

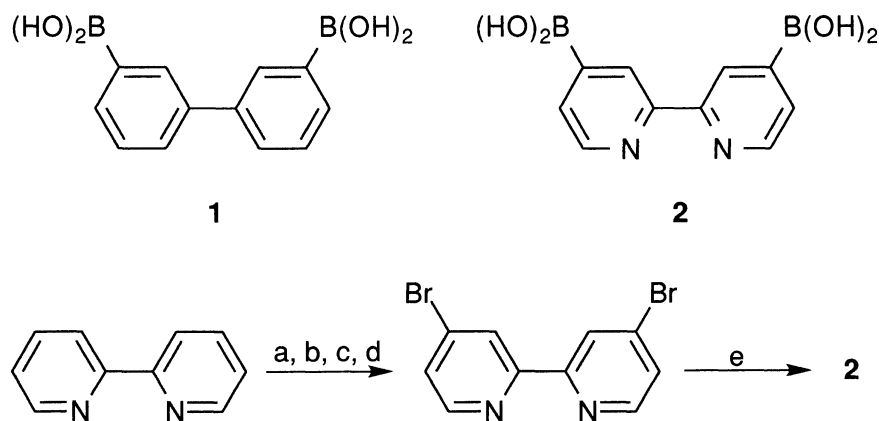
Sugar-Assisted Chirality Control of Tris(2,2'-bipyridine)-Metal Complexes

Kazuaki NAKASHIMA and Seiji SHINKAI*

Chemirecognics Project, ERATO, Research Development Corporation of Japan,
Aikawa 2432-3, Kurume, Fukuoka 830

2,2'-Bipyridine-4,4'-diboronic acid (**2**), a 2,2'-bipyridine derivative with sugar-binding sites was synthesized. The Δ vs. Λ chirality of the $\text{Fe}^{2+}\cdot\mathbf{2}_3$ complex was selectively generated in correlation with the absolute configuration of added saccharides.

Boronic acids, which have been known since a long time ago to form covalently-bonded complexes with diols in an aqueous system, now attract a great deal of attention as a new interactive tool for sugar recognition.¹⁻⁸⁾ We previously designed compound **1** to recognize disaccharides: the distance between two boronic acids in **1** with a syn conformation is *ca.* 7.4 Å, which is comparable with the distance between 1,2-diols and 4',6'-diols in disaccharides (assuming a linear conformation) serving as boronic-acid-binding sites.⁵⁾ Interestingly, only when **1** formed cyclic 1:1 complexes with disaccharides (*e.g.*, D-maltose, D-cellobiose, and D-lactose), clear exciton coupling bands appeared in circular dichroism (CD) spectroscopy because of asymmetric immobilization of the two benzene rings.⁵⁾ We considered that this concept could be further extended to the generation of novel sugar-assisted asymmetry, for example, Δ vs. Λ metal complexes by using **2** as a metal ligand: that is, the chirality generated in **2** through the complexation with disaccharides would be eventually reflected as the Δ vs. Λ enantioselectivity in the metal- $\mathbf{2}_3$ complex. To test the feasibility of this idea we synthesized **2** according to Scheme 1⁹⁾ and estimated the chirality of the Fe^{2+} complexes in the presence of saccharides by CD spectroscopy.¹⁰⁾



Conditions: a) $\text{H}_2\text{O}_2/\text{CH}_3\text{COOH}$ b) fuming HNO_3 /fuming H_2SO_4 c) $\text{CH}_3\text{COBr}/\text{CH}_3\text{COOH}$
d) $\text{PBr}_3/\text{CHCl}_3$ e) (i) $n\text{-BuLi}/\text{THF}$, -90°C (ii) $\text{B}(\text{O}i\text{Pr})_3/\text{THF}$, -90°C (iii) H_2O

Scheme 1.

Compound **2** was identified by IR, ^1H NMR, and mass spectral evidence.¹¹⁾ Figure 1 shows the CD spectra of **2** in the presence of D-maltose ($[\theta]_{205} = -2900 \text{ deg cm}^2 \text{ dmol}^{-1}$) or D-cellobiose ($[\theta]_{212} = 6600 \text{ deg cm}^2 \text{ dmol}^{-1}$). It is known that **1** shows the negative exciton coupling with the negative first Cotton effect and the positive second Cotton effect in the presence of D-maltose and the positive exciton coupling with the positive first Cotton effect and the negative second Cotton effect in the presence of D-cellobiose.⁵⁾ The coincidence between the CD sign in Fig. 1 and that of the first Cotton effect in the disaccharide-**1** complexes suggests that the bands in Fig. 1 correspond to the first Cotton effect in the exciton coupling.

