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Preparation of Hexakis(6-*O*-mesitylsulfonyl)cyclomaltooctaoses and Structural Validation of the Four Isomers Using Heteronuclear Multiple Bond Correlation Spectroscopy

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Four cyclomaltooctaose derivatives **1a–d**, which possess six mesitylsulfonyloxy groups on their C(6) atoms, were prepared. The assignment of the regiosiomers was performed by observing the long-range coupling through a glycoside linkage between H(1′) –C(4) and C(1′) –H(4) using a heteronuclear multiple-bond correlation (HMBC) method.

Cyclodextrin (CD) is a cyclic oligosaccharide composed of D-glucose residues. Its unique character is to include a variety of guest molecules in its molecular cavity. Because of this feature, CD has been regarded as being attractive in academic studies as well as industrial applications.[1] In order to improve the characteristics of the molecule, chemically-modified CD derivatives have been studied, and it has been demonstrated that multifunctionalized CDs are quite useful in generating sophisticated functionality such as found in enzymes and antibodies.[2,3] For this purpose, regiospecifically-sulfonylated derivatives are versatile synthetic intermediates. In contrast to the 6-*O*-sulfonylated cyclomaltohexaoses (α-CDs) and the 6-*O*-sulfonated cyclomaltoheptaoses (β-CDs) almost all of which have been reported,[4–9] only four regioisomeric disulfonates,[10] heptasulfonate[11] and octasulfonate[11] of cyclomaltooctaose (γ-CD) among thirty five kinds 6-*O*-sulfonates are known. This was because γ-CD composed of "eight" glucose residues gave a complicated mixture of products, which made the preparation and structure determination more difficult than in the case of α- and β-CD. Here, we report on four regioisomers of γ-CD derivatives **1a–d** possessing six mesitylsulfonyl groups at their O(6) atoms. Methods have been developed to determine the structures of the regioisomers of the sulfonates by additional sulfonylation,[4,7] Taka-amylolysis,[6] 3,6-anhydration followed by Taka-amylolysis,[7,10] 3,6-anhydration and subsequent ROESY analysis,[5,9] and 3,6-anhydration and identification with those derived from authentic compounds.[9] All of them contains chemical conversion to more easily assignable compounds. We describe here a more straightforward method to determine the structures of the regioisomers by means of heteronuclear two-dimensional ^{1}H NMR analyses of the sulfonates, themselves.

Results and Discussion

Sulfonylation of γ-CD **2** was carried out using mesitylenesulfonyl chloride in pyridine.[4–11] The reaction generated a mixture of 6-*O*-mesitylsulfonyl derivatives composed of a mixture of seven regioisomeric pentasulfonates **3**, the hexasulfonates **1a–d** and the heptasulfonate **4**.[11] As results of examining separation conditions, we found that HPLC using a phenyl-modified silica-gel column separated four regioisomers of the desired **1a–d** (Fig. 1). Accordingly, the crude reaction mixture was purified using low-pressure ODS column chromatography eluted with increasing amounts of MeCN in water, followed by preparative HPLC using a phenyl-modified silica-gel column.

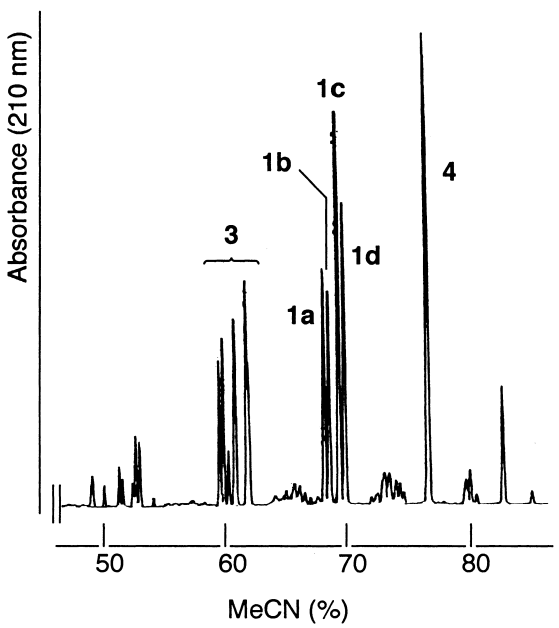


Fig. 1. RP-HPLC trace of the mixture obtained by the reaction of γ-CD **2** with mesitylenesulfonyl chloride in pyridine. A linear gradient of MeCN was applied.

