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Carbohydrate Research 324 (2000) 75–96

CARBOHYDRATE RESEARCH

Synthesis and silica-based immobilization of monofunctionalized cyclomaltoheptaose derivatives for enantioselective HPLC

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Received 11 June 1999; accepted 11 October 1999

Abstract

Heptakis(6-*O*-*tert*-butyldimethylsilyl-2,3-di-*O*-methyl)cyclomaltoheptaose (6-TBDMS-2,3-Me-β-CD) and heptakis(2,3,6-tri-*O*-methyl)cyclomaltoheptaose (per-Me-β-CD) were monofunctionalized by introduction of a 5-cyanopentyl group attached to one of the O-2, O-3 or O-6 positions and subsequent reduction with lithium aluminum hydride to give the corresponding mono-*O*-(ω-aminohexyl) derivatives. Alternatively, after attachment of a 7-octenyl group and further epoxidation the corresponding mono-ω-epoxyoctyl derivatives of 6-TBDMS-2,3-Me-β-CD were obtained. The mono-*O*-(ω-aminohexyl) derivatives were immobilized by reaction with glycidoxypropyl and 'aldehyde' silica, whereas aminopropyl silica was used for the immobilization of the monoepoxyoctyl derivatives. The immobilized cyclodextrin derivatives were partially evaluated as chiral stationary phases in high-performance liquid chromatography (HPLC) and micro-HPLC.

Keywords: Monofunctionalized cyclomaltoheptaose (β-cyclodextrin) derivatives; Migration of TBDMS group; Immobilized chiral stationary phases; Enantioselective HPLC

1. Introduction

The synthesis of monosubstituted cyclomaltooligosaccharides (cyclodextrins, CDs), in which a single hydroxy group is reacted to introduce a desired functionality, has become important over the last years. Recently, D'Souza and co-workers [1] have reviewed strategies for selective modification of cyclodextrins including methods for regioselective monofunctionalization. One of the reasons for monosubstitution is the increase of water solubility in comparison with the native cyclodextrins, which is favorable for enhancing the bioavailability of included drugs [2]. By introduction of biological markers to monofunctionalized cyclodextrins, specific site delivery of pharmacologically active compounds has been faced [3]. Monosubstituted derivatives were also used in the synthesis of defined cyclodextrin di- and oligomers, which exhibit stronger binding constants toward guest molecules than the corresponding monomers due to cooperative inclusion effects [4]. Furthermore, applications as artificial models for enzyme mimetics [5] and supramolecular sensors [6] have been reported.

Native as well as derivatized cyclodextrins are predominant as selectors in the majority of enantioselective separation techniques. In gas

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0008-6215/00/$ - see front matter
PII: S0008-6215(99)00280-3

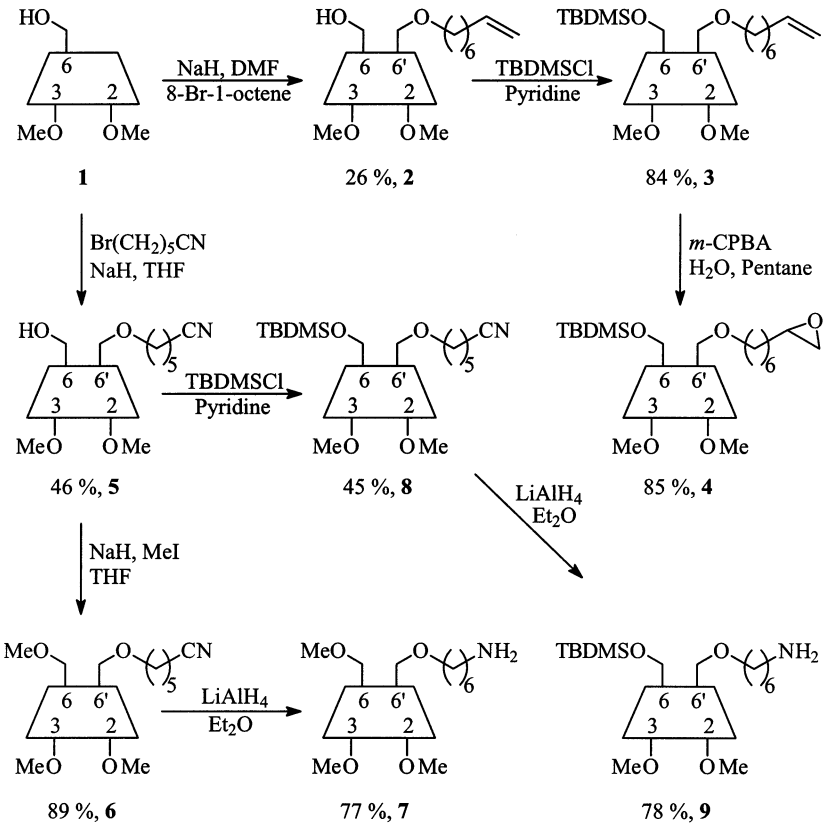
chromatography (GC), hydrophobic cyclodextrin derivatives were successfully introduced in 1988 [7]. Their superior properties as compared with previous chiral stationary phases initiated the development of a great number of CD derivatives to investigate the influence of the substitution pattern on enantioselectivity [8]. Because of the simple means of preparation and general applicability, permethylated β-CD took a leading role, but the importance of other selectively substituted CD derivatives, especially $6^{I\text{-}VII}$-hepta-*O*-*tert*-butyldimethylsilyl-$2^{I\text{-}VII}$,$3^{I\text{-}VII}$-tetradeca-*O*-methylcyclomaltoheptaose (6-TBDMS-2,3-Me-β-CD) should not be underestimated [9].

Enantioselective GC is limited to the separation of volatile and thermally stable compounds with up to approximately 20 carbon atoms [10]. In the case of highly polar or thermally labile compounds, other separation techniques are preferred. Currently applied methods are liquid chromatography (LC) [11], supercritical fluid chromatography (SFC) [12], electrochromatography (EC) [13] and capillary electrophoresis (CE) [14]. For most of these applications, it is inevitable to immobilize the CD derivative to the surface of the fused silica capillary or to polymeric material like functionalized silica. For LC applications, immobilization of the cyclodextrins was generally performed in a statistical reaction [15]. In order to obtain batch-to-batch reproducibility in chromatographic separations, it is advantageous to prepare derivatives with a defined substitution pattern via monofunctionalization prior to immobilization. Immobilized $2^{I\text{-}VII}$,$3^{I\text{-}VII}$,$6^{I\text{-}VII}$-heneicosa-*O*-methylcyclomaltoheptaose (per-Me-β-CD) has been widely used as the chiral stationary phase (CSP) in all chromatographic separation methods. For enantioselective high-performance liquid chromatography (HPLC), 6^{I}-deoxy-6^{I}-carboxy-$2^{I\text{-}VII}$, $3^{I\text{-}VII}$,$6^{I\text{-}VI}$-eicosa-*O*-methylcyclo-maltoheptaose (6′-deoxy-6′-carboxy-per-Me-β-CD)[1] was converted into the corresponding acyl chloride derivative and immobilized to aminopropyl silica [16]. Schurig et al. [17] prepared $2^{I\text{-}VII}$, $3^{I\text{-}VII}$,$6^{I\text{-}VI}$-eicosa-*O*-methyl-6^{I}-*O*-(oct-7-enyl)-cyclomaltoheptaose (6′-octenyl-per-Me-β-CD), which was bound to a dimethylpolysiloxane containing 10% Si–H moieties via hydrosilylation (Chirasil-Dex). Residual Si–H groups were used for immobilization of Chirasil-Dex on a fused-silica surface for open-tubular LC [17] and on unmodified silica gel for micro and conventional HPLC [18]. The same group recently reported the immobilization of 6′-octenyl-per-Me-β-CD on (mercaptopropyl)methyl silica [19]. Only one paper deals with the immobilization of monofunctionalized 6-TBDMS-2,3-Me-β-CD and its application in enantioselective LC [20]. Here, 6-TBDMS-2,3-Me-β-CD was covalently linked at O-6 by one ω-carboxyheptyl linker to aminopropyl silica by amide bond formation. In continuation of our work in the field of cyclodextrin CSPs for HPLC and SFC, we have monofunctionalized 6-TBDMS-2,3-Me-β-CD and per-Me-β-CD by the introduction of 6-aminohexyl groups into one of the O-2, O-3 or O-6 positions before immobilization to 3-glycidoxypropyl or aldehyde silica. As an alternative, the monoepoxyalkyl derivatives of 6-TBDMS-2,3-Me-β-CD were prepared and immobilized to 3-aminopropyl silica. The usefulness of these immobilized CD derivatives in enantioselective HPLC and micro-HPLC is demonstrated by the separation of several racemic drugs and atropisomers. The synthetic routes presented in this work can be considered as general approaches for the preparation of selectively modified cyclodextrin derivatives and can be extended to many other fields of application.

2. Results and discussion

For monosubstitution at O-6 (Scheme 1), we chose a strategy similar to that of Bradshaw and co-workers [21] to warrant a practical and economic separation of the desired product from oversubstituted by-products using normal phase column chromatography. Monofunctionalization reaction of **1**, obtained in three steps from β-CD by selective *tert*-butyldimethylsilylation at O-6 [22], permethylation of the secondary hydroxyl rim [23] and final desilylation [24], represented the pivotal

[1] The primed numbers in this notation refer to the unregularly substituted D-glucopyranosyl subunit.



Scheme 1. Synthesis of the O-6 monomodified 6-TBDMS-2,3-Me- and per-Me-β-CD derivatives.

step. Using potassium hydride (1.5 mol equiv) and a 10-fold excess of 8-bromo-1-octene, 26% of $2^{I\text{-}VII},3^{I\text{-}VII}$-tetradeca-*O*-methyl-$6^{I}$-*O*-(oct-7-enyl)cyclomaltoheptaose (6′-octenyl-2,3-Me-β-CD, **2**) was obtained. The residual six 6-hydroxy groups were silylated again (**3**) and, finally, the double bond of the octenyl residue was epoxidized to obtain 85% of the desired product **4**.

Monosubstituted CDs possess extremely complicated NMR spectra in accordance with the loss of C_n-symmetry. The extensive signal overlap makes an interpretation of the spectra very difficult and tedious. In addition, only a tentative estimation of the purity by evaluation of the NMR spectra is possible. For an unambiguous proof of the purity, all monomodified cyclodextrins were analyzed by matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF) using 4-hydroxy-α-cyanocinnamic acid as matrix [25]. Fig. 1 shows the MALDI-TOF mass spectra of **2**, **3** and **4**. For each compound, intense quasi molecular ions $[M+Na]^+$ and $[M+K]^+$ were detected exclusively, indicating their high purity.

For the preparation of the 6-mono-ω-aminohexyl substituted derivative of 6-TBDMS-2,3-Me-β-CD and per-Me-β-CD, 2,3-Me-β-CD (**1**) was monosubstituted by alkylation with 1-bromo-5-cyanopentane (10-fold excess) and potassium hydride (1.5-fold excess). The yield of 46% for 6^{I}-*O*-(5-cyanopentyl)-$2^{I\text{-}VII},3^{I\text{-}VII}$-tetradeca-*O*-methyl-β-CD [6′-(5-cyanopentyl)-2,3-Me-β-CD, **5**] was very high for a monofunctionalization reaction taking into account that 22% of the starting material could be recovered. Methylation of the residual hydroxy groups to **6**, followed by the reduction of the cyano group with $LiAlH_4$, furnished 6′-aminohexyl-per-Me-β-CD (**7**). Silylation of the 6-hydroxy groups with TBDMS (**8**) and subsequent reduction of the linker residue on the other hand provided 6′-(6-aminohexyl)-6*-TBDMS-2,3-Me-β-CD[2] (**9**) (Scheme 1).

[2] The asterisk (*) is used here to denote all unprimed (i.e., equally substituted) subunits.

Per-Me-β-CD with one ω-epoxyoctyl group at position 6 (6′-epoxyoctyl-per-Me-β-CD, **12**) was prepared by alkylation of 6′-monohydroxy-per-Me-β-CD (**10**) [26] with 8-bromo-1-octene and potassium hydride, followed by epoxidation of the double bond (Scheme 2).

For the introduction of a spacer residue at O-2 two pathways were pursued. First, both the 7-octenyl and the 5-cyanopentyl groups were directly attached to a single O-2 position by reaction of 6-TBDMS-β-CD (**13**) [22] with the corresponding bromide and potassium hydride (Scheme 3). In the case of the octenyl derivative **14**, the yield was 40%, recovering 31% of **13**, whereas the cyanopentyl derivative **17** was obtained in only 24% yield, but recovering 73% of the starting material. After permethylation of the residual secondary hydroxy groups, the octenyl derivative **15** was epoxidized and the cyanopentyl derivative **18** reduced with $LiAlH_4$ to obtain the desired final products **16** and **19**. Epoxidation of 2′-octenyl-6-TBDMS-β-CD (**14**) to **20** could even be carried out at room temperature without the formation of dimers, indicating that the secondary hydroxy groups are not sufficiently nucleophilic to open the epoxide ring.

The attachment of the octenyl residue at O-2 of **15** was proven by SMA [27] after catalytic hydrogenation of the double bond (Fig. 2). The major peak in the gas chromatogram was identified as the 2,3-di-*O*-methylated glucitol acetate and corresponded to the six equally substituted glucose units of

