The Synthesis of Functionalized Cyclodextrins As Scaffolds and Templates for Molecular Diversity, Catalysis, and Inclusion Phenomena

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α-, β-, and γ-cyclodextrins were chemically modified to selectively introduce functionality on the primary and secondary faces. Azido and substituted alkenyl groups were selectively introduced on the primary hydroxy groups to give monosubstituted derivatives. The secondary C-2 hydroxy group was selectively functionalized with allyl, 1-hexenyl, carboxymethyl, and ω-azidoalkyl groups (*n*: **3**, **4**, **5**) as ethers. The chemically modified cyclodextrins are versatile molecules for use as scaffolds and templates in conjunction with chemical diversity, catalysis, and inclusion phenomena.

The cyclodextrins are cyclic oligomers of (1→4)-α-D-glucopyranosyl units that are formed during the enzymatic degradation of starch.[1] Their structures, topologies, and architectures can be appreciated from the torus-like shapes of α-, β-, and γ-cyclodextrins consisting of six, seven, and eight α-D-glucopyranosyl units, respectively.

The dominant physical character of the cyclodextrins is their ability to include in their cavities a variety of geometrically and spatially compatible hydrophobic motifs.[1-3] This has led to their exploitation in a variety of important functions, including their use in medicinal applications,[4] in chromatographic work as supports for useful and practical separations,[5] in the study of inclusion phenomena,[1,2] in catalysis,[1,3] and in asymmetric reactions,[6] to mention a few. The cyclodextrins have been extensively studied as models for artificial enzymes.[7] The catalytic activity is invariably associated with an interplay between the affinity for hydrophobic substrates and the ability of the hydroxyl groups on the periphery of the torus-shaped molecules to act as nucleophiles, as in the well studied hydrolysis of esters.[8]

In order to enhance the catalytic activity, it has been necessary to functionalize the cyclodextrins on the primary and/or secondary hydroxyl groups.[3,9] Several reports[10] have elegantly shown the importance of designing and placing functional groups with potential catalytic sites (amines, thiols, carboxyl, imidazole, etc.) on the periphery of these molecules. Because of their availability and desirable cavity size, most of the above studies have utilized α- and β-cyclodextrins.

A large number of cyclodextrin derivatives have involved one or more of the chemically equivalent primary hydroxyl groups.[3,9] Taking advantage of the greater reactivity of the C-2 hydroxyl group, it has been also possible to effect selective peripheral functionalizations at that site (e.g., esters, ethers).[9] However, these transformations have not been as straightforward as in analogous reactions with methyl α-D-glucopyranoside which can be considered as the core saccharide. The main difficulties have been associated with selectivity, efficiency, and separation techniques. In particular, *monosubstitution* at a specific hydroxyl group with functional versatility is a major challenge in these molecules.[3,9,10]

As part of a program involving the use of cyclodextrin derivatives in catalysis, in the study of inclusion phenomena, and as functionalized scaffolds or templates for the attachment of chemically diverse groups, we explored various methods for the selective and direct functionalization of the primary and C-2 secondary hydroxyl groups individually in α-, β-, and γ-cyclodextrins which we report in this article.

Our first objective was to explore direct methods for the introduction of azide groups in α-, β-, and γ-cyclodextrins. A controlled method for monoazido, diazido, and possibly triazido cyclodextrins would make the corresponding amino derivatives accessible for a variety of chemical and physicochemical studies.

Lehn and co-workers[11] had shown that the treatment of α- and β-cyclodextrins with a mixture of triphenylphosphine, carbon tetrabromide, and lithium azide in DMF

⊗ Abstract published in *Advance ACS Abstracts,* June 15, 1995.

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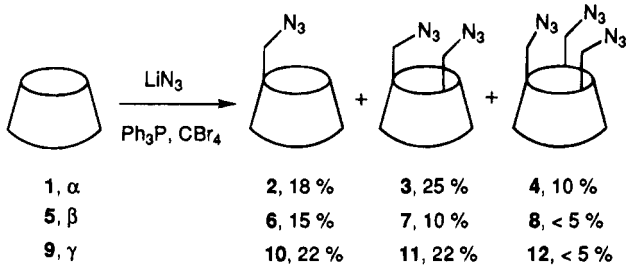
Scheme 1



as solvent in an exchange type process[12] led to the introduction of six and seven azido groups, respectively, on the primary hydroxymethyl groups. A more classical approach involved the displacement of primary tosylates with sodium azide.[13]

Efforts to obtain monoazido cyclodextrins have relied on the displacement of a monotosylate.[14] However the isolation of the monotosylate in preparatively useful yields is not simple. Bis(6-azido-6-deoxy)-β-cyclodextrin has been prepared by azide displacement of a diphenylmethane-*p,p'*-disulfonate "cap" derivative.[15] Again the yields of sulfonylation are modest and separations are effected with some difficulty resulting in the preparation of functionalized cyclodextrins in small quantities only. Symmetrical triamino α-cyclodextrins with permethylated secondary hydroxy groups have been described *via* a six-step procedure.[16]

In these and other instances, yields of azidocyclodextrins have been variable mainly because the emphasis has been to obtain workable quantities of products for the design of specific cyclodextrin derivatives as enzyme models etc. Thus, little effort has been expended for the optimization of reaction conditions.

We have studied the reaction of α-, β-, and γ-cyclodextrins in the presence of varying proportions of triphenylphosphine, carbon tetrabromide, and lithium azide. We report on conditions leading to formation and isolation of the mono-, di-, and triazido cyclodextrins as well as the assignment of substitution patterns. Thus, treatment of α-cyclodextrin (α-CD) **1** with triphenylphosphine and carbon tetrabromide (3 equiv) and lithium azide (10 equiv) in DMF at room temperature followed by column chromatography led to the isolation of monoazidomonodeoxy-α-CD **2**, diazidodideoxy-α-CD **3**, and triazidotrideoxy-α-CD **4** in consistently reproducible yields of 20%, 26%, and 5%–10% respectively, in addition to recovered α-CD (Scheme 1).

Application of essentially the same conditions to β-CD **5** with a longer reaction time (15 h instead of 6 h for α-CD) and two chromatographic separations, led to monoazido β-CD **6** and diazido β-CD **7** in yields of 15% and 10% respectively. Under these conditions, less than 5% of the triazido derivative **8** was found.

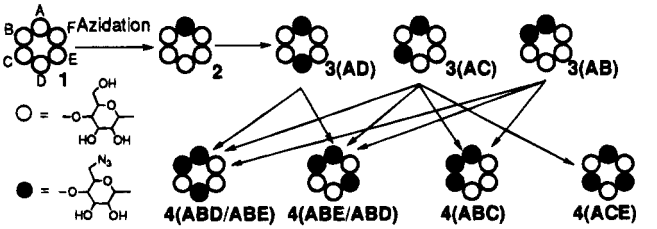


Figure 1. Assignment of substitution patterns for diazido- and triazido-α-CD **3** and **4**. A–E denote positions of the azido pyranosidic units. See also ref 18.

γ-Cyclodextrin **9** exhibited a similar reactivity pattern, affording the monoazido **10**[17] and diazido **11** derivatives in yields of 22% each. In order to obtain these mono- and diazido CD derivatives in preparatively useful quantities, the reaction conditions had to be controlled, thus avoiding the substitution of all the primary hydroxy groups. As a consequence, unreacted CD was invariably left behind in these direct azidation reactions. The modest conversions to mono, di-, and trisubstituted products are not uncommon in the cyclodextrins.[3,9]

Since a number of isomeric diazido and triazido CD derivatives could be produced in these reactions, it was deemed necessary to attempt to identify the substitution patterns.[18] Reversed-phase preparative HPLC of the mixture of diazido **3** and triazido α-CD isomers **4** allowed the separation of fractions containing single components and mixtures of two (Figure 1). ^{13}C NMR analysis of the major component of the diazido α-CD established the symmetrical substitution pattern schematically represented as **3(AD)** (Figure 1). The minor peak represented the two possible isomers **3(AB)** and **3(AC)** which could not be separated from each other (Figure 2A). The major peak in the HPLC of the triazido α-CD (Figure 2B) was identified as a mixture of isomers **4(ABD)** and **4(ABE)**. The minor peaks corresponding to faster and slower elution profiles contained the symmetrical isomer **4-(ACE)** and **4(ABC)**, respectively. The NMR characteristics of these isomeric di- and triazido α-CDs are recorded in the Experimental section. Although we have not done a similar analysis for di- and triazido β- or γ-CDs, the general pattern of substitution should not deviate much from the above analysis.[15,18]

As one of our objectives is to utilize the CD derivatives having differently substituted amino groups on the primary carbon atoms as templates for a number of model reactions in catalysis and related phenomena, we explored conditions to introduce two types of nitrogen substituent in α-CD. Thus the monoazido α-CD was transformed into the corresponding *N*-Cbz derivative **13** in good overall yield (Scheme 2). Treatment of **13** with triphenylphosphine, carbon tetrabromide, and lithium azide gave a monoazido derivative **14** which could be reduced chemoselectively to the corresponding amino derivative **15**. It should now be possible to attach a variety of motifs to each amino group (e.g., peptides) and to study phenomena related to selective inclusion, recognition, catalysis, and chemical diversity.

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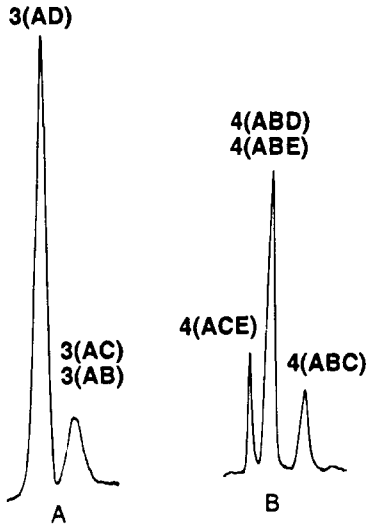
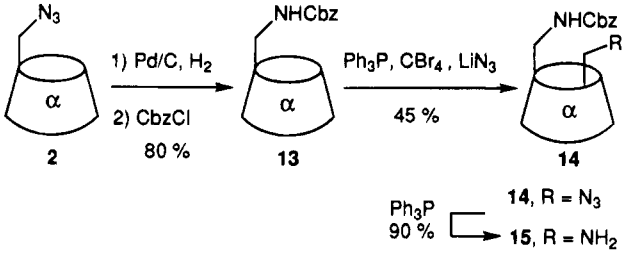


Figure 2. A. Reversed-phase HPLC of the isomer mixture of **3** (AD, AC, AB). B. Isomer mixture of **4** (ACE, ABD and ABE, ABC). A stepwise gradient elution was applied: 10% aqueous MeOH, 10 min; 50% aqueous MeOH, 20 min; then MeOH, 10 min.

Scheme 2

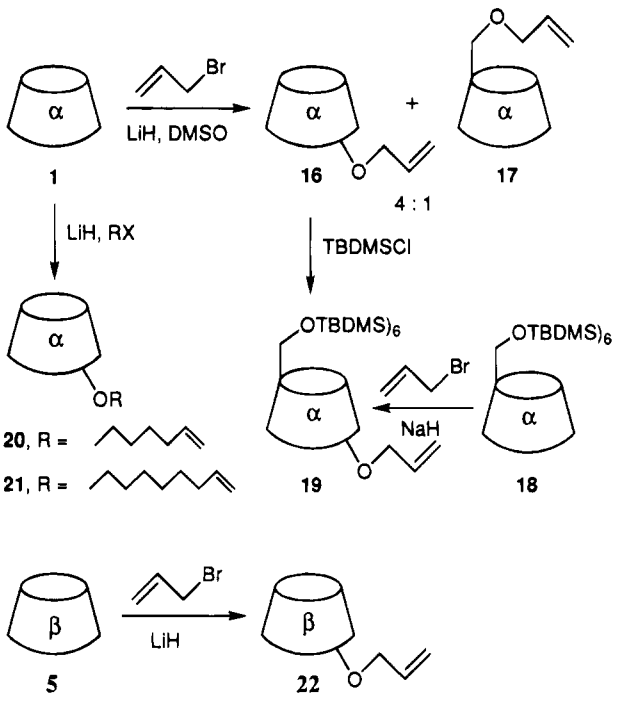


It has long been known that the selective alkylation of cyclodextrins under base-catalyzed conditions is possible at the C-2 and C-6 hydroxy groups.[9] This is attributed to the higher kinetic reactivity of the C-2 hydroxyl group due to its proximity to the anomeric center. For example, a number of 2,6-di-*O*-alkyl-β-CDs have been reported by direct alkylation with alkyl halides in the presence of base (e.g., NaH, DMF, or DMSO).[19]

Our studies led us to explore methodology for the selective monoalkylation of α- and β-CDs at the C-2 hydroxyl group.[10] Thus, treatment of α-CD with allyl bromide in the presence of sodium hydride and lithium iodide in DMSO at 55 °C led to the formation of a mixture of 2-*O*-allyl-α-CD **16** and 6-*O*-allyl α-CD **17** in a ratio of 4:1, respectively (Scheme 3). Chromatographic purification and trituration of the mixture of **16** and **17** with methanol allowed the isolation of **16** cleanly as a crystalline solid. Recrystallization from water afforded material that was suitable for single-crystal X-ray analysis.[20] A chemical structural correlation was obtained by monoallylation of hexa-*O*-*tert*-butyldimethylsilyl-α-CD[21] under the same conditions and comparing data with a sample obtained by treatment of **16** with *tert*-butyldimethylsilyl chloride.

Treatment of α-CD with 6-bromo-1-hexene and 8-bromo-1-octene in the presence of lithium iodide and lithium

Scheme 3



hydride in DMSO at 70 °C followed by chromatographic separation from dialkylated products and α-CD led to the isolation of the corresponding mono-2-*O*-(1-hexenyl) and 2-*O*-(1-octenyl) derivatives **20** and **21**, respectively (Scheme 3). The structures of these products were satisfactorily determined by detailed ^1H and ^{13}C NMR studies and by FAB mass spectrometry. Under the same conditions of allylation, β-CD afforded a 27% yield of the 2-*O*-allyl derivative **22** in addition to dialkylated products and unreacted starting material (Scheme 3).

The synthesis of the mono-2-*O*-allyl-α-CD derivative in preparatively useful quantities prompted us to further explore its potential as a source of functionalized amino and carboxylic acid derivatives. Thus ozonolysis of the double bond and reductive amination of the resulting aldehyde gave the benzylamino derivative **23** in excellent overall yield. Catalytic reduction afforded the 2-*O*-(2-aminoethyl)-α-CD analog **24** (Scheme 4).

