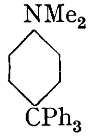
372. *The Rearrangement of the Alkylanilines. Part VI. Mechanism of the Rearrangement.*

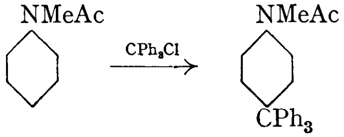
By W. J. HICKINBOTTOM.

THE rearrangement of the hydrobromides of the alkylanilines, where alkyl is *iso*butyl, *iso*amyl, or a higher group, has been shown to proceed largely through the intermediate formation of an olefin * (Hickinbottom and Preston, J., 1930, 1566; Hickinbottom and Ryder, J., 1931, 1281; Hickinbottom, J., 1932, 2396); where the alkyl group is ethyl or propyl, a notable amount of the corresponding alkyl bromide is also produced (Hickinbottom and Ryder, *loc. cit.*). It is important, therefore, to enquire what part the liberated alkyl halide plays in the transference of the alkyl group from the nitrogen to the nucleus.

There is no experimental evidence for the frequently expressed view that the alkyl halide can react with the nucleus of aniline in the absence of a catalyst. In attempts to supply such evidence it is necessary that there shall be no reaction with the amino-group and no olefin must be formed by the action of the amine on the alkyl halide. Triphenylmethyl chloride was therefore heated with dimethylaniline at 100°: 4-trityldimethylaniline (I) was formed together with a variable amount of triphenylmethane. Although triphenylmethyl chloride apparently does not give rise to quaternary ammonium salts (Hughes, J., 1933, 75), there remains the possible objection that a preliminary reaction at the amino-group may occur (compare Wieland, Dolgow, and Albert, *Ber.*, 1919, **52**, 896). This, however, is discounted by the observation that acetomethylanilide reacts in the same way to furnish 4-*tritylacetomethylanilide* (II).

(I.)





(II.)

When methylaniline hydrobromide is heated at 302° so that the volatile products can escape, methyl bromide is evolved, but the principal reaction is migration of the methyl group to the nucleus with the formation of *p*-toluidine. Methylaniline hydriodide, similarly heated, evolves only 2—6% of the theoretical amount of methyl iodide and the main change is the production of a mixture of *o*- and *p*-toluidines. The formation of *o*-toluidine is the first authentic case of the migration, in any serious amount, of an alkyl group to the ortho-position of an arylamine even when the para-position is free (Hofmann, *Ber.*, 1872, **5**, 721, recorded the formation of a liquid toluidine, not otherwise identified, when methylaniline hydriodide was heated at 350° in a sealed tube).

The formation of toluidines in relatively large amounts by heating methylaniline hydriodide or hydrobromide in open tubes is unexpected on the view that the reaction involves a preliminary dissociation into methyl halide and aniline, which then react to form toluidines. Although this hypothesis can be expanded to include these observations, the author believes that the facts receive a more adequate and logical explanation on the basis of a general hypothesis developed in the sequel.

The rearrangement of the alkylanilines can occur under conditions whereby neither olefin nor alkyl halide takes part in the migration of the alkyl group, *e.g.*, when the alkylaniline is heated with a suitable anhydrous metal salt (Hickinbottom, J., 1927, 64; 1932, 2396; Hickinbottom and Waine, J., 1930, 1558; Hickinbottom and Preston, *loc. cit.*). Mechanisms for rearrangements of this type are (a) the expulsion of the alkyl group as a free radical or an ion, which reacts with the nucleus to form an aminoalkylbenzene: (b) the alkyl group, while still attached to the nitrogen, becomes attached to a carbon atom of the nucleus; subsequent rupture of the linkage between the alkyl and the nitrogen furnishes the product of rearrangement (compare Lapworth, J., 1898, **73**, 445). Mechanism

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* In commenting on this view of the rearrangement of *iso*amylaniline hydrobromide, Kon (*Ann. Reports*, 1933, 186) has misinterpreted the experimental evidence. This salt, when heated at 302°, furnishes about 72% of the theoretical amount of amylene.

