The mixture was stirred at 0 °C for 30 min and then allowed to warm to room temperature. After washing the mixture with 10 mL of saturated sodium bicarbonate solution, the organic layer was separated, dried and distilled to give *threo*-2,3-bis(methylthio)butane as a colorless liquid [2.69 g, 90%, bp 70–73 °C (6 mm)].[11] A rubber septum was used in place of the gas inlet tube for less volatile alkenes.

***trans*-1,4-Bis(methylthio)- and -Bis(phenylthio)-2-butene.** To a solution of sodium methoxide in methanol (1 M, 200 mL, 0 °C) was added methanethiol (9.6 g, 0.2 mol) or benzenethiol (22 g, 0.2 mol). The temperature was raised briefly to 25 °C and then cooled again to 0 °C. *trans*-1,4-Dichloro-2-butene (12.5 g, 0.1 mol) was added slowly to the stirred solution such that the temperature remained below 10 °C. Thereafter, the mixture was refluxed for 1 h, cooled, and poured into 1 L of ice–water. After extraction with ether (100 mL × 3), the ether extract was dried and distilled to give a colorless oil of *trans*-1,4-bis(methylthio)-2-butene [12.4 g, 85%, bp 41–42 °C (0.15 mm), (lit.[15] bp 115 °C (19 mm))]: NMR ($CDCl_3$) δ 2.01 (s, SCH_3, 3 H), 3.05 (m, CH_2, 2 H), 5.45 (m, CH=, 1 H). With benzenethiol, a crystalline solid of *trans*-1,4-bis(phenylthio)-2-butene was obtained [mp 64–66 °C (lit.[16] mp 76–77 °C), 20 g, 74%); NMR ($CDCl_3$) δ 3.43 (m, CH_2, 2 H), 5.56 (m, CH=, 1 H), 7.20 (m, Ph, 5 H).

Methyl Phenyl Disulfide. Methyl disulfide (9.4 g, 0.1 mol) was converted to methanesulfenyl chloride by adding 7.1 g of chlorine at −40 °C. The product, as a clear reddish orange solution, was added to a cold (0 °C) solution of benzenethiol (26 g, 0.236 mol) in 200 mL of dry methanol with 20 g of powdered calcium carbonate. The mixture was stirred for an additional 2 h at room temperature. Ice–water (500 mL) was added, and when gas evolution ceased, the mixture was extracted with ether (100 mL × 3), and the ether extracts were washed with 10% NaOH and then water (100 mL × 2), dried, and fractionally distilled to give 19.6 g of the product free of symmetrical disulfides [63%, 60–61 °C (0.2 mm)]: NMR ($CDCl_3$) δ 2.44 (s, SCH_3, 3 H), 7.15–7.55 (m, Ph, 5 H).

Addition of Methyl Phenyl Disulfide to *cis*-2-Butene. To a cold solution of 10 mL each of dichloromethane and nitromethane were added *cis*-2-butene (1.1 g, 20 mmol) and boron trifluoride dimethyl etherate (0.1 mL) as described previously. The mixture was cooled to −10 °C, and methyl phenyl disulfide (1.56 g, 10 mmol) in 5 mL of 1:1 solvent mixture was added slowly with stirring. The products were obtained as described previously and the composition determined by GLPC and NMR. Tabulated NMR data are available as supplementary material.

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Supplementary Material Available: Table II, containing NMR assignments for all adducts (1 page). Ordering information is given on any current masthead page.

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Unsymmetrically Disubstituted β-Cyclodextrins. 6A,6X-Dideoxy-6A-azido-6X-[(mesitylsulfonyl)oxy] Derivatives

