

# A Calixarene Dendron with Surface Congestion at the First Generation

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**General methods.** Unless otherwise reported, all reactions were carried out under dry and deoxygenated argon atmosphere. Solvents were freshly distilled and dried before use by standard methods. All chemicals were used as purchased. Reported melting points are uncorrected and were measured in open capillaries on a Gallenkamp Melting Point apparatus. The NMR experiments ( $^1\text{H}$ ,  $^{13}\text{C}\{^1\text{H}\}$ , and ROESY) were carried out at 500 (125) MHz and reported chemical shifts ( $\delta$ ) are externally referenced to solvent residual signal and given in ppm. Mass spectra were performed on a REFLEX spectrometer by MALDI-TOF method, using dithranol as matrix and NaI as additive. Elemental analyses, performed on a LECO CHN 932 microanalyser and reported as percentage, indicated inclusion of solvent molecules for nearly all calixarene products and were supported by separate  $^1\text{H}$  NMR studies. TLC was performed on silica gel Alugram Sil G/UV254 (Macherey-Nagel).

## Experimental Part

**Synthesis of Compounds 1 and 6:** A mixture of amine **3**<sup>1</sup> (150.0 mg, 0.125 mmol) and DIEA (50  $\mu\text{L}$ , 0.347 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (1.35 mL) was slowly added (25  $\mu\text{L}/\text{min}$ ) to a solution of triphosgene (13.7 mg, 0.046 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (0.90 mL) at 10-15°C, under argon. The mixture was stirred at room temperature for 15 min and then a solution of tetramine **4**<sup>2</sup> (17.8 mg, 0.023 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (0.90 mL) was slowly added. After 24 h under stirring at 40°C the organic solution was washed with  $\text{KHSO}_4$  10%,  $\text{NaHCO}_3$  5%, water and finally dried over  $\text{MgSO}_4$ . The solvent was removed under reduced pressure and the residue was triturated in MeOH. The solid obtained was purified by three successive columns of Bio-Beads SX-1 (toluene), then by preparative thin layer chromatography (silica gel, Hexane/THF, 6:1), gave **1** (34.0 mg, 46%) and **6** (40.1 mg, 13%) as colorless solids. M.p. > 210°C (dec).  $^1\text{H}$  NMR (500 MHz,  $\text{CD}_2\text{Cl}_2$ , 25 °C, COSY, ROESY):  $\delta$  7.33 (s, 16H;  $\text{ArH}_{\text{calix}[6]\text{arene}}$ ), 7.22 (s, 8H;  $\text{ArH}_{\text{xylylenyl}}$ ), 6.85 (s, 16H;  $\text{ArH}_{\text{calix}[6]\text{arene}}$ ), 6.78 (s, 16H;  $\text{ArH}_{\text{calix}[6]\text{arene}}$ ), 6.60 (bs, 4H; NH), 6.51 (bs, 12H;  $\text{ArH}_{\text{calix}[4]\text{arene}}$  + NH), 5.03 (s, 4H;  $\text{ArH}_{\text{xylylen}}$ ), 4.46 (d,  $^2J(\text{H},\text{H}) = 14.2$  Hz, 4H;  $\text{ArCH}_2\text{Ar}_{\text{calix}[4]\text{arene}}$ ), 4.39 (d,  $^2J(\text{H},\text{H}) = 15.5$  Hz, 16H;  $\text{ArCH}_2\text{Ar}_{\text{calix}[6]\text{arene}}$ ), 4.29 (d,  $^2J(\text{H},\text{H}) = 14.2$  Hz, 8H;

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<sup>1</sup> H. Galán, A. Frago, J. de Mendoza, P. Prados, *J. Org. Chem.* **2008**, *73*, 7124-7131.

<sup>2</sup> A. M. A. van Wageningen, E. Snip, W. Verboom, D. N. Reinhoudt, H. Boerrigter, *Liebigs Ann./Recueil* 1997, 2235-2245.

ArCH<sub>2</sub>Ar<sub>calix[6]arene</sub>), 4.14 (s, 16H; ArOCH<sub>2</sub>-*m*-xylylen), 3.85 (t, <sup>3</sup>*J*(H,H) = 6.9 Hz, 8H; ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.58-3.51 (m, 32H; ArOCH<sub>2</sub>CH<sub>3</sub>), 3.38 (d, <sup>2</sup>*J*(H,H) = 15.8 Hz, 16H; ArCH<sub>2</sub>Ar<sub>calix[6]arene</sub>), 3.22-3.14 (m, 12H; ArCH<sub>2</sub>Ar<sub>calix[6]arene</sub> + ArCH<sub>2</sub>Ar<sub>calix[4]arene</sub>), 1.92-1.85 (m, 8H; ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.40 [s, 72H; C(CH<sub>3</sub>)<sub>3</sub>], 1.06 (t, <sup>3</sup>*J*(H,H) = 6.9 Hz, 48H; ArOCH<sub>2</sub>CH<sub>3</sub>), 0.97 (t, <sup>3</sup>*J*(H,H) = 7.6 Hz, 12H; ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 0.87 [s, 144H; C(CH<sub>3</sub>)<sub>3</sub>]; <sup>13</sup>C NMR (125 MHz, CD<sub>2</sub>Cl<sub>2</sub>, 25 °C, DEPT, HSQC): δ 154.2 (C=O), 153.1, 152.8, 146.5, 145.6, 139.7, 138.1, 136.9, 133.9, 133.4, 133.3, 132.5 (ArC), 128.7, 125.7, 124.7, 122.0, 117.8, 114.7 (ArH), 77.4 (ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 72.2 (ArOCH<sub>2</sub>-*m*-xylylen), 69.5 (ArOCH<sub>2</sub>CH<sub>3</sub>), 34.7, 34.5 [C(CH<sub>3</sub>)<sub>3</sub>], 32.0, 31.6 [C(CH<sub>3</sub>)<sub>3</sub>], 30.7 (ArCH<sub>2</sub>Ar<sub>calix[4]arene</sub>), 30.3, 29.8 (ArCH<sub>2</sub>Ar<sub>calix[6]arene</sub>), 23.3 (ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 16.0 (ArOCH<sub>2</sub>CH<sub>3</sub>), 10.7 (ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); MS (MALDI-TOF, dithranol + NaI): *m/z* (%): 5590.7 (100%) [M+Na]<sup>+</sup>; Anal. Calc. for C<sub>372</sub>H<sub>472</sub>N<sub>8</sub>O<sub>32</sub>.CH<sub>2</sub>Cl<sub>2</sub>: C 79.25, H 8.45, N 1.98; found: C 79.11, H 8.77, N 2.21.

Compound **6**: M.p. > 240°C (dec). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, 25 °C): δ 7.33 (s, 8H; ArH), 7.27 (s, 4H; ArH), 6.87 (s, 8H; ArH), 6.81 (s, 8H; ArH), 6.78 (bs, 2H; NH), 5.11 (s, 2H; ArH<sub>xylylenyl</sub>), 4.42 (d, <sup>2</sup>*J*(H,H) = 15.4 Hz, 8H; ArCH<sub>2</sub>Ar), 4.33 (d, <sup>2</sup>*J*(H,H) = 13.9 Hz, 4H; ArCH<sub>2</sub>Ar), 4.19 (s, 8H; ArOCH<sub>2</sub>-*m*-xylylene), 3.60 (q, <sup>3</sup>*J*(H,H) = 6.9 Hz, 16H, ArOCH<sub>2</sub>CH<sub>3</sub>), 3.33 (d, <sup>2</sup>*J*(H,H) = 15.8 Hz, 8H; ArCH<sub>2</sub>Ar), 3.24 (d, <sup>2</sup>*J*(H,H) = 14.2 Hz, 4H; ArCH<sub>2</sub>Ar), 1.46 [s, 36H; C(CH<sub>3</sub>)<sub>3</sub>], 1.12 (t, <sup>3</sup>*J*(H,H) = 6.9 Hz, 24H; ArOCH<sub>2</sub>CH<sub>3</sub>), 0.90 [s, 72H; C(CH<sub>3</sub>)<sub>3</sub>]; <sup>13</sup>C NMR (δ, 125 MHz, CDCl<sub>3</sub>, 25 °C, DEPT, HSQC): 153.3 (C=O), 152.5, 152.2, 145.8, 145.0, 139.9, 136.5, 133.4, 132.84, 132.75 (Ar), 128.0, 125.5, 125.0, 124.1, 118.6, 115.4 (ArH), 71.4 (ArOCH<sub>2</sub>-*m*-xylylene), 68.7 (ArOCH<sub>2</sub>CH<sub>3</sub>), 34.3, 34.0 [C(CH<sub>3</sub>)<sub>3</sub>], 31.7, 31.2 [C(CH<sub>3</sub>)<sub>3</sub>], 30.1, 28.8 (ArCH<sub>2</sub>Ar), 15.6 (ArOCH<sub>2</sub>CH<sub>3</sub>); MS (MALDI-TOF, dithranol + NaI): *m/z* (%): 2453.6 (100%) [M+Na]<sup>+</sup>; Anal. Calc. for C<sub>165</sub>H<sub>212</sub>N<sub>2</sub>O<sub>13</sub> CHCl<sub>3</sub>: C 78.16, H 8.42, N 1.10; found: C 78.22, H 8.93, N 1.31.

**Synthesis of Compounds 2:** A mixture of amine 3<sup>1</sup> (74.3 mg, 0.062 mmol), and DIEA (24 μL, 0.137 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (0.71 mL), was slowly added (25 μL/min) to a solution of triphosgene (3.8 mg, 0.023 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (0.48 mL) at 10-15°C, under argon. The mixture was stirred at room temperature for 15 min and then a solution of amine 5<sup>3</sup> (18.2 mg, 0.023 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (0.48 mL) was slowly added. After 24 h under stirring the organic solution was washed with KHSO<sub>4</sub> 10%, NaHCO<sub>3</sub> 5%, water and finally dried over MgSO<sub>4</sub>.

<sup>3</sup> P. Timmerman, R. H. Vreekamp, R. Hulst, W. Verboom, D. N. Reinhoudt, K. Rissanen, K. A. Udachin, J. Ripmeester, *Chem. Eur. J.* 1997, **3**, 1823-1832.

The solvent was removed under reduced pressure and the residue was triturated in MeOH. The solid obtained was purified by three successive columns of Bio-Beads SX-1 (toluene), and then by column chromatography (using a reservoir Bond Elut (Varian) of 25 mL, with 3 cm silica gel, Hexane/THF 8:1), to give **2** (36.9 mg, 49%), as a colorless solid. Some **6** (17.3 mg, 11%) was also isolated. M.p. > 198°C (dec). <sup>1</sup>H NMR (500 MHz, CD<sub>2</sub>Cl<sub>2</sub>, 25 °C, ROESY): δ 7.32 (s, 8H; ArH<sub>calix[6]arene</sub>), 7.27 (bs, 2H; NH<sub>xylylenyl</sub>), 7.11 (s, 4H; ArH<sub>calix[4]arenet-Bu</sub>), 7.08 (s, 4H; ArH<sub>xylylenyl</sub>), 6.84 (s, 8H; ArH<sub>calix[6]arene</sub>), 6.77 (s, 8H; ArH<sub>calix[6]arene</sub>), 6.11 (s, 2H; NH<sub>calix[4]arene</sub>), 5.88 (s, 4H; ArH<sub>calix[4]areneureas</sub>), 5.01 (s, 2H; ArH<sub>xylylenyl</sub>), 4.45 (d, <sup>2</sup>J(H,H) = 13.6 Hz, 4H; ArCH<sub>2</sub>Ar<sub>calix[6]arene</sub>), 4.39 (d, <sup>2</sup>J(H,H) = 15.5 Hz, 8H; ArCH<sub>2</sub>Ar<sub>calix[6]arene</sub>), 4.26 (d, <sup>2</sup>J(H,H) = 13.9 Hz, 4H; ArCH<sub>2</sub>Ar<sub>calix[4]arene</sub>), 4.13 (s, 8H; ArOCH<sub>2</sub>-*m*-xylylen), 3.96 (t, <sup>3</sup>J(H,H) = 8.2 Hz, 4H; ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.69 (t, <sup>3</sup>J(H,H) = 6.6 Hz, 4H; ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.56-3.43 (m, 16H; ArOCH<sub>2</sub>CH<sub>3</sub>), 3.37 (d, <sup>2</sup>J(H,H) = 15.8 Hz, 8H; ArCH<sub>2</sub>Ar<sub>calix[6]arene</sub>), 3.20-3.12 (m, 8H; ArCH<sub>2</sub>Ar<sub>calix[6]arene</sub> + ArCH<sub>2</sub>Ar<sub>calix[4]arene</sub>), 1.92-1.82 (m, 8H; ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.38 [s, 36H; C(CH<sub>3</sub>)<sub>3</sub>], 1.34 [s, 18H; C(CH<sub>3</sub>)<sub>3</sub>], 1.13-1.06 (m, 36H; ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> + ArOCH<sub>2</sub>CH<sub>3</sub>), 0.88 [s, 72H; C(CH<sub>3</sub>)<sub>3</sub>]; <sup>13</sup>C NMR (125 MHz, CD<sub>2</sub>Cl<sub>2</sub>, 25 °C, DEPT, HSQC): δ 156.3 (C=O), 154.7, 153.7, 153.0, 152.97, 146.4, 145.5, 145.2, 139.3, 137.7, 136.7, 135.5, 133.9, 133.5, 133.3, 132.1, 129.6 (ArC), 128.7, 126.6, 125.7, 124.6, 122.7, 117.6, 115.4 (ArH), 77.5, 77.0 (ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 72.0 (ArOCH<sub>2</sub>-*m*-xylylene), 69.5 (ArOCH<sub>2</sub>CH<sub>3</sub>), 34.7, 34.6, 34.5 [C(CH<sub>3</sub>)<sub>3</sub>], 32.2, 32.0, 31.6 [C(CH<sub>3</sub>)<sub>3</sub>], 30.6 (ArCH<sub>2</sub>Ar<sub>calix[4]arene</sub>), 30.3, 29.3 (ArCH<sub>2</sub>Ar<sub>calix[6]arene</sub>), 24.1, 23.5 (ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 16.0 (ArOCH<sub>2</sub>CH<sub>3</sub>), 11.3, 10.1 (ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). MS (MALDI-TOF, dithranol + NaI): *m/z* (%): 3215.1 (100%) ([M+Na]<sup>+</sup>), 3193.1 (15%) [M+H]<sup>+</sup>; Anal. Calc. for C<sub>214</sub>H<sub>276</sub>N<sub>4</sub>O<sub>18</sub> MeOH·CH<sub>2</sub>Cl<sub>2</sub>: C 78.39, H 8.59, N 1.69; found: C 78.25, H 8.88, N 1.67.

**Crystallographic study:** Depending of the solvent mixtures used for crystallization different solvates of compound **1** were obtained. In general, crystals were of poor quality and had a high tendency to lose solvent and degrade. After several attempts, crystals of two of the solvates could be measured. In the first case (crystal A), crystals were obtained by crystallization from a concentrated solution of the compound in a mixture of CH<sub>2</sub>Cl<sub>2</sub> and DMSO at 45 °C. In the second case (crystal B) crystallization was performed from a solution in MeOH/CH<sub>2</sub>Cl<sub>2</sub>. The crystals were prepared under inert conditions immersed in perfluoropolyether as protecting oil for manipulation and cooled down to -173 °C in the shortest time possible to avoid crystal damage.

