680. *Trisulphides and Tetrasulphides from Bunte Salts.*

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The synthesis of trisulphides by reaction of sodium *S*-alkyl thiosulphates with sodium sulphide has been improved by adding formaldehyde, which prevents subsequent partial conversion of trisulphide into disulphide by reacting preferentially with the liberated sulphite. Saturation of the reaction mixture with sodium chloride also suppresses disulphide formation, but to a smaller extent. Bunte salts react with sodium disulphide (or higher polysulphides), giving mixtures of tri- and tetra-sulphides. Mixtures of di-, tri-, and tetra-sulphides were analysed by gas–liquid chromatography; for compounds $R{\cdot}S_n{\cdot}R$, where $n = 1$—4, a plot of log (retention volume) against molecular weight was linear for each of the series, R = methyl, ethyl, and allyl.

In an earlier paper [1] the synthesis of trisulphides by reaction of Bunte salts (salts of *S*-alkyl or *S*-aryl hydrogen thiosulphates) with aqueous sodium sulphide was described. The reaction is believed to involve two nucleophilic displacements:

$$S^{2-} + RS{\cdot}SO_3^- \rightleftharpoons RS{\cdot}S^- + SO_3^{2-} \quad \ldots\ldots\ldots \quad (1)$$

$$RS{\cdot}S^- + RS{\cdot}SO_3^- \rightleftharpoons RS{\cdot}S{\cdot}SR + SO_3^{2-} \quad \ldots\ldots\ldots \quad (2)$$

In some cases disulphides were also obtained, but this side reaction could be suppressed by adding a layer of light petroleum to the stirred reaction mixture in order to extract trisulphide from the aqueous phase. This presumably minimises reaction of trisulphide with liberated sulphite ion, which could give disulphide and thiosulphate according to reaction (3):

$$SO_3^{2-} + RS{\cdot}S{\cdot}SR \rightleftharpoons RS^- + RS{\cdot}S{\cdot}SO_3^- \rightleftharpoons RS{\cdot}SR + S_2O_3^{2-} \quad \ldots\ldots \quad (3)$$

Support for this mechanism has now been obtained by allowing dimethyl trisulphide to react with sulphite ion at pH 8; considerable amounts of dimethyl disulphide were formed.

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[1] Milligan, Saville, and Swan, *J.*, 1961, 4850.

Throughout this work the relative proportions of di-, tri- and tetra-sulphide were determined by gas–liquid chromatography (g.l.c.). This technique has been used by several workers for the separation and identification of thiols, sulphides, and disulphides.[2] However, there appears to be only one previous reference to such chromatography of trisulphides,[3] and none to that of tetrasulphides.

Disulphide formation is particularly marked in the reaction of sodium *S*-methyl thiosulphate with sulphide ion, the ratio of di- to tri-sulphide being 60 : 40.* This result is probably due, in part, to the greater solubility in water of dimethyl trisulphide than of other dialkyl trisulphides.† In the presence of light petroleum, which extracts the trisulphide from the aqueous reaction mixture, the ratio of di- to tri-sulphide was lowered to 40 : 60, but the results were variable and appeared to depend on the degree of agitation.

The relative amount of trisulphide could be increased further by saturating the reaction mixture with sodium chloride, the ratio of di- to tri-sulphide then being 20 : 80. Since the solubility of dimethyl trisulphide in saturated salt solution is about one-tenth of that in water, it seems probable that the increase in the relative yield of trisulphide can be ascribed to further repression of reaction (3). In agreement, it was found that the presence of salt inhibits the formation of dimethyl disulphide from trisulphide and sulphite ion. Simultaneous addition of light petroleum did not result in further improvement.

The above methods appear to minimise the reactions (3) by removing trisulphide from the aqueous phase. Alternatively this side reaction might be suppressed by removing the sulphite ions formed in reactions (1) and (2). This has now been achieved by addition of formaldehyde, which forms a stable addition compound with sulphite at pH 8. Removal of sulphite ion favours the forward reactions (1) and (2) as well as suppressing reaction (3). Foss[4,5] used this technique when synthesising higher polythionates from tetrathionate and thiosulphate.

