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# Multiple Homo- and Hetero-functionalizations of α-Cyclodextrin through Oriented Deprotections

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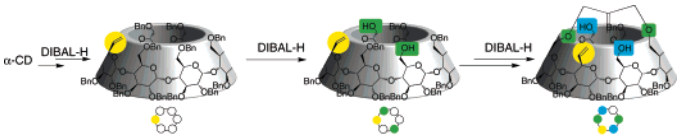


Introduction of one or more functions on a cyclodextrin in a regioselective manner is a complex task. The discovery of a blueprint strategy involving regioselective deprotection reactions of fully protected cyclodextrins, instead of functionalization of native cyclodextrins, allowed us to propose an efficient alternative to reach this goal. In this paper, we have applied previously delineated strategies, based on steric decompression, to duplicate our deprotection reaction, using a combination of mono- or di-deprotections to access cyclodextrins with two, three and five points of attachment for one, two or three different new functions. The patterns of multi-functionalization delineated here are not accessible by any other methods. Indeed, it is the first time ever a cyclodextrin bearing four different groups is synthesized in a completely controlled manner. This work paves the way to the use of cyclodextrins as multi-functional macrocyclic scaffolds, a use they have long been meant for, but lack of reliable functionalization methods hindered this development.

## Introduction

Cyclodextrins (CDs) are water soluble lamp-shade-shaped cyclic oligosaccharides presenting a hydrophobic cavity. Their applications in their native form range from deodorant to drug vectors, but further development of their potential toward more elaborated applications relies on their functionalization. A lot of effort has been invested in this field, but only a limited fraction of functionalization patterns are accessible, rarely in large practical scale.[1] Focusing on the primary hydroxyls, although their mono-functionalization is a relatively easy task,[2] the regioselective double addition of a new functionality is much more delicate but has been thoroughly investigated. The current methods vary according to the nature of the CD: for α-CD the best results are obtained with large groups relying on the steric hindrance for the selectivity;[3] for β-CD a capping strategy has been delineated on the basis of the geometry of these reagents to react with a given pair of hydroxyl groups.[4,5] Selective trisubstitution on the other hand is a largely unexplored area, indeed, out of the four possible patterns **a**−**d** for the trifunctionalisation of the primary rim of α-CD (Figure 1) only the $C_3$ symmetric **a** is currently accessible.[6] In the case of hetero-trifunctionalization of α-CDs even more patterns are possible as illustrated on Figure 1, but none have been described.[7]

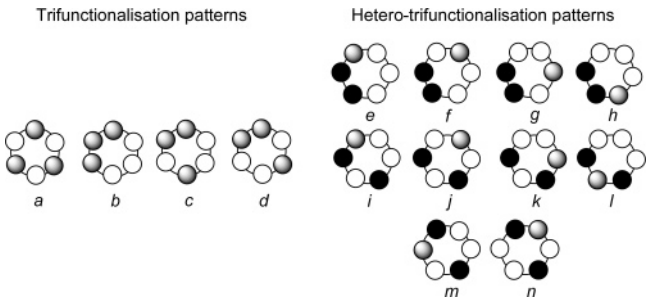


**FIGURE 1.** Trifunctionnalisation patterns on α-CD.

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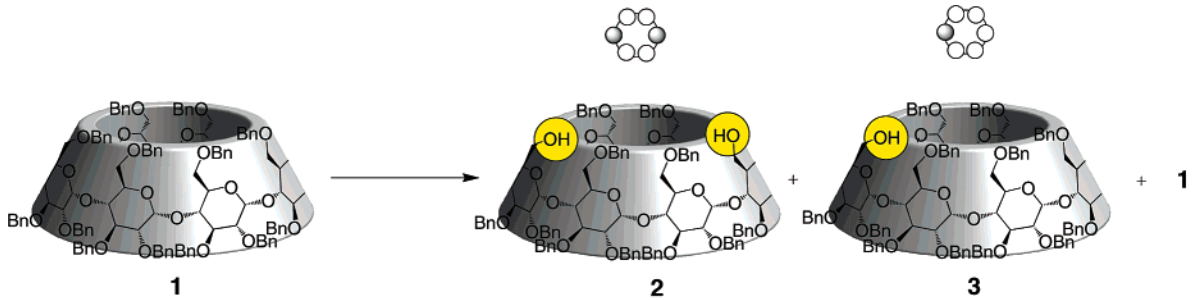
**SCHEME 1. Debenzylation of Perbenzylated α-CD 1 with DIBAL-H**




| DIBAL-H : | 2 | 3 | 1 |
|---|---|---|---|
| 120 eq, 0.5M, 50°C, 2h | 82% | 0% | 0% |
| 30 eq, 1M, 50°C, 3h | 82% | 0% | 0% |
| 30 eq, 0.1M, rt, 2h | 21% | 64% | 13% |
| 10 eq, 1M, 50°C, 30min | 0% | 49% | 32% |
| 2 eq, 1M, 50°C, 2h | 0% | 58% | 27% |

In this context the development of an efficient and scalable double deprotection of perbenzylated α- and *β*-CDs using diisobutylaluminium hydride (DIBAL-H) afforded a good alternative to previously existing methods.[8] A very important parameter in the reaction is the concentration in DIBAL-H, indeed, according to our proposed mechanism,[8] speed of reaction should be of order 2 in aluminum reagent. Therefore an increase of concentration allows the decrease in reagent excess, from 120 equiv at 0.5 M to 15 equiv at 1.5 M for example. If this balance is not respected, the reaction never goes to completion but yields a mixture of diol **2**, alcohol **3** and starting material **1**. It is hence possible to tune experimental conditions to optimize mono-deprotection of CD **1** to afford alcohol **3** in 64% yield, always accompanied by unreacted CD **1**, which can be recycled, but also by diol **2** (Scheme 1). This reaction is not as spectacular as the double deprotection because as we already mentioned, the access to mono-functional CDs have been accessible for a long time, although our yield is very competitive in this field. However, in our quest for functional pattern diversity, we believed it would be interesting to exploit this reaction in view of an iterative deprotection process yielding trifunctional CDs.

## Results and Discussion

The double deprotection can be duplicated selectively through two strategies both allowing access to CDs bearing three diametrically opposed pairs of protecting groups on their primary rims.[9] It relies on the steric decompression of the 6-position of a given pair of sugar units inducing a kinetically favored approach of the aluminum reagent and subsequent debenzylation on the clockwise sugar (view from the primary rim). The first method uses deoxy-sugars;[9,10] for example, when dideoxy-unsaturated CD **4**[9] is subjected to the action of DIBAL-H (30 equiv, 1 M) a single diol **5** is obtained with an excellent yield (90%) (Scheme 2). An extension of this work is the combination of double and simple debenzylation reactions as well as steric decompression techniques to pave the way toward trifunctionalized α-CDs.

The same unsaturated CD **4** was therefore subjected to the action of DIBAL-H at a concentration of 0.1 M and at room temperature to afford alcohol **6** in 54% yield together with 23% of diol **5** and 21% of starting material **4**. The regioselectivity of the reaction was determined indirectly through further reaction of the obtained **6** with DIBAL-H affording known diol **5**. Reductive ozonolysis of **6** affords triol **7** in 63% yield, whereas silylation and subsequent reductive ozonolysis give diol **8** (45%) bearing three different functionalities on the primary rim (Scheme 2).

Our second strategy to regioselectively duplicate the cleavage of benzyl groups is based on the conformational change induced by the bridging of a cyclodextrin as in CD **9**, giving, upon reaction with DIBAL-H, the diol **10** in 93% yield.[9,11] As in the previous case, mono-debenzylation in the same conditions afforded CD **11** in 52% as well as diol **10** in 26% and starting material **9** in 22% yield. Further debenzylation of **11** afforded diol **10** in 95% yield, confirming its structure. The same triol **7** and diol **8** as in the previous case can be obtained using $Pd^0$-assisted cleavage of the bridge in 51% and 45% yield, respectively (Scheme 3). We have hence delineated two completely regioselective routes to two new useful trifunctional

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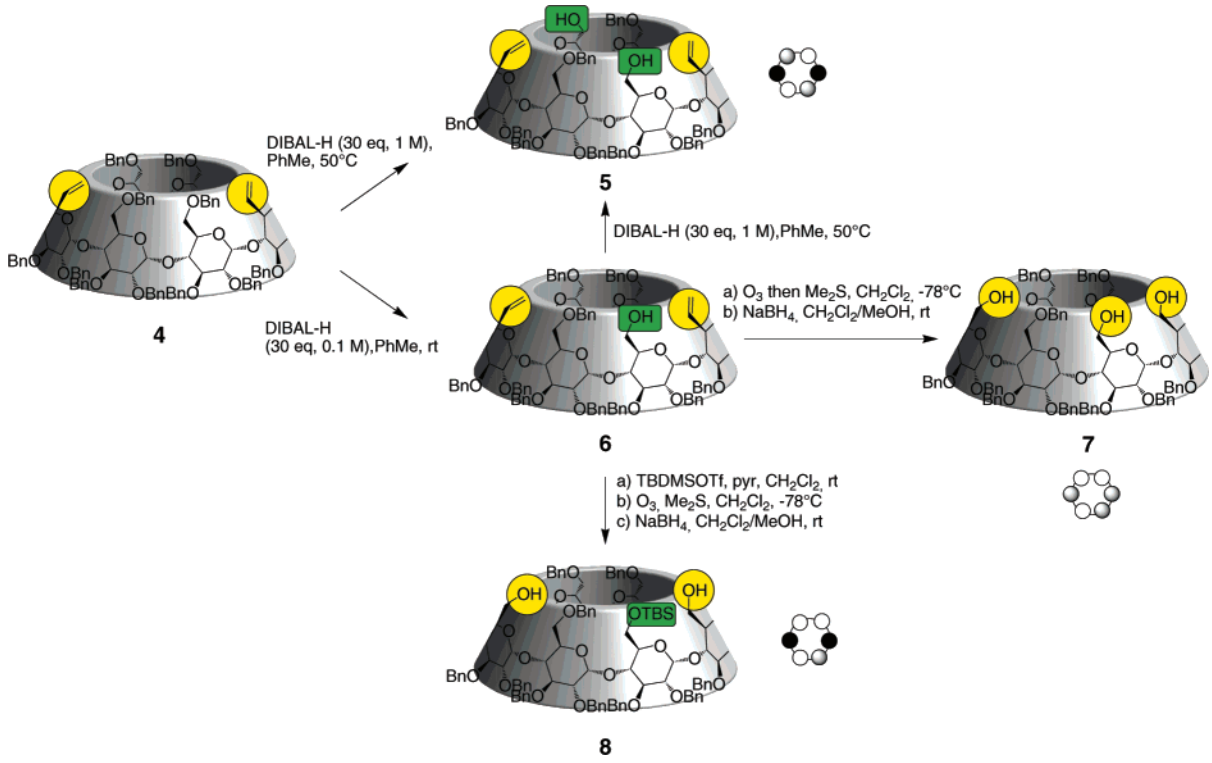
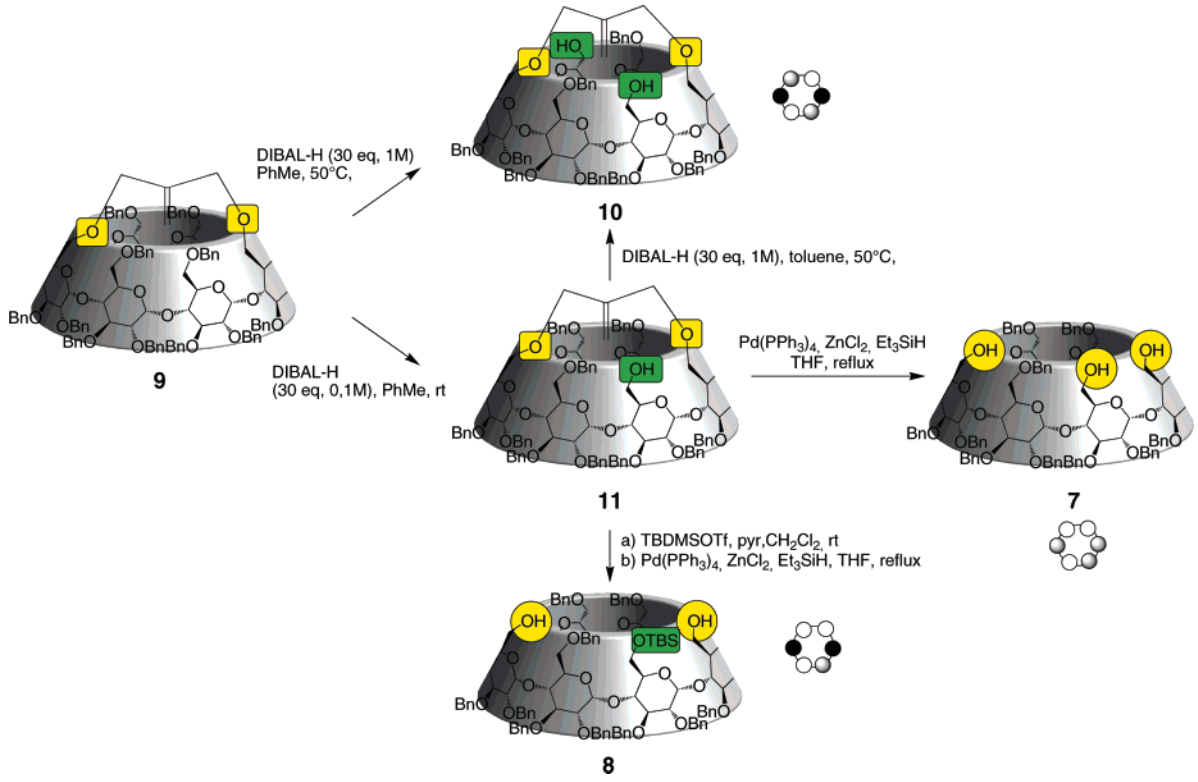
**SCHEME 2. Mono- or Di-deprotection of Dideoxy-CD 4**



