281. *ββ'-Diaminodiethylamine.*

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The object of the work was the preparation of ββ'-diaminodiethylamine (I) and the examination of its co-ordination compounds with metals (cf. Mann and Pope, *Proc. Roy. Soc.*, 1925, *A*, **107**, 80; **109**, 444; J., 1926, 482, 489; Mann, this vol., pp. 461, 466).

Ethylene chlorohydrin condensed with the sodium derivative of *p*-toluenesulphonamide to give *p*-toluenesulphon-β-hydroxyethylamide (II) as a syrup, which reacted with thionyl chloride and with hydrogen bromide to produce the β-*chloroethyl* compound (III) and the β-*bromoethyl* derivative respectively. With alcoholic ammonia in an autoclave, (III) formed a mixture of *p*-toluenesulphon-β-aminoethylamide (IV), ββ'-di-*p*-toluenesulphonamidodiethylamine (V), and a compound still under investigation. When heated with hydrochloric acid in a sealed tube, (V) gave ββ'-diaminodiethylamine trihydrochloride.

$$\begin{tikzcd}
\text{(VI.)} & C_7H_7{\cdot}SO_2{\cdot}N(CH_2Ph){\cdot}CH_2{\cdot}CH_2{\cdot}OH & C_7H_7{\cdot}SO_2{\cdot}NH{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2 & \text{(IV.)} \\
\text{(II.)} & C_7H_7{\cdot}SO_2{\cdot}NH{\cdot}CH_2{\cdot}CH_2{\cdot}OH \arrow[u] \arrow[d] \arrow[r] & C_7H_7{\cdot}SO_2{\cdot}NH{\cdot}CH_2{\cdot}CH_2Cl \arrow[u] \arrow[d] & \text{(III.)} \\
\text{(VII.)} & C_7H_7{\cdot}SO_2{\cdot}N(CH_2{\cdot}CH_2{\cdot}OH)_2 & NH(CH_2{\cdot}CH_2{\cdot}NH{\cdot}SO_2{\cdot}C_7H_7)_2 & \text{(V.)}
\end{tikzcd}$$

The dry sodium derivative of (II) reacted with benzyl chloride and with ethylene chlorohydrin to give the corresponding *benzyl* derivative (VI) and p-*toluenesulphondi*-β-*hydroxyethylamide* (VII) respectively. The compound (VII) was also obtained by the action of toluenesulphonyl chloride on " diethanolamine." From (VI) and similar substances, we propose to prepare unsymmetrical bases of the type $H_2N{\cdot}C_2H_4{\cdot}NH{\cdot}C_2H_4{\cdot}NHR$.

When (III) was treated with sodium ethoxide, ethyl sodiomalonate, or ethyl sodioacetoacetate, there was produced, in addition to the normal condensation product, 1 : 4-*di*-p-*toluenesulphonylpiperazine*. This substance was also obtained by the action of β-chloroethyl *p*-toluenesulphonate on the sodium derivative of *p*-toluenesulphonamide.

Of the unsuccessful methods which were tried for the production of ββ'-diaminodiethylamine, the following may be mentioned : (a) the condensation of potassiophthalimide with *aceto-* and *benzo-di*-β-*bromoethylamide*, (b) the reduction of αα'-dicyanodimethylamine (iminodiacetonitrile), (c) the action of ammonia on β-*phthalimidoethyl* p-*toluenesulphonate*. The benzoyl derivative of ββ'-dibromodiethylamine forms a hydrochloride and a hydrobromide which are fairly stable. ββ'-Diaminodiethylamine has previously been obtained by Hofmann (*Proc. Roy. Soc.*, 1862, **11**, 413; *Ber.*, 1890, **23**, 3711) and Fargher (J., 1920, **117**, 1353) by the action of ammonia on ethylene dihalides, and similar triamines have been prepared by Dudley, Rosenheim, and Starling (*Biochem. J.*, 1927, **21**, 95) and Foldi (*Ber.*, 1929, **62**, 1700).

Experimental.

p-*Toluenesulphon*-β-*hydroxyethylamide* (II).—*p*-Toluenesulphonamide (256 g.) was added to a solution of sodium (34·5 g.) in methyl alcohol (700 c.c.), the alcohol distilled off, and the sodio-compound distilled twice with dry benzene to remove water and alcohol. Unless this was done, the following reaction did not proceed well. Ethylene chlorohydrin (132 g.) was added to the product, and the mixture heated in an autoclave for 6 hours at 120°. The product was worked up, again treated with sodium (3·45 g.) and ethylene chlorohydrin (13·2 g.), extracted with hot ethyl alcohol, and obtained as a viscous syrup.

