Saccharide Induction of Chiral Orientation of the Aggregate Formed from Boronic-Acid-Appended Amphiphiles

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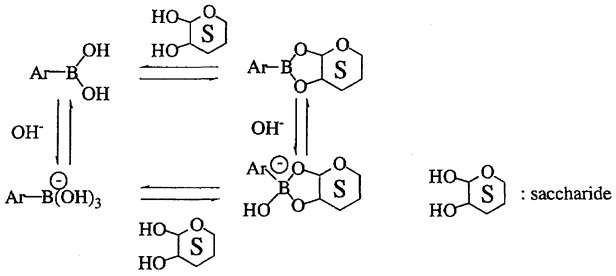
A boronic-acid-appended amphiphile bearing an azobenzene chromophore at the chain center, *N*-[4-(dihydroxyboryl)benzyl]-*N*-(10-{4-[(4-dodecyloxyphenyl)azo)]phenoxy}decyl)-*N*,*N*-dimethylammonium bromide (**4**) was synthesized. In aqueous media, compound **4** formed a scarcely-oriented aggregate in the absence of saccharides, but in the presence of saccharides the boronic acid groups formed saccharide complexes and the resultant amphiphiles formed well-ordered aggregates. The ΔH value in DSC depended on the inherent structure of the added saccharides. Although D-glucose and methyl α-D-glucopyranoside could only form less ordered aggregates, D-fructose and D-xylose formed well-ordered aggregates. The saccharide complexes with **4** became CD-active with the appearance of exciton-coupling bands inherent to the saccharides. The CD band intensity was increased with increasing saccharide concentration but decreased by a further increase in the saccharide concentration. These results indicate that the reversible boronic acid–saccharide interaction is useful to induce the chirality in the ordered aggregate structure, where saccharides are used as a trigger for the chiral induction.

It has been established that saccharides are important as signals, triggers, identification tags, etc. for biological events occurring on the cell surface. For example, it is known that certain gangliosides can impart specialized characters to the cells.[1] Saccharides, which have several structural features such as multiple chiral centers and diversiform arrangement of hydroxy groups, are useful as a unique building-block for designing information devices.[2] In an artificial system, several research groups have demonstrated that introduction of chiral substituents into amphiphiles results in unique assembly structures such as helix,[3,4] super-coil,[5] and gels,[6,7] which cannot be created without them. In most cases, however, the chiral substituents are introduced via complex synthetic processes using covalent linkages. As a result, the syntheses of such chiral amphiphiles frequently become troublesome, time-consuming, and expensive, and therefore the application has been very limited. We considered that saccharides may be useful as chiral resources for the preparation of such chiral amphiphiles. Generally saying, however, it is known that the synthetic modification of saccharides is rather difficult. Is there any good alternate idea by which one can readily and less expensively introduce saccharides into amphiphiles?

We have recently been interested in molecular design of a new sugar recognition system useful in aqueous media.[8,9] We have already demonstrated the validity of boronic acid as a saccharide receptor functional group, because the reaction with saccharides to form a covalent linkage can take place rapidly and reversibly even in aqueous media (Scheme 1).[8—12] This is a big advantage of the boronic acid function over the hydrogen-bonding function, which is nearly useless in aqueous media. It has thus become possible to use a



Scheme 1. Reversible formation of a boronate ester complex from a diol (i.e., saccharide) and an arylboronic acid.

variety of saccharide molecules, abundant natural resources, as a chiral auxiliary for boronic-acid-appended amphiphiles. Meanwhile, Fuhrhop et al.[13] demonstrated that protoporphyrin IX **1**, covalently linking two glycosamines as a chiral auxiliary, can form ordered aggregates in aqueous media. We demonstrated that similar but more diversiform chiral aggregates can be created by simply mixing saccharides with a boronic-acid-appended porphyrin **2**[14] or with a boronic-acid appended azobenzene-containing amphiphile **3** (Chart 1).[15] These novel findings suggest that the boronic acid-saccharide interaction may be useful as a novel trigger to change the morphology of aggregates formed in aqueous media. If this idea works as expected, it would become a potential model system for saccharide control of the cell morphology. We previously synthesized compound **3**, expecting that the saccharide complexation with the boronic acid moiety would create an anionic charge to disperse **3** into aqueous solution and the aggregation mode would be detected from a spectroscopic change in the azobenzene moiety.[15] In fact, however,

