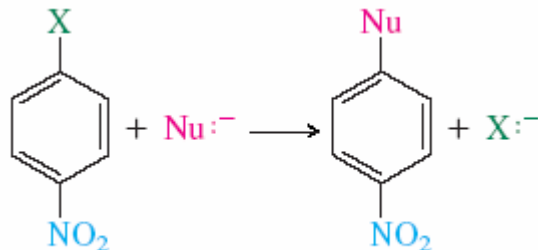


Aryl Halides

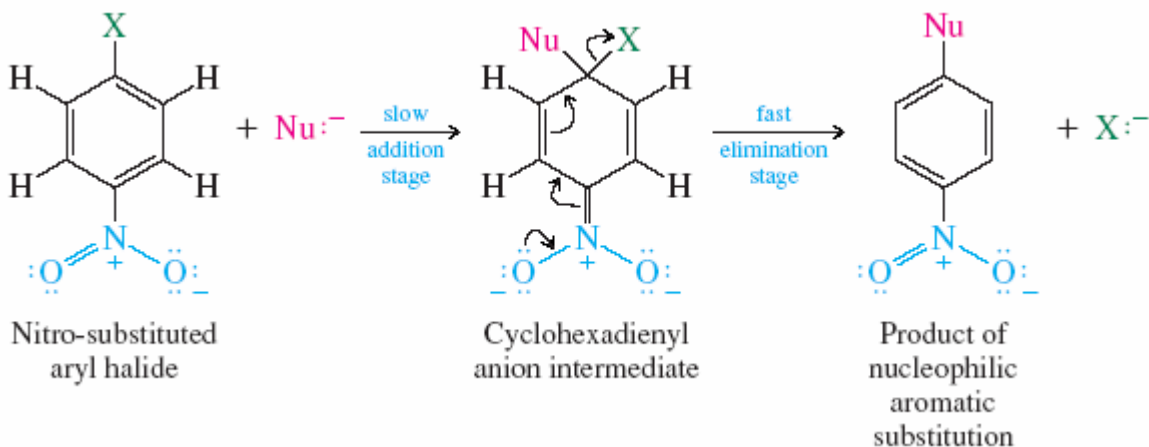
SUMMARY

- Section 23.1 Aryl halides are compounds of the type ArOX where X = F, Cl, Br, or I. The carbon–halogen bond is stronger in ArX than in an alkyl halide (RX).
- Section 23.2 Some aryl halides occur naturally, but most are the products of organic synthesis. The methods by which aryl halides are prepared were recalled in Table 23.2
- Section 23.3 Aryl halides are less polar than alkyl halides.
- Section 23.4 Aryl halides are less reactive than alkyl halides in reactions in which COX bond breaking is rate-determining, especially in nucleophilic substitution reactions.
- Section 23.5 Nucleophilic substitution in ArX is facilitated by the presence of a strong electron-withdrawing group, such as NO₂, ortho or para to the halogen.



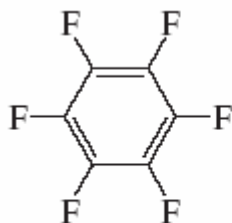
In reactions of this type, fluoride is the best leaving group of the halogens and iodide the poorest.

- Section 23.6 Nucleophilic aromatic substitutions of the type just shown follow an **addition– elimination mechanism**.

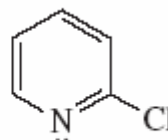


The rate-determining intermediate is a cyclohexadienyl anion and is stabilized by electron-withdrawing substituents.

- Section 23.7 Other aryl halides that give stabilized anions can undergo nucleophilic aromatic substitution by the addition–elimination mechanism. Two examples are hexafluorobenzene and 2-chloropyridine.

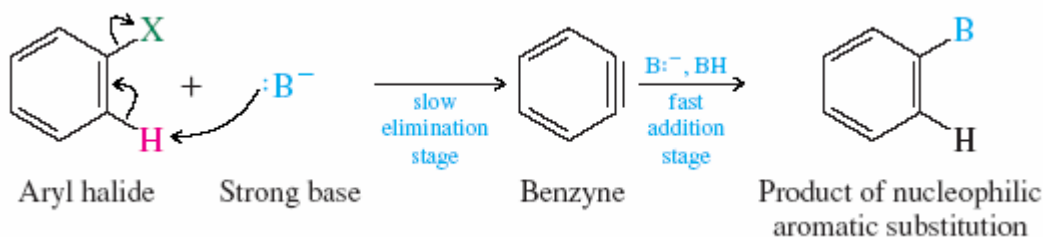


Hexafluorobenzene



2-Chloropyridine

Section 23.8 Nucleophilic aromatic substitution can also occur by an **elimination–addition mechanism**. This pathway is followed when the nucleophile is an exceptionally strong base such as amide ion in the form of sodium amide (NaNH_2) or potassium amide (KNH_2). **Benzyne** and related **arynes** are intermediates in nucleophilic aromatic substitutions that proceed by the elimination–addition mechanism.



Nucleophilic aromatic substitution by the elimination–addition mechanism can lead to substitution on the same carbon that bore the leaving group or on an adjacent carbon.

Section 23.9 Benzyne is a reactive dienophile and gives Diels–Alder products when generated in the presence of dienes. In these cases it is convenient to form benzyne by dissociation of the Grignard reagent of *o*-bromofluorobenzene.

Section 23.10 Benzyne is a reactive intermediate and capable of being studied only at low temperatures. Two isomers of benzyne, 1,3-dehydrobenzene and 1,4-dehydrobenzene, are diradicals and are even less stable. 1,4-Dehydrobenzene and compounds related to it are formed from enedynes by the Bergman cyclization. An analogous process appears responsible for the DNA cleaving properties of the antitumor enediyne antibiotics.