757. *Antituberculosis Agents. Part II.*[1] *Dehydrobromination Products and Related Bases derived from Bis-2 : 3-dibromopropyl Sulphide*

By D. Edwards and J. B. Stenlake.

Monodehydrobromination of bis-2 : 3-dibromopropyl sulphide yields 2 : 3-dibromopropyl 3-bromoprop-2-enyl sulphide (II). Further dehydrobromination gives a mixture of bis-3-bromoprop-2-enyl sulphide (VII) and 2-bromoprop-2-enyl 3-bromoprop-2-enyl sulphide (VIII), from which the former may be isolated after the latter has reacted with diethylamine to yield 3-bromoprop-2-enyl 2-diethylaminoprop-2-enyl sulphide (IX). The influence of substituents on the relative reactivity of vinylic bromides is discussed, and it is shown that whereas bis-3-bromoprop-2-enyl sulphide (VII) undergoes rapid solvolysis in 90% acetic acid, the corresponding sulphone is stable under these conditions. Oxidation of the sulphides (VII) and (VIII) with hydrogen peroxide in acetic acid is accompanied by rearrangement, which is demonstrated by the isolation of basic derivatives on subsequent reaction with diethylamine.

Bisdialkylaminoalkyl sulphides of varying chain length are more active than the corresponding sulphones against *M. tuberculosis in vitro*,[1] activity increasing with the chain length. Unsaturation enhances activity so that bis-3-diethylaminoprop-1-enyl sulphone

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[1] Part I, Edwards and Stenlake, *J. Pharm. Pharmacol.*, 1955, **7**, 852.

is nearly the equal of bis-10-diethylaminodecyl sulphone, the most active of the saturated sulphones examined. The present investigation arose out of an attempt to prepare bis-3-diethylaminoprop-1-enyl sulphide and related unsaturated sulphides for examination.

Bis-3-diethylaminoprop-1-enyl sulphone was prepared from diallyl sulphone by addition of bromine, followed by dehydrobromination, to give bis-3-bromoprop-1-enyl sulphone which was condensed with diethylamine.[1] An analogous route from diallyl sulphide was therefore considered. Rothstein [2] has shown that 2-bromo-1 : 1-diethylthiopropane, $CH_3CHBr{\cdot}CH(SEt)_2$, is readily dehydrobrominated to 1 : 1 - diethylthiopropene, $CH_3{\cdot}CH{:}CH(SEt)_2$, in accordance with the Saytzeff elimination rule. However, application of the rule to the proposed dehydrobromination of bis-2 : 3-dibromopropyl sulphide gave no indication as to the direction in which elimination might be expected, although by analogy with the corresponding sulphone αβ-elimination seemed probable.

Bis-2 : 3-dibromopropyl sulphide (I) was readily obtained from allyl sulphide,[3] but attempts to remove hydrogen bromide from it with pyridine failed. It appears, therefore, that electron accession from the lone pairs on the adjacent sulphide link inhibits attack at the α-position, these being conditions which do not obtain in the corresponding sulphone where this reaction is smooth. Rothstein [4] has shown similarly that, whilst benzyl 2-chloropropyl sulphone undergoes smooth dehydrobromination in pyridine, the isomeric benzyl 3-chloropropyl sulphone, which because of the more remote sulphone group is not activated for elimination, resists the attack. On the other hand, stronger bases such as potassium hydroxide in aqueous or absolute ethanol, readily removed acid from bis-2 : 3-dibromopropyl sulphide, the first experiment giving a tribromo-sulphide and a mixture of dibromo-sulphides (A); control of the conditions afforded only the dibromo-sulphides (A).

Ozonolysis of the tribromo-sulphide gave minute amounts of formaldehyde, but hydrobromic acid in almost theoretical yield, indicating its structure as (II). The dehydrobromination is thus analogous to that of αβ-dibromo*iso*butyraldehyde diethyl acetal (IV), which yields β-bromo-α-methylacraldehyde diethyl acetal (V) by βγ-elimination. The small yield of formaldehyde was probably due to contamination by traces of the isomeric sulphide (III), rather than to anomalous ozonolysis,[6, 7] since although the latter has been observed with 4-ethoxybut-2-ene, bis-3-bromoprop-2-enyl sulphide (VII) gives no formaldehyde. Formation of some tribromide (III), albeit in low yield, suggested that the dibromo-sulphides (A) contained the isomers (VII) and (VIII). Distillation failed to separate them, but their presence was established by ozonolysis, by isolation of bis-3-bromoprop-2-enyl sulphide (VII), and by the reactions of the base derived from 3-bromoprop-2-enyl 2-bromoprop-2-enyl sulphide (VIII) and diethylamine.

$$\underset{\text{(IV)}}{CH_2Br{\cdot}CBrMe{\cdot}CH(OEt)_2} \longrightarrow \underset{\text{(V)}}{CHBr{:}CMe{\cdot}CH(OEt)_2} \longrightarrow \underset{\text{(VI)}}{NHPh{\cdot}CH{:}CMe{\cdot}CH{:}NPh}$$

The dibromo-sulphides (A) reacted only slowly with boiling diethylamine, giving a monoacid base, $C_{10}H_{18}SNBr$: bis-3-bromoprop-2-enyl sulphide (VII) was unaffected and was recovered. The latter also failed to react with hot diethylamine, in benzene or alone under pressure. The base similarly failed to react further with diethylamine. The non-reactivity of the bromo-substituents in these two substances agrees with their formulation as vinylic halides.

