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# COMPLEXES OF BORATE IONS WITH GUAR D-GALACTO-D-MANNAN POLYMER AND RELATED MODEL COMPOUNDS

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## ABSTRACT

The prevailing borate mono- and di-complexes of a series of glycosides, particularly those representing model compounds (methyl β-D-mannopyranoside and methyl α-D-galactopyranoside) of guar D-galacto-D-mannan in aqueous alkaline solution, have been identified by $^{11}$B-n.m.r. spectroscopy, and the associated formation constants determined. These data provide some new insights into the rheological properties displayed by the polymer in alkaline medium (gelation and hydration-delay phenomenon).

## INTRODUCTION

The legume-seed D-galacto-D-mannan from guar is a polysaccharide consisting of linear chains of (1→4)-linked β-D-mannopyranosyl residues, to which are attached (1→6)-linked α-D-galactopyranosyl groups (as single-unit side chains) at O-6 of some D-mannopyranosyl units. Because of its viscosity properties, guar is extensively exploited by various industries[1]. Upon addition of borax at alkaline pH, gels are formed from guar or guar derivatives and, more generally, from a number of polysaccharides containing hydroxyl groups in a favorable position to react with the borate ion (the hydroxyl groups should be adjacent and in *cis* position). This is the case for the OH-2 and OH-3 of the D-mannose units, as well as the OH-3 and OH-4 of the D-galactose units. Gelation is supposed to take place by cross-linking of different polymer chains or, sometimes, parts of the same chain with borax, in such a way that a three-dimensional network of connected chains is formed. When the concentration of cross-linked chains is high enough, a semi-rigid gel results. However, although there have been many speculations regarding these peculiarities, the molecular basis has never been firmly established.

The formation of complexes between borate and hydroxy compounds has been recognized for a long time. It has been utilized as a tool to assign carbohydrate configuration[2], as well as in a variety of separation and chromatography

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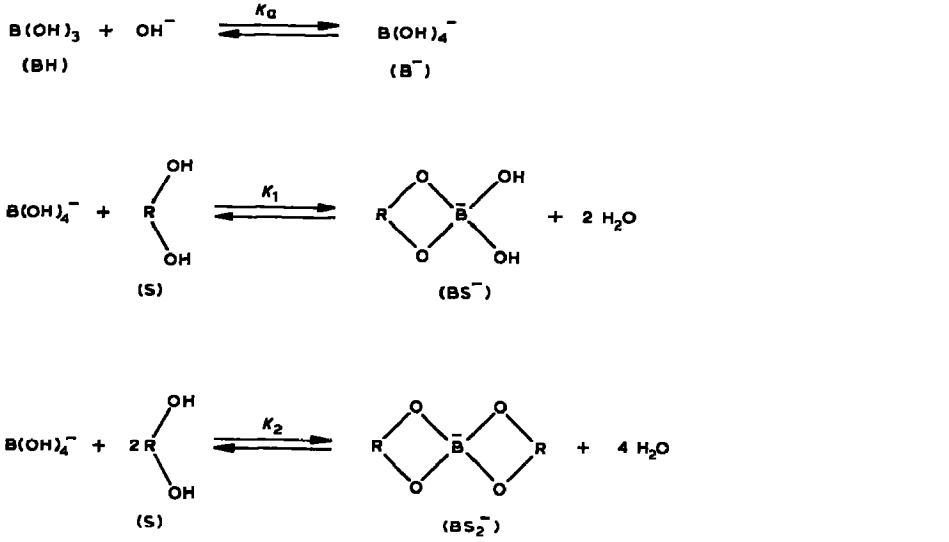
techniques[3]. Several methods have been considered for examining borate-complexing reactions, such as conductivity, pH (ref. 4), cryoscopic measurements, polarimetry[5,6], zone electrophoresis[7], and $^{1}H$-, $^{13}C$-, and $^{11}B$-spectroscopy[8–10]. The pH-dependent interconversion of aqueous boron compounds, as well as the interaction of borate ion with diols, have also been indirectly monitored by refractive index and optical rotation measurements[11]. The interaction of 1,2-diols with borate ions at pH 12 may lead to the formation of 1:1 or 2:1 anionic complexes. $^{11}B$-N.m.r. spectroscopy provides simple methods for monitoring the different forms of complexes with diols. Discrete resonances may be observed for 1:1 and 2:1 anionic complexes with both 1,2- and 1,3-diols[12].

