Carbohydrate Research, 253 (1994) 1–12
Elsevier Science B.V., Amsterdam

The structure and (local) stability constants of borate esters of mono- and di-saccharides as studied by ^{11}B and ^{13}C NMR spectroscopy

Ron van den Berg, Joop A. Peters and Herman van Bekkum

Laboratory of Organic Chemistry and Catalysis, Delft University of Technology, Julianalaan 136, 2628 BL Delft (Netherlands)

(Received February 24th, 1993; accepted June 29th, 1993)

ABSTRACT

The formation of borate esters of various mono- and di-saccharides in aqueous solution was studied by ^{11}B and ^{13}C NMR spectroscopy. Association constants $K(B^-L)$ at a carbohydrate–borate molar ratio of 1:1, pH 7, and 25°C were determined and compared with literature values obtained from potentiometry. The association constants $K(B^-L)$ were converted into local association constants $K_{loc}(B^-L)$ by using the distribution of the various anomeric forms in D_2O. In this way, values of $K_{loc}(B^-L)$ were obtained, which appear to be characteristic of the configuration concerned. They explain the favourable effect of borate in the alkaline isomerisation of lactose into lactulose. At a low molar ratio (1:3) of carbohydrate–borate, predominantly diborate esters $(B^-)_2L$ were formed.

INTRODUCTION

Boric acid and borate are known to form esters with hydroxy compounds in aqueous solution. These esters have been studied for more than a century and they have found widespread use in various fields of science and technology[1–14]. The ability of hydroxy compounds to form borate esters has been utilised in organic synthesis to protect diol functions, to increase reaction selectivities via chelation control, or to shift equilibria. An example of the latter in the carbohydrate field is the isomerisation of aldoses to ketoses in alkaline media, which is catalysed by borate[15,16]. An important industrial application is possible in the base-catalysed isomerisation of lactose into lactulose[17,18], which is a regulating medicine in the human intestine. Here, borate can shift the equilibrium towards lactulose and protect the sugars against alkaline degradation.

Much research has been done on borate esters of sugars and sugar derivatives. Verchere et al.[9–11] investigated B^-L_2 esters of mono- and di-saccharides by the use of potentiometry, and various of these esters were characterised by ^{11}B and ^{13}C NMR spectroscopy. However, many questions still remain, particularly with regard to the role of borate in the isomerisation of aldoses to ketoses. In order to get more insight into the structures and the stabilities of borate esters involved in the

SSDI 0008-6215(93)E0271-2

processes mentioned above, we undertook a systematic study of borate esters of mono- and di-saccharides by means of ^{11}B and ^{13}C NMR spectroscopy, the results of which are presented in this paper.

EXPERIMENTAL

^{11}B NMR and ^{13}C NMR spectra were recorded at 25°C with a Nicolet NT-200 WB spectrometer at 64.19 MHz with 0.1 M boric acid as the external reference and at 50.31 MHz with *tert*-butyl alcohol as the internal reference, respectively. All spectra were first recorded at a total boron concentration $c_B = 0.1$ M and a total sugar concentration $c_L = 0.1$ M. Other concentrations were also used, varying from 0.1 to 0.3 M.

The samples were prepared by dissolution of the appropriate amounts of boric acid and sugar in D_2O. The pH was adjusted with 2 M NaOH in H_2O and the total volume of each sample was 5 mL. It took some time before the pH was stable, varying from seconds to 2 h, depending on the sugar used.

All sugars used were D isomers, with the exception of sorbose.

RESULTS AND DISCUSSION

General.—A series of 17 mono- and di-saccharides was investigated (see Scheme 1. The possible equilibria between boric acid (B^0), borate (B^-), and the borate esters of carbohydrates [B^-L, B^-L_2, and $(B^-)_2L$] are exemplified in Fig. 1. Borate esters can be formed both at vicinal 1,2-diol functions and at 1,3-diol functions. At 25°C, the exchange between boric acid and borate was fast on the ^{11}B NMR time-scale, but that between borate and the borate esters was slow for the mono-

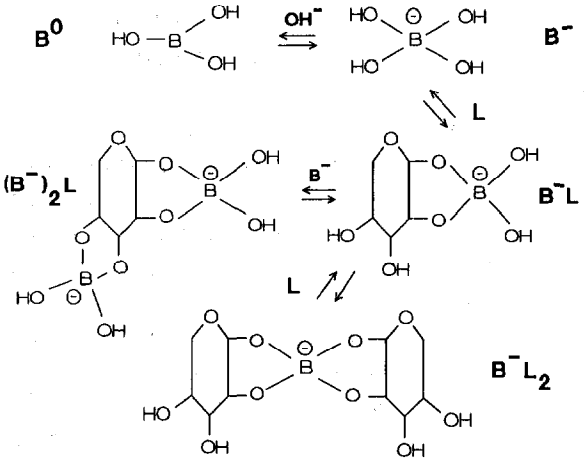


Fig. 1. Equilibria between boric acid, borate, and a sugar compound in aqueous medium. The indices "−" do not stand for the actual charge of the esters, but denote the charge of the BO_4 moieties.

