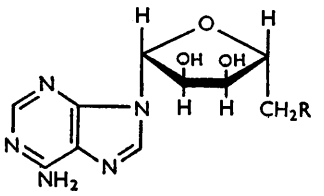
433. *Dithiols. Part XX.* The Occurrence of Transthiomethylation in Some Reactions of 2 : 3-Bismethylthiopropanol and Related Compounds.*

By PETER S. FITT and L. N. OWEN.

Treatment of 2 : 3-bismethylthiopropyl acetate with hot dilute acid gives mainly 1 : 2 : 3-trismethylthiopropane, with small amounts of 1 : 3-bismethylthiopropan-2-ol and methanethiol. The trismethylthio-compound is also formed similarly from 2 : 3-bismethylthiopropanol or its methyl ether. The probable courses of these reactions, involving sulphonium intermediates, are outlined. In the absence of a vicinal dithiol system, transthiomethylation occurs much less readily; 2-acetoxy-1 : 3-bisacetylthiopropane gives a small yield of 1 : 2 : 3-trismethylthiopropane, and 2-methylthioethanol is only slowly converted into 1 : 2-bimethylthioethane.

THE importance of methylthio-compounds in certain biological processes is well recognised, and, in particular, the rôle of methionine as a methyl donor has received much attention.[1] The so-called " active methionine " (I), originally prepared [2] enzymically from methionine and adenosine triphosphate and later synthesised,[3] is of special interest because it can not only transfer a methyl group to, for example, nicotinamide, but also [4] can be hydrolysed under mild conditions to give 5'-deoxy-5'-methylthioadenosine (II); effectively, therefore, a methylthio-group has been transferred from methionine to replace a hydroxyl group in adenosine. Active methionine is very probably [4, 5] an intermediate in the microbiological formation of (II), for which an ample supply of methionine is necessary in the



I; R = $^{+}$SMe·CH$_2$·CH$_2$·CH(NH$_2$)·CO$_2^-$]
(II; R = SMe)

$$S\{[CH_2]_2\cdot\overset{+}{S}Me\cdot[CH_2]_2\cdot CH(NH_2)\cdot CO_2H\}_2 \xrightarrow{2H_2O} 2H^+ + S\{[CH_2]_2\cdot SMe\}_2 + 2HO\cdot[CH_2]_2\cdot CH(NH_2)\cdot CO_2H$$
(III) (IV) (V)

culture medium.[5, 6] No other instances of biological transthiomethylation appear to be known, but an earlier purely chemical example was recorded by Stein and Moore,[7] who showed that methionine reacted with 2 : 2'-dichlorodiethyl sulphide (mustard gas) in aqueous hydrochloric acid to give the sulphonium salt (III), which when heated gave 2 : 2'-di(methylthio)diethyl sulphide (IV) and 2-amino-4-hydroxybutanoic acid (V) together with much methionine; breakdown around the sulphur atom was thus occurring in two of the three possible ways. The formation of sulphonium intermediates, both by inter- and intra-molecular reactions, is of course well known in analogous systems involving groups more complex than methyl, as in mustard gas itself.[8]

* Part XIX, preceding paper.

[1] Challenger, *Quart. Rev.*, 1955, **9**, 255.
[2] Cantoni, *J. Amer. Chem. Soc.*, 1952, **74**, 2942; *J. Biol. Chem.*, 1953, **204**, 403.
[3] Baddiley and Jamieson, *J.*, 1954, 4280.
[4] Baddiley, Cantoni, and Jamieson, *J.*, 1953, 2662.
[5] Weygand, Junk, and Leber, *Z. physiol. Chem.*, 1952, **291**, 191.
[6] Smith and Schlenk, *Arch. Biochem.*, 1952, **38**, 167.
[7] Stein and Moore, *J. Org. Chem.*, 1946, **11**, 681.
[8] Stahmann, Fruton, and Bergmann, *ibid.*, p. 704; Price and Wakefield, *ibid.*, 1947, **12**, 232.

