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Complexation behavior of mono- and disaccharides by the vinylbenzeneboronic acid–divinylbenzene copolymer resins packed in a high-performance liquid chromatographic column

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ABSTRACT

Using an HPLC column packed with monodispersed vinylbenzeneboronic acid–divinylbenzene (V–D) copolymer resins, the elution behaviors of the mono- and disaccharides were studied under different pH mobile phases. The monodispersed V–D copolymer resins were prepared by the copolymerization of 4-vinylbenzeneboronic acid and divinylbenzene in the presence of template silica gel particles (particle size: 5 μm; pore size: 10 nm), followed by dissolution of the template silica gel using a NaOH solution. Similarly, styrene–divinylbenzene (S–D) copolymer resins as the control resins were also synthesized. The transmission electron micrographs of these polymer resins revealed a good monodispersity. The complexation behavior of the saccharides was evaluated by comparison of the peak area eluted through the V–D column for that through the S–D column. Four aldopentoses (D-ribose, D-arabinose, D-xylose, and D-lyxose) and four aldohexoses (D-glucose, D-mannose, D-galactose, and D-talose) were retained completely at pH 11.9. Especially, ribose and talose were totally retained even under acidic and neutral conditions. For the disaccharides, unlike sucrose and maltose, palatinose was completely retained in basic mobile phases.

1. Introduction

Boronic acids are known to form cyclic boronate complexes with the molecules containing *cis*-1,2 and *cis*-1,3-diol groups (Fig. 1). These complexations have been applied for the separation of saccharides [1,2], glycated proteins [3] and glycoconjugates [4,5]. However, the formation of the saccharide-boronate complex depends on the structure of the saccharide and pH value of the mixture. Therefore, in order to evaluate the complexation behaviors, various approaches, such as ^{13}C and ^{11}B NMR spectroscopy [6,7], and the potentiometric titration [8] have been examined. Moreover, the complexation behaviors were studied in a batch-wise operation using the phenylboronic acid-bonded acrylamide copolymers [2], and the magnetite particles modified with dihydroxyborylphenyl groups [9]. From these experiments, saccharides, such as glucose and fructose are known to predominantly form a complex with boronic acids under alkaline conditions [8], and the furanose form of the saccharides are advantageous in the complexation [6]. However, these methods are not suitable for the rapid evaluation of the complexation behaviors for enormous numbers of saccharides.

By using the HPLC column packed with boronic acid-bonded polymers, which were resistant to an alkaline solution, the complexation behaviors in a wide pH range would be evaluated. For the separation and isolation of saccharides using the boronic acid containing stationary phases, silica gel [5,10–12], and bio- and synthetic polymers, such as cellulose [13], agarose [14,15] and polyacrylamide [2,16,17], have been reported as support materials. Since boronic acids predominantly form a complex with saccharides under alkaline conditions, polymer supports, such as cellulose, agarose and polyacrylamide, which are inert to the basic conditions, are more effective than silica gel. However, the immobilization of boronic acid groups on the supports is a time-consuming step and the yield is relatively low. Therefore, a one-step preparation method of monodispersed porous polymer resins containing boronic acid moieties is desirable.

The templating polymerization methods for the preparation of monodispersed porous polymer particles have been reported, i.e., the polymerization of a monomer in a porous matrix, such as silica gel, followed by dissolution of the matrix in an alkaline solution

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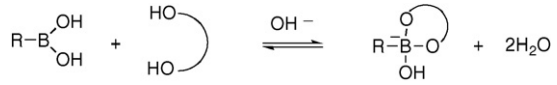

Fig. 1. Equilibria between boronic acids and diols.

[18–20]. We have previously reported the preparation of monodispersed porous polymer resins using this templating polymerization method and their application to stationary phases for the high-performance liquid chromatographic separation of carbohydrates [21].

We now report the preparation of monodispersed 4-vinylbenzeneboronic acid–divinylbenzene (V–D) copolymer resins by copolymerization in the presence of template silica gel particles (particle size: 5 μm; pore size: 10 nm), and the complexation behavior of 15 kinds of monosaccharides and three kinds of disaccharides by measuring the elution percentage through the HPLC column packed with the V–D copolymer resins.

2. Materials and methods

2.1. Materials

Nucleosil silica 100-5 (particle size: 5 μm; pore size: 10 nm) was purchased from Macherey-Nagel (Duren, Germany). The 4-vinylbenzeneboronic acid was purchased from Alfa Aesar (Ward Hill, MA, USA). Divinylbenzene (80% grade), benzoyl peroxide and the inhibitor remover were from Aldrich (Milwaukee, WI, USA). Divinylbenzene was passed through the inhibitor remover column before use. Chlorotrimethylsilane, ethylene glycol, and the mono- and disaccharides were from Tokyo Kasei (Tokyo, Japan). Two poly(vinyl alcohol) powders with the average polymerization degrees of 1000 (86–90% hydrolyzed) and 1500 (100% hydrolyzed) were from Wako (Osaka, Japan). Toluene was dried by refluxing over sodium and then distilled before use. Pyridine was dried over molecular sieve 4 Å. All other chemicals were of analytical grade and used without further purification.

