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# Synthesis of 6-O-Hexadecyl- and 6-O-Octylsucroses and Their Self-Assembling Properties Under Aqueous Conditions

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# Synthesis of 6-O-Hexadecyland 6-O-Octylsucroses and Their Self-Assembling Properties Under Aqueous Conditions

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This paper reports the synthesis and self-assembling properties of 6-O-hexadecyl- and 6-O-octylsucroses. Mono-etherification of 2,3,4,1',3',4'-hexa-O-benzylsucrose with the corresponding alkyl bromides predominantly took place at the glucose 6-position and the products were isolated by silica gel column chromatography. Benzyl groups in the isolated products were cleaved to yield the target derivatives. The SEM, TEM, XRD, and DLS results indicated that 6-O-alkylsucroses formed vesicle-type particles via formation of lamellar-like planes under aqueous conditions, which were further merged by fusion of the planes to construct larger aggregates. The self-assembling properties of the materials were different from those of the previously reported 6-O- and 6'-O-hexadecylsucroses mixture.

Keywords Sucrose; Monoalkyl ether; Self-assembly; Vesicle; Lamellar

# INTRODUCTION

Amphiphilic molecules, of which soap is a typical example, possess antagonistic hydrophilic and hydrophobic moieties in the same molecule. In aqueous media, such molecules self-assemble into various controlled morphologies,

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such as spherical micelles, cylindrical micelles, spherical vesicles, planar bilayers, and tubes, depending on the molecular shape and solution conditions.<sup>[1]</sup> Because glycolipids, which are natural amphiphiles containing carbohydrates as a hydrophilic part, exhibit important in vivo functions in living systems,<sup>[2]</sup> synthetic carbohydrate-based amphiphiles have been previously studied extensively to show a large variety of self-assembling morphologies.<sup>[1]</sup>

On the other hand, the synthetic carbohydrate-based amphiphiles have been used as an emulsifier in various food industries.<sup>[3]</sup> One of the most effective food additives, practically employed, is the sucrose fatty acid ester, which contains a sucrose residue as a hydrophilic part and a long-alkyl fatty acid moiety as a hydrophobic part.<sup>[4]</sup> Self-assembling properties of the sucrose fatty acid esters are changed depending on the lengths and types of fatty acid chains.<sup>[5]</sup> Compared with such sucrose ester amphiphiles, self-assembling studies using sucrose-based amphiphiles connecting with long-alkyl chains by ether linkages (i.e., sucrose alkyl ethers) have been less reported. As one of the examples, the effect of molecular shape on the liquid crystal properties of mono-O-(2-hydroxydodecyl)sucroses, which were prepared by the reaction of sucrose with 1,2-epoxydodecane under alkaline conditions, was reported.<sup>[6]</sup> On the basis of the above viewpoint, in the previous paper, we reported the self-assembling property of a mixture of 6-O- and 6'-O-hexadecylsucroses (6mono-C16 and 6'-mono-C16, respectively) under aqueous conditions, which were new sucrose-based amphiphiles having the structures of a sucrose residue connecting with a hexadecyl chain by the ether linkage at the 6- or 6'position.<sup>[7]</sup> From the analytical results, the following self-assembling process of such mono-O-alkylsucrose mixtures under aqueous conditions was proposed. The mixture primarily formed spherical micelles with diameters of ca. 5 to 7 nm in water. The micelles regularly organized according to face-centered cubic (FCC) structure during the drying process from the aqueous dispersion to construct nanoparticles with diameters of ca. 50 nm. Moreover, several numbers of the nanoparticles further assembled to form larger aggregates. However, the more precise study on the self-assembling properties of the individual **6-mono-C16** and **6'-mono-C16** under aqueous conditions has not been achieved because these two isomers could not be separated from the mixture by general experimental techniques such as column chromatography.

To investigate the detailed self-assembling property of such mono-O-alkylsucroses, in the continuous study, we have attempted synthesis of a sole **6-mono-C16** from sucrose. Consequently, in this paper, we report that monoetherification of 2,3,4,1',3',4'-hexa-O-benzylsucrose (**3**), which had two free hydroxy groups at the 6- and 6'-positions, predominantly took place at the glucose 6-position by the reaction with 1-bromohexadecane under selected conditions (Sch. 1). A major product (**4a**) by the etherification at the 6-position, moreover, could be separated from a minor product yielded by the etherification at the

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Scheme 1: Synthesis of 6-O-hexadecylsucrose (6-mono-C16) and 6-O-octylsucrose (6-mono-C8) from sucrose.

