Supporting Information

Depolymerization of supramolecular polymers by a covalent reaction; transforming an intercalator into a sequestrator

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General procedures

Preparation of new compounds: synthetic procedures for the preparation of **Cys-BTA** and **HexCys-BTA** are detailed on pages S3-S5. All chemicals were purchased from Sigma Aldrich, Merck, Acros Organics, or Novabiochem (protected amino acid **N-FMOC-Cys(trt)-OH**) and used without further purification. Solvents were purchased from Biosolve and used as received. Dried solvents were obtained from an SPS solvent purification system. All inert atmosphere reactions were carried out under an argon atmosphere with a standard Schlenk-Line. The deuterated solvents and spectra-grade MCH were both purchased from Sigma Aldrich and used as received.

Sample preparation

***For CD experiments*:** the stock solutions of **Cys-BTA** and **HexCys-BTA** were prepared at a concentration of 1 mM in MCH. The necessary amount of the monomers was weighed into volumetric flasks, which for the *in situ* reaction also included 3 eq. of 1-hexene and 0.3 eq. of DMPA. The flasks were then filled 3/4 full of methylcyclohexane (MCH) and put in a sonicating bath at 40 °C for 1 h. After cooling the flask to room temperature, the final volume was added.

***For FT-IR, DLS and NMR experiments*:** the same protocol was followed to prepare the 0.5 mM - 10 mM solutions of **Cys-BTA** and **HexCys-BTA**.

When performing the thiol-ene reaction on **Cys-BTA**, no trace of **Cys-BTA** oxidation and disulfide bridge were observed.

Instrumentation

For synthesis: NMR spectra were recorded on Varian Mercury Vx 400 MHz and Bruker 400 MHz Ultrashield spectrometers. Chemical shifts (δ) are reported in ppm downfield from tetramethyl silane (TMS). Peak multiplicity is abbreviated as s: singlet; d: doublet; t: triplet; q: quartet; p: pentet; m: multiplet; bs: broad singlet. Matrix Assisted Laser Desorption/Ionization Time-Of-Flight (MALDI-TOF) mass spectra were obtained on a Bruker Autoflex Speed spectrometer using α-cyano-4-hydroxycinnamic acid (CHCA) and trans-2-[3-(4-tert-

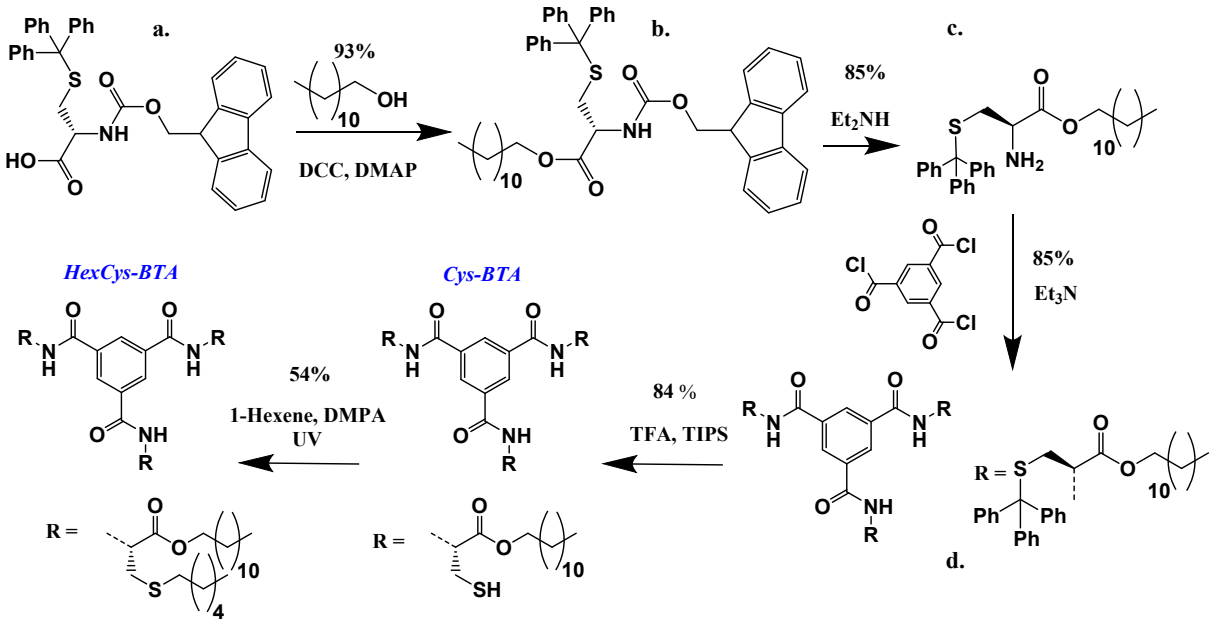
butylphenyl)-2-methyl-2-propenylidene]-malononitrile (DCTB) as matrix. Flash column chromatography was performed on a Biotage Isolera One system equipped with an ultraviolet detector.

Analysis of samples: CD measurements were performed on a Jasco J-815 spectropolarimeter where the sensitivity, time constant and scan range were chosen appropriately (sensitivity: standard, response: 0.5 s, band width: 3 nm, data pitch: 0.5 nm, scanning speed 50 nm/min). Corresponding temperature dependent measurements were performed with a Jasco PTC-348WI Peltier-type temperature controller, with a temperature range of 288-359 K and adjustable temperature slope. The molar circular dichroism ($\Delta\varepsilon$) value was calculated from $\Delta\varepsilon$ = CD intensity / (32980*c*l) in which c is the concentration in mol/L and l is the optical path length in cm. Ultraviolet–visible (UV/Vis) absorbance spectra were recorded on a Jasco V-650 UV/Vis spectrometer at 293 K with a Jasco ETCT-762 temperature controller. UV/Vis and CD measurements were performed using quartz cuvettes (5 mm and 1 mm) with a Teflon cap and Teflon tape to ensure no evaporation of the solvent at high temperature. IR spectra were recorded on a PerkinElmer FT-IR spectrometer with 16 scans and the solution-phase IR was measured in a cell of pathlength 0.5 mm. Thermal transitions were determined using a TA Q2000 DSC with both 10 and 40 °C/min heating and cooling. POM samples were placed on glass slides and imaged using a Nikon Xfinity1 Lumenera microscope with 5X magnification at room temperature. NMR spectra were recorded on Varian Mercury Vx 400 MHz and Bruker 400 MHz Ultrashield spectrometers. Chemical shifts (δ) are reported in ppm downfield from tetramethyl silane (TMS). Peak multiplicity is abbreviated as s: singlet; d: doublet; t: triplet; q: quartet; p: pentet; m: multiplet. Variable temperature IR (VT-IR) spectra were recorded on a Bruker Tensor 27 equipped with a Pike GladiATR 210 module. Full spectra of the samples were recorded every 5 ˚C upon cooling from 200 °C down to 25 °C with a cooling ramp of 5 °C/min. A baseline correction was performed on the collected spectra to correct for temperature dependent changes in the atmospheric spectrum. UV intensities were measured using an Opsyfec Radiometer RM12 fitted with a UV-A sensor of a range of 0-200 mW/cm^2.

Fitting of kinetic data

After normalization, the data were fitted to first order kinetics in the form: $y(t) = e^{(-k_1 t)}$ or in the case of low light intensities second order kinetics were used to fit: $f(t) = e^{(-k_2 t^2)}$. Fitting of the data was done using the Origin fitting toolbox with the 'Levenberg Marquardt' iteration algorithm.

Synthesis of Cys-BTA and HexCys-BTA.



Scheme 1. Synthesis of **Cys-BTA** and **HexCys-BTA**. a) THF, DCC, DMAP, 1-dodecanol, 3 H, (93%). b) ACN, DEA, 16 H, (85 %). c) DCM, 1,3,5-benzenetricarbonyltrichloride, TEA, 6 H, (85 %). d) DCM, TFA, TIPS, 2 H, (84%). e) $CHCl_3$, 1-hexene, DMPA, UV, 1 H, (54%).

