Bull. Chem. Soc. Jpn., 70, 699—705 (1997)

A Novel Sugar Sensing System Designed with a Cooperative Action of a Boronic-Acid-Appended Zinc Porphyrin and a 3-Pyridylboronic Acid Axial Ligand

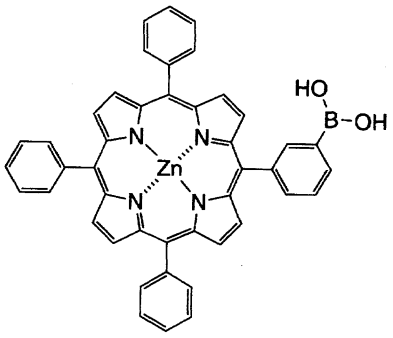
Masayuki Takeuchi, Hideomi Kijima, Itaru Hamachi, and Seiji Shinkai*

Department of Chemical Science & Technology, Faculty of Engineering, Kyushu University, Fukuoka 812

(Received October 17, 1996)

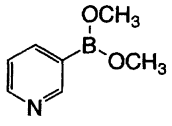
The cooperative action of two boronic acids is indispensable to the selective binding of saccharides in aqueous solution and the binding process can be spectrophotometrically monitored by using porphyrins as a chromophoric probe. It is not so easy, however, to synthesize porphyrins that satisfy these prerequisites, i.e., porphyrins bearing two appropriately-arranged boronic acid groups within a molecule. In this paper, we report that such a diboronic-acid-based porphyrin receptor can be easily designed by utilizing the self-assembling nature of a Zn(II) porphyrin and an axial ligand: That is, a mixture of boronic-acid-appended Zn(II) porphyrin (**1-Zn**) and 3-pyridylboronic acid (**2**) self-organizes to create a novel diboronic acid system for saccharide (S) recognition. Thus, the **1-Zn·2**·S ternary complexes give the CD spectral pattern inherent to saccharide absolute configuration. The present study is a new example for sugar sensing using a boronic acid-porphyrin self-assembly system.

The specific interaction between phenylboronic acids and saccharides or related compounds has been attracting increasing attention as a novel force for sugar recognition in an aqueous system.[1—5] Since one phenylboronic acid reacts with two OH groups to form a cyclic boronate ester, monosaccharides usually bearing five OH groups tend to form 1 : 2 monosaccharide/phenylboronic acid complexes.[1,6—10] However, the stability order of these complexes is always the same, depending on the structure of the monosaccharides.[2—4,11,12] Fructose is one of such monosaccharides with a high association constant, whereas glucose is one of such monosaccharides with a low association constant. In contrast, diboronic acids which can react with four of five OH groups show the different stability order, depending on the specific spatial position of two boronic acid functions. This idea was first realized with 3,3′-methylenediphenylboronic acid which showed the highest affinity towards glucose.[6] The finding offers a potential working-hypothesis that the desired monosaccharide may be selectively bound by adjusting the spatial position of two boronic acids complementary to the OH groups in the monosaccharide.[1] It is not so easy, however, to design and synthesize such a diboronic acid host complementary to a saccharide guest. Here, it occurred to us that the self-assembling nature of metalloporphyrins[13—15] might be useful to solve this problem: When both the metalloporphyrin and the axial ligand possess a boronic acid group, the complex should behave like a diboronic acid derivative and the spatial position could readily be adjusted by changing the structure of either the metalloporphyrin or the ligand. With this idea in mind we here tested a combination of 5-[3-(dihydroxyboryl)phenyl]-10,15,20-triphenylporphyrinatozinc(II) (**1-Zn**) (Chart 1) and 3-pyridylboronic acid (used as its dimethyl ester **2** (Chart 2) : It was confirmed by ^{1}H NMR spectroscopy that the exchange with diols to yield stabler cyclic boronate esters readily takes place in solution). We have found that the **1-Zn·2** complex shows a novel stability order for monosaccharides and gives CD (circular dichroism) spectra for the Soret band inherent to the absolute configuration of monosaccharides. 5,10,15,20-Tetraphenylporphyrinatozinc(II) (ZnTPP) was used as a reference compound for **1-Zn**.



1-Zn

Chart 1.



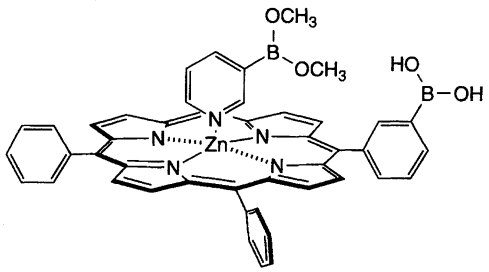
2

Chart 2.

