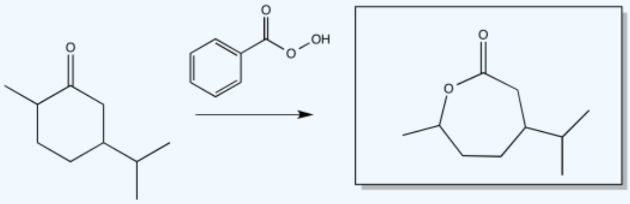


Answer



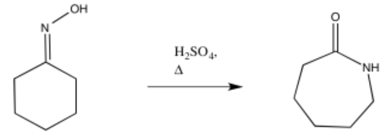




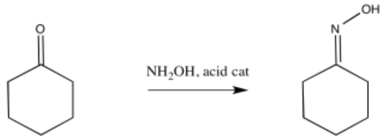


11.4: Beckmann Rearrangement

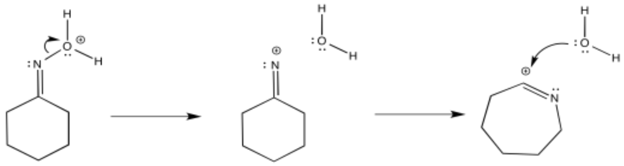
The Beckmann rearrangement results when an oxime (an N-hydroxyimine) is treated with concentrated acid and heated.



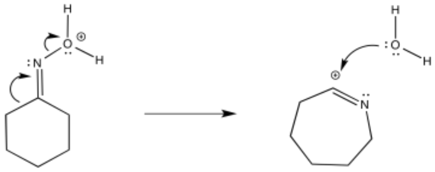
The oxime, in turn, is generated by treatment of a ketone with hydroxylamine. A catalytic amount of acid can activate the carbonyl, accelerating the otherwise sluggish reaction.



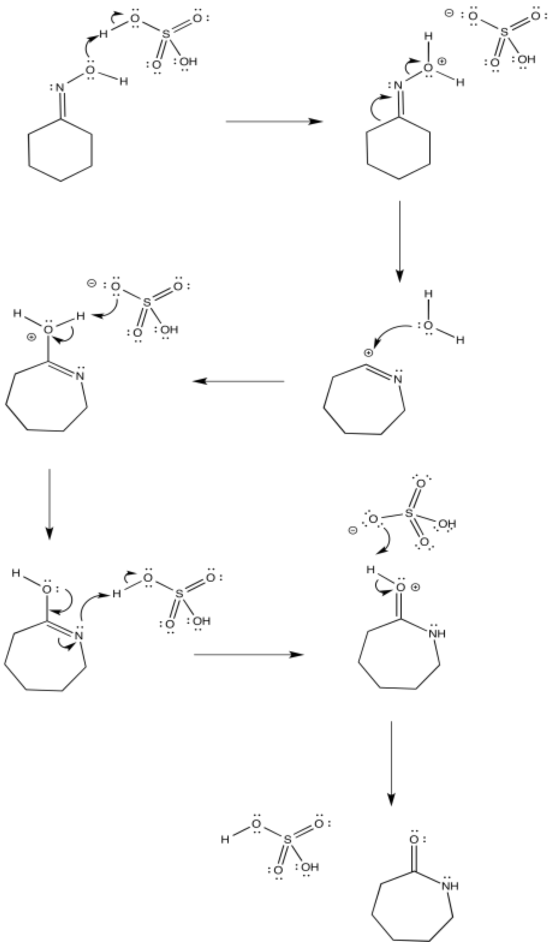
The reaction, like the pinacol rearrangement, is triggered by the loss of water from the starting material. The incipient cation that results undergoes a 1,2-shift. Subsequently, the re-addition of water to the rearranged cation results in a new compound.



By "incipient", we describe a cation that is only on the brink of forming, but has not actually occurred yet. The 1,2-shift happens as soon as the partial positive charge on the nitrogen becomes great enough to draw the electrons from the neighbouring bond.

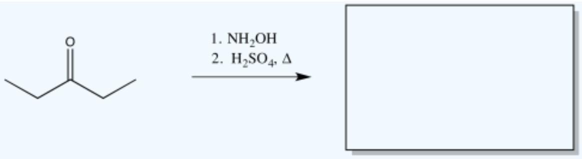


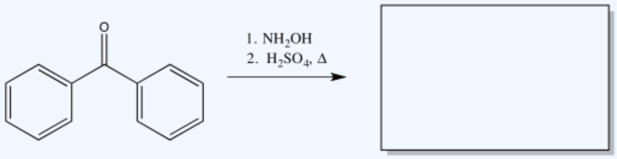
The complete mechanism is described pictorially below.