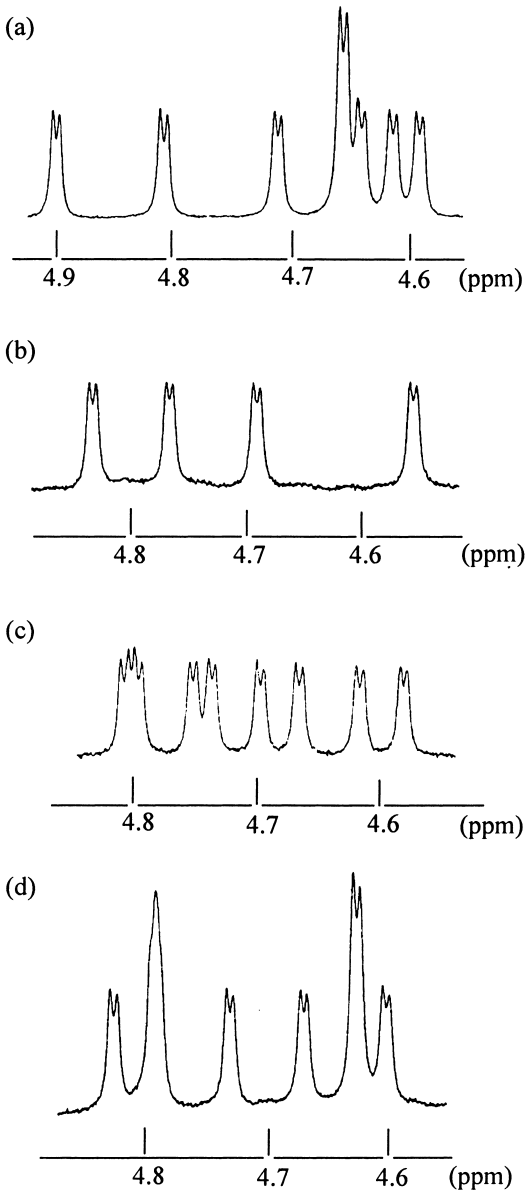
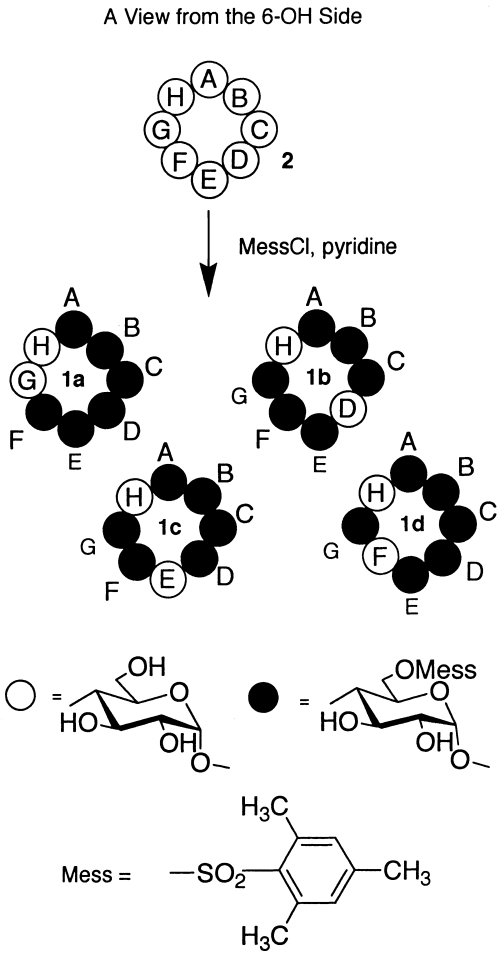


Fig. 2. The observed signals due to anomeric protons H(1) (δ 4.6–5.0) of the hexakis(6-*O*-mesitylsulfonyl) derivatives [**1a** (a), **1b** (b), **1c** (c), and **1d** (d)] on the ^{1}H-NMR (600 MHz; [$^2H_6$]DMSO) spectra.

