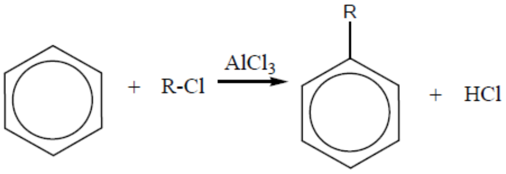
B. Sc. II (Hons)
Organic Chemistry

Friedel-Crafts reactions

Friedel-Crafts reactions, involving electrophilic aromatic substitution, are of two types: alkylation and acylation.

Friedel-Crafts alkylation

Friedel-Crafts alkylation is an important method for adding alkyl chains to aromatic rings via the reaction between an aromatic ring and an alkyl halide using a strong Lewis through the use of a strong Lewis acid, generally AlCl3 or FeCl3, as a catalyst in which, the alkyl group substitutes the chloride ion.



Alkylations are not limited to alkyl halides. Friedel-Crafts alkylation is possible with any carbocationic intermediate such as those derived from alkenes and a protic acid or lewis acid, enones and epoxides.

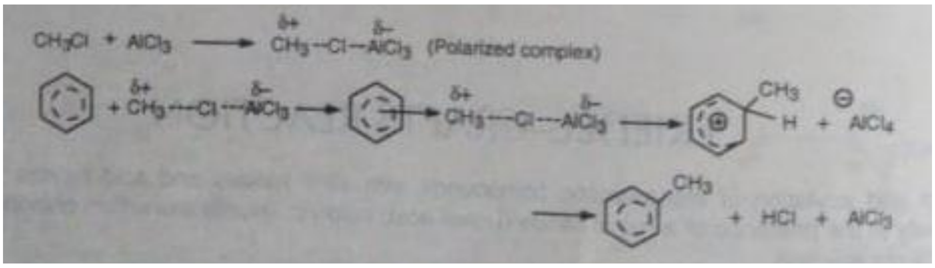
Mechanism

The mechanism of the reaction is not clearly understood. The alkylating reagent generally used is alkyl halide.

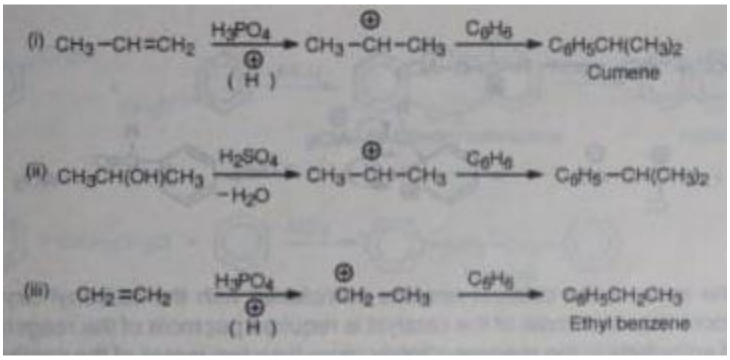
The function of the catalyst is to furnish a real or potential carbocation for the electrophilic attack on the ring. Since tertiary carbocations are stable, it is expected that a real carbocation is the attacking species when the alkylating agent is a tertiary halide.

$$R_3CX + AlCl_3 \longrightarrow R_3\overset{\oplus}{C} + \overset{\ominus}{X}AlCl_3$$

However, primary and secondary carbocations are relatively unstable. Hence it is suggested that with 1^{o} or 2^{o} halides, a polarized complex with a potential carbocation is the attacking species.



Besides alkyl halides, the alkylating agents may be aliphatic alcohols, alkenes, ethers and esters also. These in the presence of acidic catalysts, such as H_2SO_4, H_3PO_4, HF, HF-BF_3, etc., afford carbocations for the electrophilic attack on the ring.



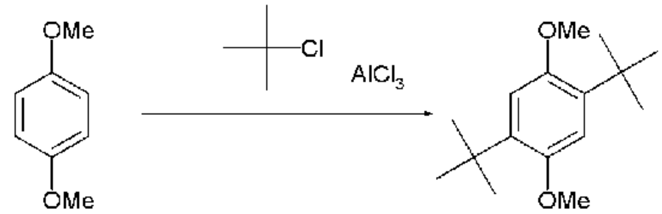
The order of effectiveness of Lewis acid catalysts has been shown to be:

$AlCl_3 > FeCl_3 > BF_3 > TiCl_3 > ZnCl_2 > SnCl_4$

Limitations

In this reaction, the product is more nucleophilic than the reactant due to the electron donating effect of alkyl-chain, therefore, another hydrogen is substituted with an alkyl-chain, which leads to over alkylation of the molecule. Further, if the chlorine is not on a tertiary carbon, carbocation rearrangement reaction occurs, attributed to the relative stability of the tertiary carbocation over the secondary and primary carbocations.

