CC.—*The Rearrangement of the Alkylanilines. Part II. The Course of the Rearrangement in Presence of Metallic Salts.*

By Wilfred John Hickinbottom and (in part) Allan Coley Waine.

The alkylanilines are converted into the corresponding aminoalkylbenzenes by heating with anhydrous metallic halides, such as cobalt, cadmium, manganous, or zinc chloride, in sealed tubes (J., 1920, **117**, 103) or in open tubes (J., 1927, 65), at temperatures above 200°. The nature of this change has now been examined more closely with the object of ascertaining as far as possible the course of the reaction (see also the following paper).

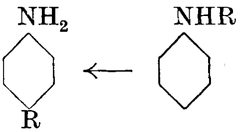
The change may be due to one of two types of reaction: either it proceeds in at least two stages with the formation of intermediate chemical compounds which are capable of isolation; or it is an isomerisation, involving an internal rearrangement, or an exchange of groups between two molecules following an internal electronic redistribution.

As the isomerisation of some other classes of *N*-substituted anilines to give nuclear-substituted amines has been shown to be the result of at least two consecutive reactions (Orton, Soper, and Williams, J., 1928, 998; Chapman, J., 1925, **127**, 2818), it appeared to be more profitable to examine the change of the alkylanilines from the point of view that the isomerisation involves the formation of definite intermediate chemical compounds. On this basis the following alternatives are the most probable : (*a*) Interaction of the metallic chloride and moisture to give hydrogen chloride with formation of the hydrochloride of the base, and subsequent rearrangement as in the well-known Hofmann and Martius change (*Ber.*, 1871, **4**, 742), $2\text{Ph·NHR} + \text{CoCl}_2 + \text{H}_2\text{O} \longrightarrow$
$2\text{Ph·NHR,HCl} + \text{CoO} \longrightarrow 2\text{R·C}_6\text{H}_4\text{·NH}_2\text{,HCl} + \text{CoO}$.

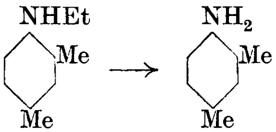
(*b*) Elimination of the alkyl, when it is ethyl or a higher group, as olefin, and subsequent reaction with the nucleus in presence of the metallic salt to give an aminoalkylbenzene, $\text{Ph·NH·Alk} \longrightarrow \text{Ph·NH}_2 + \text{C}_n\text{H}_{2n} \longrightarrow \text{Alk·C}_6\text{H}_4\text{·NH}_2$.

The scheme (*b*) has the disadvantage of requiring a separate mechanism to account for the rearrangement of methylaniline in presence of cobalt chloride (Reilly and Hickinbottom, J., 1920, **117**, 129). Nevertheless this is not sufficient to exclude the hypothesis from consideration, since it has been found that the alkylanilines may lose alkyl groups as olefin under suitable conditions; and it is known that the benzene ring reacts with olefins to form alkyl derivatives (Balsohn, *Bull. Soc. chim.*, 1879, **31**, 539; Essner, *ibid.*, 1881, **36**, 212; Böeseken, *Proc. K. Akad. Wetensch. Amsterdam*, 1912, **14**, 1035). On this hypothesis, it would be expected, when the alkylanilines are converted into aminoalkylbenzenes, that alkyl groups such as *n*-butyl, *iso*butyl, and *n*-propyl should suffer at least a partial internal isomerisation, and that the products of the rearrangement of these alkylanilines should contain appreciable proportions of the *sec.*-butyl-, *tert.*-butyl-, and *iso*propyl-aminobenzenes as a consequence of the tendency of the olefins to react to give secondary and tertiary compounds. It has now been found that when *n*-butylaniline, *n*-propylaniline, and *iso*butylaniline undergo isomerisation in presence of metallic salts the alkyl groups retain their original configuration, the products being *p*-amino-*n*-butylbenzene (I), *p*-amino-*n*-propylbenzene (I), and *p*-amino*iso*butylbenzene (following paper) respectively : in no instance is there any appreciable internal isomerisation of the alkyl group.