2.2. Microscopy and FTIR spectra

A JEM-1200EX transmission electron microscope (TEM) from JEOL (Tokyo, Japan) was employed to observe the morphology of the resulting polymer particles. The Fourier transform infrared spectroscopy (FTIR) spectra were recorded by a JASCO (Tokyo, Japan) FT/IR-470 Plus spectrometer.

2.3. High-performance liquid chromatographic instrumentation and chromatographic conditions

The HPLC analysis was performed by a system consisting of a JASCO 880-PU pump, a Rheodyne (Cotati, CA, USA) 7125 injector, and an Alltech (Deerfield, IL, USA) ELSD 2000 evaporating light scattering detector. A Chromatocorder 12 from SIC (Tokyo, Japan) was used for the data analysis. The V–D copolymer resins and the S–D copolymer resins were separately packed into 15 cm × 4.6 mm I.D. stainless-steel columns. All saccharide samples were dissolved in ultrapure water and filtered through 0.45 μm filters (Millipore, Billerica, MA, USA). The samples were eluted with four different mobile phases consisting of 60% (v/v) acetonitrile and 40% water (pH 5.4), 0.01 M trifluoroacetic acid (pH 2.1), 0.01 M triethylamine (pH 11.3) and 0.1 M triethylamine (pH 11.9), during isocratic elution at the flow rate of 0.3 mL/min. The drift tube temperatures for the evaporating light scattering detector were set at 90 °C and the nebulizing gas (air) flow rate was 1.8 L min^{-1}.

2.4. Preparation of the 4-vinylbenzeneboronic acid–divinylbenzene copolymer resins

An outline of the preparation method for the V–D copolymer resins is shown in Fig. 2. A mixture of 4-vinylbenzeneboronic acid ethylene glycol esters, divinylbenzene and benzoyl peroxide in water was vigorously stirred in the presence of silanized silica gel in order to immerse the monomers into the pores of the silica gel, then the mixture was polymerized by heating. The template silica gel was removed by dissolution using

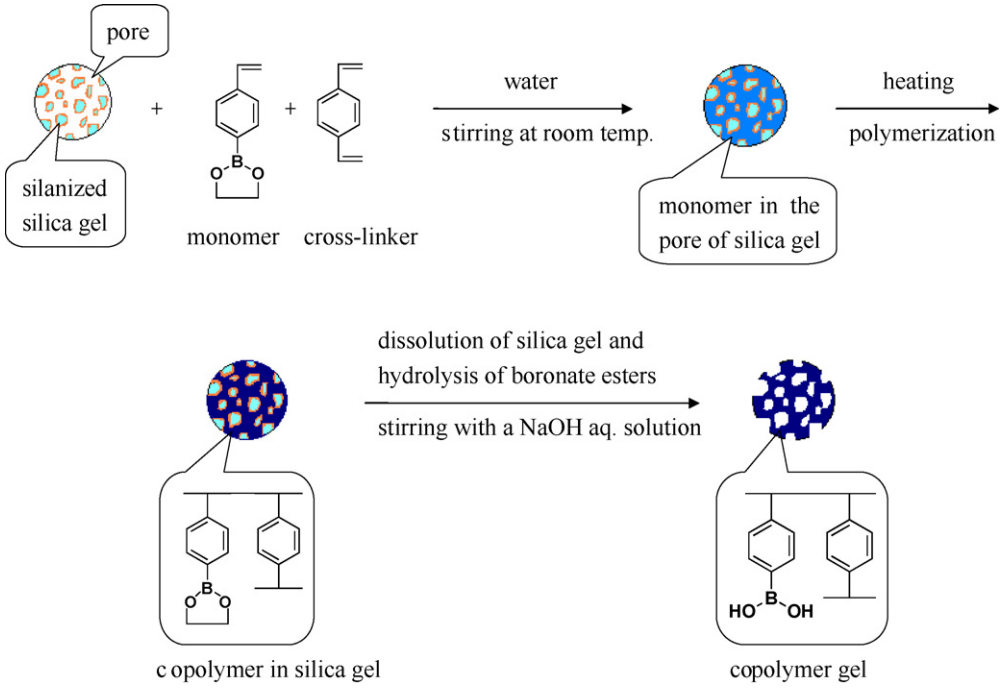

Fig. 2. Preparation of porous polymer resins by copolymerization of monomers in the template silica gel.

an alkaline aqueous solution. As a control experiment, the styrene–divinylbenzene copolymer resins were similarly prepared.