The interconversion of boric acid and borate anions, along with the interaction of borate ions with diols, may be represented by the equilibria presented in Scheme 1, where S stands for the carbohydrate molecule.

These equilibria in aqueous solution are rapidly established as a function of the pH of the solution and the configuration of the diol.

From the mass law, it follows that $K_a = [B^-]/[BH]\,[OH^-]$, $K_1 = [BS^-]/[B^-]\,[S]$, and $K_2 = [BS_2^-]/[B^-]\,[S]^2$, where $K_a$, $K_1$, and $K_2$ are the bor c acid dissociation constant and the complex formation constants, respectively.

In his pioneering work, Böeseken[2] discussed the covalent character of these complexes. This was firmly established through X-ray diffraction measurements[13–15], as well as by n.m.r. studies[16]. However, the role that hydrogen-bonding interactions might play in stabilizing the complexes has seldom been examined[11]. $^{11}B$-N.m.r. spectroscopy provides a direct measurement of the amount of boron in different environments; this technique has been applied here to study the borate complexes of guar D-galacto-D-mannan models, *i.e.*, methyl α-D-galactopyranoside and methyl β-D-mannopyranoside. The results are extended to the polysaccharide and provide a valuable molecular explanation for guar–borate gelation.




Scheme 1.

## EXPERIMENTAL

*Materials.* — Methyl α-D-glucopyranoside (**1**) and methyl α-D-galactopyranoside (**2**) were commercial compounds (Sigma Chemical Co.). Methyl α-D-mannopyranoside (**3**) and methyl β-D-mannopyranoside (**4**) were prepared according to a glycosylation reaction catalyzed by hydrogen fluoride[17].

Guar (*Cyamopsis tetragonolobus*) galactomannan was prepared and purified from commercial flour. It contained D-galactose and D-mannose in the molar ratio 19:31. Low-molecular-weight oligomers were obtained by dissolving a sample (4 g/L) in 10mM acetate buffer (pH 4.5) and treating it with a solution (50 μL) of a highly purified *A. niger* β-D-mannanase[18]. The mixture was first incubated at 40° for 4 h and then, in order to inactivate the enzyme, it was heated for 10 min at 100°. The unreacted solid material was removed by centrifugation at 15 000 r.p.m. for 30 min. Ethanol was added to obtain a 40% solution, and the guar fraction was recovered after centrifugation at 15 000 r.p.m. for 30 min.

Sodium borate solutions in $D_2O$ were prepared from commercial sodium metaborate tetrahydrate (BDH Chemicals).

*$^{11}B$-N.m.r. spectroscopy.* — Weighed quantities of glycosides or depolymerized guar fractions were dissolved in a known volume of borate solution of known concentration. After dissolution, the volume was adjusted to 2.5 mL with a hydroxide–chloride buffer solution (pH 12) at 22°. For each compound, the borate concentration remained the same, *i.e.*, 72.6mM for **2**, **3**, and **4**, 36.3mM for **1**, and 3.63mM for guar fractions, whereas the sugar concentration was increased progressively.

$^{11}B$-N.m.r. spectra were recorded at 96.28 MHz with a Bruker spectrometer equipped with an Aspect 3000 computer. The temperature was maintained at 295 K. Ethyl ether–boron trifluoride was used as external reference. The spectra were obtained in the F.t. mode with a spectral width of 4000 Hz, 8 k data points, and a pulse width of 15 μs (90° pulse) to give a resolution of 0.961 Hz per point. The signals, which were in general well resolved, were integrated by use of the integrating facilities of the spectrometer.

*Calculation of equilibrium constants.* — The values of $[B^-]$, $[BS^-]$ and $[BS_2^-]$ could be determined directly from the peak areas. [S] is the concentration of uncomplexed sugar and was calculated according to Eq. (*1*), where $[S]_0$ is the initial concentration of sugar.