A plot of $[\theta]_{205}$ against D-maltose concentration is shown in Fig. 2. The concentration dependence is biphasic with a $[\theta]_{205}$ minimum. Other disaccharides also showed a similar dependence. A similar concentration dependence was previously observed for **1**.⁵⁾ This is rationalized by the successive complex formation from a CD active cyclic 1:1 complex at the low disaccharide concentration to a CD-silent noncyclic 1:2 complex at the high disaccharide concentration (Scheme 2).¹²⁾

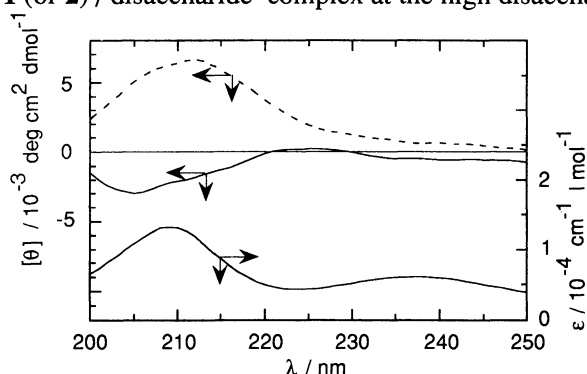


Fig. 1. CD spectra of **2** (5.0 mM) in the presence of D-maltose (50 mM, —) or D-cellobiose (50 mM, ----) and absorption spectrum of **2** (32.4 mM): 25 °C, pH = 10.5.

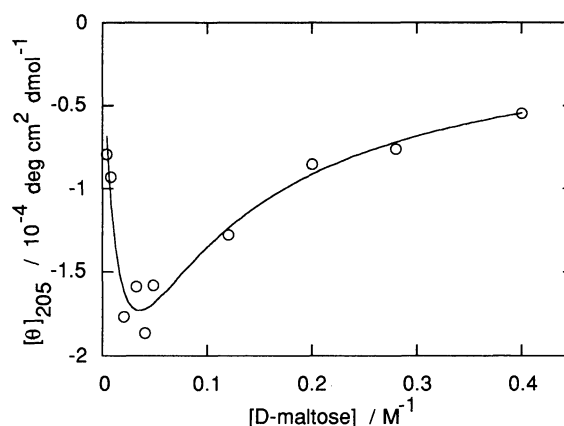
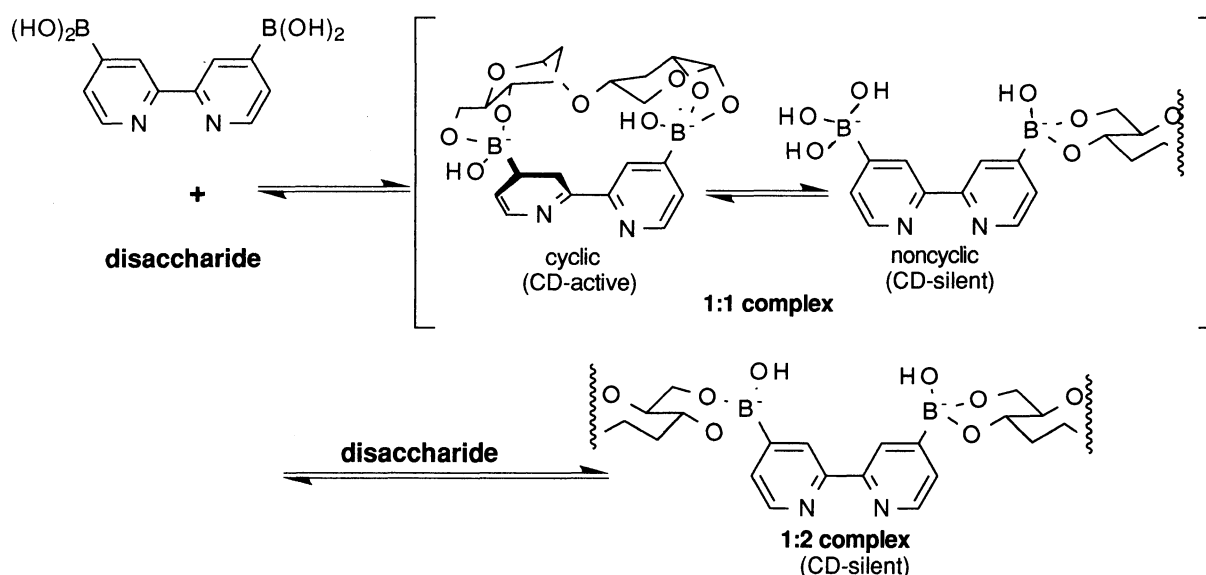


Fig. 2. Plot of $[\theta]_{205}$ vs. [D-maltose]: 25 °C, pH = 10.5, $[\mathbf{2}] = 5.0 \text{ mM}$.



