Self-Assembly

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# Size-Selective Helical Stacking and Template Polymerization of Oligosaccharides around a Linear Polymeric Guest Molecule**

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The dimensions of molecular assemblies found in biological systems are often controlled on the nano- and mesoscale as a result of molecular association, self-replication, chemical processes, and transcription. For example, the self-assembly of viruses, such as the tobacco mosaic virus, represents the propagation of a biological complex on the basis of molecular information, that is, substrate chain length. Similar phenomena are also found with DNA, proteins, and enzymes. Although these sophisticated structures have inspired the construction of synthetic macromolecules with a similar degree of control, the design of artificial structures remains challenging.[1] Herein, we show that oligosaccharides are stacked around a synthetic polymeric guest molecule axis and that the stacking process is controlled by two-way molecular communication; more specifically, recognition of the chain length of the guest and transfer of chirality information occurs from the oligosaccharide host to the guest.[2]

Recently, we have found the preferential induction of a helical conformation in the main chain of oligosilanes and oligothiophenes within the helical channel of amylose and schizophyllan, where the helical sense of the guest molecules is controlled by wrapping with host polymers that have either a left- or the right-handed helical conformation.[3] Other research groups have also reported supramolecular complexes of conjugated polymers that are wrapped with polysaccharides to provide insulated molecular wires.[4,5]

We have extended this wrapping approach to the use of short-chain linear maltooligosaccharides as host molecules. Our experimental design, together with the guest molecules that were used is illustrated in Figure 1. Maltooligosaccharides, composed of α-(1→4)-linkages between D-glucopyranose residues with over six glucose units, are essentially structural analogues of cyclodextrins, which are cyclic oligosaccharides that can form inclusion complexes with organic molecules of the appropriate size and shape.[6] However, if the size (or length) of the oligosaccharides is too small to accommodate the whole guest molecule, the oligosaccharides

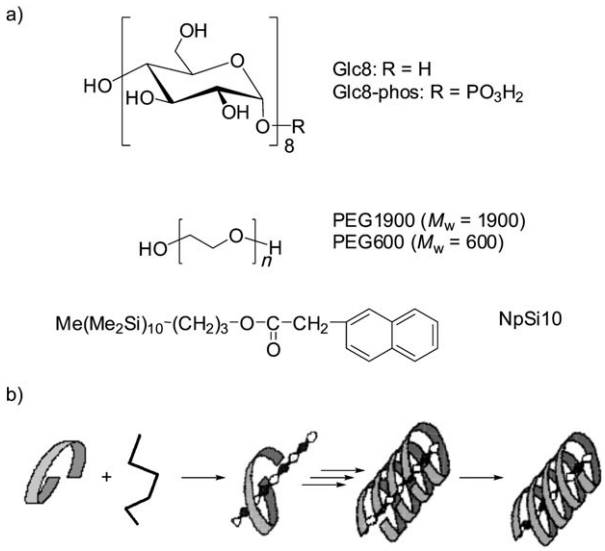


***Figure 1.*** a) Chemical structures of oligosaccharide (Glc8 and Glc8-phos) hosts and poly(ethylene glycol) (PEG1900 and PEG600) and oligosilane (NpSi10) guests. b) Schematic representation of size-selective helical stacking of oligosaccharide hosts around a polymeric guest followed by template polymerization of stacked hosts in the self-assembled system.

stack around the linear polymeric guest and hold it in the resulting cavity. In our experiments, maltooctaose (Glc8) and phosphate-functionalized maltooctaose (Glc8-phos) were used as the oligosaccharide and poly(ethylene glycol) units, PEG1900 and PEG600 (with molecular weights of 1900 ($M_w/M_n = 1.03$) and 600 ($M_w/M_n = 1.15$),[7] and an oligosilane unit (NpSi10) were examined as the guest axle molecules.

In a typical preparation of the complex, a mixture of Glc8-phos (32.3 mg, $2.32 \times 10^{-2}$ mmol) and PEG1900 ($4.02 \times 10^{-2}$ mmol repeat unit) in citric acid buffer solution (0.05 M, 5.0 mL) was dispersed by using ultrasonication for 5 minutes and stirred for 24 hours. Phosphorylase[8,9] (0.322 mg, 23 unit $mg^{-1}$, 7.64 unit) was then added to the mixture, which was stirred at 37 °C for 24 hours and analyzed by using gel permeation chromatography (GPC). Figure 2 shows the GPC profile of the mixture after the reaction and Table 1 summarizes the results of the GPC analysis. The GPC trace of the mixtures shift to the high-molecular-weight region (Figure 2a) relative to the parent Glc8 as a reference (Figure 2d).[10,11] The molecular weight ($M_w = 21\,500$) suggests that the resulting material comprises 21–22 Glc8 molecules ($M_w = 1015$), which is fairly consistent with the number of Glc8 molecules required to cover the whole PEG1900 molecule by stacking, when the molecular ratio of one α-

