

# Tetraiodoethynyl resorcinarene cavitands as multivalent halogen bond donors

*L. Turunen, N. K. Beyeh, F. Pan, A. Valkonen and K. Rissanen\**

Department of Chemistry, NanoScience Center, University of Jyväskylä, P. O. Box 35, 40014 Jyväskylä, Finland

## Electronic Supplementary Information

### Table of Contents

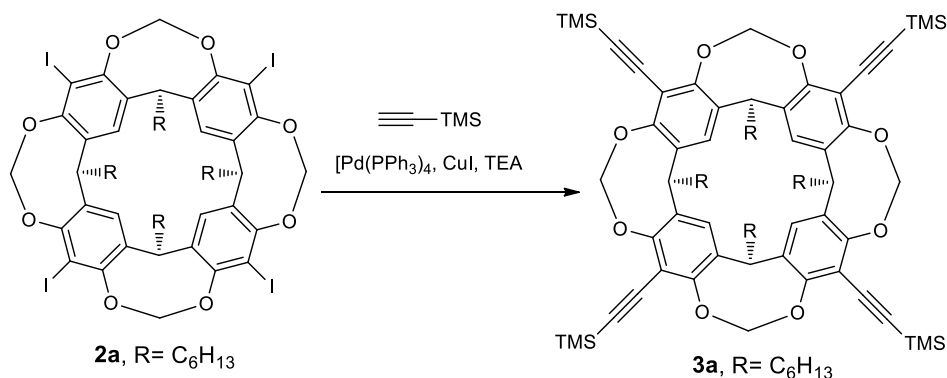
I General Information.....	2
II Synthesis.....	2
III X-Ray Crystallography.....	12
IV References.....	14

## I General Information

Reagents were purchased from commercial suppliers and used without further purification. Triethylamine was dried prior to use. The C<sub>6</sub>-resorcinarene and iodinated resorcinarene **1a** were prepared according to literature procedures.<sup>1,2</sup> Ethylene bridged cavitand **2b** was prepared according to modified literature procedure, whereby the treatment of the iodinated resorcinarene **1a** with 1-bromo-2-chloroethane in the presence of K<sub>2</sub>CO<sub>3</sub> as base gave the cavitand **2b**.<sup>2</sup> Tetra[(trimethylsilyl)ethynyl]cavitands were prepared based on modified reported procedures.<sup>3</sup> Tetrahalogenated ethyne cavitands were prepared according to literature procedure.<sup>4</sup> <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker Avance DRX 500 (500 MHz for <sup>1</sup>H and 126 MHz for <sup>13</sup>C) spectrometer. All signals are given as δ values in ppm using residual solvent signals as the internal standard. Coupling constants are given in Hz. Melting points were determined with a Mettler Toledo FP62 capillary melting point apparatus. The mass spectrometric studies were performed with a micromass LCT ESI-TOF instrument.

