Selective Tetrafunctionalisation of α-Cyclodextrin using the Supertrityl Protecting Group − Synthesis of the First C_2-Symmetric Tetraphosphane Based on a Cavitand (α-TEPHOS)

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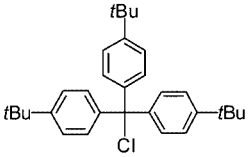
Regioselective tetraalkylation of α-cyclodextrin using supertrityl chloride enables the preparation of new C_2-symmetric cavitands.

Introduction

Cyclodextrins (CDs) are still the subject of considerable interest in many areas of molecular chemistry.[1] Chemical modification of these natural molecular receptors is often a prerequisite for the preparation of CDs displaying sophisticated properties that make use of the cavity. It is well-known, for example, that appropriate functionalisation allows an unmodified CD to be tailored to a particular guest and hence to meet the specific requirements of an anticipated host-guest complex. In a previous paper we have shown that supertrityl chloride **1** [^{s}TrCl = tris(4-*tert*-butylphenyl)methyl chloride] is a valuable reagent for the regioselective functionalisation of the α-cyclodextrin (α-CD) primary hydroxyl face.[2] Acting as a bulky alkylating agent, it allows the convenient preparation of a variety of A,D- and A,C-disubstituted α-CDs. We have recently employed phosphane- or amine-modified α-CD's of this type for the directed construction of metallacyclodextrins bearing transition metal centres located at the cavity entrance.[3−6] Extending our investigations on this reagent we now report its use in the effective preparation of tetrol **4**, a potential precursor of chiral, C_2-symmetrical cavitands. Methodology for the regioselective, multiple functionalisation of α-CD is already well documented.[7−11] However, most procedures reported in the literature are low-yielding preparations and/or require the use of large amounts of expensive reagents.[7]



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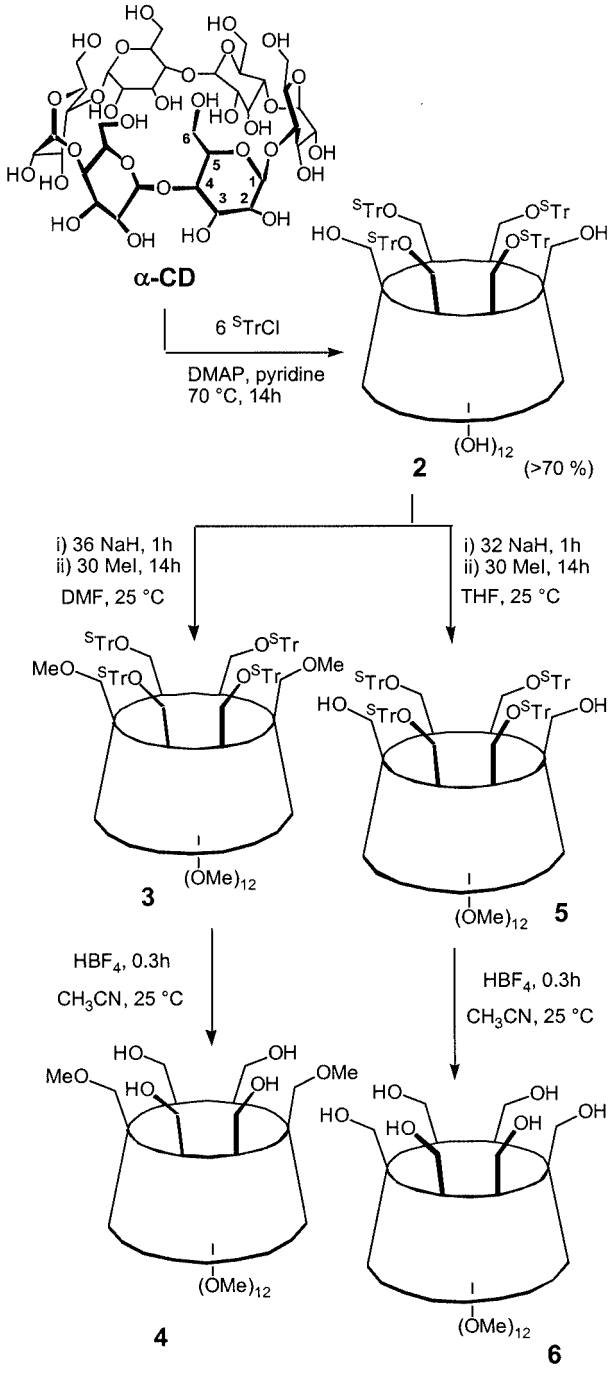
Results and Discussion

Tetrol **4** was conveniently prepared in three steps starting from α-cyclodextrin (Scheme 1). Treatment of α-CD with six equivalents of **1** in pyridine/DMAP afforded the A,B,D,E-tetraalkylated CD **2** in about 80% spectroscopic yield, together with small amounts of unidentified side-products, presumably the trialkylated compounds. Purification of **2** by column chromatography with MeOH/CH_2Cl_2 was only possible in the presence of small amounts of pyridine, which prevents cleavage of the supertrityl groups. The key compound **2** was characterised by ^{1}H and ^{13}C NMR spectroscopy as well as elemental analysis, which revealed the presence of a pyridine solvate. The presence of two *t*Bu signals and three anomeric ones in the ^{1}H NMR spectrum is in agreement with a C_2-symmetric derivative. The remarkable selectivity of this reaction, which is a direct consequence of the bulkiness of the supertrityl group, contrasts with previously reported tetrafunctionalisations. Thus, for example, tetraalkylation of α-CD with $ClCPh_3$ produces three tetraalkylated regioisomers.[10] We also found that using a large excess of ^{s}TrCl did not allow us to graft more than four ^{s}Tr groups onto α-CD. Finally, it should be emphasised that purification of **2** is not compulsory for the methylation steps outlined below.

