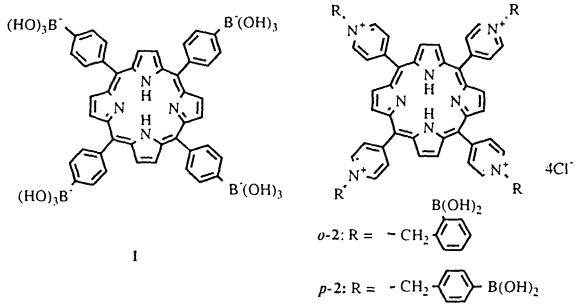
Sugar-Sensing by Chiral Orientation of Dimeric Boronic-Acid-Appended Porphyrins Which Show Selectivity for Glucose and Xylose

Susumu Arimori, Masayuki Takeuchi, and Seiji Shinkai*
Department of Chemical Science & Technology, Faculty of Engineering, Kyushu University, Fukuoka 812

(Received October 16, 1995)

5,10,15,20-Tetrakis(4-boronylphenyl)porphyrin (**1**) and 5, 10,15,20-tetrakis[*N*-(2- or 4-boronylphenyl)methyl-pyridinium] porphyrin (*o*-**2** or *p*-**2**) formed a 1:1 complex, which gave specific exciton-coupling bands in CD spectroscopy only in the presence of glucose and xylose among monosaccharides. The structural examination established that only these monosaccharides can bridge two porphyrins by covalent-bond formation with boronic acids and twist them asymmetrically.

The exploitation of artificial receptors which can specifically discriminate between guest molecules and give us reading-out physical signals has become a very active area of endeavor. We and several other groups have recently been interested in the development of new sugar recognition methods useful in an aqueous system.[1-5] It has been shown that in aqueous solution reversible covalent-bond formation is frequently superior to hydrogen-bonding interaction.[6] We previously showed that a boronic-acid-appended porphyrin (**1**) forms one-dimensional stacked aggregates in aqueous solution and in the presence of sugars the aggregates give exciton-coupling bands (ECB) specific to the absolute configuration of added sugars.[7] Since there exists a general correlation between the sign of ECB and the sugar structure, this can become a novel and promising methodology for predicting the absolute configuration. In general, sugar-binding to the boronic acid group tends to make the complex more hydrophilic and deaggregate the porphyrin stack. Hence, one has to carefully choose the water versus DMSO ratio in a mixed solvent and enhance the **1** concentration in order to preserve the stacked porphyrin aggregate.[7] Here, it occurred to us that simple dimeric porphyrins may satisfy the basic requirement to generate such ECB in the presence of sugars as does the stacked aggregate of **1** if the boronic acid groups are introduced into the appropriate positions. It is known that anionic and cationic porphyrins form dimers with a 1:1 stoichiometry due to the electrostatic interaction.[8] We thus decided to apply this concept to create dimeric boronic acid-appended porphyrins from anionic **1** and cationic *o*-**2** or *p*-**2**. The CD spectral studies have established that the dimers become CD-active only in the presence of glucose and xylose, which are composed of the partially same skeleton.



1

Compounds *o*-**2** (mp >300 °C) and *p*-**2** (mp >300 °C) were synthesized by quaternization of commercially-available 5,10,15,20-tetra-4-pyridylporphyrin with 2-bromomethylphenylboronic acid and 4-chloromethylphenylboronic acid, respectively.[9] The bromide salt of *o*-**2** was ion-exchanged to give the chloride salt. They were identified by IR and ^{1}H NMR spectral evidence and elemental analyses. The measurements were carried out in water:DMSO = 300:1 v/v at 25 °C and pH 10.0 (50 mmol dm^{-3} carbonate buffer) where boronic acids can efficiently bind sugars with the aid of OH$^-$.[1,2,4]

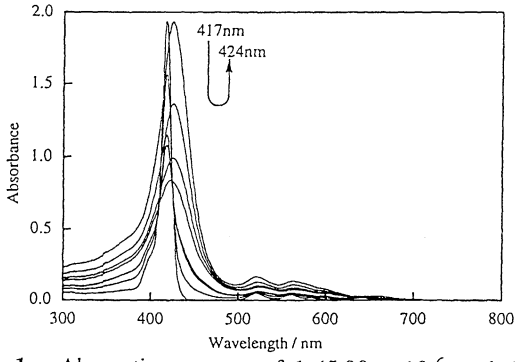


Figure 1. Absorption spectra of **1** (5.00 x 10^{-6} mol dm^{-3}) measured with increasing *o*-**2** concentration(0~7.00 x 10^{-6} mol dm^{-3})