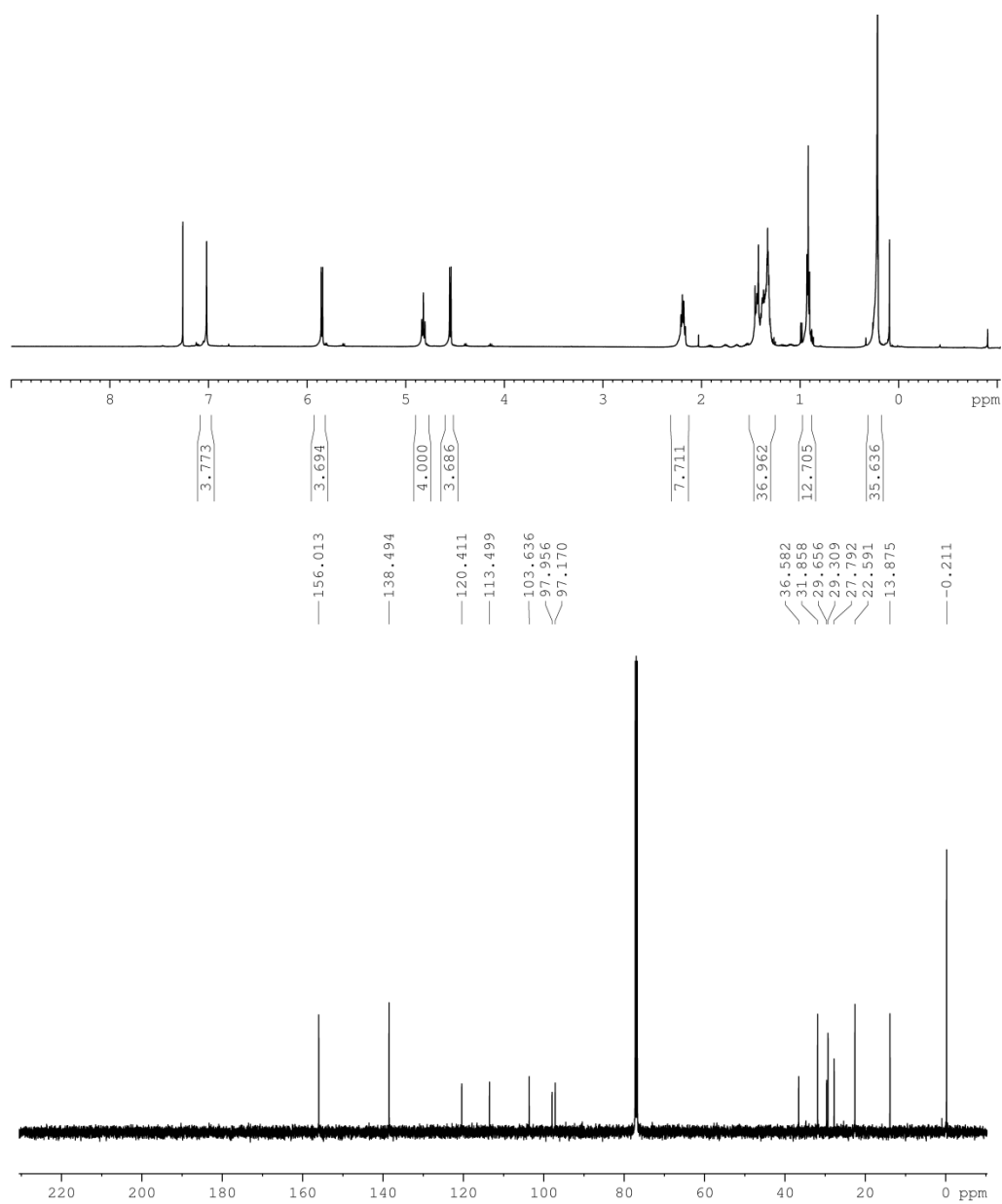
## II Synthesis

### Synthesis of tetra[(trimethylsilyl)ethynyl]cavitand **3a**



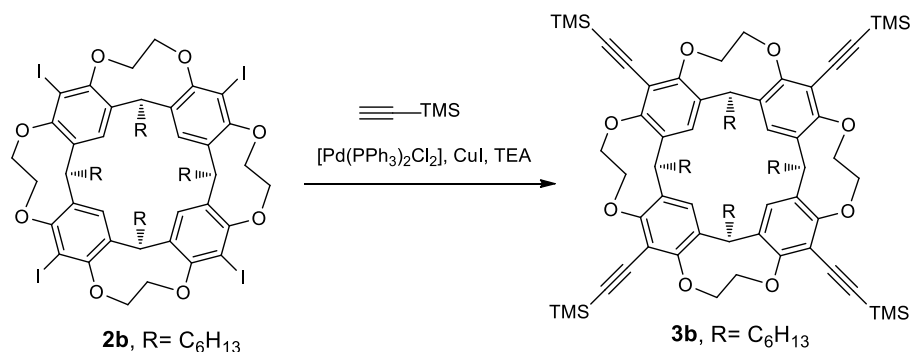
**Scheme S1.** Synthesis of tetra[(trimethylsilyl)ethynyl]cavitand **3a**.

Tetraiodocavitand **2a** (2.33 g, 1.69 mmol), [Pd(PPh<sub>3</sub>)<sub>4</sub>] (156 mg, 0.135 mmol) and copper(I) iodide (26 mg, 0.135 mmol) were evacuated and flushed with argon twice. Dry triethylamine (60 ml) and ethynyltrimethylsilane (1.19 ml, 8.45 mmol) were added via syringe. The mixture was stirred at 100°C for 18 h. Water and chloroform were added. The layers were separated and the aqueous layer was extracted twice with chloroform. The combined organic layers were dried over MgSO<sub>4</sub> and the solvent was evaporated to dryness. The crude product was purified by column chromatography (SiO<sub>2</sub>, *n*-hexane/EtOAc 20:1) to give the tetra[(trimethylsilyl)ethynyl]cavitand **3a** as a white solid (1.786 g, 84%). m.p. 254 °C; <sup>1</sup>H NMR (500 MHz, 303K, CDCl<sub>3</sub>) δ (ppm): 0.21 (s, 36H, TMS), 0.92 (t, 12H, CH<sub>3</sub>, J=7.0 Hz), 1.30-1.45 (m, 32H, (CH<sub>2</sub>)<sub>4</sub>), 2.16-2.21 (m, 8H, CH<sub>2</sub>), 4.54 (d, 4H, CH<sub>2in</sub>, J=7.3 Hz), 4.82 (t, 4H, CH, J=8.1 Hz), 5.85 (d, 4H, CH<sub>2out</sub>, J=7.3 Hz), 7.02 (s, 4H, Ar-H); <sup>13</sup>C NMR (126 MHz, 303K, CDCl<sub>3</sub>) δ (ppm): -0.21, 13.87, 22.59, 27.79, 29.31, 29.66, 31.86, 36.59, 97.17, 97.96, 103.64, 113.50, 120.41, 138.49, 156.01; LCT ESI-TOF: *m/z* = Found 1383.5887 ([M+I]<sup>-</sup>), 2.5 ppm; calc. 1383.5853.



