119. *Ribose and its Derivatives. Part VIII.* The Ring Structure* *and Periodate Oxidation of Ribose and Related Polyols.*

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A study has been made of the course of the reaction between the periodate ion and *cis-cis*-1 : 2 : 3-triols in which the hydroxyl residues are attached to a six-membered ring. It is concluded that, at the moment of dissolution in water, ribose exists in the pyranose form. The stereochemical requirements for the reaction, including the effect of conformation, are discussed. A new method is put forward for the assessment of relative stabilities of " chair " conformations of pyranose rings.

ALL natural derivatives of ribose possess the furanose structure. On the other hand, the cyclic form adopted by the free sugar is still in some doubt, since its rapid complex mutarotation probably involves more than one ring form.[1] It has been stated [2] that crystalline D-ribose exists in the pyranose form on the grounds that benzoylation at low
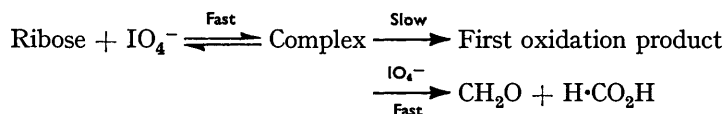
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[1] Phelps, Isbell, and Pigman, *J. Amer. Chem. Soc.*, 1934, **56**, 747.
[2] Ness, Diehl, and Fletcher, *ibid.*, 1954, **76**, 763.

temperature in presence of pyridine yields a 1 : 2 : 3 : 4-tetrabenzoate. Even under these conditions, however, interchange between the various possible structures is likely to be rapid. We have studied the ring structure of ribose by periodate oxidation, which we believe to be, under certain conditions, more rapid than the reactions associated with mutarotation.

It has been shown [3] that a number of reducing sugars are oxidised by sodium meta-periodate in their lactol forms, and 2-O-formylglyceraldehyde has been isolated after periodate oxidation of D-glucose in unbuffered solution.[4] By analogy, it was envisaged that oxidation of ribose might result in initial, rapid consumption of 2 mols. of oxidant if a furanose ring were present, or of 3 mols. if a pyranose ring were concerned. However, in unbuffered solution, 4 mols. of periodate were rapidly consumed, with no discontinuity in the rate of uptake. In presence of phosphate buffer at pH 7·0, determination of periodate by the arsenite method [5] showed the immediate disappearance of approximately 1 mol. of oxidant, with a subsequent slow further uptake. Similar results were obtained on using a phthalate buffer at pH 6·2, the secondary uptake being somewhat faster in this case. It is clear that, in the presence of these buffers, the reaction proceeds by neither of the schemes mentioned above. It may also be concluded that the behaviour is not due to combination of the phosphate and periodate ions.[6] Also, the results cannot be explained by an association of the phosphate ion with ribose, since its specific rotation after mutarotation in phosphate buffer is the same as at equilibrium in aqueous solution. Similar phases in the uptake of periodate were observed between pH 6·2 and 8·0; below pH 6·0 more than 1 mol. of oxidant was rapidly consumed.

In order to determine the nature of the reaction taking place under the conditions described above, crystalline ribose was added to one molar equivalent of sodium meta-periodate in phosphate buffer at pH 7·0, and the resulting solution was chromatographed on paper. A strong spot corresponding to ribose was obtained, and it was estimated by Baar's method [7] that approximately 60% of the original ribose was recovered. To explain this, we suggest that, under the conditions described, ribose and the periodate ion combine in equimolecular proportions to form a complex which can decompose either to give ribose and periodate again, or to give oxidation products and iodate:

$$\text{Ribose} + \text{IO}_4^- \underset{}{\overset{\text{Fast}}{\rightleftharpoons}} \text{Complex} \xrightarrow{\text{Slow}} \text{First oxidation product}$$

$$\xrightarrow[\text{Fast}]{\text{IO}_4^-} \text{CH}_2\text{O} + \text{H·CO}_2\text{H}$$

Under the conditions of the experiment, the position of equilibrium appears to lie far over to the right. In agreement with this, it was found that, with aliquot parts taken early in an experiment, the faint colour of iodine obtained at the end-point of the titration slowly increased in intensity, presumably owing to the liberation of periodate ions by decomposition of the complex. This " drift " in the end-point was not observed with later portions in which much of the complex had decomposed. The reversible nature of the initial reaction was also shown by the fact that if, after treatment of ribose with periodate at pH 7, the solution is acidified and the periodate determined with potassium iodide and sodium thiosulphate, the apparent uptake of periodate is smaller than when the titration is done in alkaline solution. The concentration of the complex at time t is proportional to the difference between the final consumption of periodate and the apparent uptake after time t. A plot of the logarithm of this difference against time indicates that, up to a point at which 75% of the ribose has been oxidised, decomposition of the complex follows a first-order equation, in accordance with the proposed scheme of reactions.

