40. *Aspects of Stereochemistry. Part III.* Acidic and Basic Hydrolysis of Some Diol Cyclic Sulphates and Related Compounds.†*

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The behaviour of the cyclic sulphates of cyclohexane-*cis*- and -*trans*-1,2-diol on acidic and basic hydrolysis has been examined. From the rates and extent of hydrolysis, the nature of the products formed, and the extent of incorporation of ^{18}O when the hydrolyses were performed in H_2O–$H_2{}^{18}O$, a qualitative reaction mechanism has been proposed.

Recent publications [1-4] have illustrated the fact that, with very few exceptions,[1] cyclic sulphite esters of 1,2- and 1,3-diols are hydrolysed by acids and bases with S–O bond cleavage only. More complex reactions occur on hydrolysis of the analogous cyclic sulphates [4] and we now record a qualitative study of the acidic and basic hydrolysis of the cyclic sulphates of cyclohexane-*cis*- and -*trans*-1,2-diol and of related compounds.

Diol cyclic sulphates may be synthesised by (1) oxidation of a diol cyclic sulphite with calcium permanganate in wet acetic acid,[4] (2) reaction of silver sulphate with a 1,2- or 1,3-alkylene dibromide,[5] (3) reaction of a diol with sulphuryl chloride,[6,7] (4) pyrolysis of

* Part II, *Tetrahedron*, 1959, **7**, 10.

† A preliminary report of a part of this work has been published: Foster, Hancock, and Overend, *Chem. and Ind.*, 1956, 1144.

1 Bunton, de la Mare, Greaseley, Llewellyn, Pratt, and Tillett, *J.*, 1958, 4751.
2 Bunton, de la Mare, and Tillett, *J.*, 1958, 4754.
3 Bunton, de la Mare, Lennard, Llewellyn, Pearson, Pritchard, and Tillett, *J.*, 1958, 4761.
4 Garner and Lucas, *J. Amer. Chem. Soc.*, 1950, **72**, 5497.
5 Baker, *J.*, 1931, 1765; Baker and Field, *J.*, 1932, 86.
6 Price and Berti, *J. Amer. Chem. Soc.*, 1954, **76**, 1211.
7 Lichtenberger and Lichtenberger, *Bull. Soc. chim. France*, 1948, **15**, 1002.

TABLE 1. *Data on some diol cyclic sulphites and cyclic sulphates.*

	Yield (%)	B. p. or m. p.	$n(t)$	Formula	Required (%) C	Required (%) H	Required (%) S	Found (%) C	Found (%) H	Found (%) S	$\nu_{max.}$ S=O * (cm.$^{-1}$)
Cyclic sulphite of:											
Cycloheptane-*cis*-1,2-diol	41	90°/0·5 mm.	1·4860 (24°)	$C_7H_{12}O_3S$	47·7	6·8		47·6	7·0		1210
Cycloheptane-*trans*-1,2-diol	38	92°/0·5 mm.	1·4865 (24°)	$C_7H_{12}O_3S$	47·7	6·8		48·2	7·0		1210
Indane-*cis*-1,2-diol	72	70°	—	$C_9H_8O_3S$	55·1	4·1	16·3	55·2	4·2	16·0	1203
1,4-Anhydroerythritol	55	106—108	—	$C_4H_6O_4S$	32·0	4·0		32·1	4·2		1195
Cyclic sulphate of:											
Cyclohexane-*cis*-1,2-diol	33	37	—	$C_6H_{10}O_4S$	40·45	5·6	18·0	40·1	5·6	17·9	1212, 1387, 1365
Cyclohexane-*trans*-1,2-diol	30	55	—	$C_6H_{10}O_4S$	40·45	5·6	18·0	40·8	5·5	18·05	1205, 1221, 1371, 1401
Ethane-1,2-diol [a]	20—23	91—92	—	$C_2H_4O_4S$							1214, 1388
Propane-1,3-diol [b]	33	61—62	—	$C_3H_6O_4S$							1196, 1380, 1395
2,2-Dimethylpropane-1,3-diol	30	79—80	—	$C_5H_{10}O_4S$	36·15	6·0	19·3	35·8	6·15	19·1	1208, 1397

* Infrared spectra of solids measured in KCl discs, other compounds as liquid films.
[a] Described by Baker and Field.[5] [b] Described by Lichtenberger and Lichtenberger.[7]

TABLE 2. *Data on hydrolysis of diol cyclic sulphates and related compounds.*

Compound	Condns. of hydrol.	Products	Isotope ratio $10^3[C^{16}O^{18}O]/[C^{16}O_2]$	Bond cleavage
Cyclohexane-*cis*-1,2-diol cyclic sulphate	H^+	*trans*-Diol + trace of *cis*-diol	9·14	(i) C–O with inversion (ii) S–O
	HO^-	*cis*-Diol monosulphate + trace of *trans*-diol	1·06 [a]	(i) S–O [(ii) C–O with inversion]
Cyclohexane-*trans*-1,2-diol cyclic sulphate	H^+	*trans*-Diol + *cis*-Diol	10·66	(i) C–O with inversion and retention; (ii) S–O
	HO^-	*trans*-Diol	9·19	(i) S–O (ii) C–O with retention (*via* epoxide)
Cyclohexene oxide	H^+	*trans*-Diol	11·1	C–O with inversion
Cyclohexane-*cis*-1,2-diol monosulphate	H^+	*cis*-Diol	0·9	S–O
Cyclohexane-*trans*-1,2-diol monosulphate	H^+	*trans*-Diol	1·5	S–O
	HO^-	*trans*-Diol	11·75	C–O with retention (*via* epoxide)
Cyclohexane-*cis*-1,2-diol disulphate	H^+	*cis*-Diol	0·44	S–O
Cyclohexane-*trans*-1,2-diol disulphate	H^+	*trans*-Diol	0·05	S–O

[a] Determined on *cis*-diol obtained after acidic hydrolysis of *cis*-diol monosulphate in normal water.

the barium salt of a diol sulphate,[7] or (5) photochemically induced reactions between certain quinones and sulphur dioxide.[8] None of these methods appears to be of completely general application; methods (1) and (2) were used in this work.