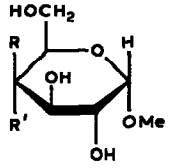
$$[S]_0 = [S] + [BS^-] + 2[BS_2^-] \qquad (1)$$

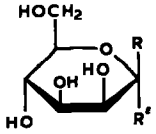
*Molecular drawings.* — Molecular drawings were generated by use of several computer programs aimed at molecular modeling; they were drawn with the aid of the PITMOS program[19].

RESULTS AND DISCUSSION

$^{11}$B-N.m.r. spectroscopy is shown to be particularly suitable to study the formation of complexes between borate and diols, provided some precautions are taken. Experiments were conducted at pH 12 where the preponderant ion is $B(OH)_4^-$ (therefore favoring complex formation) and where the reaction rate between the borate compounds proved to be sufficiently low, on the $^{11}$B-n.m.r. time scale, for sharp and well-resolved resonances to be observed[12] for the different components of the equilibrium reaction.

*$^{11}$B-N.m.r. spectroscopy of glycoside complexation with borate.* — The following model compounds were studied, methyl α-D-glucopyranoside (**1**), methyl α-D-galactopyranoside (**2**), methyl α-D-mannopyranoside (**3**), and methyl β-D-mannopyranoside (**4**).




**1** R = H, R' = OH
**2** R = OH, R' = H
**3** R = H, R' = OMe
**4** R = OMe, R' = H

In accordance with the results obtained previously with model compounds (1,2- and 1,3-diols[12], some alditols[20], and cyclitols[21]), the $^{11}$B-n.m.r. spectra obtained were easily analyzed after progressive addition of sugar to solutions of borate of known concentration. The results are consistent with the assignments published for 1,2- and 1,3-diols[12]. Thus, all the observed spectral lines could be assigned, thereby allowing the individual components present to be identified and quantified. The free borate ion resonates at $\delta$ ~1.5–2.0, and the 5-membered-ring mono- and di-complexes resonate at $\delta$ ~5.3–5.8, and ~8.9–9.7, respectively; the 6-membered-ring mono- and di-complexes exhibited resonances at $\delta$ ~1.0–1.2, and ~0.6, respectively. In some cases, the formation of the mixed spirocyclic anion (5- and 6-membered-ring di-complex) was observed as indicated by the occurrence of a $^{11}$B-n.m.r. signal at $\delta$ 5.0–6.

The results are shown in detail in Fig. 1 and Table I. In particular, the calculated values of the formation constants are given in the Table. For each compound, a mean value could be assessed from the average of different peak-area for each component. The components that were present in very low proportion have been omitted (this does not affect the calculation of $[S]_0$ significantly). Typically, they corresponded to such structures as the 6-membered-ring di-complex peak for **4**, and to the mixed, spirocyclic anion for **2**, **3**, and **4**. In both instances, the corresponding peak was overlapped by a predominant adjacent one arising from the