2.4.1. Sililation of silica gel

Silica gel was silanized with chlorotrimethylsilane for conversion of the hydrophilic silica gel surface to a hydrophobic surface. The template silica gel (Nucleosil silica 100-5) was dried in a flask under vacuum at 150 °C for 4 h. Dry toluene (80 mL), pyridine (7 mL) and chlorotrimethylsilane (5.55 g) were added to the flask containing dry silica gel (9.66 g). The mixture was stirred at 60 °C for 5 h under an argon atmosphere. The silanized silica gel was filtered through a sintered-glass filter and washed with 200 mL of toluene followed by 200 mL of dichloromethane and 300 mL of methanol, then finally dried overnight under vacuum. The yield of the silanized silica gel was 10.62 g and the extent of the silanization calculated from the increase in the weight was 1.26 mmol/g of the silanized silica gel.

2.4.2. Preparation of copolymer resins

Silanized silica gel (3.5 g), 4-vinylbenzeneboronic acid (0.62 g, 4.18 mmol), ethylene glycol (0.27 g, 4.29 mmol) and ultrapure water (50 mL) were added to a three-necked flask, and the mixture was stirred under an argon atmosphere. A mixture of divinylbenzene (2.03 g, 12.4 mmol) and benzoyl peroxide (0.10 g) was then added to the flask, followed by 30 mL of an aqueous solution of poly(vinyl alcohol) [average degree of polymerization of 1000 (4 mg) and 1500 (100 mg)]. The mixture was stirred at 700 rpm under flowing argon at room temperature for 24 h and then kept at 90 °C for 24 h. The mixture was then cooled to room temperature, and the precipitate was filtered through a sintered-glass filter and washed with 100 mL of water and 200 mL of methanol. The precipitate was added to a mixture of 90 mL of a 5 M NaOH aqueous solution and 60 mL of methanol. The mixture was stirred at room temperature for 24 h to dissolve the template silica gel and to hydrolyze the boronate esters. The particles were washed with water until the solution was neutral followed by 100 mL of methanol, then dried under vacuum at room temperature to produce the V–D copolymer resins (2.15 g) in a 78.3% yield. The elemental analysis of the resins gave $B = 1.6\%$.

The S–D copolymer resins were also synthesized in a similar way. A mixture of the silanized silica gel (5.0 g), styrene (1.6 g, 15 mmol), divinylbenzene (2.5 g, 15 mmol), and benzoyl peroxide (0.12 g) was heated at 90 °C for 24 h. After treating with a NaOH solution, the S–D copolymer resins (3.61 g) were obtained in 85.5% yield.

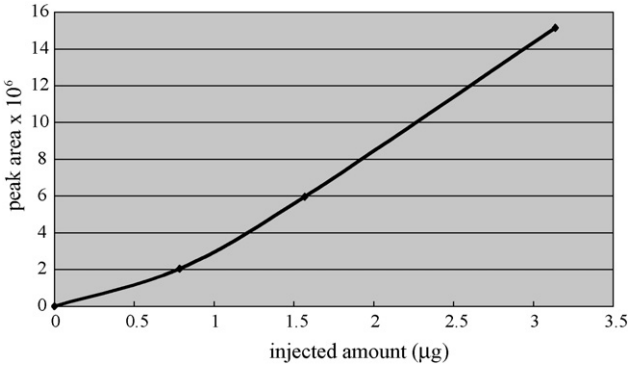

Fig. 3. Calibration curve for glucose eluted through the column packed with S–D copolymer resins under basic conditions (pH 11.3). All peaks eluted at the hold-up time. Column: 15 cm × 4.6 mm I.D., mobile phase: CH_3CN – 10 mmol-triethylamine (TEA) aq. sol. (pH 11.3) (6:4, v/v), flow rate: 0.3 mL/min, detection: evaporative light scattering detector (Alltech 2000), tube temperature 90 °C, gas flow 1.8 L min^{-1} (air).

