Supporting Information

Capsule–bowl conversion triggered by a guest reaction

Shitao Wang, Tomohisa Sawada, Makoto Fujita*

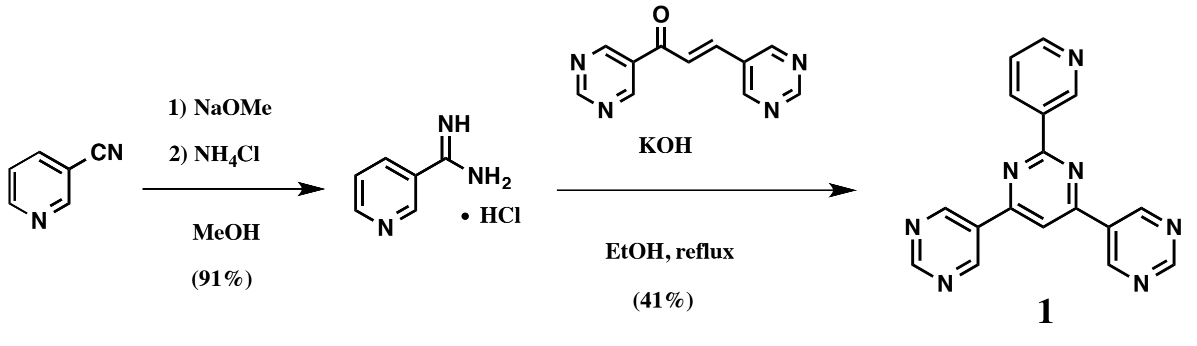
School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bukyo-ku, Tokyo, 113-8656, JAPAN

Materials and analytical instrumentation

Reagents and solvents were purchased from TCI Co., Ltd., WAKO Pure Chemical Industries, Ltd., KANTO Chemical Co., Inc., or Sigma-Aldrich. Deuterated solvents were acquired from Cambridge Isotope Laboratories, Inc. All chemicals were of reagent grades and used without any further purification. Filtration was performed with membrane syringe filter (ADVANTEC HP020AN). ^{1}H, ^{13}C, ^{31}P and 2D NMR spectral data were recorded on a Bruker AVANCE 500 MHz spectrometer equipped with a CP-TCI cryoprobe or a Bruker AVANCE III HD 500 MHz spectrometer equipped with a PABBO probe. ^{1}H NMR for D_2O solvent was set at 4.790 ppm. ESI-MS was measured on a Waters eAlliance 2695, micromass ZQ. HR-MS data were measured on a Bruker maXis. Melting points were determined on a Yanaco MP-500V micro melting point apparatus. Elemental analyses were performed at the Elemental Analysis Center (School of Science, The University of Tokyo).

Synthesis

The synthetic route to the triangular *exo*-pentadentate ligand 2-(3-pyridyl)-4,6-bis(3,5-pyrimidyl)-pyrimidine **1** was shown in scheme S1. (2*E*)-1,3-bis(3,5-pyrimidyl)propenone was synthesized according to the literature.[S2] At each step, synthesis was carried out according to the reported procedures of the analogous compounds.[S1]–[S3]



Scheme S1. Synthesis of ligand **1**

Pyridine-3-carboximidamide hydrochloride[S1] To a two-necked flask were added sodium methoxide (33 mg, 0.6 mmol) and dry MeOH (4 mL) under Ar atmosphere. After cooling to 0 °C, dry MeOH (4 mL) solution of 3-cyanopyridine (500 mg, 4.8 mmol) was slowly added and the mixture was then stirred for overnight at ambient temperature. Then ammonium chloride (326 mg, 6.1 mmol) was added and the solution was stirred for 8 h at 40 ºC. After cooling to room temperature, Et_2O (20 mL) was added. White precipitate was formed, which was filtered, washed with Et_2O and dried *in vacuo*. White powder of the product was obtained (688 mg, 91% yield). The product was used in the next step without further purifications. ^{1}H NMR (500 MHz, DMSO-d_6, 300 K): δ 8.98 (d, *J* = 2.5 Hz, 1H), 8.87 (dd, *J* = 1.5 Hz, 1.5 Hz, 1H), 8.53 (br, 4H, NH_2x2), 8.22 (tt, *J* = 8 Hz, 2.5 Hz, 1.5 Hz, 1H), 7.65 (q, 1H); ^{13}C NMR (125 MHz, DMSO-d_6, 300 K), δ 164.15, 154.03, 148.69, 136.23, 124.76, 123.70; ESI-MS (ESI+): calcd. for $[M–Cl]^+$:122.1, found: 122.2.

2-(3-pyridyl)-4,6-bis(3,5-pyrimidyl)-pyrimidine 1[S1-S3] Pyridine-5-carboximidamide hydrochloride (236 mg, 1.5 mmol) was dissolved in anhydrous EtOH (15 mL) in a 30 mL flask, and then KOH (85%) (104 mg, 1.58 mmol, 1.05 equiv.) was added (*Caution:* even slightly excess amount of KOH can decompose the compound (2*E*)-1,3-bis(3,5-pyrimidyl)propenone). The mixture was stirred at room temperature for 30 min and filtered. To the filtrate solution was added the compound (2*E*)-1,3-bis(3,5-pyrimidyl)propenone (319 mg, 1.5 mmol) and the suspended solution was then heated to reflux for 24 h. After cooled to ambient temperature, the yellow precipitate was collected by filtration, and washed with water and EtOH. After dried *in vacuo* at 60 °C for 24 h, white fluffy solid (45 mg) was obtained. The mother filtrate was added 0.4 mL of 1 M EtOH solution of KOH and heated to reflux again for additional 24 h. After cooling to ambient temperature, the precipitate was collected by filtration and washed with water and EtOH, and then dried *in vacuo* at 60 °C for 24 h. White gray solid **1** was obtained (195 mg in total, yield 41%). Sublimation >350 ºC, ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ 9.88 (d, *J* = 2 Hz, 1H), 9.60 (s, 4H), 9.44 (s, 2H), 8.92 (tt, *J* = 8 Hz, 2 Hz, 2 Hz, 1H), 8.83 (dd, *J* = 1.5 Hz, 1.5 Hz, 1H), 8.12 (s, 1H), 7.53 (q, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ 164.19, 161.24, 160.64, 155.70, 152.40, 150.29, 135.82, 132.15, 129.99, 123.61, 110.67; HR-MS (ESI+): calcd. for $[M+H]^+$: 314.1149, found: 314.1164.

Self-assembly of the empty octahedral $M_{20}L_8$ capsule 3

Ligand **1** (12.5 mg, 0.04 mmol) and (en)Pd$(ONO_2)_2$ (29.0 mg, 0.05 mmol) were suspended in an aqueous solution (1 mL) in a capped test-tube and the mixture was stirred at ambient temperature for 36 h. For isolation, slowly diffused methanol into the clear aqueous solution at refrigerator (4 °C) for three weeks. Yellow crystals were formed and collected by filtration, then dried *in vacuo* at ambient temperature for 12 h (29 mg, 70%). m.p. > 220 °C (decomposed). ^{1}H NMR (500 MHz, D_2O, 300 K): δ 11.14 (s, 8H), 10.95 (s, 8H), 10.94 (s, 8H), 10.56 (s, 8H), 10.47 (s, 8H), 9.90 (s, 8H), 9.85 (s, 8H), 9.20 (d, *J* = 5 Hz, 8H), 9.13 (d, *J* = 8 Hz, 8H), 9.11 (s, 8H), 7.81 (d, *J* = 6 Hz, 6 Hz, 8H), 3.19~3.0 (br). ^{13}C NMR (125 MHz, D_2O, 300 K): δ 163.10, 161.12, 160.92, 160.80, 160.47, 159.64, 158.74, 158.60, 156.75, 153.02, 151.74, 139.84, 135.07, 132.79, 131.53, 126.82, 113.83, 47.75 (br), 47.68 (br), 47.13 (br), 46.73 (br). Elemental analysis (%): calcd. for $C_{176}H_{248}N_{136}O_{120}Pd_{20}•50H_2O•4CH_3OH$: C 23.13, H 3.93, N 20.38; found: C 22.96, H 4.32, N 20.36.

References

[S1] T. Sawada, H. Hisada, M. Fujita, *J. Am. Chem. Soc.* **2014**, *136*, 4449−4451.

[S2] S. Wang, T. Sawada, K. Ohara, K. Yamaguchi, M. Fujita, *Angew. Chem.Int. Ed.* **2016**, *55*, 2063–2066; *Angew. Chem.* **2016**, *128*, 2103–2106.

[S3] R. M. Dodson, J. K. Seyler, *J. Org. Chem.* **1951**, *16*, 461–465.

Crystallization:

3: Yellow crystals were obtained by slow evaporation of methanol into the aqueous solution of **3** (5 mM) at 4 °C (in refrigerator) for around three weeks.

3•(8)$_2$: First, slowly evaporated the aqueous sample solution **3•(8)**$_2$ (2.5 mM) at room temperature for around two or three weeks. During the crystallization, the solution became suspended and precipitates were formed. Then, filtrated the solution, continued slowly evaporating the aqueous sample solution at room temperature for additional two or three weeks. Light-yellow crystals were finally obtained.

3•9: Yellow crystals were obtained by slow evaporation of methanol into the aqueous solution of **3•9** (5 mM) at room temperature for two or three weeks.

3′•12: First, slowly evaporated the aqueous sample solution **3′•12** (2.5 mM) in a vial at room temperature for around two or three weeks. During the crystallization, the solution became suspended and precipitates were formed. Then, filtrated the solution, continued slowly evaporating the aqueous sample solution at 4 °C (in refrigerator, with $MgSO_4$ in a sealed flask) for additional two or three weeks until the solution was almost dried. Light-yellow crystals were finally obtained.

Crystallographic study

Crystallographic diffraction data were measured on a Bruker APEX-II/CCD diffractometer or a Bruker Photon 100 CMOS diffractmeter equipped with a focusing mirror (Mo Kα radiation λ = 0.71073 Å) with a cryostat system equipped with a N_2 generator. The crystals were removed from the solution, quickly attached to a loop of nylon fiber with antifreeze reagent (paraton-N or mineral oil), and mounted on a goniometer. The structures were solved by direct methods (SHELXS) and refine by full-matrix least-squares calculations (SHELXL-2014) of F^2. Hydrogen atoms were fixed at calculated positions and refined using a riding model.

Structural analysis of **3•(8)**$_2$: The structure was refined as a 2-component twin. All atoms except for Pd(II) were isotropically refined. Solvents and nitrates were severely disordered. Due to the poor diffraction of the crystal, constraints were applied for the refinement. As for one of the $M_{20}L_8$ capsule **3**, the constraints (AFIX 66) were applied to panel ligands due to the disorder. For naphtylsilanetriols **8**, constraints (AFIX 116) were applied. Several restraints were applied on the basis of the chemical geometry.

Structural analysis of **3•9**: The thermal temperature factors of all atoms except for Pd(II) were isotropically refined due to the poor diffraction.

Table S1. Crystal data and structure refinement for **3** (CCDC 1498170).

