



Supporting Information

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Efficient Macrocyclization of Preorganized Palindromic Oligosquaramides.

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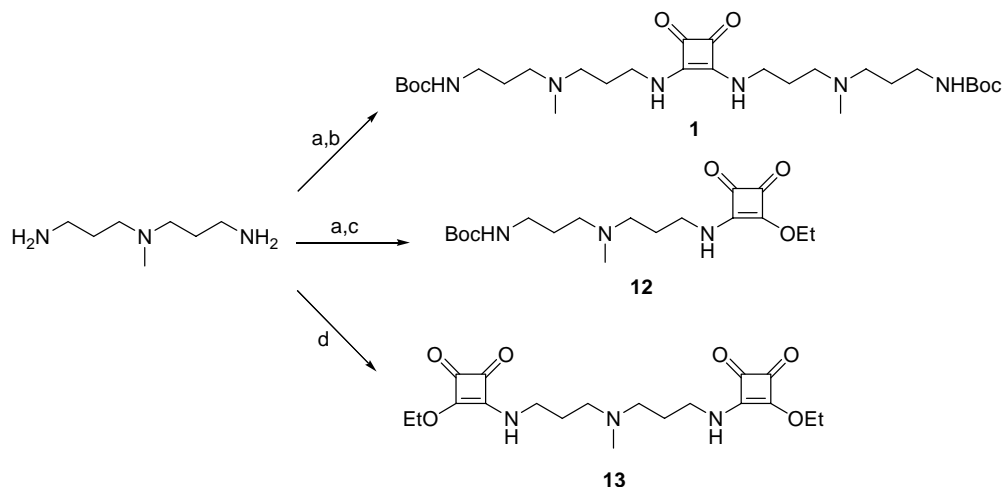
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1. General

All the reagents and solvents were commercially available and of analytical grade and were used without further purification unless otherwise stated. Diethyl ether, 1,4-dioxane and THF were distilled before compound purification. [D6] DMSO and CDCl₃ (99.8 %D) were stored on molecular sieves (3 Å). ¹H and ¹³C NMR spectra were recorded at 300 and 75 MHz at 23 °C unless otherwise specified. Chemical shifts are reported as parts per million (δ) referenced to the deuterium lock solvents and ¹³C NMR spectra in D₂O were referenced to 3-(trimethylsilyl)-1-propanesulfonic acid sodium salt. The coupling constants values *J* are given in Hz IR spectra were recorded on (FT-IR) Bruker IFS66 spectrophotometer. UV-Vis measurements were obtained on a (UV-Vis) Varian Cary 300 Bio spectrophotometer. HRMS data were obtained on a MicroMass Autospec 300 with a double focusing magnetic sector mass spectrometer operating at 3000 m/z with a cone voltage of 4V. For all the experiments the samples (10⁻⁶ M) in MeOH were injected at rate of 20 µl/min. The charge of the species corresponding to an observed ion rate were deduced directly from the spacing of the isotope peaks for masses lower than 3000 m/z. Calibration was done with PER standards giving closest peaks to the molecular ions under study.

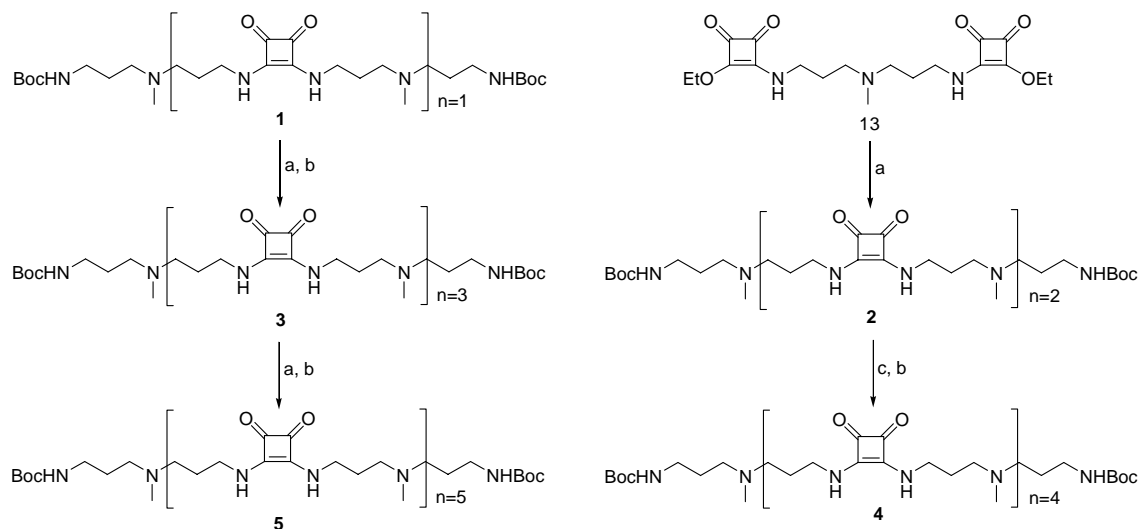
2. Synthetic procedures.

Scheme S1. Synthesis of monomer **1** and building blocks **12**, and **13**.^[1]



a: Boc-ON, dioxane, 16 h r. t., 4 h, reflux; b: diethylsquarate (0.5 equiv), EtOH, r. t. 12 h; c: diethylsquarate (1 equiv) Et₂O; d: diethylsquarate (2 equiv.), Et₂O.

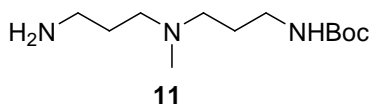
Scheme S2. Synthesis of dimer **2**, trimer **3**, tetramer **4** and pentamer **5**.



a: HCl, 50 °C, 3 h; b: **12** (2 equiv), EtOH.

[1] Synthesis of compound **13** is described in M. C. Rotger, M. N. Piña, A. Frontera, G. Martorell, P. Ballester, P. M. Deyà, A. Costa, *J. Org. Chem.* **2004**, *69*, 2302-2308.

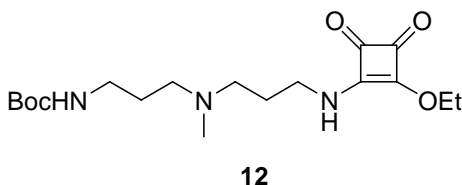
3,3'-N-Boc-aminopropyl-N-methyl-dipropylamine 11.



3,3'-diamino-N-methyl-dipropylamine (18 g, 0.12 mol) in 1,4-dioxane (30 ml) was added dropwise to a stirred solution of Boc-ON (5 g, 0.02 mol) in 1,4-dioxane (20 ml). The reaction mixture was stirred at room temperature for 12 h and then was refluxed for additional 4 h. The solvent was removed under reduced pressure and the residue dissolved in H₂O (100 ml). The aqueous solution was acidified with 3M HCl to pH=3, and extracted with Et₂O (5 x 10 ml). The aqueous layer was basified with 1M NaOH to pH=10 and extracted with CH₂Cl₂ (5 x 20 ml). The organic layer was washed with a Na₂CO₃ 5% aqueous solution (5 x 20 ml), dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure to give **11** (3.6 g, 14.8 mmol) as a pale yellow oil in 74% of yield. Bp= 190°C, 5.6 10⁻³ torr.

¹H NMR (300 MHz, CDCl₃): δ= 5.39 (br s, 1H; NH), 3.17 (q, *J*(H,H) = 7.0, 2H; CH₂), 2.74 (t, *J*(H,H) = 6.9, 2H; CH₂), 2.40 (m, 4H; CH₂), 2.18 (s, 3H; NMe), 1.61 (m, 4H; CH₂), 1.44 (s, 9H; tBuO), 1.2 (br s, 2; NH₂). ¹³C NMR (75 MHz, CDCl₃): δ=158.07, 80.70, 58.16, 57.54, 43.95, 42.38, 41.72, 32.84, 30.40, 28.91. IR ν = 3365, 1692, 1526, 1462, 1366 cm⁻¹. HRMS calcd for C₁₂H₂₈N₃O₂ 246.2182; found 246.2182 [MH⁺].

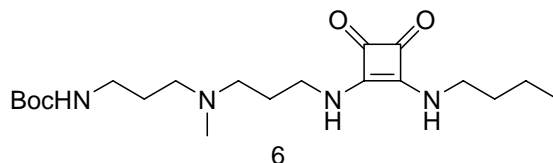
3-(3,3'-N-Boc-aminopropyl-N-methyl-dipropylamino)-4-(ethoxy)-3-cyclobutene-1,2-dione 12.



3,3'-N-Boc-aminopropyl-N-methyl-dipropylamine (832 mg, 3.2 mmol) in Et₂O (100 ml) was added dropwise to a stirred solution of diethylsquarate (600 mg, 3.5 mmol) in Et₂O (10 ml). The reaction mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue dissolved in CH₂Cl₂ and fractionated using hexane as precipitation agent to give **12** (840 mg, 2.28 mmol) as yellow oil. Yield= 72%.

¹H NMR (300 MHz, CDCl₃): δ=7.98 (br s, 0.6 H; NH), 7.62 (br s, 0.4 H; NH), 4.99 (br s, 1H; NH), 4.79 (m, 2 H CH₂), 3.78 (br s, 0.77 H; CH₂), 3.7 (m, 1.22 H; CH₂), 3.17 (m, 2 H; CH₂), 2.48 (t, *J*(H,H) = 5.7 2H; CH₂N), 2.38 (t, *J*(H,H) = 6.6 2H; NCH₂), 2.19 (s, 3H; NMe), 1.76 (m, 2 H; CH₂), 1.66 (m, 2 H; CH₂), 1.43 (s, 12 H; CH₃, tBu). ¹³C NMR (75 MHz, CDCl₃): δ=187.67, 181.47, 175.40, 170.80, 156.53, 77.51, 67.69, 54.80, 55.73, 42.83, 40.11, 37.32, 38.02, 26.76, 25.83, 14.19. IR ν = 3333, 2975, 1803, 1708, 1609, 1521, 1456, 1366 cm⁻¹. HRMS calcd. for C₁₈H₃₁N₃O₅Na 392.2161; found 392.2172 [MNa]⁺.

3-nButhylamino-4-(3,3'-N-Boc-aminopropyl-N-methyl-dipropylamino)-3-cyclobutene-1,2-dione 6.



n-Butylamine (100 mg, 1.37 mmol) in EtOH (20 ml) was added dropwise to a stirred solution of semiesther (500 mg, 1.35 mmol) in EtOH (5 ml). The reaction mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the solid crude was recrystallised from CH₂Cl₂/diethylether (30:70) to give **6** (465 mg, 1.17 mmol) as a white solid in 87% yield.

¹H NMR (300 MHz, CDCl₃): δ=7.34 (br s 1 H; NH), 6.68 (br s 1 H; NH), 4.76 (br s, 1H; NH), 3.80 (br s, 2 H CH₂), 3.64 (q *J*(H,H)=6.9 2H; CH₂), 3.23 (q *J*(H,H)=6.3 2H; CH₂), 2.51 (m, 2 H; NCH₂), 2.41 (m, 2H; CH₂N), 2.20 (s, 3H; NMe), 1.81 (m, 2 H; CH₂), 1.60 (m, 4 H; CH₂), 1.44 (s, 9 H, tBu), 1.35 (m, 2 H, CH₂), 0.94 (t *J*(H,H)=6.9 3H CH₃). ¹³C NMR (75 MHz, CDCl₃): δ=182.89, 168.52, 168.29, 156.92, 79.52, 55.52, 44.62, 43.73, 42.10, 38.94, 33.75, 28.79, 28.30, 27.54, 19.94, 14.07. IR (KBr) ν = 3414, 3170, 2957, 1803, 1689, 1639, 1584, 1543, 1431, 1363 cm⁻¹. HRMS calc. for C₂₀H₃₇N₄O₄ 397.2815 found 397.2807 [MH⁺].

Monomer 1.

3,3'-N-Boc-aminopropyl-N-methyl-dipropylamine (944 mg, 3.8 mmol) in Et₂O (30 ml) was added dropwise to a stirred solution of diethylsquarate (300 mg, 1.8 mmol) in EtOH (5 ml). The reaction mixture was stirred at room temperature for 12 h. The solvent was removed under pressure and the solid was recrystallized from CH₂Cl₂/hexane (30:70) to yield **1** (970 mg, 1.64 mmol) as a white solid. Yield= 95%.

¹H NMR (300 MHz, CDCl₃): δ= 7.09 (br s, 2H; NH), 5.02 (br s, 2H; NH), 3.73 (br s, 4H; CH₂), 3.19 (q *J*(H,H) = 7.0, 4H; CH₂), 2.43,2.38(2m, 8H; CH₂NMeCH₂), 2.17 (s, 3H; NMe), 1.77, 1.63 (2m, 8H; CH₂), 1.44 (s 18H; tBu). ¹³C NMR (75 MHz, CDCl₃): δ= 182.87, 168.12, 156.50, 79.21, 57.05, 55.35, 43.22, 41.82, 38.76, 28.47, 25.29. IR (KBr) ν = 3373, 3162, 2967, 1799, 1704, 1640, 1567, 1508, 1240 cm⁻¹. HRMS calc. for C₂₈H₅₂N₆O₆ Na 591.3856; found 591.3846 [MNa]⁺.

Dimer 2.

3,3'-N-Boc-aminopropyl-N-methyl-dipropylamine (2.58 g, 10.17 mmol) in EtOH (20 ml) was added dropwise to **13** (2 g, 5.09 mmol) in EtOH (10 ml). The reaction mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the solid residue was recrystallized from CH₂Cl₂/Et₂O (30/70) as precipitation agent to yield **2** (3.83 g, 4.83 mmol) as a white solid. Yield= 95%.

