Carbohydrate Research, 185 (1989) 39–50
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

BORATE COMPLEXATION WITH PENTITOLS: A STUDY BY ^{11}B-N.M.R. SPECTROSCOPY AND MNDO SEMI-EMPIRICAL LCAO-MO CALCULATIONS

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(Received February 19th, 1988; accepted for publication, July 13th, 1988)

ABSTRACT

The complexation of borate ions and xylitol, ribitol, and arabinitol in aqueous solution at high pH has been studied by ^{11}B-n.m.r. spectroscopy. Stability constants of the various complexes have been calculated by an iterative method and complemented by MNDO calculations.

INTRODUCTION

It has been customary to interpret experimental data on borate/polyol mixtures in aqueous solution by assuming that similar equilibria exist to those known for simple 1,2- or 1,3-diols, namely,

$$B^- + L \overset{K_1}{\rightleftharpoons} BL^- + H_2O \qquad \mathit{1}$$

$$BL^- + L \overset{K_2}{\rightleftharpoons} BL_2^- + H_2O \qquad 2$$

where L is the ligand and B^- represent $B(OH)_4^-$. At pH >12, B^- is the preponderant ion in aqueous solution; at lower pH, it is converted, at least in part, into boric acid, B, and the equilibrium

$$B + OH^- \rightleftharpoons B^-$$

becomes important. Formation of polyborates also becomes important in more concentrated solutions at lower pH.

A study[1], using differential potentiometry, of the chelation of pentitols with boric acid led to values for log K_1K_2 of 6.118 and 6.356, respectively, for ribitol and xylitol, and for log K_1 of 4.507 for D-arabinitol.

Studies of borate complexation with mannitol and glucitol using ^{11}B-n.m.r. spectroscopy[2–4] have shown, as well as the formation of BL^- and BL_2^-, the exis-

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tence of B_2L^{2-} (diborate) and B_3L^{3-} (triborate) at certain low polyol:borate ratios. In each of these four complexes, the ^{11}B resonance occurs at lower field than that of B^-, and in each complex the boron is in a 5-membered ring. In addition, the formation of another 1:1 complex, BL(6), was observed[4], the ^{11}B resonance of which was at higher field than that of B^-.

N.m.r. spectroscopy is ideally suited to the quantitative study of borate/polyol complexation, provided that the spectra can be analysed to give the percentages of each boron species present. A difficulty arises when, as for BL^-, B_2L^{2-}, and B_3L^{3-}, each boron atom has a similar environment and the resonances are almost coincident. We now report on the formation of complexes between B^- and xylitol, D-arabinitol, and ribitol in aqueous solution at pH 12. In such a system, B_3L^- cannot exist, and the composite peak due to BL^- and B_2L^- could be resolved by graphical analysis. Stability constants of the complexes could be calculated using a computer program[5] in which the sum of the squares of the errors between the experimental and calculated values for the percentages of components in a mixture was taken as the parameter to be optimised. The constants found in this way provided the best fit of experimental data, in a least squares' sense, to the proposed reaction scheme.

RESULTS AND DISCUSSION

The ^{11}B-n.m.r. data are typified by those for a 2:1 ribitol/borate mixture at pH 12. Four peaks were observed, namely, for $BL(6)^-$ (δ 1.65, $\nu_{1/2}$ 6.5 Hz), B^- (2.16, 3.3), BL^-, B_2L^{2-} (5.88, 14), and BL_2 (10.04, 30).

The reaction scheme used for the analysis of the data incorporates equilibria *3* and *4*, in addition to *1* and *2*, in which

$$B^- + L \overset{K_3}{\rightleftharpoons} BL(6)^- \tag{3}$$

$$BL^- + B^- \overset{K_4}{\rightleftharpoons} B_2L^{2-}, \tag{4}$$

and B_2L^{2-} is assumed to have two 5-membered rings each containing boron.