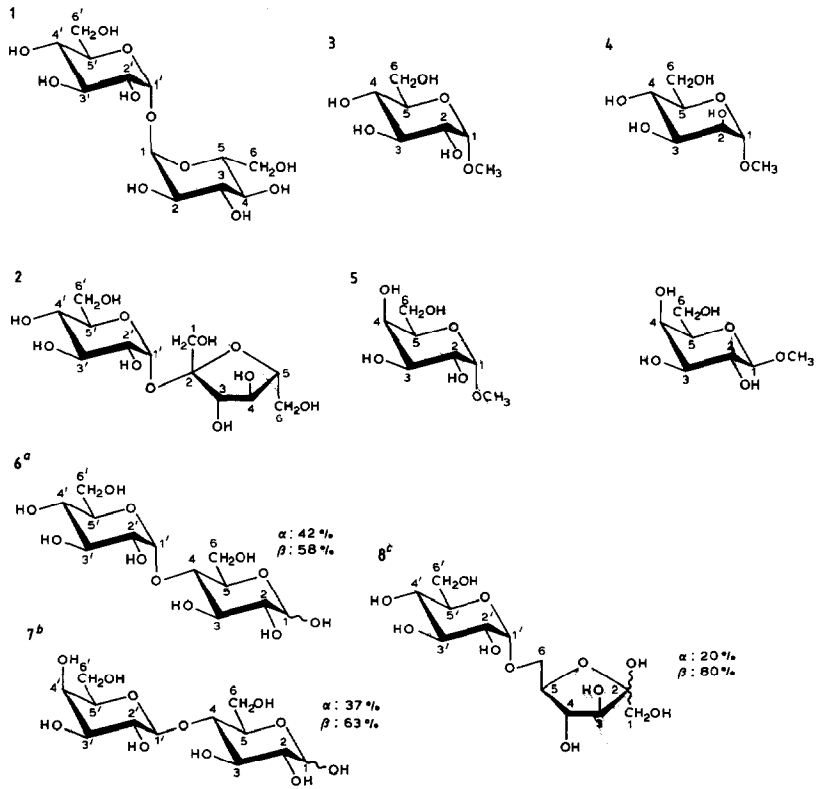
TABLE I

Characteristic values of ^{11}B chemical shifts of borate esters[19–20]

