60. *Some Aliphatic Thiols and their Derivatives. Part I. Aliphatic Mercaptoamines.*

By John Harley-Mason.

In this paper the preparation and properties of four aliphatic 2-mercaptoamines are described. All were obtained from the corresponding chloroamines by reaction with thiourea and decomposition of the resulting *iso*thiouronium salts with alkali.

Although many aliphatic hydroxyamines are well known and are commercially available, little work has been recorded on the corresponding mercaptoamines. 2-Aminoethylthiol has long been known (Gabriel, *Ber.*, 1891, **24**, 1111; see also Mills and Bogert, *J. Amer. Chem. Soc.*, 1940, **62**, 1173), and 2-diethylaminoethylthiol has recently been prepared (Albertson and Clinton, *ibid.*, 1945, **67**, 1222), but other compounds of this type, and, in particular, amines containing two or more thiol groups, have not hitherto been described. In the present paper the preparation and properties of 2 : 2′-*dimercapto-diethylamine* (I) and -*triethylamine* (II), *methyl*-2 : 2′-*dimercaptodiethylamine* (III), and 2 : 2′ : 2″-*trimercaptotriethylamine* (IV) are described.

$NH(CH_2{\cdot}CH_2{\cdot}SH)_2$	$NEt(CH_2{\cdot}CH_2{\cdot}SH)_2$	$NMe(CH_2{\cdot}CH_2{\cdot}SH)_2$	$N(CH_2{\cdot}CH_2{\cdot}SH)_3$
(I.)	(II.)	(III.)	(IV.)

All of these were prepared from the corresponding hydroxy-compounds (ethanolamines) which were first converted into the chloroamines by means of thionyl chloride. The chloroamines or their hydrochlorides reacted with thiourea in boiling ethanol to give hydrochlorides of *iso*thiourea derivatives, which on basification and warming gave the required thiols and dicyanodiamide (cf. Arndt, *Ber.*, 1921, **54**, 2236; Hall and Reid, *J. Amer. Chem. Soc.*, 1943, **65**, 1466). Three of the four *iso*thiourea derivatives, *ethyl*- and *methyl-di*-(2-iso-*thioureido*-S-*ethyl*)*amine trihydrochloride* and *tri*-(2-iso*thioureido*-S-*ethyl*)*amine tetrahydrochloride*, were well crystalline, sparingly soluble in alcohol, and very soluble in water. The free bases corresponding to these salts were also exceedingly soluble in water and no attempt was made to isolate them. When the hydrochlorides of the *iso*thiourea derivatives were treated in aqueous solution with sodium hydroxide in slight excess over that required to neutralise the hydrochloric acid, and the whole heated on the water-bath, decomposition to give the mercaptoamines occurred rapidly. The mercaptoamines were extracted with benzene and subsequently distilled under reduced pressure.

2 : 2′-Dimercaptodiethylamine (I) was first obtained as a by-product in the preparation of (IV) : a lower boiling fraction was always obtained in the final distillation, and was identified as (I) by iodine titration and analysis of the free base and its hydrochloride. Evidently it arose from the presence of diethanolamine in the commercial grade of triethanolamine used for the preparation of trichlorotriethylamine. It was observed that the hydrochloride of this amine, obtained from commercial triethanolamine and thionyl chloride, was impure since it had m. p. 112—120°, whereas the pure hydrochloride has m. p. 130—131° (Ward, *J. Amer. Chem. Soc.*, 1935, **57**, 914). The impurity was clearly 2 : 2′-dichlorodiethylamine hydrochloride, which subsequently reacted with the thiourea giving diethylamine-2 : 2′-bis*iso*thiouronium trihydrochloride, which gave the dimercaptoamine on decomposition with alkali. However, all attempts to prepare a crystalline thiouronium salt from pure 2 : 2′-dichlorodiethylamine hydrochloride and thiourea in boiling alcohol were unsuccessful. It was found that the dithiol could be prepared, though in very poor yield, by boiling 2 : 2′-dichlorodiethylamine hydrochloride with

two mols. of thiourea in alcoholic solution, removing the solvent, and treating the residual syrup with aqueous alkali. A small quantity of the dithiol was obtaining by extracting the aqueous solution with benzene.

It seems probable that the anomalous behaviour of 2 : 2′-dichlorodiethylamine hydrochloride towards thiourea is due to its rapid decomposition in boiling alcoholic solution: similar anomalies were observed in its reaction with potassium thiocyanate under the same conditions (see below). It is interesting to note, however, that the yields of the dithiol obtained as described above, from crude 2 : 2′ : 2″-trichlorotriethylamine containing the dichloroamine, are fairly satisfactory, and it is possible that the decomposition of the secondary amine is inhibited by the presence of a larger amount of the tertiary amine.