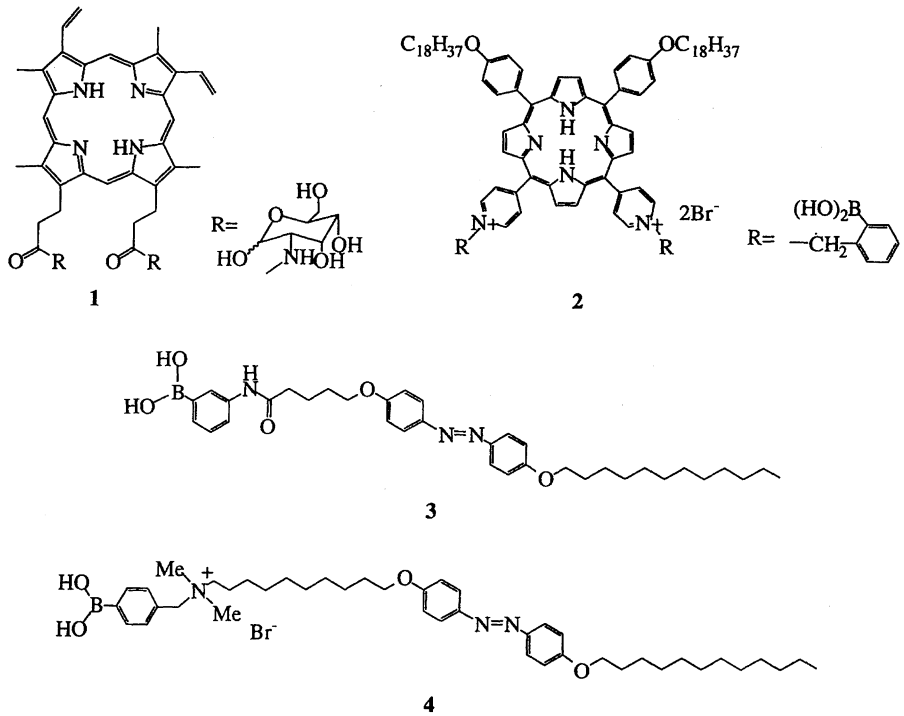


Chart 1.

3 could not be dispersed homogeneously into aqueous media even in the presence of excess saccharides but only solubilized with dipalmitoylphosphatidylcholine (DPPC).[15] To improve the water solubility we newly synthesized compound **4** with a quaternary ammonium ion. There is a precedent that such an intramolecular cationic charge facilitates the saccharide complexation that accompanies an anionic charge generation.[16] Here, we report the characterization of the aggregation mode of a boronic-acid-appended amphiphile **4** in the presence of saccharides, aiming at the control of the assembly structure by added saccharides. The chromophoric azobenzene moiety should be useful not only to detect the aggregation properties by spectroscopic methods but also to facilitate the aggregation by π–π stacking and/or hydrophobic interactions.[17]

Results and Discussion

Influence of Solvent Composition on the Aggregation Mode. The azobenzene chromophore integrated in compound **4** gives us the information to distinguish between two different aggregation modes: They are a face-to-face H-aggregation and a head-to-tail J-aggregation. They are distinguishable by the shift of the absorption maximum of the azobenzene moiety.[17] If the absorption maximum shifts to a shorter wavelength, the amphiphile adopts an H-aggregation, but if the absorption maximum shifts to a longer wavelength, the amphiphile adopts a J-aggregation. Figure 1 shows the absorption spectra of **4** in water (pH 10.5)–methanol mixtures. When **4** was dissolved in methanol, the absorption maximum (λ_{max}) appeared at 357 nm. This λ_{max} is attributed to non-aggregated **4**. Since the medium pH should be sufficiently higher than pK_a of boronic acid,[8–10,13] one can regard the hydrophilic head group as zwitterionic. When the concentration of water (adjusted to pH 10.5) was increased, the λ_{max} of **4** shifted to 328 nm. The shift to shorter wavelength implies that the chromophoric azobenzene moieties adopt an H-aggregation. It is clearly seen from Fig. 1 that a sudden shift from λ_{max} 357 nm to λ_{max} 328 nm occurs between 50 vol% methanol and 80 vol% methanol. The result supports the view that the aggregate is formed water concentrations higher than 50 vol%. When excess D-glucose was added, the λ_{max} was scarcely changed but the absorbance was significantly decreased. Although the reason for this is not yet known, there is no doubt that **4** still retains the H-type aggregate and the complexation with saccharides does affect the aggregation mode.

Characterization of the Aggregates by DLS and DSC. First, we measured dynamic light scattering (DLS) to obtain direct evidence for the aggregate formation. The measurements were done in 3 vol% methanolic solution (pH 10.5), which was commonly used for the subsequent experiments (except the DSC measurements). In Fig. 2, the average particle size of **4** in the absence and the presence of saccharides is plotted against the measurement time. In the absence of saccharides (▲ in Fig. 2) the average particle size of **4** was large (ca. 10^3 nm) and increased with the measurement time. After 2—3 h, **4** gradually precipitated from the solution. The result implies that although **4** has a zwitterionic head group, the hydrophilicity is not yet sufficient to form a stable aggregate in aqueous solution: The aggregate particles continue to grow, which eventually leads to precipitation. The similar particle-growth was also observed for **4** in the presence of D-glucose or methyl α-D-glucopyranoside (25 mmol dm^{-3} each). In general, these saccharides are known to have low association constants with phenylboronic acid derivatives.[8–12,14,16,18] Hence, one can presume that these saccharides are not suf-