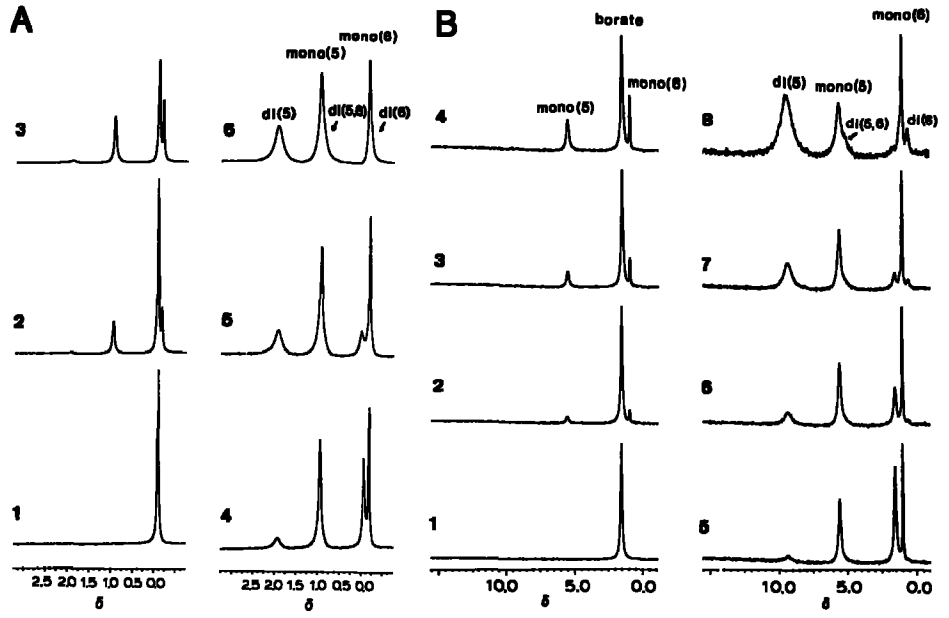



Fig. 1. $^{11}$B-N.m.r. spectra, at 96.28 MHz, of borate solutions, at pH 12 and 295 K, of **2** and **4** at different sugar concentrations: (A) methyl β-D-mannopyranoside (**4**); (B) methyl α-D-galactopyranoside (**2**).

formation of a monocomplex-type of structure.

Our data are similar to those published for other derivatives[12,20,21], but differ from the results of Malcolm *et al.*[11] who have used refractive index and optical rotation measurements to study borate–carbohydrate complex formation. Peak assignments were facilitated by comparison with previously reported values. For **1**, the only possible stereochemical arrangement is the formation of a 6-membered ring where O-4 and O-6 are involved. Assignment of the peaks corresponding to the 1:1- and 1:2-complexes was possible since the 1:1-complex forms preferentially at low sugar concentration.

Methyl α-D-galactopyranoside (**2**) is a good candidate for complex formation. In particular, all possible 5-, 6-, and mixed-membered ring dicomplexes were formed. While both 3,4- and 4,6-monocomplexes had the same occurrence, di-complexation occurred mainly *via* the 3,4-dicomplex.

For methyl α-D-mannopyranoside (**3**), on addition of sugar other products could be detected and structures were assigned according to the sequence in which they appeared as a function of increasing sugar concentration. Compound **3** may form a complex with borate either at O-2 and O-3 (5-membered ring complex), or at O-4 and O-6 (6-membered-ring complex as for **1**). The latter monocomplex was easily detected, while the corresponding dicomplex was barely seen. Also, a mixed dicomplex existed which could be detected by variation of the temperature.

Methyl β-D-mannopyranoside (**4**) formed the same complexes with the following differences. The 6-membered-ring dicomplex could be detected and the

TABLE I

$^{11}$B-N.M.R. SPECTROSCOPIC DATA, EQUILIBRIUM CONCENTRATIONS, AND CONSTANTS FOR COMPLEX FORMATION OF METHYL α-D-GLUCOPYRANOSIDE (1), METHYL α-D-GALACTOPYRANOSIDE (2), METHYL α-D-MANNOPYRANOSIDE (3), AND METHYL β-D-MANNOPYRANOSIDE (4) BY BORATE IONS[a]

*Methyl α-D-glucopyranoside* (1)

| $[S]_0$ (M) | $B^-$ | $BS^-_{4,6}$[b] | | $B(S_{4,6}{}^b)^-_2$ | |
|---|---|---|---|---|---|
| | $[B^-]$[c] | $[BS^-]$[c] | $K_1$ | $[BS^-_2]$[c] | $K_2$ |
| 0.0515 | 2.98 | 0.65 | 4.85 | | |
| 0.0936 | 2.69 | 0.94 | 3.73 | | |
| 0.206 | 2.25 | 1.38 | 3.19 | | |
| 0.412 | 1.75 | 1.88 | 2.73 | | |
| 0.824 | 1.23 | 1.88 | 1.92 | 0.52 | 0.67 |

