

## LECTURE 1

### 3. Reactions: Electrophilic Substitution

The general equation for this reaction is:

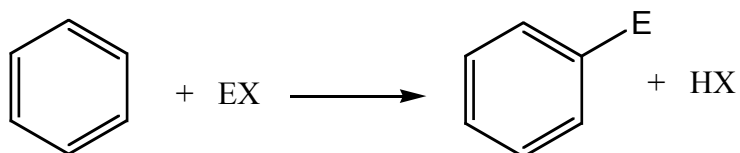


Fig. 1

The ready availability of the  $\pi$ -electrons makes benzene rings nucleophilic i.e. they are susceptible to attack by electrophiles, despite the stability of the ring.

#### (a) Arenium Ion Mechanism:

The reaction passes through an intermediate which is variously called the  $\sigma$ -complex, the Wheland intermediate or the arenium ion:

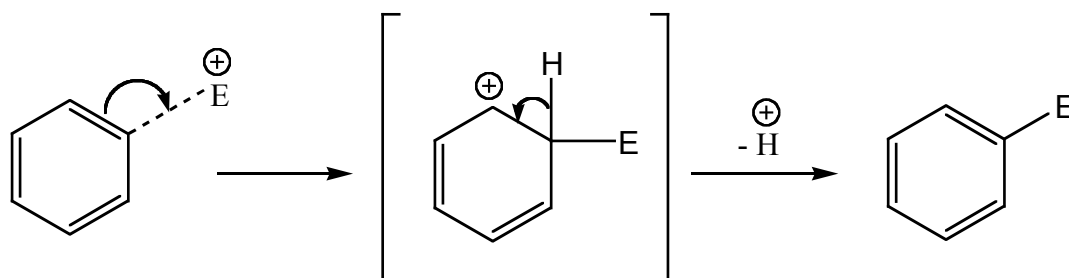


Fig. 2

Although the Wheland intermediate is stabilised by resonance

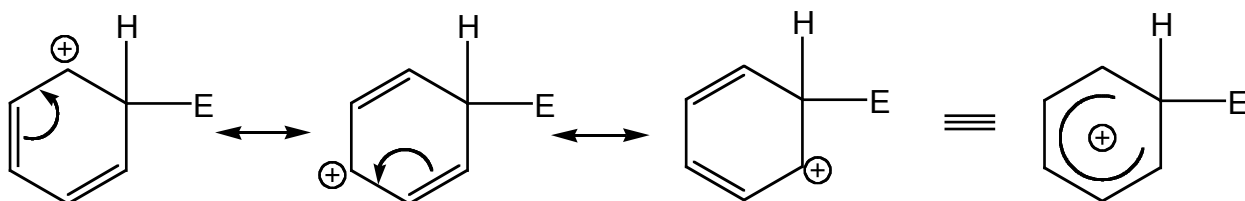


Fig. 3

we have clearly lost the aromatic stabilisation of the starting material and hence the addition of the electrophile is going to be the slow step (rds = rate determining step). The second step will be fast since we regenerate the aromatic system by loss of the proton.

The evidence for the arenium ion mechanism is

- *No deuterium/hydrogen isotope effect in most cases.* If the hydrogen departed before the electrophile added or if the arrival of the electrophile and the departure of the proton were simultaneous then we would expect an isotope effect on the rate of reaction if we replace H by its more massive isotope D (deuterated substrates undergo substitution more slowly than protonated species when C – H(D) is involved in the rate determining step because the C – H bond is weaker than the C – D bond). Thus the lack of an isotope effect means that the proton is lost after the rds.
- *Isolation of an arenium ion.* For example:

