8. *New Organic Sulphur Vesicants. Part II. Analogues of 2 : 2′-Dichlorodiethyl Sulphide and 2 : 2′-Di-(2-chloroethylthio)diethyl Ether.*

By A. H. Williams and F. N. Woodward.

Homologues [(III), (VIII), (XII), (XVII), (XVIII), (XIX), (XX), (XXI), (XXII)] of the vesicants 2 : 2′-dichlorodiethyl sulphide and 2 : 2′-di-(2-chloroethylthio)diethyl ether having one or more methyl groups as substituents on the side chain have been synthesised, as have also compounds analogous to the latter in which its sulphur and chlorine atoms have been replaced by other atoms or groups. In the course of this work the difficulty experienced by Bennett and Whincop (*J.*, 1921, **119**, 1860) in converting (XI) into (XII) with thionyl chloride has been overcome, and the method of Boëseken, Tellegen, and Henriquez (*Rec. Trav. chim.*, 1931, **50**, 909) for the preparation of 2 : 3-dichloro-1 : 4-dioxan has been improved. (VI) and (VII), intermediates in the synthesis of (III), (XVII), and (XVIII), have been obtained in admixture by the interaction of propylene oxide and hydrogen sulphide. Most of the new chloro-sulphides synthesised have but slight vesicant power.

The only previously described bis-β-chloro-sulphides of the mustard gas (H) type having one or more methyl groups as substituents on the side chain are 2-chloroethyl 2-chloro-*n*-propyl (I), 2-chloroethyl 3-chloro-*n*-butane-2 (II), 2 : 2′-dichlorodi-*n*-propyl (III), and di-(3-chloro-*n*-butane-2) (IV) Coffey, *J.*, 1921, **119**, 94; Pope and Smith, *ibid.*, p. 396; Kranzlein and Covell, U.S.P. 1,570,262; Sylvester, unpublished). No corresponding analogues of the more powerful vesicant 2 : 2′-di-(2-chloroethylthio)diethyl ether have been recorded.

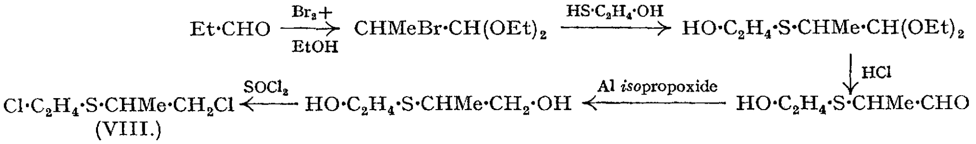
As part of a programme planned to determine the relationship between chemical constitution and vesicant power, a number of analogues of H and 2 : 2′-di-(2-chloroethylthio)diethyl ether have been synthesised and in some cases the physiological activity assessed.

Although Sylvester (*loc. cit.*) appears to have placed the orientation of (I), (II), and (IV) beyond dispute, no decisive evidence has yet been obtained as to the position of the methyl groups in (III). Pope and Smith (*loc. cit.*) assumed that the reaction between sulphur monochloride and propylene goes according to the left-hand side of the scheme

$$S_2Cl_2 + 2CHMe{:}CH_2 \longrightarrow \underset{\text{(III.)}}{S(CH_2{\cdot}CHMeCl)_2} \xleftarrow{\text{HCl}} \underset{\text{(VI.)}}{S(CH_2{\cdot}CHMe{\cdot}OH)_2} \xleftarrow{\text{Na}_2\text{S}} \underset{\text{(V.)}}{Cl{\cdot}CH_2{\cdot}CHMe{\cdot}OH}$$

On the other hand, Coffey (*loc. cit.*) making use of the interaction of propylene chlorohydrin (V) and sodium sulphide assumed, apparently without confirmatory evidence, that the chlorohydrin he used, obtained from allyl chloride and water (Oppenheim *Annalen Suppl.*, 1868, **6**, 367), was pure propylene-α-chlorohydrin (V). Pure (III) has now been obtained by Coffey's method from an authentic sample of (V) made from propylene oxide and hydrogen chloride (Smith, *Z. physikal. Chem.*, 1918, **93**, 59), and has been shown to be identical with that obtained by the earlier workers. The compound is best obtained, however, through 2 : 2′-*dihydroxydi*-n-*propyl sulphide* (VI) prepared, together with 2-*hydroxypropanethiol* (VII), by the interaction of propylene oxide and hydrogen sulphide.

