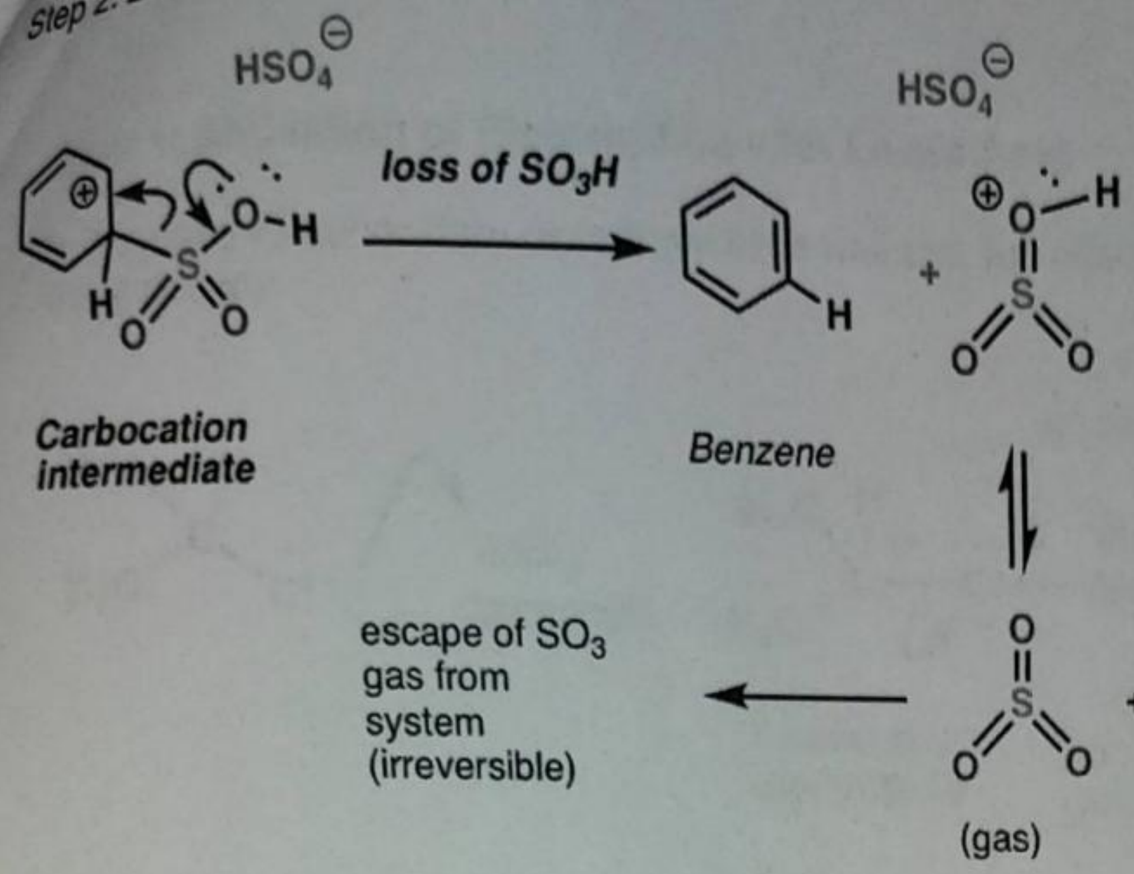
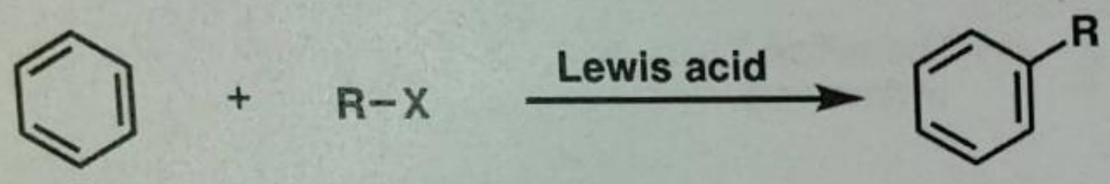
Step 2: Loss of SO_3H (restoring aromaticity)



Introduction of alkyl or acyl gp. in benzene.