¹H NMR (300 MHz, CDCl₃): δ= 8.01 (br, 2H; NH), 7.48 (br s, 2H; NH), 5.19 (br s, 2H; NH), 3.77 (br s, 8H; CH₂), 3.20 (m, 4H; CH₂), 2.49,2.39(2m, 12H; CH₂NMeCH₂), 2.23 (s, 6H; NMe), 2.17 (s, 3H; NMe), 1.88, 1.77 (2m, 8H; CH₂), 1.67 (m, 4H; CH₂), 1.43 (s 18H; tBu). ¹³C NMR (75 MHz, CDCl₃): δ = 182.99, 181.60, 169.00, 166.99, 156.50, 79.03, 55.15, 54.71, 43.52, 42.44, 42.01, 38.90, 28.88, 28.48, 28.19, 27.21. IR (KBr) ν = 3414, 3164, 2955, 1800, 1644, 1574, 1450, 1364 cm⁻¹. HRMS calc. for C₃₉H₇₀N₉O₈ 792.5347; found 792.5353 [MH]⁺.

Trimer 3.

1 (250 mg, 0.44 mmol) in H₂O (1 ml) with 6 equiv of HCl was stirred for 4h at 50°C. The solution was cooled to room temperature and Na₂CO₃ solid was carefully added until pH = 9 of the aqueous solution was reached. The solvent was removed under reduced pressure and the crude was dissolved in 20 ml of EtOH. The residual salts were filtered. To this clear solution, **12** (2.3 equiv) in EtOH (30 ml) was slowly added. The reaction mixture was stirred at room temperature for 15 h. The solvent was removed under reduced pressure and the crude was dissolved in aqueous Na₂CO₃ 5% (20 ml) and extracted with CHCl₃ (4 x 15 ml) and CHCl₃-tBuOH, 50:50 v:v (2x 15 ml). The organic layers were dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure. The solid crude was digested in 1,4-dioxane (5 x 10 ml) for 10 minutes each, to give **3** (214 mg, 0.11 mmol) as a pale yellow solid. Yield = 55%.

¹H NMR (300 MHz, CDCl₃): δ= 7.98 (br, 4H; NH), 7.6 (br s, 2H; NH), 5.14 (br s, 2H; NH), 3.75 (br s, 12H; CH₂), 3.20 (m, 4H; CH₂), 2.49, 2.40 (2m, 16H; CH₂NMeCH₂), 2.21 (s, 6H; NMe), 2.17 (s, 6H; NMe), 1.79 (m, 12H; CH₂), 1.66 (m, 4H; CH₂), 1.44 (s 18H; tBu). ¹³C NMR (75 MHz, CDCl₃): δ= 182.90, 181.80, 181.57, 169.01, 168.07, 167.04, 156.44, 78.99, 55.11, 54.72, 43.39, 42.45, 42.89, 38.96, 28.87, 28.68, 28.47, 28.22, 27.17. IR ν = 3551, 3476, 3415, 1806, 1664, 1592, 1430 cm⁻¹. HRMS calc. for C₅₀H₈₇N₁₂O₁₀ 1015.6668; found 1015.6661 [MH]⁺.

Tetramer 4.

4 was obtained from **2** using the procedure described for **3**. THF was the solvent used for crude purification to give **4** as a pale yellow solid. Yield = 55%. ¹H NMR (300 MHz, CDCl₃): δ= 8.09 (br, 6H; NH), 7.52 (br s, 2H; NH), 5.16 (br s, 2H; NH), 3.77 (br s, 16H; CH₂), 3.20 (m, 4H; CH₂), 2.49, 2.41 (2m, 20H; CH₂NMeCH₂), 2.23 (s, 6H; NMe), 2.17 (s, 9H; NMe), 1.83 (m, 16H; CH₂), 1.65 (m, 4H; CH₂), 1.44 (s 18H; tBu). ¹³C NMR (75 MHz, CDCl₃): δ= 183.22, 182.14, 181.90, 169.36, 168.43, 167.45, 156.78, 79.33, 55.40, 55.12, 43.64, 42.85, 42.27, 39.30, 29.19, 29.03, 28.82, 28.49, 27.36. IR (KBr) ν = 3415, 3172, 2953, 1800, 163, 1590, 1549, 1447, 1364 cm⁻¹. HRMS calc. for C₆₁H₁₀₄N₁₅O₁₂ 1238.7989; found 1238.8020 [MH]⁺.

Pentamer 5

5 was obtained from **3** using the procedure described for **3**. Crude purification was done using THF and acetone as washing agents to give **5** as a pale yellow solid. Yield = 55%. ¹H NMR (300 MHz, CDCl₃): δ= 8.13 (br, 8H; NH), 7.53 (br s, 2H; NH), 5.21 (br s, 2H; NH), 3.77 (br s, 20H; CH₂), 3.19 (m, 4H; CH₂), 2.52, 2.42 (2m, 24H; CH₂NMeCH₂), 2.24 (s, 6H; NMe), 2.17 (s, 12H; NMe), 1.84 (m, 20H; CH₂), 1.66 (m, 4H; CH₂), 1.44 (s 18H; tBu). ¹³C NMR (75 MHz, CDCl₃): δ= 183.27, 182.23, 181.99, 169.33, 168.37, 167.45, 156.80, 79.34, 55.41, 55.13, 43.63, 42.86, 42.24, 39.22, 29.04, 29.03, 28.82, 28.43, 28.05, 27.36. IR (KBr) ν = 3551, 3476, 3414, 2952, 1800, 1641, 1588, 1549, 1444, 1363 cm⁻¹. HRMS calc. for C₇₂H₁₂₀N₁₈O₁₄Na 1483.9129; found 1483.9108 [MNa]⁺.

Macrocycle 7

2 (300 mg, 0.37 mmol) was boc-cleaved as described above. The crude amine was dissolved in methanol (10 ml) and to this stirred solution diethylsquarate (63 mg, 0.37 mmol) was added. The reaction was stirred at room temperature for 12 h. The solvent was removed and the residue was dissolved in H₂O/HCl (10 ml) at pH=2. Then, the

solution was basified to pH=10 with NaOH 1 N and let to stand. The precipitate was filtered and dried to give **7** (200 mg, 0.3 mmol) as a white solid. Yield = 81%.

^1H NMR (300 MHz, DMSO): δ = 7.61 (br s, 6 H; NH), 3.94 (br s 12H, CH_2), 2.29 (br s, 12 H; CH_2NCH_2), 2.09 (s, 9 H NMe), 1.64 (br s, 12 H; CH_2). ^{13}C NMR (75 MHz, $\text{D}_2\text{O}/\text{HCl}$): δ = 184.30, 170.82, 55.90, 55.48, 43.75, 43.17, 27.88. IR (KBr) ν = 3473, 3414, 3174, 2950, 1800, 1643, 1581, 1434, 1361 cm^{-1} . HMRS calc. for $\text{C}_{33}\text{H}_{52}\text{N}_9\text{O}_6$ 670.4041 found 670.4062 $[\text{MH}]^+$.

Macrocycle 8.

8 was prepared and purified as described for **7** starting from **3** (375 mg, 0.37 mmol) and diethyl squarate (63 mg, 0.37 mmol). The desired product **8** (264 mg, 0.30 mmol) was obtained as white solid. Yield = 80%.

^1H NMR (300 MHz, DMSO): δ = 7.61 (br s, 8H; NH), 3.49 (br s, 16 H; CH_2), 2.29 (br s, 16 H; CH_2NCH_2), 2.09 (br s, 12 H NMe), 1.64 (br s, 16 H CH_2). ^{13}C NMR (75 MHz, $\text{D}_2\text{O}/\text{HCl}$): δ = 184.32, 170.74, 55.92, 55.62, 43.83, 43.01, 42.69, 27.96. IR (KBr) ν = 3475, 3413, 3174, 2951, 1799, 1645, 1586, 1548, 1444, 1362 cm^{-1} . HMRS calc. for $\text{C}_{44}\text{H}_{69}\text{N}_{12}\text{O}_8$ 893.53 found 893.5394 $[\text{MH}]^+$.

Macrocycle 9.

9 was prepared and purified as described for **7** starting from **4** (458 mg, 0.37 mmol) and diethyl squarate (63 mg, 0.37 mmol). The desired product **9** (338 mg, 0.3 mmol) was obtained as white solid. Yield = 82%.

^1H NMR (300 MHz, DMSO): δ = 7.61 (br s, 10H; NH), 3.49 (br s, 20 H; CH_2), 2.29 (br s, 20 H; CH_2NCH_2), 2.09 (br s, 15 H NMe), 1.64 (br s, 20 H CH_2). ^{13}C NMR (75 MHz, $\text{D}_2\text{O}/\text{HCl}$): δ = 184.30, 170.74, 55.92, 43.83, 42.69, 27.96. IR (KBr) ν = 3415, 3231, 2950, 1800, 1642, 1592, 1542, 1436, 1361 cm^{-1} . HMRS calc. for $\text{C}_{55}\text{H}_{85}\text{N}_{15}\text{O}_{10}$ Na 1138.6502 found 1138.6478 $[\text{MNa}]^+$.

Macrocycle 10.

10 was prepared and purified as described for **7** starting from **5** (540 mg, 0.37 mmol) and diethyl squarate (63 mg, 0.37 mmol). The desired product **10** (398 mg, 0.30 mmol) was obtained as white solid. Yield = 80%.

^1H NMR (300 MHz, DMSO): δ = 7.49 (br, 12 H; NH), 3.58 (br s, 24 H; CH_2), 2.38 (br s, 24 H; $\text{CH}_2\text{NMeCH}_2$), 2.18 (s, 18 H; NMe), 1.73 (br s, 24H; CH_2). ^{13}C NMR (75 MHz, $\text{D}_2\text{O}/\text{HCl}$): δ = 184.28, 170.71, 55.89, 43.80, 42.66, 27.93. IR (KBr) ν = 3478, 3212, 2953, 1802, 1644, 1591, 1487, 1446, 1363 cm^{-1} . HMRS calc. for $\text{C}_{66}\text{H}_{103}\text{N}_{18}\text{O}_{12}$ 1339.8003 found 1339.7996 $[\text{MH}]^+$.

3. NMR Studies.

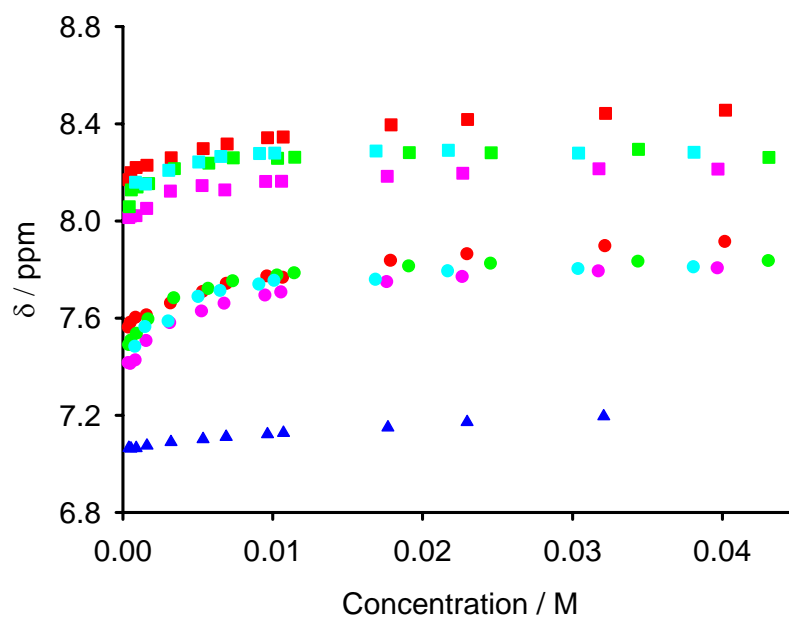


Figure S1. Plot of the observed chemical shifts of the NH squaramide protons: H_{upfield} (circle) and $H_{\text{downfield}}$ (squares) of dimer **2** (red), trimer **3** (pink), tetramer **4** (green), pentamer **5** (cyan) and monomer **1** (triangle) as function of the concentration.

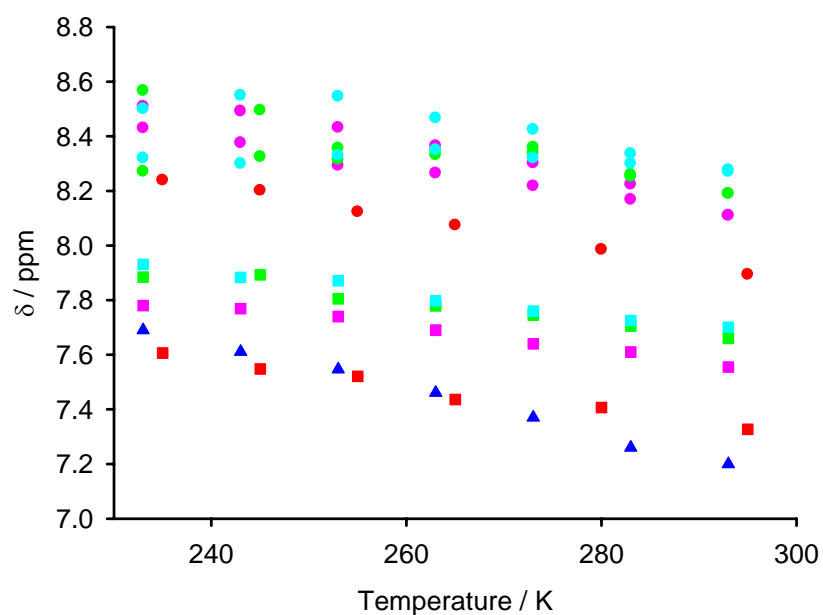


Figure S2. Plot of the observed chemical shifts of the NH squaramide protons: H_{upfield} (square) and $H_{\text{downfield}}$ (circle) of dimer **2** (red), trimer **3** (pink), tetramer **4** (green), pentamer **5** (cyan) and monomer **1** (triangle), in CDCl_3 (3mM) as function of the temperature (233-298K).