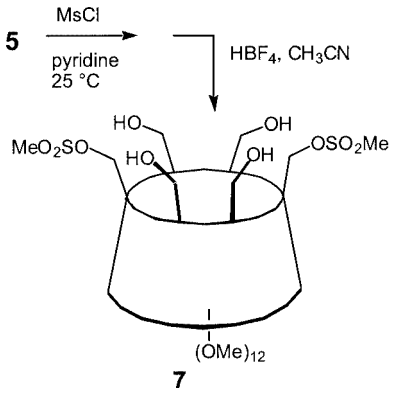
In situ permethylation of **2** was achieved at room temperature using MeI/NaH (30 equiv./36 equiv.) in DMF. This reaction afforded **3** in 46% yield[12] after workup (overall yield). As expected for a C_2-symmetrical compound, the ^{1}H NMR spectrum of **3** displays seven methyl singlets and three anomeric signals. Deprotection with HBF_4 afforded the tetrol **4** in 97% yield. Interestingly, the extent of methylation of **2** was found to depend strongly on the nature of the solvent. Thus, carrying out the reaction in THF instead of DMF afforded the dodecamethylated compound **5** in ca. 33% yield[13] and virtually no **3**. Cyclodextrin **5** has C_2 symmetry. To determine the face bearing the two non-alkylated



Scheme 1. Stepwise construction of tetrol **4** and hexol **6**

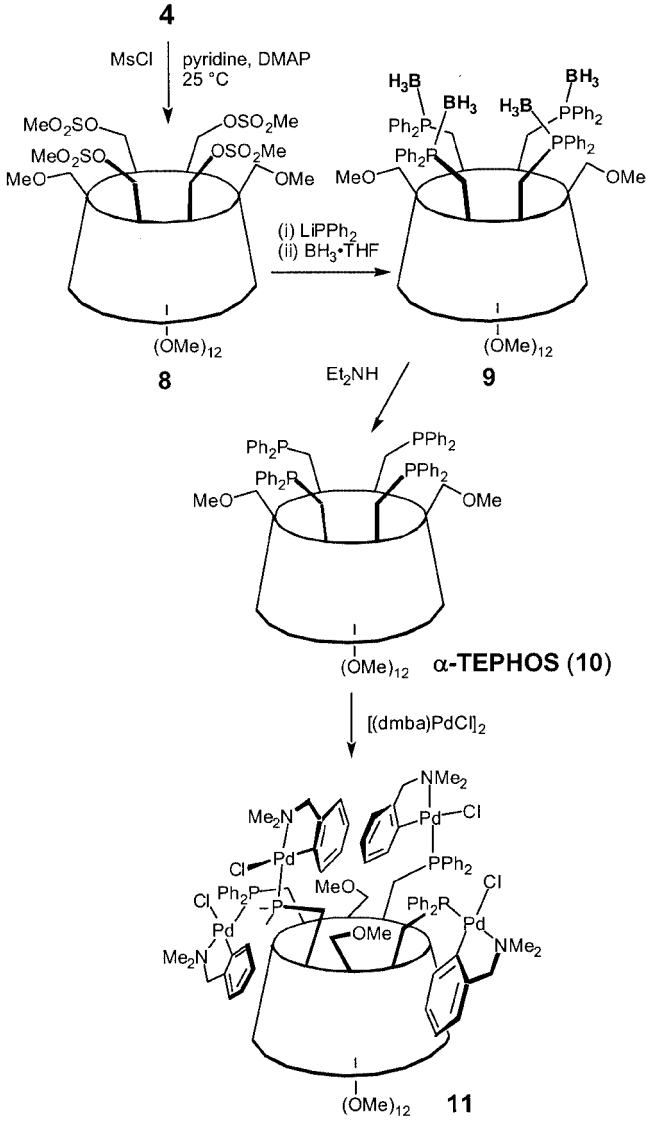
hydroxy groups, the four supertrityl groups were removed with HBF_4, giving the known C_6-symmetrical hexol **6** (Scheme 1).[14] Mesylation of **5** followed by cleavage of the ^{s}Tr groups led, after chromatography, to the C_2-symmetrical tetrol **7** (Scheme 2).

