440. *Some Sulphides containing the 2-Chloroethyl Group.*

By L. J. Goldsworthy, G. F. Harding, W. L. Norris, S. G. P. Plant, and B. Selton.

The preparation of several compounds belonging to the types R·S·CH_2·CH_2Cl, R·O·CH_2·CH_2·S·CH_2·CH_2Cl, and R·S·CH_2·CH_2·S·CH_2·CH_2Cl has been investigated on account of the possible interest attaching to these substances as vesicants. Some of the sulphides have been converted into sulphones and sulphilimines.

As part of an investigation designed to compare the vesicant properties of a series of compounds containing the S·CH_2·CH_2Cl group, several sulphides of this type not hitherto recorded have been prepared.

The reactions used by Demuth and Meyer (*Annalen*, 1887, **240**, 305) to obtain 2-chlorodiethyl sulphide, and represented by the scheme Et·SH $\longrightarrow$ Et·S·CH_2·CH_2·OH $\longrightarrow$ Et·S·CH_2·CH_2Cl, can be employed for other 2-chloroethyl alkyl sulphides (see, *e.g.*, Dawson, *J. Amer. Chem. Soc.*, 1933, **55**, 2070), and have now been applied to the preparation of *2-chloroethyl* n-*heptyl*, n-*nonyl*, and n-*undecyl sulphides.*

Four 2-alkoxyethylthiols, $R{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}SH$ (R = Me, Et, *n*-Pr, and *n*-Bu), have been obtained from the appropriate 2-alkoxyethyl halides, and converted by a similar series of reactions into *2-chloro-2′-methoxydiethyl sulphide*, $Me{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}S{\cdot}CH_2{\cdot}CH_2Cl$, and the analogous ethoxy-, n-*propoxy-*, and n-*butoxy*-compounds. The corresponding 2-alkylthioethylthiols, $R{\cdot}S{\cdot}CH_2{\cdot}CH_2{\cdot}SH$ (R = Me, Et, *n*-Pr, and *n*-Bu), obtained from the 2-chloroethyl alkyl sulphides, were transformed by similar stages into 2-chloro-2′-methylthiodiethyl sulphide, $Me{\cdot}S{\cdot}CH_2{\cdot}CH_2{\cdot}S{\cdot}CH_2{\cdot}CH_2Cl$, and its ethyl, n-*propyl*, and n-*butyl* analogues.

2-Chlorodiethyl sulphone, *2-chloro-2′-*n-*propoxydiethyl sulphone*, and *2-chloro-2′-*n-*butylsulphonyldiethyl sulphone*, $C_4H_9{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2Cl$, have been prepared from the sulphides, the conversion of some of which into sulphilimines has been studied. In this connexion, while methyl 2-chloroethyl sulphide, 2-chloroethyl allyl sulphide, 2-chloro-2′-methoxydiethyl sulphide, and 2-chloro-2′-*n*-propoxydiethyl sulphide readily gave crystalline *sulphilimines* on shaking with an aqueous solution of chloramine-T, homogeneous products were not obtained from 2-chloroethyl *n*-undecyl sulphide, 2-chloro-2′-ethoxydiethyl sulphide, the corresponding *n*-butoxy-compound, and 2-chloro-2′-*n*-propylthiodiethyl sulphide, and pure substances were not obtained on recrystallisation, except from the last-named which yielded toluene-*p*-sulphonamide. The remarkable difference in the ease with which this reaction ensues with these closely related sulphides is not without parallel, for although 2 : 2′-dichlorodiethyl sulphide readily gives a sulphilimine (Mann and Pope, *J.*, 1922, **121**, 1052), yet Davies and Oxford (*J.*, 1931, 224) obtained toluene-*p*-sulphonamide as the only pure product from 1 : 2′-dichlorodiethyl sulphide and chloramine-T.

EXPERIMENTAL.

