Materials and Methods

Materials

All commercially available chemicals were used as received and were purchased from Acros Organics (Waltham, Massachusetts, USA), Aldrich (St. Louis, Missouri, USA), Alfa Aesar (Massachusetts, USA), Iris Biotech (Marktredwitz, Germany), Fluorochem (Hadfield, UK), Fluka (St. Louis, Missouri, USA) , Merck (Darmstadt, Germany) and TCI (Tokyo, Japan).

UV/vis spectroscopy

UV/vis spectra were measured on a *Jasco V-770* spectrophotometer (Jasco Deutschland GmbH, Pfungstadt, Germany) using *High Precision SUPRASIL quartz glass cuvettes* (Hellma Analytics GmbH, Müllheim, Germany). The spectra were recorded with Spectra Manager 2, Spectra Manager Version 2.14.06 (Jasco Deutschland GmbH, Pfungstadt, Germany). The samples were dissolved in 20 mM HEPES buffer (pH = 8.01) and the baseline was measured against the same solvent. Data analysis was realized using *OriginPro 2018 b b9.5.5.409* (ORIGINLAB Corperation, Northampton, USA).

Circular Dichroism Spectroscopy

CD spectra were recorded on a *Jasco J-815* (Jasco Deutschland GmbH, Pfungstadt, Germany) using the software *Spectra Manager 2.12.00* (Jasco Deutschland GmbH, Pfungstadt, Germany). Data processing was realized using *OriginPro 2018 b b9.5.5.409* (ORIGINLAB Corperation, Northampton, USA). If not indicated otherwise, all samples were measured at 20 °C and 3 accumulations were executed. Samples were dissolved in 1 mM HEPES buffer (pH = 8.01).

Dynamic light scattering

Dynamic light scattering (DLS) was performed on a *Nano-ZS Zetasizer* (Malvern Instruments, Malvern, UK). Aqueous samples were measured in disposable 1 mL *semi-micro PMMA* cuvettes (Brand GmbH & Co. KG, Wertheim, Germany), while *High Precision SUPRASIL quartz glass cells* (Hellma Analytics GmbH, Müllheim, Germany) were used for measurements in organic solvents. Data analysis was realized with *Malvern Zetasizer software 7.12* (Malvern Instruments, Malvern, UK).

Inverted vial tests

Hydrogels were prepared by a well-established method reported by Adams[1] and co-workers. Stock solutions of Nap-GFFYS and Nap-GFFYS-AAP were prepared in MilliQ water at pH ≈ 12

by stepwise addition of NaOH. The stock solutions were diluted to the respective concentrations and M-CDV were added. This precursor solution was transferred into a vial with the respective amount of GdL present and mixed by gently shaking the vial. After leaving the vial unmoved overnight, hydrogel formation was tested by the standard inverted vial test.

Rheology

Rheological measurements were carried out on an Anton Paar *Modular Compact Rheometer MCR 102* (Anton Paar GmbH, Graz, Austria) with Anton Paar *RhepCompass V1.20.40.496* (Anton Paar GmbH, Graz, Austria) analysis software. Data processing was realized using *OriginPro 2018 b b9.5.5.409* (ORIGINLAB Corperation, Northampton, USA).

Hydrogel samples were prepared and gelated overnight. For the measurement approximately 200 µl of the hydrogel were transferred onto the rheometer. After moving to the measuring position the sample was equilibrated for 10 min before starting the first measurement.

For magneto rheological measurements the rheometer was equipped with a *MRD 70* (Anton Paar GmbH, Graz, Austria) magneto cell. Direct current was supplied through a Anton Paar *PS-MRD* (Anton Paar GmbH, Graz, Austria) direct current source. Further a parallel plate geometry using a *PP20/MRD/TI* (Anton Paar GmbH, Graz, Austria) spindle (19.951 mm plate diameter) was used. Magnetic flux density was measured with a Magnet Physik *FH54 Gaus-/Teslameter* (Magnet Physik Dr. Steingroever GmbH, Köln, Germany). All magnetorheological measurements were carried out at 20 °C, 1 mm Gap with 0.1% shear strain and 1 Hz frequency.

Photo-rheological measurements were performed by equipping the rheometer with a *P-PTD200 + H-PTD200* (Anton Paar GmbH, Graz, Austria) photo cell and a *CP25-2* (Anton Paar GmbH, Graz, Austria) spindle (25 mm plate diameter, 2 degree angle). The sample was continuously measured at 20 °C, 0.1% shear strain and a frequency of 1 Hz during irradiation with UV-(λ = 365 nm) or vis-light (λ = 520 nm) for 1 min each.

Bending Experiments

Hydrogels were prepared by a well-established method reported by Adams[1] and co-workers. 1 wt% stock solutions of Nap-GFFYS and Nap-GFFYS-AAP were prepared in MilliQ at pH ≈ 12 by stepwise addition of NaOH. 400 µL of the Nap-GFFYS and 100 µL of the Nap-GFFYS-AAP stock solution were mixed with 500 µL of a 1 mM (4 mg/ml MNPs) M-CDV solution. The obtained solution was transferred into a vial containing 20 mg GdL and was shaken until the GdL was fully dissolved. This solution was subsequently transferred into a Pasteur pipette and gelated overnight. For analysis the hydrogel was pressed out of the pipette into a 22 mL glass vial filled with MilliQ and manipulated by placing a permanent magnet at the wall of the vial.

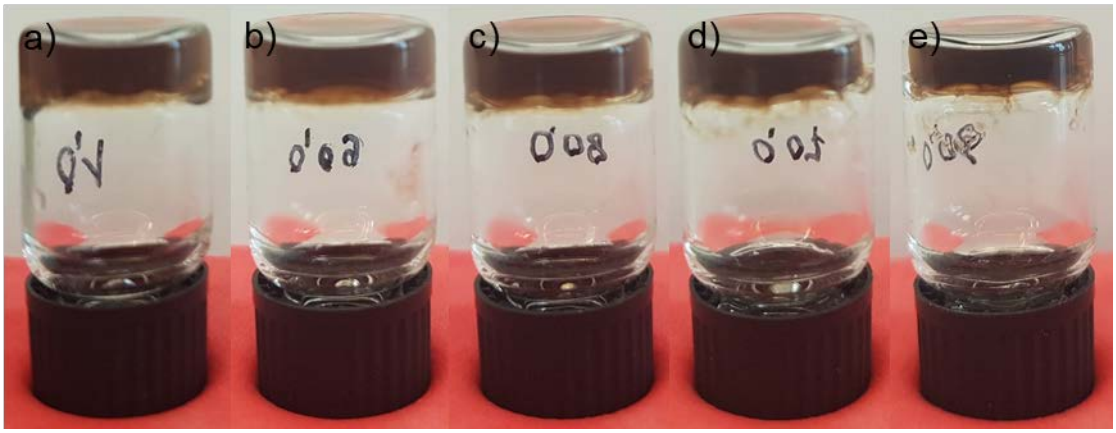


Fig. S1 Determination of the critical gelation concentration through inverted vial tests of Nap-GFFYS with 20% Nap-GFFYS-AAP and 250 µM M-CDV corresponding to 1 mg/ml $CoFe_2O_4$ nanoparticles. Total gelator concentration: a) 0.1 wt%, b) 0.09 wt%, c) 0.08 wt%, d) 0.07 wt% e) 0.06 wt%.