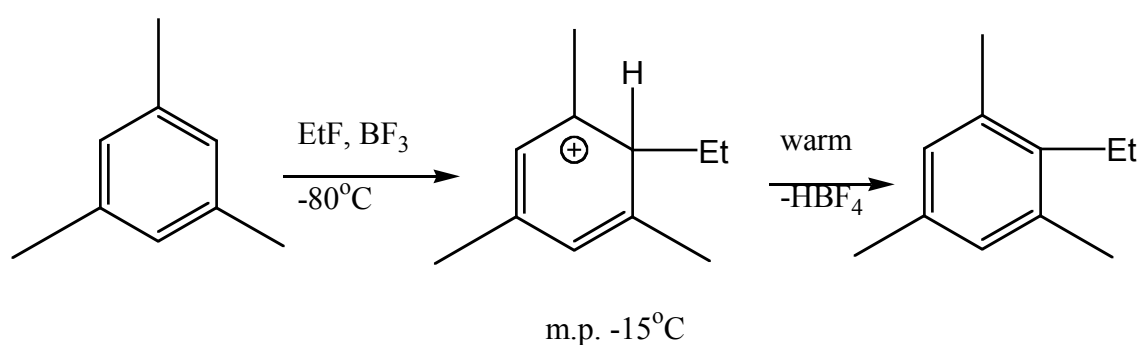
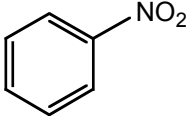
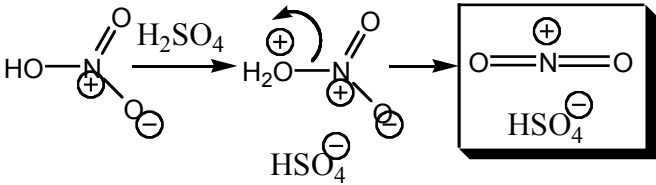
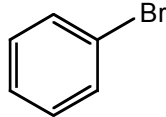
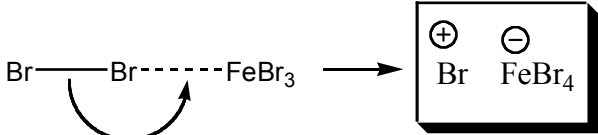
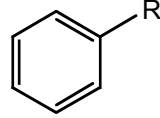
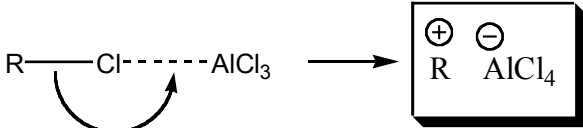
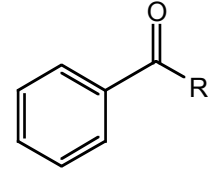
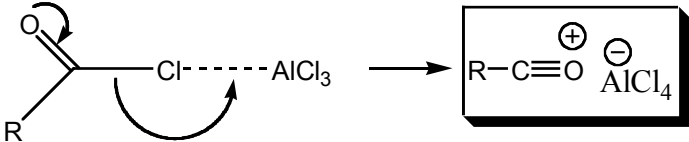
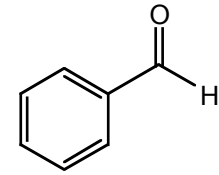
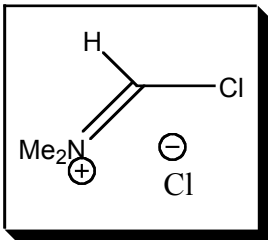
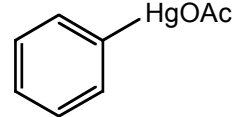
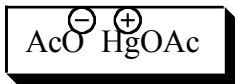
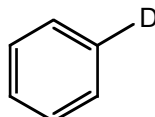

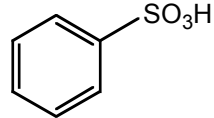
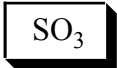


Fig. 4

Even the simplest arenium ion from benzene has been detected by NMR at low temperatures (-134 °C).

The most common types of electrophile are illustrated in the table on the following page. The last reaction on the list, namely sulphonation, is reversible. Heating benzene-sulphonic acid in dilute sulphuric acid or water converts it back to benzene.

