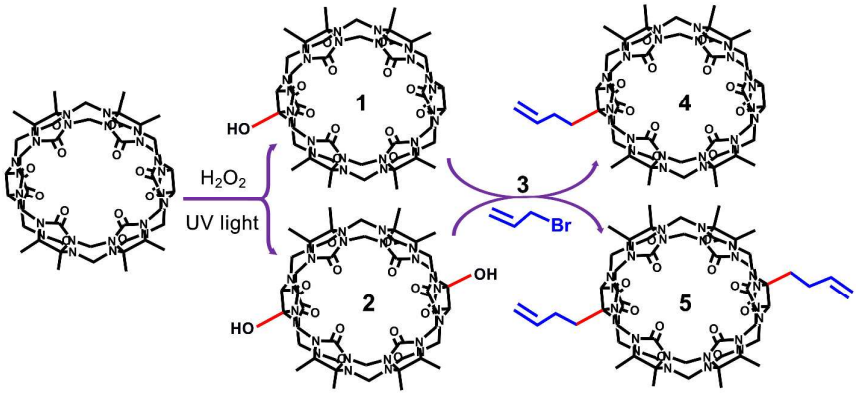
Supporting Information

Mono- and di-hydroxylated symmetrical octamethylcucurbiturils and allylated derivatives

Fang-Fang Shen,[†] Kai Chen, *,[‡] Yun-Qian Zhang,[†] Qian-Jiang Zhu,[†] Zhu Tao,[†] Hang Cong*,[†]

[†] Key Laboratory of Macrocyclic and Supramolecular Chemistry of Guizhou Province, Guizhou University, Guiyang, Guizhou 550025, China

[‡] Jiangsu Collaborative Innovation Center of Atmospheric Environment and Equipment Technology, Jiangsu Key Laboratory of Atmospheric Environment Monitoring and Pollution Control, School of Environmental Science and Engineering, Nanjing University of Information Science & Technology, Nanjing 210044, P. R. China.



Scheme S1. Synthesis of mono- and di-hydroxylated octamethylcucurbituril (**1** and **2**), and their allylated products (**4**, **5**) with allyl bromide (**3**) from a symmetrical octamethylcucurbituril (OMeQ[6]).

EXPERIMENTAL SECTION

Materials. OMeQ[6] was prepared and purified according to methods in our laboratory.[1] Chemicals such as moroxydine hydrochloride and DMSO were obtained from Aladdin and were of analytical grade and used as received without further purification. Double-distilled water was used for all experiments.

NMR measurements. To analyze the obtained compounds **1**, **2**, **4**, **5**, 2.0-2.5×10^{-3} mmol solutions and related host-guest complexes were prepared in 0.5-0.7 mL D_2O or $DMSO_{-d6}$, and NMR spectra were recorded at 20 °C on a VARIAN INOVA-400 spectrometer.

Xevo Q-TOF mass spectrometry. Mass spectral analyses were carried out using a Xevo Q-TOF mass spectrometer equipped with an electrospray ionization source (Waters, Milford, MA, USA). High-purity nitrogen was used as the nebulizer and auxiliary gas, and argon was used as the collision gas. TOF/MS analysis was performed in positive ion mode, and the mass range was set at m/z 100–2000. The ESI capillary voltage was set at 2.5 kV in positive ion mode. The source and desolvation temperature were set at 120 and 450°C, respectively. The desolvation and cone gas flows were 800 and 50 L/h, respectively. The sample and extraction cone voltage were set at 40 V and 4.0 V, respectively. The collision energy

was set at 6 eV. The data acquisition rate was set to 0.2 s, with a 0.02 s interscan delay. Mass accuracy was maintained using a lock spray with leucine enkephalin for the negative ion mode ($[M-H]^-$= 554.2615) at a concentration of 200 mg/mL and a flow rate of 10 µl/min as a reference. Data were collected in continuous mode, the lockspray frequency was set at 15 s, and data were averaged over three scans. All acquisitions and data analysis were controlled by Waters Masslynx v4.1 software. Samples were injected directly into the TOF-MS using an interactive fluidics system.

Synthesis and Separation of (OH)OMeQ[6] (1) and trans-**(OH)$_2$OMeQ[6] (2).** The photochemical reactor was a Yan Zheng Instrument (model YZ-GHX-AR) containing 16 light bulbs from Philips (254 nm, model TUV 8W, Figure S0a, Supporting Information). OMeQ[6] (1×10^{-4} mol, 128.8 mg) was introduced in a 100 mL quartz tube in a 50 mL solution (1/1 vol. %) of HPLC grade water and 10 M HCl aqueous solution. A brief period of ultrasound was applied to ensure all cucurbituril was solubilized before the addition of hydrogen peroxide (3×10^{-4} mol, 30 µL) and then was degassed under argon. The solution was vigorously stirred and subjected to UV light at a wavelength of 254 nm for 12 h. The solvent was then evaporated under reduced pressure to afford a white solid (125 mg, 97 % yield). The crude product, mainly containing OMeQ[6], **1** and **2** (2 g, Figure S0b, Supporting Information) was dissolved using 5 mL formic acid (88 %), and loaded onto a silica gel column (200-300 mesh, Cat. No. S1001, innochem)(Figure S0c, Supporting Information) and eluted using an 8:10:2 water: acetic acid: formic acid mixture within 1 day under atmospheric pressure to afford di-hydroxylated (OH)$_2$OMeQ[6] mixtures containing mainly **2 (**~0.53 g, ~ 26%, white solid**)**, **1 (**~0.53 g, ~ 26%, white solid**)**, and 0.51 g of OMeQ[6] ~25% yield.

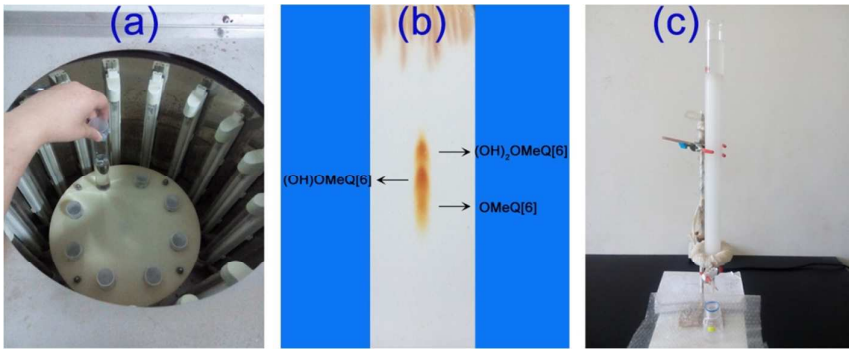


Figure S0. Pictures of (a) the photochemical reactor; (b) the TLC profile of a mixture of three Q[6]s, 1, 2 and OMeQ[6]; (c) a silica gel column for separating the OMeQ[6] mixture.

Compound 1: M.p. 354-355°C. TLC ($CH_3COOH/H_2O/HCOOH$, 10:8:2) R_f 0.38. IR (KBr, cm^{-1}): 3458s, 2059s, 1743s, 1637w, 1478s, 1294s, 1079m, 943m. ^{1}H NMR (400 MHz, D_2O): 5.68 (d, J=12.0, 2H), 5.60 (d, J=12.0, 4H), 5.58 (d, J=16.0, 4H), 5.42 (d, J=12.0, 2H), 5.44 (s, 2H), 5.24 (s, H), 4.50 (d, J=16.0, 2H), 4.34(d, J=16.0, 4H), 4.28 (d, J=12.0, 2H), 4.25 (d, J=12.0, 4H), 1.72 (d, J=12.0, 24H). ^{13}C NMR (400

MHz, D_2O):156.7, 155.5, 155.1, 93.0, 77.8, 77.5, 77.3, 77.0, 70.7, 48.0, 47.6, 43.8, 42.1, 16.62, 15.90. MS: $C_{44}H_{52}N_{24}O_{13,}$ for **1**·H·K^+: calcd. m/z 1165.1359, found m/z 1165.4052.

