A Complete Set of $2^A,6^X$-Di-*O*-diactivated α-Cyclodextrins

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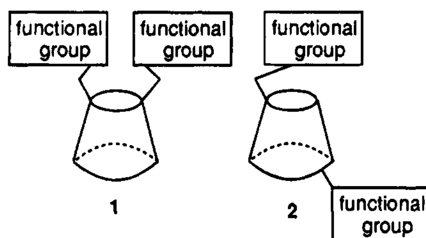
Each regioisomer of 2^A-*O*-(1-naphthalenesulfonyl)-6^X-*O*-(mesitylenesulfonyl)-α-cyclodextrins (X = A–F), which was prepared by the reaction of 2-*O*-(1-naphthalenesulfonyl)-α-cyclodextrin with mesitylenesulfonyl chloride in pyridine, was isolated and structurally determined.

Biomimetic studies on multiple recognition of enzymes and receptors have attracted much attention, where a bifunctional cyclodextrin has been one of the most important host molecules.[2] But, the studies are limited to the reaction or inclusion of bifunctional cyclodextrins which possess the functional groups on the same sides of the cyclodextrin torus (see **1**).[2] For the sake of wide study on construction of artificial enzymes and receptors, it is necessary to develop a method that enables two functional groups to locate on opposite sides on the cyclodextrin torus (see **2**). Since hydroxyl groups of cyclodextrins must be activated usually before their functionalization, specific sulfonylation of the primary and secondary hydroxyl groups is important. Some useful methods for sulfonation on C_2-OH,[3] C_3-OH,[3b,4] and C_6-OH[5] are known.



Recently, we reported the preliminary preparation, isolation, and structure-determination of $3^A,6^X$-di-*O*-diactivated α-cyclodextrins.[6a,b] However, since the 3-*O*-sulfonate does not easily react with nucleophiles and since the $2^A,3^A$-alloepoxide derived from the 3-*O*-sulfonate does not give a sole product in the reaction with a nucleophile,[7] the $3^A,6^X$-di-*O*-sulfonates may not be appropriate starting materials for the preparation of bifunctional α-cyclodextrins. On the other hand, the 2-*O*-sulfonate is very useful since the mannoepoxide obtained from it gives a sole product in the reaction with a nucleophile.

We describe here the preparation and isolation of $2^A,6^X$-di-*O*-disulfonylated α-cyclodextrins (**3**–**8**, X = A–F) and

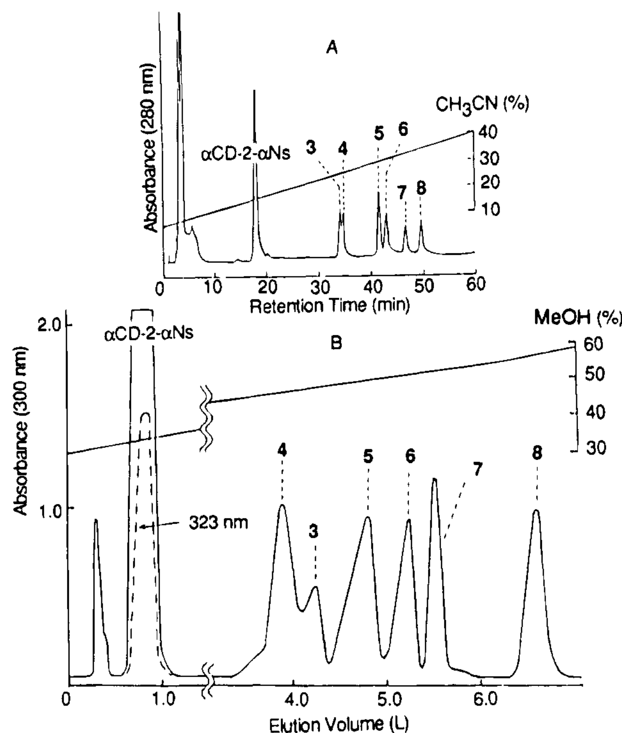


Figure 1. Reversed-phase HPLC (A) and column chromatography (B) of the mixture obtained by the reaction of 2-*O*-(1-naphthalenesulfonyl)-α-cyclodextrin (αCD-2-αNs) with mesitylenesulfonyl chloride in pyridine. A linear gradient elution of CH_3CN (A) or MeOH (B) was applied.

their structure-determination. We have reported the preparation and structure-determination of $2^A,6^X$-di-*O*-diactivated β-cyclodextrins,[6c] where the key reaction for structure-determination was the enzymatic, selective hydrolysis of the disulfonates with α-amylase (saccharifying type) of *Bacillus subtillus* var. *amylosaccharitícus* (BSA). However, this method is not effective in the present case since α-cyclodextrin and modified α-cyclodextrins are not susceptible to enzymatic hydrolysis with BSA.

