9. *New Organic Sulphur Vesicants. Part III. Homologues of 2 : 2′-Di-(2-chloroethylthio)diethyl Ether.*

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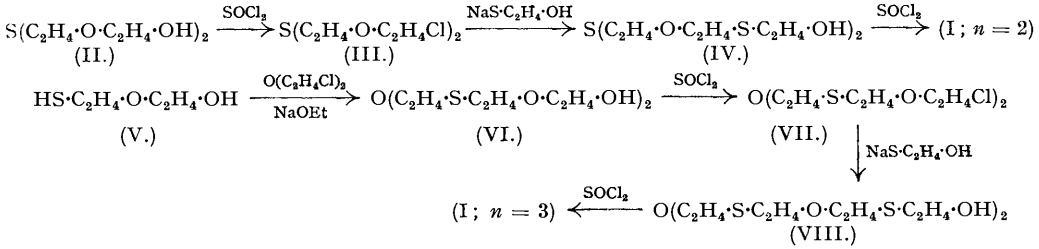
The powerful vesicants 2 : 2′-dichlorodiethyl sulphide and 2 : 2′-di-(2-chloroethylthio)-diethyl ether are the first two members of the series having the general formula (I). The third, fourth, fifth, and sixth members have now been prepared.

The four compounds mentioned above (I; n = 2, 3, 4, and 5) have not hitherto been described.

$$Cl{\cdot}[C_2H_4{\cdot}S{\cdot}C_2H_4{\cdot}O]_n{\cdot}C_2H_4{\cdot}S{\cdot}C_2H_4Cl \quad (I.)$$

1 : 17-*Dichloro*-6 : 12-*dioxa*-3 : 9 : 15-*trithiaheptadecane* * (I; $n = 2$) and 1 : 23-*dichloro*-6 : 12 : 18-*trioxa*-3 : 9 : 15 : 21-*tetrathiatricosane* (I, $n = 3$) have now been synthesised through the following stages, starting from 2 : 2′-*di*-(2-*hydroxyethoxy*)*diethyl sulphide* (II) and 2-*hydroxy*-2′-*mercaptodiethyl ether* (V) obtained by the interaction of diethylene chlorohydrin and sodium hydrogen sulphide in alcoholic solution.



$$\underset{(II.)}{S(C_2H_4{\cdot}O{\cdot}C_2H_4{\cdot}OH)_2} \xrightarrow{SOCl_2} \underset{(III.)}{S(C_2H_4{\cdot}O{\cdot}C_2H_4Cl)_2} \xrightarrow{NaS{\cdot}C_2H_4{\cdot}OH} \underset{(IV.)}{S(C_2H_4{\cdot}O{\cdot}C_2H_4{\cdot}S{\cdot}C_2H_4{\cdot}OH)_2} \xrightarrow{SOCl_2} (I;\ n = 2)$$

$$\underset{(V.)}{HS{\cdot}C_2H_4{\cdot}O{\cdot}C_2H_4{\cdot}OH} \xrightarrow[NaOEt]{O(C_2H_4Cl)_2} \underset{(VI.)}{O(C_2H_4{\cdot}S{\cdot}C_2H_4{\cdot}O{\cdot}C_2H_4{\cdot}OH)_2} \xrightarrow{SOCl_2} \underset{(VII.)}{O(C_2H_4{\cdot}S{\cdot}C_2H_4{\cdot}O{\cdot}C_2H_4Cl)_2}$$

$$\Big\downarrow NaS{\cdot}C_2H_4{\cdot}OH$$

$$(I;\ n = 3) \xleftarrow{SOCl_2} \underset{(VIII.)}{O(C_2H_4{\cdot}S{\cdot}C_2H_4{\cdot}O{\cdot}C_2H_4{\cdot}S{\cdot}C_2H_4{\cdot}OH)_2}$$

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* This terminology, sanctioned by the International Union of Chemistry (see *J.*, 1931, 1607), is adopted for the longer hetero-chains.—Editor.