Friedel-Crafts Alkylation

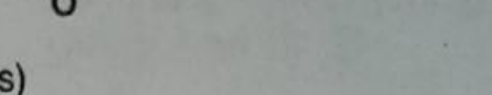
Generic example:



Bonds Formed	Bonds Broken
C–C	C–H
H–X	C–X

- R–X must be an alkyl halide (typically alkyl chorides, bromides, or iodides)
- Lewis acid often $AlCl_3$ but can vary widely (e.g. $FeCl_3$, $ZrCl_4$)
- Carbocation rearrangements can occur

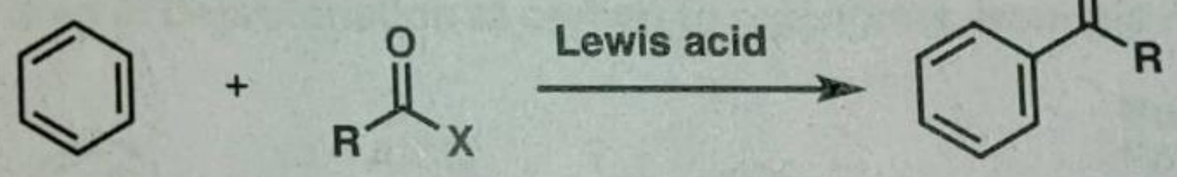
does not work for



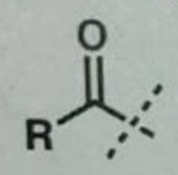
- alkenyl halides
- alkynyl halides

Friedel-Crafts Acylation

Generic example:



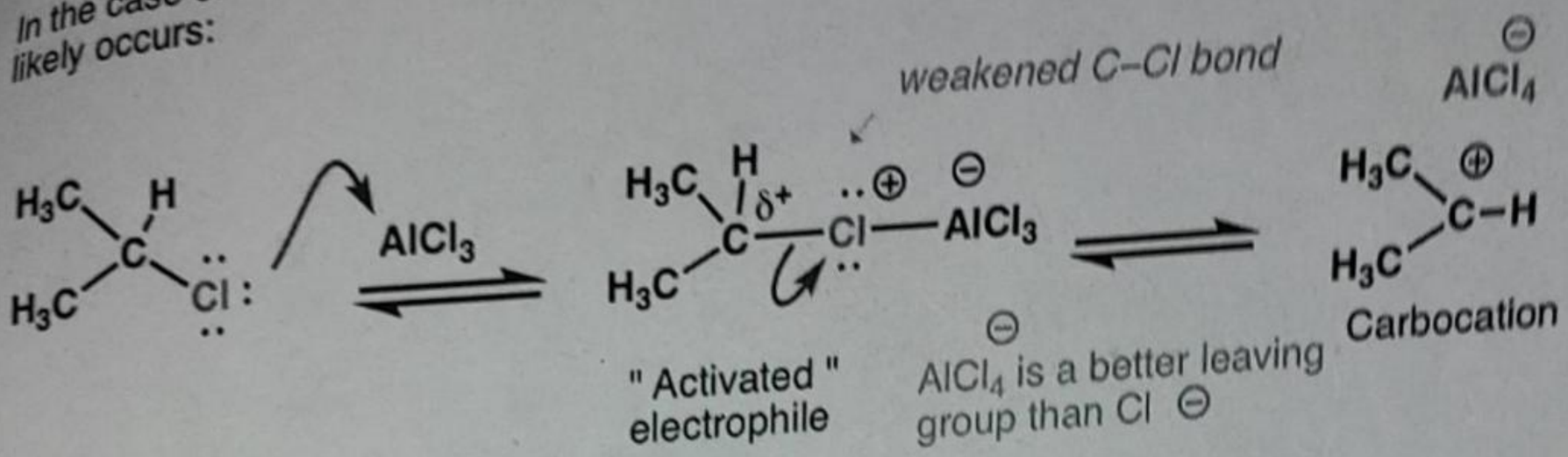
Bonds Formed	Bonds Broken
C–C	C–H
H–X	C–X

