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Note

Synthesis of 6^{I}-amino-6^{I}-deoxy-$2^{I–VII}$,$3^{I–VII}$-tetradeca-*O*-methyl-cyclomaltoheptaose

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Abstract—The preparation of 6^{I}-amino-6^{I}-deoxy-$2^{I–VII}$,$3^{I–VII}$-tetradeca-*O*-methyl-cyclomaltoheptaose is reported. Two different routes (A and B), both starting from β-cyclodextrin (βCD), have been examined. Route A involved: (i) synthesis of heptakis(6-*O*-*tert*-butyldimethylsilyl)-βCD from βCD; (ii) permethylation of the secondary hydroxyl groups with methyl iodide and sodium hydride; (iii) desilylation of the primary hydroxyls with ammonium fluoride; (iv) monotosylation at O-6 position of per-(2,3-*O*-methyl)-βCD; (5) nucleophilic replacement of the tosyl group with azide anion; (v) reduction of the azido group by catalytic transfer hydrogenation using hydrazine hydrate in the presence of Pd/C in methanol/water. Route B started from the known 6^{I}-monoazido-6^{I}-monodeoxy-β-CD (two steps from β-CD) and entailed: (i) protection of the remaining primary hydroxyls using *tert*-butyldimethylsilylchloride (TBDMSCl); (ii) exhaustive methylation of the secondary hydroxyls with methyl iodide and sodium hydride; (iii) removal of the TBDMS protecting groups with ammonium fluoride; (iv) reduction of the azido group as above. *Route A* was found to be less convenient than *Route B* due to the inherent difficulty of controlling the monotosylation of per-(2,3-*O*-methyl)-βCD.

Keywords: Methylated cyclodextrin; Selective tosylation; Aminodeoxycyclodextrin

Cyclodextrins (cyclomaltooligosaccharides, CDs) are water-soluble cyclic oligosaccharides composed, for the most common representatives, of six (α-), seven (β-), or eight (γ-) α-(1→4)-linked D-glucopyranose units arranged in a torus-shaped structure with hydrophilic exterior and a comparatively hydrophobic cavity. As a consequence of these structural features, CDs show the remarkable capacity to form host–guest inclusion complexes in aqueous solution with hydrophobic molecules of the proper size and shape.[1] Combining the cyclodextrin molecular recognition ability with proper functional groups is of significance[2a] in several research fields and applications aimed at realizing models for enzyme binding pockets,[2b] optical sensors of organic molecules in aqueous environment,[3] and systems for slow release or site-specific delivery of drugs.[4a,b] Furthermore, being chiral entities, CDs have a significant potential for asymmetric synthesis and chiral separations. Finally, attachment of properly functionalized CDs to solid surfaces, may lead to useful organic–metal composites.

With this latter objective in mind, we have recently reported the synthesis of a permethylated β-CD derivative bearing a lipoic acid unit linked via an amide bond (TRIMEB-LA), which gives strong chemisorption on colloidal gold allowing the realization of nanoparticles coated with hundreds of cyclodextrin moieties.[5] For the synthesis of TRIMEB-LA, we exploited the precursor 6^{I}-amino-6^{I}-deoxy-$2^{I–VII}$,$3^{I–VII}$-$6^{II–VII}$-decaosa-*O*-methyl-cyclomaltoheptaose (TRIMEB-NH_2), which can be conveniently prepared in a multigram scale starting from βCD using a four steps route recently reported by Jicsinszky and Ivanyi.[6] TRIMEB-NH_2 is a key compound that makes simpler the synthesis of cyclodextrin