The structure of bis-3-bromoprop-2-enyl sulphide (VII) was confirmed by ozonolysis, which gave no formaldehyde but liberated 1·70 mols. of hydrobromic acid. Ozonolysis of the mixed dibromo-sulphides (A), on the other hand, gave 0·19 mol. of formaldehyde [0·29 mol. after allowance for the presence of (VII)], in agreement with structure (VIII)

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[2] Rothstein, *J.*, 1940, 1553.

[3] McKitterick, *Ind. Eng. Chem.*, 1929, **21**, 585.

[4] Rothstein, *J.*, 1934, 684.

[5] Hamer and Rathbone, *J.*, 1945, 595.

[6] Knights and Waight, *J.*, 1955, 2830.

[7] Young, McKinnis, Webb, and Roberts, *J. Amer. Chem. Soc.*, 1946, **68**, 293.

for the second component: the alternative structure, $CHBr{:}CH{\cdot}CH_2{\cdot}S{\cdot}CHBr{\cdot}CH{:}CH_2$, for this component was rejected since its formation would require rearrangement which was considered unlikely under the alkaline conditions of the dehydrobromination.[8, 9]

Adoption of structures (VII) and (VIII) leads to an assignment of structure (IX) to the base $C_{10}H_{18}SNBr$ derived from the latter. Retention of the vinylidene group in this base was confirmed by liberation of formaldehyde on ozonolysis: the low yield (0·13 mol.) is attributed to the small scale of the reaction, comparably small yields being obtained under similar conditions with test compounds of known structure. Oxidation with hydrogen peroxide gave the sulphone (X), which similarly on ozonolysis gave hydrobromic acid and formaldehyde (0·12 mol.). Formation of a base by reaction of a vinylic halide with diethylamine at first sight seemed improbable;[10] there is some evidence, however, that suitably substituted vinylic bromides are more reactive than the corresponding chlorides, presumably owing to the greater polarisability of the bromine. For example, Hamer and Rathbone[5] have shown that β-bromo-α-methylacraldehyde diethyl acetal (V) readily gives β-anilino-α-methylacraldehyde anil (VI). On the other hand Parcell and Pollard[11] found that only the allylic bromine atom of 2 : 3-dibromopropene was replaced in reaction with diethylamine. Other replacement reactions which appear to be general to allylic bromides are the formation of lithium alkenyls[12] and replacement by metal alkoxides[13] or thioalkoxides.[14] We have now found that bis-3-bromoprop-2-enyl sulphide undergoes almost complete solvolysis in 90% acetic acid, hydrobromic acid being liberated in 91% of the theoretical yield after 1 hour's refluxing. The product, 3-acetoxyprop-2-enyl sulphide (XI), was unstable and could not be fully characterised. Reactivity in vinylic bromides, however, is not completely general, being governed by the nature of adjacent substituents. For example, Dufraisse and Netter[15] found that only the ethoxy-group of α-bromo-β-ethoxybenzylidene acetophenone reacts with piperidine. Similarly, we have found that bis-3-bromoprop-2-enyl sulphone, unlike the sulphide, does not undergo solvolysis in boiling 90% acetic acid: replacement of an electron-denoting (sulphide) group by an electron-attracting (sulphone) substituent in the 1-position exerts a profound effect on the reactivity of the halogen atom in the 3-bromoprop-2-enyl residue. The difference in reactivity of the bromo-substituents in 2-bromoprop-2-enyl 3-bromoprop-2-enyl sulphide (VIII) can be explained in the same way by the proximity of the methylenethio-group, $-S{\cdot}CH_2-$, to the vinylic halogen of the 2-bromoprop-2-enyl fragment so that substitution with diethylamine occurs in the 2-position, with the formation of 3-bromoprop-2-enyl 2-diethylaminoprop-2-enyl sulphide (IX).

Oxidation of the dehydrobromination product (A) with hydrogen peroxide in acetic acid gave an oil, which, contrary to expectation, reacted with diethylamine, permitting separation into basic and non-basic fractions. The base, $C_{10}H_{18}O_2NBrS$, was not identical with (X) and is formulated as 2-bromoprop-2-enyl 1-diethylaminoprop-2-enyl sulphone (XIII), being derived from 1-bromoprop-2-enyl 2-bromoprop-2-enyl sulphone (XII), which is formed by the thiotropic rearrangement and oxidation of the sulphide (VIII). Rothstein[8] has reported that oxidation of the thioacetal, $CH_2{:}CH{\cdot}CH(SEt)_2$, is accompanied by migration of an ethylthio-group to yield 1 : 3-diethylsulphonylpropene. A similar rearrangement of vinylic to allylic bromide is supported in the present case by the ease with which the rearranged and oxidised product reacted with diethylamine. Reaction was instantaneous at room temperature, and comparable in ease with that between bis-3-bromoprop-1-enyl sulphone and diethylamine. Ozonolysis of the sulphone (XII) was not completely satisfactory owing to the small amount of material available. Formaldehyde was obtained but in only 8% of the theoretical yield for two vinylidene groups, although this yield is comparable on a weight basis with those obtained from the sulphides (IX) and

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[8] Rothstein, *J.*, 1940, 1560.