Tetrol **4** is suitable for further functionalisation. Thus, mesylation with MsCl/pyridine afforded **8** in greater than 80% yield (Scheme 3). Reaction of **8** with excess $LiPPh_2$ (10 equiv.) and in situ treatment with BH_3·THF gave the protected tetraphosphane **9**. Deprotection of **9** with NEt_2H afforded **10** (α-TEPHOS in the following). As expected, the



Scheme 2. New entry to C_2-symmetric derivatives of α-CD

^{31}P NMR spectrum of α-TEPHOS shows two singlets of equal intensity. To the best of our knowledge α-TEPHOS is the first optically active tetraphosphane built on a macro-



Scheme 3. Preparation of the chiral, C_2-symmetric tetraphosphane **10** (α-TEPHOS)

cyclic backbone.[15,16] Reaction of α-TEPHOS with the cyclometallated dimer $[PdCl(dmba)]_2$ (dmbaH = *o*-$C_6H_5CH_2NMe_2$) led to the tetranuclear complex **11**. Again, all NMR spectroscopic data are consistent with a C_2-symmetric species. Interestingly, three pairs of exo-oriented CD protons undergo a strong deshielding (ca. 1 ppm for two symmetrical H-1 protons; >2 ppm for two pairs of symmetrical H-4 protons), suggesting the presence of at least two aromatic dmba rings near the outer CD walls.

In conclusion, supertrityl chloride can be used as an effective reagent for the regioselective A,B,D,E-tetrafunctionalisation of α-CD. As exemplified by the synthesis of the tetrapalladium complex **11**, the methodology outlined in this work opens a new entry to C_2-symmetrical metallacyclodextrins. Further work aimed at exploiting the coordinative and catalytic properties of the chiral tetraphosphane **10** will be reported in due course.

Experimental Section

$6^A,6^B,6^D,6^E$-Tetra-[*O*-tris(*p*-*tert*-butylphenyl)methyl]-α-CD (2): Tris-(*p*-*tert*-butyl-phenyl)methyl chloride (22.060 g, 49.34 mmol) and 4-dimethylaminopyridine (DMAP; 0.610 g, 5.00 mmol) were added to a solution of α-CD (8.000 g, 8.22 mmol) in pyridine (240 mL). The solution was stirred for 24 h at 70 °C, concentrated to one-third of the original volume, then poured into water (800 mL) and the precipitate collected by filtration. The white-yellow solid (31.200 g) was dried overnight under vacuum at 50 °C. The crude product (2.000 g), which still contained small amounts of pyridine (!), was subjected to column chromatography [SiO_2, MeOH/CH_2Cl_2, 10:90 (v/v)] to afford **2** [SiO_2, butanone/H_2O/*i*PrOH 13:1:1 (v/v/v); R_f = 0.58]. Yield: 1.050 g, 70%. ^{1}H NMR (500.1 MHz, $CDCl_3$, 25 °C; assignments by HMQC): δ = 1.28 (s, 54 H, *tert*-butyl), 1.32 (s, 54 H, *tert*-butyl), 2.70−4.30 (36 H, H-2, H-3, H-4, H-5, H-6), 4.00 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 2.9 Hz, 2 H, H-1),4.94 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.2 Hz, 2 H, H-1), 4.99 (br. s, OH), 5.04 (br. s, OH), 5.21 (br. s, OH), 5.38 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 2.8 Hz, 2 H, H-1), 5.79 (br. s, OH), 6.26 (br. s, OH), 6.29 (br. s, OH), 7.00−7.50 (48 H, AA′BB′ system of trityl) ppm. Two OH protons could not be detected. $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$, 25 °C): δ = 31.0, 31.4 [$C(CH_3)_3$], 34.1, 34.3 [$C(CH_3)_3$], 60.8, 62.3, 63.1 (C-6), 70.3, 71.4, 71.7, 71.9, 72.8, 73.2, 74.5, 74.7, 74.8, 80.6, 81.0, 81.7 (C-2, C-3, C-4, C-5), 85.7, 87.5 [O*C*(Ph)$_3$], 100.7, 101.1, 101.6 (C-1), 123.7, 124.6, 128.3, 128.6 (aromatic CH), 141.7, 142.0, 148.9, 149.3 (aromatic quat. C) ppm. $C_{160}H_{212}O_{30}{\cdot}2H_2O{\cdot}C_5H_5N$ (2615.46 + 115.06): calcd. C 72.58, H 8.16, N 0.51; found C 72.33, H 8.32, N 0.73.

