845. *Ionophoresis of Carbohydrates. Part VI.* A Steric Effect in the Reaction of Certain Pyran Derivatives with Borate Ions.*

By A. B. Foster.

The reaction of vicinal *cis*-hydroxyl groups in certain pyran derivatives, with borate ions, is hindered by a methoxyl group in vicinal *cis*-relationship. An explanation of this and related effects is suggested.

Extensive analytical use is now being made, in carbohydrate chemistry, of zone electrophoresis (ionophoresis) in alkaline borate buffers.[1] The value of the technique in providing structural information depends on an understanding of the reactions of borate ions with carbohydrates. Some progress towards this end has been made with derivatives of D-glucose,[2,3] and several applications of the technique in structural determination have been described.[4] The reaction of borate ions with certain pyran derivatives is now reported.

* Part V, *J.*, 1957, 1395.

[1] Part V of this series and references cited therein; see also Foster, *Adv. Carbohydrate Chem.*, 1957, **12**, 81.

[2] Foster, *J.*, 1953, 982.

[3] Foster and Stacey, *J.*, 1955, 1778.

[4] (*a*) Foster and Stacey, *Chem. and Ind.*, 1953, 279; cf. (*b*) Foster, *ibid.*, 1953, 591; Foster, Overend, Vaughan, and Stacey, *J.*, 1953, 3308; Bera, Foster, and Stacey, *J.*, 1955, 3788.

The M_G value [2] has been adopted, in these investigations, as a convenient index of the intensity of reaction of a hydroxy-compound with borate ions and it connotes the mobility of the substance compared with that of D-glucose in ionophoresis on paper under standard conditions (see p. 4218). Small differences (*i.e.*, $<10\%$) in M_G values between compounds of closely related structure are not easy to interpret since the mobility of ions of the type (A) in (1), in ionophoresis, will depend on their mass–charge ratio and on their size, which will be affected to an unknown extent by hydration. There does not appear to be selective adsorption of carbohydrates of low molecular weight on the paper during ionophoresis.[1,5] However, the significant differences in M_G values between isomeric compounds which are considered in this paper are quite large (see Table).

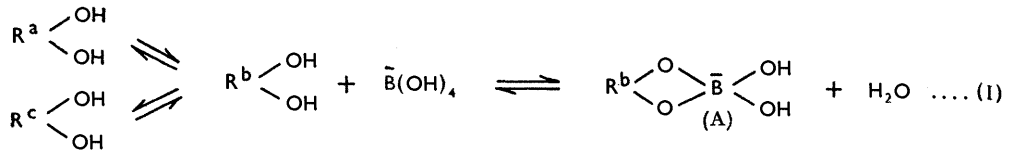
The M_G values of a series of pyran derivatives are recorded in the Table. The zero M_G values of the xylopyranose derivatives (I)—(III) indicate that vicinal *trans*-hydroxyl groups attached to a pyran ring have no affinity for borate ions. It is not possible to study this effect in pyran derivatives which contain more than three hydroxyl groups attached to separate ring carbon atoms since such compounds would be reducing sugars and capable of isomerization in solution.

M_G values of some pyran derivatives.

1 : 5-Anhydroxylitol (I)	0·00	Methyl α-D-mannopyranoside (XII)	0·42
Methyl α-D-xylopyranoside (II)	0·00	Methyl β-D-mannopyranoside (XIII)	0·31
Methyl β-D-xylopyranoside (III)	0·00	1 : 5-Anhydro-D-mannitol (XIV)	0·40
1 : 5-Anhydro-L-arabinitol (IV)	0·39	Methyl α-D-gulopyranoside (XV)	0·59
Methyl α-D-arabinopyranoside (V)	0·38	Methyl β-D-gulopyranoside (XVI)	0·72
Methyl β-D-arabinopyranoside (VI)	0·38	Methyl α-L-rhamnopyranoside (XVII)	0·31
Methyl 2-deoxy-αβ-D-ribopyranoside (VII)	0·34	Methyl β-L-rhamnopyranoside (XVIII)	0·14
Methyl α-D-lyxopyranoside (VIII)	0·45	1 : 5-Anhydro-L-rhamnitol (XIX)	0·31
Methyl β-D-lyxopyranoside (IX)	0·27	Methyl α-D-galactopyranoside (XX)	0·38
1 : 5-Anhydroribitol (X)	0·53	Methyl β-D-galactopyranoside (XXI)	0·38
Methyl β-D-ribopyranoside (XI)	0·53	1 : 5-Anhydro-D-galactitol (XXII)	0·38