Esterification of N-FMOC-Cys(trt)-OH (a)

To a solution of **N-FMOC-Cys(trt)-OH** (2.00 g, 3.4 mmol) in 20 ml THF was added 1-dodecanol (980 mg, 1.5 eq.) and a catalytic amount of DMPA (40 mg, 0.16 mmol). The resulting solution was brought to 0 °C with an ice bath. Afterwards 1.3 eq. of DCC (920 mg, 4.5 mmol) were added and after 15 minutes the ice bath was removed, and the solution was stirred at ambient temperature for 3 hours. The resulting solution was filtered (twice) and the solvent removed. The resulting solid was taken up as a slurry in a few ml of DCM and purified on a short column of silica gel (gradient elution: EtOAc/Hept 5/95 to 15/85) to obtain 2.4 g of **N-FMOC-Cys(trt)-ester** (yield = 93%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (dd, *J* = 7.7, 3.4 Hz, 2H), 7.61 (dd, *J* = 7.5, 3.5 Hz, 2H), 7.43 – 7.17 (m, 17H), 5.27 (d, *J* = 8.3 Hz, 1H), 4.43 – 4.28 (m, 3H), 4.23 (t, *J* = 7.2 Hz, 1H), 4.11 (t, *J* = 6.7 Hz, 2H), 2.64 (qd, *J* = 12.4, 5.5 Hz, 2H), 1.60 (q, *J* = 7.1 Hz, 2H), 1.34 – 1.23 (m, 18H), 0.88 (t, *J* = 6.8 Hz, 3H).

Deprotection of the N-FMOC-Cys(trt)-ester (b)

N-FMOC-Cys(trt)-ester (2.2 g, 2.91 mmol) was added to a round-bottom flask and dissolved in approximately 55 ml of acetonitrile. In one go, diethylamine (DEA, 15 ml, 0. 15 mol) was added to the flask and the mixture was stirred at RT overnight. Afterwards, the solvent was removed under vacuum and partitioned in EtOAc/H_2O, in which the water layer was extracted twice with EtOAc. The mixture was then dried with $MgSO_4$, filtered and the solvent removed. The resulting solid was taken up as a slurry in a few ml of DCM and purified on a short column of silica gel (gradient elution: MeOH/$CHCl_3$ 0/100 to 5/95) to obtain 1.5 g of **Cys(trt)-ester** (yield = 85 %).

^{1}H NMR (399 MHz, Chloroform-*d*) δ 7.51 – 7.26 (m, 12H), 7.24 – 7.17 (m, 3H), 4.04 (t, *J* = 6.6 Hz, 2H), 2.62 – 2.41 (m, 2H), 1.55 (m, 4H), 1.26 (s, 18H), 0.92 – 0.84 (m, 3H).

BTA formation with Cys(trt)-ester (c)

1,3,5-benzenetricarbonyltrichloride (228 mg, 0.86 mmol) was added to a 100 ml round-bottom flask and dissolved into ca. 50 ml of dry DCM under argon atmosphere. Subsequently, 3.3 eq. of **Cys(trt)-ester** (1.5 g, 2.8 mmol) was added in one portion and the mixture was cooled using an ice bath under argon. Afterwards, 12 eq. of triethylamine (TEA, 1.5 ml, 10.8 mmol) was added dropwise, the ice bath was removed, and the mixture was left to stir at room temperature over the weekend. 30 ml of water was added to the flask, and the crude mixture was extracted thrice with $CHCl_3$. The combined organic phases were dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure. The resulting solid was taken up as a slurry in a few ml of DCM and purified on a short column of silica gel (gradient elution: EtOAc/Hept 5/95 to 15/85) to obtain 1.4 g of **Cys(trt)-BTA** (yield = 85%).

^{1}H NMR (399 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 4.0 Hz, 1H), 7.50 – 7.29 (m, 7H), 7.25 – 7.13 (m, 7H), 6.77 (d, *J* = 7.8 Hz, 1H), 4.77 (q, *J* = 6.1 Hz, 1H), 4.14 (t, *J* = 6.5 Hz, 2H), 2.88 – 2.64 (m, 2H), 1.63 (s, 2H), 0.88 (td, *J* = 6.7, 1.7 Hz, 5H).

Deprotection of Cys(trt)-BTA (d)

Cys(trt)-BTA (1.01 g, 0.58 mmol) was added to a flask together with 20 ml of DCM and put under argon atmosphere. Afterwards, 3 eq. of triisopropylsilane (0.3 ml, 1.5 mmol) and 14 eq. of TFA (0.6 ml, 7.8 mmol) were added, causing a colour change to bright orange. The

mixture was stirred overnight under argon. Afterwards, 10 ml of a saturated solution of $NaHCO_3$ was added and extracted twice with $CHCl_3$. The organic layer was then dried with $MgSO_4$, filtered and the solvent was removed under pressure. The resulting solid was taken up as a slurry in a few ml of DCM and purified on a short column of silica gel (gradient elution: MeOH/$CHCl_3$ 0/100 to 10/90) to obtain 0.48 g of **Cys-BTA** (yield = 84 %).

^{1}H NMR (399 MHz, Chloroform-*d*) δ 8.42 (s, 1H), 7.37 (d, *J* = 7.4 Hz, 1H), 5.06 (dt, *J* = 8.2, 4.5 Hz, 1H), 4.32 – 4.15 (m, 2H), 3.23 – 3.08 (m, 2H), 1.70 (p, *J* = 7.2 Hz, 2H), 1.55 (t, *J* = 9.0 Hz, 1H), 1.27 (d, *J* = 7.5 Hz, 18H), 0.88 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.37, 165.77, 134.65, 128.93, 66.38, 54.97, 31.92, 29.64, 29.64, 29.60, 29.53, 29.35 29.24, 26.61, 25.90, 22.69, 14.11.

MALDI: Calculated for $C_{54}H_{93}NaN_3O_9S_3$ $[M+Na]^+$: 1046.60, found: 1046.61.

Thiol-ene reaction on Cys-BTA (e)

Cys-BTA (50 mg, 0.05 mmol), 0.3 eq. of DMPA (4 mg, 0.016 mmol) and 4 eq. of 1-hexene (18 mg, 0.21 mmol) were added to a round-bottom flask and dissolved in 6 ml of $CHCl_3$. The flask was flushed with argon, then irradiated with UV for 20 minutes and left to stir for approximately an hour. Then the solvent was removed under vacuum and the mixture was purified twice with a short column of silica gel (gradient elution: EtOAc/Hept 10/90 to 30/70) to obtain 35 mg of **HexCys-BTA** (yield = 54 %).

^{1}H NMR (399 MHz, Chloroform-*d*) δ 8.47 (s, 1H), 7.17 (d, *J* = 7.4 Hz, 1H), 5.00 (dt, *J* = 7.5, 5.2 Hz, 1H), 4.20 (t, *J* = 6.8 Hz, 2H), 3.11 (qd, *J* = 13.9, 5.3 Hz, 2H), 2.54 (t, *J* = 7.4 Hz, 2H), 1.68 (p, *J* = 6.8 Hz, 2H), 1.55 (q, *J* = 7.6 Hz, 2H), 1.40 – 1.20 (m, 24H), 0.87 (q, *J* = 6.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.86, 165.21, 134.70, 128.94, 66.21, 52.65, 34.15, 32.74, 31.92, 31.39, 29.66, 29.64, 29.60, 29.53, 29.49, 29.36, 29.24, 28.52, 28.46, 25.87, 22.69, 22.52, 14.12, 14.02.

MALDI: Calculated for $C_{72}H_{129}NaN_3O_9S_3$ $[M+Na]^+$: 1298.88, found: 1298.87.