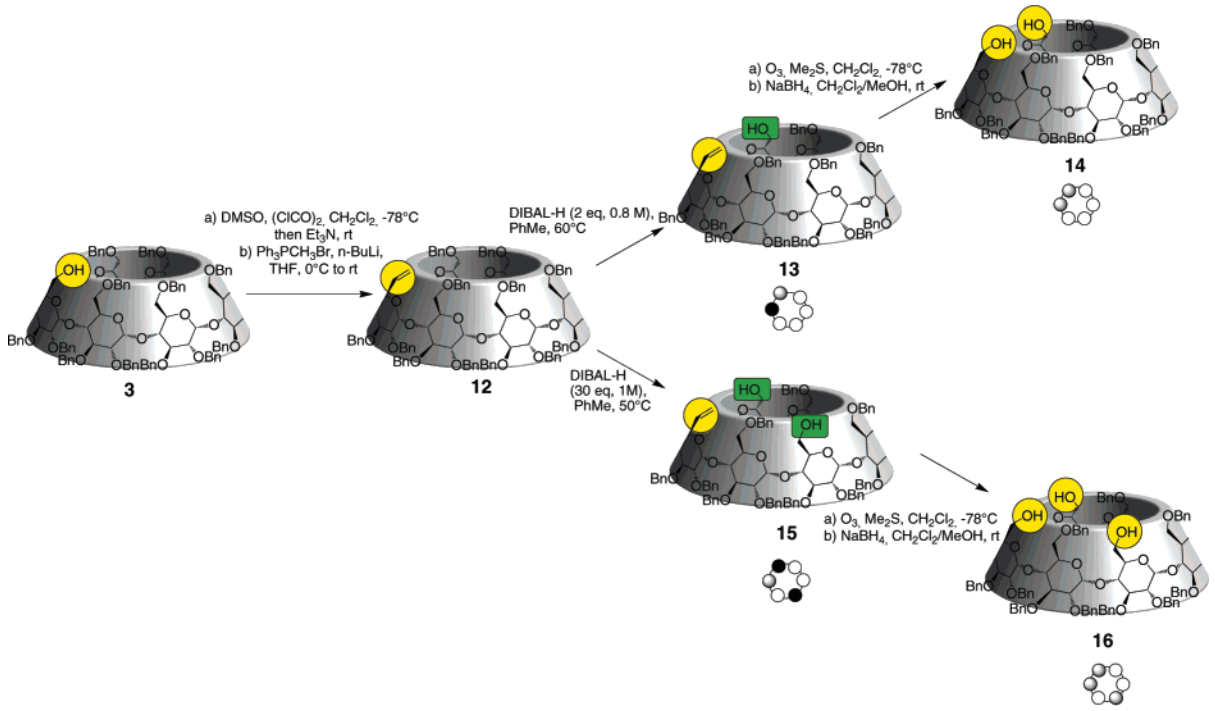

**SCHEME 3. Mono- or Di-deprotection of Bridged-CD 9**



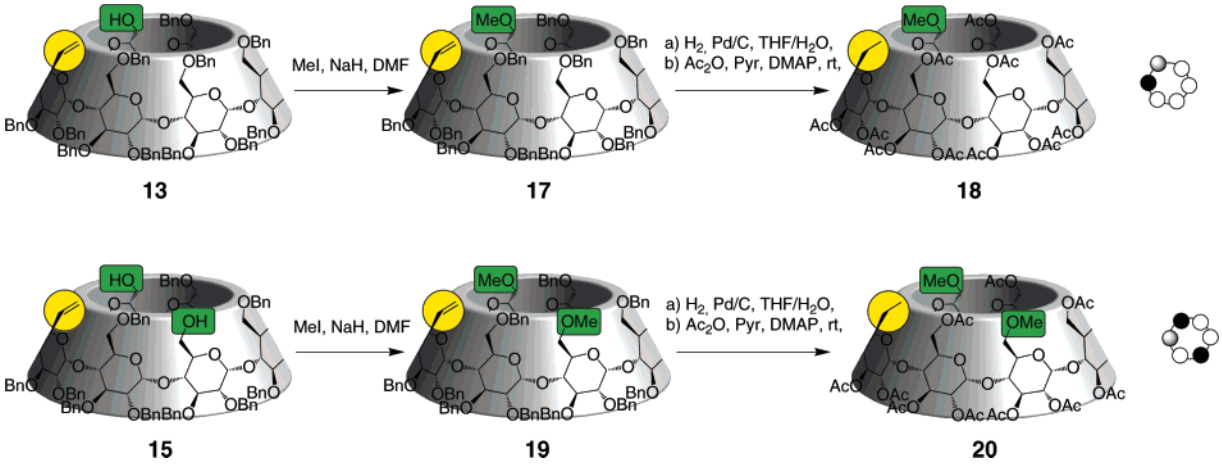

CD derivatives ready for further derivatization by one or two new functions, with so far completely unaccessible patterns.

We can also adopt the inverse strategy and start from the mono-alcohol **3** to access CDs functionalized on two or three positions via mono or di-deprotection. Alcohol **3** was therefore converted into vinyl CD **12** through Swern oxidation and Wittig olefination in 90% yield over two steps. The mono-deprotection of **12** needs careful monitoring and required some tuning of the reaction conditions. In this case, the symmetry being broken the DIBAL-H molecule needs to discriminate between five positions instead of two in the case of $C_2$ symmetric CDs **4** and **9**. In the end, we determined that treatment of alkene **12**

**SCHEME 4. Mono- or Di-deprotection of Mono-deoxy-CD 12**




**SCHEME 5. Synthesis of CDs 18 and 20 for NMR Analysis**




with 2 equiv of DIBAL-H at a concentration of 0.8 mol $L^{-1}$ for approximately 2 h at 60 °C was the most reproducible procedure to obtain alcohol **13** as a major product in 41% as well as 22% of unreacted starting material **12** and 20% of diol **15**. Alcohol **13** is a useful synthon bearing two different contiguous functionalizable positions. However, it is also possible to generate diol CD **14** with two identical contiguous functionalities through reductive ozonolysis of the olefin **13** in 50% yield. On the other hand, the usual double deprotection conditions afforded diol **15** in 77% yield from the same olefine **12**. The reaction starts with the debenzylation of the same kinetically favored position clockwise to the vinyl group, which in turn induces the selectivity of the second debenzylation process on the diametrically opposed sugar. This relay double deprotection constitutes an original regioselective process. It is also worth noting that the pattern of functionalization in CD **16** is symmetric to the one in **7**, and is readily afforded through reductive ozonolysis of CD **15** in 81% yield (Scheme 4).

The regioisomeric outcome of the previous reactions needs to be unambiguously assigned. We therefore undertook careful analysis of simplified derivatives of CDs **13** and **15** by NMR spectroscopy using a 600 MHz spectrometer using COSY, TOCSY and NOESY experiments. To this purpose, we converted CDs **13** and **15** into the peracetylated compounds **18** and **20** via methylation, hydrogenolysis with simultaneous saturation of the double bond and final peracetylation (Scheme 5).

We hence got rid of the benzylic protons that overlap some of the sugar proton signals. We also introduced tags clearly identifying the different groups on the position 6 of the sugar units: a methyl ether, a deoxygenation of the position 6, and acetyl groups. Indeed, the deoxygenated 6-position is easily detected through its chemical shift, H-6 next to acetyl groups are deshielded and the remaining H-6 presents a NOE correlation with the neighboring methyl ether. In the case of CD **18** a pair of NOE cross correlation between the unique $CH_3$ group and two H-6 identifies cycle **F** (Figure 2) and one deoxy position

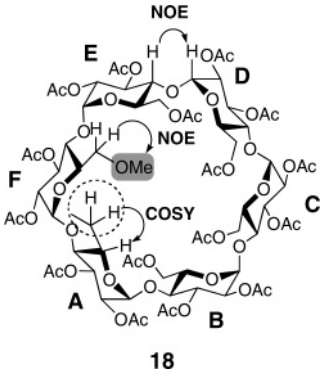



**FIGURE 2.** Structural assignment of CD **18**.

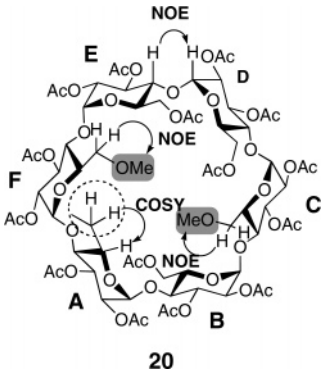



**FIGURE 3.** Structural assignment of CD **20**.

allows the assignment of unit **A** (Figure 2). In the case of CD **20** two sets of NOE correlations are detected clearly pointing out the two methylated units **C** and **F** (Figure 3) and one deoxy position allows the assignment of unit **A** (Figure 3). Having clearly identified three sets of H-6 protons, COSY and TOCSY experiments then allowed the assignment of all signals on each cycle. Finally, the sequence of the cycles was reconstituted through H-1/H-4 NOE cross correlations between different cycles (Figures 2 and 3).

Access to compound **15** allows to envisage going one step further in the diversity of functionalization of the primary rim of CDs regioselectively accessible by yet another deprotection. Indeed, capped CD **21**, product of the methalyl-bridging of diol **15** in 80% yield, is submitted to the action of DIBAL-H to afford through double deprotection diol **22** in 48% yield, a CD bearing four different functionalities on the primary rim (Scheme 6). This constitutes a completely regioselective sequence affording a CD bearing a pattern of functionalization with an unprecedented degree of complexity.

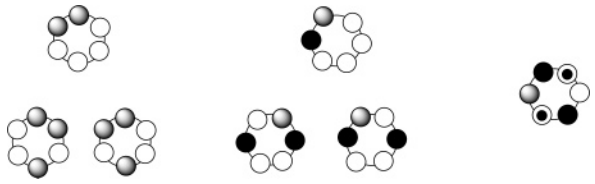


**FIGURE 4.** Patterns of functionalization accessible through the methods described in this paper.

## Conclusion

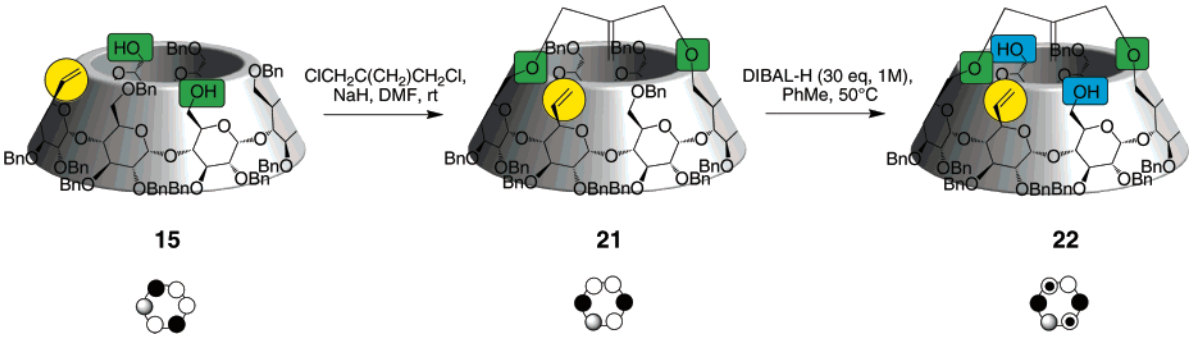
We have shown that it is possible to access a large number of previously unaccessible functionalization patterns of the primary rim of α-cyclodextrins through iterative DIBAL-H mono- and di-deprotection of judiciously protected CDs (Figure 4). A remarkable relay process has been delineated, where a first kinetic deprotection induces the selectivity of the second. An unprecedented completely regioselective synthesis of a CD bearing four different groups on its primary rim is also uncovered. The easy acces to a wide variety of easily functionalizable CDs allows the design of new applications, such as asymmetric metal ligands or organocatalysts with a spacial arrangement imposed by the structure of the cyclodextrin.