[3] Barker and Smith, *Chem. and Ind.*, 1952, 1035, and references therein.
[4] Schöpf and Wild, *Chem. Ber.*, 1954, **87**, 1571.
[5] Hughes and Nevell, *Trans. Faraday Soc.*, 1948, **44**, 941.
[6] Bell, Palmer, and Johns, *J.*, 1949, 1536.
[7] Baar. *Biochem. J.*, 1954, **58**, 175.

Isolation of the complex proved impossible owing to its progressive decomposition. In order to determine the nature of the complex, the behaviours of other polyols of known structure were studied. Buist and Bunton [8] have shown by kinetic measurements that an intermediate complex is formed at pH 4·5 between periodate and 2-methylbutane-2 : 3-diol but it will appear from the following discussion that the complex now postulated is of a different type.

In Table 3 are given the rates of uptake of periodate by a variety of polyols. In buffered solution, most hexose and pentose sugars were found to consume three or more mols. of oxidant very rapidly. Exceptions are D-ribose, D-lyxose, D-gulose, D-talose, and D-allose (compare, in Table 3, nos. 7, 8, 16, 17, and 18 with nos. 9, 10, 11, 12, 13, 14, and 15). The same distinction exists between *cis-trans-cyclo*hexane-1 : 2 : 3-triol and *cis-cis-cyclo*hexane-1 : 2 : 3-triol (nos. 20 and 21). Most pyranosides behave differently from the parent sugars in exhibiting a slow and steady uptake of periodate. Benzyl and methyl β-D-ribopyranoside are exceptional in that, like the parent sugar, they immediately consume approximately 1 mol. The subsequent uptake is even slower than in the case of the parent sugar. From these results it is seen that the immediate consumption of 1 mol. of periodate followed by a slow further uptake (the rate in this second phase varies from one case to another) is characteristic of compounds possessing a *cis-cis*-1 : 2 : 3-triol system in a six-membered ring, as an obligatory or a potential element of their structure. We attribute this anomalous behaviour to complex formation as described above for ribose and the results are summarised in Table 1 (column *A*). This behaviour is not observed with ribitol, 5-*O*-triphenylmethyl-D-ribose, or 5-*O*-methyl-D-ribose (Table 3, nos. 19, 37, 38), thus excluding acyclic or five-membered ring systems. The rates of uptake of periodate by diols cannot be analysed in the same way, but in no case was any increase in the colour of iodine observed at the end-point of the titration and we do not believe that diols undergo reversible complex formation. Furthermore, *trans-trans-cyclo*hexane-1 : 3 : 5-triol, which forms complexes with the cuprammonium ion,[9] does not interact with the periodate ion under these conditions.

It may be mentioned that Christian, Gogek, and Purves [10] observed that in the periodate oxidation of *cyclo*hexanetriols the rate of uptake of the first mol. of oxidant is very much higher by the totally *cis*-isomer than by the others, but they did not measure the rate of consumption of periodate beyond this point.

The Structure of Ribose.—From the above discussion, formation of the type of complex now described appears to be diagnostic for a *cis-cis*-triol system in a six-membered ring, from which it follows that, at the moment of dissolution, D-ribose exists in the pyranose form. The same may be said of D-lyxose, and, since the requirements for complex formation are fulfilled only in the β-structure, it is concluded that the crystalline sugar is β-D-lyxopyranose. It is interesting that, after mutarotation, D-lyxose gives no evidence of complex formation. In contrast, no distinction can be made between α- and β-D-ribopyranose on the basis of periodate oxidation, because the 1-, 2-, and 3-hydroxyl groups or those at positions 2, 3, and 4 may be involved in complex formation. However, if solutions of ribose are allowed to mutarotate for varying intervals of time, the initial uptake of periodate progressively increases to a new constant value. This is thought to imply that, during the mutarotation, structures other than α- or β-D-ribopyranose are formed. It is calculated that, at equilibrium, approximately 20% of the sugar is in a form which does not form complexes. This is in agreement with Phelps, Isbell, and Pigman's view [1] that the initial reaction during the mutarotation of ribose involves a change in the size of the ring. Cantor and Peniston [11] have deduced from polarographic measurements that, after mutarotation, solutions of ribose contain 8·5—30% of a form

[8] Buist and Bunton, *J.*, 1957, 4580.
[9] Reeves, *J. Amer. Chem. Soc.*, 1949, **71**, 2116.
[10] Christian, Gogek, and Purves, *Canad. J. Chem.*, 1951, **29**, 911.
[11] Cantor and Peniston, *J. Amer. Chem. Soc.*, 1940, **62**, 2113.

