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STUDIES ON CYCLITOLS—XVII

STRUCTURAL REQUIREMENTS FOR ABNORMAL HYDROXYLATION OF DIENES BY PERMANGANATE*

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Abstract—Abnormal hydroxylation by permanganate of cyclopentadiene (**1a**) and 1,3-cyclohexadiene (**1b**) has been described previously. This pathway, referred to as the epoxidic pathway, gives (1,2,3,4/0)-1,2-epoxydiols (**3**), and (1,2,3/4)- and (1,2,4/3)-tetrols (**5** and **6**) in addition to normal products. A second abnormal pathway, described by other authors, converts 1,5-hexadiene (**7**) and related dienes (**9**) into tetrahydrofurandiols (**8** and **10**). This is referred to as the oxacyclane pathway. The study has now been extended to include 1,4-cyclohexadiene (**11**) and 1,5-cyclooctadiene (**17**). VPC analysis using authentic markers shows that **11** gives only normal products, neither epoxydiol nor (*cis*/*trans*)-tetrol being detectable. The study of **17** is less complete; only normal products have been identified, but in the absence of authentic abnormal products for comparison, the conclusions are only tentative. **17** is a constrained analogue of **7**, and might possibly be expected to react by the oxacyclane pathway. Examination of models suggests that **17** probably cannot assume a conformation leading to the transition state necessary to give analogues of **8** by the oxacyclane pathway, and also that in any conformation that would lead to the necessary transition state, the methylenic hydrogens would seriously hinder the approach of the reagent. Measurements of the models also show that the interatomic distances, among the carbon atoms in the double bonds, are markedly different in **11** with respect to **1a** and **1b**. On the other hand, the distances in **7** are more like those in **1**. It is proposed that the epoxidic pathway requires conjugated double bonds in the substrate, and that the oxacyclane pathway requires proximity of isolated double bonds. **11** does not react by the oxacyclane route because the proposed bicyclic product **21** would be too strained to be formed.

ALKENES AND CYCLOALKENES are converted into *cis* glycols by treatment with permanganate; varying amounts of α-ketoalcohols are formed,‡ in addition, when the medium is insufficiently alkaline.[2] A different situation exists with certain dienes, for which two abnormal pathways have been described. (a) Cyclopentadiene (**1a**) and 1,3-cyclohexadiene (**1b**) gave five main products (**2–6**).[3–5] Of these, **2** and **4** were considered to have arisen by one or two normal *cis* hydroxylations, whereas **3**, **5** and **6** were considered to be the products of a different reaction, for which a reactive intermediate related to **3** was proposed.[3] We will refer to this as the *epoxidic pathway*. (b) Klein and Rojahn[6] reported that 1,5-hexadiene (**7**) and a series of substituted 1,5-hexadienes, e.g. **9**, are converted into the tetrahydrofuran diols **8** and **10**, respectively, rather than the expected tetrols. In each case the products could have been formed only by a concerted *cis* addition to both double bonds simultaneously.

