Reactions of Aromatic Compounds

3 - Reactions at Benzylic Position, Substitution and Reduction

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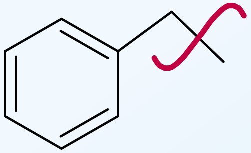
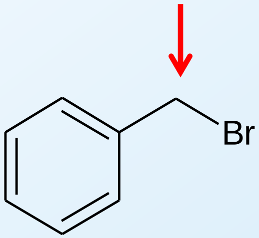
Nomenclature Review

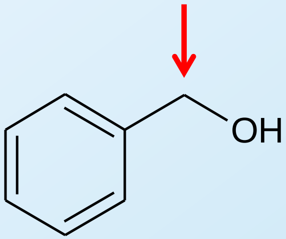
Just to remind you that a phenyl group is C_6H_5- while benzyl is $C_6H_5CH_2$-. Benzylic position is the carbon attached directly to benzene as shown by the red arrow below.



Benzyl, $C_6H_5CH_{2-}$
PhCH$_2$~



Benzylbromide



Benzylalcohol

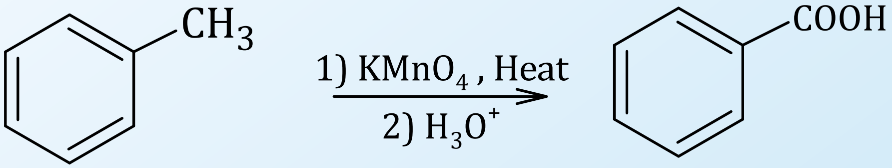
Certain reactions happen at the benzylic carbon because it is directly attached to the benzene ring, e.g., oxidation, free radical bromination. Some other reactions we will cover are just general reactions carried out on certain functional groups and are not dependent on the benzene, e.g., reduction.

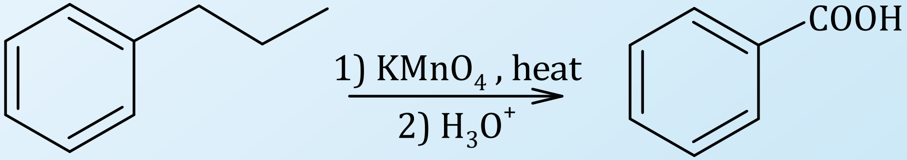
We will also cover some reactions on benzene that are unusual and not necessarily benzylic carbon reactions.

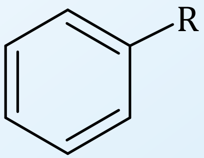
Oxidation of Benzene

Alkyl and unsaturated side chains of aromatic rings can be oxidized to the carboxylic acid using hot $KMnO_4$.

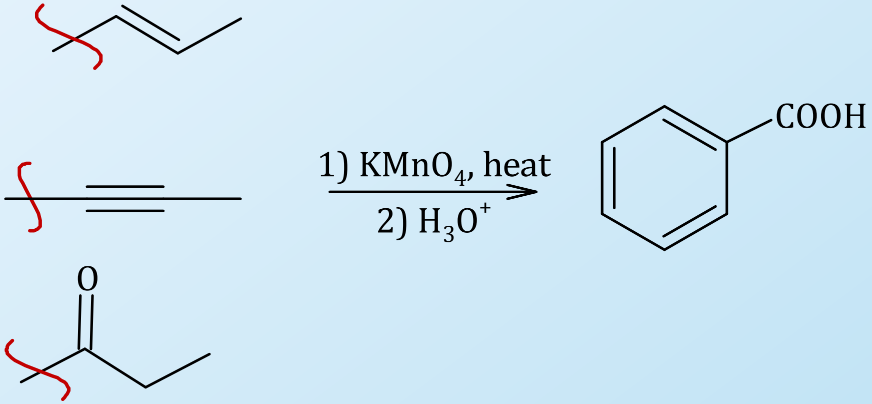
- H_2CrO_4 can also be used.