The similar M_G values of methyl α- and β-D-arabinopyranoside (V) and (VI), and 1 : 5-anhydro-L-arabinitol (IV) suggest that the reactivity, towards borate ions, of the 3 : 4-hydroxyl groups in these compounds, is independent of the presence or absence of a 1-methoxyl group. Methyl α- and β-D-galactopyranoside and 1 : 5-anhydro-D-galactitol also have similar M_G values. However, in the lyxopyranosides M_G for the α-anomer (VIII) is much higher than for the β-anomer (IX), which suggests that borate ions are sterically hindered in their reaction with the 2 : 3-hydroxyl groups in the latter glycoside. In fact, in all the pyran derivatives so far examined, the presence of a methoxyl group in vicinal *cis*-relationship to vicinal *cis*-hydroxyl groups appears to hinder those hydroxyl groups in their reaction with borate ions. This structural arrangement is present in methyl β-D-lyxopyranoside (IX), methyl β-D-mannopyranoside (XIII), methyl α-D-gulopyranoside (XV), methyl β-L-rhamnopyranoside (XVIII), and (+)-bornesitol [4a] (1-*O*-methyl-*myo*-inositol).

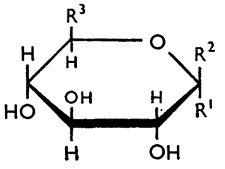
In the pyran derivatives under consideration the probable effective reaction whereby they acquire a negative charge in the presence of borate ions is shown in equation 1



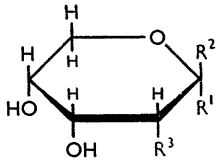
(cf. Isbell *et al.*[6]) where $R^a(OH)_2$, $R^b(OH)_2$, and $R^c(OH)_2$ are different conformations of the same molecule. The formation of " terdentate " complexes, quite different from

[5] Foster, Newton-Hearn, and Stacey, *J.*, 1956, 30.
[6] Isbell, Brewster, Holt, and Frush, *J. Res. Nat. Bur. Stand.*, 1948, **40**, 129.

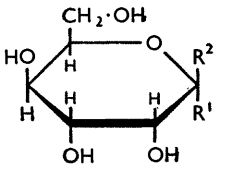
the complex A in (1), has been recognised in the reaction of borate ions with certain cyclitols.[7] The structural features necessary for terdentate complex formation suggests



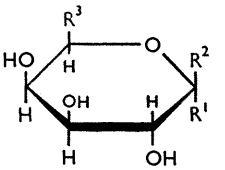
(I): $R^1 = R^2 = R^3 = H$
(II): $R^1 = OMe$, $R^2 = R^3 = H$
(III): $R^1 = R^3 = H$, $R^2 = OMe$



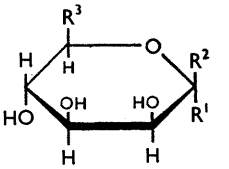
(VII): R^1, $R^2 = H$, OMe, $R^3 = H$
(X): $R^1 = R^2 = H$, $R^3 = OH$
(XI): $R^1 = H$, $R^2 = OMe$, $R^3 = OH$



(XV): $R^1 = OMe$, $R^2 = H$
(XVI): $R^1 = H$, $R^2 = OMe$



(IV): $R^1 = R^2 = R^3 = H$
(V): $R^1 = R^3 = H$, $R^2 = OMe$ (*L*-form)
(VI): $R^2 = R^3 = H$, $R^1 = OMe$ (*L*-form)
(XX): $R^1 = OMe$, $R^2 = H$, $R^3 = CH_2{\cdot}OH$
(XXI): $R^1 = H$, $R^2 = OMe$, $R^3 = CH_2{\cdot}OH$
(XXII): $R^1 = R^2 = H$, $R^3 = CH_2{\cdot}OH$