**Data Collection:** Measurements were made on a Bruker-Nonius diffractometer equipped with an APPEX 2 4K CCD area detector, a FR591 rotating anode with MoK<sub>α</sub> radiation, Montel mirrors as monochromator and a

Kryoflex low temperature device ( $T = 100$  K). Full-sphere data collection was used with  $\omega$  and  $\varphi$  scans. Programs used: Data collection Apex2 V. 1.0-22 (Bruker-Nonius 2004), data reduction Saint + Version 6.22 (Bruker-Nonius 2001) and absorption correction SADABS V. 2.10 (2003). *Structure Solution and Refinement*: SHELXTL Version 6.10 (Sheldrick, 2000) was used.

**Compound 1 crystal A:** Although compound **1** is a large and flexible molecule (formula  $C_{372}H_{472}N_8O_{32}$ ), it surprisingly crystallizes maintaining a  $C_2$  symmetry in the solid state (half molecule in the unit cell). The  $C_2$  rotation axis is centered in the molecule crossing through the centre of the calix[4]arene cone and between the four calix[6]arene moieties. The external positions of the molecule are partially disordered and in general large thermal ellipsoids can be observed in the “legs” of the calix[4]arene and in the external areas of the calix[6]arene moieties (for the thermal displacements see Figure 1). The crystal structure contains also a high number of disordered DMSO and  $CH_2Cl_2$  molecules which were omitted in the submitted dataset using the program SQUEEZE.<sup>4</sup>

**Crystal data for 1 at 100 K in crystal A:**  $C_{372}H_{472}N_8O_{32}$ , 5567.58  $g\ mol^{-1}$ , monoclinic,  $C2/c$ ,  $a = 34.2509(15)$  Å,  $b = 39.8239(18)$  Å,  $c = 27.5132(12)$  Å,  $\beta = 94.105(2)^\circ$ ,  $V = 37432(3)$  Å<sup>3</sup>,  $Z = 4$ ,  $\rho_{calcd} = 1.016$  Mg/m<sup>3</sup> (density including disordered solvent molecules in the refinement, 0.988 Mg/m<sup>3</sup> after applying SQUEEZE)<sup>4</sup>,  $R_{1obs} = 0.1364$  ( $R_{1ref} = 0.2020$ ),  $wR2_{obs} = 0.3153$  ( $wR2_{ref} = 0.3370$ ), for 15001 reflections with  $I > 2\sigma(I)$  (for 27050 reflections [ $R_{int}: 0.0820$ ] with a total measured of 248364 reflections), diffracting  $2\theta$  range:  $4.88^\circ$  to  $46.72^\circ$ , goodness-of-fit on  $F^2 = 1.702$ , largest diff. peak (hole) =  $0.615$  ( $-0.663$ )  $e\ \text{\AA}^{-3}$ .

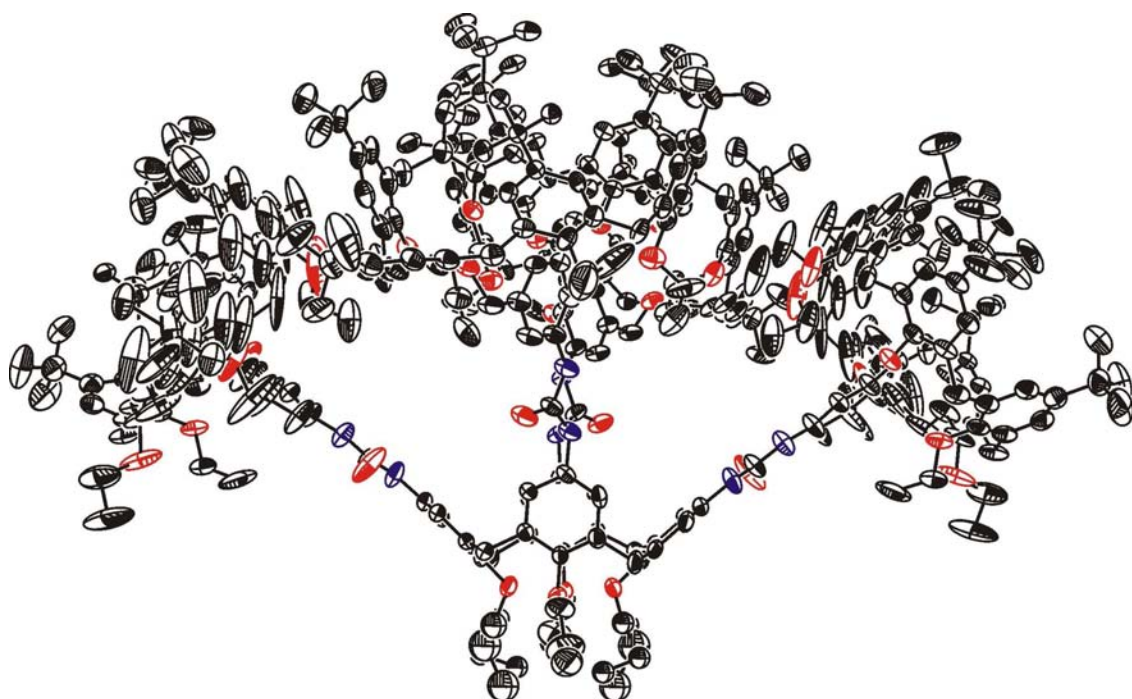
**Compound 1 crystal B:** A second structure of compound **1** could be measured corresponding to a MeOH/ $CH_2Cl_2$  solvate. In this case the crystal was of extremely poor quality and the structure could not be refined properly. Anyway the core of the structure could be solved and partially refined. In crystal B the calix[4]arene core displays a *pinched cone* conformation with  $80^\circ$  and  $29^\circ$  interplanar angles of the planes of the benzene rings. The urea subunits are mostly planar. The calix[6]arene moieties show a similar arrangement as in the previous structure and also one the six aromatic rings is tumbled into the central cavity of the ring (Figure 2).

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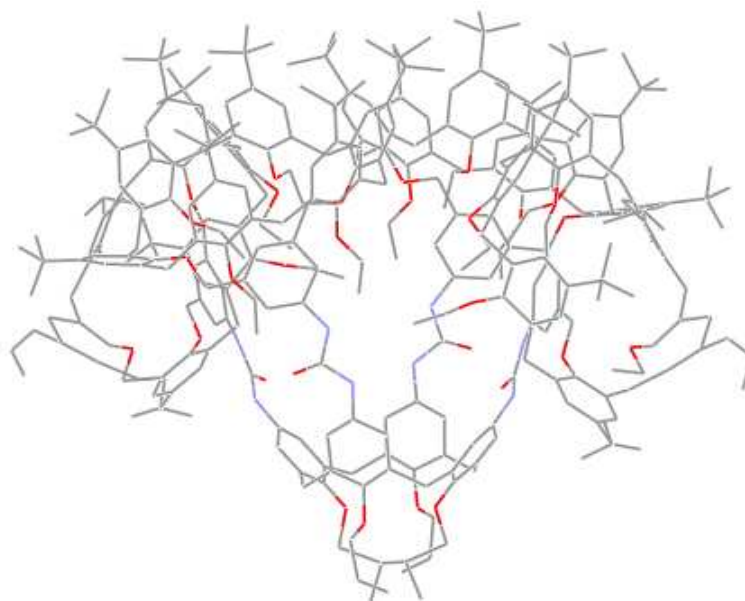
<sup>4</sup> P. van der Sluis, A. L. Spek, *Acta Cryst.* 1990, **A46**, 194-201.

**Cell data for 1 at 100 K in crystal B:** Monoclinic,  $P2/c$ ,  $a = 26.038(8) \text{ \AA}$ ,  $b = 34.769(10) \text{ \AA}$ ,  $c = 26.428(7) \text{ \AA}$ ,  $\beta = 1143.024(15)^\circ$ ,  $V = 21853(5) \text{ \AA}^3$ ,  $Z = 4$ .

CCDC 719413 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge via [www.ccdc.cam.ac.uk/conts/retrieving.html](http://www.ccdc.cam.ac.uk/conts/retrieving.html) (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; (fax: (+44) 1223-336-033; or e-mail: [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).



**Figure 1:** Ortep-Plot (thermal ellipsoids shown at 30 % probability level) of 1 in crystal A. Hydrogen atoms have been omitted for the sake of clarity.



**Figure 2:** Second structure of compound **1** (crystal B).

**Volume calculation by Swiss-Pdb viewer.** The volume of the guest and interior cavity of compound **1** was calculated by Swiss-Pdb Viewer program,<sup>5</sup> using the X-ray structures obtained for both of them.<sup>6</sup> In the case of compound **1** it was necessary to use 12H-phenalene to cover the four windows it possesses. The obtained volumes were 79 Å<sup>3</sup> and 125 Å<sup>3</sup>, respectively.

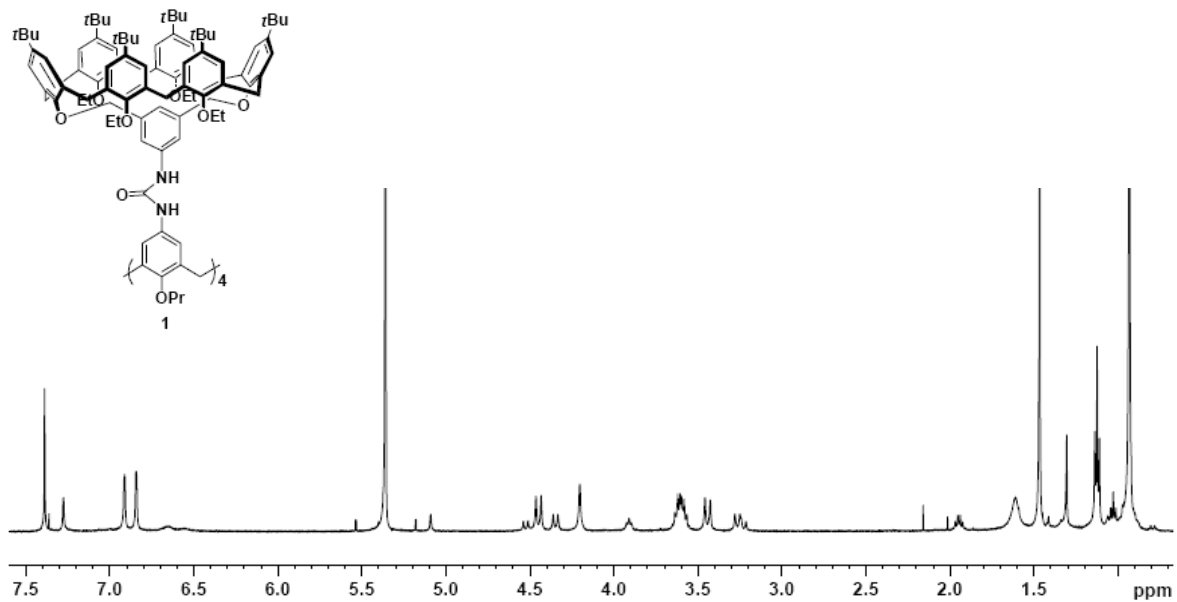
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<sup>5</sup> A. Pintar, O. Carugo, S. Pongor, *Bioinformatics* 2002, **18**, 980-984.

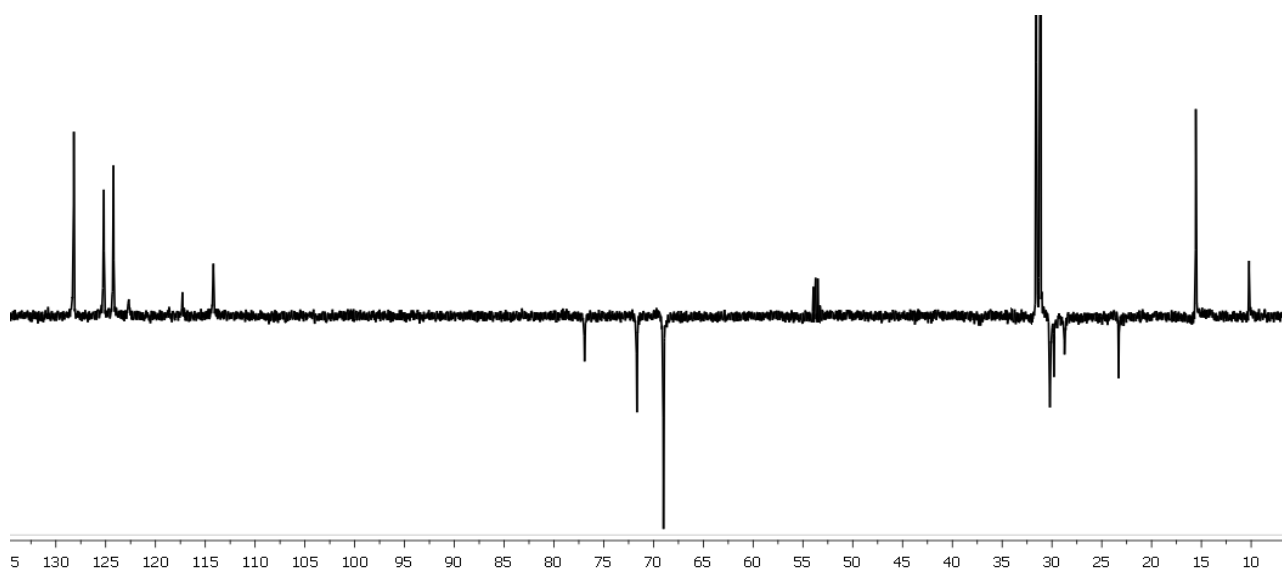
<sup>6</sup> P. A. Gale, M. E. Light, R. Quesada, *Cryst. Eng. Commun.* 2006, **8**, 178-188.

