ChemComm

New Deep Cavitand with Imidazoquinoxaline Flaps: Formation of Static Helical Alkane Inclusion Complexes by Enhanced CH/π Interactions

Electronic Supporting Information

Heung-Jin Choi,[a]* Quoc-Thiet Nguyen,[a] Yeon Sil Park,[a] Cheol-Ho Choi,[b] Kyungsoo Paek,[c‡] and Eun-Hee Kim[d]

[a] Department of Applied Chemistry, Kyungpook National University, Daegu 702-701, Korea. [b]Department of Chemistry, Kyungpook National University. [c]CAMDRC and Department of Chemistry, Soongsil University, Seoul 156-743, Korea. [d]Magnetic Resonance Team, Korea Basic Science Institute, Ochang, Chungbuk 363-883, Korea.

Synthetic Procedures

2,3,21,22,30,31,39,40-Octanitro-9,11,13,15-tetraundecyl-7,17:8,16-dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2´´,3´´:2´,3´] [1,4]benzodioxonino[10´,9´:5,6] quinoxalino [2´´,3´´:2´,3´]quinoxalino [2´´´´,3´´´´:2´´´,3´´´] [1,4]dioxonino [6´´´,5´´´:9´,10´] [1,4] benzodioxonino[6´,5´:9,10] [1,4]benzodioxonino[2,3-*b*]quinoxaline (Octanitro cavitand 5)

To sodium hydride (60% dispersion in oil, 400 mg, 10 mmol) prewashed with hexane was added a solution of resorcinarene (1.1 g, 1 mmol) in dry THF (30 mL) and stirred at 0 ^{o}C for 30 min under nitrogen atmosphere. A solution of 2,3-dichloro-5,6-dinitroquinoxaline (1.3 g, 4.4 mmol) in dry THF (30 mL) was slowly added to the stirred mixture via a syringe. The mixture was stirred for six hours and then quenched with saturated NaCl solution. The solvent was removed *in vacuo*. The residue was partitioned between CH_2Cl_2 (40 mL) and brine (40 mL) and the organic layer was separated and the aqueous layer was extracted once with CH_2Cl_2 (40 mL). The combined organic layer was dried over anhydrous $MgSO_4$, filtered through a pad of silica gel, and concentrated under reduced pressure. The solid residue was redissolved in the minimum amount of acetone and reprecipitated with the addition of methanol (50 mL). The precipitate was filtered, washed with methanol (2 x 20 mL), and dried *in vacuo* to afford yellow solid (1.78 g, 90%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.47 (s, 8H), 7.43 (s, 4H), 6.94 (br s, 4H), 3.86 (t, *J* = 7.3 Hz, 4H), 2.11 (m, 8H), 1.28-1.20 (m, 72H), 0.87 (t, *J* = 6.9 Hz, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 152.64, 151.95, 142.50, 140.25, 133.60, 125.41, 124.51, 115.64, 38.03, 32.24, 32.09, 29.98, 29.96, 29.94, 29.82, 29.75, 29.70, 27.40, 23.01, 14.45; IR (KBr): 2926, 2854, 1548 (s), 1427 (s, ν_{as} NO_2), 1346 (s, ν_s NO_2), 1182 cm^{-1}; FAB MS (NOBA): m/z 1969.78 (87%), 1970.30 (M+H, 100%), calcd for $C_{104}H_{112}N_{16}O_{24}$: m/z 1968.8035.

2,3,21,22,30,31,39,40-Octaamino-9,11,13,15-tetraundecyl-7,17:8,16-dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2´´,3´´:2´,3´][1,4]benzodioxonino[10´,9´:5,6] quinoxalino[2´´,3´´:2´,3´]quinoxalino[2´´´´,3´´´´:2´´´,3´´´][1,4]dioxonino[6´´´,5´´´:9´,10´][1,4]benzo dioxonino[6´,5´:9,10][1,4]Benzodioxonino [2,3-*b*]quinoxaline (Octaamino cavitand 6)