In connection with studies on the hydrolysis of acetylated hydroxy-thiols, which have revealed [9] that an *O*-acetate can undergo O–alkyl fission when displaced by a neighbouring thiol group, it was of interest to examine the behaviour of 2 : 3-bismethylthiopropyl acetate (VI). 2 : 3-Bismethylthiopropanol has been prepared [10] by selective methylation of 2 : 3-dimercaptopropanol with methyl sulphate and sodium hydroxide; we have now found that it is also formed by the use of diazomethane, the thiol groups, as expected, being preferentially methylated. Acetylation gave the acetate (VI) as a liquid; characterisation of this by oxidation with hydrogen peroxide in acetic acid resulted in simultaneous hydrolysis and gave 2 : 3-bismethylsulphonylpropanol (VII), which on reacetylation gave the disulphone corresponding to (VI). Alkaline hydrolysis of 2 : 3-bismethylthiopropyl acetate took place normally and gave 2 : 3-bismethylthiopropanol, but in boiling 0·7N-aqueous-methanolic hydrochloric acid there was a slow evolution of methanethiol (trapped and identified as its mercurichloride and mercaptide). After reaction for 3 hr. the products were isolated, but they could not be completely separated

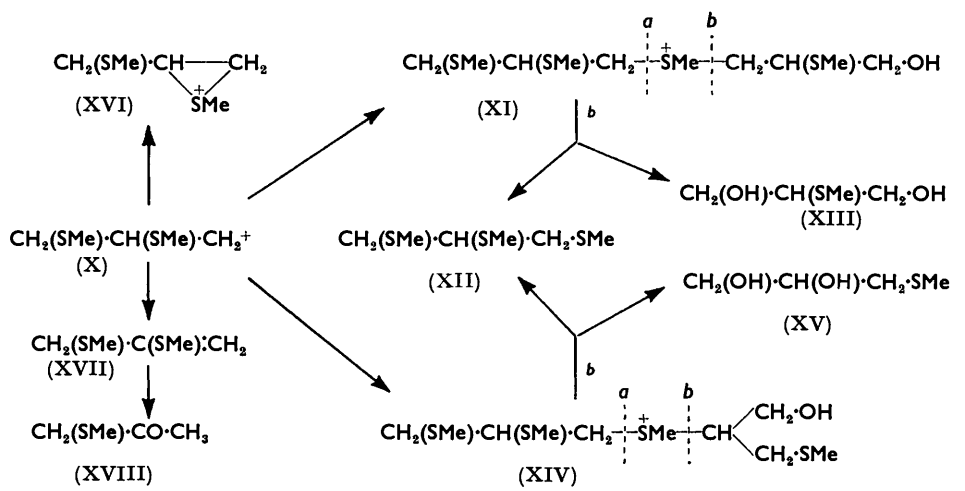
$CH_2(SMe)\cdot CH(SMe)\cdot CH_2\cdot OAc$ (VI)

$CH_2(SO_2\cdot Me)\cdot CH(SO_2\cdot Me)\cdot CH_2\cdot OH$ (VII)

$CH_2(SO_2\cdot Me)\cdot CH(SO_2\cdot Me)\cdot CH_2\cdot SO_2\cdot Me$ (VIII)

$CH_2(SO_2\cdot Me)\cdot CH(OH)\cdot CH_2\cdot SO_2\cdot Me$ (IX)

by distillation, and a puzzling feature was that the sulphur content of the higher-boiling fractions was greater than any calculated value for a likely product containing two sulphur atoms per propyl unit. The product was therefore oxidised with hydrogen peroxide in acetic acid to give a mixture of sulphones, which by a combination of extraction and fractional crystallisation was separated into three crystalline products. The major constituent was 1 : 2 : 3-trismethylsulphonylpropane (VIII), identical with authentic material prepared from propane-1 : 2 : 3-trithiol by Rheinboldt and Tetsch's method; [11] the other two were 1 : 3-bismethylsulphonylpropan-2-ol (IX), and, in smallest amount, 2 : 3-bismethylsulphonylpropanol (VII). It follows that acid hydrolysis of 2 : 3-bismethyl-



thiopropyl acetate gives mainly 1 : 2 : 3-trismethylthiopropane, with a little 1 : 3-bismethylthiopropan-2-ol, and a trace of the " normal " product. Repetition of the reaction, with 0·7N-aqueous-methanolic sulphuric acid instead of hydrochloric acid, again gave a product which on oxidation furnished the trisulphone (VIII), though in smaller yield.

[9] Fitt and Owen, preceding paper, and references there cited.
[10] Evans, Fraser, and Owen, *J.*, 1949, 248.
[11] Rheinboldt and Tetsch, *Ber.*, 1937, **70**, 680.

