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Sugar Sensing Utilizing Aggregation Properties of a Boronic-acid-appended Porphyrin

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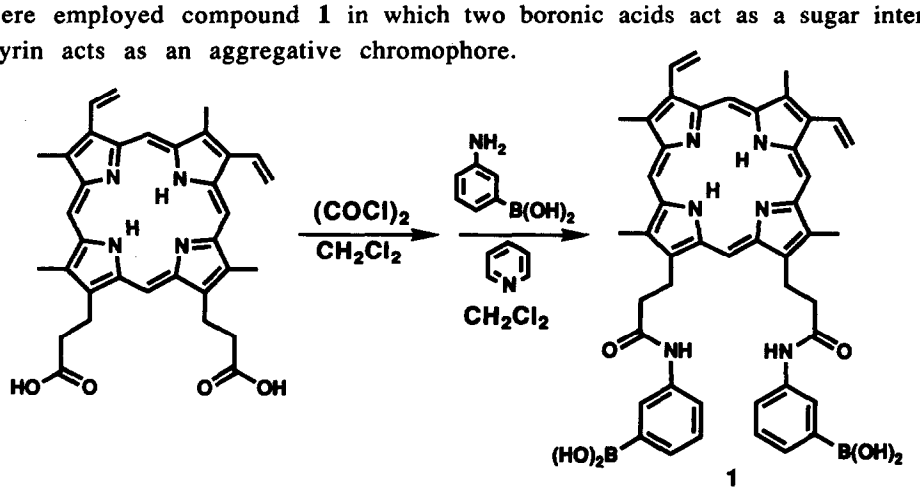
Summary: It was shown that monosaccharides can be sensitively detected utilizing aggregation properties of a boronic-acid-appended porphyrin. Since the magnitude of the spectral change is correlated with the association tendency between sugars and boronic acids, the origin of the spectral change is related to the increase in the hydrophilicity in the sugar-binding site.

The molecular design of artificial receptors has recently become a very active area of endeavor. The overview of the past literatures teaches us that hydrogen-bonding interactions are versatilely used for precise recognition of guest molecules.[1] We have currently been interested in sugar recognition and reading-out of the recognition process.[2-6] Although hydrogen-bonding interactions are also useful for sugar recognition,[7-9] the effect is exerted only in aprotic solvents. To "touch" sugars in water we have proposed to use a boronic acid which can form complexes with a variety of sugar molecules in an aqueous system.[2-5] Through these studies we learned that when boronic acid $RB(OH)_2$ forms complexes with saccharides, they become more hydrophilic than starting $RB(OH)_2$. Here, it occurred to us that if $RB(OH)_2$ is appropriately appended to chromophores which tend to aggregate in water, the aggregation-deaggregation equilibrium would be controlled by the concentration, absolute configuration, and complex stoichiometry of saccharides and the process can be "read-out" by the color change: that is, we expected that the boronic acid moiety would act as a "sugar interface". We here employed compound **1** in which two boronic acids act as a sugar interface and a porphyrin acts as an aggregative chromophore.



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Compound **1** (mp > 300 °C) was synthesized from protoporphyrin according to the above-mentioned route and identified by IR and ^{1}H NMR spectral evidence and elemental analysis.

Figure 1 shows the absorption spectra of **1** in DMSO-water mixed solvents. The sharp peak (λ_{max} 405 nm) in DMSO, which is attributed to monomeric **1**, was gradually flattened with increasing water concentration. The broad peak (λ_{max} 375 nm) is attributable to aggregated **1**. When sodium dodecylsulfate (0.10 M) was added, the peak became sharp again, indicating that **1** exists discretely in the micellar phase.

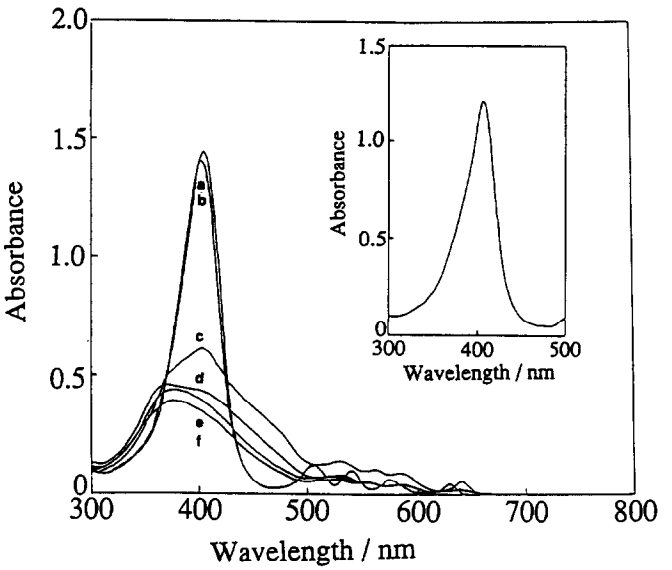

Fig. 1. Absorption spectra of **1** (1.00 X 10^{-5} M) at 25 °C in (a) DMSO, (b) DMSO:water = 2:1, (c) DMSO:water = 1:1, (d) DMSO:water = 1:2, (e) DMSO:water = 1:30, and (f) DMSO:water = 1:300. The inserted spectrum is in DMSO: water = 1:30 in the presence of 0.10 M SDS.