Results and Discussion

Complex Formation between 1-Zn and 2. Firstly, we determined the association constant between **1-Zn** and **2** (Eq. 1) in dichloromethane at 25 °C. As shown in Fig. 1, the Soret band (λ_{max} 419 nm) shifts to longer wavelength region (λ_{max} 429 nm) with increasing **2** concentration. A tight isosbestic point appears at 424 nm. From the analysis of a A_{429} vs. [**2**] plot by the Benesi–Hildebrand equation, one can estimate the association constant for the 1 : 1 complex to be 4.7×10^4 dm^3 mol^{-1}. This value is comparable with those determined for ZnTPP and pyridine derivatives (10^4—10^5 dm^3 mol^{-1}).[16]

1-Zn + **2** ⟺



(1)

To estimate the stability order of **1-Zn·2·** saccharide (S) ternary complexes toward saccharides, one has to set up measurement conditions where the ternary complex exists predominantly over other species such as **1-Zn**·S, (**1-Zn**)$_2$·S, **2**·S, (**2**)$_2$·S, etc. One can compute from the above association constant that more than 90% of **1-Zn** (1.00×10^{-5} mol dm^{-3}) can be converted into the **1-Zn·2** complex in the presence of 2.00×10^{-3} mol dm^{-3} of **2**. To suppress the formation of other species, we decided to use a solid(S)–liquid (dichloromethane) extraction system. CD and ^{1}H NMR spectroscopic studies of the extracted dichloromethane solutions established that **2** (ca. 10^{-2} mol dm^{-3}) cannot extract any saccharides by itself. On the other hand, **1-Zn** could extract certain (relatively lipophilic) saccharides by itself (probably forming the (**1-Zn**)$_2$·S complex) at the concentrations higher than 3×10^{-5} mol dm^{-3}. We thus prepared a dichloromethane solution (100 ml) containing [**1-Zn**]=7.4×10^{-6} mol dm^{-3} and [**2**]=2.1×10^{-3} mol dm^{-3} and extracted solid saccharides (10 mg) at 25 °C with sonication for 10 min (we confirmed that the extraction equilibrium is attained within 10 min). The top clear part was subjected to the CD spectroscopic examination. Under these extraction conditions the CD spectra should reflect only those of **1-Zn·2·**S complexes.

CD Spectra of 1-Zn·2·Saccharide Ternary Complexes. The molecular size of monosaccharides is about 3.0—4.0 Å. When 1,2-diol and 4,6-diol in pyranosides are used as boronic acid complexation sites,[1,6,8—10] the distance between two boronic acids in the host should be favorably adjusted to 3.5 Å. When **2** coordinates to Zn(II) in **1-Zn** as an axial ligand, the distances from the axial ligand boronic acid to *o*- and *m*-positions in the 5-phenyl ring of **1-Zn** are estimated from CPK molecular models to be 2.0 and 3.5 Å, respectively. We thus chose **1** bearing the boronic acids group at the *m*-position, expecting that the two boronic acids can cooperatively act to bind monosaccharides.

When solid saccharides were extracted with free base **1** and **2** or with ZnTPP and **2**, they were not solubilized into the dichloromethane phase at all: Neither the saccharide proton signal in ^{1}H NMR spectroscopy nor the CD spectral band was observed. In contrast, the combination of **1-Zn** and **2** extracted saccharides and gave the CD spectral pattern inherent to their absolute configuration. This means that

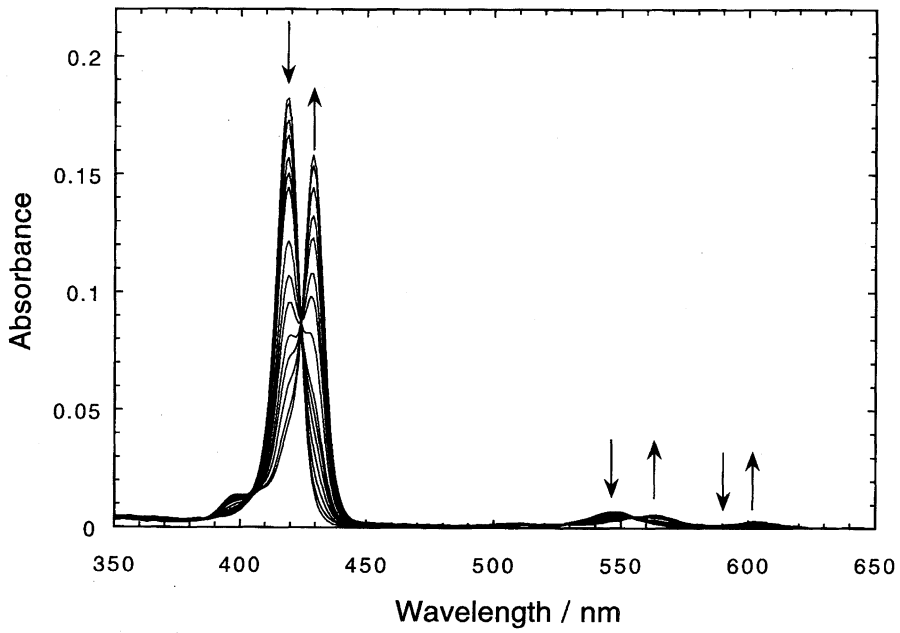
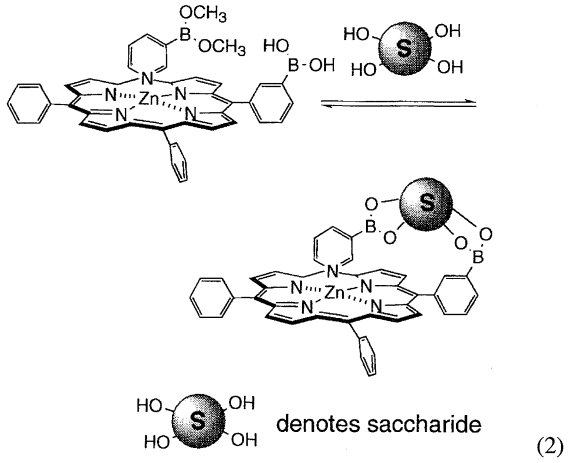


