Novel Ether-Linked Secondary Face-to-Face 2−2′ and 3−3′ β-Cyclodextrin Dimers

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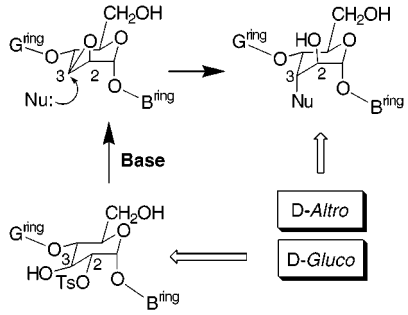
Received June 29, 1999 (Revised Manuscript Received December 8, 1999)

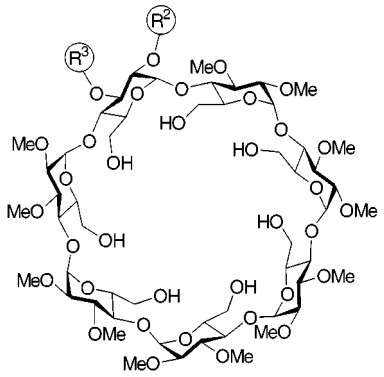
The internal hydrophobic space and external hydrophilic hydroxy groups of chemically modified cyclodextrins (CDs) make them ideal compounds for modeling enzyme−substrate binding,[1] drug delivery,[2] catalysis,[3] host−guest interactions,[4] and molecular recognition in self-assembled monolayers.[5] For applications in molecular recognition and chemical sensing, methods for selectively and efficiently modifying CDs are highly desirable. Monosubstitution on the secondary face of cyclodextrins is not straightforward, because of the presence of a large number of hydroxy groups.[6] Despite considerable research efforts expended during the past two decades, monoalkylation of the secondary face of CDs has remained a challenging problem.[7] Monoalkylation of the 3-hydroxy group has proven particularly difficult because of its weak acidity. The very few examples of this regioselective alkylation have utilized special electrophiles such as *N*-methyl-4-chloromethyl-2-nitroaniline.[8] Further functionalization of the resulting monoalkylated CDs is not easy, limiting potential applications of these synthetic methodologies. β-CD dimers, which have drawn lots of attention in the past two decades, may be considered to mimic antigen−antibody interactions because they strongly bind guest molecules in water.[9] However, most approaches to the synthesis of secondary face-to-face β-CD dimers have utilized a single bifunctional molecule to bridge the two β-CD rings and generally proceed in low yields (0.5−10%).[10] Because of the weak acidity of the hydroxy group at the 3-position, the 3−3′ dimer has generally been synthesized by using bifunctional nucleophiles to attack regioselectively the C-3 position of *manno*-mono-2,3-epoxy-β-CD. However, the introduction of these nucleophiles to C-3 generally necessitates stereochemical inversion,[8c,10a,b,11] as shown in Scheme 1. The reported 3−3′ β-CD dimers have always

Scheme 1



been amide or sulfide linked,[10a,b,12] because of the need to use strong nucleophiles. To our knowledge, no 3−3′ ether-linked dimers have yet been synthesized. In this paper, we present a method for monoalkylating the 2- or 3-position hydroxy groups of β-CD selectively and exploit the method to synthesize β-CD dimers that are ether-linked in a 2−2′ or 3−3′ fashion at their secondary faces without changing the configuration of the original stereogenic centers.

We have shown previously that β-CD derivatives **1** and **2** can be synthesized in high yield.[13] After the primary



	R2	R3
1	H	Me
2	Me	H

hydroxy groups of **1** and **2** are protected, the corresponding derivatives **3** and **4** (Scheme 2) have only one free