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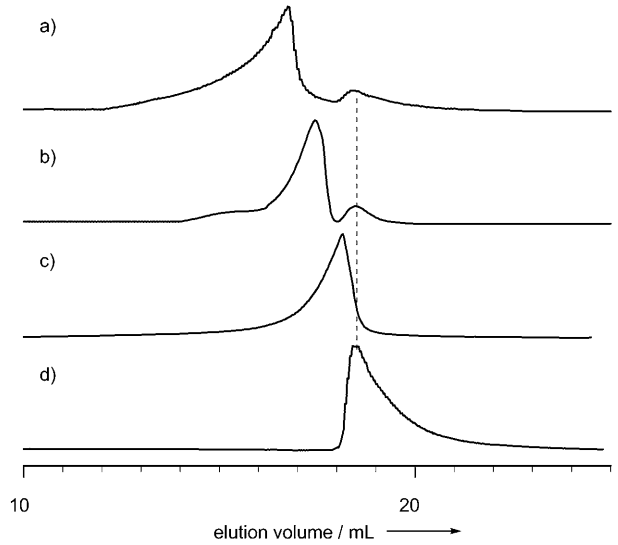


***Figure 2.*** GPC traces of mixtures of a) PEG1900, b) PEG600, and c) NpSi10 with Glc8-phos after the phosphorylase-catalyzed enzymatic reaction, and d) Glc8 alone.

***Table 1:*** GPC data for mixtures of PEG1900, PEG600, and NpSi10 with Glc8-phos after the phosphorylase-catalyzed enzymatic reaction.

| Entry | Guest | $M_{w(GPC)}$ ($M_w/M_n$)[a] | $M_{(calcd)}$[b] |
|---|---|---|---|
| 1 | PEG1900 | 21 500 (1.5) | 21 000 |
| 2 | PEG600 | 7000 (1.2) | 6600 |
| 3 | NpSi10 | 3900 (1.4) | 5300 |
| 4 | [c] | 1015 (1.4) | 1315 |
| 5 | [d] | 1870 (1.2) | – |
| 6 | [e] | 1800 (1.2) | – |

[a] Determined by using GPC with poly(ethylene glycol) standards. [b] The calculated molecular weight value based on the number of Glc8 molecules stacked along the molecular length of the guest. [c] Obtained using parent Glc8 as a reference. [d] A mixture of PEG1900 and Glc8-phos. [e] Mixture obtained by an enzymatic reaction of Glc8-phos in the absence of NpSi10.

cyclodextrin to two ethylene oxide units of PEG in the inclusion complex formed from α-cyclodextrin with six glucose units and PEG is considered.[7] In addition, the observed distribution of molecular weights is relatively narrow ($M_w/M_n = 1.5$), which indicates that the equilibrium of the dynamic process is shifted towards the complexed state. When PEG600 is employed instead of PEG1900, the GPC trace shifts to the lower-molecular-weight region, and also shows a narrow distribution (Figure 2b and Table 1, entry 2). Again, the observed molecular weight (7000) is in good agreement with the calculated value (Table 1, entry 2). On the other hand, in the absence of PEG as the linear guest, the enzymatic reaction of Glc8-phos does not proceed efficiently to produce polymeric materials under otherwise identical conditions (Table 1, entry 6). These findings clearly suggest that an inclusion complex is formed by stacking the oligosaccharide molecules around the guest polymer exclusively in a head-to-tail manner and also that the extent of stacking is dictated by the molecular weight of the guest polymer. The stacking leads, upon phosphorylase-catalyzed condensation polymerization, to the formation of amylose that has a molecular weight consistent with the chain length of the linear guest polymer (Figure 1).

To further elucidate the helical stacking of the oligosaccharides around the linear molecules, oligosilane NpSi10 was applied as the guest template. Oligosilanes show an absorption in the UV region that results from σ conjugation, which is extremely sensitive to the conformation of the main chain,[12] while Glc8 has no absorption in this region. Hence we hypothesized that the stacking process could be monitored by absorption and circular dichroism (CD) measurements, which can substantiate the influence of helically-stacked oligosaccharides on the conformation of the oligosilane guest. It was found that a mixture of NpSi10 ($3.27 \times 10^{-4}$ mmol) and Glc8 ($1.29 \times 10^{-3}$ mmol) in water (3.2 mL) shows an absorption and an induced positive CD signal at around 280 nm that arise from the oligosilane main chain (Figure 3a). When the Glc8

