439. *Amines containing 2-Halogenoethyl Groups.*

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Studies have been made of compounds related to the known vesicant bases, methyldi-(2-chloroethyl)amine and tri-(2-chloroethyl)amine. The *substances* $NR(CH_2{\cdot}CH_2Cl)_2$ (R = Ac, $CH_2Cl{\cdot}CO$, CO_2Me, CN, Cl·CO, and $CH_2{\cdot}OMe$) have been made from di-(2-chloroethyl)amine, while attempts to introduce the *n*-butoxymethyl group into the base led to the isolation of NN'-*di*-(2-*chloroethyl*)*piperazine*. The synthetical work has been extended by the preparation of NNN'N'-*tetra*-(2-*chloroethyl*)*ethylenediamine*, *tri*-(2-*chloroethylthioethyl*)*amine hydrochloride*, and *tri*-(2-*bromoethyl*)*amine*. Fluorine analogues of the above bases which have been prepared include *di*-(2-*fluoroethyl*)*amine*, *methyldi*-(2-*fluoroethyl*)*amine*, *tri*-(2-*fluoroethyl*)*amine*, 2-*chloroethyldi*-(2-*fluoroethyl*)*amine*, and *di*-(2-*chloroethyl*)-2-*fluoroethylamine*. Several derivatives of these fluorine-containing bases have been made.

In the preparation of the substances described below, which are related to the vesicant bases, methyldi-(2-chloroethyl)amine and tri-(2-chloroethyl)amine, the formation of NN'-*di*-(2-*chloroethyl*)*piperazine* requires special comment. Stewart and Bradley (*J. Amer. Chem. Soc.*, 1932, **54**, 4172) have described the preparation of *n*-butoxymethyldiethylamine, $Et_2N{\cdot}CH_2{\cdot}OC_4H_9$, from diethylamine, *n*-butanol, and paraformaldehyde under anhydrous conditions. In attempts to prepare an analogous compound similarly from di-(2-chloroethyl)amine, the only substance isolated was NN'-*di*-(2-*chloroethyl*)*piperazine dihydrochloride*, from which the base was readily obtained. It is obvious that the dihydrochloride arose from the polymerisation of the di-(2-chloroethyl)amine used, but several attempts to obtain the salt under simpler conditions from the amine alone or in *n*-butanol gave less satisfactory results. Although the instability of di-(2-chloroethyl)amine has been noted (Prelog, Driza, and Hanousek, *Chem. Zentr.*, 1932, i, 1532; Mann, *J.*, 1934, 461), there appears to be no record of any investigation of the polymerisation process.

Experimental.

N-*Acetyl*-, N-*Chloroacetyl*-, *and* N-*Carbomethoxy*-*di*-(2-*chloroethyl*)*amine*.—A solution of di-(2-chloroethyl)amine hydrochloride (35·7 g., prepared either by the method of Mann, *loc. cit.*, or by that of Ward, *J. Amer. Chem. Soc.*, 1935, **57**, 914) in water (100 c.c.) was treated with sodium hydroxide (8 g.), also dissolved in water (50 c.c.), at 0°. Acetyl chloride (20 g.), diluted with chloroform (30 c.c.), and a solution of sodium hydroxide (10 g.) in water (100 c.c.) were added simultaneously with vigorous stirring during an hour, the temperature being kept between 0° and 5°. The chloroform layer and further chloroform extracts were united, dried (Na_2SO_4), and fractionated. N-*Acetyldi*-(2-*chloroethyl*)*amine* (22 g.) was collected as a colourless syrup, b. p. 130—135°/0·2 mm. (152—156°/16 mm.) (Found : C, 38·8; H, 6·1. $C_6H_{11}ONCl_2$ requires C, 39·1; H, 6·0%).

N-*Chloroacetyldi*-(2-*chloroethyl*)*amine* (Found : C, 33·0; H, 4·4. $C_6H_{10}ONCl_3$ requires C, 33·0; H, 4·6%), a colourless oil, b. p. 160—164°/0·2 mm., was similarly prepared from chloroacetyl chloride; and N-*carbomethoxydi*-(2-*chloroethyl*)*amine* (Found : C, 36·1; H, 5·5; Cl, 35·2. $C_6H_{11}O_2NCl_2$ requires C, 36·0; H, 5·5; Cl, 35·5%), a colourless oil, b. p. 86—90°/0·06 mm., from methyl chloroformate.

