Supplementary Material (ESI) for Chemical Communications

Supramolecular Gel Formation and Self-correction Induced by Aggregation-driven Conformational Changes

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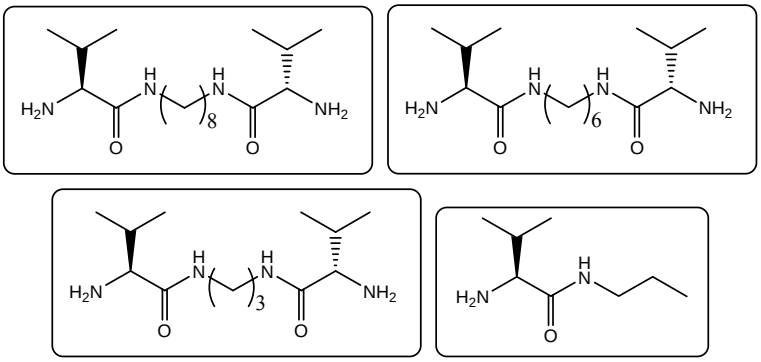
Electronic Supporting Information

Synthetic procedures:

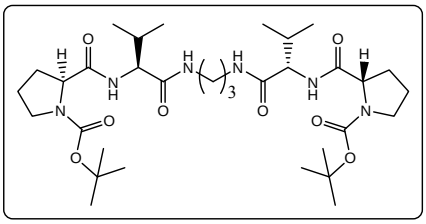
Preparation of diamino amides shown below has been previously reported[1]:



General procedure for the preparation of N-Boc-protected compounds **1a-c**:

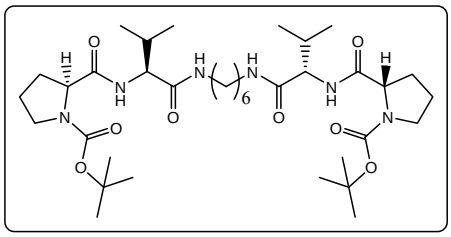
A solution of diamino amide (5.51 mmol) in 100 mL of dry DME was added dropwise over a solution of Boc-L-Pro-OSuc (11.50 mmol) in 100 mL of dry DME. The mixture was stirred at room temperature for 24 h and then at 40 ºC for 5 h. Solvent was evaporated under vacuum and the resulting white solid was dissolved in 50 mL of dichloromethane and washed with $NaHCO_3$ (3 x 15 mL). Afterwards the organic layers were dried (Na_2SO_4) and the solvent was evaporated under vacuum to yield N-Boc-protected **1a-c** as a white solids.

N-Boc-protected **1a**



Yield 89 %; m.p. 163 ºC; IR (KBr) ν = 3303, 2970, 2876, 1702, 1649, 1545 cm^{-1}; ^1H NMR (500 MHz, DMSO-d6): δ = 0.89 (12 H, br, m), 1.34-1.54 (20H, br, m), 1.76-2.12 (10H, br, m), 3.03-3.23 (4H, br, m), 3.30-3.48 (4H, br, m), 4.11 (2H, dd, J = 8.7, 7.9 Hz), 4.20-4.31 (2H, br, m), 7.72 (2H, br, d, J = 7.8 Hz), 7.90-8.08 (2H, br, m) ppm; ^{13}C NMR (300 MHz, DMSO-d6): δ = 19.157, 19.904, 23.657, 28.670, 29.830, 31.295, 31.790, 36.901, 47.224, 58.599, 60.125, 79.099, 154.055, 171.411, 172.868 ppm. ESI-MS *(m/z)* = 335.3 $[M + 2H]^{2+}$, 667.6 $[M + H]^+$, 689.6 $[M + Na]^+$, 705.5 $[M + K]^+$.

N-Boc-protected **1b:**

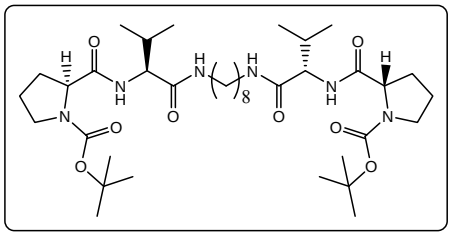


Yield = 83 %; m.p. 173 ºC; IR (KBr) ν = 3299, 2968, 2874, 1702, 1647, 1545 cm^{-1}; ^1H NMR (500 MHz, DMSO-d6): δ = 0.89 (12 H, br, m), 1.26-1.52 (26H, br, m), 1.76-2.21 (10H, br, m), 3.02-3.18 (4H, br, m), 3.30-3.47 (4H, br, m), 4.13 (2H, dd, J = 8.1, 7.9 Hz),

[1] Becerril, J; Bolte, M.; Burguete, M.I.; Galindo, F.; García-España, E.; Luis, S.V.; Miravet, J.F. *J. Am. Chem. Soc.* **2003**, *125*, 6677-6686.

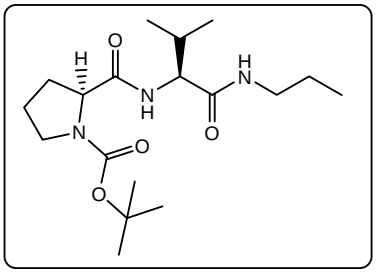
4.20-4.31 (2H, br, m), 7.68 (2H, br, d, J = 8.5 Hz), 7.90-8.03 (2H, br, m) ppm; ^{13}C NMR (500 MHz, DMSO-d6): δ = 19.133, 19.912, 23.643, 26.701, 28.655, 29.650, 31.386, 31.813, 38.961, 47.223, 58.484, 60.177, 79.105, 154.067, 171.255, 172.773 ppm; ESI-MS *(m/z)* = 709.7 $[M + H]^+$, 731.6 $[M + Na]^+$, 747.6 $[M + K]^+$.

N-Boc-protected **1c:**



Yield = 85 %; m.p. = 109 ºC. IR (KBr) ν = 3307, 2968, 2872, 1703, 1644, 1543 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d6): δ = 0.90 (12 H, br, m), 1.25-1.50 (30H, br, m), 1.75-2.20 (10H, br, m), 2.98-3.16 (4H, br, m), 3.29-3.47 (4H, br, m), 4.13 (2H, dd, J = 8.0, 7.8 Hz), 4.22-4.29 (2H, br, m), 7.67 (2H, br, d, J = 7.9 Hz), 7.87-8.05 (2H, br, m) ppm; ^{13}C NMR (300 MHz, DMSO-d6): δ = 19.111, 19.897, 23.650, 26.915, 28.663, 29.303, 29.607, 31.379, 31.798, 38.984, 47.232, 58.469, 60.163, 79.106, 154.062, 171.228, 172.761 ppm. ESI-MS *(m/z)* = 737.6 $[M + H]^+$, 759.6 $[M + Na]^+$, 775.7 $[M + K]^+$.

Synthesis of N-Boc-protected **2:**



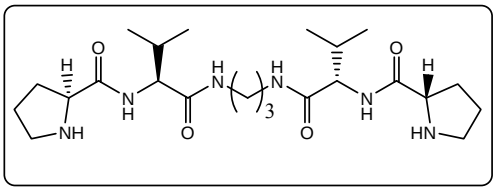
A solution of amino amide (6.32 mmol) in 100 mL of dry DME was added dropwise over a solution of Boc-L-Pro-OSuc (6.57 mmol) in 100 mL of dry DME. The mixture was stirred at room temperature for 24 h and then at 40 ºC for 5 h. Solvent was evaporated under vacuum and the resulting white solid was dissolved in 50 mL of dichloromethane and washed with $NaHCO_3$ (3 x 15 mL). Afterwards the organic layers were dried (Na_2SO_4) and the solvent was evaporated under vacuum to yield N-Boc-protected **2c** as a white solid.
Yield 84 %; m.p. = 104-105 ºC; IR (KBr) ν = 3298, 2966, 2876, 1703, 1647, 1545 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d6): δ = 0.86 (9 H, m), 1.39 (9H, s), 1.41-1.51 (2H, m), 1.77-2.23 (5H, m), 3.02-3.16 (2H, m), 3.32-3.52 (2H, m), 4.11-4.19 (1H, dd, J = 8.1, 7.9 Hz), 4.21-4.31 (1H, m), 7.69 (1H, br, d, J = 8.6 Hz), 7.91-8.06 (1H, br, m) ppm;^{13}C NMR (500 MHz, DMSO-d6): δ = 12.016, 19.134, 19.927, 22.949, 23.658, 28.647, 31.394, 31.813, 40.877, 47.232, 58.507, 60.201, 79.113, 154.075, 171.309, 172.782 ppm; ESI-MS *(m/z)* = 356.4 $[M + H]^+$, 378.4 $[M + Na]^+$, $[M + K]^+$.

Synthesis of compounds **1a-c** and **2.**

N-protected compounds (3.00 mmol) were dissolved in dichloromethane and after addition of 15 mL of TFA the mixture was stirred at room temperature for 2 h. The solvent was evaporated under vacuum and then the resulting crude oil was dissolved in water (50 mL). The solution was treated with NaOH (pH =12), and extracted with

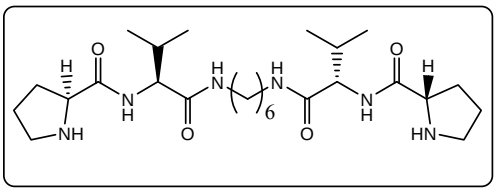
chloroform (3 x 15 mL). The organic layers were washed with water and dried (Na_2SO_4). Solvent was evaporated under vacuum to yield compounds **1a-c** and **2** as white solids.

Compound **1a:**



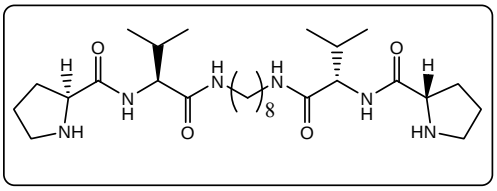
Yield 84 %, m.p. 170 ºC; IR (KBr) ν = 3289, 2959, 2870,1638, 1545 cm^{-1};^{1}H NMR (500 MHz, CD_3CN): δ = 0.89 (12 H, dd, J =19.9, 6.8 Hz), 1.53-1.60 (4H, m), 1.65-1.72 (4H, m), 1.76-1.84 (2 H, m), 2.02-2.14 (4 H, m), 2.31 (2H, br, s), 2.84-2.88 (2H, m), 3.12-3.20 (4 H, m), 3.69 (2H, dd, J = 8.8, 4.8 Hz), 4.06 (2H, dd, J = 8.8, 5.5 Hz), 6.97 (2H, br, s), 8.08 (2H, br, d, 8 Hz) ppm; ^{13}C NMR (500 MHz, CD_3CN): δ = 17.171, 19.071, 26.258, 29.264, 30.752, 30.927, 35.986, 47.141, 58.002, 60.916, 171.720, 175.321 ppm; ESI-MS *(m/z)* = 234 $[M+2]^{2+}$ $C_{23}H_{42}N_6O_4$.

Compound **1b:**



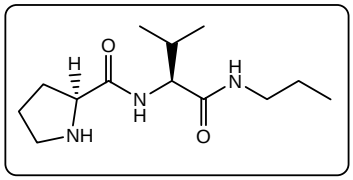
Yield 87 %; m.p. = 190 ºC; IR (KBr) ν =3285, 2956, 2861, 1641, 1541 cm^{-1}; ^{1}H NMR (500 MHz, CD_3CN): δ = 0.90 (12 H, dd, J =19.8, 7 Hz), 1.28-1.34 (4H, m), 1.42-1.49 (4H, m), 1.64-1.71 (4 H, m), 1.77-1.84 (2H, m), 2.02-2.10 (4 H, m), 2.22 (2H, br, s), 2.82-2.87 (2H, m), 3.00-3.04 (2H, m), 3.12-3.18 (4H, m) 3.65 (2H, dd, J = 4.5, 9.4 Hz), 4.09 (2H, dd, J = 8.9, 6.0 Hz), 6.77 (2H, br, s), 8.08 (2H, br, d, J = 6.70 Hz) ppm; ^{13}C NMR (500 MHz, CD_3CN): δ = 17.333, 19.047, 22.706, 26.061, 26.298, 29.219, 30.875, 31.348, 38.672, 47.209, 57.867, 60.903, 171.289, 175.149 ppm; ESI-MS *(m/z)* = 256 $[M+2]^{2+}$.

