244. *The Nature of the 2-Chloroethyl Chlorovinyl Sulphide Isomers.*

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The decomposition of 1 : 2 : 2′-trichlorodiethyl sulphide [prepared by the chlorination of 2 : 2′-dichlorodiethyl sulphide (" mustard gas ")] gives two compounds which have previously been assumed to be he 2-chloroethyl 1- and 2-chlorovinyl sulphides (I) and (II). They are now believed to be the *cis–trans* isomers of (II), since :

(*a*) A derivative of the aldehyde (III), expected from the hydrolysis of (II), has been obtained from both isomers.

(*b*) By interaction with methylthiol and subsequent oxidation the isomers could be converted to two disulphones, that from (II) having the structure (VI). These disulphones were found to be interconvertible, the " β " form giving the " α " on treatment with bromine in acetic acid. This behaviour is characteristic of geometrical isomerism, and the disulphones are therefore considered to be the *cis–trans* isomers of (VI).

An attempt to obtain rigid proof of geometrical isomerism by reduction to 2-chloroethyl 2-methylsulphonylethyl sulphone (VII) met with failure.

LAWSON and DAWSON (*J. Amer. Chem. Soc.*, 1927, **49**, 3119) showed that 1 : 2 : 2′-trichlorodiethyl sulphide was formed by the controlled chlorination of 2 : 2′-dichlorodiethyl sulphide ("mustard gas"); this trichloro-compound on being heated decomposed with the elimination of hydrogen chloride. By fractionation they obtained two compounds from the reaction product; these were thought to be the isomeric 2-chloroethyl 1- and 2-chlorovinyl sulphides [" C.E.C.V.S.," (I) and (II)].

$CH_2Cl{\cdot}CH_2{\cdot}S{\cdot}CCl{:}CH_2$ (I.) $CH_2Cl{\cdot}CH_2{\cdot}S{\cdot}CH{:}CHCl$ (II.) $CH_2(OH){\cdot}CH_2{\cdot}S{\cdot}CH_2{\cdot}CHO$ (III.)

Many other workers have since handled these compounds (cf. Lewin and Tschulkow, *J. pr. Chem.*, 1930, **128**, 171; Dawson, *J. Amer. Chem. Soc.*, 1933, **55**, 2070), but the original assumption as to their structure has not been questioned. The compound (II), however, should be capable of geometrical isomerism, and the compounds isolated by Lawson and Dawson might therefore be the *cis–trans* isomers of (II). The isomerism might, in fact, be either structural or geometrical, and none of the work previously published has thrown any light on which of these alternatives is correct. The evidence now presented supports the geometrical nature of the isomerism. It does not exclude the possibility that (I) is also formed, though no evidence of a third isomer has been obtained in this or previous work.

Hydrolysis of (II) would be expected to yield the aldehyde (III); and this compound was in fact isolated by Wadsworth after the hydrolysis of a mixture of the two isomers (private communication). The 2 : 4-*dinitrophenylhydrazone* of this aldehyde has now been isolated from the products of hydrolysis, and its structure has been confirmed by its preparation from the aldehyde (III) which was itself synthesised by the condensation of bromoacetal with the sodium salt of monothioethylene glycol, and hydrolysis of the product.

The isomers, separated by careful fractionation to constant density, were hydrolysed; from each the 2 : 4-dinitrophenylhydrazone of the aldehyde (III) was isolated, the best yields in each case being about 45—50%. Since this compound could hardly arise from (I) it appears that both isomers consisted, at least largely, of (II).

When the isomers were treated with sodium thiomethoxide, the chloroethyl group, as was expected, reacted very much more readily than the chlorovinyl group; the monothioethers so formed could be oxidised to give crystalline *disulphones*. Starting from the mixed isomeric sulphides a mixture of the two disulphones was obtained which could be separated by recrystallisation, while the pure " α " and " β " isomers gave the disulphones, m. p. 180° and 115° respectively, each apparently uncontaminated by the other; this afforded confirmation that the fractionation of the isomeric sulphides had achieved substantial separation of the two components.

These two disulphones could either have the structures (V) and (VI), or, if the sulphides were geometrical isomers, be the *cis–trans* forms of (VI).

