

ELECTROPHILIC AROMATIC SUBSTITUTION I

Department of Pharmaceutical Chemistry

Dr. Husam Hamza

ELECTROPHILIC AROMATIC SUBSTITUTION

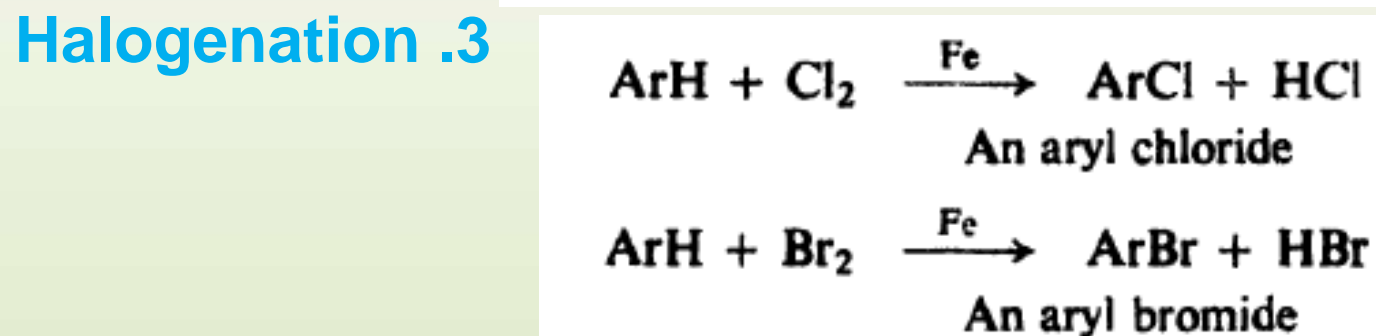
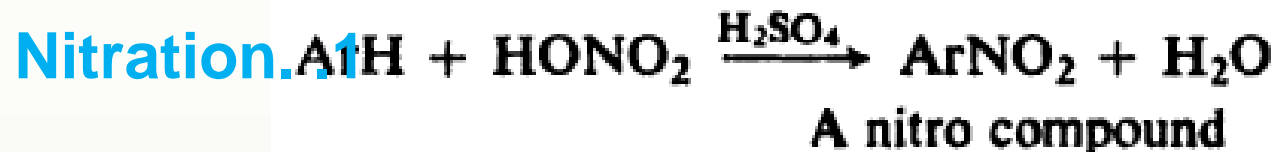
Above and below the plane of the benzene ring there is a cloud of π electrons. Because of resonance ➤

It is not surprising that *in its typical reactions the benzene ring serves as a source of electrons*, that is, as a **base**. The compounds with which it reacts are deficient in electrons, that is, are **electrophilic reagents** or **acids**. Just as the typical reactions of the alkenes are electrophilic addition reactions, so the typical reactions of the benzene ring are **electrophilic substitution reactions** ➤

These reactions are characteristic not only of benzene itself, but of the benzene ring wherever it is found and, indeed, of many aromatic rings, benzenoid and non-benzenoid ➤

Electrophilic Aromatic Substitution Reactions

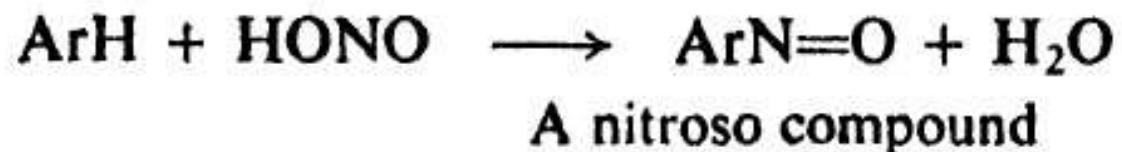
Ar = *aryl*, any aromatic group with attachment directly to ring carbon