Identification code	wang52	
Empirical formula	$C_{176}H_{532}N_{135}O_{209}Pd_{20}$	
Formula weight	10013.33	
Temperature	90(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	$P\bar{1}$	
Unit cell dimensions	a = 25.125(7) Å	α = 71.625(3) °
	b = 25.841(9) Å	β = 74.386(3) °
	c = 36.446(9) Å	γ = 67.204(3) °
Volume	20408(10) Å^3	
Z	2	
Density (calculated)	1.630 Mg•m^{-3}	
Absorption coefficient	0.970 mm^{-1}	
F(000)	10250	
Crystal size	0.18 × 0.15 × 0.15 mm^3	
θ range for data collection	1.27 to 28.64 °	
Index ranges	$-32 \leqq h \leqq 33$, $-34 \leqq k \leqq 33$, $-48 \leqq l \leqq 46$	
Reflections collected	218154	
Independent reflections	91080 [R_{int} = 0.0641]	
Completeness to θ = 28.64 °	86.9%	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	91080 / 493 / 3689	
Goodness-of-fit on F^2	1.147	
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.1458$, $\omega R_2 = 0.3654$	
R indices (all data)	$R_1 = 0.1861$, $\omega R_2 = 0.3888$	
Largest diff. peak and hole	5.379 and –2.194 e.Å^{-3}	

Table S2. Crystal data and structure refinement for **3´•12** (CCDC 1498173).

Identification code	wang73	
Empirical formula	$C_{108} H_{166} N_{55} O_{59.5} Pd_8 Si_4$	
Formula weight	4150.52	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 24.8071(15) Å	α = 90 °
	b = 18.2127(12) Å	β = 96.472(2) °
	c = 40.556(3) Å	γ = 90 °
Volume	18206(2) $Å^3$	
Z	4	
Density (calculated)	1.514 $Mg{\bullet}m^{-3}$	
Absorption coefficient	0.889 mm^{-1}	
F(000)	8396	
Crystal size	0.20 × 0.15 × 0.10 mm^3	
θ range for data collection	1.64 to 30.59 °	
Index ranges	$-35 \leqq h \leqq 35, -26 \leqq k \leqq 26, -57 \leqq l \leqq 49$	
Reflections collected	202281	
Independent reflections	55720 [R_{int} = 0.0713]	
Completeness to θ = 30.59 °	99.5%	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	55720 / 478 / 1893	
Goodness-of-fit on F^2	1.952	
Final R indices [I>2σ(I)]	R_1 = 0.1562, ωR_2 = 0.4072	
R indices (all data)	R_1 = 0.2592, ωR_2 = 0.4492	
Largest diff. peak and hole	6.632 and –2.394 e.$Å^{-3}$	

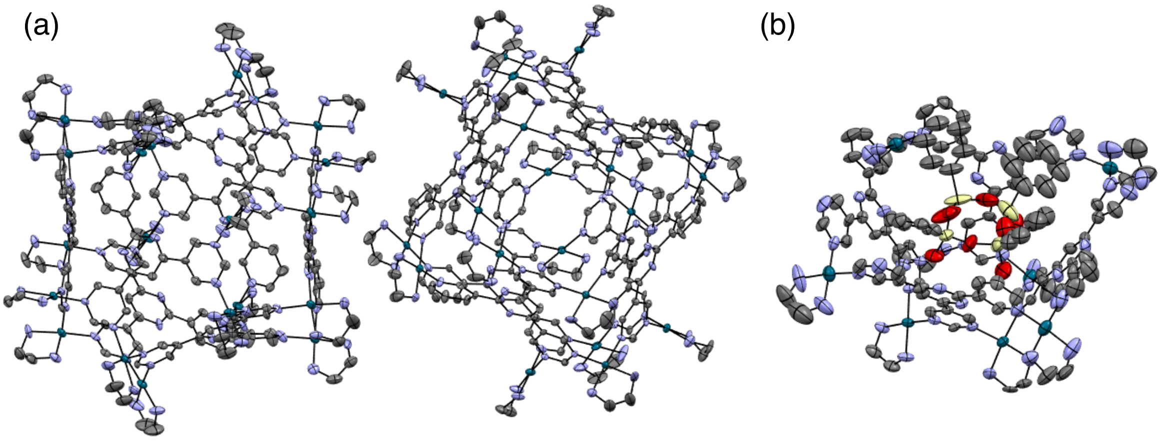


Figure S1. Thermal ellipsoids (50% probability) of the crystal structure of (a) $M_{20}L_8$ capsule **3** and (b) M_8L_4 bowl-cyclic tetrasiloxane **3´•12**. Solvents, nitrates, and hydrogen atoms were omitted for clarity.

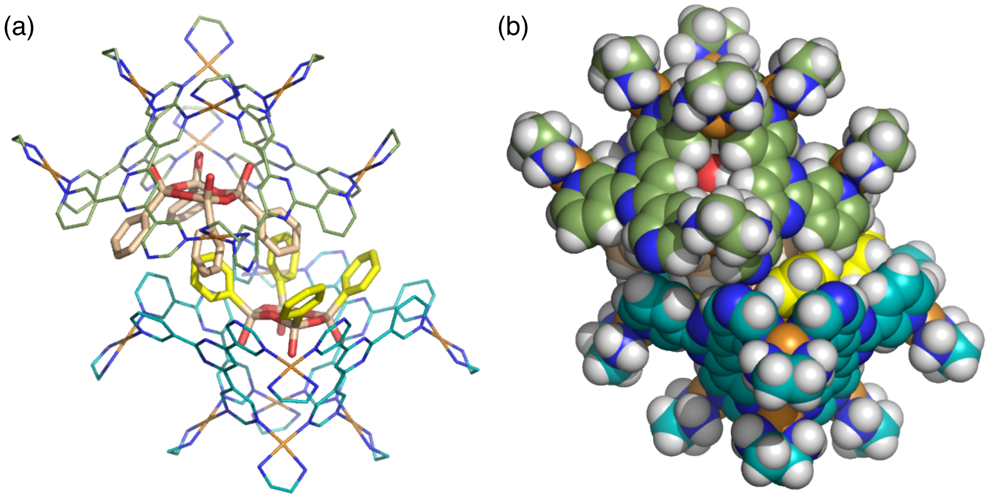


Figure S2. Dimeric formation of **3´•12** observed in the solid state representing in (a) stick and (b) space-filling models.

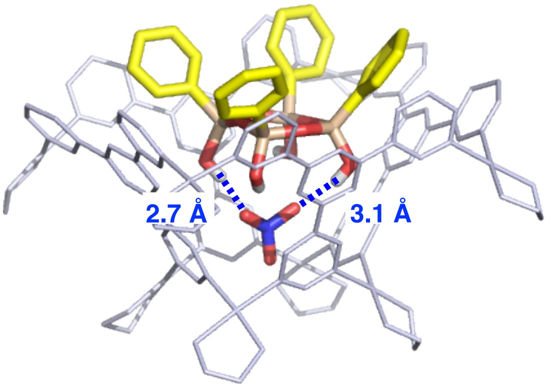


Figure S3. Interactions between cyclic tetrasiloxane **12** and nitrate within the cavity of M_8L_4 bowl **3´**. H-bond distances between O•••(H)–O were shown in this figure.

Table S3. Crystal data and structure refinement for **3**•(**8**)$_2$ (CCDC 1498172).

Identification code	wang71	
Empirical formula	$C_{196} H_{357} N_{118.5} O_{119.5} Pd_{20} Si_3$	
Formula weight	8498.25	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 46.603(6) Å	α = 90 °
	b = 25.734(3) Å	β = 113.398(3) °
	c = 37.303(5) Å	γ = 90 °
Volume	41058(9) Å^3	
Z	4	
Density (calculated)	1.375 Mg•m^{-3}	
Absorption coefficient	0.943 mm^{-1}	
F(000)	17122	
Crystal size	0.20 × 0.15 × 0.08 mm^3	
θ range for data collection	1.63 to 24.37 °	
Index ranges	$-53 \leqq h \leqq 53, -28 \leqq k \leqq 29, -39 \leqq l \leqq 38$	
Reflections collected	296082	
Independent reflections	57298 [R_{int} = 0.1049]	
Completeness to θ = 24.37 °	85.1%	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	57298 / 822 / 1918	
Goodness-of-fit on F^2	1.836	
Final R indices [I>2σ(I)]	R_1 = 0.2071, ωR_2 = 0.4916	
R indices (all data)	R_1 = 0.3022, ωR_2 = 0.5805	
Largest diff. peak and hole	4.698 and –1.694 e.Å^{-3}	

Table S4. Crystal data and structure refinement for **3•9** (CCDC 1498171).

Identification code	wang68	
Empirical formula	$C_{204} H_{351} N_{130} O_{191} Pd_{20}$	
Formula weight	9809.13	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$C2/c$	
Unit cell dimensions	a = 48.457(8) Å	α = 90 °
	b = 27.761(4) Å	β = 108.713(5) °
	c = 37.941(6) Å	γ = 90 °
Volume	48342(13) Å^3	
Z	4	
Density (calculated)	1.348 Mg•m^{-3}	
Absorption coefficient	0.815 mm^{-1}	
F(000)	19732	
Crystal size	0.29 × 0.20 × 0.04 mm^3	
θ range for data collection	1.62 to 24.22 °	
Index ranges	$-55 \leqq h \leqq 55$, $-28 \leqq k \leqq 29$, $-42 \leqq l \leqq 42$	
Reflections collected	77042	
Independent reflections	27490 [R_{int} = 0.0844]	
Completeness to θ = 24.37 °	70.6 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	27490 / 39 / 1297	
Goodness-of-fit on F^2	1.809	
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.1800$, $\omega R_2 = 0.4395$	
R indices (all data)	$R_1 = 0.2464$, $\omega R_2 = 0.4958$	
Largest diff. peak and hole	4.142 and –1.707 e.Å^{-3}	

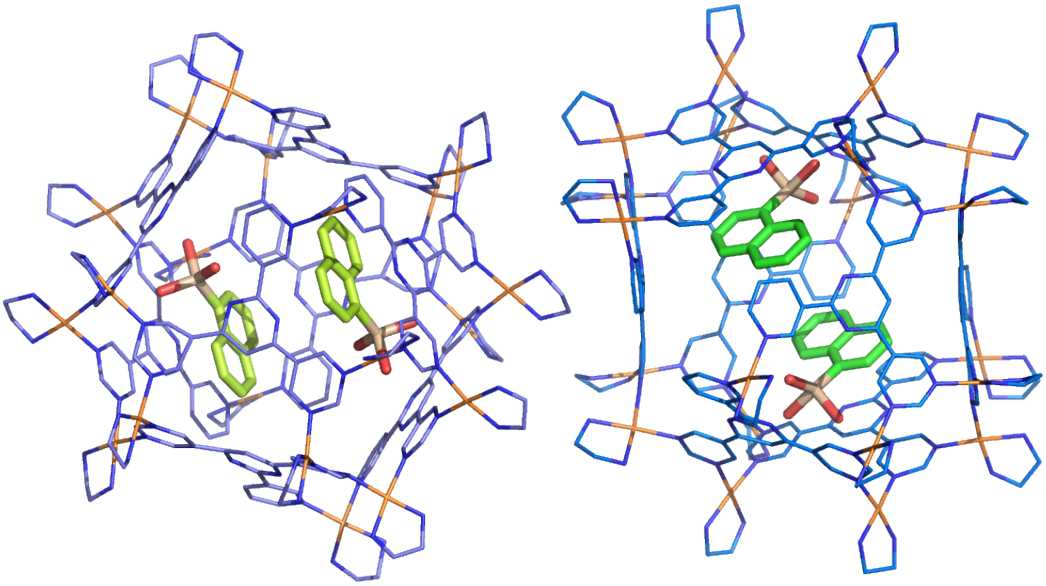


Figure S4. Crystal structure of **3**•(**8**)$_2$. Two crystallographically independent host–guest complexes were observed. Solvents and nitrates were omitted for clarity.

