Electronic Supplementary Material (ESI) for ChemComm.

A chromogenic molecular capsule attributable to dipolar amide resonance structure

Yeon Sil Park, Juwan Park, and Kyungsoo Paek,*

Department of Chemistry, Soongsil University, Seoul 156-743, Korea
kpaek@ssu.ac.kr

Supporting Information

Table of Contents

1. Syntheses

3. Acid (CH_3SO_3H) and base (DBU) titration experiments of molecular capsule $\mathbf{2}_2$

6. Methanol addition experiments of the protonated molecular capsule $\mathbf{2}_2\cdot8H^+$

1. Syntheses

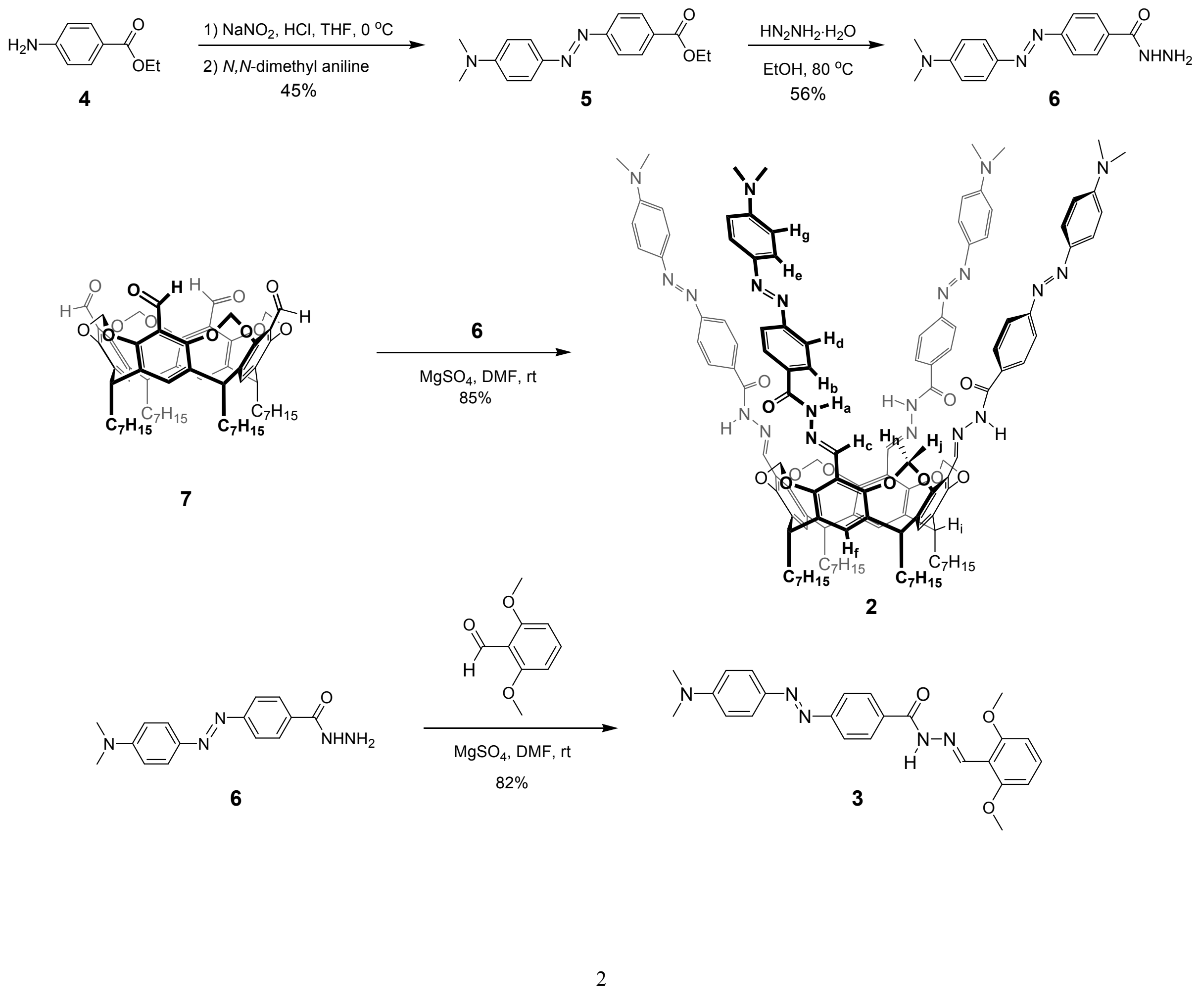
1-1. General

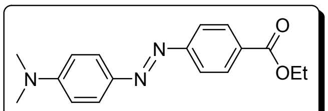
All commercially obtained solvents and reagents were used without further purification. *N*,*N*-Dimethylformamide (DMF) was obtained from Aldrich Chemical Company, Inc. as anhydrous, 99+% grade. Analytical thin-layer chromatography (TLC) was carried out on Merck silica gel 60 F_{254} glass plate and column chromatography was performed on Merck silica gel 60 (70 - 230 mesh).

NMR solvents were obtained as chloroform-*d*, 99.96 atom %D and toluene-d_8, 99.9 atom %D from Aldrich Chemical Company, Inc.; DMSO-d_6 99.8 atom %D from Cambridge Isotope Laboratories, Inc.

NMR spectra were measured on a Bruker Avance Digital 400 spectrometer at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR. Chemical shifts were recorded in parts per million (δ) using either relative to residual undeuterated solvent resonances and coupling constants in hertz (Hz). UV-Visible spectra were recorded on a JASCO V-550 spectrophotometer. Matrix assisted laser desorption/ionization mass-time of flight (MALDI-TOF) spectra were obtained using an Applied Biosytems Voyager-DE STR biospectrometer. Elemental analysis was measured on a Thermo Finnigam-Flash 2000 series.

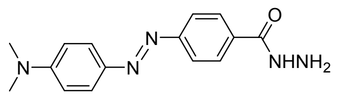
1-2. Synthetic procedures





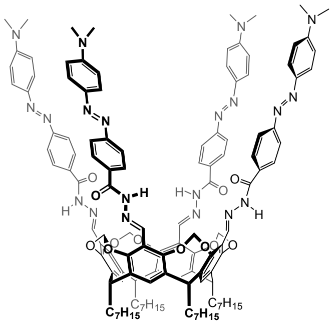
5

Compound 5 : A mixture of ethyl 4-aminobenzoate (2.60 g, 15.7 mmol) and HCl (4.5 mL) in THF (10 mL) was stirring for 30 min at 0 ^{o}C and then a solution of $NaNO_2$ (1.20 g, 17.4 mmol) in H_2O (5 mL) precooled to 0 °C was added dropwise. The reaction mixture was stirred at 0 ^{o}C for 30 min. To this solution was added slowly a solution of *N,N*-dimethylaniline (1.90 g, 15.7 mmol) in THF (4 mL) at 0 °C. After being stirred for another 16 h at 0 ^{o}C, the reaction mixture was concentrated under reduced pressure. The residue was dissolved with CH_2Cl_2 (30 mL) and was washed with 1N NaOH, water, and dried over $MgSO_4$, filtered. Removal of the solvent under reduced pressure afford the crude product, which was further recrestallized from CH_2Cl_2/CH_3OH (7:3) to give **5** as a reddish-colored solid (2.1 g, 45%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.8 Hz, 2H, Ar-*H*), 7.92 (d, *J* = 9.2 Hz, 2H, Ar-*H*), 7.87 (d, *J* = 8.8 Hz, 2H, Ar-*H*), 6.77 (d, *J* = 9.2 Hz, 2H, Ar-*H*), 4.41 (q, *J* = 7.2 Hz, 2H, $-CO_2CH_2CH_3$), 3.12 (s, 6H, $-N(CH_3)_2$), 1.43 (t, *J* = 7.2 Hz, 3H, $-CO_2CH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 156.1, 153.1, 143.9, 141.6, 130.7, 125.7, 122.1, 111.7, 61.3, 40.5, 14.6; HRMS (MALD-TOF; M + H^+) calcd for $C_{17}H_{20}N_3O_2^+$: 298.1550; found 298.1568.