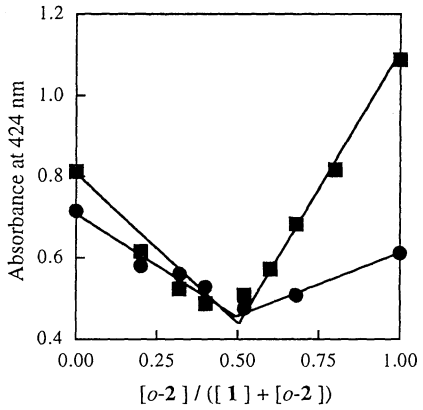


Figure 2. Continuous variation plots for [**1**] + [*o*-**2**] = 5.00 x 10^{-6} mol dm^{-3} (constant) in the absence (■) and the presence (●) of D-glucose (2.50 mmol dm^{-3})

When the **1** concentration was maintained constant while the *o*-**2** concentration was varied (Figure 1), the absorbance at the Soret band (417 nm) first decreased and then increased above the equimolar concentration, the λ_{max} shifting to 424 nm. The fluorescence maximum (655 nm) excited at 434 nm (isosbestic point in the absorption spectra at [*o*-**2**] ≦ [**1**]) decreased with increasing *o*-**2** concentration. The findings are reasonably explained by the aggregation of **1** with added *o*-**2**. To obtain firm evidence for the stoichiometry we made continuous variation plots (Figure 2). It is clearly seen from

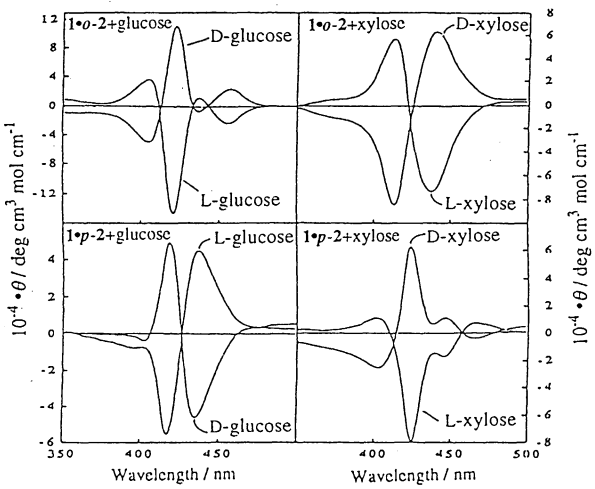
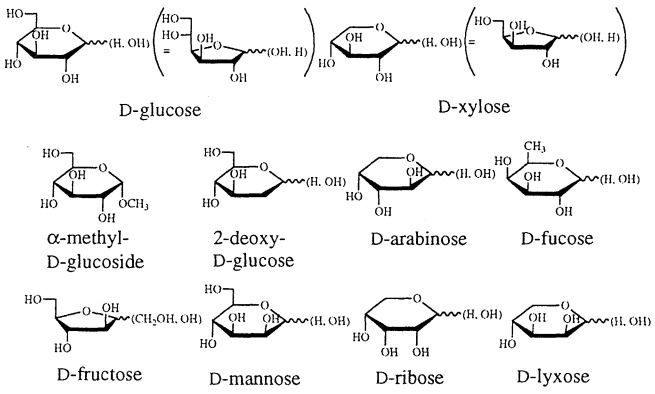


Figure 3. CD spectra: [1] = [*o*-2] = [*p*-2] = 1.00 x 10^{-5} mol dm^{-3}, [saccharide] = 5.00 x 10^{-3} mol dm^{-3}

Figure 2 that **1** and *o*-*2* form a 1:1 complex. The similar spectral properties were also observed for the **1** plus *p*-**2** system and for the presence of sugars (2.50 mmol dm^{-3}).