In order to obtain the carboxylic acid derivative **26**,[22] ozonolysis had to be done on the peracetylated derivative followed by oxidation with sodium chlorite in phosphate buffer[23] to give **25**. De-O-acetylation and chromatographic separation gave the desired acid in 66% overall yield from **16**. Finally, addition of 3-mercaptopropionic acid to the double bond[24] in **16** gave the corresponding adduct **27** in 85% yield as a novel carboxylic acid tether to α-CD (Scheme 4).

Under the same conditions of ozonolysis of the double bond and reductive amination of the resulting aldehyde, 2-*O*-allyl-β-CD gave the benzylamino derivative **28**. Catalytic reduction afforded the mono-2-*O*-(2-aminoethyl)-β-CD analog **29** in excellent overall yield (Scheme 4).

In another series of monoalkylation reactions, we explored the synthesis of ω-azidoalkyl α- and β-CDs.

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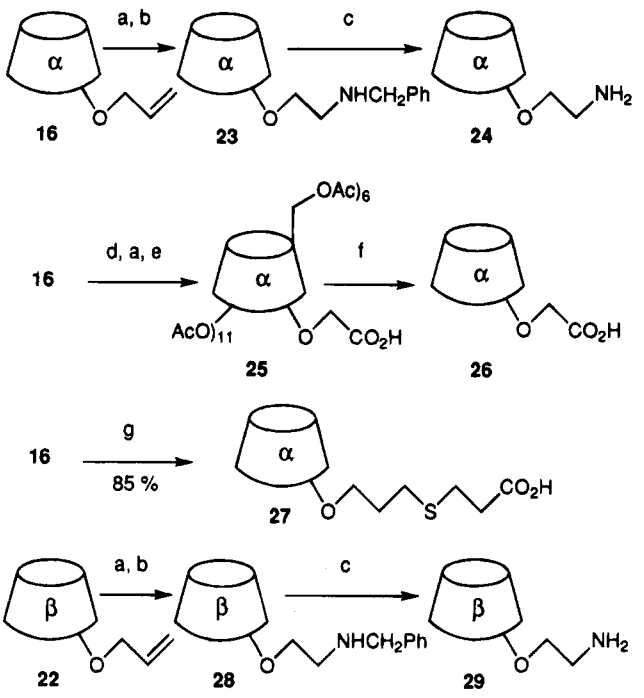
Scheme 4[a]



[a] Legend: (a) ozonolysis; (b) $PhCH_2NH_2$, $NaBH_3CN$; (c) Pd/C, H_2; (d) Ac_2O; (e) $NaClO_2$; (f) NaOMe; (g) mercaptopropionic acid.

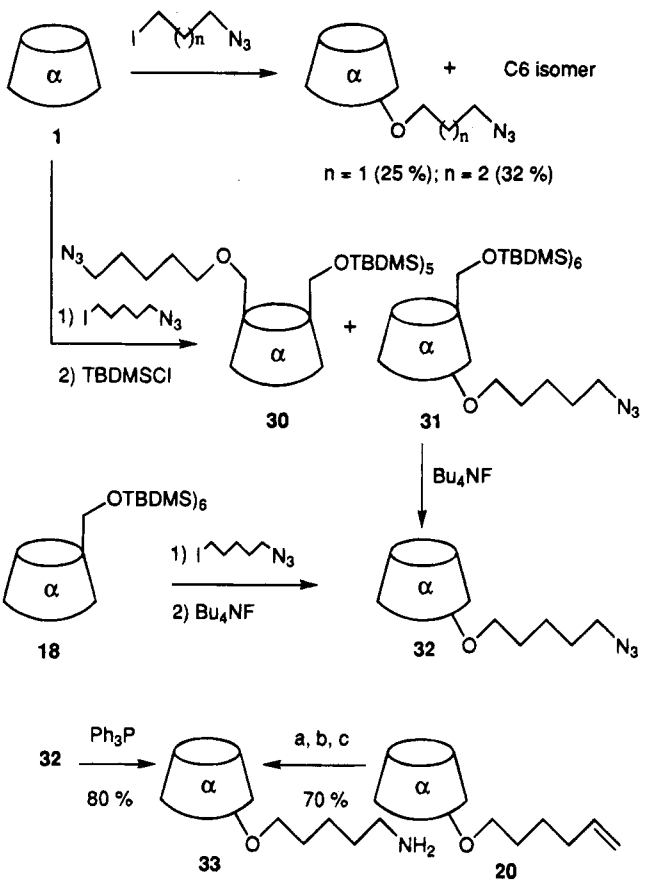
Thus, controlled alkylation of α-CD with 1-iodo-3-azidopropane easily available from the corresponding 1-bromo-3-chloropropane,[25] led to a mixture of dialkyl and monoalkyl CDs that could be separated chromatographically. ^{13}C NMR analysis showed that the monoalkyl derivatives (25%) consisted of a 1:1 ratio of the mono-6-*O*-(3-azidopropyl) and mono-2-*O*-(3-azidopropyl) isomers that could not be separated. The same result was obtained when 1-iodo-4-azidobutane and 1-iodo-5-azidopentane were used as alkylating agents (Scheme 5). In the latter case, the treatment of the mixture with *tert*-butyldimethylsilyl chloride allowed the separation of the two silylated isomers. Thus pentakis(6-*O*-*tert*-butyldimethylsilyl)mono-6-*O*-(5-azidopentyl)-α-CD **30** and hexakis-(6-*O*-*tert*-butyldimethylsilyl)mono-2-*O*-(5-azidopentyl)-α-CD **31** were obtained in 17% and 15% yield, respectively. Treatment of **31** with fluoride ion gave mono-2-*O*-(5-azidopentyl)-α-CD **32**.

Alternatively, alkylation of hexa-6-*O*-*tert*-butyldimethylsilyl-α-CD **18** with 1-iodo-5-azidopentane followed by treatment with fluoride ion led to the same derivative **32** described above. Treatment of **32** with triphenylphosphine effected reduction of the azide group to give the mono-2-*O*-(5-aminopentyl)-α-CD **33** in excellent yield. The same derivative could also be obtained from the mono-2-*O*-(1-hexenyl)-α-CD **20** by oxidative cleavage, reductive amination with benzylamine, and catalytic hydrogenolysis (Scheme 5).

ω-Azidoalkylations of β-CD, under controlled conditions utilized in the case of α-CD, were much more selective and led to the formation of the mono-2-*O*-(ω-azidoalkyl) derivatives and a small amount of dialkyl derivatives and to recovery of β-CD. Thus mono-2-*O*-(3-azidopropyl)-β-CD **34**, mono-2-*O*-(4-azidobutyl)-β-CD **35**, and mono-2-O-(5-azidopentyl)-β-CD **36** were prepared by direct alkylation followed by chromatographic separation (Scheme 6). The selective alkylation could also be done with 1-iodo-5-chloropentane (25%). Nucleophilic displacement with sodium azide in DMSO gave the monoazidopentyl analog **36** in excellent yield. Reduction of the ω-azidoalkyl ethers **34**–**36** with triphenylphosphine gave the corresponding ω-aminoalkyl derivatives **37**–**39** in excellent yields. Alternatively, reduction could be effected with 10% Pd/C under 60 psi in over 80% yield.

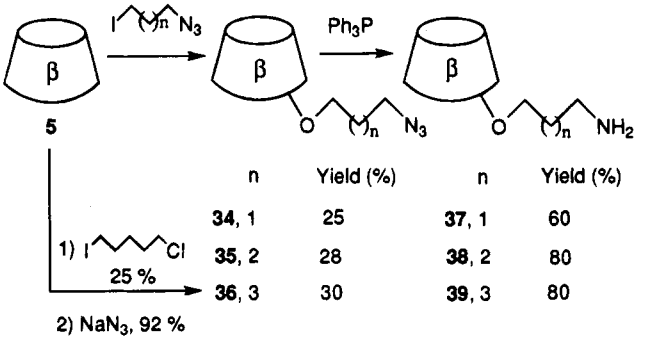
The lack of alkylation on the primary hydroxyl groups in β-CD under conditions that gave selective mono-2-O-alkylation is of interest. It is possible that the alkoxide species formed on the primary alcohol(s) are less reactive because of aggregation and association with the solvent. Inclusion of the alkylating agent and inter- or intramolecular alkylation may be favored in β-CD compared to α-CD.

Scheme 5[a]



[a] Legend: (a) Ozonolysis; (b) $PhCH_2NH_2$, $NaBH_3CN$; (c) Pd/C, H_2.

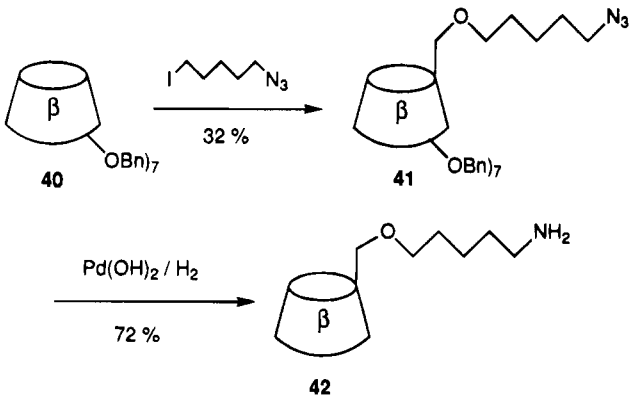
Scheme 6



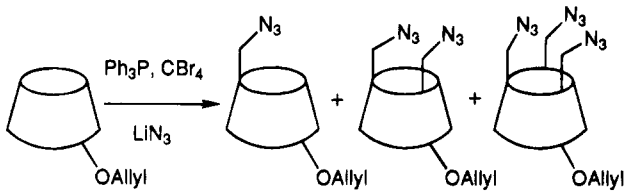
n	Yield (%)	n	Yield (%)
34, 1	25	**37**, 1	60
35, 2	28	**38**, 2	80
36, 3	30	**39**, 3	80

(25) Carboni, B.; Benalil, A.; Vaultier, M. *J. Org. Chem.* **1993**, *58*, 3736.

Scheme 7



Scheme 8



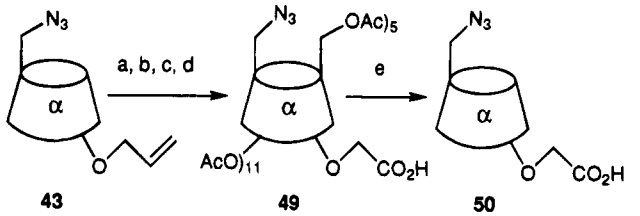
16	**43**, 26 %	**44**, 33 %	**45**, 27 %
22	**46**, 36 %	**47**, 22 %	**48**, < 5 %

We wished to prepare a mono-6-*O*-(azidoalkyl)-β-CD in connection with our interest in functionalizing both sides of β-CD. To this end, we prepared the hepta-2-*O*-benzyl ether derivative[26] **40**, *via* a selective benzylation reaction, and subjected it to the standard conditions of alkylation with 1-iodo-5-azidopentane (Scheme 7). The resulting monoalkylated product **41** (32%) was assigned the expected structure based on NMR data. Catalytic reduction gave the mono-6-*O*-(5-aminopentyl)-β-CD analog **42** which was different from its 2-*O*-substituted isomer **39**.

In an effort to obtain α-CD derivatives with different functional groups attached to the primary and secondary face, we investigated the controlled azidation of the 2-*O*-allyl derivative **16**. Under the conditions previously used for α-CD, it was possible to obtain the monoazido **43**, diazido **44**, and triazido **45** derivatives in approximately equal quantities and excellent overall yields (Scheme 8). Each of the above derivatives was isolated by chromatography and obtained as amorphous solids. They were characterized by NMR spectroscopic techniques and FAB mass spectrometry, but it was not possible to ascertain the position(s) of the azido group(s). It is thus possible that the monoazido derivative **43** is a statistical mixture of several positional isomers. The situation is probably more complicated with **44** and **45** because of the substitution pattern. Under the same conditions of azidation, the monoazido **46** and diazido β-CDs **47** were obtained in a good yield with less than 5% of the triazido-β-CD **48** being formed.

In order to obtain an amino acid type derivative within one and the same CD motif, we acetylated **43** and then cleaved the double bond by ozonolysis to the corresponding aldehyde. Oxidation with sodium chlorite[23] gave the acetylated azido acid derivative **49** as a mixture of positional isomers which was transformed to the methyl ester to facilitate the chromatographic purification (Scheme 9). Finally, base-catalysed deacetylation and deesterification followed by purification on reversed-phase column chromatography gave the desired acid **50** in excellent overall yield.

Scheme 9[a]



[a] Legend: (a) Ac_2O; (b) ozonolysis; (c) $NaClO_2$; (d) CH_2N_2; (e) NaOH: 64% overall yield for five steps.

We have described preparatively useful methods for the selective and controlled functionalization of α-, β-, and γ-cyclodextrins on primary and/or secondary faces. Several of these derivatives within each group of CDs are interesting templates for further functionalization with a variety of reagents and motifs with potenial application in catalysis, in inclusion phenomena, in simulating receptor-like cavities, in analytical and medicinal purposes, as well as for their utilization as chemical scaffolds in molecular diversity and in combinatorial chemistry.[27] Results pertaining to some of these applications are forthcoming.[28]

Experimental Section

General. Cyclodextrins and all reagents were purshased commercially and used without further purification after drying under vaccum at 90 °C for 20 h. DMF was distilled from CaH_2. HPLC was performed on a μ-Bondapak ODS column (3.9 × 300 mm^3, 10 μm) for analytical HPLC or on a Novapak ODS column (7.8 × 300 mm^2) for semipreparative HPLC using an absorbance detector (λ = 214 nm). Medium pressure chromatography was performed using a fluid-metering pump and medium pressure column (20 × 200 mm^2). The column was packed locally with Lichroprep RP18 (40–63 mm, Merck). Thin layer chromatography (TLC) was performed on glass plates coated with a 0.02-mm layer of silica gel 60 F-254. Spot detection was carried out with a molybdate reagent. Flash column chromatography on silica gel was done as described.[29] Optical rotation were measured at 25 °C at the sodium line on a Perkin-Elmer 241 spectropolarimeter. The IR spectra were recorded on a Perkin-Elmer 721 spectrophotometer on KBr pellets. Fast atom bombardment (FAB) mass spectra (carrier gas, xenon) were recorded on a Kratos MS 50 instrument. The ^1H NMR spectra were measured on a Brucker ARX 400 spectrometer operating at 400.10 MHz for ^1H and 100.6 MHz for ^{13}C or on a Varian 300 spectrometer operating at 300 MHz for ^1H and 75.5 MHz for ^{13}C. Coupling constants (*J*) are reported in hertz.

