Electronic Supplementary Information (ESI)

Self-assembly in water of amphiphilic aryl-squaramides driven by dipolar π–π interactions

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1. Experimental Methods

All solvents and reagents were purchased from Sigma-Aldrich, Merck, Scharlau, Acros Organics and Alfa-Aesar and used as received without further purification. Deionized water was obtained from water purification system ELIX10 and MilliQ (Millipore) with a maximum resistivity of 18.2 MΩ.

NMR spectroscopy: NMR spectra were recorded on an Advance (300 MHz) and Advance III (600 MHz) from Bruker at 295 K. The residual proton signal was used as the reference. Chemical shifts (δ) are given in ppm and coupling constants (J) in Hz.

UV- Vis spectroscopy: UV/Vis Absorption spectra were recorded using an Agilent Cary 60 spectrophotometer. The measurements were carried out in quartz glass cuvettes and a TrayCell, which comprises a fiber-optic measuring cell and different caps with integrated mirrors, thus covering a major range of concentrations, using deionized water prepared by water purification system ELIX10 and MilliQ (Millipore). Temperature control was accomplished by Agilent 1x0 Cell Holder Peltier system.

Microwave reactor: Microwave-assisted reactions were carried out in a Biotage Initiator reactor (microwave power supply 0-400 W, 1 W increments, IR temperature sensor, open or closed vessel mode, pressure range 0-20 bar).

Mass spectrometry: ESI-HRMS mass spectra were recorded on Thermo Scientific Orbitrap Q Exactive mass spectrometer equipped with electrospray modules.

AFM: Atomic force microscopy imaging was performed in tapping mode under ambient conditions on a MultiMode Veeco AFM microscope with a NanoScope IV controller. An HQ:NSC35/AlBS silicon tip with a cantilever length of 90 μm was employed with the resonance frequency region of 150−300 kHz and a scan rate of 1.0 Hz. Cross- section profiles were performed with WSxM software.

Rheology: The rheological measurements were performed by using a Dinamic Mechanic Analyzer DMA Q800 (TA Instruments) with 15 mm parallel plates at room temperature.

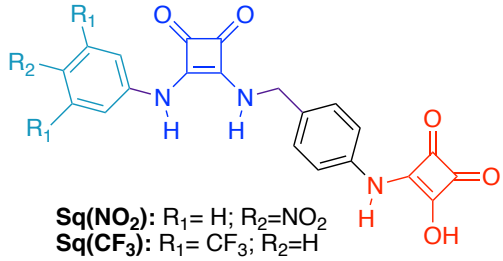
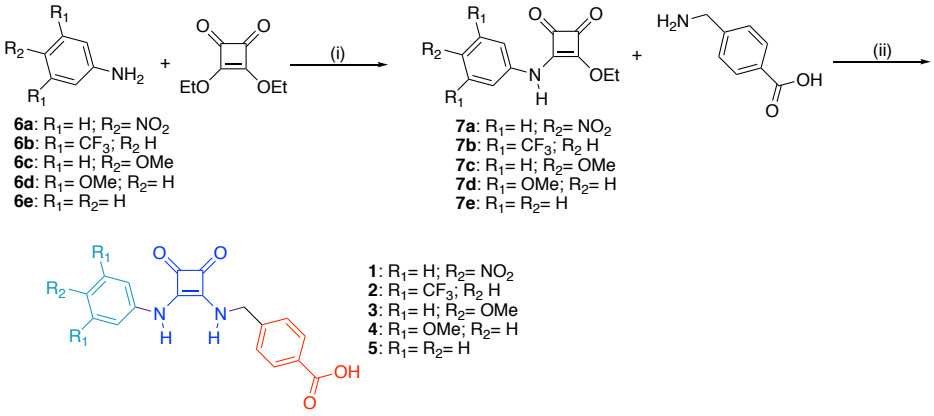


Fig. S1. Molecular structure of compounds **Sq(NO₂)** and **Sq(CF₃)**.

2. Synthetic procedures



Scheme S1. Synthetic scheme for compounds **1-5**. (i) $Zn(OTf)_2$, EtOH, RT, 4h; (ii) K_2CO_3, EtOH, MW, 135 °C, 35 min.

General procedure for the synthesis of aryl-squaramide monoesters (**7a-e**)

The corresponding aniline (**6a-e**) was dissolved in ethanol and added to a suspension of diethyl squarate (DSq) and zinc trifluoro-methanesulfonate [$Zn(OTf)_2$] in ethanol. The suspension was stirred for 4 hours at room temperature. The solvent was removed under vacuum and the residue was subsequently suspended in NH_4Cl 1M. After filtering, the solid was washed several times with NH_4Cl and water. The crude products were recrystallized in acetonitrile or ether. The final compounds were obtained in moderate to good yields comprised between 73 and 97%.

Squaramide esters **7a**, **7b** and **7e** were prepared according the general procedure and were previously reported by us in reference S1.

4-nitrophenyl squaramide ethyl ester (7a):

Prepared according to the general procedure.[S1] **6a** (1.51 g, 10.9 mmol) in 40 ml of ethanol, DSq (1.88 g, 10.6 mmol) and $Zn(OTf)_2$ (0.5 g, 1.4 mmol) in 40 ml ethanol. The crude product was purified by recrystallization in acetonitrile. **7a** was obtained as an orange solid (2.60 g, 93.4%).

δH(300 MHz, d6-DMSO) 11.24 (1H, s, NH), 8.25 (2H, d, J = 9.2, Ar-H), 7.6 (2H, d, J = 9.2, Ar-H), 4.81 (2H, q, J = 7.1, CH_2), 1.44 (3H, t, J = 7.1, CH_3); δC(75 MHz, d6-DMSO) 188.56, 18622, 181.44, 170.81, 145.79, 143.97, 126.74, 120.43, 71.67, 17.04; HRMS calcd. for $C_{12}H_{10}O_5N$ 261.0517, found 261.0515 $[M-H]^-$.

3,5-bis(trifluoromethyl)phenyl squaramide ethyl ester (7b):

Prepared according to the general procedure.[S1] **6b** (1.24 g, 5.4 mmol) in 40 ml of ethanol, DSq (0.97 g, 5.5 mmol) and $Zn(OTf)_2$ (0.25 g, 0.7 mmol) in 40 ml of ethanol. **7b** was obtained as a pale yellow solid (1.56 g, 81.6%).

δH(300 MHz, d6-DMSO) 11.21 (1H, s, NH), 8.04 (2H, s, Ar-H), 7.79 (1H, s, Ar-H), 4.80 (2H, q, J = 7.0, CH_2), 1.41 (3H, t, J = 7.0, CH_3); δC(75 MHz, d6-DMSO) 187.44, 184.50, 179.26, 169.14, 140.17, 131.14 (q, J = 32.9), 123.08 (q, J = 271.2), 119.36, 116.23(d, J = 3.7), 70.13, 15.34 ;HRMS calcd. for $C_{14}H_9F_6O_3N$ 352.0414, found 352.0408 $[M-H]^-$.

4-methoxyphenyl squaramide ethyl ester (7c):

Prepared according to the general procedure. **6c** (0.378 g, 3.1 mmol) in 15 ml of ethanol, DSq (0.505 g, 2.9 mmol) and $Zn(OTf)_2$ (0.258 g, 0.7 mmol) in 10 ml of ethanol. **7c** was obtained as a white solid (0.670 g, 95.1%).

δH(300 MHz, d6-DMSO) 10.63 (1H, s, NH), 7.26 (2H, s, Ar-H), 6.92 (2H, d, J = 8.8, Ar-H), 4.74 (2H, q, J = 7.0, CH_2), 3.73 (3H, s, OMe), 1.40 (3H, t, J = 7.0, CH_3); δC(75 MHz, d6-DMSO) 188.11, 183.23, 177.83, 169.35, 156.23, 130.99, 121.36, 114.23, 69.37, 55.32, 15.67; HRMS calcd. for $C_{13}H_{13}O_4N$ 246.0772, found 246.0765 $[M-H]^-$.

3,5-dimethoxyphenyl squaramide ethyl ester (7d):

Prepared according to the general procedure. **6d** (0.844 g, 5.5 mmol) in 30 ml of ethanol, DSq (1 g, 5.6 mmol) and $Zn(OTf)_2$ (0.246 g, 0.7 mmol) in 30 ml of ethanol. **7d** was obtained as a white solid (1.267 g, 82.9%).

δH(300 MHz, d6-DMSO) 10.67 (1H, s, NH), 6.65 (2H, s, Ar-H), 6.23 (1H, s, Ar-H), 4,77 (2H, q, J = 7.1, CH_2), 3.72 (6H, s, OMe), 1.41 (3H, t, J = 7.1, CH_3); δC(75 MHz, d6-DMSO) 187.67, 183.79, 178.31, 169.34, 139.79, 97.66, 95.97, 55.21, 15.64; HRMS calcd. for $C_{14}H_{15}O_5N$ 300.0842, found 300.0843 $[M-H]^-$.

Phenyl squaramide ethyl ester (7e):

Prepared according to the general procedure.[S1] **6e** (0.55 g, 5.9 mmol) in 30 ml of ethanol, DSq (1 g, 5.6 mmol) and $Zn(OTf)_2$ (0.250 g, 0.7 mmol) in 30 ml of ethanol. Recrystallization in diethyl ether. **7e** was obtained as a white solid, (1.197 g, 97.6%).

δH(300 MHz, d6-DMSO) 10.75 (1H, s, NH), 7.36 (4H, s, Ar-H), 7.11 (1H, s, Ar- H), 4.76 (2H, dq, *J* = 7.1, 2.3, CH_2), 1.41 (3H, dt, *J* = 7.1, 2.3, CH_3); δC(75 MHz, d6-DMSO) 187.84, 183.74, 178.25, 169.56, 137.96, 129.07, 124.04, 119.60, 69.55, 15.65 ;HRMS calcd. for $C_{12}H_{11}O_3N$ 240.0631, found 240.0609 $[M-H]^-$.

General procedure for the synthesis of aryl-squaramide-benzoic acids (**1-5**)

A mixture of 4-(aminomethyl)benzoic acid, an aryl-squaramide mono-ester (**7a-e**), K_2CO_3 and ethanol, was introduced and hermetically sealed into a microwave vial (5, 10 or 20 ml) with a magnetic stirrer. The mixture was stirred in a microwave reactor at 135 °C for 35 minutes (MW =1-400 W). Then the solvent was removed under vacuum and the solid residue was suspended in 1M HCl, stirred for 30 minutes and then filtered and washed with 1M HCl. The resulting solid was suspended in water and the pH was adjusted to 10-11 with 1M NaOH and it was stirred for additional 10 minutes. Subsequently 30 ml of 1M HCl were added and a precipitate is formed. The resulting solid was filtered and washed several times with 1M HCl. This treatment with NaOH and HCl was repeated between 3-5 times until the desired product is pure.

4-nitrophenyl squaramide-4-aminomehyl benzoic acid (1):

Prepared according to the general procedure. **7a** (1 g, 3.8 mmol), 4-(aminomethyl)benzoic acid (1 g, 6.6 mmol) and $NaCO_3$ (1.236 g, 11.7 mmol) in 150 ml of ethanol. **1** was obtained as a reddish brown solid (1.32 g, 94.2%).

δH(300 MHz, d6-DMSO) 12.98 (1H, s, COOH), 10.35 (1H, s, NH), 8.31 (1H, s, NH), 8.22 (2H, d, *J* = 8.9, Ar-H), 7.96 (2H, d, *J* = 8.1, Ar-H), 7.61 (2H, d, *J* = 8.9, Ar-H), 7.50 (2H, d, *J* = 8.1, Ar-H), 4.91 (2H, d, *J* = 5.9, CH_2); δC(75 MHz, d6-DMSO) 184.99, 179.99, 170.21, 167.14, 163.00, 145.75, 143.26, 141.38, 130.01, 129.80, 127.52, 125.69, 117.51, 47.03; HRMS calcd. for $C_{18}H_{12}N_3O_6$ 366.0721, found 366.0725 $[M-H]^-$.

3,5-bis[trifluoromethyl]phenyl squaramide-4-aminomethyl benzoic acid (2):

Prepared according to the general procedure. **7b** (305 mg, 0.9 mmol), 4-(aminomethyl)benzoic acid (165 mg, 1.1 mmol) and $NaCO_3$ (499 mg, 4.71 mmol) in 20 ml of ethanol. **2** was obtained as a yellow solid, (380 mg, 96.0%).

δH(300 MHz, d6-DMSO) 12.99 (1H, s, COOH), 10.42 (1H, s, NH), 8.29 (1H, s, NH), 8.04 (2H, s, Ar-H), 7.96 (2H, d, *J* = 7.9, Ar-H), 7.67 (1H, s, Ar-H), 7.50 (2H, d, *J* = 7.9, Ar-H), 4.91 (2H, d, *J* = 5.3, CH_2); δC(75 MHz, d6-DMSO) 184.77, 180.69, 169.55, 167.04, 162.86, 143.27, 141.06, 131.29 (q, *J* = 32.9), 130.01, 129.72, 127.57, 123.15 (q, *J* = 271.2), 118.10, 114.79, 46.94; HRMS calcd. for $C_{20}H_{12}F_6O_4N_2$ 457.0628, found 457.0620 $[M-H]^-$.

4-methoxhyphenyl squaramide-4-aminomehyl benzoic acid (3):

Prepared according to the general procedure. **7c** (196 mg, 0.79 mmol), 4-(aminomethyl)benzoic acid (148 mg, 0.98 mmol) and $NaCO_3$ (322 mg, 3.04 mmol) in 20 ml of ethanol. **3** was obtained as a white solid (209 mg, 74.8%).

δH(300 MHz, d6-DMSO) 12.92 (1H, s, COOH), 9.81 (1H, s, NH), 8.19 (1H, s, NH), 7.95 (2H, d, *J* = 8.1, Ar-H), 7.48 (2H, d, *J* = 8.1, Ar-H), 7.36 (2H, d, *J* = 9.0, Ar-H), 6.92 (2H, d, *J* = 9.0, Ar-H), 4.87 (2H, d, *J* = 6.0, CH_2), 3.73 (3H, s, OMe); δC(75 MHz, d6-DMSO) 183.33, 180.64, 168.54, 167.13, 165.12, 164.02, 155.26, 143.60, 132.19, 129.72, 127.51, 119.72, 114.51, 55.25, 46.77; HRMS calcd. for $C_{19}H_{16}O_5N_2$ 353.1132, found 353.1131 $[M-H]^-$.

3,5-dimethoxyphenyl squaramide-4-aminomehyl benzoic acid (4):

Prepared according to the general procedure. **7d** (299 mg, 1.08 mmol), 4-(aminomethyl)benzoic acid (198 mg, 1.31 mmol) and $NaCO_3$ (417 mg, 3.93 mmol) in 20 ml of ethanol. **4** was obtained as a white solid (334 mg, 81.0%).

δH(300 MHz, d6-DMSO) 10.46 (1H, s, NH), 8.80 (2H, s, Ar-H), 7.95 (2H, d, *J* = 7.4, Ar-H), 7.48 (2H, d, *J* = 7.4, Ar-H), 6.76 (2H, s, Ar-H), 6.16 (1H, s, Ar-H), 4.88 (2H, d, *J* = 5.6, CH_2), 3.71 (6H, s, OMe); δC(75 MHz, d6-DMSO) 183.85, 180.31, 169.09, 167.09, 164.05, 161.11, 143.55, 140.91, 129.92, 129.75, 127.50, 96.38, 94.73, 55.19, 46.84; HRMS calcd. for $C_{20}H_{18}O_6N_2$ 381.1081, found 381.1088 $[M-H]^-$.

Phenyl squaramide-4-aminomehyl benzoic acid (5):

Prepared according to the general procedure. **7e** (28.5 mg, 0.13 mmol), 4-(aminomethyl)benzoic acid (23.78 mg, 0.16 mmol) and $NaCO_3$ (36.7 mg, 0.35 mmol) in 3 ml of ethanol. **5** was obtained as a white solid (14.04 mg, 33.2%).

δH(300 MHz, d6-DMSO) 12.96 (1H, s, COOH), 9.98 (1H, s, NH), 8.33 (1H, s, NH), 7.95 (2H, d, *J* = 7.5, Ar-H), 7.48 (2H, d, *J* = 7.5, Ar-H), 7.46 (2H, d, *J* = 3.1, Ar-H), 7.33 (2H, t, *J* = 7.4, Ar-H), 7.02 (1H, t, *J* = 7.4, Ar-H), 4.89 (2H, d, *J* = 6.3, CH_2); δC(75 MHz, d6-DMSO) 184.03, 180.48, 169.0,0, 167.55, 164.05, 143.03, 139.12, 131.13, 129.68, 129.27, 127.46, 122.59, 118.15, 46.83 HRMS calcd. for $C_{18}H_{14}O_4N_2$ 323.1026, found 323.1027 $[M-H]^-$.

3. ^{1}H and ^{13}C NMR spectra

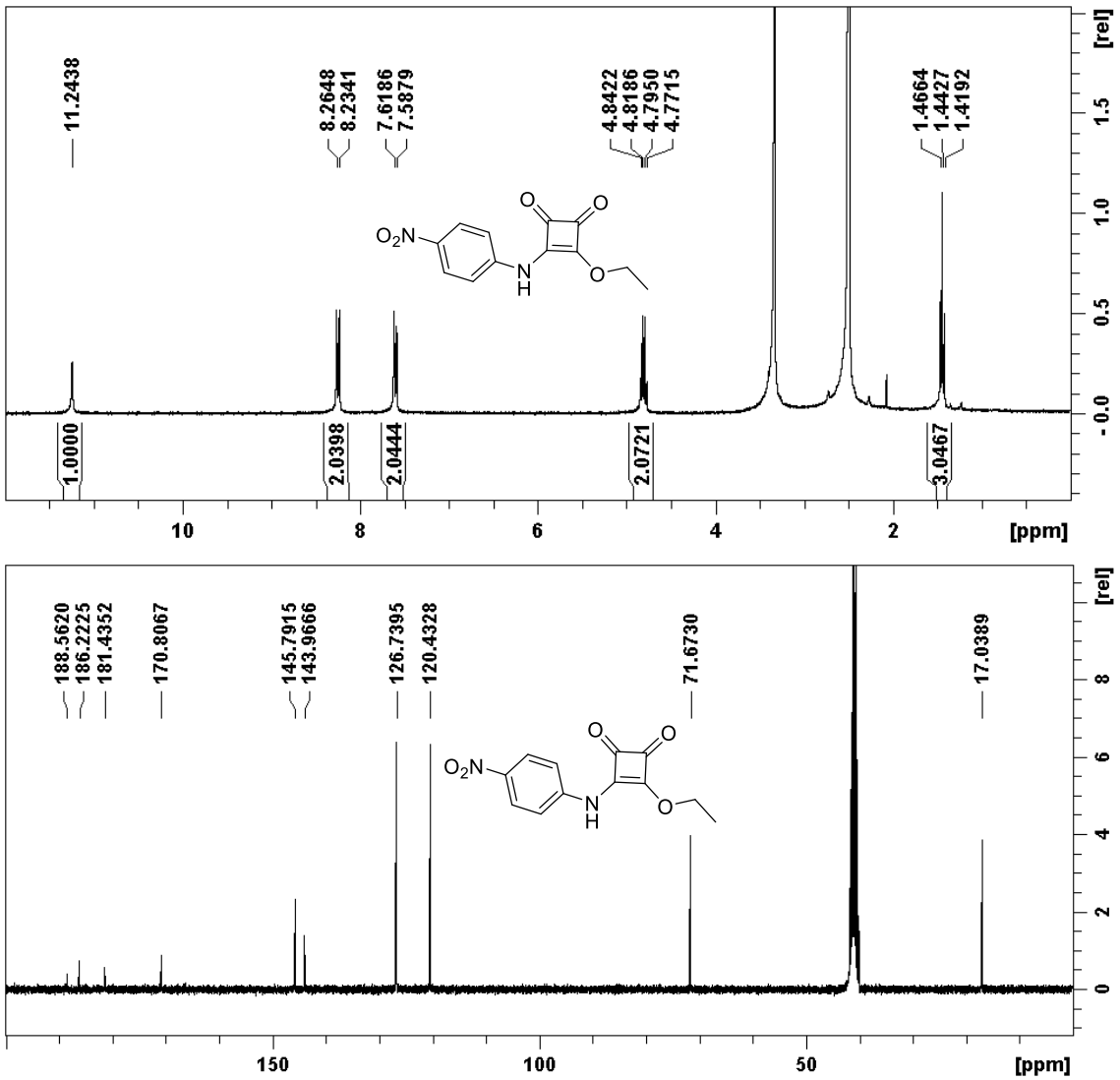


Fig. S2: ^{1}H NMR (top) and ^{13}C spectra (bottom) of **7a** in DMSO-*d6*.