To a solution of octanitro cavitand **5** (394 mg, 0.2 mmol) in DMF (10 mL) was added tin(II) chloride (3.65 g, 19.2 mmol). The mixture was stirred at room temperature for three hours. The reaction mixture was diluted with THF (100 mL) and then filtered through a pad of silica gel washing with THF. The filtrate was concentrated *in vacuo* to remove volatile THF. The concentrate was used for next reaction. An aliquot portion of the solution was concentrated to dryness *in vacuo* for NMR analysis: ^{1}H NMR (400 MHz, DMSO-d_6): δ7.95 (br s, 4H), 6.91 (br s, 8H), 6.84 (br s, 4H), 5.52 (br t, 4H), 3.40 (br s, 16H, NH), 2.40 (br m, 8H), 1.50-1.10 (m, 72H), 0.88 (br t, 12H). ^{13}C NMR (100 MHz, DMSO-d_6, delay time = 5 sec): δ 152.8 (br), 151.8 (br), 147.9 (br), 139.6 (br), 135.7 (br), 125. 0 (br), 118.5 (br), 105.5 (br), 36.2, 34.7, 31.8, 30.8, 29.5, 29.2, 22.5, 14.2.

Imidazoquinoxaline cavitand (2)

To a solution of octaamino cavitand **6** (346 mg, 0.2 mmol) in DMF (10 mL) cooled in an ice-bath was added phosphorus oxychloride (2 mL, 8 mmol) slowly. The mixture was stirred at room temperature under for three hours and then poured to a beaker of ice (100 g). The mixture was stirred until the excess phosphorus oxychloride was decomposed completely and then neutralized with sat. $NaHCO_3$ solution. The precipitate was filtered and washed with water (30 mL x 3) and then with methanol (30 mL x 3) sequentially. The precipitate dried in air was dissolved in CH_2Cl_2. The resulting solution was dried over anhydrous $MgSO_4$, filtered and then concentrated under reduced pressure. The solid residue was dissolved in a minimum amount of CH_2Cl_2 and reprecipitated with the addition of CH_3CN (50 mL). The precipitates were filtered and washed with CH_3CN (30 mL x 3) and CH_3OH (30 mL x 3). The precipitates were dried in air and then under vacuum at 100 ^{o}C yielding a brownish solid (343 mg, 97%): ^{1}H NMR ($CDCl_3$/CD_3OD, 9:1 v/v, 400 MHz): δ 8.18 (s, 4H), 8.02 (s, 4H), 7.94 (s, 8H), 7.16 (s, 4H), 5.61 (t, J = 8.0 Hz, 4H), 2.19 (t, J = 6.4 Hz, 8H), 1.38-1.11 (br m, 72H), 0.77 (t, J = 6.0 Hz, 12H); ^{1}H NMR (CD_2Cl_2/CD_3OD, 9:1 v/v, 400 MHz): δ 8.26 (s, 4H), 8.17 (s, 4H), 8.07 (s, 8H), 7.34 (s, 4H), 5.70 (t, J = 7.5 Hz, 4H), 2.34 (8H), 1.49-1.30 (br m, 72H), 0.89 (br m, 12H); ^{13}C NMR (CD_2Cl_2/CD_3OD, 9:1 v/v, 100 MHz, delay time = 10 sec) δ 155.31, 154.02, 153.82, 149.14, 138.95, 138.50, 125.94, 121.84, 114.10, 36.96, 35.22, 34.73, 32.53, 32.20, 30.86, 25.45, 16.54; ^{13}C NMR ($CDCl_3$/CD_3OD, 9:1 v/v, 100 MHz, delay time = 10 sec) δ 152.43, 151.20, 146.21, 135.89, 135.80, 123.30, 118.81, 33.99, 32.33, 31.88, 29.70, 29.65, 29.35, 28.01, 22.61, 16.52, 13.91; IR (KBr): 3422.40 (N-H), 2924.33, 2853.18 ($C_{11}H_{23}$) 1635.42, 1482.11, 1395.02, 1338.29, 1267.58, 1162.99, 892.68, 595.98 cm^{-1}; HRMS-MALDI-TOF: m/z 1769.7641 (M+H, 85.92%), 1770.7730 (100%), 1771.7713 (67.5%), 1772.7696 (30.6%), 1773.7738 (11.8%), 1774.8041 (4.59%), calcd for $C_{108}H_{120}N_{16}O_8$ m/z: 1769.9553 (M+H, 85.6%), 1770.9587 (100.0%), 1771.9620 (57.9%), 1772.9654 (22.1%), 1773.9687 (6.3%), 1774.9721 (2.2%). Anal. Calcd for $C_{108}H_{120}N_{16}O_8 \cdot 8H_2O$: C, 67.76; H, 7.15; N, 11.71. Found: C,

67.58; H, 6.96; N, 11.57.

