dried ($MgSO_4$), and the solvent was evaporated in vacuo. Chromatography (hexanes–ethyl acetate, 4:1) of the residual oil afforded **11** (0.059 g, 81%) as a colorless oil. This ketone (0.052 g, 0.17 mmol) was reduced with L-Selectride (0.21 mmol), following the procedure used for the reduction of compound **15**. After the usual workup, the corresponding alcohol was obtained as a colorless oil (0.048 g, 91%), which was not purified and was carried directly into the next step. The crude alcohol (0.044 g, 0.14 mmol) was acetylated following the same procedure employed for the preparation of **7**. After workup, the crude product was chromatographed (hexanes–ethyl acetate, 4:1) to afford the acetate **12** (0.049 g, 98.2%) as a colorless oil.

Tetrabutylammonium fluoride (0.26 mL, 1 M solution in THF) was added under nitrogen to a solution of acetate **12** (0.045 g, 0.13 mmol) in anhydrous THF (2 mL) at 0 °C. The cold bath was removed when the addition was finished. After 2 h, the solvent was evaporated in vacuo and the crude was chromatographed (chloroform–ethyl acetate, 4:1) to give the lactone **10** (0.018 g, 75%) as a solid; mp and mixture mp 79–81 °C, which presented the same chromatographic and spectroscopic characteristics as that of the lactone obtained starting with the allyl derivative **5**.

Acknowledgment. This research was supported by PHS Grant Al 16943. An MEC/Fulbright Fellowship to M.P.C. and a Consejo Nacional de Investigaciones Cientificas y Tecnicas Argentina Fellowship to L.O.J. are gratefully acknowledged. NMR spectra were obtained through the auspices of the Northeast Regional NSF/NMR Facility at Yale University, which was supported by NSF Chemistry Division Grant CHE 7916210.

Registry No. **1**, 61740-33-8; **2**, 119414-47-0; **3**, 130193-05-4; **4**, 119414-48-1; **5**, 130096-86-5; **6**, 130096-87-6; **7**, 130096-88-7; **8**, 130096-89-8; **9** (isomer 1), 130096-90-1; **9** (isomer 2), 130193-11-2; **10**, 130193-06-5; **11**, 130096-91-2; **12**, 130096-92-3; **13**, 130096-93-4; **14**, 130096-94-5; **15**, 130096-95-6; **16**, 130096-96-7; **17** (1α-OH), 130096-97-8; **17** (1β-OH), 130193-10-1; **18**, 130096-98-9; **19**, 130096-99-0; **20**, 130097-00-6; **21**, 130097-01-7; **22**, 130097-02-8; **23**, 130097-03-9; **24**, 121651-99-8; **25**, 130097-04-0; **26**, 130193-07-6; **27a**, 130193-08-7; **27b**, 130193-09-8; **28** (R = βH), 130097-05-1; **28** (R = αH), 130120-60-4; **29**, 130097-06-2; **30**, 130097-07-3; H_2C=C(OEt)OSi(Me_2)Bu-*t*, 42201-84-3; 3a,6,7,7a-tetrahydro-2-hydroxy-(3*H*,4*H*)-benzofuran-5-one (isomer 1), 130097-08-4; 3a,6,7,7a-tetrahydro-2-hydroxy-(3*H*,4*H*)-benzofuran-5-one (isomer 2), 130193-12-3; 4-allyl-3-(*tert*-butyldimethylsiloxy)cyclopentanol, 130097-09-5; allyltrimethylsilane, 762-72-1; 1,3-butadiene, 106-99-0.

Supplementary Material Available: X-ray crystallographic data for compounds **18**, **22**, and **25** (35 pages). Ordering information is given on any current masthead page.

Racemic Resolution of Free Sugars with Macroporous Polymers Prepared by Molecular Imprinting. Selectivity Dependence on the Arrangement of Functional Groups versus Spatial Requirements[1]

Günter Wulff* and Stephanie Schauhoff

Institute of Organic Chemistry and Macromolecular Chemistry, Heinrich-Heine-Universität Düsseldorf, D 4000 Düsseldorf, F.R.G.

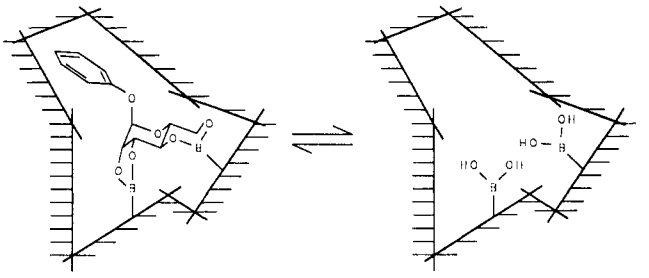
Received February 12, 1990 (Revised Manuscript Received July 11, 1990)