Scheme 2.

Very interestingly, we found that when Fe^{2+} (added as FeCl_2) is added to the solution containing the disaccharide·**2** complex, the CD spectrum with an exciton coupling band appears at the metal-ligand charge-transfer (MLCT) band region (Fig. 3). The same CD spectrum was produced when disaccharide was added to the solution containing the Fe^{2+} ·**2**₃ complex. Separately, we confirmed that the $[\text{Fe}(2,2\text{-bipyridine})_3]^{2+}$ is CD silent even in the presence of disaccharides. Hence, the CD-activity is attributable to the generation of chiral Fe^{2+} complexes which is originated from the disaccharide-diboronic acid interaction. Figure 3 shows that Fe^{2+} ·(**2**·D-maltose)₃ adopts Λ chirality while Fe^{2+} ·(**2**·D-cellobiose)₃ adopts Δ chirality.¹³⁾

Figure 4 shows a plot of $[\theta]_{556}$ ($[\theta]$ minimum) and $[\theta]_{480}$ ($[\theta]$ maximum) at the MLCT band region vs. D-maltose concentration. Strangely, the MLCT band region is still CD active in the presence of excess D-maltose while **2** itself becomes CD-silent.⁵⁾ This implies that in **2** the intramolecular cross-link of two boronic acids is indispensable to the CD-activity whereas in Fe^{2+} ·(**2**·disaccharide)₃ it is not a prerequisite to the CD-activity. This was further corroborated by the CD-activity observed in the presence of D-glucose 1-phosphate ($[\theta]_{543} = -1000$, $[\theta]_{512} = 0$, and $[\theta]_{480} = 540 \text{ deg cm}^2 \text{ dmol}^{-1}$), D-glucose 6-phosphate ($[\theta]_{561} = 1600$, $[\theta]_{524} = 0$, and $[\theta]_{486} = -870 \text{ deg cm}^2 \text{ dmol}^{-1}$), and α -methyl D-glucopyranoside ($[\theta]_{563} = -2700$, $[\theta]_{522} = 0$, and $[\theta]_{481} = 1700 \text{ deg cm}^2 \text{ dmol}^{-1}$) which have only one boronic-acid-binding site and cannot cross-link two boronic acids intramolecularly (Fig. 5). The results indicate that the $\Delta \rightleftharpoons \Lambda$ interconversion can take place even 4 °C and the CD sign for the thermodynamically more stable enantiomer appears.

At present we cannot yet determine the optical purity of the Fe^{2+} ·(**2**·disaccharide)₃ complexes because the effort toward the optical resolution (we have tried the resolution by chiral-packed columns, diastereomer formation with tartaric acid, etc.) is unsuccessful so far.

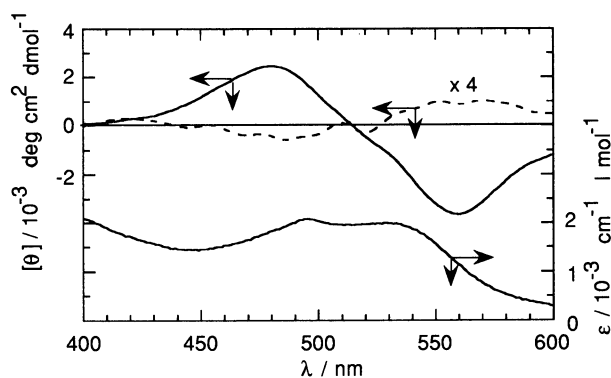


Fig. 3. CD spectra of Fe^{2+} ·**2**₃ (6.0 mM) in the presence of D-maltose (18 mM, —) and D-cellobiose (18 mM, ----): 4 °C, pH = 10.5 and absorption spectrum of Fe^{2+} ·**2**₃ (0.5 mM): 25 °C, pH = 10.5.

