

168. *The Direction of Ring Opening of Some Unsymmetrical Ethylene Oxides and Sulphides.*

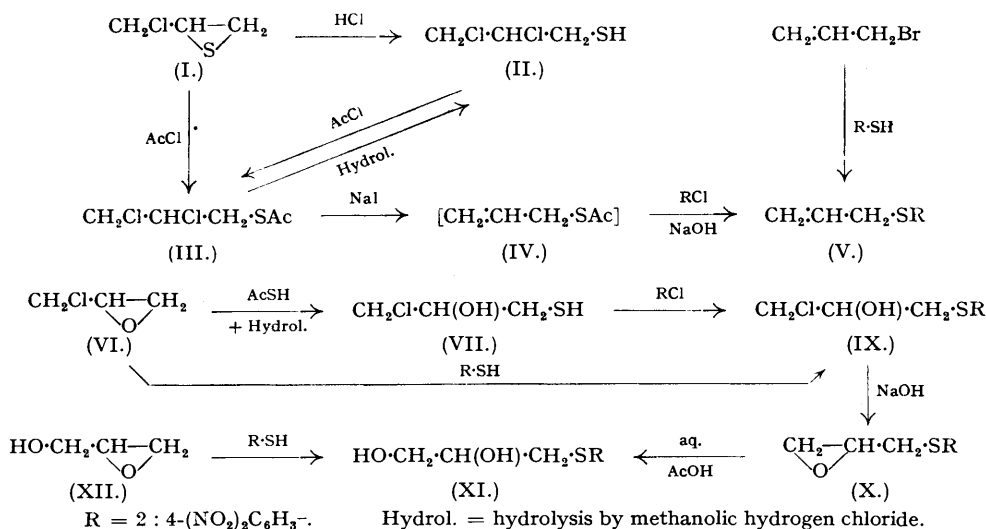
By W. DAVIES and W. E. SAVIGE.

Propylene oxide, *isobutylene* (2-methylpropylene) oxide, epichlorohydrin, and glycidol undergo normal ring fission with 2 : 4-dinitrothiophenol (forming crystalline derivatives suitable for the characterisation of ethylene oxides) and/or thiolacetic acid, the oxygen atom retaining its link with C₍₂₎. *iso-Butylene* sulphide with acetic anhydride containing pyridine also gives a "normal" product. Abnormal fissions are brought about by the interaction of chloropropylene sulphide (I) with hydrogen chloride and acetyl chloride respectively. These facts, which have now been proved, admit of a generalisation.

ACETIC ANHYDRIDE in the presence of pyridine has already been shown to react with propylene sulphide to form 2-acetylthiopropyl acetate, $\text{AcS}\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{OAc}$, and this is regarded as a

“ normal ” process (Davies and Savige, *J.*, 1950, 317) because the sulphur atom retains its link with C₍₂₎. Acetyl chloride formed the “ abnormal ” product, 2-chloropropyl thiolacetate, CHMeCl·CH₂·S·Ac, aqueous hydrogen chloride also bringing about ring fission in the same direction. The effect of these reagents on other unsymmetrical ethylene sulphides has now been studied.

The unspecified dichloropropanethiol obtained by interaction of chloropropylene sulphide (I) and hydrochloric acid (Culvenor, Davies, and Heath, *J.*, 1949, 285) is shown in the following manner to be the abnormal product—2 : 3-dichloropropane-1-thiol (II). With phenyl