From the above results it seemed likely that 2 : 3-bismethylthiopropanol itself would also undergo transthiomethylation, and when it was heated with aqueous-methanolic hydrochloric acid methanethiol was again evolved, and oxidation of the reaction product gave the trisulphone (VIII). The reaction was also carried out in the absence of organic solvent, with the same result, by heating a suspension of 2 : 3-bismethylthiopropanol in 0·7N-aqueous hydrochloric acid at 100°.

In order to determine whether etherification of the hydroxyl group would prevent the reaction, 2 : 3-bismethylthiopropyl methyl ether was synthesised by complete methylation of 2 : 3-dimercaptopropanol and also by conventional means from 2 : 3-dibromopropyl methyl ether, *via* 2 : 3-bisacetylthiopropyl methyl ether and the free dithiol. The ether proved to be much more resistant but, under the same conditions as above, methanethiol was formed, and oxidation of the product gave a small amount of the trisulphone (VIII) together with much 2 : 3-bismethylsulphonylpropyl methyl ether. Methyl ethers are not normally hydrolysed by such dilute acid, and the neighbouring sulphide group clearly has a powerful displacing effect.

The mechanism of these transthiomethylations is undoubtedly similar to those involving methionine, in that sulphonium compounds must be formed as intermediates. Under acid conditions, conversion of 2 : 3-bismethylthiopropanol, its acetate, and its methyl ether into the carbonium ion (X), followed by intermolecular attack on the sulphur atom of the primary methylthio-group of a second molecule (taken, for illustration, to be the free alcohol), would give the sulphonium ion (XI), which by breakdown at *a* or *b* respectively would either regenerate 2 : 3-bismethylthiopropanol or give the trismethylthio-compound (XII) and the monomethylthio-fragment (XIII). A similar intermolecular attack by the carbonium ion on the secondary methylthio-group would lead to the sulphonium ion (XIV), from which, according to the position of fission, either 2 : 3-bismethylthiopropanol or the trismethylthio-compound (XII) and the fragment (XV) could be formed. The sulphones derived from (XIII) and (XV) were possibly present in the liquid residues after isolation of the di- and tri-sulphones, but attempts to prove their presence were unsuccessful. The formation of 1 : 3-bismethylthiopropan-2-ol in the hydrolysis can be explained by the supposition that the carbonium ion (X) can also undergo intramolecular reaction with the neighbouring sulphur atom to give the cyclic sulphonium ion (XVI), which on fission can clearly yield either the 2 : 3- or the 1 : 3-bismethylthio-compound. The acyclic ions (XI) and (XIV) could of course arise also by a bimolecular mechanism not involving a carbonium ion, whilst the cyclic ion (XVI) could be formed by a concerted intramolecular displacement of OAc^-, OH^-, or OMe^- by the neighbouring methylthio-group. Although both uni- and bi-molecular reactions may therefore be involved, from analogy with the behaviour of mustard gas a carbonium-ion intermediate appears, however, to be favoured.

The source of the methanethiol is not immediately obvious, because its formation by breakdown of any of the possible sulphonium salts requires the simultaneous fission of the two bonds *a* and *b*, which is highly improbable. On the other hand, it appears not to be derived by direct fission of a methylthio-group from a saturated methyl sulphide, since 1 : 2-bismethylthiopropane (synthesised by direct methylation of the dithiol) was unaffected by boiling methanolic hydrochloric acid. The most likely explanation is that the carbonium ion (X) to a small extent undergoes elimination to yield the vinyl sulphide (XVII), which under acid conditions would be hydrolysed [12] to the ketone (XVIII) with loss of methanethiol. The carbonium-ion precursors of the monomethylthio-compounds (XIII) and (XV) could behave similarly. The lower-boiling fractions of the hydrolysis products did in fact give ketonic reactions, though no pure derivatives could be isolated. The number of possible products is of course not exhausted by the reactions already discussed, because other sulphonium salts, *e.g.*, derived by attack on (XIII) or (XV), can evidently be formed and lead to further by-products.

[12] Cf. Bernstein and Dorfman, *J. Amer. Chem. Soc.*, 1946, **68**, 1152; Rosenkranz, Kaufmann, and Romo, *ibid.*, 1949, **71**, 3689; Romero, Djerassi, and Rosenkranz, *ibid.*, 1951, **73**, 1528.

