



Shree H.N.Shukla College of Science Rajkot

B.Sc. (Sem- 3) (CBCS)

CHEMISTRY: [301]

Unit-2 Chapter-3: Aryl Halide

CONTENTS:

- **Introduction**
- **Direct halogenation**
- **Sandmeyer, Schiemann and Gatterman reactions**
- **Via di azonium salt**
- **Halogenation in nature**
- **Benzyne**

- **Grignard reaction**
- **Elimination addition reaction**
- **SNAR reactions**
- **Uses of aryl halide**
- **Wurtz reaction**
- **Fitting reaction**
- **Wurtz fitting reaction**
- **Question bank**



INTRODUCTION

In organic chemistry, an aryl halide (also known as haloarene or halogenoarene) is an aromatic compound in which one or more hydrogen atoms directly bonded to an aromatic ring are replaced by a halide. The haloarene are distinguished from haloalkanes because they exhibit many differences in methods of preparation and properties. The most important members are the aryl chlorides, but the class of compounds is so broad that many derivatives enjoy niche applications.

Preparation

The two main preparatory routes to aryl halides are direct halogenation and via diazonium salts.

Direct halogenation

In the Friedel-Crafts halogenation, Lewis acids serve as catalysts. Many metal chlorides are used, examples include iron(III) chloride or aluminium chloride. The most important aryl halide, chlorobenzene is produced by this route. Monochlorination of benzene is always accompanied by formation of the dichlorobenzene derivatives.

Arenes with electron donating groups react with halogens even in the absence of Lewis acids. For example, phenols and anilines react quickly with chlorine and bromine water to give multiple halogenated products. The decolouration of bromine water by electron-rich arenes is used in the bromine test.

Direct halogenation of arenes are possible in the presence of light or at high temperature. For alkylbenzene derivatives, the alkyl positions tend to be halogenated first in the free radical halogenation. To halogenate the ring, Lewis acids are required, and light should be excluded to avoid the competing reaction.

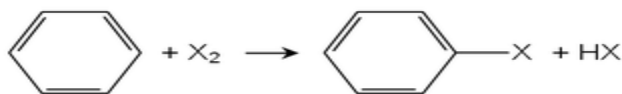


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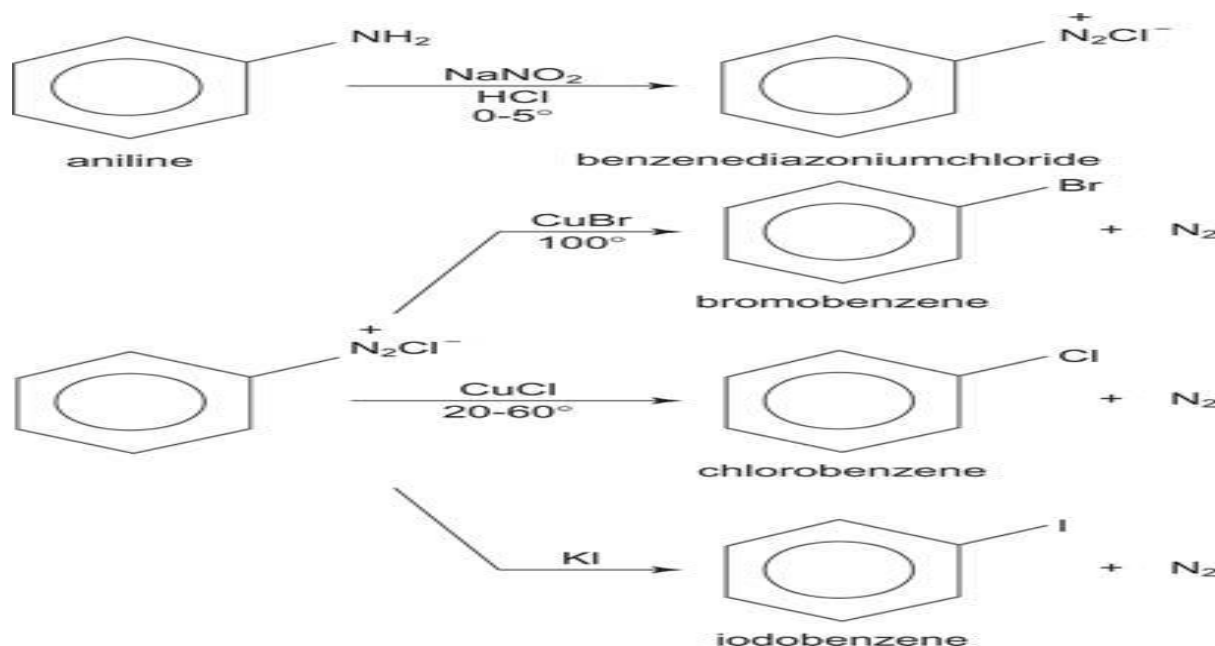
Reaction between benzene and halogen to form an halogenobenzene