$6^A,6^B,6^D,6^E$-Tetra-[*O*-tris(*p*-*tert*-butylphenyl)methyl]-$2^A,2^B,2^C,2^D,2^E,2^F,3^A,3^B,3^C,3^D,3^E,3^F,6^C,6^F$-tetradeca-*O*-methyl-α-CD (3): NaH (7.104 g, 296.00 mmol) was added to a solution of crude **2** (29.200 g) in DMF (400 mL). The mixture was stirred for 1 h, then iodomethane (35.000 g, 246.60 mmol, ca. 15.4 mL) was added dropwise to the suspension (the temperature must be kept below 35 °C). After stirring for 14 h, excess NaH was destroyed by careful addition of methanol, then of water. The products were extracted with diethyl ether (3×). The ethereal solution was washed with water, then dried over $MgSO_4$. Solvent evaporation gave a pale yellow solid which was subjected to column chromatography [SiO_2, EtOAc/hexane, step gradient: 20:80 to 50:50 (v/v)] to give **3** which eluted first [SiO_2, EtOAc/hexane, 40:60 (v/v); R_f = 0.62]; further elution gave tritritylated (ca. 35%) and ditritylated species (<5%), which were not separated. Yield: 9.830 g, 46% overall yield. M.p. > 230 °C. ^{1}H NMR (200.1 MHz, $CDCl_3$, 25 °C): δ = 1.20 (s, 54 H, *tert*-butyl), 1.22 (s, 54 H, *tert*-butyl), 2.52 (s, 6 H, 6-OMe), 3.29 (s, 6 H, OMe), 3.50 (s, 6 H, OMe), 3.51 (s, 6 H, OMe), 3.58 (s, 6 H, OMe), 3.61 (s, 6 H, OMe), 3.79 (s, 6 H, OMe), 2.40−4.20 (36 H, H-2, H-3, H-4, H-5, H-6), 4.24 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 2.7 Hz, 2 H, H-1), 4.64 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 2.5 Hz, 2 H, H-1), 5.33 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 2.9 Hz, 2 H, H-1), 7.00−7.50 (48 H, AA′BB′ system of trityl) ppm. $^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 31.4 [×2] [$C(CH_3)_3$], 34.3 [×2] [$C(CH_3)_3$], 57.2, 57.9, 58.4, 59.7, 60.2, 61.7, 61.9 (2-OCH_3, 3-OCH_3, 6-OCH_3), 61.2, 61.5 (C-$6^{A,B,D,E}$), 71.0 (C-$6^{C,F}$), 69.7, 72.2, 72.6 (C-5), 80.1, 80.7, 81.0 [×2], 81.5, 81.7, 82.1, 83.1 [×2] (C-2, C-3, C-4), 85.1, 85.7 [O*C*(Ph)$_3$], 96.3, 96.5, 97.3 (C-1), 124.2, 124.4, 128.4 [×2] (aromatic CH), 141.0, 141.7, 149.0, 149.1 (aromatic quat. C) ppm. $C_{174}H_{240}O_{30}$ (2811.84): calcd. C 74.33, H 8.6; found C 74.45, H 8.54.

$2^A,2^B,2^C,2^D,2^E,2^F,3^A,3^B,3^C,3^D,3^E,3^F,6^A,6^D$-Tetradeca-*O*-methyl-α-CD (4): An aqueous solution of tetrafluoroboric acid (1.1 mL, 34%) was added to a solution of **3** (0.690 g, 0.25 mmol) in acetonitrile (20 mL) and the resulting mixture was stirred for 20 min at room temperature. Excess acid was then neutralised with triethylamine (4 mL). Tris(*p*-*tert*-butylphenyl)methanol was precipitated by adding water to the reaction mixture and eliminated by filtration. The product was extracted with dichloromethane (4 × 40 mL). The combined organic layers were washed with a saturated solution of $NaHCO_3$ and dried over $MgSO_4$ before being evaporated to dryness to afford **4** after column chromatography [SiO_2, MeOH/CH_2Cl_2, 12:88 (v/v)] as a white product [SiO_2, MeOH/CH_2Cl_2, 10:90 (v/v); R_f = 0.25]. Yield: 0.280 g, 97%. M.p. 159−160 °C. ^{1}H NMR (200.1 MHz, $CDCl_3$, 25 °C): δ = 1.40 (t, $^3J_{OH,H\text{-}6}$ = 7.3 Hz, 2 H, OH), 3.13 (t, $^3J_{OH,H\text{-}6}$ = 7.6 Hz, 2 H, OH), 3.38 (s, 6 H, 6-OMe), 3.48 (s, 6 H, OMe), 3.50 (s, 6 H, OMe), 3.51 (s, 6 H, OMe), 3.63 (s, 6 H, OMe), 3.66 (s, 6 H, OMe), 3.68 (s, 6 H, OMe), 2.90−4.10 (36 H, H-2, H-3, H-4, H-5, H-6), 5.01 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.2 Hz, 2 H, H-1), 5.10 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.5 Hz, 2 H, H-1), 5.12 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.2 Hz, 2 H, H-1) ppm. $^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 57.7, 57.9, 58.2, 58.9, 61.3, 61.5, 61.6 (2-OCH_3, 3-OCH_3, 6-OCH_3), 62.1, 62.3, 71.7 (C-6), 71.3, 72.7 [×2] (C-5), 81.4 [×3], 81.6 [×3], 81.8, 81.9 [×2] (C-2, C-3, C-4), 98.7, 98.9, 99.1 (C-1) ppm. FAB-MS: *m*/*z* (%) = 1169.4 $[M + H]^+$ and 1191.3 $[M + Na]^+$. $C_{50}H_{88}O_{30}$ (1169.24): calcd. C 51.36, H 7.59; found C 51.44, H 7.75.