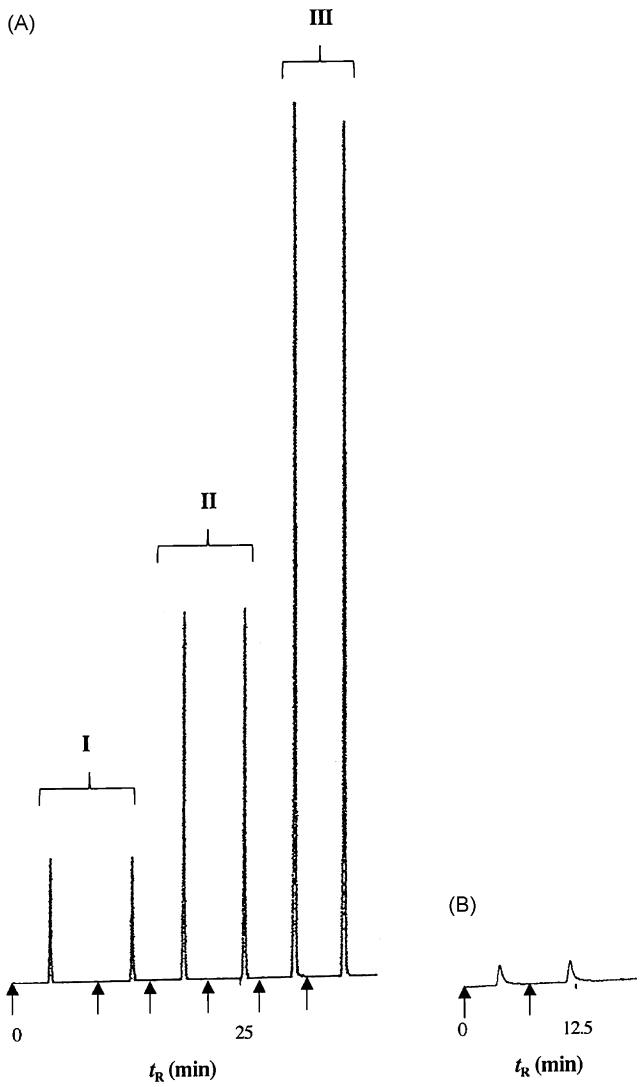

Fig. 4. HPLC profiles of glucose eluted through a column packed with S–D copolymer resins in a basic mobile phase (pH 11.3) (A), and that with V–D copolymer resins (pH 11.3) (B). Injection amounts are: (I) 0.78, (II) 1.56, (III) 3.13 and (B): 3.13 mg. All injections were duplicated.

2.5. Column packing

The V–D copolymer resins were packed into stainless-steel columns (4.6 mm I.D. × 150 mm) by a conventional slurry packing method using acetonitrile–water (6:4, v/v) as the eluent at a constant pressure of 10 MPa. For the control experiment, the S–D copolymer resins were also packed in a similar way.

2.6. Measurement of degree of complexation

Each of the saccharide solutions (5 μL) containing 0.156, 0.313 and 0.625 mg mL^{-1} of each sample was injected into the column packed with the S–D copolymer resins in the mobile phases of pH 2.1, 5.4, 11.3 and 11.9. The injection of each sample was duplicated. All analytes were eluted at the hold-up time. The calibration curves for each saccharide were created from the respective peak areas. As an example, the calibration curve for glucose under basic conditions (pH 11.3) is shown in Fig. 3. Fig. 3 shows that the calibration curve was not linear. In the case of detection of saccharides by the evaporating light scattering detector, the non-linear relationship between the amounts of sample and the peak area has also been reported in the literatures [22,23]. Each 5 μL of the sample solutions

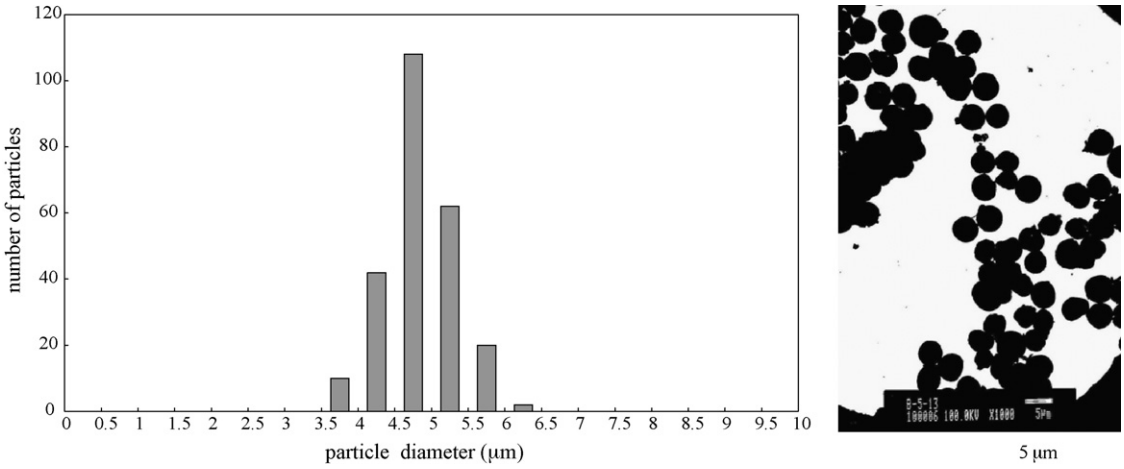

Fig. 5. TEM image of 4-vinylbenzeneboronic acid–divinylbenzene copolymer resins (V–D) and their particle size distribution. Mean particle diameter: 4.84 μm and total number of particles: 244.