## Experimental Section

**Mono Alcohol 3.** DIBAL-H (2.4 mL, 3.6 mmol, 1.5 m in toluene) was added dropwise over 2 min to a stirred solution of CD **1** (310 mg, 0.12 mmol) in anhydrous toluene (33.5 mL) at room temperature under argon. The reaction mixture was stirred at 25 °C for 100 min, when TLC (cyclohexane/EtOAc: 3/1) indicated starting material ($R_f$ 0.6), a major product ($R_f$ 0.4) and a minor product ($R_f$ 0.3). The mixture was cooled to 0 °C, water (15 mL) was added dropwise (CARE! exothermic evolution of gas), and the mixture was then stirred vigorously at room temperature for 15 min. The mixture was diluted with EtOAc (75 mL) and filtered (Celite) into a separating funnel washing thoroughly with hot EtOAc (3 × 75 mL). Water (50 mL) was added, the organic layer was washed with brine (100 mL), dried ($MgSO_4$), and filtered, and the solvent was removed in vacuo. The residue was purified by flash chromatography (eluent gradient, 20−22% EtOAc in cyclohexane) to afford recovered **1** (39 mg, 13%) and **3** as a colorless foam (193 mg, 64%), further elution gave **2** (62 mg, 21%).

$[\alpha]_D^{20}$: +33.0 (*c* 0.9, $CHCl_3$). $R_f$: 0.4 (cyclohexane/AcOEt:3/1). $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 7.50−7.21 (m, 85H, H arom), 5.68 (d, 1H, $^3J_{1,2}$ 3.7 Hz, H-1), 5.64 (d, 1H, $^3J_{1,2}$ 3.7 Hz, H-1), 5.55 (d, 1H, $^2J$ 10.6 Hz, CHPh), 5.49 (d, 1H, $^2J$ 10.6 Hz, CHPh), 5.39 (d, 1H, $^2J$ 10.6 Hz, CHPh), 5.34 (d, 1H, $^2J$ 10.9 Hz, CHPh), 5.13−4.95 (m, 12H, 4×H-1, 8×CHPh), 4.85 (d, 1H, $^2J$ 12.3 Hz, CHPh), 4.84 (d, 1H, $^2J$ 12.1 Hz, CHPh), 4.71−4.44 (m, 20H, 20×CHPh), 4.39−4.33 (m, 2H, 2×H-3), 4.31−4.21 (m, 7H, 4×H-

**SCHEME 6. Tetradifferentiation of the Primary Rim of α-CD**



3, 3×H-4), 4.18−3.99 (m, 12H, 3×H-4, 6×H-5, 3×H-6), 3.91−3.79 (m, 5H, 5×H-6), 3.74−3.69 (m, 4H, 2×H-2, 2×H-6), 3.65−3.55 (m, 6H, 4×H-2, 2×H-6), 2.76 (dd, 1H, $^3J_{6,OH}$ 5.7, $^3J_{6',OH}$ 5.7 Hz, OH). $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 139.3, 139.3, 139.25, 139.2, 139.2, 139.15, 138.5, 138.4, 138.3, 138.2, 138.2, 138.2, 138.0, 138.0, 138.0, 137.9, 137.8 (17×C arom quat), 128.3−126.3 (m, 85×C arom tert), 98.7, 98.3, 98.1, 98.0, 98.0, 97.9 (6×C-1), 81.3, 81.3, 81.1, 81.0, 80.8, 80.8, 80.7, 80.3, 80.2, 79.9 (10C, 6×C-3, 4×C-4), 79.6, 79.3, 79.1, 79.9, 78.4, 77.9 (6×C-2), 76.4 (C-4), 76.2, 76.0, 75.8, 75.8 (4×$CH_2$Ph), 75.6 (C-4), 74.6 (2×$CH_2$Ph), 73.7, 73.3, 73.3, 73.2, 73.2, 73.15, 73.1, 72.9, 72.8 (9×$CH_2$Ph), 72.3 (2×$CH_2$Ph), 71.8, 71.7, 71.6, 71.4, 71.3, 71.2 (6×C-5), 69.4, 69.3, 69.2, 69.1, 68.9, 61.4 (6×C-6). FAB MS (M + Na)$^+$: *m/z* 2526.9.

**Mono Alcohol 6.** DIBAL-H (1.5 M in toluene, 1.66 mL, 2.49 mmol, 30 equiv) was slowly added to a solution of **4**[9] (200 mg, 83.2 $\mu$mol, 1 equiv) in toluene (24 mL) under argon at room temperature (rt). The reaction mixture was stirred at rt until TLC indicated formation of monoalcohol as a major product and then poured on ice. HCl (5 mL, 1 mol $L^{-1}$ in water) and EtOAc (15 mL) were added, and the solution was stirred for 1 h. The aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vaccuo. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 4/1) gave starting material **4**[9] (42 mg, 21%), monol **6** (104 mg, 54%) and diol **5** (43 mg, 23%) as white foams.

$[\alpha]_D^{20}$: +39.9 (*c* 1.0, $CHCl_3$). $R_f$: 0.55 (cyclohexane/AcOEt: 2/1). $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 7.36−7.11 (m, 75H, H arom), 6.02 (ddd, 1H, $^3J_{5,6}$ 6.3, $^3J_{cis}$ 10.5, $^3J_{trans}$ 17.0 Hz, C*H*═$CH_2$), 5.94 (ddd, 1H, $^3J_{5,6}$ 7.0, $^3J_{cis}$ 10.3, $^3J_{trans}$ 17.2 Hz, C*H*═$CH_2$), 5.47 (d, 1H, $^2J$ 9.4 Hz, CHPh), 5.47 (d, 1H, $^3J_{1,2}$ 2.0 Hz, H-1), 5.46 (d, 1H, $^3J_{1,2}$ 3.0 Hz, H-1), 5.41 (d, 1H, $^2J$ 10.6 Hz, CHPh), 5.32 (bd, 2H, $^2J_{trans}$ 17.2 Hz, 2×CH═C$H_2$), 5.30 (d, 1H, $^2J$ 10.5 Hz, CHPh), 5.24 (d, 1H, $^2J$ 10.8 Hz, CHPh), 5.10 (bd, 1H, $^3J_{cis}$ 10.0 Hz, CH═C$H_2$), 5.07 (bd, 1H, $^3J_{cis}$ 9.5 Hz, CH═C$H_2$), 4.98 (d, 1H, $^3J_{1,2}$ 3.3 Hz, H-1), 4.95 (d, 1H, $^2J$ 11.7 Hz, CHPh), 4.93 (d, 1H, $^2J$ 12.4 Hz, CHPh), 4.88 (d, 1H, $^2J$ 11.9 Hz, CHPh), 4.86 (d, 1H, $^2J$ 10.5 Hz, CHPh), 4.84 (d, 1H, $^2J$ 10.7 Hz, CHPh), 4.81 (d, 1H, $^3J_{1,2}$ 3.3 Hz, H-1), 4.77 (d, 1H, $^3J_{1,2}$ 3.5 Hz, H-1), 4.76 (d, 1H, $^2J$ 10.4 Hz, CHPh), 4.76 (d, 1H, $^3J_{1,2}$ 3.3 Hz, H-1), 4.64 (d, 1H, $^2J$ 12.5 Hz, CHPh), 4.61 (d, 1H, $^2J$ 9.5 Hz, CHPh), 4.58−4.53 (m, 5H, H-5, 4×CHPh), 4.52−4.46 (m, 8H, H-6, 7×CHPh), 4.44−4.38 (m, 9H, 2×H-5, H-6, 6×CHPh), 4.33 (d, 1H, $^2J$ 12.9 Hz, CHPh), 4.23 (bdd, 2H, $^3J_{2,3}$ 8.3, $^3J_{3,4}$ 9.5 Hz, 2×H-3), 4.13−4.07 (m, 6H, 4×H-3, 2×H-6), 4.06−4.02 (m, 4H, 3×H-5, H-6), 3.96−3.81 (m, 5H, 4×H-4, H-6), 3.66 (bd, 2H, $^2J$ 10.4 Hz, 2×H-6), 3.59 (dd, 2H, $^3J_{3,4}$ 9.1, $^3J_{4,5}$ 8.7 Hz, 2×H-4), 3.57−3.53 (m, 3H, 3×H-2), 3.50 (dd, 1H, $^3J_{1,2}$ 3.2, $^3J_{2,3}$ 9.8 Hz, H-2), 3.46−3.42 (m, 2H, 2×H-2). $^{13}$C NMR ($CDCl_3$, 100 MHz) : $\delta$ 139.86, 139.82, 139.77, 139.75, 139.74, 139.66, 139.19, 138.92, 138.74, 138.72 (2C), 138.45, 138.41 (2C), 138.27 (15×C arom quat), 136.97, 136.82 (2×*C*H═$CH_2$), 128.77−126.65 (m, 75×C arom tert), 119.88, 119.12 (2×CH═*C*$H_2$), 99.31, 99.15, 99.02, 98.94, 98.84, 98.65 (6×C-1), 82.23, 81.98 (2×C-4), 81.91 (2C), 81.61, 81.51 (4×C-4), 81.46, 81.42, 81.31, 81.08, 80.78, 80.69 (6×C-3), 80.28, 80.10, 79.62, 79.20, 78.75, 78.62 (6×C-2), 76.89, 76.66 (2C), 76.47, 76.23, 74.74, 74.51, 73.81 (2C), 73.72 (2C), 73.47, 72.56 (2C) (14×$CH_2$Ph), 72.34, 72.29, 72.03, 71.57, 71.14, 69.55 (6×C-5), 69.46 ($CH_2$Ph), 64.26, 62.35, 60.83 (2C) (4×C-6). FAB MS (M + Na)$^+$: *m/z* 2338.9. Anal. Calcd for $C_{143}H_{150}O_{28}$•$CH_2Cl_2$: C, 72.02; H, 6.38. Found: C, 72.40; H, 6.42.

**Further Debenzylation of CD 6: Diol 5.** DIBAL-H (1.5 M in toluene, 5 mL, 7.7 mmol, 30 equiv) was slowly added to a solution of monol **6** (594 mg, 257 $\mu$mol, 1 equiv) in toluene (2.5 mL) under argon at rt. The reaction mixture was heated at 60 °C for 1 h under a flux of argon. Upon completion, it was cooled to rt and poured on ice. HCl (5 mL, 1 mol $L^{-1}$ in water) and EtOAc (10 mL) were added and the solution was stirred for 1 h. The aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vaccuo. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 3/1) gave the known diol **5** (352 mg, 62%) as a white foam. Mass and $^1$H and $^{13}$C NMR spectra were in accordance with the litterature.[9]

**Triol 7 via Ozonolysis of α-CD 6.** Compound 6 (200 mg, 86 $\mu$mol, 1 equiv) was dissolved in $CH_2Cl_2$ (30 mL). The solution was cooled to −78 °C and ozone was bubbled through it for 2 min, until the solution turned blue. Excess (1.0 mL) $Me_2S$ was then added. The reaction mixture was stirred at rt for 20 min, then evaporated, and dissolved in 5 mL of $CH_2Cl_2$/MeOH (1:1), and the solution was treated at rt by $NaBH_4$ (26 mg, 691 $\mu$mol, 8 equiv). After 2 h of stirring at rt, MeOH (5 mL) was added and the mixture was evaporated to dryness. The residue was dissolved in 3 mL of MeOH and then concentrated; this operation was repeated 3 times. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 2/1) afforded the α-CD 7 (126 g, 63%) as a white foam.