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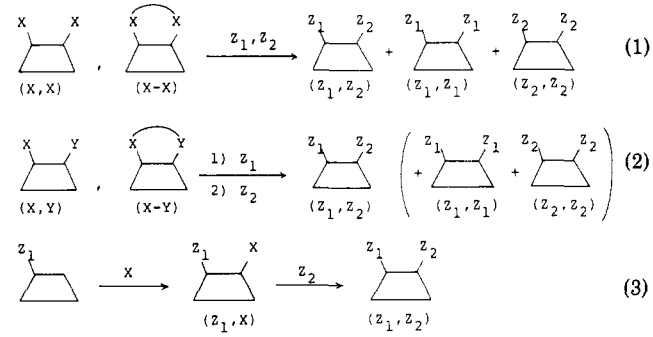
In the past decade, construction of artificial enzymes (or receptors) by chemical modification of cyclodextrins has been extensively studied. While monosubstitution of primary hydroxyl groups of cyclodextrins allowed simple designing of enzymes (or receptors),[1] transannular disulfonation (disulfonate capping) developed a new and quite interesting aspect of synthesis of symmetrically and specifically (6A,6C or 6A,6D) bifunctionalized enzyme (or receptor) mimics.[1,2] Recently, we also developed convenient preparation and effective separation of 6A,6B-, 6A,6C-, and 6A,6D-disulfonates of α- and β-cyclodextrins.[3,4] However, more sophisticated artificial enzmes (or receptors) should possess two different functional groups at desirable positions. Strategy of preparation of these artificial enzymes (or receptors) may be divided into three types as shown in Scheme I, where X and Y are activated primary hydroxyls such as sulfonates and Z_1 and Z_2 are functional groups. Since the product composition of the type (1) reaction is statistical, particular association between Z_1 and Z_2 (neither between Z_1 and Z_1 nor between Z_2 and Z_2) should be necessary for the formation of (Z_1,Z_2) in a composition more than 50% (statistical value). The type (2) reaction utilizing an unsymmetrically capped cyclodextrin (X–Y) has been reported by Tabushi.[5] This elegant and ingenious method permitted predominant production of (Z_1,Z_2), although information was not given with respect to the relative positions of Z_1 and Z_2.

Scheme I



We describe here a novel type (3) method which will permit isolation of pure (Z_1,Z_2) with respect to the relative positions of the substituents, 6A,6B-, 6A,6C-, or 6A,6D-isomers. The regioisomeric mixture of 6A,6X-dideoxy-6A-azido-6X-[(mesitylsulfonyl)oxy]-β-cyclodextrins was prepared by the reaction of 6-deoxy-6-azido-β-cyclodextrin[6] with mesitylenesulfonyl chloride in pyridine. After evaporation of pyridine, the crude mixture was applied on a reversed-phase column. After elution of water, a gradient elution of water–aqueous MeOH gave the recovered starting material (28.7%) and products 1 (11.2%), 2 (9.6%), and 3 (8.6%) (Figure 1). The products (1–3) were clearly separable from each other by reversed-phase HPLC (Figure 2A). The IR spectra of 1, 2, and 3 showed the absorptions of the azido (2100 cm^{-1}) and the sulfonate (1190, 1173, 760, and 648 cm^{-1}) in addition to the ab-

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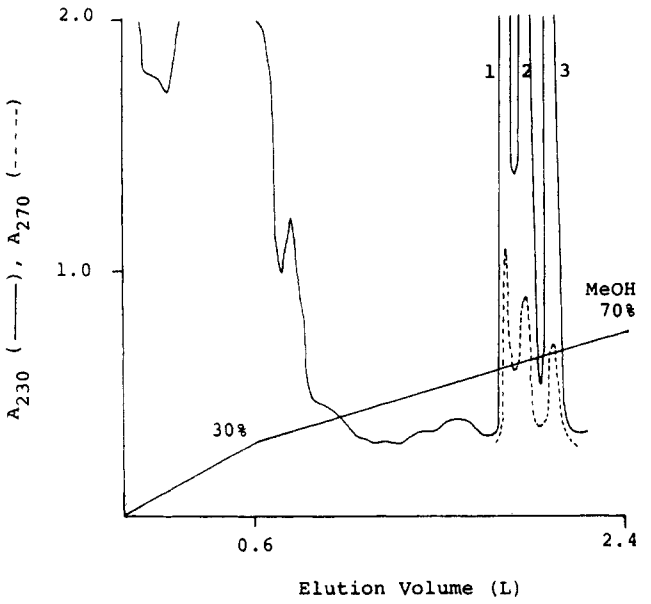
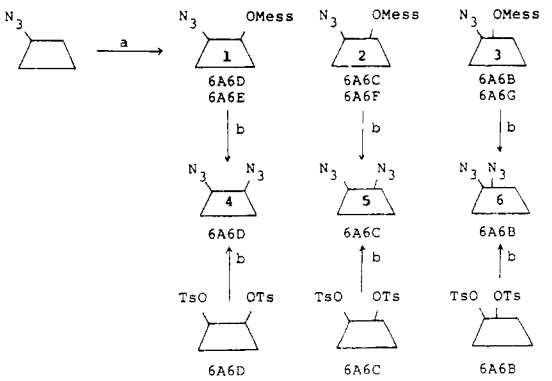