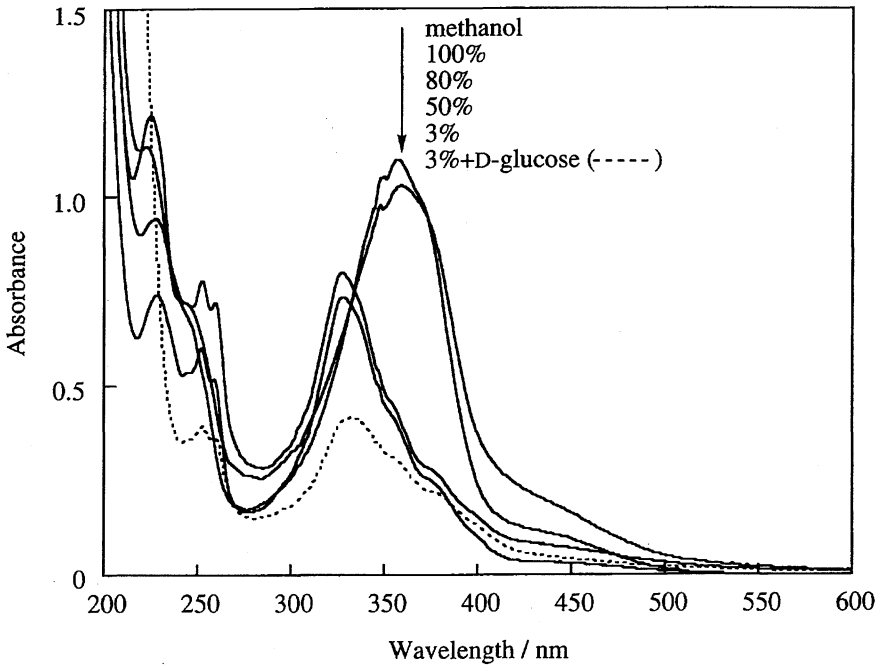


Fig. 1. Absorption spectra of **4** (5.00×10^{-5} mol dm^{-3}) at 25 °C in methanol–water (pH 10.5 with 50 mmol dm^{-3} carbonate): - - - indicates the presence of D-glucose (25.0 mmol dm^{-3}) in 3 vol% methanol.

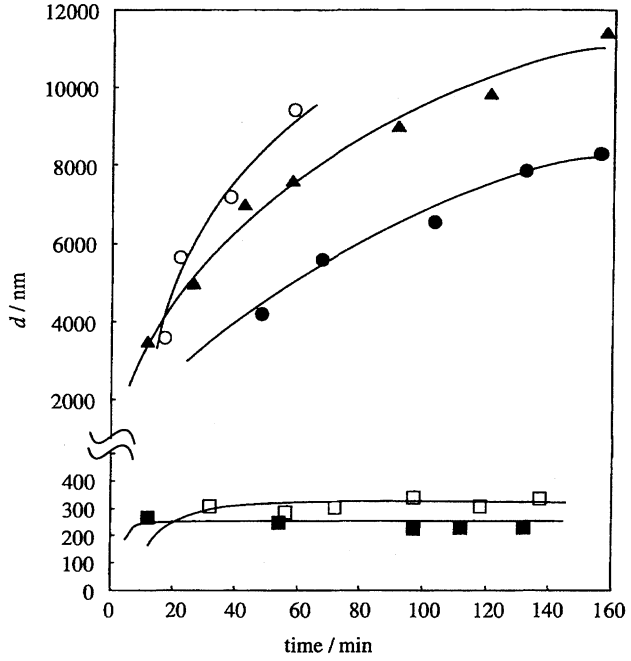


Fig. 2. Plots of the average particle size (d) versus the measurement time: [**4**] = 5.00×10^{-5} mol dm^{-3}, [saccharide] = 25.0 mmol dm^{-3}, pH 10.5 with 50 mmol dm^{-3} carbonate buffer, 3 vol% methanol: no saccharide (▲), D-fructose (■), D-xylose (□), D-glucose (●), methyl α-D-glucopyranoside (○).

ficiently bound to the boronic acid groups on the aggregate surface to particularly stabilize the aggregate structure, even though the intramolecular cationic charge facilitates the saccharide complexation by the charge neutralization.[16] In contrast, when D-fructose or D-xylose was added, the average particle size of **4** was small (200—400 nm) and kept a constant value for several hours. It is known that these saccharides have large association constants with phenylboronic acid derivatives.[8—12,14,16,18] The results support the view that these saccharides are sufficiently bound to the boronic acid groups and saccharide-linked zwitterionic head groups are hydrophilic enough for the particles to maintain the aggregate structure stably. Undoubtedly, the time-independence of the aggregate structure is indicative of the formation of stable ordered aggregates. The finding that the particles, the surface of which is "coated" by saccharides, do not fuse with each other is particularly worth mentioning.

To obtain further insights into the aggregation mode, we measured differential scanning calorimetry (DSC). To increase the concentration of **4** up to the level suitable to the DSC measurement we here used 30 vol% methanolic solutions. The DSC thermograms are shown in Fig. 3 and the resultant parameters are summarized in Table 1. It is seen from Fig. 3 that an endothermic peak reproducibly appears at T_c = 68—75 °C and the T_c value is scarcely affected by the addition of saccharides. In contrast, the ΔH value shows a drastic change. In the absence of saccharides, **4** has a small ΔH value (1.7 kJ mol^{-1}), indicating that the orientation of **4** is rather less developed in the absence of saccharides. When saccharides are added, the ΔH value increases by factors of 2.5—7.4 and as a general trend, the saccharides that can keep a constant particle size (i.e., D-fructose and D-xylose) have the ΔH larger than those which result in the time-dependent particle growth (i.e., D-glucose and methyl α-D-glucopyranoside). Figure 3 also shows that D-fructose- and D-xylose-complexed aggregates have a sharp endothermic peak, while D-glucose- and methyl α-D-glucopyranoside-complexed aggregates have a few weak peaks. These DSC

