

**355. Cyclic Sulphites derived from the Chloropropanediols.**

By P. B. D. DE LA MARE, W. KLYNE, D. J. MILLEN, J. G. PRITCHARD, and D. WATSON.

The products of the reaction between thionyl chloride and 2-chloropropane-1 : 3-diol include two crystalline products, identified as the geometric isomers of the cyclic 2-chlorotrimethylene sulphite. Infrared absorption spectra of these and of related compounds are discussed with reference to the conformational and configurational problems involved.

THE reaction of thionyl chloride with 1 : 2- and with 1 : 3-diols is known to result in the formation, often in good yield, of cyclic sulphites, and a number of these have been described.<sup>1,2</sup> Geometrical isomerism dependent on the pyramidal arrangement of the groups attached to the sulphur atom should be possible in suitably substituted sulphites, by analogy with the similar geometrical isomerism observed in sulphoxides.<sup>3</sup> In the present work, the reaction between thionyl chloride and 2-chloropropane-1 : 3-diol has been studied. Fractional distillation of the product gave two isomeric sulphites, A, m. p. 42°, and B, m. p. 62°. Their infrared spectra have been compared with those of related compounds, including the cyclic sulphite of 5 $\beta$ -cholestane-3 $\beta$  : 5-diol. In this compound, the rather rigid steroid skeleton limits the conformational possibilities for the position of the S=O bond. From the comparisons, it is deduced that compounds A and B are the geometric isomers of 2-chlorotrimethylene sulphite. Their conformations and configurations are discussed below in terms of conformational analysis.<sup>4,5</sup>

*Note added May 1st, 1956.*—Szmant and Emerson<sup>5a</sup> reported the infrared stretching frequencies of the S=O bonds in some of the cyclic sulphites examined by us. Their values for ethylene sulphite (1220 cm.<sup>-1</sup>) and propylene sulphite (1222 cm.<sup>-1</sup>) agree fairly well with ours (1214 and 1215 cm.<sup>-1</sup> respectively). Their value for trimethylene sulphite (1220 cm.<sup>-1</sup>) differs from ours; since they used a dilute solution in carbon tetrachloride, they possibly failed to resolve the two bands which we observed for this compound at 1190 cm.<sup>-1</sup> and 1234 cm.<sup>-1</sup>. From the regularity of its occurrence in 1 : 3-sulphites, we regard the former band as that of the S=O stretching vibration.

## EXPERIMENTAL

2-Chloropropane-1 : 3-diol was prepared by the method of Glattfield *et al.*<sup>6</sup> A monochlorohydrin mixture (300 g.; prepared from allyl alcohol and chlorine in the presence of aqueous sodium carbonate) was treated several times with acetone in the presence of sulphuric acid and sodium sulphate. Each time, the isopropylidene derivative of 3-chloropropane-1 : 2-diol was separated from the residual monochlorohydrin mixture, which in this way was gradually enriched in 2-chloropropane-1 : 3-diol. Finally, there was obtained a product (60 g.), b. p. 96—98°/3 mm.,  $n_D^{25}$  1.4818. Kinetic analysis<sup>7</sup> of this showed that less than 10% of the isomeric diol was present.

3-Chloropropane-1 : 2-diol was recovered from its isopropylidene derivative, obtained as a by-product in the above preparation. It had b. p. 96—98°/3 mm.,  $n_D^{25}$  1.4790, and a 0.054N-solution reacted with 0.054N-sodium hydroxide in water at 25° with  $k_2 = 10.8$  l. mole<sup>-1</sup> min.<sup>-1</sup>.

*Reaction of Thionyl Chloride with 2-Chloropropane-1 : 3-diol.*—2-Chloropropane-1 : 3-diol (20 g.) was refluxed for 12 hr. with thionyl chloride (13.4 ml.) and ether (100 ml.). The product was fractionated, giving the following materials: (i) 13 g., b. p. 67—73°/12 mm.; this solidified on cooling, and recrystallisation from water gave trans(?) 2-chlorotrimethylene sulphite as needles (A), m. p. 42° (Found: C, 22.7; H, 3.0; Cl, 22.3; S, 20.2. C<sub>3</sub>H<sub>5</sub>O<sub>3</sub>ClS requires C, 23.0; H, 3.2; Cl, 22.7; S, 20.5%). (ii) 7 g., b. p. 73—84°/12 mm., solidifying partly on cooling.

<sup>1</sup> Carlson and Cretcher, *J. Amer. Chem. Soc.*, 1947, **69**, 1952.