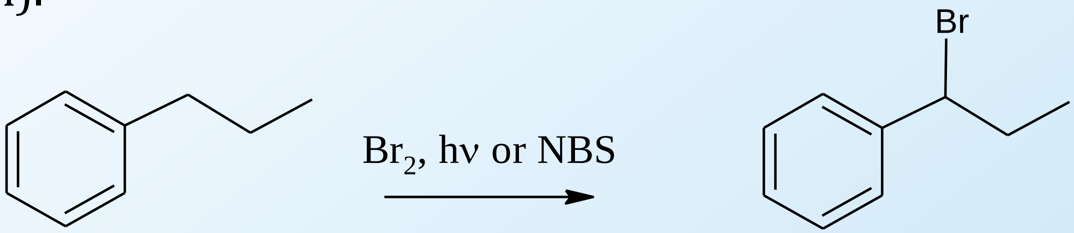
Where R can be any of these groups.



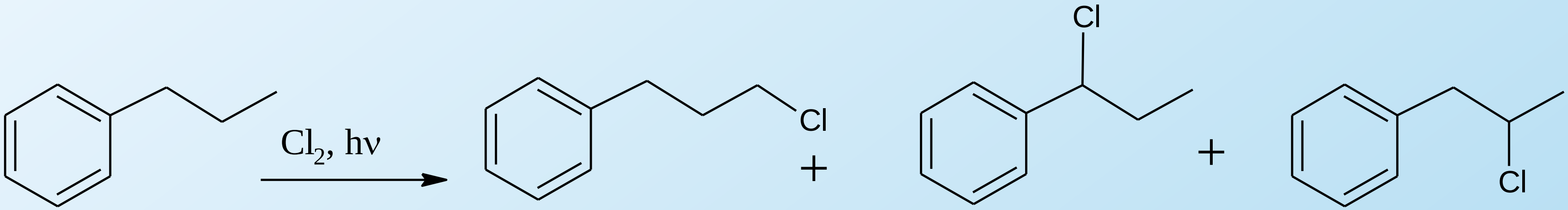
Allylic Bromination

Allylic bromination takes place under conditions which favor radical reactions. Bromination is a more specific reaction; free radical chlorination can give multiple products.

- Reaction of *N*-bromosuccinamide (NBS) with n-propylbenzene in the presence of light leads to allylic bromination. (*N*-bromosuccinamide favors radical reaction).

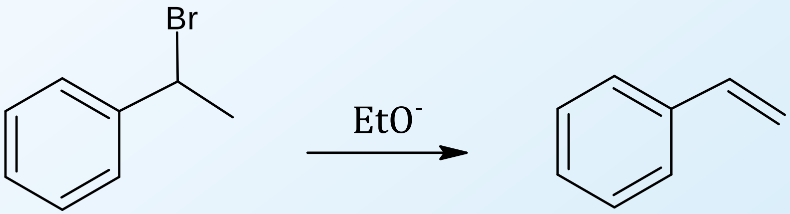


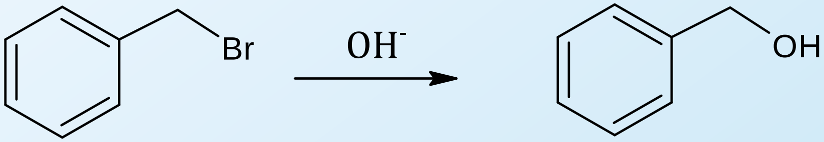
- Reaction of n-propylbenzene with excess chlorine in presence of light produces multiple chlorinations of almost equal proportions. Chlorination is not specific to the benzylic carbon.



Substitution on Benzylic Position

Once there is a leaving group (Br) is on the benzylic position, any number of substitution or elimination reactions can be carried out on the side chain.





