Supplementary Information

One-Pot Regioselective Synthesis of $2^I,3^I$-*O*-(*o*-Xylylene)-Capped Cyclomaltooligosaccharides: Tailoring the Topology and Supramolecular Properties of Cyclodextrins

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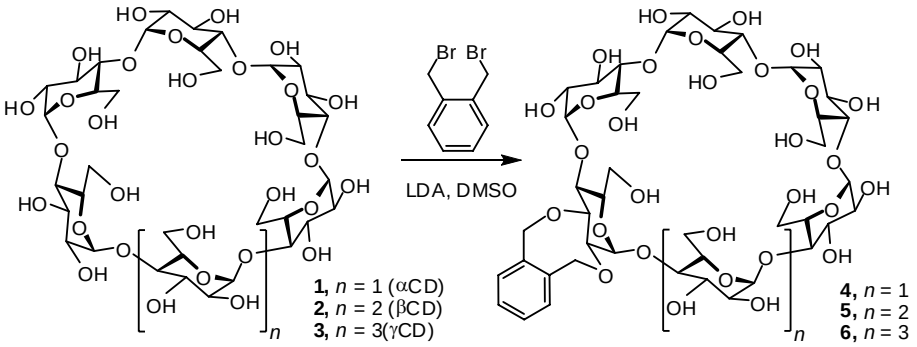
Materials and General Methods. All solvents and reagents were purchased from commercial sources and used without further purification, except for dichloromethane, which was distilled under Ar stream over CaH_2, pyridine, which was dried over KOH and distilled, DMF, which was dried over BaO, distilled and kept over 4 Å molecular sieves, and DMSO, which was distilled and kept over 4 Å molecular sieves. α, β and γCD were commercial compounds; they were dried over P_2O_5 at 85 ºC under vacuum until constant weight before using. Optical rotations were measured at 20 ºC in 1-cm or 1-dm tubes. ^{1}H (and ^{13}C NMR) spectra were recorded at 500 (125.7) MHz. 2D COSY, 2D NOESY, 1D TOCSY, HMQC and HSQC experiments were used to assist on NMR assignments. Thin-layer chromatography (TLC) was carried out on aluminium sheets coated with Kieselgel 60 F254 (E. Merck), with visualisation by UV light and by charring with 10% H_2SO_4. Analytical HPLC was carried out on a Waters 600 instrument provided with an on-line degasser and a DEDL PL ELS 1000 detector from Polymer Laboratories. The Waters chemstation used Empower software. Alltech Carbohydrate ES 5u (5μm particle size, 250 mm x 4,6 mm) and Alltech Prevail C_{18} 5u (5μm particle size, 250 mm x 4,6 mm) columns were used. Column chromatography was carried out on Silica Gel 60 (E. Merck, 230-400 mesh). The operating conditions for recording FAB mass spectra were the following: the primary beam consisted of Xe atoms with a maximum energy of 8 keV; the samples were dissolved in thioglycerol, and the positive ions were separated and accelerated over a potential of 7 keV; NaI was added as cationizing agent. MALDI-TOF mass spectra were acquired on a spectrometer operating in the positive-ion mode with an accelerating voltage of 28 keV. Samples were dissolved in acetonitrile at mM concentration and mixed with a standard solution of α-cyano-4-hydroxycinnamic acid (α-cyano; 20 mg mL^{-1} in 25:25:1 MeOH-H_2O-AcOH, 2 μL); 1 μL of the mixture was loaded onto the target plate, then allowed to airdryat room temperature. For ESI mass spectra, 0.1 pM sample concentration were used, the mobile phase consisting of 50% aq acetonitrile at 0.1 mL min^{-1}. Elemental analyses were performed at the Instituto de Investigaciones Químicas (Sevilla, Spain). Calculations were performed with the MACROMODEL 6.0 package using the MM2* force field and the GB/SA continuous solvent model for water.

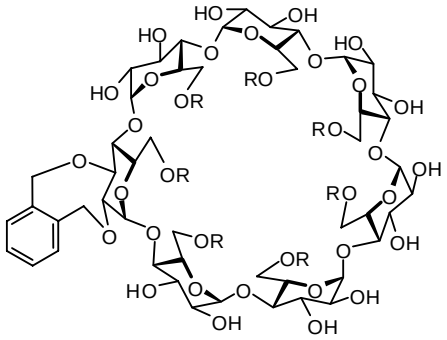


$2^{I},3^{I}$-*O*-(*o*-Xylylene)cyclomaltohexaose (4). Isolated as white needles after crystallisation from water (Found: C, 48.99; H, 5.95; $C_{44}H_{66}O_{30}$ requires: C, 49.16; H, 6.19); R_f = 0.54 (6:3:1 CH_3CN-H_2O-NH_4OH); $[\alpha]_D$ = +152.2 (*c* 1.0 in DMSO); ^{1}H NMR (500 MHz, D_2O, 333 K): δ = 7.70-7.63 (m, 4 H, Ph), 5.48 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1^{I}), 5.46, 5.40 (2 d, 2 H, $^2J_{H,H}$ = 14.6 Hz, C*H*Ph), 5.43, 5.30 (2 d, 2 H, $^2J_{H,H}$ = 13.7 Hz, C*H*Ph), 5.37-5.28 (m, 5 H, H-1^{II-VI}), 4.41-3.98 (m, 26 H, H-3^{I-VI}, H-$6a^{I-VI}$, H-$6b^{I-VI}$, H-5^{I-VI}, H-2^{I}, H-4^{I}), 3.98-3.88 (m, 5 H, H-2^{II-VI}), 3.91-3.78 (m, 5 H, H-4^{II-VI}); ^{1}H TOCSY (H-1^{I} irradiation): δ = 4.29 (d, 1 H, $J_{6a,6b}$ = 12.5 Hz, H-$6a^{I}$), 4.25 (dd, 1 H, $J_{5,6b}$ = 3.0 Hz, H-$6b^{I}$), 4.21 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.0 Hz, H-3^{I}), 4.14 (m, 1 H, H-5^{I}), 4.05 (dd, 1 H, H-2^{I}), 4.03 (t, 1 H, $J_{4,5}$ = 9.5 Hz, H-4^{I}); ^{13}C NMR (125.7 MHz, D_2O, 333 K): δ = 136.9-128.6 (Ph), 102.0, 101.9, 101.8, 101.7, 101.6 (5 C, C-1^{II-VI}), 100.9 (C-1^{I}), 82.5, 82.0, 81.9 (×2), 81.8 (5 C, C-4^{II-VI}), 80.8 (C-3^{I}), 80.4 (C-4^{I}), 79.5 (C-2^{I}), 74.2, 74.0 (×2), 73.8, 73.6 (5 C, C-3^{II-VI}), 73.8 (CH_2Ph), 72.8, 72.7 (×3), 72.5 (5 C, C-5^{II-VI}), 72.7 (CH_2Ph), 72.3, 72.2 (×2), 72.1, 71.9 (5 C, C-2^{II-VI}), 61.0 (×6) (6 C, C-6^{I-VI}); ESIMS: *m/z* 1113.2 ($[M + Na]^+$).

$2^{I},3^{I}$-*O*-(*o*-Xylylene)cyclomaltoheptaose (5). Isolated as an amorphous solid (Found: C, 48.38; H, 5.96; $C_{50}H_{76}O_{35}$ requires: C, 48.54; H, 6.19); R_f = 0.42 (6:3:1 CH_3CN-H_2O-NH_4OH); $[\alpha]_D$ = +124.2 (*c* 1.0 in DMSO); ^{1}H NMR (500 MHz, DMSO): δ = 7.26-7.12 (m, 4 H, Ph), 5.73-5.61 (m, 7 H, OH-6), 5.14, 4.88 (2 d, 2 H, $^2J_{H,H}$ = 14.3 Hz, C*H*Ph), 5.06 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1^{I}), 5.05, 4.94 (2 d, 2 H, $^2J_{H,H}$ = 14.3 Hz, C*H*Ph), 4.83-4.78 (m, 6 H, H-1^{II-VII}), 4.57-4.32 (m, 14 H, OH-2, OH-3), 3.80 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 8.9 Hz, H-3^{I}), 3.68 (m, 1 H, H-$6a^{I}$), 3.64-3.48 (m, 23 H, H-$6b^{I}$, H-5^{I},H-4^{I}, H-2^{I}, H-3^{II-VII}, H-5^{II-VII}, H-$6a^{I-VII}$), 3.35-3.21 (m, 18 H, H-4^{II-VII}, H-$6b^{II-VII}$, H-2^{II-VII}); ^{1}H 1DTOCSY (H-3^{I} irradiation): δ = 5.06 (d, 1 H, H-1^{I}), 4.50 (m, 2 H, OH-2, OH-3), 3.68 (m, 1 H, H-$6a^{I}$), 3.58 (m, 1 H, H-$6b^{I}$), 3.54 (m, 1 H, H-5^{I}), 3.52 (t, 1 H, $J_{4,5}$ = 9.5 Hz, H-4^{I}), 3.49 (dd, 1 H, $J_{2,3}$ = 8.9 Hz, H-2^{I}); ^{13}C NMR (125.7 MHz, DMSO): δ = 137.1-128.3 (Ph), 102.4 (×3), 102.3, 102.1 (×2) (6 C, C-1^{II-VII}), 100.6 (C-1^{I}), 82.5, 82.1 (×2), 81.8 (×2), 81.7 (6 C, C-4^{II-VII}), 81.7 (C-3^{I}), 81.0 (C-2^{I}), 79.1 (C-4^{I}), 73.8, 73.7 (×3), 73.6, 73.4 (6 C, C-3^{II-VII}), 73.7 (CH_2Ph), 73.2 (C-5^{I}), 73.1 (CH_2Ph), 73.0, 72.9, 72.8 (×2), 72.7 (×2), (6 C, C-2^{II-VII}), 72.6, 72.5 (×4), 72.1 (6 C, C-5^{II-VII}), 60.6, 60.5 (×2), 60.3 (×3) (6 C, C-6^{II-VII}), 60.1 (C-6^{I}). FABMS: *m/z* 1259 ($[M + Na]^+$).

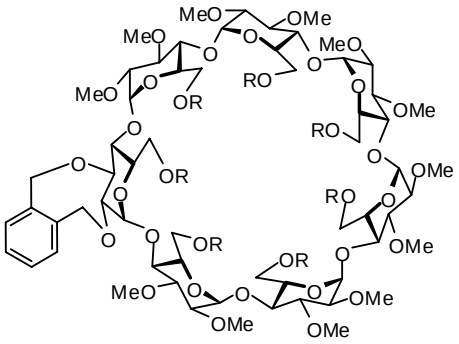
2^{I}, 3^{I}-*O*-(*o*-Xylylene)cyclomaltooctaose (6). Isolated as an amorphous solid (Found: C, 47.95; H, 6.06; $C_{56}H_{86}O_{40}$ requires: C, 48.07; H, 6.19); R_f = 0.52 (CH_3CN-H_2O-NH_4OH 6:3:1); $[\alpha]_D$ = +154.8 (*c*

0.91 in H_2O). ^{1}H NMR (500 MHz, D_2O): δ = 7.10-6.96 (m, 4 H, Ph), 5.28 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1^{I}), 5.20, 4.73 (2 d, 2 H, $^2J_{H,H}$ = 13.4 Hz, C*H*Ph), 5.16, 5.09 (2 d, 2 H, $^2J_{H,H}$ = 14.0 Hz, C*H*Ph), 5.12-4.98 (m, 7 H, H-1$^{II-VIII}$), 4.13-4.03 (m, 7 H, H-5$^{II-VIII}$), 3.97-3.62 (m, 27 H, H-3^{I-VIII}, H-6a^{I-VIII}, H-6b^{I-VIII}, H-5^{I}, H-4^{I}, H-2^{I}), 3.63-3.47 (m, 14 H, H-2$^{II-VIII}$, H-4$^{II-VIII}$); ^{1}H 1DTOCSY (H-1^{I} irradiation): δ = 3.93 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 8.3 Hz, H-3^{I}), 3.92 (m, 2 H, H-6a^{I}, H-5^{I}), 3.89 (d, 1 H, $J_{6a,6b}$ = 11.5 Hz, H-6b^{I}), 3.79 (m, 1 H, H-2^{I}), 3.75 (m, 1 H, H-4^{I}); ^{13}C NMR (125.7 MHz, D_2O): δ = 136.2-128.0 (Ph), 102.3, 102.2, 102.0, 101.7, 101.6, 101.0 (×2) (7 C, C-1$^{II-VIII}$), 100.3 (C-1^{I}), 81.7, 81.1, 80.5, 80.0, 79.8, 79.6, 79.2, 79.1 (8 C, C-4^{I-VIII}), 79.1 (C-2^{I}), 78.4 (C-3^{I}), 73.8 (CH_2Ph), 73.7, 73.5, 73.2, 72.9 (×2), 72.8, 72.7, 72.6, 72.5 (×2), 72.3, 72.1, 72.0 (×3), 71.9 (×3), 71.8 (×3), 71.7 (22 C, C-2$^{II-VIII}$, C-3$^{II-VIII}$, C-5^{I-VIII}), 60.5 (×2), 60.3 (×3), 60.1 (×2), 59.9 (8 C, C-6^{I-VIII}); ESIMS: *m/z* 1421.3 ([M + Na]$^+$).