"acyl group": 

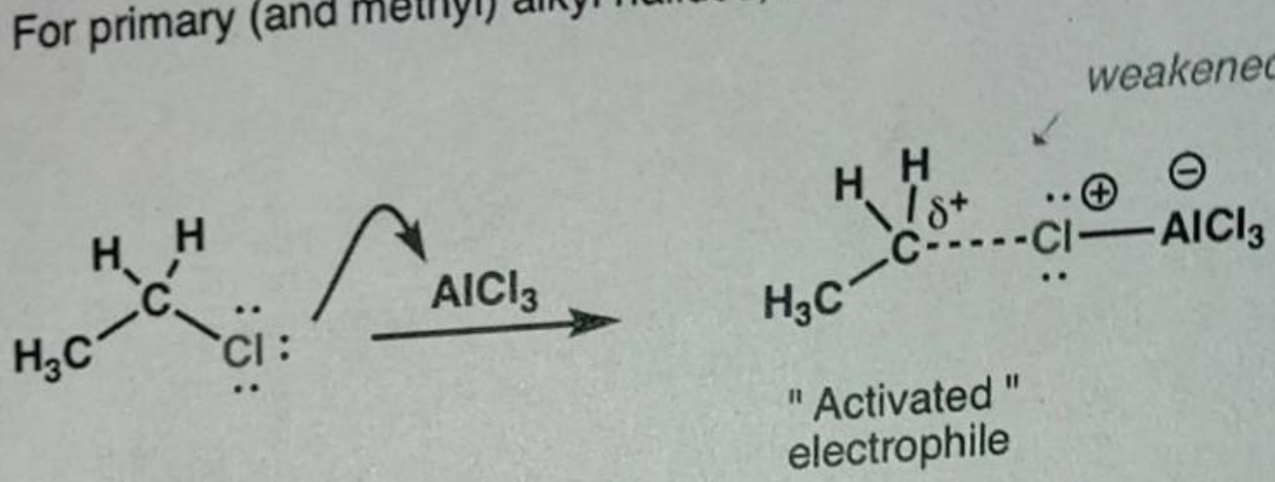
X is usually a halogen
e.g. Cl, Br, I
(although anhydrides can also be used)

Step 1: Activation of Electrophile with Lewis Acid

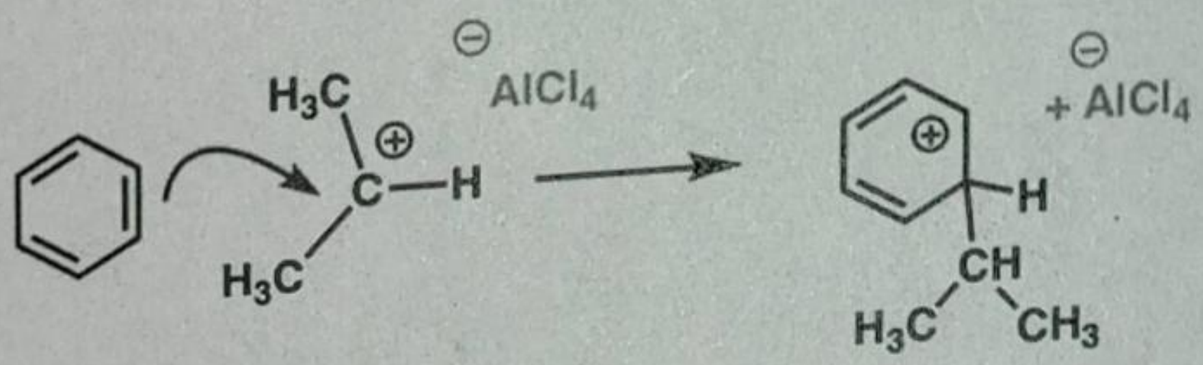
In the case of secondary or tertiary alkyl halides, full dissociation to a carbocation likely occurs:



For primary (and methyl) alkyl halides, it is unlikely that a "free" carbocation is present:

