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SUPPORTING INFORMATION

Insight in the aggregation induced emission of 1,8-Naphthalimide-based supramolecular hydrogels.

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1. Mgc determination of compound 1 in different solvents

Heating cooling method: The required amount of compounds were dissolved in the desired amount of solvent and then, heated until complete solution in a screw-capped vial (8 mL, diameter 1.5 cm). The vial was left to rest at ambient temperature for 10 minutes, gel formation was assessed by vial inversion method.

Solvent shift method: The required amount of compounds was dissolved in the desired amount of DMSO and then, water is added quickly in a screw-capped vial (8 mL, diameter 1.5 cm). The vial was left to rest at ambient temperature overnight. Gel formation was assessed by vial inversion method.

Table S1. Mgc of **1** in different solvents by heating/cooling method and solvent shift method* (only for DMSO/H2O samples)

Solvent	mgc
CH_3CN	1,54 ± 0,02 mg/ml (3,9 mM)
CH_3OH	1,82 ± 0,06 mg/ml (4,6 mM)
THF	2,3 ± 0,2 mg/ml (5,9 mM)
DMSO	6 mg/ml (15,2 mM)
DMSO/H_2O (2:8)	1.18 mg/ml (3 mM)*
BuOH	1,8 ± 0,1 mg/ml (4,5 mM)
$CHCl_3$	4,0 ± 0,3mg/ml (10,9 mM)
CH_2Cl_2	5,5 ± 0,5 mg/ml (13,9 mM)
AcOEt	2,3 ± 0,3 mg/ml (5,8 mM)

2. Self healing behaviour of gels of 1

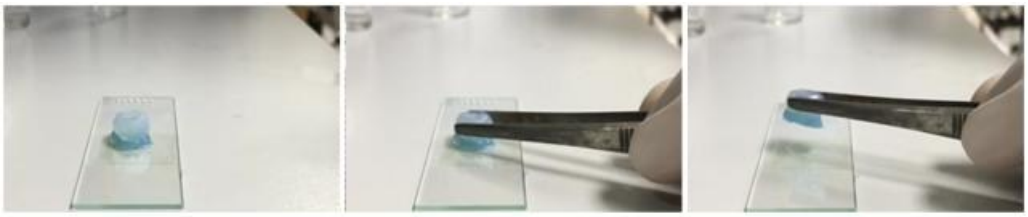


Figure S1. Picture of Gels of **1** (3 mM) presenting self healing properties. Two gels are individually formed, one of them stained with methylene blue dye. Both gels are placed one in top of the other and perfect fusion was observed after several minutes.

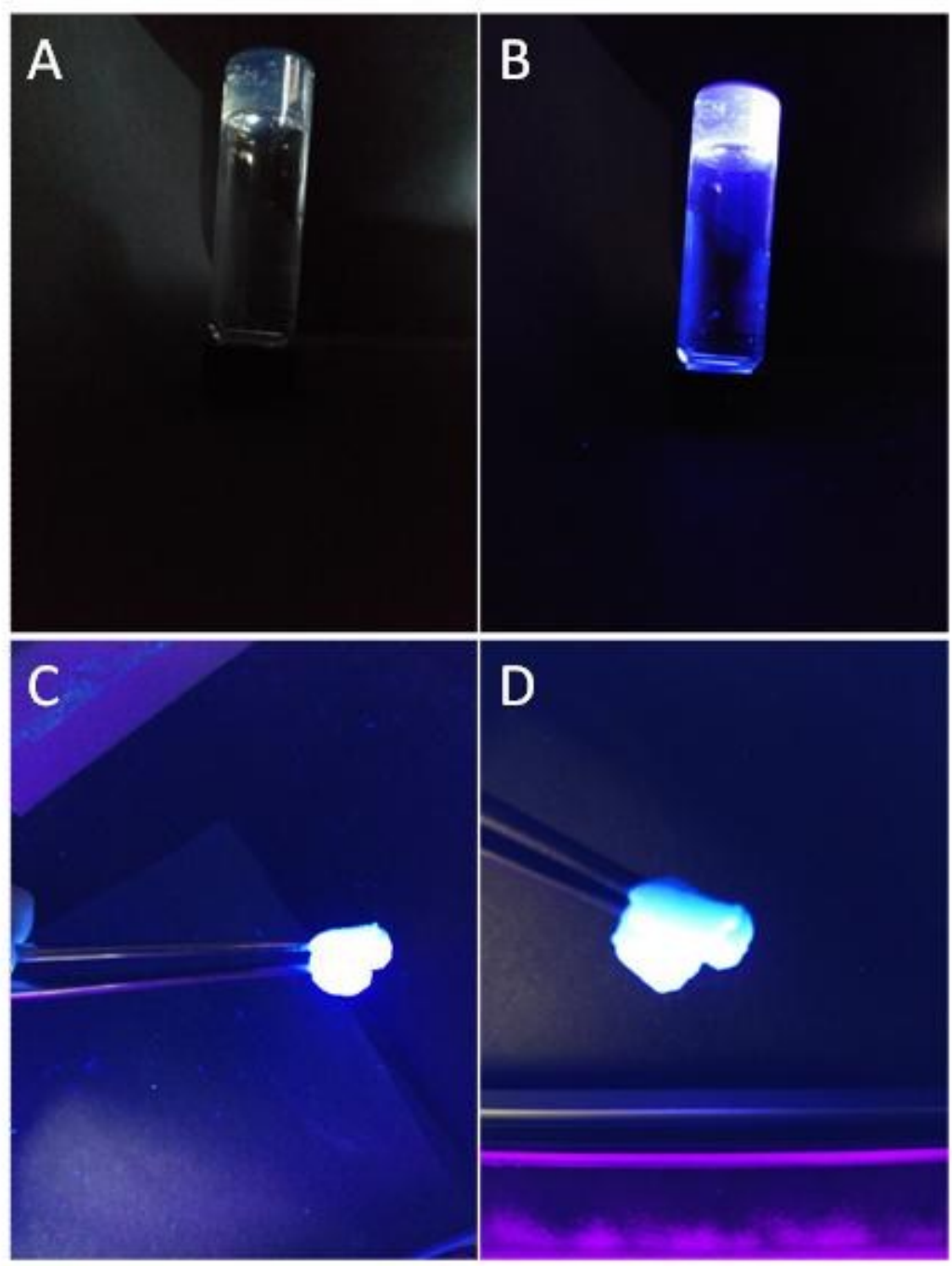
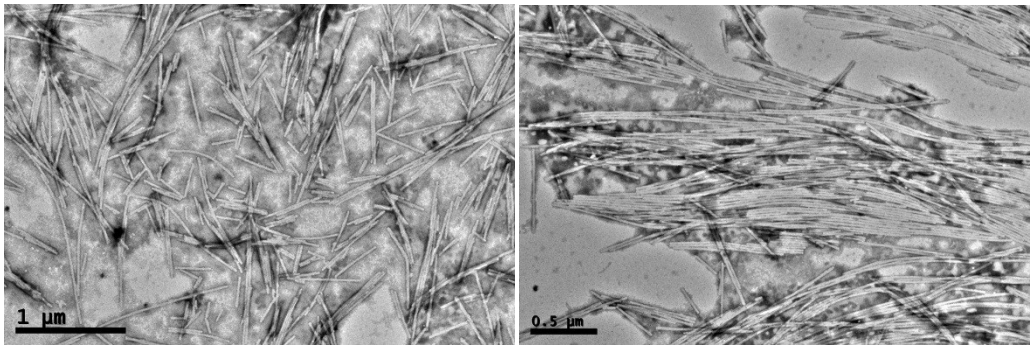
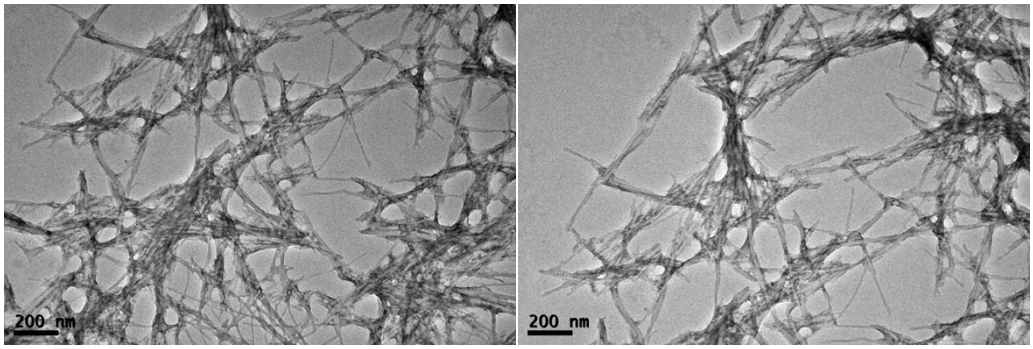


Figure S2. Pictures of Gels of **1** (3.8 mM). **A)** Under ambient light; **B)** Under UV irradiation (λ_{ex}=365); **C)** and **D)** Gels out of the vial that can be manipulated with tweezers under UV- irradiation.

