Specific Preparation and Structure Determination of $3^A,3^C,3^E$-Tri-*O*-sulfonyl-β-cyclodextrin

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A reaction of β-cyclodextrin with β-naphthylsulfonyl chloride in alkaline aqueous acetonitrile gave only one isomer ($3^A,3^C,3^E$-trisulfonate, 17.8%) of five 3,3,3-tri-*O*-sulfonyl-β-cyclodextrins. The isomer was converted to $3^A,6^A:3^C,6^C:3^E,6^E$-trianhydro-β-cyclodextrin, the structure of which was assigned by comparing its spectral and HPLC data of the trianhydro-β-cyclodextrin with those of all authentic 3,6:3,6:3,6-trianhydro-β-cyclodextrins prepared by the reactions of known 6-tri-O-sulfonylated β-cyclodextrins with aqueous alkali.

Regiospecific bifunctionalization of cyclodextrins is an approach to the construction of enzyme (or receptor) mimics.[2] In this context the study of disulfonylation is important. Many studies have been focused on di- (or poly-) sulfonylation of the primary hydroxyls.[3] Since Breslow et al. reported that β-cyclodextrin modified with a pyridoxamine moiety on its secondary hydroxyl side produced amino acids with chirality opposite to that produced from the corresponding 6-modified cyclodextrin in transamination reactions,[4] di- (or poly-) sulfonylation of the secondary hydroxyls should be investigated for the sake of wide development of chemical construction of enzyme (or receptor) mimics. However, there are few studies of sulfonylation of the secondary hydroxyl. Breslow et al.,[5a] Hattori et al.,[5b] Fujita et al.,[5c-f] and Murakami et al.[5g] prepared the 2-*O*- and/or 3-*O*-monosulfonyl cyclodextrins. Fujita et al. prepared 2,2-*O*-disulfonyl-α-cyclodextrins[5c] and 3,3-*O*-disulfonyl-β-cyclodextrins.[5d] On the other hand, there are not any studies of tri- (or poly-) O-sulfonylation. Since Knowles et al. demonstrated very interesting molecular recognition of a $6^A,6^C,6^E$-trifunctionalized α-cyclodextrin in the guest binding,[2f] it must be valuable to prepare a trisulfonate of the secondary hydroxyls. We now describe specific preparation of a $3^A,3^C,3^E$-tri-O-sulfonylated β-cyclodextrin **4** and its structure assignment.

Experimental Section

General Principles. ^1H and ^{13}C NMR spectra were determined at 500 (or 400 or 270) and 125 (or 67.5 or 25) MHz, respectively. Fast-atom-bombardment mass spectra (FABMS) were obtained with a JEOL JMS DX-300/JMA 3500 data system. 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% 1,3-dihydroxynaphthalene in $EtOH/H_2O/H_2SO_4$ (200/157/43 v/v/v). The elution solvent for TLC was n-C_3H_7OH/AcOEt/H_2O (7/7/5 v/v/v). Prepacked columns (Merck, Lobar column LiChroprep Rp18 and Rp8) were used for reverse-phase column chromatography. High-performance liquid chromatography (HPLC) was performed on a Zorbax ODS column (4.6 × 150 mm, Du Pont).

$3^A,3^C,3^E$-Tri-*O*-(β-naphthylsulfonyl)-β-cyclodextrin 4 from β-Cyclodextrin. A solution of β-cyclodextrin (1.4 g) and $Na_2HPO_4 \cdot 12H_2O$ (800 mg) in aqueous 30% acetonitrile (20 mL) was kept at 40 °C, and the pH of the solution was adjusted to 12 by addition of a small amount of concentrated NaOH. β-Naphthylsulfonyl chloride (2.8 g) was added in one portion to the solution under vigorous stirring at 40 °C. The pH of the reaction mixture became acidic after 5 min. After water (10 mL) was added to the reaction mixture, the mixture was filtered and chromatographed on a reverse-phase column with gradient elution from aqueous 20% CH_3CN (1.4 L) to aqueous 55% CH_3CN (1.4 L). The 20-mL fractions were taken in a fraction collector to give **2** (the fractions from no. 53 to 59, 168.4 mg, 9.0%), **3** (the fractions from no. 61 to 67, 126.5 mg, 6.,8%), and **4** (the fractions from no. 115 to 131, 373.5 mg, 17.8%). The fractions from no. 6 to 20 were collected, concentrated, and rechromatographed with gradient elution from water (1 L) to aqueous 25% CH_3CN (1 L). The 20-mL fractions from no. 75 to 84 gave **1** (160 mg, 9.8%).

