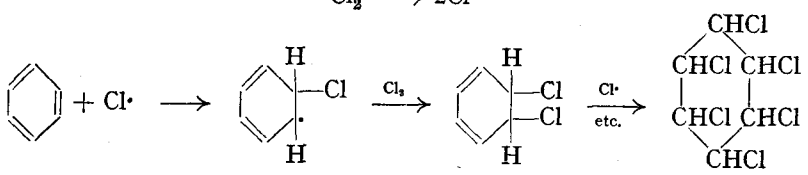
CHAPTER XXI

AROMATIC HALOGEN COMPOUNDS

THERE are three types of aromatic halogen compounds, the *addition* compounds, the *nuclear substitution* products, and the *side-chain* substitution products.

Addition compounds. When treated with chlorine or bromine in the presence of sunlight, benzene forms the benzene hexahalides, $C_6H_6Cl_6$ and $C_6H_6Br_6$, respectively. The addition probably takes place by a chain mechanism:

$$Cl_2 \xrightarrow{h\nu} 2Cl\cdot$$



Benzene hexachloride (1 : 2 : 3 : 4 : 5 : 6-hexachloro*cyclo*hexane), $C_6H_6Cl_6$, theoretically can exist in eight stereoisomeric forms (*cf.* inositol, p. 483). Until recently only five of these were known: α, β, γ, δ, ε; but Kolka *et al.* (1954) have now prepared two others, η and θ. The γ-isomer is a powerful insecticide; it is very stable and acts more quickly than D.D.T. All of the isomers have been shown to exist in the chair form, and the α-isomer has been identified as the (±)-form (Cristol, 1949). The following conformations have been assigned respectively to the α- and γ-isomers: *aeeeee* and *aaaeee*. γ-Hexachloro*cyclo*hexane is prepared commercially by treating benzene with chlorine in the presence of ultra-violet light. The α-, β-, γ- and δ-isomers are produced, the γ- to the extent of 12–14 per cent.; this is the only one that has insecticidal properties. It is very difficult to separate the isomers, but it may be done by fractional crystallisation from various organic solvents.

Mullins (1955) has suggested that molecular size and shape are critical for the action of chlorinated hydrocarbon insecticides. According to Mullins, the molecule of γ-BHC is smaller than those of the other stereoisomers and so can penetrate more readily.

Nuclear substitution products (aryl halides). These compounds may be prepared by the following methods:

1. **Direct halogenation.** *Low temperature and the presence of a halogen carrier favour nuclear substitution.* Chlorination and bromination may be very conveniently carried out at ordinary temperature in the presence of an iron or aluminium amalgam catalyst; the extent of the substitution depends on the amount of halogen used, *e.g.*, chlorobenzene is formed when benzene is treated with chlorine (1 molecule) in the presence of iron:

$$C_6H_6 + Cl_2 \xrightarrow{Fe} C_6H_5Cl + HCl \quad (90\%)$$

If 2 molecules of chlorine are used, then a mixture of *o*- and *p*-dichlorobenzenes is obtained, the latter predominating:

$$C_6H_5Cl + Cl_2 \xrightarrow{Fe} \underset{o\text{-} + p\text{-}}{C_6H_4Cl_2} + HCl$$

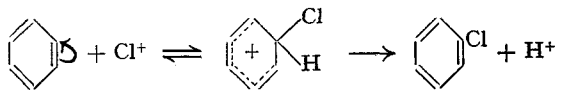
When toluene is brominated in the presence of iron (using 1 molecule of bromine), a mixture of *o*- and *p*-bromotoluenes (*tolyl bromides*) is obtained:

$$C_6H_5{\cdot}CH_3 + Br_2 \xrightarrow{Fe} \underset{o- + p-}{CH_3{\cdot}C_6H_4Br} + HBr$$

To obtain the *o*-, *m*- and *p*-toluene derivatives pure, it is best to prepare them from the corresponding toluidines (*cf.* method 3).

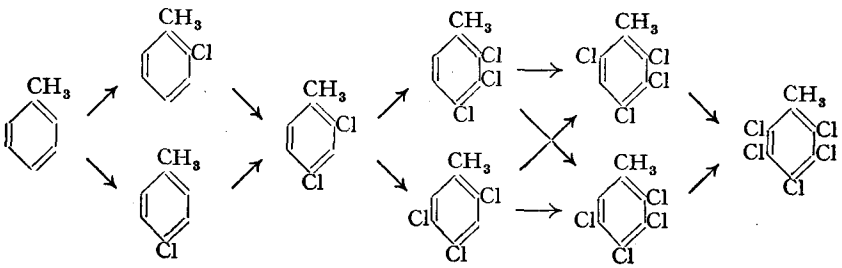
A possible mechanism for the chlorination of benzene in the presence of ferric chloride is:

$$Cl_2 + FeCl_3 \rightleftharpoons Cl^+ + FeCl_4^-$$



$$H^+ + FeCl_4^- \longrightarrow HCl + FeCl_3$$

Nuclear chlorination can be carried out with sulphuryl chloride in the presence of a catalyst, a most effective one being a mixture of sulphur monochloride and aluminium chloride; *e.g.*, sulphuryl chloride in the presence of 1 per cent. of this catalyst chlorinates benzene in the cold. Toluene can be similarly chlorinated, and the *side-chain is not attacked in the absence of organic peroxides*. Chlorination with sulphuryl chloride is stepwise, and the final product depends on the amount of this reagent used:



2. Treatment of nuclear hydroxy-compounds with phosphorus pentachloride results in the formation of nuclear-chlorinated compounds:

$$C_6H_5OH + PCl_5 \longrightarrow C_6H_5Cl + POCl_3 + HCl$$

The yield of chlorobenzene, however, is poor, the main product being triphenyl phosphate, $(C_6H_5O)_3PO$.

Rydon *et al.* (1957), however, have shown that aryl chlorides may be prepared from phenols as follows:

$$3ArOH + PCl_5 \xrightarrow{heat} 3HCl + (ArO)_3PCl_2 \xrightarrow[heat]{Ar'OH}$$

$$HCl + (ArO)_3(Ar'O)PCl \xrightarrow{heat} Ar'X + (ArO_3)PO$$

In these reactions Ar' contains a more powerful electron-attracting group than does Ar, *e.g.*, when Ar = C_6H_5 and Ar' = *p*-$NO_2{\cdot}C_6H_4$—, the product is *p*-$NO_2{\cdot}C_6H_4Cl$ (91%).

Bromides and iodides may also be prepared as follows:

$$(ArO)_3(Ar'O)PCl + RX \xrightarrow{heat} RCl + (ArO)_3(Ar'O)PX$$

$$\xrightarrow{heat} Ar'X + (ArO)_3PO$$

3. The decomposition of diazonium salts under suitable conditions is generally the most satisfactory method of preparing nuclear derivatives (see p. 585); *e.g.*, benzenediazonium chloride, in the presence of cuprous chloride, produces chlorobenzene:

$$C_6H_5{\cdot}N_2Cl \xrightarrow{CuCl} C_6H_5Cl + N_2$$

4. The silver salts of many aromatic acids react with bromine to form aryl bromides (*cf.* p. 105), *e.g.*,

$$C_6H_5{\cdot}CO_2Ag + Br_2 \longrightarrow C_6H_5Br + CO_2 + AgBr \quad (53\%)$$
$$p\text{-}NO_2{\cdot}C_6H_4{\cdot}CO_2Ag + Br_2 \longrightarrow p\text{-}NO_2{\cdot}C_6H_4Br + CO_2 + AgBr \quad (79\%)$$

Iodine compounds. Iodination is reversible, very little iodo-compound being present in the equilibrium mixture:

$$C_6H_6 + I_2 \rightleftharpoons C_6H_5I + HI$$

If, however, the iodination is carried out in the presence of an oxidising agent, *e.g.*, nitric acid, mercuric oxide, etc., the yield of iodo-compound is usually very good:

$$2C_6H_6 + I_2 \xrightarrow[HNO_3]{[O]} 2C_6H_5I + H_2O \quad (86\text{–}87\%)$$

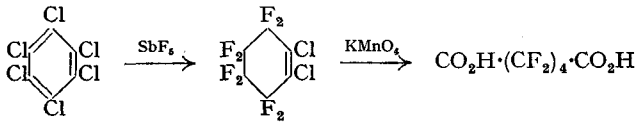
Iodine compounds are generally most conveniently prepared via the diazonium salts (method 3), but if an activating group (hydroxyl or amino-) is present in the ring, then iodine monochloride, or even iodine without the presence of an oxidising agent, may be used (see aniline, p. 569).

Fluorine compounds. Fluorination of benzene in the vapour phase in the presence of a metallic catalyst results in the formation of *no aromatic fluorine products*; instead, a complex mixture of aliphatic and alicyclic fluoro-compounds is obtained: CF_4, C_2F_6, C_3F_8, C_4F_{10}, C_5F_{12}, C_6F_{12} (in greatest amount), C_6HF_{11}, $C_{12}F_{22}$ (Bigelow *et al.*).

Perfluorobenzene, C_6F_6, may be prepared by treating perchlorobenzene with bromine trifluoride (other products are also obtained):

$$C_6Cl_6 \xrightarrow{BrF_3} C_6F_6$$

If, however, perchlorobenzene is treated with antimony pentafluoride, not all the chlorine atoms are replaced, and an *alicyclic* compound results:



This compound, when oxidised with permanganate, yields octafluoroadipic acid.

Fluorinated aromatic compounds are always prepared indirectly, the most convenient method of introducing a fluorine atom into the ring being via the diazonium salt (see p. 586).

General properties of the nuclear halogen derivatives. Nuclear halogen derivatives are colourless oils or crystalline solids, insoluble in water but soluble in organic solvents; their densities are all greater than 1. **The halogen atom is firmly attached to the nucleus, and is not easily displaced by OH(NaOH), NH_2(NH_3), CN(KCN), etc.** The aryl halides thus differ very much from the alkyl halides, but resemble the vinyl halides (p. 266). Under

special conditions, however, the halogen atom in the aryl halides may be replaced:

(i) If an aryl halide is heated with aqueous sodium hydroxide under pressure at 300°, the halogen atom is replaced by hydroxyl:

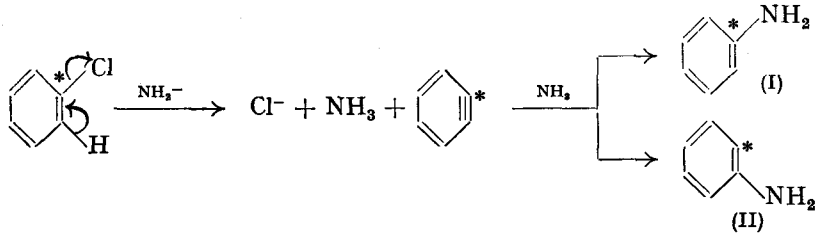
$$C_6H_5Cl + NaOH \longrightarrow C_6H_5OH + NaCl$$

Phenol is also produced when chlorobenzene and steam are passed over a silica-gel catalyst at 500° (Chiba, 1953).

(ii) When an aryl chloride is heated with aqueous ammonia in the presence of cuprous oxide at 200° under pressure, the amino-compound is formed:

$$2C_6H_5Cl + 2NH_3 + Cu_2O \longrightarrow 2C_6H_5{\cdot}NH_2 + 2CuCl + H_2O \quad (90\%)$$

Chlorobenzene also reacts with potassamide in liquid ammonia at low temperatures to form aniline. Roberts *et al.* (1953), using the isotope ^{14}C to label the carbon of the C—Cl group, showed that the amino-group entered partly at the labelled carbon and partly at the *ortho*-carbon. This behaviour has been explained by postulating a **benzyne** intermediate.



Bunnett and Zahler (1951) have proposed the name **cine-substitution** for reactions of this kind, *i.e.*, for the formation of (II) where nucleophilic aromatic substitution occurs in which the ring position taken up by the entering group is not the same as that of the displaced group.

Evidence for the benzyne mechanism (*elimination–addition* mechanism) has been provided by Roberts *et al.* (1953–56):

(*a*) The entering amino group is never further than the *o*-position from the ejected halogen atom.

(*b*) *o*-Deuterochlorobenzene reacts more slowly than the protium analogue. Thus there is a kinetic isotope effect, and from this it follows that the formation of benzyne is the rate-determining step.

(*c*) If only one benzyne intermediate is possible, then the ratio of the isomeric amines produced should be independent of the nature of the halogen atom, since the formation of benzyne is the rate-determining step and not its combination with ammonia (or amines). This has been shown to be so in practice, *e.g.*, *o*-halotoluenes gave the same mixtures of *o*- and *m*-amines with potassamide.

(iii) An aryl bromide reacts with anhydrous cuprous cyanide when heated in the presence of pyridine or quinoline, *e.g.*, bromobenzene forms phenyl cyanide:

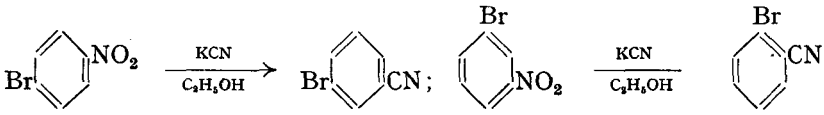
$$C_6H_5Br + CuCN \xrightarrow[200°]{\text{pyridine}} C_6H_5{\cdot}CN + CuBr$$

Pyridine or quinoline is not always necessary, and sodium cyanide may be used instead of cuprous cyanide provided a small amount of the latter is also present. Aryl chlorides may be used if the chlorine atom is activated by a nitro-group in the *o*- or *p*-position (see below).

(iv) If a strongly negative group, *e.g.*, the nitro-group is in the *o*- or *p*-position to the halogen atom, replacement of the latter halogen atom is fairly

easy, *e.g.*, *o*- and *p*-chloronitrobenzenes may be converted, at about 150–200°, by ethanolic potassium hydroxide, and ethanolic ammonia into the corresponding nitrophenols and nitroanilines. These are examples of activated nucleophilic aromatic substitution (p. 525).

A very interesting reaction of the halogenonitro-benzenes is the **von Richter reaction** (1871). In this reaction, when the compound is heated with potassium cyanide at 150°, the nitro-group is expelled and a cyano group enters the ring *ortho* to the position occupied by the former (this is an example of cine-substitution), *e.g.*,



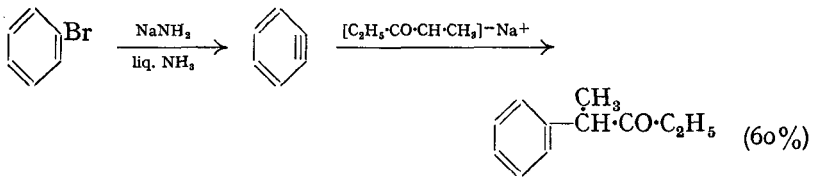
The mechanism of this reaction is uncertain. Most cine-substitutions involve a benzyne intermediate; the von Richter reaction, however, according to Bunnett *et al.* (1956), does not.

(v) An aryl halide may be converted into the parent hydrocarbon by reducing it with a nickel-aluminium alloy in the presence of alkali (Schwenk *et al.*, 1944):

$$C_6H_5Cl + 2[H] \xrightarrow[NaOH]{Ni/Al} C_6H_6 + HCl$$

This dehalogenation may also be carried out by means of reduction with hydrogen over Raney nickel in the presence of potassium hydroxide (Kämmerer *et al.*, 1958).

Aryl bromides and aryl iodides form Grignard reagents, and undergo the Ullmann reaction (p. 576). The aryl chlorides, however, form Grignard reagents in tetrahydrofuran (Ramsden *et al.*, 1958). The aryl halides do not react with sodioacetoacetic ester or with sodiomalonic ester, but they undergo the Wurtz–Fittig (p. 534) and Fittig reactions (p. 697). Ketones, however, may be directly phenylated with bromobenzene as follows, the reaction proceeding via a benzyne intermediate (Leake *et al.*, 1955):



As will be seen later, side-chain substituted halogen derivatives behave like the alkyl halides in most ways and therefore are better not to be regarded as aryl halides but as aryl-substituted alkyl halides.

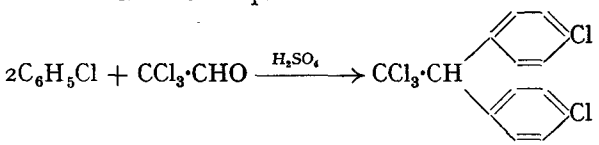
The aryl halides are difficult to mercurate, but they may be mercurated by refluxing them with mercuric acetate until a test portion gives no precipitate of mercuric oxide with aqueous sodium hydroxide. On the other hand, chloromercuri-derivatives may be prepared from aryl bromides or iodides as follows:

$$ArBr + Mg \longrightarrow Ar{\cdot}MgBr \xrightarrow{HgCl_2} Ar{\cdot}HgCl + MgClBr$$

Chlorobenzene (*phenyl chloride*), C_6H_5Cl, is produced commercially by the Raschig process: a mixture of benzene vapour, air and hydrogen chloride is passed over a catalyst (copper chloride):

$$C_6H_6 + HCl + \tfrac{1}{2}O_2 \longrightarrow C_6H_5Cl + H_2O$$

Chlorobenzene is a liquid, b.p. 132°. It is used for the manufacture of aniline, phenol, and D.D.T. D.D.T. is a contraction for *p* : *p*′-dichlorodiphenyltrichloroethane [1 : 1 : 1-trichloro-2 : 2-bis(*p*-chlorophenyl)-ethane]. It is a solid, m.p. 109–110°, and is manufactured by heating chlorobenzene and chloral with concentrated sulphuric acid:



Good commercial D.D.T. contains about 75 per cent. *p* : *p*′-D.D.T., 20 per cent. *o* : *p*′-D.D.T. (m.p. 74–75°), and 5 per cent. of other substances as impurities; it is a powerful insecticide.

Side-chain substituted compounds. Side-chain substitution is favoured by high temperature and light, and the *absence* of halogen carriers; *e.g.*, when chlorinated at its boiling point in the presence of light, toluene is converted into benzyl chloride (see also below):

$$C_6H_5{\cdot}CH_3 + Cl_2 \longrightarrow C_6H_5{\cdot}CH_2Cl + HCl$$

It is generally believed that side-chain substitution proceeds by a chain reaction (*cf.* p. 103):

$$Cl_2 \xrightarrow{h\nu} 2Cl{\cdot}$$
$$C_6H_5{\cdot}CH_3 + Cl{\cdot} \longrightarrow C_6H_5{\cdot}CH_2{\cdot} + HCl$$
$$C_6H_5{\cdot}CH_2{\cdot} + Cl_2 \longrightarrow C_6H_5{\cdot}CH_2Cl + Cl{\cdot};\ \text{etc.}$$

Side-chain substitution may be readily effected by sulphuryl chloride in the *presence* of organic peroxides. Excess of sulphuryl chloride will introduce no more than two chlorine atoms on the same carbon atom; *e.g.*, toluene gives benzylidene chloride as the final product:

$$C_6H_5{\cdot}CH_3 \xrightarrow{SO_2Cl_2} C_6H_5{\cdot}CH_2Cl \xrightarrow{SO_2Cl_2} C_6H_5{\cdot}CHCl_2$$

In these reactions it is believed that the peroxide provides traces of free radicals which then set up the chain reaction.

When the side-chain is larger than a methyl group, its halogenation is more complicated, *e.g.*, chlorination of ethylbenzene at its boiling point in the presence of light first produces a mixture of α- and β-chloroethylbenzenes, and finally pentachloroethylbenzene:

$$C_6H_5{\cdot}CH_2{\cdot}CH_3 \xrightarrow{Cl_2} \underset{\alpha\text{-isomer}}{C_6H_5{\cdot}CHCl{\cdot}CH_3} + \underset{\beta\text{-isomer}}{C_6H_5{\cdot}CH_2{\cdot}CH_2{\cdot}Cl} \xrightarrow{Cl_2} C_6H_5{\cdot}CCl_2{\cdot}CCl_3$$

The monochloro-derivatives can be isolated (using 1 molecule of chlorine), but it is extremely difficult to isolate any of the other intermediates (when chlorine is used in excess). If, however, chlorination is carried out in the cold and in the presence of light, then the main product of substitution is the α-isomer:

$$C_6H_5{\cdot}CH_2{\cdot}CH_3 \xrightarrow{Cl_2} C_6H_5{\cdot}CHCl{\cdot}CH_3 \xrightarrow{Cl_2} C_6H_5{\cdot}CCl_2{\cdot}CH_3$$

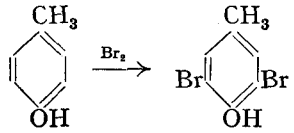
If two side-chains are present, both may be halogenated, *e.g.*,

$$CH_3{\cdot}C_6H_4{\cdot}CH_3 \xrightarrow{Cl_2} \underset{\text{methylbenzyl chloride}}{CH_3{\cdot}C_6H_4{\cdot}CH_2Cl} \xrightarrow{Cl_2}$$

$$\underset{\text{xylylene chloride}}{CH_2Cl{\cdot}C_6H_4{\cdot}CH_2Cl} \xrightarrow{Cl_2} \underset{\text{bis-(trichloromethyl)-benzene}}{C_6H_4(CCl_3)_2}$$

A curious feature of this reaction is that the fully chlorinated product cannot be obtained with *o*-xylene, but can with the *m*- and *p*-isomers. The explanation may be the steric effect.

When a hydroxyl or an amino-group (activating groups) is present in the ring, side-chain halogenation is very difficult, if not impossible; *e.g.*, bromination of *p*-cresol gives 2 : 6-dibromo-*p*-cresol:



Introduction of fluorine into the side-chain may be carried out by heating the corresponding chloro-derivative with hydrogen fluoride under pressure, or with antimony pentafluoride; *e.g.*, trifluoromethylbenzene (benzotrifluoride) from benzotrichloride and antimony pentafluoride:

$$C_6H_5{\cdot}CH_3 \xrightarrow{Cl_2} C_6H_5{\cdot}CCl_3 \xrightarrow{SbF_5} C_6H_5{\cdot}CF_3$$

The trifluoromethyl group is very resistant to attack, *e.g.*, oxidation of trifluoromethylbenzene results in the formation of trifluoroacetic acid:

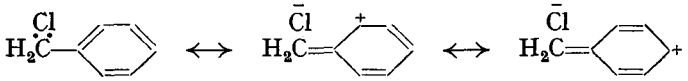
$$C_6H_5{\cdot}CF_3 \xrightarrow{[O]} CF_3{\cdot}CO_2H$$

Benzyl chloride, $C_6H_5{\cdot}CH_2Cl$, may be prepared by passing chlorine into boiling toluene until the theoretical increase in weight for benzyl chloride is obtained:

$$C_6H_5{\cdot}CH_3 + Cl_2 \longrightarrow C_6H_5{\cdot}CH_2Cl + HCl \quad (60\%)$$

Benzyl chloride may also be prepared by the chloromethylation of benzene.

Benzyl chloride is a liquid, b.p. 179°, and chemically it behaves like an alkyl halide, *e.g.*, when heated with aqueous alkali, aqueous potassium cyanide, or ethanolic ammonia, it is converted into benzyl alcohol. $C_6H_5{\cdot}CH_2OH$, benzyl cyanide, $C_6H_5{\cdot}CH_2{\cdot}CN$, and benzylamine, $C_6H_5{\cdot}CH_2{\cdot}NH_2$, respectively. Actually, the chlorine atom in benzyl chloride is more reactive than in methyl chloride. One suggestion that has been put forward to account for this is hyperconjugation:



This shows that the chlorine is largely ionised, but does not account for the fact that the $-CH_2Cl$ group is mainly *o*-*p*-orienting and not *m*- (*cf.* p. 521).

From the M.O. point of view, ionisation of the chlorine atom would leave the carbon atom with a positive charge. The " closed circuit " of the benzene ring can now extend itself to cover this carbon atom, *i.e.*, the resulting positive ion is stabilised by delocalisation (Fig. 1). It is this extension of conjugation that acts as the " driving force " in the ionisation of the chlorine atom. Conjugation is not possible in alkyl halides.

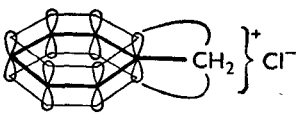


FIG. 21.1.

Benzylidene chloride (*benzal chloride*), $C_6H_5{\cdot}CHCl_2$, may be prepared by passing chlorine into boiling toluene in the presence of light until the weight increase corresponds to $C_6H_5{\cdot}CHCl_2$:

$$C_6H_5{\cdot}CH_3 + 2Cl_2 \longrightarrow C_6H_5{\cdot}CHCl_2 + 2HCl \quad (g.)$$

It may also be prepared by the action of phosphorus pentachloride on benzaldehyde:

$$C_6H_5{\cdot}CHO + PCl_5 \longrightarrow C_6H_5{\cdot}CHCl_2 + POCl_3$$

Benzylidene chloride is a liquid, b.p. 207°; it is hydrolysed by calcium hydroxide solution to benzaldehyde, and is used industrially for this purpose.

$$C_6H_5{\cdot}CHCl_2 + Ca(OH)_2 \longrightarrow C_6H_5{\cdot}CHO + CaCl_2 + H_2O$$

The conversion of toluene into benzaldehyde via benzylidene chloride is an example of *indirect* oxidation.

Benzotrichloride, $C_6H_5{\cdot}CCl_3$, may be prepared by the continued action of chlorine on boiling toluene in the presence of light:

$$C_6H_5{\cdot}CH_3 + 3Cl_2 \longrightarrow C_6H_5{\cdot}CCl_3 + 3HCl$$

It is a liquid, b.p. 214°. When heated with calcium hydroxide solution, it is converted into benzoic acid: it is used industrially for this purpose. This is another example of indirect oxidation:

$$C_6H_5{\cdot}CCl_3 + 2H_2O \xrightarrow{Ca(OH)_2} C_6H_5{\cdot}CO_2H + 3HCl$$

It can be seen from the foregoing that the properties of the side-chain halogen derivatives are very much different from those of the nuclear halogen derivatives. The former closely resemble the alkyl halides but, in general, possess a pungent smell and are lachrymatory (provided the halogen atom is on the α-carbon); they have been used in warfare.

Polyvalent iodine compounds. When a well-cooled chloroform solution of iodobenzene is treated with chlorine, a precipitate of **iodosobenzene dichloride** (*phenyliodochloride*) is formed:

$$C_6H_5I + Cl_2 \longrightarrow C_6H_5{\cdot}ICl_2 \quad (87\text{–}94\%)$$

This is a yellow crystalline solid: its structure is uncertain. When exposed to light or heated to 110°, it is converted into *p*-chloroiodobenzene:

$$C_6H_5{\cdot}ICl_2 \longrightarrow p\text{-}Cl{\cdot}C_6H_4{\cdot}I + HCl$$

When treated with alkali, iodosobenzene dichloride is converted into **iodosobenzene,** $C_6H_5I{\rightarrow}O$:

$$C_6H_5{\cdot}ICl_2 + 2NaOH \longrightarrow C_6H_5{\cdot}IO + 2NaCl + H_2O \quad (60\text{–}62\%)$$

Iodosobenzene is a yellow solid which is basic, *e.g.*, with hydrochloric acid it forms iodosobenzene dichloride, and with nitric acid, iodosobenzene dinitrate:

$$C_6H_5{\cdot}IO + 2HNO_3 \longrightarrow C_6H_5{\cdot}I(NO_3)_2 + H_2O$$

Iodosobenzene has been used to oxidise sulphides to sulphoxides (Ford-Moore, 1949), and iodosobenzene diacetate oxidises primary aromatic amines to azo-compounds (Pausacker, 1953).

When steam distilled, iodosobenzene is converted into **iodoxybenzene**:

$$2C_6H_5{\cdot}IO \longrightarrow C_6H_5{\cdot}IO_2 + C_6H_5I \quad (92\text{–}95\%)$$

This is also obtained when iodosobenzene dichloride is treated with an alkaline solution of sodium hypochlorite:

$$C_6H_5{\cdot}ICl_2 + NaOCl + H_2O \longrightarrow C_6H_5{\cdot}IO_2 + NaCl + 2HCl \quad (87\text{–}92\%)$$

Iodoxybenzene is a solid which does not melt or vaporise when heated to 230°; all iodoxy-compounds exhibit this refractory property. The structure of iodoxybenzene is not known with certainty; it may be $C_6H_5{-}I{<}\begin{matrix}O\\O\end{matrix}$. It forms salts with

inorganic acids, *e.g.*, $C_6H_5{\cdot}IO_2{\cdot}H_2SO_4$, but although these salts are fairly stable in the solid state, they are readily hydrolysed in solution. Iodoxybenzene also forms salts with alkalis, but these have not yet been isolated.

When a mixture of iodoso- and iodoxybenzene is treated with aqueous sodium hydroxide, **diphenyliodonium iodate** is formed, and this, on treatment with potassium iodide, forms **diphenyliodonium iodide**:

$$C_6H_5{\cdot}IO + C_6H_5{\cdot}IO_2 \xrightarrow{NaOH} [(C_6H_5)_2I]^+IO_3^- \xrightarrow{KI} [(C_6H_5)_2I]^+I^- \quad (70\text{–}72\%)$$

Diphenyliodonium iodide readily changes to iodobenzene on heating; the mechanism of this reaction is obscure. Diphenyliodonium iodide is the salt of the base *diphenyliodonium hydroxide* which may be prepared, in solution, by the action of " silver hydroxide " on a mixture of iodoso- and iodoxybenzene:

$$C_6H_5{\cdot}IO + C_6H_5{\cdot}IO_2 + \text{" AgOH "} \longrightarrow [(C_6H_5)_2I]^+OH^- + AgIO_3$$

QUESTIONS

1. Name the compounds and state the conditions under which they are formed when each of the following compounds is treated with chlorine: (*a*) C_6H_6, (*b*) PhMe, (*c*) o-$C_6H_4Me_2$, (*d*) PhEt, (*e*) p-$Me{\cdot}C_6H_4{\cdot}Et$.
2. Discuss the general methods of preparing:—(*a*) nuclear halogen derivatives, (*b*) side-chain halogen derivatives, and write an account of the general properties of these two types of halogen compounds.
3. Starting with benzene and any other compound you like, how would you prepare:—(*a*) PhCl, (*b*) PhI, (*c*) D.D.T., (*d*) $PhCH_2Br$, (*e*) $PhCHMeCO_2H$, (*f*) $PhCH_2{\cdot}CH_2{\cdot}NH_2$, (*g*) o-$C_6H_4(CH_2Br)_2$, (*h*) 2 : 4 : 6-tribromophenol, (*i*) p-nitrophenol, (*j*) $PhCH_2F$, (*k*) PhCHO, (*l*) $PhCO_2H$?
4. Discuss the use of sulphuryl chloride as a chlorinating agent.
5. Write an account of the aromatic polyvalent iodine compounds.
6. How would you distinguish between:—(*a*) $PhCH_2Cl$ and p-MeC_6H_4Cl; (*b*) PhCOCl and p-$ClC_6H_4CO_2H$?
7. Write an account of cine-substitution.

