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Chiroselective Re-binding of Saccharides to the Fibrous Aggregates Prepared from Organic Gels of Cholesterylphenylboronic Acid

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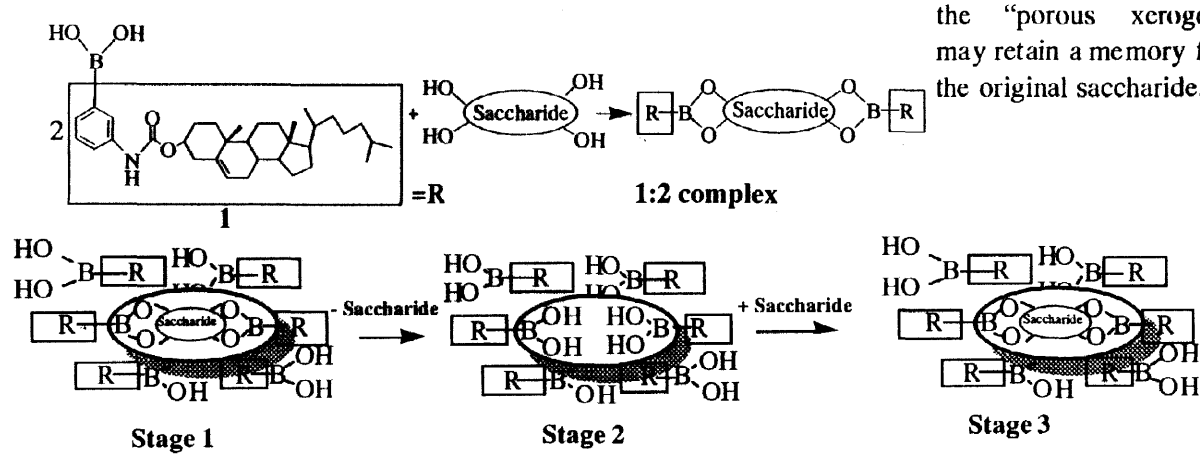
Abstract: The xerogel fibers prepared from cholesterylphenylboronic acid or its D- or L-xylose complexes show the chiral discrimination ability in the re-binding of saccharides and partially retain the memory for the original imprinted saccharide. The novel findings indicate that the sol-gel phase transition in the organic gel is utilizable to the chiral discrimination and even to the molecular imprinting.

Cholesterol is a potential natural product useful as chiral building-blocks for designing host molecules, liquid crystals, molecular assemblies, *etc.*[1,2] The rigid, chiral skeleton provides an excellent platform on which it becomes possible to build or design a variety of functionalized systems.[1] Weiss,[3,4] Terech,[5] and we[6-8] have currently been interested in cholesterol derivatives containing an appropriate substituent coupled to the C-3 OH group, which act as intriguing gelators of organic fluids. Of particular interest among those gelators is a family of saccharide complexes with the cholesterylphenylboronic acid (**1**)[8]: the 1:2 saccharide/**1** complexes efficiently gelatinize several organic fluids and the gelation properties such as the sol-gel phase-transition temperature, the xerogel fiber structure, the gel stability difference between the D- *vs.* L-complexes, *etc.* are changeable by the saccharide structure acting as a central building-block of the gelator.[8] From the thermodynamic and spectral studies, it has been established that the gel fibers are more or less crystal-like and are scarcely wetted by solvent molecules.[7,9] These results have stimulated us to apply the xerogel fibers of **1** to a "host" for chiral saccharide recognition: *i.e.*, the boronic acid groups arranged on the helical xerogel fibers should selectively bind D- or L-saccharides. Furthermore, if the saccharide can be extracted out of the fibers without destroying the xerogel structure, the "porous xerogel" may retain a memory for the original saccharide.



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The preparation of the 1:2 saccharide/**1** complexes was described previously.[8,10] When they were dissolved in organic solvents by heating and then cooled slowly to room temperature, the solutions were gelatinized. The SEM picture of a xerogel image prepared from the D-xylose·$\mathbf{1}_2$ complex is shown in Figure 1. It is seen from this picture that the xerogel consists of fibrous structure with a 20 ~ 30 nm diameter. This implies that the surface area useful for the re-binding of saccharides is very extensive.