Thus, reaction of sodium *S*-methyl thiosulphate with sulphide ions in the presence of an excess of formaldehyde gave a product containing dimethyl disulphide and trisulphide in the ratio 2 : 98; in some experiments the presence of disulphide could not be detected. However, in all cases dimethyl tetrasulphide was also formed, despite the fact that none was obtained in the absence of formaldehyde. In a typical experiment at pH 8 in the presence of formaldehyde, the ratio of di- to tri- to tetra-sulphide in the undistilled product was 2 : 90 : 8. Distillation gave almost pure dimethyl trisulphide in 65% yield. At pH values above 8 formaldehyde was less effective in preventing reaction (3), as might be expected. Thus, at pH values 9 and 10 the product ratios were, respectively, 4 : 68 : 28 and 20 : 64 : 16. When the reaction mixture (pH 8) containing formaldehyde was saturated with sodium chloride, there was a slight improvement in yield of trisulphide at the expense of tetrasulphide (ratio 2 : 95 : 3).

Our results are consistent with the formation of dimethyl tetrasulphide in accord with reaction (4), which postulates interaction of methyl hydrodisulphide anion [reaction (1)] and dimethyl trisulphide [reaction (2)].

$$\mathrm{MeS{\cdot}S^- + MeS{\cdot}S{\cdot}SMe \rightleftharpoons MeS{\cdot}S{\cdot}S{\cdot}SMe + MeS^-} \qquad \ldots\ldots\ldots \quad (4)$$

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* Molar ratios are quoted throughout.

† The solubility of dimethyl trisulphide in water at room temperature (estimated by g.l.c. of an ethereal extract of a saturated aqueous solution) was 0·025%. This is ten times greater than that of diethyl trisulphide.

[2] See, *e.g.*, "Gas Chromatography," Bayer, Elsevier, Amsterdam, 1961, p. 122; Evans and Smith, *J. Chromatog.*, 1961, **6**, 293.

[3] Carson and Wong, *J. Org. Chem.*, 1959, **24**, 175.

[4] Foss, *Acta Chem. Scand.*, 1950, **4**, 866.

[5] Foss and Kringlebotn, *Acta Chem. Scand.*, 1961, **15**, 1608.

The equilibrium (4) may be displaced to the right if methanethiol adds to formaldehyde (cf. Levi[6]):

$$\mathrm{MeS^- + CH_2O + H^+ \rightleftharpoons MeS{\cdot}CH_2{\cdot}OH} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (5)$$

In support of this scheme (5) it was shown that methanethiol is rapidly displaced from a buffer at pH 8 by a stream of nitrogen, but is only very slowly displaced if the buffer contains formaldehyde.

Indirect evidence for the validity of reaction (4) was obtained by a study of the reactions of dimethyl trisulphide with methanethiol in the presence and absence of formaldehyde. In a buffer of pH 8, dimethyl trisulphide with one equivalent of methanethiol gave a mixture of di-, tri-, and tetra-sulphide in the ratio 60 : 33 : 7, presumably by a combination of reactions (6) and (4).

$$\mathrm{MeS^- + MeS{\cdot}S{\cdot}SMe \rightleftharpoons MeS{\cdot}SMe + MeS{\cdot}S^-} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (6)$$

In the presence of formaldehyde the trisulphide was virtually unchanged, showing that combination of methanethiol with formaldehyde can inhibit processes such as (6), and by analogy, could favour processes such as (4).

Likewise, reaction of dimethyl trisulphide with sulphide ion gave di-, tri-, and tetra-sulphide in the ratio 31 : 42 : 26, but in the presence of formaldehyde the ratio was 1 : 81 : 18. A complex set of equations can be written for the disproportionation of dimethyl trisulphide by sulphide ion, involving $\mathrm{MeS^-}$, $\mathrm{MeS{\cdot}S^-}$, and $\mathrm{MeS{\cdot}S{\cdot}S^-}$ as intermediates. Of these entities, only $\mathrm{MeS^-}$ can give rise to disulphide, by reaction with tri- or tetra-sulphide, so that disulphide formation is again inhibited by formaldehyde.

Formaldehyde was also very effective in minimising disulphide formation in the synthesis of diethyl and diallyl trisulphide from the corresponding Bunte salts and sulphide. In these cases no tetrasulphide could be detected.