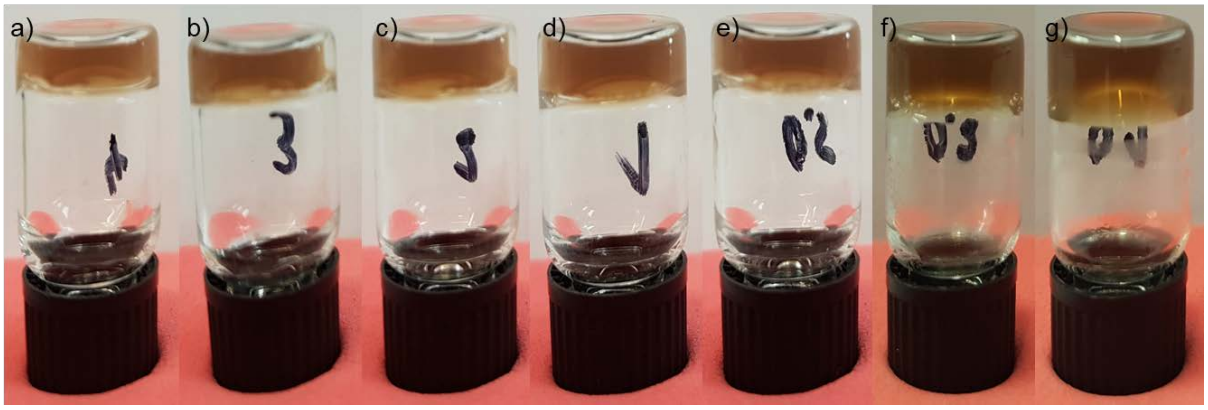


Fig. S2 Determination of the critical GdL concentration of 0.1 wt% Nap-GFFYS hydrogels with 20% Nap-GFFYS-AAP and 250 µM M-CDV corresponding to 1 mg/ml $CoFe_2O_4$ nanoparticles through inverted vial tests. GdL concentrations: a) 10 mg/ml, b) 7.5 mg/ml, c) 5 mg/ml, d) 2.5 mg/ml e) 1.25 mg/ml, f) 0.75 mg/ml, g) 0.25 mg/ml.

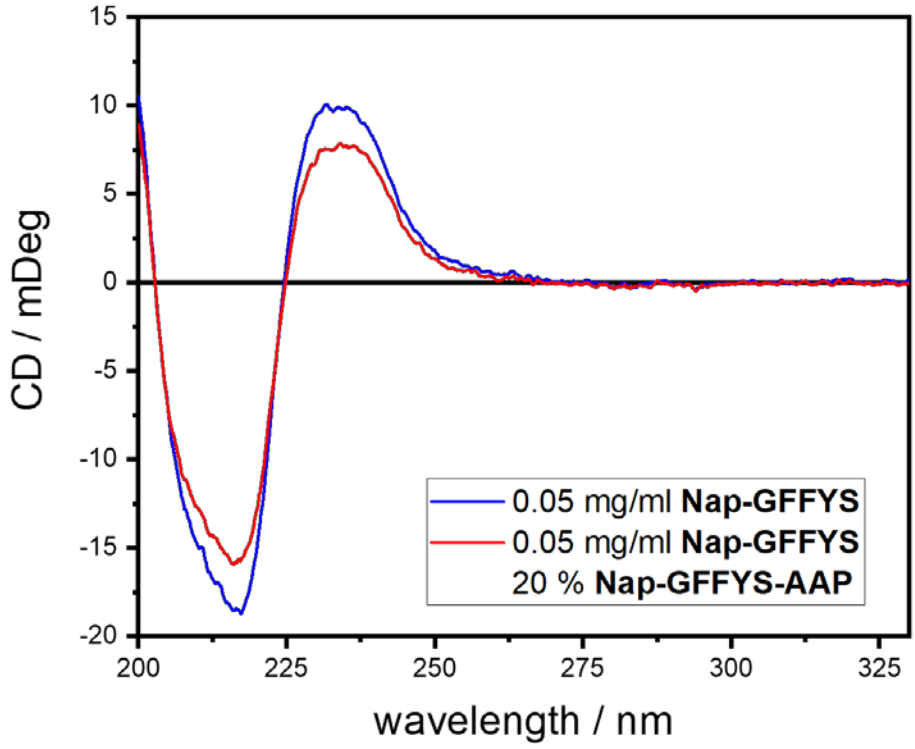


Fig. S3 CD spectra of Nap-GFFYS and Nap-GFFYS with 20% Nap-GFFYS-AAP at 0.05 mg/ml in 1 mM HEPES-buffer at pH = 8.01.

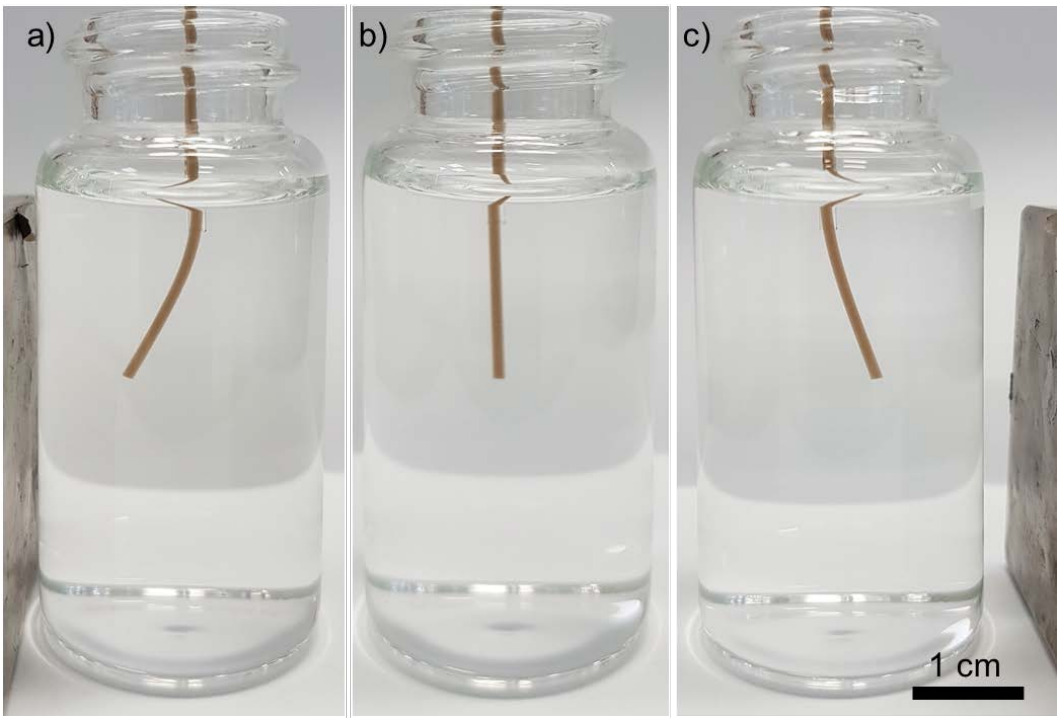


Fig. S4 Bending of a hydrogel rod consisting of 0.5 wt% Nap-GFFYS mit 20% Nap-GFFYS-AAP and 500 µM M-CDV (corresponding to 2 mg/ml MNPs) in water by placing a permanent magnet at the vial walls. a) Magnet placed on the left side of the vial, b) Hydrogel in the absence of a magnet, c) Magnet placed on the right side of the vial.

Synthesis

Cobaltferrite NPs capped with oleylamine and oleic acid

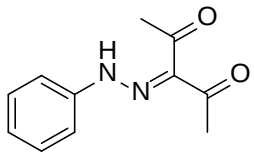
Bis(acetylacetonato)-cobalt(II) (77.1 mg, 0.3 mmol, 1 eq.) and tris(acetylacetonato)-iron(III) (212.0 mg, 0.6 mmol, 2 eq) were dissolved in 1-ocatdecene (10 ml), oleic acid (3 ml, 9.5 mmol, 31 eq.) and oleylamine (3 ml, 9.2 mmol, 30 eq.). The mixture was transferred into a flame dried Schlenk-flask with 1-octadecanol (202.9 mg, 0.75 mmol, 2.5 eq) present. The mixture was degassed for 30 min by an argon stream at room temperature. The solution was heated up to 110 °C and stirred for 30 min, before heating up to 200 °C. After stirring for 30 min the mixture was heated up to 265 °C and stirred at this temperature for 1.5 h. After cooling to room temperature the nanoparticles were precipitated upon the addition of EtOH (ca. 20 ml). The precipitated nanoparticles were separated using a bar magnet and then re-dissolved in cyclohexane (ca. 2 ml). This washing procedure was repeated 2 times. After freeze-drying from cyclohexane the cobaltferrite nanoparticles were isolated as a black powder in a yield of 19.4 mg.