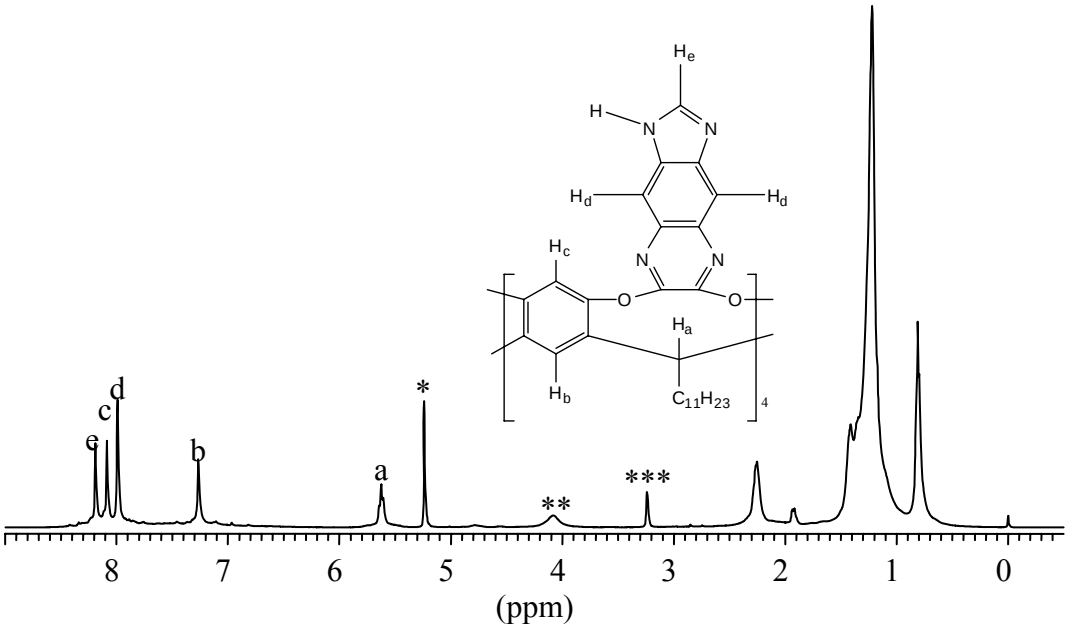

Fig. S-1. ^{1}H NMR (400 MHz) spectrum of imidazoquinoxaline cavitand **2** in CD_2Cl_2/CD_3OD (9:1, v/v) at room temperature. * Residual proton in CD_2Cl_2 , ** , *** residual protons in CD_3OD .

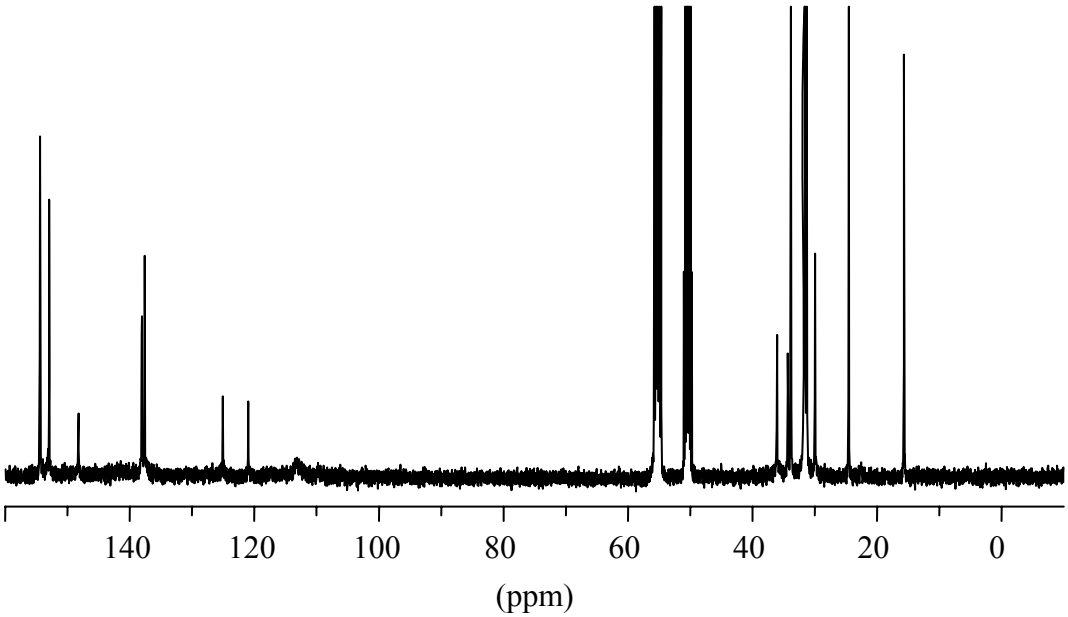

Fig. S-2. ^{13}C NMR (100 MHz) spectrum of imidazoquinoxaline cavitand **2** in CD_2Cl_2/CD_3OD (9:1) at room temperature.