[9] Jones and Weedon, *J.*, 1946, 937.

[10] Ingold and Rothstein, *J.*, 1929, 8.

[11] Parcell and Pollard, *J. Amer. Chem. Soc.*, 1950, **72**, 2385.

[12] Braude and Timmons, *J.*, 1950, 2000.

[13] Winstein, Lindegren, and Ingraham, *J. Amer. Chem. Soc.*, 1953, **75**, 155.

[14] Laevenich, Losen, and Dierichs, *Ber.*, 1927, **60**, 950.

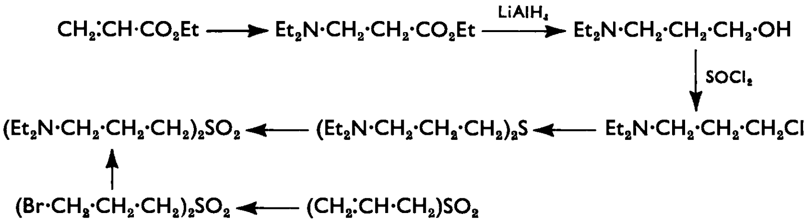
[15] Dufrasse and Netter, *Bull. Soc. chim. France*, 1932, **51**, 550.

(X). Hydrobromic acid was also obtained, indicating the retention of one vinylic bromine in the molecule.

The oily non-basic substance obtained on oxidation of the dibromo-sulphides (A), isolated after reaction with diethylamine, was separated by distillation into two fractions. One was bis-3-bromoprop-2-enyl sulphone (XIV), identical with the principal oxidation product of bis-3-bromoprop-2-enyl sulphide (VII). Its structure was confirmed by its failure to react with diethylamine, and the absence of formaldehyde and liberation of hydrobromic acid (1·66 mol.) on oxonolysis. The higher-boiling fraction afforded a material, $C_{10}H_{19}O_2BrS$, from which ozonolysis yielded hydrobromic acid but no formaldehyde, indicating the presence of an intact $CHBr{:}CH{\cdot}CH_2{\cdot}SO_2$ group in the molecule.

Oxidation of bis-3-bromoprop-2-enyl sulphide (VII) was accompanied by partial rearrangement to 1-bromoprop-2-enyl 3-bromoprop-2-enyl sulphone (XV), since the oily product reacted with cold diethylamine (indicative of an allyl bromide group) to give small yields of a monoacid base, insufficient for characterisation but presumably 3-bromoprop-2-enyl 1-diethylaminoprop-2-enyl sulphone (XVI); crystalline bis-3-bromoprop-2-enyl sulphone (XIV) was also isolated. In an experiment on a larger scale the crude base from the oxidation of the dibromo-sulphides (A) gave low equivalent weights, suggesting the presence of a diacidic base, tentatively formulated as bis-1-diethylaminoprop-2-enyl sulphone. The latter, like bis-3-diethylaminoprop-1-enyl sulphone, decomposed on distillation of the crude product, but small amounts were isolated from the undistilled material as the crystalline dihydrochloride, the melting point of which was depressed on admixture with bis-3-diethylaminoprop-1-enyl sulphone dihydrochloride.

Some experiments, with the object of comparing the reactivity of 3-bromo-substituents in various propyl sulphides and sulphones, though later found unnecessary to the present investigation, remain to be recorded. Bis-3-bromopropyl sulphone,[1] prepared by the peroxide-catalysed addition of hydrogen bromide to diallyl sulphone, with diethylamine in boiling benzene slowly gave bis-3-diethylaminopropyl sulphone. The direction of addition of hydrogen bromide, and hence the 3-position of the bromo-substituent, have now been confirmed by the preparation of bis-3-diethylaminopropyl sulphone from bis-3-diethylaminopropyl sulphide,[16] which we obtained by the following annexed routes:

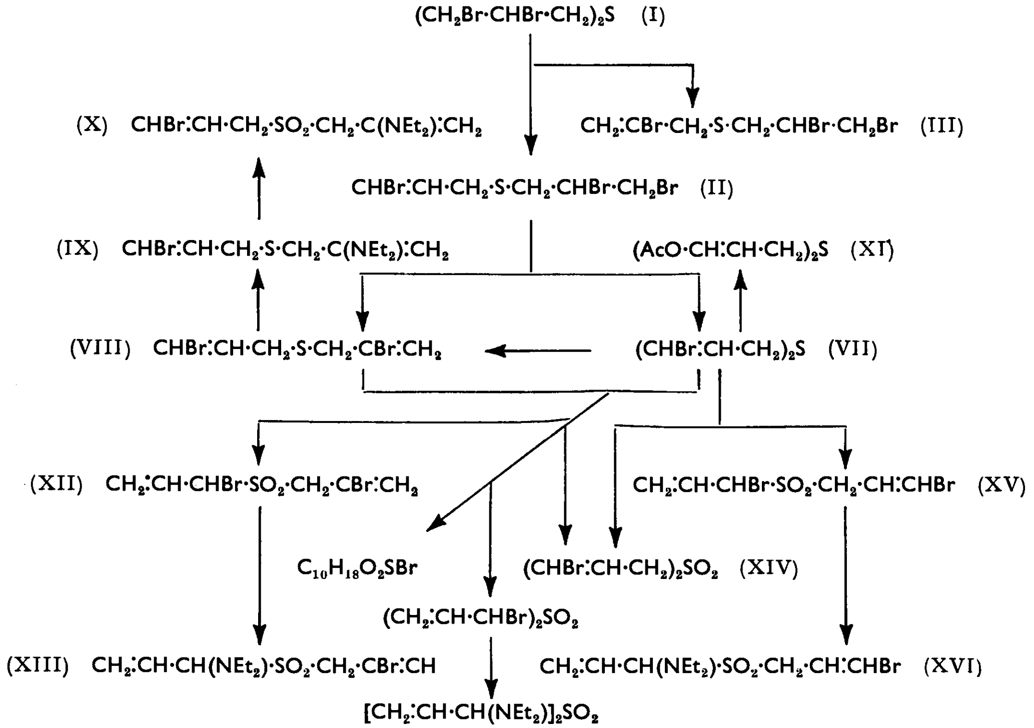


Peroxide-catalysed addition of hydrobromic acid to allyl sulphide under the conditions used for addition to the corresponding sulphone, gave bis-2-bromopropyl sulphide, and not the expected bis-3-bromopropyl sulphide. This was confirmed by its reaction with diethylamine, which was extremely slow in benzene, to give a diacidic base bis-2-diethylaminopropyl sulphide, the hydrochloride of which depressed the melting point of bis-3-diethylaminopropyl sulphide. It is conceivable that the sulphide link could offset the influence of peroxide on the course of hydrogen bromide addition, the peroxide being eliminated in an oxidation of the sulphide group. This, however, is in direct contradiction to Jones and Reid's demonstration [17] of the catalytic effects of even traces of peroxides on the course of addition of thiols to unsaturated compounds.

An attempt to prepare bis-3-bromopropyl sulphide by a controlled reaction between 1 : 3-dibromopropane and sodium sulphide gave only a small yield of a bis-3-bromopropyl tetrasulphide, which was characterised by conversion into bis-3-diethylaminopropyl tetrasulphide dihydrochloride.

[16] Andrews, Bergel, and Morrison, *J.*, 1953, 2998.

[17] Jones and Reid, *J. Amer. Chem. Soc.*, 1938, **60**, 2452; *Org. Synth.*, Coll. Vol. I, 1st. edn., p. 23.



EXPERIMENTAL

*Bis-*2 : 3*-dibromopropyl Sulphide.*—Diallyl sulphide (14·33 g.) was slowly treated in carbon tetrachloride (100 ml.) with bromine (41 g.) in carbon tetrachloride (30 ml.). The residue obtained on evaporation gave colourless needles (from carbon tetrachloride) of bis-2 : 3-dibromopropyl sulphide, m. p. 92—93·5° (31 g., 57%) (McKitterick[3] gives m. p. 94—95·5°) (Found : Br, 73·9. Calc. for $C_6H_{10}SBr_4$: Br, 73·7%).

*Dehydrobromination of Bis-*2 : 3*-dibromopropyl Sulphide.*—(*a*) To bis-2 : 3-dibromopropyl sulphide (15 g.) in warm ether (100 ml.) and ethanol (40 ml.) potassium hydroxide (4 g.) in water (3 ml.) and ethanol (20 ml.) was added slowly with stirring. On cooling, the mixture was poured into water (400 ml.) and extracted with ether. The ethereal solution was washed with water, dried (Na_2SO_4), and evaporated to yield a brown oil (10·22 g.). Fractional distillation of a portion (8·13 g.) gave fraction A, a straw-coloured liquid (A), b. p. 125—130° (bath)/4 mm., n_D^{19} 1·5990 (3·6 g.) (1·5979 after redistillation) (Found: Br, 58·5. Calc. for $C_6H_8SBr_2$: Br, 58·8%), and B, 3*-bromoprop-*2*-enyl* 2 : 3*-dibromopropyl sulphide*, a yellow liquid, b. p. 118—119°/0·75 mm., n_D^{15} 1·6125 (3·5 g.) (Found : Br, 69·3. $C_6H_8SBr_3$ requires Br, 67·9%).

(*b*) Bis-2 : 3-dibromopropyl sulphide (11·75 g.) in benzene (50 ml.) and ethanol (20 ml.) was treated with potassium hydroxide (3·1 g.) in ethanol (60 ml.) slowly with stirring. After 10 minutes' stirring, the potassium bromide was filtered off and the bulk of the solvent removed. The residual liquid was poured into water (120 ml.) and extracted with benzene. The benzene solution, after drying (Na_2SO_4) and evaporation, gave the mixture (A) of bis-3-bromoprop-2-enyl sulphide and 3-bromoprop-2-enyl 2-bromoprop-2-enyl sulphide (n_D^{20} 1·5942; 7·09 g., 95%), obtained after distillation as a straw-coloured liquid, b. p. 96—97°/1·3 mm., n_D^{20} 1·5961.