The mercaptoamines were characterised as their *hydrochlorides* and by conversion into the corresponding benzoates which formed well-crystallised *hydrochlorides*. The latter were prepared by shaking the mercaptoamines with 10% aqueous alkali and benzoyl chloride, extracting the oily benzoyl derivatives with ether, and passing dry hydrogen chloride into the ethereal solution. The dithiol (I), which might have been expected to give a non-basic *NSS*′-tribenzoyl derivative, failed to give a crystalline product with benzoyl chloride and with *o*-nitrobenzoyl chloride.

All four mercaptoamines were colourless oils of very peculiar odour, miscible with ether and benzene, but only rather sparingly soluble in water. On exposure to air, rapid oxidation occurred, giving viscous gums, presumably chain-polymeric disulphides. The normal reactions of both thiols and amines were shown, the compounds being soluble in aqueous acids and strong alkalis. Well-defined salts were formed with mineral acids, and the thiol groups could be titrated quantitatively with iodine solution. Reaction occurred readily with acrylonitrile (cf. Albertson and Clinton, *loc. cit.*) and with dichloroarsines and arsine oxides of the types $RAsCl_2$ and RAsO, giving compounds which will be described in succeeding papers. Complexes were readily formed with a large number of metal ions, those formed with nickel being particularly noteworthy (see Part III, to be published).

Another possible method of obtaining the mercaptoamines was investigated: this consisted in reduction of the corresponding thiocyanates prepared from the chloroamines and potassium thiocyanate. Methyl-2 : 2′-dichlorodiethylamine, 2 : 2′-dichlorotriethylamine, and 2 : 2′ : 2″-trichlorotriethylamine all reacted readily with potassium thiocyanate in boiling alcohol to give oily thiocyanates, which formed well-crystallised hydrochlorides. *Methyl-*2 : 2′-*dithiocyanodiethylamine hydrochloride*, 2 : 2′-*dithiocyanotriethylamine hydrochloride*, and 2 : 2′ : 2″-*trithiocyanotriethylamine hydrochloride* all formed white prisms from alcohol–ether, readily soluble in water. On addition of alkali, the oily free bases were precipitated. Reduction of these compounds with zinc and dilute sulphuric acid apparently yielded a small amount of the corresponding mercaptoamines, but isolation was too difficult and the yield too poor for the method to be of any preparative value. 2 : 2′-Dithiocyanodiethylamine could not be obtained from 2 : 2′-dichlorodiethylamine or its hydrochloride by reaction with potassium thiocyanate; a complex mixture of products was formed and was not investigated further.

In the preparation of methyl-2 : 2′-dithiocyanodiethylamine hydrochloride, another compound was isolated in small yield. This was shown to be an ionic thiocyanate by its reaction with ferric chloride and analysis indicated that it was NN′-*dimethyldi*-2-*chloroethylpiperazinium dithiocyanate*. This was undoubtedly formed by dimerisation of the chloroamine, and the piperazinium structure was confirmed by the fact that acetylene was evolved when it was boiled with concentrated alcoholic potash.

EXPERIMENTAL.

Methyldi-(2-iso*thioureido*-S-*ethyl*)*amine Trihydrochloride*.—Methyl-2 : 2′-dichlorodiethylamine hydrochloride (Eisleb, *Ber.*, 1941, **74**, 1433, 96 g.) and thiourea (80 g.) in alcohol (400 c.c.) were refluxed for 3 hours. The resulting solution was cooled in ice; some of the product then separated in a sticky condition. Dry hydrogen chloride was passed in with stirring and cooling in ice. More of the product separated, and had become completely solid at 0° overnight. It was filtered off, washed with acetone, and dried. A portion was twice recrystallised from alcohol containing a little water. The *compound* had m. p. 200° (decomp.) (Found: C, 25·7; H, 6·0; N, 20·2. $C_7H_{20}N_5Cl_3S_2$ requires C, 25·4; H, 5·8; N, 20·3%). Yield of crude product, 140 g. (80%).

