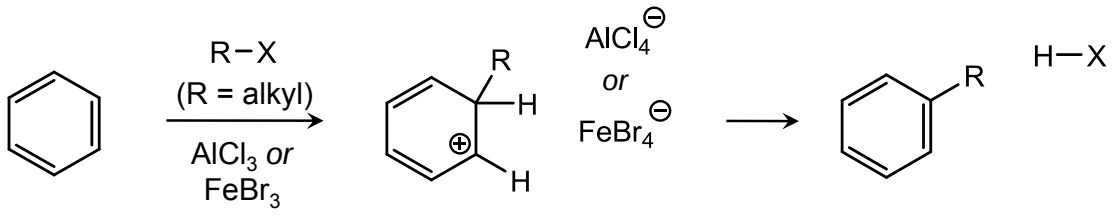
Friedel-Crafts Alkylation

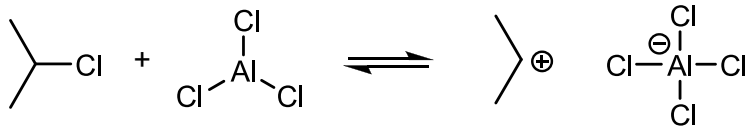
General scheme:



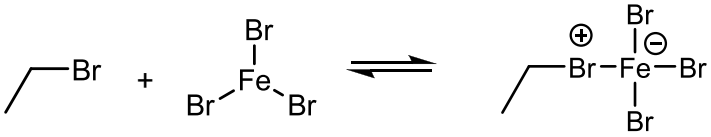
Friedel-Crafts Alkylation

Depends on formation of alkyl cation (or “incipient” cation) intermediate:

2° or 3° halide:



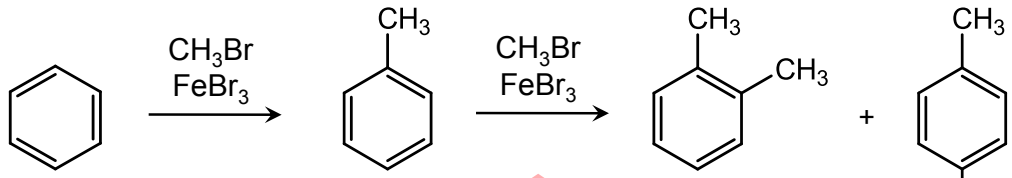
1° or CH_3 halide:



These intermediates react identically in the Friedel-Crafts alkylation reaction.

Problems with Friedel-Crafts Alkylation

1. Only succeeds for benzene, activated aromatics.
2. Alkylation makes aromatic ring more reactive to further alkylation.



2nd reaction is faster than the 1st (because aromatic ring is activated);

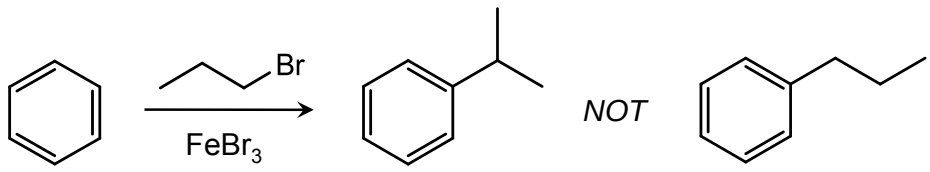
Can't stop reaction at monoalkylated product.

further alkylation

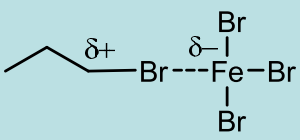
(Can address by using excess starting material.)

Problems with Friedel-Crafts Alkylation

3. Intermediate cation can rearrange (leading to unexpected products).

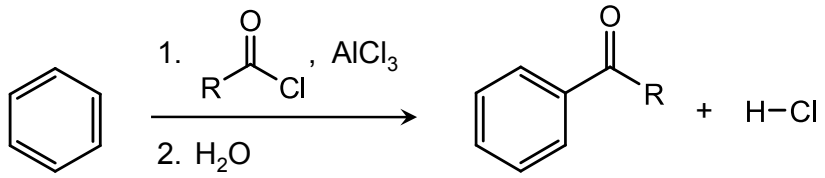


due to rearrangement of

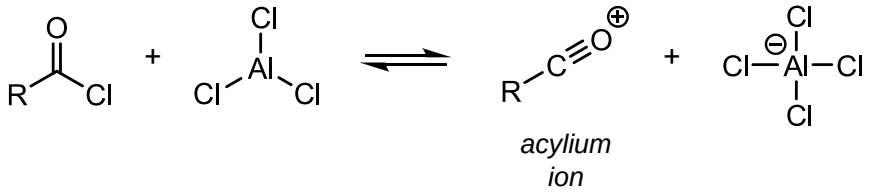


Friedel-Crafts Acylation

General scheme:



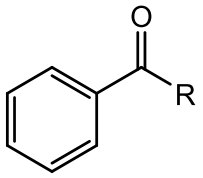
Depends on formation of acylium ion intermediate:



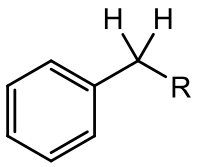
acylium ion

Reducing Carbonyls to Alkyl Carbons

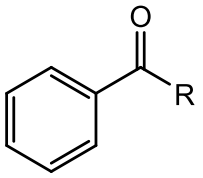
Clemmensen Reduction



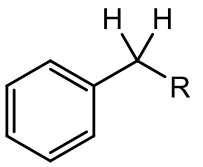
Zn(Hg), HCl/H_2O ***(acidic conditions)***



Wolff-Kishner Reduction



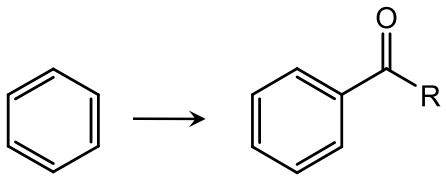
1. N_2H_4
2. KOH, Δ ***(basic conditions)***



Both useful for converting Friedel-Crafts acylation products to alkylated aromatic molecules that can't be made by Friedel-Crafts alkylation.

Characteristics of Combined Friedel-Crafts Acylation/Clemmensen Reduction

1. Still only succeeds for benzene, activated aromatics.
2. Acylation makes aromatic ring **less** reactive to further acylation.

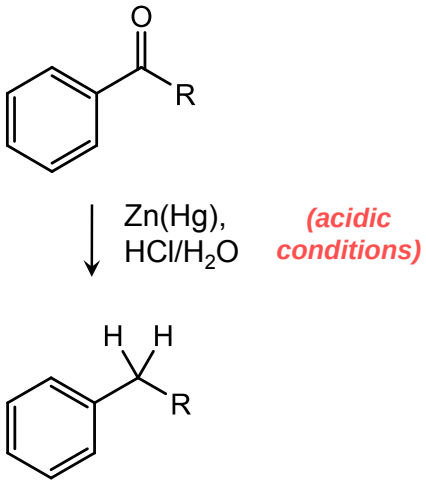


Electron-withdrawing C=O deactivates product.

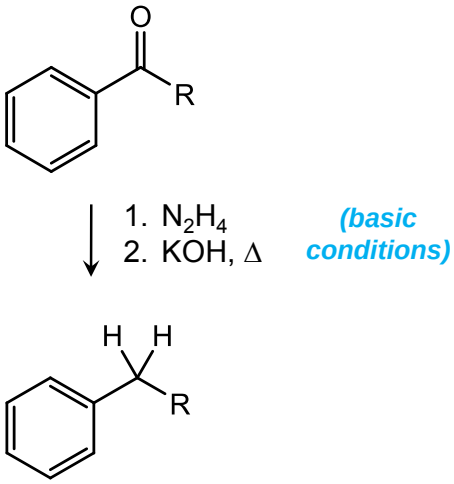
3. Acylium ion is resonance-stabilized, doesn't rearrange.

Reducing Carbonyls to Alkyl Carbons

Clemmensen Reduction



Wolff-Kishner Reduction

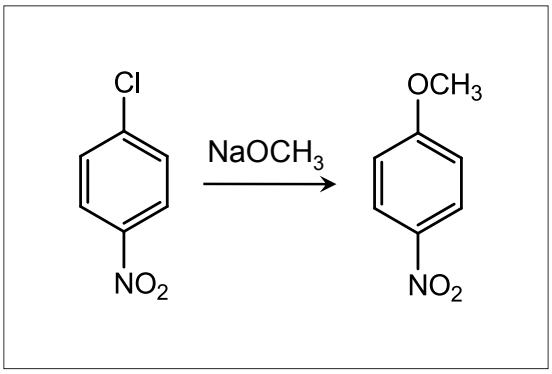


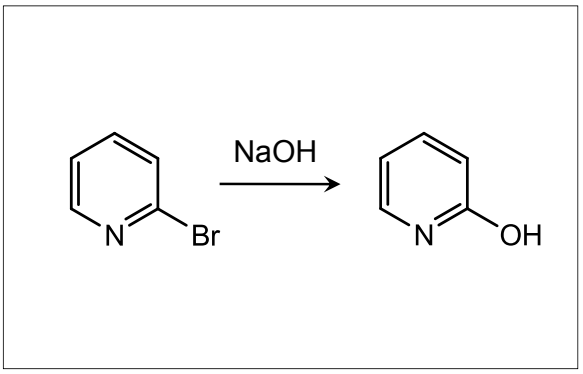
Both useful for converting Friedel-Crafts acylation products to alkylated aromatic molecules that can't be made by Friedel-Crafts alkylation.