## Spectral characterization of compound **1**

$^1\text{H}$  NMR ( $\text{CD}_2\text{Cl}_2$ , 500 MHz, 298 K) spectrum of **1**

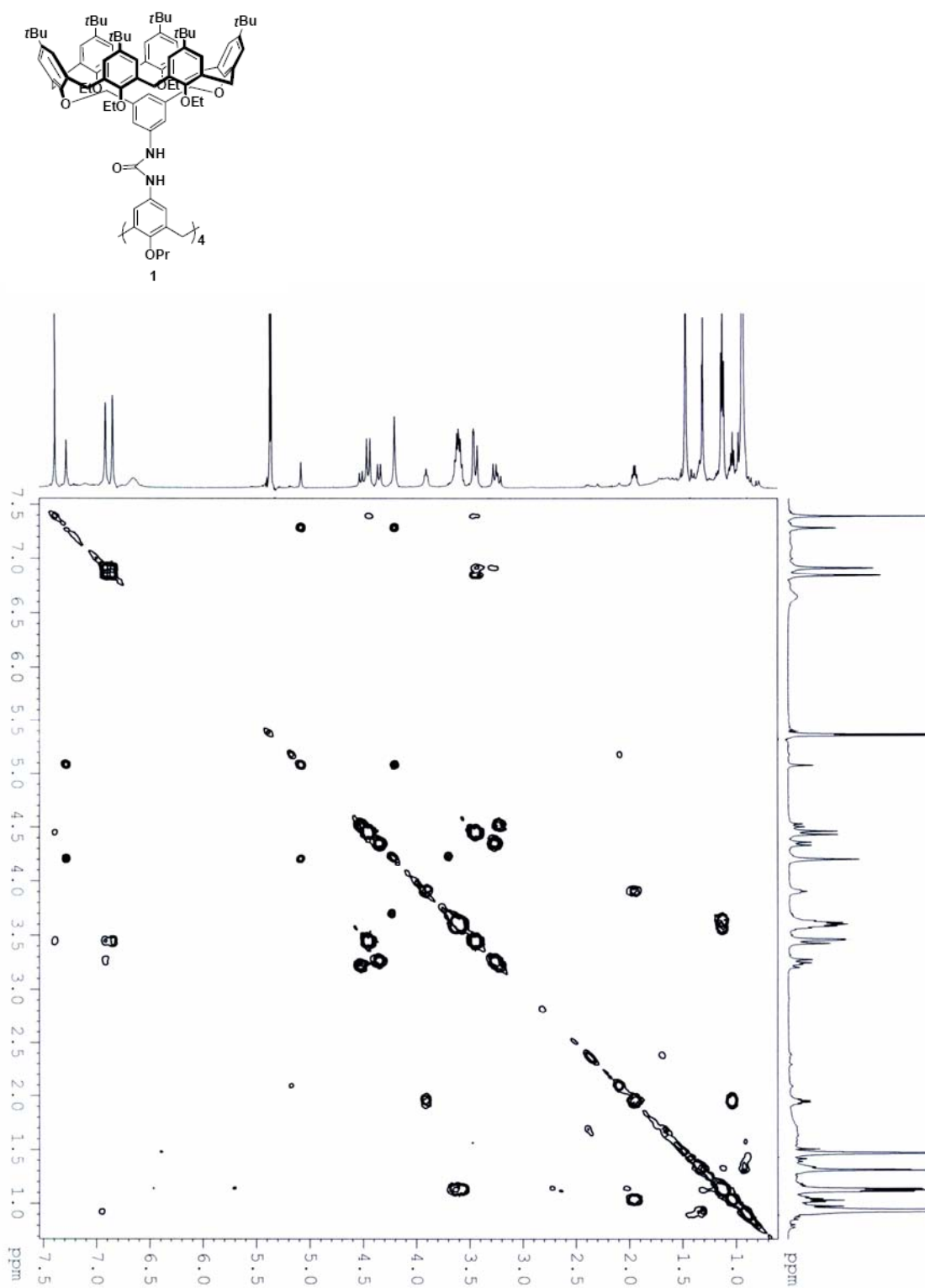


DEPT ( $\text{CD}_2\text{Cl}_2$ , 500 MHz, 298 K) spectrum of **1**

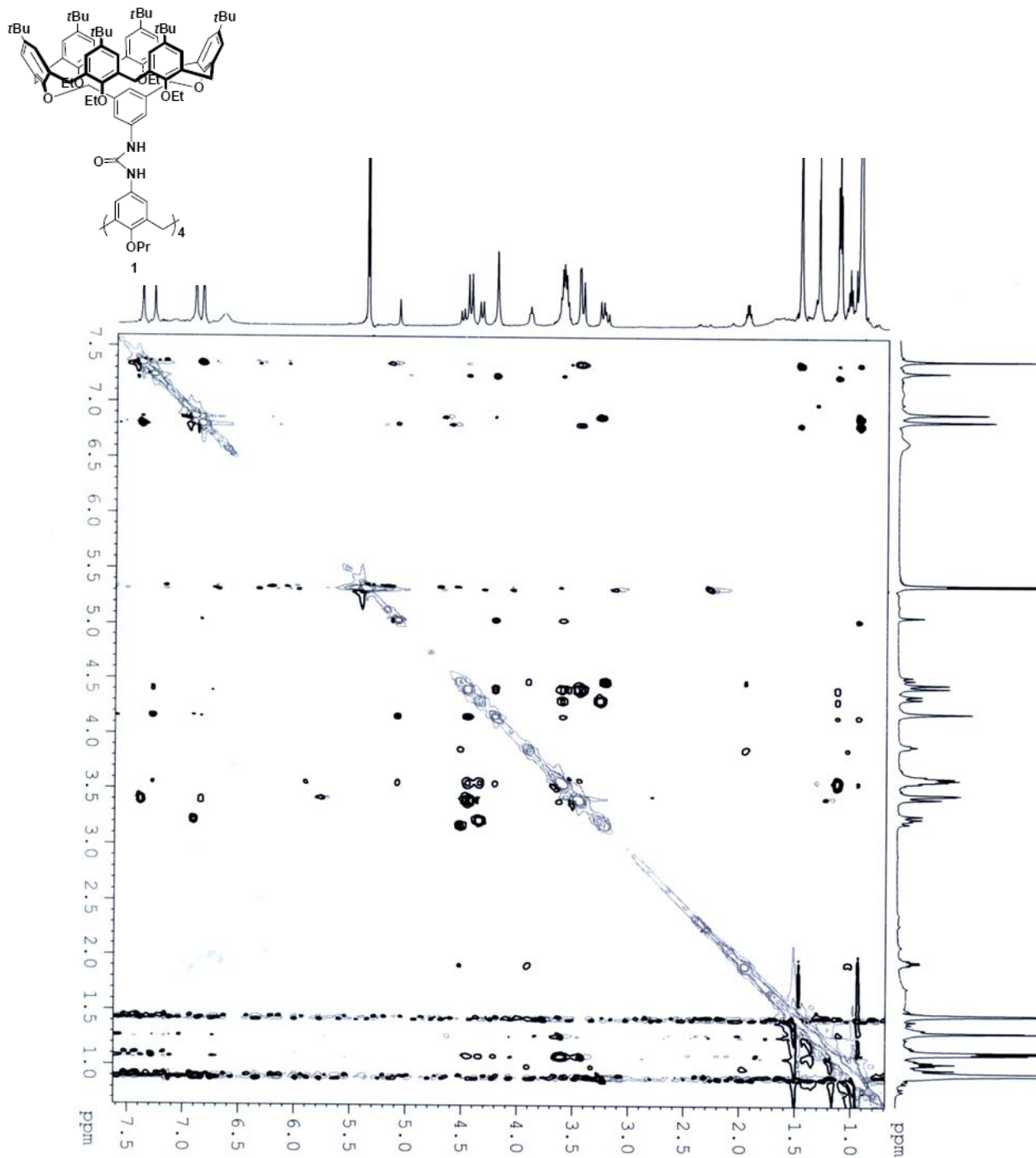




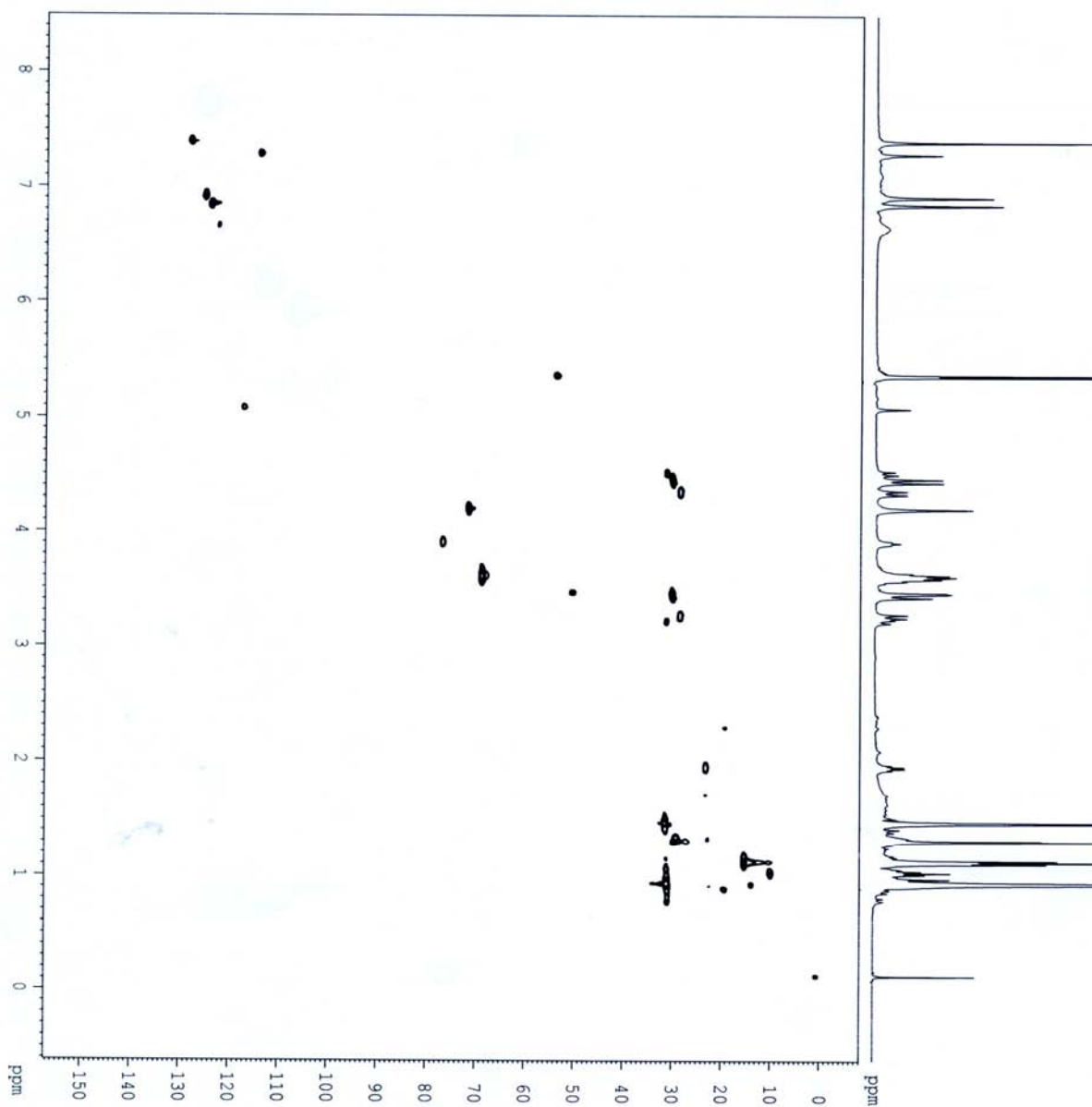
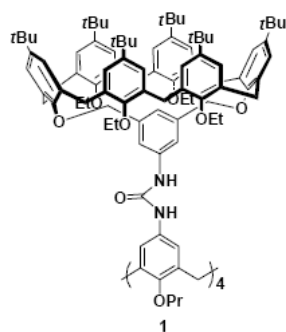
COSY ( $\text{CD}_2\text{Cl}_2$ , 500 MHz, 298 K) spectrum of **1**



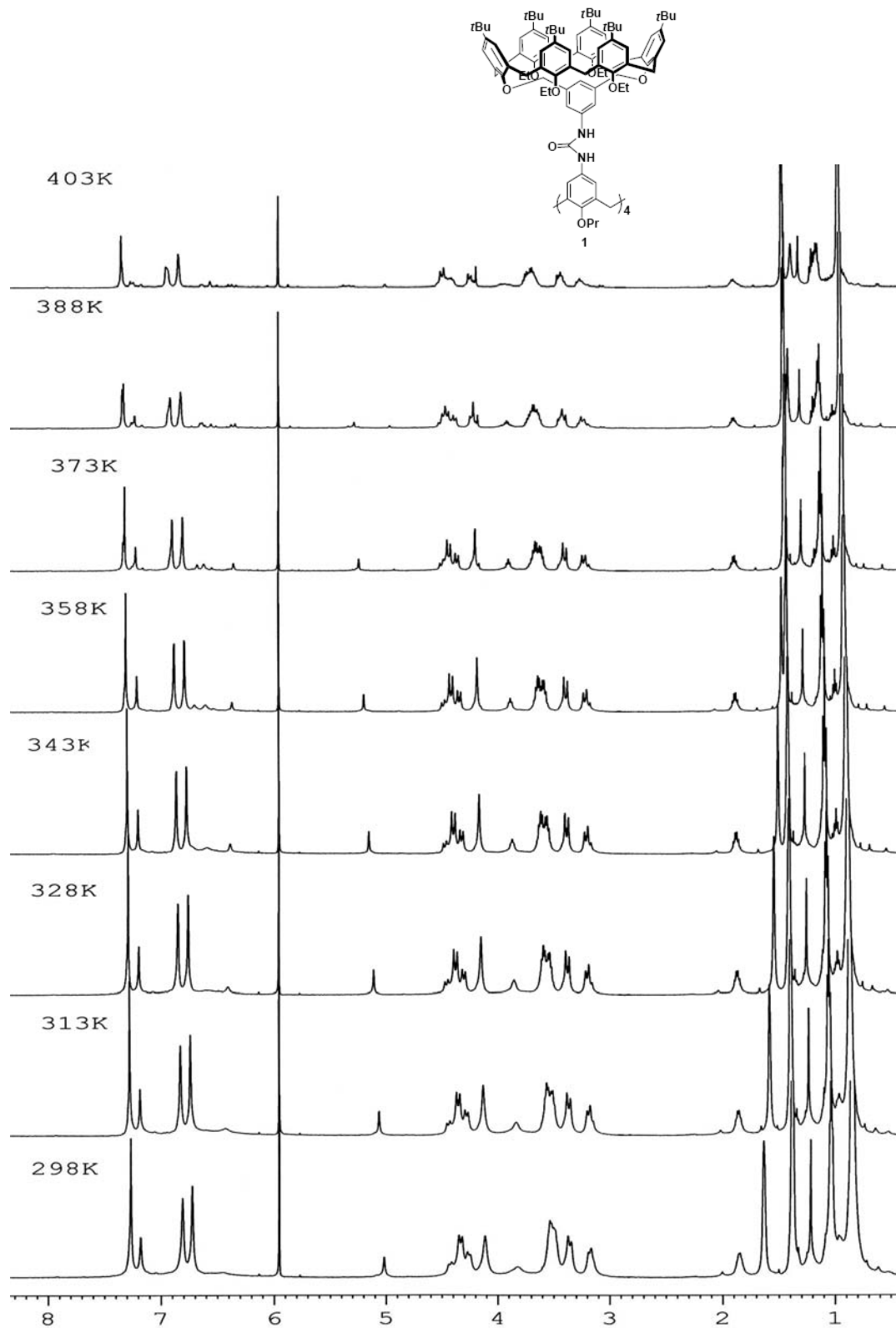
ROESY (CD<sub>2</sub>Cl<sub>2</sub>, 500 MHz, 298 K) spectrum of **1**



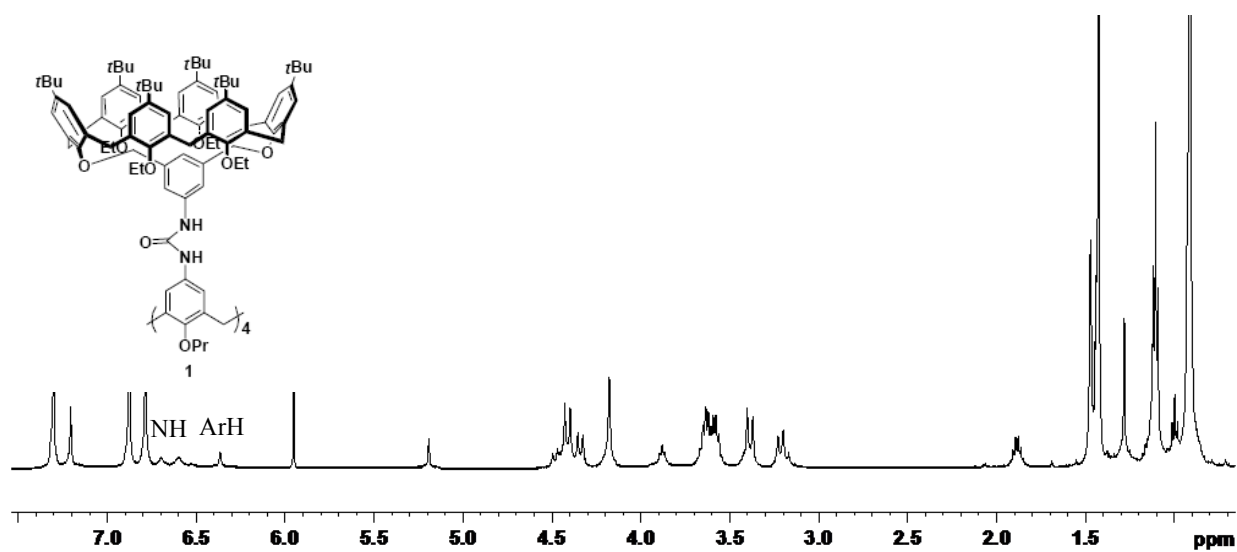
HSQC (CD<sub>2</sub>Cl<sub>2</sub>, 500 MHz, 298 K) spectrum of **1**