Sandmeyer, Schiemann and Gatterman reactions

The second main route is the Sandmeyer reaction. Anilines (aryl amines) are converted to their diazonium salts using nitrous acid. For example, copper(I) chloride converts diazonium salts to the aryl chloride. Nitrogen gas is the leaving group, which makes this reaction very favorable. The similar Schiemann reaction uses the tetrafluoroborate anion as the fluoride donor. Gatterman Reaction can also be used to convert Diazonium salt to chlorobenzene or bromobenzene by using copper powder instead of copper chloride or copper bromide. But this must be done in the presence of HCl and HBr respectively. .

Via di azonium salt

A second method for preparing aryl halides is the Sandmeyer reaction. During a **Sandmeyer reaction**, a diazonium salt reacts with copper (I) bromide, copper (I) chloride, or potassium iodide to form the respective aryl halide. The diazonium salt is prepared from aniline by reaction with nitrous acid at cold temperatures.



Halogenation in nature

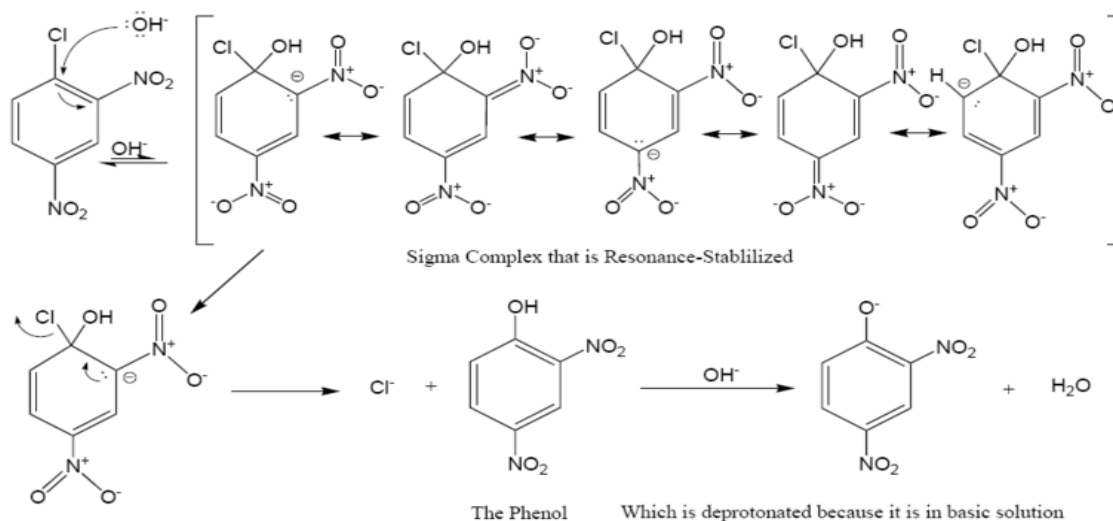
Aryl halides occur widely in nature, most commonly produced by marine organisms that utilize the chloride and bromide in ocean waters. Chlorinated and brominated aromatic compounds are also numerous, e.g. derivatives of tyrosine, tryptophan, and various pyrrole derivatives. Some of these naturally occurring aryl halides exhibit useful medicinal properties.

Reactions

Substitution

Unlike typical alkyl halides, aryl halides do not participate in conventional $\text{S}_{\text{N}}2$ reactions, as the backside attack required for an $\text{S}_{\text{N}}2$ reaction is impossible, owing to the planar structure of the aryl group. $\text{S}_{\text{N}}1$ reactions are theoretically possible, but not generally observed, as the formation of the aryl cation is not energetically favourable.

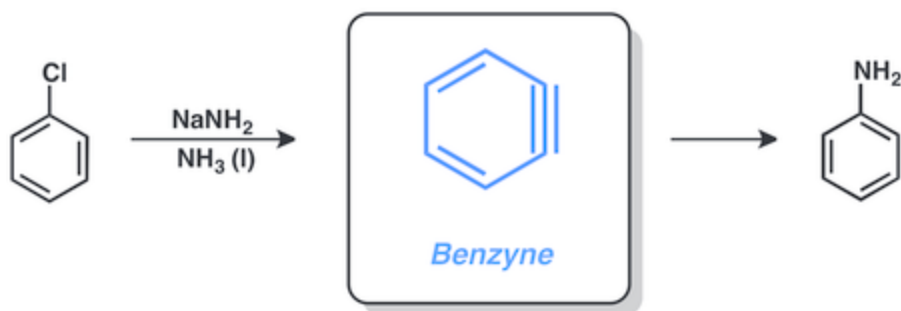
However, aryl halides with electron-withdrawing groups in the ortho and para positions, can undergo $\text{S}_{\text{N}}\text{Ar}$ reactions. For example, 2,4-dinitrochlorobenzene can react with water in basic solution to give a phenol.



