3. *The Chemical Effects of γ-Radiation on Organic Systems. Part III.*[1] *The Action of Radiation on Triethylamine Alone or Mixed with Bromobenzene.*

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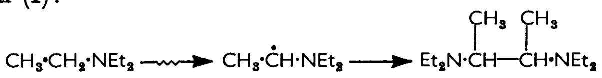
Two new bases, *meso*- and racemic 2 : 3-bisdiethylaminobutane (II), have been isolated from triethylamine which had been irradiated with γ-rays and have also been synthesised chemically. When the irradiation was carried out in the presence of bromobenzene, in addition to these two bases, diethylaniline, diphenyl, and triethylamine hydrobromide were obtained.

Previous work[1] has shown that the action of γ-radiation on alcohols $R{\cdot}CH_2{\cdot}OH$ results in the formation of radicals $R{\cdot}CH(OH){\cdot}$, *i.e.*, the hydroxyl group facilitates homolysis of the C–H bond in the system $\mathrm{H{-}\overset{|}{\underset{|}{C}}{-}O{-}}$. Following the well-known analogy between bivalent oxygen and tervalent nitrogen in organic compounds it has now been shown that a similar effect occurs in the system $\mathrm{H{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{N}{-}}$. Thus irradiation of triethylamine with γ-rays led to *meso*- and racemic-2 : 3-bisdiethylaminobutane (II), presumably formed through the radical (I):



$$CH_3{\cdot}CH_2{\cdot}NEt_2 \rightsquigarrow CH_3{\cdot}\dot{C}H{\cdot}NEt_2 \longrightarrow Et_2N{\cdot}\underset{}{\overset{CH_3}{\overset{|}{C}H}}{-}\overset{CH_3}{\overset{|}{C}H}{\cdot}NEt_2$$

(I) (II)

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[1] Part II, Swan and Wright, *J.*, 1958, 4673.

The *meso*- and the racemic form of this base were formed in approximately equal amounts (*G* value for the crude mixture 2·9) and were separated by partition chromatography with a phosphate buffer of pH 6·5 on kieselguhr as the stationary phase and ether as the mobile phase, in a manner experimentally similar to that used by Evans and Partridge[2] for the separation of a mixture of hyoscyamine and scopolamine. The *meso*-base passed rapidly through the column with the ether, the racemic base remaining on the column, from which it was later isolated by treatment with sodium hydroxide solution and ether. This difference could scarcely be due to the difference in basic strength between the two isomers and (in any case) the racemic appeared to be weaker than the *meso*-base. It is probably due to the fact that in the most stable conformation of the *meso*-form similar groups achieve maximum separation, so that the two basic groups are too far apart to form a chelate phosphate, while in the racemic form chelation can occur. This was confirmed by the fact that no separation occurs when the phosphate buffer is replaced by an acetate buffer of the same pH.

Neither form of 2 : 3-bisdiethylaminobutane appears to have been described previously, so we synthesised the two isomers by alkylation of 2 : 3-diaminobutane, obtained by reduction of dimethylglyoxime. We have here a synthesis of two new compounds by irradiation, a method which moreover involves less work than the chemical synthesis. It is possible that other tertiary amines $(R{\cdot}CH_2)_3N$ behave similarly. Indeed, from benzylamine we have obtained *meso*-stilbenediamine; we hope to report more fully on this aspect later.

We also irradiated a 1 : 10—25 molar mixture of triethylamine and bromobenzene. Triethylamine hydrobromide crystallised [*G*(HBr 6—6·4], and it was shown by a tracer experiment that more than 90% of the hydrogen of this hydrogen bromide arose from the triethylamine and not from the bromobenzene. From the non-basic portion of the residual irradiation mixture diphenyl was isolated with $G = 0{\cdot}65$, but probably much loss was involved.

The ultraviolet spectrum of the basic product of b. p. 100—130° (bath-temp.)/1 mm. resembled that of diethylaniline, although the extinction coefficient was much lower (3800 instead of 15,000 at 2600 Å). Chromatography of this fraction in a phosphate buffer of pH 6·5 afforded pure *meso*-2 : 3-bisdiethylaminobutane, and in a similar buffer of pH 5 afforded impure aniline ($G < 0{\cdot}1$), racemic 2 : 3-bisdiethylaminobutane, and a compound of acetophenone-like odour, which failed to give a 2 : 4-dinitrophenylhydrazone. A basic fraction of b. p. > 130°/12 mm. was not identified: we failed to isolate diethyl-1-phenylethylamine from it, though we synthesised this compound for a study of its chromatographic behaviour. We also irradiated a mixture of benzyl alcohol and triethylamine, but were unable to establish the formation of any coupling products of a radical $Et_2N{\cdot}CHMe{\cdot}$ with $Ph{\cdot}CH_2{\cdot}$ or $Ph{\cdot}CH(OH){\cdot}$: the basic product was mainly 2 : 3-bisdiethylaminobutane and the small amount of higher-boiling material failed to yield crystalline derivatives.