This afforded four isomeric pentasulfonates **1a–d** in isolated yields of 1.3%, 0.95%, 2.52% and 0.95%, respectively. The elemental analyses and MS spectra of **1a–d** are consistent with the hexakis-mesitylsulfonylated structure. The ^{1}H NMR spectra of **1a–d** confirmed the presence of six mesitylsulfonyl groups on γ-CD. The observed signals are characteristic for each isomer, as the H(1)s (δ 4.6–5.0) shown in Fig. 2. Eight H(1) signals exist for the sulfonates **1a**, **1c** and **1d**, while the sulfonate **1b** exhibits four kinds of H(1) signals. The C_2 symmetry of the molecule **1b** reveals its substitution pattern as (A,B,C,E,F,G) (Scheme 1).

In order to assign the remaining three possible substitution patterns, (A,B,C,D,E,F), (A,B,C,D,E,G), and (A,B,C,D,F,G), to the hexakis-sulfonylated derivatives **1a**, **1c** and **1d**, the relative position of the two unmodified glucose units must be determined. That is, a neighboring relationship between a glucose unit and either the other glucose or a 6-*O*-sulfonylated glucose unit in each isomer must be revealed. Instead of converting the sulfonates to the corresponding 3,6-anhydro derivatives, which would give proton signals sufficiently resolved to be analyzed,[5,9] we attempted a direct structural determination by means of high-resolution NMR techniques. In the case of the sulfonate **1c**, here the H(1) signals were arbitrarily numbered as 1–8 from high to low chemical shift. HOHAHA experiments allowed the isolation and correlation of the signals in each glucose unit which, along with H–H COSY experiments, enabled the assignment of the H(1)–H(5) signals (Fig. 3 and Table 1). Unfortunately, the assignment of the H(6) signals was not achieved because the correlation between H(1) and H(6) was too weak to be observed on the HOHAHA spectra, and the overlapped signals disturbed the correlation with other signals on the COSY spectra. However, proton signals of the two unmodified glucose residues were clearly discriminated from those of six other sulfonylated residues based on the observed signals. Since the 6-*O*-sulfonyaltion of a glucose residue generally causes downfield shifts of the H(5) and H(6) signals and also an upfield shift of the H(4) signal,[4,8] six sets of proton signals with higher chemical shift values for H(5) and lower chemical shift values for H(4) were determined to be



Scheme 1.

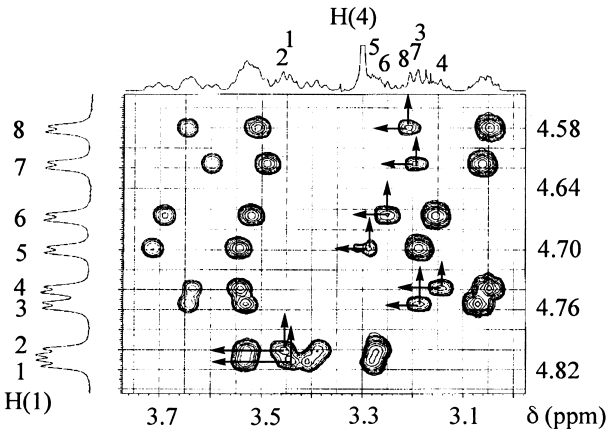


Fig. 3. HOHAHA spectrum of the sulfonate **1c** in [$^2H_6$]-DMSO. Cross peaks corresponding to H(1)–H(4) are marked with arrows.

Table 1. Observed Proton Signals of Glucose Residues in ABCDFG-Tetrasulfonylated Isomer **1c**

Residue	Chemical shift (δ/ppm)						
	H(1)	H(2)	H(3)	H(4)	H(5)	C(1)	C(4)
C	4.57	3.04	3.51	3.21	3.64	101.1	80.0
B	4.61	3.06	3.49	3.19	3.60	101.3	79.7
G	4.67	3.15	3.52	3.25	3.69	101.4	80.6
D	4.70	3.18	3.54	3.29	3.71	101.2	80.5
F	4.73	3.05	3.54	3.14	3.63	100.2	80.7
A	4.75	3.07	3.53	3.18	3.64	100.4	80.4
E[a)]	4.80	3.27	3.53	3.45	3.38	102.0	78.7
H[a)]	4.81	3.28	3.53	3.44	3.41	102.0	79.1

a) Unmodified residue.

those of the sulfonylated glucose residues, whose H(1)s resonated at a higher field, while the proton signals of the two unmodified glucose residues were identified as being those with the higher chemical shift values for H(1).