Cyclic sulphites of 1,2- and 1,3-diols may be prepared [9] by reaction of the diol with thionyl chloride in pyridine–methylene chloride. A number of new diol cyclic sulphites are shown in Table 1. The infrared spectra of these compounds as liquid films or in KCl discs had $\nu_{max.}$, characteristic [10] of S=O stretching, in the range 1203—1210 cm.$^{-1}$ in agreement with the observations by de la Mare *et al.*[11]

The diol cyclic sulphites were readily oxidised with calcium permanganate in wet acetic acid,[4] although the low yields (20—33%) suggested that some hydrolysis also occurred. Attempts to oxidise the diol cyclic sulphites with ozone,[12] with potassium permanganate in acetone,[13] and with perbenzoic acid [14] were unsuccessful. All the diol cyclic sulphates listed in Table 1 except that from ethane-1,2-diol were obtained by oxidation of their cyclic sulphites. A preliminary attempt to prepare a carbohydrate cyclic sulphate by oxidation [4] of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside 2,3-cyclic sulphite [15] was unsuccessful: although oxidation readily occurred, hydrolysis of the cyclic ester moiety could not be prevented and methyl 4,6-*O*-benzylidene-α-D-glucopyranoside was the only isolable product. The cyclic sulphates of ethane-1,2-diol and propane-1,3-diol were obtained by the action of silver sulphate on the appropriate dibromides; [5] a cyclic sulphate could not be obtained from 1,2-dibromopropane. All the diol cyclic sulphates in Table 1 were stable crystalline solids whose infrared spectra (KCl discs) showed strong absorptions, characteristic of the $-SO_2-$ group in covalent sulphates, in the ranges 1196—1221 and 1365—1401 cm.$^{-1}$. Schreiber [16] records absorptions at 1193 and 1187 cm.$^{-1}$ respectively for dimethyl and diethyl sulphate, and Colthup [17] records strong absorption in the ranges 1150—1230 and 1350—1440 cm.$^{-1}$ for covalent sulphates.

Basic Hydrolyses.—The diol cyclic sulphates listed in Table 1 were hydrolysed at 50° as 0·056M-solutions in a water–dioxan mixture (1 : 2, v/v) which was also 0·2N with respect to sodium hydroxide. The hydrolyses were followed acidimetrically and the curves obtained are shown in Figs. 1 and 2. Certain hydrolyses were carried out in water enriched with $H_2{}^{18}O$ but in these cases the rates were not followed. The ^{18}O-content of the diols formed was determined by mass spectrometry of the carbon dioxide obtained from the diols by essentially the method of Oita and Conway.[18] Table 2 shows the results obtained *; the isotope ratio $[C^{16}O^{18}O]/[C^{16}O_2]$ was determined from the mass peaks 44 and 46. Cyclohexane-*trans*-1,2-diol (isotope ratio $11{\cdot}1 \times 10^{-3}$) obtained by the acidic hydrolysis of cyclohexene oxide in H_2O–$H_2{}^{18}O$ was used as a reference labelled diol since the product is formed solely by C–O bond cleavage with consequent incorporation of ^{18}O. Qualitatively, an isotope ratio near to $11{\cdot}1 \times 10^{-3}$ would be expected for a diol if the hydrolysis of the precursor cyclic sulphate involved only one C–O bond-cleavage step.

Although a diol monosulphate could be isolated in only one case (see Table 2), the reasonable assumption is made in the following discussion that a diol monosulphate is the first product in each case on the hydrolysis of a diol cyclic sulphate.

* A preliminary report of these results has been published (Brimacombe, Foster, and Stacey, *Chem. and Ind.*, 1959, 262).

[8] Schenck and Schmidt-Thomée, *Annalen*, 1953, **584**, 199.
[9] Majima and Simanuki, *Proc. Imp. Acad.* (*Tokyo*), 1926, **2**, 545; Carlson and Cretcher, *J. Amer. Chem. Soc.*, 1947, **69**, 1952.
[10] Vogel-Högler, *Acta Phys. Austriaca*, 1948, **1**, 328; Barnard, Fabian, and Koch, *J.*, 1949, 2442.
[11] de la Mare, Klyne, Millen, Pritchard, and Watson, *J.*, 1956, 1813.
[12] Cf. Barnard, Handbook of I.U.P.A.C. Meeting 1955, p. 74.
[13] Burdon and Tatlow, *J. Appl. Chem.*, 1958, **8**, 293.
[14] Braun, *Org. Synth.*, Coll. Vol. I, p. 431.
[15] Honeyman and Morgan, *J.*, 1955, 3660.
[16] Schreiber, *Analyt. Chem.*, 1949, **21**, 1168.
[17] Colthup, *J. Opt. Soc. Amer.*, 1950, **40**, 397.
[18] Oita and Conway, *Analyt. Chem.*, 1954, **26**, 600.

The diol cyclic sulphates were, with one exception, rapidly cleaved by alkali to yield the diol monosulphates (Figs. 1 and 2); the cyclic sulphate of 2,2-dimethylpropane-1,3-diol was relatively resistant towards alkali (Fig. 2), presumably because the *gem*-dimethyl

FIG. 1.

