# A Novel Approach to the Synthesis of Some Chemically-Modified Cyclodextrins

Peter R. Ashton, Sue E. Boyd, Giuseppe Gattuso, Edward Y. Hartwell, Rainer Königer, Neil Spencer, and J. Fraser Stoddart*

*School of Chemistry, University of Birmingham, Edgbaston, Birmingham B15 2TT, U.K.*

*Received February 7, 1995*

Cyclodextrins (CDs) are a class of cyclic oligosaccharides composed of α(1–4)-linked D-(+)-glucopyranose units. In the last few decades, they have been the subject of extensive investigations.[1] It is now well established[2] that CD molecules possess the overall shapes of truncated cones, with well-defined and rigid cavities. The most appealing feature of CDs is their ability to form inclusion complexes with a wide range of guest molecules. As a consequence, CDs and their derivatives have found an enormous number of academic[3] as well as industrial applications.[4]

In order to modify the solubility properties and the binding behavior of the CDs, a wide variety of chemically-modified cyclodextrins have been synthesized.[3d,5] However, the selective modification of CDs is still a challenging task,[6] as a result of the problems associated with their highly functionalized and symmetrical nature. The isolation of homogeneous, selectively modified CDs often involves extensive purification procedures. Therefore, there is a real need to develop new methodologies for the synthesis of chemically-modified cyclodextrins in high yields.

The *tert*-butyldimethylsilyl (TBDMS) group, developed by Corey and Vankateswarlu,[7] is one of the most widely used protecting groups for alcohols. It has been employed for the preparation of the protected CDs[8] hexakis(2,6-di-*O*-TBDMS)-α-CD[9] and heptakis(2,6-di-*O*-TBDMS)-β-CD.[10]

It is known[11–14] that TBDMS groups can migrate between vicinal hydroxyl groups under basic conditions. In the period from the late 1970s to the early 1980s, TBDMS group migration in protected ribonucleosides was described[11] by a number of research groups. They observed that the treatment of 2′-O or 3′-O silylated ribose derivatives with base led to a process of thermodynamic equilibration between the possible constitutional isomers, resulting in mixtures of compounds. In 1979, Ikegami and co-workers[12] reported TBDMS group migration, under Wittig reaction conditions, during the synthesis of prostaglandin derivatives. As in the case of the ribonucleosides derivatives, they observed a thermodynamically-equilibrated mixture of isomers. In 1992, Ley *et al.*[13] reported a TBDMS group migration occurring on a *myo*-inositol derivative during an alkylation of the unprotected C-6 hydroxyl group. These authors observed the formation of only one of the possible isomers, as a result of the migration from the more hindered C-1 position—where the TBDMS group was attached—to the less sterically demanding C-6 position of the *myo*-inositol derivative.

As part of our studies on chemically-modified cyclodextrins, we decided to investigate the possibility of employing per(2,6-di-*O*-TBDMS)-CDs as synthetic intermediates in the synthesis of methylated CDs. Our aim was to find a new convenient synthetic methodology to afford octakis(2,6-di-*O*-methyl)-γ-CD in a yield higher than the 7% overall yield reported in the literature.[15] Surprisingly, however, octakis(3,6-di-*O*-methyl)-γ-CD was the final product of the synthesis. After further investigations, we observed that, under strong basic conditions, alkylation of octakis(2,6-di-*O*-*tert*-butyldimethylsilyl)-γ-CD (**1c**) was found to occur with the migration of the *tert*-butyldimethylsilyl groups from the O-2 to the O-3 positions on all eight D-glucopyranose residues, affording octakis(2-*O*-benzyl-3,6-di-*O*-*tert*-butyldimethylsilyl)-CD (**2c**) in high yield and with high selectivity. The serendipitous discovery of the behavior of these silylated derivatives provided us with an unexpected opportunity to develop successfully a novel approach to the synthesis of some chemically-modified cyclodextrins.

The syntheses of per(3,6-di-*O*-methyl)-CDs **5a–c** and heptakis(2-*O*-methyl-3,6-anhydro)-β-CD **9** are reported in this Note. These compounds, along with a number of other chemically-modified CD derivatives, have been prepared by following a new synthetic strategy which involves the use of per(2,6-di-*O*-*tert*-butyldimethylsilyl)-CDs **1a–c** as key intermediates.

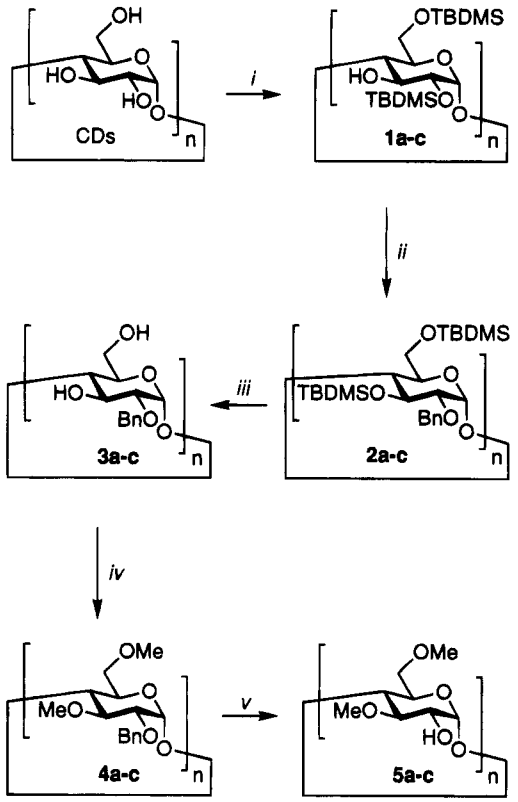
## Results and Discussion

Although the protection of CDs as their per(2,6-di-*O*-TBDMS) derivatives by reaction with TBDMS-Cl has been reported[9,10] to proceed with high selectivity and efficiency, this methodology has not yet been utilized for the synthesis of other chemically-modified CD derivatives. This reaction is reported to afford hexakis(2,6-di-*O*-TBDMS)-α-CD (**1a**) and heptakis(2,6-di-*O*-TBDMS)-β-