4. Friedel-Crafts alkylation

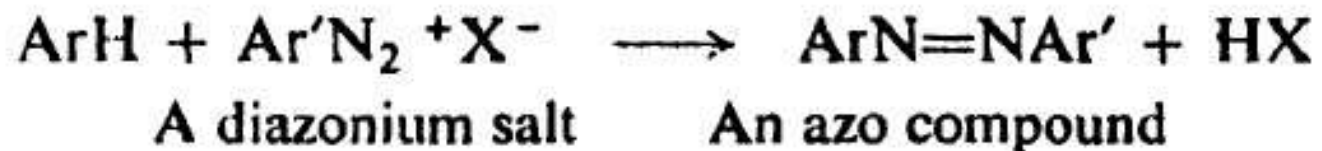


5. Nitrosation



Only for highly reactive ArH

6. Diazo coupling

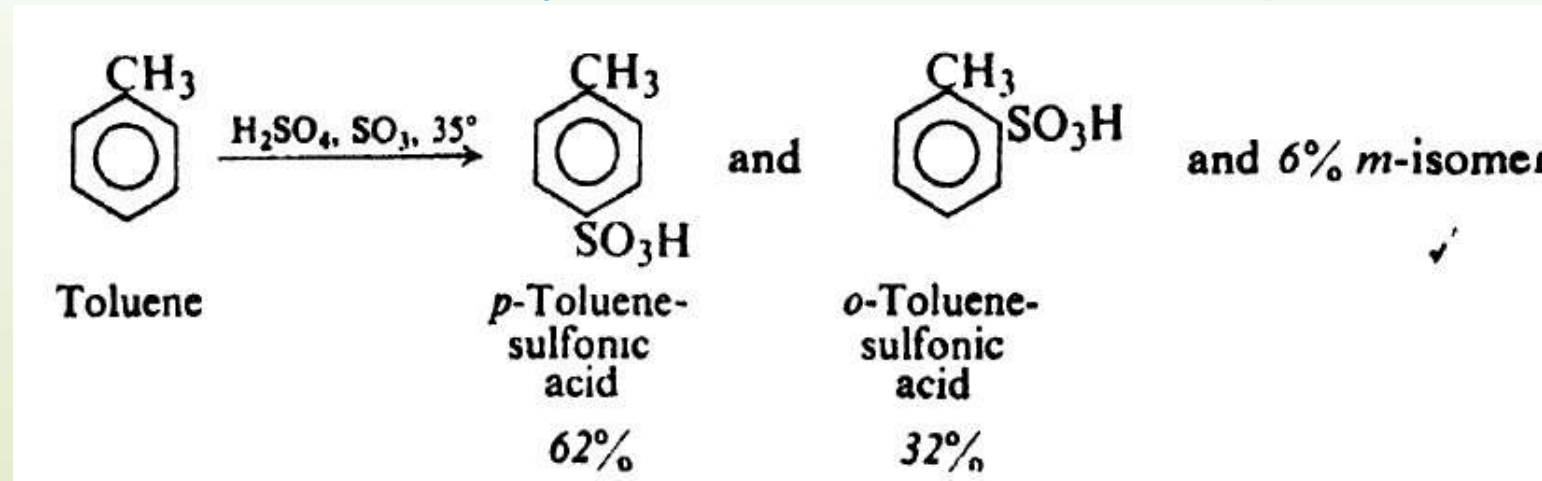


Only for highly reactive ArH


Effect of substituent groups

Like benzene, toluene undergoes electrophilic aromatic substitution: sulfonation ➤

There are three possible monosulfonation products, ➤
this reaction actually yields appreciable amounts of
only two of them: the *o*- and *p*-isomers



A group that makes the ring more reactive than benzene ➤
is called **an activating group**. A group that makes the
ring less reactive than benzene is called a **deactivating
group**



A group that causes attack to occur chiefly at positions *ortho* and *para* to it is called an *ortho*, *para* director. A group that causes attack to occur chiefly at positions *meta* to it is called a *meta* director

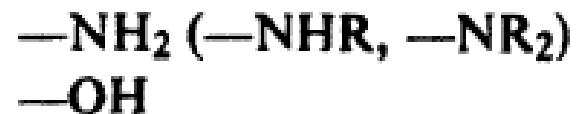
Classification of substituent groups

All groups fall into one of two classes: activating and *ortho* .*para* directing, or deactivating and *meta*-directing. The halogens are in a class by themselves, being deactivating but *ortho*.*para*-directing.