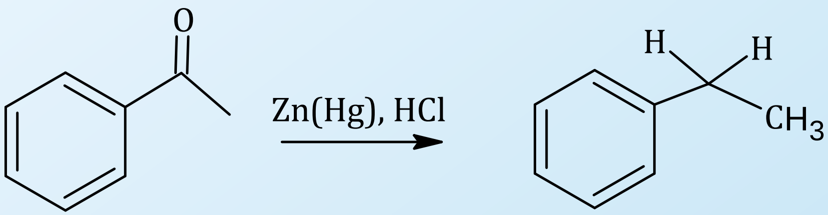
Reduction of Side Chain Group - Carbonyl

These reductions are specific to functional groups and are not driven by its benzylic position.

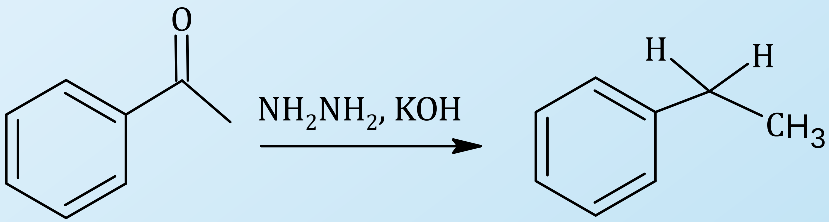
Ketones and aldehydes can be reduced to CH_2 in either an acidic or basic medium using the two reactions below.

1. The Clemmensen reduction— uses zinc and mercury with strong acid.
2. The Wolff-Kishner reduction—uses hydrazine (NH_2NH_2) and strong base (KOH).

Clemmensen Reduction



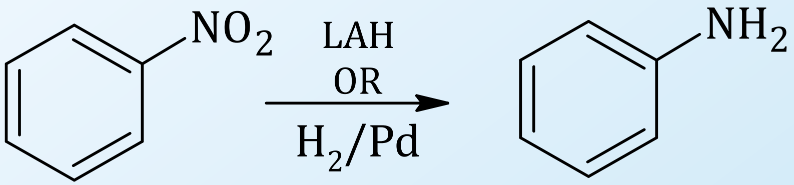
Wolf-Kishner Reduction



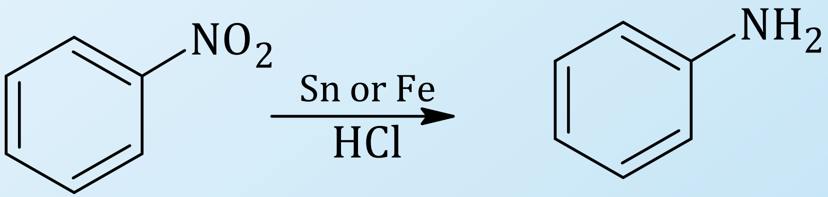
Reduction of Side Chain Group - Nitro

These reductions are specific to functional groups and are not driven by its benzylic position.

Reduction of nitro group gives an amine group. Reduction can be carried out using a strong reducing agent, lithium aluminum hydride (LAH), hydrogenation or a metal in presence of acids.



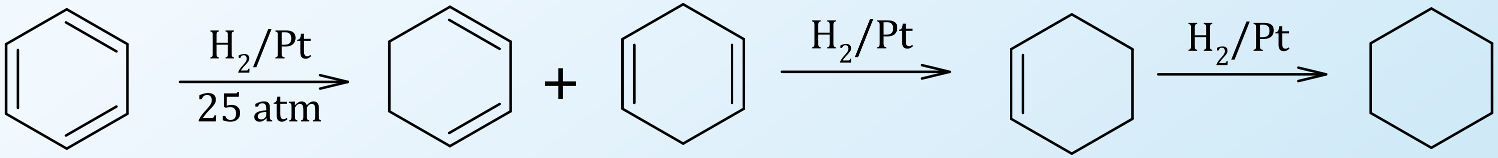
Use of acid in metal reduction is used when there are other groups on the benzene ring that may also be reduced by LAH, e.g., a carbonyl.