Nuclear Overhauser effects between H(1) of a glucose unit and H(4) of the adjoining unit are useful to determine the sequential relationship.[5,9] However, here the ROESY experiment of the sulfonate **1c** did not afford unambiguous results because of its overlapped H(4) signals. D'Souza was successful in the structural determination of 2-*O*- and 3-*O*-modified CDs by observing the C–H correlation between a modified glucose residue and its substituent.[12,13] We then surveyed the "interresidual" long range C–H correlation on the corresponding H(1′)–C(1′)–O(4)–C(4) and/or C(1′)–O(4)–C(4)–H(4) through three bonds including glycoside linkages. This was because carbon atoms were expected to give well-resolved signals sufficient to reveal any clear interresidual correlation. First, a ^{1}H-detected multiple quantum coherence (HMQC) experiment of **1c** was performed to identify eight C(4) signals correlated with the corresponding H(4)s determined above (Fig. 4a). The subsequent ^{1}H-detected multiple-bond heteronuclear multiple quantum coherence (HMBC) spectrum of the compound **1c** demonstrated a neighboring [H(1′):C(4)] correlation to reveal an interresidual relationship as we had expected. Especially, cross peaks revealing an interresidual relationship between two glucose units (unit 1 and 2) through two sulfonylated glucose

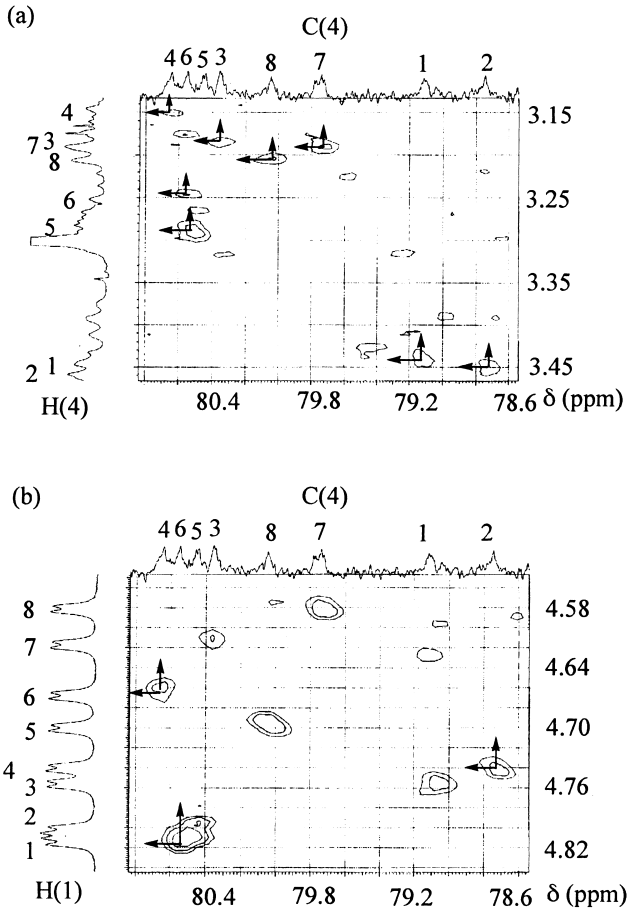


Fig. 4. Correlation of H(4)–C(4) on HMQC spectrum (a) and interresidual cross peaks between neighboring [H(1′) and C(4)] (b) on the HMBC spectrum of the sulfonate **1c** in [$^2H_6$]DMSO.

units (unit 4 and 6) were clearly observed, namely [H(1)^1 (δ 4.81):C(4)^6 (δ 80.6)], [H(1)^6 (δ 4.67):C(4)^4 (δ 80.7)] and [H(1)^4 (δ 4.73):C(4)^2 (δ 78.7)] (Fig. 4b).