$6^A,6^B,6^D,6^E$-Tetra-[*O*-tris(*p*-*tert*-butylphenyl)methyl]-$2^A,2^B,2^C,2^D,2^E,2^F,3^A,3^B,3^C,3^D,3^E,3^F$-dodeca-*O*-methyl-α-CD (5): NaH (2.760 g, 115.05 mmol) was added to a solution of crude **2** (13.710 g) in THF (270 mL). The mixture was stirred for 1 h, then iodomethane (15.320 g, 107.95 mmol, ca. 34.9 mL) was added dropwise while maintaining the temperature below 35 °C. After 14 h, excess NaH was destroyed by slow addition of methanol, then water. The products were extracted with diethyl ether (3×). The organic fractions were washed with water and dried. Solvent evaporation gave a pale yellow solid that was subjected to column chromatography [SiO_2, EtOAc/hexane, step gradient: 20:80 to 50:50 (v/v)] to afford **5** [SiO_2, EtOAc/hexane, 40:60 (v/v); R_f = 0.59]. Yield: 3.340 g, ca. 33%, overall yield. M.p. 223 °C. ^{1}H NMR (200.1 MHz, $CDCl_3$, 25 °C): δ = 0.98 (s, 54 H, *tert*-butyl), 1.28 (s, 54 H, *tert*-butyl), 3.32 (s, 6 H, OMe), 3.45 (s, 6 H, OMe), 3.50 (s, 6 H, OMe), 3.59 (s, 6 H, OMe), 3.63 (s, 6 H, OMe), 3.64 (s, 6 H, OMe), 2.50−4.50 (36 H, H-2, H-3, H-4, H-5, H-6), 4.02 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.2 Hz, 2 H, H-1), 5.04 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.0 Hz, 2 H, H-1), 5.44 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 2.2 Hz, 2 H, H-1), 7.00−7.50 (48 H, AA′BB′ system of trityl) ppm. The two OH protons were not detected. $^{13}C\{^1H\}$ NMR (50.3 MHz,

$CDCl_3$, 25 °C): δ = 31.0, 31.5 [C(CH_3)$_3$], 34.1, 34.3 [C(CH$_3$)$_3$], 57.2, 57.6, 57.8, 61.4, 61.9, 62.0 (2-OCH$_3$, 3-OCH$_3$), 60.3, 62.8, 63.9 (C-6), 71.5, 71.6, 72.7 (C-5), 80.8, 81.0, 81.3 [×3], 81.6, 81.9, 82.1, 82.3 (C-2, C-3, C-4), 85.5, 87.3 [OC(Ph)$_3$], 98.5, 99.8, 100.0 (C-1), 124.0, 124.5, 128.4, 128.6 (aromatic CH), 142.0, 142.3, 148.8, 149.2 (aromatic quat. C) ppm. $C_{172}H_{236}O_{30}$ (2783.78): calcd. C 74.21, H 8.55; found C 74.29, H 8.51.

6^A,6^D-Di-*O*-methylsulfonyl-2^A,2^B,2^C,2^D,2^E,2^F,3^A,3^B,3^C,3^D,3^E,3^F-dodeca-*O*-methyl-α-CD (7): DMAP (0.147 g, 1.20 mmol) and methanesulfonyl chloride (0.280 g, 2.62 mmol) were added successively to a solution of diol **5** (1.830 g, 0.66 mmol) in pyridine (11 mL). The mixture was stirred for 48 h at room temperature whereupon water (100 mL) was added. The precipitate was collected on a bed of Celite before being dissolved in CH_2Cl_2 (100 mL). The organic solution was then washed with water (100 mL), dried over $MgSO_4$ and finally evaporated to dryness. The residue was dissolved in acetonitrile (40 mL). Aqueous tetrafluoroboric acid (2.18 mL, 34%) was added to this solution which immediately turned yellow. Excess acid was neutralised with triethylamine (10 mL). Tris(*p*-*tert*-butylphenyl)methanol was precipitated by adding water to the reaction mixture and eliminated by filtration. The product was extracted from the filtrate with CH_2Cl_2 (4 × 50 mL). The combined organic layers were washed with a saturated solution of $NaHCO_3$ and dried over $MgSO_4$ before being evaporated to dryness. Column chromatography [SiO_2, MeOH/CH_2Cl_2, 10:90 (v/v)] of the residue afforded **7** as a colourless solid [SiO_2, MeOH/CH_2Cl_2, 12:88 (v/v); R_f = 0.26]. Yield: 0.440 g, 52%. M.p. 198 °C dec. ^{1}H NMR (300.1 MHz, $CDCl_3$, 25 °C): δ = 1.32 (t, $^3J_{H\text{-}6,OH}$ = 7.3 Hz, 2 H, OH), 3.08 (s, 6 H, OSO_2Me), 3.46 (s, 6 H, OMe), 3.47 (s, 6 H, OMe), 3.48 (s, 6 H, OMe), 3.62 (s, 12 H, OMe), 3.63 (s, 6 H, OMe), 3.07−4.12 (32 H, H-2, H-3, H-4, H-5, H-6^{B,C,E,F}), 4.53 (dd, $^3J_{H\text{-}6b,H\text{-}5}$ = 5.2, $^3J_{H\text{-}6b,H\text{-}6a}$ = 11.2 Hz, 2 H, H-6b^{A,D}), 4.60 (d, $^3J_{H\text{-}6a,H\text{-}6b}$ = 11.2 Hz, 2 H, H-6a^{A,D}), 5.00 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.5 Hz, 4 H, H-1), 5.04 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.7 Hz, 2 H, H-1) ppm. Two OH protons were not detected. ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 37.4 (SO_2CH_3), 57.9, 58.0, 58.1, 61.7 [×2], 61.8 (2-OCH$_3$, 3-OCH$_3$), 61.9, 62.4 (C-6^{B,C,E,F}), 69.6, 72.1, 72.9 (C-5), 70.1(C-6^{A,D}), 81.1, 81.2, 81.4, 81.9 [×3], 82.1 [×2], 82.8 (C-2, C-3, C-4), 99.1, 99.3, 99.8 (C-1) ppm. $C_{50}H_{88}O_{34}S_2{\cdot}3H_20$ (1297.35 + 38.04): calcd. C 44.57, H 6.73; found C 44.43, H 7.02.

