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Friedel-Crafts reactions are organic coupling mechanisms that involve electrophilic aromatic substitutions, enabling the attachment of various substituents to aromatic rings. ===== Friedel-Crafts reactions were first developed in 1877 by French chemist Charles Friedel and American chemist James Crafts. The two primary types of Friedel-Crafts reactions are alkylation and acylation, which involve the replacement of a hydrogen atom on an aromatic ring with an electrophile. The acyl benzene product is formed through a series of steps involving electrophilic attack, resonance stabilization, and deprotonation. Initially, an acyl halide forms an acylium ion by losing a halide ion, which then undergoes an electrophilic attack on the aromatic ring, leading to a complex formation. This intermediate is subsequently deprotonated, resulting in the release of HCl and the regeneration of the AlCl<sub>3</sub> catalyst. Friedel-Crafts Alkylation and Acylation: A Comparative Analysis of Their Limitations and Mechanisms ===== The Friedel-Crafts reaction, including both alkylation and acylation, is a widely used method in organic synthesis. However, its limitations and the need for alternative reactions have led to the development of new and improved methods. Carbocation Rearrangement and Compound Limitations When attempting to add a carbon chain greater than two carbons to an aromatic ring using Friedel-Crafts alkylation, carbocation rearrangements can occur due to hydride shifts and methyl shifts. This can result in the formation of unwanted products. Furthermore, the reaction is limited by the type of compound being used, with nitrobenzene and other strong deactivating systems failing to participate. Friedel-Crafts Acylation: A Solution to the Limitations Friedel-Crafts acylation was developed as a response to the limitations of Friedel-Crafts alkylation. This reaction involves the formation of an acylium ion, which then reacts with the aromatic ring to form a complex. The subsequent departure of a proton enables the ring to return to aromaticity, resulting in the formation of a ketone. Mechanism of Friedel-Crafts Acylation The mechanism of Friedel-Crafts acylation involves three stages. In the first stage, the acylium ion is formed through the reaction of an alkyl halide with aluminium chloride. In the second stage, the acylium ion attacks the aromatic ring, forming a complex. Finally, the departure of a proton enables the ring to return to aromaticity, resulting in the formation of a ketone. Simplified Mechanism The simplified mechanism of Friedel-Crafts acylation involves two stages. In the first stage, the CH<sub>3</sub><sup>+</sup> ion approaches the delocalised electrons in the benzene, forming a new bond and breaking the delocalisation. In the second stage, the AlCl<sub>4</sub><sup>-</sup> removes the hydrogen from the ring to form HCl, re-generating the aluminium chloride catalyst. Conclusion Friedel-Crafts acylation offers a solution to the limitations of Friedel-Crafts alkylation, enabling the formation of complex molecules with reduced side reactions. Understanding the mechanism and limitations of this reaction is essential for its successful application in organic synthesis. Friedel-Crafts Alkylation via electrophilic aromatic substitution occurs in chemistry. Example of toluene production. Friedel-Crafts alkylation mechanism uses aluminium chloride as catalysts. It happens in four steps under anhydrous conditions. Biphenyl can be used to limit side reactions. Carbocation rearrangements happen when alkyl halide has more than two carbons. Aniline and NR<sub>2</sub> substituted aromatic compounds don't undergo Friedel-Crafts alkylation. Polyalkylation happens when each group is added to benzene ring multiple times. Acylation occurs in electrophilic aromatic substitution reactions. It differs from alkylation. Rearrangements of primary carbocations are surprising because they shouldn't be formed in the first place, which is correct, as primary carbocations are generally not observed and instead, a complex forms in the Lewis acid-base reaction. This complex has a very electrophilic carbon connected to Cl and still promotes a 1,2-hydride shift, similar to what's seen in the dehydration of primary alcohols. Whenever possible, rearrangements will occur, resulting in a mixture of alkylated rings, with the ratio being optimized based on conditions such as concentrations and temperature. Friedel-Crafts alkylation can be avoided when using tertiary alkyl halides or methyl/ethyl alkyl halides, which cannot rearrange into more stable carbocations. For successful Friedel-Crafts alkylation, the halogen of the alkyl halide must be connected to an sp<sup>3</sup> hybridized carbon atom, as carbocations with a positive charge on an sp<sup>2</sup> carbon are unstable and don't form readily. Vinyl and aryl halides do not undergo Friedel-Crafts alkylation due to this instability. Friedel-Crafts alkylations and acylations are the slowest in electrophilic aromatic substitution reactions, so they're not suitable when a strongly deactivating group is present. In theory, any functional group that can be converted into a strong electrophile can be used in Friedel-Crafts Alkylation. For example, alcohols can be converted into carbocations using H<sub>2</sub>SO<sub>4</sub>, similar to E1 elimination reactions. Alcohols can also be activated with Lewis acids like BF<sub>3</sub>. Alkenes are converted into carbocations in the presence of dilute acids, serving as electrophiles in Friedel-Crafts alkylation reactions. Aromatic compounds with functional groups that can be converted into an electrophile can undergo intramolecular Friedel-Crafts Alkylation. =====