*Methyl α-D-galactopyranoside* (2)

| $[S]_0$ (M) | $B^-$ | $BS^-_{3,4}$[b] | | $BS^-_{4,6}$[c] | | $B(S_{3,4}{}^b)^-_2$ | | $B(S_{4,6}{}^b)^-_2$ | |
|---|---|---|---|---|---|---|---|---|---|
| | $[B^-]$[c] | $[BS^-]$[c] | $K_1$ | $[BS^-]$[c] | $K_1$ | $[BS^-_2]$[c] | $K_2$ | $[BS^-_2]$[c] | $K_2$ |
| 0.0206 | 6.39 | 0.37 | 4.87 | 0.50 | 6.58 | | | | |
| 0.0412 | 5.58 | 0.81 | 5.95 | 0.87 | 6.39 | | | | |
| 0.0724 | 4.48 | 1.39 | 6.64 | 1.28 | 6.12 | | | | |
| 0.1448 | 2.96 | 2.30 | 7.80 | 1.78 | 6.04 | 0.22 | 7.49 | | |
| 0.2906 | 1.49 | 2.68 | 8.06 | 2.12 | 6.37 | 0.97 | 13.07 | | |
| 0.5798 | 0.50 | 2.54 | 10.40 | 1.85 | 7.57 | 1.98 | 16.59 | 0.39 | 3.27 |

*Methyl α-D-mannopyranoside* (3)

| $[S]_0$ (M) | $B^-$ | $BS^-_{2,3}$[b] | | $BS^-_{4,6}$[b] | | $B(S_{2,3}{}^b)^-_2$ | |
|---|---|---|---|---|---|---|---|
| | $[B^-]$[c] | $[BS^-]$[c] | $K_1$ | $[BS^-]$[c] | $K_1$ | $[BS^-_2]$[c] | $K_2$ |
| 0.0735 | 3.91 | 2.25 | 14.4 | 0.75 | 4.80 | 0.35 | 55.9 |
| 0.1460 | 2.37 | 3.09 | 14.8 | 0.92 | 4.40 | 0.88 | 47.6 |
| 0.2074 | 1.57 | 3.44 | 16.1 | 0.81 | 3.79 | 1.43 | 49.0 |
| 0.4124 | 0.72 | 3.29 | 14.2 | 0.63 | 2.73 | 2.61 | 35.2 |
| 0.7142 | 0.16 | 2.54 | 22.2 | 0.50 | 4.37 | 4.06 | 49.7 |

*Methyl β-D-mannopyranoside* (4)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 0.0502 | 5.02 | 1.37 | 5.43 | 0.86 | 3.41 | | |
| 0.1555 | 3.61 | 2.11 | 3.76 | 1.31 | 2.33 | 0.24 | 2.75 |
| 0.3096 | 2.12 | 2.78 | 5.08 | 1.80 | 3.29 | 0.56 | 3.96 |
| 0.6270 | 0.90 | 3.06 | 6.17 | 2.09 | 4.21 | 1.21 | 4.42 |
| 1.049 | | 3.20 | | 2.08 | | 1.98 | |

[a]At pH 12 and 295 K. [b]These numbers refer to the oxygen atoms involved in the complex. [c]Concentration of boron compounds (M × 100).

formation constants were very different from those of **3**. The highest formation constants at pH 12 and 295 K were those found for the α-D anomer. Using zone electrophoresis, Foster[7] found for the same compounds that the mobility of the α-D anomer in the presence of alkaline borate was higher than that of the β-D anomer. The relative instability of the borate complexes of methyl β-D-mannopyranoside (**4**) could not be precisely explained, but was thought to arise, at least in part, from adverse, non-bonded interactions within the complexes.

The present formation constants, in particular $K_1$ and $K_2$ of the 2,3-mono- and di-complexes, respectively, may bring additional information. In the complex of the β-D anomer **4**, the aglycon methoxyl group occupies an equatorial position and will interact strongly with O-2, thereby destabilizing the corresponding