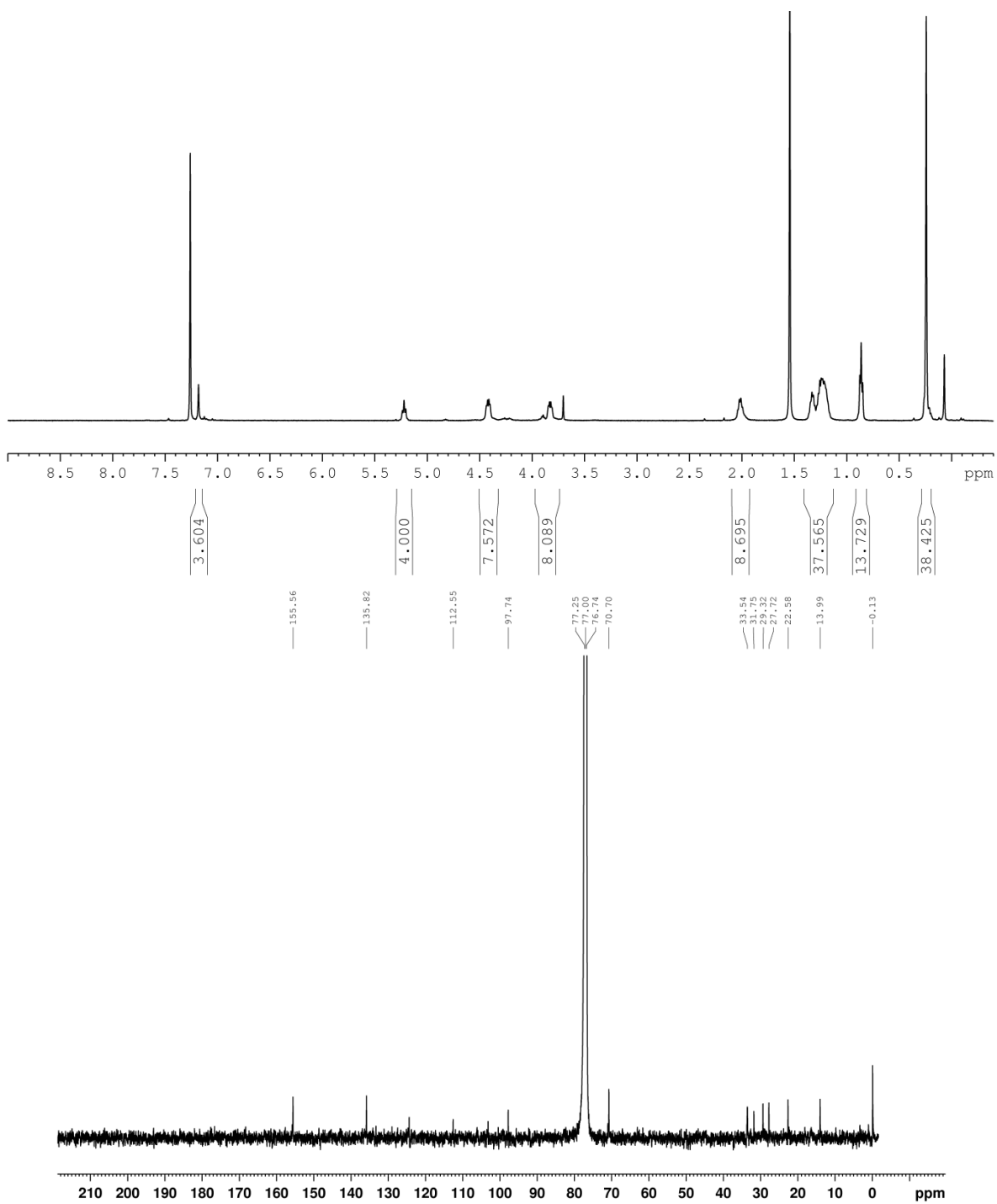
**Fig. S1.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of tetra[(trimethylsilyl)ethynyl]cavitand **3a**.

## Synthesis of tetra[(trimethylsilyl)ethynyl]cavitand **3b**



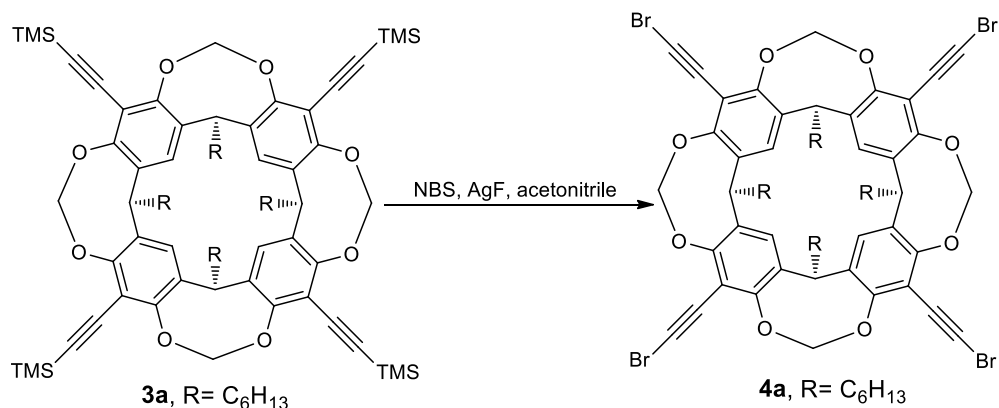
### *Scheme S2.* Synthesis of tetra[(trimethylsilyl)ethynyl]cavitand **3b**.

