77. *The Cyclic Methyleneamines. The Use of Hexamine in the Production of Aldehydes.*

By John Graymore and (in part) David R. Davies.

Sommelet showed that hexamine–benzyl chloride on hydrolysis gave benzaldehyde. It is now demonstrated that benzylamine and its derivatives can be converted into the corresponding aldehydes by means of hexamine. In a similar manner α-phenylethylamine gives acetophenone.

By hydrolysis of the quaternary compounds which hexamine forms with alkyl halides Hoch (D.R.-P. 139,394) obtained primary amines. Sommelet (*Compt. rend.*, 1913, **157**, 852) showed that, when boiled with water, the quaternary derivatives broke down to give an aldehyde other than formaldehyde as the main product, hexamine–benzyl chloride yielding 70% of benzaldehyde together with some benzylamine and methylamine. He presumed that methylenebenzylamine, formed by fission of the quaternary compound, isomerised to benzylidenemethylamine, hydrolysis of which would give benzaldehyde.

On this assumption it was obvious that benzaldehyde should be obtainable in good yield from methylenebenzylamine or indeed directly from benzylamine. The authors have found that, when benzylamine is added to formaldehyde an oil is produced which, when just dissolved in hydrochloric acid, reacts with an aqueous solution of hexamine to give benzaldehyde in 60% yield. Similarly, the solution obtained by adding concentrated hydrochloric acid to pure methylenebenzylamine till it just dissolves also gives benzaldehyde when heated with hexamine. No benzaldehyde is obtained from either benzylamine or methylenebenzylamine in absence of hexamine or in presence of an excess of hydrochloric acid.

Ingold (J., 1929, 1199) observed that methylenebenzylamine exhibits prototropic mobility in presence of sodium hydroxide at 300°. His results, which indicated a 10% conversion into benzylidenemethylamine (based on the yield of benzaldehyde obtained by hydrolysis of the product), are not comparable with those obtained by the use of hexamine in aqueous solution. The low result is probably due to polymerisation of methylenebenzylamine in presence of sodium hydroxide to tribenzyltrimethylenetriamine, whereby isomerisation to benzylidenemethylamine is precluded.

According to Clarke, Gillespie, and Weisshaus (*J. Amer. Chem. Soc.*, 1933, **55**, 4571) the production of methylamine when certain amino-acids are heated with formaldehyde in acid solution is due, in the first place, to transposition of the double bond in a Schiff's base:

$$\mathrm{CH_2{:}N{\cdot}CHR{\cdot}CO_2H \longrightarrow CH_3{\cdot}N{:}CR{\cdot}CO_2H}$$

The results now obtained show that methylenebenzylamine is initially formed as a result of the hydrolysis of hexamine–benzyl chloride. Under conditions unfavourable to the formation of tribenzyltrimethylenetriamine, isomerisation to benzylidenemethylamine ensues. Finally, benzaldehyde is produced by interaction of the benzylidenemethylamine and aminomethyl alcohol (from hexamine):

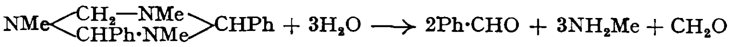
$$\mathrm{CHPh{:}NMe + H_2O + NH_2{\cdot}CH_2{\cdot}OH \longrightarrow Ph{\cdot}CHO + NHMe{\cdot}CH_2{\cdot}OH + NH_3}$$

Ammonia is evolved copiously during hydrolysis of hexamine–benzyl chloride.

o-, *m*-, and *p*-Chlorobenzylamine can be similarly converted into *o*-, *m*-, and *p*-chlorobenzaldehyde, but in considerably lower yields than that obtained from benzylamine.

The method, when extended to α-phenylethylamine gave, as expected, acetophenone.

Distillation under reduced pressure of hexamine–benzyl chloride yielded a colourless oil to which the structure (I) has been assigned. Its behaviour is similar to that of other cyclic triamines; it decomposes

(I.) 

$$\mathrm{NMe}\begin{matrix}\diagup\mathrm{CH_2{-}NMe}\diagdown\\ \diagdown\mathrm{CHPh{\cdot}NMe}\diagup\end{matrix}\mathrm{CHPh + 3H_2O \longrightarrow 2Ph{\cdot}CHO + 3NH_2Me + CH_2O}$$

readily on warming with mineral acids to give benzaldehyde, methylamine, and formaldehyde.