6^A,6^B,6^D,6^E-Tetra-*O*-methylsulfonyl-2^A,2^B,2^C,2^D,2^E,2^F,3^A,3^B,3^C,3^D,3^E,3^F,6^C,6^F-tetradeca-*O*-methyl-α-CD (8): Methanesulfonyl chloride (0.804 g, 7.02 mmol) was added to a solution of tetrol **4** (1.820 g, 1.56 mmol) and DMAP (0.620 g, 5.07 mmol) in pyridine (20 mL). The mixture was stirred for 24 h at room temperature. Water was then added and tetramesylate **8** was extracted with EtOAc (4 × 150 mL). The organic phase was washed successively with HCl (2 M), a solution of NaCl (2 M) and water, before being dried over $MgSO_4$ and the solvents evaporated. Entrapped water molecules were removed by azeotropic distillation with benzene and the resulting product was dried under vacuum to give tetramesylate **8** [SiO_2, MeOH/CH_2Cl_2, 8:92 (v/v); R_f = 0.47]. Yield: 2.01 g, 87%. M.p. 198 °C dec. ^{1}H NMR (300.1 MHz, $CDCl_3$, 25 °C): δ = 3.06 (s, 6 H, OSO_2Me), 3.07 (s, 6 H, OSO_2Me), 3.39 (s, 6 H, OMe), 3.49 (s, 12 H, OMe), 3.50 (s, 6 H, OMe), 3.62 (s, 12 H, OMe), 3.67 (s, 6 H, OMe), 3.10−4.70 (36 H, H-2, H-3, H-4, H-5, H-6), 5.01 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.3 Hz, 2 H, H-1), 5.04 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 2.8 Hz, 4 H, H-1) ppm. ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 37.3, 37.6 (SO_2CH_3), 57.6, 57.9, 58.3, 59.0, 61.5, 61.7 [×2] (2-OCH$_3$, 3-OCH$_3$, 6-OCH$_3$), 69.4, 69.8, 71.2 (C-5), 69.5, 69.9, 70.9 (C-6), 80.9 [×2], 81.0, 81.6 [×2], 82.0 [×3], 82.1 (C-2, C-3, C-4), 99.0, 99.4, 100.4 (C-1) ppm. $C_{54}H_{96}O_{38}S_4$ (1481.58): calcd. C 43.78, H 6.53, S 8.66; found C 43.79, H 6.48, S 8.21.