Tetraiodocavitand **2b** (1.00g, 0.698 mmol),  $[\text{Pd}(\text{PPh}_3)_2\text{Cl}_2]$  (39.19 mg, 0.056 mmol) and copper(I) iodide (10.63 mg, 0.056 mmol) were evacuated and flushed with argon twice. Dry triethylamine (27 ml) was added and the mixture was stirred at room temperature for 60 min. Ethynyltrimethylsilane (0.49 ml, 3.49 mmol) was added into the mixture via syringe dropwise. The mixture was stirred at 98 °C for 20 h. Water and EtOAc were added. The layers were separated and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over  $\text{MgSO}_4$  and the solvent was evaporated to dryness. The crude product was purified by column chromatography ( $\text{SiO}_2$ , *n*-hexane/EtOAc 25:1) to give the tetra[(trimethylsilyl)ethynyl]cavitand **3b** as a white solid (430 mg, 47%). m.p. 198 °C; 0.24 (s, 36H, TMS), 0.86 (t, 12H,  $\text{CH}_3$ ,  $J=6.64$ ), 1.21-1.33 (m, 32H,  $(\text{CH}_2)_4$ ), 2.00-2.02 (m, 8H,  $\text{CH}_2$ ), 3.82-3.84 (m, 8H,  $\text{CH}_{2\text{in}}$ ), 4.40-4.44 (m, 8H,  $\text{CH}_{2\text{out}}$ ), 5.24 (t, 4H, CH,  $J=7.83$ ), 7.18 (s, 4H, Ar-H);  $^{13}\text{C}$  NMR (126 MHz, 303K,  $\text{CDCl}_3$ )  $\delta$  (ppm): -0.13, 13.99, 22.58, 27.72, 29.32, 31.75, 33.54, 70.70, 97.74, 112.55, 135.82, 155.56; LCT ESI-TOF (int. calibration):  $m/z$ =Found 1335.7333 ( $[\text{M}+\text{Na}]^+$ ) 0.45 ppm; calc. 1335.73265.



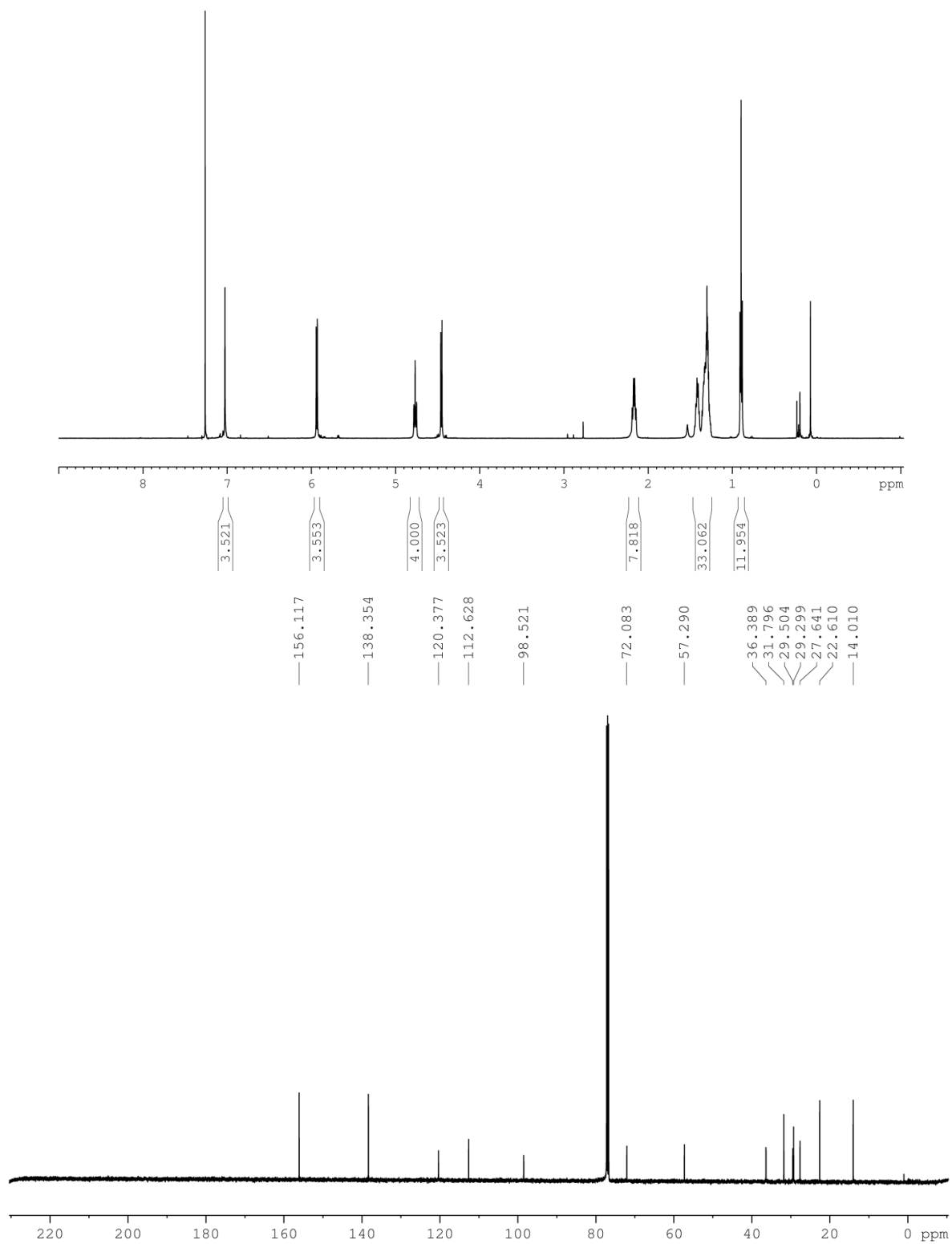
**Fig. S2.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of tetra[(trimethylsilyl)ethynyl]cavitand **3b**.