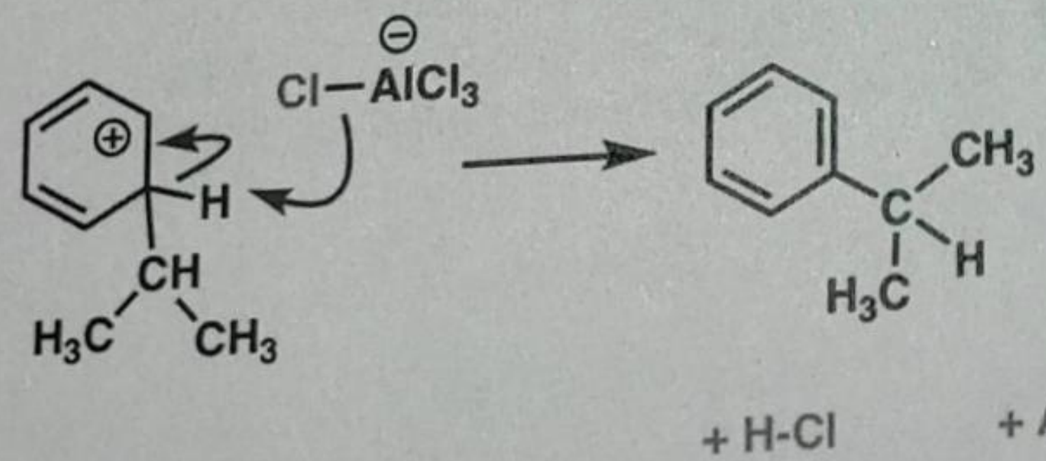


Step 2: Attack of activated electrophile by aromatic ring (rate determining step)



Bonds Formed	Bonds Broken
C–C	C–C (pi)

Step 3: Deprotonation at carbon to regenerate aromatic ring

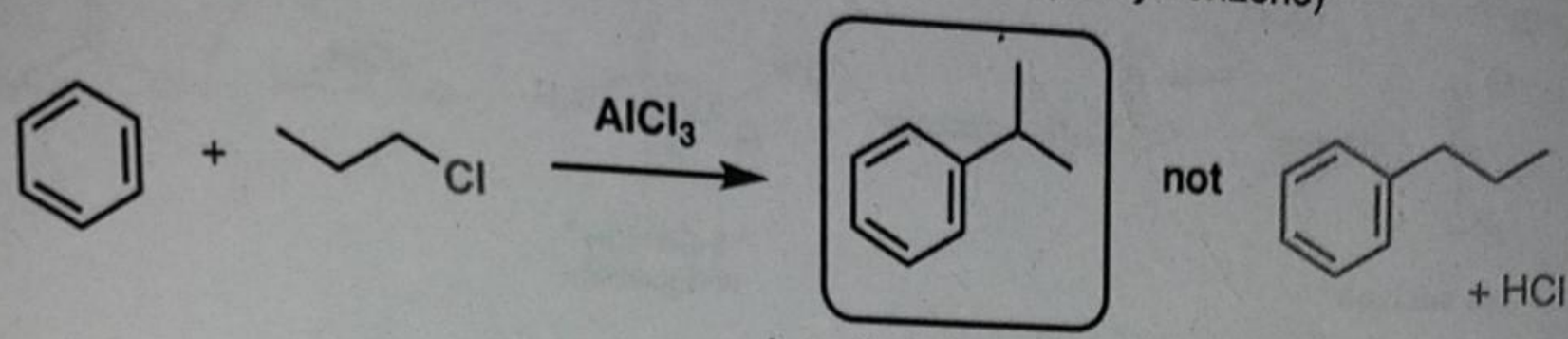


Bonds Formed	Bonds Broken
C–C (pi)	C–H
H–Cl	Al–Cl

Note that this step regenerates $AlCl_3$, which can react with more alkyl halide starting material ($AlCl_3$ is a catalyst in this reaction)