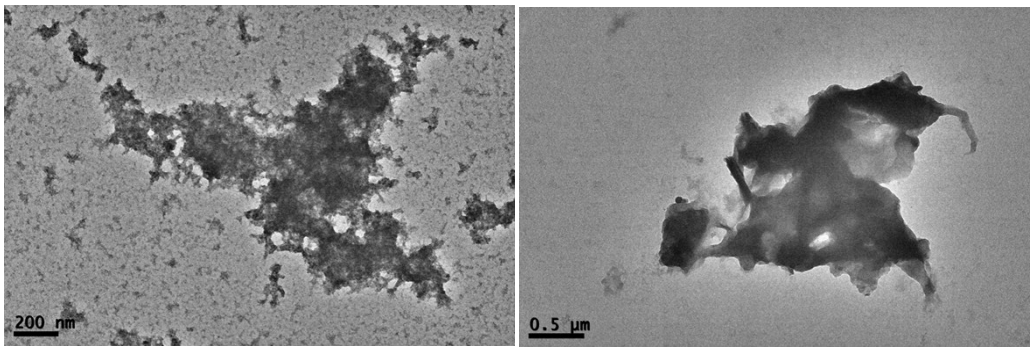
3. Additional transmission electron microscopy images



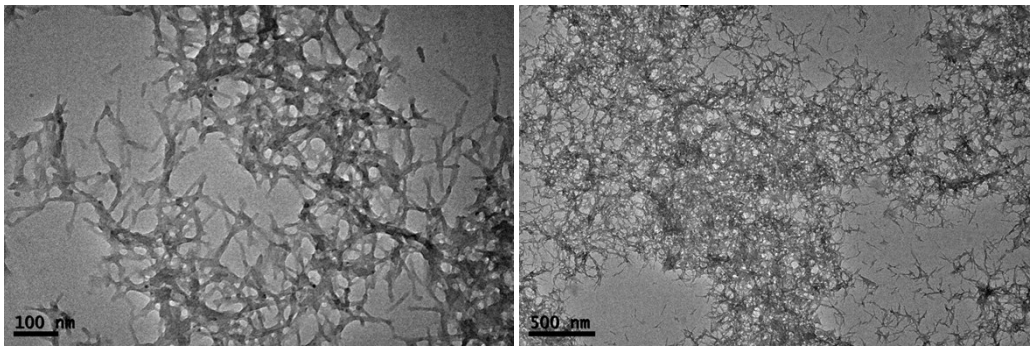
TEM of Compound **1**



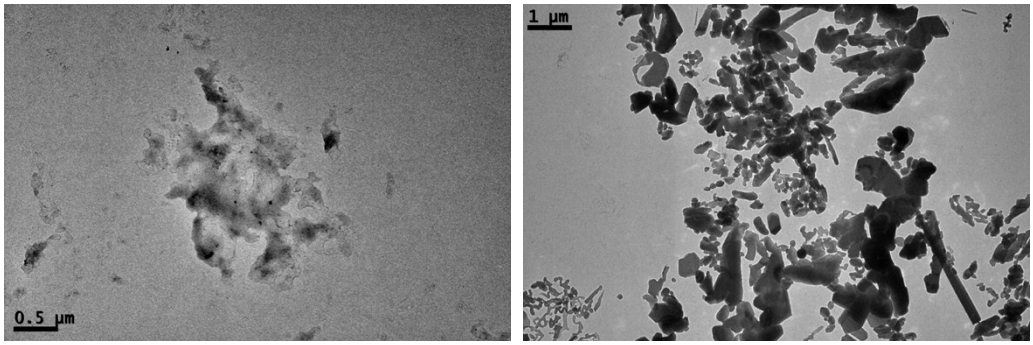
TEM of Compound **2**



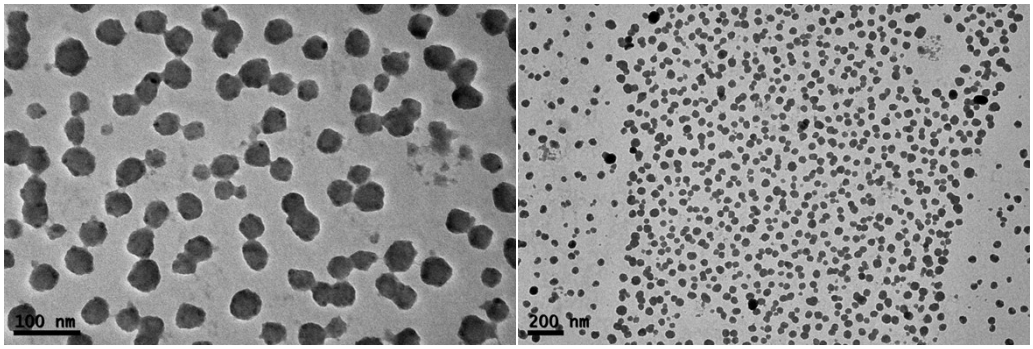
TEM of Compound **3** and **4**



TEM of Compound **5**



TEM of Compound **6**



TEM of Compound **7**

4. Additional Confocal microscopy images

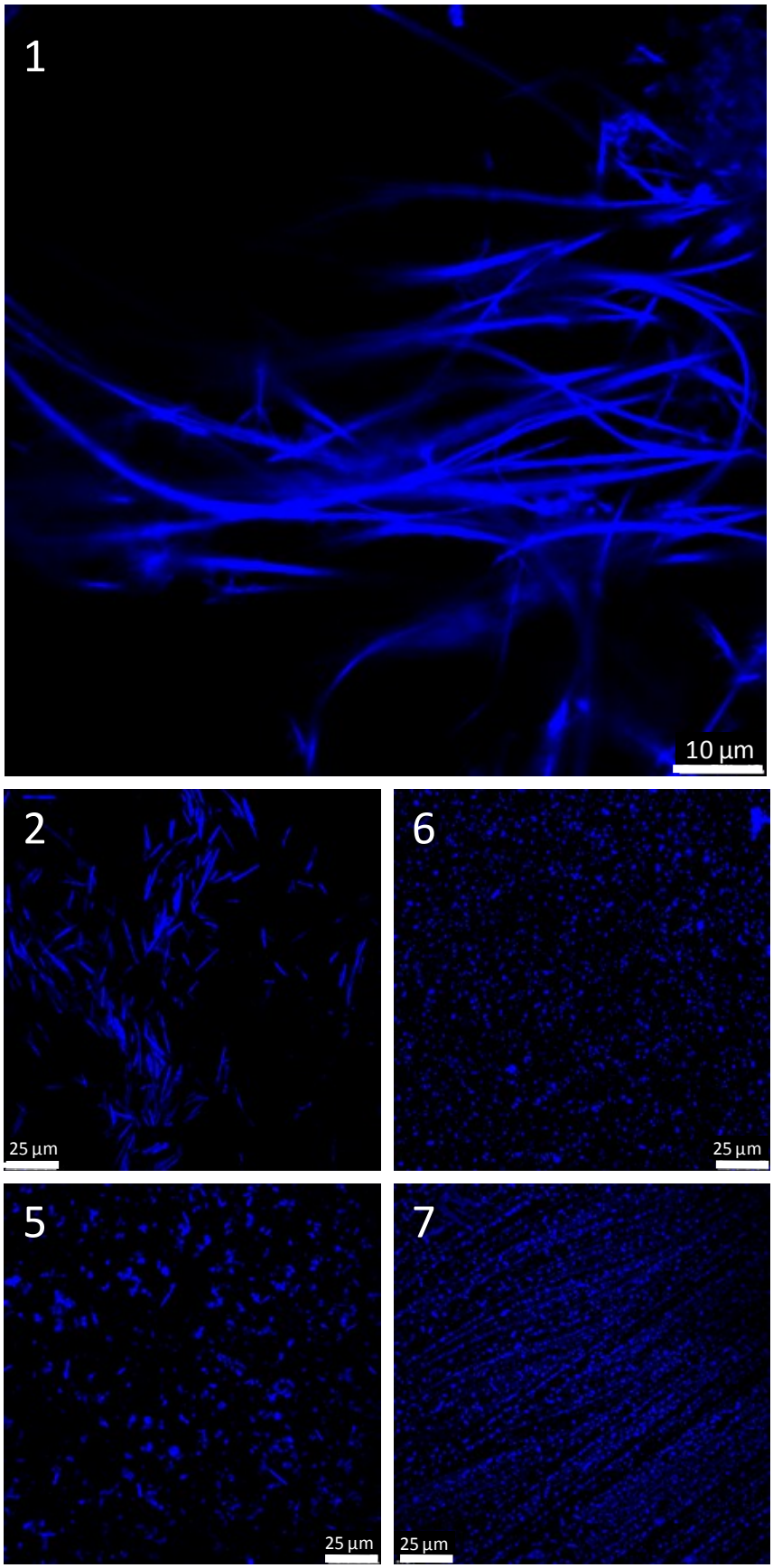


Figure S3A. CLSM images of the aggregates of **1, 2, 5, 6** and **7.** 2 mM in DMSO/H_2O (5/95) mixture λ_{ex} = 405 nm λ_{em} = 410-500 nm.