Mono-6-azido-6-deoxy-α-cyclodextrin (2), 6,6′-Diazido-6,6′-dideoxy-α-cyclodextrins (3), and 6,6′,6″-Triazido-6,6′,6″-trideoxy-α-cyclodextrins (4). To a solution of dried α-cyclodextrin (2.54 g, 2.61 mmol) in DMF (20 mL) were added lithium azide (1.28 g, 10 equiv), triphenylphosphine (2.05 g, 3 equiv) and carbon tetrabromide (2.60 g, 3 equiv). The addition of the latter caused a mildly exothermic reaction, and the solution turned yellow. The reaction was stirred under argon

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(27) For recent reviews, see: Gordon, E. M.; Barrett, R. W.; Dower, W. J.; Fodor, S. P. A.; Gallop, M. A. *J. Med. Chem.* **1994**, *37*, 1386. Gallop, M. A.; Barrett, R. W.; Dower, W. J.; Fodor, S. P. A.; Gordon, E. M. *J. Med. Chem.* **1994**, *37*, 1233. Moos, W. H.; Green, G. D.; Paria, M. R. *Ann. Rep. Med. Chem.* **1993**, *28*, 315.

(28) Hanessian, S.; Benalil, A.; Phan Viet, M. T. *Tetrahedron*, in press.

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at room temperature for 6 h. TLC on silica gel (CH_3CN-H_2O, 4:1) showed four major products having R_f values of 0.50, 0.35, 0.20, and 0.09, and corresponding, respectively, to triazido-, diazido-, monoazido-α-cyclodextrins, and starting material in addition to other minor products. After addition of MeOH (10 mL), the brown solution was concentrated to about half the volume by rotary evaporation under reduced pressure and then poured into acetone (500 mL) to precipitate α-cyclodextrin and its derivatives. The precipitate was filtered and washed with acetone (100 mL) to give 3.0 g of crude products, which were purified by flash chromatography on a silica gel column (4 × 40 cm^2) eluting with CH_3CN-H_2O, 9:1 (2 L) and then 4:1 (1.5 L). The pure fractions were combined and then concentrated in vacuo to give compounds **2** (470 mg, 18%) and **3** (670 mg, 25%). The fractions of triazido-α-cyclodextrins contaminated with tetraazido derivatives were purified a second time to give compound **4** (270 mg, 10%).

Data for **2**: mp 190 °C (decomp); $[\alpha]^{25}_D$ +133° (*c* 0.2, H_2O) (lit.[14] mp 217 °C (decomp); $[\alpha]^{25}_D$ +128° (*c* 0.4, H_2O)); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 300 MHz, the A notation refers to the glucose unit bearing the azide group) δ 3.20–3.45 (m, H2, H4, $H6^A$, H_2O), 3.52–3.70 (m, 18H, H5, H6), 3.71–3.87 (m, 6H, H3), 4.40–4.60 (m, 5H, OH6), 4.72–4.82 (m, 5H, H1), 4.83 (d, 1H, J = 3.2, $H1^A$), 5.31–5.49 (m, 6H, OH3), 5.49–5.62 (m, 6H, OH2); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 51.3 ($C6^A$), 60.0 (C6), 70.4 ($C5^A$), 71.6, 71.7, 71.8, 71.9, 72.1 (C2, C5), 72.3 ($C2^A$), 72.7 ($C3^A$), 72.9, 73.0, 73.1 (C3), 82.1, 82.2, 82.4 (C4), 83.2 ($C4^A$), 101.7 ($C1^A$), 102.0, 102.1, 102.3 (C1); HRMS (FAB) calcd for $C_{36}H_{59}O_{29}N_3$, 1020.3132 (M + Na), found, 1020.3055.

Data for **3** (AD isomer): A quantity of the diazido product (36 mg) was purified by semipreparative reversed-phase HPLC using a stepwise gradient elution with 10% aqueous MeOH for 10 min and then 50% aqueous MeOH for 20 min with intermittent washing with MeOH between injections. Evaporation of the eluents gave the AD isomer: mp 165 °C (decomp); $[\alpha]^{25}_D$ +77° (*c* 0.11, H_2O); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 300 MHz, the A, D notation refers to the glucose units bearing the azide groups) δ 3.11–3.48 (m, H2, H4, $H6^A$, $H6^D$, H_2O), 3.48–3.70 (m, 18H, H5, H6), 3.70–3.90 (m, 6H, H3), 4.42–4.68 (m, 4H, OH6), 4.76 (d, 2H, J = 3.6, H1), 4.78 (d, 2H, J = 3.3, H1), 4.84 (d, 2H, J = 2.4, $H1^A$, $H1^D$), 5.30–5.72 (m, 12H, OH2, OH3); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 51.3 ($C6^A$, $C6^D$), 60.0, 60.3 (C6), 70.4 ($C5^A$, $C5^D$), 72.0, 72.1 (C2, C5), 72.4, ($C2^A$, $C2^D$), 72.9 ($C3^A$, $C3^D$), 73.2 (C3), 82.2, 82.4 (C4), 83.2 ($C4^A$, $C4^D$), 101.7 ($C1^A$, $C1^D$), 102.0, 102.2 (C1); HRMS (FAB) calcd for $C_{36}H_{59}O_{28}N_6$, 1023.3377 (M + H), found, 1023.3435. Anal. Calcd for $C_{36}H_{58}O_{28}N_6 \cdot 4H_2O$: C, 39.48; H, 6.03; N, 7.67. Found: C, 39.20; H, 5.79; N, 8.00.

For compound **4**, a quantity of the triazido product (100 mg) was purified by semipreparative reversed-phase HPLC as described above. Evaporation of three pooled fractions gave four isomers.

Data for the ACE isomer of **4**: mp 178 °C (decomp); $[\alpha]^{25}_D$ +165° (*c* 0.2, MeOH); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 300 MHz, the A, C, E notation refers to the glucose units bearing the azide group) δ 3.25–3.55 (m, H2, H4, $H6^A$, $H6^C$, $H6^E$, H_2O), 3.55–3.83 (m, 24H, H5, H6, H3), 4.65–4.76 (m, 3H, OH6), 4.78 (d, 3H, J = 3.2, H1), 4.85 (d, 3H, J = 3.1, $H1^A$, $H1^C$, $H1^E$), 5.40–5.80 (m, 12H, OH2, OH3); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 51.3 ($C6^A$, $C6^C$, $C6^E$), 60.2 (C6), 70.4 ($C5^A$, $C5^C$, $C5^E$), 71.9, (C2, C5), 72.4 ($C2^A$, $C2^C$, $C2^E$), 73.0 ($C3^A$, $C3^C$, $C3^E$), 73.2 (C3), 82.5 (C4), 83.2 ($C4^A$, $C4^C$, $C4^E$), 101.8 ($C1^A$, $C1^C$, $C1^E$), 102.2 (C1); HRMS (FAB) calcd for $C_{36}H_{58}O_{27}N_9$, 1048.3442 (M + H); found, 1048.3324.

Data for the ABD and ABE isomers of **4**: mp 190 °C (decomp); $[\alpha]^{25}_D$ +144° (*c* 0.11, MeOH); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 300 MHz, the A, B, D and A, B, E notations refer to the glucose units bearing the azide group) δ 3.25–3.48 (m, H2, H4, $H6^A$, $H6^B$, $H6^D$, and $H6^A$, $H6^B$, $H6^E$, H_2O), 3.51–3.88 (m, 24H, H5, H6, H3), 4.48–4.68 (m, 3H, OH6), 4.76–4.82 (m, 3H, H1), 4.86 (m, 3H, $H1^A$, $H1^B$, $H1^D$, and $H1^A$, $H1^B$, $H1^E$), 5.35–5.70 (m, 12H, OH2, OH3); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 51.1, 51.2, 51.4 ($C6^A$, $C6^B$, $C6^D$, and $C6^A$, $C6^B$, $C6^E$), 59.8, 59.9, 60.2 (C6), 70.1, 70.2, 70.3, 70.4, 70.5, 70.6 ($C5^A$, $C5^B$, $C5^D$, and $C5^A$, $C5^B$, $C5^E$), 71.7, 71.8, 71.9 (C2, C5), 72.2, 72.27, 72.3 ($C2^A$, $C2^B$, $C2^D$, and $C2^A$, $C2^B$, $C2^E$), 72.7, 72.8, 72 9 ($C3^A$, $C3^B$, $C3^D$, and $C3^A$, $C3^B$, $C3^E$), 73.1, 73.2 (C3), 82.0, 82.1, 82.3, 82.4, 82.5 (C4), 83.1, 83.3 ($C4^A$, $C4^B$, $C4^D$, and $C4^A$, $C4^B$, $C4^E$), 101.60, 101.68, 101.70, 101.74 ($C1^A$, $C1^B$, $C1^D$, and $C1^A$, $C1^B$, $C1^E$), 101.9, 102.0, 102.1, 102.2 (C1); HRMS (FAB) calcd for $C_{36}H_{58}O_{27}N_9$, 1048.3442 (M + H); found, 1048.3469.

Data for the ABC isomer of **4**: mp 160 °C (decomp); $[\alpha]^{25}_D$ +141° (*c* 0.12, MeOH); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 300 MHz, the A, B, C notation refers to the glucose units bearing the azide group) δ 3.20–3.48 (m, H2, H4, $H6^A$, $H6^B$, $H6^C$, H_2O), 3.49–3.90 (m, 24H, H5, H6, H3), 4.45–4.76 (m, 3H, OH6), 4.78–4.85 (m, 3H, H1), 4.88 (m, 3H, $H1^A$, $H1^B$, $H1^C$), 5.42–5.75 (m, 12H, OH2, OH3); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 51.3, 51.4 ($C6^A$, $C6^B$, $C6^C$), 59.8, 59.9, 60.2 (C6), 70.2, 70.4, 70.5 ($C5^A$, $C5^B$, $C5^C$), 71.7, 71.8, 71.9, 72.00, 72.07, 72.1, 72.3 (C2, C5), 72.7, 72 78, 72.8 ($C3^A$, $C3^B$, $C3^C$), 73.1, 73.2 (C3), 82.0, 82.2, 82.4 (C4), 83.3, 83.4 ($C4^A$, $C4^B$, $C4^C$), 101.7, 101.8, 101.9 ($C1^A$, $C1^B$, $C1^C$), 102.0, 102.1 (C1); HRMS (FAB) calcd for $C_{36}H_{58}O_{27}N_9$, 1048.3442 (M + H); found, 1048.3521.

Mono-6-azido-6-deoxy-β-cyclodextrin (6) and 6,6′-Diazido-6,6′-dideoxy-β-cyclodextrins (7). Essentially the same procedure was used as for α-CD starting with β-CD (930 mg, 0.80 mmol) to give after 15 h a mixture of mono-, di-, and (a small amount of) triazido-β-CD. After two purifications by silica gel column chromatography using CH_3CN-H_2O 9:1 to 75:25 as eluent, compounds **6** (140 mg, 15%) and **7** (100 mg, 10%) were obtained as solids.

Data for **6**: mp 200 °C (decomp); $[\alpha]^{25}_D$ +100° (*c* 1.0, DMSO), (lit.[14] mp 206 °C (decomp); $[\alpha]^{25}_D$ +108.2° (*c* 0.4, H_2O)); R_f 0.28 (CH_3CN-H_2O, 7.5:2.5); IR (KBr) 3400 (OH), 2100 (N_3); ^{13}C NMR (DMSO-d_6, 100.6 MHz, the A notation refers to the glucose unit bearing the azide group) δ 51.9 ($C6^A$), 60.6, 60.8, 61.0 (C6), 71.0 ($C5^A$), 73.0, 73.1, 73.3 (C2, C5), 73.7, 73.9 (C3), 82.3, 82.4, 82.7 (C4), 83.8 ($C4^A$), 102.4, 102.8, 103.1 (C1).

Data for **7**:[15] mp 190 °C (decomp); $[\alpha]^{25}_D$ +141.0° (*c* 0.74, DMSO); R_f 0.48 (CH_3CN-H_2O, 7.5:2.5); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 400 MHz, the A notation refers to the glucose unit bearing the azide group) δ 3.20–3.45 (m, H2, H4, $H6^A$, H_2O), 3.45–3.80 (m, H5, H6, H3), 4.40–4.62 (OH6), 4.80–4.90 (m, H1), 4.90–4.95 (m, $H1^A$), 5.60–5.85 (m, OH2, OH3); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 51.9 ($C6^A$), 60.4, 60.7, 60.8, 61.0 (C6), 70.9, 71.0, 71.3 ($C5^A$), 72.9, 73.1, 73.3 (C2, C5), 73.7, 73.8, 73.9 (C3), 82.4, 82.7 (C4), 83.8, 84.0 ($C4^A$), 102.4, 102.8, 103.1 (C1).

Mono-6-azido-6-deoxy-γ-cyclodextrin (10) and 6,6′-Diazido-6,6′-dideoxy-γ-cyclodextrins (11). Essentially the same procedure was used as for α-CD starting with γ-CD (1.2 g, 0.92 mmol) to give a mixture of mono-, di-, and (a small amount of) triazido-γ-CD. After purification by silica gel column chromatography using CH_3CN-H_2O 9:1 to 75:25 as eluent, compounds **10** (260 mg, 22%) and **11** (262 mg, 22%) were obtained as solids.

Data for **10**:[17] mp 185 °C (decomp); $[\alpha]^{25}_D$ +142.8° (*c* 0.28, H_2O); R_f 0.27 (CH_3CN-H_2O, 7.5:2.5); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 400 MHz, the A notation refers to the glucose unit bearing the azide group) δ 3.20–3.45 (m, H2, H4, $H6^A$, H_2O), 3.45–3.80 (m, H5, H6, H3), 4.38–4.62 (OH6), 4.78–4.90 (m, H1), 4.90–4.95 (m, $H1^A$), 5.60–5.80 (m, OH2, OH3); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 51.9 ($C6^A$), 60.7, 60.8, 61.0 (C6), 71.3 ($C5^A$), 73.0, 73.2, 73.5, 73.7, 73.8 (C2, C3, C5), 81.6, 81.8, 81.9, 82.0, 82.1 (C4), 83.5 ($C4^A$), 102.1, 102.5, 102.7, 103.1 (C1); HRMS (FAB) calcd for $C_{48}H_{79}O_{39}N_3$, 1344.4188 (M + Na); found, 1344.4146.