The striking difference in behaviour towards alkaline hydrolysis shown by 2 : 3-bisacetylthiopropyl acetate, which readily yields an episulphide, and 2-acetoxy-1 : 3-bisacetylthiopropane, which undergoes normal hydrolysis,[9] is an illustration of the special effect which a vicinal dithiol system has upon the reactivity of a neighbouring group. It was therefore important to compare the acid hydrolysis of 2-acetoxy-1 : 3-bisacetylthiopropane (XIX) with that of the 2 : 3-isomer discussed above. Selective methylation of 1 : 3-dimercaptopropan-2-ol gave the di-*S*-methyl compound (characterised as the disulphone) which on acetylation furnished the required acetate. When this was treated as before with boiling 0·7N-aqueous-methanolic hydrochloric acid, methanethiol was again evolved; oxidation of the product gave a small proportion of the trisulphone (VIII), the material being mostly 1 : 3-bismethylsulphonylpropan-2-ol. Further evidence on this point was provided by a study of 2-methylthioethanol (XX). When this was heated with 0·7N-aqueous hydrochloric acid at 100° no methanethiol could be detected, but the formation of 1 : 2-bismethylthioethane (XXI) was evident from the characteristically obnoxious odour produced, though after 3 hr. the conversion was so small that it was not possible after oxidation to isolate the crystalline disulphone. Prolongation of the reaction for 20 hr., however, and distillation of the product, gave an oil with a sulphur content intermediate

$CH_2(SMe)\cdot CH(OAc)\cdot CH_2\cdot SMe$ (XIX)

$CH_2(SMe)\cdot CH_2R$ (XX; R = OH) (XXI; R = SMe)

$CH_2(S\cdot CH_2Ph)\cdot CH(S\cdot CH_2Ph)\cdot CH_2\cdot OH$ (XXII)

between those of (XX) and (XXI), and which on oxidation readily furnished 1 : 2-bismethylsulphonylethane. Transthiomethylation therefore occurs in these cases, but much less readily than when a vicinal bismethylthio-system is present.

In contrast to the results obtained with 2 : 3-bismethylthiopropanol, 2 : 3-bisbenzylthiopropanol (XXII) was recovered unchanged after treatment with boiling 0·7N-aqueous-methanolic hydrochloric acid. Increase in acid concentration merely resulted in the formation of 2 : 3-bisbenzylthiopropyl chloride, since oxidation of the product gave only the corresponding sulphone, no trisbenzylsulphonylpropane being detected.

Experimental

2 : 3-*Bismethylthiopropanol*.—A solution of diazomethane in *cyclo*hexane (200 c.c.), prepared from methylnitrosourea (11·4 g.), was slowly added to a stirred suspension of 2 : 3-dimercaptopropanol (2·6 g.) in *cyclo*hexane (50 c.c.). The mixture was set aside overnight, then shaken for a few minutes with acid-moistened charcoal and filtered. Concentration, and distillation of the residue, gave a main fraction (1·0 g.) of 2 : 3-bismethylthiopropanol, b. p. 89°/1 mm., n_D^{21} 1·5460. The same product was also prepared by Evans, Fraser, and Owen's method.[10] The α-naphthylurethane, recrystallised from light petroleum (b. p. 100—120°), had m. p. 84°; Evans, Fraser, and Owen gave m. p. 71°, but recrystallisation of their original specimen gave material with m. p. and mixed m. p. 82—83°.

2 : 3-*Bismethylthiopropyl Acetate*.—2 : 3-Bismethylthiopropanol (3·8 g.), fused sodium acetate (1 g.) and acetic anhydride (25 c.c.) were heated together at 100° for 8 hr. The cooled solution was then poured into water, and the oil, isolated by extraction with chloroform, on distillation afforded the *acetate* (4·9 g.), b. p. 88°/0·1 mm., n_D^{19} 1·5131 (Found: C, 43·35; H, 7·2; S, 33·3. $C_7H_{14}O_2S_2$ requires C, 43·3; H, 7·3; S, 33·0%).

2 : 3-*Bismethylsulphonylpropanol*.—(i) 2 : 3-Bismethylthiopropanol (0·6 g.) in acetic acid (2·5 c.c.) was treated dropwise with 30% hydrogen peroxide (2 c.c.). After the vigorous reaction had moderated, more hydrogen peroxide (2 c.c.) was added, and the solution was evaporated to dryness on the steam-bath. Recrystallisation of the residue from ethanol furnished the *disulphone* (0·6 g.), m. p. 123—124° (Found: C, 28·0; H, 5·7; O, 37·1; S, 29·2. $C_5H_{12}O_5S_2$ requires C, 27·8; H, 5·6; O, 37·0; S, 29·6%).