A molecular imprinting procedure was adopted to prepare highly cross-linked polymers for racemic resolution of free sugars. This is the first example illustrating a racemic resolution of free sugars on a support. For this purpose β-D-fructopyranose 2,3:4,5-bis-*O*-((4-vinylphenyl)boronate) **2** and α-D-galactopyranose 1,2:3,4-bis-*O*-((4-vinylphenyl)boronate) **3**, easily prepared from their parent free sugars in a single step, were copolymerized with a large amount of cross-linking agent. After splitting off the respective templates these polymers were used for racemic resolution of the racemates of the templates with separation factors α as high as α = 2.36 in the batch procedures. Surprisingly, polymers prepared from **2** preferably absorb D-fructose from D,L-fructose, but L-galactose from D,L-galactose. Similarly, polymers prepared from **3** preferably absorb D-galactose but L-fructose from the corresponding racemates. From these results and similar studies carried out with mannose derivatives, important conclusions can be drawn with regard to the separation mechanism on polymers prepared by molecular imprinting with templates. The influence of the arrangement of functional groups within the cavities versus the spatial requirements (shape selectivity) on selectivity is discussed in detail. In the examples presented here, the orientation of the functional groups inside the cavity is the dominating factor; shape selectivity is only of secondary importance. These findings offer new possibilities for the construction of selective adsorbents and enzyme-analogue-built catalysts.

Introduction

Several years[2,3] ago we introduced a new synthetic methodology to prepare specific binding sites in cross-linked polymers having a predetermined shape as well as an arrangement of functional groups with a defined steric orientation. For this purpose an imprinting procedure was used with the aid of template molecules. Suitable polymerizable binding groups were linked to a template molecule, and this was copolymerized to form highly cross-linked polymers. Removal of the templates leaves behind cavities

Scheme I. Schematic Representation of the Polymerization of the Template Monomer 1 and the Removal of the Template



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possessing a shape and an arrangement of the functional groups corresponding to that of the template. The maintenance of the stereochemical arrangement of the functional groups as well as the shape of the cavities has been evaluated by molecular recognition abilities of the polymers for the template molecules used for their preparation. Thus, for optically active templates the ability for racemic resolution of the racemate of the template was taken as a measure for the exactness of the shape of the cavity and of the orientation of functional groups within the free cavities.

In case of phenyl α-D-mannopyranoside as the template with two molecules (4-vinylphenyl)boronic acid as the binding sites (see 1 and Scheme I) the resulting polymers showed high selectivity for racemic resolution of the racemate of the template.[2d,4] The separation factor α (ratio of the distribution factors for the D and L compounds) obtained in the batch procedure was as high as 4.5. Furthermore, by using these polymers as chromatographic supports[5] base-line separations were obtained in a short time with a resolution of R_s = 4.3. Besides sugar derivatives, amino acid derivatives, hydroxycarboxylic acids, dialdehydes, and several other classes of compounds have been successfully used as templates by our group.[3] Using this approach it was also possible to locate two functional groups within a distinct distance from each other in a cross-linked polymer[6] and on the surface of silica.[6a,c] Other research groups have utilized this principle of molecular imprinting and have widened the scope of this approach by using a variety of templates.[7] The group of Mosbach[8] has concentrated on the use of noncovalent interactions for fixation of the template during polymerization. In this case, too, complete chromatographic separation of racemates has been achieved.[8b,9]

For racemic resolution of racemates on this type of chromatographic supports in most cases (as with other chromatographic racemic separations) the racemates need to be transformed to specific derivatives. This is particularly true for noncovalent interactions.[8,9] In this case the template (amino acid derivatives) and the substrate to be chromatographed need to be derivatized in order to provide suitable interactions between substrate and binding sites as well as for having rigid substituents of considerable size.[8b] We have now attempted to use underivatized sugars as templates and to separate the racemates of the free sugars directly. This would certainly facilitate the racemic resolution process considerably and has not been achieved until now.

Table I. Preparation of the Polymers[a]

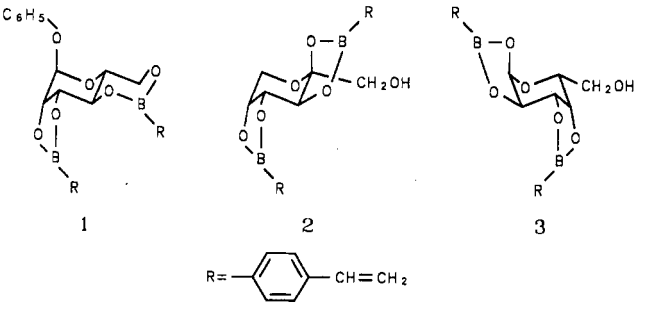
polymer	monomer (template)	wt %	mol %	EGDMA[b] wt %
FP-1	2 (Fruc)	3.7	1.9	96.3
FP-2	2 (Fruc)	7.7	3.9	92.3
FP-3	2 (Fruc)	11.1	5.8	88.9
GP-1	3 (Gal)	3.7	1.9	96.3
GP-2	3 (Gal)	7.7	3.9	92.3
GP-3	3 (Gal)	11.1	5.8	88.9
PMP	1 (Phen-Man)	4.8	2.0	95.2

[a] Monomers were polymerized after addition of 1 mL of THF per gram of monomer mixture and 0.8 mol % 2,2'-azobis(isobutyronitrile), 48 h at 65 °C and afterwards 24 h at 100 °C. In case of FP-1 polymerization was performed 96 h at 65 °C. [b] EGDMA = ethylene glycol dimethacrylate.