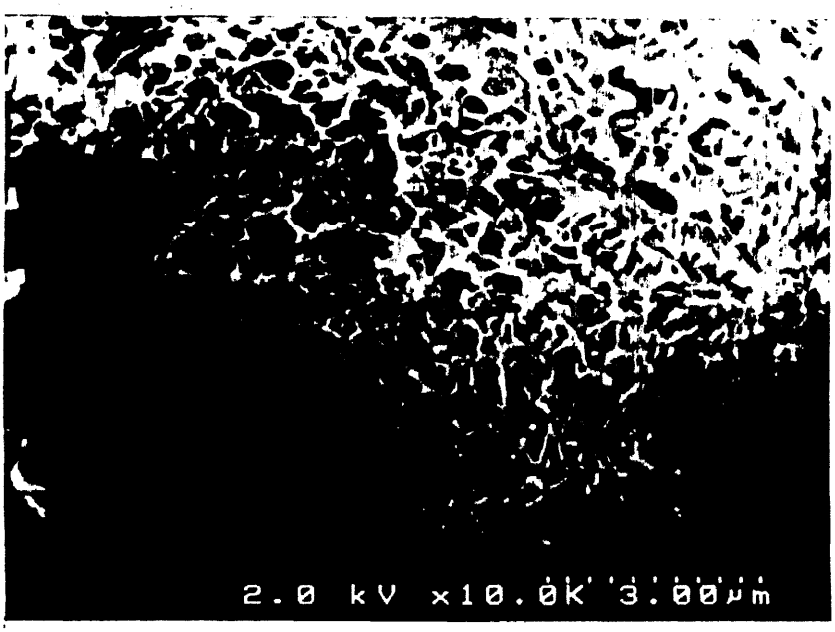

Figure 1. SEM picture of a xerogel obtained from D-xylose·$\mathbf{1}_2$(5.0 wt%) in CCl_4

Here, we chose the benzene gels of the D- or L-xylose·$\mathbf{1}_2$ complexes for the evaluation of the selective saccharide re-binding, because their benzene solutions were readily gelatinized and the frozen sample could be conveniently concentrated to dryness. It is known that L-xylose·$\mathbf{1}_2$ features the higher cohesion than D-xylose·$\mathbf{1}_2$ in their aggregation properties.[8,10] Careful observation of these two benzene gels revealed that less cohesive D-xylose·$\mathbf{1}_2$ forms the very stable, homogeneous gels whereas the gel containing more cohesive L-xylose·$\mathbf{1}_2$ is somewhat cloudy and sometime affords the precipitate. We thus used a mixture of **1** (2 mol) and L-xylose·$\mathbf{1}_2$ (1 mol) to obtain the homogeneous gel.

In Stage 1, the benzene solution (5.0 wt% gelator) was gelatinized and the xerogel was obtained by freeze-drying. In Stage 2, the xerogel was washed with aqueous 15 vol% acetic acid solution for 2 days and then water-methanol (1:1 wt/wt) for 4 days at room temperature. The content of the residual xylose in the "porous xerogel" was determined by a ^{1}H NMR spectroscopic method (for the detail of the method see Ref. 10). In Stage 3, the "porous xerogel"(10 mg) was finely powdered and dispersed in a water-methanol (1:1 wt/wt) solution (1.0 ml) containing the re-binding saccharide (0.10 mol dm^{-3}). After stirring for 40 h at room temperature, the xerogel was recovered by filtration. The amount of the re-bound saccharide was determined by a ^{1}H NMR spectroscopic method.[10] We confirmed that in Stages 2 and 3 neither **1** nor L-xylose·$\mathbf{1}_2$ is not solubilized into solvent media. The results are summarized in Table 1.

From examination of Table 1, one can raise several intriguing recognition abilities of this cholesterol gel system. Firstly, even in the **1** gel prepared in the absence of saccharides L-xylose is bound more efficiently than D-xylose (Entries 1 and 2). This implies that basically, the boronic acid groups arranged on the **1** gel fiber have the chiral recognition ability. Secondly, the re-binding ability of the mixture gels is largely dependent upon the original xylose (Entries 3-6). When the original xylose is D-isomer, the

amount of the re-bound xylose is similar between D-isomer and L-isomer. In contrast, when the original xylose is L-isomer, L-xylose is re-bound 4 times more efficiently than D-xylose. The result indicates that D-xylose rather disorders the chiral gel structure and loses its own "memory" whereas L-xylose constructs the oriented structure suitable to the re-binding of the L-isomer used as the template. Thirdly, the "porous xerogel" prepared only from D-xylose·$\mathbf{1}_2$ shows the slightly higher affinity with L-xylose than with D-xylose (Entries 7 and 8). These results consistently support the view that as already observed in related systems,[8,10] the helical structure of **1** is more complementary to L-xylose rather than to D-xylose. Thus, L-xylose·$\mathbf{1}_2$ (used as a mixture with **1**) can provide the well-ordered gel structure which can differentiate L-isomer from D-isomer (Entries 5 and 6).