2-*Chloroethyl* 2-*chloro*iso*propyl sulphide* (VIII) has been obtained as a colourless liquid, b. p. 88°/7 mm. (sulphilimine, m. p. 132°), by the following reactions :



$$\begin{array}{l} Et{\cdot}CHO \xrightarrow[\text{EtOH}]{Br_2+} CHMeBr{\cdot}CH(OEt)_2 \xrightarrow{HS{\cdot}C_2H_4{\cdot}OH} HO{\cdot}C_2H_4{\cdot}S{\cdot}CHMe{\cdot}CH(OEt)_2 \\ \hfill \downarrow \text{HCl} \\ \underset{\text{(VIII.)}}{Cl{\cdot}C_2H_4{\cdot}S{\cdot}CHMe{\cdot}CH_2Cl} \xleftarrow{SOCl_2} HO{\cdot}C_2H_4{\cdot}S{\cdot}CHMe{\cdot}CH_2{\cdot}OH \xleftarrow{\text{Al } \textit{iso}\text{propoxide}} HO{\cdot}C_2H_4{\cdot}S{\cdot}CHMe{\cdot}CHO \end{array}$$

It closely resembles its β-analogue (IX) (b. p. 88°/4 mm.; *sulphilimine*, m. p. 129—130°).

2 : 2′-Di-(2-hydroxyethylthio)diethyl sulphide (XI) was obtained by Bennett and Whincop (*loc. cit.*) by condensing H with 2-hydroxyethanethiol (X) in alcoholic sodium ethoxide solution, but failed to convert it into the corresponding *chloro*-compound (XII). This conversion has now been effected by the controlled action of thionyl chloride in chloroform solution. (XII) readily forms a *platinochloride*, m. p. 136°, and its piperidino-derivative gave a *dipicrate*, m. p. 180°. In common with other β-chloro-sulphides it possesses extremely reactive chlorine atoms, completely removed by boiling alcoholic silver nitrate in 5 minutes and by boiling water in 45 minutes, and the *iodo-*, *thiocyanato-*, *phenoxy-*, α-naphthoxy-, β-*naphthoxy-*, s-*tribromophenoxy-*, and *thiophenoxy*-derivatives are easily obtained.

2 : 2′-*Di*-(2-*bromoethylthio*)*diethyl sulphide* was obtained by interaction of (XI) and phosphorus tribromide, but attempts to synthesise the corresponding cyano-compound by the interaction of H and 2-cyanoethanethiol failed, the reaction actually proceeding as follows :

$$S(C_2H_4Cl)_2 + 2NaS{\cdot}C_2H_4{\cdot}CN \longrightarrow S(CH_2{\cdot}CH_2)_2S + 2S(C_2H_4{\cdot}CN)_2 + 2NaCl$$

Oxidation of (XII) afforded the *trisulphone*, $SO_2(C_2H_4{\cdot}SO_2{\cdot}C_2H_4Cl)_2$. 2 : 2′-*Di*-(2-*chloroethylthio*)*diethyl sulphoxide*, *sulphone*, *disulphide* (XIV), and the 1 : 4-*dioxan* have been obtained by methods similar to those employed in the synthesis of (XII). The requisite initial chloro-compounds were obtained by recognised methods with the exception of 2 : 3-dichloro-1 : 4-dioxan required for the synthesis of the last. Although this had been obtained by Boëseken, Tellegen, and Henriquez (*loc. cit.*), repetition of their work showed that higher chloro-derivatives were always obtained in quantity, a fact subsequently borne out by the work of Butler and Cretcher (*J. Amer. Chem. Soc.*, 1932, **54**, 2987), Summerbell and Christ (*ibid.*, p. 3778), and Baker (*J.*, 1932, 2666). By using mixed sulphuryl chloride and sulphur monochloride in the presence of aluminium chloride as described by Silberrad (*J.*, 1922, **121**, 1016), the chlorination was easily controlled and afforded the desired dichlorodioxan in good yield in 3 hours. The 2 : 2′-dichlorodiethyl disulphide (XV) required for the synthesis of (XIV) was obtained by Bennett's method (*J.*, 1921, **119**, 424) although we separated and distilled the intermediate *hydroxy*-compound (XVI), which readily afforded a *bis*-α-*naphthylurethane* and *diphenoxy-*, *dieugenoxy-*, and *di*-s-*tribromophenoxy*-derivatives.

