

174. The Methyl Thioethers derived from 2 : 2'-Dichlorodiethyl Sulphide and its Analogues. Part III. Synthetic Experiments.

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The syntheses summarised in the schemes below have been carried out in order to confirm the structures of various compounds [*e.g.*, (III), (VI), (IX), (X), (XIII), and (XVIII)] described in Parts I and II.

Various additions of thiols to vinyl sulphides, postulated in Part II, have been shown to occur spontaneously. The products have all been straight chain compounds, as opposed to the alternative possibility of the thioacetal type, RS·CHMe·SR'. The addition therefore proceeds to give the "abnormal" products: it thus falls into line with the addition of thiols to other classes of vinyl compound, when the "abnormal" products are usually obtained.

In Part I (Meade and Moggridge, this vol., p. 813) it was found that the action of sodium thiomethoxide on 2 : 2'-dichlorodiethyl sulphide ("mustard gas") gave, in addition to the expected product (VI), small amounts of (X) and (XIII). This result was so unexpected as to make desirable a direct synthetic confirmation of the structures of these compounds and of such related derivatives as (IX) and (XVIII). In addition, in Part II (Charnock and Moggridge, preceding paper) the spontaneous occurrence of several additions of thiols to vinyl compounds [*e.g.*, (III) to phenyl- and methyl-thiols, (III) to (VIII), (XVI) to (VIII)] was postulated; it was desirable to confirm their occurrence with synthetic specimens.

The following related schemes of synthesis were therefore undertaken (see opposite).

It is seen that the structures of the key compounds listed above are amply confirmed, (VI), (IX), and (X) by two syntheses, (XIII) by four, and (XVIII) by one synthesis and by the fission of its sulphone to give (XX). The products were in all cases identical with the compounds as prepared in the usual way.

Most of the reactions concerned were straightforward and call for little comment. Some [the formation of (VI) and (VIII) from (VII), and of (XX) from 2 : 2'-dichlorodiethyl sulphone and sodium methanesulphinate]

EXPERIMENTAL.

Methyl 2-Chloroethyl Sulphide (VII).—This was prepared from methyl 2-hydroxyethyl sulphide as described in *Org. Synth.* (Collective Vol. II, 136). The hydroxy compound was prepared either by the method given in *Org. Synth.* (Collective Vol. II, 345) or by the following method. Methylthiol (25 g.) was distilled into an ice-cooled mixture of ethylene oxide (22 g.) and methyl alcohol (200 c.c.) during one hour. The solvent was then removed by distillation, and the residue distilled to give the desired product, b. p. 63–64°/56 mm., in 75% yield.

Methyl Vinyl Sulphide (III).—Methyl 2-chloroethyl sulphide (25 g.) was refluxed for 30 minutes with a solution prepared from sodium (5.2 g.) and *n*-amyl alcohol (200 c.c.). The mixture was then distilled, and the material boiling below 135° collected and redistilled to give methyl vinyl sulphide in 50% yield, b. p. 69–70° (cf. Part II for its isolation after pyrolysis of 2 : 2'-dimethylthiodiethyl sulphide).

1-Phenylsulphonyl-2-methylsulphonylthioethane (I).—(a) Methyl vinyl sulphide (III) was treated with phenylthiol and the product oxidised with peracetic acid as described in Part II. The disulphone (I) was obtained, m. p. 172°, identical by mixed m. p. with that obtained in Part II.

(b) Methyl 2-chloroethyl sulphide (VII) (6.2 g.) was treated with a solution of sodium thiophenoxide, prepared from 36 c.c. of 1.67*N*-sodium ethoxide solution and 7.2 g. of phenylthiol; the mixture was kept for 10 minutes, and then refluxed for a further 10 minutes. Chloroform and dilute hydrochloric acid were then added, the chloroform layer separated, dried, and concentrated, and the residue distilled to give 1-phenylthio-2-methylthioethane (II) in 80% yield, b. p. 110°/0.5 mm., 115°/1 mm. Oxidation gave the disulphone (I) in 90% yield, identical by mixed m. p. with the two preceding preparations.