<sup>2</sup> Majima and Simanuki, *Proc. Imp. Acad. (Tokyo)*, 1926, **2**, 545.

<sup>3</sup> Bell and Bennett, *J.*, 1927, 1798; 1929, 15.

<sup>4</sup> Barton, *J.*, 1953, 1027.

<sup>5</sup> Klyne, "Progress in Stereochemistry," Butterworths, London, 1954, p. 36.

<sup>6</sup> Glattfield, Seavell, Spieth, and Hutton, *J. Amer. Chem. Soc.*, 1931, **53**, 3169.

<sup>7</sup> Smith, *Z. phys. Chem.*, 1918, **92**, 717.

(iii) 3 g., b. p. 96°/12 mm., solidifying on cooling. Recrystallisation from water gave *cis*(?)-2-chlorotrimethylene sulphite as plates (B), m. p. 62° (Found: C, 23.0; H, 3.2; Cl, 23.1; S, 20.4%). The materials A and B were not dimorphic forms of the same substance, since they had different b. p.s. and a mixture of the two was liquid at room temperature.

*Reaction of Thionyl Chloride with 3-Chloropropene-1:2-diol.*—3-Chloropropene-1:2-diol (10 g.) was refluxed for 12 hr. with thionyl chloride (6.7 ml.), toluene (50 ml.), and ether (50 ml.). Fractional distillation gave 3-chloropropylene sulphite (9.5 g.), b. p. 95°/12 mm., 210°/760 mm.,  $n_D^{25}$  1.4808 (Found: C, 23.4; H, 3.6; Cl, 19.7; S, 22.5%).

Reaction of thionyl chloride with this diol in the presence of pyridine gave mixtures containing also dichlorohydrins and trichloropropane.

*Cyclic Sulphite of 5 $\beta$ -Cholestane-3 $\beta$ :5-diol.*—This was prepared by the method used for anhydrostrophanthidin 3:5-sulphite by Plattner, Segre, and Ernst.<sup>8</sup> The diol (135 mg., double m. p. 141—142°, 150—152°; Plattner, Heusser, and Kulkarni<sup>9</sup> report m. p. 149°) was dissolved in dry chloroform (15 ml.), and *ca.* 5 ml. of chloroform were distilled off. The solution

*Infrared absorption bands (cm.<sup>-1</sup>) of cyclic sulphites.*

(a) Ethylene sulphite; (b) propylene sulphite; (c) 3-chloropropylene sulphite; (d) trimethylene sulphite; (e) 1:3-butylene sulphite; (f) sulphite A; (g) sulphite B; (h) cyclic sulphite from 5 $\beta$ -cholestane-3 $\beta$ :5-diol.

1:2-Sulphites			1:3-Sulphites				
(a)	(b)	(c)	(d)	(e)	(f)	(g)	(h)
—	—	—	611w	620w	614w	611w	—
—	—	—	622m	635m	628m	623m	—
—	—	—	—	—	670w	666w	—
672s	675m	678m	675s	—	689m	674s	—
—	—	—	708s	690m	—	700s	—
—	—	733m	—	724m	730s	—	—
744s	742m	—	749m	—	—	—	—
—	—	768m	—	—	—	—	—
—	—	—	—	822m	816w	818w	—
—	830m	—	—	—	826w	828m	—
—	—	843m	855s	846w	848s	838s	—
875w	—	—	—	—	—	870m	—
—	—	888w	—	888s	—	880w	—
921s	—	—	904w	—	917w	927w	—
—	—	—	935s	934w	—	—	—
965m	969s	962s	—	952s	969s	—	—
—	—	—	—	974w	998m	986m	—
1011s	—	1026m	1019s	1017m	—	1008s	1001s
—	1061m	1050m	—	1061m	—	1078m	1048m
1090w	—	1078w	—	—	—	1087s	1097s
—	1105w	1106w	—	—	—	—	—
1128w	1141w	—	1141w	1133w	1122s	—	—
—	—	—	—	1153w	1153w	1152w	1159w
—	—	—	—	—	1160w	1184m	1177m
—	—	—	1190s	1195s	1188s	1189s	1192s
1214s	1215s	1213s	—	—	—	—	—
—	—	—	1234m	1230w	1239m	1230m	—
—	—	—	—	1250w	—	—	—
—	—	—	1277m	—	1274m	1288s	—
—	1308w	1298w	—	1315w	—	1303m	—
—	—	—	—	1333w	1330m	—	—
1362m	1385m	—	1367m	1387m	1388m	—	—
—	—	1428m	1428s	—	—	1448m	—
1472s	—	1454m	1467m	1467m	1467m	1467m	—

s = strong; m = medium; w = weak.

was cooled to -12°, and pyridine (1 ml.) and thionyl chloride (0.75 ml.) were added. The mixture was kept for 36 hr. at room temperature and then cooled to 0°, and ice, water, and ether were added. The ethereal solution was washed with water, dilute sodium hydrogen carbonate solution, and water again, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. The residue (135 mg.) was chromatographed on alumina (acid-washed, activity II; 4 g.). The bulk of the material was eluted

<sup>8</sup> Plattner, Segre, and Ernst, *Helv. Chim. Acta*, 1947, **30**, 1432.