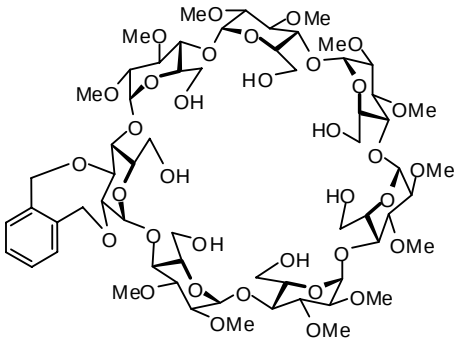
7, R = TBDMS

Heptakis(6-*O*-*tert*-butyldimethylsilyl)-2^{I},3^{I}-*O*-(*o*-xylylene)cyclomaltoheptaose (7). To a solution of **5** (300 mg, 0.24 mmol) in dry pyridine (3 mL), TBDMSCl (304 mg, 2.02 mmol) was added. The reaction mixture was stirred at room temperature for 24 h, then concentrated and the resulting residue was purified by column chromatography using 60:1→6:1 CH_2Cl_2-MeOH (0.5% Et_3N) as eluent, to yield **7** (458 mg, 93%) as an amorphous solid (Found: C, 53.98; H, 8.36; $C_{92}H_{174}O_{35}Si_7$ requires: C, 54.25; H, 8.61); R_f = 0.34 (9:1 CH_2Cl_2-MeOH); [α]$_D$ = +133.8 (*c* 0.73 in $CHCl_3$); ^{1}H NMR (500 MHz, CD_3OD): δ = 7.29-7.156 (m, 4 H, Ph), 5.28, 4.99 (2 d, 2 H, $^2J_{H,H}$ = 14.1 Hz, C*H*Ph), 5.12, 5.07 (2 d, 2 H, $^2J_{H,H}$ = 14.7 Hz, C*H*Ph), 5.12 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1^{I}), 5.01-4.94 (m, 6 H, H-1^{II-VII}), 4.11-3.91 (m, 8 H, H-6a^{I-VII}, H-3^{I}), 3.90-3.82 (m, 6 H, H-3^{II-VII}), 3.79-3.73 (m, 7 H, H-6b^{I-VII}), 3.69-3.64 (m, 8 H, H-5^{I-VII}, H-4^{I}), 3.59-3.52 (m, 7 H, H-4^{II-VII}, H-2^{I}), 3.44-3.36 (m, 6 H, H-2^{II-VII}), 0.89 (s, 63 H, *(CH$_3$)$_3$*C), 0.02 (s, 42 H, *(CH$_3$)$_2$*Si); ^{1}H TOCSY (H-1^{I} irradiation): δ = 4.11 (bd, 1 H, $J_{6a,6b}$ = 11.5 Hz, H-6a^{I}), 3.97 (m, 1 H, H-3^{I}), 3.76 (m, 1 H, H-6b^{I}), 3.69 (m, 2 H, H-4^{I}, H-5^{I}), 3.54 (dd, 1 H, $J_{2,3}$ = 8.8 Hz, H-2^{I}); ^{13}C NMR (125.7 MHz, CD_3OD): δ = 136.3-127.8 (Ph), 102.4, 102.3 (×2), 102.2, 101.9, 101.6 (6 C, C-1^{II-VII}), 100.7 (C-1^{I}), 81.7, 81.0, 80.9, 80.8 (×2), 80.7 (6 C, C-4^{II-VII}), 80.8 (C-2^{I}), 80.4 (C-3^{I}), 78.4 (C-4^{I}), 73.7, 73.6, 73.4, 73.3, 73.2 (×2) (6 C, C-3^{II-VII}), 73.2 (*C*H$_2$Ph), 73.1, 73.0 (×2), 72.9 (x3) (6 C, C-2^{II-VII}), 72.9 (*C*H$_2$Ph), 72.7 (x2), 72.5 (×3), 72.4 (6 C, C-5^{II-VII}), 72.1 (C-5^{I}), 62.2, 62.1, 61.9 (×4) (6 C, C6^{II-VII}), 61.8 (C-6^{I}), 25.2 (21 C, *(CH$_3$)$_3$*C), 17.9 (7 C, (CH$_3$)$_3$*C*); FABMS: *m/z* 2059 ([M + Na]$^+$).



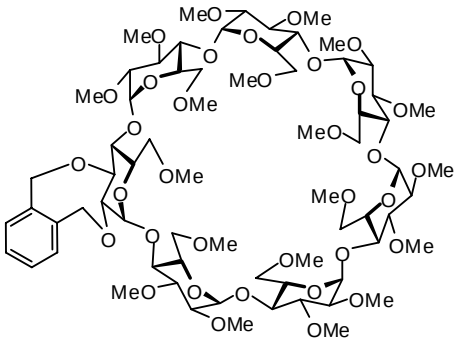
8, R = TBDMS

Heptakis(6-*O*-*tert*-butyldimethylsilyl)-2^{II-VII},3^{II-VII}-dodeca-*O*-methyl-2^{I},3^{I}-*O*-(*o*-xylylene)cyclomaltoheptaose (8). Compound **7** (114 mg, 0.06 mmol) was dissolved in dry DMF (4.5 mL). NaH (60% in mineral oil, 134 mg, 3.36 mmol) and MeI (209 mL, 3.36 mmol) were then added at 0 ºC under Ar and the reaction mixture was stirred at room temperature for 2 h, then quenched with water (10 mL) and extracted with Et_2O (4 × 10 mL). The combined organic layers were washed with water (3 × 5 mL), dried (Na_2SO_4), concentrated and purified by column chromatography (1:4→1:3 EtOAc-petroleum ether) to yield **8** (69 mg, 56%) as an amorphous solid (Found: C, 56.62; H, 8.78; $C_{104}H_{198}O_{35}Si_7$ requires: C, 56.64; H, 9.05); R_f = 0.34 (1:3 EtOAc-petroleum ether); $[\alpha]_D$ = +96.9 (*c* 1.0 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.22-7.05 (m, 4 H, Ph), 5.26, 4.73 (2 d, 2 H, $^2J_{H,H}$ = 12.7 Hz, C*H*Ph), 5.18, 5.12 (2 d, 2 H, $^2J_{H,H}$ = 11.6 Hz, C*H*Ph), 5.19-5.12 (m, 7 H, H-1^{I-VII}), 4.10-4.01 (m, 7 H, H-6a^{I-VII}), 3.79 (m, 1 H, H-3^{I}), 3.79-3.61 (m, 6 H, H-4^{II-VII}), 3.61-3.47 (m, 8 H, H-6b^{I-VII}, H-4^{I}), 3.59-3.35 (m, 14 H, H-5^{I-VII}, H-3^{II-VII}, H-2^{I}), 3.11-3.00 (m, 6 H, H-2^{II-VII}), 3.75, 3.70, 3.64, 3.62, 3.57, 3.56, 3.52, 3.50, 3.49, 3.47, 3.43, 3.25 (12s, 36 H, Me), 0.85 (s, 63 H, *(CH$_3$)$_3$*C), 0.01 (s, 42 H, *(CH$_3$)$_2$*Si); ^{1}H 1DTOCSY (H-3^{I} irradiation): δ = 5.15 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1^{I}), 4.10 (d, 1 H, $J_{6a,6b}$ = 12.2 Hz, H-6a^{I}), 3.61 (d, 1 H, H-6b^{I}), 3.56 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.5 Hz, H-4^{I}), 3.53 (m, 1 H, H-5^{I}), 3.41 (dd, 1 H, $J_{2,3}$ = 9.0 Hz, H-2^{I}); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 138.4-126.8 (Ph), 99.8 (C-1^{I}), 98.6, 98.2, 98.1 (×2), 98.0, 97.9 (6 C, C-1^{II-VII}), 82.3 (×6), 82.2, 82.0 (×3), 81.8 (×2) (12 C, C-2 $^{II-VII}$, C-3^{II-VII}), 82.0 (C-2^{I}), 80.2, 79.2, 78.8, 78.7, 78.6, 78.5, 78.2 (7 C, C-4^{I-VII}), 79.0 (C-3^{I}), 74.8 (CH_2Ph), 72.4 (CH_2Ph), 72.3 (C-5^{I}), 72.3, 72.2 (×3), 72.0, 71.9 (6 C, C-5^{II-VII}), 62.6 (×2), 62.3 (×2), 62.2 (×2), 61.7 (×2), 61.5 (×2), 61.4 (×2), 61.3, 58.8, 58.7, 58.6 (×3), 58.5 (19 C, C-6^{I-VII}, Me), 26.0 (21 C, *(CH$_3$)$_3$*C), 18.5 (7 C, (CH$_3$)$_3$*C*); MALDI-TOFMS: *m/z* 2226.2 ([M + Na]$^+$).



9

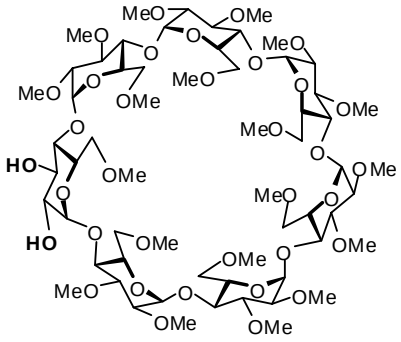
2^{II-VII},3^{II-VII}-Dodeca-*O*-methyl-2^{I},3^{I}-*O*-(*o*-xylenylene)cyclomaltoheptaose (9). A solution of **8** (170 mg, 0.08 mmol) in TFA-H_2O (1:1, 10 mL) was stirred at 45 ºC for 2 h. The acid was eliminated by coevaporation with water under reduced pressure and the resulting residue was dissolved in water and freeze dried to give **9** (108 mg, 96%) as a white foam (Found: C, 52.77; H, 7.15; $C_{62}H_{100}O_{35}$ requires: C, 52.98; H 7.17); R_f = 0.47 (10:1:1 CH_3CN-H_2O-NH_4OH); $[\alpha]_D$ = +108.7 (*c* 1.0 in H_2O); ^{1}H NMR (500 MHz, D_2O): δ = 7.35-7.14 (m, 4 H, Ph), 5.25 (d, 1 H, $J_{1,2}$ = 3.4 Hz, H-1^{I}), 5.35-5.19 (m, 6 H, H-1^{II-VII}), 5.09, 4.98 (2 d, 2 H, $^2J_{H,H}$ = 14.7 Hz, C*H*Ph), 4.85 (bs, 2 H, CH_2Ph), 3.92-3.76 (m, 7 H, H-$6a^{I-VII}$), 3.79-3.68 (m, 7 H, H-$6b^{I-VII}$), 3.79-3.62 (m, 7 H, H-5^{I-VII}), 3.78-3.38 (m, 7 H, H-3^{I-VII}), 3.67-3.52 (m, 7 H, H-4^{I-VII}), 3.39-3.21 (m, 7 H, H-2^{I-VII}), 3.60 (×2), 3.55, 3.52, 3.50, 3.49, 3.42, 3.41, 3.27 (×4) (7 s, 36 H, 12 Me); ^{1}H 1DTOCSY (H-1^{I} irradation): δ = 3.90 (m, 1 H, H-$6a^{I}$), 3.78 (m, 2 H, H-3^{I}, H-5^{I}), 3.74 (m, 1 H, H-$6b^{I}$), 3.62 (m, 1 H, H-4^{I}), 3.39 (dd, 1 H, H-2^{I}); ^{13}C NMR (125.7 MHz, D_2O): δ = 136.8-128.0 (Ph), 98.1 (x2), 97.9, 97.6, 96.7, 96.0 (6 C, C^{II-VII}), 97.8 (C-1^{I}), 81.9, 81.8, 81.4 (x2), 81.2, 80.9 (6 C, C-3^{II-VII}), 80.8, 80.5, 80.4, 80.3, 80.2 (×2) (6 C, C-2^{II-VII}), 80.2 (C-2^{I}), 79.9 (C-3^{I}), 78.6, 78.3 (×3), 76.8, 75.4, 75.0 (7 C, C-4^{I-VII}), 73.3, 73.0 (2 C, CH_2Ph), 70.2, 71.9 (×2), 71.8 (×2), 71.6, 70.5 (7 C, C-5^{I-VII}), 60.7 (×2), 60.6 (×4), 60.5, 60.4 (×2), 60.3 (×3), 60.2, 59.6, 58.4 (×2), 58.1 (×3) (19 C, C-6^{I-VII}, Me); FABMS: *m/z* 1428 ($[M + Na]^+$).



10

2^{II-VII},3^{II-VII},6^{I-VII}-Nonadeca-*O*-methyl-2^{I},3^{I}-*O*-(*o*-xylylene)cyclomaltoheptaose (10). To a solution of **5** (192 mg, 0.16 mmol) in dry DMF (12 mL), NaH (60% in mineral oil, 589 mg, 14.73 mmol) and MeI (917 μL, 14.73 mmol) were carefully added at 0 ºC under Ar. The reaction mixture was stirred for 12 h, then quenched with water (15 mL) and extracted with Et_2O (4 × 15 mL). The combined organic layer

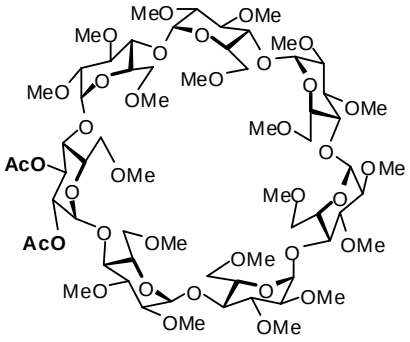
were washed with water (3 × 10 mL), dried (Na_2SO_4), concentrated and purified by column chromatography (20:1 CH_2Cl_2-MeOH) to yield **10** (243 mg, 99%) as an amorphous solid (Found: C, 54.93; H, 7.46; $C_{69}H_{114}O_{35}$ requires: C, 55.12; H 7.64); R_f = 0.23 (CH_2Cl_2: MeOH 20:1); $[\alpha]_D$ = +164.3 (*c* 1.0 $CHCl_3$); ^{1}H NMR (500 MHz, D_2O): δ = 7.25-7.13 (m, 4 H, Ph), 5.26-5.14 (m, 7 H, H-1$^{I\text{-}VII}$), 4.98, 4.91 (2 d, 2 H, $^2J_{H,H}$ = 14.6 Hz, C*H*Ph), 4.95, 4.92 (2 d, 2 H, $^2J_{H,H}$ = 14.5 Hz, C*H*Ph), 3.85 (m, 1 H, H-6a^{I}), 3.79-3.67 (m, 6 H, H-6a$^{II\text{-}VII}$), 3.68-3.52 (m, 7 H, H-4$^{I\text{-}VII}$), 3.66-3.43 (m, 7 H, H-6b$^{I\text{-}VII}$), 3.64-3.43 (m, 8 H, H-3$^{I\text{-}VII}$, H-2^{I}), 3.58-3.40 (m, 7 H, H-5$^{I\text{-}VII}$), 3.28-3.17 (m, 6 H, H-2$^{II\text{-}VII}$), 3.57, 3.53, 3.48, 3.47, 3.44, 3.43, 3.41, 3.38 (×2), 3.36, 3.27 (×3), 3.26 (×3), 3.25, 3.23, 3.17 (15 s, 57 H, Me); ^{1}H 1DTOCSY (H-6a^{I} irradiation): δ = 5.17 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1^{I}), 3.78 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, H-3^{I}), 3.67 (dd, 1 H, $J_{6a,6b}$ = 11.0 Hz, $J_{5,6b}$ = 4.0 Hz,H-6b^{I}), 3.60 (t, 1 H, $J_{4,5}$ = 10.5, H-4^{I}), 3.57 (m, 1 H, H-5^{I}), 3.44 (dd, 1 H, H-2^{I}); ^{13}C NMR (125.7 MHz, D_2O): δ = 136.7-128.1 (Ph), 98.1 (C-1^{I}), 97.7, 97.6, 97.5, 97.3, 96.7, 96.2 (6 C, C-1$^{II\text{-}VII}$), 81.6, 81.5, 81.2 (×2), 81.0 (×2) (6 C, C-3$^{II\text{-}VII}$), 80.5, 80.3, 80.2 (x4) (6 C, C-2$^{II\text{-}VII}$), 79.9 (C-3^{I}), 79.2 (C-2^{I}), 77.9 (x2), 77.8, 77.7, 76.9, 76.0, 75.6 (7 C, C-4$^{I\text{-}VII}$), 73.3 (CH_2Ph), 72.4 (CH_2Ph), 70.6 (×5), 70.5 (×2) (7 C, C-5$^{I\text{-}VII}$), 70.9, 70.8, 70.6, 70.5 (×2), 70.4 (6 C, C-6$^{II\text{-}VII}$), 69.5 (C-6^{I}), 60.2, 60.6 (×2), 60.0 (×2), 59.7, 58.5, 58.4 (×8), 58.3, 58.2, 58.0 (×2) (19 C, Me); FABMS: *m/z* 1526 ([M + Na]$^+$).