Supplementary Figures

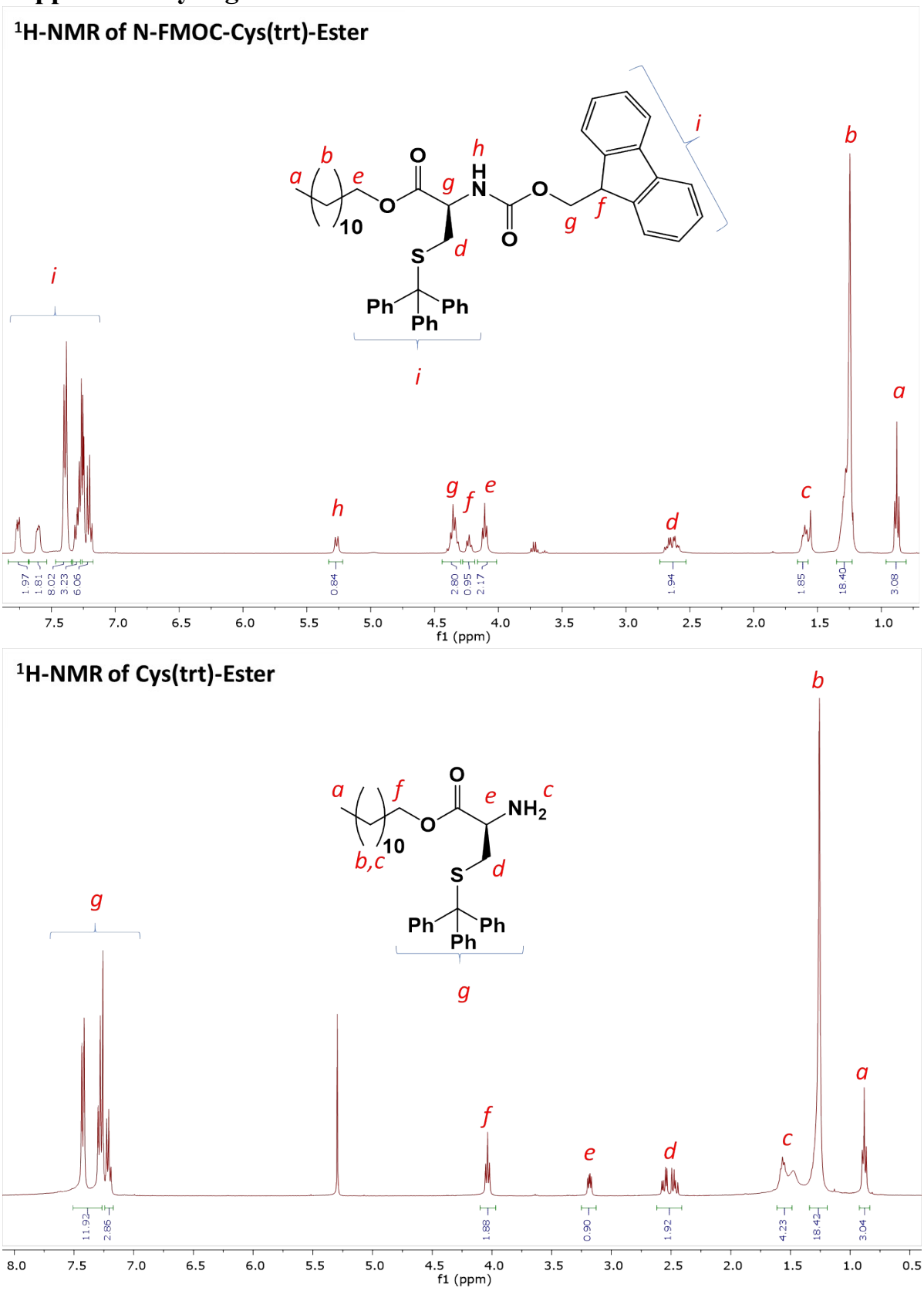


Figure S1. ^{1}H-NMR spectra of **N-FMOC-Cys(trt)-ester** and **Cys(trt)-ester** at 5 mM in $CDCl_3$ at 20 °C. All peaks have been assigned to the molecular structure, which is also displayed in the spectrum.

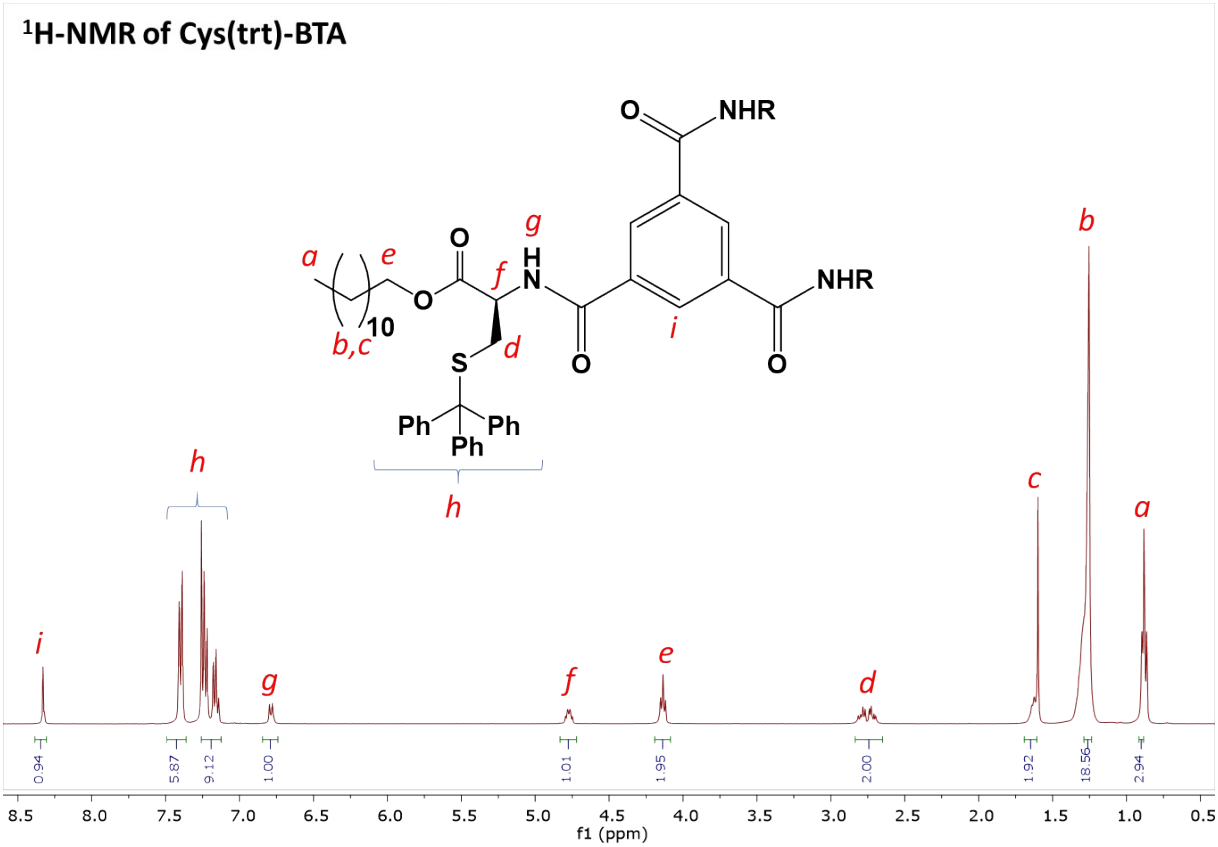


Figure S2. ^{1}H-NMR spectrum of **Cys-(trt)-BTA** at 5 mM in $CDCl_3$ at 20 °C. All peaks have been assigned to the molecular structure, which is also displayed in the spectrum.