Formaldehyde could not be used in the synthesis of trisulphides containing substituents such as amino- or activated methylene groups, since these can react with formaldehyde. Thus sodium *S*-phenacyl thiosulphate and sodium *S*-*o*-aminophenyl thiosulphate gave non-crystalline products with sodium sulphide and formaldehyde. In the absence of formaldehyde, diphenacyl trisulphide and a crystalline mixture of di-(*o*-aminophenyl) di- and tri-sulphide, respectively, were obtained. Reaction of sodium *S*-*o*-nitrophenyl thiosulphate with sodium sulphide gave a mixture of di-(*o*-nitrophenyl) di- and tri-sulphide in the ratio 85 : 15 (estimated from a sulphur analysis of the crude product). It was not possible to isolate the trisulphide by fractional crystallisation owing to the ease with which it decomposed to disulphide, as also observed by Lecher and Simon.[7] However, addition of formaldehyde resulted in only a moderate improvement in the relative yield of trisulphide, and decomposition mechanisms other than that of reaction (3) may be operating in this case.

The reaction of Bunte salts with sodium disulphide in place of sodium sulphide has been found to afford tetrasulphides:

$$\mathrm{S_2^{2-} + RS{\cdot}SO_3^- \rightleftharpoons RS{\cdot}S{\cdot}S^- + SO_3^{2-}} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (7)$$

$$\mathrm{RS{\cdot}S{\cdot}S^- + RS{\cdot}SO_3^- \rightleftharpoons RS{\cdot}S{\cdot}S{\cdot}SR + SO_3^{2-}} \quad . \; . \; . \; . \; . \; . \; . \; . \quad (8)$$

The major products, however, were trisulphides, even when formaldehyde was present. Attempts to prepare pentasulphides by using sodium trisulphide were unsuccessful, dialkyl tri- and tetra-sulphides and elemental sulphur being formed. In solution sodium disulphide is in equilibrium with sodium sulphide and higher polysulphides,[8] and the

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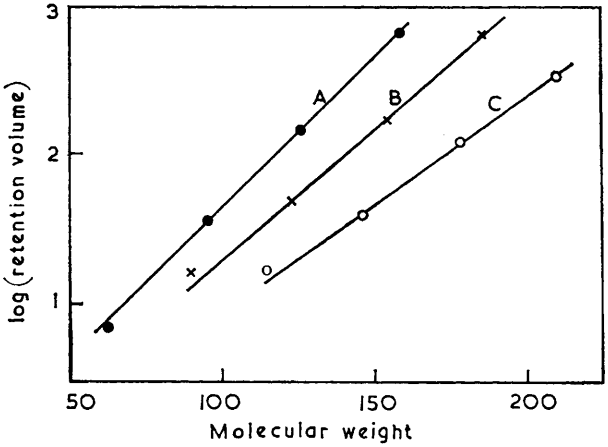
[6] Levi, *Gazzetta*, 1932, **62**, 776.

[7] Lecher and Simon, *Ber.*, 1922, **55**, 2430.

[8] Pearson and Robinson, *J.*, 1930, 1473.

above results can be explained by assuming that the nucleophilicity of sulphide ions to Bunte salts follows the sequence $S^{2-} > S_2^{2-} \gg S_{3-5}^{2-}$.

The identities of the dialkyl di- and tri-sulphides were confirmed by comparison of retention volumes on gas chromatography with those of authentic samples. Samples of diethyl tetrasulphide, prepared by reaction of sodium *S*-ethyl thiosulphate and sodium disulphide, and also from ethanethiol and disulphur dichloride, had identical retention volumes on gas chromatography. A linear relation was observed on plotting log (retention volume) against the molecular weight for the series diethyl mono-, di-, tri-, and tetra-sulphides (see Figure). Straight-line plots were also obtained for the corresponding methyl and allyl series, thus confirming the identity of chromatographic peaks ascribed to dimethyl and diallyl tetrasulphide. Relations of this kind have been widely observed for homologous series involving successive introduction of methylene groups,[9] but this is the first instance involving successive insertions of an atom other than carbon. Incidentally, this result is further evidence for the linear nature of polysulphide chains.[10]



Relation between log (retention volume) and molecular weight for sulphides, $R{\cdot}S_{1-4}{\cdot}R$, where R = (A) Me, (B) Et, and (C) allyl.

