128. *The Periodate Oxidation of the Inositols.*

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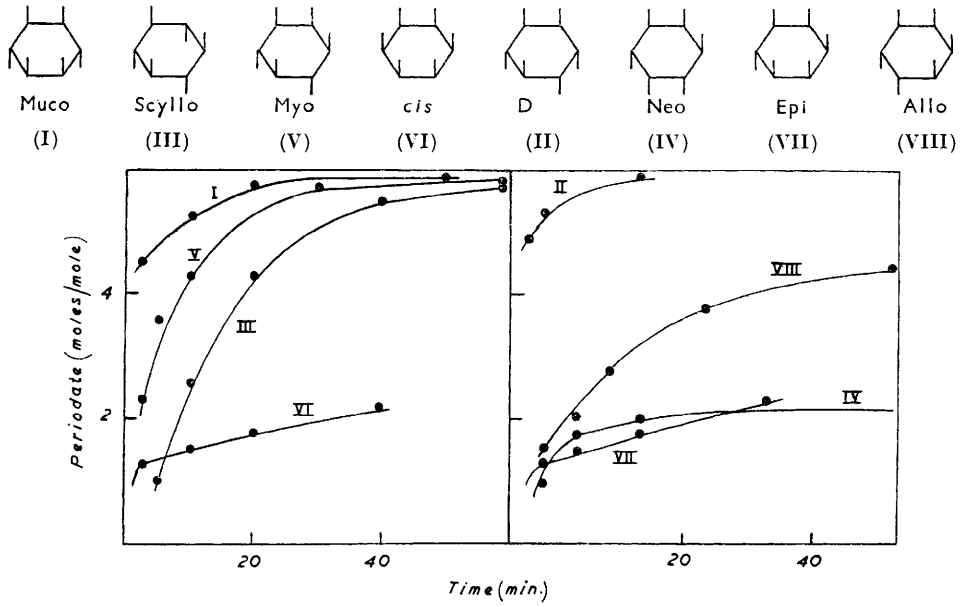
The structures of the isomeric inositols are in line with their behaviour towards periodate when this is interpreted according to Barker and Shaw's views [1] on complex formation.

It has recently been found by Barker and Shaw [1] that, in solutions buffered at pH 7, the periodate ion reacts with certain cyclic *cis-cis*-1,2,3-triols to form complexes which decompose relatively slowly to give the oxidation products. It was assumed that the formation of such complexes requires the adoption of the conformation of the six-membered ring in which two of the participating hydroxyl groups occupy axial positions, and this is in agreement with an explanation of the stability of triesters of periodic acid subsequently put forward by Nevell.[2] Thus the progress of periodate oxidation under these conditions can yield information concerning both configuration and conformation in six-membered cyclic triols. Since the configurations of some of the inositols are based on complex arguments, it was of interest to examine their behaviour towards periodate.

Of the nine isomeric inositols, muco-, D- (and L-) and scyllo-inositol have no *cis-cis*-triol system, and in agreement with this gave no evidence of complex formation (see curves I, II, and III).

In presence of neoinositol, determination of free periodate indicated a rapid consumption of 2 mols. after which reaction was slow (curve IV). This is in agreement with the presence in the molecule of two *cis-cis*-triol systems, both of which can simultaneously take up the required shape for complex formation. Myoinositol possesses a *cis-cis*-triol structure, but was completely oxidised rapidly (curve V) and showed no evidence of complex formation; this is attributed to the fact that formation of a complex would necessitate the adoption of a highly unfavourable conformation in which all but one

hydroxyl group occupy axial positions. Differences between total atomic overlap in the two conformations have been calculated for the inositols as previously carried out for the pyranose sugars [1] and are shown in Table 1. These calculations show that in the case of



Rate of reaction of inositols with periodate at pH 7.

myoinositol, the difference between overlaps is of the same order as for β-mannose which also failed to form a complex.[1] It may also be seen from Table 1 that in the case of neoinositol, which also can form a complex only in the unpreferred conformation, the difference between overlaps is approximately half that for myoinositol. Thus the behaviours of these two inositols are in agreement with their accepted structures.