Figure 1. Reversed-phase column chromatography of the mixture obtained by the reaction of 6-deoxy-6-azido-β-cyclodextrin with mesitylenesulfonyl chloride. A gradient elution of water–aqueous MeOH was applied.

Scheme II[a]



[a] (a) MessCl/py; (b) NaN_3/DMF; Mess = 2,4,6-$Me_3C_6H_2SO_2$.

sorptions characteristic to the cyclodextrin. The ^1H NMR spectrum showed that **1**, **2**, or **3** was a monosulfonate. Moreover, the FABMS spectrum demonstrated that each compound was indeed the mesitylenesulfonated azidocyclodextrin. There are no significant differences in spectral data among **1–3**. Therefore, the spectra are not useful for regiostructure determination of **1–3**. Even if they were different from one another, the assignment would be still difficult since there is no accumulation of spectral data for such systems. The assignments of the regiochemistry of **1–3** were carried out as shown in Scheme II. The azido sufonates **1–3** were converted to the corresponding diazido derivatives **4–6** by the reaction with sodium azide, which were ascertained by the FABMS and IR spectra and TLC and reversed-phase HPLC, which can separate **4–6** as shown in Figure 2B. The azido derivatives (**4–6**) were assigned to 6A,6D-, 6A,6C-, and 6A,6B-isomers, respectively, by comparing the HPLC retention times of **4–6** with those of the corresponding authentic compounds which were prepared by the reaction of 6A,6D-, 6A,6C-, and 6A,6B-ditosylates of β-cyclodextrin[4] with sodium azide. Therefore, the relative position of the two substituents of **1**, **2**, or **3** is 6A,6D, 6A,6C, or 6A,6B, respectively.

Thus, β-cyclodextrins substituted with two different kinds of functional groups including an amino group on

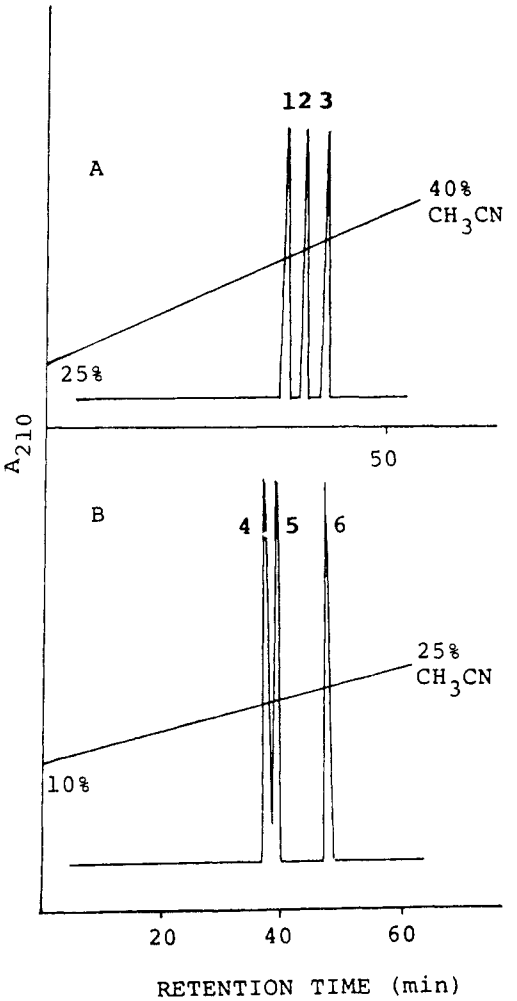


Figure 2. Reversed-phase HPLC of a mixture of 6A,6X-dideoxy-6A-azido-6X-[(mesitylsulfonyl)oxy]-β-cyclodextrins **1–3** (A) and a mixture of 6A,6X-dideoxy-6A,6X-diazido-β-cyclodextrins **4–6** (B). A gradient elution of aqueous CH_3CN was applied.

given positions of the primary hydroxyl side become now available through our method, since the azido can be easily reduced to an amino function and the sulfonyloxyl group is also convertible to various functional groups by nucleophilic substitution. However, since the sulfonation on the azidocyclodextrin is expected to show no regioselectivity, the isolated compound **1**, **2**, or **3** is most likely a mixture of 6A,6D and 6A,6E, 6A,6C and 6A,6F, or 6A,6B and 6A,6G isomers, respectively.