Unlike in other substitution reactions, fluoride is the best leaving group, and iodide the worst, due to the fluoride's high electronegativity allowing better stabilization of the negatively charged intermediate

Benzyne

Aryl halides are capable of doing reactions via the benzyne mechanism, involving sodium amide in liquid ammonia. For example, chlorobenzene can be converted to aniline under these conditions.

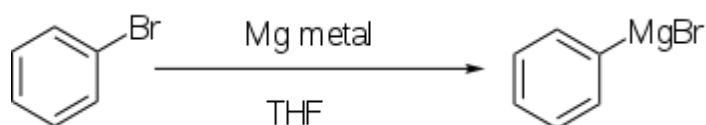


Organometallic reagent formation

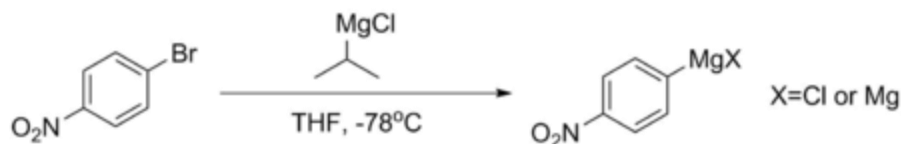


Aryl halides react with metals, generally lithium or magnesium, to give more reactive derivatives that behave as sources of aryl anions.

Direct formation of Grignard reagents, by adding the magnesium to the aryl halide in an ethereal solution, works well if the aromatic ring is not significantly deactivated by electron-withdrawing groups.



Compounds such as para-bromonitrobenzene cannot form stable Grignards directly, as their aromatic rings are too deactivated. If such a Grignard is needed, it's usually made by magnesium-halogen exchange involving isopropyl magnesium chloride at -78°C . This reaction takes place because the pK_a of the aromatic protons is much lower—generally around 45, while that of the aliphatic alkane exceeds 50. The Grignards made using this procedure are generally used immediately, to avoid decomposition.



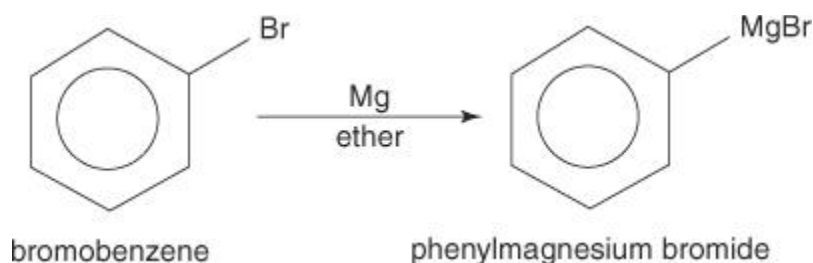
Other reactions

The halides can be displaced by strong nucleophiles via reactions involving radical anions. Alternatively aryl halides, especially the bromides and iodides, undergo oxidative addition, and thus are subject to Buchwald–Hartwig amination-type reactions.

Chlorobenzene was once the precursor to phenol, which is now made by oxidation of cumene. At high temperatures, aryl groups react with ammonia to give anilines.

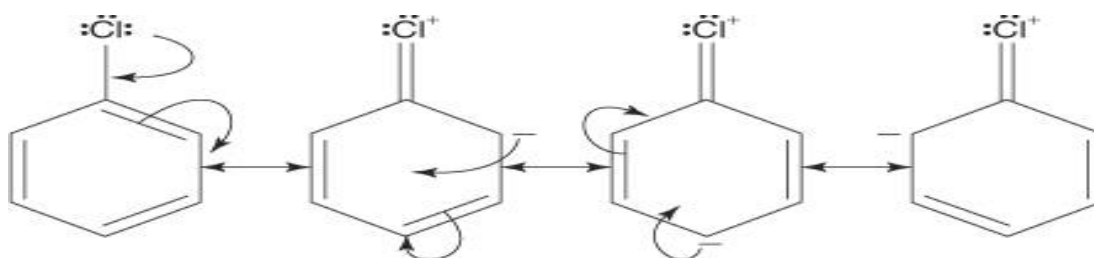
Grignard reaction

Aryl halides form Grignard reagents when reacted with magnesium.