(a) is adopted, for mechanism (b), which is somewhat similar to that successfully applied to account for the conversion of phenyl allyl ether into *o*-hydroxyallylbenzene (Claisen and Tietze, *Ber.*, 1925, **58**, 275; Claisen, Kremers, Roth, and Tietze, *Annalen*, 1925, **442**, 221), is unsatisfactory in that it is difficult to account for the very high proportion of para-substitution which generally occurs in this rearrangement (on statistical grounds a high proportion of ortho-compound would be expected) and, moreover, the transference of a small alkyl group such as methyl or even ethyl to the para-position requires a considerable and rather improbable distortion of the molecule.

Although it is possible to account satisfactorily for the rearrangement of the alkylanilines and the formation of all the products of the thermal decomposition of their halogen hydride salts on the assumption that the alkyl group is expelled as a free radical, the hypothesis presents serious difficulties. Of these, the most important is the known instability of the free alkyl radicals higher than ethyl (Paneth and Lautsch, *Ber.*, 1931, **64**, 2702, 2703; Rice, *Trans. Faraday Soc.*, 1934, **30**, 152). At no time have the known decomposition products of these radicals been isolated during the rearrangement of the alkylanilines under the influence of metal salts. Further, it might be reasonably expected that free methyl and ethyl radicals would give rise to detectable amounts of ethane and butane. This has not yet been observed. The application of this hypothesis to the alkylaniline salts raises the further difficulty of assuming the expulsion of a neutral group from an amine salt.

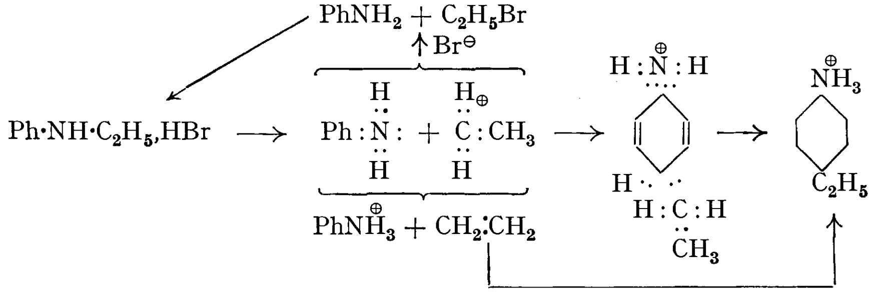
These objections disappear if it is assumed that the alkyl group is eliminated as a positively charged group. Support for the conception that such groups may react as " ions " is derived from the work of Meerwein (*Annalen*, 1927, **453**, 31; Meerwein and Vortmann, *ibid.*, 1923, **435**, 190). Hughes and Ingold have recently cited experimental evidence to support the contention that an alkyl group may be split out from quaternary ammonium and sulphonium compounds as a charged ion (*Nature*, 1933, **132**, 933). Moreover, the idea of a positively charged alkyl ion has been applied by Whitmore (*J. Amer. Chem. Soc.*, 1932, **54**, 3274) to account for some of the internal rearrangements which accompany the dehydration of alcohols.

On such a hypothesis, the rearrangement of alkylanilines in presence of metal halides is represented by reaction of the positive alkyl " ion " with the aniline nucleus reacting in the quinonoid form. The expelled " ion," in general, suffers no internal rearrangement, either on account of the stabilising effect of the metal salt or because its reaction with the nucleus is catalysed by the metal salt.

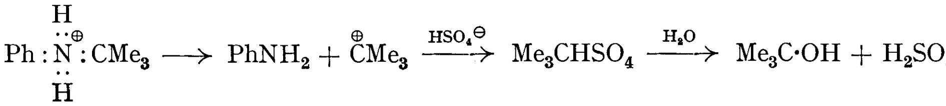
This hypothesis explains the thermal decomposition of the halogen hydrides of the alkylanilines. When such salts are heated, the transference of the alkyl " ion " to the nucleus is restricted by the occurrence of side reactions. Thus alkyl halide results by combination with the halogen ion, and, if the structure permits, a proton is expelled with the formation of an olefin. Simultaneously with these side reactions, the migration of the alkyl group occurs by reaction of the surviving alkyl " ion " with the nucleus. The rearrangement due to the last reaction is surprisingly large with methylaniline hydriodide, which yields more than 50% of the theoretical amount of *o*- and *p*-toluidines when heated at 305—310° in an open tube for 1 hour. Ethylaniline hydrobromide may furnish up to 50% of the theoretical amount of *p*-aminoethylbenzene when heated under similar conditions at 302° for 2 hours. With increasing size of alkyl group, the rearrangement diminishes, with a corresponding increase in the yield of olefin, until with *iso*butyl and *iso*amyl and higher alkylanilines the isomerisation due to this cause is very small. The extent of this rearrangement is seen in the table given by Hickinbottom and Ryder (*loc. cit.*) for the relative proportion of the products formed by the thermal decomposition of the hydrobromides of the alkylanilines. The rearrangement of the higher alkylaniline hydrobromides is therefore dependent largely on the reaction of the secondary products, such as olefin, with the nucleus and must be effected in sealed tubes if it is to proceed to any extent.

