

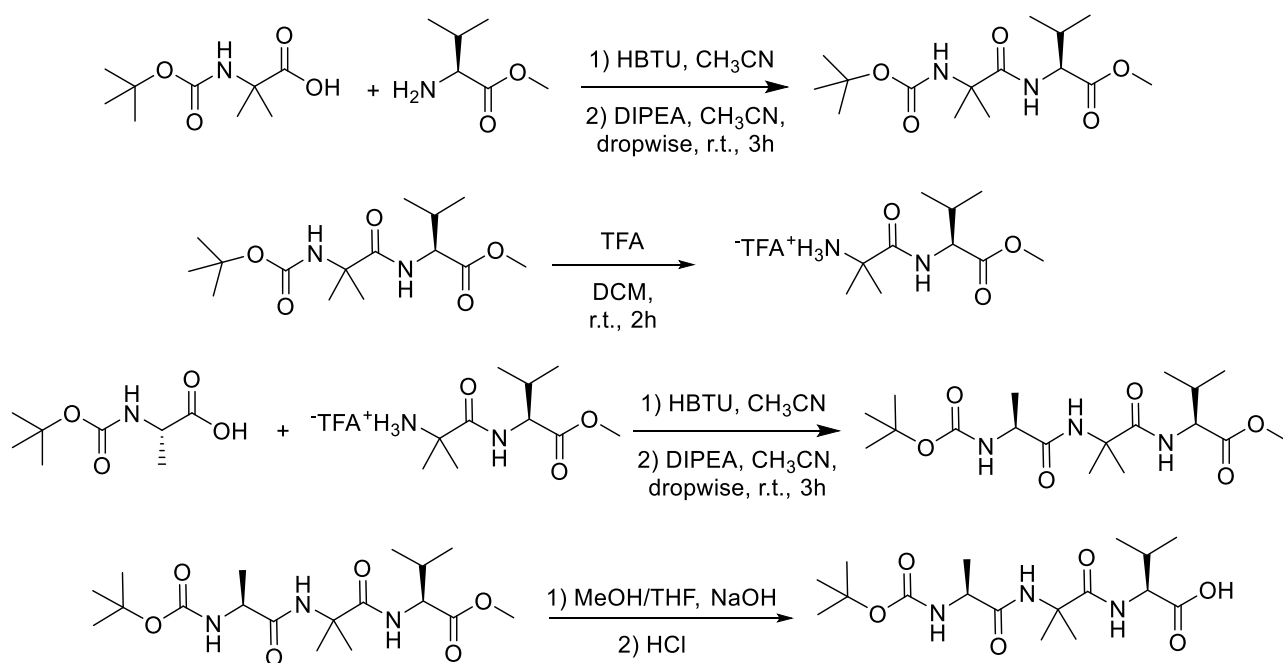
CHEM**NANO**MAT

Supporting Information

Water Remediation from Pollutant Agents by the Use of an Environmentally Friendly Supramolecular Hydrogel

Demetra Giuri⁺, Simone D'Agostino⁺, Paolo Ravarino, Davide Faccio, Giuseppe Falini,^{*} and Claudia Tomasini^{*}

Boc-AUV-OH (A)



Scheme S1. Preparation of compound A.

Synthesis of compound A.

900 mg of Boc-Aib-OH, (4.43 mmol) are dissolved in 60 mL of dry CH₃CN and 2 g of HBTU (5.21 mmol) are added under inert atmosphere at room temperature. A solution containing 782 mg of L-Val-OMe*HCl (4.43 mmol), 20 mL of dry CH₃CN and 2.34 mL of DIPEA (13.73 mmol) is added dropwise to the first one. The reaction is left under stirring for 3 h, then the solvent is removed under vacuum, the residue suspended in 20 mL of H₂O, extracted with ethyl acetate (3 x 50 mL) and washed with HCl 1 M (2x30 mL), saturated solution of NaHCO₃ (2x30 mL) and brine (2x30 mL). The organic layer is dried over Na₂SO₄ and the solvent evaporated under vacuum. The product, Boc-Aib-L-Val-OMe was obtained as a white solid with 95% yield (4.22 mmol, 1,34 g).

Boc-Aib-L-Val-OMe (4.22 mmol, 1.34 g) is dissolved in 40 mL of dry CH₂Cl₂, then 5.9 mL of trifluoroacetic acid (75.96 mmol) are added under inert atmosphere. The reaction is left under vigorous stirring for 2 h at room temperature, then the solvent is removed under reduced pressure. The whole residue, made of the remaining TFA and the desired intermediate [F₃CCO₂⁻H₃N-Aib-L-Val-OMe], is used for the next step of the reaction, considering a quantitative yield for this one.

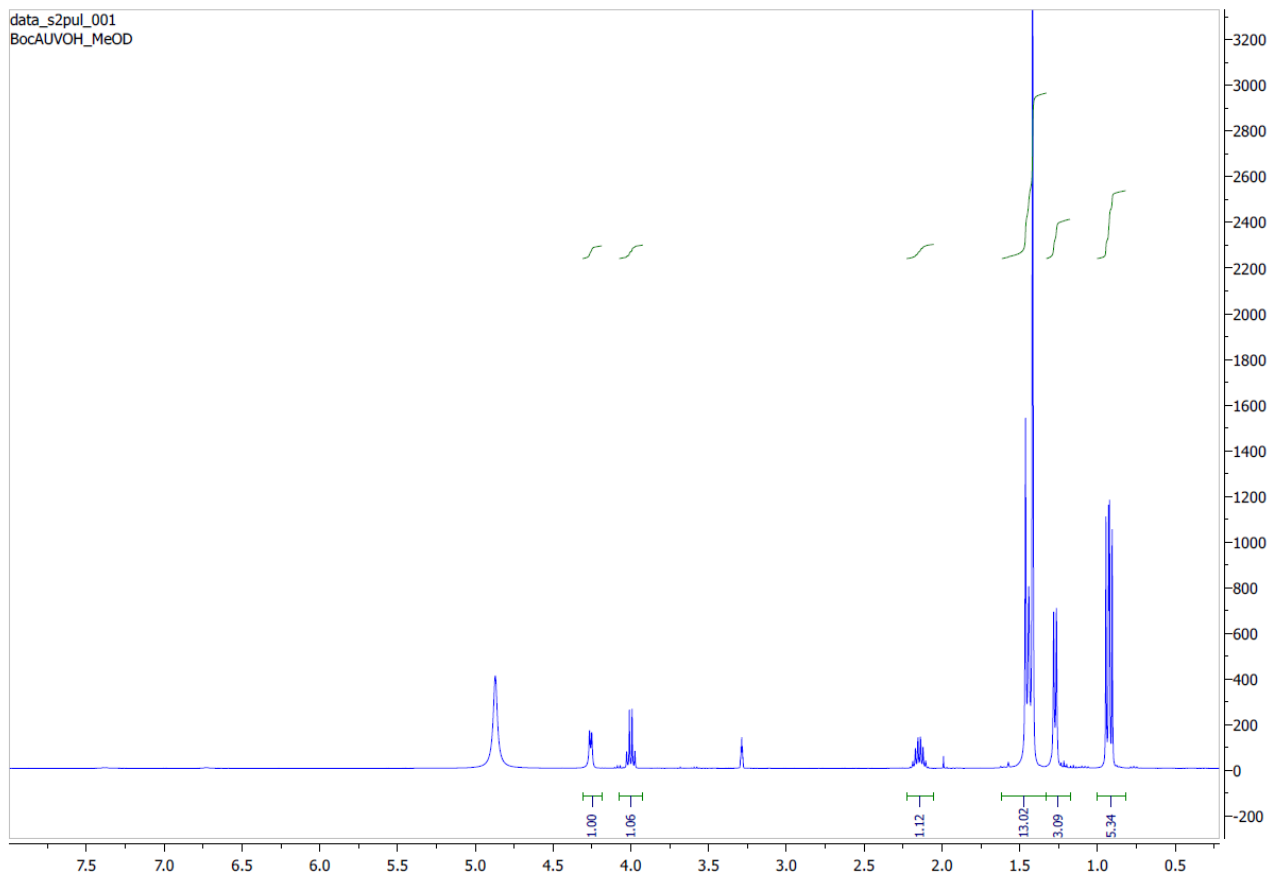
799 mg of Boc-L-Ala-OH, **10** (4.22 mmol) are dissolved in 60 mL of dry CH₃CN and 1.76 g of HBTU (4.64 mmol) are added under N₂ atmosphere at room temperature. A solution containing the residue of the former step, 20 mL of CH₃CN and 3.7 mL of DIPEA (22.0 mmol) is added dropwise to the first one. The reaction is left under stirring for 3 h, then the solvent is removed under vacuum, the residue suspended in 10 mL of H₂O, extracted with ethyl acetate (3x50 mL) and washed with HCl 1 M (15 mL), Brine (15 mL), saturated solution of NaHCO₃ (15 mL) and brine once again (15 mL). The organic layer is dried over Na₂SO₄ and the solvent evaporated under vacuum. The product is eventually purified through a flash chromatography (CH₂Cl₂ 100%, CH₂Cl₂:EtOAc 80:20, CH₂Cl₂:EtOAc 70:30). Boc-L-Ala-Aib-L-Val-OMe is obtained as a white solid with a yield of 84% (3.54 mmol, 1.37 g).

