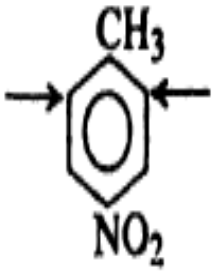
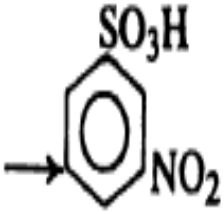
Orientation in disubstituted benzenes

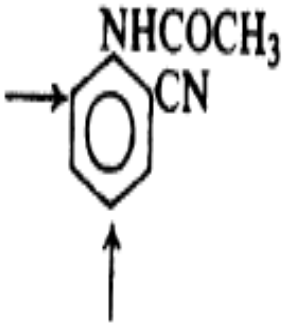
The presence of two substituents on a ring makes the problem of orientation more complicated, but even here we can frequently make very definite predictions. First of all, the two substituents may be located so that the directive influence of one reinforces that of the other for example, in I, II, and III the orientation clearly must be that indicated by the arrows.



I



II

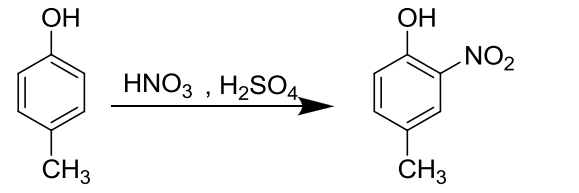


III

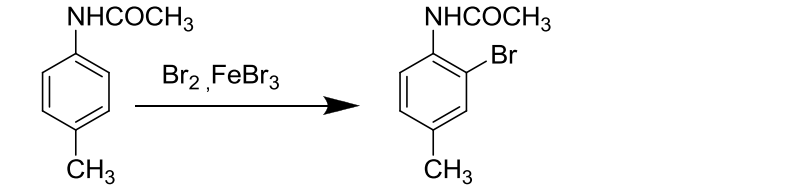
On the other hand, when the directive effect of one group opposes that of the other, it may be difficult to predict the major product; in such cases complicated mixtures of several products are often obtained.Even where there are opposing effects, however, it is still possible in certain cases to make predictions in accordance with the following generalizations.

(a) Strongly activating groups generally win out over deactivating or weakly activating groups. The differences in directive power in the sequence
$-NH_2$, $-OH$ > $-OCH_3$, $-NHCOCH_3$ > $-C_6H_5$, $-CH_3$ > Meta directors

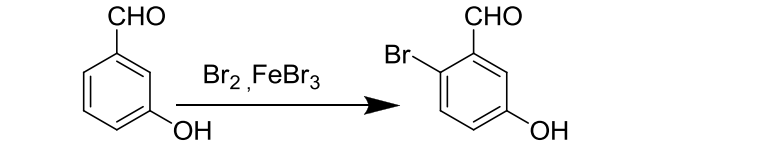
For example:



p-cresol 4-methyl-2-nitrophenol

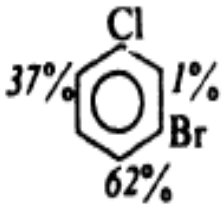


N-*p*-tolylacetamide *N*-(2-bromo-4-methylphenyl)acetamide

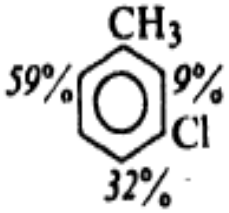


3-hydroxybenzaldehyde 2-bromo-5-hydroxybenzaldehyde
Chief product

(b) There is often little substitution between two groups that are Meta to each other. In many cases it seems as though there just is not enough room between two groups located Meta to each other for appreciable substitution to occur there, as illustrated by IV and V.



Nitration
IV

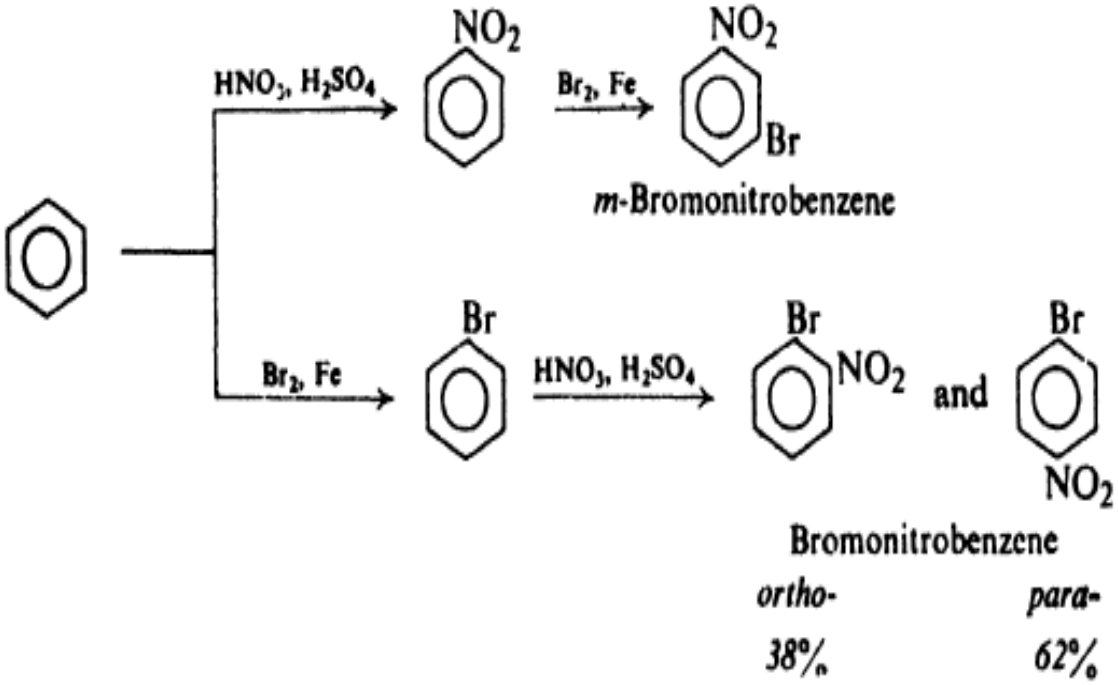


Nitration
V

Orientation and synthesis

A laboratory synthesis is generally aimed at obtaining a single, pure compound. Whenever possible we should avoid use of a reaction that produces a mixture, since this lowers the yield of the compound we want and causes difficult problems of purification. With this in mind, let us see some of the ways in which we can apply our knowledge of orientation to the