MALDI-TOF Mass Spectrum of Imidazoquinoxaline Cavitand 2

The MALDI-TOF mass spectrum was obtained with a Voyager-DE STR Biospectrometer using Dithranol matrix.

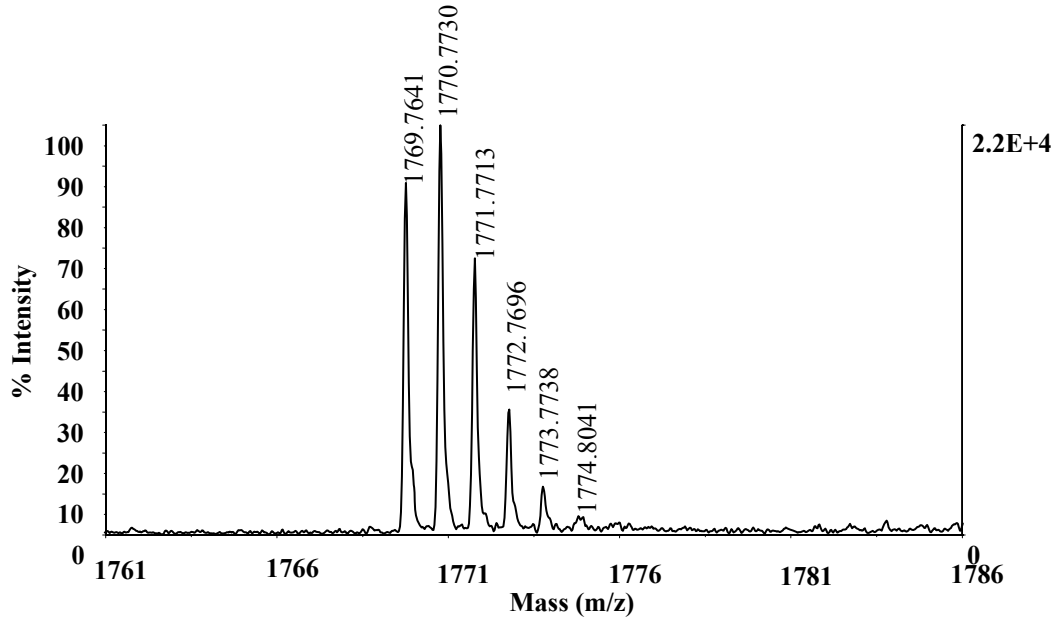

Fig. S-3. MALDI-TOF Mass Spectrum of Imidazoquinoxaline Cavitand **2**.

Table S-1. Observed and calculated data for MALDI-TOF Mass Spectrum of Imidazoquinoxaline Cavitand **2**

Observed		Calculated for $C_{108}H_{120}N_{16}O_8 + H^+$	
m/z	rel %	m/z	rel %
1769.764125	85.9	1769.9553	84.4 (M+H)
1770.772979	100.0	1770.9587	100.0
1771.771261	67.5	1771.9620	66.0
1772.769564	30.6	1772.9654	28.0
1773.773791	11.8	1773.9689	9.0
1774.804073	4.6	1774.9721	2.2

Molecular Modeling:

To obtain the geometries and the energetics of the complexes, electronic structure calculations based on density functional theory (DFT) were performed with B3LYP functional. All calculations reported here were performed with the general atomic and molecular electronic structure system (GAMESS)[1]. The all-electron 6-31(d)[2] basis set was used throughout this work. The magnetic shielding tensors were calculated with gauge including atomic orbital (GIAO) method[3] with HF/6-31G(d) level of theory.

The depth of the cavity of **2**·4MeOH, the distance between the plane connecting four top-carbons of imidazole moieties and the plane connecting four C5 carbons of the resorcinol rings was measured as 10.08 Å, and the width of the cavity, the distance of two crossing C2 carbon atoms of imidazole moieties was measured as 8.23 Å.