Substitution reaction

Aryl halides are relatively unreactive toward nucleophilic substitution reactions. This lack of reactivity is due to several factors. Steric hindrance caused by the benzene ring of the aryl halide prevents S_N2 reactions. Likewise, phenyl cations are unstable, thus making S_N1 reactions impossible. In addition, the carbon-halogen bond is shorter and therefore stronger in aryl halides than in alkyl halides. The carbon-halogen bond is shortened in aryl halides for two reasons. First, the carbon atom in aryl halides is sp^2 hybridized instead of sp^3 hybridized as in alkyl halides. Second, the carbon-halogen bond has partial double bond characteristics because of resonance.



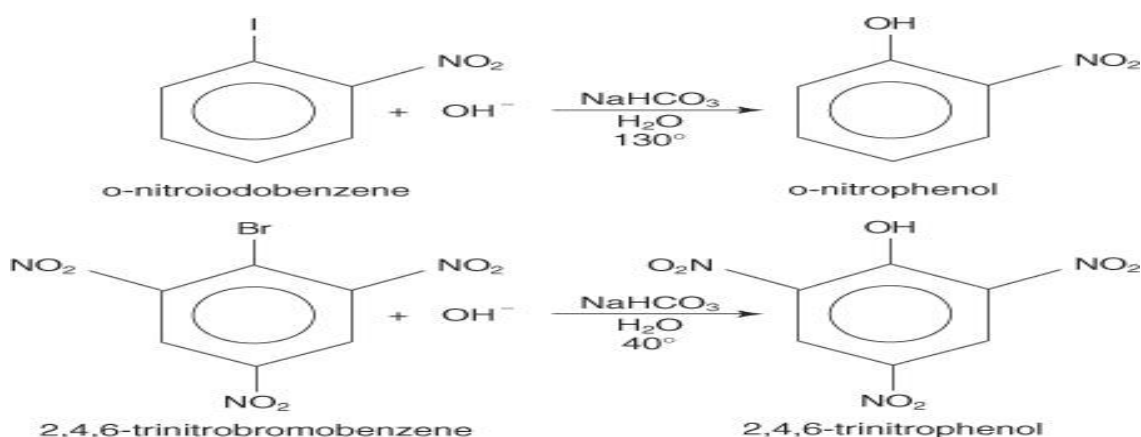
Because three of the four resonance structures show a double bond between the carbon and halogen atoms, the hybrid structure must have double bond character.



S_NAR reactions

Nucleophilic substitution reactions can occur with aryl halides, provided that strong electron-withdrawing groups (deactivators) are located ortho and/or para to the carbon atom that's attached to the halogen. (This arrangement makes the carbon susceptible to nucleophilic attack.)

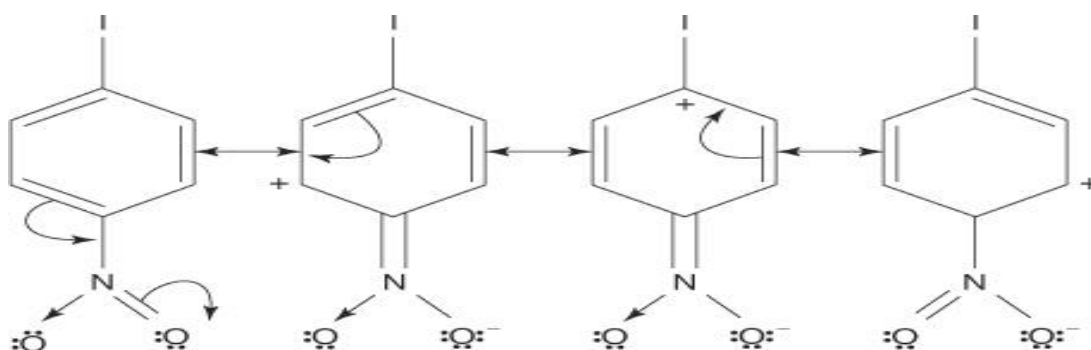
The examples below illustrate S_N substitutions on deactivated aryl halides.



S_NAR mechanism

The S_NAR mechanism is an addition-elimination mechanism that proceeds through a carbanion with delocalized electrons (a Meisenheimer complex). The following steps show the mechanism for the formation of p-nitrophenol from p-nitroiodobenzene.