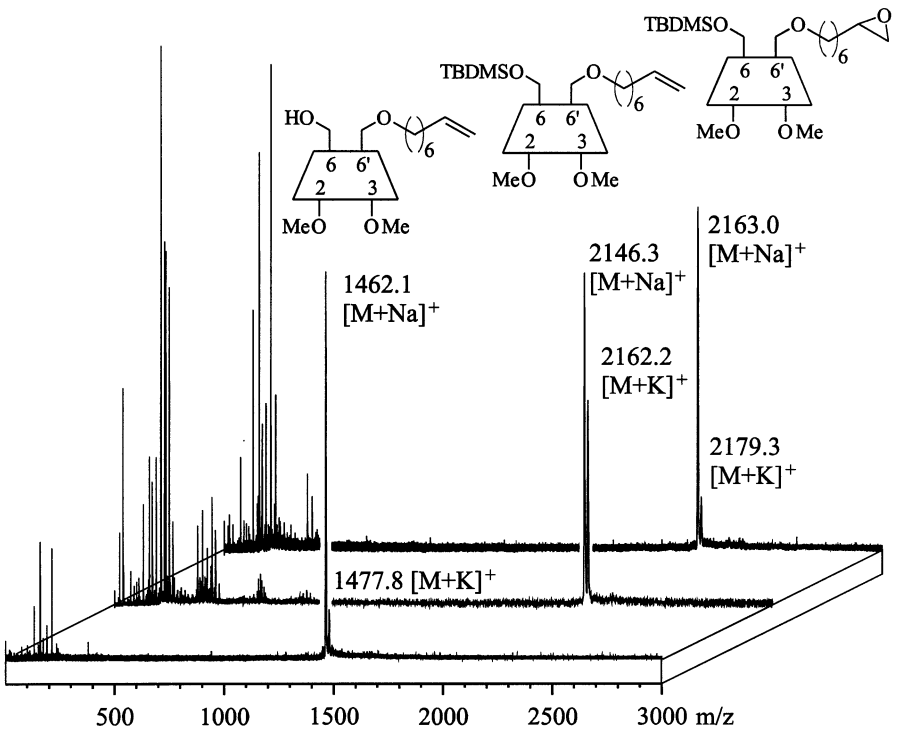
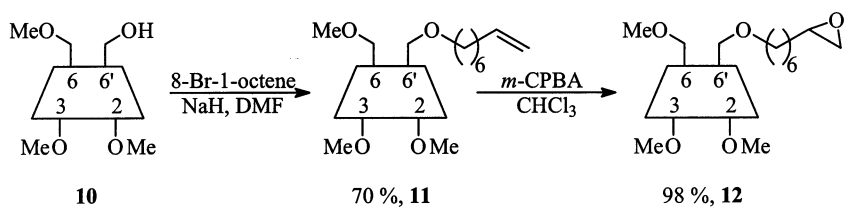
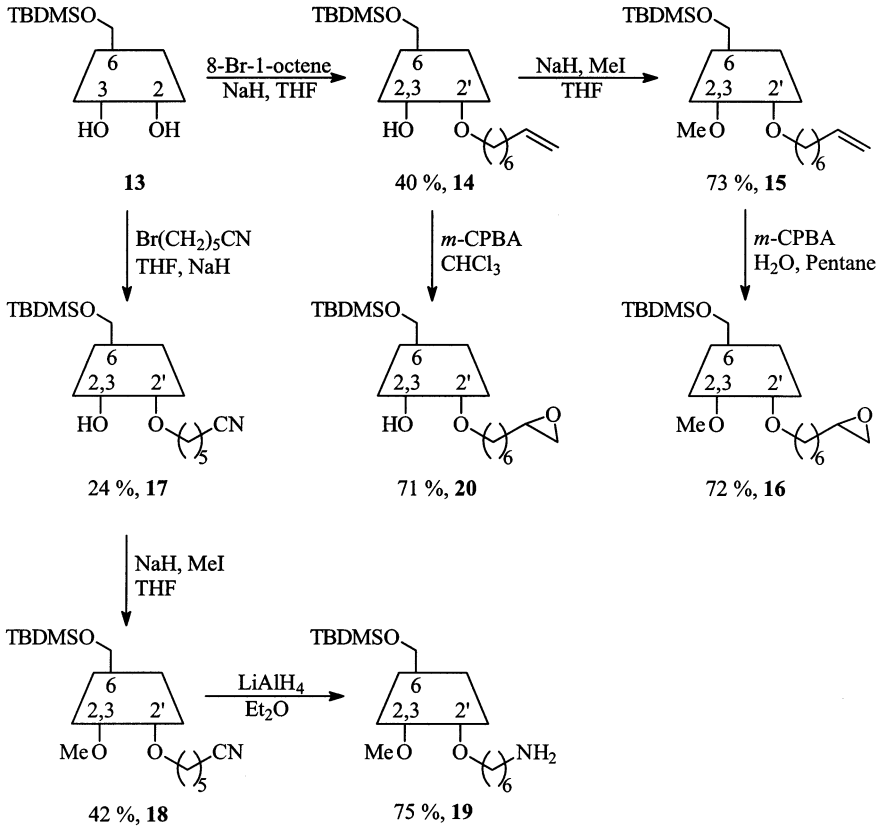


Fig. 1. MALDI-TOF mass spectra of O-6 monomodified CD derivatives: 6′-octenyl-2,3-Me-β-CD (**2**) ($C_{64}H_{112}O_{35}$, $M = 1441.6$ Da), 6′-octenyl-6*-TBDMS-2,3-Me-β-CD (**3**) ($C_{100}H_{196}O_{35}Si_6$, $M = 2127.2$ Da), 6′-epoxyoctyl-6*-TBDMS-2,3-Me-β-CD (**4**) ($C_{100}H_{196}O_{36}Si_6$, $M = 2143.2$ Da).



Scheme 2. Synthesis of per-Me-β-CD with one ω-epoxyoctyl residue attached to O-6.



Scheme 3. Synthesis of the O-2 monosubstituted 6-TBDMS-2,3-Me-β-CD derivatives by direct alkylation of 6-TBDMS-β-CD (**13**).

the monoderivatized CD derivative. The minor peak corresponded to 3-*O*-methyl-2-*O*-octyl glucitol acetate representing the monofunctionalized glucose unit. If the double bond was not hydrogenated prior to SMA, three peaks were observed in the gas chromatogram due to the fact that Markownikoff and anti-Markownikoff addition products were formed during the hydrolysis step.

During the preparation of 6-TBDMS-β-CD, 21% of $2^{I},6^{I\text{-}VII}$-octa-*O*-*tert*-butyldimethylsilyl-cyclomaltoheptaose (2′,6-TBDMS-β-CD) was obtained in 21% yield from β-CD as a side product during selective per-*tert*-butyldimethylsilylation at O-6 [20]. Following already reported reaction sequences [20], 2′,6-TBDMS-β-CD was transformed into the selectively functionalized derivative **21**, which contains a single unreacted hydroxyl group at O-2. Compound **21** was converted into the ω-alkenyl derivative **15**, which was epoxidized to give the final product **16** (Scheme 4).

Adopting the reaction pathway described by Dönnecke et al. [20], 2′,6-TBDMS-β-CD was also used as starting material for the preparation of the 6-TBDMS-2,3-Me-β-CD derivatives **22** and **23** with a single ω-alkenyl group at O-3. Epoxidation of **22** and **23** furnished the desired final products **24** and **25** (Scheme 4). Because epoxidation of the mono-ω-alkenyl derivatives can proceed from both sides of the double bond, the formation of diastereoisomeric epoxides is expected. No indication of the formation of diastereoisomers was observed in the ^{1}H NMR spectra, except for 3′-epoxypropyl-6-TBDMS-2,3-Me-β-CD (**24**), for which two dd-signals for each CH_2(epoxy)-proton appeared. As expected, the ^{13}C NMR spectrum of **24** showed two signals for epoxy-CH_2 (at 44.54, 45.06 ppm), epoxy-CH (at 50.90, 51.00 ppm) and α-CH_2 (at 74.73, 75.39 ppm), respectively. For 3′-epoxyoctyl-6-TBDMS-2,3*-Me-β-CD (**25**) two signals were found for the methylene carbon adjacent to CH(epoxy) at 32.45 and 32.47 ppm.

2′-Aminohexyl- and 3′-aminohexyl-per-Me-β-CD were prepared starting from **21** and

6^{I-VII}-hexa-*tert*-butyldimethylsilyl-$2^{I-VII},3^{I-VI}$-trideca-*O*-methylcyclomaltoheptaose (3′-OH-6-TBDMS-2,3-Me-β-CD, **30**) [20], to which a 5-cyanopentyl group was attached providing 2′-cyanopentyl-6-TBDMS-2*,3-Me-β-CD (**18**) and 3′-cyanopentyl-6-TBDMS-2,3-Me-β-CD (**31**), respectively. Desilylation to **26** and **33** and subsequent permethylation of the O-6 position furnished 2′-cyanopentyl-per-Me-β-CD (**27**) and 3′-cyanopentyl-per-Me-β-CD (**34**), which were reduced to render the O-2 and O-3 monosubstituted aminohexyl per-Me-β-CDs **28** and **35**. Reduction of **18** and **31** provided the O-2 and O-3 monosubstituted aminohexyl 6-TBDMS-2,3-Me-β-CDs **19** and **32**. Compound **27** was also transformed into the corresponding carboxylic acid **29** by treatment with ethanolic NaOH (Scheme 5).

The epoxyalkylated derivatives were covalently linked to aminopropyl silica and the aminohexyl derivatives either to 3-glycidoxypropyl silica or to aldehyde silica, which was prepared in situ inside the packed capillary by periodate cleavage of diol silica before immobilization via reductive amination [28,29] (Scheme 6). The immobilization yields were determined by elemental analysis and reached from 80 to 120 mmol immobilized CD/g modified silica. Table 1 lists the batch immobilization conditions and immobilization ra-

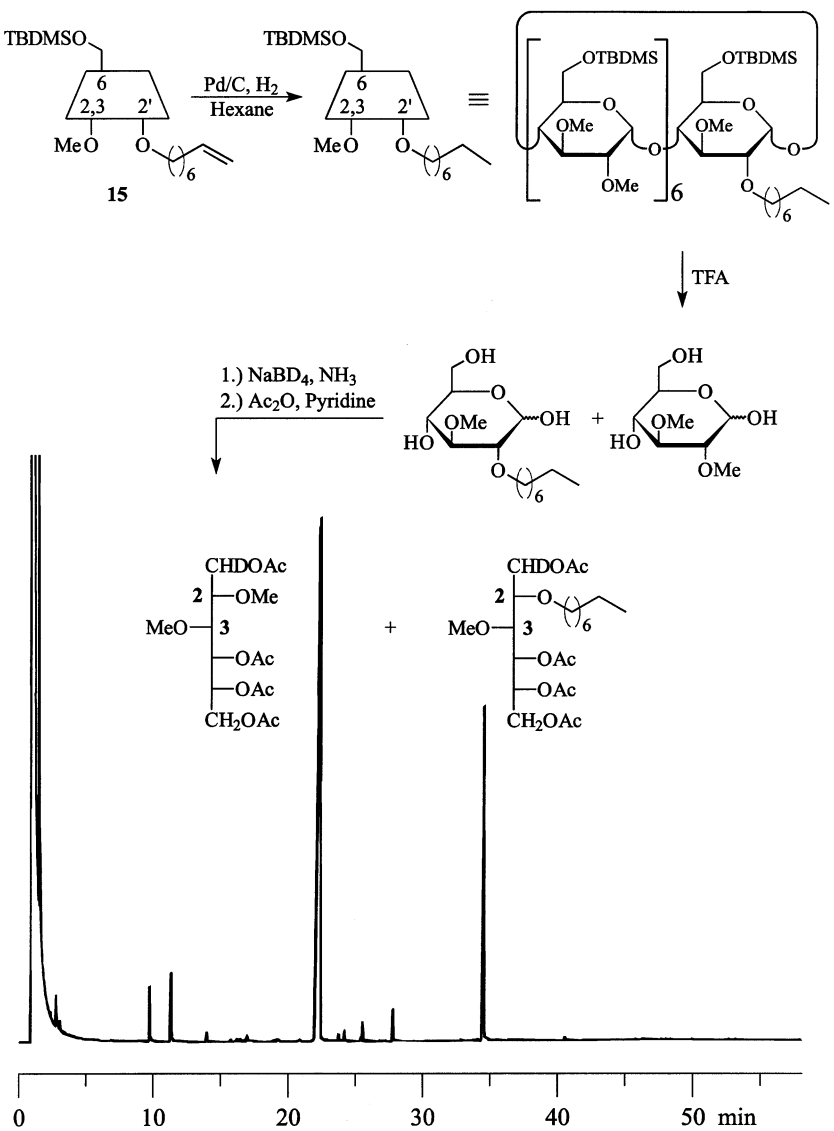
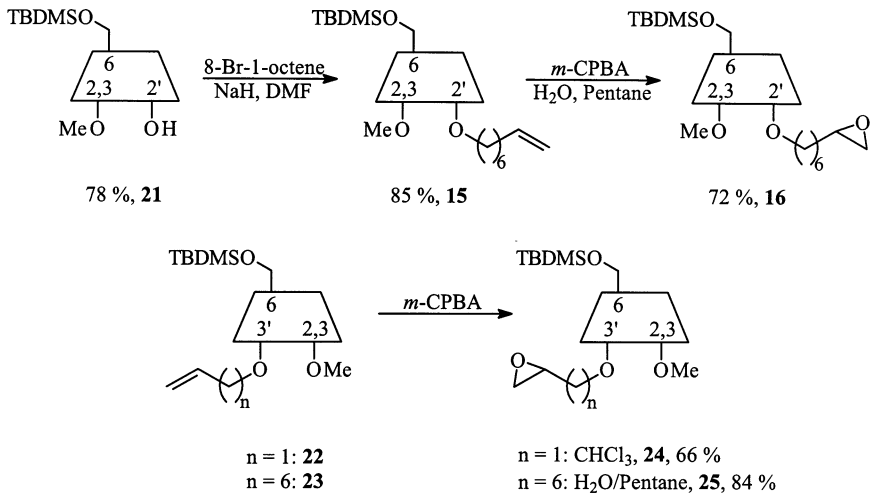


Fig. 2. Standard methylation analysis of 2′-octenyl-6-TBDMS-2*,3-Me-β-CD (**15**); GC, 25 m CPSil 8 CB; 70 °C, 1 min isothermal, 30 °C/min to 130 °C, 4 °C/min to 290 °C; on-column injection.



Scheme 4. Synthesis of O-2 and O-3 monosubstituted CD derivatives using 2′,6-TBDMS-β-CD as starting material. DTBPy, 2,6-di-*tert*-butylpyridine; TBAF, tetrabutylammonium fluoride.

tios for selected cyclodextrin derivatives. Although the batch procedure allows better control of the reaction and analysis of the product, it takes fairly large amounts of selector. The 'on-column' immobilization in the capillary is a simple method that only consumes the commercially available silica gel for packing and, in addition, small amounts (2–5 mg) of the cyclodextrin derivative, but also requires a fast and smooth reaction. The reductive amination of an amino-substituted selector to aldehyde silica seems to be an especially preferable method, which was successfully applied for α-chymotrypsin [28] and vancomycin [29].

The immobilized CD derivatives were partially evaluated as CSPs in micro-LC in the reversed phase mode. Fig. 3 shows enantiomer separations of some chiral drugs on a capillary with 6-TBDMS-2,3-Me-β-CD immobilized over an epoxyoctyl spacer in position 6 to aminopropyl silica. By decreasing the amount of organic modifier in the mobile phase the separation factor α increases, but longer retention times must be taken into account. In contrast to 6-TBDMS-2,3-Me-β-CD bonded over position O-6 by one ω-carboxyheptyl linker to aminopropyl silica by an amide bond [20], none of our numerous phases based on 6-TBDMS-2,3-Me-β-CD was able to separate neither ephedrine nor *N*-methylephedrine, although immobilization ratios were comparable. It can be concluded that the type of spacer and the bonding function play an important role in the chiral recognition, as well as in the discriminating process. Surprisingly, neither the bonding position O-2, O-3 or O-6 of the spacer molecule nor the mode of immobilization seems to influence noticeably the enantioselectivity.