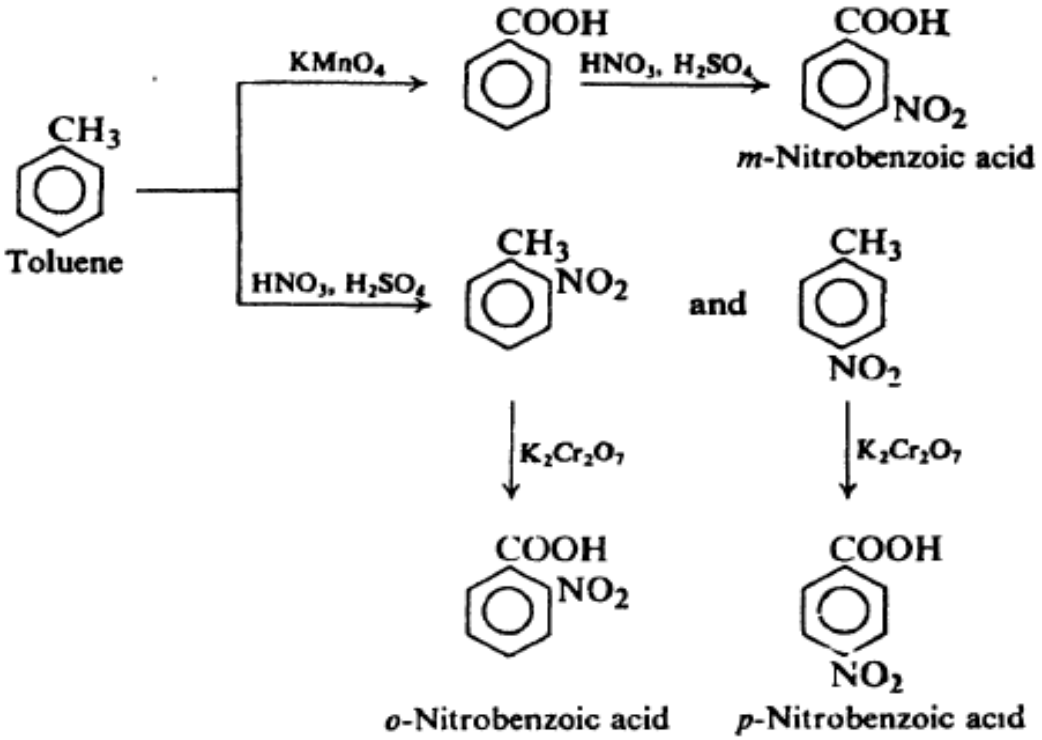
synthesis of pure aromatic compounds. First of all, we must consider the order in which we introduce these various substituents into the ring. In the preparation of the bromonitrobenzenes, for example, it is obvious that if we nitrate first and then brominate, we will obtain the ***m***-isomer; whereas if we brominate first and then nitrate, we will obtain a mixture of the ***o***- and ***p***-isomers. The order in which we decide to carry out the two steps, then, depends upon which isomer we want