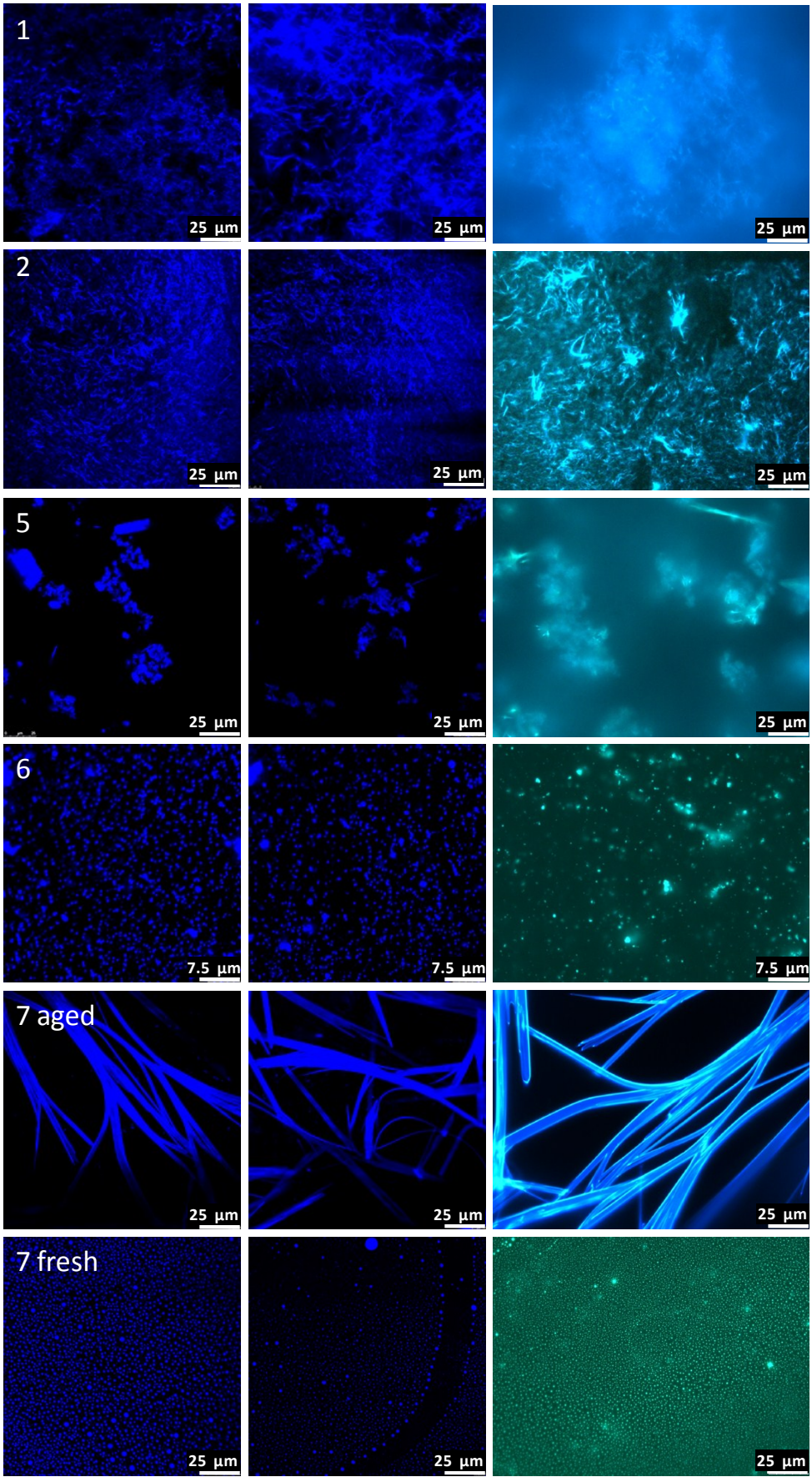


Figure S3B. CLSM images of the aggregates of **1, 2, 5, 6** and **7.** 2 mM in DMSO/H_2O (20/80) mixture. Left and central column: λ_{ex} = 405 nm λ_{em} = 410-500 nm. Right column: λ_{ex} = 405 nm, detection by Microscope Camera DFC7000 with DAPI filter.

5. Aggregation of compound 1 followed by ^{1}H NMR

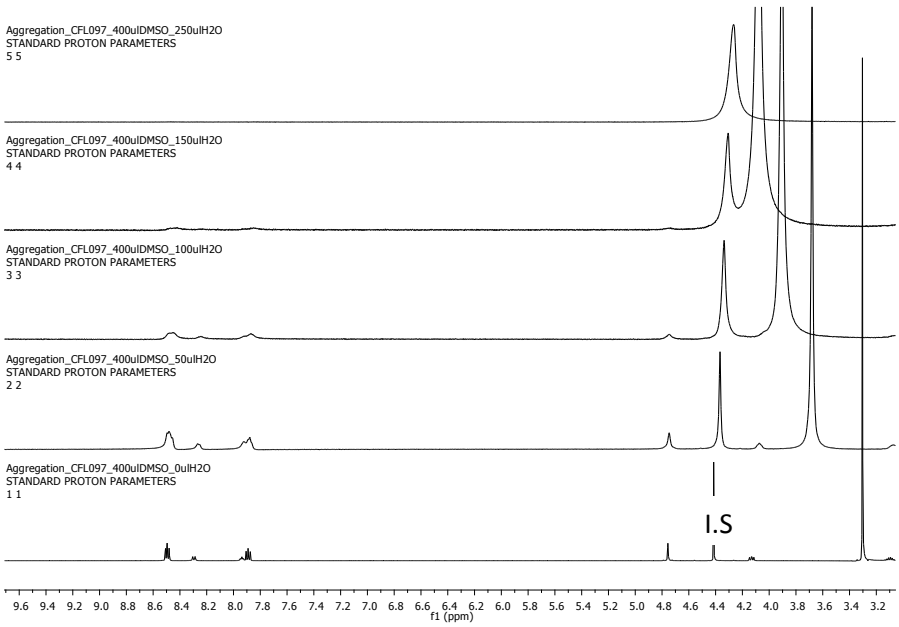


Figure S4. Aggregation process of **1** in DMSO/H_2O; % H_2O= 0, 11.1, 20.0, 27.3 and 38.5 using 0.5 µl of nitromethane as internal standard (singlet at 4.4 ppm) the experiment is performed by adding amounts of water to the same NMR tube, the formation of aggregates can be seen by the progressive disappear and broadening of the signals as the water enters on the system.