Table S1. Observed coefficients for the temperature rate of change for the NH-squaramide protons.

Compound			
Monomer 1			-6.59
Dimer 2	-6.65	-4.02	
Trimer 3	-6.65	-3.75	-5.33
Tetramer 4	-6.28	-3.73	-1.35
Pentamer 5	-3.71	-3.83	-0.83

DOSY measurements.

All NMR 2D-DOSY experiments were carried out on a Bruker 500 MHz Avance equipped with a 5-mm inverse broadband probehead with a gradient set capable of generating magnetic field pulse-gradients (in the z-direction). The measurement of *D* was made using the bipolar-gradient LED pulse sequence^[2] and all calculations were made using the DOSY package provided in the Bruker Topspin software. The strength of the gradient was first calibrated by measuring the self-diffusion coefficient of the residual HDO signal in a 100% D₂O sample at 298 K.

Convection effects were minimized using sample rotation as described by Esturau *et al.*^[3] The temperature regulation system eurotherm VT-3000 supplied by the manufacturer was used. Temperature calibration on the spectrometer was performed using a standard methanol sample. In all experiments temperature was stabilized into a range of ± 0.1 K using an air flow rate of 270 L/h. Sample spinning of 20 Hz was used.

Table S2. Diffusion coefficients *D* of **1-5** in CDCl₃ at 301 K.

Compounds ^[a]	Mw	D/10¹⁰ m²s⁻¹
Monomer 1	568.75	5.28
Dimer 2	792.02	3.84
Trimer 3	1014.66	3.16
Tetramer 4	1238.33	2.17
Pentamer 5	1461.84	1.83

[a] [Oligomer] = 5 mM.

[2] Wu, A. Chen, C. S. Johnson, Jr., *J. Magn. Reson. A*, 1995, **115**, 260.

[3] N. Esturau, F. Sánchez-Ferrando, J. A. Gavin, C. Roumestand, M. Delsuc, T. Parella, *J. Magn. Reson.*, 2001, **153**, 48.

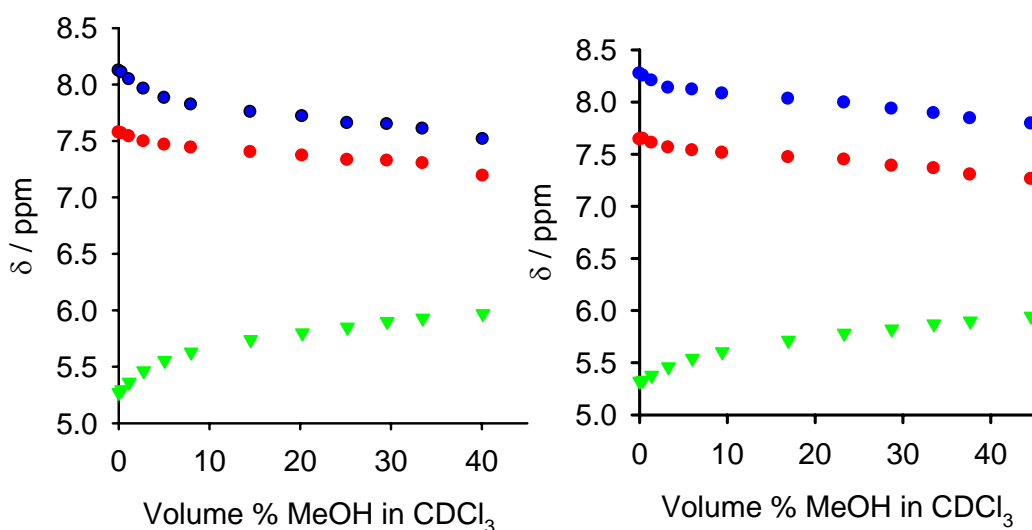


Figure S3. Chemical shift of NH-squaramide protons (circle) and NH-carbamate (triangle) as function of MeOH in CDCl_3 for dimer **2** (left) and tetramer **4** (right) at 283 K. [Oligomer] = 3mM.

4. Differential scanning calorimetry (DSC) studies.

DSC measurements were performed in duplicates using the Microcal (marca) with a cell volume of 1.98 ml and pressure of N_2 (2 atm) applied over the cells. The scans for **2-5** were performed by increasing the temperature from 10 °C to 80 °C at scan rate of 60 °C/h. The compound concentration used for calorimetric experiments was 2-3 mM in the solvent mixture EtOH- CHCl_3 95:5 v:v. Solvent scans were run under the same experimental conditions. DSC data was analyzed using Origin software from MicroCalInc. Solvent scans were subtracted from sample scans prior to the determination of molar excess heat capacities (C_p), by normalizing the experimental thermograms with concentrations and the volume of the calorimeter cell. The apparent denaturation temperature T_m was determined as the temperature corresponding to maximum C_p ($C_{p_{\max}}$) and the calorimetric enthalpy ΔH was calculated as the integrated area under the peak. A linear connected baseline was subtracted prior to the determination of the thermodynamic parameters.

Tabla S2. Observed ΔH and T_m for **2-5** in EtOH- CHCl_3 95/5 v:v (2-3 mM).

Compound	ΔH cal/mol	T_m C°
Dimer 2	165	61
Trimer 3	370	64
Tetramer 4	475	63
Pentamer5	611	63

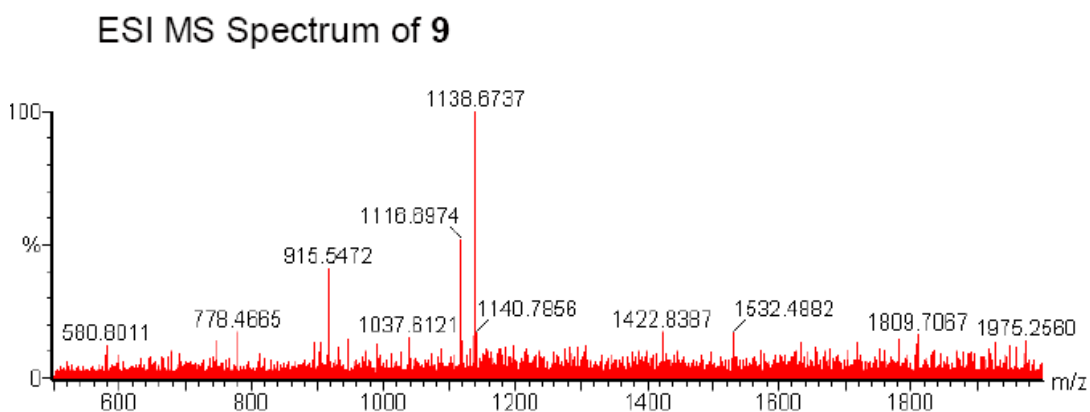
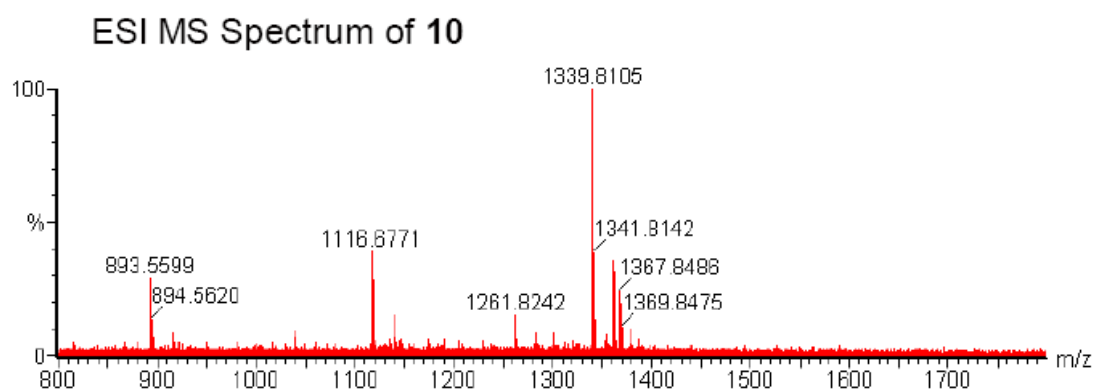
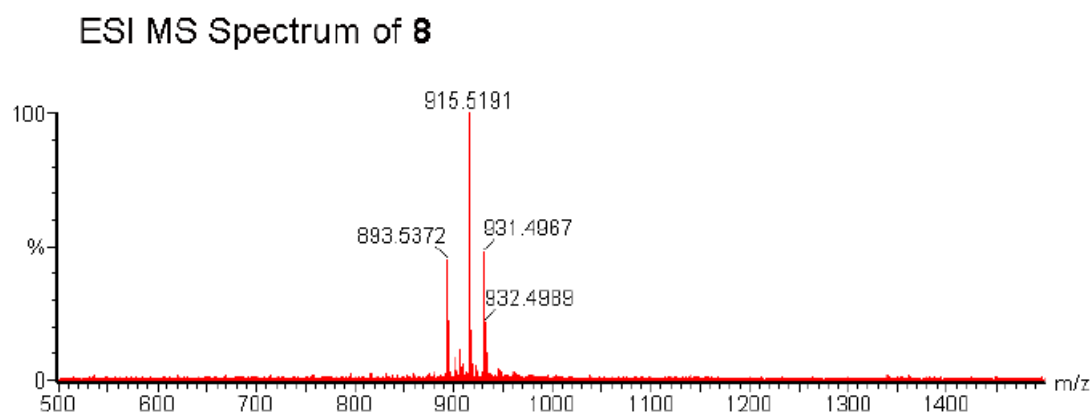
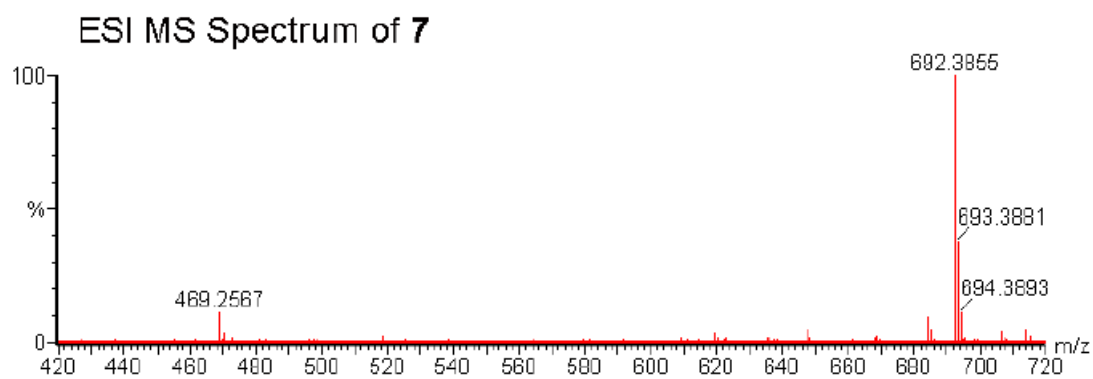
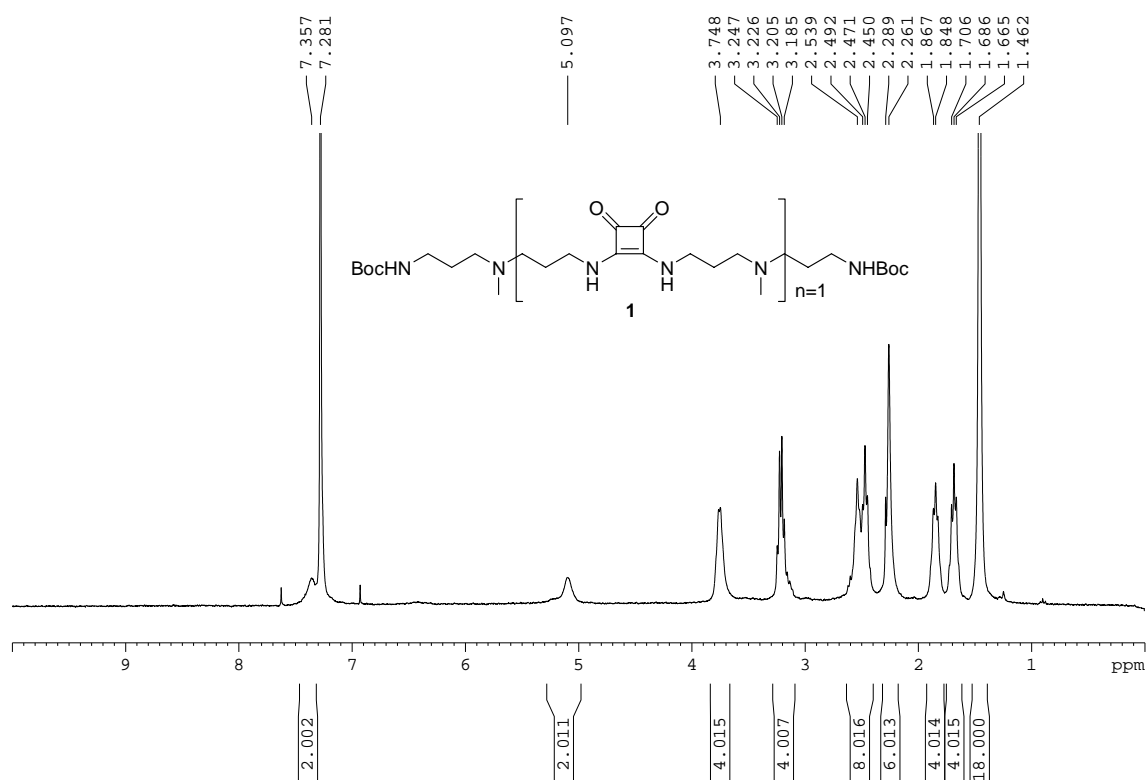
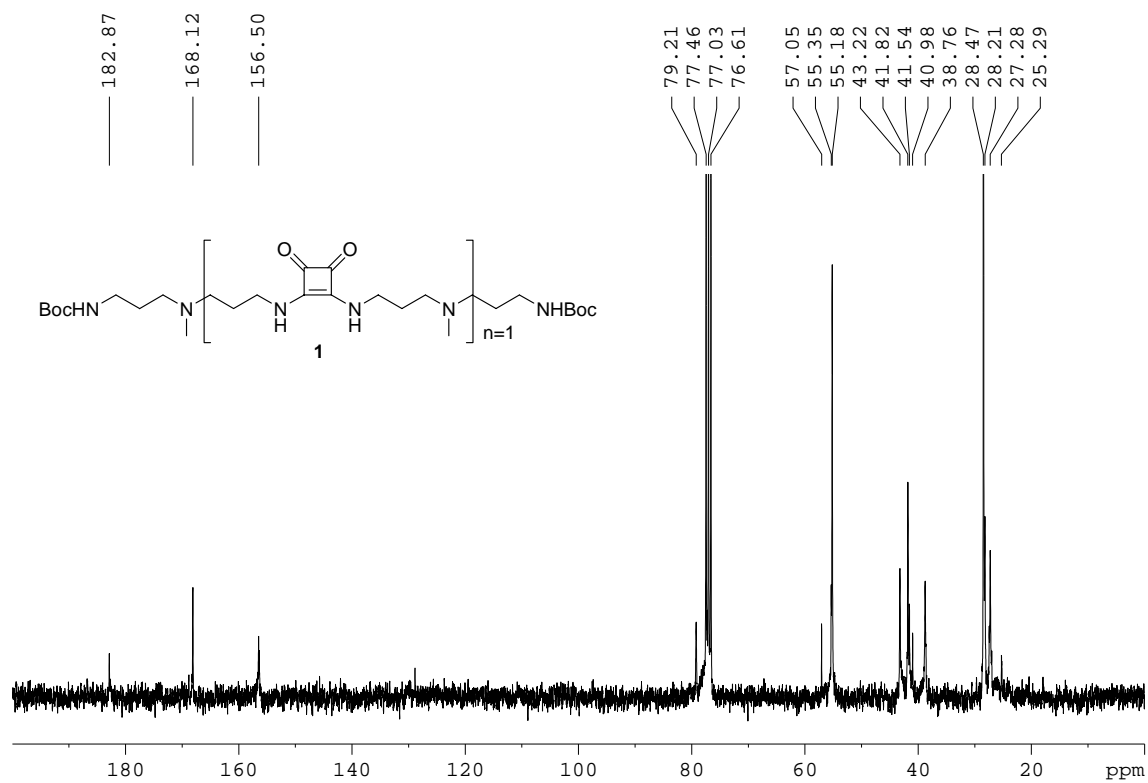