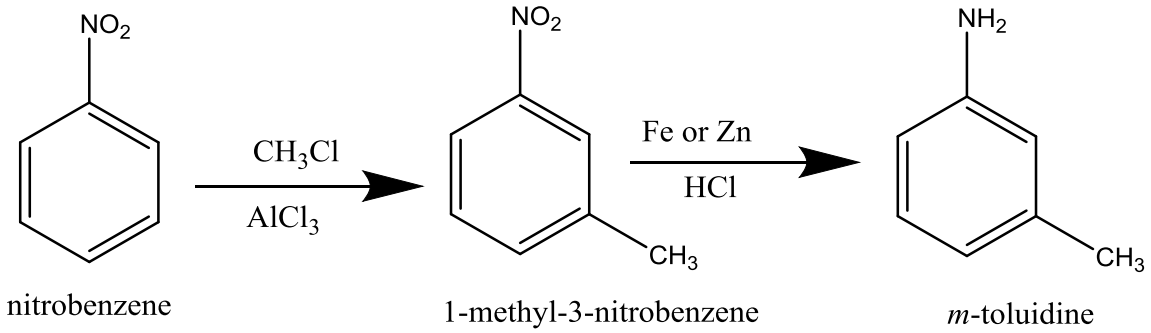


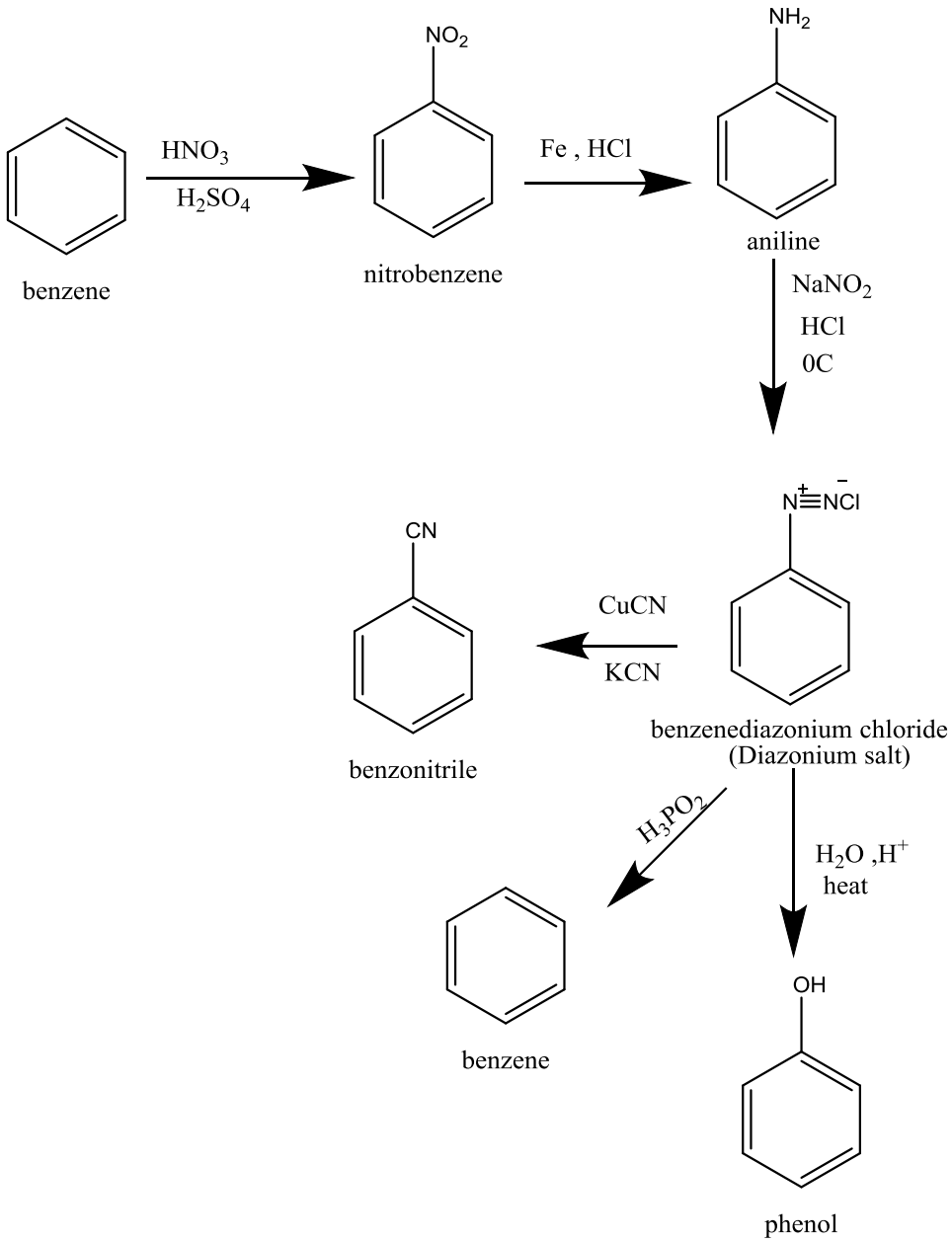
Next, if our synthesis involves conversion of one group into another, we must consider the proper time for this conversion. For example, oxidation of a methyl group yields a carboxyl group. In the preparation of nitrobenzoic acids from toluene, the particular product obtained depends upon whether oxidation or nitration is carried out first.

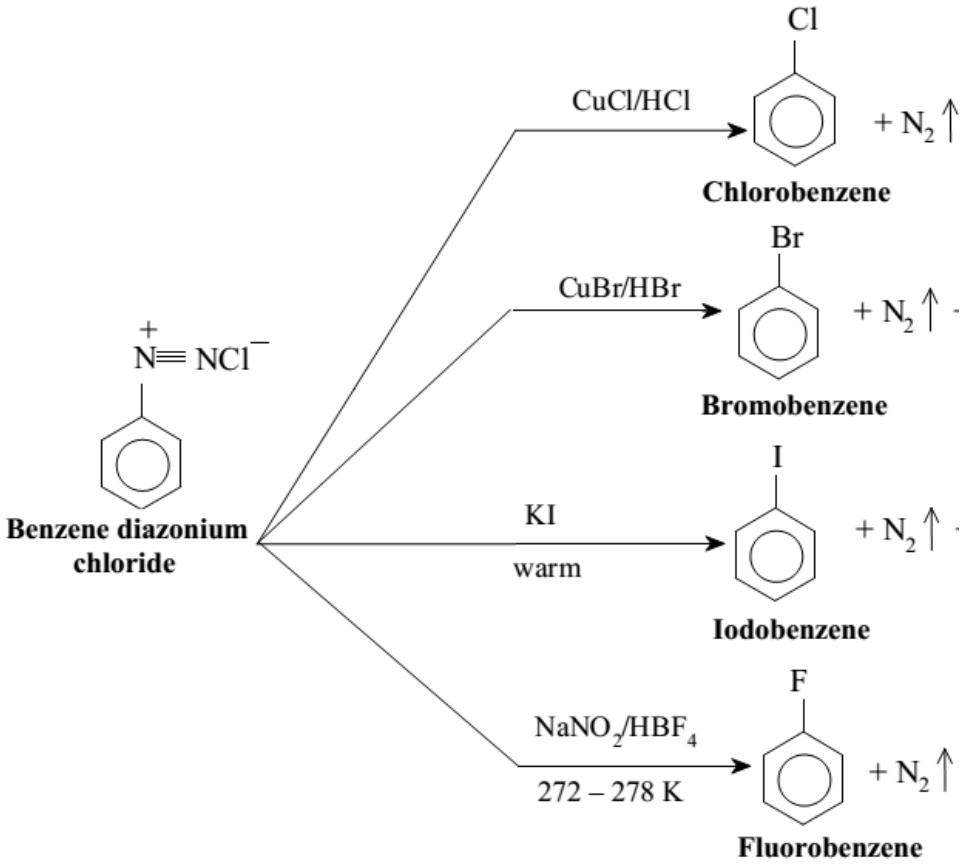
Substitution controlled by an activating group yields a mixture of *ortho* and *para* isomers; nevertheless, we must often make use of such reactions, as in the examples just shown. It is usually possible to obtain the pure *para* isomer from the mixture by fractional crystallization. As the more symmetrical isomer, it is the less soluble, and crystallizes while the solvent still retains the soluble *ortho* isomer. Some *para* isomer, of course, remains