Experimental.

Hexamine–p-*nitrobenzyl Bromide*.—*p*-Nitrobenzyl bromide (1 mol.) was added to hexamine (1 mol.) in chloroform, and the mixture refluxed (2 hrs.). The quaternary *compound* separated in needles, m. p. 168° (decomp.) (Found: Br, 22·4. $C_{13}H_{18}O_2N_5Br$ requires Br, 22·5%).

Hexamine–o-*nitrobenzyl iodide*, obtained in a similar way, crystallised in deep yellow needles, m. p. 154° (Found: I, 31·7. $C_{13}H_{18}O_2N_5I$ requires I, 31·5%).

Preparation of Benzaldehyde from Benzylamine.—Benzylamine (25 g.) was dissolved in water (25 c.c.), and formaldehyde (25 c.c. of 40%) added with cooling. The sticky oil which separated was dissolved by the addition of concentrated hydrochloric acid (25 c.c.), and the solution heated to its b. p. under reflux. Hexamine (25 g.), dissolved in a small quantity of warm water, was added, and the whole refluxed (15 mins.). After excess of acid had been added and the solution again refluxed (5 mins.) to decompose any condensation product which the benzaldehyde might have formed, the latter was extracted with ether, dried over calcium chloride, and distilled, b. p. 179° (16 g., 66%).

When only 10 g. of hexamine were used, a considerably smaller yield of the aldehyde was obtained, and from benzylamine (25 g.), water (25 c.c.), formaldehyde (25 c.c. of 40%), and excess of concentrated hydrochloric acid (65 c.c.) together with hexamine (10 g.), no benzaldehyde resulted.

Action of Hexamine on Methylenebenzylamine.—A solution of methylenebenzylamine (10 g.) in concentrated hydrochloric acid (10 c.c.) was heated to its b. p. under reflux, hexamine (10 g.) added, and, after refluxing for 15 mins., the mixture was made acid with excess of hydrochloric acid. The oil which had separated was removed in ether, recovered, and distilled; benzaldehyde (5 g.) was obtained.

Distillation of Hexamine–Benzyl Chloride.—Hexamine–benzyl chloride (30 g.), prepared by heating hexamine with benzyl chloride in chloroform solution, was heated under 30 mm. The mass rapidly charred, ammoniacal vapours were given off, and an oil distilled at 68—75°. On redistillation a colourless oil was obtained, b. p. 70—72°/30 mm. (Found: C, 76·5; H, 8·6; N, 15·1. $C_{18}H_{23}N_3$ requires C, 76·8; H, 8·2; N, 15·0%).

Hydrolysis. After the oil (5 g.) had been refluxed with excess of hydrochloric acid for 10 minutes, the benzaldehyde which had separated was extracted with ether, dried, and distilled, b. p. 179° (phenylhydrazone, m. p. and mixed m. p. 153°) (1·8 g.). The residual liquor after the extraction was evaporated to dryness on the water-bath; formaldehyde was evolved. The residue was dissolved in alcohol (in which it was completely soluble) and evaporated to remove traces of formaldehyde. Addition of sodium hydroxide liberated methylamine, identified by conversion into 2 : 4-dinitrophenylmethylamine, m. p. and mixed m. p. 175°.

Action of Hexamine Hydrochloride on Methylenebenzylamine.—Hexamine hydrochloride (9 g.), precipitated from a chloroform solution of hexamine by dry hydrogen chloride, was intimately mixed with methylenebenzylamine (9 g., prepared by addition of formaldehyde to an aqueous solution of benzylamine, the sticky oil, after repeated washing with water, being dried over concentrated sulphuric acid and crystallised from light petroleum; m. p. 45—46°) and heated under reduced pressure. Considerable charring with evolution of ammoniacal vapours ensued and a small quantity of oil, which on redistillation gave a colourless oil (2 g.), was obtained, b. p. 72°/30 mm. (Found: N, 15·2. $C_{18}H_{23}N_3$ requires N, 15·0%). Hydrolysed with hydrochloric acid, it gave benzaldehyde, methylamine, and formaldehyde.