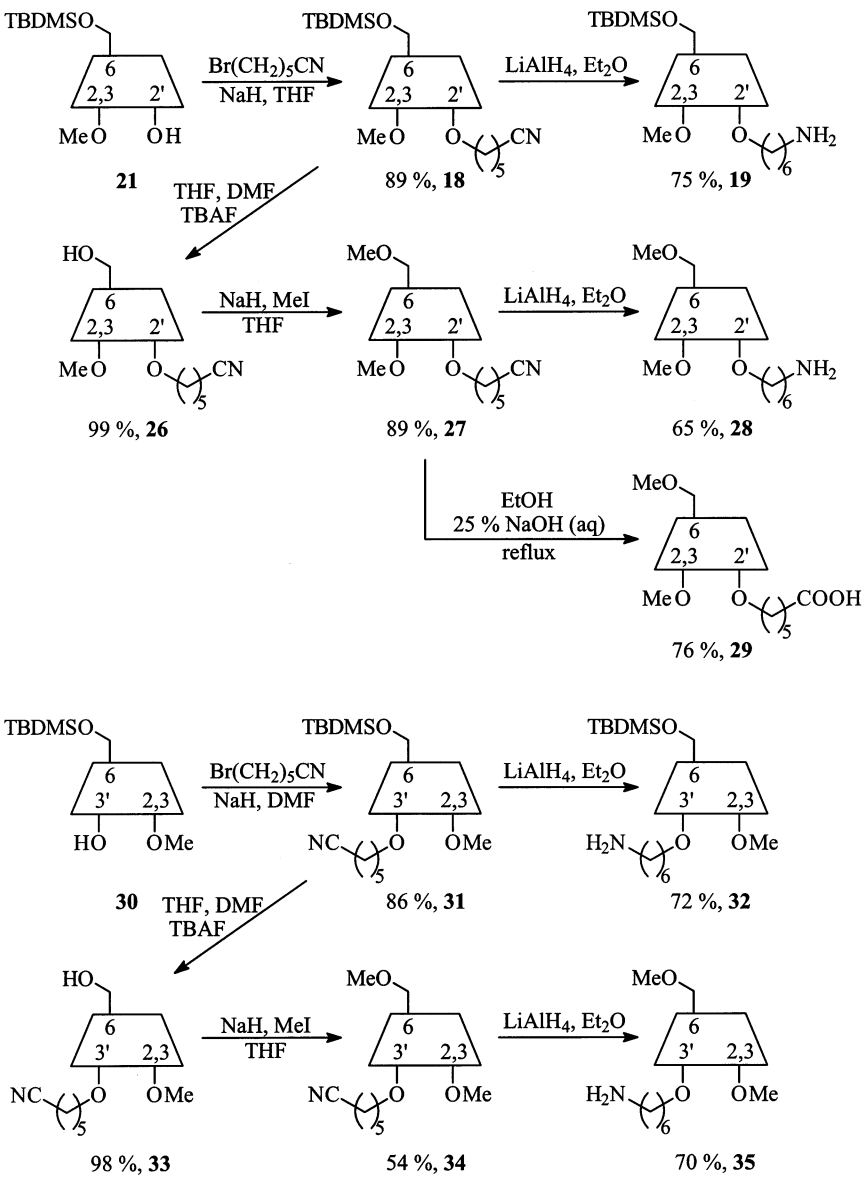
In the case of immobilized per-Me-β-CD, only the chiral support prepared by bonding **15** (with an epoxyoctyl spacer in 6-position) to aminopropyl silica was thoroughly investigated in micro-LC, as well as in conventional HPLC (25 cm × 4 mm column). We succeeded in separating quite a number of drugs (e.g., ciprofibrate, etozoline, pentobarbital, methohexital). This CSP showed enhanced recognition capabilities for atropisomeric compounds like chiral biphenyls and diazaparacyclophanes (Fig. 4). It was noted that there was almost no difference in column efficiency when the same samples were run under conventional or micro LC conditions. Although the scope of enantiomeric discrimination capability has not yet been fully evaluated, it can be concluded that, similarly to GC, the substitution pattern of the cyclodextrin derivatives and the type of linker play an important role in chiral recognition.

3. Experimental

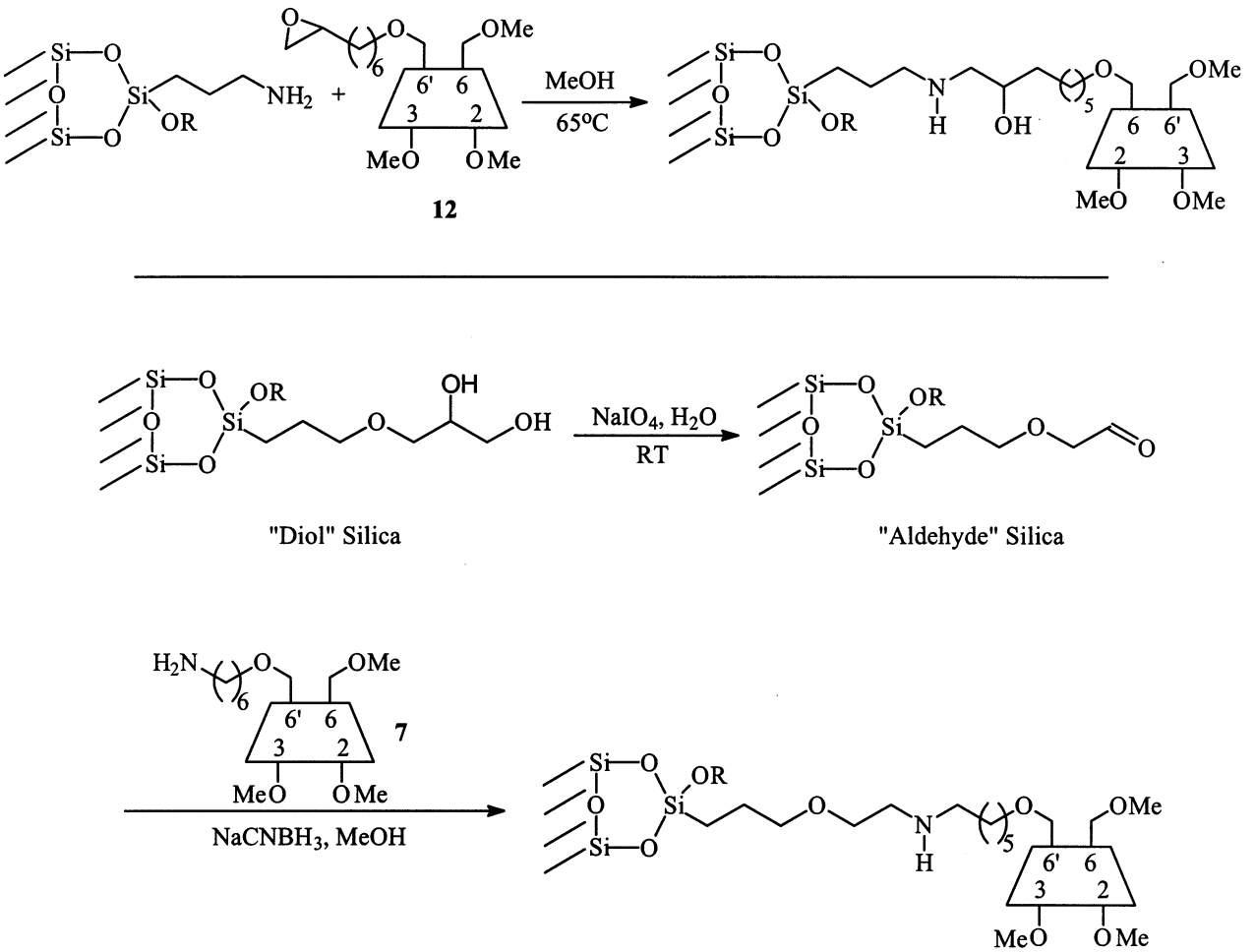
Instrumentation and general methods.—Optical rotations were measured with a Perkin–

Elmer polarimeter 341. NMR spectra (^{1}H, 400 MHz; ^{13}C, 100.62 MHz) were recorded with a Bruker WM 400 instrument. The assignment of ^{1}H and ^{13}C signals was supported by ^{1}H–^{1}H and ^{1}H–^{13}C COSY experiments. Diastereotopic protons were distinguished by *a* and *b*. Carbon and hydrogen atoms of the substituents are designated α, β, γ, etc. For example 5-cyanopentyl: -*O*-CH_2(α)–CH_2(β)–CH_2(γ)–CH_2(δ)–CH_2(ε)–CN.

The purity of synthetic products was established by NMR spectroscopy, MALDI-TOF mass spectra (Bruker Biflex instrument in the reflector mode and with 4-hydroxy-α-cyano cinnamic acid in EtOH as matrix) and thin-layer chromatography (TLC). GC–MS measurements were performed under electron impact (70 eV) conditions using a 25 m (0.25 mm ID) fused silica capillary column with CP-Sil 5 CB (Chrompack) polydimethylsiloxane phase. All reactions were monitored by TLC on Silica Gel foil 60 F_{256} (E. Merck, Darmstadt, Germany) with H_2SO_4 (10% in EtOH) detection. Amine derivatives were additionally detected by spraying with ninhydrin solution after heating. Dried solvents were purchased from Fluka, Buchs, Switzerland. Except for the epoxidations, all reactions were



Scheme 5. Synthesis of per-Me-β-CD and 6-TBDMS-2,3-Me-β-CD with one aminohexyl group attached to position O-2 and O-3, respectively.



Scheme 6. Immobilization of the synthesized cyclodextrin derivatives (e.g., per-Me-β-CD) on functionalized silica via nucleophilic ring opening (above) and reductive amination (below).

Table 1
Immobilization conditions and ratios of selected monofunctionalized cyclodextrin derivatives [a]

CD derivative	Immobilization site spacer	Excess of CD (w/w)	T (°C) solvent	Reaction time (days)	CD/modified silica [% w/w (μmol/g)]
16	C-2 epoxyoctyl	1.6	97 l-propanol	3	20.2 (90.0)
24	C-3 epoxypropyl	3.3	97 l-propanol	8	26.9 (119.9)
25	C-3 epoxypropyl	1.6	97 l-propanol	3	26.3 (121.0)
4	C-6 epoxypropyl	1.6	97 l-propanol	3	17.9 (83.5)
9	C-6 epoxypropyl	1.6	65 l-propanol	3	18.5 (87.2)
12	C-6 epoxypropyl	0.4	65 l-propanol	3	12.9 (83.4)
7	C-6 epoxypropyl	1.8	65 l-propanol	3	18.2 (120.2)

[a] The aminohexyl derivatives were bound to 3-glycidoxypropyl silica, the monoepoxyalkylated cyclodextrins to 3-aminopropyl silica.

carried out in a nitrogen atmosphere. Column chromatography was performed either at atmospheric pressure (Silica Gel 60, 70–230 mesh; E. Merck) or under flash conditions (Silica Gel 60, 230–400 mesh; E. Merck). For enantiomer separations and packing procedures, HPLC grade solvents were used. Before immobilization the cyclodextrin derivatives

were dissolved in $CHCl_3$ and freed from insoluble particles by filtration using 0.45 mm pore size filters to avoid possible plugging of the capillaries. Standard methylation analysis was carried out as described [27].

$2^{I\text{-}VII}$,$3^{I\text{-}VII}$-Tetradeca-O-*methyl*-6^{I}-O-*(oct*-7-*enyl)cyclomaltoheptaose* (**2**).—Sodium hydride (130 mg, 5.42 mmol; washed with petroleum ether) was added in three portions to a stirred solution of lyophilized 2,3-Me-β-CD (**1**) (4.6 g, 3.46 mmol) in 100 mL anhyd DMF at 0 °C. After 20 min, 5.8 mL (34.47 mmol) 8-bromo-1-octene was added dropwise and stirring was continued at 0 °C for 30 min, then at room temperature (rt) for 15 h. Excess NaH was decomposed by addition of MeOH after cooling the reaction mixture to 0 °C. The reaction product was concentrated under reduced pressure (1 Torr) and subsequently co-distilled with 1:1 toluene–1-butanol (200 mL) to remove traces of DMF. For removal of salts, the crude product was dissolved in $CHCl_3$ and

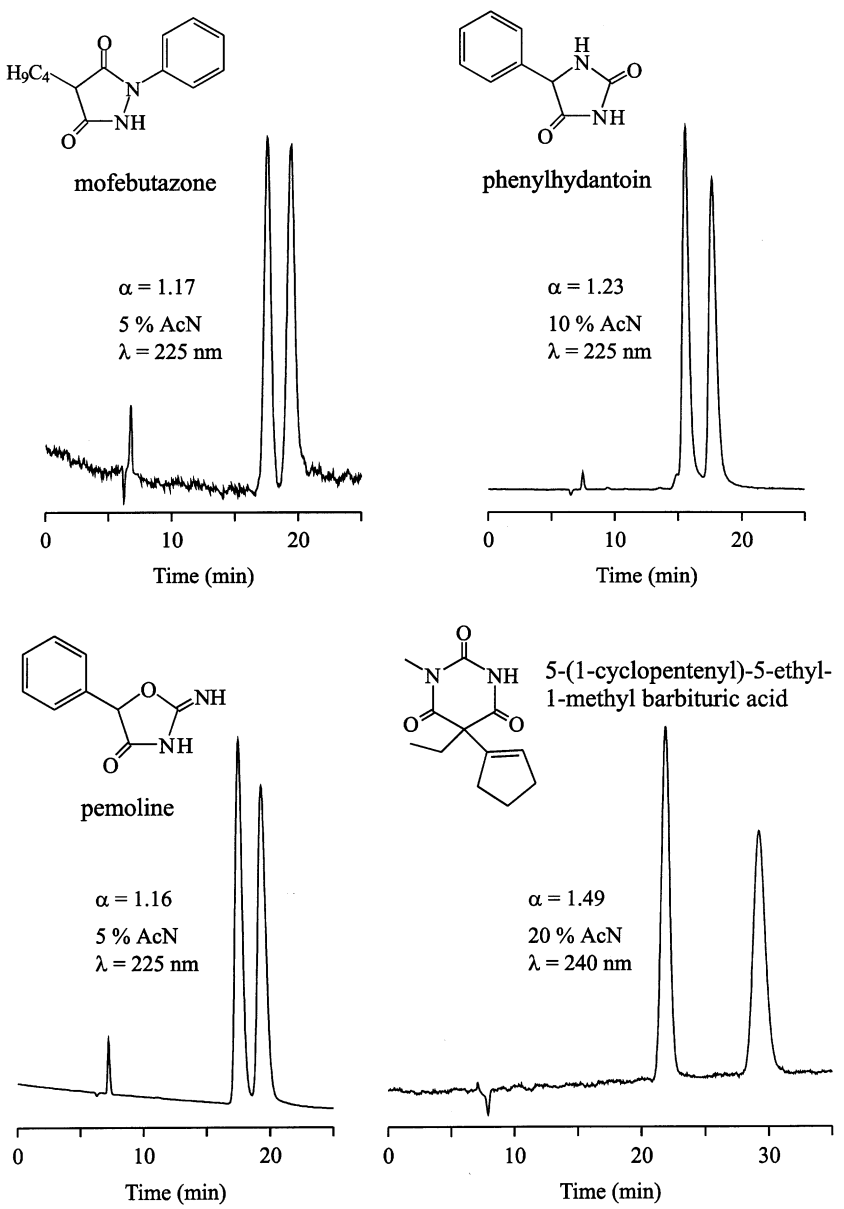


Fig. 3. Micro-HPLC separation of mofebutazone, phenylhydantoin, pemoline, and 5-(1-cyclopentenyl)-5-ethyl-1-methyl barbituric acid on 60 cm capillary (180 μm ID) packed with 6-TBDMS-2,3-Me-β-CD immobilized on aminopropyl silica over one epoxyoctyl linker at O-6; mobile phase, phosphate buffer pH 4.0/MeCN, ion strength = 0.1; $p = 300$ bar.