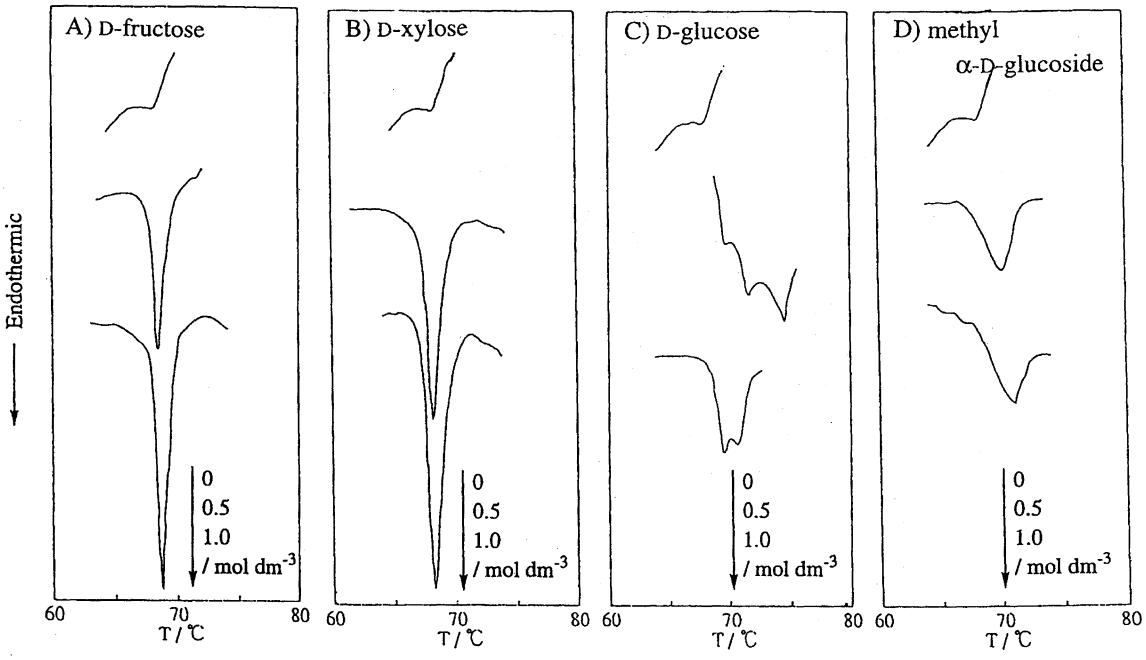


Fig. 3. DSC thermograms of **4** (1.00×10^{-2} mol dm^{-3}) in the presence of saccharides: (A) D-fructose, (B) D-xylose, (C) D-glucose, (D) methyl α-D-glucopyranoside in aqueous solution [water (pH 10.5 with 50 mmol dm^{-3} carbonate buffer)–methanol, 70 : 30 v/v].

Table 1. DSC Parameters of **4**[a)]

Saccharide	Saccharide concentration / mmol dm^{-3}	T_c / °C	ΔH / kJ mol^{-1}
No saccharide	0	69.0	1.7
D-Fructose	500	68.7	6.5
	1000	69.0	10.4
D-Xylose	500	68.2	7.1
	1000	69.4	12.6
D-Glucose	500	70.2, 72.0, 74.6	6.1
	1000	69.8, 70.9	6.6
Methyl α-D-glucopyranoside	500	70.3	5.5
	1000	71.3	4.3

a) Measurement conditions are similar to those recorded in a caption to Fig. 3.

data consistently indicate that the former two aggregates have a uniformly-oriented, stable aggregate structure but the latter two aggregates consist of a few metastable aggregate structures. As described above, this is not only due to the structural difference but also due to the low affinity of these saccharides for the boronic acid group.[8—12,14,16,18)]

Observation of the Aggregates by Transmission Electron Micrograph (TEM). To obtain a visual insight into the aggregate structure, we observed the aggregation mode of **4** in the presence of saccharides by TEM. The amphiphiles were first sonicated in an aqueous solution with saccharides and then shadowed with phosphotungstic acid (for the detailed method see Experimental Section). As saccharides, D-fructose and D-xylose, which resulted in stable aggregates, were used. As shown in Fig. 4, fibrous aggregates with a 12—25 nm diameter were observable. This diameter is comparable with or slightly longer than that assuming the formation of a bilayer membrane,[17)] because the chain length of **4** is estimated (the CPK molecular model) to be about 5 nm. We previously observed SEM pictures of fibrous aggregates formed in organic gels prepared from azobenzene-appended cholesterols and tried to find some possible correlation between the fibril structure and CD spectroscopy.[6a)] Very interestingly, the cholesterol derivatives showing a positive exciton-coupling band ((*R*)-chirality) gave right-handed helical fibrils while those showing the negative exciton-coupling band ((*S*)-chirality) gave left-handed helical fibrils:[6a)] That is, the microscopic CD spectral difference is correlated with the macroscopic aggregate morphology. We thus expected that the chirality in saccharides complexed with **4** induces the chiral orientation of **4**. Although we carefully checked the TEM pictures, the chiral structure related to the

