Electronic Supplementary Material (ESI) for Chemical Communications

Hydrogen-bond driven assembly of a molecular capsule facilitated by supramolecular chelation

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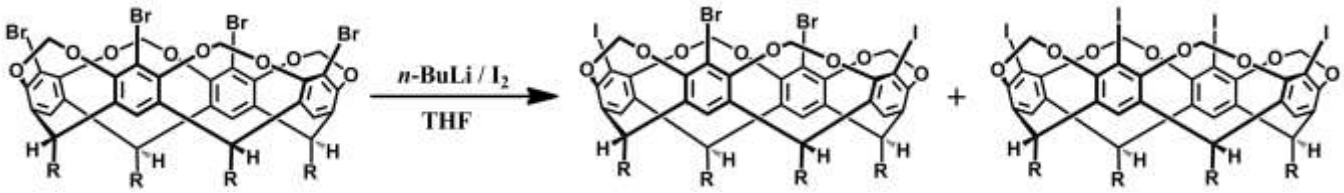
Supplementary Information

Synthesis

All chemicals were purchased from Aldrich and Strem chemicals and used without further purification. The determinations of melting points were carried out on Fisher-Johns melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Unity plus 200 MHz or 400 MHz spectrometer in $CDCl_3$ or D_6-DMSO. Compounds were prepared for infrared spectroscopic (FT-IR) analysis as a mixture in KBr. MALDI-TOF / TOF-MS was carried out on a Bruker Daltonics Ultraflex TOF/TOF.

Synthesis of C-pentyltetraiodocavitand, *2*[1, 2]



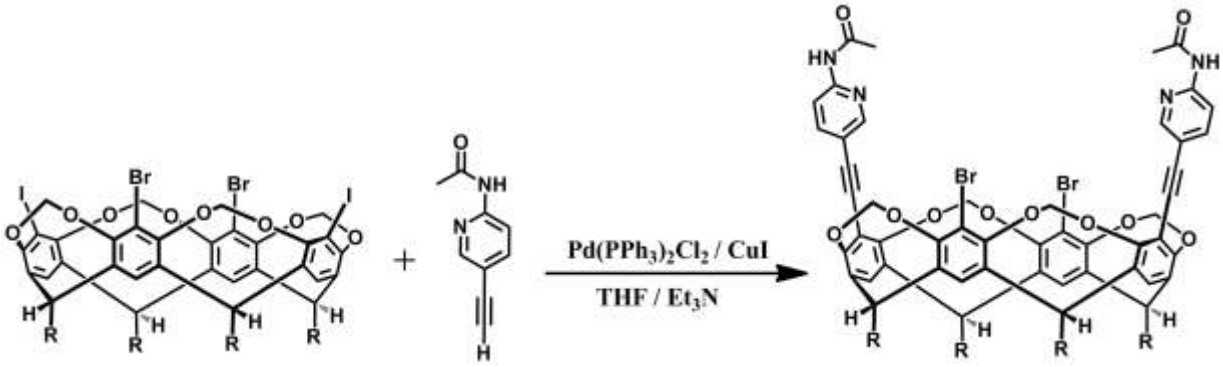
R = $(CH_2)_4CH_3$ **1** **2**

C-Pentyltetrabromocavitand (2.0 g, 1.8 mmol) was placed in a round bottomed flask and warmed to 50 ºC with stirring for about 30 mins. Dry, freshly distilled THF (50 mL) was added to it and the solution cooled to -78 ºC using dry ice/acetone bath. The reaction mixture was stirred under dinitrogen and *n*-butyllithium (6.0 equiv., 6.6 mL, ca. 1.6 M solution in hexanes) was rapidly added using syringe. After stirring for 1 hr, iodine (3.6 g, 14.2 mmol in THF (5 mL)) was added. The cooling bath was removed and the reaction mixture was allowed to warm to room temperature. The stirring was continued for 2 hrs and then the reaction mixture was cooled to 0 ºC using ice bath and quenched with a saturated aqueous sodium thiosulfate solution. The aqueous phase was extracted with ethyl acetate (3 x 75 mL), washed with brine and dried with magnesium sulfate. The solvent was removed on a rotary evaporator to obtain a white residue. It was purified by column chromatography using a hexanes/dichloromethane mixture as eluent, whereupon small amounts of *C*-pentyl-1,3-dibromo-2,4-diiodocavitand, **1** was also isolated. The product **2** was further purified by recrystallization with dichloromethane yielding a white powder, (1.70 g, 73 %). M. P. >280 ˚C; ^{1}H NMR (δH; 200 MHz, $CDCl_3$): 7.07 (s, 4H), 5.98 (d, J = 6.0Hz, 4H), 4.86 (t, J = 8.0