Data for **11**: mp 195 °C (decomp); $[\alpha]^{25}_D$ +150.2° (*c* 0.22, MeOH); R_f 0.42 (CH_3CN-H_2O, 7.5:2.5); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 400 MHz, the A notation refers to the glucose unit bearing the azide group) δ 3.20–3.45 (m, H2, H4, $H6^A$, H_2O), 3.45–3.80 (m, H5, H6, H3), 4.40–4.62 (OH6), 4.80–4.90 (m, H1), 4.90–4.95 (m, $H1^A$), 5.60–5.85 (m, OH2, OH3); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 51.9, 52.2 ($C6^A$), 60.8 (C6), 71.1, 71.3 ($C5^A$), 73.0, 73.3, 73.5, 73.6, 73.7 (C2, C3, C5), 81.4, 81.6, 81.8, 82.1 (C4), 83.5, 83.6 ($C4^A$), 102.0, 102.3, 102.4, 102.6, 103.0, 103.1 (C1); HRMS (FAB) calcd for $C_{48}H_{78}O_{38}N_6$, 1369.4252 (M + Na); found, 1369.4305.

Mono-6-amino-6-deoxy-α-cyclodextrin. A solution of **2** (200 mg, 0.2 mmol) in MeOH−H_2O, 1:1 (50 mL), was reduced with palladium on charcoal (10%, 20 mg) at 30 psi of hydrogen on a Parr hydrogenator for 18 h. After removal of the catalyst by filtration, the solution was evaporated to dryness to give 6-amino-6-deoxy-α-cyclodextrin (180 mg, 90%): mp 180 °C (decomp); $[\alpha]^{25}D$ +135° (*c* 0.38, H_2O) (lit.[14] mp 200 °C (decomp); $[\alpha]^{25}D$ +117° (*c* 0.4, H_2O)); R_f 0.20 (*n*-PrOH−H_2O−NH_4OH, 6:2:1); ^1H NMR (D_2O, 300 MHz, the A notation refers to the glucose unit bearing the amino group) δ 2.92 (dd, 1H, *J* = 12.7, 7.3, $H6^A$), 3.20 (d, 1H, *J* = 12.7, $H6'^A$), 3.50 (t, 1H, *J* = 8.9, $H4^A$), 3.58−3.74 (m, 11H, H2, H4), 3.82−3.98 (m, 16H, H5, H6), 4.20 (t, 6H, *J* = 9.3, H3), 5.10 (s, 6H, H1); ^{13}C NMR (D_2O, 75.5 MHz) δ 39.9 ($C6^A$), 58.9 (C6), 70.2 (C5), 70.5 (C2), 71.7 ($C3^A$), 71.8 (C3), 79.7 (C4), 81.5 ($C4^A$), 99.7 ($C1^A$), 99.8 (C1); HRMS (FAB) calcd for $C_{36}H_{62}O_{29}N$, 972.3407 (M + H); found, 972.3448.

6-Benzyloxycarbonylamino-6-deoxy-α-cyclodextrin (13). To a solution of the above compound (170 mg, 0.17 mmol) in water (20 mL) were added sodium bicarbonate (600 mg), dichloromethane (5 mL), and benzyl chloroformate (250 μL, 10 equiv). The mixture was stirred overnight at room temperature and then extracted with dichloromethane (2 × 10 mL). The aqueous phase was concentrated to about 10 mL and then applied on a reversed-phase column (Lichroprep C18, 2 × 20 cm^2), eluting with H_2O (50 mL), 10% aqueous MeOH (100 mL), and then 50% aqueous MeOH (100 mL). The pure fractions were combined and concentrated to dryness to give the product as a solid (170 mg, 87%): mp 195 °C (decomp); $[\alpha]^{25}D$ +81° (*c* 0.11, H_2O); R_f 0.40 (CH_3CN−H_2O, 4:1); IR (KBr) 3400 (OH), 1710 (CO); ^1H NMR (DMSO-d_6, 300 MHz, the A notation refers to the glucose unit bearing the NHCbz group) δ 3.15−3.85 (m, H2, H3, H4, H5, H6), 4.40−4.75 (m, 5H, OH6), 4.75−4.80 (m, 5H, H1), 4.86 (d, 1H, *J* = 3.3, $H1^A$), 4.92 (d, 1H, *J* = 12.6, benzyl), 5.20 (d, 1H, *J* = 12.8, benzyl), 5.60−6.10 (m, 12H, OH2, OH3), 7.25−7.40 (m, 5H, Ph), 7.50−7.60 (m, 1H, NH); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 60.3, 60.5 (C6), 65.3 ($C6^A$), 70.5 ($C5^A$), 72.2, 72.5, 72.7, 72.8, 73.3 (C2, C5, benzyl), 73.6, 73.65 (C3), 82.6, 82.7, 82.8 (C4), 84.5 ($C4^A$), 102.1 ($C1^A$), 102.3 (C1), 127.7, 128.5, 137.8 (Ph), 175.7 (CO); HRMS (FAB) calcd for $C_{44}H_{67}O_{31}N$, 1128.3595 (M + Na); found, 1128.3557.

6-Benzyloxycarbonylamino-6′-azido-6,6′-dideoxy-α-cyclodextrins (14). To a solution of dry **13** (200 mg, 0.18 mmol) in DMF (10 mL) was added triphenylphosphine (120 mg, 2.5 equiv), lithium azide (100 mg, 2.5 equiv) and carbon tetrabromide (150 mg, 2.5 equiv). The yellow solution was stirred at room temperature for 4 h. TLC on silica gel (CH_3CN−H_2O, 4:1) showed two major products having R_f values of 0.75 and 0.56, corresponding, respectively, to the trisubstituted derivative and the expected product **14**. After addition of MeOH (2 mL), the solution was concentrated in vacuo and then the residue was applied to a silica gel column (2.5 × 45 cm^2), eluting with CH_3CN−H_2O 95:5 then 9:1, gave the title compound (90 mg, 45%): mp 216 °C (decomp); $[\alpha]^{25}D$ +114.0° (*c* 0.22, MeOH); IR (KBr) 3400 (OH), 2100 (N_3), 1720 (CO); ^1H NMR (DMSO-d_6, 400 MHz, The A, X notation refers to the glucose units bearing the azide and NHCbz groups, X = B, C, D, E, or F) δ 3.15−3.85 (m, H2, H3, H4, H5, H6), 4.38−4.62 (m, 4H, OH6), 4.65−5.08 (m, 8H, H1, benzyl), 5.38−5.62 (m, 12H, OH2, OH3), 7.18−7.22 (m, 1H, NH), 7.25−7.42 (m, 5H, Ph); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 51.2 ($C6^A$), 59.83, 59.89, 59.90, 59.93 (C6), 65.2, 65.3 ($C6^X$), 70.0, 70.1, 70.2, 70.35, 70.37, 70.5 ($C5^A$, $C5^X$), 71.80, 71.87, 71.92, 71.96, 72.0, 72.11, 72.13, 72.27, 72.3 (C2, C5, benzyl), 72.8, 72.9, 73.1, 73.20, 73.26, 73.3 (C3), 81.94, 81.95, 82.04, 82.06, 82.11, 82.12, 82.2 (C4), 83.1, 83.24, 83.26, 83.6, 83.8 ($C4^A$, $C4^X$), 101.7, 102.00, 102.05, 102.17, 102.20 (C1), 127.70, 127.78, 127.83, 128.36, 128.40, 137.18, 137.20, 137.23, 137.25 (Ph), 156.29, 156.31, 156.33, 156.35, 156.37 (CO); HRMS (FAB) calcd for $C_{44}H_{67}O_{30}N_4$, 1131.3840 (M + H); found, 1131.3730.

6-Benzyloxycarbonylamino-6′-amino-6,6′-dideoxy-α-cyclodextrins (15). Compound **14** (100 mg, 0.08 mmol) was suspended in dioxane−methanol (10:2 mL). To the slightly milky solution was added triphenylphosphine (70 mg, 0.26 mmol). After 1 h, 1 mL of concentrated ammonia was added and stirring was continued for 20 h. After removal of the solvents in vacuo, the white residue was suspended in water (20 mL) and then washed twice with dichloromethane (10 mL). The aqueous solution was concentrated in vacuo and then applied to a reversed-phase column (Lichroprep C18, 2 × 20 cm). The column was stepwise eluted with water (300 mL), 10% aqueous MeOH (200 mL), and then 20% aqueous MeOH (200 mL). The pure fractions were concentrated in vacuo to give the product as a white solid (90 mg, 90%): mp 205 °C (decomp); $[\alpha]^{25}D$ +107.6° (*c* 0.3, MeOH); R_f 0.50 (*n*-butanol−acetic acid−water−pyridine, 15:3:12:10); IR (KBr) 3400 (OH), 1700 (CO); ^1H NMR (DMSO-d_6, 400 MHz, The A, X notation refers to the glucose units bearing the amino and NHCbz groups, X = B, C, D, E, or F) δ 2.68−2.92 (m, 2H, $H6^A$), 3.18−3.85 (m, H2, H3, H4, H5, H6), 4.38−4.60 (m, 4H, OH6), 4.64−5.08 (m, 8H, H1, benzyl), 5.38−5.62 (m, 12 H, OH2, OH3), 7.12−7.22 (m, 1H, NH), 7.25−7.42 (m, 5H, Ph), ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 40.5 ($C6^A$), 60.7 (C6), 66.1 ($C6^X$), 70.9 ($C5^A$, $C5^X$), 72.8, 72.9 (C2, C5, benzyl), 74.0 (C3), 82.9 (C4), 84.5 ($C4^A$, $C4^X$), 102.6, 102.7, 102.9 (C1), 128.4, 128.6, 128.7, 129.2, 138.0 (Ph), 157.1, 157.2 (CO); HRMS (FAB) calcd for $C_{44}H_{69}O_{30}N_2$, 1105.3935 (M + H); found, 1105.3900.

Mono-2-*O*-allyl-α-cyclodextrin (16). To a solution of dried α-cyclodextrin (2.88 g, 2.96 mmol) in DMSO (30 mL) was added lithium hydride (35 mg, 1.5 equiv). The mixture was stirred under argon until the solution became clear (24 h). To this solution were added allyl bromide (256 μL, 1 equiv) and lithium iodide (10 mg). The mixture stood at 55 °C for 4 h. TLC on silica gel (CH_3CN−H_2O, 4:1) showed three products having R_f values of 0.24, 0.16, 0.09, corresponding respectively to diallyl, monoallyl-α-cyclodextrins, and starting material. α-Cyclodextrin and its derivatives were precipitated by the addition of acetone (500 mL). The precipitate was filtered and washed with acetone (100 mL) to give 3.0 g of crude product, which was purified by flash chromatography on a silica gel column (4 × 40 cm^2), eluting with CH_3CN−H_2O, 9:1 (1 L) then 4:1 (1.5 L). The pure fractions of monoallyl-α-cyclodextrin were combined and then concentrated in vacuo to give a solid (900 mg, 30%). The proton NMR spectra showed that it was a mixture of 2-*O*- and 6-*O*-allyl-α-cyclodextrins. The latter was present in about 20% (based on the integration of the alkenyl protons). Trituration of the solid in MeOH (3 mL) for 20 h and then filtration gave pure 2-*O*-monoallyl-α-cyclodextrin (720 mg, 24%) as a colorless solid. A portion was crystallized after slow evaporation of an aqueous solution: mp 270 °C (decomp); $[\alpha]^{25}D$ +55° (*c* 0.1, H_2O); IR (KBr) 3400 (OH); ^1H NMR (DMSO-d_6, 300 MHz, the A notation refers to the glucose unit bearing the allyl group) δ 3.20 (dd, 1H, *J* = 3.3, 9.0, $H2^A$) 3.22−3.48 (m, H2, H4, H_2O), 3.50−3.70 (m, 18H, H5, H6), 3.70−3.82 (m, 5H, H3), 3.85 (td, 1H, *J* = 9.0, 2.2, $H3^A$), 4.16 (dd, 1H, *J* = 12.8, 5.7, allyl), 4.28 (dd, 1H, *J* = 12.8, 5.7, allyl), 4.38−4.52 (m, 6H, OH6), 4.79 (s, 5H, H1), 4.95 (d, 1H, *J* = 3.3, $H1^A$), 5.18 (dd, 1H, *J* = 10.4, 1.8, allyl), 5.29 (dd, 1H, *J* = 17.3, 1.8, allyl), 5.40−5.70 (m, 11H, OH2, OH3), 5.80−5.95 (m, 1H, allyl); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 60.1 (C6), 71.9, 72.2 (C2, C5), 72.4 (allyl), 72.8 ($C3^A$), 73.2, 73.3, 73.4 (C3), 79.6 ($C2^A$), 82.2, 82.4 (C4), 82.8 ($C4^A$), 100.2 ($C1^A$), 101.2, 102.0, 102.1, (C1), 117.7 (allyl), 134.8 (allyl); HRMS (FAB) calcd for $C_{39}H_{64}O_{30}$, 1035.3380 (M + Na); found, 1035.3385. Anal. Calcd for $C_{39}H_{64}O_{30}·5H_2O$: C, 42.46; H, 6.71. Found: C, 42.40; H, 6.23. The structure was confirmed by X-ray analysis.[20]

Treatment of **16** with *tert*-butyldimethylsilyl chloride in DMF containing imidazole (20 h) gave after usual work up the corresponding 6-*O*-hexa-*tert*-butyldimethylsilyl derivative **19** in 71%: $[\alpha]^{25}D$ +79.2° (*c* 2.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz, the A notation refers to the glucose unit bearing the allyl group) δ 0.04 (s, 36H, (CH_3), 0.88 (s, 54H, *t*-Bu), 3.24 (dd, 1H, *J* = 9.7, 2.3, $H2^A$), 3.42−4.20 (m, 35H, H2, H3, H4, H5, H6), 4.38 (dd, 1H, *J* = 13.1, 5.3, allyl), 4.52 (d, 1H, *J* = 9.6, allyl), 4.82−4.95 (m, 6H, H1), 5.05−5.38 (m, 8H, OH3, allyl), 5.87−6.42 (m, 6H, OH2, allyl); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −5.4, −5.3, −5.26, −5.20 (CH_3), 18.1, 18.2, 18.3 (*t*-Bu), 25.7, 25.8, (*t*-Bu), 61.5, 61.7, 61.9, 62.1, 62.2 (C6), 71.8, 71.9, 72.1, 72.6, 72.7, 72.9, 73.1, 73.5, 73.8, 74.2, 74.4 (C2, C3, C5, allyl), 80.2, 80.4, 80.7, 81.2, 81.3, 81.9 (C4), 100.8, 101.3, 101.4, 101.5, 101.8, 102.9 (C1), 119.6 (allyl), 134.0 (allyl); FAB-MS *m*/*z* 1827

(M + thioglycerol + Na). The same product was obtained by monoallylation of α-cyclodextrin 6-*O*-hexa-*tert*-butyldimethylsilyl ether **18** in 22%.