6. Absorption and emission spectra of studied compounds: Evolution upon water addition

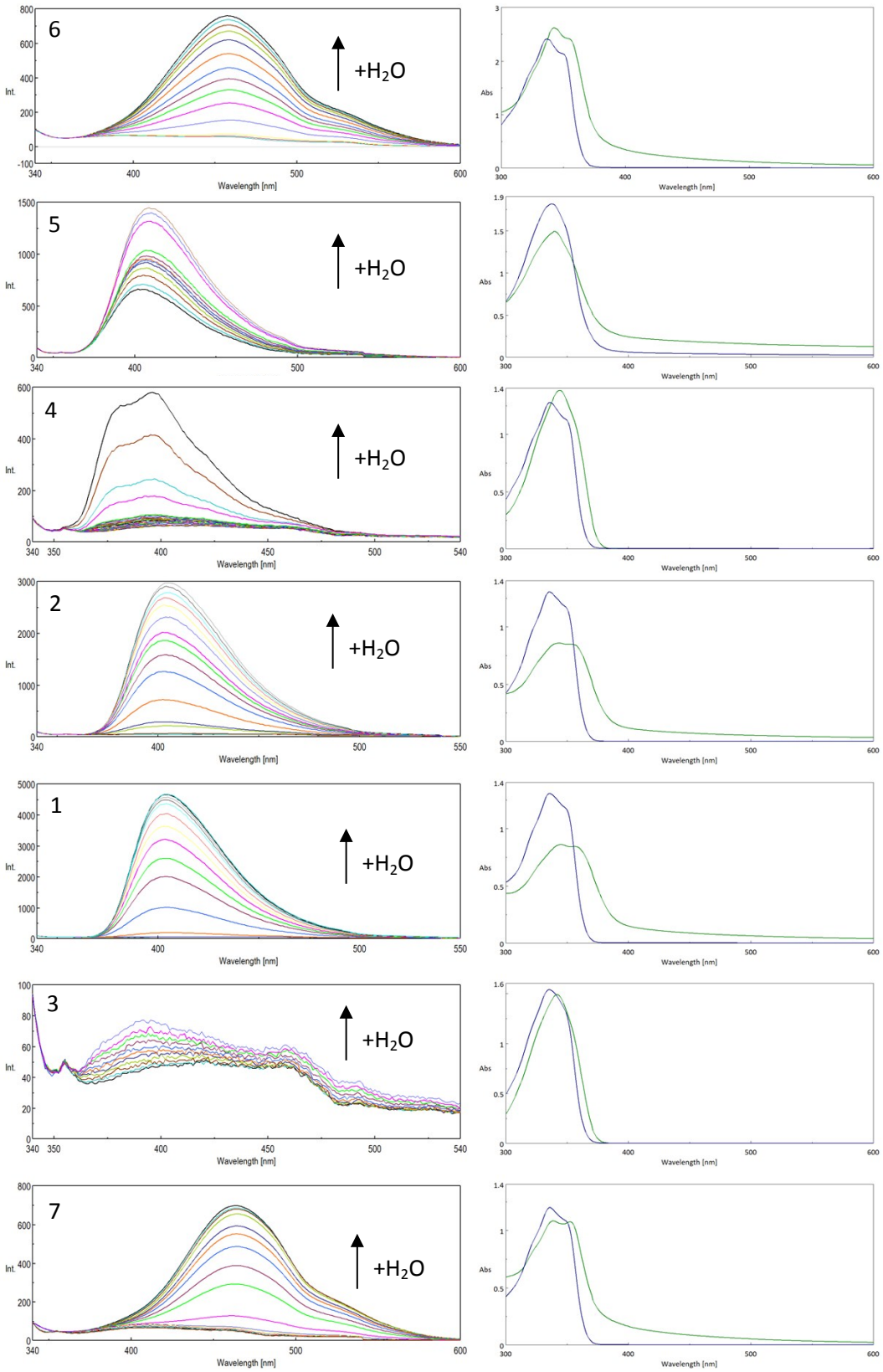


Figure S5. Left: Evolution of fluorescence emission spectra of studied compounds 3.16 mM in DMSO when adding H_2O. Right: Absorption spectra of studied compounds in DMSO (Blue line) and DMSO/H_2O (5/95 green line) 100 µM. Fluorescence rises as H_2O content increases in all cases. From 0 to 1500 µL (ΔV_{H2O} = 50µL).

7. Absorption spectra of compound 5 at different concentrations.

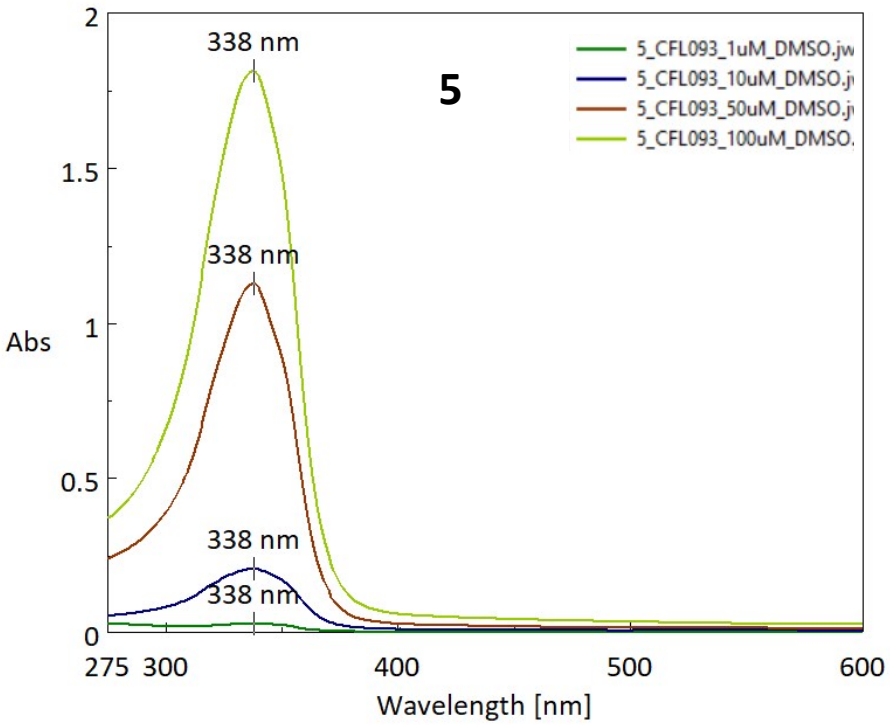


Figure S6. Evolution of UV-Vis spectra of compound 5 in DMSO 1, 10, 50 and 100 µM.

8. Spectroscopic information of all compounds in DMSO and DMSO/H_2O mixtures.

Table S2. Spectroscopic characterization of studied compounds and packing behaviour observed by TEM microscopy in H_2O/DMSO (80/20) mixtures. Absorption spectra recorded at 1 mM in suprasil 1mm quartz cuvette; fluorescence recorded at 3.16 mM with triangular cuvette setup.

	DMSO		**DMSO/H_2O**				**Solid**
Compound	λabs max / nm	λem max / nm	λabs max / nm	λem max / nm	Em max intensity / a.u.	Emitting species	λem max / nm
1	335	391	342	405	4672	F	415
2	335	391	341	405	2975	F	412
3	335	391	341	392	1447	S	453
4	336	391	341	395	77	S	442
5	338	402	339	409	97	F	432
6	336	391	343	458	780	NF	469
7	335	391	341	462	718	NF	471
TPE	307	452	335	462	544	NF	453

S= Soluble, F= Fibrillar aggregates, NF= non fibrillar aggregates

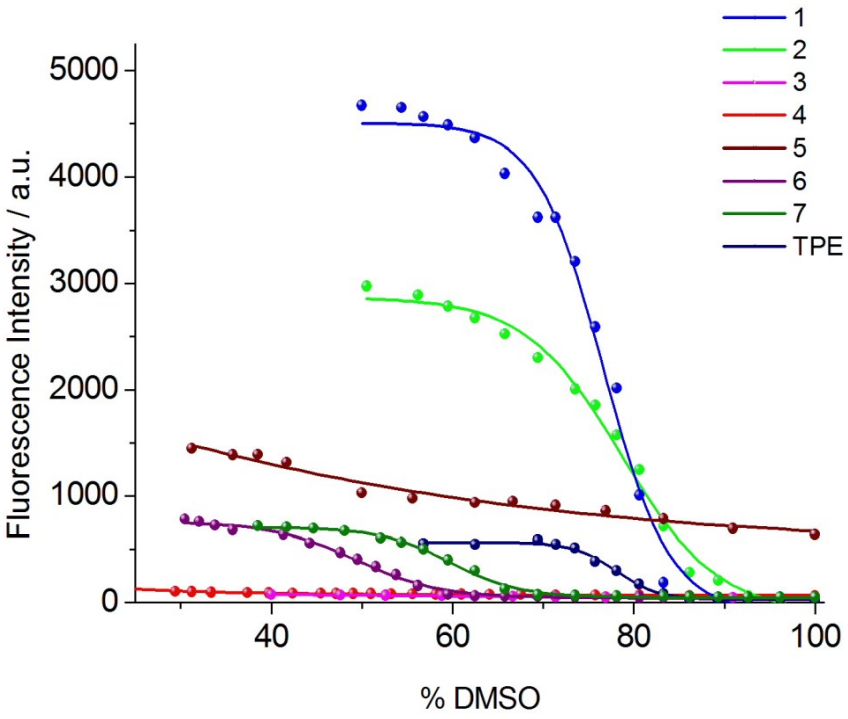


Figure S7. Fluorescence intensity vs % DMSO in DMSO/H_2O mixtures with different compounds at the same concentration (3.16 mM). Measurements done with triangular cuvette λex on the absorption maxima of each compound, the naphthalimide-based compounds at 330 nm and the tetraphenlyethene at 350 nm; λem recorded at the emission maxima of each compound. Start with 100% DMSO previously dried with molecular sieves and add ΔVol=40 µL of H_2O

9. Evolution of metastable systems by UV-Vis spectroscopy and CLSM

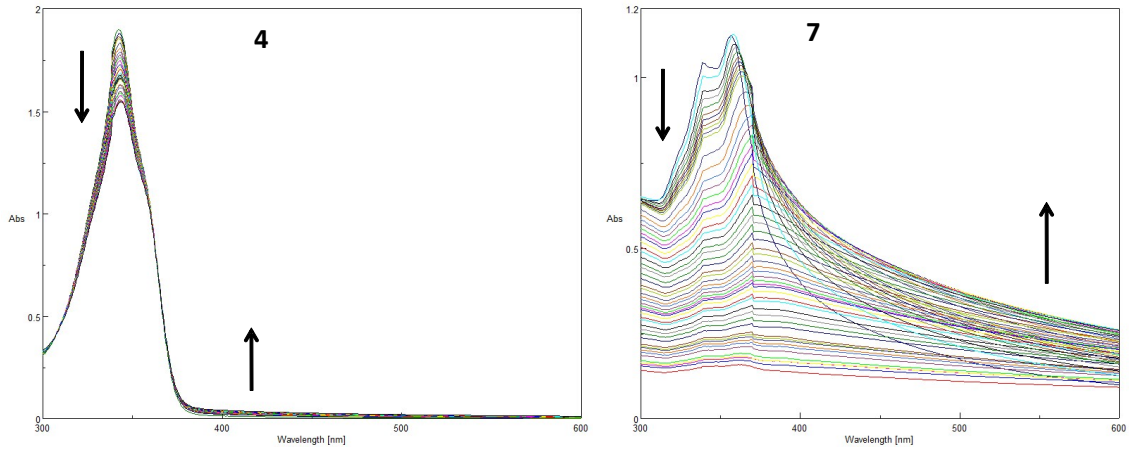
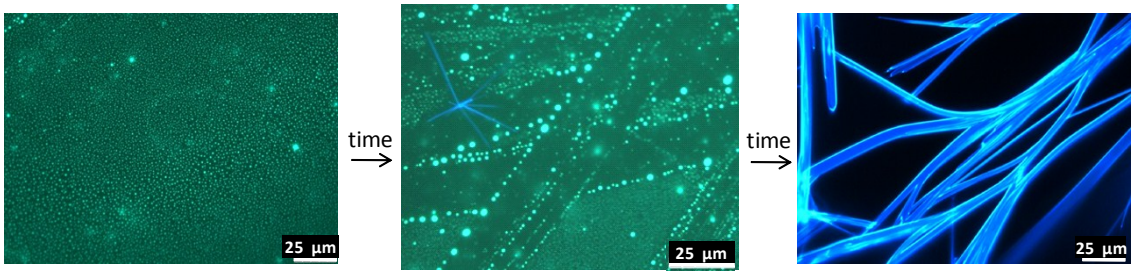


Figure S8. UV-Vis spectroscopy kinetics of the evolution from NPS to crystals/fibres of compound **4** and **7**. 1 mM, DMSO/H2O 5/95. Δt = 10 min, total time 700 min.