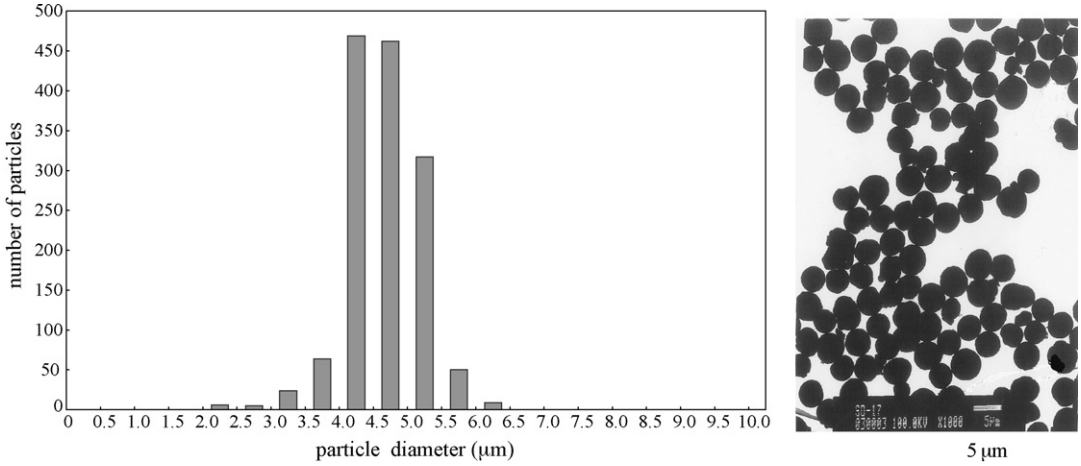

Fig. 6. TEM image of styrene–divinylbenzene copolymer resins (S–D) and their particle size distribution. Mean particle diameter: 4.65 μm and total number of particles: 1406.

Table 1
Retention (%) of saccharides on 4-vinylbenzeneboronic acid–divinylbenzene copolymer resins.

Saccharide			Retention (%)			
			pH of mobile phase			
			2.1	5.4	11.3	11.9
Monosaccharide	Aldopentose	D-Ribose	100	100	100	100
		D-Arabinose	34	27	100	100
		D-Xylose	49	45	100	100
		D-Lyxose	42	27	100	100
	Aldohexose	D-Glucose	16	46	84	100
		D-Mannose	22	26	67	100
		D-Galactose	59	58	100	100
		D-Talose	100	100	100	100
	Ketohexose	D-Fructose	70	74	100	100
	Deoxy sugar	L-Fucose	37	36	62	100
	Cyclohexitol	*myo*-Inositol	15	17	77	100
		scyllo-Inositol	10	17	18	23
	Uronic acid	D-Glucuronic acid	27	19	21	47
	Aminosugar	*N*-Acetyl-D-glucosamine	18	0	6	26
		N-Acetyl-D-galactosamine	54	48	39	100
Disaccharide		Sucrose	14	9	16	31
		Maltose	16	8	31	48
		Palatinose	43	44	100	100

of 0.625 mg mL^{-1} (absolute amount: 3.13 μg) was injected into the column packed with the V–D copolymer resins under the same pH conditions. From the peak area of the analyte, the corrected weight (B, μg) of the analyte eluted through the V–D column was calculated using its own calibration curve. The degree of retention (%) of each saccharide was determined by the following equation.

$$\text{Degree of retention}\,(\%) = \left[\frac{(3.13\,\mu g - B)}{3.13\,\mu g}\right] \times 100$$

After each injection, the retained analytes were not washed from the column, because the binding capacity of the column for saccharides (approximately 1.5 mmol/column) is extremely higher than the injected amount of saccharides (approximately 9–17 nmol/injection). The repeated experiment for the retention degree of glucose also showed good reproducibility.

The HPLC profiles for determination of the degree of complexation of glucose under basic conditions (pH 11.3) are shown in Fig. 4.

3. Results and discussion

3.1. Characterization of copolymer resins

The V–D and the S–D copolymer resins were prepared by the templating polymerization method as shown in Fig. 2. The infrared absorption spectra of the V–D copolymer resins show the absorptions at 1346 cm^{-1} and 3435 cm^{-1}, which are the characteristics of the stretching vibration of B–O and O–H, respectively [24]. The boronic acid group content per 1 g of the copolymer resins was calculated to be 1.5 mmol/g from the boron elemental analysis.

Figs. 5 and 6 show the TEM images and the size distribution of the V–D and S–D copolymer resins, respectively. These resins had a good size monodispersity (mean particle size: 4.84 μm for V–D and 4.65 μm for S–D) and were free from non-spherical by-products.

The V–D and the S–D copolymer resins were packed into stainless-steel columns for the HPLC analysis.

3.2. Complexation of mono- and disaccharides with V–D copolymer resins

For evaluation of the complexation of saccharides with boronoic acids, the solution of each mono- and disaccharide was injected into the columns packed with the V–D and S–D copolymer resins in the acidic, neutral and basic mobile phases. The degree of retention was calculated from the equation in Section 2.6 and is summarized in Table 1.