## Synthesis of tetrabrominated ethyne cavitand **4a**



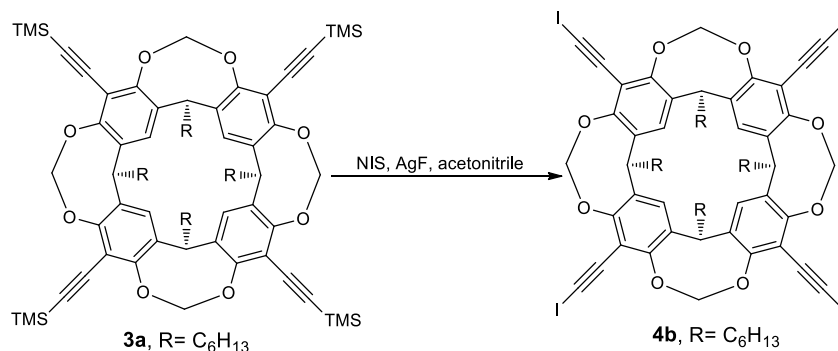
### *Scheme S3.* Synthesis of tetrabrominated ethyne cavitand **4a**.

Acetonitrile (6.7 ml) was added to the mixture of tetra[(trimethylsilyl)ethynyl]cavitand **3a** (0.50 g, 0.40 mmol) and AgF (0.26 g, 2.06 mmol). The flask was wrapped in aluminium foil and NBS (0.35 g, 1.99 mmol) was added. The mixture was stirred for 24h at room temperature. Water and chloroform were added. The layers were separated and the aqueous layer was extracted twice with chloroform. The combined organic layers were dried over MgSO<sub>4</sub> and the solvent was evaporated to dryness. The crude product was filtered through a silica plug (n-hexane/ethyl acetate, 2:1) to give the tetrabrominated ethyne cavitand **4a** as a white solid (488 mg, 96 %); m.p. > 300 °C; <sup>1</sup>H NMR (500 MHz, 303K, CDCl<sub>3</sub>) δ (ppm): 0.90 (t, 12H, CH<sub>3</sub>, J = 6.8 Hz), 1.27-1.43 (m, 32H, CH<sub>2</sub>)<sub>4</sub>, 2.14-2.19 (m, 8H, CH<sub>2</sub>), 4.45 (d, 4H, CH<sub>2in</sub>, J = 7.3 Hz), 4.77 (t, 4H, CH, J = 8.2 Hz), 5.93 (d, 4H, CH<sub>2out</sub>, J = 7.3 Hz), 7.03 (s, 4H, Ar-H); LCT ESI-TOF: m/z = Found 1407.0662 ([M+I]<sup>-</sup>) 3.2 ppm; calc. 1407.0692.



**Fig. S3.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of tetrabrominated ethyne cavitaand **4a**.

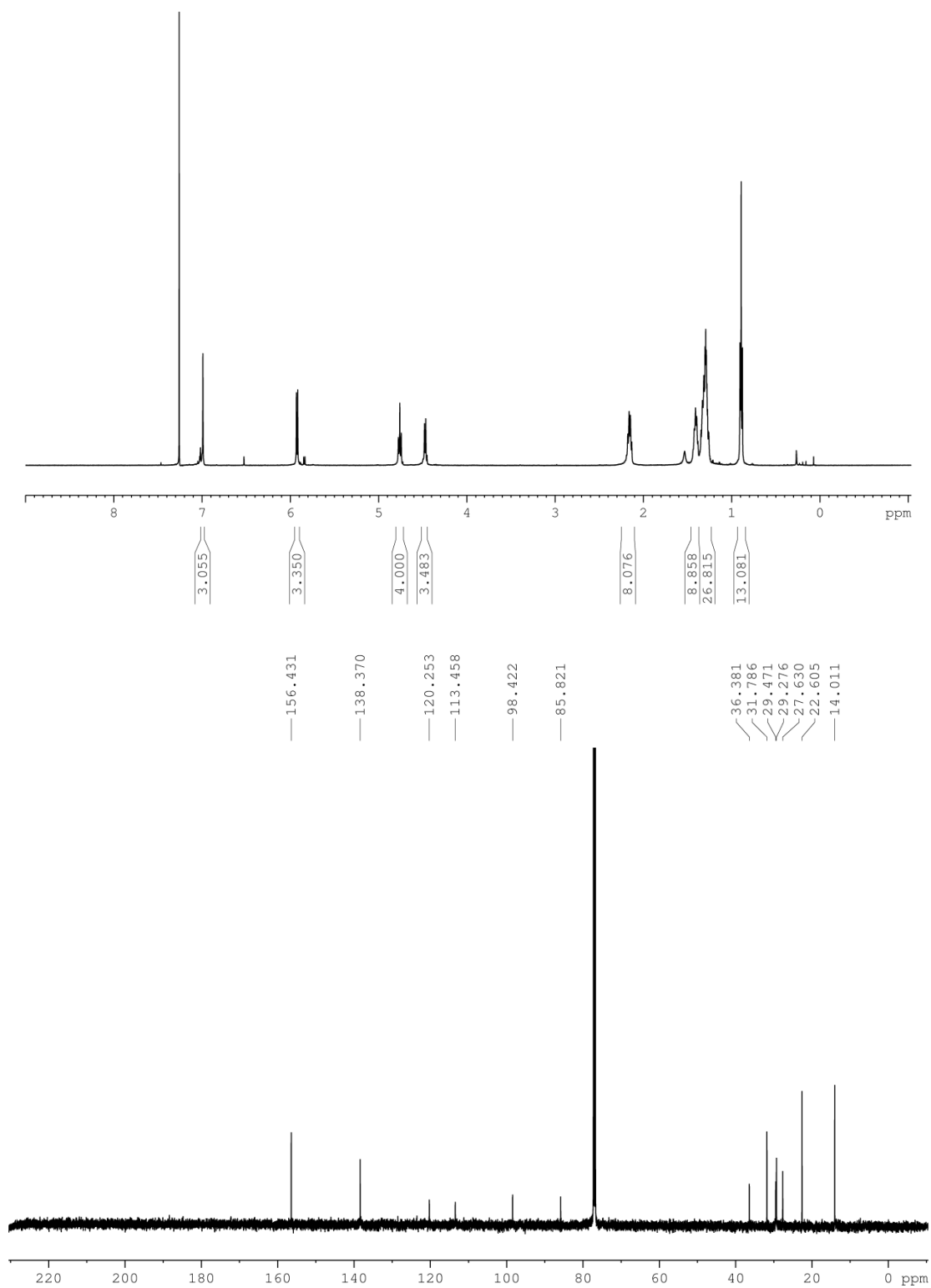
## Synthesis of tetraiodinated ethyne cavitand **4b**