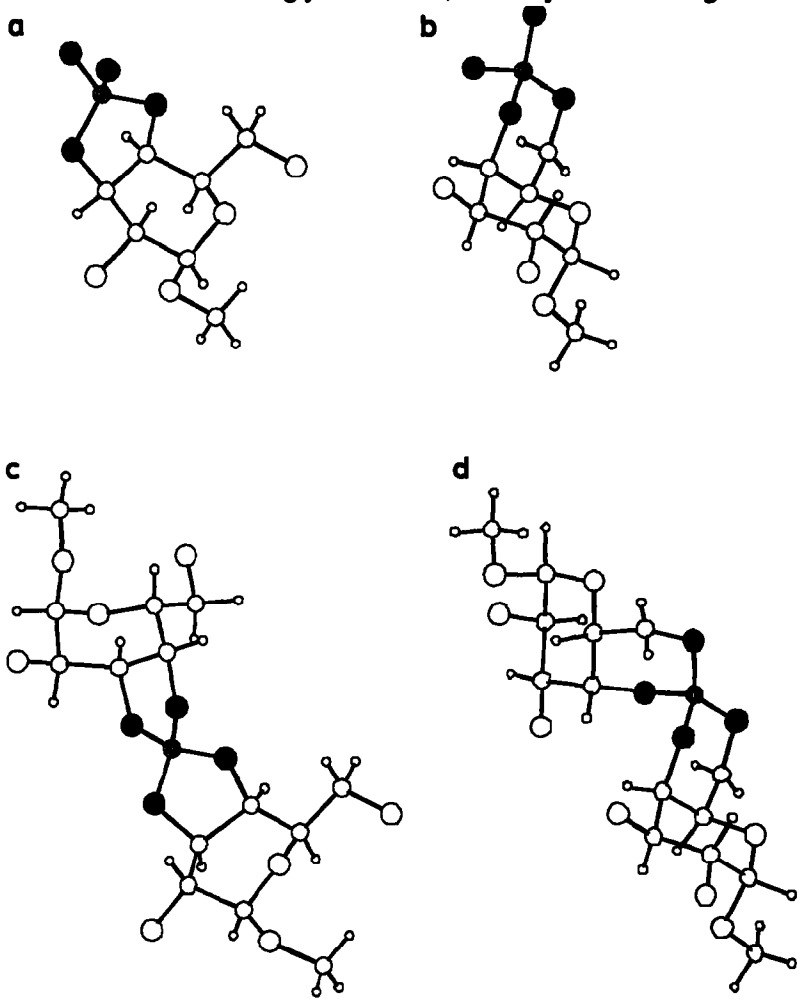



Fig. 2. Computer representations showing feasible models of methyl α-D-galactopyranoside (**2**): 5- (a) and 6-membered-ring (b) monocomplexes, (*R*)- (c) and (*S*)-isomers (d) of 5- and 6-membered-ring di-complexes.

complex. This is particularly true if one considers that complex formation is always accompanied by a slight ring deformation. As a result of the destabilization of the 5-membered-ring complex of the β-D anomer **4**, the 6-membered dicomplex could be detected as a minor component.

*Molecular modeling of the glycoside–borate complex.* — Computer drawings of the stable conformations of the 5- and 6-membered-ring mono- and di-complexes of methyl α-D-galactopyranoside (**2**) were obtained with the aid of the PITMOS program[19] (Fig. 2). These complexes were constructed by use of the data derived from X-ray investigations of α-D-galactose[22], methyl 3,4-*O*-ethylidene-β-D-galactopyranoside[23], and also of some borate esters[13–15]. Positions of the hydrogen atoms were computed according to neutron-diffraction studies of carbohydrates[24].

The 4,6-mono- and di-complexes were easily drawn with a *gauche-gauche* conformation of the hydroxymethyl group of the D-galactose unit. This led to a O-4···O-6 distance of 2.40 Å, as compared to a O···O distance (within the free borate ion) of 2.42 Å. For such a dicomplex, two isomers, namely bis(methyl α-D-galactopyranoside) (*R*)- and (*S*)-4,6:4′,6′-borates had to be considered. The same isomerization was found for the 3,4-dicomplex; both bis(methyl α-D-galactopyranoside) (*R*)- and (*S*)-3,4:3′,4′-borates were present. Computer drawings for these 3,4-mono- and di-complexes suggested the existence of some deformation of the D-galactose ring. For strain-free α-D-galactose, the distance O-3···O-4 is 2.82 Å. The O···O distance of borate of 2.42 Å can be fitted only if one allows some strain in the sugar unit. Similar deformation is caused by the ethylidene group linked to O-3 and O-4 of methyl 3,4-*O*-ethylidene-β-D-galactopyranoside[23]. In this compound, the O-3···O-4 distance is 2.28 Å, closer to the O···O distance of the borate ion. The true situation must be in between and can be envisaged as arising from a slight flattening of the normal $^4C_1$(D) conformation.