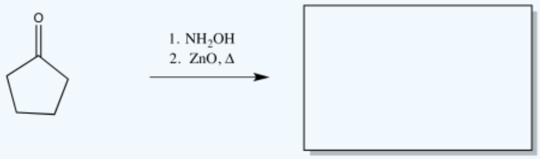


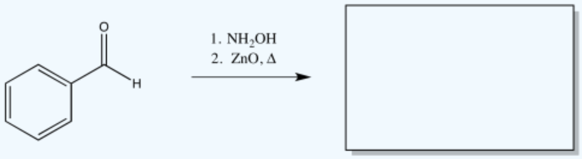
Exercise 11.4.1

Predict the products of the following Beckmann rearrangements.

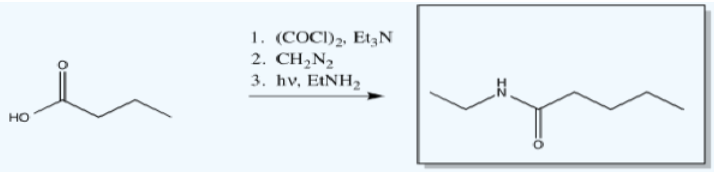

O
1. NH₂OH
2. H₂SO₄, Δ

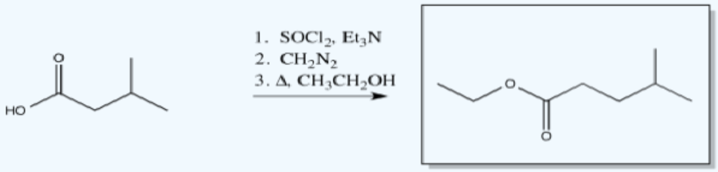

O
1. NH₂OH
2. H₂SO₄, Δ

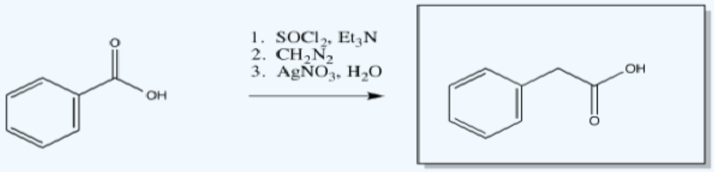

O
1. NH₂OH
2. ZnO, Δ

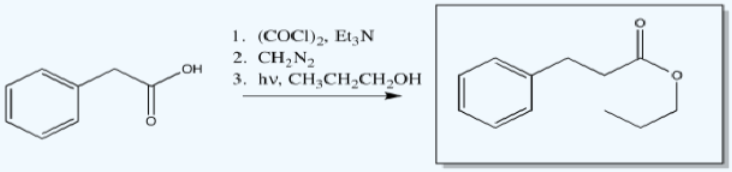

O
H
1. NH₂OH
2. ZnO, Δ

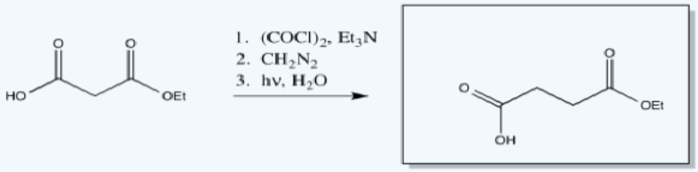
Answer

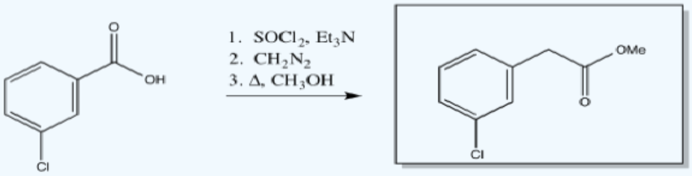

HO
O
1. (COCl)2, Et3N
2. CH2N2
3. hν, EtNH2
H
N
O

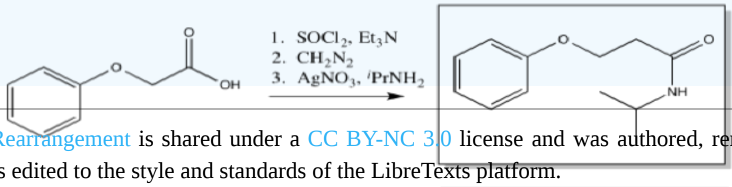

HO
O
1. SOCl2, Et3N
2. CH2N2
3. Δ, CH3CH2OH
O
O

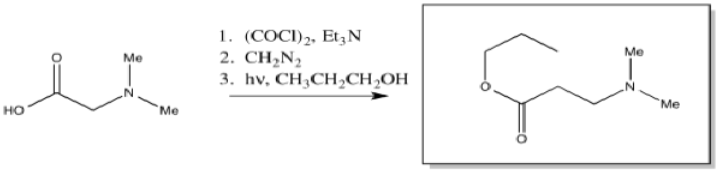

O
OH
1. SOCl2, Et3N
2. CH2N2
3. AgNO3, H2O
OH
O


OH
O
1. (COCl)2, Et3N
2. CH2N2
3. hν, CH3CH2CH2OH
O
O


HO
O
O
OEt
1. (COCl)2, Et3N
2. CH2N2
3. hν, H2O
O
OH
O
OEt