<sup>9</sup> Plattner, Heusser, and Kulkarni, *ibid.*, 1948, **31**, 1885.

with light petroleum (b. p. 40—60°) containing 10% or 20% of benzene. After crystallisation from pentane, the sulphite formed small prisms, m. p. 160—162° (a polymorphic form, prisms, m. p. 135—137°, was sometimes obtained from pentane or from methanol) (Found: C, 72.0; H, 10.2; S, 6.5.  $C_{27}H_{46}O_3S$  requires C, 72.0; H, 10.2; S, 7.1%);  $[\alpha]_D +4.5^\circ$  (*c* 1.4 in  $CHCl_3$ ),  $[M]_D +20^\circ$ .

*Other Cyclic Sulphites.*—These were prepared by refluxing the appropriate diol with thionyl chloride. The products, which were washed with water, dried ( $K_2CO_3$ ), and fractionated, had the following properties: ethylene sulphite,<sup>1</sup> b. p. 90°/42 mm.,  $n_D^{25}$  1.4448; propylene sulphite,<sup>10</sup> b. p. 92°/40 mm.,  $n_D^{25}$  1.4354; trimethylene sulphite,<sup>2</sup> b. p. 90—91°/38 mm.,  $n_D^{25}$  1.4498; cyclic sulphite<sup>10</sup> of ( $\pm$ )-butane-1 : 3-diol, b. p. 59°/10 mm.,  $n_D^{25}$  1.4437. We are indebted to Mr. D. J. Phillips for the preparation of the last compound.

*Infrared Spectra.*—These were recorded with a Hilger D209 spectrometer, used as a single-beam instrument. The liquids were placed between rock-salt or potassium bromide windows, depending on the region being scanned. The solids A and B were melted, then placed between the appropriate windows, and allowed to crystallise before their spectra were recorded. No washers were used, the films being of capillary thickness. The cyclic sulphite of 5 $\beta$ -cholestane-3 $\beta$  : 5-diol was examined only in the region 1000—1300  $cm^{-1}$ , as a crystalline film obtained by evaporation of a solution in carbon disulphide.

The spectral maxima are recorded in the Table. A number of bands, recorded in the region 3000  $cm^{-1}$ , result presumably from C-H vibrations and have not been included.

#### DISCUSSION

That the compounds A and B are cyclic sulphites is proved by analysis, in conjunction with the facts that neither chlorine nor sulphur dioxide is readily displaced in acidic or neutral hydrolysis, whereas sulphite ion is rapidly and quantitatively liberated in alkaline solution at room temperature. The possibility of rearrangement during the reaction of the diol with thionyl chloride, giving 3-chloropropylene sulphite, is unlikely on *a priori* grounds, for one would not expect carbon-oxygen fission during the condensation. Rearrangement is made still more unlikely by the fact that the latter sulphite can be prepared independently and has properties different from those of A, B, or a mixture of A and B.

The infrared absorption spectra give conclusive evidence that A and B are indeed 1 : 3-sulphites. First, the 1 : 2-sulphites, including 3-chloropropylene sulphite, have no absorption bands in the region 600—640  $cm^{-1}$ . The simple 1 : 3-sulphites, however, including A and B, have a characteristic weak band at 610—620  $cm^{-1}$ , and another of medium intensity at 620—635  $cm^{-1}$ . These bands, which have similar contours, can, from their low frequencies, be attributed most plausibly to vibrations of the six-membered ring. Their absence in the more rigid 5-membered ring-structure is on this basis not surprising. Secondly, all the 1 : 2-sulphites, including 3-chloropropylene sulphite, have a strong absorption band at about 1214  $cm^{-1}$ , almost certainly to be attributed to the S=O stretching frequency, which customarily appears in this region.<sup>11</sup> The 1 : 3-sulphites, including the compounds A and B, also have a similar band, but it is consistently displaced by about 25  $cm^{-1}$ , to about 1190  $cm^{-1}$ .