(V.) $CH_3{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2{\cdot}SO_2{\cdot}CCl{:}CH_2$ $CH_3{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2{\cdot}SO_2{\cdot}CH{:}CHCl$ (VI.)

(VII.) $CH_3{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2Cl$ $CH_3{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2{\cdot}SO_2{\cdot}CH_2{\cdot}CH_3$ (VIII.)

It was then found that the compound of m. p. 115° could be converted into that of m. p. 180° if it were heated in acetic acid in the presence of a catalyst such as bromine, bromate, or iodate. This phenomenon falls into line with many similar cases of conversion of *cis-* into *trans*-isomers; it is, however, very difficult to explain if the isomerism is structural (V and VI). It is therefore considered probable that the compound of m. p. 115° is the *cis-*, and that of m. p. 180° the *trans-*, isomer of (VI).

If it were possible to reduce the vinyl group of the disulphones without removing the chlorine atom, a rigid proof of the nature of the isomerism should be obtained; the geometrical isomers of (VI) would give the same compound (VII), while (V) would give the corresponding 1-chloroethyl derivative. The compound (VII) was accordingly synthesised by the action of one equivalent of sodium methanesulphinate on 2 : 2′-dichlorodiethyl sulphone (Helfrich and Reid, *J. Amer. Chem. Soc.*, 1920, **42**, 1208). Attempts were then made to reduce the chlorovinyl sulphones catalytically. Unfortunately, no reduction occurred using palladium chloride–gum arabic or platinum–platinum oxide catalysts, and the use of palladised barium sulphate led to the hydrogenation of the double bond and replacement of the chlorine atom. The structure of the 2-*methylsulphonyldiethyl sulphone* (VIII) resulting from the reduction was confirmed by synthesis; ethyl iodide was condensed with the sodium salt of *methyl 2-mercaptoethyl sulphide* (prepared from methyl 2-chloroethyl sulphide), and the product oxidised to the disulphone.

The preparation of (VIII) from the isomeric chlorovinyl disulphones affords general confirmation of their structure; it does not, however, have any bearing on the nature of the isomerism of the sulphides, since (VIII) could be derived from either (V) or (VI). Attempts to prove the structure by reduction were therefore abandoned.

The opportunity is taken to record the preparation of 2-chloroethyl thiolacetate, since it was analogous to the 2-hydroxyethyl thiolacetate expected to be formed on hydrolysis of (I). Neither this compound, nor the diacetate of 2-hydroxyethylthiol, nor the solutions obtained by their hydrolysis, showed any signs of reaction with 2 : 4-dinitrophenylhydrazine.

Experimental.

1 : 2 : 2′-*Trichlorodiethyl Sulphide.*—The following modification of the method of Lawson and Dawson (*loc. cit.*) was normally used. A current of dry air was led over a weighed amount of cooled liquid chlorine, and then into well stirred and cooled 2 : 2′-dichlorodiethyl sulphide (1 mol.) (Gibson and Pope, *J.*, 1920, **117**, 271) without solvent. The rate of chlorine addition was adjusted so that the temperature of the reaction mixture was kept at about 0°. When the addition was finished the mixture was stirred for a further ½ hour at room temperature with an air current; the product was used without further purification for the preparation of the mixed sulphides.

Chloroethyl Chlorovinyl Sulphides.—Crude 1 : 2 : 2′-trichlorodiethyl sulphide was kept at 100° for 6 hours in a current of dry air and then distilled. After redistillation through a Widmer column to remove unchanged 2 : 2′-dichlorodiethyl sulphide the material was used as " mixed sulphides ".

The author is indebted to Dr. R. J. Rossner and to Mr. E. Booth for the samples of the pure isomers used in this work. They were prepared by systematic fractionation of " mixed sulphides "; in the second case the fractionation was continued until no further change in density resulted from redistillation.

The properties of the preparations were as follows :—

β-Isomer	(*a*)	b. p. 58°/2 mm.; $n_{D}^{20°}$ 1·5493; $d_{4°}^{20°}$ 1·3220
	(*b*)	b. p. 79—81°/6·5 mm.; $d_{4°}^{20°}$ 1·3222
α-Isomer	(*a*)	b. p. 54°/2 mm.; $n_{D}^{20°}$ 1·5486; $d_{4°}^{20°}$ 1·3031
	(*b*)	b. p. 69—73·5°/6·5 mm.; $d_{4°}^{20°}$ 1·3015.