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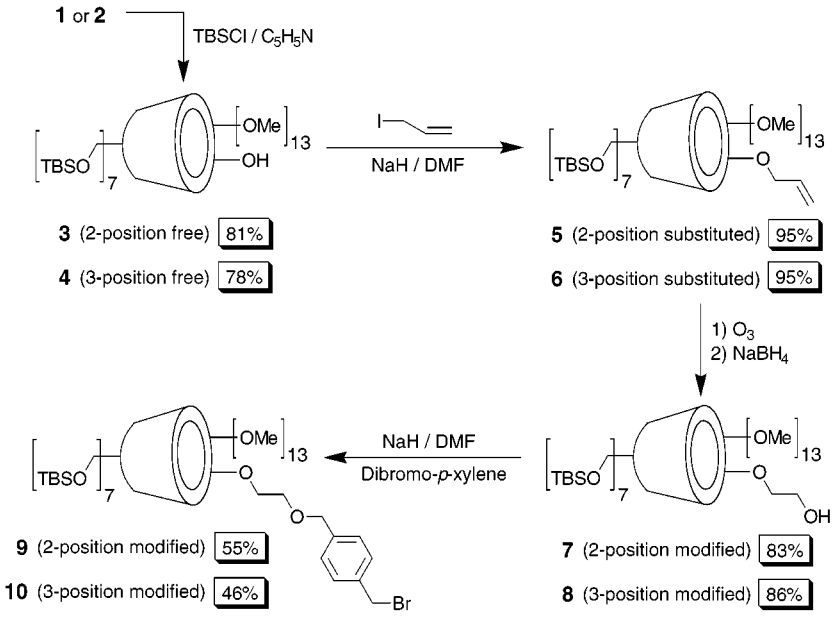
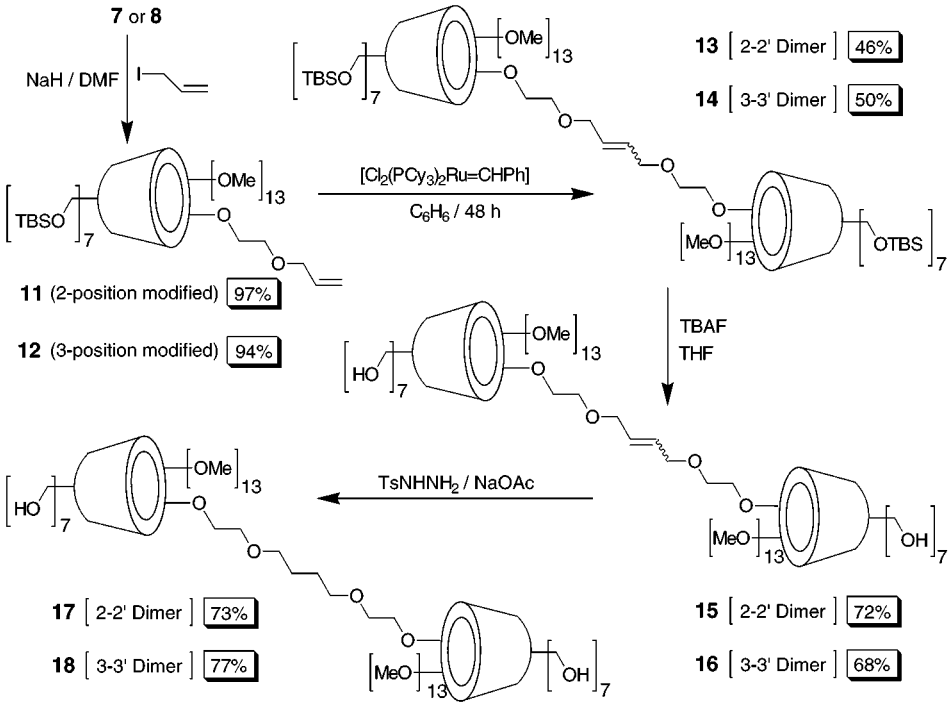
10.1021/jo9910381 CCC: $19.00
Published on Web 04/13/2000

Scheme 2



Scheme 3



hydroxy group on their secondary face. This secondary hydroxy group may be too sterically hindered to be a good nucleophile as evidenced by the fact that there is no reaction when the alcohols **3** and **4** are exposed to α,α′-dibromo-*p*-xylene under basic conditions. Allyl iodides reacts with both **3** and **4** to generate the alkene derivatives **5** and **6** in near-quantitative yield. The alkenes **5** and **6** are converted into the alcohols **7** and **8** after ozonolysis and $NaBH_4$ reduction. The newly generated primary hydroxy groups of compound **7** and **8** are now much more reactive. α,α′-Dibromo-*p*-xylene reacts readily with the alcohols **7** and **8** to generate the bromobenzene derivatives **9** and **10**.

Initial attempts, starting with alkenes **5** and **6**, gave low yields in the "self-metathesis"[14] reaction, so alkenes

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11 and **12** were synthesized to avoid possible steric hindrance (Scheme 3). As expected, alkenes **11** and **12** can easily be dimerized to the corresponding 2−2′ and 3−3′ β-CD dimers **13** and **14**, respectivly, in about 50% yields.[15] To our knowledge, compound **14** is the first ether-linked 3−3′ β-cyclodextrin dimer and also the first 3−3′ dimer that preserves all the original stereogenic centers present in the β-CD nucleus. The cis,trans selectivity of this dimerization reaction, although high,[16] was not determined. Since these alkene isomers were not easy to separate, both of them were converted into the same alkane by hydrogenating their carbon−carbon double bonds. However, Pd/C and hydrogen gas caused hydrogenolysis rather than hydrogenation, giving alcohol **8** from dimer **14** in 70% yield. Hydrogenation of the alkene dimer **14** using diimide gave products that were difficult to separate or identify. To characterize the product definitively, desilylation was carried out before reduction. The silyl groups were removed with tetrabutylammonium fluoride and the resulting β-CD polyol dimers **15** and **16** were reduced to the desired saturated β-CD dimers **17** and **18** using diimide reductions.