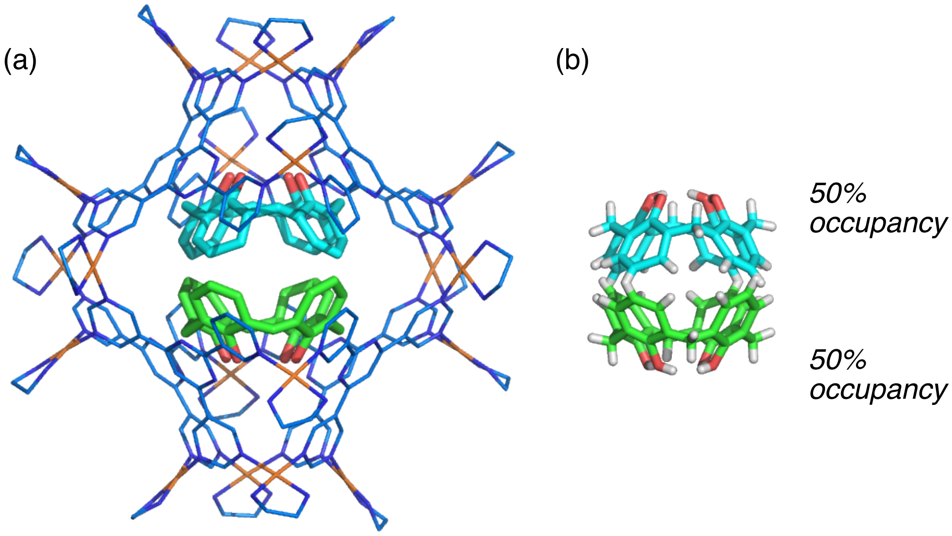


Figure S5. Crystal structure of **3**•**9**. (a) Within the cavity of **3**, calix[4]arene **9** was disordered at two positions (green and cyan, 50% occupancies). (b) Close-up view of the guest disorder. Solvents and nitrates were omitted for clarity.

NMR Spectra

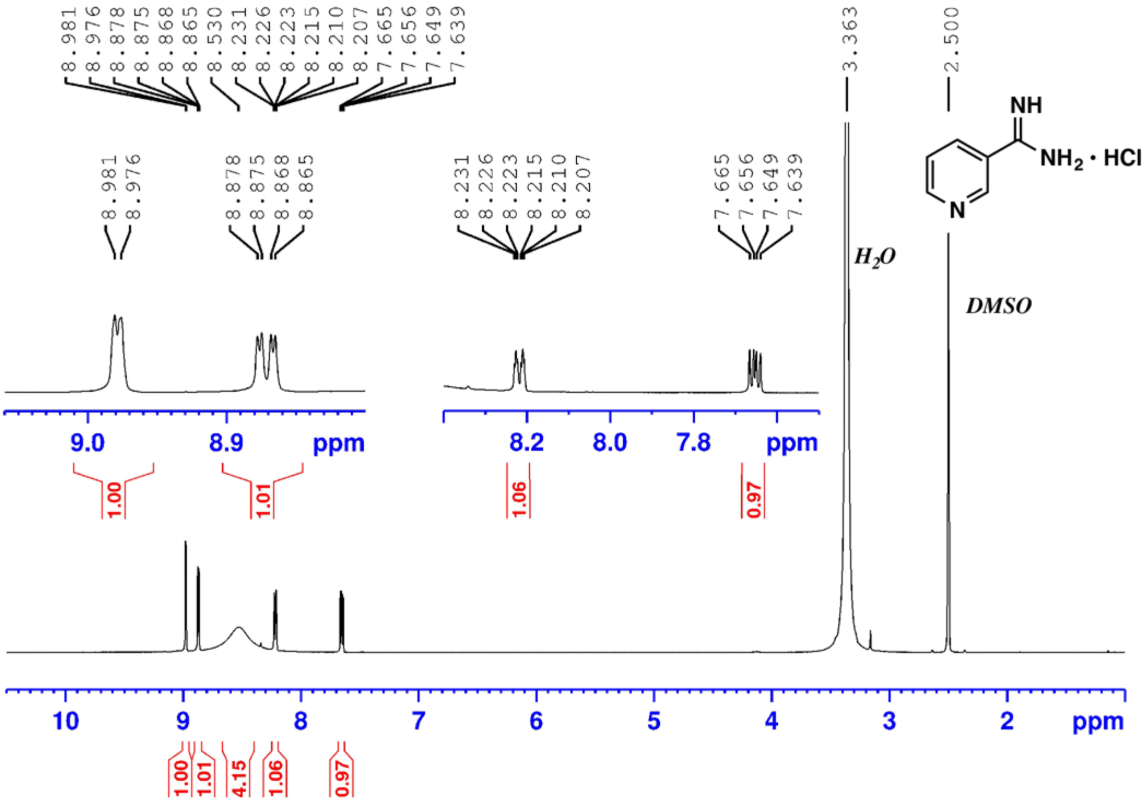


Figure S6. ^{1}H NMR spectrum of pyridine-3-carboxamidamide hydrochloride (500 MHz, 300 K, DMSO-d_6)

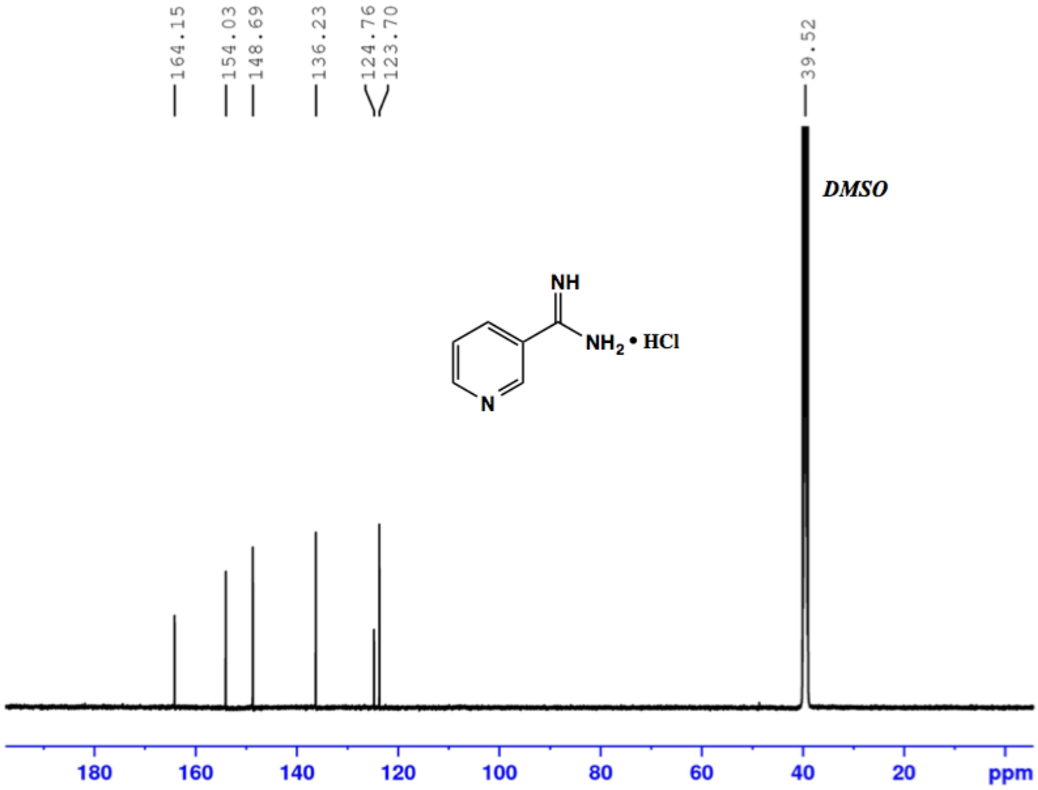


Figure S7. ^{13}C NMR spectrum of pyridine-3-carboximidamide hydrochloride (125 MHz, 300 K, DMSO-d_6)

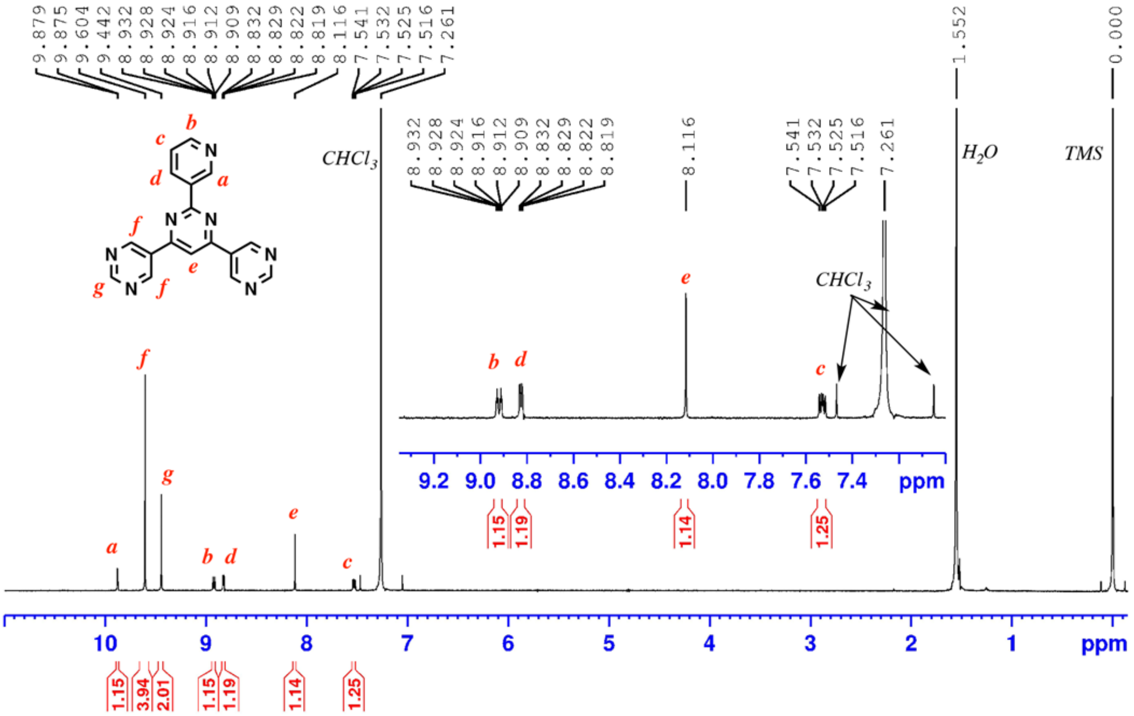


Figure S8. ^{1}H NMR spectrum of ligand **1** (500 MHz, 300 K, $CDCl_3$, TMS).