TABLE 1.

Compound	A Complex formation with periodate	B Total overlap (Å) (1C–Cl)	C Anhydride (%)	Compound	A Complex formation with periodate	C Total overlap (Å) (1C–Cl)
β-D-Glucose ...		1·82	2	α-D-Gulose		0·33
β-D-Galactose ...		1·70	Small	α-D-Altrose		0·28
β-D-Mannose ...	—	1·65	Small	β-D-Arabinose	—	0·23
β-D-Talose	+	1·53	Small	α-D-Idose *	—	0·16
β-D-Allose	+	1·30	14	α-D-Xylose	—	0·06
β-D-Gulose † ...	+	1·18	43	α-D-Lyxose		−0·23
β-D-Altrose	—	1·13	57	α-D-Ribose		−0·37
β-D-Idose *	—	1·01	75	α-D-Arabinose		−0·54
α-D-Glucose ...	—	0·98		cis-cis-cycloHexane-1 : 2 : 3-		
α-D-Galactose ...	—	0·85		triol	+	0·43
α-D-Mannose ...		0·80		CH₂Ph β-D-ribopyranoside	+	0·40
β-D-Xylose		0·71		Me β-D-ribopyranoside ...	+	0·40
α-D-Talose		0·68		Me β-D-xylopyranoside......	—	0·71
β-D-Lyxose	+	0·54		Me α-D-lyxopyranoside......	—	−0·23
α-D-Allose		0·45		Me α-D-glucopyranoside ...	—	0·98
β-D-Ribose	+	0·40		CH₂Ph β-D-glucopyranoside	—	1·82

Compound	A Complex formation with periodate	Compound	A Complex formation with periodate
Lævoglucosan	—	cis-cycloPentane-1 : 2-diol	—
1 : 6-Anhydro-D-allopyranose...	+	trans-cycloPentane-1 : 2-diol	—
Benzyl β-D-ribofuranoside	—	cis-cycloHexane-1 : 2-diol	—
5-O-Triphenylmethyl-D-ribose	—	trans-cycloHexane-1 : 2-diol	—
5-O-Methyl-D-ribose	—	cis-cis-trans-cycloHexane-1 : 2 : 3-triol	—
Ribitol	—	trans-trans-cycloHexane-1 : 3 : 5-triol	—

* The syrupy anomeric mixture was used.   † The crystalline calcium chloride compound was used.

which is more rapidly reduced than the rest. We cannot conclude from our results anything concerning the nature of the structures produced during the mutarotation of ribose, since neither an acyclic nor a furanose form would be expected to give a stable complex with periodate. We emphasise, however, that since the initial reaction is not an anomerisation, it is not permissible to conclude from the direction of the initial change of rotation that crystalline ribose is β-D-ribopyranose. Only the size of the ring can be regarded as established.

The Nature of the Complex and the Behaviour of Mannose.—It has been suggested [12] that the rate-determining step in the fission of glycols by periodate is the formation of a cyclic diester of periodic acid. On the assumption that the complexes formed between the periodate ion and triols are triesters, it appeared that the size of the periodate ion might be a critical factor in determining the stability of the complex. We therefore investigated the possibility of reaction between triols and the tellurate ion, since this ion approximates closely in size to that of the periodate ion. The possibility also existed of isolating a complex with telluric acid since there would be no tendency toward oxidative decomposition. It was first ascertained that, in the absence of buffer at pH 8, the formation of a complex between a triol and periodate was accompanied by a sharp drop in pH, followed by a slow increase, whereas with those triols which do not form complexes, a slow but small increase in pH is observed. The pH of a solution of telluric acid, previously adjusted to pH 8·0 with sodium hydroxide, fell after the addition of ribose or other compounds which form complexes with periodate, whereas no change in pH was observed with compounds which do not form complexes. This is taken to indicate that the tellurate ion forms complexes analogous to those with the periodate ion. In this case, however, complex formation took place much more slowly and it was not possible to isolate the

[12] Price and Knell, *J. Amer. Chem. Soc.*, 1942, **64**, 552, and references therein.

complex. Further evidence for complex formation with tellurate is that the initial uptake of periodate by *cis-cis-cyclo*hexane-1 : 2 : 3-triol is considerably reduced by prior addition of tellurate. No such effect was obtained in the oxidation of the *cis-cis-trans*-isomer. The analogous behaviour of the two ions of similar size confirmed our view that the formation of complexes with triols depends on specific stereochemical factors and we therefore next considered the conformations of triols which undergo this reaction.