EXPERIMENTAL

Analysis of Products.—Mixtures of dialkyl di-, tri-, and tetra-sulphides were analysed by gas–liquid chromatography, using an F and M instrument (model 500). Separations were effected with (*a*) a 2-ft. stainless steel ($\frac{1}{4}$ in. outside diameter) U-shaped column of silicone gum rubber (20%) on Chromosorb P, or (*b*) an 8-ft. spiral column packed with Silicone Oil 550 (20%) on Chromosorb P. Column (*b*) was useful only for separating di- and tri-sulphides, since tetrasulphides were not displaced at its maximum operating temperature (*ca.* 180°). Mixtures of di- and tri-sulphides, or of tri- and tetra-sulphides could be separated isothermally on column ( ), although temperature-control over the range 75—200° was necessary for clean separation of all three types.

Operational details of the chromatograph were as follows: Carrier gas, helium; inlet pressure, 28 lb./in.^{2}; flow rate, 50 ml./min.; injection port temperature, 170°; hot-wire thermal-conductivity detector, 150 mA; block temperature, 250°.

The relative molar proportions of di-, tri-, and tetra-sulphides in admixture were estimated from peak areas by cutting and weighing the appropriate areas from the chart. The validity of this technique was checked using known mixtures of dimethyl di- and tri-sulphides; reasonable agreement was obtained. In order to check whether disproportionation of tri- or tetra-sulphides occurred on the column, mixtures were separated at different column temperatures, but this had no appreciable effect on the relative peak areas. Pure samples of diethyl and diallyl trisulphide gave single peaks, proving the absence of thermal decomposition.

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[9] James and Martin, *Biochem. J.*, 1952, **50**, 679; Keulemans, "Gas Chromatography," Reinhold Publ. Corp., New York, 2nd edn., 1960, p. 27.

[10] Foss, in "Organic Sulfur Compounds," ed. Kharasch, Pergamon Press, New York, 1961, Vol. I, p. 75.

Retention volumes, adjusted for column dead space, are given for dimethyl, diethyl, and diallyl mono-, di-, tri-, and tetra-sulphide in Table 1.

TABLE 1.

Adjusted retention volumes (c.c.) for dialkyl mono-, di-, tri-, and tetra-sulphides.

	Column (*a*)			Column (*b*)	
Compound	100°	125°	160°	150°	175°
Dimethyl sulphide	8				
Dimethyl disulphide	40			140	
Dimethyl trisulphide	160	75	35	490	
Dimethyl tetrasulphide	675	280	100		
Diethyl sulphide		18			
Diethyl disulphide		55		370	200
Diethyl trisulphide		190	80		620
Diethyl tetrasulphide		680	230		
Diallyl sulphide			19		
Diallyl disulphide		130	45		415
Diallyl trisulphide		410	130		
Diallyl tetrasulphide			360		

General Procedure for Synthesis of Dialkyl Trisulphides.—Sodium sulphide (13 ml., 0·4 molar) was added dropwise during 15 min. to a stirred solution of the Bunte salt (0·01 mole) in 0·2M-phosphate buffer (pH 8; 25 ml.) containing 35% w/v formaldehyde solution (2—3 ml.). 2N-Hydrochloric acid was added simultaneously to maintain pH 8. After a further 1 hr. the mixture was extracted with ether (3 × 10 ml.) and the dried ethereal solution was analysed directly by gas chromatography.

This method was modified in certain experiments as shown in Table 2.

TABLE 2.

Ratio of di-, tri-, and tetra-sulphide in the products from reaction of sodium *S*-alkyl thiosulphates ($RS{\cdot}SO_3Na$) with sodium sulphide at pH 8.