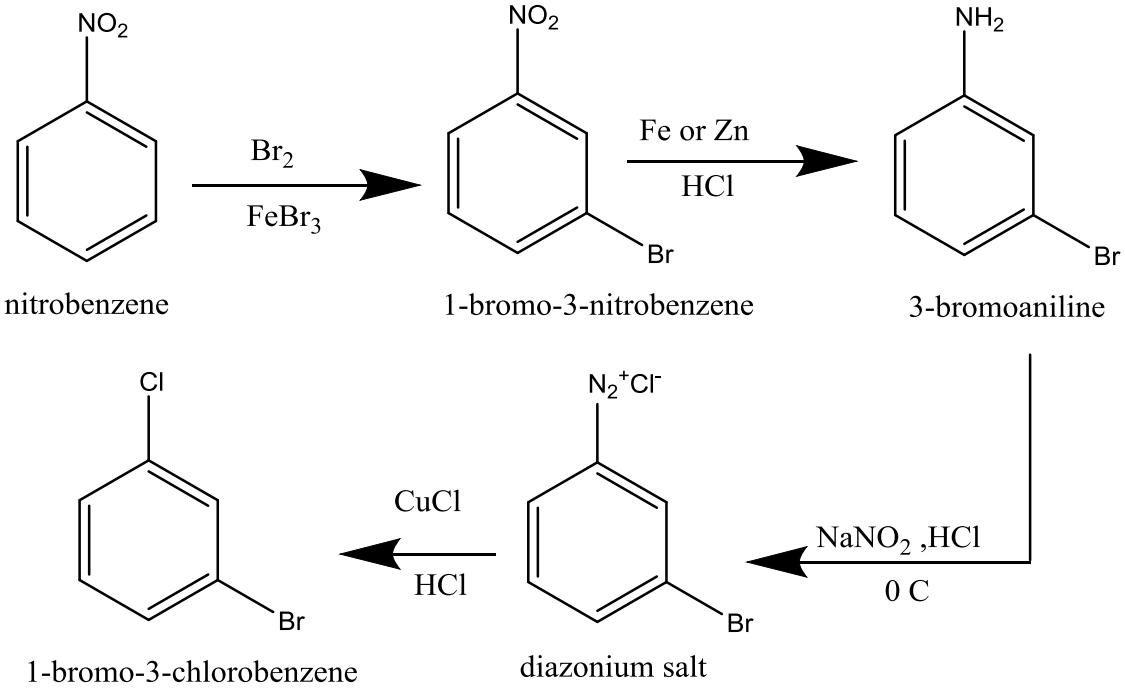
in solution to contaminate the *ortho* isomer, which is therefore difficult to purify. As we shall see, special approaches are often used to prepare ortho isomers






benzene
HNO3
H2SO4
NO2
nitrobenzene
Fe , HCl
NH2
aniline
NaNO2
HCl
0C
N≡NCl
benzenediazonium chloride
(Diazonium salt)
CuCN
KCN
CN
benzonitrile
H3PO2
H2O ,H+
heat
benzene
OH
phenol

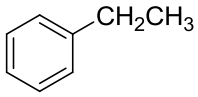

Cl
CuCl/HCl
+ N2
Chlorobenzene
Br
CuBr/HBr
+ N2
Bromobenzene
+
N≡ NCl−
Benzene diazonium chloride
I
KI
warm
+ N2
Iodobenzene
F
NaNO2/HBF4
272 – 278 K
+ N2
Fluorobenzene


NO2
Br2
FeBr3
Br
nitrobenzene
1-bromo-3-nitrobenzene
Fe or Zn
HCl
NH2
Br
3-bromoaniline
NaNO2 ,HCl
0 C
N2+Cl-
Br
diazonium salt
CuCl
HCl
Cl
Br
1-bromo-3-chlorobenzene

Aliphatic-aromatic hydrocarbons

Many important compounds are not just aliphatic or just aromatic, however, but contain both aliphatic and aromatic units; hydrocarbons of this kind are known collectively as arenes. ***Ethylbenzene***, for example, contains a benzene ring and an aliphatic side chain

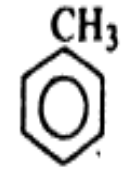
.



ethylbenzene

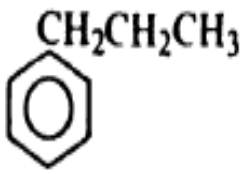
The ring of ethylbenzene undergoes the electrophilic substitution characteristic of benzene, and the side chain undergoes the free radical substitution characteristic of ethane. Second, the properties of each portion of the molecule should be modified by the presence of the other portion. The ethyl group should modify the aromatic properties of the ring, and the ring should modify the aliphatic properties of the side chain .Treatment of ethylbenzene with nitric acid and sulfuric acid, for instance, introduces a nitro group into the ring; treatment with bromine in the presence of light introduces a bromine atom into the side chain. But because of the ethyl group, nitration takes place more readily than with benzene itself, and occurs chiefly at the positions *ortho* and *para* to the ethyl group; and because of the ring, bromination takes place more readily than with ethane, and occurs exclusively on the carbon nearer the ring. Thus each portion of the molecule Affects the reactivity of the other portion and determines the orientation of attack

The simplest of the alkyl benzenes, methylbenzene, is given the special name of toluene. Compounds containing longer side chains are named by prefixing the name of the alkyl group to the word -benzene, as, for example, in ethylbenzene, n-propyl benzene, and isobutyl benzene.

