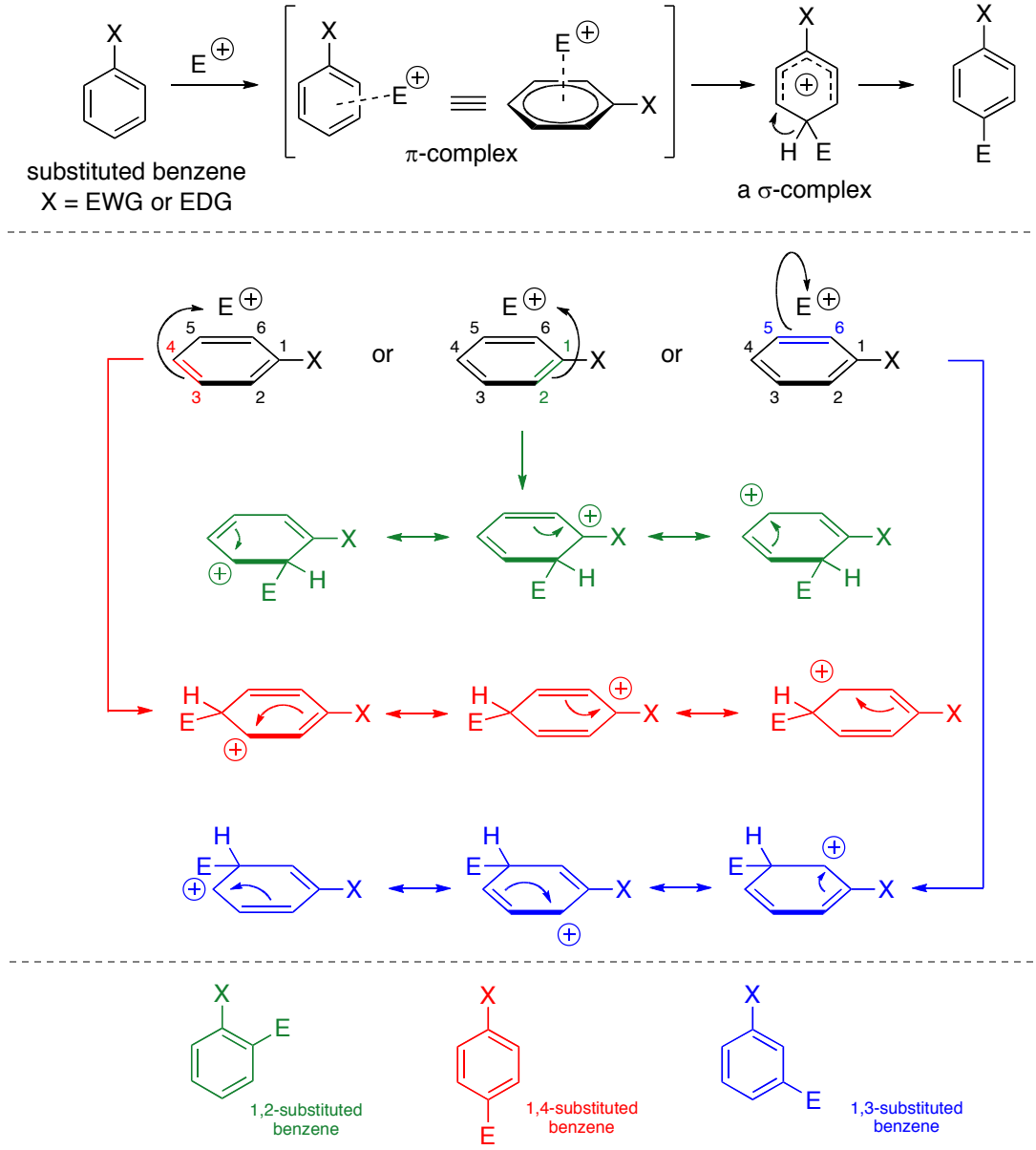
CHEM 30121

THEORY OF ELECTROPHILIC AROMATIC SUBSTITUTION

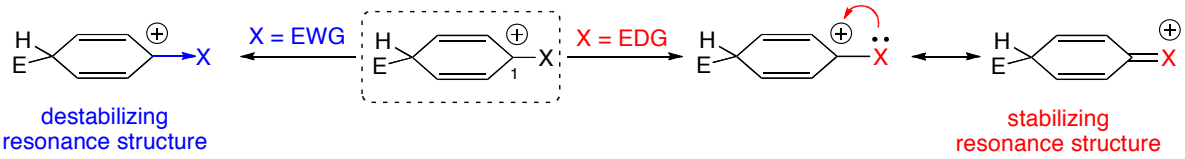
Although the aromatic ring is a π-system, its chemistry is quite different from that of a simple double or triple bond. Alkenes and alkynes undergo addition to the multiple bond when treated with most electrophilic reagents. Typical reactions include addition of HX (X = halogen), addition of X_2 (X = Cl or Br), acid-catalyzed addition of H_2O, hydroboration, etc. The process is usually exothermic since π-electrons become lower energy σ-electrons when the multiple bond is destroyed. However, the 6 π-electron system in an aromatic ring enjoys a special stability that makes addition reactions to the ring very difficult. Instead, the aromatic ring prefers to undergo substitution during which a hydrogen atom on the ring is replaced by another group thus preserving the aromatic nucleus in the product. The scope of this class of reaction is very broad. Although a wide range of electrophilic species and a variety of aromatic substrates are available, all of these reactions can be explained by a common mechanism shown at the top of Scheme 1. In the first step, the electrophile attacks the