Di-(2-*chloroethyl*)*cyanamide*.—An ice-cold solution of di-(2-chloroethyl)amine hydrochloride (53·6 g.) in water (50 c.c.) was shaken with a cold solution of potassium hydroxide (17 g.) in water (30 c.c.), and the oily base was taken up in ether. The ethereal extract was dried ($MgSO_4$) and filtered, and the magnesium sulphate was washed with more ether. Cyanogen bromide (15·9 g.) in dry ether (30 c.c.) was gradually added, with shaking and cooling in ice-water, to the ethereal solution of the base. The reaction (compare Wallach, *Ber.*, 1899, **32**, 1872) was completed within a few minutes with the separation of di-(2-chloroethyl)amine hydrobromide. This was removed by filtration, the filtrate fractionated, and *di*-(2-*chloroethyl*)*cyanamide* collected at 135°/0·15 mm. (Found : C, 34·1; H, 4·8; N, 16·6; Cl, 39·1. $C_5H_8Cl_2N_2$ requires C, 35·9; H, 4·8; N, 16·8; Cl, 42·5%).

N-*Chloroformyldi*-(2-*chloroethyl*)*amine*.—A solution of di-(2-chloroethyl)amine in dry benzene (400 c.c.), obtained from the hydrochloride (21 g.) by a process similar to that used for the ethereal solution described above, was cooled in a freezing mixture, and added gradually during ½ hour with mechanical stirring to carbonyl chloride (7·3 g.) dissolved in benzene (100 c.c.), the temperature being kept below 10°. After the mixture had been left for several hours, the precipitate of di-(2-chloroethyl)amine hydrochloride was removed by filtration, and the benzene distilled off on the water-bath. When the residue was distilled under reduced pressure, N-*chloroformyldi*-(2-*chloroethyl*)*amine* was obtained as a pale yellow oil (6·8 g.), b. p. 92—96°/0·1 mm. (Found : C, 29·8; H, 4·2; Cl, 52·2. $C_5H_8ONCl_3$ requires C, 29·3; H, 3·9; Cl, 52·1%).

Methoxymethyldi-(2-*chloroethyl*)*amine*. A solution of di-(2-chloroethyl)amine in dry chloroform (60 c.c.) was made from the hydrochloride (17·9 g.) as above. Methoxymethyl chloride (8·4 g., prepared as described by Wedekind, *Ber.*, 1903, **36**, 1383) in chloroform (20 c.c.) was added during ½ hour to a mixture of the chloroform solution of the base and an excess of powdered, dry potassium carbonate which was rapidly stirred and cooled in ice-water. After stirring had been continued for a further 2 hours without cooling, the potassium chloride and potassium carbonate were removed by filtration, and the chloroform distilled off under reduced pressure. When the residue was distilled, a considerable amount of solid was formed in the flask, but *methoxymethyldi*-(2-*chloroethyl*)*amine* was collected as a colourless oil, b. p. 106—108°/13 mm. (Found : C, 39·2; H, 7·0; N, 7·7; Cl, 37·2. $C_6H_{13}ONCl_2$ requires

C, 38·7; H, 7·0; N, 7·5; Cl, 38·2%). The base was unstable, and gradually changed into a colourless solid.