(I), (XVII), and (XVIII) have been prepared by the interaction of (VII) and the appropriate chloro-compound, followed by the controlled action of thionyl chloride on the hydroxy-sulphide formed. Similarly, (III) with (X) and with (VII) affords (XX) and (XXI), respectively, whilst subjection of (VI) to the action of hydrogen chloride at 100° affords a mixture of (III) and (XIX).

The physiological activity of certain of these analogues was assessed by the Physiological Section, Chemical Defence Experimental Station, Porton. The " empirical vesicant power " compared with an arbitrarily chosen standard H = 100, was obtained by comparison of the size of vesicles resulting from the application of the test and standard compounds in an inert solvent to the fore-arms of male volunteers. Table I gives details of the compounds tested.

TABLE I.

	M. p.	B. p.	Empirical vesicant power (H = 100).
2 : 2′-Dichloro-di-*n*-propyl sulphide (III)	−40°	105°/10 mm.	10
2-Chloroethyl 2-chloro-*n*-propyl sulphide (VIII)	−23	88/4 mm.	30
2-Chloroethyl 2-chloro*iso*propyl sulphide (I)	−24·5	88/7 mm.	50
2 : 2′-Di-(2-chloro-*n*-propylthio)diethyl ether (XVII)	—	95—98/0·02 mm.	20
2 : 2′-Di-(2-chloro-*n*-propylthio)di*iso*propyl ether (XIX)	—	90/0·01 mm.	10
2 : 2′-Di-(2-chloroethylthio)diethyl sulphide (XII)	73—75	—	20
2 : 2′-Di-(2-chloro-*n*-propylthio)diethyl sulphide (XVIII)	43·5	—	30
2 : 2′-Di-(2-chloro-*n*-propylthio)di-*n*-propyl sulphide (XXI)	—	108—109/0·02 mm.	20
2 : 2′-Di-(2-chloroethylthio)di-*n*-propyl sulphide (XX)	—	—	50

EXPERIMENTAL.

2-*Hydroxypropanethiol* (VII) *and* 2 : 2′-*Dihydroxydi*-n-*propyl Sulphide* (VI).—The apparatus and technique described by Woodward for the production of thiodiglycol (in the press) being used, liquid propylene oxide was introduced at 0·7 c.c. per min. and hydrogen sulphide throughout at 45 l./hr., the reaction being continuous at 60°. In the course of six experiments, 680 g. of propylene oxide were used, giving a product (948 g.) which on distillation gave 2-*hydroxypropanethiol* (488 g.), b. p. 44·5—45°/8 mm.; $n_D^{18\cdot0^\circ}$ 1·4850 (Found : S, 35·1; SH, 35·6. C_3H_8OS requires S, 34·8; SH, 35·9%), and 2 : 2′-*dihydroxydi*-n-*propyl sulphide* (390 g.), b. p. 125°/4 mm. (Found : S, 21·3; OH, 22·4. $C_6H_{14}O_2S$ requires S, 21·3; OH, 22·7%).

2 : 2′-*Dichlorodi*-n-*propyl Sulphide* (III).—By proceeding essentially according to Smith (*loc. cit.*),

2-chloro*iso*propyl alcohol was obtained, and the fraction, b. p. 126—128°, shown to be substantially pure by oxidation with nitric acid to chloro*iso*nitrosoacetone (Henry, *Bull. Acad. roy. Belg.*, 1903, **6**, 397; 1902, **5**, 535). The chlorohydrin (20 g.) was condensed with sodium sulphide (8·3 g.) in alcohol (70 c.c.), the mixture being boiled under reflux for 10 minutes. The precipitated salt was filtered off, and after removal of the solvent the 2 : 2′-dihydroxydi-*n*-propyl sulphide was distilled under reduced pressure, b. p. 114°/3 mm.

The hydroxy-sulphide (50 g.) obtained by either of the above methods was dissolved in chloroform (200 c.c.) and treated dropwise with thionyl chloride (62 c.c., 20% excess). After subsidence of the vigorous reaction, the mixture was boiled over the water-bath for 30 minutes, and the solvent then removed by distillation. The 2 : 2′-*dichlorodi*-n-*propyl sulphide* was once distilled under reduced pressure (Found : Cl, 37·6. $C_6H_{12}SCl_2$ requires Cl, 37·9%). Its sulphilimine, crystallised from alcohol, had m. p. 166° and was identical with that obtained from the chloro-sulphide prepared by the method of Pope and Smith (*loc. cit.*).