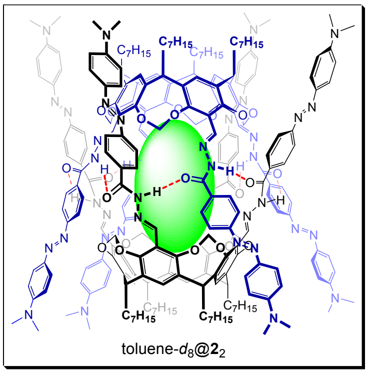
6

Compound 6: To a solution of compound **5** (1.0 g, 3.4 mmol) in ethanol (30 mL) was added hydrazine hydrate (85%, 20 mL). The solution was heated to reflux for 4 h and then cooled to room temperature. The reaction mixture was concentrated under reduced pressure and the formed precipitate was collected by filtration and washed with water and methanol to give the required product **6** as a red solid (0.54 g, 56%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.87 (s, 1H, -CON*H*-NH$_2$), 7.96 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 7.82 (d, *J* = 8.8 Hz, 2H, Ar-*H*), 7.80 (d, *J* = 8.8 Hz, 2H, Ar-*H*), 6.85 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 4.53 (s, 2H, -CONH-N*H*$_2$), 3.08 (s, 6H, $-N(CH_3)_2$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.3, 153.9, 152.8, 142.6, 133.6, 128.1, 125.1, 121.5, 111.6, 39.8; HRMS (MALD-TOF; M + H^+) calcd for $C_{15}H_{18}N_5O^+$: 284.1506; found 284.1517.



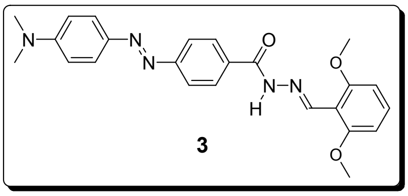
2

Cavitand 2: A mixture of tetraformyl cavitand **7** (1.00 g, 0.96 mmol), compound **6** (1.15 g, 4.0 mmol), $MgSO_4$ (3 g), and anhydrous DMF (50 mL) was stirred for 4 days at room temperature under an argon atmosphere. The reaction mixture was concentrated under reduced pressure. The residue was dissolved with toluene (80 mL), filtered through a pad of celite. After removal of solvent, purification by short column chromatography on silica gel (CH_2Cl_2/EtOAc = 7:3) provided the product as a white solid (1.7 g, 85%): ^{1}H NMR of cavitand **2** (400 MHz, 10% CD_3OD/toluene-d_8) δ 8.80 (s, 4H, imine -C*H*=N-), 8.07 (d, *J* = 8.0 Hz, 8H, Ar-*H*), 8.00-7.96 (m, 16H, Ar-*H*), 7.55 (s, Ar-*H*), 6.56 (d, *J* = 7.6 Hz, 4H, $-OCH_{out}H_{in}O-$), 6.40 (d, *J* = 9.2 Hz, 8H, Ar-*H*), 5.40 (t, *J* = 8.0 Hz, 4H, -C*H*-), 5.00 (d, *J* = 7.6 Hz, 4H, $-OCH_{out}H_{in}O-$), 2.46 (s, 24H, $-N(CH_3)_2$), 2.41 (m, 4H, $-CH_2-$), 1.45 - 1.28 (m, 40H, $-(CH_2)_5-$), 0.92 (t, *J* = 6.8 Hz, 12H, $-CH_3$); Anal. Calcd for $C_{124}H_{140}N_{20}O_{12}$: C, 70.83; H, 6.71; N, 13.32. Found: C, 70.69; H, 6.84; N, 13.24.



toluene-d_8@**2**$_2$

^{1}H NMR of **capsule** (400 MHz, toluene-d_8) δ 12.79 (s, 8H, amide -N*H*), 9.07 (d, *J* = 8.8 Hz, 16H, Ar-*H*), 8.83 (s, 4H, imine -C*H*=N-), 8.32 (d, *J* = 8.8 Hz, 16H, Ar-*H*), 8.07 (d, *J* = 9.2 Hz, 16H, Ar-*H*), 7.24 (s, 8H, Ar-*H*), 6.41 (d, *J* = 9.2 Hz, 16H, Ar-*H*), 6.33 (d, *J* = 7.6 Hz, 8H, -OC*H*$_{out}$H$_{in}$O-), 4.89 (t, *J* = 8.0 Hz, 8H, -C*H*-), 4.35 (d, *J* = 7.6 Hz, 8H, -OCH$_{out}$*H*$_{in}$O-), 2.41 (s, 48H, -N(CH_3)$_2$), 1.84 (m, 8H, -CH_2-), 1.20 - 1.09 (m, 80H, -(CH_2)$_5$-), 0.84 (t, *J* = 7.2 Hz, 24H, -CH_3); ^{13}C NMR of **capsule** (100 MHz, toluene-d_8) δ 164.4, 156.7, 155.9, 154.0, 153.3, 145.4, 144.5, 137.9, 133.9, 130.5, 126.3, 123.7, 122.3, 121.9, 112.2, 101.6, 40.0, 37.4, 32.6, 30.9, 30.5, 30.0, 28.5, 23.3, 14.6.



3

Model compound 3: This compound was prepared as an orange solid (82%) from the reaction of 2,6-dimethoxybenzaldehyde and compound **6** following the procedure described above for preparing cavitand **2**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.76 (s, 1H, -CON*H*-NH$_2$), 8.65 (s, 1H, imine -C*H*=N-), 8.07 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 7.87 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 7.84 (d, *J* = 9.2 Hz, 2H, Ar-*H*), 7.36 (t, *J* = 8.4 Hz, 1H, Ar-*H*), 6.86 (d, *J* = 9.2 Hz, 2H, Ar-*H*), 6.74 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 3.82 (s, 6H, -OCH_3), 3.09 (s, 6H, -N(CH_3)$_2$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.1, 158.7, 154.2, 152.9, 143.6, 142.7, 133.8, 131.2, 128.8, 125.2, 121.6, 111.6, 111.1, 104.4, 56.0, 39.8; HRMS (MALD-TOF; M + H$^+$) calcd for $C_{24}H_{26}N_5O_3^+$: 432.2030; found 432.2042.

