210. *The Preparation of Benzylamines from Benzyl Halides and Hexamethylenetetramine.*

By John Graymore.

A new method for the preparation of cyclic methyleneimines and thence the corresponding primary amines is described, as is also a method for the preparation of benzylmethylamine. The work also shows that these methyleneimines may be converted into the corresponding aldehydes by heating with hydrochloric acid providing the methyleneimine be in excess.

Various investigators have described methods for the preparation of primary amines from hexamine–alkyl halides (Delépine, *Compt. rend.*, 1895, **120**, 501; *Bull. Soc. chim.*, 1897, **17**, 290;

Compt. rend., 1897, **124**, 292; Galat and Elion, *J. Amer. Chem. Soc.*, 1939, **61**, 3585). The present method depends on the preparation of a methyleneimine by decomposition of an aqueous solution of a quaternary compound such as hexamine–benzyl chloride in the presence of excess of ammonia, and subsequent hydrolysis of the cyclic methyleneimine by excess of hydrochloric acid :

$$6(\mathrm{CH_2})_6\mathrm{N_4},\mathrm{C_6H_5{\cdot}CH_2Cl} + 8\mathrm{NH_3} \longrightarrow 3(\mathrm{C_6H_5{\cdot}CH_2{\cdot}N{:}CH_2})_2 + 5(\mathrm{CH_2})_6\mathrm{N_4} + 6\mathrm{NH_4Cl}$$

$$3(\mathrm{C_6H_5{\cdot}CH_2{\cdot}N{:}CH_2})_2 + 6\mathrm{HCl} + 6\mathrm{H_2O} \longrightarrow 6\mathrm{C_6H_5{\cdot}CH_2{\cdot}NH_2,HCl} + 6\mathrm{CH_2O}$$

Hoch (D.R.-P. 139,394) showed that the oil obtained by adding excess of sodium hydroxide to hexamine–alkyl halides gave a cyclic methyleneimine when gently heated. The cyclic methyleneimine could not, however, be obtained directly by heating an aqueous solution of hexamine–alkyl halide with sodium hydroxide. Heated alone, an aqueous solution of the quaternary compound gives benzaldehyde (Sommelet, *Compt. rend.*, 1913, **157**, 852).

The ammonia serves the double purpose of ensuring the alkalinity of the solution, thus facilitating the polymerisation of the benzylmethyleneamine and so preventing its isomerisation to benzylidenemethylamine, and also combines with the liberated formaldehyde.

The hydrochlorides of benzylamine and of *p*-nitro-, *p*-chloro- and *m*-methyl-benzylamine were obtained. The molecular weight (Rast) of the solid methyleneimine, obtained either by the above method or by direct condensation of benzylamine with formaldehyde, indicated it to be a mixture of the dimeride and the trimeride of $\mathrm{CH_2{:}N{\cdot}CH_2Ph}$, although it is possible that at the high temperature of melting camphor depolymerisation occurs. Analysis of the addition product of the methyleneimine with methyl iodide also seemed to indicate that the methyleneimine is a mixture. Decomposition of the addition product by heating with water at 80° gave the hydriodide of benzylmethylamine, a benzylmethyleneimine, formaldehyde, and a small quantity of a substance apparently the *methiodide* of the trimeride :

$$2(\mathrm{C_6H_5{\cdot}CH_2{\cdot}N{:}CH_2})_2,\mathrm{CH_3I} + 2\mathrm{H_2O} \longrightarrow 2\mathrm{C_6H_5{\cdot}CH_2{\cdot}NH{\cdot}CH_3,HI} + (\mathrm{C_6H_5{\cdot}CH_2{\cdot}N{:}CH_2})_2 + \mathrm{CH_2O}$$

The aqueous solution yields benzylmethylamine hydriodide. The method is thus suitable for providing the secondary amine pure and in good yield. The breakdown of quaternary derivatives obtained from the cyclic methyleneimines to give secondary amines has been demonstrated previously (Graymore, *J.*, 1938, 1311) but the above decomposition differs in that the secondary amine is readily recoverable by virtue of the fact that the other products, save formaldehyde, are insoluble in cold water.

It has been shown (Graymore, *J.*, 1945, 293), following a suggestion of Sommelet (*loc. cit.*), that the condensation product of benzylamine with formaldehyde, dissolved in hydrochloric acid, gave benzaldehyde when heated with hexamine. A similar result has now been achieved by heating the condensation product with two-thirds of the quantity of hydrochloric acid as required by the equation $(\mathrm{C_6H_5{\cdot}CH_2{\cdot}N{:}CH_2})_2 + 2\mathrm{HCl} = 2\mathrm{C_6H_5{\cdot}CH_2{\cdot}N{:}CH_2,HCl}$, the excess of cyclic methyleneimine replacing the hexamine previously used.