6'-position by the simple silica gel column chromatographic technique. Thus, the following debenzylation of the isolated product gave a pure **6-mono-C16**. Self-assembling property of the obtained **6-mono-C16** was evaluated according to the similar experimental manners as those of the previously reported 6-mono-C16 and 6'-mono-C16 mixture using the SEM, TEM, powder Xray diffraction (XRD), and dynamic light scattering (DLS) measurements.<sup>[7]</sup> Consequently, it was found that **6-mono-C16** showed a hierarchically selfassembling process based on the primary formation of lamellar planes, leading to vesicle-type particles. The particles further assembled to construct larger aggregates probably by fusion of the planes between the particles. These results indicated that the self-assembling process of the sole 6-mono-C16 molecule was completely different from that of its mixture with the regioisomer, 6'**mono-C16**, which took place based on the primary formation of the spherical micelles. It is also reported in this paper that other 6-O-alkylsucrose with a different chain length, that is, 6-O-octylsucrose (6-mono-C8), was also synthesized from sucrose according to the same procedure, and its self-assembling process was found to be similar to that of 6-mono-C16.

# **RESULTS AND DISCUSSION**

We first attempted synthesis of **6-mono-C16** via mono-tritylation, followed by the appropriate reactions because the isolation of 6-O-tritylsucrose from the products containing 6'-O-tritylsucrose by mono-tritylation of sucrose was

already reported.<sup>[8]</sup> However, the complete separation according to such literature procedure was not achieved well by us at present. As the alternative approach to that via mono-tritylation, therefore, we selected the procedure through di-tritylation, followed by benzylation, detritylation, etherification, and debenzylation. During the present approach, we found that monoetherification of 2,3,4,1',3',4'-hexa-O-benzylsucrose (3) having two free hydroxy groups at the 6- and 6'-positions, which was prepared by di-tritylation of sucrose, followed by benzylation and detritylation, with 1-bromohexadecane predominantly took place at the glucose 6-position under selected conditions because of the higher reactivity of the 6-hydroxy group than the 6'-hydroxy group. Furthermore, it was also found that 6-hexadecylated derivative 4a as a major product could be separated from 6'-hexadecylated derivative as a minor product by simple silica gel column chromatography owing to relatively different values in rates of flow  $(R_{\rm f})$  of the two materials eluted with ethyl acetate:hexane = 1:50 (v/v) on silica gel. This fact was much different from that which appeared in other 6- and 6'-regioisomers of sucrose such as 6-mono-C16 and 6'-mono-C16 because such regioisomers generally eluted at the almost same  $R_{\rm f}$  value on silica gel.

Accordingly, the synthesis of 6-mono-C16 was carried out by five reaction steps from sucrose according to Scheme 1, which were successive di-tritylation at the 6- and 6'-posititons, benzylation of other free hydroxy groups, detritylation, etherification at the 6-posititon, and debenzylation.<sup>[9-11]</sup> Although the first tritylation selectively took place at the primary hydroxy groups, three kinds of the tritylated products (i.e., mono-, di-, and tri-O-tritylsucroses) were formed. Therefore, a target molecule of 6,6'-di-tritylated sucrose 1 was separated from the crude products by silica gel column chromatography, and accordingly the isolated yield was not high (27.4%). It was confirmed further by its acetylation experiment using acetic anhydride and pyridine that the trityl groups were present at the 6- and 6'-positions, but not at the 1'-position of the other primary hydroxy group in the isolated compound. The <sup>1</sup>H NMR spectrum  $(CDCl_3)$  of the acetylated derivative showed that chemical shifts of the signals assignable to the H-6 and H-6' protons were not changed compared with those before the acetylation, whereas the signals due to the protons at other positions (besides H-1) were shifted to the lower magnetic field. These data indicated that the 6- and 6'-positions were tritylated in the aforementioned product and, accordingly, were not acetylated by acetic anhydride.