Results and Discussion

2-*O*-(1-Naphthalenesulfonyl)-α-cyclodextrin[3c] was 6-*O*-sulfonylated with mesitylenesulfonyl chloride in pyridine and the mixture of products (disulfonates) was chromatographed on a reversed-phase column to give the recovered starting material (43.5%), **3** (5.8%), **4** (2.1%), **5** (7.2%), **6** (5.0%), **7** (3.5%), and **8** (4.5%) (Figure 1). Of the many kinds of sulfonyl chloride examined for 6-*O*-sulfonylation,

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(2) Tabushi, I.; Kuroda, Y.; Mizutani, T. *J. Am. Chem. Soc.* **1986**, *108*, 4514 and references cited therein.

(3) (a) Ueno, A.; Breslow, R. *Tetrahedron Lett.* **1982**, *23*, 3451. (b) Fujita, K.; Nagamura, S.; Imoto, T. *Tetrahedron Lett.* **1984**, *25*, 5673. (c) Fujita, K.; Nagamura, S.; Imoto, T.; Tahara, T.; Koga, T. *J. Am. Chem. Soc.* **1985**, *107*, 3233. (d) Murakami, T.; Harata, K.; Morimoto, S. *Tetrahedron Lett.* **1987**, *28*, 321. (e) Rong, D.; D'Souza, V. T. *Ibid.* **1990**, *31*, 4275.

(4) Fujita, K.; Tahara, T.; Imoto, T.; Koga, T. *J. Am. Chem. Soc.* **1989**, *108*, 2030.

(5) Fujita, K.; Yamamura, H.; Imoto, T. *Tetrahedron Lett.* **1991**, *32*, 6737 and references cited therein.

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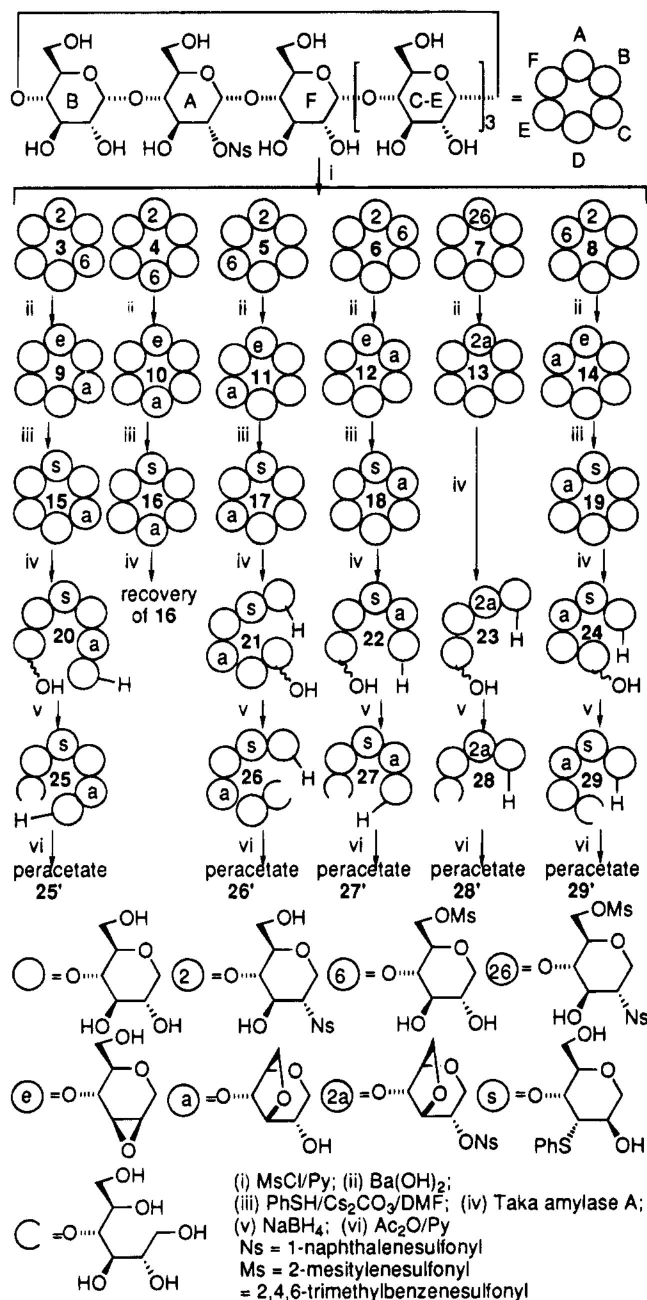
Scheme 1. Preparation and Structure-Determination of a Complete Set of 2^A-*O*-(1-naphthalenesulfonyl)-6^X-*O*-(mesitylenesulfonyl)-α-cyclodextrins 3–8 (X = A–F)



mesitylenesulfonyl chloride performed best to give a mixture of disulfonates which could be separated by reversed-phase column chromatography.