4: ^{13}C NMR (25 MHz, Me_2SO-d_6, characteristic nonaromatic absorptions) δ 59.97, 70.03, 71.90, 72.76, 76.46, 80.47, 82.27, 84.30, 100.55; FABMS, m/z 1705 ($M + H^+$); R_f value on TLC 0.60.

Effect of Buffer Concentration on the Yields of Sulfonates 1–4. These experiments were carried out similarly to that described in the preparation of **4** from β-cyclodextrin except the amount of $Na_2HPO_4 \cdot 12H_2O$ was changed from 0 to 600 mg (almost saturated concentration, 16.8×10^{-2} M). The result was shown in Figure 1.

$3^A,3^C,3^E$-Tri-*O*-(β-naphthylsulfonyl)-β-cyclodextrin 4 from $3^A,3^D$-Disulfonate 2 or $3^A,3^C$-Disulfonate 3. Immediately after 7 mL of aqueous 10% NaOH was added to a solution of **2** (50 mg) in aqueous 30% acetonitrile (20 mL), β-naphthylsulfonyl chloride (100 mg) was added in one portion to the solution under vigorous stirring at room temperature. The amount of aqueous 10% NaOH necessary to adjust the pH of an aqueous 30% CH_3CN solution (20 mL) of β-cyclodextrin (43 mg, equimolar amount to that of **2**) to 12 was determined by a separate experimental result. After

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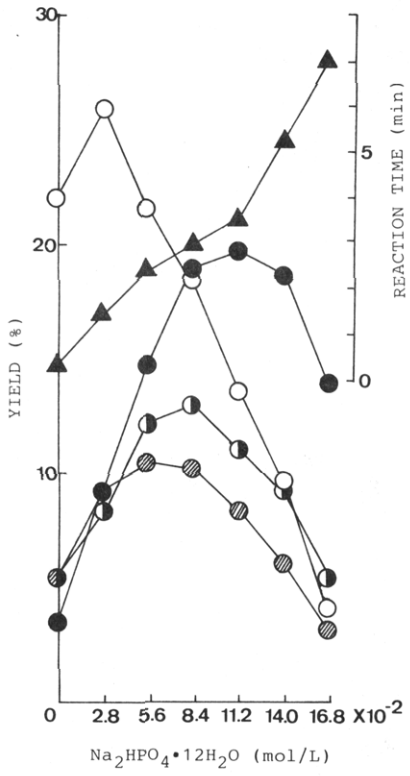

Figure 1. Effect of the buffer concentration on the yield of **1** (○), **2** (◐), **3** (⊘), and **4** (●) and on the reaction time (▲) required for the pH of the reaction mixture to change from 12 to 8.

112 s, the mixture became acidic. The workup procedures similar to those described above gave **4** (12.9 mg, 16.6%) and **2** (33.0 mg, 66%). Similarly, the reaction of **3** (50 mg) with β-naphthylsulfonyl chloride (100 mg) for 117 s gave **4** (20.9 mg, 41.8%) and **3** (21.8 mg, 28.1%).

$2^A,3^A:2^C,3^C:2^E,3^E$-Trianhydro-(3^AS),(3^CS),(3^ES)-β-cyclodextrin 8 from 4. A solution of **4** (160 mg) in a mixture of 0.1 N aqueous $Ba(OH)_2$ (15 mL) and ethanol (7 mL) was stirred at 25 °C for 1 h. The reaction mixture was neutralized with 0.1 N H_2SO_4 and filtered. The filtered solution was chromatographed on a reverse-phase column with water to give **8** (82.2 mg, 81.0%).

8: ^1H NMR (400 MHz, D_2O, H-1 absorptions) δ 5.08–5.15 (4 H), 5.36 (1 H, d, J = 3.42 Hz), 5.40 (1 H, d, J = 2.93 Hz), 5.42 (1 H, d, J = 3.42 Hz); ^{13}C NMR (25 MHz, D_2O, characteristic absorptions) δ 56.69, 56.89, 59.11, 62.66, 63.36, 71.78, 74.12, 75.09, 75.37, 75.99, 76.50, 81.18, 81.41, 82.07, 83.67, 97.28, 97.47, 97.71, 98.41, 101.92, 102.58, 103.21, 103.67, 108.95; FABMS, m/z 1081 (M + H^+); R_f value on TLC 0.13.