Fig. 1. Absorption spectra of **1-Zn** (3.00×10^{-7} mol dm^{-3}) in the presence of **2** in CH_2Cl_2 at 25 °C. Arrows indicate the direction of the absorbance change with increasing **2** concentration.

it is indispensable for efficient saccharide extraction to intramolecularly organize two boronic acids with the aid of the Zn(II)–pyridine interaction. These results allow us to propose that saccharides are bound to the **1-Zn·2** complex by a cooperative action of two boronic acids (as shown in Eq. 2). Typical CD spectra are shown in Fig. 2 and the CD parameters (λ_{max} and θ_{obs}) obtained from the extraction system are summarized in Table 1.



(2)

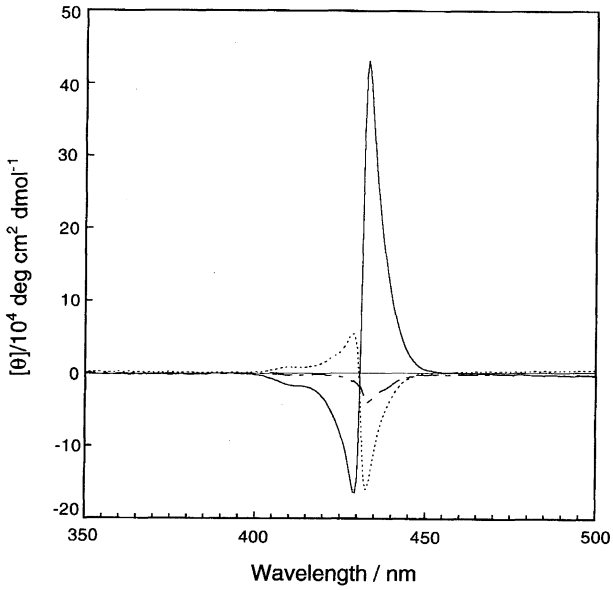


Fig. 2. CD spectra obtained from extraction of solid saccharides into the dichloromethane solution at 25 °C: [**1-Zn**] = 7.40×10^{-6} mol dm^{-3}, [**2**] = 2.10×10^{-3} mol dm^{-3}: — D-fucose, - - - D-arabinose, – • – D-threitol.

The CD parameters [λ_{max} (θ_{obs})] in Table 1 are data observed for the mixture of uncomplexed **1-Zn·2** and complexed **1-Zn·2**·S. We tried to determined the extractability (Ex%) of saccharides per **1-Zn·2** from which one can draw the true CD spectra for 100 %-complexed **1-Zn·2**·S. This purpose can be basically accomplished by estimating the ratio of **1-Zn·2** vs. **1-Zn·2**·S by ^{1}H NMR spectroscopy.

Table 1. λ_{max} (nm), θ_{obs} (deg cm^{-2} dmol^{-1}), and Ex% under the CD Concentration[a] and Ex% and θ_{corr} (deg cm^{-2} dmol^{-1}) under the NMR Concentration[b]

Saccharide(s)	CD		NMR	
	λ_{max} (θ_{obs})	Ex% (CD)[c]	Ex% (NMR)[d]	θ_{corr}[e]
D-Glucose	429.0 (4.73×10^4)	31	12	1.58×10^5
	435.5 (-9.01×10^4)			-2.87×10^5
D-Fructose	429.0 (9.74×10^4)	37	33	3.90×10^5
	435.5 (-1.49×10^5)			-4.02×10^5
D-Fucose	429.0 (-1.64×10^5)	97	30	-1.83×10^5
	432.0 (4.31×10^5)			4.46×10^5
L-Fucose	429.0 (1.76×10^5)	85	—	—
	432.0 (-3.78×10^5)			
D-Arabinose	429.0 (5.38×10^4)	55	10	1.69×10^5
	432.5 (-1.57×10^5)			-2.84×10^5
L-Arabinose	429.0 (-5.47×10^4)	56	—	—
	432.5 (1.60×10^5)			
D-Xylose[f]	429.0 (-3.5×10^4)	2	6	-4.4×10^5
	433.5 (1.6×10^4)			7.9×10^5
D-Threitol	433.5 (-7.17×10^4)	18	10	-4.00×10^5
L-Threitol	431.0 (7.83×10^4)	19	—	—

a) 25 °C, [**1-Zn**] = 7.40×10^{-6} mol dm^{-3}, [**2**] = 2.10×10^{-3} mol dm^{-3}. b) 25 °C, [**1-Zn**] = [**2**] = 4.00×10^{-3} mol dm^{-3}. c) The Ex% (CD) is defined as the ratio of θ_{obs} versus θ_{corr}. d) The Ex% (NMR) was determined by the ratio of saccharide protons versus total (complexed and uncomplexed) porphyrin protons. e) The NMR spectral measurement solution was directly subjected to the CD measurement and the θ_{obs} was corrected for 100% complex by Ex% (NMR). f) As the CD bands are considerably weak, the θ values are not so precise as others. The λ_{max} under the NMR conditions appeared at 426 nm, which was different by 3 nm from the λ_{max} (429 nm) under the CD conditions. The difference implies that extraction of xylose by **1-Zn·2** is so difficult that alternate extraction species (**1-Zn**)$_2$·S (more advantageous under the NMR conditions) increases the Ex% (NMR).