It is reasonable to assume that, in order to form a complex with periodic acid, a cyclic *cis-cis*-1 : 2 : 3-triol adopts the conformation in which two hydroxyl groups occupy axial positions and one an equatorial position. However, this is not the preferred conformation in many cases, and it is concluded that a compound may take up an unfavourable conformation in order to form a complex with periodate. In agreement, it was found that 1 : 6-anhydro-D-allopyranose,[13] in which the conformation with two axial hydroxyl groups is obligatory, behaved exactly as other complex-forming triols. Consequently, the behaviour of mannose needs further consideration.

β-D-Mannose is the only compound we have examined having a potential *cis-cis*-1 : 2 : 3-triol system in a six-membered ring which does not form a complex with periodate. We believe this to be due to the reluctance of the compound to adopt the necessary conformation. Reeves[9] predicted that both conformations will normally be present in this sugar, but we feel that the method of assessing relative stabilities suggested by Reeves is based on an arbitrary allotment of significance to the various factors. We therefore put forward what we believe to be a more accurate method of assessment.

The Stabilities of the Conformations of Pyranose Rings.—Reeves[14] gave strong evidence for excluding all but the two " chair " conformations of pyranose rings and only these two conformations will be considered in this discussion. It is assumed that the degree of distortion in a molecule is determined by the total amount of overlap of non-bonded atoms, overlap between each pair being calculated separately and added together. In considering each pair of atoms, it is assumed that the other atoms in the molecule are not displaced from their normal positions. This assumption, though necessary for calculations, is not strictly justified since overlap between one pair of atoms will result in the readjustment of the positions of all the atoms in the molecule. The following atomic dimensions have been used: C–C bond, 1·54 Å; C–H bond, 1·07 Å; C–O bond, 1·43 Å;[15] van der Waals radius of carbon, 1·60 Å;[16] hydrogen, 1·20 Å (see below); oxygen, 1·40 Å.[15] It has been assumed that all the carbon and oxygen valency angles are 109° 28′. This is the usual value taken for the carbon valency angle in calculations of this kind, although in propane the angle is 111·5°.[17] Similarly, the oxygen valency angle in dimethyl ether is 111°,[18] but an alteration of approximately 2° in the values taken does not affect the conclusions to be drawn later.

On the above basis, we have calculated values for the overlaps of various pairs of atoms in the pyranose forms of sugars (see Table 2). From these values the difference between the total overlaps for the 1C and C1 conformations of each compound concerned have been calculated. Thus in the case of β-D-glucose, the pertinent interactions in the C1 conformation are between $H_{(O-1)}$ and $C_{(5)}$, $C_{(1)}$ and $H_{(O-5)}$, $C_{(6)}$ and $O_{(O-4)}$, $C_{(6)}$ and $H_{(O-4)}$, $H_{(O-5)}$ and $C_{(3)}$, $C_{(5)}$ and $H_{(O-3)}$, $H_{(O-4)}$ and $C_{(2)}$, $C_{(4)}$ and $H_{(O-2)}$, $H_{(O-3)}$ and $C_{(1)}$, $C_{(3)}$ and $H_{(O-1)}$, $H_{(O-1)}$, and $H_{(O-5)}$. In the 1C conformation, interactions to be considered occur between $O_{(O-1)}$ and $C_{(5)}$, $C_{(1)}$ and $C_{(6)}$, $C_{(6)}$ and $C_{(3)}$, $C_{(6)}$ and $H_{(O-4)}$, $C_{(5)}$ and $O_{(O-3)}$, $O_{(O-4)}$ and $C_{(2)}$, $C_{(4)}$ and $O_{(O-2)}$, $O_{(O-3)}$ and $C_{(1)}$, $C_{(3)}$ and $O_{(O-1)}$, $O_{(O-1)}$ and $C_{(6)}$, $C_{(6)}$ and $O_{(O-3)}$, $O_{(O-3)}$ and $O_{(O-1)}$, $O_{(O-2)}$ and $O_{(O-4)}$. Interactions between atoms within the rings are omitted since they are the same in both conformations. The differences in total overlap between the 1C and C1 conformations are listed in Table 1

[13] Pratt and Richtmyer, *J. Amer. Chem. Soc.*, 1955, **77**, 1906.
[14] Reeves, *ibid.*, 1950, **72**, 1499.
[15] Pauling, " The Nature of the Chemical Bond," Cornell Univ. Press, 1948, p. 164.
[16] Dostrovsky, Hughes, and Ingold, *J.*, 1946, 173.
[17] Pauling and Brockway, *J. Amer. Chem. Soc.*, 1937, **59**, 1223.
[18] Klyne in " Progress in Stereochemistry," Butterworths, London, 1954, p. 364.