***P*,*P*′,*P*′′,*P*′′′-(6^A,6^B,6^D,6^E-Tetradeoxy-6^A,6^B,6^D,6^E-tetra{diphenylphosphinyl}-2^A,2^B,2^C,2^D,2^E,2^F,3^A,3^B,3^C,3^D,3^E,3^F,6^C,6^F-tetradeca-*O*-methyl-α-CD)tetraborane (9):** *n*-Butyllithium (7.7 mL of a 1.6 M solution in hexane, 12.27 mmol) was added dropwise at −78 °C to a stirred solution of diphenylphosphane (2.514 g, 13.5 mmol, ca. 2.35 mL) in THF (10 mL). After 30 min, the thus-obtained phosphide solution was added slowly (within 1 h) with a cannula to a stirred solution, maintained at −5 °C, of tetramesylate **8** (2.000 g, 1.35 mmol) in THF (75 mL). The solution was then allowed to reach room temperature and stirred for a further 14 h before being cooled to −5 °C. A BH_3/THF solution (1 M, 18.9 mL) was added subsequently and the mixture was stirred for one hour. The reaction mixture was poured onto ice and extracted with dichloromethane (4 × 120 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and the solvents evaporated. The product precipitated upon addition of diethyl ether and pure **9** was recovered by filtration [SiO_2, MeOH/CH_2Cl_2, 8:92 (v/v); R_f = 0.40]. Yield: 2.55 g, 100%. M.p. 172−174 °C. ^{1}H NMR (300.1 MHz, $CDCl_3$, 25 °C): δ = 0.70−1.50 (12 H, P-BH_3), 2.81 (s, 6 H, OMe), 3.41 (s, 6 H, OMe), 3.45 (s, 6 H, OMe), 3.49 (s, 6 H, OMe), 3.52 (s, 6 H, OMe), 3.64 (s, 6 H, OMe), 3.65 (s, 6 H, OMe), 2.50−4.50 (36 H, H-2, H-3, H-4, H-5, H-6), 4.53 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.0 Hz, 2 H, H-1), 4.75 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 2.7 Hz, 2 H, H-1), 5.50 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.0 Hz, 2 H, H-1), 6.80−8.00 (40 H, aromatic H) ppm. ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 26.9 (d, $^1J_{C,P}$ = 31.0 Hz, C-6^{A,D} or C-6^{B,E}), 27.3 (d, $^1J_{C,P}$ = 34.1 Hz, C-6^{B,E} or C-6^{A,D}), 57.2, 57.8, 58.7, 59.0, 61.0, 61.3, 61.7 (2-OCH$_3$, 3-OCH$_3$, 6-OCH$_3$), 68.8, 70.1, 71.2 (C-5), 70.2 (C-6^{C,F}), 79.6, 80.4, 80.6, 81.0, 81.1, 81.6, 82.4, 83.4, 85.0 (C-2, C-3, C-4), 97.6, 98.6, 99.6 (C-1), 128.0 (d, $^2J_{C,P}$ = 11.2 Hz, *o*-C), 128.2 (d, $^2J_{C,P}$ = 9.9 Hz, *o*-C), 128.5 (d, $^2J_{C,P}$ = 9.9 Hz, *o*-C), 128.6 (d, $^2J_{C,P}$ = 57.7 Hz, *ipso*-C), 128.6 (d, $^3J_{C,P}$ = 9.9 Hz, *o*-C), 130.2 (*p*-C), 130.6 (*p*-C), 130.7 (*p*-C), 130.8 (d, $^1J_{C,P}$ = 56.5 Hz, *ipso*-C), 131.1 (*p*-C), 131.6 (d, $^2J_{C,P}$ = 8.7 Hz, *m*-C), 131.9 (d, $^3J_{C,P}$ = 9.3 Hz, *m*-C), 132.0 (d, $^3J_{C,P}$ = 8.7 Hz, *m*-C), 132.4 (d, $^1J_{C,P}$ = 58.9 Hz, *ipso*-C), 132.8 (d, $^3J_{C,P}$ = 9.9 Hz, *m*-C), 132.8 (d, $^1J_{C,P}$ = 55.9 Hz, *ipso*-C) ppm. ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$, 25 °C): δ = 11.6 (s), 13.9 (s) ppm. $C_{98}H_{136}B_4O_{26}P_4{\cdot}CH_2Cl_2$ (1897.30 + 84.93): calcd. C 59.99, H7.02; found C 60.27, H 7.08.

6^A,6^B,6^D,6^E-Tetradeoxy-6^A,6^B,6^D,6^E-tetra{diphenylphosphinyl}-2^A,2^B,2^C,2^D,2^E,2^F,3^A,3^B,3^C,3^D,3^E,3^F,6^C,6^F-tetradeca-*O*-methyl-α-CD (10; α-TEPHOS): Compound **9** (1.00 g, 0.53 mmol) was added to diethylamine (100 mL) and the resulting solution was heated at 55−60 °C for 10 h. The precipitate was filtered off over Celite. The amine was then removed under vacuum to afford analytically pure **10** [SiO_2, MeOH/CH_2Cl_2, 8:92 (v/v); R_f = 0.31]. Yield: 0.930 g, 96%. −^{1}H NMR (300.1 MHz, $CDCl_3$, 25 °C): δ = 2.84 (s, 6 H, OMe), 3.34 (s, 6 H, OMe), 3.51 (s, 6 H, OMe), 3.54 (s, 6 H, OMe), 3.63 (s, 6 H, OMe), 3.65 (s, 6 H, OMe), 3.71 (s, 6 H, OMe), 2.30−4.30 (36 H, H-2, H-3, H-4, H-5, H-6), 4.45 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 2.7 Hz, 2 H, H-1), 5.03 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 2.6 Hz, 2 H, H-1), 5.12 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.1 Hz, 2 H, H-1), 6.80−7.60 (40 H, aromatic H) ppm. ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 29.7 (d, $^1J_{C,P}$ = 16.1 Hz, C-6^{A,D} or C-6^{B,E}), 32.4 (d, $^1J_{C,P}$ = 13.7 Hz, C-6^{B,E} or C-6^{A,D}), 57.5, 57.6, 57.7, 58.0, 61.4, 61.5, 61.8 (2-OCH_3, 3-OCH$_3$, 6-OCH$_3$), 70.1 (C-6^{C,F}), 70.3 (d, $^2J_{C,P}$ = 9.2 Hz, C-5^{A,B} or C-5^{D,E}), 70.4 (C-5^{C,F}), 71.3 (d, $^2J_{C,P}$ = 14.9 Hz, C-5^{D,E} or C-5^{A,B}), 80.6, 80.9, 81.0 [×2], 81.7, 82.2, 82.3 (C-2, C-3, C-4^{C,F}), 85.9 (d, $^3J_{C,P}$ = 12.6 Hz, C-4^{A,B} or C-4^{D,E}), 87.1 (d, $^3J_{C,P}$ = 9.3 Hz, C-4^{D,E} or C-4^{A,B}), 98.9 [×2], 99.9 (C-1), 126.5−134.0 (aromatic CH), 138.7 (d, $^1J_{C,P}$ = 11.8 Hz, *ipso*-C), 139.2 (d, $^1J_{C,P}$ = 12.4 Hz, *ipso*-C), 139.5 (d, $^1J_{C,P}$ = 11.2 Hz, *ipso*-C), 141.0 (d, $^1J_{C,P}$ = 11.2 Hz, *ipso*-C) ppm. ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$, 25 °C): δ = −24.8 (s),