1-3. ^{1}H , ^{13}C NMR, and 2D-NOESY Spectra

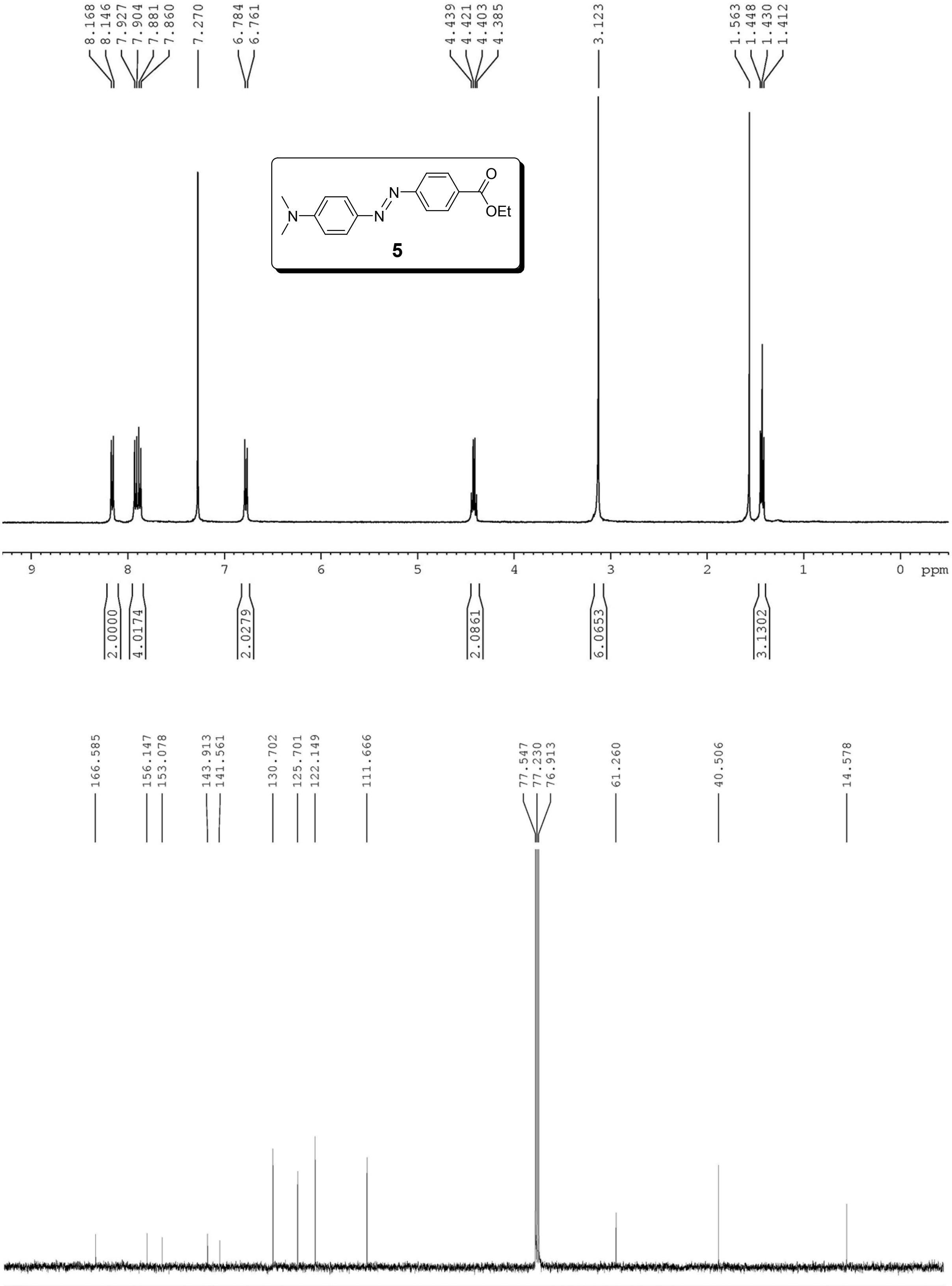


Fig. S1. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of compound **5** in $CDCl_3$.

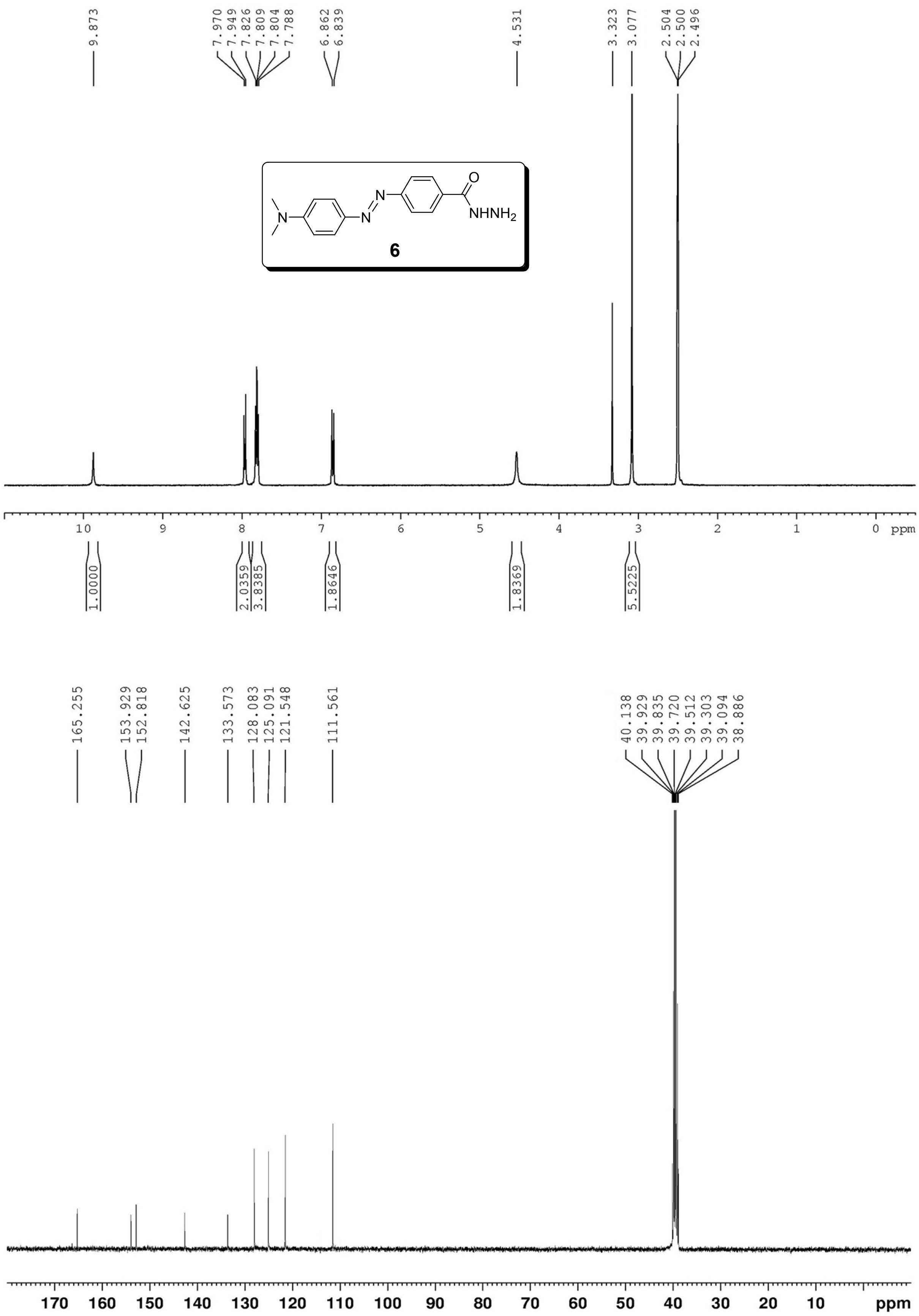


Fig. S2. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of compound **6** in DMSO-d_6.