TABLE 2. *Overlap of pairs of atoms in the chair conformations of the pyranose ring.*

Substituents
(a = axial; e = equatorial)

Interactions between H and H		Overlap (Å)	Interactions between ring atom and subst.		Overlap (Å)
1a	5a	0·19	**O**		
O and O			$C_{(5)}$	1a	0·33
2a	3e	0·04	$C_{(5)}$	3a	0·03
2e	3a	0·04	$C_{(4)}$	2a	0·03
3a	4e	0·04	$C_{(3)}$	1a	0·10
3e	4a	0·04	$C_{(2)}$	4a	0·03
1a	3a	0·19	$C_{(1)}$	3a	0·03
2a	4a	0·11			
H and O			**H**		
1a	5a	0·38	$C_{(1)}$	5a	0·28
5a	1a	0·38	$C_{(3)}$	1a	0·06
C and H			$C_{(3)}$	5a	0·06
5a	1a	0·56			
5a	3a	0·17	**C**		
5a	4a	0·06	$C_{(1)}$	5a	0·47
5e	4a	0·07	$C_{(3)}$	5a	0·25
5e	4e	0·06			
C and O					
5a	1a	0·83			
5a	3a	0·38			
5a	4e	0·11			
5e	4a	0·11			
5e	4e	0·10			

(column *B*). It must be emphasised that these figures are intended only to be used to arrange the compounds in the correct order of stabilities of the two conformations. For those compounds having a high value for the difference, the C1 conformation is preferred; those in the middle range are expected to change readily from one conformation to the other; a negative value for the difference implies that the 1C conformation is the more stable. Predictions on this basis, in many cases, agree with those of Reeves.[19] The chief exceptions are as follows: We consider β-D-altrose, β-D-mannose, and β-D-talose to be appreciably less stable in the 1C conformation. α-D-Lyxose now appears to favour the C1 conformation. We consider α-D-allose, β-D-ribose, and α-D-xylose to favour the 1C rather than the C1 conformation.

It is seen that the new method satisfactorily predicts that, of those sugars having a potential *cis-cis*-1 : 2 : 3-triol system, mannose is the least likely to take up the conformation necessary for complex formation with periodate. Furthermore, each compound which forms a complex can do so without adopting a highly unfavourable conformation. For instance, although in β-D-talose the C1 conformation is preferred this sugar is able to form complexes in both conformations. α-D-Ribose also can do this but β-D-ribose can form a complex only in the 1C conformation. It is impossible to state whether ribose forms its complex in the slightly less favourable conformation of the β-form, or in the more favourable α-form. These alternatives serve to emphasise the point made earlier that it is not satisfactory to regard crystalline ribose necessarily as β-D-ribopyranose. The α-D-ribopyranose structure could equally explain the properties of the natural sugar.

Further justification for the method of analysis, put forward for comparing stabilities of different chair conformations, is provided by the formation of 1 : 6-anhydrohexopyranoses in acid solution. The formation of these anhydrides necessitates the adoption of the 1C conformation by the β-form of the sugar. In Table 1 (column C) are listed the percentages of anhydride in equilibrium with the hexose sugar in acid solution, and it is seen that there is good inverse correlation between these figures and the differences in overlap between the 1C and the C1 form of the β-hexoses. Thus a small amount of

[19] Reeves, *Adv. Carbohydrate Chem.*, 1951, **6**, 107.