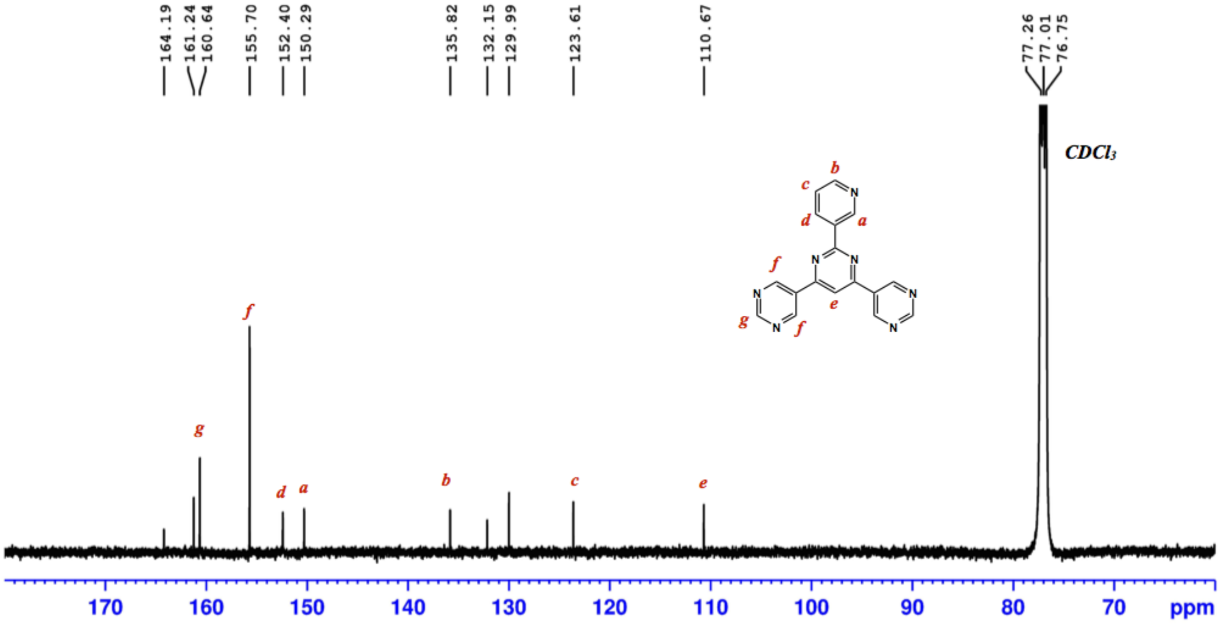


Figure S9. ^{13}C NMR spectrum of ligand **1** (125 MHz, 300 K, $CDCl_3$, TMS).

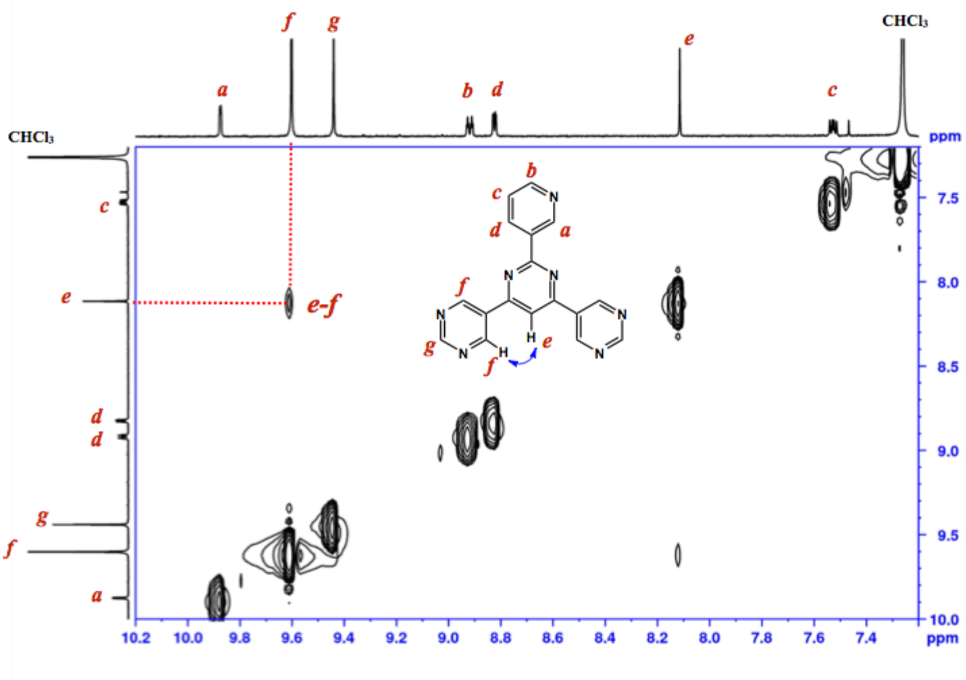


Figure S10. NOE spectrum of ligand **1** (500 MHz, 300 K, $CDCl_3$, TMS)

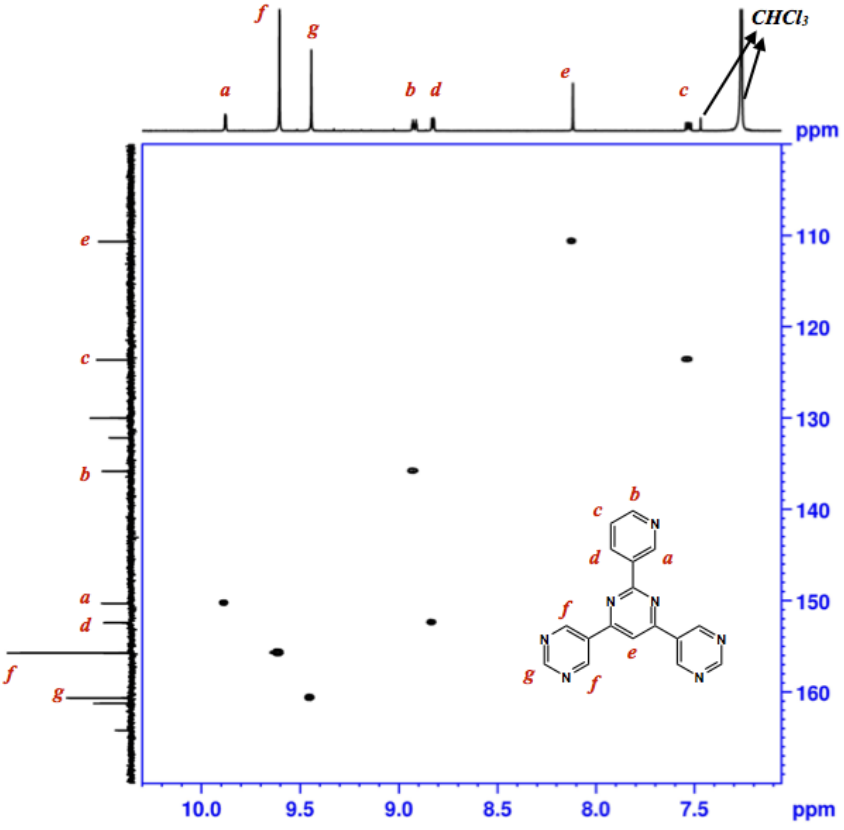


Figure S11. $^1H/^{13}C$ HSQC spectrum of ligand **1** (500 MHz, 300 K, $CDCl_3$, TMS)

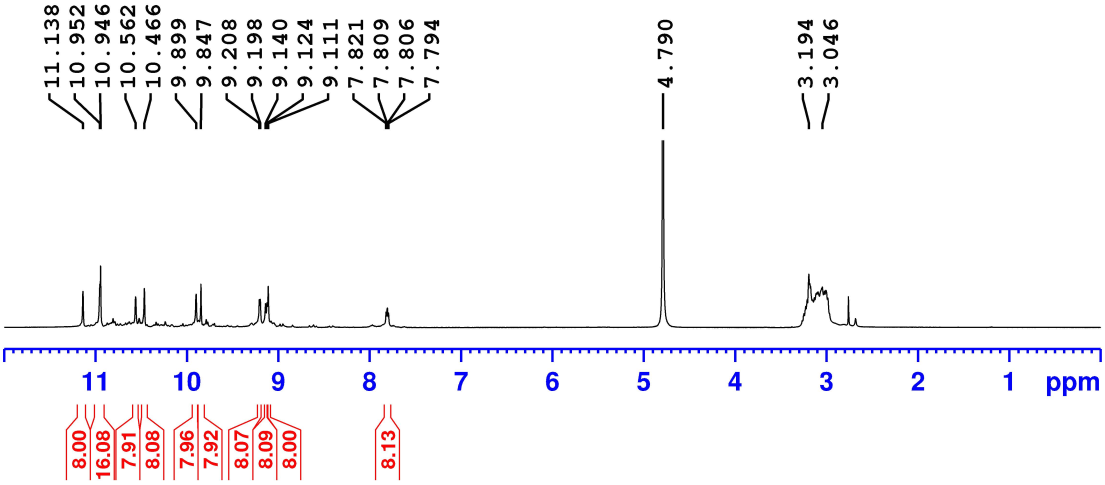


Figure S12. ^{1}H NMR spectrum of $M_{20}L_8$ capsule **3** (500 MHz, 300 K, D_2O)

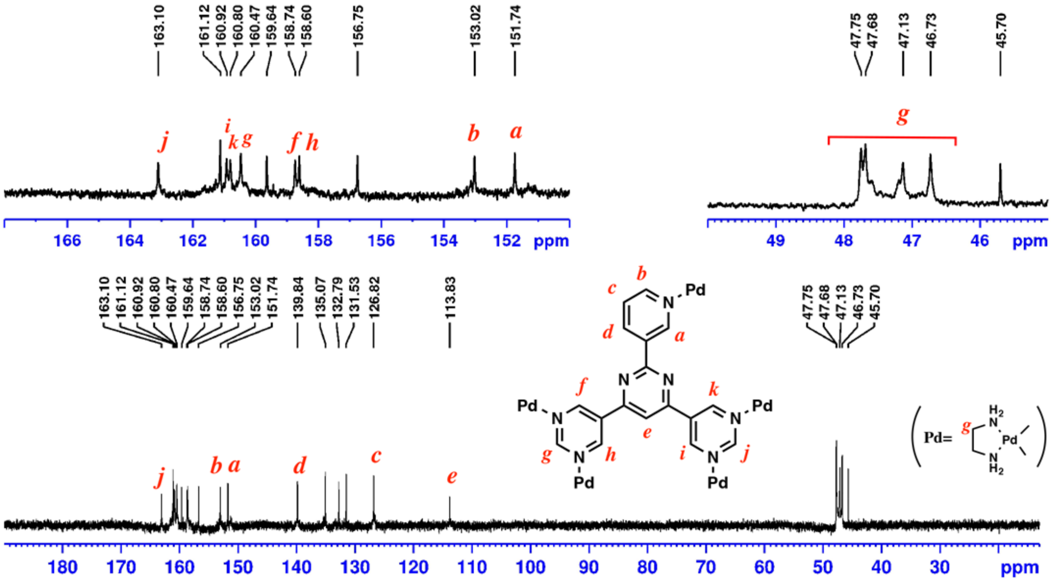


Figure S13. ^{13}C NMR spectrum of $M_{20}L_8$ capsule **3** (125 MHz, 300 K, D_2O)