2-*Chloroethyl* 2-*Chloro*iso*propyl Sulphide* (VIII).—Bromine (45 c.c.), dissolved in ethyl acetate (100 c.c.), was added dropwise during 3 hours to a stirred mixture of propaldehyde (58 g.) and ethyl acetate (300 c.c.) kept between − 5° and 0° by immersion in ice–salt. When addition was complete, the mixture was poured into absolute alcohol (500 c.c.) and kept at room temperature for 18 hours. Some solvent (500 c.c.) was then removed under vacuum on a water-bath at 70°. The remaining solution was added to potassium carbonate (300 g.) dissolved in water (300 c.c.), and the precipitated oil separated quickly and washed with water. After drying (Na_2SO_4), the liquid was distilled in a vacuum, and the fraction, b. p. 60—68°/11 mm., separated. This on redistillation gave α-bromopropaldehyde diethyl acetal, b. p. 67°/13 mm. To sodium (8·2 g.) dissolved in absolute alcohol (200 c.c.) was added 2-hydroxyethanethiol (27·8 g.), followed by the acetal (75 g.). No immediate precipitation of sodium bromide occurred, and the mixture was refluxed on the water-bath for 25 hours before the odour of the bromoacetal disappeared completely. The precipitated sodium bromide was filtered off, and the alcohol removed under reduced pressure. The residual dark oil, distilled in a vacuum, gave a light yellow distillate, b. p. 86—90°/0·5 mm. On redistillation, α-(2-*hydroxyethylthio*)*propaldehyde diethyl acetal* was obtained as a colourless liquid, b. p. 87°/0·5 mm. (Found : S, 15·6. $C_9H_{20}O_3S$ requires S, 15·4%). The acetal sulphide (40 g.) was dissolved in 3% hydrochloric acid (1200 c.c.) and allowed to stand for 24 hours. After neutralisation with magnesium carbonate, saturation with salt, and filtration, the aqueous solution (1400 c.c.) was extracted with five 300 c.c. portions of ether. The ethereal extract, after drying (Na_2SO_4), was freed from solvent on the water-bath, the last traces being removed in a vacuum. α-(2-*Hydroxyethylthio*)-*propaldehyde* remained as a colourless oil (Found : S, 23·6. $C_5H_{10}O_2S$ requires S, 23·9%). Reduction of the aldehyde was carried out with aluminium *iso*propoxide by the method of Young, Hartung, and Crossley (*J. Amer. Chem. Soc.*, 1936, **58**, 100). On distillation of the reaction product, the fraction of b. p. 135—143°/5 mm. was collected and redistilled to give relatively pure 2-*hydroxyethyl* 2-*hydroxy*iso-*propyl sulphide*, b. p. 136—137°/5 mm. (Found : S, 22·2; OH, 22·8. $C_5H_{12}O_2S$ requires S, 23·5; OH, 25·0%). Conversion into the chloro-compound, b. p. 105°/12 mm., followed in the usual manner. The sulphilimine, from aqueous alcohol, had m. p. 132°; admixture with *p*-toluenesulphonamide depressed this to m. p. 115°, whilst addition of the sulphilimine of the isomeric 2-chloroethyl 2-chloro-*n*-propyl sulphide (m. p. 130°) gave mixed m. p. 128°.

2 : 2′-*Di*-(2-*chloroethylthio*)*diethyl Sulphide* (XII).—2 : 2′-Di-(2-hydroxyethylthio)diethyl sulphide (9·5 g.; 1 mol.), prepared by the method of Bennett (*loc. cit.*), in chloroform (100 c.c.) was treated dropwise with redistilled thionyl chloride (11·5 g.; 20% excess), a vigorous reaction occurring. After 30 mins.' heating over the steam-bath, the solvent and excess of thionyl chloride were removed by distillation, and the residual solid, after two crystallisations from alcohol–chloroform (1 : 2) and finally from absolute methyl alcohol, was obtained as silvery scales, m. p. 73—75° (Found : S, 34·0; Cl, 25·5. $C_8H_{16}Cl_2S_3$ requires S, 34·4; Cl, 25·4%). Its *platinochloride*, m. p. 136°, separated as a mustard-coloured, amorphous solid 10 minutes after a solution of platinic chloride (0·5 g.) in acetone was added to the chloro-compound (0·1 g.) also in acetone (Found : Pt, 31·7. $C_8H_{16}Cl_6S_3Pt$ requires Pt, 31·7%). The piperidide, roseate crystals from alcohol, was converted into its *picrate*, m. p. 180° (decomp.), micro-crystals from alcohol (Found : C, 43·5; H, 5·2. $C_{30}H_{42}O_{14}N_8S_3$ requires C, 43·7; H, 5·0%).