DLS (Diameter number mean): 9.2 ± 0.4 nm

M-CDV preparation

M-CDV were prepared using a method presented by Ravoo[2] and co-workers. Oleic acid and oleylamine capped cobaltferrite NPs and amphiphilic β-CD were dissolved in chloroform. The solvent was slowly evaporated from the solution in an argon stream while continually rotating the flask. The residual solvent was removed from the film in strong vacuum. The film was hydrated by the addition of MilliQ and vigorous stirring overnight. This solution was sonicated for 10 s and then passed repetitively through a 100 nm pore size polycarbonate membrane in a *Liposofast* manual extruder.

3-(2-Phenylhydrazono)pentane-2,4-dione



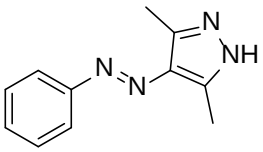
Aniline (1,86 g, 20 mmol, 1.82 ml, 1 eq.) and HCl (12 M, 4,6 ml) were dissolved in AcOH (30 ml) at 0 °C. $NaNO_2$ (1,66 g, 24 mmol, 1.2 eq.) dissolved in a minimum amount of water (ca. 5 ml) was added dropwise and stirred for 1 hr. The resulting mixture was dropwise added into a suspension of NaOAc (2.46 mg, 30 mmol, 3 eq.) and Pentane-2,4-dione (2.60 g, 26 mmol, 2.65 ml, 1.3 eq.) in EtOH/water 10:6 (32 ml). The mixture was stirred for 1 hr and the yellow precipitate was collected *via* filtration. The solid was washed with EtOH (50 ml) and water/EtOH 1:1 (50 ml) and dried under vacuum. The product was isolated as a yellow solid in a yield of 2.52 g (12.3 mmol, 62%)[3].

^{1}H NMR: (400 MHz, $CDCl_3$) δ [ppm]= 14.74 (s, 1H, -N**H**-), 7.49 – 7.35 (m, 4H, *o,m*-Ph **H**), 7.24 – 7.15 (m, 1H, *p*-Ph **H**), 2.61 (s, 3H, -C**H**$_3$), 2.50 (s, 3H, -C**H**$_3$).

^{13}C NMR: (101 MHz, $CDCl_3$) δ [ppm]= 197.97, 197.16, 141.53, 133.22, 129.68, 125.92, 116.28, 31.71, 26.67.

ESI-MS: [*m*/*z*]: found: 227.0798, calculated: 227.0791 $[M+Na]^+$.

3,5-Dimethyl-4-(phenyldiazenyl)-1*H*-pyrazole



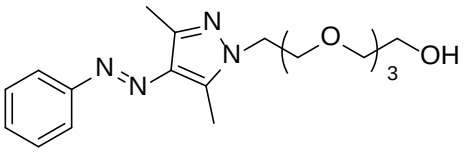
3-(2-Phenylhydrazono)pentane-2,4-dione (2.52 g, 12.3 mmol, 1 eq.) and Hydrazine x Hydrate (396 mg, 12.3 mmol, 0.48 ml, 1 eq.) were dissolved in EtOH (125 ml) and the solution was refluxed for 3 h. The orange solution was concentrated under reduced pressure and the 3,5-Dimethyl-4-(phenyldiazenyl)-1H-pyrazole was isolated as a yellow solid without further purification in a yield of 2.392 g (11.95 mmol, 97%)[3].

^{1}H NMR: (400 MHz, $CDCl_3$) δ [ppm]= 10.20 (s, 1H, -N**H**-), 7.87 – 7.74 (m, 2H, *o*-Ph **H**), 7.52 – 7.44 (m, 2H, *m*-Ph **H**), 7.43 – 7.36 (m, 1H, *p*-Ph **H**), 2.64 (s, 6H, -C**H**$_3$).

^{13}C NMR: (101 MHz, $CDCl_3$) δ [ppm]= 153.55, 141.49, 134.74, 129.51, 128.94, 121.86, 12.20.

ESI-MS: [*m*/*z*]: found: 201.1146, calculated: 201.1135 $[M+H]^+$.

(*E*)-2-(2-(2-(3,5-Dimethyl-4-(phenyldiazenyl)-1*H*-pyrazol-1-yl)ethoxy)ethoxy)ethan-1-ol (**AAP-TEG**)



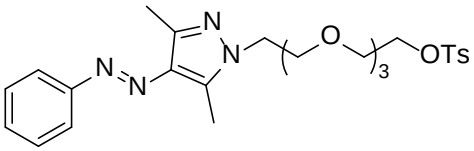
3,5-Dimethyl-4-(phenyldiazenyl)-1*H*-pyrazole (2.39 g, 12 mmol, 1 eq.), K_2CO_3 (8.26 g, 59.8 mmol, 5 eq.) and LiBr (catalytic amount) were dissolved in dry acetonitrile (100 ml) and TEG-Tos (4.99 g, 14.3 mmol, 1.2 eq.) dissolved in dry acetonitrile (50 ml) was added. After refluxing for 5 days the mixture was allowed to cool to room temperature and the solved was removed under vacuum. The residue was re-dissolved in DCM (150 ml) and washed with water (100 ml) and brine (3 x 100 ml). After drying over $MgSO_4$ the solution was concentrated under vacuum. The residue was purified *via* column chromatography (DCM/EtOAc 9:1, R_f = 0.65) and **AAP-TEG** was isolated as a dark orange oil in a yield of 4 g (10.64 mmol, 89%)[3].

^{1}H NMR: (300 MHz, $CDCl_3$) δ [ppm]= 7.82 – 7.70 (m, 2H, *o*-Ph **H**), 7.51 – 7.40 (m, 2H, *m*-Ph **H**), 7.39 – 7.31 (m, 1H, *p*-Ph **H**), 5.28 (s, 1H, -O**H**), 4.20 (t, *J* = 5.4 Hz, 2H, -N-C**H**$_2$-CH_2-O-), 3.86 (t, *J* = 5.4 Hz, 2H, -N-CH_2-C**H**$_2$-O-), 3.71 – 3.50 (m, 12H, -O-C**H**$_2$-C), 2.61 (s, 3H, -C**H**$_3$), 2.49 (s, 3H, -C**H**$_3$).

^{13}C NMR: (75 MHz, $CDCl_3$) δ [ppm]= 153.58, 142.47, 140.48, 134.94, 129.28, 128.89, 121.73, 72.48, 70.70, 70.58, 70.51, 70.31, 69.89, 61.64, 49.03, 14.16, 9.92.

ESI-MS: [*m*/*z*]: found: 399.2019, calculated: 399.2003 $[M+Na]^+$.

(*E*)-2-(2-(2-(2-(3,5-Dimethyl-4-(phenyldiazenyl)-1*H*-pyrazol-1-yl)ethoxy)ethoxy)ethyl 4-methylbenzenesulfonate (**AAP-TEG-Tos**)



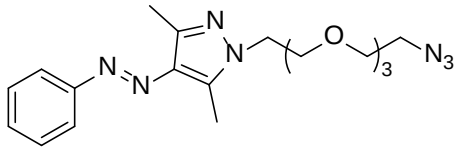
AAP-TEG (4 g, 10.6 mmol, 1 eq.), triethylamine (1.18 g, 11.66 mmol, 1.62 ml, 1.1 eq.) and 4-dimethylaminopyridine (catalytic amount) were in dissolved in DCM (70 ml) and cooled to 0 °C. Tosylchloride (2.22 g, 11.66 mmol, 1.1 eq.) dissolved in DCM (70 ml) was added dropwise over 1 h. The mixture was allowed to warm to room temperature and was stirred for 48 h. After washing with water (100 ml) and brine (2 x 100 ml) the organic layer was dried over $MgSO_4$. The solution was then concentrated under vacuum and the residue was purified by column chromatography (EtOAc, R_f = 0.35). **AAP-TEG-Tos** was isolated as an orange oil in a yield of 2.97 g (5.59 mmol, 53%)[4].