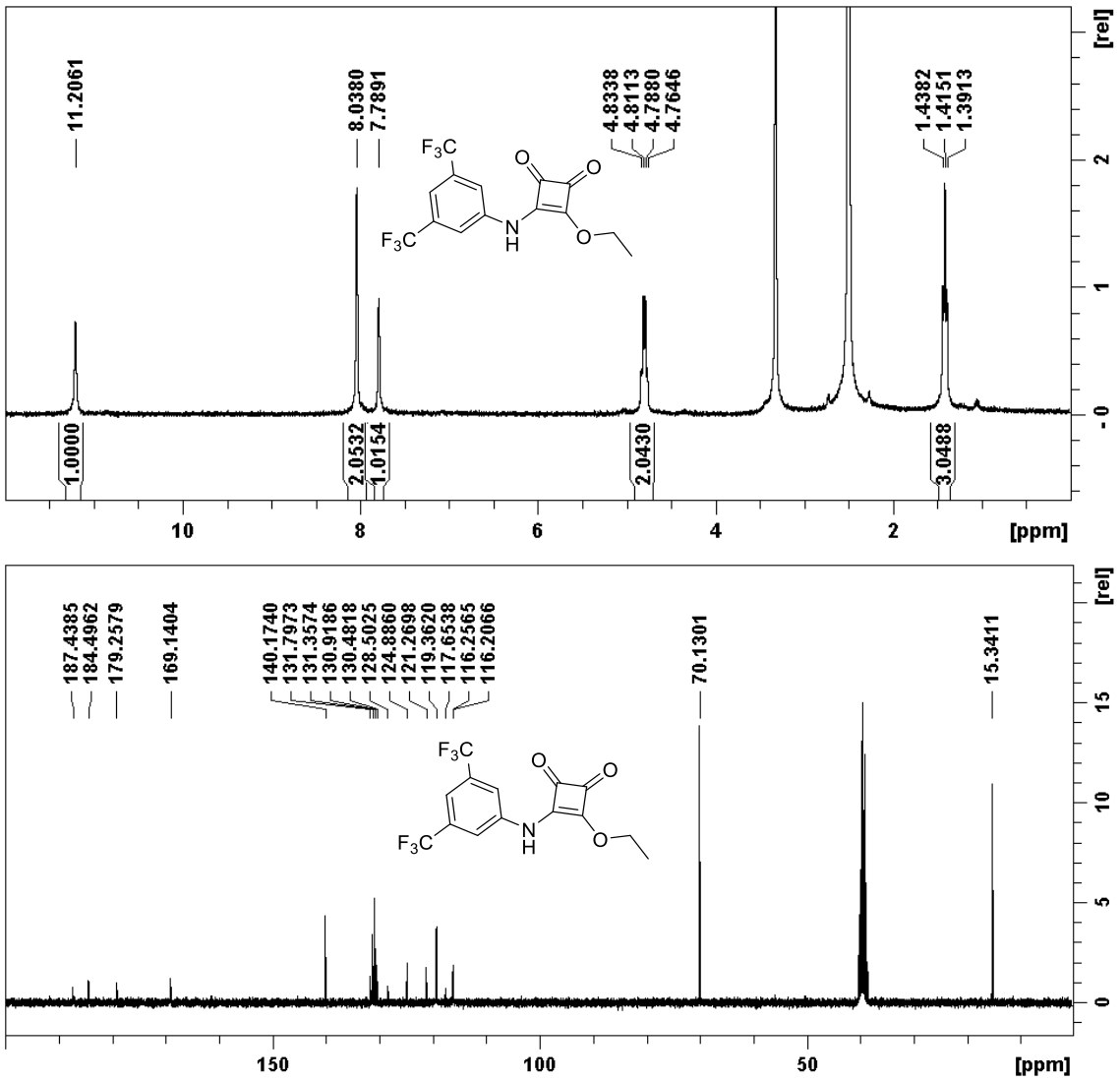


Fig. S3: ^{1}H NMR (top) and ^{13}C spectra (bottom) of **7b** in DMSO-*d6*.

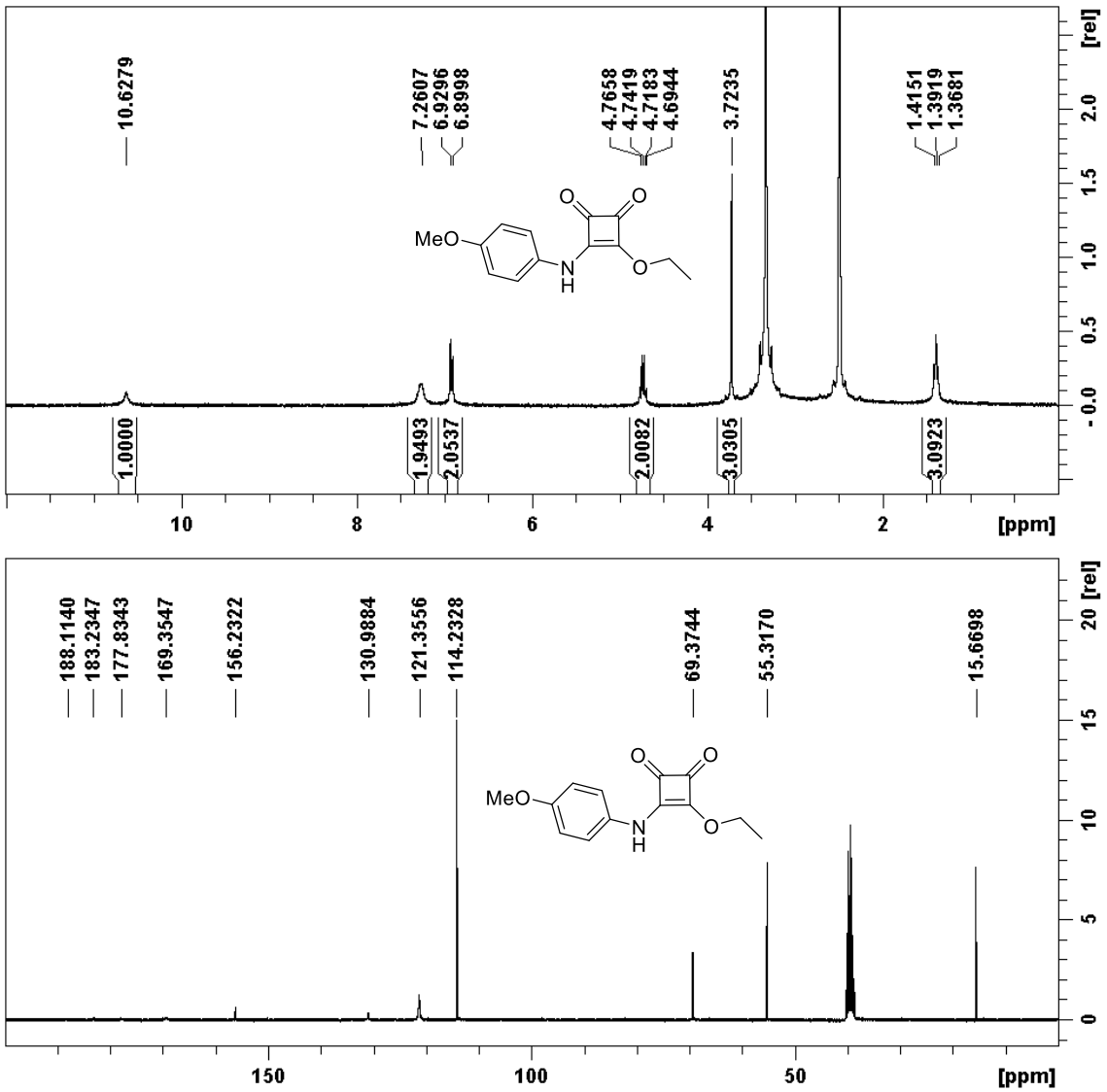


Fig. S4: ^{1}H NMR (top) and ^{13}C spectra (bottom) of **7c** in DMSO-*d6*.

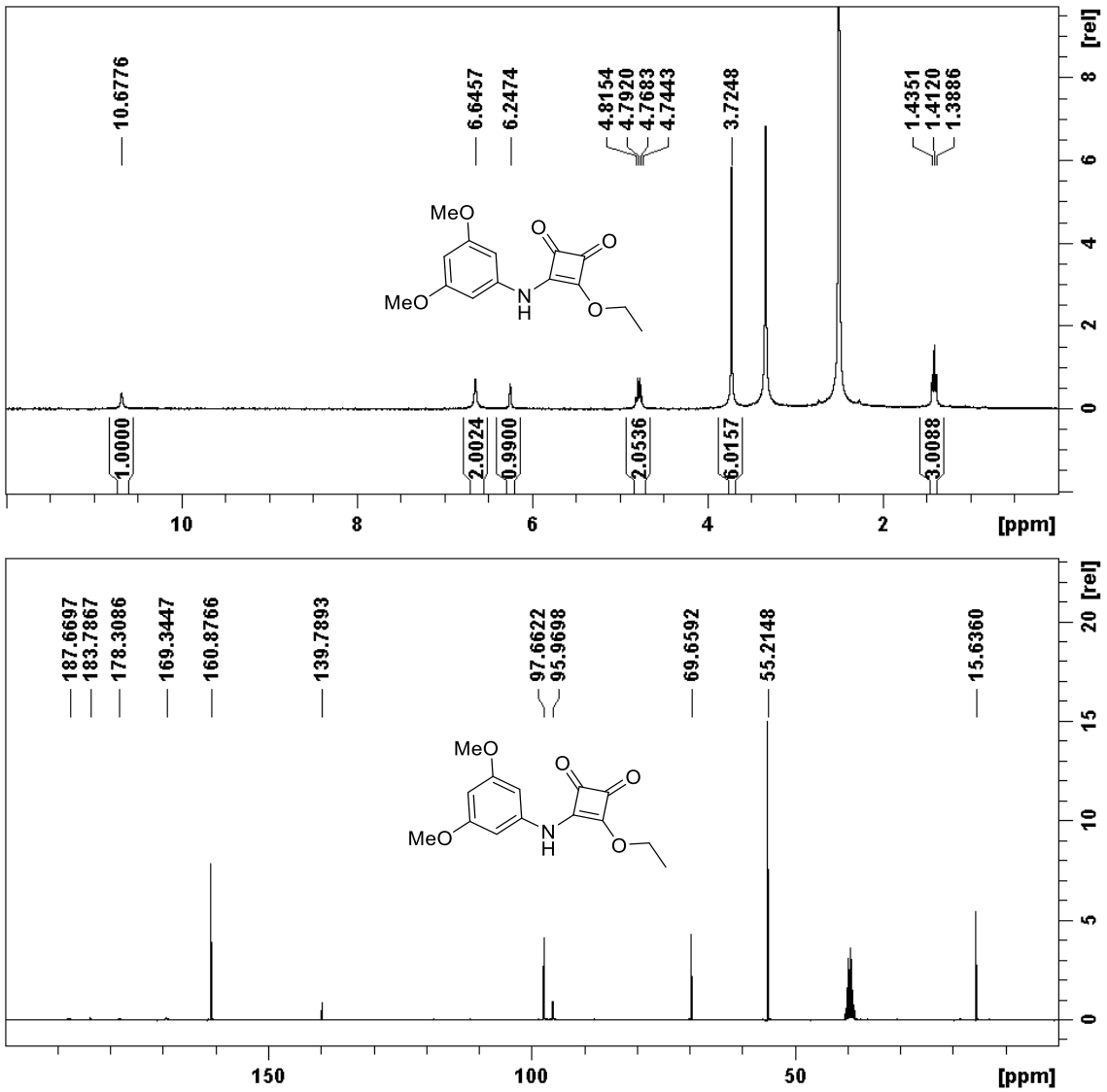


Fig. S5: ^{1}H NMR (top) and ^{13}C spectra (bottom) of **7d** in DMSO-*d6*.

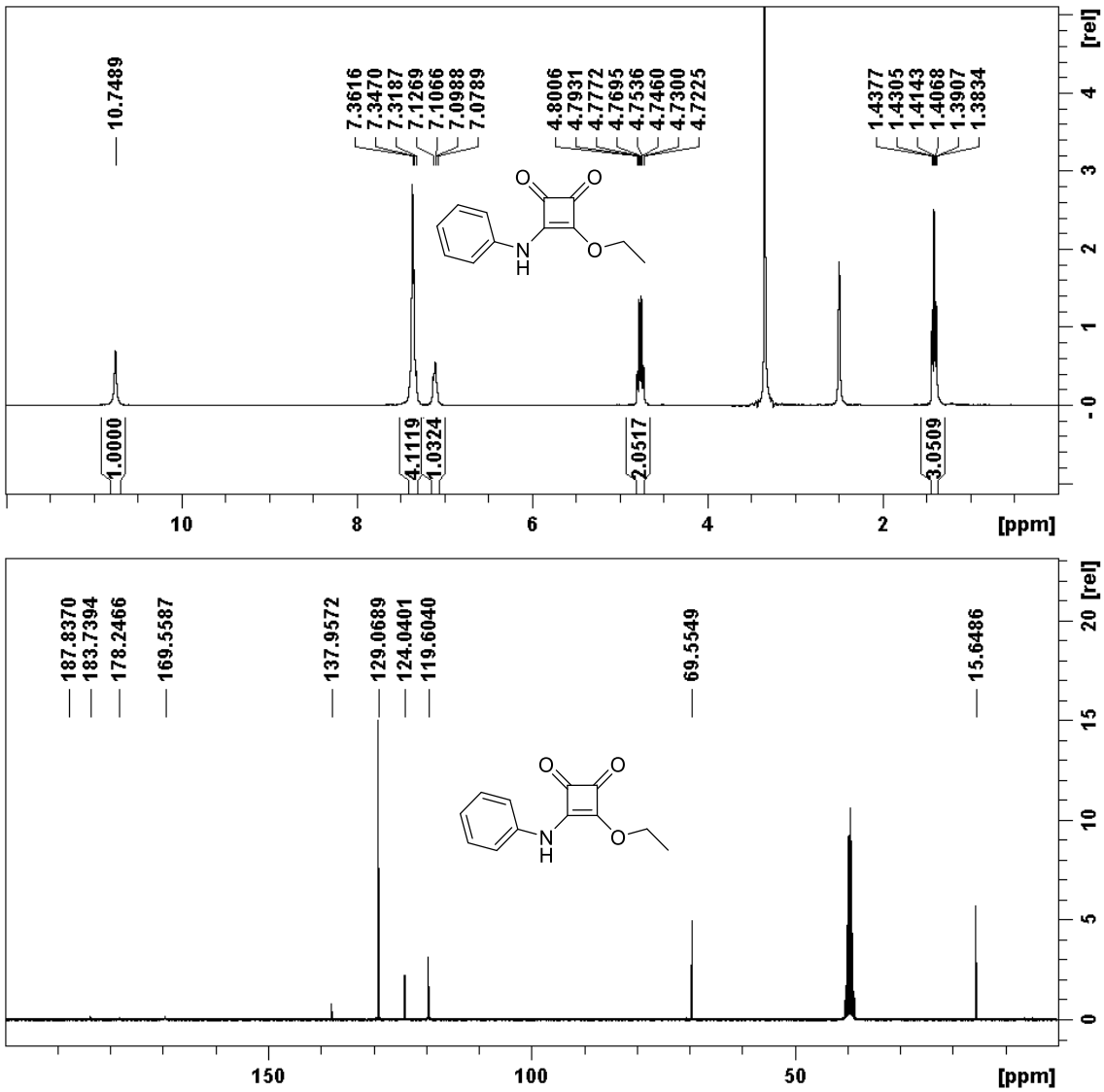


Fig. S6: ^{1}H NMR (top) and ^{13}C spectra (bottom) of **7e** in DMSO-*d6*.

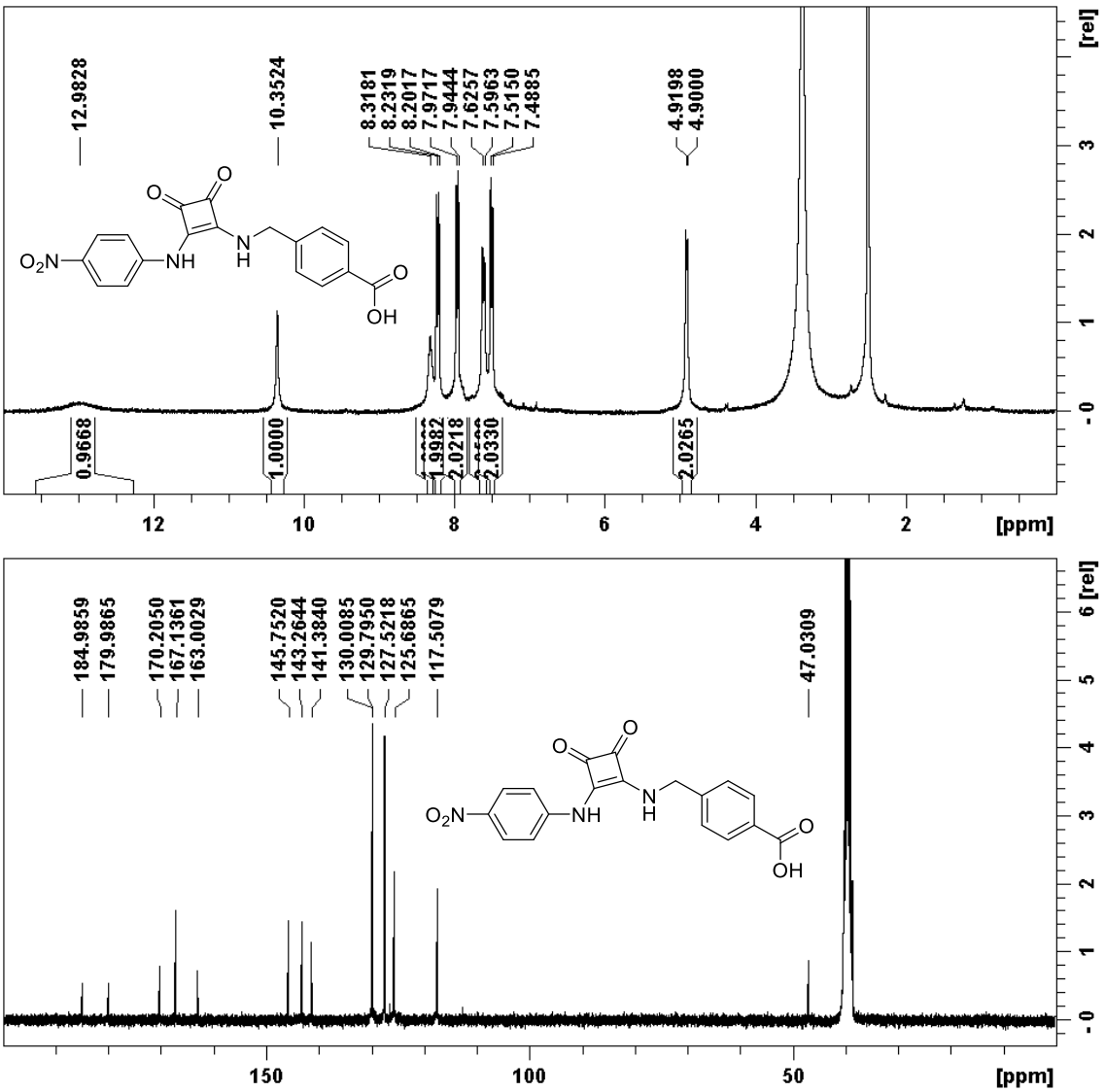


Fig. S7: ^{1}H NMR (top) and ^{13}C spectra (bottom) of **1** in DMSO-*d6*.