Several *ethers* (see Table II) were obtained by the following general method : 2 : 2′-di-(2-chloroethylthio)diethyl sulphide (0·01 mol.) in alcohol (20 c.c.) was refluxed for 1 hour with the phenol (0·02 mol.) in the requisite amount of alcoholic sodium ethoxide, and the ether separated by addition of water (60 c.c.).

TABLE II.

Ethers and thio-ethers from $S(C_2H_4{\cdot}S{\cdot}C_2H_4Cl)_2$.

Ether.	Crystal form from EtOH–CHCl$_3$.	M. p.	Formula.	Found, %.			Required, %.		
				C.	H.	S.	C.	H.	S.
Phenoxy-	Colourless rhombs	59°	$C_{20}H_{26}O_2S_3$	60·3	6·2	—	60·9	6·6	—
α-Naphthoxy-	Lustrous needles	56	—	—	—	—	—	—	—
β-Naphthoxy-	Silvery plates	122	$C_{28}H_{30}O_2S_3$	—	—	19·1	—	—	19·4
s-*Tribromo-phenoxy-*	Irregular plates	107	$C_{20}H_{20}O_2Br_6S_3$	—	—	11·5 §	—	—	11·1
Eugenoxy-	Felted needles	86	$C_{28}H_{38}O_4S_2$	62·5	7·1	—	62·9	7·1	—
Thiophenoxy-	Silvery leaflets	92—94	$C_{20}H_{26}S_5$	—	—	37·3	—	—	37·5

§ Found : Br, 55·3. $C_{20}H_{20}O_2Br_6S_3$ requires Br, 55·3%.

2 : 2′-*Di*-(2-*iodoethylthio*)*diethyl Sulphide*.—The chloro-compound (1·3 g.) in methyl alcohol (10 c.c.) was refluxed with a saturated solution of sodium iodide in methyl alcohol (60 c.c.) for 10 minutes. The precipitated salt, after filtration, was extracted with boiling chloroform (50 c.c.), and the residual *iodo*-compound obtained on removal of solvent from the combined solution and washings separated as a white solid, m. p. 102—103°, which, unlike its hydroxy-analogue and 2 : 2′-di-iododiethyl sulphide, is perfectly stable (Found : I, 53·6. $C_8H_{16}I_2S_3$ requires I, 55·0%).

2 : 2′-*Di*-(2-*thiocyanatoethylthio*)*diethyl Sulphide*.—The chloro-compound (1·8 g.) in acetone (20 c.c.) was refluxed for 16 hours with a saturated acetone solution of potassium thiocyanate (60 c.c.), the solvent then removed by distillation, and water (60 c.c.) added. The oil which separated was taken up in ether, the solution dried (Na_2SO_4), and the crude *thiocyanato*-compound obtained by removal of the solvent was crystallised from alcohol–chloroform (4 : 1), from which it separated as glistening plates, m. p. 52° (Found * : C, 37·2; H, 5·2; S, 49·7. $C_{10}H_{16}N_2S_5$ requires C, 37·0; H, 4·9; S, 49·4%).

Attempted Synthesis of 2 : 2′-*Di*-(2-*cyanoethylthio*)*diethyl Sulphide*.—Interaction of ethylene cyanohydrin (0·2 mol.) and 2 : 2′-dichlorodiethyl sulphide (0·1 mol.) in presence of the theoretical amount of alcoholic sodium ethoxide afforded an oil on removal of the solvent from the filtered reaction mixture. This on crystallisation from alcohol yielded long needles of dithian, m. p. 110° (mixed with authentic specimen, m. p. 110°), and gradual addition of chloroform to the mother-liquors thus obtained precipitated crude 2 : 2′-dicyanodiethyl sulphide which, on recrystallisation from alcohol–chloroform (1 : 1), was obtained as plates, m. p. 28° (mixed m. p. with authentic sample kindly supplied by Dr. R. J. Rosser, 28°).