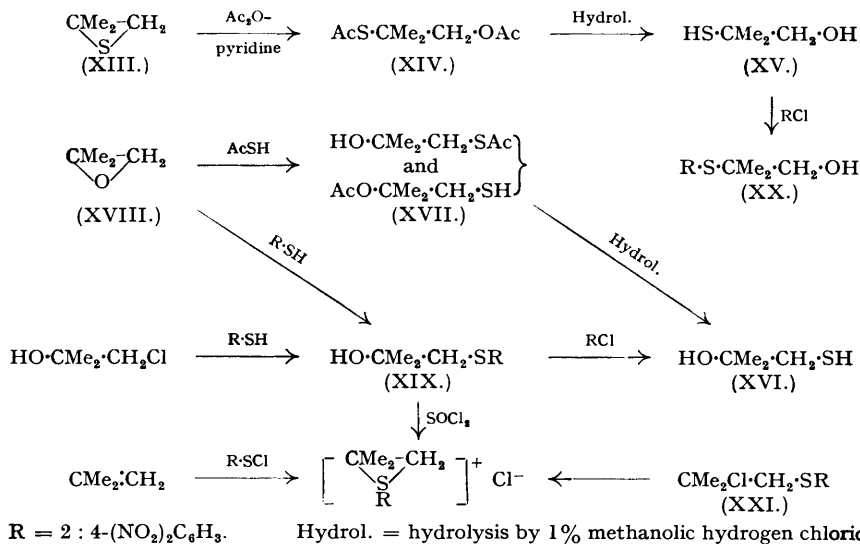


isocyanate and triphenylmethyl chloride severally, it gives crystalline derivatives identical with those formed from the dichloropropanethiol produced by hydrolysis of the product (III) obtained from (I) and acetyl chloride. Moreover, (III) [which is also made by acetylation of (II)] is dehalogenated by sodium iodide in the manner characteristics of 1 : 2-dihalides. The resulting unstable allyl thiolacetate (IV) is converted into allyl 2 : 4-dinitrophenyl sulphide (V), identical with the product obtained from allyl bromide and 2 : 4-dinitrothiophenol. Hence the abnormal ring fission of chloropropylene sulphide with both hydrogen chloride and acetyl chloride is definitely established.

On the other hand, epichlorohydrin (VI) undergoes normal fission with thiolacetic acid, for the product on acid hydrolysis (Sjöberg, *Ber.*, 1941, 74, 64) yields 3-chloro-2-hydroxypropane-1-thiol (VII). This gives no ethylene sulphide derivative with mild alkali (cf. Coltof, U.S.P. 2,183,860/1938), and therefore cannot be the isomeric 3-chloro-2-mercaptopropan-1-ol, CH₂Cl·CH(SH)·CH₂·OH (VIII). Moreover, (VII) forms a 2 : 4-dinitrophenyl sulphide (IX) which is also obtained by interaction of epichlorohydrin and 2 : 4-dinitrothiophenol in a mild alkaline environment. The chlorohydrin (IX) is readily convertible by cold alkali into the corresponding ethylene oxide (X); on the other hand, it is to be expected that cyclisation of the dinitrophenyl sulphide from the isomer (VIII) would be relatively difficult, and the product would be a trimethylene oxide derivative. The oxide (X) is readily hydrolysed in dilute acetic acid to the glycol (XI), also obtained by interaction of glycidol (XII) and 2 : 4-dinitrothiophenol.

*iso*Butylene (2-methylpropylene) sulphide (XIII) is converted by acetic anhydride containing pyridine into 2-acetylthio-2-methylpropyl acetate (XIV), which is hydrolysed to 2-mercapto-2-methylpropanol (XV). On the other hand, the isomeric 2-hydroxy-2-methylpropane-1-thiol (XVI) is formed on hydrolysis of the mixture (XVII) (owing to “ acetyl wandering ”; cf. Sjöberg, *Ber.*, 1942, 75, 27) of 1-acetylthio-2-methylpropan-2-ol and 2-acetoxy-2-methylpropane-1-thiol, produced by interaction of thiolacetic acid and *isobutylene oxide* (XVIII). The mercaptobutanol (XV), but not (XVI), with nascent nitrous acid gives the green and then red colours characteristic of the formation of thionitrites. These colours can be obtained from tertiary, but not from primary or secondary, thiols (Rheinboldt, *Ber.*, 1927, 60, 184; 1926, 59, 1311). The isomers (XV) and (XVI) also form different crystalline 2 : 4-dinitrophenyl sulphides. Moreover, the sulphide (XIX) derived from (XVI) is also obtained by interaction of

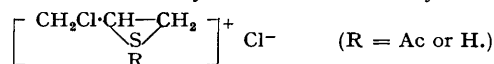
2 : 4-dinitrothiophenol and either *isobutylene* α -chlorohydrin or *isobutylene* oxide in an alkaline environment. Also, thionyl chloride converts (XIX) without re-arrangement (cf. Fuson, Price, and Burness, *J. Org. Chem.*, 1946, **11**, 477) into the corresponding chloro-sulphide (XXI), previously prepared by Kharasch and Buess (*J. Amer. Chem. Soc.*, 1949, **71**, 2724) from 2 : 4-dinitrobenzenesulphenyl chloride and *isobutylene*.