The 2 : 4-*Dinitrophenylhydrazone of* 2-*Hydroxyethylthioacetaldehyde* (III).—(a) *Isolation experiments.* Samples of the α- or β-isomer (0·3 to 0·5 g.) and water (100 parts) were refluxed for various times; the mixture became homogeneous after about ½ hour. At the end of the hydrolysis the solutions were added to 2 : 4-dinitrophenylhydrazine (1 equiv.) in cold 2N-hydrochloric acid, and the mixtures kept overnight. The *product* was deposited as long needles, and after recrystallisation from aqueous alcohol or from ethyl acetate–petrol melted at 78·5° (Found : C, 40·7; H, 4·3; N, 18·2; S, 10·34. $C_{10}H_{12}O_5N_4S$ requires C, 40·0; H, 4·0; N, 18·7; S, 10·66%). The yields after varying periods of hydrolysis were as follows :

β-Isomer	6	hours	hydrolysis,	51%	yield of	product,	m. p. 78°
	18	,,	,,	45%	,,	,,	,, 75°
α-Isomer	6	,,	,,	4%	,,	,,	,, 73°
	12	,,	,,	41%	,,	,,	,, 75°
	18	,,	,,	45%	,,	,,	,, 74°

(b) *Synthesis.* Bromoacetal (Freunder and Ladra, *Compt. rend.*, 1905, **140**, 794) (27·5 g.) was added gradually to a warm solution of 2-hydroxyethylthiol (11 g.; cf. Bennett, *J.*, 1921, 423) in sodium ethoxide solution (from 3·1 g. of sodium and 50 c.c. of alcohol). Sodium bromide was rapidly precipitated; the reaction was completed by refluxing for 1 hour, and the mixture was then cooled, acidified with dilute hydrochloric acid, and extracted with chloroform. Concentration of the extracts gave a brown oily residue which appeared to decompose on distillation and was therefore, without further purification, hydrolysed by being kept for 24 hours with hydrochloric acid (600 c.c., 2·5%). The solution was then neutralised by addition of magnesium carbonate, and sodium chloride added. Repeated ether extraction followed by concentration gave the required aldehyde as a partially crystalline mass, which was purified by recrystallisation from petrol; m. p. 56°. The *p*-nitrophenylhydrazone formed needles, m. p. 126° (Wadsworth, *loc. cit.*, records for the aldehyde as isolated from the hydrolysis of the mixed sulphides, m. p. 56·5°; *p*-nitrophenylhydrazone, m. p. 124—125°); the 2 : 4-dinitrophenylhydrazone had m. p. 78°, identical by mixed m. p. with samples prepared as above from the α- and β-isomers.

2-*Methylsulphonylethyl* 2-*Chlorovinyl Sulphones.*—(1) *Preparation.* (*a*) The α-sulphide (1·57 g.) was refluxed for ½ hour with an alcoholic solution of sodium thiomethoxide (12 c.c., 2N, made by distilling methylthiol (*Org. Synth.*, Coll. Vol. **2**, 346) into the equivalent amount of sodium ethoxide solution). The mixture was allowed to cool, dilute acid and chloroform were added, and the chloroform layer was separated, dried, and evaporated to dryness under reduced pressure. The residue, without further purification, was treated with glacial acetic acid (15 c.c.) and hydrogen peroxide (15 c.c., 100 vol.) and heated at 100° for 1 hour. The *α-disulphone* was deposited on cooling in a yield (crude) of about 70%; it could be recrystallised from a mixture of equal volumes of water and glacial acetic acid, from which it was obtained sometimes as needles, sometimes as plates; both melted at 180°, as did a mixture of the two, and interconversion of the two was frequently observed during recrystallisation (Found : C, 26·0; H, 4·3; Cl, 15·5; S, 27·8. $C_5H_9O_4ClS_2$ requires C, 25·8; H, 3·9; Cl, 15·25; S, 27·5%).