Another important question which still remains unsolved in the molecular imprinting procedure is the precise mechanism of molecular recognition. The high selectivity observed is believed on one hand to be mainly due to the shape of the cavity and the binding sites within the cavity which are primarily responsible for the driving force to bring the substrates inside the cavity. On the other hand, molecular recognition could also be due to the spatial arrangement of the functional groups (binding sites) within the cavity. Certainly, the shape of the cavity plays an important role since templates with only a one-point binding generate selective cavities.[7f,10] A recent revelation by Shea and Sasaki[6d] showed that shape selectivity may be the most important factor for molecular recognition. Results presented in this paper lead to the conclusion that in our examples the orientation of the functional groups at the recognition sites is the predominating factor.

Results

Synthesis of the Monomers and Polymers. As templates D-fructose, D-galactose, and phenyl α-D-mannopyranoside were chosen. Reaction of 2 mol of (4-vinylphenyl)boronic acid with 1 mol of D-fructose with azeotropic removal of the formed water yields the new monomer β-D-fructopyranose 2,3:4,5-bis-*O*-((4-vinylphenyl)boronate), **2**. It is known with other boronic acids that unsubstituted D-fructose yields 2,3:4,5-diboronates leaving the OH group at C-6 free.[11] NMR and mass spectral data confirm the assumed structure **2** to be correct.



1 2 3

More complicated was the situation in case of the reaction of (4-vinylphenyl)boronic acid with D-galactose. It is well known that reaction of D-galactose with alkyl- or arylboronic acids yields a mixture of at least two di-

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Table II. Properties of the Polymers

polymer	splitting percentage	inner surface area, m^2/g	swelling ability in methanol	enantiomeric enrichment, %	separation factor α in 98% methanol[a]
FP-1	72	403	1.59	4.9	1.47 (1.40)[b]
FP-2	66	308	1.56	6.0	1.63
FP-3	67	248	1.68	5.4	1.54
GP-1	80	395	1.55	2.2	1.19 (1.38)[b]
GP-2	64	316	1.55	2.4	1.22
GP-3	62	266	1.63	2.0	1.18
PMP	99	192	1.75	10.3	2.96

[a] Equilibration of the polymers (freed from the templates) with the racemate of the template used. Equilibration at room temperature in 98% methanol under conditions that half of the racemate is bound to the polymer. Separation factor α is calculated (from the enantiomeric enrichment in solution and at the polymer) as the ratio of the distribution coefficients of D and L compounds between polymer and solution. [b] Equilibration at 60 °C.

Table III. Properties of Polymers Prepared from 2 in Relation to Polymerization Time[a]

polymer	polymerization time, h	splitting percentage	inner surface area, m^2/g	swelling ability in methanol	recovering percentage[b]	enantiomeric enrichment, %	separation factor α
FP-1	96	72	403	1.59	49	4.9	1.47
FP-1					29	8.7	2.36[c]
FP-4	48	85	350	1.93	n.d.	4.8	1.46[c]
FP-5	24	87	380	1.75	48	4.5	1.48
FP-5					22	6.3	2.19[c]
FP-6	9	92	371	1.73	43	5.4	1.63
FP-7	6	93	374	2.09	39	5.4	1.55
FP-8	4	95	367	1.79	37	5.0	1.50

[a] Composition of the monomeric mixture was the same as for FP-1 (see Table I). Polymerization was performed at 65 °C for the time given in the table. Equilibration of the polymers with D,L-fructose in methanol with 2% water at room temperature. [b] Percentage of cavities which are newly covered by the template during equilibration. [c] The equilibration in this case was performed in pure methanol at room temperature under which conditions around 75% of the racemate is bound to the polymer.

boronates.[12] The structures of these compounds were not elucidated. Investigation of the reaction product of D-galactose with (4-vinylphenyl)boronic acid by ^1H NMR and mass spectroscopy revealed the presence of two main products in a ratio of 9:1. By comparison of ^1H NMR data of the known 1,2:3,4-diisopropylidene-α-D-galactopyranose and 1,2-isopropylidene-α-D-galactopyranose 3,4-(phenylboronate)[13] with that of the major component of this reaction product, its structure could be ascribed to be α-D-galactopyranose 1,2:3,4-bis-*O*-((4-vinylphenyl)boronate), **3**. It was not possible to isolate the minor component in pure state since transesterification reactions occurred during purification procedures. Therefore the compound containing 90% of **3** was directly used as such for the preparation of the polymers.