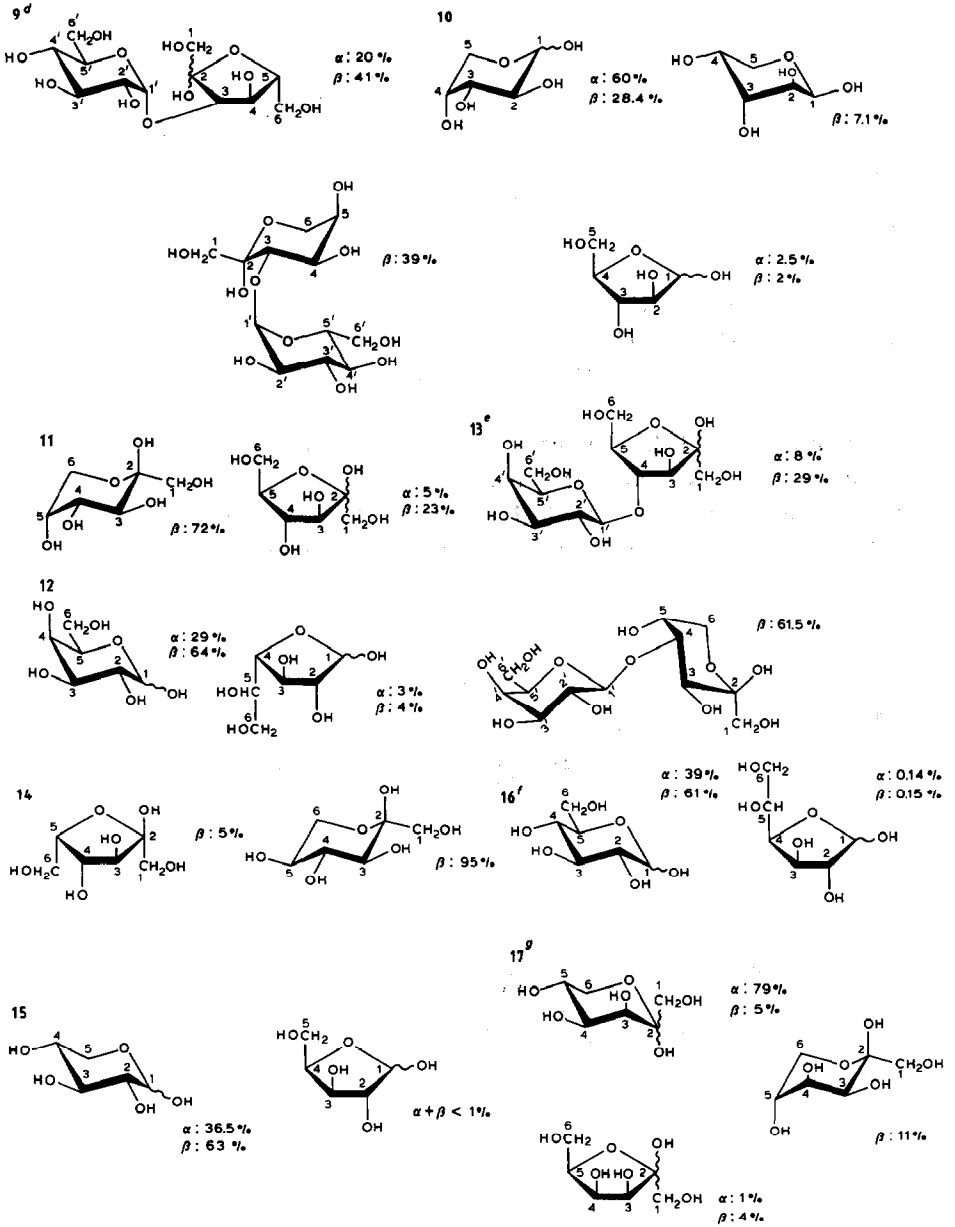
Ester type	^{11}B Chemical shift range (ppm)	
	B^-L	B^-L_2
1,2-Bidentate	−12.6 to −14.9	−7.7 to −11.9
1,3-Bidentate	−17.9 to −18.5	−18.4 to −19.0
1,3,5-Tridentate	−18.1 to −19.4	

and di-saccharides investigated. Thus, separate signals were observed for free and complexed boron species. The borate mono- and di-esters of 1,2- and 1,3-diols have characteristic values[12], which allows a distinction between these types (Table I).

For determination of the binding sites for borate in the saccharides, ^{13}C NMR was often applied. The exchange between the free sugar ligand and the borate esters was always slow on the ^{13}C NMR time-scale. Upon borate ester formation, a substituent effect of 3–10 ppm to higher frequency was usually observed for the



Scheme 1. Anomeric equilibria of the carbohydrates studied in D_2O at pH 7 and 31°C[4]. [a] $T = 34°C$[31]; [b] $T = 20°C$[32]; [c] $T = 20°C$[30]; [d] $T = 36°C$[27]; [e] $T = 25°C$[27]; [f] $T = 27°C$, pH 4.8[29]; [g] $T = 27°C$[27].



Scheme 1 (continued).

^{13}C nuclei in the borate ester ring. The various anomers of the sugars could be identified by their characteristic chemical shift ranges, which persisted upon borate ester formation. The ^{13}C chemical shift difference between corresponding $B^{-}L$ and $B^{-}L_2$ esters was always small for these compounds, which suggests that steric interactions between the two organic ligands in the $B^{-}L_2$ esters are rather small.

TABLE II

^{11}B Chemical shifts of $(B^-)_2L$, B^-L, and B^-L_2 in D_2O and association constants of B^-L borate esters of mono- and di-saccharides at 25°C and pH 7