NN′-*Di*-(2-*chloroethyl*)*piperazine*.—A mixture of di-(2-chloroethyl)amine (28 g., obtained from its dry ethereal solution by evaporation under reduced pressure), *n*-butanol (18·8 g.), and paraformaldehyde (6 g.) was slowly warmed to 35°. At this point the temperature of the reaction mixture rose to 39·5°, and the whole was left to cool overnight. After potassium carbonate (6 g.) had been added and the mixture left for a further 24 hours, the solid was removed by filtration, and the pale yellow, viscous filtrate was heated to 80° under reduced pressure to remove *n*-butanol. The residue soon solidified, and, after it had been ground with warm alcohol, NN′-*di*-(2-*chloroethyl*)*piperazine dihydrochloride* (4·5 g.), m. p. 315° (decomp.), remained in a pure condition. It separated from aqueous alcohol in colourless prisms (Found : Cl , 24·9, 25·1; total Cl, 50·7, 51·7. $C_8H_{16}N_2Cl_2,2HCl$ requires Cl′, 25·0; total Cl, 50·0%). When the dihydrochloride was dissolved in the minimum quantity of water at room temperature, and the solution filtered and treated with concentrated aqueous potassium carbonate, NN′-*di*-(2-*chloroethyl*)*piperazine* separated as an oil which rapidly solidified. It was dried in a desiccator, freed from a little inorganic material by dissolving in dry ether, and recovered by removing the ether from the filtered solution under reduced pressure. It then remained as a colourless solid, m. p. 41—43° (Found : C, 45·5; H, 7·4; Cl, 33·8; *M*, 207. $C_8H_{16}N_2Cl_2$ requires C, 45·5; H, 7·6; Cl, 33·6%; *M*, 211). It could not be distilled unchanged, even under reduced pressure, owing to further polymerisation with the formation of a high-melting solid which dissolved in water and contained chloride ion.

Methyldi-(2-*hydroxyethyl*)*amine*.—(*a*) After di-(2-hydroxyethyl)amine (105 g.) had been carefully neutralised with concentrated hydrochloric acid and the water removed under reduced pressure at 60—70°, paraformaldehyde (50 g.) was added and the mixture heated under reflux in an oil-bath (compare Eschweiler, *Ber.*, 1905, **38**, 880). Evolution of carbon dioxide began when the temperature of the bath reached 140° and continued steadily for 1—1½ hours at 160—165°. After 3 hours at this temperature, the product was cooled, neutralised with solid sodium hydroxide, and distilled. The fraction (92 g.) boiling at 125—135°/14 mm. was redistilled, and methyldi-(2-hydroxyethyl)amine (75 g.; 63% yield) collected at 130°/14 mm. as a colourless oil.

(*b*) Di-(2-hydroxyethyl)amine (52·5 g.) was neutralised with anhydrous formic acid (23 g.) and heated with paraformaldehyde (15 g.) (compare Hanby and Rydon, *J.*, 1947, 513). Evolution of carbon dioxide began at 50°, was torrential at 100—110°, and was practically complete after 10 minutes. At the end of ½ hour, methyldi-(2-hydroxyethyl)amine (55 g.; 92% yield) was isolated by distilling the mixture.

Methyliminodiacetic Acid.—When a mixture of iminodiacetic acid (13·3 g.), formic acid (4·6 g.), aqueous formaldehyde (10 c.c. of 36%), and water (5 c.c.) was heated on a steam-bath, gentle evolution of carbon dioxide ensued. After 2 hours, the whole was boiled under reflux for 10 minutes and then treated with alcohol. The precipitated methyliminodiacetic acid was crystallised from aqueous alcohol (charcoal) and obtained in colourless prisms (12·2 g.), m. p. 223—225° (decomp.) (Found : C, 40·6; H, 6·1. Calc. for $C_5H_9O_4N$: C, 40·8; H, 6·1%).

NNN′N′-*Tetra*-(2-*chloroethyl*)*ethylenediamine*.—The dihydrochloride of *NNN′N′*-tetra-(2-hydroxyethyl)ethylenediamine was obtained as a syrup, which slowly solidified, when the base, prepared by the method of Knorr and Brownsdon (*Ber.*, 1902, **35**, 4470), was dissolved in a slight excess of hydrochloric acid and the solution evaporated under reduced pressure. A suspension of the salt (50 g.) in chloroform (55 c.c.) was treated gradually with a solution of thionyl chloride (92 c.c.) in chloroform (100 c.c.) while the temperature was maintained at 55°, and the whole was then refluxed until the evolution of hydrogen chloride ceased. All volatile material was expelled under reduced pressure at 50°, the residue dissolved in dilute hydrochloric acid, and a small quantity of insoluble oil removed with ether. The basic product was recovered from the aqueous solution by the cautious addition of solid sodium carbonate and extracted with ether. After the extract had been dried ($MgSO_4$) and evaporated at 50° under reduced pressure, NNN′N′-*tetra*-(2-*chloroethyl*)*ethylenediamine* remained as a brown oil (Found : Cl, 43·4, 42·9. $C_{10}H_{20}N_2Cl_4$ requires Cl, 45·8%). It was not possible to distil this product, since on being heated to 130°/0·02 mm. the whole became solid as a result of quaternary salt formation. This was confirmed by the fact that the solid gave the test for chloride ion when dissolved in water. In fact, salt formation occurred so readily that the oily base became partly solid on being kept for a short time at room temperature.

