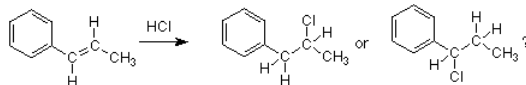


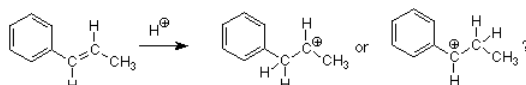
1.32: Side Chain Oxidations, Phenols, Arylamines

Carbocations Stabilized by Resonance

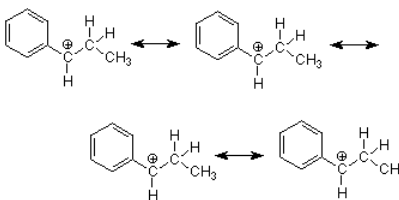
Let's begin by looking at the addition of HCl to an alkene in which one of the alkene carbons is directly attached to the benzene ring.



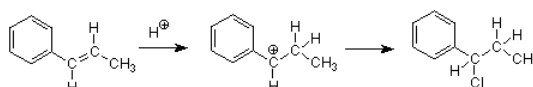
In this example each of the alkene carbons has the same number of hydrogens so the direct application of Markovnikov's rule is stymied. We find that we must go beyond Markovnikov's rule to its explanation in terms of the relative stability of the two carbocations which might be formed. Here are the two carbocations which would be formed by the attack of H^+ on the alkene:



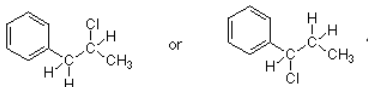
Which of these carbocations has the lower energy? Will the phenyl group donate electrons more effectively than the methyl group? The key thing to notice in answering these questions is that the pi electrons of the benzene ring are directly adjacent to the carbocation carbon in the structure on the left. This is reminiscent of the situation we saw in the addition of HCl to 1,3-butadiene where we encountered resonance stabilization of the carbocation by the pi electrons of the neighboring double bond. The same situation occurs here, and we can symbolize the resonance stabilization with the following resonance structures.



The effect of this resonance is to make the carbocation more stable when the charge and the electron deficiency are located on a carbon which is directly bonded to the phenyl group. Such a carbon is called a "benzylic" carbon. Since there is no such resonance stabilization available when a simple alkyl group is bonded to the carbocationic carbon, the benzylic carbocation is more stable, is formed faster, and the product formed from it is the only one we see.



With this background, we can quickly decide which of the two alkyl halides below will react faster by way of an S_N1 mechanism.



The more reactive alkyl halide is the one which give the more stable carbocation. The more stable carbocation (since both will be secondary carbocations) is the one where benzylic resonance is possible. (The resonance structures are given above.) Only the alkyl halide on the right will make a carbocation in which the carbocation carbon is directly attached to a phenyl group. Consequently we understand why the alkyl halide on the right is more reactive.

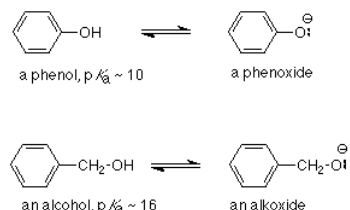
Bases Stabilized by Resonance

We've seen that benzylic carbocations are stabilized by resonance. What happens if the atom directly attached to the benzene ring has an unshared pair of electrons -- in other words, it is electron rich rather than electron poor. We can see the effects of this arrangement in the acid-base properties of phenols and aromatic amines.

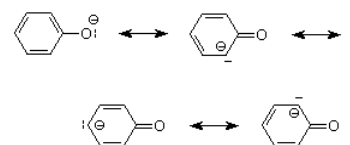
A phenol is an alcohol whose R group is a phenyl group. It is essential that the oxygen and the benzene ring be directly attached to each other. If there is a tetrahedral carbon between them, the compound is not a phenol but an alcohol.



An important difference between phenols and alcohols lies in their acidities. Recall that alcohols, like water, have pK_a 's of about 16. Phenols in contrast typically have pK_a 's of about 10, making them considerably stronger acids than alcohols. Since the stronger acid has the weaker conjugate base, we need to ask why a phenoxide (the conjugate base of a phenol) is weaker than an alkoxide (the conjugate base of an alcohol).

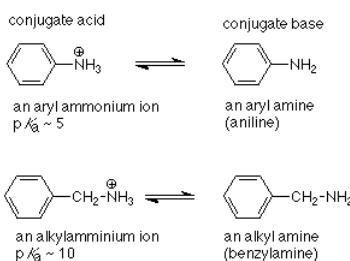


Since it is the unshared electron pair which makes either of the bases a base, we can ask why the unshared electron pair on the phenoxide ion is less available to bond with a proton than the unshared electron pair on the alkoxide ion. Again, the reason is found in resonance.