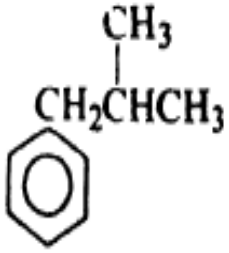


Toluene

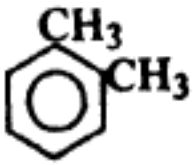
Ethylbenzene



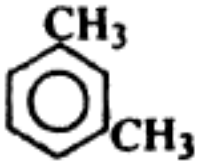
n-Propylbenzene



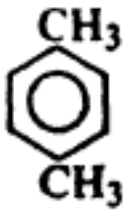
Isobutylbenzene



o-Xylene

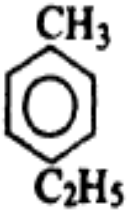


m-Xylene

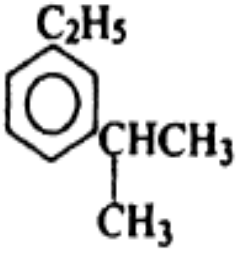


p-Xylene

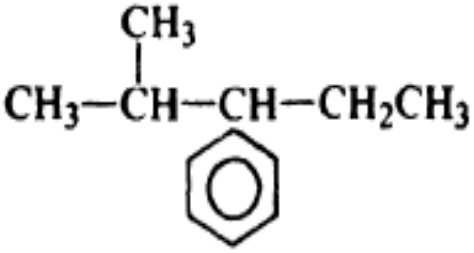
A compound containing a very complicated side chain might be named as a phenyl alkane (***C_6H_5* = *phenyl***). Compounds containing more than one benzene ring are nearly always named as derivatives of alkanes.



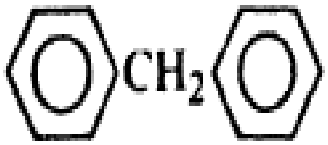
p-Ethyltoluene



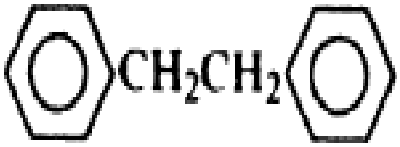
m-Ethylisopropylbenzene



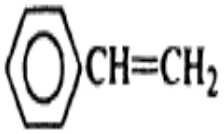
2-Methyl-3-phenylpentane



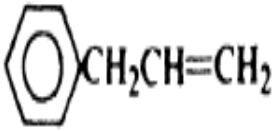
Diphenylmethane



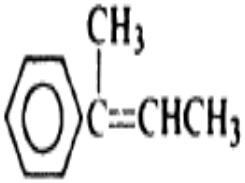
1,2-Diphenylethane



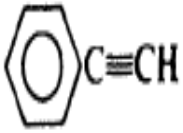
Styrene
(Vinylbenzene)
(Phenylethylene)



Allylbenzene
(3-Phenylpropene)



