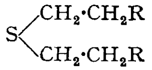
172. *The Methyl Thioethers derived from 2 : 2′-Dichlorodiethyl Sulphide and its Analogues. Part I. Possible Uses for Analysis.*

By E. M. Meade and (the late) R. C. G. Moggridge.

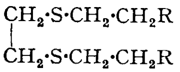
2 : 2′-Dichlorodiethyl sulphide (" mustard gas ") (I) and its higher analogues (II—IV) react with sodium thiomethoxide to give the corresponding methyl thioethers (V—VIII). These are low-melting solids and can be separated by distillation. Attempts have been made to use them for analysis of mixtures of mustard gas and its higher analogues, for which no other method of separation is available. Only partial success has been achieved, since it has been found that small amounts of the thioethers (VI) and (VIII) can be isolated after treatment of pure mustard gas with the thiomethoxide.

The study of mixtures of 2 : 2′-dichlorodiethyl sulphide (" mustard gas ") (I) with its higher analogues, *e.g.*, 1 : 2-di-(2-chloroethylthio)ethane (II), 2 : 2′-di-(2-chloroethylthio)diethyl ether (III), or 2 : 2′-di-(2-chloroethylthio)diethyl sulphide (IV), is complicated by the difficulty of separating the constituents; it is hard to obtain even approximate estimates of the amounts of the various compounds present. Their chemical similarity makes it hard to devise any chemical differentiation; and, while mustard gas can be distilled at reduced pressures without decomposition, the other three compounds decompose on attempted distillation at pressures of the order of 1—5 mm. (unpublished work; cf. also Davies and Oxford, *J.*, 1931, 224).



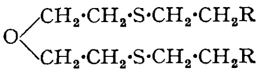
$S\left\langle\begin{matrix}CH_2\cdot CH_2R\\CH_2\cdot CH_2R\end{matrix}\right.$

(I; R = Cl.)
(V; R = SMe.)



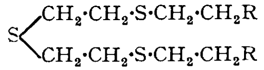
$\begin{matrix}CH_2\cdot S\cdot CH_2\cdot CH_2R\\|\\CH_2\cdot S\cdot CH_2\cdot CH_2R\end{matrix}$

(II; R = Cl.)
(VI; R = SMe.)



$O\left\langle\begin{matrix}CH_2\cdot CH_2\cdot S\cdot CH_2\cdot CH_2R\\CH_2\cdot CH_2\cdot S\cdot CH_2\cdot CH_2R\end{matrix}\right.$

(III; R = Cl.)
(VII; R = SMe.)



$S\left\langle\begin{matrix}CH_2\cdot CH_2\cdot S\cdot CH_2\cdot CH_2R\\CH_2\cdot CH_2\cdot S\cdot CH_2\cdot CH_2R\end{matrix}\right.$

(IV; R = Cl.)
(VIII; R = SMe.)

This paper describes an attempt to overcome these difficulties by preliminary conversion into the *methyl thioethers* (V—VIII). These are readily obtained in very high yield by the action of alcoholic sodium thiomethoxide on the chloro-compounds. They crystallise readily and can be distilled without apparent decomposition; their stability and non-vesicant nature make them much easier to handle than the parent chloro-compounds. The corresponding *sulphones* are obtained by action of peracetic acid.

The methyl thioethers appeared to be suitable for distillation analysis, and reasonable results were obtained in control experiments with synthetic mixtures of (I), (II), and (IV). It was therefore hoped that the method would prove useful for approximate analyses of mustard gas mixtures. In the course of such analytical experiments, however, two observations were made which suggested that the application of the method to problems requiring any delicacy of analysis was unsound. Thus :

(*a*) During analyses, particularly in cases when, owing to the presence of tarry residues, the mixtures had to be heated strongly to ensure complete distillation, low-boiling products were observed. These presumably indicated the presence of decomposition reactions, and therefore cast doubt on the quantitative nature of the analysis. An investigation into the nature of the products of decomposition of (V) is described in Part II of this series (Charnock and Moggridge, following paper).