In addition, the C(1) signals were also determined in relation to the H(1) signals by an HMQC experiment, and an HMBC experiment gave three cross peaks due to the interresidual correlation between C(1′) and H(4), namely [C(1)^1 (δ 102.0):H(4)^6 (δ 3.25)], [C(1)^6 (δ 101.4):H(4)^4 (δ 3.14)] and [C(1)^4 (δ 100.2):H(4)^2 (δ 3.45)]. Both spectra showed that the two unmodified glucose residues were separated by two sulfonylated residues (Scheme 1). This identified compound **1c** as being the ABCDFG isomer. Also, 2D NMR experiments revealed another interresidual relationship in **1c**, and the residues 1,2,3,4,5,6,7 and 8 were identified as H, E, A, F, D, G, B and C, respectively.

Proton and carbon signals of the isomer **1d** were assigned similarly. In its HMBC spectrum, the cross peaks showed interresidual relationships between two glucose units (unit F and H) through one sulfonylated glucose (unit G) {[H(1)^H (δ 4.83):C(4)^G (δ 80.9)], [H(1)^G (δ 4.80):C(4)^F (δ 79.1)], [C(1)^H (δ 101.9):H(4)^G (δ 3.24)] and [C(1)^G (δ 100.5):H(4)^F (δ 3.44)]}. Accordingly, the structure of **1d** was determined to be ABCDEG-isomer (Scheme 1).

In the case of the sulfonate **1a**, the cross peak between C(1′)

Table 2. Observed Proton Signals of Glucose Residues in ABCDEF-Tetrasulfonylated Isomer **1a**

Residue	Chemical shift (δ/ppm)						
	H(1)	H(2)	H(3)	H(4)	H(5)	C(1)	C(4)
F	4.59	3.04	3.51	3.21	3.61	100.9	80.6
B	4.61	3.03	3.48	3.19	3.62	101.2	79.8
1[a)]	4.64	3.08	3.51	3.26	3.65	101.2	—[b)]
2[a)] and 3[a)]	4.66	3.10	3.52	3.26	3.63	101.0	—[b)]
		3.17			3.70		
A	4.71	3.06	3.52	3.14	3.61	100.6	80.3
G[c)]	4.81	3.30	3.56	3.44		102.0	79.8
H[c)]	4.90	3.27	3.56	3.37	3.42	101.4	79.8

a) The residues 1, 2 and 3 could not correspond to each of C, D and E residues. b) Three peaks for C(4) of residues C, D and E were observed at δ 79.5, 79.6 and 79.9. c) Unmodified residue.

Table 3. Observed Proton Signals of Glucose Residues in ABCDEG-Tetrasulfonylated Isomer **1d**

Residue	Chemical shift (δ/ppm)						
	H(1)	H(2)	H(3)	H(4)	H(5)	C(1)	C(4)
1	4.60	3.06	3.51	3.21	3.61	101.0	79.6
2	4.63	3.06	3.53	3.23	3.61	101.3	79.6
		(or 3.08)			(or 3.65)		
3	4.63	3.08	3.53	3.23	3.65	101.0	79.6
		(or 3.06)			(or 3.61)		
E	4.67	3.17	3.53	3.27	3.68	101.0	80.4
A	4.74	3.05	3.52	3.16	3.64	100.5	80.4
G	4.80	3.16	3.56	3.24	3.71	100.5	80.9
F[a)]	4.80	3.27	3.54	3.44	3.40	102.0	79.1
H[a)]	4.83	3.27	3.52	3.43	3.35	101.9	79.1

a) Unmodified residue.

of one unmodified glucose and H(4) of the other [$C(1)^H$ (δ 101.4):$H(4)^G$ (δ 3.44)], and also that between H(1′) and C(4) [$H(1)^H$ (δ 4.90):$C(4)^G$ (δ 79.8)], were observed on its HMBC spectrum, which demonstrated that the two units were directly linked by a glycoside linkage. Therefore, the structure of the sulfonate **1a** was unambiguously established as ABCDEF-hexasulfonate (Scheme 1). The observed signals of the glucose residues of **1a** and **1d** are listed in Tables 2 and 3.