11

2$^{II\text{-}VII}$,3$^{II\text{-}VII}$,6$^{I\text{-}VII}$-Nonadeca-*O*-methylcyclomaltoheptaose (11). To a solution of **10** (243 mg, 0.16 mmol) in 1:1 EtOAc-MeOH (10 mL) and aq HCOOH (10%, 1.6 mL), 10% Pd/C (80 mg) was added. The resulting suspension was hydrogenated at 1 atm for 16 h, then filtered through Celite, concentrated and the resulting residue purified by column chromatography (10:1 CH_3CN-H_2O→10:1:0.5 CH_3CN-H_2O-NH_4OH) to yield **11** (137 mg, 60%) as an amorphous solid (Found: C, 52.32; H, 7.78; $C_{61}H_{108}O_{35}$ requires: C 52.28, H 7.77); R_f = 0.42 (10:1:0.5 CH_3CN-H_2O-NH_4OH); $[\alpha]_D$ = +158.7 (*c* 1.0 in $CHCl_3$); ^{1}H NMR (500 MHz, D_2O): δ = 5.18-5.14 (m, 6 H, H-1$^{II\text{-}VII}$), 4.94 (d, 1 H, $J_{1,2}$ = 3.6, H-1^{I}), 3.80-3.64 (m, 8 H, H-6a$^{I\text{-}VII}$, H-3^{I}), 3.66-3.63 (m, 6 H, H-4$^{II\text{-}VII}$), 3.66-3.43 (m, 10 H, H-6b$^{I\text{-}VII}$, H-4^{I}, H-5^{I}, H-2^{I}), 3.62-3.53 (m, 6 H, H-3$^{II\text{-}VII}$), 3.29-3.21 (m, 6 H, H-2$^{II\text{-}VII}$), 3.52, 3.49 (x5), 3.43, 3.40 (x4), 3.27 (x4), 3.26 (x4) (7 s, 57 H, Me); ^{1}H 1DTOCSY (H-1^{I} irradiation): δ = 3.79 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, H-3^{I}), 3.64 (dd, 1 H, $J_{6a,6b}$ = 11.5 Hz, H-6a^{I}), 3.57 (m, 1 H, H-6b^{I}), 3.50 (m, 2 H, $J_{4,5}$ = 9.5 Hz, H-4^{I}, H-5^{I}), 3.45 (dd, 1 H, H-

2^{I}); ^{13}C NMR (125.7 MHz, D_2O): δ = 100.3 (C-1^{I}), 98.2, 97.6, 97.4, 97.1, 96.9, 96.8 (6 C, C-1^{II-VII}), 81.5, 81.2, 81.1, 80.9 (×2), 80.7, 80.4, 80.2 (×3), 80.0 (×2) (12 C, C-2^{II-VII}, C-3^{II-VII}), 77.8, 77.3 (×3), 77.0 (×2), 76.6 (7 C, C-4^{I-VII}), 73.0 (C-3^{I}), 71.8 (C-2^{I}), 70.8 (×4), 70.7, 70.6, 70.5, 70.4 (×3), 70.3 (×2), 70.2 (14 C, C-5^{I-VII}, C-6^{I-VII}), 60.3, 59.8 (×2), 59.7, 59.5, 59.4, 58.9, 58.4 (×6), 58.2 (×3), 58.1 (×2), 58.0 (19 C, Me); ESIMS: *m/z* 1423 ($[M + Na]^+$).

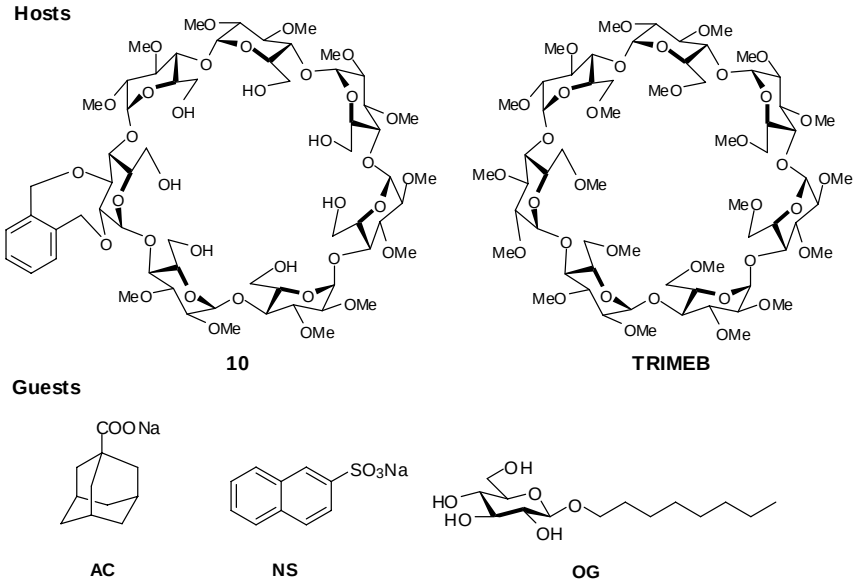


12

2^{I},3^{I}-Di-*O*-acetyl-2^{II-VII},3^{II-VII},6^{I-VII}-nonadeca-*O*-methylcyclomaltoheptaose (12). Compound **11** (80 mg, 0.06 mmol) was dissolved in Ac_2O-pyridine (1:1, 1 mL) and stirred at 45 ºC for 4 days. H_2O (10 mL) was then added and the mixture was extracted with CH_2Cl_2 (4 × 5 mL). The combined organic layer was washed with H_2SO_4 (2 M, 3 × 5 mL), saturated aqueous $NaHCO_3$ (2 × 5 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified by column chromatography (20:1 CH_2Cl_2-MeOH) to yield **12** (53 mg, 60%) as an amorphous solid (Found: C, 52.46; H, 7.71; $C_{65}H_{112}O_{37}$ requires: C, 52.55; H, 7.60) R_f = 0.18 (20:1 CH_2Cl_2-MeOH); $[\alpha]_D$ = +145.2 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ = 5.51 (dd, 1 H, $J_{2,3}$ = 10.6 Hz, $J_{3,4}$ = 9.4 Hz, H-3^{I}), 5.21 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1^{I}), 5.15-4.93 (m, 6 H, H-1^{II-VII}), 4.76 (dd, 1 H, H-2^{I}), 3.98 (dd, 1 H, $J_{5,6b}$ = 10.9 Hz, $J_{5,6a}$ = 3.5 Hz, H-$6a^{I}$), 3.87-3.71 (m, 14 H, H-4^{I-VII}, H-$6a^{II-VII}$, H-5^{I}), 3.60-3.44 (m, 13 H, H-5^{II-VII}, H-$6b^{I-VII}$), 3.53-3.48 (m, 6 H, H-3^{II-VII}), 3.63, 3.62, 3.60, 3.58, 3.55, 3.53, 3.48, 3.46 (x4), 3.42, 3.37, 3.35 (x6) (12 s, 57 H, Me), 3.17-3.05 (m, 6 H, H-2^{II-VII}), 2.06 (2 s, 6 H, OAc); ^1H 1DTOCSY (H-1^{I} irradiation): δ = 5.51 (dd, 1 H, H-3^{I}), 4.76 (dd, 1 H, H-2^{I}), 3.98 (dd, 1 H, H-$6a^{I}$), 3.86 (m, 1 H, H-5^{I}), 3.75 (t, 1 H, $J_{4,5}$ = 9.5 Hz, H-4^{I}), 3.55 (d, 1 H, H-$6b^{I}$); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 170.7, 170.2 (CO), 99.5, 99.3, 98.9 (x4) (6 C, C-1^{II-VII}), 98.2 (C-1^{I}), 82.7, 82.4, 82.1, 82.0, 81.9, 81.8 (6 C, C-2^{II-VII}), 81.7 (×3), 81.5 (×2), 81.2 (6 C, C-3^{II-VII}), 80.7, 80.6, 80.4 (x2), 79.6 (×2) (6 C, C-4^{II-VII}), 78.6 (C-4^{I}), 71.8, 71.6, 71.5 (×2), 71.4, 71.3, 71.2, 71.0, 70.9 (×2), 70.8 (12 C, C-5^{II-VII}, C-6^{II-VII}), 71.4 (C-2^{I}), 70.6 (C-6^{I}), 69.7 (C-3^{I}), 61.6 (C-5^{I}), 61.5 (×2), 61.4, 61.2, 60.3, 59.1, 59.0, 58.9 (×6), 58.7 (×2), 58.6 (×2), 58.3 (×2) (19 C, Me), 21.0, 20.8 (2 C, OAc); ESIMS: *m/z* 1507.7 ($[M + Na]^+$); 1523.7 ($[M + K]^+$).

NMR Aggregation Studies for 10: Comparative ^1H NMR experiments for **10** in D_2O at different concentrations (range 1 to 14 mM) and temperatures (range 25 to 80 ºC) confirmed the formation of aggregates. The aggregation process was fully reversible and was disrupted in $CDCl_3$ solution, supporting

the hydrophobic nature of the interactions at work during aggregation. The high temperature spectra resemble the spectra at low concentration and, conversely, the spectra al low temperatures resembled those at high concentration, in agreement with a thermodynamically favoured association. From the chemical shift variations of spectra recorded at 25 ºC for different concentrations, an association number $n = 2$ was derived.



Comparative NMR Inclusion Studies for 10 and TRIMEB: The association constants at 298 K in D_2O were experimentally determined by measuring the proton chemical shift changes of 3 mM solutions of the capped cyclodextrin receptor **10** or heptakis(2,3,6-tri-O-methyl)cyclomaltoheptaose (TRIMEB) upon increased amounts of the guest (OG). Smooth variations of the chemical shifts as a function of the host:guest ratio were observed. The absence of new peaks arising from the complex indicated that the inclusion process is in a fast exchange regime in the NMR time scale. In a typical titration experiment, a 3 mM solution of host in D_2O was prepared, a 500-μL aliquot was transferred to a 5-mm NMR tube, and the initial NMR spectrum was recorded. A solution (25-50 mM) of guest in the previous host solution was prepared and then added via microsyringe initially in 10 μL portions. These amounts were increased until complete complexation of the host. The ^{1}H NMR spectrum of each solution was recorded and the chemical shift of the diagnostic sugar protons obtained at 12-15 different host-guest concentration ratios were used in an iterative least-squares fitting procedure (see, e.g., Figure 1S).

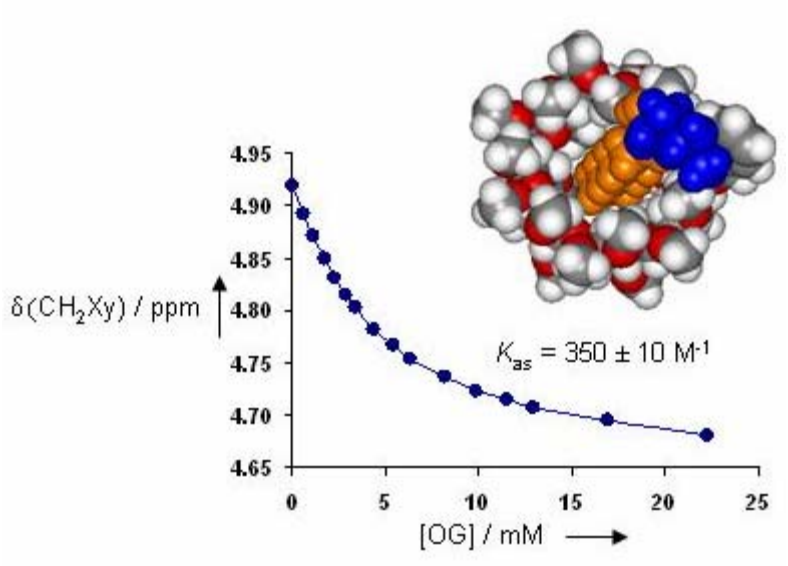


Figure 1S. Binding isotherm for the **10**:OG complex. A three-dimensional model showing the spatial proximity between the sugar moiety in OG (in blue) and the xylylene moiety in **10**, assuming inclusion of the hydrocarbon chain (in orange) in the cavity, is depicted. This proximity is probably translated into stabilising interactions that, are their turn, would explain the three-fold increase in K_{as} when compared with the analogous TRIMEB:OG complex ($K_{as} = 112 \pm 5\ M^{-1}$).

Fluorescence Aggregation Studies for 10: Fluorescence decay measurements were performed on a TCSPC FL900 Edinburgh Instruments Spectrometer by using a thyratron-gated lamp filled with hydrogen and equipped with two concave grating monochromators at both the excitation and emission paths and a red sensitive photomultiplier immersed in a Peltier cooled housing. The data acquisition was carried out by using 1024 channels and a time window width of 200 ns with a total of 10.000 counts at the maximum peak of intensity. The instrumental response function was regularly obtained by measuring the scattering of a Ludox solution. Temperature was controlled (Techne TE-8A). Right angle geometry, magic angle and cylindrical 2 mm diameter cells were used. Al measurements were performed in the range of temperatures from 5 to 45 ºC at 10 ºC intervals.

Decay intensity profiles were fitted to a sum of exponential decay functions as

$$I(t) = \sum_{i=1}^{n} A_i e^{-t/\tau_i} \qquad (1)$$

by the iterative reconvolution method. The average lifetime of a multiple-exponential decay function was then defined as

$$\langle \tau \rangle = \frac{\sum_{i=1}^{n} A_i \tau_i^2}{\sum_{i=1}^{n} A_i \tau_i} \qquad (2)$$

where A_i is the pre-exponential factor of the component with a lifetime τ_i of the multi-exponential function intensity decay.

The fractional contribution f_i of each decay time to the steady-state intensity which represents the fraction of total fluorescence intensity, I of *i*-component at the wavelength of observation is given by

$$f_i = \frac{A_i \tau_i}{\sum_{i=1} A_i \tau_i} = \frac{I_i}{\sum_{i=1} I_i} \qquad (3)$$

The intensity weighted average lifetime <τ> from a dilute solution of a pair of emitting species, 1 and 2, that do not interact during excited state lifetime can be obtained as

$$\langle \tau \rangle = f_1 \tau_1 + f_2 \tau_2 \qquad (4)$$

For the dimer formation equilibrium

$$2\,CD \rightleftharpoons CD_2 \qquad (5)$$

described by the following association constant

$$K = \frac{[CD_2]}{[CD]^2} \qquad (6)$$

the $[CD_2]$ and $[CD]$ at the equilibrium can be obtained as

$$[CD_2] = \frac{(4K[CD]_0 + 1) - \sqrt{8K[CD]_0 + 1}}{8K} \qquad (7)$$

and

$$[CD] = \frac{\sqrt{8K[CD]_0 + 1} - 1}{4K} \qquad (8)$$

The total fluorescence intensity, measured as area under the emission spectra, can be written as sum of contribution due to the CD and CD_2 dimer as

$$I = I_{CD} + I_{CD_2} = k\phi_{CD}[CD] + k\phi_{CD_2} K[CD]^2 \qquad (9)$$

where k is a constant which depends on instrumental conditions: detector and monochromator response, geometry of the detection…, and ϕ_{CD} and ϕ_{CD_2} are the proportionality constants between fluorescence and concentration of free CD and CD_2, which are related to their fluorescence quantum yields and molar absorptivities at the excitation wavelength.