	Donor sites (borate ester)	Chemical shift (ppm)			Association constant (K_{loc})
		$(B^-)_2L$	B^-L	B^-L_2	B^-L
1. Trehalose	4/6+4′/6′		−18.0		3
2. Sucrose	4′/6′		−18.0		3
3. Methyl α-D-glucopyranoside	4/6		−18.0		3
4. Methyl α-D-mannopyranoside	2/3		−13.9	−10.3	15
	4/6		−18.0		3
5. Methyl α- and β-D-galactopyranoside	3/4		−13.6	−9.7	10
	4/6		−18.2		3
6. α-Maltose	1/2		−13.7	−9.5	20
Maltose	4′/6′		−18.0		3
7. α-Lactose	1/2		−14.0	−10.0	15
Lactose	3′/4′		−13.6		15
	4′/6′		−18.2		6
8. β-Isomaltulose	2/3		−13.1	−8.7	2500
Isomaltulose	4′/6′		−18.0		[a]
9. β-Turanopyranose	1/2		−13.0	−8.7	250
	1/2+4/5	−13.6			[a]
β-Turanofuranose	1/2		−13.0	−8.7	50
α-Turanofuranose	1/2		−13.0	−8.7	100
Turanose	4′/6′		−18.0		[a]
10. β-Arabinofuranose	1/2		−13.7	−9.2	6000
	1/2/5		−13.0		[a]
β-Arabinopyranose	1/2+3/4	−13.6			[a]
11. β-Fructofuranose	2/3		−13.7	−8.8	6000
	2/3/6		−13.0		[a]
β-Fructopyranose	1/2		−13.0	−8.8	500
	1/2/3+4/5	−13.6			[a]
12. α-Galactofuranose	1/2		−14.0	−9.0	3500
	1/2/5(6?)		−13.0		[a]
α-Galactopyranose	1/2+3/4	−13.6			[a]
Galactopyranose	4/6		−18.2		[a]
13. β-Lactulofuranose	2/3		−13.7	−8.7	4500
	2/3/6		−13.0		[a]
β-Lactulopyranose	1/2		−13.0	−8.7	250
Lactulose	3′/4′		−13.6		[a]
	4′/6′		−18.2		[a]
14. β-Sorbofuranose	2/3		−13.1	−8.7	40000
	2/3+*4/6*	−18.7			[a]
15. α-Xylofuranose	1/2		−13.0	−8.5	>16000
	1/2+*3/5*	−18.7			[a]
16. α-Glucofuranose	1/2		−13.0	−8.5	45000
	1/2+*5/6*	−15.1			[a]
	1/2+*3/5*	−17.5			[a]
	1/2+*3/5/6*	−15.8			[a]
Glucopyranose	4/6		−18.0		[a]
17. α-Tagatopyranose	1/2		−13.0	−8.5	1500
β-Tagatofuranose	3/4		−13.4		10000
	3/4+1/2	−13.0			[a]

[a] The association constants $K_{loc}(B^-L)$ of these esters could not be determined because of the low amount of free carbohydrate (L) present under the conditions in which these esters occurred.

The ^{13}C chemical shifts of the B^-L_2 esters of the monosaccharides were in good agreement with those reported by Verchere et al.[11].

The relative amounts of boric acid/borate and borate esters could be determined by integration of the various ^{11}B signals. Then by using mass balances *1* and *2* and the equilibrium constant for the system boric acid/borate (*3*), the various stability constants of the borate esters (*4–6*) were calculated:

$$c_B = [B^0] + [B^-] + [B^-L] + [B^-L_2] + 2[(B^-)_2L] \quad (1)$$

$$c_L = [L] + [B^-L] + 2[B^-L_2] + [(B^-)_2L] \quad (2)$$

$$K(B^-) = [B^-][H^+]/[B^0] = 4.0 \times 10 \exp(-10) \quad (3)$$

$$K(B^-L) = [B^-L]/[B^-][L] \quad (4)$$

$$K(B^-L_2) = [B^-L_2]/[B^-L][L] \quad (5)$$

$$K(B_2^-L) = [(B^-)_2L]/[B^-L][B^-] \quad (6)$$

The organic ligand L usually consists of a mixture of anomers. In order to get an impression of the affinity for borate of the various types of diol functions in each saccharide anomer, the effects of the anomeric equilibria were eliminated by taking as [L] in eqs. *4* and *5* the concentration of the anomer involved in the formation of the borate ester under study. Literature values[4,27–32] for the anomeric compositions in D_2O of the mono- and di-saccharides were used and these are included in Scheme 1. In this way, overall association constants $K(B^-L)$ were converted into local association constants $K_{loc}(B^-L)$. The anomeric compositions are dependent on temperature[27–30,33] and, because they have not always been reported for room temperature, small deviations may occur when $K(B^-L)$ is converted into $K_{loc}(B^-L)$.

The ^{11}B and ^{13}C chemical shifts of the various species and the stability constants obtained are compiled in Tables II and III.