Tri-(2-*chloroethylthioethyl*)*amine Hydrochloride* [$(CH_2Cl{\cdot}CH_2{\cdot}S{\cdot}CH_2{\cdot}CH_2)_3N,HCl$].—Tri-(2-chloroethyl)-amine hydrochloride (16·1 g.) and monothioethylene glycol (16 g.) in cold alcohol (180 c.c.) were added to a solution of sodium (6·1 g.) in alcohol (120 c.c.) containing potassium iodide (1 g.). On warming, sodium chloride was rapidly precipitated, and, after heating for ½ hour under reflux, the liquid was filtered and evaporated. The colourless, syrupy residue, a specimen of which decomposed on attempted distillation at 0·05 mm., was dissolved in concentrated hydrochloric acid (150 c.c.), and the solution heated for 2 hours on the steam-bath. The red oil which gradually separated was extracted with chloroform, and the extract dried (Na_2SO_4) and evaporated. The residual syrupy *tri*-(2-*chloroethylthioethyl*)*amine hydrochloride* (15 g.) could not be crystallised (Found: N, 3·2; Cl, 36·9; S, 22·6. $C_{12}H_{25}NCl_4S_3$ requires N, 3·3; Cl, 33·8; S, 22·8%).

2-*Chloro- and* 2-*Bromo*-2′-*phthalimidodiethyl Sulphide*.—Monothioethylene glycol (7·8 g.) and sodium iodide (1 g.) were dissolved in a solution of sodium (2·3 g.) in alcohol (50 c.c.), and the whole treated with phthalo-2-bromoethylimide (25·4 g.) in alcohol (75 c.c.). Sodium bromide was rapidly precipitated, and, after 10 minutes on a steam-bath, the solution was cooled, filtered, and evaporated. The syrupy hydroxy-compound was dissolved in chloroform (25 c.c.) and treated with thionyl chloride (15 g.). After 2 hours, the solution was evaporated under reduced pressure, and when the residue was crystallised from alcohol, 2-chloro-2′-phthalimidodiethyl sulphide (compare Gabriel, *Ber.*, 1891, **24**, 3098) was obtained in colourless needles, m. p. 75—76° (Found : C, 53·3; H, 4·3. Calc. for $C_{12}H_{12}O_2NClS$: C, 53·4; H, 4·5%).

When a solution of the above syrupy hydroxy-compound in hot hydrobromic acid (*d* 1·5) was kept for a few minutes at 100°, an oil separated, and this solidified on cooling. After it had been crystallised from methyl alcohol, 2-bromo-2′-phthalimidodiethyl sulphide (compare Gabriel, *loc. cit.*) was obtained in colourless plates, m. p. 87—88° (Found : C, 46·2; H, 3·9. Calc. for $C_{12}H_{12}O_2NBrS$: C, 45·9; H, 3·8%).

Tri-(2-*bromoethyl*)*amine.*—Tri-(2-hydroxyethyl)amine hydrobromide (46 g.), suspended in chloroform (50 c.c.), was treated with phosphorus pentabromide (130 g.), and the reaction completed by heating the mixture under reflux on a water-bath. When cold, the *tri-*(2-*bromoethyl*)*amine hydrobromide* (60 g.) was filtered off, washed with chloroform, and crystallised from aqueous acetone, from which it separated in colourless needles, m. p. 153—154° (Found : C, 16·5; H, 3·3. $C_6H_{13}NBr_4$ requires C, 17·2; H, 3·1%). The *base* was liberated as an oil, which rapidly solidified, when a solution of the hydrobromide in the minimum quantity of warm water was treated with the calculated quantity of solid sodium carbonate. When distilled, it was obtained as a colourless liquid, b. p. 145°/0·05 mm., which solidified, and then melted again at 30° (Found : N, 4·1. $C_6H_{12}NBr_3$ requires N, 4·1%).