Mono-2-*O*-(1-hexenyl)-α-cyclodextrin (20). To a solution of dried α-cyclodextrin (2.5 g, 2.57 mmol) in DMSO (20 mL) was added lithium hydride (40 mg, 2 equiv). To this mixture, stirred under argon for 24 h and then treated with 6-bromo-1-hexene (850 mg, 2 equiv) and lithium iodide (10 mg). After stirring at 70 °C for 10 h, TLC on silica gel (CH_3CN-H_2O, 4:1) showed three products having R_f values of 0.50, 0.70, and 0.09, corresponding respectively to dihexenyl, monohexenyl-α-cyclodextrins, and starting material. The residue obtained after concentration of the solvent in vacuo was applied on a silica gel column (4 × 40 cm²) eluted with CH_3CN-H_2O, 9:1 (1 L) then 4:1 (1.5L). The pure fractions of monohexenyl-α-cyclodextrin were combined and then concentrated in vacuo to give a solid (750 mg, 30%): mp 230 °C (decomp); $[\alpha]^{25}_D$ +109.4° (*c* 0.27, DMSO); ^{1}H NMR (DMSO-d_6, 300 MHz, the A notation refers to the glucose unit bearing the hexenyl group) δ 1.30–1.60 (m, 4H, hexenyl), 1.95–2.10 (m, 2H, hexenyl), 3.10–3.20 (m, 1H, H2^A), 3.20–3.50 (m, H2, H4, H_2O), 3.50–3.70 (m, 18H, H5, H6), 3.70–3.85 (m, 7H, H3, hexenyl), 3.85–3.95 (m, 1H, H3^A), 4.40–4.60 (m, 6H, OH6), 4.70–4.85 (m, 5H, H1), 4.90–5.05 (m, 3H, H1^A, hexenyl), 5.35–5.90 (m, 12H, OH2, OH3, hexenyl); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 24.6, 28.9, 33.0 (hexenyl), 60.0 (C6), 71.6, 71.9, 72.2 (C2, C5, hexenyl), 72.9, 73.2, 73.3 (C3), 80.4 (C2^A), 82.2, 82.4, 82.7 (C4), 100.2 (C1^A), 102.1, (C1), 115.0 (hexenyl), 138.7 (hexenyl); FAB-MS *m*/*z* 1094 (M + K, glycerol/KI as matrix).

Mono-2-O-(1-octenyl)-α-cyclodextrin (21). Essentially the same procedure was used to give the product as a solid, yield 22%; $[\alpha]^{25}_D$ +97.6° (*c* 0.25, MeOH); R_f 0.45 (CH_3CN-H_2O, 4:1); ^{1}H NMR (DMSO-d_6, 300 MHz, the A notation refers to the glucose unit bearing the octenyl group) δ 1.20–1.60 (m, 8H, octenyl), 1.95–2.10 (m, 2H, octenyl), 3.17 (dd, 1H, *J* = 10.1, 3.4, H2^A), 3.20–3.48 (m, H2, H4, H_2O), 3.47–3.70 (m, 18H, H5, H6), 3.70–3.95 (m, H3, octenyl), 4.42–4.58 (m, 6H, OH6), 4.70–4.85 (m, 5H, H1), 4.90–5.05 (m, 3H, H1^A, octenyl), 5.30–5.82 (m, 12H, OH2, OH3, octenyl); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 25.2, 28.4, 28.5, 29.5, 33.3 (octenyl), 60.2 (C6), 72.0, 72.3 (C2, C5, octenyl), 73.0, 73.4 (C3), 80.5 (C2^A), 82.3, 82.5 (C4), 100.3 (C1^A), 102.2, (C1), 115.0 (octenyl), 139.0 (octenyl); FAB-MS *m*/*z* 1083 (M + Na).

Mono-2-*O*-allyl-β-cyclodextrin (22). Essentially the same procedure was used as for **16** starting with β-CD (2.5 g, 2.20 mmol) to give a mixture of mono- and diallyl-β-CD derivatives, which were separated by chromatography. 2-*O*-Monoallyl-β-cyclodextrin was isolated as a solid (700 mg, 27%): $[\alpha]^{25}_D$ +110.0° (*c* 1.07, DMSO); R_f 0.14 (CH_3CN-H_2O, 4:1); ^{1}H NMR (DMSO-d_6, 300 MHz, the A notation refers to the glucose unit bearing the allyl group) δ 3.24–3.45 (m, H2, H4, H_2O), 3.45–3.64 (m, 26H, H3, H5, H6), 3.76 (td, 1H, *J* = 9.3, 1.1, H3^A), 4.15 (dd, 1H, *J* = 12.3, 6.2, allyl), 4.30 (dd, 1H, *J* = 12.3, 5.9, allyl), 4.45–4.54 (m, 7H, OH6), 4.81 (m, 6H, H1), 4.95 (d, 1H, *J* = 3.5, H1^A), 5.16 (dd, 1H, *J* = 11.4, 1.8, allyl), 5.28 (dd, 1H, *J* = 15.7, 1.8, allyl), 5.68–5.93 (m, 14H, OH2, OH3, allyl); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 60.1 (C6), 72.0, 72.2, 72.5, 72.7 (C2, C5, allyl), 73.1, 73.3 (C3), 79.9 (C2^A), 81.7 (C4), 82.4 (C4^A), 100.5 (C1^A), 102.1, (C1), 118.1 (allyl), 134.8 (allyl); FAB-MS *m*/*z* 1306 (M + Na).

Mono-2-*O*-(2-(benzylamino)ethyl)-α-cyclodextrin (23). Through a solution of **16** (200 mg, 0.2 mmol) in MeOH–H_2O, 1:1 (50 mL) at 0 °C was bubbled ozone until TLC indicated complete disappearance of starting material (2 h). Argon was bubbled through the solution to remove excess ozone. Excess methyl sulfide was added, and the reaction mixture was warmed to room temperature and then concentrated in vacuo to give the aldehyde derivative as a white solid used without further purification in the next step. To a suspension of the aldehyde derivative in MeOH (20 mL) was added benzylamine (1 mL). The pH of the solution was adjusted to 6 by addition of concentrated hydrochloric acid and then sodium cyanoborohydride (60 mg, 5 equiv) was added. The mixture was stirred at room temperature for 48 h. Concentrated hydrochloric acid was added until pH 3 to decompose excess sodium cyanoborohydride, and then the solvent was removed in vacuo to give a residue which was partitioned between water and dichloromethane. The aqueous layer was washed with dichloromethane, and then potassium carbonate was added until pH 9. The solution was concentrated to about 10 mL, then applied on a reversed-phase column (Lichroprep C18, 2 × 20 cm²). Stepwise elution with water (300 mL), 10% MeOH (400 mL), and then 20% MeOH (300 mL) gave **23** (160 mg, 73%): mp 210 °C (decomp); $[\alpha]^{25}_D$ +120° (*c* 0.15, H_2O); R_f 0.60 (*n*-PrOH–H_2O–NH_4OH, 6:2:1); ^{1}H NMR (D_2O, 400 MHz, the A notation refers to the glucose bearing the (benzylamino)ethyl group) δ 2.80–3.00 (m, 2H, CH_2N), 3.40–3.70 (m, 12H, H2, H4), 3.75–4.10 (m, 26H, H5, H6, H3, O–CH_2–CH_2N), 5.00–5.18 (m, 7H, H1, benzyl), 5.19 (d, 1H, *J* = 3.1, H1^A), 7.30–7.60 (m, 5H, Ph); ^{13}C NMR (D_2O, 100.6 MHz) δ 44.7 (CH_2N), 49.4 (CH_2Ph), 57.0 (C6), 66.2 (O–CH_2–CH_2N), 68.4, 68.8, 68.9 (C2, C5), 69.8, 70.0 (C3), 76.5 (C2^A), 78.0, 78.2, 78.4 (C4), 96.0 (C1^A), 98.1, 98.2 (C1), 124.4, 125.5, 125.6, 134.7 (Ph); HRMS (FAB) calcd for $C_{45}H_{71}O_{30}N$, 1106.4139 (M + H); found, 1106.4226.

Mono-2-*O*-(2-aminoethyl)-α-cyclodextrin (24). A solution of **23** (120 mg, 0.1 mmol) in MeOH (20 mL) was hydrogenated in the presence of palladium on charcoal (200 mg) at atmospheric pressure for 1 day. After removal of the catalyst by filtration through a bed of Celite, the solution was concentrated in vacuo to give a solid (90 mg, 90%); mp 205 °C (decomp); $[\alpha]^{25}_D$ +108.3° (*c* 0.27, H_2O); R_f 0.34 (*n*-PrOH–H_2O–NH_4OH, 6:3:1); ^{1}H NMR (D_2O, 400 MHz, the A notation refers to the glucose unit bearing the aminoethyl group) δ 2.62–2.81 (m, 2H, CH_2N), 3.51 (dd, 1H, *J* = 3.1, 10.0, H2^A), 3.58–3.74 (m, 13H, H2, H4), 3.80–4.08 (m, 25 H, H3, H5, H6, O–CH_2–CH_2N), 4.10 (t, 1H, *J* = 9.0, H3^A), 5.08–5.12 (m, 5H, H1), 5.27 (d, 1H, *J* = 3.1, H1^A); ^{13}C NMR (D_2O, 100.6 MHz) δ 58.2 (CH_2N), 61.0, 61.1, 61.2 (C6), 68.0 (O–CH_2–CH_2N), 72.4 (C5), 72.7, 72.8 (C2), 73.7, 74.0, 74.1 (C3), 80.6 (C2^A), 82.0, 82.1, 82.2 (C4), 99.6 (C1^A), 102.0, 102.1, 102.2, 102.3 (C1).

Per-O-acetylated 2-*O*-Carboxymethyl-α-cyclodextrin (25). To a solution of **16** (310 mg, 0.3 mmol) in pyridine (5 mL) was added acetic anhydride (5 mL), and the mixture was heated at 80 °C for 20 h. The residue obtained after usual workup was dissolved in CH_2CL_2–MeOH (10:10 mL). Through this solution was bubbled ozone at −78 °C until TLC indicated complete disappearence of starting material (15 min). The residue obtained after usual workup was dissolved in MeOH (10 mL) and isobutene (3 mL). To this solution cooled at 0 °C was added dropwise a solution of sodium chlorite (240 mg) and sodium dihydrogenphosphate in water (3 mL). The reaction mixture was stirred at room temperature overnight. The residue obtained after removal of the solvents under vacuum was dissolved in water. The solution was acidified to pH 4 with HCl (1 N) and extracted with ethyl acetate. The organic layers were dried and concentrated in vacuo to give a residue, which was purified by flash chromatography on a silica gel column. Stepwise elution with EtOAc–MeOH, 6:1, 3:1, and then 1:1 gave the desired compound **25** (400 mg, 75%).

Mono-2-*O*-carboxymethyl-α-cyclodextrin (26).[30] A solution of **25** (400 mg, 0.23 mmol) in MeOH (10 mL) was treated with 1 N sodium methoxide in MeOH (2 mL) overnight. The suspension was diluted with water, neutralized with Amberlyst, and then filtered to give, after removal of the solvents in vacuo, the title compound (210 mg, 88% from **25** and 66% from **16**): mp 224 °C (decomp); $[\alpha]^{25}_D$ +129.6° (*c* 0.28, H_2O); R_f 0.31 (*n*-butanol–acetic acid–water–pyridine, 15:3:12:10); IR (KBr) 3400 (OH), 1720 (CO); ^{1}H NMR (D_2O, 400 MHz, the A notation refers to the glucose unit bearing the carboxymethyl group) δ 3.42–3.58 (m, H2, H4), 3.58–3.85 (m, 18H, H5, H6), 3.85–3.94 (m, 5H, H3), 4.04 (t, 1H, *J* = 9.0, H3^A), 4.28 (AB, 1H, *J* = 16.5, CH_2COOH), 4.33 (AB, 1H, *J* = 16.5, CH_2COOH), 4.92–5.00 (m, 5H, H1), 5.17 (d, 1H, *J* = 3.2, H1^A); ^{13}C NMR (D_2O, 100.6 MHz) δ 60.9, 61.1 (C6), 69.9 (CH_2–COOH), 72.0, 72.30, 72.37, 72.5, 72.9, 73.1, 73.3, 73.6, 73.8, 73.90, 74.0 (C2, C3, C5), 80.9 (C2^A), 81.8, 82.1, 82.5 (C4), 100.3 (C1^A), 102.00, 102.06 (C1), 173.8 (CO); HRMS (FAB) calcd for $C_{38}H_{63}O_{32}$, 1031.3302 (M + H); found, 1031.3281.

(30) Compound **26** has been prepared by alkylation of α-CD with iodoacetic acid, and the product was used after characterization by IR, see ref 22.