2-Chloroethyl Alkyl Sulphides.—After *n*-heptylthiol (44 g.) had been dissolved in a solution of sodium (7·7 g.) in alcohol (130 c.c.), ethylene chlorohydrin (27 g.) was gradually added with shaking and cooling. The mixture was then heated for ½ hour on a steam-bath, and, when cold, the precipitate of sodium chloride was removed by filtration and washed with a little alcohol. The solvent was removed from the united alcoholic solutions by distillation and the residual oil was decanted from a further small quantity of sodium chloride. It was then distilled under reduced pressure, and 2-hydroxyethyl *n*-heptyl sulphide was collected at 153—154°/33 mm. in good yield. Thionyl chloride (26·5 g.) in chloroform (60 c.c.) was gradually added with shaking to the hydroxy-compound (35 g.) in chloroform (30 c.c.), the temperature being maintained at about 40° until the evolution of gas had slackened. The mixture was then kept at 60° to effect completion of the reaction, and the solvent and excess of thionyl chloride were removed by distillation from a steam-bath. When the residual oil was fractionated, *2-chloroethyl* n-*heptyl sulphide* was obtained as a colourless oil, b. p. 139—140°/25 mm. (Found : Cl, 17·8; S, 16·4. $C_9H_{19}ClS$ requires Cl, 18·3; S, 16·5%).

The following were similarly prepared : *2-chloroethyl* n-*nonyl sulphide*, colourless oil, b. p. 164—166°/20 mm. (Found : Cl, 15·4. $C_{11}H_{23}ClS$ requires Cl, 15·9%), *via* 2-hydroxyethyl *n*-nonyl sulphide, b. p. 174—176°/20 mm.; *2-hydroxyethyl* n-*undecyl sulphide*, m. p. 26—27°, b. p. 185—186°/15 mm. (Found : C, 66·9; H, 12·1. $C_{13}H_{28}OS$ requires C, 67·2; H, 12·1%); *2-chloroethyl* n-*undecyl sulphide*, colourless oil, b. p. 175—179°/14 mm. (Found : C, 62·4; H, 10·9; Cl, 14·3. $C_{13}H_{27}ClS$ requires C, 62·3; H, 10·8; Cl, 14·2%); 2-chlorodiethyl sulphide, b. p. 154—155° (compare Demuth and Meyer, *loc. cit.*); 2-chloroethyl *n*-propyl sulphide, b. p. 74—75°/22 mm. (compare Dawson, *loc. cit.*); 2-chloroethyl *n*-butyl sulphide, b. p. 89°/20 mm. (compare Whitner and Reid, *J. Amer. Chem. Soc.*, 1921, **43**, 636; Dawson, *loc. cit.*); 2-chloroethyl benzyl sulphide, b. p. 137—138°/12 mm. (Found : Cl, 19·1. Calc. for $C_9H_{11}ClS$: Cl, 19·0%) (compare Dawson, *loc. cit.*).

2-Chloro-2′-alkoxydiethyl Sulphides.—The 2-alkoxyethanols, $R{\cdot}O{\cdot}CH_2{\cdot}CH_2OH$ (R = Me, *n*-Pr, and *n*-Bu), were prepared by the methods of Cretcher and Pittenger (*J. Amer. Chem. Soc.*, 1924, **46**, 1503) and converted into the corresponding bromides as described by Palomaa and Kenetti (*Ber.*, 1931, **64**, 797), and 2-ethoxyethyl chloride was made from ethylene chlorohydrin by the method of Swallen and Boord (*J. Amer. Chem. Soc.*, 1930, **52**, 651).

2-Methoxyethyl bromide (99 g.) was added to a solution of potassium hydrogen sulphide made by saturating potassium hydroxide (80 g.) in methyl alcohol (300 c.c.) with hydrogen sulphide. After the mixture had been quickly shaken, it was placed in a pressure bottle and left overnight. The thiol, b. p. 109—110°, was isolated by diluting the mixture with water, extracting with light petroleum, and fractionating the dried extract. The yield (9 g.; 14%) was poor, and since there was only a small quantity of the corresponding sulphide in the form of higher-boiling material, it seems probable that a considerable amount of the original bromide was transformed into methyl vinyl ether. The theoretical quantity of ethylene chlorohydrin was added to a solution of the thiol in alcohol containing slightly more than one molecular proportion of sodium ethoxide. After the whole had been refluxed for an hour, it was cooled, and the sodium chloride removed by filtration. When the alcohol was removed from the filtrate and the residue fractionated, 2-hydroxy-2′-methoxydiethyl sulphide was obtained as a colourless oil, b. p. 112°/15 mm. (Found : C, 43·4; H, 8·4. Calc. for $C_5H_{12}O_2S$: C, 44·1; H, 8·8%). This compound has been isolated by Kretov (*J. Russ. Phys. Chem. Soc.*, 1929, **61**, 2345) from the products of the action of zinc on 2 : 2′-dichlorodiethyl sulphide in the presence of methyl alcohol. The process used to replace hydroxyl by chlorine in the substance was similar to that described above for the preparation of 2-chloroethyl *n*-heptyl sulphide, and *2-chloro-2′-methoxydiethyl sulphide* was obtained as a colourless oil, b. p. 88°/12 mm. (Found : Cl, 23·0. $C_5H_{11}OClS$ requires Cl, 23·0%).

