

09_ Notes

Nucleophilic aromatic substitution has a historical reaction the Dow's process of making phenol from chlorobenzene by hydrolysis with NaOH at 350°C and 300 atm pressure under industrial conditions. The reaction curiously gets easier and easier with introduction of electron withdrawing groups at ortho and para positions. For example, with p-nitrochlorobenzene the reaction takes place at pH 14 at 160°C.

2,4-dinitrochlorobenzene requires a pH of 10 and temperature of 100°C.

With 2,4,6-trinitrochlorobenzene the hydrolysis takes place in warm water. To account for this, the addition-elimination mechanism was proposed (S_NAr mechanism). In this mechanism the nucleophile attacks the aromatic ring at the same carbon atom as the leaving group leading to formation of a carbanion which is stabilised by resonance. Since the negative charge is localised at the two ortho and para positions, the presence of electron withdrawing groups at these positions leads to additional stability. The leaving group then leaves in a fast second step leading to the product. It is pertinent to note that presence of an electron withdrawing group at meta does not assist the reaction in any way and m-nitrochlorobenzene does not react with weak bases like NaHCO₃.

But then something unexpected was noticed. Chlorobenzene when treated with potassium amide in liquid ammonia at -30°C gave aniline. Compared to the industrial reaction first referred to, the conditions are totally different. Then another observation was that 2,4,6-trimethylbromobenzene does not undergo hydrolysis under the same conditions. A third observation was that when compounds of the type o-methylbromobenzene where the bromine is attached to a carbon which is labelled with ¹⁴C, gave 50% product i.e. o-toluidine with the amino group attached to the labelled carbon (normal substitution) and 50% of the product with the amino group at the position ortho to the labelled carbon (cine substitution).

To account for these observation, another mechanism was proposed. The elimination-addition or the 'benzyne' mechanism. In this mechanism the incoming nucleophile picks up a proton from the position ortho to the leaving group leading to the formation of a carbanion at the ortho position. This explains why compounds with no proton at the ortho position to the leaving group do not react. The carbanion then knocks out the leaving group leading to the formation of an intermediate 'Benzyne', a species where there is a triple bond between two carbon atoms of the benzene ring. Benzyne is a symmetrical intermediate. In the second step, the incoming nucleophile attacks any one of the carbon atoms linked by the triple bond and this is followed by protonation leading to the two products, the normal and cine substituted products.

The formation of a benzyne intermediate has been proved by trapping it in a Diels-Alder reaction with a suitable diene.