(1) Stoddart, J. F. *Carbohydr. Res.* **1989**, *192*, xii–xv.
(2) Saenger, W. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Eds.; Academic Press: London, 1984; Vol. 2, pp 231–259.
(3) (a) Bender, M. L.; Komiyama, M. *Cyclodextrin Chemistry*; Springer-Verlag: Berlin, 1978. (b) Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 846–848. (c) Li, S.; Purdy, W. C. *Chem. Rev.* **1992**, *92*, 1457–1470. (d) Wenz, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 803–822. (e) Takahashi, K.; Hattori, K. *J. Incl. Phenom.* **1994**, *17*, 1-24. (f) Breslow, R. *Pure Appl. Chem.* **1994**, *66*, 1573–1582.
(4) (a) *Cyclodextrins and Their Industrial Uses*; Duchêne, D., Ed.; Editions de Santé: Paris, 1987. (b) Szejtli, J. *Cyclodextrin Technology*; Kluwer: Dordrecht, 1988. (c) Eastburn, S. D.; Tao, B. Y. *Biotech. Adv.* **1994**, *12*, 325–339.
(5) Croft, A. P.; Bartsch, R. A. *Tetrahedron* **1983**, *39*, 1417–1474.
(6) Boger, J.; Concoran, R. J.; Lehn, J.-M. *Helv. Chim. Acta* **1978**, *61*, 2190–2218.
(7) Corey, E. J.; Vankateswarlu, L. *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191.
(8) (a) Takeo, K.; Mitoh, H.; Uemura, K. *Carbohydr. Res.* **1989**, *187*, 203–221. (b) Pregel, M. J.; Buncel, E. *Can J. Chem.* **1991**, *69*, 130–137. (c) Tian, S.; D'Souza, V. T. *Tetrahedron Lett.* **1994**, *35*, 9339–9342.
(9) Michalski, T. J.; Kendler, A.; Bender, M. L. *J. Incl. Phenom.* **1983**, *1*, 125–128.
(10) (a) Wife, R. L.; Reed, D. E.; Leworthy, D. P.; Barnett, D. M.; Regan, P. D.; Volger, H. C. In *Proceedings of the First International Symposium on Cyclodextrins*; Szejtli, J., Ed.; Akadémiai Kiadó: Budapest, 1982; pp 301–325. (b) Fügedi, P. *Carbohydr. Res.* **1989**, *192*, 366–369.
(11) (a) Ogilvie, K. K.; Beaucage, S. L.; Schifman, A. L.; Theriault, N. Y.; Sadana, K. L. *Can. J. Chem.* **1978**, *56*, 2768–2780. (b) Jones, S. S.; Reese, C. B. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2762–2764. (c) Ogilvie, K. K.; Entwistle, D. W. *Carbohydr. Res.* **1981**, *89*, 203–210.
(12) Torisawa, Y.; Shibasaki, M.; Ikegami, S. *Tetrahedron Lett.* **1979**, *21*, 1865–1868.
(13) Ley, S. V.; Yeung, L. L. *Synlett* **1992**, 997–998.
(14) Howard, C.; Newton, R. F.; Reynolds, D. P.; Roberts, S. M. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2049–2054.
(15) (a) Spencer C. M.; Stoddart, J. F.; Zarzycki, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1323–1336. (b) Irie, T.; Fukunaga, K.; Pitha, J.; Uekama, K.; Fales, H. M.; Sokolowski, E. A. *Carbohydr. Res.* **1989**, *192*, 167–172. (c) Takeo, K. *Carbohydr. Res.* **1990**, *200*, 481–485. (d) Tanimoto, T.; Kubota, Y.; Nakanishi, N.; Koizumi, K. *Chem. Pharm. Bull.* **1990**, *38*, 318–322.

0022-3263/95/1960-3898$09.00/0 

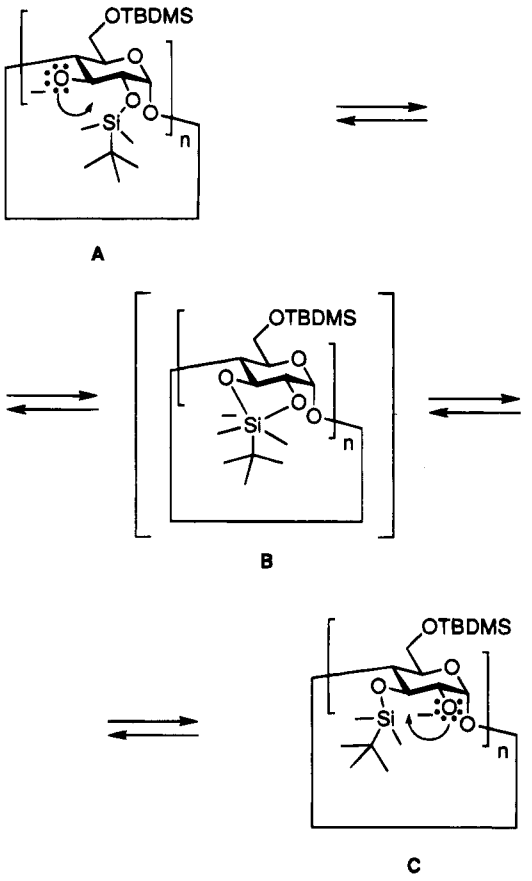
**Scheme 1. Synthesis of the Per(3,6-di-*O*-methyl)-cyclodextrins 5a-c** [a]




[a] For the α-CDs, $n = 6$; for the β-CDs, $n = 7$; for the γ-CDs, $n = 8$. Reagents: *(i)* TBDMS-Cl/DMAP/ DMF/$C_5H_5N$; *(ii)* BnBr/NaH/ THF; *(iii)* $Bu_4NF$/THF; *(iv)* MeI/NaH/THF; *(v)* 10% Pd/C/MeOH.

CD (**1b**) in high yields with excellent purities.[9,10] We believed that such protected CDs would be convenient intermediates to achieve further modifications. The use of TBDMS groups is particularly beneficial, because these protected CDs are extremely soluble in organic solvents and insoluble in water, a fact which facilitates the workup and purification procedures. We prepared **1a** and **1b**, along with octakis(2,6-di-*O*-TBDMS)-γ-CD (**1c**), following a modification of the literature procedure,[9,10] by reacting CDs with a 1.5-fold excess of TBDMS-Cl in a mixture of dry DMF and pyridine (Scheme 1). The conversion of **1a–c** into per(2-*O*-benzyl-3,6-di-*O*-TBDMS)-CDs **2a–c** was achieved by treating the cyclodextrins **1a–c** with sodium hydride and benzyl bromide in dry THF. Initially, a surprising aspect of this reaction to us was the migration of the silyl protecting groups from the O-2 to the O-3 positions of the CDs. We believe that the migration is an intramolecular process and that it most probably involves a five-membered ring intermediate[11b,12,14] containing a pentacovalent silicon atom (**B**, Scheme 2). The alkylations occur under kinetic control, *i.e.* the species **A** is more stable than the isomeric species **C** but **C** is more reactive as a result of the proximity of the 2-OH to the anomeric center. This selectivity can be interpreted by reference to the Curtin–Hammett principle.[16] Furthermore, it is worth noting the high yields of these reactions—especially for β-CD (78%) and γ-CD (76%), but less so for α-CD (49%)—considering

**Scheme 2**




that six, seven, or eight TBDMS groups migrate on the same molecule during the overall reaction! The lower yield of the benzylation of the α-CD derivative **1a** is probably a consequence of the higher steric hindrance of the smaller α-CD ring and the bulky substituents, *i.e.* TBDMS and benzyl groups. This evidence suggests that a cooperative effect operates during the reaction, *i.e.* it is likely that the migration of a TBDMS group on one of the D-glucopyranoside residues aids the migration of a silyl group on an adjacent residue. The structures of compounds **2a–c** were confirmed by 2D NMR spectroscopy. The spectra of compounds **2a,b** at room temperature were extremely broad, as a consequence of the hindered rotation[17] of the bulky TBDMS and benzyl substituents on the NMR time scale (300 MHz). Warming up of the samples provided sharpening of the signals sufficient to allow their characterization. An inverse C–H correlation experiment optimized for three-bond $^1H-^{13}C$ coupling at less than 5 Hz showed coupling between the benzylic protons and C-2 of the cyclodextrin, giving evidence, beyond any doubt, that the benzyl group is attached to the position O-2. Furthermore, evidence supporting benzyloxy substitution at the C-2 position can be observed in the 2D NOESY spectra of **2a** (400 MHz,

(16) (a) Curtin, D. Y. *Rec. Chem. Progr.* **1954**, *15*, 111–128. (b) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83–134. (c) Seeman, J. I. *J. Chem. Educ.* **1986**, *63*, 42–48. (d) Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; John Wiley & Sons, Inc.: New York, 1994; pp 647–654.