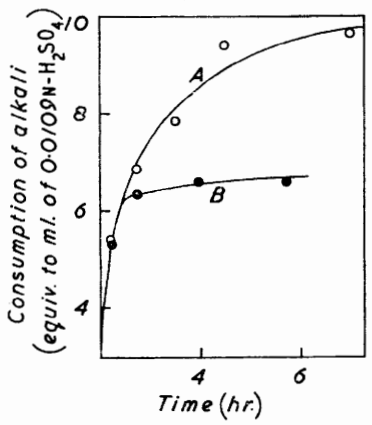
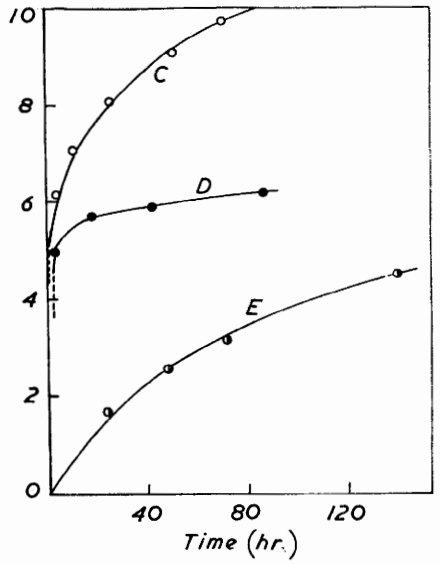


FIG. 2.



FIGS. 1 and 2. *Alkaline hydrolysis of the cyclic sulphates of* (*A*) *cyclohexane*-trans-1,2-*diol*, (*B*) *cyclo hexane-cis*-1,2-*diol*, (*C*) *ethane*-1,2-*diol*, (*D*) *propane*-1,2-*diol*, *and* (*E*) 2,2-*dimethylpropane*-1,3-*diol*. *An uptake of* 10·3 *ml. of alkali is equivalent to complete hydrolysis.*

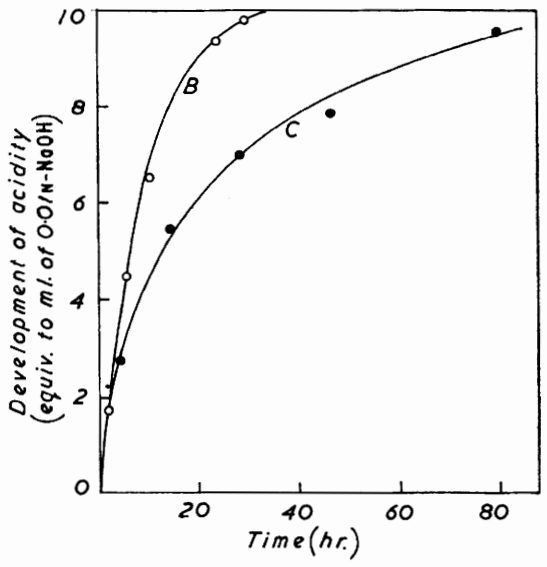


FIG. 3. *Acidic hydrolysis of the diol cyclic sulphates. Theoretical total hydrolysis corresponds to the development of acidity equivalent to* 11·2 *ml. of* 0·01N-*sodium hydroxide.* [*For* (*B*) *and* (*C*) *see Fig.* 1.]

group impedes attack by hydroxide ions. Further hydrolysis of the diol monosulphate intermediates derived from the cyclic sulphates of cyclohexane-*trans*-1,2-diol and ethane-1,2-diol occurred although at quite different rates (Figs. 1 and 2) and presumably through epoxide intermediates. That the diol monosulphate intermediate in the hydrolysis of

cyclohexane-*trans*-1,2-diol cyclic sulphate had the *trans*-configuration was shown by the fact that authentic cyclohexane-*trans*-1,2-diol monosulphate was smoothly hydrolysed by alkali in H_2O–$H_2{}^{18}O$ to yield cyclohexane-*trans*-1,2-diol only, with an isotope ratio of $11{\cdot}75 \times 10^{-3}$. A similar result would be expected if basic hydrolysis of cyclohexane-*trans*-1,2-diol monosulphate proceeded by C–O bond cleavage in the C–O·SO_3^- grouping with retention of configuration. However, were this mechanism operative it would be difficult to account for the alkali-stability of cyclohexane-*cis*-1,2-diol monosulphate (see below). Thus, the ester ring in cyclohexane-*trans*-1,2-diol cyclic sulphate is opened by alkali predominantly, if not exclusively, with S–O bond cleavage.

Cyclohexane-*trans*-1,2-diol monosulphate was obtained by treatment of *trans*-2-benzoyloxycyclohexanol [19] with the pyridine–sulphur trioxide complex [20] followed by catalytic hydrogenolysis [21] of the benzyl group. The *trans*-configuration of the compound was demonstrated when acidic hydrolysis in H_2O–$H_2{}^{18}O$ gave cyclohexane-*trans*-1,2-diol only, with a low isotope ratio ($1{\cdot}5 \times 10^{-3}$) indicative of S–O bond cleavage in the hydrolysis.

The diol monosulphates obtained on basic hydrolysis of the cyclic sulphates of propane-1,3-diol and cyclohexane-*cis*-1,2-diol were markedly resistant towards further hydrolysis since epoxide formation is precluded. The *cis*-monosulphate from the latter was easily isolated and its configuration was proved by the formation of cyclohexane-*cis*-1,2-diol only, with a low isotope ratio ($0{\cdot}9 \times 10^{-3}$), on acidic hydrolysis of the diol monosulphate in H_2O–$H_2{}^{18}O$. The cyclohexane-*cis*-1,2-diol obtained after conversion of cyclohexane-*cis*-1,2-diol cyclic sulphate into the *cis*-diol monosulphate in H_2O–$H_2{}^{18}O$ and acidic hydrolysis of the *cis*-diol monosulphate in normal water, also had a low isotope ratio ($1{\cdot}06 \times 10^{-3}$). Thus, in the presence of alkali, the ester ring in cyclohexane-*cis*-1,2-diol cyclic sulphate is cleaved predominantly, if not exclusively, by S–O bond cleavage. Prolonged basic hydrolysis of cyclohexane-*cis*-1,2-diol monosulphate gave traces of a product which was not isolated but appeared (on zone electrophoresis) to be cyclohexane-*trans*-1,2-diol. A parallel for this result is provided by Burwell and Holmquist's [22] observation that sodium (+)-butan-2-ol sulphate is only slowly hydrolysed by alkali but yields (—)-butan-2-ol. The marked difference in behaviour of the cyclohexane-*cis*- and -*trans*-1,2-diol monosulphates on treatment with alkali elegantly illustrates the molecular geometrical requirements for epoxide formation.[23] Percival [24] has commented on the stability of sodium methyl sulphate towards alkali and has emphasised that, unless an anhydro-ring can be formed, non-reducing carbohydrate sulphates are only slowly hydrolysed by alkali. Garner and Lucas [4] observed that basic hydrolysis of D-(—)-butane-2,3-diol cyclic sulphate gave mainly DL-butane-2,3-diol and suggested the formation of an epoxide intermediate.

The reaction pattern which results when the cyclohexane-*cis*- and -*trans*-1,2-diol cyclic sulphates are treated with alkali is shown in Fig. 4.

Brown and Higson [25] have found that cyclohexane-*cis*-1,3-diol cyclic phosphate shows a remarkable stability towards alkali. Attempts to prepare the analogous cyclic sulphate were unsuccessful; the reaction of cyclohexane-*cis*-1,3-diol with thionyl chloride gave ill-defined products.

Acidic Hydrolyses.—The diol cyclic sulphates were hydrolysed at 50° as 0·056M-solutions in water–dioxan (1 : 2, v/v) which was also 0·2N with respect to sulphuric acid, and the curves shown in Fig. 3 were obtained alkalimetrically. Acid hydrolyses were also performed in H_2O–$H_2{}^{18}O$, and the isotope ratios of the products are recorded in Table 2.

From Fig. 3 it may be seen that cyclohexane-*cis*-1,2-diol cyclic sulphate is hydrolysed

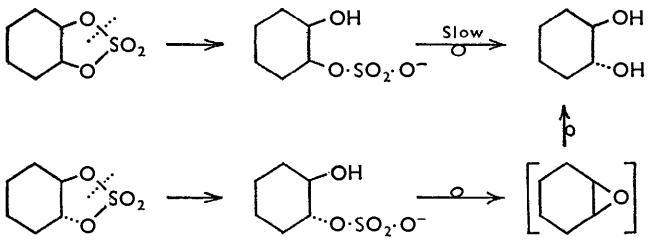
[19] McKusick, *J. Amer. Chem. Soc.*, 1948, **70**, 1976.
[20] Sisler and Audrieth, *Inorg. Synth.*, Vol. II, p. 173.
[21] Mozingo, *Org. Synth.*, 1946, **26**, 77; McCloskey, *Adv. Carbohydrate Chem.*, 1957, **12**, 137.
[22] Burwell and Holmquist, *J. Amer. Chem. Soc.*, 1948, **70**, 878.
[23] Cf. Newth, *Quart. Rev.*, 1959, **13**, 30.
[24] Percival, *ibid.*, 1949, **3**, 369.
[25] Brown and Higson, *J.*, 1957, 2034.

somewhat more rapidly than the *trans*-isomer ($t_{\frac{1}{2}}$ hydrolyses 7·5 and 13 hr. respectively). Both these cyclic sulphates are attacked by acid much more slowly than they are by alkali (compare Figs. 1 and 3). The cyclic sulphate of 2,2-dimethylpropane-1,3-diol was found to be much more resistant to attack by acid than any of its analogues (Fig. 3; compare with the behaviour in basic media). The acid catalysis of these reactions was not examined in detail.

From the low isotope ratios (Table 2) of the diols produced by acidic hydrolysis of the monosulphates of cyclohexane-*cis*- and -*trans*-1,2-diol it is clear that reaction proceeds predominantly if not exclusively by S–O bond cleavage so that incorporation of ^{18}O into the diols finally produced by hydrolysis of the diol cyclic sulphates can only occur during the first stage of the reaction, *i.e.*, when the cyclic esters are opened.

Acidic hydrolysis of cyclohexane-*cis*-1,2-diol cyclic sulphate gave a mixture of cyclohexane-*cis*- and -*trans*-1,2-diol in which the latter greatly predominated. A satisfactory quantitative method for the separation of the two diols on a macro-scale was not encountered

FIG. 4. *Reaction pattern of the cyclic sulphates of cyclohexane*-cis- *and* -trans-1,2-*diol on treatment with alkali.*



(see p. 209). The diols could be separated on a micro-scale by zone electrophoresis (ionophoresis) on paper, with a borate buffer and the enclosed strip technique;[26] the M_G values[27] were respectively 0·07—0·09 and 0·00 for the *cis*- and the *trans*-diol. Visual inspection of the pherograms[28] indicated that $\gtrsim\sim 10\%$ of the *cis*-diol in the above mixture. Infrared spectroscopy confirmed the identity of the components and their approximate proportion in the mixture. The high isotope ratio ($9{\cdot}14 \times 10^{-3}$) of the diol mixture and the formation of the *trans*-diol as the predominant product indicated that, in the initial stage of the hydrolysis of cyclohexane-*cis*-1,2-diol cyclic sulphate, the ester ring opened by C–O bond cleavage with inversion of configuration. The trace of *cis*-diol could have resulted from initial C–O bond cleavage with retention of configuration, or by S–O bond cleavage: the available evidence does not permit a distinction.

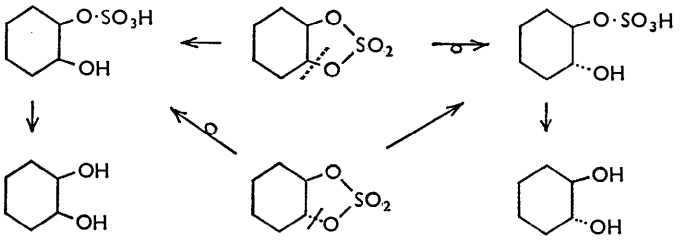
Acidic hydrolysis of cyclohexane-*trans*-1,2-diol cyclic sulphate also gave a mixture of cyclohexane-*cis*- and -*trans*-1,2-diol in which the latter apparently slightly predominated (zone electrophoresis and infrared spectroscopy). The high isotope ratio ($10{\cdot}66 \times 10^{-3}$) for the diol mixture indicated that both components were labelled and that the initial reaction of the diol cyclic sulphate involved C–O bond cleavage with both inversion and retention of configuration, the latter process being slightly predominant. It is of interest that Garner and Lucas[4] observed that acidic hydrolysis of D-(—)-butane-2,3-diol cyclic sulphate yielded *meso*-butane-2,3-diol, *i.e.*, reaction had occurred by C–O bond cleavage with inversion of configuration. The conformational flexibility of cyclohexane-*cis*-1,2-diol cyclic sulphate and of cyclohexane-*cis*- and -*trans*-1,2-diol complicates discussion of the possible steric control in the acidic hydrolysis of cyclohexane-*cis*- and -*trans*-1,2-diol cyclic sulphate. It is hoped that the study, now in progress, of the acid-hydrolytic behaviour of the cyclic sulphates of decalin-2α,3α- and -2α,3β-diol, in which conformational flexibility is eliminated, will throw more light on the mechanism of these reactions in general.

[26] Foster, *Chem. and Ind.*, 1952, 1050.
[27] Foster, *J. Chem. Soc.*, 1953, 982.
[28] Bücher, Matzelt, and Pette, *Klin. Wochenschr.*, 1952, **30**, 325.

The reaction pattern of the acidic hydrolysis of the cyclic sulphates of cyclohexane-*cis*- and -*trans*-1,2-diol is shown in Fig. 5.

Sequential application of basic and acidic hydrolysis to dextran sulphate [29] yields mannose and other hexoses in addition to glucose; acidic hydrolysis of dextran sulphate yields D-glucose only. Overend and Ricketts [30] have accounted for the formation of

FIG. 5. *Reaction pattern of the cyclic sulphates of cyclohexane*-cis- *and* -trans-1,2-*diol on treatment with acid. The* cis-*diol formed from the* cis-*cyclic sulphate is the minor product and could also have arisen by* S–O *bond cleavage in the first stage.*



mannose by an epoxide-migration mechanism. An alternative explanation might involve the conversion by alkali of a glucose 2,3-disulphate unit in the polysaccharide chain into a mannose 2,3-cyclic sulphate unit which would be expected to react further with alkali to yield a mannose 2(or 3)-monosulphate unit and finally mannose on acidic hydrolysis. However, such a mechanism seems unlikely since sequential application of basic and acidic hydrolysis to the disulphates of cyclohexane-*cis*- and -*trans*-1,2-diol did not cause any inversion of configuration.

EXPERIMENTAL

Preparation and Characterisation of Diols.—The *cis*- and the *trans*-forms of cyclopentane-, cyclohexane-, and cycloheptane-1,2-diol were prepared by methods previously described.[31] Ethane-1,2-diol (b. p. 198—200°, n^{20} 1·4270) and propane-1,3-diol (b. p. 130—135°/20—25 mm., n^{20} 1·4398) were commercial samples purified by fractional distillation. 2,2-Dimethylpropane-1,3-diol (neopentyl glycol) was a gift from Imperial Chemical Industries Limited and had m. p. 127° after recrystallisation from benzene; it readily afforded a *dibenzoate* m. p. 48—49° (from aqueous ethanol) (Found: C, 72·8; H, 6·4. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·4%), a *ditoluene*-p-*sulphonate*, m. p. 119—121° (from ethanol) (Found: C, 55·3; H, 5·9. $C_{19}H_{24}O_6S_2$ requires C, 55·3; H, 5·8%), and a *ditrityl ether*, m. p. 168—170° (Found: C, 87·5; H, 6·7. $C_{43}H_{40}O_2$ requires C, 87·7; H, 6·8%).

Preparation of Cyclic Sulphites.[9]—To a solution of cyclohexane-*trans*-1,2-diol (11·6 g.) and dry pyridine (19 ml.) in methylene chloride (200 ml.) was added, during 2 hr., with stirring and cooling (0°), a solution of thionyl chloride (7·2 ml.) in methylene chloride (50 ml.). The precipitated pyridine hydrochloride was removed and the filtrate was washed successively with 0·01N-hydrochloric acid, aqueous sodium hydrogen carbonate, and water. After drying ($MgSO_4$), the solvent was evaporated under reduced pressure and the residue distilled to yield cyclohexane-*trans*-1,2-diol cyclic sulphite (72%), b. p. 72—75°/0·1 mm., n^{21} 1·4845. Price and Berti [6] give b. p. 94—96°/2 mm., n^{20} 1·4817. By essentially the above method, the cyclic sulphites listed in Table 1 were obtained.

Preparation of Cyclic Sulphates.—(*a*) A filtered solution of calcium permanganate (9 g.) in water (9 ml.) was slowly added [4] to a solution of 2,2-dimethylpropane-1,3-diol cyclic sulphite [6] (5 g.) in glacial acetic acid (25 ml.) with continuous stirring and cooling (0°). The temperature was not allowed to exceed 15° and when the reaction was complete (permanent pink colour) the mixture was poured into an ice-cold solution of sodium carbonate (50 g.) in water (100 ml.), and sufficient sodium metabisulphite was added to decompose the excess of permanganate. The mixture was extracted with ether (6 × 100 ml.), and the combined and dried ($MgSO_4$) extracts

[29] Ricketts, *J.*, 1956, 3752.
[30] Overend and Ricketts, *Chem. and Ind.*, 1957, 632.
[31] Brimacombe, Foster, Stacey, and Whiffen, *Tetrahedron*, 1958, **4**, 351.

were evaporated. Recrystallisation of the residue from ether afforded 2,2-*dimethylpropane*-1,3-*diol cyclic sulphate*. By essentially the above method the cyclic sulphates of cyclohexane-*cis*- and -*trans*-1,2-diol and propane-1,3-diol were obtained from the corresponding cyclic sulphites. Analytical and other data on these compounds are recorded in Table 1. When the above method was applied to methyl 4,6-*O*-benzylidene-α-D-glucopyranoside 2,3-cyclic sulphite [15] (6·5 g.; m. p. 176—177°, $[\alpha]_D$ +114·3° in chloroform), no sulphur-containing organic product was detected and methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (3·34 g.), m. p. 161—162° alone or in admixture with the authentic compound, was isolated.

(*b*) A mixture [5] of 1,2-dibromoethane (10 g.) and silver sulphate (20 g.) in boiling xylene (10 ml.) was shaken for 15 min. Insoluble material was then removed and the filtrate was fractionally distilled under diminished pressure. Addition of light petroleum (b. p. 80—100°) to the distillate obtained after removal of the solvent yielded ethane-1,2-diol cyclic sulphate (1·3 g.) which recrystallised from this petroleum. Propane-1,3-diol cyclic sulphate was similarly prepared from 1,3-dibromopropane. Data on these compounds are recorded in Table 1.

Sodium Cyclohexane-trans-1,2-*diol Monosulphate*.—A mixture of cyclohexene oxide (11 g.; b. p. 129—130°/~760 mm.) and benzyl alcohol (50 ml.) was treated with sodium (0·15 g.), heated at 180—200° for 22 hr. and thereafter fractionally distilled. *trans*-2-Benzoyloxycyclohexanol (6·5 g.) was obtained having b. p. 96—97°/0·05 mm., n^{20} 1·5300. McKusick [19] gives b. p. 110—112°/0·3 mm., n^{25} 1·5290.

trans-2-Benzoyloxycyclohexanol (6 g.) in dry pyridine (150 ml.) was heated with the pyridine–sulphur trioxide complex [20] (17 g.) at 80° for 2—3 hr. whilst a vigorous stream of nitrogen was continuously passed through the mixture. Thereafter the mixture was poured, with stirring, into water in which an excess of barium carbonate was suspended. After removal of insoluble material the filtrate was concentrated initially (to ~40 ml.) at 35—40° (bath)/15 mm. in the presence of a little barium carbonate and finally by freeze-drying. The residue was extracted (4 times) with hot ethyl acetate, then dissolved in water and freed from insoluble material. Freeze-drying yielded a hygroscopic solid (8·2 g.) which, surprisingly, did not contain barium ions and was apparently hydrated trans-2-*benzoyloxycyclohexyl sulphate* (Found: C, 53·3, 53·1; H, 6·0, 6·0. $C_{13}H_{18}O_5S,\frac{1}{2}H_2O$ requires C, 52·9; H, 6·4%). The infrared spectrum (KCl disc) showed $\nu_{max.}$ at 1190 (S=O) and 1500, 752, and 676 cm.$^{-1}$ (benzene ring).

This sulphate (1 g.) in water (50 ml.) was shaken at room temperature under a slight overpressure of hydrogen with palladium hydroxide–barium sulphate [21] (500 mg.) until 1 mol. of hydrogen (*ca.* 60 ml.) had been absorbed. The catalyst was removed and the filtrate neutralised with barium carbonate, filtered, and freeze-dried, to yield *barium cyclohexane*-trans-1,2-*diol monosulphate* (0·64 g.) as a white powder [Found: C, 27·7; H, 4·5. $(C_6H_{11}O_5S)_2Ba$ requires C, 27·3; H, 4·2%], $\nu_{max.}$ (KCl disc) 1207 cm.$^{-1}$ (S=O).

Sodium Cyclohexane-cis-1,2-*diol Monosulphate*.—Cyclohexane-*cis*-1,2-diol cyclic sulphate (0·3 g.) in dioxan–water (1 : 2 v/v; 10 ml.) was treated with sodium hydroxide (50 mg.) at 50° for 3—4 hr. Unchanged sulphate was removed by ether-extraction (2 × 50 ml.), and the aqueous solution then freeze-dried. Extraction of the residue with ethyl acetate left *sodium cyclohexane*-cis-1,2-*diol monosulphate* (0·22 g.) as a white powder (Found: C, 32·8; H, 5·0. $C_6H_{11}O_5SNa$ requires C, 33·0; H, 5·05%).

Rates of Hydrolysis of Cyclic Sulphates.—(a) *In alkali*. The sulphate (*ca.* 100 mg., 0·56 mmole) in dioxan–water (8 ml.; 1 : 2 v/v) at 50° was treated with N-sodium hydroxide (2 ml.) at the same temperature which was subsequently maintained. Aliquot parts (1 ml.) were diluted at suitable times with ice-water (5 ml.) and rapidly titrated with sulphuric acid (~0·01N) with Bromothymol Blue as indicator. Blank values were obtained from mixtures from which the cyclic sulphate had been omitted. The results are shown in Figs. 1 and 2.

(b) *In acid*. A solution of the cyclic sulphate (*ca.* 100 mg., 0·56 mmole) in dioxan–water (8 ml.; 1 : 2 v/v) at 50° was treated with N-sulphuric acid (2 ml.) at the same temperature which was subsequently maintained. Aliquot parts (1 ml.) were diluted at suitable times with ice-water (5 ml.) and rapidly titrated with sodium hydroxide (*ca.* 0·01N) (Bromothymol Blue). Blank values were determined as in (a). The results are shown in Fig. 3.

Hydrolyses in H_2O–$H_2{}^{18}O$.—The isotopically enriched water employed in all the hydrolyses contained approx. 2—3 atom % of ^{18}O and traces of ^{17}O.

(a) *Acidic hydrolyses*. (1) Cyclohexene oxide. The oxide (1 g.) was boiled in H_2O–$H_2{}^{18}O$ (3 ml.) containing 1 drop of concentrated sulphuric acid under reflux for 1·5 hr., thereafter the

solution was neutralised with barium carbonate and the H_2O–$H_2{}^{18}O$ removed by freeze-drying and recovered. (The H_2O–$H_2{}^{18}O$ was recovered in this way in the subsequent hydrolyses.) Water (5 ml.) was added to the residue, insoluble material was removed, and the filtrate freeze-dried. Recrystallisation of the residue from ethyl acetate gave ^{18}O-labelled cyclohexane-*trans*-1,2-diol (0·8 g.), m. p. 102—104°, isotope ratio $11{\cdot}1 \times 10^{-3}$. This indicates that the enriched water contained approx. 2·2 atom % of ^{18}O.

(2) Cyclohexane-*trans*-1,2-diol cyclic sulphate. A suspension of the cyclic sulphate (0·2 g.) in H_2O–$H_2{}^{18}O$ (20 ml.) was treated with concentrated sulphuric acid (0·15 ml.) and the mixture stored at 50° for 4 days to ensure complete hydrolysis. The solution was neutralised with barium carbonate, centrifuged, and freeze-dried. The residue was extracted with hot ethyl acetate. Concentration of the extract yielded the product (52 mg.) of isotope ratio $10{\cdot}66 \times 10^{-3}$. This method of diol isolation was employed in the subsequent acid hydrolyses. Analysis of the product by zone electrophoresis on Whatman No. 3 paper with the enclosed strip technique [26] with a borate buffer [32] of pH 10 under a potential gradient of 20—30 v/cm. and detection with silver nitrate revealed both cyclohexane-*cis*- and -*trans*-1,2-diol, with the latter slightly predominating as determined by visual inspection of the pherograms. (Subsequent reference to zone electrophoresis implies the use of this method.) The infrared spectrum (KCl disc) of the product confirmed the identity and approximate composition of the mixture.

Attempts to analyse mixtures of cyclohexane-*cis*- and -*trans*-1,2-diol quantitatively were unsuccessful although it was not difficult to make an approximate qualitative determination by the above methods. The small difference in mobilities of the diols (M_G values: [27] *trans*-diol 0·00, *cis*-diol 0·07—0·08) in microscale zone electrophoresis prevented a successful translation to a macroscale. The reported [33] paper-chromatographic separation of the diols by means of the organic phase of water–xylene–ethyl methyl ketone (1 : 1 : 1) could be used to demonstrate the presence of the diols in a mixture, but since a substantial part of the diol mixture introduced on the paper remained at the origin and there was extensive " tailing " of the spots the method was not quantitative. Other paper-chromatographic methods [34] were also unsuitable. Only a partial separation of the bis-(4-phenylazobenzoates) of the two diols could be effected [35] by chromatography on alumina, but no separation [35] by paper chromatography by Wickberg's method.[36] Vapour-phase chromatography [37] did not separate the bis(trimethylsilyl) ethers of the diols.

(3) Cyclohexane-*cis*-1,2-diol cyclic sulphate. The procedure was as in (2). Analysis of the product (isotope ratio $9{\cdot}14 \times 10^{-3}$) by zone electrophoresis and infrared spectroscopy showed that it contained predominantly cyclohexane-*trans*-1,2-diol with a small amount (*ca.* 10% or less) of the *cis*-isomer.

(4) Sodium cyclohexane-*cis*-1,2-diol monosulphate. A solution of the sodium salt (0·16 g.) in H_2O–$H_2{}^{18}O$ (10 ml.) was made 2N with respect to sulphuric acid by the addition of concentrated acid and then heated at 95—100° for 4—5 hr. The product was isolated in the usual way. Cyclohexane-*cis*-1,2-diol (20 mg.), of isotope ratio $0{\cdot}9 \times 10^{-3}$ (homogeneous by zone electrophoresis), was thus obtained. In an analogous experiment with normal water the product had m. p. 93—94°.

(5) Barium cyclohexane-*trans*-1,2-diol monosulphate. The barium salt (400 mg.) in H_2O–$H_2{}^{18}O$ (10 ml.) was treated with concentrated sulphuric acid (0·25 ml.), and the insoluble material removed by centrifugation. The supernatant liquid was heated at 95—100° for 2 hr. and the product isolated in the usual way. Cyclohexane-*trans*-1,2-diol (80 mg.), m. p. 100—102°, isotope ratio $1{\cdot}5 \times 10^{-3}$, which appeared homogeneous on zone electrophoresis, was thus obtained.

(6) Barium cyclohexane-*cis*-1,2-diol disulphate. The barium salt [38] (0·5 g.) in H_2O–$H_2{}^{18}O$ (5 ml.) was treated with sufficient concentrated sulphuric acid (*ca.* 3 ml.) to make the solution

[32] Foster, Newton-Hearn, and Stacey, *J.*, 1956, 30.
[33] Henbest and Wilson, *J.*, 1957, 1958; cf. Partridge, *Nature*, 1946, **158**, 270; Hough, *ibid.*, 1950, **165**, 400.
[34] Angyal, McHugh, and Gilham, *J.*, 1957, 1432; Angyal and McHugh, *J.*, 1957, 3682; Angyal, Gilham, and MacDonald, *J.*, 1957, 1417; Posternak, Reymond, and Fricdli, *Helv. Chim. Acta*, 1955, **38**, 205.
[35] Bose and Foster, unpublished results.
[36] Wickberg, *Acta Chem. Scand.*, 1958, **12**, 615.
[37] Hedgley and Overend, unpublished method.
[38] Derx, *Rec. Trav. chim.*, 1922, **41**, 313.

4N. After centrifugation the solution was heated at 100° for 6 hr. and the product was isolated in the usual way. Cyclcohexane-*cis*-1,2-diol (58 mg.), m. p. 93—94°, isotope ratio $0{\cdot}44 \times 10^{-3}$, which appeared homogeneous on zone electrophoresis, was thus obtained.

(7) Barium cyclohexane-*trans*-1,2-diol disulphate. By a procedure similar to that detailed for the *cis*-isomer in (6) the barium salt of cyclohexane-*trans*-1,2-diol disulphate [38] yielded homogeneous (zone electrophoresis) cyclohexane-*trans*-1,2-diol (80 mg.), m. p. 102—103°, isotope ratio $0{\cdot}05 \times 10^{-3}$.