By substitution of (8) into (9) and (3), from eq (4) the intensity weighted average lifetime <τ> from the CD and CD_2 emission can be related to the initial $[CD]_0$ by

$$\langle \tau \rangle = \frac{\tau_{CD} + \Phi \tau_{CD_2} \left(\sqrt{8K[CD]_0 + 1} - 1 \right)}{1 + \Phi \left(\sqrt{8K[CD]_0 + 1} - 1 \right)} \qquad (10)$$

where Φ is proportional to the ϕ_{CD}/ϕ_{CD_2} ratio.

Figure 2S (a) depicts the variation of <τ> with [**10**] and temperature. Curves are fitted to equation (10) by assuming Φ = 2, which reasonably reproduces de fluorescence intensity changes for [**10**]. The following parameters were obtained:

Temperature (ºC)	τ_{mono} (ns)	τ_{dimer} (ns)	K (M^{-1})
5	4.8 ± 0.3	16.2 ± 0.9	260 ± 80
15	4.6 ± 0.3	14.2 ± 0.8	239 ± 75
25	4.4 ± 0.2	12.3 ± 0.9	200 ± 85
35	4.3 ± 0.2	10.9 ± 1.4	122 ± 75
45	4.0 ± 0.3	9.0 ± 2.4	77 ± 70

ΔH^0 (-22.7 ± 4.4 kJ/mol) and ΔS^0 (-34 ± 15 J/Kmol) values were obtained from the linear van't Hoff plot depicted in Figure 2S (b) by using the K values collected in Table 1. This is consistent with an enthalpy-driven dimerization process, enthropically disfavored. Figure 3S depicts three-dimetional models for the monomer in the "capped" conformation and the corresponding dimer in the head-head (HH) arrangement.

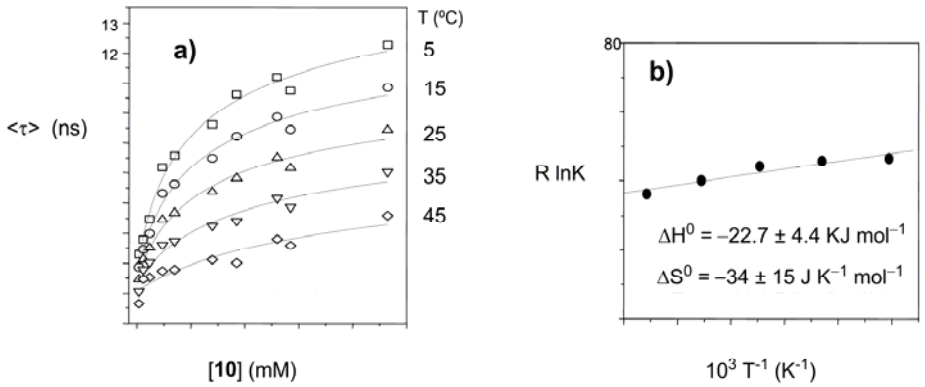


Figure 2S. Average lifetimes as a function of total concentration of **10** to determine K at different temperatures (a) and linear van't Hoff plot for the monomer-to-dimer equilibrium (**b**).

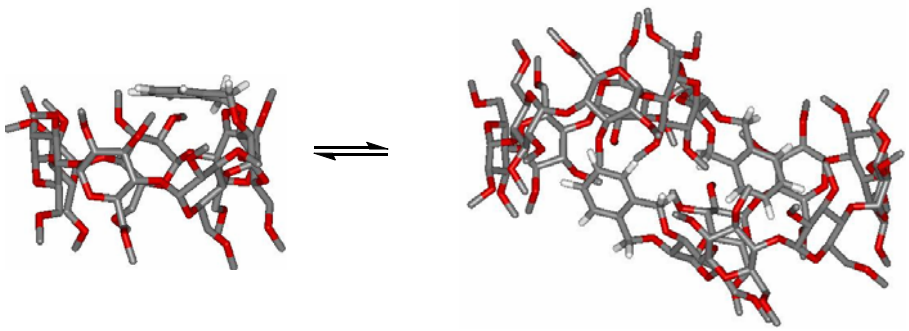


Figure 3S. Three dimesional models for the monomeric and dimeric species present in a water solution of **10**. The monomer is depicted in the most stable "capped" conformation and the dimer in the HH arrangement, in agreement with NMR data. Only the protons at the xylylene moiety are represented for clarity.

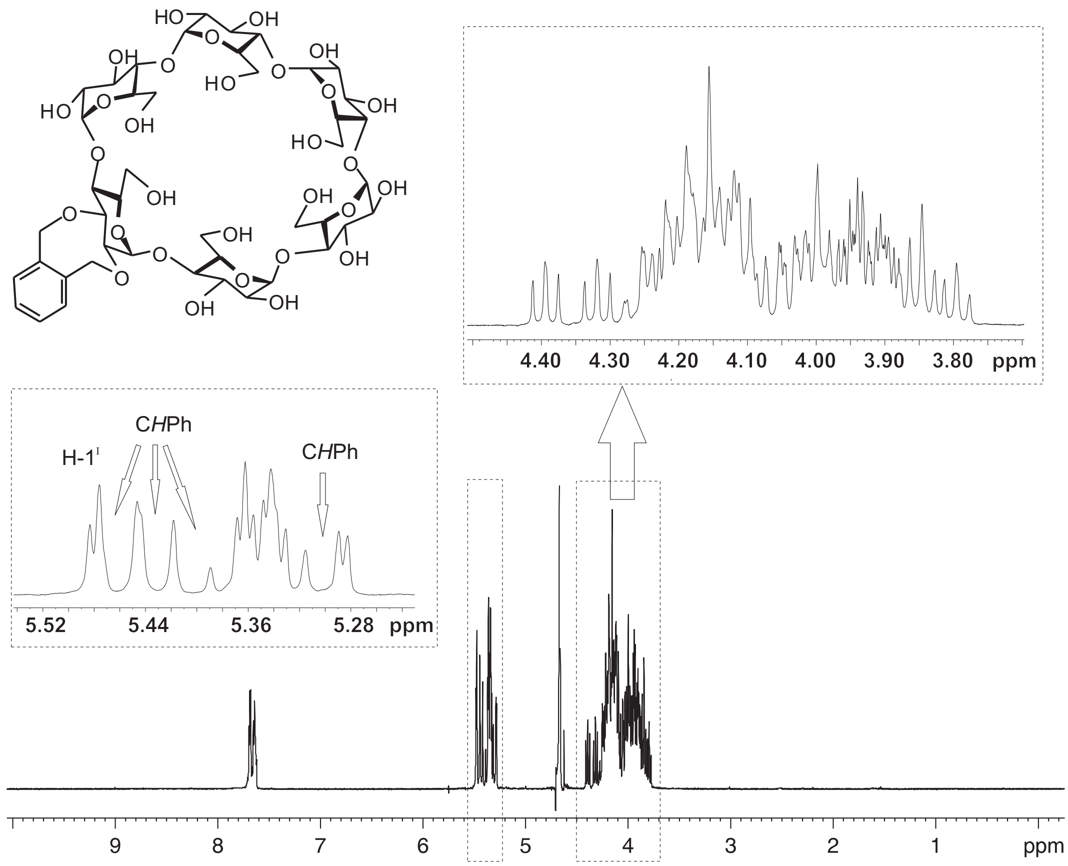
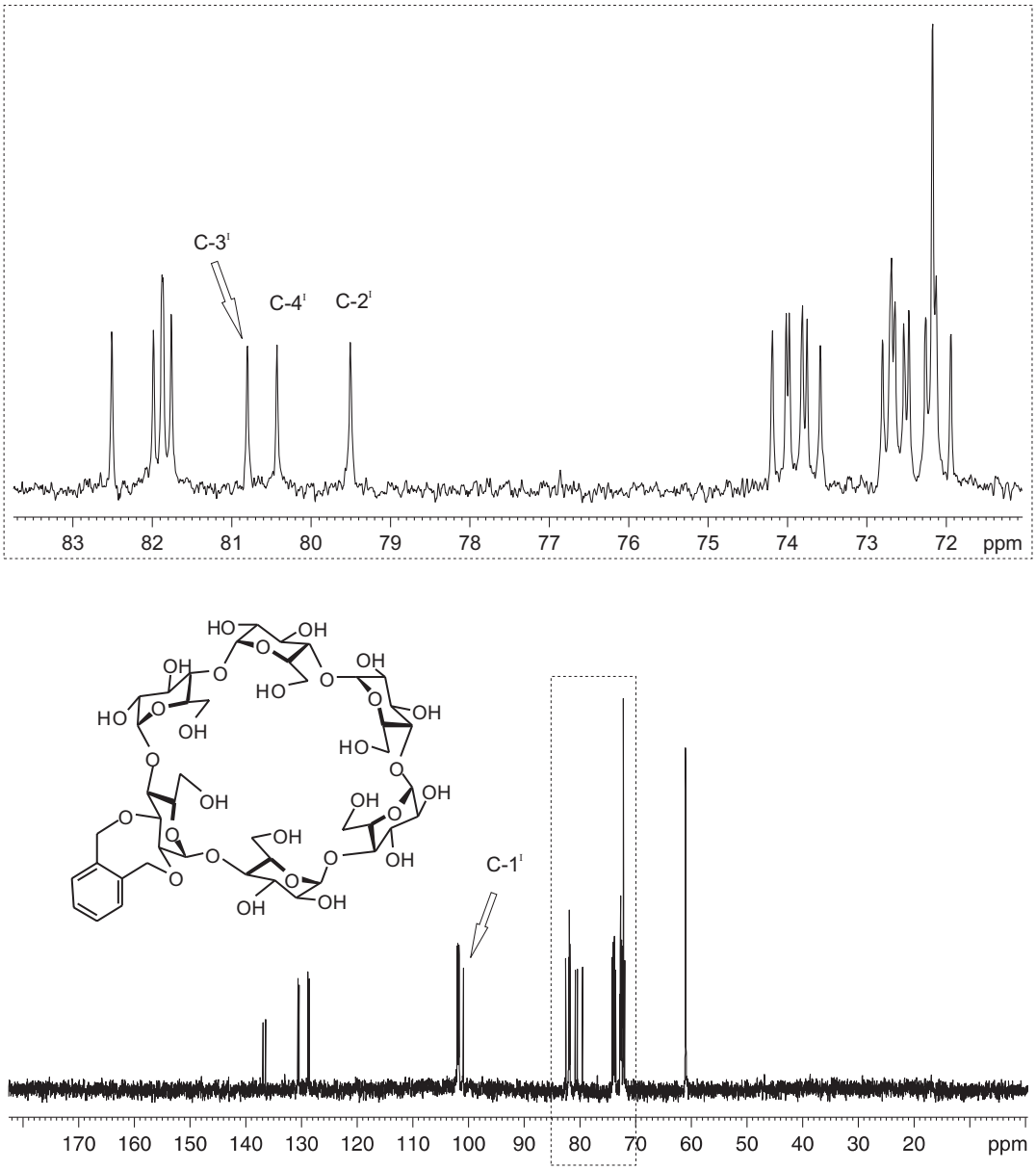


Figure 3S. ^{1}H NMR spectrum (500 MHz, D_2O, 333 K) of compound **4**.



Figur3 4S. ^{13}C NMR spectrum (125.7 MHz, D_2O, 333 K) of compound **4**.

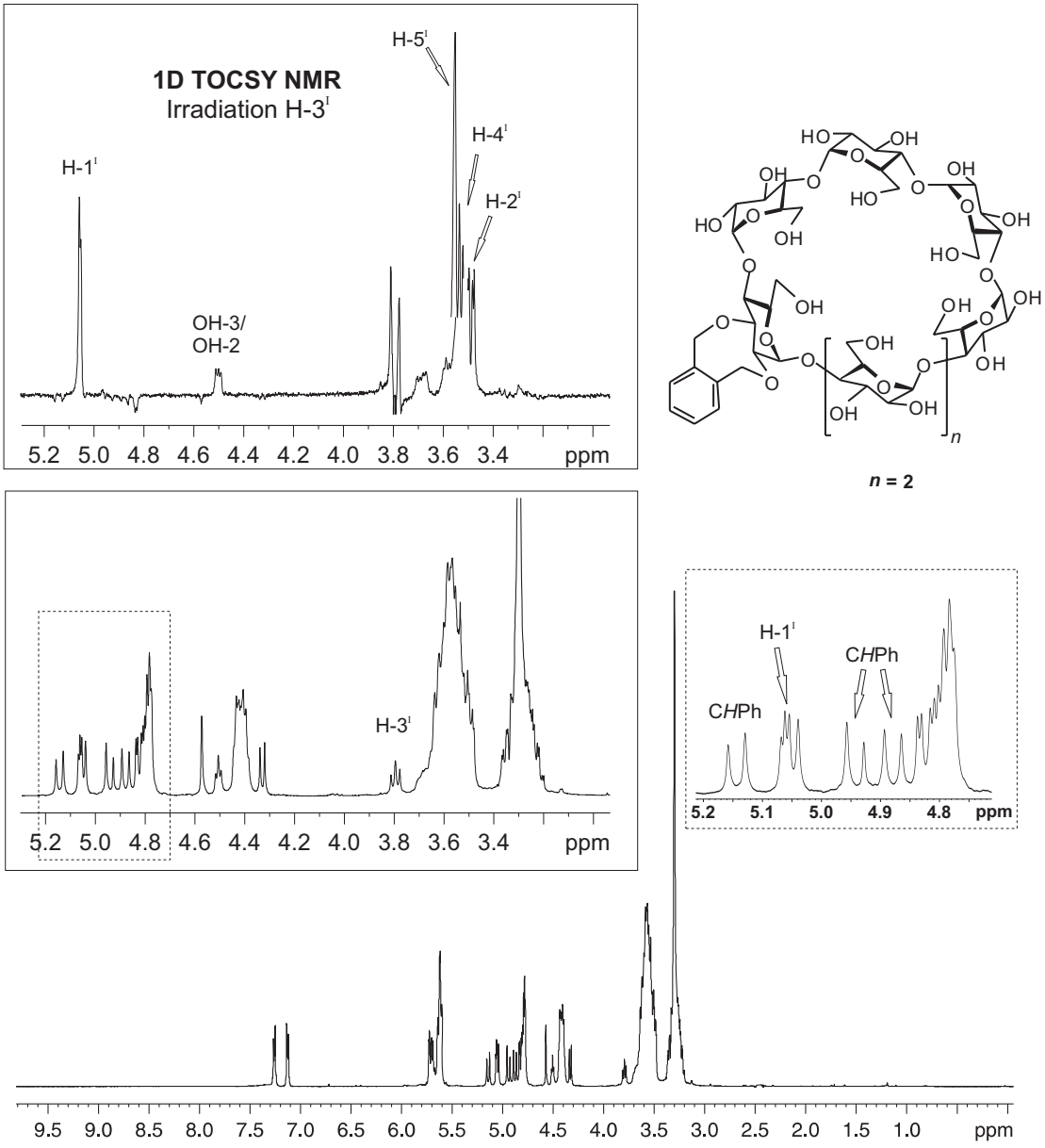
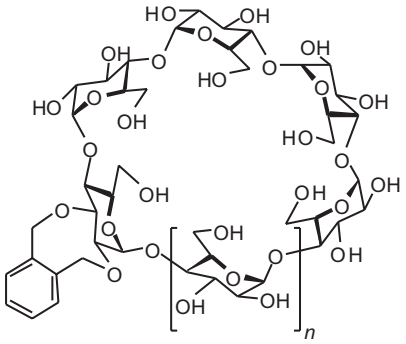


Figure 5S. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of compound **5**.