In this paper, we have demonstrated that we can monoalkylate the secondary face of β-CD selectively and leave all the original stereogenic centers intact. The ether-linked 3−3′ β-CD dimer **18** represents a new selective functionalization, while the intermediates **7**-**10** are amenable to further chemical modifications.

Experimental Section

Methods and Materials. All glassware, stir-bars, and needles were either oven- or flame-dried prior to use. Dry solvents were freshly distilled according to literature procedures. All reagents, unless otherwise indicated, were obtained from commercial suppliers and used directly without further purification. Reactions were carried out under either a nitrogen or argon atmosphere. Organic solvents were removed by rotary evaporation under reduced pressure.

Hexakis(2^{A},2^{B},2^{C},2^{D},2^{E},2^{F}-*O*-methyl)heptakis(3-*O*-methyl)heptakis(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (3). Pyridine (3 mL) was added via a syringe at room temperature to a flame-dried round-bottomed flask charged with the β-CD derivative **1** (220 mg, 0.167 mmol) and *tert*-butyldimethylsilyl chloride (0.6 g, 3.98 mmol). The reaction mixture was stirred at room temperature for 24 h, before being partitioned between CH_2Cl_2 (100 mL) and H_2O (100 mL). The organic layer was separated and washed with 5% aq HCl (3 × 100 mL), dried ($MgSO_4$), and concentrated. Column chromatography, using 30% EtOAc in hexane as eluant, gave **3** as a white solid (285 mg, 81%): mp 117−119 °C; FAB-MS 2139 for $[M + Na]^+$, calcd for $C_{97}H_{194}O_{35}Si_7$ 2117; ^{1}H NMR (360 MHz, $CDCl_3$) δ −0.01 (s, 42H), 0.85 (s, 63H), 3.00−3.10 (m, 7H), 3.37−3.72 (m, 65H), 4.00−4.90 (m, 8H), 4.34 (d, 1H), 4.89 (d, 1H), 5.13−5.20 (m, 7H); ^{13}C NMR (90 MHz, $CDCl_3$) δ −5.4, −5.3, −5.3, −5.2, −5.2, −5.2, −5.0, −5.0, −4.9, 18.2, 18.2, 18.3, 25.9, 25.9, 58.3, 58.4, 58.5, 58.6, 58.8, 60.8, 61.1, 61.3, 61.4, 61.4, 61.5, 61.7, 62.3, 62.4, 72.0, 72.0, 72.1, 72.1, 72.2, 72.5, 73.0, 74.3, 78.5, 78.5, 78.7, 78.7, 79.1, 81.3, 82.0, 82.0, 82.1, 82.4, 82.5, 83.1, 84.2, 97.7, 98.1, 98.5, 98.7, 101.6. Anal. Calcd for $C_{97}H_{194}O_{35}Si_7$: C, 55.03; H, 9.24. Found: C, 55.43; H, 9.20.

Hexakis(3^{A},3^{B},3^{C},3^{D},3^{E},3^{F}-*O*-methyl)heptakis(2-*O*-methyl)heptakis(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (4). Compound **4** was prepared from the β-CD derivative **2** in 78% yield using the same procedure as that described for the preparation of **3** from **1**. Data for **4**: mp 118−120 °C; FAB-MS 2139 for $[M + Na]^+$, calcd for $C_{97}H_{194}O_{35}Si_7$ 2117; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.08 (s, 42H), 0.86 (s, 63H), 3.02−3.14 (m, 7H), 3.37−3.72 (m, 67H), 3.90−4.20 (m, 7H), 4.96 (d, 1H), 5.13−5.22 (m, 7H); ^{13}C NMR (90 MHz, $CDCl_3$) δ −5.3, −5.3, −5.2, −5.1, −5.0, −5.0, −4.9, −4.9, 18.2, 18.3, 18.3, 25.9, 25.9, 25.9, 58.3, 58.4, 58.6, 58.8, 58.9, 59.0, 60.0, 61.2, 61.4, 61.5, 61.6, 61.7, 62.4, 62.4, 62.5, 71.2, 71.6, 71.9, 72.0, 72.1, 72.2, 72.3, 72.6, 78.4, 78.5, 78.8, 79.3, 81.3, 81.9, 81.9, 82.0, 82.1, 82.2, 82.2, 82.3, 82.4, 82.5, 82.7, 83.3, 97.7, 97.7, 98.1, 98.4, 98.4, 98.6, 100.3. Anal. Calcd for $C_{97}H_{194}O_{35}Si_7$: C, 55.03; H, 9.24. Found: C, 55.43; H, 9.18.