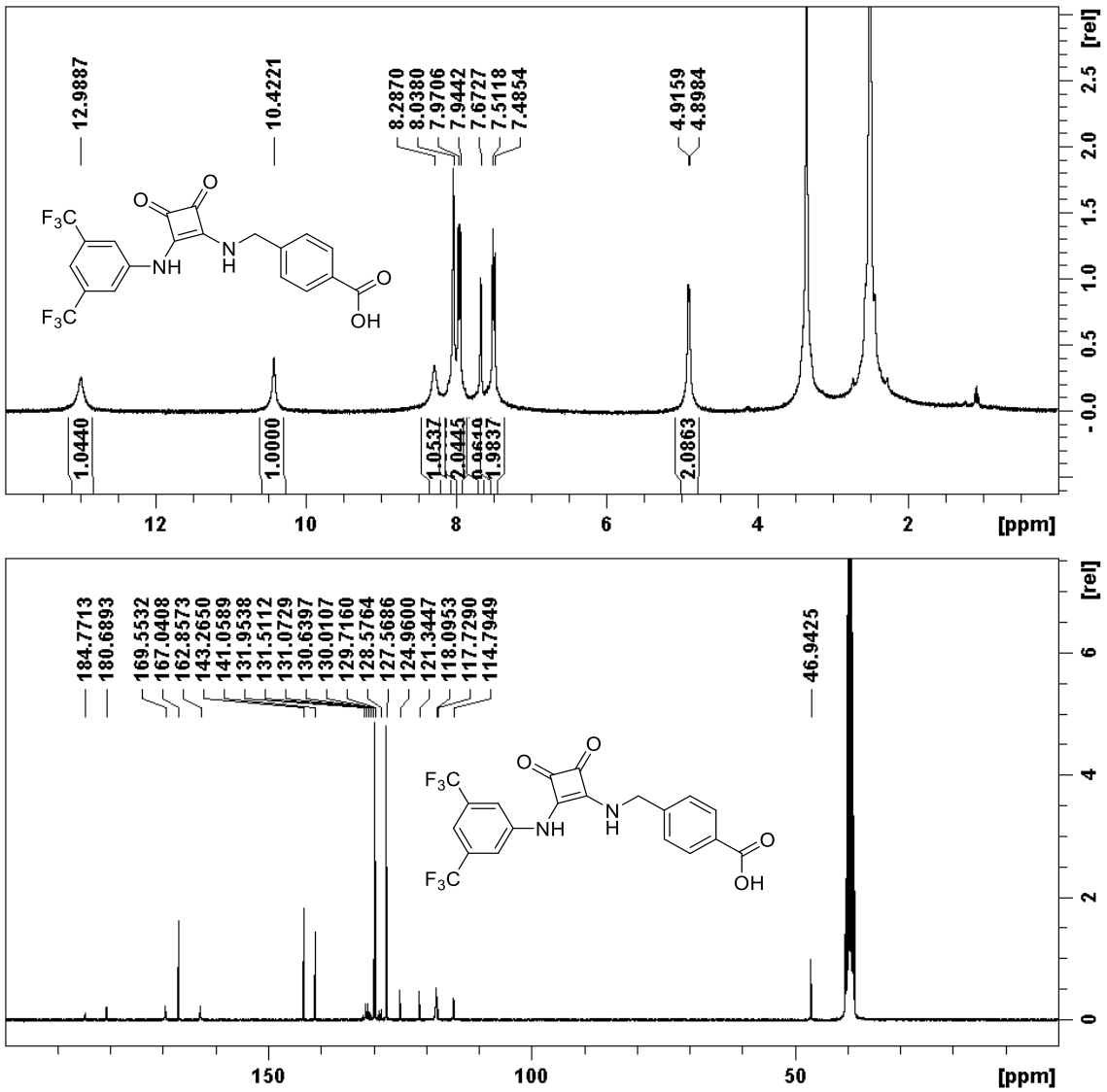


Fig. S8: ^{1}H NMR (top) and ^{13}C spectra (bottom) of **2** in DMSO-*d6*.

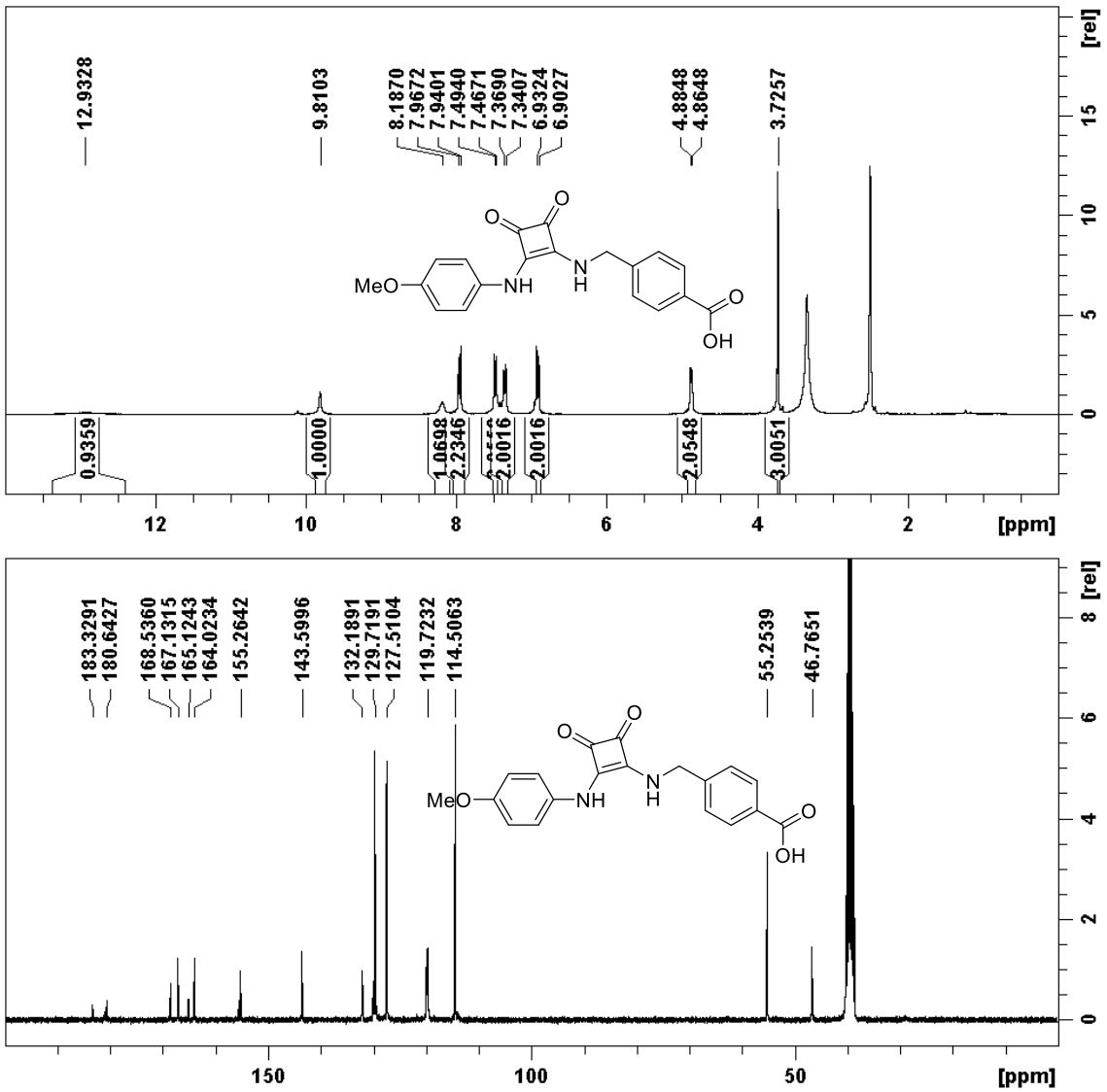


Fig. S9: ^{1}H NMR (top) and ^{13}C spectra (bottom) of **3** in DMSO-*d6*.

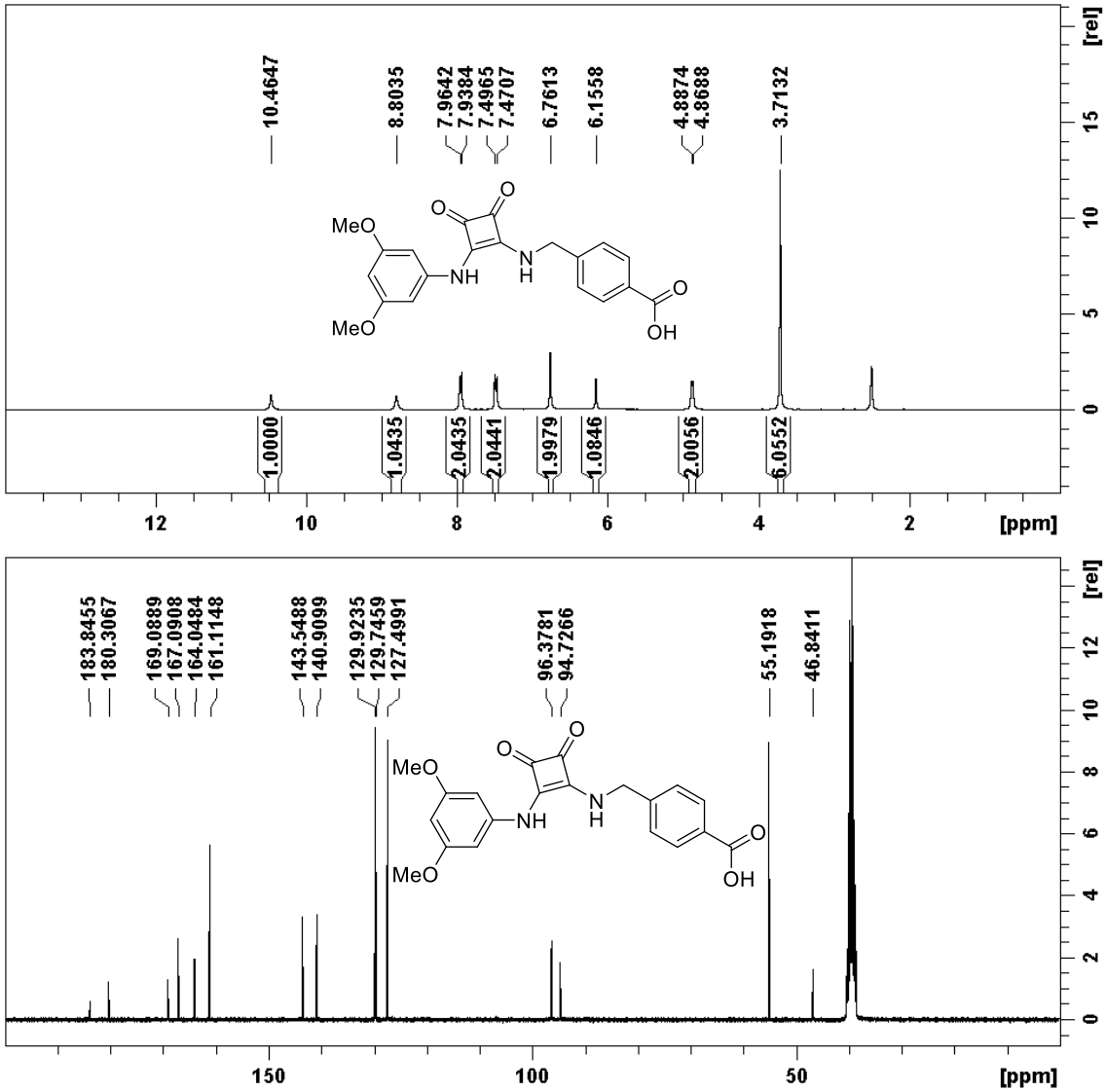


Fig. S10: ^{1}H NMR (top) and ^{13}C spectra (bottom) of **4** in DMSO-*d6*.

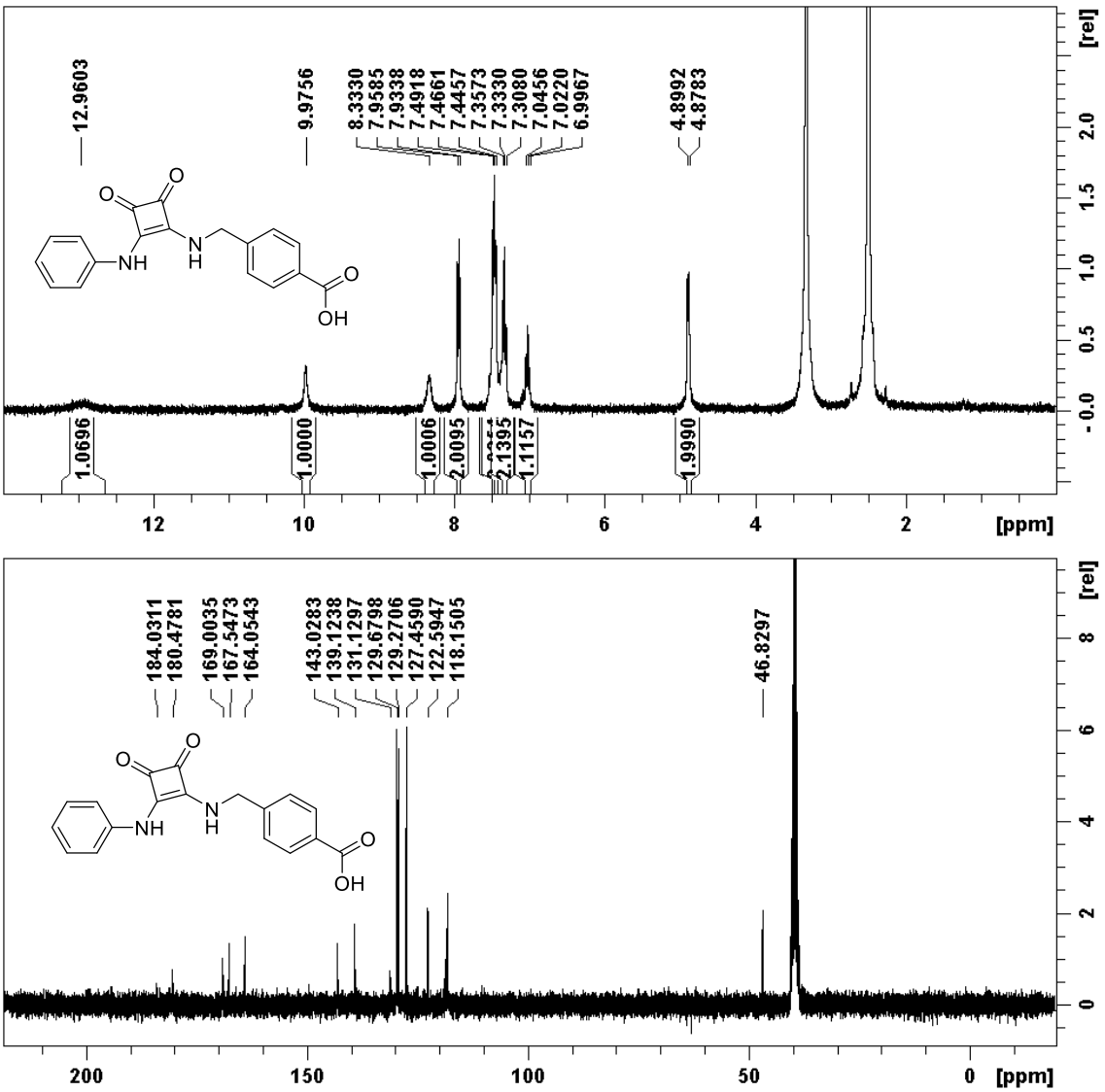


Fig. S11: ^{1}H NMR (top) and ^{13}C spectra (bottom) of **5** in DMSO-*d6*.

4. Atomic Force Microscopy (AFM)

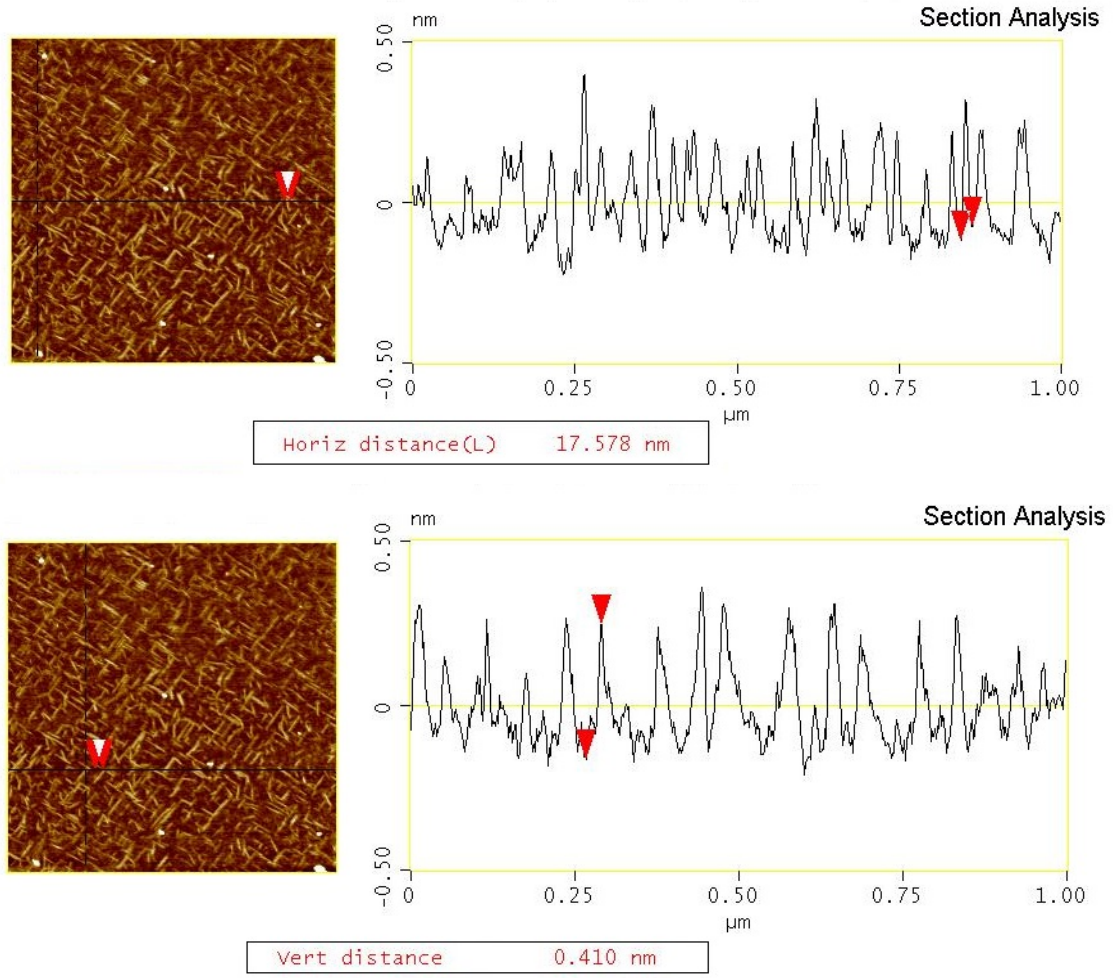


Fig. S1. AFM images and profiles of fibers of compound **1** in PBS ($1.0x10^{-4}$ M) spin coated on a mica surface. Width (top) and high (bottom)