***n* = 2**

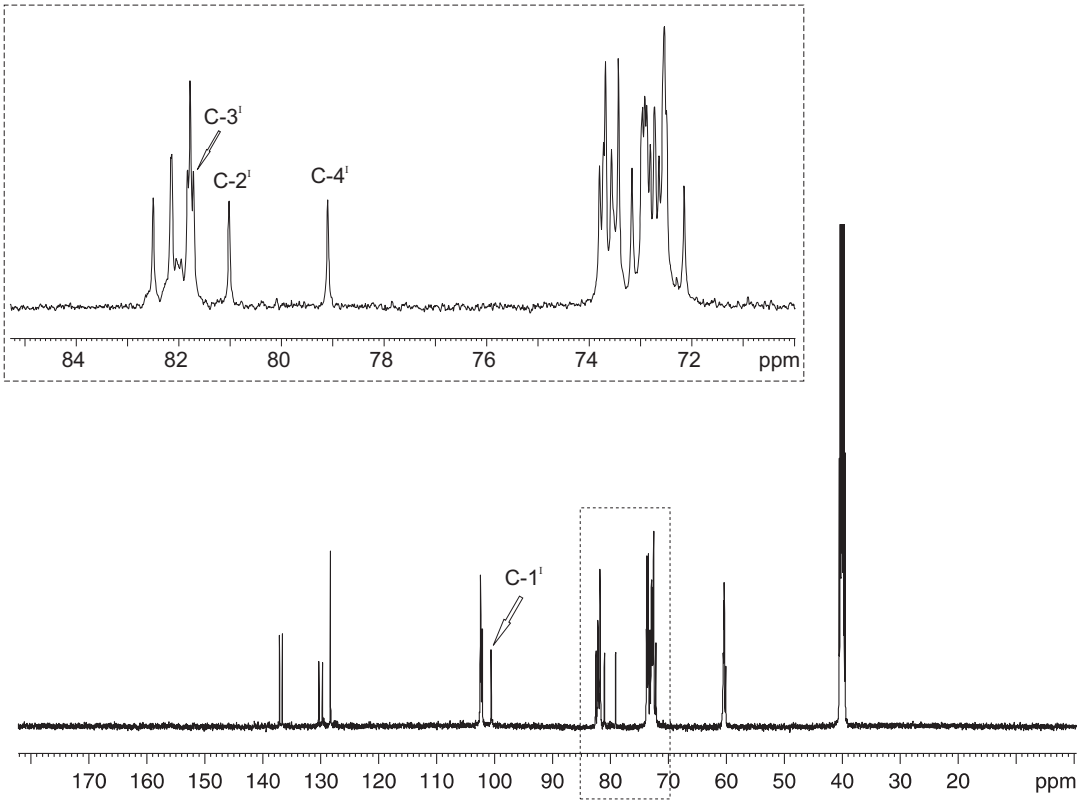


Figura 6S. ^{13}C NMR spectrum (125.7 MHz, DMSO-d_6) of compound **5**.

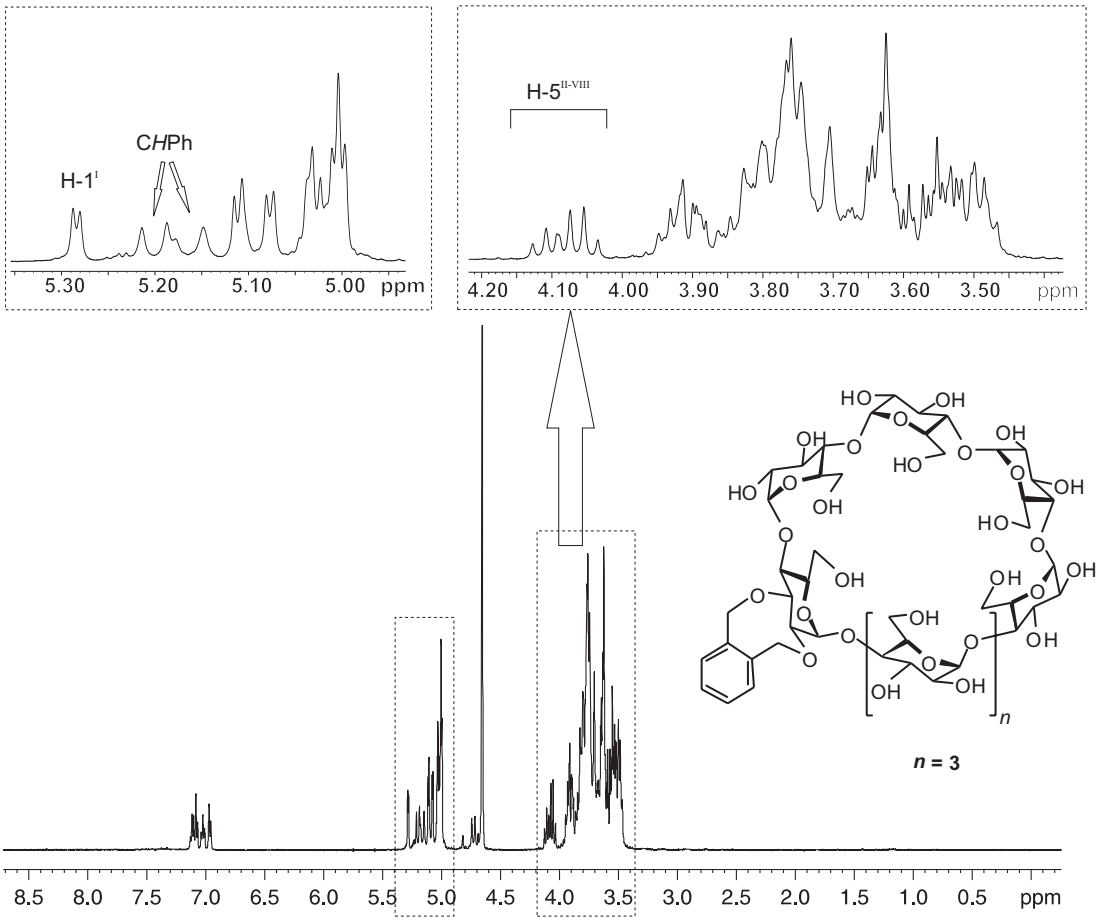


Figure 7S. ^{1}H NMR spectrum (500 MHz, D_2O) of compound **6**.

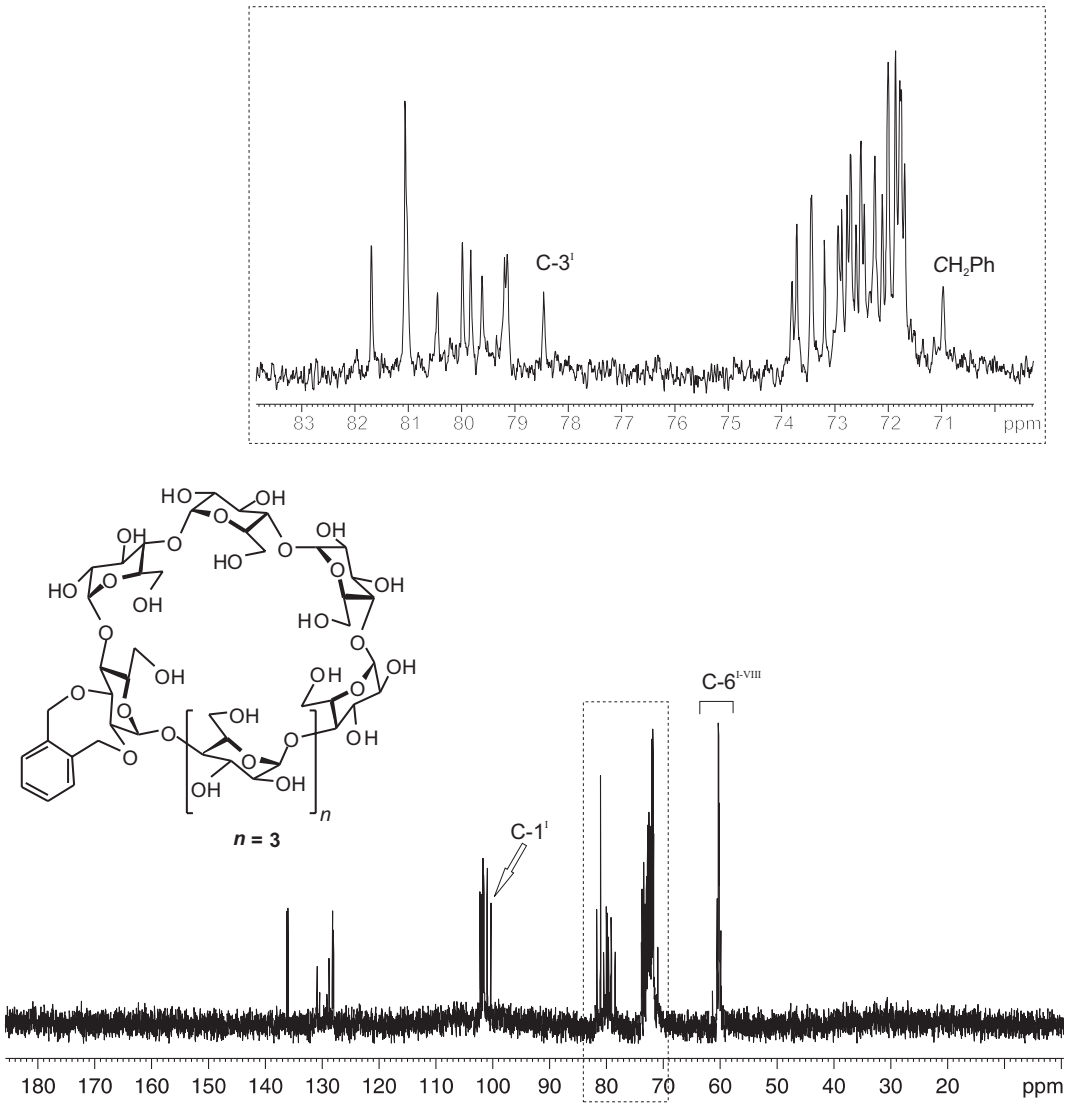
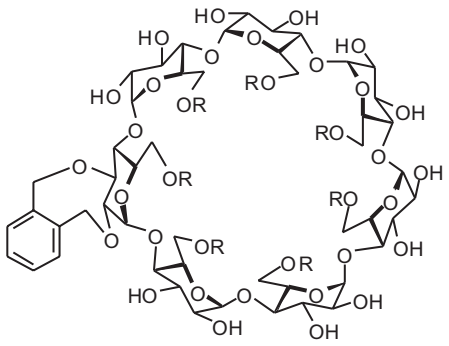


Figure 8S. ^{13}C NMR spectrum (125.7 MHz, D_2O) of compound **6**.



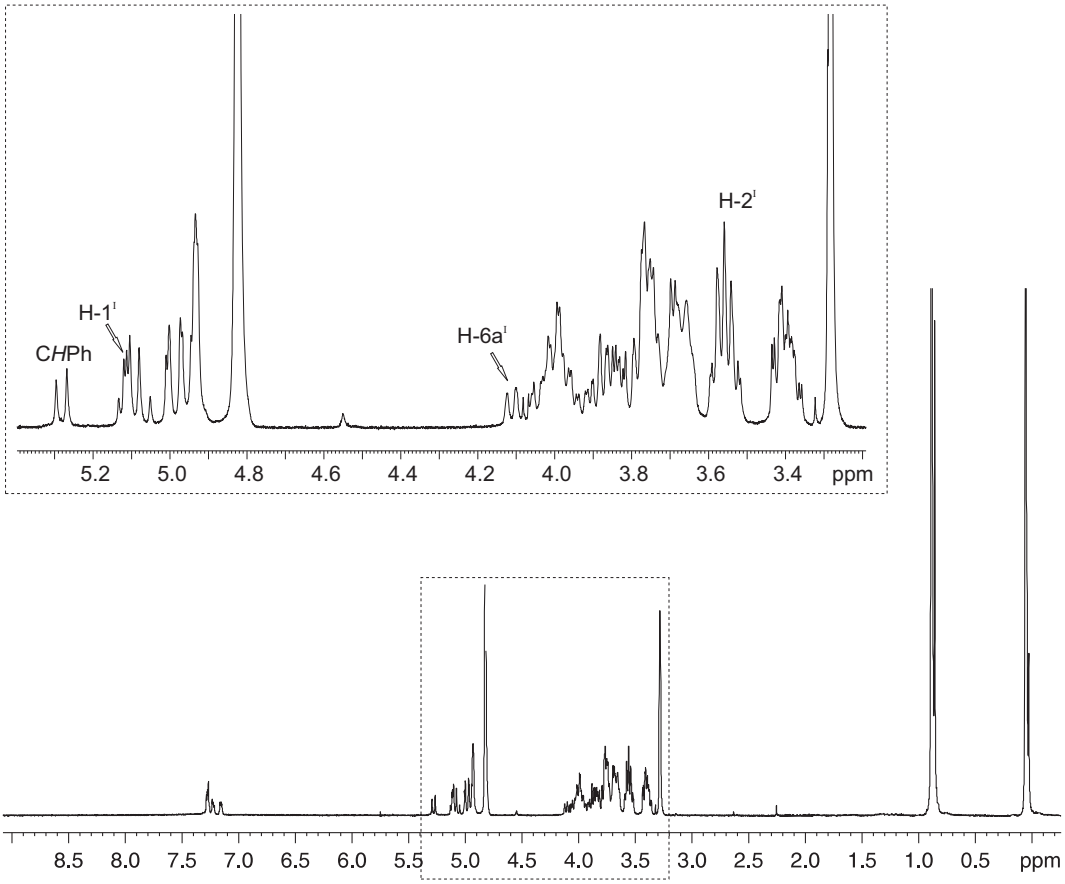
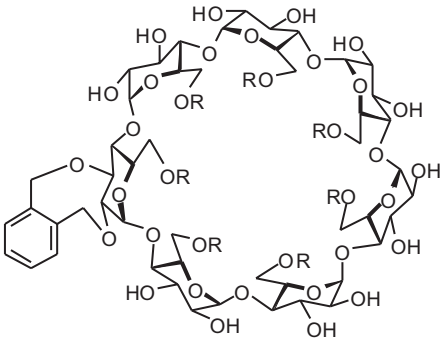


Figura 9S. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound **7**.