$3^A,6^A:3^C,6^C:3^E,6^E$-Trianhydro-β-cyclodextrin 18 from 8. A solution of **8** (25 mg) in 0.25 N aqueous $Ba(OH)_2$ (0.5 mL) was stirred at 90 °C for 46 h. After being neutralized with 0.1 N H_2SO_4 and filtered, the solution was chromatographed on a reverse-phase column with gradient elution from water (1 L) to aqueous 30% methanol (1 L) to give **18** (18.7 mg, 74.8%).

18: ^1H NMR (500 MHz, D_2O), Figure 2; ^{13}C NMR (125 MHz, D_2O, C-1 absorptions) δ 101.71, 101.99, 102.21, 102.58, 103.29, 103.66, 103.94; FABMS, m/z 1081 (M + H^+); R_f value on TLC 0.13.

3,6:3,6:3,6-Trianhydro-β-cyclodextrins 17–21 from 6,6,6-Tri-*O*-(*p*-tosyl)-β-cyclodextrins 22–26. Following the procedure described previously,[6] the title trisulfonates were prepared by the reaction of β-cyclodextrin with *p*-tosyl chloride in pyridine. A solution of $6^A,6^B,6^E$-tri-*O*-(*p*-tosyl)-β-cyclodextrin **22** (14.1 mg) in a mixture of 0.1 N aqueous $Ba(OH)_2$ (1.4 mL) and acetonitrile (0.7 mL) was stirred at 40 °C for 48 h. After being neutralized with 0.1 N H_2SO_4 and filtered, the solution was chromatographed on a reverse-phase column with gradient elution from water (1 L) to aqueous 30% methanol (1 L) to give $3^A,6^A:3^B,6^B:3^E,6^E$-trianhydro-β-cyclodextrin **17** (9.2 mg, 96.8%). Similarly, **23** (12.7 mg) and **26** (23.6 mg) gave the trianhydro-β-cyclodextrins **18** (8.5 mg, 98.8%) and **21** (11.1 mg, 69.4%), respectively. The conversions

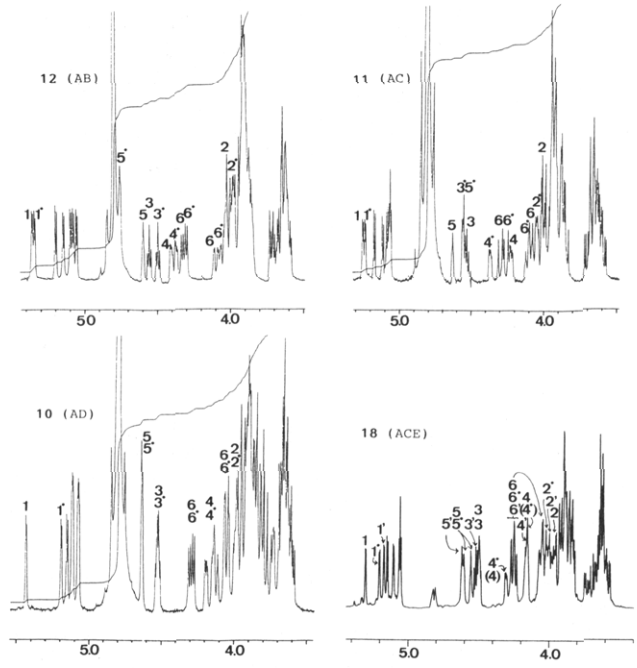

Figure 2. ^1H NMR spectra of **10** (400 MHz), **11** (400 MHz), **12** (400 MHz), and **18** (500 MHz) in D_2O.

of **24** to **19** and of **25** and **20** have been described elsewhere in order to assign the regiochemistry of **24** and **25**.[6] The trianhydrides **17–21** were cleanly separated from one another by reverse-phase HPLC with elution of aqueous 3% acetonitrile.

17: ^1H NMR (270 MHz, D_2O, H-1 absorptions) δ 5.06 (1 H, d, J = 3.96 Hz), 5.12–5.14 (2 H), 5.19 (1 H, d, J = 3.63 Hz), 5.26-5.30 (3 H); ^{13}C NMR (125 MHz, D_2O, C-1 absorptions) δ 100.46, 100.81, 100.89, 100.39, 101.59, 102.88, 103.87; FABMS, m/z 1081 (M + H^+), 1103 (M + Na^+); R_f value on TLC 0.10.