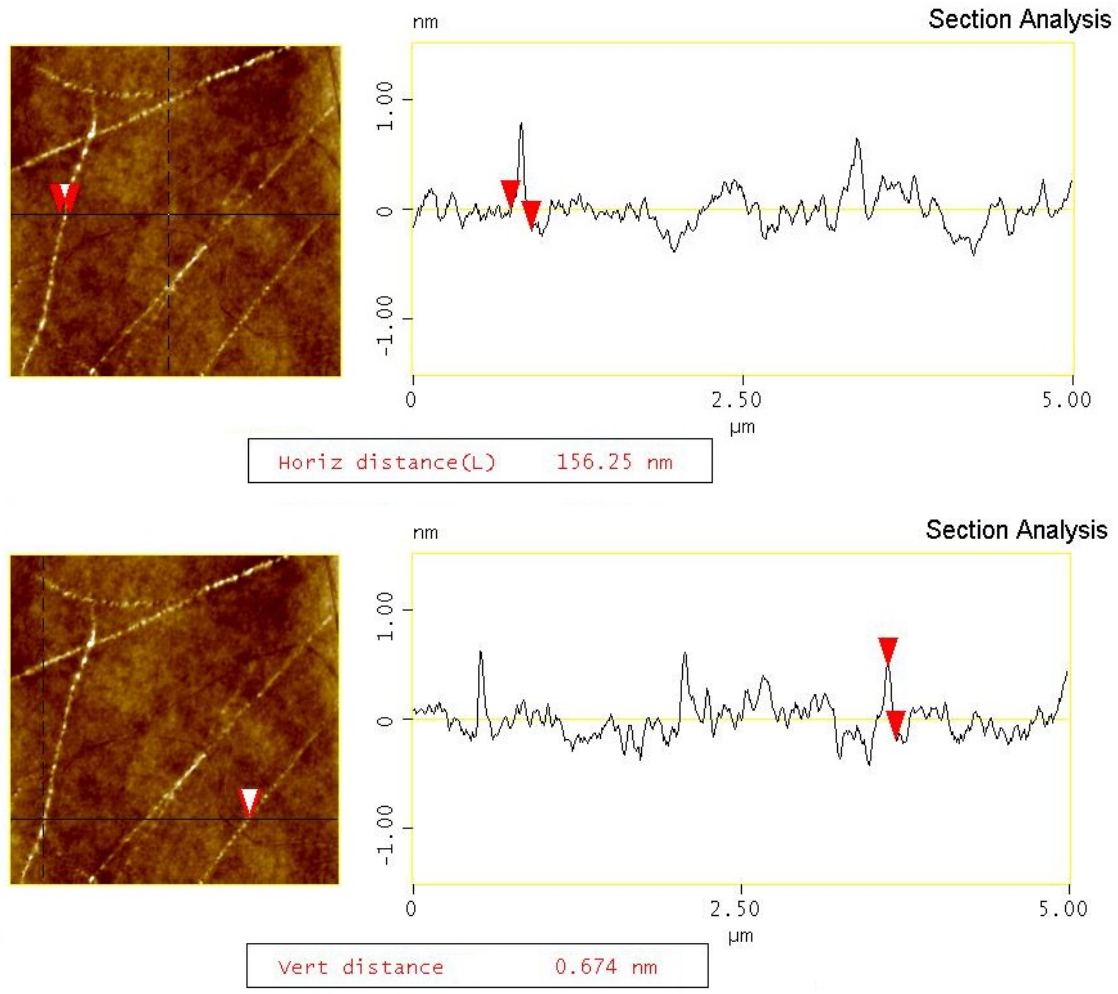


Fig. S13. AFM images and profiles of fibers of compound **2** in PBS ($1.0x10^{-4}$ M) spin coated on a mica surface. Width (top) and high (bottom).

5. ^{1}H NMR Concentration Dependent Experiments

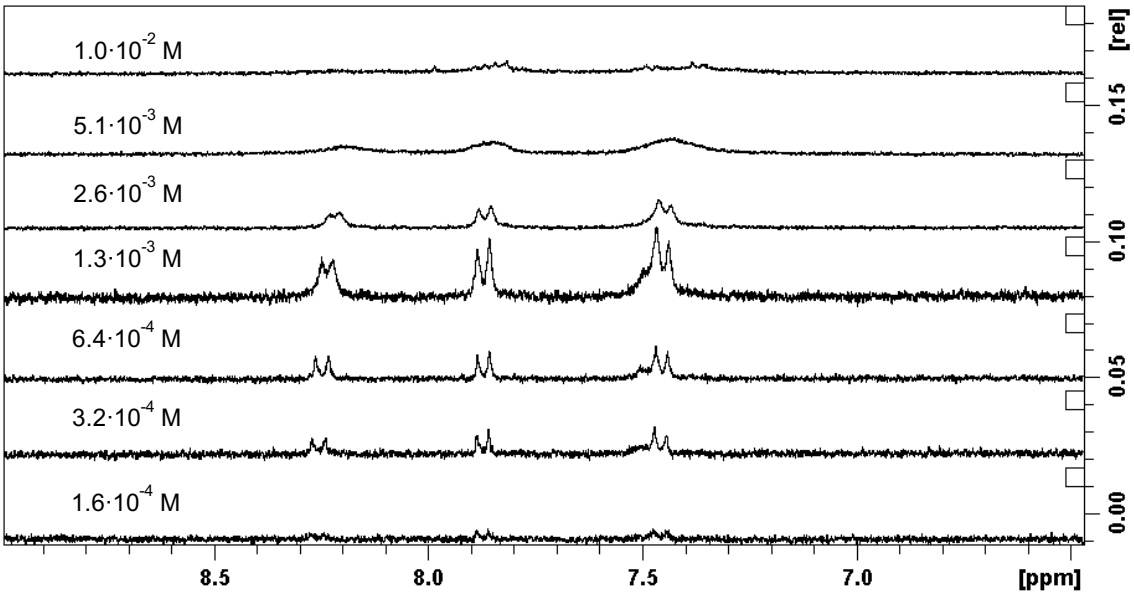


Fig. S2: Superposition of ^{1}H NMR spectra of **1** at different concentrations in D_2O/NaOD.

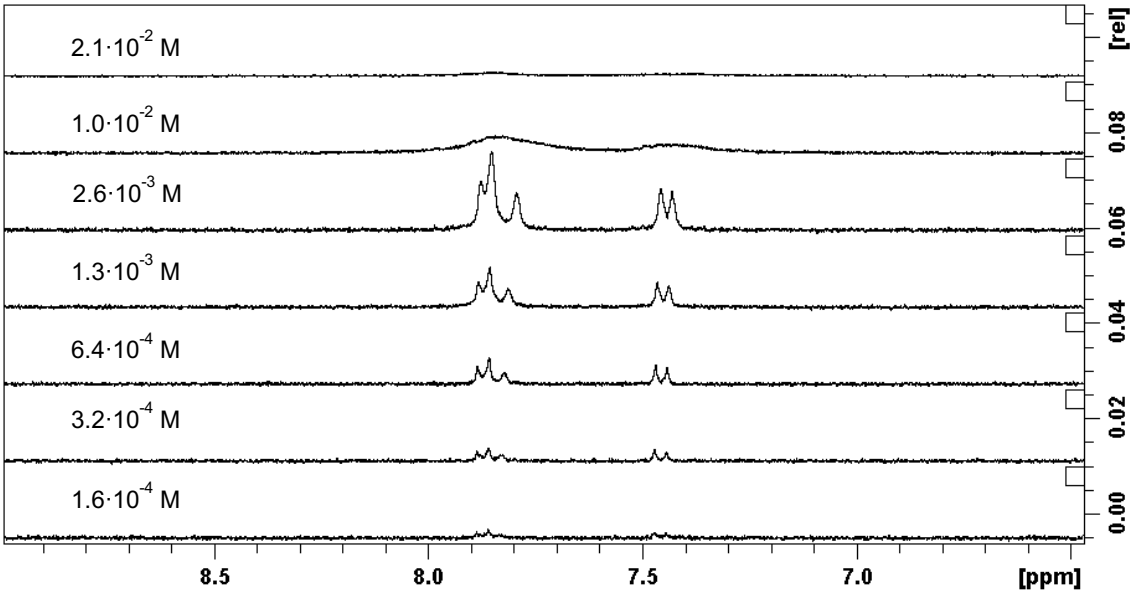


Fig. S3: Superposition of ^{1}H NMR spectra of **2** at different concentrations in D_2O/NaOD.

6. Temperature Dependent NMR Experiments

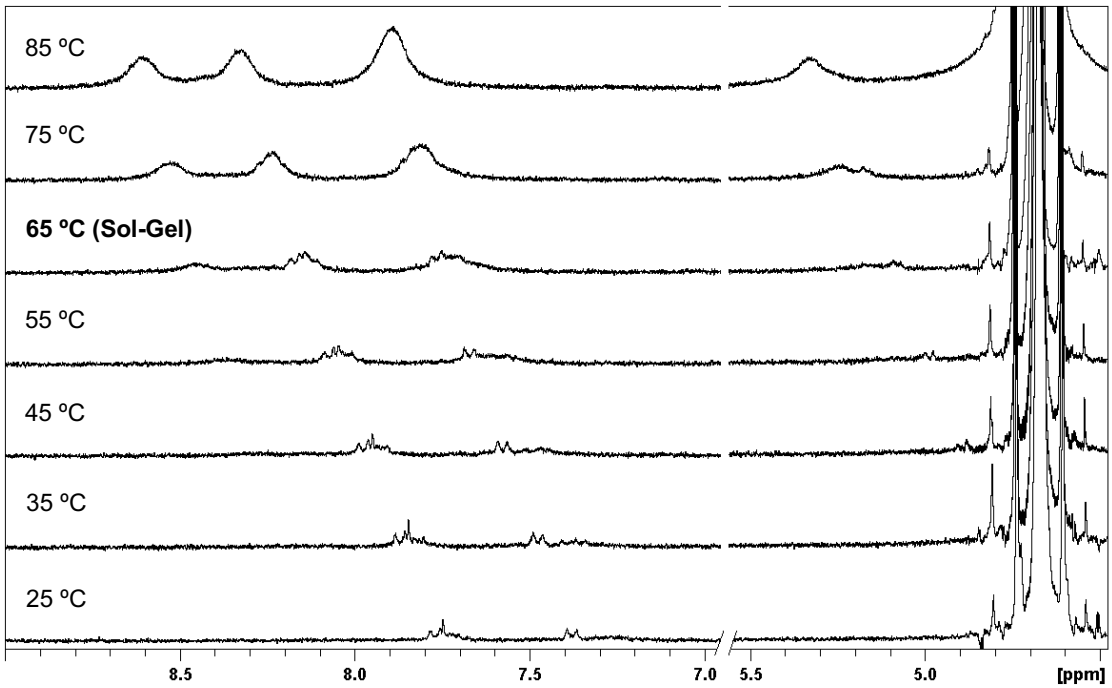


Fig. S4: Superposition of ^{1}H NMR spectra of **1** (0.6 wt%; 1.63×10^{-2} M) at different temperatures in D_2O/PBS.

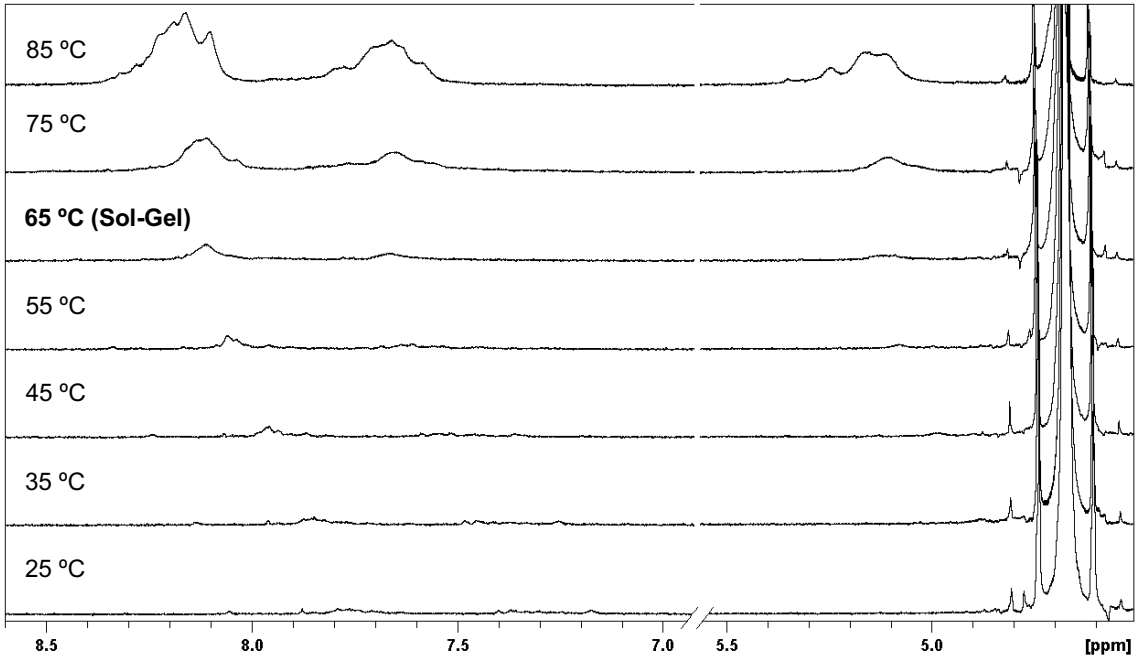


Fig. S5: Superposition of ^{1}H NMR spectra of **2** (1.0 wt%; 2.19×10^{-2} M) at different temperatures in D_2O/PBS.

7. Rheology Experiments

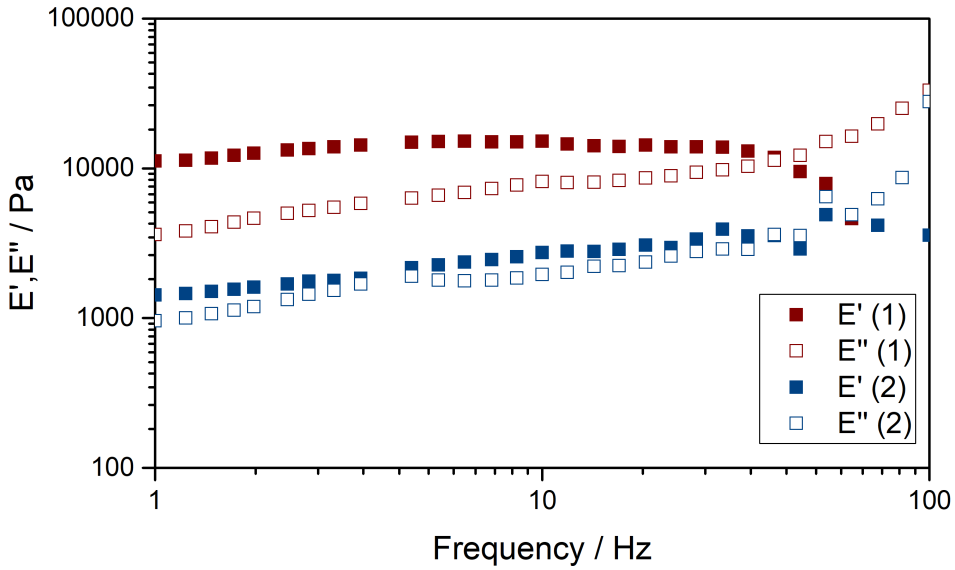


Fig. S6: (a) Storage modulus (E') of **1** (2 wt%, NaOH) (red)and **2** (2 wt%, NaOH) (blue) hydrogels as function of the frequency. (b) Loss modulus (E'') of **1** (2 wt%, NaOH) (red) and **2** (2 wt%, NaOH) hydrogels (blue) as function of the frequency. All the experiments were carried out at 25 °C.

8. UV-Vis Experiments

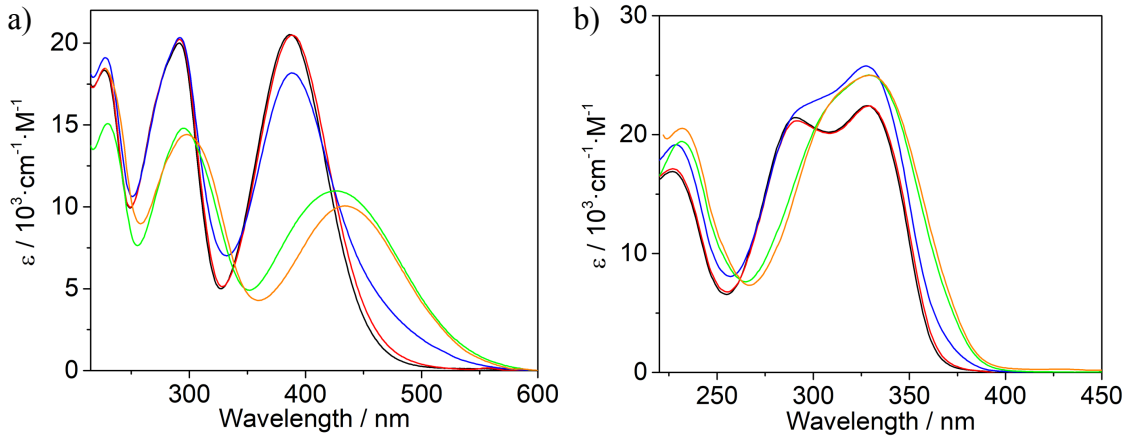


Fig. S19. a) UV-Vis spectra of **1** (3×10^{-5} M) at pH 7 (black line), pH 8 (red line), pH 9 (purple line), pH 10 (green line) and pH 12 (orange line). b) UV-Vis spectra of **2** ((3×10^{-5} M) at pH 7 (black line), pH 8 (red line), pH 9 (purple line), pH 10 (green line) and pH 12 (orange line). The spectra at pH 7 and 8 are overlapped. The samples at pH 7 and 8 were prepare in a phosphate buffer solution (PBS) (0.1 M). The samples at pH 9 and 10 were prepare in a borate buffer solution (0.1 M). The samples at pH 12 were prepared by adjusting the pH with an NaOH solution (1 M).

The red-shift of the UV-Vis bands is indicative of the first deprotonation of the squaramidic NHs. This process starts at pH~9, and therefore at pHs ranging between 7 and 8 (conditions used in the present work) the squaramides have two NH groups.