Ozonolysis of the Mixed Dibromo-sulphides (*A*).—The mixture (A) (1·022 g.) was ozonised in chloroform (25 ml.) for 1 hr. The solvent was removed under pressure, and the oily product hydrolysed by refluxing with water (40 ml.) for 30 min. Steam-distillation and treatment of the distillate with dimedone yielded the formaldehyde–dimedone derivative (0·211 g., 0·193 mol.). Treatment of the aqueous solution, remaining after steam-distillation, with nitric acid (1 ml.) and an excess of silver nitrate solution gave silver bromide (0·92 g., 1·3 mols.).

Ozonolysis of 3*-Bromoprop-*2*-enyl* 2 : 3*-Dibromopropyl Sulphide.*—3-Bromoprop-2-enyl 2 : 3-dibromopropyl sulphide (0·944 g.) was ozonised in chloroform as described above, and yielded the formaldehyde–dimedone derivative (0·023 g., 0·29 mol.) and hydrobromic acid (as silver bromide, 0·502 g., 0·92 mol.).

Reaction of the Mixed Dibromo-sulphides (*A*) *with Diethylamine*.—The mixture (A) (9·5 g.) in benzene (120 ml.) was refluxed with diethylamine (25 ml.) for 1 hr. Excess of diethylamine and benzene were removed by distillation, and the residue washed in benzene with water and extracted with dilute hydrochloric acid. The aqueous solution was made alkaline with sodium hydroxide solution, and the liberated base extracted with benzene. This benzene solution was washed with water, dried (Na_2SO_4), and evaporated to a yellow liquid (5·42 g.) which on distillation gave 3-*bromoprop*-2-*enyl* 2-*diethylaminoprop*-2-*enyl sulphide*, b. p. 123—128° (bath)/3·5 mm., n_D^{19} 1·5300 (Found: N, 5·2%; equiv., 263·6. $C_{10}H_{18}NSBr$ requires N, 5·3%; equiv., 264·2).

The benzene solution remaining after extraction with hydrochloric acid was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure to a liquid (2·69 g.) which on distillation gave *bis*-3-*bromoprop*-2-*enyl sulphide* as a pale straw-coloured liquid, b. p. 120—125° (bath)/3·5 mm., n_D^{20} 1·5958 (Found: C, 26·5; H, 3·15. $C_6H_8SBr_2$ requires C, 26·5; H, 3·0%).

Ozonolysis of 3-*Bromoprop*-2-*enyl* 2-*Diethylaminoprop*-2-*enyl Sulphide*.—This sulphide (0·679 g.), ozonised as described above, yielded the formaldehyde–dimedone derivative (0·0979 g., 0·13 mol.) and hydrobromic acid (not estimated).

Ozonolysis of Bis-3-*bromoprop*-2-*enyl Sulphide*.—The sulphide (0·962 g.), ozonised as above, gave only a trace of formaldehyde–dimedone derivative. Treatment of the aqueous solution remaining after steam-distillation with nitric acid (1 ml.) and silver nitrate, gave silver bromide (1·125 g., 1·69 mols.).

Attempts to Condense Bis-3-*bromoprop*-2-*enyl Sulphide with Diethylamine*.—(*a*) The sulphide (1 g.) in benzene (20 ml.) was refluxed with diethylamine (2·5 ml.) for 2 hr., and the mixture left at room temperature overnight, then evaporated to dryness and dissolved in benzene, washed with water, and extracted with dilute hydrochloric acid. The residual solution was washed, dried (Na_2SO_4), and evaporated, to yield unchanged bis-3-bromoprop-2-enyl sulphide (0·93 g.), n_D^{20} 1·5959. The acid aqueous extract was made alkaline with sodium hydroxide solution and extracted with benzene. The benzene solution was washed, dried (Na_2SO_4), and evaporated, to yield a trace of a reddish base, $n_D^{22\cdot5}$ 1·5262, insufficient for characterisation.

(*b*) Bis-3-bromoprop-2-enyl sulphide (3·63 g.) was heated with diethylamine (6 ml.) at 130—140° for 2·5 hr. in a steel bomb (40 ml. capacity). On cooling and extraction as above unchanged sulphide (3·45 g.), n_D^{20} 1·5956, was obtained, together with traces of a base, n_D^{20} 1·5278.

Reaction of Bis-3-*bromoprop*-2-*enyl Sulphide with* 90% *Acetic Acid*.—The sulphide (1·093 g.) was heated at 100° for 1 hr. in acetic acid (15 ml.) and water (1·5 ml.). The solution became dark red. After dilution with water (60 ml.) and partial neutralisation with sodium hydroxide the then cloudy solution was extracted with benzene. The benzene solution was washed with water, dried (Na_2SO_4), and evaporated to yield a liquid (0·75 g.) which distilled with considerable decomposition, yielding a pale yellow oil (0·266 g.), b. p. 95—100° (bath)/0·35 mm., n_D^{14} 1·5605. The oily product did not restore the colour to Schiff's reagent or reduce ammoniacal silver nitrate solution, but caused immediate reduction of Tollens's reagent. Sodium hydroxide solution elicited a pleasant odour, but the solution rapidly resinified. The product was unstable and decomposed rapidly, so that analytical figures could not be obtained. The residual aqueous liquid from the benzene extraction, on addition of nitric acid and excess of silver nitrate, gave silver bromide (1·369 g., 1·81 mols.).