Thus, four isomers of γ-CD derivatives possessing six mesitylsulfonyl groups on their primary hydroxy groups were prepared. The use of inverse NMR techniques to observe a long-range H–C correlation is a very powerful method to determine the interunit relationship, and is widely applicable. Studies of other 6-*O*-sulfonates of γ-CD, namely seven isomers of trisulfonates, ten isomers of tetra sulfonates, and seven isomers of pentasulfonates are in progress, while aiming towards the establishment of a completely indexed "library" of CD sulfonates for the development of novel modified CDs.

Experimental

^{1}H and ^{13}C NMR spectra were recorded at 30 °C on a Varian UNITY-plus 600 operating at 600 and 150 MHz, respectively. Each of the hexasulfonates **1a–d** was dissolved in [$^2H_6$]DMSO (8.4×10^{-3} mol dm^{-3}). Proton signals were assigned using COSY and HOHAHA (mixing time, 120 ms) experiments. Carbon signals were assigned using ghmqc, ghsqc and ghmbc experiments and their number of transients were 32, 8, and 64, respectively. FAB mass measurements were carried out with a Shimadzu-Kratos CONCEPT 32IH spectrometer. TLC was run on precoated silica-gel plates (Art 5554, Merck) using 1-propanol: ethyl acetate: water (7:7:5, v/v/v) as the eluent and visualizing using UV light and/or staining with 0.1% 1,3-naphthalenediol in EtOH–water–H_2SO_4 [200:157:43 (v/v/v)]. A prepacked ODS column [LiChroprep RP-18, size B (25 × 310 mm), Merck] was used for low-pressure RP column chromatography. Analytical RP-HPLC was carried out using a YMC-pack Ph column (4 μm; 4.6 × 150 mm, YMC Inc.). Preparative HPLC was performed using a YMC-Pack Ph column (5 μm; 20 × 250 mm, YMC Inc.) with a YMC-Guard pack Ph (5 μm; 20 × 50 mm, YMC Inc.).

Hexakis(6-*O*-mesitylenesulfonyl)-γ-CD 1a-d. Lyophilized γ-CD **2** (500 mg, 3.80×10^{-4} mol) was treated with mesitylenesulfonyl chloride (2.61 g, 1.13×10^{-2} mol) in dry pyridine (15 cm^3) at −10 °C for 5 h. After the addition of H_2O (5 cm^3), the solvent was removed under reduced pressure and the residue was dissolved in a 60% aq MeCN solution (110 cm^3) and neutralized with solid $NaHCO_3$, which was subjected to low-pressure RP chromatography. Elution with 60% aq MeCN (500 cm^3) and gradient elution from 60% aq MeCN (1.0 dm^3) to 100% MeCN (1.0 dm^3) were applied to give a mixture of the hexasulfonates **1a–d** (111 mg). The mixture dissolved in 70% aq MeCN (30 cm^3) was applied to preparative RP-HPLC to afford A,B,C,D,E,F-hexasulfonate **1a** (11.6 mg, 1.3%), the ABCEFG isomer **1b** (8.5 mg, 0.95%), the ABCDFG isomer **1c** (22.5 mg, 2.5%) and the ABCDEG isomer **1d** (8.5 mg, 0.95%).

1a R_f 0.63; t_R [column: YMC-pack Ph; gradient, 30–90% MeCN in water (120 min); flow rate, 1.0 cm^3/min] 69.0 min (Found: C, 48.99; H, 5.82; S, 7.59. Calcd for $C_{102}H_{140}O_{52}S_6 \cdot 6H_2O$:

C, 49.03; H, 6.13; S, 7.69%). NMR δ_H (600 MHz; [$^2H_6$]DMSO) 2.25, 2.26, 2.27, 2.42, 2.44, 2.45, 2.47 and 2.49 (Me), 6.98, 7.01 and 7.04 (12 H, ArH), those of glucose residues are shown in Table 2, δ_C (150 MHz; [$^2H_6$]DMSO) 20.5 and 21.9 (Me), 59.3, 59.4, 67.9, 68.2, 69.1, 69.2, 69.3, 69.4, 71.6, 71.7, 71.8, 72.0, 72.1, 72.3, 72.4, 72.5, 72.7, 79.5, 79.6 and 79.8 [C(3, 5 and 6)], 130.3, 130.4, 130.5, 131.3, 131.4, 138.9, 139.0 and 143.1 (aromatic carbons), those of C(1) and C(4) were shown in Table 2. MS *m/z* (+FAB, LR) 2412.6 [(M + Na)$^+$], 2429.6 [(M + K)$^+$], (HR) 2411.6861 [(M + Na)$^+$ $C_{102}H_{140}O_{52}S_6Na$ requires 2411.6532], (−FAB, LR) 2388.5 [(M)$^-$], 2542.8 [(M + nitrobenzyl alcohol)$^-$], 2588.6 [(M + mesitylenesulfonate)$^-$], (HR) 2587.8128 [(M + mesitylenesulfonate)$^-$. $C_{102}H_{140}O_{52}S_6{\cdot}C_9H_{11}O_3S$ requires *m/z*, 2587.7061].

1b R_f 0.63; t_R [column: YMC-pack Ph; gradient, 30–90% aq MeCN (120 min); flow rate, 1.0 cm^3/min] 69.4 min (Found: C, 49.58; H, 6.03; S, 8.12. Calcd for $C_{87}H_{120}O_{45}S_5{\cdot}3.8H_2O$: C, 49.82; H, 6.05; S, 7.83%). NMR δ_H (600 MHz; [$^2H_6$]DMSO) 2.25, 2.27, 2.39 and 2.44 (Me), 4.56 (2H, d, J = 3.4 Hz), 4.69 (2H, d, J = 3.4 Hz), 4.75 (2H, d, J = 3.1 Hz), 4.83 (2H, d, J = 3.2 Hz) [H(1)], 6.96, 7.01 and 7.06 (12H, ArH). MS *m/z* (+FAB, LR) 2412.7 [(M + Na)$^+$], 2428.7 [(M + K)$^+$], (HR) 2411.6519 [(M + Na)$^+$ $C_{87}H_{120}O_{45}S_5Na$ requires 2411.6433], (−FAB, LR) 2388.8 [(M)$^-$], 2542.8 [(M + nitrobenzyl alcohol)$^-$], 2588.8 [(M + mesitylenesulfonate)$^-$], (HR) 2587.7658 [(M + mesitylenesulfonate)$^-$. $C_{102}H_{140}O_{52}S_6{\cdot}C_9H_{11}O_3S$ requires *m/z*, 2587.7064].

1c R_f 0.63; t_R [column: YMC-pack Ph; gradient, 30–90% aq MeCN (120 min); flow rate, 1.0 cm^3/min] 70.3 min, (Found: C, 48.99; H, 5.82; S, 7.59. Calcd for $C_{102}H_{140}O_{52}S_6{\cdot}6H_2O$: C, 49.03; H, 6.13; S, 7.69%). NMR δ_H (600 MHz; [$^2H_6$]DMSO) 2.26, 2.27, 2.43, 2.44, 2.45, 2.47, 2.48 and 2.51 (Me), 6.99, 7.01, 7.03, 7.04 and 7.06 (12 H, ArH), those of glucose residues were shown in Table 1, δ_C (150 MHz; [$^2H_6$]DMSO) 20.5, 21.9, and 22.0 (Me), 59.0, 59.2, 68.0, 68.1, 69.1, 69.2, 69.3, 69.4, 71.5, 71.7, 71.8, 72.0, 72.1, 72.2, 72.4 and 72.5 [C(3, 5 and 6)], 130.2, 130.3, 130.4, 130.6, 131.3, 131.4, 138.8, 138.9, 139.0, 139.1, 143.0 and 143.1 (aromatic carbon), those of C(1) and C(4) were shown in Table 1. MS *m/z* (+FAB, LR) 2412.6 [(M + Na)$^+$], 2425.6 [(M + K)$^+$], (HR) 2411.6295 [(M + Na)$^+$ $C_{102}H_{140}O_{52}S_6Na$ requires 2411.6533], (−FAB, LR) 2388.7 [(M)$^-$], 2542.7 [(M + nitrobenzyl alcohol)$^-$], 2588.7 [(M + mesitylenesulfonate)$^-$], (HR) 25878.7264 [(M + mesitylenesulfonate)$^-$. $C_{102}H_{140}O_{52}S_6{\cdot}C_9H_{11}O_3S$ requires 2587.7064].