### *Scheme S4.* Synthesis of tetraiodinated ethyne cavitand **4b**.

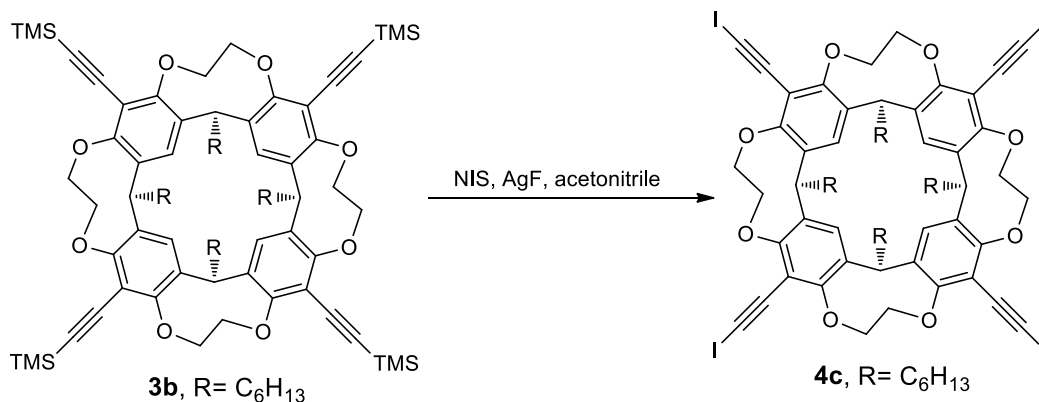
Acetonitrile (6 ml) was added to the mixture of tetra[(trimethylsilyl)ethynyl]cavitand **3a** (0.50 g, 0.40 mmol) and AgF (0.21 g, 1.59 mmol). The flask was wrapped in aluminium foil and NIS (0.36 g, 1.59 mmol) was added. The mixture was stirred for 24h at room temperature. The mixture was stirred for 5 hours at room temperature. To the mixture were added 2 ml of deionised water and 2 ml of THF and the mixture was stirred for 18 h more. The mixture was filtered. The precipitate was filtered through a silica plug (n-hexane/ethyl acetate, 2:1) to give the tetraiodinated ethyne cavitand **4b** as a white solid (258 mg, 44%); m.p. > 300 °C; <sup>1</sup>H NMR (500 MHz, 303K, CDCl<sub>3</sub>) δ (ppm): 0.90 (t, 12H, CH<sub>3</sub>, J = 6.8 Hz), 1.27-1.43 (m, 32H, (CH<sub>2</sub>)<sub>4</sub>), 2.14-2.19 (m, 8H, CH<sub>2</sub>), 4.45 (d, 4H, CH<sub>2in</sub>, J = 7.3 Hz), 4.77 (t, 4H, CH, J = 8.2 Hz), 5.93 (d, 4H, CH<sub>2out</sub>, J = 7.3 Hz), 7.03 (s, 4H, Ar-H); <sup>13</sup>C NMR (126 MHz, 303K, CDCl<sub>3</sub>) δ (ppm): 14.01, 22.61, 27.63, 29.28, 29.47, 31.79, 36.38, 85.82, 98.42, 113.46, 120.25, 138.37, 156.43; LCT ESI-TOF: m/z = Found 1599.0142 ([M + I]<sup>-</sup>), 0.30 ppm; calc. 1599.0138.