Compound **1c:**



Yield 79 %; m.p. 177 ºC; IR (KBr) ν = 3289, 2957, 2854, 1640, 1540 cm^{-1}; ^{1}H NMR (500 MHz, CD_3CN): δ = 0.90 (12 H, dd, J =19.4, 6.9 Hz), 1.25-1.36 (8H, m), 1.41-1.50 (4H, m), 1.65-1.72 (4 H, m), 1.78-1.85 (2H, m), 2.03-2.10 (4 H, m), 2.29 (2H, br, s), 2.83-2.88 (2H, m), 3.00-3.04 (2H, m), 3.12-3.19 (4H, m) 3.67 (2H, dd, J = 4.6, 9.3 Hz), 4.01 (2H, dd, J = 9.0, 6.2 Hz), 6.77 (2H,br, s), 8.08 (2H, br, d, J = 9.04 Hz) ppm; ^{13}C NMR (500 MHz, CD_3CN): δ = 17.289, 19.087, 22.706, 26.291, 26.467, 28.839, 29.289, 30.836, 31.410, 38.955, 47.217, 57.791, 60.896, 171.188, 175.102 ppm; ESI-MS *(m/z)*= 269 $[M+2]^{2+}$.

Compound **2:**



Yield = 79 %; m.p. = 127 ºC; IR (KBr) ν = 3303, 2963, 2873, 1467, 1518 cm^{-1}; ^{1}H NMR (500 MHz, CD_3CN): δ = 0.86-0.92 (9 H, m), 1.45-1.52 (2 H, m), 1.66-1.71 (2 H, m), 1.78-1.84 (1 H, m), 2.02-2.10 (2H, m), 2.39 (1H, br, s), 2.83-2.87 (1H, m), 3.00-3.05 (1H, m), 3.07-3.19 (2H, m), 3.67 (1H, dd, J = 9.2, 5Hz), 4.11 (1 H, dd, J =8.9, 6.1 Hz), 6.70 (1H, br, s), 8.07 (1H, br, d, J = 6.70 Hz) ppm; ^{13}C NMR (500 MHz, CD_3CN): δ = 10.971, 173.323, 19.032, 22.706, 26.288, 30.878, 31.484, 40.838, 47.205, 57.757, 60.878, 171.231, 175.089 ppm; ESI-MS *(m/z)* = 256 $[M+H]^+$, 278 $[M+Na]^{+.}$

Gelation studies.

Typically, the desired amount of the gelator in the corresponding solvent was heated in a screw-capped vial until it was completely dissolved and, afterwards, it was left to cool by two different methods:

Spontaneous cooling:
The sample was cooled at room temperature during 24 h and afterwards it was stabilized at r.t. during 12 h.

Slow cooling:
The sample was cooled in a thermoregulated bath (0.5 ºC / min) and stabilized at r.t. during 12 h.

To determine the minimum gel concentration values reported, 5-20 mmol of the studied compounds were dissolved in 1 mL of hot solvent in a screw-capped cylindrical glass vial (diameter = 2 cm). The formation of a gel was checked by turning the vial upside down. Thus, when, upon vial inversion, all the solvent remains entrapped within the gel and does not fall-down we consider it as a gel (G).

Table S1. Gelation of compounds **1a-c** in different organic solvents after spontaneous cooling at 25 ºC.[a]

	1a	**1b**	**1c**
Tetrahydrofuran	G (30)	S	S
Dimethoxyethane	G (24)	S	S
Toluene	G (50)	G (7)	G (11)
Ethyl acetate	G (6)	G (7)	G (9)
Acetonitrile	G (34)	G (16)	G (14)

a. G: gel; S: soluble. Minimum gel concentration (mM) in parentheses.

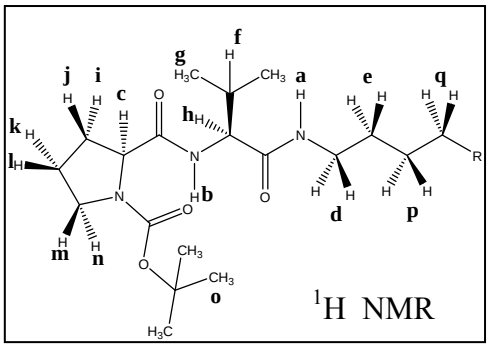
Scanning Electron Microscopy. Scanning electron micrographs were taken in a LEO 440I microscope equipped with a digital camera. Samples of the xerogels were prepared by placing the gel on top of a tin plate and, after vacuum drying of the solvent, sputtering with Au/Pd in a Polaron SC7610 Sputter Coater from Fisons Instruments.

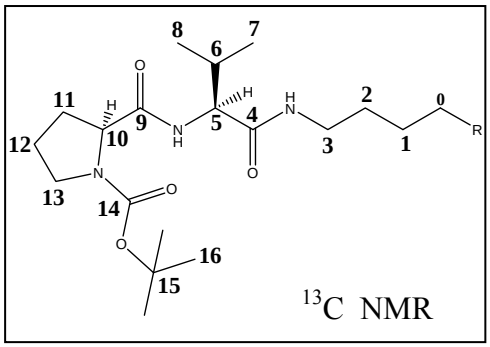
NMR. ^{1}H and ^{13}C NMR spectra were recorded in a Varian Mercury 300 MHz spectrometer at 30 ºC. NOE (1D-NOESY and NOESY) measurements were carried out in a Varian Inova 500 MHz spectrometer. Gel samples were prepared by transferring a hot solution of the gelator in CD_3CN to the NMR tube. Upon cooling to room temperature a gel was formed and the sample obtained was analyzed using the same parameters as for solution NMR (except in the case of NOE experiments where the mixing time for gel samples was 20 ms -to avoid spin diffusion- and for solutions 500 ms).

Molecular modeling. The models reported were obtained by molecular mechanics calculations performed with MACROMODEL 8.0 using AMBER* as force-field and a GB/SA simulation of chloroform as solvent. The structures of the isolated molecules correspond to minimum energy conformers found after exhaustive Monte Carlo conformational search. The models for the aggregates were energetically minimized.

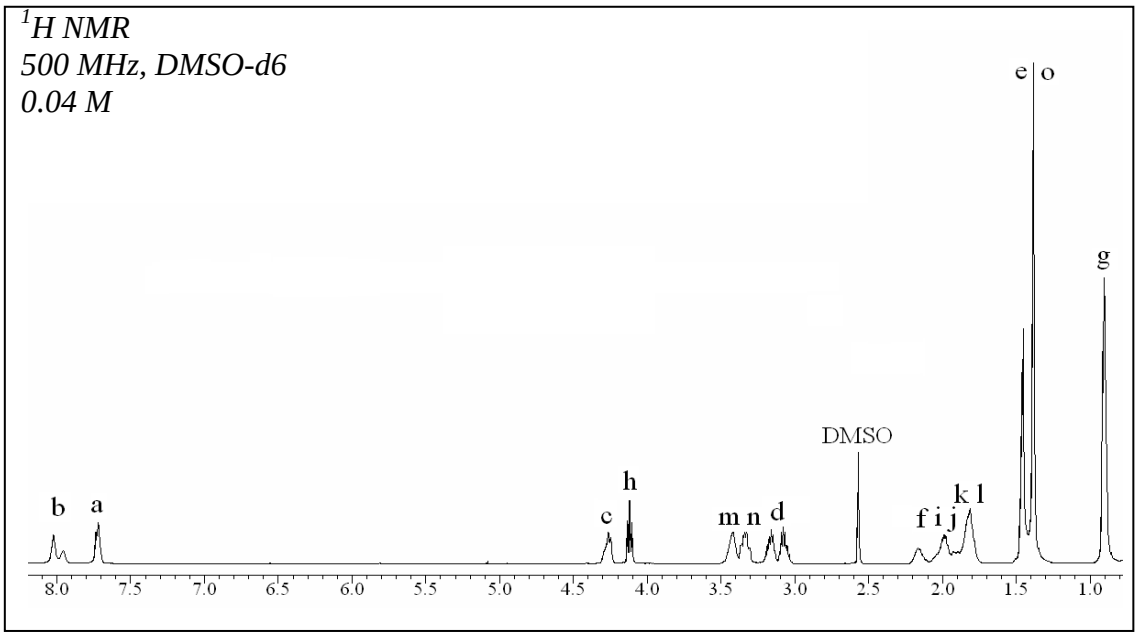
X-ray powder diffraction. Data collection was performed at room temperature on a Siemens D5000 diffractometer using Cu-K_α radiation. Samples of the powdered solids were placed on a quartz sample holder and data were collected for 2θ values between 3º and 35º with a step size of 0.05º and a time step of 20 s.

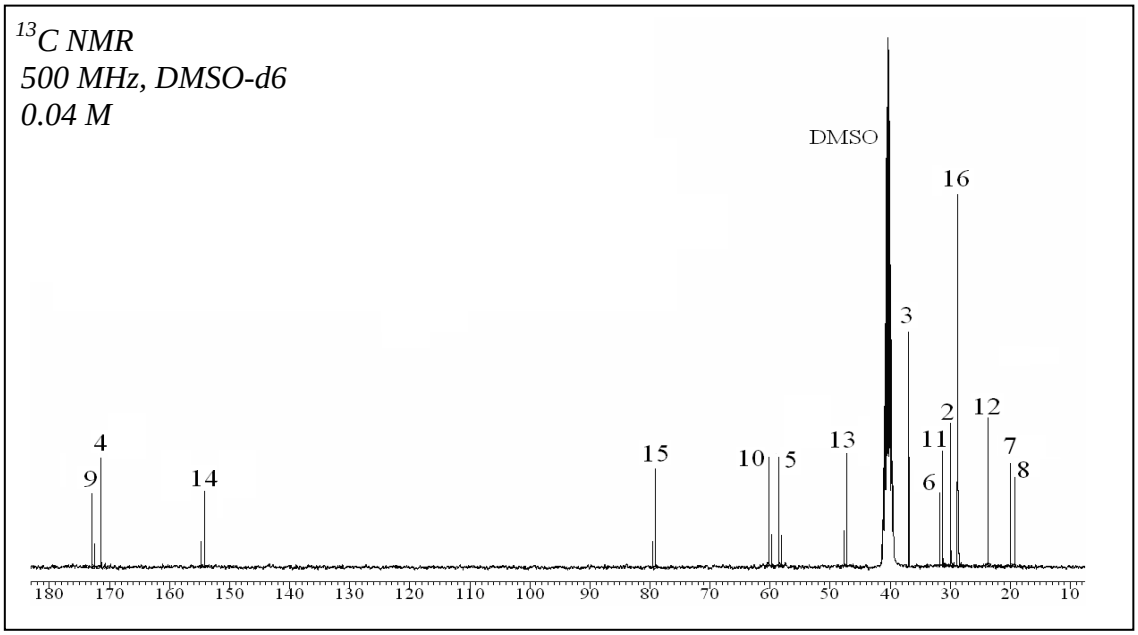
CD spectroscopy. CD spectra were recorded in a Jasco J-810 spectropolarimeter equipped with a Peltier heating device. The samples were prepared in quartz cuvettes of 1 mm and 0.5 mm of path length.