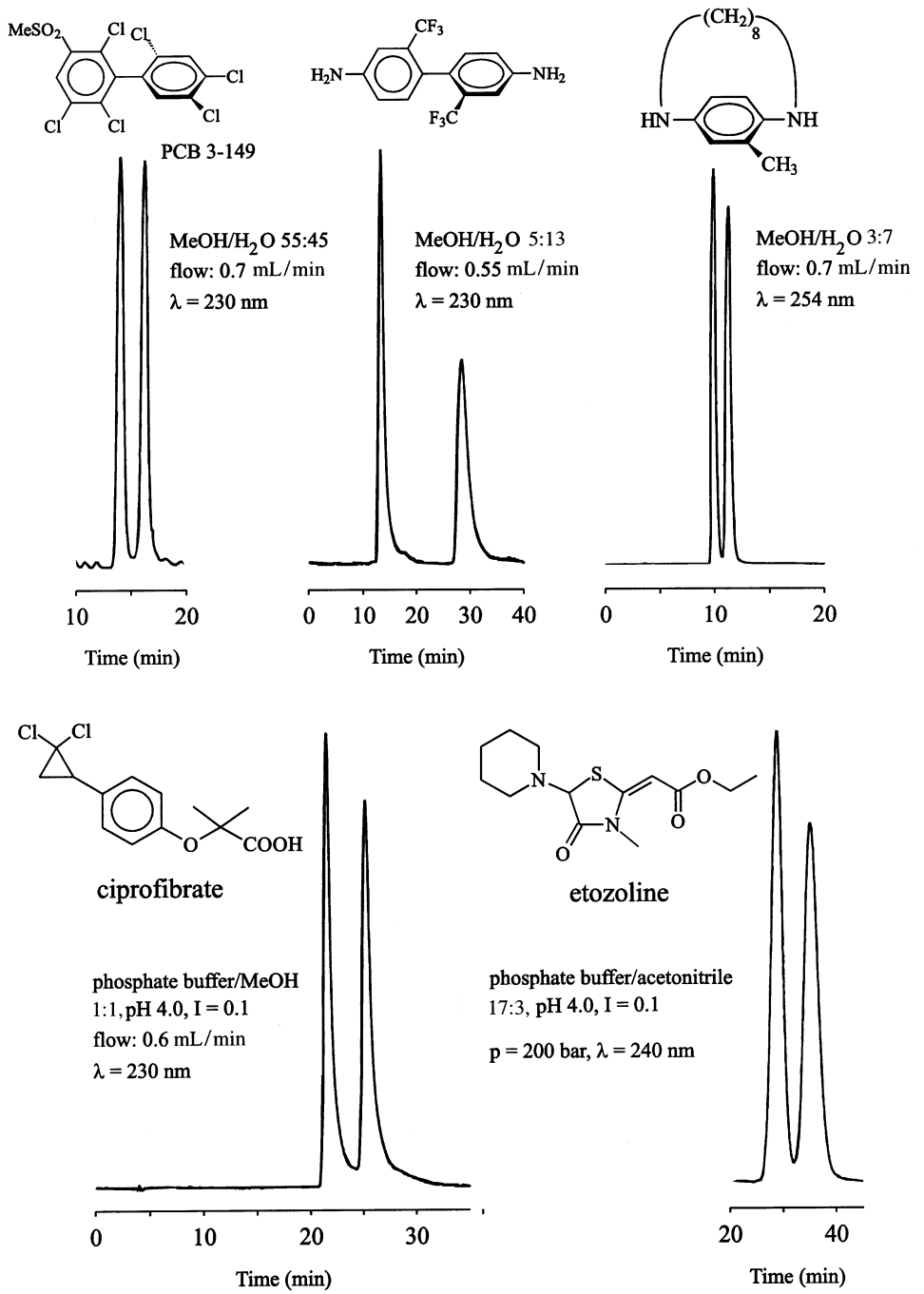


Fig. 4. HPLC enantioseparation (250 × 4 mm steel column) of PCB 3-149, bis(trifluoromethyl)benzidin, 2′-methyl-1,10-diaza[10]-paracyclophane, and ciprofibrate on per-Me-β-CD immobilized over one epoxyoctyl spacer in the O-6 position to aminopropyl silica and micro-HPLC separation of etozoline on per-Me-β-CD immobilized over one aminohexyl spacer in the O-6 position to 3-glycidoxypropyl silica (60 cm, 180 μm ID capillary).

extracted with water. The organic phase was dried over $MgSO_4$, filtered and concentrated. Flash chromatography of the residue (10:1–4:1 $CHCl_3$–MeOH, stepwise) afforded **2** (1.29 g, 0.89 mmol, 26%); $[\alpha]_D^{22}$ +138.0° (*c* 0.8, $CHCl_3$); TLC (7:1 $CHCl_3$–MeOH) R_f 0.20; ^{1}H NMR (400 MHz, MeOH-d_4): δ 5.87 (ddt, 1 H, $J_{CH_2-CH=}$ 6.6 Hz, C*H*=CH_2), 5.28–5.20 (m, 7 H, H-1), 5.04 (m, 1 H, J_E 17.3 Hz, CH=CH_2), 4.70 (m, 1 H, J_Z 10.2 Hz, CH=CH_2), 4.07–3.73 (m, 21 H, H-5,6a,6b), 3.73–3.62 (m, 7 H, H-4), 3.68, 3.56 (s, 42 H, OCH_3), 3.62–3.46 (m, 9 H, H-3, α-CH_2), 3.24–3.16 (m, 7 H, H-2), 2.12 (m, 2 H, CH_2–CH=), 1.70–1.54 (m,

2 H, β-CH_2), 1.53–1.30 (m, 6 H, γ,δ,ε-CH_2); ^{13}C NMR (100.62 MHz, MeOH-d_4): δ 140.37 (*C*H=CH_2), 115.17 (CH=*C*H_2), 99.95–99.60 (C-1), 83.84–83.45 (C-2,3), 81.14–80.71 (C-4), 73.93–72.91 (C-5), 72.68 (α-CH_2), 71.25–62.45 (C-6), 62.15–59.21 (OCH_3), 35.21 (*C*H_2–CH=), 31.08 (β-CH_2), 30.49, 30.42, 25.59 (γ-,δ-,ε-CH_2); $C_{64}H_{112}O_{35}$ 1441.57, MALDI-TOF MS: *m*/*z* 1463.0 $[M + Na]^+$, 1479.2 $[M + K]^+$.

6^{I-VI}-Hexa-O-tert-*butyldimethylsilyl-2^{1-VII},3^{I-VII}-tetradeca*-O-*methyl-6^{I}*-O-*(oct-7-enyl)-cyclomaltoheptaose* (**3**).—*tert*-Butyldimethylsilyl chloride (425 mg, 2.82 mmol) was added to a solution of freeze-dried 6′-octenyl-2,3-Me-β-CD (**2**) (317.7 mg, 0.22 mmol) in anhyd pyridine (40 mL). After 18 h stirring at rt the reaction was stopped by the addition of water. The solvent was removed by co-distillation with toluene and the residue dissolved in petroleum ether and extracted with a satd NaCl solution. The organic layer was dried over $MgSO_4$ and evaporated after filtration. Column chromatography (3:1 petroleum ether–EtOAc) furnished **3** (399.8 mg, 0.188 mmol, 85%); $[\alpha]_D^{22}$ +70.0° (*c* 0.8, $CHCl_3$); TLC (2:1 petroleum ether–EtOAc) R_f 0.35; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.76 (ddt, 1 H, $J_{CH_2-CH=}$ 6.6 Hz, CH_2–C*H*=), 5.24–5.11 (m, 6 H, H-1), 5.09 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.95 (m, 1 H, J_E 17.3 Hz, CH=CH_2), 4.90 (m, 1 H, J_Z 10.2 Hz, CH=CH_2), 4.19–3.85 (m, 7 H, H-6a), 3.65–3.61, 3.49–3.47 (s, 42 H, OCH_3), 3.78–3.39 (m, 28 H, H-3,4,5,6b), 3.39–3.27 (m, 2 H, α-CH_2), 3.14 (dd, 1 H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.7 Hz, H-2), 3.08–2.96 (m, 6 H, H-2), 2.00 (m, 2 H, CH_2–CH=), 1.62–1.44 (m, 2 H, β-CH_2), 1.40–1.31 (m, 2 H, ε-CH_2), 1.31–1.17 (m, 4 H, δ,γ-CH_2), 0.88–0.81 (s, 54 H, $SiCMe_3$), 0.03–0.06 (s, 36 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 138.94 (*C*H=CH_2), 114.23 (CH=*C*H_2), 98.51–97.97 (C-1), 82.28–81.85 (C-2,3), 79.69–78.13 (C-4), 71.46 (α-CH_2), 72.18–71.20 (C-5), 69.04, 62.45–62.25 (C-6), 61.62–58.38 (OCH_3), 33.72 (*C*H_2–CH=), 29.72 (β-CH_2), 28.91 (ε-CH_2), 28.99, 26.15 (δ,γ-CH_2), 25.96, 25.88 ($SiCMe_3$), 18.35–18.26 ($SiCMe_3$), 4.87–5.25 ($SiMe_2$); $C_{100}H_{196}O_{35}Si_6$ 2127.15, MALDI-TOF MS: *m*/*z* 2146.4 $[M + Na]^+$, 2162.2 $[M + K]^+$.

6^{I-VI}-Hexa-O-tert-*butyldimethylsilyl-6^{I}*-O-*(7-epoxyoctyl)-2^{I-VII},3^{I-VII}-tetradeca*-O-*methyl-cyclomalto-heptaose* (**4**).—To a dispersed solution of **3** (156.5 mg, 73.57 μmol) in pentane (3 mL) and water (5 mL) was added 56 mg *m*-chloroperbenzoic acid (85–95%, Aldrich) at 0 °C under stirring. After 8 days stirring at rt, the reaction mixture was diluted with additional pentane and the organic phase washed successively with 20% aq $Na_2S_2O_3$, 10% aq Na_2CO_3 (3 ×) and satd aq NaCl. The organic layer was dried over $MgSO_4$, filtered and concentrated. The crude product was chromatographed (5:2–2:1 petroleum ether–EtOAc) to obtain **4** (134.8 mg, 62.90 μmol, 85%); $[\alpha]_D^{27}$ +97.0° (*c* 1, $CHCl_3$); TLC (1:1 petroleum ether–EtOAc) R_f 0.46; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.22–5.11 (m, 6 H, H-1), 5.07 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.18–3.85 (m, 7 H, H-6a), 3.64–3.60, 3.48–3.46 (s, 42 H, OCH_3), 3.76–3.38 (m, 28 H, H-3,4,5,6b), 3.38–3.27 (m, 2 H, α-CH_2), 3.12 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 9.7 Hz, H-2), 3.07–2.97 (m, 6 H, H-2), 2.85 (m, 1 H, CH_{epoxy}), 2.70 (dd, 1 H, $^2J = {}^3J = 4.7$ Hz, CH_{2epoxy}), 2.41 (dd, 1 H, ^3J 2.5, ^2J 5.1 Hz, CH_{2epoxy}), 1.63–1.50 (m, 2 H, β-CH_2), 1.50–1.44 (m, 2 H, CH_2–CH_{epoxy}), 1.44–1.36 (m, 2 H, ε-CH_2), 1.36–1.23 (m, 4 H, δ,γ-CH_2), 0.87–0.81 (s, 54 H, $SiCMe_3$), 0.01–0.04 (s, 36 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 98.54–97.96 (C-1), 82.30–81.84 (C-2,3), 79.75–78.13 (C-4), 71.41 (α-CH_2), 72.17–71.20 (C-5), 69.04, 62.45–62.24 (C-6), 61.61–58.37 (OCH_3), 52.21 (CH_{epoxy}), 46.98 (CH_{2epoxy}), 32.43 (*C*H_2–CH_{epoxy}), 29.69 (β-CH_2), 29.32, 26.88 (γ,δ-CH_2), 26.21 (ε-CH_2), 25.95, 25.87 ($SiCMe_3$), 18.34–18.24 ($SiCMe_3$), 4.89–5.26 ($SiMe_2$); $C_{100}H_{196}O_{36}Si_6$ 2143.15, MALDI-TOF MS: *m*/*z* 2163.0 $[M + Na]^+$, 2179.0 $[M + K]^+$.

6^{I}-O-*(5-Cyanopentyl)-2^{1-VII},3^{I-VII}-tetradeca*-O-*methylcyclomaltoheptaose* (**5**).—Sodium hydride (68 mg, 2.83 mmol, washed with petroleum ether) was added to a vigorously stirred solution of lyophilized 2,3-Me-β-CD (**1**) (2.5 g, 1.88 mmol) in 90 mL anhyd THF at 0 °C. After 20 min 2.5 mL (18.74 mmol) 1-bromo-5-cyanopentane was added dropwise and stirring was continued at 0 °C for 30 min, then at rt for 12 h. Excess NaH was decomposed by the addition of MeOH after cooling

the reaction mixture to 0 °C. The crude product was concentrated under diminished pressure, dissolved in $CHCl_3$ and washed with water. The organic layer was dried over $MgSO_4$, filtered and concentrated. Column chromatography (7:1–4:1 $CHCl_3$–MeOH, stepwise) afforded pure **5** (1.22 g, 0.86 mmol, 46%); $[\alpha]_D^{20}$ +140.9° (*c* 1, $CHCl_3$); TLC (3:1 $CHCl_3$–MeOH) R_f 0.55; ^{1}H NMR (400 MHz, pyridine-d_5): δ 6.36–6.10 (m, 6 H, OH), 5.67–5.56 (m, 6 H, H-1), 5.48 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.55–4.29 (m, 11 H, H-6), 4.28–4.06 (m, 15 H, 6 × H-4, 7 × H-5, 2 × H-6), 4.04–3.87 (m, 9 H, 7 × H-3, 1 × H-4, 1 × H-6), 3.85–3.82, 3.55–3.49 (s, 42 H, OCH_3), 3.46–3.28 (m, 9 H, H-2, α-CH_2), 2.23 (t, 2 H, $J_{\delta,\varepsilon}$ 6.6 Hz, ε-CH_2), 1.59–1.46 (m, 2 H, β-CH_2), 1.46–1.28 (m, 4 H, γ,δ-CH_2); ^{13}C NMR (100.62 MHz, pyridine-d_5): δ 120.46 (CN), 99.58–99.27 (C-1), 83.06–82.75 (C-2,3), 81.44–80.38 (C-4), 73.45–71.88 (C-5), 71.00 (α-CH_2), 70.35 (C-6), 61.65–61.48 (OCH_3, C-6), 58.52–58.35 (OCH_3), 29.28 (β-CH_2), 25.74, 25.51 (γ,δ-CH_2), 16.81 (ε-CH_2); $C_{62}H_{107}NO_{35}$ 1426.52, MALDI-TOF MS: *m*/*z* 1446.7 $[M+Na]^+$, 1462.6 $[M+K]^+$.