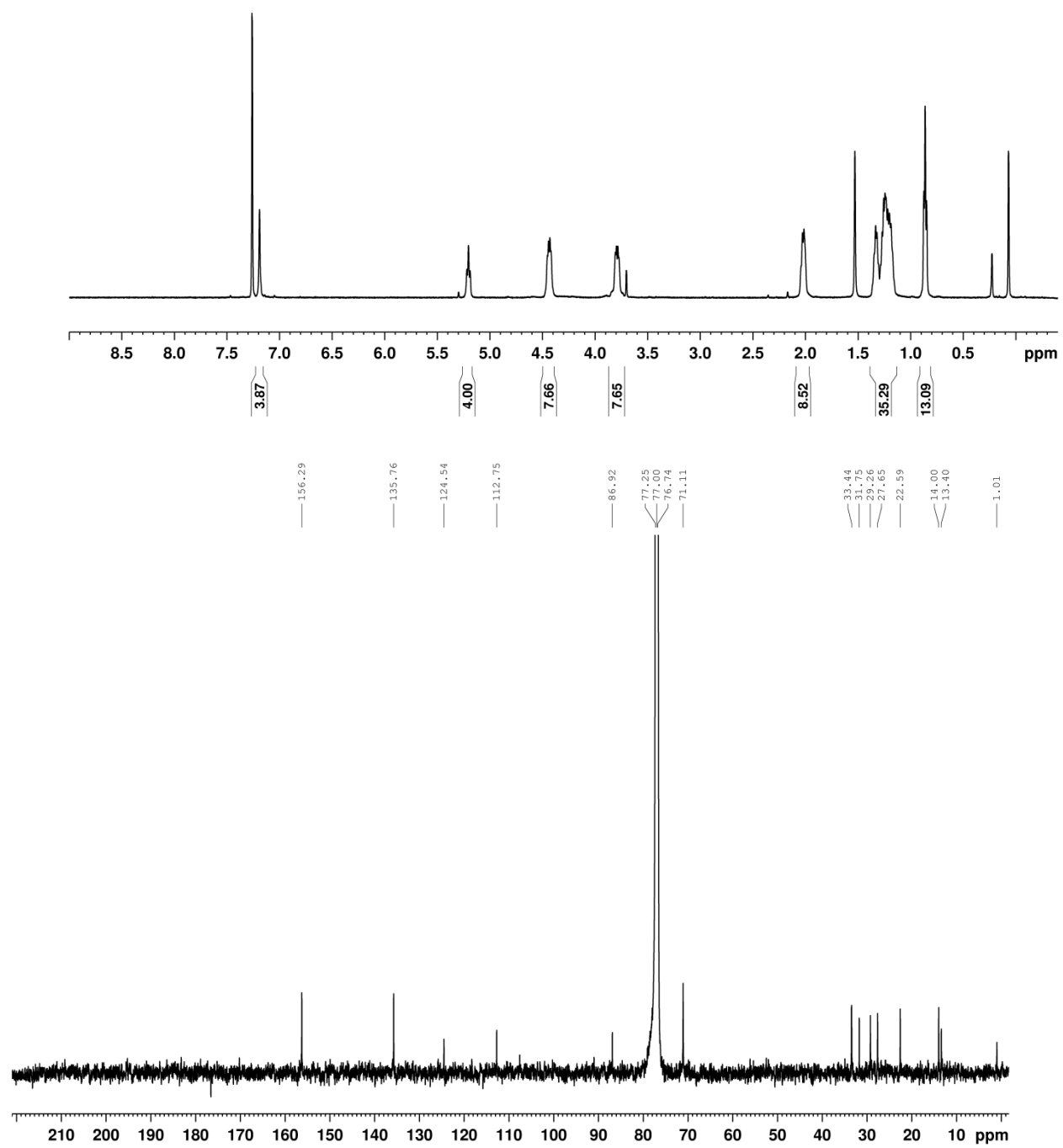
**Fig. S3.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of tetraiodinated ethyne cavitant **4c**.

## Synthesis of tetraiodinated ethyne cavitand **4c**



### *Scheme S4.* Synthesis of tetraiodinated ethyne cavitand **4c**.

Acetonitrile (5.9 ml) was added to the mixture of tetra[(trimethylsilyl)ethynyl]cavitand **3b** (0.37 g, 0.28 mmol) and AgF (0.22 g, 1.73 mmol). The flask was wrapped in aluminium foil and NIS (0.38g, 1.68 mmol) was added. The mixture was stirred overnight at room temperature. Water and chloroform were added. The layers were separated and the watery layer was extracted twice more with chloroform. The combined organic layers were dried over MgSO<sub>4</sub> and the solvent was evaporated to dryness. The crude product was purified by column chromatography (SiO<sub>2</sub>; n-hexane/ethyl acetate, 2:1) to give the tetraiodinated ethyne cavitand **4d** as a white solid (300 mg, 69 %). m.p. > 300 °C; <sup>1</sup>H NMR (500 MHz, 303K, CDCl<sub>3</sub>) δ (ppm): 0.86 (t, 12H, CH<sub>3</sub>, J = 5.5 Hz), 1.19-1.33 (m, 32H, (CH<sub>2</sub>)<sub>4</sub>), 2.01-2.03 (m, 8H, CH<sub>2</sub>), 3.74-3.83 (m, 4H, CH<sub>2in</sub>), 4.42-4.45 (m, 4H, CH<sub>2out</sub>), 5.20 (t, 4H, CH, J = 6.85.0 Hz), 7.19 (s, 4H, Ar-H); <sup>13</sup>C NMR (126 MHz, 303K, CDCl<sub>3</sub>) δ (ppm): 1.01, 13.40, 14.00, 22.59, 27.65, 29.26, 31.75, 33.44, 71.11, 86.96, 112.75, 124.54, 135.76, 156.29; LCT ESI-TOF (int. calibration): m/z = Found 1551.1549 ([M+Na]<sup>+</sup>), 4.0 ppm; calc. 1551.1611.



*Fig. S4.*  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of tetraiodinated ethyne cavitanol **4d**.