Hz, 4H), 4.32 (d, 6.0Hz, 4H), 2.22 – 2.19 (m, 8H), 1.39 (br, 24H), 0.92 (t, J = 7Hz, 12 H); ^{13}C NMR (δH; 200 MHz, $CDCl_3$): 155.03, 138.80, 120.85, 98.90, 93.25, 38.14, 32.06, 30.23, 27.61, 22.84, 14.27.

The product **1** was further purified by recrystallization with dichloromethane yielding a white powder, (0.25 g). M. P. >280 ˚C; ^{1}H NMR (δH; 200 MHz, $CDCl_3$): 7.07 (s, 2H), 7.04 (s, 2H), 5.98 (d, J = 8.0Hz, 4H), 4.86 (t, J = 8.0 Hz, 4H), 4.37 (d, 6.0Hz, 4H), 2.19 – 2.22 (m, 8H), 1.39 (br, 24H), 0.92 (t, J = 7Hz, 12 H).

Synthesis of C-pentyl-1,3-di-(2-acetamidopyridyl-5-ethynyl)-2,4-dibromocavitand, *3*

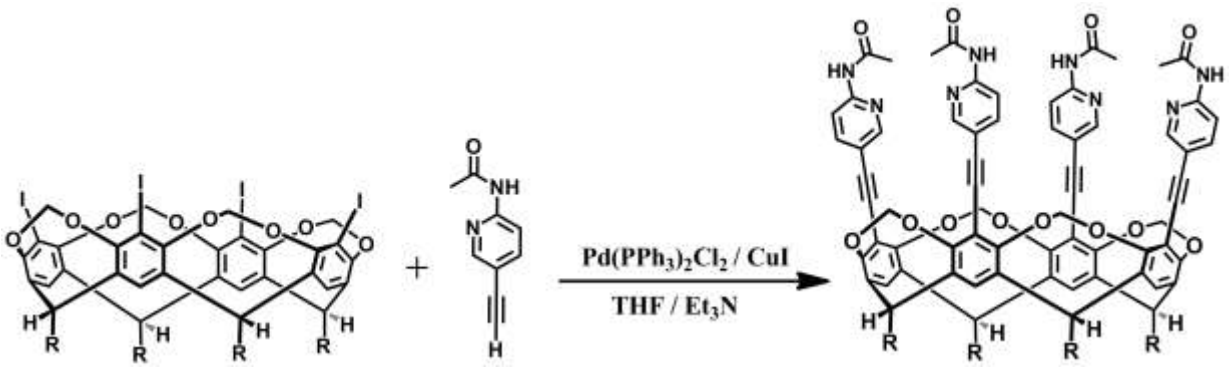


1 **3**

C-Pentyl-1,3-dibromo-2,4-diiodocavitand **2** (0.200 g, 0.163 mmol) was placed in a round bottomed flask and warmed to 50 ºC with stirring for 30 minutes to remove moisture. 2-Acetamido-5-ethynylpyridine (0.075 g, 0.470 mmol), *bis*(triphenylphosphine)palladium (II) dichloride (0.005 g, 0.007 mmol), triphenylphosphine (0.002 mg, 0.008 mmol), and copper(I) iodide (0.001 mg, 0.005 mmol) was added to it along with dry, freshly distilled THF (5 mL) and triethylamine (3 mL). Dinitrogen was bubbled through the mixture for 10 minutes and refluxed at 70 ºC under dinitrogen. The reaction was monitored by TLC and upon completion (36 hrs) was cooled to room temperature. The solution was then diluted with ethyl acetate (100 mL), washed with water (3 x 100 mL) and saturated aqueous sodium chloride solution (1 x 100 mL). The organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was removed on a rotary evaporator and the residue was chromatographed on silica with hexane/ethyl acetate/methanol mixture as eluant. The