If the concentrations of B^- and L, respectively, are designated as x and y, the following equations represent the percentages of boron as

$$\begin{aligned} B^- &= 100/(1 + K_1y + K_1K_2y^2 + K_3y + 2K_1K_4xy) \\ &= 100/D \\ BL^- &= 100K_1y/D \\ BL_2^- &= 100K_1K_2y^2/D \\ BL(6)^- &= 100K_3y/D \\ B_2L^{2-} &= 200K_1K_4xy/D. \end{aligned}$$

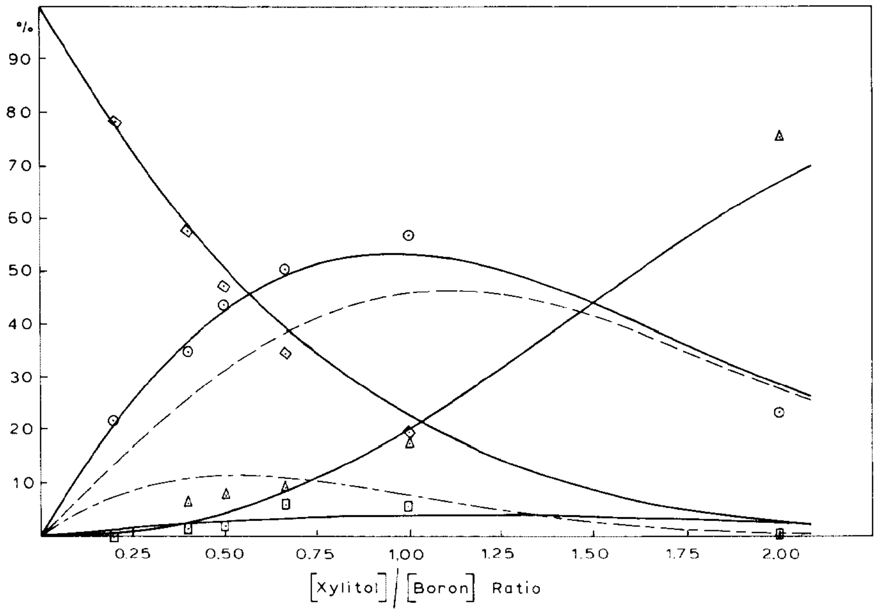


Fig. 1. Comparison of calculated and experimental values of the amounts of different species present in xylitol–borate mixtures as a function of xylitol–borate ratio (B concentration, 0.162M): B^-, ◇; BL_2^-, △; B_2L^{2-} + BL^-, ○; $BL(6)^-$, □; BL^-, ————; B_2L^{2-}, - - - - - -.

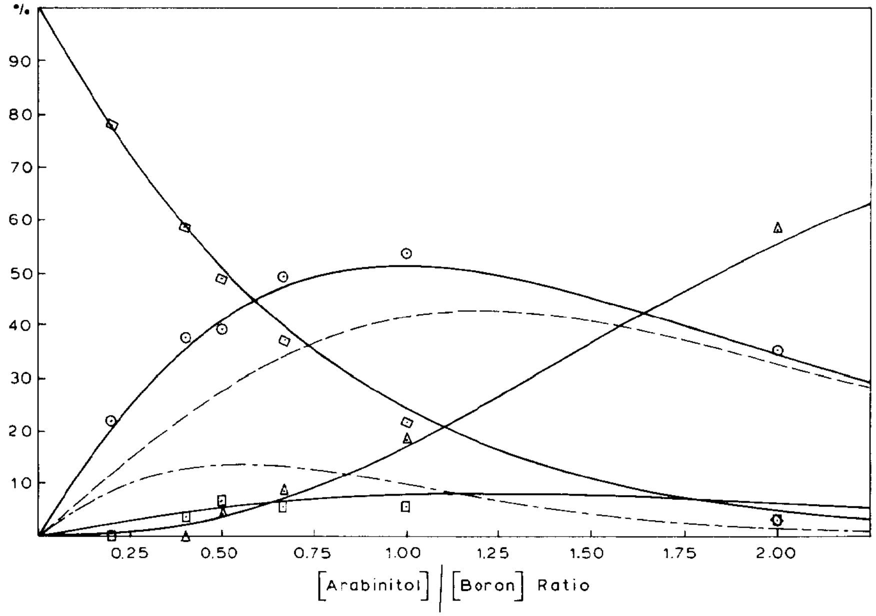


Fig. 2. Comparison of calculated and experimental values of the amounts of different species present in arabinitol–borate mixtures as a function of arabinitol–borate ratio (boron concentration, 0.162M): symbols as in Fig. 1.