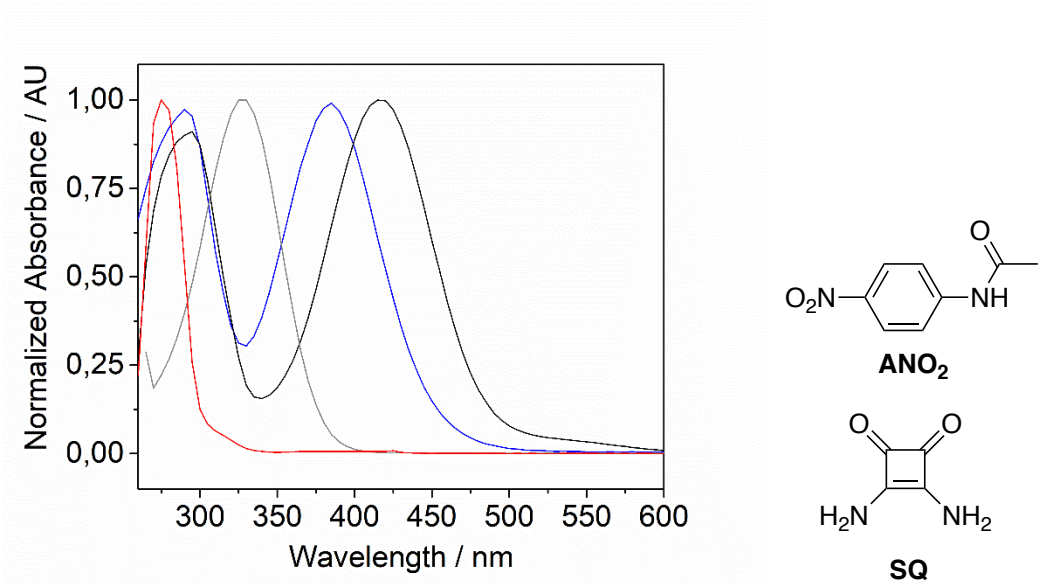


Fig. S20. UV-Vis spectra of **1** in PBS (blue), **1** in DMF (black), **ANO_2** in DMF (grey) and **SQ** in DMF (red). Concentrations 1×10^{-4} M. Right image shows the chemical structures of **ANO_2**[S2] and **SQ**.[S3]

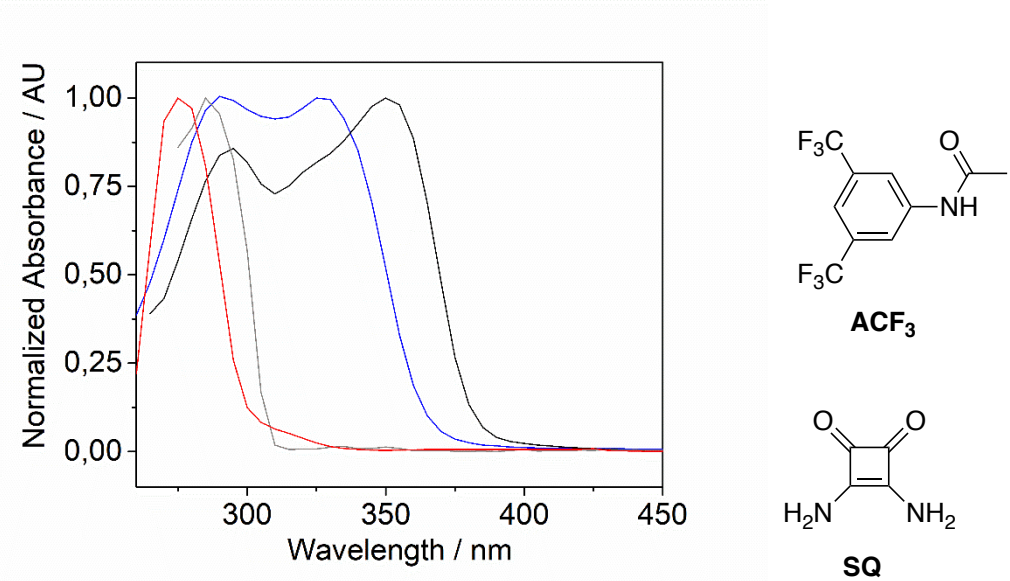


Fig. S21. UV-Vis spectra of **2** in PBS (blue), **2** in DMF (black), **ACF$_3$** in DMF (grey) and **SQ** in DMF (red). Concentrations 1×10^{-4} M. Right image shows the chemical structures of **ACF$_3$**[S2] and **SQ**.[S3]

9. UV-Vis Concentration Dependent Experiment

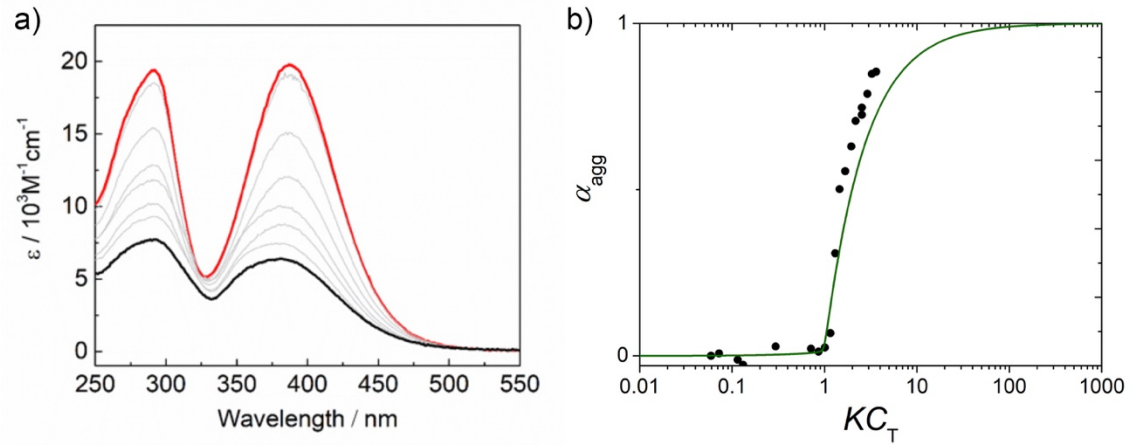


Fig. S22. (a) UV-Vis spectra of **1** in PBS at different concentrations (4.1×10^{-5} M, red line; 2.5×10^{-3} M, black line). (b) Fraction of aggregated molecules α_{agg} plotted as a function of KcT ($\sigma = 0.006$) (black dots) and fitted according to the cooperative nucleation-elongation model (green line).[S4] The experimental absorption data of **1** in PBS (4.1×10^{-5} M to 2.5×10^{-3} M) at 385 nm (see Figure S18a). $K \simeq 1.4\ 10^3\ M^{-1}$; $K_2 \simeq 9\ M^{-1}$.

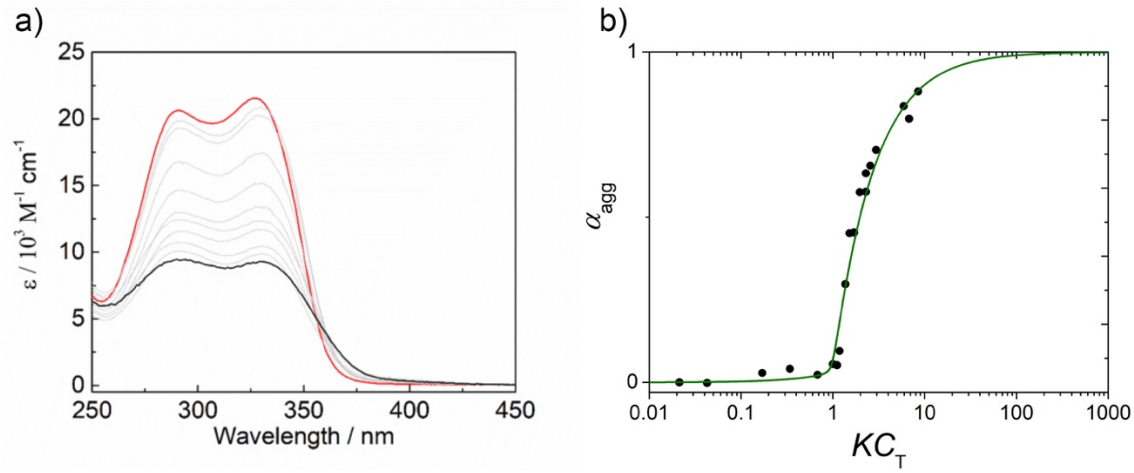


Fig. S23. (a) UV-Vis spectra of **2** in PBS at different concentrations (1.3×10^{-5} M, red line; 5.0×10^{-3} M, black line). (right) (b) Fraction of aggregated molecules α_{agg} plotted as a function of KcT ($\sigma = 0.015$) (black dots) and fitted according to the cooperative nucleation-elongation model (green line).[S4] The experimental absorption data of **2** in PBS (1.3×10^{-5} M to 5.0×10^{-3} M) at 327 nm (see Figure S18a). $K \simeq 1.7\ 10^3\ M^{-1}$; $K_2 \simeq 25\ M^{-1}$.

10. FT-IR Experiments

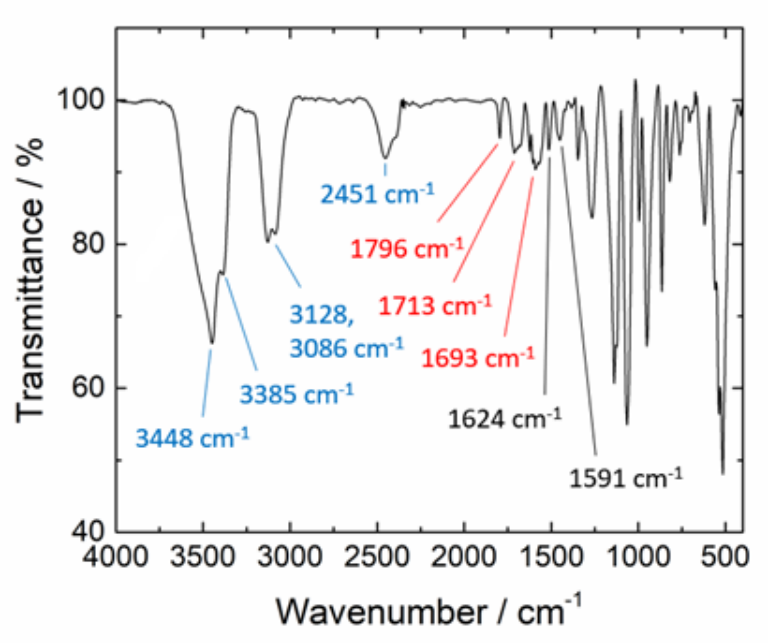


Fig. S24. FT-IR spectra in KBr of xerogels of **1** prepared with PBS.

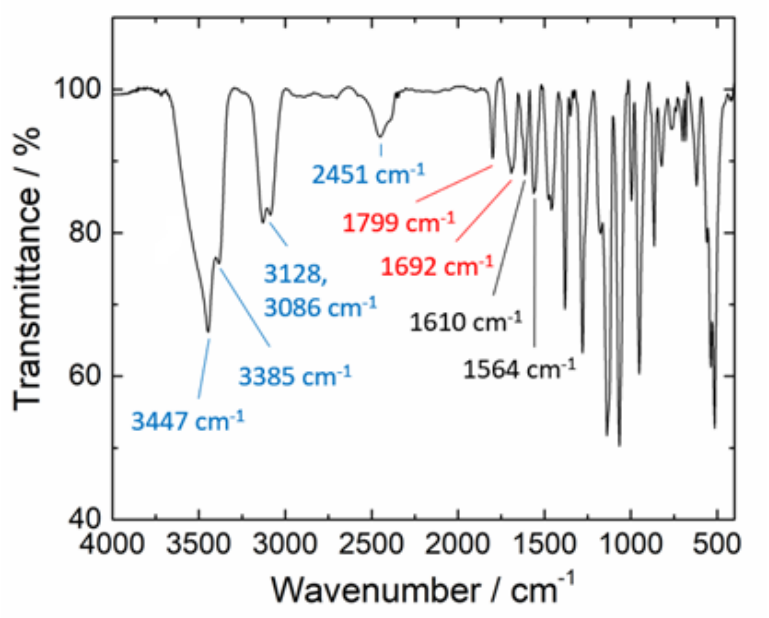


Fig. S25. FT- IR spectra in KBr of xerogels of **2** prepared with PBS.

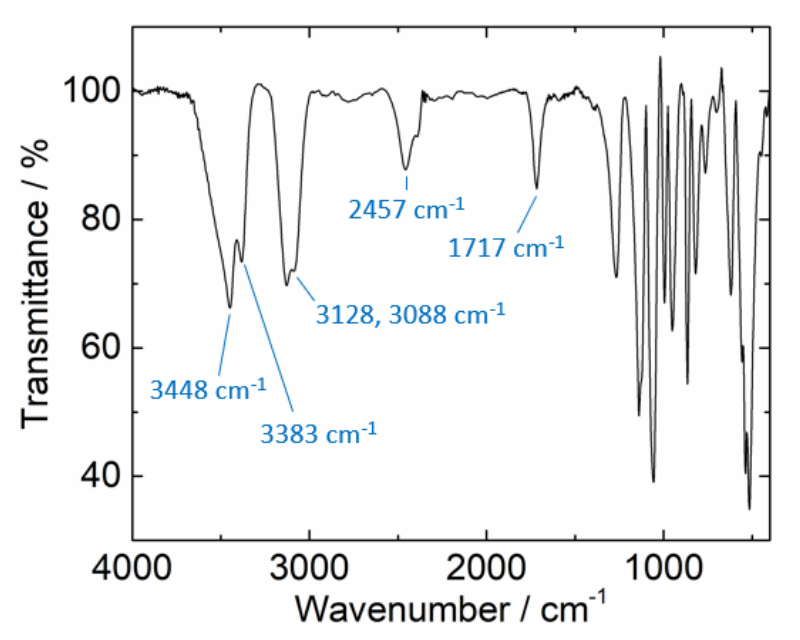


Fig. S26. FT- IR spectra in KBr of PBS.

11. ^{1}H NMR H_2O/DMSO

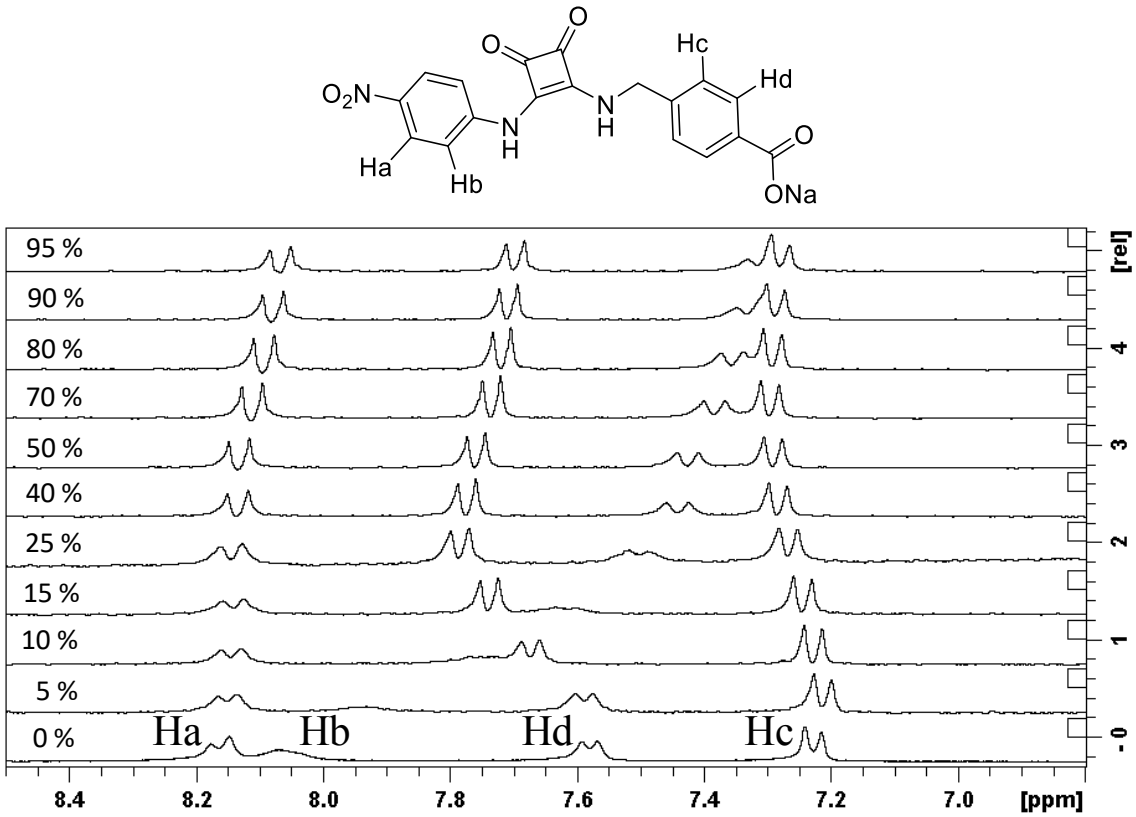


Fig. S27. Superposition of ^{1}H NMR spectra of **1(Na)** (1.0×10^{-3} M) in different ratios of H_2O/DMSO-*d6* solvent mixtures. % indicates the ratio of water.

12. ^{1}H NMR NOESY

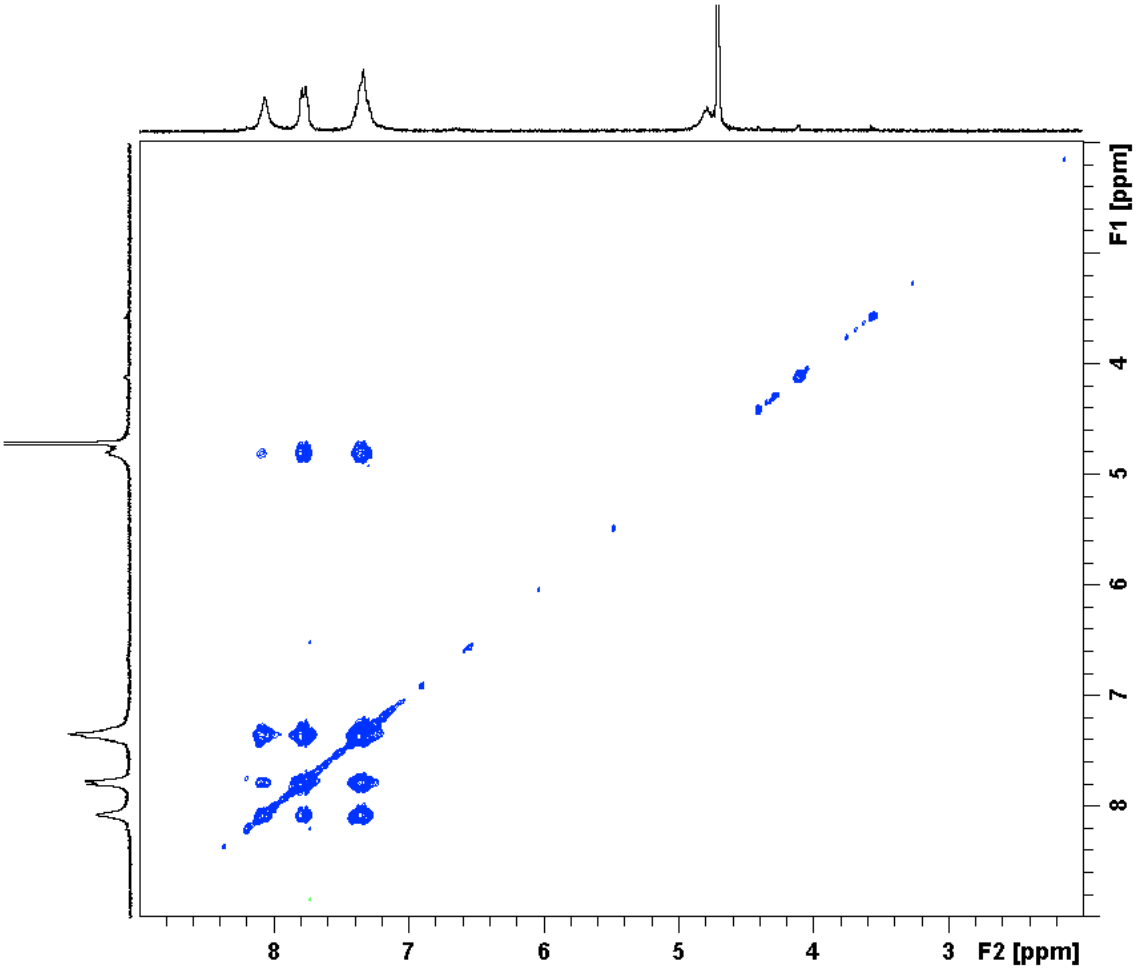


Fig. S28. NOESY spectrum of **1** in D_2O/NaOD (5.1×10^{-3} M).