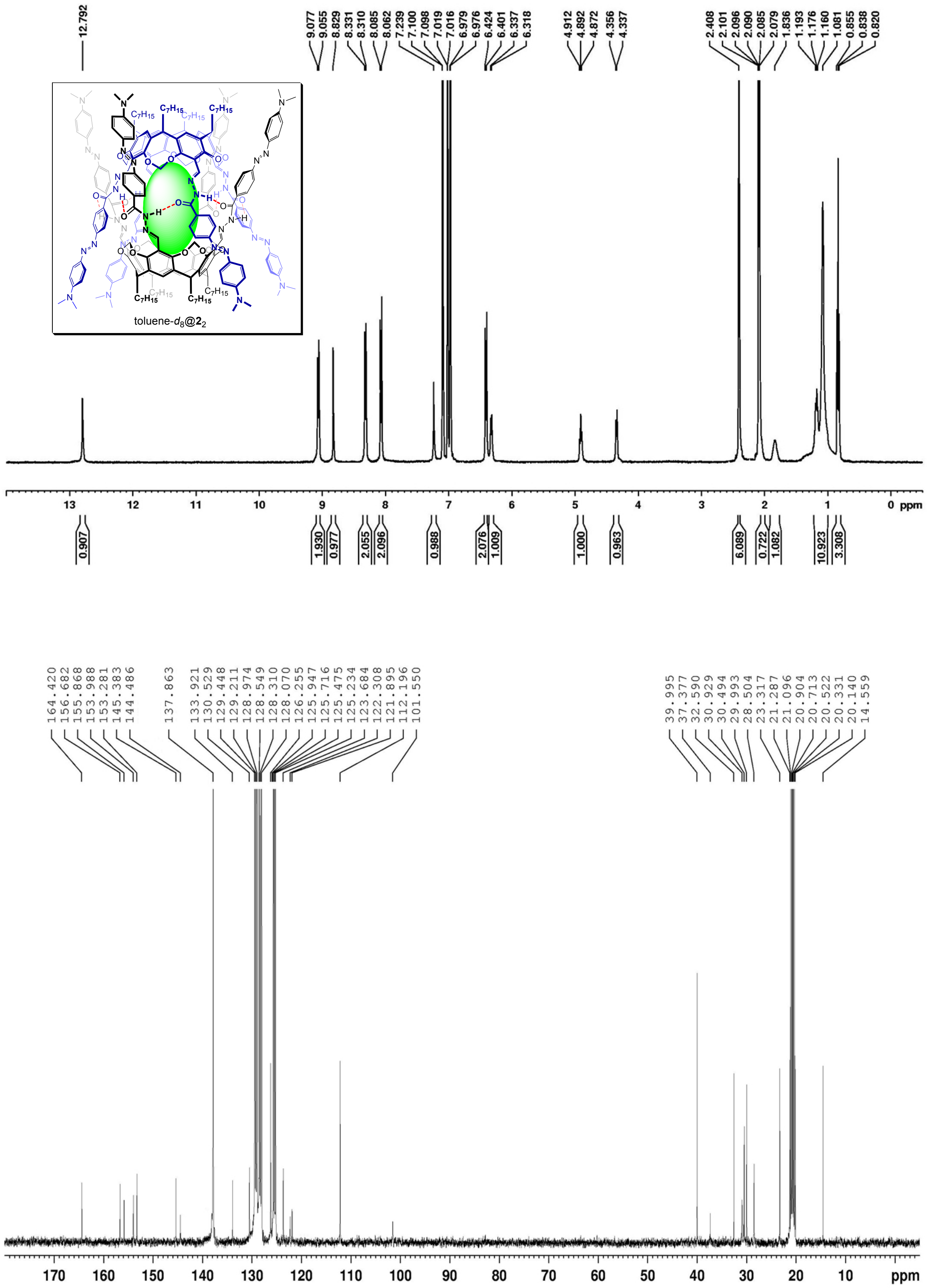


Fig. S3-1. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of molecular capsule (toluene-*d*$_8$@**2**$_2$) in toluene-*d*$_8$.

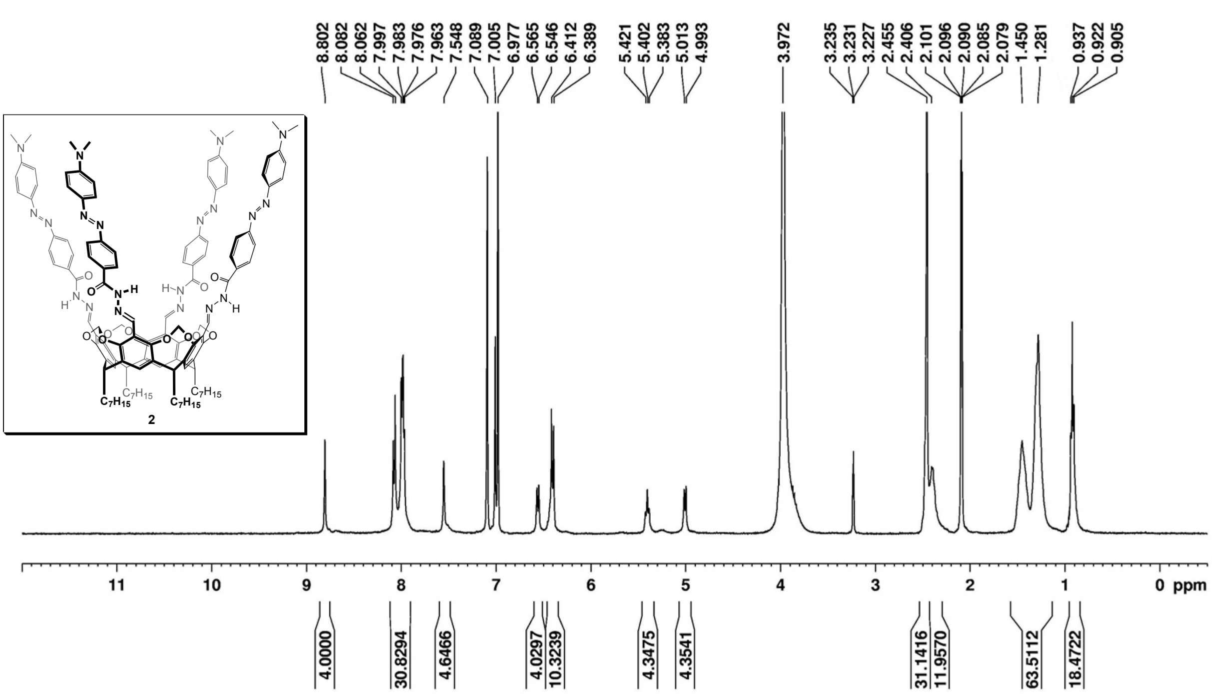


Fig. S3-2. ^{1}H NMR spectrum of cavitand **2** in 10% CD_3OD/toluene-d_8.