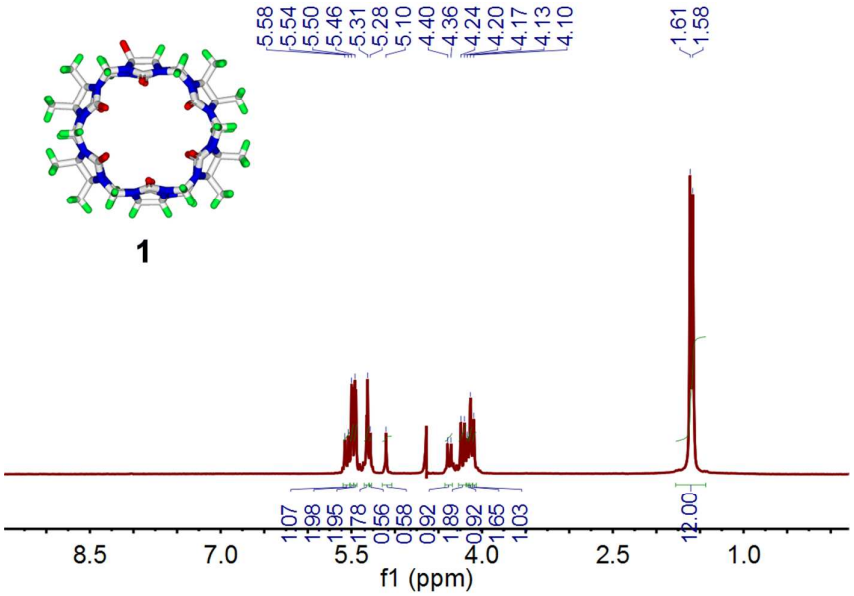


Figure S1. ^{1}H NMR spectra of **1** in D_2O.

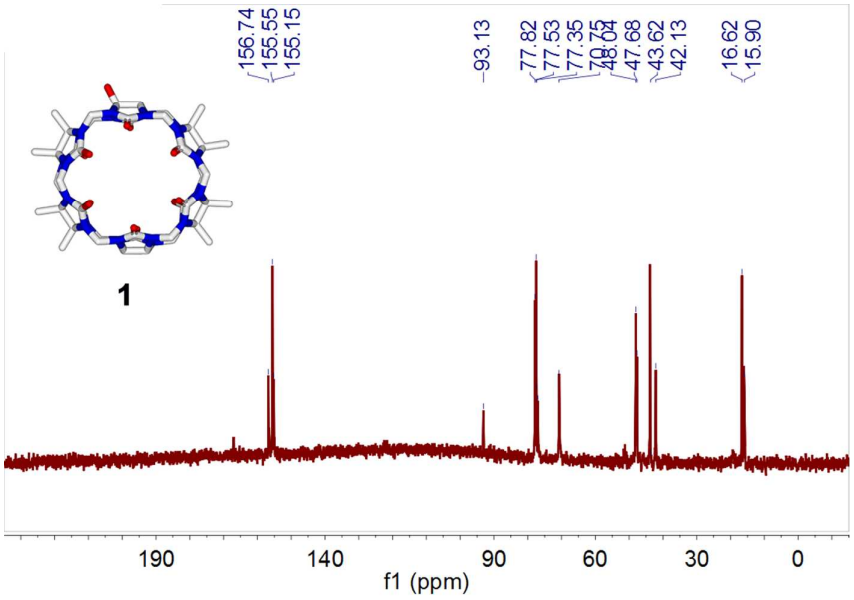


Figure S2. ^{13}C NMR spectra of **1** in D_2O.

Compound 2: M.p. 348-349°C. TLC ($CH_3COOH/H_2O/HCOOH$, 10:8:2) R_f 0.50. IR (KBr, cm^{-1}): 3454s, 2066s, 1731s, 1487s, 1372w, 1294s, 1215w, 1064m, 936w, 736w. ^{1}H NMR (400MHz, D_2O): 5.61 (d, J=16.0,4H), 5.52 (d, J=16.0,4H), 5.35 (d, J=16.0, 4H), 5.15 (s, 2H), 4.42 (d, J=16.0, 4H), 4.27 (d, J=20.0,4H), 4.20 (d, J=16.0, 4H), 1.65 (d, J=12.0, 24H). ^{13}C NMR (400 MHz, D_2O): 155.5, 155.1, 93.0,

77.8, 77.5, 77.3, 77.0, 47.6, 43.8, 42.1, 16.6, 15.9. MS: $C_{44}H_{52}N_{24}O_{14}$, for **2**·H·K^+,calcd. m/z 1181.1353, found m/z 1181.4122; for **2**·3Na^{3+}: calcd. m/z 403.0, found m/z 403.0987(3).

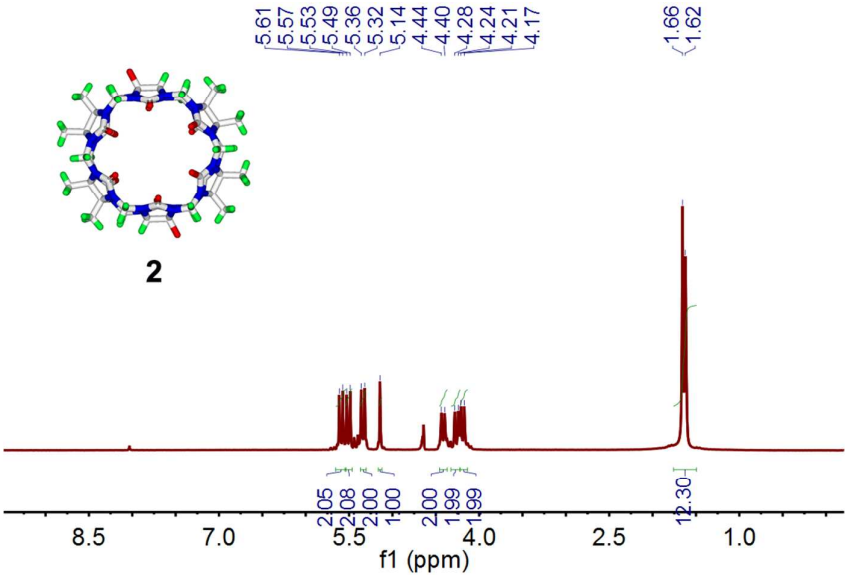


Figure S3. ^{1}H NMR spectra of **2** in D_2O.

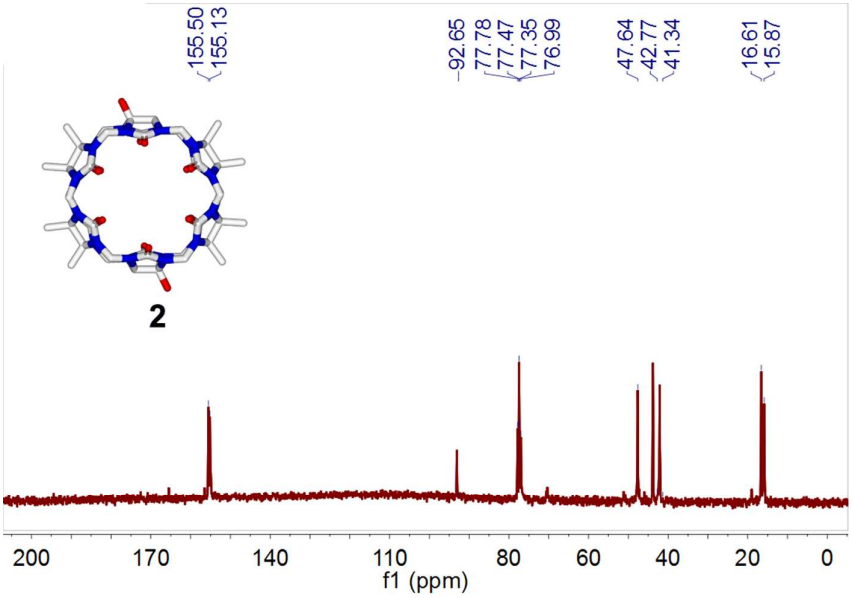


Figure S4. ^{13}C NMR spectra of **2** in D_2O.