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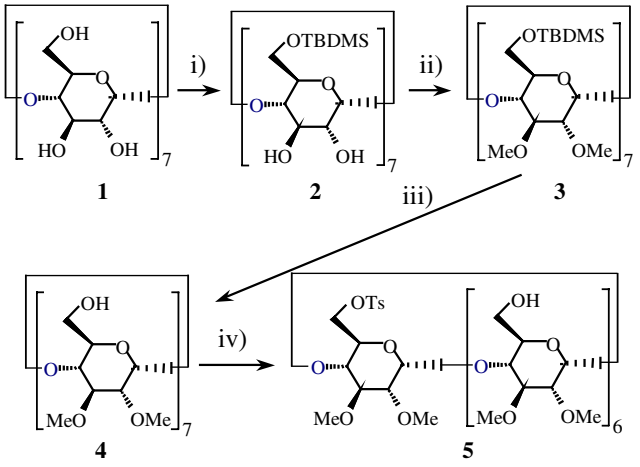
conjugates for at least two reasons: (i) TRIMEB-NH_2 has only one reactive amino group, which can be coupled by standard peptide chemistry protocols to molecules containing a carboxyl functionality, without requiring any protection/deprotection step; (ii) the lipophilic nature of the permethylated cyclodextrin moiety, produces βCD conjugates soluble not only in water but also in common organic solvents and that makes straightforward their purification by standard flash column chromatography on silica gel. This latter point is of crucial importance for applications in which pure cyclodextrin derivatives rather than mixtures of positional isomers or homologous derivatives are needed.

Although the synthesis and purification of TRIMEB-LA and other derivatives of TRIMEB-NH_2 bearing an appended chromophore or fluorophore proved to be easy, their use as molecular sensors or supramolecular receptors was rather disappointing. In fact, we consistently found that the pendant group is so strongly self-included into the cavity or into a counter molecule that the cyclodextrin cavity is almost unavailable for binding of any target substrate. In order to capitalize upon the ease of purification of derivatives like TRIMEB-LA (or similar compounds), we addressed 6^{I}-amino-6^{I}-deoxy-$2^{I–VII}$,$3^{I–VII}$-tetradeca-*O*-methyl-cyclomaltoheptaose **10**, as an attractive substitute of TRIMEB-NH_2, despite the predictable synthetic difficulties. As a matter of fact, its preparation involves two of the most challenging synthetic problems in the chemical modification of cyclodextrins: (i) monosubstitution at the 6-position and; (ii) exclusive peralkylation at the 2- and 3-positions.

Although there are some well-established methods that might provide a solution to the above problems one at a time,[7a,b] the reactivity of the primary hydroxyl groups in substitution reactions, when all secondary hydroxyls are alkylated, was never confronted. So, we envisaged the synthetic plan indicated as *Route A* in Scheme 1. It involves the preparation of per-2,3-*O*-methyl-βCD (**4**),[10b] followed by introduction of the amino group.

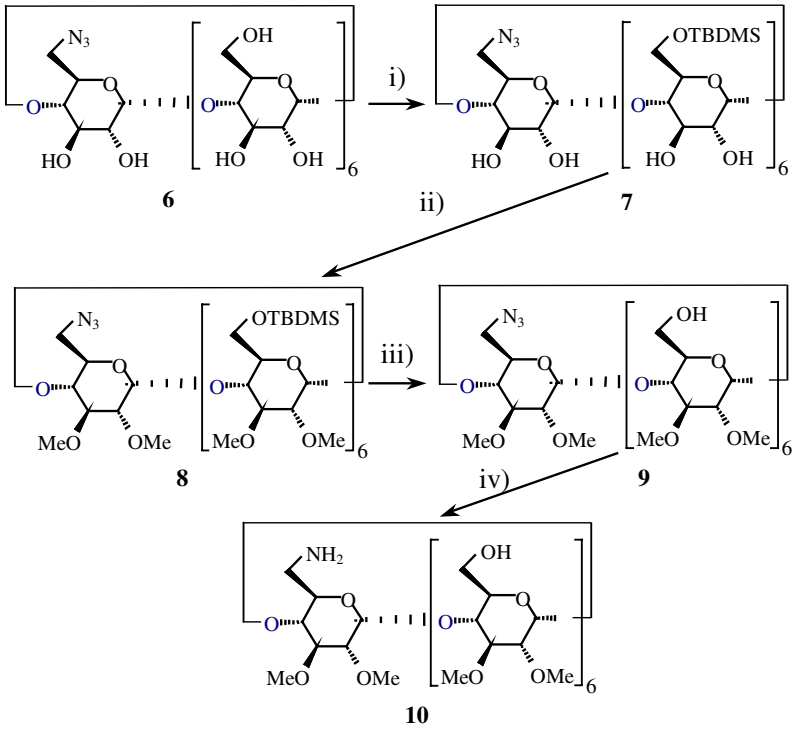
In order to synthesize **4**, all the primary hydroxyl groups of βCD were protected by reaction with TBDMSCl in dry pyridine.[8,10a,b] Kinetic studies revealed that one-portion addition of TBDMSCl results in more efficient control on the substitution range. Using low temperature is necessary only at the starting period of the reaction. Application of the higher reaction temperature makes the purification procedure easier due to the reduced amounts of the lower silylated products. These modifications of Fügedi[10a] and Takeo et al.[10b] resulted in an easily crystallizable crude product. Preparation of the corresponding α- and γ-cyclodextrin by this modified method also did not require chromatography. The desired per-(6-*O*-*tert*-butyldimethylsilyl)-βCD (**2**) was obtained in good yield (>75%) by recrystallization from various solvent mixtures, *without purification by column chromatography on silica gel*. The identity of the product was confirmed by ^{1}H NMR[8] and by ESIMS. Heptakis(6-*O*-*tert*-butyldimethylsilyl-2,3-di-*O*-methyl)cyclomaltoheptaose (**3**) was obtained from **2** in 86% yield by exhaustive methylation of the secondary hydroxyl groups with a large excess of NaH/iodomethane in dry THF at room temperature. Further desilylation of **3** was accomplished with ammonium fluoride hydrogen fluoride in methanol under reflux.