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CHAPTER XXII

AROMATIC NITRO-COMPOUNDS

AROMATIC nitro-compounds are almost invariably prepared by direct nitration, using one of the following reagents:

(i) *Concentrated nitric acid*, density about 1·5.

(ii) *Fuming nitric acid* (6–12 per cent. nitrogen dioxide).

(iii) *Mixed acid.* This is a mixture of nitric acid (concentrated or fuming) and various amounts of concentrated sulphuric acid (sometimes fuming sulphuric acid is used). Mixed acid is by far the most important nitrating agent. Occasionally other acids besides sulphuric acid are used, *e.g.*, glacial acetic acid.

Boron trifluoride is a very effective catalyst for nitration (Thomas *et al.*, 1940). One equivalent of catalyst must be used:

$$ArH + HNO_3 + BF_3 \longrightarrow Ar{\cdot}NO_2 + BF_3{\cdot}H_2O$$

The yields are better and the products purer than by the above methods. Furthermore, boron trifluoride is particularly useful for nitrating compounds containing a negative group, *e.g.*,

$$C_6H_5{\cdot}NO_2 + HNO_3 \xrightarrow{BF_3} m\text{-}C_6H_4(NO_2)_2 \quad (87\%)$$

Oláh *et al.* (1956) have shown that nitronium tetrafluoroborate (a stable compound) is a useful nitrating agent.

$$ArH + (NO_2^+)(BF_4^-) \longrightarrow Ar{\cdot}NO_2 + HF + BF_3 \quad (g.\text{–}ex.)$$

This method of nitration gives direct preparative proof of the electrophilic character of nitration through the nitronium cation (see below).

(iv) *Acetyl nitrate*, $CH_3{\cdot}CO{\cdot}O{\cdot}NO_2$, is useful as a nitrating agent in certain cases, since it introduces a nitro-group into the *o*-position, and produces almost only the mononitro-derivative. Acetyl nitrate, however, is somewhat dangerous to use, since it tends to explode when heated.

The nitrating agent used depends on the nature of the compound to be nitrated and the object in view, *i.e.*, the introduction of one or more nitro-groups. In any case, whichever reagent is used, it is usually difficult to stop the nitration process at one nitro-group (except with acetyl nitrate).

As an outcome of a great deal of experimental work, it has been shown that nitration with mixed acid, *i.e.*, nitration in sulphuric acid, is due to some substance produced from the nitric acid and not the nitric acid itself. According to Bennett *et al.* and Ingold *et al.* (1946), the active nitrating agent is the *nitronium cation*, NO_2^+, which, they believe, is formed as follows:

$$HNO_3 + 2H_2SO_4 \rightleftharpoons NO_2^+ + H_3O^+ + 2HSO_4^-$$

The evidence for the existence of the nitronium cation is shown:

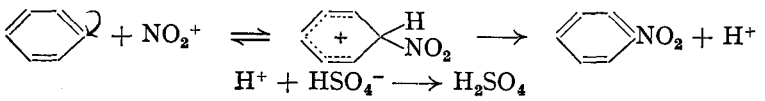
(i) By electrolysis experiments, *e.g.*, it has been found that nitric acid in oleum migrates to the cathode.

(ii) By cryoscopic experiments in which it has been shown that *i* (the van't Hoff factor) is 4; this value satisfies the equation given above.

(iii) By the isolation of salts of the nitronium ion, *e.g.*, nitronium perchlorate, $(NO_2^+)(ClO_4^-)$, and nitronium tetrafluoroborate, $(NO_2^+)(BF_4^-)$ [see (iii) above].

(iv) By spectroscopic analysis (which has shown the existence of the nitronium ion).

Nitration (with mixed acid) thus possibly proceeds as follows:



$$H^+ + HSO_4^- \longrightarrow H_2SO_4$$

Nitration in concentrated aqueous nitric acid and in organic solvents is also believed to be via the nitronium ion:

$$2HNO_3 \rightleftharpoons NO_2^+ + H_2O + NO_3^-$$

On the other hand, in more dilute nitric acid solutions, it is probably the *nitracidium cation* that is involved in nitration:

$$2HNO_3 \rightleftharpoons H_2NO_3^+ + NO_3^-$$

The catalytic effect of boron trifluoride is believed to be due to the formation of the nitronium ion:

$$HNO_3 + BF_3 \rightleftharpoons NO_2^+ + HO{-}BF_3$$

According to Norman *et al.* (1960), the active species with acetyl nitrate (and other organic nitrates) is dinitrogen pentoxide.

General properties of the nitro-compounds. Most nitro-compounds are yellow crystalline solids; a few, including nitrobenzene, are yellow liquids. Many are steam-volatile, and except for a few mononitro-derivatives, cannot be distilled under atmospheric pressure because, when strongly heated, they decompose, often with explosive violence. All the nitro-compounds are denser than water, in which they are insoluble; they are, however, readily soluble in organic solvents. The nitro-group is firmly atttached to the nucleus and may be replaced only under certain conditions (see later). Nitro-compounds form addition products with many aromatic compounds; their most important reaction is their reduction by various reducing agents.

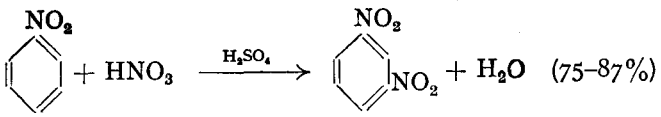
Nitrobenzene (*oil of mirbane*), $C_6H_5{\cdot}NO_2$, may be prepared by the action of cold mixed acid on benzene, and then warming to complete the reaction:

$$C_6H_6 + HNO_3 \longrightarrow C_6H_5{\cdot}NO_2 + H_2O \quad (85\%)$$

It is a pale yellow oil, b.p. 211°, with a smell like benzaldehyde. It is almost insoluble in water, but is steam-volatile; its vapour is poisonous. It is used for scenting cheap soaps, in the manufacture of floor polishes, aniline, benzidine and some azo-dyes, etc. It is used as a solvent, and is used occasionally as an oxidising agent in organic chemistry, *e.g.*, in the preparation of quinoline.

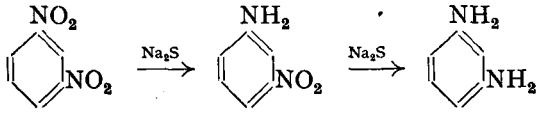
When heated with solid potassium hydroxide, nitrobenzene produces a mixture of *o*- and *p*-nitrophenols and some azoxybenzene.

Dinitrobenzenes. When nitrobenzene is heated with mixed acid (fuming nitric acid and concentrated sulphuric acid), the main product is *m*-dinitrobenzene:

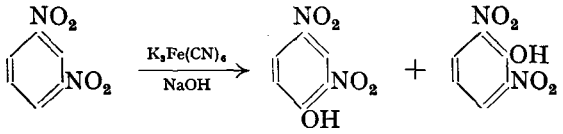


Nitric acid alone may be used to introduce one nitro-group; mixed acid must be used to introduce the second nitro-group into nitrobenzene.

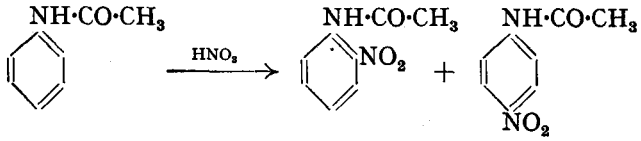
m-Dinitrobenzene is a pale yellow solid, m.p. 90°, practically insoluble in water, but is steam-volatile. It may be reduced stepwise by, *e.g.*, sodium sulphide, to *m*-nitroaniline, and then to *m*-phenylenediamine:



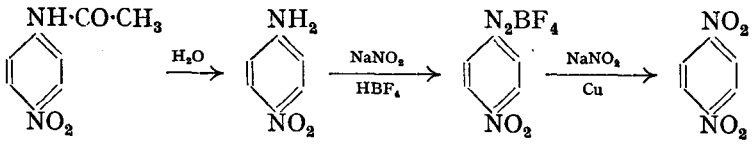
The hydrogen atom *o*- or *o-p*- to two nitro-groups is easily displaced by oxidation, but not by substitution; *e.g.*, *m*-dinitrobenzene is oxidised by an alkaline solution of potassium ferricyanide to a mixture of 2 : 4-dinitrophenol (mainly) and 2 : 6-dinitrophenol (small amount):



***o*-Dinitrobenzene** can be isolated after removing the *m*-isomer when nitrobenzene is nitrated. Nitration of acetanilide gives a mixture of *o*- and *p*-nitroacetanilides:

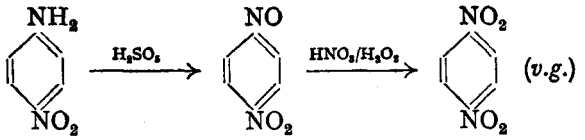


These isomers are separated; each is deacetylated, and by replacing the amino-group by a nitro-group (see p. 586), the *o*- and *p*-dinitrobenzenes may be obtained pure, *e.g.*,

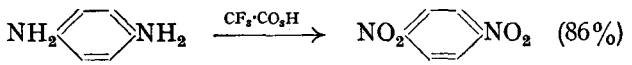


It is necessary to " protect " compounds with a hydroxyl or amino-group in the ring, since these compounds are very easily oxidised instead of nitrated by nitric acid.

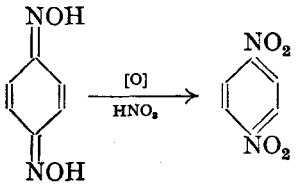
An alternative method for preparing *o*- and *p*-dinitrobenzenes is to oxidise the corresponding nitroaniline with Caro's acid, and then to oxidise the product, the nitro-nitroso-derivative, with a mixture of nitric acid and hydrogen peroxide:



On the other hand, peroxytrifluoroacetic acid oxidises the amino-group directly to the nitro-group (Emmons *et al.*, 1953), *e.g.*,

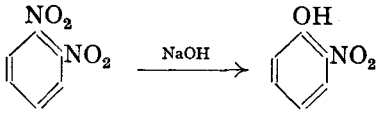


***p*-Dinitrobenzene** may also be prepared by oxidising *p*-benzoquinone dioxime (p. 672) with nitric acid:



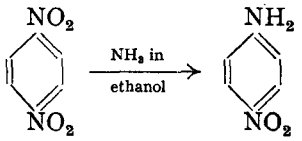
o- and *p*-Dinitrobenzenes are colourless solids, melting points 118° and 173°, respectively. They resemble the *m*-isomer in many ways, but differ in the following respects.

(i) When *o*- and *p*-dinitrobenzenes are boiled with aqueous sodium hydroxide, one nitro-group is replaced by hydroxyl to give the corresponding nitrophenol:

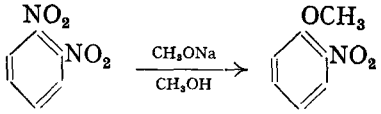


This reaction is used to separate *m*-dinitrobenzene from its *o*- and *p*-isomers in the industrial preparation of *m*-dinitrobenzene.

(ii) When boiled with ethanolic ammonia, *o*- and *p*-dinitrobenzenes are converted into the corresponding nitroanilines, one nitro-group being displaced by an amino-group:

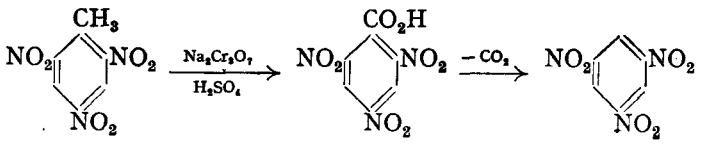


(iii) When boiled with methanolic sodium methoxide, *o*- and *p*-dinitrobenzenes are converted into the corresponding nitroanisoles, one nitro-group being replaced by a methoxyl group:



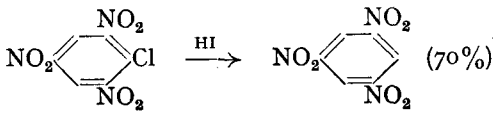
These nucleophilic substitutions are characteristic of polynitro-compounds in which two nitro-groups are in the *o*- or *p*-positions, one nitro-group being replaced by a hydroxyl, amino-, or methoxyl group.

s-Trinitrobenzene may be prepared by the nitration of *m*-dinitrobenzene with mixed acid consisting of fuming nitric acid and fuming sulphuric acid. This reaction takes five days to complete; it is very difficult to introduce the third nitro-group, and it is impossible to introduce more than three nitro-groups by direct nitration. A better method of preparing *s*-trinitrobenzene is to oxidise 2 : 4 : 6-trinitrotoluene, and to decarboxylate the trinitrobenzoic acid so produced by heating it in acetic acid solution:



(43–46%)

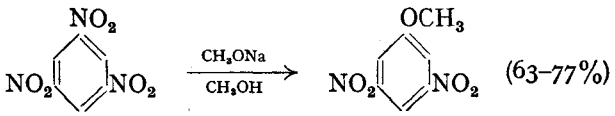
It may also be prepared by the removal of the chlorine atom in picryl chloride by means of hydrogen iodide generated from sodium iodide and acetic acid in acetone solution (Blatt *et al.*, 1952):



(70%)

s-Trinitrobenzene is a colourless solid, m.p. 122°. It forms well-defined addition compounds with many aromatic compounds such as hydrocarbons, phenols, etc. Many polynitro compounds form these complexes, and the forces that hold the two components together have been the subject of much discussion. It has been suggested that these complexes are *charge-transfer complexes*, the closed aromatic sextet of the nitro-compound forming a π-complex with the other component. The stabilisation of the complex depends on the overlap between the highest filled M.O. of the donor molecule and the lowest unfilled M.O. of the acceptor molecule (Mulliken, 1952). However, there are also complexes which are held together by dipole–dipole interactions, van der Waals forces, etc. The term " polarisation bonding " (first used by McKeown *et al.*, 1951) has been used by Mulliken (1952) to include both charge-transfer bonding and the weaker polar interactions. Wallwork (1961), from his X-ray analysis work, has concluded that: (*a*) polarisation bonding in complexes between aromatic molecules results in a characteristic plane-to-plane structure in the crystal lattice, and (*b*) where charge-transfer forces predominate, the relative orientations and positions of the components are found to be such as to allow the maximum degree of overlap between their molecular π-orbitals.

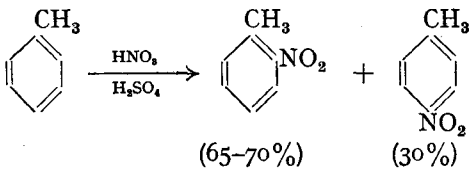
When three nitro-groups are present in the ring as in *s*-trinitrobenzene, one may be removed by the reagents which attack the *o*- and *p*-dinitrocompounds; *e.g.*, when heated with methanolic sodium methoxide, *s*-trinitrobenzene forms 3 : 5-dinitroanisole:



(63–77%)

Benzene may be oxidised and nitrated simultaneously to dinitrophenol and picric acid by mercuric nitrate in nitric acid solution (see p. 628).

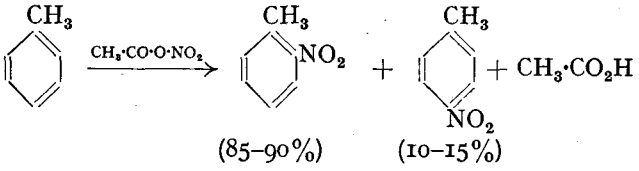
Nitrotoluenes. Benzene homologues are more readily nitrated than benzene itself, due to the activating effect of the alkyl group. When nitrated with mixed acid, toluene forms a mixture of *o*- and *p*-nitrotoluenes:



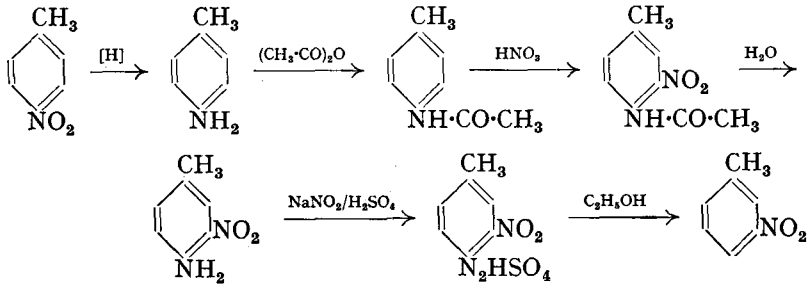
(65–70%) (30%)

These isomers may readily be separated by fractional distillation under reduced pressure: *o*-isomer, m.p. −4°, b.p. 222°; *p*-isomer, m.p. 54°, b.p. 238°.

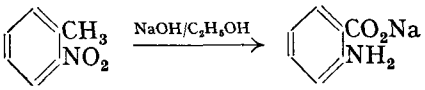
A larger yield of *o*-nitrotoluene may be obtained by nitrating toluene with acetyl nitrate:



m-Nitrotoluene, m.p. 16°, b.p. 227°, may be prepared by reducing the *p*-isomer, acetylating the *p*-toluidine, nitrating the acetyl derivative, deacetylating, and replacing the amino-group by hydrogen (see p. 584):



All the nitrotoluenes may be reduced to the corresponding toluidines. A very interesting oxidising effect of a nitro-group is the internal oxidation of *o*-nitrotoluene to *o*-aminobenzoic acid when heated with ethanolic sodium hydroxide:

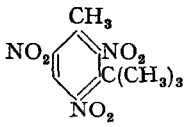


Dinitrotoluenes. Nitration of any of the nitrotoluenes gives a mixture of 2 : 4- and 2 : 6-dinitrotoluenes.

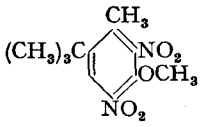
2 : 4 : 6-Trinitrotoluene (T.N.T), m.p. 81°, may be prepared by nitrating toluene with mixed acid consisting of fuming nitric and fuming sulphuric acids. This reaction takes place far more readily than with benzene because of the activation of the ring by the methyl group.

Trinitrotoluene is used as an explosive; mixed with ammonium nitrate, it forms the explosive *amatol*.

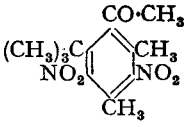
Artificial musks. Polynitro-derivatives of benzene containing a tertiary butyl group, possess odours resembling musk, and are used in perfumery, *e.g.*,



"toluene-musk"



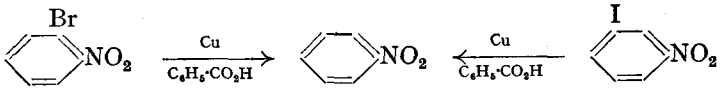
"musk ambrette"



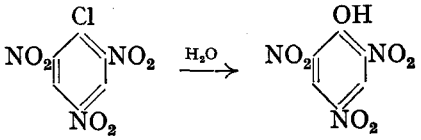
"musk ketone"

Halogeno-nitrobenzenes. Nitration of phenyl halides produces a mixture of the *o*- and *p*-halogeno-nitrobenzenes; these may be separated by freezing and filtration, the *p*-isomer having the higher melting point. The halogen atom *o*- or *p*- to a nitro-group is fairly reactive, and is replaced when heated with alkali, ethanolic ammonia, etc., to form respectively nitrophenols, nitroanilines, etc. Smith *et al.* (1953) have shown that the halogen atom in halogenonitro-compounds may be removed by heating with copper powder

and benzoic acid. Chlorine and bromine may be removed when *o*- or *p*- to a nitro-group; iodine is removed from *any* position, and fluorine not at all, *e.g.*,

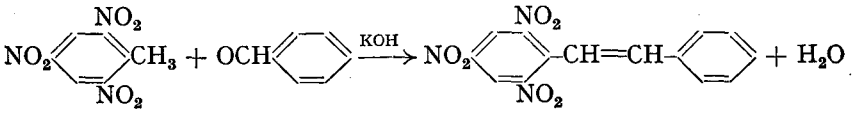


When two nitro-groups are present in the *o*- and *p*-positions (with respect to the halogen atom), the halogen atom is more reactive, and when three nitro-groups are present in the *p*- and two *o*-positions, the halogen atom is so reactive that it can be replaced by hydroxyl merely by warming with water, *e.g.*, picryl chloride forms picric acid:

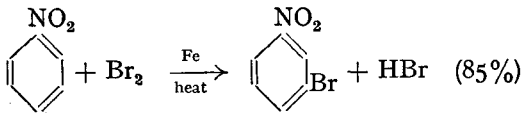


It is also interesting to note that the fluorine atom in 1-fluoro-2 : 4-dinitrobenzene is strongly activated. This compound condenses with amino-groups to form *N*-2 : 4-dinitrophenyl derivatives. This reaction has been used in protein and peptide studies (Sanger, 1945).

A methyl group is also made reactive by a nitro-group in the *o*- or *p*-position, *e.g.*, trinitrotoluene condenses with benzaldehyde in the presence of ethanolic potassium hydroxide to form *trinitrostilbene*:



Halogenation of nitrobenzene produces mainly the *m*-derivative:

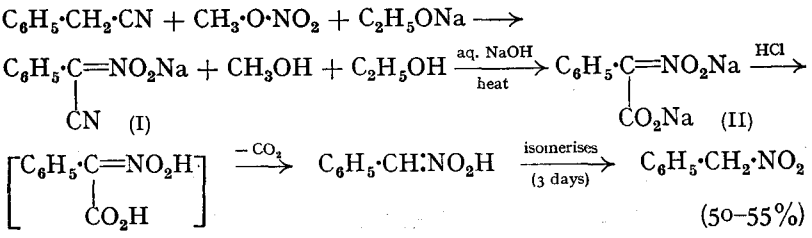


A halogen atom *m*- to a nitro-group shows the same unreactivity as the halogen atom in a phenyl halide.

Phenylnitromethane, $C_6H_5{\cdot}CH_2{\cdot}NO_2$, may be prepared by heating toluene with dilute nitric acid in a sealed tube at 100°, or by heating benzyl chloride with aqueous ethanolic silver nitrite:

$$C_6H_5{\cdot}CH_3 + HNO_3 \longrightarrow C_6H_5{\cdot}CH_2{\cdot}NO_2 + H_2O \quad (p.)$$
$$C_6H_5{\cdot}CH_2Cl + Ag{\cdot}O{\cdot}NO \longrightarrow C_6H_5{\cdot}CH_2{\cdot}NO_2 + AgCl \quad (f.g.).$$

Phenylnitromethane is best prepared as follows:

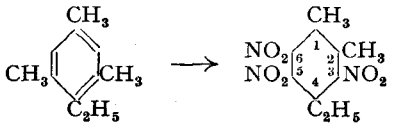


(I) is sodio-phenyl*aci*nitroacetonitrile, and (II) is the sodium salt of phenylnitroacetic acid.

Phenylnitromethane behaves as a true primary aliphatic nitro-compound; both the nitro- and *aci*nitro-forms have been isolated (*cf.* p. 304):

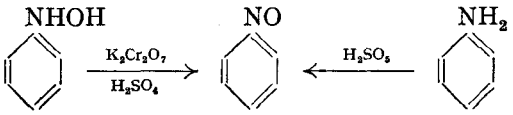
$$\underset{\text{yellow oil}\\ \text{b.p. } 226^\circ}{C_6H_5{\cdot}CH_2{\cdot}NO_2} \rightleftharpoons \underset{\text{solid}\\ \text{m.p. } 84^\circ}{C_6H_5{\cdot}CH{=}NO_2H}$$

Abnormal nitration. When nuclear-substituted aromatic compounds are nitrated, there are many cases where an alkyl, halogen, alkoxyl, acyl, carboxyl, or sulphonic acid group is replaced by a nitro-group; in some cases, a hydrogen atom in the side-chain is replaced by the *nitrate* group. Generally, abnormal nitration is more likely to occur in the nitration of polysubstituted benzene compounds, particularly the polyalkylbenzenes. Mono-, di- and trialkylbenzenes (where the alkyl group is methyl or ethyl) give the expected nitro-compounds. Polyalkylbenzenes containing three or more alkyl groups in some cases give normal products, and in others, abnormal; *e.g.*, ethylmesitylene, when nitrated with mixed acid (fuming nitric and sulphuric), gives 3:5:6-trinitro-4-ethyl-*o*-xylene:



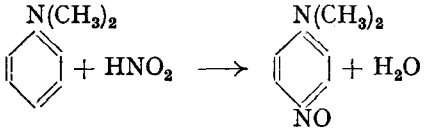
AROMATIC NITROSO-COMPOUNDS

The simplest aromatic nitroso-compound is **nitrosobenzene,** $C_6H_5{\cdot}NO$. This may be prepared by oxidising phenylhydroxylamine with dichromate-sulphuric acid mixture, or by oxidising aniline with Caro's acid:



Nitrosobenzene may also be prepared by the electrolytic reduction of nitrobenzene (see later).

Nitroso-compounds containing certain other groups in the ring may be prepared directly by the action of nitrous acid on the compound, *e.g.*, dimethylaniline forms *p*-nitrosodimethylaniline:



Nitrosobenzene, in the solid state, exists as colourless crystals, m.p. 68°; this is the dimer. According to Lüttke (1956, 1957), dimeric nitrosobenzene exists in the *cis*-form. In the liquid (fused) state, in solution, or in the gaseous state, nitrosobenzene is green; this is the monomer (*cf.* p. 307).

Reactions of nitrosobenzene. Nitrosobenzene is reduced by hydrogen in the presence of palladium (on a calcium carbonate support) to *azobenzene*:

$$2C_6H_5{\cdot}NO + 2H_2 \xrightarrow{Pd} C_6H_5{\cdot}N{:}N{\cdot}C_6H_5 + 2H_2O \quad (100\%)$$

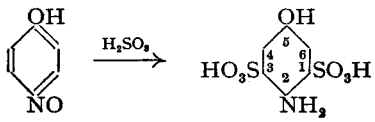
When reduced with concentrated hydriodic acid-red phosphorus, nitrosobenzene gives phenylhydroxylamine:

$$C_6H_5{\cdot}NO + 2HI \xrightarrow{P} C_6H_5{\cdot}NH{\cdot}OH + I_2$$

Reduction with metal and acid gives aniline:

$$C_6H_5{\cdot}NO + 4[H] \xrightarrow{Fe/HCl} C_6H_5{\cdot}NH_2 + H_2O$$

Reduction of nitroso-compounds with sulphur dioxide or sodium hydrogen sulphite is often accompanied by the simultaneous introduction of a sulphonic acid group, *e.g.*, *p*-nitrosophenol forms 2-amino-5-hydroxybenzene-1:3-disulphonic acid:



Nitrosobenzene is oxidised by alkaline hydrogen peroxide, dilute nitric acid, or a mixture of nitric acid and hydrogen peroxide, to nitrobenzene:

$$C_6H_5{\cdot}NO + H_2O_2 \xrightarrow{NaOH} C_6H_5{\cdot}NO_2 + H_2O$$

Nitrosobenzene condenses with aniline to form azobenzene:

$$C_6H_5{\cdot}NO + C_6H_5{\cdot}NH_2 \longrightarrow C_6H_5{\cdot}N{:}N{\cdot}C_6H_5 + H_2O$$

It will also condense with compounds containing a reactive methylene group, *e.g.*,

$$C_6H_5{\cdot}NO + C_6H_5{\cdot}CH_2{\cdot}CN \longrightarrow C_6H_5{\cdot}C(CN){:}N{\cdot}C_6H_5 + H_2O$$

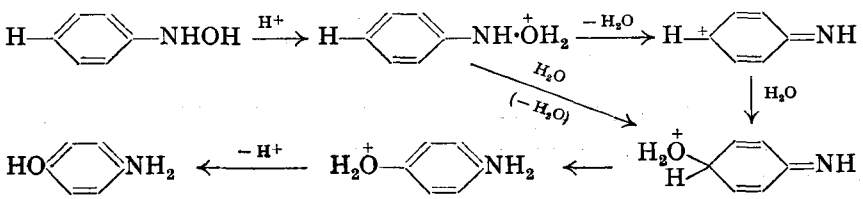
The orienting influence of the nitroso-group has been discussed on p. 522.

Phenylhydroxylamine, $C_6H_5{\cdot}NH{\cdot}OH$, may be prepared by reducing nitrobenzene with zinc dust and aqueous ammonium chloride (yield: 62–68 per cent.), or by the electrolytic reduction of nitrobenzene in an aqueous solution of acetic acid containing sodium acetate.

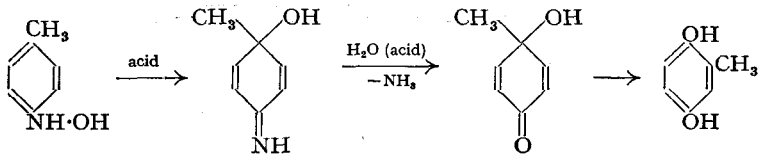
Phenylhydroxylamine is a white solid, m.p. 81°, soluble in water, ethanol and ether. It is a powerful reducing agent, *e.g.*, it reduces ammoniacal silver nitrate and Fehling's solution. It readily absorbs oxygen from the air to form nitrosobenzene; this can react with unchanged phenylhydroxylamine to give *azoxybenzene*:

$$C_6H_5{\cdot}NH{\cdot}OH + C_6H_5{\cdot}NO \longrightarrow C_6H_5{\cdot}\overset{\overset{O}{\uparrow}}{N}{:}N{\cdot}C_6H_5 + H_2O$$

In dilute acid solution, phenylhydroxylamine rearranges to *p*-aminophenol. According to Hughes and Ingold (1951), the mechanism is possibly:



If the *p*-position is occupied by a methyl group, the rearrangement can still take place, but in this case ammonia is eliminated and a methylquinol is formed; this methylquinol then readily rearranges to a quinol:



Phenylhydroxylamine is used to prepare **cupferron**; an ethereal solution of phenylhydroxylamine is treated with dry ammonia gas, and then *n*-butyl nitrite is added:

$$C_6H_5{\cdot}NH{\cdot}OH + C_4H_9{\cdot}O{\cdot}NO + NH_3 \longrightarrow C_6H_5{\cdot}N(NO){\cdot}ONH_4 + C_4H_9OH \quad (85\text{–}90\%)$$

Cupferron is the ammonium salt of *N*-nitrosophenylhydroxylamine, and was originally used for the quantitative estimation of copper and iron (hence its name). Cupferron is a colourless solid, and the structure of its metallic complexes is uncertain.