1.37 g of Boc-L-Ala-Aib-L-Val-OMe in 6 mL of MeOH and 12 mL of THF was cooled to 0 °C and treated with 4.4 mL of NaOH 1M. The ice bath was removed. The mixture warmed to room temperature with stirring for 18 hours. A solution of 5.3 ml of HCl 1M was added to the reaction mixture, which was concentrated in vacuo to remove the volatiles. The reduced volume was then extracted with three portions of CH₂Cl₂ (3 x 30 mL). The organic phase was combined, washed with water (60 mL), dried over Na₂SO₄, filtered and evaporated in vacuo, to afford pure Boc-L-Ala-Aib-L-Val-OH (95%) as a white solid.

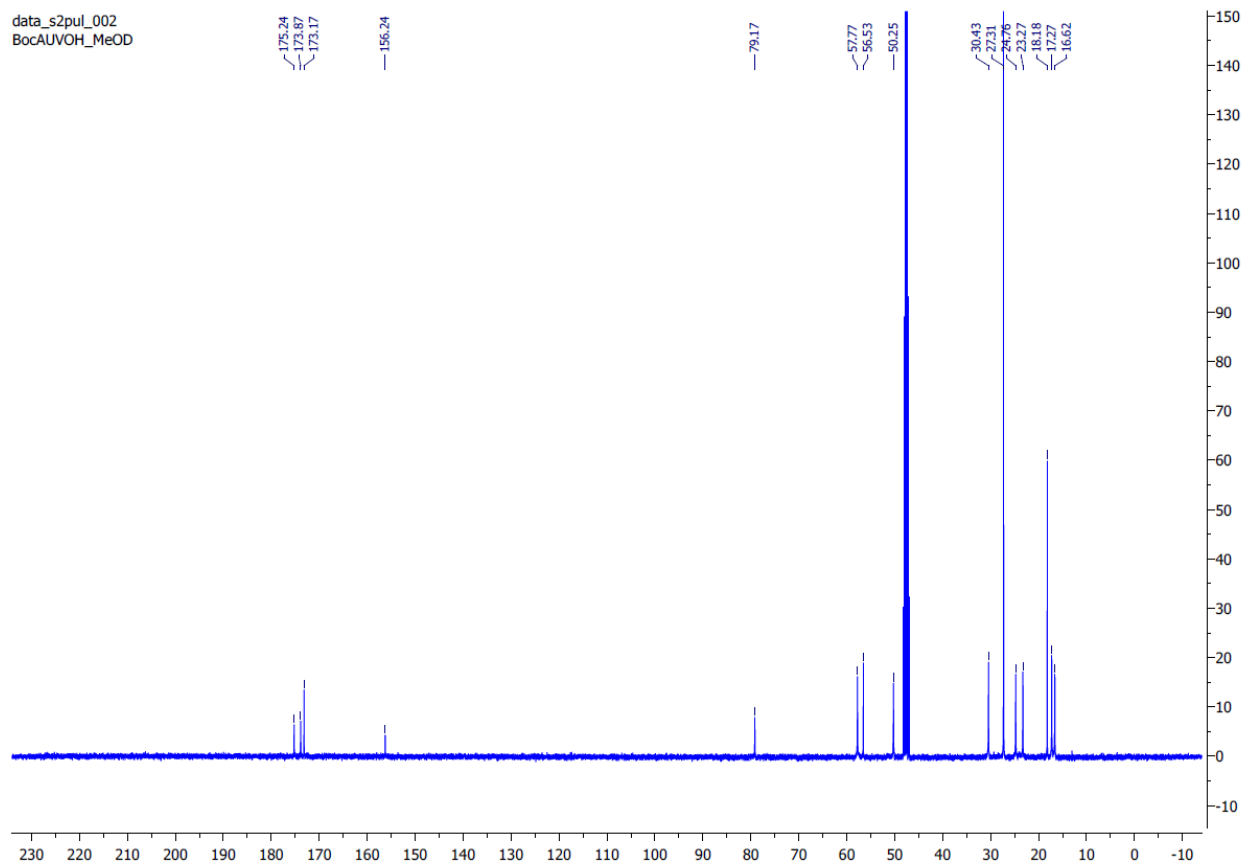
m.p. : 175-182 °C; [α]_D²⁵ : -20 (c = 5 mg/mL in MeOH); **IR (ATR-IR)**: ν 3507, 3412, 3395, 3330, 3294, 3279, 3072, 2978, 2932, 1701, 1685, 1670, 1645, 1558, 1524.