Attempts to synthesise the fifth and sixth members of the series by a similar series of reactions starting from (III) and (VII) were unsuccessful on account of the difficulties encountered in purifying the essential intermediate compounds $S(C_2H_4\cdot O\cdot C_2H_4\cdot S\cdot C_2H_4\cdot O\cdot C_2H_4Cl)_2$ and $O(C_2H_4\cdot S\cdot C_2H_4\cdot O\cdot C_2H_4\cdot S\cdot C_2H_4\cdot O\cdot C_2H_4\cdot S\cdot C_2H_4Cl)_2$ neither of which could be distilled or crystallised. An alternative route was therefore chosen dependent upon 2-*mercapto*-2′-(2-*hydroxyethylthio*)*diethyl ether* (IX) as starting material. This was obtained in 40% yield, together with 2 : 2′-di-(2-hydroxyethylthio)diethyl ether, by treating di-2-mercaptoethyl ether with one equivalent each of sodium ethoxide and ethylene chlorohydrin. The parent hydroxy-compounds of the desired 1 : 29-*dichloro*-6 : 12 : 18 : 24-*tetraoxa*-3 : 9 : 15 : 21 : 27-*pentathianonacosane* (I; $n = 4$) and 1 : 35-*dichloro*-6 : 12 : 18 : 24 : 30-*pentaoxa*-3 : 9 : 15 : 21 : 27 : 33-*hexathiapentatriacontane* (I; $n = 5$) were obtained by interaction of the sodium salt of (IX) with (III) and (VII), respectively. Conversion into the chloro-compounds and the formation of various derivatives followed the usual lines. Confirmation of the structure of various intermediates was obtained by means of the alternative synthesis of (VIII) from di-2-chloroethyl ether and (IX). Another structural confirmation was obtained by the preparation of the methylthio-ether of (I; $n = 2$) by the two routes :

$$(\text{I};\ n = 2) + 2\text{SMeNa} \longrightarrow S(C_2H_4\cdot O\cdot C_2H_4\cdot S\cdot C_2H_4SMe)_2 \longleftarrow (\text{III}) + 2\text{NaS}\cdot C_2H_4\cdot \text{SMe}$$

The chloro-compounds (I; $n = 2$, 3, 4, and 5) are colourless, low-melting solids which, like their derivatives, are difficult to purify; their crystallising power is low, and preparations melting 5—10° below their true m. p.s were frequently encountered and the m. p.s could not be raised by repeated crystallisation. This fact explains the necessity for rigid purification of intermediates in the above syntheses.

EXPERIMENTAL.

Diethylene Chlorohydrin.—A modification of the method of Fourneau and Ribas (*Bull. Soc. chim.*, 1927, **41**, 1046) afforded the chlorohydrin in 35% yield. Ethylene oxide was distilled into a mixture of ethylene chlorohydrin (500 c.c.) and concentrated sulphuric acid (9 c.c.) in a flask fitted with an inlet tube and a reflux condenser cooled with solid carbon dioxide–alcohol, during ½ hour. The contents of the flask were then boiled for a further 5 minutes, and the sulphuric acid neutralised by addition of sodium carbonate. The sludge was removed by filtration, and distillation of the filtrate afforded three fractions : (i) b. p. 110—130°, unchanged chlorohydrin mixed with a small amount of dioxan, (ii) b. p. 80—110°/15 mm., the crude dichlorohydrin, and (iii) b. p. 110—150°/15 mm., presumably a mixture of higher homologues. The diethylene chlorohydrin was freed from traces of ethylene glycol by washing with an equal volume of water, extracting with ether, drying (Na_2SO_4), and fractionally distilling. The pure compound had b. p. 85—93°/10 mm., 92—100°/15 mm. (Found : Cl, 28·3; OH, 13·9. Calc. for $C_4H_9O_2Cl$: Cl, 28·5; OH, 13·7%).

2-*Hydroxy*-2′-*mercaptodiethyl Ether* (V) *and* 2 : 2′-*Di*-(2-*hydroxyethoxy*)*diethyl Sulphide* (II).—Sodium (23 g.) was dissolved in absolute alcohol (500 c.c.), and the solution saturated with hydrogen sulphide and left overnight with a slow stream of hydrogen sulphide passing through. The stream of gas was continued both whilst diethylene chlorohydrin (125 g.) was added during ½ hour and also during the subsequent heating of the mixture to 50° for 30 minutes and to the b. p. for a further 30 minutes. The precipitated salt was then filtered off, the alcoholic solution made slightly acid with concentrated hydrochloric acid, the alcohol removed, and the product distilled. The crude *ether* (V) first distilled, b. p. 78—80°/1 mm. (Found : SH, 26·0. $C_4H_{10}O_2S$ requires SH, 27·0%), followed by the *sulphide* (II), b. p. 180°/1·5 mm. (Found : S, 16·0. $C_8H_{18}O_4S$ requires S, 15·3%).