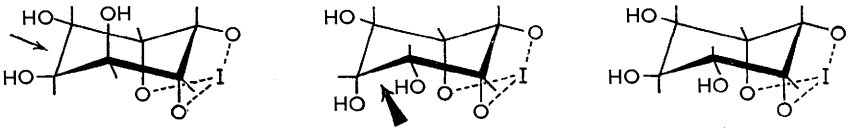
TABLE 1. *Difference between total atomic overlaps for two chair conformations of inositol rings.*

Compound	Difference between overlaps (Å)	Compound	Difference between overlaps (Å)	Compound	Difference between overlaps (Å)
Alloinositol	0	D-Inositol	0·70	Myoinositol	1·48
cis-Inositol	0	Neoinositol	0·74	Scylloinositol	2·22
Mucoinositol	0	Epi-inositol	0·84		

cis-Inositol and epi-inositol behaved very similarly to each other (curves VI and VII). The shape of the curves suggests that complex formation may take place with one mol. of periodate, but the break in the curve is not as marked as with *cis-cis*-cyclohexane-1,2,3-triol.[1] This slightly different behaviour cannot be due to failure to adopt the required conformation, since both forms would be expected to form complexes. (It should be noted that, although *cis*-inositol possesses two *cis-cis*-triol systems, only one set of three hydroxyl groups can take up, at a given time, the positions necessary for complex formation.) The behaviour of these two inositols is tentatively ascribed to the fact that, after a complex has been formed, there remain two 1,2-glycol groups which can be attacked by periodate with fission of carbon–carbon bonds in the usual way. Similar behaviour would be expected with alloinositol for the same reason, since, here also, both conformations would allow of complex formation. It was found, however, that disappearance of free periodate in presence of alloinositol (curve VIII) took place much more rapidly than with *cis*- and

epi-inositol. Reaction of alloinositol with periodate was not as rapid as with, for instance, muco-, and D-inositol and its behaviour is believed to be due to initial complex formation followed by a rapid secondary attack by periodate on the already complexed molecule. Secondary attack on complexes *cis*- and epi-inositol is believed to take place more slowly for reasons outlined below.

First, examination of the complex assumed to be formed initially with alloinositol (A), suggests that secondary attack by periodate will take place readily along the direction shown by the arrow. On the other hand, secondary attack on complexed *cis*-inositol would have to take place from a sterically unfavourable side of the molecule as shown (B). Such a steric effect cannot explain, however, why disappearance of free periodate in presence of epi-inositol takes place more slowly, after the first few minutes, than with alloinositol. It is suggested that this is due to the fact that all free hydroxyl groups in complexed epi-inositol are equatorial (C). It is seen (curve III) that oxidation of scyllo-



inositol takes place more slowly than that of other non-complexing isomers, and it is almost certain (see Table 1) that this inositol carries all its hydroxyl groups in equatorial positions. The slower oxidative fission of a diequatorial diol may possibly be due to the unfavourable positions taken up by the oxygen atoms in such a cyclic triol. If complex formation takes place with three hydroxyl groups as indicated in (A—C), it follows that the pair of oxygen atoms occupying respectively axial and equatorial positions on adjacent carbon atoms are favourably placed for combination with periodate. The distance between these oxygen atoms cannot be calculated but will be different from that between adjacent equatorial oxygen atoms because the ring will be distorted by repulsions between non-bonded atoms, but it would appear likely that the distance between an equatorial and an adjacent axial oxygen atom in the distorted molecule is more favourable for attack by periodate than the distances between adjacent equatorial oxygen atoms either in a distorted molecule or in a relatively undistorted molecule such as in scylloinositol.

It is seen that only in the case of neo-inositol can positive evidence in support of the configuration of the hydroxyl groups be obtained from periodate oxidation. Absence of complex formation is expected with muco-, D- (and L-), scyllo-, and myo-inositol. The behaviours of *cis*-, epi-, and allo-inositol are more complex, but are believed to be in accordance with the accepted structures.

Experimental

Periodate Oxidations.—These were carried out as previously described,[1] except that in the case of neoinositol, which dissolves only slowly, the compound was dissolved in water before addition of oxidant.

Calculation of Atomic Overlaps.—The same values for bond lengths and van der Waals radii of atoms were used as previously.[1] In view of the shorter length of the C–O bond than of the C–C bond, interatomic distances in carbohydrate molecules were calculated by spherical trigonometry, but the greater symmetry of the inositol ring enables a simpler method of calculation to be used. This involves the assumptions, first, that the $C_{(1)}$–$C_{(2)}$ and $C_{(4)}$–$C_{(5)}$ bonds

Table 2. *Overlap of pairs of atoms in the chair conformations of the inositols.*

(*ax* = axial)

Interaction between	Overlap (Å)
$C_{(1)}$ and $H_{(C-3)}$ (*ax*)	0·07
$C_{(1)}$ and $O_{(C-3)}$ (*ax*)	0·11
$O_{(C-1)}$ (a) and $H_{(C-3)}$ (*ax*)	0·06
$O_{(C-1)}$ (a) and $O_{(C-3)}$ (*ax*)	0·29

are parallel and, secondly, that the bonds of adjacent carbon atoms are in the fully staggered position. These assumptions result in only a small difference in total overlap when compared with the figure arrived at by the previous method of calculation. The overlaps of pairs of atoms attached to the ring and of ring atoms and substituents are shown in Table 2.

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