Hexamine–Chlorobenzyl Chlorides.—*p*-, *o*-, and *m*-Chlorobenzyl chloride with hexamine (1 mol. of each) in hot chloroform gave the corresponding quaternary derivatives, white crystals, m. p. 198° (Found: Cl, 23·7. Calc. for $C_{13}H_{18}N_4Cl_2$: Cl, 23·6%), white solid, m. p. 204—205° (Found: Cl, 23·8%), and white crystals, m. p. 205° (Found: Cl, 23·7%), respectively.

p-*Chlorobenzylamine.*—Hexamine-*p*-chlorobenzyl chloride (50 g.) was dissolved in excess of hydrochloric acid, the solution steam-distilled until evolution of formaldehyde ceased, and the liquor evaporated to 150 c.c. On cooling, *p*-chlorobenzylamine hydrochloride crystallised; recrystallised from aqueous alcohol, it formed needles (22 g.), m. p. 250° (Found: N, 7·9. Calc. for C_7H_8NCl,HCl: N, 7·9%). The base was obtained from it as an oil (13 g.) b. p. 218—224°/775 mm. (Found: N, 9·9. Calc. for C_7H_8NCl: N, 9·9%).

m-Chlorobenzylamine hydrochloride (25 g.), obtained in a similar way from hexamine-*m*-chlorobenzyl chloride (50 g.), crystallised from alcohol in flakes, m. p. 225° (Found: N, 7·9%). The base was obtained as an oil, b. p. 226°/760 mm.

o-Chlorobenzylamine (15 g.) was prepared by decomposition of the corresponding quaternary derivative (35 g.). After evaporation of the residual liquor almost to dryness, the base was liberated by addition of sodium hydroxide, extracted in ether, and distilled; b. p. 220°/775 mm. (Found: N, 9·8%). 2 : 4-*Dinitrophenyl*-o-*chlorobenzylamine*, obtained from the base and 2 : 4-dinitrochlorobenzene in alcohol, formed yellow needles, m. p. 116—117°, from alcohol (Found: N, 13·6. $C_{13}H_{10}O_4N_3Cl$ requires N, 13·7%).

p-*Chlorobenzaldehyde.*—To *p*-chlorobenzylamine (10 g.) was added formaldehyde (5 c.c. of 40%), followed by sufficient hydrochloric acid (50 : 50) to dissolve the condensation product. The solution was made up to 100 c.c. and brought to the b. p., hexamine (5 g.) added, and the mixture refluxed (15 mins.). An excess of hydrochloric acid was now added, and the mixture boiled for 5 minutes and cooled. The oil, which solidified, was extracted with ether, from which it crystallised, m. p. 45°, yield 5 g. It was identified as *p*-chlorobenzaldehyde by conversion into the 2 : 4-dinitrophenylhydrazone, m. p. 265°.

o-*Chlorobenzaldehyde.*—To *o*-chlorobenzylamine (8 g.) formaldehyde (4 c.c. of 40%) was added. The emulsion formed was just cleared by addition of hydrochloric acid, and the solution diluted to 100 c.c. Addition of hexamine (5 g.), followed by refluxing (½ hr.), resulted in the separation of an oil, which was extracted with ether. From the extract, after washing with hydrochloric acid and drying over calcium chloride, *o*-chlorobenzaldehyde (3 g.) was obtained, b. p. 210—214°; it was identified by conversion into its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 207°.

m-*Chlorobenzaldehyde.*—By the method described in the preceding case, *m*-chlorobenzylamine (10 g.), formaldehyde (5 c.c. of 40%), and hexamine (10 g.) gave *m*-chlorobenzaldehyde (5 g.), b. p. 212—214°, identified by conversion into its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 245°.

Acetophenone from α-Phenylethylamine.—Formaldehyde (13 c.c. of 40%) and water (50 c.c.) were added to α-phenylethylamine (20 g.). The emulsion was shaken (15 mins.) to complete the reaction, just cleared by addition of dilute hydrochloric acid, and brought to its b. p. Hexamine (12 g.) was added, and the mixture refluxed (1 hr.). After cooling, the oil which had separated was extracted with ether, washed with dilute hydrochloric acid, dried over calcium chloride, and distilled, b. p. 202°. It was identified as acetophenone. Yield, 6 g.

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