Product	Electrophilic Species (boxed)	Reaction Name
		Nitration
		Bromination
		Friedel-Crafts Alkylation
		Friedel-Crafts Acylation
	$\text{Me}_2\text{NCHO} + \text{POCl}_3 \longrightarrow$ 	Vilsmaier-Haack Formylation
		Mercuration
	$\ominus$ 	Deuteration
		Sulphonation

The mechanism for the formation of the Vilsmaier-Haack formylating agent is as follows:

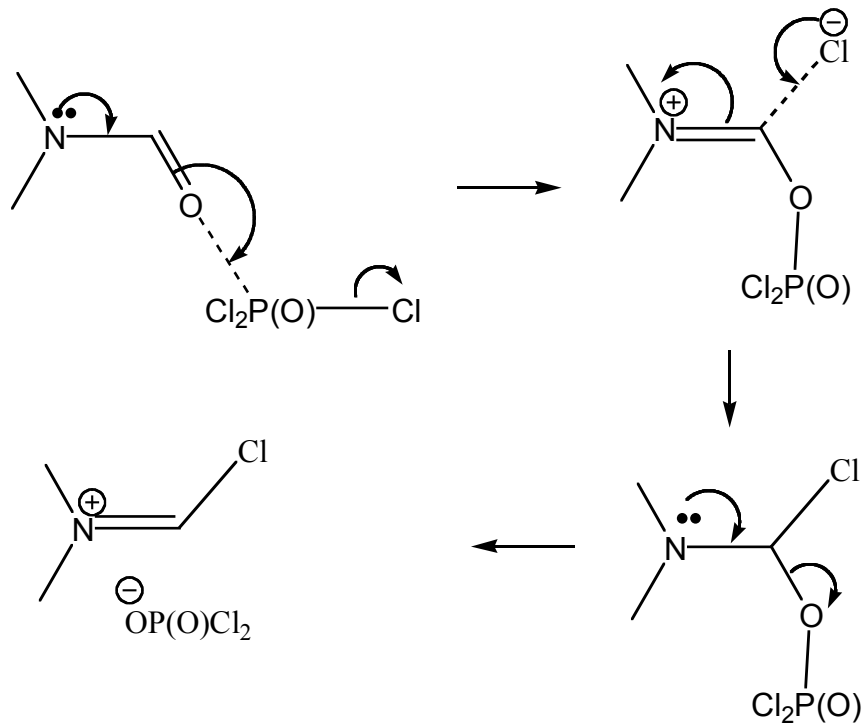


Fig. 5

(b) Reactivity and Orientation: definitions

What do we mean by these terms? If we have a mono-substituted benzene instead of benzene itself then attack by the electrophile can occur in four possible positions (ipso, ortho, meta and para):

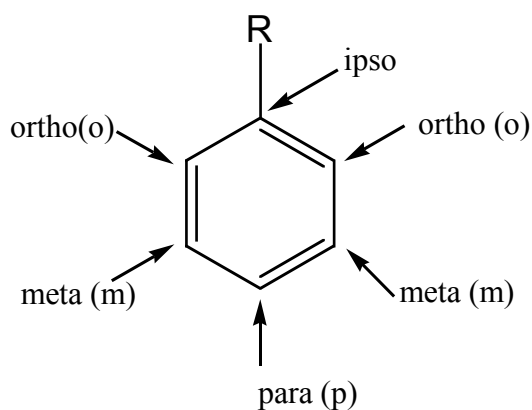


Fig. 6

Which of these sites is attacked is called the Orientation of the reaction.

When compared with benzene, the rate of the reaction of a mono-substituted benzene may be slower or faster. This is the Reactivity of the reaction. If the reaction is slower the substituent is said to deactivate the ring; if faster it activates it. The following illustrate the differences in orientation and reactivity that we may observe:

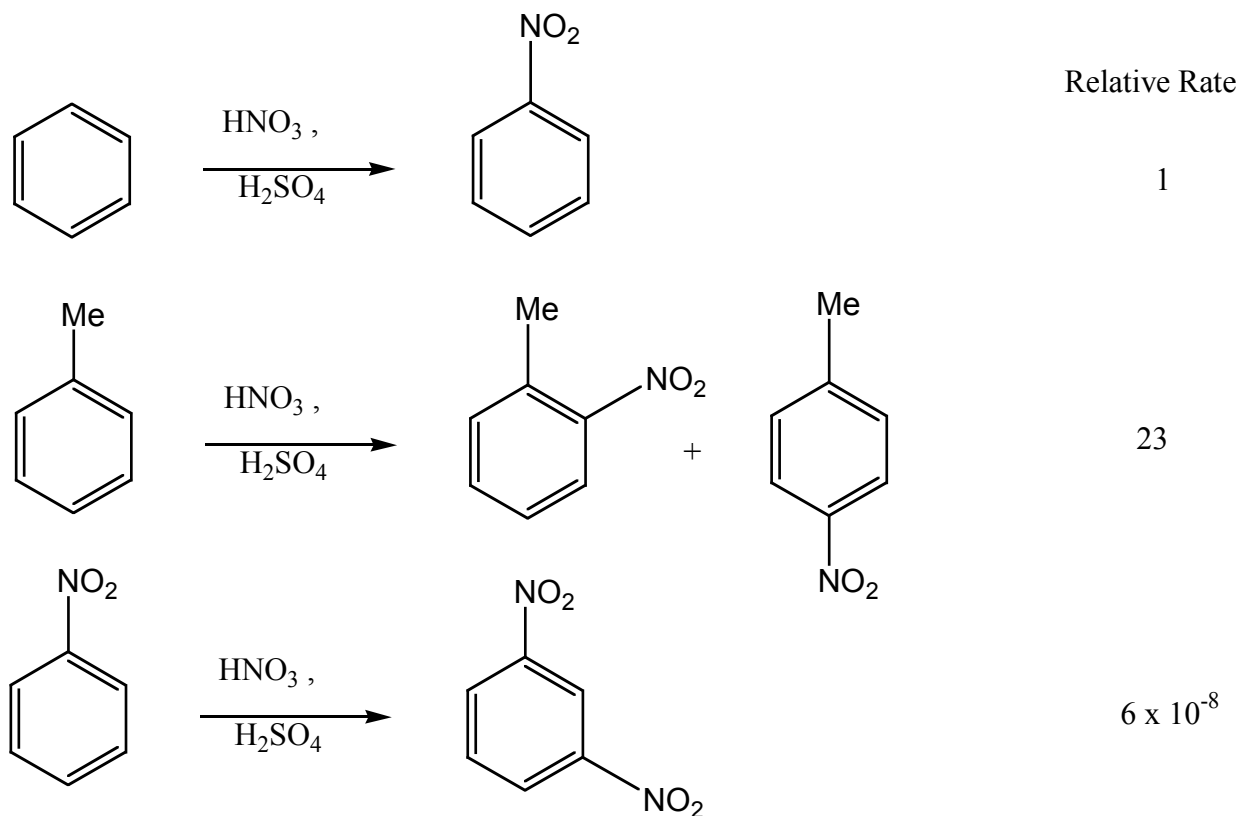


Fig. 7

Thus toluene reacts 23 times faster than benzene and gives a mixture of ortho and para products whereas nitrobenzene is very much less reactive and only gives the meta product.

(c) Reactivity and Orientation: ortho / para – and meta – directors

We must now attempt to classify the groups, R, according to their influence on both reactivity and orientation. Two properties of R have a major influence, namely, inductive (I) effects and resonance (sometimes known by the older term, mesomeric)(Re or M) effects.

The groups, R, fall into the following categories:

- $\text{O}^-$ ,  $\text{NR}_2$ ,  $\text{NHR}$ ,  $\text{NH}_2$ ,  $\text{OH}$ ,  $\text{OR}$ ,  $\text{NHCOR}$ ,  $\text{OCOR}$
- $\text{NO}_2$ ,  $\text{CN}$ ,  $\text{SO}_3\text{H}$ ,  $\text{CHO}$ ,  $\text{COR}$ ,  $\text{CO}_2\text{H}$ ,  $\text{CONH}_2$
- R
- $\text{CO}_2^-$
- $^+\text{NR}_3$ ,  $^+\text{NH}_3$ ,  $\text{CCl}_3$ ,  $\text{CF}_3$
- F, Cl, Br, I

We will now discuss each of these categories in turn.