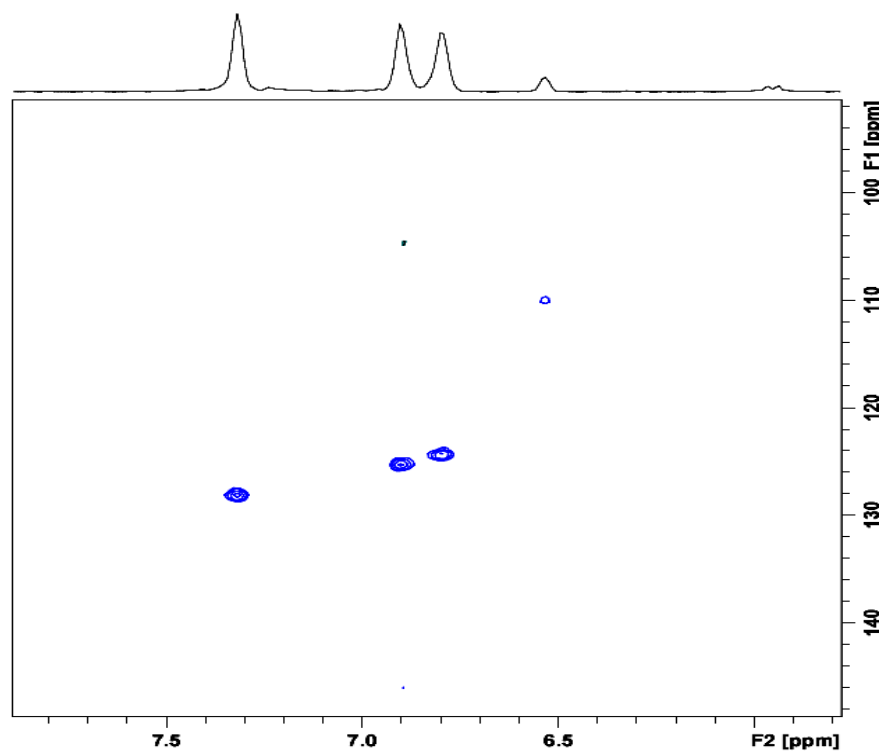
VT-<sup>1</sup>H NMR (C<sub>2</sub>D<sub>2</sub>Cl<sub>4</sub>, 500 MHz, 403–298 K) spectra of **1**



$^1\text{H}$  NMR ( $\text{C}_2\text{D}_2\text{Cl}_4$ , 500 MHz, 358 K) spectrum of **1**

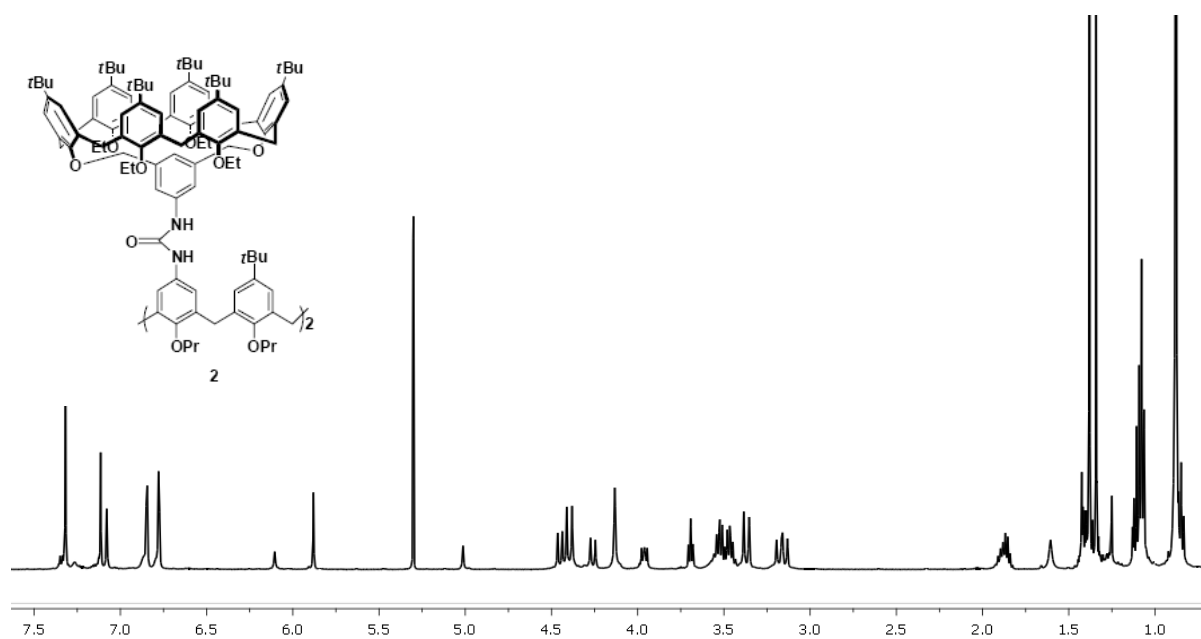


HSQC ( $\text{C}_2\text{D}_2\text{Cl}_4$ , 500 MHz, 358 K) fragment spectrum of **1**

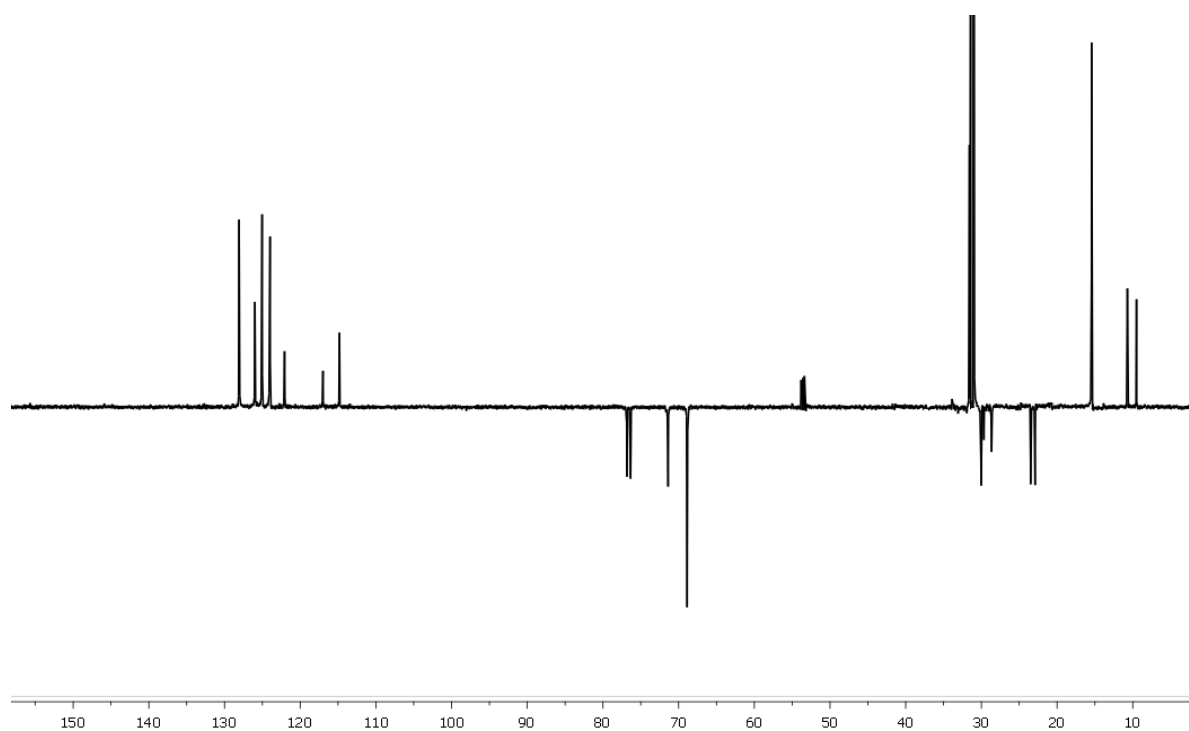


## Spectral characterization of compound **2**

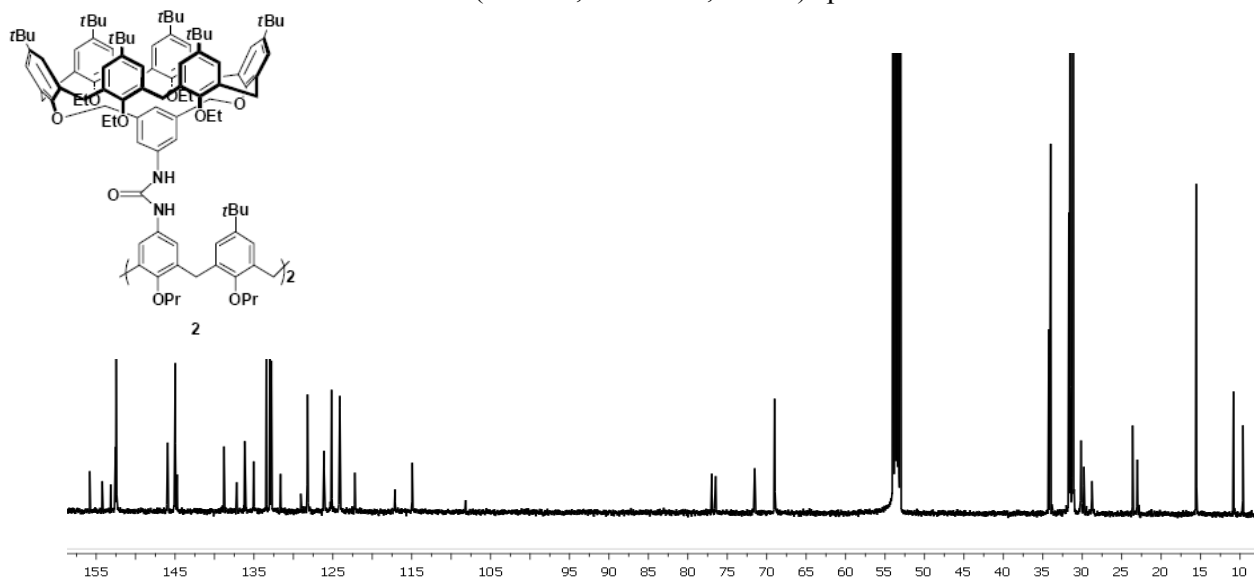
$^1\text{H}$  NMR ( $\text{CD}_2\text{Cl}_2$ , 500 MHz, 298 K) spectrum of **2**



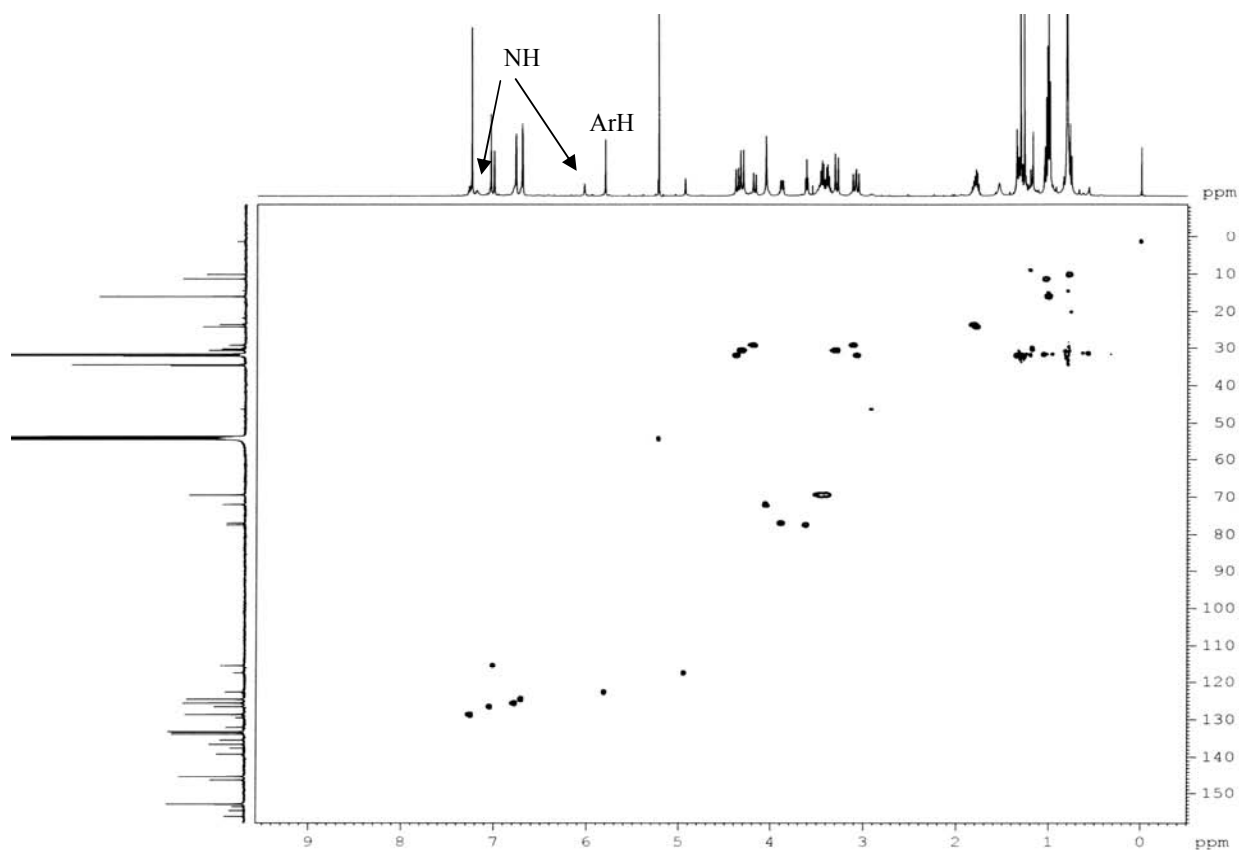
DEPT ( $\text{CD}_2\text{Cl}_2$ , 500 MHz, 298 K) spectrum of **2**