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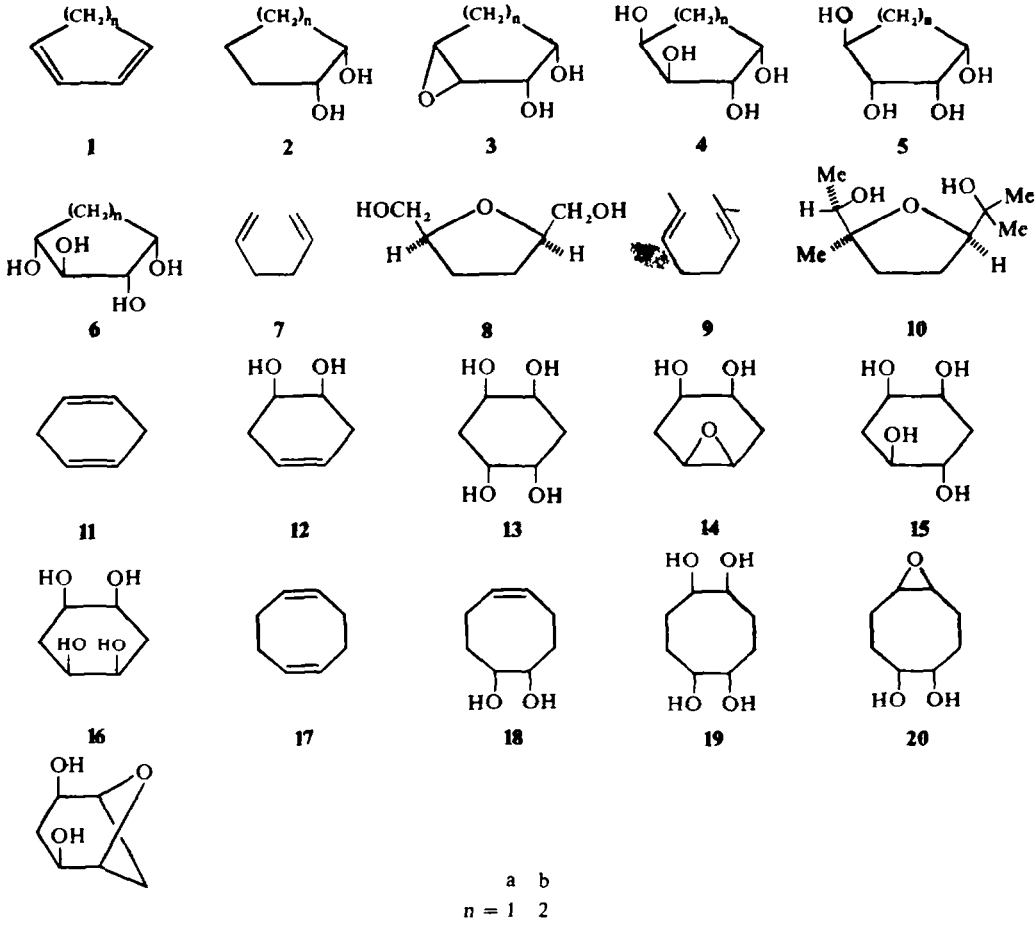
‡ A similar anomalous product has been observed[24] in the oxidation of 3-cyclohexenol benzoate by $AgClO_3/OsO_4$.

We will refer to this pathway as the *oxacyclane* pathway. The reactive intermediate proposed by these authors[6] is similar to the intermediate proposed by us[3] for the oxidation of **1**. In an attempt to elucidate the structural requirements for abnormal hydroxylation, we have now extended our studies to include 1,4-cyclohexadiene (**11**) and 1,5-cyclooctadiene (**17**).

RESULTS AND DISCUSSION

The unconjugated dienes **11** and **17** behave differently from **1a** and **1b**. In the studies with the conjugated dienes, buffered (neutral) as well as alkaline permanganate were useful[3] both for mechanistic studies and for preparative work.

CHART I



Neutral hydroxylation with $Zn(MnO_4)_2$ is convenient because the inorganic products, MnO_2 and $Zn(OH)_2$, are insoluble, and their removal leaves an ion-free solution

whose subsequent work-up is simple. However, in repeated experiments with **11** or **17** as the substrate, we failed to isolate diols or tetrols, and only small amounts were detected by TLC. Qualitative phenylhydrazine tests were strongly positive, suggesting that the principal products were ketoalcohols.[2] Consequently the oxidant used in the present experiments was either $KMnO_4$, with which the medium becomes alkaline as the reaction progresses, or $KMnO_4$–K_2CO_3. The dienes are poorly soluble in water, and are therefore dissolved in acetone or EtOH. In the oxidation of **1a**, **1b** and **17**, we are unable to ascribe consistent differences to the use of either solvent. However in the case of **11**, EtOH is superior, the yields of isolated products being 5–10 times larger than when acetone is the solvent. Regardless of solvent, the oxidation of **11** and **17** is markedly slower than that of the conjugated dienes. Addition of oxidant to the conjugated dienes can be carried out in 2–4 hours,[3] whereas with **11** and **17** under the same conditions of temperature and concentrations, 4–12 hours were required.

The products of hydroxylation were also different. From the oxidation of **11** only the known compounds[7,8] **12** and **13** were isolated. These can be formed by one or two normal *cis* hydroxylations. The diol was identified[7] by its elemental analysis, spectroscopic properties and m.p. Its subsequent conversion into the epoxydiol (**14**) by *m*-Cl-$PhCO_3H$ (see Experimental) and into tetrol[8] **13** by alkaline $KMnO_4$ confirmed the identification. Compounds **12**, **13**, **14** and **15** were easily separable by VPC (Table 1), and under conditions which would easily have allowed detection of a component which was 0·1% of the total product, neither **14** nor **15** was found. A minor component in the tetrol region, representing about 5% of the total product, has not

TABLE 1. VPC ANALYSIS OF PRODUCTS OF HYDROXYLATION OF 1,4-CYCLOHEXADIENE
Freshly distilled 1,4-cyclohexadiene 10 ml, was dissolved in 450 ml EtOH and chilled to −10° with dry-ice EtOH. An aqueous solution of $KMnO_4$, 23 g, and K_2CO_3 13 g in 300 ml H_2O was added over a period of 2½ hr. The resulting solution was continously extracted with CH_2Cl_2 for 3 days and the CH_2Cl_2-soluble and H_2O-soluble fractions were analyzed separately by VPC (Experimental)

Substance or mixture	RT	Substance or mixture	RT	%
	min		min	
Diol **12**	2·1	CH_2Cl_2-Soluble[a]	2·1	99·9
Epoxydiol **14**	4·9			
Tetrol **13**	12·6		12·8	93·3
Tetrol **15**	15·4	H_2O-Soluble[b]	16·6	6·7

[a] In one experiment there was a small amount of a component with the same retention time as epoxydiol **14**. However when the material was refluxed in 0·05N H_2SO_4 for an hour, the component did not disappear, so it could not have been epoxydiol (see Experimental).

[b] In an identical experiment the components of RT 12·8 and 16·6 min were 98·2% and 1·8% of this fraction. As little as 0·5% of **15** would have been detected, if it were present.

been identified. A similar tetrol mixture was obtained when **12** was oxidized with $KMnO_4$. By analogy with many other studies, successive *cis* hydroxylations are expected to give predominantly *cis–anti-cis* (**13**) because of steric hindrance to the second addition. Since some *cis–syn-cis* product (**16**) could be formed in small

amounts, (e.g. see McCasland *et al.*[8a]) it is conceivable that the minor product may be **16**. However, in the absence of authentic material, definite assignment cannot be made.

The study of the cyclooctane system is less complete. Oxidation of **17** gave a mixture separable into two solubility groups by continuous extraction of an aqueous solution of the crude product[3] with CH_2Cl_2. In a series of 10 experiments, the "CH_2Cl_2 fraction" yielded a substance identified as **18**. In the same series the "H_2O layer" gave a tetrol shown (see below) to be (*cis*-1,2), (*cis*-5,6)-cyclooctanetetrol (**19**), but whether the configuration is (1, 2, 5, 6/0) or (1, 2/5, 6) has not been determined. The yield of diol (from 20 g of **17**) was 0·24–1·2 g; the yield of tetrol was 0·8–2·3 g, except in one experiment in which 9·5 g were obtained. The structure of **18** was established from its elemental analysis, from its catalytic reduction to a diol identical with authentic *cis*-cyclooctane-1,2-diol, and by its oxidation to **19** (see below). The structure proof of **19** was obtained as follows: (a) By oxidation with $KMnO_4$ at room temperature, under conditions which converted cyclooctane-1,2-diol into suberic acid, **19** was converted into succinic acid. Only a 1,2,5,6-tetrol could give this result. (b) Treatment of **18** with $AgClO_3$–OsO_4 gave a tetrol identical with **19**. Since **18** has a *cis* glycol function, and since OsO_4 produces *cis* glycols from alkenes, the postulated structure is substantiated. For some unexplained reason, periodate oxidation gave anomalous results. On an analytical scale, the tetrol consumed only 1·2–1·3 molar equivalents of periodate. No explanation of the observation is apparent.*

As noted above, oxidation with buffered permanganate gave poor yields. IR spectra of products isolated from the CH_2Cl_2 extract (Experimental) showed carbonyl groups ($\sim 1700\ cm^{-1}$) and intramolecularly bonded OH ($\sim 3500\ cm^{-1}$) suggesting that α-ketoalcohols were present. TLC studies were inconclusive because of the presence of such products. Data on some of the purified products are shown in Table 2, with one crude mixture for comparison. The crude mixture apparently contains only tetrol and diol, with a small amount of faster-moving unknown component. Although this would seem to be proof that there is no epoxide formed, the abnormal hydroxylation could produce an "abnormal" tetrol with the same R_f as that of **19**, or other, unexpected products.

A substance was prepared which is probably either the (1,2,5,6/0) or the (1,2/5,6) isomer of **20**. Treatment of **18** with *m*-Cl-$PhCO_3H$ under the usual conditions gave a crystalline substance with correct elemental analysis. Study of Dreiding models shows that in the (1,2,5,6/0)-isomer, transannular, intramolecular H-bonds, involving the OH groups and the oxirane oxygen atom, are conformationally feasible, and should be detectable for examination of the O—H stretching mode. In all our previous work, characteristic frequencies in the IR spectra of diols, epoxydiols and acetals were detectable because the compounds were soluble in CS_2, a solvent whose IR spectrum obscures few of the bands of interest in the compounds under study. Because of the poor solubility of many of the cyclooctane derivatives in CS_2, spectra had to be measured on solutions in CH_2Cl_2, a solvent which has many strong bands throughout the spectrum, or in Nujol mulls. Spectra of a dispersion of the compound in KBr

* A referee has made the following valuable suggestions. The anomalous periodate uptake is possibly due to hemiacetal formation by the intermediate 4,5-dihydroxyoctanedial. Another possibility would be a cyclic periodate ester. Such abnormal reactions may be favored by the special steric situation in cyclooctane derivatives, which may lead to transannular interactions.

would not have been any more useful in this connection, since they would have given no information on the presence or absence of intramolecular H-bonds. The spectra of the presumed **20** contained the strong band at 840–845 cm^{-1} which we have shown[3,9] to be characteristic of the cycloalkene oxides we have studied. The C—H stretching region was obscured. The O—H stretching frequency near 3600 cm^{-1} was present, but in the absence of detailed studies of solutions in CH_2Cl_2 no conclusions can be drawn about the presence or absence of intramolecular H-bonds. The m.p. of **20** was hard to determine, possibly because the product was a mixture of isomers. The analytical sample had m.p. 136–142°. Hydrolysis of the supposed epoxydiol gave a product of m.p. 112–115°, which had an R_f in TLC analysis similar to that of **19**, but which was not

TABLE 2. TLC ANALYSIS OF CYCLOOCTANE AND CYCLOCTENE DERIVATIVES

TLC analysis was performed on silica gel G; the developing solvent was butanone, glacial acetic acid, 2% boric acid (9:1:1 by volume); the detecting reagent was a permanganate–periodate spray (Experimental)

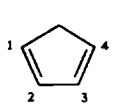
Substance analyzed	R_f
cis-Cyclooctane-1,2-diol	0·73–0·75
Cyclooctenediol **18**	0·76
Cyclooctane epoxydiol **20**	0·60
Cyclooctanetetrol **19**	0·32–0·36
Crude hydroxylation product[a]	0·34, 0·79, 0·90[b]

[a] In this experiment the oxidant was $KMnO_4$–K_2CO_3. After centrifugation to remove the MnO_2 the solution was adjusted to pH 5 with $HClO_4$ and then chilled. $KClO_4$ was filtered and the filtrate concentrated as usual, more $KClO_4$ being precipitated with ethanol, and the filtrate again concentrated to a small volume.

[b] The substance of R_f 0·90 was at most 3–5% of the mixture of products.

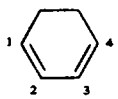
further characterized. TLC analysis of crude products obtained from the hydroxylation by $KMnO_4$ was unsatisfactory, because of the large content of inorganic solutes, and no statement can be made about the presence of minor components which might be products of abnormal hydroxylation.

Examination of Dreiding models of several of the dienes studied by us and by others[3,6] shows differences which may be the basis for the different tendencies to give normal and abnormal products. The interatomic distances C_1–C_3 and C_1–C_4 in **1a** are distinctly less than in **1b**, and the abnormal reaction is more marked in the former.[3] Comparison of distances in **1b** and **11** shows C_1–C_4 in the latter only 0·05 Å longer than C_1–C_4 in **1b**, and C_1–C_5 only 0·10 Å longer than C_1–C_3. If positions 1, 2, 5 and 4 of **11** correspond to positions 1, 2, 3 and 4 of **1b**, with respect to the possible formation of a reactive intermediate postulated for the formation of **3b**, then it is probably unreasonable to ascribe the total absence of the epoxidic pathway to the 0·05–0·10 Å greater distances in **11**. A more reasonable explanation would then be that the reactive intermediate can only form when the double bonds are conjugated, as in **1**. On the



1a

1-3: 2·25 Å
1-4: 2·40 Å

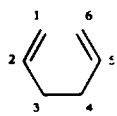


1b

2·50 Å
2·85 Å

11

1-4: 2·90 Å
1-5: 2·60 Å



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other hand, it may be just as reasonable to assume that the distance C_1–C_4 of **11** should be compared with C_1–C_3 of **1**, and C_1–C_5 with C_1–C_4 of **1**. In that case one interatomic distance is larger and the other smaller, compared with **1b**. One would then have to consider that the dimensions of **11** may be wrong for accommodating the oxidant in a manner that can lead to the formation of the reactive intermediate of the epoxidic pathway. To choose between these two explanations, we have measured the corresponding interatomic distances in **7**, assuming that the C_2–C_5 distance corresponds to C_1–C_4 in **1**, and C_1–C_5 of **7** to C_1–C_3 of **1**. The values reported are the range for two conformers with C_3 and C_4 eclipsed, but with the double bonds *syn* in one and *anti* in the other. Values for the *syn* conformer are given first in each case. C_1–C_5: 2·35–2·40 Å; C_1–C_6: 2·35–2·50 Å; C_2–C_5: 2·60 Å; C_2–C_6: 3·20–2·50 Å. Interference between hydrogen atoms on C_1 and C_6 prevents **7** from being planar, and this restriction adds to the difficulty of evaluating the potential mechanisms. However, the distances are reasonably close to those for **1a** and **1b**, but the epoxidic pathway does not operate. We are therefore inclined to the position that operation of the epoxidic pathway requires a conjugated diene as the substrate, rather than some given interatomic distances among the carbon atoms of the diene. The oxacyclane pathway, leading to tetrahydrofurandiols, related to **10**, requires proximity of two isolated double bonds, achieved when the molecule assumes a conformation favorable for the formation of the necessary reactive intermediate. If these postulations are correct, **11** cannot react by the epoxidic pathway because of the absence of conjugation, while the oxacyclane pathway would be slow or absent, because of the relatively strained nature of the required product **21**; that is, the restrictions imposed on **11** by its cyclic nature would make difficult the accommodation of the entering reagent in the manner required by the reactive intermediate.

As indicated, the study of the cyclooctane series is incomplete because of the experimental difficulties, and only tentative conclusions can be drawn. It is noteworthy, however, that only normal hydroxylation products have been identified. In a formal sense, **17** is cyclic homologue of **7**; furthermore the conformational mobility of **17** and of transition states related to it must be greater than for the system related to **11**. Nevertheless, two factors seem to oppose the operation of the oxacyclane pathway. First, the flexibility may still not be great enough to allow the substrate to assume the proper conformation for the reaction to occur. Second, even if the requisite conformation could theoretically be achieved, the concomitant rotation about C—C single bonds is likely to bring methylenic hydrogen atoms into positions where they would effectively block the approach of the reagent, and as a result the normal pathway, however slow, would predominate or occur to the complete exclusion of the abnormal pathway.

Recently another abnormal hydroxylation reaction has been observed. Nace and Rieger[10] obtained 5β-6β-oxidopregnan-3β-ol-20-one-3-acetate from treatment of the

corresponding pregnenolone with $KMnO_4$–HIO_4 in pyridine–water. It is expected that detailed investigation of other "specific" hydroxylating reagents will lead to the discovery of still more unexpected products and mechanisms.

Spectroscopic studies

Tetrabenzoate of tetrol **13**. In the NMR spectrum[8] of **13**, the CH_2 signal is a triplet, indicating a time-averaged equivalence of the CH_2 protons due to rapid chair $\rightleftharpoons$ chair interconversion. The tetrabenzoate of **13** was prepared, and its spectrum in $CDCl_3$ measured. The CH_2 signal is again a triplet, showing that the conformational interchange is still too rapid, with respect to the NMR time scale, for the individual conformers to be observed. Because of the limited solubility of the tetrabenzoate, low-temperature studies were not carried out.

Epoxydiol **14**. The IR spectrum of CS_2 solutions of the epoxydiol had bands at 3568 and 3506 cm^{-1}, indicative of two different intramolecularly H-bonded O—H groups. There was no absorption in the 3600–3630 cm^{-1} region, nor in the 3400 cm^{-1} region, showing the absence of free and intermolecularly H-bonded species. This phenomenon has also been observed[3] in the case of **3a** and **3b**, and the interpretation is identical; i.e., one OH group is bonded to the oxygen of the vicinal OH, which is itself bonded to the oxirane oxygen atom.

We reported previously[9] that all the cyclopentanoid epoxides had C—H stretching bands at 3010–3040 cm^{-1}, but that in the cyclohexanoid epoxides the oxirane C—H stretching mode occurred at lower frequency. In this respect, **14** resembles the other cyclohexane epoxides we studied,[3] in having a band at 2998 cm^{-1} and no C—H absorption above 3000 cm^{-1}. A strong oxirane band, near 840 cm^{-1} is found in the spectra of all the cyclopentene oxides and in many other cycloalkene oxides as well.[3,9] The spectrum of **14** has a band at 852 cm^{-1} which probably represents the same vibrational mode, but it is weaker than normal, since it is only about half as strong as the band at 803 cm^{-1}.

The NMR spectrum in D_2O is completely consistent with the proposed structure. The following signals are observed: CH_2, δ 2·17 (4), two unresolved broad singlets; oxirane CH, δ 3·31 (2), broad singlet; OCH, δ 3·77 (2), triplet of unresolved multiplets.

EXPERIMENTAL

Microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee. IR spectra were measured with a Perkin–Elmer 237B spectrophotometer. The samples were examined as Nujol mulls (solids), or thin films or as dilute solns in CS_2 or chlorinated hydrocarbons. NMR spectra were recorded in $CDCl_3$ or D_2O, with a Varian Associates A-60 NMR Spectrometer, with TMS or DSS as internal reference. Values are reported on the δ-scale in p.p.m. M.p's were determined on a Kofler Micro hot stage, and are corrected. B.p's are uncorrected.

TLC was carried out with silica gel G as backing, and the developing solvent was butanone–glacial acetic acid–2% boric acid (9:1:1 by volume). The detecting reagent was usually a permanganate–periodate spray,[11] except that for the detection of carbonyl compounds a benzidine–HCl soln was used. VPC was carried out with a Victoreen Gas Chromatograph, under the following conditions: stainless steel column 6 ft × $\frac{1}{8}$ in (O.D.), packed with 6% Silicone SE 30 on ABS 90/100 mesh; oven temp 150°; injection temp 250°; flame ionization detector temp 280°. The sample, 10 mg, was dissolved in 1 ml anhyd. pyridine, and 0·2 ml hexamethyldisilazane and 0·1 ml trimethylchlorosilane were added,[12] and allowed to react at least 5 min; samples of 0·4–0·5 µl were injected on the column. The per cent of each cpd was determined from the area

(height × width at half-height) under the curve, corrected for the attenuation. Control samples were run for each expt.

Oxidation of 1,4-*cyclohexadiene* **11**. Freshly distilled 1,4-cyclohexadiene (Aldrich) 24 ml, in 1200 ml EtOH was maintained at −5° (dry ice–acetone) while 52·8 g $KMnO_4$–27·6 g K_2CO_3 in 600 ml H_2O was added dropwise over 3 hr, stored at −10° overnight, then 52·8 g $KMnO_4$ in 500 ml H_2O added over 2 hr. The mixture was centrifuged at 3000 × g in a refrigerated centrifuge. Supt soln was decanted, ppt washed with 70% EtOH, and combined solns were conc. in a rotary evaporator to about 400 ml, adjusted to pH 6 with $HClO_4$, chilled in ice, $KClO_4$ filtered and washed with cold EtOH. Conc again to remove EtOH, and extracted continuously for 2 days with CH_2Cl_2. Evap of CH_2Cl_2 gave 3·25 g of **12**, m.p. 74–78·5°; recryst from toluene gave 3·01 g, m.p. 77–79° (lit.[7b] 80–81°) The aq. soln was chilled in ice, filtered and deionized with Duolite A-4-OH^- and Dowex 50-H^+ resins, the resin columns washed with large vols H_2O, and soln conc to a syrup.* Cryst from 80% EtOH gave **13** m.p. 237–241°; recryst gave 0·47 g, m.p. 238–241° (lit.[8] 240–241°). In another prep the temp was kept at −20° to −25° and the second $KMnO_4$ soln was added right after the first. Yields 1·34 g **12** and 2·96 g **13**.

Oxidation of 1,5-*cyclooctadiene* **17** was carried out essentially as described above for **11**. Cyclooctenediol **18** was obtained from the CH_2Cl_2 extract, and tetrol **19** from the aqueous layer.

5-*Cyclooctene*-1,2-*cis diol* **18**, was recryst from EtOAc, m.p. 102–4°. (Found: C, 67·37; H, 9·72. $C_8H_{14}O_2$ requires C, 67·57; H, 9·92%). Hydroxylation of **18**: 200 mg treated with 90 mg $AgClO_3$, 20 mg OsO_4 in H_2O, final vol 200 ml, in brown bottle, 3 weeks at room temp.[5] AgCl filtered, evap to oil and cryst from EtOH; m.p. 172–174°; m.m.p. with authentic **19**, 172–175°. *Reduction* of **18**: 80 mg in 70 ml H_2O, 75 mg PtO_2, stirred at room temp 3 hr while H_2 gas bubbled through. Catalyst removed, solvent evap and residue cryst from EtOAc, m.p. 75–77·5°. Authentic *cis*-1,2-cyclooctanediol prep by oxid of *cis*-cyclooctene, m.p. 75–77° (lit.[13], 76–79°); m.m.p. 75·5–78°.