Mono(2^{A}-*O*-allyl)hexakis(2^{B},2^{C},2^{D},2^{E},2^{F},2^{G}-*O*-methyl)heptakis(3-*O*-methyl)heptakis(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (5). DMF (1 mL) was slowly added to **3** (70 mg, 0.033 mmol) and NaH (10 mg, 0.416 mmol), and the solution was cooled to 0 °C. The reaction mixture was stirred at 0 °C for 5 min, warmed to room temperature, and charged with allyl iodide (0.05 mL, 0.547 mmol). The solution was stirred at room temperature until compound **3** was consumed. The reaction was quenched with MeOH (1 mL) and then poured into CH_2Cl_2 (30 mL) and H_2O (30 mL). The organic layer was separated, washed with H_2O (30 mL), dried ($MgSO_4$), and evaporated. Column chromatography, using 30% EtOAc in hexane as eluant, gave **5** as a white solid (68 mg, 95%): mp 122−124 °C; FAB-MS 2180 for $[M + Na]^+$, calcd for $C_{100}H_{198}O_{35}Si_7$ 2157; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.01 (s, 42H), 0.86 (s, 63H), 3.04 (dd, 6H), 3.20 (dd, 1H), 3.50−3.72 (m, 67H), 4.04−4.24 (m, 9H), 5.11−5.31 (m, 9H), 5.92 (m, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ −5.2, −5.2, −5.2, −4.9, 18.3, 25.9, 58.5, 58.6, 58.6, 58.6, 58.8, 61.4, 61.5, 61.5, 62.3, 61.5, 71.6, 72.1, 72.2, 78.3, 78., 78.6, 78.7, 78.8, 79.8, 81.9, 82.0, 82.1, 82.2, 82.3, 98.0, 98.1, 98.4, 116.4, 135.4. Anal. Calcd for $C_{100}H_{198}O_{35}Si_7$: C, 55.68; H, 9.25. Found: C, 56.12; H, 9.29.

Mono(3^{A}-*O*-allyl)hexakis(3^{B},3^{C},3^{D},3^{E},3^{F},3^{G}-*O*-methyl)heptakis(2-*O*-methyl)heptakis(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (6). Compound **6** was prepared from **4** in 95% yield employing the same procedure as that described for preparation of **5** from **3**. Data for **6**: mp 121−124 °C; FAB-MS 2180 for $[M + Na]^+$, calcd for $C_{100}H_{198}O_{35}Si_7$ 2157; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.01 (s, 42H), 0.86 (s, 63H), 3.03−3.10 (m, 7H), 3.47−3.80 (m, 67H), 4.05−4.26 (m, 8H), 4.53 (m, 1H), 5.11−5.31 (m, 9H), 6.08 (m, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ −5.3, −5.2, −5.2, −4.9, 18.3, 25.9, 25.9, 58.5, 58.6, 58.6, 58.7, 59.0, 61.4, 61.5, 62.3, 72.1, 72.2, 72.3, 74.9, 78.3, 78.5, 78.8, 80.1, 82.0, 82.1, 82.2, 82.3, 97.8, 98.2, 98.3, 116.1, 136.3. Anal. Calcd for $C_{100}H_{198}O_{35}Si_7$: C, 55.68; H, 9.25. Found: C, 56.02; H, 9.35.

Mono(2^{A}-*O*-hydroxyethyl)hexakis(2^{B},2^{C},2^{D},2^{E},2^{F},2^{G}-*O*-methyl)heptakis(3-*O*-methyl)heptakis(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (7). O_3 was bubbled into a solution of **5** (70 mg, 0.032 mmol) in CH_2Cl_2 (1 mL) at −78 °C. After the solution had turned deep blue, excess PPh_3 was added. The reaction mixture was warmed to room temperature and diluted with CH_2Cl_2 (30 mL). The organic layer was washed with H_2O (2 × 30 mL), dried ($MgSO_4$), and concentrated. The crude mixture was dissolved in EtOH (2 mL) and treated with an excess of $NaBH_4$ at room temperature. The solution was stirred for 1 h and diluted with CH_2Cl_2 (30 mL). The organic layer was washed with H_2O (2 × 30 mL), dried ($MgSO_4$), and evaporated. Column chromatography, using 40% EtOAc in hexane as eluant, gave **7** as a white solid (58 mg, 83%): mp 123−125 °C; FAB-MS 2184 for $[M + Na]^+$, calcd for $C_{99}H_{198}O_{36}Si_7$ 2161; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.01 (s, 42H), 0.86 (s, 63H), 3.02−3.17 (m, 7H), 3.47−3.80 (m, 72H), 3.90−4.17 (m, 7H), 5.18−5.21 (m, 7H); ^{13}C NMR (90 MHz, $CDCl_3$) δ −5.5, −5.4, −5.3, −5.3, −5.1, −5.0, 18.1, 18.1, 18.2, 18.2, 25.7, 25.7, 25.8, 58.3, 58.4, 58.5, 58.7, 59.2, 61.0, 61.2, 61.2, 61.4, 61.4, 61.4, 61.0, 62.1, 62.2, 62.3, 62.4, 71.9, 72.1, 72.1, 72.3, 72.4, 78.0, 78.3, 78.6, 78.7, 78.8, 78.9, 81.6, 81.7, 81.8, 81.9, 81.9, 82.0, 82.1, 82.2, 82.2, 82.4, 97.7, 97.9, 97.9, 98.0, 98.0, 98.4, 98.6. Anal. Calcd for $C_{99}H_{198}O_{36}Si_7$: C, 55.02; H, 9.23. Found: C, 55.51; H, 9.43.