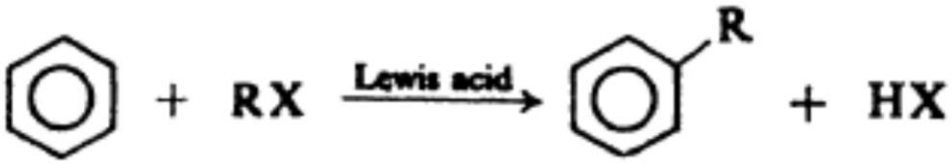
2-Phenyl-2-butene



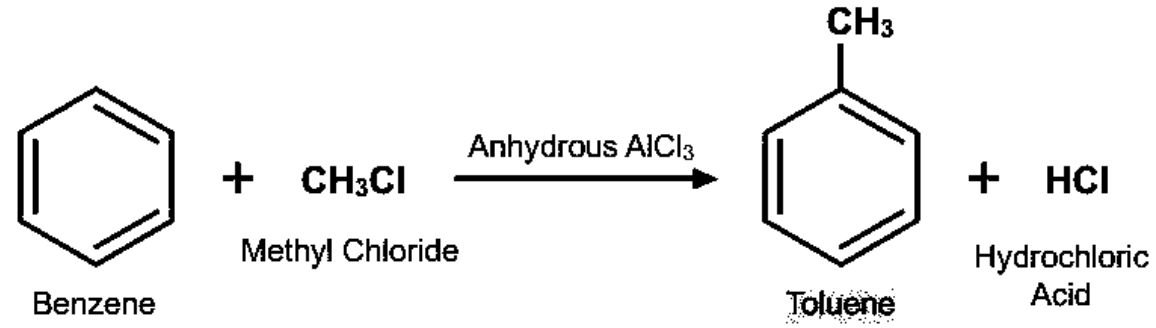
Phenylacetylene

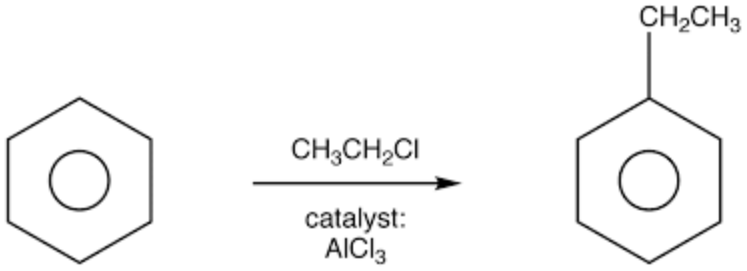
Preparation of alkylbenzenes

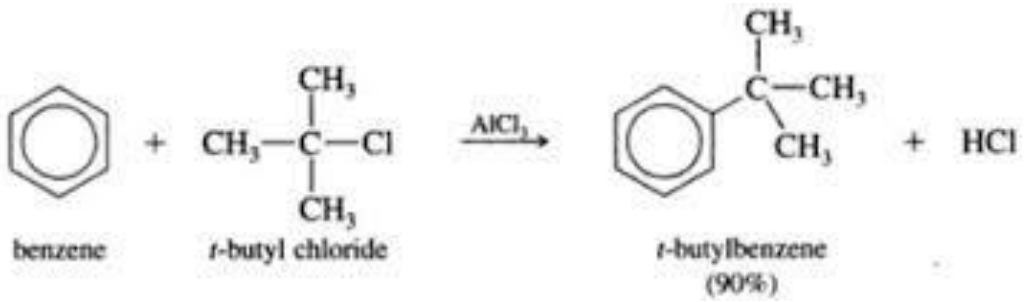
1. Friedel-Crafts alkylation

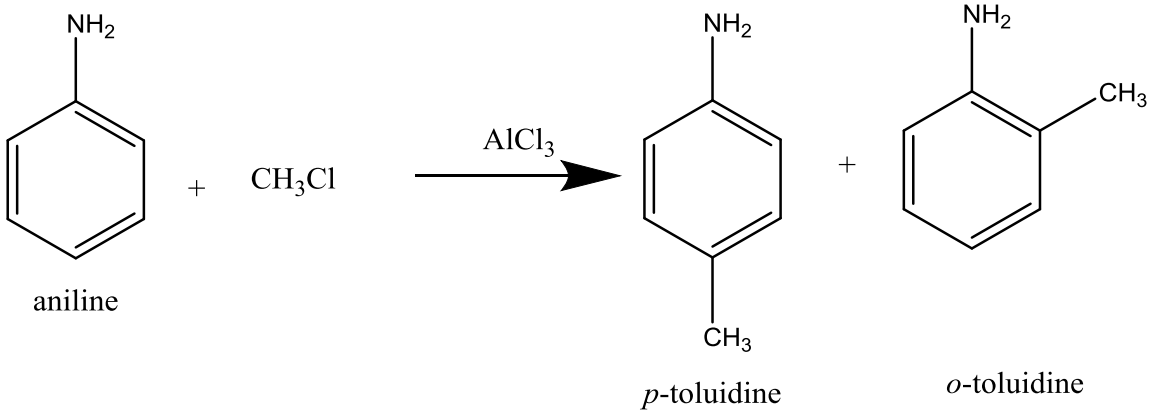


Lewis acid: $AlCl_3$, BF_3, HF, etc.

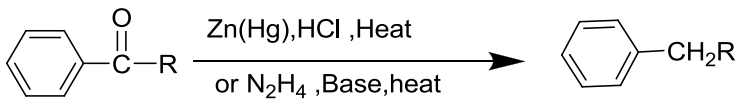

CH3
+ CH3Cl
Anhydrous AlCl3
+ HCl
Methyl Chloride
Benzene
Toluene
Hydrochloric Acid


CH2CH3
CH3CH2Cl
catalyst:
AlCl3

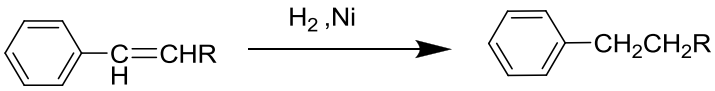

CH3
CH3—C—Cl
CH3
AlCl3
C—CH3
CH3
+ HCl
benzene
t-butyl chloride
t-butylbenzene
(90%)

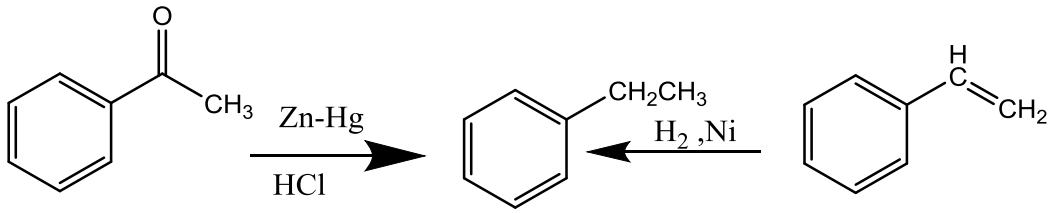

NH2
+ CH3Cl
AlCl3
NH2
CH3
+
NH2
CH3
aniline
p-toluidine
o-toluidine

2. Conversion of side chain



Ketone



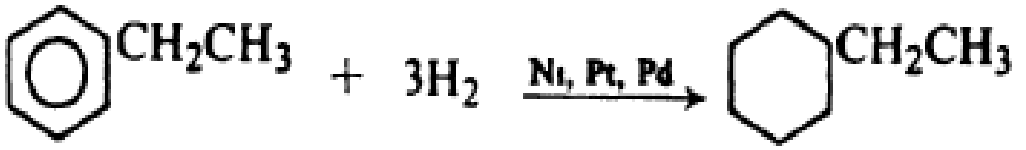


acetophenone ethylbenzene styrene

<u>Reactions of alkylbenzenes:</u>

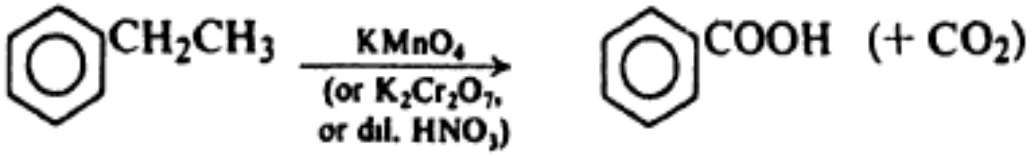
The most important reactions of the alkyl benzenes are outlined below, with toluene and ethylbenzene as specific examples; essentially the same behavior is shown by compounds bearing other side chains. Except for hydrogenation and oxidation, these reactions involve either ***electrophilic substitution in the aromatic ring*** or ***free-radical substitution in the aliphatic side chain.***