Systems with pyranose rings.—No 1,2-diol borate esters were observed in systems with pyranoses having exclusively equatorial hydroxyl groups, such as trehalose (**1**), sucrose (**2**), and methyl α-D-glucopyranoside (**3**). In these cases, the ^{11}B spectrum showed a single borate ester peak at δ −18 ppm, which is characteristic of a 1,3-diol borate ester (B^-L) (see Table I). The only sterically possible binding sites for such an ester are C-4 and C-6 (C-4′ and C-6′). The association constant $K(B^-L)$ of this exocyclic *trans*-C-4/C-6 ester is 3. Apparently, *eq,eq* 1,2-diol sequences of pyranose systems are not involved in borate ester formation, which can be ascribed to the large steric strain that would be present in the corresponding borate ester.

However, in pyranose systems with an *eq,ax* 1,2-diol sequence, borate ester formation occurred. Methyl α-D-mannopyranoside (**4**) and methyl α,β-D-galactopyranoside (**5**) showed B^-L and very weak B^-L_2 esters of this kind. The association constants $K(B^-L)$ are 15 and 10, respectively. In addition, an exocyclic *cis*-1,3-diol borate ester at C-4 and C-6 of **5** was detected with a stability that is the

TABLE III

^{13}C Chemical shifts (ppm) of mono- and di-saccharides and of their B^-L, B^-L_2, and $(B^-)_2L$ borate esters at pH 7 and 25°C [a]

		C-1	C-2	C-3	C-4	C-5	C-6
5. Methyl α-D-galactopyranoside	L	101.0	71.0	69.8	70.8	72.3	62.8
3/4	B^-L	101.0	[69.7–74.7] [b]				63.5
Methyl β-D-galactopyranoside	L	105.4	72.3	74.4	70.3	76.7	62.6
3/4	B^-L	104.7	[71.3–78.2] [b]				63.3
8. β-Isomaltulose	L	64.2	103.3	76.8	76.1	80.5	69.4
2/3	$B^-L+B^-L_2$	65.8	112.2	85.2	79.2	84.3	69.1
10. β-Arabinopyranose	L	94.1	70.1	70.1	70.1	64.0	
1/2+3/4	$(B^-)_2L$	96.0	[69.5/71.5/73.2]			64.3	
β-Arabinofuranose	L	96.7	77.8	75.8	82.9	62.7	
1/2	$B^-L+B^-L_2$	105.0	84.5	78.3	87.0	63.6	
1/2/5	B^-L	101.8	81.2	80.0	86.4	65.2	
11. β-Fructopyranose	L	65.4	99.6	69.1	71.2	70.8	64.9
1/2	$B^-L+B^-L_2$	[c]	104.8	[70.2/71.0/72.3]			64.9
1/2/3+4/5	$(B^-)_2L$	68.1	101.9	[69.6/71.3/74.1]			65.3
β-Fructofuranose	L	64.2	103.0	76.9	76.0	82.2	64.0
2/3	$B^-L+B^-L_2$	65.7	112.0	85.0	78.7	86.9	63.7
2/3/6	B^-L	65.7	110.1	82.2	80.5	87.0	65.9
12. α-Galactopyranose	L	93.9	70.9	69.9	70.7	72.0	62.8
1/2+3/4	$(B^-)_2L$	96.1	[70.9/71.3/71.5/72.6]				63.7
α-Galactofuranose	L	96.5	77.8	75.8	82.3	73.4	64.0
1/2	$B^-L+B^-L_2$	104.5	84.6	78.3	85.5	72.8	64.5
1/2/5(6?)	B^-L	102.0	[80.4/80.8]		85.5	72.8	64.9
14. β-Sorbofuranose	L	64.7	103.0	77.4	76.6	79.0	62.0
2/3	$B^-L+B^-L_2$	65.4	111.9	84.9	77.5	81.7	61.3
2/3+4/6	$(B^-)_2L$	65.8	111.9	85.1	78.4	81.7	62.1
15. α-Xylofuranose [d]	L	96.0	77.8	76.2	79.3	61.6	
1/2	$B^-L+B^-L_2$	103.8	84.1	77.3	80.8	61.3	
1/2+3/5	$(B^-)_2L$	104.0	84.0	77.5	80.8	61.4	
16. α-Glucofuranose [d]	L	97.0	77.7	76.6	78.8	70.7	64.2
1/2	$B^-L+B^-L_2$	104.2	83.6	77.3	79.5	70.3	65.2
1/2+3/5/6	$(B^-)_2L$	104.9	83.9	[79.1/79.2]		73.1	65.3
17. α-Tagatopyranose	L	65.5	99.8	71.4	72.5	67.9	63.8
1/2	$B^-L+B^-L_2$	68.3	104.4	75.1	73.1	71.3	63.8
β-Tagatofuranose	L	64.2	104.0	72.4	72.5	81.6	62.6
3/4	B^-L	65.1	106.6	81.0	78.3	82.3	61.7
3/4+1/2	$(B^-)_2L$	68.1	111.6	81.1	78.3	83.7	62.8