Methyl-2 : 2′-*dimercaptodiethylamine* (III).—To a solution of the above crude trihydrochloride (103 g.) in water (200 c.c.), 20% sodium hydroxide solution (180 c.c.) was added. The solution was rapidly heated to 95° and then cooled. The dithiol, some of which had separated as an oil, was extracted with benzene (3 × 100 c.c.). The benzene solution was dried (Na_2SO_4), the solvent removed, and the residue distilled under reduced pressure. The *dithiol* (27·5 g.; 61%) was obtained as a clear colourless liquid, b. p. 105—107°/11 mm. (Found: C, 40·0; H, 8·8; N, 8·9. $C_5H_{13}NS_2$ requires C, 39·7; H, 8·6; N, 9·3%). Titration with 0·1N-iodine indicated a purity of 97%. The *hydrochloride*, white needles, very hygroscopic, prepared in ether and recrystallised from alcohol-ether, had m. p. 104° (Found: C, 31·6; H, 7·8. $C_5H_{14}NClS_2$ requires C, 32·0; H, 7·5%).

A small portion of the dithiol was shaken with 10% aqueous sodium hydroxide and benzoyl chloride, and the oily product was dissolved in benzene. Dry hydrogen chloride was passed into the benzene solution; the *dibenzoate hydrochloride* was then precipitated as needles, m. p. 135° (from alcohol–ether) (Found: C, 55·5; H, 5·6. $C_{19}H_{22}O_2N_2ClS_2$ requires C, 55·9; H, 5·4%).

Ethyldi-(2-iso*thioureido-*S-*ethyl)amine.*—2 : 2′-Dichlorotriethylamine (Ward, *loc. cit.*) (170 g.) and thiourea (152 g.) in alcohol (600 c.c.) were refluxed for 3 hours. After cooling, dry hydrogen chloride was passed into the mixture with stirring and cooling in ice. The *trihydrochloride* (335 g.) which had separated was filtered off and washed with acetone. A portion, recrystallised from alcohol containing a little water, formed white needles, m. p. 238—239° (decomp.) (Found, after drying at 100°: C, 26·6; H, 6·4; N, 19·8. $C_8H_{22}N_5Cl_3S_2$ requires C, 26·8; H, 6·2; N, 19·5%).

2 : 2′-*Dimercaptotriethylamine* (II).—To a solution of the trihydrochloride (300 g.) in water (400 c.c.), 20% sodium hydroxide solution (500 c.c.) was added. After being heated to 95° for a few minutes the solution was cooled, and the mercapto-amine, some of which had separated as an oil, was extracted with benzene (3 × 250 c.c.). The extract was dried (Na_2SO_4), the solvent removed, and the residue distilled under reduced pressure. The *dithiol* (75 g.; 55%) was obtained as a colourless liquid, b. p. 108—109°/4 mm. (Found: C, 36·5; H, 7·5; N, 7·3. $C_6H_{15}NS_2$ requires C, 36·5; H, 7·5; N, 7·1%). The *hydrochloride* formed hygroscopic white needles from alcohol–ether, m. p. 97—99° (Found: C, 36·1; H, 8·1. $C_6H_{16}NClS_2$ requires C, 35·7; H, 7·9%). The *dibenzoate hydrochloride*, prepared as for that of (III), formed needles from alcohol, m. p. 159° (Found: C, 58·7; H, 6·2. $C_{20}H_{24}O_2N_2ClS_2$ requires C, 58·8; H, 5·9%).

Tri-(2-iso*thioureido-*S-*ethyl)amine Tetrahydrochloride.*—Pure 2 : 2′ : 2″-trichlorotriethylamine hydrochloride (Ward, *loc. cit.*) (m. p. 130°; 120 g.) and thiourea (115 g.) were refluxed in alcohol (400 c.c.) for 2 hours. On cooling, the *product* crystallised (203 g.; m. p. 216°). A small fraction was recrystallised from alcohol containing a little water and formed prisms, m. p. 219° (decomp.) (Found: Cl, 30·5; N, 20·3. $C_9H_{25}N_7Cl_4S_3$ requires Cl, 30·3; N, 20·9%).