*2-Chloro-2′-*n-*propoxydiethyl sulphide*, colourless oil, b. p. 109—110°/12 mm. (Found : Cl, 19·6.

$C_7H_{15}OClS$ requires Cl, 19·5%), was similarly prepared *via* 2-*n*-propoxyethylthiol, b. p. 48—50°/17 mm. (yield 65%), and 2-hydroxy-2′-*n*-propoxydiethyl sulphide, b. p. 128—129°/12 mm. 2-*Chloro*-2′-n-*butoxydiethyl sulphide*, colourless oil, b. p. 124°/12 mm. (Found: Cl, 17·7. $C_8H_{17}OClS$ requires Cl, 18·1%), was also similarly obtained *via* 2-*n*-butoxyethylthiol, b. p. 167° (yield: 68%), and 2-hydroxy-2′-*n*-butoxydiethyl sulphide, b. p. 141°/15 mm.

2-Ethoxyethylthiol was prepared from 2-ethoxyethyl chloride by the method of Swallen and Boord (*loc. cit.*) and converted by a process similar to that described above for the methoxy-compound into 2-hydroxy-2′-ethoxydiethyl sulphide, b. p. 115—117°/13 mm., which has been obtained in small amounts from 2 : 2′-dichlorodiethyl sulphide by Kretov (*loc. cit.*) by the action of zinc in the presence of alcohol, and by Davies and Oxford (*loc. cit.*) by hydrolysis with aqueous-alcoholic potassium hydroxide. The hydroxy-compound (158 g.) in dimethylaniline (191 g.) was kept cold while thionyl chloride (188 g.) was gradually added. After a short time the mixture was heated for 15 minutes on a steam-bath and then poured into an excess of dilute hydrochloric acid. The product was extracted with chloroform, dried ($CaCl_2$), and fractionated. 2-Chloro-2′-ethoxydiethyl sulphide was obtained as a colourless oil (147 g.), b. p. 92·5°/11 mm. (Found: C, 42·9; H, 7·5; Cl, 20·6. Calc. for $C_6H_{13}OClS$: C, 42·7; H, 7·7; Cl, 21·1%) (compare Kretov, *loc. cit.*).

2-*Chloro*-2′-*alkylthiodiethyl Sulphides*.—A solution of sodium (1·1 mols.) in alcohol was saturated with hydrogen sulphide at 0°, mixed with methyl 2-chloroethyl sulphide (prepared as described in *Org. Synth.*, **14**, 18), and heated in a pressure bottle at 60—65° for 6 hours. 2-Methylthioethylthiol, b. p. 57—61°/15 mm. (compare Moggridge, *J.*, 1946, 1105), was isolated by pouring the mixture into water, and purified by distillation. The thiol was dissolved in an alcoholic solution of sodium ethoxide (1·05 mols.), and the whole raised to boiling with stirring under reflux on a water-bath. The flame was removed while ethylene chlorohydrin (1·1 mols.) was gradually added during ½—1 hour with continued stirring. After the sodium chloride had been filtered off, the alcohol was removed on a steam-bath and the residue distilled under reduced pressure. 2-Hydroxy-2′-methylthiodiethyl sulphide was collected at 139—140°/9·5 mm. (compare Brown and Moggridge, *J.*, 1946, 816, who made this substance from monothioethylene glycol). A solution of the hydroxy-compound in twice its volume of chloroform was boiled under reflux in an all glass apparatus (the use of corks led to a dark brown material, the purification of which was difficult), and the flame was removed while thionyl chloride (1·1 mols.) in four times its volume of chloroform was fairly rapidly added down the condenser. The whole was refluxed until hydrogen chloride was no longer evolved (1½—3 hours). When all volatile material had been removed on the steam-bath, finally under reduced pressure, 2-chloro-2′-methylthiodiethyl sulphide (compare Brown and Moggridge, *loc. cit.*) remained as a colourless oil, which solidified on being cooled and then melted again between 7° and 13° (Found: C, 35·2; H, 6·7; Cl, 19·4. Calc. for $C_5H_{11}ClS_2$: C, 35·2; H, 6·5; Cl, 20·8%).