The fast-atom-bombardment mass (FAMBS) spectra of **3–8** demonstrated that they were mesitylenesulfonates of 2-*O*-(1-naphthalenesulfonyl)-α-cyclodextrin. That the mesitylenesulfonyl group must be located on the 6-*O* position is reasonably deduced from many results of similar sulfonylation reactions in pyridine.[5]

The positional determination was carried out as shown in Scheme 1. While the disulfonates other than **7** gave dianhydrides of α-cyclodextrin by treatment with aqueous alkali, only **7** afforded a naphthalenesulfonate (**13**) of anhydro-α-cyclodextrin. The FAB mass spectrum of **13** contained the molecular ion and the ^{1}H NMR (500 MHz) showed the characteristic signals of the 1-naphthalenesulfonyl part at δ 7.70–8.57 and of the 2-*O*-sulfonyl-3,6-anhydroglucoside part at δ 4.48 (m, C_2-H), 4.54 (t, J = 4.8 Hz, C_3-H), and 4.57 (m, C_5-H). The hydrolysis of **13** by Taka-amylase A (TAA) gave a derivative of maltotetraose **23**, which reduced with aqueous $NaBH_4$ to give **28**. Complete acetylation of **28** by the conventional method with acetic anhydride–pyridine gave **28′**. FABMS spectral analysis of **28′** (Figure 2) demonstrated that **23** was 3″,6″-anhydro-2″-*O*-(1-naphthalenesulfonyl)maltotetraose. Therefore, **13** and **7** are assigned to $3^A,6^A$-anhydro-2^A-*O*-(1-naphthalenesulfonyl)-α-cyclodextrin and $2^A,6^A$-di-*O*-disulfonylated α-cyclodextrin, respectively.

As mentioned above, the disulfonates (**3–6** and **8**) were converted to the dianhydrides (**9–12** and **14**) by treatment with aqueous $Ba(OH)_2$, respectively. This chemical change is easily understandable on the basis of previous observations that 6-*O*-sulfonylated cyclodextrins and 2-*O*-sulfonylated cyclodextrins were selectively converted to 3,6-anhydrocyclodextrins[8] and 2,3-anhydrocyclodextrins,[3c] respectively, with alkali treatment. The FABMS spectrum of each dianhydride contained the molecular ion. The ^{1}H NMR spectrum showed the characteristic signals of the 3,6-anhydroglucoside part,[8] and the ^{13}C NMR spectrum demonstrated the presence of oxirane ring.[3c] Therefore, the anhydrides are assigned to $2^A,3^A$:$3^X,6^X$-dianhydro-(2AS)-α-cyclodextrins.

Although the enzymatic hydrolysis with BSA was an effective method for determining the location of modified glucoside units in β-cyclodextrin derivatives, it is not applicable to the present case since BSA cannot hydrolyze α-cyclodextrin and its derivatives. The enzymatic hydrolysis method using TAA followed by analysis of the mass spectral fragmentation is also a very useful method for determining the location of modified glucoside units in α, β, γ-cyclodextrins and their derivatives. But this method is not appropriate in this case since both of 3,6-anhydrocyclodextrins and 2,3-anhydrocyclodextrins are converted to anhydromaltotetraoses which possess the anhydroglucoside as the second unit from the nonreducing end. Therefore, we employed the oxirane ring opening with thiophenol for discriminating the two anhydrides. In order to test the usefulness of this method, we carried out the following separate experiments (Scheme 2). The reaction of $2^A,3^A$-anhydro-(2AS)-α-cyclodextrin (**30**) with thiophenol gave 3^A-*S*-phenyl-(2AS,3^AR)-3^A-thio-α-cyclodextrin (**31**) as the major product. The location of phenylthio group on the C_3 in **31** was demonstrated by the presence of the carbon signal at δ 56.3 which was assigned to a secondary carbon attached to SR instead of OH and also assigned to the C_3 from ^{1}H, ^{13}C COSY, and ^{1}H, ^{1}H COSY NMR. From the coupling constant $J_{1,2}$ (6.4 Hz), the sugar unit having the phenylthio group at the C_3 was 3-deoxy-3-phenylthio-altroside of $^1C_4$ conformation. The phenylthio derivative **31** was hydrolyzed enzymatically by TAA to give (2″S,3″R)-

(6) (a) Fujita, K.; Egashira, Y.; Tahara, T.; Imoto, T.; Koga, T. *Tetrahedron Lett.* **1989**, *30*, 1285. (b) Fujita, K.; Tahara, T.; Egashira, Y.; Imoto, T.; Koga, T. *Tetrahedron Lett.* **1992**, *33*, 5385. (c) Fujita, K.; Ishizu, T.; Obe, K.; Minamiura, N.; Yamamoto, T. *J. Org. Chem.* **1992**, *57*, 5606.