Dimethyldi-(2-*chloroethyl*)*ammonium Chloride.*—After an excess of methyl iodide had been added to a solution of methyldi-(2-chloroethyl)amine in a small amount of benzene, and the whole left for a few hours, the solid methiodide was collected and washed with acetone. It was dissolved in water, and the solution shaken at room temperature for a short time with an excess of freshly precipitated silver chloride. When the solvent was removed from the filtered solution under reduced pressure, and the residue ground with acetone and crystallised from alcohol, *dimethyldi-*(2-*chloroethyl*)*ammonium chloride* was obtained in colourless prisms which turned brown and decomposed at 218° (Found : C, 35·2; H, 6·9; Cl, 52·0. $C_6H_{14}NCl_3$ requires C, 34·9; H, 6·8; Cl, 51·6%).

Di-(2-*fluoroethyl*)*amine.*—Dry ammonia was passed into a solution of 2-fluoroethyl bromide (100 g., prepared from 2-fluoroethanol and phosphorus tribromide under conditions communicated by Dr. H. McCombie and Dr. B. C. Saunders) in alcohol (400 c.c.) until the weight had increased by 21 g., and the whole was heated for 7 hours in an autoclave at 70°. When cold, it was found that a large amount of solid had separated. Concentrated hydrochloric acid was added until the mixture was acidic, and the alcohol was removed as completely as possible by heating on a water-bath under reduced pressure. After the residue had been made alkaline with a concentrated solution of sodium hydroxide, with cooling, the mixture was submitted to prolonged continuous extraction with ether. The extract was dried ($MgSO_4$), and the solvent removed through a fractionating column. When the residue was distilled from a flask fitted with a short column, *di-*(2-*fluoroethyl*)*amine* (10 g.) was collected as a colourless liquid in the form of a well-defined fraction, b. p. 123—126°/764 mm. (Found : N, 12·6; equiv., 111. $C_4H_9NF_2$ requires N, 12·8%; equiv., 109). The base, which is very soluble in water, showed no apparent change on being kept for several weeks.

In the fractionation of the above extract a small quantity of liquid was collected at 35—42° and when dry hydrogen chloride was passed into it, the hydrochloride of 2-fluoroethylamine (2 g.) was precipitated as a colourless, hygroscopic solid. After it had been recrystallised from alcohol, the salt (1·1 g.) was dissolved in water containing sodium hydroxide (1 g.), and the solution shaken for several hours with toluene-*p*-sulphonyl chloride (1·3 g.) dissolved in ether. When the aqueous layer was acidified with hydrochloric acid, *toluene-*p*-sulphon-*2*-fluoroethylamide* was precipitated. It was recrystallised from aqueous alcohol and obtained in colourless needles, m. p. 104° (Found : N, 7·0. $C_9H_{12}O_2NFS$ requires N, 6·5%).

N-*Phenyl-*N′N′-*di-*(2-*fluoroethyl*)*urea.*—Di-(2-fluoroethyl)amine (0·5 g.) was kept cold while phenyl *iso*cyanate (0·5 g.) was gradually added. When the product, which rapidly solidified, was crystallised from benzene–petroleum (b. p. 60—80°), N-*phenyl-*N′N′-*di-*(2-*fluoroethyl*)*urea* separated in colourless needles, m. p. 91° (Found : N, 12·4. $C_{11}H_{14}ON_2F_2$ requires N, 12·3%).

*Toluene-*p*-sulphondi-*(2-*fluoroethyl*)*amide.*—A solution of the secondary base (1 g.) in water (20 c.c.) containing sodium hydroxide (0·37 g.) was mechanically shaken for 8 hours with toluene-*p*-sulphonyl chloride (1·74 g.) in ether (18 c.c.). After the ethereal layer had been dried ($MgSO_4$) and evaporated and the residual solid crystallised from petroleum (b. p. 80—100°), *toluene-*p*-sulphondi-*(2-*fluoroethyl*)*amide* was obtained in colourless needles, m. p. 79° (Found : N, 4·8. $C_{11}H_{15}O_2NF_2S$ requires N, 5·3%).