2 : 2′ : 2″-*Trimercaptotriethylamine* (IV).—To a solution of the tetrahydrochloride above (156 g.) in water (200 c.c.), 20% sodium hydroxide solution (275 c.c.) was added. The solution was rapidly heated just to boiling; most of the trithiol then separated as an oil. After rapid cooling, the mixture was extracted with benzene (3 × 100 c.c.), the benzene solution was separated and dried (Na_2SO_4), and the solvent was removed. The residual oil was distilled under reduced pressure. The *trithiol* (30 g.; 45%) was obtained as a viscous oil, b. p. 145—147°/7 mm. (Found: C, 36·2; H, 8·0; N, 7·3. $C_6H_{15}NS_3$ requires C, 36·5; H, 7·5; N, 7·1%). The *hydrochloride*, prepared in ether and recrystallised from alcohol–ether, formed very hygroscopic white needles, m. p. 82—83° (Found: C, 30·9; H, 7·4. $C_6H_{16}NClS_3$ requires C, 30·8; H, 6·9%). The *tribenzoate hydrochloride*, prepared as for (III), formed needles from alcohol, m. p. 131° (Found: C, 59·9; H, 5·4. $C_{27}H_{28}O_3NClS_3$ requires C, 59·4; H, 5·2%).

2 : 2′-*Dimercaptodiethylamine* (I).—The crude product obtained from thionyl chloride and commercial triethanolamine (m. p. 112—120°; 120 g.) and thiourea (115 g.) were refluxed in alcohol (400 c.c.) for 2 hours. The solvent was distilled off, and the semi-solid residue dissolved in water (200 c.c.). 20% Sodium hydroxide solution (270 c.c.) was then added and the mixture heated to boiling. After rapid cooling, the mixture was extracted with benzene (5 × 100 c.c.), the benzene solution separated, dried (Na_2SO_4), and the solvent removed. The residual oil was distilled under reduced pressure and the main fraction (42 g.; b.p. 100—150°/7 mm.) was collected and then redistilled using a 12 cm. column. Two fractions were obtained: the *dithiol*, b. p. 100—105°/7 mm. (12 g.) (Found: C, 35·1; H, 8·0; N, 10·2. $C_4H_{11}NS_2$ requires C, 35·0; H, 8·0; N, 10·2%), and the trithiol (IV), b. p. 144—147°/7 mm. (24 g.). The *hydrochloride* of the dithiol formed hygroscopic white plates, m. p. 161° (from alcohol–ether) (Found: C, 27·9; H, 7·2. $C_4H_{12}NClS_2$ requires C, 27·6; H, 6·9%).

*Methyl-*2 : 2′-*dithiocyanodiethylamine Hydrochloride.*—Methyl-2 : 2′-dichlorodiethylamine (5·2 g.) was added to a solution of potassium thiocyanate (7 g.) in water (100 c.c.) and alcohol (50 c.c.). The mixture was boiled for 0·5 hour, water added, and the alcohol distilled off; the product then separated as an oil, which was dissolved in benzene. The benzene solution was dried, and dry hydrogen chloride passed in. The *hydrochloride* which separated was recrystallised from alcohol–ether; m. p. 121—122° (Found: N, 17·4. $C_7H_{12}N_3ClS_2$ requires N, 17·7%). Partial evaporation of the mother liquor after benzene extraction gave a compound which separated in small plates, m. p. 192° (decomp.). This gave a red colour with ferric chloride solution, indicating it to be an ionic thiocyanate, and, on boiling with 20% alcoholic potash, acetylene was evolved, indicating that the substance was probably a piperazinium diquaternary salt, *i.e.*, NN′-*dimethyldi-*2-*chloroethylpiperazinium dithiocyanate* (Found: N, 15·3; Cl, 20·0. $C_{12}H_{22}N_4Cl_2S_2$ requires N, 15·7; Cl, 19·8%).

2 : 2-*Dithiocyanotriethylamine Hydrochloride.*—Prepared exactly as above, from 2 : 2′-dichlorotriethylamine (5·5 g.) and potassium thiocyanate (7 g.), this *salt* formed white needles (from alcohol), m. p. 113—114° (Found: N, 16·8. $C_8H_{14}N_3ClS_2$ requires N, 16·7%).

2 : 2′ : 2″-*Trithiocyanotriethylamine Hydrochloride.*—Prepared exactly as above, from 2 : 2′ : 2″-trichlorotriethylamine (4 g.) and potassium thiocyanate (6 g.), this *salt* formed white needles (from alcohol), m. p. 153—155° (Found: N, 17·8. $C_9H_{13}N_4ClS_2$ requires N, 18·1%).

The greater part of this work was done in No. 2 Anti-Gas Laboratory, R.E., during 1944, and it was completed at the Chemical Defence Experimental Station, Porton, Wilts.

We are indebted to the Director General of Scientific Research (Defence), Ministry of Supply, and to the War Office, for permission to publish these results, and to Mr. J. H. R. Slade for much experimental assistance.

Micro-analyses were performed by Mr. G. Ingram.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE.

[*Received, June 29th,* 1946.]