(ii) Similar treatment of 2 : 3-bismethylthiopropyl acetate (0·45 g.) gave the same product (0·5 g.), m. p. and mixed m. p. 123—124°.

2 : 3-*Bismethylsulphonylpropyl Acetate.*—Acetyl chloride (0·4 g.) was cautiously added to a solution of the above disulphone (0·8 g.) in dry pyridine (3 c.c.). The mixture was then heated on the steam-bath for 30 min., then concentrated under reduced pressure, and diluted with water. Extraction with chloroform gave a solid (0·3 g.), which on recrystallisation from methanol afforded 2 : 3-*bismethylsulphonylpropyl acetate*, m. p. 117—119° (Found : C, 33·0; H, 5·8; O, 37·2. $C_7H_{14}O_6S_2$ requires C, 32·55; H, 5·5; O, 37·2%).

2 : 3-*Bisacetylthiopropyl Methyl Ether.*—2 : 3-Dibromopropyl methyl ether [13] (23 g.), potassium thiolacetate (25 g.), and ethanol (300 c.c.) were stirred and heated under reflux in an atmosphere of nitrogen for 2 hr. The cooled mixture was filtered, then concentrated under reduced pressure and diluted with water. The oil which separated was isolated by extraction with ether, and on distillation furnished 2 : 3-bisacetylthiopropyl methyl ether (18 g.), b. p. 72—73°/0·3 mm., n_D^{20} 1·5146. Previously prepared by another route it was reported [14] to have b. p. 158—159°/13 mm., n_D^{25} 1·5143.

2 : 3-*Dimercaptopropyl Methyl Ether.*—The above bisthiolacetate (13 g.), methanol (90 c.c.), and concentrated hydrochloric acid (10 c.c.) were boiled under reflux for 6 hr. in nitrogen. Most of the methanol was then removed under reduced pressure and the residue was diluted with water and extracted with ether to give the dithiol (4·1 g.), b. p. 57—63°/2 mm., n_D^{22} 1·515—1·518 (lit.,[15] b. p. 63—65°/6 mm., n_D^{25} 1·5178).

2 : 3-*Bismethylthiopropyl Methyl Ether.*—(i) Methyl sulphate (2·5 g.) was added dropwise to a stirred solution of the above dithiol (2·5 g.) in 30% aqueous sodium hydroxide (20 c.c.) at *ca.* 60°, under nitrogen. Stirring and heating were continued for 3 hr., and the mixture was then cooled and extracted with ether to give 2 : 3-*bismethylthiopropyl methyl ether* (1·0 g.), b. p. 110—114°/15 mm., n_D^{21} 1·5122 (Found : C, 43·7; H, 8·6; S, 37·7. $C_6H_{14}OS_2$ requires C, 43·4; H, 8·5; S, 38·6%). On oxidation with 30% hydrogen peroxide in acetic acid it gave 2 : 3-*bismethylsulphonylpropyl methyl ether*, which after recrystallisation from methanol had m. p. 112—113° (Found : C, 31·25; H, 6·3; O, 34·9. $C_6H_{14}O_5S_2$ requires C, 31·3; H, 6·1; O, 34·7%).

(ii) (With L. W. C. Miles.) Methyl sulphate (40 g.) was added, during 1 hr., to a stirred solution of 2 : 3-dimercaptopropanol (10 g.) in 30% aqueous sodium hydroxide (100 c.c.); the heat of reaction maintained the temperature at about 60°. Stirring was maintained for a further hour at 50° and for 30 min. at 100°, and the solution was then cooled and extracted with ether. Distillation of the product gave the *OSS*-trimethyl derivative (4·3 g.), b. p. 64—66°/1 mm., n_D^{20} 1·5155 (Found : S, 38·8%).

1 : 2-*Bismethylthiopropane.*—1 : 2-Dibromopropane (28 g.), potassium thiolacetate (35 g.), and ethanol (200 c.c.) were heated and stirred together under reflux for 8 hr. Concentration of the mixture, dilution of the residue with water, and extraction with ether gave 1 : 2-bisacetylthiopropane (21 g.), b. p. 79—80°/0·01 mm., n_D^{22} 1·5190. For a preparation by a different method the reported [16] constants were b. p. 93°/1 mm., n_D^{21} 1·5197.