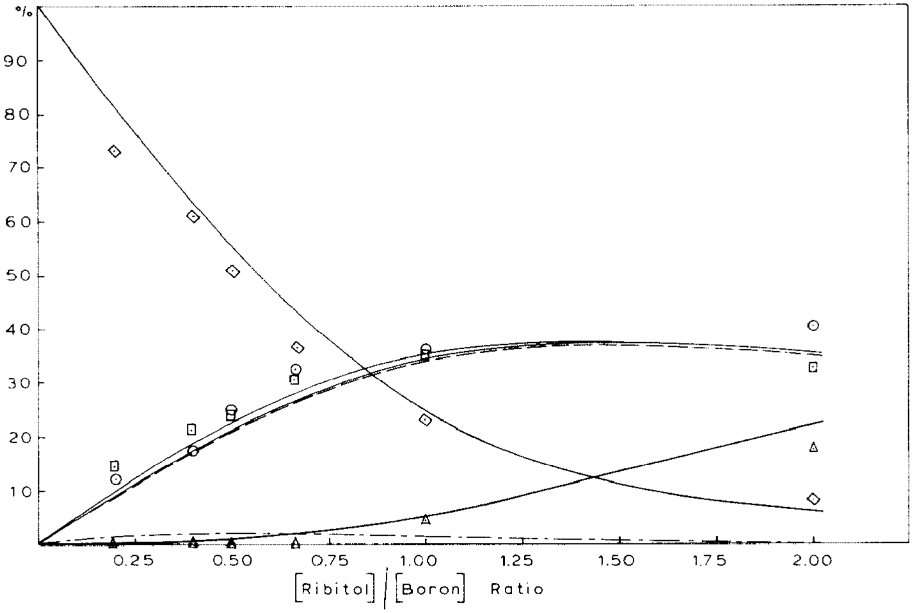


Fig. 3. Comparison of calculated and experimental values of the amounts of different species present in ribitol–borate mixtures as a function of ribitol–borate ratio (B concentration, 0.162M): symbols as in Fig. 1.

TABLE I

STABILITY CONSTANTS FOR BORATE/PENTITOL COMPLEXES

	Ribitol	D-*Arabinitol*	*Xylitol*
K_1	42.3	89.8	192.2
K_3	42.5	17.1	17.1
K_1K_2	194.6	1885.8	7995.5
K_1K_4	25.4	269.4	422.8

Figs. 1–3 show the experimental and calculated values for the various species present in mixtures of borate complexes with ribitol, xylitol, and D-arabinitol. The K values listed in Table I give the best degree of self-consistency such that least-squares errors are minimised.

The stability of BL^- (the mono 5-membered complex) and BL_2^- [the spiro(5,5) complex] increases in the sequence ribitol < D-arabinitol < xylitol. The xylitol diborate is approximately twice as stable as the diborate of arabinitol, both of which appear to be considerably more stable than ribitol diborate. The sequence for BL^- and BL_2^- has been reported[6] and, presumably, reflects increasing ease of complexation, mainly as a consequence of differences in the conformations of each polyol and of the borate/complex in the mixture.

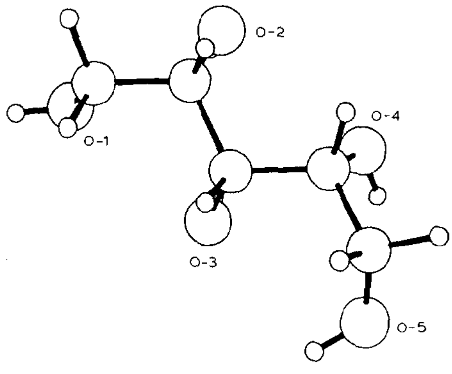
According to Angyal *et al.*[7], the tendency of three vicinal oxygens in an alditol to complex with a metal ion appears to decrease in the following order: t–t (adjacent *threo* pairs), ω–t (a *threo* pair adjacent to a primary OH group), e–t (an *erythro–threo* grouping), ω–e (an *erythro* pair adjacent to a primary OH group), and e–e (an *erythro–erythro* grouping). It is evident that *threo* pairs are energetically more favourable than *erythro* pairs for complex formation. In accordance with this sequence, xylitol [(t–t) + 2(ω–t)] forms stronger complexes with borate than arabinitol [(e–t) + (ω–t) + (ω–e)] which, in turn, complexes more strongly than ribitol [2(ω–e) + (e–e)].

For $BL(6)^-$ (the mono 6-membered complex), the order of stability is ribitol > D-arabinitol = xylitol. It is apparent from molecular models that the formation of a 6-membered 2,4-borate complex involves conformations derived, in each of the three pentitols, from the less stable of the two possible idealised geometries so that analogy with metal complexation breaks down.