6^I-O-(5-Cyanopentyl)-2$^{I\text{-}VII}$,3$^{I\text{-}VII}$,6$^{I\text{-}VI}$-eicosa-O-methylcyclomaltoheptaose (**6**).—Iodomethane (0.92 mL, 14.71 mmol) was added to a solution of **5** (350 mg, 245.35 μmol) and NaH (177 mg, 7.38 mmol) in dry THF at 0 °C. After 30 min the mixture was allowed to warm up to rt and stirring was continued for 3 h. Excess NaH was decomposed by the addition of MeOH after cooling the reaction mixture to 0 °C. The crude product was evaporated, dissolved in $CHCl_3$, washed with water, and dried over $MgSO_4$. After filtration and evaporation, column chromatography rendered pure **6** (328.6 mg, 217.52 μmol, 89%); $[\alpha]_D^{20}$ +143.0° (*c* 1, $CHCl_3$); TLC (20:1 $CHCl_3$–MeOH) R_f 0.47; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.16–5.01 (m, 7 H, H-1), 3.92 (dd, 1 H, $J_{5,6a}$ 3.6, $J_{6a,6b}$ 10.7 Hz, H-6a), 3.86–3.68 (m, 13 H, H-5, 6 × H-6a), 3.62–3.59, 3.48–3.47 (s, 42 H, 2,3-OCH_3), 3.67–3.39 (m, 23 H, H-3,4,6b, α-CH_2), 3.34, 3.33 (s, 18 H, 6-OCH_3), 3.19–3.10 (m, 7 H, H-2), 2.30 (t, 2 H, $J_{\varepsilon,\delta}$ 7.1 Hz, ε-CH_2), 1.69–1.54 (m, 4 H, β,δ-CH_2), 1.53–1.40 (m, 2 H, γ-CH_2); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 119.45 (CN), 98.94–98.79 (C-1), 82.10–81.95 (C-2), 81.85–81.68 (C-3), 80.58–79.82 (C-4), 71.46–69.37 (C-6, α-CH_2), 71.13–70.82 (C-5), 58.97–58.85 (6-OCH_3), 61.50–61.27, 58.62–58.37 (2,3-OCH_3), 28.81 (β-CH_2), 25.31 (γ-CH_2), 25.17 (δ-CH_2), 17.00 (ε-CH_2); $C_{68}H_{119}NO_{35}$ 1510.68, MALDI-TOF MS: *m*/*z* 1531.1 $[M+Na]^+$, 1547.0 $[M+K]^+$.

6^I-O-(6-Aminohexyl)-2$^{I\text{-}VII}$,3$^{I\text{-}VII}$,6$^{I\text{-}VI}$-eicosa-O-methylcyclomaltoheptaose (**7**).—$LiAlH_4$, 100 μL of a 1 M solution (100 mmol) in Et_2O, was added to a stirred solution of **6** (280.4 mg, 185.61 μmol) in 10 mL anhyd Et_2O. After 2 h of stirring at rt, the reaction was quenched by addition of one drop of iced water. The precipitated aluminium hydroxide was filtered off and washed intensively with Et_2O. The filtrate was dried over $MgSO_4$, filtered and concentrated. Column chromatography (7:1 $CHCl_3$–MeOH) of the residue afforded **7** (216.7 mg, 143.06 μmol, 77%); $[\alpha]_D^{20}$ +139.0° (*c* 1, $CHCl_3$); TLC (5:1 $CHCl_3$–MeOH) R_f 0.35; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.15–5.03 (m, 7 H, H-1), 3.91–3.68 (m, 14 H, H-5,6a), 3.62–3.60, 3.47–3.46 (s, 42 H, 2,3-OCH_3), 3.67–3.35 (m, 23 H, H-3,4,6b, α-CH_2), 3.34, 3.33 (s, 18 H, 6-OCH_3), 3.14 (dd, 7 H, $J_{1,2}$ 3.6, $J_{2,3}$ 9.7 Hz, H-2), 2.76–2.60 (m, 2 H, CH_2–NH_2), 1.63–1.48 (m, 2 H, β-CH_2), 1.48–1.38 (m, 2 H, ε-CH_2), 1.37–1.23 (m, 4 H, γ,δ-CH_2); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 98.95–98.65 (C-1), 82.11–81.86 (C-2), 81.81–81.73 (C-3), 80.48–79.94 (C-4), 71.41–69.40 (C-6, α-CH_2), 71.18–70.85 (C-5), 58.97, 58.91 (6-OCH_3), 61.50–61.30, 58.58–58.39 (2,3-OCH_3), 41.71 (CH_2–NH_2), 32.86 (ε-CH_2), 29.61 (β-CH_2), 26.67, 25.96 (γ,δ-CH_2); $C_{68}H_{123}NO_{35}$ 1514.71, MALDI-TOF MS: *m*/*z* 1513.9 $[M+H]^+$, 1535.5 $[M+Na]^+$, 1551.6 $[M+K]^+$.

6$^{I\text{-}VI}$ - Hexa - O - tert - butyldimethylsilyl - 6^I - O - (5 - cyanopentyl) - 2$^{I\text{-}VII}$,3$^{I\text{-}VII}$ - tetradeca - O - methylcyclomalto - heptaose (**8**).—A solution of **5** (300 mg, 210.30 μmol) and *tert*-butyldimethylsilyl chloride (288 mg, 1.91 mmol) in 10 mL dry pyridine was stirred overnight at rt and stopped by quenching with water. Pyridine was totally removed by co-distillation with toluene under vacuum. Column chromatography (2:1 petroleum ether–EtOAc) furnished **8** (201.8 mg, 95.55 μmol, 45%); $[\alpha]_D^{20}$ +95.1° (*c* 1, $CHCl_3$); TLC (1:1 petroleum

ether–EtOAc) R_f 0.59; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.23–5.10 (m, 6 H, H-1), 5.05 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.17–3.89 (m, 7 H, H-6a), 3.65–3.61, 3.49–3.47 (s, 42 H, OCH_3), 3.77–3.33 (m, 30 H, H-3,4,5,6b, α-CH_2), 3.12 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 9.7 Hz, H-2), 3.09–2.98 (m, 6 H, H-2), 2.29 (t, 2 H, $J_{\delta,\varepsilon}$ 7.1 Hz, ε-CH_2), 1.70–1.37 (m, 6 H, β,γ,δ-CH_2), 0.89–0.81 (s, 54 H, $SiCMe_3$), 0.03–0.03 (s, 36 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 119.45 (CN), 98.83–97.96 (C-1), 82.35–81.85 (C-2,3), 80.00–78.18 (C-4), 72.22–71.20 (C-5), 70.89 (α-CH_2), 69.17, 62.45–62.26 (C-6), 61.63–58.41 (OCH_3), 28.99 (β-CH_2), 25.95–25.88 (SiC*Me*$_3$), 25.47 (γ-CH_2), 25.30 (δ-CH_2), 18.36–18.26 (Si*C*Me$_3$), 17.07 (ε-CH_2), 4.87–5.24 ($SiMe_2$); $C_{98}H_{191}NO_{35}Si_6$ 2112.09, MALDI-TOF MS: m/z 2131.4 $[M + Na]^+$, 2147.6 $[M + K]^+$.

6^I-O-(6-Aminohexyl)-6$^{I\text{-}VI}$-hexa-O-tert-*butyldimethylsilyl-2$^{I\text{-}VII}$,3$^{I\text{-}VII}$-tetradeca*-O-*methylcyclomalto-heptaose* (**9**).—Compound **8** (201.8 mg, 95.36 mmol) was reduced with $LiAlH_4$ as described for **7**, yielding **9** (157.1 mg, 74.24 μmol, 78%) after column chromatography (8:1 $CHCl_3$–MeOH); $[\alpha]_D^{20}$ +98.2° (*c* 1, $CHCl_3$); TLC (6:1 $CHCl_3$–MeOH) R_f 0.36; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.24–5.10 (m, 6 H, H-1), 5.07 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.18–3.85 (m, 7 H, H-6a), 3.65–3.61, 3.49–3.47 (s, 42 H, OCH_3), 3.76–3.27 (m, 30 H, H-3,4,5,6b, α-CH_2), 3.13 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 9.7 Hz, H-2), 3.08–2.97 (m, 6 H, H-2), 2.70 (m, 2 H, C*H*$_2$–NH_2), 1.64–1.50 (m, 2 H, β-CH_2), 1.50–1.40 (m, 2 H, ε-CH_2), 1.39–1.18 (m, 4 H, γ,δ-CH_2), 0.88–0.81 (s, 54 H, $SiCMe_3$), 0.02–0.04 (s, 36 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 98.57–97.96 (C-1), 82.33–81.86 (C-2,3), 79.82–78.15 (C-4), 72.19–71.23 (C-5), 71.38 (α-CH_2), 69.06, 62.47–62.25 (C-6), 61.60–61.14, 58.85–58.37 (OCH_3), 41.66 (CH_2–NH_2), 32.63 (ε-CH_2), 29.76 (β-CH_2), 26.74, 26.07 (γ,δ-CH_2), 25.95, 25.88 (SiC*Me*$_3$), 18.34–18.25 (Si*C*Me$_3$), 4.88–5.26 ($SiMe_2$); $C_{98}H_{195}NO_{35}Si_6$ 2116.13, MALDI-TOF MS: m/z 2114.1 $[M + H]^+$, 2135.7 $[M + Na]^+$, 2151.8 $[M + K]^+$.

2$^{I\text{-}VII}$,3$^{I\text{-}VII}$,6$^{I\text{-}VI}$-Eicosa-O-*methyl-6^I*-O-*(oct-7-enyl)cyclomaltoheptaose* (**11**).—8-Bromo-1-octene (1.35 mL, 8.05 mmol) was added dropwise at 0 °C to a stirred solution of 6′-hydroxy-per-Me-β-CD (**10**) (2.27 g, 1.60 mmol), prepared by adapting the procedure of Bradshaw et al. [21], and NaH (0.2 g, 8.33 mmol) in dry DMF (350 mL). After 2 h, the ice bath was removed, allowing the reaction mixture to warm up to rt. Stirring was continued overnight. Excess NaH was then decomposed at 0 °C by the addition of MeOH, and the solvent subsequently removed by distillation under high vacuum. The residue was dissolved in EtOAc, washed with water, dried over $MgSO_4$, filtered and concentrated. Column chromatography (20:1 EtOAc–MeOH) afforded **11** (1.71 g, 1.12 mmol, 70%); $[\alpha]_D^{20}$ +139.4° (*c* 1, $CHCl_3$); TLC (20:1 EtOAc–MeOH) R_f 0.23; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.75 (ddt, 1 H, $J_{CH_2-CH=}$ 6.6 Hz, C*H*=CH_2), 5.14–5.04 (m, 7 H, H-1), 4.94 (m, 1 H, J_E 17.3 Hz, CH=CH_2), 4.88 (m, 1 H, J_Z 10.2 Hz, CH=CH_2), 3.89–3.69 (m, 14 H, H-5,6a), 3.47–3.46, 3.62–3.60 (s, 42 H, 2,3-OCH_3), 3.68–3.36 (m, 23 H, H-3,4,6b, α-CH_2), 3.34, 3.33 (s, 18 H, 6-OCH_3), 3.19–3.11 (m, 7 H, H-2), 1.99 (m, 2 H, C*H*$_2$–CH=), 1.64–1.44 (m, 2 H, β-CH_2), 1.41–1.16 (m, 6 H, γ,δ,ε-CH_2); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 138.85 (*C*H=CH_2), 114.24 (CH=*C*H_2), 98.97–98.65 (C-1), 82.10–81.88 (C-2), 81.81–81.73 (C-3), 80.50–80.03 (C-4), 71.18, 70.89 (C-5), 71.45–71.35, 69.52 (C-6, α-CH_2), 58.94, 58.90 (6-OCH_3), 61.46–61.32, 58.52–58.41 (2,3-OCH_3), 33.65 (*C*H_2–CH=), 29.62 (β-CH_2), 28.93 (ε-CH_2), 28.82 (γ-CH_2), 26.03 (δ-CH_2); $C_{70}H_{124}O_{35}$ 1525.73, MALDI-TOF MS: m/z 1547.4 $[M + Na]^+$, 1563.3 $[M + K]^+$.

6^I-O-(7-Epoxyoctyl)-2$^{I\text{-}VII}$,3$^{I\text{-}VII}$,6$^{I\text{-}VI}$-eicosa-O-*methylcyclomaltoheptaose* (**12**).—6′-Octenylper-Me-β-CD (**11**) (1.71 g, 1.12 mmol) was treated with 0.3 g *m*-chloroperbenzoic acid, as described for **4**, but using $CHCl_3$ (150 mL) as solvent instead of pentane and water. Pure **12** (1.7 g, 1.10 mmol; 98%) was obtained by column chromatography (29:1 EtOAc–MeOH); $[\alpha]_D^{20}$ +134.8° (*c* 1, $CHCl_3$); TLC (15:1 EtOAc–MeOH) R_f 0.29; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.14–5.04 (m, 7 H, H-1), 3.90–3.69 (m, 14 H, H-5,6a), 3.62–3.60, 3.47–3.46 (s, 42 H, 2,3-OCH_3), 3.67–3.35 (m, 23 H, H-3,4,6b, α-CH_2), 3.34–3.33 (s, 18 H, 6-OCH_3), 3.18–3.10 (m, 7 H, H-2), 2.87–2.81 (m, 1 H, CH_{epoxy}), 2.69 (dd, 1 H, ^3J 4.4 Hz,

CH_{2epoxy}), 2.40 (dd, 1 H, ^2J 5.1, ^3J 2.5 Hz, CH_{2epoxy}), 1.63–1.23 (m, 10 H, β,γ,δ,ε-CH_2, CH_2–CH_{epoxy}); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 98.95–98.62 (C-1), 82.09–81.69 (C-2,3), 80.48–79.94 (C-4), 71.15–70.82 (C-5), 71.39–71.32, 69.40 (C-6, α-CH_2), 58.96, 58.90 (6-OCH_3), 61.51–61.32, 58.57–58.39 (2,3-OCH_3), 52.19 (CH_{epoxy}), 46.96 (CH_{2epoxy}), 32.37 (CH_2–CH_{epoxy}), 29.56 (β-CH_2), 29.27 (γ-CH_2), 26.08, 25.93 (δ,ε-CH_2); $C_{70}H_{124}O_{36}$ 1541.73, MALDI-TOF MS: m/z 1562.4 $[M + Na]^+$, 1578.4 $[M + K]^+$.

$6^{I\text{-}VII}$-Hepta-O-tert-*butyldimethylsilyl-2^I-O-(oct-7-enyl)cyclomaltoheptaose* (**14**).—Sodium hydride (43 mg, 1.79 mmol, washed with petroleum ether) was added to a stirred solution of lyophilized **13** (0.5 g, 258.42 μmol) [22] in 20 mL anhyd THF at 0 °C. After 20 min, 0.43 mL (2.56 mmol) 8-bromo-1-octene was added dropwise and stirring was continued at 0 °C for 10 min, and then at rt for 44 h. Excess NaH was decomposed by the addition of MeOH after cooling the system to 0 °C. The solvent was evaporated under vacuum, the residue dissolved in $CHCl_3$ and washed with water. After drying over $MgSO_4$ and filtration and evaporation the crude product was purified by column chromatography (8:1–3:1 $CHCl_3$—MeOH, stepwise) yielding **14** (210.6 mg, 102.98 μmol, 40%); $[\alpha]_D^{21}$ +81.0° (*c* 1, $CHCl_3$), TLC (6:1 $CHCl_3$—MeOH) R_f 0.27; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.67–5.12 (13 s, 13 H, OH), 5.79 (ddt, 1 H, $J_{CH_2-CH=}$ 6.6. Hz, C*H*=CH_2), 4.96 (m, 1 H, J_E 16.8 Hz, CH=CH_2), 4.93–4.80 (m, 8 H, H-1, 1 × CH=CH_2), 4.16–3.75 (m, 15 H, H-3,6a, 1 × α-CH_2), 3.74–3.40 (m, 28 H, 6 × H-2, H-4,5,6b, 1 × α-CH_2), 3.16 (dd, 1 H, $J_{1,2}$ 3.1, $J_{2,3}$ 9.7 Hz, H-2), 2.01 (m, 2 H, CH_2–CH=), 1.66–1.47 (m, 2 H, β-CH_2), 1.40–1.30 (m, 2 H, ε-CH_2), 1.30–1.20 (m, 4 H, γ,δ-CH_2), 0.88–0.82 (s, 63 H, $SiCMe_3$), 0.04 to −0.01 (s, 42 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 138.94 (*C*H=CH_2), 114.33 (CH=*C*H_2), 102.98–100.80 (C-1), 82.08–79.87 (C-2), 73.16 (α-CH_2), 74.05–72.26 (C-3,4,5), 62.24–61.37 (C-6), 33.75 (CH_2–CH=), 29.15 (β-CH_2), 28.81 (γ-CH_2), 28.76 (ε-CH_2), 25.89, 25.83 (SiC*Me*$_3$), 25.46 (δ-CH_2), 18.33–18.18 (Si*C*Me_3), −5.04 to −5.30 ($SiMe_2$); $C_{92}H_{182}O_{35}Si_7$ 2045.03, MALDI-TOF MS: m/z 2066.0 $[M + Na]^+$, 2081.8 $[M + K]^+$.