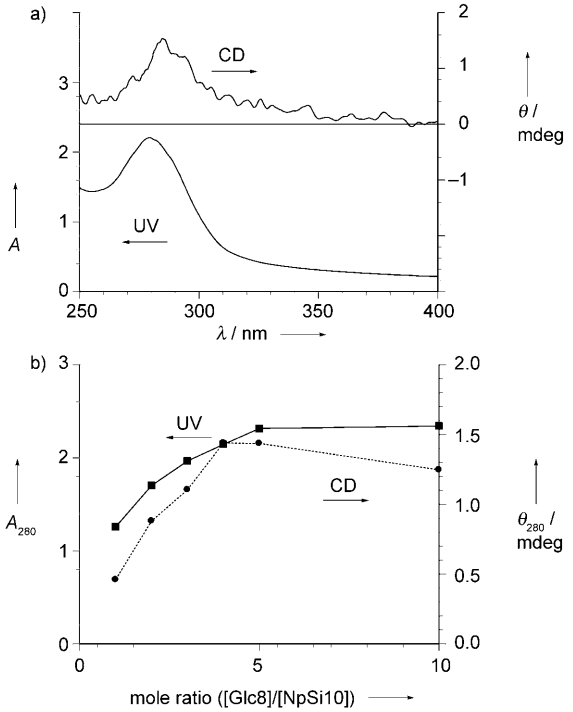


***Figure 3.*** a) Absorption and circular dichroism spectra of a mixture of Glc8 and NpSi10 ([Glc8]/[NpSi10=4]) in $H_2O$. b) Intensities of the absorption ($A_{280}$) and induced circular dichroism ($\theta_{280}$) spectra at 280 nm as a function of the mole ratio ([Glc8]/[NpSi10]).

content increases towards Glc8/NpSi10 = 4, the intensities of the absorption and the induced positive Cotton signal increase and then become almost constant at even higher ratios.[13,14] These spectral features are consistent with those of inclusion complexes of NpSi10 with γ-cyclodextrin[15] or amylose,[3] although the dissymmetry ratio of the complex, $g_{abs}$ ($\Delta\varepsilon/\varepsilon$), which is usually used to characterize helical structures such as right- and left-handed helix populations,[16] is $2.0 \times 10^{-5}$ at Glc8/NpSi10 = 4, which is somewhat low compared to the value for the amylose-wrapped oligosilane system ($2.3 \times 10^{-4}$).[3] The minimum Glc8/NpSi10 ratio

  

required to produce the full intensity of the CD signal and absorption in the spectral titrations was approximately 4. These observations clearly demonstrate that the oligosilane adopts a helical conformation in the channel constructed by the one-turn helical stacking of oligosaccharides, which proceeds with size-specific recognition of the guest substrate. In addition, the phosphorylase-catalyzed enzymatic reaction after the complexation of NpSi10 and Glc8-phos was carried out. The observed molecular weight of the product (3900) is comparable to the calculated value, which is about four times larger than that of the parent Glc8, as shown in the GPC analysis (Table 1, entry 3 and Figure 2c). This molecular weight value is also consistent with the value derived from the absorption and CD analysis as mentioned above.

In conclusion, we have demonstrated the helical stacking of oligosaccharides around axial polymeric guest molecules with transcription of molecular information, such as the transfer of guest chain length to the assembled helical hosts, and host chirality to the guest. This system represents a higher-level control of self-assembly through complexation and also affords a basis for a new and simple concept for molecular communication in molecular and macromolecular objects.

## Experimental Section

A typical synthetic procedure is as follows: An aqueous solution of PEG1900 ($4.01\times10^{-2}$ mmol per unit) in citric acid buffer solution (0.05 M, 5 mL, pH 7.10) was added to Glc8-phos (32.3 mg, $2.32\times10^{-2}$ mmol). A citric acid buffer solution (0.05 M, 5.0 mL) was added to the mixture. The mixture was dispersed by using ultrasonication for 5 min and stirred for 24 h, after which time phosphorylase (0.332 mg, 23 units $mg^{-1}$, 7.64 units) was added to the mixture. The mixture was stirred at 37 °C for 24 h and was subsequently analyzed by using GPC ($M_w = 21\,500$, $M_w/M_n = 1.5$).

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[2] In this study, it is convenient to define oligosaccharides and linear polymeric molecules as "host" and "guest", respectively.

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[8] Phosphorylase ($M_w = 97$ kDa) catalyzes the enzymatic polymerization with the regio- and stereoselective construction of an α-glycosidic bond, which leads to the direct formation amylose, a α-(1→4)-glucan chain; a) S. Kobayashi, H. Uyama, S. Kimura, *Chem. Rev.* **2001**, *101*, 3793; b) S. Shoda, R. Izumi, M. Fujita, *Bull. Chem. Soc. Jpn.* **2003**, *76*, 1; c) S. Kobayashi, M. Ohmae, S. Fujikawa, H. Ochiai, *Macromol. Symp.* **2005**, *226*, 147; d) S. Kobayashi, M. Ohmae, *Adv. Polym. Sci.* **2006**, *194*, 159; e) G. Ziegast, B. Pfannemüller, *Carbohydr. Res.* **1987**, *160*, 185.

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[10] A small peak around 19 mL and a shoulder around 15 mL are due to uncomplexed Glc8-phos and phosphorylase, respectively. The tail on the peak in the GPC trace of Glc8 is probably due to a mixture of anomers.

[11] The GPC and NMR data before and after filtration (pore size 0.45 μm) to avoid formation of aggregation show the same spectroscopic features.

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[14] A preliminary experiment shows that eight sugar units in the oligosaccharide are not a critical length for wrapping the oligosilanes (see the Supporting Information for details).

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