(7) The reaction with ammonia, sodium azide, thiophenol, and benzyl mercaptan gave two products. Fujita, K.; Egashira, Y.; Tahara, T.; Ohta, K.; Okabe, Y.; Imoto, T.; Koga, T., to be published.

(8) Fujita, K.; Yamamura, H.; Imoto, T.; Tabushi, I. *Chem. Lett.* **1988**, 543. Fujita, K.; Yamamura, H.; Imoto, T.; Fujioka, T.; Mihashi, K. *J. Org. Chem.* **1988**, *53*, 1943. Fujita, K.; Tahara, T.; Yamamura, H.; Koga, T.; Fujioka, T.; Mihashi, K. *J. Org. Chem.* **1990**, *55*, 877. Yamamura, H.; Fujita, K. *Chem. Pharm. Bull.* **1991**, *39*, 2505.

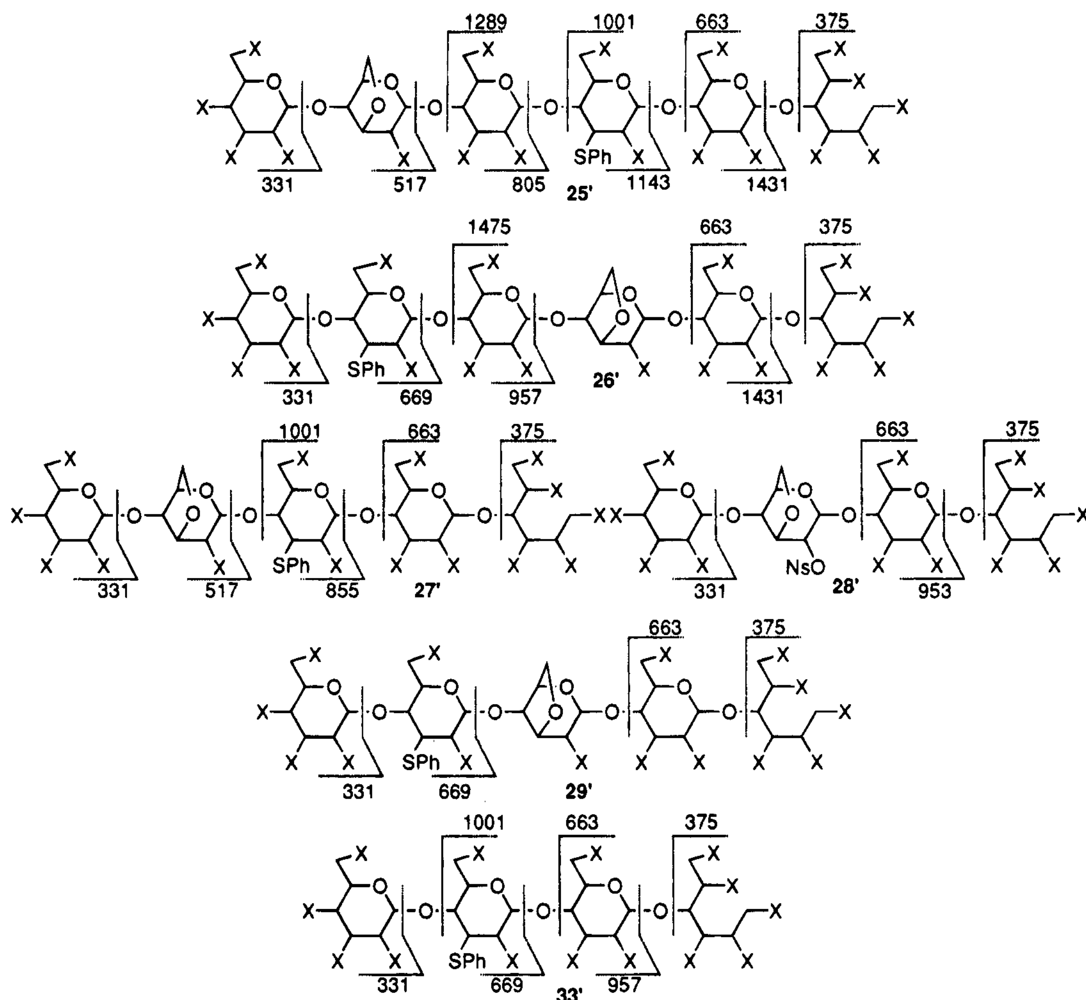
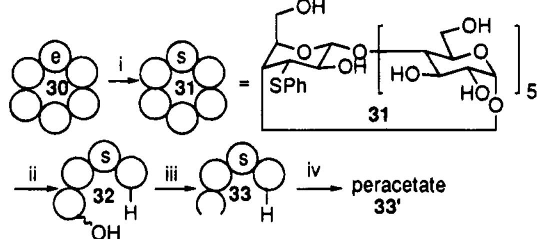


Figure 2. FAB MS spectral fragmentation patterns of the peracetates, **25'–29'** and **33'**. X = OAc, Ns = 1-naphthalenesulfonyl.