¹H NMR (CD₃OD, 400 MHz): δ 0.93 (6H, dd, J = 9.2 Hz, CH₃CH₃CH Val), 1.27 (3H, d, 7.1 Hz, CH₃CH Ala), 1.42 (9H, s, *t*-Bu), 1.44 (3H, s, CH₃CH₃CNH Aib), 1.46 (3H, s, CH₃CH₃CNH Aib), 2.23 – 2.04 (1H, m, CHCH₃CH₃ Val), 3.93 - 4.06 (1H, q, J = 7.1 Hz), 4.23 (1H, d, J = 5.6 Hz), 6,72 (1H, d, *NH*Boc, J = 5.6 Hz), 7.38 (1H, d, *NH*CH Val, J = 8.3 Hz), 8.04 (1H, s, NHC(CH₃)₂ Aib).

¹³C (CD₃OD, 100 MHz): δ 16.62, 17.27, 18.18, 23.27, 24.76, 27.31, 30.43, 50.25, 56.53, 57.77, 79.17, 156.24, 173.17, 173.87, 175.24.

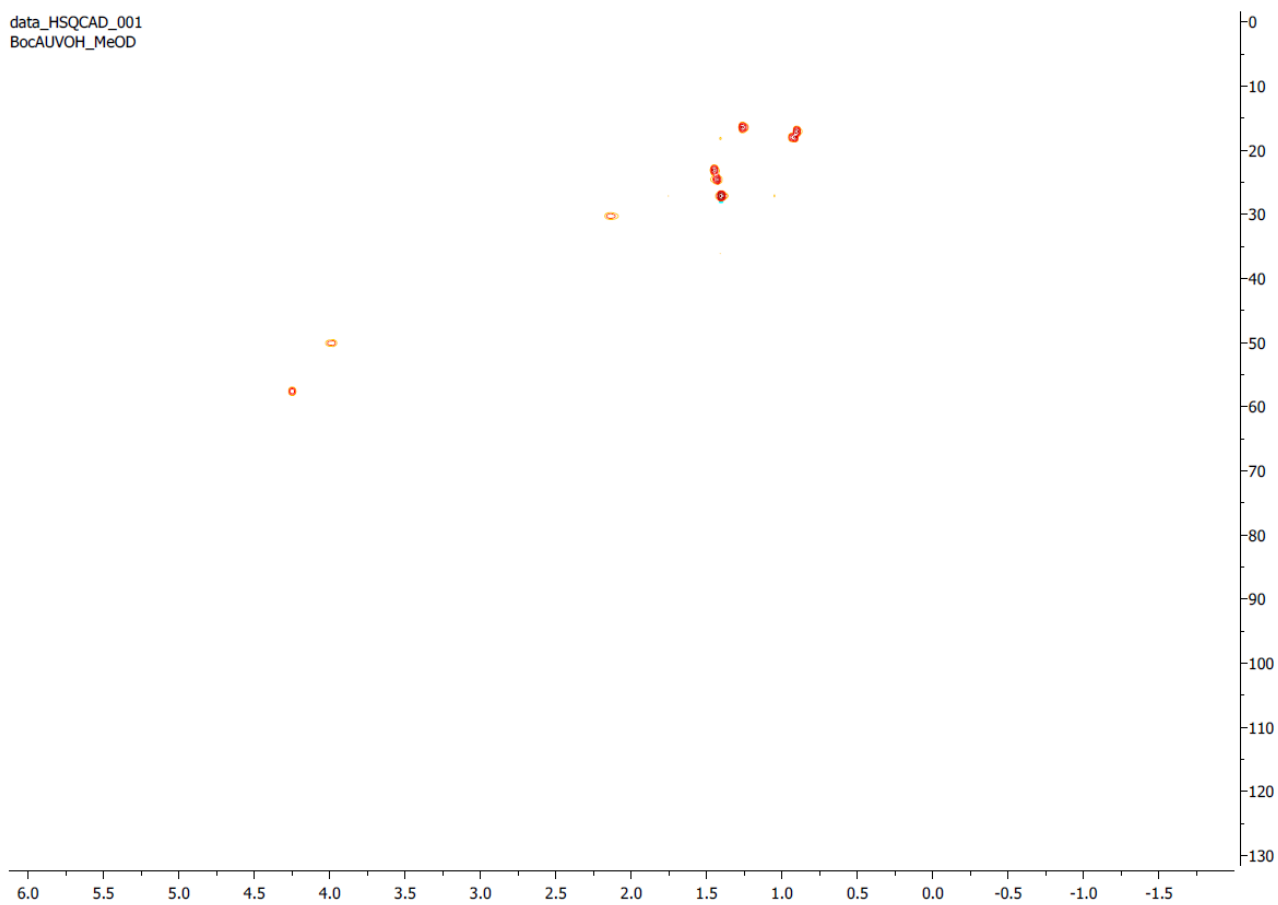


¹H NMR spectrum of Boc-L-Ala-Aib-L-Val-OH (A) in CD₃OD.

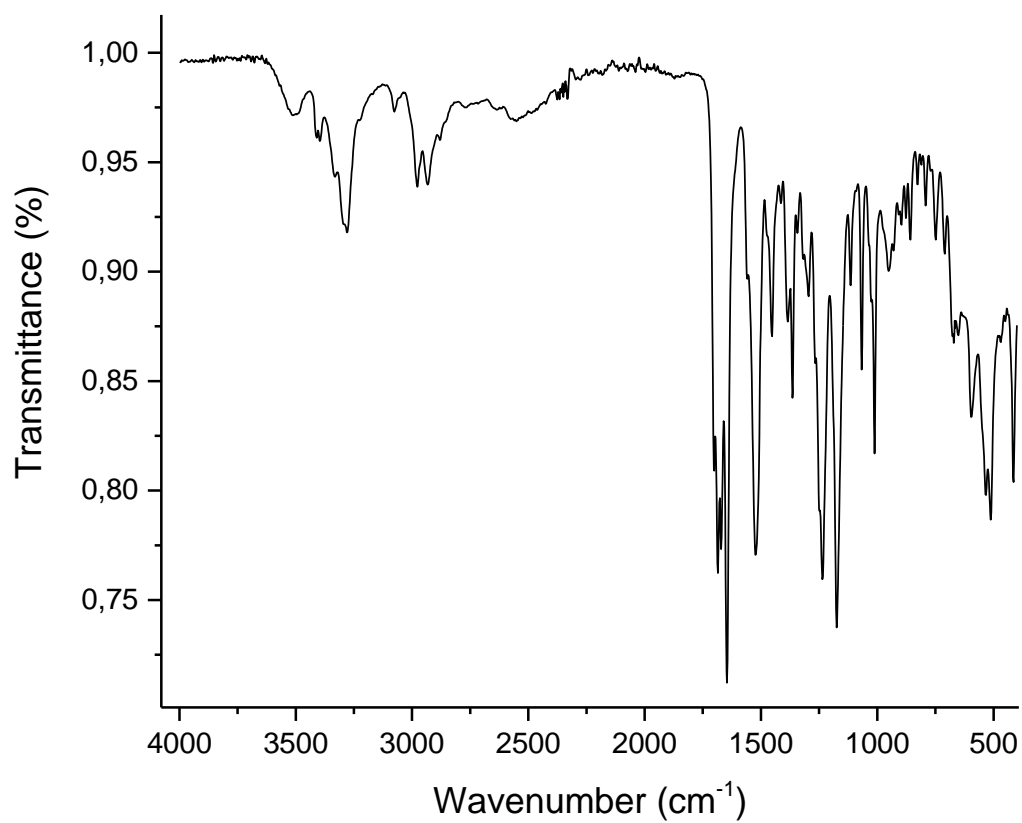


^{13}C NMR spectrum of Boc-L-Ala-Aib-L-Val-OH (A) in CD_3OD .