Monomer **1** has been prepared according to literature procedures.[4]

Polymers were prepared in a manner as described earlier[4] using ethylene glycol dimethacrylate as the cross-linking agent. A typical polymerization recipe consists of 1.9–5.8 mol % of either of the template monomers **1**, **2**, or **3** and of the cross-linking agent. Macroporous polymers were obtained by polymerizing in presence of 1 mL of THF per gram of monomeric mixture. Detailed experimental procedures dealing with polymer preparation and isolation are described earlier[4] and monomeric composition data are summarized in Table I.

Properties of the Polymers. In all cases macroporous polymers were obtained (see Table II). Inner surface areas of the polymers were found to lie between 192 and 403 m^2/g, which were dependent on the degree of cross-linking. Template molecules could be split off to the extent of 62–99% from these polymers. The nonremovable templates are hidden in highly cross-linked portions of the polymer. The swellability of these polymers does not differ considerably. The polymers swelled in methanol to about 155–175% of the volume in dry state. These data are very similar to the earlier reported polymers obtained with other templates.[2,4]

The selectivity was determined by equilibration of the polymers with the racemate of its template, i.e. with D,L-fructose, D,L-galactose, and phenyl α-D,L-mannoside, respectively, in the batch procedure. The reaction conditions were adjusted in such a manner that half of the racemate is bound to the polymer. The selectivity was expressed as the separation factor α, i.e. the ratio of the distribution coefficients of the D and the L form. The separation factors α for polymers FP-1–2 using D,L-fructose as substrate were found to lie between 1.47 and 1.63 and for polymers GP-1–3 using D,L-galactose between 1.18 and 1.22, and for polymer PMP using phenyl α-D,L-mannopyranoside at 2.96. Similar to earlier results using other templates, in the present case highest selectivity was found for the polymer FP and GP with 7.7 wt % (3.9 mol %) of the template in the monomeric mixture. The selectivity was dependent on the temperature of equilibration in the batch procedure. The polymer properties and their selectivity behavior are summarized in Table II.

The selectivity behavior of the polymers was also found to be influenced by the polymerization conditions. Table III illustrates the influence of different polymerization times on enantiomer selectivity. With decreasing polymerization time the splitting percentage increases, suggesting greater accessibility of the chiral cavities within the highly cross-linked part of the matrices. With shorter polymerization times less cross-linking is expected. At the same time the amount of substrate taken up during equilibration is reduced. This is possibly due to the fact that less cross-linking leads to flexible networks, and some of the chiral cavities loose their shape and cannot take up the substrate.

As a result of these two opposing influences there is an optimum time of polymerization for selectivity at around 9 h of polymerization.

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Table IV. Results of the Equilibration with Different Racemates

polymer	template	racemate	sugar enriched at the polymer	enantiomeric enrichment, %	separation factor α[a]
GP-1	D-galactose	D,L-galactose	D-galactose	2.2	1.19
GP-1	D-galactose	D,L-fructose	L-fructose	2.6	1.25
GP-1	D-galactose	D,L-mannose	-	0.0	1.00
FP-6	D-fructose	D,L-fructose	D-fructose	5.4	1.63
FP-6	D-fructose	D,L-galactose	L-galactose	2.1	1.17
FP-6	D-fructose	D,L-mannose	-	0.0	1.00
PMP	phenyl α-D-mannopyranoside	phenyl α-D,L-mannopyranoside	phenyl α-D-mannopyranoside	10.3	2.96
PMP	phenyl α-D-mannopyranoside	D,L-mannose	D-mannose	nd	1.60[b]
PMP	phenyl α-D-mannopyranoside	D,L-fructose	D-fructose	3.0	1.34
PMP	phenyl α-D-mannopyranoside	D,L-galactose	-	0.0	1.00

[a] Equilibration as in Table II at room temperature. For the calculation of α from the ratio of the distribution coefficients always the distribution coefficient of that enantiomer is set in the numerator that is enriched at the polymer. This means for a better comparison no α values are below 1.00. [b] Separation factor α was determined by chromatography.[18]

With lower loading of the polymer during equilibration the selectivity is considerably enhanced. α values up to 2.36 in case of FP-1 are obtained.