Mono-2-*O*-(3-(propionylthio)propyl)-α-cyclodextrin (27). To a solution of **16** (61.5 mg, 0.06 mmol) in water (3 mL) and acetonitrile (2 mL), was added 3-mercaptopropionic acid (0.5 mL). After bubbling argon through the solution for 30 min to remove oxygen, the solution was placed under a mercury UV lamp for 18 h. TlC (CH_3CN-H_2O, 4:1) showed a new product having an R_f value of 0.11 and complete disappearance of starting material. The solution was then evaporated to dryness and washed with acetone followed by centrifugation five times (until the odor of mercaptopropionic acid was no longer present) to give the product as a colorless solid (58 mg, 85 %): $[\alpha]^{25}D$ +98.0° (*c* 1.1, DMSO); IR (KBr) 3400 (OH), 1720 (CO); ^1H NMR (DMSO-d_6, 300 MHz, the A notation refers to the glucose unit bearing the propionylthiopropyl group) δ 1.73 (quint, 2H, *J* = 6.7, thiopropyl), 2.40–2.70 (m, 6H, propionylthiopropyl), 3.17 (dd, 1H, *J* = 2.1, 9.5, H2^A), 3.20–3.48 (m, 12H, H2, H4), 3.47–3.70 (m, 20H, H5, H6, O–CH_2), 3.70–3.81 (t, 5H, H3), 3.90 (t, 1H, *J* = 9.0, H3^A), 4.42–4.58 (m, 6H, OH6), 4.78 (m, 5H, H1), 4.94 (m, 1H, H1^A), 5.30–5.80 (m, 11H, OH3, OH2); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 26.5, 27.6, 29.8, 34.9 (propionylthiopropyl), 60.1 (C6), 70.4 (C5^A), 71.9, 72.2 (C2, C5, O-CH_2), 72.8 (C3^A), 73.4 (C3), 80.6 (C2^A), 82.2, 82.4 (C4), 82.7 (C4^A), 100.1 (C1^A), 102.1 (C1), 173.4 (CO); FAB-MS *m*/*z* 1141 (M + Na).

Mono-2-*O*-(2-(benzylamino)ethyl)-β-cyclodextrin (28). The same procedure described for compound **23** was used to give the product as a solid. Starting from compound **22** (100 mg, 0.08 mmol), 70 mg (65%) of **28** was obtained after reversed-phase column chromatography. The column was eluted with water (200 mL) and then with MeOH 10% (300 mL): mp 210 °C (decomp); $[\alpha]^{25}D$ +106° (*c* 0.30, H_2O); R_f 0.60 (*n*-PrOH–H_2O–NH_4OH, 6:2:1); ^1H NMR (D_2O, 300 MHz, the A notation refers to the glucose bearing the (benzylamino)ethyl group) δ 2.85–3.05 (m, 2H, CH_2N), 3.48–4.15 (m, H2, H3, H4, H5, H6, O–CH_2–CH_2N), 4.80–5.15 (m, H1, benzyl), 5.20 (d, 1H, *J* = 3.1, H1^A), 7.28–7.50 (m, 5H, Ph); ^{13}C NMR (D_2O, 100.6 MHz) δ 46.2 (CH_2N), 51.3 (benzyl), 59.1, 59.3 (C6), 68.0 (O–CH_2–CH_2N), 70.7, 70.8, 71.0, 71.1 (C2, C5), 72.2, 72.4 (C3), 79.3 (C2^A), 79.8, 79.9, 80.0, 80.1, 80.2 (C4), 98.8 (C1^A), 100.8, 101.0 (C1), 127.7, 127.8, 127.9, 128.1, 128.2, 135.0 (Ph); HRMS (FAB) calcd for $C_{51}H_{82}O_{35}N$, 1268.4668 (M + H); found, 1268.4719.

Mono-2-*O*-(2-aminoethyl)-β-cyclodextrin (29). The hydrogenolysis of **28** (60 mg, 0.04 mmol) gave compound **29** (60 mg, 100%): mp 214 °C (decomp); $[\alpha]^{25}D$ +122.9° (*c* 0.41, H_2O); R_f 0.16 (*n*-PrOH–H_2O–NH_4OH, 6:2:1); ^1H NMR (D_2O, 400 MHz, the A notation refers to the glucose unit bearing the aminoethyl group) δ 3.12–3.32 (m, 2H, CH_2N), 3.57 (dd, 1H, *J* = 3.1, 10.2, H2^A), 3.57–3.78 (m, H2, H4), 3.82–4.18 (m, H3, H5, H6, O–CH_2–CH_2N), 4.12 (t, 1H, *J* = 9.6, H3^A), 5.08–5.16 (m, 6H, H1), 5.27 (d, 1H, *J* = 3.2, H1^A); ^{13}C NMR (D_2O, 100.6 MHz) δ 40.2 (CH_2N), 61.0 (C6), 68.9 (O–CH_2–CH_2N), 72.1, 72.6, 72.7 (C2, C5), 73.2, 73.5, 73.8 (C3), 80.8 (C2^A), 81.8 (C4), 100.1 (C1^A), 102.6 (C1); HRMS (FAB) calcd for $C_{44}H_{76}O_{35}N$, 1178.4198 (M + H); found, 1178.4236.

Mono-6-*O*- and Mono-2-*O*-(3-azidopropyl)-α-cyclodextrins. To a solution of dried α-cyclodextrin (2.4 g, 2.46 mmol) in DMSO (15 mL) was added lithium hydride (40 mg, 2 equiv). The mixture was stirred under argon until the solution became clear (24 h). To this solution was added 1-iodo-3-azidopropane (780 mg, 1.5 equiv). The mixture stood at 70 °C for 10 h. TLC on silica gel (CH_3CN-H_2O, 4:1) showed three products corresponding to dialkyl, monoalkyl-α-cyclodextrin, and starting material. After usual workup, the residue was applied to a silica gel column (4 × 40 cm). Elution with CH_3CN-H_2O, 9:1, removed the dialkyl derivative. Monoalkyl derivative and starting material were eluted with CH_3CN-H_2O, 4:1. The pure fractions of monoalkyl-α-cyclodextrin were combined and then concentrated in vacuo to give a solid. The ^{13}C NMR spectra showed that the alkylation had occurred at the C-2 and C-6 positions in almost the same ratio (650 mg, 25%).

Mono-6-*O*- and mono-2-*O*-(4-azidobutyl)-α-cyclodextrins. Essentially the same procedure was used to give the product as a mixture of C2 and C6 isomers, yield 32%.

Mono-6-*O*- and Mono-2-*O*-(5-azidopentyl)-α-cyclodextrins 30 and 31. Essentially the same procedure was used to give the product as a mixture of C2 and C6 isomers, yield 30%. The treatment of 630 mg of the above mixture with *tert*-butyldimethylsilyl chloride in DMF containing imidazole (20 h) gave after usual workup and purification on silica gel column ($CHCl_3$–MeOH, 15:1 to 9:1) three fractions corresponding to pentakis(6-*O*-*tert*-butyldimethylsilyl)mono-6-*O*-(5-azidopentyl)-α-CD (**30**, 180 mg, 17%), hexakis(6-*O*-*tert*-butyldimethylsilyl)mono-2-*O*-(5-azidopentyl)-α-CD (**31**, 160 mg, 15%), and a mixture of **30** and **31** (320 mg, 31%).

Data for **30**: mp 250 °C (decomp); $[\alpha]^{25}D$ +78.6° (*c* 1.0, $CHCl_3$); R_f 0.30 ($CHCl_3$–MeOH, 8:1); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.04 (s, 36H, (CH_3), 0.88 (s, 54H, (*t*-Bu), 1.32–1.47 (m, 2H, pentyl), 1.52–1.75 (m, 4H, pentyl), 3.16 (dd, *J* = 9.8, 2.0, 1H, H6a), 3.25 (t, *J* = 6.8, 2H, CH_2-N_3), 3.40 (dd, *J* = 10.0, 2.2), 3.45–4.12 (m, H2, H3, H4, H5, H6, pentyl), 4.80–4.92 (m, 6H, H1), 5.70–6.50 (m, OH2, OH3); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −5.4, −5.3 (CH_3), 18.1, 18.2 (*t*-Bu) 22.5 (pentyl), 25.7, 25.8, (*t*-Bu), 28.4, 28.5, 51.0 (pentyl), 61.7, 61.9 (C6), 71.9, 72.0, 72.1, 72.4, 72.7, 73.0, 73.7, 74.1, 74.3 (C2, C3, C5, pentyl), 80.4, 80.7, 81.1, 81.3, 81.6, 81.9 (C4), 100.4, 101.46, 101.5, 102.0, 102.9 (C1); FAB-MS *m*/*z* 1790 (M + Na).

Data for **31**: mp 255 °C (decomp); $[\alpha]^{25}D$ +94.0° (*c* 1.0, $CHCl_3$); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.04 (s, 36H, (CH_3), 0.88 (s, 54H, (*t*-Bu), 1.42 (quint, 2H, *J* = 7.5, pentyl), 1.63 (quint, 2H, *J* = 7.7, pentyl), 1.70–1.88 (m, 2H, pentyl), 3.27 (t, 2H, *J* = 6.9, CH_2-N_3), 3.35–4.18 (m, H2, H3, H4, H5, H6, pentyl), 4.75–5.20 (m, H1, OH3), 5.60–6.10 (m, OH2); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −5.4, −5.3, −5.2 (CH_3) 18.2, 18.3 (*t*-Bu), 23.0 (pentyl), 25.7, 25.8, (*t*-Bu), 28.4, 28.8, 51.4 (pentyl), 61.7 (C6), 72.1, 72.3, 72.4, 72.7, 72.8, 73.3, 73.7, 74.0, 74.4 (C2, C3, C5, pentyl), 80.3, 80.7, 80.8, 80.9, 81.2 (C4), 101.5, 101.7, 101.9, 102.2, 102.4 (C1); FAB-MS *m*/*z* 1790 (M + Na).

The same product was obtained by alkylation of **18**. To a solution of **18** (740 mg, 0.44 mmol) in DMF (15 mL) was added sodium hydride (30 mg, 60% mineral oil) followed, 2 h later, by 1-iodo-5-azidopentane (220 mg, 2 equiv). The reaction mixture was stirred overnight and then quenched with MeOH. After the usual workup, the crude product was purified on a silica gel column using $CHCl_3$–MeOH, 15:1 to 9:1 as eluent, to give the product as a solid (210 mg, 26%). The spectral properties are identical to those described previously for **31**.

Mono-2-*O*-(5-azidopentyl)-α-cyclodextrin (32). Tetrabutylammonium fluoride in THF (1M, 3 mL) was added to a solution of **31** (200 mg, 0.1 mmol). The mixture was stirred under reflux for 2 h and then concentrated in vacuo. The residue was dissolved in water, and the solution was washed with chloroform, concentrated in vacuo, and then applied on a reversed-phase column (Lichroprep C18, 2 × 20 cm^2). Elution with water (500 mL), 10% MeOH (200 mL), and then 30% MeOH (150 mL) gave **32** (100 mg, 80%): mp 180 °C (decomp); $[\alpha]^{25}D$ +113.2° (*c* 0.22, H_2O); R_f 0.29 (CH_3CN-H_2O, 4:1); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 400 MHz, the A notation refers to the glucose unit bearing the azidopentyl group) δ 1.20–1.40 (m, 2H, pentyl), 1.45–1.65 (m, 4H, pentyl), 3.20–3.52 (m, H2, H4, CH_2N_3, H_2O), 3.52–3.84 (m, 25H, H3, H5, H6, pentyl), 3.84–3.97 (m, 1H, H3^A), 4.45–4.65 (m, 6H, OH6), 4.75–4.82 (m, 6H, H1), 5.40–6.60 (m, 11H, OH2, OH3); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 22.8, 28.2, 29.0, 50.7, (pentyl), 60.1 (C6), 71.1 (pentyl), 72.0, 72.1, 72.2, 72.3, 72.6, 72.8, 73.2, 73.4, 73.5, 73.7 (C2, C3, C5), 79.5 (C2^A), 80.9, 81.6, 82.0, 82.1, 82.5 (C4), 101.90, 101.96, 102.11, 102.16 (C1); HRMS (FAB) calcd for $C_{41}H_{70}O_{30}N_3$, 1084.4044 (M + H); found, 1084.3997.

Mono-2-*O*-(5-aminopentyl)-α-cyclodextrin (33). A. From 32: The azide **32** (86.6 mg, 0.08 mmol) was subjected to reduction as described for compound **14** to give after purification on a reversed-phase column (elution with 500 mL of water) the amine **33** (68 mg, 80%): mp 195 °C (decomp); $[\alpha]^{25}D$ +117.6° (*c* 0.34, H_2O); R_f 0.12 (*n*-PrOH–H_2O–NH_4OH, 6:2:1); ^1H NMR (D_2O, 300 MHz) δ 1.67–1.80 (m, 2H, pentyl), 1.88–2.05 (m, 4H, pentyl), 3.16 (t, *J* = 6.8, 2H, CH_2-NH_2), 3.65–4.10 (m, 38H, H2, H3, H4, H5, H6, pentyl), 4.98–5.08 (m, 6H, H1); ^{13}C NMR (D_2O, 75.5 MHz) δ 20.5, 24.8, 26.9, 37.7 (pentyl), 58.7, 58.8 (C6), 69.80, 69.84, 69.9, 70.0., 70.1, 70.3, 70.4, 70.8, 71.6, 71.7, 71.8 (C2, C3, C5, pentyl), 77.2 (C2^A), 78.9, 79.5, 79.6,

79.8 (C4), 99.3 ($C1^A$), 99.6, 99.7, 99.9 (C1); HRMS (FAB) calcd for $C_{41}H_{72}O_{30}N$, 1058.4139 (M + H); found, 1058.4062.

B. From 20: The aldehyde **20** (120 mg, 0.11 mmol) was subjected to ozonolysis and reductive amination with benzylamine as described for **23** to give the corresponding (benzylamino)pentyl ether (86 mg, 66%): mp 190 °C (decomp); $[\alpha]^{25}D$ +123.3° (*c* 0.21, H_2O); ^1H NMR (D_2O, 400 MHz) δ 1.30–1.80 (m, 6H, pentyl), 2.50 (m, 2H, CH_2–NH_2), 3.40–4.18 (m, H2, H3, H4, H5, H6, $-CH_2O$), 4.95–5.22 (m, H1, benzyl), 7.30–7.65 (m, Ph); ^{13}C NMR (D_2O, 100.6 MHz) δ 23.8, 28.8, 29.4, 48.3 (pentyl), 52.8 (benzyl), 61.0 (C6), 72.1 ($-CH_2O$), 72.5, 72.7, 72.9, 73.0 (C2, C5), 73.8, 74.2, 74.3 (C3), 80.2 ($C2^A$), 82.0, 82.1, 82.8 (C4), 101.0 ($C1^A$), 102.4 (C1), 127.5, 128.0, 129.4, 129.5, 139.5 (Ph); HRMS (FAB) calcd for $C_{48}H_{78}O_{30}N$, 1148.4608 (M + H); found, 1148.4654.

Hydrogenolysis of the above compound, as described for **23**, gave **33** as a solid (in quantitative yield). The spectral properties are the same as described above.