### III X-Ray Crystallography:

Crystals of **4c•Pyridine** were obtained by slow evaporation from a pyridine solution. Crystals of **4c•TPABr** were obtained by slow evaporation from CHCl<sub>3</sub> with a few drops of methanol, while **4b•1,4-Dioxane** crystals were grown from CHCl<sub>3</sub> with a few drops of 1,4-dioxane. Data were collected at 123 K with an Agilent Super-Nova diffractometer using mirror-monochromatized Cu-K $\alpha$  ( $\lambda$  = 1.54184 Å) radiation. *CrysAlisPro*<sup>5</sup> was used for the data collection and processing. The intensities were corrected for absorption using the analytical face index absorption correction method. The structures were solved by direct methods with *SHELXS*<sup>6</sup> or *SIR2011*<sup>7</sup> (for **4b•1,4-Dioxane**) and refined by full-matrix least-squares methods using the *OLEX2*<sup>8</sup> which utilizes the *SHELXL-97*<sup>6</sup> module. All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were introduced in proper positions with isotropic thermal parameters using the ‘riding model’. One hexyl chain end (2 C atoms) and 1.7 1,4-dioxane molecules in **4b•1,4-Dioxane**, two hexyl chains and one iodoethynyl group in **4c•Pyridine**, and the chloroform molecule in **4c•TPABr** were disordered and they were split over two positions with additional geometry constraints/restraints if necessary. Restraints on neighbouring anisotropic displacement parameters (SIMU 0.01 0.02) were also applied for disordered moieties in **4b•1,4-Dioxane**. Moreover, some of the non-H atoms with sharp anisotropic ellipsoids due to thermal vibration in **4c•Pyridine** and **4c•TPABr** were restrained to be approximately isotropic with “ISOR 0.02 or ISOR 0.01” commands. Crystal data, information regarding the data collection, reduction and convergence results were documented in table S1.

**Table S1. Crystallographic details**

	<b>4b•1,4-Dioxane</b>	<b>4c•Pyridine</b>	<b>4c•TPABr</b>
Crystal data			
Chemical formula	C <sub>64</sub> H <sub>68</sub> I <sub>4</sub> O <sub>8</sub> ·3.7(C <sub>4</sub> H <sub>8</sub> O <sub>2</sub> )·0.3O	C <sub>68</sub> H <sub>76</sub> O <sub>8</sub> I <sub>4</sub> ·7(C <sub>5</sub> H <sub>5</sub> N)	C <sub>68</sub> H <sub>76</sub> O <sub>8</sub> I <sub>4</sub> ·CHCl <sub>3</sub> ·2(Br)·2(C <sub>12</sub> H <sub>28</sub> N)·H <sub>2</sub> O·2(C <sub>3</sub> H <sub>6</sub> O)
<i>M<sub>r</sub></i>	1803.56	2082.58	2314.95
Crystal system, space group	Triclinic, <i>P</i> -1	Monoclinic, <i>C</i> 2/ <i>c</i>	Monoclinic, <i>P</i> 2 <sub>1</sub> / <i>c</i>
Temperature (K)	123	123	123
<i>a</i> (Å)	14.9822(4)	27.3028(5)	24.4168(7)
<i>b</i> (Å)	16.9494(5)	12.2692(2)	24.5753(13)
<i>c</i> (Å)	17.6201(4)	29.3240(5)	19.1408(6)
<i>α</i> (°)	96.532(2)	90	90
<i>β</i> (°)	101.5835(19)	90.8176(15)	106.621(3)
<i>γ</i> (°)	113.200(3)	90	90
<i>V</i> (Å <sup>3</sup> )	3935.34(19)	9822.0(3)	11005.6(8)
<i>Z</i>	2	4	4
<i>μ</i> (mm <sup>-1</sup> )	12.945	10.42	10.82
Crystal size (mm)	0.30 × 0.18 × 0.04	0.51 × 0.15 × 0.12	0.17 × 0.09 × 0.08
Data collection			
<i>T<sub>min</sub></i> , <i>T<sub>max</sub></i>	0.104, 0.454	0.040, 0.232	0.208, 0.420
No. of measured, independent and observed [ <i>I</i> > 2σ( <i>I</i> )] reflections	22925, 13955, 11795	19709, 10048, 8788	40510, 22103, 15779
<i>R<sub>int</sub></i>	0.047	0.036	0.049
(sin θ/λ) <sub>max</sub> (Å <sup>-1</sup> )	0.692	0.632	0.631
Refinement			
<i>R</i> [ <i>F</i> <sup>2</sup> > 2σ( <i>F</i> <sup>2</sup> )], <i>wR</i> ( <i>F</i> <sup>2</sup> ), <i>S</i>	0.073, 0.209, 1.02	0.043, 0.120, 1.03	0.057, 0.164, 1.03
No. of reflections	13955	10048	22103
No. of parameters	1036	592	1163
No. of restraints	433	43	68
Δρ <sub>max</sub> , Δρ <sub>min</sub> (e Å <sup>-3</sup> )	4.52, -1.68	1.16, -0.80	1.83, -1.80

#### IV References:

- 1 P. Timmerman, W. Verboom and D. N. Reinhoudt, *Tetrahedron*, 1996, **52**, 2663.
- 2 F. Gruppi, F. Boccini, L. Elviri and E. Dalcanale, *Tetrahedron*, 2009, **65**, 7289.
- 3 (a) C. Aakeröy, N. Schultheiss and J. Desper, *CrystEngComm*, 2007, **9**, 211. (b) C. Grave, D. Lentz, A. Schäfer, P. Samori, J. P. Rabe, P. Franke and A. D. Schlüter, *J. Am. Chem. Soc.*, 2003, **125**, 6907. (c) J. Lieffrig, O. Jeannin and M. Fourmigué, *J. Am. Chem. Soc.*, 2013, **135**, 6200.
- 4 K. Osowska, T. Lis and S. Szafert, *Eur. J. Org. Chem.*, **2008**, 4598–4606.
- 5 *CrysAlisPro*, Agilent Technologies, version 1.171.36.28, 2013.
- 6 G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 2008, **64**, 112.
- 7 M. C. Burla, R. Caliandro, M. Camalli, B. Carrozzini, G. L. Cascarano, C. Giacovazzo, M. Mallamo, A. Mazzone, G. Polidori and R. Spagna, *J. Appl. Crystallogr.*, 2012, **45**, 357.
- 8 O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Cryst.*, 2009, **42**, 339.