^{1}H NMR: (300 MHz, $CDCl_3$) δ [ppm]= 7.83 – 7.70 (m, 4H, Aryl-**H**), 7.51 – 7.40 (m, 2H, Aryl-**H**), 7.39 – 7.23 (m, 3H, Aryl-**H**), 4.25 – 4.15 (m, 2H, N-C**H**$_2$-CH_2-O-), 4.14 – 4.05 (m, 2H, -O-CH_2-C**H**$_2$-O-S), 3.88 – 3.80 (m, 2H, N-CH_2-C**H**$_2$-O-), 3.70 – 3.44 (m, 10H, -O-C**H**$_2$-C), 2.64 – 2.56 (m, 3H, AAP-C**H**$_3$), 2.53 – 2.46 (m, 3H, AAP-C**H**$_3$), 2.45 – 2.38 (m, 3H, Tosyl-C**H**$_3$).

^{13}C NMR: (75 MHz, $CDCl_3$) δ [ppm]= 153.58, 144.79, 142.43, 140.51, 134.95, 132.93, 129.81, 129.28, 128.90, 127.96, 121.73, 70.73, 70.52, 70.48, 69.92, 69.20, 68.64, 49.06, 28.06, 21.65, 14.18, 9.93

ESI-MS: [*m*/*z*]: found: 553.2109, calculated: 553.2091 $[M+Na]^+$.

(*E*)-1-(2-(2-(2-(2-Azidoethoxy)ethoxy)ethoxy)ethyl)-3,5-dimethyl-4-(phenyldiazenyl)-1*H*-pyrazole (**AAP-TEG-Azide**)



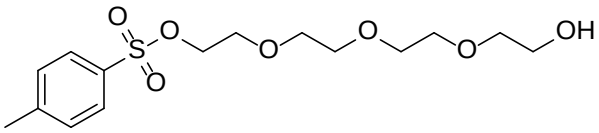
AAP-TEG-Tos (2.97 g, 5.6 mmol, 1 eq.) and NaN_3 (1.82 g, 28 mmol, 5 eq.) were dissolved in DMF (70 ml). After refluxing for 4 days the mixture was allowed to cool to room temperature and the solvent was removed under vacuum. The residue was re-dissolved in DCM (100 ml) and was washed with water (3 x 100 ml) and brine (3 x 100 ml). The organic layer was dried over $MgSO_4$ and the solvent was removed under vacuum. The product was isolated without further purification as a dark red oil in a yield of 1.43 g (3.6 mmol, 64%)[4].

^{1}H NMR: (300 MHz, $CDCl_3$) δ [ppm]= 7.86 – 7.73 (m, 2H, *o*-Ph **H**), 7.53 – 7.42 (m, 2H, *m*-Ph **H**), 7.42 – 7.34 (m, 1H, *p*-Ph **H**), 4.30 – 4.14 (m, 2H, N-C**H**$_2$-CH_2-O-), 3.94 – 3.79 (m, 2H, N-CH_2-C**H**$_2$-O-), 3.74 – 3.46 (m, 10H, -O-C**H**$_2$-C), 3.34 (t, *J* = 5.0 Hz, 2H, -O-CH_2-C**H**$_2$-N_3), 2.68 – 2.57 (m, 3H, -C**H**$_3$), 2.56 – 2.46 (m, 3H, -C**H**$_3$).

^{13}C NMR: (101 MHz, $CDCl_3$) δ [ppm]= 153.60, 142.46, 140.49, 129.26, 128.88, 121.72, 70.79, 70.66, 70.60, 70.57, 69.99, 69.93, 61.64, 50.60, 49.08, 14.17, 9.93.

ESI-MS: [*m*/*z*]: found: 424.2064, calculated: 424.2067 $[M+Na]^+$.

2-(2-(2-(2-Hydroxyethoxy)ethoxy)ethoxy)ethyl 4-methylbenzenesulfonate (**TEG-Tos**)



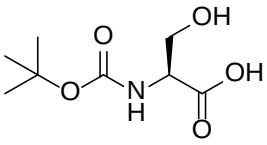
Tetraethyleneglycol (61.18 g, 315 mmol, 54.6 ml, 10.5 eq.) was dissolved in THF (11 ml) and cooled to 0 °C. NaOH (1.92 g, 48 mmol, 1.6 eq.) dissolved in water (11 ml) was slowly added and the resulting solution was stirred for 30 min at 0 °C. After that time, a solution of tosylchloride (5.72 g, 30 mmol, 1 eq.) in THF (28 ml) was added over 1 h and the resulting mixture was stirred for 2 h. The reaction mixture was poured into ice water (ca. 100 ml) and DCM (ca. 50 ml) was added to separate the phases. The aqueous layer was extracted with DCM (3 x 50 ml) and the combined organic phases were washed with brine (2 x 50 ml). After drying over $MgSO_4$ the solvent was removed under vacuum. The residue was purified *via* column chromatography (EtOAc, R_f = 0.3) and TEG-Tos was isolated as a colourless oil in a yield of 7.2 g (20.7 mmol, 69%).

^{1}H NMR: (300 MHz, $CDCl_3$) δ [ppm]= 7.75 (d, 2H, Aryl-**H**), 7.31 (d, *J* = 8.1 Hz, 2H, Aryl-**H**), 4.12 (t, *J* = 5.7, 3.9 Hz, 2H, S-O-C**H**$_2$-), 3.70 – 3.52 (m, 14H, -O-C**H**$_2$-C), 2.63 (s, 1H, -O**H**), 2.41 (s, 3H, -C**H**$_3$).

^{13}C NMR: (101 MHz, $CDCl_3$) δ [ppm]= 144.84, 132.89, 129.84, 127.95, 72.47, 70.69, 70.61, 70.42, 70.28, 69.28, 68.66, 61.66, 21.64.

ESI-MS: [*m*/*z*]: found: 371.1146, calculated: 371.1135 $[M+Na]^+$.

(*tert*-Butoxycarbonyl)-*L*-serine



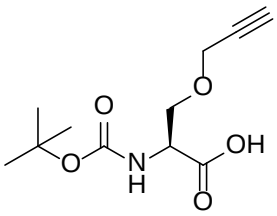
L-Serine (7.36 g, 70 mmol, 1 eq.) and Na_2CO_3 (7.42 g, 70 mmol, 1 eq.) were dissolved in 100 ml of a 50% saturated $NaHCO_3$ solution. After cooling to 0 °C di-*tert*-butyldicarbonate (18.33 g, 84 mmol, 1.2 eq.) dissolved in 18 ml dioxane was added dropwise. The mixture was stirred for 30 min at 0 °C. After warming to room temperature the reaction mixture was stirred for 2 days. The solvents were removed by two thirds in vacuum. The concentrated solution was then acidified to pH=2 using conc. HCl (ca. 25 ml) at 0 °C and brine (10 ml) was added. The acidified solution was then extracted with Ethylacetate (6 x 50 ml) and the combined organic phases were dried over $MgSO_4$. After concentration under vacuum (*tert*-butoxycarbonyl)-*L*-serine was isolated as a colourless, viscous oil without further purification in a yield of 14.99 g (73 mmol, quant.)[5].

^{1}H NMR: (400 MHz, $CDCl_3$) δ [ppm]= 5.79 (d, *J* = 7.8 Hz, 1H, -N**H**-), 4.44 – 4.17 (m, 1H, *α*-**H**), 4.07 – 3.94 (m, 1H, -C**H**$_2$-), 3.91 – 3.72 (m, 1H, -C**H**$_2$-), 1.45 (s, 9H, -C**H**$_3$).