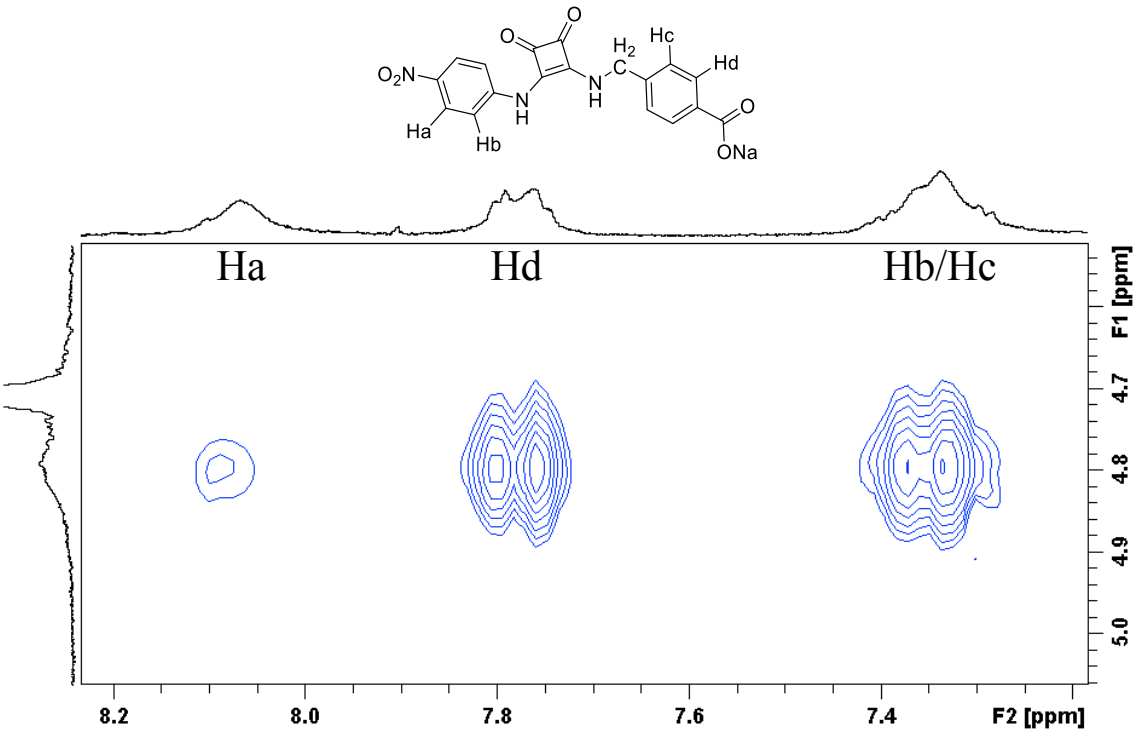


Fig. S29. Selected relevant part of the NOESY spectrum of **1** in D_2O/NaOD (5.1×10^{-3} M).

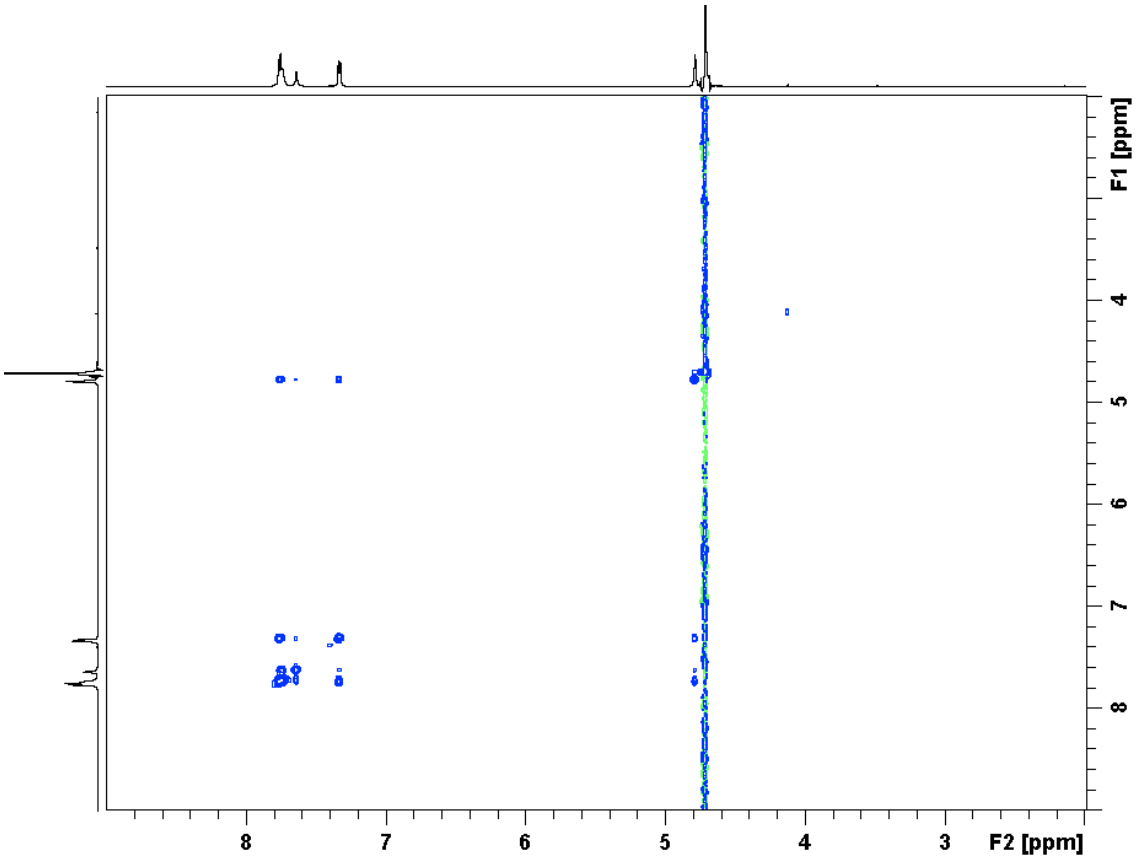


Fig. S30. NOESY spectrum of **2** in D_2O/NaOD (6.7×10^{-3} M).

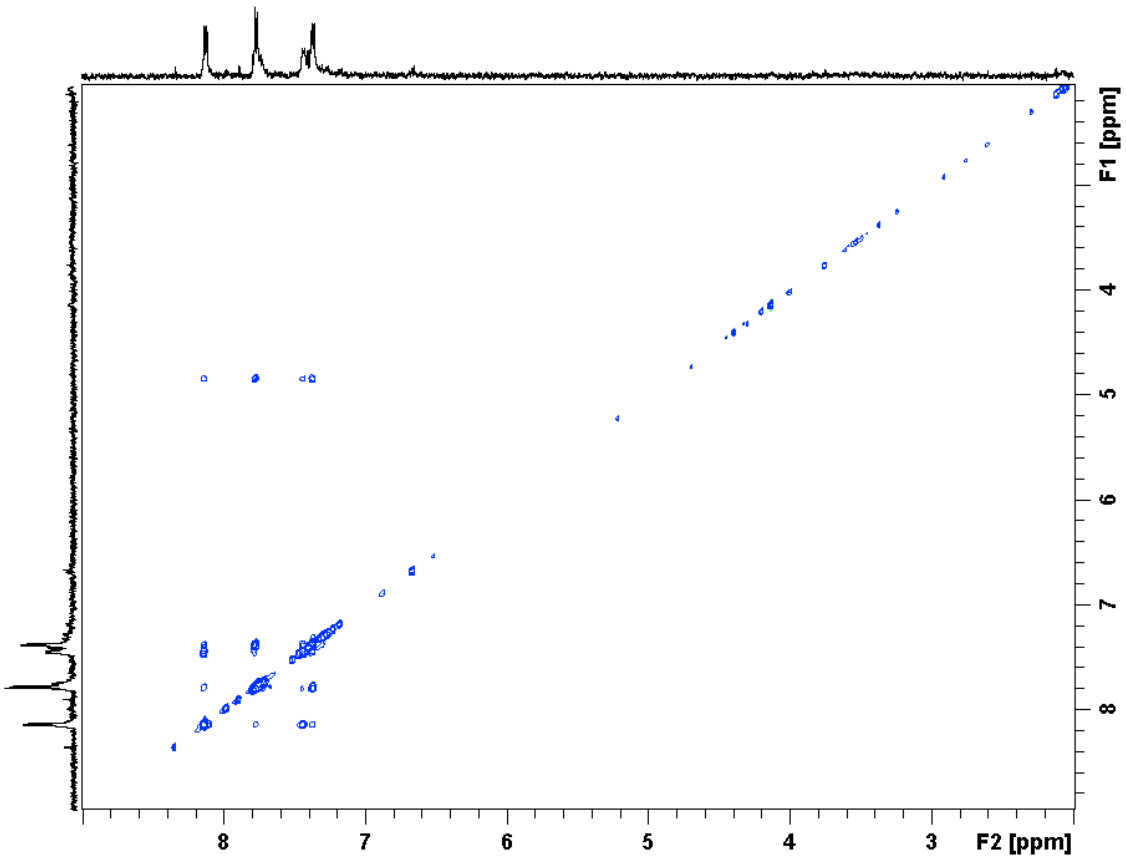


Fig. S31. NOESY spectrum of **1** in PBS (2.7×10^{-3} M) at r.t.

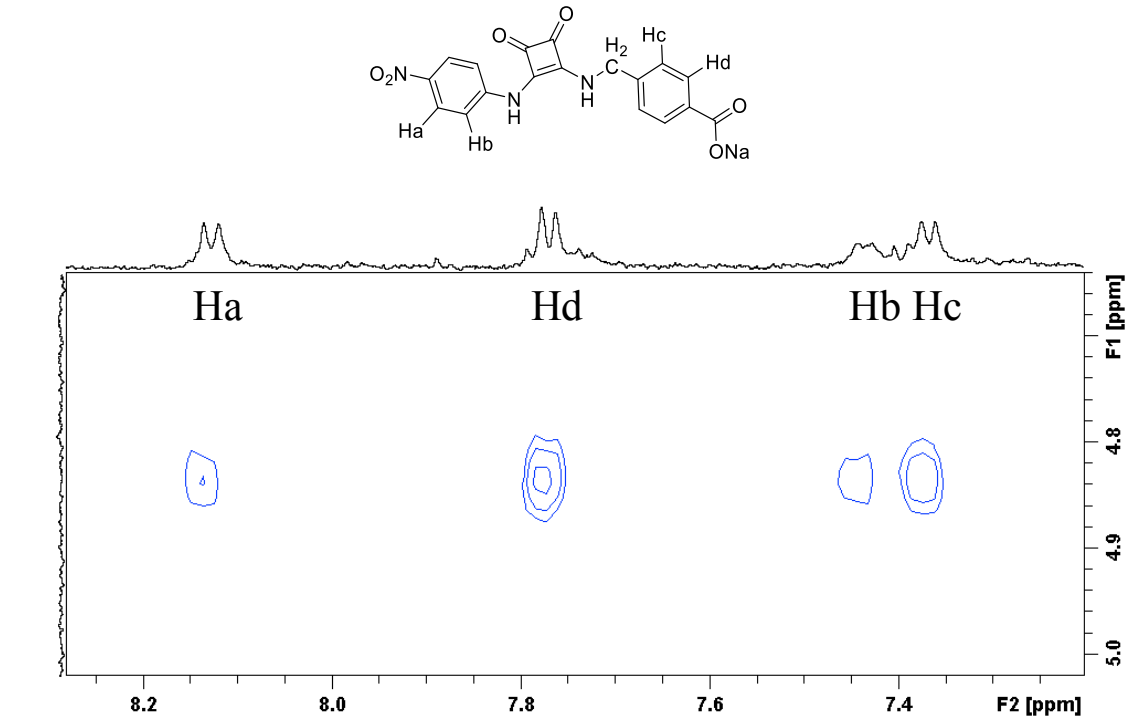


Fig. S32. Selected relevant part of the NOESY spectrum of **1** in PBS (2.7×10^{-3} M) at r.t.

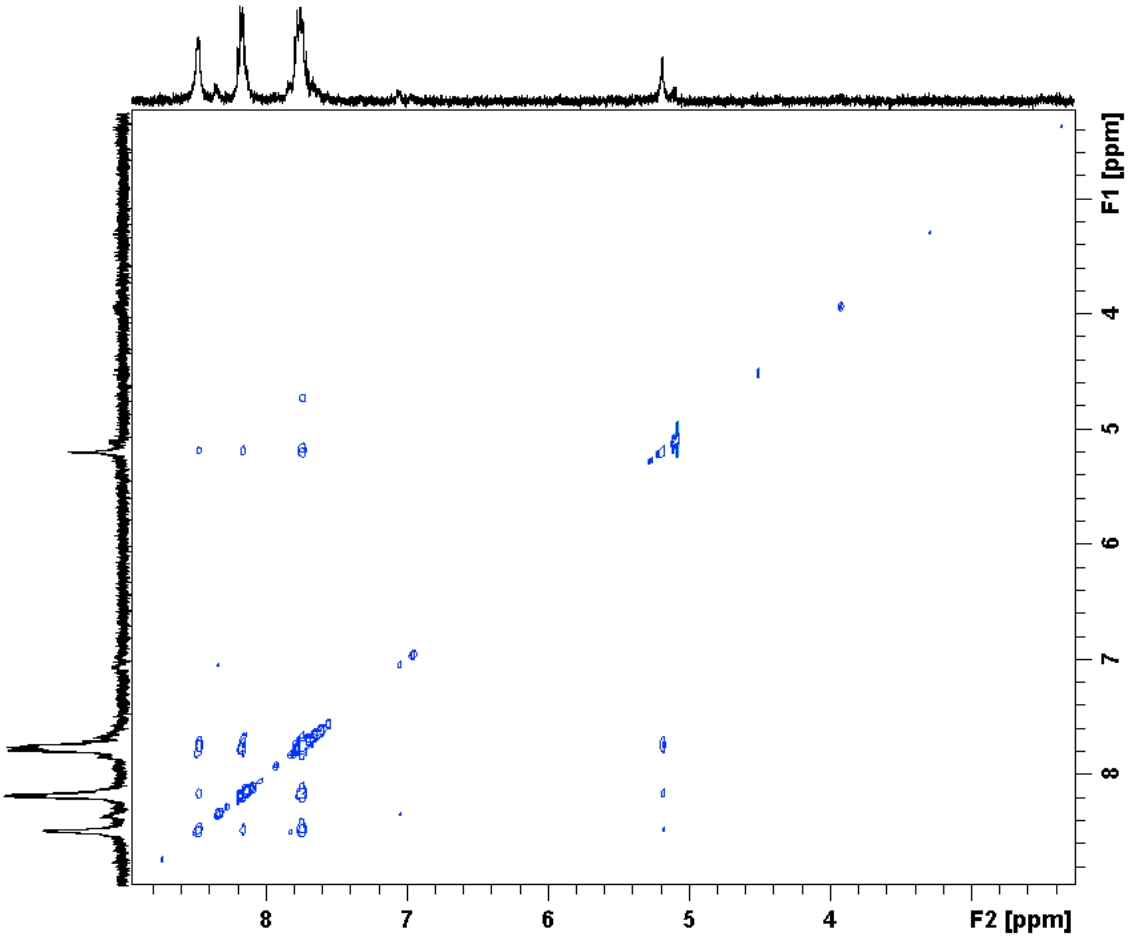


Fig. S33. NOESY spectrum of **1** in PBS (8.15×10^{-3} M) at 65 ºC.

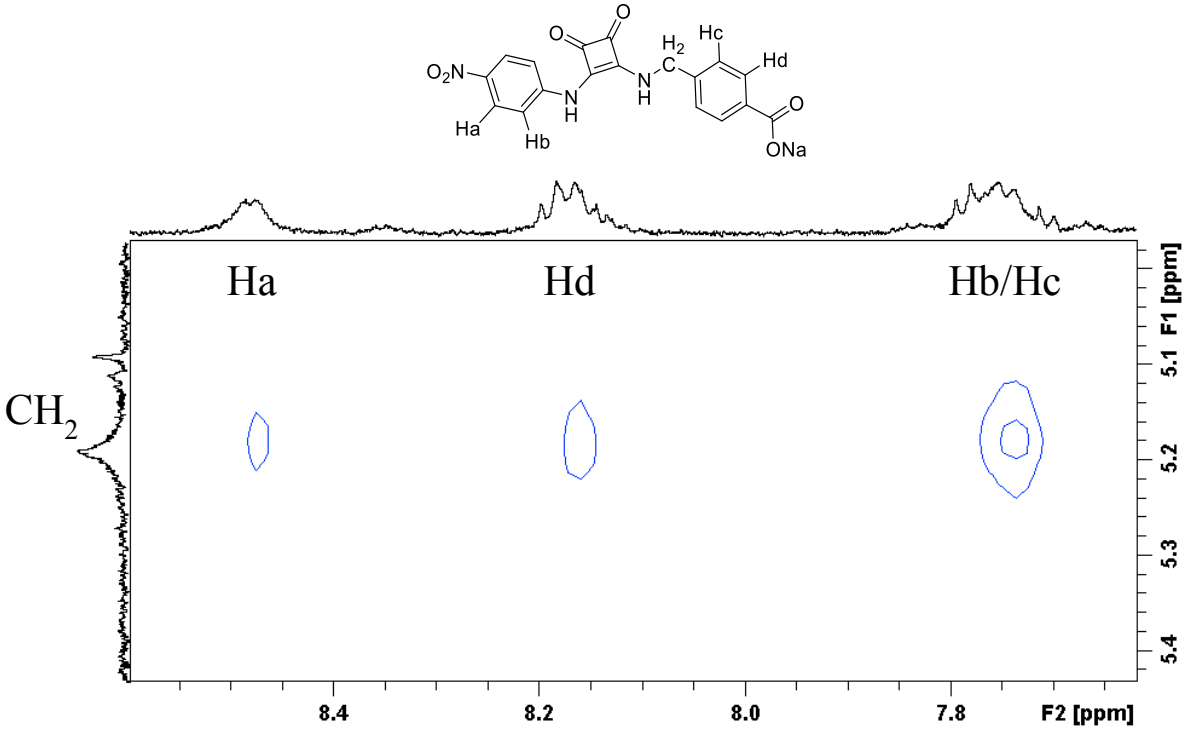


Fig. S34. Selected relevant part of the NOESY spectrum of **1** in PBS (8.15×10^{-3} M) at 65 ºC.

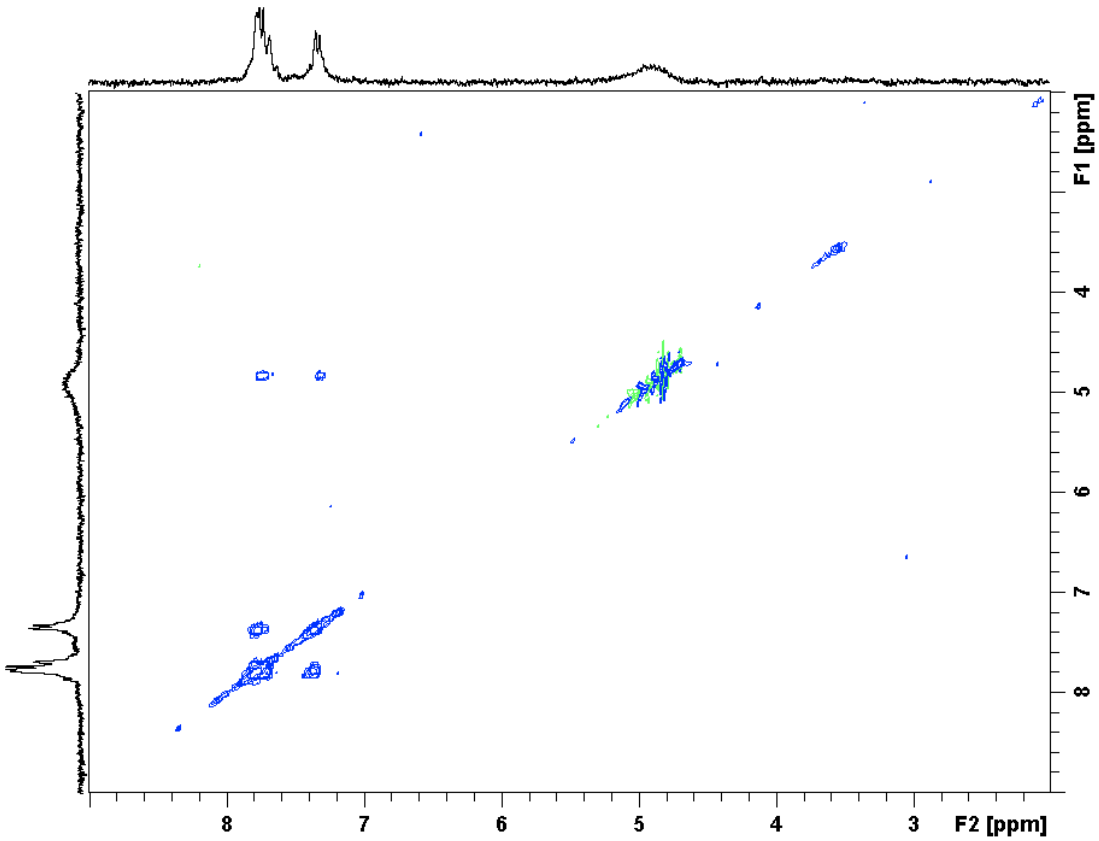


Fig. S35. NOESY spectrum of **2** in PBS (4.36×10^{-3} M) at r.t.