Scheme 1. Route A: (i) TBDMSCl, pyridine; (ii) NaH/CH_3I, THF; (iii) NH_4F, MeOH; (iv) TsCl, 5:1 CH_2Cl_2–pyridine.

By analogy with the reported preparations of 6^{I}-amino-6^{I}-deoxy-βCD via the corresponding 6^{I}-*O*-tosyl derivative,[6,9a–c] tosylation of **4** was attempted in 5:1 CH_2Cl_2–pyridine. However, TLC monitoring of the reaction mixture showed that **5** was formed together with a considerable amount of polytosylated derivatives. Extensive purification by flash chromatography allowed to obtain compound **5** in 21% yield and its identity was established by ^{1}H NMR spectroscopy and ESIMS. Changes in the tosyl chloride/cyclodextrin ratio did not lead to any improvement of the O-6 monotosylation. Alternative tosylation methods reported in the literature[7a,9] were also pursued but considerable amounts of ditosylated derivatives were always obtained. Moreover, purification of **5** was successful only in a 100 mg scale by column chromatography and failed for any larger amounts. For this reason, this route was abandoned to follow the alternative one depicted in Scheme 2 (*Route B*).

Compound **6** was obtained in two steps from βCD by selective monotosylation at O-6 (33% yield) followed by nucleophilic displacement of the tosyl group with a 20% molar excess of sodium azide in DMF at 105–110 °C (quantitative), following literature procedures.[6] The basic idea behind *Route B* was to relegate the tosylation step to the very beginning of the synthesis where a low yield is more acceptable since it only involves a loss of the commercially available βCD. Treatment of **6** with TBDMSCl in dry pyridine afforded the cyclodextrin



Scheme 2. Route B: (i) TBDMSCl, dry pyridine; (ii) NaH/MeI, DMF; (iii) NH_4F, MeOH; (iv) hydrazine hydrate/Pd/C.

derivative **7** (70% isolated yield), in which all the primary hydroxyl groups were silylated. The ^{1}HNMR spectrum of **7** in $CDCl_3$ was consistent with the proposed structure. Furthermore, the corresponding ESIMS spectrum in the presence of NH_4Cl as cationizing agent gave the expected signal at m/z 939 ($[\mathbf{7}+2(NH_4)]^{2+}$). Permethylation of the remaining secondary hydroxyl groups of **7** by a large excess of methyl iodide and sodium hydride in dry DMF gave **8** in 88% isolated yield. Desilylation of **8** was carried out as above described for **4** and resulted in compound **9** (63% yield). Finally, reduction of the azido group of **9** by catalytic transfer hydrogenation using hydrazine hydrate in the presence of Pd/C in water gave the desired cyclodextrin derivative **10** in 90% yield. Then, the overall yield for the target compound **10** from commercial βCD was 11.5%.