^{13}C NMR: (101 MHz, $CDCl_3$) δ [ppm]= 173.89, 156.28, 80.72, 62.98, 55.41, 28.30.

ESI-MS: [*m*/*z*]: found: 228.0843, calculated: 228.0842 $[M+Na]^+$.

N-(*tert*-Butoxycarbonyl)-O-(prop-2-yn-1-yl)-*L*-serine



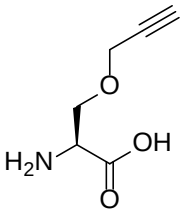
(*tert*-Butoxycarbonyl)-*L*-serine (5.4 g, 26 mmol, 1 eq.) was dissolved in DMF (150 ml) and cooled to 0 °C. NaH (60% in mineral oil, 1.25 g, 52 mmol, 2 eq.) was added portion wise. After effervescence ceased, propargyl-bromide (80% in toluene, 3.01 g, 26 mmol, 2.9 ml, 1 eq.) was added over 15 min. After stirring for 2 h at 0 °C the reaction was quenched by the addition of water (50 ml). The solvent was removed under vacuum and the residue was re-dissolved in water (100 ml). After washing with Et_2O (2 x 50 ml) the aqueous phase was acidified to pH = 2 with a 10% $NaHSO_4$ solution. The aqueous layer was extracted with DCM (3 x 100 ml) and the combined organic phases were washed with a 10% $NaHSO_4$ solution (3 x 100 ml) and brine (2 x 100 ml). After drying over $MgSO_4$ the solvent was evaporated under vacuum and the product was isolated as a red oil in a yield of 4.71 g (19.38 mmol, 75%)[6].

^{1}H NMR: (300 MHz, $CDCl_3$) δ [ppm]= 11.01 (s, 1H, -N**H-**), 4.52 – 4.38 (m, 1H, -NH-C**H**-COOH), 4.23 – 4.08 (m, 2H, -O-C**H**$_2$-C≡), 3.97 (m, 1H, -CH-C**H**$_2$-O-), 3.79 (m, 1H, -CH-C**H**$_2$-O-), 2.44 (t, *J* = 2.4 Hz, 1H, -C≡C**H**), 1.43 (s, 9H, -C**H**$_3$).

^{13}C NMR: (75 MHz, $CDCl_3$) δ [ppm]= 174.04, 155.65, 80.17, 78.83, 75.19, 69.62, 58.63, 53.64, 28.30.

ESI-MS: [*m*/*z*]: found: 266.1004, calculated: 266.0999 $[M+Na]^+$.

O-(Prop-2-yn-1-yl)-*L*-serine



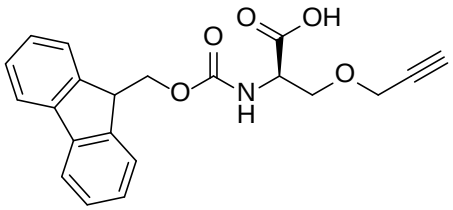
N-(*tert*-Butoxycarbonyl)-O-(prop-2-yn-1-yl)-*L*-serine (15.19 g, 62 mmol) was dissolved in Ethylacetate (40 ml) and HCl (10 m, 50 ml) was added. The resulting mixture was stirred at room temperature overnight. After evaporation of the solvent under vacuum, the residue was re-dissolved in water (60 ml). The aqueous solution was washed with DCM (3 x 50 ml) and Et_2O (3 x 50 ml). The combined organic layers were re-extracted with water (100 ml) and the combined aqueous layers were concentrated under vacuum. The title product was isolated as a brownish solid in a yield of 15 g (quant.)[4].

^{1}H NMR: (400 MHz, DMSO-*d*6) δ [ppm]= 8.40 (s, 2H, -N**H**$_2$), 4.22 (t, *J* = 2.7 Hz, 2H, -O-C**H**$_2$-≡), 4.19 – 4.13 (m, 1H, H_2N-C**H**-COOH), 3.91 – 3.78 (m, 2H, -CH-C**H**$_2$-O-), 3.56 (t, *J* = 2.4 Hz, 1H, -≡C**H**).

^{13}C NMR: (101 MHz, DMSO-*d*6) δ [ppm]= 182.62, 79.86, 78.64, 67.61, 58.51, 52.73.

ESI-MS: [*m*/*z*]: found: 178.0282, calculated: 178.0276 $[M+Cl]^-$.

N-(((9*H*-Fluoren-9-yl)methoxy)carbonyl)-*O*-(prop-2-yn-1-yl)-*D*-serine
(Fmoc-*O*-propargyl-*L*-serine)



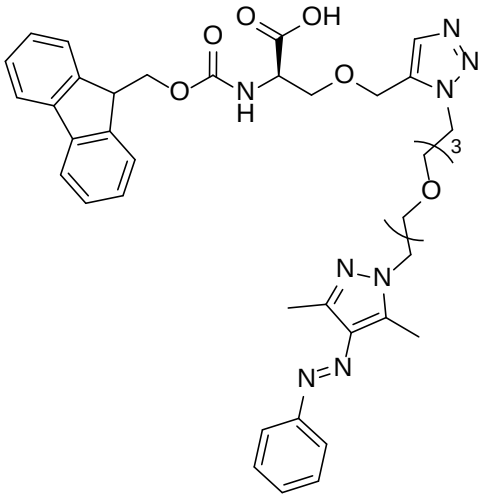
O-Propargyl-*L*-serine (1.5 g, 10.5 mmol, 1 eq) was dissolved in dioxane/water (75 ml, 2:1) and Na_2CO_3 (1.1 g, 10.5 mmol, 1 eq.) was added. The mixture was cooled to 0 °C and Fmoc-OSu (4.2 g, 12.6 mmol, 1.2 eq.) dissolved in dioxane (25 ml) was added dropwise. After stiring for 3 h at 0 °C the mixture was acidified to pH = 2 using 1 M HCl. The aqueous phase was extracted with ethylacetate (2 x 100 ml) and the combined organic layers were washed with 1 M HCl, water and brine (100 ml each). The organic layer was dried over $MgSO_4$ and concentrated under vacuum. The title product was isolated as a white solid in a yield of 4.7 g (quant.)[4].

^{1}H NMR: (400 MHz, DMSO-d_6) δ [ppm]= 12.85 (s, 1H, -COO**H**), 7.92 – 7.87 (m, 2H, Aryl-**H**), 7.75 (d, *J* = 7.5 Hz, 2H, Aryl-**H**), 7.64 (d, *J* = 7.4 Hz, 1H, Aryl-**H**), 7.43 – 7.39 (m, 2H, Aryl-**H**), 7.35 – 7.30 (m, 2H, Aryl-**H**), 4.33 – 4.22 (m, 4H, *α*-**H** Serine*, -C**H**-CH_2-O-COON-, -CH-C**H**$_2$-O-COON-), 4.17 (d, *J* = 2.4 Hz, 2H, -O-C**H**$_2$-C≡), 3.73 (d, *J* = 5.5 Hz, 2H, -NH-CH-C**H**$_2$-O-), 3.48 (t, *J* = 2.4 Hz, 1H, -C≡C**H**).

^{13}C NMR: (101 MHz, DMSO-d_6) δ [ppm]= 171.97, 156.53, 144.29, 139.90, 127.59, 127.56, 125.38, 120.51, 80.35, 78.03, 69.16, 66.28, 58.17, 54.44, 47.08.

ESI-MS: [*m*/*z*]: found: 388.1157, calculated: 388.1155 $[M+Na]^+$.