Preparation of A. $MgCl_2$ (12.48 mg, 0.061 mmol), $CdCl_2·2H_2O$ (11.30 mg, 0.050 mmol), and **1** (10 mg, 0.0077 mmol) were dissolved in 2.0 mL of 3.0 mol/L HCl with stirring. The solution was left to stand to allow slow evaporation of the volatiles in air at room temperature. Colourless crystals were obtained from the solution within a week. A compound with the composition **1**·$[Cd_2Cl_8]^{4-}$·$4H_3O$·$6H_2O$ (**A**) was obtained. $C_{44}H_{76}N_{24}O_{23}Cd_2Cl_8$ (%): C 29.07; H 4.21; N 18.49, found: C 29.23; H 4.11; N 18.64.

Preparation of B. di-hydroxylated $(OH)_2$OMeQ[6] mixtures containing mainly **2** (50 mg, 0.038 mmol) was dissolved in 10 mL H_2O, and the solution was left to stand to allow slow evaporation of the volatiles in air at room temperature. Colourless crystals were obtained from the solution within a week. A compound with the composition **2**·20H_2O (**B**) was obtained. $C_{44}H_{92}N_{24}O_{34}$ (%): C 35.20; H 6.18; N 22.39, found: C 35.50; H 6.06; N 22.53.

X-ray crystallography. A suitable single crystal **A** or **B** (~0.2 × 0.2 × 0.1 mm) was embedded in paraffin oil and mounted on a Bruker SMART Apex II CCD diffractometer equipped with a graphite-monochromator Mo K_α radiation source (λ = 0.71073 Å, μ = 0.828 mm^{-1}) that was operated in the ω-scan mode under a nitrogen stream (–50°C). Data were corrected for Lorentz and polarization effects using the SAINT program, and semi-empirical absorption corrections based on equivalent reflections were also applied using SADABS. The structure was elucidated through direct methods and refined by the full-matrix least-squares method on F^2 values using SHELXS-97 and SHELXL-97, respectively.[2,3] All non-hydrogen atoms were refined anisotropically, and carbon-bound hydrogen atoms were introduced at calculated positions and treated as riding atoms with an isotropic displacement parameter equal to 1.2 times that of the parent atom. Most of the water molecules in **A** and **B** were omitted using the SQUEEZE option in the PLATON program (10 and 20 water molecules for compounds **A** and **B**, respectively). Analytical expressions for neutral-atom scattering factors were employed, and anomalous dispersion corrections were incorporated. Details of the crystal parameters, data collection conditions, and refinement statistics are summarized in **Table S1**, and crystallographic data have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication No. CCDC-1496522 (**A**), 1496523 (**B**). These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033).

Synthesis of mono-allylated OMeQ[6] (4) and trans-di-allylated OMeQ[6] (5). To a solution of **1** (30 mg) in a 1:1 molar ratio of **1**:**6** in anhydrous DMSO (2 mL), NaH (10 mg, 0.4 mmol) was added and stirred at room temperature for 15 min. **3** (0.5 mL, 5.8 mmol) was added subsequently at 0ºC and the reaction mixture was stirred at room temperature for 12 h. The reaction was then diluted with 50 mL diethyl ether and filtered. The remaining solid was triturated with acetone (3×50mL) and dried under vacuum to give a yellow solid (**4**; 26 mg, 83.6 %). To a solution of **2** (30 mg) in a 1:1 molar ratio of **1**:**6** in anhydrous DMSO (2 mL), NaH (10 mg, 0.4 mmol) was added and stirred at room temperature for 15 min. **3** (0.5 mL, 5.8 mmol) was added subsequently at 0ºC and the reaction mixture was stirred at room temperature for 12 h. The reaction was then diluted with 50 mL diethyl ether and filtered. The remaining solid was triturated with acetone (3×50mL) and dried under vacuum to give a yellow solid (**5**; 27 mg, 84.0 %).

Compound 4: M.p. 373-374°C. IR (KBr, cm^{-1}): 3459s, 2059s, 1741s, 1630w, 1475s, 1308s, 1072m, 936m, 764w. ^{1}H NMR (400 MHz, D_2O): 5.92 (m, H), 5.54 (m, 15H), 5.34 (d, J=16.0, H), 5.22 (d, J=8.0, H), 4.30 (m, 12H), 3.95 (s, H), 1.70 (m, 24H). ^{13}C NMR (400 MHz, D_2O): 156.94, 155.66, 155.54,

131.91, 119.23, 96.27, 78.04, 77.76, 77.64, 70.82, 64.53, 47.94, 43.87, 42.61, 38.67, 16.65, 15.68. MS: $C_{47}H_{57}N_{24}O_{13.}$ for **4**·2Na^{+}: calcd. m/z 605.5, found m/z 605.2078(2).

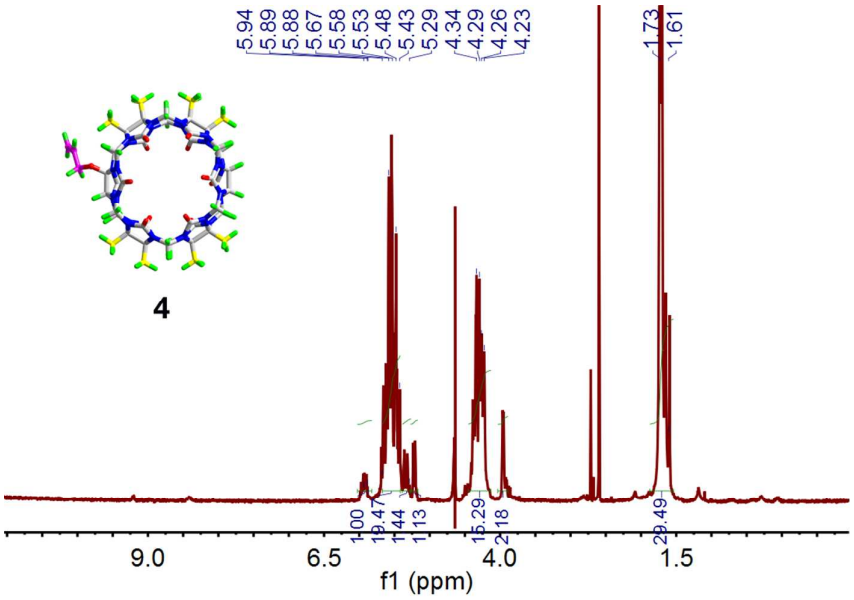


Figure S5. ^{1}H NMR spectra of **4** in D_2O.

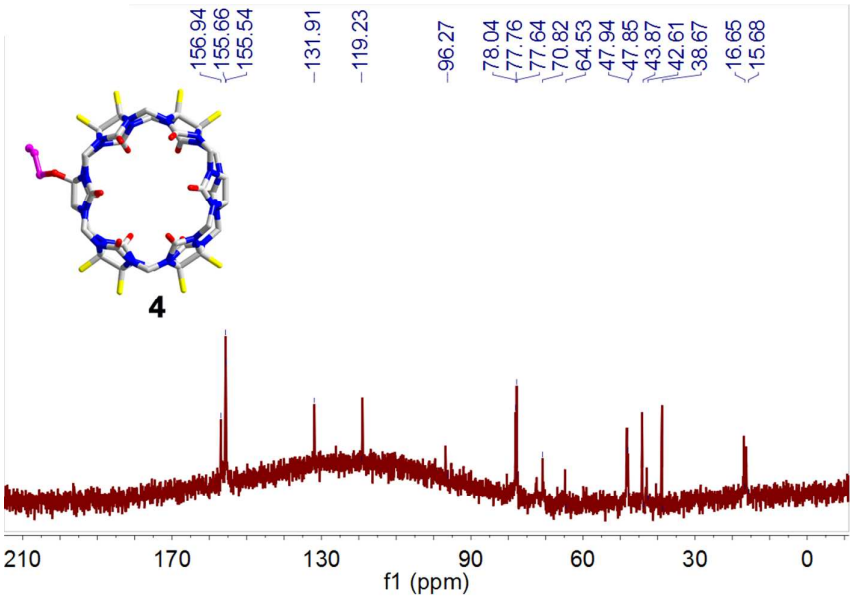


Figure S6. ^{13}C NMR spectra of **4** in D_2O.