This hypothesis was also examined from another point of view. As the intermediate products postulated by it are volatile, it should be possible under suitable conditions to remove them from the reacting system and thus hinder the rearrangement. When, however, a stream of nitrogen was passed through the mixture of alkylaniline and metallic halide at 210—250°, there was no appreciable elimination of the alkyl group as olefin from ethylaniline, *n*- or *iso*-butylaniline, or *n*-propylaniline and the rearrangement proceeded smoothly, giving, due allowance being made for unchanged secondary amine, 95—100% conversion into the corresponding *p*-aminoalkylbenzene. Ethyl-*m*-4-xylidine (II) under these conditions gave *m*-4-xylidine with the complete removal of the ethyl group : rearrangement cannot be effected, however, even when its hydrobromide is heated in a sealed tube.



(I; R = Et, Pr^{α}, Pr^{β}, or *n*-Bu).



(II.)

It was possible also to bring about the rearrangement of *n*-butylaniline and of ethylaniline to the corresponding *p*-aminoalkylbenzenes by heating with metallic salts under diminished pressure.

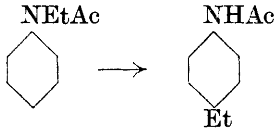
On the evidence recorded above, it must be concluded that the change under investigation is not represented by the scheme (*b*) on p. 1559.

When a mixture of *iso*propylaniline and a metallic halide was heated, a considerable quantity of aniline was produced together with *p*-amino*iso*propylbenzene; the isomerisation, however, was not inhibited even when a rapid stream of nitrogen was bubbled through the heated mixture. In view of the smooth conversion of the other alkylanilines examined under these conditions, it is probable that with *iso*propylaniline two simultaneous reactions occur, namely, a normal rearrangement, giving *p*-amino*iso*propylbenzene, and an elimination of propylene, yielding aniline.

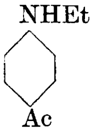
The mechanism (*a*)(p. 1559) resembles that established by Chapman (*loc. cit.*) for the conversion of the diacylanilides into acylamidoacetophenones. It has already been shown that when normal precautions have been taken to dry the materials used in the reaction the change still proceeds smoothly (Hickinbottom, J., 1927, 65). It appeared, however, desirable to re-examine this as a possible mechanism, in view of the exceptional catalytic action of traces of moisture and the difficulty of ensuring absolute dryness of the materials and apparatus (Baker, J., 1929, 1661).

According to this hypothesis, the hydrogen halides of the alkylanilines are produced as a result of the interaction of moisture with the metallic halide. Now, since the hydrogen halides of the alkylanilines tend to dissociate above their melting points into aniline and either alkyl halide or olefin (unpublished observation), it might be expected that when nitrogen is bubbled through the mixture of amine and metallic chloride, or when the pressure is diminished, the dissociation would be facilitated by the removal of the volatile products. The rearrangement would then be retarded or even prevented and the product would contain a considerable proportion of aniline. This expectation is not, however, fulfilled by the experimental results.

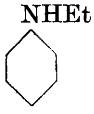
This hypothesis was further tested by experiments on the rearrangement of *N*-ethylacetanilide (III). In this compound the acetyl group is known to be more sensitive than the alkyl group towards acids. Consequently it would be expected, if hydrogen chloride or hydrogen bromide is an intermediate product of the change in presence of a metallic salt, that deacetylation would be the principal reaction and that the product would contain ethylaniline (VI), unchanged ethylacetanilide, and cobalt oxide if the acetyl chloride is removed by means of a rapid stream of nitrogen. If, on the other hand, hydrogen halide has no part in the isomerisation, it should be possible to effect a partial rearrangement of the ethyl group without displacement of the acetyl group: the product should then contain a high proportion of acetylated primary amine in addition to the products formed by the isomerisation of the acetyl group alone. It was found experimentally that deacetylation to ethylaniline did not constitute the main reaction and that the product contained a high proportion of acetylated primary amines, principally *p*-ethylacetanilide (IV).