1. Experimental

1.1. Reagents

β-Cyclodextrin was a Wacker product, and all other reagents were purchased from Fluka and used as supplied. 6^I-*O*-*p*-Tolylsulfonylcyclomaltoheptaose, 6^I-azido-6^I-deoxy-cyclomaltoheptaose (**6**), and heptakis(6-*O*-*tert*-butyldimethylsilyl)cyclomaltoheptaose are also commercial products and can be obtained from Cyclolab R&D Lab. (Budapest, Hungary). Chloroform for TLC was distilled before use to remove EtOH (stabilizer). Pyridine was stored on molecular sieves. TLC plates (E. Merck 5554 F_{254}) were developed in saturated chamber on 10 cm; spots were visualized by UV 254 nm and charring of H_2SO_4–EtOH sprayed plates at 110 °C.

1.2. Heptakis(6-*O*-*tert*-butyldimethylsilyl)cyclomaltoheptaose (2)

Freshly dried βCD (22.7 g, 0.020 mol) was dissolved in dry pyridine (230 mL) at room temperature. Then, TBDMSCl (24.1 g, 0.160 mol) was added in one portion with external water bath cooling. The reaction mixture was stirred for 4.5 h at room temperature. When the reaction did not show any change in the desired product by TLC (40:10:1 $CHCl_3$–MeOH–water) the reaction mixture was poured onto water (2.5 L). The precipitate formed was collected by filtration, washed with water (2 × 200 mL) and acetone (200 mL). The crude product (35.7 g) was recrystallized twice from CH_2Cl_2 (50 mL) and MeOH (350 mL) and once from CH_2Cl_2 (25 mL) and acetone (200 mL). The obtained product (17.6 g, 46% yield) was suitable for further reactions (>95% purity). A second crop of crystals (12.1 g, 32% yield) was obtained from mother liquors after several recrystallizations (total yield 29.7 g, 78%): mp 304–308 °C (acetone), lit.[10a] 314–318 °C, lit.[10b] 299–302 °C, $[\alpha]_D^{25}$ + 105.3 (*c* 2, $CHCl_3$), lit.[10a] +105°, lit.[10b] +113° (at 22 °C); R_F 0.45–0.46 (40:10:1 $CHCl_3$–MeOH–water); ESIMS (1:1 water–MeOH): m/z 983.5 ($[(\mathbf{2})+2\ NH_4]^{2+}$, calcd 984.0), 993.3 ($[(\mathbf{2})+2\ NH_4+H_2O]^{2+}$, calcd 993.0).

1.3. Heptakis(6-*O*-*tert*-butyldimethylsilyl-2,3-di-*O*-methyl)cyclomaltoheptaose (3)

Compound **2** (29.0 g, 0.015 mol) was dissolved in peroxide-free THF (290 mL), then NaH was added (7.2 g, 0.30 mol, dispersed in oil, 80%). The reaction mixture was heated up to 40 °C and iodomethane (42.6 g, 18.6 mL, 0.30 mol) was added in 3 mL portions within a 15–30 min period. After 30 min stirring at 40 °C, more sodium hydride (1.8 g, 0.075 mol) and iodomethane (10.7 g, 4.7 mL, 0.075 mol) in two portions were added and the reaction mixture was further stirred overnight at room temperature.

The excess of sodium hydride and iodomethane was decomposed by addition of MeOH (50 mL). Volatile compounds were removed by evaporation under diminished pressure resulting in a sticky solid, which was suspended in *n*-hexane (320 mL). The solid was filtered off and discarded. The solvent was removed in a rotatory evaporator under diminished pressure yielding a yellow oil (34 g), which contained some oil from sodium hydride. Removal of the oil could be achieved at this point by filtration through a silica gel bed, or after the desilylation step, but due to technical reasons the latter is recommended: $[\alpha]_D^{25} + 130.6$ (*c* 2, $CHCl_3$), lit.[10b] +97° (at 26 °C); R_F 0.91–0.93 (50:25:1 $CHCl_3$–MeOH–water); ESIMS (1:1 water–MeOH): *m*/*z* 1081.9 ($[(\mathbf{3}) + 2\ NH_4]^{2+}$, calcd 1082.0); 1108.4 ($[(\mathbf{3}) + 2\ NH_4 + 3H_2O]^{2+}$, calcd 1109.0).