Inverse Selectivity of the Polymers. In order to elucidate the molecular recognition abilities of the polymers for different racemates the most selective polymers GP-1 (with D-galactose as template), FP-6 (with D-fructose as template), and PMP (with phenyl α-D-mannopyranoside as template) were individually equilibrated with D,L-galactose, D,L-fructose, and D,L-mannose each (see Table IV). The study gives rise to the interesting result that while the polymer imprinted with D-galactose preferably absorbs D-galactose from the racemate, on the contrary it absorbs the L enantiomer from the racemate of D,L-fructose and shows no selectivity for D,L-mannose. On the other hand FP-6 absorbs the D enantiomer from D,L-fructose but the L enantiomer from D,L-galactose, and D,L-mannose is again not separated at all in this case. Interestingly, the inverse selectivity on GP-1 for D,L-fructose is even more pronounced than for its own template. The polymer PMP prepared with phenyl α-D-mannopyranoside is also selective for the racemic resolution of the free sugar racemate D,L-mannose. Whereas no selectivity was found for the resolution of D,L-galactose, D,L-fructose can be separated with D-fructose being preferably incorporated on PMP (α value 1.34).

Discussion

The free sugars D-fructose and D-galactose have been used as templates and transformed to the diboronates **2** and **3**. These sugars have been chosen because the racemic resolution of their enantiomers is of practical interest. L-Fructose is considered as a sugar substitute in diets, and synthetic attempts have been made to prepare this sugar.[14] L-Galactose occurs in nature, in several cases in mixture with D-galactose. In both cases the detection of optical purity or of the ratio of the enantiomers is important. Until now only derivatized sugar enantiomers have been separated by capillary gas chromatography.[15] Polymers from monomer **1** with phenyl α-D-mannopyranoside as template have been prepared earlier.[4]

From the polymers obtained with the template monomers **1**, **2**, and **3** the templates, i.e. phenyl α-D-mannopyranoside, D-fructose, and D-galactose, respectively, could be split off to a high percentage. The polymers contained free chiral cavities with two boronic acids per cavity (see Schemes I and II). Considering the similarity of the shape of the two enantiomers and the existence of a mutarotational equilibrium the selectivity shown for the new polymers GP-1–3 and FP-1–8 for racemic resolution in the batch procedure was rather high (see Tables II and III).

Scheme II. Schematic Representation of the Polymerization of the Template Monomer 2 as Well as Removal and Uptake of D-Fructose

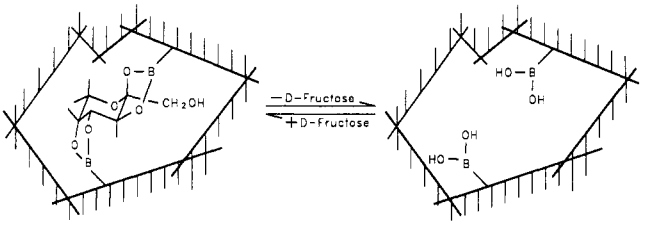

Table V. Composition of Mutarotational Equilibrium of D-Fructose[16] and D-Galactose[17] in Water

	composition in %			
	β-D-pyranose	α-D-pyranose	β-D-furanose	α-D-furanose
D-fructose at 25 °C	73	2	20	5
D-fructose at 60 °C	58	3	30	9
D-galactose at 31 °C	64	29	4	3
D-galactose at 71 °C	56	34	4.5	5.5

The selectivity compared to equilibrations with phenyl α-D,L-mannopyranoside on PMP should be lower. Fructose as well as galactose exists in water and in methanol in a mutarotational equilibrium. Table V shows the ratio of the isomers for D-fructose[16] and D-galactose[17] in water. In methanol we found similar values. This implies that the correct conformer corresponding to the template is present only to a certain degree, in case of D-fructose 73% and in case of D-galactose only 29% at room temperature. Therefore during binding the equilibrium has to be shifted toward the correct conformer. This should lead to a lower selectivity, especially in the case of D-galactose, and is consistent with observed results. The mutarotational equilibrium is strongly temperature dependent. With increasing temperature while the percentage of the β-D-fructopyranose is decreasing, that of α-D-galactopyranose somewhat increases. In accordance with this fact the selectivity in case of D,L-fructose decreases, while the selectivity of D,L-galactose increases at higher temperature (see Table II). This effect is overlapping with another factor, since the selectivity generally increases at higher temperature due to faster mass transfer.[5b,c]

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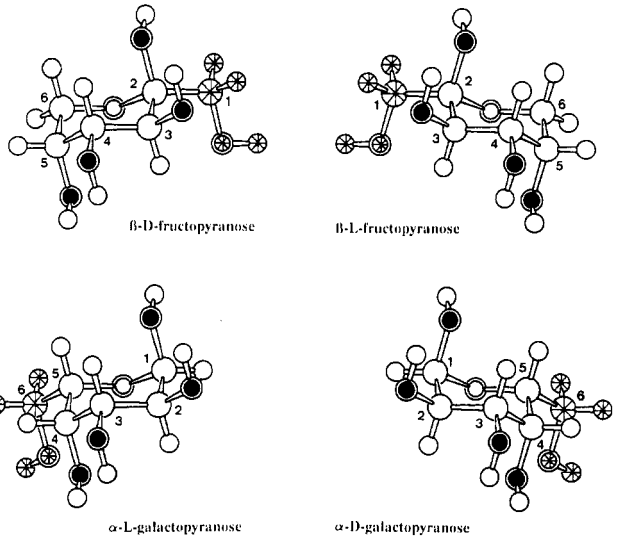