Reduction products of the nitro-compounds. The course of the reduction of nitro-compounds has been shown to take place through the following stages:

$$C_6H_5{\cdot}NO_2 \longrightarrow C_6H_5{\cdot}NO \longrightarrow C_6H_5{\cdot}NH{\cdot}OH \longrightarrow C_6H_5{\cdot}NH_2\ .$$

The nature of the final product, however, depends mainly on the *p*H of the solution in which the reduction is carried out.

(i) In acid solution (metal and acid), aniline is obtained:

$$C_6H_5{\cdot}NO_2 + 6[H] \xrightarrow{\text{metal/acid}} C_6H_5{\cdot}NH_2 + 2H_2O$$

In acid solution, the intermediate products nitrosobenzene and phenylhydroxylamine are reduced far more rapidly than nitrobenzene, and so these intermediates are never isolated.

(ii) In neutral solution, *e.g.*, with zinc dust and ammonium chloride solution, the main product of the reduction is phenylhydroxylamine.

(iii) In alkaline solution the compound obtained depends on the nature of the reducing agent used (see p. 599). The complex compounds that may be obtained are:

(*a*) *Azoxybenzene.* This is believed to be formed by interaction of the intermediate products nitrosobenzene and phenylhydroxylamine:

$$C_6H_5{\cdot}NO + C_6H_5{\cdot}NH{\cdot}OH \longrightarrow C_6H_5{\cdot}\overset{\overset{O}{\uparrow}}{N}{:}N{\cdot}C_6H_5 + H_2O$$

(*b*) *Azobenzene.* This is believed to be formed by reaction between two molecules of phenylhydroxylamine:

$$2C_6H_5{\cdot}NH{\cdot}OH \longrightarrow C_6H_5{\cdot}N{:}N{\cdot}C_6H_5 + 2H_2O$$

(*c*) *Hydrazobenzene.* This is apparently formed by the reduction of azobenzene:

$$C_6H_5{\cdot}N{:}N{\cdot}C_6H_5 + 2[H] \longrightarrow C_6H_5{\cdot}NH{\cdot}NH{\cdot}C_6H_5$$

Thus by choosing a suitable alkaline reducing agent, it is possible to isolate (*a*), (*b*), or (*c*).

In weakly acid solution, the main product is aniline; but in strongly acid solution, the product is *p*-aminophenol, formed by the rearrangement of phenylhydroxylamine. On the other hand, aromatic nitro-compounds are reduced to azo-compounds by lithium aluminium hydride. If, however, this reduction is carried out in the presence of a small amount of metal chloride, *e.g.*, Fe, Sn, etc. (but *not* Al), nitrobenzene (and azobenzene) gives hydrazobenzene (yield: good; Oláh, 1959).

The course of catalytic reduction (with Raney nickel) has not been investigated in detail. It is quite likely that it takes place in the same way as those discussed above; the final product is often almost a quantitative yield of amine.

QUESTIONS

1. Write an account of the mechanism of nitration with (*a*) mixed acid, (*b*) with concentrated aqueous nitric acid.

2. Starting with benzene or toluene, how would you prepare each of the following:—(*a*) $PhNO_2$, (*b*) *o*-, *m*- and *p*-$C_6H_4(NO_2)_2$, (*c*) *s*-$C_6H_3(NO_2)_3$, (*d*) *o*-, *m*- and *p*-$MeC_6H_4{\cdot}NO_2$, (*e*) T.N.T., (*f*) *o*-, *m*- and *p*-$ClC_6H_4{\cdot}NO_2$, (*g*) $Ph{\cdot}CH_2{\cdot}NO_2$?

In each case indicate the principles upon which you have based your method.

3. What are the important differences in behaviour between *o*-, *m*- and *p*-dinitrobenzene? Which of these isomers resemble *s*-trinitrobenzene in chemical properties?

4. Discuss the effect of a nitro-group on the reactivity of:—(*a*) a halogen atom, (*b*) a methyl group, (*c*) another nitro-group, in aromatic compounds.

5. Write an account of the preparation and properties of:—(*a*) PhNO, (*b*) *p*-$Me_2N{\cdot}C_6H_4{\cdot}NO$, (*c*) $Ph{\cdot}NH{\cdot}OH$.

6. Write an account of the reduction products of nitrobenzene.

7. A compound has the formula $C_7H_7O_2N$. Write out the structures of the possible isomers and show how you would distinguish between them.

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Murrell, The Theory of Charge-Transfer Spectra, *Quart. Reviews* (*Chem. Soc.*), 1961, **15**, 191.
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CHAPTER XXIII

AROMATIC AMINO-COMPOUNDS

AROMATIC amines are of two types, one in which the amino-group is attached directly to the ring, and the other in which the amino-group is in the side-chain. The latter behave very much like the aliphatic amines, and so may be regarded as aryl-substituted aliphatic amines.

Nuclear amino-compounds fall into the same three classes as the aliphatic amines, *viz.*, *primary amines*, $Ar{\cdot}NH_2$; *secondary amines*, Ar_2NH and $Ar{\cdot}NH{\cdot}R$; and *tertiary amines*, Ar_3N, $Ar_2N{\cdot}R$ and $Ar{\cdot}NR_2$.

Purely aromatic quaternary compounds, *i.e.*, compounds of the type $Ar_4\overset{+}{N}\}X^-$, have not yet been prepared; compounds of the type $Ar_3\overset{+}{N}{\cdot}R\}X^-$, however, are known.

General methods of preparation of primary amines. 1. Primary aromatic amines are nearly always prepared by the reduction of the corresponding nitro-compound. Various reducing reagents may be used, *e.g.*, tin, iron, or zinc, with hydrochloric or acetic acid:

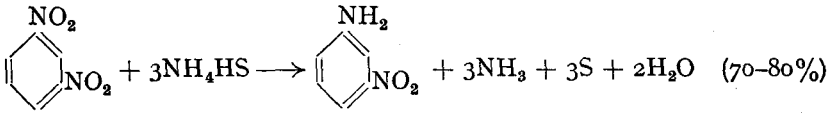
$$Ar{\cdot}NO_2 + 6[H] \xrightarrow{\text{metal/acid}} Ar{\cdot}NH_2 + 2H_2O \quad (v.g.\text{–}ex.)$$

Zinc and hydrochloric acid often produce the chloroamino-compound as well as the desired amino-compound. Acetic acid is very useful for compounds which contain a group that is attacked by inorganic acid; *e.g.*, reduction of *p*-nitro-acetanilide in hydrochloric acid solution leads to some hydrolysis of the acetyl group; use of acetic acid prevents this deacetylation.

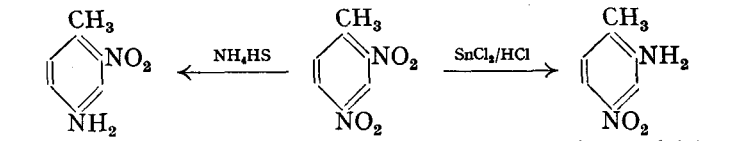
Titanous chloride in hydrochloric acid reduces nitro-compounds to amines, and may be used for the quantitative estimation of nitro-groups in a compound:

$$Ar{\cdot}NO_2 + 6TiCl_3 + 6HCl \longrightarrow Ar{\cdot}NH_2 + 6TiCl_4 + 2H_2O$$

By means of aqueous ethanolic ammonium hydrogen sulphide, aqueous sodium sulphide, or stannous chloride in hydrochloric acid, nitro-groups in a polynitro-compound can be reduced one at a time, *e.g.*, *m*-nitroaniline from *m*-dinitrobenzene:

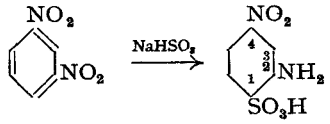


It appears that ammonium hydrogen sulphide and sodium sulphide will not reduce a nitro-group in the *o*-position to an alkyl group, whereas stannous chloride in hydrochloric acid reduces this nitro-group preferentially:



3-nitro-*p*-toluidine 5-nitro-*o*-toluidine

Sulphur dioxide or sodium hydrogen sulphite may also be used to reduce one nitro-group in polynitro-compounds, but in certain cases the reduction is accompanied by the introduction of a sulphonic acid group, *e.g.*,



4-nitro-orthanilic acid

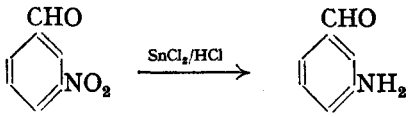
Nitro-compounds may be reduced catalytically to the corresponding amine at 200–400°; if Raney nickel or platinum is used as catalyst, the reduction may be carried out at room temperature. Catalytic reduction is particularly useful for compounds which contain a group that is hydrolysable in acid solution, *e.g.*, *p*-nitroacetanilide, $p\text{-}NO_2\cdot C_6H_4\cdot NH\cdot CO\cdot CH_3$. Although organic sulphur compounds poison the Raney nickel catalyst, nitro-compounds containing a thiol, sulphide, etc., linkage can nevertheless still be reduced by using a large excess of the catalyst (Fel'dman, 1949). The reduction of nitro-compounds may also be effected with hydrazine hydrate. The reaction is slow, but is catalysed by Raney nickel (Balcom *et al.*, 1953). Dewar *et al.* (1956) have shown that palladised charcoal is a more convenient catalyst, the yields of amine varying from 60–81 per cent.

Nitro-compounds may also be reduced by means of *cyclo*hexene and palladium, and if more than one nitro-group is present, it is possible to reduce only one (see p. 483).

Certain nitro-compounds may be reduced to the corresponding amine in liquid ammonia solution by sodium and methanol, or sodium and ammonium bromide (Watt *et al.*, 1947), *e.g.*,

$$C_6H_5\cdot NO_2 \xrightarrow{Na/CH_3OH} C_6H_5\cdot NH_2 \quad (92\%)$$

If a nitro-compound contains an unsaturated chain or an aldehyde group in the nucleus, alkaline ferrous sulphate may be used as the reducing agent to avoid reduction of these other groups. If only an aldehyde group is present, then stannous chloride may be used as the reducing agent; *e.g.*, *m*-nitrobenzaldehyde may be reduced to *m*-aminobenzaldehyde:



2. Amino-compounds may be prepared by reduction of nitroso-compounds:

$$C_6H_5\cdot NO + 4[H] \xrightarrow{Sn/HCl} C_6H_5\cdot NH_2 + H_2O$$

3. Reduction of azo- and hydrazo-compounds, usually with sodium hyposulphite (dithionite), gives very good yields of amino-compound:

$$Ar\cdot N{:}N\cdot Ar' + 2Na_2S_2O_4 + 4H_2O \longrightarrow Ar\cdot NH_2 + Ar'\cdot NH_2 + 4NaHSO_3$$

Reduction of azo-compounds is very useful in certain cases (see, *e.g.*, p. 598).

4. Amino-compounds may be prepared by the Hofmann reaction; *e.g.*, benzamide gives aniline:

$$C_6H_5\cdot CO\cdot NH_2 \xrightarrow{Br_2/KOH} C_6H_5\cdot NH_2$$

5. The Schmidt reaction may be used to prepare amines:

$$Ar{\cdot}CO_2H + HN_3 \xrightarrow{H_2SO_4} Ar{\cdot}NH_2 + CO_2 + N_2$$

6. Ammonolysis of halogeno- and hydroxy-compounds may be used in certain cases to prepare amino-compounds (see, *e.g.*, aniline).

7. Many amino-compounds may be prepared by means of rearrangement reactions (see, *e.g.*, p. 602).

Aniline (*aminobenzene*), $C_6H_5{\cdot}NH_2$, was discovered by Unverdorben (1826), who obtained it by distilling indigo; this name was given to it by Fritzsche (1841), who derived it from *anil*, the Portuguese word for indigo.

In the laboratory, aniline is prepared by the reduction of nitrobenzene with metal and acid, *e.g.*, tin and hydrochloric acid:

$$C_6H_5{\cdot}NO_2 + 6[H] \longrightarrow C_6H_5{\cdot}NH_2 + 2H_2O \quad (80\%)$$

The aniline remains in solution as aniline stannichloride $(C_6H_5{\cdot}NH_2)_2{\cdot}H_2SnCl_6$; when the solution is made alkaline and steam distilled, the aniline comes over in the distillate.

Commercially, aniline is prepared:

(i) By the reduction of nitrobenzene with iron, water and a small amount of hydrochloric acid (one fortieth of the theoretical amount).

The mechanism of the reduction is uncertain, but there is some evidence to show it may be as follows:

$$Fe + 2HCl \longrightarrow FeCl_2 + 2[H]$$
$$C_6H_5{\cdot}NO_2 + 6[H] \longrightarrow C_6H_5{\cdot}NH_2 + 2H_2O$$
$$FeCl_2 + 2H_2O \longrightarrow Fe(OH)_2 + 2HCl$$
$$C_6H_5{\cdot}NO_2 + 6Fe(OH)_2 + 4H_2O \longrightarrow C_6H_5{\cdot}NH_2 + 6Fe(OH)_3$$

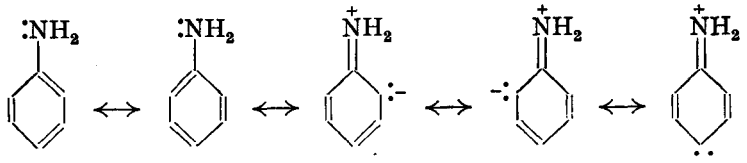
(ii) By the catalytic reduction (nickel catalyst) of nitrobenzene.

(iii) By heating chlorobenzene with excess aqueous ammonia in the presence of cuprous oxide at 200° under pressure. The cuprous oxide renders the reaction irreversible by decomposing the ammonium chloride formed in the reaction:

$$2C_6H_5Cl + 2NH_3 + Cu_2O \longrightarrow 2C_6H_5{\cdot}NH_2 + 2CuCl + H_2O \quad (90\%)$$

Aniline (whose properties are characteristic of primary aromatic amines in general) is, when freshly prepared, a colourless liquid, b.p. 184°; it has an unpleasant odour and is poisonous. When exposed to air, it rapidly darkens, since it is very sensitive to oxidation. It is practically insoluble in water, but is steam-volatile; it is readily soluble in organic solvents.

Aniline forms crystalline salts with strong inorganic acids, and these salts are considerably hydrolysed in solution. Aniline is a weaker base than the primary aliphatic amines, and this may be explained by resonance (which is not possible in aliphatic primary amines):



In aniline, owing to resonance, the lone pair of electrons on the nitrogen atom is less available for co-ordinating with a proton; at the same time, the small

positive charge on the nitrogen atom would tend to repel a proton. Alternatively, since there are more resonating structures possible for aniline itself than for the cation $C_6H_5{\cdot}\overset{+}{N}H_3$, the former will be stabilised with respect to the latter.

The decreased basicity of aniline may be explained from M.O. theory as follows. The lone pair of electrons on the nitrogen atom conjugate with the p_z electrons of the benzene ring, thereby reducing their availability for accepting a proton owing to partial delocalisation (see Fig. 20.4, p. 528).

Hydrogen atoms of the amino-group are replaceable by halogen when aniline is treated with hypohalous acid. When aniline is heated with sodium or potassium, the metal dissolves with the evolution of hydrogen;

$$C_6H_5{\cdot}NH_2 + K \longrightarrow [C_6H_5{\cdot}NH]^-K^+ + \tfrac{1}{2}H_2$$

Aniline combines with alkyl halides to give finally a quaternary ammonium compound:

$$C_6H_5{\cdot}NH_2 + 3CH_3Cl \longrightarrow [C_6H_5{\cdot}N(CH_3)_3]^+Cl^-$$

Aniline gives the iso*cyanide reaction* when heated with chloroform and ethanolic potassium hydroxide (see p. 297):

$$C_6H_5{\cdot}NH_2 + CHCl_3 + 3KOH \longrightarrow C_6H_5{\cdot}NC + 3KCl + 3H_2O$$

Aniline is readily acetylated, and condenses with aromatic aldehydes to form anils or Schiff bases; *e.g.*, when warmed with benzaldehyde, it forms benzylideneaniline:

$$C_6H_5{\cdot}NH_2 + C_6H_5{\cdot}CHO \longrightarrow C_6H_5{\cdot}N{:}CH{\cdot}C_6H_5 + H_2O \quad (84\text{–}87\%)$$

These Schiff bases are easily hydrolysed to the free amine, and so their formation offers a means of " protecting " an amino-group, *e.g.*, during nitration. Schiff bases may also be used to prepare secondary amines:

$$C_6H_5{\cdot}N{:}CH{\cdot}Ar \xrightarrow[Ni]{H_2} C_6H_5{\cdot}NH{\cdot}CH_2{\cdot}Ar$$

On the other hand, benzylideneaniline undergoes reductive cleavage to aniline by hydrogen transfer with *cyclo*hexene and palladium (Braude *et al.*, 1954; see also p. 483).

When refluxed with ethanolic carbon disulphide and solid potassium hydroxide, aniline forms **s-diphenylthiourea** (*thiocarbanilide*), m.p. 154°, which is used as a rubber accelerator:

$$CS_2 + 2C_6H_5{\cdot}NH_2 + 2KOH \longrightarrow S{:}C(NH{\cdot}C_6H_5)_2 + K_2S + 2H_2O \quad (70\%)$$

When treated with concentrated hydrochloric acid, diphenylthiourea is converted into phenyl *iso*thiocyanate:

$$S{:}C(NH{\cdot}C_6H_5)_2 + HCl \longrightarrow C_6H_5{\cdot}NCS + C_6H_5{\cdot}NH_2{\cdot}HCl$$

Phenyl *iso*thiocyanate may be conveniently prepared by running aniline into a cooled mixture of carbon disulphide and concentrated aqueous ammonium hydroxide, and decomposing the precipitated ammonium phenyldithiocarbamate with lead nitrate solution:

$$C_6H_5{\cdot}NH_2 + CS_2 + NH_4OH \longrightarrow C_6H_5{\cdot}NH{\cdot}CS_2NH_4 + H_2O \xrightarrow{Pb(NO_3)_2} C_6H_5{\cdot}NCS + NH_4NO_3 + HNO_3 + PbS \quad (74\text{–}78\%)$$

Baxter *et al.* (1956) have shown that aryl *iso*thiocyanates may be prepared by heating arylthioureas in chlorobenzene solution at 150°, *e.g.*,

$$C_6H_5{\cdot}N{\cdot}CS{\cdot}NH_2 \longrightarrow C_6H_5{\cdot}NCS + NH_3 \quad (44\%)$$

The oxidation products of aniline are far more complex than those obtained from primary aliphatic amines (p. 316). Nitrosobenzene, nitrobenzene, phenylhydroxylamine, *p*-benzoquinone, azobenzene, azoxybenzene, aniline black (a dye), etc., may be isolated, the actual substance obtained depending on the nature of the oxidising agent used, *e.g.*, Caro's acid oxidises aniline to a mixture of nitroso- and nitrobenzene; peroxytrifluoroacetic acid oxidises aniline to nitrobenzene (89%; Emmons, 1954); chromic acid gives *p*-benzoquinone; sodium hypochlorite gives a purple coloration—this reaction is characteristic of aniline.

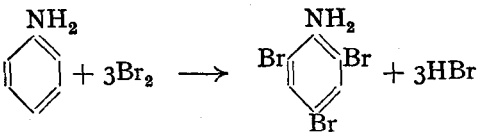
Aniline may be easily mercurated with an aqueous ethanolic solution of mercuric acetate in the cold or on warming.

The most important difference between aniline and primary aliphatic amines is their behaviour towards nitrous acid; aliphatic amines liberate nitrogen (see p. 316), whereas aniline (and all other primary aromatic monoamines) forms *diazonium salts*, which are stable in cold aqueous solution:

$$C_6H_5{\cdot}NH_2 + HNO_2 + HCl \longrightarrow \underset{\text{benzenediazonium chloride}}{C_6H_5{\cdot}N_2Cl} + 2H_2O$$

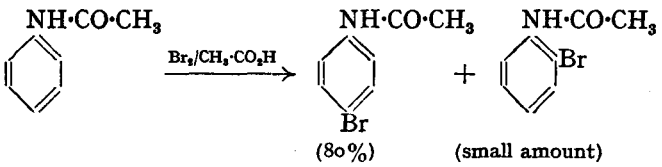
Acetanilide (*N-phenylacetamide*), $C_6H_5{\cdot}NH{\cdot}CO{\cdot}CH_3$, may be readily prepared, in very good yield, by heating aniline with acetyl chloride, acetic anhydride, or glacial acetic acid. It is a white crystalline solid, m.p. 114°, almost insoluble in cold water but readily soluble in hot. It is hydrolysed by strong acids or alkalis to aniline. It is used in medicine, under the name of *antifebrin*, as a febrifuge. It is a useful intermediate in various reactions of aniline in which it is desirable to " protect " the amino-group, *e.g.*, in nitration, halogenation, etc.; the acetamido-group is predominantly *p*-orienting. The *N*-phenyl derivative of the amide of any acid is known as an *anilide*.

Halogenated anilines. The amino-group in aniline activates the *o*- and *p*-positions to a very large degree; *e.g.*, when aniline is treated with excess chlorine- or bromine-water, an immediate precipitate of the 2 : 4 : 6-*trihalogeno-derivative* is obtained:



The yield is quantitative, and so this reaction is used to estimate aniline.

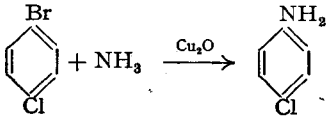
In order to introduce only one chlorine or bromine atom, the activating effect of the amino-group must be lowered; this may be done by acetylation:



These, on hydrolysis, yield the corresponding bromoanilines, which may be separated by steam distillation (the *o*-compound being steam volatile).

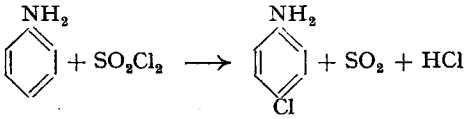
The deactivating effect of the acetyl group may be due to the inductive effect of the carbonyl group, thereby inhibiting, to a certain extent, the lone pair entering into resonance.

An interesting method of preparing *p*-chloroaniline is to heat *p*-chlorobromobenzene with ammonia in the presence of cuprous oxide:



This is possible due to the more ready displacement of bromine compared with chlorine.

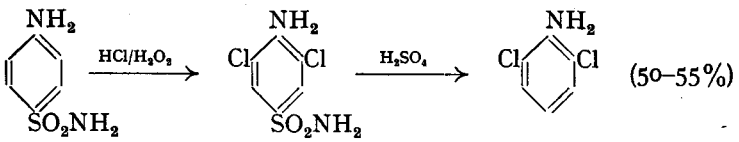
Aniline is readily chlorinated by sulphuryl chloride, in the *absence* of catalysts, to form the mono-, di- and trichloroanilines, *e.g.*,



***p*-Iodoaniline** may be prepared by the action of iodine on aniline in the presence of aqueous sodium hydrogen carbonate (*cf.* p. 546). Oxidising agents cannot be used to remove the hydrogen iodide, since they will oxidise the aniline; hence the use of sodium hydrogen carbonate.

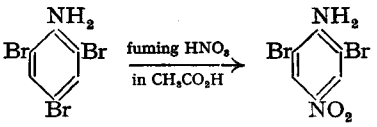
m-Chloro- and bromo-anilines may be prepared by reducing the corresponding halogeno-nitrobenzenes. They are also formed by the halogenation of aniline in concentrated sulphuric acid, the *m*-orienting effect being due to the presence of the $-\overset{+}{N}H_3$ group (see p. 520).

2 : 6-Dichloroaniline may be prepared by first blocking the *p*-position of aniline with a sulphonamide group, refluxing the sulphanilamide with hydrochloric acid and hydrogen peroxide, and subsequently refluxing the product, 3 : 5-dichlorosulphanilamide, with 70 per cent. sulphuric acid, thereby removing the sulphonamide group:



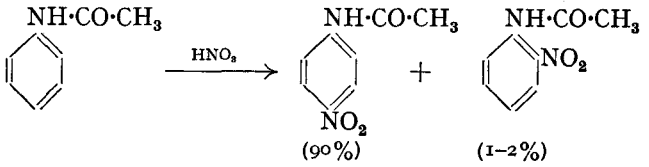
The presence of a halogen atom, particularly in the *o*- or *p*-position, decreases the basic properties of aniline; *e.g.*, the salts of the trihalogeno-anilines are completely hydrolysed in aqueous solution (*cf.* nitroanilines below).

An interesting point about trihalogeno-anilines is their anomalous nitration:



Nitroanilines. Direct treatment of aniline with nitric acid gives a complex mixture of mono-, di- and trinitro-compounds, and oxidation products. If, however, the amino-group is protected (and deactivated) by acetylation

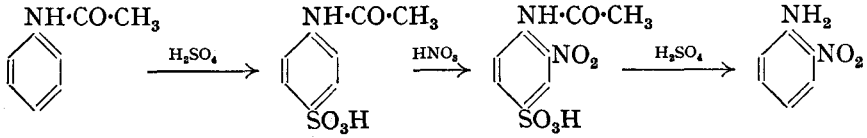
or by the formation of the benzylidene derivative, the main product on nitration is the *p*-nitro-derivative:



The nitroacetanilides may be separated by digesting the mixture with chloroform in which the *o*-derivative is soluble and the *p*-, insoluble. Alternatively, they may be separated by keeping the *o*-compound liquid (m.p. 93°) and filtering off the solid *p*-isomer (m.p. 215°); or by chromatographic adsorption, since the *o*-compound chelates. After separation, the nitroanilines may be obtained by hydrolysis with alkali.

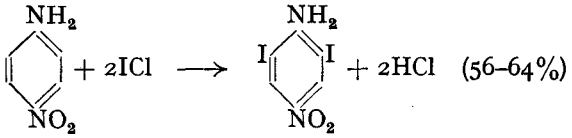
Nitration of aniline derivatives is accelerated by nitrous acid. This is believed to be due to the formation of the nitroso-compound, followed by its oxidation to the nitro-compound (see phenol, p. 626).

***o*- and *p*-Nitroanilines** may be prepared by heating *o*- and *p*-chloronitrobenzenes with ammonia (*cf.* p. 558). The *o*-isomer, however, is best prepared as follows:

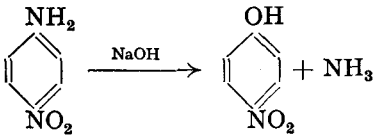


***m*-Nitroaniline** (m.p. 114°) may be prepared by the partial reduction of *m*-dinitrobenzene with ammonium hydrogen sulphide (yield: 70–80 per cent.), sodium sulphide (yield: 70 per cent.), or stannous chloride in hydrochloric acid. *m*-Nitroaniline may also be prepared by the direct nitration of aniline *in the presence of concentrated sulphuric acid* (*cf. m*-chloroaniline, above). Industrially, it is prepared by reducing *m*-dinitrobenzene with the calculated quantity of iron (for one nitro-group) and a small amount of hydrochloric acid.

All three nitroanilines may be reduced by metal and acid to the corresponding diamines. All can be halogenated in the *o*-position; iodine monochloride in boiling acetic acid is used to prepare the iodo-compound:

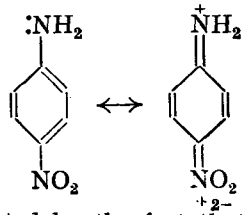


o- and *p*-Nitroanilines, but not *m*-, react with boiling aqueous sodium hydroxide to give the corresponding nitrophenol (*cf.* chloronitrobenzenes, p. 588):



All the nitroanilines are weaker bases than aniline. This may be due to the inductive effect of the nitro-group tending to withdraw electrons from the ring, thereby decreasing the availability of the lone pair on the nitrogen

atom of the amino-group; the net result is an increased contribution of the charged state, due to resonance, to the actual state of the molecule:

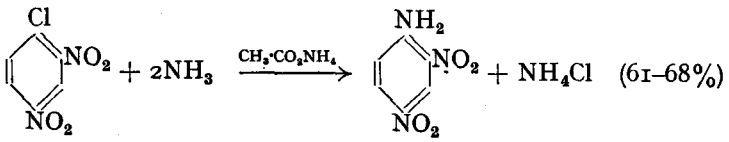


This explanation is supported by the fact that the dipole moment of *p*-nitroaniline is greater than the sum of the dipole moments of the amino- and nitro-groups.

Increasing the number of nitro-groups decreases the basic properties of the compound due to an increase in resonance. A nitro-group in the *o*- or *p*-position has a much greater effect than one in the *m*-position.

From the point of view of M.O. theory, the decreased basicity may be accounted for by the fact that in nitroanilines, the nitrogen atoms of both nitro- and amino-groups enter into conjugation with the benzene ring. Also, since the nitrogen atom of the nitro-group has a positive charge and consequently attracts the electron cloud, partial delocalisation of the lone pair on the amino-group will be greater than had the nitro-group been absent. Calculation shows that this effect of the nitro-group is greater in the *o*- and *p*-positions than in the *m*-position.

2:4-Dinitroaniline, m.p. 180°, may be prepared by passing ammonia gas into a heated mixture of 1-chloro-2:4-dinitrobenzene and ammonium acetate:



Aminobenzenesulphonic acids (see p. 615).

Toluidines (*tolylamines*). These may be obtained by reduction of the corresponding nitrotoluenes. *o*- and *m*-Toluidines are oils, b.p. 201° and 200°, respectively; *p*-toluidine is a solid, m.p. 45°, b.p. 200°.

Nitration of toluene gives a mixture of *o*- and *p*-nitrotoluenes, and this, when reduced with iron and dilute hydrochloric acid, gives a mixture of the corresponding toluidines.

When the reaction mixture is steam distilled, both pass over; when the distillate is cooled, the hydrate of the *p*-isomer crystallises out, the *o*-compound remaining as an oil (yield of *o*- and *p*-isomers is 90–95 per cent.). Both isomers are used in the preparation of dyes.

m-Nitrotoluene is prepared via a diazonium salt (p. 584).