1.4. Heptakis(2,3-di-*O*-methyl)cyclomaltoheptaose (4)

To compound **3** (34 g, 0.015 mol, which contained about 2 g of oil, were added MeOH (340 mL), and ammonium fluoride (20 g, 0.35 mol). The oily material slowly dissolved at reflux; the desilylation was completed after 5 h reflux as confirmed by TLC (40:10:1 $CHCl_3$–MeOH–water). MeOH was removed by evaporation and the crude product was dissolved in CH_2Cl_2, and filtered through an aluminum oxide bed (60 g, diam 70 mm, height 17 mm), to obtain **4** (17.0 g, 85%), which is oil-free: mp 160–166 °C (amorphous), lit.[10b]: 168–172 °C; $[\alpha]_D^{25} + 155.3$ (*c* 2, $CHCl_3$), lit.[10b] +176° (at 24 °C); R_F 0.42–0.43 (50:25:1 $CHCl_3$–MeOH–water); ^{1}H NMR (250 MHz, Me_2SO-d_6): δ 5.12 (m, 7H, H-1), 4.54 (m, 7H, OH-6) 3.75–3.29 (m, 77H, H-2, H-3, H-4, H-5, H-6a, H-6b, Me-2, Me-3); ESIMS (1:1 water–MeOH): *m*/*z* 681.9 ($[(\mathbf{4}) + 2\ NH_4]^{2+}$, calcd 683.0); 1347 ($[(\mathbf{4}) + NH_4]^{+}$, calcd 1348). Anal. Calcd for $C_{56}H_{98}O_{35}$: C, 50.52; H, 7.42. Found: C, 50.6; H, 7.46.

1.5. Heptakis(2,3-di-*O*-methyl)-6^I-*O*-*p*-tolylsulfonyl-cyclomaltoheptaose (5)

Compound **4** (5.0 g, 0.038 mol) was solubilized in CH_2Cl_2 (50 mL) and pyridine (10 mL) and *p*-toluenesulfonyl chloride (0.82 g, 0.043 mol) in CH_2Cl_2 (50 mL) was added dropwise within ~10 min. The reaction was monitored by TLC (50:10:1 $CHCl_3$–MeOH–water). After 24 h, some starting material was still present together with the expected product and some polytosylated derivatives. In the attempt to increase the yield, more tosyl chloride (0.36 g, 0.019 mol) in CH_2Cl_2 (15 mL) was added. After 5 h, the solvents were removed by evaporation and the solid residue was purified by column chromatography (silica gel, 9:1 → 4:1 $CHCl_3$–MeOH); yield: 1.2 g (21%): mp 194–195 °C [dec] (amorphous); $[\alpha]_D^{25}$ +151 (*c* 1, $CHCl_3$); R_F 0.32–0.33 (50:10:1 $CHCl_3$–MeOH–water); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.79 (d, 2H, H-2′,6′), 7.36 (d, 2H, H-3′,5′), 5.13 (m, 7H, H-1), 4.46 (m, 6H, OH-6), 3.98–3.46 (m, 77 H), 3.17 (m, 7H), 2.44 (s, 3H, CH_3–Ar); ESIMS (1:1 water–MeOH): *m*/*z* 759.0 ($[(\mathbf{5}) + 2\ NH_4]^{2+}$, calcd 760.0); 1501.1 ($[(\mathbf{5}) + 2\ NH_4]^{2+}$, calcd 1502). Anal. Calcd for $C_{63}H_{104}O_{37}S$: C, 50.94; H, 7.06; S, 2.16. Found: C, 51.11; H, 7.11; S, 2.01.