Compound 5: M.p. 362-363°C. IR (KBr, cm^{-1}): 3456s, 2059s, 1736s, 1637w, 1478s, 1380w, 1322s, 1072m, 936m, 750w. ^{1}H NMR (400 MHz, D_2O): 5.91 (m, H), 5.52 (m, 14H), 5.32 (d, J=16.0, H), 5.21 (d, J=8.0, H), 4.30 (m, 12H), 3.94 (s, H), 1.70 (m, 24H). ^{13}C NMR (400MHz, D_2O): 155.54, 155.42, 131.43,

118.69, 96.28, 77.94, 77.68, 77.59, 77.33, 64.57, 47.79, 44.03, 42.75, 38.59, 16.67, 16.0. MS: $C_{50}H_{62}N_{24}O_{14}$, for **5**·2Na^{+}: calcd. m/z 634.0, found m/z 633.2208(2).

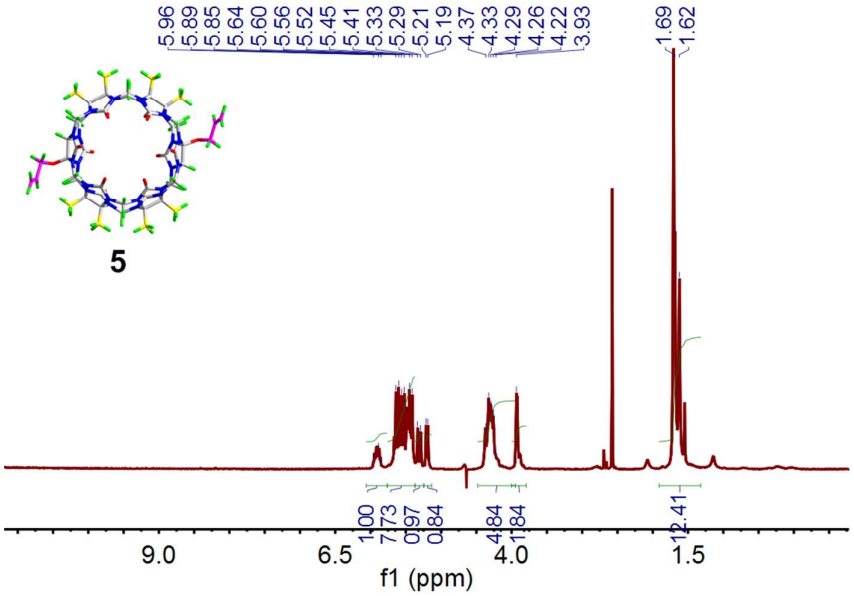


Figure S7. ^{1}H NMR spectra of **5** in D_2O.

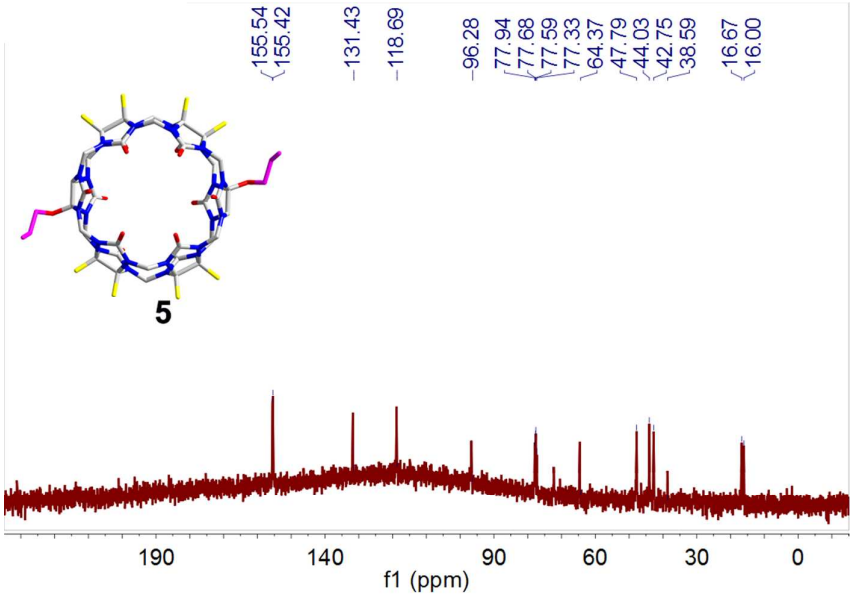


Figure S8. ^{13}C NMR spectra of **5** in D_2O.

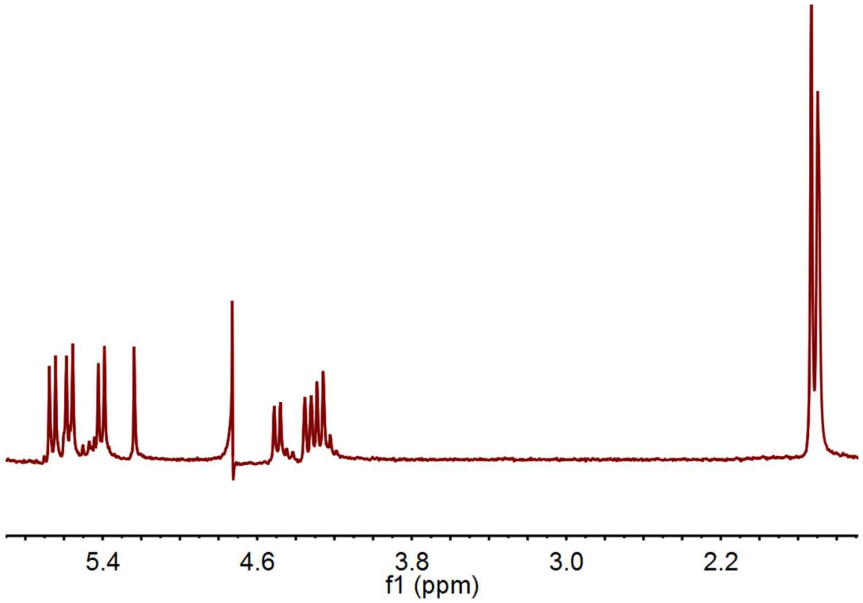


Figure S9. ^{1}H NMR spectra of di-hydroxylated $(OH)_2$OMeQ[6] mixture in D_2O.

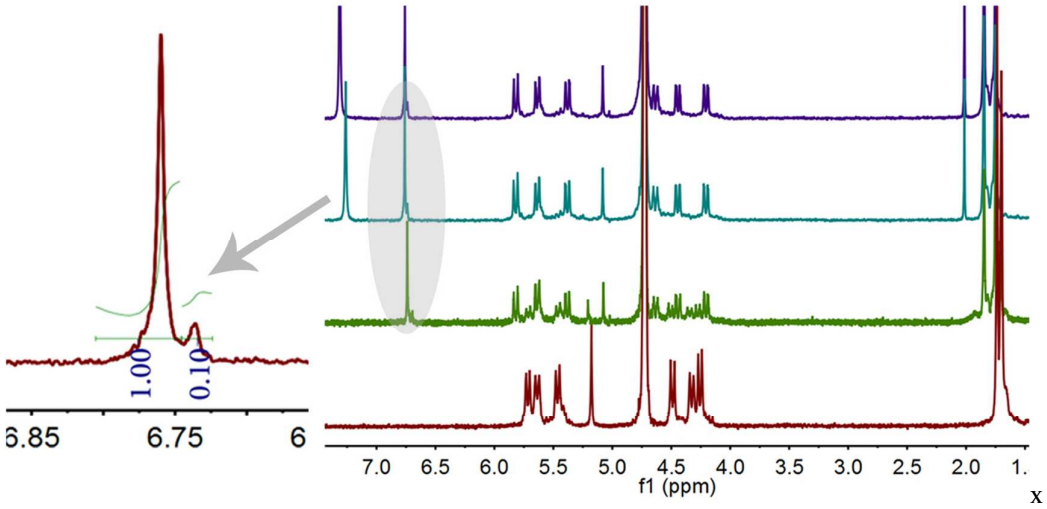


Figure S10. ^{1}H NMR spectra of di-hydroxylated $(OH)_2$OMeQ[6] mixtures with guest *p*-phenylene diammonium chloride salt in D_2O.