(17) It is possible that the broadening on the signals in the $^1H$ NMR spectra of the derivatives **2a** and **2b** is a result of the loss of the $C_6$ or $C_7$ symmetry, respectively, possibly as a result of conformational isomerism similar to that which has been observed for per-substituted CD derivatives bearing bulky substituents. It has been proposed that, in solution at room temperature, the insertion of one of the primary rim substituents in the CD cavity can occur. For a complete discussion of conformational isomerism in highly substituted CD derivatives, see: (a) Ellwood, P.; Spencer, C. M.; Spencer, N.; Stoddart, J. F.; Zarzycki, R. *J. Incl. Phenom.* **1992**, *12*, 121–150. (b) Jullien, L.; Canceill, J.; Lacombe, L.; Lehn, J.-M. *J. Chem. Soc., Perkin Trans. 2* **1994**, 989–1002.

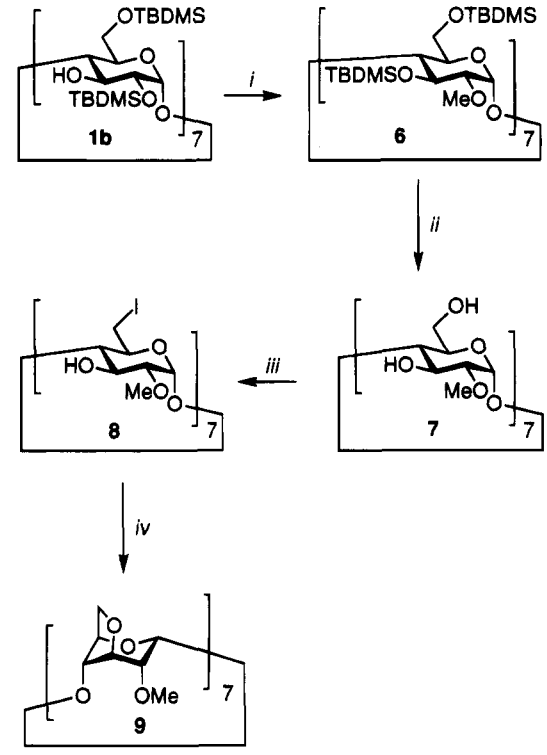
355 K, 2K × 400, $\tau_m$ = 400 ms). Clear cross peaks were observed between resonances for the benzylic protons and protons H-1, H-2, and H-3 on the CD and the aromatic ring protons.

Cleavage of the silyl groups from **2a–c**, using tetrabutylammonium fluoride in THF, proceeded in very high yields, affording the per(2-*O*-benzyl)-CDs **3a–c**. Hexakis(2-*O*-benzyl-3,6-di-*O*-methyl)-α-CD (**4a**) and heptakis(2-*O*-benzyl-3,6-di-*O*-methyl)-β-CD (**4b**) have been prepared following the literature method reported by Takeo *et al.*,[8a] and octakis(2-*O*-benzyl-3,6-di-*O*-methyl)-γ-CD (**4c**) has been prepared in a similar manner by treating the CD **3c** with sodium hydride and methyl iodide in THF. Debenzylation of **4a** and **4b** was performed according to the literature procedure,[8a] and in an analogous manner **4c** was debenzylated, by hydrogenolysis with 10% palladium on carbon. The final per(3,6-di-*O*-methyl)-CDs were obtained pure during the last steps of these reactions.

In order to gain additional evidence for the silyl group migration and to demonstrate the usefulness of this new synthetic methodology, the synthesis of the heptakis(2-*O*-methyl-3,6-anhydro)-β-CD (**9**) was also undertaken, following a procedure similar to that reported for the preparation of heptakis(3,6-anhydro)-β-CD[18] (Scheme 3). The CD **1b** was methylated with sodium hydride and methyl iodide in THF to afford heptakis(2-*O*-methyl-3,6-di-*O*-TBDMS)-β-CD (**6**) in high yield. Once again, the alkylation involved the migration of the TBDMS groups from the O-2 to the O-3 positions. Compound **6** was desilylated with tetrabutylammonium fluoride in THF, affording heptakis(2-*O*-methyl)-β-CD (**7**). The CD **7** was then iodinated[18d] with iodine/triphenylphosphine in DMF to afford heptakis(2-*O*-methyl-6-deoxy-6-iodo)-β-CD (**8**). Treatment of this compound with KOH in aqueous methanol gave **9** in very high yield. The success of the preparation of **9** provides further synthetic evidence for the O-2 to O-3 migration of the TBDMS groups. It is obvious that 3,6-anhydration could not have occurred if the methylation of **1b** had taken place at its 3-position. Furthermore, we expect the CD **9** to be a good host for metal and inorganic cations, on the basis of the properties that have been reported for the per(3,6-anhydro)-CDs.[18e] Studies on the binding properities of this new compound are being carried out at present.

The mass spectra of all the compounds—with the exception of the iodinated derivative **8**—have been recorded employing a matrix-assisted laser desorption ionization–time of flight (MALDI–TOF) mass spectrometry technique. It has already been reported[19] that this technique provides good results in the analysis of mixtures of linear and cyclic oligosaccharides. In the case of the cyclodextrins described in this Note, it proved to be an extremely effective technique, giving very strong peaks for the $[M + Na]^+$ and $[M + K]^+$ ions, especially for the very nonpolar silylated derivatives **1a–c**, **2a–c**, and **6**, which were not amenable to analysis by fast atom bombardment mass spectrometry (FABMS). A MALDI–TOF mass spectrum of the iodinated CD **8** showed peaks indicative of the loss of three, four, and five HI molecules, respectively—but no molecular ion, as a consequence of its instability under the conditions by which the MALDI–TOF mass spectrum was obtained. The mass spectrum of **8** was also recorded using a liquid secondary ion mass spectroscopy (LSIMS) technique. In this case, we observed the molecular ion, as well as peaks indicative of the progressive loss of HI—up to five molecules—presumably resulting in anhydration of the glucopyranose residues.

**Scheme 3. Synthesis of the Per(2-*O*-methyl-3,6-anhydro)-β-cyclodextrin 9**[a]




[a] Reagents: *(i)* MeI/NaH/THF; *(ii)* $Bu_4NF$/THF; *(iii)* $I_2/PPh_3$/DMF; *(iv)* KOH/$H_2O$/MeOH.

Finally, it is important to emphasize that all the compounds described herein were efficiently and easily purified by crystallization or column chromatography on silica gel. Indeed, the use of more sophisticated and expensive techniques such as HPLC or reversed-phase chromatography—which too often are needed to produce chemically-modified cyclodextrins in high purity—has been avoided. Thus, we are confident that this convenient and novel synthetic methodology will be employed on a regular basis for the routine syntheses of a range of chemically-modified CD derivatives.

