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STUDIES ON CYCLIC POLYOLS

PART IX. DIRECTIVE EFFECTS IN THE REACTIONS OF POLYSUBSTITUTED CYCLOPENTANES*

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INTRODUCTION

In previous studies[1-3], directive influences in the synthesis and reactions of different classes of substituted cyclopentanes were investigated, and the preparation of several isomeric members of some of these series (*e.g.*, tetrols, aminotriols, aminotetrols, diaminotriols, and anhydrotetrols) was described. Conformational factors play a major role in determining the stereoselectivity of reactions of cyclohexane derivatives, but are of minor or negligible importance in reactions involving the corresponding cyclopentane derivatives. The observed selectivity could be rationalized on the basis of other directive influences, such as steric hindrance, inductive effects, and participation of neighboring groups.

In the present report, further examples are presented that appear to substantiate the general validity of the earlier conclusions about the directive influence, on epoxide opening, of an adjacent, electronegative substituent. *cis*-1,2:3,4-Diepoxycyclopentane has been prepared, and its behavior in nucleophilic, epoxide-opening reactions has been studied; when either water or Br^- is the nucleophile, no selectivity is seen in the direction of opening of the first of the two epoxide rings. A rational approach to stereoselective synthesis of the five known cyclopentanetetrols is indicated, and several new derivatives are described. In addition, the relative ease of hydrolysis of *O*-isopropylidene groups and epoxide rings present in the same molecule has been investigated; in the presence of dilute mineral acid, the *O*-isopropylidene residue is found to be hydrolyzed more easily than the epoxide ring. Many of the compounds synthesized are suitable for i.r. spectroscopy in nonaqueous solvents, permitting the detection of intramolecular hydrogen bonds (H-bonds). Usually, only one (or two)

*The nomenclature used for cyclitols has varied from author to author. Definitive proposals for official nomenclature for this field are at present being considered by the IUPAC/IUB Nomenclature Commission. Until a decision is reached by this Commission, no nomenclature may be considered official. The nomenclature used in this paper is the "Modified Maquenne" system proposed by Professors S. J. Angyal and L. Anderson. Although some of the compounds described in this paper are not strictly cyclitols (cycloalkanes containing one hydroxyl group on each of four or more ring atoms), the relationships among the compounds are such that it seems preferable to name all of them by one system. In the present paper, the same enantiomer is shown in each case, except where it is necessary to do otherwise to illustrate a sequence of reactions.

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of the possible conformations is consistent with the indicated presence of a strong, intramolecular H-bond, and, on this basis, tentative conformational assignments have been made.

RESULTS

Epoxide opening. — Earlier studies[1,2] showed that, in the presence of dilute acid, the epoxide ring of the *cis*-anhydrotetrol **1** is opened, by water or Br^-, stereo-

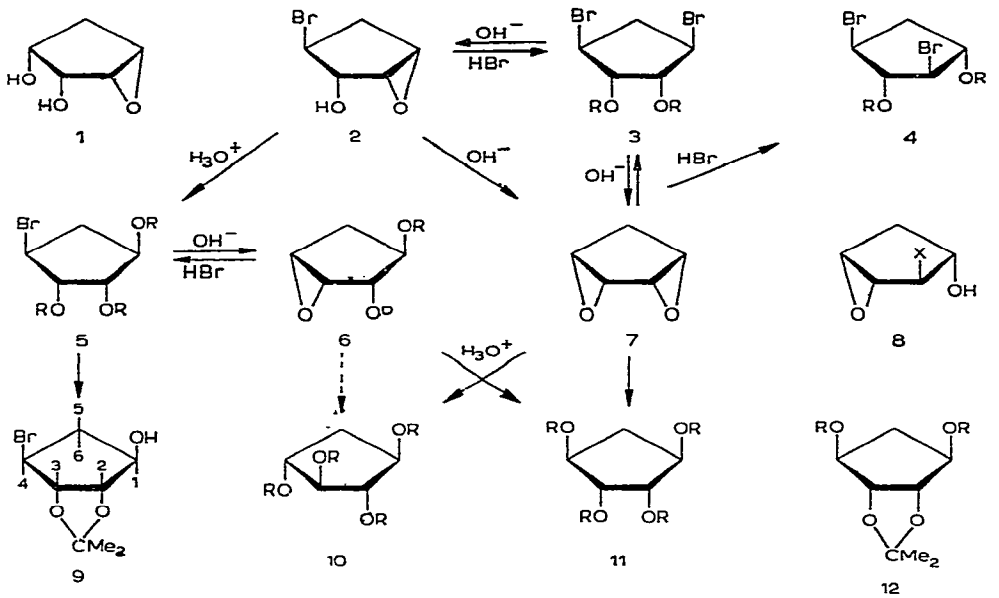

Fig. 1. Formation and opening of some epoxides of cyclopentane: R = H (a); Bz (b); X = OH (c); Br (d). The numbers in formula 9 show the numbering used in the discussion of the n.m.r. spectra.

selectively at the position farthest from an electronegative hydroxyl group. In the present work, similar results were obtained when the epoxybromohydrin[4] **2** and the anhydrotetrol **6a** were subjected to the same conditions. In ethanolic hydrogen bromide, **2** was converted into a product that crystallized during processing; it had m.p. 68–71° (compared with a m.p. for authentic **3a** of 75.5–76.5°). It was easily purified by a single recrystallization, and was identified as the dibromoglycol **3a**. Hydrolysis by dilute sulfuric acid converted **2** into a bromotriol identified, for several reasons, as **5a**. Thus, benzoylation of the product gave a tribenzoate **5b** that crystallized during processing, and that melted sharply at 136–7° after a single recrystallization. In our previous studies, such ease of purification has been characteristic only of mixtures consisting preponderantly of a single isomer. Acetonation of the presumed bromotriol **5a** gave a liquid *O*-isopropylidene derivative **9**. No conclusions concerning the stereoselectivity of opening of **2** in the hydrolytic reaction can be based on the yield of **9**, because yields of *O*-isopropylidene derivatives in our previous work have

been far from quantitative. However, the configurational assignment as **9** is unequivocal; the dioxolane ring can only be fused *cis* to the cyclopentane ring, and the n.m.r. spectrum[5] is consistent only with the 1,4/2,3 configuration. This proves that no rearrangement occurred during hydrolysis of the epoxide.

When the crude bromotriol **5** is treated with aqueous alkali, the *trans*-bromohydrin is converted into an epoxide, and the anhydrotetrol **6a** (m.p. 103.5–104.5°) is obtained in 49% yield; this constitutes further proof that the principal bromotriol present is **5a**. Previously[2], we were unable to distinguish between the two possible configurations **6** or **8c** for the anhydrotetrol, but since **5a** is the parent compound, structure **8** is untenable. Consistent with the proposed configuration is the observation[3c] that epoxides having a *trans*-hydroxyl group adjacent to one end of the oxirane ring, as in the epoxydiol **8c**, open stereoselectively at the less-hindered site. The product obtained by hydrolysis of **8c** should therefore be the 1,3/2,4 tetrol (**10a**), but the product actually obtained from the epoxydiol is preponderantly the 1,4/2,3 tetrol **11a** (see below). Unequivocal proof of its configuration was obtained by treatment of the anhydrotetrol **6a** with hydrogen bromide. That the resulting bromotriol is **5a** was shown by its conversion into an *O*-isopropylidene derivative whose i.r. spectrum was identical with that of an analytically pure sample of **9**.

In an earlier study[1], *trans*-1,2-cyclopentenediol (**13**) was epoxidized with peroxybenzoic acid (see Fig. 2) and the product was then hydrolyzed directly to a

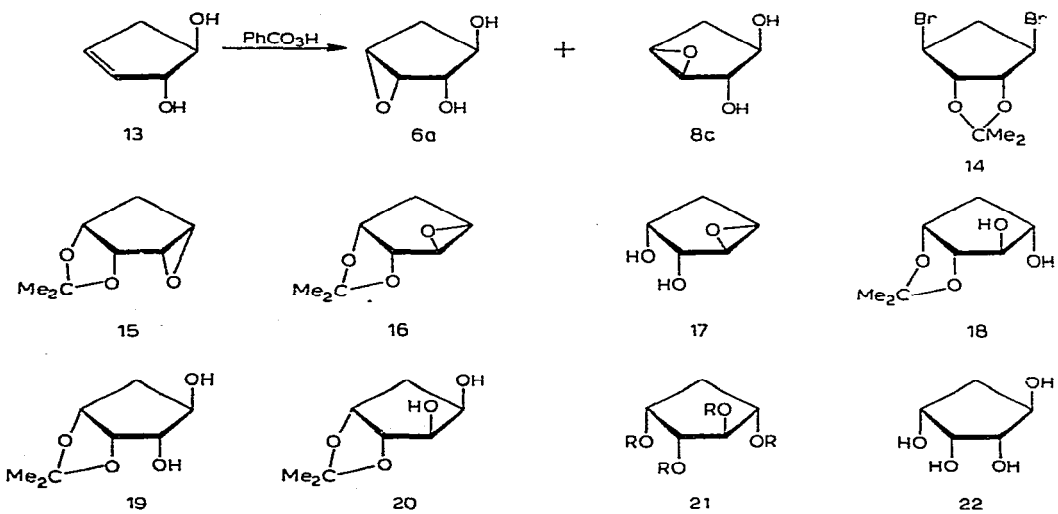

Fig. 2. Intermediates in synthetic reactions. **21a**, R = H; **21b**, R = Bz.

mixture of tetrols, composed of about 20–25% of **10a** and 75–80% of **11a**. The *cis*-directing influence of an allylic hydroxyl group in such epoxidation reactions is well known[6] and has been amply substantiated in our earlier studies[1–3a]. However, Darby *et al.*[7] have shown that a homoallylic hydroxyl group is also *cis*-directing, so that the

epoxydiol produced could have been a mixture of **6a** and **8c**, and no conclusions concerning stereoselectivity of epoxide opening could be drawn. In the present work, two different lines of evidence indicated the preferential opening of the oxirane ring of the epoxydiol **6a** at the position adjacent to the methylene group, *i.e.*, remote from an electronegative substituent. When the anhydrotetrol was hydrolyzed, the product crystallized during removal of the solvent. A single recrystallization gave the 1,4/2,3 tetrol **11a**, m.p. 132–4°, identical with authentic material previously prepared[1]. A more reliable indication of stereoselectivity is the quantitative analysis of the hydrolyzate by n.m.r. spectroscopy. As the methylene protons and the adjacent O–C–H protons of the tetrol **11a** form an AKX_2 system[8a,9], each of the methylene protons is represented in the spectrum by a six-line multiplet (doublet of triplets) (see Table III). The corresponding four protons of the tetrol **10a** form an A_2X_2 system, the methylene protons of which gave a triplet. Fortuitously, the two methylene signals of **11** are widely separated, and the methylene signal of **10** falls between them. Consequently, the composition of a mixture of these two isomers may be analyzed by comparing the integrated areas of the corresponding methylene signals, and such an analysis showed that the hydrolyzate consisted of 90% of **11** and 10% of **10**.

An entirely different and unexpected result was obtained when the opening of the diepoxide **7** was investigated (see below for the synthesis and proof of structure of **7**). When **7** was hydrolyzed and the hydrolyzate was analyzed by the n.m.r. method, 58% of the 1,3/2,4 tetrol **10a** and 42% of the 1,4/2,3 tetrol **11a** were found. For the following reasons, this result indicates that the first attack by water at an inner or outer end of an oxirane ring shows only slight stereoselectivity. If the first attack occurs at an outer position, the intermediate product would be the anhydrotetrol **6a**, and the final product would therefore contain 90% of the tetrol **11a**. On the other hand, if the first attack occurred at an inner position, the intermediate product would be the anhydrotetrol **8c**, and the final product would consist largely of the tetrol **10a**. We therefore conclude that both anhydrotetrols are intermediates in the hydrolysis, although no direct proof of the formation of either has been obtained. Partial hydrolysis was performed, and the hydrolyzate was examined by t.l.c. under conditions in which anhydrotetrols and tetrols are readily distinguished. At no time during the hydrolysis did demonstrable amounts of anhydrotetrols accumulate, presumably because the latter are hydrolyzed more rapidly than the parent diepoxide.

A similar lack of selectivity was observed when the diepoxide **7** was treated with aqueous hydrobromic acid. Quantitative analysis of the product was not accomplished, but evidence was obtained for the presence of both dibromoglycols, **3a** and **4a**. Treatment of the mixture with acetone and copper(II) sulfate produced a small amount of an *O*-isopropylidene derivative that could not be purified, but which is presumably **14**. The material that resisted acetonation was benzoylated and, after five recrystallizations of the product, a dibenzoate having m.p. 117.5–119° was isolated. A dibenzoate **3b**, prepared from the authentic dibromoglycol **3a**, melted at 123.5–124°, and a mixture of the two dibenzoates melted at 95°, proving that the two substances are not identical. The structure of the dibenzoate having m.p. 117.5–119° is probably **4b**, for the follow-

ing reasons. The first attack by Br^- can occur at an inner or outer end of either of the equivalent oxirane rings. Attack at an outer position would lead to the epoxybromohydrin **2**, which would then be opened stereoselectively by the second attack of Br^- to give **3a**, as was noted above. On the other hand, if the first attack occurs at an inner end of an oxirane ring, the epoxybromohydrin **8d** would be formed first. The bromo group of **8d** hinders the approach of the second Br^-, and the hindrance will be greater at the adjacent end than at the distant end of the oxirane ring; this would lead to the formation of the 1,3/2,4 dibromoglycol **4a**. The n.m.r. spectrum of the dibenzoate is consistent with the proposed structure **4b**, although application of computer techniques will be required for detailed analysis of the spectrum. Quantitative analysis of the crude mixture, by examination of the n.m.r. spectrum, could not be effected on the mixture of dibromoglycols, because of overlap of the methylene signals of the two compounds.

*Hydrolysis of anhydro-*O*-isopropylidene-tetrols.* — The anhydro-*O*-isopropylidene-tetrols **15** and **16** were previously found[1,2] to yield chiefly the 1,2,3/4 tetrol **22** and the 1,2,4/3 tetrol **21**, respectively, when subjected to acid-catalyzed hydrolysis, and preliminary evidence was obtained that the anhydrotetrols **1** and **17**, instead of the 1,2-mono-*O*-isopropylidenetetrols **18** and **19**, were intermediate products in the hydrolytic sequence. Further investigation has shown that the sequences are indeed **15**→**1**→**22**, and **16**→**17**→**21**. Authentic samples of each of these substances have been prepared, and used as reference materials in t.l.c. analysis. Table I shows the results of typical experiments in which partial hydrolyzates of the anhydro-*O*-isopropylidene-tetrols were analyzed by this technique (see Experimental for details). It is evident that, although compounds whose R_F values corresponded to those of the expected anhydrotetrols accumulated in partial hydrolyzates, the corresponding mono-*O*-isopropylidenetetrols could never be detected. In other experiments, not shown in Table I, known mixtures containing different proportions of the two tetrols **21** and **22** were used as reference materials for comparison with the tetrols contained in the complete hydrolyzate. By this semiquantitative method, we have estimated that, by acid hydrolyzis, the *cis*-anhydro-*O*-isopropylidene-tetrol **15** is converted into a mixture containing 90–98% of **22**, whereas the other isomer (**16**) yields 99% of **21**. The greater ease of acetal hydrolysis relative to the epoxide-opening reaction is in accord with a similar finding by Buchanan and Schwarz[11] concerning the *O*-benzylidene group in anhydro-*O*-benzylidene pyranoside derivatives of sugars.

cis-*1,2:3,4-Diepoxycyclopentane* (**7**). — The epoxybromohydrin **2** is an important intermediate for the synthesis of many of the compounds that we have studied, and it has been prepared many times by the procedure of Young *et al.*[4], *viz.*, by incubation of the dibromoglycol **3a** with aqueous alkali at room temperature. Usually, the observed yield of **2** has been lower than that reported by Young *et al.*, and the boiling point and viscosity of the product were often abnormal. A fraction having a boiling point lower than that of the epoxybromohydrin was obtained by fractional distillation. The i.r. spectrum of the low-boiling fraction showed no absorption in the O–H stretching region (3500–3600 cm^{-1}). Treatment of **2** with aqueous sodium

TABLE I

THIN-LAYER CHROMATOGRAPHIC ANALYSIS OF HYDROLYZATES OF ANHYDRO-*O*-ISOPROPYLIDENETETROLS[a]

Substance hydrolyzed	*Hydrolyzate*[b]			*Reference compounds*[b]					
				Tetrol		*Anhydrotetrol*		*Mono-O-isopropylidenetetrol*	
				21	**22**	**1**	**17**	**18**	**19**
15	0.19 (major)	0.30 (minor)	0.52	0.30	(0.18)[c]	0.51		0.70	0.59
16	0.17 (minor)	0.27 (major)	0.63	0.27	(0.18)[c]	0.47	0.62	0.70	0.58

[a]Both experiments were performed with silica gel G and the developing solvent was butanone–acetic acid–2% boric acid (9:1:1 by volume). The detecting reagent was a periodate–permanganate spray[10]. [b]The numbers are R_F values and, unless otherwise stated, all the values in a row were determined on the same thin-layer plate. [c]These values were measured in a separate but comparable experiment.

TABLE II

INTRAMOLECULAR HYDROGEN BONDING

Compound		*Solvent*	$\Delta\nu$ *in* cm^{-1} *for H-bonded OH*[a]	*Bond length OH···O, Å*	*Compound*		*Solvent*	$\Delta\nu$ *in* cm^{-1} *for H-bonded OH*[a]
Dibromoglycol	**3a**	CS_2	40			**12a**	[e]	66
	28[b]	CCl_4	61	1.84		**18**	$CHCl_3$	51
	29[c]	CCl_4	63	1.82	Isopropylidenetetrols	**19**	CH_2Cl_2; $CHCl_3$	45
	32[b]	CCl_4	73	1.70		**20**	$CHCl_3$; CS_2	51
Diols	**30**[b]	CCl_4	39	2.22	Bromo-*O*-isopropyl-	**35**	CS_2	~50[f]
	31[b]	CCl_4	32	2.36	idenetriols	**9**	[e]	32
	33[d]	CCl_4	103	1.42				
	34[d]	CCl_4	102	1.41				

[a]The values of $\Delta\nu$ are considered accurate to ± 5 cm^{-1}. [b]Data of Kuhn[14]. [c]Data of Darby *et al.*[7]. [d]Data of Kwart and Vosburgh[15]. [e]The value is an average of measurements made on solutions of **12a** in CS_2, $CHCl_3$, or CH_2Cl_2, and **9** in CS_2 or $CHCl_3$. [f]The value is based on an average position of 3610–3615 cm^{-1} for an unbonded OH.

hydroxide gave material whose i.r. spectrum was identical with that of the low-boiling fraction. The spectrum showed two strong bands at 3020 cm^{-1} and 3047 cm^{-1}, characteristic of oxirane or vinyl C–H stretching. The strongest band in the spectrum was at 845 cm^{-1}, coinciding exactly with the strong band that is found in the spectra of all of the epoxides we have studied. In our series, there was no absorption in the region (700–725 cm^{-1}) characteristic of out-of-plane C–H deformation[12] of vinylic compounds nor in the 1600–1680 cm^{-1} region characteristic[12] of C=C stretching. Consequently, the assignment as a diepoxide was considered certain. Since both oxirane rings originate from the *trans*-bromohydrin, functional groups of the dibromoglycol **3**, the *cis* configuration was anticipated[4], and this expectation is substantiated by the n.m.r. spectrum (see Fig. 3). Only two cyclopentane diepoxides are possible, the 1,2:3,4 (*i.e.*, *cis*, *syn cis*), and the 1,2/3,4 (*i.e.*, *cis*, *anti cis*). In the former compound

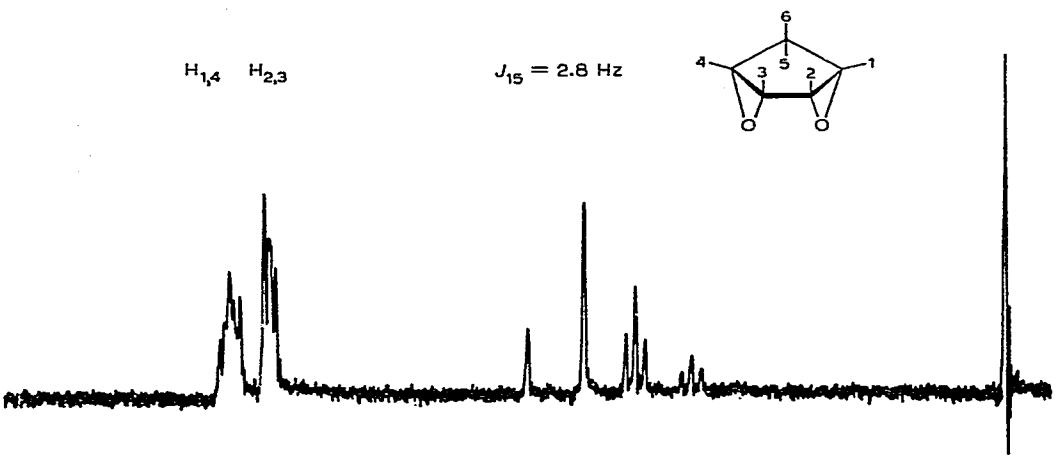

Fig. 3. 60-MHz n.m.r. spectrum of diepoxide **7**.

the protons of the methylene group are not equivalent, and are expected to be represented by an AB system in the spectrum[8,9], whereas for the (1,2/3,4)-diepoxide, the methylenic protons would be chemically equivalent and would be seen either as a single line, or as the A_2 portion of an A_2X_2 system; in the latter case, the signal would be a triplet. The spectrum shows an AB portion of an ABX_2 system in the methylene region, and the proposed *cis* configuration is, therefore, established. A more detailed discussion of the n.m.r. spectrum is given below.

Tetrols and O-isopropylidenetetrols. — Improved methods for synthesis of some of the tetrols have been developed. These methods, and the preparation of some *O*-isopropylidene derivatives useful in their purification, are reported.

The (1,2,4/3)-tetrol was originally prepared[1] by *trans*-hydroxylation of *cis*-1,3-cyclopentenediol (**23**). Although the product requires little purification, the starting material is difficult to prepare, and therefore, the tetrol is now prepared routinely by acid hydrolysis of the more readily accessible[1,2] anhydro-*O*-isopropylidenetetrol **16**. The tetrol has been obtained crystalline, m.p. 127.5–129°, and the small proportion of

contaminating (1,2,3/4)-tetrol is removed by recrystallization. The (1,2/3,4)-tetrol **24** was prepared[1] by *cis*-hydroxylation of the dibenzoate (**25b**) of *cis*-1,2-cyclopentenediol. A better preparative route involves *cis*-hydroxylation of the corresponding *O*-isopropylidene derivative **26**. The product is the corresponding mono-*O*-isopropyl-

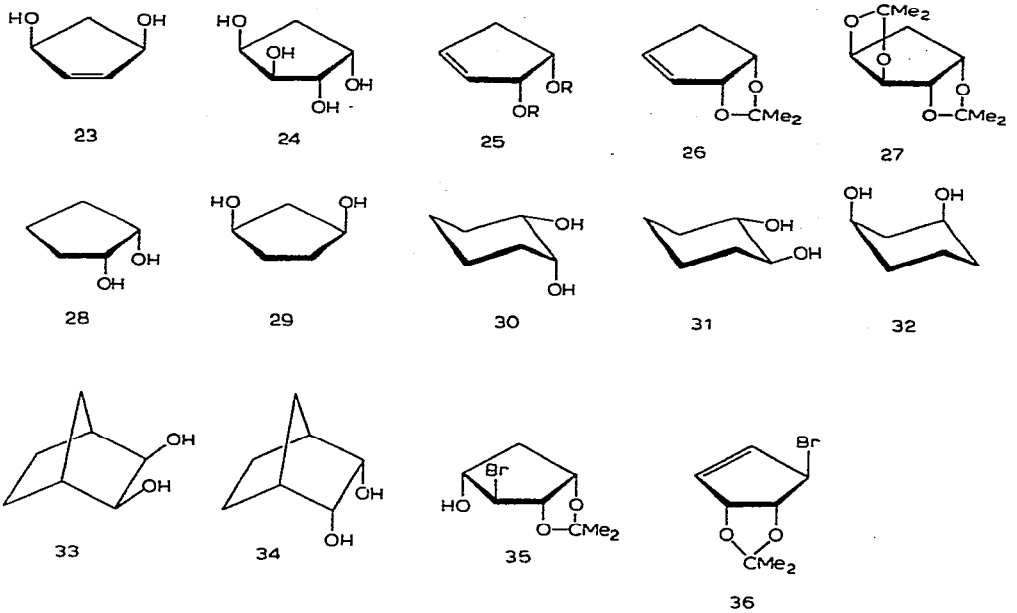

Fig. 4. Other compounds studied; **25a**, R = H; **25b**, R = Bz.

idenetetrol **20**, which is readily purified and then hydrolyzed to give the free tetrol. The preparation of the (1,4/2,3)-tetrol **11a** was formerly accomplished by *cis*-hydroxylation of *cis*-1,3-cyclopentenediol (**23**) with osmium tetraoxide, or by *trans*-hydroxylation of *trans*-1,2-cyclopentenediol (**13**). Both starting materials are difficult to obtain; and consequently, the tetrol **11a** is now prepared by the sequence **3a**→**2**→**5a**→**6a**→**11a**.

The mono-*O*-isopropylidene derivatives of the tetrols are useful intermediates in the synthesis and purification of the tetrols. They may be purified by sublimation, are soluble in a variety of solvents (water, ethanol, ethyl acetate, ether, hot benzene, and dichloromethane), can be selectively extracted from mixtures, and are readily recrystallized. Only the (1,2,3/4) isomer (**19**) has previously been described[1], although four halo-*O*-isopropylidenetriols were also described in the earlier work[2]. In the present study, the (1,4/2,3) and the (1,2,4/3) isomers, (**12a**) and (**18**), were prepared by the usual procedure of stirring the parent tetrol in an excess of dry acetone, with anhydrous copper(II) sulfate as the dehydrating agent and catalyst. When the (1,2/3,4)-tetrol **24** was treated in this way, the product did not contain a significant proportion of the mono-*O*-isopropylidene derivative **20**; but instead, a 94% yield of the di-*O*-isopropylidene derivative **27** was obtained. The i.r. and n.m.r.[9] spectra were consistent only with the proposed structure.

Production of the diol **23** by treatment of the corresponding dibromide with tetraethylammonium acetate and subsequent saponification[1b] suggested that tetrols might be produced directly from the *O*-isopropylidene derivative of the dibromoglycol **14**. The only product that could be identified when **14** was treated with tetraethylammonium acetate was, however, the corresponding, unsaturated, monobromo compound **36**, indicating that elimination of hydrogen bromide occurred, instead of nucleophilic displacement of bromide; this result is probably attributable to steric hindrance related to the *endo* methyl group of the *O*-isopropylidene residue.

Conformational analysis. — Substituted cyclopentanes are known to exist in nonplanar conformations[13a], either as an envelope form, in which one ring atom is out of the plane of the other four, or as a twist conformer in which one atom is above and an adjacent atom is below the plane of the other three. The relief of nonbonded repulsions thus obtained more than compensates for the increased angular strain caused by the "pseudorotation". We believe that the all-*cis* diepoxide **7** may be an exception to this rule. Examination of Dreiding models and of plane projections of

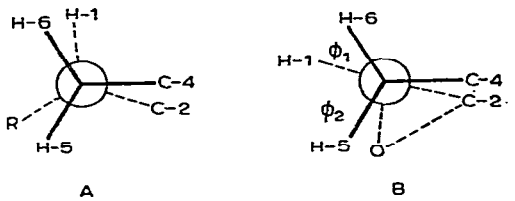

Fig. 5. Comparison of dihedral angles and internuclear distances. A, "planar" cyclopentane. Dihedral angle (H-1)–C–C–(H-6), 0°; H-1 to H-6 internuclear distance 2.2–2.3Å. B, Diepoxide **7**, planar conformation. Dihedral angles: $\varphi_1 = 35$–$38°$; $\varphi_2 = 82$–$85°$. Distances: H-1 to H-6 = 2.55 Å; H-1 to H-5 = 2.8 Å. In both cases, the observer is looking at the methylenic carbon atom (C-5), in the direction of the bond from C-5 to C-1. See reference 13b for an explanation of the Newman projections used.

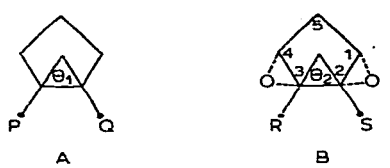

Fig. 6. Projected valence-angles and internuclear distances. A "planar" cyclopentane; $\theta_1 = 70°$; distance PQ = 2.2–2.3 Å. B, Diepoxide **7**; $\theta_2 = 78°$; distance RS = 2.6–2.7 Å.

these models shows the relations illustrated in Figs. 5 and 6. Atoms H-5 and H-6 are not eclipsed with the vicinal hydrogen atoms H-1 and H-4 of the oxirane ring, but the four oxirane hydrogen atoms are mutually eclipsed, *i.e.*, H-1 with H-2, H-2 with H-3, and H-3 with H-4. However, the internuclear distance is 2.6–2.7 Å, as against 2.2–2.3 Å in the eclipsed, ethane-like portion of cyclopentane. Furthermore, the projected, vicinal C–H bonds in cyclopentane intersect at an angle of 70°, whereas those of the diepoxide intersect at an angle of 78°. For all of these reasons, the non-

bonded repulsions in the diepoxide are expected to be significantly smaller than those in a saturated derivative of cyclopentane. In addition, because of the rigidity of the three-membered ring, H-1 (H-4) would tend to remain eclipsed with H-2 (H-3), and the only repulsion that might be relieved is that of H-2 with H-3. The energetic cost of puckering this fused-ring system would probably far exceed the small gain obtained from the relief of eclipsing. This explanation also agrees with the generalization[13a]* that "an sp^2-hybridized atom in planar surroundings is not seriously troubled by bond eclipsing". For all of these reasons, we propose that the cyclopentane ring of 7 exists in the planar conformation.

The conformations of the tetrols and related compounds are more difficult to assign. Many of the substances (but not the tetrols) are sufficiently soluble in non-hydroxylated solvents to permit detection and assessment of the strength of intramolecular H-bonds by i.r. spectroscopy. The presence of such bonds defines an additional ring, and thus diminishes the number of conformations possible. Some of the relevant data are shown in Table II. The difference, $\Delta\nu$, in O–H stretching frequency between free and H-bonded hydroxyl groups has been related[14] to the length of the H-bond. The value found for *cis*-1,2-cyclopentanediol (**28**) is compatible only with a conformation in which there is a torsional angle of 20–30°, and an O··· H bond-length of 1.84 Å. Darby *et al.*[7] reported that $\Delta\nu$ for *cis*-1,3-cyclopentanediol (**29**) is 63 cm^{-1}, corresponding to an O··· H distance of 1.82 Å. Examination of Dreiding models shows that, in order that this H-bond may exist, the cyclopentane ring must be puckered (see Fig. 7). The simplest puckering produces the V conformation (the terminology is that suggested by Hall[16] and used by Bishop and Cooper[17]). In order to accommodate the H-bond in the molecule, C-2 must be displaced by 0.4 to 0.5 Å out of the plane of the other ring atoms, in the direction away from the oxygen atoms. Although this conformation is logical in the sense that it explains the length of the H-bond, it still includes an eclipsed, ethane conformation involving C-4 and C-5, with a corresponding increase in energy of about 3 kcal[13b]. Consequently, the T_2^3 conformation, which also can accommodate the H-bond, must be considered. Similar arguments apply to the dibromoglycol 3a. In this case, the alternative conformations T_2^1 and T_1^5 differ with respect to the carbon atom (C-4 or C-3, respectively) that has its substituents in the bisectional orientation. Somewhat different considerations apply to **18**. Again, the simplest deformation would produce either the V^3 or V^5 conformation, depending on whether O-2 or O-1 is involved in the intramolecular H-bond. For the reasons outlined above, a twist conformer seems more likely; and, in the T_2^3 and T_1^5 conformations (see Fig. 7), the substituents are correctly disposed for H-bonding to O-2 and O-1, respectively. These conformations differ in the orientation of the C-3 hydroxyl group. In the T_2^3 conformation, the C-3 hydroxyl is quasi-axial; whereas, in the T_1^5 conformation, it is bisectional and one of the methylenic hydrogen atoms is quasi-axial (see Discussion).

*In this discussion, we have assumed that the diepoxide 7 resembles cyclopropane[13c] with respect to the approximate sp^2 hybridization of the orbitals involved in the C–H bonds.

Nuclear magnetic resonance studies. — Configurational assignments for many cyclopentane cyclitols and related compounds have previously been made on both chemical and spectroscopic grounds[1,2,9], and further details of the n.m.r. spectra of

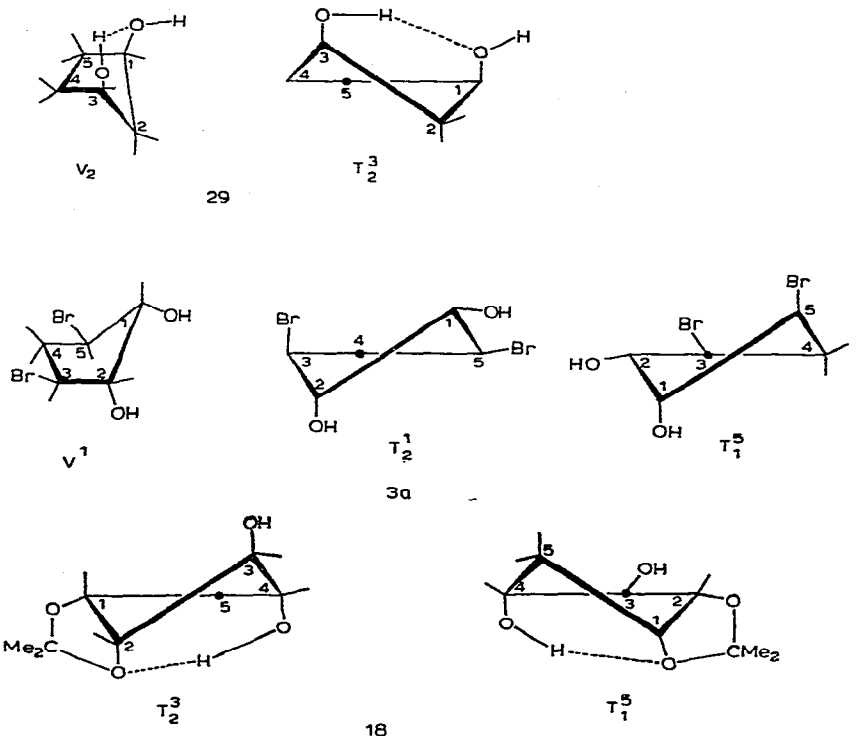

Fig. 7. Conformations considered reasonable for compounds **3a**, **18**, and **29**.

these compounds have been reported[5]. The spectral parameters of several of the compounds now reported are listed in Table III. In some cases, unequivocal assignments of some of the signals cannot yet be made; but the partial descriptions are included, because the spectra have nevertheless been useful in identifying the compounds. The numbering of the protons is as shown for **9** in Fig. 1, in which H-6 is *cis* and H-5 is *trans* with respect to H-1.

The spectrum of the dibenzoate **3b** resembles in general that of **3a**, reported earlier[9]. In the spectrum of that dibenzoate for which structure **4b** is proposed, the difference in chemical shift between H-5 and H-6 is much smaller than the corresponding difference in chemical shift in the spectrum of **3b**. The principal reason for this difference is the angular dependence of the deshielding effect of the vicinal, electronegative substituents[9,18]. In a compound having configuration **4**, the deshielding effects on the two methylenic protons should be approximately equal, whereas in compounds having configuration **3**, the methylenic proton that is *trans* to both vicinal substituents is subjected to a stronger deshielding influence

than is the *cis* proton. The spectrum of the unsymmetrical dibromoglycol supports, therefore, the proposed configurational assignment **4b**.

Most of the compounds under consideration having the same geometry as tetrol

TABLE III

N.M.R. SPECTROSCOPIC DATA[a]

Substance	*Protons*	*Appearance of signal*	δ	*Coupling constants*[a], *Hz*			
				$J_{1,2}$	$J_{1,5}$	$J_{1,6}$	$J_{5,6}$
3b	H-1,4	multiplet of at least 8 lines	~4.45[b]				
	H-2,3	multiplet of at least 4 lines	5.29	4.5	7.2	8.1	15.5
	H-5	doublet of triplets	2.60				
	H-6	5-line multiplet	3.36				
4b	H-5,6	irregular multiplet of at least 8 lines	~2.76[b]	width 27 Hz			
	All Br-C-H	irregular multiplet	~4.47[b]	width 24 Hz			
	O-C-H	quartet	5.67	"J" = 4.3 Hz			
	O-C-H	triplet	5.93	"J" = 4.3 Hz			
7	H-1,4	6-line multiplet[c]	3.75	width 5.6 Hz			
	H-2,3	4-line multiplet[c]	3.56	width 3.1 Hz			
	H-5	doublet of triplets	1.69[d]	?	2.8	0	16.5
	H-6	doublet	2.13[d]				
24	H-5,6	triplet	2.03	"J_{AX}" = 5.2 Hz			
	All O-C-H	irregular multiplet	4.06[b]	width 26 Hz			
10a	H-5,6	triplet	1.98	"J_{AX}" = 7.4 Hz			
	O-C-H	multiplet (probably H-2,3)	3.71[b]	width 13 Hz			
	O-C-H	multiplet (probably H-1,2)	4.03[b]	width 23 Hz			
11a	H-5	multiplet of at least 24 lines[e]	~1.4	width ~30 Hz			
	H-6	multiplet of at least 20 lines	~2.5	width ~32 Hz	6.5[e]	7.5[e]	17[e]
	All O-C-H	multiplet	~3.95	width ~30 Hz			
22	H-5,6	multiplet	2.00[b]	width 49 Hz			
	All O-C-H	irregular multiplet	4.12[b]	width 42 Hz			
21	H-5	doublet of multiplets	1.55	width 29 Hz			
	H-6	doublets of multiplets	2.48	width 38 Hz			
				$J_{5,6}$ ~16 Hz			
	All O-C-H	irregular multiplet	3.9[b]	width 37 Hz			

[a] **3b**, **4b**, and **7**: solutions in chloroform-*d*, with internal TMS; **10a**, **21**, **22**, and **24**: solutions in deuterium oxide, with internal DSS. The coupling constants shown are averages of all of the appropriate line separations in each of the signals in which the coupling may be assigned. Unless otherwise stated, the chemical shifts reported are the central point of the appropriate signals. [b] Value given is the midpoint of this multiplet, and is not necessarily the chemical shift of either of the nuclei represented. [c] The apparent multiplicity was determined from a spectrum recorded on an expanded scale at a lower sweep-rate. [d] Chemical shifts of H-5 and H-6 were in this case calculated by treating these two protons as an AB system[8b]. [e] See text for explanation.

11 (for example, **3a**, **3b**, **11b**, **12a**, **12b**, and **14**) have simple spectra that are amenable to first-order analysis[5,9]. In all of these instances, the bonds (H-5)–C–C–C–(H-2) and (H-5)–C–C–C–(H-3) assume the "W" conformation, which is known to favor long-range coupling[5]; and, in the examples cited, this long-range coupling is also amenable to first-order interpretation. The only compound in this series whose spectrum cannot be interpreted by the first-order rules is the free tetrol **11a**. The signals of H-5 and H-6 are not the simple doublets of triplets observed in the other cases, and the signals of H-1 (H-4) and H-2 (H-3) comprise an overlapping multiplet. On the basis of the total width of each of these signals, and the recurrence of certain separations between spectral lines, tentative values for $J_{1,5}$, $J_{1,6}$ and $J_{5,6}$, are reported in Table III, but these values will have to be confirmed by computation before they may be considered to have been established. The reason for the complexity of the spectrum is not easy to assess. One possible explanation is that the spectrum observed is the result of combined real and virtual[8c] coupling, which causes each proton in the molecule to be involved in non-zero coupling with all of the other protons.

For the diepoxide **7**, at least two different interpretations are possible. The assignment of the signals of H-5 and H-6 has been made by analogy with compounds of similar geometry in which the internal chemical shift[9,18] between H-1 (H-4) and H-5 is larger than that between H-1 (H-4) and H-6. We have assumed that this assignment is valid for substituted epoxides of cyclopentane. However, we have observed strong, long-range shielding and deshielding effects[19], ascribed to the diamagnetic anisotropy of the C–O bonds of the oxirane ring, and it is conceivable that the assignment of resonance frequencies to the two methylenic protons should be reversed (*cf.*, Tori *et al.*[20] and Jefferies *et al.*[21]). Consequently, until the assumption is unequivocally proved, *e.g.*, by specific replacement of H-5 or H-6 by deuterium, the assignment can be only tentative. In the epoxycyclopentanes that we have studied[9,19], and in anhydrofuranosides[16], vicinal spin–spin coupling of sp^3-hybridized protons with oxirane protons is associated with small or zero line-separation in the n.m.r. spectra. The relation between the dihedral angle and the magnitude of such vicinal coupling constants is not known. If the assignment of the resonance frequencies of the methylenic protons is correct, the tripling of the H-5 signal may be ascribed to $J_{1,5} = J_{4,5} =$ 2.8 Hz. If this conclusion is correct, it follows that $J(85°)$ is much larger than $J(35°)$, opposite to the situation described by Karplus' calculations[22]. This apparently anomalous coupling adds to the uncertainty of the assignments of the protons of the methylene group. A spin–spin decoupling experiment, by nuclear-magnetic, double resonance[19], showed that the nuclei corresponding to the signal at δ 3.75 are coupled to the nuclei that we have designated H-5. The signal at δ 3.75 is, therefore, assigned to H-1 (H-4). The remaining signal, at δ 3.56, must, therefore, be that of H-2 (H-3). If first-order rules for multiplicity apply, the signal at δ 3.75 should be a doublet of doublets due to $J_{1,2}$ ($J_{3,4}$) and $J_{1,5}$ ($J_{4,5}$); the signal at δ 3.56 should be a doublet due to $J_{1,2}$. The additional multiplicity might then be ascribed to long-range coupling ($J_{1,3}$ and $J_{2,4}$); indeed, the C–H bonds concerned appear to be well oriented for such long-range coupling.

An entirely different interpretation of the spectrum seems equally reasonable. The methylenic protons might be assumed not to be coupled with H-1 and H-4. Instead, the tripling in the signal at highest field is ascribed to long-range coupling equally with H-2 and H-3. The latter nuclei would, therefore, be assigned to the signal at δ 3.75. In addition, H-2 is coupled with H-1 and, by long range, with H-4. Since H-1 and H-4 have the same chemical shift, the line-splitting caused in H-2 is one half of $(J_{1,2} + J_{2,4})$, causing a tripling[23] of the signal; H-2 appears, therefore, as a six-line signal. H-1 (H-4) is a "triplet" due to $J_{1,2}$ and $J_{1,3}$; the coupling constants are unequal, but, as the chemical shifts of H-2 and H-3 are identical, the line-separation in the H-1 (H-4) signal is one half of $(J_{1,2} + J_{1,3})$.

DISCUSSION

Conformational analysis of cyclopentanoid systems is subject to more uncertainty than that of cyclohexanoid or pyranoid systems. In the examples cited above, the conformations proposed are not necessarily valid, except in the solutions in non-hydroxylic solvents in which the intramolecular hydrogen-bonds were observed. Even in these restricted situations, the choice between alternative possibilities (see Fig. 7) does not yet have an unequivocal basis. For example, in cyclohexanoid systems, the choice between conformers corresponding to T_2^3 and T_1^5 of the mono-*O*-isopropylidene tetrol **18** would be relatively easy; that conformer having fewer axial substituents would be favored, because of the decreased 1,3-diaxial repulsion. In the example shown in Fig. 7, the cost in energy of the quasi-axial hydroxyl group is probably much less than that of an axial group in a cyclohexanoid system, because the hydroxyl group of T_2^3 does not enter into serious 1,3-interaction with another group. Consequently, we favor conformation T_2^3 over T_1^5 because the mutual repulsion between the C-3 and C-4 hydroxyl groups in the former is minimized. Gagnaire and Vottero[24] have studied a related system (2,4/3,5)-3,4-dibromo-2,5-dimethoxytetrahydrofuran. On the basis of n.m.r. coupling-constants of the ring protons, these authors have concluded that a T_3^4 conformation, with all the bulky groups in quasi-axial orientation, is favored. In this example also, the mutual repulsions of the substituents are minimized.

Assignment of absorption bands in the 1300–800 cm^{-1} region of the i.r. spectra to particular modes of vibration of epoxides is still associated with some uncertainty[12b]. The band at 845 cm^{-1} that is characteristic of cyclopentane epoxides is probably the same as the band at 830 cm^{-1} that some authors have tentatively assigned to ring vibrations in *cis*-epoxides[12b]. In general, this region of the spectrum is related to alkyl C–O stretching and to C–H rocking vibrations. Cope *et al.*[25] prepared *cis*-cyclodecene oxide and the corresponding compound in which the oxirane hydrogen atoms are replaced by deuterium. In December, 1964, Professor Cope sent us tracings of the i.r. spectra of the normal and deuterated epoxides, determined with thin films of the pure liquids. Both spectra have strong bands in the 845–835 cm^{-1} region. The possibility that this band is due to a C–H rocking mode is, therefore, eliminated.

Biological studies of the compounds reported have not yet been conducted.

Diepoxides have been found to be good alkylating agents, and they are cytotoxic, mutagenic, and carcinogenic[26-31]. It will be interesting to test the diepoxide **7** and other compounds, such as the epoxybromohydrin and dibromoglycol **2** and **3a**, which may also be good bis-alkylating agents.

EXPERIMENTAL

I.r. spectra were measured with a Perkin–Elmer Model 237B spectrophotometer. n.m.r. spectra were measured with a Varian Associates A-60 n.m.r. spectrometer, with either tetramethylsilane (TMS) or sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) as the internal standard. Melting points were determined on a Kofler micro hot-stage (Athur H. Thomas and Co.) and are corrected. Boiling points are uncorrected. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee.

cis-*1,2:3,4-Diepoxycyclopentane* (**7**). — A. *From 3,5-dibromo-(1,2/3,5)-cyclopentane-1,2-diol* (**3a**). The dibromoglycol **3a** (12.8 g, 49 mmoles) was dissolved in 70 ml of 0.72N sodium hydroxide (50 mmoles) and the solution was extracted with ether continuously for several h. The syrupy residue obtained after evaporation of the ether was separated into two fractions by vacuum distillation; (a) b.p. 62° (0.7 torr), and (b) b.p. 87° (0.3 torr). Fraction (b) was identified as **2** by its i.r. spectrum. Fraction (a) was redistilled to give **7**, b.p. 35° (0.2 torr).

Anal. Calc. for $C_5H_6O_2$: C, 61.21; H, 6.17, Found: C, 61.15; H, 6.22.

B. *From* DL-*1,2-anhydro-4-bromo-(1,2,3/4)-cyclopentane-1,2,3-triol* (**2**). The epoxybromohydrin **2** (2.9 g, 16.2 mmoles) was treated with sodium hydroxide as above, the aqueous solution was extracted for 42 h with dichloromethane and the residue was distilled, giving 1.5 g of **7** (15.4 mmoles, 95%).

DL-*Tri*-O-*benzoyl-4-bromo-(1,4/2,3)-cyclopentane-1,2,3-triol* (**5b**) *and* DL-4-*bromo-2,3*-O-*isopropylidene-(1,4/2,3)-cyclopentane-1,2,3-triol* (**9**). — A solution of **2** in 0.25N sulfuric acid was heated for 1h at 100° to produce **5a**. Excess barium carbonate was added, barium sulfate was removed by filtration, and the solvent was evaporated under diminished pressure. An aliquot sample of the resulting syrup (126 mg) was dissolved in 0.6 ml of pyridine, the solution was chilled in ice, 0.4 ml of benzoyl chloride was added and the mixture was kept overnight at room temperature. The product was isolated in the usual way[2] and it crystallized after brief contact with ethanol. Recrystallization gave **5b**, m.p. 136–7°.

Anal. Calc. for $C_{26}H_{21}BrO_6$: C, 61.31; H, 4.15; Br, 15.69. Found: C, 61.02; H, 4.13; Br, 15.80.

The remainder of the syrup (1.2 g) was stirred for 40 h with 100 ml of anhydrous acetone to which was added 2 g of anhydrous copper(II) sulfate and 3 drops of conc. hydrochloric acid. Conc. aqueous ammonia was added, the mixture was filtered, and the solvent was evaporated in a current of warm air. The residue was extracted with dichloromethane and the solvent was evaporated to give a semi-solid product. The product was extracted with carbon disulfide, and after removal of this solvent the oily residue was distilled to give **9**, yield 282 mg, b.p. 100–110° (0.3 torr).

Anal. Calc. for $C_8H_{13}BrO_3$: C, 40.52; H, 5.52; Br, 33.70. Found: C, 40.45; H, 5.65; Br, 33.66.

DL-*1,2-Anhydro-(1,2,3/4)-cyclopentane-1,2,3,4-tetrol* (**6a**). — The crude bromotriol **5a** (13.5 g, 68 mmoles) was added to a solution of 2.7 g (68 mmoles) of sodium hydroxide in 70 ml of water, and the solution was extracted with ether for 24 h. The ether was evaporated and the syrupy product was crystallized from hot ethyl acetate, yield 3.95 g (35 mmoles, 50%), m.p. 103.5–104.5°.

Anal. Calc. for $C_5H_8O_3$: C, 51.72; H, 6.94. Found: C, 51.76; H, 7.07.

The dibenzoate **6b** was prepared from the anhydrotetrol **6a** (70 mg) in 0.19 ml of pyridine, with 0.14 ml of benzoyl chloride; recrystallized from ethanol it had m.p. 119–120°.

Anal. Calc. for $C_{19}H_{16}O_5$: C, 70.86; H, 4.97. Found: C, 70.43; H, 5.08.

2,3-O-Isopropylidene-(1,4/2,3)-cyclopentane-1,2,3,4-tetrol (**12a**) *and its dibenzoate* (**12b**). — The anhydrotetrol **6a** was hydrolyzed by heating for 1 h at 100° in 0.25N sulfuric acid, and the solution was neutralized (barium carbonate) and evaporated. The syrupy product crystallized spontaneously. Analysis by n.m.r. spectroscopy showed that 90% of tetrol **11a** and 10% of tetrol **10a** had been produced. The hydrolyzate was stirred with acetone and copper(II) sulfate for two days and worked up in the usual way. The product (**12a**) crystallized spontaneously and was recrystallized from benzene; it had m.p. 136.5–138.5°.

Anal. Calc. for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.34; H, 8.25.

Benzoylation of **12a** (71 mg) with benzoyl chloride (0.09 ml) and pyridine (0.4 ml) gave the product **12b**, which crystallized rapidly from ethanol, and was recrystallized from the same solvent; it had m.p. 139–141°.

Anal. Calc. for $C_{26}H_{22}O_6$: C, 69.10; H, 5.80. Found: C, 68.91; H, 5.76.

DL-*(1,2,4/3)-Cyclopentane-1,2,3,4-tetrol* (**21a**). — The *O*-isopropylideneanhydrotetrol **16** was prepared as described previously[1a], and hydrolyzed (N sulfuric acid, 1 h, 100°) and worked up as usual. The syrup obtained after removal of solvent was desiccated for several weeks, during which time crystals formed slowly. After recrystallization from absolute ethanol, the product **21a** melted at 127.5–129°.

Anal. Calc. for $C_5H_{10}O_4$: C, 44.77; H, 7.52. Found: C, 44.64; H, 7.38.

Benzoylation of **21a** gave a product identical[1a] with authentic **21b**.

DL-*1,2-O-Isopropylidene-(1,2,4/3)-cyclopentane-1,2,3,4-tetrol* (**18**). — The cyclopentanetetrol **21** was prepared in the usual way, and the syrupy product was stirred overnight with anhydrous acetone and copper(II) sulfate. After the mixture had been filtered, the acetone was evaporated in a stream of warm air, and the residue was extracted with dichloromethane. The solvent was evaporated as before, and the liquid obtained was subjected to a high vacuum for 1h. After a few h at room temperature, the oil solidified to a mass of crystals, m.p. 60–65°. The product was purified by sublimation at 65° (0.3 torr) with the condenser at 0°; the product had m.p. 65–66°.

Anal. Calc. for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.20; H, 8.13.

DL-*1,2-O-Isopropylidene-(1,2/3,4)-cyclopentane-1,2,3,4-tetrol* (**20**). — A solution of *cis*-1,2-*O*-isopropylidene-3-cyclopentene-1,2-diol[4] (**26**) (3 g, 21.4 mmoles) in 300 ml

of acetone was cooled to −10° and 60 ml of 5% (w/v) aqueous potassium permanganate added dropwise, with good stirring, during 2.5 h. Stirring was continued and the temperature was maintained for 0.5 h at 0° after the addition had been completed. When the solution was allowed to warm slightly, the precipitate became flocculent and was removed by filtration. The filtrate was concentrated, and the resultant syrup was desiccated under vacuum for 2 days, during which time **20** crystallized, yield 2.0 g (11.3 mmoles, 53%), m.p. 87–92°. The product was dissolved in hot ether, and the solution was filtered and evaporated to give crystals, m.p. 91–94°, and the product was finally recrystallized from benzene; m.p. 95–96°.

Anal. Calc. for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.32; H, 8.00.

Hydrolysis of **20** under the usual conditions gave the free tetrol **24**, m.p. 124.5–127°, and benzoylation of the latter under the usual conditions gave the tetrabenzoate, m.p. 144–6°. The tetrol and the tetrabenzoate were identical to the authentic materials previously described[1a].

DL-*1,2:3,4-Di*-O-*isopropylidene-(1,2/3,4)-cyclopentane-1,2,3,4-tetrol* (**27**). — The tetrol **24** (0.50 g, 3.73 mmoles) was dissolved in 100 ml of anhydrous acetone, 3 drops of conc. hydrochloric acid and 2 g of anhydrous copper(II) sulfate were added, and the mixture was stirred overnight. After having been adjusted to pH 7 with conc. ammonium hydroxide, the mixture was filtered and the solvent was evaporated in a stream of cool air to give a white, crystalline product. Sublimation at 55° (0.3 torr), with the condenser at 0°, gave **27** (0.75 g, 3.50 mmoles, 94%) m.p. 49–50°.

Anal. Calc. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.39%; H, 8.50.

DL-*5-Bromo-1,2*-O-*isopropylidene-(1,2/5)-3-cyclopentene-1,2-diol* (**36**). — A solution of 3,5-dibromo-1,2-*O*-isopropylidene-(1,2/3,5)-cyclopentane-1,2-diol[4] **14** (2.5 g, 8.3 mmoles) in 15 ml of anhydrous acetone was added over a period of 20 min to a solution of tetraethylammonium acetate (3.4 g, 16.5 mmoles) in 25 ml of anhydrous acetone, and the temperature was maintained at 0°. A white precipitate formed slowly during the addition. The mixture was stirred for 24 h at room temperature, filtered and the solvent was evaporated. The syrupy residue was distilled, giving 0.2 ml of **36**, b.p. 68° (120 torr). The i.r. spectrum showed bands characteristic of vinyl C-H vibrations at 690, 755, and 3065 cm^{-1}, and of *O*-isopropylidene groups at 1370–1380, 1253, and 1154 cm^{-1}.

Anal. Calc. for $C_8H_{11}BrO_2$: C, 43.86; H, 5.06; Br, 36.47. Found: C, 44.01; H, 5.12; Br, 36.23.

Epoxide opening of epoxybromohydrin **2**. — Hydrolysis of **2** is described above. For opening by hydrogen bromide, 0.28 g of **2** was dissolved in 10 ml of abs. ethanol, and hydrogen bromide gas was bubbled vigorously through the solution for 1 min. The solution became hot. It was kept for 0.5 h and then concentrated. The syrup was diluted with 15 ml of water, the pH was adjusted to 6 by addition of solid sodium hydrogen carbonate, and the solution was extracted overnight with dichloromethane. Evaporation of the extract gave a crystalline product, m.p. 68–71°. The i.r. spectrum showed that the substance was the dibromoglycol **3a**. After recrystallization from

dichloromethane–low-boiling petroleum[4], it had m.p. 75.5–76.5°, mixture m.p. with authentic **3a** 75–77°.

Epoxide opening of anhydrotetrol **6a**. — A. *Hydrolysis.* Substance **6a** (300 mg) was dissolved in 0.02N sulfuric acid (50 ml) and the solution was heated for 1h at 100°. Excess barium carbonate was added, the mixture was filtered, and solvent was removed under vacuum. The product was dissolved in deuterium oxide (0.60 ml) and the n.m.r. spectrum of the solution was recorded.

B. *Opening with hydrogen bromide.* Substance **6a** (0.253 g, 2.2 mmoles) was dissolved in 25 ml of ethanol, and hydrogen bromide gas was bubbled vigorously through the solution for 2 min. The solution was kept overnight at room temperature and then concentrated *in vacuo* to an orange syrup. Anhydrous acetone (50 ml) and copper(II) sulfate (3 g) were added and the mixture was stirred for 22 h at room temperature. The pH was adjuted to 7 with conc. ammonium hydroxide, the mixture was filtered, and the solvent was removed by a current of cool air. The syrupy product was extracted with dichloromethane, the extract was evaporated, and the residue was distilled; b.p. 120° (0.75 torr), yield 0.234 g (0.1 mmole, 45%). The i.r. and n.m.r. spectra of the *O*-isopropylidene derivative were identical to those of **9** prepared from epoxybromohydrin **2**.

Epoxide opening of the diepoxide **7**. — A. *Hydrolysis.* Substance **7** (290 mg) was dissolved in 0.02N sulfuric acid (50 ml), the solution was heated for 1 h at 100°, and the product was worked up as described above. The syrupy product (118 mg) was dissolved in deuterium oxide (0.50 ml) and its n.m.r. spectrum was recorded.

B. *Opening by hydrogen bromide.* Substance **7** (1.67 g, 17 mmoles) was added to 15 ml of N aqueous hydrobromic acid and kept overnight at room temperature. The solution was neutralized with N sodium hydroxide and was then extracted for 3 days with dichloromethane. Evaporation of the solvent gave 1.2 g of an oil, which was treated overnight with acetone (70 ml) and copper(II) sulfate (2 g), and the product was worked up as usual. A yellow oil was obtained, which was extracted with low-boiling petroleum (35–60°); most of the material was insoluble. Evaporation of the petroleum left a liquid whose i.r. spectrum was identical to that of authentic[4] **14**. The petroleum-insoluble material was benzoylated in 8 ml of pyridine with 5.5 ml of benzoyl chloride. The product, DL-1,3-di-*O*-benzoyl-2,4-dibromo-(1,3/2,4)-1,3-cyclopentane-diol (**4b**), recrystallized 5 times from abs. ethanol, had m.p. 117.5–119°.

Anal. Calc. for $C_{19}H_{16}Br_2O_4$: C, 48.75; H, 3.44; Br, 34.12. Found: C, 48.69; H, 3.25; Br, 34.14.

The dibenzoate **3b**, prepared from the authentic dibromoglycol **3a**, had m.p. 123.5–124°. *Anal.* Found: C, 48.63; H, 3.51; Br, 34.24. The mixture m.p. of **3b** and **4b** was 97–107°.

Products of hydrolysis of the O-*isopropylideneanhydrotetrols* **15** *and* **16**. — A. *Partial hydrolysis.* Aqueous solutions were prepared, containing 7 mg/ml of the respective compounds. Aliquots (0.4 ml) were added to 1.2 ml of 1.8×10^{-3}N sulfuric acid, and the solutions were heated for 5 min at 100°. The reaction was stopped by chilling in ice and adding an excess of barium carbonate. The mixtures were filtered,

the filtrates were evaporated to dryness, and the residues were dissolved in water (0.2 ml). These solutions were used for t.l.c. analysis.

B. *Semi-quantitative analysis of products of complete hydrolysis.* Mixtures, prepared as above, were heated for 30 min and analyzed as described.

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SUMMARY

Earlier conclusions that an electronegative substituent exerts a strong influence on the direction of opening of an unhindered, adjacent epoxide by a nucleophilic reagent have been substantiated; the nucleophile attacks stereoselectively at the end of the oxirane ring farthest from the vicinal, electronegative substituent (OH or Br). *cis*-1,2:3,4-Diepoxycyclopentane **7** has been prepared, and, unlike the substituted monoepoxides of cyclopentane, this compound shows no stereoselectivity for the attack of a nucleophile (Br^- or H_2O). When the anhydro-*O*-isopropylidene cyclopentanetetrols are subjected to acid-catalyzed hydrolysis, the first products are anhydrotetrols, because of the greater lability of the *O*-isopropylidene residue. The corresponding *O*-isopropylidenetetrols are not detected in partial hydrolyzates, which contain tetrols, anhydrotetrols, and starting material. When a hindered halocyclopentane, 3,5-dibromo-1,2-*O*-isopropylidene-(1,2/3,5)-1,2-cyclopentane-diol (**14**), reacts with tetraethylammonium acetate, the expected nucleophilic displacement of halogen by acetate is not observed; instead a 1,2-elimination of hydrogen bromide occurs. Favored conformations of several derivatives of cyclopentane cyclitols are assigned, on the basis of the presence of strong, intramolecular, hydrogen bonds and the need to minimize nonbonded repulsion. Improved methods of synthesis, and several new derivatives of cyclopentane cyclitols, are described. The strong band near 840 cm^{-1} in the infrared spectra of epoxides is assigned to a C–O stretching, rather than to a C–H rocking mode.

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