19: ^1H NMR (500 MHz, D_2O, H-1 absorptions) δ 5.05 (1 H, d, J = 3.66 Hz), 5.08 (2 H, d, J = 3.66 Hz), 5.10 (1 H, d, J = 3.30 Hz), 5.17 (1 H, d, J = 2.93 Hz), 5.23 (1 H, d, J = 2.95 Hz); ^{13}C NMR (125 MHz, D_2O, C-1 absorptions) δ 97.94, 98.95, 101.90, 101.94, 102.59, 102.97, 103.17; FABMS, m/z 1081 (M + H^+); R_f value on TLC 0.12.

20: ^1H NMR (500 MHz, D_2O, H-1 absorptions) δ 5.05 (1 H, d, J = 3.67 Hz), 5.07 (1 H, d, J = 3.67 Hz), 5.08 (1 H, d, J = 3.66 Hz), 5.19 (1 H, d, J = 4.39 Hz), 5.22 (1 H, d, J = ca. 1 Hz), 5.26 (1 H, d, J = 2.93 Hz), 5.31 (1 H, d, J = 2.94 Hz); ^{13}C NMR (125 MHz, D_2O, C-1 absorptions) δ 99.49, 100.71, 100.92, 101.08, 103.17, 103.34, 103.74; FABMS, m/z 1081 (M + H^+); R_f value on TLC 0.09.

21: ^1H NMR (270 MHz, D_2O, H-1 absorptions) δ 5.02–5.04 (2 H), 5.07 (1 H, d, J = 3.63 Hz), 5.16 (1 H, d, J = 3.96), 5.26 (1 H, d, J = 3.13 Hz), 5.34 (1 H, J = 2.81 Hz), 5.38 (1 H, d, J = 3.14 Hz); ^{13}C NMR (67.5 Hz, D_2O, C-1 absorptions) δ 98.88, 100.54, 101.32, 102.40, 103.10, 103.34, 103.80; FABMS, m/z 1081 (M + H^+), 1119 (M + Na^+); R_f value on TLC 0.08.

3,6:3,6-Dianhydro-β-cyclodextrins 10–12 from 6,6-Di-*O*-(*p*-tosyl)-β-cyclodextrins 14–16. A solution of the ditosylate **16** (185 mg) in 0.1 N aqueous $Ba(OH)_2$ (10 mL) was stirred at 40 °C for 19 h. After being neutralized with 0.1 N H_2SO_4 and filtered, the solution was chromatographed on a reverse-phase column with water (700 mL), aqueous 1% methanol (1 L), aqueous 3% methanol (300 mL), and aqueous 7% methanol (300 mL) and then with gradient elution from aqueous 10% methanol (200 mL) to aqueous 30% methanol (200 mL) to give the dianhydro-β-cyclodextrin **12** (90 mg, 63.5%). Similarly, **14** (185 mg) and **15** (185 mg) gave the dianhydro-β-cyclodextrins **10** (86 mg, 61.5%) and **11** (133 mg, 94.6%), respectively.

10: ^1H NMR (400 MHz, D_2O), Figure 2; ^{13}C NMR (67.5 MHz, D_2O, C-1 absorptions) δ 101.21, 103.05, 103.13, 103.35, 104.06, 104.25, 104.75; FABMS, m/z 1099 (M + H^+); R_f value on TLC 0.09.

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11: ^1H NMR (400 MHz, D_2O), Figure 2; ^{13}C NMR (67.5 MHz, D_2O, C-1 absorptions) δ 101.26, 101.44, 102.43, 102.55, 103.45 (three C-1 absorptions); FABMS, m/z 1099 ($M + H^+$), 1121 ($M + Na^+$); R_f value on TLC 0.09.

12: ^1H NMR (400 MHz, D_2O), Figure 2; FABMS, m/z 1099 ($M + H^+$); R_f value on TLC 0.09.

3,6:3,6-Dianhydro-β-cyclodextrins 10 and 11 from Diepoxides 6 and 7. A solution of **6** (100 mg) in 0.25 N aqueous $Ba(OH)_2$ (81 mL) was stirred at 90 °C for 48 h. After neutralized with 0.1 N H_2SO_4 and filtered, the solution was chromatographed by a reverse-phase column to give **10** (49.9 mg, 49.9%). Similarly, **7** (100 mg) gave **11** (73.8 mg, 73.8%).