data_HSQCAD_001
BocAUVOH_MeOD

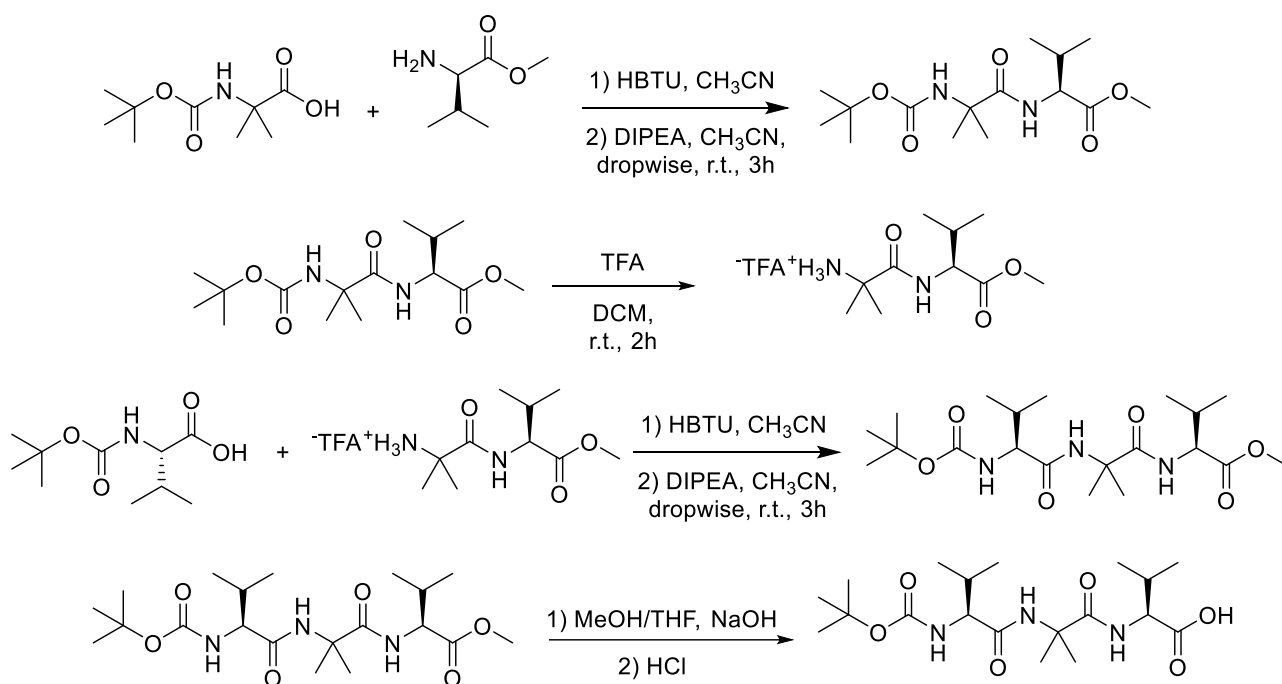


HSQC NMR spectrum of Boc-L-Ala-Aib-L-Val-OH (A) in CD₃OD.



IR-ATR spectrum of Boc-L-Ala-Aib-L-Val-OH (A)

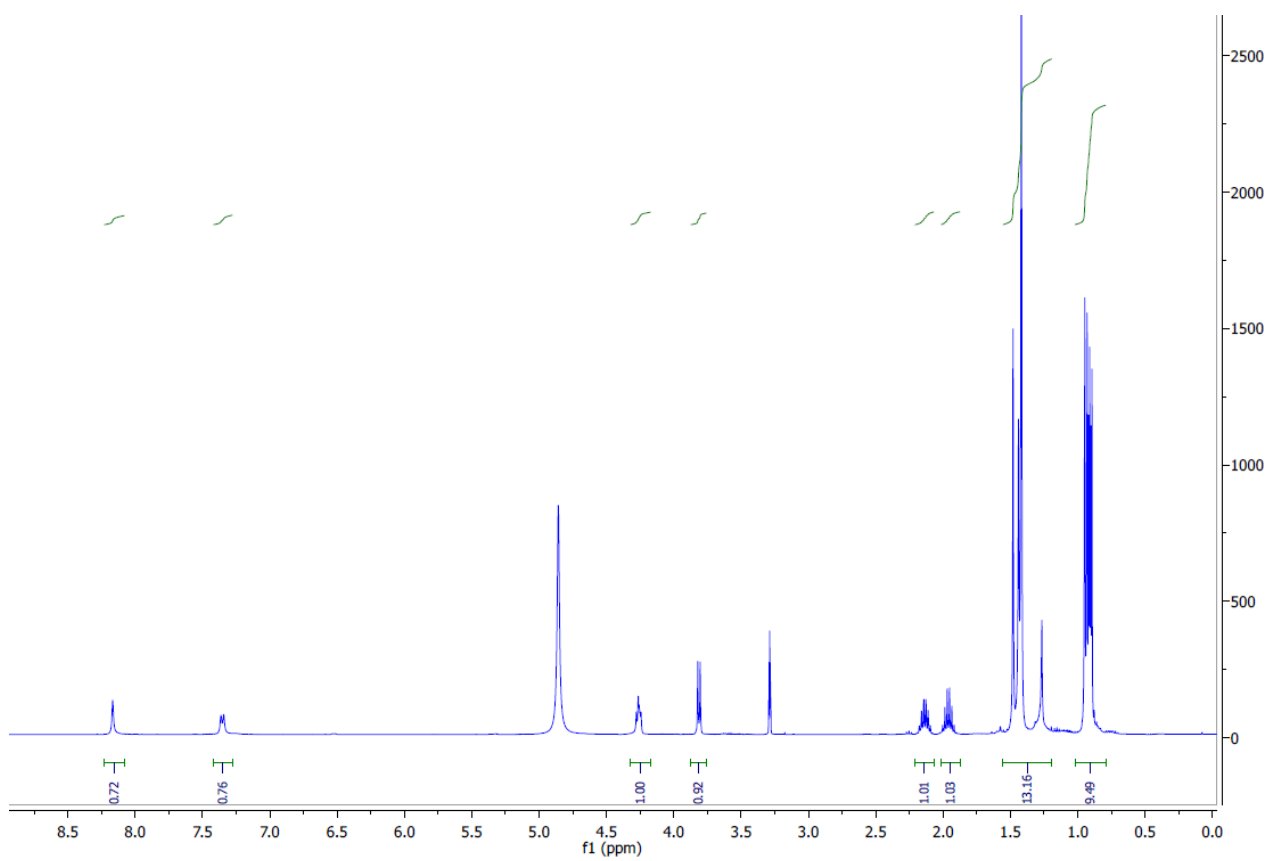
Boc-VUV-OH (B)