**Triol 7 via Deprotection of the Bridge of α-CD 11.** $Pd^0(PPh_3)_4$ (15 mg, 12.6 $\mu$mol, 0.1 equiv), prepared according to the Rosevear methodology,[12] is added to a solution of compound **11** (300 mg, 126 $\mu$mol, 1 equiv) in THF (10 mL). A 1 M solution of anhydrous $ZnCl_2$ in THF (1.89 mL, 1.89 $\mu$mol, 15 equiv) is added dropwise to the reaction mixture at rt 10 min later; $ET_3SiH$ (305 $\mu$L, 1.89 $\mu$mol, 15 equiv) is added slowly. The reaction mixture is refluxed for 12 h under argon and then cooled to rt, water (5 mL) is added, the layers are separated, and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vaccuo. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 3/1) gave **7** (150 mg, 51%) as a white foam.

$[\alpha]_D^{20}$: +37.7 (*c* 1.0, $CHCl_3$). $R_f$: 0.60 (cyclohexane/AcOEt: 1/1); $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 7.21−6.79 (m, 75H, H arom), 5.49 (d, 1H, $^3J_{1,2}$ 3.7 Hz, H-1), 5.47 (d, 1H, $^3J_{1,2}$ 3.9 Hz, H-1), 5.25 (d, 1H, $^2J$ 10.5 Hz, CHPh), 5.24 (d, 1H, $^2J$ 10.7 Hz, CHPh), 5.13 (d, 1H, $^2J$ 10.5 Hz, CHPh), 5.12 (d, 1H, $^2J$ 10.7 Hz, CHPh), 4.82 (d, 1H, $^3J_{1,2}$ 3.5 Hz, H-1), 4.80 (d, 1H, $^2J$ 10.8 Hz, CHPh), 4.78 (d, 1H, $^3J_{1,2}$ 3.9 Hz, H-1), 4.77 (d, 1H, $^2J$ 10.3 Hz, CHPh), 4.76 (d, 1H, $^2J$ 10.3 Hz, CHPh), 4.75 (d, 1H, $^2J$ 9.2 Hz, CHPh), 4.70 (d, 1H, $^2J$ 10.7 Hz, CHPh), 4.69 (d, 1H, $^2J$ 10.5 Hz, CHPh), 4.64 (d, 1H, $^2J$ 12.3 Hz, CHPh), 4.62 (d, 1H, $^2J$ 12.7 Hz, CHPh), 4.61 (d, 1H, $^2J$ 10.3 Hz, CHPh), 4.59 (d, 1H, $^2J$ 11.8 Hz, CHPh), 4.57 (d, 1H, $^3J_{1,2}$ 3.3 Hz, H-1), 4.56 (d, 1H, $^2J$ 10.1 Hz, CHPh), 4.54 (d, 1H, $^3J_{1,2}$ 3.3 Hz, H-1), 4.49 (bd, 4H, $^2J$ 12.3 Hz, 4×CHPh), 4.44 (d, 1H, $^2J$ 10.1 Hz, CHPh), 4.40 (d, 1H, $^2J$ 11.0 Hz, CHPh), 4.37 (d, 1H, $^2J$ 10.7 Hz, CHPh), 4.36 (d, 1H, $^2J$ 12.1 Hz, CHPh), 4.34 (d, 1H, $^2J$ 12.0 Hz, CHPh), 4.29 (d, 1H, $^2J$ 12.7 Hz, CHPh), 4.28 (bs, 4H, 2×$CH_2$Ph), 4.25 (d, 1H, $^2J$ 12.9 Hz, CHPh), 4.12−4.08 (m, 2H, 2×H-3), 4.05−3.93 (m, 7H, 4×H-3, 3×H-6), 3.90−3.84 (m, 8H, 5×H-5, 3×H-6), 3.82−3.78 (m, 3H, H-4, 2×H-6), 3.74 (dd, 1H, $^3J_{3,4}$ 9.0, $^3J_{4,5}$ 9.2 Hz, H-4), 3.70−3.60 (m, 6H, 3×H-4, H-5, 2×H-6), 3.59−3.55 (m, 3H, H-4, 2×H-6), 3.46 (dd, 1H, $^3J_{1,2}$ 3.9, $^3J_{2,3}$ 9.6 Hz, H-2), 3.43 (dd, 1H, $^3J_{1,2}$ 3.7, $^3J_{2,3}$ 9.9 Hz, H-2), 3.39 (dd, 1H, $^3J_{1,2}$ 3.3, $^3J_{2,3}$ 9.9 Hz, H-2), 3.35 (dd, 1H, $^3J_{1,2}$ 3.9, $^3J_{2,3}$ 8.5 Hz, H-2), 3.33 (dd, 1H, $^3J_{1,2}$ 3.2, $^3J_{2,3}$ 7.7 Hz, H-2), 3.29 (dd, 1H, $^3J_{1,2}$ 3.5, $^3J_{2,3}$ 9.6 Hz, H-2). $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 139.31, 139.25 (3C), 139.20 (2C), 138.55, 138.46, 138.23, 138.19, 138.11, 138.04, 137.98, 137.78, 137.49 (15×C arom quat), 128.42−126.35 (m, 75×C arom tert), 98.27, 98.25, 97.98, 97.76 (2C), 97.70 (6×C-1), 82.09 (C-4),81.65, 81.46, 81.45 (3×C-3), 80.99, 81.98 (2×C-4), 80.73, 80.52, 80.41 (3×C-3), 80.21 (C-4), 79.86, 79.61, 78.97, 78.82, 78.15, 78.03 (6×C-2), 76.36 (2C), 75.80, 75.75 (4×$CH_2$Ph), 75.38, 75.16 (2×C-4), 74.32 (2C), 73.55, 73.54, 73.45, 73.42, 73.28 (2C), 73.11 (9×$CH_2$Ph), 72.97 (C-5), 72.55, 72.44 (2×$CH_2$Ph), 72.23, 71.94, 71.66, 71.64, 71.49 (5×C-5), 69.88, 69.60, 69.50, 62.88, 61.82, 61.70 (6×C-6); FAB MS (M + Na)$^+$: *m/z* 2346.9. Anal. Calcd for $C_{141}H_{150}O_{30}$: C, 72.85; H, 6.50. Found: C, 72.67; H, 6.67.

(12) Rosevear, D. T.; Stone, F. G. H *J. Chem. Soc. A* **1968**, 164.

**Tridifferentiated CD 8 from Bridged-CD 6.** A solution of **6** (382 mg, 166 $\mu$mol, 1 equiv), pyridine (40 $\mu$L, 495 $\mu$mol, 3 equiv) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (114 $\mu$L, 495 $\mu$mol, 3 equiv) in dichloromethane (5 mL) was stirred at rt for 1 h. Upon completion of the reaction, the reaction mixture was washed with water (5 mL), dried over $MgSO_4$, filtered and concentrated. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 5/1) gave the silylated compound (397 mg, 99%) as a white foam directly used in the next step. $R_f$ 0.70 (cyclohexane/AcOEt: 2/1).

The sylilated compound (200 mg, 82.4 $\mu$mol, 1 equiv) was dissolved in $CH_2Cl_2$ (30 mL). The solution was cooled to −78 °C, and ozone was bubbled through it for 2 min, until the solution turned blue. Excess (0.5 mL) of $Me_2S$ was then added. The reaction mixture was stirred at rt for 20 min, then evaporated, dissolved in 5 mL of $CH_2Cl_2$/MeOH (1:1) and treated at rt by $NaBH_4$ (25 mg, 659 $\mu$mol, 8 equiv). After 2 h of stirring at rt, MeOH (5 mL) was added and the mixture was evaporated to dryness. The residue was dissolved in 3 mL of MeOH and then concentrated; this operation was repeated 3 times. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 2:1) afforded the α-CD **8** (91 mg, 45%) as a white foam.

**Tridifferentiated CD 8 from Bridged-CD 11.** A solution of **11** (1.30 g, 569 $\mu$mol, 1 equiv), pyridine (356 $\mu$L, 3.415 mmol, 6 equiv) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (784 $\mu$L, 3.415 mmol, 6 equiv) in dichloromethane (10 mL) was stirred at rt for 1 h. Upon completion of the reaction, the reaction mixture was washed with water (5 mL), dried over $MgSO_4$, filtered and concentrated. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 5/1) gave the silylated compound (498 mg, 91%) as a white foam directly used in the next step. $R_f$ 0.60 (cyclohexane/AcOEt: 3/1) $Pd^0(PPh_3)_4$ (57 mg, 49.4 $\mu$mol, 0.1 equiv), prepared according to the Rosevear methodology,[12] is added to a solution of the sylilated compound (1.24 g, 498 $\mu$mol, 1 equiv) in THF (10 mL). A 1 M solution of anhydrous $ZnCl_2$ in THF (7.4 mL, 7.4 mmol, 15 equiv) is added dropwise to the reaction mixture at rt 10 min later, $ET_3SiH$ (1.2 mL, 7.4 mmol, 1 equiv) is added slowly. The reaction mixture is refluxed for 12 h under argon and then cooled to rt, water (5 mL) is added, the layers are separated, and the aqueous layer is extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vaccuo. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 5/1) gave **8** (547 mg, 45%) and the starting material (650 mg, 52%) as white foams.

$[\alpha]_D^{20}$: +25.6 (*c* 1.0, $CHCl_3$). $R_f$: 0.70 (cyclohexane/AcOEt: 2/1). $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 7.22−6.96 (m, 75H, H arom), 5.62 (d, 1H, $^3J_{1,2}$ 3.7 Hz, H-1), 5.57 (d, 1H, $^3J_{1,2}$ 3.7 Hz, H-1), 5.37 (d, 1H, $^2J$ 10.3 Hz, CHPh), 5.35 (d, 1H, $^2J$ 10.5 Hz, CHPh), 5.08 (bd, 2H, $^2J$ 10.5 Hz, 2×CHPh), 4.87 (d, 1H, $^3J_{1,2}$ 3.1 Hz, H-1), 4.80 (d, 1H, $^2J$ 10.3 Hz, CHPh), 4.79 (d, 1H, $^2J$ 10.5 Hz, CHPh), 4.76 (d, 1H, $^2J$ 10.1 Hz, CHPh), 4.75 (d, 1H, $^2J$ 10.3 Hz, CHPh), 4.72 (d, 1H, $^2J$ 12.0 Hz, CHPh), 4.69 (d, 1H, $^2J$ 10.0 Hz, CHPh), 4.67 (d, 1H, $^2J$ 11.2 Hz, CHPh), 4.66 (d, 1H, $^2J$ 11.0 Hz, CHPh), 4.64 (d, 1H, $^3J_{1,2}$ 3.5 Hz, H-1), 4.62 (d, 1H, $^3J_{1,2}$ 3.7 Hz, H-1), 4.61 (d, 1H, $^3J_{1,2}$ 3.5 Hz, H-1), 4.53 (d, 1H, $^2J$ 12.3 Hz, CHPh), 4.50 (d, 1H, $^2J$ 10.0 Hz, CHPh), 4.49 (d, 1H, $^2J$ 12.5 Hz, CHPh), 4.48 (d, 1H, $^2J$ 12.3 Hz, CHPh), 4.47 (d, 1H, $^2J$ 12.1 Hz, CHPh), 4.43 (d, 1H, $^2J$ 8.9 Hz, CHPh), 4.42 (d, 1H, $^2J$ 12.7 Hz, CHPh), 4.38 (d, 1H, $^2J$ 10.1 Hz, CHPh), 4.36 (d, 1H, $^2J$ 12.5 Hz, CHPh), 4.35 (d, 1H, $^2J$ 11.0 Hz, CHPh), 4.33 (d, 1H, $^2J$ 10.2 Hz, CHPh), 4.32 (d, 1H, $^2J$ 12.0 Hz, CHPh), 4.31 (bd, 2H, $^2J$ 12.1 Hz, 2×CHPh), 4.26 (bd, 2H, $^2J$ 8.6 Hz, 2×CHPh), 4.22 (bd, 2H, $^2J$ 8.1 Hz, 2×CHPh), 4.18−4.08 (m, 4H, 3×H-3, H-5), 4.06−3.94 (m, 5H, 3×H-3, 2×H-5), 3.91−3.83 (m, 6H, 2×H-4, 3×H-5, H-6), 3.81−3.78 (m, 2H, H-4, H-6), 3.75−3.73 (m, 4H, 4×H-6), 3.71−3.66 (m, 4H, H-4, 3×H-6), 3.63−3.56 (m, 4H, H-4, 3×H-6), 3.48 (dd, 1H, $^3J_{1,2}$ 3.7, $^3J_{2,3}$ 9.8 Hz, H-2), 3.42 (dd, 1H, $^3J_{1,2}$ 3.1, $^3J_{2,3}$ 9.9 Hz, H-2), 3.41 (dd, 1H, $^3J_{1,2}$ 3.7, $^3J_{2,3}$ 9.6 Hz, H-2), 3.37−3.31 (m, 3H, 2×H-2, H-4), 3.30 (dd, 1H, $^3J_{1,2}$ 3.5, $^3J_{2,3}$ 9.6 Hz, H-2), 0.85 (s, 9H, $SiC(CH_3)_3$), 0.00 (s, 3H, $SiCH_3$), −0.01 (s, 3H, $SiCH_3$); $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 138.36, 138.27 (2C), 138.24 (2C) 138.18, 137.59, 137.52 (2C), 137.31, 137.30, 137.00, 136.99, 136.84, 136.80 (15×C arom quat), 127.32−125.32 (m, 75×C arom tert), 97.40, 97.18, 96.84, 96.66, 96.60, 96.37 (6×C-1), 80.86, 80.77 (2×C-4), 80.63, 80.59, 80.06, 79.90, 79.80 (5×C-3), 79.62 (C-3, C-4), 78.83, 78.79, 78.12, 78.08, 76.93, 76.72 (6×C-2), 76.22 (C-4), 75.42, 75.32, 75.08, 75.06 (4×$CH_2$Ph), 73.43 (C-4), 73.03 ($CH_2$-Ph), 73.00 (C-4), 72.93 ($CH_2$Ph), 72.43−72.37 (m, 7×$CH_2$Ph), 72.00, 71.81 (2×$CH_2$Ph), 71.78 (C-5), 71.32, 71.25 (2×C-6), 71.05, 70.98, 70.69, 70.23 (2C) (5×C-5), 68.70, 62.07, 60.89, 60.84 (4×C-6), 25.03 ($SiC(CH_3)_3$), 21.67 ($SiC(CH_3)_3$), −5.98, −6.24 (2×$SiCH_3$). FAB MS $(M + Na)^+$: *m*/*z* 2461.0. Anal. Calcd for $C_{147}H_{164}O_{30}$·Si·2MeOH: C, 71.50; H, 6.93. Found: C, 71.15; H, 7.05.