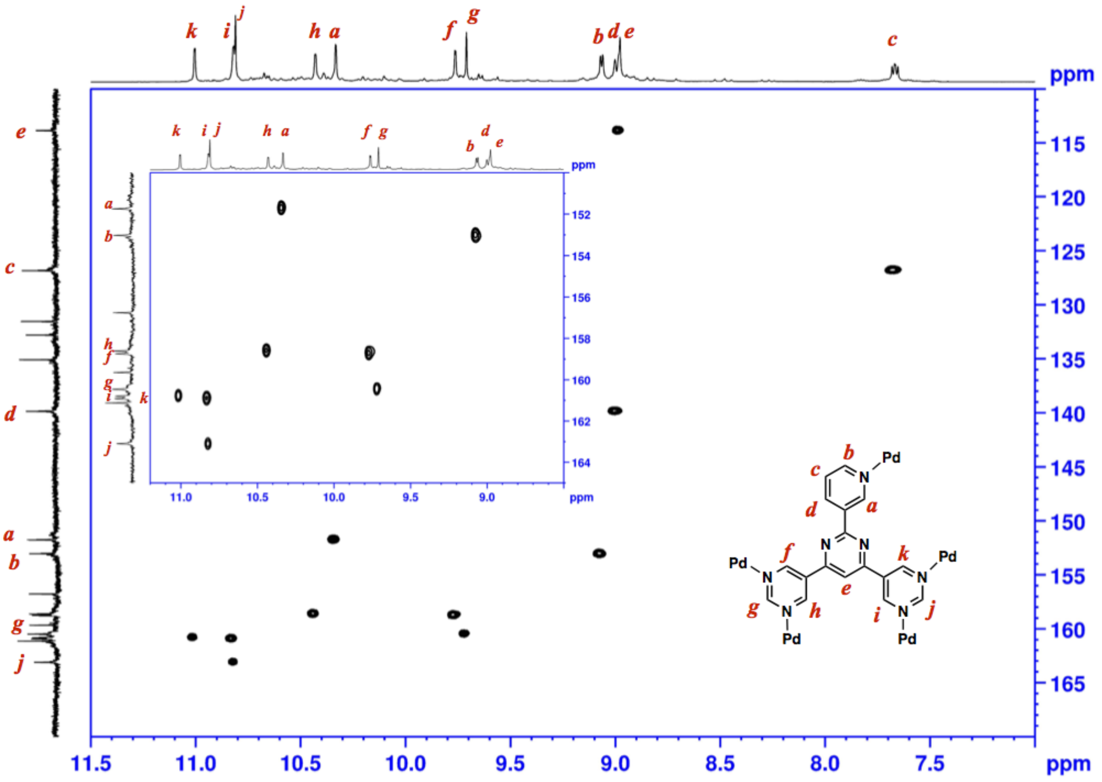


Figure S14. ^{1}H/^{13}C HSQC spectrum of $M_{20}L_8$ capsule **3** (500 MHz, 300 K, D_2O)

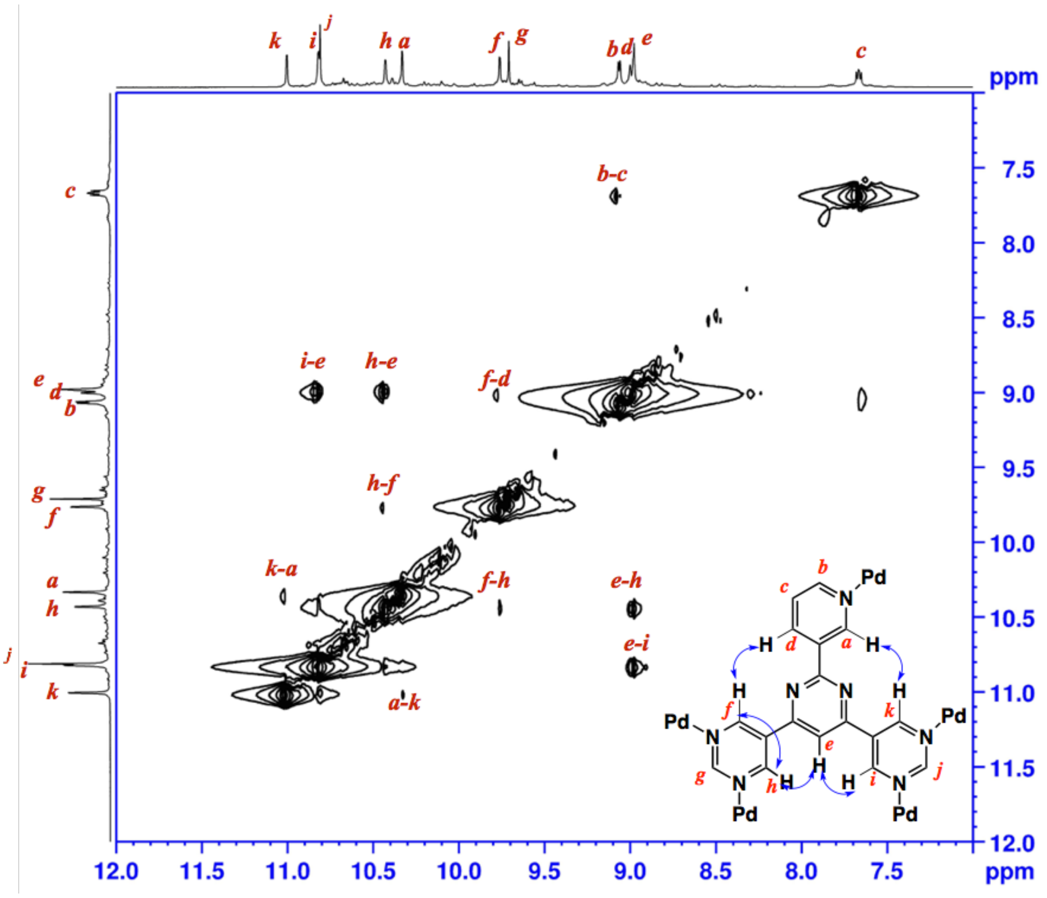


Figure S15. NOE spectrum of $M_{20}L_8$ capsule **3** (500 MHz, 300 K, D_2O)

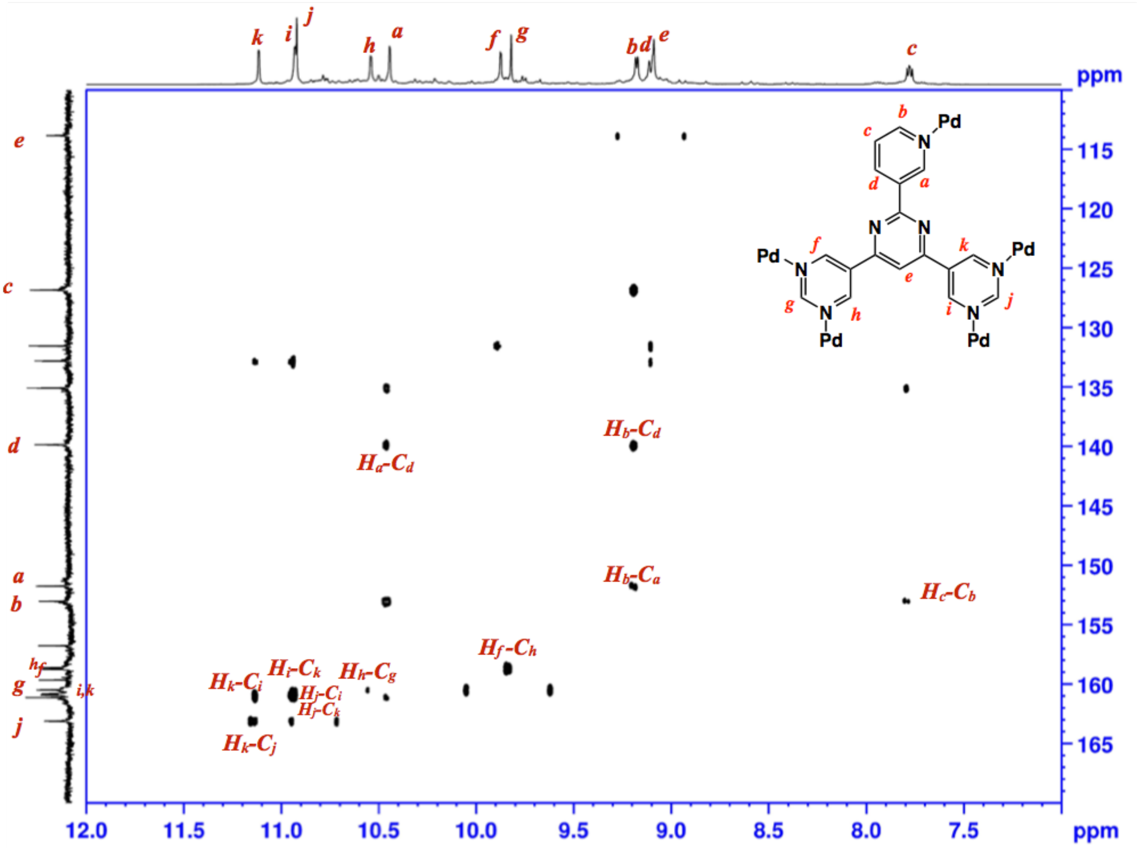


Figure S16. ^{1}H/^{13}C HMBC spectrum of $M_{20}L_8$ capsule **3** (500 MHz, 300 K, D_2O)