A further complication is introduced by the tendency of the surviving alkyl " ion," if its structure is favourable, to undergo internal rearrangement in the manner postulated by Whitmore (*J. Amer. Chem. Soc.*, 1932, **54**, 3274).

On the hypothesis just outlined, the behaviour of ethylaniline hydrobromide on heating is represented by the following scheme :



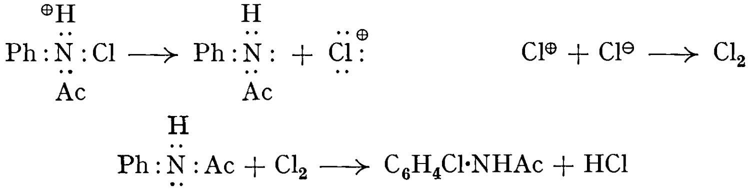
The hypothesis can also be applied to represent the hydrolysis of the alkylanilines containing tertiary alkyl groups (Hickinbottom, J., 1933, 1070) and it fits in with the general electronic theory of reactions developed by Lapworth and by Robinson (" Outline of the Electrochemical Theory of the Course of Organic Reactions," 1932). In these compounds, the induced effect of three alkyl groups attached to one carbon atom is sufficiently intense to cause the transfer of an electron from the tertiary alkyl group, provided that the conditions are suitable and reagents are present to take advantage of this tendency. Similar conditions apply to the hydrolysis of the tertiary alkyl halides.



$$\mathrm{Ph}:\overset{\overset{\mathrm{H}}{\cdot\cdot\oplus}}{\underset{\underset{\mathrm{H}}{\cdot\cdot}}{\mathrm{N}}}:\mathrm{CMe_3} \longrightarrow \mathrm{PhNH_2} + \overset{\oplus}{\mathrm{C}}\mathrm{Me_3} \xrightarrow{\mathrm{HSO_4^{\ominus}}} \mathrm{Me_3CHSO_4} \xrightarrow{\mathrm{H_2O}} \mathrm{Me_3C{\cdot}OH} + \mathrm{H_2SO_4}$$

A simple extension of the hypothesis appears to afford a satisfactory basis for representing a number of similar rearrangements.

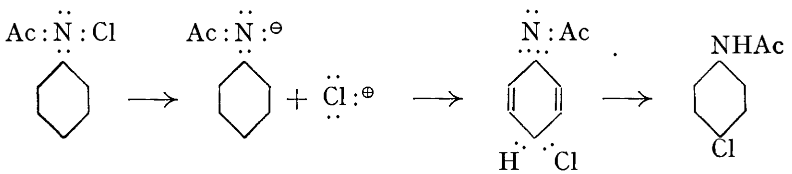
The conversion of *N*-chloroacetanilide into *p*-chloroacetanilide under the influence of hydrochloric acid depends on the intermediate formation of chlorine (Orton and Jones, *Rep. Brit. Assoc.*, 1910, 85). This is represented by the following scheme :