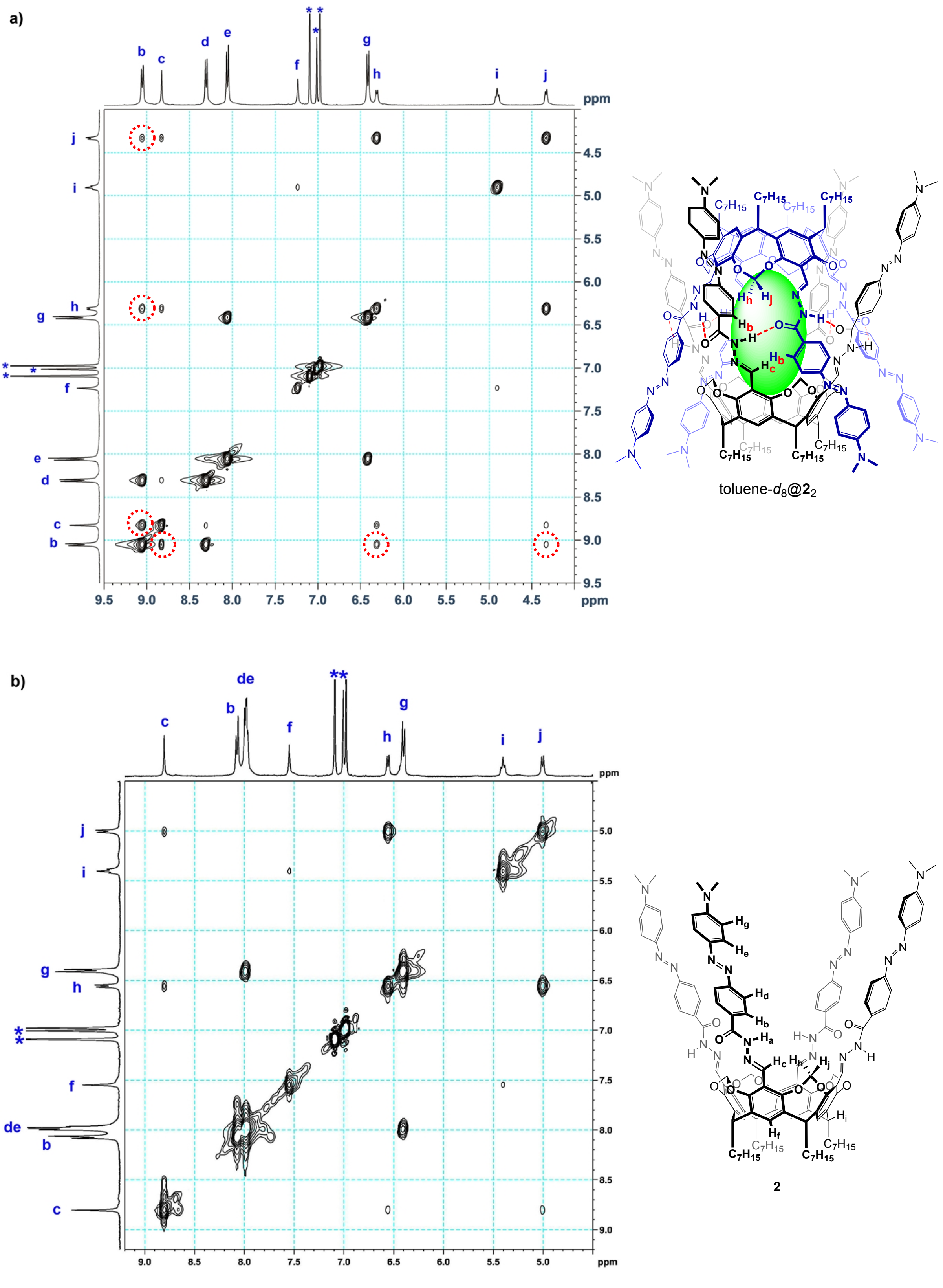


Fig. S3-3. Partial regions of the 2D-NOESY spectra of a) molecular capsule (toluene-d_8@$\mathbf{2}_2$) in toluene-d_8; b) cavitand **2** in 10% CD_3OD/toluene-d_8

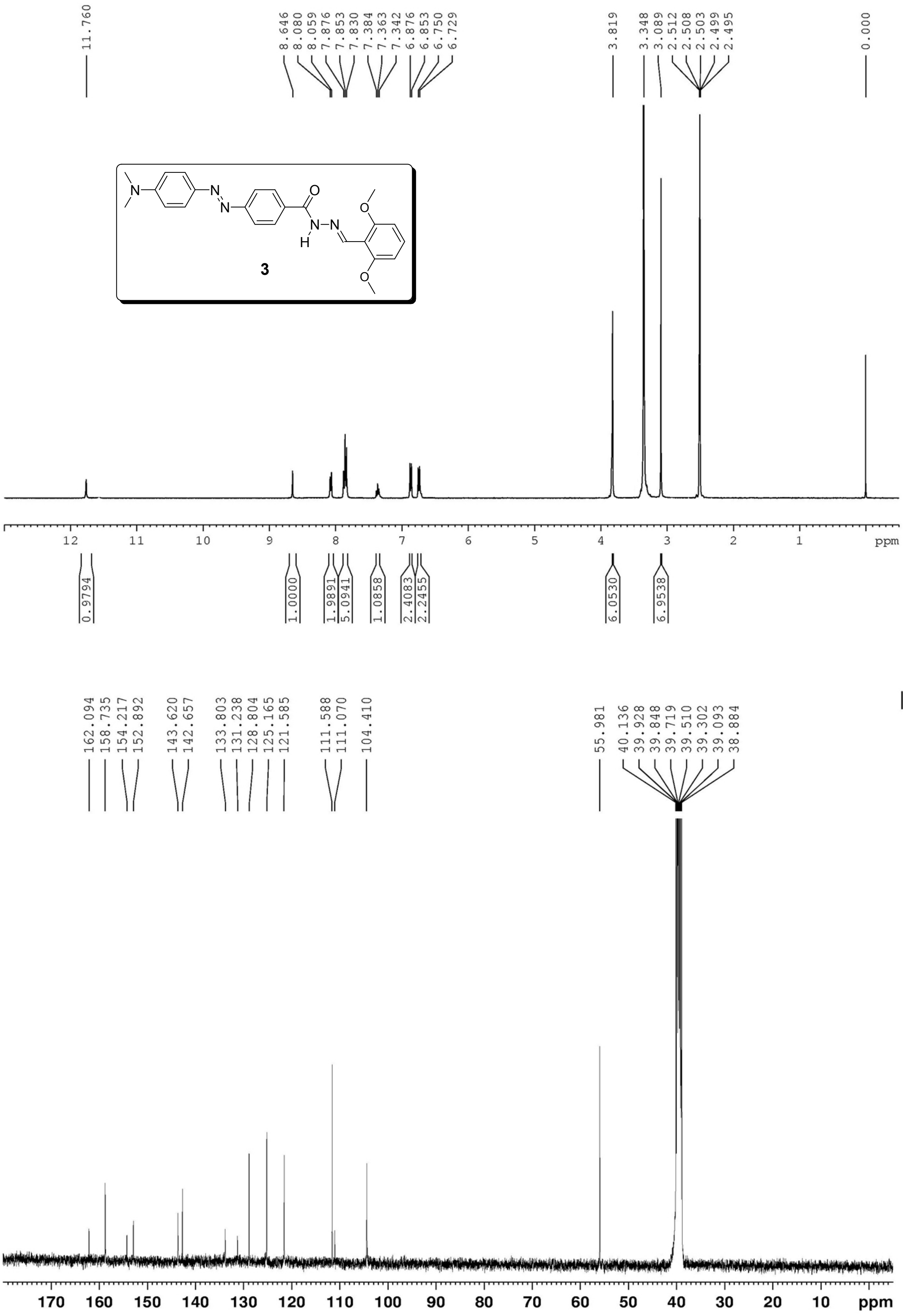
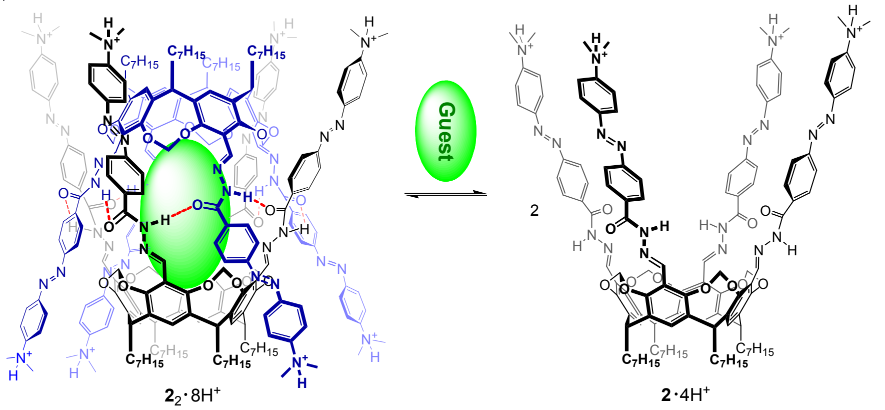


Fig. S4. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of model compound **3** in DMSO-d_6.

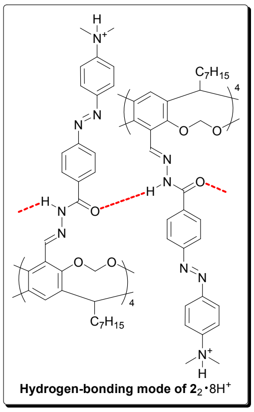
2. Molecular Modeling

The structures of molecular capsule $\mathbf{2}_2\cdot 8H^+$ and cavitand $\mathbf{2}\cdot 4H^+$ are built and minimized Semi-Empirical PM3 level using the PC model program: Spartan'06 V112. The heptyl side chains in molecular capsule $\mathbf{2}_2\cdot 8H^+$ and cavitand $\mathbf{2}\cdot 4H^+$ are replaced to methyl groups.