Scheme 1

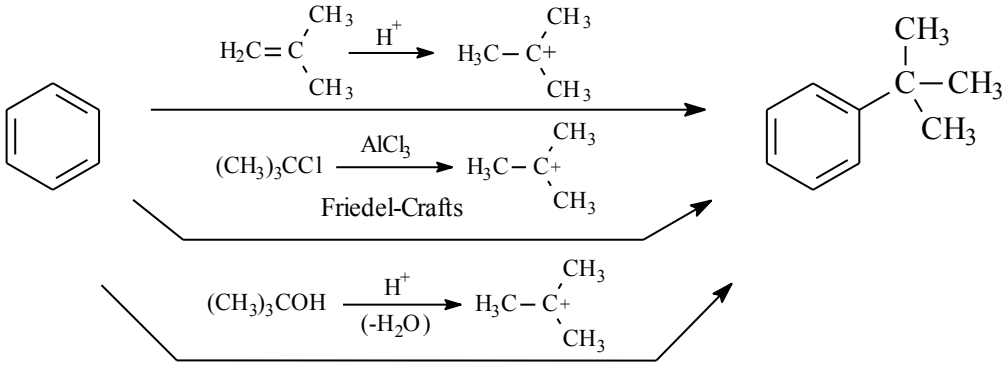
electron-rich aromatic ring to generate a π-complex that collapses rapidly to the σ-complex. The σ-complex is a stabilized (conjugated) carbocation that loses a proton (deprotonation) in the last step to restore the aromaticity in the final product.

If X = H in this equation, then the substrate is benzene and the product is a monosubstituted aromatic ring. However, if X is a substituent group on the aromatic substrate, then the product is a disubstituted benzene ring. Thus, there are three possible isomeric products from the reaction as shown by the green, red, and blue structures at the bottom of Scheme 1. These products arise from three different positions of attack by the electrophile on the aromatic ring. The route leading to the green product (1,2-disubstituted or *ortho* isomer) involves a σ-complex formed by electrophilic attack at either carbon 2 or carbon 6 of the substrate. The blue product (1,3-disubstituted or *meta* isomer) is formed by electrophilic attack at either carbon 3 or carbon 5 of the substrate; and the red product (1,4-disubstituted or *para* isomer) is the result of electrophilic attack at carbon 4. The group X on the substrate determines which isomer(s) will be produced as the major product(s) in the reaction. For example, if X is an electron-donating group, this can result in extra stabilization of the carbocation leading to formation of both the *ortho* and the *para* products (*i.e.*, X is an *ortho/para* director). On the other hand, if X is an electron-withdrawing group, this can (but not always) destabilize the cation leading to the *ortho* and *para* products and cause the *meta* isomer to the major product. These groups are called *meta* directors.



The electronic nature of the group X also has a dramatic impact on the reactivity of the ring. If X is electron withdrawing (-NO_2, -CN, -SO_3H, carbonyl functions, etc.), the substrate becomes less reactive that benzene toward substitution. If X is electron donating (alkyl, -OH, OCH_3, -NH_2, etc.), the substrate is more reactive than benzene.

The most common electrophiles for electrophilic aromatic substitution include carbocations, nitronium ($^+NO_2$), halonium (Cl^+, Br^+), $^+SO_3H$ and acylium. Specific sets of reagents are used in the generation of each of these electrophiles. For example, carbocations can be produced by at least three familiar pathways. If a solution of isobutylene gas dissolved in benzene is treated with a very strong mineral acid such as sulfuric acid, the protonation of isobutylene gives the *t*-butyl carbocation.



This cation attacks the benzene ring and gives *t*-butylbenzene as the product. The famous Friedel-Crafts reaction uses *t*-butyl chloride and $AlCl_3$ to generate the same carbocation. Finally, *t*-butyl

alcohol with a strong acid is also a source of *t*-butyl carbocation via protonation of the oxygen and loss of water.

PROBLEM SET – Electrophilic Aromatic Substitution

1. What is the role of acetic acid in the electrophilic aromatic substitution reaction you did in the laboratory?

2. What is the structure of the most likely product from the reaction of methoxybenzene with an excess of *t*-butyl alcohol under the same conditions you used in the laboratory? What other products did you discount and why?

3. In the electrophilic aromatic substitution reaction you did in the laboratory, the substitution of the second *t*-butyl group on the ring is faster than the first substitution. Explain why this is true.