Figure 1. Ball-and-stick models of the preferred conformations of the enantiomers of fructose and galactose. In the same line the mirror images are shown. Each two formula being vertically arranged have the same spatial arrangement of the OH groups responsible for interaction with the boronic acids in GP and FP (marked black). The hydroxymethyl groups giving the two vertical molecules a different shape are marked with spokes. Oxygen is represented by a double circle. The models represent idealized structures. The coordinates for the atoms were taken from X-ray structures. Plotting was effected with the Schakal program.

Polymers imprinted with D-fructose, D-galactose, and phenyl α-D-mannopyranoside as templates show a surprising behavior when equilibrated with other sugar racemates (see Table IV). The polymer imprinted with D-fructose binds preferably L-galactose from D,L-galactose racemate and that imprinted with D-galactose binds preferably L-fructose. D,L-Galactose is separated with nearly the same enantiomeric enrichment on a polymer imprinted with D-galactose (GP-1) as on a polymer imprinted with D-fructose (FP-6), however, with inverse selectivity. In case of D,L-fructose the inverse selectivity on GP-1 is less than the selectivity on its "own" polymer FP-6.

D,L-Mannose on the contrary is not separated on both polymers. This racemate is separated on polymer PMP prepared using phenyl α-D-mannopyranoside as the template (i.e. from template monomer 1).[18] Chromatographic separations show that D-mannose is the more retarded enantiomer and separation factors α of around 1.60 can be obtained. Polymer PMP is also capable of separating D,L-fructose while for other sugar racemates like D,L-glucose, or D,L-galactose, no selectivity was observed using PMP.

The inverse selectivity observed on polymers prepared from D-fructose (FP-6) and from D-galactose (GP-1) can be explained by inspecting molecular models of the preferred conformations of the free sugars. Figure 1 shows ball-and-stick models of β-D- and β-L-fructopyranose as well as of α-D- and α-L-galactopyranose. Since binding occurs under thermodynamic control the most stable diboronates will be formed. In the case of the galactose this is from the α-D- and α-L-galactopyranose. Even if this form is only existent in 29% in the mutarotational equilibrium the equilibrium will be shifted during binding similarly as in case of the formation in solution. It can be seen that the spatial arrangements of the hydroxyl functions responsible for the interaction with the boronic acid binding sites at the polymer (oxygens marked black) is identical

(18) See also results of a preliminary report, in ref 5d.

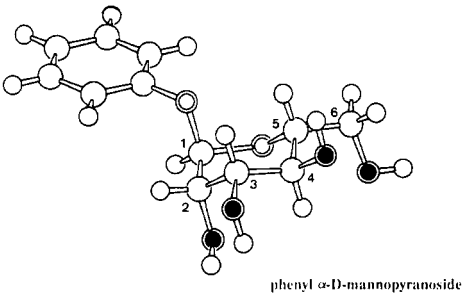

Figure 2. Representation as in Figure 1.

for D-galactose and L-fructose as well as for D-fructose and L-galactose. For both the enantiomers of mannose, on the contrary, the hydroxyl groups possess a different steric arrangement.

On the other hand, polymer PMP prepared from 1 with phenyl α-D-mannopyranoside as template has the appropriate orientation of the boronic acids in the cavity (Scheme I) to accommodate also the free D-mannose. For the equilibration of D-fructose on FP-1–8 apparently the hydroxyl groups 2,3 and 4,5 are used to form the boronate esters (see Scheme II) as is the case in the template monomer 2. These hydroxyl groups cannot be used to form a boronate diester in cavities of polymer PMP (see Scheme I) since they possess a different spatial arrangement. By comparison of the molecular models of β-D-fructopyranose (in Figure 1) with phenyl α-D-mannopyranoside (Figure 2) it is evident that the hydroxyl groups 2,3 and 4,6 in the mannoside possess the same spatial arrangement as those in 1,3 and 4,5 of the β-D-fructopyranose. Therefore D-fructose can be bound on polymer PMP, and this polymer shows selectivity in racemic resolution of D,L-fructose. The steric arrangement of the diol groupings of D,L-galactose or D,L-glucose are such that no selective two-point binding in PMP is possible in these cases.

Conclusions

The findings of this study as discussed above have a number of important consequences for the concept of molecular imprinting with templates:

(a) They present a deeper insight to the question pertaining to the origin of the selectivity for racemic resolution. The chiral construction of the cavities is stabilized by means of the cross-linking points in the polymer chains. This type of chirality can arise from the configuration of the cross-linking points as well as from asymmetric conformations of the polymer chains which are stabilized by cross-linking.[19] The chiral configurations of the linear portions of the chains are not expected to contribute to the asymmetry of the cavity since no asymmetric cyclopolymerization[20] is possible for the examples presented in this paper.