From these facts, it is deduced that compounds A and B, prepared from 2-chloropropane-1 : 3-diol, are 1 : 3-sulphites, obtained without rearrangement. The conformational arrangement of the C-Cl bonds in these compounds can be assigned with a fair degree of certainty. For such bonds, it has been established that higher stretching frequencies are to be associated with equatorial than with axial substituents. This was first shown by Larnaudie,<sup>12</sup> who investigated a number of substituted cyclohexanes, including the chloro-cyclohexanes. Recent work by Barton, Page, and Shoppee,<sup>13</sup> to whom we are indebted for details made available to us before publication, has confirmed this generalisation by comparison of the spectra of a large number of isomeric pairs of halogeno-steroids. For the compounds investigated in this work, the strong absorption bands, at 730  $cm^{-1}$  for A and at 700  $cm^{-1}$  for B, can very reasonably be identified as C-Cl stretching frequencies,

<sup>10</sup> Myles and Pritchard, U.S.P. 2,465,915; *Chem. Abs.*, 1949, **43**, 4853.

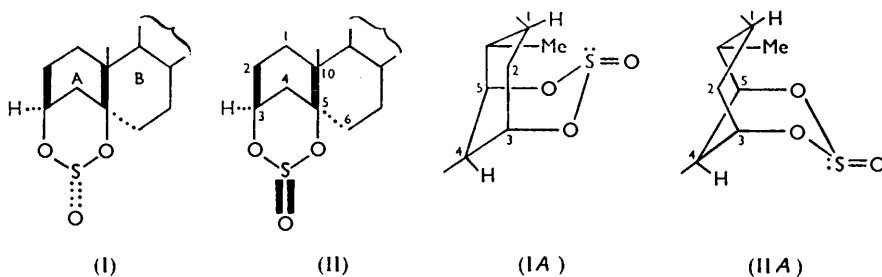
<sup>11</sup> Vogel-Högler, *Acta Phys. Austriaca*, 1948, **1**, 328; Barnard, Fabian, and Koch, *J.*, 1949, 2442

<sup>12</sup> Larnaudie, *Compt. rend.*, 1952, **235**, 154; 1953, **236**, 909.

<sup>13</sup> Barton, Page, and Shoppee, *J.*, 1956, 331.

since, in the chlorocyclohexanes, equatorial and axial C-Cl bonds have frequencies of absorption in these regions, and separated, in isomeric pairs, by about this amount.<sup>12, 13</sup> It seems very probable, therefore, that compound A has an equatorial C-Cl bond, and compound B has an axial C-Cl bond; and it seems likely that both of these compounds, in the crystalline state, exist substantially in one conformation.

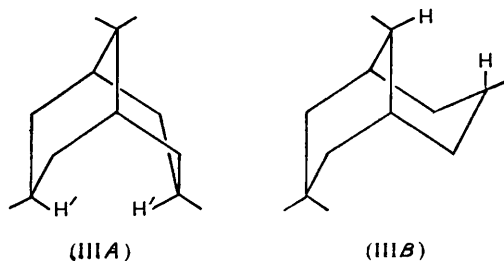
All the simple 1:3-sulphites have absorption bands, which may reasonably be attributed to the S=O stretching frequency, at about 1190  $\text{cm}^{-1}$ . The cyclic sulphite prepared from 5 $\beta$ -cholestane-3 $\beta$ :5-diol also has a strong absorption band at 1192  $\text{cm}^{-1}$ , almost identical with those observed in the spectra of the other 1:3-sulphites: it must have configuration (I) or (II), where the sulphite-containing ring is represented as in the plane of the paper: the S=O bond is *trans* in (I), and *cis* in (II), to the bridge formed by the remainder of the steroid A-ring. For each configuration, two conformations are possible, with the sulphite ring in the chair or boat form respectively. The two preferred conformations are (I; chair) and (II; boat), shown in perspective as (IA) and (IIA) respectively, in each of which the S=O bond is equatorial. In the other two conformations, (I; boat) and (II; chair), the axial position of the S=O group would involve a prohibitively large



repulsion between the oxygen atom and the 4 $\beta$ - or 1 $\beta$ -hydrogen atom respectively. Hence, whichever geometrical isomer (I or II) has been obtained, the S=O bond must be equatorial.\*

It must now be considered whether the nearly identical position of the S=O absorption band in compounds A and B, and in the other 1:3-sulphites including the cyclic sulphite from 5 $\beta$ -cholestane-3 $\beta$ :5-diol, can be taken as evidence that the conformational arrangement of the S=O linkage is the same in all these compounds. For substituted steroids, absorption-frequency differences of similar magnitude between axial and equatorial