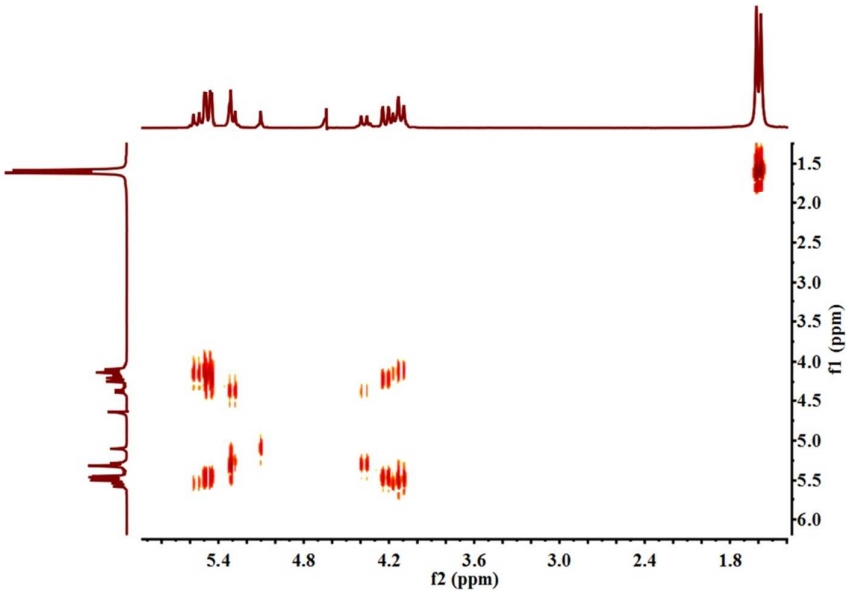


Figure S11. gCOSY 2D NMR spectrum of **1** in 0.50 ml D_2O at 20ºC.

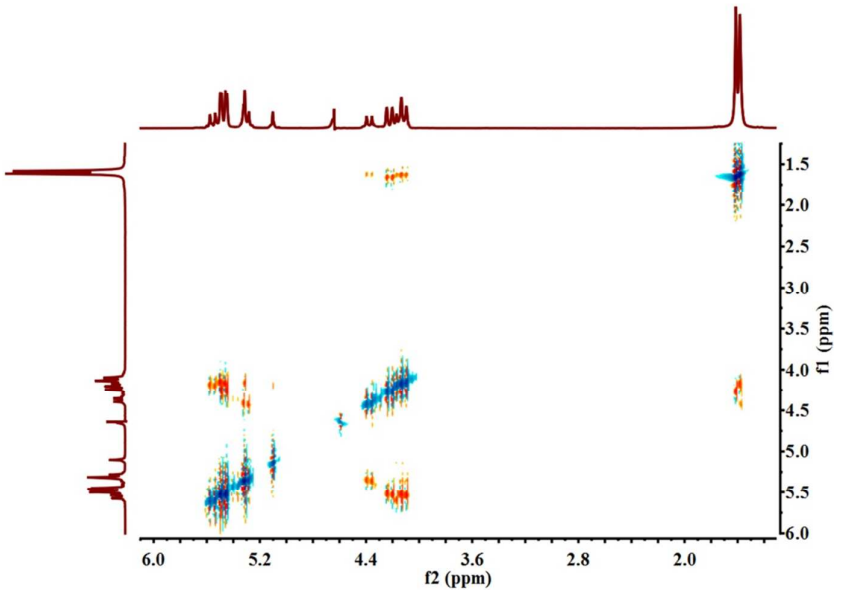


Figure S12. ROESY 2D NMR spectrum of **1** in 0.50 ml D_2O at 20 ºC.

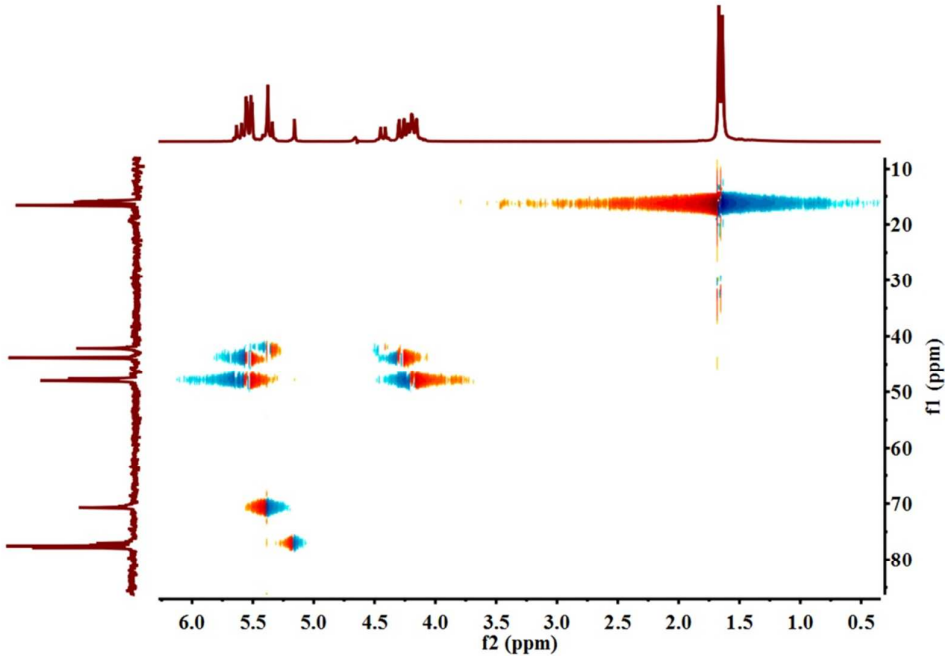


Figure S13. gHSQC 2D NMR spectrum of **1** in 0.50 ml D_2O at 20 ºC.

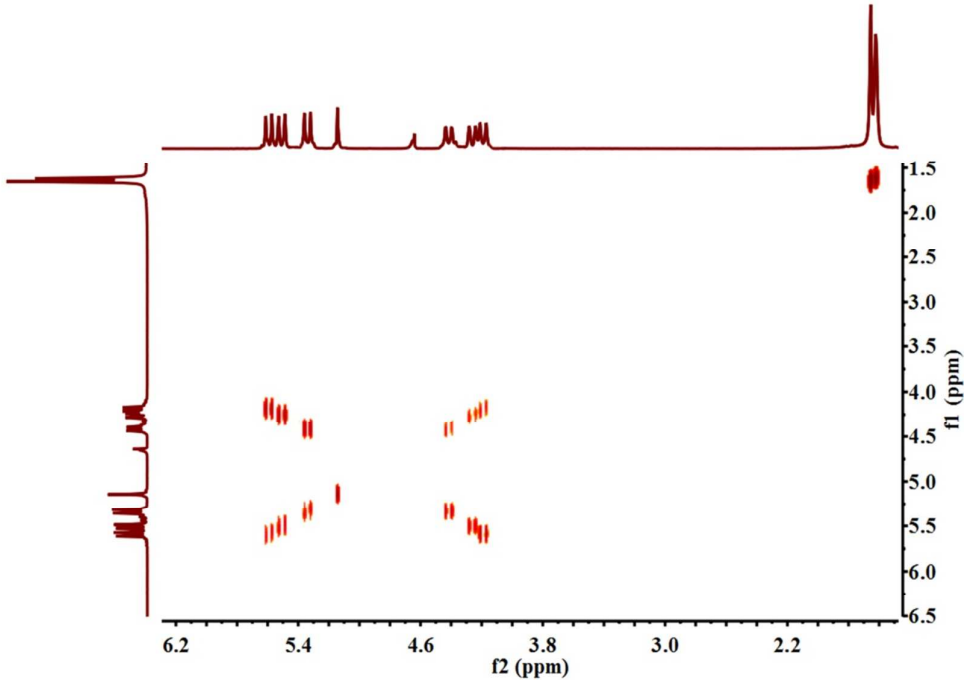


Figure S14. gCOSY 2D NMR spectrum of **2** in 0.50 ml D_2O at 20ºC.