Mono-2-*O*-(3-azidopropyl)-β-cyclodextrin (34). To a solution of dried β-cyclodextrin (2.4 g, 2.11 mmol) in DMSO (15 mL) was added lithium hydride (34 mg, 2 equiv). The mixture was stirred under argon until the solution became clear (24 h). To this solution was added 1-iodo-3-azidopropane (670 mg, 1.5 equiv). The mixture was allowed to stand at 70 °C for 10 h. TLC on silica gel (CH_3CN–H_2O, 4:1) showed three products corresponding to dialkyl; monoalkyl-β-cyclodextrin, and starting material. After usual workup, the residue was applied on a silica gel column (4 × 40 cm^2). Elution with CH_3CN–H_2O, 9:1, removed the dialkyl derivative. The monoalkyl derivative was eluted with CH_3CN–H_2O, 4:1. The pure fractions of 2-*O*-(3-azidopropyl)-β-cyclodextrin were combined and then concentrated in vacuo to give a solid (640 mg, 25%): mp 210 °C (decomp); $[\alpha]^{25}D$ +141.3° (*c* 0.22, MeOH); R_f 0.19 (CH_3CN–H_2O, 4:1); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 300 MHz, the A notation refers to the glucose unit bearing the azidopropyl group) δ 1.68–1.85 (m, 2H, propyl), 3.00–3.48 (m, H2, H4, CH_2–N_3, H_2O), 3.49–3.90 (m, 30H, H3, H5, H6, propyl), 4.40–4.60 (m, 7H, OH6), 4.78–4.90 (m, 6H, H1), 4.95–5.05 (m, 1H, $H1^A$), 5.60–6.10 (m, 13H, OH2, OH3); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 28.9, 47.6 (propyl), 60.0 (C6), 68.9 (propyl), 71.9, 72.1, 72.3, 72.5 (C2, C5), 72.7, 73.1 (C3), 80.8 ($C2^A$), 81.6, 81.7 (C4), 82.2 ($C4^A$), 100.2 ($C1^A$), 101.9, 102.0 (C1); HRMS (FAB) calcd for $C_{45}H_{75}O_{35}N_3$, 1240.4079 (M + Na); found, 1240.3967. Anal. Calcd for $C_{45}H_{75}O_{35}N_3 \cdot 7H_2O$: C, 40.20; H, 6.62; N, 3.12. Found: C, 40.05; H, 5.88; N, 3.10.

Mono-2-*O*-(4-azidobutyl)-β-cyclodextrin (35). Essentially the same procedure was used to give the product as a colorless solid, yield 25%: mp 224 °C (decomp); $[\alpha]^{25}D$ +127.1° (*c* 0.22, H_2O); R_f 0.20 (CH_3CN–H_2O, 4:1); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 300 MHz, the A notation refers to the glucose unit bearing the azidobutyl group) δ 1.50–1.65 (m, 4H, butyl), 3.22 (dd, 1H, *J* = 3.3, 10.0, $H2^A$), 3.22–3.48 (m, H2, H4, CH_2–N_3, H_2O), 3.48–3.82 (m, 30H, H3, H5, H6, butyl), 4.45 (t, 7H, *J* = 5.2, OH6), 4.78–4.86 (m, 6H, H1), 4.96 (d, 1H, *J* = 3.5, $H1^A$), 5.55–6.00 (m, 13H, OH2, OH3); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 24.8, 26.5, 50.5 (butyl), 60.0 (C6), 71.3 (butyl), 71.8, 71.9, 72.1, 72.3, 72.5 (C2, C5), 72.8, 73.1, 73.2 (C3), 80.7 ($C2^A$), 81.6, 81.8, 81.9 (C4), 82.3 ($C4^A$), 100.4 ($C1^A$), 101.9, 102.0 (C1); HRMS (FAB) calcd for $C_{46}H_{77}O_{35}N_3$, 1254.4235 (M + Na); found, 1254.4200. Anal. Calcd for $C_{46}H_{77}O_{35}N_3 \cdot 7H_2O$: C, 40.67; H, 6.70; N, 3.09. Found: C, 40.73; H, 5.85; N, 3.15.

Mono-2-*O*-(5-azidopentyl)-β-cyclodextrin (36). A. From β-Cyclodextrin 5: Essentially the same procedure described above was used to give the product as a colorless solid, yield 30%: mp 230 °C (decomp); $[\alpha]^{25}D$ +115.5° (*c* 0.20, MeOH); R_f 0.21 (CH_3CN–H_2O, 4:1); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 300 MHz, the A notation refers to the glucose unit bearing the azidopentyl group) δ 1.28–1.40 (m, 2H pentyl), 1.47–1.60 (m, 4H, pentyl), 3.21 (dd, 1H, *J* = 3.3, 9.7, $H2^A$), 3.21–3.48 (m, H2, H4, CH_2-N_3, H_2O), 3.48–3.82 (m, 30H, H3, H5, H6, pentyl), 4.47 (t, 7H, *J* = 5.3, OH6), 4.78–4.87 (m, 6H, H1), 4.96 (d, 1H, *J* = 3.3, $H1^A$), 5.55–6.00 (m, 13H, OH2, OH3); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 22.5, 28.0, 28.8, 50.6 (pentyl), 60.0 (C6), 71.7 (pentyl), 71.8, 72.1, 72.3, 72.5 (C2, C5), 72.8, 73.1 (C3), 80.7 ($C2^A$), 81.6, 81.8 (C4), 82.3 ($C4^A$), 100.4 ($C1^A$), 101.9, 102.0 (C1); HRMS (FAB) calcd for $C_{47}H_{79}O_{35}N_3$, 1268.4392 (M + Na); found, 1268.4441. Anal. Calcd for $C_{47}H_{79}O_{35}N_3 \cdot 6H_2O$: C, 41.68; H, 6.72; N, 3.10. Found: C, 41.62; H, 6.52; N, 3.20.

B. From Mono-2-*O*-(5-chloropentyl)-β-cyclodextrin: Treatment of β-cyclodextrin (1.8 g, 1.58 mmol) in DMSO (15 mL) with lithium hydride (25 mg, 2 equiv) and then with 1-iodo-5-chloropentane (740 mg, 2 equiv) as described for **34** gave after chromatographic separation (CH_3CN–H_2O, 9:1, then 4:1) pure 2-*O*-(5-chloropentyl)-β-cyclodextrin as a solid (480 mg, 25%): mp 208 °C (decomp); $[\alpha]^{25}D$ +122.9° (*c* 0.24, DMSO); R_f 0.20 (CH_3CN–H_2O, 4:1); ^1H NMR (DMSO-d_6, 400 MHz, the A notation refers to the glucose unit bearing the chloropentyl group) δ 1.35–1.62 (m, 6H, pentyl), 3.20 (dd, 1H, *J* = 3.8, 9.8, $H2^A$), 3.25–3.40 (m, H2, H4, CH_2–Cl, H_2O), 3.50–3.70 (m, 27H, H3, H5, H6), 3.70–3.80 (m, 3H, H3A, pentyl), 4.35–4.45 (m, 7H, OH6), 4.78–4.85 (m, 6H, H1), 4.95 (d, 1H, *J* = 3.8, $H1^A$), 5.55–5.90 (m, 13H, OH2, OH3); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 23.5, 29.3, 32.6, 46.2 (pentyl), 60.8 (C6), 72.2 (pentyl), 72.5, 72.6, 72.9, 73.1, 73.3 (C2, C5), 73.6, 73.9, 74.0 (C3), 81.5 ($C2^A$), 82.4, 82.6, 83.1 (C4), 101.2 ($C1^A$), 102.7, 102.8 (C1); FAB-MS *m*/*z* 1261 (M + Na).

Treatment of the above compound (150 mg) in DMSO (10 mL) with sodium azide (40 mg, 5 equiv) for 20 h at 90 °C followed by concentration in vacuo and filtration on a short silica gel column using CH_3CN–H_2O, 4:1, as eluent gave **36** as a solid (140 mg, 92%). The spectral properties are the same as described above.

Mono-2-*O*-(3-aminopropyl)-β-cyclodextrin (37). The azide **34** (100 mg, 0.08 mmol) was subjected to reduction as described for compound **14** to give after purification on reverse-phase column (stepwise elution with 500 mL of water and then 300 mL of 5% aqueous MeOH) the amine **37** (60 mg, 61%): mp 210 °C (decomp); $[\alpha]^{25}D$ +137.6° (*c* 0.25, H_2O); R_f 0.22 (*n*-butanol–acetic acid–water–pyridine, 15:3:12:10); ^1H NMR (D_2O, 300 MHz, the A notation refers to the glucose unit bearing the aminopropyl group) δ 1.82–1.96 (m, 2H, propyl), 2.95–3.05 (m, 2H, propyl), 3.43–3.52 (m, 1H, $H2^A$), 3.43–4.09 (m, 43H, H2, H3, H4, H5, H6, propyl), 5.04–5.10 (m, 6H, H1), 5.18–5.24 (m, 1H, $H1^A$); ^{13}C NMR (D_2O, 75.5 MHz) δ 27.0, 35.8 (propyl), 58.6 (C6), 68.0 (propyl), 69.9, 70.1, 70.2, 70.3 (C2, C5), 71.3, 71.4 (C3), 78.7 ($C2^A$), 79.4, 79.6 (C4), 79.7 ($C4^A$), 98.1 ($C1^A$), 100.0, 100.1 (C1); HRMS (FAB) calcd for $C_{45}H_{78}O_{35}N$, 1192.4354 (M + H); found, 1192.4405.

Mono-2-*O*-(4-aminobutyl)-β-cyclodextrin (38). Essentially the same procedure was used to give the product as a colorless solid, yield 80%: mp 203 °C (decomp); $[\alpha]^{25}D$ +136.4° (*c* 0.25, H_2O); R_f 0.28 (*n*-butanol–acetic acid–water–pyridine, 15:3:12:10); ^1H NMR (DMSO-d_6, 300 MHz, the A notation refers to the glucose unit bearing the aminobutyl group) δ 1.30–1.70 (m, 4H, butyl), 2.56–2.75 (m, 2H, butyl), 3.00–3.85 (m, 44H, H2, H3, H4, H5, H6, butyl), 4.35–4.58 (m, 7H, OH6), 4.78–4.88 (m, 6H, H1), 4.95 (d, 1H, *J* = 2.5, $H1^A$), 5.60–6.00 (m, 13H, OH2, OH3); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 26.8, 27.5, 40.4 (butyl), 60.0, 60,10, 60.11 (C6), 71.7 (butyl), 71.9, 72.0, 72.2, 72.3, 72.5 (C2, C5), 73.0, 73.2, 73.4 (C3), 80.6 ($C2^A$), 81.60, 81.67 (C4), 82.3 ($C4^A$), 100.4 ($C1^A$), 101.9, 102.0 (C1); HRMS (FAB) calcd for $C_{46}H_{80}O_{35}N$, 1206.4510 (M + H); found, 1206.4498.

Mono-2-*O*-(5-aminopentyl)-β-cyclodextrin (39). Essentially the same procedure was used to give the product as a colorless solid: mp 205 °C (decomp); $[\alpha]^{25}D$ +131.5° (*c* 0.20, H_2O); R_f 0.31 (*n*-butanol–acetic acid–water–pyridine, 15:3:12:10); ^1H NMR (DMSO-d_6, 300 MHz, the A notation refers to the glucose unit bearing the aminopentyl group) δ 1.24–1.55 (m, 6H, pentyl), 2.52–2.68 (m, 2H, pentyl), 3.20 (dd, 1H, *J* = 2.8, 9.9, $H2^A$), 3.22–3.85 (m, 43H, H2, H3, H4, H5, H6, pentyl), 4.78–4.88 (m, 6H, H1), 4.94 (d, 1H, *J* = 3.0, $H1^A$); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 22.4, 28.9, 30.0, 40.0 (pentyl), 59.8 (C6), 71.7, 72.0, 72.3, 72.6 (C2, C5, pentyl), 73.0, 73.1 (C3), 80.5 ($C2^A$), 81.40, 81.44, 81.5, 81.6 (C4), 82.1 ($C4^A$), 100.3 ($C1^A$), 101.7, 101.9, 102.0 (C1); HRMS (FAB) calcd for $C_{47}H_{82}O_{35}N$, 1220.4667 (M + H); found, 1220.4746.

Hepta(2-*O*-benzyl)mono-6-*O*-(5-azidopentyl)-β-cyclodextrin (41). To a solution of **40**[26] (1.5 g, 0.85 mmol) in DMF (20 mL) was added sodium hydride (60 mg, 60% mineral oil).

The mixture was stirred for 2 h at room temperature and then 1-iodo-5-azidopentane (250 mg, 1.0 mmol) was added. After stirring for 20 h, MeOH was added to decompose excess hydride, and the residue obtained after usual workup was purified by silica gel column chromatography (CH_2Cl_2–MeOH, 15:1 to 10:1) to give the product as a solid (520 mg, 32%): mp 170 °C (decomp); $[\alpha]^{25}D$ +162.0° (*c* 0.50, $CHCl_3$); R_f 0.50 (CH_2Cl_2–MeOH, 8:1); IR (KBr) 3400 (OH), 2070 (N_3); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.20–1.52 (m, 6H, pentyl), 3.05–4.15 (m, H2, H3, H4, H5, H6, pentyl), 4.60–5.12 (m, H1, benzyl), 7.20–7.51 (m, Ph); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 23.1, 28.4, 28.9, 51.2 (pentyl), 61.1, 61.4 (C6), 68.6 ($C6^A$), 70.3 ($C5^A$), 71.0 (pentyl), 71.3, 71.4, 71.5, 71.6 (benzyl), 73.6, 73.9 (C2, C5), 78.0, 78.1, 78.2, 78.3, 78.4 (C3), 82.5, 83.2, 83.4, 83.5, 83.8, 84.1 (C4), 101.4, 101.6, 101.7, 102.1 (C1), 128.0, 128.3, 128.8, 137.3, 137.5 (Ph); FAB-MS *m/z* 1898 (M + Na).