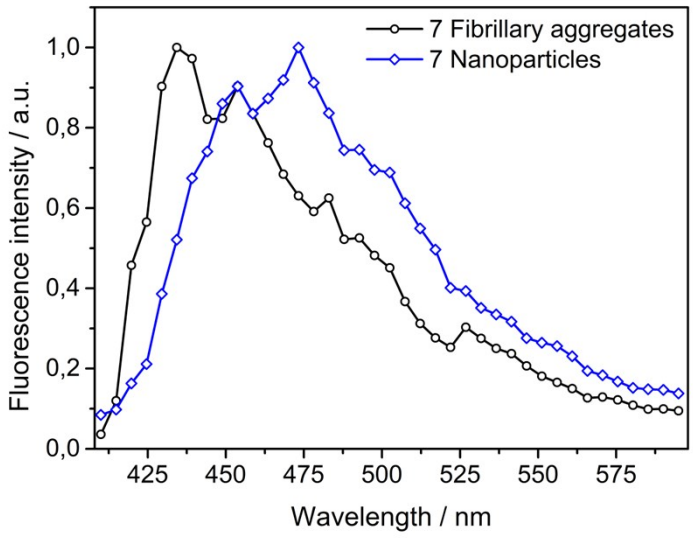
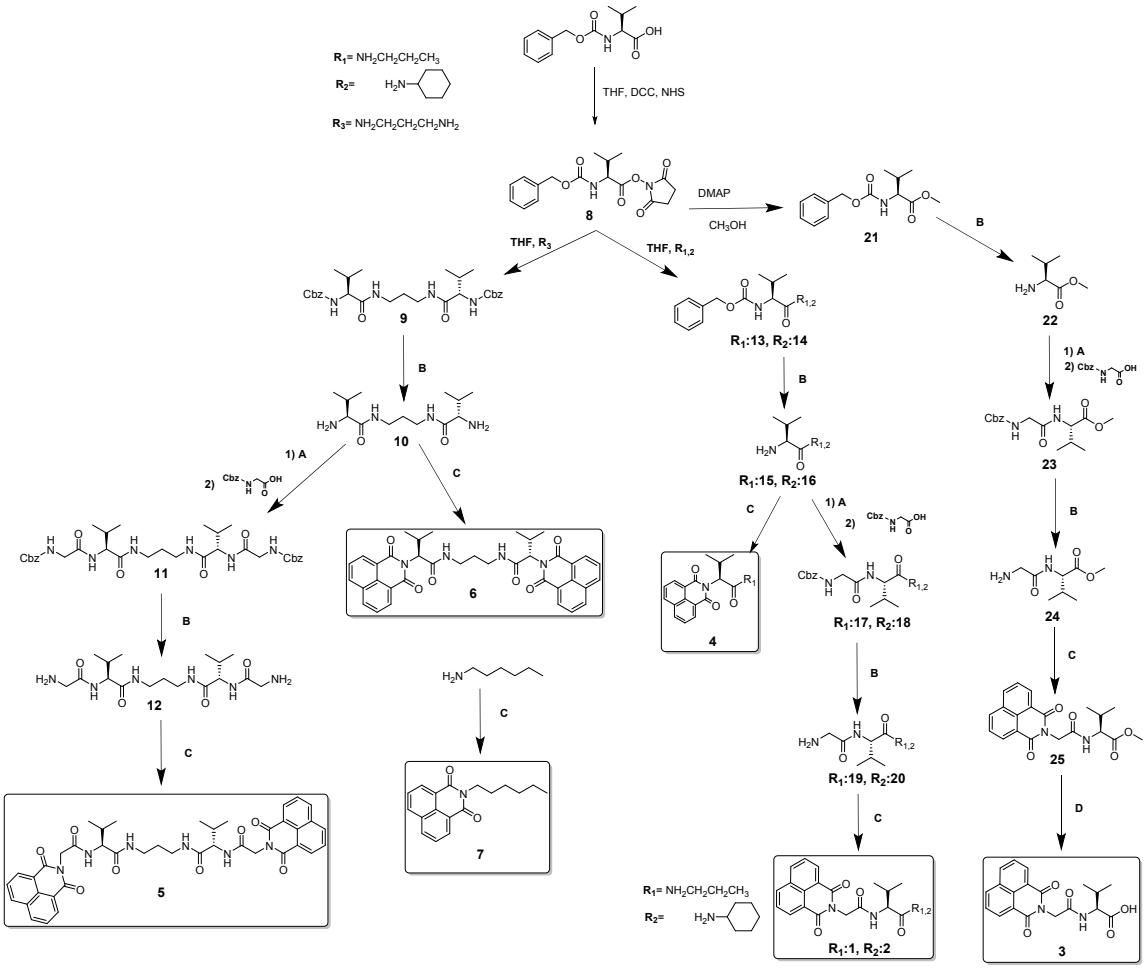


Figure S9. Top row: Evolution from nanoparticles to fibrillar aggregates in compound **7** with the time. **Bottom:** Fluorescence spectra of recorded inside the CLSM showing the transformation from greenish excimeric emission of nanoparticles to bluish fibrillary emission. λex = 405 nm, 2mM in 20/80 DMSO/H_2O mixtures.

Table S3. Evolution of nanoparticles of **4** at 3 mM in 95/5 H_2O/DMSO mixtures with time.

Time / min	Zav / nm	Di / nm	Dn / nm
0	345	372	244
36	496	519	414
64	634	681	424
76	646	718	395

10. General synthetic procedures



Scheme S1. Synthesis of peptide-naphthalimide derivatives A) THF, Et_3N, ClCOOEt, r.t., 8h; B) MeOH, Pd/C, H_2, r.t., 4 h; C) MeOH, 1,8-naphthalyc anhydride, 70 ^oC, 8 h; D) THF/H_2O, LiOH (1.4 eq), r.t., 1h

Synthetic procedure for aminoacid activation with N-Hydroxysuccinimide.

A solution of commercial available Carbobenzyloxy-L-Valine (70 mmol) and Nhydroxysuccinimide (70 mmol, 1.0 eq.) in THF (300 mL) was added dropwise to a solution of N,N'- dicyclohexylcarbodiimide (70.7 mmol, 1.01 eq.) in THF (150 mL). The mixture was further stirred for 1 h at 0 ºC. The solution was then allowed to stand into refrigerator for 2 h, which caused precipitation of N,N'-dicyclohexylurea. After this time, the mixture was filtered under vacuum. The crude residue was purified by crystallization in isopropanol to yield the respective activated ester.

2,5-dioxopyrrolidin-1-yl ((benzyloxy)carbonyl)-L-valinate ***(8, Z-ValOSu)****:*

A white solid was obtained (yield 92 %); the NMR spectra were consistent with those described in the literature[1]

Synthetic procedure for esterification between amino-acid and alcohol.

A solution DMAP (31 mmol, 1.03 eq) in THF (100 mL) was added dropwise to a solution of the corresponding alcohol (30 mmol) in THF (100 mL) at 0ºC and stir until the addition is complete. After 5 minutes, a solution of Z-activated amino acid in (30 mmol) in THF (100 mL) was added dropwise and the system heated to reflux at 60 ºC for 12 hours. The crude is then vacuum dried and oily mixture is obtained. The product is solved with CH_2Cl_2 and washed several times with HCl 0,1 M, then washed again with an aqueous solution of saturated NH_4Cl. The organic layer is dried with anhydrous $MgSO_4$ and dried in the rotary evaporator.

Methyl ((benzyloxy)carbonyl)-L-valinate ***(21, Z-Val-OMe)*** Transparent oil (84 %)*:*

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 7.46 – 7.21 (m, 5H), 5.42 (d, J = 8.3 Hz, 1H), 5.10 (s, 2H), 4.36 – 4.18 (m, 1H), 3.71 (s, 3H), 2.14 (td, J = 12.8, 6.3 Hz, 1H), 0.95 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H). NMR and spectra were consistent with those described in the literature.[2]

General procedure for coupling amino-acid and amine (A).