$6^{I\text{-}VII}$-Hepta-O-tert-*butyldimethylsilyl-$2^{I\text{-}VI}$, $3^{I\text{-}VII}$-trideca*-O-*methyl-2^I*-O-*(oct-7-enyl)cyclomalto-heptaose* (**15**).—(a) Iodomethane (0.60 mL, 9.60 mmol) was added to a stirred solution of **14** (303.5 mg, 148.41 μmol) and NaH (139 mg, 5.79 mmol) in 20 mL of dry THF at 0 °C. After 30 min the reaction mixture was allowed to warm up to rt by removing the ice bath, and stirring was continued for 3.5 h. Excess NaH was degraded with MeOH at 0 °C and the solvent was evaporated under vacuum. The crude product was dissolved in $CHCl_3$, washed with water, dried over $MgSO_4$, filtered and concentrated. Purification by column chromatography (4:1 petroleum ether–EtOAc) afforded **15** (240.3 mg, 107.88 μmol, 73%); $[\alpha]_D^{20}$ +90.7° (*c* 1, $CHCl_3$); TLC (3:1 petroleum ether–EtOAc) R_f 0.26; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.78 (ddt, 1 H, $J_{CH_2-CH=}$ 6.6 Hz, C*H*=CH_2), 5.21–5.11 (m, 7 H, H-1), 4.96 (m, 1 H, J_E 16.8 Hz, CH=CH_2), 4.90 (m, 1 H, J_Z 10.2 Hz, CH=CH_2), 4.20 (dd, 1 H, $J_{5,6a}$ 2.0, $J_{6a,6b}$ 11.7 Hz, H-6a), 4.15–3.95 (m, 6 H, H-6a), 3.65–3.62, 3.49–3.48 (OCH_3), 3.79–3.36 (m, 30 H, H-3,4,5,6b, α-CH_2), 3.10 (dd, 1 H, $J_{1,2}$ 3.1, $J_{2,3}$ 9.7 Hz, H-2), 3.07–2.98 (m, 6 H, H-2), 2.01 (m, 2 H, CH_2–CH=), 1.65–1.50 (m, 2 H, β-CH_2), 1.43–1.20 (m, 6 H, γ,δ,ε-CH_2), 0.85 (s, 63 H, $SiCMe_3$), −0.01 (s, 42 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 139.14 (*C*H=CH_2), 114.13 (CH=*C*H_2), 98.13–97.91 (C-1), 82.25–81.09 (C-2,3), 78.91–77.92 (C-4), 72.26–72.02 (C-5), 70.81 (α-CH_2), 62.44–62.24 (C-6), 61.61–58.50 (OCH_3), 30.08 (β-CH_2), 28.98 (γ-CH_2), 28.91 (ε-CH_2), 25.93, 25.89 (SiC*Me*$_3$), 18.31–18.22 (Si*C*Me_3), −4.87 to −5.27 ($SiMe_2$); $C_{105}H_{208}O_{35}Si_7$ 2227.38, MALDI-TOF MS: m/z 2248.1 $[M + Na]^+$, 2264.3 $[M + K]^+$.

(b) 8-Bromo-1-octene (1.1 mL, 6.56 mmol) was added dropwise to a stirred mixture of 2′-OH-6-TBDMS-2*,3-Me-β-CD (**21**), prepared by adapting the procedure of Dönnecke et al. [20], and NaH (170 mg, 7.083 mmol) in 75 mL anhyd DMF at 0 °C. Stirring was continued for 20 min at 0 °C, and then at rt for a further 17 h. Excess NaH was decomposed by adding MeOH at 0 °C. The reaction mixture was diluted with water and extracted with $CHCl_3$. The organic phase was dried over $MgSO_4$, filtered, and concentrated under vac-

uum. Residual DMF was removed by two-fold co-distillation with 90 mL of 1:1 1-butanol–toluene. Finally, the crude product was purified by column chromatography (4:1 petroleum ether–EtOAc) to afford **15** (997.1 mg, 0.448 mmol, 85%).

$6^{I\text{-}VII}$-Hepta-O-tert-*butyl-dimethylsilyl-2^{I}*-O-*(7-epoxyoctyl)-$2^{I\text{-}VI}$,$3^{I\text{-}VII}$-trideca*-O-*methyl-cycloheptaose* (**16**).—Compound **15** (228 mg, 102.36 μmol) was treated with 40 mg *m*-chloroperbenzoic acid in pentane (10 mL) and water (10 mL), as described above for **4**. Column chromatography (5:2 petroleum ether–EtOAc) yielded pure **16** (164.2 mg, 73.19 μmol, 72%); $[\alpha]_D^{20}$ +92.8° (*c* 1, $CHCl_3$); TLC (2:1 petroleum ether–EtOAc) R_f 0.26; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.22–5.10 (m, 7 H, H-1), 4.20 (dd, 1 H, $J_{5,6a}$ 2.0, $J_{6a,6b}$ 11.7 Hz, H-6a), 4.15–3.97 (m, 6 H, H-6a), 3.65–3.61, 3.49–3.48 (OCH_3), 3.79–3.36 (m, 30 H, H-3,4,5,6b, α-CH_2), 3.09 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 10.2 Hz, H-2), 3.06–2.96 (m, 6 H, H-2), 2.90–2.83 (m, 1 H, CH_{epoxy}), 2.71 (dd, 1 H, ^3J 4.1 Hz, CH_{2epoxy}), 2.43 (dd, 1 H, ^3J 2.5, ^2J 5.1 Hz, CH_{2epoxy}), 1.65–1.54 (m, 2 H, β-CH_2), 1.54–1.47 (m, 2 H, CH_2–CH_{epoxy}), 1.47–1.29 (m, 6 H, γ,δ,ε-CH_2), 0.84 (s, 63 H, $SiCMe_3$), −0.01 (s, 42 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 98.12–97.89 (C-1), 82.26–81.13 (C-2,3), 78.94–77.91 (C-4), 72.26–72.03 (C-5), 70.71 (α-CH_2), 62.43–62.19 (C-6), 61.64–58.50 (OCH_3), 52.32 (CH_{epoxy}), 47.08 (CH_{2epoxy}), 32.43 (CH_2–CH_{epoxy}), 30.03 (β-CH_2), 29.29 (γ-CH_2), 25.93–25.88 ($SiCMe_3$), 18.31–18.22 ($SiCMe_3$), 4.87–5.27 ($SiMe_2$); $C_{105}H_{208}O_{36}Si_7$ 2243.38, MALDI-TOF MS: *m*/*z* 2264.1 $[M+Na]^+$, 2280.0 $[M+K]^+$.

$6^{I\text{-}VII}$-Hepta-O-tert-*butyldimethylsilyl-2^{I}*-O-*(5-cyanopentyl)cyclomaltoheptaose* (**17**).—Sodium hydride (42 mg, 1.79 mmol, washed with petroleum ether) was added to a vigorously stirred solution of lyophilized **13** (0.5 g, 258.42 μmol) [22] in 20 mL anhyd THF at 0 °C. After 20 min, 1-bromo-5-cyanopentane (0.34 mL, 2.55 mmol) was added dropwise and stirring was continued at 0 °C for 10 min, then at rt overnight. Excess NaH was decomposed by the addition of MeOH at 0 °C. The reaction mixture was concentrated under vacuum and partitioned between $CHCl_3$ and water. The organic layer was dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (8:1 $CHCl_3$–MeOH) yielding **17** (125.9 mg, 62.02 μmol, 24%); $[\alpha]_D^{20}$ +68.0° (*c* 15, $CHCl_3$); TLC (4:1 $CHCl_3$–MeOH) R_f 0.30; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.69–5.15 (12 s, 12 H, OH), 4.95–4.76 (m, 8 H, H-1, 1 × OH), 4.15–3.73 (m, 15 H, H-3,6a, 1 × α-CH_2), 3.73–3.35 (m, 28 H, 6 × H-2, H-4,5,6b, 1 × α-CH_2), 3.18 (dd, 1 H, $J_{1,2}$ 3.1, $J_{2,3}$ 9.7 Hz, H-2), 2.31 (dt, 2 H, $J_{\gamma,\varepsilon}$ 1.5, $J_{\delta,\varepsilon}$ 7.1 Hz), 1.71–1.53 (m, 4 H, β,δ-CH_2), 1.52–1.38 (m, 2 H, γ-CH_2), 0.88–0.81 (s, 63 H, $SiCMe_3$), 0.04–0.03 (s, 42 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 119.57 (CN), 102.68–100.33 (C-1), 82.04–79.74 (C-2), 72.37 (α-CH_2), 73.91–72.15 (C-3,4,5), 62.32–61.33 (C-6), 28.36 (β-CH_2), 25.90–25.80 ($SiCMe_3$), 25.08, 24.70 (γ,δ-CH_2), 18.33–18.16 ($SiCMe_3$), 16.97 (ε-CH_2), 5.07–5.32 ($SiMe_2$); $C_{90}H_{177}NO_{35}Si_7$ 2029.98, MALDI-TOF MS: *m*/*z* 2050.2 $[M+Na]^+$, 2066.3 $[M+K]^+$.

$6^{I\text{-}VII}$-Hepta-O-tert-*butyldimethylsilyl-2^{I}*-O-*(5-cyanopentyl)-$2^{I\text{-}VI}$,$3^{I\text{-}VII}$-trideca*-O-*methyl-cyclomalto-heptaose* (**18**).—(a) Compound **17** (157.5 mg, 77.59 μmol) was treated with NaH and iodomethane, as described for the preparation of **15**, yielding pure **18** (72.9 mg, 32.95 μmol; 42%) after column chromatography (3:1–2:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ +88.2° (*c* 1, $CHCl_3$); TLC (2:1 petroleum ether–EtOAc) R_f 0.23; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.22–5.10 (m, 7 H, H-1), 4.20 (dd, 1 H, $J_{5,6a}$ 2.0, $J_{6a,6b}$ 11.7 Hz, H-6a), 4.16–3.97 (m, 6 H, H-6a), 3.65–3.61, 3.49–3.48 (OCH_3), 3.78–3.39 (m, 30 H, H-3,4,5,6b, α-CH_2), 3.09 (dd, 1 H, $J_{1,2}$ 3.1, $J_{2,3}$ 9.7 Hz, H-2), 3.06–2.96 (m, 6 H, H-2), 2.32 (t, 2 H, $J_{\delta,\varepsilon}$ 7.1 Hz, ε-CH_2), 1.73–1.65 (m, 2 H, δ-CH_2), 1.65–1.60 (m, 2 H, β-CH_2), 1.60–1.50 (m, 2 H, γ-CH_2), 0.85 (s, 63 H, $SiCMe_3$), −0.01 (s, 42 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 119.70 (CN), 98.17–97.73 (C-1), 82.25–81.24 (C-2,3), 79.04–78.05 (C-4), 72.24–72.01 (C-5), 70.00 (α-CH_2), 62.37–62.13 (C-6), 61.72–58.44 (OCH_3), 29.24 (β-CH_2), 25.90–25.84 ($SiCMe_3$), 25.23 (γ,δ-CH_2), 18.28–18.21 ($SiCMe_3$), 17.09 (ε-CH_2), 4.88–5.29 ($SiMe_2$); $C_{103}H_{203}NO_{35}Si_7$ 2212.33, MALDI-TOF MS: *m*/*z* 2232.1 $[M+Na]^+$, 2248.3 $[M+K]^+$.

(b) 1-Bromo-5-cyanopentane (0.75 mL, 5.62 mmol) was added dropwise to a stirred solution of **21** (0.9 g, 425.09 μmol) and NaH (135 mg, 5.63 mmol, washed with petroleum ether) in 45 mL anhyd THF at 0 °C. After 20 min, the reaction mixture was allowed to warm up to rt and stirring was continued overnight. Excess NaH was degraded with MeOH after cooling the system to 0 °C. After evaporation of the solvent the residue was dissolved in $CHCl_3$ and washed with water. The organic phase was dried over $MgSO_4$, filtered and concentrated. For purification, the crude product was chromatographed on silica gel (3:1–3:2 petroleum ether–EtOAc, stepwise). Low weight impurities were finally removed by exclusion chromatography (Sephadex LH-20, MeOH) yielding **18** (837.1 mg, 378.38 μmol, 89%); TLC (4:1 petroleum ether–acetone) R_f 0.43.

2^I-O-(6-Aminohexyl)-$6^{I\text{-}VII}$-hepta-O-tert-butyldimethylsilyl-$2^{I\text{-}VI}$,$3^{I\text{-}VII}$-trideca-O-methyl-cyclomalto-heptaose (**19**).—Compound **18** (150.0 mg, 67.80 μmol) was reduced with $LiAlH_4$, as described for **7**, yielding **19** (112.7 mg, 50.85 μmol; 75%) after column chromatography (6:1 $CHCl_3$–MeOH); $[\alpha]_D^{20}$ +92.0° (*c* 1, $CHCl_3$); TLC (4:1 $CHCl_3$–MeOH) R_f 0.40; ^{1}H NMR (400 MHz, MeOH-d_4): δ 5.36–5.25 (m, 7 H, H-1), 4.35 (dd, 1 H, $J_{5,6a}$ 2.0, $J_{6a,6b}$ 11.7 Hz, H-6a), 4.29–4.08 (m, 6 H, H-6a), 3.56–3.55, 3.73–3.69 (s, 42 H, OCH_3), 3.90–3.47 (m, 30 H, H-3,4,5,6b, α-CH_2), 3.17 (dd, 1 H, $J_{1,2}$ 3.1, $J_{2,3}$ 9.7 Hz, H-2), 3.14–3.05 (m, 6 H, H-2), 2.82 (t, 2 H, ^3J 7.1 Hz, CH_2–NH_2), 1.79–1.67 (m, 2 H, β-CH_2), 1.67–1.58 (m, 2 H, ε-CH_2), 1.58–1.50 (m, 2 H, γ-CH_2), 1.50–1.39 (m, 2 H, δ-CH_2), 0.98–0.95 (s, 63 H, $SiCMe_3$), 0.14–0.10 (s, 42 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, MeOH-d_4): δ 99.57–99.29 (C-1), 83.93–82.81 (C-2,3), 72.20 (α-CH_2), 64.12–63.89 (C-6), 62.51–59.36 (OCH_3), 41.97 (CH_2–NH_2), 31.68 (ε-CH_2), 31.43 (β-CH_2), 27.92 (δ-CH_2), 27.23 (γ-CH_2), 26.98–26.85 ($SiCMe_3$), 19.65–19.53 ($SiCMe_3$), 3.94–4.38 ($SiMe_2$); $C_{103}H_{207}NO_{35}Si_7$, MALDI-TOF-MS: *m/z* 2215.5 $[M+H]^+$, 2237.4 $[M+Na]^+$, 2253.4 $[M+K]^+$.