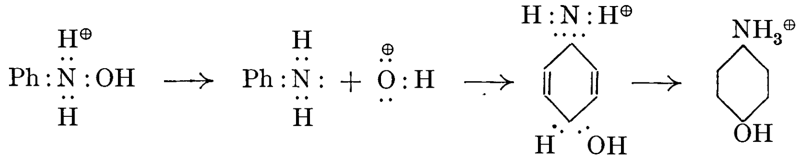
$$\mathrm{Ph}:\overset{\overset{\oplus\mathrm{H}}{\cdot\cdot}}{\underset{\underset{\mathrm{Ac}}{\cdot\cdot}}{\mathrm{N}}}:\mathrm{Cl} \longrightarrow \mathrm{Ph}:\overset{\overset{\mathrm{H}}{\cdot\cdot}}{\underset{\underset{\mathrm{Ac}}{\cdot\cdot}}{\mathrm{N}}}: + \overset{\cdot\cdot\oplus}{\underset{\cdot\cdot}{\mathrm{Cl}}}: \qquad \mathrm{Cl^{\oplus}} + \mathrm{Cl^{\ominus}} \longrightarrow \mathrm{Cl_2}$$

$$\mathrm{Ph}:\overset{\overset{\mathrm{H}}{\cdot\cdot}}{\underset{\cdot\cdot}{\mathrm{N}}}:\mathrm{Ac} + \mathrm{Cl_2} \longrightarrow \mathrm{C_6H_4Cl{\cdot}NHAc} + \mathrm{HCl}$$

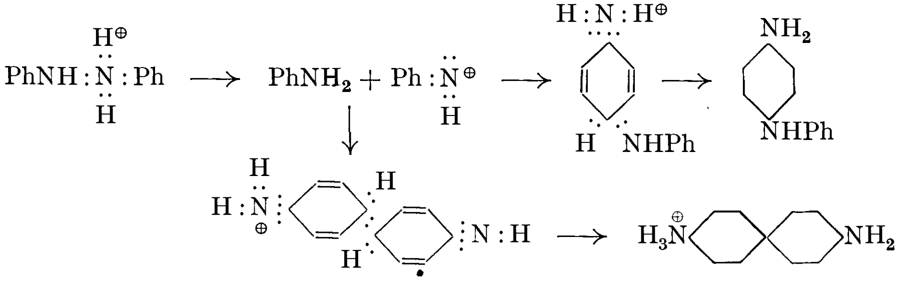
This isomerisation also occurs on exposure to sunlight or on heating in the absence of added catalysts (Blanksma, *Rec. trav. chim.*, 1902, **21**, 290; Chattaway, *Proc.*, 1902, **18**, 200; Porter and Wilbur, *J. Amer. Chem. Soc.*, 1927, **49**, 2145). It can be represented thus :



The isomerisation of the nitroamines when heated or exposed to sunlight or under the influence of sulphuric acid is formulated similarly, the nitro-group being expelled as a negatively charged group. The conversion of the β-arylhydroxylamines into aminophenols is effected by the action of acids : schemes to account for the change have been proposed by Bamberger (*Ber.*, 1900, **33**, 3600) and Hope (*J. Soc. Chem. Ind.*, 1934, **53**, 425). On the basis of the " positive ion " hypothesis now developed, the rearrangement receives an explanation which brings it into line with that of the alkylanilines and the nitroamines and accounts for the formation of such characteristic by-products as quinoles and quinols.



The benzidine rearrangement is represented in the following way according to the " positive ion " hypothesis :



Although the Fischer–Hepp rearrangement of nitrosoamines can be formulated as proceeding by reaction of the positive nitroso-ion with the nucleus, it is highly probable that the positive ion is captured by the chloridion from the hydrogen chloride used to promote the change, with the formation of nitrosyl chloride.

EXPERIMENTAL.

Reaction of Triphenylmethyl Chloride with Dimethylaniline.—Dimethylaniline was treated with acetic anhydride, and was distilled before each preparation, the first fractions being rejected. Triphenylmethyl chloride was crystallised from benzene till of constant m. p. and stored over anhydrous barium perchlorate in a vacuum desiccator.

Triphenylmethyl chloride (2·01 g.) and dimethylaniline (6 g.) were heated at 100—115° for 8 hours, access of moisture being prevented. After addition of aqueous ammonia, steam-distillation removed the excess of dimethylaniline. The reddish-violet aqueous solution was decanted, and the brownish solid product dissolved in warm acetone; 4-trityldimethylaniline separated as a white crystalline mass from the solution. The filtrate was diluted with water and extracted repeatedly with ether. This removed basic products, which were recovered by several extractions with dilute hydrochloric acid and subsequent basification; crystallisation of the flocculent precipitate from alcohol gave a further quantity of 4-trityldimethylaniline (total yield, 1·05 g.).