Propylene oxide, which was previously shown to undergo normal fission with thiolacetic acid (Sjöberg, *loc. cit.*; Davies and Savige, *loc. cit.*) is now found to give the "normal" product, 1-(2 : 4-dinitrophenylthio)propan-2-ol when condensed with 2 : 4-dinitrothiophenol. This product is converted by phosphorus pentachloride into the corresponding chloro-sulphide. The readily crystallisable sulphides derived from 2 : 4-dinitrothiophenol are now found to be eminently suitable for characterisation of ethylene oxides, for they are prepared at room temperatures in a weakly alkaline medium. 2 : 4-Dinitrophenyl sulphides have been used to characterise alkyl halides (Willgerodt, *Ber.*, 1885, **18**, 325) and have also been recommended for the characterisation of thiols (Bost, Turner, and Norton, *J. Amer. Chem. Soc.*, 1932, **54**, 1985) and olefins (Kharasch and Buess, *loc. cit.*). In the present work, no difficultly separable mixture of the two possible isomers has yet been obtained from unsymmetrical ethylene oxides, as has been encountered in their reaction with alkali nitrophenoxides (Boyd and Marle, *J.*, 1914, **105**, 2117) or in the reaction of 2 : 4-dinitrobenzenesulphenyl chloride with propylene (Kharasch and Buess, *loc. cit.*).

The normal cleavage of propylene and *isobutylene* oxides, epichlorohydrin, and glycidol occurs almost quantitatively both with 2 : 4-dinitrothiophenol in cold aqueous sodium hydrogen carbonate and with thiolacetic acid. (Fission of glycidol with thiolacetic acid—also with hydrogen sulphide in the presence of alkali—was carried out by Sjöberg, *Ber.*, 1941, **74**, 64.) This recalls similar results with *isopropylidene* 5 : 6-anhydroglucose and hydrogen sulphide or thiols (Ohle and Mertens, *Ber.*, 1935, **68**, 2176), and also the interaction of alkali salts of thiols with unsymmetrical ethylene oxides (Gilman and Fullhart, *J. Amer. Chem. Soc.*, 1949, **71**, 1478). These reactions doubtless belong to the large class based on bimolecular nucleophilic displacements on carbon (cf. Elderfield, "Heterocyclic Compounds," Vol. I, p. 27, Wiley, 1950).

The normal ring fission of *isobutylene* sulphide with acetic anhydride containing pyridine is probably a similar reaction, owing to the presence of pyridine acetate. On the other hand, the abnormal products of the reaction of chloropropylene sulphide with hydrochloric acid and acetyl chloride respectively can be ascribed, as in the case of propylene sulphide (Davies and Savige, *loc. cit.*, p. 319), to the intermediary formation of an ethylenesulphonium ion such as :



In such cases the nature of the group (*e.g.*, CH_2Cl) attached to the ethylene sulphide ring should

decide the manner of fission of the C-S bonds in the above ion, but further investigation of this aspect is necessary. Although in several cases the amount of abnormal product from ethylene oxides and acidic reagents is over 50% (Elderfield, *loc. cit.*, pp. 37-39), it is in general small in comparison with the amounts of abnormal products from ethylene sulphides. This is regarded as caused by the smaller tendency of oxygen, as compared with sulphur, to form 'onium ions. These generalisations co-ordinate some reactions of simple unsymmetrical sulphides and oxides, and also clarify some statements in the literature.