EXPERIMENTAL.

Cyclic Benzylmethyleneimine.—Hexamine–benzyl chloride (90 g.) was dissolved in water (400 c.c.) containing an excess of ammonia (70 c.c.; *d* 0·88) and the solution heated under reflux (1½ hours). Formaldehyde (20 c.c.; 40%) was now added to remove excess of ammonia and to precipitate any free benzylamine as cyclic methyleneimine. The oily cyclic base was allowed to settle, the greater part of the supernatant liquor decanted, and the residue poured into a large quantity of cold water; solidification of the oil was hastened by vigorous stirring. The solid was then ground, and washed well with cold sodium hydroxide and finally with cold water. The crude product (35—36 g.), *bis*(*benzylmethyleneimine*), recrystallised from cold benzene or light petroleum, had m. p. 46° and was identified by comparison with sample prepared directly from benzylamine and formaldehyde [Found : *M* (Rast), 254. $(\mathrm{C_6H_5{\cdot}CH_2{\cdot}N{:}CH_2})_2$ requires *M*, 238]. From the decanted liquor, 50 g. of a mixture of hexamine and ammonium chloride were recovered.

Benzylamine hydrochloride. The cyclic imine (10 g., crude), dissolved in excess of concentrated hydrochloric acid, was steam-distilled to remove formaldehyde and traces of benzaldehyde, and evaporated to small bulk; benzylamine hydrochloride crystallised in large plates (11 g.), m. p. and mixed m. p. 248—249°

Benzaldehyde from the cyclic base. To the cyclic methyleneimine (10 g.) was added concentrated hydrochloric acid (6 c.c.) and the mixture was gently heated under reflux (1 hr.). The solution was now made strongly acid with dilute hydrochloric acid, refluxed for a minute, and the precipitated benzaldehyde removed by ether and identified; yield 4 c.c. (50%).

Bis-(p-*nitrobenzylmethyleneimine*).—Hexamine–*p*-nitrobenzyl bromide (60 g.) dissolved in water (300 c.c.) containing ammonia (60 c.c.; *d* 0·88), was heated under reflux until the semi-solid orange liquid which separated had formed a buff or buff-orange solid (1½ hrs.); this was cooled, removed (yield 23 g.), ground, and recrystallised from hot benzene, forming small needles, m. p. 158°. It dissolved in dilute hydrochloric acid and was reprecipitated as a buff powder. It was slightly soluble in alcohol but very soluble in ethyl acetate [Found : C, 58·5; H, 5·0; N, 16·8; *M* (Rast), 329. $(C_8H_8O_2N_2)_2$ requires C, 58·5; H, 4·9; N, 17·07%; *M*, 328].

(i) This *dimer* (14 g.) was dissolved in excess of hydrochloric acid (20 c.c., *d* 1·19, in 200 c.c. of water). Steam-distillation removed most of the formaldehyde, and the solution on concentration yielded *p*-nitrobenzylamine hydrochloride in yellow crystals (15 g., crude). Most of the yellow colour was extracted by washing with a small quantity of warm alcohol, and recrystallisation from water afforded needles decomposing at 256° (Found : Cl, 18·8. Calc. for $C_7H_8O_2N_2,HCl$: Cl, 18·8%).

(ii) To the cyclic methyleneimine (6 g.) was added hydrochloric acid (*d* 1·19; 2·6 c.c.) and the mixture was gently refluxed (¼ hr.). After addition of an excess of dilute hydrochloric acid with cooling, *p*-nitrobenzaldehyde separated (0·8 g.); a further quantity was obtained on dilution of the filtrate with water. Recrystallised from hot water, it was obtained as a pale yellow substance, m. p. 106°, identified by conversion into its 2 : 4-dinitrophenylhydrazone.

*Decomposition of Hexamine–*p*-Chlorobenzyl Chloride.*—The quaternary compound (30 g.), dissolved in water (100 c.c.) containing ammonia (*d* 0·88; 30 c.c.), was heated under reflux (1 hr.). After cooling, the supernatant liquor was decanted from the oily methyleneimine, the latter washed several times with water, extracted with ether, and dried over solid sodium hydroxide. After removal of the ether, the base p-*chlorobenzylmethyleneimine* was distilled under reduced pressure and obtained as a viscous oil, b. p. 220°/100 mm. (Found : C, 62·5; H, 5·21. C_8H_8NCl requires C, 62·6; H, 5·2%). The molecular weight was not determined.