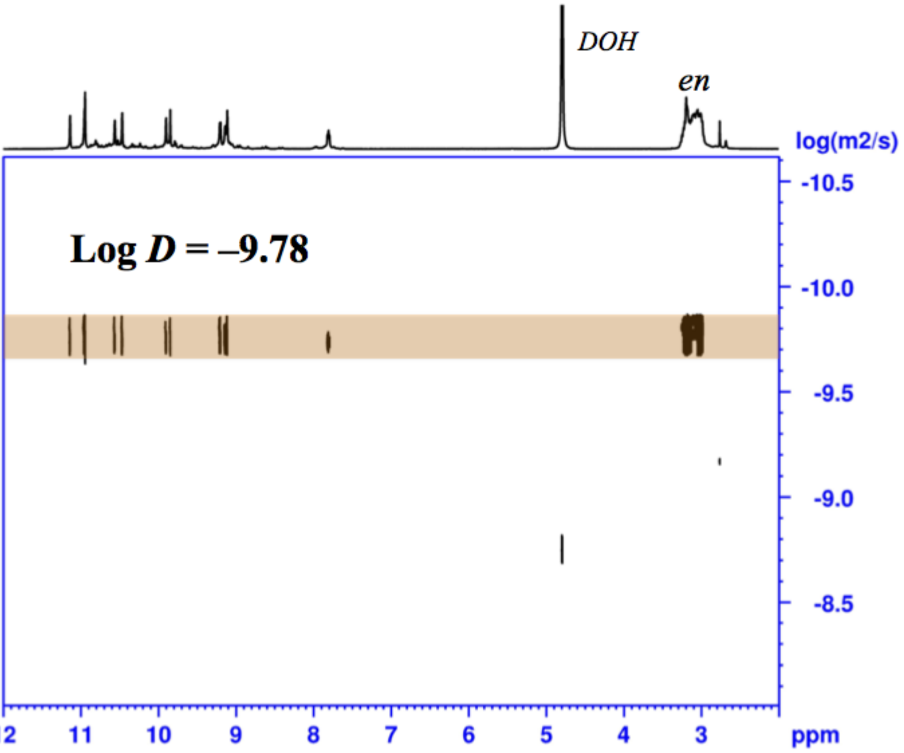
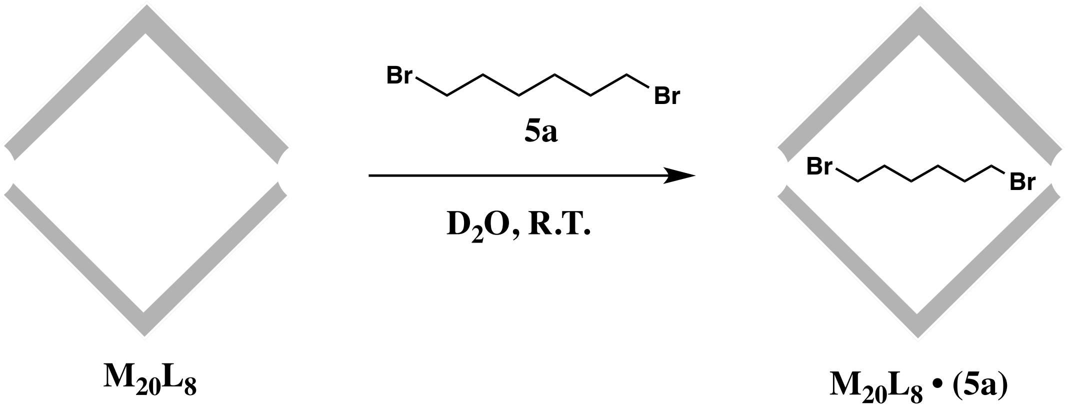


Figure S17. ^{1}H-DOSY spectrum of $M_{20}L_8$ capsule **3** (500 MHz, 300 K, D_2O)

Guest Encapsulation



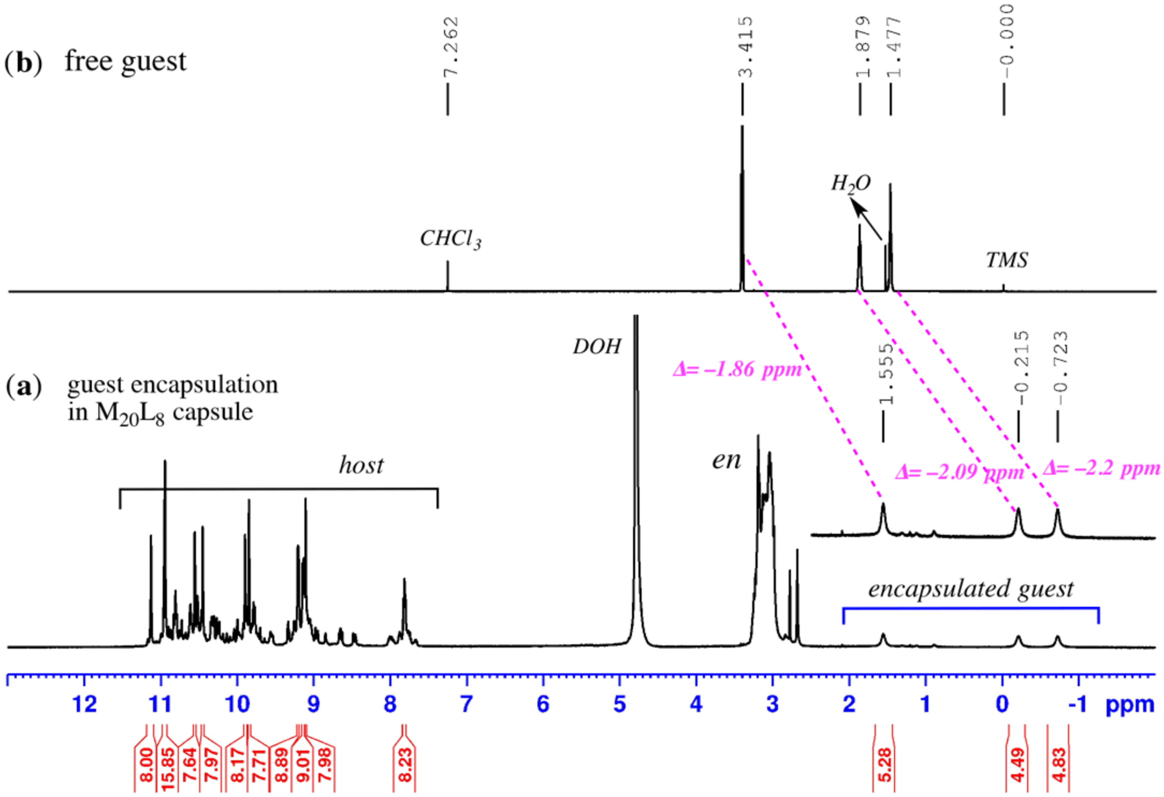


Figure S18. ^{1}H NMR spectra (500 MHz, 300 K) of (a) **3•5a** (guest: 1,6-dibromohexane) in D$_2$O and (b) free guest **5a** in CDCl$_3$ solvent.

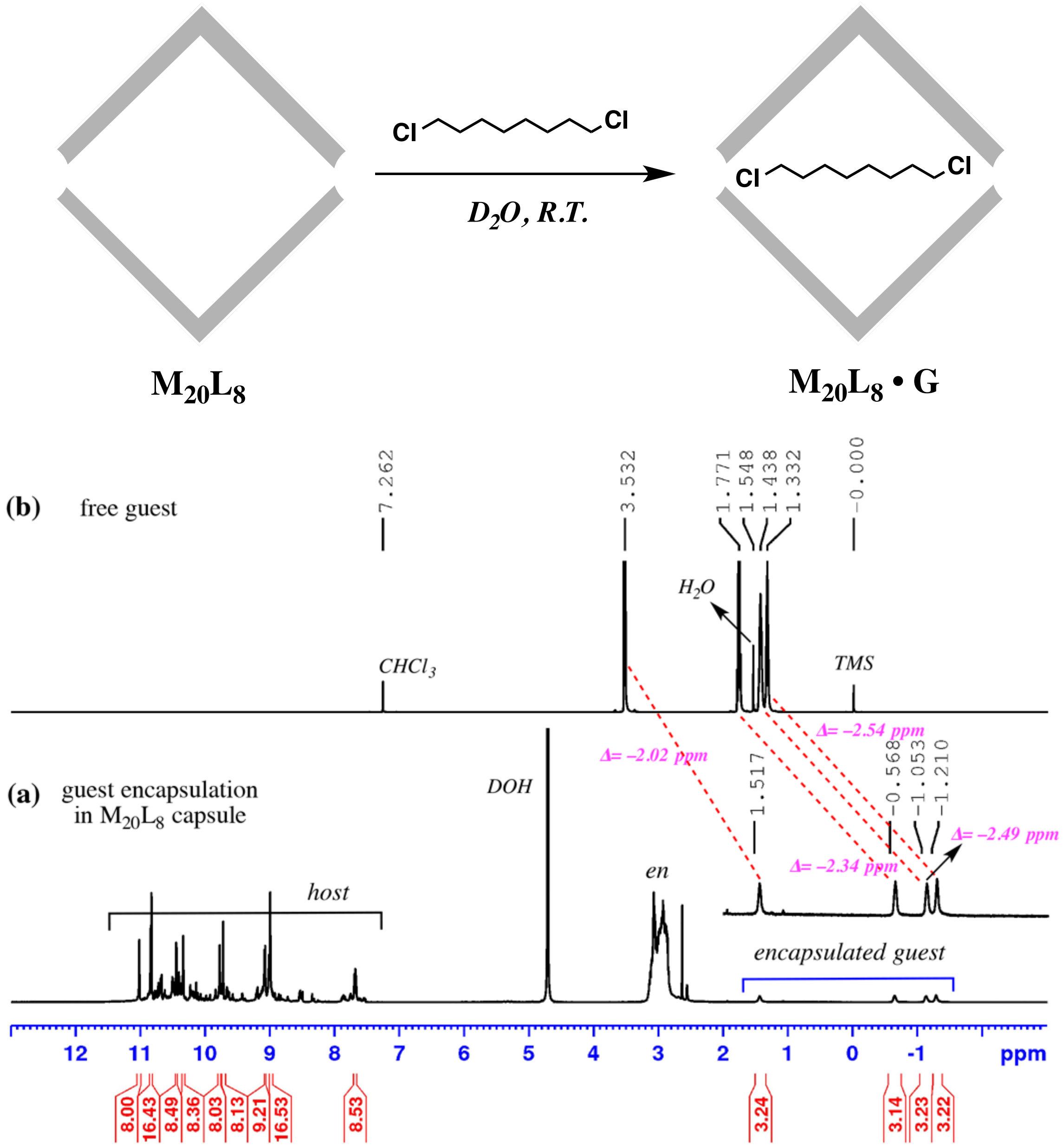
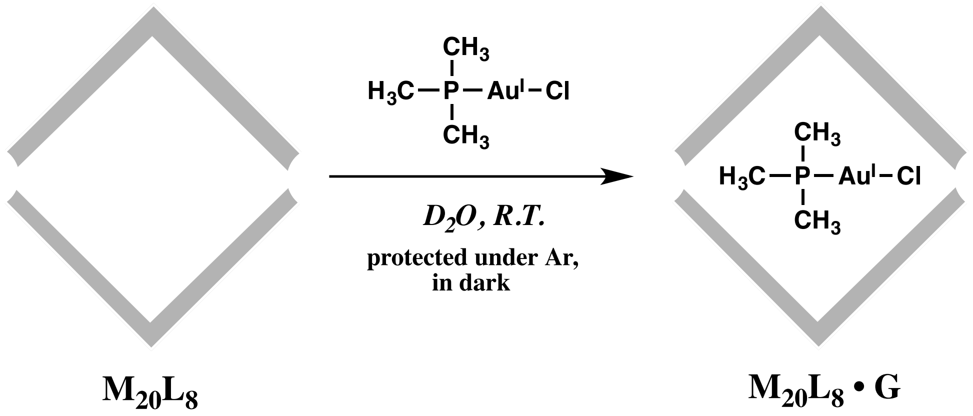


Figure S19. ^{1}H NMR spectra (500 MHz, 300 K) of (a) **3•5b** (guest: 1,8-dichlorooctane) in D_2O and (b) free guest **5b** in $CDCl_3$ solvent.