−20.0 (s) ppm. $C_{98}H_{124}O_{26}P_4$ (1841.96): calcd. C 63.90, H 6.79; found C 63.73, H 6.75.

***P*,*P*′,*P*′′,*P*′′′-(6^A,6^B,6^D,6^E-Tetradeoxy-6^A,6^B,6^D,6^E-tetra{diphenylphosphinyl}-2^A,2^B,2^C,2^D,2^E,2^F,3^A,3^B,3^C,3^D,3^E,3^F,6^C,6^F-tetradeca-*O*-methyl-α-CD)-tetrakis[chloro(*o*-dimethylbenzylaminomethylphenyl-*C*,*N*)]palladium(II) (11):** To a solution of **10** (0.100 g, 0.05 mmol) in CH_2Cl_2 (10 mL) was added a solution of [Pd(*o*-$C_6H_4CH_2NMe_2$)Cl]$_2$ (0.060 g, 0.11 mmol) in CH_2Cl_2 (5 mL). After 1 h the solution was concentrated to *ca* 2 mL. Addition of pentane afforded **11** as a brown powder [SiO_2, MeOH/CH_2Cl_2, 8:92 (v/v); R_f = 0.68]. Yield: 0.140 g, 71%. M.p. 161 °C dec. ^{1}H NMR (300.1 MHz, $CDCl_3$, 25 °C): δ (assignments by HMQC) = 2.73 (br. d, $^4J_{P,H}$ = 2 Hz, 6 H, NMe), 2.75 (br. d, $^4J_{P,H}$ = 2 Hz, 6 H, NMe), 2.95 (s, 12 H, OMe), 2.96 (br. d, $^4J_{P,H}$ = 2 Hz, 6 H, NMe), 3.01 (br. d, $^4J_{P,H}$ = 2 Hz, 6 H, NMe), 3.43 (s, 6 H, OMe), 3.49 (s, 6 H, OMe), 3.58 (s, 6 H, OMe), 3.71 (s, 6 H, OMe), 3.97 (s, 6 H, OMe), 2.50−4.80 (32 H, H-2, H-3, H-4, H-5, H-6), 5.37 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.7 Hz, 2 H, H-1), 5.51 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 2.4 Hz, 2 H, H-1), 5.72 (t, aver. ^3J = 8.5 Hz, 2 H, H-4), 5.84 (t, aver. ^3J = 7.6 Hz, 2 H, arom. H of dmba), 5.99 (t, aver. ^3J = 7.5 Hz, 2 H, H-4), 6.18 (t, J = 7.1 Hz, 2 H, arom. H of dmba), 6.50 (t, J = 7.3 Hz, 2 H, arom. H of dmba), 6.62 (m, 4 H, arom. H of dmba), 6.65 (d, $^3J_{H\text{-}1,H\text{-}2}$ = 3.1 Hz, 2 H, H-1), 6.80 (t, J = 7.3 Hz, 2 H, arom. H of dmba), 6.85−8.20 (44 H, aromatic H) ppm (NCH_2 protons not assigned). ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 24.6 (d, $^1J_{C,P}$ = 28.5 Hz, C-6^{A,D} or C-6^{B,E}), 29.0 (d, $^1J_{C,P}$ = 32.9 Hz, C-6^{B,E} or C-6^{A,D}), 50.1, 50.3, 52.1 [×2] (NCH_3), 58.0, 58.9, 59.3, 60.7, 61.9, 62.1 (2-OCH_3, 3-OCH_3, 6-OCH_3), 69.9, 71.1, 71.9, 72.3, 78.6, 80.4, 80.7 [×2], 80.9, 81.4, 82.6, 83.0 (C-2, C-3, C-4, C-5), 71.3 (C-6^{C,F}), 72.8 (d, $^3J_{C,P}$ = 2.4 Hz, NCH_2), 73.2 (d, $^3J_{C,P}$ = 2.9 Hz, NCH_2), 94.0, 96.5, 97.1 (C-1), 121.7−150.6 (aromatic C) ppm. ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$, 25 °C): δ = 22.3 (s), 24.1 (s) ppm. $C_{134}H_{172}Cl_4N_4O_{26}P_4Pd_4$·2$CH_2Cl_2$ (2946.18 + 169.87): calcd. C 52.42, H 5.69, N 1.80; found C 52.40, H 5.69, N 1.64.

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