The following benzylation smoothly proceeded and the product 2 was isolated in a relatively high yield (87.3%) by recrystallization. Because a glycosidic linkage in the sucrose derivatives was weak under the acidic conditions,<sup>[11]</sup> detritylation of the product was carefully performed under the mild conditions, but the yield of **3** was not high (31.6%). The subsequent etherification using an equivalent of 1-bromohexadecane for **3** with sodium hydride at rt for 1 h predominantly took place at the 6-position. The product **4a** was separated from the 6'-etherified product by silica gel chromatography, although the isolated yield was low (8.0%). Then, debenzylation of the product was conducted by catalytic hydrogenation to give **6-mono-C16**.

The structure of **6-mono-C16** was determined by the <sup>1</sup>H NMR analysis in CD<sub>3</sub>OD as shown in Figure 1a. The signals' assignments are as follows:  $\delta$ 0.82 (t, 3H, CH<sub>3</sub>, J = 6.8 Hz), 1.03–1.19 (m, 26H, -(CH<sub>2</sub>)<sub>13</sub>-CH<sub>3</sub>), 1.50–1.54 (m, 2H, -O-CH<sub>2</sub>-CH<sub>2</sub>-), 3.21–4.00 (m, 15H, H-1',2,3,3',4,4',5,5',6,6', -O-CH<sub>2</sub>-CH<sub>2</sub>-), 5.27 (d, 1H, H-1, J = 3.6 Hz). The mono-etherified structure was confirmed by the integrated ratio of the signals due to CH<sub>3</sub> of the hexadecyl group to the signal due to an H-1 proton of the glucose residue, which was 3:1. The MALDI-TOF MS showed a significant peak corresponding to the molecular mass of [**6-mono-C16**]Na<sup>+</sup> (found; m/z 589.4320, calcd; m/z 589.3564). The structure of the product was confirmed further by its acetylation experiment using acetic



Figure 1: <sup>1</sup>H NMR spectra of (a) **6-mono-C16** (CD<sub>3</sub>OD) and (b) its acetylated derivative (CDCl<sub>3</sub>).

anhydride and pyridine. The <sup>1</sup>H NMR spectrum in  $CDCl_3$  (Fig. 1b) of the acetylated derivative showed that chemical shift of the signals assignable to the H-6 protons was not changed compared with that before acetylation (Fig. 1a), whereas the signals due to other positions including the H-6' position were shifted to the lower magnetic field. This data indicated that only the 6-position was etherified in the aforementioned product and, accordingly, was not acetylated by acetic anhydride. All the above analytical and acetylation results can be taken to support the structure of **6-mono-C16**.

The other derivative, 6-O-octylsucrose (**6-mono-C8**), was also synthesized by the same manner as previously mentioned. The structure of the product was confirmed by the <sup>1</sup>H NMR spectrum and MALDI-TOF MS (see Experimental section). Then, two derivatives, **6-mono-C16** and **6-mono-C8**, were subjected to the following self-assembling investigations under aqueous conditions.

In the SEM image (Fig. 2a) of a sample of **6-mono-C16** on an aluminum plate, which was prepared by drying its dispersion in water  $(1.0 \times 10^{-5} \text{ mol/L})$ , particle-type nanoaggregates with an average diameter of ca. 51 nm were seen. Although this value was similar to that observed in the previously reported SEM image of a sample of the **6-mono-C16** and **6'-mono-C16** mixture prepared by the same procedure, the standard deviation in the diameters of the present particles was much larger than that in the diameters of the particles from the mixture (12.8 and 4.34, respectively). The SEM image in Figure 2a,



**Figure 2:** SEM images of the samples prepared from dispersions of (a) **6-mono-C16** and (b) **6-mono-C8**; TEM images of the samples prepared from dispersions of (c) **6-mono-C16** and (d) **6-mono-C8** in water  $(1.0 \times 10^{-5} \text{ mol/L})$ ; and (e) a magnified TEM image of (d).

furthermore, did not show larger aggregates by further assembly from the several particles as observed in that of the mixture. The TEM image (Fig. 2c) of a sample of **6-mono-C16** prepared from its dispersion in water  $(1.0 \times 10^{-5} \text{ mol/L})$  exhibited vesicle-like particles, which further assembled to form larger aggregates, whereas such vesicle morphology in the particles was not seen in the TEM image of a sample of the **6-mono-C16** and **6'-mono-C16** mixture (image not shown). These results suggested that the self-assembling process of a sole **6-mono-C16** under aqueous conditions was probably different from that of the **6-mono-C16** mixture under the same conditions.