The binding energy between helical-octane and free cavitand **2**·4MeOH was calculated from the energy difference between inclusion complex helical-octane@**2**·4MeOH and decomplexed **2**·4MeOH − free extended-octane. The CH-π stabilization of the inclusion complex helical-octane@**2**·4MeOH was calculated to be −6.726 kcal/mol considering the energy 4.716 kcal/mol required helical formation from extended octane.

helical-Octane − *anti*-Octane= 4.716 kcal/mol
Binding Energy of inclusion complex= −2.010 kcal/mol
CH-π Stabilization = −6.726 kcal/mol

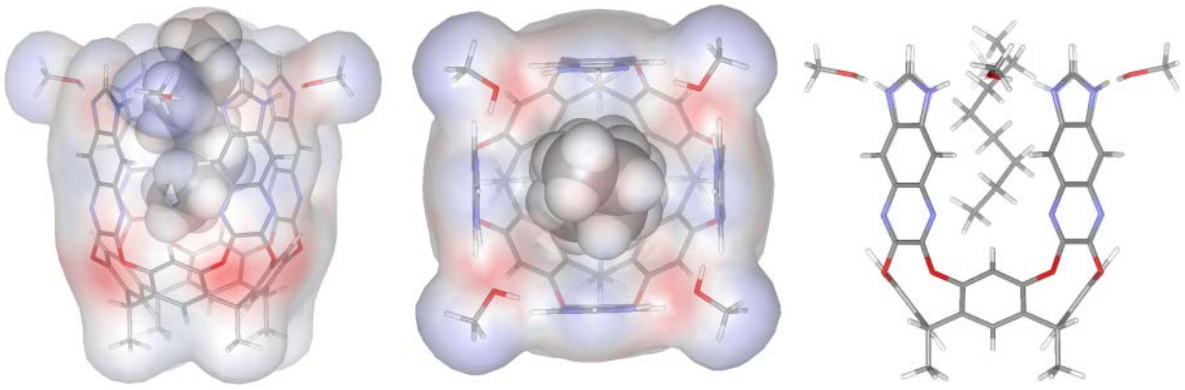

Fig. S-4. Energy-minimized structure of helical-octane@**2**·4MeOH as obtained with B3LYP/6-31G*. For clarity, the alkyl pendants are replaced by methyls.

Table S-2. The proton chemical shifts of the octane enclosed in the cavity of **2**·4MeOH

Number of carbon [a]	*helical*-octane calcd δ (ppm) [b]	*extended*-octane calcd δ (ppm) [b]	octane obsd, δ (ppm) [c]
C1(CH_3)	−4.82 (-4.769, -5.074, -4.626)	−4.93 (-5.29, -5.27, -4.23)	−4.49
C2 (CH_2)	−4.42 (-4.180, -4.654)	−4.78 (-4.79, -4.76)	−4.08
C3 (CH_2)	−4.34 (-4.582, -4.094)	−4.91 (-4.94, -4.88)	−4.13
C4 (CH_2)	−3.91 (-4.040, -3.779)	−4.26 (-4.28, -4.23)	−4.18
C5 (CH_2)	−3.33 (-3.514, -3.144)	−3.39 (-3.42, -3.36)	−3.58
C6 (CH_2)	−2.09 (-1.932, -2.248)	−1.80 (-1.80, -1.79)	−2.63
C7 (CH_2)	−0.77 (-1.078, -0.458)	−0.11 (-0.12, -0.10)	−0.87
C8 (CH_2)	−0.10 (-0.226, 0.222, -0.309)	0.85 (1.17, 0.69, 0.69)	0.13

[a]The proton chemical shifts are the average values of each proton on a carbon calculated with HF/6-31G* level at B3LYP/6-31G* geometry. [b]The numbers of carbon atoms of octane were assigned from the deepest carbon in the cavity. [c] taken by 800 MHz, 10 mM **2** + 100 mM octane in CD_3OD/ $CDCl_3$ (35:65, v/v) at 273 K.

(1) (a) M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. Su, T. L. Windus, M. Dupuis and J. A. Montgomery, Jr., *J. Comp. Chem.*, 1993, **14**, 1347. (b) G. D. Fletcher, M. W. Schmidt and M. S. Gordon, *Adv. Chem. Physics*, 1999, **110**, 267.

(2) W. J. Hehre, R. Ditchfield and J. Pople, *J. Chem. Phys.*, 1972, **56**, 2257.

(3) I. Ando and G. A. Webb, Theory of NMR Parameters. Academic Press, New York (1983).

Determination of the association constants, K_a for the inclusion complexes of *n*-alkanes with imidazoquinoxaline cavitand 2 in $CD_3OD/CDCl_3$ (35:65, v/v) at 273 K.