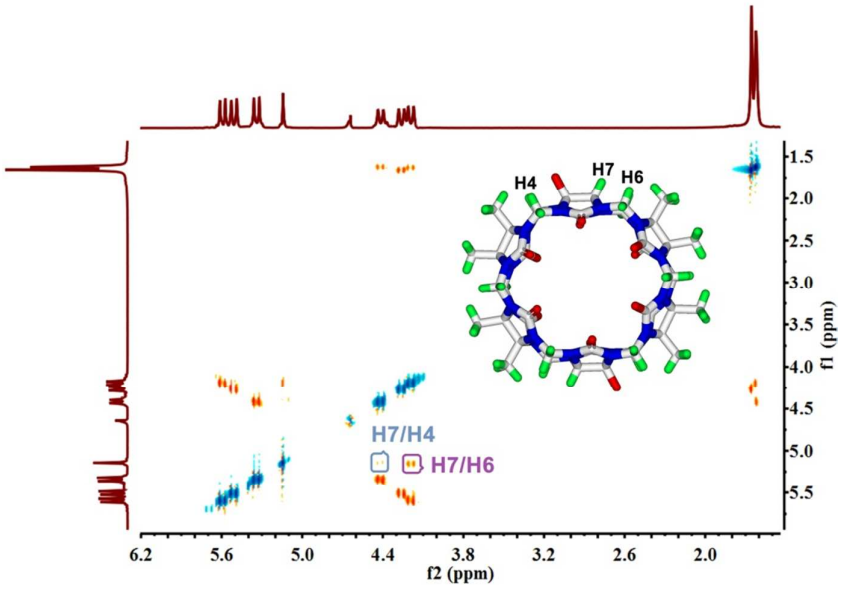


Figure S15. ROESY 2D NMR spectrum of **2** in 0.50 ml D_2O at 20 ºC.

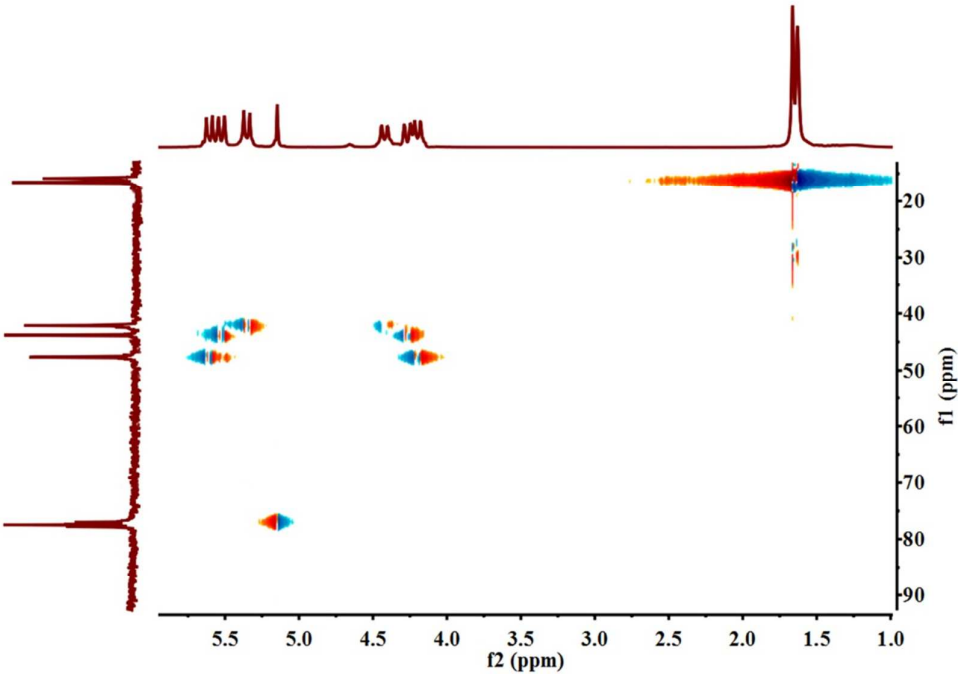


Figure S16. gHSQC 2D NMR spectrum of **2** in 0.50 ml D_2O at 20 ºC.

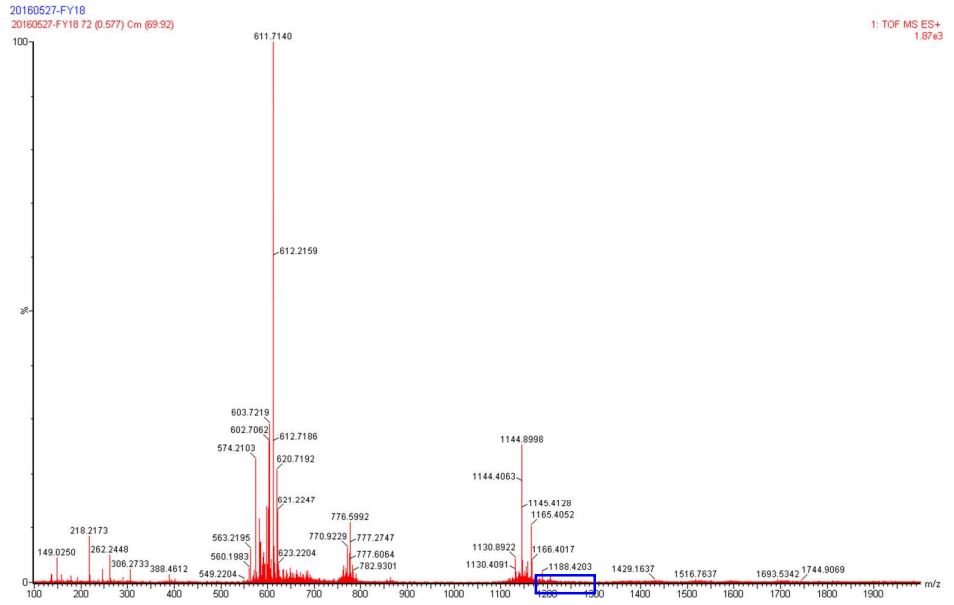


Figure S17. Q-TOF mass spectrum of **1**: for **1**·H·K^{+}: calcd. m/z 1165.1359, found m/z 1165.4052.