2-*Fluoroethyl Toluene-*p*-sulphonate.*—A mixture of 2-fluoroethanol (150 g.) and toluene-*p*-sulphonyl chloride (180 g.) was refluxed for 10 hours, access of moisture being prevented by a calcium chloride tube. After the excess of 2-fluoroethanol (b. p. 103·5°) had been distilled off, the residue was dissolved in ether, and shaken first with water, then twice with dilute aqueous sodium carbonate, and finally again with water. The ethereal solution was dried ($MgSO_4$), the solvent removed, and the residue distilled under reduced pressure. 2-*Fluoroethyl toluene-*p*-sulphonate* (148 g.) was obtained as a colourless oil, b. p. 135—136°/1 mm. (Found : C, 49·7; H, 5·3; F, 8·9. $C_9H_{11}O_3FS$ requires C, 49·5; H, 5·0; F, 8·7%).

Methyldi-(2-*fluoroethyl*)*amine.*—Dry methylamine was passed into alcohol until the concentration, found by titration, was 62 g. per litre. A mixture of 2-fluoroethyl toluene-*p*-sulphonate (124 g.) and the alcoholic methylamine (275 c.c.) was heated in pressure bottles in a water-bath at 50—55° for 9 hours. The reaction mixture was treated as described for di-(2-fluoroethyl)amine, and *methyldi-*(2-*fluoroethyl*)*amine* (8·6 g.) was obtained as a colourless liquid, b. p. 123—124°/762 mm. (Found : C, 48·9; H, 9·3; N, 11·8; F, 30·3; equiv., 124. $C_5H_{11}NF_2$ requires C, 48·8; H, 8·9; N, 11·4; F, 30·9%; equiv., 123). The base is very soluble in water, and remained clear on being kept for several days.

Dimethyldi-(2-*fluoroethyl*)*ammonium Iodide.*—When the above tertiary base (1 g.) was stirred with methyl iodide (2·5 g.), a solid rapidly separated. After the excess of methyl iodide had been evaporated, the residue was crystallised from acetone, and *dimethyldi-*(2-*fluoroethyl*)*ammonium iodide* obtained in colourless prisms, m. p. 200° (decomp.) (Found : I, 47·8. $C_6H_{14}NF_2I$ requires I, 47·9%).

Tri-(2-*fluoroethyl*)*amine.*—After di-(2-fluoroethyl)amine (13·6 g.), 2-fluoroethyl bromide (16·0 g.), and alcohol (50 c.c.) had been heated together in a pressure bottle at 70° for 7 hours, the mixture was treated as described for di-(2-fluoroethyl)amine. A considerable quantity (6·7 g.) of unchanged secondary base was collected at 122—125°, and *tri-*(2-*fluoroethyl*)*amine* (2 g.) then distilled at 73—74°/25 mm. (Found : N, 9·2; F, 36·7; equiv., 156. $C_6H_{12}NF_3$ requires N, 9·0; F, 36·8%; equiv., 155). The tertiary base is a colourless liquid, and not very soluble in water.

2-*Chloroethyldi-*(2-*fluoroethyl*)*amine.*—Di-(2-fluoroethyl)amine (14 g.) was slowly added with mechanical stirring to a mixture of water (3·5 g.) and ethylene oxide (8·5 g.) cooled to 9° in an apparatus fitted with a reflux condenser which consisted of a coil surrounded by a mixture of ice and salt. After the mixture had been kept at 15—20° for 19 hours, the temperature was raised to 40° for 3 hours and then to 50°