2-Chloro-2′-ethylthiodiethyl sulphide (Found: C, 38·1; H, 7·0; Cl, 18·8. Calc. for $C_6H_{13}ClS_2$: C, 39·0; H, 7·0; Cl, 19·2%), similarly prepared, was obtained as a pale yellow oil which solidified in a freezing mixture and then melted between 4° and 10° (compare Demuth and Meyer, *loc. cit.*). 2-*Chloro*-2′-n-*propylthiodiethyl sulphide* (Found: C, 42·1; H, 7·8; Cl, 17·8. $C_7H_{15}ClS_2$ requires C, 42·3; H, 7·6; Cl, 17·9%) was obtained as a pale yellow oil, which solidified on being cooled and then melted between 1° and 7°, by a similar process *via* 2-*n*-propylthioethylthiol, b. p. 75—77°/11 mm., and 2-hydroxy-2′-*n*-propylthiodiethyl sulphide, b. p. 151—154°/10 mm. 2-*Chloro*-2′-n-*butylthiodiethyl sulphide* (Found: C, 44·9; H, 7·7; Cl, 15·9. $C_8H_{17}ClS_2$ requires C, 45·2; H, 8·0; Cl, 16·7%), a colourless oil which solidified in a freezing mixture and melted again between −8° and −2°, was similarly obtained *via* 2-*n*-butylthioethylthiol b. p. 90—92°/10 mm., and 2-hydroxy-2′-*n*-butylthiodiethyl sulphide, b. p. 163—165°/10 mm. It was not possible satisfactorily to distil any of these four chloro-compounds, owing to the ease with which they decomposed to give 1 : 4-dithian and the corresponding alkyl chloride.

Sulphones.—The following were prepared from the corresponding sulphides by a process similar to that used by Brown and Moggridge (*loc. cit.*) for methyl 2-chloroethyl sulphone: 2-*chlorodiethyl sulphone*, b. p. 154—155°/18 mm., m. p. 20° (Found: Cl, 22·4. $C_4H_9O_2ClS$ requires Cl, 22·7%), 2-*chloro*-2′-n-*propoxydiethyl sulphone*, pale yellow oil, b. p. 165—167°/9 mm. (Found: Cl, 16·7. $C_7H_{15}O_3ClS$ requires Cl, 16·6%), and 2-*chloro*-2′-n-*butylsulphonyldiethyl sulphone*. The last was not distilled, but was purified by crystallisation from glacial acetic acid, from which it separated in colourless plates, m. p. 188—189° (Found: Cl, 12·6. $C_8H_{17}O_4ClS_2$ requires Cl, 12·8%).

Sulphilimines.—The *sulphilimines* now described were prepared by shaking the corresponding sulphide with an aqueous solution of chloramine-T (10% excess) until the product had solidified, and were purified by crystallisation from alcohol. That of methyl 2-chloroethyl sulphide was obtained in colourless prisms, m. p. 121° (Found: Cl, 12·7. $C_{10}H_{14}O_2NClS_2$ requires Cl, 12·7%), that of 2-chloroethyl allyl sulphide (the thio-ether was prepared as described by Scherlin and Wasilewsky, *J. pr. Chem.*, 1929, **121**, 173) in colourless prisms, m. p. 60—61° (Found: Cl, 11·6. $C_{12}H_{16}O_2NClS_2$ requires Cl, 11·6%), that of 2-chloro-2′-methoxydiethyl sulphide in colourless needles, m. p. 113° (Found: Cl, 11·1. $C_{12}H_{18}O_3NClS_2$ requires Cl, 11·0%), and that of 2-chloro-2′-*n*-propoxydiethyl sulphide in colourless prisms, m. p. 77—78° (Found: Cl, 10·3. $C_{14}H_{22}O_3NClS_2$ requires Cl, 10·1%).

We are indebted to Sir Robert Robinson for his interest in these investigations, and to the Chief Scientist, Ministry of Supply, for permission to publish the work.

Dyson Perrins Laboratory, Oxford University. [*Received, February 20th*, 1948.]
