

17.10: REACTIONS OF PHENOLS

OBJECTIVES

After completing this section, you should be able to

1. explain why phenols and phenoxide ions are very reactive towards electrophilic aromatic substitution (see Section 16.4 of the textbook).
2. write an equation to illustrate the oxidation of a phenol or an arylamine to a quinone, and identify the reagents used to oxidize phenols.
3. write an equation to illustrate the reduction of a quinone to a hydroquinone, and identify the reagents used to reduce quinones.
4. describe, briefly, the biological importance of the redox properties of quinones.

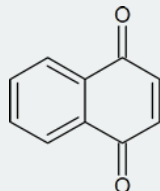
KEY TERMS

Make certain that you can define, and use in context, the key terms below.

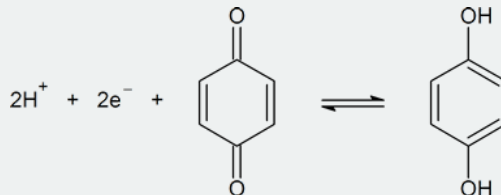
- hydroquinone
- quinone
- ubiquinone

STUDY NOTES

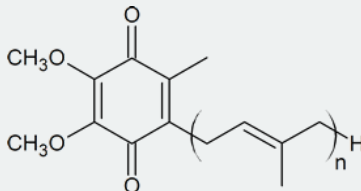
“Quinone” is a term used to describe cyclohexadiendiones in general, and *p*-benzoquinone in particular. In addition to benzene, other aromatic systems also give rise to quinones; for example, 1,4-naphthoquinone



“Hydroquinones” are produced by the reduction of quinones according to the following half-reaction:

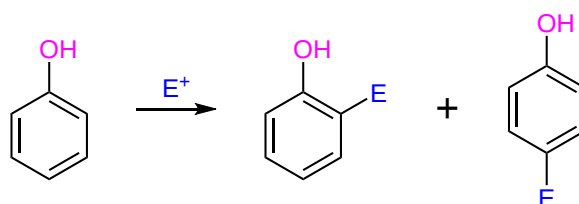


“Ubiquinones” are naturally occurring quinones whose role is to transfer a pair of electrons from one substance to another in enzyme-catalyzed reactions. Ubiquinones are also called coenzymes Q.



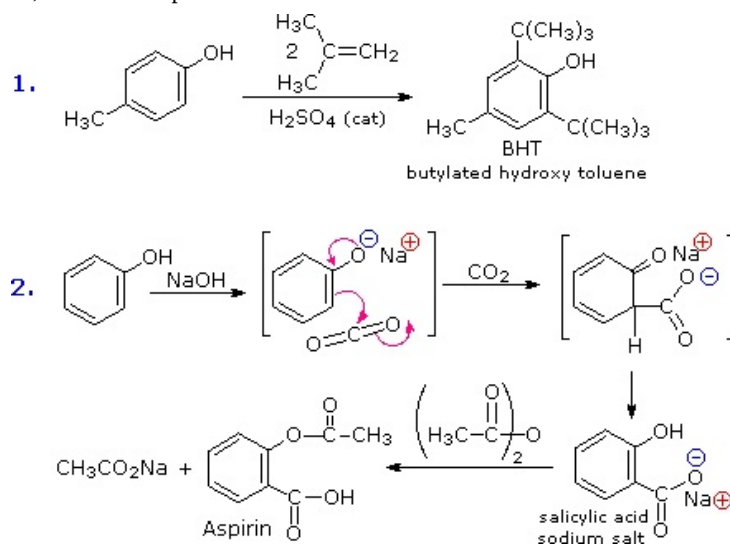
ELECTROPHILIC AROMATIC SUBSTITUTION REACTIONS

The hydroxyl substituent of phenol is *ortho* and *para* directing and makes the aromatic ring strongly activated towards electrophilic aromatic substitution reaction (Section 16-4). In fact, phenols are strongly activating that often times electrophilic addition is difficult to limit to a single addition.



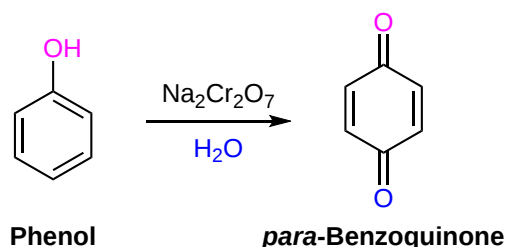
The ease with which the aromatic ring of phenols and phenol ethers undergoes electrophilic substitution is shown in the two examples in the diagram below. The first shows the Friedel-Crafts synthesis of the food preservative BHT from *para*-cresol. In this example, an electrophilic is added to both of the *ortho* positions to the alcohol of *para*-cresol.