3.2.1. Monosaccharides

Fig. 7 depicted the influence of the pH of the mobile phase on the retention behaviors of the eight investigated aldoses. Fig. 7 clearly showed that these saccharides were strongly retained on the boronic acid copolymer resins under basic conditions. D-Fructose and L-fucose also showed the same tendency to be retained under basic conditions (Table 1). Our observations of the complexing behavior estimated from the retention manner of eight aldoses, D-fructose and L-fucose using the boronic acid column were consistent with the results reported by James et al., which suggested that the reaction of boronic acid with the saccharides occurs in the alkaline solutions [8].

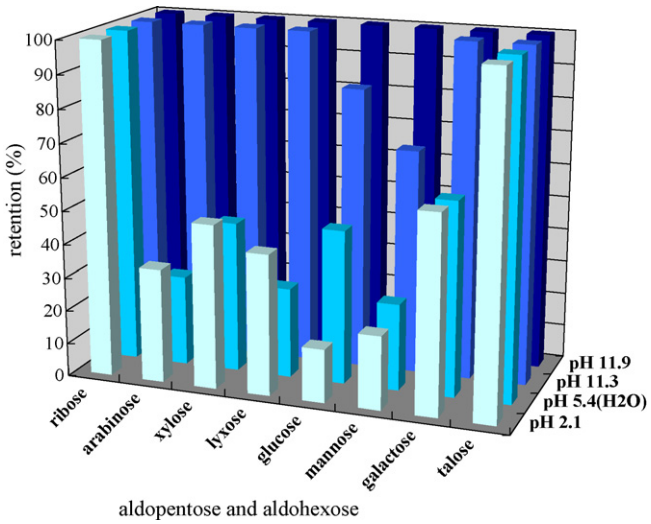

Fig. 7. The retention percentages of aldopentoses and aldohexoses on boronic acid polymer resins.

It is noteworthy that D-ribose and D-talose were completely retained even under neutral and acidic conditions. It is known that among the aldoses, these two saccharides significantly exist in the furanose form in a neutral aqueous solution (ribose: 20%; talose: 29%) (Table 2, [25]). The other saccharides predominantly exist as pyranose forms under neutral conditions. Fig. 8 shows the pyranose and furanose forms of some aldoses. The furanose forms of ribose and talose have the *cis*-1,2-diol structure. Bekkum et al. [6] reported that from the ^{11}B and ^{13}C NMR spectroscopic study, the decreasing order of the association constants of sugar-borate esters is as follows: *cis*-1,2-diol furanose ≫ exocyclic-1,2-diol pyranose > exocyclic-1,2-diol furanose > *cis*-1,2-diol pyranose > exocyclic *cis*/*trans*-4,6-diol pyranose ≫ *trans*-1,2-diol pyranose/furanose. This report suggests that the *cis*-1,2-diol furanose forms would be the most favorable for the complexation, and in our experiment D-ribose and D-talose were strongly retained even under neutral and acidic conditions.

The retention behavior of two stereoisomeric inositoles, the *myo*- and *scyllo*-inositoles, was examined. Table 1 shows that *myo*-inositol was more strongly retained than the *scyllo*-inositol over the entire pH range, and was totally retained in the basic mobile phase. Unlike aldoses, these two inositoles do not take isomers such as the furanose form. The structural difference in the two isomers is that

Table 2
The percentage composition of sugars in aqueous solution at equilibrium.[a].

Saccharides	Temperature (°C)	α-Pyranose (%)	β-Pyranose (%)	α-Furanose (%)	β-Furanose (%)
Ribose	31	21.5	58.5	6.5	13.5
Arabinose	31	60	35.5	2.5	2
Xylose	31	36.5	63	<1	<1
Lyxose	31	70	28	1.5	0.5
Glucose	31	38	62		0.14
Mannose	44	64.9	34.2	0.6	0.3
Galactose	31	30	64	2.5	3.5
Talose	22	42	29	16	13
Fructose	31	2.5	65	6.5	25

[a] Collins and Ferrier [25].