Strange Things Afoot In The Friedel-Crafts Alkylation Reaction

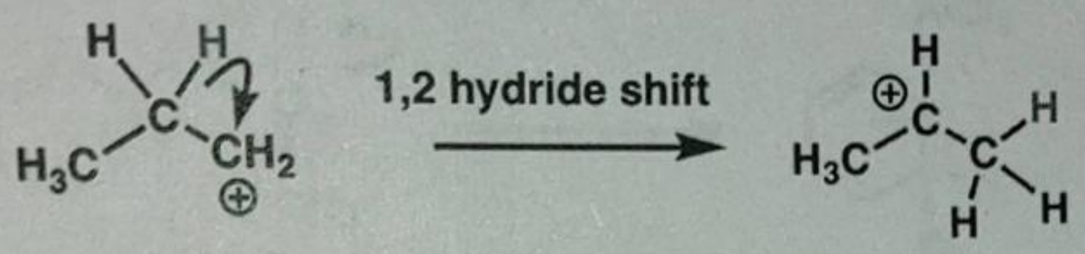
The Friedel-Crafts alkylation reaction between propyl chloride and benzene does not give propylbenzene, but isopropyl benzene (1-methylethylbenzene)



1-methylethylbenzene ("isopropylbenzene")

propylbenzene

What happened here?



Primary carbocation (less stable)

Secondary carbocation (more stable)

+ Rearrangement

Limitations of the Freidel-Crafts Alkylation

Final note on the Friedel-Crafts alkylation: a few drawbacks.

- First, as we've seen, carbocation rearrangements can occur. [There are ways of circumventing this issue indirectly, which we'll hint at below [skip to bottom].
- Second, the Friedel-Crafts alkylation tends not to work well with electron-poor aromatic rings, particularly strongly deactivating substituents such as CF_3, NO_2, SO_3H, and so forth. Halogens are OK.
- Third – and this is more of a practical issue than anything else, so is often ignored – the product of the FC alkylation is often a better nucleophile than the starting material. (Recall that alkyl groups are activating.) The result can be a bit like the Cookie Monster in a Chips Ahoy! factory – it can't stop at just one, resulting in multiple alkylations.
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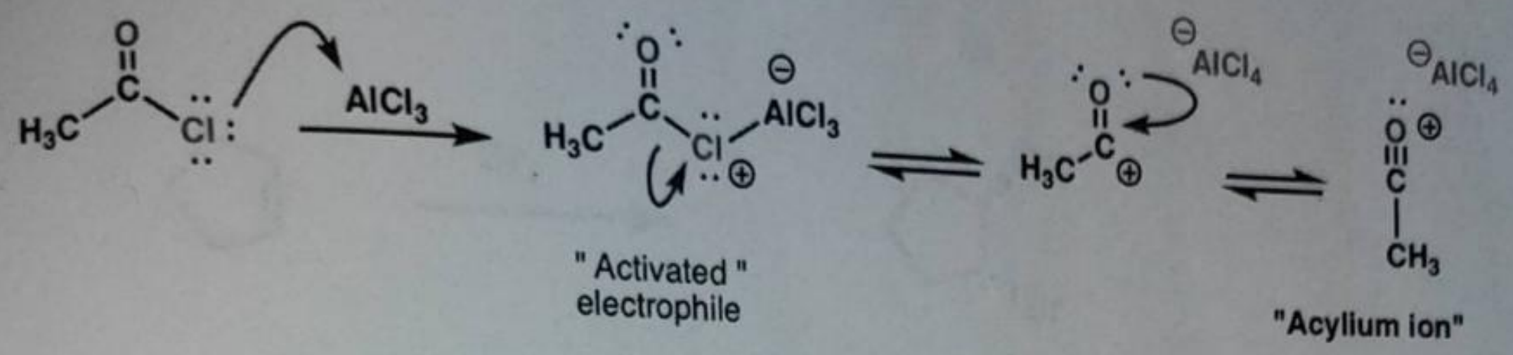
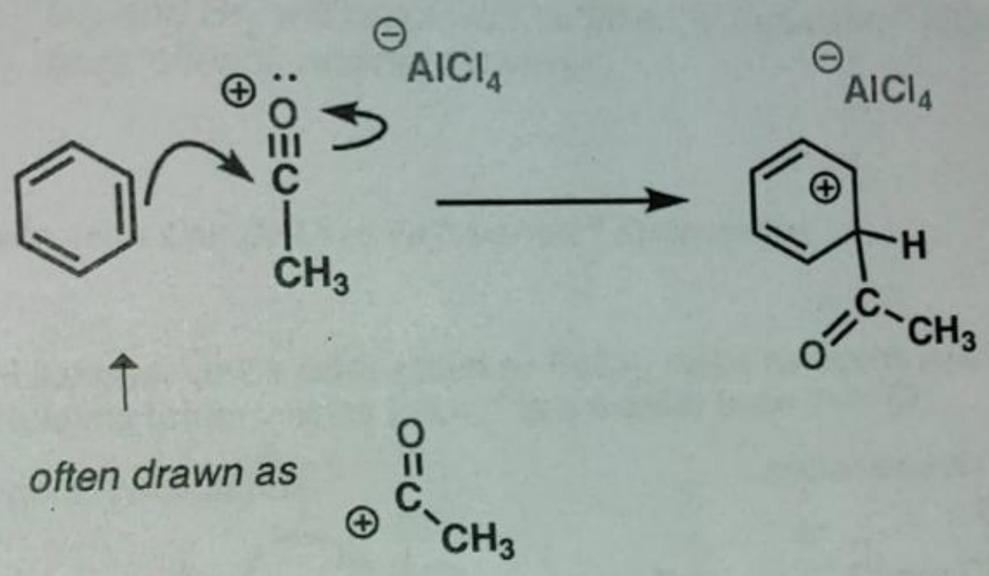
The Mechanism Of The Friedel-Crafts Acylation Reaction