Nucleophilic Aromatic Substitution

Electron-withdrawing groups/atoms facilitate substitution with nucleophiles. But mechanism not quite like S_N1/S_N2.

Examples:

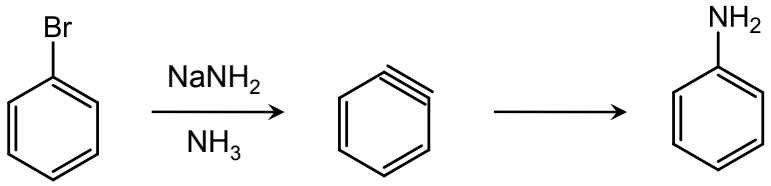




Successful only if electron-withdrawing group is ortho- *or* para- *to site of substitution.*

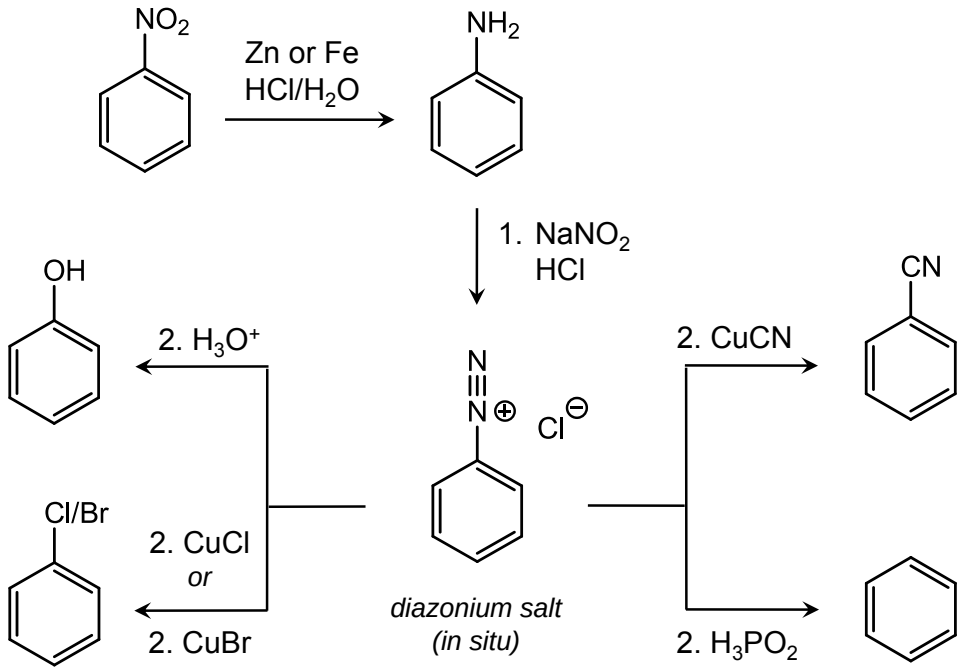
Nucleophilic Aromatic Substitution via the Benzyne Mechanism

Pretty unusual.
Works only for $^-OH/H_2O$, $^-NH_2/NH_3$.



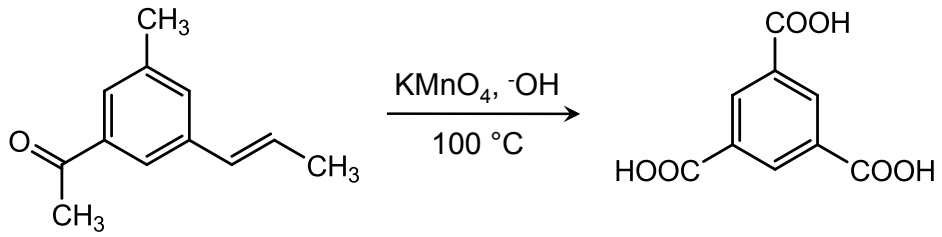
benzyne

Substitution of Arenediazonium Salts (Sandmeyer Reaction)



Reactions at Benzylic Carbons

Oxidation: $KMnO_4$ will convert any benzylic carbon to –COOH.



Reduction: Benzylic functional groups readily reduced all the way to hydrocarbon.

(X = halogen, -OH, -OR)