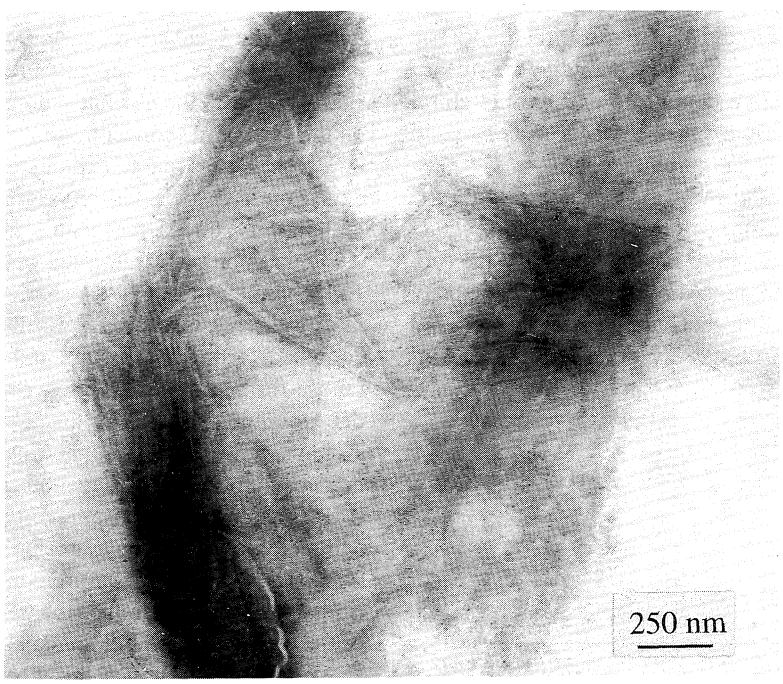


Fig. 4. TEM picture of **4** in the presence of D-fructose.

saccharide chirality (e.g., helical structure) was not visually confirmed in this system. Hence, we tried to find evidence for chiral orientation from CD spectroscopy of the azobenzene moieties, which is a powerful tool to sensitively detect the chirality in molecular assemblies.

Chiral Orientation of the Aggregates as Detected by CD Spectroscopy. To obtain an insight into the saccharide-induced chiral orientation of **4** we measured CD spectra of **4** in the presence of saccharides (Fig. 5). It is seen from Fig. 5 that there is a clear plus-to-minus or minus-to-plus CD band with $\theta = 0$ at around 335 nm (except D-glucose). Comparison with Fig. 1 establishes that this band is complementary to λ_{max} 328 nm in the absorption spectra and therefore ascribable to an exciton-coupling band. According to the principle of the exciton-coupling interaction,[19] the amphiphiles complexed with D-fructose and methyl α-D-glucopyranoside give a sign of (*R*)-chirality with the positive first Cotton effect and the negative second Cotton effect, indicating that the azobenzene moieties are oriented in a clockwise direction, while the amphiphile complexed with D-xylose gives a sign of (*S*)-chirality with the negative first Cotton effect and the positive second Cotton effect, indicating that the azobenzene

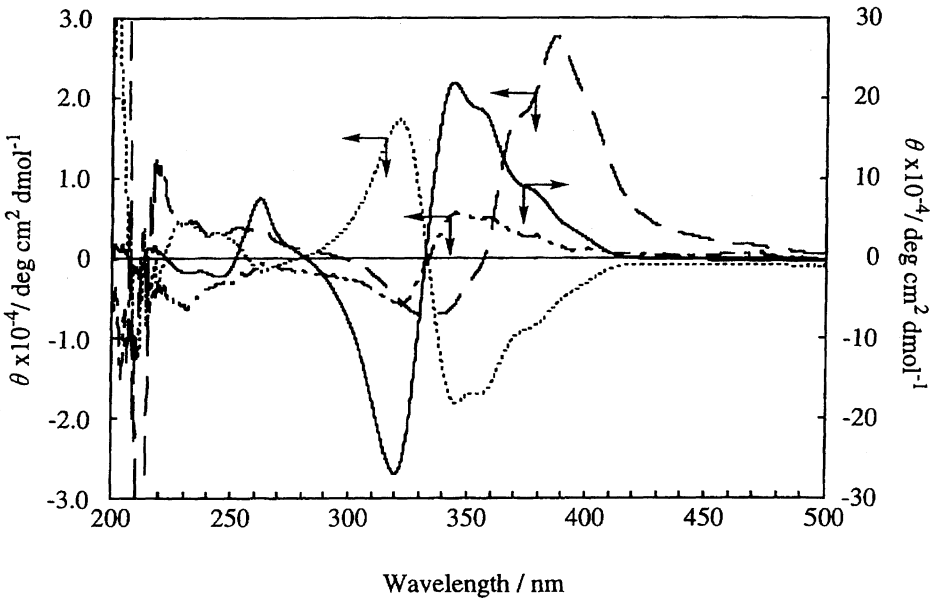


Fig. 5. CD spectra of **4** (5.00×10^{-5} mol dm^{-3}) in the presence of saccharides: – • – D-fructose (0.30 mmol dm^{-3}), •••• D-xylose (0.50 mmol dm^{-3}), - - - D-glucose (10.0 mmol dm^{-3}), — methyl α-D-glucopyranoside (100 mmol dm^{-3}), pH 10.5 with 50 mmol dm^{-3} carbonate buffer, 3 vol% methanol. The saccharide concentrations used for the measurements are those at the largest CD intensity.

moieties are oriented in an anti-clockwise direction. The result show that saccharides covalently bound to the surface of the aggregate are effective enough to enforce the chiral orientation of chromophoric azobenzene segments situated at the central position of the amphiphilic chain.