These characteristics led to the conclusions that methyl α-D-galactopyranoside (**2**) presents two main possible complex formation (3,4 and 4,6), the latter, although unfavored energetically because of an 1,3-diaxial interaction at O-4 and O-6, being favored kinetically and the former being stabilized by deformation.

*Extension to the galactomannan polymer.* — The $^{11}$B-n.m.r. spectrum, at pH 12 and 295 K, of a fraction of guar galactomannan obtained by hydrolysis of a purified guar sample by β-D-mannanase is shown in Fig. 3. This fraction exhibited the same mannose-to-galactose ratio as that of the parent polymer, but its solubility in water was greatly enhanced owing to the partial backbone cleavage. The spectra obtained for various polymer concentrations suggested the complexes that were formed. Although it was difficult to discriminate between the complexes of D-galactopyranosyl *v.s.* D-mannopyranosyl residues, it was readily possible to establish the presence of 5-membered-ring mono- ($\delta$ 5.6) and di-complexes ($\delta$ 9.4), as well as 6-membered-ring mono-($\delta$ 0.9) and di-complexes ($\delta$ 0.5). Comparison between the formation constants determined for the two model glycosides and the displayed lines indicated that both mono- and di-complex formation occurred mainly *via* 5-membered-ring complexes (O-2···O-3 for the D-mannopyranosyl and

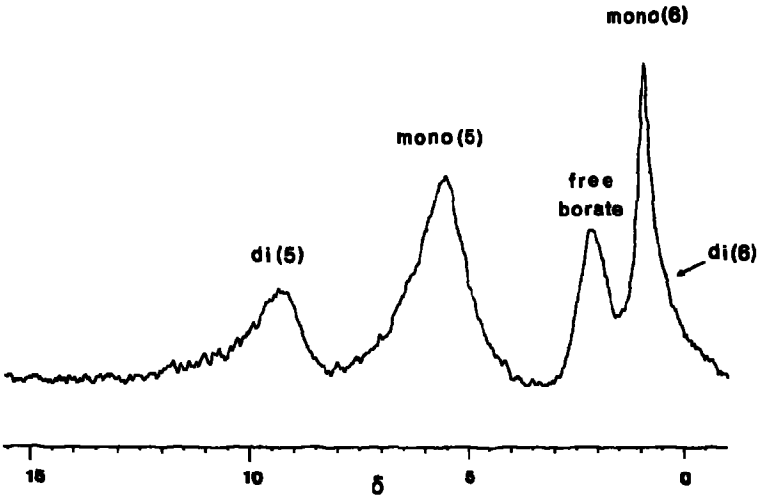



Fig. 3. $^{11}$B-N.m.r. spectrum (96.28 MHz) of borate–guar galactomannan fraction at pH 12 and 295 K.

O-3···O-4 for the D-galactopyranosyl residues). Moreover, the formation constants found for the two glycosides agreed with previous findings[16]. All the aforementioned evidence led to the conclusion that the guar galactomannan–borate complex forms more readily with the D-galactosyl side-groups than with the D-mannosyl residues of the backbone. Also, the respective $K_2$ values pointed towards a selective involvement of the D-galactosyl side-groups during dicomplex formation (or cross-linking of the chains leading to gelation for the polymer in alkaline media). The present study corroborated these findings and improved our understanding of the polymer properties resulting from complex formation. Therefore, a direct correspondence between dicomplex formation and gelation, as well as between monocomplex formation and hydration-delay phenomenon, could be established. When dispersed in water, hot or cold, galactomannans hydrate rapidly to form colloidal solutions of unusually high viscosity characteristics, even at very low concentrations. In contrast, when the gum, in powder form, is introduced into an alkaline borate solution at room temperature, it disperses easily but neither hydrates, nor develops viscosity. This inhibiting action can be overcome by lowering the pH to 7 or by raising the temperature. This phenomenon[1] may be used as a method of dispersing guar-containing products that tend to lump. According to our study, the monocomplex formation of borate ions on the particles of guar gum may prevent water from properly hydrating the polymer chains and, therefore, explain the delay observed.

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