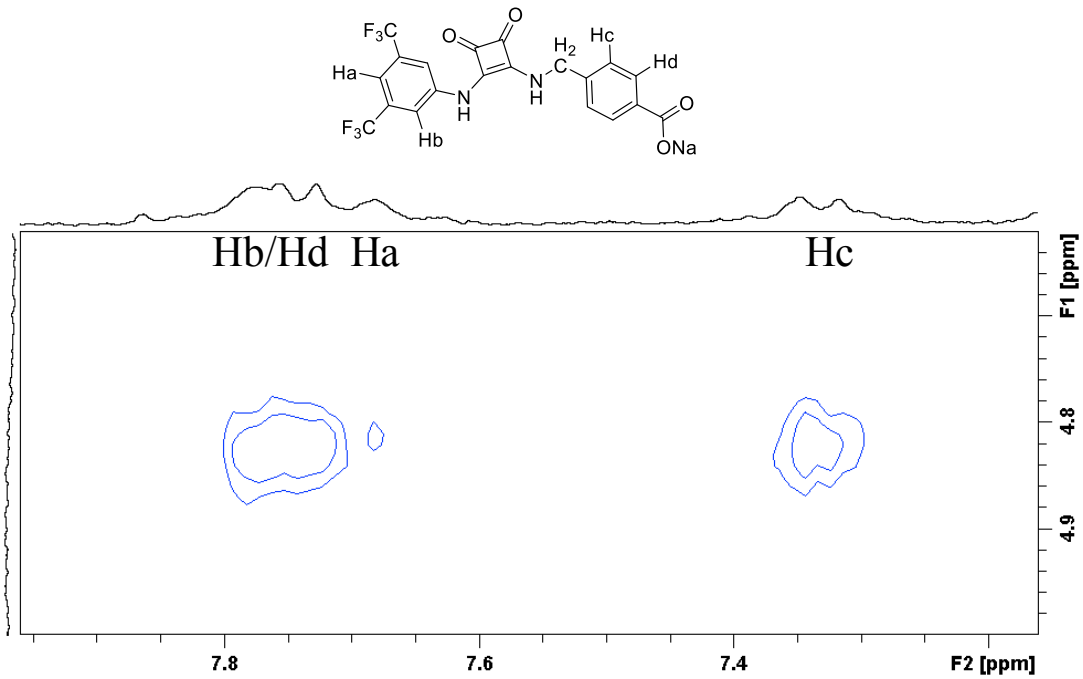


Fig. S36. Selected relevant part of the NOESY spectrum of **2** in PBS (4.36×10^{-3} M) at r.t.

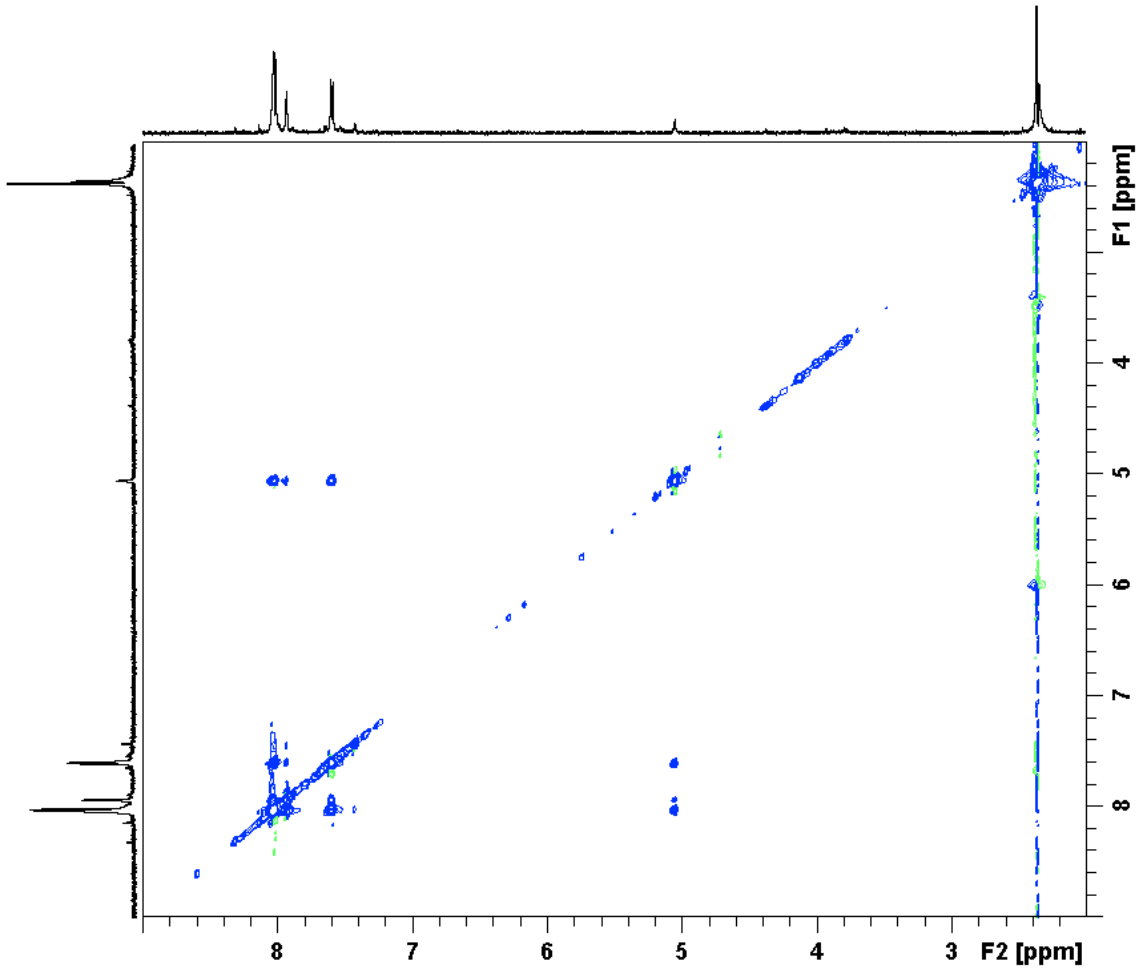


Fig. S37. NOESY spectrum of **2** in PBS (6.55×10^{-3} M) at 50 ºC.

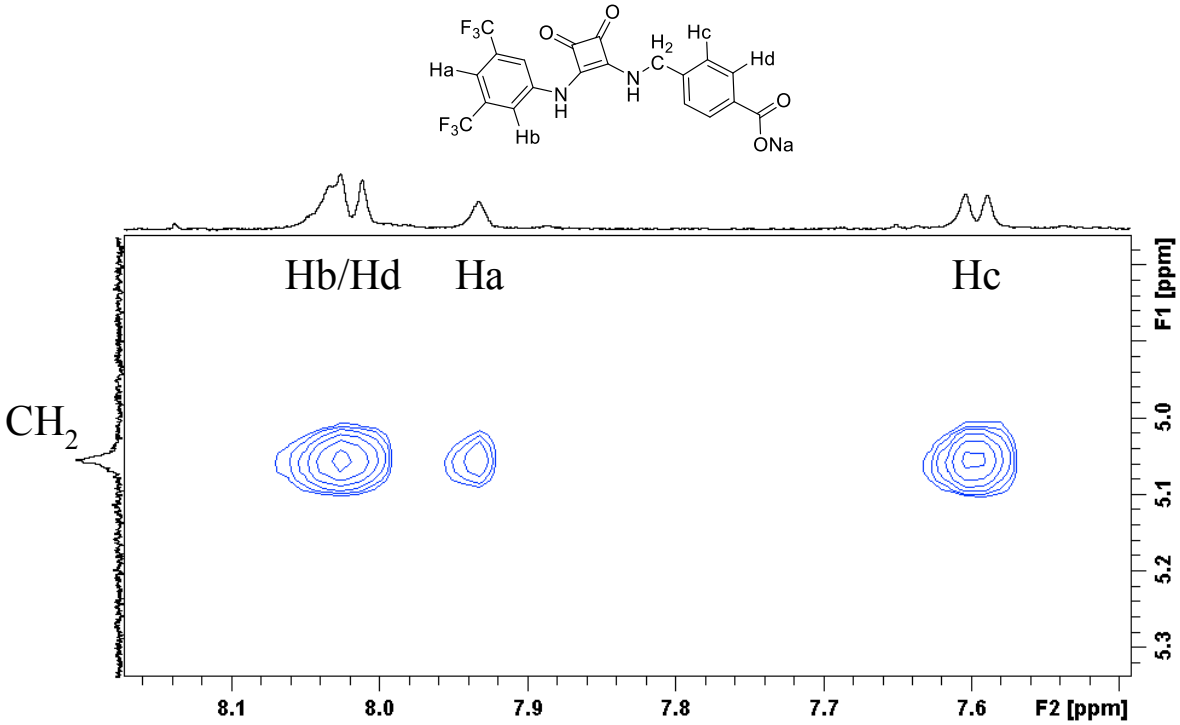


Fig. S38. Selected relevant part of the NOESY spectrum of **2** in PBS (6.55×10^{-3} M) at 50 ºC.

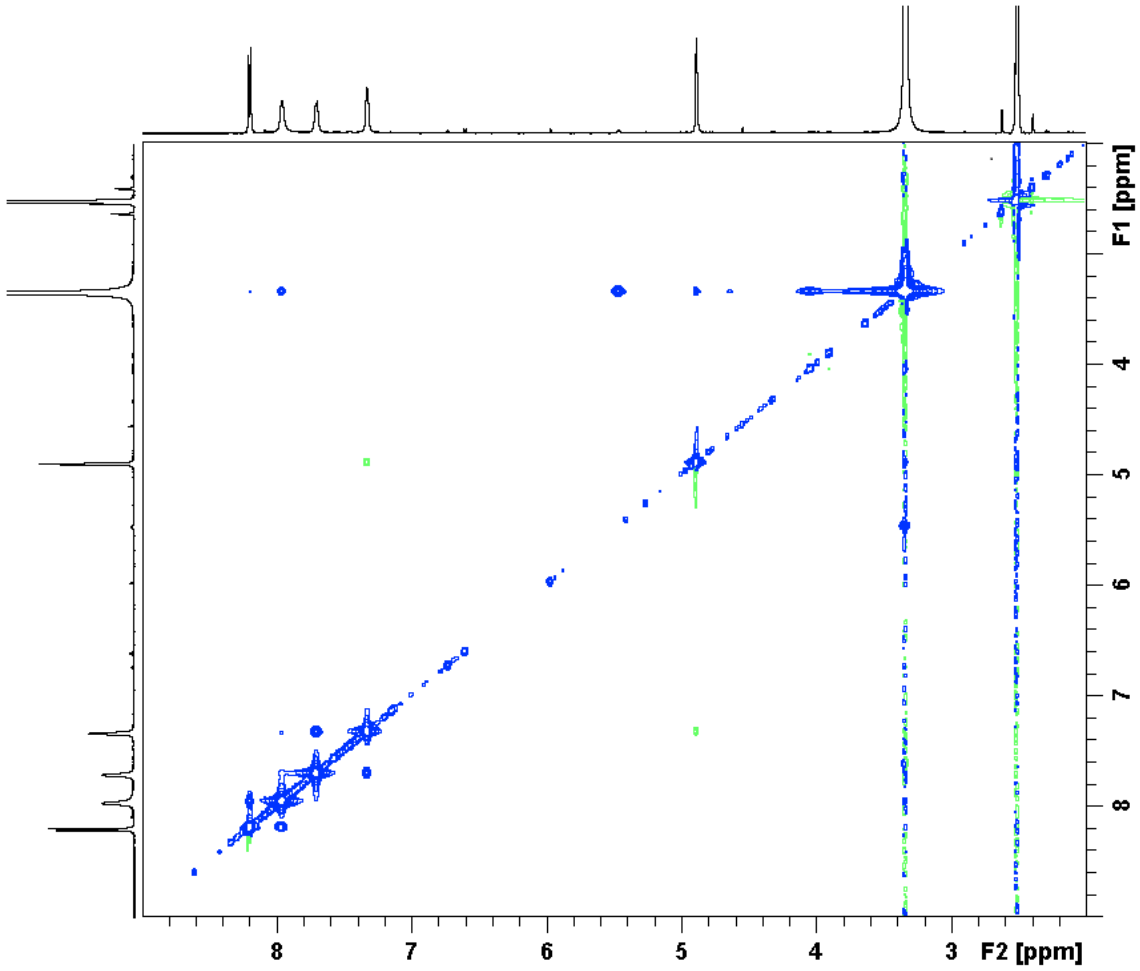


Fig. S39. NOESY spectrum of **1(Na)** in DMSO-*d6* (4.8×10^{-3} M) at r.t.

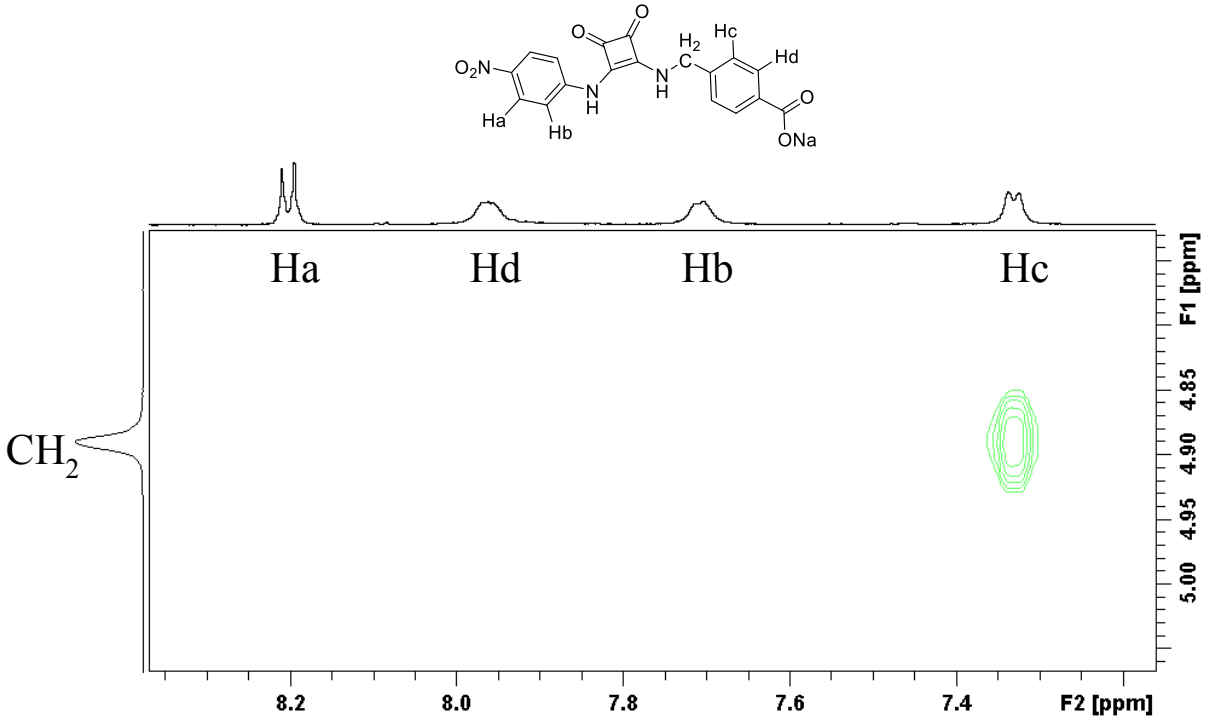


Fig. S40. Selected relevant part of the NOESY spectrum of **1(Na)** in DMSO-*d6* (4.8×10^{-3} M) at r.t.

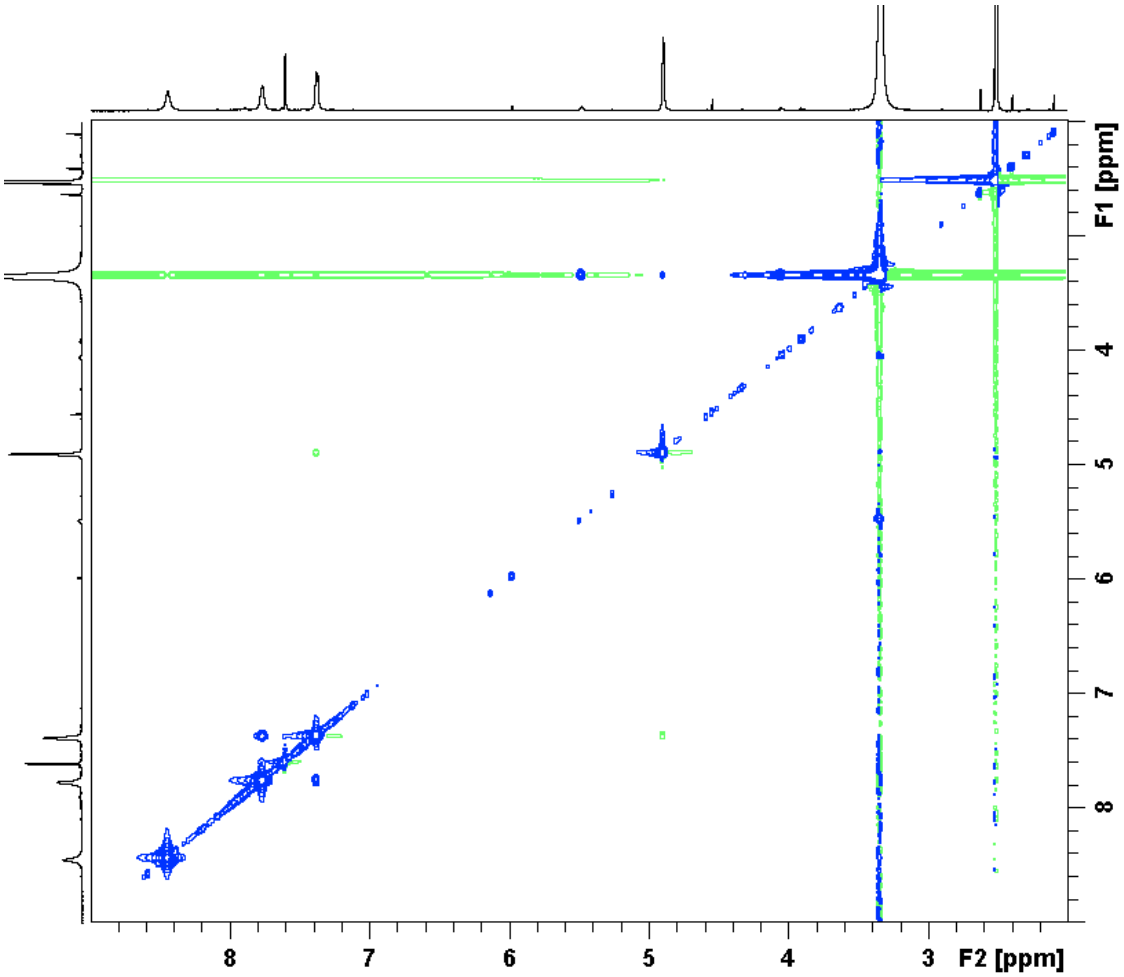


Fig. S41. NOESY spectrum of **2(Na)** in DMSO-*d6* (6.4×10^{-3} M) at r.t.