Hydrolysis of the bisthiolacetate (19 g.) by boiling a solution in methanol (120 c.c.) and concentrated hydrochloric acid (6 c.c.) for 3 hr., followed by concentration, dilution with water, and extraction with ether, furnished 1 : 2-dimercaptopropane (3·8 g.), b. p. 52—56°/25 mm., n_D^{20} 1·527—1·531 (lit.,[17] b. p. 72—74°/55 mm.).

Methyl sulphate (7·5 g.) was slowly added to a stirred solution of this dithiol (3·8 g.) in sodium hydroxide (3 g.) and water (10 c.c.), and the temperature was finally raised to 95° for 30 min. Extraction of the cooled mixture with ether gave 1 : 2-*bismethylthiopropane* (2·1 g.), b. p. 75—76°/18 mm., n_D^{23} 1·5150 (Found : C, 44·35; H, 9·0. $C_5H_{12}S_2$ requires C, 44·1; H, 8·9%). Oxidation with 30% hydrogen peroxide in acetic acid, and recrystallisation of the product from methanol, gave 1 : 2-*bismethylsulphonylpropane*, m. p. 115—117° (Found : C, 30·1; H, 6·0; S, 31·6. $C_5H_{12}O_4S_2$ requires C, 30·0; H, 6·0; S, 32·0%).

1 : 3-*Bismethylthiopropan-2-ol.*—A stirred solution of 1 : 3-dimercaptopropan-2-ol [18] (8 g.) in 20% aqueous sodium hydroxide (40 c.c.) was treated with methyl sulphate (16 g.) during 30 min. at 75—90°. Extraction of the cooled mixture with ether gave the *di*-S-*methyl* derivative (3·5 g.), b. p. 66—68°/0·2 mm., n_D^{20} 1·5371 (Found : C, 39·4; H, 7·9; S, 41·3. $C_5H_{12}OS_2$

[13] Irvine, Macdonald, and Soutar, *J.*, 1915, **107**, 349.
[14] Bader, Cross, Heilbron, and Jones, *J.*, 1949, 619.
[15] Pavlic and Peppel, U.S.P. 2,397,689/1946.
[16] Chapman and Owen, *J.*, 1950, 579.
[17] Culvenor, Davies, and Heath, *J.*, 1949, 282.
[18] Johary and Owen, *J.*, 1955, 1303.

requires C, 39·4; H, 7·9; S, 42·1%). Oxidation with hydrogen peroxide in acetic acid gave 1 : 3-*bismethylsulphonylpropan-2-ol*, which after recrystallisation from methanol had m. p. 133—135° (Found : C, 27·6; H, 5·7; O, 36·7. $C_5H_{12}O_5S_2$ requires C, 27·8; H, 5·6; O, 37·0%).

2-Acetoxy-1 : 3-*bisacetylthiopropane*.—1 : 3-Bismethylthiopropan-2-ol (3 g.), fused sodium acetate (1 g.), and acetic anhydride (20 c.c.) were heated together at 100° for 5 hr. The product, isolated as described above for the 2 : 3-isomer, on distillation gave the *acetate* (1·5 g.), b. p. 99—101°/3 mm., n_D^{20} 1·5060 (Found : C, 43·6; H, 7·2; S, 33·1. $C_7H_{14}O_2S_2$ requires C, 43·3; H, 7·3; S, 33·0%).

2-*Methylthioethanol*.[19]—Methyl sulphate (25 g.) was added to a stirred solution of 2-mercaptoethanol (15 g.) in 25% aqueous sodium hydroxide (45 c.c.) at such a rate that the temperature was maintained at 60—70°. Stirring was maintained for a further 30 min. and the product was then isolated by extraction with ether. Distillation afforded 2-methylthioethanol (11·7 g.), b. p. 61°/10 mm., n_D^{20} 1·4930 (lit.,[20] b. p. 81°/30 mm., n_D^{30} 1·4867).

Alkaline Hydrolysis of 2 : 3-*Bismethylthiopropyl Acetate*.—The acetate (1·9 g.) was vigorously stirred for 6 hr. with a solution of sodium hydroxide (4 g.) in water (50 c.c.). Extraction with ether then furnished an oil, which on distillation gave 2 : 3-bismethylthiopropanol (1·0 g.), b. p. 81°/0·02 mm., n_D^{20} 1·5462, characterised as the α-naphthylurethane, m. p. and mixed m. p. 80—82°.