1 : 17-*Dichloro*-6 : 12-*dioxa*-3 : 9 : 15-*trithiaheptadecane* (I, $n = 2$).—The foregoing sulphide (50 g.) was dissolved in dry chloroform (200 c.c.), and pure thionyl chloride (40 c.c.) run in rapidly. After standing for 30 minutes, the mixture was heated on the water-bath for 10 minutes, and the chloroform and unchanged thionyl chloride then removed in a vacuum at 30°. On distillation, impure 2 : 2′-*di*-(2-*chloroethoxy*)*diethyl sulphide* (III), b. p. 145°/1 mm., was obtained in 50% yield (Found : Cl, 29·0; S, 14·0. $C_8H_{16}O_2Cl_2S$ requires Cl, 28·4; S, 13·0%). The chloro-sulphide (10 g.) was added to a solution of 2-hydroxyethanethiol (6·3 g.) in sodium ethoxide (1·8 g. of sodium) and boiled for ½ hour on the water-bath. The precipitated salt was filtered off, and removal of the alcohol left the *sulphide* (IV) as a pale yellow oil solidifying on cooling; needles, m. p. 48—49°, from ether. The *a-naphthylurethane* formed needles, m. p. 83°, from ethyl acetate–petrol (Found : S, 14·1. $C_{34}H_{40}O_6N_2S_3$ requires S, 14·4%). Conversion into the *chloro*-compound (I; $n = 2$) with thionyl chloride was effected in the normal manner. Extraction of the product with boiling light petroleum (b. p. 40—60°) and cooling in ice gave needle rosettes, m. p. 18°, which were filtered off on a cold filter (Found : Cl, 19·4; S, 26·4. $C_{12}H_{24}O_2Cl_2S_3$ requires Cl, 19·1; S, 26·2%). The *bis*(*methylthio*)-*ether*, m. p. 42°, was obtained either by interaction of the chloro-sulphide with 10% excess of the sodium mercaptide of (III) with methyl 2-mercaptoethyl sulphide in the requisite amount of sodium ethoxide (Found : S, 40·5. $C_{14}H_{30}O_2S_5$ requires S, 41·0%); the *dithiophenoxide*, needle rosettes, had m. p. 44° from ethyl acetate–alcohol (Found : S, 31·2. $C_{24}H_{34}O_2S_5$ requires S, 31·1%).

1 : 23-*Dichloro*-6 : 12 : 18-*trioxa*-3 : 9 : 15 : 21-*tetrathiatricosane* (I; $n = 3$).—Dichlorodiethyl ether (29·3 g.) was added rapidly to a solution of 2-hydroxy-2′-mercaptodiethyl ether (50 g.) in sodium ethoxide (9·5 g. of sodium). The mixture was kept for ½ hour and then heated for a futher ½ hour on the water-bath, filtered from salt, and the alcohol removed. On distillation of the residual oil, the *com-*

pound (VI), b. p. 230°/1 mm., was obtained as a colourless viscous oil (Found: S, 20·7. $C_{12}H_{26}O_5S_2$ requires S, 20·4%). The pyridine–acetic anhydride method of estimating hydroxyl groups was inapplicable to this and analogous compounds. Conversion into the *chloro*-compound (VII) was carried out in the normal manner, thionyl chloride being used. It could not be distilled without decomposition at 1 mm. (b. p. 200—210°) but distilled smoothly at 125—130°/0·02 mm. (Found: Cl, 21·0; S, 17·2. $C_{12}H_{24}O_3Cl_2S_2$ requires Cl, 20·2; S, 17·2%). The chloro-compound (10 g.) was added rapidly to a solution of 2-hydroxyethanethiol (5 g.) in sodium ethoxide (1·3 g. of sodium) and heated for ½ hour on the water-bath. The precipitated salt was filtered off and the alcohol removed to leave 1 : 23-dihydroxy-6 : 12 : 18-trioxa-3 : 9 : 15 : 21-tetrathiatricosane (VIII) as a pale yellow oil which solidified on cooling; needles, m. p. 58—58·5°, from ether; *a-naphthylurethane*, needles, m. p. 69°, from ethyl acetate–light petroleum (Found: S, 16·6. $C_{38}H_{48}O_7N_2S_4$ requires S, 16·6%). The method of conversion into the *chloro*-compound (I; $n = 3$) and the isolation procedure were identical with those employed in the synthesis of the lower analogue (I; $n = 2$). It was obtained as needle rosettes, m. p. 28·5°, from ethyl acetate–alcohol (Found: Cl, 15·5; S, 27·6. $C_{16}H_{32}O_3Cl_2S_4$ requires Cl, 15·1; S, 27·2%). The *bismethylthioether* was obtained as needle rosettes, m. p. 45°, from ethyl acetate–alcohol (Found: S, 39·1. $C_{18}H_{38}O_3S_6$ requires S, 38·9%), and the *dithiophenoxide*, m. p. 50°, was similarly obtained (Found: S, 30·6. $C_{28}H_{42}O_3S_6$ requires S, 31·1%).