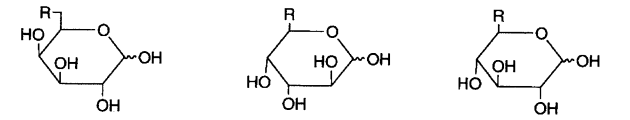


Chart 3.

However, a dilemma arises that we must use the high **1-Zn** concentration for the ^{1}H NMR measurement where undesired (**1-Zn**)$_2$·S may be partially formed. We considered that undesired (**1-Zn**)$_2$·S, even if it is formed, could be converted into desired **1-Zn**·**2**·S in the presence of excess **2**. The CD spectroscopic study proved that this is the case: as shown in Fig. 3, extraction of L-threitol with **1-Zn** gives a positive exciton coupling band which is assignable to the (**1-Zn**)$_2$·L-threitol complex. When excess **2** was added to this solution, the CD spectrum changed to a simple positive ICD band which coincides with that obtained for **1-Zn**·**2**·L-threitol under the diluted extraction conditions (see λ_{max} (θ_{obs}) in Table 1). Hence, we extracted saccharides with the high **1-Zn** and **2** concentrations (4.0×10^{-3} mol dm^{-3}) and determined the Ex% by ^{1}H NMR spectroscopy. The typical ^{1}H NMR spectrum is shown in Fig. 4. The integral intensity ratio of 1-H in saccharides and β-protons of pyrroles in **1-Zn** is useful for this calculation.[17] The solution was directly subjected to the CD spectral measurement with a 0.1 mm thickness cell and the θ_{corr} (θ_{obs} (NMR)/Ex%) for 100%-complexed **1-Zn**·**2**·S was estimated. By dividing θ_{obs} (CD) by θ_{corr} (NMR), one can estimate the Ex% (CD) under the diluted extraction conditions. The results are all summarized in Table 1.

It is seen from Table 1 that the Ex% defined as S/**1-Zn**·**2** is higher in the diluted CD conditions than in the concentrated NMR conditions (except for xylose: see footnote f to Table 1). In particular, fucose and arabinose which correspond, respectively, to 6-deoxygalactose and 6-de(hydroxymethyl)-altorose and therefore should be more lipophilic than glucose

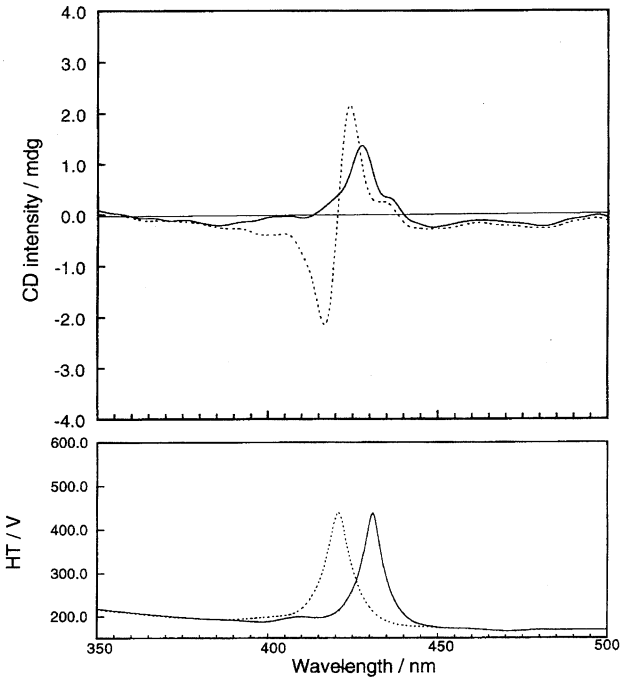


Fig. 3. HT voltages and CD spectra of **1-Zn** (6.60×10^{-5} mol dm^{-3} in 1.0 ml of dichlomethane at 25 °C): - - - after extraction of L-threitol (solid, 1.0 mg), —— after addition of **2** (4.00×10^{-3} mol dm^{-3}).