Acid Hydrolysis of 2 : 3-*Bismethylthiopropyl Acetate*.—(i) The acetate (21 g.), methanol (100 c.c.), and 2N-aqueous hydrochloric acid (50 c.c.) were boiled together under reflux for 3 hr. in a slow stream of nitrogen, the gases being passed through (*a*) aqueous mercuric cyanide and (*b*) aqueous mercuric chloride. Methanethiol, m. p. 176—177° (lit., 176°), and methanethiol mercurichloride (Found : C, 4·2; H, 1·2. Calc. for $CH_3{\cdot}SHgCl$: C, 4·2; H, 1·0%) were respectively precipitated. The solution was then cooled, made alkaline with aqueous sodium hydroxide, then just acidified with hydrochloric acid and extracted continuously with ether overnight. Evaporation of the dried (Na_2SO_4) extracts gave a yellow oil (13·5 g.) which contained no free thiol and no halogen (Found : S, 43·85. Calc. for $C_5H_{12}OS_2$: S, 42·1. Calc. for $C_6H_{14}S_3$: S, 52·7%).

Repeated distillation of a portion of this oil failed to give any pure material, though a higher-boiling fraction, b. p. 139—142°/8 mm., n_D^{16} 1·5558, had a significantly high sulphur content (Found : S, 47·3%).

To a portion of the crude oil (6·7 g.), in acetic acid (60 c.c.), 30% hydrogen peroxide (60 c.c.) was added dropwise. The solution was then heated on a steam-bath for 1 hr. and evaporated to dryness. The product was stirred with 30% hydrogen peroxide (40 c.c.) and again evaporated to dryness. The crystalline residue was extracted with hot methanol, and the insoluble portion (2·86 g.), m. p. 203—205°, was recrystallised from water to give 1 : 2 : 3-trismethylsulphonylpropane, m. p. and mixed [11] m. p. 205—207° (Found : C, 26·4; H, 5·0; S, 34·5. Calc. for $C_6H_{14}O_6S_3$: C, 25·9; H, 5·1; S, 34·6%). The methanol extracts were concentrated to give a viscous residue which partly crystallised. The solid (0·9 g.) was collected, drained on a porous tile and then extracted with boiling chloroform; the insoluble residue on recrystallisation from methanol gave 1 : 3-bismethylsulphonylpropan-2-ol (0·3 g.), m. p. and mixed m. p. 132—133°. The porous tile was extracted with methanol to give a viscous brown oil (5·1 g.) which decomposed on attempted distillation.

Similar oxidation of the higher-boiling fraction mentioned above (0·4 g.) gave 1 : 2 : 3-trismethylsulphonylpropane (0·25 g.), m. p. and mixed m. p. 205—206°. Concentration of the methanolic extract and fractional crystallisation of the residue gave a few mg. of 2 : 3-bismethylsulphonylpropanol, m. p. and mixed m. p. 124—126°.

(ii) 2 : 3-Bismethylthiopropyl acetate (1 g.), methanol (10 c.c.), and 2N-aqueous sulphuric acid (5 c.c.) were boiled under reflux for 3 hr. in a slow stream of nitrogen. The product, isolated as a crude oil as described above, was oxidised in acetic acid with hydrogen peroxide to yield a mixture of sulphones (0·65 g.). This was extracted with hot methanol, and the insoluble residue (0·08 g.) on recrystallisation from water gave 1 : 2 : 3-trismethylsulphonylpropane, m. p. and mixed m. p. 207—208°. The methanol extracts were concentrated to a pasty solid, which on recrystallisation from methanol gave 2 : 3-bismethylsulphonylpropane, m. p. and mixed m. p. 124—125°. No methanethiol could be detected in the nitrogen stream.

[19] Cf. Albertson and Tullar, *J. Amer. Chem. Soc.*, 1945, **67**, 502.
[20] Kirner, *ibid.*, 1928, **50**, 2451.

Reaction of 2 : 3-*Bismethylthiopropanol with Hydrochloric Acid.*—(i) 2 : 3-Bismethylthiopropanol (2·4 g.), methanol (10 c.c.), and 2N-aqueous hydrochloric acid (5 c.c.) were boiled together for 5 hr. in a slow stream of nitrogen. Methanethiol was evolved and detected as described above. The product on oxidation with hydrogen peroxide gave 1 : 2 : 3-trismethylsulphonylpropane (0·6 g.), m. p. and mixed m. p. 207—208°.

(ii) A suspension of 2 : 3-bismethylthiopropanol (0·8 g.) in 0·7N-aqueous hydrochloric acid (10 c.c.) was stirred at 100° for 20 hr. in a slow stream of nitrogen; methanethiol was slowly evolved. The cooled mixture was then extracted with ether to yield an oil, which on oxidation furnished the above trisulphone (0·3 g.), m. p. and mixed m. p. 205—207°.