2 : 2′-*Di*-(2-*chloroethylsulphonyl*)*diethyl Sulphone*.—To a solution of 2 : 2′-di-(2-chloroethylthio)diethyl sulphide (1·0 g.) in glacial acetic acid (50 c.c.) was added 30% hydrogen peroxide (24 c.c.; 6 mols.) during 1 hour with intermittent shaking. After removal of the solvent by distillation, the crude *tri-sulphone*

Compound.	Solvent.	Crystalline form.	M. p. or b. p.	Formula.	Found, %		Required, %.
2 : 2′-Di-(2-hydroxyethyl thio)diethyl sulphoxide	—	Long needles	57°	$C_8H_{18}O_3S_3$	S	37·3	37·2
2 : 2′-Di-(2-chloroethylthio)diethyl sulphoxide	Acetone–alcohol	Micro-crystals	63	$C_8H_{16}OCl_2S_3$	Cl	24·2	24·0
2 : 2′-Di-(2-hydroxyethylthio)diethyl sulphone	Acetone	Plates	85—86	$C_8H_{18}O_4S_3$	S	35·8	35·0
2 : 2′-Di-(2-chloroethylthio)diethyl sulphone	Alcohol	Prisms	107—109	$C_8H_{16}O_2Cl_2S_3$	S	31·1	30·9
2 : 2′-Di-(2-hydroxyethylthio)diethyl disulphide	Alcohol	Amorphous powder	79—81	$C_4H_9OS_2$	S	48·7 §	46·7
2 : 2′-Di-(2-hydroxy-*n*-propylthio)diethyl sulphide	Benzene–light petroleum	—	59	$C_{10}H_{22}O_2S_3$	S	35·7	35·6
2 : 2′-Di-(2-chloro-*n*-propylthio)diethyl sulphide (XVIII)	Light petroleum	—	43·5	$C_{10}H_{20}Cl_2S_3$	Cl	23·1	23·1
2 : 3-Di-(2-hydroxyethylthio)-1 : 4-dioxan †	—	Oil	—	$C_8H_{16}O_4S_2$	S	25·8	26·7
2 : 3-Di-(2-chloroethyl thio)-1 : 4-dioxan	—	—	138—141/ 15 mm.	$C_8H_{14}O_2Cl_2S_2$	S Cl	23·1 25·5	23·1 25·6
2-Hydroxyethyl 2-hydroxypropyl sulphide	—	—	154/8 mm.	$C_5H_{12}O_2S$	S OH	23·5 25·2	23·5 25·0
2-Chloroethyl 2-chloro-*n*-propyl sulphide (I)	—	—	88/4 mm.	$C_5H_{10}Cl_2S$	Cl	41·2	41·1
2 : 2′-Di-(2-hydroxy-*n*-propylthio)diethyl ether	—	—	217—218/ 5 mm.	$C_{12}H_{22}O_3S_2$	S	25·5	25·2
2 : 2′-Di-(2-chloro-*n*-propylthio)diethyl ether (XVII)	—	—	95—98/ 0·02 mm.	$C_{10}H_{20}Cl_2OS_2$	Cl	24·1	24·4
2 : 2′-Di-(2-hydroxy-ethylthio)di-*n*-propyl sulphide	—	—	240/ 1·5 mm.	$C_{10}H_{22}O_2S_3$	S	35·8	35·6
2 : 2′-Di-(2-chloroethylthio)di-*n*-propyl sulphide (XX)	—	—	—	$C_{10}H_{20}Cl_2S_3$	Cl	23·0	23·2
2 : 2′-Di-(2-hydroxy-*n*-propylthio)di-*n*-propyl sulphide	—	—	210/ 0·5 mm.	$C_{12}H_{26}O_2S_3$	S	32·3	32·2
2 : 2′-Di-(2-chloro-*n*-propylthio)di-*n*-propyl sulphide (XXI)	—	—	108—109/ 0·02 mm. (slight decomp.)	$C_{12}H_{24}Cl_2S_3$	Cl	22·1	21·2

§ High S content due to dissolved dithian (cf. Bennett, *J.*, 1921, **119**, 424).