(*b*) When the formation of the methyl thioether from mustard gas was studied carefully, it was found that the product contained small amounts of (VI) and (VIII); the amounts isolated from pure mustard gas were of the order of 1% and 0·02% (molar ratios) respectively. Pure (V) could be repeatedly redistilled without any sign of (VI) or (VIII) being observed; it therefore appears that these compounds were produced not during the distillation but during the reaction with the thiomethoxide. The occurrence of this reaction was so unexpected as to cast some doubt on the structure of the compounds concerned; these have, however, since been confirmed by independent syntheses (cf. Part III, Brown and Moggridge, this vol., p. 816). It seems possible that the mechanism of this reaction may be similar to that proposed by Bell, Bennett, and Hock (*J.*, 1927, 1803) for the analogous formation of 1 : 2-di-(2-cyanoethylthio)ethane when mustard gas is treated with potassium cyanide (Davies, *J.*, 1920, **117**, 297).

The occurrence of this reaction, even though only to a small extent, clearly attacks the logical basis of the analytical method. It is concluded that the results given by the method can at best only be regarded as rough approximations; in particular, that the isolation of small amounts of (VI) and (VIII) must not be taken as evidence of the presence of (II) and (IV) in the original mixture.

EXPERIMENTAL.

Starting materials were mustard gas (I) (cf. Clarke, *J.*, 1912, **101**, 1583); 1 : 2-di-(2-chloroethylthio)ethane (II) (cf. Bennett and Whincop, *J.*, 1921, 1862); 2 : 2′-di-(2-chloroethylthio)diethyl ether (III) (cf. Davies and Oxford, *loc. cit.*; Woodward, private communication); and 2 : 2′-di-(2-chloroethylthio)diethyl sulphide (IV) (Woodward, private communication).

Preparation of the Thioethers.—To the chloro-compound (1 equiv.) in a large flask fitted with an efficient reflux was added a solution of sodium thiomethoxide in alcohol, prepared by distilling methylthiol (1·3 equivs.; *Org. Synth.*, Coll. Vol. 2, 346) into sodium ethoxide solution (from 1·25 equivs. of sodium). The mixture was cautiously warmed, and the vigorous reaction which ensued was completed by refluxing for 30 minutes. Then, either (*a*) the mixture was cooled, sodium chloride removed by filtration, and the filtrate evaporated to dryness under reduced pressure, or (*b*) equal volumes of chloroform and dilute acid were added to the mixture, and the chloroform layer was separated. The aqueous layer was again extracted with chloroform, and the combined extracts were dried and evaporated to dryness under reduced pressure. In either case the crude thioether was obtained in almost theoretical yield and was purified by distillation; yield of distilled material 80—90%.

For conversion into the sulphone the thioether was treated with a large excess (in a typical case 20 c.c. for 0·25 g. of thioether) of a mixture (1 : 1) of perhydrol and glacial acetic acid. A reaction occurred with evolution of heat; it was completed either by keeping at room temperature for 24—48 hours, or by heating at 100° for 1 hour. The crude sulphone was in either case deposited from the reaction mixture in 80—90% yield.

2 : 2′-*Dimethylthiodiethyl sulphide* (V) had m. p. 24·3°, b. p. 118°/1 mm., 125°/2·5 mm., 137°/6 mm., about 260°/760 mm.; d^{25° 1·08935 (temperature gradient, 0·00085 per degree); n^{25° 1·55835 (temperature gradient, 0·00045 per degree); [*R*] 53·89 (calc., 53·83) (Found : S, 52·4. $C_6H_{14}S_3$ requires S, 52·7%). 2 : 2′-*Dimethylsulphonyldiethyl sulphone* formed colourless plates from aqueous acetic acid (50%), m. p. (no decomp.) 265° (Found : C, 25·5; H, 4·95; S, 35·16. $C_6H_{14}O_6S_3$ requires C, 25·85; H, 5·08; S, 34·5%).