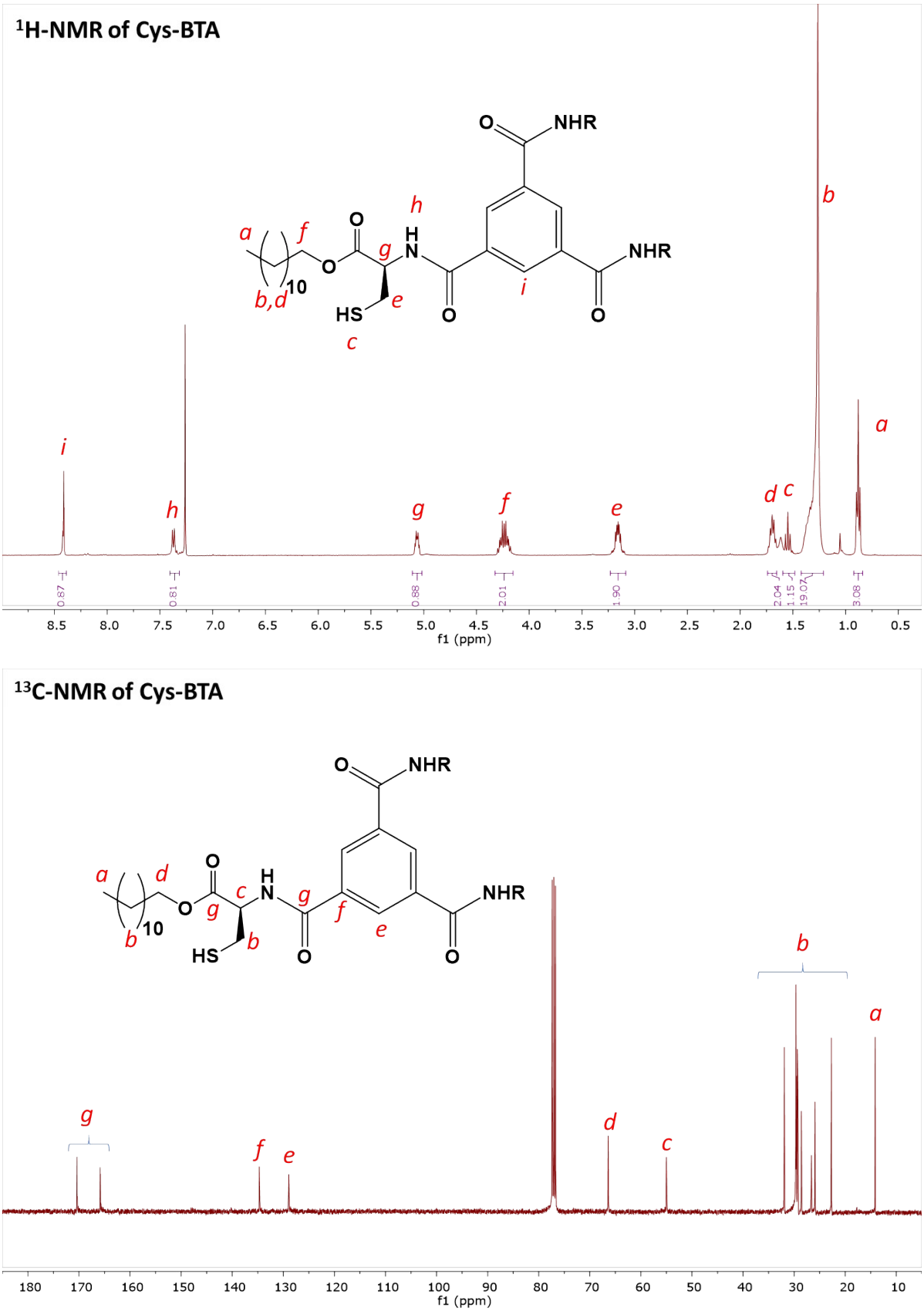


Figure S3. ^{1}H-NMR and ^{13}C-NMR spectra of **Cys-BTA** at 5 mM in $CDCl_3$ at 20 °C. All peaks have been assigned to the molecular structure, which is also displayed in the spectrum.

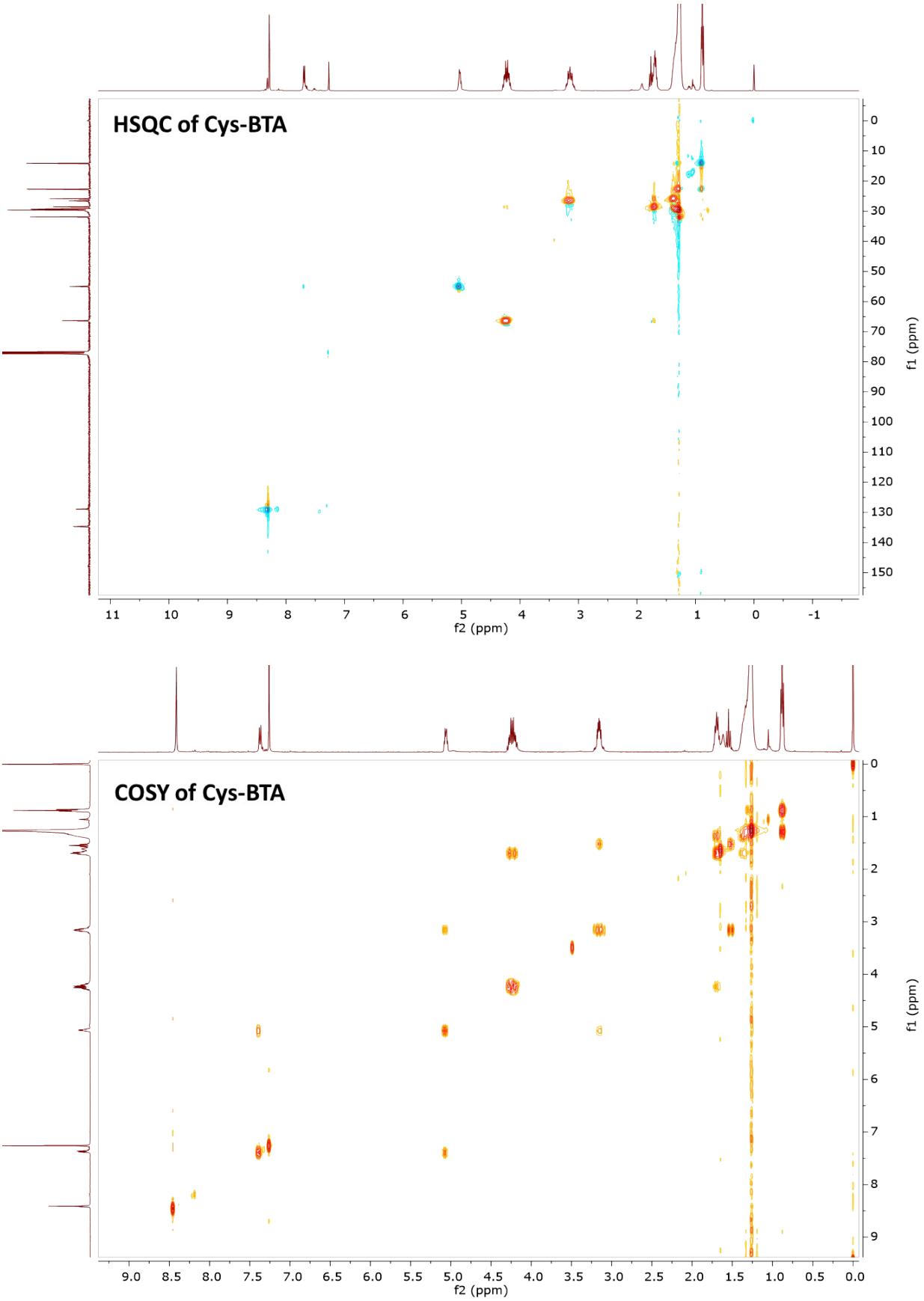


Figure S4. HSQC and COSY spectra of **Cys-BTA** at 5 mM in $CDCl_3$ at 20 °C.