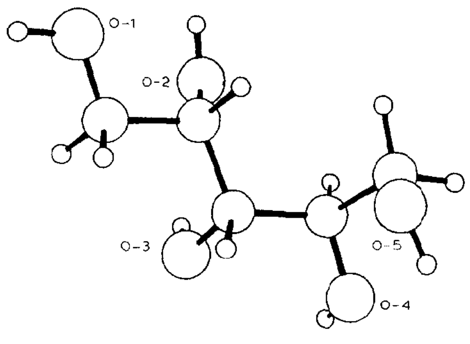
It is not valid to compare the magnitude of the constants reported here with those published[6] because the latter were derived by potentiometry for the pH range 6–8 where B^- is a relatively small proportion of the borate/boric acid equilibrium. Moreover, the results were calculated on the assumption that only the mono(5) and spiro(5,5) species were present, which is not so at pH 12.

Conformations of pentitols and structure of their borate complexes. — MNDO calculations with complete geometry optimisation, performed for several possible conformations of each pentitol and for their mono- and di-borate complexes, provide a guide to the relative thermodynamic stabilities.

The calculated heats of formation of seven conformers of xylitol are given in Table II. The conformation in which there is a planar zigzag C_5 skeleton is unstable[1,8,10] because of the non-bonded interaction of O-2 and O-4 which are in positions equivalent to syn-diaxial. If the planar zigzag is preserved in the calculation, then the results are those for conformer I, which is the least stable. When this constraint is removed, the more stable conformer V (**1**) results in which C-1,2,3,4 are nearly coplanar but the O-2,4 interaction has been reduced by rotation around the C-3–C-4 bond so that C-5 lies well outside the plane of C-1,2,3,4.



1 (Xylitol, relaxed zigzag)



2 (Xylitol, relaxed sickle C-1 240°)

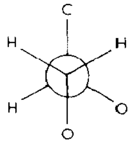
TABLE II

MNDO DATA FOR XYLITOL CONFORMERS AND BORATE COMPLEXES

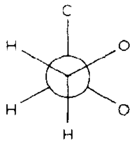
Xylitol	$-\Delta H_f$ *(kJ.mol^{-1})*
I Forced planar zigzag	991.47
II Relaxed sickle C-5 120°	996.90
III Relaxed sickle C-5 240°	999.12
IV Relaxed sickle C-1 120°	1000.21
V Relaxed zigzag (**1**)	1001.25
VI Relaxed sickle	1008.5
VII Relaxed sickle C-1 240° (**2**)	1012.4
Borate complexes	
Sickle 1,3-borate	1839.68
Sickle 4,5-borate	1852.39
Zigzag 2,4-borate (**7**)	1854.98
Sickle 1,2-borate (**6**)	1864.81
Sickle 3,4-borate	1882.43
Sickle 1,2:4,5-diborate	2466.92

When a large rotation about the C-3–C-4 bond takes place, the C_5 skeleton assumes a sickle shape. The other 5 conformers examined are derived from this structure but with various conformations of the terminal CH_2OH groups. Conformer VI represents a relaxed sickle structure. The values of the twist angles C-1–C-2–C-3–C-4 of 167.6° and C-2–C-3–C-4–C-5 of −54.92° indicate that although C-1,2,3,4 are nearly coplanar, C-5 is far removed from this plane. Conformers II and III are derived from VI by rotations of 120° and 240°, respectively, about the C-4–C-5 bond and each is less stable than VI. Conformer IV results from a rotation of 120° about the C-1–C-2 bond only and conformer VII is derived from IV by a further rotation of 120° about the C-1–C-2 bond. Conformer VII (**2**) is the most stable of all those examined.

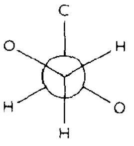
The relationship between conformers IV, VI, and VII is visualised most easily in terms[7] of the idealised geometries of the terminal CH_2OH group O_e, (**3**, oxygen extends the carbon chain), O_g (**4**, O-1,2 are *gauche*), and O_t (**5**, O-1,2 are *trans*). In each, the conformation about C-5 can be regarded as O_g.