We estimated the dependence of the CD intensity on the saccharide concentration (Fig. 6). In Fig. 6, the θ_{345} value at the CD maximum or minimum is plotted against the saccharide concentration. The plots show that the CD intensity first increases with increasing saccharide concentration, but addition of excess saccharides rather decreases the CD intensity. The saccharide concentration where the largest CD intensity is observed depends on the kind of added saccharide. Why does the CD intensity give a biphasic dependence on the saccharide concentration?

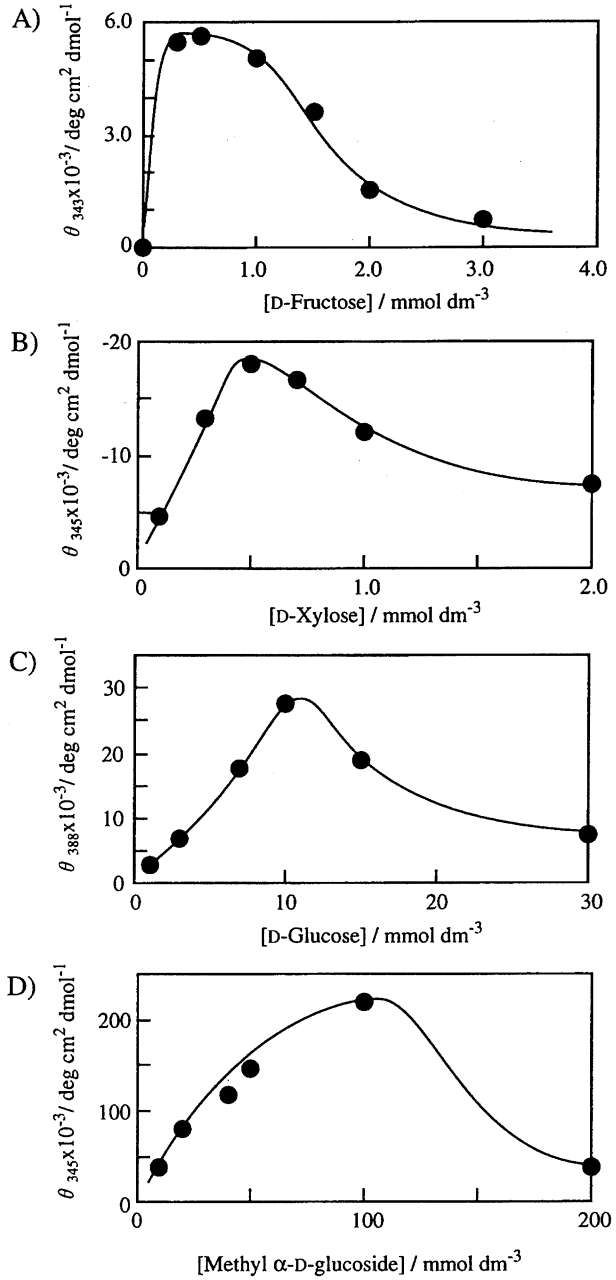


Fig. 6. Plots of θ_{max} or θ_{min} (observed) versus saccharide concentration: [**4**] = 5.00×10^{-5} mol dm^{-3}, pH 10.5 with 50 mmol dm^{-3} carbonate buffer, 3 vol% methanol: (A) D-fructose, (B) D-xylose, (C) D-glucose, (D) methyl α-D-glucopyranoside.

To find a reasonable explanation for the biphasic dependence we here consider the origin of the CD activity in this system. To find a reasonable mechanism one must clarify which complex is formed between saccharide and **4**, a 1 : 1 complex or a 1 : 2 saccharide/**4** complex.[9] For example, D-glucose is known to form 1 : 2 glucose/boronic acid complexes using 1,2-*cis*-diol and 4,6- or 5,6-diol (in the pyranose form and the furanose, respectively).[8,9,20—22] Hence, one possible rationale is that already reported for related systems,[8,9,20—22] a stoichiometrical change from 1 : 2 to 1 : 1 may result in a biphasic dependence. In this system, although D-fructose and D-glucose have two binding sites, D-xylose and methyl α-D-glucopyranoside have only one binding site (Chart 2).[9] The CD measurements showed that all saccharides tested here can induce the CD-active spectra, regardless of the number of the binding site. This means that even the 1 : 1 complex can induce chiral orientation of the aggregates and the formation of the 1 : 2 complex is not a prerequisite for the chiral orientation of the azobenzene moieties. Presumably, the CD activity of the complexes with θ = 0 at around 335 nm (i.e., D-fructose, D-xylose, and methyl α-D-glucopyranoside) should stem from the same origin, which is most likely associated with the formation of 1 : 1 complexes. On the other hand, D-glucose is one of the monosaccharides that tend to form 1 : 2 saccharide/boronic acid complexes.[8,9,20—22] Thus, the exceptional CD spectrum observed for the D-glucose complex (Fig. 5) may be due to the mixing of the CD bands arising from the 1 : 1 and the 1 : 2 complex. In particular, the largest θ_{max} observed at red-shifted 385 nm suggests that this strong CD band arises instead from the J-aggregated species. Careful examination of Fig. 1 indicates that in the absorption spectrum of **4** in the presence of D-glucose, the ε_{328} ascribable to an H-aggregation decreases and a new shoulder ascribable to a J-aggregation appears at around 380 nm. We now consider that D-glucose partly forms a 1 : 2 D-glucose/**4** complex, which eventually enforces the J-type aggregation. In this molecular assembly system, however, it is rather difficult to experimentally measure the stoichiome-