(*E*)-*N*-(((9*H*-Fluoren-9-yl)methoxy)carbonyl)-*O*-((1-(2-(2-(2-(2-(3,5-dimethyl-4-(phenyldiazenyl)-1*H*-pyrazol-1-yl)ethoxy)ethoxy)ethoxy)ethyl)-1*H*-1,2,3-triazol-5-yl)methyl)-*D*-serine (Fmoc-Ser*-AAP)



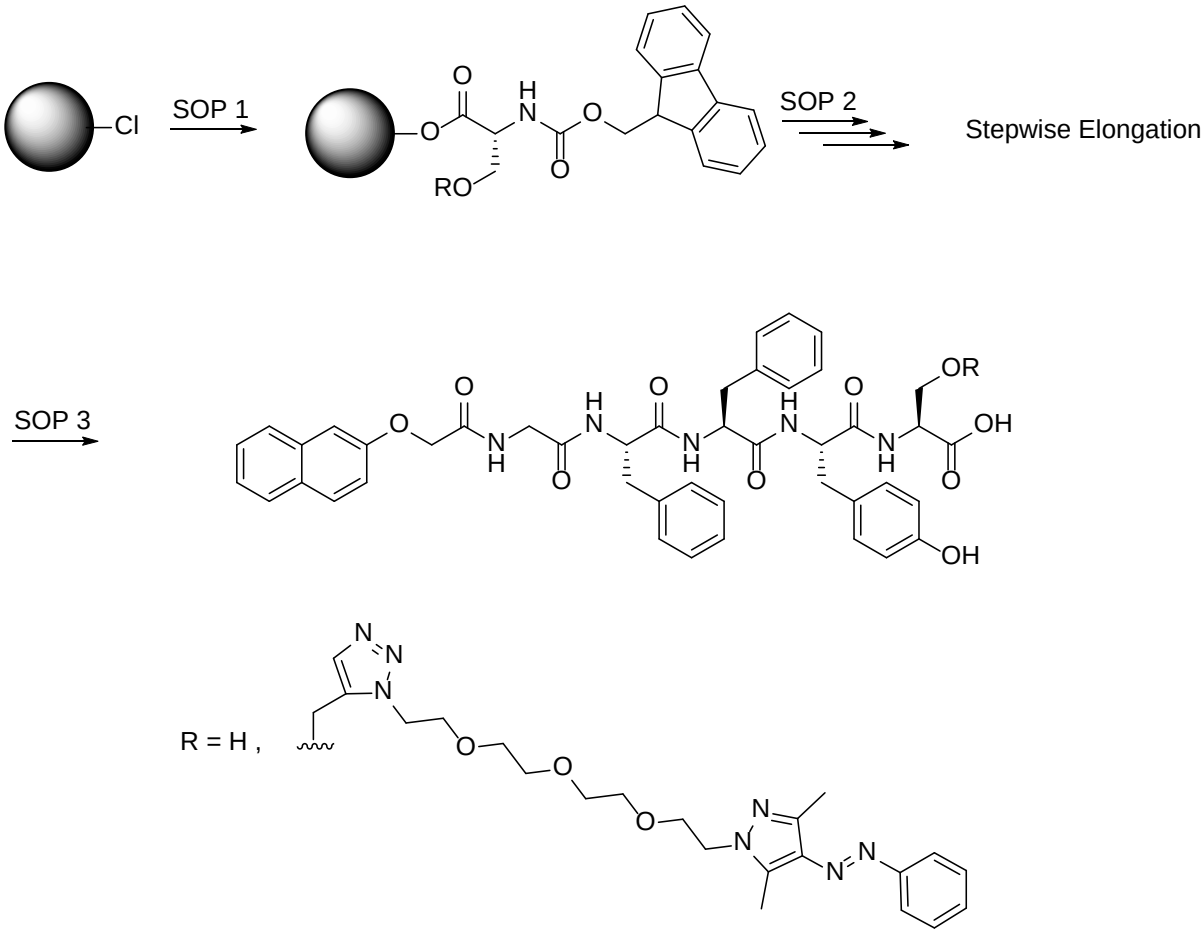
Fmoc-*O*-propargyl-*L*-serine **2** (909 mg, 2.5 mmol, 1 eq.), AAP-TEG-Azide **3** (1.5 g, 3.74 mmol, 1.5 eq.) and Cu(II)SO_4 x 5 H_2O (3.7 g, 14.9 mmol, 6 eq.) were suspended in DMF (80 ml). Sodiumascorbate (2 g, 10 mmol, 4 eq.) was suspended in DMF (20 ml) and added to the mixture. After stirring for 4 days at room temperature the solvent was removed under vacuum. The residue was re-dissolved in DCM (100 ml) and insoluble fraction was removed *via* filtration. The organic phase was washed with 1 M HCl (2 x 100 ml) and brine (2 x 100 ml) and the combined aqueous layers were re-extracted with DCM (100 ml). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The residue was purified via column chromatography (DCM/methanol 9:1; R_f = 0.1) and the title product was isolated as an orange oil in a yield of 484 mg (0.6 mmol, 25%)[4].

^{1}H NMR: (300 MHz, DMSO-d_6) δ [ppm]= 8.04 – 7.94 (m, 1H, Triazole-**H**), 7.88 (d, J = 7.7 Hz, 2H, Aryl-**H**), 7.79 – 7.60 (m, 4H, Aryl-**H**), 7.56 – 7.46 (m, 2H, Aryl-**H**), 7.45 – 7.36 (m, 2H, Aryl-**H**), 7.36 – 7.17 (m, 3H, Aryl-**H**), 7.02 – 6.96 (m, 1H, -N**H**-), 4.50 (s, 2H, -O-C**H**$_2$-Triazole), 4.44 (t, J = 5.2 Hz, 2H, -O-CH$_2$-C**H**$_2$-AAP), 4.30 – 4.16 (m, 3H, -C**H**-CH$_2$-O-COON-, -CH-C**H**$_2$-O-COON-), 4.03 (t, J = 5.3 Hz, 1H, α-**H** Serine*), 3.73 (t, J = 5.3 Hz, 4H, -NH-CH-C**H**$_2$-O-, Triazole-C**H**$_2$-CH$_2$-O-), 3.52 – 3.31 (m, 10H, -O-C**H**$_2$-C**H**$_2$-O-), 2.56 (s, 3H, -C**H**$_3$), 2.36 (s, 3H, -C**H**$_3$).

^{13}C NMR: (75 MHz, DMSO-d_6) δ [ppm]= 173.03, 155.76, 153.44, 144.26, 141.32, 141.16, 141.06, 134.72, 129.90, 129.61, 128.09, 127.53, 125.79, 124.77, 121.82, 120.54, 70.25, 70.10, 70.04, 69.97, 69.72, 69.51, 69.10, 66.24, 61.99, 56.69, 49.75, 49.05, 47.06, 14.49, 9.86.

ESI-MS: [m/z]: found: 765.3370, calculated: 765.3366 $[M-H]^-$.

Solid Phase Peptide Synthesis (SPPS)



Solid-phase peptide synthesis of Nap-GFFYS and Nap-GFFYS-AAP

Standard Operating Procedure (SOP) 1 (Loading of the resin)

The first Fmoc-protected amino acid (Fmoc-Serine(tBu), Fmoc-Ser*-AAP or Fmoc-Ser*-Ad, 1.5 eq. relative to the amount of active functionalities on the resin) was dissolved in dry DCM (20 ml). The solution was added to the 2-chlorotrityl-resin (1.6 mmol/g) under argon atmosphere. DIPEA (2 eq. relative to the amount of active functionalities on the resin) was added and the mixture was agitated for 5 min by the argon stream. A second portion of DIPEA (3 eq. relative to the amount of active functionalities on the resin) was added. After agitating for 2 hr by the argon stream methanol (1 ml/g resin) was added and the resulting mixture was agitated for further 15 min to quench the remaining resin functionalities. After filtration of the reaction mixture the resin was washed with DCM p.a. (3 x 20 ml), DMF p.a. (3 x 20 ml), DCM p.a. (3 x 20 ml) and methanol (3 x 20 ml). The resin was dried under vacuum to determine the loading ratio by the weight increase.