***N*-Alkylanilines.** The commonest *N*-alkylanilines are mono- and dimethylaniline. These may be prepared by heating aniline with methyl iodide:

$$C_6H_5{\cdot}NH_2 + CH_3I \longrightarrow C_6H_5{\cdot}NH{\cdot}CH_3{\cdot}HI$$
$$C_6H_5{\cdot}NH{\cdot}CH_3 + CH_3I \longrightarrow C_6H_5{\cdot}N(CH_3)_2{\cdot}HI$$

Commercially, these methylanilines are prepared by heating a mixture of aniline, methanol and sulphuric acid under pressure at 230°. No quaternary compound is formed under these conditions (*cf.* p. 309). Monomethylaniline is the main product (50 per cent.) when about 1·2 molecules of methanol

are used; dimethylaniline and unchanged aniline are also present. Dimethylaniline is obtained as the main product (95 per cent.) by using a large excess of methanol; monomethylaniline and unchanged aniline are also present, but these are removed by acetylating the mixture and distilling off the dimethylaniline.

To prepare higher *N*-alkyl derivatives of aniline, hydrochloric acid is used instead of sulphuric, since the latter tends to dehydrate the alcohol to olefin.

An interesting example of *reductive methylation* is the conversion of aniline into dimethylaniline; aniline and formaldehyde, in aqueous ethanolic sulphuric acid, is hydrogenated in the presence of platinum as catalyst (Pearson *et al.*, 1951).

$$C_6H_5{\cdot}NH_2 + 2CH_2O + 2H_2 \xrightarrow{Pt} C_6H_5{\cdot}N(CH_3)_2 + 2H_2O \quad (74\%)$$

Mono- and dimethylaniline are liquids, b.p. 196° and 193°, respectively, and, due to the closeness of their boiling points, cannot be readily separated by fractional distillation. They can be separated, however, by acetylating the monomethyl derivative (as indicated above).

Pure monomethylaniline may be prepared by treating the sodium derivative of acetanilide with methyl iodide in toluene solution:

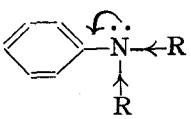
$$[C_6H_5{\cdot}N{\cdot}CO{\cdot}CH_3]^-Na^+ + CH_3I \longrightarrow C_6H_5{\cdot}N(CH_3){\cdot}COCH_3 + NaI \xrightarrow{KOH} C_6H_5{\cdot}NH{\cdot}CH_3 \quad (90\%)$$

Pure monomethylaniline may also be prepared as follows:

$$C_6H_5{\cdot}NH_2 + C_6H_5{\cdot}SO_2Cl \longrightarrow C_6H_5{\cdot}NH{\cdot}SO_2{\cdot}C_6H_5 \xrightarrow[NaOH]{(CH_3)_2SO_4} C_6H_5{\cdot}N(CH_3){\cdot}SO_2{\cdot}C_6H_5 \xrightarrow{H_2O} C_6H_5{\cdot}NH{\cdot}CH_3$$

Secondary amines, particularly those in which one group is of the type $Ar{\cdot}CH_2$—, may be readily prepared by the catalytic reduction of the corresponding anil (p. 312).

Mono- and dimethylaniline are slightly *weaker* bases than aniline itself. The reason for this is not certain, but it may be due to the electron-releasing property of an alkyl group. This would tend to increase resonance and consequently the lone pair on the nitrogen atom would be less available for proton co-ordination in these bases than in aniline. On the other hand, phenyltrimethylammonium hydroxide $C_6H_5{\cdot}\overset{+}{N}(CH_3)_3\}OH^-$, is strongly basic.



Mono- and dimethylaniline resemble secondary and tertiary aliphatic amines in many ways, but differ in that they can also undergo substitution reactions (in the *o*- and *p*-positions) due to the presence of the benzene ring. Monoalkylanilines form pale yellow *N*-nitrosoamines with nitrous acid, and these give Liebermann's nitroso-reaction (p. 317):

$$C_6H_5{\cdot}NH{\cdot}CH_3 + HNO_2 \longrightarrow C_6H_5{\cdot}N(NO){\cdot}CH_3 + H_2O \quad (87\text{–}93\%)$$

This may be converted into the original compound by heating with hydrochloric acid:

$$C_6H_5{\cdot}N(NO){\cdot}CH_3 + H_2O \xrightarrow{HCl} C_6H_5{\cdot}NH{\cdot}CH_3 + HNO_2$$

The nitroso-compound may also be reduced by nascent hydrogen to *as*-methylphenylhydrazine:

$$C_6H_5{\cdot}N(NO){\cdot}CH_3 + 4[H] \xrightarrow{Zn/CH_3{\cdot}CO_2H} C_6H_5{\cdot}N(CH_3){\cdot}NH_2 + H_2O \quad (52\text{–}56\%)$$

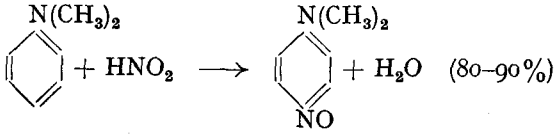
***N*-Methylformanilide,** $C_6H_5{\cdot}N(CH_3){\cdot}CHO$, may be prepared by distilling a mixture of methylaniline, formic acid and toluene:

$$C_6H_5{\cdot}NH{\cdot}CH_3 + H{\cdot}CO_2H \longrightarrow C_6H_5{\cdot}N(CH_3){\cdot}CHO + H_2O \quad (93\text{–}97\%)$$

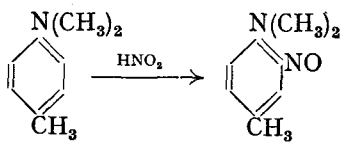
It may also be prepared (in 80 per cent. yield) by oxidising *N* : *N*-dimethylaniline with hydrated manganese dioxide (Henbest *et al.*, 1957).

It is a liquid, b.p. 253°, and is used as a formylating agent in the preparation of aldehydes (see p. 657).

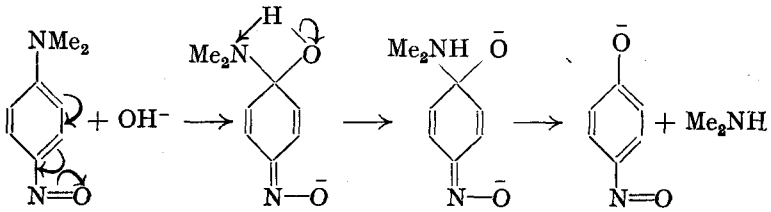
Dialkylanilines form *p*-nitroso-compounds with nitrous acid, *e.g.*, dimethylaniline forms *p*-nitrosodimethylaniline (green flakes):



If the *p*-position is occupied, the *o*-nitroso-compound is formed:

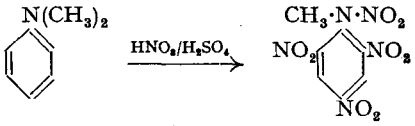


The nitroso-group activates the dimethylamino-group, *e.g.*, when boiled with aqueous sodium hydroxide, *p*-nitrosodimethylaniline forms *p*-nitrosophenol; the mechanism is possibly:

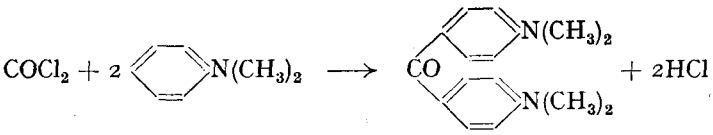


p-Nitrosodimethylaniline is readily oxidised by permanganate to *p*-nitrodimethylaniline, and may be reduced to *p*-aminodimethylaniline.

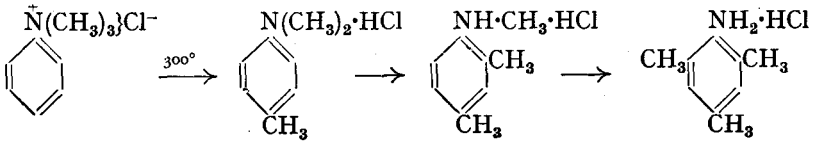
When dimethylaniline is dissolved in concentrated sulphuric acid and then nitrated with nitric acid at 40–55°, a tetranitro-derivative is obtained in which one methyl group has been replaced by a nitro-group:



The dimethylamino-group activates the *p*-hydrogen atom so much that dimethylaniline will condense with formaldehyde and carbonyl chloride to form diphenylmethane derivatives, and with aromatic aldehydes to form triphenylmethane derivatives; *e.g.*, with carbonyl chloride, it forms *Michler's ketone*:



A remarkable property of the mono- and dialkylanilines (and the quaternary compounds) is the ability of their hydrochlorides (or hydrobromides) to undergo rearrangement on strong heating, an alkyl group migrating from the nitrogen atom and entering preferentially the *p*-position, or, if this is occupied, the *o*-; *e.g.*, when phenyltrimethylammonium chloride is heated under pressure, the following rearrangement takes place:



This reaction is known as the **Hofmann–Martius rearrangement** (1871); it may be used to prepare aniline homologues.

Many mechanisms have been proposed for the Hofmann–Martius rearrangement. Hughes and Ingold (1952) have proposed the following, based largely on the suggestion of Hickinbottom (1934) that the rearrangement occurs via the formation of an alkyl carbonium ion:

$$C_6H_5\cdot\overset{+}{N}H_2\cdot C_2H_5\}Cl^- \rightleftharpoons C_6H_5\cdot NH_2 + C_2H_5Cl$$

$$C_2H_5Cl \rightleftharpoons C_2H_5^+ + Cl^-$$

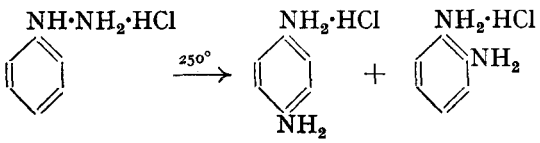
$$C_6H_5\cdot NH_2 + C_2H_5^+ \rightleftharpoons C_6H_5\cdot NH_3^+ + C_2H_4$$

$$C_2H_5^+ + C_6H_5\cdot NH_2 \longrightarrow p\text{-}C_2H_5\cdot C_6H_4\cdot NH_2 + H^+$$

$$H^+ + C_6H_5\cdot NH_2 \rightleftharpoons C_6H_5\cdot NH_3^+$$

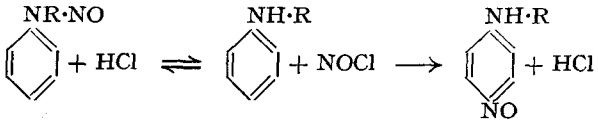
Some evidence given by Hickinbottom to support this mechanism is that alkyl halides have been shown to be formed during the rearrangement, and when the alkyl group is ethyl or a higher homologue, then olefins are also produced. Hickinbottom also showed that alkyl groups may rearrange during the reaction, *e.g.*, when *N-iso*butylaniline hydrobromide is rearranged the product is *p-t*-butylaniline. This product was also obtained when aniline hydrobromide was heated with *iso*butylene. All these facts clearly demonstrate that the rearrangement is intermolecular.

Rearrangements of this kind have been observed to take place with aniline derivatives of the type $C_6H_5\cdot\overset{|}{N}—Z$, where Z is R, X, NH_2, NO, or NO_2, *e.g.*,



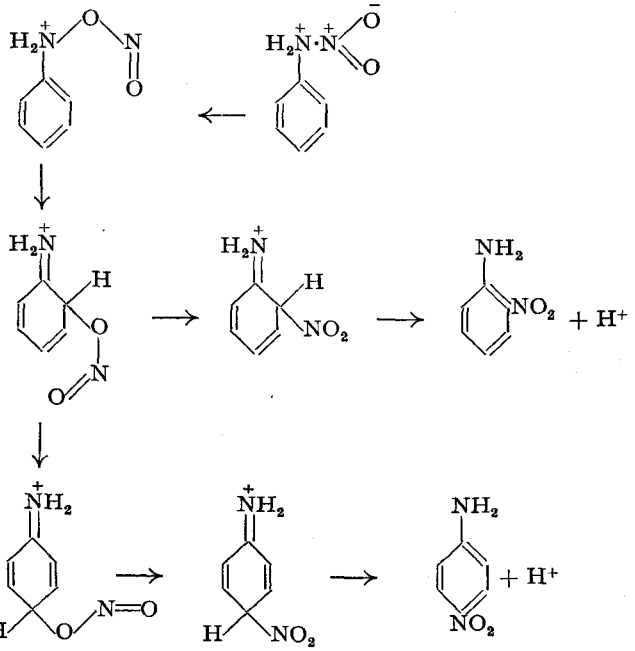
When Z is NO, *i.e.*, the compound is the *N*-nitroso-derivative of a secondary aromatic amine, the rearrangement is known as the **Fischer–Hepp rearrangement** (1886).

The main product in the Fischer–Hepp rearrangement is the *p*-isomer, and the mechanism is believed to be *intermolecular* and possibly as follows:

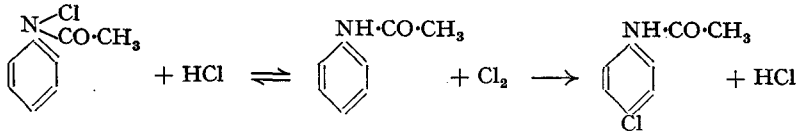


This mechanism was proposed by Houben (1913), who was led to suggest it because he found that in certain cases the yield of rearranged product was increased by the addition of sodium nitrite. This mechanism is supported by, *e.g.*, the fact that when the reaction is carried out in the presence of urea, no *C*-nitroso compound is formed; only secondary amine is produced (Macmillan *et al.*, 1929). This is readily explained on the basis that nitrosyl chloride is decomposed by reaction with urea.

Hughes *et al.* (1956) have studied the rearrangement of phenylnitramine in sulphuric acid in the presence of enriched ^{15}N tracer. The products were *o*- and *p*-nitroaniline and they contained the normal amount of ^{15}N, thus showing that the rearrangement is *intramolecular*. According to Hughes and Ingold (1952), the mechanism is:



The mechanism of the rearrangement of *N*-chloroacetanilide in hydrochloric acid (which acts as a catalyst) is believed to be:



This is an example of the **Orton rearrangement** (1909), which is the rearrangement of *N*-halogenoacylanilides in which the halogen migrates to the *p*-position and sometimes to the *o*-position. The rearrangement may be effected:

(i) By means of halogen acids as catalysts; the intermolecular mechanism given above was proposed by Orton. Orton, *e.g.*, isolated both acetanilide and

chlorine from solution during the rearrangement, and also showed that the proportions of *p*- to *o*-chloro-compound were the same when the starting materials were *N*-chloroacetanilide and hydrochloric acid or acetanilide and chlorine. This mechanism is supported by Olson *et al.* (1936–1938) who used hydrochloric acid containing radioactive chlorine, some of which appeared in the chloroacetanilide produced.

(ii) By the action of heat or photochemically; these reactions probably occur by a free-radical mechanism. Hickinbottom *et al.* (1955) have shown that this rearrangement is also effected by benzoyl peroxide in the absence of light. Thus the rearrangement in this case is a homolytic intermolecular chlorination.

(iii) With carboxylic acids or phenols in aprotic solvents. The mechanism of the rearrangement under these conditions is not certain; some workers (Soper *et al.*, 1945) believe it to be intermolecular, and others (Bell *et al.*, 1934–1939) intramolecular. According to Soper, the mechanism is:

$$C_6H_5{\cdot}NX{\cdot}CO{\cdot}CH_3 + HOY \longrightarrow C_6H_5{\cdot}NH{\cdot}CO{\cdot}CH_3 + XOY \longrightarrow p\text{-}X{\cdot}C_6H_4{\cdot}NH{\cdot}CO{\cdot}CH_3 + HOY$$

where X is the halogen and HOY the acid catalyst. Work by Dewar *et al.* (1959) appears to show that the mechanism is much more involved than that given by Soper.

The rearrangement of phenylhydroxylamine in acid solution to *p*-aminophenol (p. 561) may be regarded as the case where Z is OH.

Diphenylamine $(C_6H_5)_2NH$, may be prepared by heating phenol with aniline in the presence of zinc chloride at 260°:

$$C_6H_5OH + C_6H_5{\cdot}NH_2 \xrightarrow{ZnCl_2} (C_6H_5)_2NH + H_2O$$

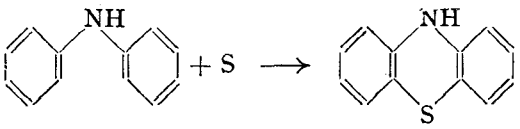
It may also be prepared by the **Ullmann reaction**; this is carried out by refluxing acetanilide, potassium carbonate, bromobenzene and a little copper powder in nitrobenzene solution (copper accelerates the reaction):

$$C_6H_5{\cdot}NH{\cdot}CO{\cdot}CH_3 + C_6H_5Br + K_2CO_3 \xrightarrow{Cu} (C_6H_5)_2NH + CO_2 + CH_3{\cdot}CO_2K + KBr \quad (60\%)$$

Commercially, diphenylamine is prepared by heating aniline with aniline hydrochloride at 140° under pressure:

$$C_6H_5{\cdot}NH_2 + C_6H_5{\cdot}NH_2{\cdot}HCl \longrightarrow (C_6H_5)_2NH + NH_4Cl \quad (85\%)$$

Diphenylamine is a colourless, pleasant-smelling solid, m.p. 54°. It is a weaker base than aniline, and its salts are completely hydrolysed in solution. It forms an *N*-nitroso-derivative with nitrous acid. A solution of diphenylamine in phosphoric acid gives a blue colour with oxidising agents; this reaction is used as a test for nitric acid. When melted with sulphur, diphenylamine forms *phenothiazine* (*thiodiphenylamine*):



Diphenylamine is used for making certain dyes.

When heated with sodium or sodamide, diphenylamine is converted into the sodium salt:

$$(C_6H_5)_2NH + Na \longrightarrow [(C_6H_5)_2N]^-Na^+ + \tfrac{1}{2}H_2$$

When treated with iodine, sodiodiphenylamine forms *tetraphenylhydrazine*:

$$2(C_6H_5)_2N^-Na^+ + I_2 \longrightarrow (C_6H_5)_2N{\cdot}N(C_6H_5)_2 + 2NaI$$

Tetraphenylhydrazine is best prepared by oxidising diphenylamine with potassium permanganate in acetone solution. It is a colourless crystalline solid, but in benzene solution (or any other non-ionising solvent) it produces a green colour due to the formation of the free hydrazine radical, *diphenylnitrogen*, in which the nitrogen is bivalent:

$$(C_6H_5)_2N{-}N(C_6H_5)_2 \rightleftharpoons 2(C_6H_5)_2N{\cdot}$$

When the solution is diluted, the colour deepens, thereby showing increased dissociation; the colour also deepens on warming and fades on cooling. That we are dealing with a free radical is shown, apart from the colour phenomena (the colour intensity does not obey Beer's law), by the immediate reaction of the substance (in solution) with *e.g.*, nitric oxide, a reaction which is characteristic of free radicals:

$$(C_6H_5)_2N{\cdot} + NO \longrightarrow (C_6H_5)_2N{-}NO$$

The stability of this free hydrazine radical is believed to be due to its being a resonance hybrid (*cf.* triphenylmethyl, p. 703).

Triphenylamine $(C_6H_5)_3N$, may be prepared by the reaction between sodiophenylamine and bromobenzene:

$$(C_6H_5)_2N^-Na^+ + C_6H_5Br \longrightarrow (C_6H_5)_3N + NaBr$$

A better method of preparation is the Ullmann reaction; diphenylamine, iodobenzene, potassium carbonate and a little copper powder are heated in nitrobenzene solution:

$$2(C_6H_5)_2NH + 2C_6H_5I + K_2CO_3 \xrightarrow{Cu} 2(C_6H_5)_3N + CO_2 + 2KI + H_2O \quad (82\text{–}85\%)$$

Triphenylamine is a colourless crystalline solid, m.p. 127°, and is too weak a base to combine with acids. The decreasing basic character of aniline, diphenylamine and triphenylamine may be explained by the increasing number of resonating structures (reaching a maximum in triphenylamine), thereby decreasing the availability of the lone pair on the nitrogen atom.

Triphenylamine dissolves in concentrated sulphuric acid to give a blue solution.

Benzylamine (*α-aminotoluene*), $C_6H_5{\cdot}CH_2{\cdot}NH_2$, may be prepared by the reduction of phenyl cyanide or benzaldoxime:

$$C_6H_5{\cdot}CN \xrightarrow{Na/C_2H_5OH} C_6H_5{\cdot}CH_2{\cdot}NH_2 \xleftarrow{Na/C_2H_5OH} C_6H_5{\cdot}CH{:}N{\cdot}OH$$

It may also be prepared by heating benzyl chloride with ammonia under pressure, or by the Hofmann reaction on phenylacetamide:

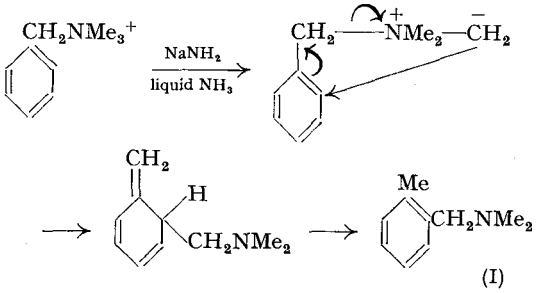
$$C_6H_5{\cdot}CH_2{\cdot}CO{\cdot}NH_2 \xrightarrow{Br_2/KOH} C_6H_5{\cdot}CH_2{\cdot}NH_2 + CO_2$$

Benzylamine is a colourless liquid, b.p. 185°, which resembles the aliphatic amines, and is best regarded (as far as the amino-group is concerned) as a phenyl-substituted methylamine; *e.g.*, it differs from the primary aromatic

amines in that it is soluble in water, basic (more so than aniline), and with nitrous acid does not form a diazonium salt but gives benzyl alcohol:

$$C_6H_5{\cdot}CH_2{\cdot}NH_2 + HNO_2 \longrightarrow C_6H_5{\cdot}CH_2OH + N_2 + H_2O$$

A special type of nucleophilic rearrangement is the *Hauser rearrangement* (1951–1956); this occurs with quaternised benzylamine:



(I)

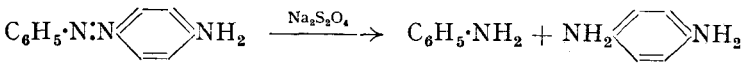
(I) can be quaternised and the process repeated until all the ring positions are filled.

Diamines

The aromatic diamines may be prepared:

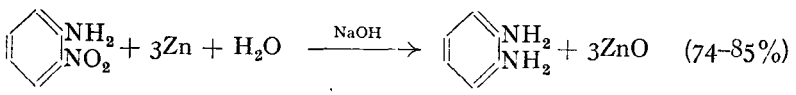
1. By reduction of dinitro-compounds.
2. By the reduction of nitroamines.
3. By the reduction of *C*-nitrosoamines.
4. By reducing an aminoazo-compound with sodium hyposulphite;

e.g., reduction of aminoazobenzene gives aniline and *p*-phenylenediamine:



The diamines are colourless or white crystalline solids which turn brown when exposed to the air. They are " diacid " bases, and their reactions are characterised by those of the three phenylenediamines.

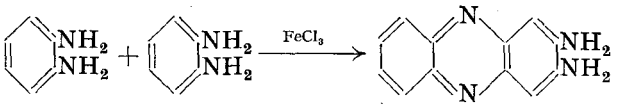
***o*-Phenylenediamine** (*benzene*-1 : 2-*diamine*, 1 : 2-*diaminobenzene*) is best prepared by reducing *o*-nitroaniline with zinc dust and aqueous ethanolic sodium hydroxide:



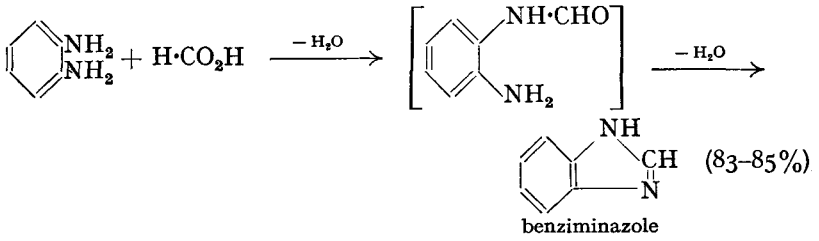
It is manufactured by reduction of *o*-nitroaniline with iron and dilute hydrochloric acid.

It is a white crystalline solid, m.p. 102°. The most characteristic property of *o*-diamines is the ease with which they form heterocyclic compounds.

(i) When *o*-phenylenediamine is treated with ferric chloride solution, a dark red colour is produced due to the formation of 2 : 3-*diaminophenazine*:

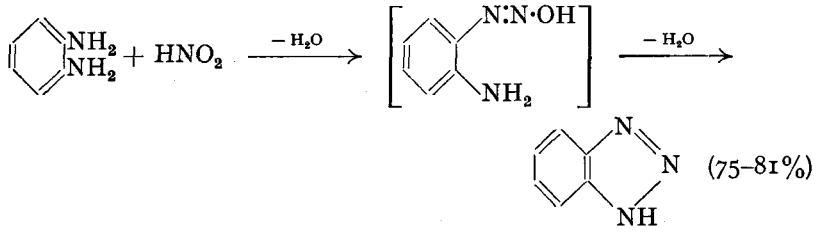


(ii) *Benziminazoles* are formed when *o*-phenylenediamine is heated with organic acids, *e.g.*,

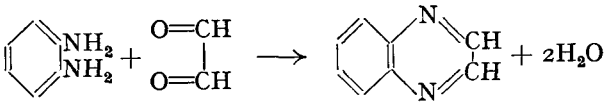


benziminazole

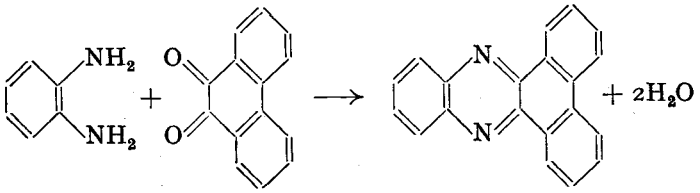
(iii) When *o*-phenylenediamine is treated with nitrous acid (a solution of the diamino-compound in acetic acid is treated with aqueous sodium nitrite), *benztriazole* is formed:



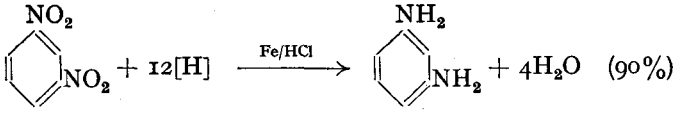
(iv) *o*-Phenylenediamine condenses with α-dicarbonyl compounds to form *quinoxalines*; *e.g.*, with glyoxal, quinoxaline is formed:



This reaction is used to identify *o*-diamines; the α-dicarbonyl compound employed for this purpose is phenanthraquinone, resulting in the formation of a sparingly soluble phenazine derivative:

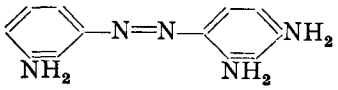


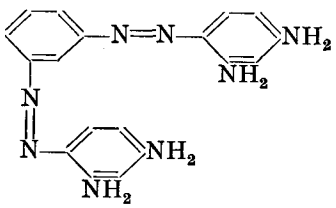
m-Phenylenediamine (*benzene*-1 : 3-*diamine*, 1 : 3-*diaminobenzene*) is best prepared by the reduction of *m*-dinitrobenzene with iron and hydrochloric acid:



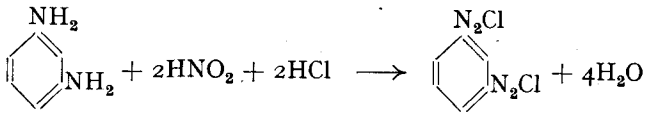
It is a white crystalline solid, m.p. 63°. The most characteristic reaction of *m*-phenylenediamine is the formation of brown dyes—*Bismarck Brown*—

when it is treated with nitrous acid; a monazo- and a bisazo-compound are formed:



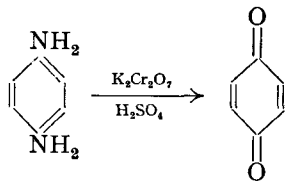


This reaction is used as a colorimetric method for the determination of nitrites in water; even when nitrites are present in traces, a yellow colour is produced. On the other hand, by dissolving *m*-phenylenediamine in concentrated hydrochloric acid, and by keeping the nitrous acid always in excess, both amino-groups may be diazotised to give the tetrazo-compound:



m-Phenylenediamine is used in the preparation of dyes.

p-Phenylenediamine (*benzene*-1 : 4-*diamine*, 1 : 4-*diaminobenzene*) may be prepared by the reduction of *p*-nitroaniline or aminoazobenzene. It is a white crystalline solid, m.p. 147°. On vigorous oxidation it forms *p*-benzoquinone:



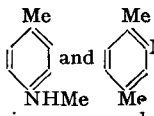
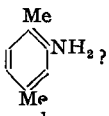
p-Phenylenediamine can be diazotised in the ordinary way, and is used in the preparation of dyes.

QUESTIONS

1. Compare and contrast the reactions of $PhNH_2$ and $EtNH_2$.
2. How may primary aromatic amines be prepared? In your answer, discuss the advantages and disadvantages of the various reducing agents that may be used.
3. Starting with C_6H_6 or PhMe, how would you prepare:—(*a*) *o*-, *m*- and *p*-nitroaniline, (*b*) *o*-, *m*- and *p*-nitrotoluidine, (*c*) *p*-aminobenzaldehyde, (*d*) PhNCS, (*e*) *o*-, *m*- and *p*-bromoaniline, (*f*) 2 : 6-dibromoaniline, (*g*) 2 : 6-dibromo-*p*-phenylenediamine, (*h*) 2 : 4-dinitroaniline, (*i*) $PhMeN{\cdot}NH_2$, (*j*) PhNMe·CHO, (*k*) *s*-trimethylaniline, (*l*) 3-bromo-4-aminotoluene?
4. How are the following compounds prepared commercially and what are their uses:—(*a*) $PhNH_2$, (*b*) $PhNH{\cdot}CO{\cdot}CH_3$, (*c*) $m\text{-}NO_2{\cdot}C_6H_2{\cdot}NH_2$, (*d*) *o*- and *p*-toluidines, (*e*) PhNHMe, (*f*) $PhNMe_2$, (*g*) Ph_2NH?
5. Write an essay on the basic properties of aniline and its halogeno-, nitro-, and halogeno-nitro-derivatives.
6. Write an account of the rearrangement of the *N*-substituted aniline compounds.
7. Name the compounds and state the conditions under which they are formed when $PhNH_2$, PhNHMe and $PhNMe_2$, are respectively treated with:—(*a*) HNO_2, (*b*) MeI, (*c*) $Ar{\cdot}SO_2Cl$, (*d*) Ac_2O, (*e*) CS_2, (*f*) $CHCl_3$, (*g*) chromic acid, (*h*) Ph·CHO, (*i*) $H{\cdot}CO_2H$, (*j*) Br_2, (*k*) HNO_3, (*l*) $COCl_2$, (*m*) HCl and heat.
8. Write an account of the preparation and properties of (*a*) Ph_2NH, (*b*) Ph_3N, (*c*) $PhCH_2{\cdot}NH_2$.