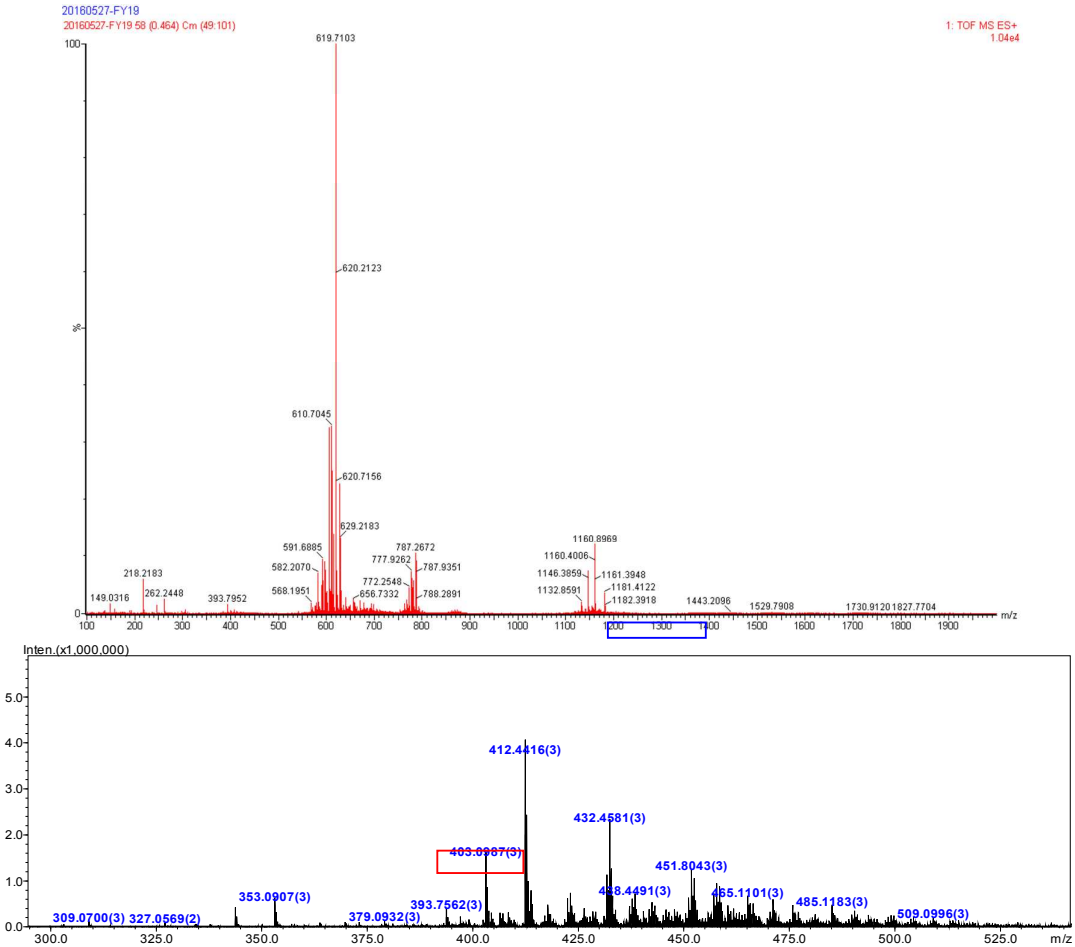


Figure S18. Q-TOF mass spectrum of **2**: (top) for **2**·H·K^{+}: calcd. m/z 1181.1353, found m/z 1181.4122; (bottom) for **2**·3Na^{+}: calcd. m/z 403.0, found m/z 403.0987(3).

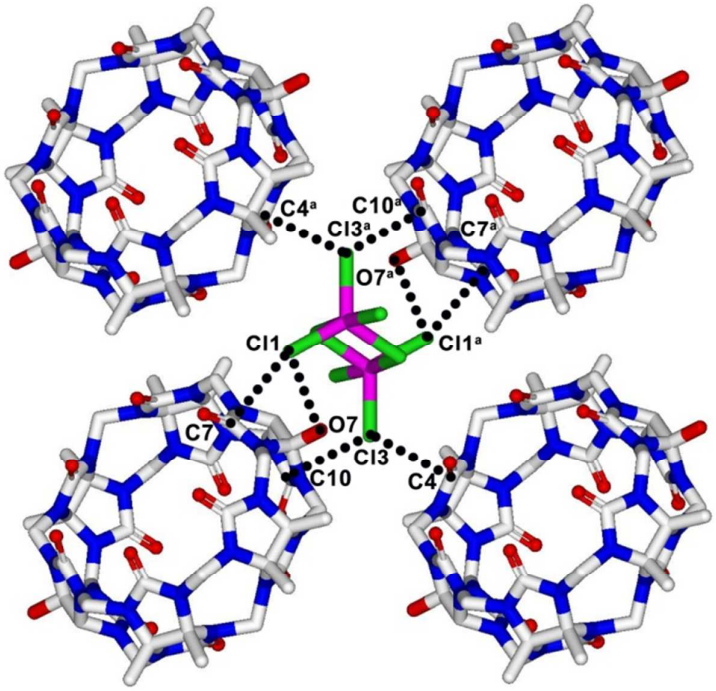


Figure S19. X-ray crystal structure of complex of **1** with $[Cd_2Cl_8]^{4-}$ anions interacting through the outer surface interaction of Q[*n*]s.

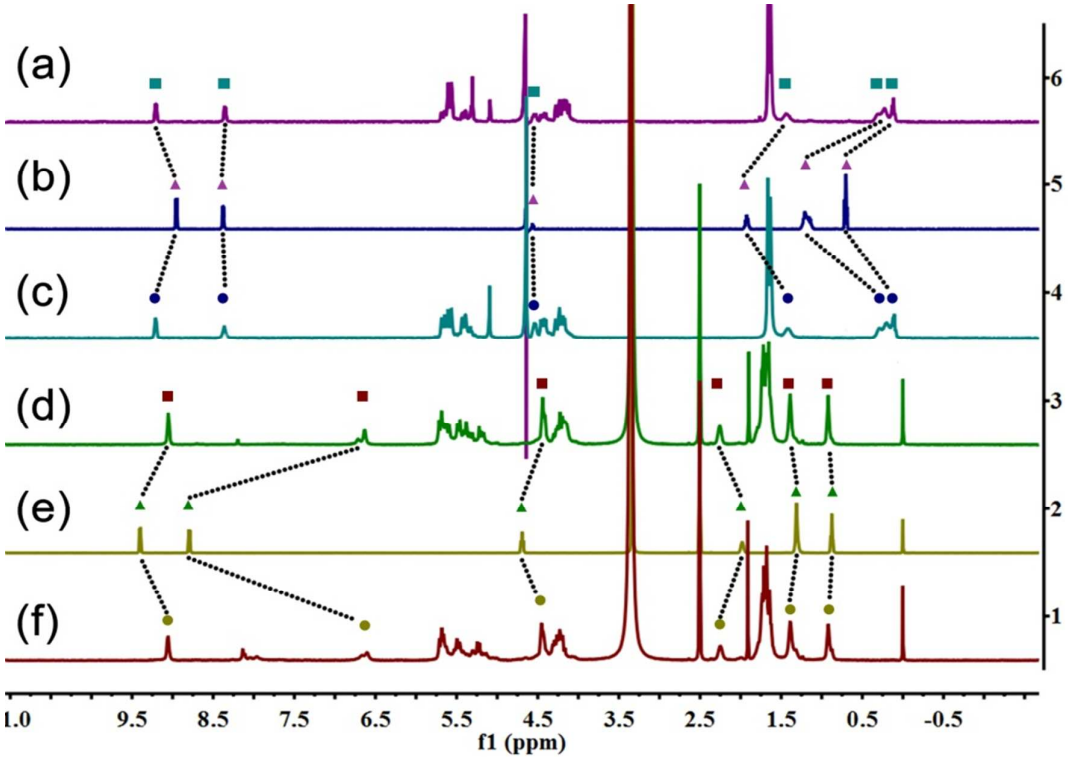


Figure S20. ^{1}H NMR spectra of (a) **1** with **6**; (b) neat **6**; (c) **2** with **6** in D_2O. ^{1}H NMR spectra of (d) **1** with **6**; (e) neat **6**; (f) **2** with **6** in $DMSO_{-d6}$.