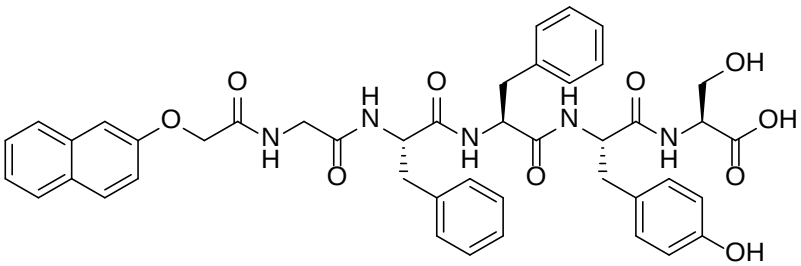
SOP 2 (stepwise elongation)

The dry resin was pre-swollen by shaking in DMF (20 ml) for 5 min. The pre-swollen resin was washed with DMF (2 x 20 ml) and the Fmoc-group was cleaved by shaking in 20% piperidine solution in DMF (20 ml). After sucking off the solution another portion of 20% piperidine solution in DMF (20 ml) was added and shaken for 20 min to ensure complete deprotection. The resin was washed with DMF (7 x 20 ml) and the second Fmoc-protected amino acid (Fmoc-tyrosine(tBu), 3 eq. relative to resin loading, 0.5 M solution in DMF) was added. HOBt (4 eq. relative to resin loading, 0.4 M solution in DMF) and DIPCDI (4 eq. relative to resin loading, 0.4 M solution in DMF) were added and the mixture was shaken for 2.5 h. After washing with DMF (3 x 20 ml) the procedure was repeated for the following amino acid derivatives: Fmoc-phenylalanine, Fmoc-phenylalanine and Nap-glycine (3 eq. to resin loading each, 0.5 M solution in DMF).

SOP 3 (cleavage of the peptide from the resin)

The resin was suspended in a solution of TFA:H_2O:Tri-isopropylsilane (95:2.5:2.5, 20 ml) and stirred for 4 h. The reaction mixture was sucked off and the resin was washed with TFA (3 x 5 ml). In the following the peptide was precipitated by the addition of cold Et_2O:pentane solution (3:1). The precipitate was collected *via* centrifugation and the remaining water was removed *via* lyophilisation. The dried powder was re-dissolved in a minimal amount of DMSO and precipitated by the addition of MilliQ. The precipitate was collected *via* centrifugation and the remaining water was removed *via* lyophilisation.

Nap-GFFYS

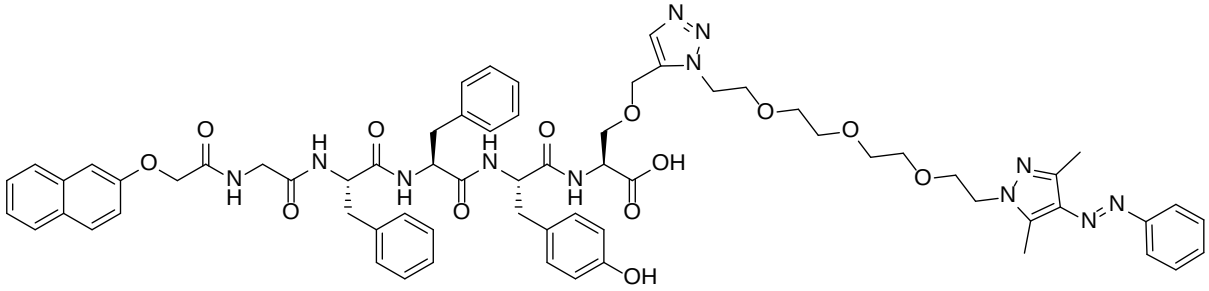


The peptide was synthesized as described in SOP 1, SOP 2 and SOP 3 by using Fmoc-serine(tBu) as the first amino acid. The peptide was obtained without further purification as a white powder.

^{1}H NMR: (300 MHz, DMSO-d_6) δ [ppm]= 9.15 (s, 1H, Amide-**H**), 8.30 – 8.20 (m, 1H, Amide-**H**), 8.17 (d, *J* = 8.2 Hz, 1H, Amide-**H**), 8.11 – 8.03 (m, 2H, Nap-Aryl-**H**), 7.89 – 7.82 (m, 3H, Nap-Aryl-**H**, Amide-**H**), 7.79 (d, *J* = 8.2 Hz, 1H, Amide-**H**), 7.52 – 7.42 (m, 1H, Nap-Aryl-**H**), 7.40 – 7.31 (m, 2H, Nap-Aryl-**H**), 7.29 – 7.11 (m, 10H, Phenylalanine-Aryl-**H**), 7.11 – 7.03 (m, 2H, Tyrosine-Aryl-**H**), 6.67 – 6.58 (m, 2H, Tyrosine-Aryl-**H**), 5.09 – 4.96 (m, 1H, Serine-O**H**), 4.61 (s, 2H, Nap-C**H**$_2$), 4.59 – 4.43 (m, 3H, 2 x α-**H** Phenylalanine, α-**H** Tyrosine), 4.35 – 4.25 (m, 1H, α-**H** Serine), 3.83 – 3.58 (m, 4H, α-C**H**$_2$ Serine, -C**H**$_2$- Glycine), 3.04 – 2.89 (m, 3H, 2 x α-C**H**$_2$ Phenylalanine, α-C**H**$_2$ Tyrosine), 2.84 – 2.62 (m, 3H, 2 x α-C**H**$_2$ Phenylalanine, α-C**H**$_2$ Tyrosine).

HR-MS: [*m*/*z*]: found: 826.20661, calculated: 826.30586 $[M+Na]^+$.

Nap-GFFYS-AAP



The peptide was synthesized as described in SOP 1, SOP 2 and SOP 3 by using Fmoc-Ser*-AAP **4** as the first amino acid. The peptide was obtained without further purification as a yellow powder.

^{1}H NMR: (300 MHz, DMSO-d_6) δ [ppm]= 9.17 (s, 1H, Amide-**H**), 8.43 (d, *J* = 7.9 Hz, 1H, Triazole-**H**), 8.25 (t, *J* = 5.8 Hz, 1H, Amide-**H**), 8.15 (d, *J* = 8.1 Hz, 1H, Amide-**H**), 8.10 – 8.02 (m, 2H, Nap-Aryl-**H**), 8.00 (s, 1H, Tyrosine-O**H**), 7.89 – 7.76 (m, 4H, 2 x Amide-**H**, Nap-Aryl-**H**), 7.75 – 7.68 (m, 2H, AAP-Phenyl-**H**), 7.55 – 7.30 (m, 6H, Nap-Aryl-**H**, AAP-Phenyl-**H**), 7.27 – 7.03 (m, 12H, Phenylalanine-Aryl-**H**, Tyrosine-Aryl-**H**), 6.68 – 6.58 (m, 2H, Tyrosine-Aryl-**H**), 4.65 – 4.41 (m, 9H, 2 x α-**H** Phenylalanine, α-**H** Tyrosine, Nap-C**H**$_2$, -O-C**H**$_2$-Triazole, Triazole-C**H**$_2$-CH$_2$-O-), 4.19 (t, *J* = 5.2 Hz, 1H, α-**H** Serine), 3.84 – 3.59 (m, 8H, α-C**H**$_2$ Serine, -C**H**$_2$- Glycine, Triazole-CH$_2$-C**H**$_2$-O-, -O-CH$_2$-C**H**$_2$-AAP), 3.49 – 3.33 (m, 10H, -O-C**H**$_2$-C**H**$_2$-O-, -O-C**H**$_2$-CH$_2$-AAP), 3.05 – 2.88 (m, 3H, 2 x α-C**H**$_2$ Phenylalanine, α-C**H**$_2$ Tyrosine), 2.81 – 2.62 (m, 3H, 2 x α-C**H**$_2$ Phenylalanine, α-C**H**$_2$ Tyrosine), 2.56 (s, 3H, -C**H**$_3$), 2.37 (s, 3H, -C**H**$_3$).

MALDI-MS: [*m*/*z*]: found: 1243.52, calculated: 1243.56 $[M+H]^+$.