Mono(3^{A}-*O*-hydroxyethyl)hexakis(3^{B},3^{C},3^{D},3^{E},3^{F},3^{G}-*O*-methyl)heptakis(2-*O*-methyl)heptakis(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (8). Compound **8** was prepared from **6** using the same procedure as that described for prepara-

(15) For some reason, a large amount of Grubbs' catalyst was required in this reaction, and even then, ∼30% of starting allyl β-CD was recovered. Using more catalyst or extending the reaction time did not give better results.

(16) Because of symmetry, the vinyl protons of both isomers gave a singlet peak in the ^{1}H NMR spectrum. A 9:1 isomer ratio was suggested from integration.

tion of **7** from **5** (86%). Data for **8**: mp 120−122 °C; FAB-MS 2184 for $[M + Na]^+$, calcd for $C_{99}H_{198}O_{36}Si_7$ 2161; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.02 (s, 42H), 0.86 (s, 63H), 3.03−3.11 (m, 7H), 3.49−3.79 (m, 72H), 3.98−4.18 (m, 8H), 4.35 (d, 1H), 5.15−5.25 (m, 7H); ^{13}C NMR (90 MHz, $CDCl_3$) δ −5.4, −5.3, −5.2, −5.2, −5.1, −4.9, −4.8, 18.2, 18.3, 18.3, 25.8, 25.9, 25.9, 25.9, 26.0, 58.4, 58.4, 58.5, 58.6, 58.7, 59.1, 61.2, 61.2, 61.3, 61.5, 61.5, 61.7, 62.1, 62.2, 62.3, 62.5, 72.0, 72.1, 72.1, 72.2, 72.3, 72.6, 75.8, 77.6, 78.2, 78.3, 78.5, 79.0, 79.3, 79.3, 79.5, 81.8, 82.0, 82.0, 82.2, 82.3, 82.4, 82.5, 82.5, 82.8, 83.0, 97.0, 98.1, 98.1, 98.2, 98.3. Anal. Calcd for $C_{99}H_{198}O_{36}Si_7$: C, 55.02; H, 9.23. Found: C, 55.35; H, 9.22.

Mono(2^A-*O*-(*p*-(bromomethyl)benzyloxyethyl))hexakis-(2^B,2^C,2^D,2^E,2^F,2^G-*O*-methyl)heptakis(3-*O*-methyl)heptakis-(6-*O*-*tert*-butyldimethylsilyl)-*β*-cyclodextrin (9). DMF (0.2 mL) was added slowly to **7** (20 mg, 0.009 mmol) and NaH (6 mg, 0.25 mmol) at room temperature. The solution was stirred for 10 min, and then α,α-dibromo-*p*-xylene (0.1 g, 0.38 mmol) was added. The reaction mixture was stirred in the dark at room temperature for 6 h. The reaction was quenched with MeOH (0.1 mL) and the mixture poured into CH_2Cl_2 (20 mL) and H_2O (20 mL). The organic layer was washed with H_2O (20 mL), dried ($MgSO_4$), and concentrated. Column chromatography, using 40% EtOAc in hexane as eluent, gave **9** as a white solid (12 mg, 55%): mp 119−121 °C; FAB-MS 2366 for $[M + Na]^+$, calcd for $C_{107}H_{205}O_{36}Si_7$ 2344; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.02 (s, 42H), 0.87 (s, 63H), 3.01−3.07 (m, 6H), 3.24 (d, 1H), 3.50−3.75 (m, 70H), 3.80−3.90 (m, 1H), 4.07−4.56 (m, 7H), 4.48 (s, 2H), 4.56 (s, 2H), 5.16−5.21 (m, 7H), 7.30−7.36 (m, 4H); ^{13}C NMR (90 MHz, $CDCl_3$) δ −5.2, −5.2, −5.2, −4.9, 18.3, 18.3, 25.9, 25.9, 33.4, 58.5, 58.6, 58.7, 58.8, 61.4, 61.5, 61.5, 61.5, 61.6, 61.6, 62.3, 62.4, 70.0, 70.0, 72.1, 72.2, 72.3, 72.6, 78.1, 78.5, 78.6, 78.7, 78.9, 81.4, 81.8, 81.9, 82.0, 82.0, 82.1, 82.2, 82.2, 98.0, 98.1, 127.8, 129.0, 136.9, 139.1. Anal. Calcd for $C_{107}H_{205}O_{36}Si_7Br$: C, 54.82; H, 8.81. Found: C, 55.15; H, 8.95.