Step 1: Activation of Electrophile with Lewis Acid

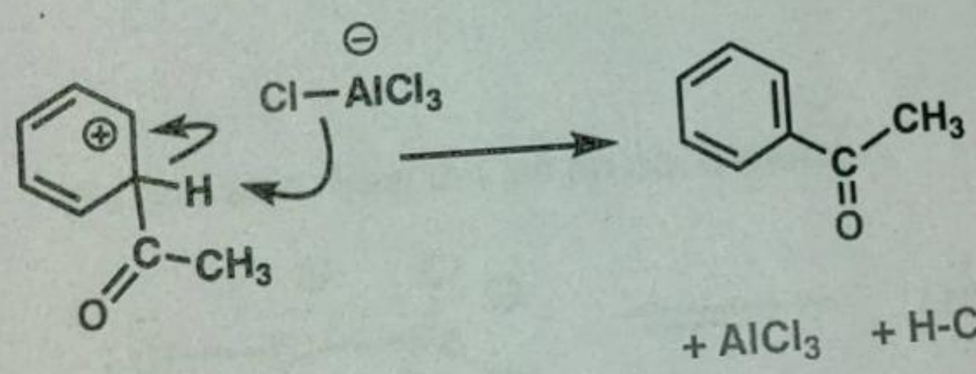


Step 2: Attack of activated electrophile by aromatic ring (rate determining step)



Bonds Formed	Bonds Broken
C–C	C–C (π)
	C–O (π)

Step 3: Deprotonation at carbon to regenerate aromatic ring



Bonds Formed	Bonds Broken
C–C (π)	C–H
H–Cl	Al–Cl

No Rearrangements Occur In The Friedel-Crafts Acylation

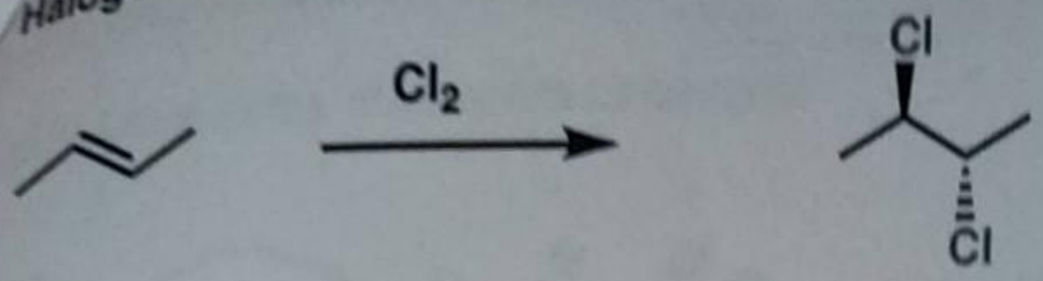
Limitations of The Friedel-Crafts Acylation