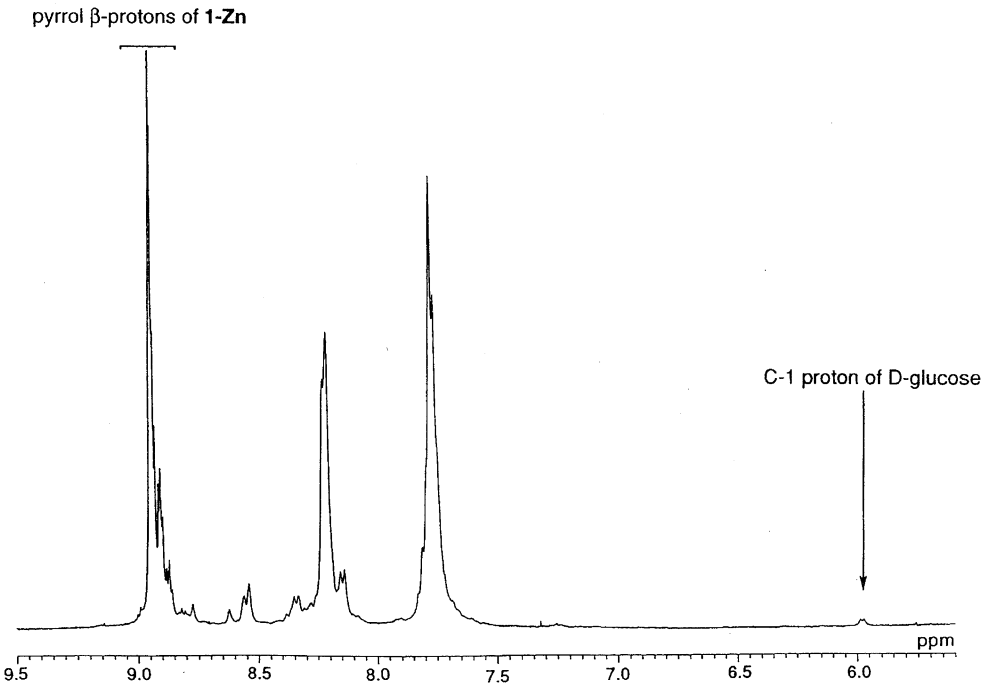
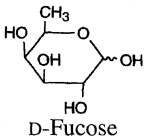
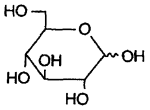
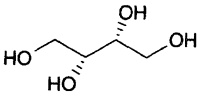
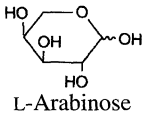
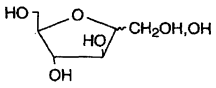
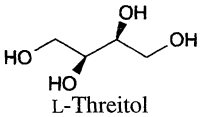
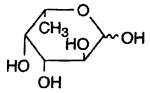
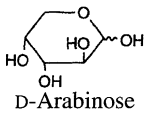


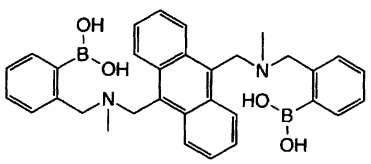
Fig. 4. Pratial ^{1}H NMR spectrum obtained after extraction of D-glucose (solid) to a CD_2Cl_2 solution containing **1-Zn** (4.00×10^{-3} mol dm^{-3}) and **2** (4.00×10^{-3} mol dm^{-3}): 400 MHz, 25 °C.

Table 2. Classification of Saccharides from the CD Sign

Positive exciton-coupling	Negative exciton-coupling	ICD
 D-Fucose	 D-Glucose	 D-Threitol
 L-Arabinose	 D-Fructose	 L-Threitol
	 L-Fucose	
	 D-Arabinose	

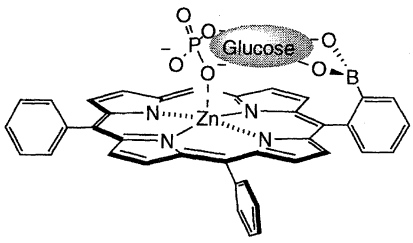
and fructose, show the high Ex% values (Chart 3). However, xylose, which corresponds to 6-de(hydroxymethyl)glucose and therefore should be relatively lipophilic, is extracted only to a smaller extent. The difference is reasonably explained by the difference in the absolute configuration. In fucose and arabinose, the 3,4-diol possesses the *cis* configuration and the 1,2-diol can adopt the *cis* configuration in their one anomeric form: Hence, both diols are favorably preorganized for the boronate ester formation. In xylose, on the other hand, the 1,2-diol can adopt the *cis* configuration, but the 3,4-diol possesses the *trans* configuration. Thus, fucose and arabinose which can bind two boronic acids through two *cis*-diols are more advantageous than xylose for the formation of the **1-Zn·2**·S ternary complex.

Glucose, which is known to frequently form cyclic complexes with diboronic acid compounds,[1,6—10] results in the relatively low Ex% and small θ_{corr} in the present system. Examination of CPK molecular models reveals that when two boronic acids in the **1-Zn·2** complex are intramolecularly bridged by glucose, the 5-phenyl ring in **1-Zn** and the pyridine ring in **2** are forced to become parallel to each other and a serious steric hindrance appears between *o*-H in the 5-phenyl ring and bound glucose. Because of this steric problem, the **1-Zn·2** complex cannot create a diboronic-acid cleft favorable to the glucose binding. We previously reported that compound **3** strongly binds glucose in its pyranose form (Chart 4).[10] The ^{1}H NMR study showed that 3-OH (which is not used for complexation) of bound glucose exists in the proximity of the anthracene plane.[10] Provided that **1-Zn·2** also adopts the similar binding mode for glucose, the space surrounded by the 5-phenyl ring and bound glucose will become even more crowded. This is another reason why the Ex% for glucose is very low.