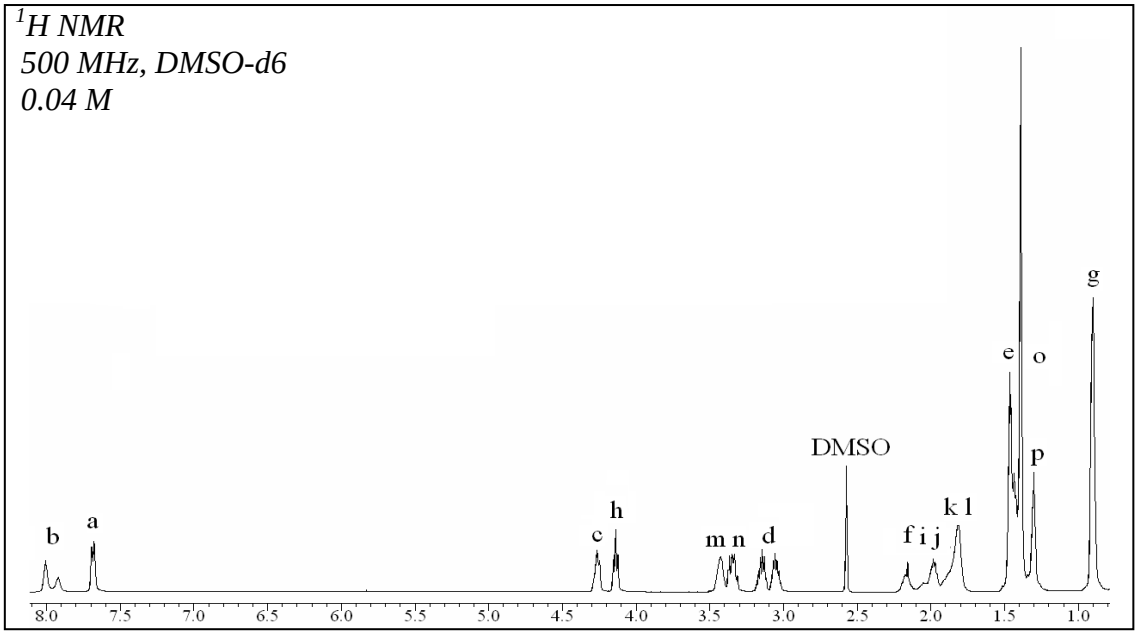


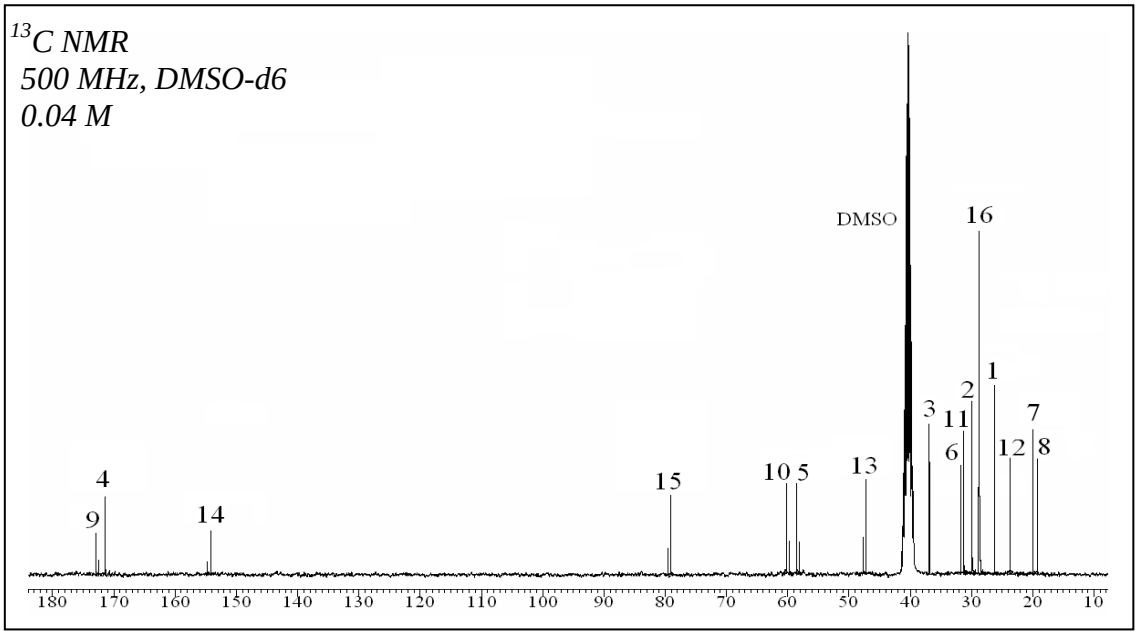
N-Boc-protected **1a.**



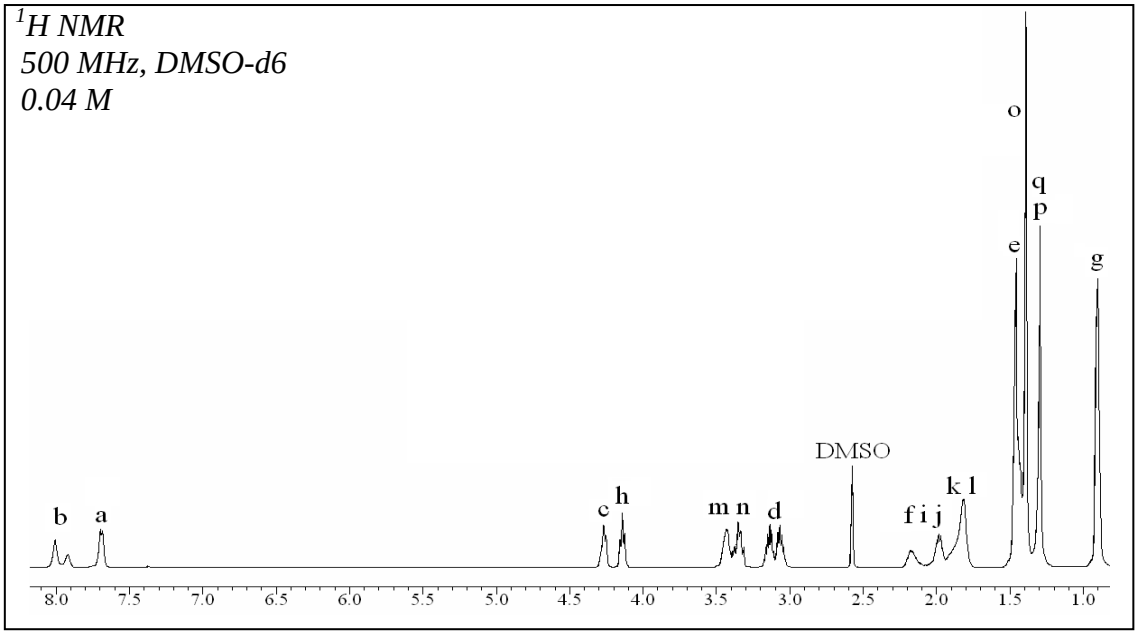


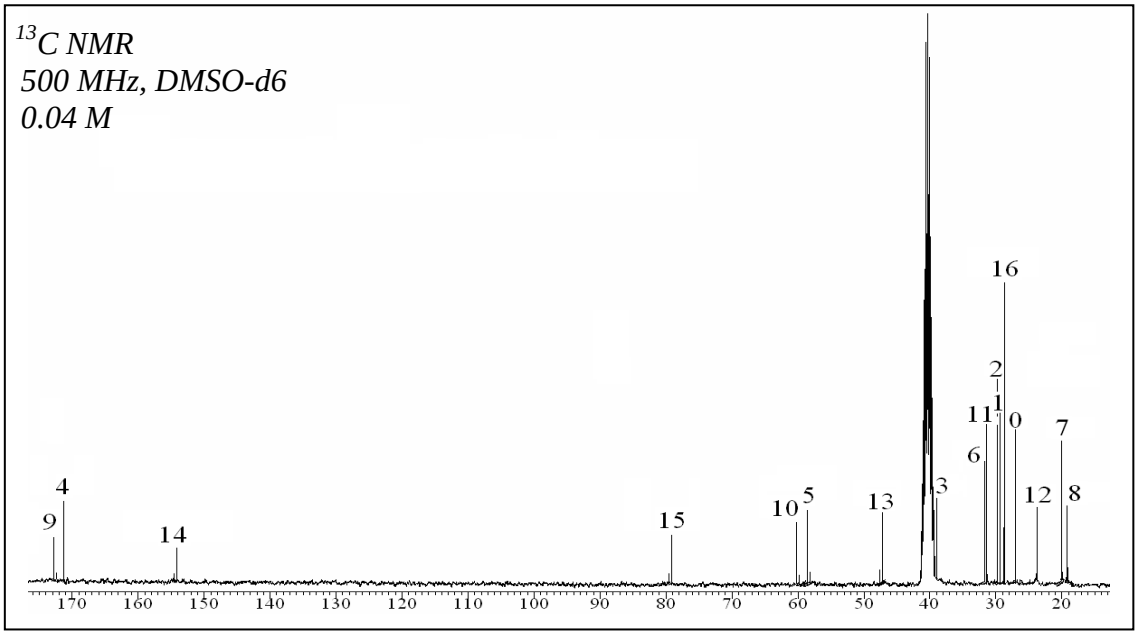
N-Boc-protected **1b.**





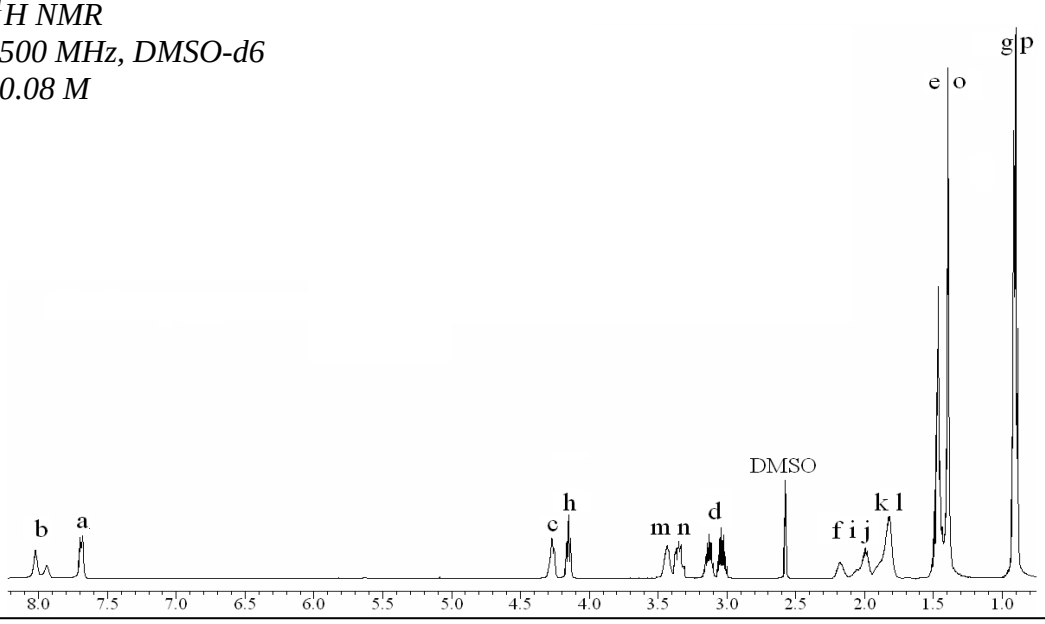
N-Boc-protected **1c.**



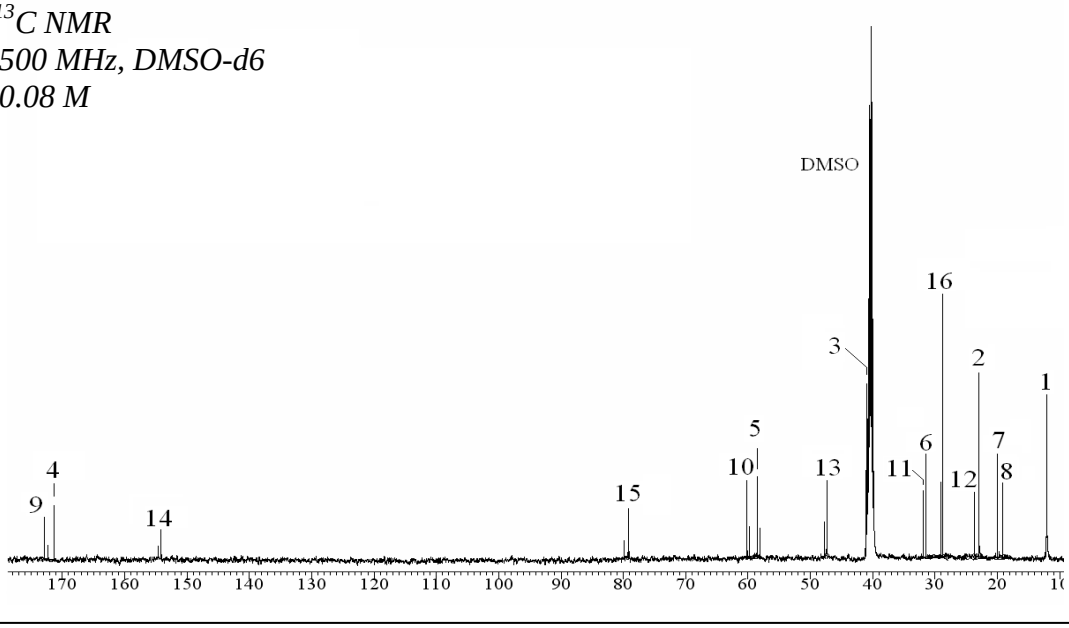


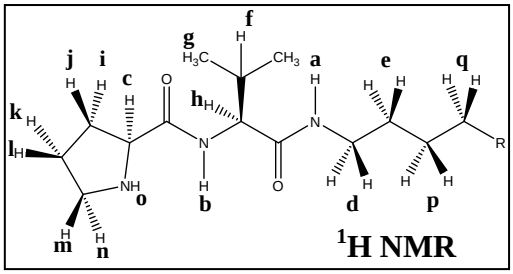