p-*Toluenesulphon*-β-*chloroethylamide* (III).—Into the substance (II) (225 g.), thionyl chloride (96 c.c.) was stirred at 15—20° during 2—3 hours. Stirring was continued (cooling in ice and water) for 4 hours, then (next day) the temperature was kept at 60—70° for 2 hours and finally at 100° for 1 hour, a considerable evolution of sulphur dioxide now taking place. The product set to a hard granular mass (220 g.) when poured into cold water, and crystallised from ethyl or methyl alcohol in stout prisms, m. p. 99° (Found : N, 6·0; Cl, 15·4. $C_9H_{12}O_2NClS$ requires N, 6·0; Cl, 15·2%). When heated with an alcoholic solution of sodium phenoxide, the substance (III) gave *p*-toluenesulphon-β-phenoxyethylamide, m. p. 104° alone or in admixture with an authentic specimen (Marckwald and Chain, D.R.-P. 122,047).

p-*Toluenesulphon-β-bromoethylamide,* prepared by treating the substance (II) (27 g.) with sodium bromide (16 g.), concentrated sulphuric acid (20 g.), and water (14 c.c.), and crystallised from methyl alcohol, had m. p. 88—90° [Found (micro) (Schoeller) : C, 40·2; H, 4·55; S, 12·4. $C_9H_{12}O_2NBrS$ requires C, 38·8; H, 4·3; S, 11·5%].

p-*Toluenesulphon-β-aminoethylamide* (IV) *and the Hydrochloride of ββ'-Di-*p-*toluenesulphonamidodiethylamine* (V).—The substance (III) (50 g.) was heated with 6*N*-alcoholic ammonia (400 c.c.) for 6 hours in an autoclave at 100—120°. The alcohol was distilled off, and the sticky product treated with warm water (40—50°) : this extracted the hydrochloride of (IV); the base (10—14 g.), liberated on neutralisation and crystallised from boiling water, had m. p. 124° (Found : C, 49·6; H, 6·4; N, 12·4. Calc. for $C_9H_{14}O_2N_2S$: C, 50·4; H, 6·5; N, 13·0%) (Moore, Boyle, and Thorn, J., 1929, 50, give m. p. 121°). The residue was repeatedly extracted with boiling dilute hydrochloric acid : on cooling, the solution deposited *p*-toluenesulphonamide and the sparingly soluble *hydrochloride* of (V) (6—7 g.), which crystallised from hot water or aqueous acetone in needles, m. p. 163° (Found : Cl, 7·6; N, 9·5. $C_{18}H_{25}O_4N_3S_2,HCl$ requires Cl, 7·9; N, 9·4%). The gummy residue (15—20 g.) on treatment with dilute aqueous ammonia, set to a hard mass, which crystallised from methyl alcohol or acetic acid in large rhombohedra, m. p. 104°, and is still under investigation.

*Tri-*p-*toluenesulphonyl-ββ'-diaminodiethylamine,* prepared from (V) and crystallised from glacial acetic acid, had m. p. 173° (Found : C, 53·2; H, 5·4; N, 7·45. $C_{25}H_{31}O_6N_3S_3$ requires C, 53·1; H, 5·5; N, 7·4%). *Benzodi-β-*p-*toluenesulphonamidoethylamide,* prepared by the action of benzoyl chloride on (V) and crystallised from boiling ethyl alcohol, had m. p. 167° (Found : N, 8·3. $C_{25}H_{29}O_5N_3S_2$ requires N, 8·15%). The *acid sulphate* of (V) crystallised readily from hot water containing a little sulphuric acid; m. p. 228° (Found : N, 8·6. $C_{18}H_{25}O_4N_3S_2,H_2SO_4$ requires N, 8·25%). The base (IV), acted upon by *p*-toluenesulphonyl chloride, gave *di-*p-*toluenesulphonylethylenediamine,* m. p. 155°, unchanged by admixture with the product obtained by the action of *p*-toluenesulphonyl chloride (2 mols.) on ethylenediamine (Found : N, 7·25. $C_{16}H_{20}O_4N_2S_2$ requires N, 7·6%). The *benzoyl* derivative of (IV), crystallised from ethyl alcohol–acetone, had m. p. 135° (Found : N, 8·6. $C_{16}H_{18}O_3N_2S$ requires N, 8·8%).

ββ'-Diaminodiethylamine Trihydrochloride.—The hydrochloride of (V) (5 g.) was heated for 6 hours with concentrated hydrochloric acid (35 c.c.) in a sealed tube at 160°. The trihydrochloride obtained (1·6 g.) had m. p. 215—220° (cf. Mann, *loc. cit.*, p. 465) and separated from alcohol in colourless plates on addition of hydrochloric acid and ether [Found: N (micro), 18·3. Calc. : N, 19·8%]. When solutions of the trihydrochloride and copper sulphate were mixed, and caustic soda added, a deep blue solution of the complex salt was formed. Ferric chloride, treated similarly, gave a precipitate of ferric hydroxide.

p-*Toluenesulphondi-β-hydroxyethylamide* (VII).—The substance (II) (213 g.) was converted into the dry monosodium derivative and heated with ethylene chlorohydrin (80 g.) for 5 hours in an autoclave at 110—120°. The product was extracted with alcohol, treated with sodium and with ethylene chlorohydrin (one-tenth of the previous quantities), and again extracted with alcohol. The viscous product slowly crystallised and was then drained on porous plate (yield, 44 g.) and recrystallised from aqueous acetone; m. p. 101° (Found : C, 51·2; H, 6·6; N, 5·3. $C_{11}H_{17}O_4NS$ requires C, 50·9; H, 6·6; N, 5·4%).