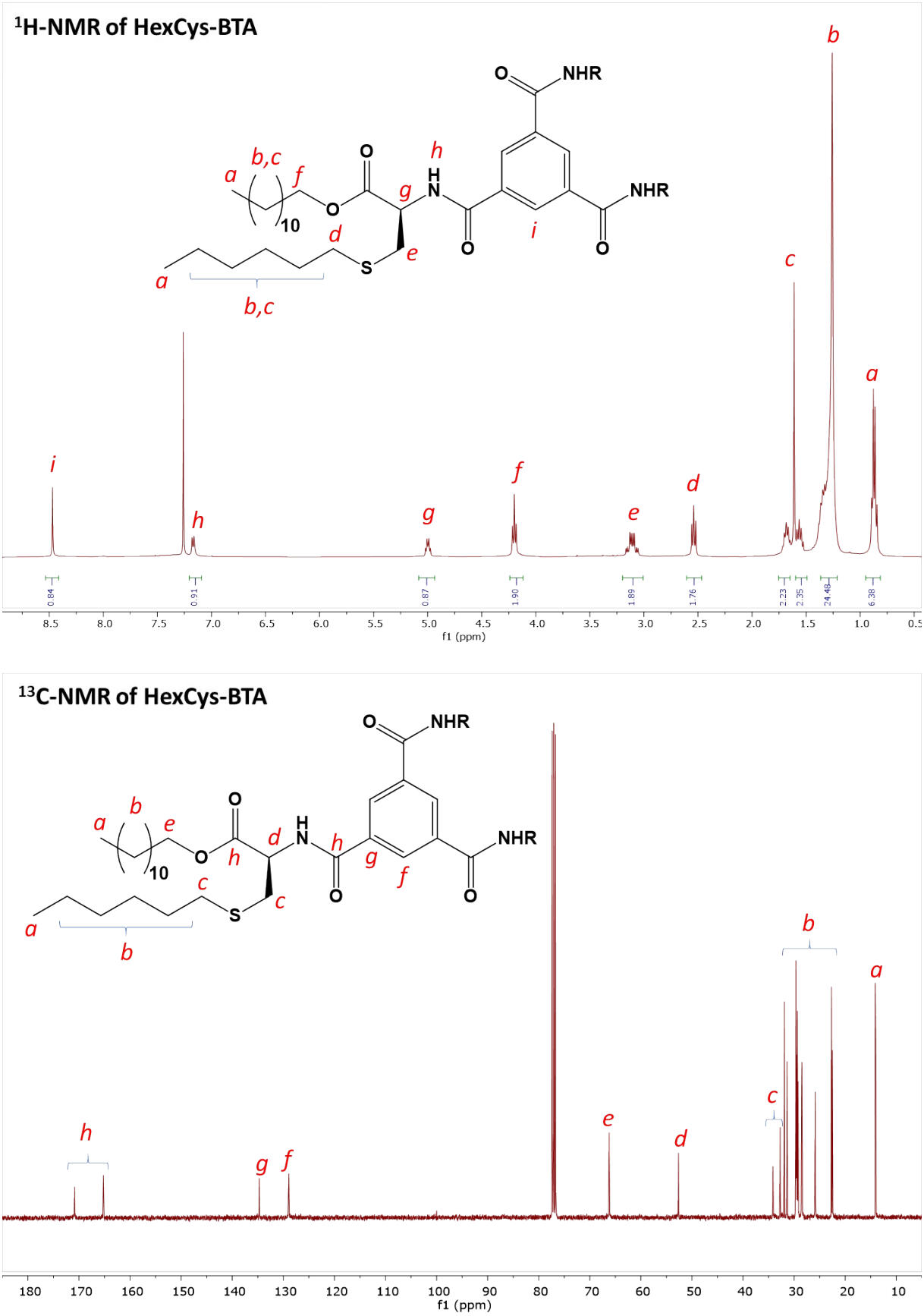


Figure S5. ^{1}H-NMR and ^{13}C-NMR spectra of **HexCys-BTA** at 5 mM in $CDCl_3$ at 20 °C.

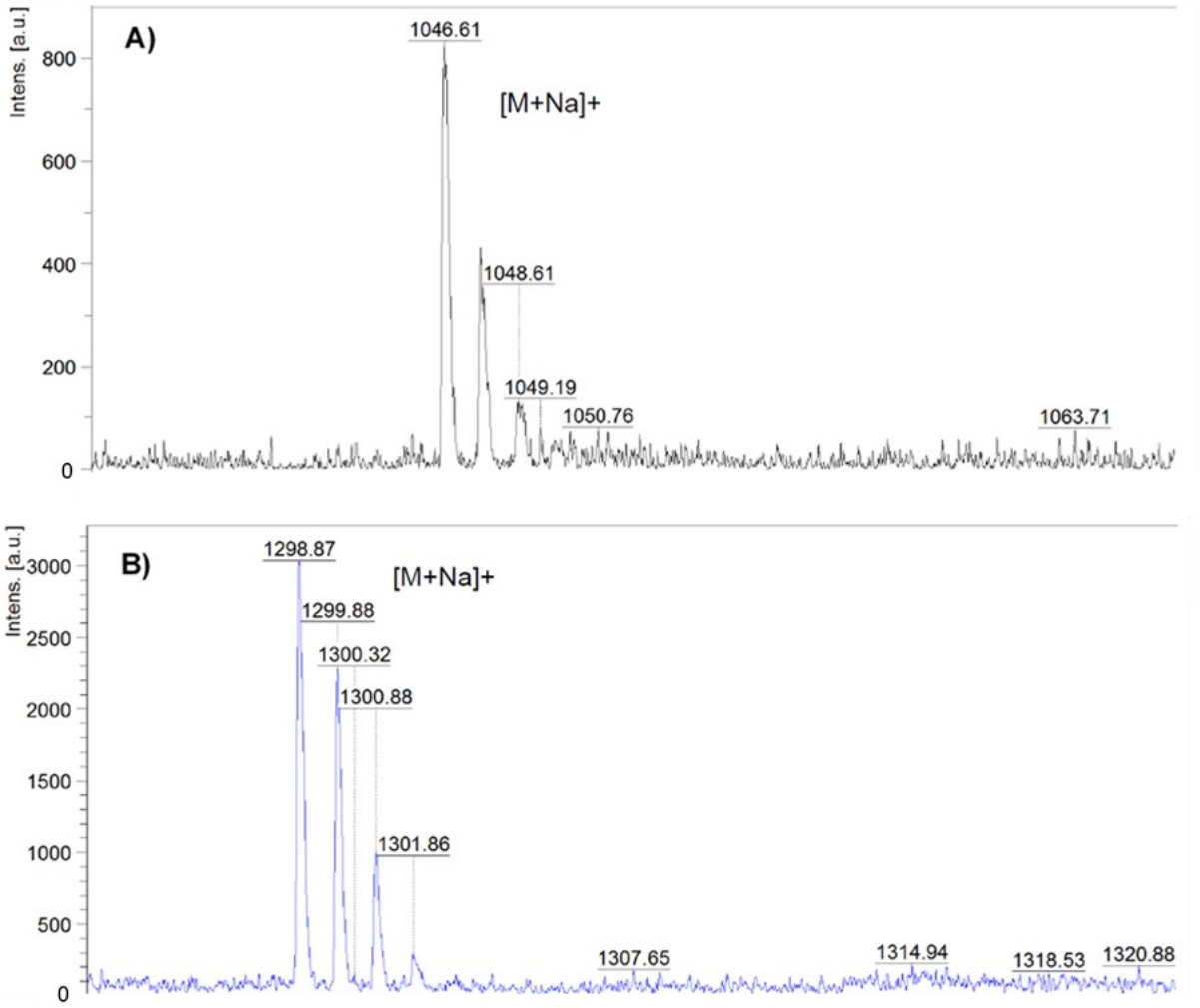


Figure S6. MALDI spectra of A) **Cys-BTA** and B) **HexCys-BTA** with the found molar mass annotated with [M + Na].

Homoaggregation of Cys-BTA and Dimerization of HexCys-BTA.

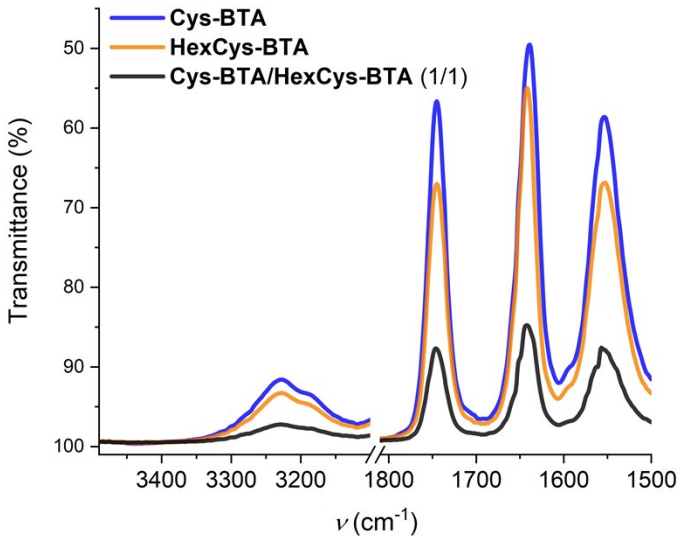


Figure S7. The bulk IR spectra of the **Cys-BTA** (blue), **HexCys-BTA** (orange), and their 1/1 mixture (black) at 20°C. All spectra display the characteristic bands of the helical stacks.