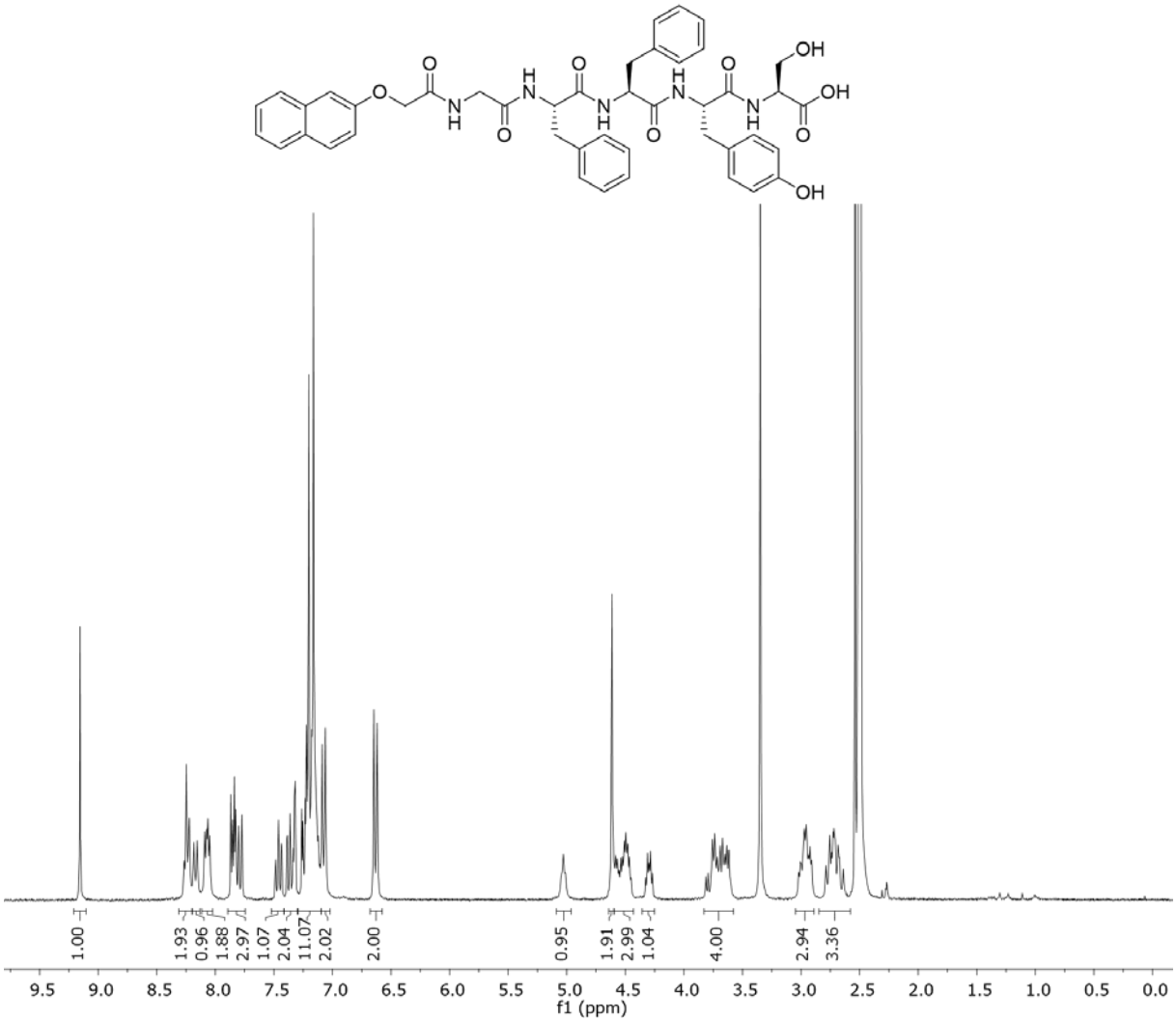


Fig. S5 ^{1}H-NMR spectra of Nap-GFFYS (300 MHz, DMSO-*d6*, 300 K).

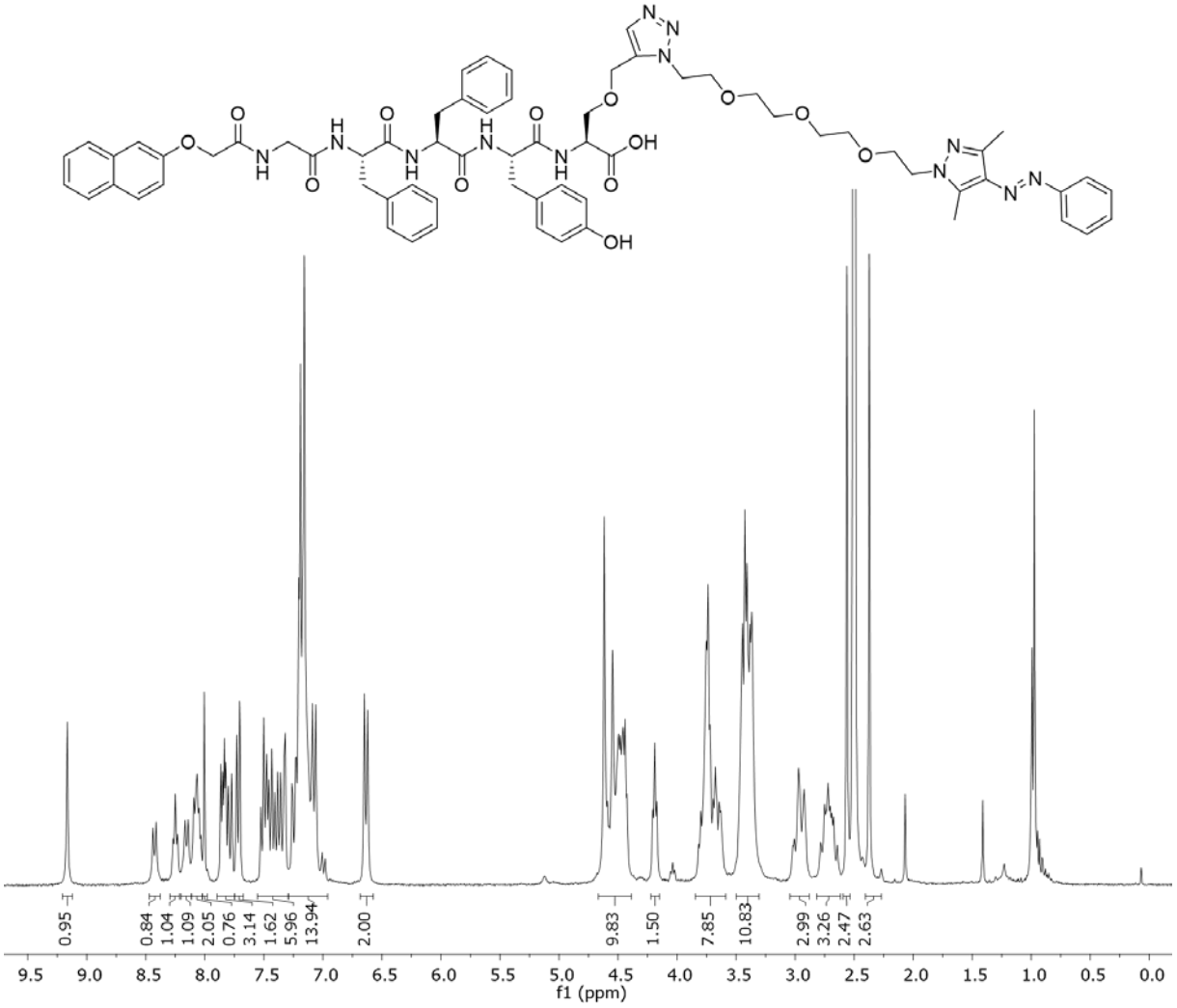


Fig. S6 ^{1}H-NMR spectra of Nap-GFFYS-AAP (300 MHz, DMSO-*d6*, 300 K).

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