From the above considerations, it is likely that the condensation product of two molecules of propylene sulphide with one of *n*-butylamine (Reppe and Nicolai, D.R.-P. 631,016/1936; Frdl., 23, 244) is $\text{NBu}^{\text{II}}(\text{CH}_2\cdot\text{CHMe}\cdot\text{SH})_2$ and not $\text{NBu}^{\text{II}}(\text{CHMe}\cdot\text{CH}_2\cdot\text{SH})_2$. The latter formula has also been queried by Snyder, Stewart, and Zeigler (*J. Amer. Chem. Soc.*, 1947, 69, 2672), who showed that the main products of interaction of equimolecular amounts of *isobutylene* sulphide and strongly basic primary and secondary amines are normal, e.g., $\text{HS}\cdot\text{CMe}_2\cdot\text{CH}_2\cdot\text{NR}_2$. Their demonstration that the interaction of *isobutylene* sulphide and thiols in the presence of an acid reagent (boron trifluoride) is chiefly abnormal is in accord with the results of the present paper. On the other hand, their isolation of chiefly abnormal products ($\text{RS}\cdot\text{CMe}_2\cdot\text{CH}_2\cdot\text{SH}$) from *isobutylene* sulphide and thiols in the presence of basic catalysts is, at first reading, contrary to the above generalisations. It is, however, noteworthy that they use a mere trace of basic catalyst (sodium ethoxide), and the large proportion of free thiol may function as an acid environment, leading to some abnormal product. Moreover, as equimolecular amounts of *isobutylene* sulphide and thiol yield only about 40% of the mixed normal and abnormal products, it is not certain that the latter (which usually comprises about 60-80% of the mixture) is in fact the chief product. The results of the present work are more definite, for the normal products (XIV) and the abnormal products (II) and (III) are isolated in yields of over 50% (usually over 80%), and any products of the reverse type that may be formed are in quantities too small to be isolated.

EXPERIMENTAL.

Derivatives of Chloropropylene Sulphide.—2 : 3-Dichloropropane-1-thiol (II), b. p. 74-76°/20 mm., n_D^{20} 1.5245, a liquid having a most unpleasant odour, was prepared from 3-chloropropylene sulphide (I), b. p. 57-60°/45 mm. (cf. Culvenor, Davies, and Pausacker, *J.*, 1946, 1050), and concentrated hydrochloric acid as described by Culvenor, Davies, and Heath (*loc. cit.*) who record b. p. 81°/33 mm. Culvenor (private communication) heated (II) with excess of acetyl chloride on the water-bath for 2 hours and on distillation obtained 2 : 3-dichloropropyl thiolacetate (III), b. p. 122°/25 mm., n_D^{20} 1.5155, a liquid with a characteristic ester odour if pure, but rather unpleasant if contaminated with small amounts of free thiol. The ester (III), b. p. 99-103°/11 mm., was also obtained by heating chloropropylene sulphide and acetyl chloride at 50-55° for 5 hours (cf. Culvenor, Davies, and Heath, *loc. cit.*, who give b. p. 115°/18 mm., n_D^{20} 1.5157), this sample on hydrolysis with 2% of hydrogen chloride in methanol for 2 hours giving a good yield of (II), b. p. 74-77°/20 mm., n_D^{20} 1.5235. Both samples of (II) were unchanged in refractive index throughout the distillation, and identical reactions are as follows. Attempts to cause (II) to react with 1-chloro-2 : 4-dinitrobenzene, 1-fluoro-2 : 4-dinitrobenzene, or picryl chloride were unsuccessful, the alkaline medium (sodium hydroxide, sodium hydrocarbonate, or sodium acetate) converting (II) into 3-chloropropylene sulphide, as discernible by odour (cf. Coltof, U.S.P. 2,183,860). The thiol (II) and phenyl isocyanate in light petroleum at 160° during 3 hours gave a *thiolcarbanilate*, m. p. 100°, prisms from benzene-light petroleum (Found : N, 5.0; S, 12.1. $\text{C}_{10}\text{H}_{11}\text{ONCl}_2\text{S}$ requires N, 5.3; S, 12.1%), which when heated with aqueous sodium hydroxide gave the odour of 3-chloropropylene sulphide. The thiol (II) and triphenylmethyl chloride in light petroleum at 100° during 4 hours (cf. von Meyer and Fischer, *J. pr. Chem.*, 1910, [ii], 82, 524) gave 2 : 3-dichloropropyl triphenylmethyl sulphide, m. p. 128°, plate-like prisms from low-boiling light petroleum in which it is moderately soluble (Found : C, 67.95; H, 5.15. $\text{C}_{22}\text{H}_{20}\text{Cl}_2\text{S}$ requires C, 68.2; H, 5.15%).