TABLE 3. *Uptake of periodate (mol.).*

No.	Compound	Buffer	Uptake at time (min.)											
			1	2·5	5	10	15	20	25	30	40	60	120	240
1	β-D-Ribose	A	2·03	2·55	2·88	3·42	3·70	—	3·94	—	4·05	4·06	—	—
2	β-D-Ribose	D	0·33	0·38	—	—	0·56	—	—	1·06	—	—	2·20	3·99
3	β-D-Ribose	E	0·93	1·42	1·68	2·29	—	3·06	—	3·60	—	4·19	—	—
4	β-D-Ribose	C	1·28	—	—	2·12	2·80	—	—	3·53	2·18	—	4·19	4·20
5	β-D-Ribose	F	1·12	—	1·12	1·38	1·80	1·80	—	—	1·52	2·95	3·74	4·04
6	β-D-Ribose	G	1·09	1·12	1·31	2·06	—	1·38	—	—	1·75	—	2·26	4·04
7	β-D-Ribose	B	1·27	1·53	—	—	—	—	—	—	—	—	—	3·39
8	β-D-Lyxose	B	1·35	3·70	3·8	3·91	—	2·67	—	3·23	—	3·72	4·02	—
9	α-D-Xylose	B	3·20	—	—	—	—	3·94	—	—	—	3·97	4·00	—
10	β-D-Arabinose	B	3·57	3·85	—	4·74	—	3·85	—	—	—	3·94	4·10	—
11	α-D-Glucose	B	3·04	3·86	—	4·11	—	4·88	—	—	—	4·94	—	5·07
12	α-D-Galactose	B	3·77	—	—	—	—	4·35	—	—	—	4·68	4·90	5·07
13	D-Idose	B	5·25	4·91	—	—	5·30	5·15	—	—	—	—	—	—
14	D-Altrose	B	—	4·27	4·99	4·86	—	5·02	—	—	—	5·15	—	—
15	β-D-Mannose	B	3·72	1·30	—	2·01	1·46	2·12	—	—	—	—	5·04	—
16	D-Gulose-calcium chloride	B	—	1·07	1·15	—	—	—	—	—	3·20	—	4·95	—
17	β-D-Talose	B	—	1·39	—	2·03	2·57	—	—	—	1·86	—	2·40	—
18	β-D-Allose	B	—	3·93	3·93	—	3·93	—	—	3·36	—	4·48	5·07	—
19	Ribitol	B	—	2·04	2·07	—	—	—	—	—	—	—	—	—
20	cis-cis-trans-cycloHexane-1:2:3-triol	B	1·92	0·98	—	1·11	1·00	—	—	2·07	—	—	—	—
21	cis-cis-cycloHexane-1:2:3-triol	B	0·97	0·14	—	0·18	1·21	—	—	1·36	—	1·56	—	—
22	cis-cis-cycloHexane-1:2:3-triol	J	0·14	1·36	—	—	0·23	—	—	—	—	—	—	—
23	cis-cis-trans-cycloHexane-1:2:3-triol	J	1·25	—	—	1·63	1·87	—	—	—	—	—	—	—
24	trans-cycloHexane-1:3:5-triol	B	0	—	—	0	0	—	—	—	0	—	—	—
25	CH₂Ph β-D-ribopyranoside	B	—	1·03	1·05	1·02	1·00	—	0·94	1·03	—	—	1·01	1·09
26	Me α-D-lyxopyranoside	B	0·92	0·90	0·89	0·89	1·45	—	—	1·86	—	—	—	1·44
27	Me β-D-lyxopyranoside	B	0·17	0·10	0·99	0·18	0·37	—	—	0·69	—	1·99	2·07	2·07
28	Me β-D-xylopyranoside	B	0·04	0·17	—	0·28	—	—	—	1·04	—	1·00	—	2·01
29	Me α-D-glucopyranoside	B	0·07	0·12	0·10	0·16	0·30	—	—	—	—	—	1·80	2·09
30	CH₂Ph β-D-glucopyranoside	B	0·12	0·09	—	0·13	0·23	—	—	—	—	—	1·43	2·01
31	Laevoglucosan	B	0·09	1·29	—	1·52	1·52	—	1·79	1·87	—	—	1·07	1·58
32	1:6-Anhydro-D-allopyranose	B	1·25	—	—	—	—	0·98	—	—	2·02	0·55	—	—
33	trans-cycloPentane-1:2-diol	B *	0·65	0·79	0·90	—	0·97	—	—	—	—	—	—	1·00
34	cis-cycloPentane-1:2-diol	B *	0·96	0·96	0·97	0·98	1·02	—	—	—	—	—	—	0·99
35	trans-cycloHexane-1:2-diol	B *	0·54	0·75	0·90	1·05	—	—	—	—	—	1·02	—	—
36	cis-cycloHexane-1:2-diol	B *	1·00	—	—	—	—	—	—	—	—	1·10	—	—
37	5-O-Triphenylmethyl-D-ribose	H	2·98	2·95	3·05	2·95	3·10	—	—	3·16	—	3·16	—	—
38	5-O-Methyl-D-ribose	B	—	—	—	2·95	—	—	—	—	—	2·95	—	—
39	CH₂Ph β-D-ribofuranoside	B *	1·03	—	1·01	1·01	—	1·01	—	—	—	1·06	—	—