A solution of Et_3N (2.30 mL, 16.3 mmol, 1 eq) in THF (40 mL) was added dropwise to a solution of commercially available Carbobenzyloxy-*L*-amino acid (4.125 g, 16.22 mmol) in THF (60 mL) under N_2 flow on an ice bath 0 ºC. To this mixture, an ice bath cooled solution of ethyl chloroformate (1.70 ml, 17.7 mmol, 1.1 eq) in THF (50 mL) was added dropwise. The reaction was left at 0 ºC for 30 minutes. Finally, a solution of the free-amine derivatives (19.8 mmol, 1.2 eq.) in THF (50 mL) was added dropwise for 15 minutes at 0 ºC. The reaction was left for 12 hours at room temperature. After this time, the solvent was removed under reduced pressure and the residue was poured into HCl 0.1 M. The mixture was sonicated during 5 minutes. It was filtered under vacuum, and the residue was washed with water KOH 0.1 M and H_2O until pH = 7. The residue was dried under reduced pressure at 50 ºC overnight.

Dibenzyl ((2S,2'S)-(propane-1,3-diylbis(azanediyl))bis(3-methyl-1-oxobutane-1,2-diyl))dicarbamate ***(9, Z-Val-3)*** White solid (92 %) *:*

^{1}H NMR (500 MHz, D_6-DMSO) δ (ppm) 7.89 (t, *J* = 4.9 Hz, 1H), 7.45 – 7.26 (m, 5H), 7.22 (d, *J* = 8.7 Hz, 1H), 5.02 (s, 2H), 3.77 (dd, *J* = 7.9 Hz, 1H), 3.18 – 2.96 (m, 2H), 1.99 – 1.84 (m, 1H), 1.59 – 1.46 (m, 1H), 0.90 – 0.74 (m, 6H). ^{13}C NMR (75 MHz, D_6-DMSO, 30 °C) δ (ppm): 18.4, 19.4, 29.3, 30.3, 36.4, 60.5, 65.5, 127.6, 128.3, 137.1, 156.0, 171.0. NMR and spectra were consistent with those described in the literature.[1]

Dibenzyl ((4S,12S)-4,12-diisopropyl-2,5,11,14-tetraoxo-3,6,10,13-tetraazapentadecane-1,15-diyl)dicarbamate ***(11, Z-Gly-Val-3)*** White solid (90 %)*.*

^{1}H NMR (300 MHz, D_6-DMSO) δ (ppm): 7.90 (s, 2H), 7.73 (d, *J* = 8.8 Hz, 2H), 7.50 – 7.16 (m, 10H), 5.15 – 4.92 (m, 4H), 4.22 – 3.99 (m, 2H), 3.77 – 3.56 (m, 4H), 3.18 – 2.88 (m, 6H), 1.92 (dd, *J* = 13.3, 6.7 Hz, 2H), 1.62 – 1.40 (m, 2H), 0.81 (t, *J* = 5.5 Hz, 12H). ^{13}C NMR (75 MHz, dmso) δ (ppm): 171.11, 169.36, 156.91,

137.51, 128.76, 128.19, 128.08, 65.87, 58.13, 46.02, 43.88, 36.75, 31.10, 29.52, 19.59, 18.53. HRMS (ESI-TOF, positive mode): m/z calcd. For $C_{33}H_{47}N_6O_8^+$ 655.3455; found 655.3460 $[M+H]^+$ (Δ= 0.8 ppm).

benzyl (S)-(3-methyl-1-oxo-1-(propylamino)butan-2-yl)carbamate ***(13, Z-Val-Pr)*** White solid (96 %)*:*

^{1}H NMR (300 MHz, D_6-DMSO) δ (ppm): 7.86 (t, *J* = 4.9 Hz, 1H), 7.46 – 7.24 (m, 5H), 7.17 (d, *J* = 8.9 Hz, 1H), 5.03 (s, 2H), 3.78 (t, *J* = 7.9 Hz, 1H), 3.18 – 2.87 (m, 2H), 2.04 – 1.79 (m, 1H), 1.51 – 1.20 (m, 2H), 0.96 – 0.62 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 11.2, 17.9 19.2, 22.7, 30.1, 41.2, 60.7, 67.0, 128.0, 128.2, 128.5, 136.3, 156.4, 171.1. ESI-MS m/z = 293.4 ($M + H^+$). NMR spectra were consistent with those described in the literature.[3]

benzyl (S)-(1-(cyclohexylamino)-3-methyl-1-oxobutan-2-yl)carbamate ***(14, Z-Val-Chx)*** White solid (93 %)*:*

^{1}H NMR (300 MHz, D_6-DMSO) δ (ppm): 7.43 (t, J = 7.2 Hz, 1H), 7.39 – 7.27 (m, 5H), 6.73 (s, 1H), 5.05 (s, 2H), 3.85 (t, J = 17.2, 9.0 Hz, 1H), 3.63 – 3.48. (m, 1H), 1.95 (sext, J = 6.0, 9.0, 12.0, 21.0 Hz, 1H), 1.70 (t, J = 12.1 Hz, 4H), 1.60 – 1.45 (m, 1H), 1.38 – 1.05 (m, 5H), 0.87 (d, J = 6.1 Hz, 3H), 0.84 (d, J = 6.1 Hz, 3H). ^{13}C NMR (75 MHz, D_6-DMSO) δ (ppm): 169.6, 136.8 (C=O), 127.9 (x3) (CH), 127.3 (C), 127.1 (x2) (CH), 65.1 (CH2), 60.0, 47.2 (CH), 32.0, 31.8 (CH2), 30.2 (CH), 24.9, 24.0 (x2) (CH2), 18.7, 17.7 (CH3). HR ESMS: m/z: calcd. for $C_{19}H_{28}N_2O_3$: 333.2178; found: 333.2173 $[M + H^+]$. NMR spectra were consistent with those described in the literature.[4]

methyl ((benzyloxy)carbonyl)glycyl-L-valinate ***(23, Z-Gly-Val-OMe)*** White solid (94 %)*:*

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.32 – 7.22 (m, 4H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.04 (t, *J* = 5.4 Hz, 1H), 5.08 (s, 2H), 4.50 (dd, *J* = 8.8, 5.3 Hz, 1H), 3.89 (d, *J* = 4.9 Hz, 2H), 3.65 (s, 3H), 2.09 (dq, *J* = 13.4, 6.7 Hz, 1H), 0.85 (dd, *J* = 10.9, 6.9 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 172.36, 169.44, 156.74, 136.31, 128.43, 128.05, 127.92, 66.96, 57.21, 52.07, 44.37, 31.08, 18.86, 17.75. NMR spectra were consistent with those described in the literature.[5]

benzyl (S)-(2-((3-methyl-1-oxo-1-(propylamino)butan-2-yl)amino)-2-oxoethyl)carbamate ***(17, Z-Gly-Val-Pr)*** White solid (96 %)*:*

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.93 (t, *J* = 4.9 Hz, 1H), 7.68 (d, *J* = 8.8 Hz, 1H), 7.42 (t, *J* = 5.7 Hz, 1H), 7.38 – 7.24 (m, 5H), 5.01 (s, 2H), 4.09 (t, *J* = 7.8 Hz, 1H), 3.66 (d, *J* = 6.0 Hz, 2H), 3.13 – 2.86 (m, 2H), 2.00 – 1.81 (m, 1H), 1.38 (sext, *J* = 6.5 Hz, 2H), 0.91 – 0.72 (m, 9H). ^{13}C NMR (75 MHz, dmso) δ (ppm): 171.11, 169.36, 156.91, 137.51, 128.76, 128.19, 128.08, 65.87, 58.13, 46.02, 43.88, 36.75, 31.10, 29.52, 19.59, 18.53. NMR spectra were consistent with those described in the literature.[6]

*benzyl (S)-(2-((1-(cyclohexylamino)-3-methyl-1-oxobutan-2-yl)amino)-2-oxoethyl)carbamate (****18, Z-Gly-Val-Chx****)* White solid (98 %)*:*

^{1}H NMR (500 MHz, D_6-DMSO) δ (ppm) 7.83 (d, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 8.9 Hz, 1H), 7.45 (t, *J* = 5.8 Hz, 1H), 7.39 – 7.28 (m, 5H), 5.03 (s, 2H), 4.16 – 4.08 (m, 1H), 3.66 (d, *J* = 6.0 Hz, 2H), 3.57 – 3.47 (m, 1H), 1.94 – 1.83 (m, 1H), 1.76 – 1.59 (m, 5H), 1.53 (d, *J* = 12.4 Hz, 1H), 1.31 – 1.04 (m, 5H), 0.81 (dd, *J* = 11.3, 6.7 Hz, 6H). ^{13}C NMR (126 MHz, D_6-DMSO) δ (ppm): 170.06, 169.26, 156.93, 137.50, 128.78, 128.21, 128.06, 65.88, 57.87, 47.88, 43.92, 32.89, 32.61, 31.44, 25.65, 24.97, 24.89, 19.51, 18.59. HRMS: m/z: calcd. for C21H32N3O4: 390.2388; found: 390.2386 [M + H^+] (Δ= 1.2 ppm).