3-*Bromoprop*-2-*enyl* 2-*Diethylaminoprop*-2-*enyl Sulphone*.—3-Bromoprop-2-enyl 2-diethylaminoprop-2-enyl sulphide (1 g.) was treated in glacial acetic acid (15 ml.) at 5° with 30% hydrogen peroxide (3 ml.) and set aside overnight at room temperature. The solution was then heated to 80—85° for 1 hr., cooled, and diluted with water (50 ml.). A slight excess of sodium hydroxide solution was added, and the liberated base extracted with benzene. The benzene extracts were washed, dried (Na_2SO_4), and evaporated under reduced pressure, to yield 3-*bromoprop*-2-*enyl* 2-*diethylaminoprop*-2-*enyl sulphone*, b. p. 140° (bath)/1·4 mm., $n_D^{15\cdot5}$ 1·5343, d^{19} 1·284 (0·32 g., 29·2%) (Found: N, 4·6%; equiv., 294·3. $C_{10}H_{18}O_2NBrS$ requires N, 4·7%; equiv., 296·2).

This sulphone (0·27 g.) was ozonised in chloroform, and the ozonide hydrolysed to yield formaldehyde, isolated as the dimedone derivative (0·033 g., 0·124 mol.), and hydrobromic acid (not estimated).

Oxidation of the Mixed Dibromo-sulphides (*A*).—The dibromo-sulphides (A) (5·614 g.) were oxidised in acetic acid (70 ml.) with 30% hydrogen peroxide (14 ml.), as above. The mixture was poured into water (300 ml.) and extracted with benzene. Evaporation of the benzene solution gave a yellow oil (5·467 g.), $n_D^{24·5}$ 1·5683, subsequently shown to be a mixture of bis-3-bromoprop-2-enyl sulphone, 1-bromoprop-2-enyl 2-bromoprop-2-enyl sulphone, bis-1-bromoprop-2-enyl sulphone, and a substance $C_{10}H_{19}O_2BrS$.

Reaction of the Mixed Dibromo-sulphones with Diethylamine.—The mixed product from the above reaction (5·45 g.) in benzene (50 ml.) was treated with diethylamine (7 ml.) and heated on a water-bath for 5 min. to complete the reaction (apparently instantaneous). After removal of the solvent under reduced pressure, the residue was washed with water and extracted with benzene. The benzene solution was extracted with dilute hydrochloric acid, and the acid solution basified with aqueous sodium hydroxide and extracted with benzene, to give an oily base (2·296 g.), n_D^{14} 1·5110 (Found : equiv., 247·6. Calc. for $C_{14}H_{28}O_2N_2S$: equiv., 144·2. Calc. for $C_{10}H_{18}O_2NSBr$: equiv., 296·2). The crude mixed bases (1·131 g.) were distilled with considerable decomposition, to yield 2-*bromoprop*-2-*enyl* 1-*diethylaminoprop*-2-*enyl sulphone* as a yellow oil (0·453 g.), b. p. 170—175° (bath)/1·7 mm., n_D^{14} 1·5158, d^{19} 1·307 (Found : N, 4·9%; equiv., 295·3. $C_{10}H_{18}O_2NBrS$ requires N, 4·7%; equiv., 296·2). The crude mixed bases (0·2 g.) were dissolved in dilute hydrochloric acid and carefully evaporated. The residue (from ethanol–ether) gave a small yield of colourless bis-1-diethylaminoprop-2-enyl sulphone dihydrochloride, m. p. 189—190° (insufficient for analysis), mixed m. p. with bis-3-diethylaminoprop-1-enyl sulphone hydrochloride (m. p. 192—193°) 176—179°.

Non-basic oxidation products were obtained by evaporation of the benzene solution remaining after the extraction of bases with hydrochloric acid as a reddish-brown oil (2·24 g.), n_D^{14} 1·5624, containing some crystals. Distillation yielded fractions A and B. Fraction A was a yellowish liquid (1·2 g.), b. p. 160—165° (bath)/1·3 mm., which solidified. The solid was separated from traces of oil by chromatography from ether on alumina. The crystalline product isolated from the first fraction of the eluate gave [from light petroleum (b. p. 40—60°)] colourless plates of *bis*-3-*bromoprop*-2-*enyl sulphone*, m. p. 65·5—66·5° (Found : C, 23·8; H, 3·0; Br, 52·15. $C_6H_8O_2Br_2S$ requires C, 23·7; H, 2·7; Br, 52·6%). Fraction B was a yellow oil (1·5 g.), b. p. 180—200° (bath)/1·3 mm., which solidified to yield a *bromo-compound* as colourless prisms (from ether), m. p. 73—74° (Found : C, 42·95, 41·9; H, 6·3, 6·5; Br, 28·1. $C_{10}H_{19}O_3SBr$ requires C, 42·4; H, 6·8; Br, 28·2%).