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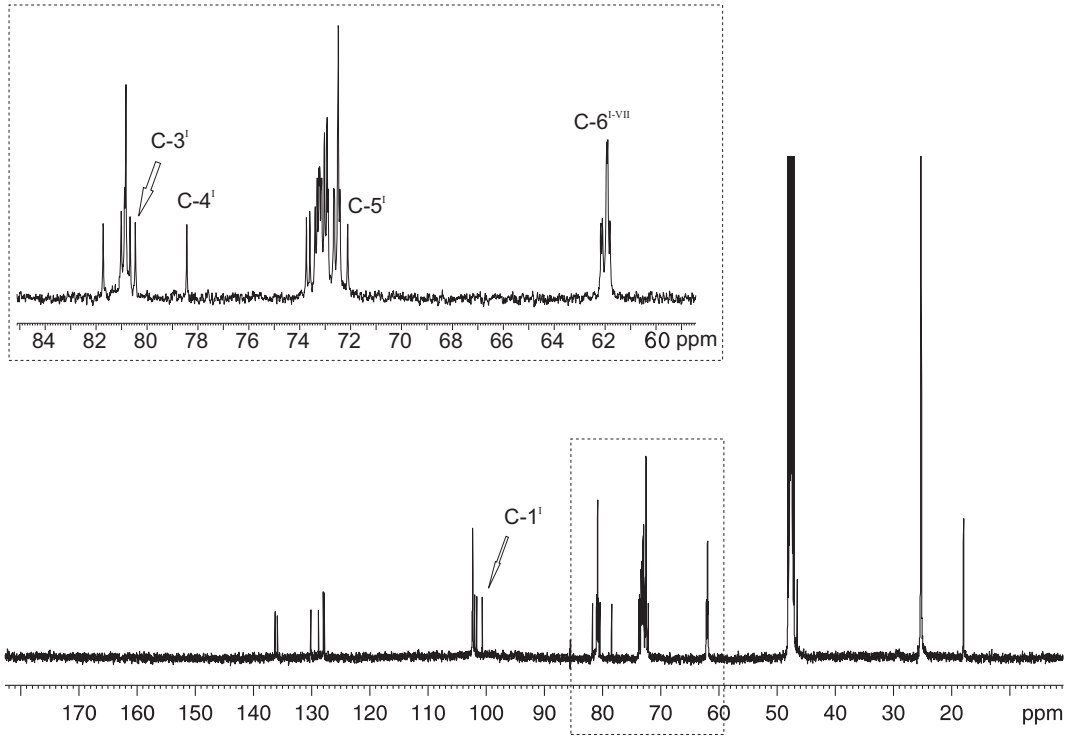
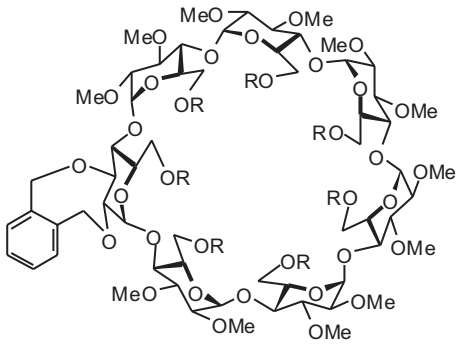


Figura 10S. ^{1}H NMR spectrum (125.7 MHz, CD_3OD) of compound **7**.



R = TBDMS

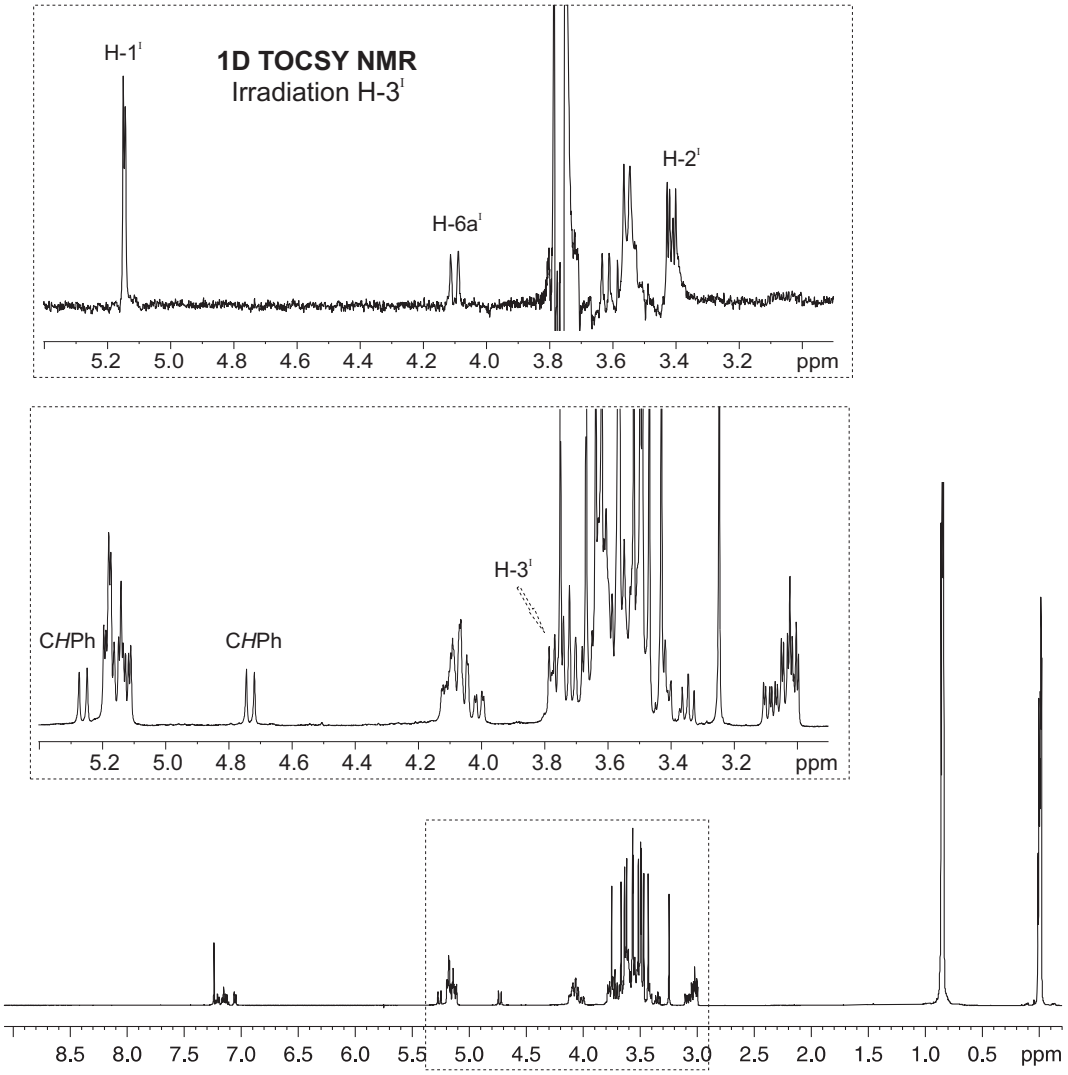
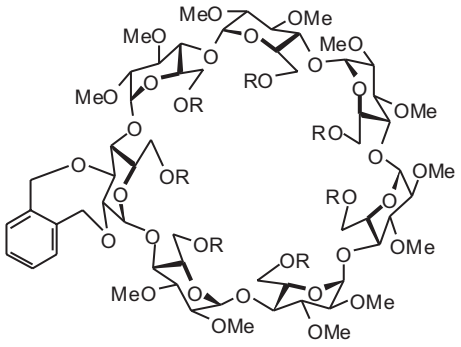


Figura 11S. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **8**.



R = TBDMS

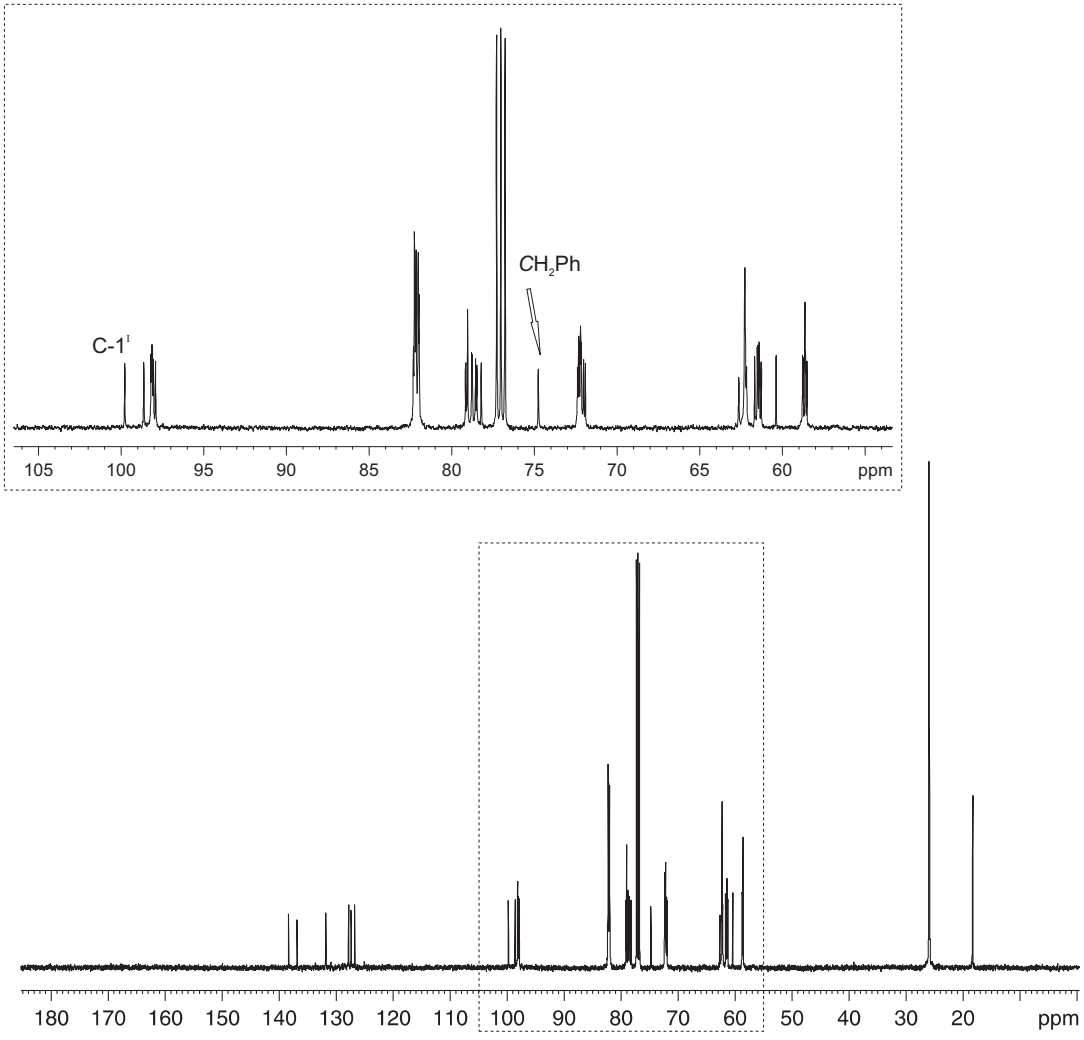


Figura 12S. ^{13}C NMR spectrum (125.7 MHz, $CDCl_3$) of compound **8**.

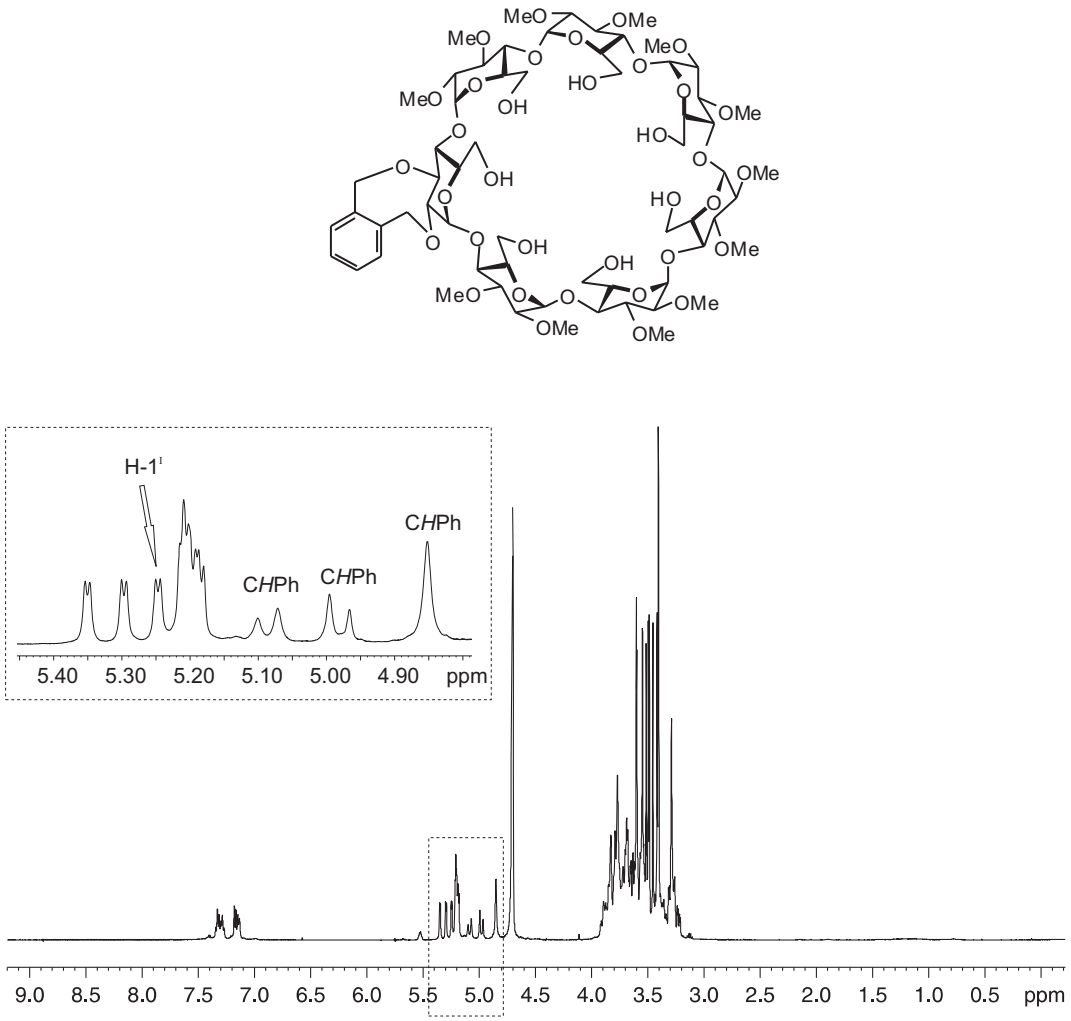
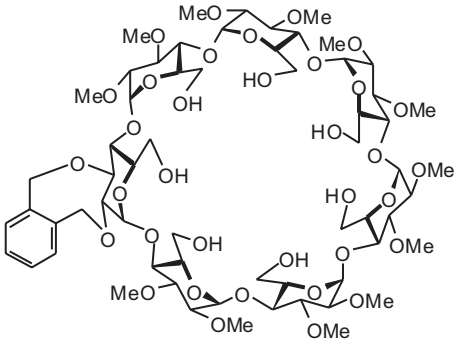


Figure 13S. ^{1}H NMR spectra (500 MHz, D_2O) of compound **9**.