Results and Discussion

Preparation of $3^A,3^C,3^E$-Tri-*O*-(β-naphthylsulfonyl)-β-cyclodextrin 4. By the reaction of β-cyclodextrin with β-naphthylsulfonyl chloride in a mixture of acetonitrile and phosphate buffer (pH 12) at 40 °C, $3^A,3^C,3^E$-tri-*O*-(β-naphthylsulfonyl)-β-cyclodextrin **4** was specifically prepared together with 3-sulfonate (**1**) and $3^A,3^D$- (**2**) and $3^A,3^C$-disulfonate (**3**).

In this sulfonylation reaction, the initial pH of the solution of β-cyclodextrin in the mixed solvent was adjusted to 12 and the pH was allowed to decrease during the reaction with β-naphthylsulfonyl chloride. The products were chromatographed on a reverse-phase column to afford the sulfonates **1** (9.8%), **2** (9.0%), **3** (6.8%), and **4** (17.8%). Structure assignment of **4** are described later. We already reported the specific preparation of **1–3** in aqueous acetonitrile, where the yields of **2** and **3** were dependent on the reaction time.[5d] In this reaction, the high pH condition was essentially necessary to dissociate the secondary hydroxyls for the sulfonylation reaction, although the products **1–3** were converted to the corresponding allo-epoxides **5–7** under such conditions. Therefore, the reaction time that the pH of reaction mixture was kept alkaline was very important for the preparation of **1–3**. The reaction time in preparation of **2** and **3** was changed by changing the acetonitrile content in the solvent, and the optimum acetonitrile content was determined to 30%. In the present preparation of **4**, the situation is similar to that mentioned above. However, similar employment of 30% aqueous acetonitrile as the solvent did not necessarily give the best reaction time for the preparation of **4**. To change the reaction time required for the pH of the reaction mixture to change from 12 to 8, we employed a mixture of acetonitrile and a phosphate buffer solution as the solvent, where the content of acetonitrile was fixed at 30% and the concentration of the buffer was changed. The effect of the reaction time on the yield of **4** is shown in Figure 1. The optimum yield of **4** was obtained when 11.2×10^{-2} M of the buffer was used. Also, the reaction condition gave the disulfonates **2** and **3** in better yields than those in the previous report.[5d]

Additional sulfonylation of **2** or **3** with β-naphthylsulfonyl chloride in aqueous acetonitrile for 112 or 117 s at room temperature also gave **4** exclusively in 16.6% or 28.1% yield together with the recovered starting material **2** or **3** in 66% or 41.8% yield, respectively. Interestingly, only one isomer (the A,C,E-trisulfonate, **4**) was produced from β-cyclodextrin, although formation of five isomers (A,B,C, A,B,D, A,B,E, A,B,F, and A,C,E isomers) was possible. Similarly, the A,C,E-trisulfonate was only one product in the sulfonylation of the A,D- (**2**) and A,C-disulfonates (**3**) although four (A,B,D, A,B,E, A,B,F, and A,C,E isomers) and four trisulfonates (A,B,C, A,B,D, A,B,F, and A,C,E isomers) were expected to form, respectively. These are explicable by inhibition of $3^A,3^B$-di-O-sulfonylation, i.e., steric repulsion between two naphthylsulfonyl moieties on the neighboring two glucose units. This idea is consistent with the observation that only the A,D (**2**) and A,C (**3**) isomers were produced in the reaction although the A,B isomer was not.

Structure Assignment of $3^A,3^C,3^E$-Tri-*O*-(β-naphthylsulfonyl)-β-cyclodextrin 4. The sulfonylation of three hydroxyls in **4** was confirmed by the FABMS and ^1H NMR spectra. The ^{13}C NMR spectrum showed the absence of upfield-shifted absorption of C-1, demonstrating sulfonylation on three 3-OH's.[5d,f]