The SEM image (Fig. 2b) of a sample of **6-mono-C8** on an aluminum plate prepared by the same procedure as above also showed particle-type nanoaggregates, but their average diameter (ca. 117 nm) was larger than that in Figure 2a (the standard deviation, 14.4). The TEM image (Fig. 2d) of a sample of **6mono-C8** also showed vesicles and their assemblies as observed in Figure 2c. Furthermore, the image showed that the vesicle was constructed from lamellar planes of 10-odd alternating black and white layers, where the former and latter probably corresponded to the self-organized hydrophilic sucrose and hydrophobic octyl layers, respectively. Interestingly, the lamellar planes at the interfacial area between the two vesicles were merged as observed in the magnified TEM image (Fig. 2e).

To confirm the self-assembling processes of the present materials further, the XRD and DLS measurements were conducted. In the XRD profiles (Fig. 3) of the samples, which were prepared by drying aqueous dispersions of 6-mono-C16 and 6-mono-C8 ( $1.0 \times 10^{-3}$  mol/L), diffraction peaks due to (001) (Figs. 3a and 3b) and further peaks assignable to the (002), (003), and (004) Bragg reflections (Fig. 3a) of lamellar patterns were observed. From the XRD patterns, widths of the lamellar layers were calculated to be 3.9 nm for 6-mono-C16 and 2.9 nm for **6-mono-C8** as decreased with decreasing the alkyl chain lengths. Both the DLS results (Fig. 4) of dispersions of **6-mono-C16** and **6-mono-C8** in water  $(1.0 \times 10^{-5} \text{ mol/L})$  showed monomodal profiles with relatively narrow distributions. An average diameter of the former (99.8 nm) was smaller than that of the latter (105.7 nm), and thus, the tendency was similar to that which appeared in the SEM measurement. The difference in the average diameters by the DLS and SEM measurements was probably because of the different calculation methods for the average diameters in both the measurements, in which the average diameter in the DLS measurement was calculated from the intensity of scattering light, which was proportional to  $d^6$  (d: diameter of a particle), whereas number distribution was used for calculation of the average diameter of particles in the SEM measurement.<sup>[12]</sup> Furthermore, the wet and dry sample conditions in the two measurements probably affected the difference in the particle sizes. The XRD and DLS results of the 6-mono-C16 and 6'-mono-C16 mixture measured under the same conditions were completely



Figure 3: XRD profiles of the samples prepared from dispersions of (a) **6-mono-C16** and (b) **6-mono-C8** in water  $(1.0 \times 10^{-3} \text{ mol/L})$ .

different from the present results. The XRD profile of the mixture showed the pattern assignable to the FCC organization, and an average diameter of the particles in the DLS measurement of the mixture in water was 7.1 nm, corresponding to a diameter of the spherical micelle.<sup>[7]</sup>

The above analytical results indicated that both of the self-assembling processes of **6-mono-C16** and **6-mono-C8** under aqueous conditions equally took place, in which the vesicle-like particles were primarily obtained on the basis of lamellar planes, which were constructed by the self-organized alternating hydrophilic sucrose and hydrophobic alkyl layers. Some of the vesicles were merged further by fusion of the planes at the interfacial area (Fig. 5). Thus, the particles observed in the SEM images and the DLS profiles probably corresponded to a sole vesicle or the merged vesicles. As we previously reported,<sup>[7]</sup> however, the self-assembly of the **6-mono-C16** and **6'-mono-C16** mixture did not induce the formation of a vesicle-like particle, but led to the spherical micelle in water, which was separately present in aqueous dispersion as indicated by the DLS measurement. The spherical micelles assembled further according



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Figure 4: DLS profiles of (a) 6-mono-C16 and (b) 6-mono-C8 in water ( $1.0 \times 10^{-5}$  mol/L).

to the FCC organization by drying the aqueous dispersion to construct the nanoparticles and larger aggregates by their assembly. The reason for the difference in the self-assembling processes of the sole **6-mono-C16** (or **6-mono-C-8**) and the **6-mono-C16** and **6'-mono-C16** mixture is not yet clear, but it is assumed that a couple of regioisomers, **6-mono-C16** and **6'-mono-C16**, construct the favorable structure to assemble the spherical micelle.