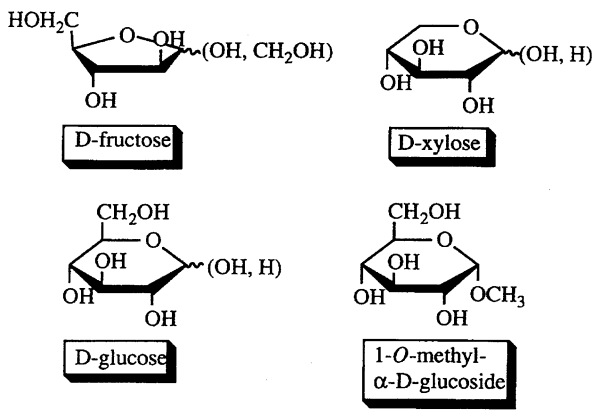


Chart 2.

try. The survey of past references suggests that glucose, the bonding sites [1,2-diol and 4,6 (or 5,6)-diol] of which react with phenylboronic acids independently, tends to form a 1 : 2 glucose/boronic acid complex[8,9,20—22] but fructose tends to form a 1 : 1 complex with the boronic acid group interacting with three OH groups.[23] This conjecture is compatible with the DSC data that the **4**+D-glucose complex affords the plural endothermic peaks at the phase transition region.

Next we compare the results of CD measurements with those of DSC spectra. The saccharides that gave a sharp endothermic peak (i.e., D-fructose and D-xylose) have weak CD intensities. In contrast, the saccharides that gave broad endothermic peaks (i.e., D-glucose and methyl α-D-glucopyranoside) have strong CD intensities (when compared at the largest θ value in Fig. 6). This suggests that when the orientation of amphiphiles is moderately disordered, the aggregate has a large θ value. If an ample amount of saccharides is added to these moderately disordered system, **4** would form a more ordered aggregate structure, which eventually leads to the large θ value (although it appears at a fairly high saccharide concentration: see Figs. 6C and 6D). In the ordered aggregate, on the other hand, the orientation of the azobenzene moieties would be more influenced by the packing of hydrophobic segments than by the chirality of saccharides present at the hydrophilic surface. At low saccharide concentrations, however, the aggregate formed from **4** would have some disorder, allowing the azobenzene moieties to be twisted asymmetrically. Thus, the largest θ value appears at the low saccharide concentrations: see Figs. 6A and 6B.

Conclusion. This study demonstrated that the aggregation mode of **4** can be partially controlled by a boronic acid–saccharide interaction that occurs at the aggregate surface. We consider that this attempt is interesting in relation to the imitation of certain cell membranes which have saccharide-recognition sites on the cell surface and change their morphology in response to added saccharide structures.[1] More in general, we believe that this concept will become a novel method for the control of aggregate morphology by physiologically-nontoxic saccharides. The research toward these new potentials is currently been done in this laboratory.

Experimental

Measurements. Spectroscopic data were obtained by a Bruker ARX-300(300 MHz) FT-NMR (AC-250P) for ^{1}H NMR spectroscopy using tetramethylsilane or sodium 3-(trimethylsilyl)-propane-1-sulfonate as a reference. Mass spectrometry was done on a Hitachi M-2500 instrument. IR spectra were recorded on a JASCO infrared spectrophotometer (JASCO A-100). The absorption spectroscopy and circular dichroism spectroscopy were measured by a Shimadzu UV-visible spectrophotometer (UV-160A) and a JASCO spectropolarimeter (J-720), respectively. The DLS was measured with an Otsuka Electronics super dynamic light scattering spectrophotometer (VLS-70). The phase transition behavior was studied with a differential scanning calorimeter (Seiko Instruments SSC/5200). Aggregate morphology was examined by transmission electron microscopy (Hitachi H-600).

4-[(4-Dodecyloxyphenyl)azo]phenol. The preparation of this compound from 4-dodecyloxyacetanilide via 4-dodecyloxyaniline has already been reported:[15] Yield 34.5 g (53%) from 4-dodecyloxyaniline, mp 108.7—110.6 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.88 (t, J = 6.8 Hz, 3H), 1.27—1.43 (m, 18H), 1.85 (p, J = 6.6 Hz, 2H), 4.06 (t, J = 6.6 Hz, 2H), 7.04 (m, 4H), 7.89 (m, 4H), 8.48 (s, 1H). MS Calcd for $C_{24}H_{34}O_2N_2$: M, 382.6. Found: m/z 382.