[a] Assignments of the free carbohydrates (L) according to refs. 21–26. [b] The signals of C-2 to C-5 were broad and overlapping, and could not be assigned. [c] Not resolved. [d] The shifts of α-xylofuranose and α-glucofuranose were assigned by comparison with the corresponding methyl furanosides[23].

same as those of **1**, **2**, and **3** [$K(B^-L) = 3$]. Another type of *cis*-1,2-diol borate ester was observed at C-1 and C-2 of α-maltose (**6**). The association constant $K_{loc}(B^-L)$ of this ester is 20, assuming that the amount of α-maltose in solution was 42% (Table I). Lactose (**7**) gave a mixture of all types of borate esters described above, with association constants of about the same magnitudes.

Much stronger borate ester formation (B^-L_2 and B^-L) was observed with β-turanopyranose (**9**), β-fructopyranose (**11**), β-lactulopyranose (**13**), and α-

tagatopyranose (**17**). These carbohydrates have in common that they have a CH_2OH group at the anomeric centre, and form a relatively stable borate ester at C-1 and C-2, resulting in an exocyclic compound. Determination of the association constants $K_{loc}(B^-L)$ of these esters was hampered by the presence of borate esters at the furanose ring, which had about the same chemical shift in the ^{11}B spectrum. However, the anomeric carbon atoms of the various borate esters had well-separated peaks in the ^{13}C spectrum which allowed estimation of the distribution of the various esters. The association constants $K(B^-L)$ of these exocyclic borate esters (250 to 1500) are comparable with those of borate esters of acyclic polyhydroxy compounds such as D-mannonate[13]. The small differences in stability between the various esters of this type can be ascribed to steric effects.

Systems with furanose rings.—No 1,2-diol borate esters were observed in systems with furanoses having exclusively *trans* hydroxy groups, such as **2**. Isomaltulose (**8**), however, showed very strong borate ester formation. Both B^-L_2 and B^-L esters were observed (^{11}B: δ −8.7 and −13.1 ppm), while a ^{13}C NMR spectrum showed only 6 single signals and 6 signals with threefold splitting. The latter signals could be assigned to the carbon atoms of the fructofuranose ring on the basis of their relatively high chemical shifts. It is well known that pyranose rings have lower chemical shifts for the carbon atoms than furanose rings[21–26]. The chemical shifts indicated that only the C-2/C-3 borate ester of β-isomaltulose was formed, which is in agreement with the literature[11]. The threefold splitting of the ^{13}C signals for the fructose ring can then be explained by the presence of one B^-L and two diastereomeric B^-L_2 esters. Remarkably, the ^{13}C chemical shift increment for borate ester formation is much larger on the furanose ring than on the pyranose ring (9 compared to < 5 ppm). The association constant $K_{loc}(B^-L)$ of the C-2/C-3 ester is ca. 2500, which shows that systems with a *cis*-1,2-diol configuration on the furanose ring produce very stable borate esters. The reason for this is the favourable distance between the two preorganised hydroxyl groups, which results in borate esters with a low ring strain and in a small decrease of entropy of the ligand.

Similar borate esters were formed from β-arabinofuranose (**10**), β-fructofuranose (**11**), α-galactofuranose (**12**), β-lactulofuranose (**13**), β-sorbofuranose (**14**), α-xylofuranose (**15**), and α-glucofuranose (**16**). Once again, it can be seen that the stability constants $K_{loc}(B^-L)$ of these borate esters depend strongly on steric effects. In the compounds β-isomaltulose (**8**), β-arabinofuranose (**10**), β-fructofuranose (**11**), α-galactofuranose (**12**), and β-lactulofuranose (**13**), the borate group is sterically hindered by a group which is on the same side of the ring. The larger the group the smaller the association constant. However, β-sorbofuranose (**14**), α-xylofuranose (**15**), and α-glucofuranose (**16**) have the borate group and the other groups on opposite sides of the ring. Consequently, the association constants $K_{loc}(B^-L)$ of β-sorbofuranose (**14**) and α-glucofuranose (**16**) are relatively high (40000 and 45000, respectively). It was not possible to determine $K_{loc}(B^-L)$ of α-xylofuranose (**15**) because the anomeric equilibrium of xylose is not exactly

known. When it is assumed that the association constant of this ester is the same as that of β-sorbofuranose (**14**), the amount of α-xylofuranose in solution can be calculated to be ca. 0.4%.