Figure S4. ESI MS Spectrum of macrocycles **7-10**.

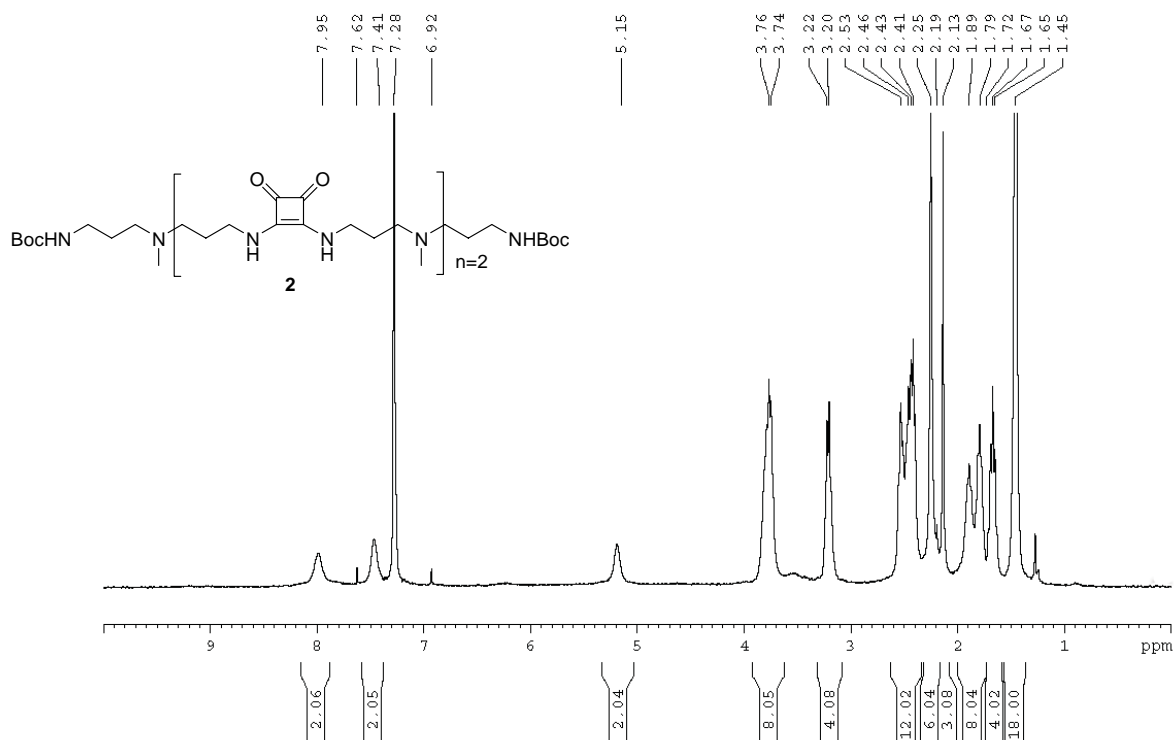
^1H RMN spectrum of monomer **1** in CDCl_3



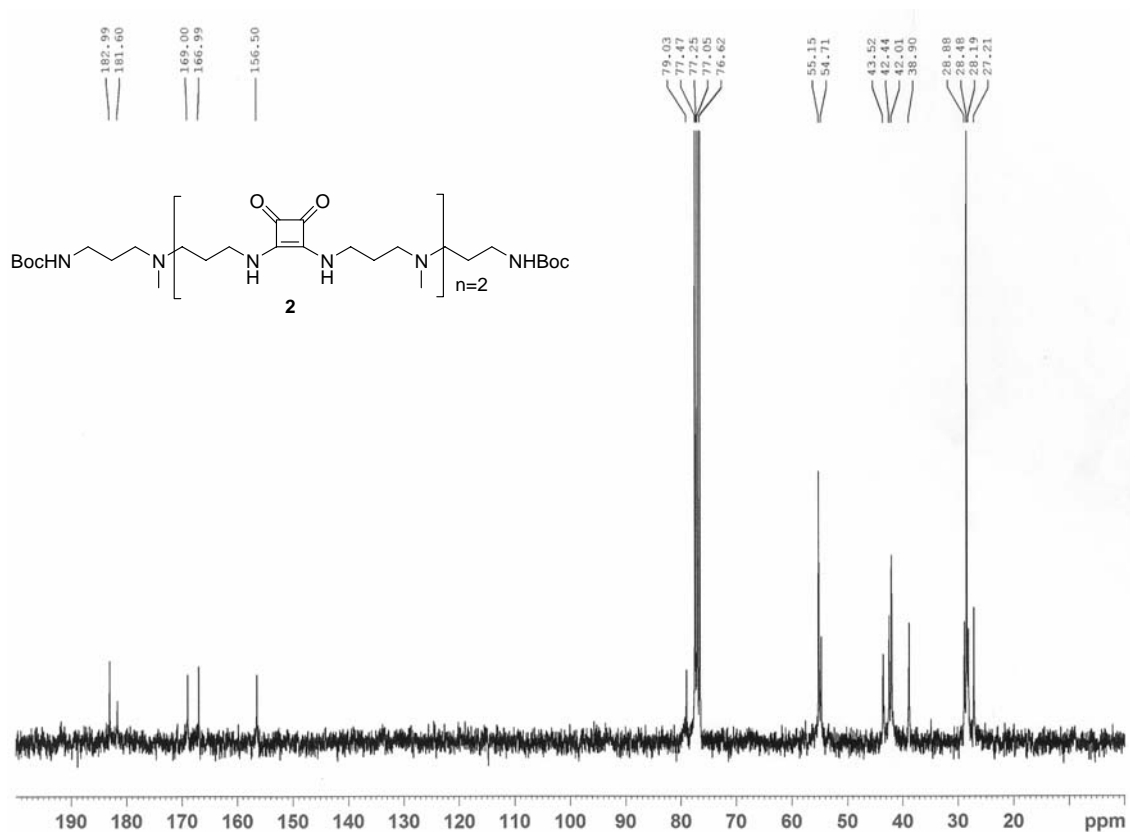
^{13}C RMN spectrum of monomer **1** in CDCl_3



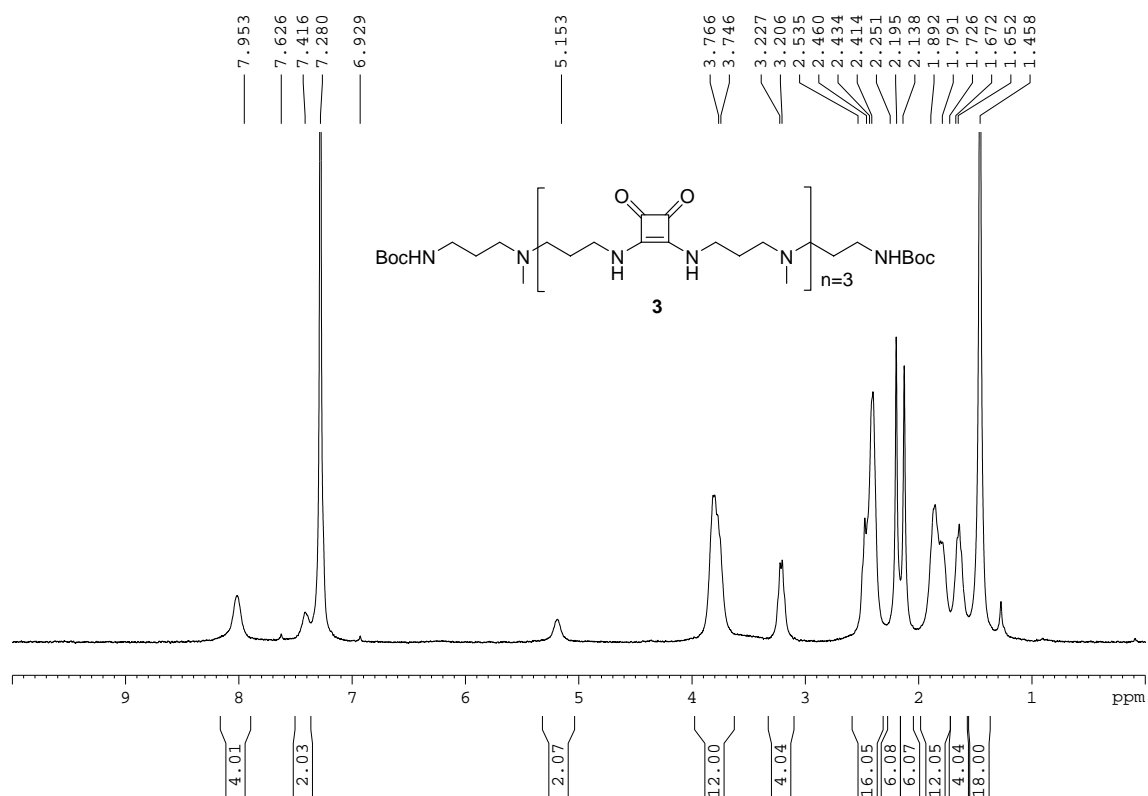
^1H RMN spectrum of dimer **2** in CDCl_3