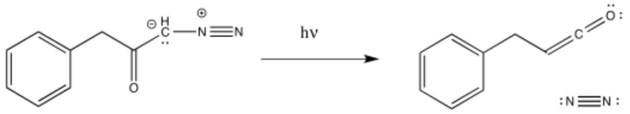

O
OH
Cl
1. SOCl2, Et3N
2. CH2N2
3. Δ, CH3OH
OMe
O
Cl


O
O
OH
1. SOCl2, Et3N
2. CH2N2
3. AgNO3, iPrNH2
O
O
NH

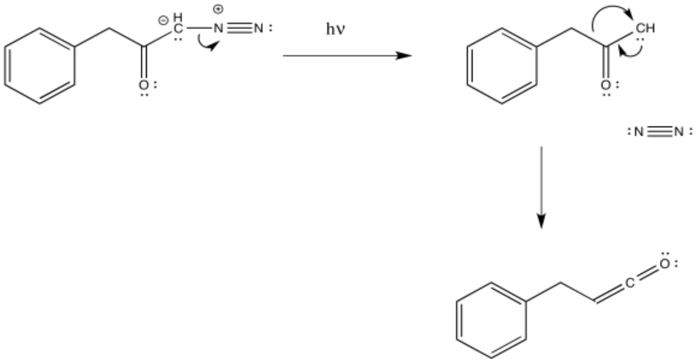

HO
O
Me
N
Me
1. (COCl)2, Et3N
2. CH2N2
3. hν, CH3CH2CH2OH
O
O
Me
N
Me

11.5: Wolff Rearrangement

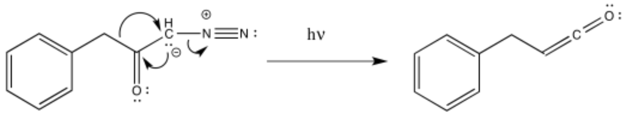
The Wolff rearrangement is the conversion of a diazoketone to a ketene, usually under photolytic conditions.



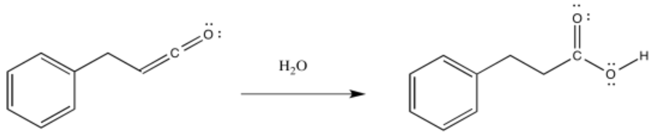
The loss of dinitrogen from the diazonium compound would result in an electron-deficient carbene. Like a carbocation, the carbene would be susceptible to a 1,2-shift. If accompanied by π-donation from the carbene to the carbonyl, a ketene would result.



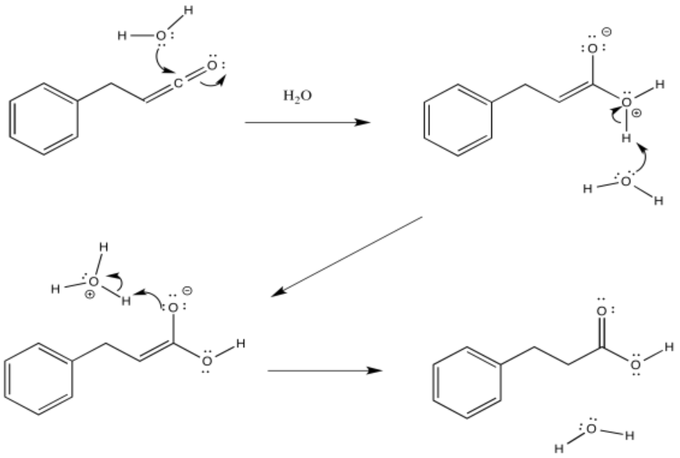
As with other rearrangements, the 1,2-shift could occur at the same time as the loss of the dinitrogen.