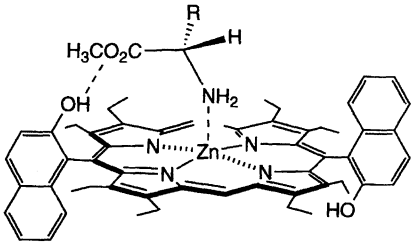


3
Chart 4.

Here, we discuss the origin of the CD activity in the present ternary complexes. We can raise several possible explanations: (i) ICD spectra are induced by complexation with chiral saccharides, (ii) the boronic-acid-appended 5-phenyl



4-Zn·glucose-6-phosphate complex[19]
Chart 5.



5-Zn·α-amino acid complex[20]
Chart 6.

ring is chirally immobilized by saccharides to afford a sort of chiral atropisomer, (iii) the porphyrin plane is deformed in a chiral manner (ruffling of the porphyrin plane[18]) and (iv) exciton coupling between the porphyrin dipole moment and the pyridine dipole moment. Possibility (i) is incompatible with the fact that most saccharides bound to **1-Zn·2** give an exciton-coupling band. We previously studied the saccharide sensing with an *o*-boronic acid isomer of **1-Zn** (**4-Zn**) in aqueous solution.[19] It was shown that unless saccharides have some additional group for the interaction with Zn(II), the saccharide complexes do not show any CD activity.[19] Similarly, **1-Zn** in aqueous solution did not show the CD activity upon addition of saccharides used herein. The results mean that the chiral rotation and immobilization of the 5-phenyl ring (i.e., possibility (ii)) is not the origin of the CD activity. Possibility (iii) is also unlikely, because a macrocyclic ring created in the **1-Zn·2·**S is not so rigid as to deform the porphyrin plane: The steric hindrance is easily relaxed by the rotation of the axial ligand pyridine. Therefore, it is most reasonable to attribute the CD activity to possibility (iv). The finding that the **4-Zn·**glucose-6-phosphate complex (Chart 5) and the **5-Zn·** α-amino acid complex (see below for the structure of **5-Zn**) (Chart 6) give the clear exciton-coupling band because of the interaction between the porphyrin dipole moment and P=O or C=O dipole moment[19,20] is also compatible with this proposal.

Saccharides in Table 1 can be classified into three categories: (i) D-fucose and L-arabinose which show the positive exciton-coupling band, (ii) D-glucose, D-fructose, L-fucose, and D-arabinose which show the negative exciton-coupling band, and (iii) D- and L-threitol which show the simple ICD band (Table 2). It is known that when 4-OH and 6-OH in the pyranose form a six-membered ring with a boronic acid, the direction of the C–O–B–O–C plane is controlled by the configuration of 4-OH.[6,7,9,10] Careful examination of Table 1, taking this concept into consideration, reveals that category (i) includes such saccharides that can form a downward five-membered ring with 1,2-*cis*-diol and an upward six-membered ring with 4,6-*trans*-diol. As a result, these saccharides provide a ⌙ -shaped architecture upon complexation with two boronic acids. One can consider that immobilization of the 5-[3-(dihydroxyboryl)phenyl] group and the pyridylboronic acid with this "lock" is the origin of the positive exciton-coupling band. Category (ii) (except D-glucose) includes such saccharides that can form the first upward ring and the second downward ring. Therefore, these saccharides provide a ⌐┘-shaped architecture upon complexation with two boronic acids. As expected, their CD sign (negative exciton-coupling band) is symmetrical to that of category (i). According to this classification, D-glucose forms the first downward ring and the second downward ring. This down–down configuration is advantageous to the formation of intramolecular complexes with diboronic acid compounds.[1,6] In the present system, however, the bridging by D-glucose is hampered by the steric crowding with the 5-phenyl group. We consider, therefore, that this steric problem brings forth an exceptional CD sign (i.e., negative exciton-coupling) for D-glucose. In category (iii), threitol is a relatively flexible molecule and cannot make the pyridine plane so rigid as to give the distinct exciton-coupling band. As a result, a simple ICD band is observed.

These results consistently support the view that the CD sign in **1-Zn·2·**S complexes appears in correlation with the absolute configuration of saccharides acting as a "lock".

Conclusions. Through the past studies on exploitation of boronic-acid-based saccharide sensing systems, it has been established that the cooperative action of intramolecularly-situated two boronic acids is indispensable to realize the high affinity and high selectivity towards specific saccharides.[1,6–10] In general, however, the synthesis of such diboronic acid compounds is not so easy. On the other hand, the present study demonstrates that the self-assembly of monoboronic acids can act as a diboronic acid mimic, also exhibiting the high affinity and selectivity which reflect the absolute configuration of saccharides. From the synthetic viewpoint, monoboronic acids are much easier than diboronic acids. Furthermore, the "fine-tuning" of the boronic acid-boronic acid distance is possible by simply changing the connection method of each assembly unit. This is exactly the main advantageous point of self-assembled systems which is difficult to attain in monomeric host systems. Further extension to polymeric self-assembled boronic acid systems is currently continued to create more elaborated sugar sensing systems.

Experimental

Materials. 3-Pyridylboronic acid dimethyl ester (**2**) was synthesized from diethyl-3-pyridylborane according to the literature:[21] mp>300 °C, yield 19% (lit,[21] mp>300 °C, 25%).