General procedure for deprotection of carbobenzyloxy group (B).

Palladium catalyst (10% *w/w*) was suspended in MeOH (250 mL) and stirred under H_2 at room temperature for 10 min. Subsequently, a solution of carbobenzyloxy amino compound in MeOH (150 mL) was added via syringe, followed by stirring under H_2 at room temperature for 2–4 h. The reaction mixture was then filtered through HPLC filters (nylon, 0.46 μm), and the solvent was removed under reduced pressure to yield the respective amine.

(2S,2'S)-N,N'-(propane-1,3-diyl)bis(2-amino-3-methylbutanamide) ***(10, NH2-Val-3)*** transparent solid (86 %):

^{1}H NMR (500 MHz, D_6-DMSO) δ (ppm): 7.83 (t, *J* = 5.1 Hz, 2H), 3.14 – 3.01 (m, 4H), 2.89 (d, *J* = 5.1 Hz, 2H), 1.93 – 1.77 (m, 2H), 1.52 (p, *J* = 6.7 Hz, 2H), 0.82 (dd, *J* = 40.9, 6.8 Hz, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 15.8, 19.2, 29.3, 30.6, 35.1, 59.8, 174.3; ESI-MS (m/z) 273.1 (M + H+), 295.1 (M + Na^+). NMR and spectra were consistent with those described in the literature.[1]

(2S,2'S)-N,N'-(propane-1,3-diyl)bis(2-(2-aminoacetamido)-3-methylbutanamide) ***(12,NH2-Gly-Val-3)*** yellowish solid (96 %)*:*

^{1}H NMR (300 MHz, D_6-DMSO) δ 8.05 (s, 2H), 7.98 (s, 2H), 4.11 (s, 2H), 3.16 (s, 4H), 3.12 – 2.92 (m, 4H), 1.91 (dt, *J* = 12.9, 6.3 Hz, 2H), 1.58 – 1.42 (m, 2H), 0.82 (t, *J* = 5.6 Hz, 12H). ^{13}C NMR (75 MHz, D_6-DMSO) δ (ppm): 172.40, 171.16, 57.73, 44.52, 36.66, 31.31, 29.49, 19.62, 18.49.

(S)-2-amino-3-methyl-N-propylbutanamide ***(15, NH2-Val-Pr)*** transparent oil (99%):

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 0.77 (d, 3H, *J*=6.5 Hz), 0.87 (t, 3H, *J*=8.5 Hz), 0.92 (d, 3H, *J*=7.5 Hz), 1.34 (br s, 2H), 1.47 (m, 2H), 2.22 (m, 1H), 3.16 (m, 3H), 7.28 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 11.4, 16.1, 19.7, 23.0, 30.9, 40.7, 60.3, 174.3. NMR and spectra were consistent with those described in the literature.[7]

(S)-2-amino-N-cyclohexyl-3-methylbutanamide ***(16, NH2-Val-Chx)*** yellowish solid (98%)*:*

^{1}H NMR (500 MHz, D_6-DMSO) δ (ppm): 7.59 (d, J = 7.7 Hz, 1H), 3.63 – 3.48 (m,δ 1H), 3.48 (br, 2H), 2.87 (d, J = 5.3 Hz, 1H), 1.86 – 1.75 (m, 1H), 1.74 – 1.60 (m, 4H), 1.58 – 1.50 (m, 1H), 1.32 – 1.21 (m, 2H), 1.21 – 1.09 (m, 3H), 0.85 (d, J = 6.8 Hz, 3H), 0.77 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d6) δ (ppm):

173.5 (C=O), 59.9 (CH), 48.6 (MeOH) 47.1 (CH), 32.5, 32.4 (CH2), 31.8 (x2) (CH, CH2), 25.2, 24.5 (CH2), 19.5, 17.2 (CH3). HRMS: m/z: calcd. for C11H22N2O: 199.1810; found: 199.1813 [M + H^+]. NMR and spectra were consistent with those described in the literature.[4]

(S)-2-(2-aminoacetamido)-3-methyl-N-propylbutanamide ***(19, NH2-Gly-Val-Pr)*** White solid (94 %):

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.72 (d, *J* = 7.4 Hz, 1H), 6.10 (t, *J* = 5.4 Hz, 1H), 4.14 (t, *J* = 8.5 Hz, 1H), 3.38 (s, 2H), 3.33 – 3.09 (m, 2H), 2.24 – 2.08 (m, 1H), 1.60 – 1.45 (sext, *J* = 7.2 Hz, 2H), 1.01 – 0.84 (m, 9H). ^{13}C NMR (75 MHz, D_6-DMSO) δ (ppm): 172.75, 171.04, 57.55, 44.83, 40.66, 31.47, 22.71, 19.59, 18.50, 11.82. HRMS (ESI-TOF, positive mode): m/z calcd. For $C10H22N3O2^+$ 216.1712; found 216.1710 $[M+H]^+$ (Δ=1.2ppm). NMR and spectra were consistent with those described in the literature.[6]

(S)-2-(2-aminoacetamido)-N-cyclohexyl-3-methylbutanamide ***(20, NH2-Gly-Val-Chx)*** White solid (98 %):

^{1}H NMR (300 MHz, D_6-DMSO) δ (ppm): 7.89 (d, J = 7.8 Hz, 1H), 4.15 (t, J = 7.7 Hz, 1H), 3.60 – 3.43 (m, 1H), 3.10 (s, 2H), 1.87 (td, J = 13.6, 6.9 Hz, 1H), 1.67 (s, 4H), 1.54 (d, J = 12.3 Hz, 1H), 1.33 – 1.02 (m, 5H), 0.82 (t, J = 6.6 Hz, 6H). ^{13}C NMR (75 MHz, D_6-DMSO) δ (ppm): 172.85, 170.09, 57.24, 47.84, 44.98, 32.92, 32.62, 31.85, 25.65, 24.96, 24.88, 19.52, 18.62. HRMS (ESI-TOF, positive mode): m/z calcd. For $C13H25N3O2^+$ 256.2025; found 256.2020 $[M+H]^+$ (Δ= 2.0 ppm).

methyl L-valinate ***(22, NH2-Val-OMe)*** transparent oil (99 %):

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.73 (s, 3H), 3.38 (d, *J* = 4.9 Hz, 1H), 2.11 – 2.01 (m, 1H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H). NMR and spectra were consistent with those described in the literature.[8]

Methyl glycyl-L-valinate ***(24, NH2-Gly-Val-OMe)*** transparent oil (95 %):

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.79 – 7.60 (m, 1H), 4.52 (dd, *J* = 9.0, 5.1 Hz, 1H), 3.71 (s, 2H), 3.37 (s, 2H), 2.17 (td, *J* = 13.5, 6.8 Hz, 1H), 0.92 (t, *J* = 6.9 Hz, 6H). ^{13}C NMR (75 MHz, $cdcl_3$) δ (ppm): 172.82, 172.45, 56.70, 52.03, 44.67, 31.13, 18.97, 17.76. NMR and spectra were consistent with those described in the literature.[9]

General procedure for preparing Naphthalimide derivatives (C).

1,8-Naphthalic anhydride (1.94 mmol, 1 eq.) was suspended in a closed opaque vial with CH_3OH (15 mL) and vigorous stirring at room temperature. A solution of free-amino derivative (1.95 mmol) in CH_3OH (15 mL) was added dropwise. The vial was closed and the reaction mixture was heated to 75 ^{o}C for 8 hours. Dissolution of the suspension was observed as the temperature increases and appearance of voluminous solid was observed. After this time, the reaction mixture was left at room temperature and the brown solid was filtered through sintered funnel and washed with hot CH_3OH several times until light brown/white solid is obtained.

(2S,2'S)-N,N'-(propane-1,3-diyl)bis(2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-3-methylbutanamide). ***(6, Naph-Val-3)***. Light brown solid (97 %):

^{1}H NMR (300 MHz, dmso) δ 8.46 (d, *J* = 6.6 Hz, 8H), 7.86 (t, *J* = 7.7 Hz, 4H), 7.70 (t, *J* = 5.5 Hz, 2H), 4.97 (d, *J* = 9.1 Hz, 2H), 2.92 (tt, *J* = 12.1, 5.9 Hz, 4H), 2.63 – 2.51 (m, 2H), 1.40 – 1.28 (m, 2H), 1.06 (d, *J* = 6.3 Hz, 6H), 0.54 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (75 MHz, dmso) δ 168.80, 164.06, 134.76, 131.76, 131.33, 128.14, 127.66, 122.65, 58.94, 36.72, 29.39, 26.71, 23.20, 19.24. HRMS (ESI-TOF, positive mode): m/z calcd. C37H36N4O6Na+ 655.2533; found 655.2537 $[M+Na]^+$ (Δ= 0.6 ppm).