## Summary

The serendipitous discovery of the silyl shift on the secondary rim of the CD rings gives us the opportunity to report a novel, highly efficient synthetic strategy for the preparation of some chemically-modified CDs. This approach, relying on the readily-available per(2,6-di-*O*-TBDMS)-CDs **1a–c** as key intermediates, has proved to

(18) For a discussion of 3,6-anhydro-CDs, see: (a) Ashton, P. R.; Ellwood, P.; Staton, I.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 80–81. (b) Ashton, P. R.; Ellwood, P.; Staton, I.; Stoddart, J. F. *J. Org. Chem.* **1991**, *56*, 7274–7280. (c) Yamamura, H., Fujita, K. *Chem. Pharm. Bull.* **1991**, *39*, 2505–2508. (d) Gadelle, A.; Defaye, J. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 78–79. (e) Yamamura, H.; Ezuka, T.; Kawase, Y.; Kawai, M.; Butsugan, Y.; Fujita, K. *J. Chem. Soc., Chem. Commun.* **1993**, 636–637. For a discussion of other anhydro CD derivatives, see: (f) Fujita, K.; Egashira, Y.; Imoto, T.; Fujioka, T.; Mihashi, K.; Tahara, T.; Koga, T. *Chem. Lett.* **1989**, 429–432. (g) Fujita, K.; Tahara, T.; Sasaki, H.; Egashira, Y.; Shingu, T.; Imoto, T.; Koga, T. *Chem. Lett.* **1989**, 917–920. (h) Khan, A. R.; Barton, L.; D'Souza, V. T. *J. Chem. Soc., Chem. Commun.* **1992**, 1112–1114. (i) Coleman, A. W.; Zhang, P.; Ling, C.-C.; Mahuteau, J.; Parrot-Lopez, H.; Miocque, M. *Supramol. Chem.* **1992**, *1*, 11–14.

(19) Stahl, B.; Steup, M.; Karas, M.; Hillenkamp, F. *Anal. Chem.* **1991**, *63*, 1463–1466.

be extremely useful and simple to employ. The efficiency and reliability of this new methodology has been demonstrated by preparing the per(3,6-di-*O*-methyl)-CDs **5a–c** and heptakis(2-*O*-methyl-3,6-anhydro)-β-CD **9** with very good overall yields and in high purities.

## Experimental Section

**General.** All chemicals were purchased from Aldrich and used as received. Cyclodextrins were dried before use over $P_4O_{10}$ at 90 °C for 24 h. Solvents were dried according to literature procedures. Thin-layer chromatography (TLC) was carried out on aluminum sheets coated with silica gel. The plates were inspected under UV light and developed with $H_2SO_4$ (5%) in EtOH. Column chromatography was performed on silica gel. Microanalyses were performed by the University of Birmingham Microanalytical Service or by the University of Sheffield Microanalytical Service. $^1$H NMR spectra were recorded at 300.1 or 400.1 MHz. $^{13}$C NMR spectra were recorded at 67.8, 75.5 or 100.6 MHz. All chemical shifts are quoted in ppm, referenced to tetramethylsilane (TMS) using the residual solvent. Coupling constants (*J*) are quoted in hertz.

**Hexakis(2,6-di-*O*-*tert*-butyldimethylsilyl)-α-cyclodextrin[9] (1a).** *tert*-Butyldimethylsilyl chloride (27.94 g, 185.4 mmol, 1.5 equiv per OH group) and 4-(*N*,*N*-dimethylamino)pyridine (ca. 20 mg) were added to a solution of α-cyclodextrin (10.0 g, 10.3 mmol) in dry DMF (100 ml) and dry pyridine (60 mL) under nitrogen. The resulting mixture was heated at 100 °C for 18 h. After cooling, the solvents were removed under high vacuum. The solid was partitioned between water (150 mL) and $CH_2Cl_2$ (150 mL). The organic layer was retained and washed successively with $KHSO_4$ (0.5 M, 150 mL) and with water (150 mL). After drying ($MgSO_4$), the solvent was removed under reduced pressure to afford a white solid. Column chromatography ($SiO_2$, $CH_2Cl_2$) afforded an amorphous solid (20.76 g, 8.86 mmol, 86%), which was characterized as hexakis(2,6-di-*O*-*tert*-butyldimethylsilyl)-α-cyclodextrin (**1a**), mp 281–283 °C (lit.[9] mp 274 °C dec): $^1$H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 36H), 0.13 (s, 18H), 0.14 (s, 18H), 0.88 (s, 54H), 0.90 (s, 54H), 3.47 (t, *J* = 9, 6H), 3.53 (dd, *J* = 3.5, 9, 6H), 3.65–3.75 (m, 12H), 3.90–4.02 (m, 12H), 4.36 (s, 6H), 4.89 (d, *J* = 3.5, 8H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ −5.1, −4.7, −4.6, 18.4, 18.8, 25.9, 26.3, 62.3, 72.0, 72.4, 74.6, 82.6, 102.7; MALDI-TOFMS *m*/*z* 2379 for $[M + K]^+$, calcd for $C_{108}H_{228}O_{30}Si_{12}$ M = 2340. Anal. Calcd for $C_{108}H_{228}O_{30}Si_{12}{\cdot}C_6H_{14}$: C, 56.34; H, 10.04. Found: C, 56.57; H, 10.15.

**Heptakis(2,6-di-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin[10b] (1b).** **1b** was prepared from β-cyclodextrin (10.0 g, 8.81 mmol) using the procedure described above for **1a**. Column chromatography ($SiO_2$, $CH_2Cl_2$) afforded an amorphous solid (20.95 g, 7.66 mmol, 87%), which was characterized as heptakis(2,6-di-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (**1b**), mp 285 °C dec. (lit.[10b] mp 289–291 °C): $^1$H NMR (400 MHz, $CDCl_3$, 50 °C) δ 0.03 (s, 21H), 0.04 (s, 21H), 0.16 (s, 21H), 0.17 (s, 21H), 0.88 (s, 63H), 0.93 (s, 63H), 3.47 (t, *J* = 9, 7H), 3.55 (dd, *J* = 3.3, 9, 7H), 3.63 (m, 7H), 3.69 (br d, *J* = 11.5, 7H), 3.88 (t, *J* = 9, 7H), 3.99 (dd, *J* = 11.5, 3, 7H), 4.36 (s, 7H), 4.87 (d, *J* = 3.3, 7H); $^{13}$C NMR (100.6 MHz, $CDCl_3$) δ −5.2, −5.0, −4.6, −4.5, 18.3, 18.9, 25.9, 26.3, 61.9, 71.9, 72.1, 74.9, 82.0, 102.6; MALDI-TOFMS *m*/*z* 2773 for $[M + K]^+$, calcd for $C_{126}H_{266}O_{35}Si_{14}$ M = 2734. Anal. Calcd for $C_{126}H_{266}O_{35}Si_{14}{\cdot}C_6H_{14}$: C, 56.20; H, 10.01. Found: C, 55.96; H, 9.98.