3 (O_e)



4 (O_g)



5 (O_t)

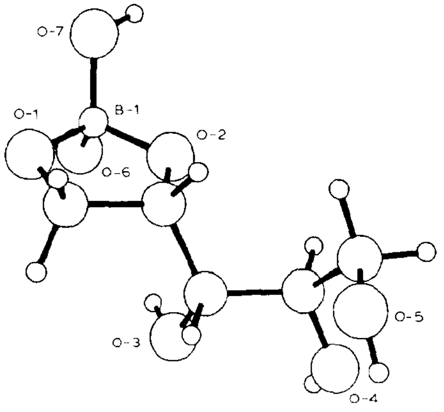
Conformers IV, VI, and VII each possesses a distorted sickle shape. The twist angles C-1–C-2–C-3–C-4 (169.4°) and C-3–C-2–C-1–O-1 (183.2°) indicate that the five atoms involved are almost coplanar (**2**) and are approximately zigzag. The dihedral angle C-2–C-3–C-4–C-5 is −56.04° which is a measure of the distortion in the sickle structure.

Thus, the MNDO data confirm that sickle geometry is more stable than zigzag geometry. The similarity of the ΔH_f values for I–VII (Table II) shows that, for xylitol in solution, there is likely to be a complex mixture of conformers.

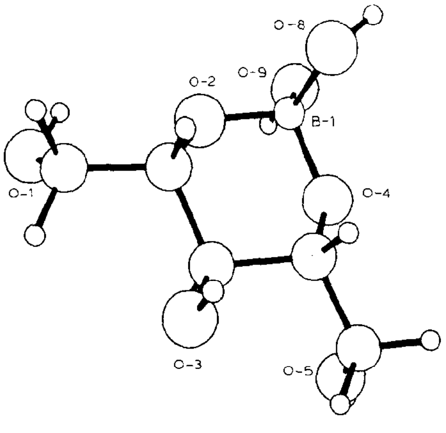
Hawkes and Lewis[8], on the basis of a 400-MHz ^{1}H-n.m.r. study of xylitol in solution in D_2O, concluded that the conformer with a planar zigzag chain constituted only 12% of the molecules in solution and found that the percentages of the three idealised geometries for terminal CH_2OH were O_e 52, O_g 29, and O_t 19. In the solid state[9], the molecule has a sickle conformation with C-1,2,3,4 coplanar to within 0.025 Å, O-1 forms a planar zigzag arrangement with C-1,2,3 and O-3, and each hydroxyl group is involved in two intermolecular hydrogen bonds.

Intermolecular forces in condensed phases will influence the stability of conformers, but MNDO calculations with complete geometry optimisation are still a good guide to the relative stabilities of the various geometries possible for the isolated molecule.

Data for xylitol borates are also given in Table II. The sickle 5-membered 3,4-borate is the most stable of the five examined and may be identified with BL^{-} observed in solution. Xylitol 2,3-borate is enantiomeric with the 3,4-borate so that the heats of formation will be identical. Inner (4,5) complexation rather than "terminal" (1,2) complexation is thermodynamically favoured. BL(6)$^{-}$, probably formed between a zigzag conformer and B^{-}, is more stable by 15.3 kJ.mol^{-1} than the corresponding 6-membered ring complex of a sickle conformer. It is noteworthy that the more stable 6-membered ring complex is derived from the less stable conformers of the parent pentitol. The structures of the 1,2-borate and BL(6)$^{-}$, derived from the MNDO data, are shown in **6** and **7**.

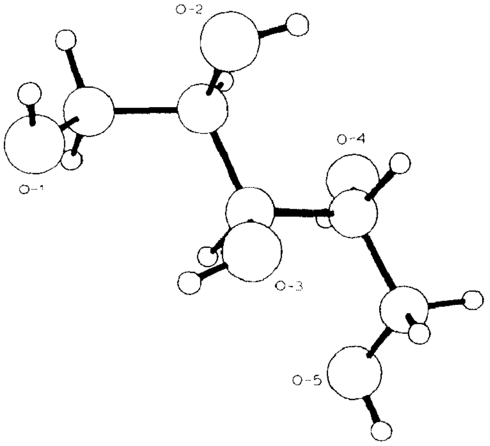


6 (Sickle xylitol 1,2-borate)