(III.) (IV.)



(V.)



(VI.)

Here also the experimental evidence is at variance with the deduction from the hypothesis which requires the intervention of traces of moisture. Further, apparently decisive evidence against the hypothesis that the isomerisation of the alkylanilines, when promoted by metallic salts, is due to the intermediate formation of hydrogen halide is discussed in the next paper.

EXPERIMENTAL.

Rearrangement in a Current of Nitrogen.—The apparatus consisted of a wide tube having a sealed-in delivery tube, and a vertical side arm carrying a short condenser. To ensure efficient stirring by the nitrogen, the lower end of the delivery tube was blown into a bulb and pierced with a number of small holes.

The procedure in all the experiments was substantially the same. A measured quantity of the secondary amine was introduced into the tube together with about half its weight of the finely powdered anhydrous metallic salt. The mixture was maintained at 210—250° while a vigorous stream of dry nitrogen was passed through it. After 12—18 hours, the reaction mixture solidified on cooling. It then consisted of the additive compound of the metallic salt with the primary amine formed in the reaction, together with unchanged secondary amine.

Ethylaniline : *Formation of* p-*aminoethylbenzene.* The product obtained from freshly distilled ethylaniline (9·6 g.) and 5 g. of anhydrous cobalt chloride (13 hours at 200—235°) was a greenish-blue crystalline mass containing oily matter. It was dissolved in warm dilute hydrochloric acid and the solution was diluted with water, filtered from oily matter, and treated with a slight excess of aqueous ammonia. The liberated amines were extracted by ether, washed, dried with potassium carbonate, and recovered. The primary amine was isolated as the sparingly soluble zincichloride (Morgan, E.P. 102,834, 1916), which was freed from ethylaniline by extraction with light petroleum and treated with cold concentrated aqueous ammonia. *p*-Aminoethylbenzene, thus obtained in an almost pure state (yield, 6·7 g.), gave an acetyl derivative, m. p. (after one crystallisation from alcohol) and mixed m. p. 93—94°.

n-*Propylaniline* : *Formation of* p-*amino*-n-*propylbenzene.* The following table summarises the results of four typical experiments with pure *n*-propylaniline. The product of each experiment was worked up as described above. The yield of primary amine is calculated from the weight of dry zincichloride. The remainder of the product consisted of unchanged secondary amine, with traces of substituted diphenylamines if the reaction had been unduly prolonged.

Wt. of secondary amine.	Catalyst.	Duration.	Temp. (oil-bath).	Yield of primary amine.
9·45 g.	$CoBr_2$	16 hrs.	230—240°	4·61 g.
9·40 ,,	$ZnBr_2$	12 ,,	220—230	4·68 ,,
9·43 ,,	$CoBr_2$	11·5 ,,	200—230	3·47 ,,
9·45 ,,	$CoCl_2$	15 ,,	210—235	7·01 ,,

Fractional crystallisation of the sulphate and of the acetyl derivative of the primary amine from each preparation showed that no appreciable quantity of aniline was present. Fractional distillation of the primary amine obtained in a series of similar experiments also failed to separate aniline.

The aminopropylbenzene was characterised by its acetyl derivative, m. p. 96—96·5°, and benzoyl derivative, m. p. 116—117°. The melting points recorded in the literature are: *p*-acetamido-*n*-propylbenzene, 87° (Louis, *Ber.*, 1883, **16**, 105); *p*-benzamido-*n*-propylbenzene, 115° (Schultz, *Ber.*, 1909, **42**, 3614); *p*-acetamido*iso*propylbenzene, 102—102·5° (Constam and Goldschmidt, *Ber.*, 1888, **21**, 1159); *p*-benzamido*iso*propylbenzene, 114° (Louis, *loc. cit.*). Accordingly, *p*-amino-*n*-propylbenzene was prepared from *n*-propylbenzene (b. p. 157—161° uncorr.) by nitration, subsequent reduction, and separation of the resulting *o*- and *p*-aminopropylbenzenes by crystallisation of their oxalates from aqueous alcohol, the oxalate of the *p*-isomeride being the less soluble. The orientation of the propyl group was determined by converting the pure amine through the diazo-compound into *n*-propylchlorobenzene and oxidation of this with chromic acid in dilute sulphuric acid to *p*-chlorobenzoic acid, m. p. 234°.

