18.10: NUCLEOPHILIC AROMATIC SUBSTITUTION - THE ADDITION-ELIMANTION MECHANISM

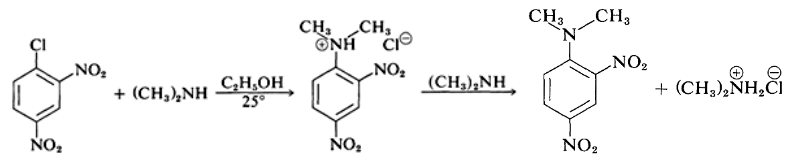
A NUCLEOPHILIC AROMATIC DISPLACEMENT REACTIONS OF ARYL HALIDES

The carbon-halogen bonds of aryl halides are like those of alkenyl halides in being much stronger than those of alkyl halides. The simple aryl halides generally are resistant to reaction with nucleophiles in either S_N1 or S_N2 reactions. However, this low reactivity can be changed dramatically by changes in the reaction conditions and the structure of the aryl halide. In fact, nucleophilic displacement becomes quite rapid

a. when the aryl halide is activated by substitution with strongly electron-attracting groups such as $N0_2$, and
b. when very strongly basic nucleophilic reagents are used.

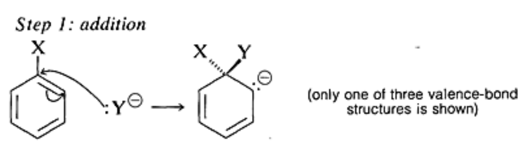
ADDITION-ELIMINATION MECHANISM OF NUCLEOPHILIC SUBSTITUTION OF ARYL HALIDES

Although the simple aryl halides are inert to the usual nucleophilic reagents, considerable activation is produced by strongly electron-attracting substituents provided these are located in either the ortho or para positions, or both. For example, the displacement of chloride ion from 1-chloro-2,4-dinitrobenzene by dimethylamine occurs readily in ethanol solution at room temperature. Under the same conditions chlorobenzene completely fails to react; thus the activating influence of the two nitro groups amounts to a factor of at least 108:



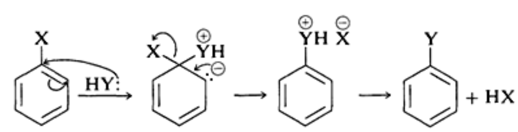
In general, the reactions of activated aryl halides closely resemble the S_N2-displacement reactions of aliphatic halides. The same nucleophilic reagents are effective (e.g., CH_3O^-, HO^-, and RNH_2); the reactions are second order overall (first order in halide and first order in nucleophile); and for a given halide the stronger the nucleophile, the faster the reaction. However, there must be more than a subtle difference in mechanism because an aryl halide is unable, to pass through the same type of transition state as an alkyl halide in S_N2 displacements.

The generally accepted mechanism of nucleophilic aromatic substitution of aryl halides carrying activating groups involves two steps that are closely analogous to those described for alkenyl and alkynyl halides. The first step involves the nucleophile $Y:^-$ reacting with the carbon bearing the halogen substituent to form an intermediate carbanion (Equation 14-3). The aromatic system is destroyed on forming the anion, and the carbon at the reaction site changes from planar (sp^2 bonds) to tetrahedral (sp^3 bonds).



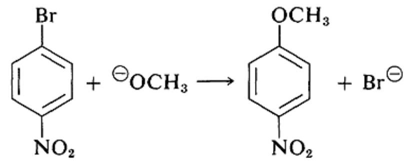
(14-3)

In the second step, loss of an anion, X^- or Y^-, regenerates an aromatic system. If X^- is lost, the overall reaction is nucleophilic displacement of X by Y. In the case of a neutral nucleophilic reagent, Y or HY, the reaction sequence would be the same except for the necessary adjustments in the charge of the intermediate:



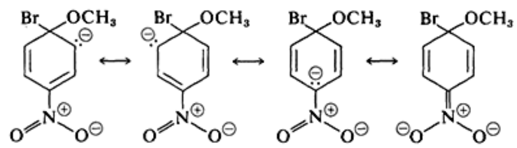
Why is this reaction pathway generally unfavorable for the simple aryl halides? The answer is that the anionic intermediate is too high in energy to be formed at any practical rate. Not only has the anion lost the aromatic stabilization of the benzene ring, but its formation results in transfer of negative charge to the ring carbons, which themselves are not very electronegative:

However, when strongly electron-attracting groups are located on the ring at the ortho-para positions, the intermediate anion is stabilized by delocalization of electrons from the ring carbons to more favorable locations on the substituent groups. As an example, consider the displacement of bromine by $^-OCH_3$ in the reaction of 4-bromonitrobenzene and methoxide ion:



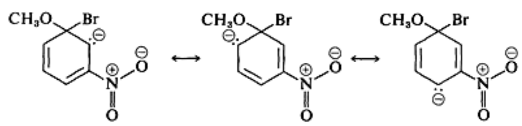
4-nitromethoxybenzene

The anionic intermediate formed by addition of methoxide ion to the aryl halide can be described by the valence-bond structures 5a-5d. Of these structures 5d is especially important because the charge is transferred from the ring carbons to the electronegative oxygen of the nitro substituent:

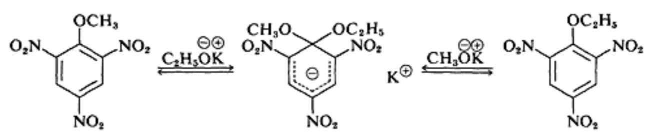


5a 5b 5c 5d

Substituents in the meta positions have much less effect on the reactivity of an aryl halide because delocalization of electrons to the substituent is not possible. No formulas can be written analogous to 5c and 5d in which the negative charges are both on atoms next to positive nitrogen, $\overset{\ominus}{C}-\overset{\oplus}{N}-\overset{\ominus}{O}$ and $\overset{\ominus}{O}-\overset{\oplus}{N}-\overset{\ominus}{O}$,



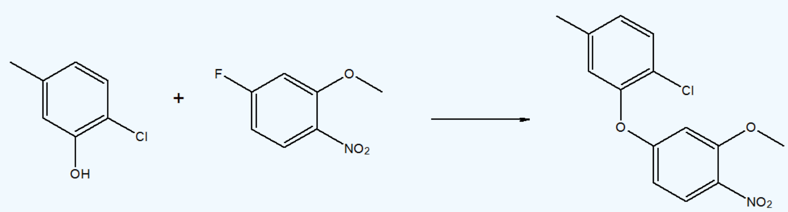
In a few instances, stable compounds resembling the postulated reaction intermediate have been isolated. One classic example is the complex 7 (isolated by J. Meisenheimer), which is the product of the reaction of either the methyl aryl ether 6 with potassium ethoxide, or the ethyl aryl ether 8 and potassium methoxide:



6 7 8

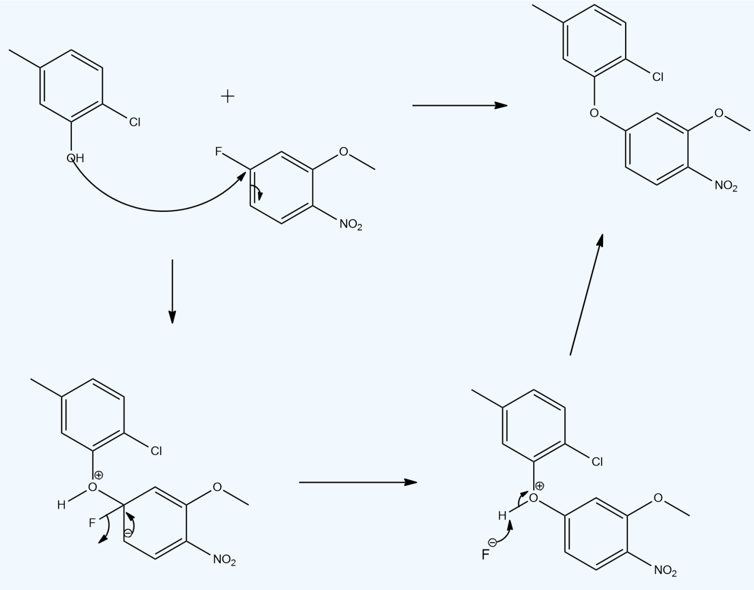
Exercise

24. Propose a mechanism for the following reaction:



Answer

24.



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