Mono-6-*O*-(5-aminopentyl)-β-cyclodextrin (42). A solution of **41** (380 mg, 0.2 mmol) was hydrogenated in the presence of palladium hydroxide (500 mg) at 120 psi for 2 days and then filtered through a bed of Celite which was washed with MeOH. The combined filtrate were concentrated in vacuo to give the product as a solid, which was further purified by reverse-phase column chromatography (elution with water 200 mL) to give the pure amine (180 mg, 72%): mp 195 °C (decomp); $[\alpha]^{25}D$ +162.3° (*c* 0.17, H_2O); R_f 0.31 (*n*-butanol–acetic acid–water–pyridine, 15:3:12:10); ^1H NMR (D_2O, 400 MHz, the A notation refers to the glucose unit bearing the aminopentyl group) δ 1.40–1.55 (m, 2H, pentyl), 1.62–1.80 (m, 4H, pentyl), 3.05 (t, 2H, *J* = 7.3, pentyl), 3.55–3.78 (m, H2, H4), 3.80–4.12 (m, H3, H5, H6, pentyl), 4.72–4.95 (m, 6H, H1), 5.12 (d, 1H, *J* = 2.6, $H1^A$); ^{13}C NMR (D_2O, 100.6 MHz) δ 23.1, 27.3, 28.9, 40.1 (pentyl), 60.0 (C6), 69.5 ($C6^A$), 71.4 ($C5^A$), 71.7 (pentyl), 72.6 (C5), 72.8 (C2), 73.8 (C3), 81.8 (C4), 102.4 ($C1^A$), 102.6 (C1); FAB-MS *m/z* 1220 (M + H).

Mono-2-*O*-allyl-6-monoazido-6-deoxy-α-cyclodextrins (43), Mono-2-*O*-allyl-6,6′-diazido-6,6′-dideoxy-α-cyclodextrins (44), and Mono-2-*O*-allyl-6,6′,6″-triazido-6,6′,6″-trideoxy-α-cyclodextrins (45). To a solution of dried **16** (740 mg, 0.73 mmol) in DMF (30 mL) were added lithium azide (358 mg, 10 equiv), triphenylphosphine (574 mg, 3 equiv), and carbon tetrabromide (728 mg, 3 equiv). The addition of the latter caused a mildly exothermic reaction, and the solution turned yellow. The reaction was stirred under argon at room temperature for 6 h. TLC on silica gel (CH_3CN–H_2O, 4:1) showed three major products having R_f values of 0.68, 0.54, and 0.40, corresponding respectively to **45**, **44**, and **43**, in addition to other minor products. After addition of MeOH (5 mL), the brown solution was concentrated to about 3 mL by rotary evaporation under reduced pressure and then applied on a silica gel column (4 × 40 cm^2), eluting with CH_3CN–H_2O, 92:8 (1 L), 9:1 (1.5 L), and then 85:15 (1.5 L). The pure fractions were combined and then concentrated in vacuo to give **43** (200 mg, 26%), **44** (260 mg, 33%), and **45** (214 mg, 27%).

Data for **43**: mp 175 °C (decomp); $[\alpha]^{25}D$ +153° (*c* 0.1, H_2O); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 400 MHz, the A notation refers to the glucose unit bearing the allyl group; the X notation refers to the glucose units bearing the azide group; X = A, B, C, D, E, or F) δ 3.20–3.46 (m, H2, H4, $H6^X$), 3.50–3.70 (m, 18H, H5, H6), 3.70–3.88 (m, 5H, H3), 3.88–3.98 (m, 1H, $H3^A$), 4.15 (dd, 1H, *J* = 12.8, 5.8, allyl), 4.28 (dd, 1H, *J* = 12.7, 5.7, allyl), 4.33–4.60 (m, 5H, OH6), 4.74–5.02 (m, 6H, H1), 5.15 (dd, 1H, *J* = 10.4, 1.8, allyl), 5.28 (dd, 1H, *J* = 17.3, 1.8, allyl), 5.32–5.80 (m, 11H, OH2, OH3), 5.80–5.92 (m, 1H, allyl); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 51.3 ($C6^X$), 60.0, 60.3 (C6), 70.1, 70.4 ($C5^X$), 71.8, 71.9, 72.1, 72.2, 72.3 (C2, C5, allyl), 72.9, 73.2, 73.3 (C3), 79.3, 79.6 ($C2^A$), 82.10, 82.16, 82.2, 82.3, 82.4 (C4), 82.70, 82.75 ($C4^A$), 83.21, 83.28 ($C4^X$), 101.1 ($C1^A$), 101.8, 101.90, 101.93, 102.0, 102.2 (C1), 117.6, 117.7 (allyl), 134.71, 134.78, 134.8 (allyl); HRMS (FAB) calcd for $C_{39}H_{63}O_{29}N_3$, 1038.3625 (M + H); found, 1038.3556. Anal. Calcd for $C_{39}H_{63}O_{29}N_3 \cdot 4H_2O$: C, 42.20; H, 6.40; N, 3.78. Found: C, 42.16; H, 6.23; N, 3.90.

Data for **44**: mp 172 °C (decomp); $[\alpha]^{25}D$ +131° (*c* 0.1, H_2O); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 400 MHz, The A notation refers to the glucose unit bearing the allyl group; the X notation refers to the glucose units bearing the azide group; X = A, B, C, D, E, or F) δ 3.20–3.46 (m, H2, H4, $H6^X$, H_2O), 3.48–3.85 (m, 23H, H3, H5, H6), 3.85–3.98 (m, 1H, $H3^A$), 4.12–4.22 (m, 1H, allyl), 4.24–4.30 (m, 1H, allyl), 4.32–4.70 (m, 4H, OH6), 4.71–5.05 (m, 6H, H1), 5.15 (dd, 1H, *J* = 10.3, 1.8, allyl), 5.28 (dd, 1H, *J* = 17.3, 1.8, allyl), 5.38–5.79 (m, 11H, OH2, OH3), 5.80–5.92 (m, 1H, allyl); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 51.3 ($C6^X$), 60.0, 60.3 (C6), 70.0, 70.1, 70.33, 70.36 ($C5^X$), 71.7, 71.8, 72.0, 72.1, 72.2, 72.3, 72.4, 72.7, 72.8, 72.9, 73.2 (C2, C3, C5, allyl), 79.2, 79.5 ($C2^A$), 82.1, 82.2, 82.50, 82.53, 82.6, 82.7, 82.8, 83.0, 83.1, 83.3 (C4), 99.9, 100.1, 100.2 ($C1^A$), 101.6, 101.7, 101.8, 101.9, 102.0, 102.1, 102.2 (C1), 117.6, 117.7 (allyl), 134.72, 134.77, 134.8 (allyl); HRMS (FAB) calcd for $C_{39}H_{62}O_{28}N_6$, 1063.3690 (M + H); found, 1063.3764.

Data for **45**: mp 168 °C (decomp); $[\alpha]^{25}D$ +110° (*c* 0.11, MeOH); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 400 MHz, The A notation refers to the glucose unit bearing the allyl group; the X notation refers to the glucose units bearing the azide group; X = A, B, C, D, E, or F) δ 3.20–3.45 (m, H2, H4, $H6^X$, H_2O), 3.50–3.86 (m, 23H, H3, H5, H6), 3.86–3.97 (m, 1H, $H3^A$), 4.12–4.21 (m, 1H, Hd), 4.24–4.30 (m, 1H, allyl), 4.35–4.73 (m, 3H, OH6), 4.73–5.08 (m, 6H, H1), 5.15 (dd, 1H, *J* = 10.3, 1.8, allyl), 5.28 (dd, 1H, *J* = 17.3, 1.8, allyl), 5.38–5.75 (m, 11H, OH2, OH3), 5.79–5.95 (m, 1H, allyl); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 51.3, 51.4 ($C6^X$), 60.0, 60.2 (C6), 69.8, 70.3, 70.5, 71.9, 72.3, 72.7, 72.8, 73.2 (C2, C3, C5, allyl), 79.2, 79.4 ($C2^A$), 82.1, 82.6, 82.8, 83.1, 83.3 (C4), 99.9, 100.1 ($C1^A$), 101.7, 102.0 (C1), 117.6, 117.7 (allyl), 134.5, 134.7, 134.8 (allyl); HRMS (FAB) calcd for $C_{39}H_{61}O_{27}N_9$, 1088.3755 (M + H); found, 1088.3861.

Mono-2-*O*-allyl-6-monoazido-6-deoxy-β-cyclodextrins (46) and Mono-2-*O*-allyl-6,6′-diazido-6,6′-dideoxy-β-cyclodextrins (47). Essentially the same procedure was used, starting from **22** (560 mg, 0.47 mmol), to give 2-*O*-allyl-6-azido-6-deoxy-β-cyclodextrins **46** (210 mg, 36%), 2-*O*-allyl-6,6′-diazido-6,6′-dideoxy-β-cyclodextrins **47** (130 mg, 22%), and a small amount of the triazido derivative **48**.

Data for **46**: mp 200 °C (decomp); $[\alpha]^{25}D$ +135.1° (*c* 0.22, MeOH); R_f 0.38 (CH_3CN–H_2O, 4:1); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 400 MHz; the A notation refers to the glucose unit bearing the allyl group; the X notation refers to the glucose units bearing the azide group; X = A, B, C, D, E, or F) δ 3.20–3.82 (m, H2, H3, H4, H5, H6), 4.18 (dd, 1H, *J* = 12.7, 5.3, allyl), 4.28 (dd, 1H, *J* = 12.8, 5.7, allyl), 4.40–4.65 (m, OH6), 4.78–5.05 (m, 7H, H1), 5.16 (dm, 1H, *J* = 10.3, allyl), 5.28 (dm, 1H, *J* = 17.3, allyl), 5.60–6.00 (m, OH2, OH3, allyl); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 52.0 ($C6^X$), 60.8 (C6), 71.1 ($C5^X$), 72.6, 73.0, 73.1, 73.3, 73.4, 73.9 (C2, C3, C5, allyl), 80.6 ($C2^A$), 82.4, 82.7, 83.1, 83.4 (C4), 83.8 ($C4^A$), 101.1 ($C1^A$), 102.5, 102.6, 102.8 (C1), 118.7 (allyl), 135.5 (allyl); FAB-MS *m/z* 1200 (M + H).

Data for **47**: mp 195 °C (decomp); $[\alpha]^{25}D$ +126.5° (*c* 0.27, MeOH); R_f 0.54 (CH_3CN–H_2O, 4:1); IR (KBr) 3400 (OH), 2100 (N_3); ^1H NMR (DMSO-d_6, 400 MHz; the A notation refers to the glucose unit bearing the allyl group; the X notation refers to the glucose units bearing the azide group; X = A, B, C, D, E, or F) δ 3.20–3.82 (m, H2, H3, H4, H5, H6), 4.18 (dd, 1H, *J* = 12.7, 5.3, allyl), 4.28 (dd, 1H, *J* = 12.8, 5.7, allyl), 4.40–4.65 (m, OH6), 4.78–5.05 (m, 7H, H1), 5.16 (dm, 1H, *J* = 10.3, allyl), 5.28 (dm, 1H, *J* = 17.3, allyl), 5.60–6.00 (m, OH2, OH3, allyl); ^{13}C NMR (DMSO-d_6, 100.6 MHz) δ 52.0 ($C6^X$), 60.8, 61.0 (C6), 70.9, 71.1, 71.2 ($C5^X$), 72.6, 72.9, 73.1, 73.3, 73.4, 73.7, 73.9 (C2, C3, C5, allyl), 80.4, 80.6 ($C2^A$), 82.5, 82.7, 83.4 (C4), 83.8, 84.3 ($C4^A$), 101.2 ($C1^A$), 102.5, 102.8, 103.1 (C1), 118.7, 135.5 (allyl); FAB-MS *m/z* 1225 (M + H).

Per-O-acetylated Mono-6-azido-6-deoxy-2-*O*-methoxycarbonylmethyl-α-cyclodextrins (49). The acetylation of **41** (320 mg, 0.3 mmol), ozonolysis, and then oxidation were effected as described for compound **16**. Protection of the acid derivative, dissolved in MeOH, with diazomethane in ether followed by purification on silica gel column (CH_2Cl_2–MeOH, 50:1 to 40:1 as eluent) gave **49** (320 mg, 64%): ^1H NMR ($CDCl_3$, 400 MHz, the A notation refers to the glucose unit bearing the methoxycarbonylmethyl group) δ 1.80–2.34 (m, CH_3–CO), 3.31 (dd, *J* = 2.3, 9.9, $H2^A$), 3.55–3.90 (m, H4, CH_2N_3), 3.92–4.55 (m, H5, H6, CH_2COOH), 4.62–4.82 (m, H2), 4.82–5.20

(m, H1), 5.25–5.78 (m, H3); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 20.3, 20.6, 20.8 (CH_3CO), 51.1, 51.2, 51.4 (CH_2N_3), 51.80, 51.86 (CO_2CH_3), 62.9, 63.1, 63.2 (C6), 68.2, 68.3 ($-CH_2-CO_2CH_3$), 68.5–73.6 (C2, C3, C5), 75.7–79.8 ($C2^A$, C4), 95.6–99.4 (C1), 168.9–170.2 (CO).

Mono-6-azido-6-deoxy-2-*O*-carboxymethyl-α-cyclodextrins (50). Deprotection of **49** (130 mg, 0.07 mmol) with 1 N NaOH in MeOH at room temperature overnight gave, after purification on reverse-phase column, stepwise elution with H_2O (350 mL), and then 10% MeOH (200 mL), the title compound **50** as a colorless solid (64 mg, 80%): mp 210 °C (decomp); R_f 0.32 (*n*-butanol–acetic acid–water–pyridine, 15:3:12:10); $[\alpha]^{25}_D$ +127.0° (*c* 0.20, H_2O); IR (KBr) 3400 (OH), 2100 (N_3), 1720 (CO); ^{1}H NMR (D_2O, 400 MHz, the A notation refers to the glucose unit bearing the carboxymethyl group) δ 3.52–3.78 (m, H2, H4, CH_2N_3), 3.78–4.05 (m, H3, H5, H6), 4.12–4.19 (m, $H3^A$), 4.41 (AB, 1H, J = 17.4, CH_2COOH), 4.48 (AB, 1H, J = 17.4, CH_2COOH), 5.05–5.12 (m, 5H, H1), 5.25–5.32 (m, 1H, $H1^A$); ^{13}C NMR (D_2O, 100.6 MHz) δ 52.1 (CH_2N_3), 61.1, 61.2 (C6), 71.4 (CH2–COOH), 72.1–74.2 (C2, C3, C5), 80.8, 81.0 ($C2^A$), 82.0–83.8 (C4), 100.5 ($C1^A$), 102.2 (C1), 174.2 (CO); HRMS (FAB) calcd for $C_{38}H_{61}O_{31}N_3$, 1078.3187 (M + Na); found, 1078.3147.

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Supporting Information Available: Copies of ^{1}H NMR and ^{13}C NMR spectra of **2–4**, **14**, **16**, **20**, **24**, **26**, **29**, **33**, **36**, **39**, **42**, and **46** (25 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.

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