R	CH_2O *	Sodium chloride * NaCl *‡	Pet.*†	Ratio of products (detd. by g.l.c.) di : tri : tetra	Comments
Me	—	—	—	65 : 35 : 0	Average of 3 expts.
	—	—	+	45 : 55 : 0	For 2 expts.
				18 : 82 : 0	Different stirring rate
	—	+	—	22 : 78 : 0	
	—	+	+	24 : 76 : 0	
	+	—	—	2 : 88 : 10	Average of 7 expts.
				0 : 92 : 8	In an atmosphere of nitrogen
				3 : 69 : 28	At pH 9
				20 : 64 : 16	At pH 10
				1 : 94 : 5	With acetaldehyde in place of formaldehyde
	+	+	—	<1 : 96 : 4	
	+	+	+	<1 : 97 : 3	
Et	—	—	—	4 : 96 : 0	
	+	—	—	0 : 100 : 0	
Allyl	—	—	—	10 : 90 : 0	Average of 2 expts.
	+	—	—	2 : 98 : 0	,, ,,

* + denotes presence; — denotes absence. † Light petroleum (b. p. 55—70°) (10 ml.). ‡ To saturation.

Dimethyl Trisulphide.—(i) Reaction of sodium *S*-methyl thiosulphate (8·8 g.) according to the general procedure above gave a crude product containing dimethyl di-, tri-, and tetra-sulphide in the ratio < 1 : 96 : 4. Distillation gave a main fraction (2·4 g., 65%), b. p. 56—59°/14 mm., n_D^{20} 1·5982, which contained no disulphide and <2% of tetrasulphide.

(ii) A suspension of methyl iodide (71 g.) in a solution of sodium thiosulphate heptahydrate (125 g.) in water (200 ml.) was stirred vigorously at 30° until a homogeneous solution resulted (*ca.* 2 hr.). After extraction with ether (3 × 50 ml.) to remove any dimethyl disulphide, the aqueous phase was saturated with sodium chloride, and 35% w/v formaldehyde (100 ml.) was added. M-Sodium sulphide (250 ml.) was then added with stirring during ½ hr., the pH of the mixture being maintained at 7—8 by simultaneous addition of 6N hydrochloric acid; it was also necessary to use external cooling to keep the temperature in the range 20—30°. After a further 1½ hours' stirring, the product was extracted with ether (3 × 50 ml.). The ethereal extract contained (g.l.c.) dimethyl di-, tri-, and tetra-sulphide in the ratio <1 : 97 : 3. Distillation gave dimethyl trisulphide (18·0 g., 57% based on methyl iodide), shown (g.l.c.) to contain no disulphide and <1% of tetrasulphide.

Diethyl Trisulphide.—Ethyl bromide (21·8 g.) and sodium thiosulphate heptahydrate (50 g.) were heated under reflux in 1 : 1 aqueous ethanol (200 ml.) until a homogeneous solution was obtained. The alcohol was distilled off under reduced pressure, and 35% w/v formaldehyde (40 ml.) added to the residue, which was treated with M-sodium sulphide (100 ml.) in the usual way, at pH 8. In this case the mixture was kept for 4 hr. before isolation of the product, which contained (g.l.c.) di- and tri-sulphide in the ratio 2 : 98. Distillation gave a main fraction (9·5 g., 62%) which was free from disulphide.

Reaction of Dimethyl Trisulphide with Sodium Sulphite.—(i) Dimethyl trisulphide (0·12 g.) and 0·1M-sodium sulphite (5 ml.) were shaken for 2 hr. with 0·2M-phosphate buffer (pH 8; 20 ml.). The mixture was then extracted with ether (3 × 5 ml.) and the dried extracts were analysed directly (g.l.c.). Dimethyl di- and tri-sulphide, in the ratio 50 : 50, were detected.

(ii) As for (i), 35% w/v formaldehyde (1 ml.) being added to the original mixture. The product contained less than 1% of disulphide.

(iii) As for (i), the mixture being saturated with sodium chloride, and the pH then adjusted to 8. The product contained di- and tri-sulphide in the ratio 28 : 72.

Reaction of Dimethyl Trisulphide with Methanethiol.—(i) Dimethyl trisulphide (0·25 g.), and methanethiol (0·2 g.) were shaken vigorously with 0·2M-phosphate buffer (pH 8; 25 ml.) for 2 hr., and the products were then extracted with ether (3 × 5 ml.). Gas-chromatographic analysis showed the presence of dimethyl di-, tri-, and tetra-sulphide in the ratio 60 : 33 : 7. (ii) As for (i), but 35% w/v formaldehyde (2 ml.) was also added. The product contained di-, tri-, and tetra-sulphide in the ratio 4 : 94 : 2.