$6^{I\text{-}VII}$-Hepta-O-tert-butyldimethylsilyl-2^I-O-(7-epoxyoctyl)cyclomaltoheptaose (**20**).—Compound **14** (161 mg, 78.73 μmol) was subjected to epoxidation, as described for **12**. Purification by column chromatography (9:1 $CHCl_3$–MeOH) afforded pure **20** (114.4 mg, 55.51 μmol; 71%); $[\alpha]_D^{20}$ +99.0° (*c* 1, $CHCl_3$); TLC (6:1 $CHCl_3$–MeOH) R_f 0.29; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.68–5.14 (s, 12 H, 2,3-OH), 4.93–4.78 (m, 8 H, H-1, 1 × OH), 4.15–3.75 (m, 15 H, H-3,6a, 1 × α-CH_2), 3.74–3.40 (m, 29 H, 6 × H-2, H-4,5,6b, 1 × α-CH_2), 3.16 (dd, 1 H, $J_{1,2}$ 2.5, $J_{2,3}$ 9.7 Hz), 2.87 (m, 1 H, Ch_{epoxy}), 2.71 (dd, 1 H, $^2J = {}^3J = 4.1$ Hz, CH_{2epoxy}), 2.43 (dd, 1 H, ^3J 2.5, ^2J 5.1 Hz, CH_{2epoxy}), 1.65–1.53 (m, 2 H, β-CH_2), 1.53–1.46 (m, 2 H, CH_2–CH_{epoxy}), 1.46–1.37 (m, 2 H, ε-CH_2), 1.37–1.21 (m, 4 H, γ,δ-CH_2), 0.88–0.80 (s, 63 H, $SiCMe_3$), 0.05–0.04 (s, 42 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 102.99–100.79 (C-1), 82.09–79.90 (C-2), 73.08 (α-CH_2), 74.05–72.27 (C-3,4,5), 62.25–61.38 (C-6), 52.25, 52.23 (CH_{2epoxy}), 47.05, 47.03 (CH_{epoxy}), 32.43, 32.40 (CH_2–CH_{epoxy}), 29.10 (β-CH_2), 25.89–25.83 ($SiCMe_3$), 29.13, 25.54 (γ,δ-CH_2), 18.33–18.18 ($SiCMe_3$), 5.04–5.30 ($SiMe_2$); $C_{92}H_{182}O_{36}Si_7$ 2061.03, MALDI-TOF MS: *m/z* 2082.0 $[M+Na]^+$, 2097.8 $[M+K]^+$

$6^{I\text{-}VII}$-Hepta-O-tert-butyldimethylsilyl-3^I-O-(2-epoxypropyl)-$2^{I\text{-}VII}$,$3^{I\text{-}VI}$-trideca-O-methyl-cyclomalto-heptaose (**24**).—3′-All-6-TBDMS-2,3*-Me-β-CD (**22**) (437.2 mg, 202.67 μmol) was prepared according to the procedure of Dönnecke et al. [20], and epoxidized as described for **12**. Purification by column chromatography (5:2–2:1 petroleum ether–EtOAc) yielded **24** (291.3 mg, 134.04 μmol, 66%); $[\alpha]_D^{20}$ +95.3° (*c* 1, $CHCl_3$); TLC (2:1 petroleum ether–EtOAc) R_f 0.21; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.24–5.10 (m, 7 H, H-1), 4.25–3.93 (m, 8 H, H-6a, 1 × α-CH_2), 3.65–3.61, 3.51–3.47 (s, 39 H, OCH_3), 3.85–3.36 (m, 29 H, H-3,4,5,6b, 1 × α-CH_2), 3.35–3.25 (m, 1 H, CH_{epoxy}), 3.11–2.99 (m, 7 H, H-2), 2.81–2.76 (2 × dd, 1 H, CH_{2epoxy}), 2.64 (dd, 0.38 H, ^2J 5.1, ^3J 3.1 Hz, CH_{2epoxy}), 2.61 (dd, 0.62 H, ^2J 5.1, ^3J 3.1 Hz, CH_{2epoxy}), 0.84 (s, 63 H, $SiCMe_3$), −0.01 (s, 42 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 98.36–97.55 (C-1), 82.35–81.70 (C-2,3), 79.06–78.07 (C-4), 75.39, 74.73 (α-CH_2), 72.19, 71.99 (C-5), 62.31–62.20 (C-6), 61.58–58.44 (OCH_3), 51.00, 50.90 (CH_{epoxy}), 45.06, 44.54 (CH_{2epoxy}), 25.89 ($SiCMe_3$), 18.27 ($SiCMe_3$), 4.86–5.23

($SiMe_2$); $C_{100}H_{198}O_{36}Si_7$ 2173.25; MALDI-TOF MS: m/z 2192.5 $[M+Na]^+$, 2208.55 $[M+K]^+$.

$6^{I\text{-}VII}$-Hepta-O-tert-butyldimethylsilyl-3^I-O-(7-epoxyoctyl)-$2^{I\text{-}VII},3^{I\text{-}VI}$-trideca-O-methyl-cyclomalto-heptaose (**25**).—3′-Octenyl-6-TBDMS-2,3*-Me-β-CD (**23**) (303.6 mg, 136.30 μmol) was prepared according to Dönnecke et al. [20], and epoxidized as described for **4**. Column chromatography (3:1–2:1 petroleum ether–EtOAc) afforded **27** (255.5 mg, 113.89 μmol, 84%); $[\alpha]_D^{20}$ +89.4° (*c* 1, $CHCl_3$); TLC (3:1 petroleum ether–EtOAc) R_f 0.15; ^1H NMR (400 MHz, $CDCl_3$): δ 5.22–5.11 (m, 7 H, H-1), 4.22–3.94 (m, 8 H, H-6a, 1 × α-CH_2), 3.64–3.62, 3.49–3.46 (s, 39 H, OCH_3), 3.78–3.41 (m, 29 H, H-3,4,5,6b, 1 × α-CH_2), 3.07–2.98 (m, 7 H, H-2), 2.86 (m, 1 H, CH_{epoxy}), 2.71 (dd, 1 H, ^3J 4.1 Hz, CH_{2epoxy}), 2.42 (dd, 1 H, ^2J 5.1, ^3J 2.5 Hz, CH_{2epoxy}), 1.68–1.55 (m, 2 H, β-CH_2), 1.54–1.46 (m, 2 H, CH_2–CH_{epoxy}), 1.46–1.40 (m, 2 H, δ-CH_2), 1.40–1.29 (m, 4 H, γ,ε-CH_2), 0.84 (s, 63 H, $SiCMe_3$), −0.01 (s, 42 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 98.24–97.71 (C-1), 82.26–80.14 (C-2,3), 78.89–78.23 (C-4), 74.01 (α-CH_2), 72.26–72.07 (C-5), 62.32–62.24 (C-6), 61.53–58.49 (OCH_3), 52.33 (CH_{epoxy}), 47.06 (CH_{2epoxy}), 32.47, 32.45 (CH_2–CH_{epoxy}), 30.31 (β-CH_2), 29.54, 26.08 (γ,ε-CH_2), 25.98 (δ-CH_2), 25.89 ($SiCMe_3$), 18.27 ($SiCMe_3$), 4.86–5.28 ($SiMe_2$); $C_{105}H_{208}O_{36}Si_7$ 2243.38, MALDI-TOF MS: m/z 2261.7 $[M+Na]^+$, 2277.7 $[M+K]^+$.

2^I-O-(5-Cyanopentyl)-$2^{I\text{-}VI},3^{I\text{-}VII}$-trideca-O-methylcyclomaltoheptaose (**26**).—A solution of **18** (685 mg, 309.63 μmol) and tetrabutylammonium fluoride trihydrate (98 mg, 319.60 μmol) in 12 mL anhyd 1:1 THF–DMF was stirred for 22 h at rt. The solvent was evaporated under diminished pressure. Traces of DMF were removed by co-distillation with 1-butanol and toluene. The residue was dissolved in MeOH and stirred slowly (rotatory evaporator) with mixed bed ion-exchange resin (Amberlite MB-3, E. Merck) to remove the tetrabutylammonium salts. The resin was filtered off and the solution was taken to dryness. Column chromatography (3:1 $CHCl_3$–MeOH) of the crude product furnished pure **26** (439.2 mg, 310.94 μmol, > 99%); $[\alpha]_D^{20}$ +144.1° (*c* 1, $CHCl_3$); TLC (3:1 $CHCl_3$–MeOH) R_f 0.21; ^1H NMR (400 MHz, pyridine-d_5): δ 6.60–6.06 (m, 7 H, OH), 5.69–5.54 (m, 7 H, H-1), 4.64–4.09 (m, 28 H, H-4,5,6a,6b), 4.03–3.89 (m, 7 H, H-3), 3.80–3.87 (s, 21 H, 3-OCH_3), 3.76–3.65 (m, 1 H, 1 × α-CH_2), 3.53–3.48 (s, 18 H, 2-OCH_3), 3.45–3.28 (m, 8 H, H-2, 1 × α-CH_2), 2.33 (t, 2 H, $J_{\delta,\varepsilon}$ 6.6 Hz, ε-CH_2), 1.68–1.38 (m, 6 H, β,γ,δ-CH_2); ^{13}C NMR (100.62 MHz, pyridine-d_5): δ 120.51 (CN), 99.50–99.23 (C-1), 83.02–81.86 (C-2,3), 80.99–80.18 (C-4), 73.64–73.26 (C-5), 70.26 (α-CH_2), 61.98–61.50 (3-OCH_3), 61.53–61.35 (C-6), 58.63–58.24 (2-OCH_3), 29.50 (β-CH_2), 25.46 (γ,δ-CH_2), 16.90 (ε-CH_2); $C_{61}H_{105}NO_{35}$ 1412.49, MALDI-TOF MS: m/z 1435.7 $[M+Na]^+$, 1451.7 $[M+K]^+$.

2^I-O-(5-Cyanopentyl)-$2^{I\text{-}VI},3^{I\text{-}VII},6^{I\text{-}VII}$-eicosa-O-methylcyclomaltoheptaose (**27**).—Compound **26** (439.2 mg, 310.94 μmol) was methylated with NaH and iodomethane, as described for the preparation of **15**, yielding pure **27** (415.8 mg, 275.24 μmol, 89%) after column chromatography (30:1 $CHCl_3$–MeOH); $[\alpha]_D^{20}$ +139.2° (*c* 1, $CHCl_3$), TLC (20:1 $CHCl_3$–MeOH) R_f 0.39; ^1H NMR (400 MHz, $CDCl_3$): δ 5.15–5.04 (m, 6 H, H-1), 5.01 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 3.92 (dd, 1 H, $J_{5,6a}$ 3.6, $J_{6a,6b}$ 10.7 Hz, H-6a), 3.87–3.68 (m, 13 H, H-5, 6 × H-6a), 3.62–3.58, 3.47–3.46 (2,3-OCH_3), 3.68–3.38 (m, 23 H, H-3,4,6b, α-CH_2), 3.34 (s, 21 H, 6-OCH_3), 3.20 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 9.7 Hz, H-2), 3.18–3.10 (m, 6 H, H-2), 2.31 (t, 2 H, $J_{\delta,\varepsilon}$ 7.1 Hz, ε-CH_2), 1.72–1.45 (m, 6 H, β,γ,δ-CH_2); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 119.62 (CN), 99.00–98.68 (C-1), 82.05–80.96 (C-2,3), 80.47–79.69 (C-4), 71.50–71.07 (C-6), 71.00–70.71 (C-5), 70.06 (α-CH_2), 58.93–58.88 (6-OCH_3), 61.66–61.23, 58.73–58.28 (2,3-OCH_3), 29.13 (β-CH_2), 25.16 (γ,δ-CH_2), 17.05 (ε-CH_2); $C_{68}H_{119}NO_{35}$ 1510.68, MALDI-TOF MS: m/z 1533.4 $[M+Na]^+$, 1549.4 $[M+K]^+$.

2^I-O-(6-Aminohexyl)-$2^{I\text{-}VI},3^{I\text{-}VII},6^{I\text{-}VII}$-eicosa-O-methylcyclomaltoheptaose (**28**).—Compound **27** (221.1 mg, 146.36 μmol) was reduced with $LiAlH_4$, as described for **7**, yielding **28** (144.4 mg, 95.33 μmol, 65%) after column chromatography (5:1 $CHCl_3$–MeOH); $[\alpha]_D^{20}$ +134.7° (*c* 1, $CHCl_3$); TLC (3:1 $CHCl_3$–MeOH) R_f 0.39; ^1H NMR (400 MHz, MeOH-

d_4): δ 5.27–5.15 (m, 6 H, H-1), 5.13 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.02 (dd, 1 H, $J_{5,6a}$ 3.6, $J_{6a,6b}$ 10.7 Hz, H-6a), 3.98–3.79 (m, 13 H, H-5, 6 × H-6a), 3.70–3.67, 3.56–3.55 (s, 39 H, 2,3-OCH_3), 3.79–3.47 (m, 23 H, H-3,4,6b, α-CH_2), 3.407, 3.401 (s, 21 H, 6-OCH_3), 3.29–3.14 (m, 7 H, H-2), 2.71 (t, 2 H, ^3J 7.1 Hz, CH_2–NH_2), 1.79–1.62 (m, 2 H, β-CH_2), 1.61–1.48 (m, 4 H, γ,ε-CH_2), 1.48–1.36 (m, 2 H, δ-CH_2); ^{13}C NMR (100.62 MHz, MeOH-d_4): δ 99.85–99.75 (C-1), 83.83–83.68 (C-3), 83.55–82.43 (C-2), 81.37–80.58 (C-4), 73.26–72.91 (C-6), 72.80–72.53 (C-5), 72.22 (α-CH_2), 59.71–59.65 (6-OCH_3), 62.41–62.00, 59.53–59.23 (2,3-OCH_3), 42.68 (CH_2–NH_2), 33.71 (ε-CH_2), 31.50 (β-CH_2), 28.10 (δ-CH_2), 27.32 (γ-CH_2); $C_{68}H_{123}NO_{35}$ 1514.71, MALDI-TOF MS: m/z 1514.9 $[M + H]^+$, 1536.9 $[M + Na]^+$, 1553.0 $[M + K]^+$.