for an hour. The whole was then cooled in a freezing mixture and acidified with concentrated hydrochloric acid. When the solution was evaporated to dryness on a steam-bath under a pressure of 40 mm., the hydrochloride of di-(2-fluoroethyl)-2-hydroxyethylamine remained as a pale yellow, viscous syrup. A solution of thionyl chloride (23 g.) in chloroform (70 c.c.) was gradually added to a mechanically stirred mixture of the above hydrochloride and chloroform (60 c.c.) at 60° in an apparatus fitted with a reflux condenser. After the whole had been kept at 60° for an hour, methyl alcohol (8 c.c.) was added, and all volatile material removed by warming at a pressure of 25 mm. The residual 2-chloroethyldi-(2-fluoroethyl)amine hydrochloride solidified, on cooling, to a deliquescent mass which was dissolved in water (20 c.c.). After the addition of chloroform, the whole was cooled below 0° and mechanically stirred while a solution of potassium hydroxide (7·5 g.) in water (50 c.c.) was gradually added. The chloroform solution was dried and the solvent removed through a short column under reduced pressure. When the residue was distilled, 2-*chloroethyldi*-(2-*fluoroethyl*)*amine* (9·4 g.) was collected as a colourless liquid, b. p. 95—97°/19 mm. (Found : N, 8·2; Cl, 20·8; F, 21·8. $C_6H_{12}NClF_2$ requires N, 8·2; Cl, 20·7; F, 22·2%). The base is not very soluble in water and is comparatively stable; only a trace of solid had separated after a fortnight.

When the base was treated with an equivalent amount of picric acid in dry benzene, the *picrate* quickly separated. It was recrystallised from alcohol and obtained in yellow needles, m. p. 121° (Found : C, 36·2; H, 3·8; Cl, 8·8. $C_{12}H_{15}O_7N_4ClF_2$ requires C, 36·0; H, 3·7; Cl, 8·9%).

Di-(2-*chloroethyl*)-2-*fluoroethylamine*.—A mixture of potassium phthalimide (160 g.) and 2-fluoroethyl bromide (180 g.) was heated at 180—190° for 8 hours in sealed tubes, and the product heated and stirred for an hour with water (800 c.c.) on a steam-bath. The mixture was cooled to the point at which the crude alkylphthalimide solidified, and rapidly filtered. After the solid had been ground with cold methyl alcohol (120 c.c.), it was further purified by dissolving it in chloroform (400 c.c.) at room temperature, filtering the solution from a small amount of insoluble material, and removing the solvent. When the residue was crystallised from alcohol, *phthalo*-2-*fluoroethylimide* (132 g.) was obtained in long, fawn-coloured needles, m. p. 100° (Found : C, 62·5; H, 4·2. $C_{10}H_8O_2NF$ requires C, 62·2; H, 4·1%). After a solution of this substance (63·6 g.) in alcohol (200 c.c.) had been treated with hydrazine hydrate (16·5 g.) and boiled under reflux for ½ hour, the whole was acidified with concentrated hydrochloric acid, and boiling was continued for an hour (compare Ing and Manske, *J.*, 1926, 2348). When cold, the mixture was filtered, the solid washed twice with water, and the combined filtrate and washings were evaporated to dryness under reduced pressure. A filtered solution of the residue in water (100 c.c.) was shaken for 2½ hours with salicyl aldehyde (40 c.c.) to remove hydrazine, and all insoluble material extracted with ether. When the aqueous liquid was again evaporated to dryness, 2-fluoroethylamine hydrochloride (23·8 g.) remained as a brown syrup which set to a deliquescent glassy solid (compare Traube and Peiser, *Ber.*, 1920, **53**, 1501). Its composition was confirmed by converting a little of it into toluene-*p*-sulphon-2-fluoroethylamide, identical with the substance described above. A solution of this hydrochloride (48 g.) in water (125 c.c.) was treated with aqueous potassium hydroxide (288 c.c. of 1·68N) and then gradually added with mechanical stirring to ethylene oxide (100 g.) at 9—11° under a reflux condenser which was surrounded by a mixture of ice and salt. After stirring had been continued for 3 hours at this temperature, the whole was left overnight. The isolation of the hydrochloride of the dihydroxy-compound and its conversion into *di*-(2-*chloroethyl*)-2-*fluoroethylamine* followed along lines similar to those described for 2-chloroethyldi-(2-fluoroethyl)amine. The product (12·7 g.) was collected as an almost colourless liquid, b. p. 115°/13 mm. (Found : C, 38·5; H, 6·5; Cl, 38·1. $C_6H_{12}NCl_2F$ requires C, 38·3; H, 6·4; Cl, 37·8%). The base is not very soluble in water and is comparatively stable. It remained clear for several days, but a specimen which was kept for 5 weeks deposited a small amount of white solid and a few drops of a dark brown, gummy material.

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