**Octakis(2,6-di-*O*-*tert*-butyldimethylsilyl)-γ-cyclodextrin (1c).** **1c** was prepared from γ-cyclodextrin (4.43 g, 3.41 mmol) using the procedure described above for **1a**. Column chromatography ($SiO_2$, $CH_2Cl_2$) afforded an amorphous solid (9.07 g, 2.90 mmol, 85%), which was characterized as octakis(2,6-di-*O*-*tert*-butyldimethylsilyl)-γ-cyclodextrin (**1c**), mp 181 °C (from EtOH): $^1$H NMR (300 MHz, $CDCl_3$) δ 0.00 (s, 24H), 0.01 (s, 24H), 0.14 (s, 24H), 0.15 (s, 24H), 0.84 (s, 72H), 0.90 (s, 72H), 3.43 (t, *J* = 9, 8H), 3.49–3.61 (m, 16H), 3.65 (d, *J* = 11.5, 8H), 3.84 (t, *J* = 9, 8H), 3.96 (dd, *J* = 11.5, 3, 8H), 4.26 (s, 8H), 4.92 (d, *J* = 3.3, 8H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ −5.2, −4.9, −4.2, 18.3, 18.8, 25.9, 26.3, 62.1, 72.0, 72.2, 75.1, 81.1, 102.0; MALDI-TOFMS *m*/*z* 3148 for $[M + Na]^+$, calcd for $C_{144}H_{304}O_{40}Si_{16}$ M = 3125. Anal. Calcd for $C_{144}H_{304}O_{40}Si_{16}$: C, 55.34; H, 9.80. Found: C, 55.36; H, 9.98.

**Hexakis(2-*O*-benzyl-3,6-di-*O*-*t*-butyldimethylsilyl)-α-cyclodextrin (2a).** Compound **1a** (5.0 g, 2.13 mmol) was dissolved in dry THF (25 mL) under nitrogen. NaH (1.22 g, 51 mmol) was added in one portion, and the mixture was stirred for 30 min at room temperature. The reaction was cooled to 0 °C, and benzyl bromide (8.72 g, 51 mmol) was added dropwise. The mixture was heated under reflux for 19 h. The reaction mixture was then allowed to cool down to room temperature, MeOH (10 mL) was added, and the solvents were removed under vacuum. The residue was partitioned between water (100 mL) and $CH_2Cl_2$ (100 mL), the organic layer was washed with water (2 × 100 mL) and dried ($MgSO_4$), and the solvent was removed under reduced pressure. Column chromatography ($SiO_2$, *n*-hexane/acetone 98:2) afforded a white solid characterized as hexakis(2-*O*-benzyl-3,6-di-*O*-*tert*-butyldimethylsilyl)-α-cyclodextrin (**2a**) (3.00 g, 1.04 mmol, 49%), mp 238–239 °C: $^1$H NMR (400 MHz, $C_6D_{12}$, 72 °C) δ 0.06 (s, 18H), 0.10 (s, 18H), 0.12 (s, 18H), 0.13 (s, 18H), 0.90 (s, 54H), 0.93 (s, 54H), 3.31 (dd, *J* = 2.5, 6, 6H), 3.81–3.87 (br m, 6H), 3.93 (t, *J* = 6, 6H), 4.08 (br s), 4.27 (br s, 6H), 4.35 (t, *J* = 6, 6H), 4.61, 4.71 (AB system, $J_{AB}$ = 12.6, 14H), 5.00 (br s, 6H), 7.07–7.20 (m, 18H), 7.26–7.32 (m, 12H); $^{13}$C NMR (100 MHz, $C_6D_{12}$, 72 °C) δ −3.4, −3.3, −2.4, −2.2, 19.5, 19.6, 27.4, 27.6, 63.8, 74.2, 74.9, 75.9, 78.7, 79.5, 98.6, 128.6, 129.3, 130.0, 139.9; MALDI-TOFMS *m*/*z* 2907 for $[M + Na]^+$, calcd for $C_{150}H_{264}O_{30}Si_{12}$ M = 2884. Anal. Calcd for $C_{150}H_{264}O_{30}Si_{12}{\cdot}C_6H_{14}$: C, 63.07; H, 9.43. Found: C, 63.32; H, 9.48.

**Heptakis(2-*O*-benzyl-3,6-di-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (2b).** The cyclodextrin **1b** (10.0 g, 3.66 mmol) was treated following the procedure described for **2a**. Column chromatography ($SiO_2$, *n*-hexane/acetone 98:2) afforded a white solid, which was characterized as heptakis(2-*O*-benzyl-3,6-di-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (**2b**) (9.59 g, 2.85 mmol, 78%), mp 214–216 °C: $^1$H-NMR (400 MHz, $CDCl_3$, 55 °C) δ −0.05 (s, 21H), −0.01 (s, 21H), 0.02 (s, 21H), 0.05 (s, 21H), 0.81 (s, 63H), 0.88 (s, 63H), 3.28 (dd, *J* = 3.5, 8, 7H), 3.75–3.80 (m, 7H), 3.93–3.95 (m, 14H), 4.13–4.16 (m, 7H), 4.21–4.25 (m, 7H), 4.49, 4.59 (AB system, $J_{AB}$ = 12.5, 14H), 5.08 (s, *J* = 3.5, 7H), 7.18–7.21 (m, 35H); $^{13}$C NMR (100 MHz, $CDCl_3$, 55 °C) δ −4.6, −4.4, −3.7, −3.6, 18.2, 18.4, 26.2, 26.4, 62.4, 72.6, 73.8, 77.5, 77.6, 96.7, 105.7, 116.0, 116.1, 117.0; MALDI-TOFMS *m*/*z* 3389 for $[M + Na]^+$, calcd for $C_{175}H_{308}O_{35}Si_{14}$ M = 3366. Anal. Calcd for $C_{175}H_{308}O_{35}Si_{14}{\cdot}C_6H_{14}$: C, 62.98; H, 9.40. Found: C, 63.29; H, 9.40.

**Octakis(2-*O*-benzyl-3,6-di-*O*-*tert*-butyldimethylsilyl)-γ-cyclodextrin (2c).** The cyclodextrin **1c** (10 g, 2.56 mmol) was treated according to the procedure described above for **1a**. Column chromatography ($SiO_2$, *n*-hexane/acetone 98:2) and recrystallization from EtOH/acetone afforded a white crystalline compound, which was characterized as octakis(2-*O*-benzyl-3,6-di-*O*-*tert*-butyldimethylsilyl)-γ-cyclodextrin (**2c**) (7.48 g, 1.95 mmol, 76%), mp 199 °C (from EtOH/acetone): $^1$H NMR (300 MHz, $CDCl_3$) δ −0.04 (s, 24H), −0.01 (s, 24H), 0.00 (s, 24H), 0.02 (s, 24H), 0.81 (s, 72H), 0.86 (s, 72H), 3.29–3.40 (br m, 8H), 3.76 (m, 8H), 3.91 (br s, 16H), 4.00–4.12 (m, 8H), 4.15–4.24 (m, 8H), 4.49, 4.61 (AB system, $J_{AB}$ = 12, 16H), 5.17 (br s, 8H), 7.25–7.37 (m, 40H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ −4.7, −4.4, −3.8, 18.1, 18.4, 26.2, 26.3, 62.1, 72.7, 73.4, 73.9, 96.5, 127.3, 128.1, 138.5; MALDI-TOFMS *m*/*z* 3869 for $[M + Na]^+$, calcd for $C_{200}H_{352}O_{40}Si_{16}$ M = 3846. Anal. Calcd for $C_{200}H_{352}O_{40}Si_{16}$: C, 62.46; H, 9.22. Found: C, 62.20; H, 9.22.