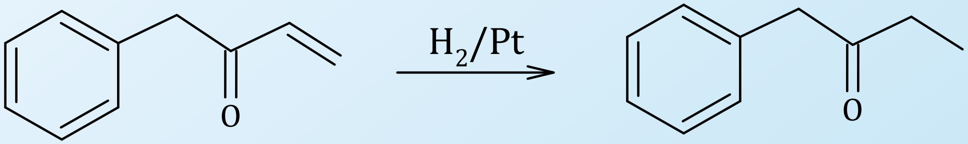
Reduction of Benzene and Alkenes on Benzene

Hydrogenations are possible in benzene and outside the benzene ring.

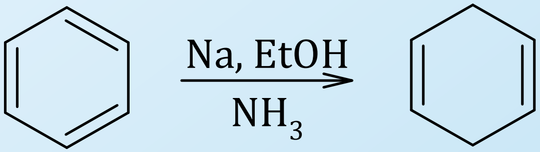
Hydrogenation can reduce benzene all the way to cyclohexane. The first step is the hardest as the benzene is aromatic, once aromaticity is gone, hydrogenation is similar to alkenes. Also note that the first hydrogenation gives two products, in equal proportion. This kind of hydrogenation is not practical due to the high pressure involved.



It is easy to carry out outside the benzene ring because the ring cannot be reduced under these conditions.



<u>Birch Reduction</u> – is very specific in reducing benzene to give the non conjugated diene.

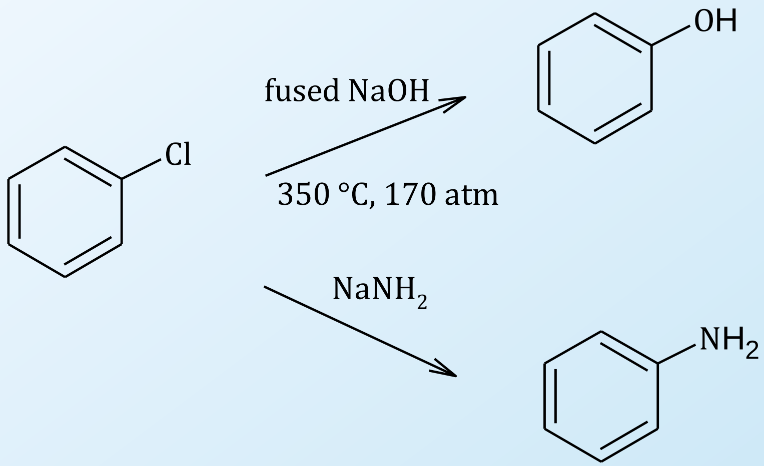


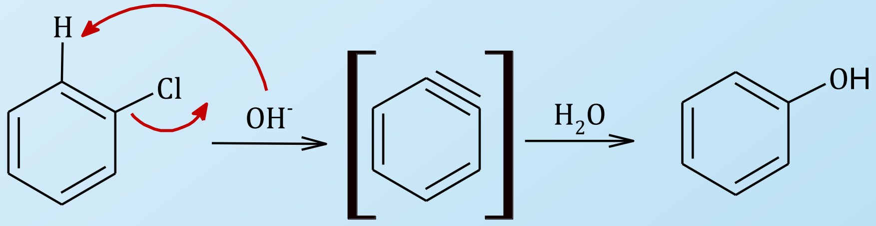
Nucleophilic Substitution on Benzene Ring

Aryl halides do not readily undergo nucleophilic substitution by either S_N1 or S_N2 mechanism since benzene itself is a good nucleophile.

However, substitution can be carried out but by mechanisms quite different from those of aliphatic nucleophilic substitution. Chlorobenzene can be converted to phenol and aniline in industrial conditions.