N-Boc-protected **2.**

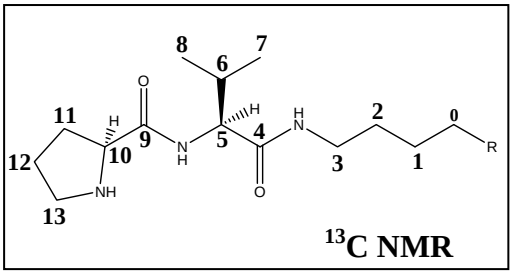
^{1}H NMR
500 MHz, DMSO-d6
0.08 M



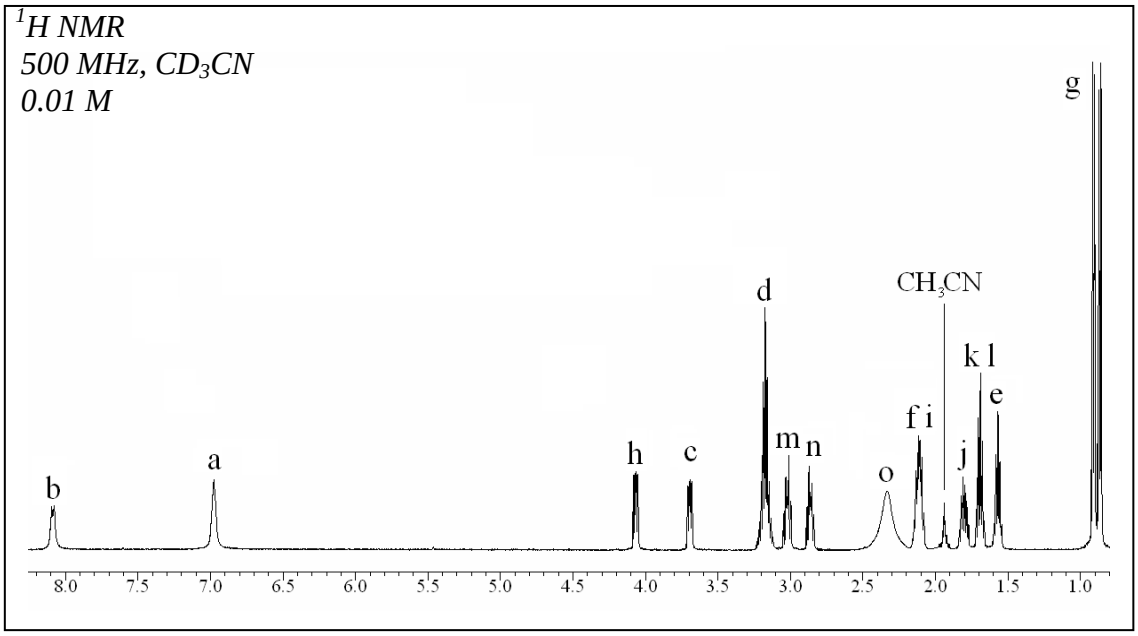
^{13}C NMR
500 MHz, DMSO-d6
0.08 M

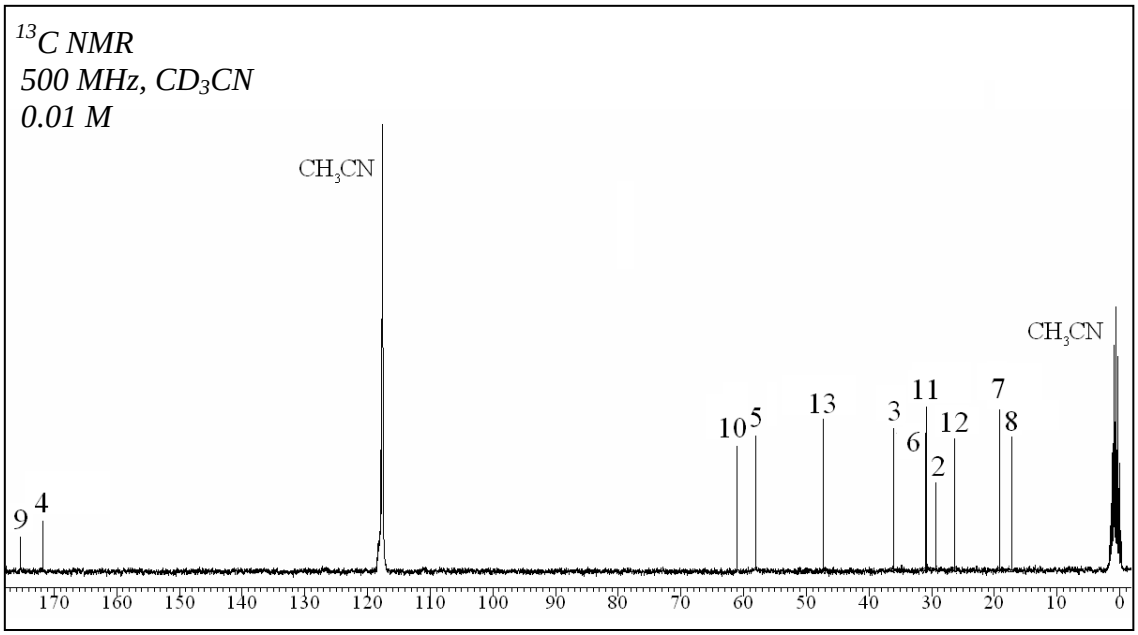



^{1}H NMR

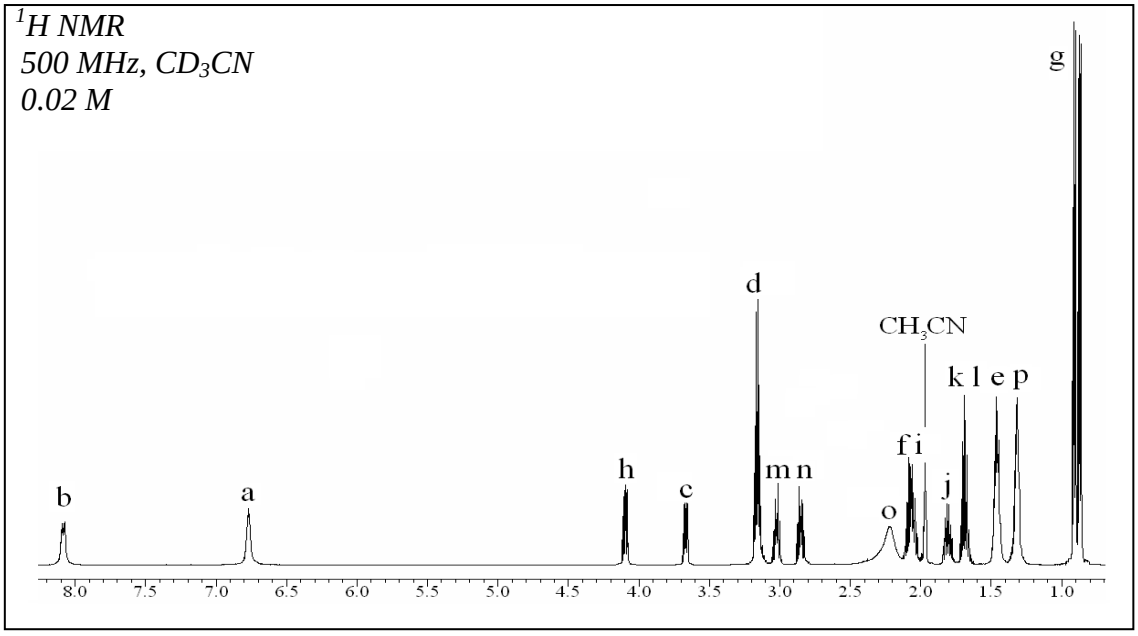

^{13}C NMR

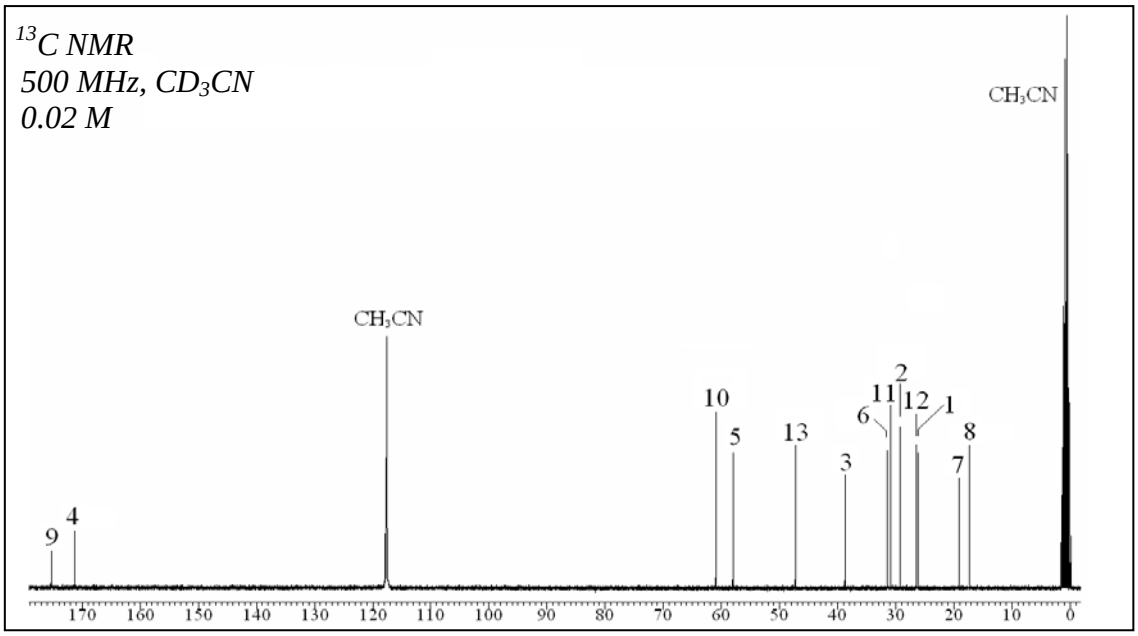
Compound 1a:


^{1}H NMR
500 MHz, CD_3CN
0.01 M
CH_3CN

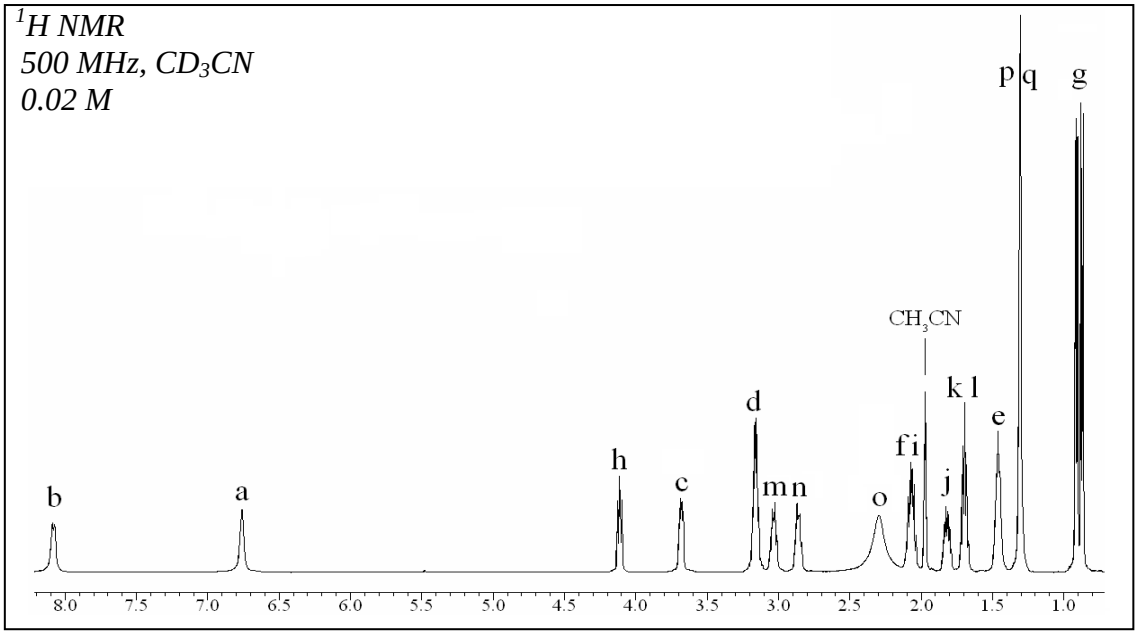

^{13}C NMR
500 MHz, CD_3CN
0.01 M
CH_3CN
CH_3CN

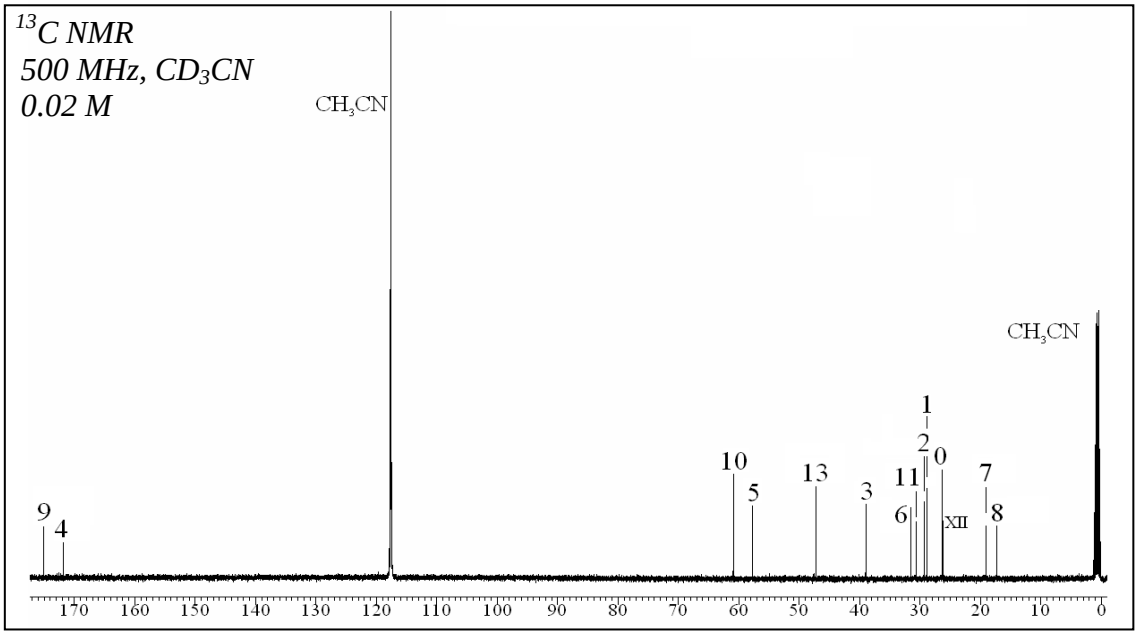
Compound 1b:


^{1}H NMR
500 MHz, CD_3CN
0.02 M
g
d
CH_3CN
k l e p
f i
h
m n
j
b
a
c
o
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0

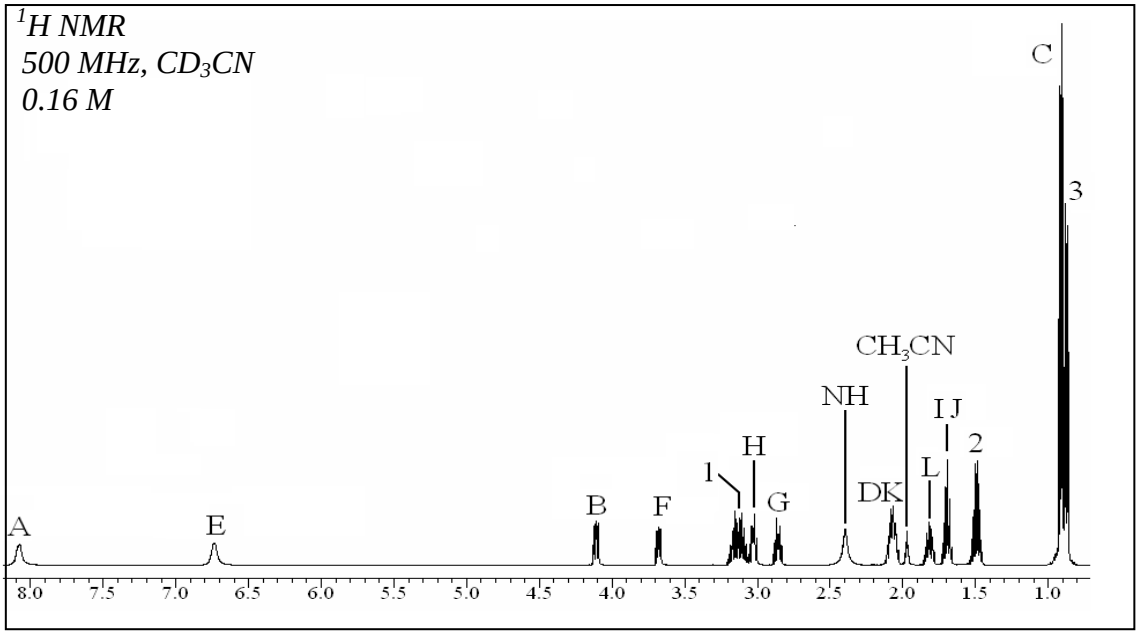

^{13}C NMR
500 MHz, CD_3CN
0.02 M
CH_3CN
CH_3CN
10
2
11
12
1
6
5
13
8
3
7
9
4
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

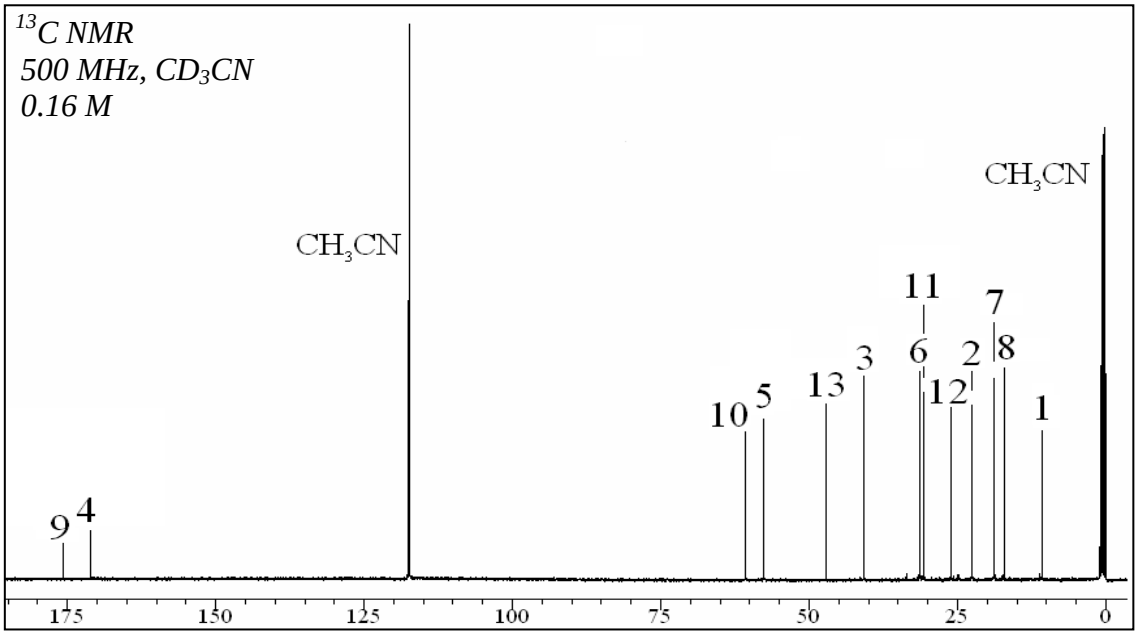
Compound 1c:


^{1}H NMR
500 MHz, CD_3CN
0.02 M
p q g
CH_3CN
k l
d
e
f i
h
j
c
m n
b
a
o
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0

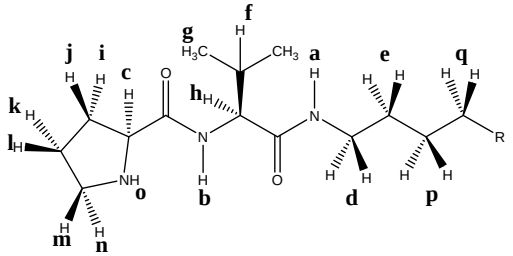

^{13}C NMR
500 MHz, CD_3CN
0.02 M
CH_3CN
CH_3CN
1
2
0
10
13
11
7
5
3
6
XII
8
9
4
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

Compound 1d:


^{1}H NMR
500 MHz, CD_3CN
0.16 M
C
3
CH_3CN
NH
IJ
H
2
1
L
DK
G
B
F
A
E
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

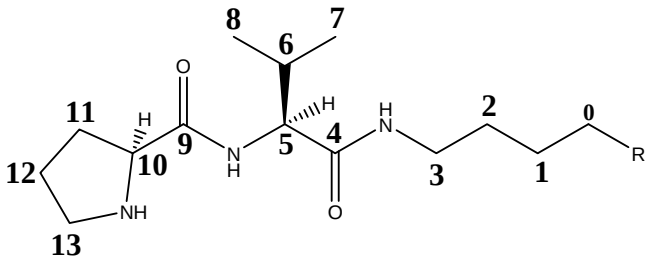

^{13}C NMR
500 MHz, CD_3CN
0.16 M
CH_3CN
CH_3CN
11
7
6
2
8
3
13
12
10
5
1
9
4
175
150
125
100
75
50
25
0

^{1}H-RMN
CD_3CN



	Compound **1a** 0.002 M	Compound 1**b** 0.001 M	Compound 1**c** 0.002 M	Compound **2** 0.004 M
Signal	δ (ppm)	δ (ppm)	δ (ppm)	δ (ppm)
a	6.98	6.71	6.72	6.61
b	8.09	8.07	8.07	8.04
c	3.67	3.67	3.69	3.68
d	3.17	3.15	3.16	3.13
e	1.54	1.45	1.46	1.49
f	2.08	2.05	2.07	2.05
g	0.89	0.90	0.87	0.90
h	4.05	4.08	4.10	4.10
i	2.08	2.05	2.07	2.05
j	1.78	1.80	1.82	1.80
k	1.67	1.69	1.70	1.69
l	1.67	1.69	1.70	1.69
m	3.00	3.02	3.04	3.02
n	2.87	2.85	2.87	2.84
o	2.15	2.15	2.18	2.15
p	---	1.32	1.30	0.87
q	---	---	1.30	---