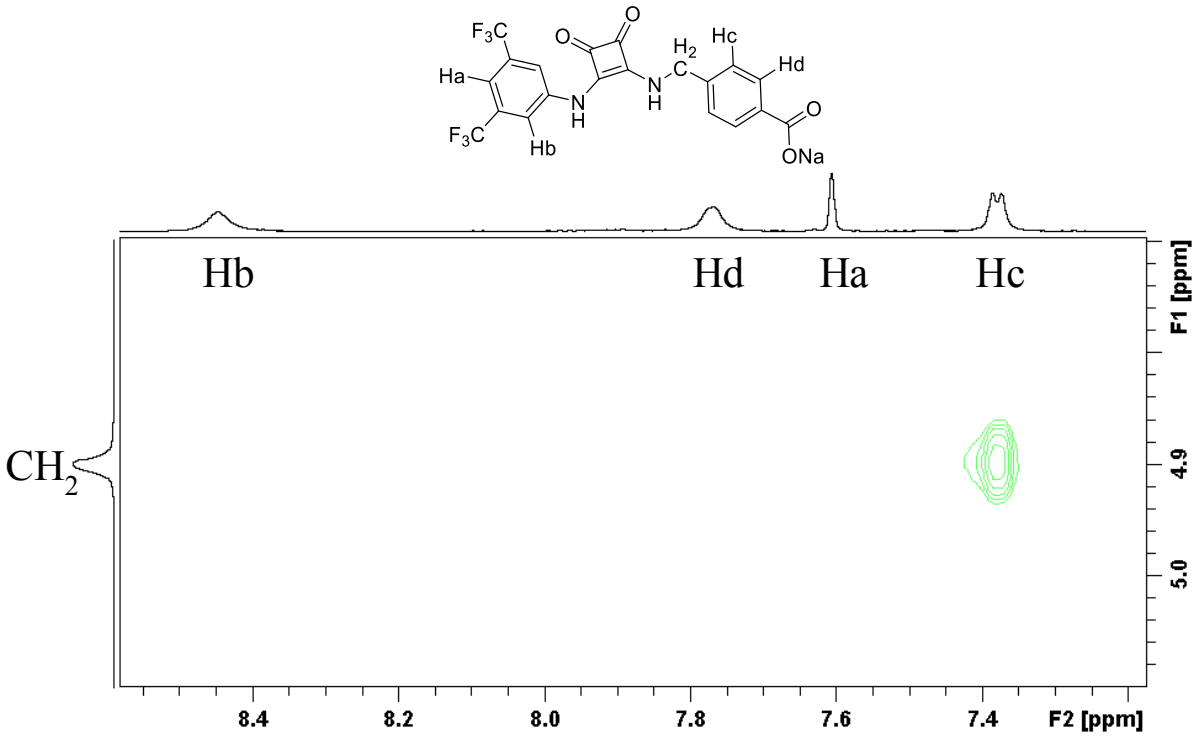


Fig. S42. Selected relevant part of the NOESY spectrum of **2(Na)** in DMSO-*d6* (6.4×10^{-3} M) at r.t.

13. Theoretical calculations

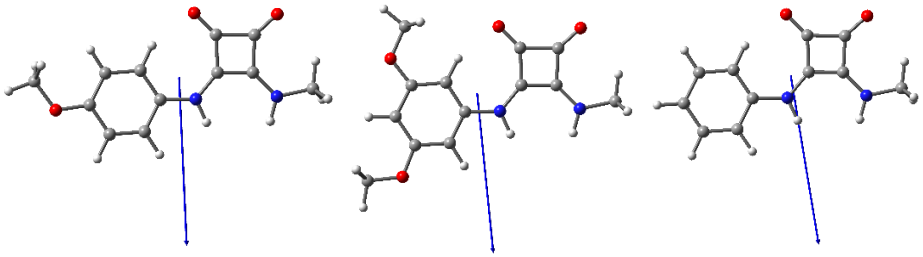


Fig. S43. Dipole moments in the aryl-squaramide part of compounds **3** (left), **4** (middle) and **5** (right).

Table S1. Calculated dipole moments for compounds **1-5**.

Compound	Dipole moment (D)
1	10.1
2	8.5
3	6.6
4	6.4
5	7.5

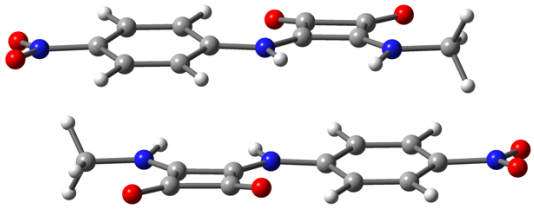


Fig. S44. B3LYP-D/6-31+G* optimised dimer of compound **1**. The dipole vectors are represented using pink arrows

Cartesian coordinates

Compound 1

Center Number	Atomic Number	Coordinates (Angstroms) X	Y	Z
1	6	-3.192905	-0.385318	-0.000042
2	6	-3.609307	1.044693	0.000225
3	6	-2.116980	1.413877	-0.000325
4	6	-1.832077	-0.053723	-0.000544
5	8	-4.673488	1.624778	0.000623
6	8	-1.475495	2.442836	-0.000531
7	7	-3.898241	-1.524141	-0.000119
8	7	-0.740352	-0.875546	-0.001262
9	1	-0.937006	-1.869065	-0.001403
10	1	-3.414361	-2.412934	0.000043
11	6	0.626451	-0.570953	-0.000755
12	6	1.527481	-1.653770	-0.000668
13	6	1.116827	0.746468	-0.000452
14	6	2.895289	-1.432791	-0.000243
15	1	1.150507	-2.674216	-0.000944
16	6	2.488691	0.964098	-0.000029
17	1	0.432023	1.588699	-0.000524
18	6	3.367032	-0.119902	0.000084
19	1	3.600495	-2.254528	-0.000128
20	1	2.887940	1.970991	0.000194
21	7	4.809193	0.119017	0.000559

22	8	5.553523	-0.864598	0.000928
23	8	5.198441	1.288018	0.000555
24	6	-5.360550	-1.558476	0.001269
25	1	-5.733969	-2.072502	0.893917
26	1	-5.727857	-0.531452	0.000846
27	1	-5.735513	-2.073795	-0.889971

Compound 2

Center Number	Atomic Number	Coordinates (Angstroms) X	Y	Z
1	6	-3.835484	-0.733587	-0.002954
2	6	-4.390277	0.647826	0.013488
3	6	-2.941749	1.161250	0.018621
4	6	-2.513760	-0.270003	0.001713
5	8	-5.506587	1.120727	0.019356
6	8	-2.400695	2.246817	0.031382
7	7	-4.424776	-1.937220	-0.016203
8	7	-1.344445	-0.974259	-0.007689
9	1	-1.434288	-1.982599	-0.024157
10	1	-3.855113	-2.773382	-0.025496
11	6	-0.013320	-0.524923	-0.005098
12	6	0.993806	-1.500863	-0.036788
13	6	0.337138	0.831643	0.028642
14	6	2.333963	-1.126160	-0.034902
15	1	0.734411	-2.555477	-0.068470
16	6	1.687282	1.182836	0.025262
17	1	-0.429248	1.601383	0.059068
18	6	2.696003	0.220402	-0.005982
19	6	-5.876130	-2.116211	-0.021515
20	1	3.738905	0.511630	-0.007099
21	6	3.399712	-2.190345	0.005219
22	6	2.054225	2.647141	-0.006707
23	9	3.295713	2.860667	0.483319
24	9	1.195967	3.393423	0.714728
25	9	2.038830	3.127589	-1.270150
26	9	3.723412	-2.517717	1.276892
27	9	2.993535	-3.329706	-0.601274
28	9	4.534686	-1.786941	-0.601112
29	1	-6.199382	-2.678557	0.861612
30	1	-6.196542	-2.652090	-0.922027
31	1	-6.343698	-1.130779	-0.007708

Compound 3

Center Number	Atomic Number	Coordinates (Angstroms) X	Y	Z
1	6	2.946546	-0.325668	-0.000107
2	6	3.298483	1.113706	-0.000220
3	6	1.794683	1.418242	-0.000033
4	6	1.568298	-0.062066	-0.000027
5	8	4.338934	1.742851	-0.000387
6	8	1.108143	2.419865	0.000102
7	7	3.700326	-1.437740	-0.000208
8	7	0.519862	-0.923696	0.000057
9	1	0.756103	-1.908254	0.000010
10	1	3.252959	-2.344914	0.000486
11	6	-0.873899	-0.676645	0.000027
12	6	-1.728977	-1.791084	-0.000200
13	6	-1.426674	0.606364	0.000225
14	6	-3.106144	-1.627739	-0.000226
15	1	-1.312838	-2.797194	-0.000363
16	6	-2.814203	0.768875	0.000182
17	1	-0.783954	1.481247	0.000393
18	6	-3.664395	-0.341853	-0.000031
19	6	5.160741	-1.407275	0.000475
20	1	5.561432	-1.904391	-0.890654
21	1	5.560675	-1.902881	0.892800
22	1	5.479852	-0.363944	-0.000249
23	1	-3.213553	1.776569	0.000306
24	1	-3.770112	-2.486238	-0.000406
25	8	-5.029863	-0.285201	-0.000135
26	6	-5.644141	0.993295	0.000164
27	1	-5.375749	1.571390	-0.894203
28	1	-6.720005	0.808658	0.000123
29	1	-5.375740	1.570968	0.894800

Compound 4

Center Number	Atomic Number	Coordinates (Angstroms) X	Y	Z
1	6	-3.136487	-0.659054	-0.000063
2	6	-3.665954	0.725670	-0.000443
3	6	-2.212931	1.215535	-0.000538
4	6	-1.802171	-0.224166	-0.000156
5	8	-4.775989	1.220647	-0.000637

6	8	-1.660657	2.297973	-0.000759
7	7	-3.743577	-1.856284	0.000148
8	7	-0.656702	-0.954344	-0.000179
9	1	-0.771334	-1.960332	-0.000214
10	1	-3.184714	-2.699509	0.000866
11	6	0.694689	-0.543020	0.000000
12	6	1.660931	-1.548611	-0.000240
13	6	1.053166	0.812815	0.000406
14	6	3.018829	-1.198530	-0.000087
15	1	1.393913	-2.601537	-0.000594
16	6	2.411410	1.133380	0.000508
17	1	0.288795	1.579070	0.000527
18	6	3.405171	0.139378	0.000274
19	6	-5.196131	-2.012331	0.001056
20	1	4.441638	0.450356	0.000365
21	1	-5.528625	-2.554801	0.893675
22	1	-5.529365	-2.557188	-0.889810
23	1	-5.646806	-1.018730	-0.000070
24	8	2.879839	2.411238	0.000846
25	8	3.888094	-2.251105	-0.000344
26	6	1.931637	3.474133	0.000274
27	1	1.294118	3.443752	-0.891209
28	1	1.293834	3.444442	0.891588
29	1	2.519894	4.393478	0.000031
30	6	5.279143	-1.969109	-0.000407
31	1	5.576137	-1.406424	0.894147
32	1	5.780413	-2.938850	-0.000743
33	1	5.575949	-1.405895	-0.894690

compound 5

Center Number	Atomic Number	Coordinates (Angstroms) X	Y	Z
1	6	2.096990	-0.415543	-0.000093
2	6	2.564684	0.992162	-0.000068
3	6	1.089633	1.417474	0.000195
4	6	0.745897	-0.040024	-0.000008
5	8	3.651829	1.534616	-0.000098
6	8	0.487717	2.471217	0.000433
7	7	2.758395	-1.584133	-0.000374
8	7	-0.368333	-0.819154	0.000188
9	1	-0.207864	-1.819020	0.000052
10	1	2.239081	-2.452288	0.000334
11	6	-1.736105	-0.467855	0.000091
12	6	-2.667682	-1.517729	0.000264
13	6	-2.182597	0.860303	-0.000218
14	6	-4.032842	-1.244466	0.000119
15	1	-2.321548	-2.550179	0.000510
16	6	-3.553799	1.114716	-0.000343
17	1	-1.470668	1.679581	-0.000318
18	6	-4.486166	0.075613	-0.000175
19	6	4.216679	-1.673037	-0.000014
20	1	-5.550636	0.290689	-0.000298
21	1	4.574665	-2.200728	-0.891634
22	1	4.574277	-2.200481	0.891907
23	1	4.620765	-0.659622	-0.000071
24	1	-3.892049	2.147401	-0.000605
25	1	-4.740978	-2.068678	0.000253

dimer of 1

Center Number	Atomic Number	Coordinates (Angstroms) X	Y	Z
1	6	-1.788163	-0.725123	-2.051035
2	6	-1.371532	-2.121501	-2.378193
3	6	-0.933610	-2.245073	-0.925783
4	6	-1.506317	-0.920902	-0.677897
5	8	-1.322934	-2.787837	-3.383758
6	8	-0.278523	-3.077300	-0.295234
7	7	-2.194296	0.306027	-2.765372
8	7	-1.630584	-0.030097	0.339072
9	1	-1.918953	0.914390	0.045126
10	1	-2.267784	1.210398	-2.284622
11	6	-1.406557	-0.209441	1.695206
12	6	-1.489782	0.931171	2.524896
13	6	-1.096354	-1.461359	2.265926
14	6	-1.240500	0.837247	3.885930
15	1	-1.699435	1.902946	2.072857
16	6	-0.841075	-1.553414	3.629344
17	1	-1.038015	-2.351178	1.641387
18	6	-0.905606	-0.408290	4.428838
19	1	-1.258903	1.717247	4.527479
20	1	-0.584560	-2.508146	4.088318
21	7	-0.582107	-0.506799	5.852944
22	8	-0.806154	0.463434	6.559393
23	8	-0.087488	-1.556758	6.252112
24	6	-2.402117	0.247166	-4.207757

25	1	-1.804345	1.021378	-4.712533
26	1	-2.097713	-0.742244	-4.576356
27	1	-3.466636	0.408563	-4.450031
28	6	1.788163	0.725123	2.051035
29	6	1.371532	2.121501	2.378193
30	6	0.933610	2.245073	0.925783
31	6	1.506317	0.920902	0.677897
32	8	1.322934	2.787837	3.383758
33	8	0.278523	3.077300	0.295234
34	7	2.194296	-0.306027	2.765372
35	7	1.630584	0.030097	-0.339072
36	1	1.918953	-0.914390	-0.045126
37	1	2.267784	-1.210398	2.284622
38	6	1.406557	0.209441	-1.695206
39	6	1.489782	-0.931171	-2.524896
40	6	1.096354	1.461359	-2.265926
41	6	1.240500	-0.837247	-3.885930
42	1	1.699435	-1.902946	-2.072857
43	6	0.841075	1.553414	-3.629344
44	1	1.038015	2.351178	-1.641387
45	6	0.905606	0.408290	-4.428838
46	1	1.258903	-1.717247	-4.527479
47	1	0.584560	2.508146	-4.088318
48	7	0.582107	0.506799	-5.852944
49	8	0.806154	-0.463434	-6.559393
50	8	0.087488	1.556758	-6.252112
51	6	2.402117	-0.247166	4.207757
52	1	1.804345	-1.021378	4.712533
53	1	3.466636	-0.408563	4.450031
54	1	2.097713	0.742244	4.576356
55	8	2.003990	-2.467853	0.882978
56	1	2.613309	-3.166172	0.607811
57	8	-2.003990	2.467853	-0.882978
58	1	-2.613309	3.166172	-0.607811
59	1	1.104061	-2.768486	0.578604
60	1	-1.104061	2.768486	-0.578604

dimer of **2**

Center Number	Atomic Number	Coordinates (Angstroms) X	Y	Z
1	6	-2.075132	-0.291516	-1.852887
2	6	-2.037260	-1.740547	-2.208062
3	6	-1.472665	-1.984329	-0.819156
4	6	-1.704240	-0.569451	-0.515195
5	8	-2.272648	-2.385790	-3.200689
6	8	-0.954783	-2.954197	-0.261200
7	7	-2.303595	0.809705	-2.543115
8	7	-1.530801	0.294999	0.515442
9	1	-1.664184	1.287502	0.273183
10	1	-2.117019	1.708924	-2.082685
11	6	-1.211168	0.013520	1.839344
12	6	-0.993220	1.103341	2.707598
13	6	-1.080887	-1.291186	2.335022
14	6	-0.645434	0.882114	4.035197
15	1	-1.060008	2.122062	2.322394
16	6	-0.716219	-1.488324	3.669729
17	1	-1.235992	-2.152361	1.686940
18	6	-0.502749	-0.418728	4.535144
19	6	-2.709357	0.787537	-3.943498
20	6	2.075132	0.291516	1.852887
21	6	2.037260	1.740547	2.208062
22	6	1.472665	1.984329	0.819156
23	6	1.704240	0.569451	0.515195
24	8	2.272648	2.385790	3.200689
25	8	0.954783	2.954197	0.261200
26	7	2.303595	-0.809705	2.543115
27	7	1.530801	-0.294999	-0.515442
28	1	1.664184	-1.287502	-0.273183
29	1	2.117019	-1.708924	2.082685
30	6	1.211168	-0.013520	-1.839344
31	6	0.993220	-1.103341	-2.707598
32	6	1.080887	1.291186	-2.335022
33	6	0.645434	-0.882114	-4.035197
34	1	1.060008	-2.122062	-2.322394
35	6	0.716219	1.488324	-3.669729
36	1	1.235992	2.152361	-1.686940
37	6	0.502749	0.418728	-4.535144
38	6	2.709357	-0.787537	3.943498
39	8	1.524322	-2.826186	0.645496
40	1	1.948646	-3.667856	0.431921
41	8	-1.524322	2.826186	-0.645496
42	1	-1.948646	3.667856	-0.431921
43	1	0.558617	-2.956032	0.442155
44	1	-0.558617	2.956032	-0.442155
45	1	0.214986	0.586249	-5.572468
46	1	-0.214986	-0.586249	5.572468

47	6	-0.430645	2.038089	4.983935
48	6	0.430645	-2.038089	-4.983935
49	6	-0.453023	-2.902572	4.119367
50	6	0.453023	2.902572	-4.119367
51	9	-0.374982	-3.012891	5.454081
52	9	0.374982	3.012891	-5.454081
53	9	-1.388471	-3.756954	3.685018
54	9	1.388471	3.756954	-3.685018
55	9	0.733920	-3.340664	3.620933
56	9	-0.733920	3.340664	-3.620933
57	9	-1.436283	2.107312	5.880330
58	9	1.436283	-2.107312	-5.880330
59	9	-0.374451	3.216424	4.352942
60	9	0.374451	-3.216424	-4.352942
61	9	0.704134	1.880668	5.688010
62	9	-0.704134	-1.880668	-5.688010
63	1	-3.785973	1.013038	-4.042446
64	1	3.785973	-1.013038	4.042446
65	1	-2.141368	1.544824	-4.500185
66	1	2.141368	-1.544824	4.500185
67	1	-2.510499	-0.206331	-4.366968
68	1	2.510499	0.206331	4.366968

14. References

S1 C. López, M. Ximenis, F. Orvay, C. Rotger and A. Costa, *Chem Eur. J.*, 2017, **23**, 7590-7594.

S2 M. Lee, L. Zhang, Y. Park and H. Park, *Tetrahedron*,2012, **68**, 1452-1459.

S3 N. Fu, A. D. Allen, S. Kobayashi, T. T. Tidwell, S. Vukovic, S. Arumugam, V. V. Popik and M. Mishima *J. Org. Chem*., 2007, **72**, 1951-1956.

S4 T. E. Kaiser, V. Stepanenko and F. Würthner, *J. Am. Chem. Soc.*, 2009, **131**, 6719-6732.