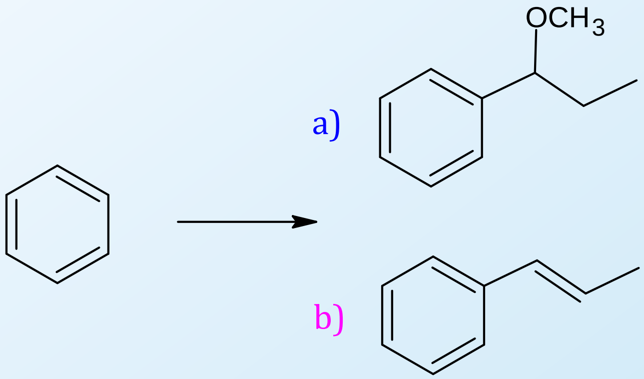
- Phenol can be prepared treatment of chlorobenzene with dilute aqueous NaOH at 340 °C under high pressure.
- Aniline can be synthesized by using sodium amide.
- The reaction mechanism in both cases involves an elimination reaction that gives a triple bond, and the intermediate is called benzyne.



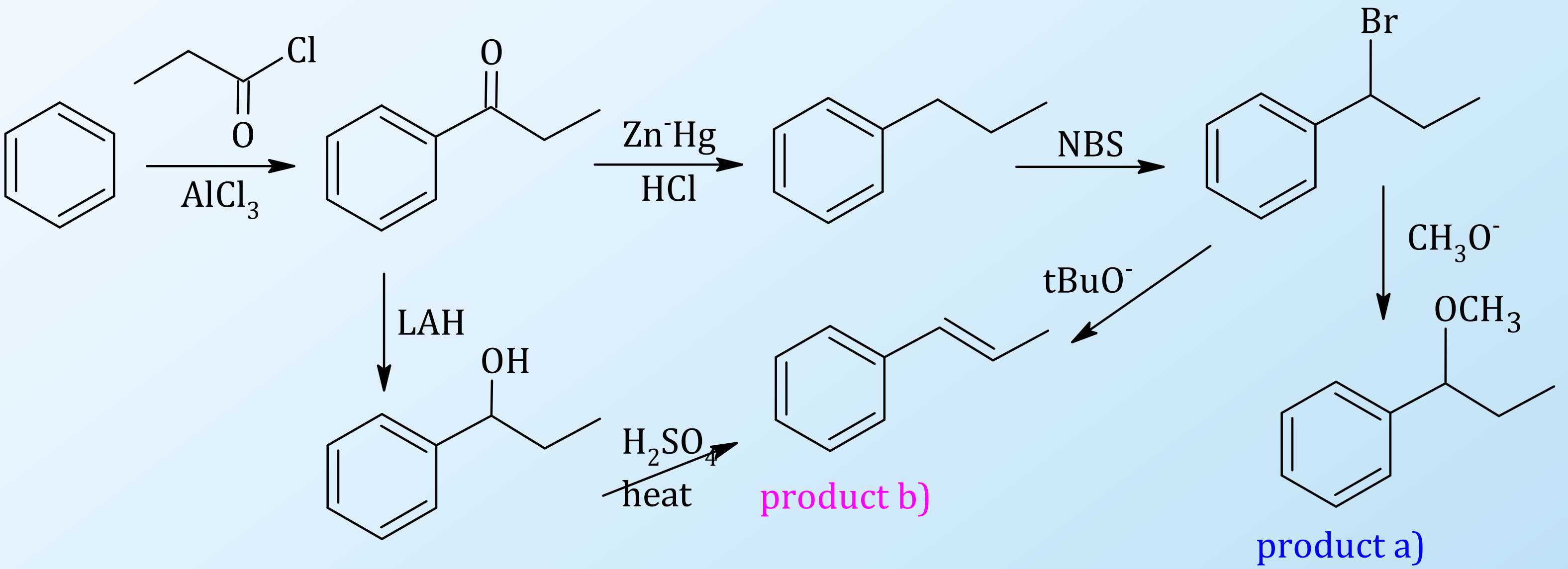


Worked Example

Carry out the following synthesis using appropriate reagents and any organic substances needed.



Answer: Both are side reactions of benzene so we can start the same way – FC acylation to make a propyl group, then do side reactions as appropriate for products a and b. ***NOTE***: I have given two different ways to make b.



Key Concepts

- Oxidation of side chain
- Side chain reactions (benzylic position reactions)
- Reductions
- Nucleophilic reaction on benzene