In the case of 6-poly-*O*-(arenesulfonyl)cyclodextrins, the assignment of the regioisomers are carried out by extended Körner method[3e,f] and/or by hydrolysis with Taka amylase A.[3d,e,g,h] In the former method, the number and kinds of the products obtained from a sulfonate by additional sulfonylation are employed as criteria for the structure assignment. Therefore, this method requires that all of the possible isomers are formed in the additional sulfonylations. But this condition is not satisfied in the present case where only one trisulfonate **4** was formed in the additional sulfonylation of **2** and **3**. Hydrolysis of **4** with Taka amylase A is expected to give 3′,3‴,3⁗⁗⁗-tri-*O*-(β-naphthylsulfonyl)maltoheptaose from the result of the enzymatic hydrolysis of 3-*O*-(β-naphthylsulfonyl)-β-cyclodextrin **1**, but the reaction of **4** was extremely slow and not useful. The tri-allo-epoxide **8** obtained from **4** with treatment with $Ba(OH)_2$ was unaffected by Taka amylase. Only when **8** is $2^A,3^A:2^C,3^C:2^E,3^E$-(3^AR),(3^CR),(3^ER)-trianhydro-β-cyclodextrin is this observation in accord with the expectation on the basis of the enzymatic hydrolysis where the mono-allo-epoxide **5** gave 2″,3″-anhydro-(3″*R*)-maltotetraose.[5d,f] However, this is not a satisfactory assignment since the other isomeric triepoxides are not necessarily expected to be enzymatically hydrolyzed smoothly.

Recently, we reported the conversion of 6-*O*-(arenesulfonyl)-β-cyclodextrin **13** to $3^A,6^A$-anhydro-β-cyclodextrin **9**[7] and the conversion of $2^A,3^A$-anhydro-(3^AR)-β-cyclodextrin **5** to $3^A,6^A$-anhydro-β-cyclodextrin **9**.[8] Since the alloepoxide **5** is obtained from 3-*O*-(β-naphthylsulfonyl)-β-cyclodextrin **1**, the 3-sulfonate can be correlated with the 6-sulfonate via the 3,6-anhydride (Scheme I). Before employed in the assignment of the 3,3,3-trisulfonate **4**, this method was tested in the correlation of the 3-disulfonates **2** and **3** with $6^A,6^X$-di-*O*-(*p*-tosyl)-β-cyclodextrins (X = B, X = C, and X = D, Scheme I).

The known $6^A,6^X$-di-*O*-(*p*-tosyl)-β-cyclodextrins **14** (X = D), **15** (X = C), and **16** (X = B)[3g] were easily converted to $3^A,6^A:3^X,6^X$-dianhydro-β-cyclodextrins **10** (X = D), **11** (X = C), and **12** (X = B), respectively, by treatment with aqueous alkali. The FABMS spectra of **10–12** contained the corresponding molecular ions. The ^{13}C and/or ^1H NMR (Figure 2) spectra demonstrated the presence of two 3,6-anhydroglucose units in **10–12**. The assignment of the 3,6-anhydroglucose units in Figure 2 was carried out by the COSY ^1H NMR spectra.

The $3^A,3^X$-disulfonates **2** and **3** were converted to **6** and **7**, respectively, according to the reported procedure.[5d] Treatment of the diepoxides **6** with aqueous $Ba(OH)_2$ at 90 °C gave a 3,6:3,6-dianhydro-β-cyclodextrin, which was assigned to **10** by comparing its retention time in reverse-phase HPLC and ^{13}C and ^1H NMR spectra with those of **10–12** obtained from **14–16**. Similarly, a 3,6:3,6-dianhydro-β-cyclodextrin that was obtained from **7** was

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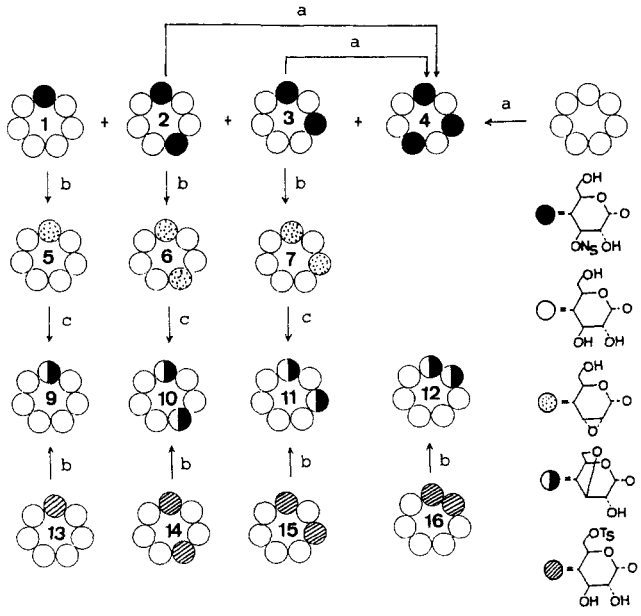
Scheme I. Synthesis of $3^A,3^C,3^E$-Tri-*O*-sulfonyl-β-cyclodextrin 4 and Correlation of 3-*O*-Sulfonyl-β-cyclodextrins 1–3 with 6-*O*-Sulfonyl-β-cyclodextrins 13–16 via 3,6-Anhydro-β-cyclodextrins 9–12[a]