**Mono Alcohol 11.** DIBAL-H (1.5 M in toluene, 1.62 mL, 2.44 mmol, 30 equiv) was slowly added to a solution of **9**[11] (200 mg, 81.2 $\mu$mol, 1 equiv) in toluene (24 mL) under argon at rt. The reaction mixture was stirred at rt until TLC indicated formation of monoalcohol as a major product and then poured on ice. HCl (5 mL, 1 mol $L^{-1}$ in water) and EtOAc (15 mL) were added, and the solution was stirred for 1 h. The aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vaccuo. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 3/1) gave starting material **9** (46 mg, 22%), monol **11** (100 mg, 52%) and diol **10** (50 mg, 26%) as white foams.

$[\alpha]_D^{20L}$: +34.1 (*c* 1.0, $CHCl_3$). $R_f$: 0.50 (cyclohexane/AcOEt: 2/1) . $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 7.38−7.13 (m, 75H, H arom), 5.65 (d, 1H, $^3J_{1,2}$ 4.2 Hz, H-1), 5.63 (d, 1H, $^2J$ 10.5 Hz, CHPh), 5.62 (d, 1H, $^2J$ 10.5 Hz, CHPh), 5.58 (d, 1H, $^3J_{1,2}$ 4.1 Hz, H-1), 5.34 (d, 1H, $^2J$ 10.6 Hz, CHPh), 5.33 (d, 1H, $^2J$ 10.7 Hz, CHPh), 5.13 (bs, 1H, $(OCH_2)_2C{=}CH_2$), 5.06 (bs, 1H, $(OCH_2)_2C{=}CH_2$), 5.04 (d, 2H, $^2J$ 10.6 Hz, 2×CHPh), 4.87−4.96 (m, 6H, 6×CHPh), 4.85 (d, 1H, $^3J_{1,2}$ 3.5 Hz, H-1), 4.83 (d, 1H, $^3J_{1,2}$ 3.7 Hz, H-1), 4.80 (d, 1H, $^3J_{1,2}$ 2.8 Hz, H-1), 4.76 (d, 1H, $^3J_{1,2}$ 3.6 Hz, H-1), 4.61−4.44 (m, 13H, 13×CHPh), 4.41−4.33 (m, 10H, 2×H-4, 3×H-5, 5×H-6), 4.30 (d, 2H, $^2J$ 12.6 Hz, 2×CHPh), 4.23−4.13 (m, 6H, 4×H-3, 2×H-6), 4.07−4.00 (m, 6H, H-4, 2×H-5, 2× $(OCH_2)_2C{=}CH_2$, CHPh), 3.98−3.89 (m, 7H, 2×H-4, H-5, 2× $(OCH_2)_2C{=}CH_2$ , CHPh), 3.84 (d, 1H, $^2J$ 11.1 Hz, CHPh), 3.81−3.78 (m, 2H, 2×H-3), 3.69 (dd, 1H, $^3J_{1,2}$ 4.1, $^3J_{2,3}$ 10.0 Hz, H-2), 3.66 (dd, 1H, $^3J_{1,2}$ 2.2, $^3J_{2,3}$ 11.1 Hz, H-2), 3.65−3.61 (m, 2H, H-4, H-6), 3.58−3.48 (m, 7H, 2×H-2, H-4, 4×H-6), 3.44 (dd, 1H, $^3J_{1,2}$ 3.3, $^3J_{2,3}$ 7.9 Hz, H-2), 3.42 (dd, 1H, $^3J_{1,2}$ 3.2, $^3J_{2,3}$ 7.9 Hz, H-2), 1.34 (t, 1H, $^3J$ 7.1 Hz, OH). $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 142.93 ($(OCH_2)_2C{=}CH_2$), 139.62, 139.60, 139.35, 139.31 (2C), 139.26, 138.74, 138.62, 138.40, 138.30, 138.26, 138.14, 138.02, 137.82, 137.80 (15×C arom quat), 128.25−127.39 (m, 75×C arom tert), 114.16 ($(OCH_2)_2C{=}CH_2$), 99.67, 99.57, 99.49, 99.33, 97.84, 97.82 (6×C-1), 82.10 (C-3), 81.95 (C-4), 81.61 (C-3), 81.53 (C-4), 81.12 (2×C-3), 81.08 (C-4), 80.73 (C-3), 80.65 (C-4), 80.45 (C-3), 80.05 (2×C-2), 79.33, 79.09 (2×C-2), 78.87, 78.79 (2×C-4), 77.76, 77.64 (2×C-2), 76.57, 76.49, 76.04, 76.03 (4×$CH_2$Ph), 73.66−72.77 (m, 13C, 11×$CH_2$-Ph, 2×$(OCH_2)_2C{=}CH_2$), 72.58 (C-5), 71.97 (2×C-5), 71.91, 71.83 (2×C-6), 71.81 (2×C-5), 71.76, 69.50 (2×C-6), 69.13 (C-5), 69.01 (C-6), 62.18 ($CH_2OH$). FAB MS $(M + Na)^+$: *m*/*z* 2399.3. Anal. Calcd for $C_{145}H_{154}O_{30}$·$CH_2Cl_2$: C, 71.23; H, 6.39. Found: C, 71.23; H, 6.50.

**Further Debenzylation of CD 11: Diol 10.** DIBAL-H (1.5 M in toluene, 840 $\mu$L, 1.26 mmol, 30 equiv) was slowly added to a solution of monol **11** (100 mg, 42.0 $\mu$mol, 1 equiv) in toluene (400 $\mu$L) under argon at rt. The reaction mixture was heated at 60 °C for 1 h under a flux of argon. Upon completion, it was cooled to rt and poured on ice. HCl (1 mL, 1 mol $L^{-1}$ in water) and EtOAc (5 mL) were added, and the solution was stirred for 1 h. The aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vaccuo. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 2/1) gave the known diol **10** (77 mg, 80%)

as a white foam. Mass and $^1$H and $^{13}$C NMR spectra were in accordance with the litterature.[11]

**Olefinic α-CD 12.** DMSO (2.48 mL, 34.97 mmol, 5 equiv) was added dropwise to a solution of oxalyl chloride (1.5 mL, 17.49 mmol, 2.5 equiv) in $CH_2Cl_2$ (10 mL) cooled to −78 °C under argon. The reaction mixture was stirred at −78 °C for 30 min, and then a solution of monol 3[8] (17.5 g, 6.994 mmol, 1 equiv) in $CH_2Cl_2$ (100 mL) was added to it. After 2 h at −78 °C, $Et_3N$ (4.91 mL, 34.97 mmol, 5 equiv) was added and the reaction mixture was warmed to rt over 30 min. It was then treated with water (40 mL). The aqueous layer was extracted with $CH_2Cl_2$ (3 × 40 mL). Organic layers were combined, dried over $MgSO_4$, filtered and concentrated to give the aldehyde. $Ph_3PCH_3Br$ (12.5 g, 34.97 mmol, 5 equiv) was suspended in THF (50 mL), cooled to −40 °C and treated dropwise by *n*BuLi (2.5 M in hexane, 13.99 mL, 34.97 mmol, 5 equiv). The reaction mixture was stirred at −40 °C for 15 min and then at 0 °C for 5 min, and a solution of the previously obtained crude mono-aldehyde diluted in THF (50 mL) was added. The reaction mixture was stirred at rt for 12 h under argon. Water (50 mL) and $CH_2Cl_2$ (50 mL) were then added. The layers were separated. The aqueous layer was extracted with $CH_2Cl_2$ (3 × 50 mL). The organic layers were combined, dried over $MgSO_4$, filtered and concentrated. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 95/5, then 3/1) gave the olefinic CD 12 (15.71 g, 90% over two steps) as a white foam.

$[\alpha]_D^{20}$: +36 (*c* 0.5, $CHCl_3$). $R_f$: 0.75 (cyclohexane/AcOEt: 2/1). $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 7.35−7.14 (m, 85H, H arom), 6.04 (ddd, 1H, $^3J_{5,6}$ 6.7, $^3J_{cis}$ 10.3, $^3J_{trans}$ 17.1 Hz, C*H*═$CH_2$), 5.55 (d, 2H, $^3J_{1,2}$ 3.7 Hz, 2×H-1), 5.49 (d, 1H, $^2J$ 10.6 Hz, CHPh), 5.45 (d, 1H, $^2J$ 10.6 Hz, CHPh), 5.33 (bd, 1H, $^3J_{trans}$ 17.3 Hz, CH═C$H_2$), 5.28 (d, 1H, $^2J$ 10.7 Hz, CHPh), 5.27 (d, 1H, $^2J$ 10.8 Hz, CHPh), 5.14 (dd, 1H, $^3J_{cis}$ 10.2, $^2J$ 1.3 Hz, CH═C$H_2$), 5.03−4.86 (m, 12H, 4×H-1, 8×CHPh), 4.75 (d, 2H, $^2J$ 12.1 Hz, 2×CHPh), 4.60 (d, 1H, $^2J$ 12.7 Hz, CHPh), 4.55 (d, 1H, $^2J$ 12.4 Hz, CHPh), 4.52−4.38 (m, 17H, H-5, 16×CHPh), 4.35 (d, 1H, $^3J$ 10.8 Hz, CHPh), 4.32 (d, 1H, $^2J$ 11.7 Hz, CHPh), 4.29 (dd, 1H, $^3J_{3,4}$ 7.2, $^3J_{4,5}$ 9.7 Hz, H-4), 4.27 (dd, 1H, $^3J_{3,4}$ 9.7, $^3J_{4,5}$ 9.7 Hz, H-4), 4.23−4.13 (m, 9H, 4×H-3, 3×H-6, H-4, H-5), 4.10−4.04 (m, 5H, 2×H-3, H-5, 2×H-6), 3.98−3.92 (m, 5H, H-4, 3×H-5, H-6), 3.67−3.61 (m, 6H, 2×H-2, H-4, 2×H-6), 3.58−3.46 (m, 7H, 4×H-2, H-4, 2×H-6). $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 139.36, 139.35, 139.34, 139.30, 139.28, 139.22, 138.51, 138.50, 138.38, 138.27, 138.24, 138.23, 138.14, 138.08 (2C), 138.02, 138.00 (17×C arom quat), 136.87 (*C*H═$CH_2$), 128.25−126.37 (m, 85×C arom tert), 118.75 (CH═*C*$H_2$), 98.69, 98.59, 98.52, 98.25, 98.14, 97.88 (6×C-1), 81.22, 81.17, 81.10, 81.08, 81.04, 80.99 (6×C-4), 80.72, 80.64 (2C), 80.36, 79.97 (5×C-3), 79.71, 79.55, 79.02, 78.80, 78.34 (2C) (6×C-2), 76.84 (C-3), 76.20, 76.12, 75.86, 75.73, 74.54, 74.28 (6×$CH_2$-Ph), 73.49−73.08 (m, 7×$CH_2$Ph), 72.82, 72.72, 72.28, 72.10 (4×$CH_2$Ph), 71.74, 71.58, 71.24, 71.17, 71.01, 70.97 (6×C-5), 69.41, 69.35, 69.33, 69.13, 68.98 (5×C-6). FAB MS $(M + Na)^+$: *m*/*z* 2522.9. Anal. Calcd for $C_{156}H_{162}O_{29}$: C, 74.92; H, 6.53. Found: C, 74.72; H, 6.66.