Here, we measured CD spectroscopy for the following eight monosaccharides and two glucose derivatives. Among them only glucose and xylose gave CD-active complexes with **1**·*o*-**2** and **1**·*p*-**2** dimers (Figure 3). Since 2-deoxy-D-glucose and α-methyl-D-glucoside did not give any CD-active species and it is sterically impossible for two proximal boronic acids to bind one monosaccharide intramolecularly, the CD activity observed for glucose and xylose should stem from the bridging of two porphyrins using four OH groups in glucose or xylose.[10]



It is not clear yet why only glucose and xylose can give the CD-active species. However, careful examination of the saccharide structure and the CD spectra provides us with the following pieces of information: (i) for the Soret band D-xylose affords the positive ECB for both **1**·*o*-**2** and **1**·*p*-**1** whereas D-glucose affords the positive ECB for **1**·*o*-**2** and the negative ECB for **1**·*p*-**2**, (ii) the pyranose form of xylose having only one *cis*-diol (at 1,2-position) useful for complexation with the boronic acid group cannot bridge two porphyrins, so that the furanose form should act as a cross-linker in the complex, and (iii) the basic skeleton of xylose is involved in that of glucose. In **1**·*o*-**2** the intermolecular distance between two boronic acids is relatively short and they face each other to create a cleft. To reasonably explain (i) ~ (iii) one may consider that D-xylofuranose is immobilized in **1**·*o*-**2** and the resultant complex affords the positive ECB. D-Glucofuranose, including the basic skeleton of D-xylofuranose and affording the positive ECB, should be immobilized in a similar manner in **1**·*o*-**2** (*i.e.*, using 1, 2- and 3, 5-diols). In **1**·*p*-**2** the intermolecular distance between two boronic acids is relatively long and they adopt a parallel orientation. D-Xylose, affording the positive ECB again, should be immobilized in the D-xylofuranose form. On the other hand, D-glucose affords the negative ECB and therefore should adopt the different binding mode: the possible boronic acid binding-sites are to use 1, 2- and 5, 6-diols in D-glucofuranose or 1, 2- and 4, 6-diols in D-glucopyranose.

In conclusion, the present study shows that dimeric boronic-acid-appended porphyrins generated from cationic and anionic porphyrins give the CD sign selectively for glucose and xylose and characteristically for their absolute configuration. The results indicate that combination of boronic acid functions as a sugar-binding site with porphyrins as a physical signal reporter is very promising for designing reading-out-type sugar sensing systems.

This work is supported by the grant-in-aid from the Ministry of Education, Science and Culture.

References and Notes

1 K. Tsukagoshi and S. Shinkai, *J. Org. Chem.*, **56**, 4089 (1991); K. Kondo, Y. Shiomi, M. Saisho, T. Harada, and S. Shinkai, *Tetrahedron*, **48**, 8239 (1992).

2 H. Murakami, T. Nagasaki, I. Hamachi, and S. Shinkai, *Tetrahedron Lett.*, **34**, 6273 (1993); H. Murakami, T. Nagasaki, I. Hamachi, and S. Shinkai, *J. Chem. Soc., Perkin Trans. 2*, **1994**, 975.

3 T. D. James, K. R. A. S. Sandanayake, and S. Shinkai, *Angew. Chem. Int. Ed. Engl.*, **33**, 2207 (1994); T. D. James, K. R. A. S. Sandanayake, and S. Shinkai, *Nature*, **374**, 345 (1995).

4 J. Yoon and A. W. Czarnik, *J. Am. Chem. Soc.*, **114**, 5874 (1992); M.-F. Paugan and B. D. Smith, *Tetrahedron Lett.*, **34**, 3723 (1993).

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

6 For a comprehensive review see F. Ohseto, K. Nakashima, and S Shinkai, *Yukagaku*, **43**, 845 (1994). For sugar recognition by porphyrins using the hydrogen-bonding interaction see T. Mizutani, T. Murakami, N. Matsumi, T. Kurahashi, and H. Ogoshi, *J. Chem. Soc., Chem. Commun.*, **1995**, 1257.

7 T. Imada, H. Murakami, and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, **1994**, 1557.

8 T. La, R. Richard, and G. M. Miskelly, *Inorg. Chem.*, **33**, 3159 (1994); J. F. Lispskier and T. L. Tran-Thi, *Inorg. Chem.*, **32**, 722 (1993); T. Shimizu and T. Iyoda, *Chem. Lett.*, **1981**, 853; U. Hofstra, R. B. M. Koehorst, and T. J. Schaafsma, *Chem. Phys. Lett.*, **130**, 555 (1986).

9 S. Arimori, M. Takeuchi, and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, **1995**, 961.

10 5,10,15,20-Tetrakis(*N*-methyl-4-pyridinium)porphyrin tetra-tosylate (**3**) forms a 2:1 **1**·**3** complex (evidenced by the continuous variation plot). Neither glucose nor xylose gave any CD-active species with the trimeric complex. The result also supports the view that the CD-active species with the dimeric **1**·**2** complexes stem from the bridging of two porphyrins by these monosaccharides.