The second example is interesting in that it further demonstrates the delocalization of charge that occurs in the phenolate anion. Carbon dioxide is a weak electrophile and normally does not react with aromatic compounds; however, the negative charge concentration on the phenolate ring enables the carboxylation reaction shown in the second step. The sodium salt of salicylic acid is the major product, and the preference for *ortho* substitution may reflect the influence of the sodium cation. This is called the **Kolbe-Schmidt reaction**, and it has served in the preparation of aspirin, as the last step illustrates.

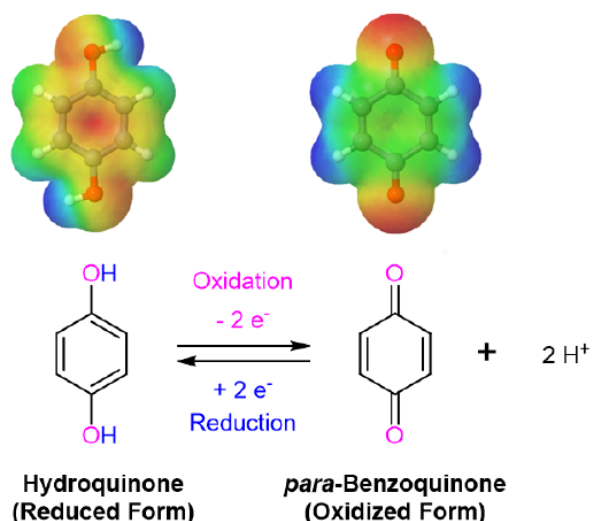


OXIDATION OF PHENOLS: QUINONES

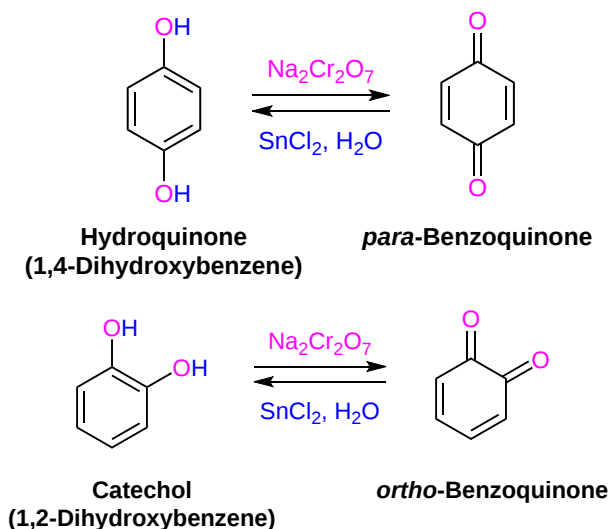
Phenols are rather easily oxidized despite the absence of a hydrogen atom on the hydroxyl bearing carbon. Among the colored products from the oxidation of phenol by chromic acid is the dicarbonyl compound **para-benzoquinone** (also known as 1,4-benzoquinone).



Quinones are an important class of compounds because of their redox equilibrium with their dihydroxybenzene analogs. The difference in electron density is seen in the electron potential map of hydroquinone and *para*-benzoquinone. The reduced compound, hydroquinone, has a greater electron density in the ring seen as a yellow/red color. The oxidized compound, *para*-benzoquinone, has significantly less electron density around the ring shown by the presence of green and blue colors.

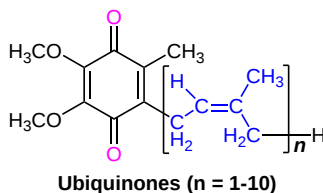


Dihydroxybenzenes can easily be oxidized to the corresponding quinones by a wide variety of oxidizing agents including: sodium dichromate ($\text{Na}_2\text{Cr}_2\text{O}_7$), chromium trioxide (CrO_3), and potassium nitrosodisulfonate $[(\text{KSO}_3)_2\text{NO}]$ called **Fremy's salt**. Likewise, quinone can be easily reduced back to hydroquinones using reagents such as stannous chloride (SnCl_2) or sodium borohydride (NaBH_4).



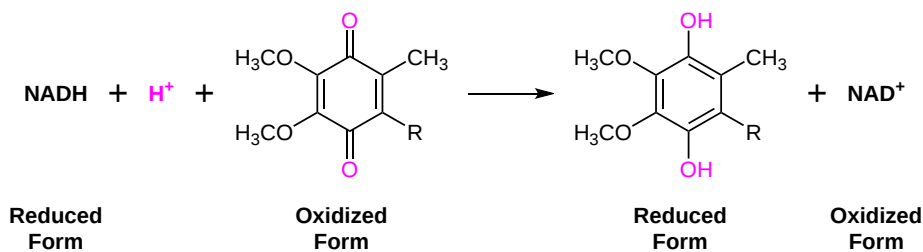
UBIQUINONES

The redox abilities of quinones are utilized as biological oxidizing agents in the mitochondria of cells of aerobic organism. These quinone containing compounds called ubiquinones or coenzymes Q are a coenzyme family that is ubiquitous in all animals and bacteria which is the source of their name.