1d R_f 0.63; t_R [column: YMC-pack Ph; gradient, 30–90% aq MeCN (120 min); flow rate, 1.0 cm^3/min] 70.7 min (Found: C, 48.83; H, 5.69; S, 7.47. Calcd for $C_{102}H_{140}O_{52}S_6{\cdot}6H_2O$: C, 49.03; H, 6.13; S, 7.70%). NMR δ_H (600 MHz; [$^2H_6$]DMSO) 2.27, 2.46, 2.47, 2.48, 2.50 and 2.51 (Me), 6.98, 7.02, 7.03 and 7.04 (12 H, ArH), those of glucose residues were shown in Table 3, δ_C (150 MHz; [$^2H_6$]DMSO) 20.5, 21.9 and 22.0 (Me), 59.1, 67.9, 68.4, 69.1, 69.3, 69.4, 71.8, 71.9, 72.0, 72.1, 72.3 and 72.7 [C(3, 5 and 6)], 130.1, 130.2, 130.4, 130.5, 131.3, 131.4, 138.9, 139.0, 139.1, 143.1 and 143.2 (aromatic carbons), those of C(1) and C(4) were shown in Table 3. MS *m/z* (+FAB, LR) 2412.6 [(M + Na)$^+$], 2428.6 [(M + K)$^+$], (HR) 2412.6394 [(M + Na)$^+$ $C_{102}H_{140}O_{52}S_6Na$ requires 2411.6533], (−FAB, LR) 2388.6 [(M)$^-$], 2542.6 [(M + nitrobenzyl alcohol)$^-$], 2588.7 [(M + mesitylenesulfonate)$^-$], (HR) 2587.6543 [(M + mesitylenesulfonate)$^-$. $C_{102}H_{140}O_{52}S{\cdot}C_9H_{11}O_3S$ requires *m/z*, 2587.7064].

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References

1 "Comprehensive Supramolecular Chemistry," ed by J. L. Atwood, J. E. D. Davies, D. D. MacNicol, F. Vögtle, and J.-M. Lehn, Elsevier Science Ltd., Oxford (1996), Vol. 3.

2 R. Breslow and C. Shmuck, *J. Am. Chem. Soc.*, **118**, 6601 (1996).

3 E. Fasella, S. D. Dong, and R. Breslow, *Bioorg. Med. Chem.*, **7**, 709 (1999).

4 K. Fujita, H. Yamamura, A. Matsunaga, T. Imoto, K. Mihashi, and T. Fujioka, *J. Am. Chem. Soc.*, **108**, 4509 (1986).

5 H. Yamamura, H. Nagaoka, K. Saito, M. Kawai, Y. Butsugan, T. Nakajima, and K. Fujita, *J. Org. Chem.*, **58**, 2936 (1993).

6 K. Fujita, A. Matsunaga, and T. Imoto, *Tetrahedron Lett.*, **25**, 5533 (1984).

7 K. Fujita, T. Tahara, and T. Koga, *Chem. Lett.*, **1989**, 821.

8 H. Yamamura and K. Fujita, *Chem. Pharm. Bull.*, **39**, 2505 (1991).

9 H. Yamamura, I. Iida, S. Araki, K. Kobayashi, R. Katakai, K. Kano, and M. Kawai, *J. Chem. Soc., Perkin Trans. 1*, **1999**, 3111.

10 K. Fujita, H. Yamamura, T. Imoto, T. Fujioka and K. Mihashi, *J. Org. Chem.*, **53**, 1943 (1989).

11 H. Yamamura, Y. Kawase, M. Kawai, and Y. Butsugan, *Bull. Chem. Soc. Jpn.*, **66**, 585 (1993).

12 P. Forgo and V. T. D'Souza, *J. Org. Chem.*, **64**, 306 (1999).

13 P. Forgo and V. T. D'Souza, *Tetrahedron Lett.*, **40**, 8533 (1999).