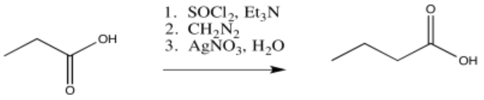


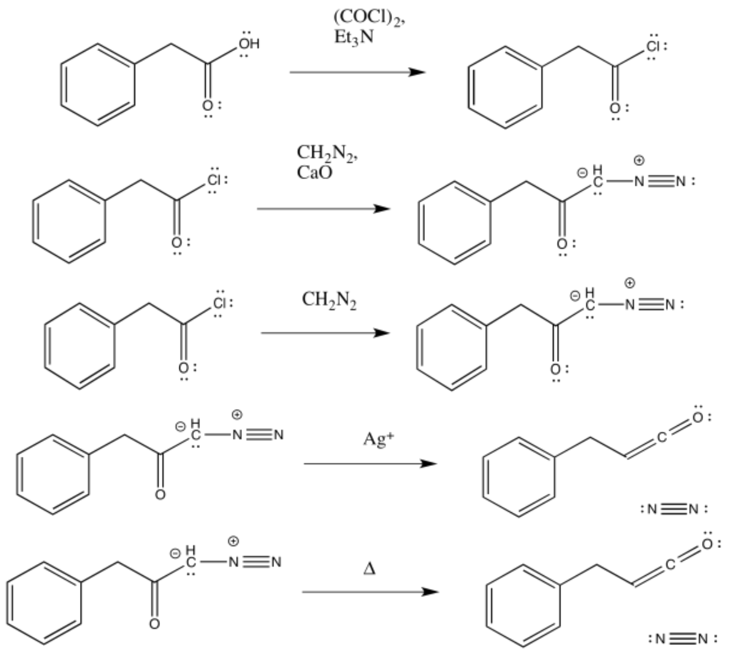
Ketenes are not terribly stable. In the presence of nucleophilic solvents such as water or alcohol, the ketene easily undergoes nucleophilic addition. Addition of water would result in a carboxylic acid.



The mechanism of that addition involves keto-enol tautomerism.

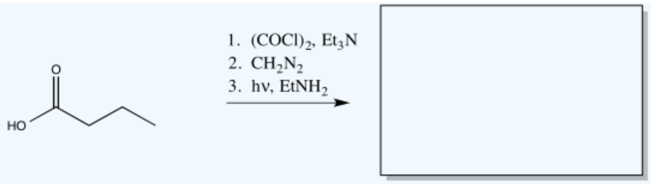


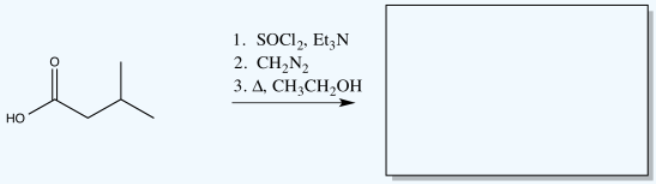


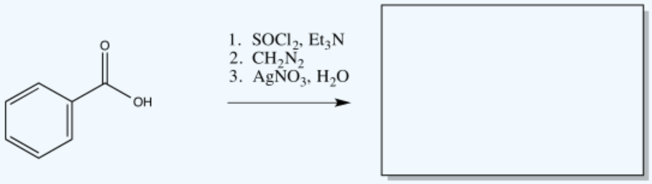


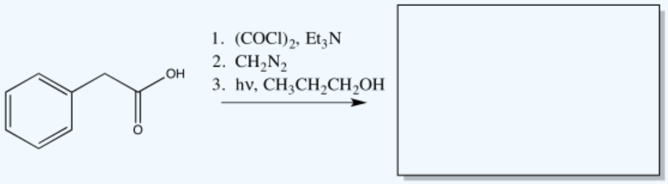
Exercise 11.5.1

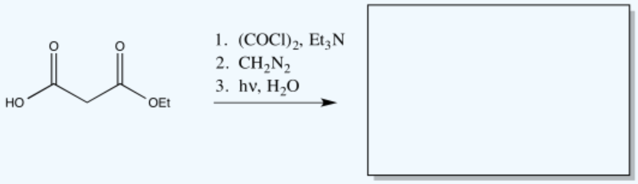
Predict the products of the following Wolff rearrangements.