Ozonolysis of 2-*Bromo*-2-*enyl* 1-*Diethylaminoprop*-2-*enyl Sulphone.*—This sulphone (0·247 g.), ozonised in chloroform, gave formaldehyde, isolated as the dimedone derivative (0·039 g., 0·158 mol.) and hydrobromic acid (not estimated).

Ozonolysis of Bis-2-*bromoprop*-2-*enyl Sulphone.*—The sulphone (0·413 g.), ozonised in chloroform, yielded only a trace of formaldehyde. Treatment of the aqueous solution, remaining after steam-distillation, with nitric acid (1 ml.) and excess of silver nitrate gave silver bromide (0·421 g., 1·63 mol.).

Ozonolysis of the Neutral Compound, $C_{10}H_{19}O_2BrS$.—This compound (0·289 g.) gave no formaldehyde, but gave hydrobromic acid in good yield (not estimated).

Oxidation of Bis-3-*bromoprop*-2-*enyl Sulphide and Reaction of the Products with Diethylamine.*—Bis-3-bromoprop-2-enyl sulphide (2·33 g.) in acetic acid (30 ml.) was oxidised with 30% hydrogen peroxide (5·5 ml.) as described in the preparation of 3-bromoprop-2-enyl 2-diethylaminoprop-2-enyl sulphone. The resulting solution was poured into water (150 ml.) and extracted with benzene. The benzene solution was washed, dried (Na_2SO_4), and evaporated under reduced pressure to a yellow oil (2·45 g.), which partly crystallised. The oil was dissolved in benzene (20 ml.), warmed with diethylamine (2·5 ml.) for 5 min., evaporated to dryness, and extracted with benzene. Separation of basic and non-basic products by benzene and dilute acid as before gave a basic fraction, probably 3-*bromoprop*-2-*enyl* 1-*diethylaminoprop*-2-*enyl sulphone,* a reddish-brown oil (0·117 g.), n_D^{14} 1·5123 (Found: equiv., 293·3. $C_{10}H_{18}O_2NBrS$ requires equiv., 296·2), and a non-basic yellow oil (2·091 g.), n_D^{14} 1·5649, which gave, on distillation, a colourless oil (1·75 g.), b. p. 145—150° (bath)/0·6 mm., which solidified and when chromatographed from ether on alumina and recrystallised from light petroleum gave colourless plates of bis-3-bromoprop-2-enyl sulphone, m. p. and mixed m. p. 65·5—66·5°.

Attempted Solvolysis of Bis-3-*bromoprop*-2-*enyl Sulphone.*—The sulphone (1·38 g.) was heated with acetic acid (19 ml.) and water (2 ml.) for 1·25 hr. on a boiling-water bath, cooled, poured into water (150 ml.), and extracted with benzene. Evaporation of the benzene gave unchanged bis-3-bromoprop-2-enyl sulphone (1·232 g.), m. p. and mixed m. p. 65·5—66·5°.

Other Materials.—Ethyl 3-diethylaminopropionate, prepared by Adamson's method,[18] had b. p. 87°/15 mm., $n_D^{17·5}$ 1·4290. Adamson reports b. p. 87—88°/15 mm.

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[18] Adamson, *J.*, 1949, S 144.

Diethyl-3-hydroxypropylamine, prepared by lithium aluminium hydride reduction of ethyl β-diethylaminopropionate (82 g.), had b. p. 81°/15 mm., $n_{\rm D}^{17\cdot5}$ 1·4430 (50·8 g., 81·8%). Von Braun [19] reports b. p. 84°/20 mm.

3-*Chloropropyldiethylamine.* Thionyl chloride (37 ml.) in benzene (90 ml.) was slowly added to a solution of diethyl-3-hydroxypropylamine (50·8 g.) in benzene (250 ml.). The solvent was removed under reduced pressure to yield a brown crystalline mass. The product was dissolved in water (60 ml.), cooled to 0°, basified by 20% sodium hydroxide solution (85 ml.), and extracted with ether. The ethereal solution was washed, dried (Na_2SO_4), and evaporated, and the residual oil distilled to give 3-chloropropyldiethylamine, b. p. 62—65°/16 mm., $n_{\rm D}^{20}$ 1·4417 (49·22 g., 84·9%) (lit.,[20] b. p. 53—57°/12 mm.).

Bis-3-*diethylaminopropyl sulphide.* 3-Chloropropyldiethylamine (36·51 g.) in ethanol (24 ml.) was slowly added to a hot solution of anhydrous sodium sulphide (13 g.) in water (14 ml.) and ethanol (35 ml.), and the mixture was refluxed for 3·5 hr. with continuous stirring. The residual liquor, after removal of the bulk of the ethanol by distillation, was poured into water (350 ml.), and extracted with ether. The ethanol solution was washed, dried (Na_2SO_4), and evaporated. Fractional distillation of the residual oil gave a forerun of unchanged 3-chloropropyldiethylamine followed by bis-3-diethylaminopropyl sulphide, b. p. 133—136°/2·5 mm., $n_{\rm D}^{18}$ 1·4758 (21·71 g., 68·4%). Andrews, Bergel, and Morrison [16] gave b. p. 80—81°/0·03 mm., $n_{\rm D}^{21}$ 1·4731 (Found: equiv., 131·1. Calc. for $C_{14}H_{32}N_2S$: equiv., 130). Its *dihydrochloride* (from ethanol) has m. p. 222·5—223·5° (Found: N, 8·5; Cl, 21·4. $C_{14}H_{34}N_2Cl_2S$ requires N, 8·4; Cl, 21·3%).