1. Hydrogenation:

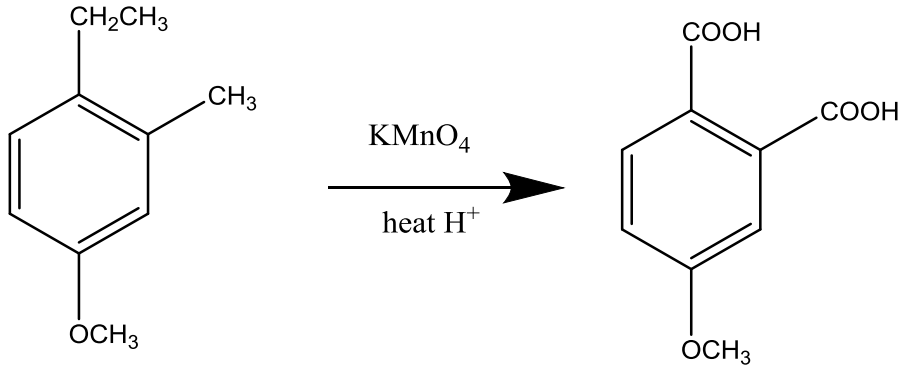


Ethylbenzene Ethylcyclohexane

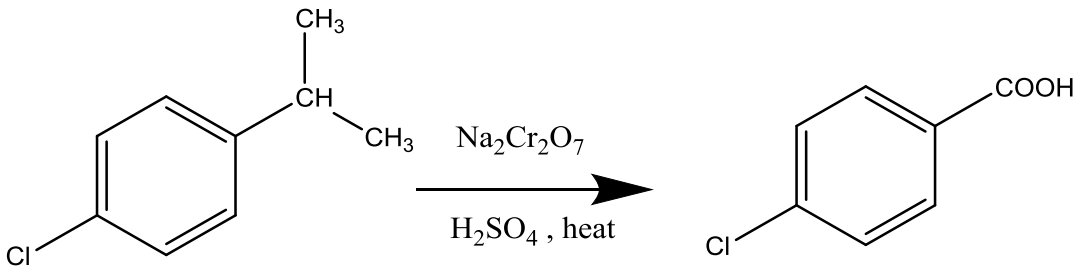
2. Oxidation



Ethylbenzene — Benzoic acid

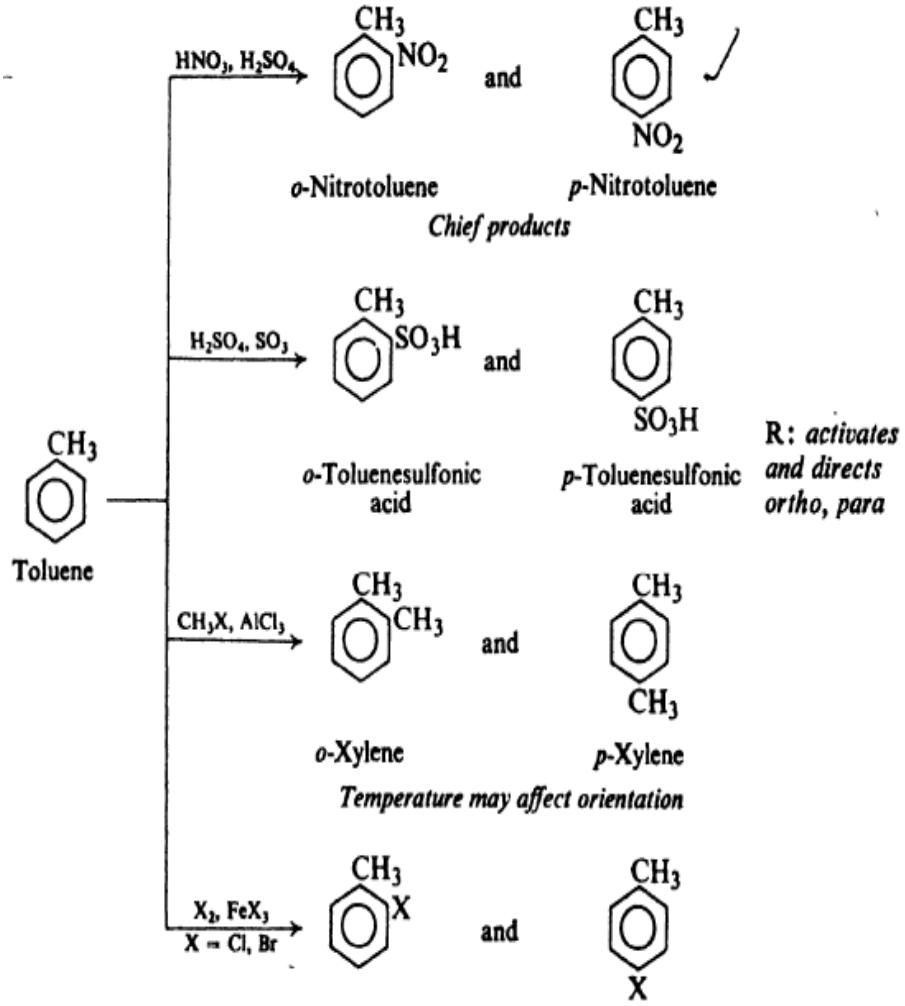


1-ethyl-4-methoxy-2-methylbenzene — 4-methoxyphthalic acid



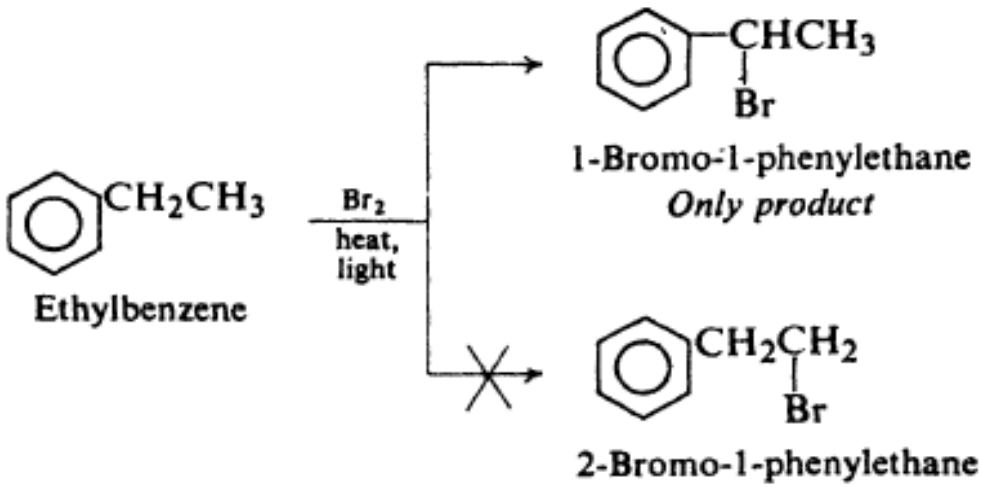
1-chloro-4-isopropylbenzene — 4-chlorobenzoic acid

2) Electrophilic aromatic substitution

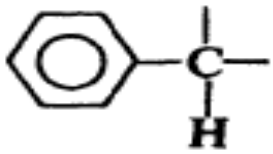


3) Side-chain halogenation (Free-radical halogenations) of alkylbenzenes

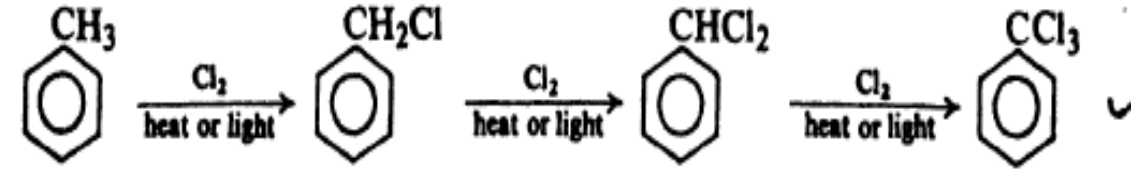
An alkyl benzene with a side chain more complicated than methyl offers more than one position for attack, and so we must consider