Dehalogenation of 2 : 3-Dichloropropyl Thiolacetate (III).—2 : 3-Dichloropropyl thiolacetate (12.5 g.), sodium iodide (15 g.), and magnesium (10 g.) were refluxed in methyl ethyl ketone (25 ml.) for 24 hours, then poured into water and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and distilled. The halogen-free distillate b. p. 40-160°, was collected and submitted to repeated fractionation, but a constant-boiling fraction could not be obtained. The formation of high-boiling residue during each distillation indicated that polymerisation was occurring. The fraction of b. p. 50-100° (mainly methyl ethyl ketone) contained free thiol, as shown by the characteristic odour and positive reaction with aqueous sodium nitroprusside. The fraction of b. p. 100-140° (of which about 3 ml. were obtained) (1 g.), 1-chloro-2 : 4-dinitrobenzene (0.4 g.), sodium hydroxide (0.4 g.), water (0.5 ml.), and alcohol (10 ml.) were warmed on the water-bath for 15 minutes. Cooling gave *allyl* 2 : 4-dinitrophenyl sulphide (V), small yellow plates (0.4 g.), m. p. 71° on recrystallisation from 90% alcohol (Found : N, 11.6; S, 13.5, 13.2. $\text{C}_9\text{H}_8\text{O}_4\text{N}_2\text{S}$ requires N, 11.65; S, 13.35%). The sulphide (V) was also obtained (m. p. and mixed m. p. 71°) on warming of allyl bromide (0.12 g.) with a filtered solution of 2 : 4-dinitrothiophenol (0.2 g.) and sodium hydroxide (0.4 g.) in alcohol (10 ml.) on the water-bath for 15 minutes, the mixture being then concentrated to 3 ml. and filtered hot and water (0.5 ml.) added (cf. Willgerodt, *loc. cit.*). The product was purified by recrystallisation from aqueous alcohol, then from light petroleum containing a few drops of benzene, and finally dissolved in a mixture of benzene (1 part) and light

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petroleum (3 parts), and the solution passed through a small column of alumina and developed with the same solvent.

1-(2 : 4-Dinitrophenylthio)-3-chloropropan-2-ol (IX), m. p. 81—82°, yellow prisms from benzene-light petroleum (Found : C, 37.35; H, 2.75; S, 11.2; N, 9.7. $C_9H_9O_5N_2ClS$ requires C, 36.95; H, 3.05; S, 10.95; N, 9.6%), was obtained from exactly equimolar amounts of 1-chloro-3-mercaptopropan-2-ol (VII) (prepared according to Sjöberg's method, *loc. cit.*), 1-chloro-2 : 4-dinitrobenzene, and sodium hydroxide in alcohol (cf. Bennett and Whincop, *J.*, 1921, 119, 1863). As shown by a mixed m. p., (IX) was also obtained on mixing epichlorohydrin (0.1 g.) in alcohol with a filtered solution of 2 : 4-dinitrothiophenol (0.2 g.) in saturated aqueous sodium hydrogen carbonate and keeping the mixture for 10 minutes.

2 : 3-Epoxypropyl 2 : 4-dinitrophenyl sulphide (X), m. p. 94—95°, yellow, halogen-free prisms from benzene-light petroleum (Found : N, 11.0; S, 12.65. $C_9H_9O_5N_2S$ requires N, 10.95; S, 12.5%) was obtained when (IX) in ether-benzene was stirred for 1 hour with excess of cold 40% aqueous sodium hydroxide, and the mixture then poured into water, the organic layer being separated, washed, dried, and freed from solvent. Warming the sulphide (X) with aqueous sodium thiosulphate rapidly produced alkali, which is characteristic of ethylene oxides (cf. Culvenor, Davies, and Heath, *J.*, 1949, 278).