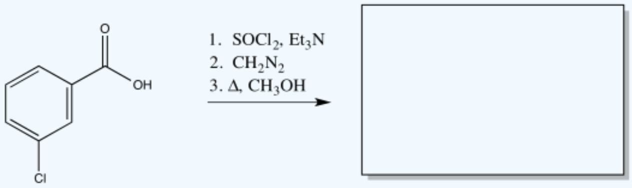

HO
O
1. $(COCl)_2$, Et_3N
2. CH_2N_2
3. hv, $EtNH_2$

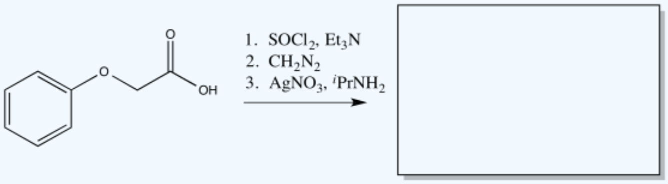

HO
O
1. $SOCl_2$, Et_3N
2. CH_2N_2
3. Δ, CH_3CH_2OH

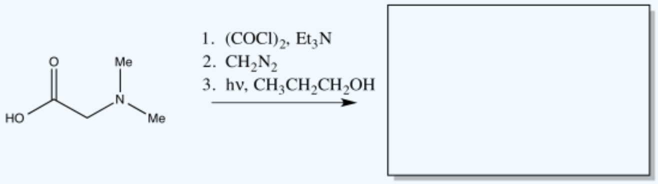

O
OH
1. $SOCl_2$, Et_3N
2. CH_2N_2
3. $AgNO_3$, H_2O


OH
O
1. $(COCl)_2$, Et_3N
2. CH_2N_2
3. hv, $CH_3CH_2CH_2OH$

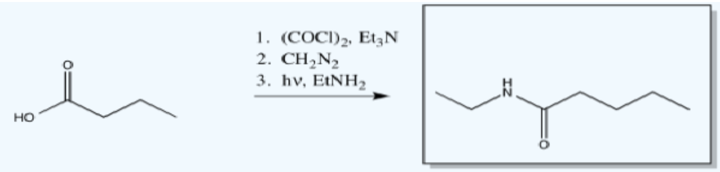

O
O
HO
OEt
1. $(COCl)_2$, Et_3N
2. CH_2N_2
3. hv, H_2O

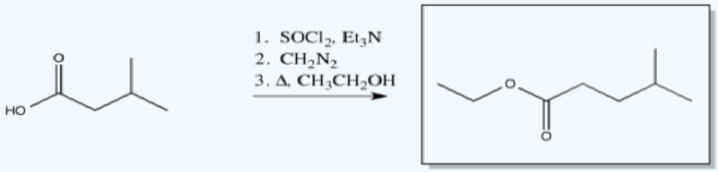

O
OH
Cl
1. $SOCl_2$, Et_3N
2. CH_2N_2
3. Δ, CH_3OH

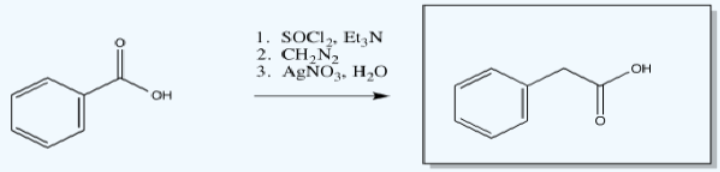

O
O
OH
1. $SOCl_2$, Et_3N
2. CH_2N_2
3. $AgNO_3$, $^{i}PrNH_2$

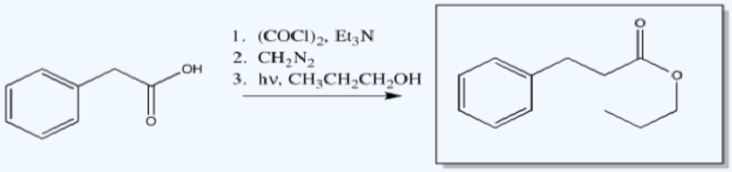

O
Me
N
Me
HO
1. $(COCl)_2$, Et_3N
2. CH_2N_2
3. hv, $CH_3CH_2CH_2OH$

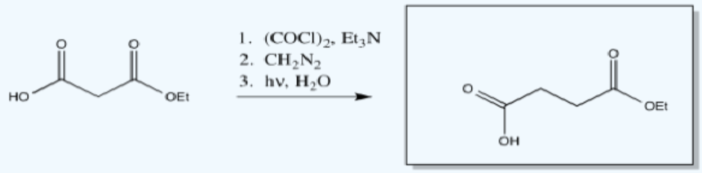
Answer

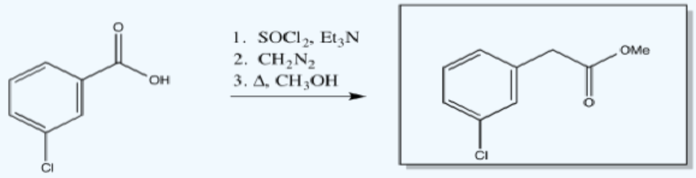

1. $(COCl)_2$, Et_3N
2. CH_2N_2
3. hν, $EtNH_2$
HO
O
H
N
O

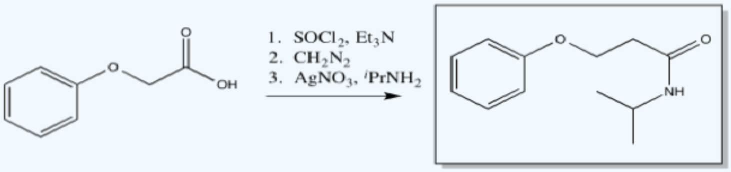

1. $SOCl_2$, Et_3N
2. CH_2N_2
3. Δ, CH_3CH_2OH
HO
O
O
O

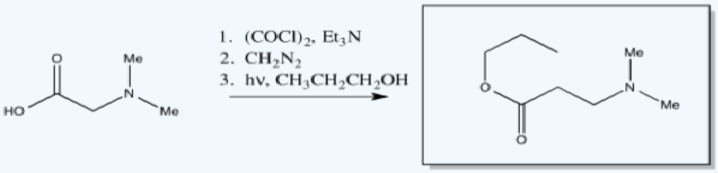