All measurements of periodate were done by the arsenite method, except as indicated in D.
A, Unbuffered. B, 0·03M-Phosphate buffer, pH 7. C, 0·02M-Phthalate buffer, pH 6·2. D, 0·03M-Phosphate buffer, pH 7; periodate determined by thiosulphate method. E, 0·02M-Acetate buffer, pH 5·9. F, Phosphate buffer, pH 6·6. G, Phosphate buffer, pH 8·0. H, As in B, but in presence of 50% ethanol. J, As in B, but after standing with sodium tellurate.
* In these experiments, no reappearance of the colour of iodine was observed.

anhydride is found when adoption of the 1C conformation would involve a high total overlap (glucose,[20] galactose,[21] mannose,[22] talose,[23] and allose [13]). On the other hand, the anhydride is readily formed in the cases of gulose,[24] altrose,[20] and idose,[20] in which the relative stability of the 1C conformation is higher. According to Reeves's method of prediction, mannose and talose would be expected to yield more anhydride relative to allose and gulose than is found experimentally.

It has been suggested [25] that 0·6 Å should be taken as an interference value for hydrogen instead of the van der Waals radius of 1·2 Å. If this figure is used, all overlaps involving hydrogen atoms in pyranose rings are eliminated. However, it may be shown that on this basis the order of the sugars given in Table 1 is little affected. The only differences arise with the β-pentopyranoses which appear a little higher in the middle range of the list. None of the conclusions reached is affected.

We consider that the agreement between prediction and experiment justifies our method as a semiquantitative approach to the comparison of different conformations in the series of pyranose sugars. It also adds weight to our claim that the behaviour of ribose and related polyols towards periodate is due to the formation of a complex involving three-point attachment of the ion.

EXPERIMENTAL

Periodate Oxidations.—To a weighed quantity of the material under test ($\sim$5 mg.) was added a 0·05N-solution of sodium metaperiodate in water or the appropriate buffer (10 c.c.). All the materials used dissolved immediately and aliquot parts (1 c.c., measured in an " Agla " burette) were added, at intervals, to 0·05N-sodium arsenite containing potassium iodide (2% w/v) and sodium hydrogen carbonate (5% w/v) (1 c.c. measured in an " Agla " burette). The solutions were kept for 15 min., then titrated with 0·1N-iodine (" Agla " burette). Some experiments were also done on ten times this scale with conventional burettes. In both cases, titrations were reproducible within 1%. Owing to the time taken to manipulate burettes, the times of reaction are given to the nearest minute. The results are in Table 3. Results obtained over a protracted experiment with D-ribose are given in Table 4.

TABLE 4. *Rate of consumption of periodate by D-ribose in second phase of the reaction.*

Time (min.)	Periodate consumed (mol.) (a)	log (4·13 − a)	Time (min.)	Periodate consumed (mol.) (a)	log (4·13 − a)	Time (min.)	Periodate consumed (mol.) (a)	log (4·13 − a)
1	1·16	0·47	132	2·81	0·12	300	3·75	−0·42
16	1·45	0·43	170	3·09	0·02	522	4·03	−1·00
36	1·76	0·37	230	3·41	−0·14	630	4·05	−1·09
78	2·29	0·26	275	3·63	−0·30	2050	4·13	—
104	2·57	0·19						

TABLE 5.

Time of muta-rotation (min.)	Initial uptake of periodate (mol.)		Time of muta-rotation (min.)	Initial uptake of periodate (mol.)	Time of muta-rotation (min.)	Initial uptake of periodate (mol.)	
	D-Ribose	D-Lyxose		D-Ribose		D-Ribose	D-Lyxose
0·1	1·04	1·00	2·5	1·48	15	1·59	2·9
0·25	1·15	—	5	1·48	25	1·59	2·9
0·5	1·18	2·2	10	1·63	780	1·58	3·2
1·0	1·30	—					

Mutarotation of Ribose in Phosphate Buffer.—D-Ribose (0·0980 g.) was dissolved in phosphate buffer (pH 7·0) (20 c.c.). $[\alpha]_D^{20}$ was −14·5° (1·5 min.), −15·5° (2 min.), −17·5° (3 min.), −18·5° (5 min.), −18·5° (7 min.), −19·5° (10 min.), −20·0° (100 min.).

[20] Stewart and Richtmyer, *J. Amer. Chem. Soc.*, 1955, **77**, 424.
[21] Turton, Bebbington, Dixon, and Pacsu, *ibid.*, 1955, **77**, 2565.
[22] Pacsu and Mora, *ibid.*, 1950, **72**, 1045.
[23] See p.
[24] Stewart and Richtmyer, *J. Amer. Chem. Soc.*, 1955, **77**, 1021.
[25] Braude and Waight in " Progress in Stereochemistry," Vol. I, Butterworths Scientific Publications, London, 1954, p. 146.