1-(2 : 4-Dinitrophenylthio)propane-2 : 3-diol (XI), m. p. 142—143°, yellow warts from benzene-acetone (Found : S, 11.5. $C_9H_{10}O_6N_2S$ requires S, 11.7%), was obtained in >60% yield when (X) was refluxed in aqueous acetic acid for 4 hours. The diol, which is readily soluble in alcohol and in acetone, but insoluble in benzene, was also obtained when a slight excess of glycidol was mixed with a filtered solution of 2 : 4-dinitrothiophenol (0.2 g.), sodium carbonate (0.2 g.), and sodium hydrogen carbonate (0.2 g.) in water (10 ml.) and the mixture kept for 30 minutes. The solid product was dried at 100°. Its solution in acetone (2 parts) and benzene (1 part) was poured through a narrow column of alumina (10 cm. in length), and the chromatogram developed with acetone. The first yellow fraction yielded (XI) (0.2 g.), identical with the above (mixed m. p.). There appeared to be a small amount of a secondary product contained in a small band near the top of the column, but this gave no crystalline material.

Reaction of isoButylene Sulphide with Acetic Anhydride.—*iso*Butylene sulphide (XIII) was prepared (cf. Culvenor, Davies, and Pausacker, *loc. cit.*) by adding *isobutylene oxide* (23.2 g.) to a well-stirred solution of thiourea (27 g.) in methanol (100 ml.) at a rate such that the temperature was kept at 35—40°. The mixture was then stirred at 40° for an additional 3 hours, diluted with water (200 ml.), extracted with ether, dried, distilled, and refractionated. The yield was 16.5 g. (63%), and the b. p. 84—86°, and 5 ml. of unchanged *isobutylene oxide* were recovered.

*iso*Butylene sulphide (7.1 g.), acetic anhydride (9 g.), and pyridine (0.6 ml.) were heated on the water-bath for 1 hour, and then at 130° for a further 15 hours. The product distilled over the range 110—116°/14 mm., further fractionation yielding 2-acetylthio-2-methylpropyl acetate (XIV), b. p. 114°/15 mm. (9.0 g.) (Found : C, 50.7; H, 7.6. $C_8H_{14}O_3S$ requires C, 50.55; H, 7.4%). The odour resembles that of the propyl homologue (cf. Davies and Savage, *loc. cit.*). Hydrolysis with hot 1% methanolic hydrogen chloride (6 hours) gave a fraction (3 g.), b. p. 56—64°/15 mm., which gave a light red colour with nitrous acid. Refractionation gave 2-mercapto-2-methylpropan-1-ol (XV) (2.5 g.), b. p. 70°/30 mm., n_D^{25} 1.469 (Found : C, 45.7; H, 9.3. $C_4H_{10}OS$ requires C, 45.3; H, 9.4%). This is partly miscible with water, has the unpleasant odour characteristic of thiols, gives a mauve colour with sodium nitroprusside, and explodes on contact with sodium peroxide. Nitrous acid (cf. Rheinboldt, *loc. cit.*) gives a green flash which soon changes to a light red colour.

2-(2 : 4-Dinitrophenylthio)-2-methylpropan-1-ol (XX), m. p. 108.5°, thick yellow needles from benzene-light petroleum (Found : N, 10.5. $C_{10}H_{12}O_5N_2S$ requires N, 10.3%), was obtained from (XV), 1-chloro-2 : 4-dinitrobenzene, and sodium hydroxide in alcohol [method as for (IX)]. Initial crystallisation was effected by adding light petroleum to a dry benzene solution of the crude oily product and keeping the mixture at 0°.