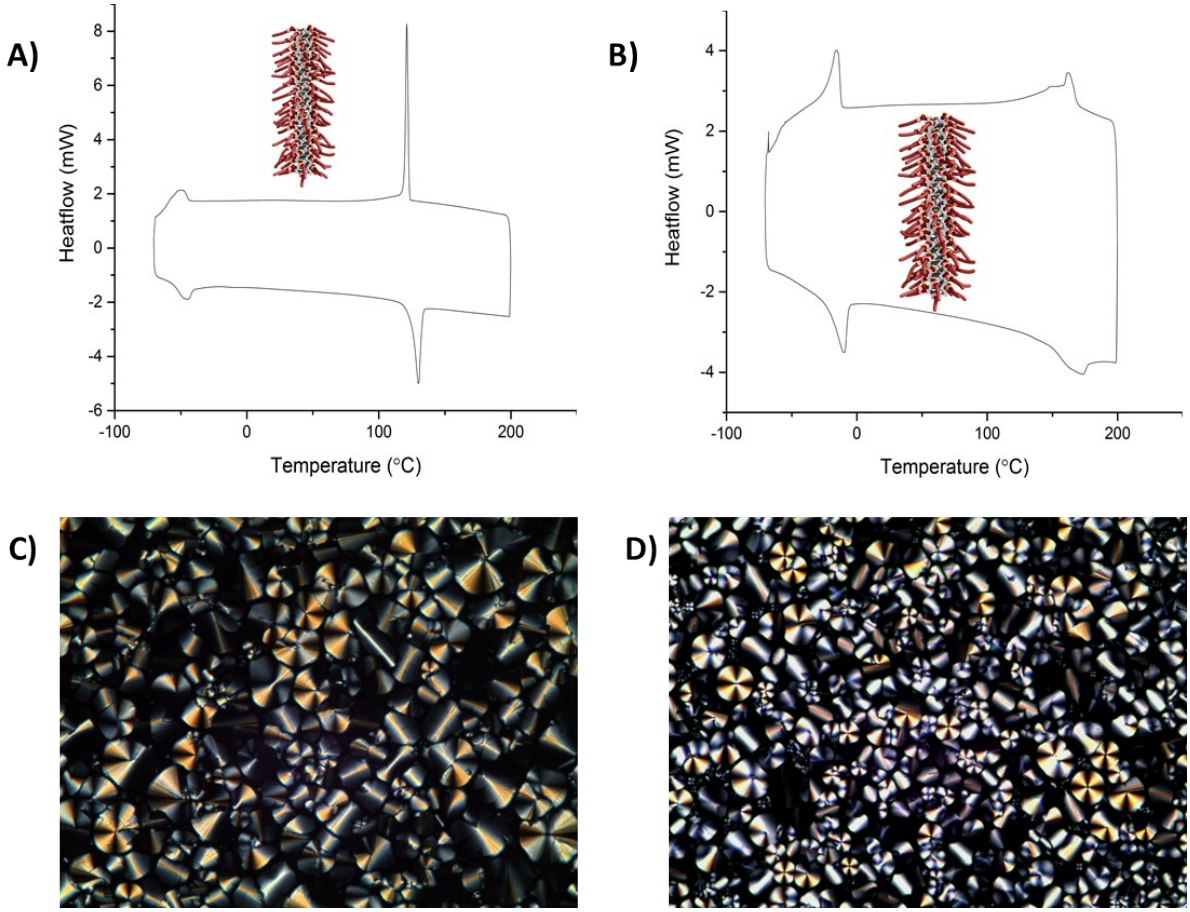


Figure S8. The DSC traces of A) **HexCys-BTA** and B) **Cys-BTA**. Both spectra display the 2nd heating run (20°C.min^{-1}) with the exotherm in the upwards direction. POM photos of C) **HexCys-BTA** and D) **Cys-BTA** show the presence of a focal conic texture just below their respective clearing temperatures (130 °C and 170 °C) characteristic of the hexagonal phase, confirming the presence of helical stacks.

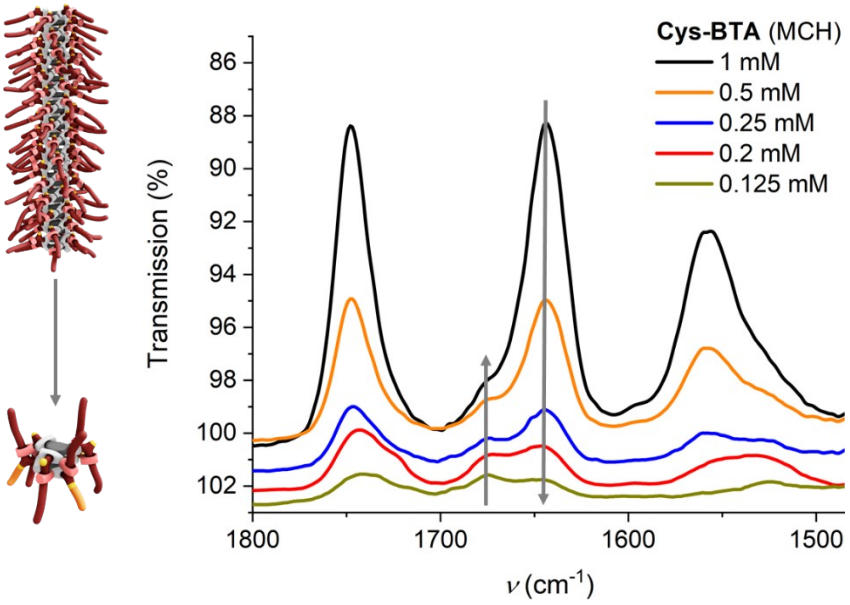


Figure S9. The IR spectra of **Cys-BTA** at different concentrations in MCH at 20 °C. The decrease of concentration in **Cys-BTA** leads to a shift in IR bands. Most notably the shift of the band at ≈ 1640 cm^{-1} to ≈ 1675 cm^{-1} indicates the disassembly of the helical structures and the formation of dimers upon dilution.

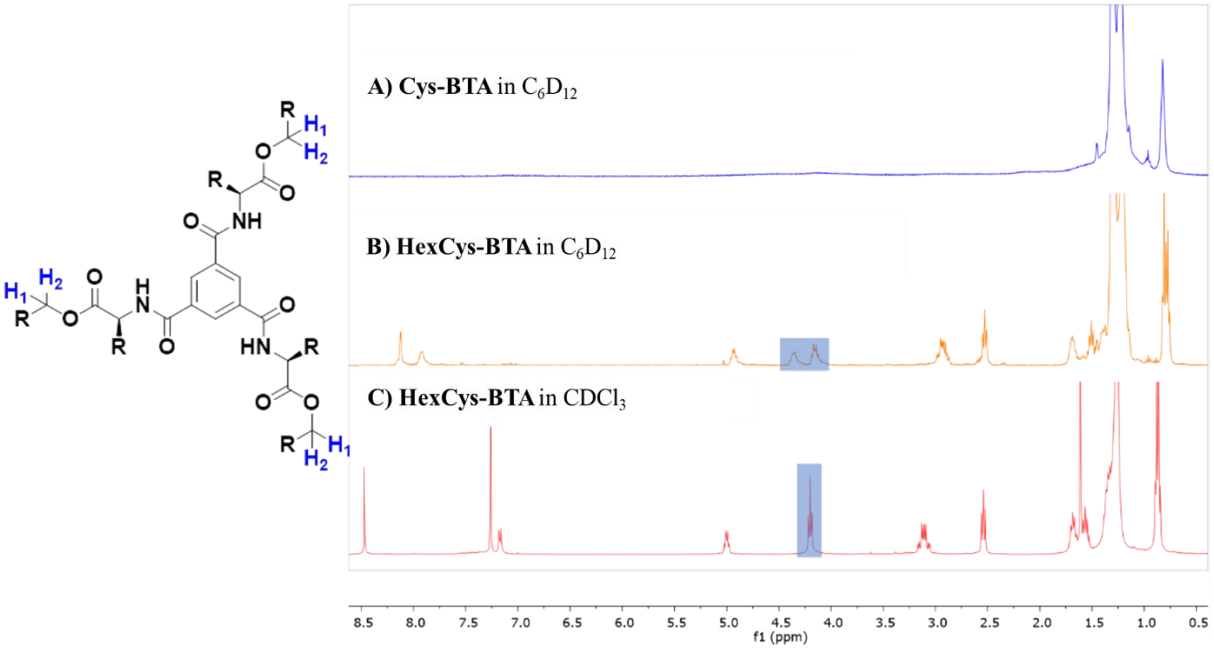


Figure S10. The ^{1}H-NMR spectra of A) **Cys-BTA** in C_6D_{12} and **HexCys-BTA** in B) $CDCl_3$ and C) C_6D_{12} solvent at a concentration of 5 mM at 20 °C. Additionally, the general structure of ester-BTA is shown. The blue protons correspond to the highlighted signals in the ^{1}H-NMR spectra B and C.