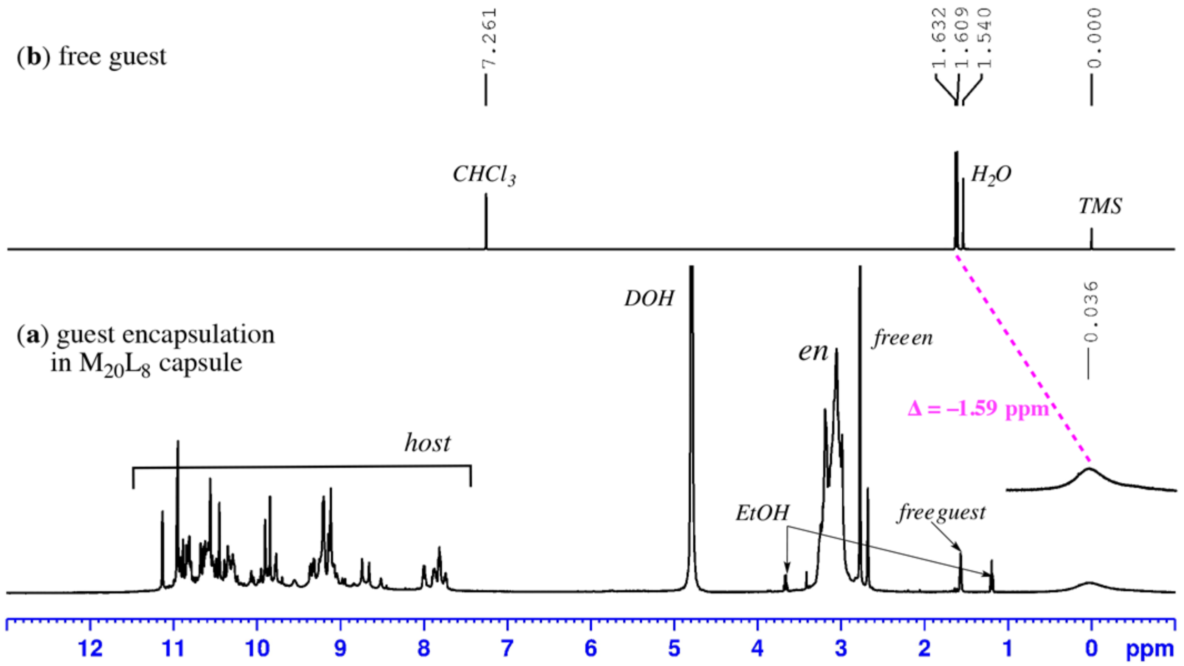


Figure S20. ^{1}H NMR spectra (500 MHz, 300 K) of (a) **3•6** in D_2O and (b) free guest **6** in $CDCl_3$ solvent. (note: the gold complex **6** is slightly souble in water)

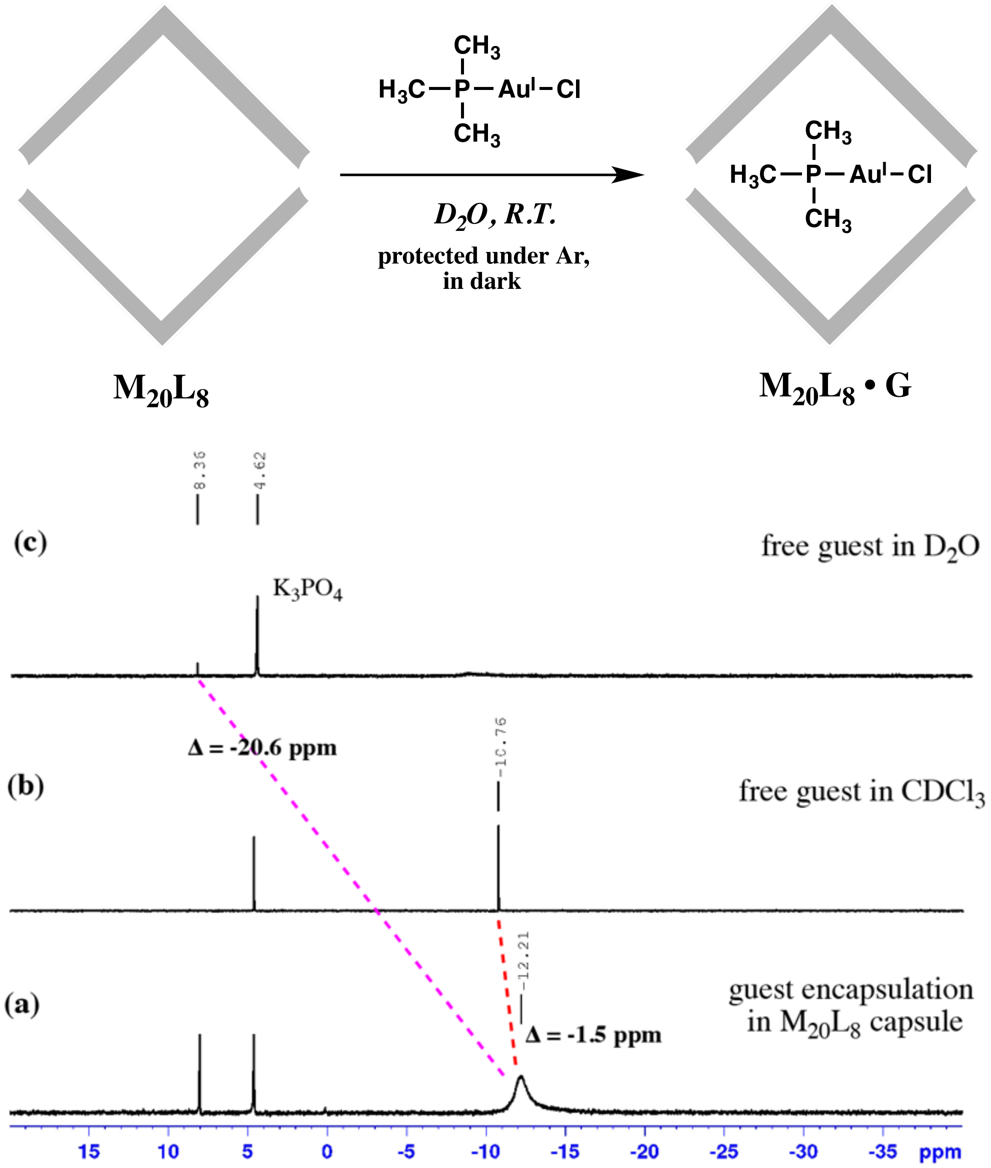
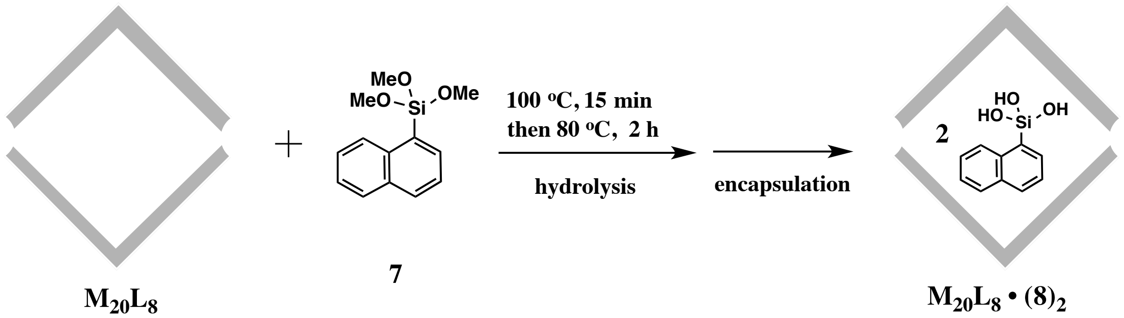


Figure S21. ^{31}P NMR spectra (202 MHz, 300 K) of (a) **3•6**, (b) free guest **6** in CDCl$_3$ solvent (c) free guest **6** in D$_2$O solvent (inner standard: K$_3$PO$_4$/D$_2$O in a sealed capillary). (note: the gold complex **6** is slightly soluble in water).



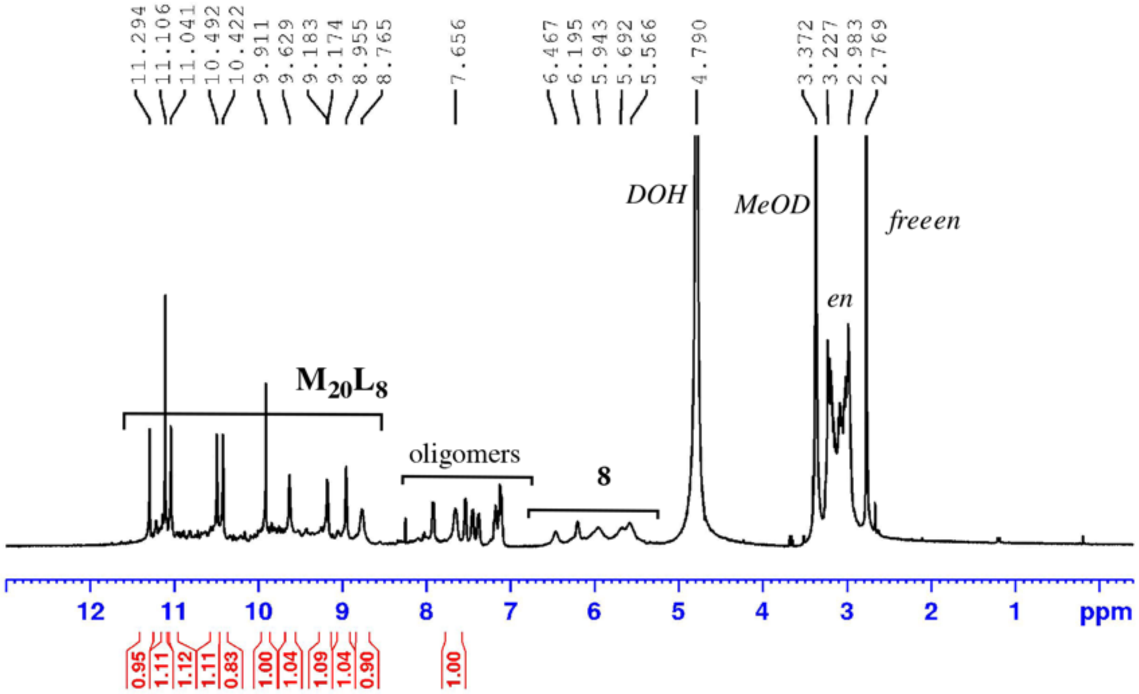
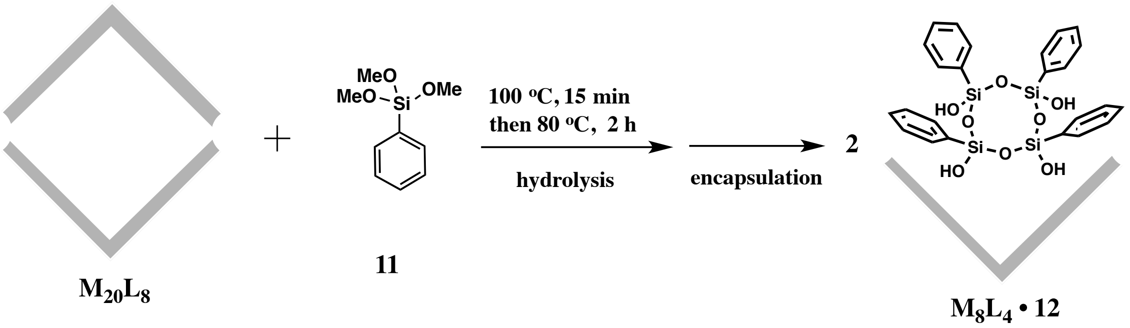


Figure S22. ^{1}H NMR spectrum (500 MHz, 300 K) of (a) **3•(8)$_2$** in D_2O.