(b) *Basic hydrolyses.* (1) Cyclohexane-*trans*-1,2-diol cyclic sulphate. A suspension of the cyclic sulphate (105 mg.) in H_2O–$H_2{}^{18}O$ (10 ml.) was heated with sodium hydroxide (80 mg.) at 50° for 16 hr. A slight excess of concentrated sulphuric acid was added and the solution was finally neutralised with barium carbonate. The product was isolated in the usual way. Cyclohexane-*trans*-1,2-diol (10·4 mg.), isotope ratio $9{\cdot}19 \times 10^{-3}$, which appeared homogeneous on zone electrophoresis, was obtained. After a parallel hydrolysis by ordinary water the product had m. p. 103—104°.

(2) Cyclohexane-*cis*-1,2-diol cyclic sulphate. The sulphate (0·3 g.) in H_2O–$H_2{}^{18}O$ (10 ml.) was treated with sodium hydroxide (60 mg.) at 50° for 3—4 hr. Unchanged sulphate was removed by ether (2 % 30 ml.), and the remaining solution freeze-dried. The residue after extraction with hot ethyl acetate was sodium cyclohexane-*cis*-1,2-diol monosulphate (0·2 g.). The *cis*-diol obtained after acidic hydrolysis of the monosulphate in ordinary water had an isotope ratio of $1{\cdot}06 \times 10^{-3}$.

(3) Sodium cyclohexane-*trans*-1,2-diol monosulphate. The barium salt of the monosulphate obtained as described above was converted into the sodium salt by passage of its aqueous solution through a column of Amberlite IR-120 (Na^+ form). A solution of the sodium salt (100 mg.) in H_2O–$H_2{}^{18}O$ (10 ml.) was heated with sodium hydroxide (80 mg.) at 50° for 2 days. A slight excess of concentrated sulphuric acid was then added and the solution neutralised with barium carbonate. The product, isolated in the usual way, was homogeneous (zone electrophoresis) cyclohexane-*trans*-1,2-diol (21 mg.), m. p. 102—103°, isotope ratio $11{\cdot}75 \times 10^{-3}$.

Determination of the Isotope Ratio of the ^{18}O*-Labelled Cyclohexane-1,2-diols.*—The method used was essentially that of Oita and Conway [18] whereby the diol (10—20 mg.) was pyrolysed over platinised carbon at 900°, to yield carbon monoxide which was quantitatively oxygenated by iodine pentoxide at 120°. The resultant carbon dioxide was dried, collected, and analysed in the mass spectrometer. The isotope abundance of ^{18}O was determined by comparison of the mass peaks 44 ($C^{16}O_2$) and 46 ($C^{16}O^{18}O$) and the isotopic ratio is given by $[C^{16}O^{18}O][C^{16}O_2]$. The values obtained are in Table 2. Blank values were obtained by pyrolysing isotopically normal samples of cyclohexane-*cis*- and -*trans*-1,2-diol. From a series of blank determinations carried out at intervals throughout the investigation it became clear that the apparatus had no memory of any preceding run. For the purpose of this work it was not essential to obtain a complete recovery of the oxygen from the diol as carbon dioxide; however, in typical experiments where the carbon dioxide was absorbed and weighed the oxygen values obtained were 26·9 and 26·7% respectively for the *cis*- and the *trans*-diol (Calc.: 27·6%).

Bis(trimethylsilyl) Ethers of the Cyclohexane-1,2-diols.—Cyclohexane-*trans*-1,2-diol (3 g.) in dry pyridine (50 ml.) was treated with trimethylchlorosilane (8·2 g.) overnight at room temperature. Excess of reagent and solvent were removed under reduced pressure and the residue was extracted with ether by decantation. Evaporation of solvent from the extract and distillation of the residue yielded trans-1,2-*bis(trimethylsilyloxy)cyclohexane* (5·3 g.), b. p. 84—86°/0·3 mm., n^{22} 1·4328 (Found: C, 55·35; H, 11·0. $C_{12}H_{28}O_2Si_2$ requires C, 55·4; H, 10·8%).

In the same way cyclohexane-*cis*-1,2-diol (2 g.) yielded cis-1,2-*bis(trimethylsilyloxy)cyclohexane* (3·9 g.), b. p. 72°/0·5 mm., n^{22} 1·4338 (Found: C, 55·1; H, 11·1%). The infrared spectra (liquid films) of these compounds showed $\nu_{max.}$ near 1259, 841, and 755 $cm.^{-1}$ characteristic [39] of the $SiMe_3$ grouping and at *ca.* 1100 $cm.^{-1}$ characteristic [39] of the Si–O–C grouping.

Di-(p-phenylazobenzoates) of the Cyclohexane-1,2-diols (this experiment was carried out by Dr. J. L. Bose).—Cyclohexane-*trans*-1,2-diol (0·21 g.) was heated with a solution of *p*-phenylazobenzoyl chloride (0·95 g.) in dry pyridine (14 ml.) at 95° for 5—6 hr. Water (0·1 ml.) was added and the mixture was poured on ice. The precipitate was collected, washed with water, dissolved in chloroform, and washed successively with aqueous cadmium chloride (*ca.* 2%) and sodium hydrogen carbonate and water. The dried ($MgSO_4$) solution was freed from *p*-phenylazobenzoic acid by passage through a column of alumina. Evaporation of the eluate and

[39] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1958, p. 336.

recrystallisation of the residue (1·0 g.) from benzene–light petroleum (b. p. 60—80°) gave trans-1,2-*di*-(p-*phenylazobenzoyloxy*)*cyclohexane*, m. p. 184—185° (Found: C, 72·7; H, 5·3. $C_{32}H_{28}O_4N_4$ requires C, 72·2; H, 5·3%). In the same way cis-1,2-*di*-(p-*phenylazobenzoyloxy*)-*cyclohexane*, m. p. 162°, was obtained (Found: C, 72·5; H, 5·4%).

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