The results on equilibration with different racemates clearly suggest that for selectivity, at least for the present cases, the orientation of the functional groups inside the cavity is primarily responsible for molecular recognition. Shape selectivity is only of secondary importance. A comparison of the structure of β-D-fructopyranose and α-L-galactopyranose, which are both preferably taken up by FP-6, shows that they do not differ (in their preferred conformation) in the orientation of the interacting hydroxyl groups (marked black in Figure 1) but the hydroxy

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methyl groups (marked with spokes in Figure 1) are at different places in the molecule. This renders these compounds to possess considerably different shapes. Because of this fact the selectivity did not change but was only reduced to some extent. The same is true if phenyl α-D-mannopyranoside as the template is compared with D-mannose and D-fructose both of which can be incorporated in polymer PMP. The large phenyl substituent in the mannoside alters the shape quite considerably (compare β-D-fructopyranose in Figure 1 with Figure 2). Still only the extend of selectivity is reduced on equilibration with D,L-mannose and D,L-fructose on polymer PMP.

(b) If the orientation of the interacting groups inside the cavity is the principal factor governing the selectivity, other molecules than the templates but with a similar orientation of their functional groups can be separated. In this case it is possible to prepare a well-defined monomer as in case of 1 from phenyl α-D-mannopyranoside and separate D,L-mannose or D,L-fructose afterwards. Furthermore the concept of inverse selectivity might be of importance under the situation where pure enantiomers of the racemate in question are not easily accessible.

(c) In contrast to imprinting with noncovalent interactions[8,9] in our systems the functional groups are present in a defined number and orientation per active center. With noncovalent interactions an excess (usually 4-fold[8b]) of binding sites need to be incorporated to obtain reasonable selectivity. This implies that only a quarter of the functional groups is arranged in an oriented manner, the rest being irregularly arranged all over the polymer. This may be an important shortcoming for the construction of active centers behaving in a catalytic mode. With covalent interactions certain functionalities can be introduced in a defined number and orientation into the active site, and these groups can be transformed to other functionalities. This is especially true for the boronic acid moiety that can be easily replaced by a variety of other functional groups.[21]

(d) Not only is it possible to prepare active centers with a defined orientation of functional groups and with a particular shape to selectively bind certain substances or catalyze certain reactions, it is also possible to introduce additional pockets or niches at the active centers. This can be achieved by attaching bulky substituents at the template molecule. Thus, in case of 1 the phenyl ring provides additional space in the active centers (compare Schemes I and II). This principle can find application in the construction of catalytically active polymers.

Experimental Section

General Procedure. Elemental analyses were performed in the microanalytical laboratories of the Faculty of Natural Sciences of the Heinrich-Heine-University of Düsseldorf. ^1H and ^{13}C NMR spectra were recorded on Varian EM 390 and VXR 300 spectrometers. Optical rotations were measured with a Perkin-Elmer Model 241 polarimeter. Specific inner surface areas (BET) were measured with a Ströhlein Areameter II. Quantitative chromatographic determinations of the free sugars were carried out by HPLC using a 30 × 0.8 cm column filled with Aminex A-7/Ca^{2+} with eluent water at 80 °C.

Preparation of the Sugar Monomers: General Procedure. A 2-g (11-mmol) sample of sugar was esterified with 2.9 g (7.4 mmol) of tris(4-vinylphenyl)boroxine[2c,22] in 30 mL of dioxane solution by azeotropic distillation (bp 88 °C) of the water formed during the reaction. When no additional water was formed the solvent was removed in vacuo.

β-D-**Fructopyranose 2,3:4,5-bis-*O*-((4-vinylphenyl)boronate), 2**: recrystallization from CH_2Cl_2/hexane; yield 3.3 g (81%); mp 125–126 °C; $[\alpha]^{20}_D$ = −34.4° ($CHCl_3$, c = 1.0); ^1H NMR ($CDCl_3$) of the protons in the sugar part δ 2.28 (br s, 1 H at OH), 3.63 (d, $J_{1,1'}$ = 12 Hz, 1 H at C-1), 3.81 (d, 1 H′ at C-1), 3.72 (dd, $J_{6,6'}$ = 13 Hz, $J_{6,5}$ = 2 Hz, 1 H at C-6), 3.93 (d, 1 H′ at C-6), 4.64 (dd, $J_{4,5}$ = 8.5 Hz, 1 H at C-5), 4.82 (d, $J_{3,4}$ = 2.4 Hz, 1 H at C-3), 5.08 (dd, 1 H at C-4) [^1H NMR reported for β-D-fructopyranose 2,3:4,5-di-*O*-(phenylboronate):[11] δ 3.60 (d, $J_{1,1'}$ = 12 Hz, 1 H at C-1), 3.81 (d, 1 H′ at C-1), 3.75 (dd, $J_{6,6'}$ = 13 Hz, $J_{6,5}$ < 1 Hz, 1 H at C-6), 3.93 (d, 1 H′ at C-6), 4.64 (dd, $J_{4,5}$ = 8.4 Hz, 1 H at C-5), 4.76 (d, $J_{3,4}$ = 2.4 Hz, 1 H at C-3), 5.07 (dd, 1 H at C-4)]. Anal. Calcd for $C_{22}H_{22}B_2O_6$: C, 65.40; H, 5.49. Found: C, 65.40; H, 5.55.