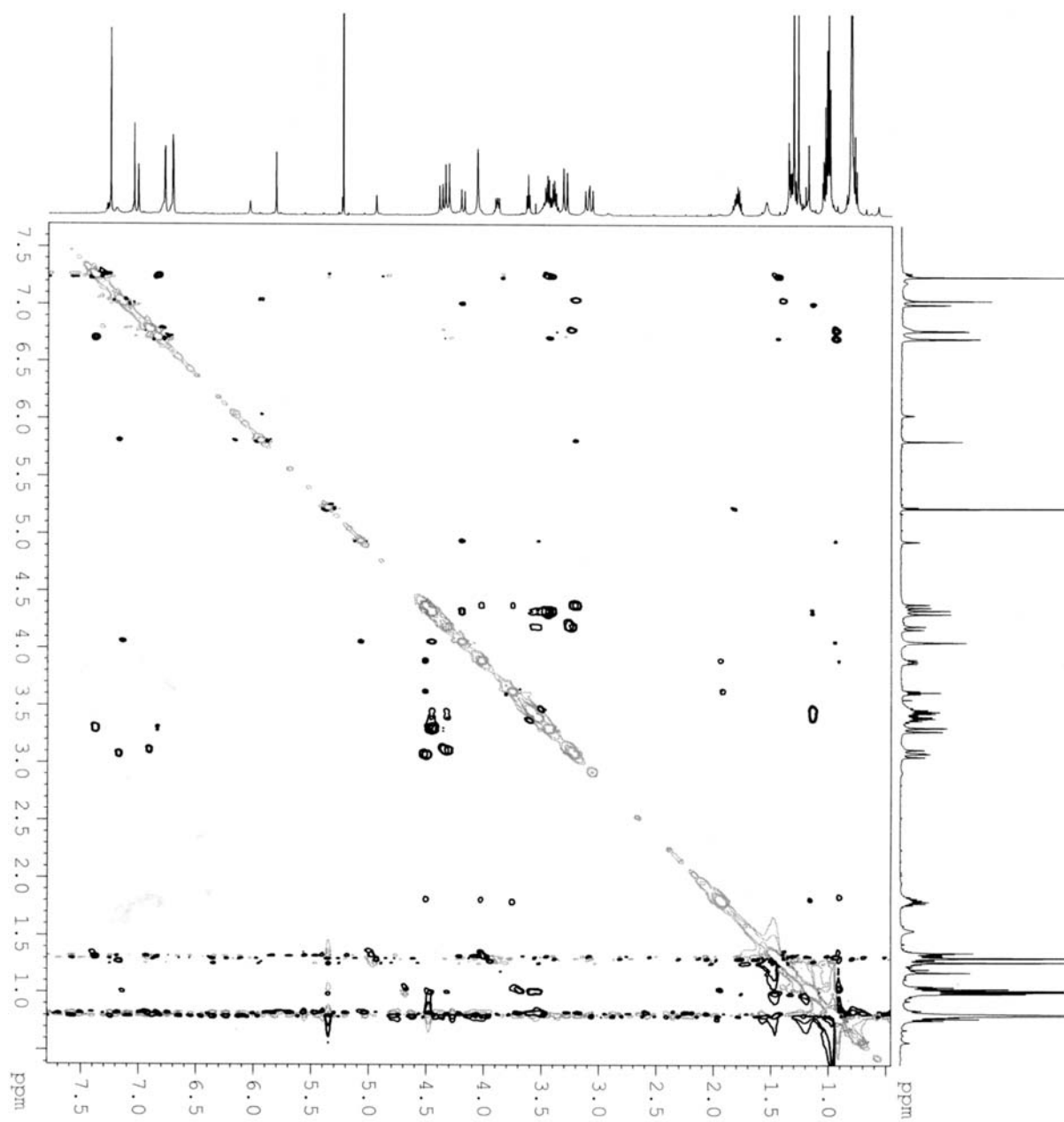
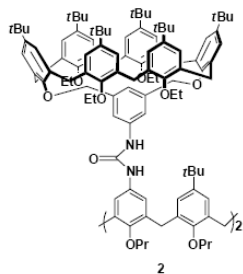
$^{13}\text{C}$  NMR ( $\text{CD}_2\text{Cl}_2$ , 500 MHz, 298 K) spectrum of **2**



HSQC ( $\text{CD}_2\text{Cl}_2$ , 500 MHz, 298 K) spectrum of **2**

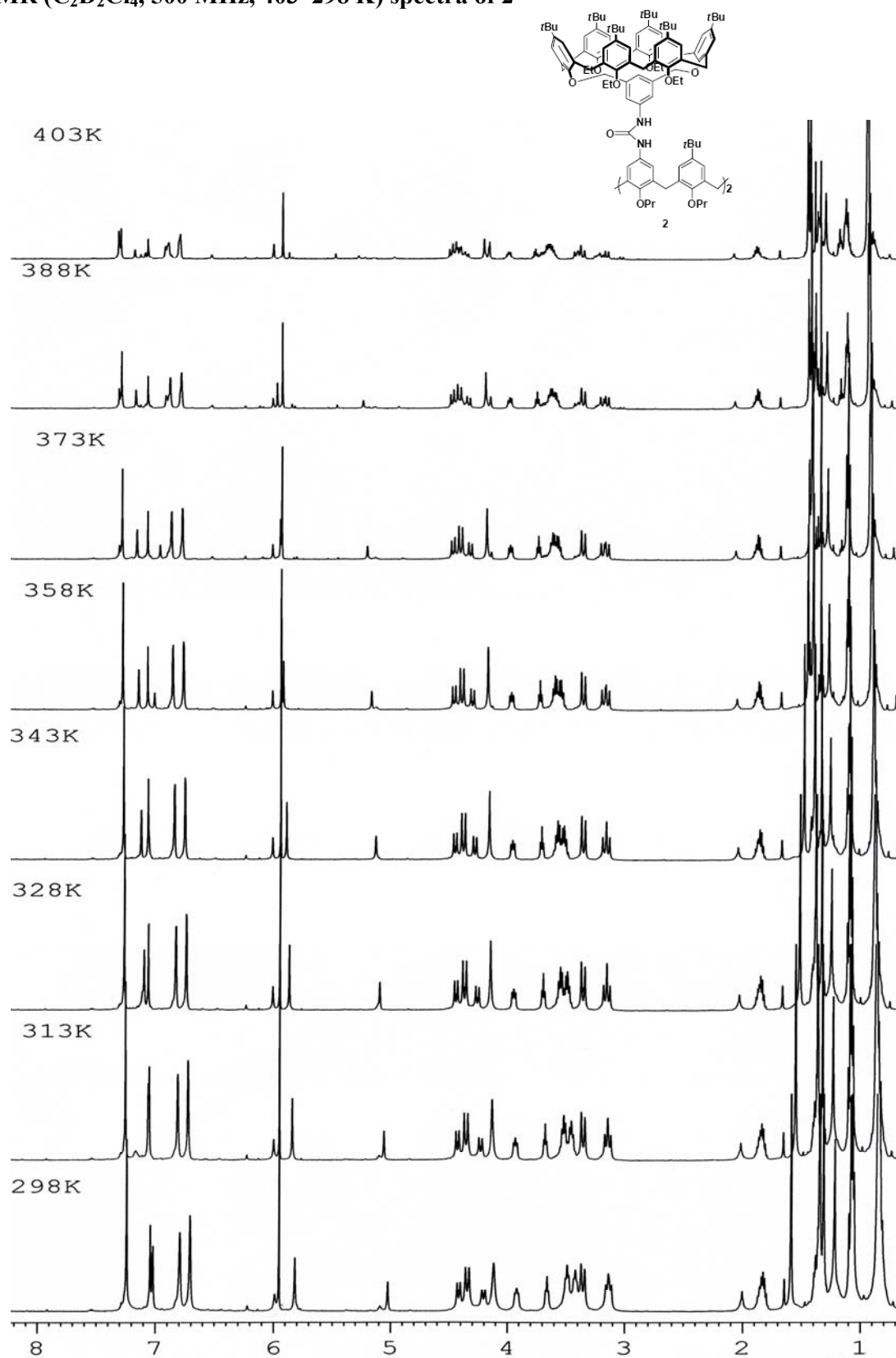


ROESY (CD<sub>2</sub>Cl<sub>2</sub>, 500 MHz, 298 K) spectrum of **2**

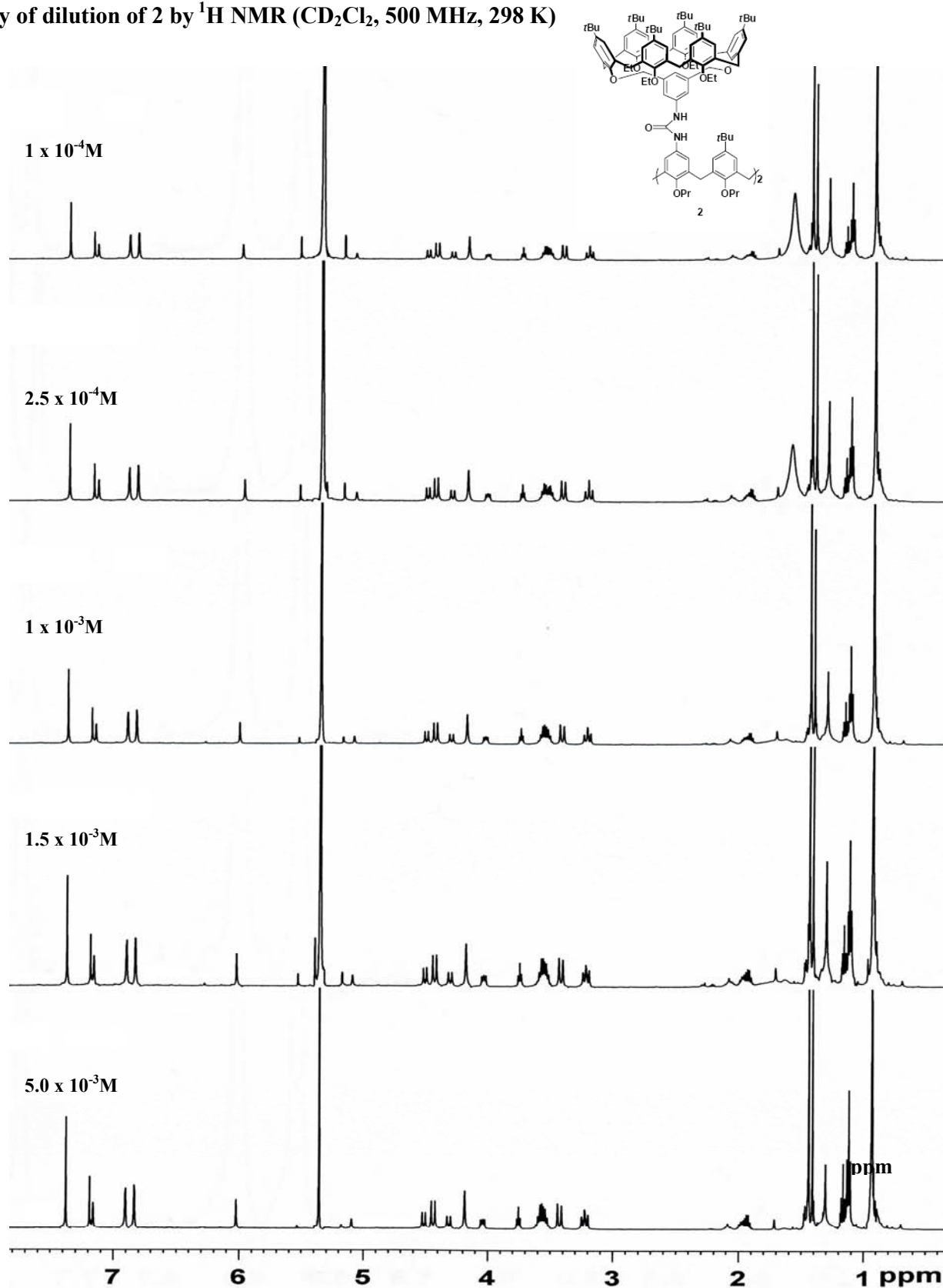




VT- $^1\text{H}$  NMR ( $\text{C}_2\text{D}_2\text{Cl}_4$ , 500 MHz, 403–298 K) spectra of **2**

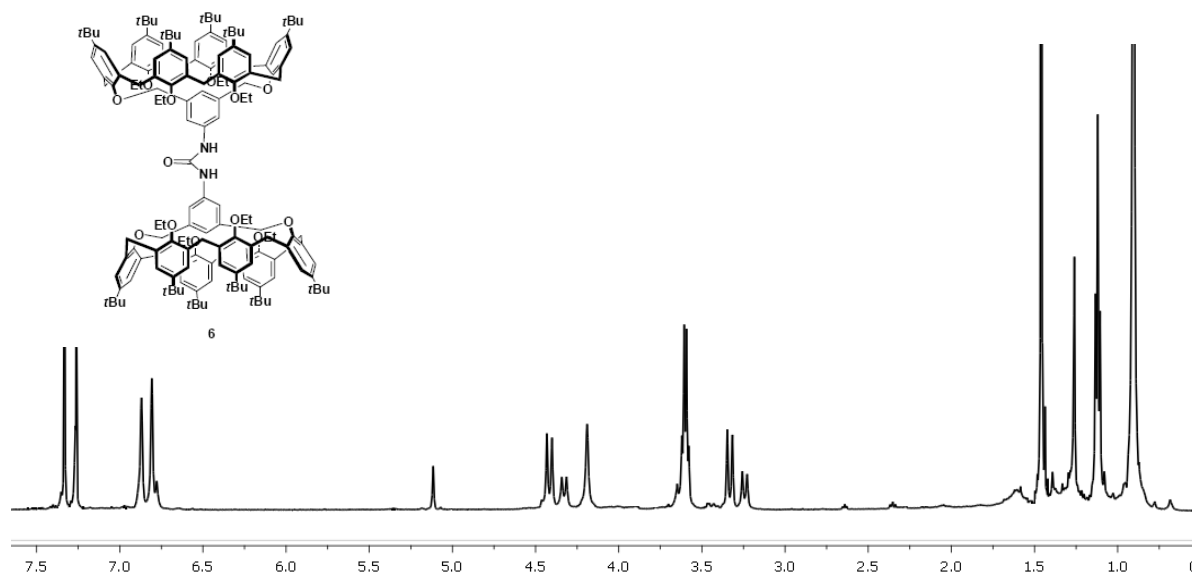


Study of dilution of **2** by  $^1\text{H}$  NMR ( $\text{CD}_2\text{Cl}_2$ , 500 MHz, 298 K)