p-Amino-*n*-propylbenzene so prepared gave an acetyl derivative, m. p. 96—96·5°, and a benzoyl derivative, m. p. 116—117°, identical (mixed m. p.) with those of the amine obtained by the rearrangement of *n*-propylaniline. The amine was further characterised by its p-*toluenesulphonyl* derivative, stout tablets, m. p. 113—114°, from alcohol (Found : N, 4·8. $C_{14}H_{19}O_2NS$ requires N, 4·8%).

p-n-*Propyldiphenylthiocarbamide*, $NHPh{\cdot}CS{\cdot}NH{\cdot}C_6H_4Pr$, prepared by warming a slight excess of the amine in light petroleum with phenylthiocarbimide, separated from alcohol in glistening plates, m. p. 127—128° (Found : N, 10·4. $C_{16}H_{18}N_2S$ requires N, 10·3%).

p-Amino-*n*-propylbenzene yielded with aqueous zinc chloride a curdy white precipitate of the *zincichloride*, sparingly soluble in water and in light petroleum and slightly soluble in ether. It separated from alcohol in clusters of slender needles [Found : Cl, 17·6. $(C_{10}H_{13}N)_2,ZnCl_2$ requires Cl, 17·5%].

The *cobaltobromide* separated as a blue crystalline mass when dry concentrated alcoholic solutions of the components were mixed [Found: N, 5·7; Co, 11·9. $(C_{10}H_{13}N)_2,CoBr_2$ requires N, 5·7; Co, 12·0%]. It was purified for analysis by crystallisation from warm dry ethyl acetate.

iso*Propylaniline* : *Formation of* p-*amino*iso*propylbenzene*. When *iso*propylaniline was heated at 210—250° with anhydrous cobalt chloride, zinc bromide, or cadmium chloride in open tubes or in a current of nitrogen, the product obtained was a mixture of primary amines. A partial separation by fractional distillation yielded *p*-amino*iso*propylbenzene and aniline in approximately equal amounts, together with a smaller quantity of an amine of much higher boiling point. A sharper separation was effected by fractional crystallisation of the sulphates. The sulphate of *p*-amino*iso*propylbenzene is the less soluble in water. The free amine was characterised by its acetyl derivative, m. p. 105°, identical with *p*-acetamido-*iso*propylbenzene prepared from *iso*propylbenzene by Constam and Goldschmidt's method (*loc. cit.*).

Ethyl-m-4-*xylidine* : *Formation of* m-4-*xylidine*. (1) *In an open tube*. The secondary amine (5·85 g.) was heated for 14½ hours at 220—240° with 1·37 g. of anhydrous cobalt chloride. There resulted a dark blue crystalline mass, and a small layer of bright green crystals on the bottom of the tube. The primary amine, isolated as zincichloride (yield, 3·44 g.) and recovered by treatment with ammonia, was acetylated in aqueous suspension. Evaporation of the crude acetylation mixture yielded a brownish crystalline mass, m. p. 120°. Crystallisation from alcohol furnished the pure acetyl compound, m. p. and mixed m. p. 127—128° (Found : N, 8·6. Calc. : N, 8·6%).