In Fig. 2, we showed the UV-visible spectral change induced by added D-fructose. With increasing D-fructose concentration the absorbance gradually increased and the λ_{max} at 375 nm shifted to 380 nm (ε 8.9 X 10^4 M^{-1}cm^{-1}). According to Inamura and Uchida,[10] protoporphyrin dispersed in basic aqueous solution gives the Soret band at 380 nm (ε 9.5 X 10^4 M^{-1}cm^{-1}), which is ascribed to the dimer. The coincidence in λ_{max} and ε supports the view that the binding of D-fructose to the boronic acids changes aggregated **1** to dimeric **1**. In Fig. 3, the absorbance at 380 nm was plotted against sugar concentrations. Among four monosaccharides tested herein, D-fructose showed the largest deaggregation effect. In contrast, the spectrum of protoporphyrin was scarcely changed by the addition of these monosaccharides.

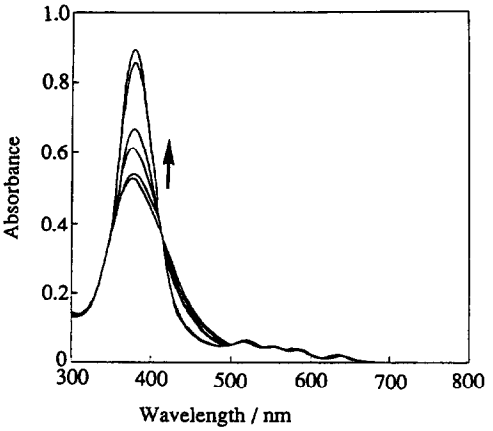

Fig. 2. Spectral change induced by the addition of D-fructose: [1] = 1.00 X 10^{-5} M, DMSO:water = 1:30, pH 10.5 with 0.067 M carbonate, 25 °C.

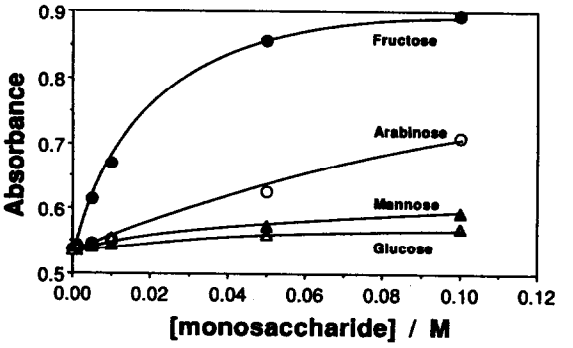

Fig. 3. Absorbance increase at 380 nm plotted against sugar concentrations.

We found that the sugar-binding process can be read-out more sensitively with a fluorescence technique. In the absence of sugars **1** was nonfluorescent because of aggregation (Fig. 4). With increasing sugar concentrations the fluorescence intensity at 632 nm increases conspicuously. Among four monosaccharides tested herein, D-fructose again showed the largest fluorescence increase (Fig. 5). We have confirmed that even 0.5 mM of D-fructose can be detected by this method. In contrast, the fluorescence change in protoporphyrin was scarcely induced by the addition of these four monosaccharides.

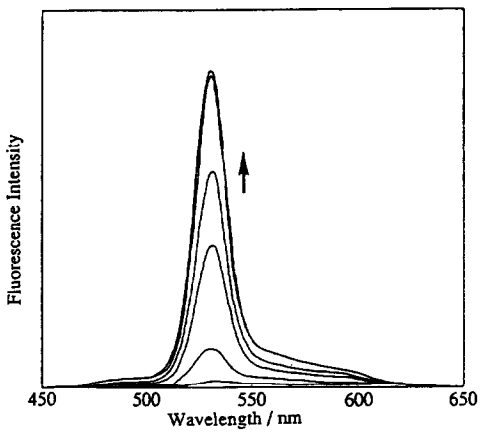

Fig. 4. Fluorescence spectral change induced by the addition of D-fructose: [1] = 1.00 X 10^{-5} M, DMSO:water = 1:30, pH 10.5 with 0.067 M carbonate, 25 °C, excitation 415 nm (isosbestic point in Fig. 2).

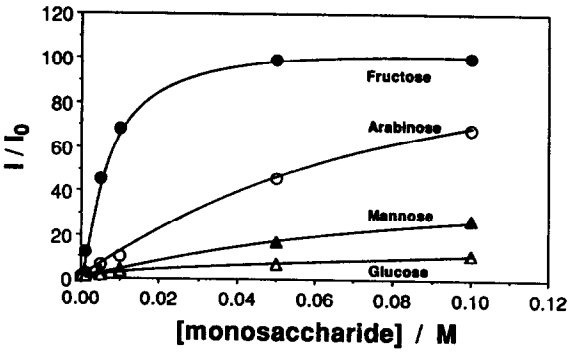

Fig. 5. Fluorescence intensity at 632 nm plotted against sugar concentrations.

What is the origin of sugar-induced spectral changes? The association constants of monosaccharides for boronic acids have been determined.[3,6,11] The order of the association constants is exactly in line with the order of the spectral change order: *i.e.*, D-fructose > D-arabinose > D-mannose ≧ D-glucose. This implies that the complexation of the boronic acids with sugars makes **1** more hydrophilic and the sugar that shows the higher affinity with the boronic acids can induce the deaggregation more efficiently.

In conclusion, the present letter demonstrated that the sugars can be sensitively detected by utilizing the aggregation properties of **1**. We believe that the fine molecular design of the boronic site will further enable the selective binding of sugars and eventually, the energy-transfer phenomena occurring in a porphyrin system will be controlled by the sugar-binding event.

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