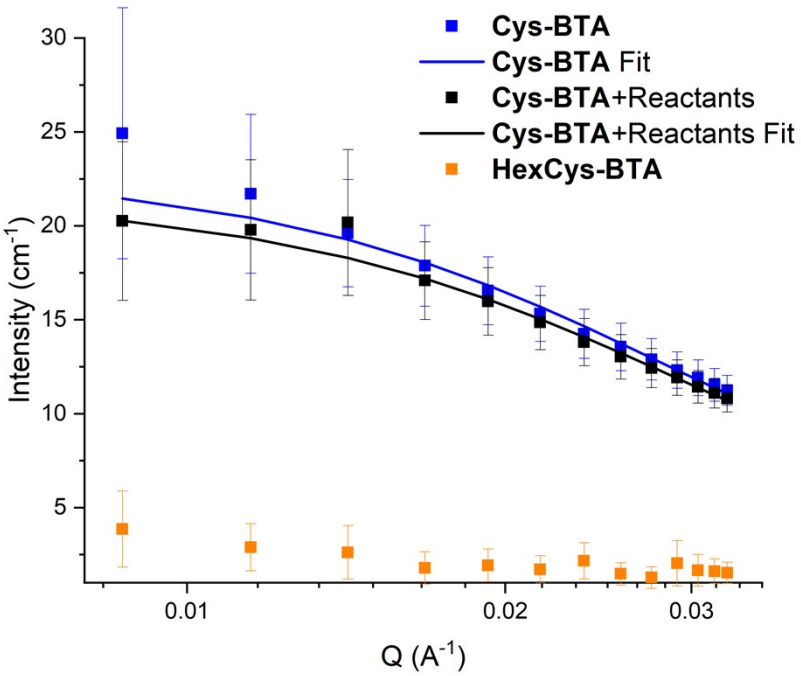


Figure S11. SLS data and their respective fits of **Cys-BTA** (blue), **Cys-BTA** with reactants (3 eq. of 1-hexene and 0.3 eq. of DMPA) in black, and **HexCys-BTA** in orange. All solutions are measured in 0.5 mM MCH solutions at 20 ºC. No significant change between the samples of **Cys-BTA** and **Cys-BTA** + reactants are observed indicating that the reactants do not negatively affect the formation of the elongated aggregates.

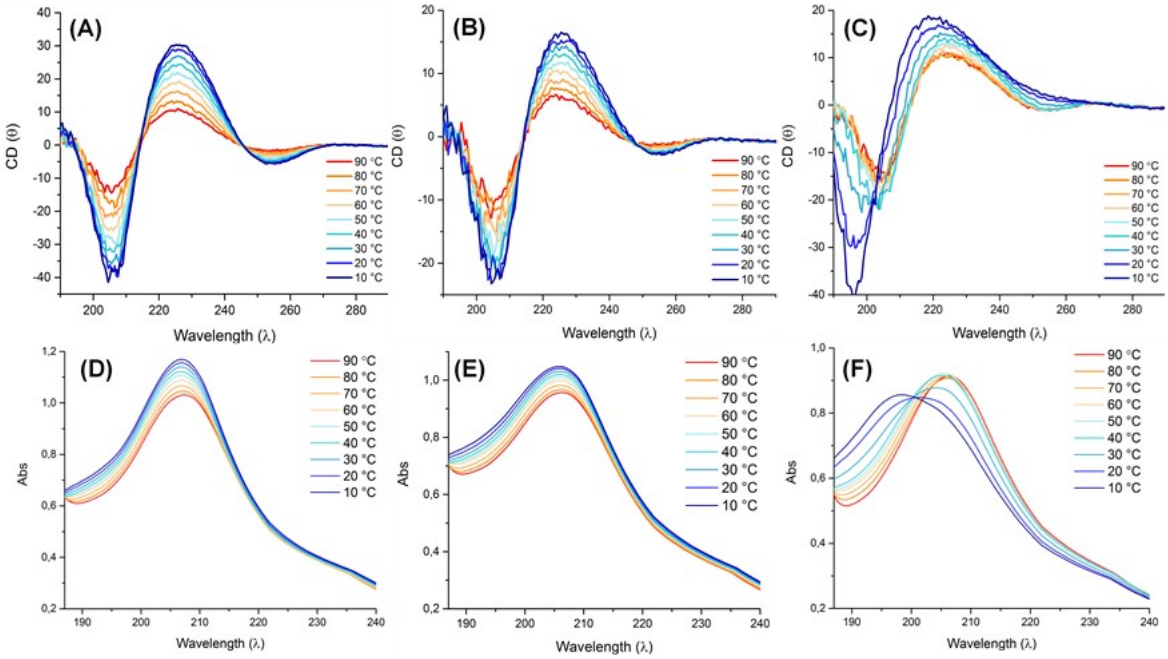


Figure S12. The VT-CD spectra between 10 °C and 90 °C of (A**) HexCys-BTA**, (B) a 1/1 mixture of **HexCys-BTA** and **Cys-BTA**, and (C) **Cys-BTA** in 0.2 mM MCH solutions. UV spectra under the same conditions are shown for (D) **HexCys-BTA,** (E) a 1/1 mixture of **HexCys-BTA** and **Cys-BTA**, and (F) **Cys-BTA**.

Supramolecular depolymerization of Cys-BTA 1D fibres into HexCys-BTA dimers upon covalent reaction.

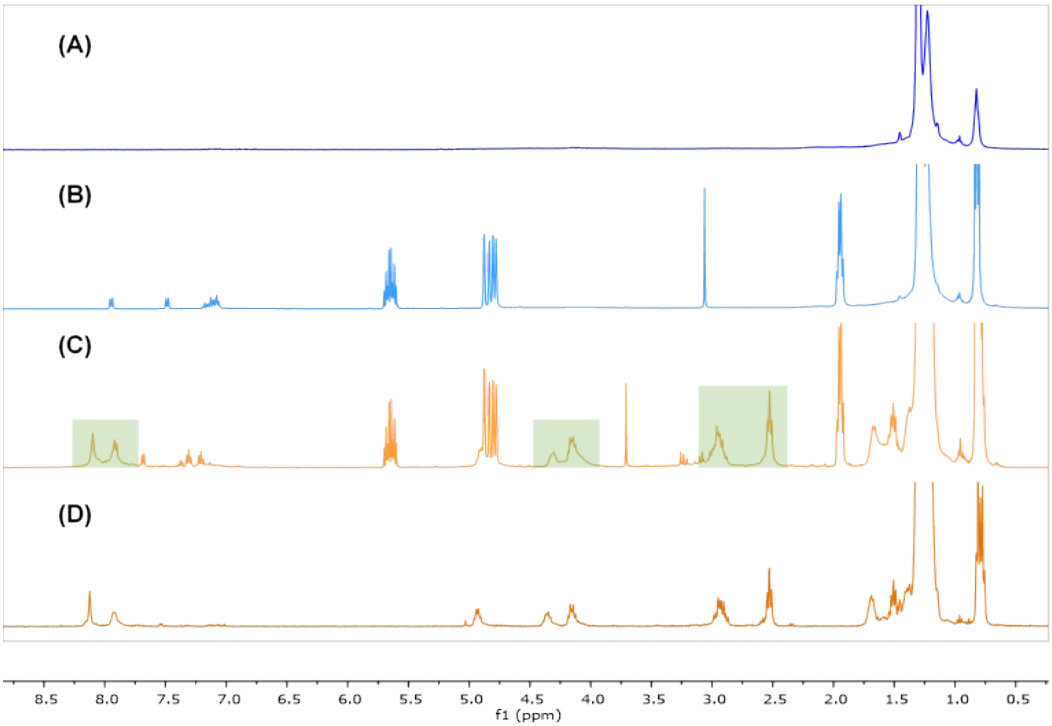


Figure S13. ^{1}H-NMR spectra of A) **Cys-BTA**, B) **Cys-BTA** and reactants (excess 6 eq. 1-hexene and DMPA), C) the spectrum of B after 10 min of UV irradiation (λ = 365 nm, 70 mW/cm^2), and D) **HexCys-BTA**. All spectra were measured at 3 mM in C_6D_{12} at 20 °C.