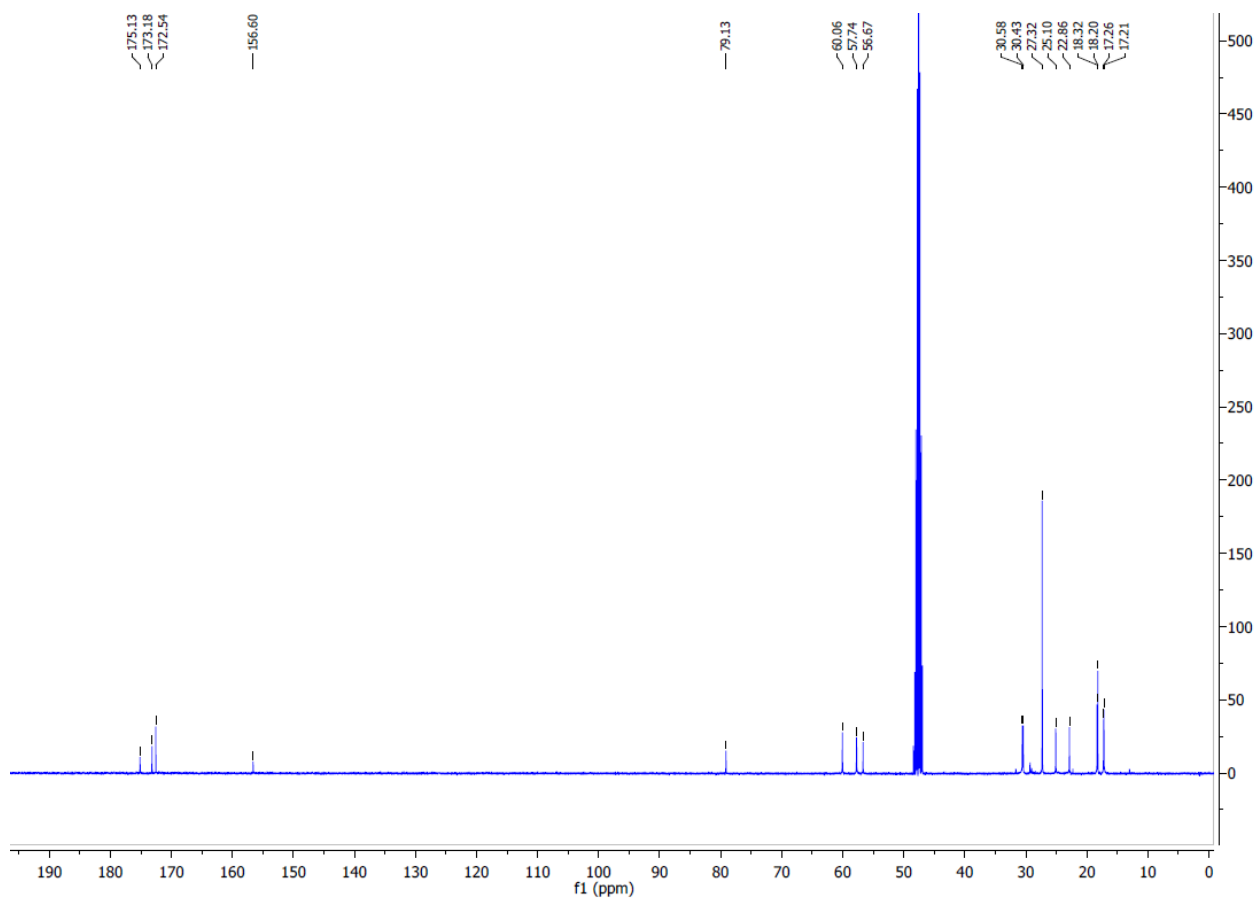
Scheme S2. Synthesis of Boc-VUV-OH (B).

Synthesis of gelator B. $F_3CCO_2^- + H_3N$ -Aib-L-Val-OMe was synthesised as described above.

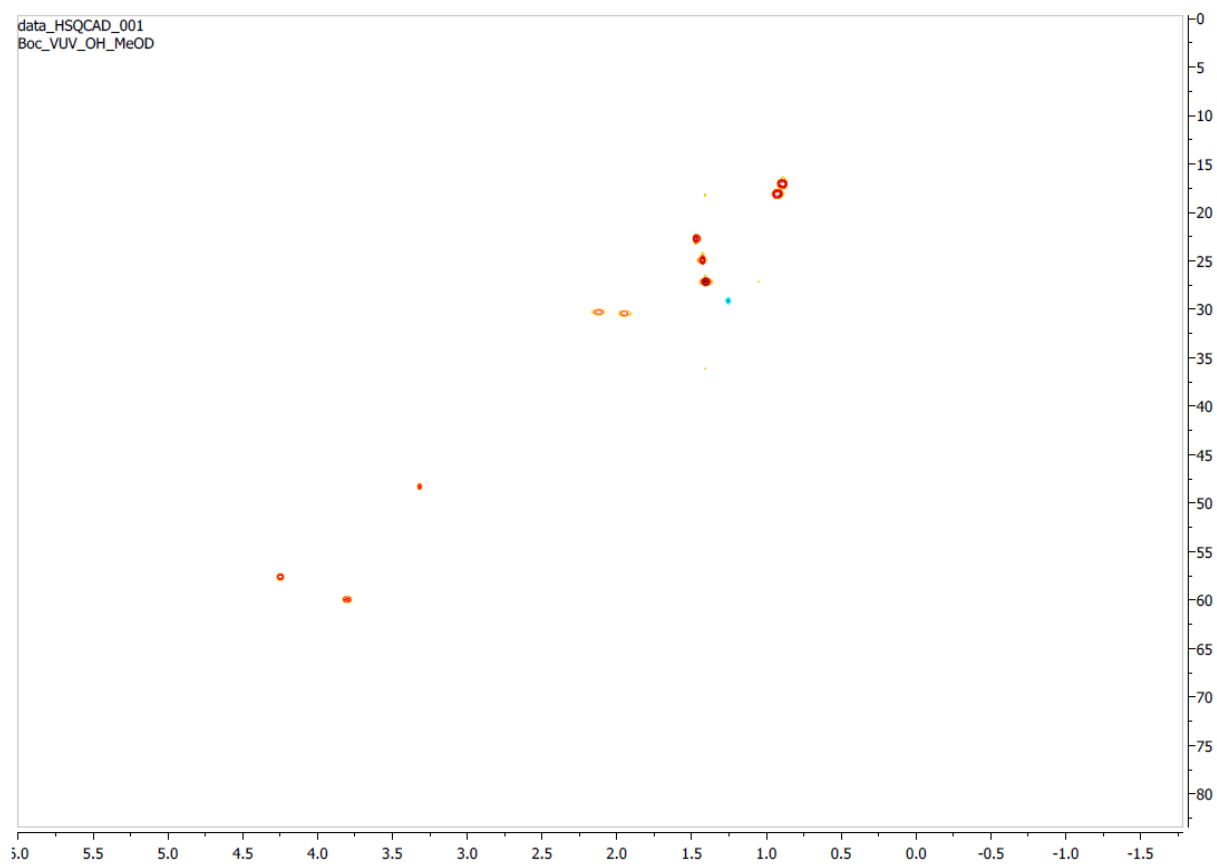
917 mg of Boc-L-Val-OH (4,22 mmol) are dissolved in 60 mL of dry CH_3CN and 1,76 g of HBTU (4,64 mmol) are added under N_2 atmosphere. A solution containing $F_3CCO_2^- + H_3N$ -Aib-L-Val-OMe, 20 mL of dry CH_3CN and 3,7 mL of DIPEA (22,0 mmol) is added dropwise to the first one. The reaction is left under stirring for 3 h at room temperature, then the solvent is removed under vacuum, the residue suspended in 10 mL of H_2O , extracted with ethyl acetate (3 x 50 mL) and washed with HCl 1 M (15 mL), Brine (15 mL), saturated solution of $NaHCO_3$ (15 mL) and brine once again (15 mL). The organic layer is dried over Na_2SO_4 and the solvent evaporated under vacuum. The product is eventually purified through a flash chromatography (Cyclohexane:Ethyl acetate 80:20, Cyclohexane:Ethyl acetate 70:30). Boc-L-Val-Aib-L-Val-OMe is obtained as a white solid with a yield of 80%. **m.p.** : 97-103 °C; $[\alpha]_D^{25}$: -10 (c = 5 mg/mL in MeOH); **IR (ATR-IR)**: ν 3447, 3347, 3259, 3220, 3065, 2970, 2928, 2877, 2853, 1721, 1702, 1666, 1547, 1519 cm^{-1} . **1H NMR** (CD_3OD , 400 MHz): δ 0.92 (12H, 2d, $J = 6.8$ Hz, CH_3CH), 1.42 (9H, s, t -Bu), 1.48 (6H, s, CH_3CNH), 1.96 (1H, dq, $J = 6.8, 6.8$ Hz, $CHCH_3$), 2.14 (1H, dq, $J = 5.6, 6.8$ Hz, $CHCH_3$), 3.80 (1H, d, $J = 7.2$ Hz, $C_\alpha H$), 4.26 (1H, m, $C_\alpha H$), 7.35 (1H, s, $NHBoc$), 8.17 (1H, d, $J = 8$ Hz, $NHC_\alpha CH_3$). **^{13}C** (CD_3OD , 100 MHz): δ 17.21, 17.26, 18.20, 18.32, 22.86, 25.10, 27.32, 30.43, 30.58, 56.67, 57.74, 60.06, 79.13, 156.60, 172.54, 173.18, 175.13.