Reaction of Dimethyl Trisulphide with Sodium Sulphide.—(i) Dimethyl trisulphide (0·12 g.) was added to a solution containing 0·1M-sodium sulphide (5 ml.) and 0·2M-phosphate buffer (pH 8; 20 ml.), which had been re-adjusted to pH 8. After being shaken for 2 hr., the mixture was extracted with ether (3 × 5 ml.). Gas chromatography showed the presence of dimethyl di-, tri-, and tetra-sulphide in the ratio 33 : 40 : 27. (ii) As for (i), including 35% w/v formaldehyde (2 ml.). The ratio of di-, tri-, and tetra-sulphide in the product was 1 : 82 : 17.

Di-(p-*nitrobenzyl*) *Trisulphide.*—Reaction of sodium *S-p*-nitrobenzyl thiosulphate (1·36 g.) with sodium sulphide by the general procedure gave the trisulphide (0·64 g., 70%), having m. p. 123° after crystallisation from ethyl acetate (Found: S, 25·7. $C_{14}H_{12}N_2O_4S_3$ requires S, 26·1%).

Di-(o-*aminophenyl*) *Trisulphide.*—Reaction of sodium *S-o*-aminophenyl thiosulphate according to the general method, but without formaldehyde, gave a mixture of di- and tri-sulphides, m. p. *ca.* 83° (from light petroleum). Chromatography on Woelm alumina (activity 1), with light petroleum as eluent, followed by fractional crystallisation of the last quarter of the eluted material, gave the *trisulphide*, yellow needles, m. p. 117° (Found: N, 10·0; S, 34·0. $C_{12}H_{12}N_2S_3$ requires N, 10·0; S, 34·3%).

Di-(o-*nitrophenyl*) *Di- and Tri-sulphide.*—(i) Reaction of sodium *S-o*-nitrophenyl thiosulphate and sodium sulphide at pH 8 gave a crude product which was washed successively with water, ethanol, ether, carbon disulphide, and ether, and then dried under reduced pressure at room temperature (Found: S, 21·6. Calc. for $C_{12}H_{10}N_2O_4S_2$: S, 20·6. Calc. for $C_{12}H_{10}N_2O_4S_3$: S, 28·2%). (ii) The reaction was repeated in the presence of formaldehyde (Found: S, 23·0%).

Dialkyl Tetrasulphides.—These were obtained, together with the corresponding trisulphides, by reaction of Bunte salts with sodium disulphide or polysulphide (prepared by dissolving the appropriate amounts of sulphur in 0·4M-sodium sulphide) at pH 8, either in the presence or absence of formaldehyde. The results are summarised in Table 3.

Diethyl Tri- and Tetra-sulphide.—The product from the reaction of ethanethiol (6·2 g.) and disulphur dichloride (6·8 g.) in anhydrous ether gave, on distillation, a main fraction, b. p. 102—112°/20 mm., shown (g.l.c.) to contain diethyl tri- and tetra-sulphide in the molar ratio 83 : 17. This figure was confirmed by elemental analysis (S, 63·7%), which corresponds to a ratio of 79 : 21.

TABLE 3.

Ratio of di-, tri-, and tetra-sulphide in the products from reaction of sodium *S*-alkyl thiosulphates ($RS{\cdot}SO_3Na$) with sodium polysulphides at pH 8.

R	Reagent	CH_2O	Ratio of products di : tri : tetra	Comments
Me	Na_2S_2	—	13 : 51 : 36	
	Na_2S_2	+	1 : 56 : 43	
	Na_2S_3	+	0 : 55 : 45	No pentasulphide detected
	Na_2S_5	+	0 : 53 : 47	,, ,,
Et	Na_2S_2	—	5 : 77 : 18	
	Na_2S_2	+	0 : 68 : 32	Average of 3 expts.
	Na_2S_3	+	0 : 56 : 44	No pentasulphide detected
Allyl	Na_2S_2	+	13 : 73 : 14	
	Na_2S_2	—	30 : 62 : 8	
			5 : 85 : 10	

We are grateful to Mr. A. S. Inglis for the elemental microanalyses.

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[*Received, November 26th,* 1962.]