Reaction of 2 : 3-*Bismethylthiopropyl Methyl Ether with Hydrochloric Acid.*—The ether (2·2 g.), methanol (10 c.c.), and 2N-aqueous hydrochloric acid (5 c.c.) were boiled under reflux for 5 hr. in nitrogen; methanethiol was evolved. The product on oxidation gave the same trisulphone (0·10 g.), m. p. and mixed m. p. 206—207°, and 2 : 3-bismethylsulphonylpropyl methyl ether (1·2 g.), m. p. and mixed m. p. 112—113°.

Stability of 1 : 2-*Bismethylthiopropane towards Acid Hydrolysis.*—1 : 2-Bismethylthiopropane (0·76 g.), methanol (4 c.c.), and 2N-aqueous hydrochloric acid (2 c.c.) were boiled under reflux for 3 hr. in a slow stream of nitrogen; no methanethiol could be detected. The product was oxidised to give 1 : 2-bismethylsulphonylpropane (0·76 g.), m. p. and mixed m. p. 115—117°. No other sulphone could be detected.

Reaction of 2-*Acetoxy*-1 : 3-*bisacetylthiopropane with Hydrochloric Acid.*—The acetate (0·7 g.), methanol (4 c.c.), and 2N-aqueous hydrochloric acid (2 c.c.) were boiled under reflux for 3 hr. in nitrogen; methanethiol was evolved. Oxidation of the product gave 1 : 2 : 3-trismethylsulphonylpropane (0·02 g.), m. p. and mixed m. p. 205—207°, and 1 : 3-bismethylsulphonylpropan-2-ol (0·23 g.), m. p. and mixed m. p. 134—135°.

Reaction of 2-*Methylthioethanol with Hydrochloric Acid.*—A solution of 2-methylthioethanol (2 g.) in 0·7N-aqueous hydrochloric acid (4 c.c.) was heated at 100° in nitrogen for 20 hr.; no methanethiol was detected. During the reaction an insoluble oil was gradually formed. The cooled mixture was then extracted with chloroform, and the product was distilled to give a highly odoriferous mobile liquid (0·6 g.), b. p. 63—65°/11 mm., n_D^{18} 1·5020 (Found : S, 39·2. Calc. for C_3H_8OS : S, 34·8. Calc. for $C_4H_{10}S_2$: S, 52·4%). A portion (0·25 g.) in acetic acid (1 c.c.) was oxidised with 30% hydrogen peroxide (3 c.c.), and the solid product on recrystallisation from water gave 1 : 2-bismethylsulphonylethane, m. p. and mixed m. p. 193—194° (Found : C, 26·0; H, 5·5. Calc. for $C_4H_{10}O_4S_2$: C, 25·8; H, 5·4%). Mathias [21] gives m. p. 191—192°.

Reaction of 2 : 3-*Bisbenzylthiopropanol with Hydrochloric Acid.*—(i) A solution of 2 : 3-bisbenzylthiopropanol [18] (4·5 g.) in methanol (25 c.c.) and 2N-aqueous hydrochloric acid (12·5 c.c.) was boiled under reflux for 2 hr. in nitrogen; no toluene-ω-thiol was evolved. The mixture was worked up as before to give unchanged 2 : 3-bisbenzylthiopropanol (4·3 g.) identified by oxidation to 2 : 3-bisbenzylsulphonylpropanol, m. p. and mixed m. p. 170—172°.

(ii) 2 : 3-Bisbenzylthiopropanol (4 g.), methanol (20 c.c.), and concentrated hydrochloric acid (20 c.c.) were treated as described above; no toluene-ω-thiol was evolved. The cooled mixture was diluted with water, and the oil which separated was taken up in ether. The dried (Na_2SO_4) ethereal solution was concentrated and the residue (3·5 g.) was oxidised in the usual way with 30% hydrogen peroxide. The product (1·4 g.), after recrystallisation from acetic acid, furnished 2 : 3-*bisbenzylsulphonylpropyl chloride*, m. p. 204—205° (Found : C, 52·7; H, 5·1; Cl, 9·0. $C_{17}H_{19}O_4S_2Cl$ requires C, 52·8; H, 4·95; Cl, 9·2%).

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[21] Mathias, *Chem. Abs.*, 1946, **40**, 2792.