(*b*) The β-sulphide was treated with sodium thiomethoxide exactly as above, and the crude product oxidised as before. The resulting *β-disulphone* was deposited in yield (crude) of 60%, and after recrystallisation from alcohol was obtained as mixed needles and plates, m. p. 111° (Found : C, 26·1; H, 4·2; Cl, 14·7%). Repeated recrystallisation from ethyl acetate–petrol gave plates, m. p. 115°, while on heating in a sealed tube to 120° for 1 hour the compound was obtained as needles, m. p. 107°. The mixture of the two melted at 111°, and either, on recrystallisation from alcohol, gave mixed needles and plates.

In both these preparations concentration of the mother liquor gave small crops of the disulphones contaminated with oily products; in neither was any sign of the isomeric disulphone observed.

(*c*) The mixed sulphides on treatment as above gave a mixture of the two disulphones which could be separated by recrystallisation from aqueous acetic acid, the compound of m. p. 115° being considerably more soluble than that of m. p. 180°. In a typical experiment the sulphides (19·5 g.) was refluxed for ½ hour with sodium thiomethoxide (2·5N, 53 c.c.) and the product isolated as above and distilled to give the mixed thioethers (15·2 g.), b. p. 95—105°/3 mm., or, on redistillation, 93—98°/3 mm. This material (2 g.) was treated with glacial acetic acid (15 c.c.) and hydrogen peroxide (15 c.c., 100 vol.) and kept at room temperature for 48 hours. The α-disulphone was deposited and collected; 0·665 g., m. p. 178°. The mother liquors were evaporated to dryness and the residue recrystallised from aqueous acetic acid; the product (0·1 g., m. p. 140—155°) was discarded, while the mother liquors were again concentrated to dryness and recrystallised, this time from alcohol, to give the β-disulphone; 1·2 g., m. p. 107°.

(2) *Interconversion.* The β-disulphone, m. p. 115°, was heated to 100° for 1 hour in a sealed tube with acetic acid containing a trace of bromine. On cooling a solid, m. p. 176°, was deposited; after recrystallisation from aqueous acetic acid it had m. p. 180° and was shown by mixed m. p. to be identical with the α-disulphone prepared as above; yield, almost theoretical. This conversion was also observed if bromine were replaced by potassium bromate or iodate; the compound m. p. 115° was recovered unchanged, however, if heated with acetic acid alone, or with acetic acid and traces of chlorine, iodine, hydrogen chloride, phosphorus pentachloride, or sulphuryl chloride. This conversion could,

if so desired, be applied to the preparation of the disulphone, m. p. 180°, from the mixed sulphides, the reaction mixture from the peracetic acid oxidation being sealed up with a trace of bromine and heated to 100° for 1 hour. The overall yield of pure α-disulphone obtained by this method was 54%.

(3) *Attempted reduction.* The α-disulphone, m. p. 180°, was used for the following experiments:

(*a*) Palladous chloride (1 g.) (cf. Skita *et al.*, *Ber.*, 1909, **42**, 1627; 1912, **45**, 3312, 3579; 1915, **48**, 1486) was dissolved in dilute hydrochloric acid (100 c.c.). The disulphone (0·5 g.) in glacial acetic acid (63 c.c.), dilute hydrochloric acid (7 c.c.), the palladous chloride solution (1 c.c.), and gum arabic (1% solution in water, 2 c.c.) were shaken in an atmosphere of hydrogen for 5 hours at room temperature. The disulphone was recovered unchanged, both in this and in another experiment in which the amount of catalyst was increased tenfold.

(*b*) The platinum–platinum oxide catalyst (*Org. Synth.*, Coll. Vol. **1**, 463) was tried both in alcohol and in acetic acid containing hydrochloric acid; in both cases the disulphone was recovered unchanged.

(*c*) Palladised barium sulphate was prepared by the formaldehyde reduction of palladous chloride in presence of barium sulphate (cf. Schmidt, *Ber.*, 1919, **52**, 409). The disulphone (0·5 g.) in glacial acetic acid (63 c.c.) and dilute hydrochloric acid (7 c.c.) was shaken with the catalyst (0·5 g.) in an atmosphere of hydrogen for 4 hours. The product was recrystallised from aqueous acetic acid; needles m. p. 120°, identical by mixed m. p. with the 2-methylsulphonyldiethyl sulphone prepared as below.