**Hexakis(2-*O*-benzyl)-α-cyclodextrin[8a] (3a).** The cyclodextrin **2a** (5.0 g, 1.73 mmol) was dissolved in a solution of $Bu_4NF$ in THF (1 M, 5.5 mL) and stirred at room temperature for 20 h. The solvent was then removed under reduced pressure to afford a yellow oil. The crude product was dissolved in $CH_2Cl_2$ (60 mL) and washed with water (3 × 120 mL), before being dried ($MgSO_4$), and the solvent was evaporated under vacuum to yield a pale yellow solid. Column chromatography ($SiO_2$, $CHCl_3$/MeOH 90:10) and recrystallization from $CHCl_3$/*n*-pentane afforded a white crystalline compound, which was characterized as hexakis(2-*O*-benzyl)-α-cyclodextrin (**16**) (2.094 g, 1.38 mmol, 80%), mp 270 °C dec (lit.[8a] mp 237–242 °C): $^1$H NMR (300 MHz, $CDCl_3$) δ 3.18 (t, *J* = 9.5, 6H), 3.38 (dd, *J* = 3.5, 9.5, 6H), 3.45–3.57 (m, 6H), 3.66–3.75 (m, 6H), 3.80 (br d, 6H), 4.10 (t, *J* = 9.5, 6H), 4.59 (s, 6H), 4.66 (d, *J* = 3.5, 6H), 4.71, 4.94 (AB system, $J_{AB}$ = 11.5, 12H), 7.27–7.40 (m, 30H); $^{13}$C NMR (75 MHz, $CD_3OD$) δ 62.4, 73.7, 75.6, 75.7, 80.7, 84.8, 102.9, 129.8, 130.1, 130.5,

139.6; MALDI-TOFMS $m/z$ 1537 for $[M + Na]^+$, calcd for $C_{78}H_{96}O_{30}$ M = 1514. Anal. Calcd for $C_{78}H_{96}O_{30}\cdot 3H_2O$: C, 59.76; H, 6.56. Found: C, 59.43; H, 6.10.

**Heptakis(2-*O*-benzyl)-β-cyclodextrin[8a] (3b).** The cyclodextrin **2b** (8.0 g, 2.37 mmol) was treated according to the procedure described for **2a**. Column chromatography ($SiO_2$, $CHCl_3$/MeOH 90:10) and recrystallization from $CHCl_3$/*n*-pentane afforded a white crystalline compound, which was characterized as heptakis(2-*O*-benzyl)-β-cyclodextrin (**3b**) (3.82 g, 2.16 mmmol, 91%), mp 208–210 °C (lit.[8a] mp 198–205 °C): $^1$H NMR (300 MHz, $CDCl_3$) δ 3.14 (t, $J$ = 9.5, 7H), 3.36 (dd, $J$ = 3.5, 10, 7H), 3.50–3.58 (m, 7H), 3.62–3.70 (m, 7H), 3.73–3.81 (m, 7H), 3.94 (t, $J$ = 10, 7H), 4.65 (d, $J$ = 3.5, 7H), 4.68 (d, part of an AB system, $J_{AB}$ = 10.5, 7H), 4.80 (s, 7H), 4.91 (d, part of an AB system, $J_{AB}$ = 10.5, 7H), 7.21–7.39 (m, 35H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 61.6, 71.9, 73.8, 74.1, 78.3, 84.0, 101.8, 128.1, 128.4, 128.9, 137.5; MALDI-TOFMS $m/z$ 1790 for $[M + Na]^+$, calcd for $C_{91}H_{112}O_{35}$ M = 1766. Anal. Calcd for $C_{91}H_{112}O_{35}\cdot 4H_2O$: C, 59.47; H, 6.58. Found: C, 59.64; H, 6.19.

**Octakis(2-*O*-benzyl)-γ-cyclodextrin (3c).** The cyclodextrin **2c** (7.0 g, 1.82 mmol) was treated according to the procedure described above for **1c**. Column chromatography ($SiO_2$, $CHCl_3$/MeOH 90:10) and recrystallization from $CHCl_3$/*n*-pentane afforded a white crystalline compound, which was characterized as octakis(2-*O*-benzyl)-γ-cyclodextrin (**3c**) (3.49 g, 1.73 mmmol, 95%), mp 219–222 °C (from $CHCl_3$/*n*-pentane): $^1$H NMR (300 MHz, $CDCl_3$) δ 3.18 (t, $J$ = 9.5, 8H), 3.40 (dd, $J$ = 4, 9.5, 8H), 3.56–3.78 (m, 16H), 3.78–3.84 (m, 8H), 3.98 (t, $J$ = 9.5, 8H), 4.92 (d, $J$ = 4, 8H), 4.72 (d, part of an AB system, $J_{AB}$ = 11.5, 8H), 4.85 (s, 8H), 4.95 (d, part of an AB system, $J_{AB}$ = 11.5, 8H), 7.30–7.39 (m, 40H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 61.5, 71.7, 73.8, 74.1, 78.6, 83.7, 102.1, 128.1, 128.4, 129.0, 137.5; MALDI-TOFMS $m/z$ 2041 for $[M + Na]^+$, calcd for $C_{104}H_{128}O_{40}$ M = 2018. Anal. Calcd for $C_{104}H_{128}O_{40}\cdot 2H_2O$: C, 60.81; H, 6.47. Found: C, 60.85; H, 6.55.

**Hexakis(2-*O*-benzyl-3,6-di-*O*-methyl)-α-cyclodextrin[8a] (4a).** Compound **4a** was prepared, following a literature procedure, from **3a**. The spectroscopic and analytical data are in agreement with the published data. **4a:** $^1$H NMR (300 MHz, $CDCl_3$) δ 3.34 (s, 18H), 3.36 (dd, $J$ = 3.5, 9, 6H), 3.53 (s, 18H), 3.55–3.69 (m, 18H), 3.75–3.85 (m, 12H), 4.64, 4.80 (AB system, $J_{AB}$ = 12.5, 12H), 4.95 (d, $J$ = 3.5, 6H) 7.21–7.37 (m, 18H), 7.41–7.49 (m, 12H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 58.9, 62.0, 71.2, 71.5, 72.3, 80.0, 81.5, 82.5, 100.8, 127.4, 127.7, 128.2, 139.0; MALDI-TOFMS $m/z$ 1705 for $[M + Na]^+$, calcd for $C_{90}H_{120}O_{30}$ M = 1682.