9. Define and give examples of:—(*a*) the Schmidt reaction, (*b*) the Hofmann reaction, (*c*) the Hofmann rearrangement, (*d*) the Fischer–Hepp rearrangement, (*e*) the Ullmann reaction, (*f*) an anilide, (*g*) the Orton rearrangement.

10. Write an account of the preparation and properties of the three isomeric phenylenediamines.

11. How would you distinguish between PhNHEt, $PhNMe_2$,  and  ?

12. Discuss the various methods for distinguishing between primary, secondary and tertiary aromatic amines.

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CHAPTER XXIV

DIAZONIUM SALTS AND THEIR RELATED COMPOUNDS

WHEN a primary aliphatic amine is treated with nitrous acid, the nature of the product depends on the amine used (see p. 316); nitrogen is always evolved:

$$R{\cdot}NH_2 + HNO_2 \longrightarrow ROH + N_2 + H_2O$$

When, however, a primary aromatic amine is treated with nitrous acid in a well-cooled solution, the product is an unstable compound known as a **diazonium salt**:

$$Ar{\cdot}NH_2 + HNO_2 + HCl \longrightarrow Ar{\cdot}N_2Cl + H_2O$$

Diazo-compounds may be obtained with primary aliphatic amines provided that the amino-group is attached to a carbon atom which is adjacent to a negative group such as acyl, carbalkoxy, or cyano; *e.g.*, aminoacetic ester forms diazoacetic ester (p. 329):

$$CH_2(NH_2){\cdot}CO_2C_2H_5 \xrightarrow{HNO_2} CHN_2{\cdot}CO_2C_2H_5$$

The formation of a diazonium compound by the interaction of sodium nitrite, an inorganic acid (usually) and a primary aromatic amine, in ice-cold solution, is known as *diazotisation*. This reaction was discovered by Griess in 1858.

The diazonium compounds are salts of the strong base *diazonium hydroxide*, $Ar{\cdot}N_2OH$, which has not yet been isolated, but is known in aqueous solution. Most diazonium salts of the inorganic acids are colourless solids, extremely soluble in water, and many, particularly the nitrate, are explosive (in the solid state). They form complex salts with many metallic salts, of which one of the most important is zinc chloride, $(Ar{\cdot}N_2)_2{}^{2+}ZnCl_4{}^{2-}$. These complex salts are stable in solution, and hence offer a means of stabilising a diazonium salt solution.

The diazonium salts are very important synthetic reagents, being the starting point in the preparation of various aromatic compounds, dyes and drugs. As pointed out previously, the preparation of a diazonium salt in the solid state is usually a hazardous process. Fortunately, however, the aqueous solutions of the diazonium salts undergo practically all the necessary reactions (*cf.* the Grignard reagents).

There are various methods of preparing a solution of a diazonium salt, but the usual procedure is to dissolve (or suspend) the amine in excess dilute inorganic acid (usually hydrochloric or sulphuric) cooled in ice and to add slowly, with stirring, a cooled aqueous solution of sodium nitrite, the addition of which is completed when the reaction mixture produces a blue colour with potassium iodide-starch paper, thereby showing the presence of free nitrous acid.

When dealing with a mono-*o*- or *p*-substituted amine, *e.g.*, nitro- or chloro-amine, it is necessary to use a more concentrated acid (than for the unsubstituted amine) because of the weakened basic character of the amino-group (p. 570). An alternative method is to mix the amine and sodium nitrite in aqueous solution and to pour this on to a mixture of cracked ice and concentrated hydrochloric acid. When dealing with di-(*o* : *o*'- or *o* : *p*-) or tri-(*o* : *o*' : *p*-)substituted amines, diazotisation may usually be effected by dissolving the amine in concentrated sulphuric acid and adding solid sodium nitrite, concentrated aqueous sodium nitrite, or sodium nitrite dissolved in concentrated sulphuric acid.

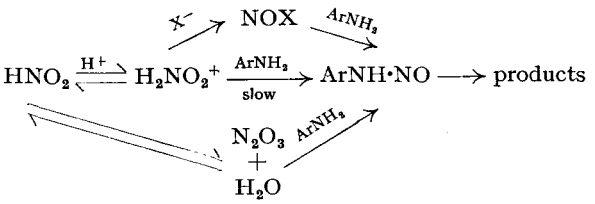
Tedder (1957) has shown that aromatic compounds containing activating groups may be converted *directly* to the diazonium salt by the action of excess of nitrous acid:

$$ArH + 2HNO_2 + HX \longrightarrow ArN_2X + 2H_2O + 2[O]$$

Deactivated aromatic nuclei, when treated with nitrosylsulphuric acid in the presence of mercuric sulphate as catalyst, are also converted to the diazonium salt.

The mechanism of diazotisation is still not settled, but it seems certain that the rate-determining step involves the *free* base.

Hughes, Ingold *et al.* (1958) have studied the diazotisation of various aromatic primary amines in weakly acidic solutions containing small amounts of perchloric acid as the only strong acid. They studied the effect of changes in reaction conditions, including the addition of halide ion, and on their kinetic results it was found that the reaction could proceed by any of the following routes (depending on the amine and the conditions):



Larkworthy (1959) has shown that with a given amine the mechanism of diazotisation depends on the extent of the acidity and the reactant concentration. This author has demonstrated that the active agent may be, *e.g.*, NO^+, $NO{\cdot}OH_2^+$, $NO{\cdot}NO_2$, NO·OH.

Nomenclature. The name of the diazonium salt is obtained by adding diazonium chloride, diazonium sulphate, etc., to the name of the parent hydrocarbon, *e.g.*, $C_6H_5{\cdot}N_2Cl$, benzenediazonium chloride; *p*-$CH_3{\cdot}C_6H_4{\cdot}N_2HSO_4$, *p*-toluenediazonium sulphate.

Reactions of the diazonium salts. These may be divided into two groups: those which involve the liberation of nitrogen gas and the displacement of the diazo-group, $-N_2X$, by another univalent group, and those in which the two nitrogen atoms are retained.

REPLACEMENT REACTIONS

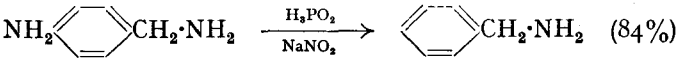
1. **Replacement by hydroxyl.** When a diazonium sulphate solution is boiled or steam distilled, the diazo-group is replaced by hydroxyl, *e.g.*,

$$C_6H_5{\cdot}N_2HSO_4 + H_2O \longrightarrow C_6H_5OH + N_2 + H_2SO_4 \quad (g.)$$

The solution should be fairly strongly acid in order to avoid coupling (p. 589) which leads to tar formation. The hydrolysis of diazonium salts has been improved by running the aqueous solution down a chilled tube in a vessel containing boiling 20 per cent. sulphuric acid through which steam is passing, *e.g.*, *o*-toluenediazonium chloride gives *o*-cresol in 89 per cent. yield (Lambooy, 1950). This reaction occurs by the nucleophilic unimolecular mechanism (p. 524).

2. **Replacement by hydrogen.** Replacement of the diazo-group by hydrogen offers a means of preparing substituted aromatic compounds in

which the substituents are in positions which they would not take up by direct substitution. According to Kornblum (1944, 1949), the most reliable method of replacing the diazo-group by hydrogen is by means of hypophosphorous acid. Furthermore, Kornblum *et al.* (1949) have shown that the aromatic primary amino-group may be selectively replaced by hydrogen in aliphatic-aromatic diamines by dissolving the diamine in hypophosphorous acid and adding sodium nitrite at 0–5°, *e.g.*,



Another common method of replacing the diazo-group by hydrogen is to dissolve the amine in a mixture of ethanol and concentrated sulphuric acid, add sodium nitrite and then warm (sometimes in the presence of copper as catalyst). According to Griess (1864), benzenediazonium sulphate reacted as follows:

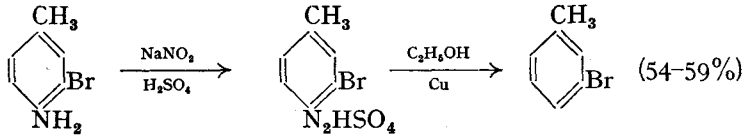
$$C_6H_5{\cdot}N_2HSO_4 + C_2H_5OH \longrightarrow C_6H_6 + CH_3{\cdot}CHO + N_2 + H_2SO_4$$

Remsen *et al.* (1887), however, showed that this was incorrect; the main product was shown to be phenetole together with a small amount of benzene. This was confirmed by Hantzsch *et al.* (1901) who obtained the following results in absolute ethanol:

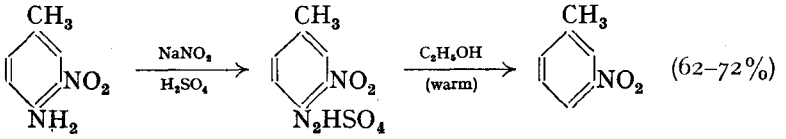
$$C_6H_5{\cdot}N_2Cl + C_2H_5OH \longrightarrow \underset{(61\%)}{C_6H_5{\cdot}O{\cdot}C_2H_5} + \underset{(5\%)}{C_6H_6}$$

When methanol was used instead of ethanol, no benzene was obtained at all; the product was anisole, $C_6H_5{\cdot}O{\cdot}CH_3$ (70%). As a result of much work it appears that the amount of side-reactions, *i.e.*, formation of ether, depends on the structure of the diazonium salt and the nature of the alcohol used; *e.g.*, if a negative group is in the *o*-position, the diazo-group is replaced in good yield by hydrogen when ethanol is used. On the other hand, if methanol is used instead of ethanol, the main product is an aryl methyl ether; this offers a means of preparing methyl ethers:

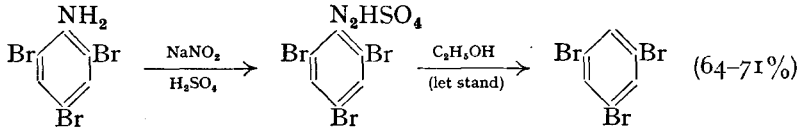
m-*Bromotoluene*



m-*Nitrotoluene*



s-*Tribromobenzene*



The mechanism of the decomposition of diazonium salts with alcohols is uncertain. According to Hey and Waters (1937), the reaction takes place by a free-radical mechanism:

$$C_6H_5{-}N{=}N{-}Cl \longrightarrow C_6H_5\cdot + N_2 + Cl\cdot$$
$$C_6H_5\cdot + CH_3{\cdot}CH_2OH \longrightarrow C_6H_6 + CH_3{\cdot}\dot{C}HOH$$
$$CH_3{\cdot}\dot{C}HOH + Cl\cdot \longrightarrow CH_3{\cdot}CHO + HCl$$

Side-reaction

$$C_6H_5\cdot + C_2H_5{-}O{-}H \longrightarrow C_6H_5{-}O{-}C_2H_5 + H\cdot$$
$$H\cdot + Cl\cdot \longrightarrow HCl$$

or

$$C_2H_5{-}O{-}H + Cl\cdot \longrightarrow C_2H_5O\cdot + HCl$$
$$C_6H_5\cdot + C_2H_5O\cdot \longrightarrow C_6H_5{\cdot}O{\cdot}C_2H_5$$

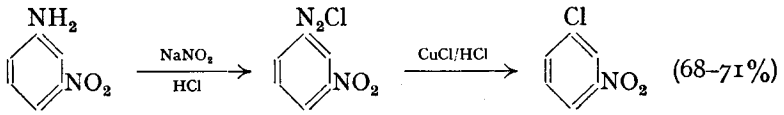
Hey and Waters believe, however, that this free-radical decomposition is *not* generally produced in *aqueous* solution, but that their formation is possible in *non-ionising* solvents, *e.g.*, ethanol, acetone, ethyl acetate, etc. When diazonium salts are decomposed in these solvents in the presence of metals, the metal is attacked to form an organo-metallic compound. This has been used to prepare aromatic derivatives of mercury, antimony, arsenic and tellurium.

Many reagents have been used to replace the diazo-group by hydrogen; the two usual methods have been described above. Roe *et al.* (1952) have now shown that this reaction can be carried out in reasonable yields by decomposing the fluoroborate in ethanol in the presence of zinc dust.

$$Ar{\cdot}NH_2 \longrightarrow Ar{\cdot}N_2BF_4 \xrightarrow[Zn]{C_2H_5OH} ArH \quad (47\text{–}85\%)$$

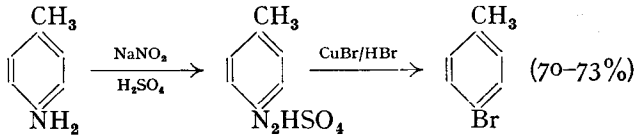
3. **Replacement by halogen.** (i) **Sandmeyer reaction** (1884). When a diazonium salt solution is run into a solution of cuprous halide dissolved in the corresponding halogen acid, the diazo-group is replaced by a halogen atom, *e.g.*,

m-*Chloronitrobenzene*



(68–71%)

p-*Bromotoluene*



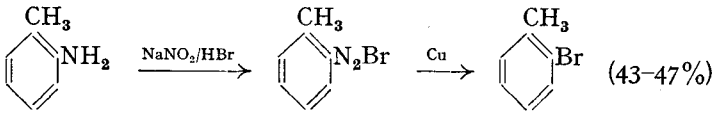
(70–73%)

The diazotisation may be carried out with hydrobromic acid, but in practice sulphuric acid is used, since it is cheaper and only slightly affects the yield of aryl bromide.

The important point to note in the Sandmeyer reaction is that it is the *halogen joined to the copper that enters the nucleus.* The mechanism of the reaction is uncertain. Cowdrey and Davies (1949) have investigated the reaction kinetics of the Sandmeyer reaction and suggest that the mechanism is (*a*) slow co-ordination of the terminal N atom of $Ar{\cdot}N_2^+$ to the copper in the $CuCl_2^-$ ion to form the complex $Ar{\cdot}N_2{\cdot}CuCl_2$, (*b*) decomposition of this to ArCl, or (*c*) further fast addition to it of $Ar{\cdot}N_2^+$ to give $[(Ar{\cdot}N_2)_2CuCl_2]^+$, which either (*d*) decomposes to ArCl or (*e*) reacts with $CuCl_2^-$ to give $Ar{\cdot}N{:}N{\cdot}Ar$.

Pfeil *et al.* (1949) have obtained *p*-chloronitrobenzene in 98 per cent. yield by treating *p*-nitrobenzenediazonium chloride with *cupric* chloride in hydrochloric acid. It appears that cupric chloride is effective only if the diazotised amine contains a *negative* group.

(ii) **Gattermann reaction** (1890). This reaction is carried out by dissolving the amine in hydrochloric or hydrobromic acid, cooling, adding cooled aqueous sodium nitrite, and then warming the diazonium salt solution in the presence of copper powder, *e.g.*,



Iodo-compounds may be prepared by boiling the diazonium salt solution with aqueous potassium iodide:

$$C_6H_5{\cdot}N_2Cl + KI \longrightarrow C_6H_5I + KCl + N_2 \quad (74\text{–}76\%)$$

This is usually the best method for introducing iodine into the benzene ring.

Fluoro-compounds may be prepared by the **Balz–Schiemann reaction** (1927). When borofluoric acid is added to a diazonium salt solution, the insoluble diazonium borofluoride is precipitated. This is collected by filtration, dried and heated gently:

$$C_6H_5{\cdot}N_2Cl + HBF_4 \longrightarrow C_6H_5{\cdot}N_2BF_4 + HCl \longrightarrow C_6H_5F + N_2 + BF_3 \quad (51\text{–}57\%)$$

Borofluoric acid may be prepared by adding hydrochloric acid to sodium borofluoride, or by dissolving boric acid in 50 per cent. hydrofluoric acid (contained in a lead vessel); the latter usually gives better yields.

Fluoro-compounds may also be prepared by dissolving the amine in cold anhydrous hydrofluoric acid, adding solid sodium nitrite and then allowing the solution to stand until the excess acid has evaporated; the residue consists of a mixture of aryl fluoride and sodium fluoride (Aelony, 1934):

$$Ar{\cdot}NH_2 \xrightarrow{NaNO_2/HF} Ar{\cdot}N_2F \longrightarrow Ar{\cdot}F + N_2$$

4. **Replacement by a cyano-group.** This is a special case of the Sandmeyer and Gattermann reactions, and is carried out by treating a diazonium salt solution with cuprous cyanide dissolved in aqueous potassium cyanide or with aqueous potassium cyanide in the presence of copper powder:

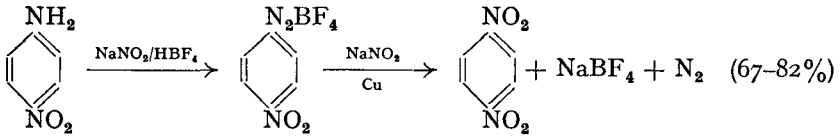
$$C_6H_5{\cdot}N_2Cl \xrightarrow{K_3Cu(CN)_4} C_6H_5{\cdot}CN + N_2 \quad (65\%)$$

$$C_6H_5{\cdot}N_2HSO_4 + KCN \xrightarrow{Cu} C_6H_5{\cdot}CN + KHSO_4 + N_2 \quad (60\%)$$

5. **Replacement by a nitro-group.** This was originally carried out by treating a diazonium salt solution with an equivalent amount of nitrous acid in the presence of cuprous oxide:

$$C_6H_5{\cdot}N_2Cl + HNO_2 \xrightarrow{Cu_2O} C_6H_5{\cdot}NO_2 + N_2 + HCl$$

A better method is to decompose the diazonium borofluoride with aqueous sodium nitrite containing copper powder:



Hodgson and Marsden (1944) have found that the decomposition of a diazonium cobaltinitrite $(Ar{\cdot}N_2)_3{}^{3+}Co(NO_2)_6{}^{3-}$, in the cold, by aqueous sodium nitrite in the presence of cuprous oxide and copper sulphate gives nitro-compounds in yields higher than 60 per cent. The diazonium cobaltinitrite is prepared by adding sodium cobaltinitrite to a diazonium salt solution previously neutralised with calcium carbonate; the yield is almost quantitative.

Ward *et al.* (1960) have shown that in certain cases the addition of the diazonium salt solution to sodium nitrite solution containing sodium hydrogen carbonate gives good yields of nitro-compound, *e.g.*, *o*-nitroaniline gives *o*-dinitrobenzene (97 per cent. yield).

6. **Replacement by an arsonic acid group, AsO_3H_2.** One method is **Bart's reaction** (1910). This is carried out by decomposing a diazonium salt with sodium arsenite in the presence of a copper salt, *e.g.*, phenylarsonic acid:

$$C_6H_5{\cdot}N_2Cl + Na_3AsO_3 \xrightarrow{CuSO_4} C_6H_5{\cdot}AsO_3Na_2 + N_2 + NaCl \xrightarrow{HCl} C_6H_5{\cdot}AsO_3H_2 \quad (39\text{–}45\%)$$

The yield may be increased by buffering the solution with sodium carbonate (Blas, 1940).

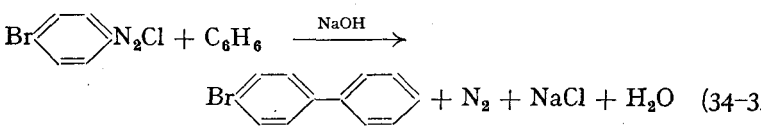
An alternative method to the Bart reaction is to add a suspension of a diazonium borofluoride to an aqueous solution of sodium meta-arsenite in the presence of a small amount of cuprous chloride (Ruddy *et al.*, 1942):

$$C_6H_5{\cdot}N_2BF_4 + NaAsO_2 + H_2O \xrightarrow{CuCl} C_6H_5{\cdot}AsO_3H_2 + NaF + N_2 + BF_3 \quad (58\%)$$

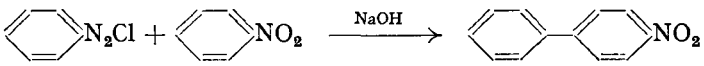
7. **Replacement by an aryl group.** This may be carried out by treating a diazonium sulphate with ethanol and copper powder, *e.g.*, diphenyl from benzenediazonium sulphate:

$$2C_6H_5{\cdot}N_2HSO_4 \xrightarrow[Cu]{C_2H_5OH} C_6H_5{\cdot}C_6H_5 + 2N_2 + 2H_2SO_4 \quad (25\%)$$

This is really a special case of the Gattermann reaction. Alternatively, a diaryl may be prepared by adding an aromatic compound to an *alkaline* solution of a diazonium salt, *e.g.*, *p*-bromodiphenyl from *p*-bromobenzenediazonium chloride and benzene:

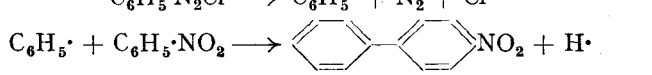


This method of preparation is known as the **Gomberg reaction** (1924), and experiment has shown that whatever is the nature of a substituent in the second component, *o*- or *p*-substitution always occurs; *e.g.*, benzenediazonium chloride forms *p*-nitrodiphenyl when treated with nitrobenzene:



This anomalous orienting effect of the nitro-group led Hey *et al.* (1934) to suggest that the reaction takes place by a free-radical mechanism:

$$C_6H_5{\cdot}N_2Cl \longrightarrow C_6H_5{\cdot} + N_2 + Cl{\cdot}$$



$$H{\cdot} + Cl{\cdot} \longrightarrow HCl$$

The Gomberg reaction is very useful for closing rings.

Arylation with diazonium salts may also be carried out by the **Meerwein reaction** (1939). Diazonium salts react with compounds containing an activated ethylenic bond to give arylated products. The reaction is carried out in acetone solution in the presence of sodium acetate and a cupric salt, *e.g.*, benzenediazonium chloride and cinnamic acid give stilbene:

$$C_6H_5N_2Cl + C_6H_5{\cdot}CH{=}CH{\cdot}CO_2H \longrightarrow C_6H_5{\cdot}CH{=}CH{\cdot}C_6H_5 + N_2 + CO_2 + HCl$$

The mechanism of this reaction is believed to be a free-radical one.

8. **Replacement by a chloromercuri-group.** This is an example of indirect mercuration (*cf.* p. 540), and may be carried out by heating the double compound of a diazonium chloride and mercuric chloride in acetone or ethanol solution with copper powder:

$$Ar{\cdot}N_2Cl{\cdot}HgCl_2 + 2Cu \longrightarrow Ar{\cdot}HgCl + N_2 + 2CuCl \quad (40\%)$$

By this means it is possible to prepare the mercuri-compounds of aromatic hydrocarbons, aryl halides, nitro-compounds, amines, phenols, acids and esters. If the double compound is heated in acetone solution with copper powder and then with copper powder in aqueous ammonia, the diaryl mercury compound is obtained:

$$2Ar{\cdot}N_2Cl{\cdot}HgCl_2 + 6Cu \longrightarrow Ar_2Hg + Hg + 6CuCl + N_2$$

The diazo-group may be replaced by many other groups, *e.g.*,

(i) $Ar{\cdot}N_2Cl \xrightarrow{CuSCN} Ar{\cdot}SCN$

(ii) $Ar{\cdot}N_2Cl \xrightarrow{KNCO/Cu} Ar{\cdot}NCO$

(iii) $2Ar{\cdot}N_2Cl \xrightarrow{(NH_4)_2S} Ar_2S$

(iv) $Ar{\cdot}N_2HSO_4 + SO_2 + Cu \longrightarrow Ar{\cdot}SO_2H + N_2 + CuSO_4$

(v) $Ar{\cdot}N_2Cl + S{:}C\begin{matrix}SK\\OC_2H_5\end{matrix} \longrightarrow S{:}C\begin{matrix}SAr\\OC_2H_5\end{matrix} \xrightarrow{H_2O} ArSH$

(vi) Beech (1954) has shown that formaldoxime reacts with diazonium salts to give products which, on hydrolysis, yield aldehydes. Other oximes, under similar conditions, give alkyl aryl ketones (R = H or R):

$$Ar{\cdot}N_2Cl + R{\cdot}CH{=}NOH \xrightarrow{NaOH} Ar{\cdot}CR{=}NOH \xrightarrow{H_2O} Ar{\cdot}CO{\cdot}R$$

In certain cases, diazotisation may lead to abnormal reactions; *e.g.*,

(i) Diazotisation of *o*-diamines produces triazoles (p. 579).

(ii) Treatment of *m*-phenylenediamine with nitrous acid gives Bismarck Brown (p. 579).

REACTIONS OF THE DIAZONIUM SALTS IN WHICH THE NITROGEN ATOMS ARE RETAINED

1. When bromine and hydrobromic acid are added to a diazonium salt solution, a crystalline precipitate of *diazonium perbromide*, $Ar{\cdot}N_2Br_3$, is obtained. This, on heating, forms the aryl bromide. On the other hand, if the perbromide is treated with aqueous ammonia, the azide, $Ar{\cdot}N_3$, is produced.

Phenyl azide may also be prepared by the action of hydrazoic acid on nitrosobenzene (Maffei *et al.*, 1954):

$$C_6H_5{\cdot}NO + 2HN_3 \longrightarrow C_6H_5{\cdot}N_3 + H_2O + 2N_2 \quad (92\%)$$

2. When reduced with stannous chloride and hydrochloric acid, or with sodium sulphite, diazonium salts form phenylhydrazines:

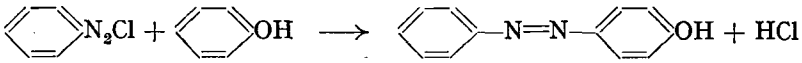
$$Ar{\cdot}N_2Cl + 4[H] \xrightarrow{SnCl_2/HCl} Ar{\cdot}NH{\cdot}NH_2{\cdot}HCl$$

If vigorous reducing agents are used, *e.g.*, zinc and hydrochloric acid, the product is an aromatic amine:

$$Ar{\cdot}N_2Cl \xrightarrow{Zn/HCl} [Ar{\cdot}NH{\cdot}NH_2] \xrightarrow{Zn/HCl} Ar{\cdot}NH_2 + NH_3$$

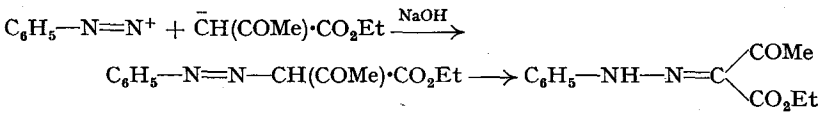
3. Diazonium salts readily undergo *coupling* reactions. This is the reaction between a diazonium salt and another substance containing a labile hydrogen, the result being the formation of an *azo-compound.*

The most important groups of compounds that couple with diazonium salts are phenols, naphthols and primary, secondary and tertiary aromatic amines; *e.g.*, benzenediazonium chloride couples with phenol to form *p*-hydroxyazobenzene:



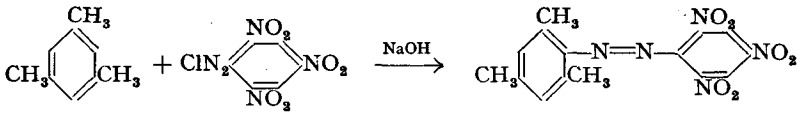
With primary and secondary amines, coupling may take place at the nitrogen atom to form *diazoamino-compounds* (*N*-azo-compounds), or directly with the nucleus to form *aminoazo-compounds* (*C*-azo-compounds). Generally, the nature of the amino-compound and the *p*H of the solution decide which type of coupling takes place (see p. 596).

Compounds containing an active methylene group, *e.g.*, acetoacetic ester, and certain hydrocarbons, *e.g.*, mesitylene, *iso*durene, butadiene, also couple with diazonium salts. The mechanism for the reaction between E.A.A. and benzenediazonium chloride is believed to be:

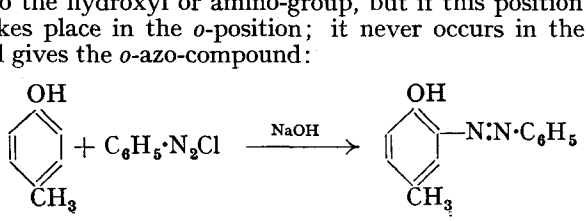


This coupling reaction is often used to detect the presence of the enolic form in the keto-enol mixtures, and is then referred to as the **Japp–Klingermann reaction** (1887).

Simple diazonium salts do not couple with hydrocarbons, but the nitro-derivatives couple readily; *e.g.*, diazotised picramide (*s*-trinitroaniline) couples with mesitylene:

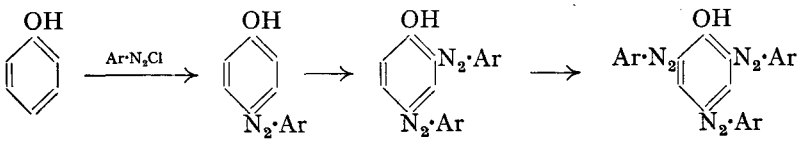


With phenols, coupling is best carried out in faintly alkaline solution; with amines, in faintly acid solution. The azo-group enters mainly the *p*-position to the hydroxyl or amino-group, but if this position is occupied, coupling takes place in the *o*-position; it never occurs in the *m*-position; *e.g.*, *p*-cresol gives the *o*-azo-compound:

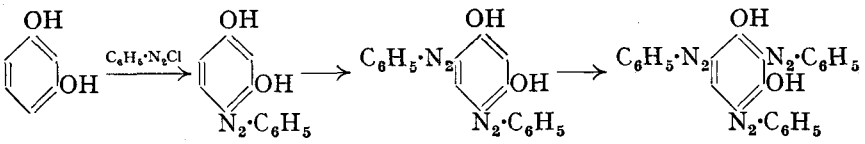


It has also been found that the rate of coupling is increased if the diazonium salt contains a negative group such as nitro-, sulphonic acid, or chlorine (*cf.* coupling with hydrocarbons, above).