**Mono Alcohol 13.** DIBAL-H (1.5 M in toluene, 530 μL, 800 μmol, 2 equiv) was slowly added to a solution of **12** (1.0 g, 400 μmol, 1 equiv) in toluene (500 μL) under argon at rt. The reaction mixture was heated at 60 °C for 2 h, until TLC indicated formation of mono-alcohol as a major product, and then cooled to rt and poured on ice. HCl (5 mL, 1 mol $L^{-1}$ in water) and EtOAc (10 mL) were added, and the solution was stirred for 1 h. The aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vaccuo. Silica gel chromatography of the residue (cyclohexane/EtOAc: 5/1) gave starting material **12** (217 mg, 22%), monol **13** (400 mg, 41%) and diol **15** (187 mg, 20%) as white foams.

$[\alpha]_D^{20}$: +32.9 (*c* 1.0, $CHCl_3$). $R_f$: 0.30 (cyclohexane/AcOEt: 2/1). $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 7.21−6.98 (m, 80H, H arom), 6.17 (ddd, 1H, $^3J_{5,6}$ 5.5, $^3J_{cis}$ 10.8, $^3J_{trans}$ 16.7 Hz, C*H*═$CH_2$), 5.30 (d, H, $^3J_{1,2}$ 3.7 Hz, H-1), 5.28 (d, 1H, $^2J$ 11.4 Hz, CHPh), 5.26 (d, H, $^3J_{1,2}$ 3.1 Hz, H-1), 5.24 (d, 1H, $^2J$ 10.1 Hz, CHPh), 5.16 (bd, 1H, $^3J_{trans}$ 17.3 Hz, CH═C$H_2$), 5.04 (bd, 1H, $^3J_{cis}$ 11.4 Hz, CH═C$H_2$), 5.01 (d, H, $^3J_{1,2}$ 2.6 Hz, H-1), 5.00 (d, H, $^3J_{1,2}$ 2.0 Hz, H-1), 4.97 (d, 1H, $^2J$ 11.0 Hz, CHPh), 4.96 (d, 1H, $^2J$ 11.2 Hz, CHPh), 4.95 (d, 1H, $^2J$ 11.0 Hz, CHPh), 4.84 (d, 1H, $^2J$ 11.2 Hz, CHPh), 4.80 (d, 1H, $^2J$ 12.7 Hz, CHPh), 4.79 (d, 1H, $^2J$ 10.7 Hz, CHPh), 4.76 (d, 1H, $^2J$ 11.0 Hz, CHPh), 4.72 (d, 2H, $^2J$ 11.0 Hz, 2×CHPh), 4.67 (d, 1H, $^3J_{1,2}$ 3.5 Hz, H-1), 4.64 (d, 1H, $^3J_{1,2}$ 3.5 Hz, H-1), 4.57 (d, 1H, $^2J$ 12.3 Hz, CHPh), 4.55 (d, 1H, $^2J$ 12.3 Hz, CHPh), 4.48 (d, 1H, $^2J$ 12.1 Hz, CHPh), 4.45 (d, 1H, $^2J$ 12.0 Hz, CHPh), 4.42 (d, 1H, $^2J$ 13.0 Hz, CHPh), 4.41 (d, 1H, $^2J$ 10.7 Hz, CHPh), 4.39 (d, 1H, $^2J$ 12.3 Hz, CHPh), 4.37 (s, 2H, $CH_2$Ph), 4.36 (d, 2H, $^2J$ 10.1 Hz, 2×CHPh), 4.35 (d, 1H, $^2J$ 12.3 Hz, CHPh), 4.34 (d, 2H, $^2J$ 12.7 Hz, 2×CHPh), 4.33 (d, 1H, $^2J$ 12.9 Hz, CHPh), 4.31 (d, 1H, $^2J$ 13.6 Hz, CHPh), 4.29 (d, 1H, $^2J$ 12.5 Hz, CHPh), 4.25 (bd, 2H, $^2J$ 11.6 Hz, 2×CHPh), 4.22 (dd, 1H, $^3J_{4,5}$ 9.2, $^3J_{5,6}$ 5.5 Hz, H-5), 4.16 (d, 1H, $^2J$ 10.5 Hz, CHPh), 4.14 (d, 1H, $^2J$ 12.0 Hz, CHPh), 4.10−4.04 (m, 3H, 3×H-3), 4.02−3.94 (m, 6H, 3×H-3, H-5, 2×H-6), 3.92−3.79 (m, 8H, 3×H-4, 3×H-5, 2×H-6), 3.74−3.70 (m, 2H, H-5, H-6), 3.68−3.59 (m, 3H, 3×H-6), 3.46−3.37 (m, 7H, 4×H-2, 2×H-4, H-6), 3.32−3.26 (m, 4H, 2×H-2, H-4, H-6). $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 139.31, 139.26 (2C), 139.23, 139.20, 139.15, 138.46, 138.39, 138.34, 138.28, 138.22, 138.18, 138.04, 138.02, 137.86, 137.82 (16×C arom quat), 136.49 (*C*H═$CH_2$), 129.78−126.58 (m, 80×C arom tert), 117.65 (CH═*C*$H_2$), 98.84, 98.28, 98.13, 97.81, 97.74, 97.70 (6×C-1), 84.27 (C-4A), 81.53, 81.37, 81.19, 80.98 (4×C-4), 80.88, 80.87, 80.68, 80.65 (4×C-3), 79.62 (C-4), 79.41, 79.27 (2C), 79.14, 78.39, 78.24 (6×C-2), 77.20 (2×C-3), 76.17 (2C), 75.48 (2C), 75.03, 74.83, 73.37 (2C), 73.25, 73.21, 73.14 (2C), 72.95, 72.65 (2C), 72.49, (16×$CH_2$-Ph), 71.87, 71.71, 71.42, 71.32, 70.92, 70.86 (6×C-5), 69.41 (2C), 68.74 (2C), 61.17 (5×C-6). FAB MS $(M + Na)^+$: *m*/*z* 2432.1. Anal. Calcd for $C_{149}H_{156}O_{29}$•$CH_3OH$: C, 73.75; H, 6.60. Found: C, 73.75; H, 6.58.

**Diol 14.** Compound **13** (40 mg, 16.6 μmol, 1 equiv) was dissolved in $CH_2Cl_2$ (20 mL). The solution was cooled to −78 °C, and ozone was bubbled through it for 2 min, until the solution turned blue. Excess (50 μL) of $Me_2S$ was then added. The reaction mixture was stirred at rt for 20 min, then evaporated, dissolved in 5 mL of $CH_2Cl_2$/MeOH (1:1) and treated at rt by $NaBH_4$ (2.5 mg, 66.4 μmol, 4 equiv). After 2 h of stirring at rt, MeOH (5 mL) was added and the solution was concentrated. This operation was repeted three times. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 2/1) afforded the α-CD **14** (20 mg, 50%) as a white foam.

$[\alpha]_D^{20}$: +29.7 (*c* 1.0, $CHCl_3$). $R_f$: 0.4 (cyclohexane/AcOEt: 2/1). $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 7.22−7.00 (m, 80H, H arom), 5.16 (d, 1H, $^2J$ 10.5 Hz, CHPh), 5.19 (d, 1H, $^2J_{1,2}$ 3.3 Hz, H-1), 5.18 (d, 1H, $^2J$ 10.8 Hz, CHPh), 5.16 (d, 1H, $^3J_{1,2}$ 3.1 Hz, H-1), 5.09 (d, 1H, $^3J_{1,2}$ 3.5 Hz, H-1), 5.07 (d, 1H, $^3J_{1,2}$ 3.5 Hz, H-1), 5.04 (d, 1H, $^2J$ 11.2 Hz, CHPh), 4.98 (d, 1H, $^2J$ 11.2 Hz, CHPh), 4.94 (d, 1H, $^2J$ 11.6 Hz, CHPh), 4.91 (d, 1H, $^2J$ 11.8 Hz, CHPh), 4.81−4.70 (m, 6H, 6×CHPh), 4.68 (d, 1H, $^3J_{1,2}$ 3.1 Hz, H-1), 4.64 (d, 1H, $^3J_{1,2}$ 3.3 Hz, H-1), 4.56 (d, 1H, $^2J$ 12.1 Hz, CHPh), 4.54 (d, 1H, $^2J$ 12.1 Hz, CHPh), 4.49 (d, 1H, $^2J$ 11.8 Hz, CHPh), 4.45−4.38 (m, 7H, 7×CHPh), 4.34 (bd, 6H, $^2J$ 12.5 Hz, 6×CHPh), 4.28 (d, 1H, $^2J$ 9.9 Hz, CHPh), 4.25 (d, 1H, $^2J$ 9.4 Hz, CHPh), 4.21 (d, 1H, $^2J$ 11.8 Hz, CHPh), 4.15 (d, 1H, $^2J$ 12.1 Hz, CHPh), 4.09−4.01 (m, 5H, 4×H-3, H-5), 3.99−3.93 (m, 5H, 2×H-3, 3×H-5), 3.86−3.69 (m, 14H, 4×H-4, 2×H-5, 8×H-6), 3.58 (bd, 2H, $^2J$ 10.7 Hz, 2×H-6), 3.46 (bd, 2H, $^2J$ 9.5 Hz, 2×H-6), 3.44−3.38 (m, 5H, 4×H-2, H-4), 3.35−3.30 (m, 2H, H-2, H-4), 3.22 (dd, 1H, $^3J_{1,2}$ 3.3, $^3J_{2,3}$ 9.9 Hz, H-2). $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 139.85, 139.55, 139.25, 139.21, 139.14 (2C), 138.43, 138.34, 138.30, 138.26, 138.20 (2C), 137.99, 137.96, 137.91, 137.73 (16×C arom quat), 128.28−126.99 (m, 80×C arom tert), 98.47, 98.42, 98.20, 97.92, 97.77, 97.73 (6×C-1), 81.34 (2C), 81.15, 80.99 (2C), 80.59 (6×C-4), 80.35 (2C), 79.46, 79.16, 79.09, 78.94 (6×C-3), 78.85, 78.56, 78.41, 77.96, 77.75 (2C) (6×C-2), 76.08, 76.02, 75.36 (2C), 75.03 (2C), 73.56 (2C), 73.43, 73.34, 73.21, 73.16, 72.83 (2C),

72.69 (2C) (16×$CH_2$Ph), 72.21, 72.03, 72.02, 71.67, 71.43, 71.23 (6×C-5), 69.49 (2C), 68.70, 62.11, 62.06, 61.96 (6×C-6). FAB MS $(M + Na)^+$: *m*/*z* 2436.8. Anal. Calcd for $C_{148}H_{156}O_{30}$: C, 73.61; H, 6.51. Found: C, 74.02; H, 6.68.