**Heptakis(2-*O*-benzyl-3,6-di-*O*-methyl)-β-cyclodextrin[8a] (4b).** Compound **4b** was prepared, following a literature procedure, from **3b**. The spectroscopic and analytical data are in agreement with the published data. **4b:** $^1$H NMR (300 MHz, $CDCl_3$) δ 3.32 (s, 21H), 3.41 (dd, $J$ = 3.5, 9, 7H), 3.48–3.73 (m, 21H), 3.56 (s, 21H), 3.74–3.90 (m, 7H), 4.70, 4.76 (AB system, $J_{AB}$ = 14, 14H), 5.05 (d, $J$ = 3.5, 7H), 7.22–7.48 (m, 35H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 58.9, 61.4, 71.0, 71.4, 72.7, 79.4, 79.7, 82.1, 99.3, 127.4, 127.8, 128.2, 138.8; MALDI-TOFMS $m/z$ 1984 for $[M + Na]^+$, calcd for $C_{105}H_{140}O_{35}$ M = 1962.

**Octakis(2-*O*-benzyl-3,6-di-*O*-methyl)-γ-cyclodextrin (4c).** NaH (1.14 g, 47.6 mmol) was added under nitrogen to a solution of dry **3c** (3.0 g, 1.49 mmol, dried over $P_4O_{10}$ at 60 °C for 24 h) in dry THF (80 mL), and the mixture was stirred for 1 h at room temperature. Methyl iodide (6.76 g, 47.6 mmol) was added dropwise, and the reaction mixture was heated under reflux for 13 h. The reaction was then allowed to cool to room temperature, MeOH (8 mL) was added, and the solvents were evaporated under reduced pressure. The residue was partitioned between $CH_2Cl_2$ (100 mL) and water (100 mL), the organic layer was washed with water (2 × 100 mL) and dried ($MgSO_4$), and the solvent was removed under reduced pressure. Column chromatography ($SiO_2$, $CHCl_3$/MeOH 98:2) on the resulting amorphous solid and recrystallization from MeOH/$CH_2Cl_2$ afforded a white crystalline compound which was characterized as octakis(2-*O*-benzyl-3,6-di-*O*-methyl)-γ-cyclodextrin (**4c**) (2.67 g, 1.19 mmol, 80%), mp 102–104 °C (from MeOH/$CH_2Cl_2$): $^1$H NMR (400 MHz, $CDCl_3$) δ 3.29 (s, 24H), 3.40–3.50 (m, 16H), 3.59–3.68 (m, 8H), 3.61 (s, 24H), 3.72–3.76 (m, 16H), 3.82 (br d, $J$ = 10, 8H), 4.72, 4.76 (AB system, $J_{AB}$ = 12.5, 16H), 5.07 (d, $J$ = 4, 8H), 7.23–7.45 (m, 40H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 58.9, 61.5, 71.0, 71.2, 72.9, 78.2, 79.3, 82.4, 98.6, 127.5, 128.0, 128.2, 138.7; MALDI-TOFMS $m/z$ 2265 for $[M + Na]^+$, calcd for $C_{120}H_{160}O_{40}$ M = 2242. Anal. Calcd for $C_{120}H_{160}O_{40}$: C, 64.27; H, 7.19. Found: C, 64.23; H, 7.17.

**Hexakis(3,6-di-*O*-methyl)-α-cyclodextrin[8a] (5a).** Compound **5a** has been prepared, following a literature procedure, from **4a**. The spectroscopic and analytical data are in agreement with the published data. **5a:** $^1$H NMR (300 MHz, $C_6D_6$) δ 3.24 (s, 18H), 3.56 (t, $J$ = 9.5, 6H), 3.64 (s, 18H), 3.60–3.78 (m, 24H), 3.96–4.05 (m, 6H), 4.35 (d, $J$ = 10, 6H), 4.78 (d, $J$ = 3.5, 6H); $^{13}$C NMR (75 MHz, $C_6D_6$) δ 58.7, 59.3, 71.5, 72.5, 74.1, 80.1, 83.8, 103.4; MALDI-TOFMS $m/z$ 1164 for $[M + Na]^+$, calcd for $C_{48}H_{84}O_{30}$ M = 1141.

**Heptakis(3,6-di-*O*-methyl)-β-cyclodextrin[8a] (5b).** Compound **5b** has been prepared, following a literature procedure, from **4b**. The spectroscopic and analytical data are in agreement with the published data. **5b:** $^1$H NMR (300 MHz, $C_6D_6$) δ 3.25 (s, 21H), 3.54 (t, $J$ = 10, 7H), 3.73 (s, 21H), 3.67–3.83 (m, 21H), 3.86–3.95 (m, 7H), 4.05–4.14 (m, 7H), 4.86 (d, $J$ = 10, 7H), 4.90 (d, $J$ = 3.5, 7H); $^{13}$C NMR (75 MHz, $C_6D_6$) δ 58.7, 59.8, 71.5, 72.5, 74.6, 80.6, 84.2, 104.1; MALDI-TOFMS $m/z$ 1353 for $[M + Na]^+$, calcd for $C_{56}H_{98}O_{35}$ M = 1331.

**Octakis(3,6-di-*O*-methyl)-γ-cyclodextrin (5c).** A solution of the cyclodextrin **4c** (2.50 g, 1.11 mmol) in MeOH (80 mL) was subjected to hydrogenolysis in the presence of 10% Pd/C (0.100 g) at atmospheric pressure for 2 h at room temperature, before being filtered through a layer of Celite and washed with MeOH (100 mL). The combined filtrate and washings were evaporated to dryness, and the residual solid was crystallized from $CHCl_3$/*n*-hexane to afford a white crystalline compound characterized as octakis(3,6-di-*O*-methyl)-γ-cyclodextrin (**5c**) (1.44 g, 0.948 mmol, 85%), mp 243 °C (from $CHCl_3$/*n*-hexane): $^1$H NMR (400 MHz, $C_6D_6$) δ 3.49 (s, 24H), 3.71 (t, $J$ = 9.4, 8H), 3.78 (t, $J$ = 9.4, 8H), 3.80 (s, 24H), 3.82–3.96 (m, 24H), 4.14–4.18 (m, 8H), 4.71 (d, $J$ = 9.3, 8H), 5.07 (d, $J$ = 3.5, 8H); $^{13}$C NMR (75 MHz, $C_6D_6$) δ 58.7, 59.9, 71.1, 72.5, 74.8, 80.0, 84.0, 103.4; MALDI-TOFMS $m/z$ 1544 for $[M + Na]^+$, Calcd for $C_{64}H_{112}O_{40}$ M = 1521. Anal. Calcd for $C_{64}H_{112}O_{40}$: C, 50.52; H, 7.42. Found: C, 50.22; H, 7.52.