Scheme 2 Preparation and Selective Enzymatic Hydrolysis of 3^A-S-Phenyl-(2AS,3^AR)-3^A-thio-α-cyclodextrin 31



(i) $PhSH/Cs_2CO_3$/DMF; (ii) Taka amylase A; (iii) $NaBH_4$; (iv) Ac_2O/Py

3″-(phenylthio)maltotetraose (**32**), whose regiochemical structure was easily determined by reduction of the reducing end followed by complete acetylation and FABMS spectral fragmentation analysis (Figure 2). In conclusion, this method is applicable to the present structure-determination of **9–12** and **14**.

The dianhydrides, **9–12** and **14**, were converted to the corresponding phenylthio-derivatives, **15–19**, which were enzymatically hydrolyzed to give phenylthio-anhydro-oligosaccharides, **20–22** and **24**, respectively, as shown in Scheme 1. Only **16** was not susceptible to the enzymatic hydrolysis. The oligosaccharides, **20–22** and **24**, were reduced with aqueous $NaBH_4$ to give the glucitol derivatives, **25–27** and **29**, respectively. Complete acetylation of **25–27** and **29** by the conventional method with acetic anhydride–pyridine followed by FABMS spectral analysis (Figure 2) demonstrated that the structures were as shown in Scheme 1.

On the basis of the above finding, **3** and **5–8** are assigned to $2^A,6^C$-, $2^A,6^E$-, $2^A,6^B$-, $2^A,6^A$-, and $2^A,6^F$-isomers, respectively. Therefore, **4** is assigned to the $2^A,6^D$-isomer. This is supported by the observation that **16** was not hydrolyzed by TAA. In conclusion, a complete set of $2^A,6^X$-di-O-diactivated α-cyclodextrins **3–8** and a complete set of reactive α-cyclodextrin derivatives **9–14** are now available for preparing bifunctional cyclodextrins which have the functionalities on the opposite sides of cyclodextrin torus. Furthermore, **9–14** and **15–19** have unique and deformed cavities which will show unique molecular recognition toward appropriate inclusion-guest molecules.

Experimental Section

General. ^{13}C and ^1H NMR spectra were determined in DMSO-d_6 at 125 and 500 MHz, respectively, unless otherwise noted. Merck Lobar prepacked columns of Rp18 were used for reversed-phase column chromatography. HPLC was performed on a TSKgel ODS-80TM (4.6 × 250 mm, TOSOH) or a Zorbax ODS (4.6 × 150 mm, Du Pont) column. Thin-layer chromatography (TLC) was run with precoated silica gel plates (Merck, Art. No. 5554). Spot detection was carried out by UV light and/or staining with 0.1% 1,2-naphthalenediol in EtOH/H_2O/H_2SO_4 (200/157/43 (v/v/v)). The elution solvent for TLC was A or B: A; n-C_3H_7OH/AcOEt/H_2O (7/7/5 v/v/v)), B; benzene/

methanol (9/1 v/v)). TAA was purchased from Sigma (α-amylase Type X-A).