**Diol 15.** DIBAL-H (1.5 M in toluene, 4.4 mL, 6.51 mmol, 30 equiv) was slowly added to a solution of **12** (542 mg, 217 μmol, 1 equiv) in toluene (2.2 mL) under argon at rt. The reaction mixture was heated at 60 °C for 1 h under a flux of argon. Upon completion, it was cooled to rt and poured on ice. HCl (5 mL, 1 mol $L^{-1}$ in water) and EtOAc (10 mL) were added and the solution was stirred for 1 h. The aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vaccuo. Silica gel chromatography of the residue (cyclohexane/EtOAc: 3/1) gave **15** (385 mg, 77%) as a white foam.

$[\alpha]_D^{20}$: +44.8 (*c* 1.0, $CHCl_3$). $R_f$: 0.50 (cyclohexane/AcOEt: 2/1). $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.33−7.16 (m, 75H, H arom), 6.22 (ddd, 1H, $^3J_{5,6}$ 5.9, $^3J_{cis}$ 10.6, $^3J_{trans}$ 16.8 Hz, C*H*═$CH_2$), 5.61 (d, 1H, $^3J_{1,2}$ 3.7 Hz, H-1), 5.56 (d, 1H, $^3J_{1,2}$ 3.9 Hz, H-1), 5.42 (d, 1H, $^2J$ 9.9 Hz, CHPh), 5.39 (d, 1H, $^2J$ 10.3 Hz, CHPh), 5.40 (dd, 1H, $^3J_{trans}$ 15.5, $^2J$ 1.2 Hz, CH═C$H_2$), 5.24 (dd, 1H, $^3J_{cis}$ 11.0, $^2J$ 1.0 Hz, CH═C$H_2$), 5.16 (d, 1H, $^2J$ 11.0 Hz, CHPh), 5.15 (d, 1H, $^2J$ 10.9 Hz, CHPh), 4.97 (d, 1H, $^3J_{1,2}$ 3.6 Hz, H-1), 4.94−4.89 (m, 8H, 8×CHPh), 4.87 (d, 1H, $^3J_{1,2}$ 3.6 Hz, H-1), 4.83 (d, 1H, $^2J$ 10.9 Hz, CHPh), 4.82 (d, 1H, $^2J$ 11.2 Hz, CHPh), 4.81 (d, 1H, $^3J_{1,2}$ 4.5 Hz, H-1), 4.78 (d, 1H, $^2J$ 10.2 Hz, CHPh), 4.74 (d, 1H, $^3J_{1,2}$ 3.7 Hz, H-1), 4.73 (d, 1H, $^2J$ 11.6 Hz, CHPh), 4.61 (d, 1H, $^2J$ 9.3 Hz, CHPh), 4.56 (d, 1H, $^2J$ 11.0 Hz, CHPh), 4.55 (d, 1H, $^2J$ 11.9 Hz, CHPh), 4.51 (s, 2H, $CH_2$Ph), 4.51−4.40 (m, 9H, 9×CHPh), 4.35 (dd, 1H, $^3J_{4,5}$ 9.3, $^3J_{5,6}$ 5.9 Hz, H-5), 4.23−4.04 (m, 7H, 6×H-3, H-5), 4.02−3.72 (m, 15H, 5×H-4, 4×H-5, 10×H-6), 3.60 (dd, 1H, $^3J_{1,2}$ 3.7, $^3J_{2,3}$ 5.1 Hz, H-2), 3.58 (dd, 1H, $^3J_{1,2}$ 4.1, $^3J_{2,3}$ 5.4 Hz, H-2), 3.54 (dd, 1H, $^3J_{1,2}$ 3.5, $^3J_{2,3}$ 6.5 Hz, H-2), 3.52 (dd, 1H, $^3J_{3,4}$ 9.1, $^3J_{4,5}$ 9.2 Hz, H-4), 3.47 (dd, 1H, $^3J_{1,2}$ 3.5, $^3J_{2,3}$ 4.8 Hz, H-2), 3.44 (dd, 1H, $^3J_{1,2}$ 3.6, $^3J_{2,3}$ 5.4 Hz, H-2), 3.43 (dd, 1H, $^3J_{1,2}$ 4.1, $^3J_{2,3}$ 7.7 Hz, H-2). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 139.32 (2C), 139.26, 139.23, 139.18, 138.50, 138.47, 138.27, 138.18, 138.14, 138.08, 138.03 (2C), 137.78, 137.68 (15×C arom quat), 135.89 (*C*H═$CH_2$), 128.33−126.67 (m, 75×C arom tert), 118.24 (CH═*C*$H_2$), 98.54, 98.27, 98.09, 98.06, 97.66, 97.39 (6×C-1), 85.09 (C-4), 81.74 (C-3), 81.34, 81.25 (2×C-4), 81.22 (C-3, C-4), 81.18, 81.11 (2×C-4), 80.79, 80.73, 80.69, 80.61 (4×C-3), 79.95, 79.51, 79.23, 79.16, 78.14, 77.78 (6×C-2), 76.05, 75.99, 75.95, 75.81, 74.52, 74.21, 73.46, 73.42, 73.37, 73.31, 73.22, 72.90, 73.77 (2C), 73.47 (15×$CH_2$Ph), 72.00, 71.92, 71.76, 71.61, 71.37, 71.18 (6×C-5), 69.71, 69.48, 69.46, 61.94, 61.37 (5×C-6). FAB MS $(M + Na)^+$: *m*/*z* 2341.1. Anal. Calcd for $C_{142}H_{150}O_{29}$: C, 73.49; H, 6.51. Found: C, 73.52; H, 6.65.

**Triol 16.** Compound **15** (500 mg, 216 μmol, 1 equiv) was dissolved in $CH_2Cl_2$ (20 mL). The solution was cooled to −78 °C, and ozone was bubbled through it for 1 min, until the solution turned blue. Excess (0.5 mL) of $Me_2S$ was then added. The reaction mixture was stirred at rt for 20 min, then evaporated, and dissolved in 6 mL of $CH_2Cl_2$/MeOH (1:1), and the solution was treated at rt by $NaBH_4$ (33 mg, 863 μmol, 4 equiv). After 2 h of stirring at rt, MeOH (5 mL) was added and the solution was concentrated. This operation was repeted three times. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 3/2) afforded the α-CD **16** (409 mg, 81%) as a white foam.

$[\alpha]_D^{20}$: +36.7 (*c* 0.9, $CHCl_3$). $R_f$: 0.50 (cyclohexane/AcOEt: 1/1). $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.36−7.21 (m, 75H, H arom), 5.79 (d, 1H, $^3J_{1,2}$ 3.9 Hz, H-1), 5.76 (d, 1H, $^3J_{1,2}$ 3.9 Hz, H-1), 5.54 (d, 1H, $^2J$ 10.3 Hz, CHPh), 5.53 (d, 1H, $^2J$ 10.4 Hz, CHPh), 5.22 (d, 2H, $^2J$ 10.8 Hz, 2×CHPh), 4.99−4.94 (m, 4H, 4×CHPh), 4.91−4.86 (m, 4H, 4×CHPh), 4.83−4.79 (m, 5H, 3×H-1, 2×CHPh), 4.74 (d, 1H, $^3J_{1,2}$ 3.0 Hz, H-1), 4.69 (d, 1H, $^2J$ 12.1 Hz, CHPh), 4.66 (d, 1H, $^2J$ 12.1 Hz, CHPh), 4.61 (d, 1H, $^2J$ 12.5 Hz, CHPh), 4.60 (d, 2H, $^2J$ 12.3 Hz, 2×CHPh), 4.58 (d, 2H, $^2J$ 12.0 Hz, 2×CHPh), 4.57 (d, 1H, $^2J$ 13.7 Hz, CHPh), 4.53 (d, 1H, $^2J$ 12.0 Hz, CHPh), 4.52 (d, 1H, $^2J$ 12.0 Hz, CHPh), 4.46 (bd, 6H, $^2J$ 10.7 Hz, 6×CHPh), 4.32−4.27 (m, 2H, 2×H-3), 4.25−4.18 (m, 4H, 4×H-3), 4.16−4.02 (m, 9H, 5×H-5, 4×H-6), 3.99−3.93 (m, 4H, 2×H-4, H-5, H-6), 3.92−3.87 (m, 3H, 2×H-4, H-6), 3.84−3.80 (m, 3H, 3×H-6), 3.77−3.71 (m, 4H, H-4, 3×H-6), 3.68−3.64 (m, 2H, 2×H-2), 3.58−3.54 (m, 2H, H-2, H-4), 3.51 (dd, 1H, $^3J_{1,2}$ 3.3, $^3J_{2,3}$ 9.6 Hz, H-2), 3.46 (dd, 1H, $^3J_{1,2}$ 3.0, $^3J_{2,3}$ 9.9 Hz, H-2), 3.43 (dd, 1H, $^3J_{1,2}$ 3.3, $^3J_{2,3}$ 10.1 Hz, H-2). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 139.80, 139.76, 139.70 (2C), 139.65 (2C), 139.05, 139.04, 138.79, 138.72, 138.42, 138.40, 138.39, 138.26, 137.87 (15×C arom quat), 128.90−126.78 (m, 75×C arom tert), 98.75, 98.52, 98.49, 98.34, 98.17, 97.96 (6×C-1), 82.62, 82.20 (2×C-4), 81.98, 81.94 (2×C-3), 81.91, 81.77 (2×C-4), 81.49, 81.39, 81.04, 80.90 (4×C-3), 80.44, 80.38, 79.55, 79.41, 78.37, 78.21 (6×C-2), 76.78, 76.74, 76.68, 76.59 (4×$CH_2$Ph), 75.60, 75.43 (2×C-4), 74.43 ($CH_2$Ph), 74.41 (C-5), 73.96 (2C), 73.91 (2C), 73.89, 73.82, 73.48, 73.36 73.00, 72.97 (10×$CH_2$Ph), 72.56, 72.39, 72.08 (2C), 71.91 (5×C-5), 70.99, 70.22, 69.89, 63.78, 62.82, 62.29 (6×C-6). FAB MS $(M + Na)^+$: *m*/*z* 2346.7. Anal. Calcd for $C_{141}H_{150}O_{30}$: C, 72.85; H, 6.50. Found: C, 72.68; H, 6.47.

**Methylated α-Cyclodextrin 17.** To a solution of **13** (316 mg, 131 μmol, 1 equiv) in DMF (5 mL) was added NaH (60% in oil, 11 mg, 262 μmol, 2 equiv) at 0 °C under argon. The reaction mixture was stirred at 0 °C for 10 min. MeI (16 μL, 262 μmol, 2 equiv) was added. The reaction mixture was stirred for 2 h at rt, then treated by MeOH (1 mL) and concentrated. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 3/1) gave the mono-methylated cyclodextrin **17** (290 mg, 91%) as a white foam, and it was directly engaged in the next step.

$R_f$: 0.45 (cyclohexane/AcOEt: 2/1).

**Peracetylated α-Cyclodextrin 18.** Compound **17** (290 mg, 120 μmol, 1 equiv) was dissolved in a mixture THF/$H_2O$ (1 mL:1 mL) together with Pd/C 10% (290 mg). The reaction mixture was stirred under an $H_2$ atmosphere for 12 h, filtered through a Celite pad and concentrated.

The residue was dissolved in pyridine (4 mL), and $Ac_2O$ (2 mL) and DMAP (10 mg) were added. The reaction mixture was stirred at rt for 12 h and then concentrated and purified by silica gel flash chromatography ($CH_2Cl_2$/MeOH: 20/1) to afford the peracetylated cyclodextrin **18** (111 mg, 56% over 2 steps).

$R_f$: 0.75 (AcOEt/MeOH: 10/1). FAB MS $(M + Na)^+$: *m*/*z* 1679.6. HRMS (ESI): calcd for $C_{70}H_{96}O_{45}Na$, 1679.51158; found, 1679.50993 (−1 ppm). Full NMR analysis is available in the Supporting Information.

**Methylated α-Cyclodextrin 19.** To a solution of **15** (385 mg, 166 μmol, 1 equiv) in DMF (5 mL) was added NaH (60% in oil, 27 mg, 664 μmol, 4 equiv) at 0 °C under argon. The reaction mixture was stirred at 0 °C for 10 min. MeI (41 μL, 664 μmol, 4 equiv) was added. The reaction mixture was stirred for 1 h at rt, treated by MeOH (1 mL) and concentrated. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 3/1) gave the bis-methylated cyclodextrin **19** (330 mg, 85%) as a white foam, and it was directly engaged in the next step.

$R_f$: 0.65 (cyclohexane/AcOEt: 2/1).

