Electrophilic Aromatic Substitutions

Transcript

00:00:00:16 - 00:00:11:70
Dr.Jessie Key: Hello again, Dr. Jessie Key here. In this slide show, you'll be exploring Electrophilic Aromatic Substitutions, one of the most powerful reactions for modifying an aromatic ring.

00:00:11:70 - 00:00:40:34
Dr.Jessie Key: You'll learn about the mechanism and see several specific examples of this class of reaction. Aromatic compounds may not be able to undergo addition reactions, but they can react with a variety of electrophiles. Let's explore the mechanism of this class of reaction generally first, using E+ as an electrophilic species.

00:00:40:50 - 00:01:23:36
Dr.Jessie Key: One of the pi bonds from the aromatic ring performs a nucleophilic attack to form a new sigma bond to the electrophilic center of the electrophile. A resonance-stabilized positively charged intermediate species is generated, known as the sigma complex, which then undergoes a proton transfer to re-establish aromaticity. In the proton transfer, a species acting as a base removes the proton from the carbon where the electrophile was added, resulting in the substitution of a proton for the electrophilic atom or group.

00:01:26:54 - 00:01:53:18
Dr.Jessie Key: Halogenation can be performed using a Lewis-acid catalyst. Bromination and chlorination are common, but fluorination is usually avoided due to its violent reactivity, and iodination is less common because of low yields. Br2 is commonly used with Lewis Acid catalyst iron tribromide, while Cl2 is commonly used with aluminum trichloride.

00:01:54:51 - 00:02:23:39
Dr.Jessie Key: The primary function of the Lewis Acid catalyst is to improve the electrophilicity of the halogen by formation of an adduct. For example, when Br2 is used with iron tribromide, a nucleophilic attack from the bromine lone pair to the central iron atom occurs to form a new sigma bond. This creates a Lewis acid-base adduct which has enhanced electrophilicity, essentially acting as Br+.

00:02:25:22 - 00:02:56:83
Dr.Jessie Key: The aromatic ring pi bond can then act as a nucleophile and attack the outermost bromine of the Lewis acid-base adduct, which causes the bromine bromine sigma bond to break and give the resonant stabilized sigma complex. Sulfonation can be performed using the regent known as “fuming sulfuric acid”. Fuming sulfuric acid is a mixture of sulfuric acid, (H2SO4) and sulfur trioxide, (SO3).

00:02:56:87 - 00:03:22:84
Dr.Jessie Key: Sulfur trioxide is a good electrophile because of poor p-orbital overlap between the sulfur and the oxygen. This results in a species that behaves more like a sulfur with a formal positive charge, single bonded to oxygens bearing negative charges. It is the sulfur trioxide that acts as the electrophile in the sulfonation mechanism.

00:03:22:84 - 00:03:53:95
Dr.Jessie Key: The aromatic pi bond performs a nuclephilic attack on the electrophilic sulfur atom, which causes one of the sulfur oxygen double bonds to move onto the oxygen as a lone pair. The resulting sigma complex then undergoes proton transfer with water acting as the base. The sulfonate ion then performs a subsequent proton transfer from the resulting hydronium ion to give the sulfonation product.

00:03:53:95 - 00:04:09:71
Dr.Jessie Key: The spontaneity of the sulfonation reaction depends on the concentration. The equilibrium favors the sulfonation product when concentrated fuming sulfuric acid is used. However, when dilute sulfuric acid is used, the reverse reaction is favored.

00:04:09:71 - 00:04:35:71
Dr.Jessie Key: This makes sulfonation a useful tool to temporarily occupy one position on the aromatic ring. A mixture of sulfuric acid and nitric acid is used to accomplish nitration. Sulfuric acid is a stronger acid with a pK of approximately -3 ($pKa1 \approx -3$), and donates a proton to the nitric acid, which has a pK of approximately -1.64 ($pKa = -1.64$).

00:04:35:71 - 00:05:13:86
Dr.Jessie Key: You can show this with curved arrow notation by starting at the lone pair of the hydroxyl oxygen of nitric acid and draw an arrow to form a new sigma bond to the proton of the sulfuric acid. This breaks the sulfuric acid O-H sigma bond, and those electrons move onto the oxygen as a lone pair. The resulting protonated nitric acid undergoes a subsequent loss of water, where a lone pair from the oxygen bearing the formal negative charge forms a new oxygen nitrogen pi bond, which causes the adjacent nitrogen oxygen sigma bond to break, ejecting water as a leaving group.