Figure 5: Plausible self-assembling processes of 6-mono-C16 and 6-mono-C8 under aqueous conditions.

# CONCLUSION

This study investigated the synthesis of 6-mono-C16 and 6-mono-C8 through mono-etherification of a sucrose derivative having two free hydroxy groups at the 6- and 6'-positions with the corresponding alkyl bromides under selected conditions. The mono-etherification at the glucose 6-position predominantly took place against that at the 6'-position and the 6-monoether derivative as a major product was separated from the 6'-monoether derivative as a minor product by silica gel column chromatography. The structures of the products were established by the <sup>1</sup>H NMR and MALDI-TOF MS measurements as well as the acetylation experiment. The self-assembling properties of these materials under aqueous conditions were evaluated by the SEM, TEM, XRD, and DLS measurements. They primarily formed the vesicle-type particles via the formation of lamellar-like planes in water, and some of which merged further because of fusion of the planes at the interfacial area between the vesicles. The self-assembling processes of the present materials were completely different from those of the **6-mono-C16** and **6'-mono-C16** mixture reported in our previous paper, which progressed via the FCC organization of the primary formed spherical micelles. The detailed study to reveal the reason for the difference in the self-assembling properties of a sole 6-O-alkylsucrose and its mixture with the regioisomer, 6'-O-alkylsucrose is now in progress in our group and will be published in a forthcoming paper.

### EXPERIMENTAL

#### General

All reagents were available commercially and used without further purification. DMF was purified by distillation over calcium hydride. Other solvents were used as received. <sup>1</sup>H NMR spectra were recorded on a JEOL ECX400 spectrometer. MALDI-TOF MS measurements were carried out by using SHIMADZU Voyager Biospectrometry Workstation Ver .5.1 with 2.5-dihydroxybenzoic acid as matrix containing 0.05% trifluoroacetic acid under positive ion mode. SEM images were obtained using a Hitachi S-4100H electron microscope. TEM measurements were operated using Jeol JEM-3010 under 200 kV. XRD measurements were conducted using a PANalytical X'Pert Pro MPD with Ni-filtered CuK $\alpha$  radiation ( $\lambda = 0.15418$  nm). DLS measurements were performed on a Zetasizer Nano ZS (Malvern Instruments).

#### Synthesis of 6-O-Hexadecylsucrose

Under argon, to a dispersion of sucrose (3.42 g, 10.0 mmol) in pyridine (20.0 mL) was added a solution of triphenylmethyl chloride (5.57 g, 10.0 mL)

20.0 mmol) in pyridine (10.0 mL) at rt, and the mixture was stirred for 72 h at that temperature. After the reaction mixture was concentrated and diluted with chloroform, the solution was successively washed with 10% KHSO<sub>4</sub> aq. and water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated. The residue was subjected to column chromatography on silica gel (eluent; chloroform:methanol = 22:1 (v/v)) to give **1** (2.27 g, 2.74 mmol) in 27.4% yield. <sup>1</sup>H NMR (CD<sub>3</sub>OD):  $\delta$  3.14–4.20 (m, 13H, H-1',2,3,3',4,4',5,5',6,6'), 5.47 (d, 1H, H-1, J = 2.2 Hz), 7.13–7.20 (m, 30H, aromatics).