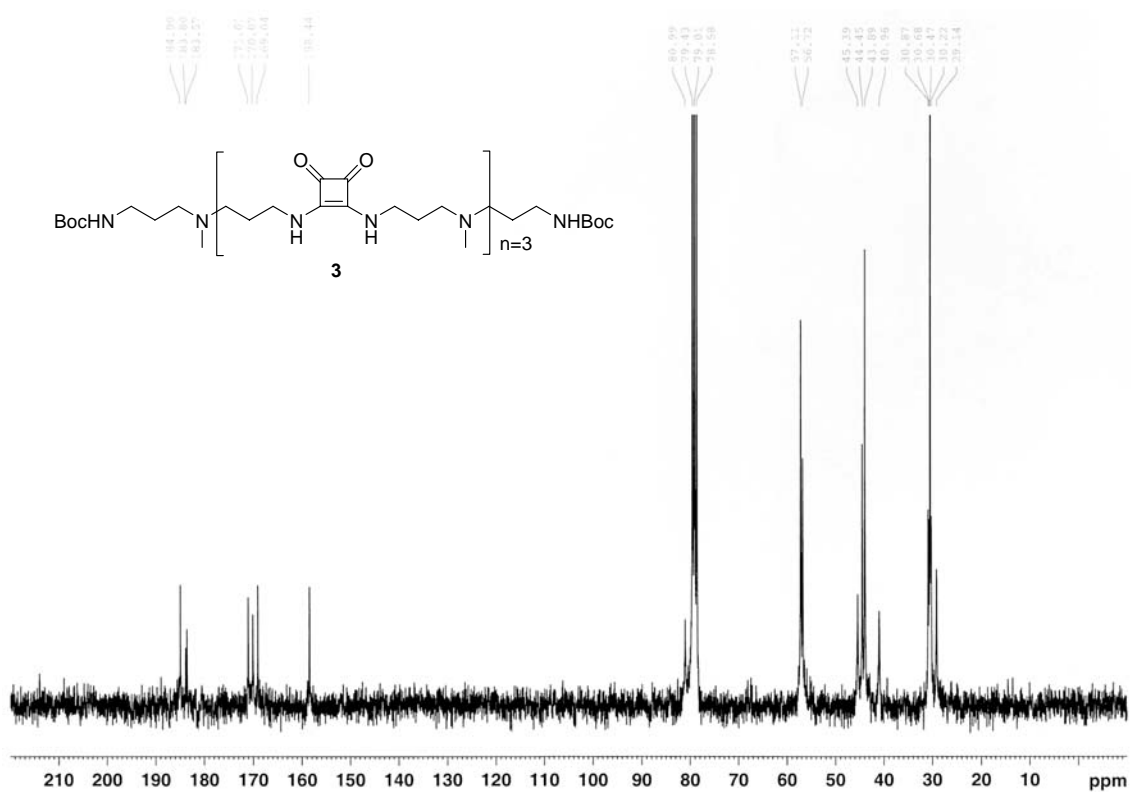
^{13}C RMN spectrum of dimer **2** in CDCl_3



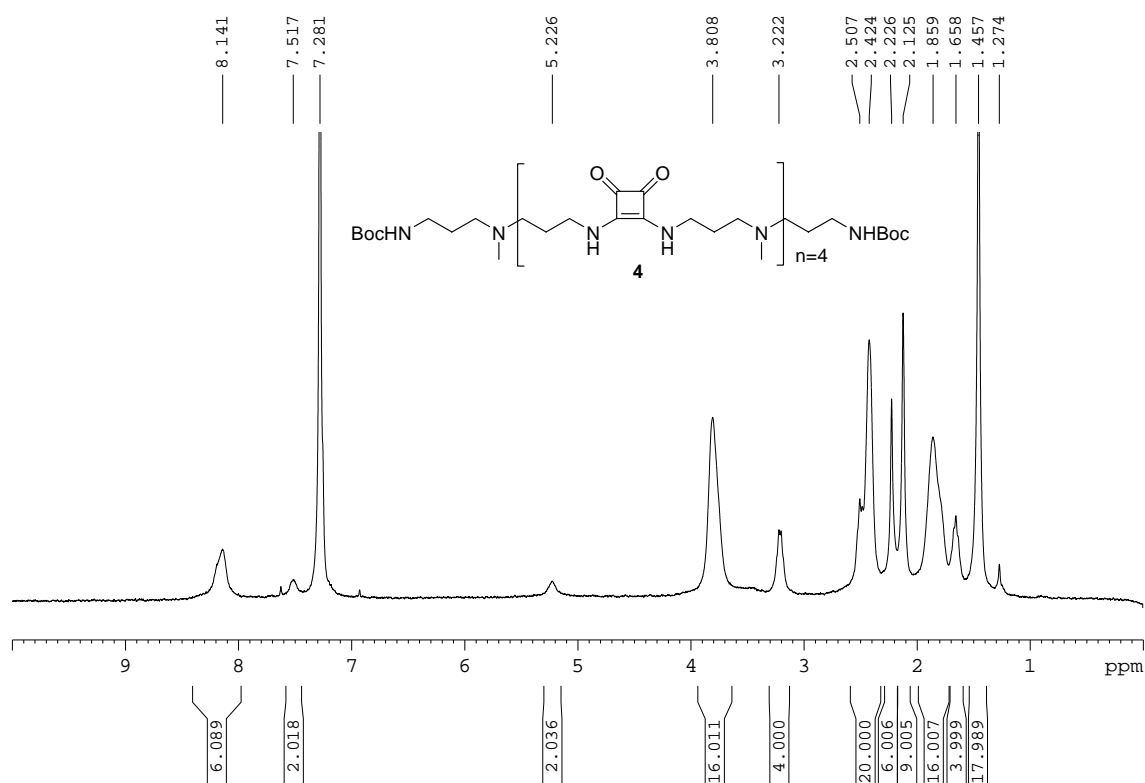
^1H RMN spectrum of trimer **3** in CDCl_3



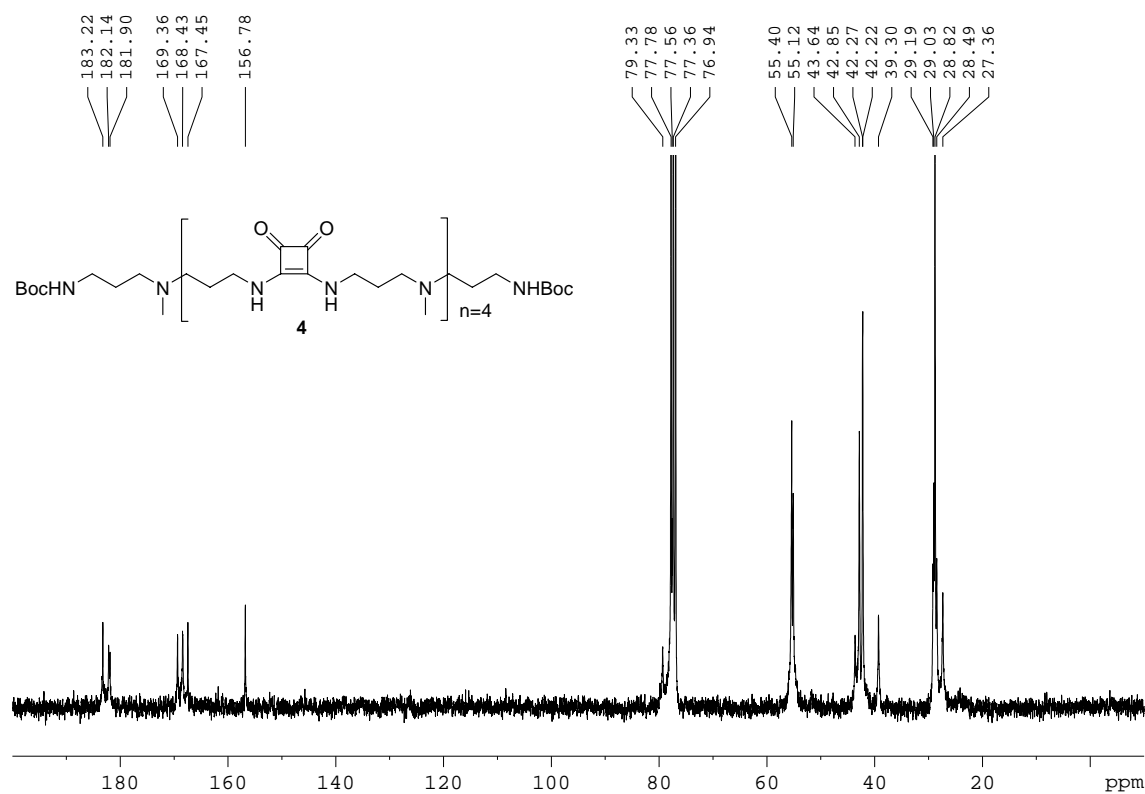
^{13}C RMN spectrum of trimer **3** in CDCl_3



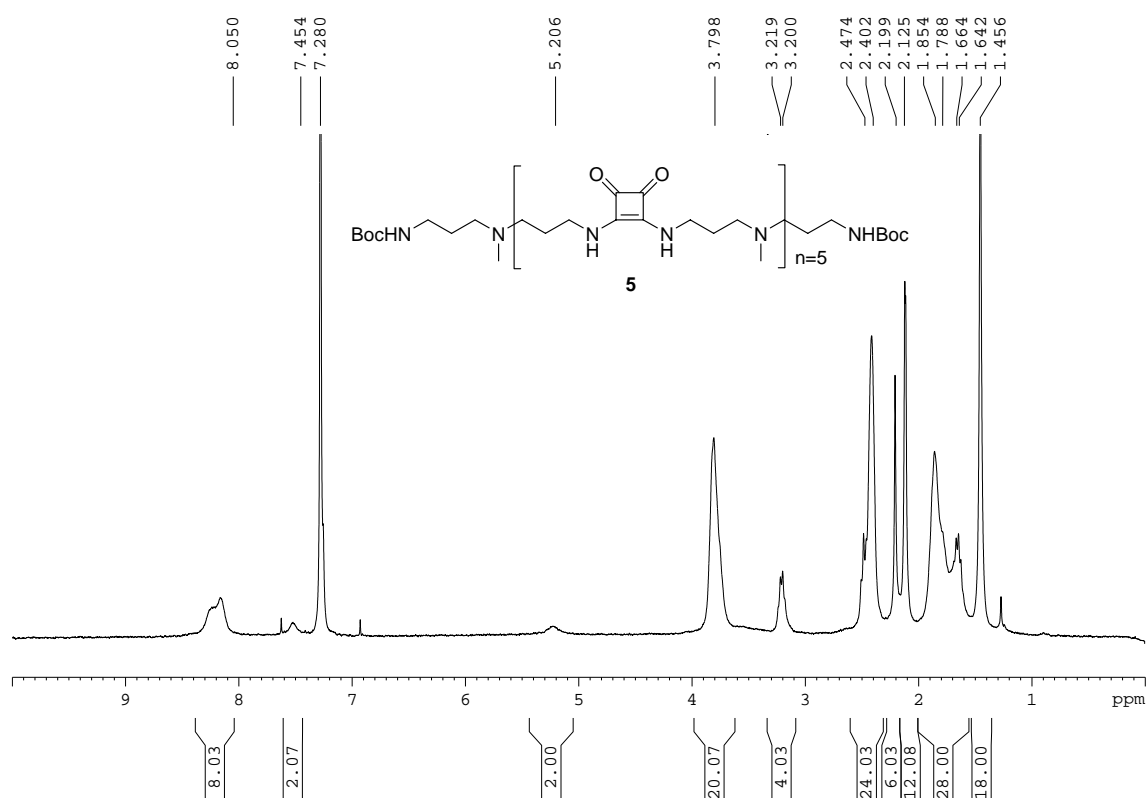
^1H RMN spectrum of tetramer **4** in CDCl_3



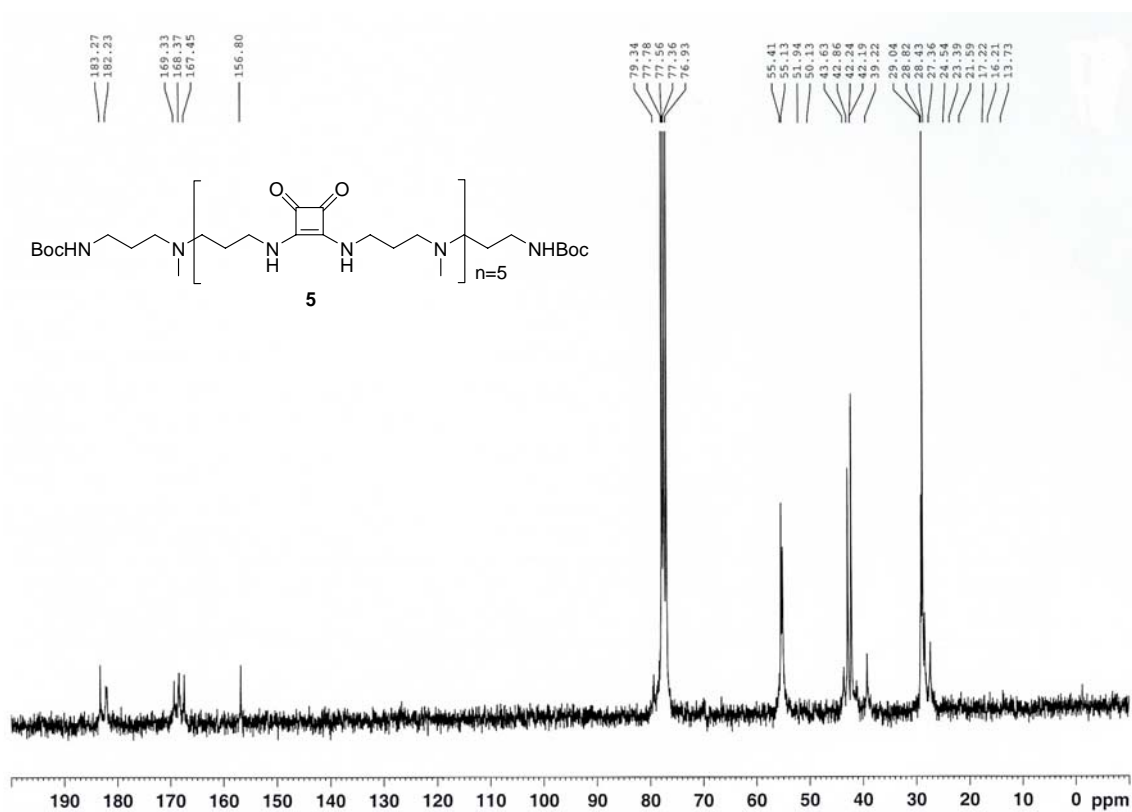
^{13}C RMN spectrum of tetramer **4** in CDCl_3