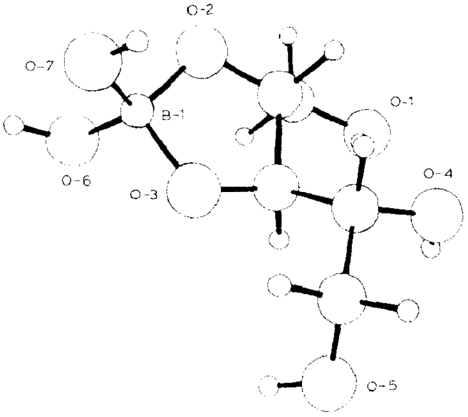


7 (Zigzag xylitol 2,4-borate)

The planar zigzag conformation of arabinitol does not involve the O-2,4 interaction of the other two pentitols and there is little impetus to form a sickle conformation. In accordance with this expectation, a sickle conformation of arabinitol is markedly less stable than any of the conformers (I–V in Table III) derived from the zigzag structure by considering the effect of various orientations of the terminal CH_2OH groups. The conformers listed in Table III are labelled according to rotations imposed about the C-1–C-2 or C-4–C-5 bond. In conformer V, both CH_2OH groups are O_g. The near-planarity of the carbon skeleton is indicated by twist angles of 202.45° for C-1–C-2–C-3–C-4 and 185.1° for C-2–C-3–C-4–C-5, and structure **8** shows that the terminal oxygens lie well outside the plane of the carbon zigzag.



8 (Arabinitol)



9 (Arabinitol 2,3-borate)

TABLE III

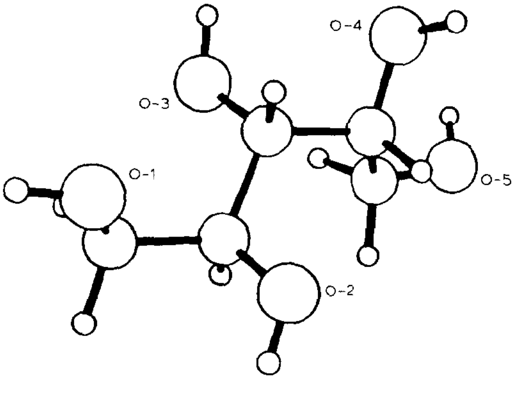
MNDO DATA FOR ARABINITOL CONFORMERS AND BORATE COMPLEXES

Arabinitol	$-\Delta H_f$ *(kJ.mol^{-1})*
Relaxed sickle (**8**)	989.11
I C-1 0°	999.54
II C-1 240° C-5 120°	1000.75
III C-1 240° C-5 240°	1003.01
IV C-1 120°	1003.3
V C-1 240°	1010.11
Borate complexes	
Zigzag (distorted) 2,4-borate	1832.72
Sickle 3,4-borate	1850.51
1,2-Borate	1856.85
4,5-Borate	1860.85
Zigzag 2,3-borate (**9**)	1865.97
1,2:4,5-Diborate	2482.69

In solution in D_2O, arabinitol adopts[7] a mainly planar zigzag conformation for the C_5 skeleton and, with regard to the end CH_2OH group, a preponderance of O_e. The two terminal groups are not equivalent. For C-1, the reported populations are O_e 57, O_g 17, and O_t 26%. Corresponding values for C-5 are 57, 42, and 1%. The crystal structure of DL-arabinitol[10] shows that the molecule adopts an almost planar zigzag conformation of the C_5 skeleton with hydroxyl groups located above and below the plane. The CH_2OH groups have the conformations O_t (C-1) and O_g (C-5). This geometry corresponds with conformer I for arabinitol, the least stable of the five considered according to the MNDO results. The extensive net-work of hydrogen bonds present in the crystal appears to have stabilised a conformation which would be expected to be relatively unstable in the isolated molecule.

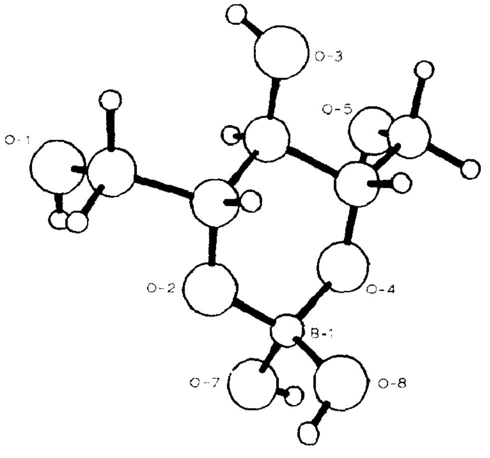
The 2,3-borate derived from the zigzag conformer (**9**) is more stable than either terminal borate or the 3,4-borate derived from the sickle conformer; for a planar zigzag carbon skeleton, O-3 and O-4 are not close enough to chelate boron unless a considerable change in conformation occurs to give a structure closer to that of the unstable sickle skeleton.