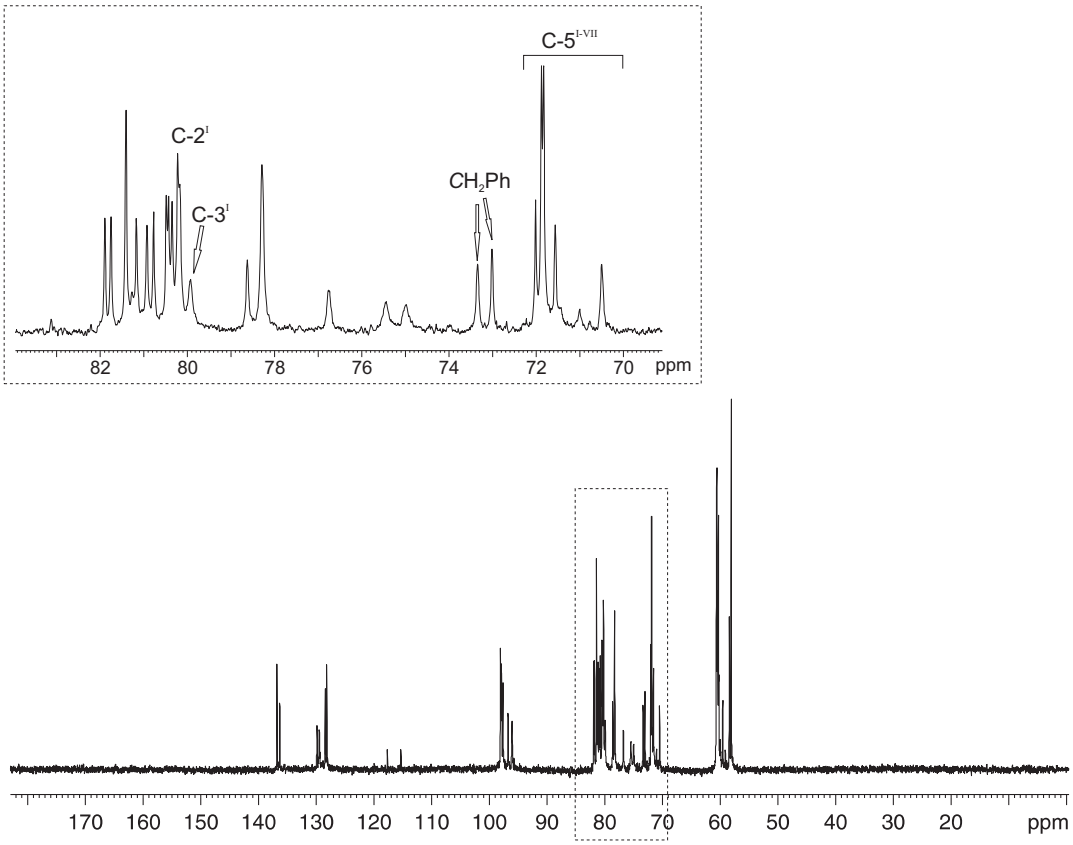


Figure 14S. ^{13}C NMR spectra (125.7 MHz, D_2O) of compound **10**.

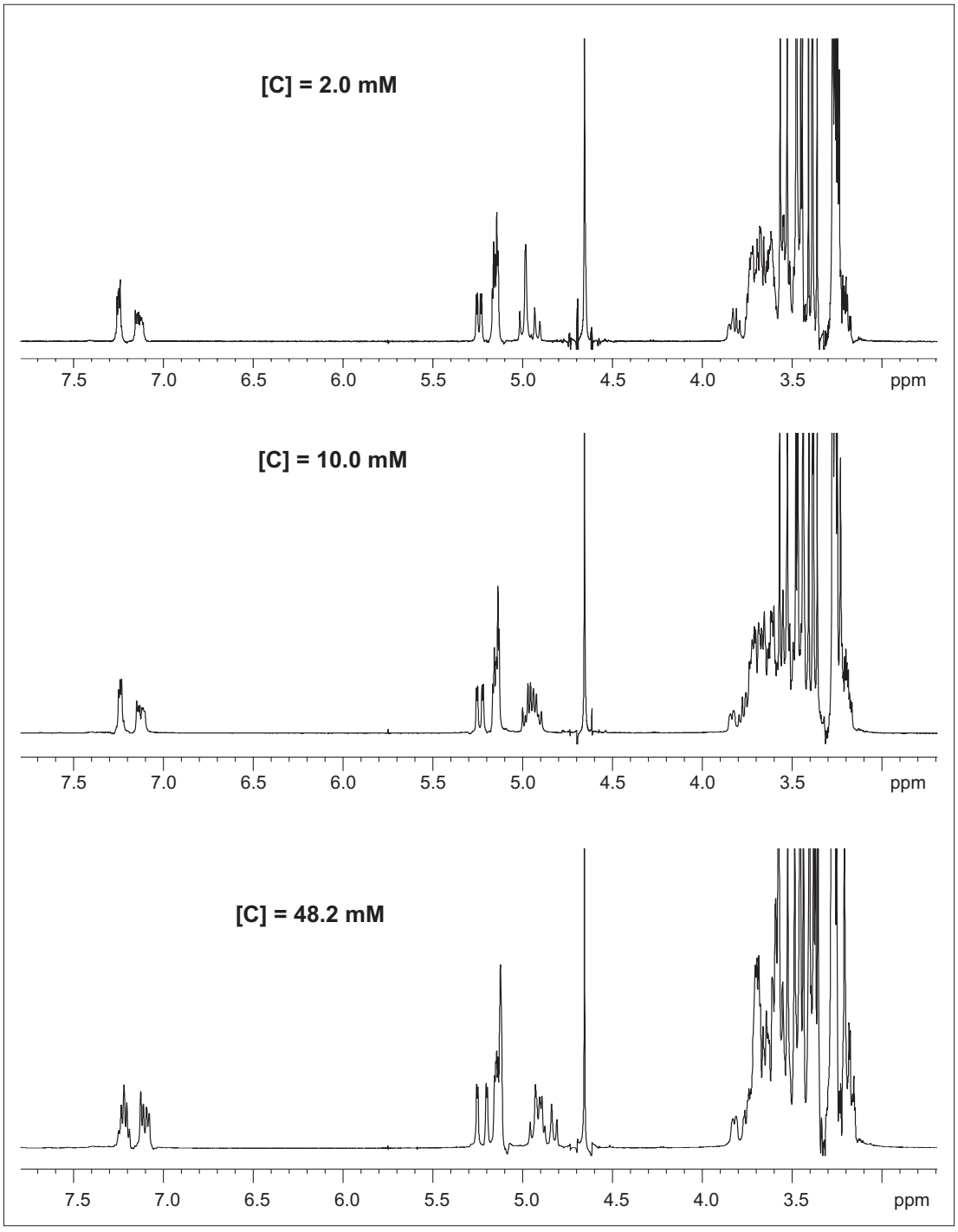


Figure 15S. ^{1}H NMR spectra (500 MHz, D_2O, 298 K) of compound **10** at different concentrations.

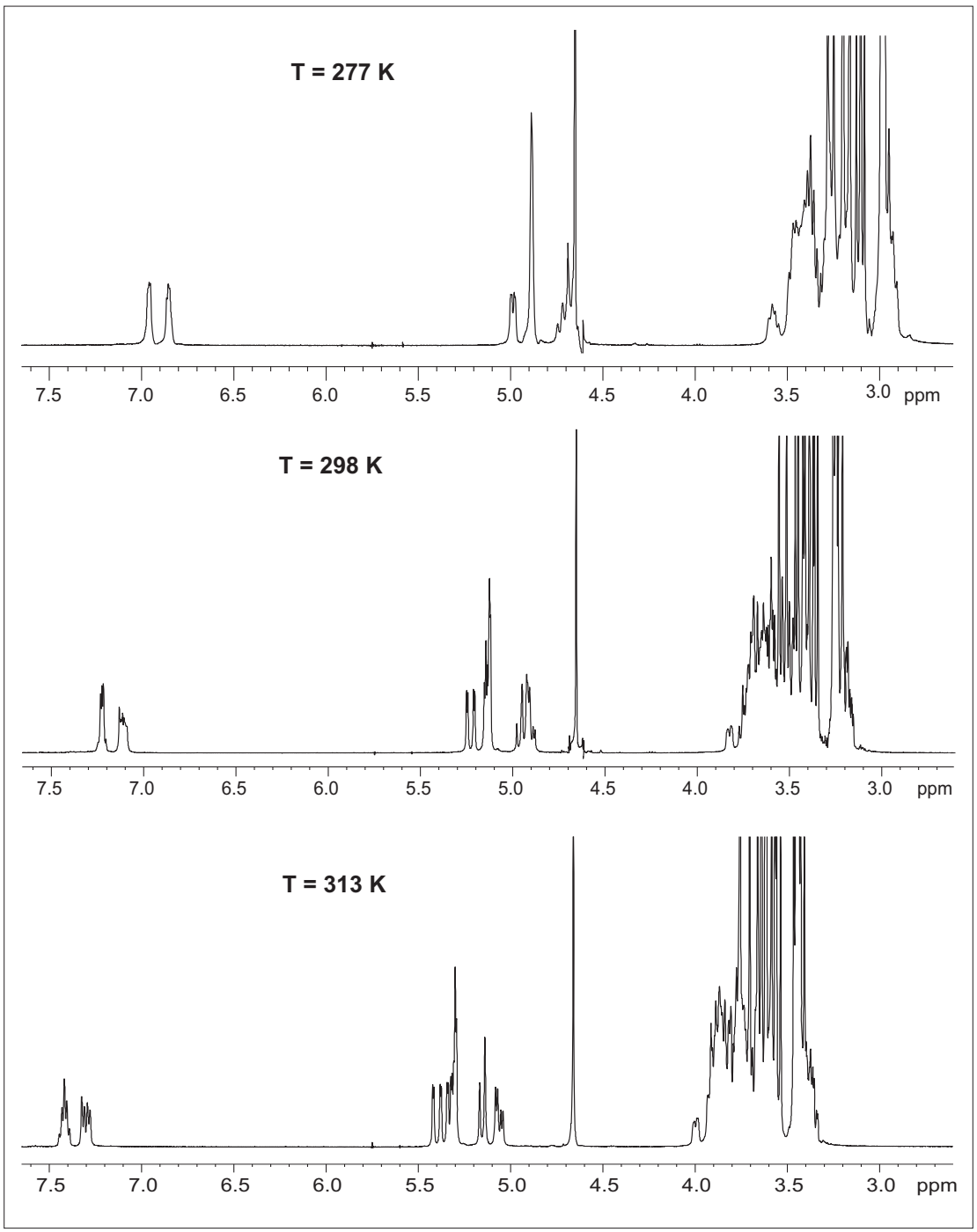


Figure 16S. ^{1}H NMR spectra (500 MHz, D_2) of compound **10** (10 mM) at different temperatures.