When an excess of diazonium salt is used, the *bisazo-* (*o-* and *p-*) and the *trisazo-compound* may be formed:

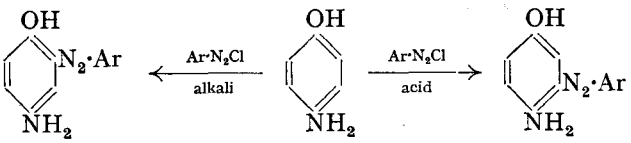


Experiment has shown that the introduction of a second azo-group is facilitated by the presence of an alkyl group in the *p*-position to the hydroxyl group, or by two hydroxyl groups in the *m*-positions; *e.g.*, resorcinol readily forms the trisazo-derivative:

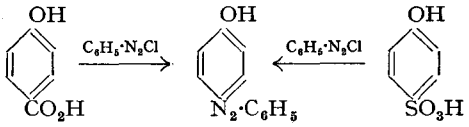


The introduction of the second (and third) azo-group takes place more slowly than the first, and so it is possible to introduce two (or three) different azo-groups.

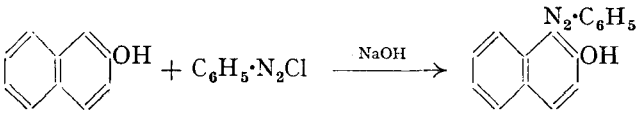
When a compound contains a hydroxyl and an amino-group in the *p*-positions, the amino-group directs coupling to the *o*-position in acid solution and the hydroxyl group to the *o*-position in alkaline solution:



Unusual cases of coupling may occur when the phenol contains a carboxyl or a sulphonic acid group in the *p*-position to the hydroxyl group, the carboxyl or sulphonic acid group being replaced by an azo-group; *e.g.*,

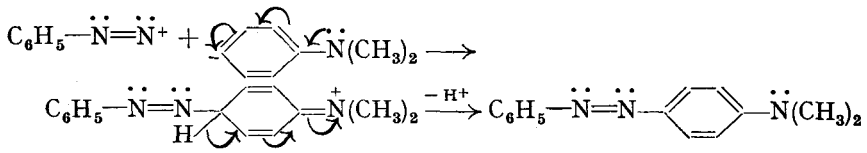


The coupling reaction with 2-naphthol is used to detect the presence of a primary aromatic amine. The compound is treated with sodium nitrite in acid solution, and this solution is added to an alkaline solution of 2-naphthol. A red precipitate of azo-2-naphthol (insoluble in alkali) shows that the original compound was a primary aromatic amine; *e.g.*, benzenediazonium chloride forms 1-phenylazo-2-naphthol:

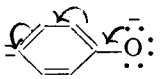


The mechanism of coupling is still a subject of discussion. Recent work indicates that coupling takes place by direct attack at the carbon atom, the

active components in the coupling reaction being the diazonium cation and the free amine or the phenoxide ion (Wistar and Bartlett, 1941; Hauser and Breslow, 1941):



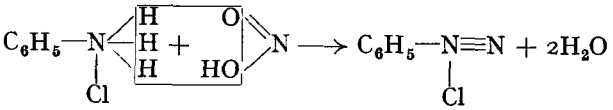
The phenoxide ion also undergoes the resonance effect in a similar manner:



Structure of the diazonium salts. Griess (1864) believed that each nitrogen atom in benzenediazonium chloride was attached to the benzene ring, and he proposed the formula $\overline{C_6H_4—N=N}\!<^{H}_{Cl}$. Kekulé (1866), however, believed that only one of the two nitrogen atoms was directly attached to the ring, his reason being that diazonium salts are converted into *monosubstituted* derivatives of benzene, *e.g.*, *mono*hydric phenols, *mono*halogen derivatives, etc., *i.e.*, the N_2Cl group is replaced by a *univalent* radical. Kekulé also suggested that the structure of benzenediazonium chloride was similar to its best-known derivatives, the azo-compounds, the structure of which was known to be Ar—N=N—Ar'. Kekulé therefore proposed the formula $C_6H_5—\overset{a}{N}=\overset{b}{N}—Cl$, arguing that the attachment of the chlorine atom to $\overset{b}{N}$ was shown by the fact that the coupling reaction of benzenediazonium chloride produced the azo-compounds.

The attachment of only one nitrogen atom to the benzene ring was proved by Langfurth (1878), who showed that the tetrabromo-sulphonic acid of aniline yields a diazo-compound in which the four bromine atoms and the sulphonic acid group are still present.

In 1869, Blomstrand suggested the formula $C_6H_5\cdot\overset{Cl}{\overset{\cdot}{N}}{:}N$, his reason being that since the diazonium salts closely resembled the ammonium salts (in basic character, solubility in water, etc.), both must contain quinquevalent nitrogen. Blomstrand also thought that this formula readily explained the formation of a diazonium salt from a primary aromatic amine:



In modern terminology this formula is written $C_6H_5—\overset{+}{N}\equiv N{:}\}Cl^-$.

Electrical conductivity measurements by Goldschmidt (1890) showed that diazonium salts dissociated into two ions, thus supporting Blomstrand's formula. Strecker (1871) upheld Blomstrand's formula on the grounds of dissimilarity between the properties of the diazonium compounds and the azo-compounds. The former are unstable (and explosive in the solid state), whereas the latter are very stable; hence the structures of the two compounds must be completely different. Le Fèvre *et al.* (1955) have obtained evidence from the infrared absorption spectra of diazonium salts that a triple bond is present.

In 1892, von Pechmann proposed the nitrosamine structure, Ar·NH·NO, for the diazonium hydroxides, basing his arguments on the fact that toluenediazonium chloride gave nitrosobenztoluidide when treated with benzoyl chloride and aqueous sodium hydroxide:

$$CH_3{\cdot}C_6H_4{\cdot}NH{\cdot}NO + C_6H_5{\cdot}COCl \xrightarrow{NaOH} CH_3{\cdot}C_6H_4{\cdot}N(NO){\cdot}CO{\cdot}C_6H_5 + HCl$$

In 1894, the problem of the structure of the diazonium compounds was further complicated by the discovery of two forms of the *diazoates* (*diazotates*); one was called the *n*-diazoate, and the other the *iso*diazoate. Von Pechmann proposed structural isomerism to account for their existence, suggesting that the *n*-diazoate was the salt of *normal* diazohydroxide, Ar·N:H·OH, and that the *iso*diazoate was the salt of *iso*diazohydroxide, which he believed to have the nitrosamine structure, Ar·NH·NO.

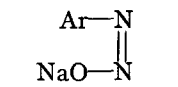
In 1895, Hantzsch, who was influenced by his work on the aromatic oximes (p. 666), proposed geometrical isomerism to account for the existence of the two forms of the diazoates. He adopted the Kekulé formula, since this can give rise to geometrical isomerism (assuming there is no free rotation about an N=N double bond). Geometrical isomerism is not possible with the Blomstrand formula (*cf.* the acetylenic dicarboxylic acids, p. 428). According to Hantzsch, the " diazo-compounds " (the name originally given to them by Griess) have the Blomstrand formula in acid solution, and these Hantzsch called the *diazonium salts*, *i.e.*, diazonium salts have the formula $[Ar{-}N{\equiv}N]^+X^-$, where X is Cl, Br, HSO_4, NO_3, etc. These are the salts of *diazonium hydroxide*, $[Ar{-}N{\equiv}N]^+OH^-$, which has never been isolated. When a diazonium salt solution is made alkaline, the diazonium hydroxide liberated rapidly rearranges to the *diazohydroxide*, the salts of which Hantzsch called the *diazoates* (*diazotates*). The mechanism of these changes may be as follows:

$$[Ar{-}N{\equiv}N:]^+Cl^- \xrightarrow{NaOH} [Ar{-}N{\equiv}N:]^+OH^-$$

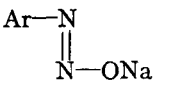
$$Ar{-}\overset{+}{N}{\equiv}N: \longleftrightarrow Ar{-}\overset{\cdot\cdot}{N}{=}\overset{+}{N}: \overset{OH^-}{\rightleftharpoons} Ar{-}\overset{\cdot\cdot}{N}{=}\overset{\cdot\cdot}{N}{-}OH \xrightarrow{NaOH}$$

$$[Ar{-}\overset{\cdot\cdot}{N}{=}\overset{\cdot\cdot}{N}{-}\overset{\cdot\cdot}{\underset{\cdot\cdot}{O}}:]^-Na^+$$

These diazoates exist in two geometrical isomeric forms, the *syn*-(*cis*-) and *anti*-(*trans*-):



sodium *n*-diazoate
syn-form



sodium *iso*diazoate
anti-form

The *syn*-form, the *n*-diazoate, is produced in weakly alkaline solution and is unstable, slowly changing into the *anti*-form, the *iso*diazoate; this change is accelerated by making the solution strongly alkaline. Hantzsch found that one form produces dyes with phenols and amines far more readily than the other, and assumed that the *syn*-isomer was the reactive form (*cis*-isomers contain more internal energy than the *trans*).

This led to a controversy between Hantzsch and Bamberger, who supported the theory of structural isomerism (of von Pechmann). Hantzsch supported his contentions by making use of physico-chemical methods, a procedure rarely used before in organic chemistry; and in 1912, Bamberger agreed with Hantzsch.

In 1926, Angeli reopened the question by proposing structural isomerism

for the existence of the two diazoates, suggesting that the *n*-diazohydroxide was Ar—N(↑O)=NH and the *iso*diazohydroxide, Ar—N=N·OH. Hantzsch once again attempted to defend his theory of geometrical isomerism, but this time he was not so successful as against Bamberger. At the present time, chemists have reverted to the two original schools of thought, the geometrical isomerism of Hantzsch and the structural isomerism of either von Pechmann or Angeli; *e.g.*, Hodgson and Marsden (1945) believe:

(i) that the solid *syn*-(*n*-) diazoates are represented by the formula Ar·N=NOM (where M is a metal), and in aqueous solution hydrolyse to give an equilibrium mixture of diazohydroxide and diazonium hydroxide:

$$Ar{\cdot}N{=}NOM \xrightarrow{H_2O} Ar{\cdot}N{=}NOH \rightleftharpoons Ar{\cdot}N_2^+ + OH^-$$

(ii) that the *anti*-(*iso*-) diazotes are either nitrosamines $Ar{\cdot}\overset{-}{N}(NO)\}\overset{+}{M}$, or equilibrium mixtures in alkaline solution of the ionised *n*-diazoate and nitrosamine:

$$Ar{\cdot}N{=}\overset{-}{N}O\}\overset{+}{M} \rightleftharpoons Ar{\cdot}\overset{-}{N}(NO)\}\overset{+}{M}$$

The strongest evidence brought forward by Hantzsch in favour of geometrical isomerism was the existence of two *diazosulphonates* and two *diazocyanides*.

The diazosulphonates. When a solution of a diazonium salt is treated with a cold alkaline solution of potassium sulphite, an orange or red precipitate is obtained. This compound couples immediately with phenols, is oxidised by iodine to the diazonium sulphate, and liberates sulphur dioxide when treated with inorganic acids. On standing in solution, this reactive form changes to a stable form which is paler in colour, does not couple with phenols, is not oxidised by iodine, and does not liberate sulphur dioxide when treated with inorganic acids.

Bamberger (1874) suggested that the labile and stable forms were *structural* isomers, the former being the *sulphite*, $Ar{\cdot}N_2{\cdot}O{\cdot}SO_2K$, and the latter the *sulphonate*, Ar—N=N—SO_3K. Hantzsch found that the absorption spectra of both compounds were similar, and therefore believed that the labile and stable forms were geometrical isomers, the former being the *syn*- and the latter the *anti*-.

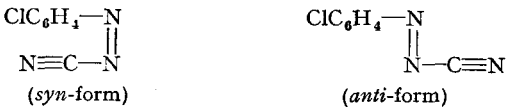
Marsden and Hodgson (1943), however, have reopened the question. These authors argue that it is difficult to explain the ease of coupling of the *syn*- and the impossibility of coupling of the *anti*-diazosulphonate if they are stereoisomers. On the other hand, if the compounds are structural isomers, then the difference in coupling power is explained by the ready rupture of the N—O bond in the *syn*-form (sulphite) and the non-rupture of the N—S bond in the anti-form (sulphonate). Furthermore, these authors argue that the liberation of nitrogen from the *syn*- but not from the *anti*-form by copper sulphate is in accord with the sulphite formula for the *syn*-form; it is oxidised to the diazonium sulphate, followed by decomposition by the cuprous salt thereby produced.

The diazocyanides. When a diazonium salt solution is treated with potassium cyanide in slightly acid solution at temperatures below −5°, a yellow precipitate is obtained. The physical properties of these compounds, *e.g.*, insolubility, colour and non-electrolytes, appear to indicate that they cannot be diazonium salts. Hantzsch therefore believed these compounds to have the structure Ar—N=N—CN (this azo-structure would account for their physical properties).

When allowed to stand in the solid state or in ethanolic solution, the yellow precipitate turns red. This red form may also be prepared by adding potassium cyanide to a diazonium salt solution at temperatures above 0°.

Hantzsch and Schultze (1895) prepared two forms of *p*-chloro- and *p*-nitrobenzenediazocyanides and showed that one form, the *labile* yellow form, coupled with 2-naphthol, and was decomposed into aryl cyanide by copper powder. The other form, the *stable* red form, did not couple with 2-naphthol, and was not

attacked by copper. Hantzsch proposed geometrical isomerism to explain the existence of the two forms, the labile being the *syn*-, and the stable, the *anti*-:



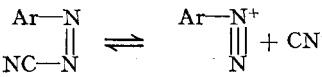
(*syn*-form) (*anti*-form)

Orton (1903) believed that the labile form was the cyanide Ar—N=N—CN, and the stable form the *iso*cyanide, Ar—N=N—NC. This, however, could not be reconciled with the work of Hantzsch and Schultze, who had shown that the labile and stable diazocyanides, on boiling with acid, both gave the same acid amide and same carboxylic acid. These hydrolytic products are characteristic of cyanides; *iso*cyanides give amines.

$$Ar{\cdot}N{=}N{\cdot}CN \xrightarrow{H_2O} Ar{-}N{=}N{-}CO{\cdot}NH_2 \xrightarrow{H_2O} Ar{-}N{=}N{-}CO_2H$$

Le Fèvre *et al.* (1938, 1947, 1949) examined the dipole moments, refractivities, magnetic optical rotatory powers, diamagnetic susceptibilities and ultraviolet spectra of the diazocyanides, and believe that their results agree with geometrical isomerism. Sheppard and Sutherland (1947), from an examination of the vibrational spectra of some pairs of diazocyanides, also believe that the diazocyanides are geometrical isomers (both forms being the cyanide).

In 1939, Stephenson and Waters claimed that the reactivity, *i.e.*, the coupling power, of the *syn*-diazocyanide is associated with the fact that in ionising solvents, the covalent diazocyanide (I) exists in equilibrium with the diazonium cyanide (II) to which the ionic reactivity (*i.e.*, coupling) is due, whereas the *anti*-diazocyanides do not yield (II) in this way:



(I) (II)

Hydrazines. The most important substituted hydrazine is **phenylhydrazine,** $C_6H_5{\cdot}NH{\cdot}NH_2$. This may be prepared by the reduction of benzenediazonium chloride with stannous chloride and hydrochloric acid:

$$C_6H_5{\cdot}N_2Cl + 4[H] \xrightarrow{SnCl_2/HCl} C_6H_5{\cdot}NH{\cdot}NH_2{\cdot}HCl \quad (90\%)$$

The reduction may also be carried out with sodium sulphite; the benzenediazonium chloride is poured into aqueous sodium sulphite, concentrated hydrochloric acid is added, and the solution is then heated on a water-bath. The mechanism of the reduction may be as follows, sodium benzene-*anti*-diazosulphonate, (III), and the sodium salt of phenylhydrazine sulphonate, (IV), being intermediate products:

$$[C_6H_5{\cdot}N{:}N]^+Cl^- \xrightarrow{Na_2SO_3} C_6H_5{-}N{=}N{-}SO_3Na \quad (III) \xrightarrow{H_2SO_3}$$

$$\left[\begin{matrix} C_6H_5{\cdot}N{\cdot}NH{\cdot}SO_3Na \\ | \\ SO_3H \end{matrix}\right] \xrightarrow{H_2O} C_6H_5{\cdot}NH{\cdot}NH{\cdot}SO_3Na + H_2SO_4 \quad (IV) \xrightarrow{HCl}$$

$$C_6H_5{\cdot}NH{\cdot}NH_2{\cdot}HCl \xrightarrow{NaOH} C_6H_5{\cdot}NH{\cdot}NH_2 \quad (80\text{–}84\%)$$

Phenylhydrazine is a colourless liquid when freshly distilled, b.p. 241°. It is readily oxidised when exposed to the air. It is very slightly soluble in water but is very soluble in organic solvents. Phenylhydrazine is strongly basic and forms well-defined salts, *e.g.*, phenylhydrazine hydrochloride,

$C_6H_5{\cdot}NH{\cdot}NH_2{\cdot}HCl$; these salts are relatively stable to atmospheric oxidation. Phenylhydrazine is a powerful reducing agent, reducing Fehling's solution in the cold:

$$C_6H_5{\cdot}NH{\cdot}NH_2 + 2CuO \longrightarrow C_6H_6 + Cu_2O + N_2 + H_2O$$

Hardie *et al.* (1957) have described a new method of phenylation by oxidising phenylhydrazine with metallic oxides (preferably silver) in an aromatic solvent, *e.g.*,

$$C_6H_5{\cdot}NH{\cdot}NH_2 \xrightarrow{Ag_2O} [C_6H_5{\cdot}N{=}NH] \longrightarrow C_6H_5{\cdot} \xrightarrow{ArH} C_6H_5{\cdot}Ar + N_2 + H{\cdot}$$

$C_6H_5{\cdot}Ar$; $C_6H_5{\cdot}C_6H_5$ (by-product) ; C_6H_6 (by-product)

When reduced with vigorous reducing agents, *e.g.*, zinc and hydrochloric acid, phenylhydrazine gives aniline and ammonia; this shows the structure of phenylhydrazine:

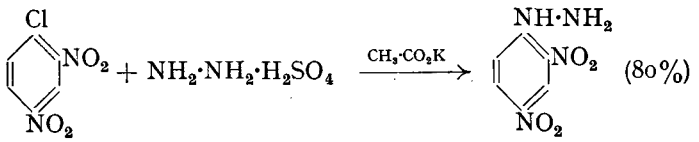
$$C_6H_5{\cdot}NH{\cdot}NH_2 + 2[H] \xrightarrow{Zn/HCl} C_6H_5{\cdot}NH_2 + NH_3$$

The most important reaction of phenylhydrazine is with carbonyl compounds to form *phenylhydrazones*, and with simple sugars to form *osazones*. These derivatives are usually well-defined crystalline solids, and so are useful for the identification of carbonyl compounds. Many phenylhydrazones are decomposed by strong inorganic acids to reform the carbonyl compound. When reduced with zinc and acetic acid, phenylhydrazones form primary amines:

$$C_6H_5{\cdot}NH{\cdot}N{:}CH{\cdot}R + 4[H] \longrightarrow C_6H_5{\cdot}NH_2 + R{\cdot}CH_2{\cdot}NH_2$$

Phenylhydrazine is used for making antipyrine (p. 755).

Various derivatives of phenylhydrazine are used instead of phenylhydrazine, since these produce compounds which crystallise more readily, *e.g.*, *p*-nitro, 2 : 4-dinitro- and *p*-bromophenylhydrazine. Of these, 2 : 4-dinitrophenylhydrazine is most commonly used, and this is prepared by the action of hydrazine sulphate and potassium acetate on 1-chloro-2 : 4-dinitrobenzene:



It is a red crystalline solid, m.p. 194°.

DIAZOAMINO- AND AMINOAZO-COMPOUNDS

Diazo-compounds have the structure Ar—N=N—Y, where Y is a group that is not attached to the nitrogen atom by carbon, **Azo-compounds,** on the other hand, have the structure Ar—N=N—Ar, each aryl group being attached to a nitrogen atom by carbon.

Diazoaminobenzene, $C_6H_5{\cdot}N{=}N{\cdot}NH{\cdot}C_6H_5$, is formed by the interaction of benzenediazonium chloride and aniline. It may be prepared by treating aniline hydrochloride solution with sodium nitrite just sufficient to diazotise *half* of the aniline, and then adding sodium acetate:

$$C_6H_5{\cdot}N_2Cl + C_6H_5{\cdot}NH_2 + CH_3{\cdot}CO_2Na \longrightarrow C_6H_5{\cdot}N{=}N{\cdot}NH{\cdot}C_6H_5 + NaCl + CH_3{\cdot}CO_2H \quad (82\text{–}85\%)$$

Diazoaminobenzene is often formed during the diazotisation of aniline, especially when the solution is only weakly acid. It exists in two forms, one as golden-yellow prisms, m.p. 98°, and the other, yellow prisms, m.p. 80°. Diazoaminobenzene explodes when heated rapidly, and is insoluble in water but soluble in ethanol. It is feebly basic and does not form stable salts. When boiled with dilute sulphuric acid, diazoaminobenzene liberates nitrogen forming phenol and aniline:

$$C_6H_5{\cdot}N{:}N{\cdot}NH{\cdot}C_6H_5 + H_2O \xrightarrow{H_2SO_4} C_6H_5OH + N_2 + C_6H_5{\cdot}NH_2$$

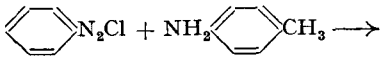
When boiled with concentrated hydrobromic acid, diazoaminobenzene forms bromobenzene and aniline, and when treated with sodium nitrite and hydrochloric acid, it forms benzenediazonium chloride.

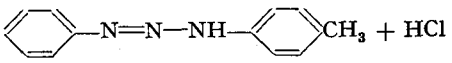
When 1 molecule of aniline, in ethanol solution, is treated with 2 molecules of benzenediazonium chloride, bisdiazoaminobenzene is formed:

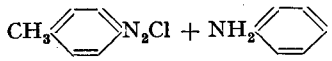
$$C_6H_5{\cdot}NH_2 + 2C_6H_5{\cdot}N_2Cl \longrightarrow C_6H_5{\cdot}N(-N{=}N{\cdot}C_6H_5)_2 + 2HCl$$

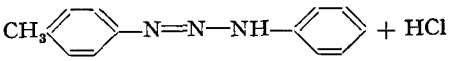
A very important property of diazoaminobenzene is its tendency to rearrange to aminoazobenzene (see below).

Tautomerism of the diazoamino compounds. When benzenediazonium chloride is added to *p*-toluidine, the product obtained is the same as that formed by adding *p*-toluenediazonium chloride to aniline:

A. 



B. 

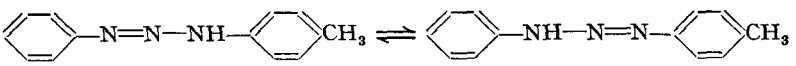


Since the same product is obtained in reactions *A* and *B*, the explanation may be either that only one form, the *stable* form, is present, the other, the *labile* form, changing into the stable form; or that both forms are present in equilibrium, thereby forming a tautomeric system. Two compounds have been shown to be present as follows:

(i) By reduction with tin and hydrochloric acid. Reduction of *A* would (presumably) give aniline and *p*-tolylhydrazine, and *B*, *p*-toluidine and phenylhydrazine. In practice, all four compounds are obtained.

(ii) By hydrolysis with sulphuric acid. Hydrolysis of *A* would give phenol and *p*-toluidine, and *B*, *p*-cresol and aniline. Again, in practice, all four compounds are obtained.

These results therefore show that both *A* and *B* are present in equilibrium:



A. *B.*

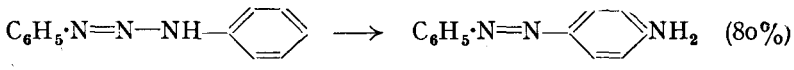
Further support for the existence of this equilibrium mixture has been provided by Hardie *et al.* (1958). They showed that heating unsymmetrical diazoaminobenzenes in chlorobenzene at 150–160°, the latter underwent phenylation by a free-radical mechanism to give mixtures of amines and diaryls. The formation of these products shows that the diazoaminobenzenes undergo decomposition in both tautomeric forms:

$$\begin{array}{l} Ar{\cdot}N{=}N{-}NH{\cdot}Ar' \longrightarrow Ar{\cdot} + Ar'NH{\cdot} + N_2 \\ \quad\quad\Updownarrow \\ Ar{\cdot}NH{-}N{=}N{\cdot}Ar' \longrightarrow ArNH{\cdot} + Ar'{\cdot} + N \end{array}$$

Thus *four* free radicals are produced, two aryl and two anilino, the former giving two diaryls with the solvent chlorobenzene and the latter two amines with the chlorobenzene.

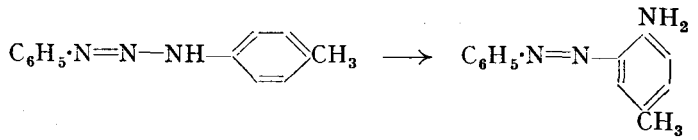
This tautomeric system is known as the *diazoamino triad system*, the *three nitrogen system*, or the *triazene* system. Since such a system has never been separated into the two forms (as is the case when a mobile hydrogen atom is attached to a *carbon* atom), Hunter (1945) called this type of tautomerism *meso-hydric tautomerism*.

***p*-Aminoazobenzene** is formed when diazoaminobenzene is warmed at 30–40° with a small amount of aniline hydrochloride:

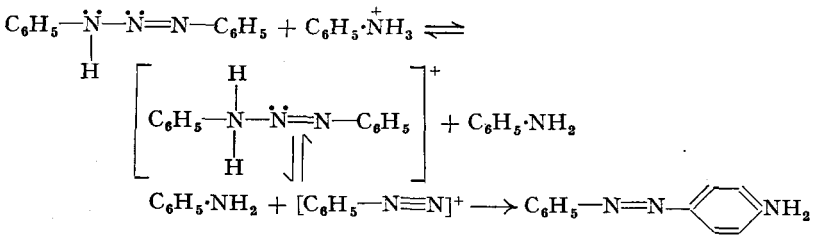


This isomeric change also takes place when the precipitate of diazoaminobenzene is left in contact with its mother liquor for several days.

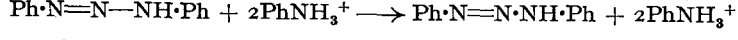
If the *p*-position in the anilino-group is occupied, then the isomeric change occurs more slowly, the azo-group taking up the *o*-position to the amino-group:



The mechanism of diazoamino-aminoazo rearrangement is still uncertain; one proposed recently is that the diazoamino-compound accepts a proton from the catalyst (amine salt), and this intermediate breaks down into a diazonium cation and amine, these two then coupling in the *p*-position:



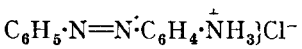
Evidence for this mechanism is to be found in the fact that if the amine salt, $Ar{\cdot}\overset{+}{N}H_3\}Cl^-$, is used as the catalyst instead of aniline hydrochloride, the product of the rearrangement consists of two azo-compounds, $C_6H_5{\cdot}N{=}N{-}C_6H_4{\cdot}NH_2$ and $C_6H_5{\cdot}N{=}N{-}Ar'{\cdot}NH_2$ (Ar′ is Ar less a hydrogen atom). This shows that the rearrangement is *intermolecular* (*i.e.*, separates into parts), the $C_6H_5{\cdot}NH_2$ and $Ar{\cdot}NH_2$ molecules competing for the diazonium cation (Kidd, 1937). This intermolecular mechanism is supported by Clusius *et al.* (1952) who showed that diazoaminobenzene containing ^{15}N reacts quantitatively with aniline hydrochloride according to the following equation:



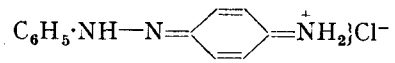
An interesting point here is that the PhN fragment of the *azo-part* of the molecule is set free. This is understandable on the basis of the tautomerism of diazoamino compounds (see previous section).

Aminoazobenzene forms brilliant orange-red plates, m.p. 126°. It is insoluble in water but may be rendered soluble by sulphonation (*cf.* p. 773). Aminoazobenzene is manufactured in large quantities for the preparation

of bisazo-dyes and indulines. Aminoazobenzene forms two series of salts with acids. When one equivalent of hydrochloric acid is used, the salt formed is yellow and unstable, and probably has the structure (I) (since this



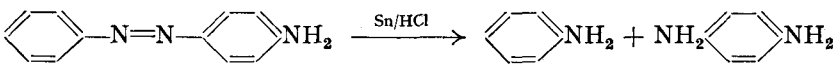
(I)



(II)

has the same type of spectrum as azobenzene). When, however, a large excess of hydrochloric acid is used, the salt produced is dark violet and stable, and its structure is probably (II), *i.e.*, the salt of the quinone-iminohydrazone (see p. 775); the spectrum of this salt is different from that of azobenzene.

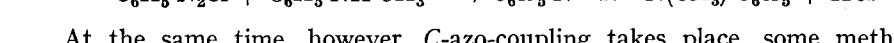
On vigorous reduction, aminoazobenzene is converted into aniline and *p*-phenylenediamine:



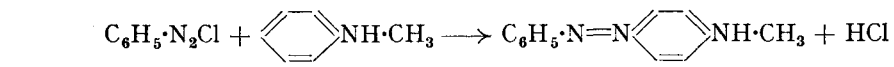
If titanous chloride is used as the reducing agent, the reaction is quantitative, and so may be used for the volumetric determination of aminoazo-dyes.

Aminoazobenzene is oxidised by manganese dioxide and sulphuric acid to *p*-benzoquinone.