(i) This imine (6 g.) was dissolved in excess of hydrochloric acid, steam-distilled to remove formaldehyde, and evaporated to small bulk, *p*-chlorobenzylamine hydrochloride crystallising out on cooling; recrystallised from alcohol, it melted at 250° (6 g.) (Found : N, 7·9. Calc. for C_7H_8NCl,HCl : N, 7·9%).

(ii) To the imine (6 g.) was added hydrochloric acid (*d* 1·19; 3 c.c.), and the mixture was heated gently under reflux (10 mins.). Excess of hydrochloric acid was now added, and boiling continued for 5 mins. On cooling, *p*-chlorobenzaldehyde separated as an oil which was extracted with ether. On removal of the ether it solidified (yield 2·5 g.). It was identified by oxidation to *p*-chlorobenzoic acid, m. p. and mixed m. p. 236°.

m-*Methylbenzylamine Hydrochloride.*—To hexamine–*m*-methylbenzyl bromide (25 g.), dissolved in water (100 c.c.), was added ammonia (*d* 0·88; 30 c.c.), and the solution heated under reflux (1 hr.). The syrupy oil which separated was removed, washed with cold water, dissolved in excess of hydrochloric acid, steam-distilled to remove formaldehyde, and the solution concentrated. *m*-Methylbenzylamine hydrochloride separated, and recrystallised from water in needles (7 g.) (Found : Cl, 22·5. Calc. for $C_8H_{12}NCl$: Cl, 22·5%).

cyclo*Hexylmethyleneimine.*—Addition of *cyclo*hexylamine (50 g.) slowly to formaldehyde (40 c.c., 40%) precipitated an oil which solidified. From alcohol it crystallised in long prisms, m. p. 75° [Found : C, 75·1; H, 11·7; N, 12·7; *M* (Rast), 144. $C_7H_{13}N$ requires C, 75·6; H, 11·7; N, 12·6%; *M*, 111. $C_6H_{11}N{:}CH_2$ requires *M*, 111].

Benzylmethyleneimine Methiodide.—To benzylmethyleneimine [1 mol. calculated as $(C_6H_5{\cdot}CH_2{\cdot}N{:}CH_2)_3$], recrystallised from light petroleum and dissolved in dry ether, was added methyl iodide (1½ mols.). After one day the precipitated *methiodide* was filtered off [Found : C, 59·1; H, 5·32; N, 8·1; I, 27·4. $(C_6H_5{\cdot}CH_2{\cdot}N{:}CH_2)_2,CH_3I$ requires C, 53·7; H, 5·5; N, 7·37; I, 33·4%. $(C_6H_5{\cdot}CH_2{\cdot}N{:}CH_2)_3,CH_3I$ requires C, 60·1; H, 6·0; N, 8·4; I, 25·5%].

Hydrolysis of Cyclic Benzylmethyleneimine Methiodide : Preparation of Benzylmethylamine Hydriodide.—The foregoing addition compound (18 g.) was suspended in water (250 c.c.) in an open vessel and heated at 70—80° for one hour. The methiodide slowly decomposed, a sticky oil was deposited, and formaldehyde was evolved. On cooling, the oil partly solidified and a small quantity of a white solid (A, see below) separated in needles (slightly soluble in hot water). The filtrate was evaporated on the water-bath to dryness, formaldehyde being evolved, and gave benzylmethylamine hydriodide in yellow needles (9 g., crude). Crystallised from hot alcohol (twice), it formed white needles, m. p. 164° (Emde, *Arch. Pharm.*, 1909, **247**, 364, gives m. p. 124°) (Found : C, 38·7; H, 4·8; N, 5·3; I, 51·2. Calc. for $C_8H_{12}NI$: C, 38·6; H, 4·8; N, 5·6; I, 51·0%). It was further identified by conversion into *p*-toluenesulphonbenzylmethylamide, m. p. 92—93° (Found : S, 11·4. Calc. for $C_{15}H_{17}O_2NS$: S, 11·6%). The residue (A, above) was ground, and extracted with ether. The ethereal solution yielded cyclic benzylmethyleneimine, m. p. 46° (4 g.) [Found : C, 80·6; H, 7·6; *M* (Rast), 242. Calc. for $(C_8H_9N)_2$: C, 80·6; H, 7·6%; *M*, 238]. The residue from the ethereal extract recrystallised from hot alcohol in needles, m. p. 160—161°, of the *methiodide* of tris(benzylmethyleneimine) (4 g.) (Found : I, 25·3; N, 8·17. $C_{25}H_{30}N_3I$ requires I, 25·5; N, 8·4%). Heated with water at 80°, it decomposed slowly to give benzylmethylamine hydriodide, formaldehyde, and cyclic benzylmethyleneimine. At higher temperatures under reflux a small quantity of benzaldehyde is formed.

Analysis and molecular-weight determinations were by Drs. Weiler and Strauss.

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