The association constants, K_a were determined from ^1H NMR spectra of a solution of (20 mM Host and 500 mM Guest) in $CDCl_3/CD_3OD$ (65:35, v/v) at 273 K. The spectra were taken with a Bruker Avance Digital 400 spectrometer. The inclusion complexes of *n*-alkane@**2**·4MeOH were kinetically stable, thus the NMR signals of the guests, alkanes of the complexes were well resolved from free guest, and clearly observed in slow-exchange within the NMR time scale.

$$H + G \rightleftharpoons H\text{-}G$$

$$K_a = \frac{[C]}{([H]_0 - [C])([G]_0 - [C])}$$

Where $[H]_0$ and $[G]_0$ are the initial concentration of host and guest, and C stands for complex H-G. The relative signal integrals (X_c) at $\delta_H(I_H)$ and $\delta_C(I_C)$ is represented by

$$x_C = \frac{I_C}{I_h + I_C}$$

Then

$$K_a = \frac{x_C/[H]_0}{(1 - x_C)(r - x_C)}$$

Where $[C] = Xc[H]_0$ and $r = [G]_0/[H]_0$

The NMR signal around -4.49 ppm was due to methyl group of the guest enclosed in the host cavity resulting in I_C = (integrals at -4.49 ppm)/3. And the peak at 5.6 ppm from four methine protons was well resolved and its integral represents the sum of integration from free and complexed host resulting in $(I_h + I_c)$ = (integrals at 5.6 ppm)/4

Table S-3. The association constants of the inclusion complexes of *n*-alkanes with imidazoquinoxaline cavitand **2** in CD_3OD/ $CDCl_3$ (35:65, v/v) at 273 K

Guest	$[G]_o$ (M)	$[H]_o$ (M)	$(I_h + I_c)$	I_c	X_c	r	K_a (M^{-1})	ΔK_a
n-hexane	0.5	0.020	3.087/4	1/4	0.324	25	0.97	±0.5
n-heptane	0.5	0.020	3.03/4	1/3	0.440	25	1.60	±0.5
n-octane	0.5	0.020	2.63/4	1/3	0.507	25	2.10	±0.5
n-nonane	0.5	0.020	2.70/4	1/3	0.494	25	1.99	±0.5
n-decane	0.5	0.020	2.81/4	1/3	0.474	25	1.84	±0.5
n-undecane	0.5	0.020	2.98/4	1/3	0.447	25	1.65	±0.5
n-dodecane	0.5	0.020	3.06/4	1/3	0.436	25	1.57	±0.5

NMR data for Inclusion complexation of Imidazoguinoxaline cavitand 2:

***n*-Octane:**

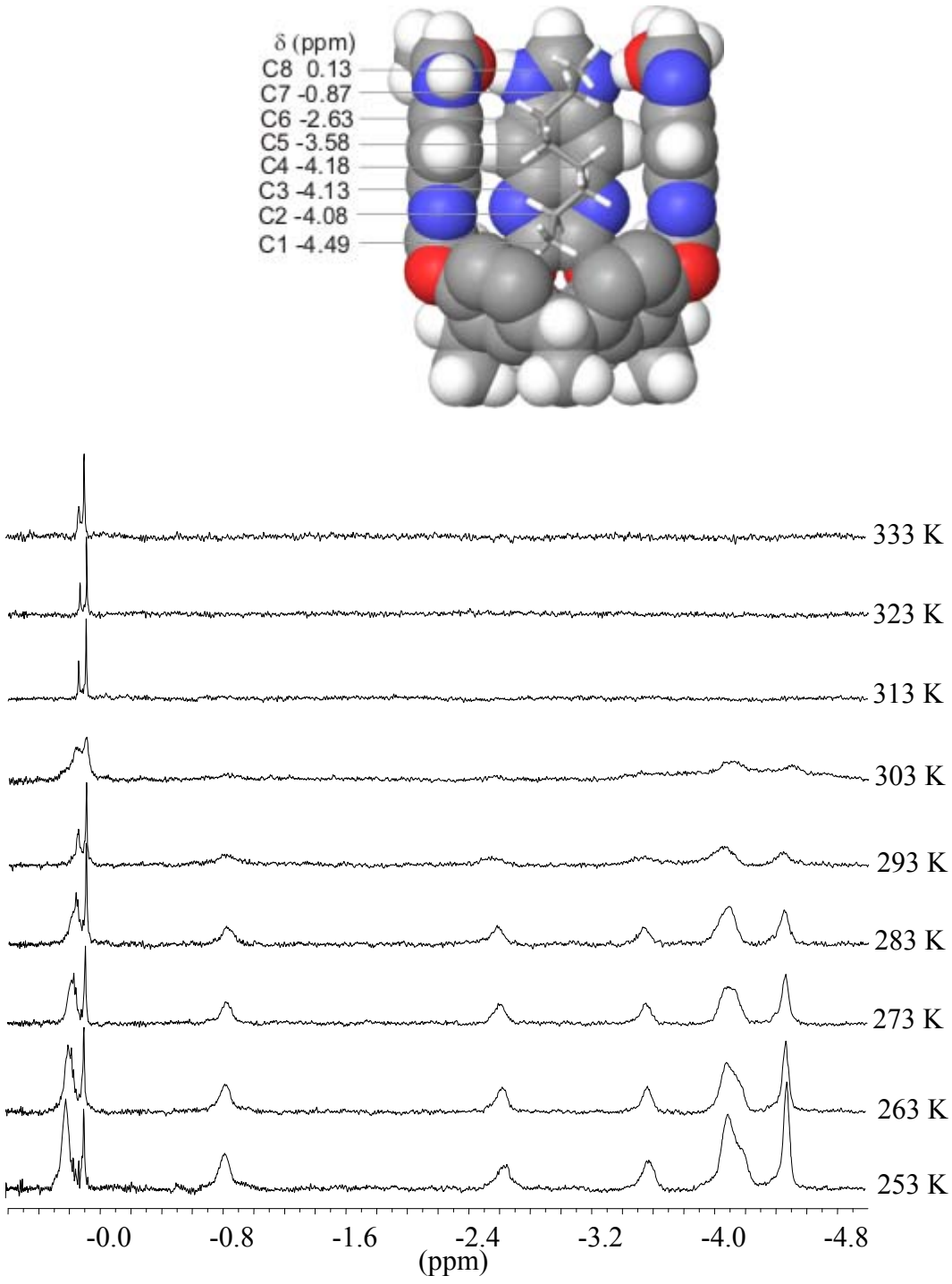

Fig. S-5. Upfield region of ^{1}H NMR (400 MHz) spectra of a mixture of host and guest (20 mM **2** + 500 mM *n*-octane) in $CD_3OD/CDCl_3$ (35:65, v/v) at various temperatures.

n-Hexane

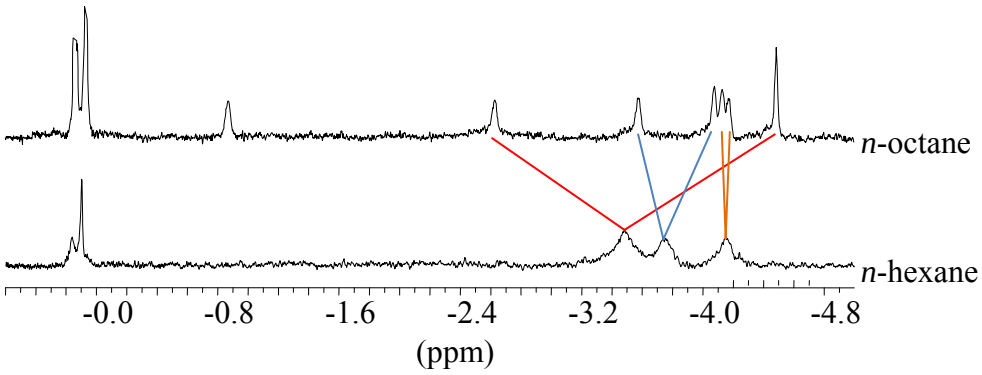

Fig. S-6. Averaged chemical shifts of tumbling *n*-hexane in cavitand **2**.

Table S-4. Observed and predicted chemical shifts of *n*-hexane enclosed in the cavity of cavitand **2**, based on observed chemical shifts of *n*-octane enclosed in the cavity

n-octane Observed δ's (ppm)	*n*-hexane	Predicted δ's (ppm)	Observed δ's (ppm)	Δ(Predt-Obsd) (ppm)
C1: -4.49	$C_1 \leftrightarrow C_6$	-3.56	-3.51	-0.05
C2: -4.08	$C_2 \leftrightarrow C_5$	-3.83	-3.79	-0.04
C3: -4.13	$C_3 \leftrightarrow C_4$	-4.16	-4.18	0.02
C4: -4.18				
C5: -3.58				
C6: -2.63				
C7: -0.87				
C8: +0.13				