α-D-**Galactopyranose 1,2:3,4-Bis-*O*-((4-vinylphenyl)boronate), 3.** The crude product obtained from the reaction contained 90% of the compound 3 as indicated by NMR. The remaining 10% was due to of another isomer, probably α-D-galactopyranose 1,2:4,6-bis-*O*-((4-vinylphenyl)boronate). During repeated recrystallizations transesterification reactions occurred leading to a mixture of four different isomers which could not be separated. For this reason the esterification was performed for a minimum period of time and the crude product containing 90% 3 was used directly without further purification.

^1H NMR in $CDCl_3$ of the protons in the sugar part of the main product: δ 5.99 (d, $J_{1,2}$ = 6 Hz, 1 H at C-1), 4.81 (dd, $J_{2,3}$ = 2.2 Hz, 1 H at C-2), 5.11 (dd, $J_{3,4}$ = 8.6 Hz, 1 H at C-3), 4.74 (dd, $J_{4,5}$ = 2.0 Hz, 1 H at C-4), 3.75 (m, 1 H at C-5), 3.88 (m, 2 H at C-6), 2.13 (br s, 1 H at O-6). For comparison of the coupling constants the ^1H NMR in C_6D_6 of 6-desoxy-α-L-galactopyranose 1,2:3,4-di-*O*-(phenylboronate) is given:[11] δ 5.67 (d, $J_{1,2}$ = 5.9 Hz, 1 H at C-1), 4.35 (dd, $J_{2,3}$ = 2.2 Hz, 1 H at C-2), 4.84 (dd, $J_{3,4}$ = 8.1 Hz, 1 H at C-3), 3.98 (dd, $J_{4,5}$ = 1.9 Hz, 1 H at C-4), 4.74 (dq, $J_{5,6}$ = 6.4 Hz, 1 H at C-5), 1.22 (d, 3 H at C-6). Proton of the minor product δ 6.02 (d, J = 6 Hz, 1 H at C-1). Due to overlap of signals resonance of the other protons of the minor product cannot be unambiguously identified. Anal. Calcd for $C_{22}H_{22}B_2O_6$: C, 65.40; H, 5.49. Found: C, 65.70; H, 5.12.

Preparation of the Polymers. The preparation and subsequent working up procedures of the polymers were carried out according to our previous procedure.[2c,4a] Details are given in Tables I and III.

Characterization of the Polymers. The details of methods for the determination of the inner surface area, the swelling ability, and the splitting percentage have been reported elsewhere.[2c,4a]

For the equilibration experiments in the batch procedure 1 g of polymer was stirred at room temperature for 48 h with a solution of the racemate (c = 0.5 mg/mL) in methanol containing 2% of water. The amount of racemate usually corresponded to 80% of the free cavities in the polymer (calculated from the splitting percentage). Afterwards the polymer was filtered off and the sugar bound to the polymer was split off by treatment with methanol/water, 1:1. The sugar content in the filtrate and at the polymer was determined by HPLC using D-glucose as internal standard. Measurement of optical rotations of the fractions from solution and from the polymer, respectively, yielded the enantiomeric excess and can be used to calculate the separation factor α.[2c]

The optical rotation is measured in aqueous solution after a time when the mutarotational equilibrium has been reached. In the calculation of the enrichment of the antipodes the optical rotation of the mutarotational equilibrium of the pure antipodes is used as reference.

Acknowledgment. We thank Fonds der Chemischen Industrie and Deutsche Forschungsgemeinschaft for financial support.

Registry No. 1, 99473-34-4; 2, 130613-23-9; 3, 130613-24-0; PMP, 108278-80-4; FP, 130613-25-1; GP, 130613-26-2; EGDMA, 97-90-5; tris(4-vinylphenyl)boroxine, 16396-62-6; DL-galactose, 39665-52-6; DL-fructose, 6035-50-3; DL-mannose, 40866-07-7; D-galactose, 59-23-4; L-fructose, 7776-48-9; D-fructose, 57-48-7; L-galactose, 15572-79-9; D-mannose, 3458-28-4; phenyl α-DL-mannopyranoside, 104759-98-0; phenyl α-D-mannopyranoside, 21797-50-2.

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