The configuration of ribitol is such that, like xylitol, the planar conformation would have lower stability because of the O-2,4 interaction. MNDO calculations (Table IV) have been carried out on five conformers. Of these, V, which has a sickle conformation and O_g at C-1, is the most stable (**10**). A measure of the distortion needed to produce V from III, which has a locked zigzag conformation, is indicated by the twist angles of −176.5° for C-1–C-2–C-3–C-4 and 59.83° in V compared with the fixed value of 180° for each of these angles in III.

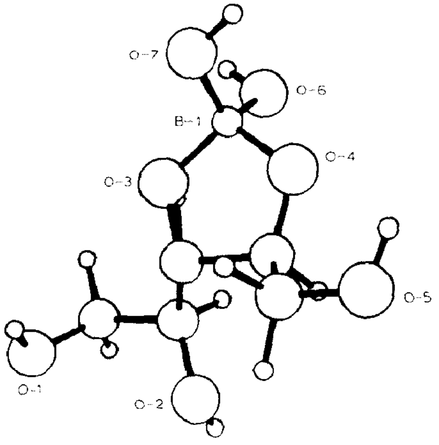


10 (Sickle ribitol)

Conformers I–III differ only in the conformations of the CH_2OH group, the stability sequence being $O_g > O_t > O_e$. In solution in D_2O, only 8% of ribitol appears to be in the planar zigzag form, in equilibrium with 92% of the sickle conformation. For the CH_2OH group, O_e (65%) is favoured over O_g (35%). The



11 (Zigzag ribitol 2,4-borate)



12 (Sickle ribitol 3,4-borate)

ribitol molecule in the crystal is sickle-shaped[11] and, as with the other pentitols, there is extensive hydrogen bonding. Thus, n.m.r. spectroscopy and X-ray crystallography show that ribitol in the solid state has a sickle-shaped molecule and MNDO calculations show this to be true of the isolated molecule.

The reported[8] conformational composition of the three pentitols in solution is based on idealised geometries (O_g, O_t, and O_e; planar zigzag and sickle forms), whereas MNDO calculations always lead to conformations that are less regular. The simple geometries remain useful reference structures.

Of the ribitol–borate structures examined, the sickle 3,4-borate (**12**) is the most stable and, as for xylitol, the 2,3- and 3,4-borates are enantiomeric so that

TABLE IV

MNDO DATA FOR RIBITOL CONFORMERS AND BORATE COMPLEXES

Ribitol	$-\Delta H_f$ *(kJ.mol^{-1})*
I Zigzag (CH_2OH 120°, O_e)	983.06
II Zigzag locked (CH_2OH 240°, O_t)	983.15
III Zigzag locked (O_g)	993.46
IV Zigzag relaxed (O_g)	1000.25
V Sickle (C-1–O_g) (**10**)	1002.05
Borate complexes	
Sickle 1,3-borate	1840.90
Zigzag 2,4-borate (**11**)	1852.35
Sickle 1,2-borate	1857.47
Sickle 4,5-borate	1858.40
Sickle 3,4-borate (**12**)	1871.1
Sickle 1,2:3,4-diborate	2470.44
Sickle 1,2:4,5-diborate	2478.14

their ΔH_f values will be identical. Of the two possible 6-membered ring 1:1 complexes, MNDO calculations favour the 2,4-borate (**11**) formed from the zigzag conformer. Ribitol is similar to xylitol in that the less stable molecular conformer appears to be that which forms the 1:1 6-membered ring complex. This is probably the mono(6) complex detected by ^{11}B-n.m.r. spectroscopy. For the ribitol diborates, the 1,2:4,5 complex is the more stable since steric crowding in the 1,2:3,4 complex probably causes destabilisation.