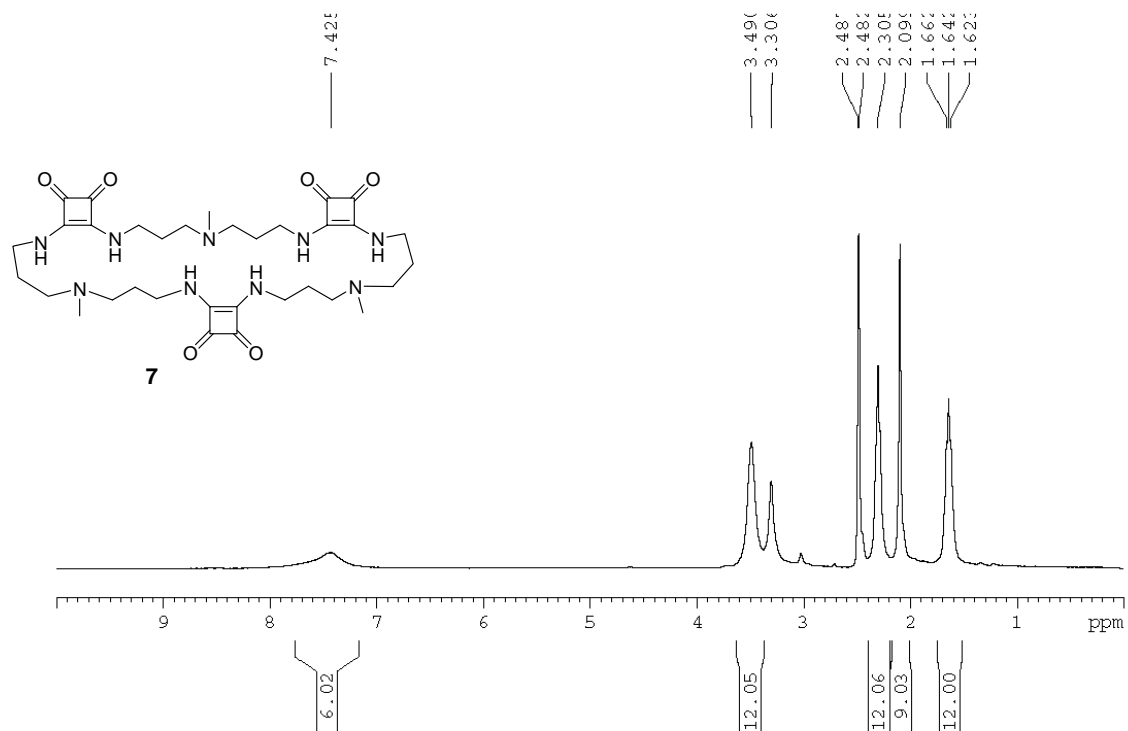
^1H RMN spectrum of pentamer **5** in CDCl_3



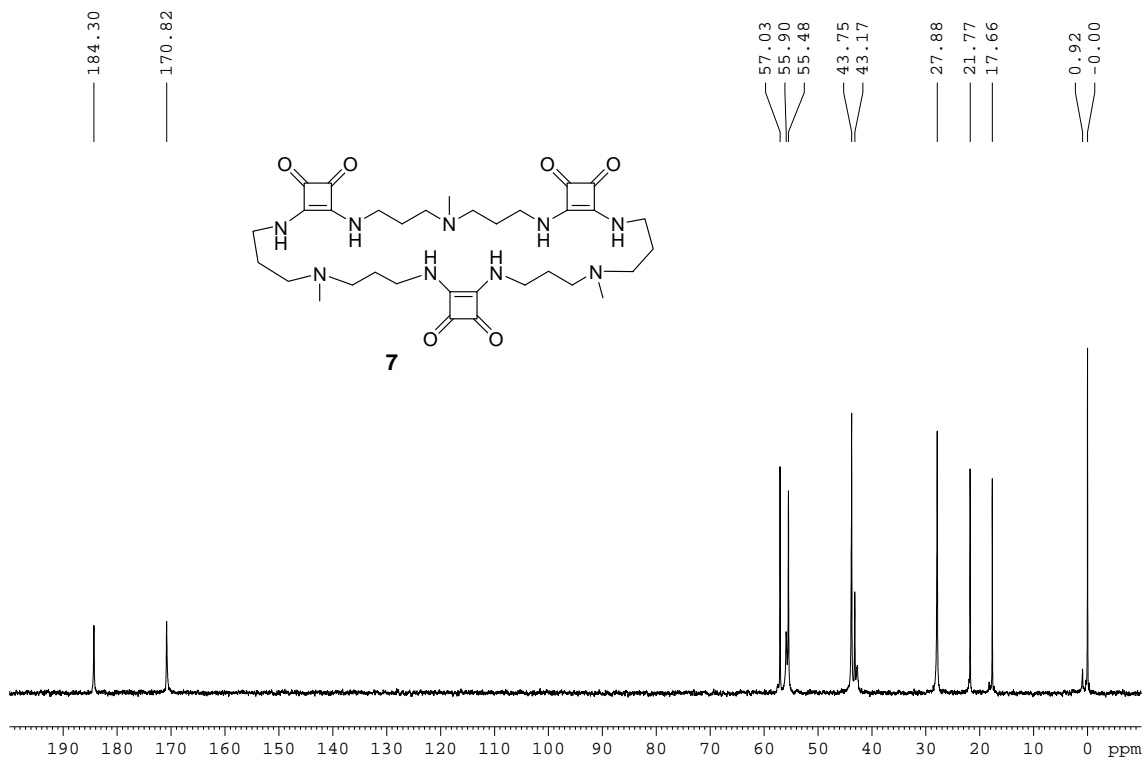
^{13}C RMN spectrum of pentamer **5** in CDCl_3



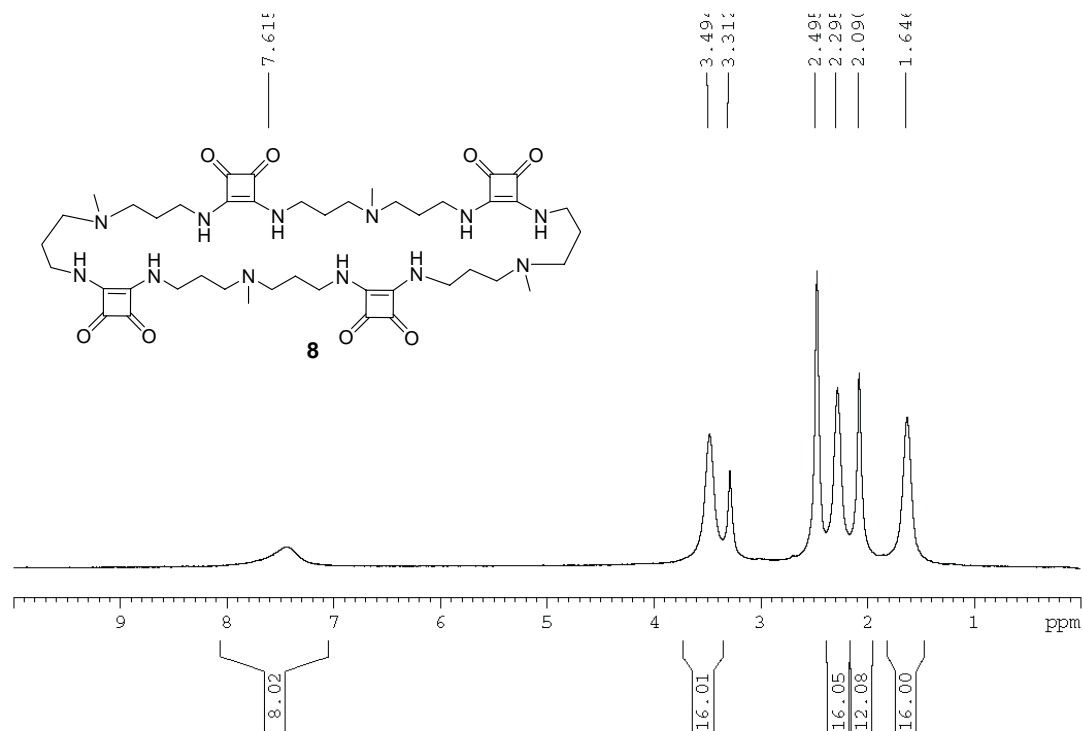
^1H NMR spectrum of macrocycle **7** in DMSO.



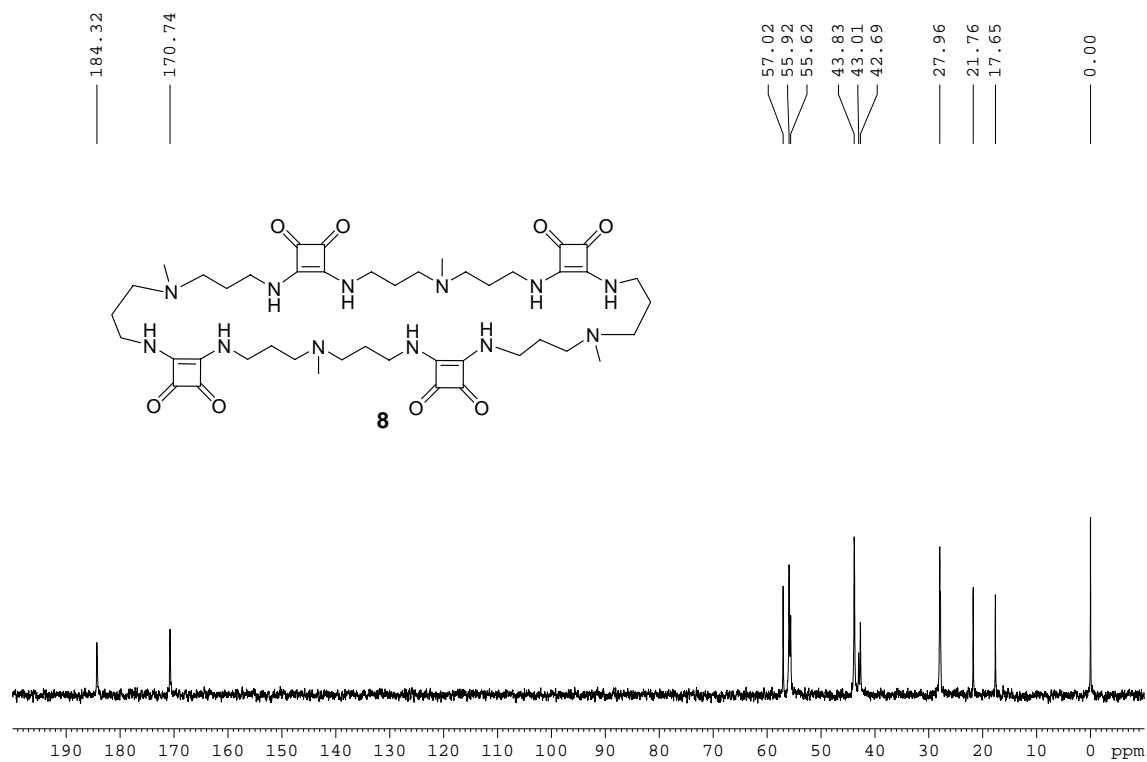
^{13}C NMR spectrum of macrocycle **7** D₂O/HCl.



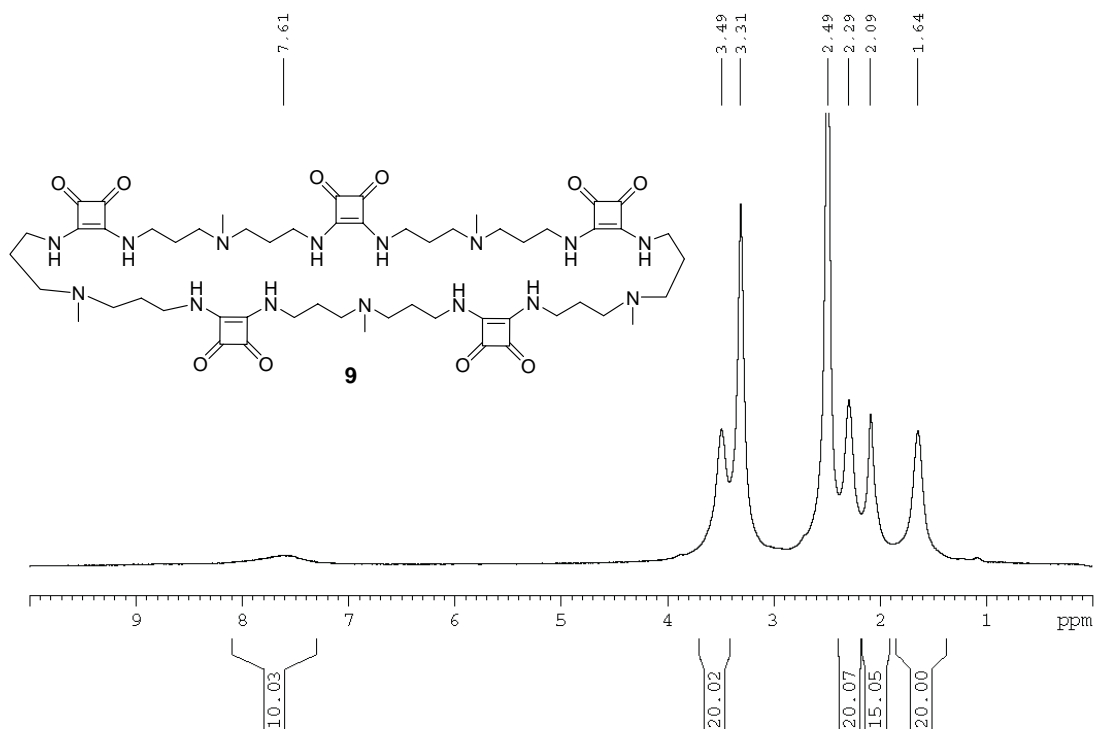
^1H NMR spectrum of macrocycle **8** in DMSO.