1 : 2-Dimethylsulphonylthioethane (V).—Excess of methylthiol was distilled into methyl vinyl sulphide (III) (1 g.) and the mixture was kept for some hours at room temperature. The crude 1 : 2-dimethylthioethane (IV) was, without further purification, treated with perhydrol-acetic acid, the solvent removed under reduced pressure, and the residue crystallised from water to give the disulphone (V) (0.7 g.), m. p. 190°. This was shown by mixed m. p. to be identical with the compound prepared as described in Part II.

2-Methylthioethylthiol (VIII) (cf. Moggridge, in the press).—The 2 : 2'-dimethylthiodiethyl sulphide (VI) obtained during this preparation was identified by oxidation to its trisulphone (IX), m. p. 264°, identical by mixed m. p. with a specimen prepared by the normal route.

2 : 2'-Di-(2-methylthioethylthio)diethyl Sulphide (X).—(a) 2-Methylthioethylthiol (VIII) (0.93 g.) was dissolved in sodium methoxide solution (from 0.2 g. of sodium), pure mustard gas (0.45 c.c., m. p. 14.3°) added, and the mixture refluxed for 10 minutes. Water (100 c.c.) was then added, and the crude product (1.0 g.), m. p. 72–77°, collected and crystallised from methyl alcohol. After one recrystallisation it melted at 84°, and was shown by mixed m. p. to be identical with the material prepared as in Part I.

This reaction was also carried out in aqueous media, the reactants being kept with occasional shaking for 30 minutes at room temperature and 30 minutes at 100°. Yield of (X), 60–70%.

(b) 2 : 2'-Dimercaptodiethyl sulphide (prepared from ethylene sulphide, Meade, private communication; cf. Meadow and Reid, *J. Amer. Chem. Soc.*, 1934, **56**, 2177) was dissolved in sodium methoxide solution (2 equivs.); methyl 2-chloroethyl sulphide (VII, 2 equivs.) was added, and the mixture refluxed for 30 minutes. The mixture was filtered hot; the filtrate on cooling deposited the required product, m. p. (after one crystallisation from alcohol) 84°. This compound was shown by mixed m. p. to be identical with that prepared by the other two methods.

Methyl 2-Chloroethyl Sulphone (XI).—Methyl 2-chloroethyl sulphide (VII; 9.0 g.) was treated with perhydrol (50 c.c.) and glacial acetic acid (50 c.c.). Heat was evolved. The mixture was kept overnight at room temperature, the solvents were then removed under reduced pressure, and the residue was distilled to give the required product in 72.5% yield; colourless oil, b. p. 112°/1 mm., m. p. 9° (Found : Cl, 24.9. Calc. for C₃H₇O₂ClS : Cl, 24.9%). Walter (*Ber.*, 1894, **27**, 3045) gives m. p. 9°.

2 : 2'-Dimethylsulphonyldiethyl Sulphide (XII).—The chlorosulphone (XI) was treated in the cold with an aqueous alcoholic solution of sodium sulphide (100% excess); the required product (XII) was then deposited in 96% yield. The yield became extremely low if the reaction mixture were heated. Long needles from water, m. p. 127° (Found : S, 38.9. C₆H₁₄O₄S₃ requires S, 39.0%).

2 : 2'-Dimethylsulphonyldiethyl Sulphone (IX).—(a) The disulphone (XII) on treatment with perhydrol-acetic acid in the usual way gave the required product in 65% yield; plates from aqueous acetic acid, m. p. 264°.

(b) Methanesulphonic acid was prepared by the action of sulphur dioxide on methylmagnesium iodide (cf. Boeseken and Ockenberg, *Rec. Trav. chim.*, 1914, **33**, 317). This reaction proceeded smoothly, and the magnesium salt of the required acid was obtained by concentration of its aqueous solution under reduced pressure. It was washed with alcohol, decomposed by the addition of sodium hydroxide solution (1 equiv.), and the sodium methanesulphinate obtained by concentration of the filtered solution under reduced pressure. A solution of 2 : 2'-dichlorodiethyl sulphone (1 equiv.) in aqueous alcohol was added; a crystalline solid was then deposited almost immediately. The mixture was refluxed for 15 minutes, cooled, and the product (IX) collected in 65% yield, m. p. 262°.