(2S,2'S)-N,N'-(propane-1,3-diyl)bis(2-(2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)acetamido)-3-methylbutanamide). ***(5, Naph-Gly-Val-3)*** white solid (80 %):

^{1}H NMR (400 MHz, $CDCl_3$/HFIPA) δ 8.47 (d, *J* = 7.2 Hz, 3H), 8.19 (d, *J* = 8.1 Hz, 3H), 7.72 (t, *J* = 7.8 Hz, 3H), 7.04 (s, 2H), 6.97 (d, *J* = 8.2 Hz, 2H), 4.90 (dd, *J* = 50.3, 15.9 Hz, 4H), 3.40 – 3.15 (m, 4H), 2.11 (dq, *J* = 13.5, 6.8 Hz, 2H), 1.76 – 1.62 (m, 3H), 0.94 (t, *J* = 6.9 Hz, 14H). ^{13}C NMR (101 MHz, $CDCl_3$/HFIPA) δ 172.71, 169.31, 165.33, 135.60, 132.22, 131.55, 127.99, 127.15, 120.85, 59.89, 42.71, 36.49, 30.25, 28.06, 18.37, 17.09. HRMS (ESI-TOF, positive mode): *m/z*calcd. For C41H42N6O8Na$^+$ 769.2962; found 769.2974 $[M+Na]^+$ (*Δ*= 1.6 ppm).

2-hexyl-1H-benzo[de]isoquinoline-1,3(2H)-dione. ***(7, Naph-C_6)*** white solid (95 %)*:*

^{1}H NMR (400 MHz, DMSO) δ 8.39 (dd, *J* = 15.0, 7.8 Hz, 4H), 7.79 (t, *J* = 7.7 Hz, 2H), 4.03 – 3.89 (m, 2H), 1.64 – 1.51 (m, 2H), 1.36 – 1.19 (m, 6H), 0.83 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 163.72, 134.64, 131.66, 131.06, 127.69, 127.56, 122.39, 40.05, 31.40, 27.86, 26.65, 22.43, 14.33. HRMS (ESI-TOF, positive mode): *m/z*calcd. For C23H27N3O3Na$^+$ 304.1313; found 304.1313 $[M+Na]^+$ (*Δ*= 0.0 ppm).

(S)-2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-3-methyl-N-propylbutanamide. ***(4, Naph-Val-Pr)*** white solid (75 %)*:*

^{1}H NMR (300 MHz, DMSO) δ 8.50 (ddd, *J* = 7.3, 5.6, 1.1 Hz, 1H), 7.89 (dd, *J* = 8.3, 7.3 Hz, 1H), 7.79 (t, *J* = 5.6 Hz, 1H), 5.03 (d, *J* = 9.2 Hz, 1H), 3.06 – 2.84 (m, 1H), 2.80 – 2.65 (m, 1H), 1.39 – 1.24 (m, 1H), 1.19 (t, *J* = 7.7 Hz, 1H), 0.72 (t, *J* = 7.4 Hz, 1H), 0.62 (d, *J* = 7.0 Hz, 1H). ^{13}C NMR (75 MHz, DMSO) δ 168.71, 164.13, 134.80, 131.80, 131.34, 128.18, 127.75, 122.77, 58.98, 40.99, 26.81, 23.33, 22.63, 19.29, 11.78. HRMS (ESI-TOF, positive mode): *m/z*calcd. For C20H22N2O3Na$^+$ 361.1528; found 361.1522 $[M+Na]^+$ (*Δ*= 1.5 ppm).

(S)-2-(2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)acetamido)-3-methyl-N-propylbutanamide. ***(1, Naph-Gly-Val-Pr)*** white solid (89 %):

^{1}H NMR (400 MHz, DMSO) δ 8.50 (ddd, *J* = 6.8, 5.2, 1.0 Hz, 1H), 8.30 (d, *J* = 9.0 Hz, 1H), 7.94 (t, *J* = 5.6 Hz, 1H), 7.89 (dd, *J* = 8.2, 7.3 Hz, 1H), 4.76 (s, 1H), 4.14 (dd, *J* = 9.0, 7.2 Hz, 1H), 3.11 (td, *J* = 13.0, 6.9 Hz, 1H), 2.97 (td, *J* = 12.4, 7.0 Hz, 1H), 2.04 – 1.88 (m, 1H), 1.42 (h, *J* = 7.3 Hz, 1H), 0.86 (dt, *J* = 14.6, 5.4 Hz, 2H). ^{13}C NMR (101 MHz, DMSO) δ 171.01, 166.99, 163.75, 135.02, 131.85, 131.34, 127.95, 127.76, 122.40,

58.44, 42.70, 40.75, 40.69, 31.25, 22.71, 19.66, 18.70, 11.87. HRMS (ESI-TOF, positive mode): *m/z*calcd. For $C_{22}H_{25}N_3O_4Na^+$ 418.1743; found 418.1736 $[M+Na]^+$ (*Δ*= 1.7 ppm).

(S)-N-cyclohexyl-2-(2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)acetamido)-3-methylbutanamide. ***(2, Naph-Gly-Val-Chx)*** white solid (91 %)*:*

^{1}H NMR (400 MHz, $CDCl_3$/HFIPA) δ 8.58 (dd, *J* = 7.4, 1.0 Hz, 2H), 8.33 (d, *J* = 7.8 Hz, 2H), 7.85 – 7.78 (m, 2H), 6.71 (d, *J* = 8.6 Hz, 1H), 6.20 (d, *J* = 8.2 Hz, 1H), 4.86 (s AB system, *J* = 41.0, 15.6 Hz, 2H), 2.05 (dq, *J* = 13.7, 6.8 Hz, 1H), 1.91 – 1.79 (m, 2H), 1.79 – 1.67 (m, 2H), 1.67 – 1.59 (m, 1H), 1.43 – 1.26 (m, 2H), 1.26 – 1.08 (m, 3H), 0.95 (t, *J* = 6.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.61, 169.03, 165.25, 135.65, 132.36, 131.72, 128.22, 127.23, 121.14, 77.12, 59.92, 49.38, 42.84, 32.46, 32.05, 30.83, 25.14, 24.44, 18.50, 17.66. HRMS (ESI-TOF, positive mode): *m/z*calcd. For $C_{25}H_{29}N_3O_4Na^+$ 458.2063; found 458.2063 $[M+Na]^+$ (*Δ*= 0.0 ppm).

Methyl (2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)acetyl)-L-valinate ***(25, Naph-Gly-Val-OMe)*** white solid (86 %)*:*

^{1}H NMR (500 MHz, D_6-DMSO) *δ* (ppm): 8.59 (d, *J* = 8.4 Hz, 1H), 8.49 (t, *J* = 7.3 Hz, 4H), 7.89 (t, *J* = 7.7 Hz, 2H), 4.77 (s AB system, *J* = 16.1 Hz, 2H), 4.23 (dd, *J* = 8.0, 6.8 Hz, 1H), 3.66 (s, 2H), 2.05 (td, *J* = 13.4, 6.7 Hz, 1H), 0.91 (dd, *J* = 12.1, 6.8 Hz, 6H). ^{13}C NMR (126 MHz, D_6-DMSO) *δ* (ppm): 172.36, 167.42, 163.68, 135.02, 131.81, 131.33, 127.90, 127.72, 122.30, 57.93, 52.19, 42.48, 30.68, 19.41, 18.68. HRMS (ESI-TOF, positive mode): m/z calcd. $C_{20}H_{20}N_2O_5Na$+ 391.1270; found 391.1268 $[M+Na]^+$ (Δ= 0.5 ppm).

General procedure for base hydrolysis (D).

A solution suspension of naphthalimide derived ester (1.33 mmol) in THF (60 mL) at r.t. was mixed with a solution of LiOH (50 mg, 2.1mmol, 1.6 eq) in water (20 mL) and stirred at room temperature for several hours until obtain a transparent solution. The reaction was followed by TLC (hexane/ethyl acetate 1:1). Then the reaction mixture was evaporated in vacuo to remove the THF and the crude product was washed with diethyl ether. The aqueous phase was then acidified with HCl 1 M and voluminous solid precipitates. The solid was then filtered and washed with saturated NH_4Cl and dried under vacuum at 60 ^{o}C.

(2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)acetyl)-L-valine. ***(3, Naph-Gly-Val-OH)*** white solid (87 %):

^{1}H NMR (400 MHz, DMSO) δ 8.50 (ddd, *J* = 6.2, 4.6, 1.0 Hz, 4H), 8.46 (d, *J* = 8.8 Hz, 1H), 7.89 (dd, *J* = 8.2, 7.3 Hz, 2H), 4.77 (s AB system, 2H), 4.19 (dd, *J* = 8.7, 5.9 Hz, 1H), 2.06 (dq, *J* = 13.5, 6.8 Hz, 1H), 0.91 (dd, *J* = 6.8, 2.7 Hz, 6H). ^{13}C NMR (101 MHz, DMSO) δ 173.34, 167.27, 163.72, 135.04, 131.84, 131.35, 128.05, 127.77, 122.35, 57.76, 42.53, 30.64, 19.62, 18.46. HRMS (ESI-TOF, positive mode): m/z calcd. For $C_{19}H_{18}N_2O_5Na^+$ 377.1113; found 377.1113 $[M+Na]^+$ (Δ= 0.0 ppm).

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