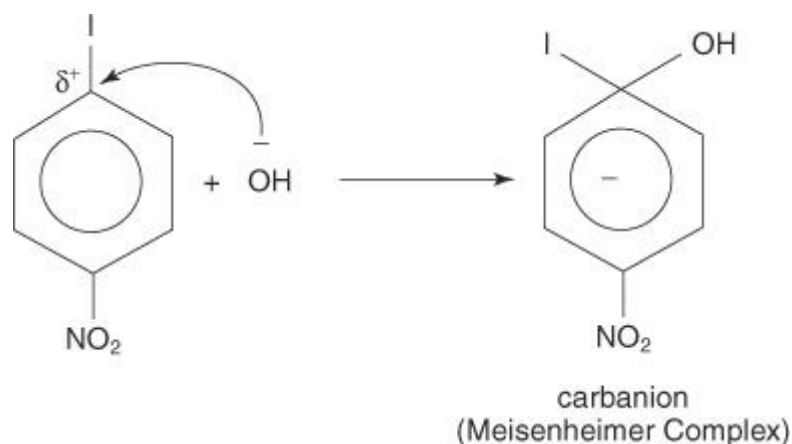
1. The nitro group, a strong deactivating group, produces a partial positive charge on the carbon that bears the halogen atom in the aryl halide.



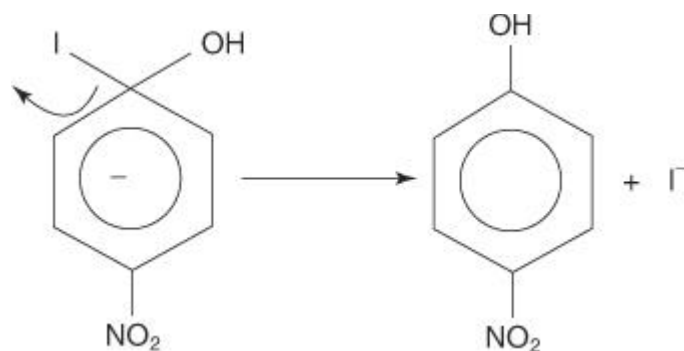


Because one of the resonance structures has a positive charge on the carbon attached to the halogen, this carbon acts as a weak nucleus.

2. The hydroxide ion is attracted to the weak nucleus, forming a carbocation with delocalized electrons.

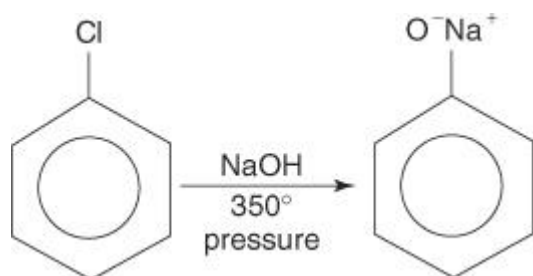


3. The complex eliminates an iodide ion to form a phenol.

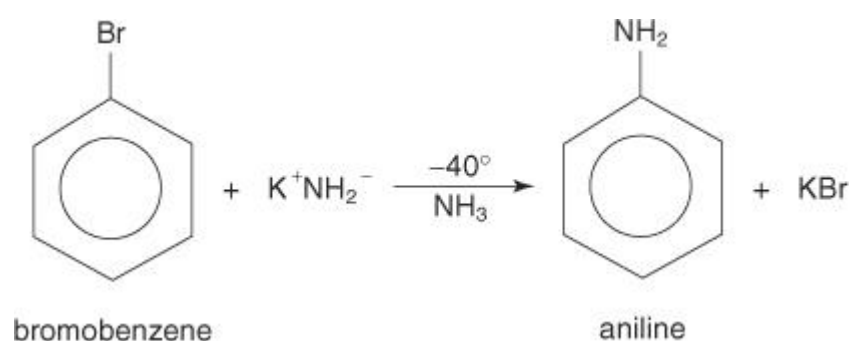


Elimination addition reaction

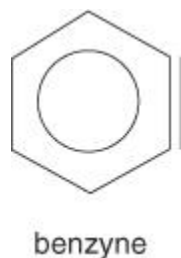
Aryl halides generally do not undergo substitution reactions. However, under conditions of high temperature and pressure, these compounds can be forced to undergo substitution reactions. For example, under high temperature and pressure, chlorobenzene can be converted into sodium phenoxide when reacted with sodium hydroxide.



Similarly, at a very low temperature, bromobenzene reacts with potassium amide (KNH_2) dissolved in liquid ammonia to form aniline.