Experimental Section

IR spectra were recorded with a Hitachi 215 grating infrared spectrophotometer. ^1H NMR spectra were determined with a JEOL FX-100 spectrometer (100 MHz). UV absorptions were obtained with a Hitachi Model 200-10 spectrophotometer. Fast atom bombardment mass (FABMS) spectra were recorded with a JEOL JMS DX-300/JMA 3500 data system. Thin-layer chromatography (TLC) was run with precoated silica gel plates (Merck, Art 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). An elution solvent of TLC was n-$C_3H_7OH/AcOH/H_2O$ (7/7/5). Merck Lobar prepacked column (LiChroprep RP18 column, Size B, 25 × 310 mm or LiChroprep RP8, Size A, 10 × 240 mm) was used for reversed-phase column chromatography. High-performance liquid chromatography (HPLC) was performed analytically on a Hitachi 635A with a TSKgel ODS 120A column (4 × 300 mm, 5 μm, Toyo Soda, Japan).

6A,6X-Dideoxy-6A-azido-6X-[(mesitylsulfonyl)oxy]-β-cyclodextrin (1–3). To a solution of 6-deoxy-6-azido-β-cyclodextrin[6] (250 mg) in dry pyridine (2 mL) was added mesitylenesulfonyl chloride (210 mg). The solution was stirred at room temperature for 9 h. The progress of reaction was monitored by TLC. The R_f value of the products (1–3) on TLC was 0.49. The amount of the sulfonyl chloride was dependent on the dryness of the reagents. After water (0.5 mL) was added to the solution to stop the progress of reaction, the mixture was concentrated in vacuo. The residue was dissolved in 20% aqueous EtOH (8 mL), filtered to remove the insoluble material, and chromatographed through a reversed-phase column (Lobar column LiChroprep RP18 Size B). After elution of water (500 mL), a gradient elution of water (300 mL)–30% aqueous MeOH (300 mL) followed by a gradient elution of 30% aqueous MeOH (800 mL)–80% aqueous MeOH (800 mL) was applied. Each fraction was monitored by UV absorption at 230 ann 270 nm and by TLC. The fractions of recovered starting material, **1**, **2**, or **3** were collected and concentrated in vacuo. The residue was dissolved in a small amount of water and lyophilized: the recovered starting material, 43.1 mg (28.7%); **1**, 19.4 mg (11.2%); **2**, 16.9% (9.7%); **3**, 14.9 mg (8.6%). The ^{1}H NMR spectra (Me_2SO-d_6) of **1–3** are very similar to each other: δ 2.29 (s, 3 H, CH_3), 2.54 (s, 6 H, 2 CH_3), 4.2–4.6 (5 H, OH), 4.65–5.00 (7 H, C_1H of cyclodextrin), 5.5–6.6 (14 H, OH), 7.10 (s, 2 H). The IR spectra (KBr) of **1–3** were also very similar to each other: 2100 (N_3), 1190, 1173, 760, 648 (sulfonate) cm^{-1}. FABMS: m/z 1142 (M + H), 1364 (M + Na).