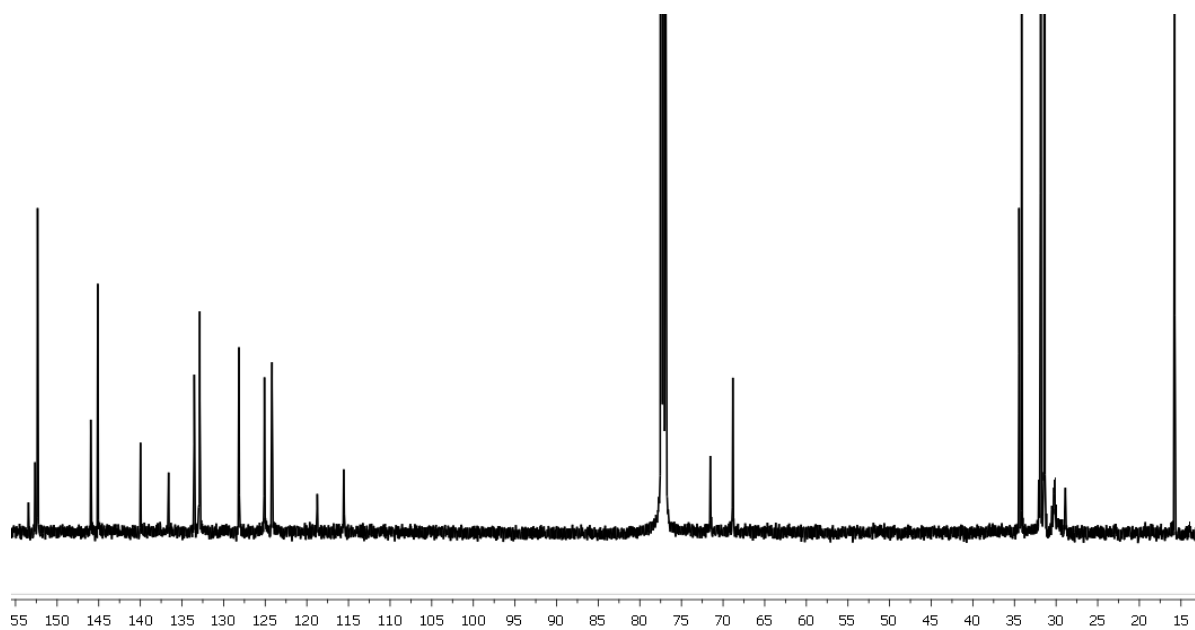


## Spectral characterization of compound **6**

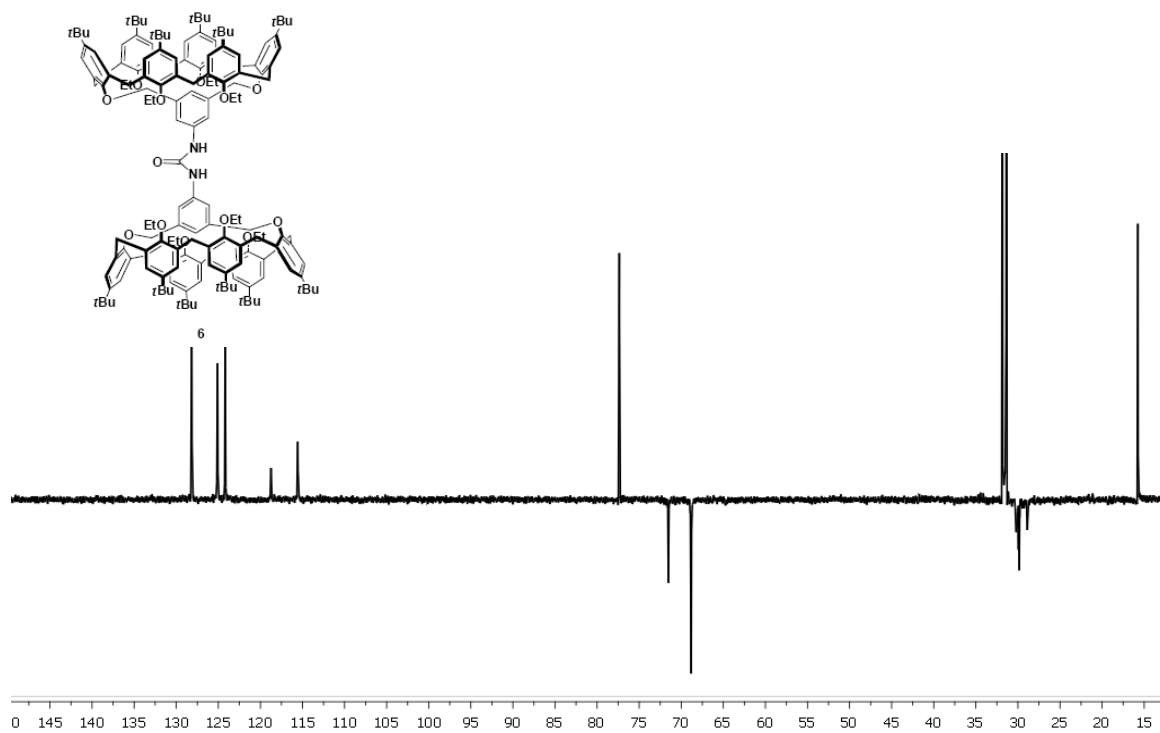
$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz, 298 K) spectrum of **6**



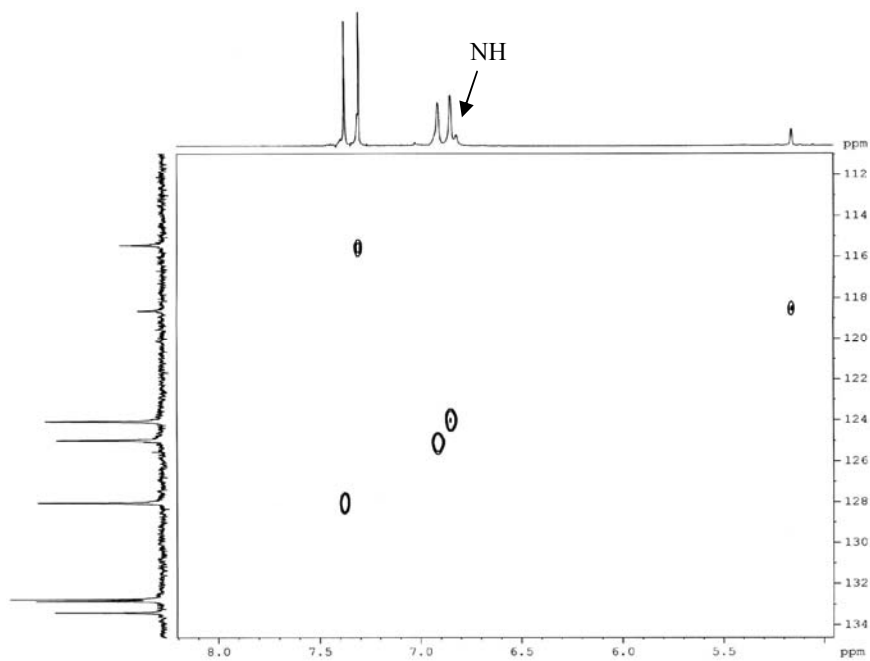
$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 500 MHz, 298 K) spectrum of **6**



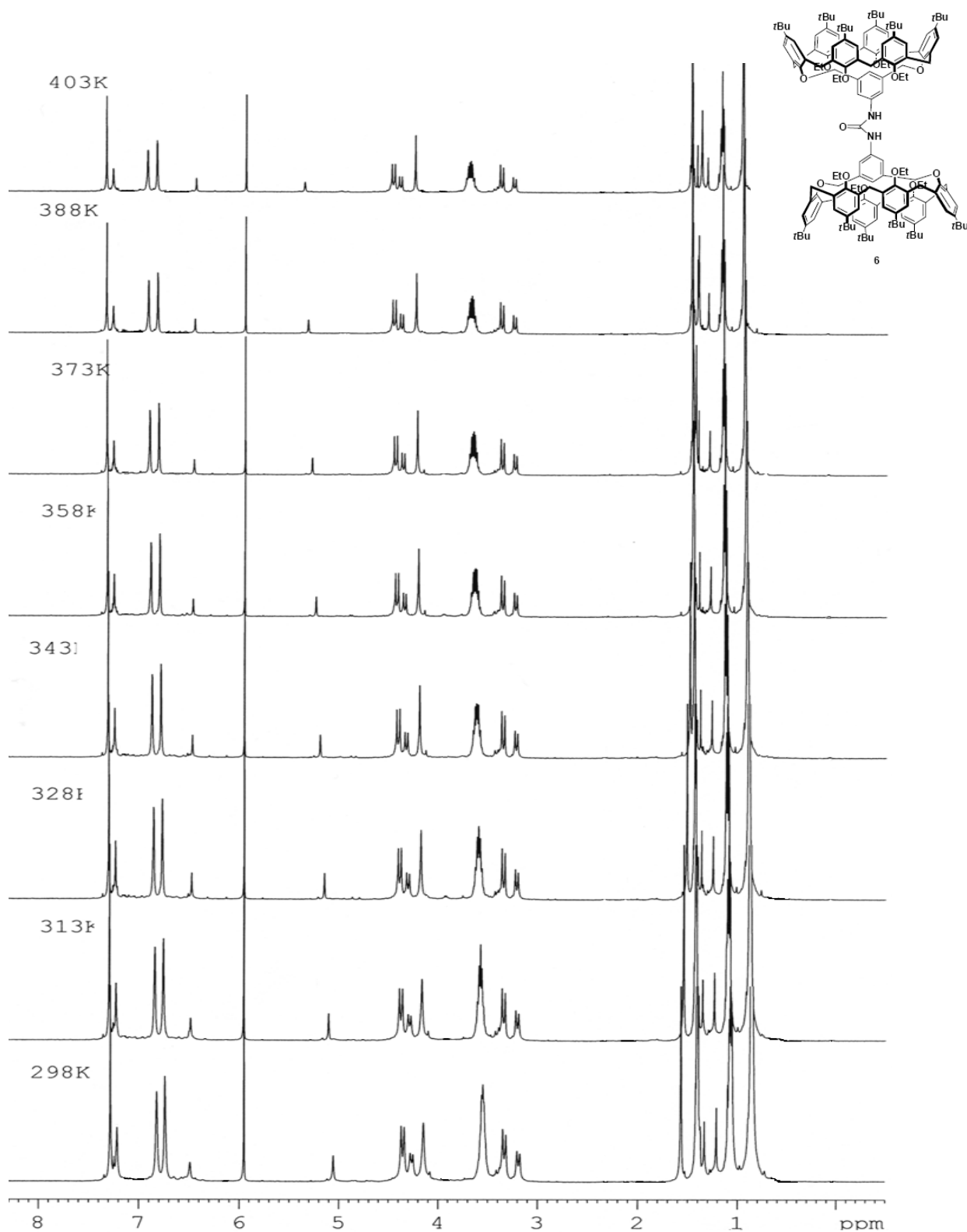
DEPT (CDCl<sub>3</sub>, 500 MHz, 298 K) spectrum of **6**



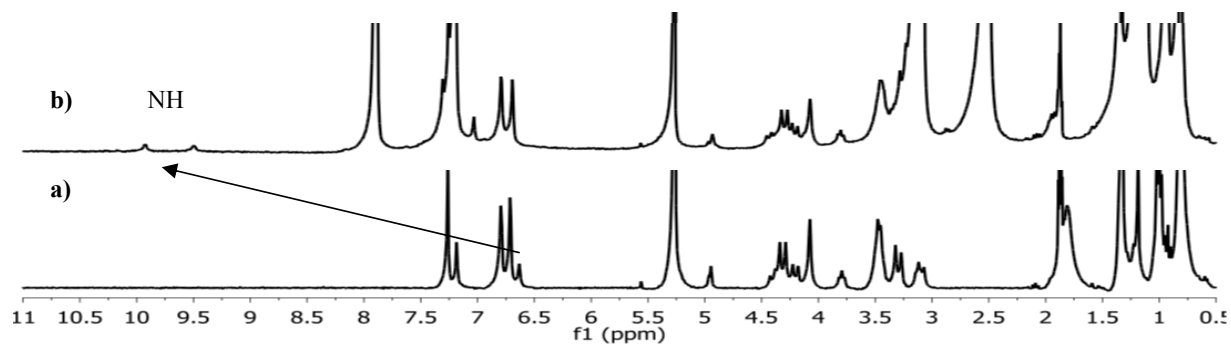
HSQC (CDCl<sub>3</sub>, 500 MHz, 298 K) spectrum fragment of **6**



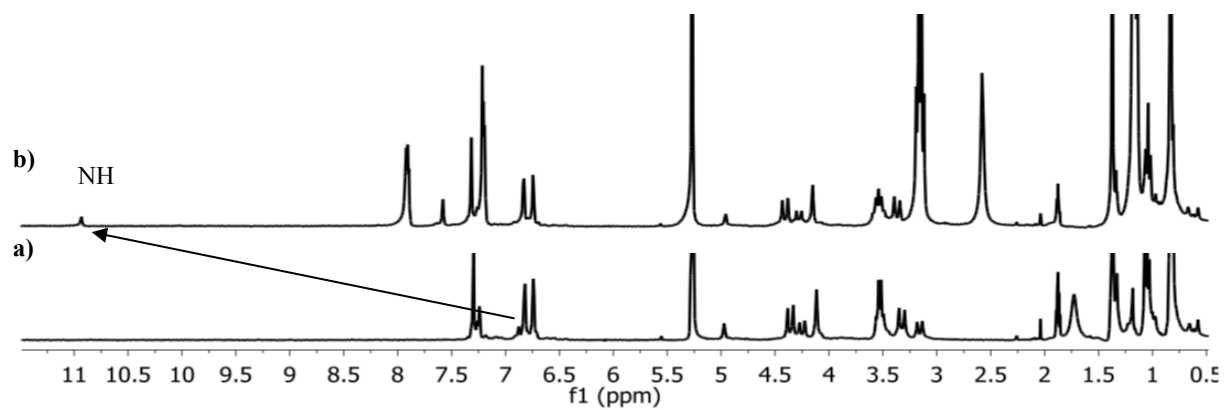
VT-<sup>1</sup>H NMR (C<sub>2</sub>D<sub>2</sub>Cl<sub>4</sub>, 500 MHz, 403–298 K) spectra of **6**



<sup>1</sup>H NMR [300 MHz, CD<sub>2</sub>Cl<sub>2</sub>/CD<sub>3</sub>CN (9:1), 298 K] spectra of **1** a) before and b) after addition of 8 equivalents of (TEA)C<sub>6</sub>H<sub>5</sub>CO<sub>2</sub>

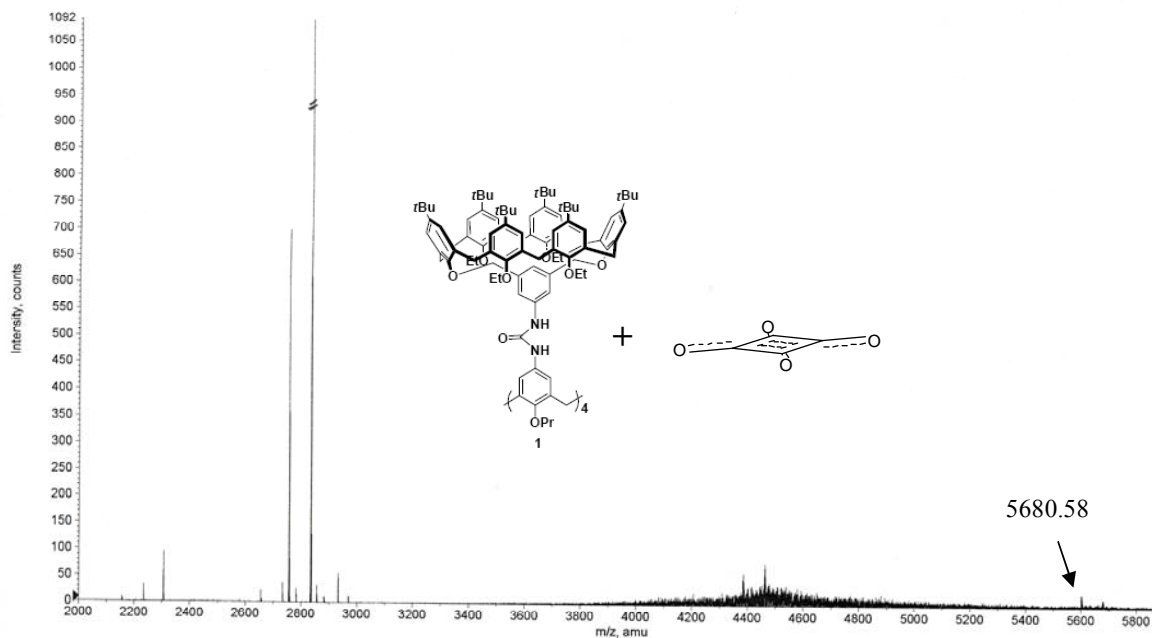


<sup>1</sup>H NMR [300 MHz, CD<sub>2</sub>Cl<sub>2</sub>/CD<sub>3</sub>CN (9:1), 298 K] spectra of **6** a) before and b) after addition of 8 equivalents of (TEA)C<sub>6</sub>H<sub>5</sub>CO<sub>2</sub>