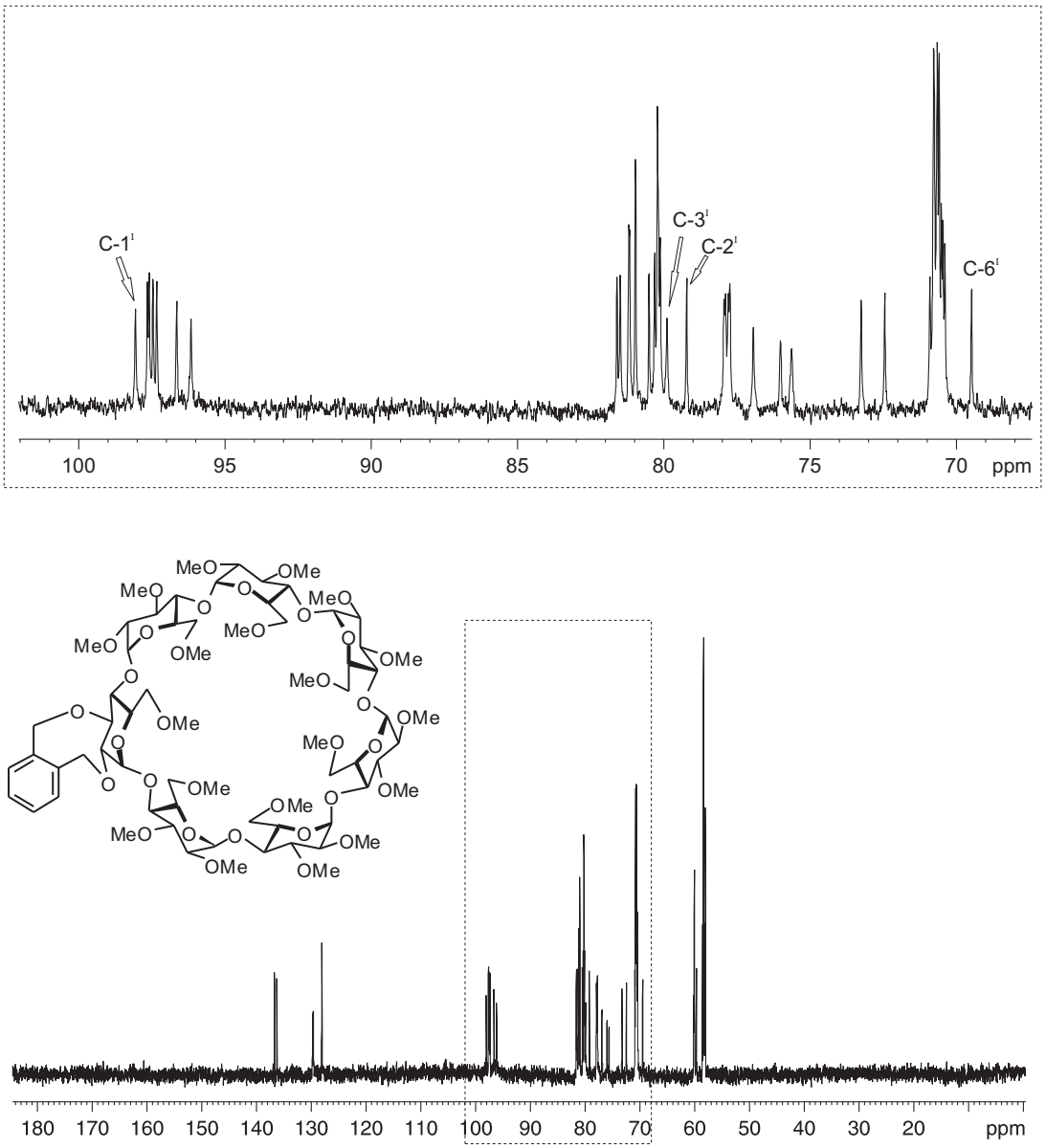


Figure 17S. ^{13}C NMR spectra (500 MHz, D_2O, 298 K) of compound **10**

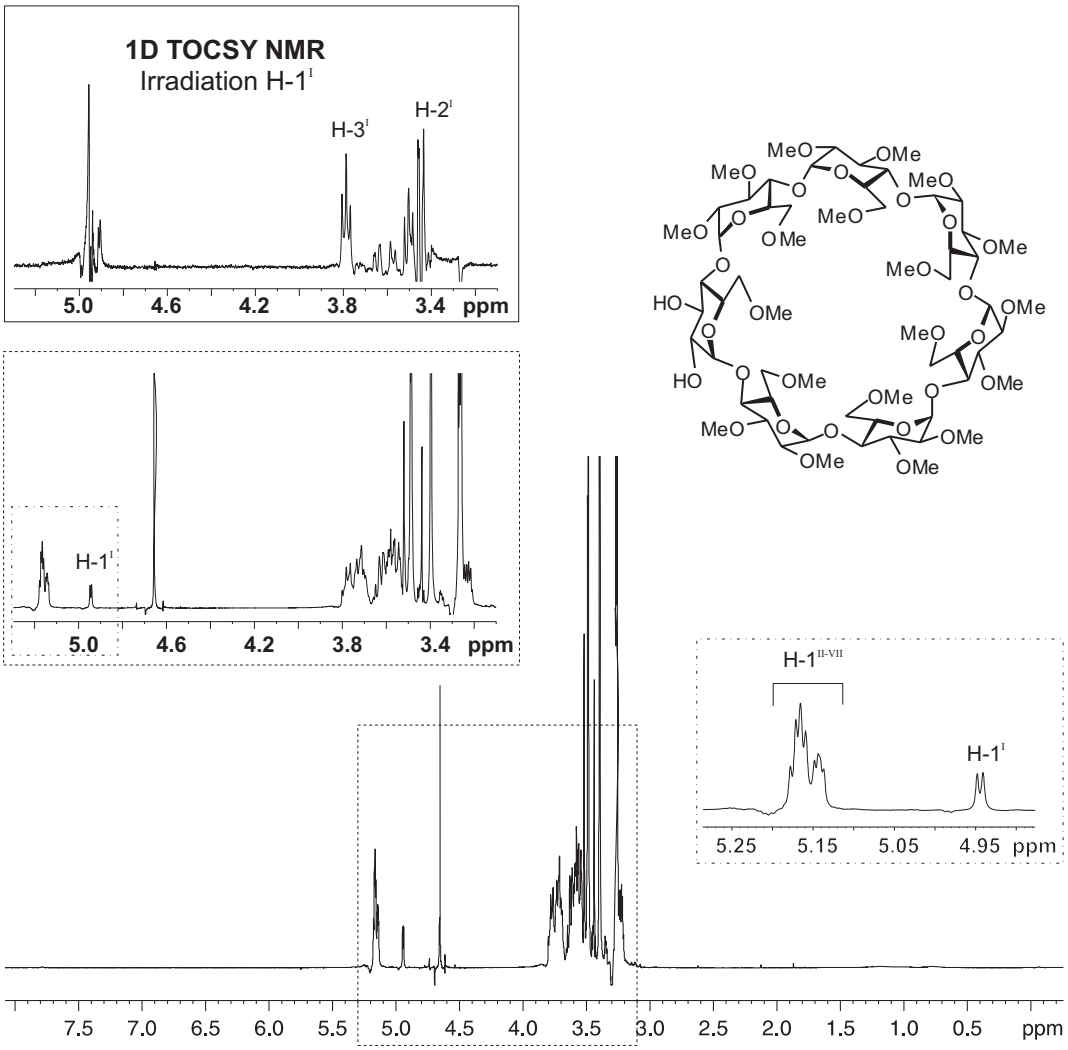


Figure 18S. ^{1}H NMR spectrum (500 MHz, D_2O) of compound **11**.

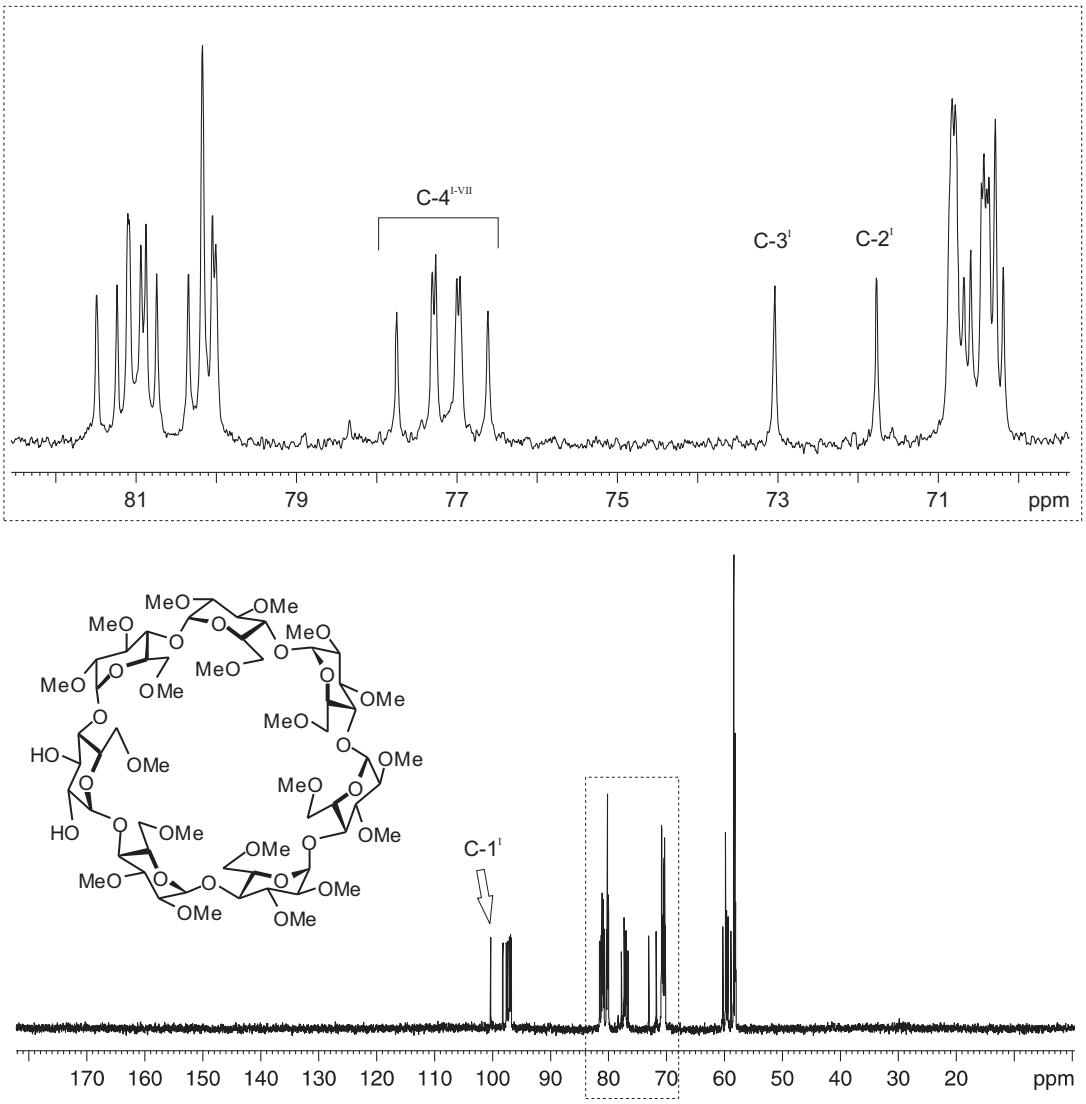


Figure 19S. ^{13}C NMR spectrum (125.7 MHz, D_2O) of compound **11**.

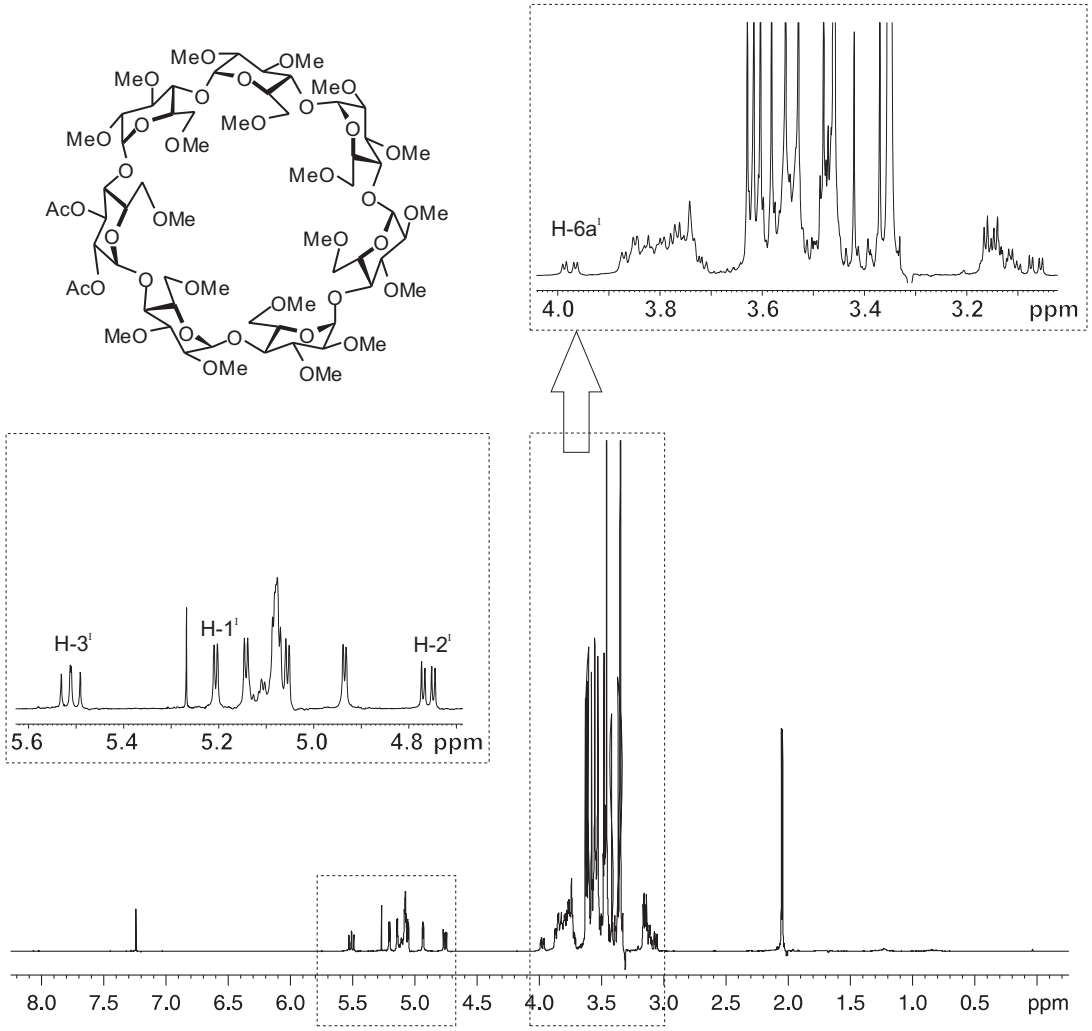


Figura 20S. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **12**.

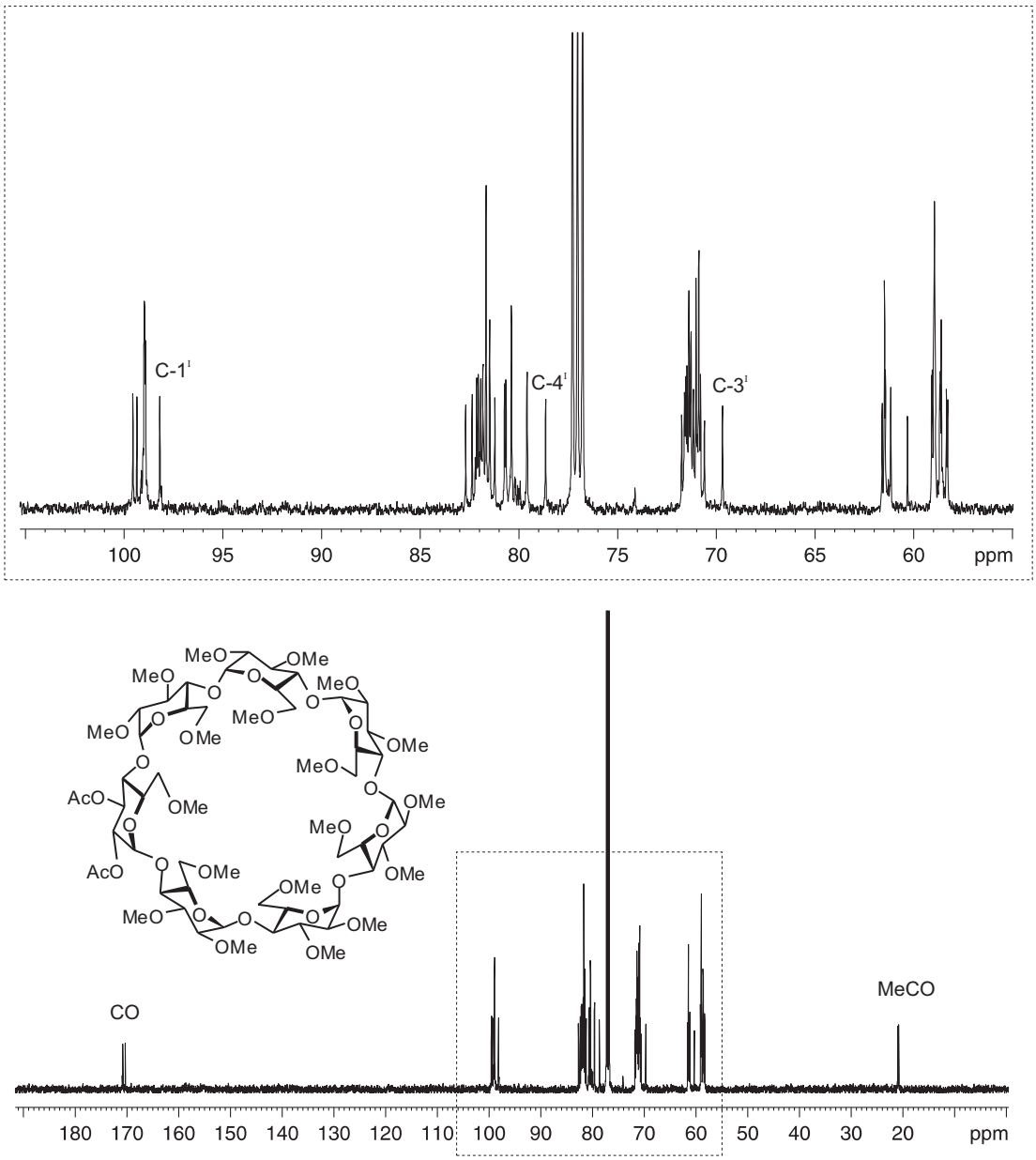


Figure 21S. ^{13}C NMR spectrum (125.7 MHz, D_2O) of compound **12**.