Secondary amines behave similarly to aniline in their reaction towards diazonium salts; *e.g.*, methylaniline couples with benzenediazonium chloride to form methyldiazoaminobenzene:

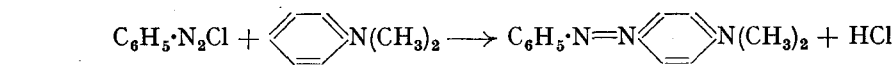


At the same time, however, *C*-azo-coupling takes place, some methylaminoazobenzene being formed:

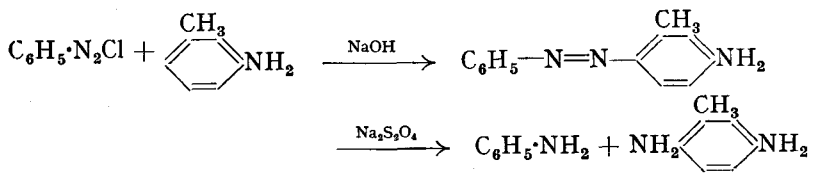


This is also formed by the rearrangement of methyldiazoaminobenzene.

With tertiary amines, the formation of a diazoamino-compound is impossible; the aminoazo-compound is always formed by direct coupling in the *p*-position; *e.g.*, dimethylaminoazobenzene from dimethylaniline and benzenediazonium chloride:



Reduction of azo-compounds with sodium hyposulphite, or stannous chloride and hydrochloric acid offers a relatively simple method of preparing diamines (or amino-phenols) in a pure state; *e.g.*, 2 : 5-diaminotoluene from *m*-toluidine:



It should be noted that the azo-compound, 4-amino-2-methylazobenzene, is formed by direct coupling with the nucleus. Generally, the diazoamino-compound (*N*-coupling) is formed by reaction between diazonium salts and

primary aromatic amines (*cf.* p. 595); *m*-toluidine and the naphthylamines always form the *C*-azo-compound.

Azoxybenzene may be prepared by reducing nitrobenzene with methanolic sodium methoxide (which is oxidised to sodium formate). It may be conveniently prepared by refluxing nitrobenzene with alkaline sodium arsenite:

$$4C_6H_5{\cdot}NO_2 + 3As_2O_3 + 18NaOH \longrightarrow 2C_6H_5{\cdot}\overset{\overset{O}{\uparrow}}{N}{=}N{\cdot}C_6H_5 + 6Na_3AsO_4 + 9H_2O \quad (85\%)$$

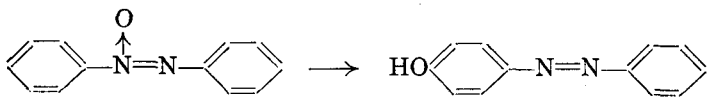
Reduction of nitro-compounds with glucose in alkaline solution gives azoxy-compounds, *e.g.*, nitrobenzene gives azoxybenzene (83 per cent. yield; Galbraith *et al.*, 1951). Metallic thallium also reduces nitro-compounds in ethanolic solution to the corresponding azoxy-compounds (McHatton *et al.*, 1953), *e.g.*,

$$2C_6H_5{\cdot}NO_2 + 6Tl + 6C_2H_5OH \longrightarrow C_6H_5{\cdot}N{=}N(O){\cdot}C_6H_5 + 6TlOC_2H_5 + 3H_2O \quad (84\%)$$

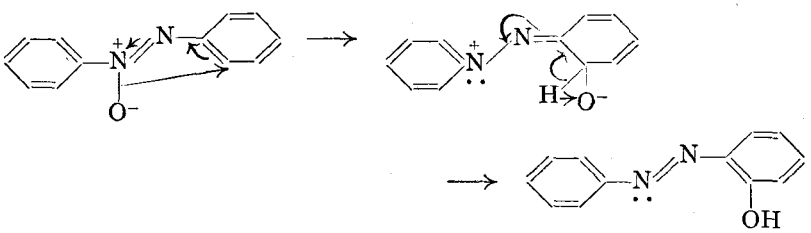
Oxidation of aniline with peracetic acid also gives an 85 per cent. yield of azoxybenzene (Greenspan, 1947).

Azoxybenzene is a yellow crystalline solid, m.p. 36°, insoluble in water but soluble in ethanol and ether. When warmed with iron filings, it is reduced to azobenzene. When reduced with ammonium sulphide, azoxybenzene gives hydrazobenzene, and with metal and acid it gives aniline.

When warmed with concentrated sulphuric acid, azoxybenzene rearranges to hydroxyazobenzene; this is an example of the **Wallach transformation** (1880). Gore *et al.* (1950) have shown that azoxybenzene gives 65 per cent. of *p*-hydroxyazobenzene when heated at 90° for 30 minutes with 83 per cent. sulphuric acid.

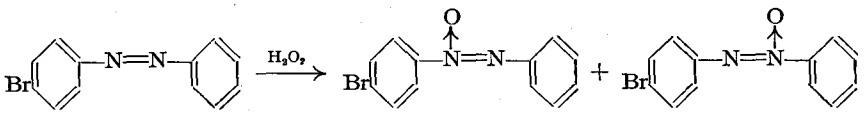


With 98 per cent. sulphuric acid at 25°, however, only 9·5 per cent. of *p*-hydroxyazobenzene was obtained, together with 58 per cent. of azobenzene and some other products. It was found that high temperatures increase the yield of the hydroxyazo-compound, and high concentrations of sulphuric acid increase the yield of the azo-compound. On the other hand, Badger *et al.* (1954) have isomerised a number of azoxy derivatives to *o*-hydroxyazo-derivatives exclusively (or almost exclusively) by exposure to sunlight. An intramolecular mechanism has been proposed for this *ortho*-rearrangement.



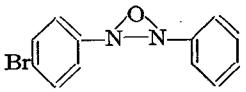
Formerly, the formula of azoxybenzene was believed to contain a three-membered ring (*cf.* V). This was shown to be incorrect by Angeli (1913), who

obtained two bromoazoxybenzenes when *p*-bromoazobenzene was oxidised with hydrogen peroxide in acetic acid:



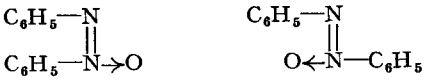
(III) (IV)

If the structure of *p*-bromoazoxybenzene were (V), it would make no difference whether the bromine atom was in one ring or the other. If, however, the oxygen is attached to one or other nitrogen atom by a co-ordinate link, the structure is unsymmetrical and therefore two isomers are possible (III and IV).



(V)

Azoxybenzene exists in two forms which are geometrical isomers:



cis, m.p. 86° *trans*, m.p. 36°

This *trans*-isomer is " ordinary " azoxybenzene.

Azobenzene may be prepared by carefully warming azoxybenzene with three times its weight of iron filings, or by the reaction between nitrosobenzene and aniline:

$$C_6H_5{\cdot}NO + C_6H_5{\cdot}NH_2 \longrightarrow C_6H_5{\cdot}N{=}N{\cdot}C_6H_5 + H_2O$$

It may be conveniently prepared by reducing nitrobenzene with sodium amalgam, alkaline sodium stannite, or best with zinc dust and methanolic sodium hydroxide:

$$2C_6H_5{\cdot}NO_2 + 8[H] \xrightarrow{Zn/NaOH} C_6H_5{\cdot}N{:}N{\cdot}C_6H_5 + 4H_2O \quad (84\text{–}86\%)$$

Lithium aluminium hydride also reduces nitrobenzene to azobenzene. Another convenient preparation is to gently reflux hydrazobenzene (yield is 50 per cent. of each compound):

$$2C_6H_5{\cdot}NH{\cdot}NH{\cdot}C_6H_5 \longrightarrow C_6H_5{\cdot}N{:}N{\cdot}C_6H_5 + 2C_6H_5{\cdot}NH_2$$

Azobenzene crystallises in orange-red plates, m.p. 68°, insoluble in water but soluble in organic solvents. According to Hartley (1938), azobenzene exists as geometrical isomers, the *trans*-form being " ordinary " azobenzene:

cis, m.p. 71·4° *trans*, m.p. 68°

It is of interest to note that the reduction of *cis*-azoxybenzene with lithium aluminium hydride gives *trans*-azobenzene (Badger *et al.*, 1953).

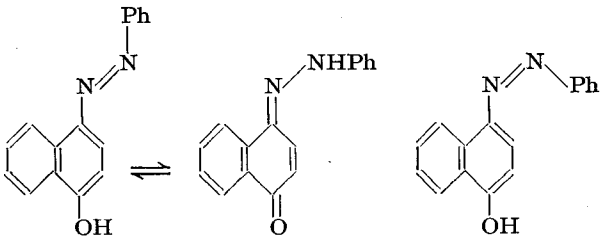
Azobenzene is reduced by zinc dust and aqueous sodium hydroxide to hydrazobenzene, and by stannous chloride or titanous chloride in acid solution, and by alkaline sodium hyposulphite, to aniline. Azobenzene is

not reduced by sodium sulphide. Sodium hydrogen sulphite adds on to azobenzene to form a bisulphite compound:

$$C_6H_5{\cdot}N{=}N{\cdot}C_6H_5 + NaHSO_3 \longrightarrow C_6H_5{\cdot}NH{\cdot}N(C_6H_5){\cdot}SO_3Na$$

Azobenzene is oxidised by hydrogen peroxide in acetic acid to azoxybenzene. Oxidation of *cis*-azobenzene with perbenzoic acid gives *cis*-azoxybenzene. The *trans*-compound gives *trans*-azoxybenzene on oxidation in the dark, but in sunlight some *cis*-isomer is also obtained (Badger *et al.*, 1953). The most outstanding property of the azo-compounds is their colour, and this is used to great advantage in the manufacture of azo-dyes.

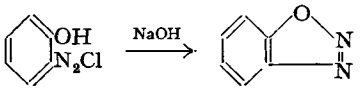
Hydroxyazo-compounds (azophenols). The reaction between diazonium salts and phenols has been the subject of much research. Chemical evidence has been used to support the structure as hydroxyazo-compounds, *e.g.*, 4-phenylazo-1-naphthol (I), and as hydrazones (II):



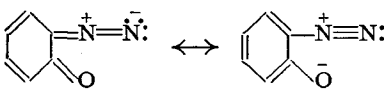
(I) (II) (III)

This compound has been prepared in two ways: (i) by direct coupling between benzenediazonium chloride and naphthol (corresponding to I); (ii) by reaction between phenylhydrazine and 1:4-naphthaquinone (corresponding to II). Kuhn *et al.* (1935), from ultraviolet spectra studies, concluded that both forms (I) and (II) existed in solution as a tautomeric equilibrium mixture. No evidence for tautomeric equilibrium has been found in the spectra of hydroxyazobenzenes or hydroxyazoanthracenes; the former behave spectrally as phenolic compounds (Burawoy *et al.*, 1952), and the latter as hydrazones (Shingu, 1938; Ospenson, 1951). On the other hand, Fischer *et al.* (1959) have confirmed, by spectroscopic evidence, the existence of this equilibrium (I $\rightleftharpoons$ II) in solution, but have also shown that, on cooling, the equilibrium shifts towards (II) in methyl*cyclo*hexane, or towards (I) in alcohol. These authors also showed that the alcoholic solution at $-140°$ contains practically only the hydroxyazo-form as the *trans*-isomer (I) which, on irradiation with light, forms an equilibrium mixture with its *cis*-isomer (III). Between $-135°$ and $-90°$, the unstable *cis*-isomer (III) is converted into the stable *trans*-isomer (I) via (II). Morgan (1961) has shown, from infrared studies, the presence of an azo-hydrazone tautomerism both in the *solid* and in solutions of 1-arylazo-2-naphthols and 4-arylazo-1-naphthols. Furthermore, the equilibrium moves towards the hydrazone in polar solvents and under the influence of electron-withdrawing substituents in the aryl group.

Another problem of structure is that of the diazo-oxides. When *o*-hydroxybenzenediazonium chloride (*o*-diazophenol) is treated with alkali, the diazo-oxide is formed, the structure of which was thought to be an oxide ring:



A quinonoid structure has also been suggested. It now appears that the properties of *o*-diazophenol are best explained on the basis of a resonance hybrid (involving the quinonoid structure):

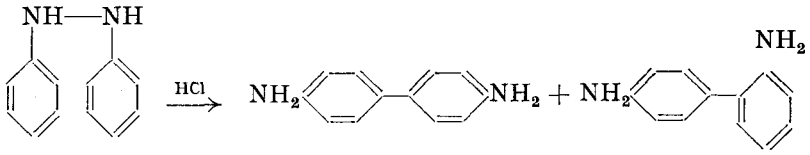


Similarly, *p*-diazophenol is also believed to be a resonance hybrid:

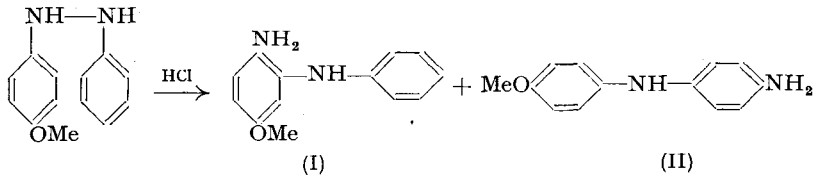
Hydrazobenzene (*s-diphenylhydrazine*), $C_6H_5{\cdot}NH{\cdot}NH{\cdot}C_6H_5$, may be prepared by reducing nitrobenzene or azobenzene with zinc dust and aqueous sodium hydroxide. It is also formed when azoxybenzene is reduced electrolytically; azobenzene has never been isolated as an intermediate product in this reduction.

Hydrazobenzene is a colourless crystalline solid, m.p. 126°. It is slowly oxidised by atmospheric oxygen to azobenzene; this oxidation is rapid with sodium hypobromite. Hydrazobenzene is reduced by stannous chloride and hydrochloric acid to aniline, and when heated, forms azobenzene and aniline (see azobenzene, above).

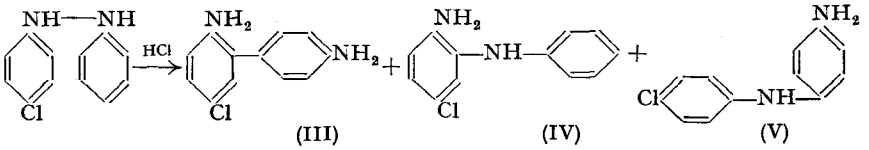
The most important reaction of hydrazobenzene is its rearrangement to *benzidine* (4 : 4′-*diaminodiphenyl*) when warmed with hydrochloric acid. The rearrangement, however, is not completely in the *p* : *p*′positions; some *diphenyline* (2 : 4′-*diaminodiphenyl*) is also formed:



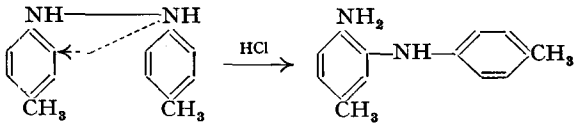
When the *p*-position of one nucleus is occupied, *o*: *p*′-coupling (*i.e.*, diphenyline formation) or the *o*- and *p*-**semidine transformations** take place, according to the nature of the group in the *p*-position. When a methyl, methoxyl, or an ethoxyl group is in the *p*-position, the main product is an *o*-semidine, accompanied by a small amount of the *p*-semidine (in the case of the methyl group, apparently only the *o*-semidine is formed); *e.g.*, *p*-methoxyhydrazobenzene gives mainly anilinomethoxyaniline (I) (the *o*-semidine), together with some methoxyanilinoaniline (II) (the *p*-semidine):



On the other hand, if the *p*-position is occupied by Cl, Br, I, or $N(CH_3)_2$, the main product is a diphenyline derivative, accompanied by a small amount of *o*- and *p*-semidines; *e.g.*, *p*-chlorohydrazobenzene gives chlorodiphenyline (III), anilinochloroaniline (IV) (the *o*-semidine), and chloroanilinoaniline (V) (the *p*-semidine):



When both *p*-positions are occupied, then only the *o*-semidine transformation takes place (the *p*-rearrangement is now impossible); *e.g.*, *p*-hydrazotoluene gives *o*-amino-(4 : 3′)-ditolylamine:

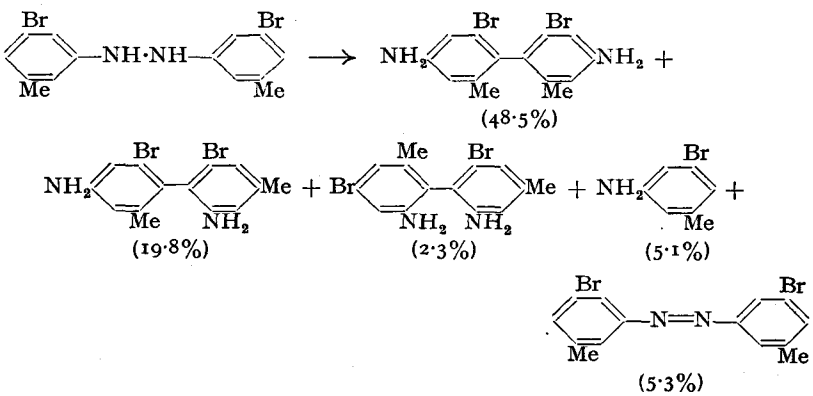


Some groups, particularly carboxyl and sulphonic acid, may be eliminated during the rearrangement, *e.g.*, hydrazobenzene-4-carboxylic acid gives benzidine in very high yield.

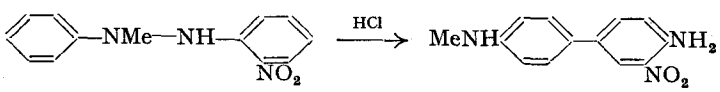
All of these rearrangements, under the influence of acids such as hydrochloric or sulphuric, are included under the heading of the **benzidine rearrangement.**

According to Večeřa *et al.* (1956), in the rearrangement of hydrazobenzene, not only benzidine and diphenyline are formed, but also 2 : 2′-diaminodiphenyl, 2-aminodiphenylamine, and 4-aminodiphenylamine. All of these products were identified by means of paper chromatography. Thus the semidine transformation also occurs to some extent even though the *p*-positions of *both* rings are unoccupied.

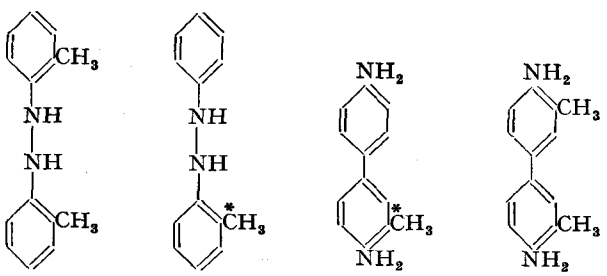
Carlin *et al.* (1956) have carried out the benzidine rearrangement on 3 : 3′-dibromo-5 : 5′-dimethylhydrazobenzene in sulphuric acid and obtained the following products:



Clemo *et al.* (1954) have shown that an *N*-methylhydrazobenzene also undergoes the normal benzidine rearrangement:

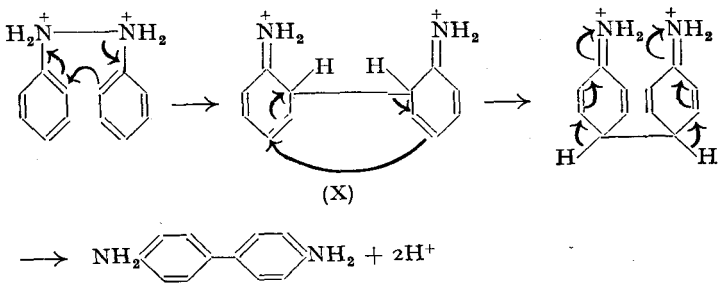


The mechanism of the above transformations is still uncertain. The benzidine transformation has been shown to be intramolecular; *e.g.*, Ingold and Kidd (1933) found that when a mixture of the hydrazobenzenes ANH·NHA and BNH·NHB rearranged, the result always was a mixture of NH_2–A–A–NH_2 and NH_2–B–B–NH_2; the compound NH_2–A–B–NH_2 was never formed. This is



also supported by Wheland *et al.* (1952) who prepared (VI) and (VII) ($\overset{*}{C} = {}^{14}C$), and carried out the rearrangement with the mixture. Compounds (VIII) and (IX) were obtained, and since (VIII) contained almost all of the tracer atom, the mechanism is thus intramolecular. (Actually IX did contain about 0·03 per cent. of the tracer atom.)

Hammond and Shine (1950) have shown that the velocity of the benzidine rearrangement is proportional to the square of the hydrogen ion concentration. Thus it has been suggested that the rearrangement proceeds via an intermediate which contains two protons. Hammond *et al.* (1955) showed that *p*:*p'*-dideuterohydrazobenzene rearranges to benzidine at about the same rate as hydrazobenzene. It therefore appears that breaking of the *p*-C—H bond occurs *after* and not *during* the rate-determining step. Hughes *et al.* (1956), on the basis of their study of the rearrangement of phenylnitramine (p. 575), have proposed the following mechanism (the two benzene rings lie in approximately parallel planes):



(X)

In a similar way, the left-hand ring in (X) can use its nitrogen atom to link either with the *p*- or the remaining *o*-position of the right-hand ring, thereby giving a semidine rearrangement.

QUESTIONS

1. Starting with benzene or toluene, show how you would prepare:—(*a*) *m*-bromotoluene, (*b*) *m*-nitrotoluene, (*c*) *s*-tribromobenzene, (*d*) *p*-iodotoluene, (*e*) *m*-fluoronitrobenzene, (*f*) *o*-tolunitrile, (*g*) *p*-dinitrobenzene, (*h*) phenylarsonic acid, (*i*) *m*-nitrophenylmercuric chloride, (*j*) 2 : 4-diaminophenol, (*k*) 3 : 4-diaminophenol, (*l*) 2 : 5-diaminotoluene, (*m*) 1 : 2 : 3-tribromobenzene, (*n*) 4-chloro-1 : 3-dinitrobenzene, (*o*) 3 : 4-dinitrotoluene, (*p*) 1 : 3-dinitro-4-hydroxybenzene, (*q*) 3-amino-4-hydroxytoluene, (*r*) *p*-methylazobenzene.
2. Write an account of the synthetic uses of the diazonium salts.
3. Describe the preparation and properties of:—(*a*) phenylhydrazine, (*b*) 2 : 4-dinitrophenylhydrazine, (*c*) diazoaminobenzene, (*d*) aminoazobenzene, (*e*) methylaminoazobenzene, (*f*) methyldiazoaminobenzene, (*g*) dimethylaminoazobenzene, (*h*) azoxybenzene, (*i*) azobenzene, (*j*) hydrazobenzene, (*k*) benzidine, (*l*) diphenyline.
4. Write an account of the coupling reactions of the diazonium salts.
5. Write an essay on the structure of the " diazo-compounds ".
6. Discuss the rearrangements of compounds with the structures Ar–N=N–NHAr' and Ar–NH·NH–Ar'.
7. Write an account of the structure of the hydroxyazo-compounds.
8. Define and give examples of:—(*a*) diazotisation, (*b*) Sandmeyer reaction, (*c*) Gattermann reaction, (*d*) Balz–Schiemann reaction, (*e*) Bart's reaction, (*f*) benzidine transformation, (*g*) semidine transformation, (*h*) Wallach transformation.

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CHAPTER XXV

SULPHONIC ACIDS

ONE of the most characteristic properties of the aromatic hydrocarbons and their derivatives is the ease with which they can be sulphonated with concentrated or fuming sulphuric acid, or with chlorosulphonic acid. The saturated aliphatic hydrocarbons are not so readily sulphonated, and so this reaction can be used to separate saturated aliphatic hydrocarbons from aromatic hydrocarbons.

Aromatic sulphonic acids are usually prepared by direct sulphonation, since this is far more convenient than indirect methods. The usual sulphonating agents are:

(i) *Concentrated sulphuric acid* (98 per cent.); *e.g.*, benzene readily forms benzenesulphonic acid (note the reversibility of the reaction):

$$C_6H_6 + H_2SO_4 \rightleftharpoons C_6H_5{\cdot}SO_3H + H_2O$$

(ii) *Sulphur trioxide* in an inert solvent such as sulphuric acid, *i.e.*, *oleum* (*fuming sulphuric acid*), or as an addition product with pyridine or dioxan. Oleum with a free sulphur trioxide content up to about 70 per cent. is particularly useful for those cases where sulphonation is difficult, *e.g.*, the sulphonation of compounds containing *m*-orienting groups in the ring (nitro-compounds, sulphonic acids, etc.).

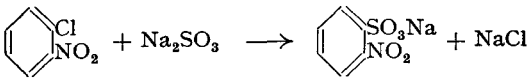
(iii) *Chlorosulphonic acid.* This results in the formation of either a sulphonic acid by carrying out the reaction in carbon tetrachloride solution (using one molecule of reagent), or a sulphonyl chloride (using excess of reagent):

$$ArH + ClSO_3H \longrightarrow Ar{\cdot}SO_3H + HCl$$
$$Ar{\cdot}SO_3H + ClSO_3H \longrightarrow Ar{\cdot}SO_2Cl + H_2SO_4$$

(iv) *Sulphuryl chloride* in the presence of aluminium chloride sulphonates aromatic compounds in the cold to form a sulphonyl chloride:

$$ArH + SO_2Cl_2 \longrightarrow Ar{\cdot}SO_2Cl + HCl$$

An example of indirect sulphonation is the replacement of an "activated" halogen atom by sulphonic acid group, *e.g.*, *o*-chloronitrobenzene reacts with sodium sulphite to form *o*-nitrobenzenesulphonic acid:

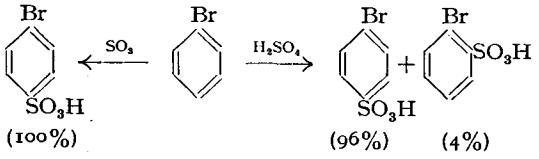


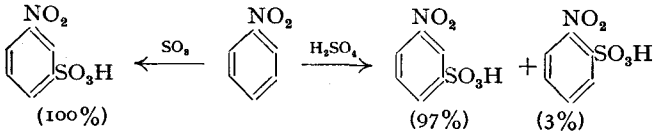
Another example of indirect sulphonation is the reduction of nitro- or nitroso-compounds with sulphur dioxide (see p. 565).

When a compound containing an *o*-*p*-orienting group is sulphonated with sulphuric acid or oleum, the temperature at which the reaction is carried out affects the ratio of the *o*- and *p*-isomers. Generally, lower temperatures favour *o*-substitution and higher temperatures, *p*-substitution; both isomers, however, are always obtained.

Lauer (1935) found that the presence of water also influenced the *o*-*p* ratio. When concentrated sulphuric acid (98 per cent.) is used, the product is mainly a mixture of the *o*- and *p*-isomers, together with a small amount of the *m*-isomer;

or vice versa. When sulphur trioxide (gaseous or in oleum) is used, 100 per cent. *o-p-* or *m*-substitution is obtained; *e.g.*,





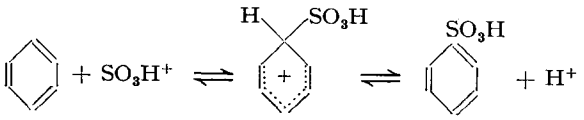
Very few catalysts are known for sulphonation; the salts of mercury, silver and vanadium, and iodine, seem the best. It has also been found that a mercury catalyst may change the orientation of sulphonation (see anthraquinone, p. 733).

Chlorosulphonic acid, at low temperatures, usually gives a high yield of the *o*-isomer when the compound contains an *o-p*-orienting group (see p. 612).

Many mechanisms have been suggested for sulphonation with sulphuric acid or sulphur trioxide, but none is certain. It is certain, however, that sulphonation with these reagents is *reversible*. The difficulty in ascertaining the mechanism appears to be that it is not completely clear what is the active sulphonating species. Price (1941) believed that the active species in sulphuric acid was the SO_3H^+ cation, which is produced as follows:

$$2H_2SO_4 \rightleftharpoons HSO_4^- + H_3SO_4^+ \rightleftharpoons H_2O + SO_3H^+$$

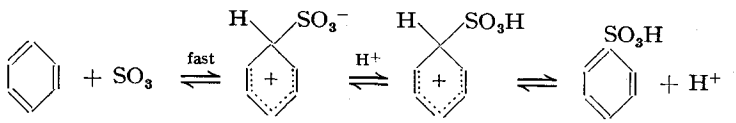
Sulphonation then occurs with this ion:



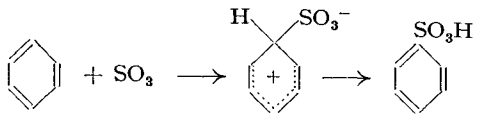
This mechanism was supported by Hinshelwood *et al.* (1948) from their kinetic studies on sulphonation. Brand *et al.* (1950, 1952) proposed that the active species in *oleum* was also the SO_3H^+ ion, and believed it was produced as follows:

$$SO_3 + H^+ \rightleftharpoons SO_3H^+$$

This then reacts according to the mechanism proposed by Price. However, later experiments of Brand *et al.* (1959) have shown that this mechanism is unacceptable; the SO_3H^+ ion is not believed to be the active species with sulphonations in oleum. These authors conclude that sulphur trioxide is the active species:

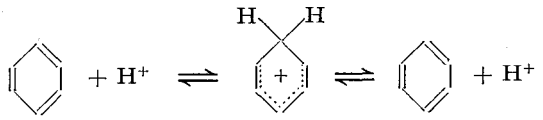


An interesting point here is that Gold *et al.* (1956) have proposed the following mechanism in *aqueous* sulphuric acid (but the authors are not certain about the intervening steps):

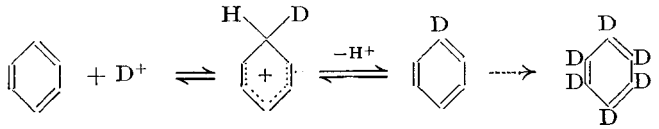


The mechanisms of sulphonation given above are all electrophilic reactions. It is also possible that the following electrophilic reaction could occur:

$$H\overset{\curvearrowright}{-}OSO_2OH \rightleftharpoons H^+ + HSO_4^-$$



As the experiment stands, there is no way of telling whether this reaction occurs or not. It was, however, shown to occur by using deuterosulphuric acid, D_2SO_4, the final product being hexadeuterobenzene (Ingold *et al.*, 1936):



Benzenesulphonic acid, $C_6H_5{\cdot}SO_3H$, may be readily prepared by heating benzene with concentrated sulphuric acid at 80°:

$$C_6H_6 + H_2SO_4 \rightleftharpoons C_6H_5{\cdot}SO_3H + H_2O \quad (75\text{–}80\%)$$

Owing to the reversibility of this reaction, the accumulation of water tends to regenerate the benzene by desulphonation of the sulphonic acid. Hence to obtain the maximum yield of sulphonic acid, it is necessary to remove the water from the reaction mixture as the reaction proceeds. The simplest way in which this may be done is by using oleum, the water being removed chemically by combination with free sulphur trioxide:

$$SO_3 + H_2O + H_2SO_4$$

Alternatively, the water may be removed by carrying out the reaction at high temperature or under reduced pressure, or by passing an inert gas, *e.g.*, nitrogen, through the mixture, or by forming a constant-boiling mixture with an inert liquid, *e.g.*, kerosene. On the other hand, Thomas *et al.* (1940) have shown that boron trifluoride (one equivalent) is an effective catalyst in aromatic sulphonation, *e.g.*,

$$C_6H_6 + H_2SO_4 + BF_3 \longrightarrow C_6H_5{\cdot}SO_3H + BF_3{\cdot}H_2O \quad (98\%)$$

During sulphonation a small amount of sulphone is produced as a by-product, *e.g.*, *diphenylsulphone*:

$$2C_6H_6 + H_2SO_4 \longrightarrow (C_6H_5)_2\,SO_2 + 2H_2O$$

Since these sulphones are insoluble in water, they may be readily separated from the sulphonic acid by filtration.