The elimination-addition mechanism for the formation of aniline proceeds via a benzyne intermediate. A **benzyne** is a benzene molecule that contains a theoretical triple bond. Thus, the following structure represents benzyne:



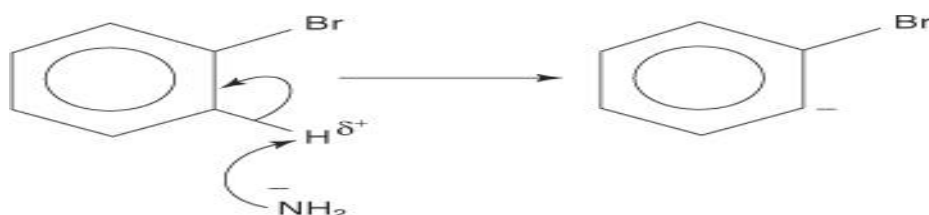
A triple bond doesn't exist in the true benzyne structure. The extra bond results from the overlap of sp^2 orbitals on adjacent carbon atoms of the ring. The axes of these sp^2 orbitals are in the same plane as the ring, and therefore, they don't overlap with the π orbitals of the aromatic system. Consequently, there's little to no interference with the aromatic system. The additional bond is weak and



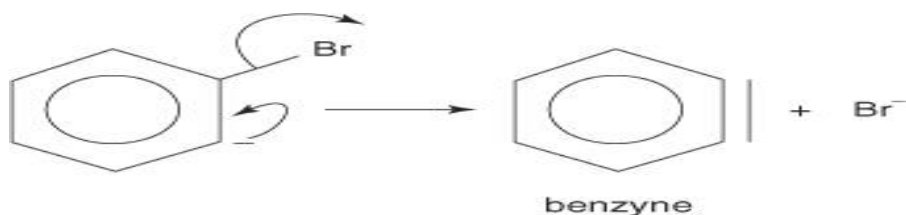
benzyne is thus highly unstable and highly reactive. Figure shows the true structure of benzyne:

The following four steps outline the mechanism for aniline formation.

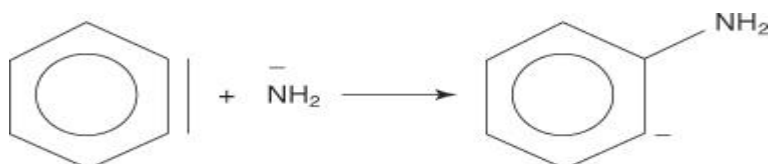
1. An amide ion, a very strong base, removes a weak proton from the carbon that is alpha to the carbon bonded to the bromine.



2. The carbanion electrons are stabilized by being attracted to the electronegative bromine, which results with the loss of a bromide ion.



3. The highly unstable and very reactive benzyne reacts with a second amide ion, creating a new carbanion.



4. The new carbanion abstracts a proton from an ammonia molecule in an acid-base reaction, leading to the formation of aniline.



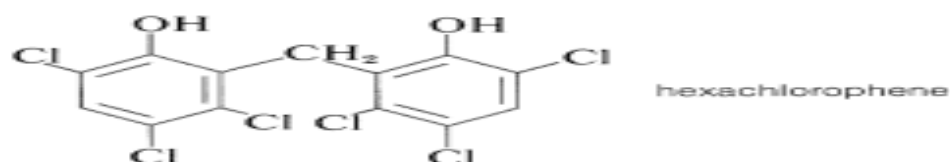
Uses for Aryl Halogen Compounds

As with most organic halides, aryl halides most often are synthetic intermediates for the production of other useful substances. For example,

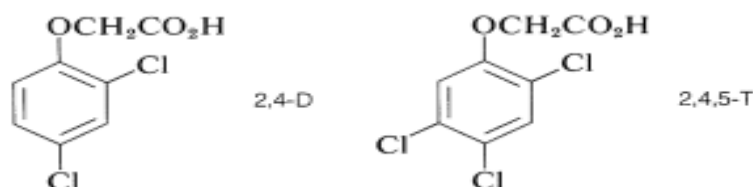


chlorobenzene is the starting aryl halide for the synthesis of DDT; it also is a source of benzenol which, in turn, has many uses.

Several aromatic chloro compounds are used extensively as insecticides, herbicides, fungicides, and bactericides. They also have acquired much notoriety because in some instances their indiscriminate usage has led to serious problems. For example, hexachlorophene is an external bactericide that until recently was used in cosmetic preparations such as soaps, deodorants, and so on. Its use has been discontinued because of compelling evidence that it can be absorbed through the skin in amounts that are dangerous, if not lethal, for infants and small children.



Other pesticides, notably DDT and the herbicides 2,4-D and 2,4,5-T have been partially banned for different reasons.