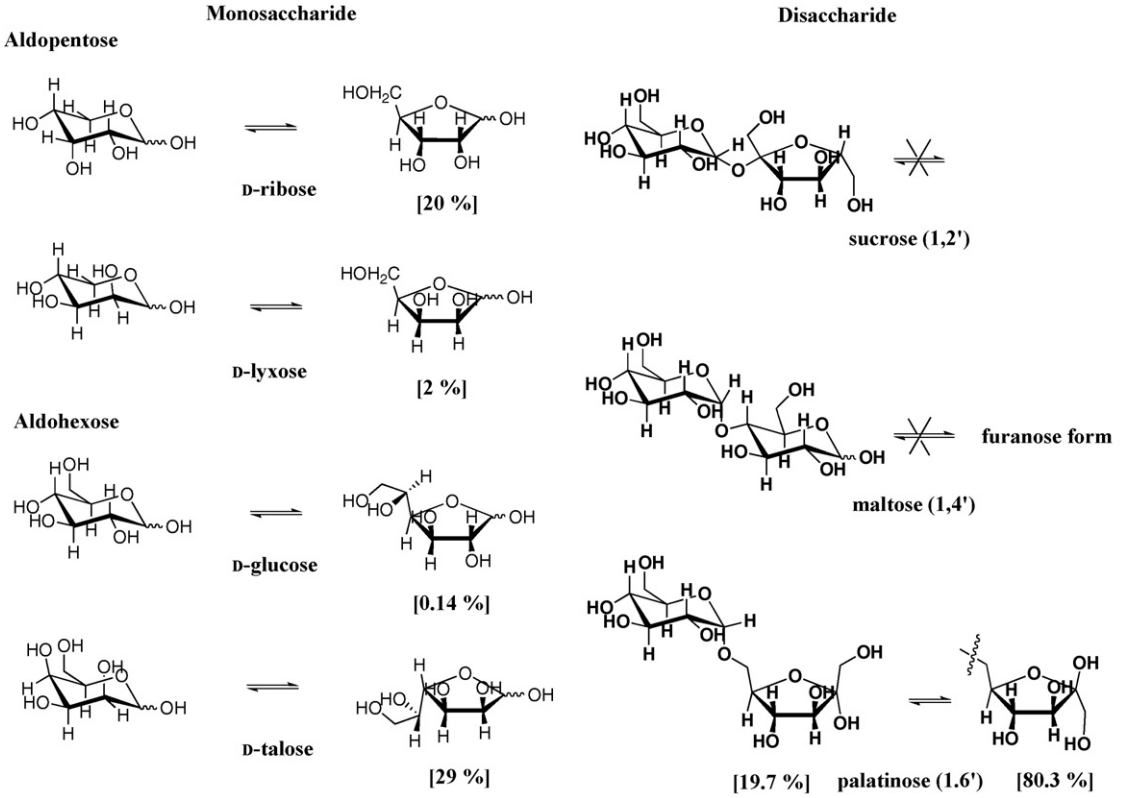

Fig. 8. Equilibrium of mono- and disaccharides in an aqueous solution.

the *myo*-inositol contains the *cis*-1,2-diol moiety whereas the *scyllo*-inositol does not contain the *cis*-1,2-diol, but the *cis*-1,3-diol moiety (Fig. 9). These results support the fact that the *cis*-1,2-diol structure is predominant in the complexation with the boronic acids.

The retention behaviors of the two aminosugars were also examined. *N*-Acetyl-D-galactosamine containing *cis*-1,2-diol groups showed stronger retentions on the boronic acid column than the *N*-acetyl-D-glucosamine.

3.2.2. Disaccharides

The retention behaviors of sucrose, maltose and palatinose were examined, and the results are shown in Fig. 10. Palatinose showed a relatively strong retention over the entire pH range compared to sucrose and maltose, especially, under the basic conditions, palatinose was completely retained. Sucrose has no hemiacetal group, therefore it does not exhibit any mutarotation, and all the vicinal diol groups are fixed in the *trans*-form (Fig. 8). Maltose and palatinose are both reducing sugars and show mutarotation. Maltose has the 1,4′-α-glycoside bond linkage which prevents it from having the furanose form. On the other hand, palatinose having the 1,6′-α-glycoside bond linkage allows the furanose form. Among these disaccharides, only palatinose can be present as the *cis*-1,2-diol furanose forms. This probably suggests the reason for the strong retention of palatinose by the boronic acid column.

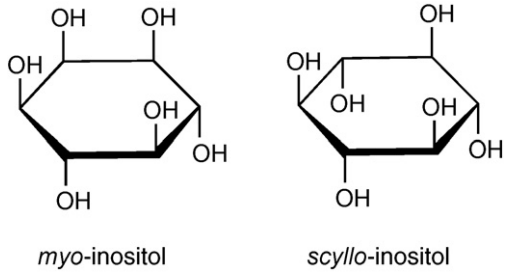

Fig. 9. The structures of *myo*- and *scyllo*-inositol.

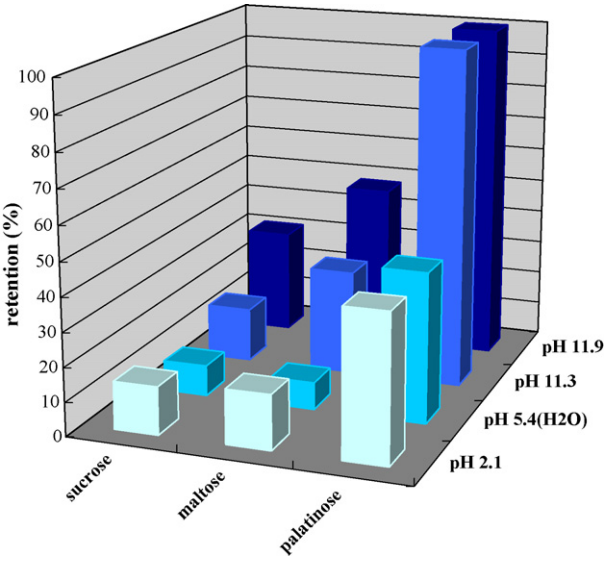

Fig. 10. The retention percentages of disaccharides on V–D copolymer resins.