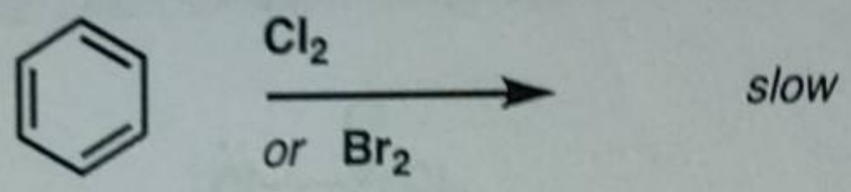
- Similarly to alkylation, Friedel-Crafts acylation tends to fail on aromatic rings with strongly deactivating groups such as nitro, CF_3, sulfonyl and so on. Halogenated aromatics still work, however.

6

Halogenation

Halogenation works well for alkenes, but benzene is not reactive enough:

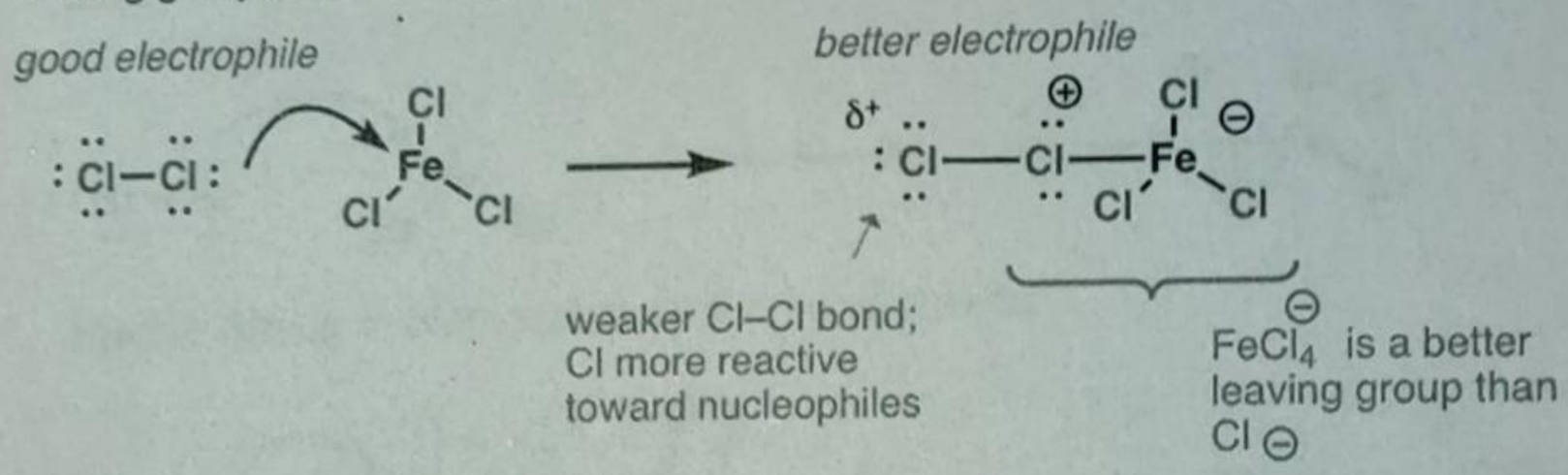




Cl_2 and Br_2 will react with sufficiently "activated" aromatic species (e.g. phenol, aniline) however

Lewis Acids Can Be Used To "Activate" Electrophiles

•Likewise, Lewis acids (such as $FeCl_3$) make halogens (such as Cl) into better leaving groups, since $FeCl_4^-$ is a weaker base than Cl^-



We can also draw this as an equilibrium: