INTRAMOLECULAR HYDROGEN BONDING IN SOME ACYCLIC ALCOHOLS

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Abstract—The extent of intramolecular hydrogen bonding, occurring in dilute CCl_4 solutions, of members of the series (n = 2-5) HO.(CH_2)_n.OH and MeO.(CH_2)_n.OH has been determined. The results permit the interpretation of the patterns of hydrogen bonding in the three monomethyl ethers of butane-1,2,4-triol and in 1,4-dimethoxybutan-2-ol. In these compounds, where hydrogen bonding allows the formation of rings of different sizes the sequence of preference 5 > 6 > 7 was observed.

THE intramolecular hydrogen bonding occurring between hydroxyl groups or between a hydroxyl group and a suitable proton acceptor (usually oxygen) has been determined for a wide range of diols and related compounds.¹ Measurements are usually made on solutions of the alcohols in carbon tetrachloride which are sufficiently dilute to preclude intermolecular hydrogen bonding. The effect of structural variation on the extent of intramolecular hydrogen bonding has been rationalized in many cases^{1,2} and the converse approach has been used in the structural determination of certain diols.² However, in all those compounds studied so far, where more than one type of intramolecular hydrogen bond can be formed, for example involving secondary and tertiary hydroxyl groups,³ the alternatives require the formation of rings of the same size. Apparently, no example has been reported where alternative intramolecular hydrogen bonds involve the formation of rings of different size. Information obtained from a study of such systems may be of potential value in considering the patterns of intramolecular hydrogen bonding in carbohydrates with relation to their effect on reactivity. There is now considerable evidence⁴⁰ which indicates that the rate and/or direction of a variety of reactions can be markedly influenced by intramolecular hydrogen bonding involving hydroxyl groups.

As a first stage we have examined the patterns of intramolecular hydrogen bonding in the series of acyclic alcohols shown in the Tables.

Whereas ethane-1,2-diol and butane-1,4-diol were readily purified by fractional distillation of commercial products, commercial propane-1,3-diol, which contains a significant percentage of periodate oxidizable material,⁵ cannot be so purified. Conversion to the crystalline⁶ 2-phenyl-1,3-dioxan, by reaction with benzaldehyde, followed by acidic hydrolysis of the cyclic acetal gave pure propane-1,3-diol. Pentane-1,5-diol

¹ M. Tichy, Chem. Listy 54, 506 (1960).

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⁸ E. Fischer, Ber. Dtsch. Chem. Ges. 27, 1524 (1894).

No.	Alash 1	ν_{\max} (cm ⁻¹) and (ε) ^a			
	Alconor	Free OH	Bonded OH	$-\Delta v$	
1	Ethane-1,2-diol	3645 (20)	3619 (24)	26	
2	2-Methoxyethanol	3641°(16)	3610 (55)	31	
3	Propane-1,3-diol ^b	3641 (53)	3565 (27)	76	
4	3-Methoxypropanol	3641 (34)	3554 (44)	87	
5	Butane-1,4-diol	3640 (29)	3484 (11)	156	
6	4-Methoxybutanol	3640 (40)	3460 (36)	180	
7	Pentane-1,5-diol ^b	3641 (15)			
8	5-Methoxypentanol	3641 (56)	35004(5)	141	
9	1,4-Dimethoxybutan-2-ol		3598 (45)	31•	
			3538 (28)	91•	
10	4-Methoxybutane-1,2-diol	3641 (33)	3597 (60)	44	
			3534 (57)	107	
			3439(18)	202	
11	2-Methoxybutane-1,4-diol ^b	3641 (29)	3597 (21)	44	
	· · · ·		3556(15)	85	
			3500 (11)	141	
12	4-Methoxybutane-1,3-diol	3641 (49)	3597 (74)	44	
			3562 (79)	79	

TABLE 1. INFRA-RED SPECTRAL DATA ON CERTAIN ALCOHOLS

 Determined for solutions in CCl₄> 0.005 M.
 Spectra measured on saturated solutions of undetermined concentration. Extinction coefficients are relative.

^o Shoulder. The extinction coefficients for these absorptions are not corrected for band overlap and hence must be considered as approximate. ^d Broad.

Calc. assuming an absorption of 3629 cm⁻¹ for unbonded secondary hydroxyl groups (cf. ref.).
 Arithmetical difference between absorptions for free and bonded hydroxyl groups.

No.	Yield (%)	M.p.	Formula	Found (%)			Required (%)		
				C	н	N	C	н	N
1	79	211–214°	C ₃₈ H ₂₂ N ₄ O ₄	69.95	4·3	11.9	70.3	4.6	11.7
2	61	74–75	C16H16N2O2	67.8	5.5	9.7	67.6	5.7	9.9
3	69	196–198	C ₁₉ H ₁₄ N ₄ O ₄	71.05	4.6	11.1	70.7	4.9	11.4
4	50	52-54	C17H18N2O2	68·2	5.75	9.5	68.4	6.1	9.4
5	66	199-200	C30H16N4O4	70.75	5.1	11.3	71.1	5.2	11-1
6	76	71–72	C18H20N2O2	69.1	6.55	8∙7	69·2	6.5	8.9
7	69	164–165	C ₈₁ H ₂₈ N ₄ O ₄	71.6	5-25	10.85	71.5	5.4	10.8
8	57	45-46	$C_{19}H_{22}N_{2}O_{3}$	69.6	6.6	8.3	69.9	6.8	8.6
9		oil	C19H23N2O4	66.7	6.85	8.1	66-65	6.5	8 ·2
10	75	113-114	C ₃₁ H ₃ -N ₄ O ₅	69.6	5.3	10·2	69.4	5.3	10.45
11	50	133–136	C31H38N4O5	69.4	5.35	10.4	69·4	5-3	10.45
12	95	109–111	C31H28N4O5	69.6	5.3	10.5	69-4	5.3	10.45

TABLE 2. ANALYTICAL DATA OF p-PHENYLAZOBENZOATES OF THE ALCOHOLS IN TABLE 1

was conveniently obtained by reduction of tetrahydropyran-2-ol with sodium borohydride. The monomethyl ethers were readily obtained by treatment of the diols with ca. 0.3 mole of sodium followed by methyl iodide.⁷

1,4-Dimethoxybutan-2-ol was obtained from cis-but-2-ene-1,4-diol. Treatment of the olefin with silver oxide and methyl iodide gave the dimethyl ether which reacted slowly with perbenzoic acid in chloroform at room temperature affording erythro-2,3epoxy-1,4-dimethoxybutane. Oxidant was slowly consumed when an aqueous solution (pH 4.5) of the epoxide also containing sodium periodate was stored, due to slow hydrolysis of the epoxide. Treatment of the epoxide with boiling 0.1N-sulphuric acid afforded a product, presumably 1,4-di-O-methyl-DL-threitol, which rapidly consumed 1 mole of periodate. The more rapid epoxidation of cis-but-2-ene-1,4-diol⁵ than of its dimethyl ether is probably due to an intramolecular hydrogen bonding effect analogous to that observed^{4a} for cyclohex-2-enol. Reduction of erythro-2,3epoxy-1,4-dimethoxybutane with lithium aluminium hydride gave 1,4-dimethoxybutan-2-ol. The structure of this compound may be allocated on analogy with reactions of other epoxides⁸ and it is substantiated by the facts that it did not react with periodate or yield any periodate oxidizable product on treatment with boiling 0.1N-sulphuric acid.

4-Methoxybutane-1,2-diol and 4-methoxybutane-1,3-diol were prepared from butane-1,2,4-triol. Acid catalysed condensation of the triol with acetone gave 4-(2'hydroxyethyl)-2,2-dimethyl-1,3-dioxolan. Methylation of the cyclic ketal followed by acidic cleavage of the ketal group gave 4-methoxybutane-1,2-diol. The diol consumed 0.95 mole of periodate thereby confirming the structure.

Acid-catalysed condensation of butane-1,2,4-triol with benzaldehyde gave a mixture of cyclic acetals in which 4-hydroxymethyl-2-phenyl-1,3-dioxan predominated as demonstrated by the following facts. Methylation of the cyclic acetal mixture followed by acidic hydrolysis of the acetal group from the product afforded a mixture of methoxybutane diols which consumed 0.05-0.1 mole of periodate. Therefore the original cyclic acetal mixture contained only 5-10 per cent of 4-(2'-hydroxyethyl)-2phenyl-1,3-dioxolan. p-Phenylazobenzoylation⁹ of the cyclic acetal mixture gave 71 per cent of a pure ester indentified as a 2-phenyl-4-p-phenylazobenzoyloxy-1,3-dioxan since, after application in sequence of saponification, methylation and acidic hydrolysis, a methoxybutane diol was obtained which was different from 4-methoxybutane-1,2-diol and 2-methoxybutane-1,4-diol (as revealed by comparison of the p-phenylazobenzoates) and therefore must have been 4-methoxybutane-1,3-diol. Authentic 2-methoxybutane-1,4-diol is known.¹⁰

With one exception, the alcohols in the tables gave crystalline p-phenylazobenzoates thus further exemplifying the value of this derivative for characterization.⁹

The infra-red spectra in the hydroxyl stretching region of the alcohols in the table were determined for >0.005 M solutions in carbon tetrachloride. At this concentration intermolecular hydrogen bonding is insignificant² and the proportion of free and intramolecularly bonded hydroxyl groups may be assessed³ approximately from the extinction coefficients of the relative absorptions. The arithmetical difference, Δv , between the frequencies (v) for free and bonded hydroxyl is an index of the strength

⁷ R. Pummerer and M. Schönamsgruber, Ber. Disch. Chem. Ges. 72, 1834 (1939).
⁸ W. G. Overend and G. Vaughan, Chem. & Ind. 995 (1955).
⁹ N. Baggett, A. B. Foster, A. H. Haines and M. Stacey, J. Chem. Soc. 3528 (1960).
¹⁰ K. Brenneisen, C. Tamm and T. Reichstein, Helv. Chim. Acta 39, 1233 (1956).

of the hydrogen bond² and also reflects the size of the ring formed by the intramolecular hydrogen bond². Thus, for the series HO.(CH₂)_n·OH the Δv values for five (n = 2), six (n = 3), and seven membered rings (n = 4) are 26, 76, and 156 respectively. No absorption for bonded hydroxyl groups could be detached for $HO.(CH_2)_5.OH$. These results agree well with Kuhn's findings.²

It is not easy to assess the proportions of free and bonded hydroxyl groups for members of the series HO.(CH₂)_n.OH and attention was therefore turned to the series MeO. $(CH_2)_n$.OH where n = 2-5 and where only one intramolecular hydrogen bond can be formed for each member. Wall and Claussen¹¹ examined the spectra of the series EtO.(CH₂)_n.OH but since they used a spectrometer equipped with a rock salt prism the degree of resolution was relatively poor, for example, they did not recognize the intramolecular hydrogen bond in ethane-1,2-diol. The Δv values for members of the series MeO.(CH₂)_n.OH where n = 2-4 were, in each case, slightly larger than those for the corresponding diols suggesting² a slightly stronger hydrogen bond and reflecting the higher basicity of the proton acceptor oxygen atom. Whereas Kuhn² found only absorption (3607 cm⁻¹) for bonded hydroxyl groups in 2-ethoxyethanol we have detected absorptions for both free and bonded hydroxyl groups in 2-methoxyethanol but only a minor proportion of the hydroxyl groups are free. Likewise, for all members of the series MeO. $(CH_2)_n$.OH where n = 3-5, absorption for both free and bonded hydroxyl groups was observed. The absorption for bonded hydroxyl groups in MeO.(CH₂)₅.OH was very weak indicating that there is little tendency for eight membered rings to be formed. The presence of absorption for free hydroxyl groups in all these cases shows that the intramolecular hydrogen bonds are too weak to hold the molecules in one conformation. Further, as the ring formed by the intramolecular hydrogen bond increases in size from five- to seven-membered, a parallel increase in $\Delta \nu$ occurs but the extent of bonding decreases thereby reflecting the decreasing probability¹² of the molecules adopting a conformation suitable for the formation of an intramolecular hydrogen bond. What little evidence their is indicates that intramolecular hydrogen bonding involving a four-membered ring does not occur. Thus, only one hydroxyl group in 5,5-dihydroxy-2-phenyl-1,3dioxan is intramolecularly hydrogen bonded and this involves the ring oxygen atoms.

Restriction of rotation in suitable compounds may permit intramolecular hydrogen bonding to give rings with more than eight members. Certainly, restriction of rotation about the bond between the carbon atoms carrying the hydroxyl groups in vicinal diols has a marked effect on Δv as illustrated by the series ethane-1,2-diol (26), cyclohexane-cis-1,2-diol (39)², cyclopentane-cis-1,2-diol (61)² and exo-cis-2,3-dihydroxybicyclo-[2,2,1]-heptane (103).¹³ In addition to restriction of rotation, the presence of bulky groups may cause molecular deformation of vicinal diols with consequent increase of Δv in certain cases. The effect is illustrated by the series HOCH₂.CH₂. OH(26), (Me₂CH)₂.COH.CH₂OH (70), threo-Me₃C.CHOH.CHOH.CMe₃ (94) and (Me₃C)₂.COH.COH.(CMe₃)₂ (170) and has been discussed by Kuhn.¹⁴ The range of $\Delta \nu$ values for vicinal diols therefore overlaps that for 1,3-diols. However, for the compounds in the table, effects of the above types will be of little significance and the Δv values can be confidently associated with ring size.

¹¹ F. T. Wall and W. F. Claussen, J. Amer. Chem. Soc. 61, 2679 (1939).

J. A. Mills, Adv. Carbohyd. Chem. 10, 1 (1955).
 H. Kwart and W. G. Vosburgh, J. Amer. Chem. Soc. 76, 5400 (1954).
 L. P. Kuhn, J. Amer. Chem. Soc. 80, 5950 (1958).

The hydrogen bond patterns observed for the series HO.(CH₂)_n.OH and MeO.-(CH₂)_n.OH may be used to assign absorptions for more complex molecules. Two intramolecular hydrogen bonds are possible for 1,4-dimethoxybutan-2-ol involving five- and six-membered rings. Absorption for free hydroxyl groups could not be detected for this alcohol and the $\Delta \nu$ values 31 and 91 (calculated on the basis of absorption at 3629 cm⁻¹ for free secondary hydroxyl groups³) for the observed absorptions 3598 (ε 45) and 3538 cm⁻¹ (ε 28) correspond well with those (31 and 87) for MeO(CH₂)₂.OH and MeO.(CH₂)₃.OH. The relative extinction coefficients indicates that the five-membered ring predominates. From a consideration of molecular models it is clear that the conformation of 1,4-dimethoxybutan-2-ol which contains a planar zig-zag arrangement¹⁵ of the carbon chain will allow either or both intramolecular hydrogen bond. Thus, in the absence of adverse steric effects, a hydroxyl group will tend to form an intramolecular hydrogen bond involving a five-membered ring not exclusively but in preference to one giving a six-membered ring.

The series of monomethyl ethers of butane-1,2,4-triol variously offer possibilities for bonding of primary and secondary hydroxyl groups with the formation of five-, six- and seven-membered rings. Thus, 4-methoxybutane-1,3-diol showed absorption at 3641 cm⁻¹ (ε 49) for free hydroxyl and at 3597 ($\Delta \nu$ 44, ε 74) and 3562 cm⁻¹ ($\Delta \nu$ 79, ε 79) for bonded hydroxyl groups involved in five- and six-membered rings. The absorptions may be assigned to the C₃.OH \rightarrow C₄.O and C₁.OH \rightarrow C₃.O hydrogen bonds respectively (I). By analogy with MeO.(CH₂)₂.OH the C₃.OH would be expected to be almost completely bonded to C₄.O thereby reducing its basicity and diminishing the tendency to form a hydrogen bond with C₁.OH. In fact no absorption could be detected which might be associated with a C₁.OH \rightarrow C₄.O hydrogen bond. By further analogy with MeO.(CH₂)₃.OH, the C₁.OH would be expected to be incompletely bonded to C₃.O and this is reflected by the absorption for free hydroxyl. The conformation of 4-methoxybutane-1,3-diol in which the carbon chain has the favoured¹⁵ planar zig-zag arrangement allows simultaneous formation of the C₁.OH \rightarrow C₄.O hydrogen bonds.

The spectra of 4-methoxybutane-1,2-diol and 2-methoxybutane-1,4-diol were more complex, each showing three absorptions for bonded hydroxyl groups in addition to absorption for free hydroxyl. The main absorptions (3597 cm⁻¹, $\Delta \nu$ 44, ε 60 and 3534 cm⁻¹, Δv 107, ε 57) for 4-methoxybutane-1,2-diol may be assigned to $C_1.OH \rightarrow C_2.O$ and $C_2.OH \rightarrow C_4.O$ hydrogen bonds (II). A $C_1.OH \rightarrow C_2.O$ hydrogen bond is more likely than a $C_2OH \rightarrow C_1O$ bond because of the greater acidity of the primary hydroxyl group. Preferential hydrogen bonding of secondary hydroxyl groups to a tertiary hydroxyl oxygen atom has been demonstrated by Cole and Jefferies.³ The cumulation of hydrogen bonds $C_1.OH \rightarrow C_2.O$ and C_2 .OH $\rightarrow C_4$.O can occur in that conformation of the molecule which has a planar zig-zag carbon chain. A different conformation would be necessary to allow the C_1 .OH $\rightarrow C_4$.O hydrogen bond which does occur to some extent (3439 cm⁻¹, $\Delta \nu$ 202, ε 18) probably because the C₂.OH is incompletely bonded to C₄.O. This also accounts for the absorption for free hydroxyl (3641 cm⁻¹ ε 33). The $\Delta \nu$ values (107 and 202) respectively associated with the C_2 .OH $\rightarrow C_4$.O and C_1 .OH $\rightarrow C_4$.O hydrogen bonds are significantly larger than those (87 and 180) for MeO.(CH₂)₃.OH and MeO. $(CH_2)_4$.OH and they indicate stronger hydrogen bonds.

¹⁵ S. A. Barker, E. J. Bourne and D. H. Whiffen, J. Chem. Soc. 905 (1952).

Absorption (3641 cm⁻¹, ε 29) for free hydroxyl in 2-methoxybutane-1,4-diol is stronger than each of the absorptions for bonded hydroxyl groups, which progressively diminish with increasing ring size and may be assigned to the following hydrogen bonds $C_1.OH \rightarrow C_2.O$ (3597 cm⁻¹, $\Delta \nu$ 44, ϵ 21), $C_4.OH \rightarrow C_2.O$ (3556 cm⁻¹, $\Delta \nu$ 85, ϵ 15) and C₁.OH \leftrightarrow C₄.OH (3500 cm⁻¹, $\Delta \nu$ 141, ε 11). The relatively large proportion of free hydroxyl groups is possibly due to the competition of C_1 .OH and C_4 .OH in hydrogen bond formation with C2.O, a factor which could also account for the relatively extensive formation of the $C_1.OH \leftrightarrow C_4.OH$ hydrogen bond.

The above results suggest that, for compounds containing a limited number of hydroxyl groups, the pattern of intramolecular hydrogen bonds may be of value in structural studies. It is also clear, that, for polyhydroxy compounds, a complex pattern of intramolecular hydrogen bonds is likely in which rings of five, six and seven members will be important.



EXPERIMENTAL

Preparation of diols. Ethane-1,2-diol and butane-1,4-diol were obtained by fractional distillation of commercial products.

Commercial propane-1,3-diol contains a significant proportion of periodate-oxidizable impurity.⁵ It was purified by conversion to 2-phenyl-1,3-dioxan, m.p. 47-49° by acid-catalysed reaction with benzaldehyde using the method of Boekelheide et al.¹⁶ The diol was recovered as follows: 2-phenyl-1,3-dioxan (ca. 100 g) was shaken vigorously with 0.5N-hydrochloric acid (ca. 300 ml) for 15 min and the mixture was then stored overnight at room temp. The mixture was neutralized with potassium carbonate, benzaldehyde was removed by distillation and the remaining aqueous solution was continuously extracted with chloroform for 1 day. Concentration of the dried (K₂CO₃) extract and distillation of the residue gave propane-1,3-diol, b.p. $110-112^{\circ}/\sim 12 \text{ mm}, n_D^{18.5} 1.4398$.

Pentane-1,5-diol was obtained as follows. A solution of tetrahydropyran-2-ol⁴⁰ (10 g) and sodium borohydride (1.42 g) in water (ca. 30 ml) was stored at room temp for 2 hr. The solution was then neutralized with acetic acid, basified with potassium carbonate and continuously extracted with ether overnight. The extract was concentrated, dried (Na2SO4) evaporated and the residue distilled to yield pentane-1,5-diol (8.6 g, 86%), b.p. 92-93°/0.2 mm, $n_D^{20.5}$ 1.4512.

Preparation of w-Methoxyalkanols. Pummerer and Schönamsgrubers' method' was used to obtain the following monomethyl ethers from the corresponding diols: 2-methoxyethanol¹⁷ b.p. $122^{\circ}/\sim760$ mm, n_D^{so} 1.4020; 3-methoxypropanol⁷ b.p. 149–150/~760 mm, n_D^{10} 1.4150; 4-methoxybutanol¹⁸ b.p. $71-72^{\circ}/\sim 12 \text{ mm}, n_{\rm D}^{17.5}$ 1.4225; 5-methoxypentanol¹⁸ b.p. 94-96°/~12 mm, $n_{\rm D}^{18}$ 1.4297.

Reaction of butane-1,2,4-triol with benzaldehyde. Redistillation of commercial butane-1,2,4-triol gave a fraction b.p. $131-132^{\circ}/0.15$ mm n_D^{P} 1.4758. The triol consumed 1 mole of periodate under standard conditions.¹⁹ It was homogeneous on paper ionophoresis²⁰ in borate buffer pH 10 ($M_{\rm G}$ 0.22)

M. H. Palomaa and R. Jansson, Ber. Disch. Chem. Ges. 64, 1606 (1931).
 E. L. Jackson, Org. Reactions 2, 361 (1944).

²⁰ A. B. Foster, Chem. & Ind. 1050 (1952); J. Chem. Soc. 982 (1953).

¹⁶ V. Bockelheide, L. Liberman, J. Figueras, C. Krespan, F. C. Pennington and D. S. Tarbell, J. Amer. Chem. Soc. 71, 3303 (1949).

¹⁷ R. C. Tallman, J. Amer. Chem. Soc. 56, 126 (1934).

and in paper chromatography $[R_{p} 0.47 \text{ for the organic phase of a butanol-ethanol-water } (4:1:5) solvent system] and detection with silver nitrate.³¹$

A mixture of benzene (100 ml), butane-1,2,4-triol (6 g), benzaldehyde (6.6 g, 1.1 moles) and conc sulphuric acid (4 drops) was boiled under reflux for 1.5 hr in an apparatus which permitted the collection of water from the azeotrope. The acid was then neutralized with potassium carbonate, the solution was filtered, concentrated and the residue distilled to yield a mixture of O-benzylidene derivatives (5.0 g, 43%) b.p. $125-126^{\circ}/0.2 \text{ mm}$, n_{D}^{34} 1.5338. (Found: C, 68.1; H, 7.2. $C_{11}H_{14}O_3$ requires: C, 68.0; H, 7.3%). Using Jacksons' method¹⁹ the product was found to contain ca. 5% of periodate oxidizable material.

The mixed O-benzylidene derivatives (1.9 g) were dissolved in benzene (50 ml), sodium wire (2 g) was added and the mixture was boiled under reflux for 23 hr. The cooled solution was decanted from excess sodium, methyl iodide (5 g) was added and the solution was boiled under reflux overnight. The cooled solution was filtered, concentrated and the residue distilled to yield mixed methyl ethers (0.9 g, 45%) b.p. $151-153^{\circ}/12 \text{ mm}, n_{\text{B}}^{18}$ 1.5112 (Found: C, 68.95; H, 7.9. C₁₂H₁₀O₃ requires: C, 69.2; H, 7.8%).

A solution of the mixed methyl ethers (0.94 g) in N-sulphuric acid (12 ml) was shaken overnight at room temp. After extraction with light petroleum (b.p. 60–80°) to remove benzaldehyde the acid was neutralized with potassium carbonate and the solution was extracted continuously with chloroform for 24 hr. Concentration of the extract and distillation of the residue gave a mixture (0.24 g) of 4-methoxybutane-1,3-diol and 4-methoxybutane-1,2-diol b.p. 77–80°/0.04 mm, n_D^{30} 1.4496 (Found: C, 50.3; H, 10.2. C₅H₁₃O₅ requires: C, 50.0; H, 10.1%). Oxidation of the mixture using essentially Jackson's procedure¹⁹ indicated the presence of 5–10% of 4-methoxybutane-1,2-diol.

4-Hydroxymethyl-2-phenyl-1,3-dioxan. A solution of the mixed O-benzylidene derivatives of butane-1,2,4-triol (5.6 g) described above, in pyridine (100 ml), was treated with p-phenylazobenzoyl chloride (8 g) at 100° for 3 hr. The p-phenylazobenzoate was isolated as previously described⁹ and recrystallized from benzene to yield 2-phenyl-4-p-phenylazobenzoyloxymethyl-1,3-dioxan (8 g, 71%) m.p. 164-166° (Found: C, 71.4; H, 5.4; N, 7.2. $C_{14}H_{12}N_{10}O_{4}$ requires: C, 71.6; H, 5.5; N, 70%).

A mixture of the *p*-phenylazobenzoate (7.6 g), ethanol (250 ml) and potassium hydroxide (5 g) was boiled under reflux for 10 hr. The cooled solution was filtered, concentrated, then diluted with water and extracted continuously with chloroform for 24 hr. The extract was washed twice with water (50 ml) dried (Na₃SO₄), concentrated and the residue distilled to yield 4-hydroxymethyl-2-phenyl-1,3dioxan (3.1 g) as a pale yellow oil b.p. 146°/0.2 mm, n_D^{26} 1.5356 (Found: C, 68.0; H, 7.5. C₁₁H₁₄O₃ requires: C, 68.0; H, 7.3%).

4-Methoxybutane-1,3-diol. 4-Hydroxymethyl-2-phenyl-1,3-dioxan (2·1 g) was methylated as described below to yield 4-methoxymethyl-2-phenyl-1,3-dioxan (1·3 g, 60%) b.p. 162-164°/12 mm, n_{2}^{n1} 1·5128 (Found: C, 69·05; H, 8·1. C₁₂H₁₆O₃ requires: C, 69·2; H, 7·8%).

The methyl ether (1·1 g) was hydrolysed by the method described above to yield 4-methoxy-butane-1,3-diol (0·33 g, 50%) b.p. 130°/12 mm, n_D^{24*6} 1·4472 (Found: C, 50·1; H, 10·1. C₆H₁₉O₃ requires: C, 50·0; H, 10·1%). Oxidation of the compound using essentially Jackson's method¹⁹ revealed that it contained <2.5% of periodate oxidizable material. The mixed m.p. of the di-*p*-phenylazobenzoate of the product (m.p. 109–111°) with the di-O-*p*-phenylazobenzoate of 4-methoxybutane-1,2-diol (m.p. 113–114°) was 93–100°.

4-Methoxybutane-1,2-diol. Butane-1,2,4-triol (7 g) was added to acetone (50 ml) containing a few drops of conc sulphuric acid and the mixture was boiled under reflux for 24 hr. The solution was neutralized with potassium carbonate, filtered and concentrated. A solution of the residue in chloro-form was washed with aqueous potassium carbonate, dried (Na₂SO₄), concentrated and the residue distilled to yield 4-(2'-hydroxyethyl)-2,2-dimethyl-1,3-dioxolan (5.7 g, 57%) b.p. 100-102°/12 mm, $n_{\rm p}^{30}$ 1.4389 (Found: C, 57.2; H, 9.4. C₇H₁₄O₃ requires: C, 57.5; H, 9.7%).

A <0.005 M solution of the cyclic ketal in CCl₄ showed v_{max} at 3641 (ε 39) and 3566 cm⁻¹ (ε 37) for free and intramolecularly bonded hydroxyl groups.

Sodium wire (2 g) was added to a solution of the dioxolan derivative (5·12 g) in dry benzene (50 ml) and the mixture was boiled under reflux for 24 hr. The cooled solution was decanted from excess sodium, methyl iodide (10 g) was added and the solution boiled under reflux for 24 hr. The cooled and filtered solution was concentrated and the residue distilled to yield 4-(2'-methoxyethyl)-2,2-dimethyl-1,3-dioxolan (2·5 g, 45%) b.p. 175-178°/760 mm, n_D^{16} 1·4220 (Found: C, 60·4; H, 10·2. C₈H₁₆O₃ requires: C, 60·0; H, 10·1%).

³¹ W. E. Trevelyan, D. P. Proctor and J. S. Harrison, Nature, Lond. 166, 444 (1950).

A solution of the above methyl ether (2 g) in N-sulphuric acid (25 ml) was stored at room temp for 24 hr. The acid was neutralized with potassium carbonate and the solution was continuously extracted with chloroform for 24 hr. The dried (Na₂SO₄) extract was concentrated and the residue distilled to yield 4-*methoxybutane*-1,2-*diol* (1.36 g) b.p. 123-124°/12 mm, n_{23}^{28} 1·4460 (Found: C, 50·1; H, 10·1. C₅H₁₂O₃ requires: C, 50·0; H, 10·1%). Oxidation of the compound using essentially Jackson's method¹⁹ gave an uptake of 0·95 mole periodate.

2-Methoxybutane-1,4-diol. Prepared by essentially the method of Brenneisen et al.¹⁰ the compound had b.p. 136–137°/12 mm, n_D^{10} 1·4490 (Found: C, 49·9; H, 10·3. Calc. for C₈H₁₂O₈: C, 50·0; H, 10·1%).

1,4-Dimethoxybutan-2-ol. To a mixture of cis-but-2-ene⁵ (10 g, b.p. 95-97°/0.5 mm, n_D^{17*8} 1.4782) and methyl iodide (200 g), silver oxide (30 g) was added portionwise. The vigorously stirred mixture was boiled under reflux for 1 hr, when more silver oxide (15 g) was added and the boiling continued for 2 hr. The methyl iodide was distilled and the residue was extracted with ether. The extract was washed with water, dried (Na₈SO₄) evaporated and the residue distilled to yield 1,4-dimethoxy-cis-but-2-ene (5.4 g, 41%) b.p. 80-81°/10 cm, n_D^{20} 1.4235. Johnson²⁸ records b.p. 77°/36 mm, n_D^{20} 1.4220 for the compound prepared from 1,4-dibromo-cis-but-2-ene.

A mixture of 1,4-dimethoxy-cis-but-2-ene (5.4 g), perbenzoic acid²³ (7.7 g) and chloroform (157 ml) was stored at room temp for 8 days. The solution was then washed with 10% aqueous potassium carbonate (3 × 10 ml), water, dried (Na₂SO₄) and evaporated. Distillation of the residue gave *erythro*-2,3-epoxy-1,4-dimethoxybutane (3.6 g, 59%), b.p. 72-74°/11 mm, n_{2}^{20} 1.4250 (Found: C, 54.8; H, 9.5. C₆H₁₂O₃ requires: C, 54.5; H, 9.2%). The product slowly consumed periodate (0.04 mole in 24 hr at room temp) as the epoxide ring was slowly cleaved. After treatment with 0.1 N-sulphuric acid at 100° for 3 hr the product consumed 0.99 mole of periodate.

To a stirred suspension of lithium aluminium hydride (5 g) in ether (100 ml) a solution of the foregoing epoxide (2.9 g) in ether (20 ml) was added and the mixture was boiled under reflux for 3 hr. More reductant (1 g) was then added and the boiling continued for 1 hr. Excess hydride was decomposed with ethyl acetate and the alcoholates with water in the usual manner. The solution was filtered, dried (Na₂SO₄), concentrated and the residue distilled to yield 1,4-*dimethoxybutan*-2-ol (1.47 g, 50%), b.p. 80-81°/14 mm, n_D^{20} 1.4255 (Found: C, 54.0; H, 10.3. C₆H₁₄O₃ requires: C, 53.7; H, 10.5%). Treatment of the product with 0.1 N-sulphuric acid at 100° for 3 hr did not yield any periodate oxidizable material.

Preparation of p-phenylazobenzoates. The esters were prepared using the method previously described.⁹ It was essential to pass chloroform solutions of the crude esters through alumina in order to remove contaminating p-phenylazobenzoic acid. The yields and m.p.s. of the esters are recorded in the table.

Infra-red spectra. The spectra in the hydroxyl stretching region were obtained from CCl₄ solutions of the alcohols in 2 or 3 cm layers (fused quartz cells), by means of a Unicam S.P. 100 spectrometer equipped with a grating (3000 lines per in.). Frequencies were checked against water vapour and ammonia bands. The CCl₄ was repeatedly distilled from phosphorus pentoxide before use. The concentration of the alcohols was always <0.005 M in order to eliminate intermolecular hydrogen bonding;³ the extinction coefficients, ε , are maximum values and are equal to $(1/cl) \log_{10} (I_0/l)$ with l in cm and c in moles/l. In certain cases a 0.005 M solution could not be obtained and a saturated solution was used. The concentrations of these solutions were not determined and consequently the extinction coefficients for absorptions of free and bonded hydroxyl groups for these compounds are not absolute values and should not be compared with extinction coefficients obtained for other compounds. For a given compound the extinction coefficients for absorptions of free and bonded hydroxyl groups may be compared.

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²² A. W. Johnson, J. Chem. Soc. 1009 (1946).

²³ G. Braun, Org. Synth. Coll. Vol. I. 431 (1932).