the likelihood of obtaining a mixture of isomers. Bromination of ethylbenzene, for example, could theoretically yield two products: **1-bromo-l-phenylethane** and **2-bromo-l-phenylethane.**



Practically the 1-Bromo product is the only product. Abstraction of the hydrogen's attacked to the carbon next to the aromatic ring is greatly preferred .Hydrogen atoms attached to carbon joined directly to an aromatic ring are called **benzylic hydrogens.**



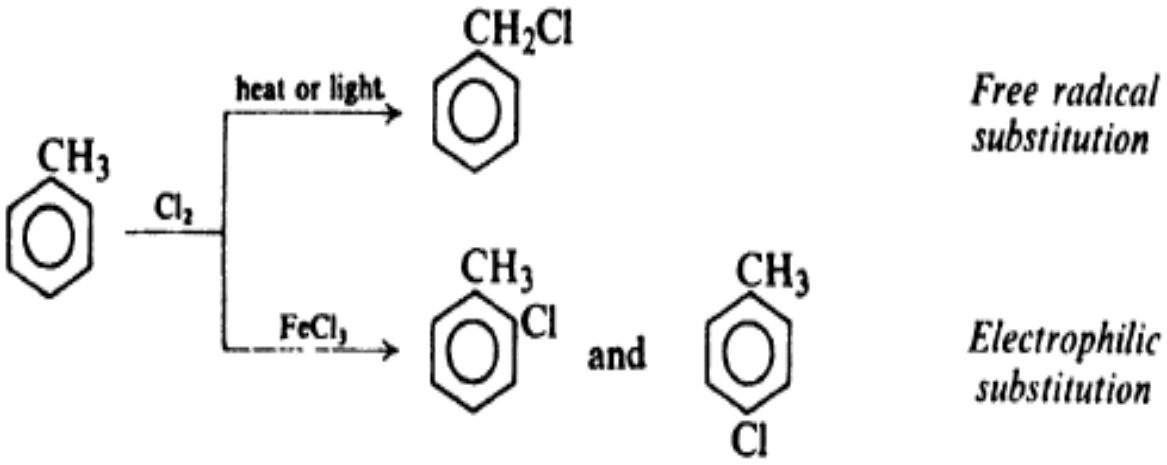
Benzylic hydrogen:



Toluene Benzyl chloride Benzal chloride Benzotrichloride

Ethylbenzene α-Phenylethyl chloride β-Phenylethyl chloride

Chief product



Free radical substitution

Electrophilic substitution