10-{4-[4-(Dodecyloxyphenyl)azo]phenoxy}decyl Bromide. A mixture of 4-[(4-dodecyloxyphenyl)azo]phenol (1.0 g, 1.3 mmol), 1,10-dibromodecane (1.2 g, 4.0 mmol), KOH (200 mg, 3,6 mmol), and ethanol (150 ml) was stirred at reflux temperature for 12 h. After cooling, water (20 ml) was added. The precipitate was collected by filtration, and was purified by flash chromatography over silica gel with chloroform and recrystallized from chloroform–ethanol: Yield 820 mg (52%), mp 99.0—99.9 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ = 0.87 (t, J = 6.85 Hz, 3H), 1.10—1.60 (m, 32H), 1.80 (m, 4H), 3.41 (t, J = 6.84 Hz, 2H), 4.03 (t, J = 6.54 Hz, 4H), 6.98 (d, J = 8.90 Hz, 4H), 7.85 (d, J = 8.85 Hz, 4H). IR (KBr) ν_{C-H} 2950—2800 cm^{-1}, ν_{B-O} 1311 cm^{-1}, ν_{C-O} 1239, 1009cm^{-1}.

***N*-(10-{4-[4-(Dodecyloxyphenyl)azo]phenoxy}decyl)-*N*,*N*-dimethyl Amine.** 10-{4-[4-(Dodecyloxyphenyl)azo]phenoxy}decyl bromide (740 mg, 1.2 mmol) was dissolved in THF. After dimethylamine gas was bubbled into this solution for 30 min at 0 °C, NaOH (750 mg, 19 mmol) was added. The mixture was stirred at 0 °C for 5 h and at room temperature for 12 h. The mixture was concentrated to dryness and the residue was dissolved in chloroform. The organic layer was washed with water and dried over anhydrous magnesium sulfate. The product was recrystallized from chloroform–methanol: Yield 630 mg (95 %), mp 102.0—103.6 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ = 0.87 (t, J = 6.78 Hz, 3H), 1.00—1.50 (m, 32H), 1.68 (s, 2H), 1.81 (m, 4H), 2.21 (m, 6H), 4.03 (t, J = 6.53 Hz, 4H), 6.98 (d, J = 8.83 Hz, 4H), 7.85 (d, J = 8.83 Hz, 4H). IR (KBr) ν_{C-H} 3000—2800 cm^{-1}, ν_{B-O} 1307 cm^{-1}, ν_{C-O} 1235, 1011 cm^{-1}.

***N*-[4-(Dihydroxyboryl)benzyl)]-*N*-(10-{4-[(4-dodecyloxyphenyl)azo]phenoxy}decyl)-*N*,*N*-dimethylammonium Bromide (4).** A mixture of *N*-(10-{4-[4-(dodecyloxyphenyl)azo]phenoxy}decyl)-*N*,*N*-dimethyl amine (70 mg, 0.27 mmol), 2-[4-(bromomethyl)phenyl]-1,3,2-dioxaborynane[24] (120 mg, 0.47 mmol) in THF (10 ml) was stirred at room temperature for 48 h. After removal of THF, the residue was recrystallized from chloroform–hexane: Yield 60 mg (77%), mp 180.0—195.0 °C. ^{1}H NMR (250 MHz, $CDCl_3$–DMSO-d_6 1 : 1) δ = 0.87 (t, 3H), 1.00—1.50 (m, 32H), 1.79 (m, 4H), 2.99 (bs, 6H), 3.50 (m, 2H), 4.05 (m, 4H), 4.55 (s, 2H), 6.81 (s, 2H), 7.03 (d, J = 8.83 Hz, 4H), 7.82 (d, J = 7.90 Hz, 4H), 7.49 (d, J = 7.78 Hz, 2H), 7.91 (d, J = 7.78 Hz, 2H). IR (KBr) ν_{O-H} 3600—3000 cm^{-1}, ν_{C-H} 2950—2800 cm^{-1}, ν_{B-O} 1300 cm^{-1}, ν_{C-O} 1235, 1013 cm^{-1}.

Preparation of the Samples for CD, DLS, and TEM. The DLS and CD samples were prepared as follows. To a buffered aqueous solution were added saccharide and a methanol stock solution of **4**. The resultant mixed solution (water–methanol, 97 : 3 v/v; pH 10.5 with 50 mmol dm^{-3} carbonate buffer) containing **4** (5.0×10^{-5} mol dm^{-3}) and saccharide was sonicated for 30 s. The CD samples were left at 25 °C for 15 min for aging. The sample solutions for TEM observation were prepared by a similar operation using an aqueous solution [water (pH 10.5 with 50 mmol dm^{-3} carbonate buffer)–methanol, 70 : 30 v/v] containing **4** (2.00 mmol dm^{-3}) and saccharide (200 mmol dm^{-3}). Since the addition of phosphotungstic acid before sonication changes the solution pH and affects the boronic acid–monosaccharide complexation equilibrium, this method cannot be used. After drying on a metal mesh, several drops of an aqueous solution containing 2 wt% phosphotungstic acid were added to the samples. The resultant meshed samples

were dried again and then observed by TEM.

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