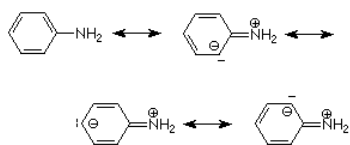


The resonance structures which improve the description of the phenoxide ion show that the electron pair on oxygen is partly moved into a pi bond position between the oxygen and the phenyl carbon it is attached to. To that extent the electron pair on a phenoxide ion is less available for attachment to a proton and the phenoxide ion is a weaker base than an alkoxide ion in which no such resonance is possible.

The same situation occurs in when an amino nitrogen is directly connected to an aromatic ring.



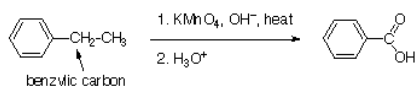
We see that the ammonium ion in which the nitrogen is directly attached to the phenyl group is a stronger acid than the one in which the nitrogen is attached to an sp^3 hybridized carbon atom. This means that the conjugate base, the aryl amine, in which the nitrogen is attached to the phenyl group is also weaker than its alkyl amine counterpart. This is understood by resonance between the unshared electron pair on nitrogen and the aromatic ring, only possible if the connection is direct, which makes the unshared electron pair less available to serve as a base.



The resonance possibilities for an aromatic group allow it to serve either as an electron donating substituent when the attached atom needs electrons (carbocation) or as an electron withdrawing substituent when the attached atom has an unshared pair to share (oxygen or nitrogen).

Side Chain Oxidation

There is another reaction which occurs at the atom directly attached to an aromatic ring. This is known as "side chain oxidation." When a compound which has an alkyl group directly attached to an aryl group is treated with a strong oxidizing agent like chromic acid, the benzylic carbon is oxidized to a carboxylic acid group which remains attached to the aryl group. Any other carbon-carbon bonds are broken. There is one further restriction -- the benzylic carbon must have a hydrogen attached.

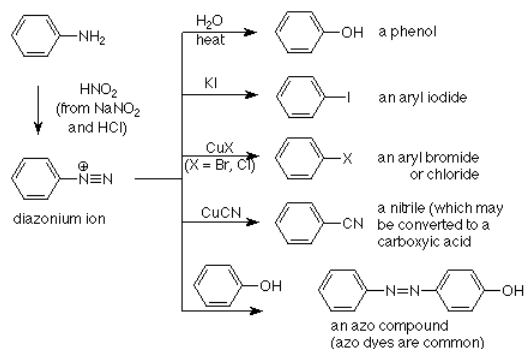


The mechanism of this reaction is obscure, but the fact that it specifically requires that there be a benzylic C-H bond suggests that breaking this bond is essential. Any intermediate that might be formed by breaking this bond will be stabilized by resonance with the aryl group, which provides an explanation for the specificity of attack at the benzylic position. Such reactions also occur in a biological context. Enzymes oxidize alkyl side chains on aromatic rings as part of making such compounds soluble enough to be eliminated.

Diazonium Ions

When primary aryl amines are reacted with nitrous acid (HNO_2 , generated from sodium nitrite (NaNO_2 and HCl) a reaction occurs which makes a new nitrogen-nitrogen triple bond. We will not be concerned with the mechanism, but the product (called a diazonium ion) is a valuable synthetic intermediate.

The diazonium ion is seldom isolated (diazonium ions can be explosive) so instead it is used in the solution it is made in. The N_2 group can be replaced by a variety of other groups and can also be an electrophile itself toward a sufficiently activated aromatic ring. The possibilities are outlined in the following chart:

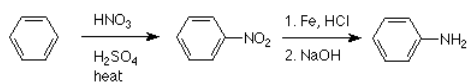


The first four reactions on this chart are examples of the replacement of the N_2 group by a nucleophile. These reactions provide a way to do nucleophilic substitutions on a carbon of an aromatic ring which are not possible by normal $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ mechanisms. The great stability of molecular nitrogen (N_2) makes it a very good leaving group, but the mechanisms of these reactions are not simple.

The last reaction in the table is one in which the diazonium group acts as an electrophile. It is not a particularly good electrophile, so it requires a reactive ring as a target. Such a ring needs to have a strong electron donating group like OH or NH_2 to increase its reactivity in an electrophilic aromatic substitution mechanism.

The product of the electrophilic coupling of a diazonium ion with a reactive aromatic ring includes a nitrogen-nitrogen double bond. These compounds are often intensely colored and are useful as dyes. A variety of other functional groups, often carrying ionic charges, may be included to make them stick tighter to cloth. Terms such as aniline dyes or azo dyes are often used to refer to these compounds.

Diazonium salts are versatile synthetic intermediate materials and we know that they are made from aniline or similar molecules. Where do aniline and its analogs come from? The most common route is by reduction of nitrobenzene or substituted nitrobenzenes. The usual reducing agent is tin (in the laboratory) or iron (in industrial practice) used in aqueous HCl solution. Since nitration is a commonly used route to nitrobenzene, the usual sequence for the production of aniline is:



The use of NaOH in the final step is to neutralize the HCl so that the basic amine (which would otherwise be in the form of its conjugate acid ammonium ion) is non-polar enough to be extracted from the water.

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