Reaction of isoButylene Oxide with Thiolacetic Acid (cf. Sjöberg, *loc. cit.*).—*iso*Butylene oxide (7.2 g.) and thiolacetic acid (7.6 g.) were warmed together on the water-bath for 7 hours. The product, apparently consisting of a mixture (XVII) (9.6 g.) of 2-hydroxy-2-methylpropyl thiolacetate and 2-acetoxy-2-methylpropane-1-thiol, distilled over the range 80—100°/12 mm. The first drops of distillate had n_D^{25} 1.4650, whilst the fraction boiling constantly at ca. 100° had n_D^{25} 1.4831. Both fractions gave a mauve colour with aqueous sodium nitroprusside. Hydrolysis of (XVII) with 1% methanolic hydrogen chloride (8 hours, reflux) followed by distillation gave a few drops of halogen-containing thiol, b. p. ca. 44°/17 mm., then a fraction of b. p. 72—74°/17 mm. The first few drops of this fraction had n_D^{25} 1.4619 and the last few drops n_D^{25} 1.4600. Both portions gave a deep red colour with nitrous acid and a purple colour with sodium nitroprusside, and were partly miscible with water. Redistillation gave pure 2-hydroxy-2-methylpropane-1-thiol (XVI) (80%), b. p. 73—74°/17 mm. (Found : S, 28.5. $C_4H_{10}OS$ requires S, 28.3%).

1-(2 : 4-Dinitrophenylthio)-2-methylpropan-2-ol (XIX), m. p. 95.5°, yellow warts or prisms from benzene-light petroleum (Found : N, 10.55. $C_{10}H_{12}O_5N_2S$ requires N, 10.3%), was readily obtained from (XVI), 1-chloro-2 : 4-dinitrobenzene, and sodium hydroxide in alcohol [method as for (IX)]. It was also obtained, as shown by mixed m. p., (i) on warming of equimolar amounts of *isobutylene* α -chlorohydrin, 2 : 4-dinitrothiophenol, and sodium hydroxide in alcohol on the water-bath for 0.5 hour, then filtration from disulphide and dilution with water, or (ii) from *isobutylene oxide*, 2 : 4-dinitrothiophenol, and aqueous sodium hydrogen carbonate [method as for (IX)], the mixture being kept for 1 hour]. The sulphide (XIX) was converted into 2-chloro-2-methylpropyl 2 : 4-dinitrophenyl sulphide (XXI) (Found : C, 41.45; H, 3.65. Calc. for $C_{10}H_{11}O_4N_2ClS$: C, 41.3; H, 3.75%), when warmed on the water-bath with a two-fold excess of thionyl chloride for 0.5 hour, followed by removal of excess of

thionyl chloride by evaporation both before and after addition of small quantities of benzene. The oily product was purified by percolation in benzene-light petroleum through a small column of alumina. The first yellow band was collected, the solvent removed, and the solid residue finally recrystallised from alcohol-light petroleum, giving fine yellow needles, m. p. 86—87°. Kharasch and Buess (*loc. cit.*) also record this m. p. for 2-chloro-2-methylpropyl 2 : 4-dinitrophenyl sulphide.

Reaction of Propylene Oxide with 2 : 4-Dinitrothiophenol.—This reaction in aqueous sodium hydrogen carbonate [method as for (XIX)] gave 1-(2 : 4-dinitrophenylthio)propan-2-ol, m. p. 94°, identified by mixed m. p. with sample prepared by Davies and Savige (*loc. cit.*) from 1-mercaptopropan-2-ol, 1-chloro-2 : 4-dinitrobenzene, and sodium hydroxide in alcohol. This was dissolved in chloroform, and phosphorus pentachloride added in portions until effervescence ceased, then ether was added and the solution washed with water. Evaporation of the ether gave 2-chloropropyl 2 : 4-dinitrophenyl sulphide, m. p. 75—77°, yellow, halogen-containing crystals from aqueous methanol and then from chloroform-light petroleum (Found : S, 11.4. Calc. for $C_9H_9O_4N_2ClS$: S, 11.6%). Kharasch and Buess (*loc. cit.*) record m. p. 75—76° for this compound, and 108.5—109.5° for the other possible isomer, both of which they obtained from propylene and 2 : 4-dinitrobenzene sulphenyl chloride.

The microanalyses were made by Miss E. E. Rutherford and Messrs. R. B. Campbell and N. L. Lottkowitz.

ORGANIC CHEMISTRY LABORATORY, UNIVERSITY OF MELBOURNE. [Received, October 13th, 1950.]