5-[3-(5,5-Dimethyl-1,3,2-dioxaborinane-2-yl)phenyl]-10,15,20-triphenylporphyrin (6). 2-(3-Formylphenyl)-1,3,2-dioxaborinane (3.8 g, 20 mmol), benzaldehyde (3.0 ml, 30 mmol), and pyrrole (3.5 ml, 50 mmol) were dissolved in propionic acid (200 ml) and the solution was refluxed for 3 h. After cooling, the solution was concentrated in vacuo to 10 ml and poured into 150 ml of hexane. The precipitate thus formed was recovered by filtration. The product was purified by column chromatography (silica gel, chloroform : hexane = 10 : 1 v/v). However, the purple band was so broadened in the column that the desired product could not be isolated. We considered that the band broadening is due to the decomposition of the protecting group (1,3-propanediol). We thus added 2,2-dimethyl-1,3-propanediol (1.0 g/100 ml) to eluent solution. As expected the band broadening could be suppressed by this method and **1** was isolated as the 2,2-dimethyl-1,3-propanediol-protected title compound **6**: mp>300 °C, yield 1%; ^{1}H NMR ($CDCl_3$; 25 °C) $\delta_H = -2.76$ (2H, s, NH of pyrrole), 1.07 (6H, s, Me), 3.80 (4H, s, CH_2), 7.77 and 8.23 (19H, ArH), 8.84 (8H, s, CH of pyrrole).

5-[3-(Dihydroxyboryl)phenyl]-10,15,20-triphenylporphyrin (1). Deprotection of 1,3-propanediol derivatives from the boronic acid group is usually accomplished by the treatment with acid (e.g., trifluoroacetic acid). In the present system, however, the 2,2-dimethyl-1,3-propanediol group is too stable to remove by the conventional method. We thus developed a new method using *N*-methylbis(2-hydroxyethyl)amine which forms strong complexes with boronic acids but is readily removed by the acid treatment.[22]

Compound **6** (5.0 mg, 6.9 μmol) was stirred with *N*-methylbis(2-hydroxyethyl)amine (0.16 ml, 1.4 mmol) in a mixed solvent of THF (200 ml) and buffered water (40 ml, pH 10.5 with 50 mmol dm^{-3} carbonate). After 8 h, 1 mol dm^{-3} HCl aqueous solution (20 ml) was added. The organic layer was separated, washed with 5% Na_2CO_3 aqueous solution (100 ml) saturated with sodium borate and dried over Na_2SO_4. The concentration of the solution under reduced pressure gave **1** as purple powder: mp>300 °C, yield 66%; ^{1}H NMR ($CDCl_3$; 25 °C) δ_H=−2.78 (2H, s, NH of pyrrol), 7.74 and 8.20 (19H, ArH), 8.80 (8H, s, CH of pyrrol).

5-(3-Dihydroxyborylphenyl)-10,15,20-triphenylporphyrinatozinc(II) (1-Zn). Compound **1** (0.11 g, 0.17 mmol) in chloroform (20 ml) and $(CH_3COO)_2$ Zn·$2H_2O$ (1.83 g, 8.4 mmol) in methanol (15 ml) were mixed and the resultant solution was stirred at room temperature for 30 min. The solution was concentrated to dryness and the residual solid was subjected to the preparative TLC separation (silica gel, chloroform : ethylacetate=5 : 1 v/v): mp>300 °C, yield 81%; ^{1}H NMR ($CDCl_3$; 25 °C) δ_H=7.75 and 8.28 (19H, ArH), 8.79 (8H, s, CH of pyrrol). Found: C, 72.19; H, 4.59; N, 7.07%. Calcd for $C_{44}H_{29}BN_4O_2Zn$·0.5CH_3 $COOC_2H_5$: C, 72.13; H, 4.34; N, 7.31%.

Typical Proceadure of Liquid-Solid Extraction. A dichloromethane solution (98.36 ml) of **2** (2.13×10^{-3} mol dm^{-3}) was added to a dichloromethane solution (1.64 ml) containing **1-Zn** (7.4×10^{-6} mol dm^{-3}). To the resulting solution of the **1-Zn·2** complex well-powdered solid saccharides (10 mg, large excess) were added at 25 °C with sonication (Mitamura Riken Kogyo CA-40) for 10 min (we confirmed that the extraction equilibrium has been attained within 10 min). The top clear part was subjected to the CD spectroscopic examination. Under these extraction conditions the CD spectra should reflect only those of **1-Zn·2·S** complexes.

Miscellaneous. Spectroscopic data were obtained by means of a Brucker 250 MHz FT-NMR (AC-250P) and a JEOL 400 MHz FT-NMR (GSX-400) for ^{1}H NMR spectroscopy using tetramethylsilane as a reference. The absorption spectroscopy and circular dichroism were measured by a Shimadzu UV-visible spectrophotometer (U-3000) and a JASCO spectropolarimeter (J-720), respectively.

References

1) For recent comprehensive reviews see : T. D. James, K. R. A. S. Sandanayake, and S. Shinkai, *Supramol. Chem.*, **6**, 141 (1995); T. D. James, P. Linnane, and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, **1996**, 281.