Evaporation of the residual ethereal solution yielded a gum, which crystallised when rubbed with benzene. Drying on porous tile (yield, 0·54 g.; m. p. 85—87°) and recrystallisation from benzene gave triphenylmethane, m. p. and mixed m. p. 92—93°.

4-Trityldimethylaniline crystallised from acetone in very small needles, m. p. 204—205° (Found : C, 88·9; H, 7·2; N, 4·05. Calc. for $C_{27}H_{25}N$: C, 89·2; H, 6·9; N, 3·9%), identical with a specimen prepared by the method of Fischer and Luckmann (*Z. physiol. Chem.*, 1921, **115**, 93).

From a not too dilute solution in methyl iodide, 4-*tritylphenyltrimethyl ammonium iodide* separated on standing; this crystallised from warm chloroform in slender white needles, m. p. 206—207° (Found : I, 24·6. $C_{28}H_{28}NI$ requires I, 25·1%), fairly soluble in warm alcohol or acetone, sparingly in benzene or boiling water, and almost completely soluble in warm dilute aqueous ammonia.

Reaction of Triphenylmethyl Chloride with Acetomethylanilide.—Carefully dried acetomethylanilide (6 g.) was heated with dry triphenylmethyl chloride (2 g.) at 140—150° for 10 hours, moisture being excluded : hydrogen chloride was soon liberated. The cooled product was dissolved in benzene and shaken with successive quantities of dilute hydrochloric acid and then with successive quantities of concentrated hydrochloric acid. The latter treatment produced a white precipitate, which was filtered off. The benzene solution was washed with water and with very dilute aqueous ammonia, dried, and evaporated. Treatment of the residue with ether caused the separation of a white, sparingly soluble, crystalline mass, which was recrystallised from absolute alcohol, separating in well-formed transparent prisms, m. p. 191—192°, of 4-*tritylacetomethylanilide* (Found : C, 85·8, 85·7; H, 6·7, 6·7; N, 3·8. $C_{28}H_{25}ON$ requires C, 85·9; H, 6·4; N, 3·6%), identical with a specimen prepared by the method described below. The ethereal solution on evaporation, yielded a brownish gum, from which triphenylmethane, m. p. and mixed m. p. 92—93°, was obtained.

Preparation of 4-*Tritylmethylaniline.*—Methylaniline hydrochloride (10 g.) and triphenylcarbinol (5 g.) in glacial acetic acid (30 g.) were heated under reflux for 5 hours. The solvent was then evaporated, and the residue basified with aqueous ammonia and steam-distilled to remove unchanged methylaniline. The greyish solid remaining crystallised from absolute alcohol, in which it was not readily soluble, in needles (3·52 g.), m. p. 211—212° (Found : C, 89·0, 89·3; H, 6·8, 6·9; N, 4·1. $C_{26}H_{23}N$ requires C, 89·4; H, 6·6; N, 4·0%), very sparingly soluble in ether, not very soluble in hot acetone, and more readily in benzene or chloroform. Acetylation of the *amine* by acetic anhydride in pyridine yielded 4-tritylacetomethylanilide, m. p. 191—192°, identical with the product already described.

Behaviour of the Halogen Hydride Salts of Methylaniline on Heating.—(a) *Methylaniline hydriodide.* The pure dry salt (31·74 g.) was heated at 305—310° for 1 hour in a long, wide, open test-tube. The product solidified, on cooling, to a dark crystalline mass which had a faint smell of ammonia. The amine was liberated by the addition of alkali and treated with 50% aqueous zinc chloride. The primary amines, precipitated as zincichlorides, were collected and extracted with boiling light petroleum after being washed with water—yield, 17·3 g. of dry zincichlorides, and 2·82 g. of amines (B) not combined with zinc chloride.

The primary amines liberated from the zincichlorides yielded 7·97 g. (A) boiling between 180° and 205° and a residue (1·23 g.) of much higher b. p. The latter product was not further examined.