Cyclooctaneepoxydiol **20**. To diol **18**, 250 mg in 10 ml $CHCl_3$, added 700 mg *m*-Cl-$PhCO_3H$ in 13 ml $CHCl_3$, 2 days in dark room temp. Solvent evap, added 50 ml H_2O, filtered and soln extr with ether. Evap of water gave residue 342 mg, m.p. 123–130°. Recryst twice from abs. EtOH gave m.p. 136–142°. (Found: C, 60·53; H, 8·94. $C_8H_{14}O_3$ requires C, 60·74; H, 8·92%).

(cis-1,2), (cis-5,6) *Cyclooctanetetrol* **19**. The aqueous layer obtained after exhaustive extraction with CH_2Cl_2 was deionized as above, conc to a syrup in a rotary evaporator. The syrup cryst spontaneously in a few days, m.p. 158–164°; recryst several times from abs EtOH, m.p. 174–176°. (Found: C, 54·41; H, 8·94. $C_8H_{16}O_4$ requires: C, 54·53; H, 9·15%). Acetylation in the usual way[1] gave the tetraacetate; recryst from EtOH, m.p. 89·5–90°. (Found: C, 56·09; H, 7·03. $C_{16}H_{24}O_8$ requires C, 55·80; H, 7·03%).

Structure proof of Cyclooctane tetrol. To cyclooctanediol 835 mg in 100 ml H_2O was added dropwise over 1 hr $KMnO_4$, 1·5 g in 100 ml H_2O, and stirred overnight at room temp. Then 5N H_2SO_4, 10 ml and $NaHSO_3$, 4 g were added to discharge MnO_2. Filtered, conc and neut to pH 6·5, ext with ether 18 hr, adjusted to pH 2–3 and ext again 24 hr. Evap of ether gave 0·70 g, recryst from H_2O gave 0·45 g suberic acid, m.p. 140–141·5°; authentic suberic acid, m.p. 141–142·5° (lit.[14] 139–141°); m.m.p. 139·5–141°.

Under the same conditions, tetrol **19**, 0·82 g and $KMnO_4$ 3·75 g gave 0·74 g crude succinic acid, m.p. 170–184°. *p*-NO_2-Benzyl ester prep: 200 mg crude product titrated to pH 6·5, dried, and refluxed 2 hr with 200 mg *p*-NO_2-benzyl-Br in 10 ml abs EtOH. Product recryst from EtOH, m.p. 93–93·5°; product from authentic succinic acid m.p. 94–94·5° (lit.[14] 88°), m.m.p. 95·5–97°.

Treatment of **19** with anhyd. acetone, $CuSO_4$ and a drop of H_2SO_4 as usual and sublimation gave a cpd m.p. 58·5–60·5° whose spectral properties were those of a diisopropylidene tetrol. Elemental analysis was not done.

Cyclohexane epoxydiol **14**. To diol **12**, 1·0 g in 45 ml $CHCl_3$ was added *m*-Cl-$PhCO_3H$, 2·93 g, left 2 hr at room temp, then 2 days in refrigerator. Solvent evap, solid product suspended in H_2O, filtered, the soln stirred with solid $BaCO_3$ and refiltered. Filtrate continuously extracted 2 days with CH_2Cl_2. Removal of CH_2Cl_2 left an oil, which was distilled in vac (bath at 100–120°, 0·5 Torr, b.p. not recorded). The product cryst in the condenser; m.p. uncertain: melts 69–71°, solidifies and becomes a glass between 100–120°. (Found: C, 55·52; H, 7·84. $C_6H_{10}O_3$ requires: C, 55·37; H, 7·75%).

DL-(1,2,4/5)-cyclohexanetetrol **15**. Epoxydiol **14** was hydrolyzed in 0·02N H_2SO_4, 100°, 1 hr. Neut with $BaCO_3$, filtrate evap and cryst twice from EtOH; m.p. 209–212° (lit.[8a] 208–209°).

* This type of deionization is fairly common in biochemical laboratories, and has the advantage of greatly diminishing the amounts of resins that must be used. A possible disadvantage is that occasionally the desired product, especially if they are ionizable, may co-precipitate with the $KClO_4$.

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