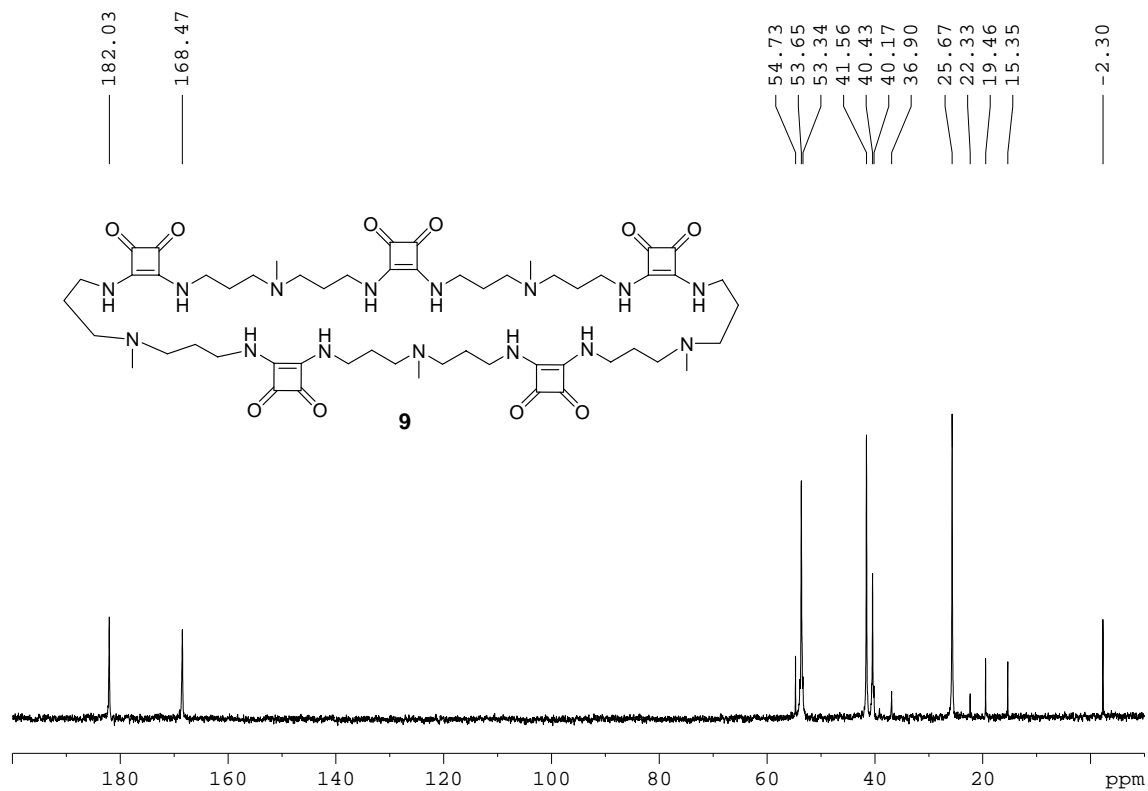
^{13}C NMR spectrum of macrocycle **8** $\text{D}_2\text{O}/\text{HCl}$.



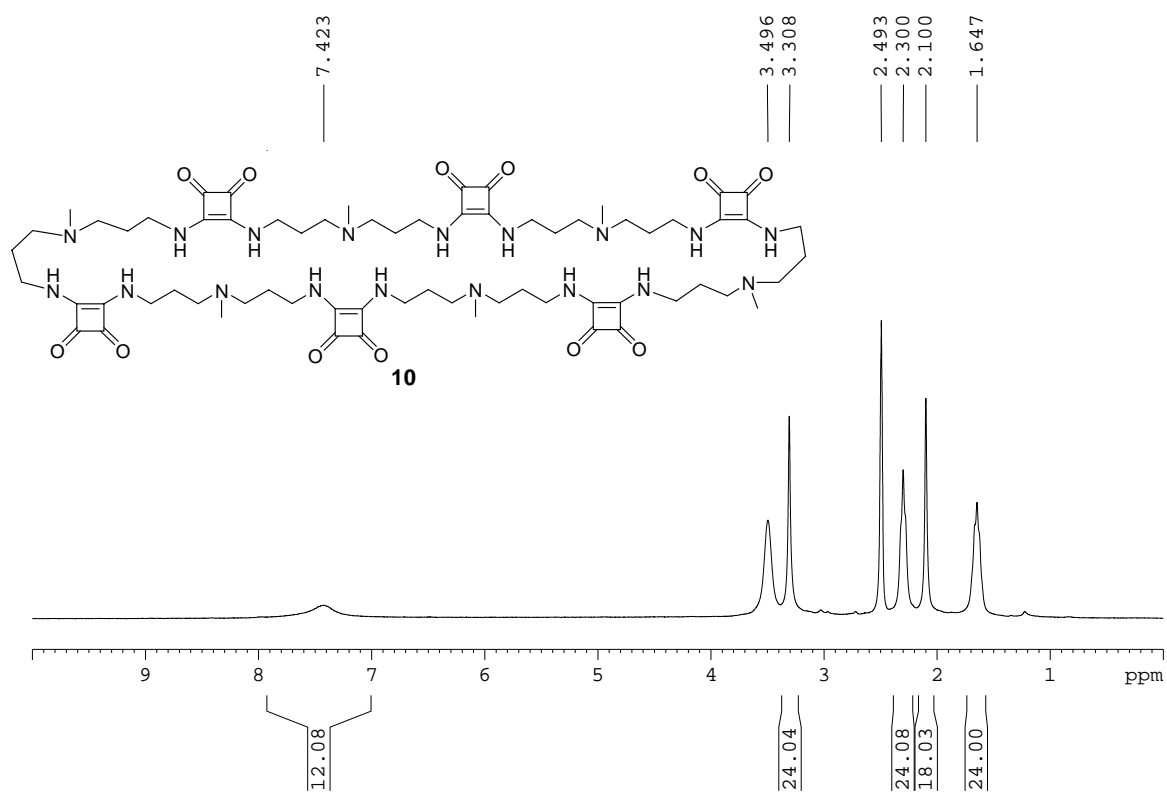
^1H NMR spectrum of macrocycle **9** in DMSO.



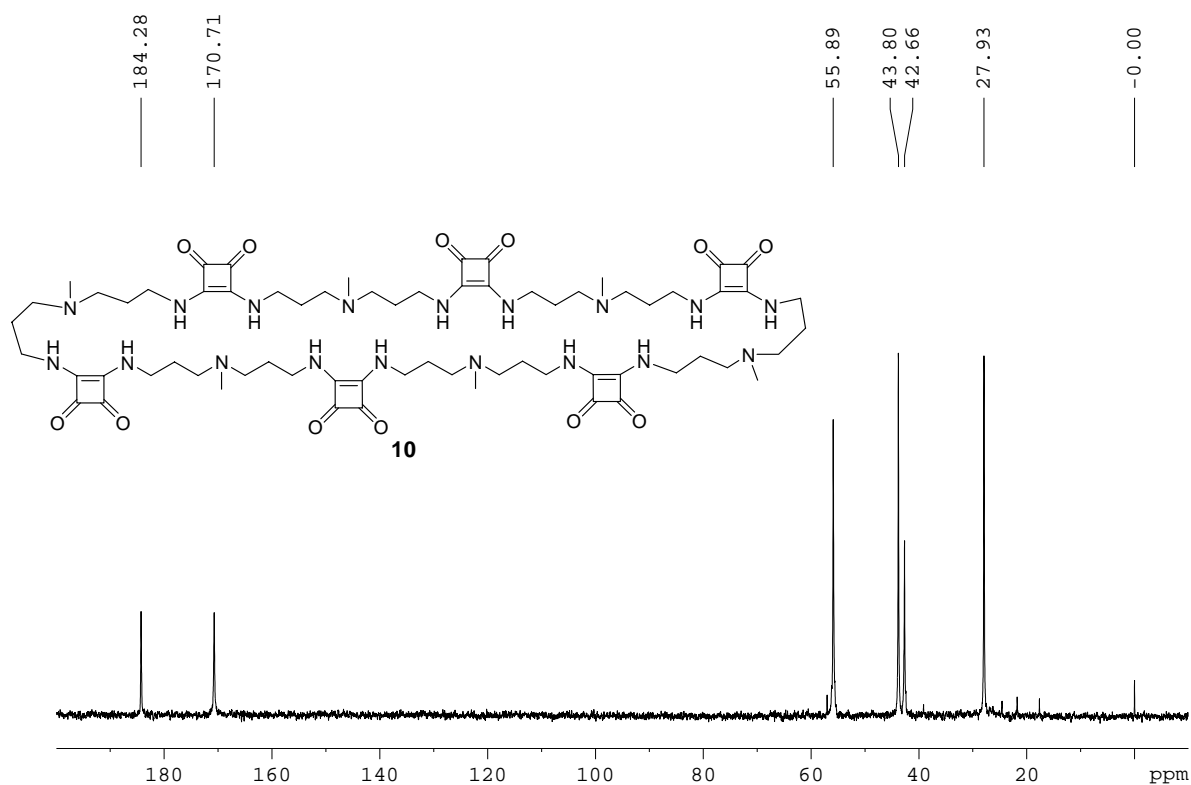
^{13}C NMR spectrum of macrocycle **9** $\text{D}_2\text{O}/\text{HCl}$.



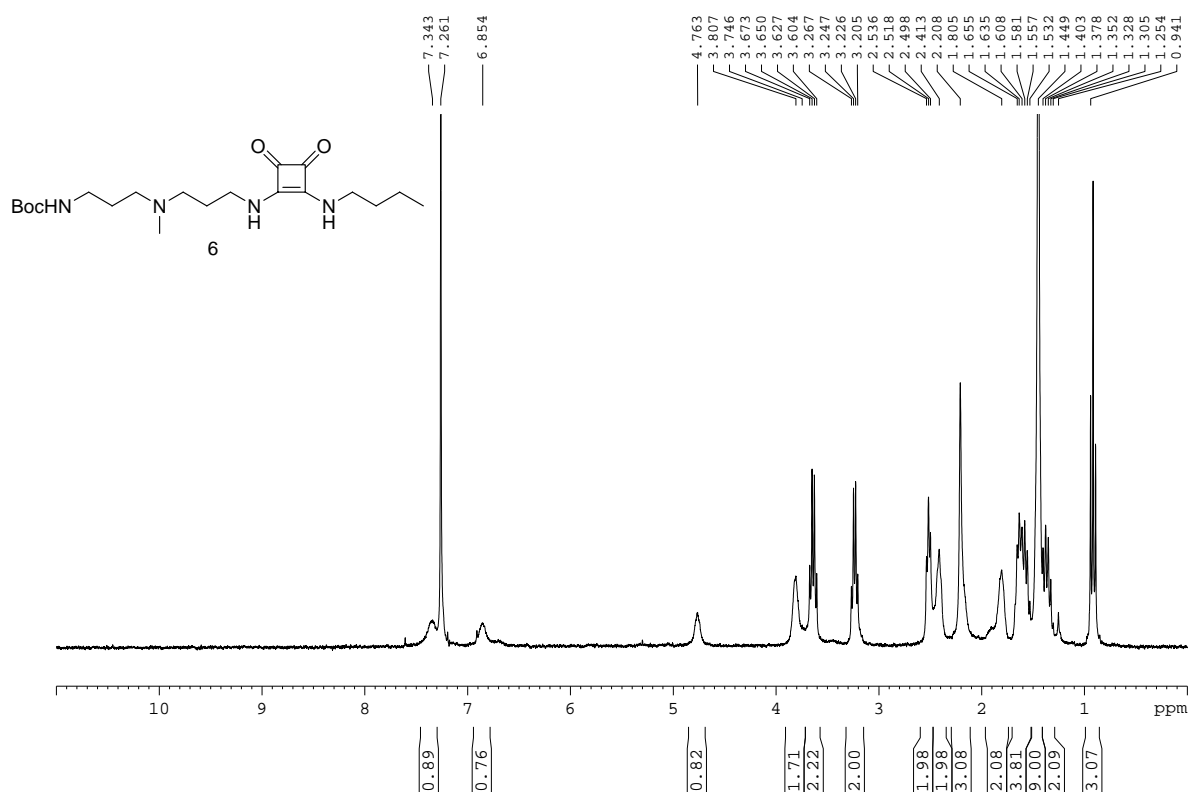
^1H NMR spectrum of macrocycle **10** in *DMSO*.