The products from both these syntheses were shown by mixed m. p. to be identical with the compound as prepared by direct oxidation of (VI) (cf. Part I).

2-Hydroxy-2'-methylthiodiethyl Sulphide (XIV).—To monothioethylene glycol (21.7 g.; cf. Bennett, *J.*, 1921, 423), dissolved in sodium ethoxide solution (from 6.25 g. of sodium), methyl 2-chloroethyl sulphide (VII; 30 g.) was added, and the mixture refluxed for 1 hour; after removal of sodium chloride and alcohol the residue was distilled to give the required product (XIV), 39 g., b. p. 125°/3 mm. (Found : S, 42.4. C₅H₁₂OS₂ requires S, 42.1%).

2-Chloro-2'-methylthiodiethyl Sulphide (XV).—The hydroxy-compound (XIV) (32 g.) in dry chloroform (150 c.c.) was treated with thionyl chloride (18.5 c.c.). The mixture was refluxed for 30 minutes after the initial vigorous reaction had subsided, and the solution was then decanted from some white gummy material and concentrated. Distillation of the residue gave the required chloro-compound (XV) as a colourless oil, b. p. 112°/3 mm., yield 30 g., which, on standing, slowly decomposed with deposition of a white solid (Found : Cl, 21.1; S, 36.85. C₅H₁₁ClS₂ requires Cl, 20.85; S, 37.55%).

2-Methylthioethyl Vinyl Sulphide (XVI).—To the chloro-compound (XV; 10 g.) in boiling alcohol, sodium ethoxide solution (from 1.35 g. of sodium) was added gradually during 15 minutes; the mixture was refluxed for a further hour, and sodium chloride and alcohol were then removed. Distillation of the residue gave the required compound (XVI) as a colourless oil showing no tendency to polymerise; b. p. 65°/2 mm. (Found : S, 47.3. C₅H₁₀S₂ requires S, 47.75%).

2-Phenylsulphonyl-2'-methylsulphonyldiethyl Sulphone (XXI).—The vinyl compound (XVI; 0.6 g.) and phenylthiol (0.485 g.) were mixed, and the initial reaction completed by heating at 100° in a sealed tube for 30 minutes. The crude thioether (XVII) without further purification was treated with perhydrol-acetic acid in the usual manner; the required trisulphone (XXI) was deposited; it crystallised from aqueous acetic acid in plates, m. p. 217° (yield, 85%) (Found : S, 28.15. C₁₁H₁₆O₆S₃ requires S, 28.25%).

1 : 2-Di-(2-methylthioethylthio)ethane (XIII).—(a) Ethylene dibromide (1.74 g.) was added to a solution of 2-methyl-

thioethylthiol (VIII; 2 g.) in sodium ethoxide solution (from 0.43 g. of sodium), and the mixture refluxed for 30 minutes. Sodium bromide was removed by filtration; the filtrate on cooling deposited the required product, m. p. 66.5°.

(b) Methyl 2-chloroethyl sulphide (VII; 0.41 g.) was added to a solution of ethylenedithiol [from ethylene sulphide (Meade, private communication), 0.38 g.] in sodium ethoxide solution (2 equivs.) and the mixture refluxed for 30 minutes. Chloroform and dilute acid were then added, and the chloroform layer was separated, dried, and concentrated under reduced pressure. The residue was purified by distillation and crystallisation to give the required product, m. p. 63°.

(c) 2-Chloro-2'-methylthiodiethyl sulphide (XV; 2.55 g.) was added to a solution of the thiol (VIII) (1.6 g.) in sodium ethoxide solution (from 0.34 g. of sodium), and the mixture was refluxed for 30 minutes. Sodium chloride was removed by filtration; the filtrate on cooling deposited the required product, m. p. (after recrystallisation from ethyl acetate-light petroleum) 64°.