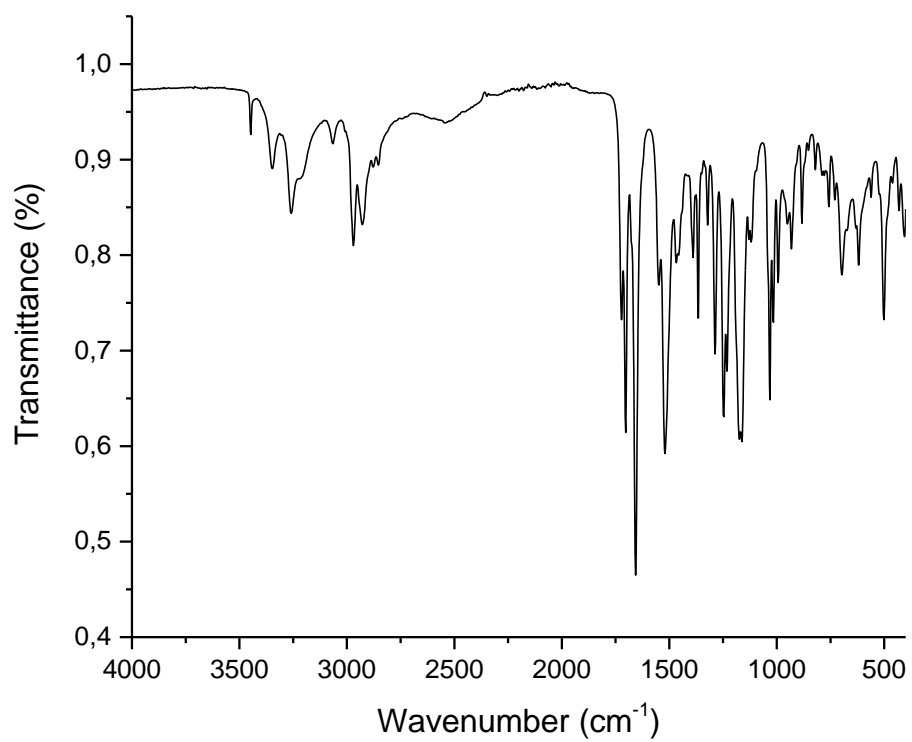
^1H NMR spectrum of Boc-L-Val-Aib-L-Val-OH (B) in CD_3OD .



^{13}C NMR spectrum of Boc-L-Val-Aib-L-Val-OH (B) in CD_3OD .



HSQC spectrum of Boc-L-Val-Aib-L-Val-OH (B) in CD₃OD.



IR-ATR spectrum of Boc-L-Val-Aib-L-Val-OH (B).

Table S1. Gelation properties of compounds **A** (10 mg) or **B** (10 mg) in different mixtures of MeOH, EtOH or *i*PrOH and water (1% w/w final concentration).

Solvent 1 (μL)	Water (μL)	Sample	Peptide	Outcome	Sample	Peptide	Outcome
MeOH (330)	660	1	A	PG	10	B	C
MeOH (500)	500	2	A	C	11	B	C
MeOH (660)	330	3	A	P	12	B	S
EtOH (330)	660	4	A	G	13	B	C
EtOH (500)	500	5	A	C	14	B	S
EtOH (660)	330	6	A	S	15	B	S
<i>i</i> PrOH (330)	660	7	A	G	16	B	C
<i>i</i> PrOH (500)	500	8	A	P	17	B	S
<i>i</i> PrOH (660)	330	9	A	S	18	B	S

G = gel; PG = partial gel; S = solution; C = crystals; P = precipitate

XRD Analysis.**Table S2.** Crystal data and refinement details for crystalline AUV (**A**) and VUV (**B**).