Under argon, to a dispersion of NaH (4.92 g, 82.1 mmol) in DMF (76.0 mL) was added a solution of 1 (4.54 g, 5.47 mmol) in DMF (61.0 mL) at rt, and the mixture was stirred at that temperature for 30 min. After a solution of tetrabutylammonium bromide (small amount) in DMF and benzyl bromide (5.90 mL, 49.2 mmol) were added to the mixture, the reaction was conducted at rt for 48 h. The reaction was stopped by addition of methanol to the reaction mixture. After the resulting mixture was concentrated and diluted with chloroform, the solution was washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated. The residue was recrystallized from methanol/acetone (20:1 (v/v)) to give 2 (6.54 g, 4.77 mmol) in 87.3% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  2.89–4.04 (m, 13H, H-1',2,3,3',4,4',5,5',6,6'), 4.18–4.81 (m, 12H, CH<sub>2</sub>-Ph), 6.34 (d, 1H, H-1, J = 4.0 Hz), 7.05–7.53 (m, 60H, aromatics).

To a solution of **2** (0.778 g, 0.638 mmol) in ice-cold dichloromethane-acetic acid (4.5 mL, 2 : 1 (v/v)) was added dropwise a small amount of conc. HCl. After the reaction was carried out at the ice-cold temperature for 3.5 h, the reaction mixture was diluted with dichloromethane, neutralized with saturated NaHCO<sub>3</sub> aq., washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated. The residue was subjected to column chromatography on silica gel (eluent; ethyl acetate:hexane = 1:6 (v/v)) to give **3** (0.178 g, 0.202 mmol) in 31.6% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  3.41–4.15 (m, 13H, H-1',2,3,3',4,4',5,5',6,6'), 4.29–4.81 (m, 12H, CH<sub>2</sub>-Ph), 5.49 (d, 1H, H-1, J = 3.6 Hz), 7.21–7.33 (m, 30H, aromatics).

Under argon, to a dispersion of NaH (0.0069 g, 0.11 mmol) in DMF (1.0 mL) was added a solution of **3** (0.099 g, 0.11 mmol) in DMF (2.0 mL) at rt and the mixture was stirred at that temperature for 30 min. After a solution of tetrabutylammonium bromide (small amount) in DMF and 1-bromohexadecane (0.034 mL, 0.11 mmol) were added to the mixture, the reaction was conducted at rt for 1 h. The reaction was stopped by addition of methanol to the reaction mixture. After the resulting mixture was concentrated and diluted with chloroform, the solution was washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated. The residue was subjected to chromatography on silica gel (eluent; ethyl acetate:hexane = 1:50 (v/v)) to give **4a** (0.0097 g, 0.0088 mmol) in 8.0% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  0.88 (t, 3H, CH<sub>3</sub>, J = 7.0 Hz), 1.23–1.25 (m, 26H, -(CH<sub>2</sub>)<sub>13</sub>-CH<sub>3</sub>), 1.56–1.70 (m, 2H, -O-CH<sub>2</sub>-CH<sub>2</sub>-), 3.25–4.08 (m, 15H, H-1',2,3,3',4,4',5,5',6,6', -O- $CH_2$ - $CH_2$ -), 4.24–4.88 (m, 12H,  $CH_2$ -Ph), 5.52 (d, 1H, H-1, J = 3.2 Hz), 7.19–7.34 (m, 30H, aromatics).

To a solution of **4a** (0.020 g, 0.018 mmol) in a mixed solvent of butanol (6.4 mL), methanol (0.64 mL), and water (0.16 mL) was added 10% palladium on carbon (0.0051 g) and the mixture was stirred at rt for 8 days under hydrogen atmosphere. After the reaction mixture was filtered and the filtrate was evaporated, the residue was subjected to column chromatography on silica gel (eluent; chloroform:methanol = 10:1) to give 6-*O*-hexadecylsucrose (**6-mono-C16**, 1, 0.0010 g, 0.018 mmol) in 99.0% yield. <sup>1</sup>H NMR (CD<sub>3</sub>OD):  $\delta$  0.82 (t, 3H, CH<sub>3</sub>, J = 6.8 Hz), 1.03–1.19 (m, 26H, -(CH<sub>2</sub>)<sub>13</sub>-CH<sub>3</sub>), 1.50–1.54 (m, 2H, -O-CH<sub>2</sub>-CH<sub>2</sub>-), 3.21–4.00 (m, 15H, H-1',2,3,3',4,4',5,5',6,6', -O-CH<sub>2</sub>-CH<sub>2</sub>-), 5.27 (d, 1H, H-1, J = 3.6 Hz). MALDI-TOF MS: Calcd [C<sub>28</sub>H<sub>54</sub>O<sub>11</sub>]Na<sup>+</sup>: m/z 589.3564. Found: m/z 589.4320.