1. $SOCl_2$, Et_3N
2. CH_2N_2
3. $AgNO_3$, H_2O
O
OH
OH
O


1. $(COCl)_2$, Et_3N
2. CH_2N_2
3. hν, $CH_3CH_2CH_2OH$
OH
O
O
O


1. $(COCl)_2$, Et_3N
2. CH_2N_2
3. hν, H_2O
HO
O
O
OEt
O
OH
O
OEt

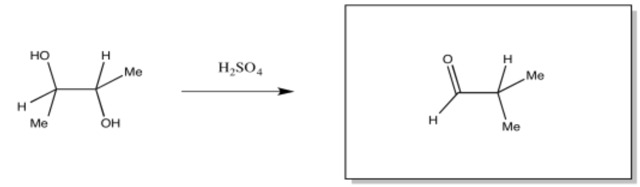

1. $SOCl_2$, Et_3N
2. CH_2N_2
3. Δ, CH_3OH
O
OH
Cl
OMe
O
Cl

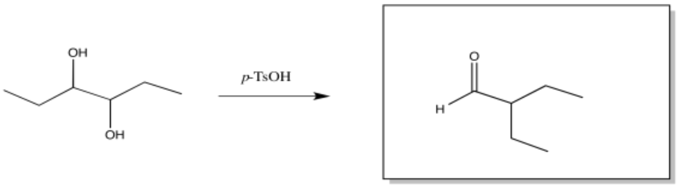

1. $SOCl_2$, Et_3N
2. CH_2N_2
3. $AgNO_3$, ^{i}PrNH$_2$
O
O
OH
O
O
NH

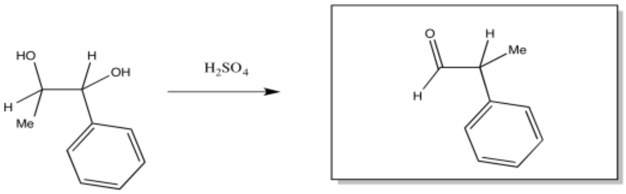

1. $(COCl)_2$, Et_3N
2. CH_2N_2
3. hν, $CH_3CH_2CH_2OH$
HO
O
Me
N
Me
O
O
Me
N
Me

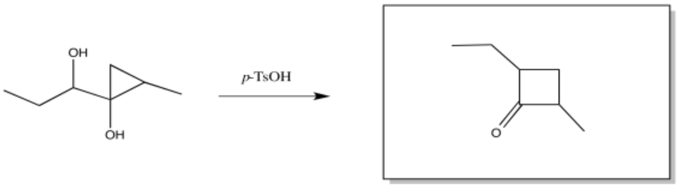
11.6: Solutions

Exercise 11.1.1:









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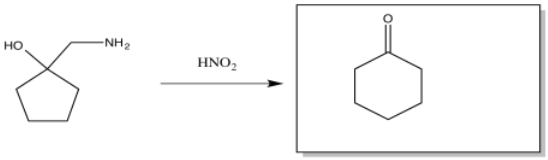

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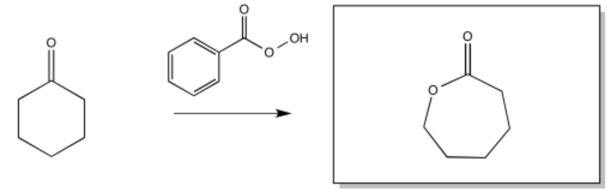

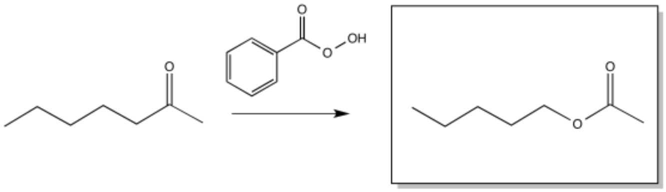

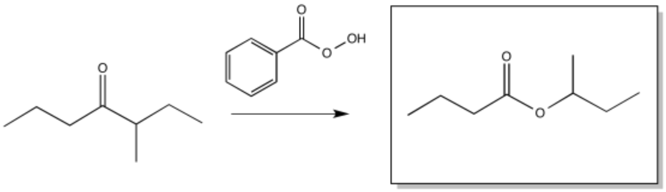

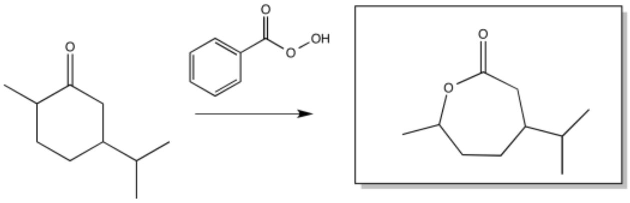

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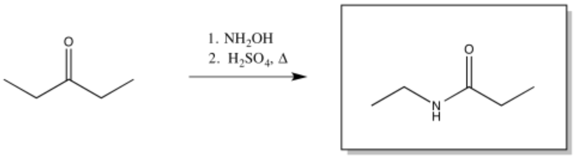