$\mathbf{2}_2\cdot 8H^+$

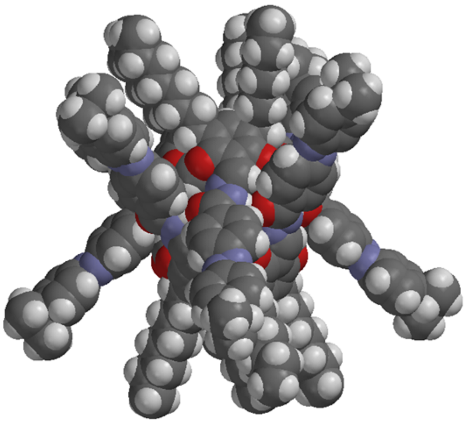
$\mathbf{2}\cdot 4H^+$



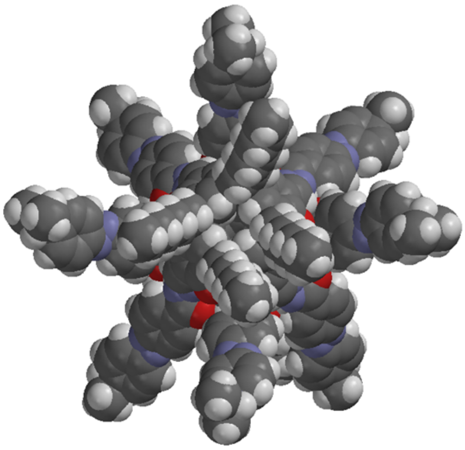
Hydrogen-bonding mode of $\mathbf{2}_2\cdot 8H^+$

< Molecular capsule $\mathbf{2}_2\cdot 8H^+$ >

Side view

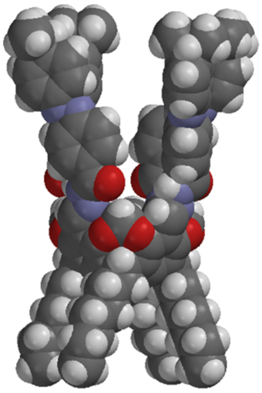


Top view

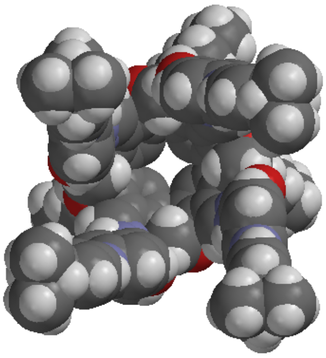


< Cavitand, $\mathbf{2}\cdot 4H^+$ >

Side view



Top view



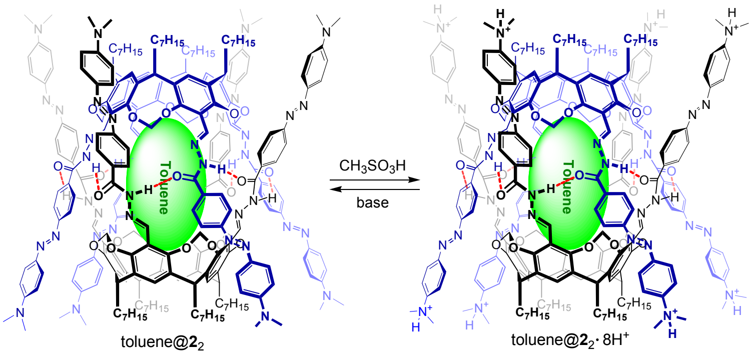
3. Acid (CH_3SO_3H) and base (DBU) titration experiments of molecular capsule $\mathbf{2}_2$

3-1. Acid (CH_3SO_3H) titration experiments of molecular capsule $\mathbf{2}_2$

Titration of 2.0 mL (4.7×10^{-6} M) solution of capsule $\mathbf{2}_2$ with stepwise addition of 0-40 equiv. of CH_3SO_3H (7.52×10^{-3} M) was followed by UV-Vis spectrophotometry, and spectrum was recorded after each addition.

Table 1. Acid titration data points for CH_3SO_3H (7.52×10^{-3} M) with capsule $\mathbf{2}_2$ (4.7×10^{-6} M, 2.0 mL) in toluene.

Molar ratio		Added volume of Guest each titration	Total volume of Titration ($\mathbf{2}_2$+acid)	Concentration [M]	
capsule $\mathbf{2}_2$	acid			$[\mathbf{2}_2]_0$	$[\text{acid}]_0$
1	0	0 μL	2000 μL	4.700×10^{-6}	0.000
1	8	10 μL	2010 μL	4.677×10^{-6}	3.742×10^{-5}
1	16	20 μL	2020 μL	4.654×10^{-6}	7.446×10^{-5}
1	24	30 μL	2030 μL	4.631×10^{-6}	1.111×10^{-4}
1	32	40 μL	2040 μL	4.608×10^{-6}	1.475×10^{-4}
1	40	50 μL	2050 μL	4.585×10^{-6}	1.834×10^{-4}



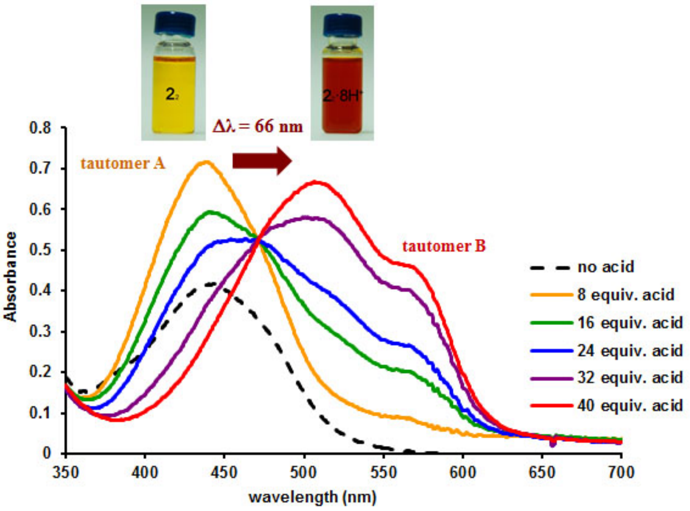


Fig. S5. Changes in UV-Vis absorption spectra of molecular capsule, toluene@$\mathbf{2}_2$ (4.7×10^{-6} M in toluene) upon addition of CH_3SO_3H.

3-2. Base (DBU) titration experiments of the protonated molecular capsule $2_2 \cdot 8H^+$

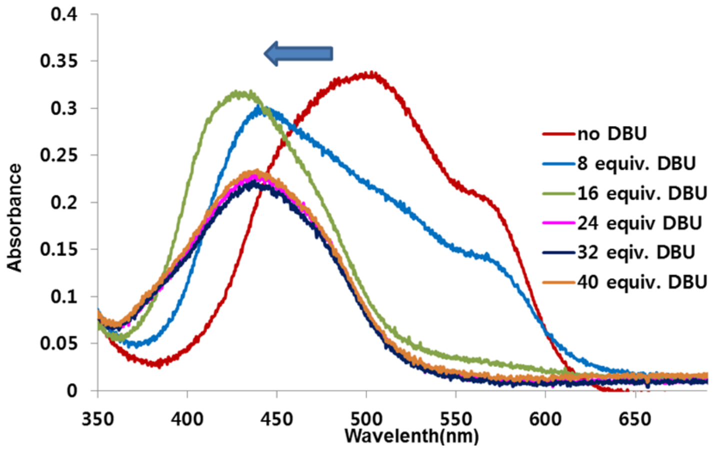


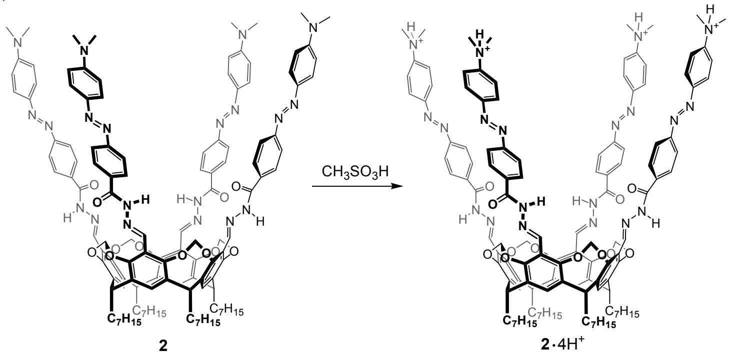
Fig. S6. Changes in UV-Vis absorption spectra of toluene@$\mathbf{2}_2 \cdot 8H^+$ (2.6×10^{-6} M in toluene) upon addition of DBU.