1.6. 6^I-Azido-6^I-deoxy-hexakis(6-*O*-*tert*-butyldimethylsilyl)cyclomaltoheptaose (7)

Dried 6^I-azido-6^I-deoxycyclomaltoheptaose[6] (23.2 g, 0.02 mol) was dissolved in pyridine (230 mL) at room temperature and immersed in a cold-water bath. *tert*-Butyldimethylsilyl chloride (21.1 g, 0.14 mol) was added and the reaction mixture was allowed to warm up to room temperature (26 °C) and further stirred for 9 h. When no more change was observed by TLC (40:10:1 $CHCl_3$–MeOH–water), the reaction mixture was poured onto water (2 L) and allowed to stand for crystallization overnight. The waxy crystals were filtered off and washed with water (3 × 100 mL), then after changing the collector, with acetone (2 × 50 mL). The resulting white crystalline material (32.5 g) contained some pyridine and smelled TBDMSOH. A second crop of crude product was obtained by evaporation of the acetone solution (6.2 g, strong TBDMSOH smell). Recrystallization from 1:3 CH_2Cl_2–acetone (25 mL) gave a material, which was practically identical to the first crystalline product (3.1 g). The two crude crops were combined (35.6 g, 96.5%) and recrystallized twice from 1:3 CH_2Cl_2–acetone (144 mL and 100 mL, respectively). The resulting product (23.5 g, 63%) had purity higher than 95% and it was suitable for further reactions. A second portion of the product could be obtained from the concentrated mother liquors of recrystallization after a short-column chromatography (silica gel, 100 g, elution with CH_2Cl_2) and recrystallization from MeOH and 1:3 CH_2Cl_2 and acetone (6.3 g, 17%, 80% combined yield): mp 266–270 °C [dec] (acetone), $[\alpha]_D^{25}$ +105.9 (*c* 1, $CHCl_3$); R_F 0.41–0.45 (50:25:1 $CHCl_3$–MeOH–water); ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.70 (m, 7H, OH-2), 5.22 (m, 7H, OH-3) 4.90 (m, 7H, H-1), 4.06–3.36 (m, 42H, H-2, H-3, H-4, H-5, H-6a, H-6b), 0.87 (m, 54H, CH_3–CMe_2–Si),

0.04 (*m*, 36H, Me_2–Si); ESIMS (1:1 water–MeOH): *m/z* 939.1 ([(**7**) + 2 NH_4]$^{2+}$, calcd 939.5). Anal. Calcd for $C_{78}H_{153}N_3O_{34}Si_6$: C, 50.76; H, 8.36; N, 2.28. Found: C, 50.71; H, 8.45; N, 2.35.

1.7. 6^{I}-Azido-6^{I}-deoxy-heptakis(2,3-di-*O*-methyl)-hexakis(6^{II-}-*O*-*tert*-butyldimethylsilyl)cyclomaltoheptaose (8)

Acetone and CH_2Cl_2 free compound **7** (18.5 g, 0.01 mol) was dissolved in dry and peroxide-free THF (185 mL) and NaH was added (4.8 g, 0.20 mol, dispersed in oil 80%) then the reaction mixture was heated up to 40 °C and iodomethane (42.6 g, 18.6 mL, 0.20 mol) was added in 3 mL portions. After 30 min stirring at ~40 °C, more NaH (1.8 g, 0.075 mol) and iodomethane (10.7 g, 4.7 mL, 0.075 mol) were added. The reaction mixture was stirred for an additional hour at ~40 °C, then heated up to reflux and stirred for an additional hour. The reaction mixture was cooled and the excess of NaH was decomposed with MeOH (50 mL) then volatile compounds were removed by distillation. To the sticky solid, *n*-heptane (420 mL) was added and the solid was filtered off. Removal of the solvent resulted in a dense, yellow oil (22.8 g). Removal of oil (from NaH) could be done at this point (by filtration through a silica gel bed) or after the desilylation step. Our experiences suggested that purification of the desilylated product is easier: mp 144–150 °C (amorphous); $[\alpha]_D^{25}$ +135.4 (*c* 1, $CHCl_3$); R_F 0.87–0.89 (50:25:1 $CHCl_3$–MeOH–water); ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.22–5.08 (m, 7H, H-1), 4.17–4.05 (m, 7H), 3.76–3.50 (m, 70H), 3.11–3.03 (m, 7H), 0.87 (m, 54H, *tert*-butyl-Si), 0.04 (m, 36H, Me_2–Si); ESIMS (1:1 water–MeOH): *m/z* 1036.7 ([(**8**) + 2 NH_4]$^{2+}$, calcd 1037.5). Anal. Calcd for $C_{92}H_{181}O_{34}N_3Si_6$: C, 54.11; H, 8.93, N, 2.06. Found: C, 54.04; H, 8.87; N, 2.12.