	A	B
Formula	C ₁₇ H ₃₃ N ₃ O ₇	C ₂₁ H ₄₁ N ₃ O ₇
FW	391.46	447.57
Temperature	RT	RT
Cryst. System	Triclinic	Orthorhombic
Space group	P1	P2 ₁ 2 ₁ 2 ₁
Z	1	4
a (Å)	6.0267(6)	9.816(1)
b (Å)	9.3387(9)	10.360(2)
c (Å)	20.099(2)	26.572(5)
α (deg)	89.281(7)	90
β (deg)	84.010(7)	90
γ (deg)	82.622(8)	90
V (Å³)	1115.7(1)	2773.0(7)
D_{calc} (g/cm³)	0.583	1.072
μ (mm⁻¹)	0.045	0.080
Measd reflns	13096	7915
Indep reflns	8985	4697
Largest diff. peak/hole (e/Å³)	0.75/-0.63	0.13/-0.12
R₁[on F_o², I>2σ(I)]	0.2294	0.0745
wR₂ (all data)	0.5682	0.1479

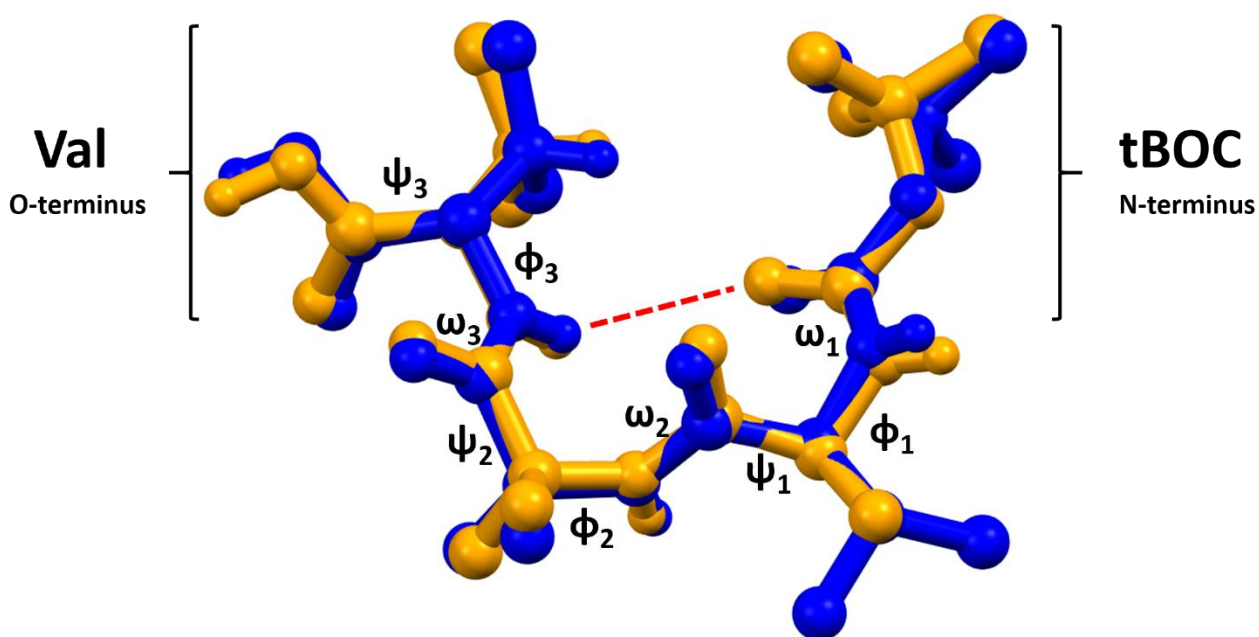


Figure S1. Overlay of the molecular structures of crystalline **B** (blue) and **A** (orange) highlighting the subtle differences among folded conformations deriving from the intramolecular hydrogen bonds (dashed red line).

Table S3. Selected backbone torsion angles for the compounds AUV (**A**) and VUV (**B**).

	ω_1 (°)	ϕ_1 (°)	ψ_1 (°)	ω_2 (°)	ϕ_2 (°)	ψ_2 (°)	ω_3 (°)	ϕ_3 (°)	ψ_3 (°)
A	179	-50	144	161	62	34	176	-62	142
B	177	-76	141	172	58	34	172	-73	157

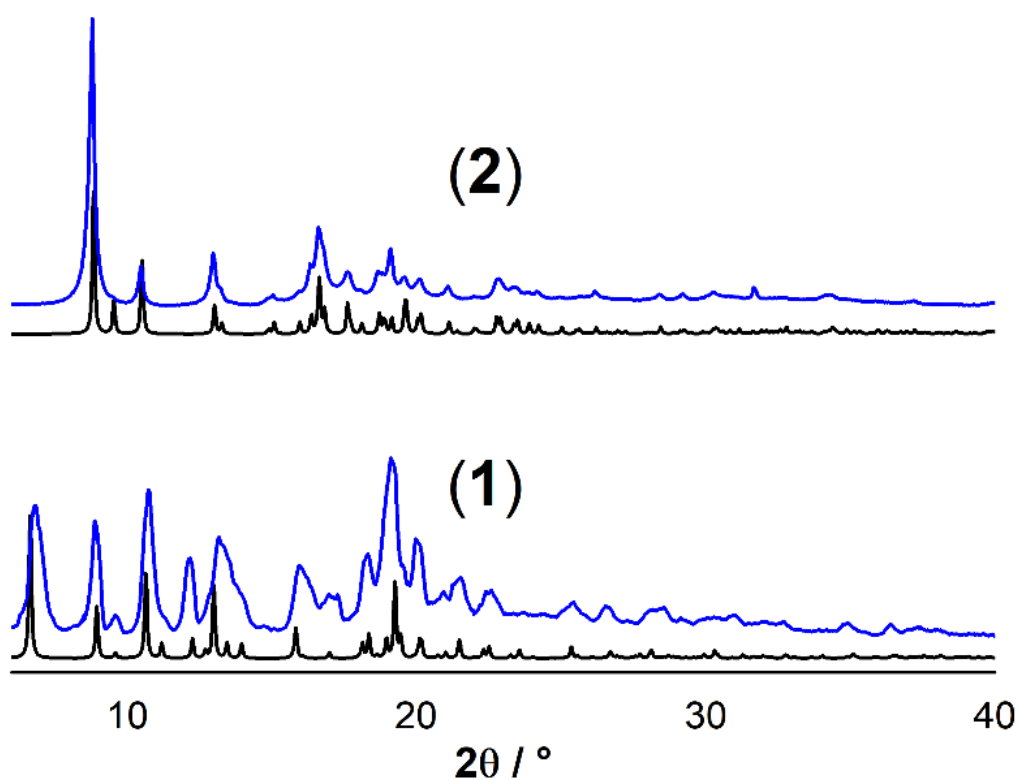


Figure S2. Comparison between XRD diffraction patterns for crystalline **B** (1) and **A** (2): experimental (blue-line) and calculated on the basis of single-crystal structure (black-line).