product was isolated as a white solid, which was recrystallized from ethyl acetate. (100 mg, 48 %). M. P. >285 ºC; ^{1}H NMR (δH; 200 MHz, $CDCl_3$): 8.34 (s, 2 NH), 8.18 (d, 2H), 8.03 (s, 2H), 7.73 (d, J = 8.0 Hz, 2H), 7.09 (s, 2 H), 7.07 (s, 2 H), 6.00 (d, J = 8.0 Hz, 4H), 4.86 (t, J = 6.0 Hz, 4H), 4.51 (d, 8.0 Hz, 4H), 2.23 (s, 14H), 1.40 (m, 24H), 0.93 (m, 12 H); ^{13}C NMR (δH; 200 MHz, $CDCl_3$): 155.44, 152.21, 150.66, 141.05, 139.63, 138.56, 113.30, 37.29, 32.04, 29.83, 27.60, 24.97, 22.84, 14.25. MALDI-TOF / TOF-MS *m/z* 1290 ([**3** + Na]$^{+}$).

Synthesis of C-pentyltetra-(2-acetamidopyridyl-5-ethynyl)cavitand, *4*



R = $(CH_2)_4CH_3$ R = $(CH_2)_4CH_3$

2 **4**

C-Pentyltetraiodocavitand **2** (0.20 g, 0.15 mmol) was placed in a round bottomed flask and warmed to 50 ºC with stirring for about 30 mins to remove moisture. 2-acetamido-5-ethynylpyridine (0.14 g, 0.88 mmol), *bis*(triphenylphosphine)palladium (II) dichloride (0.010 g, 0.014 mmol), triphenylphosphine (0.004 g, 0.016 mmol), and copper(I) iodide (0.002 g, 0.010 mmol) was added along with dry, freshly distilled THF (10 mL) and triethylamine (5 mL). Dinitrogen was bubbled through the mixture for 10 minutes and refluxed at 70 ºC under dinitrogen. The reaction was monitored by TLC and upon completion (36 hrs) was cooled to room temperature. The solution was then diluted with ethyl acetate (100 mL), washed with water (3 x 100 mL) and saturated aqueous sodium chloride solution (1 x 100 mL). The organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was removed on a rotary evaporator and the residue was chromatographed on silica with hexane/ethyl acetate/methanol mixture as eluant. The product was isolated as a white solid, which was recrystallized from ethyl acetate. (125 mg,

58 %). M. P. >285 ºC; ^{1}H NMR (δH; 200 MHz, $CDCl_3$): 9.14 (br, 4 NH), 8.27 (s, 4H), 8.22 (s, 4H), 7.74 (d, J = 8.0 Hz, 4H), 7.12 (s, 4 H), 6.01 (d, J = 6.0 Hz, 4H), 4.86 (t, J = 8Hz, 4H), 4.59 (d, 6.0 Hz, 4H), 2.25 (s, 12H), 2.18 – 2.21 (m, 8H), 1.41 – 1.27 (m, 24H), 0.93 (m, 12 H); ^{13}C NMR (δH; 200 MHz, $CDCl_3$): 169.45, 155.44, 151.11, 150.04, 141.24, 138.73, 120.71, 115.81, 113.96, 112.95, 94.26, 83.92, 36.72, 32.02, 29.66, 27.61, 24.84, 22.84, 14.26. FT-IR (KBr pellet): υ (cm^{-1}) 3293, 2930, 2863, 1697, 1573, 1517, 1368, 1292, 974. MALDI-TOF / TOF-MS *m/z* 1448 ([**4** + Na]$^{+}$)

Table 1 Crystal data and structure refinement for ***3*** and ***4***

Parameter	**3**	**4**
Empirical formula	C79 H93 Br2 N4 O12	C100.60 H113.30 N8 O16.80
M	1450.39	1703.29
T/ºK	120(2)	120(2)
Wavelength/Å	0.71073	0.71073
Crystal system	Monoclinic	Triclinic
Space group	P2(1)/m	P-1
a/Å	13.3457(7)	14.7722(7)
b/Å	19.5826(9)	15.9370(8)
c/Å	14.0550(8)	22.1716(11)
α/º	90	109.733(3)
β/º	99.793(2)	96.094(3)
γ/º	90	93.890(3)
V/Å^3	3619.7(3)	4855.4(4)
Z	2	2
D(calculated)	1.331 g/cm^3	1.165 Mg/m^3
Absorption coefficient	1.184 mm-1	0.080 mm-1
F(000)	1522	1815
Crystal size (mm^3)	0.28 x 0.24 x 0.10	0.30 x 0.20 x 0.10
Theta range for data collection	1.47 to 29.13°	0.99 to 28.40°
Index ranges	-18<=h<=18, -26<=k<=26, -14<=l<=19	-19<=h<=19, -21<=k<=21, -28<=l<=29
Reflections collected	45929	99701
Independent reflections	9980 [R(int) = 0.0389]	23980 [R(int) = 0.0575]
Completeness to theta	99.7 %	98.4 %
Absorption correction	None	None
Max. and min. transmission	0.8907 and 0.7327	0.9921 and 0.9765
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data / restraints / parameters	9980 / 44 / 481	23980 / 45 / 1136
Goodness-of-fit on F^2	1.251	1.806
Final R indices [I>2sigma(I)]	R1 = 0.0823, wR2 = 0.2499	R1 = 0.1055, wR2 = 0.2969
R indices (all data)	R1 = 0.1321, wR2 = 0.2791	R1 = 0.1804, wR2 = 0.3241
Largest diff. peak and hole (e.Å^{-3})	1.441 and -1.063	1.223 and -0.708