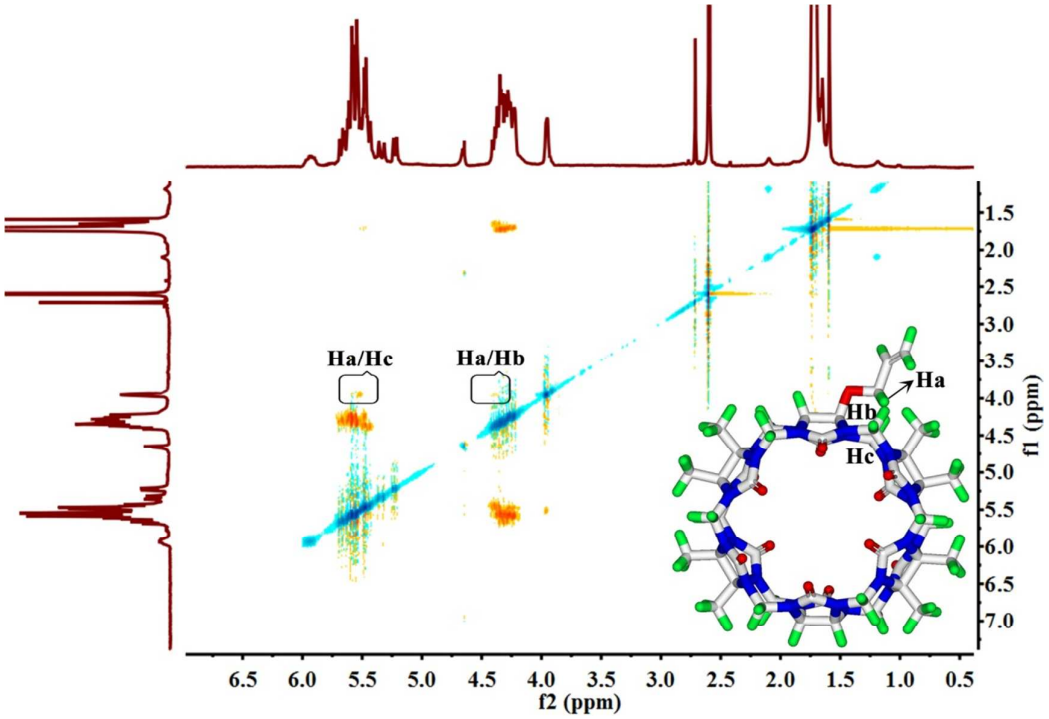


Figure S21. ROESY 2D NMR spectrum of **4** in 0.50 ml D_2O at 20ºC.

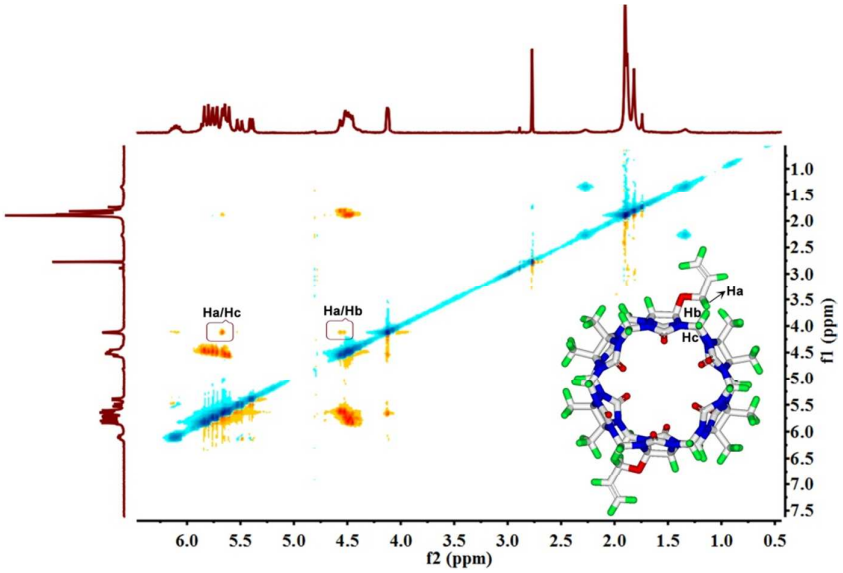


Figure S22. ROESY 2D NMR spectrum of **5** in 0.50 ml D_2O at 20ºC.

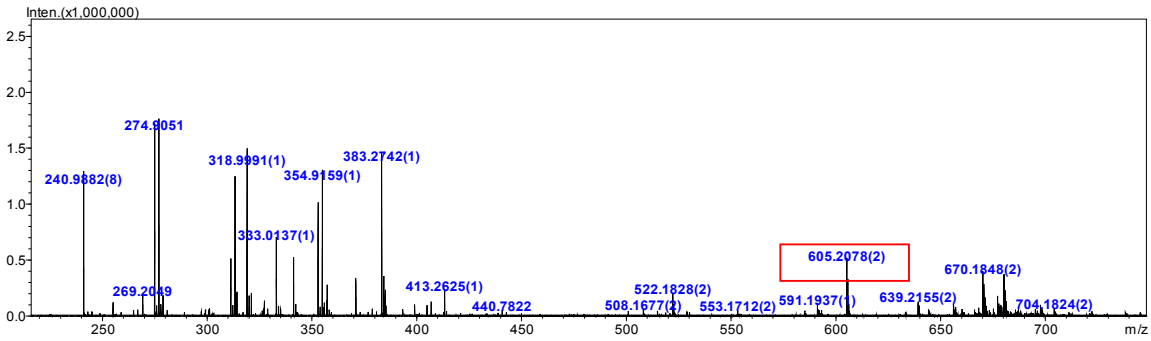


Figure S23. Q-TOF mass spectrum of **4**: for **4**·2Na^{+}: calcd. m/z 605.5, found m/z 605.2078(2).

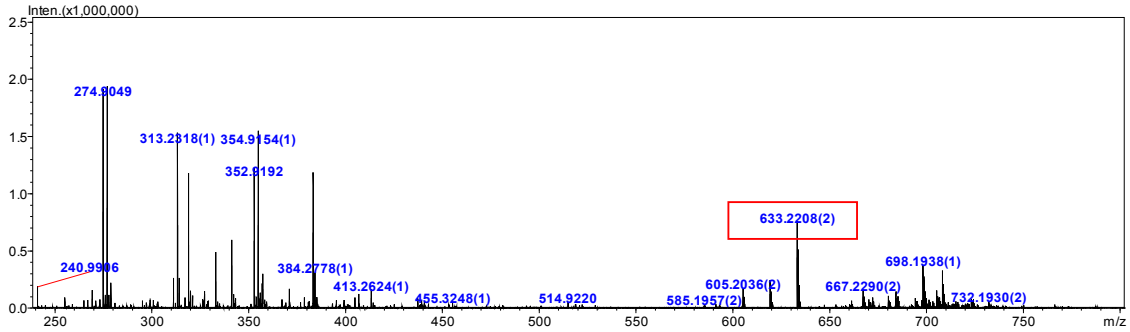


Figure S24. Q-TOF mass spectrum of **5**: for **5**·2Na^{+}: calcd. m/z 634.0, found m/z 633.2208(2).

Table S1. Crystal data and structure refinement of compounds **A** and **B**.

Compound	**A**	**B**
Empirical formula	$C_{44}H_{76}N_{24}O_{23}Cd_2Cl_8$	$C_{44}H_{92}N_{24}O_{34}$
Formula weight	1817.69	1501.34
Crystal system	Triclinic	Triclinic
Space group	P_{-1}	P-1
a (Å)	12.548(18)	12.400(17)
b (Å)	12.643(2)	12.726(18)
c (Å)	13.187(19)	34.039(5)
α(°)	62.56(3)	83.66(3)
β (°)	77.54(3)	83.95(3)

γ(°)	80.14(4)	82.86(4)
T (K)	293(2)	293(2)
V (Å^3)	1806.7(5)	5274.3(13)
Z	1	3
Dc (g·cm^{-3})	1.671	1.418
μ (mm^{-1})	0.972	0.122
F(000)	924	2388
Data collected	12965	18609
Independent data	7415	10563
R_{int}	0.033	0.059
GOFs	1.074	1.042
R_1 [I>2σ (I)]	0.0814	0.0979
wR$_2$ [I>2σ (I)]	0.1209	0.1334
R_1 (all data)[a]	0.2226	0.2807
wR$_2$ (all data)[b]	0.2430	0.3021

[a] $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR_2 = |\Sigma w(|F_o|^2 - |F_c|^2)|/\Sigma|w(F_o)^2|^{1/2}$, where $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$. $P = (F_o^2 + 2F_c^2)/3$

REFERENCES

1 Zhou, J. J.; Yu, X.; Zhao, Y. C.; Xiao, X.; Zhang, Y. Q.; Zhu, Q. J.; Xue, S. F.; Zhang, Q. J.; Liu, J. X.; Tao, Z. *Tetrahedron* **2014**, *70*, 800.

2 Sheldrick, G. M. *Acta Crystallogr. Sect. A* **2008**, *64*, 112.

3 Sheldrick, G. M. SHELXL-97 Program for the Solution and Refinement of Crystal structures, University of Göttingen, Germany, **1997**.