4. Acid (CH_3SO_3H) titration experiments of cavitand 2

Titration of 2.0 mL (4.7 × 10^{-6} M in 8% methanol/toluene) solution of cavitand **2** with stepwise addition of 0-20 equiv. of CH_3SO_3H (3.76 × 10^{-3} M in 8% methanol/toluene) was followed by UV-Vis spectrophotometry, and spectrum was recorded after each addition.

Table 2. Acid titration data points for CH_3SO_3H (3.76 × 10^{-3} M) with cavitand **2** (4.7 × 10^{-6} M, 2.0 mL) in 8% methanol/toluene.

Molar ratio		Added volume of Guest each titration	Total volume of Titration (**2**+acid)	Concentration [M]	
cavitand **2**	acid			**[2]**$_0$	[acid]$_0$
1	0	0 μL	2000 μL	4.700 × 10^{-6}	0.000
1	4	10 μL	2010 μL	4.677 × 10^{-6}	1.871 × 10^{-5}
1	8	20 μL	2020 μL	4.654 × 10^{-6}	3.723 × 10^{-5}
1	12	30 μL	2030 μL	4.631 × 10^{-6}	5.557 × 10^{-5}
1	16	40 μL	2040 μL	4.608 × 10^{-6}	7.373 × 10^{-5}
1	20	50 μL	2050 μL	4.585 × 10^{-6}	9.170 × 10^{-5}



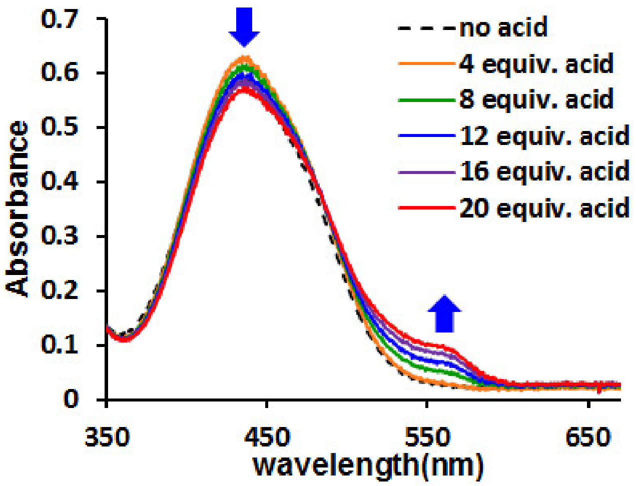


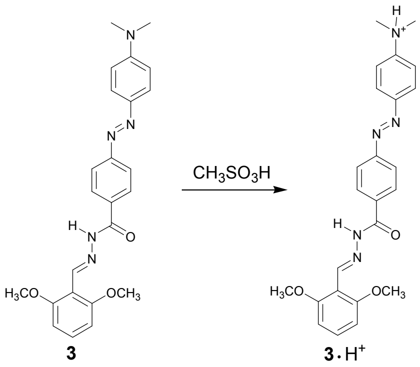
Fig. S7. Changes in UV-Vis absorption spectra of cavitand **2** (4.7 × 10^{-6} M in 8% methanol/toluene) upon addition of CH_3SO_3H.

5. Acid (CH_3SO_3H) titration experiments of model compound 3

Titration of 2.0 mL (1.4×10^{-4} M in toluene) solution of model compound **3** with stepwise addition of 0-20 equiv. of CH_3SO_3H (2.8×10^{-2} M in toluene) was followed by UV-Vis spectrophotometry, and spectrum was recorded after each addition.

Table 2. Acid titration data points for CH_3SO_3H (3.76×10^{-3} M) with model compound **3** (4.7×10^{-6} M, 2.0 mL) in toluene.

Molar ratio		Added volume of Guest each titration	Total volume of Titration (**3**+acid)	Concentration [M]	
Model compound **3**	acid			$[\mathbf{3}]_0$	$[\text{acid}]_0$
1	0	0 μL	2000 μL	1.400×10^{-4}	0.000
1	1	10 μL	2010 μL	1.393×10^{-4}	1.393×10^{-4}
1	2	20 μL	2020 μL	1.386×10^{-4}	2.772×10^{-4}
1	3	30 μL	2030 μL	1.379×10^{-4}	4.137×10^{-4}
1	4	40 μL	2040 μL	1.373×10^{-4}	5.492×10^{-4}
1	5	50 μL	2050 μL	1.366×10^{-4}	6.830×10^{-4}



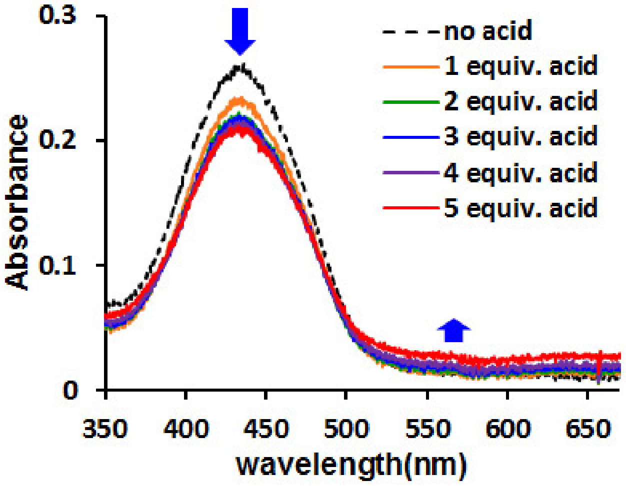


Fig. S8. Changes in UV-Vis absorption spectra of model compound **3** (1.4×10^{-4} M in toluene) upon addition of CH_3SO_3H.