Mono(3^A-*O*-(*p*-(bromomethyl)benzyloxyethyl))hexakis-(3^B,3^C,3^D,3^E,3^F,3^G-*O*-methyl)heptakis(2-*O*-methyl)heptakis-(6-*O*-*tert*-butyldimethylsilyl)-*β*-cyclodextrin (10). Compound **10** was prepared from **8** in 46% yield employing the same procedure as that described for the preparation of **9** from **7**. Data for **10**: mp 119−121 °C; FAB-MS 2366 for $[M + Na]^+$, calcd for $C_{107}H_{205}O_{36}Si_7$ 2344; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.02 (s, 42H), 0.87 (s, 63H), 3.04−3.10 (m, 7H), 3.45−3.82 (m, 70H), 3.90−4.20 (m, 8H), 4.48 (s, 2H), 4.58 (s, 2H), 5.18−5.24 (m, 7H), 7.33 (s, 4H); ^{13}C NMR (90 MHz, $CDCl_3$) δ −5.2, −5.2, −4.9, 18.3, 25.9, 33.4, 58.5, 58.6, 58.8, 59.1, 61.4, 61.5, 62.3, 72.1, 72.2, 72.4, 78.4, 78.7, 78.9, 82.0, 82.2, 97.6, 98.1, 98.3, 98.8, 127.9, 129.0, 136.9, 139.2. Anal. Calcd for $C_{107}H_{205}O_{36}Si_7Br$: C, 54.82; H, 8.81. Found: C, 55.14; H, 8.87.

Mono(2^A-*O*-allyloxyethyl)hexakis(2^B,2^C,2^D,2^E,2^F,2^G-*O*-methyl)heptakis(3-*O*-methyl)heptakis(6-*O*-*tert*-butyldimethylsilyl)-*β*-cyclodextrin (11). DMF (2.5 mL) was added slowly to **7** (170 mg, 0.079 mmol) and NaH (24 mg, 1 mmol), and the solution was cooled to 0 °C. The solution was stirred at 0 °C for 5 min, warmed to room temperature, and then charged with allyl iodide (0.12 mL, 1.3 mmol). The reaction mixture was stirred at room temperature until compound **7** was consumed. The reaction was quenched with MeOH (2 mL) before being poured into CH_2Cl_2 (100 mL) and H_2O (100 mL). The organic layer was washed with H_2O (100 mL), dried ($MgSO_4$), and concentrated. Column chromatography, using 30% EtOAc in hexane as eluant, gave **11** as a white solid (168 mg, 97%): mp 115−117 °C; FAB-MS 2223.4 for $[M + Na]^+$, calcd for $C_{102}H_{202}O_{36}Si_7$ 2201; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.00 (s, 42H), 0.85 (s, 63H), 3.00−3.06 (m, 6H), 3.19−3.23 (dd, 1H), 3.49−3.85 (m, 71H), 4.00−4.18 (m, 9H), 5.11−5.27 (m, 9H), 5.82−5.93 (m, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ −5.3, −5.2, −4.9, 18.2, 25.9, 58.5, 58.6, 58.6, 58.8, 61.3, 61.4, 61.5, 61.5, 62.3, 69.8, 70.0, 72.0, 72.1, 78.1, 78.5, 78.6, 78.7, 81.3, 81.9, 81.9, 82.1, 82.2, 98.1, 98.2, 116.5, 135.0. Anal. Calcd for $C_{102}H_{202}O_{36}Si_7$: C, 55.65; H, 9.25. Found: C, 56.10; H, 9.40.