(VIII): $R^1 = OMe$, $R^2 = R^3 = H$
(IX): $R^1 = R^3 = H$, $R^2 = OMe$
(XII): $R^1 = OMe$, $R^2 = H$, $R^3 = CH_2{\cdot}OH$
(XIII): $R^1 = H$, $R^2 = OMe$, $R^3 = CH_2{\cdot}OH$
(XIV): $R^1 = R^2 = H$, $R^3 = CH_2{\cdot}OH$
(XVII): $R^1 = OMe$, $R^2 = H$, $R^3 = Me$ (*D*-form)
(XVIII): $R^1 = H$, $R^2 = OMe$, $R^3 = Me$ (*D*-form)
(XIX): $R^1 = R^2 = H$, $R^3 = Me$ (*D*-form)

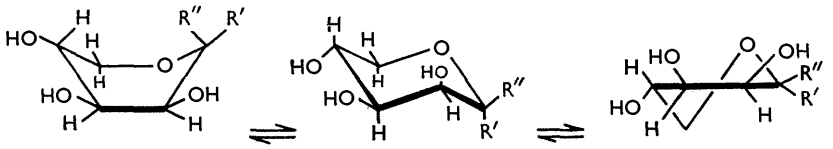
that they are unlikely to be formed in the reaction of the pyran derivatives noted in the Table with borate ions. Clearly, the position of the equilibrium (1) will be governed, *inter alia*, by the stereochemical disposition of the hydroxyl groups in $R^b(OH)_2$ and the stability of the borate complex (A).

Note has been made [8] of the fact that the O–O distance in the preferred chair conformation of both *cyclo*hexane *cis*- and *trans*-1 : 2-diol is identical. The O–O distance in the *cis*-diol is, however, a maximum and the hydroxyl groups will approach more closely during the normal conformational oscillation. It has been suggested [9] that condensation with, for example, acetone, occurs during this process. The O–O distance in the *trans*-diol is a minimum and, as such, is too great to permit condensation with acetone. This argument also applies to the reaction of these diols with borate ions since the *cis*-diol has an M_G value of 0·11 whereas the *trans*-diol does not react with borate ions. It is of interest that Böeseken, in his classical work [10] on the reaction of boric acid with polyhydric alcohols, observed [11] no reaction with *cyclo*hexane-*cis*-1 : 2-diol in boric acid at pH 5. Clearly, and as expected,[12] the polyhydric alcohol–borate ion reaction is much more intense in alkaline media.

[7] Angyal and McHugh, *Chem. and Ind.*, 1956, 1147.
[8] Angyal and Mills, *Rev. Pure Appl. Chem.*, 1952, **2**, 185.
[9] Angyal and MacDonald, *J.*, 1952, 686.
[10] Böeseken, *Adv. Carbohydrate Chem.*, 1949, **4**, 189.
[11] Böeseken and Giffen, *Rec. Trav. chim.*, 1920, **39**, 183.
[12] Consden and Stanier, *Nature*, 1952, **169**, 783.

Since the geometry of the pyran ring is similar to that of the *cyclo*hexane ring,[13] the above considerations may be applied to the reaction, with borate ions, of the appropriate pyran derivatives in the Table. Thus the important point is made that, in the reaction of borate ions with pyran derivatives which contain vicinal *cis*-hydroxyl groups, conformations other than the preferred chair forms may be involved.

The O–O distance of vicinal *cis*-hydroxyl groups in the methyl D-lyxopyranosides (VIII) and (IX) will be a minimum (*i.e.*, they will be in eclipsed positions) in the boat and half-chair forms represented below (the conformation in which the pyran ring is planar is not considered). By analogy with *cyclo*hexene,[14] which can adopt either of two types of conformation structurally related to the boat and half-chair forms (XXIV) and (XXV), the half-chair conformation (XXV) is probably preferred to the boat-form (XXIV). If it is assumed that the half-chair conformation (XXV) is the one involved in complex formation with borate ions during ionophoresis, then a possible explanation may be offered for the steric effects noted above. As the preferred chair conformation (XXIII) is converted into the half-chair form (XXV), the 1-substituent R″ moves towards an eclipsed position with the 2-hydroxyl group. The dihedral angle between 2-OH and 1-R″ decreases from 60° to *ca.* 20° during this process. [The precise value of this angle depends[15] on (*a*) the magnitude, in the half-chair form (XXV), of the angles $C_{(1)}C_{(2)}C_{(3)}$ and $C_{(2)}C_{(3)}C_{(4)}$ and (*b*) the