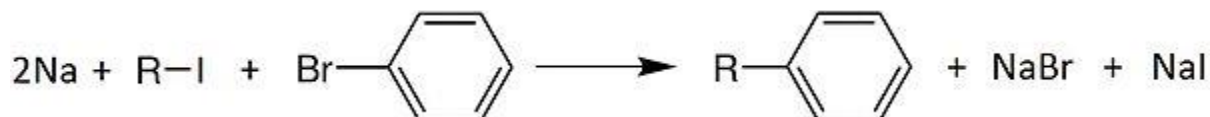


The Wurtz–Fittig

The Wurtz–Fittig reaction is the chemical reaction of aryl halides with alkyl halides and sodium metal in the presence of dry ether to give substituted aromatic compounds. Charles Adolph Wurtz reported what is now known as the Wurtz reaction in 1855, involving the formation of a new carbon-carbon bond by coupling two alkyl halides. Work by Wilhelm Rudolph Fittig in the 1860s extended the approach to the coupling of an alkyl halide with an aryl



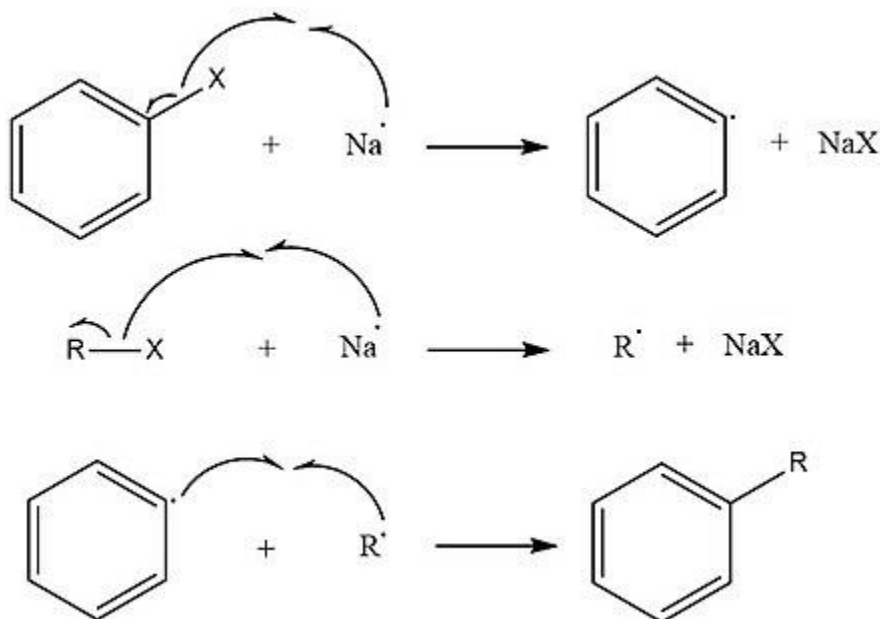
halide. This modification of the Wurtz reaction is considered a separate process and is named for both scientists.



The reaction works best for forming asymmetrical products if the halide reactants are somehow separate in their relative chemical reactivities. One way to accomplish this is to form the reactants with halogens of different periods. Typically the alkyl halide is made more reactive than the aryl halide, increasing the probability that the alkyl halide will form the organosodium bond first and thus act more effectively as a nucleophile toward the aryl halide. Typically the reaction is used for the alkylation of aryl halides; however, with the use of ultrasound the reaction can also be made useful for the production of biphenyl compounds.

Mechanism

There are two approaches to describing the mechanism of the Wurtz–Fittig reaction. The first involves the sodium-mediated formation of both alkyl and aryl radicals. The alkyl and aryl radicals then combine to form a substituted aromatic compound.

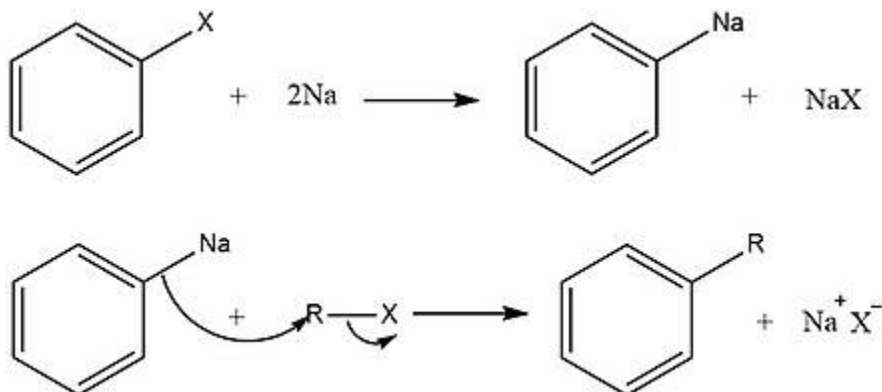


Radical Mechanism for the Wurtz–Fittig Reaction

PREPARED BY MR. ASHWIN MOLIYA



The second approach involves the formation of an intermediate organo-alkali compound followed by nucleophilic attack of the alkyl halide.