NMR data

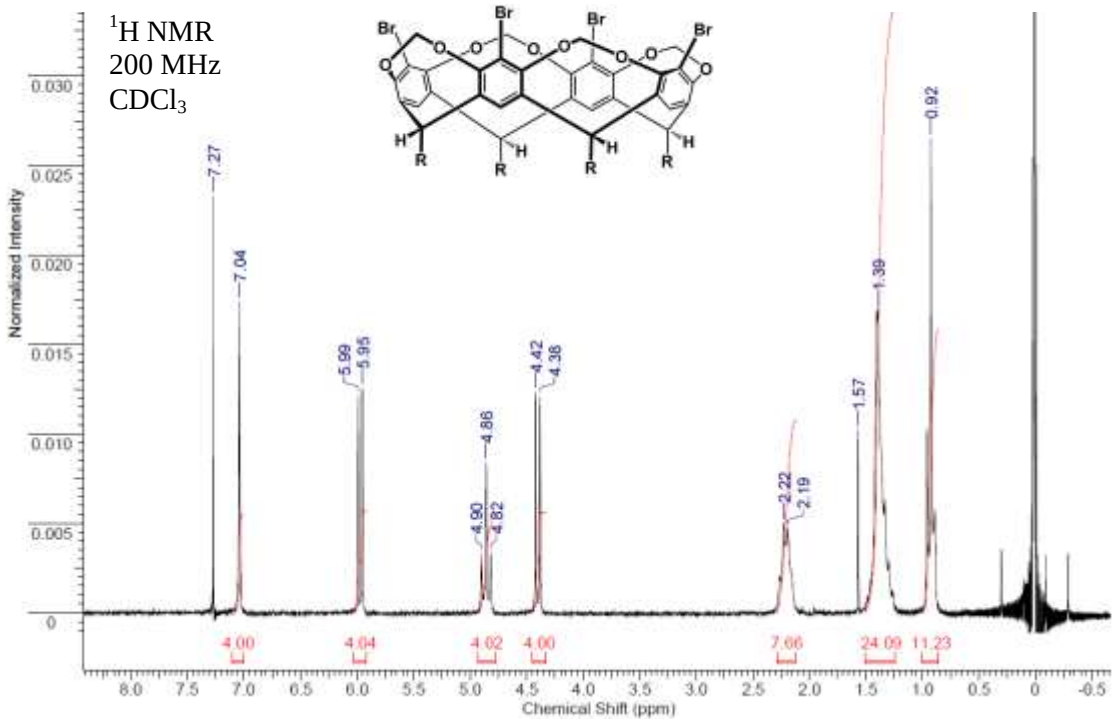


Fig. 1 ^{1}H NMR for C-Pentyltetrabromocavitand

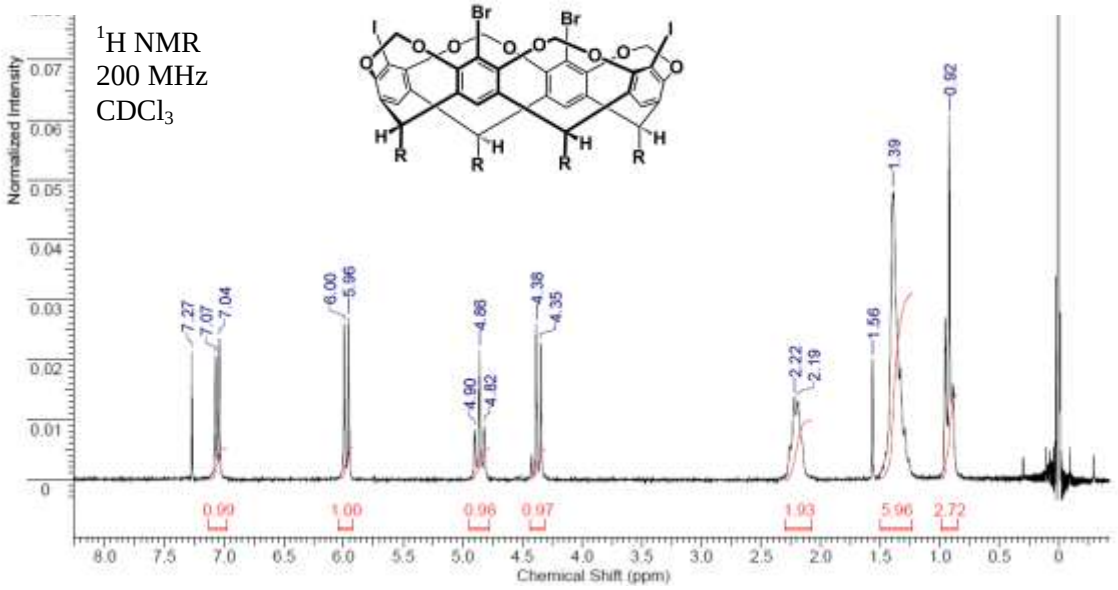


Fig. 2 ^{1}H NMR for *C*-Pentyl-1,3-dibromo-2,4-diiodo-cavitand, ***1***

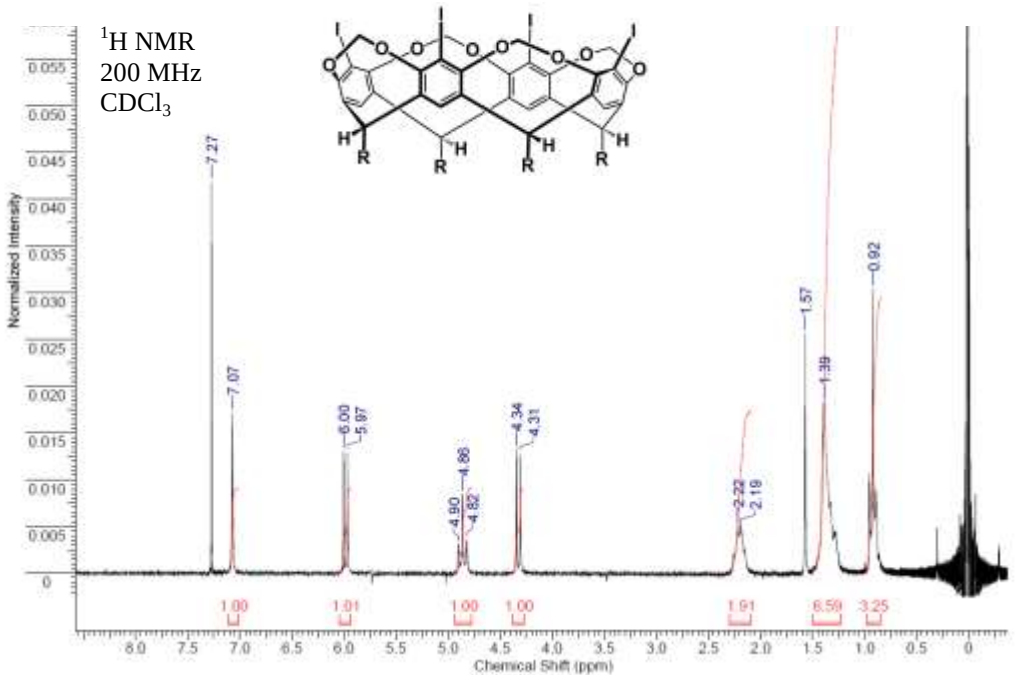


Fig. 3 ^{1}H NMR for *C*-Pentyltetraiodocavitand, ***2***

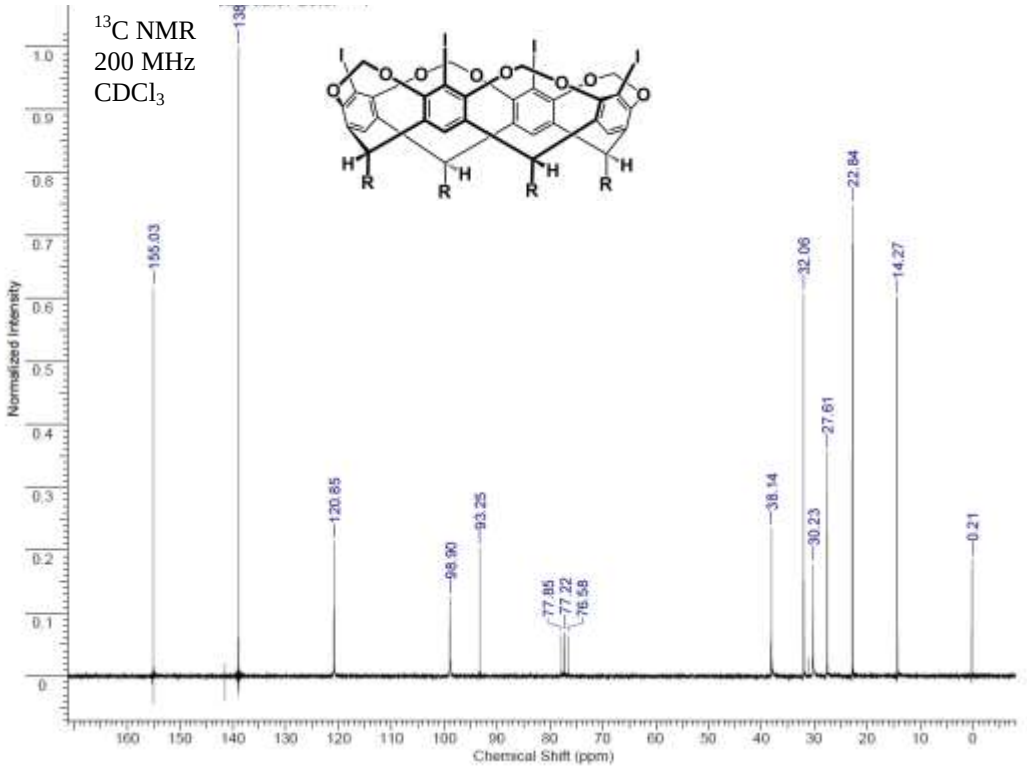