^{13}C-RMN CD_3CN



	Compound **1a** 0.004 M	Compound 1**b** 0.004 M	Compound 1**c** 0.004 M	Compound **2** 0.004 M
Signal	δ (ppm)	δ (ppm)	δ (ppm)	δ (ppm)
0	---	---	26.467	---
1	---	26.061	28.839	10,927
2	29.278	29.219	29,289	22,694
3	35.973	38.672	38,955	40,820
4	171.715	171.289	171,188	171,193
5	58.003	57.867	57,791	57,830
6	30.929	31.348	31,410	31,382
7	19.073	19.047	19,089	19,015
8	17.167	17.333	17,289	17,249
9	175.278	175.149	175,102	174,854
10	60.923	60.903	60,896	60,850
11	30.753	30.875	30,836	30,835
12	26.261	26.298	26,291	26,237
13	47.149	47.209	47,217	47,201

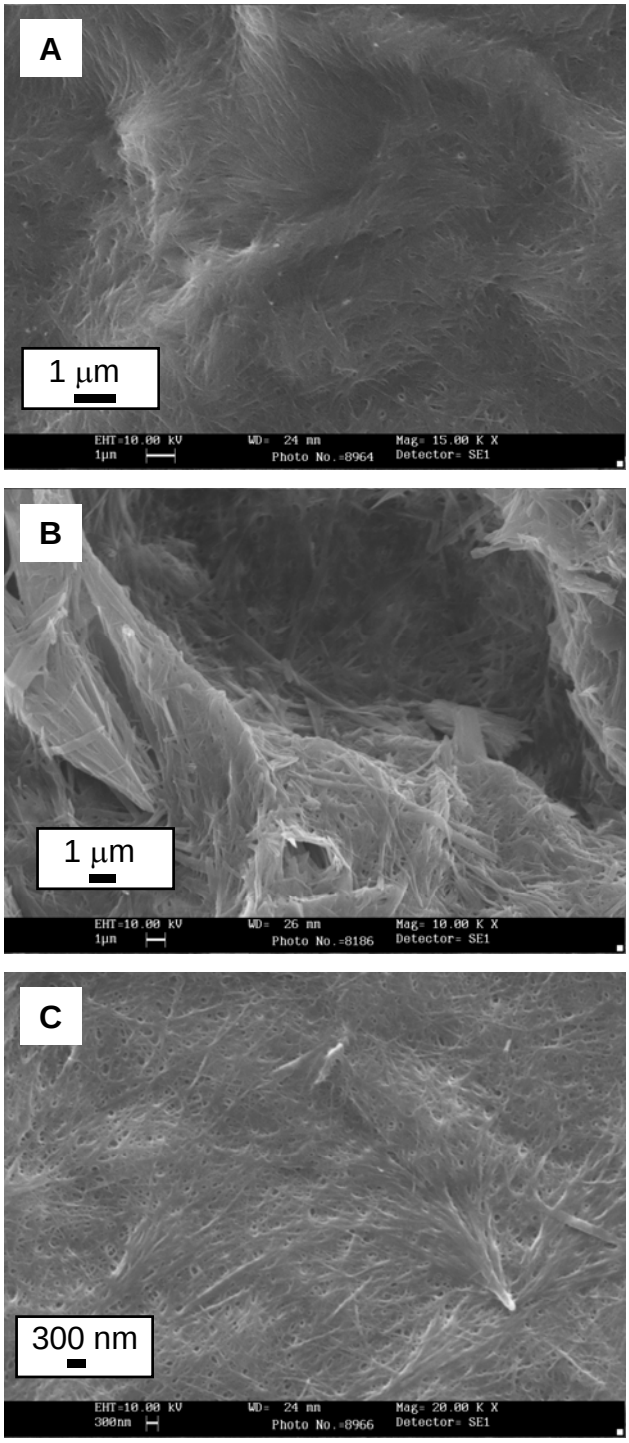


Figure S1. SEM images of xerogels of compound **1b**: A) CH_3CN, spontaneous cooling; B) *idem*, slow cooling; C) toluene, spontaneous cooling.

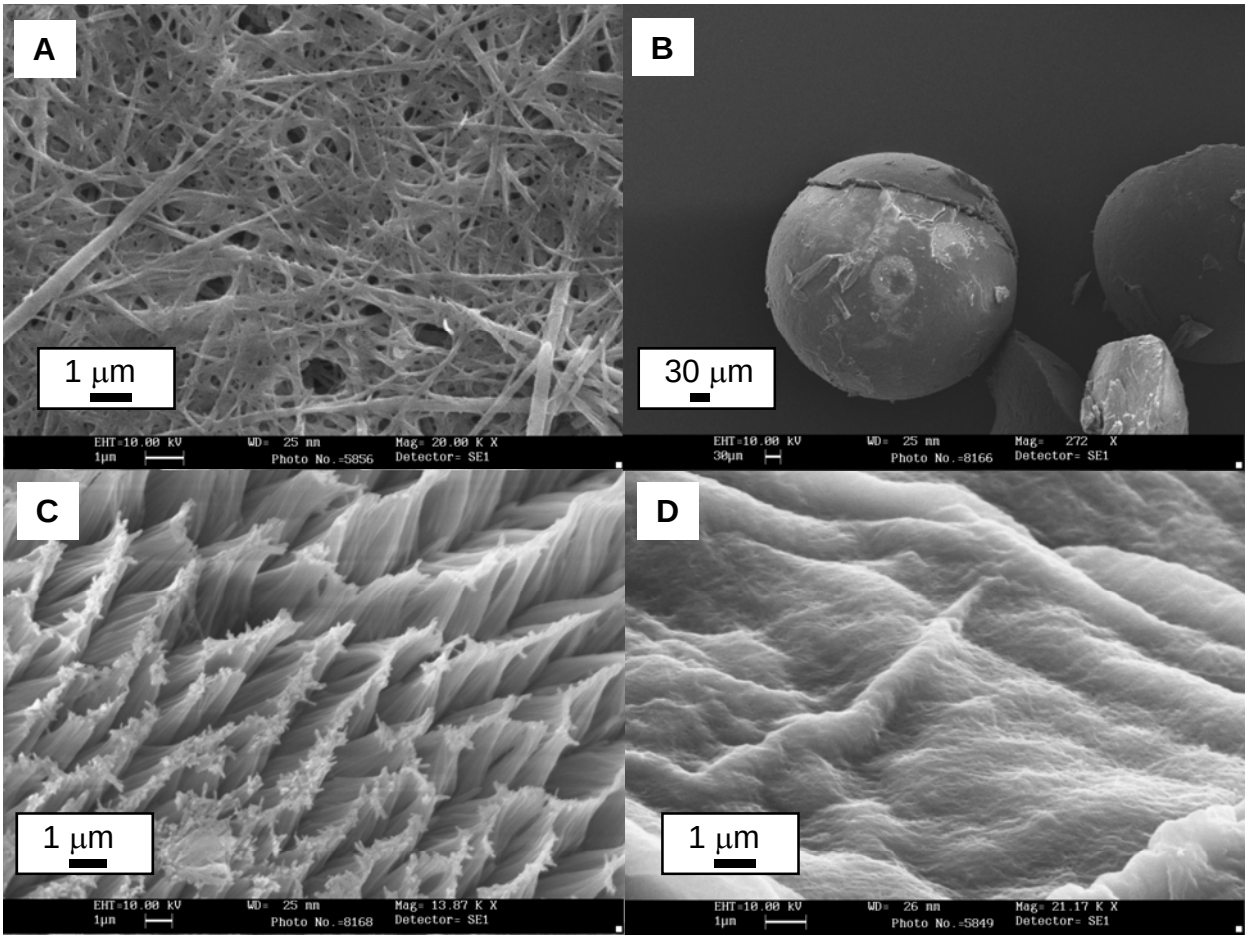


Figure S2. SEM images of xerogels and crystalline precipitates of compound **1c**: A) CH_3CN, spontaneous cooling; B,C) *idem*, slow cooling; D) EtOAc, spontaneous cooling.

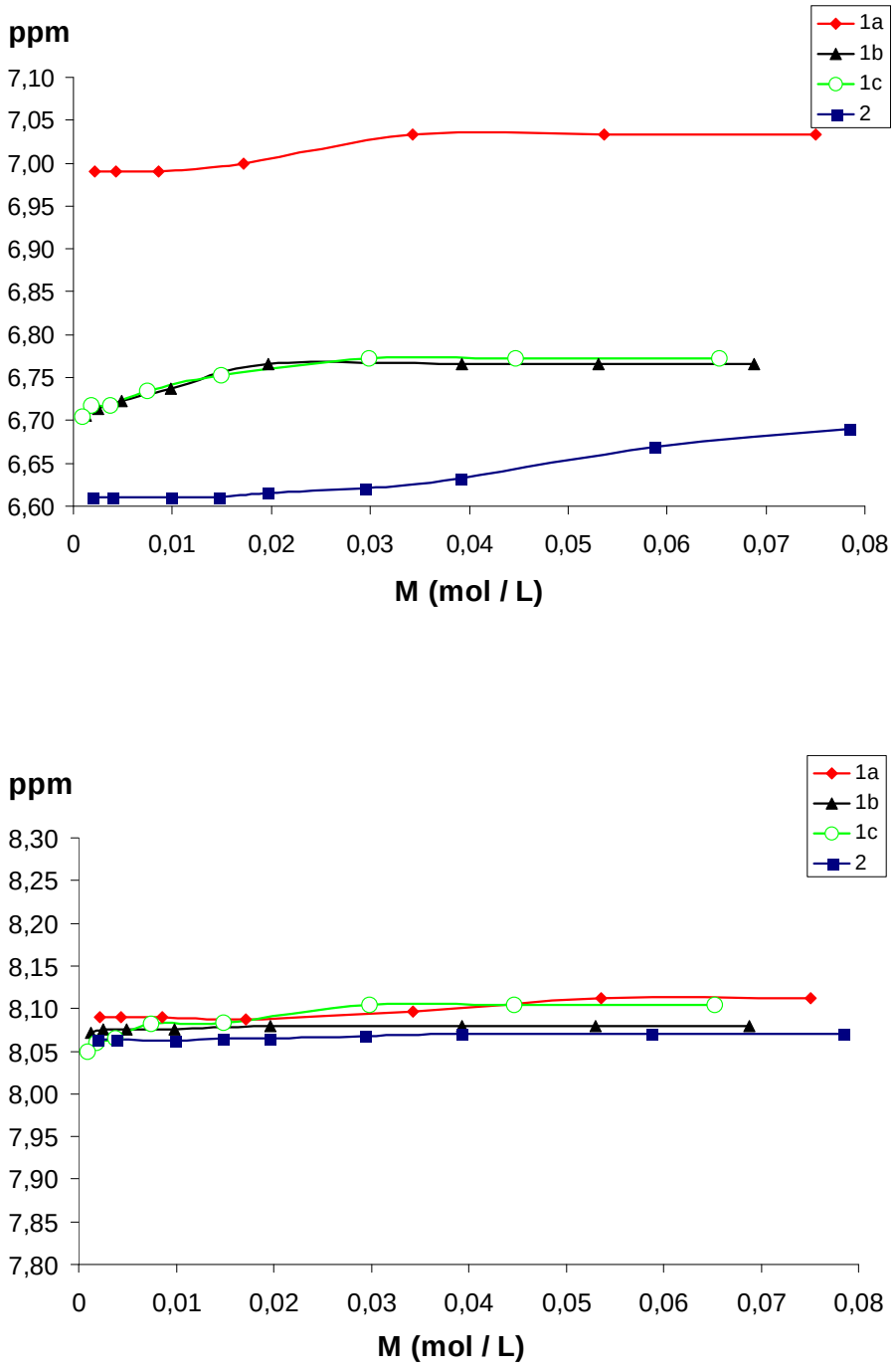
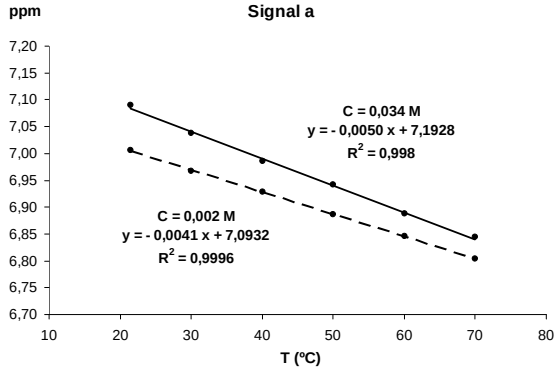
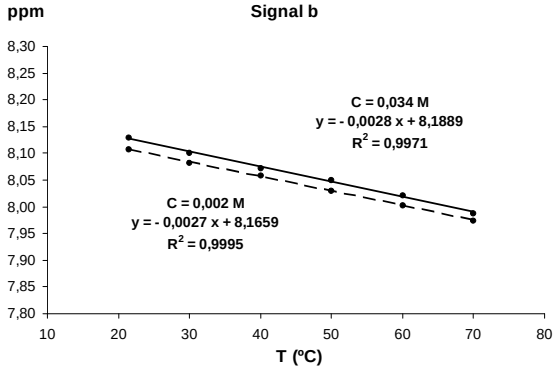