Category 1:  $\text{O}^-$ ,  $\text{NR}_2$ ,  $\text{NHR}$ ,  $\text{NH}_2$ ,  $\text{OH}$ ,  $\text{OR}$ ,  $\text{NHCOR}$ ,  $\text{OCOR}$

In each case the atom directly attached to the benzene ring is more electronegative than carbon and, therefore, each group has a inductive electron withdrawing, -I, effect (the only exception to this is the  $\text{O}^-$  group where the negative charge repels electrons in the C – O bond). However, countering that effect is a strong +Re effect because each

group has a lone pair of electrons which it is able to donate to the ring by resonance:

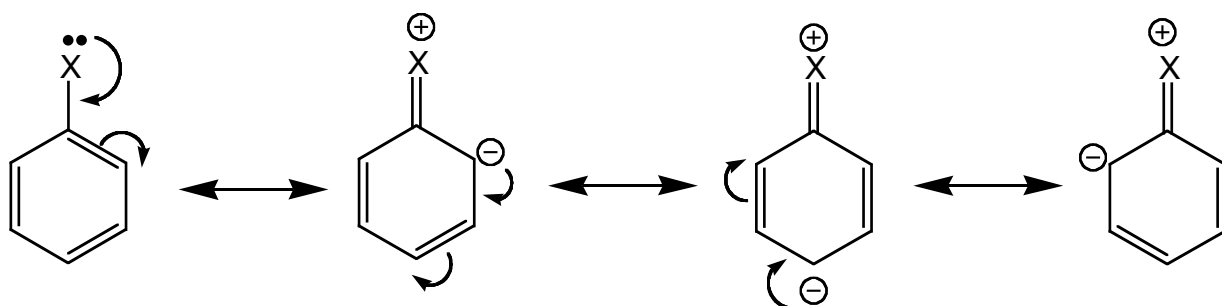


Fig. 8 For  $O^-$ ,  $NR_2$ ,  $NHR$ ,  $NH_2$ ,  $OH$ ,  $OR$   $+Re \gg -I$   
 For  $NHCOR$ ,  $OCOR$   $+Re > -I$

Every one of these groups, therefore, makes the ring more electron rich than benzene and thereby makes the ring more susceptible to attack by electrophiles i.e. aromatics bearing these groups react faster than benzene and the groups are said to be **activating**, strongly so for  $O^-$ ,  $NR_2$ ,  $NHR$ ,  $NH_2$ ,  $OH$ ,  $OR$  and moderately so for  $NHCOR$ ,  $OCOR$ . The latter are less activating than the former because the lone pairs on N or O are to some extent also being delocalised into the carbonyls:

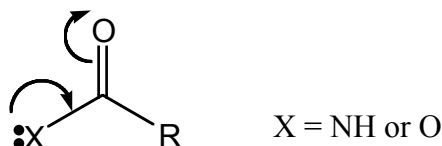


Fig. 9

With regard to the orientation we may explain the product distribution by the charge build up in the starting aromatic, by the stabilisation of the Wheland intermediate or by both. In these cases the resonance effect builds up negative charge only on the *ortho* and *para* positions in the starting material as shown above and, therefore, we would expect the electrophile to attack those positions selectively. The same conclusion is reached if we look at the stabilisation of the Wheland intermediate after such attack compared to attack at the *meta* position (see next page).

Notice that in the attack at either *ortho* or *para* positions the Wheland intermediate has an extra canonical form in which the positive charge may be delocalised onto the atom X by involvement of the lone pair on X; this is not possible on attack at the *meta* position and hence this latter intermediate is less stable than those from either *ortho* or *para* attack. Thus this category of groups is ***ortho* / *para* (o/p) directing** as well as activating.