1.8. 6^{I}-Azido-6^{I}-deoxy-heptakis(2,3-di-*O*-methyl)cyclomaltoheptaose (9)

Compound **8** (14.26 g, 0.007 mol) was suspended in MeOH (250 mL) and stirred until complete solubilization. Then, NH_4F (10.44 g, 0.242 mol) was added and the mixture was refluxed. The outcome of the reaction was monitored by TLC (40:10:1 $CHCl_3$–MeOH–water). After 18 h, the reaction was completed. The solvent was distilled off and the residue was solubilized in CH_2Cl_2 (200 mL) and extracted with brine (3 × 1 L). The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated in a rotatory evaporator obtaining a residue, which was purified by column chromatography (silica gel, 9:1 → 1:4 $CHCl_3$–MeOH); yield: 6.0 g (63%): mp 173–178 °C [dec] (amorphous); $[\alpha]_D^{25}$ + 160 (*c* 1, $CHCl_3$); R_F 0.59 (40:10:1 $CHCl_3$–MeOH–water); ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.10 (s, 7H, H-1), 4.37 (m, 6H, OH-6), 3.82–3.40 (m, 77H), 3.20 (m, 7H); ESIMS (1:1 water–MeOH): *m/z* 694.4 ([(**9**) + 2 NH_4]$^{2+}$, calcd 695.5). Anal. Calcd for $C_{56}H_{97}N_3O_{34}$: C, 49.59; H, 7.21; N, 3.10. Found: C, 49.77; H, 7.27; N, 3.14.

1.9. 6^{I}-Amino-6^{I}-deoxy-heptakis(2,3-di-*O*-methyl)cyclomaltoheptaose (10)

Compound **9** (2.50 g, 0.0018 mol) was dissolved in water (45 mL). The solution was bubbled with nitrogen then Pd (10%) supported on carbon (0.35 g) was added. After 10 min, hydrogen was applied to the reaction and kept under stirring at room temperature. The reaction was monitored by TLC (40:10:1 $CHCl_3$–MeOH–water). After 18 h, the solution was filtered then, removal of solvent resulted in a white solid; yield 2.20 g (90%): mp 244–247 °C [dec]; $[\alpha]_D^{25}$ +151 (*c* 1, $CHCl_3$); R_F 0.32 (40:10:1 $CHCl_3$–MeOH–water); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.79 (d, 2H, H-2′,6′), 7.36 (d, 2H, H-3′,5′), 5.13 (m, 7H, H-1), 4.46 (m, 6H, OH-6), 3.98–3.46 (m, 77H), 3.17 (m, 7H, H-2-5, H-6ab, Me-2, Me-3), 2.44 (s, 3H, Me–Ar); ESIMS (1:1 water–MeOH): *m/z* 759.0 ([(**10**) + 2 NH_4]$^{2+}$, calcd 760.0); 1501.1 ([(**10**) + 2 NH_4]$^{2+}$, calcd 1502). Anal. Calcd for $C_{56}H_{99}NO_{34}$: C, 50.56; H, 7.50; N, 1.05. Found: C, 50.61; H, 7.57; N, 1.03.

Compound **10** was converted into its hydrochloride by addition of aq 0.01 M HCl to its water solution, and freeze-dried to prevent carbonatation: mp 228–233 °C [dec] (amorphous); $[\alpha]_D^{25}$ +149 (*c* 1, water). Anal. Calcd for $C_{56}H_{100}ClNO_{34}$: C, 49.21; H, 7.37; N, 1.02, Cl 2.59. Found: C, 49.32; H, 7.41; N, 1.05; Cl, 2.44.

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