When the substance (VII) was treated with *p*-toluenesulphonyl chloride and caustic soda, it gave the *di-*p-*toluenesulphonate,* which formed crystals from ethyl alcohol, m. p. 65—67° (to a turbid liquid clearing at 75°) (Found : C, 52·8; H, 5·1. $C_{25}H_{29}O_8NS_3$ requires C, 52·9; H, 5·2%).

p-*Toluenesulphonbenzyl-β-hydroxyethylamide* (VI).—The substance (II) (21·5 g.) was converted into the dry sodium derivative and heated with benzyl chloride (12·7 g.) for 4 hours at 120—140°. The viscous product slowly crystallised from ethyl alcohol; m. p. 107° (Found : N, 4·4. $C_{16}H_{19}O_3NS$ requires N, 4·6%).

β-Phthalimidoethyl p-*Toluenesulphonate.*—Phthalo-β-hydroxyethylimide (Dersin, *Ber.*, 1921, **54**, 3158, gives the m. p. wrongly as 88—89°; the correct m. p. is 126·5—127·5°; Gabriel and Ohle, *Ber.*, 1888, **21**, 572) was heated for 6 hours at 100—120° with *p*-toluenesulphonyl chloride (1 mol.). The product, crystallised from acetone–ethyl alcohol, had m. p. 142° (Found : C, 58·8; H, 4·5. $C_{17}H_{15}O_5NS$ requires C, 59·1; H, 4·3%), and when heated with alcoholic ammonia gave phthalo-β-hydroxyethylimide, phthalimide, and *NN'*-diphthalylethylenediamine.

1 : 4-*Di-*p-*toluenesulphonylpiperazine.*—β-Chloroethyl *p*-toluenesulphonate (7·0 g.) (Clemo and Tenniswood, J., 1931, 2550) was heated with an aqueous solution of *p*-toluenesulphonamide

(5·1 g.) and caustic soda (1·2 g.) on a water-bath until the mixture was neutral (7 hours). Further quantities of the chloro-ester and caustic soda were added and the heating was repeated. No *p*-toluenesulphondi-β-chloroethylamide was formed, but only the piperazine *derivative*, which was crystallised from glacial acetic acid; m. p. 286° (Found: C, 54·7; H, 5·8; N, 7·6; S, 16·3. $C_{18}H_{22}O_4N_2S_2$ requires C, 54·8; H, 5·6; N, 7·1; S, 16·25%).

ββ'-*Dibromodiethylamine Hydrobromide*.—This was prepared from the ββ'-diphenoxy-compound by Gabriel and Eschenbach's method (*Ber.*, 1897, **30**, 810), but more conveniently as follows. "Diethanolamine" (16·8 g.) was heated with hydrobromic acid (80 c.c., saturated at 0°) for 5 hours in a sealed tube at 120—130°. The product, crystallised from ether–alcohol, yielded 20 g., m. p. 210°. Treatment of the base with an ethereal solution of *p*-toluenesulphonyl chloride as for the benzoyl derivative did not give the *p*-toluenesulphonyl derivative.

Acetodi-β-*bromoethylamide*.—The preceding hydrobromide (3·0 g.) was dissolved in water (1—2 c.c.) and benzene (20 c.c.) and caustic soda (2 c.c. of 33%) were added. The benzene layer was rapidly separated, filtered through a paper moistened with benzene, and mixed with acetic anhydride (5 c.c.). The mixture rapidly warmed and next day crystals had separated. These were removed, and more were obtained from the mother-liquor on concentration. The product was soluble in water and was recrystallised from ethyl acetate and from alcohol–ether; m. p. 107° (Found: N, 5·2. $C_6H_{11}ONBr_2$ requires N, 5·1%). It decomposed at 25—30° after some months.

Benzodi-β-*bromoethylamide*.—ββ'-Dibromodiethylamine hydrobromide (6·24 g.) was dissolved in water (10 c.c.) and solutions of benzoyl chloride (3·5 g.) in ether (80 c.c.) and caustic soda (25 c.c. of 2*N*) were slowly added with good shaking. The aqueous layer still gave a turbidity with caustic soda, and more benzoyl chloride and caustic soda were added until this reaction was no longer shown. Next day the ethereal layer was washed with dilute caustic soda solution, and hydrochloric acid (20 c.c. of 10%) added. A heavy oil separated which soon crystallised. Recrystallised from aqueous alcohol containing a little hydrochloric acid, the product had m. p. 165° (Found: N, 3·9. $C_{11}H_{13}ONBr_2,HCl$ requires N, 3·8%). From the *hydrochloride* the *hydrobromide* was prepared; it crystallised from ethyl alcohol, containing hydrogen bromide, in fine silky needles, m. p. 135° (Found: N, 3·4. $C_{11}H_{13}ONBr_2,HBr$ requires N, 3·4%).

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