Table 1. Selectivity for the re-binding of D- and L-xylose

Entry	Template saccharide	Stage 1[1]	Stage 2[2]	Xylose for re-binding	Stage 3[3]	Re-binding		
						Increase[4]	Ratio[5]	L/D[6]
1	None	0	0	D	18	18	18	
2	None	0	0	L	24	24	24	1.3
3	D-Xylose	50	29	D	42	13	18	
4	D-Xylose	50	29	L	44	15	22	1.2
5	L-Xylose	50	28	D	38	10	14	
6	L-Xylose	50	28	L	70	42	58	4.1
7	D-Xylose	100	4	D	22	18	19	
8	D-Xylose	100	4	L	28	24	25	1.3

1) Stage 1: the percentage of saccharide to host in the gel phase.

2) Stage 2: the percentage of saccharide to host after washing: the relative error is within 5 % of the indicated values.

3) Stage 3: the percentage of saccharide to host after re-binding for 40 h: percentage = xylose·$\mathbf{1}_2$ / (2×1 + xylose·$\mathbf{1}_2$)×100%. The relative error is within 10 % of the indicated values.

4) Increase: Stage 3 - Stage 2.

5) Ratio: the ratio of re-bound saccharide to empty host (Stage 2): re-binding ratio = (increase) / (100 - Stage 2).

6) L/D: the ratio of re-bound saccharides.

The re-binding selectivity of the "porous xerogel" was tested for 6 different monosaccharides. D-Isomers were used as re-bound saccharides except xylose. In our previous study,[8,10] these complexes were characterized by reflectance wavelength in the cholesteric liquid crystal (mixture of cholesteryl nonanoate and cholesteryl chloride). Reflectance wavelengths for the complexes of D-mannose, L-xylose, D-fructose, D-galactose, and D-lyxose caused a blue shift, indicating that their structures are complementary to the cholesterol helical groove.[10] On the other hand, the complexes of D-glucose and D-xylose caused a red shift, indicating that their structures are not complementary to it. The results shown in Table 2 well agreed with this trend: that is, the former saccharides compatible with the cholesterol helical groove are preferably bound to the latter saccharides incompatible with it.

In conclusion, the present study demonstrated for the first time that the xerogels prepared from **1** and xylose show the chiral discrimination ability and partially retains the "memory" for the original imprinted saccharide. The selectivity is originated from the crystal-like aggregation phase of the present gelators. The "memory" imprinted in the gel fibers should be readily erased by the gel-to-sol phase transition. We thus believe that further elaboration of the present sol-gel system would eventually lead to a novel and

more generalized reversible memory-imprinting system utilizing the phase transition phenomena.

Table 2. Selectivity for the re-binding of monosaccharides

Entry	Template saccharide	Stage 1[1]	Stage 2[2]	Saccharide for re-binding	Stage 3[3]	Re-binding		
						Increase[4]	Ratio[5]	L/none[6]
1	None	0	0	D-Mannose	3	3	3	
2	L-Xylose	50	31	D-Mannose	9	9	12	4.1
3	None	0	0	D-Fructose	21	21	21	
4	L-Xylose	50	31	D-Fructose	10	10	15	0.7
5	None	0	0	L-Xylose	15	15	15	
6	L-Xylose	50	31	L-Xylose	65	34	50	3.4
7	None	0	0	D-Galactose	21	21	21	
8	L-Xylose	50	31	D-Galactose	15	15	22	1.1
9	None	0	0	D-Glucose	4	4	4	
10	L-Xylose	50	31	D-Glucose	0	0	0	0.0
11	None	0	0	D-Lyxose	25	25	25	
12	L-Xylose	50	31	D-Lyxose	15	15	20	0.8

1)~5) For the details of each column see footnotes to Table1.

3) Stage 3: the percentage of saccharide to host after re-binding for 13 h.

6) L/none: the ratio of re-bound saccharides between L-xylose-template and none-template.

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