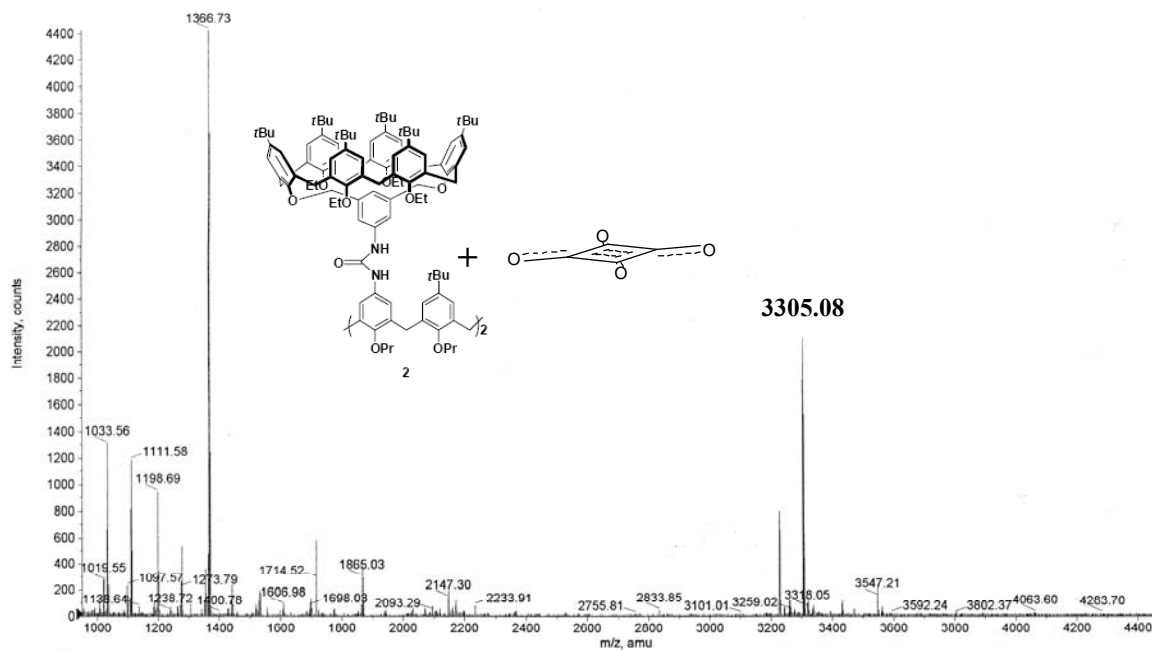


## Mass spectra of 1:SQ and 2:SQ complexes

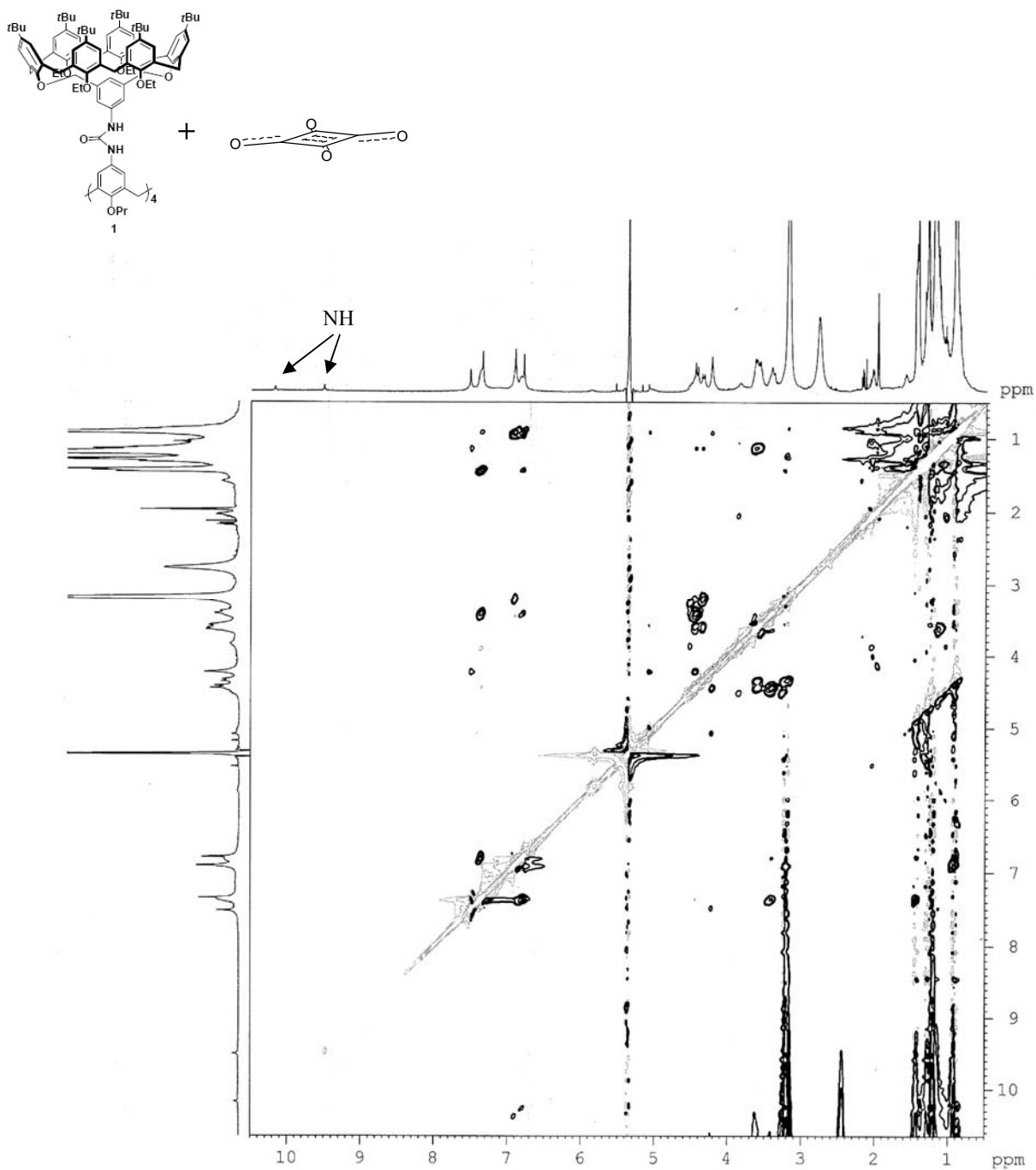
Mass spectrum 1:SQ complex (negative electrospray, solvent CH<sub>3</sub>CN/CH<sub>2</sub>Cl<sub>2</sub>)



Mass spectrum 2:SQ complex (negative electrospray, solvent CH<sub>3</sub>CN/CH<sub>2</sub>Cl<sub>2</sub>)



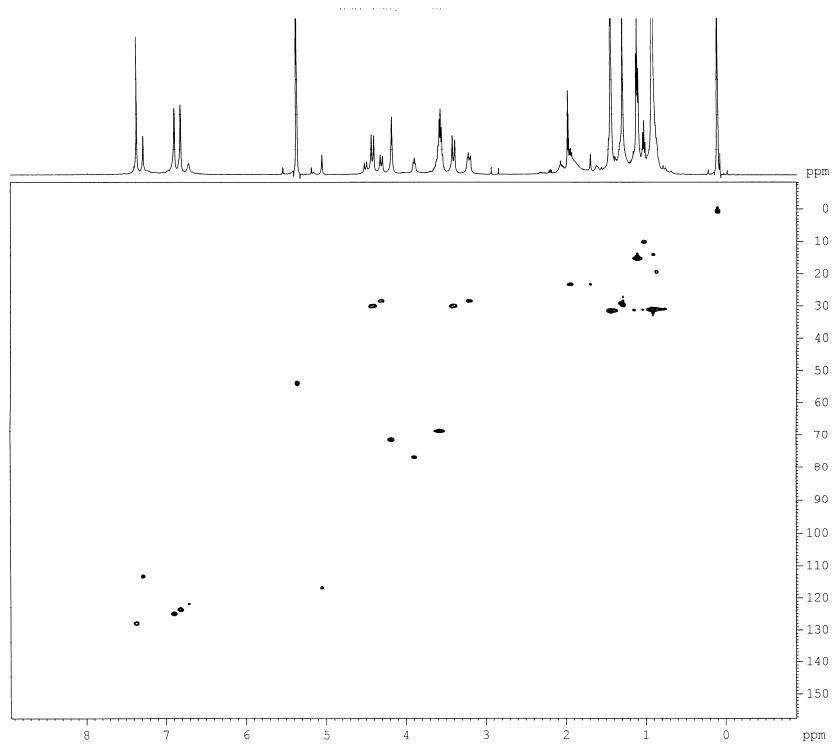
ROESY [500 MHz, CD<sub>2</sub>Cl<sub>2</sub>/CD<sub>3</sub>CN (9:1), 298 K] spectrum of 1·SQ complex



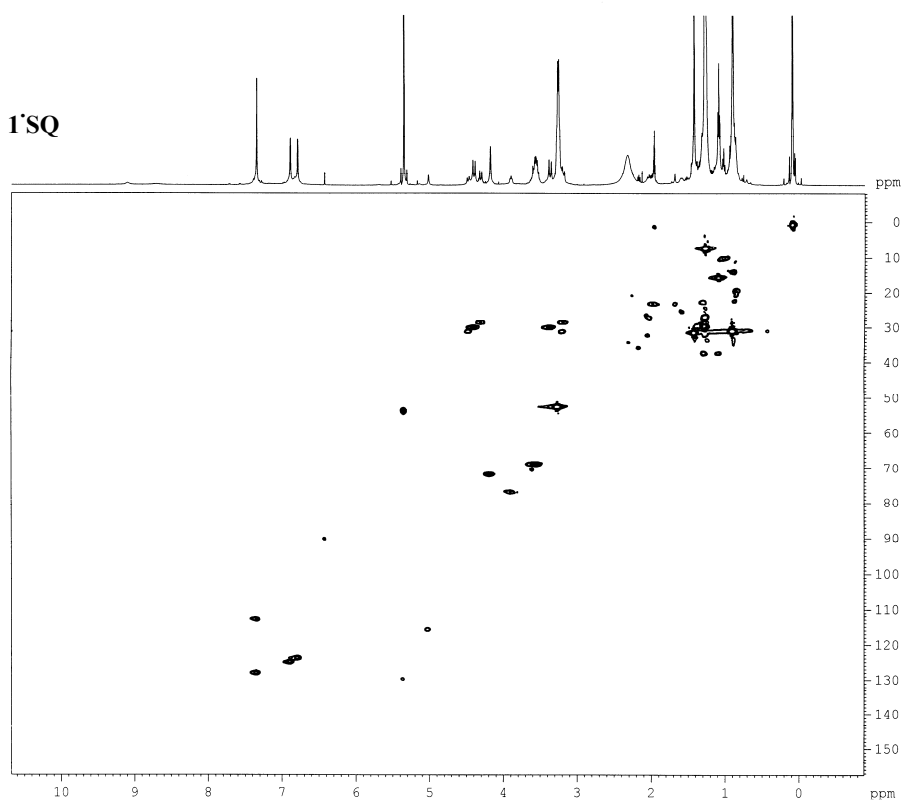


HSQC [500 MHz, CD<sub>2</sub>Cl<sub>2</sub>/CD<sub>3</sub>CN (9:1), 298 K] spectra of: a) **1**; b) **1**:SQ complex

a) **1**

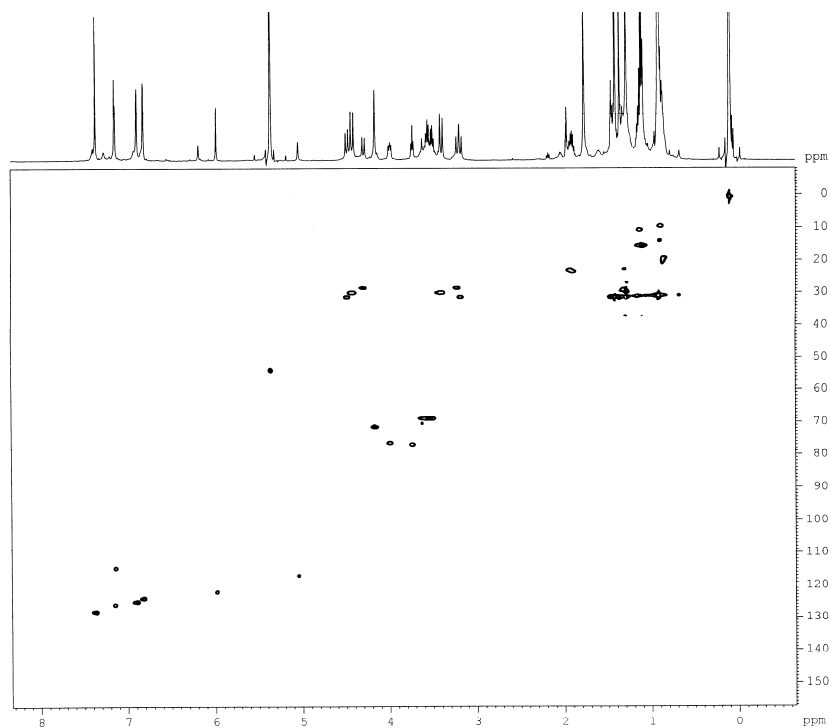


b) **1**:SQ

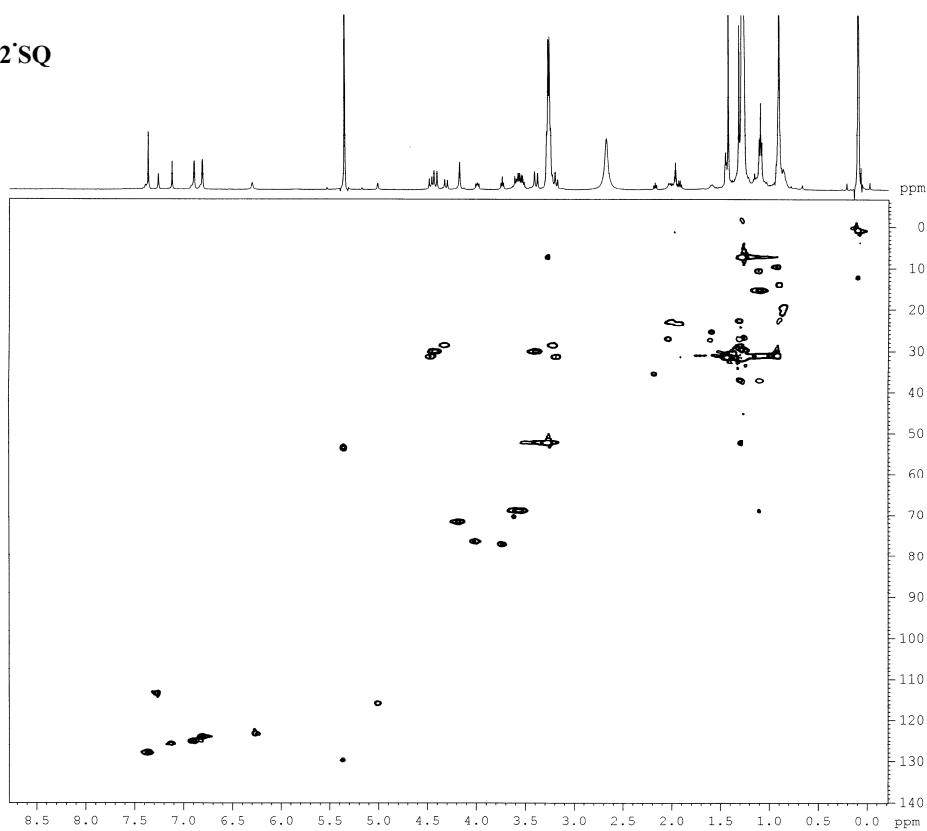


HSQC [500 MHz, CD<sub>2</sub>Cl<sub>2</sub>/CD<sub>3</sub>CN (9:1), 298 K] spectra of: a) 2; b) 2'SQ complex