† *Bis-α-naphthylurethane*, m. p. 152° from benzene (Found : S, 11·2, $C_{30}H_{30}O_6N_2S_2$ requires S, 11·1%).

remained as a white solid, sparingly soluble in water, rectified spirits, and glacial acetic acid. After two crystallisations from the last, it was obtained in white nodules, m. p. 174·5° (Found: S, 25·2; Cl, 19·5. $C_8H_{16}O_6Cl_2S_3$ requires S, 25·5; Cl, 19·2%).

2 : 2′-*Di*-(2-*bromoethylthio*)*diethyl Sulphide*.—2 : 2′-Di-(2-hydroxyethylthio)diethyl sulphide (4 g.) in chloroform (60 c.c.) was refluxed for 2 hours with phosphorus tribromide (8 g.), the solvent removed, water (50 c.c.) added, and the residue extracted with chloroform. The extract, after drying (Na_2SO_4) and removal of solvent, left a solid which, after crystallising twice from chloroform, had m. p. 87·5—88·5° (Found: Br, 43·0. $C_8H_{16}Br_2S_3$ requires Br, 43·4%).

The *compounds* (Table, p. 41) were prepared by the general method used in the synthesis of 2 : 2′-di-(2-chloroethylthio)diethyl sulphide and its hydroxy-precursor.

Of the requisite starting materials, 2 : 2′-dichlorodiethyl sulphoxide and sulphone were obtained by the methods of Helfrich and Reid (*J. Amer. Chem. Soc.*, 1920, **42**, 1211) and Steinkopf, Herold, and Stohr (*Ber.*, 1920, **53**, 1007), respectively.

2 : 2′-Dichlorodiethyl disulphide was prepared by Bennett's method (*loc. cit.*), except that the intermediate 2 : 2′-*dihydroxydiethyl disulphide* was distilled at 158—163°/3·5 mm. (Found: S, 40·9. $C_4H_{10}O_5S_2$ requires S, 41·5%). The *bis-α-naphthylurethane* had m. p. 150—152° (Found *: C, 63·7; H, 5·1; N, 5·6; S, 13·0. $C_{26}H_{24}O_4N_2S_2$ requires C, 63·4; H, 4·9; N, 5·7; S, 13·0%). Conversion of the hydroxy-disulphide into the chloro-compound, b. p. 132—134°/5 mm., is best effected by means of thionyl chloride. The *di*-s-*tribromophenoxy*-derivative crystallised from methyl alcohol, m. p. 76° (Found: Br, 61·3. $C_8H_6OBr_3S$ requires Br, 61·6%). The *dieugenoxy*-derivative was obtained as long rhombs, m. p. 97°, from methyl alcohol–chloroform (1 : 2) (Found: S, 14·7. $C_{12}H_{15}O_2S$ requires S, 14·4%).

2 : 3-*Dichloro*-1 : 4-*dioxan*.—The method of Boëseken, Tellegen, and Henriquez (*loc. cit.*), involving passage of chlorine through dioxan (200 g.) for 16 hours at 90°, was only partly successful, as higher chloro-compounds were principally obtained. The reaction proceeded smoothly, however, and was completed in 50 minutes, when sulphur monochloride (1·5 g.) in sulphuryl chloride (150 g.) was slowly added down a reflux condenser to a mixture of dioxan (88 g.) and aluminium chloride (10 g.) at 70°. After cooling, the mixture was treated with water and extracted with benzene, the extract dried ($CaCl_2$), and solvent removed; fractional distillation afforded unreacted dioxan (28 g.) and 2 : 3-dichloro-1 : 4-dioxan (25 g.), b. p. 82·5—84°/14 mm. (Boëseken *et al.* give b. p. 82·4°/14 mm.).

2 : 2′-*Di*-(2-*chloro*-n-*propylthio*)*di*iso*propyl Ether* (XIX).—Distillation of the reaction product obtained by the action of hydrogen chloride on 2 : 2′-dihydroxydi-*n*-propyl sulphide at 100° during 1 hour afforded 2 : 2′-dichlorodi-*n*-propyl sulphide, b. p. 100°/7 mm., and the desired *ether*, b. p. 90°/0·01 mm. (Found: Cl, 22·4. $C_{12}H_{24}Cl_2OS_2$ requires Cl, 22·4%).

Microanalyses marked * were carried out by Drs. Weiler and Strauss.

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