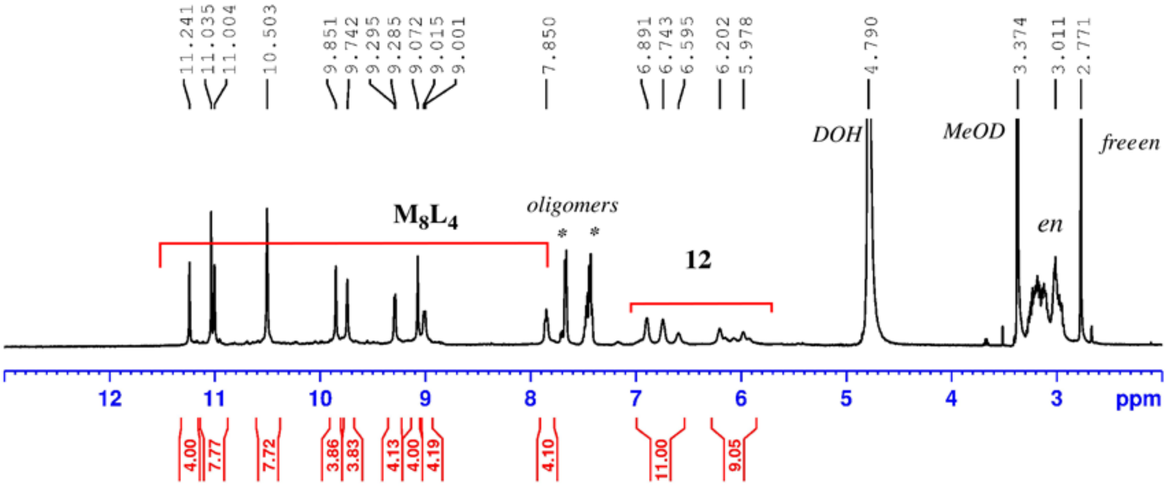


Figure S23. ^{1}H NMR spectrum (500 MHz, 300 K, D_2O) of **3′•12**.

MS analysis

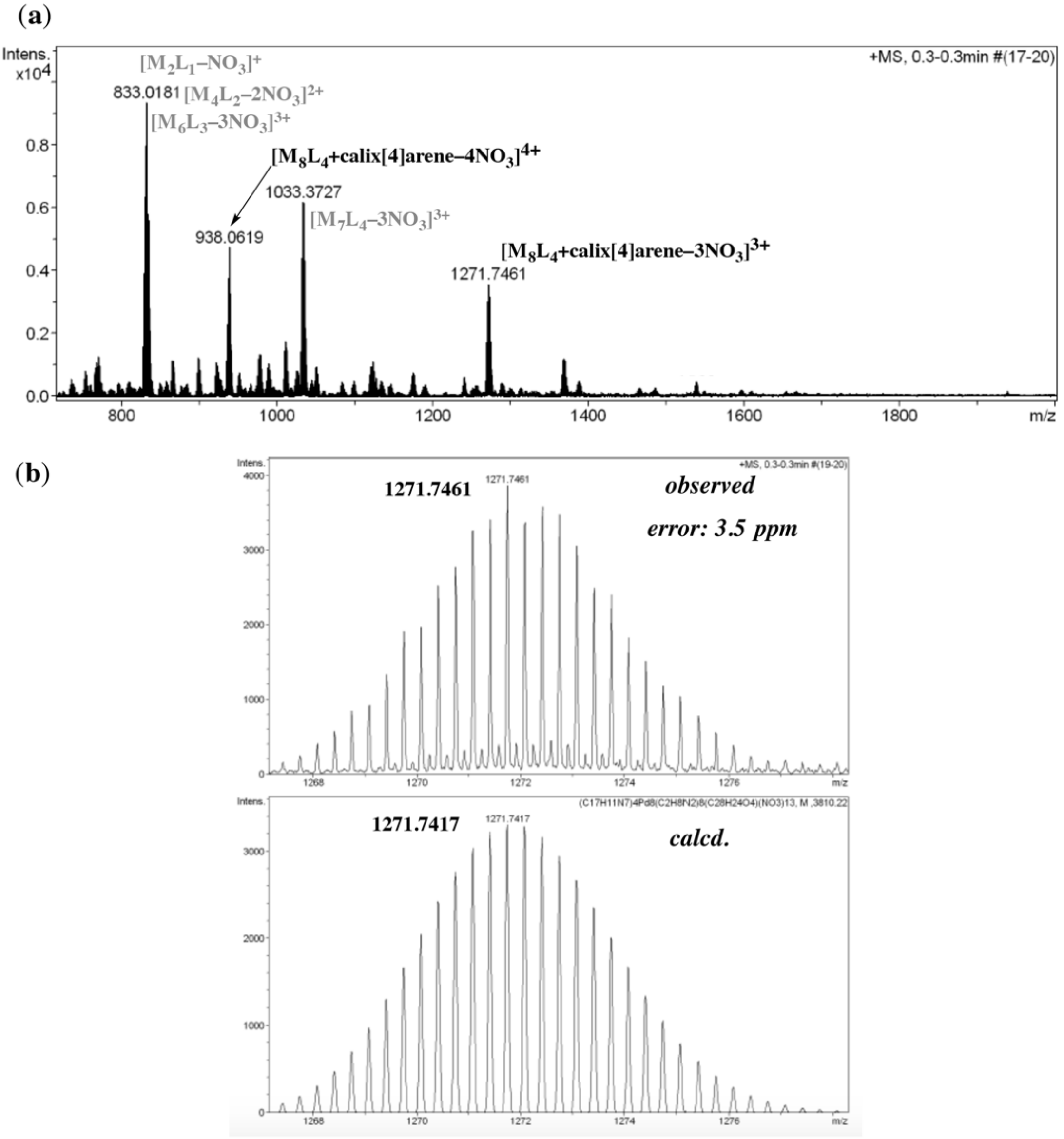


Figure S24. High resolution ESI–MS spectra of **3´•9** of (a) all region and (b) isotope pattern of the signal at *m/z* = 1272 (solvent: H_2O, ISCID 2 eV, Quadropole Ion Energy 5 eV, Collision Cell Energy 1 eV. Sample ([**1**] = 16 mM) was diluted 10 times for measurement).

Molecular modeling

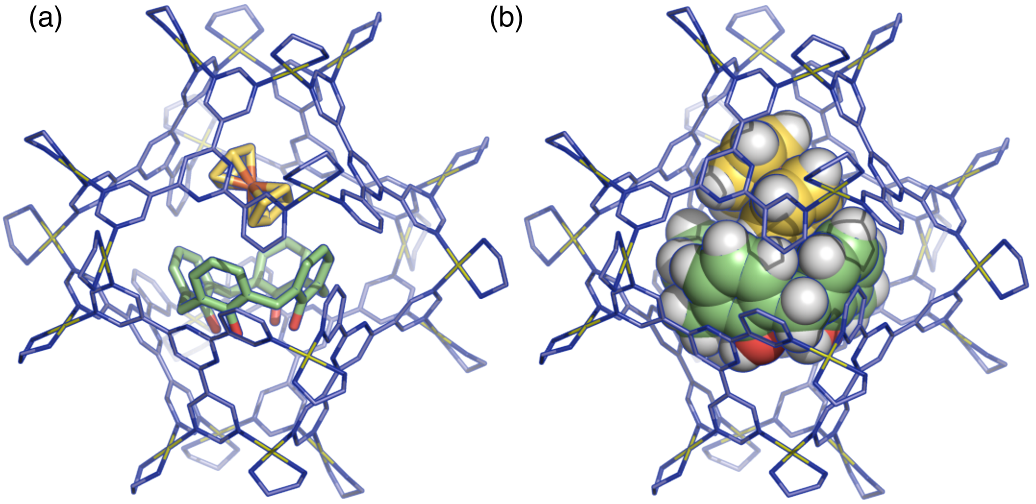


Figure S25. Geometry-optimized structure of **3**•(**9**•**10**). The pairwisely-encapsulated guests were represented in (a) stick and (b) space-filling models. Material Studio 2016 (BIOVIA®) was used for this calculation.

Comparison of the capsular frameworks 3 and 4

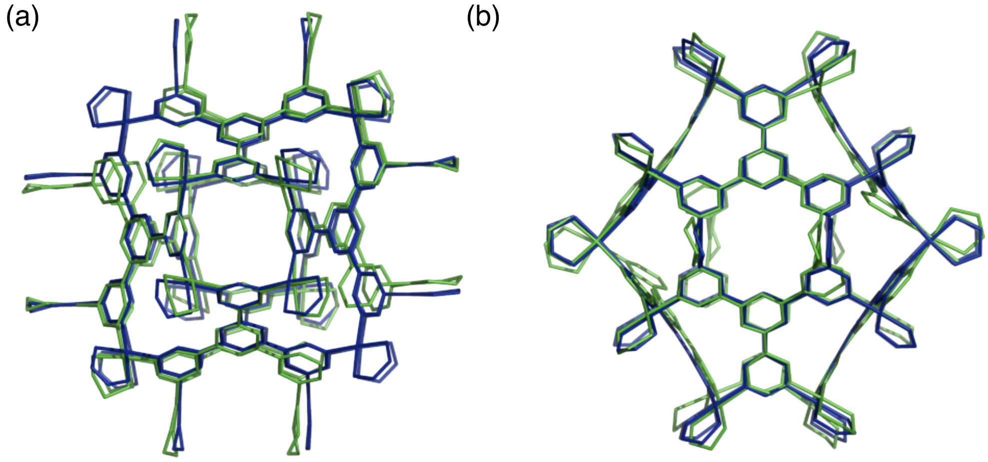


Figure S26. Overlay of the crystal structures of the capsular frameworks **3** (green) and **4** (blue) shown as (a) top and (b) side views. The coordinates of **4** are from the previous reports (ref 4).