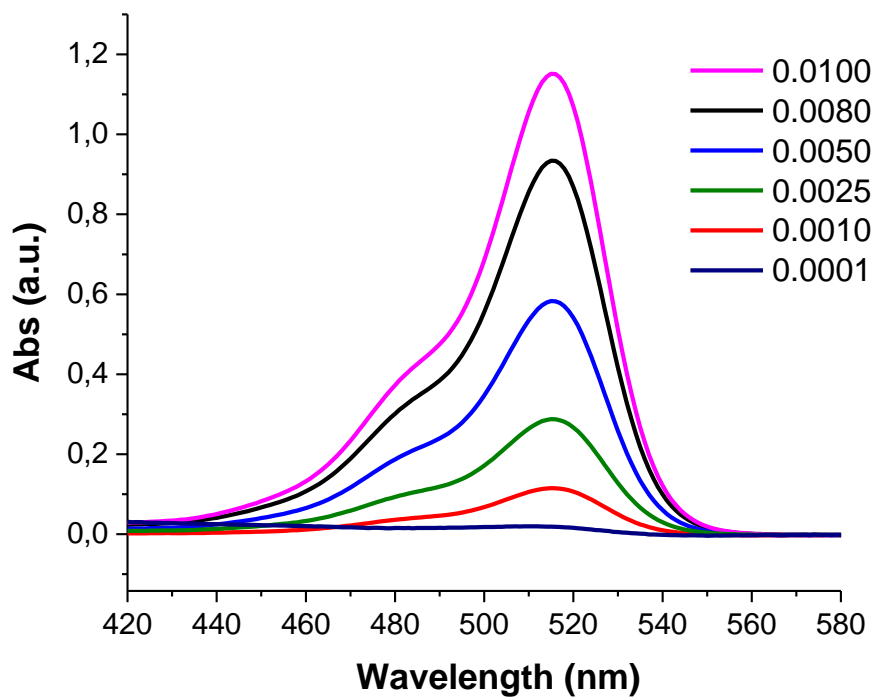
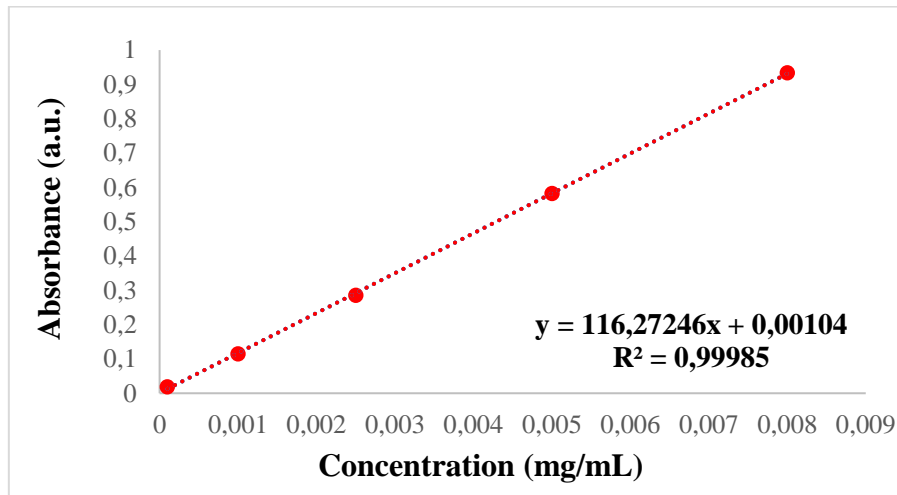
Table S4. G' and G'' moduli from amplitude sweep ($\gamma = 0.0214\%$) for compounds **4**, **7** and **19**. The measurements were repeated three times and mean values and standard deviation calculated and plotted.

Sample	G' (KPa)	G'' (KPa)
4	40,66±9,70	9,61±1,74
7	31,55±3,47	8,46±0,73
19	247,34± 18,53	47,53± 5,15

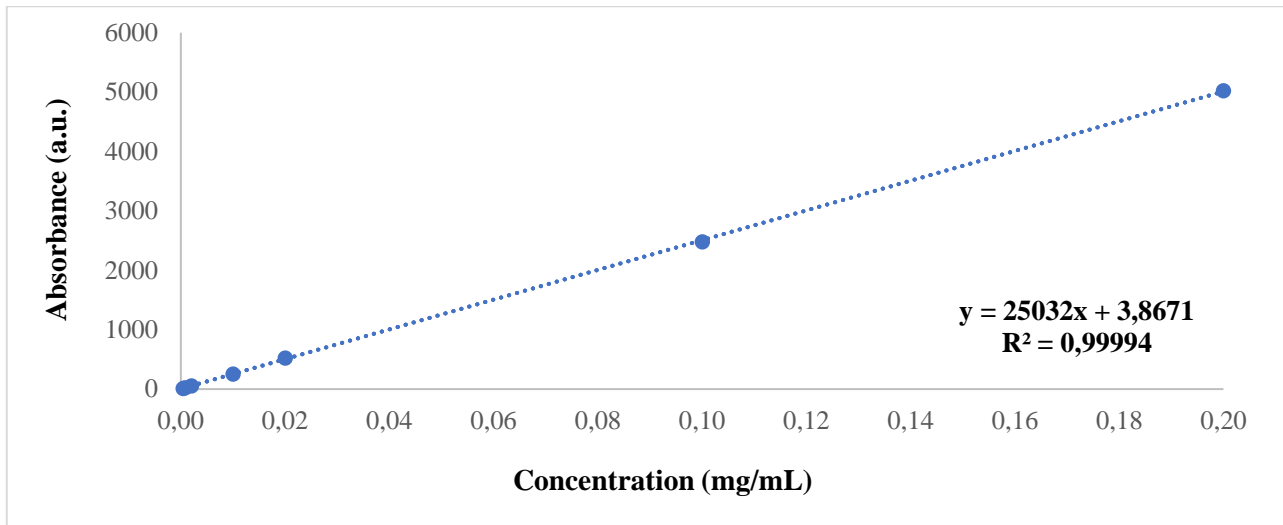
Pollutant adsorption.

Calibration curve of Eosine Y obtained with a Uv-vis spectrophotometer, absorbance reading at

$\lambda_{\max} = 515 \text{ nm}$.



Calibration curve of **Diclofenac sodium** obtained with a HPLC (DAD = 280 nm).



Concentration (mg/mL)	Area
0,2000	5021,30566
0,1000	2481,05054
0,0200	525,68408
0,0100	253,97585
0,0020	54,11948
0,0008	20,66679
0,0004	11,08909

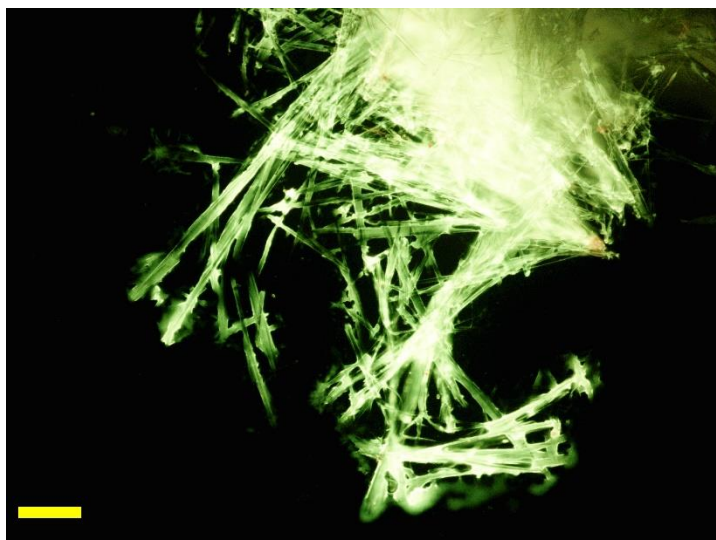


Figure S3. Epifluorescence microscope image of a sample of **7** after absorption of Eosine Y.