6. Methanol addition experiments of the protonated capsule, toluene@$\mathbf{2}_2$·8H$^+$

6-1. UV –Vis absorption spectra upon addition of methanol

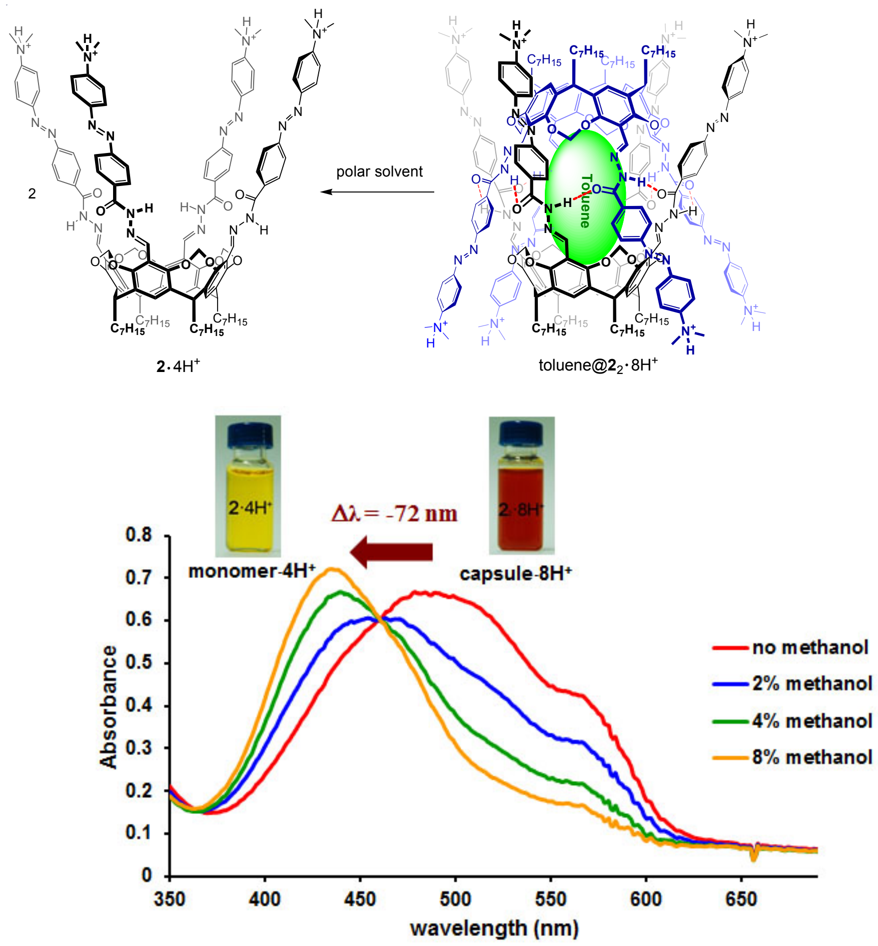
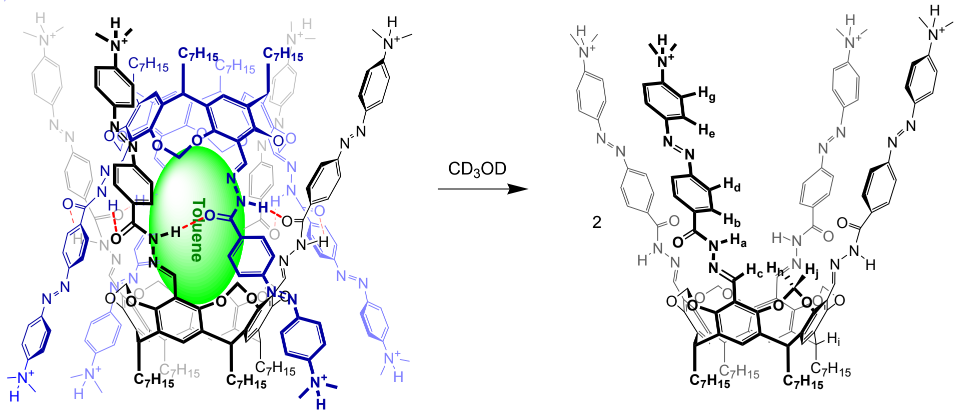


Fig. S9. Changes in UV-Vis absorption spectra of toluene@$\mathbf{2}_2$·8H$^+$ (4.7×10^{-6} M in toluene) upon addition of methanol.

6-2. ^{1}H NMR spectra upon addition of methanol



toluene@2_2·8H$^+$ $\qquad$ 2·4H$^+$

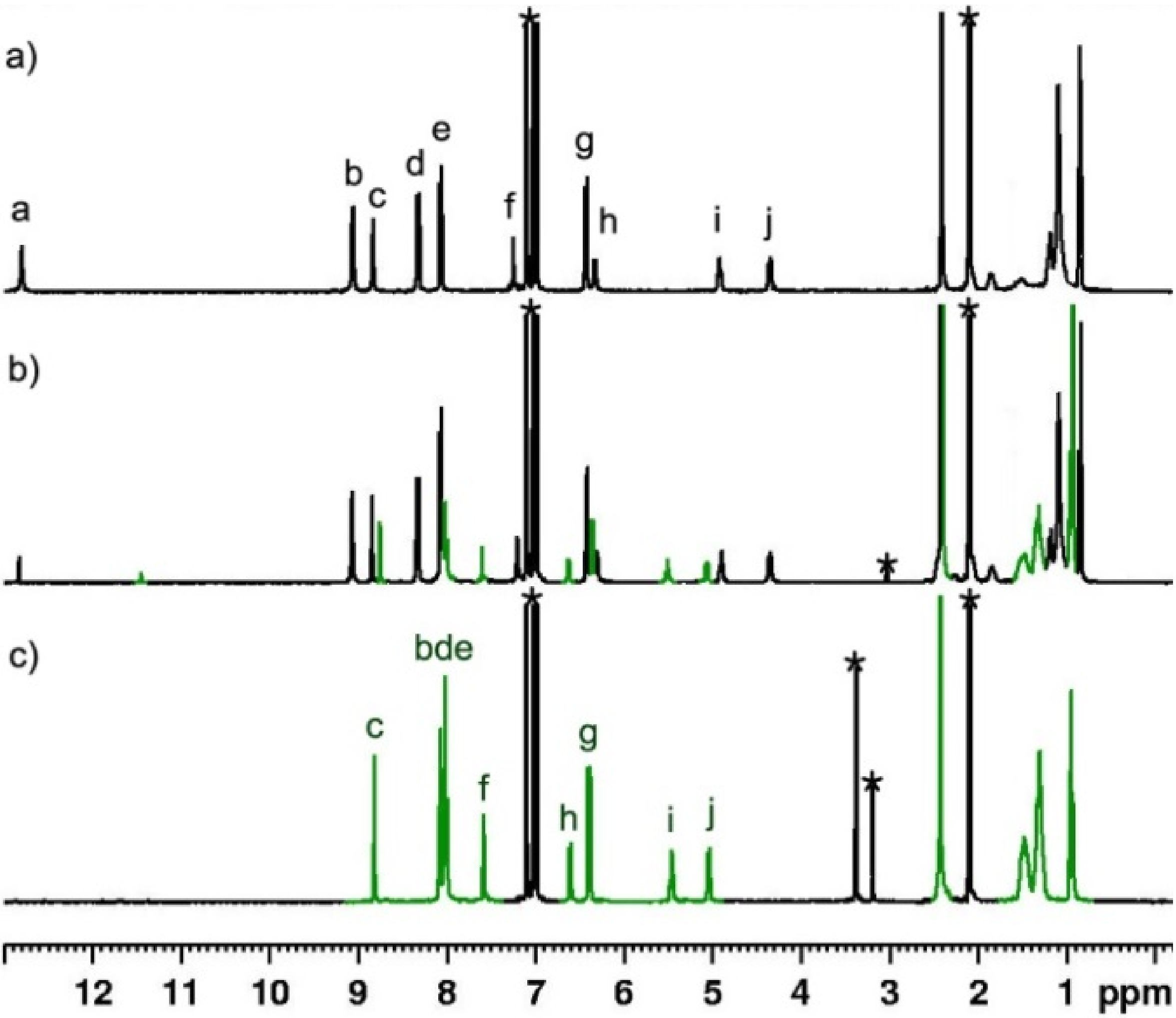


Fig. S10. ^{1}H NMR spectra (400 MHz) in toluene-d_8 at 298 K of: a) toluene-d_8@$\mathbf{2}_2$·8H$^+$ b) after the addition of 2% CD_3OD, c) after the addition of 8% CD_3OD. [$\mathbf{2}_2$] = 5 mM. The signals of capsule $\mathbf{2}_2$·8H$^+$ (**black**) and cavitand $\mathbf{2}$·4H$^+$ (**green**) are highlighted. The residual peaks of solvents are marked "*".