Authentic 6A,6X-Dideoxy-6A,6X-diazido-β-cyclodextrin (4–6). A mixture of 6A,6B-dideoxy-6A,6B-bis(tosyloxy)-β-cyclodextrin[4] (30 mg) and sodium azide (40 mg) in dry DMF (0.7 mL) was stirred at 70 °C for 3 h. After evaporation of DMF in vacuo, the residue was dissolved in water (1 mL) and was applied on a reversed-phase column (Lobar column LiChroprep RP8 Size A). After elution of 10% aqueous EtOH (100 mL), a gradient elution of 10% aqueous EtOH (200 mL)–40% aqueous EtOH (200 mL) was used for the development. The fraction of the diazido-β-cyclodextrin was easily detected by monitoring the UV absorption at 210 nm. The fractions of the diazido-β-cyclodextrin were collected and concentrated in vacuo to give a pasty solid, which was dissolved in water and lyophilized to give **6**, 18 mg (73%). By the similar procedures, the 6A,6C- (**5**) (9.7 mg, 40%) and 6A,6D- (**4**) (14.3 mg, 48%) diazido isomers were prepared from the corresponding authentic ditosylates. The ^{1}H NMR spectra (D_2O) of **4–6** were very similar to each other: δ 5.0 (7 H, C_1H), 3.2–4.1 (other protons). The IR spectra (KBr) spectra of **4–6** were also very similar to each other: 2100 cm^{-1}. FABMS: m/z 1185 (M + H), 1207 (M + Na).

Conversion of 6A,6X-Dideoxy-6A-azido-6X-[(mesitylsulfonyl)oxy]-β-cyclodextrin to 6A,6X-Dideoxy-6A,6X-diazido-β-cyclodextrin. A mixture of 6A,6X-dideoxy-6A-azido-6X-[(mesitylsulfonyl)oxy]-β-cyclodextrin (**1**, **2**, or **3**) (15 mg) and sodium azide (11 mg) in dry DMF (0.5 mL) was stirred at 60 °C for 6 h. The progress of reaction was monitored by TLC. Only one product was detected by TLC (R_f 0.36). After evaporation of DMF in vacuo, the residue was dissolved in water (5 mL) and was adsorbed into a short reversed-phase column (SEP-PAK C_{18} cartridge, Waters Ltd.). After washing it with water (20 mL), 5% (10 mL), 10% (10 mL), 15% (10 mL), and then 20% (10 mL) aqueous EtOH solutions were stepwise applied. Concentration in vacuo and lyophilization of the 10% and 15% EtOH fractions gave 11 mg of 6A,6X-dideoxy-6A,6X-diazido-6β-cyclodextrin (**4**, **5**, or **6**). This product showed the correct molecular weight in the FABMS spectrum and demonstrated the same IR spectrum, the same R_f value on TLC, and the same retention time on HPLC as those of the corresponding authentic diazido-β-cyclodextrin **4**, **5**, or **6**.

Acknowledgment. We are indebted to Japan Maise Products Co. Ltd. for the generous gift of β-cyclodextrin.

Registry No. 6A,6D-1, 98126-94-4; 6A,6E-1, 98126-95-5; 6A,6C-2, 98169-86-9; 6A,6F-2, 98126-96-6; 6A,6B-3, 98126-97-7; 6A,6G-3, 98126-98-8; 4, 98126-99-9; 4 (6A,6D-ditosylate), 95475-65-3; 5, 98169-67-6; 5 (6A,6C-ditosylate), 95509-72-1; 6, 80781-22-2; 6 (6A,6B-ditosylate), 95475-64-2; 6-deoxy-6-azido-β-cyclodextrin, 98169-85-8; mesitylenesulfonyl chloride, 773-64-8.

Crystal and Molecular Structure of *anti*-Sesquinorbornene[1]

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Since the recent preparation of the *syn*- and *anti*-sesquinorbornenes, **1**[3] and **2**,[4] respectively, several studies on their molecular structure and features associated with their molecular structure have been reported.[5–15] Theoretical calculations on the parent compound **1**[9–15] and X-ray structure analysis of several derivatives of *syn*-sesquinorbornene[7–9] and *syn*-oxasesquinorbornene[16] show that the syn isomer prefers a nonplanar, endo-bent arrangement around the double bond with the deviation from planarity being 12–22°. This conformation preference has been rationalized by diminished hyperconjugative destabilization by bending[13,14] and/or relief of unfavorable torsional interactions by bending.[15]

The molecular structure of *anti*-sesquinorbornene (**2**) has been a matter of dispute. Molecular mechanics calculations indicate a preference for a conformation with a bent double bond,[10–12] although Houk et al.[15] have shown that this preference disappears by eliminating torsional contributions. X-ray structure analysis has been reported

(1) Systematic name: Tetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodec-2(7)-ene. Previously named: 1,2,3,4,5,6,7,8-Octahydro-1,4:5,8-dimethanonaphthalene.

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