1 : 23-*Dihydroxy*-3 : 9 : 15 : 21-*tetraoxa*-6 : 12 : 18-*trithiatricosane*.—2 : 2-Di-(2-chlorethoxy)diethyl sulphide (10 g.) was added to a solution of 2-hydroxy-2′-mercaptodiethyl ether (10·4 g.) in sodium ethoxide (2 g. of sodium) and heated on the water-bath for one hour. The precipitated salt was filtered off and the solvent removed, leaving a pale yellow oil which solidified on cooling to 0°. Distillation of this oil gave a colourless solid, b. p. 230°/0·01 mm., m. p. 19°. An attempt to convert this into the chloro-compound under conditions similar to those employed in the preparation of the analogous (VII) failed, as a dark red oil which would not solidify and decomposed on distillation was formed. Condensation of this crude chloro-compound with 2-hydroxyethanethiol failed to give the desired dihydroxy-compound corresponding to (I; $n = 4$).

2-*Mercapto*-2′-(2-*hydroxyethylthio*)*diethyl Ether* (IX).—Ethylene chlorohydrin (80·5 g.) was added gradually to a solution of 2 : 2′-dimercaptodiethyl ether (138 g.) in sodium ethoxide (23 g. of sodium). After the reaction had subsided, the mixture was heated on the water-bath for ½ hour, filtered from salt, and the alcohol removed. Distillation of the product gave, besides unreacted ether, the required 2-*mercapto*-2′-(2-*hydroxyethylthio*)*diethyl ether*, b. p. 60°/1·5 mm., in 40% yield (Found: SH, 18·1. $C_6H_{14}O_2S_2$ requires SH, 18·1%), and 2 : 2′-di-(2-hydroxyethylthio)diethyl ether (30% yield), identified by mixed m. p. with an authentic specimen, m. p. 29—30°.

1 : 29-*Dichloro*-6 : 12 : 18 : 24-*tetraoxa*-3 : 9 : 15 : 21 : 27-*pentathianonacosane* (I, $n = 4$).—2 : 2′-Di-(2-chlorethoxy)diethyl sulphide (6·8 g.) was added to a solution of 2-mercapto-2′-(2-hydroxyethylthio)diethyl ether (10 g.) in sodium ethoxide (1·25 g. of sodium) and heated on the water-bath for one hour. The precipitated salt was filtered off, and the solution left to crystallise, the pentathiodiglycol being obtained as needles from alcohol, m. p. 60—61°; *a-naphthylurethane*, needles from ethyl acetate–light petroleum, m. p. 73—74° (Found: S, 18·3. $C_{42}H_{56}O_8N_2S_5$ requires S, 18·3%). Thionyl chloride (3 c.c.) was added to the pentathiodiglycol (5 g.) in chloroform (40 c.c.), and by employing the procedure used in the preparation of (I; $n = 2$), the *compound* (I, $n = 4$) was obtained as needle rosettes, m. p. 32—33°, from ethyl acetate–alcohol (Found: Cl, 12·2; S, 28·3. $C_{20}H_{40}O_4Cl_2S_5$ requires Cl, 12·3; S, 27·8%); *dithiophenoxide*, needle rosettes, m. p. 55°, from ethyl acetate–alcohol (Found: S, 31·1. $C_{32}H_{50}O_4S_7$ requires S, 31·0%).

1 : 35-*Dichloro*-6 : 12 : 18 : 24 : 30-*pentaoxa*-3 : 9 : 15 : 21 : 27 : 33-*hexathiapentatriacontane* (I, $n = 5$).—The ether (VII, 9 g.) was added to a solution of 2-mercapto-2′-(2-hydroxyethylthio)diethyl ether (10 g.) and sodium ethoxide (1·25 g. of sodium), and heated on the water-bath for one hour. After removal of the precipitated salt the hexathiodiglycol crystallised and was obtained as needles, m. p. 62·5°, from alcohol; *a-naphthylurethane*, needles, m. p. 79°, from ethyl acetate–light petroleum (Found: S, 19·4. $C_{46}H_{64}O_9N_2S_6$ requires S, 19·6%). Interaction of the hexathiodiglycol (10 g.) with thionyl chloride (4 c.c.) in chloroform (70 c.c.) gave the desired *chloro*-compound as needle rosettes, m. p. 37° from ethyl acetate (Found: Cl, 10·2; S, 29·0. $C_{24}H_{48}O_5Cl_2S_6$ requires Cl, 10·5; S, 28·3%); *dithiophenoxide*, needle rosettes, m. p. 57°, from ethyl acetate–alcohol (Found: S, 30·8. $C_{36}H_{58}O_5S_8$ requires S, 31·0%).

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