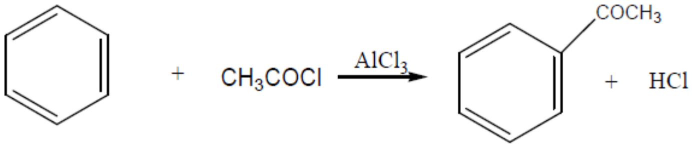
Steric hindrance can be exploited to limit the number of alkylations, as in the tertiary butylation of 1,4-dimethoxybenzene.



Friedel-Crafts alkylation reactions catalyzed by homogeneous Lewis acid catalysts generally give complex reaction mixtures. The formation of reactant (and product) catalyst complexes, the increased tendency of alkylated products towards further alkylation and isomerization, coupled with the long contact of the reactant with the catalyst, result in decreased product selectivity.

Friedel-Crafts acylation

Friedel-Crafts acylation involves the reaction of an acyl chloride or acid anhydride with aromatic compounds in presence of a strong Lewis acid catalyst.

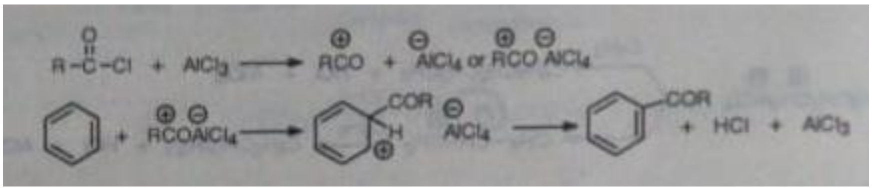


Due to the electron-withdrawing effect of the carbonyl group, the ketone product is always less reactive than the original molecule, therefore multiple acylations do not occur, which is an advantage over the alkylation reaction. Also, there are no carbocation rearrangements, as the carbocation is stabilized by a resonance structure in which the positive charge is on the oxygen, inhibiting intra molecular reactions. The viability of the Friedel-Crafts acylation depends on the stability of the acyl chloride reagent.

Mechanism

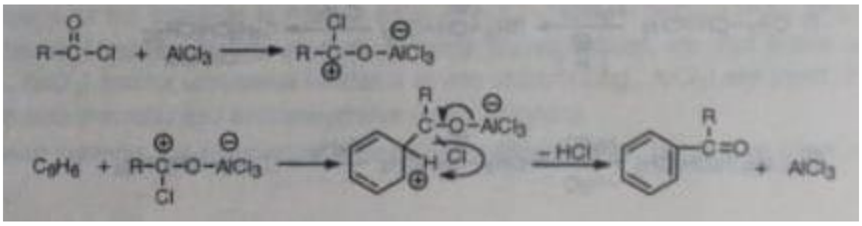
The acylating reagents are acid chlorides or acid anhydrides. Depending on the conditions probably two mechanisms operate,

1) generation of attacking species which may be a free acyl cation or an ion pair.



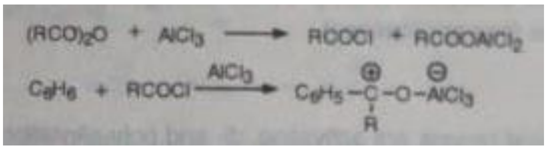
With sterically hindered acyl halides the attacking species may be the acyl cation.

2) Generation of 1:1 complex for the electrophilic attack.



In either case, one mole of the catalyst remains complexed with the carbonyl oxygen of the ketone formed. Hence, a little more than one mole of the catalyst is required per mole of the reagent.

When acid anhydride is the reagent, slightly more than two moles of the catalyst is required. This is because one mole of the catalyst is used up in liberating acyl halide and another mole for complexing with the product, ketone.



$$(RCO)_2O + AlCl_3 \longrightarrow RCOCl + RCOOAlCl_2$$

$$C_6H_6 + RCOCl \xrightarrow{AlCl_3} C_6H_5-\underset{R}{\overset{\oplus}{C}}-\overset{\ominus}{O}-AlCl_3$$