The formation of diethylaniline from triethylamine and bromobenzene involves fission of a C–N bond, but it is not clear whether this is due to direct radiolysis:

$$Et_2N{\cdot}Et \rightsquigarrow Et_2N{\cdot} + {\cdot}Et$$

or is the result of a secondary reaction (*e.g.*, oxidation) of the primarily formed radical $Et_2N{\cdot}CHMe{\cdot}$. However, a large peak at mass number 72 points to the ready fission of the C–N bond of triethylamine in the mass-spectrometer. Bamford[3] reported that photolysis of trimethylamine gave hydrogen, methane, ethane, and polymers, and Gesser, Mullhaupt and Griffiths[4] reported the formation of an unidentified "liquid" instead of polymer. The production of ethane suggests the formation of $Me_2N{\cdot}$ and $Me{\cdot}$ radicals, and the former might give rise to tetramethylhydrazine: Rice and Grelecki's[5] isolation

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[2] Evans and Partridge, *Quart. J. Pharm. Pharmacol.*, 1948, **12**, 399.

[3] Bamford, *J.*, 1939, 17.

[4] Gesser, Mullhaupt, and Griffiths, *J. Amer. Chem. Soc.*, 1957, **79**, 4834.

[5] Rice and Grelecki, *ibid.*, p. 2679.

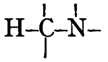
of the $Me_2N\cdot$ radical as a violet solid, stable at $-196°$, but giving tetramethylhydrazine at $-160°$ is relevant. The latter authors [6] also suggested the formation of the $Me\cdot NH\cdot CH_2\cdot$ radical from dimethylamine in the field of a high-frequency oscillator, where there was no evidence of the formation of tetramethylhydrazine. Thermal decomposition of trimethylamine yields mainly methane and methylmethyleneimine together with small amounts of hydrogen and ethane.[7]

Cosgrove and Waters [8] obtained acetaldehyde, glyoxal, and diethylamine by the action of *N*-bromosuccinimide on triethylamine, and Braude and Waight [9] isolated triethylamine hydrobromide and succinimide from the same reaction. We have repeated the reaction to ascertain whether 2 : 3-bisdiethylaminobutane was also formed; but we were unable to isolate it. More recent work by Dunstan and Henbest [10] has, however, indicated that the reaction with *N*-bromosuccinimide takes the course:

$$2Et_3N + Br\cdot N(CO\cdot CH_2)_2 \longrightarrow Et_2N\cdot CH{:}CH_2\cdot + Et_3N,HBr + NH(CO\cdot CH_2)_2$$

$$Et_2N\cdot CH{:}CH_2 + H_2O \longrightarrow Et_2NH + CH_3\cdot CHO$$

Buckley, Dunstan, and Henbest have also shown that triethylamine is dehydrogenated to diethylvinylamine by chloranil [11] or benzoyl peroxide,[12] the former case being consistent with hydride-ion transfer from the amine to the quinone, yielding $Et_2N\cdot CHMe^+$, followed by loss of proton, although single-electron transfer could not be excluded. Our observation that the radical $Et_2N\cdot CHMe\cdot$ appears to dimerise readily supports the hydride-ion transfer mechanism in the chemically induced case. On the other hand, Buckley *et al.*[11] found that, although 1-ethylpiperidine undergoes a similar reaction with chloranil, reaction of the *N*-methyl compound proceeds only in the presence of light, indicating that attack on the piperidine ring is more difficult than on the ethyl group and perhaps pointing to a homolytic mechanism.

A chemical reaction which resembles, at least superficially, the radiation-induced reaction of triethylamine described above is that between amines and olefins, induced by peroxide or, in low yield, by light [13] [*e.g.*, the formation of (±)-coniine by the interaction of piperidine and propene in the presence of *tert.*-butyl peroxide]. The photo-sensitised oxidation of amines recently studied by Schenk [14] is a further example of free-radical attack on the  $H-\overset{|}{\underset{|}{C}}-\overset{|}{N}-$ group.