2) J. Yoon and A. W. Czarnik, *J. Am. Chem. Soc.*, **114**, 5874 (1992); L. K. Mohler and A. W. Czarnik, *J. Am. Chem. Soc.*, **115**, 2998 (1993).

3) M. F. Paugan and B. D. Smith, *Tetrahedron Lett.*, **34**, 3723 (1993); G. T. Morin, M. P. Hughes, M.-F. Paugam, and B. D. Smith, *J. Am. Chem. Soc.*, **116**, 8895 (1994); P. R. Westmark and B. D. Smith, *J. Am. Chem. Soc.*, **116**, 9343 (1994).

4) Y. Nagai, K. Kobayashi, H. Toi, and Y. Aoyama, *Bull. Chem. Soc. Jpn.*, **66**, 2965 (1993).

5) G. Wulff, B. Heide, and G. Helfmeier, *J. Am. Chem. Soc.*, **108**, 1089 (1986); G. Wulff and H.-G. Poll, *Makromol. Chem.*, **188**, 741 (1987).

6) K. Tsukagoshi and S. Shinkai, *J. Org. Chem.*, **56**, 4089 (1991); Y. Shiomi, M. Saisho, K. Tsukagoshi, and S. Shinkai, *J. Chem. Soc., Perkin Trans. 1*, **1993**, 2111.

7) T. D. James, T. Harada, and S. Shinkai, *J. Chem., Soc., Chem. Commun.*, **1993**, 857.

8) K. Nakashima and S. Shinkai, *Chem. Lett.*, **1995**, 443; K. R. A. S. Sandanayake, T. D. James, and S. Shinkai, *Chem. Lett.*, **1995**, 503.

9) J. C. Norrild and H. Eggert, *J. Am. Chem. Soc.*, **117**, 1479 (1995).

10) T. D. James, K. R. A. S. Sandanayake, R. Iguchi, and S. Shinkai, *J. Am. Chem. Soc.*, **117**, 8982 (1995), and references cited therein.

11) J. P. Lorand and J. O. Edwards, *J. Org. Chem.*, **24**, 769 (1959).

12) H. Murakami, T. Nagasaki, I. Hamachi, and S. Shinkai, *Tetrahedron Lett.*, **34**, 6273 (1993); *J. Chem. Soc., Perkin Trans. 2*, **1994**, 975; T. Imada, H. Murakami, and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, **1994**, 1557; S. Arimori, H. Murakami, M. Takeuchi, and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, **1995**, 961; S. Arimori, M. Takeuchi, and S. Shinkai, *Chem. Lett.*, **1996**, 77; *J. Am. Chem. Soc.*, **118**, 245 (1996).

13) C. A. Hunter and L. D. Sarson, *Angew. Chem., Int. Ed. Engl.*, **33**, 2313 (1994); X. Chi, A. J. Guerin, R. A. Haycock, C. A. Hunter, and L. D. Sarson, *J. Chem. Soc., Chem. Commun.*, **1995**, 2567.

14) H. L. Anderson, C. A. Hunter, M. N. Meah, and J. K. M. Sanders, *J. Am. Chem. Soc.*, **112**, 5780 (1990); H. L. Anderson and J. K. M. Sanders, *J. Chem. Soc., Chem. Commun.*, **1989**, 1714; S. Anderson, H. L. Anderson, and J. K. M. Sanders, *Acc. Chem. Res.*, **26**, 469 (1993).

15) L. D. Sarson, K. Ueda, M. Takeuchi, and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, **1996**, 619.

16) K. M. Kadish, L. R. Shue, R. K. Rhodes, and L. A. Bottomly, *Inorg. Chem.*, **20**, 1274; H. Imai and E. Kyuno, *Inorg. Chem.*, **29**, 2416 (1990).

17) The chemical shifts (δ_H/ppm) of saccharide protons we used in order to calculate the Ex% are 6.01 (1-H, fucose), 6.02 (1-H, arabinose), 5.97 (1-H, glucose), 5.33 (2- or 3-H, fructose), and 4.60 (-CH-, threitol). We tried to assign the remaining chemical shifts by 2D ^{1}H NMR and NOESY but failed. The failure is due to the serious line-broadening and the serious overlap of the chemical shifts.

18) K. M. Barkigia, M. D. Berber, J. Fajor, C. J. Medforth, M. W. Renner, and K. M. Smith, *J. Am. Chem. Soc.*, **112**, 8851 (1990).

19) T. Imada, H. Kijima, M. Takeuchi, and S. Shinkai, *Tetrahedron Lett.*, **36**, 2093 (1995); *Tetrahedron*, **52**, 2817 (1996).

20) T. Mizutani, T. Ema, T. Yoshida, T. Renne, and H. Ogoshi, *Inorg. Chem.*, **33**, 3558 (1994); T. Mizutani, T. Murakami, T. Kurahashi, and H. Ogoshi, *J. Org. Chem.*, **61**, 539 (1996).

21) M. Terashima, H. Kakimi, M. Ishikura, and K. Kamata, *Chem. Pharm. Bull.*, **31**, 4573 (1983).

22) H. Suenaga, K. Nakashima, M. Mikami, and S. Shinkai, *Chem. Lett.*, **1995**, 73.