Another *cis*-1,2-diol borate ester on a furanose ring was observed with β-tagatofuranose (**17**). In this case, the borate ester was at C-3 and C-4, as was shown by the ^{13}C chemical shift increments upon borate ester formation. A borate ester at C-2 and C-3 could not detected in contrast to conclusions mentioned in ref 11.

No *cis*-1,2-diol borate esters are possible for α- and β-turanofuranose (**9**). In this case, an exocyclic borate ester was formed at C-1/C-2. The stability of this ester is much lower than that of the furanose borate esters mentioned above (50–100).

With β-arabinofuranose (**10**), β-fructofuranose (**11**), α-galactofuranose (**12**), and β-lactulofuranose (**13**), a tridentate borate ester was observed at high pH (> 9). Sharp, single ^{13}C signals were observed for this ester, in contrast to the bidentate esters which showed broad peaks with splittings. The ^{13}C chemical shifts demonstrate that the borate ester is on the furanose ring. Donor sites for borate are the *cis*-1,2-diol and the CH_2OH group, which are on the same side of the ring. At pH 10, the amount of this tridentate ester was comparable with the amount of the *cis*-1,2-diol bidentate ester (B^-L). Inspection of molecular models shows that a large steric strain may explain the relatively low stability of the tridentate ester.

Diborate esters $(B^-)_2L$.—$(B^-)_2L$ esters were observed in the presence of an excess of borate. At a sugar–borate molar ratio of 1:3, **10**, **11**, and **12** showed only 5 or 6 peaks in a ^{13}C NMR spectrum at high pH (> 9). The chemical shifts indicated a pyranose structure. Arabinose (**10**) can only form a $(B^-)_2L$ ester with borate groups at C-1/C-2 and C-3/C-4 of the pyranose form. The ^{11}B spectrum of **12** showed only a signal at δ −13.6 ppm, which indicates that a $(B^-)_2L$ ester was present with borate groups at C-1/C-2 and C-3/C-4 and that no C-4/C-6 ester had been formed. As seen before, β-fructopyranose (**11**) could form a stable borate ester at C-1 and C-2, so a $(B^-)_2L$ ester with borate groups at C-1/C-2 and C-4/C-5 of β-fructopyranose would be expected. However, the relatively small borate-induced ^{13}C chemical shift of the anomeric C-2 atom ($\Delta\delta$ 2.3 ppm) seems to refer to a C-2/C-3 and C-4/C-5 ester, because, in the case of a C-1/C-2 borate ester, a larger increment of the anomeric C-2 atom ($\Delta\delta$ 4.8 ppm) would be expected. On the other hand, the relatively large chemical shift change of the C-1 atom ($\Delta\delta$ 2.7 ppm) seemed to refer to the expected $(B^-)_2L$ ester again. Probably the $(B^-)_2L$ pyranose ester with borate groups at C-1/C-2/C-3 and C-4/C-5 was present. It must be emphasised that the $(B^-)_2L$ pyranose ester was only dominating at high pH. Fructose, for example, gave, at a sugar–borate ratio of 1:3, predominantly the C-2/C-3-β-furanose borate ester at pH 7.5.

For turanose (**9**) at a sugar–borate ratio of 1:3 and pH 10.5, the $(B^-)_2L$ ester with borate groups at C-1/C-2 and C-4/C-5 of β-turanopyranose was dominating. The intensity ratio between the $(B^-)_2L$ and B^-L ester of β-turanopyranose, as obtained by integration of the anomeric peaks in a ^{13}C spectrum, was ca. 5:1.

Furanose esters were not detectable in this case. With **14**, **15**, **16**, and **17**, exclusively the $(B^-)_2L$ ester of the furanose form was obtained at a carbohydrate–borate ratio of 1:3.

β-Sorbofuranose (**14**) and α-xylofuranose (**15**) formed a $(B^-)_2L$ ester which consisted of the stable *cis*-1,2-diol ester and a 1,3-diol ester at C-4/C-6 and C-3/C-5, respectively. The ^{11}B chemical shift of the 1,3-diol ester was −18.7 ppm, with which it distinguished itself from all other B^-L bidentate borate esters (Table I).