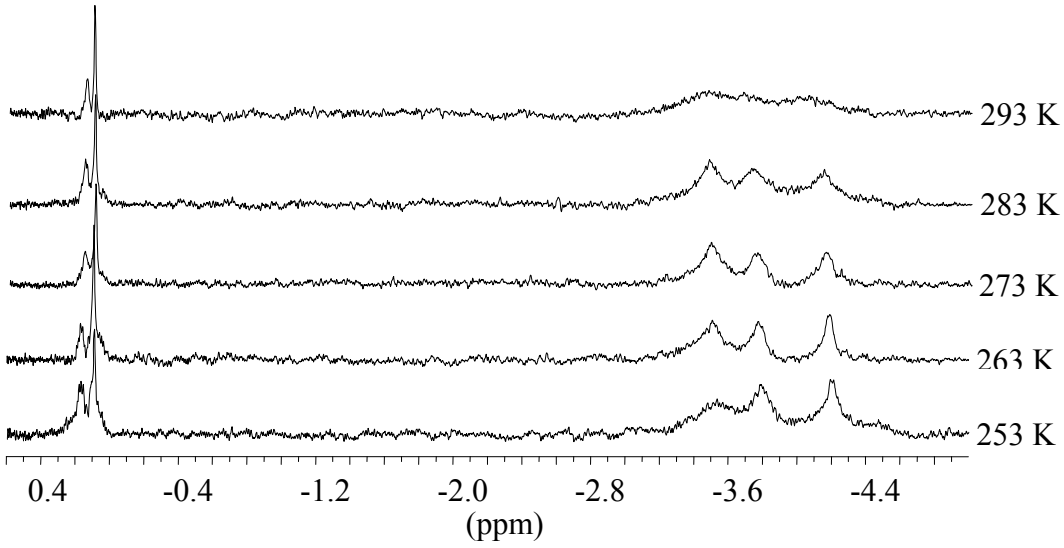

Fig. S-7. Upfield region of ^{1}H NMR (400 MHz) spectra of a mixture of host and guest (20 mM **2** + 500 mM *n*-hexane) in $CD_3OD/CDCl_3$ (35:65, v/v) at various temperatures.

n-Dodecane

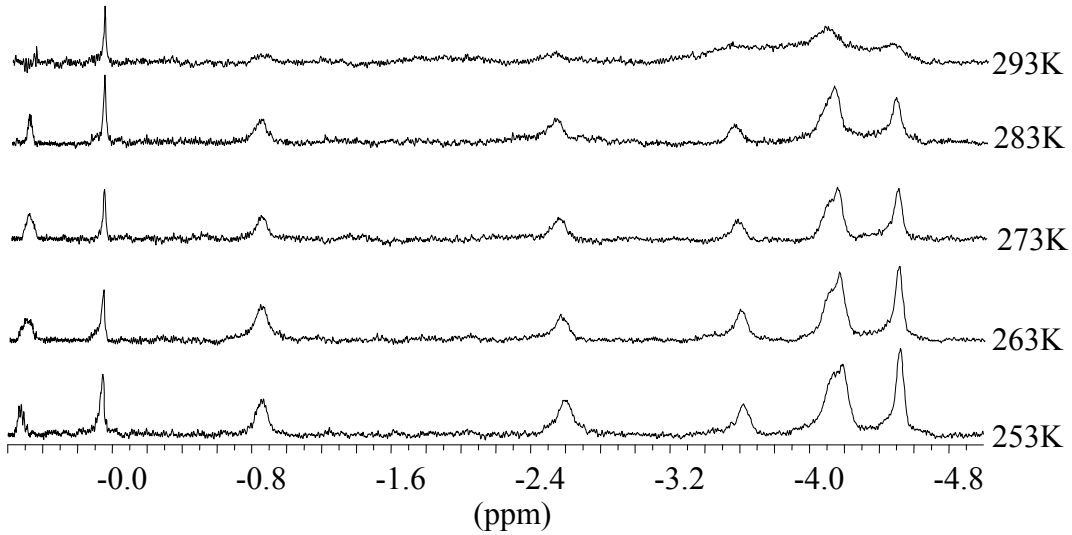

Fig. S-8. Upfield region of ^{1}H NMR (400 MHz) spectra of a mixture of host and guest (20 mM **2** + 500 mM *n*-dodecane) in $CD_3OD/CDCl_3$ (35:65, v/v) at various temperatures.