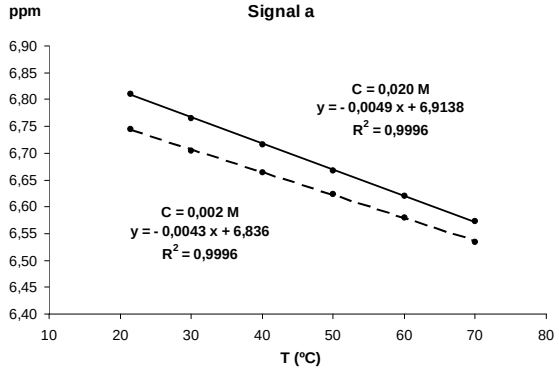
Figure S3. $\Delta\delta$ vs concentration for the amide signals **a** and **b** of compounds **1a-c** and **2** (CD_3CN, 30 ºC)

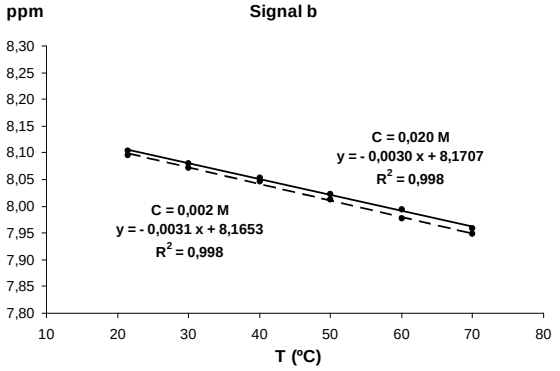
Compound 1a



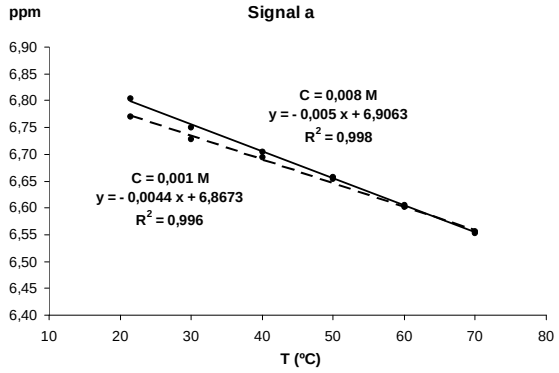


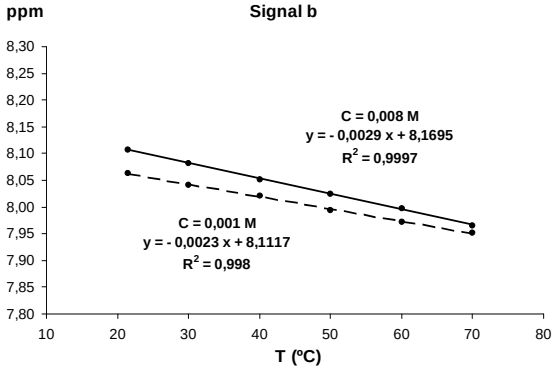
Compound 1b



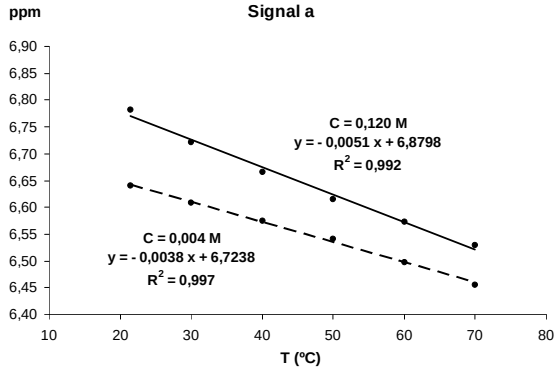


Compound 1c





Compound 2



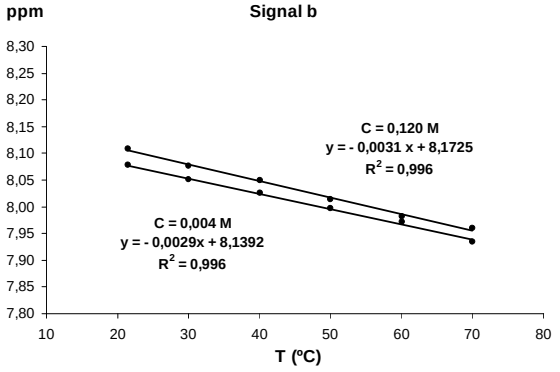


Figure S4. $\Delta\delta$ vs temperature for the amide signals **a** and **b** of compounds **1a-c** and **2** (CD_3CN, 30 ºC)

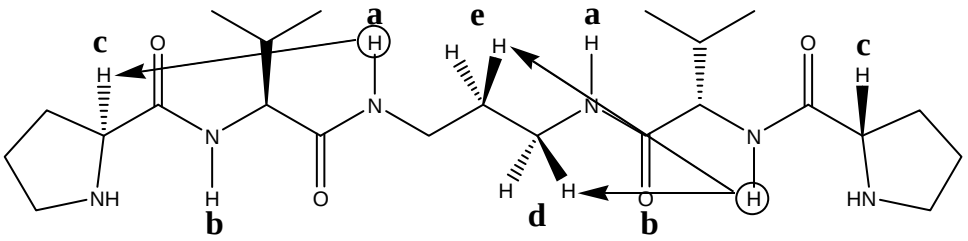


Figure S5. Informative NOE contacts for non-aggregated solutions of compounds **1a** (CD_3CN, 30 ºC)

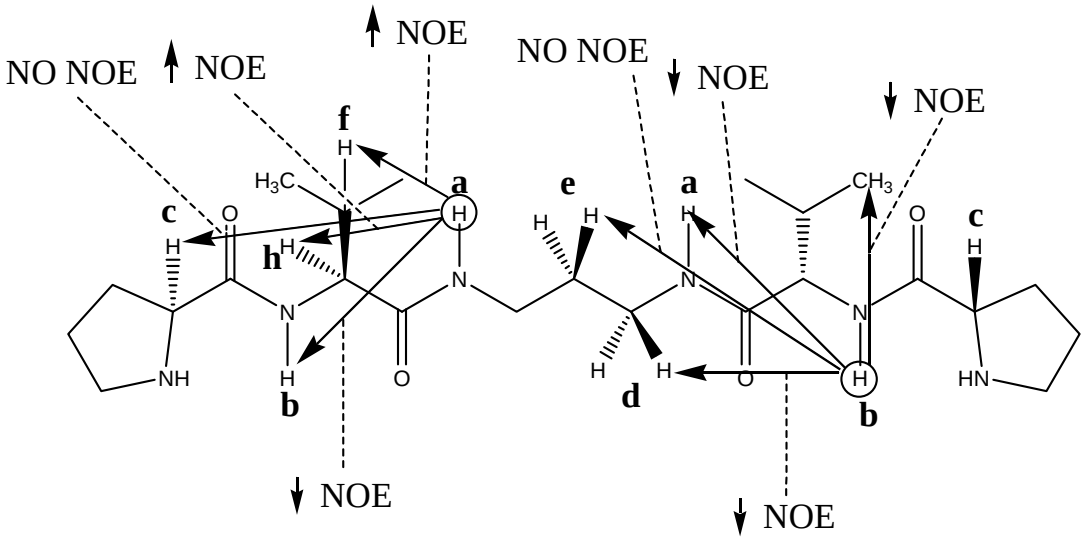


Figure S6. Transfer-NOE contacts for gels of compounds **1a** (CD_3CN, 30 ºC). Arrows indicate variations from diluted solution.

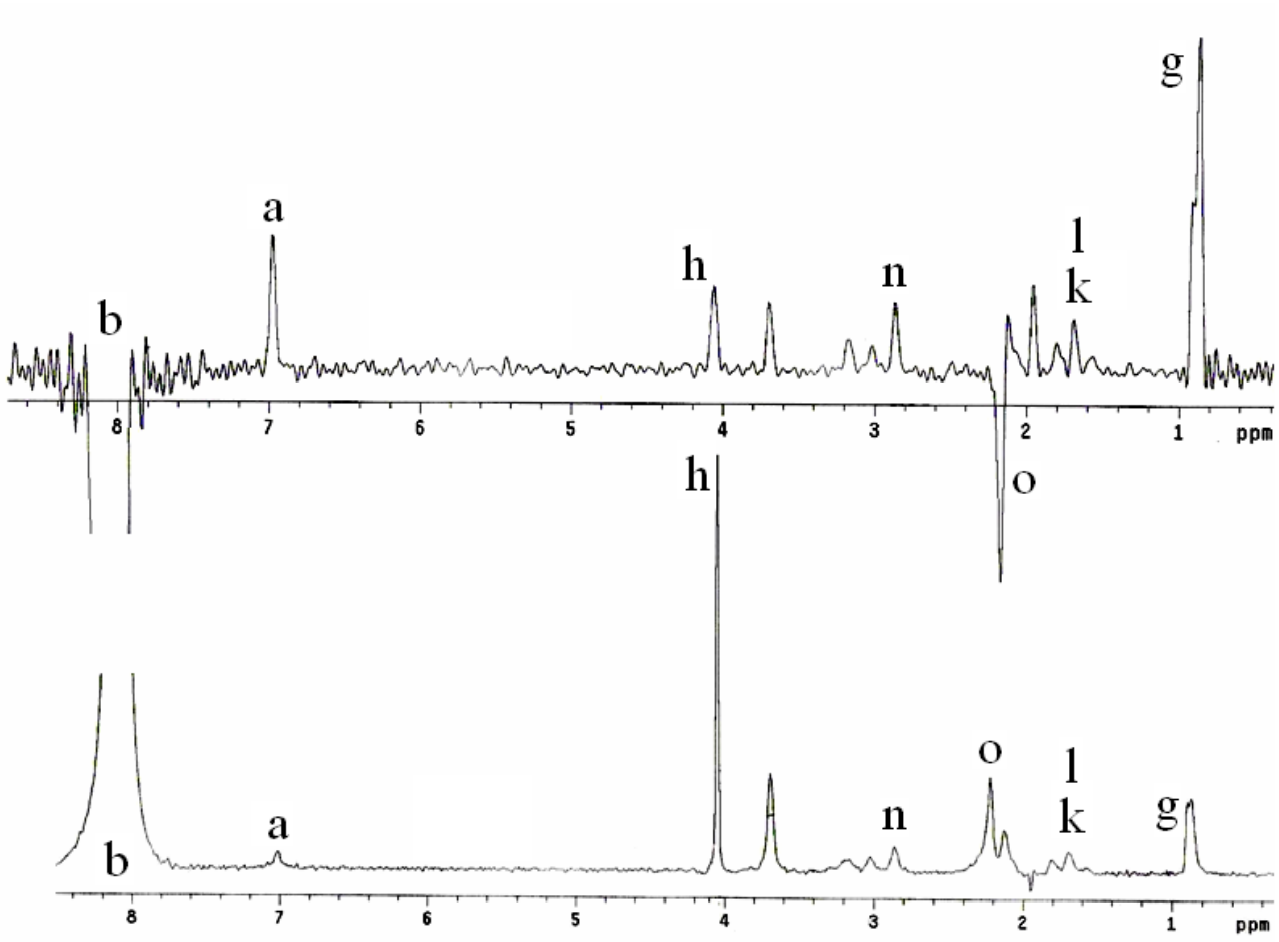
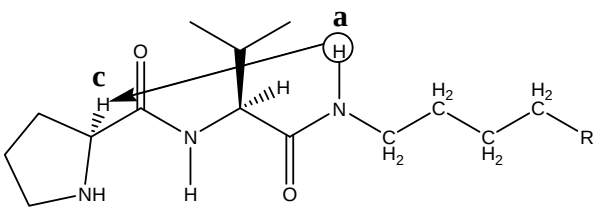
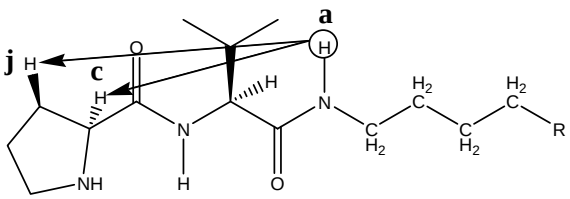