\* The possibility should be noted that in the bicyclo[3:3:1]nonane system (III) and its relevant hetero-analogues, of which the above cyclic sulphite is an example, one of the two rings may in general exist in a boat form (III $B$ ). For one of the major factors considered to contribute to the instability of boats in simple cyclohexane derivatives is the repulsion between the two "flagpole" hydrogen atoms (written as H, H in formula III $B$ ), 1.83 Å apart.<sup>14</sup> In the two-chair conformation (III $A$ ), however, the distance between the two hydrogen atoms H', H' is only about 1.2 Å, and so (III $A$ ) is likely to be less stable than (III $B$ ), which may be the preferred conformation. Nitrogen-containing analogues of this steric type belonging to the sparteine series have recently been discussed.<sup>15</sup>



<sup>14</sup> Angyal and Mills, *Rev. Pure Appl. Chem. (Australia)*, 1952, **2**, 185.

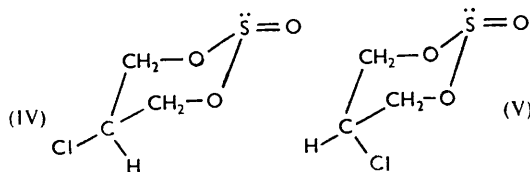
<sup>15</sup> Leonard, Thomas, and Gash, *J. Amer. Chem. Soc.*, 1955, **77**, 1552; cf. Lewis and Shoppee, *J.*, 1956, 313.

substituents have been established for the chloro-, bromo-, iodo-, hydroxy-, methoxy-, acetoxy-, and deuterio-substituents.<sup>13, 16-18</sup> A theoretical interpretation has been given<sup>13, 16</sup> for the direction of this difference, namely, that in the stretching vibration of an equatorial bond the motion of the ring-atom corresponds essentially with the stretching and compression of the six-membered ring, whereas, for an axial substituent, bending of the ring is involved. This would be expected to lead to a higher frequency for the stretching of the equatorial than of the axial bond, since the forces resisting ring-stretching and -compression are greater than those opposing ring-bending.

There seems to be no reason why the same principle should not apply to the S=O group, the infrared absorption characteristics of which are known to be markedly affected by change in the environment of the bond.<sup>11</sup> However, since as yet no definite evidence has been given concerning the absorption frequency to be associated with the stretching of axial S=O groups, the possibility exists that axial and equatorial S=O groups, in sulphites, should be assigned the same absorption frequency.

We prefer the alternative opinion, however, that all the 1 : 3-sulphites described in this paper have the S=O bond in the equatorial conformation. To assign the configurations of the isomeric 2-chlorotrimethylene sulphites on this basis, it has to be considered whether chair or boat conformations are most likely in these systems. In these sulphites, repulsions between "flagpole" hydrogen atoms are absent. On the other hand, both the C-Cl and the S=O group are strongly dipolar. Electrostatic interactions would, therefore, tend to keep these groups apart, and make boat forms unstable with respect to chair forms. Analogously, the chair predominates over the boat form in *cyclohexane-1 : 4-dione*<sup>19</sup> by the ratio of approximately 9 : 1. We consider, therefore, that similar repulsions would make chair forms preferred to boat forms in the cyclic sulphites under consideration.

If the above assumptions are well founded, then the sulphite A, m. p. 42°, is the diequatorial *trans*-2-chlorotrimethylene sulphite (IV), and the isomer B, m. p. 62°, is *cis*-2-chlorotrimethylene sulphite (V) with the chlorine substituent axial and the S=O group equatorial. We propose this as a tentative assignment of the configurations of these compounds.



We are indebted to Professor C. K. Ingold, F.R.S., and to Dr. A. Wassermann for valuable comments. Technical assistance by Messrs. T. J. Collins and C. Bilby is gratefully acknowledged. Analyses are partly by Mr. A. V. Winter, of the William Ramsay and Ralph Forster Laboratories.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES, UNIVERSITY COLLEGE,  
GOWER STREET, LONDON, W.C.1.  
POSTGRADUATE MEDICAL SCHOOL, DUCANE ROAD,  
LONDON, W.12.

[Received, November 14th, 1955.]

<sup>16</sup> Cole, Jones, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 5571.

<sup>17</sup> Page, *J.*, 1955, 2017.

<sup>18</sup> Corey, Snee, Danaher, Young, and Rutledge, *Chem. and Ind.*, 1954, 1294.

<sup>19</sup> Le Fèvre and Le Fèvre, *J.*, 1935, 1696.