4. Conclusion

Monodispersed boronic acid group-bonded polymer resins (V–D) were prepared by the copolymerization of 4-vinylbenzeneboronic acid and divinylbenzene in the presence of a

template porous silica gel (particle size: 5 μm; pore size: 10 nm) silanized with chlorotrimethylsilane on the surface, followed by dissolution of the template silica gels by an alkaline solution. The S–D copolymer resins were also synthesized from styrene and divinylbenzene in a similar manner. Using these copolymer resins, the mono- and disaccharides were analyzed by HPLC. The retention was strongly dependent on the pH of the mobile phase. A strong retention was observed under basic conditions. The saccharides containing high proportions of the furanose form at equilibrium in an aqueous solution were retained even under neutral and acidic conditions.

These polymer resins have a great potential as catch and release sorbents for the separation of saccharides by changing the pH of the mobile phase.

References

[1] J.M. Sugihara, C.M. Bowman, J. Am. Chem. Soc. 80 (1958) 2443.
[2] D. Shiino, A. Kubo, Y. Murata, Y. Koyama, K. Kataoka, A. Kikuchi, Y. Sakurai, T. Okano, J. Biomater. Sci., Polymer Ed. 7 (1996) 697.
[3] F. Frantzen, K. Grimsrud, D.E. Heggli, E. Sundrehagen, J. Chromatogr. B 670 (1995) 37.
[4] Y. Tomono, K. Abe, K. Watanabe, Anal. Biochem. 184 (1990) 360.
[5] I. Uda, A. Sugai, K. Kon, S. Ando, Y.H. Itoh, T. Itoh, Biochim. Biophys. Acta 619 (1980) 367.
[6] R. van den Berg, J.A. Peters, H. van Bekkum, Carbohydr. Res. 253 (1994) 1.
[7] M. Van Duin, J.A. Peters, A.P.G. Kieboom, H. Van Bekkum, Tetrahedron 40 (1984) 290.
[8] L.I. Bosch, T.M. Fyles, T.D. James, Tetrahedron 60 (2004) 11175.
[9] M. Shimomura, T. Abe, Y. Sato, K. Oshima, T. Yamauchi, S. Miyauchi, Polymer 44 (2003) 3877.
[10] M. Glad, S. Ohlson, L. Hansson, M.O. Mánsson, K. Mosbach, J. Chromatogr. 200 (1980) 254.
[11] L. Hansson, M. Glad, C. Hansson, J. Chromatogr. 265 (1983) 37.
[12] P. Martin, B. Leadbetter, I.D. Wilson, J. Pharm. Biomed. Anal. 11 (1993) 307.
[13] E.C. Moore, D. Peterson, L.Y. Yang, C.Y. Yeung, N.F. Neff, Biochemistry 13 (1974) 2904.
[14] X.C. Liu, Wi.H. Scouten, J. Chromatogr. A 687 (1994) 61.
[15] B.M. Brena, F.B. Viera, L. Rydén, J. Porath, J. Chromatogr. 604 (1992) 109.
[16] B.J.B. Johnson, Biochemistry 20 (1981) 6103.
[17] H. Miyazaki, A. Kikuchi, Y. Koyama, T. Okano, Y. Sakurai, K. Kataoka, Biochem. Biophys. Res. Commun. 195 (1993) 829.
[18] J.H. Knox, M.T. Gilbert, US Patent 4 263 268 (1981).
[19] M.T. Gilbert, J.H. Knox, B. Kaur, Chromatographia 16 (1982) 138.
[20] B. Feibush, N.H. Li, US Patent 4 933 372 (1990).
[21] K. Kitahara, Y. Hirai, I. Yoshihama, T. Hanada, K. Nagashima, S. Arai, J. Yamashita, Anal. Sci. 17 (2001) i1225.
[22] B. Beilmann, P. Langguth, H. Häusler, P. Grass, J. Chromatogr. A 1107 (2006) 204.
[23] S. Cárdenas, M. Gallego, M. Valcárcel, Anal. Chim. Acta 402 (1999) 1.
[24] W.J. Dale, J.E. Rush, J. Org. Chem. 27 (1962) 2598.
[25] P.M. Collins, R.J. Ferrier, Monosaccharides, Wiley, Chichester, 1984, p. 41.