Methyl 2-Mercaptoethyl Sulphide.—Sodium (5·5 g.) was dissolved in alcohol (200 c.c.) and the solution saturated with hydrogen sulphide. Methyl 2-chlorethyl sulphide (*Org. Synth.*, Coll. Vol. **2**, 345) (26·5 g.) was now added, and the solution heated to 50° for 30 minutes, and then refluxed for a further 30 minutes. Sodium chloride was removed by filtration, and the filtrate concentrated under reduced pressure. Distillation of the residue gave both the required *thiol* (8 g., b. p. 75—77°/30 mm.) and 2 : 2′-dimethylthiodiethyl sulphide (11 g., cf. Meade and Moggridge, *J.*, 1946, 813). Difficulty was found in getting satisfactory analyses for thiol (Found: SH, 28·0. $C_3H_8S_2$ requires SH, 30·5%); it was, however, satisfactorily characterised by conversion into its *α-naphthylcarbamate*, needles from ethyl acetate–petrol, m. p. 119° (Found: C, 61·5; H, 5·6; N, 5·0; S, 23·3. $C_{14}H_{15}ONS_2$ requires C, 60·7; H, 5·5; N, 5·05; S, 23·1%).

2-*Methylsulphonyldiethyl Sulphone.*—Methyl 2-mercaptoethyl sulphide was added to sodium ethoxide (1 equiv.) in alcohol and the mixture refluxed with ethyl iodide (1 equiv.) for 1 hour. The mixture was then shaken with water and chloroform and the chloroform layer separated, dried, and concentrated; the residue was oxidised by heating at 100° for 1 hour with excess of peracetic acid. The required *disulphone* was deposited on cooling as needles, m. p. 120° (Found: S, 32·2. $C_5H_{12}O_4S_2$ requires S, 32·0%).

2-*Chloroethyl* 2-*Methylsulphonylethyl Sulphone.*—Solutions of 2 : 2′-dichlorodiethyl sulphone (Helfrich and Reid, *loc. cit.*) and sodium methanesulphinate (1 equiv.; cf. Boeseken and Ockenberg, *Rec. Trav. chim.*, 1914, **33**, 317) in 80% alcohol were mixed and kept at room temperature for 2 hours. The solution was then concentrated under reduced pressure, and the residue recrystallised (with filtration in the hot) from water; the *product* was deposited in 40% yield as needles, m. p. 162° (Found: Cl, 15·2; S, 26·9. $C_5H_{11}O_4ClS_2$ requires Cl, 15·15; S, 27·3%). On being warmed with pure pyridine this compound gave an insoluble quaternary salt, which was collected, washed with ether, and recrystallised from aqueous alcohol. This *compound* was not deliquescent, though it was readily soluble in water to give a solution containing free chloride ions; on being warmed with alkali it decomposed with liberation of pyridine. Yield, 85—90%; m. p. 242° (decomp.) (Found: Cl′, 11·3; S, 20·9. $C_{10}H_{16}O_4NClS_2$ requires Cl′, 11·3; S, 20·4%).

2-*Chloroethyl Thiolacetate.*—To ethylene sulphide (Canadian patent 392,681; B.P. 465,662; also Meade, private communication) (18 g.) in chloroform (100 c.c.) was added redistilled acetyl chloride (26·5 g.), and the mixture was refluxed for ½ hour. The solvent was then removed under reduced pressure and the residue distilled to give the desired *product* in 82% yield, b. p. 54°/4 mm., 62°/7·5 mm. (Found: Cl, 25·7; S, 23·2. C_4H_7OClS requires Cl, 25·65; S, 23·15%).

2-*Acetoxyethyl Thiolacetate.*—2-Hydroxyethylthiol (40 g.) in benzene (100 c.c.) was treated with freshly distilled acetyl chloride; hydrogen chloride was evolved in the cold. The mixture was refluxed for 1 hour and then concentrated under reduced pressure. The residue on distillation gave the required product in almost theoretical yield; b. p. 80—82°/4 mm. (Rojahn and Lemme, *Arch. Pharm.*, 1925, **263**, 612, give b. p. 118—120°/25 mm.) (Found: S, 19·6. Calc. for $C_6H_{10}O_3S$: S, 19·75%).

Neither this nor the previous compound showed any sign of reaction with 2 : 4-dinitrophenylhydrazine, nor did the solutions obtained after refluxing them with water (1 and 5 hours), sodium bicarbonate solution (½ hour), or dilute hydrochloric acid (½ hour).

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