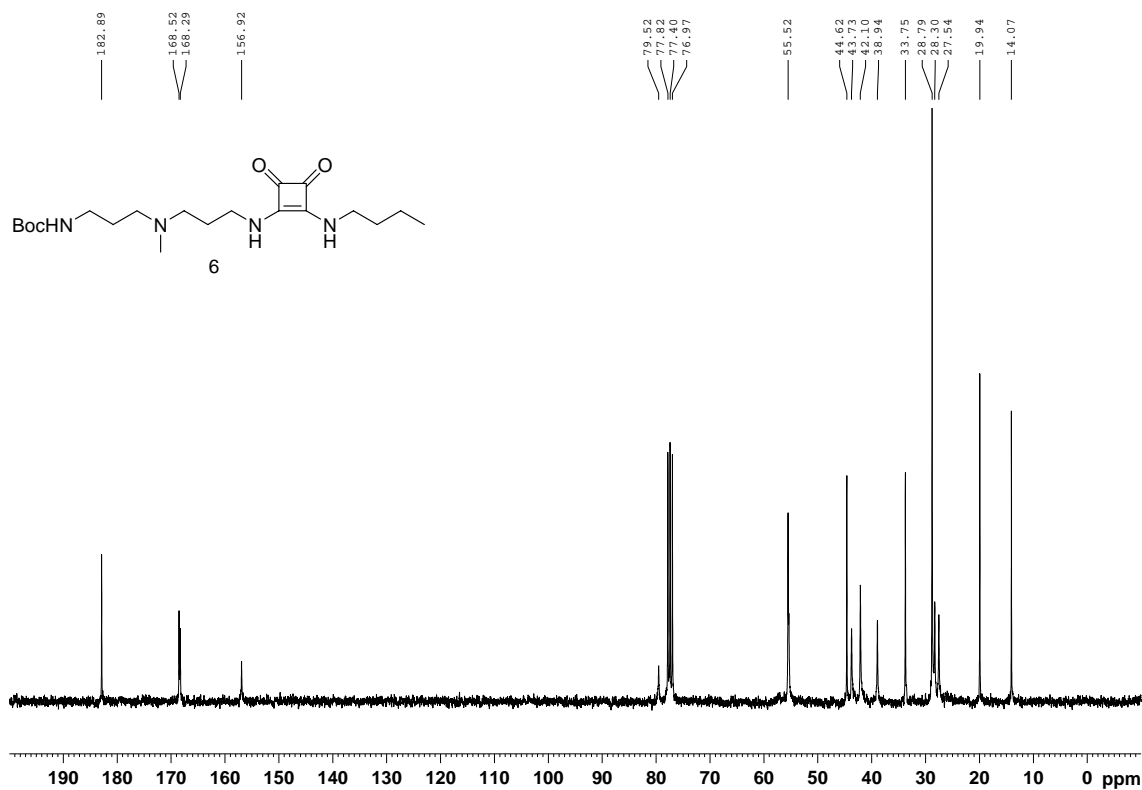
^{13}C NMR spectrum of macrocycle **10** in $\text{D}_2\text{O}/\text{HCl}$.



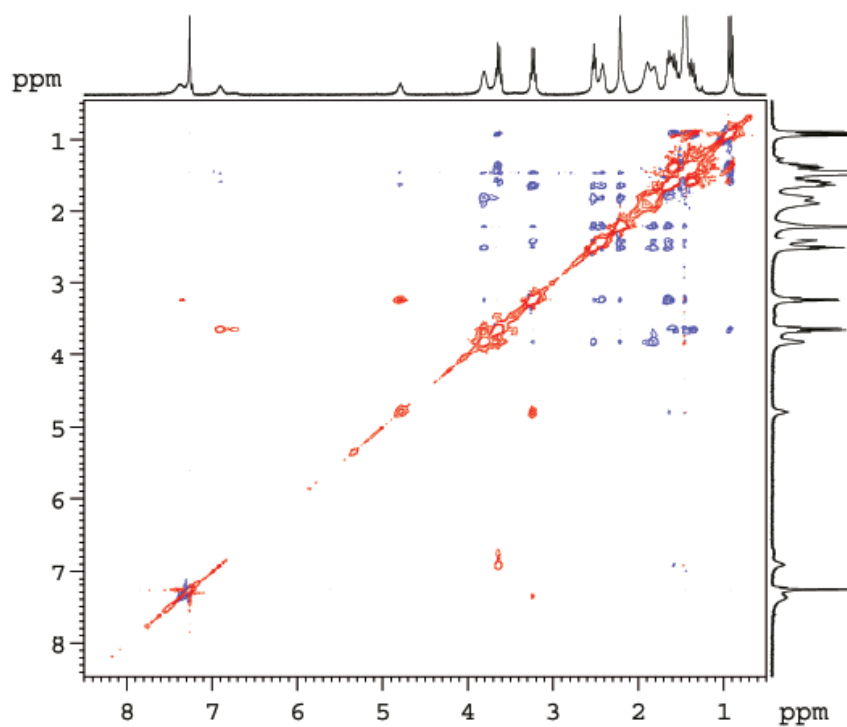
^1H NMR spectrum of **6** in CDCl_3 .



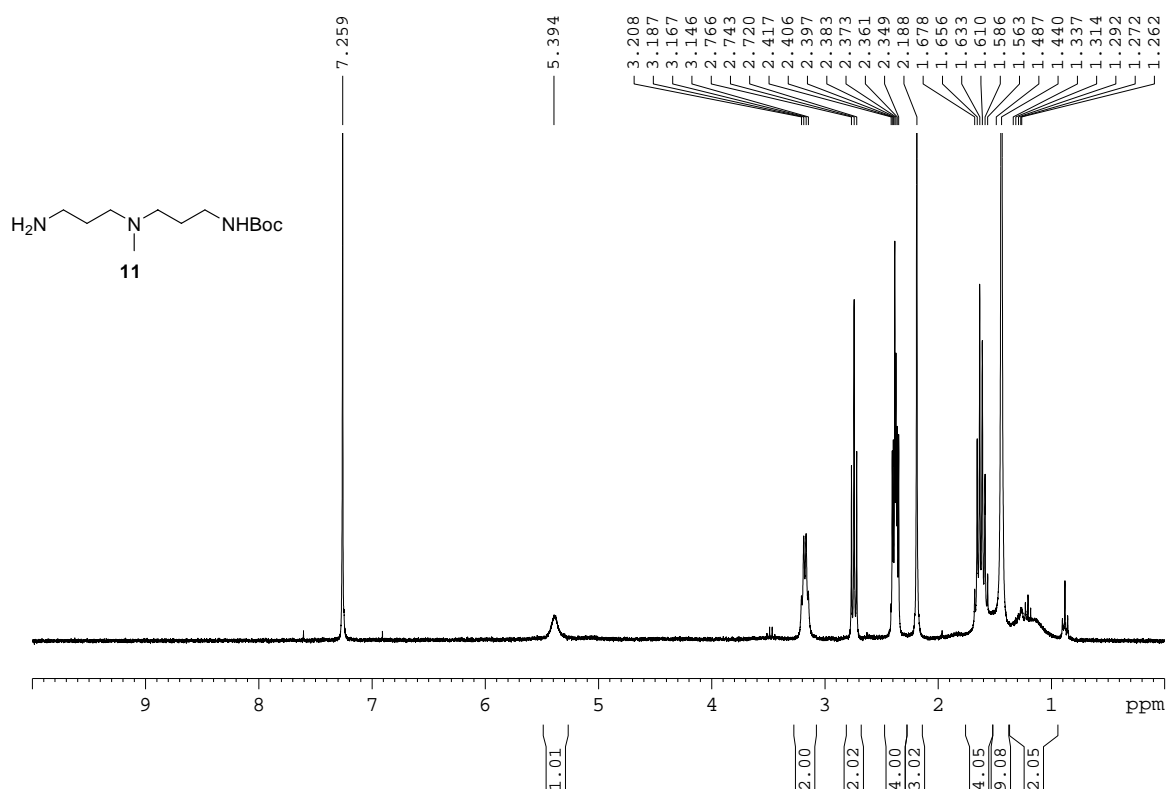
^{13}C NMR spectrum of **6** in CDCl_3 .



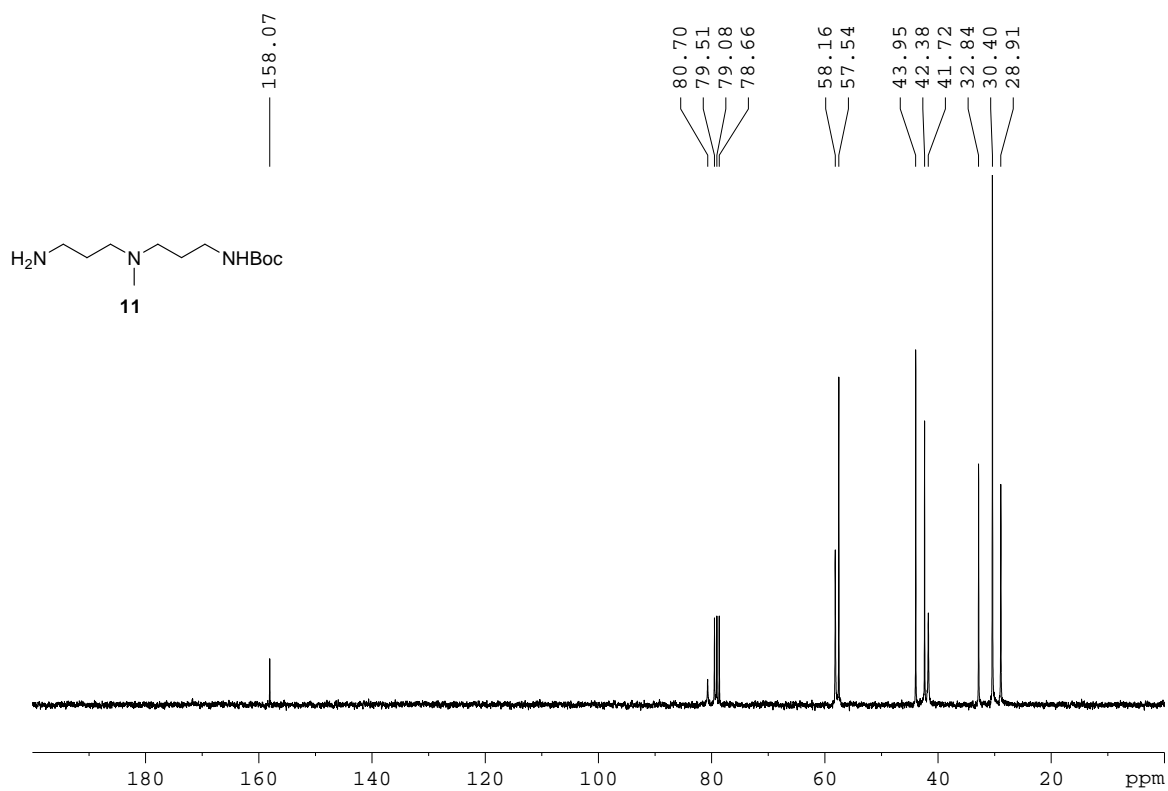
2D-NMR ROESY spectrum of **6** in CDCl₃, (300 MHz, 3mM, 298K, mixing time 500 ms).



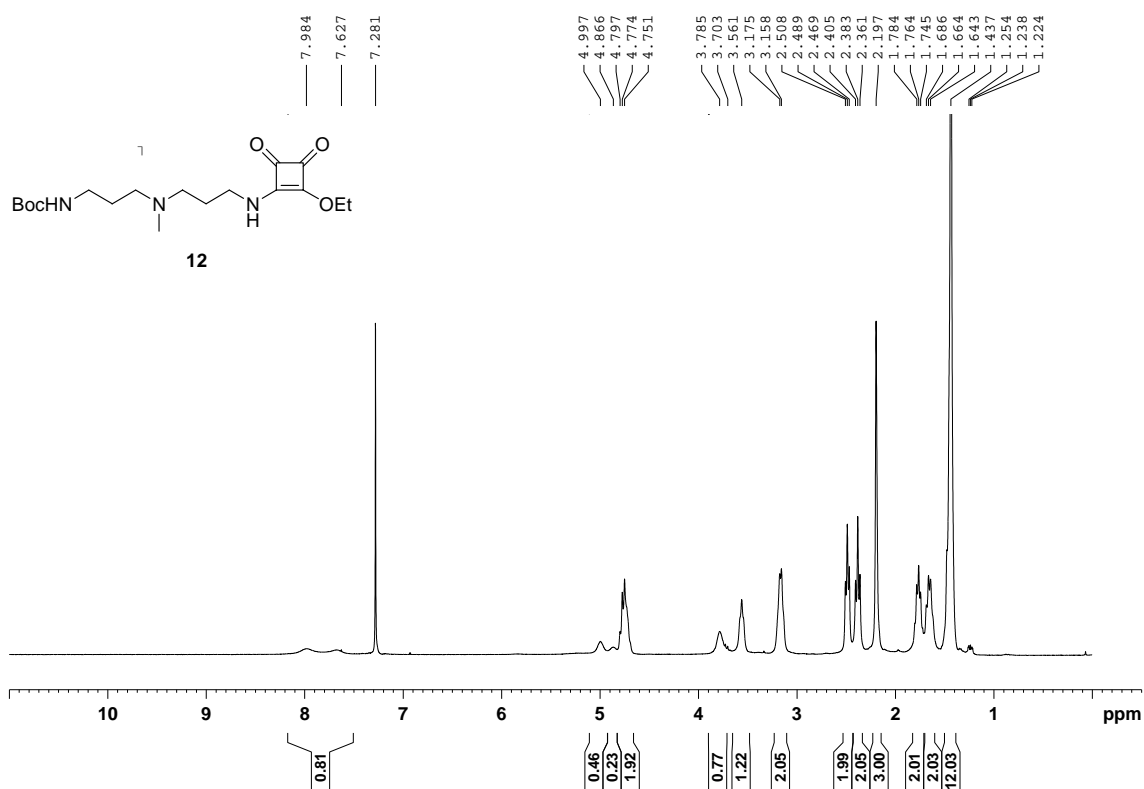
^1H NMR spectrum of **11** in CDCl_3 .



^{13}C NMR spectrum of **11** in CDCl_3 .



^1H NMR spectrum of **12** in CDCl_3 .



^{13}C NMR spectrum of **12** in CDCl_3 .