Figure S7. NOE spectra for a non-aggregated solution (top) and a gel (bottom) of compound **1a** (CD_3CN, 30 ºC).

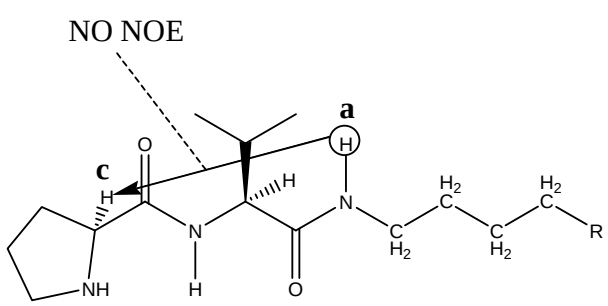


1b

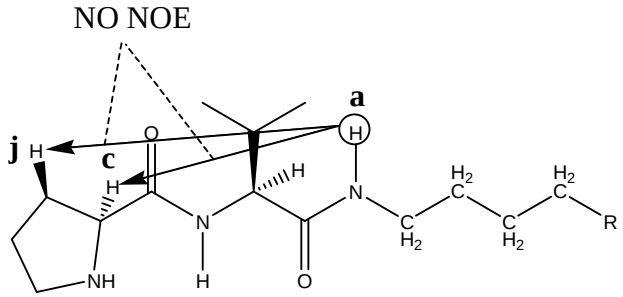


1c

Figure S8. informative NOE contacts for non-aggregated solutions of compounds **1b - c** (CD_3CN, 30 ºC)



1b



1c

Figure S9. Changes in-NOE contacts for gels of compounds **1b-c** (CD_3CN, 30 ºC)

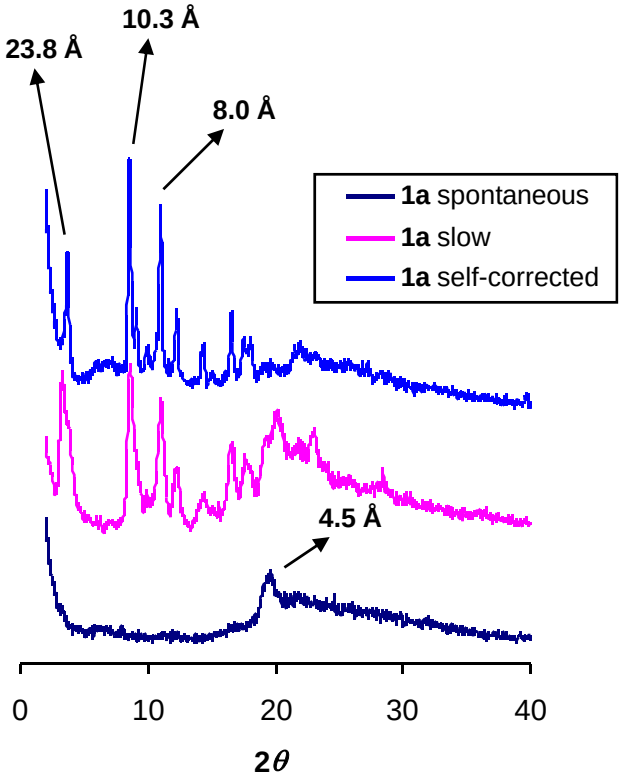


Figure S10. WAXD patters of xerogels of compound **1a**.

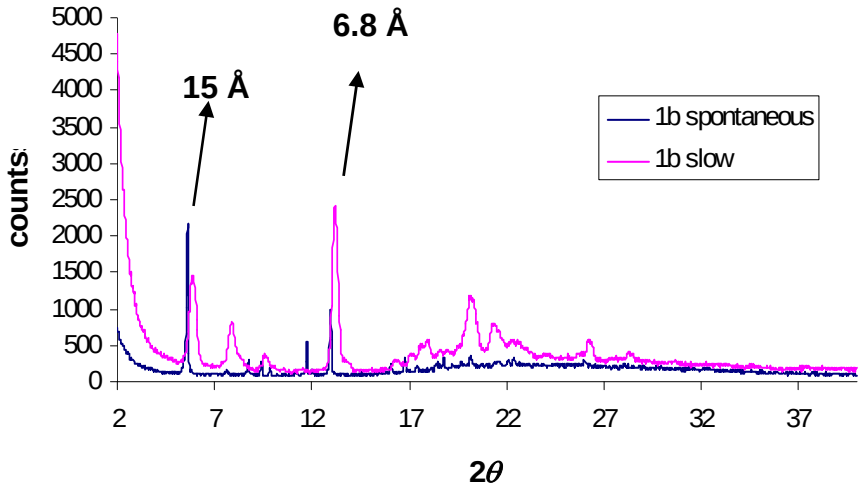


Figure S11. WAXD patters of compound **1b**.

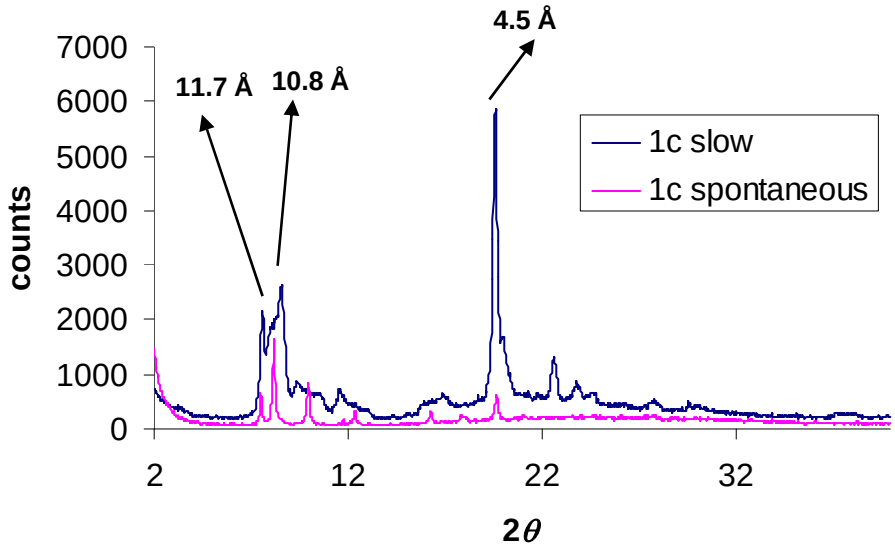


Figure S12. WAXD patters of compound **1c**.

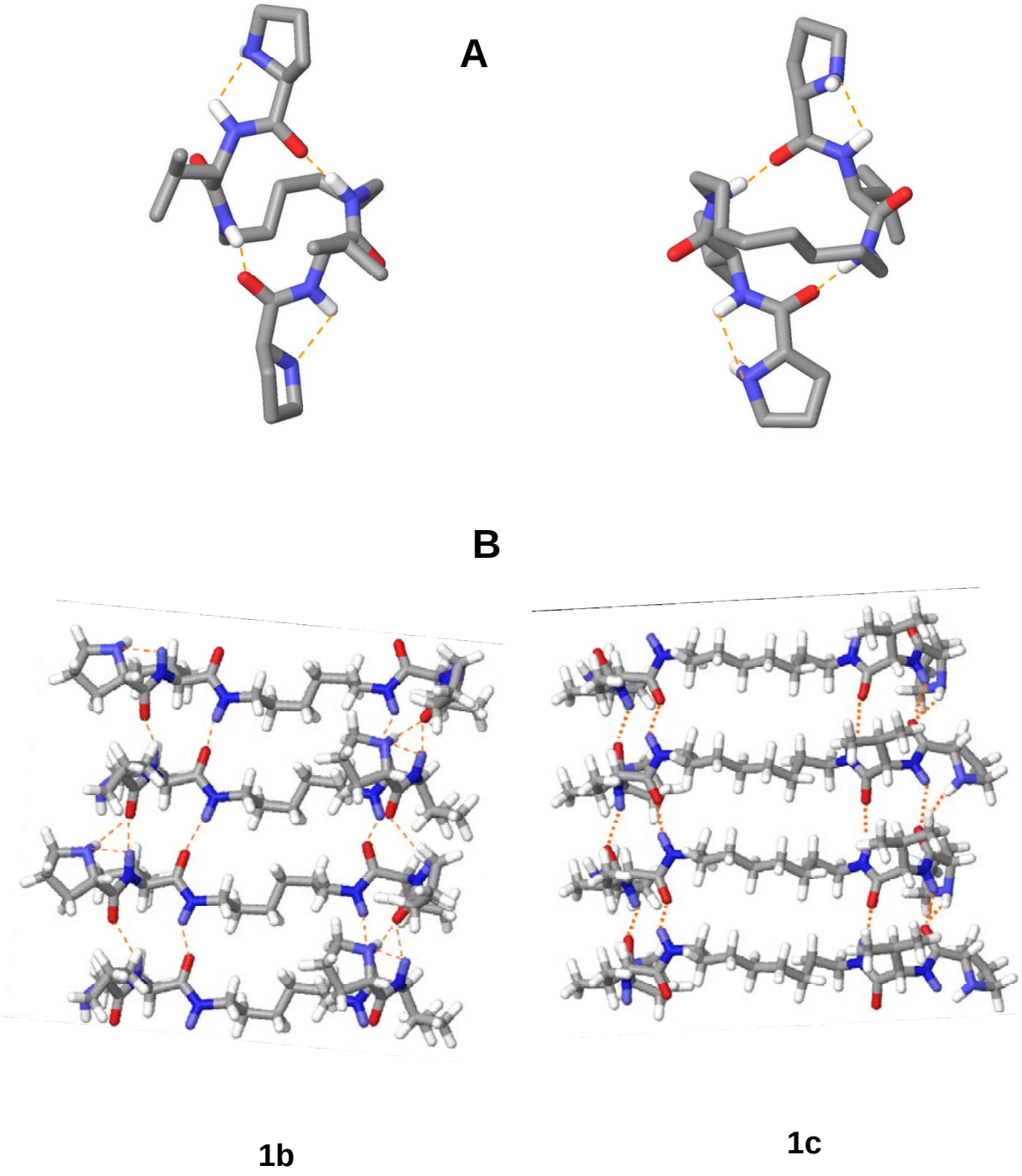


Figure S13. Molecular models for compounds **1b** and **1c** in solution (A) and in aggregates (B). (Macromodel 9, AMBER*, $CHCl_3$)