2^I - O - (5 - Carboxypentyl) - $2^{I\text{-}VI}$,$3^{I\text{-}VII}$,$6^{I\text{-}VII}$-eicosa-O-*methylcyclomaltoheptaose* (**29**).—Compound **27** (200 mg, 132.39 μmol) was dissolved in aq 25% NaOH (6.5 mL) and EtOH (1 mL) and heated under reflux until the formation of ammonia ceased (21 h). After cooling the reaction vessel to 0 °C, the pH was carefully brought down to pH 6 with aq 20% H_2SO_4 under vigorous stirring, and the free acid was extracted several times with $CHCl_3$. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. The crude product was purified by exclusion chromatography (Sephadex LH-20, MeOH) to give **29** (154.9 mg, 101.26 μmol, 76%); $[\alpha]_D^{20}$ +130.0° (*c* 1, $CHCl_3$); TLC (10:1 $CHCl_3$–MeOH) R_f 0.37; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.14–5.05 (m, 6 H, H-1), 5.00 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 3.90 (dd, 1 H, $J_{5,6a}$ 3.5, $J_{6a,6b}$ 10.4 Hz, H-6a), 3.87–3.68 (m, 13 H, H-5, 6 × H-6a), 3.61–3.57, 3.47–3.46 (s, 39 H, 2,3-OCH_3), 3.68–3.40 (m, 23 H, H-3,4,6b, α-CH_2), 3.34, 3.33 (s, 21 H, 6-OCH_3), 3.21 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 9.8 Hz, H-2), 3.18–3.11 (m, 6 H, H-2), 2.29 (t, 2 H, $J_{\delta,\varepsilon}$ 7.6 Hz, ε-CH_2), 1.67–1.52 (m, 4 H, β,δ-CH_2), 1.47–1.35 (m, 2 H, γ-CH_2); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 177.51 (C=O), 98.95–98.82 (C-1), 82.04–80.81 (C-2), 81.79–81.69 (C-3), 80.43–79.76 (C-4), 71.50–71.16 (C-6), 71.05–70.76 (C-5), 70.54 (α-CH_2), 58.92, 58.90 (6-OCH_3), 61.59–61.23, 58.68–58.33 (2,3-OCH_3), 33.81 (ε-CH_2), 29.57 (β-CH_2), 25.39 (γ-CH_2), 24.51 (δ-CH_2); $C_{68}H_{120}O_{37}$ 1529.68; MALDI-TOF MS: m/z 1551.9 $[M + Na]^+$, 1567.9 $[M + K]^+$.

$6^{I\text{-}VII}$-Hepta-O-tert-*butyldimethylsilyl-3^I*-O-*(5-cyanopentyl)-$2^{I\text{-}VII}$,$3^{I\text{-}VI}$-trideca*-O-*methylcyclomalto-heptaose* (**31**).—To a stirred solution of **30** [20] (0.3 g, 141.70 μmol) and NaH (45 mg, 1.88 mmol, washed with petroleum ether) in 15 mL anhyd DMF was added dropwise 1-bromo-5-cyanopentane (0.5 mL, 3.74 mmol) at 0 °C. The mixture was kept at 0 °C for 30 min and then warm up to rt by removing the ice bath. After 3 days the reaction was stopped by quenching with MeOH at 0 °C. The solvent was evaporated under high vacuum. Residual DMF was removed by co-distillation with 40 mL of 1:1 1-butanol–toluene. The crude product was dissolved in $CHCl_3$, washed with water and dried over $MgSO_4$. After filtration and evaporation the residue was chromatographed (5:2–2:1 petroleum ether–EtOAc, stepwise). Low-weight impurities were finally removed by exclusion chromatography (Sephadex LH-20, MeOH) yielding **31** (270.6 mg, 122.31 μmol, 86%); $[\alpha]_D^{20}$ +79.0° (*c* 1, $CHCl_3$); TLC (2:1 petroleum ether–EtOAc) R_f 0.23; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.20 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.19–5.13 (m, 6 H, H-1), 4.20 (dd, 1 H, $J_{5,6a}$ 1.9, $J_{6a,6b}$ 11.7 Hz, H-6a), 4.15–3.97 (m, 7 H, 6 × H-6a, 1 × α-CH_2), 3.65–3.62, 3.50–3.46 (s, 39 H, OCH_3), 3.80–3.40 (m, 29 H, H-3,4,5,6b, 1 × α-CH_2), 3.07–2.99 (m, 7 H, H-2), 2.33 (t, 2 H, $J_{\delta,\varepsilon}$ 7.1 Hz, ε-CH_2), 1.76–1.65 (m, 2 H, δ-CH_2), 1.65–1.59 (m, 2 H, β-CH_2), 1.59–1.49 (m, 2 H, γ-CH_2), 0.84 (s, 63 H, $SiCMe_3$), −0.01 (s, 42 H $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 119.73 (CN), 98.16–97.63 (C-1), 82.30–80.07 (C-2,3), 78.97–78.06 (C-4), 73.30 (α-CH_2), 72.29–72.02 (C-5), 62.33, 62.22 (C-6), 61.58–61.31, 58.94–58.46 (OCH_3), 29.45 (β-CH_2), 25.92–25.88 ($SiCMe_3$), 25.44 (δ-CH_2), 25.42 (γ-CH_2), 18.29, 18.26, ($SiCMe_3$), 17.13 (ε-CH_2), 4.85–5.29 ($SiMe_2$); $C_{103}H_{208}NO_{35}Si_7$ 2212.33, MALDI-TOF MS: m/z 2232.2 $[M + Na]^+$, 2248.4 $[M + K]^+$.

3^I-O-(6-Aminohexyl)-$6^{I\text{-}VII}$-hepta-O-tert-*butyldimethylsilyl-$2^{I\text{-}VII}$,$3^{I\text{-}VI}$-trideca*-O-*methylcyclomalto-heptaose* (**32**).—Compound **33** (206.5 mg, 93.34 μmol) was reduced with

$LiAlH_4$, as described for **7**, yielding **32** (149.1 mg, 67.27 μmol, 72%) after column chromatography (8:1 $CHCl_3$–MeOH); $[\alpha]_D^{20}$ + 90.0° (*c* 1, $CHCl_3$); TLC (6:1 $CHCl_3$–MeOH) R_f 0.30; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.22–5.10 (m, 7 H, H-1), 4.17 (dd, 1 H, $J_{5,6a} < 0.5$, $J_{6a,6b}$ 11.0 Hz, H-6a), 4.14–3.99 (m, 6 H, H-6a), 3.95 (m, 1 H, 1 × α-CH_2), 3.64–3.61, 3.49–3.45 (s, 39 H, OCH_3), 3.79–3.37 (m, 29 H, H-3,4,5,6b, 1 × α-CH_2), 3.08–2.95 (m, 7 H, H-2), 2.91–2.73 (m, 2 H, C*H*$_2$–NH_2), 1.68–1.52 (m, 4 H, β,ε-CH_2), 1.45–1.29 (m, 4 H, γ,δ-CH_2), 0.84 (s, 63 H, $SiCMe_3$), −0.02 (s, 42 H, $SiMe_2$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 98.18–97.64 (C-1), 82.21–80.10 (C-2,3), 78.86–78.20 (C-4), 73.77 (α-CH_2), 72.21–72.04 (C-5), 62.29 (C-6), 61.51–58.47 (OCH_3), 41.04 (CH_2–NH_2), 30.71 (ε-CH_2), 30.23 (β-CH_2), 25.87 (SiC*Me*$_3$), 26.81, 25.77 (γ,δ-CH_2), 18.24 (Si*C*Me_3), 4.89–5.30 ($SiMe_2$); $C_{103}H_{207}NO_{35}Si_7$ 2216.36, MALDI-TOF MS: *m*/*z* 2235.9 $[M + Na]^+$, 2251.9 $[M + K]^+$.

3^I-O-(5-Cyanopentyl)-2$^{I\text{-}VII}$,3$^{I\text{-}VI}$-trideca-O-methylcyclomaltoheptaose (**33**).—Compound **31** (550 mg, 248.61 μmol) was desilylated, as described for **26**, yielding pure **33** (344.5 mg, 243.90 μmol, 98%) after column chromatography (4:1 $CHCl_3$–MeOH); $[\alpha]_D^{20}$ + 144.2° (*c* 1, $CHCl_3$); TLC (3:1 $CHCl_3$–MeOH) R_f 0.25; ^{1}H NMR (400 MHz, pyridine-d_5): δ 6.36–6.12 (m, 7 H, 6-OH), 5.65–5.56 (m, 7 H, H-1), 4.61–4.08 (m, 29 H, H-4,5,6a,6b, 1 × α-CH_2), 3.86–3.81 (s, 18 H, 3-OCH_3), 4.07–3.78 (m, 8 H, H-3, 1 × α-CH_2), 3.54–3.49 (s, 21 H, 2-OCH_3), 3.38–3.26 (m, 7 H, H-2), 2.36 (t, 2 H, $J_{\delta,\varepsilon}$ 6.6 Hz, ε-CH_2), 1.84–1.71 (m, 1 H, 1 × β-CH_2), 1.71–1.62 (m, 1 H, 1 × β-CH_2), 1.62–1.48 (m, 4 H, γ,δ-CH_2); ^{13}C NMR (100.62 MHz, pyridine-d_5): δ 120.53 (CN), 99.43–98.87 (C-1), 83.08–82.65 (C-2,3), 80.87–80.32 (C-4, 1 × C-3), 73.35 (α-CH_2), 73.60–73.30 (C-5), 61.57–61.45 (C-6), 61.55–61.47 (3-OCH_3), 58.70–58.30 (2-OCH_3), 29.81 (β-CH_2), 25.73, 25.63 (γ,δ-CH_2), 16.97 (ε-CH_2); $C_{61}H_{105}NO_{35}$ 1412.49; MALDI-TOF MS: *m*/*z* 1432.2 $[M + Na]^+$, 1448.2 $[M + K]^+$.

3^I-O-(5-Cyanopentyl)-2$^{I\text{-}VII}$,3$^{I\text{-}VI}$,6$^{I\text{-}VII}$-eicosa-O-methylcyclomaltoheptaose (**34**).—Methylation of **33** (281.6 mg, 199.36 μmol) with NaH and iodomethane, as described for **15**, yielded pure **34** (163.7 mg, 108.36 μmol, 54%) after column chromatography (40:1 $CHCl_3$–MeOH); $[\alpha]_D^{20}$ + 143.8° (*c* 1, $CHCl_3$); TLC (20:1 $CHCl_3$–MeOH) R_f 0.35; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.16–5.03 (m, 7 H, H-1), 4.01–3.88 (m, 2 H, 1 × H-6a, 1 × α-CH_2), 3.87–3.68 (m, 13 H, H-5, 6 × H-6a), 3.61–3.59, 3.48–3.45 (s, 39 H, 2,3-OCH_3), 3.68–3.39 (m, 22 H, H-3,4,6b, 1 × α-CH_2), 3.34, 3.33 (s, 21 H, 6-OCH_3), 3.19–3.08 (m, 7 H, H-2), 2.31 (t, 2 H, $J_{\delta,\varepsilon}$ 7.1 Hz, ε-CH_2), 1.72–1.44 (m, 6 H, β,γ,δ-CH_2); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 119.62 (CN), 98.88–98.38 (C-1), 82.04–81.70 (C-2,3), 80.47–79.71 (1 × C-3, C-4), 73.15 (α-CH_2), 71.50–71.24 (C-6), 71.03–70.74 (C-5), 58.91–58.86 (6-OCH_3), 61.46–61.22, 58.72–58.31 (2,3-OCH_3), 29.31 (β-CH_2), 25.34 (γ-CH_2), 25.32 (δ-CH_2), 17.06 (ε-CH_2); $C_{68}H_{119}NO_{35}$ 1510.68, MALDI-TOF MS: *m*/*z* 1531.7 $[M + Na]^+$, 1547.1 $[M + K]^+$.

3^I-O-(6-Aminohexyl)-2$^{I\text{-}VII}$,3$^{I\text{-}VI}$,6$^{I\text{-}VII}$-eicosa-O-methylcyclomaltoheptaose (**35**).—Compound **34** (165.0 mg, 108.93 μmol) was reduced with $LiAlH_4$, as described for **7**, yielding **35** (115.2 mg, 76.05 μmol, 70%) after column chromatography (7:1 $CHCl_3$–MeOH); $[\alpha]_D^{20}$ + 139.1° (*c* 1, $CHCl_3$); TLC (5:1 $CHCl_3$–MeOH) R_f 0.17; ^{1}H NMR (400 MHz, MeOH-d_4): δ 5.24–5.15 (m, 7 H, H-1), 4.06–3.97 (m, 2 H, 1 × H-6a, 1 × α-CH_2), 3.96–3.78 (m, 13 H, H-5, 6 × H-6a), 3.68–3.67, 3.55 (s, 39 H, 2,3-OCH_3), 3.77–3.48 (m, 22 H, H-3,4,6b, 1 × α-CH_2), 3.41 (s, 21 H, 6-OCH_3), 3.22–3.14 (m, 7 H, H-2), 2.70 (t, 2 H, ^3J 7.1 Hz, C*H*$_2$–NH_2), 1.78–1.60 (m, 2 H, β-CH_2), 1.60–1.50 (m, 2 H, ε-CH_2), 1.50–1.36 (m, 4 H, γ,δ-CH_2); ^{13}C NMR (100.62 MHz, MeOH-d_4): δ 99.84–99.37 (C-1), 84.01–83.23 (C-2,3), 81.87–80.63 (1 × C-3, C-4), 75.19 (α-CH_2), 73.18–73.02 (C-6), 72.84–72.59 (C-5), 59.72, 59.66 (6-OCH_3), 62.15–62.03, 59.70–59.24 (2,3-OCH_3), 42.67 (CH_2–NH_2), 33.62 (ε-CH_2), 31.62 (β-CH_2), 28.30, 27.42 (γ,δ-CH_2); $C_{68}H_{123}NO_{35}$ 1514.71, MALDI-TOF MS: *m*/*z* 1537.0 $[M + Na]^+$, 1552.7 $[M + K]^+$.

Immobilization of cyclodextrin derivatives on silica

Batch procedure. The monoaminoalkyl derivatives were immobilized to glycidoxypropyl silica gel (5 μm particle size, 100 Å pore size; Macherey–Nagel, Düren, Germany) and the monoepoxyalkyl derivatives on

aminopropyl silica gel (7 μm particle size, 100 Å pore size, Macherey–Nagel, Düren, Germany) applying the conditions listed in Table 1. Stirring was performed slowly using a rotatory evaporator to avoid the degradation of the spherical silica gel particles by a stirring bar [30]. The modified silica was thoroughly washed with MeOH, acetone, and CH_2Cl_2 and dried under high vacuum at 50 °C overnight. Finally, immobilization ratios were determined by elemental analysis (Table 1).

On-column procedure. The fused silica capillary (1 m, 150–180 μm ID, 370 μm OD, Microquartz, Munich, Germany) was packed with the diol silica (5 μm particle size, 100 Å particle size, E. Merck, Darmstadt, Germany) and suspended in acetonitrile by the slurry technique, as described previously [31]. Periodate cleavage of the diol silica was performed by pumping an aq soln of $NaIO_4$ (14 mg/mL) through the capillary at 350 bar for 2 h. Excess $NaIO_4$ was washed out of the capillary with water to protect the cyclodextrin selector against cleavage. Finally, 4 mg of the monoaminoalkyl cyclodextrin and 2 mg $NaCNBH_3$ were dissolved in 1 mL MeOH and pressed through the column at 250 bar overnight.

Acknowledgements

We thank Macherey–Nagel, Düren (Germany) for supplying aminopropyl- and glycidoxypropyl silica. This work was funded by the European Union in the frame of the FAIR programme, project no. PL 95 0300.

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