Typical interatomic parameters calculated by MNDO are illustrated by those for sickle conformers of xylitol and its 3,4-borate. The O-3,4 interatomic distances in these sickle conformers, listed in Table II, are in the range 2.80–2.95 Å. In sickle xylitol 3,4-borate, the O-3,4 distance is 2.34 Å. The difference (0.46–0.61 Å) represents the amount by which O-3 and O-4 have to approach each other before chelation with boron can occur. The theoretical B–O bond-lengths are B–O-3 1.497 and B–O-4 1.483 Å (*cf.* the average B–O length[12] of 1.472 Å in metaboric acid), O–B–O bond angles are within 1° of the tetrahedral value.

Scyllitol diborate is one of the few borates of saturated polyhydroxy organic compounds whose structure has been reported[13]. In this complex, the B–$O_{org.}$ bond-lengths are in the range 1.486–1.503 Å. The interatomic distance of the chelate ring oxygens is 2.55 Å. Structurally, the scyllitol diborate is different from the borate complexes of pentitols because scyllitol is tridentate towards boron.

The spectroscopic study of pentitol/borate mixtures in solution has established that the stabilities of the mono(5) and spiro(5,5) complexes follow the same sequence as for pentitol/metal ion complexes and accord with the sequence expected from the configurations of the polyols. MNDO calculations with complete geometry optimisation yield minimum energy structures in good agreement with known structural data on the three pentitols. Zigzag (for arabinitol) and sickle (for ribitol and xylitol) conformations are the most stable idealised limiting structures, and structures derived therefrom are involved in the formation of 5-membered ring complexes with boron. Nevertheless, considerable distortions from the idealised forms must occur during complexation to reach the optimum boron/oxygen distances. MNDO provides quantitative data on these distortions, and interatomic distances and bond angles are very close to those observed in related compounds containing 4-covalent boron. For the mono(6) complexes, it is noteworthy that the various conformations are more closely related, for each of the pentitols, to the *less* stable idealised geometry. Complexation with borate stabilises this geometry by reducing the C–C and C–O interactions in the conformer which are primarily responsible for its relative instability in the uncomplexed state.

EXPERIMENTAL

D-Arabinitol, ribitol, and xylitol were commercial samples.

^{11}B-N.m.r. spectra (external Et_2OBF_3) were recorded at 28.75 MHz at 30° on a Jeol FX90 QFT spectrometer. Boric acid and the pentitol were dissolved in distilled water, the pH was increased to 12 by the addition of aqueous sodium hydroxide, and the final volume was adjusted to 25 mL.

MNDO calculations were performed at the University of London Computer Centre, using QCPE Program No. 438.

ACKNOWLEDGMENTS

We thank Mr. D. Parkinson (Royal Holloway and Bedford New College) for measurements of the ^{11}B-n.m.r. spectra, and Dr. C. R. Theocharis for his help in the preparation of this paper.

REFERENCES

1 E. Huttunen, *Finn. Chem. Lett.*, (1979) 48–52.
2 M. van Duin, J. A. Peters, A. P. G. Kieboom, and H. van Bekkum, *Tetrahedron*, 41 (1985) 3411–3421.
3 M. Makkee, A. P. G. Kieboom, and H. van Bekkum, *Recl. Trav. Chim. Pays-Bas*, 104 (1985) 230–235.
4 J. G. Dawber and S. I. E. Green, *J. Chem. Soc., Faraday Trans. 1*, 82 (1986) 3407–3413.
5 C. F. Bell, R. D. Beauchamp, and E. L. Short, *Carbohydr. Res.*, 147 (1986) 191–203.
6 W. J. Evans, E. J. McCourtney, and W. B. Carney, *Anal. Biochem.*, 95 (1979) 383–386.
7 S. J. Angyal, D. Greeves, and J. A. Mills, *Aust. J. Chem.*, 27 (1974) 1447–1456.
8 G. E. Hawkes and D. Lewis, *J. Chem. Soc., Perkin Trans. 2*, (1984) 2073–2078.
9 H. S. Kim and G. A. Jeffrey, *Acta Crystallogr., Sect. B*, 25 (1969) 2607–2613.
10 F. D. Hunter and R. D. Rosenstein, *Acta Crystallogr., Sect. B*, 24 (1968) 1652–1660.
11 H. S. Kim, G. A. Jeffrey, and R. D. Rosenstein, *Acta Crystallogr., Sect. B*, 25 (1969) 2223–2230.
12 W. H. Zachariasen, *Acta Crystallogr., Sect. B*, 16 (1963) 380–384.
13 C. T. Grainger, *Acta Crystallogr., Sect. B*, 37 (1981) 563–568.