Bis-3-*diethylaminopropyl sulphone.* Potassium permanganate (3%) in acetic acid (50%) was added during 20 min. to an ice-cold solution of bisdiethylaminopropyl sulphide (3·5 g.) in 50% acetic acid (6 ml.) until present in slight excess. After a further 20 min. the solution was decolorised with sulphur dioxide and evaporated to dryness under reduced pressure. Sodium carbonate solution was added to alkalinity, and the solution again evaporated to dryness. The solid residue, on continuous extraction with ether, removal of solvent, and distillation, gave *bis*-3-*diethylaminopropyl sulphone,* b. p. 186°/3·5 mm., $n_{\rm D}^{24\cdot5}$ 1·4707 (3·5 g., 90%) (Found: C, 57·75; H, 10·8; N, 9·5. $C_{14}H_{32}O_2N_2S$ requires C, 57·5; H, 11·0; N, 9·6%). Its dihydrochloride had m. p. 186·5—187°, mixed m. p. with bis-3-diethylaminopropyl sulphone dihydrochloride 186·5—187°.

Addition of Hydrogen Bromide to Diallyl Sulphide.—Diallyl sulphide (7·27 g.) was dissloved in carbon tetrachloride (100 ml.). A crystal of benzoyl peroxide was added, the solution heated to the b. p., and dry hydrogen bromide passed in whilst the solution was cooling and thereafter for 22 hr. The solution was brought to the b. p. at 3-hourly intervals, being allowed to cool to room temperature during the intervening periods. Evaporation of the solvent under reduced pressure gave a yellow liquid (13·7 g.), which yielded on distillation 2-*bromopropyl prop*-2-*enyl sulphide,* b. p. 49—50°/1·7 mm., $n_{\rm D}^{17\cdot5}$ 1·5275 (5·5 g.) (Found: Br, 41·8. $C_6H_{11}BrS$ requires Br, 41·0%), and *bis*-2-*bromopropyl sulphide,* b. p. 95°/0·95 mm., $n_{\rm D}^{19}$ 1·5547 (7·1 g.) (Found: Br, 58·3. $C_6H_{12}Br_2S$ requires Br, 58·0%).

Bis-2-*diethylaminopropyl Sulphide.*—Bis-2-bromopropyl sulphide (1·042 g.) in benzene (12 ml.) was refluxed with diethylamine (2 ml.) for 5 hr. The basic product, extracted in the usual way as a yellow oil (0·461 g.), b. p. 80°/1·2 mm., $n_{\rm D}^{18}$ 1·4747 (Found: equiv., 142·3. $C_{14}H_{32}N_2S$ requires equiv., 130·1), was treated with dilute hydrochloric acid, to give *bis*-2-*diethylaminopropyl sulphide dihydrochloride,* m. p. 224—226° (decomp.) (from ethanol–ether) (Found: N, 8·45; Cl, 21·3. $C_{14}H_{34}N_2Cl_2S$ requires N, 8·4; Cl, 21·3%). A mixed m. p. with bis-3-diethylaminopropyl sulphide dihydrochloride (m. p. 222·5—223·5°) was depressed to 211—212·5°.

Bis-3-*bromopropyl Tetrasulphide.*—1 : 3-Dibromopropane (40·4 g.) [17] was added to a stirred solution of sodium sulphide (7·8 g.) in water (10 ml.) and ethanol (45 ml.). The mixture was refluxed for 3·5 hr., cooled, poured into water (250 ml.), and extracted with benzene. The benzene solution was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure, to a brown oil, which on distillation gave *bis*-3-*bromopropyl tetrasulphide* as a pale yellow oil (6·32 g., 17%), b. p. 121—125°/1·2 mm., $n_{\rm D}^{13}$ 1·5538 (Found: 42·4. $C_6H_{12}Br_2S_4$ requires Br, 42·9%).

Bis-3-*diethylaminopropyl Tetrasulphide Dihydrochloride.*—Bis-3-bromopropyl tetrasulphide (2·31 g.) in benzene (20 ml.) was refluxed with diethylamine (4 ml.) for 1·5 hr. The basic product was extracted in the usual way as a yellow oil (1·34 g.), which on distillation gave a

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[19] Von Braun, *Ber.*, 1916, **49**, 966.

[20] Von Marxer, *Helv. Chim. Acta,* 1941, **24**, 209E.

colourless oil, b. p. 155—160° (bath)/1·6 mm., $n_D^{17.5}$ 1·4988. This gave *bis-3-diethylaminopropyl tetrasulphide dihydrochloride*, needles, m. p. 245·5—246·5° (from ethanol) (Found: C, 39·8; H, 7·5; N, 6·7; Cl, 17·0. $C_{14}H_{34}N_2Cl_2S_4$ requires C, 39·1; H, 8·0; N, 6·5; Cl, 16·5%).

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