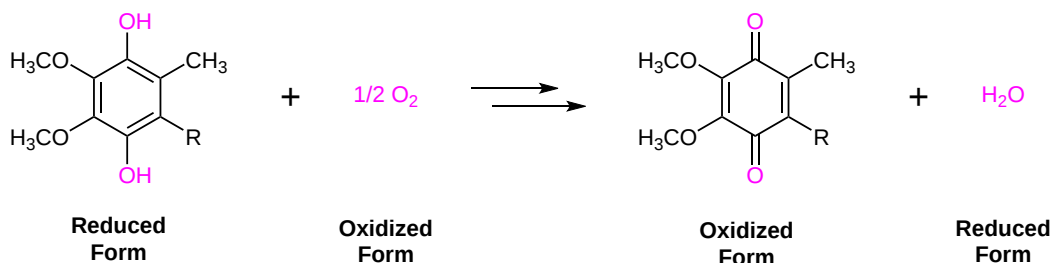


During the production of energy in cells, the redox capabilities of ubiquinones is utilized to mediate the electron-transfer process in which electrons are transferred from the biological reducing agent NADH to molecular oxygen. This process occurs in a series of steps. Initially, a ubiquinone reduced to its corresponding dihydroxy benzene in order to oxidize NADH to NAD^+ . Later, the dihydroxy benzene is oxidized back to its ubiquinone form allowing for oxygen (O_2) to be reduced to water. When looking at the overall process NADH is oxidized to NAD^+ and oxygen is reduced to water. The ubiquinone only acts as an intermediate and is unchanged during this process.

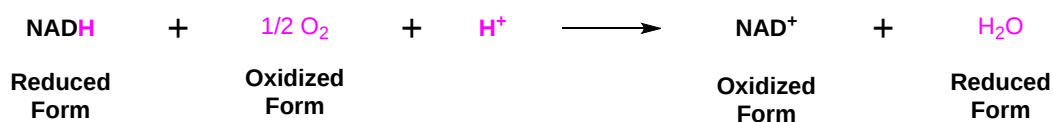
STEP 1



STEP 2



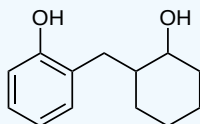
OVERALL PROCESS



EXERCISES

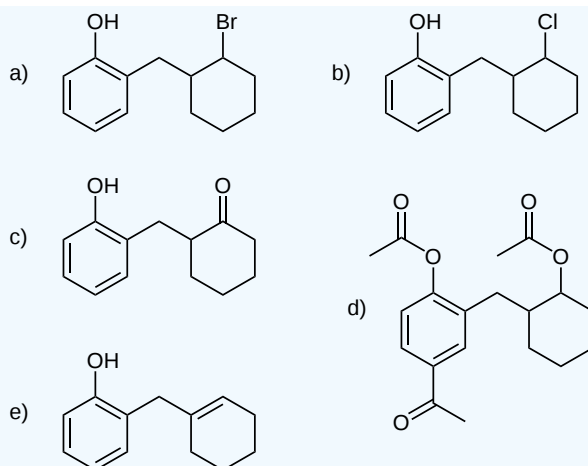
? EXERCISE 17.10.1

Predict the major product if the following reagents/reagents were used. No reaction is also a possible answer.



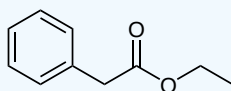
- 1 equivalent of PBr_3
- 1 equivalent of SOCl_2
- Dess–Martin periodinane
- 3 equivalents of acetyl chloride and AlCl_3 as a catalyst
- Heat and H_2SO_4 (assume the phenol does not act as a nucleophile in this case)

Answer



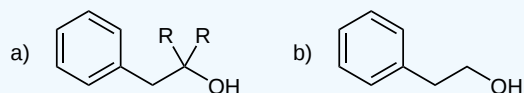
? EXERCISE 17.10.2

Predict the major product if the following reagents/conditions were used. No reaction is also a possible answer.



- 2 equivalents of RMgBr and H_3O^+ work-up
- LiAlH_4 and H_3O^+ work-up
- NaBH_4 and H_3O^+ work-up

Answer



CONTRIBUTORS AND ATTRIBUTIONS

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- William Reusch, Professor Emeritus ([Michigan State U.](#)), [Virtual Textbook of Organic Chemistry](#)
- James Kabrhel (University of Wisconsin - Green Bay, Sheboygan Campus)

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