Preparation of $2^A,6^X$-Di-*O*-disulfonylated α-Cyclodextrins (3–8, X = A–F). Mesitylenesulfonyl chloride (600 mg) was added to a solution of 2-*O*-(1-naphthalenesulfonyl)-α-cyclodextrin[3c] (600 mg) in pyridine (12 mL), and the solution was stirred at room temperature. The progress of the reaction was monitored by TLC, and the reaction was stopped by addition of water (1 mL) when the maximum amount of monomesitylenesulfonate was reached. The solution was concentrated in vacuo and chromatographed on a reversed-phase column with gradient elution from 30% aqueous MeOH (3.5 L) to aqueous 60% MeOH (3.5 L) to give the recovered starting material (261.1 mg, 43.5%), **3** (40.5 mg, 5.8%), **4** (14.8 mg, 2.1%), **5** (49.6 mg, 7.2%), **6** (34.4 mg, 5.0%), **7** (24.1 mg, 3.5%), and **8** (31.4 mg, 4.5%). **3**; ^{1}H NMR (characteristic signals) δ 8.63–7.69 (7H), 7.09 (2H, s), 2.52 (6H, 2), 2.28 (3H, s). ^{13}C NMR (characteristic signals); δ 143.1–124.3, 22.0, 20.4. FAB MS (*m/z*); 1345 (M + H$^+$). TLC (A); R_f 0.66. **4**; ^{1}H NMR (characteristic signals) δ 8.64–7.69 (7H), 7.09 (2H, s), 2.52 (6H, s), 2.29 (3H, s). ^{13}C NMR (characteristic signals); δ 143.2–124.4, 21.9, 20.5. FAB MS (*m/z*); 1345 (M + H$^+$). TLC (A); R_f 0.65. **5**; ^{1}H NMR (characteristic signals) δ 8.64–7.69 (7H), 7.10 (2H, s), 2.52 (6H, s), 2.29 (3H, s). ^{13}C NMR (characteristic signals); δ 143.2–124.3, 21.9, 20.4. FAB MS (*m/z*); 1345 (M + H$^-$). TLC (A); R_f 0.60. **6**; ^{1}H NMR (characteristic signals) δ 8.63–7.63 (7H), 7.06 (2H, s), 2.50 (6H, s), 2.27 (3H, s). ^{13}C NMR (characteristic signals); δ 143.1–124.3, 21.9, 20.4. FAB MS (*m/z*); 1345 (M + H$^+$). TLC (A); R_f 0.60. **7**; ^{1}H NMR (characteristic signals) δ 8.62–7.70 (7H), 7.05 (2H, s), 2.50 (6H, s), 2.27 (3H, s). ^{13}C NMR (125 MHz, DMSO-d_6, characteristic signals); δ 143.3–124.3, 21.8, 20.5. FAB MS (*m/z*); 1367 (M + Na$^+$). TLC (A); R_f 0.57. **8**; ^{1}H NMR (characteristic signals) δ 8.63–7.70 (7H), 7.06 (2H, s), 2.51 (6H, s), 2.28 (3H, s). ^{13}C NMR (characteristic signals); δ 143.3–124.3, 22.0, 20.4. FAB MS (*m/z*); 1345 (M + H$^+$). TLC (A); R_f 0.58.

Conversion of $2^A,6^X$-Di-*O*-disulfonylated α-Cyclodextrins (3–8, X = A–F) to Anhydrides (9–14). A mixture of **3** (25.4 mg), 0.1 N $Ba(OH)_2$ (2.5 mL), and 95% EtOH (1 mL) was stirred at 40 °C for 16 h, neutralized with 0.1 N H_2SO_4, and filtered. The filtrate was chromatographed on a reversed-phase column with gradient elution from water (1 L) to aqueous 40% MeOH (1 L) to give **9** (17.6 mg, 99.4%). Similarly, the anhydrides **10** (28.6 mg, 74.7%), **11** (44.5 mg, 82.3%), **12** (31.5 mg, 99.4%), **13** (28.1 mg, 75.1%), and **14** (24.5 mg, 83.1%) were obtained from **4** (54.4 mg), **5** (77.7 mg), **6** (45.5 mg), **7** (44.2 mg), and **8** (42.3 mg), respectively. **9**; ^{1}H NMR (D_2O, characteristic signals) δ 5.29 (1H, s), 5.17 (1H, d, J = 2.0 Hz), 4.61 (1H, broad s), 4.51 (1H, t, J = 4.6 Hz). ^{13}C NMR (D_2O, characteristic signals); δ 54.9, 51.1. FAB MS (*m/z*); 937 (M + H$^+$), 959 (M + Na$^+$). TLC (A); R_f 0.17. **10**; ^{1}H NMR (D_2O, characteristic signals) δ 5.44 (1H, s), 5.20 (1H, d, J = 2.8 Hz), 4.59 (1H, broad s), 4.51 (1H, t, J = 5.5 Hz). ^{13}C NMR (D_2O, characteristic signals); δ 55.2, 50.7. FAB MS (*m/z*); 937 (M + H$^+$), 959 (M + Na$^+$). TLC (A); R_f 0.16. **11**; ^{1}H NMR (D_2O, characteristic signals) δ 5.44 (1H, s), 5.15 (1H, d, J = 1.8 Hz), 4.59 (1H, broad s), 4.50 (1H, t, J = 4.6 Hz). ^{13}C NMR (D_2O, characteristic signals); δ 57.0, 51.8. FAB MS (*m/z*); 937 (M + H$^+$). TLC (A); R_f 0.17. **12**; ^{1}H NMR (D_2O, characteristic signals) δ 5.26 (2H, s), 4.57 (1H, broad s), 4.49 (1H, t, J = 5.0 Hz). ^{13}C NMR (D_2O, characteristic signals); δ 56.6, 52.1. FAB MS (*m/z*); 937 (M + H$^+$), 959 (M + Na$^+$). TLC (A); R_f 0.17. **13**; ^{1}H NMR (D_2O, characteristic signals) δ 8.60–7.65 (7H), 5.09 (1H, broad s), 4.44 (1H, broad s), 4.39 (1H, t, J = 4.6 Hz). ^{13}C NMR (D_2O, characteristic signals); δ 102.3, 101.8, 101.1, 100.3, 98.5, 96.8. FAB MS (*m/z*); 1145 (M + H$^+$), 1167 (M + Na$^+$). TLC (A); R_f 0.35. **14**; ^{1}H NMR (characteristic signals) δ 5.24 (1H, s), 5.14 (1H, d, J = 2.2 Hz), 4.68 (1H, broad s), 4.50 (1H, t, J = 5.1 Hz). ^{13}C NMR (characteristic signals); δ 57.4, 52.2. FAB MS (*m/z*); 937 (M + H$^+$), 959 (M + Na$^+$). TLC (A); R_f 0.17.