The main product (A) was a mixture of *o*- and *p*-toluidines with some aniline. The proportion of toluidines and aniline was determined by evaporating two separate portions with alcoholic hydrogen chloride and determining the hydrogen chloride in the dry residue (Found : HCl, 25·54, 25·60%). The average of these figures corresponds to an aniline content of 6%, the remainder being a mixture of *o*- and *p*-toluidines.

o-Toluidine was separated as its sparingly soluble picrate (in alcohol)—yield, 8·15 g. of picrate, m. p. 202—204° (decomp.), corresponding to 2·58 g. of approximately pure *o*-toluidine. The amine was characterised by its acetyl derivative, m. p. and mixed m. p. 108—109°, and by its pure picrate, m. p. 215—217° (decomp.).

The mother-liquor from the separation of the *o*-toluidine picrate yielded *p*-toluidine oxalate (1·0 g.), m. p. 172—173°, and further amounts of less pure material were also obtained. From these, *p*-toluidine was isolated, m. p. and mixed m. p. 42—43°.

The amines not precipitated as zincichlorides were a mixture of primary amines of undetermined constitution (1·20 g.), secondary amines (0·23 g., calc. as methylaniline), and tertiary amines (0·96 g.) which appeared to be largely of the acridine or phenanthridine type.

(b) *Methylaniline hydrobromide.* The dry salt (15·5 g.) was heated at 305° for 2 hours in an open tube. The product, treated in the manner described above, yielded 4·37 g. of primary amines, 0·11 g. of secondary amines, and 2·3 g. of tertiary amines.

The primary amines furnished 83% distilling between 180° and 205°, the remainder having a much higher b. p. The main fraction consisted essentially of *p*-toluidine and aniline; there was distinct evidence of the presence of xylidine, but the amount was too small for isolation. A determination of the approximate proportion of aniline and *p*-toluidine was made by evaporating some of the amine to dryness with alcoholic hydrogen chloride. The hydrogen chloride content of the dried salt (Found : HCl, 25·71%) corresponded to 11% of aniline in the mixture. The actual proportion was slightly higher owing to the presence of a trace of xylidine. The *p*-toluidine in the mixture, isolated as oxalate, had m. p. and mixed m. p. 42—43°.

The tertiary amines yielded about 40%, distilling between 175° and 200°, which did not react with nitrous acid; the remainder had a very high boiling point.

Estimation of the Alkyl Halide formed during the Thermal Decomposition of Methylaniline Hydrobromide and Hydriodide.—The salt was heated by boiling diphenylamine vapour (302°) in the apparatus described by Hickinbottom and Ryder (*loc. cit.*), the conditions being comparable with those designated (b) (p. 1287). The methyl halide evolved was collected in dry pyridine, and the resulting halidion estimated gravimetrically. The results, which were checked by determinations of the halogen hydride content of the salt before and after heating, are summarised below.

Salt.	Wt., g.	Time, hrs.	Halogen hydride, g.		Methyl halide, g., determined		% Methyl group as methyl halide, calculated	
			Before heating.	After heating.	directly.	from loss.	directly.	from loss.
Hydrobromide	5·0888	1	2·179	2·116	0·0740	0·0747	2·9	2·9
	4·5155	2	1·944	1·852	0·0946	0·1068	4·1	4·8
	8·2530	2	3·535	3·170	0·4288	0·4286	10·0	10·0
	7·2680	2	3·130	2·687	—	0·5201	—	13·6
	5·4610	4	2·352	2·029	0·2752	0·3793	10·0	13·8
Hydriodide	3·3014	½	1·764	1·660	0·1123	0·1162	5·6	5·8
	4·2773	1	2·286	2·257	0·0495	0·0324	1·8	1·3
	3·9118	1	2·091	2·053	0·0543	0·0424	2·3	1·8
	9·5704	1	5·113	5·031	—	0·0916	—	1·6

The liberation of methyl bromide and iodide was established by isolating them as pyridinium methobromide, m. p. 140—142° (Found: Br, 45·7. Calc.: Br, 45·9%), and pyridinium methiodide, m. p. and mixed m. p. 114—116°, in some preliminary decompositions.

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