1 : 2-*Di*-(2-*methylthioethylthio*)*ethane* (VI) formed colourless plates from alcohol or light petroleum, m. p. 66·5°, b. p. 180—185/6 mm. (Found : S, 52·95. $C_8H_{18}S_4$ requires S, 52·9%). 1 : 2-*Di*-(2-*methylsulphonylethylsulphonyl*)*ethane* formed colourless needles from aqueous acetic acid (50%), m. p. 210° (Found : S, 34·8. $C_8H_{18}O_8S_4$ requires S, 34·6%).

2 : 2′-*Di*-(2-*methylthioethylthio*)*diethyl ether* (VII) formed colourless plates from light petroleum, m. p. 37°, b. p. 210°/1 mm. (Found : S, 44·35. $C_{10}H_{22}OS_4$ requires S, 44·7%). 2 : 2′-*Di*-(2-*methylsulphonylethylsulphonyl*)*diethyl ether* formed colourless plates from aqueous acetic acid (50%), m. p. 198° (Found : S, 31·1. $C_{10}H_{22}O_9S_4$ requires S, 30·95%).

2 : 2′-*Di*-(2-*methylthioethylthio*)*diethyl sulphide* (VIII) formed colourless needles from alcohol or light petroleum, m. p. 88° (Found : S, 53·2. $C_{10}H_{22}S_5$ requires S, 53·0%). 2 : 2′-*Di*-(2-*methylsulphonylethylsulphonyl*)*diethyl sulphone* was insoluble in all normal solvents, but was crystallised from a mixture of water and concentrated nitric acid (equal vols.); colourless needles, m. p. 220° (decomp.) (Found : S, 34·4. $C_{10}H_{22}O_{10}S_5$ requires S, 34·6%).

Control Analytical Experiments.—The following is typical of several control experiments. The synthetic dichloro-compounds (I), (II), and (IV) were mixed in a weight ratio of 10, 75, and 15% respectively. 19·7 G. of this mixture were converted into the thioethers, which were separated by distillation; weights of fractions 2·7, 14·8, and 2·65 g. respectively, giving ratio of chloro-compounds found 13, 73·5, and 13·5% respectively.

Isolation of (VI) *and* (VIII) *from the Products of Interaction of Mustard Gas and Sodium Thiomethoxide.*—In these experiments the reaction with the thiomethoxide solution was carried out as usual and the crude product twice distilled. The residues from these distillations were mixed and distilled in small solid-distillation flasks until the (VI) fraction was obtained solid at room temperature. Final purification was then effected by recrystallisation. The residues from the solid distillations were recrystallised to give (VIII).

The results of these experiments are given below. The m. p. of pure mustard gas is generally given as 14·35°. The quoted yields refer to material melting at 63° for (VI), and 84° for (VIII). The purification necessary refers to (VI). Both compounds were identified by mixed m. p. with synthetic specimens.

(1) 76 G. of mustard gas, m. p. 13·8°. Residue split by distillation into three fractions; purification necessary ranged from 2 distillations and 1 recrystallisation to 4 distillations and 2 recrystallisations. Total yields—(VI), 1·9 g.; (VIII), 0·02 g.

(2) 133 G. of mustard gas, m. p. 14·1°. Purification necessary, 2 distillations, 3 recrystallisations. Yield of (VI), 1·4 g.; of (VIII), 0·04 g.

(3) 100 G. of mustard gas, m. p. 14·35°. Purification necessary, 1 distillation, 3 recrystallisations. Yield of (VI), 1·4 g.; of (VIII), 0·04 g.

Control Experiments.—(*a*) Pure (V) was repeatedly redistilled under conditions identical with those used in the above experiments. The distillation residues were very small and no sign of (VI) or (VIII) could be detected by their distillation or recrystallisation.

(*b*) Pure (VI) was added to batches of 17—20 g. of pure (V), and isolation experiments carried out exactly as above. The results were as follows :

(i) 3·0 G. of (VI) added. Purification necessary, one distillation. Recovery, 87%.
(ii) 1·5 G. of (VI) added. Purification necessary, one distillation. Recovery, 73%.
(iii) 1·0 G. of (VI) added. Purification, 1 distillation and 2 recrystallisations. Recovery, 50%.

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RESEARCH ESTABLISHMENT, SUTTON OAK.

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