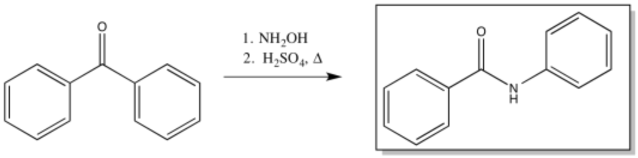

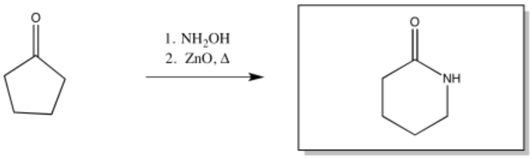

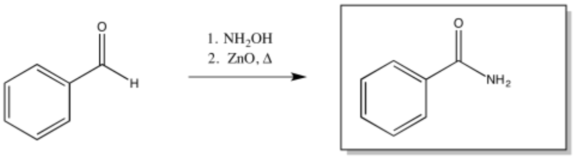

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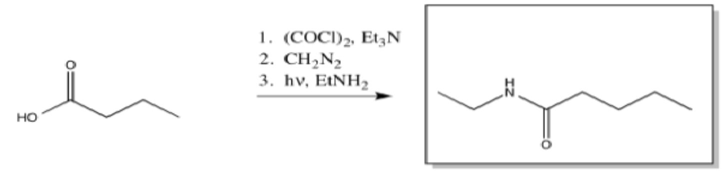