Fig. 4 ^{13}C NMR for *C*-Pentyltetraiodocavitand, ***2***

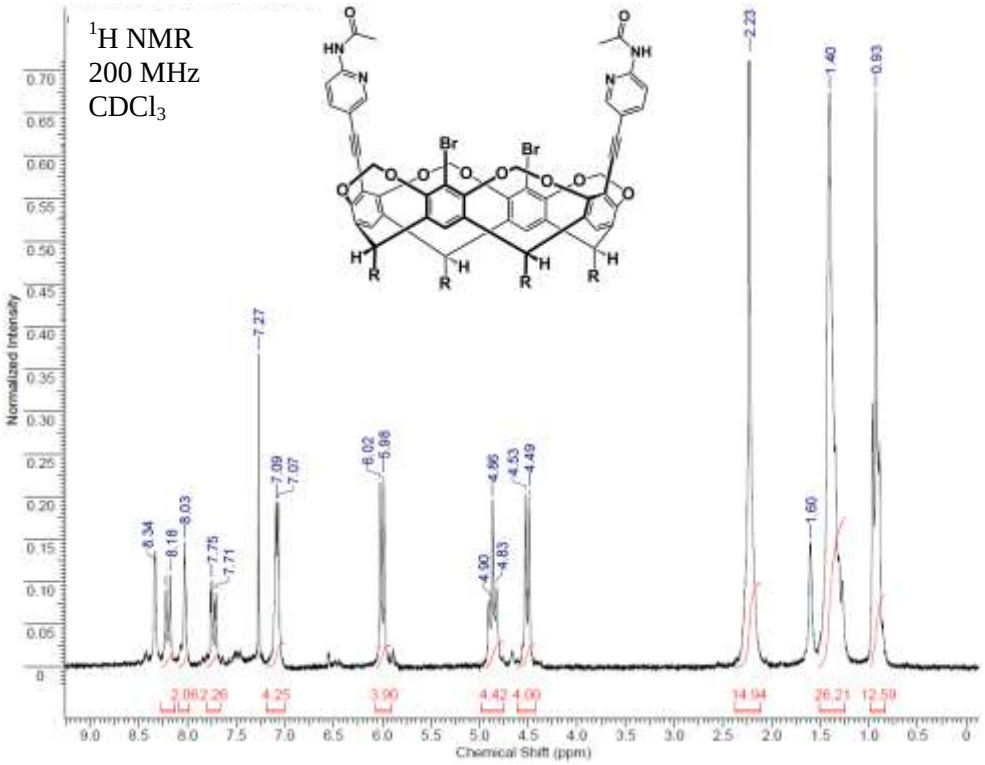


Fig. 5 ^{1}H NMR for *C*-Pentyl-1,3-di-(2-acetamidopyridyl-5-ethynyl)-2,4-dibromocavitand, ***3***