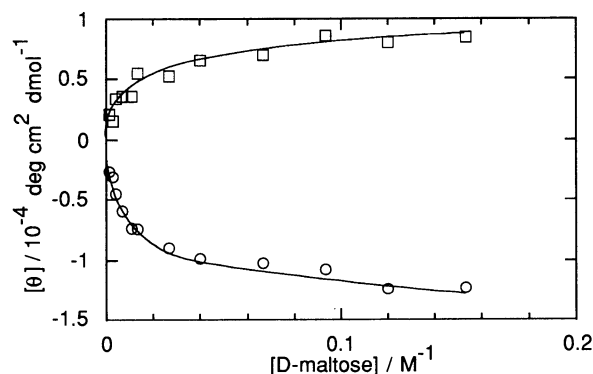


Fig. 4. Plot of $[\theta]_{556}$ (O) and $[\theta]_{480}$ (□) vs. [D-maltose]: 25 °C, pH = 10.5, $[\text{Fe}^{2+}$ ·**2**₃] = 6.0 mM.

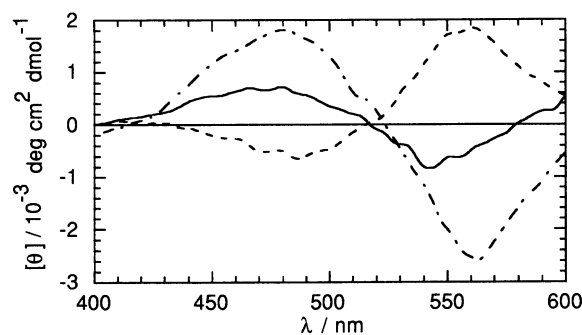


Fig. 5. CD spectra of $[\text{Fe}^{2+}$ ·**2**₃] (6.0 mM) in the presence of D-glucose 1-phosphate (added as dipotassium salt, 600 mM, —), D-glucose 6-phosphate (added as potassium salt, 600 mM, ----), and α -methyl D-glucopyranoside (600 mM, — · —): 4 °C, pH = 10.5.

Judging from the $[\theta]$ value determined for optically-pure $[\text{Fe}(\text{2,2'-(bipyridine)}_3)]^{2+}$,¹³⁾ we presume that the optical purity of $\text{Fe}^{2+} \cdot (\text{2-D-maltose})_3$ which gives the largest $[\theta]$ value in the present system is *ca.* 20%.

In conclusion, the present study has demonstrated that the Δ vs. Λ chirality of the $\text{Fe}^{2+} \cdot \mathbf{2}_3$ complex can be selectively generated by the saccharide addition and the selectivity is correlated with the absolute configuration of added saccharides. This is a novel application of a boronic-acid-dependent sugar-interface to the chirality control of metal complexes.

References

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- 9) 4,4'-Dibromo-2,2'-bipyridine was synthesized according to the following papers: J. Haginiwa, *Yakugaku Zasshi*, **75**, 731 (1955); G. Maerker and F. H. Case, *J. Am. Chem. Soc.*, **80**, 2745 (1958); D. Wenkert and R. B. Woodward, *J. Org. Chem.*, **48**, 283 (1983). However, we modified the reaction conditions to attain the higher yields: see a caption to Scheme 1.
- 10) Fe^{2+} was chosen to make the system simple because $[\text{Fe}(\text{bpy})_3]^{2+}$ is formed in preference to $[\text{Fe}(\text{bpy})_2]^{2+}$ and $[\text{Fe}(\text{bpy})]^{2+}$; see M. R. McWhinnie and J. D. Miller, *Adv. Inorg. Chem. Radiochem.*, **12**, 135 (1969).
- 11) Compound **2** was obtained as white powder; mp 463 °C (dec.); IR (KBr) 3450 cm^{-1} (OH); ^1H NMR (CD_3OD) δ = 7.56 (2H, dd, H_5 and $\text{H}_{5'}$), 8.17 (2H, s, broad, H_3 and $\text{H}_{3'}$), 8.37 (2H, dd, H_6 and $\text{H}_{6'}$), $J_{3,5} = J_{3',5'} = 1.0$ Hz, $J_{3,6} = J_{3',6'} = 1.0$ Hz, $J_{5,6} = J_{5',6'} = 4.9$ Hz; MS (SIMS(-)) m/z 243 ((M-1)-).
- 12) UV absorption spectra of **2** were scarcely affected by the addition of saccharides. So, we think that there is no big difference in the dihedral angle between free **2** and 1:1 2-disaccharide complex. Thus, the CD spectra should arise from the shift of the equilibrium between (R)- and (S)-atropisomers.
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