(2) *In a sealed tube*. Dry ethyl-*m*-4-xylidine hydrobromide (5 g.) was heated in a sealed tube for 6 hours at 280—290°. After cooling, a small quantity of a colourless volatile liquid had condensed in the capillary projecting from the furnace. There was no escape of gas when the tube was opened. The hydrobromide had been converted into a greyish, apparently amorphous mass. The primary amine present in the mixture was isolated as zincichloride (yield, 1·2 g.) and consisted of pure *m*-4-xylidine.

Rearrangement under Diminished Pressure.—When the rearrangement of the alkylanilines was attempted by heating under diminished pressure with metallic chlorides, difficulties were encountered such as irregular boiling, and excessive loss of the amine at comparatively low pressures during the early stages of the experiment. These were circumvented to a large extent by heating the mixture of secondary amine and the metallic salt initially at 100—200 mm., the pressure being gradually lowered and the temperature raised in the later stages of the experiment. It was also found advantageous to employ a moderate excess of the metallic halide.

The apparatus used in the later experiments consisted of a flask fitted with a ground-in stopper and having a wide, bent side arm to act as a reflux condenser. The flask was inclined so that the side arm was vertical. Its cooling effect was supplemented by an inclined water-jacketed condenser attached to the upper end of the side arm. Between the apparatus and the water-pump a train of soda-lime tubes was inserted to prevent access of moisture.

Ethylaniline : *Formation of* p-*aminoethylbenzene*. Ethylaniline (10 g.) with its own weight of anhydrous cobalt bromide was maintained at 190—200° under 200 mm. for about 10 hours. Thereafter the temperature was gradually raised to 230°, and the pressure gradually reduced to 100 mm. during 23 hours. A solid greenish-blue mass was obtained on cooling. The amines were isolated in the manner already described. Conversion of a portion into *p*-toluenesulphonyl derivatives and analysis by Hinsberg's method showed that 58% of the product was primary amine. The remainder was separated by means of zinc chloride and the primary amines were acetylated. The crude acetyl compound, after being washed with water, had m. p. 80—82°, raised to 93° by crystallisation from alcohol; it was identified as *p*-acetamidoethylbenzene by a mixed melting point with an authentic specimen. There was present also in the reaction mixture another primary amine which gave an acetyl derivative more soluble in water than *p*-acetamidoethylbenzene, but the amount was too small to permit of its isolation.

n-*Butylaniline* : *Formation of* p-*amino*-n-*butylbenzene*. Butylaniline (10 g.) and anhydrous cobalt chloride (10 g.) were heated at 190°/200 mm. The pressure was gradually reduced to 40 mm., and the temperature raised to 210°, during 30 hours. The mixture was finally heated for 9 hours at 230—250°/40 mm. The product contained 47% of primary amine. Acetylation of the primary amines yielded a crude solid, m. p. 85—90°, which after crystallisation from alcohol melted at 102°, alone or mixed with authentic *p*-acetamido-*n*-butylbenzene.

Rearrangement of N-*Ethylacetanilide* : *Formation of* p-*Acetamidoethylbenzene*.—A vigorous stream of nitrogen was passed through the deep blue solution of anhydrous cobalt chloride (10 g.) in *N*-ethylacetanilide (30 g.) at 250—280° for 10 hours. The greenish product was shaken with water and benzene. The benzene layer, after being filtered from tar and washed with water to remove cobalt chloride, was extracted several times with *N*-hydrochloric acid, the product thus being separated into neutral acetyl compounds (17·35 g.) and amines (6·2 g.). The latter consisted largely of secondary amines, distilled for the most part between 230° and 290°, and appeared to contain *p*-ethylaminoacetophenone (V). The neutral acetyl compounds, after hydrolysis and separation of the resulting amines by means of zinc chloride, gave 8·95 g. of zincichloride. The primary amines consisted principally of *p*-aminoethylbenzene, identified by its acetyl derivative, m. p. 93°, with smaller amounts of an amine of higher boiling point, and an aminoethylbenzene which was probably the *o*-compound.

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UNIVERSITY OF BIRMINGHAM,
EDGBASTON.

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