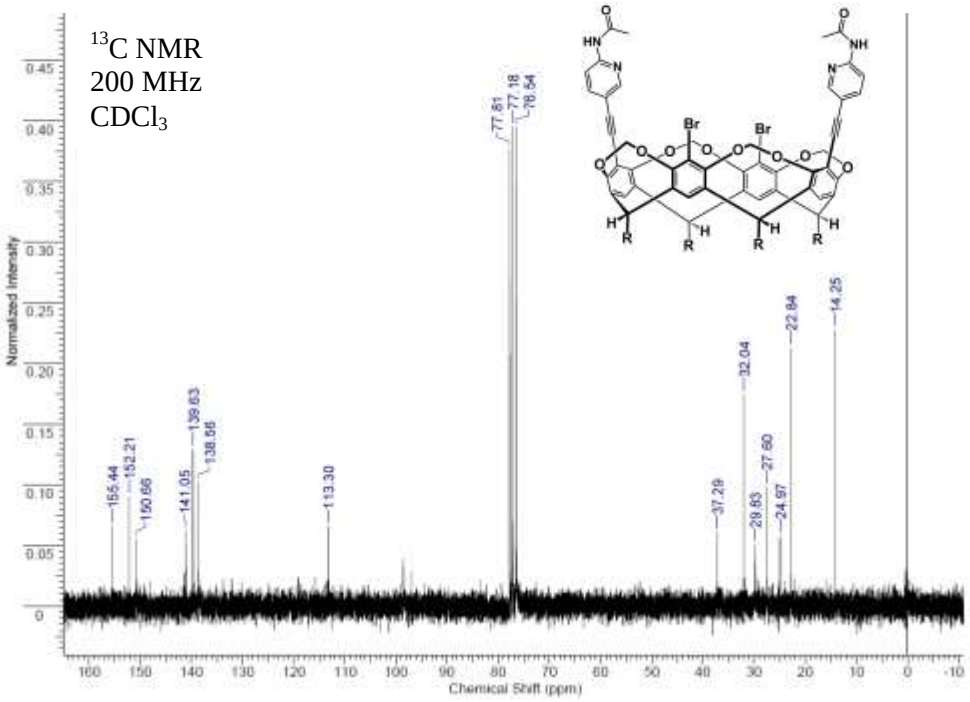


Fig. 6 ^{13}C NMR for *C*-Pentyl-1,3-di-(2-acetamidopyridyl-5-ethynyl)-2,4-dibromocavitand, ***3***