(d) 2-Methylthioethyl vinyl sulphide (XVI; 1.24 g.) was cooled to 0° and the thiol (VIII; 1 g.), also at 0°, added. The mixture was kept overnight at room temperature; by morning it had set to a solid mass, and, after recrystallisation from ethyl acetate-light petroleum, gave the required product, m. p. 66.5°.

The products from each of these four syntheses were shown by mixed m. p. to be identical with the compound prepared as in Part I.

2 : 2'-Di-(2-methylthioethylthio)diethyl Ether (XVIII).—Methyl 2-chloroethyl sulphide (VII; 2 equivs.) was added to a solution of 2 : 2'-dithiodiethyl ether (Bäcker and Stienstra, *Rec. Trav. chim.*, 1933, **52**, 1038; one equiv.) in sodium ethoxide solution (*ca.* 2N; 2 equivs.) and the mixture refluxed for 30 minutes. Chloroform and dilute acid were then added, and the chloroform layer was separated, dried, and concentrated. The residue was distilled and subsequently crystallised from benzene-light petroleum; m. p. 35.5°, identical by mixed m. p. with the compound prepared as in Part I.

2-Chloro-2'-methylsulphonyldiethyl Sulphone (XX).—(a) 2-Chloro-2'-methylthiodiethyl sulphide (XIV) was oxidised as usual with perhydrol-acetic acid. The product (XX) was deposited in almost theoretical yield on cooling; needles from water, m. p. 162°.

(b) 2 : 2'-Di-(2-methylsulphonylethylsulphonyl)diethyl ether (XIX; cf. Part I) was recovered unchanged after being heated to 150° with concentrated hydrochloric acid for 4 hours. When, however, the compound (0.2 g.) was heated with glacial acetic acid (1 c.c.) and concentrated hydrochloric acid (1 c.c.) in a sealed tube at 200° for 4 hours, the chloro-disulphone (XX) was deposited in 80% yield on cooling, m. p. 160°.

The products from these two syntheses were shown by mixed m. p. to be identical with the compound as prepared from sodium methanesulphinate and dichlorodiethyl sulphone (Moggridge, in the press).

2-Bromo-2'-methylsulphonyldiethyl Sulphone.—2 : 2'-Di-(2-methylsulphonylethylsulphonyl)diethyl ether (XIX) was recovered unchanged after being heated to 150° for 4 hours with a mixture of glacial acetic and concentrated hydrobromic acids. When, however, the compound (4.2 g.) was heated at 200° for 3 hours with hydrobromic acid (16 c.c.; *d* 1.5) and bromine (1 c.c.), the required bromo-compound was deposited on cooling in 75% yield; needles from water or from glacial acetic acid, m. p. 185° (Found : Br, 28.65. $C_8H_{11}O_4BrS_2$ requires Br, 28.7%). On being warmed with pure pyridine the compound gave an insoluble *pyridinium* salt, which, after crystallisation from aqueous alcohol, had m. p. 245° (decomp.) (Found : Br, 22.9. $C_{10}H_{16}O_4NBrS_2$ requires Br, 22.4%).

2-Iodo-2'-methylsulphonyldiethyl Sulphone.—The tetrasulphone (XIX; 4 g.) and hydriodic acid (16 c.c.; *d* 1.7) were heated in a sealed tube to 150° for 4 hours; the iodo-compound was deposited on cooling; it crystallised from glacial acetic acid in plates, m. p. 219° (yield, 70%) (Found : I, 38.6; S, 19.4. $C_8H_{11}O_4IS_2$ requires I, 38.9; S, 19.6%). The *pyridinium* compound, prepared as for the bromo-derivative, had m. p. 220° (decomp.); mixed m. p. with the iodo-compound showed marked depression (Found : I, 31.0. $C_{10}H_{16}O_4NIS_2$ requires I, 31.3%).

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