**Peracetylated α-Cyclodextrin 20.** Compound **19** (330 mg, 141 μmol, 1 equiv) was dissolved in a mixture THF/$H_2O$ (2 mL:2 mL) together with Pd/C 10% (300 mg). The reaction mixture was stirred under an $H_2$ atmosphere for 12 h, filtered through a Celite pad and concentrated. The residue was dissolved in pyridine (5 mL), and $Ac_2O$ (2.5 mL) and DMAP (10 mg) were added. The reaction mixture was stirred at rt for 12 h, then concentrated and purified by silica gel flash chromatography ($CH_2Cl_2$/MeOH: 20/1) to afford the peracetylated cyclodextrin **20** (214 mg, 93% over 2 steps).

$R_f$: 0.75 (AcOEt/MeOH: 10/1). FAB MS $(M + Na)^+$: *m*/*z* 1651.6. HRMS (ESI): calcd for $C_{69}H_{96}O_{44}Na$, 1651.51667; found, 1651.51592 (−0.5 ppm). Full NMR analysis is available in the Supporting Information.

**Capped α-CD 21.** Sodium hydride (60% w/w in oil, 275 mg, 6.81 mmol, 6 equiv) was added at rt under argon to a solution of diol **15** (2.63 g, 1.135 mmol, 1 equiv) in dry DMF (100 mL). The

reaction mixture was stirred for 30 min, and then 3-chloro-2-chloromethyl-1-propene (145 $\mu$L, 1.248 mmol, 1.1 equiv) was added. After 12 h of stirring, MeOH (5 mL) was slowly added and the solvents were removed in vaccuo. The residue was dissolved in EtOAc (20 mL) and washed with a saturated aqueous solution of $NH_4Cl$ (20 mL). The aqueous layer was extracted with EtOAc (3 × 20 mL), and the organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated. Silica gel flash chromatography of the residue (cyclohexane/EtOAc: 4/1) gave **21** (2.141 g, 80%) as a white foam.

$[\alpha]_D^{20}$: +39.8 (*c* 1.0, $CHCl_3$). $R_f$: 0.60 (cyclohexane/AcOEt: 2/1). $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 7.34−7.02 (m, 75H, H arom), 6.57 (ddd, 1H, $^3J_{5,6}$ 4.1, $^3J_{cis}$ 10.8, $^3J_{trans}$ 15.9 Hz, C*H*═$CH_2$), 5.65 (d, 1H, $^3J_{1,2}$ 4.0 Hz, H-1), 5.61 (d, 1H, $^2J$ 10.4 Hz, CHPh), 5.59 (d, 1H, $^2J$ 10.0 Hz, CHPh), 5.58 (d, 1H, $^3J_{1,2}$ 3.7 Hz, H-1), 5.28 (d, 1H, $^2J$ 10.3 Hz, CHPh), 5.27 (d, 1H, $^2J$ 10.5 Hz, CHPh), 5.25 (bd, 1H, $^3J_{trans}$ 16.6 Hz, CH═C$H_2$), 5.08 (bd, 1H, $^3J_{cis}$ 11.1 Hz, CH═C$H_2$), 5.03 (bd, 1H, $^2J$ 9.7 Hz, CHPh), 5.01 (bd, 1H, $^2J$ 11.7 Hz, CHPh), 4.99 (bs, 2H, 2×$(OCH_2)_2$C═C$H_2$), 4.91−4.79 (m, 8H, 8×CHPh), 4.78 (d, 1H, $^3J_{1,2}$ 3.4 Hz, H-1), 4.76 (d, 1H, $^3J_{1,2}$ 3.0 Hz, H-1), 4.74 (d, 1H, $^2J$ 13.0 Hz, CHPh), 4.70 (d, 1H, $^3J_{1,2}$ 3.0 Hz, H-1), 4.65 (d, 1H, $^3J_{1,2}$ 3.0 Hz, H-1), 4.58 (d, 1H, $^2J$ 11.6 Hz, CHPh), 4.52−4.38 (m, 14H, 14×CHPh), 4.37−4.23 (m, 7H, 3×H-5, 4×H-6), 4.16−4.08 (m, 4H, 4×H-3), 4.06 (d, 1H, $^2J$ 8.7 Hz, $(OCH_2)_2$C═$CH_2$), 3.99−3.89 (m, 6H, 2×H-3, H-4, 3×H-5), 3.85 (d, 1H, $^2J$ 10.3 Hz, $(OCH_2)_2$C═$CH_2$), 3.78 (bd, 1H, $^2J$ 9.6 Hz, H-6), 3.71 (bd, 2H, $^2J$ 10.4 Hz, 2×H-6), 3.67−3.59 (m, 6H, 2×H-2, 2×H-4, H-6, $(OCH_2)_2$C═$CH_2$), 3.56 (bd, 2H, $^2J$ 10.1 Hz, 2×H-6), 3.51−3.47 (m, 3H, 2×H-4, $(OCH_2)_2$C═$CH_2$), 3.45 (dd, 1H, $^3J_{1,2}$ 2.6, $^3J_{2,3}$ 9.7 Hz, H-2), 3.42 (dd, 1H, $^3J_{1,2}$ 3.0, $^3J_{2,3}$ 9.4 Hz, H-2), 3.39 (dd, 1H, $^3J_{1,2}$ 2.9, $^3J_{2,3}$ 9.9 Hz, H-2), 3.37 (dd, 1H, $^3J_{1,2}$ 3.3, $^3J_{2,3}$ 9.6 Hz, H-2), 3.28 (dd, 1H, $^3J_{3,4}$ 8.8, $^3J_{4,5}$ 8.9 Hz, H-4). $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 143.12 ($(OCH_2)_2C$═$CH_2$), 140.10, 140.00, 139.84, 139.83, 139.78, 139.77, 139.23, 139.22, 138.89, 138.88, 138.69, 138.62, 138.54, 138.35, 138.23 (15×C arom quat), 136.29 (*C*H═$CH_2$), 128.83−126.37 (m, 75×C arom tert), 115.92 (CH═*C*$H_2$), 114.74 ($(OCH_2)_2$C═*C*$H_2$), 100.25, 99.88, 99.75, 99.64, 98.42, 98.24 (6×C-1), 88.32, 82.45 (2×C-4), 82.29 (C-3), 82.02 (C-4), 81.68, 81.64, 81.61, 81.60, 81.12 (5×C-3), 80.91 (C-4), 80.85, 80.49 (2×C-2), 79.79 (C-4), 79.35, 79.22 (2×C-2), 79.22 (C-4), 78.27, 78.21 (2×C-2), 77.11, 76.96, 76.59, 76.56, 74.03, 73.97, 73.84, 73.76, 73.74, 73.63 (2C), 73.29, 73.09, 72.72, 72.57 (15×$CH_2$Ph), 72.49 (C-5), 72.33 ($(OCH_2)_2$C═$CH_2$), 72.29(C-6), 72.22 (C-5), 72.10, 72.04 (2×C-6), 71.99, 71.09 (2×C-5), 69.98 ($(OCH_2)_2$C═$CH_2$), 69.77 (C-5), 69.47, 69.37 (2×C-6), 69.32(C-5). FAB MS $(M + Na)^+$: *m*/*z* 2394.9. Anal. Calcd for $C_{146}H_{154}O_{29}$: C, 73.90; H, 6.54. Found: C, 74.00; H, 6.75.

**Diol 22.** DIBAL-H (1.5 M in toluene, 6 mL, 9.01 mmol, 10 equiv) was slowly added to a solution of 21 (2.140 g, 901 mmol, 1 equiv) in toluene (3 mL) under argon at rt. The reaction mixture was heated at 60 °C for 4 h under a flux of argon. Upon completion, it was cooled to rt and poured on ice. HCl (5 mL, 1 mol $L^{-1}$ in water) and EtOAc (10 mL) were added, and the solution was stirred for 1 h. The aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vaccuo. Silica gel chromatography of the residue (cyclohexane/EtOAc: 3/1) gave 22 (954 mg, 48%) as a white foam.

$[\alpha]_D^{20}$: +35.1 (*c* 1.0, $CHCl_3$). $R_f$: 0.20 (cyclohexane/AcOEt: 2/1). $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 7.26−6.91 (m, 65H, H arom), 6.42 (ddd, 1H, $^3J_{5,6}$ 4.4, $^3J_{cis}$ 11.0, $^3J_{trans}$ 17.1 Hz, C*H*═$CH_2$), 5.48 (d, 1H, $^3J_{1,2}$ 3.9 Hz, H-1), 5.47 (d, 1H, $^2J$ 10.5 Hz, CHPh), 5.42 (d, 1H, $^2J$ 10.7 Hz, CHPh), 5.33 (d, 1H, $^3J_{1,2}$ 4.3 Hz, H-1), 5.26 (bd, 1H, $^3J_{trans}$ 17.1 Hz, CH═C$H_2$), 5.15 (d, 2H, $^2J$ 10.7 Hz, 2×CHPh), 5.01 (bd, 1H, $^3J_{cis}$ 11.0 Hz, CH═C$H_2$), 4.99 (bs, 2H, 2×$(OCH_2)_2$C═C$H_2$), 4.89 (d, 1H, $^2J$ 10.5 Hz, CHPh), 4.88 (d, 1H, $^2J$ 10.3 Hz, CHPh), 4.77 (d, 1H, $^3J_{1,2}$ 2.6 Hz, H-1), 4.75−4.67 (m, 6H, 6×CHPh), 4.66 (d, 1H, $^3J_{1,2}$ 3.3 Hz, H-1), 4.58 (d, 1H, $^3J_{1,2}$ 3.3 Hz, H-1), 4.56 (d, 1H, $^3J_{1,2}$ 3.1 Hz, H-1), 4.45−4.31 (m, 9H, 9×CHPh), 4.27−4.13 (m, 11H, 4×H-3, H-5, $(OCH_2)_2$C═$CH_2$ , 5×CHPh), 4.02−3.95 (m, 6H, 2×H-3, 2×H-5, 2×H-6), 3.91−3.85 (m, 3H, 3×H-5), 3.81−3.73 (m, 7H, 3×H-4, $(OCH_2)_2$C═$CH_2$, 3×H-6), 3.71−3.66 (m, 2H, H-6, $(OCH_2)_2$C═$CH_2$), 3.60 (bd, 1H, $^2J$ 9.0 Hz, H-6), 3.53−3.42 (m, 6H, 2×H-2, 2×H-4, H-6, $(OCH_2)_2$C═$CH_2$), 3.39−3.29 (m, 5H, 3×H-2, 2×H-6), 3.25 (dd, 1H, $^3J_{1,2}$ 3.1, $^3J_{2,3}$ 9.6 Hz, H-2), 3.22 (dd, 1H, $^3J_{3,4}$ 8.3, $^3J_{4,5}$ 9.0 Hz, H-4). $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 142.59 ($(OCH_2)_2C$═$CH_2$), 139.62, 139.54, 139.30 (3C), 139.24, 138.65, 138.56, 138.31, 138.27, 137.98, 137.82, 137.78 (13×C arom quat), 135.49 (*C*H═$CH_2$), 128.42−126.00 (m, 65×C arom tert), 116.10 (CH═*C*$H_2$), 114.73 ($(OCH_2)_2$C═*C*$H_2$), 99.91, 99.57, 99.50, 99.40, 97.87, 97.49 (6×C-1), 87.41, 82.09, 81.83, 81.67, 81.31, 81.05 (6×C-4), 80.84, 80.75, 80.53, 80.43 (2C), 79.81 (6×C-3), 79.81, 78.97, 78.73, 78.53, 77.72 (2C) (6×C-2), 76.62, 76.41, 76.14, 75.98, 73.90, 73.73, 73.53, 73.29, 73.24 (2C), 72.93, 72.78 (12×$CH_2$Ph), 72.70, 72.45 (2×C-5), 72.41 ($CH_2$Ph), 72.25 (C-5), 72.14 (C-6), 71.95 (C-5), 71.91 (2C), 71.84, 71.74 (4×C-6), 70.92 ($(OCH_2)_2$C═$CH_2$), 70.88, 69.42 (2×C-5), 69.07 ($(OCH_2)_2$C═$CH_2$). FAB MS $(M + Na)^+$: *m*/*z* 2214.7. Anal. Calcd for $C_{132}H_{142}O_{29}$: C, 72.31; H, 6.53. Found: C, 72.21; H, 6.77.

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**Supporting Information Available:** NMR spectra, as well as the full NMR analysis of compounds **18** and **20**. This material is available free of charge via the Internet at http://pubs.acs.org.

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