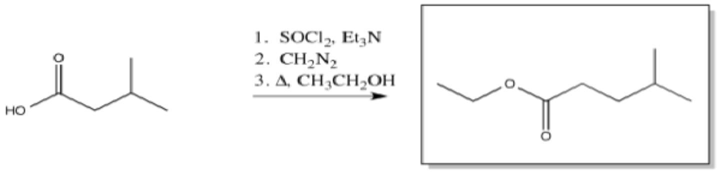

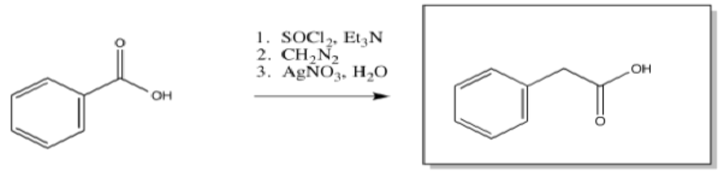

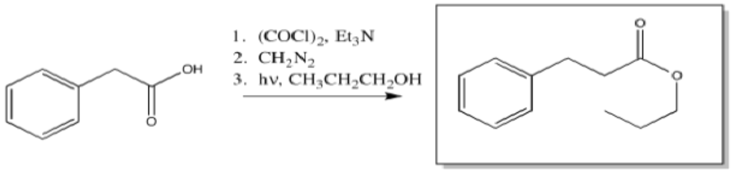

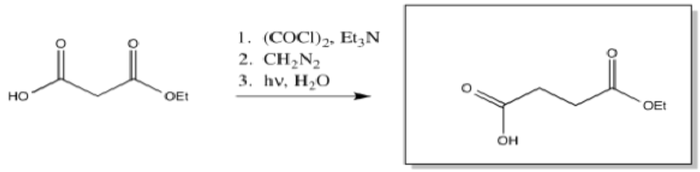

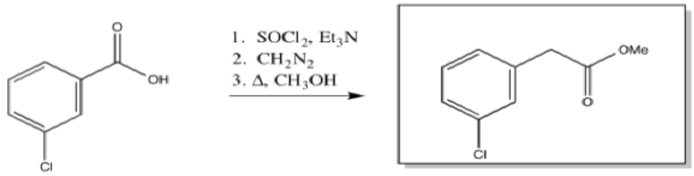

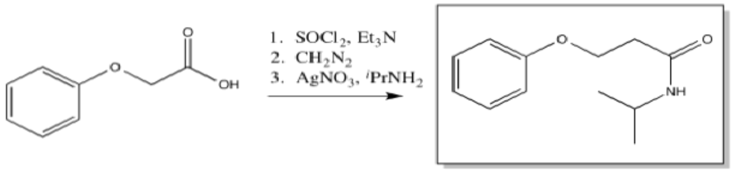

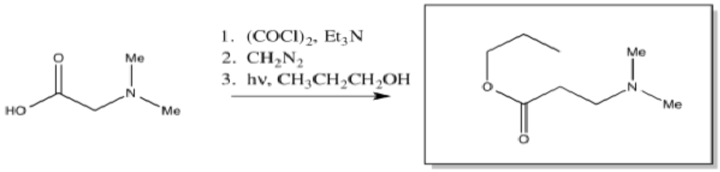

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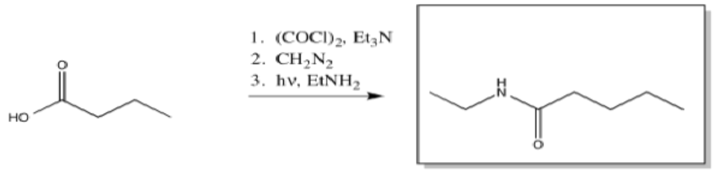
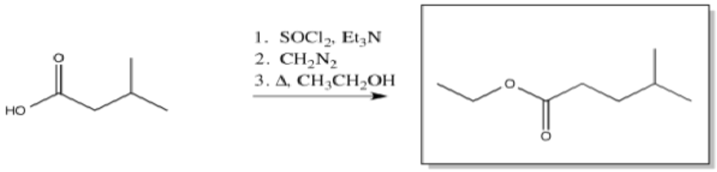
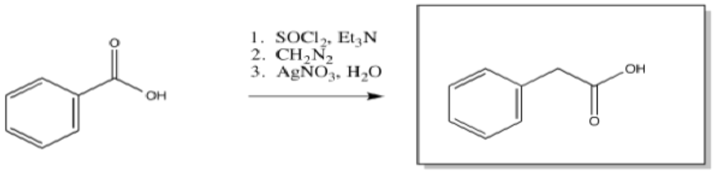
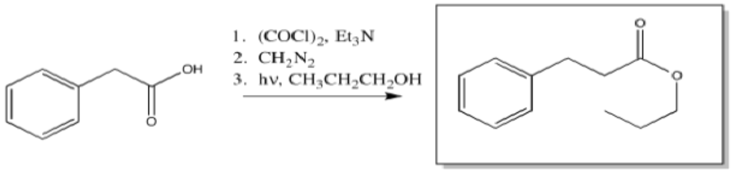
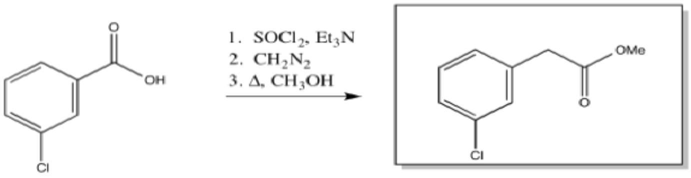

HO
O
1. $(COCl)_2$, Et_3N
2. CH_2N_2
3. hν, $EtNH_2$
H
N
O

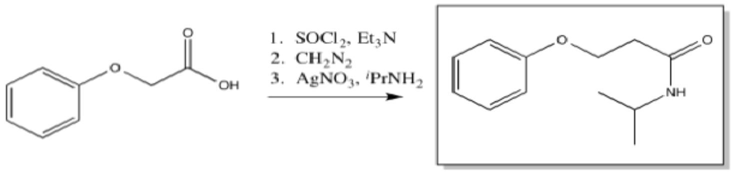

HO
O
1. $SOCl_2$, Et_3N
2. CH_2N_2
3. Δ, CH_3CH_2OH
O
O

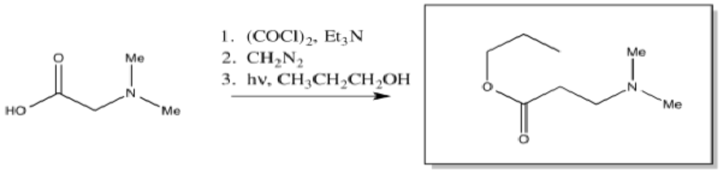

O
OH
1. $SOCl_2$, Et_3N
2. CH_2N_2
3. $AgNO_3$, H_2O
OH
O


OH
O
1. $(COCl)_2$, Et_3N
2. CH_2N_2
3. hν, $CH_3CH_2CH_2OH$
O
O


HO
O
O
OEt
1. $(COCl)_2$, Et_3N
2. CH_2N_2
3. hν, H_2O
O
OH
O
OEt


O
OH
Cl
1. $SOCl_2$, Et_3N
2. CH_2N_2
3. Δ, CH_3OH
OMe
O
Cl


O
O
OH
1. $SOCl_2$, Et_3N
2. CH_2N_2
3. $AgNO_3$, $^iPrNH_2$
O
O
NH


HO
O
Me
N
Me
1. $(COCl)_2$, Et_3N
2. CH_2N_2
3. hν, $CH_3CH_2CH_2OH$
O
O
Me
N
Me

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