EXPERIMENTAL

Arrangements for the irradiations and spectroscopic measurements were as described in Part I.

meso- *and Racemic* 2 : 3-*Bisdiethylaminobutane* (II).—2 : 3-Diaminobutane (7 g.), prepared by reduction of dimethylglyoxime,[15] was converted into the dihydrochloride, which was boiled with methanol (90 ml.) for a few minutes. The insoluble *meso*-dihydrochloride (5·5 g.) was collected and when crystallised from aqueous methanol had m. p. >290°. Concentration of the methanol mother-liquors afforded the crude racemic dihydrochloride, m. p. 255°.

A mixture of *meso*-2 : 3-diaminobutane dihydrochloride (2·3 g.), ethyl iodide (8·9 g., 4 mol.), sodium carbonate (9 g.), and water (70 ml.) was refluxed for 20 hr. The basic material was extracted with ether and then warmed for 2 hr. with acetic anhydride (6 ml.) in benzene (6 ml.). The excess of anhydride was decomposed by washing with sodium carbonate solution, and the benzene layer was dried and distilled, giving *meso*-2 : 3-bisdiethylaminobutane (0·77 g.), b. p.

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[6] Rice and Grelecki, *J. Phys. Chem.*, 1957, **61**, 824.

[7] Carter, Bosanquet, Silcocks, Travers, and Wilshire, *J.*, 1939, 495.

[8] Cosgrove and Waters, *J.*, 1949, 907.

[9] Braude and Waight, *J.*, 1952, 1116.

[10] Dunstan and Henbest, *J.*, 1957, 4905.

[11] Buckley, Dunstan, and Henbest, *J.*, 1957, 4880.

[12] *Idem, ibid.*, p. 4901.

[13] Urry, Juveland, and Stacey, *J. Amer. Chem. Soc.*, 1952, **74**, 6155.

[14] Schenk, *Angew. Chem.*, 1957, **69**, 579.

[15] Dickey, Fickett and Lucas, *J. Amer. Chem. Soc.*, 1952, **74**, 944; Strack and Schwaneberg, *Ber.*, 1934, **67**, 1006.

110° (bath-temp.)/15 mm., affording a *dihydrochloride*, m. p. 238° (from ethanol) (Found: C, 53·3; H, 11·45. $C_{12}H_{30}N_2Cl_2$ requires C, 52·8; H, 11·0%), and a *dipicrate*, m. p. 178° (Found: C, 44·05; H, 5·25. $C_{24}H_{34}O_{14}N_8$ requires C, 43·75; H, 5·15%).

The crude racemic dihydrochloride, when ethylated as above, gave a base, b. p. 100° (bath-temp.)/12 mm., yielding a picrate which was not homogeneous. A solution of this base (136 mg.) in ether was therefore passed through a column of kieselguhr (30 g.) and 0·5M-phosphate buffer of pH 6·5 (30 g.). The first 150 ml. of ether eluted 30 mg. of base which was discarded. The column was then treated with 20% sodium hydroxide solution; an ether extract of the eluate yielded racemic 2 : 3-bisdiethylaminobutane, affording a deliquescent *dihydrochloride*, m. p. 233° (Found: C, 52·7; H, 11·5%), and a *dipicrate*, m. p. 137° (from ethanol in which it is more soluble than is the *meso*-dipicrate) (Found: C, 43·7; H, 5·35%). As measured by the use of a glass electrode, a solution of the racemic dihydrochloride (14·8 mg.) in triply distilled water (10 ml.) had pH 2·9, whereas one of the *meso*-dihydrochloride (16·2 mg.) in water (10 ml.) had pH 4·1.

Irradiation of Triethylamine.—Pure triethylamine (275 ml.) was irradiated for 300 hr. (total dose $2 \cdot 08 \times 10^{23}$ ev) and unchanged material was then removed by distillation. The residue (2 g.) distilled at 90—125°/30 mm. and consisted mainly of *meso*- and racemic 2 : 3-bisdiethylaminobutane. Part of this mixture (407 mg.) was separated into its components by partition chromatography, as described above. The first 100 ml. of ether yielded the *meso*-diamine (130·5 mg.), which with picric acid gave a 92% yield of pure picrate, m. p. and mixed m. p. 179°. Treatment of the column with sodium hydroxide solution then liberated crude racemic diamine (152·4 mg.) which was isolated by ether. This was purified by partition chromatography at pH 8, the later fractions yielding the pure racemic picrate, m. p. and mixed m. p. 136°. The picrate from the earlier fractions, after recrystallisation from ethanol, yielded the same, pure picrate. Chromatography at pH 7·0 or 7·4 failed to affect sharp separation from the impurity.