#### Synthesis of 6-O-Octylsucrose

In the same way as **4a**, **4b** was prepared by the reaction of **3** with 3 equivalents of 1-bromooctane at 80°C for 2 days in 7.2% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  0.87 (t, 3H, CH<sub>3</sub>, J = 8.2 Hz), 1.23–1.27 (m, 10H, -(CH<sub>2</sub>)<sub>5</sub>-CH<sub>3</sub>), 1.56–1.70 (m, 2H, -O-CH<sub>2</sub>-CH<sub>2</sub>-), 3.25–4.08 (m, 15H, H-1',2,2',3,3',4,4',5,5',6,6', -O-CH<sub>2</sub>-CH<sub>2</sub>-), 4.27–4.88 (m, 12H, CH<sub>2</sub>-Ph), 5.52 (d, 1H, H-1, J = 3.2 Hz), 7.21–7.32 (m, 30H, aromatics).

Then, synthesis of 6-O-octylsucrose (**6-mono-C8**) was carried out in the same way as **6-mono-C16** from **4b** in 45.0% yield. <sup>1</sup>H NMR (CD<sub>3</sub>OD):  $\delta$  0.80 (t, 3H, CH<sub>3</sub>, J = 6.8 Hz), 1.28–1.29 (m, 10H, -(CH<sub>2</sub>)<sub>5</sub>-CH<sub>3</sub>), 1.50–1.56 (m, 2H, -O-CH<sub>2</sub>-CH<sub>2</sub>-), 3.20–4.25 (m, 15H, H-1',2,3,3',4,4',5,5',6,6', -O-CH<sub>2</sub>-CH<sub>2</sub>-), 5.36 (d, 1H, H-1, J = 3.6 Hz). MALDI-TOF MS: Calcd [C<sub>20</sub>H<sub>38</sub>O<sub>11</sub>]Na<sup>+</sup>: m/z 477.2312. Found: m/z 477.3399.

#### Acetylation of 6-Mono-C16

A typical example is as follows. Under argon, a mixture of **6-mono-C16** (0.0041 g, 0.0072 mmol), acetic anhydride (0.15 mL), and pyridine (0.15 mL) was stirred at rt for 24 h. The reaction mixture was poured into a large amount of water to precipitate the product. The precipitate was dried under reduced pressure to give the acetylated product (0.0050 g, 0.0058 mmol) in 80.0% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  0.88 (t, 3H, -CH<sub>2</sub>-CH<sub>3</sub>, J = 6.8 Hz), 1.28–1.29 (m, 26H, -(CH<sub>2</sub>)<sub>13</sub>-CH<sub>3</sub>), 1.57–1.60 (m, 2H, -O-CH<sub>2</sub>-CH<sub>2</sub>-), 2.02–2.18 (7s, 21H, O=C-CH<sub>3</sub>), 3.36–3.55 (m, 4H, H-6, -O-CH<sub>2</sub>-CH<sub>2</sub>-), 4.13–4.33 (m, 6H, H-1'5,5',6'), 4.86 (dd, 1H, H-2, J = 5.4, 1.8 Hz), 5.15 (t, 2H, H-4,4', J = 9.8 Hz), 5.15–5.46 (m, 2H, H-3,3'), 5.70 (d, 1H, H-1, J = 3.6 Hz).

# Preparation of Samples for SEM Measurement

A dispersion of **6-mono-C16** or **6-mono-C8**  $(1.0 \times 10^{-5} \text{ mol/L})$  was placed on an aluminum plate and it was left standing under ambient atmosphere until water was evaporated. Then, the resulting solid sample was subjected to the measurement.

### Preparation of Samples for TEM Measurement

A dispersion of **6-mono-C16** or **6-mono-C8**  $(1.0 \times 10^{-5} \text{ mol/L})$  was placed on carbon film-coated copper grids. The negative-staining technique was used for TEM sample preparation. Then, the preparative material was left standing under ambient atmosphere until water was evaporated. Then, the resulting solid sample was subjected to the measurement.

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