Properties of benzenesulphonic acid. Benzenesulphonic acid is a colourless crystalline deliquescent solid, m.p. 44°. It is very soluble in water and the solution is strongly acid (about as strong as sulphuric acid). Benzenesulphonic acid and other aromatic sulphonic acids are useful catalysts in esterification and dehydration, being better than sulphuric acid, since they attack the reaction constituents far less than does sulphuric acid. The sulphonic acids are valuable as synthetic reagents because of the ease with which the sulphonic group can be replaced by a hydrogen, amino, hydroxyl, cyano, thiol, or a nitro-group. Furthermore, since the presence of a sulphonic acid group makes the compound soluble in water, sulphonation is an

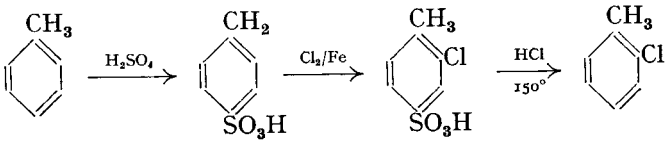
extremely important process in the preparation of dyes and drugs (converting them into soluble derivatives).

Reactions of benzenesulphonic acid. The following reactions are typical of all sulphonic acids.

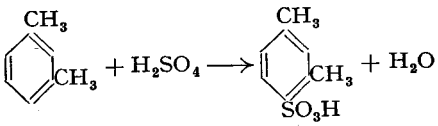
1. As pointed out above, sulphonation is a reversible reaction, but the ease of desulphonation depends on the nature of the aromatic nucleus. Benzenesulphonic acid may be desulphonated by heating with dilute hydrochloric acid under pressure at 150–200°:

$$C_6H_5{\cdot}SO_3H + H_2O \xrightarrow[150^\circ]{HCl} C_6H_6 + H_2SO_4 \quad (v.g.)$$

With some sulphonic acids the sulphonic acid group may be eliminated merely by steam distillation. This desulphonation is very useful for preparing certain isomers, *e.g.*, *o*-chlorotoluene may be prepared as follows:



Desulphonation may also be used to separate certain isomers, *e.g.*, the three xylenes. The xylene fraction from coal tar may be treated with cold 80 per cent. sulphuric acid. Under these conditions, the *m*-isomer is readily sulphonated to *m*-xylene-4-sulphonic acid, the *o*- and *p*-isomers remaining unaffected:



Thus only the *m*-isomer dissolves, and hence may be separated from the other two. The mixture of *o*- and *p*-xylenes is then sulphonated with concentrated sulphuric acid (98 per cent.), and the resulting *o*-xylene-4-sulphonic acid and *p*-xylene-2-sulphonic acid may be separated by fractional crystallisation from the diluted sulphonated mixture; the *p*-derivative is less soluble than the *o*-. The xylenes are then regenerated by heating their sulphonic acid derivatives with dilute hydrochloric acid under pressure.

2. When sodium benzenesulphonate is fused with sodamide, aniline is obtained:

$$C_6H_5{\cdot}SO_3Na + NaNH_2 \longrightarrow C_6H_5{\cdot}NH_2 + Na_2SO_3 \quad (f.g.\text{–}g.)$$

3. Fusion with sodium hydroxide converts sodium benzenesulphonate into sodium phenoxide:

$$C_6H_5{\cdot}SO_3Na + NaOH \longrightarrow Na_2SO_3 + C_6H_5OH \xrightarrow{NaOH} C_6H_5ONa \quad (g.\text{–}v.g.)$$

4. When sodium benzenesulphonate is fused with sodium cyanide, phenyl cyanide is formed:

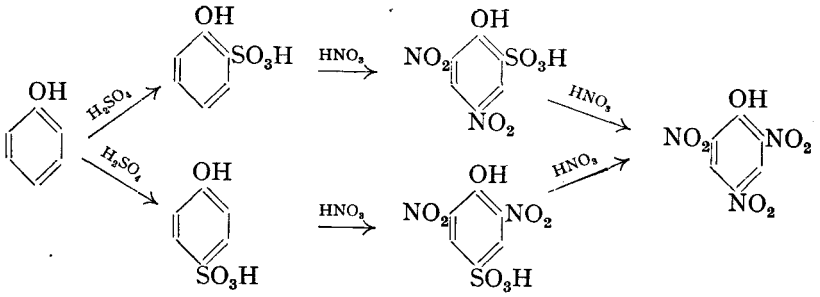
$$C_6H_5{\cdot}SO_3Na + NaCN \longrightarrow C_6H_5{\cdot}CN + Na_2SO_3 \quad (f.g.)$$

5. When the potassium salt of benzenesulphonic acid is fused with potassium hydrogen sulphide, thiophenol is formed:

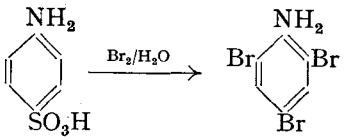
$$C_6H_5{\cdot}SO_3K + KSH \longrightarrow C_6H_5SH + K_2SO_3 \quad (f.g.)$$

6. The sulphonic acid group is often readily replaced by a nitro-group. This offers a means of preparing nitro-derivatives of compounds that are

easily oxidised by nitric acid, since the sulphonic acid derivatives are not easily oxidised; *e.g.*, picric acid from phenol:



Halogen may also replace a sulphonic acid group which is either *o*- or *p*- to a hydroxyl or to an amino-group; *e.g.*, when treated with bromine water, sulphanilic acid forms *s*-tribromoaniline:



Sulphonic acids form many derivatives that are analogous to those of the carboxylic acids, *e.g.*, salts, esters, acid chlorides, amides, etc. The acid chloride may be prepared by treating a sulphonic acid or its sodium salt with phosphorus pentachloride, *e.g.*, benzenesulphonyl chloride:

$$C_6H_5{\cdot}SO_3H + PCl_5 \longrightarrow C_6H_5{\cdot}SO_2Cl + HCl + POCl_3 \quad (g.—ex.)$$
$$C_6H_5{\cdot}SO_3Na + PCl_5 \longrightarrow C_6H_5{\cdot}SO_2Cl + NaCl + POCl_3 \quad (75–80\%)$$

The aromatic sulphonyl chlorides, however, are usually best prepared by treating an aromatic compound with excess of chlorosulphonic acid:

$$C_6H_6 + 2ClSO_3H \longrightarrow C_6H_5{\cdot}SO_2Cl + HCl + H_2SO_4 \quad (75–77\%)$$

Thionyl chloride has no action on sulphonic acids (and some carboxylic acids), but in the presence of dimethylformamide, the sulphonyl chloride is obtained in excellent yield (Bosshard *et al.*, 1959). The reaction proceeds through the amide chloride $Me_2N{\cdot}CHCl_2$.

The sulphonyl chlorides are decomposed very slowly by water but rapidly by alkali; they react with alcohols in the presence of alkali to form esters:

$$Ar{\cdot}SO_2Cl + ROH + NaOH \longrightarrow Ar{\cdot}SO_3R + NaCl + H_2O$$

It is important to note that the esters of the sulphonic acids *cannot* be prepared by direct esterification. The sulphonic acid esters are very good alkylating agents for alcohols and amines:

$$ROH + Ar{\cdot}SO_3R' \longrightarrow R{\cdot}O{\cdot}R' + Ar{\cdot}SO_3H$$
$$R{\cdot}NH_2 + Ar{\cdot}SO_3R' + NaOH \longrightarrow R{\cdot}NH{\cdot}R' + Ar{\cdot}SO_3Na + H_2O$$

It is because of this alkylating action on alcohols that sulphonic esters cannot be prepared by direct esterification.

Benzenesulphonyl chloride is reduced to benzenesulphuric acid or thiophenol by lithium aluminium hydride, depending on the conditions (Field *et al.*, 1951).

When shaken with concentrated ammonia, the sulphonyl chlorides form sulphonamides; *e.g.*, benzenesulphonamide from benzenesulphonyl chloride:

$$C_6H_5{\cdot}SO_2Cl + 2NH_3 \longrightarrow C_6H_5{\cdot}SO_2{\cdot}NH_2 + NH_4Cl$$

These sulphonamides are well-defined crystalline solids, and so are used to characterise the sulphonic acids. Better derivatives for characterising the sulphonic acids are their *S*-benzyl*iso*thiouronium salts:

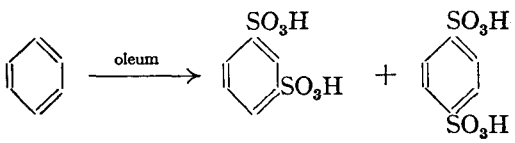
$$C_6H_5{\cdot}CH_2{\cdot}S{\cdot}C(=\overset{+}{N}H_2)(NH_2)\,Cl^- + Ar{\cdot}SO_3Na \longrightarrow C_6H_5{\cdot}CH_2{\cdot}S{\cdot}C(=\overset{+}{N}H_2)(NH_2)\,SO_3{\cdot}Ar^- + NaCl$$

Sulphonyl chlorides also react with primary and secondary amines to form *N*-substituted sulphonamides. These derivatives may be used to separate the three classes of amines (see the Hinsberg separation, p. 309), and for this purpose it is better to use *p*-toluenesulphonyl chloride than benzenesulphonyl chloride, since the former is a solid (m.p. 69°) and the latter a liquid (b.p. 246°, with decomp.).

Sulphonic acid anhydrides have been prepared by heating the acid with excess of phosphorus pentoxide (Field *et al.*, 1952), *e.g.*,

$$2C_6H_5{\cdot}SO_3H \xrightarrow[(-H_2O)]{P_2O_5} (C_6H_5{\cdot}SO_2)_2O \quad (70\%)$$

Benzenedisulphonic acids. When heated with excess of fuming sulphuric acid at 200°, benzene forms benzene-*m*-disulphonic acid as the main product and the *p*-isomer in a small amount:

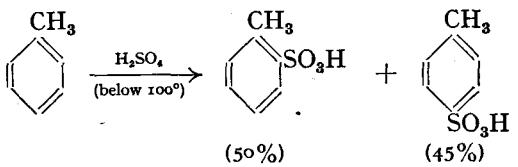


Continued heating of the *m*-isomer in sulphuric acid causes it to rearrange to the *p*-isomer. Thus the *m*-compound is the kinetically controlled product, and the *p*-compound the thermodynamically controlled product. Benzene-*o*-disulphonic acid may be prepared by sulphonating *m*-aminobenzenesulphonic acid, and then replacing the amino-group by hydrogen (diazotising, etc.).

When fused with potassium hydroxide, *m*- and *p*-benzenedisulphonic acids both form resorcinol (*m*-dihydroxybenzene); benzene-*o*-disulphonic acid forms catechol (*o*-dihydroxybenzene).

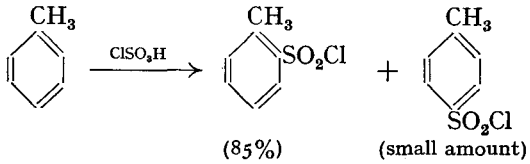
s-Benzenetrisulphonic acid may be prepared by heating benzene-*m*-disulphonic acid with fuming sulphuric acid.

Toluenesulphonic acids. When toluene is treated with concentrated sulphuric acid, the *o*- and *p*-toluenesulphonic acids are formed, low temperatures (below 100°) favouring the formation of the *o*-isomer, and high temperatures (above 100°) the *p*-:



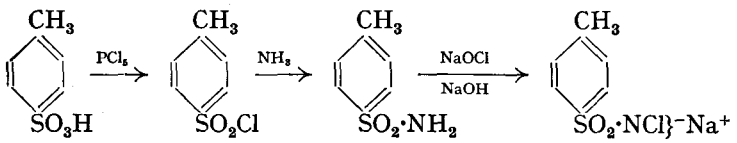
Both isomers are crystalline solids, the *o*- melting at 67·5°, and the *p*- at 106°. They may be separated by treating the mixture of the isomers with phosphorus pentachloride and then filtering; *p*-toluenesulphonyl chloride is a solid, m.p. 69°, whereas the *o*-compound is an oil.

A much better yield of *o*-toluenesulphonic acid may be obtained by treating toluene with chlorosulphonic acid at low temperatures:

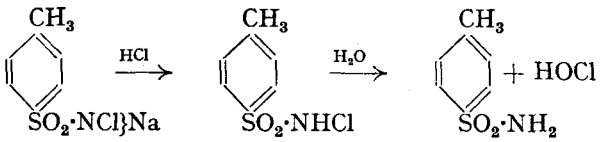


These are separated by filtration and converted into the sulphonic acids by heating with alkali, and then acidifying the solution.

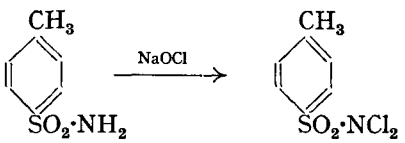
o-Toluenesulphonyl chloride is used in the preparation of saccharin (p. 681); *p*-toluenesulphonic acid is used in the preparation of antiseptics, chloroamine T and dichloramine T. **Chloramine T** is the sodium salt of *N*-chloro-*p*-toluenesulphonamide (*toluene*-p-*sulphonsodiochloramide*), and may be prepared as follows:



In addition to being used as an antiseptic, chloramine T is also used as a laboratory reagent instead of hypochlorite salts, since it is stable and liberates hypochlorous acid when acidified:



When treated with a large excess of sodium hypochlorite solution, *p*-toluenesulphonamide forms **dichloramine T** (N : N-*dichloro*-p-*toluenesulphonamide*):



The *p*-toluenesulphonyl group is often referred to as the **tosyl** group, and is denoted by Ts. Tosylates are useful for preparing, *e.g.*, ethers (with ROH), cyanides (with KCN), thiols (with KSH) thioethers (with K_2S), thiocyanates (with KSCN), alkyl iodides (with NaI), alkanes (with Grignard reagents), etc. (see text).

m-*Toluenesulphonic acid* (an oil) may be prepared by replacing the amino-group in *p*-toluidine-*m*-sulphonic acid by hydrogen:

Isolation of the sulphonic acids. It is usually difficult to isolate the sulphonic acids due to their great solubility in water and their non-volatility. Generally, the isolation of the acids is not attempted, since their salts undergo the desired synthetic reactions. The sulphonic acids (or their salts) may be isolated by any one of the following methods, the actual method used depending on the properties of the acid under investigation:

(i) When the sulphonic acid is not very soluble, the sulphonating mixture is cooled and filtered (through glass wool).

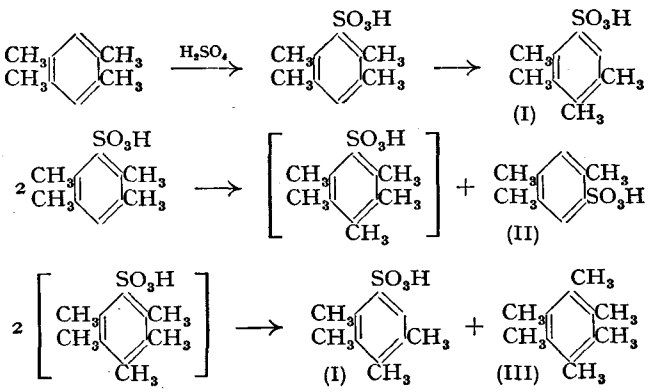
(ii) The sulphonating mixture is allowed to flow into a saturated solution of sodium chloride; in many cases the sodium sulphonate is precipitated.

(iii) The usual method for isolating the sulphonic acids is to dilute the sulphonating mixture and neutralise the liquid with the carbonate of calcium, barium or lead. The insoluble sulphate is collected by filtration, and the filtrate, which contains the soluble salt of the sulphonic acid, is evaporated to dryness under reduced pressure; this gives the dry salt. To obtain the sulphonic acid the solution of the lead salt is decomposed with hydrogen sulphide, filtered and the filtrate evaporated to dryness under reduced pressure. The sodium salt of a sulphonic acid may readily be prepared by adding aqueous sodium carbonate to the calcium or barium sulphonate solution until all the calcium or barium has been precipitated. The liquid is filtered and evaporated to dryness under reduced pressure.

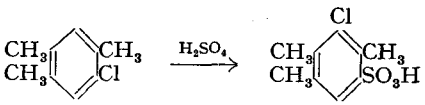
Since the free sulphonic acids are hygroscopic liquids or solids, they are very difficult to purify; some sulphonic acids have not yet been isolated in a pure state.

The separation of a mixture of isomeric sulphonic acids is usually difficult. The method to be employed must be found by experiment. Many are used, *e.g.*, fractional crystallisation of the acids from water or from organic solvents; fractional crystallisation of the salts from suitable solvents; conversion of the sulphonic acids into their sulphonyl chlorides, which are then separated.

Jacobsen rearrangement (1886). During sulphonation polyalkylbenzenes, halogenated polyalkylbenzenes, or polyhalogenated benzenes fairly readily undergo isomerisation due to the migration of an alkyl group or a halogen atom. This is known as the *Jacobsen rearrangement*, and two types of migrations are possible: intramolecular (no " free parts "), in which a group moves from one position to another in the *same* molecule; and intermolecular (involving " free parts "), in which one or more groups are transferred from one molecule to another. Experiment has shown that both types of migrations usually occur simultaneously in the Jacobsen rearrangement, and that an alkyl group always migrates to the vicinal position. Thus the Jacobsen rearrangement offers a means of preparing *vic*-compounds from non-*vic*-compounds; *e.g.*, sulphonation of durene gives 70 per cent. *prehnitenesulphonic acid* (I) and very small amounts of *5-ψ-cumenesulphonic acid* (II) and *hexamethylbenzene* (III); sulphur dioxide, carbon dioxide and about 30 per cent. of a brown amorphous material are also obtained (Smith and Cass, 1932). The reaction possibly takes place as follows:



An example of the migration of a halogen atom is the rearrangement of 5-chloro-ψ-cumene- to 3-chloro-ψ-cumene-sulphonic acid:



The mechanism of the Jacobsen rearrangement is uncertain; the only certain thing appears to be that it is the sulphonic acid, and not the hydrocarbon, that rearranges. It has also been found (so far) that the Jacobsen rearrangement does not take place when the compound contains an amino-, nitro-, methoxyl, or a carboxyl group.

Sulphinic acids, ArSO·OH. The general methods of preparing the aromatic sulphinic acids may be illustrated by the preparation benzenesulphinic acid:

(i) By warming benzenesulphonyl chloride with zinc dust and water, and then acidifying the liquid:

$$C_6H_5{\cdot}SO_2Cl \xrightarrow{Zn/H_2O} (C_6H_5{\cdot}SO_2)_2Zn \xrightarrow{HCl} 2C_6H_5{\cdot}SO_2H \quad (g.)$$

Alternatively, the reduction of the sulphonyl chloride may be effected by means of a hot aqueous solution of sodium sulphide:

$$C_6H_5{\cdot}SO_2Cl + 2Na_2S \longrightarrow C_6H_5{\cdot}SO_2Na + NaCl + Na_2S_2 \quad (g.)$$

Alkaline sodium sulphite is also widely used:

$$C_6H_5{\cdot}SO_2Cl + Na_2SO_3 + 2NaOH \longrightarrow C_6H_5{\cdot}SO_2Na + NaCl + Na_2SO_4 + H_2O$$

Aryl esters of sulphonic acids are reduced by lithium aluminium hydride to sulphinic acids.

$$C_6H_5{\cdot}SO_3Ar \xrightarrow{LiAlH_4} C_6H_5{\cdot}SO_2H + ArOH$$

Alkyl esters, on the other hand, usually give the sulphonic acid.

$$C_6H_5{\cdot}SO_3R \xrightarrow{LiAlH_4} C_6H_5{\cdot}SO_3H + RH$$

(ii) By the action of copper powder on a solution of a diazonium salt saturated with sulphur dioxide:

$$C_6H_5{\cdot}N_2HSO_4 + SO_2 + Cu \longrightarrow C_6H_5{\cdot}SO_2H + N_2 + CuSO_4 \quad (g.)$$

(iii) By the action of sulphur dioxide on benzene in the presence of anhydrous aluminium chloride:

$$C_6H_6 + SO_2 \xrightarrow{AlCl_3} C_6H_5{\cdot}SO_2H \quad (g.)$$

(iv) By the action of sulphur dioxide on an arylmagnesium bromide.

$$C_6H_5MgBr + SO_2 \xrightarrow{-40^\circ} C_6H_5{\cdot}SO_2MgBr \xrightarrow{H_2O} C_6H_5{\cdot}SO_2H \quad (g.)$$

The usual by-product in this reaction is the sulphoxide.

$$C_6H_5{\cdot}SO_2MgBr + C_6H_5MgBr \longrightarrow (C_6H_5)_2SO + (MgBr)_2O$$

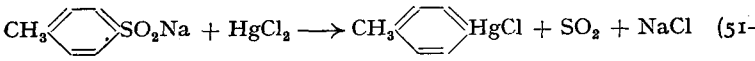
(v) Sulphinic acids may be prepared by fusion of sulphones with potassium hydroxide at 200° (see p. 338).

The sulphinic acids are unstable solids which readily oxidise in the air to sulphonic acids. They are reduced by zinc and hydrochloric acid to thiols; *e.g.*, benzenesulphinic acid gives *thiophenol*:

$$C_6H_5{\cdot}SO_2H + 4[H] \xrightarrow{Zn/HCl} C_6H_5SH + 2H_2O$$

The sulphinic acids are decomposed when warmed with water, forming the sulphonic acid and the *disulphoxide*. The most useful reaction of the sulphinic

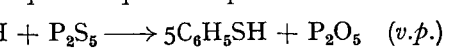
acids is the ease with which the sulphinic acid group is replaced by a chloromercuri-group (this is an example of indirect mercuration); *e.g.*, *p*-tolylmercuric chloride may be prepared by boiling an aqueous solution of sodium *p*-toluenesulphinate with mercuric chloride:



The structure of disulphoxides has been under discussion for some time. Two favoured structures are (I) and (II) (the latter is the thiolsulphonate):

Chemical evidence has been obtained which supports both structures, but Cymerman *et al.* (1951) have shown from spectroscopic evidence that (II) is the correct one. This is also supported by the work of Crenshaw *et al.* (1961), who used a compound labelled with ^{35}S (Ar = *p*-MeC_6H_4; S of SO_2 labelled).

Thiophenol, C_6H_5SH, is the simplest aryl thiol, and may be prepared by the action of phosphorus pentasulphide on phenol:



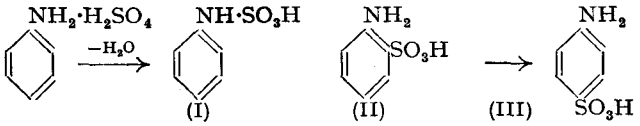
A far better method of preparation is to reduce benzenesulphonyl chloride with zinc and sulphuric acid:

This reaction shows that in the sulphonic acids the sulphur atom is directly attached to a carbon atom in the ring. Lithium aluminium hydride also reduces sulphonyl chlorides to thiols (Marvel *et al.*, 1950).

Thiophenol is a colourless liquid, b.p. 170°, with a nauseating odour. It undergoes the usual reactions of the thiols, and is a stronger acid than phenol (*cf.* the aliphatic thiols, p. 333).

Sulphanilic acid (p-*aminobenzenesulphonic acid*), *p*-$NH_2{\cdot}C_6H_4{\cdot}SO_3H$, is formed as the main product when aniline is sulphonated with oleum (containing 10 per cent. sulphur trioxide) at 180°; some metanilic and a little orthanilic acid are also produced. With excess of oleum, a second sulphonic acid group may be introduced into the *o*-position (to the amino-group), and a third into the *o'*-position. Sulphanilic acid is prepared commercially by the " baking process "; the acid sulphate of aniline (prepared by mixing about equal weights of aniline and concentrated sulphuric acid) is heated for some time at 200°; again, the other two isomers are produced, but less of the metanilic acid in this case.

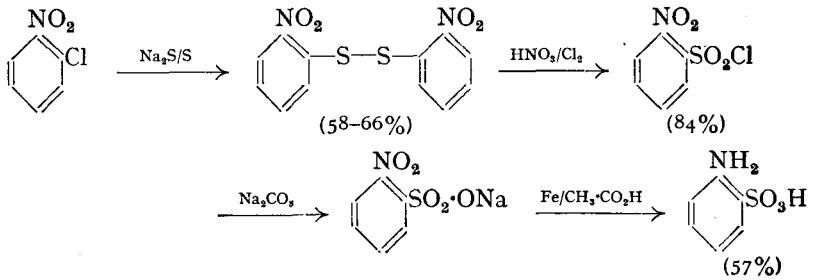
The mechanism of the baking process is uncertain. According to Bamberger (1897), the acid sulphate of aniline is converted into *phenylsulphamic acid* (I), which then rearranges to *orthanilic acid* (II), which, in turn, rearranges to sulphanilic acid (*cf.* the Hofmann–Martius rearrangement, p. 574):



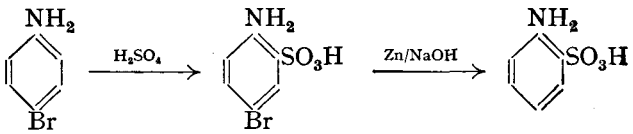
In support of this mechanism, Bamberger prepared phenylsulphamic acid (which, however, has not been isolated as an intermediate in the above reaction), and showed that when carefully heated, it formed orthanilic acid which, on heating at 180°, rearranged to sulphanilic acid. On the other hand, sulphonation in oleum is believed to occur by *direct* sulphonation, and the formation of a larger amount of metanilic acid may be accounted for by the sulphonation of the anilinium ion (p. 520).

Sulphanilic acid is a white solid, m.p. 288° (with decomp.), almost insoluble in cold water but fairly easily soluble in hot. It forms salts with bases but does not combine with acids. The latter may be due to sulphanilic acid existing as an inner salt, p-$H_3\overset{+}{N}\cdot C_6H_4\cdot SO_3^-$ (sulphonic acids are as strong as the inorganic acids). When sulphanilic acid is treated with nitric acid, the sulphonic acid group is replaced by a nitro-group to form p-nitroaniline. Similarly, bromine water attacks sulphanilic acid to form s-tribromoaniline. Sulphanilic acid may be diazotised, but there is reason to believe that the diazonium salt may be an inner salt, p-$N{:}\overset{+}{N}\cdot C_6H_4\cdot SO_3^-$. Sulphanilic acid is a very important intermediate in dye chemistry, and its substituted amides form the sulphanilamide drugs.

Orthanilic acid (*o-aminobenzenesulphonic acid*) may be prepared by refluxing o-chloronitrobenzene with sodium sulphide and sulphur in ethanol solution heating the product di-o-nitrophenyl sulphide with concentrated nitric acid in the presence of chlorine (which is passed in), refluxing the o-nitrobenzenesulphonyl chloride with aqueous sodium carbonate, and finally reducing the o-nitrobenzenesulphonic acid with iron and acetic acid:



Orthanilic acid may also be prepared by sulphonating p-bromoaniline, and then removing the bromine atom with zinc dust and aqueous sodium hydroxide:



Orthanilic acid is a crystalline solid which, on heating with concentrated sulphuric acid, isomerises to sulphanilic acid (see above).

Metanilic acid (m-*aminobenzenesulphonic acid*) may be prepared by reducing m-nitrobenzenesulphonic acid. It is a crystalline solid, and is used in the manufacture of dyes.

QUESTIONS

1. Write an account of the sulphonating agents that may be used in aromatic chemistry and discuss, where possible, the mechanism of their action.

2. Starting with benzene or toluene, show how you would prepare:—(*a*) $PhSO_3H$, (*b*) p-MeC_6H_4SH, (*c*) picric acid, (*d*) $PhSO_2Cl$, (*e*) p-$MeC_6H_4\cdot SO_2\cdot NH_2$, (*f*) o- m- and p-$C_6H_4(SO_3H)_2$, (*g*) o-, m- and p-$MeC_6H_4\cdot SO_3H$, (*h*) chloramine T, (*i*) $PhSO_2H$, (*j*) m-$MeC_6H_4\cdot SO_2H$, (*k*) p-$MeC_6H_4\cdot HgCl$, (*l*) PhSH, (*m*) sulphanilic acid, (*n*) orthanilic acid, (*o*) metanilic acid, (*p*) o-$NO_2\cdot C_6H_4\cdot SO_3H$, (*q*) p-NO_2-toluene-o-sulphonic acid, (*r*) 5-NO_2-2-NH_2-benzenesulphonic acid.

3. Write an account of the isolation of the sulphonic acids, and discuss their use as synthetic reagents.

4. Compare and contrast the reactions of the sodium salts, acid chlorides, ammonium salts, amides and esters of the sulphonic acids and the carboxylic acids.

5. Write notes on:—(*a*) the Jacobsen rearrangement, (*b*) the sulphonation of aniline.
6. Show how you would distinguish between the following compounds: *p*-$MeC_6H_4 \cdot SO_2Cl$, *p*-$CH_2Cl \cdot C_6H_4 \cdot SO_3H$ and *o*-Cl-*p*-toluenesulphonic acids.
7. Discuss the preparation and properties of the aromatic sulphonic acids.

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