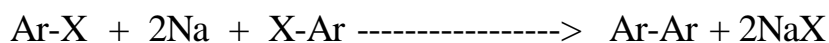
Organo-alkali Mechanism of the Wurtz-Fittig Reaction

There is empirical evidence for both approaches. The free radical mechanism is supported by the observation of side products whose formation cannot be explained by an organo-alkali mechanism. In a reaction between sodium and chlorobenzene, Bachmann and Clarke find that one of the many side products is triphenylene. They contend that the only way to explain the formation of triphenylene is through a free radical mechanism.

Fitting reaction

In Fittig reaction, two aryl halides are coupled in presence of sodium metal in dry ether or tetrahydrofuran to furnish biaryls.

Dry Ether



Where Ar = aryl group, X = halogen

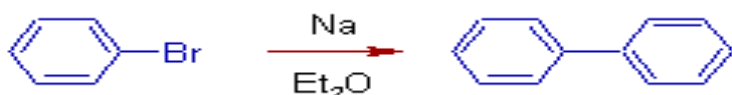
The yields will be improved by using ultrasound, especially in two-phase reactions.

A modification of reaction which involves, an alkyl halide and an aryl halide is called Wurtz-Fittig reaction.



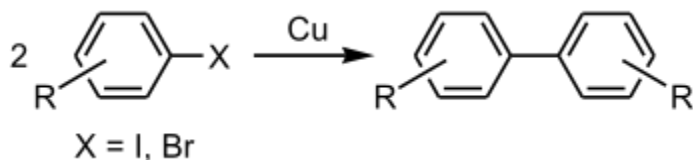
Refer Wurtz reaction for the reaction conditions and the detailed mechanism.

1) Biphenyl can be prepared by Fittig method as follows:

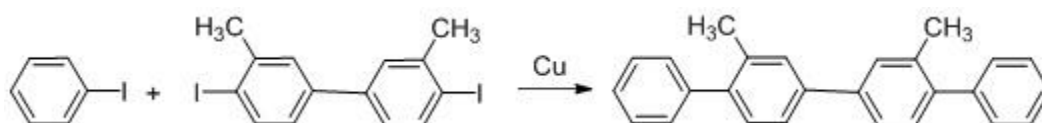
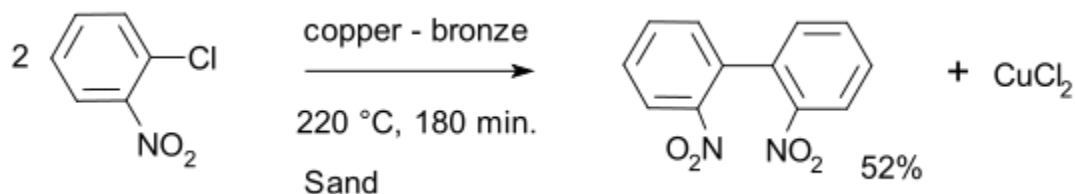


Ullmann reaction

The Ullmann reaction or Ullmann coupling is a coupling reaction between aryl halides and copper. The reaction is named after Fritz Ullmann.



A typical example of classic Ullmann biaryl coupling is the conversion of ortho-chloronitrobenzene into 2,2'-dinitrobiphenyl with a copper - bronze alloy.



The traditional version of the Ullmann reaction requires harsh reaction conditions, and the reaction has a reputation for erratic yields. Because of these problems many improvements and alternative procedures have been introduced.



Short question

- What is aryl halide ?
- Which common lewis acid is used for Friedel-Crafts halogenation ?
- Write down only reaction of Sandmeyer.
- Write down only reaction of Gatterman reactions.
- Write down only reaction of Schiemann.
- Write down only reaction of benzyne.
- Write down the reaction of halogenation.
- Write down the reaction aryl halide with Grignard reagent.
- Write down only reaction of elimination addition reaction.
- Write down only reaction of Ullman.
- Write down only reaction of wurtz fitting.
- Write down only reaction of fitting.
- Which solvent is used for Ullman reaction.
- Which metal is used for Ullman reaction.

Long question

- ❖ Write down reaction of elimination addition reaction in detail.
- ❖ Write down the detail structure of benzyne.
- ❖ Write down the reaction and mechanism of ullaman reaction.
- ❖ Write down the reaction and mechanism of wurtz fittig reaction.
- ❖ Write down the reaction and mechanism of fitting reaction.
- ❖ Write down the reaction of Sandmeyer reaction in detail.
- ❖ Write down the reaction of Gatterman in detail.
- ❖ Write down the reaction of Schiemann in detail.

ALL THE BEST