Periodate Oxidation after Mutarotation in Water.—The sugar (0·05 g.) was dissolved in water (10 c.c.) at 20° and, after a given time, the solution was added to a solution of sodium meta-periodate (as above) and aliquot parts (10 c.c.) were titrated with sodium arsenite and iodine as described above. This was repeated for various times of mutarotation. The uptake of periodate in each case was plotted against time and the initial rapid uptake was determined by extrapolation to zero time. The results are given in Table 5.

Recovery of Ribose after Treatment with Sodium Metaperiodate.—D-Ribose (0·0402 g.) was added with shaking to a mixture of 0·268M-sodium metaperiodate (1 c.c.), phosphate buffer (pH 7·0) (5 c.c.), and water (4 c.c.) (solution A). After 1 min. an aliquot part of solution A was heated with a solution containing potassium iodide and sodium hydrogen carbonate. No iodine was liberated, indicating the absence of free periodate. Solution A was kept at room temperature for 24 hr. and then chromatographed on paper with butan-1-ol–pyridine–water (10 : 3 : 3) as solvent. The aniline phthalate spray disclosed a dark spot having the same R_F value as ribose run on the same paper and two faint streaks with high R_F values. Aliquot parts of solution A (0·015, 0·020, 0·025 c.c.) were applied to Whatman No. 1 paper and were chromatographed on the same paper as spots containing 25, 50, 75, and 100 μg. of D-ribose. The air-dried paper was dipped in Baar's reagent,[7] excess of the reagent was removed with a rubber roller, and appropriate areas were cut from the paper and the colours determined as described by Baar.[7] A calibration curve was constructed by using the spots containing known amounts of ribose and it was calculated from the results for the three " unknown " spots that the recovery of ribose from the original solution A (10 c.c.) was 27, 24, and 22 mg. respectively.

Change of pH *of Solutions of Sodium Metaperiodate in Presence of Polyols.*—The pH of 0·0048M-sodium metaperiodate (60 c.c.) at 25° was adjusted to the desired value with 0·01N-sodium hydroxide, the polyol (0·387 g.) was added, and the pH was measured at intervals. The results are shown in Table 6.

TABLE 6. *Changes of* pH *during periodate oxidation of* cis-trans- *and* cis-cis-*cyclo-hexane-1 : 2 : 3-triol at various initial* pH.

	pH at time (min.)							
Compound	0	1	2	5	10	20	40	60
cis-trans-	7·99	8·03	8·24	8·44	8·67	8·94	9·03	9·06
cis-trans-	9·69	9·70	9·84	10·14	10·24	—	10·69	—
cis-cis-	7·26	5·86	5·85	5·90	6·25	6·51	—	—
cis-cis-	8·66	7·80	7·29	7·02	7·22	7·56	8·00	—
cis-cis-	9·09	8·78	8·62	8·41	8·35	8·44	8·58	8·63

Change of pH *of Sodium Tellurate Solutions in Presence of Polyols.*—0·0032M-Telluric acid (25 c.c.) at 25° was adjusted to pH 8·0 with 0·01N-sodium hydroxide. The polyol was added and the pH was measured at intervals. The results are shown in Table 7.

TABLE 7. *Changes of* pH *of solutions of sodium tellurate in presence of various polyols.*

	pH at time (min.)					
Compound added	0	5	20	30	60	120
D-Ribose	8·00	7·75	—	7·28	—	6·46
D-Glucose	7·99	7·86	—	7·80	7·80	7·78
D-Lyxose	7·99	—	7·57	6·88	—	6·41
D-Xylose	8·02	7·82	7·71	7·67	7·65	—
D-Arabinose	7·97	7·80	—	7·58	—	7·35
Me β-D-ribopyranoside	7·98	—	7·41	7·11	—	6·54
Me α-D-glucopyranoside	7·98	7·85	—	7·81	7·81	7·77

Action of Dilute Acid on D-*Talose.*—D-Talose (0·025 g.) was heated at 100° for 5 hr. with N-hydrochloric acid (5 c.c.). Chloride ions were removed with silver carbonate and the solution was concentrated and chromatographed on paper with butan-1-ol–water. The paper was sprayed with ammoniacal silver nitrate and a spot (R_F 0·1) corresponding to talose was observed together with some slow-moving material which probably contained polysaccharide. No

material moving faster than talose, as would be expected if an anhydride were formed, was detected.

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