Irradiation of a Mixture of Triethylamine and Bromobenzene.—(*a*) A mixture of triethylamine (25 ml.) and bromobenzene (250 ml.) was irradiated for 144 hr. (total dose $2 \cdot 37 \times 10^{23}$ ev). The precipitated triethylamine hydrobromide (4·3 g.) was collected and unchanged triethylamine was removed by distillation. The residue was extracted with 5N-hydrochloric acid. Basification of the extract followed by re-extraction with ether gave an oil (0·375 g.), b. p. 100—110° (bath-temp.)/15 mm., and a residue not distilling at 130°/10 mm. The bromobenzene was removed by distillation from the acid-washed irradiation product, and the residue was chromatographed on alumina, giving diphenyl, m. p. 69° (0·39 g.). (*b*) A similar experiment in which the same volume (275 ml.) of a 1 : 10 mol. mixture of triethylamine and bromobenzene was irradiated for 300 hr. (total dose $4 \cdot 04 \times 10^{23}$ ev) yielded triethylamine hydrobromide (7·8 g.) and basic fractions: (i) b. p. 100—130° (bath-temp.)/12 mm. (0·52 g.), and (ii) residue, a black tar (2·35 g.). Fraction (i) was subjected to partition chromatography, with a phosphate buffer of pH 6·5. The first three ether fractions contained 137, 86, and 32 mg., respectively, of base. The third of these portions yielded a hydrochloride, m. p. 238°, and a highly insoluble picrate, m. p. 178°, identical with *meso*-2 : 3-bisdiethylaminobutane picrate (Found: C, 44·05; H, 5·25%). These three fractions were recombined and subjected to partition chromatography in a phosphate buffer of pH 5. The ether which passed through yielded a base (150 mg.) which gave diethylaniline picrate, m. p. and mixed m. p. 137—138° (Found: C, 50·55; H, 4·5. Calc. for $C_{16}H_{18}O_7N_4$: C, 50·8; H, 4·75%); this base, however, on distillation yielded two fractions, b. p. 75° (bath-temp.)/12 mm. and (the greater part), b. p. 115° (bath-temp.)/12 mm., the extraction coefficient of which (10,900 at 2600 Å) indicated the presence of 70% of diethylaniline, *meso*-2 : 3-Bisdiethylaminobutane was isolated from the pH 5 column by treatment with sodium hydroxide solution and ether. The impure racemic isomer was similarly isolated from the pH 6·5 column and was purified by partition chromatography in a phosphate buffer of pH 8, the first few ether fractions giving gummy picrates, but the later fractions yielding a picrate, m. p. 137°, identical with racemic 2 : 3-bisdiethylaminobutane picrate.

Fraction (ii) was subjected to partition chromatography at pH 6·5. Approximately 1 g. passed through with ether, but only a small proportion of this distilled at 160°/1 mm. (Found: C, 70·85, 71·75; H, 9·25, 9·1%) and this showed no characteristic ultraviolet absorption, only a gradual rise in optical density from 2900 to 2200 Å. No further base was eluted by ether or chloroform, but treatment of the column with 20% sodium hydroxide solution released 0·7 g. of unidentified base.

Irradiation of a Mixture of Triethylamine and Bromodeuterobenzene.—Deuterobenzene [16] was brominated as described for the preparation of bromobenzene by Gattermann.[17] This bromodeuterobenzene (7·85 g.), the hydrogen of which contained 12·0% of deuterium, and triethylamine (5·05 g.) were irradiated for 70 hr. (total dose $3{\cdot}61 \times 10^{21}$ ev), and the resulting triethylamine hydrobromide (92·6 mg.; m. p. 242—243°) was collected. The hydrogen of the salt was enriched with respect to deuterium to the extent of 0·068%. The deuterium content of these compounds was determined by Mr. P. Kelly, M.Sc. by combustion [18] and reduction of the resulting water by Graff and Rittenberg's procedure,[19] before mass-spectrometic assay. The result quoted in the introductory part of the paper was calculated by neglecting any isotope effect and is therefore bound to be inaccurate as it is known that hydrogen atoms are abstracted more easily than deuterium atoms.[20]

*Diethyl-*1*-phenylethylamine.*—A mixture of 1-phenylethylamine (12·1 g.), ethyl iodide (31·2 g., 2 mol.), sodium carbonate (21·2 g.), and water (200 ml.) was refluxed for 20 hr., cooled, and extracted with ether. The ether was removed from the dried extract, and the residue was warmed with acetic anhydride (10 ml.) and benzene (10 ml.) for 2 hr., cooled, treated with water and sodium carbonate solution, and extracted with ether. Distillation of the dried extract yielded the base (5·5 g.), b. p. 94°/12 mm., affording a *picrate*, m. p. 131°, from ethanol (Found: C, 52·95; H, 5·5. $C_{18}H_{22}O_7N_4$ requires C, 53·2; H, 5·4%).

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