Reaction of 9–12, 14, and 30 with Thiophenol. A mixture of **9** (15.2 mg), Cs_2CO_3 (12 mg), and thiophenol (100 μL) in DMF (2 mL) was stirred at 80 °C for 5 h. After addition of water (1 mL), the mixture was acidified with HCl, extracted with ether, neutralized with $NaHCO_3$, and concentrated in vacuo. The residue was dissolved into water and chromatographed on a reversed-phase column with gradient elution from water (500 mL) to aqueous 50% MeOH (500 mL) to give **15** (12.1 mg, 71.2%). Similarly, **16** (15.7 mg, 80.7%), **17** (31.7 mg, 63.9 mg), **18** (19.9 mg, 68.2%), **19** (15.9 mg, 44.7%), and **31** (253.1 mg, 82.3%) were obtained from **10** (17.4 mg), **11** (44.4 mg), **12** (26.1 mg), **14** (31.8 mg), and **30** (275.7 mg), respectively. **15**; ^{1}H NMR (D_2O, characteristic signals) δ 7.56–7.30 (5H), 4.53 (1H, broad s). FAB MS (*m/z*); 1047 (M + H$^+$), 1069 (M + Na$^+$). TLC (A); R_f 0.44. **16**; ^{1}H NMR (D_2O, characteristic signals) δ 7.58–7.35 (5H), 4.62 (1H, broad s). FAB MS (*m/z*); 1047 (M + H$^+$), 1069 (M + Na$^+$). TLC (A); R_f 0.39. **17**; ^{1}H NMR (D_2O, characteristic signals) δ 7.58–7.34 (5H), 4.60 (1H, broad s). FAB MS (*m/z*); 1047 (M + H$^+$), 1069 (M + Na$^+$). TLC (A); R_f 0.42. **18**; ^{1}H NMR (D_2O, characteristic signals) δ 7.62–7.33 (5H), 4.91 (1H, d, J = 2.8 Hz), 4.80 (1H, d, J = 10.1 Hz), 4.52 (1H, broad s). FAB MS (*m/z*); 1047 (M + H$^+$), 1069 (M + Na$^+$). TLC (A); R_f 0.42. **19**; ^{1}H NMR (D_2O, characteristic signals) δ 7.92–7.38 (5H), 4.64 (1H, broad s). FAB MS (*m/z*); 1047 (M + H$^+$), 1069 (M + Na$^+$). TLC (A); R_f 0.39. **31**; ^{1}H NMR (D_2O, characteristic signals of 3-deoxy-3-phenylthio-altroside) δ 7.60–7.39 (5H), 4.88 (1H, d, J = 6.4 Hz), 4.34 (1H, m), 4.25 (1H, t, J = 3.2 Hz). ^{13}C NMR (D_2O, characteristic signals of 3-deoxy-3-phenylthio-altroside) δ 106.7, 82.1, 78.3, 56.3. FAB MS (*m/z*); 1065 (M + H$^+$), 1087 (M + Na$^+$). TLC (A); R_f 0.39.