a) 2

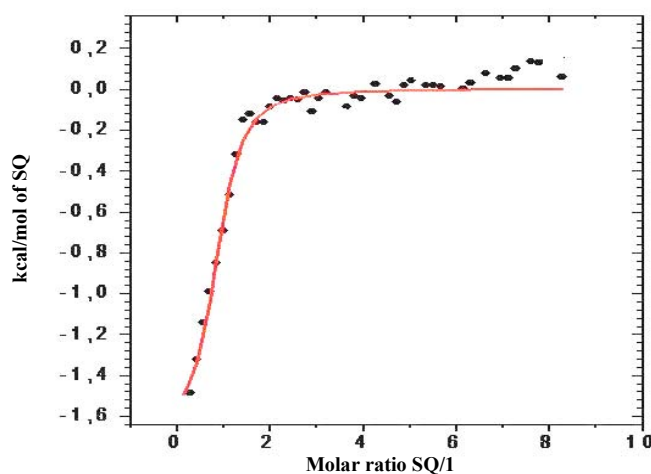


b) 2'SQ



**Measurement of complexation constants by ITC.** ITC titrations with receptor **1**, **2** and **6** were performed using an isothermal titration Microcal VP-ITC microcalorimeter. All measures were performed at 298 K. The dry solvents (acetonitrile and chloroform) were previously degassed by sonication for 15 minutes, and mixed in a 1:3 ratio. The tetraethylammonium squarate salt was weighted in a dry box. The host solutions (**1**, **2** and **6**) were filled into the cell of the ITC instrument and guest solution (tetraethylammonium squarate salt) was added with a syringe (300 rpm). A blank was registered for each experiment by addition of salt solution on solvent, and was subtracted to the data set. Titrations were repeated three times and found to be fully reproducible. Analysis and curve fitting was done using “one set of sites” algorithm of software *Origin* (Microcal, Inc).

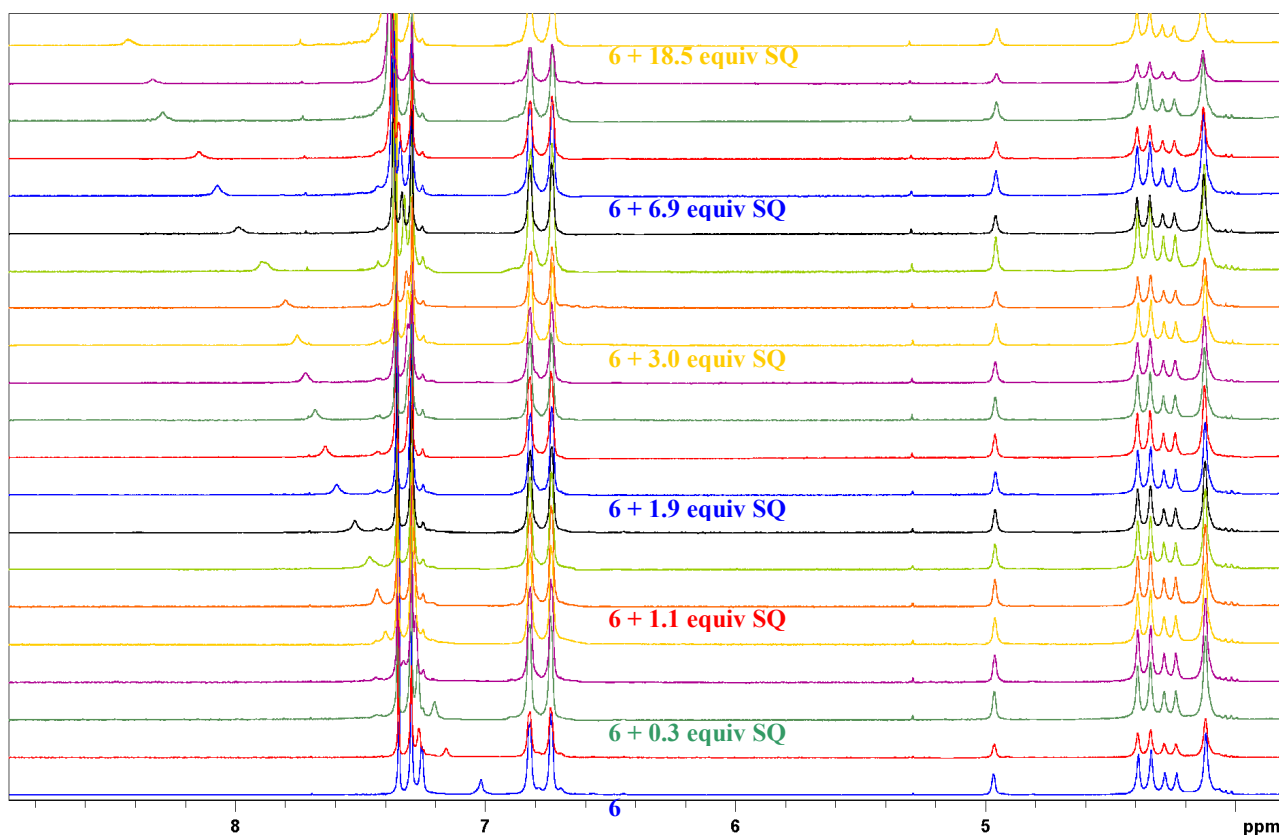
The experiment with receptor **1** and tetraethylammonium squarate dianion were carried out under the following conditions:  $[1] = 0.1 \text{ mM}$  and  $[(\text{TEA})_2\text{C}_4\text{O}_4] = 4 \text{ mM}$  in  $\text{MeCN}/\text{CHCl}_3$  (1:3 v:v). Thermodynamic parameters obtained:  $\Delta S = 17.3 \text{ cal mol}^{-1} \text{ K}^{-1}$ ;  $\Delta H = -1.69 \pm 0.14 \text{ kcal mol}^{-1}$ ,  $\Delta G = -6.84 \text{ kcal mol}^{-1}$  (Figure 3).



**Figure 3:** ITC normalized integration data of the evolved heat per injection plotted against the molar ratio **SQ-1**. To determine the values of the thermodynamic variables ( $\Delta H$ ,  $\Delta G$  and  $\Delta S$ ) the ITC data have been fitted to a 1 : 1 binding model (red line).

**Measurement of complexation constants by  $^1\text{H}$  NMR.**  $^1\text{H}$  NMR (300 MHz) titrations with receptors **1**, and **6** were performed at 298 K and with dry solvents ( $\text{CD}_3\text{CN}$  and  $\text{CDCl}_3$  or  $\text{CD}_2\text{Cl}_2$ ) that were previously mixed in the specified ratios. The host solutions (**1** or **6**) were introduced into the NMR tube and guest solutions (tetraethylammonium squarate salt) was added. Changes in the chemical shifts of the N-H groups were used,

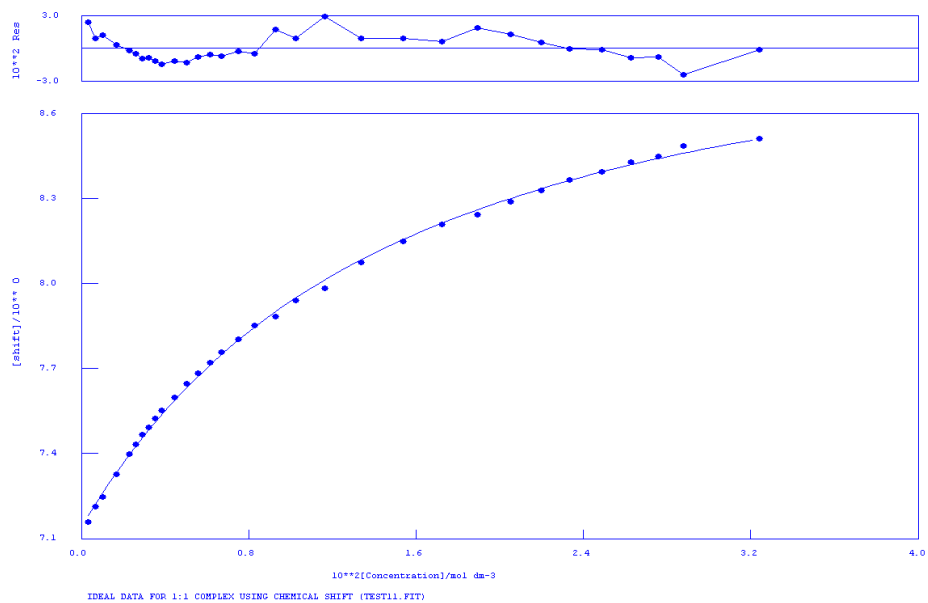
using the EQNMR software to analyze the results.<sup>7</sup>



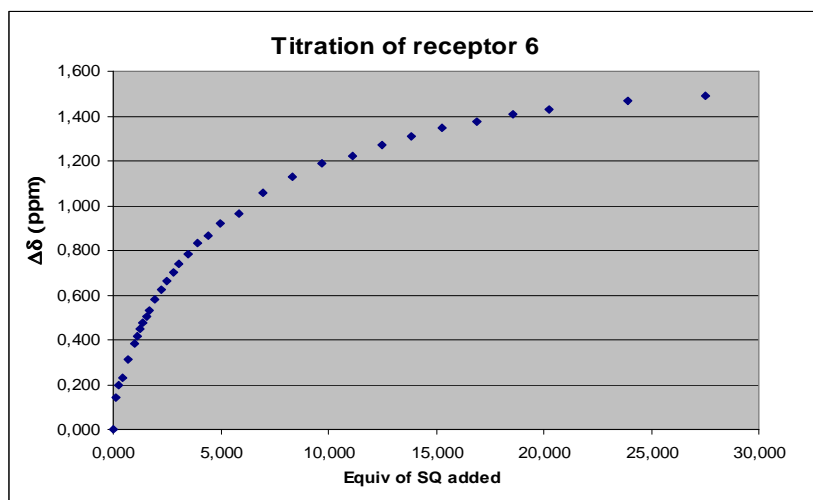
**Figure 4:** Variation of  $^1\text{H}$  NMR [300 MHz,  $\text{CDCl}_3/\text{CD}_3\text{CN}$  (3:1), 298 K] spectrum of **6** (2.5 mM) by addition of tetraethylammonium squarate salt (61.5 mM).

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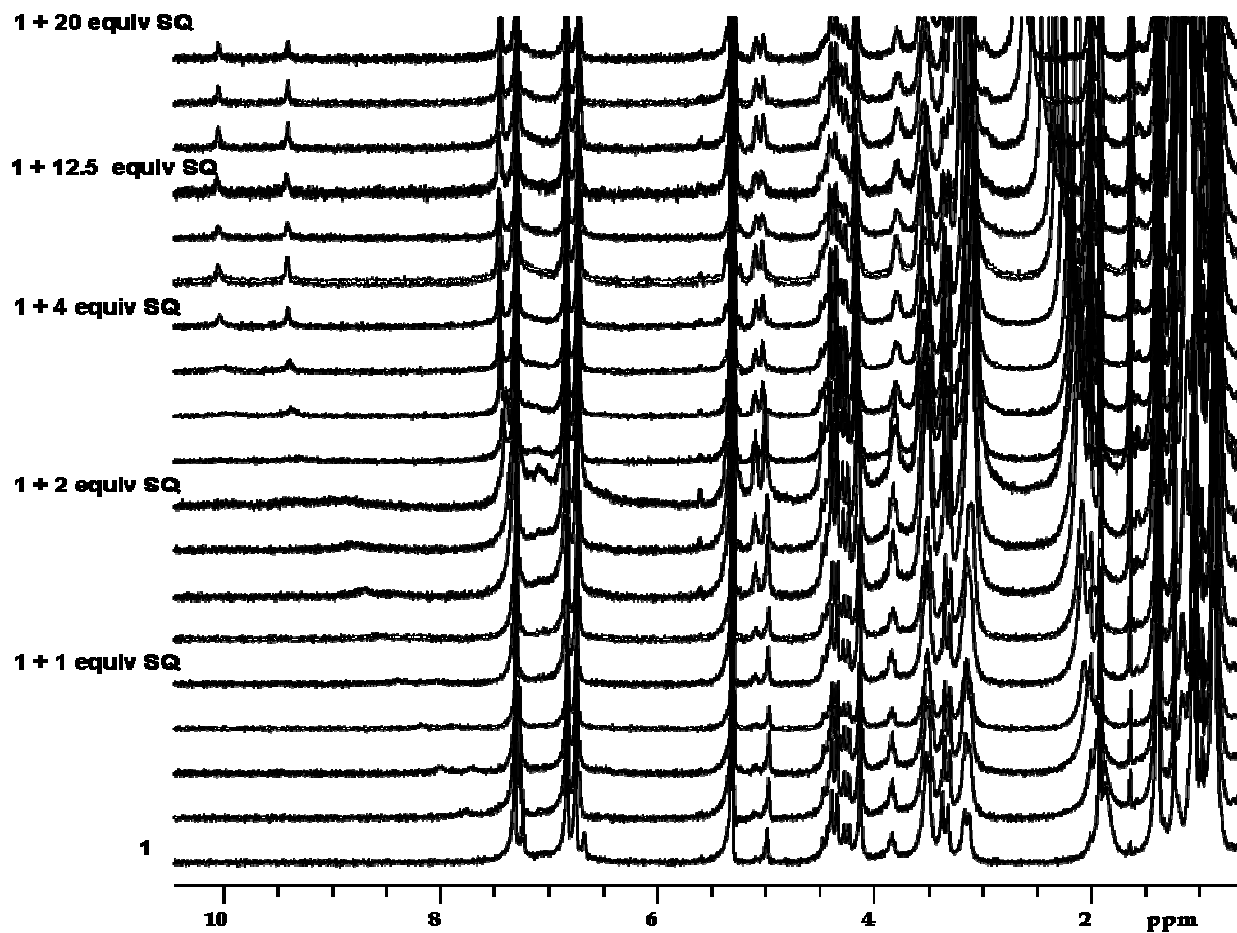
<sup>7</sup> M. J. Hynes, *J. Chem. Soc., Dalton Trans.* 1993, 311-312.



**Figure 5:** Fit plot corresponding to the titration experiment of compound **6** and tetraethylammonium squarate salt.



**Figure 6:** Variations on the N-H chemical shifts urea groups in compound **6** by addition of tetraethylammonium squarate salt.



**Figure 7:** Variation of  $^1\text{H}$  NMR [300 MHz,  $\text{CD}_2\text{Cl}_2/\text{CD}_3\text{CN}$  (9:1), 298 K] spectrum of 1 (1mM) by addition of tetraethylammonium squarate salt (26.7 mM).