**Heptakis(2-*O*-methyl-3,6-di-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (6).** Sodium hydride (1.44 g, 60 mmol) was added to a solution of **1b** (2.45 g, 0.896 mmol) in dry THF (65 mL) carefully with cooling. Once the evolution of hydrogen had subsided, methyl iodide (3 mL) was added and stirring was commenced. The reaction was protected from light and placed under an atmosphere of nitrogen. Cooling was maintained for the first hour of the reaction, after which the suspension was allowed to warm to room temperature. After 48 h, the reaction mixture was cooled on an ice bath and methanol (5 mL) was added. THF was then removed under reduced pressure and the residue was suspended in $CH_2Cl_2$ (100 mL). The $CH_2Cl_2$ layer was washed with water (2 × 50 mL), followed by saturated aqueous sodium chloride solution (2 × 50 mL). The $CH_2Cl_2$ layer was recovered, dried ($MgSO_4$), and evaporated to dryness to yield a yellowish solid. Column chromatography ($SiO_2$, *n*-hexane/acetone 99:1) afforded heptakis(2-*O*-methyl-3,6-di-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (**6**) (1.92 g, 0.690 mmol, 77%) as a white solid, mp 220–222 °C: $^1$H NMR (300 MHz, $CDCl_3$) δ 0.02 (s, 42H), 0.09 (s, 21H), 0.11 (s, 21H), 0.89 (s, 126H), 3.03 (dd, $J$ = 3, 8, 7H), 3.35 (s, 21H), 3.69 (br d, $J$ = 11, 7H), 3.74–3.87 (m, 14H), 4.12 (t, $J$ = 8, 7H), 4.21 (br d, $J$ = 11, 7H), 5.27 (d, $J$ = 3, 7H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ −5.1, −4.7, −3.8, −3.7, 18.3, 18.4, 26.0, 26.3, 57.3, 62.9, 72.2, 73.1, 78.1, 81.2, 96.2; MALDI-TOFMS $m/z$ 2854 for $[M + Na]^+$, calcd for $C_{133}H_{280}O_{35}Si_{14}$ M = 2831. Anal. Calcd for $C_{133}H_{280}O_{35}Si_{14}$: C, 56.4; H, 9.96. Found: C, 56.6; H, 9.90.

**Heptakis(2-*O*-methyl)-β-cyclodextrin[8a] (7).** The cyclodextrin **6** (6.42 g, 2.31 mmol) was dissolved in a tetrabutylammonium fluoride solution in THF (1 M, 40 mL), heated under reflux for 4 h, then cooled to room temperature, and stirred for a further 12 h. The solvent was removed under reduced pressure and the residue sonicated in $Et_2O$ for 1 h. The precipitate was filtered, dissolved in water (10 mL), and reprecipitated with acetone. The suspension was allowed to settle before being filtered. To remove residual tetrabutylammonium salt, the solid was dissolved in water and continuously extracted with $CH_2Cl_2$. The aqueous layer was recovered and the solvent removed to yield a white solid characterized as heptakis(2-*O*-methyl)-β-cyclodextrin (**7**) (2.21 g, 1.82 mmol, 79%), mp 275 °C dec (lit.[8a] mp 318–323 °C dec): $^1$H NMR (400 MHz, $D_2O$) δ 3.48 (dd, $J$ = 3, 9, 7H), 3.65 (s,

21H), 3.69 (t, $J$ = 9, 7H), 3.86–4.00 (m, 21H), 4.07 (t, $J$ = 9, 7H), 5.34 (d, $J$ = 3, 7H); $^{13}$C NMR (75 MHz, $D_2O$) $\delta$ 61.9, 63.0, 74.1, 74.7, 84.0, 84.1, 101.8; MALDI-TOFMS $m/z$ 1253 for [M + Na]$^+$, calcd for $C_{49}H_{84}O_{35}$ M = 1230. Anal. Calcd for $C_{49}H_{84}O_{35}\cdot 4H_2O$: C, 45.09; H, 7.10. Found: C, 44.85; H, 6.82.

**Heptakis(2-*O*-methyl-6-deoxy-6-iodo)-$\beta$-cyclodextrin (8).** The cyclodextrin **7** (1.00 g, 0.81 mmol) was added under nitrogen to a stirred solution of triphenylphosphine (5.96 g, 22.7 mmol) and iodine (5.76 g, 22.7 mmol) in dry DMF (25 mL) at room temperature. The reaction mixture was heated to 80 °C for 15 h. After cooling, the volume of the solvent was halved by evaporation under reduced pressure. Freshly prepared MeONa (3M in MeOH, 7.5 mL) was added while the temperature was maintained at 0 °C. The resulting mixture was stirred with cooling for 30 min. The solvents were then removed under reduced pressure, and the resulting brown tar was dissolved in $C_6H_6$ (100 mL) and stirred with an aqueous solution of $NaS_2O_3$ (17.9 g, 200 mL $H_2O$). The organic layer was separated and washed with water (2 x 100 mL) before being dried ($MgSO_4$) and evaporated to dryness. Column chromatography ($SiO_2$, *n*-hexane/acetone 50:50) on the resulting solid afforded heptakis-(2-*O*-methyl-6-deoxy-6-iodo)-$\beta$-cyclodextrin (**8**) (0.416 g, 0.337 mmol, 42%) as a white solid, mp 295 °C dec.: $^1$H NMR (300 MHz, $CD_3COCD_3$) $\delta$ 3.30–3.43 (m, 14H), 3.51–3.60 (m, 7H), 3.64 (s, 21H), 3.64–3.73 (m, 7H), 3.85 (dd, $J$ = 2, 11, 7H) 3.96 (t, $J$ = 9, 7H), 5.11 (s, 7H), 5.16 (d, $J$ = 3.5, 7H); $^{13}$C NMR (67.8 MHz, $CDCl_3$) $\delta$ 30.9, 60.5, 70.4, 72.5, 81.7, 87.6, 101.0; HRMS calcd for $C_{49}H_{77}O_{28}I_7Na$ [M + Na]$^+$ = 2024.7812, found 2024.7857.

**Heptakis(2-*O*-methyl-3,6-anhydro)-$\beta$-cyclodextrin (9).** Cyclodextrin **8** (0.0613 g, 0.0306 mmol) was dissolved in MeOH (20 mL). An aqueous potassium hydroxide solution (1 M, 5 mL) was then added, which resulted in partial precipitation of cyclodextrin **8**. The reaction was heated to a very gentle reflux for 1 h, at which point the suspension cleared. The mixture was placed under an inert atmosphere and stirred at this temperature for a further 49 h. The reaction was allowed to cool before the solvents were evaporated under reduced pressure. The solid residue was taken up in water (50 mL) and continuously extracted with $CH_2Cl_2$ for 47 h. The $CH_2Cl_2$ was then recovered and evaporated to dryness under reduced pressure to yield a yellow, clear glass. Column chromatography ($SiO_2$, $CH_2Cl_2$/MeOH from 95:5 to 90:10) afforded heptakis(2-*O*-methyl-3,6-anhydro)-$\beta$-cyclodextrin (**9**) (0.033 g, 0.0300 mmol, 98%), mp 165–170 °C dec: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.49 (s, 21H), 3.51 (t, $J$ = 3.5, 7H), 3.96 (dd, $J$ = 2.5, 11, 7H), 4.05 (dd, $J$ = 2.5, 5, 7H), 4.18 (d, $J$ = 11, 7H), 4.33 (dd, $J$ = 3.5, 5, 7H), 4.61 (br s, 7H), 5.18 (d, $J$ = 3.5, 7H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 60.4, 69.2, 71.6, 73.6, 76.5, 77.7, 98.2; HRMS calcd for $C_{49}H_{70}O_{28}$-Na [M + Na]$^+$ = 1129.3951, found 1129.3974.

**Supplementary Material Available:** Expanded general Experimental Section and a list of $^1$H and $^{13}$C NMR spectroscopic data—including the two-dimensional NMR experimental procedure—for all the compounds presented in the paper. All the peaks have been assigned by means of two-dimensional NMR experiments (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO950237R