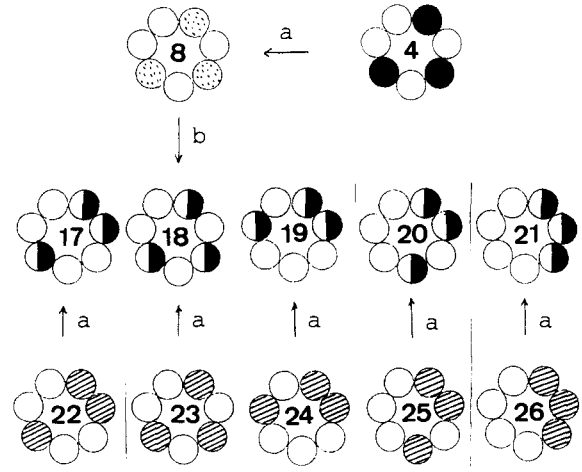


[a] (a) β-Naphthylsulfonyl chloride; (b) 0.1 N $Ba(OH)_2$, 25 °C; (c) 0.25 N $Ba(OH)_2$, 90 °C.

assigned to **11**. Therefore, **2** and **3** are assigned to the $3^A,3^D$- and $3^A,3^C$-disulfonates, respectively. This assignment is consistent with the previous structure determination of **2** and **3** and supports the previous conclusion that the $3^A,3^B$-*O*-di(β-naphthylsulfonyl)-β-cyclodextrin was produced, if any, in negligible amounts in the reaction of β-cyclodextrin with β-naphthylsulfonyl chloride.[5d] On the basis of these results, we used the correlation method for the structure assignment of **4** as shown below.

Each 6,6,6-tri-*O*-(*p*-tosyl)-β-cyclodextrin **22–26**, the preparation and structure assignment of which were already reported elsewhere,[6] was converted to the corresponding 3,6:3,6:3,6-trianhydro-β-cyclodextrin **17–21**, respectively (Scheme II). The FABMS of **17–21** contained the corresponding molecular ions. The ^{13}C and ^1H NMR spectra demonstrated the presence of three 3,6-anhydroglucose units in **17–21**. They were clearly separated by reverse-phase HPLC. Thus, all of isomeric 3,6:3,6:3,6-

Scheme II. Structure Determination of $3^A,3^C,3^E$-Tri-*O*-sulfonyl-β-cyclodextrin 4 through Its Conversion to Trianhydride 18 via Triepoxide 8[a]



[a] (a) 0.1 N $Ba(OH)_2$, 25 °C; (b) 0.25 N $Ba(OH)_2$, 90 °C.

trianhydro-β-cyclodextrins were obtained as the authentic compounds.

The triepoxides **8** were converted to the corresponding 3,6-trianhydro-β-cyclodextrin (Scheme II), which was assigned to $3^A,6^A:3^C,6^C:3^E,6^E$-trianhydro-β-cyclodextrin **18** by comparing its retention time in reverse-phase HPLC and ^{13}C and ^1H NMR spectra with those of the authentic compounds **17–21**. Therefore, the trisulfonate **4** is assigned to $3^A,3^C,3^E$-tri-*O*-(β-naphthylsulfonyl)-β-cyclodextrin.

In conclusion, $3^A,3^C,3^E$-tri-*O*-sulfonyl-β-cyclodextrin is now available through the convenient method. From this compound, some enzyme (or receptor) mimics that have three functional groups at the given positions of the secondary hydroxyl side will be prepared. Also, 3,6:3,6:3,6-trianhydro-β-cyclodextrins described in this report will afford unique cavities for guest binding. The structure determination method through the correlation of 3-O-sulfonylated cyclodextrins with 6-O-sulfonylated cyclodextrins will be applicable for more complicated cases of structure determination of polysubstituted cyclodextrins.

Acknowledgment. We thank Japan Maize Products Co. Ltd. for a generous gift of β-cyclodextrin.

Supplementary Material Available: ^1H and/or ^{13}C NMR spectra of **4**, **8**, and **17–21** (13 pages). Ordering information is given on any current masthead page.