Mono(3^A-*O*-allyloxyethyl)hexakis(3^B,3^C,3^D,3^E,3^F,3^G-*O*-methyl)heptakis(2-*O*-methyl)heptakis(6-*O*-*tert*-butyldimethylsilyl)-*β*-cyclodextrin (12). Compound **12** was prepared from **8** in 94% yield using the same procedure as that described for the preparation of **11** from **7**. Data for **12**: mp 113−116 °C; FAB-MS 2223 for $[M + Na]^+$, calcd for $C_{102}H_{202}O_{36}Si_7$ 2201; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.00 (s, 42H), 0.85 (s, 63H), 3.02−3.10 (m, 7H), 3.45−3.73 (m, 71H), 3.73−4.19 (m, 11H), 5.11−5.27 (m, 9H), 5.84−5.95 (m, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ −5.3, −5.3, −5.2, −4.9, 18.2, 25.9, 58.5, 58.5, 58.6, 58.6, 58.7, 59.1, 61.4, 61.5, 61.5, 62.2, 62.3, 69.8, 71.9, 72.1, 72.2, 72.7, 78.4, 78.5, 78.7, 78.8, 78.8, 81.0, 81.6, 81.9, 82.0, 82.1, 82.2, 97.6, 98.1, 98.1, 98.2, 98.3, 116.5, 135.1. Anal. Calcd for $C_{102}H_{202}O_{36}Si_7$: C, 55.65; H, 9.25. Found: C, 55.95; H, 9.38.

The 2−2′ *β*-Cyclodextrin Dimer 13. Grubbs' catalyst (4 mg, 0.005 mmol) was added to a solution of **11** (39 mg, 0.018 mmol) in C_6H_6 (1 mL). After 24 h at 40 °C, additional catalyst (2 mg, 0.002 mmol) was added, and the mixture was left to stir for another 24 h. The solvent was removed, and the residue was loaded directly onto a silica gel column and purified with a gradient of 20−40% EtOAc in hexane. The desired dimer **13** (18 mg, 46%) and starting material **11** (11 mg, 28%) were isolated as white solids. Data for **13**: mp 105−107 °C; MALDI-TOF-MS 4398 for $[M + Na]^+$, calcd for $C_{202}H_{400}O_{72}Si_{14}$ 4375; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.01 (s, 84H), 0.87 (s, 126H), 3.04−3.21 (m, 14H), 3.50−3.82 (m, 142H), 4.01−4.21 (m, 18H), 5.14−5.20 (m, 14H), [5.77 (s), 6.00 (s), 2H]; ^{13}C NMR (90 MHz, $CDCl_3$) δ −5.2, −5.2, −5.2, −4.9, 18.3, 25.9, 58.5, 58.6, 58.6, 58.7, 58.8, 61.3, 61.4, 61.5, 61.6, 61.6, 62.3, 62.4, 69.7, 69.8, 71.1, 72.0, 72.1, 72.2, 77.2, 77.4, 78.4, 78.7, 78.9, 81.8, 81.9, 82.1, 98.0, 98.1, 98.2, 129.3. Anal. Calcd for $C_{202}H_{400}O_{72}Si_{14}$: C, 55.46; H, 9.22. Found: C, 55.78; H, 9.37.

The 3−3′ *β*-Cyclodextrin Dimer 14. Compound **14** was prepared from **12** in 50% yield using the same procedure as that described for the preparation of **13** from **11**. The starting material **12** was recovered in 30% yield. Data for **14**: mp 103−105 °C; FAB-MS 4398 for $[M + Na]^+$, calcd for $C_{202}H_{400}O_{72}Si_{14}$ 4375; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.01 (s, 84H), 0.86 (s, 126H), 3.02−3.11 (m, 14H), 3.45−3.83 (m, 138H), 3.83−4.21 (m, 22H), 5.18−5.22 (m, 14H), {5.68 (s), 5.80 (s), 2H}; ^{13}C NMR (90 MHz, $CDCl_3$) δ −5.3, −5.2, −5.2, −4.9, 18.3, 25.9, 58.5, 58.6, 58.6, 58.6, 58.7, 59.1, 61.4, 61.5, 61.5, 62.2, 69.9, 71.0, 72.1, 72.2, 72.7, 78.5, 78.6, 78.9, 81.1, 81.7, 82.0, 82.1, 82.2, 97.6, 98.1, 98.4, 129.4. Anal. Calcd for $C_{202}H_{400}O_{72}Si_{14}$: C, 55.46; H, 9.22. Found: C, 55.91; H, 9.36.

The 2−2′ *β*-Cyclodextrin Dimer 15. THF (2 mL) was added via a syringe to a flame-dried round-bottomed flask charged with **13** (70 mg, 0.016 mmol) and *tetra*-butylamonium fluoride (105 mg, 0.333 mmol). The reaction mixture was stirred at room temperature for 24 h before being concentrated. The residue was loaded directly onto a silica gel column and purified with a gradient of 20−40% MeOH in CH_2Cl_2 to give compound **15** as a white solid (32 mg, 72%): mp 155−158 °C; FAB-MS 2798 for $[M + Na]^+$, calcd for $C_{118}H_{204}O_{72}$ 2775; ^{1}H NMR (360 MHz, D_2O) δ 3.18−3.25 (s, 14H), 3.25−4.00 (m, 174H), [5.00 (s), 5.20 (s) 14H], [5.65 (s), 5.73 (s), 2H]; ^{13}C NMR (90 MHz, D_2O) δ 59.6, 60.4, 60.7, 61.2, 62.2, 62.7, 64.5, 71.6, 72.1, 72.9, 73.2, 74.0, 74.8, 78.9, 79.5, 80.3, 81.8, 82.5, 83.4, 84.3, 98.7, 99.6, 100.5, 131.9, 132.7. Anal. Calcd for $C_{118}H_{204}O_{72}\diamond 9H_2O$: C, 48.26; H, 7.62. Found: C, 48.33; H, 7.81.