Enzymatic Hydrolysis of 15–19 and 31 by Taka-amylase A. A solution of **15** (15.1 mg), Taka-amylase A (α-amylase A type X-A, Sigma, 15.1 mg) in 0.2 M acetate buffer (pH 5.5, 1.5 mL) containing 0.01 M $CaCl_2$ was kept at 40 °C for 45 h and then the pH of the solution was adjusted to 11 with 10% NaOH. After centrifuging, the supernatant liquid was neutralized with HCl and chromatographed on a reversed-phase column with gradient elution from water (500 mL) to aqueous 50% MeOH (500 mL) to give **20** (15.0 mg, 97.4%). Similarly, enzymatic reactions of **13** (10.5 mg), **17** (31.5 mg), **18** (19.4 mg), **19** (18.4 mg), and **31** (170 mg) for 48, 46, 20, 95, and 168 h afforded **23** (7.6 mg, 98.7%), **21** (26.3 mg, 82.4%), **22** (9.2 mg, 55.0%), **24** (9.7 mg, 61.1%), and **32** (110 mg, 90.8%), respectively. Even after the similar reaction for 94 h, **16** (15 mg) was unaffected and recovered by reversed-phase column chromatography in 90.0%. **20**; FAB MS (*m/z*); 1087 (M + Na$^+$). TLC (A); R_f 0.30. **21**; FAB MS (m/z); 1065 (M + H$^+$), 1087 (M + Na$^+$). TLC (A); R_f 0.24. **22**; FAB MS (*m/z*); 903 (M + H$^+$), 925 (M + Na$^+$). TLC (A); R_f 0.39. **23**; FAB MS (*m/z*); 839 (M + H$^+$). TLC (A); R_f 0.49. **24**; FAB MS (*m/z*); 903 (M + H$^+$), 925 (M + Na$^+$). TLC (A); R_f 0.40. **32**; FAB MS (*m/z*); 759 (M + H$^+$). TLC (A); R_f 0.46.

Reduction of 20–24 and 32 with $NaBH_4$. A solution of **20** (14.0 mg) in aqueous 1% $NaBH_4$ (1.4 mL) was stirred at room temperature for 1.5 h, neutralized with HCl, and chromatographed on a reversed-phase column with gradient elution from water (500 mL) to aqueous 50% MeOH (500 mL) to give **25** (8.1 mg, 58%). Similarly, **21** (14.0 mg), **22** (9.2 mg), **23** (8.6 mg), **24** (7.5 mg), and **32** (82.0 mg) gave **26** (10.0 mg, 71%), **27** (8.5 mg, 92%), **28** (7.6 mg, 68%), **29** (4.5 mg, 60%), and **33** (78.1 mg, 95.0%), respectively. **25**; FAB MS (*m/z*); 1067 (M + H$^+$), 1089 (M + Na$^+$). TLC (A); R_f 0.26. **26**; FAB MS (*m/z*); 1089 (M + Na$^+$). TLC (A); R_f 0.23. **27**; FAB MS (*m/z*); 927 (M + Na$^+$). TLC (A); R_f 0.31. **28**; FAB MS (*m/z*); 841 (M + H$^+$). TLC (A); R_f 0.47. **29**; FAB MS (*m/z*); 905 (M + H$^+$), 927 (M + Na$^+$). TLC (A); R_f 0.34. **33**; FAB MS (*m/z*); 761 (M + H$^+$), 783 (M + Na$^+$). TLC (A); R_f 0.42.

Acetylation of 25–29 and 33 with Acetic Anhydride and Pyridine. A solution of **25** (5.9 mg) was treated conventionally with acetic anhydride (0.5 mL) and pyridine (0.5 mL) at room temperature for 2 d. The crude product was chromatographed on a short silica gel column (SEP-PAK SILICA cartridge, Waters) with elution of benzene (28 mL) and then benzene–MeOH (9/1 v/v, 12 mL) to give peracetate **25′** (4.7 mg, 47%). Similarly, **26** (5.0 mg), **27** (5.0 mg), **28** (3.9

mg), **29** (4.3 mg), and **33** (10.0 mg) gave **26′** (2.6 mg, 31%), **27′** (5.1 mg, 60%), **28′** (5.0 mg, 81%), **29′** (2.0 mg, 27%), and **33′** (13.0 mg, 73%), respectively. **25′**; FAB MS (*m/z*); 1823 ($M + H^+$), 1845 ($M + Na^+$). TLC (B); R_f 0.30. **26′**; FAB MS (*m/z*); 1845 ($M + Na^+$). TLC (B); R_f 0.27. **27′**; FAB MS (*m/z*); 1557 ($M + Na^+$). TLC (B); R_f 0.31. **28′**; FAB MS (*m/z*); 1345 ($M + H^+$), 1367 ($M + Na^+$). TLC (B); R_f 0.18. **29′**; FAB MS (*m/z*); 1557 ($M + Na^+$). TLC (B); R_f 0.34. **33′**; FAB MS (*m/z*); 1349 ($M + H^+$), 1371 ($M + Na^+$). TLC (B); R_f 0.23.

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Supplementary Material Available: ^{13}C NMR spectra of **3**–**14** and **31** and ^{1}H NRM spectra of **3**–**19** and **31** (31 pages). This material is contained in libraries on microfilm, immediately follows this article in the micofilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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