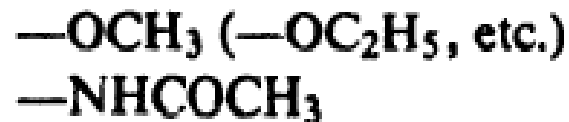
EFFECT OF GROUPS ON ELECTROPHILIC AROMATIC SUBSTITUTION

Activating: *Ortho,para* Directors

Strongly activating



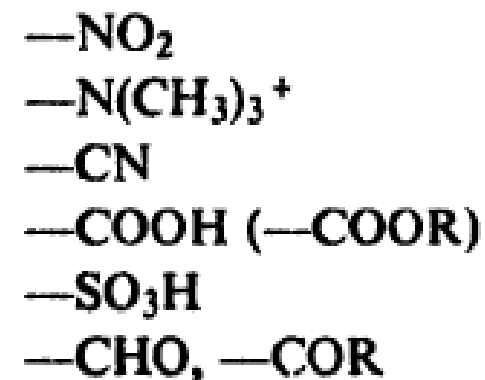
Moderately activating



Weakly activating



Deactivating: *Meta* Directors

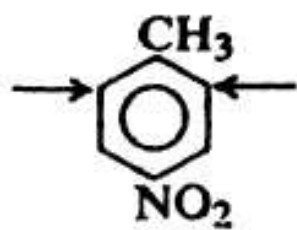


Deactivating: *Ortho,para* Directors

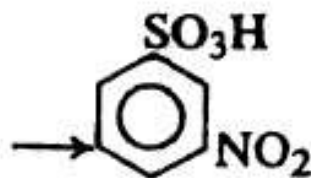


Orientation in disubstituted benzenes

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

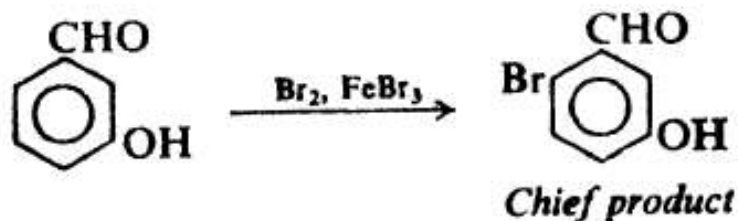
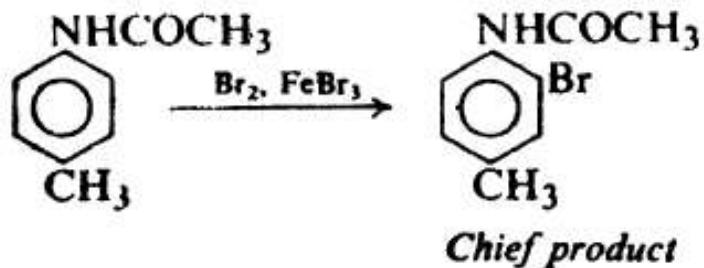
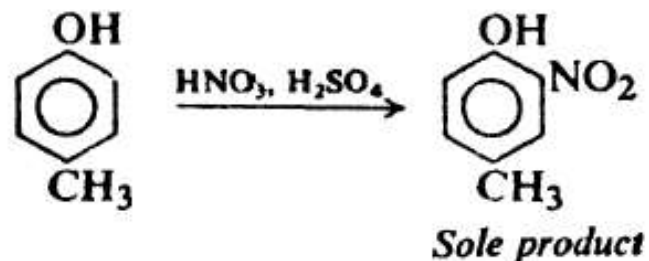


III

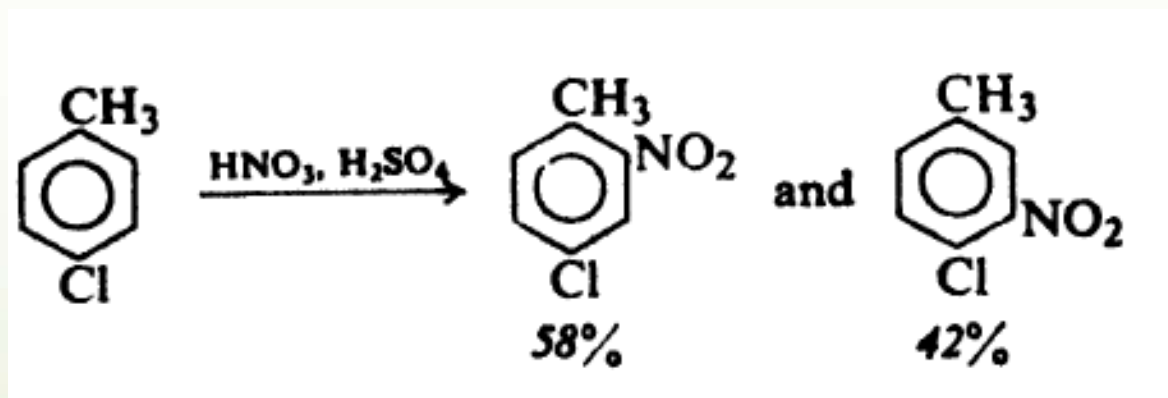
When the directive effect of one group **opposes** that of the other, it may be difficult to predict the major product; in such cases complicated mixtures of several products are often obtained.

(a) Strongly activating groups generally **win out** over **deactivating** or weakly activating groups. The differences in directive power in the sequence

$-\text{NH}_2, -\text{OH} > -\text{OCH}_3, -\text{NHCOCH}_3 > -\text{C}_6\text{H}_5, -\text{CH}_3 > \textit{meta}$ directors



There must be, however, a fairly large difference in the effects of the two groups for clear-cut results; otherwise one gets results like these:



(b) There is often little substitution between two groups that are meta to each other.