A sample with a glucose–borate ratio of 1:3 at pH 9.6 gave a ^{13}C NMR spectrum with only 6 sharp peaks. The chemical shifts did not allow an unambigious determination of the donor sites for borate in the $(B^-)_2L$ ester. Obviously, one of the borate esters is at C-1/C-2, but the other could be at C-5/C-6, C-3/C-5, or C-3/C-5/C-6. The ^{11}B spectrum displayed peaks at δ −13.0 and −15.8 ppm. At a glucose–borate ratio of 1:1 and pH < 9, peaks at δ −8.5 and −13.0 ppm were observed, but when the pH was raised (> 9) two additional peaks developed at δ −15.1 and −17.5 ppm. With 6-deoxyglucose, under analogous conditions, only a ^{11}B signal at δ −17.6 was observed, which can be assigned to the C-3/C-5 borate ester of 6-deoxy-α-glucofuranose. In this case, no signal was observed at −15.1 ppm. Therefore, it is concluded that, in the case of **16** at a glucose–borate ratio of 1:1 and pH > 9, two $(B^-)_2L$ esters were present, namely C-1/C-2–C-3/C-5 (δ −17.5) and C-1/C-2–C-5/C-6 (δ −15.1) of α-glucofuranose. However, at a glucose–borate ratio of 1:3 and pH 9.6, only one $(B^-)_2L$ ester was present, namely C-1/C-2–C-3/C-5/C-6 (δ −15.8). This observation resembles the behaviour of fructose, which also formed a tridentate ester at a sugar–borate ratio of 1:3 and at high pH.

Tagatose (**17**) is an interesting sugar because in principle it has good donor sites for borate at both its pyranose and its furanose ring. However, at a sugar–borate ratio of 1:3 and pH 9.5, mainly a $(B^-)_2L$ ester of β-tagatofuranose with borate groups at C-1/C-2 and C-3/C-4 was formed, according to ^{11}B and ^{13}C NMR data. Apparently the $(B^-)_2L$ ester of the pyranose form is sterically less favourable.

CONCLUSIONS

In Table IV, the association constants $K(B^-L)$ of sugar compounds are compared with data from the literature, which were determined with potentiometry.

When the association constants $K(B^-L)$ are converted into local association constants $K_{loc}(B^-L)$, by using percentages of the various anomeric forms in solution (D_2O), characteristic values are obtained. The sequence of the stability $[K_{loc}(B^-L)]$ of these B^-L esters of carbohydrates is: *cis*-1,2-diol furanose (2500–45000) ≫ exocyclic-1,2-diol pyranose (250–1500) > exocyclic-1,2-diol furanose (50–100) > *cis*-1,2-diol pyranose (10–20) > exocyclic *cis*/*trans*-4,6-diol pyranose (3-6) ≫ *trans*-1,2-diol pyranose/furanose (0).

TABLE IV

Association constants $K(B^-L)$ of sugar–borate esters found in the literature and in this work

	log $K(B^-L)$	
	This work [a]	Literature[9–11]
2 Sucrose	0.60	0.86/0.75
6 Maltose	1.04	1.41/1.36
7 Lactose	1.41	1.43/1.51
8 Isomaltulose	3.30	
9 Turanose	2.18	1.91
10 Arabinose	2.10	2.14
11 Fructose	3.23	2.82
12 Galactose	2.10	1.99/1.97
13 Lactulose	3.18	2.91
14 Sorbose	3.30	< 3.5
15 Xylose	2.20	1.95
16 Glucose	1.81	1.80/2.07
17 Tagatose	3.30	

[a] Carbohydrate–borate ratio = 1:1, pH = 7, and T = 25°C.

Steric factors play an important role in the stability of borate esters of the same group. For example, β-sorbofuranose (**14**), α-xylofuranose (**15**), and α-glucofuranose (**16**) have very large association constants $K_{loc}(B^-L)$, because all other substituents in the ring are in *trans* position with respect to the borate group.

The large affinity of borate for *cis*-1,2-diol furanoses explains the favourable effect that borate has, for example, in the alkaline isomerisation of lactose into lactulose.

An important factor for the formation of sugar/borate esters is the molar ratio of sugar–borate. When an excess of borate is used, a $(B^-)_2L$ ester, if possible, will be preferred.

ACKNOWLEDGMENTS

This investigation was carried out with the support of the Dutch National Innovation Oriented Program Carbohydrates (IOP-k), Solvay Duphar B.V., and DMV International. We thank H. Pluim, M.C. Heslinga, and R. de Boer for helpful discussions.

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