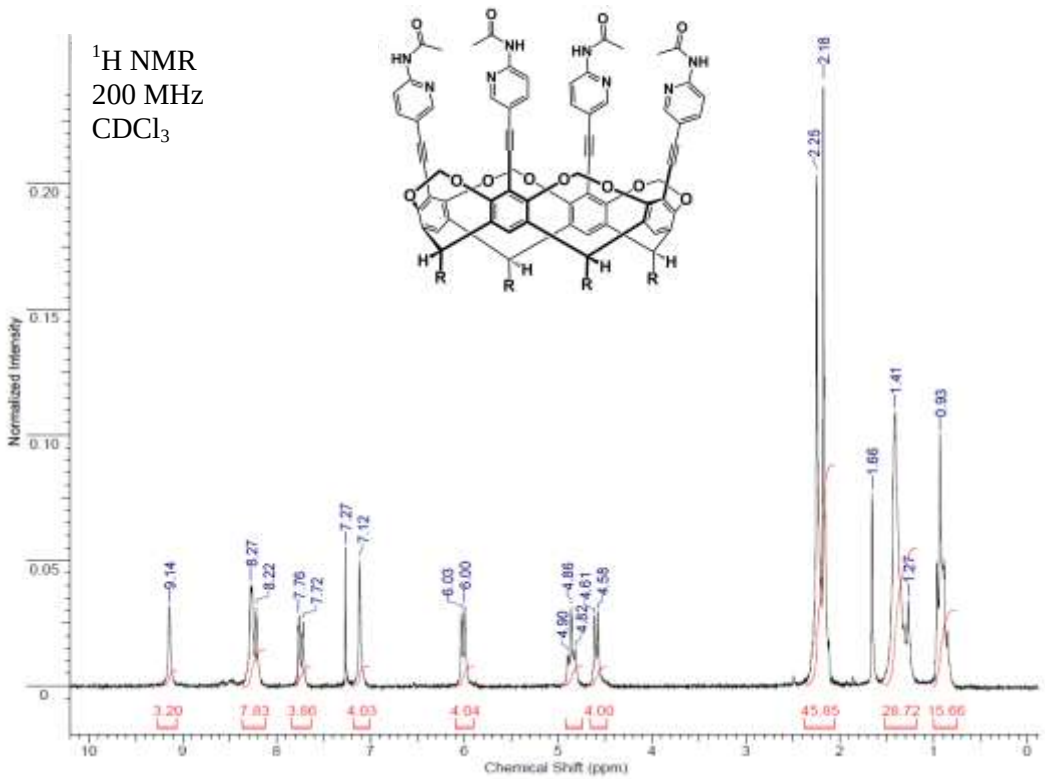


Fig. 7 ^{1}H NMR for *C*-Pentyl-tetra-(2-acetamidopyridyl-5-ethynyl)cavitand, ***4***

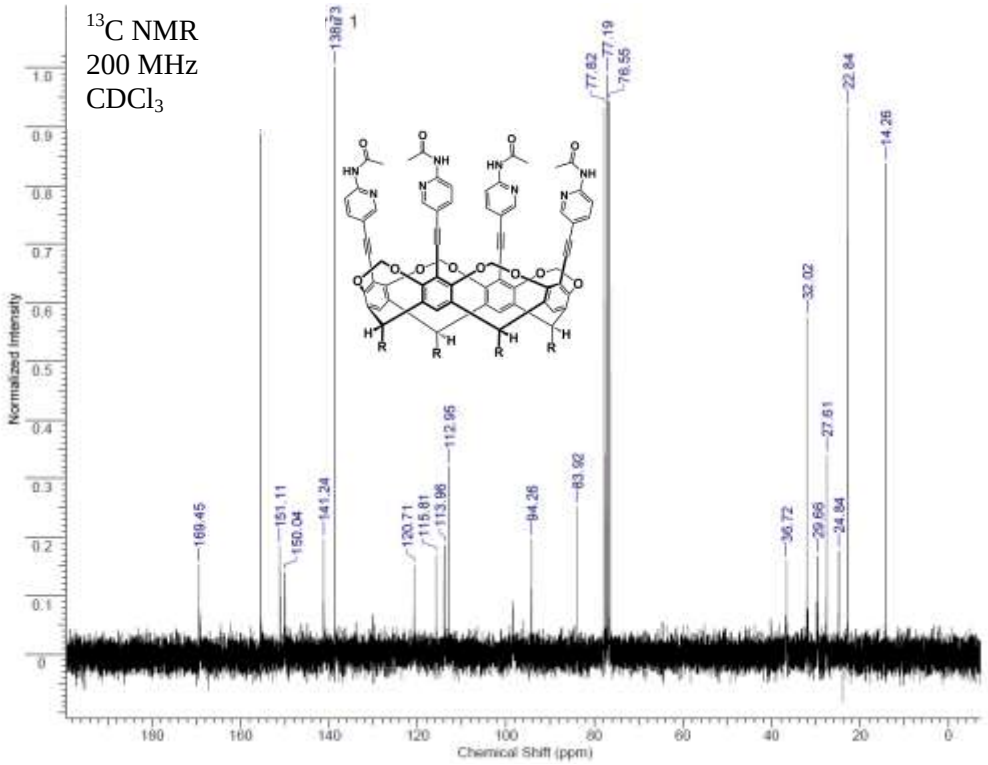


Figure 8 ^{13}C NMR for *C*-Pentyl-tetra-(2-acetamidopyridyl-5-ethynyl)cavitand, ***4***

[1] X. Liu and R. Warmuth, *Nature Protocols.*, 2007, **2**, 1288.
[2] J. A. Bryant, M. T. Blanda, M. Vincenti and D. J. Cram, *J. Am. Chem. Soc.*, 1991, **113**, 2167.