00:05:13:86 - 00:05:46:95
Dr.Jessie Key: This generates the highly electrophilic nitronium ion NO2+ species. Nitration is a particularly common electrophilic aromatic substitution because the nitro group can easily be reduced to an amine by treatment with iron or zinc with hydrochloric acid.

Carbon-carbon bond formation can be performed on aromatic rings using the Friedel-Crafts alkylation.

00:05:46:95 - 00:06:09:09
Dr.Jessie Key: This reaction is named after French chemist Charles Friedel and American chemist James Crafts, who discovered it in 1877. The Fridel-Crafts reaction uses alkyl halides in the presence of a Lewis Acid catalyst. Again, we see the Lewis Acid form an adduct to generate a better electrophile, a carbocation.

00:06:09:09 - 00:06:43:59
Dr.Jessie Key: A lone pair on the halogen chlorine atom can perform a nucleophilic attack on the central aluminum atom of AlCl3 the Lewis Acid. The resulting adduct then breaks the carbon chlorine bond to move the electrons onto the chlorine atom, generating the carbocation electrophile and the byproduct tetrachloroaluminate , (AlCl4-). The aromatic pi bond can then perform a nucleophilic attack on the alkyl cation electrophile to form the resonance-stabilized sigma complex.

00:06:44:23 - 00:07:27:42
Dr.Jessie Key: The tetrachloroaluminate acts as the base in the subsequent proton transfer using one of the aluminum chlorine sigma bonds as the electron source to form the new sigma bond to the aromatic proton. This restores the aromaticity, giving us the alkylation substitution product, hydrochloric acid, and the regenerated aluminum trichloride catalyst. One of the main drawbacks of the Friedel-Crafts reaction is that primary alkyl halides tend to give rearrangement products, as seen in this example, where substitution with chlorobutane gives the rearrangement product sec-butylbenzene in 65% yield and only 35% of the non-rearrangement product butylbenzene.

00:07:27:42 - 00:07:55:31
Dr.Jessie Key: To avoid an unstable primary carbocation, the Lewis acid base adduct is either directly attacked by the pi bond electrons or alternatively, hydride shift rearrangements occur to give the more stable secondary or tertiary carbocation. There are several other limitations to Friedel-Crafts alkylation. Vinyl and aryl alkyl halides do not work, as the resulting carbocations are too unstable.

00:07:56:11 - 00:08:30:83
Dr.Jessie Key: Polyalkylation may occur as the electron-donation of the newly added alkyl group by hyperconjugation can make the aromatic ring a better nucleophile. As well, the presence of a strong electron withdrawing group like a nitro group can make the aromatic ring too poor of a nucleophile and destabilize the sigma complex resulting in no reaction. To overcome the limitations of Friedel-Crafts alkylation, acylation can be performed instead using similar reaction conditions.

00:08:31:02 - 00:09:00:82
Dr.Jessie Key: Acylations occur through an analogous mechanism to alkylation, where Lewis acid base adduct is formed, followed by loss of the tetrachloroaluminate ion to form a

carbocation intermediate. However, in this case, the intermediate is a resonance stabilized acylium ion which will not undergo rearrangement. The electrophilic aromatic substitution mechanism of acylation proceeds through the same mechanism as seen before.

00:09:00:82 - 00:09:42:00
Dr.Jessie Key: With the aromatic pi bond performing a nucleophilic attack this time on the resonance stabilized acylium ion, the resulting sigma complex is deprotonated by the tetrachloroaluminate using one of the aluminum chlorine sigma bonds as the electron source to form the new sigma bond to the aromatic proton. This restores the aromaticity, giving us the acylation substitution product, hydrochloric acid, and the regenerated aluminum trichloride catalyst. The aryl ketone products obtained from Friedel-Crafts acylation can be utilized to generate rearrangement free alkylation by subsequent reduction to an alkane.

00:09:42:00 - 00:10:14:19
Dr.Jessie Key: The Clemmensen reduction, named after Danish-American chemist Erik Christian Clemmensen is commonly used to accomplish this reduction. It uses a zinc mercury amalgam with hydrochloric acid and heat to reduce an aryl ketone to an alkyl chain. Another benefit of using Friedel-Crafts acylation instead of alkylation is that polyacylation does not occur since the acyl group is electron withdrawing, which makes the mag ring less nucleophilic.