The 3−3′ *β*-Cyclodextrin Dimer 16. Compound **16** was prepared from **14** in 68% yield using the same procedure as that described for the preparation of **15** from **13**. Data for **16**: mp 154−156 °C; FAB-MS 2797.4 for $[M + Na]^+$, calcd for $C_{118}H_{204}O_{72}$ 2775; ^{1}H NMR (360 MHz, D_2O) δ 3.10−3.30 (s, 14H), 3.30−4.00 (m, 174H), 5.10−5.20 (s, 14H), {5.65 (s), 5.72 (s), 2H}; ^{13}C NMR (90 MHz, D_2O) δ 59.6, 59.7, 60.0, 60.4, 60.5, 60.5, 60.6, 60.8, 61.3, 61.4, 62.2, 62.3, 62.9, 64.5, 71.5, 72.8, 73.2, 73.9, 74.0, 74.8, 78.7, 79.5, 80.3, 81.6, 82.4, 82.5, 83.3, 83.5, 84.2, 98.3, 98.6, 99.2, 99.6, 100.1, 100.5, 131.9. Anal. Calcd for $C_{118}H_{204}O_{72}\cdot 10H_2O$: C, 47.96; H, 7.64. Found: C, 48.06; H, 7.73.

The 2−2′ *β*-Cyclodextrin Dimer 17. 1,2-Dimethoxyethane (1 mL) and three drops of H_2O were added to a flame-dried round-bottomed flask charged with **15** (30 mg, 0.011 mmol) and *p*-toluenesulfonyl hydrazide (150 mg, 0.806 mmol). The reaction mixture was heated to reflux and then treated with NaOAc (150 mg in 1 mL of H_2O). After 5 h, the mixture was cooled to room temperature. Solvents were removed under reduced pressure, and the residue was purified by flash chromatography on a silica gel column employing a gradient of 20−40% MeOH in CH_2Cl_2 to afford **17** as a white solid (22 mg, 73%): mp 162−164 °C; FAB-MS 2800 for $[M + Na]^+$, calcd for $C_{118}H_{206}O_{72}$ 2777; ^{1}H NMR (360 MHz, D_2O) δ 1.49 (s, 4H), 3.10−3.80 (m, 188H), {5.07 (s),

5.13 (s) 14H}; ^{13}C NMR (90 MHz, D_2O) δ 27.9, 59.7, 60.4, 60.5, 60.7, 61.3, 62.2, 62.9, 64.5, 72.1, 73.0, 73.2, 73.7, 74.0, 74.8, 78.9, 79.3, 79.6, 79.7, 80.3, 81.7, 82.1, 82.5, 83.4, 83.5, 83.9, 84.2, 98.7, 99.6, 100.6. Anal. Calcd for $C_{118}H_{206}O_{72}\cdot H_2O$: C, 50.71; H, 7.50. Found: C, 50.29; H, 7.04.

The 3−3′ *β*-Cyclodextrin Dimer 18. Compound **18** was prepared from **16** in 77% yield using the same procedure as that described for the preparation of **17** from **15**. Data for **18**: mp 162−164 °C; FAB-MS 2799.7 for $[M + Na]^+$, calcd for $C_{118}H_{206}O_{72}$ 2777; ^{1}H NMR (360 MHz, D_2O) δ 1.49 (s, 4H), 3.18−3.25 (s, 14H), 3.25−3.90 (m, 174H), 5.13 (s, 14H); ^{13}C NMR (90 MHz, D_2O) δ 27.8, 58.1, 59.7, 60.5, 60.8, 61.3, 62.2, 62.3, 62.9, 64.5, 72.0, 73.0, 73.9, 74.0, 74.8, 78.6, 79.5, 80.2, 81.5, 82.4, 82.5, 83.3, 84.1, 98.3, 98.6, 99.2, 99.6, 100.5. Anal. Calcd for $C_{118}H_{206}O_{72}\cdot 6H_2O$: C, 49.13; H, 7.62. Found: C, 48.84; H, 7.42.

Acknowledgment. We thank the University of California, Los Angeles, for generous financial support of this work.

Supporting Information Available: ^{1}H and ^{13}C NMR for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9910381