(XXIV) (XXIII) (XXV)

Chair, boat, and half-chair forms of the methyl D-*lyxopyranosides.* α-*Anomer,* R′ = OMe, R″ = H, β-*anomer,* R′ = H, R″ = OMe. *Only one of each of the two possible boat and half-chair forms which contain eclipsed* 2 : 3-*hydroxyl groups is shown.*

degree of staggering about the ring-oxygen–$C_{(6)}$ bond.] The consequent increase in adverse non-bonded interaction will be proportional to the bulk of R″ which is OMe in methyl β-D-lyxopyranoside and H in the α-anomer; it is the β-anomer which has the low M_G value. Similar interpretations apply to the anomeric methyl D-mannopyranosides, L-rhamnopyranosides, D-gulopyranosides and 1-*O*-methyl*myo*inositol.[4a] A closely analogous conformational argument has been invoked by Lemieux and Brice [16] to relate the configuration of the 3-acetoxy-grouping with the reactivity of the 1-acetoxy-group in a series of 1 : 2-*trans* sugar acetates.

It is also possible that the above steric effect could operate in the ribopyranoside series which contains three vicinal *cis*-hydroxyl groups. Borate-complex formation of each pair of vicinal *cis*-hydroxyl groups would then be hindered by the third hydroxyl group. There is little evidence to support this although the M_G value (0·53) of 1 : 5-anhydroribitol (X) is considerably less than twice that (0·38) of 1 : 5-anhydro-L-arabinitol (IV).

The low M_G value of *cyclo*hexane-1 : 2 : 3-triol [17] and the resistance of *myo*inositol towards the formation of an *iso*propylidene derivative [9] may well be due to the operation of a steric effect similar to that described above.

The appreciably higher M_G value of methyl β-D-lyxopyranoside than of the methyl D-arabinopyranosides may be due in part to the fact that the 2-hydroxyl group, which is

[13] See Maccoll, in Klyne's "Progress in Stereochemistry," Butterworths, London, 1954, Vol. I, p. 361 for details of bond angles, bond lengths, etc.
[14] Barton, Cookson, Klyne, and Shoppee, *Chem. and Ind.*, 1954, 21.
[15] Personal communication from Dr. D. H. Whiffen.
[16] Lemieux and Brice, *Canad. J. Chem.*, 1956, **34**, 1006.
[17] Angyal and McHugh, *J.*, 1957, 1423.

involved in complex formation in the D-lyxopyranoside derivative, is more acidic than the other hydroxyl groups (cf. Wolfrom and El-Taraboulsi [18]).

Experimental

The apparatus and technique employed in ionophoresis have been described previously.[19] Ionophoreses were carried out on Whatman No. 3 paper in sodium borate [5] at pH 10 under potential gradients of 20—40 v/cm. Slight variations in M_G values were encountered in successive runs; factors which influence the M_G value have been noted in Part IV.[20] The M_G values in the Tables are comparative. The non-reducing carbohydrates and the *cyclo*hexane derivatives were detected, after ionophoresis, by means of ammoniacal silver nitrate [21] (10%).

The author acknowledges the interest of Professor M. Stacey, F.R.S., in this work and thanks Dr. D. H. Whiffen for helpful discussion. He thanks also Dr. G. R. Barker (methyl β-D-ribopyranoside), Dr. H. G. Fletcher (methyl L-rhamnopyranosides), Dr. H. S. Isbell (methyl D-lyxopyranosides, methyl D-gulopyranosides), Dr. R. W. Jeanloz (1 : 5-anhydroribitol), and Dr. W. G. Overend (methyl D-arabinopyranosides) for specimens of the derivatives mentioned. The expenses were covered by a grant from Imperial Chemical Industries Limited.

Chemistry Department, The University, Edgbaston,
Birmingham, 15. [*Received, April 1st,* 1957.]

[18] Wolfrom and El-Taraboulsi, *J. Amer. Chem. Soc.*, 1953, **75**, 5350.
[19] Foster, *Chem. and Ind.*, 1952, 1050.
[20] Bourne, Foster, and Grant, *J.*, 1956, 4311.
[21] Hough, *Nature*, 1950, **165**, 400.