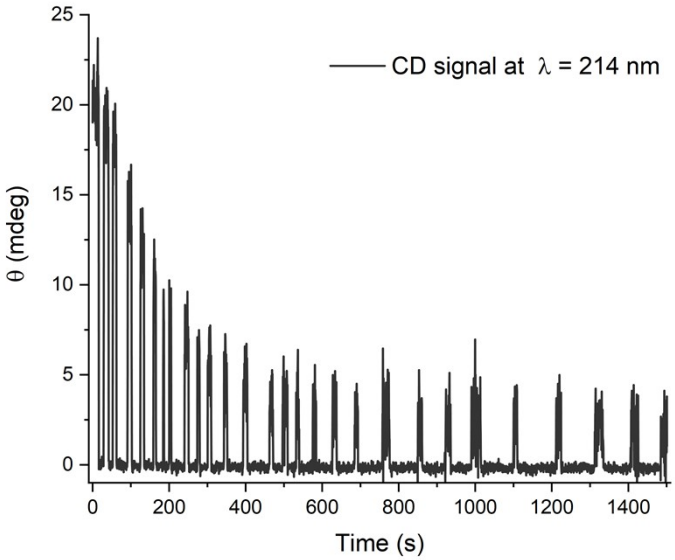


Figure S14. The kinetic data for the change in CD intensity at λ = 214 nm of a 0.2 mM MCH solution of **Cys-BTA** with reactants (3 eq. of 1-hexene and 0.3 eq. of DMPA) upon irradiation with UV (λ = 365 nm, 70 mW/cm^2) measured for 25 minutes, at 20°C. During irradiation with UV, the sensor is unable to register the signal, which explains the intermittent absence of signal in the spectrum.

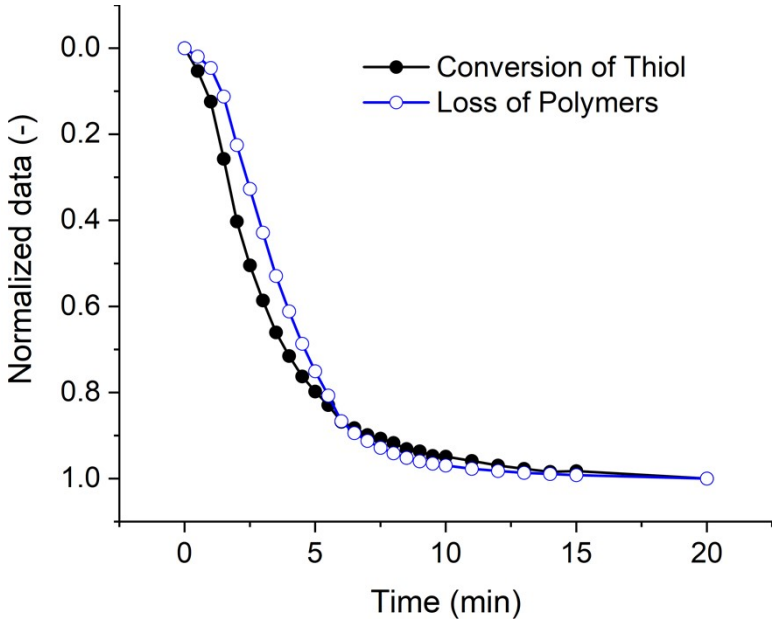


Figure S15. The normalized kinetic data of the change in IR intensities of the band of the thiol at ν = 2560 cm^{-1} and of the loss of polymer at ν = 3229 cm^{-1}.

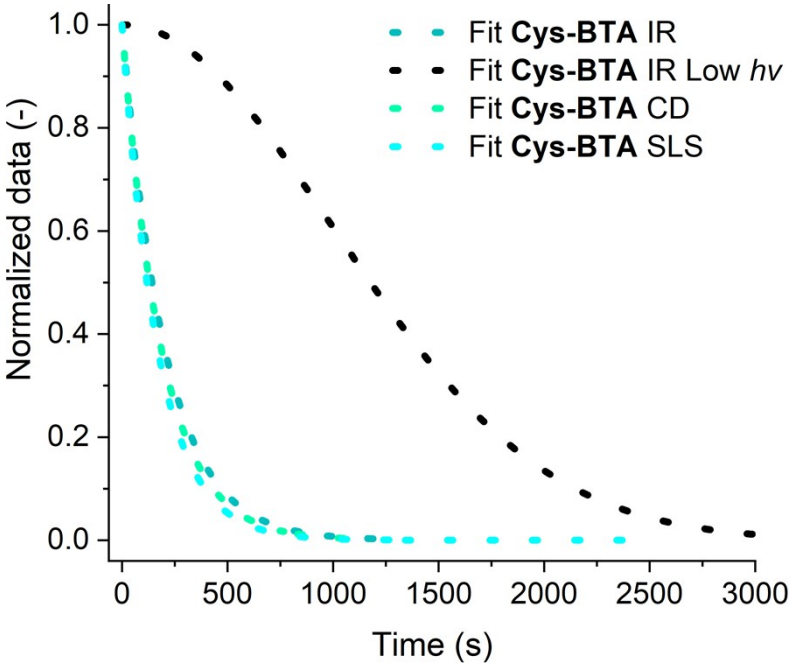


Figure S16. The fits of the IR, CD and SLS data presented in figure 5A. Data of ***Cys-BTA*** *IR, CD,* and *SLS* have been fitted to first order kinetics $f(t) = e^{(-k_1 t)}$ with $k_1 \approx 5 \cdot 10^{-3}$ s^{-1} for all of them, while ***Cys-BTA*** *IR low hv (7 mW/cm²)* has been fitted to second order kinetics $f(t) = e^{(-k_2 t^2)}$ with $k_2 \approx 3 \cdot 10^{-3}$ s^{-2}.

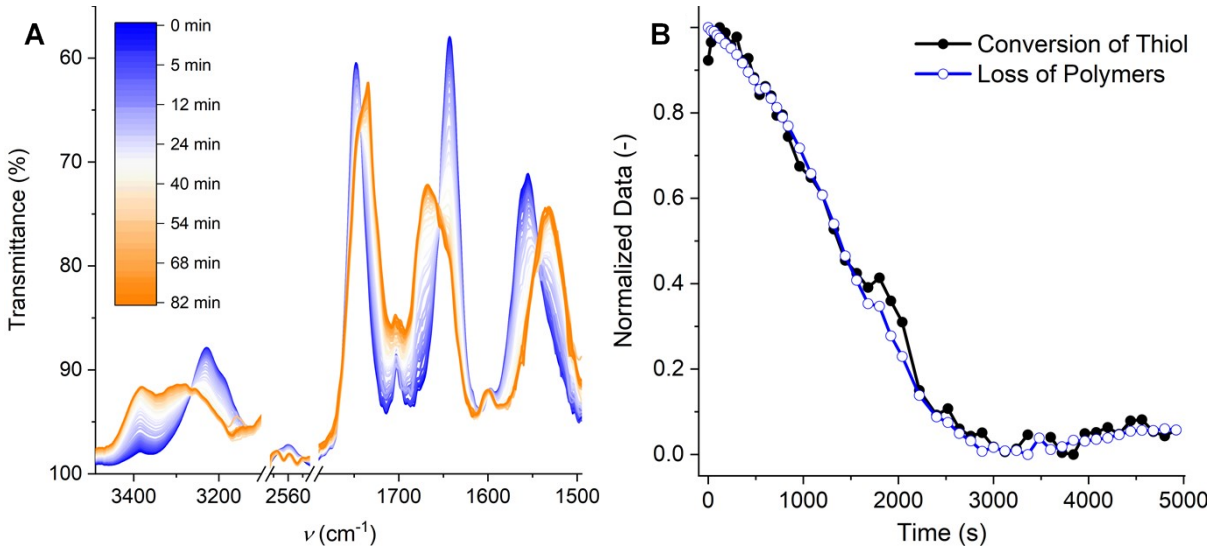


Figure S17. A) The change in FT-IR spectra over time of a 2 mM **Cys-BTA** solution with reactants (3 eq. of 1-hexene and 0.3 eq. of DMPA) at low light intensity (λ = 365 nm, ~ 7 mW/cm^2) over the course of 80 minutes in MCH at 20 °C. B) The normalized kinetic data of the change in IR intensities of the band of the thiol at ν = 2560 cm^{-1} and of the loss of polymer at ν = 3229 cm^{-1}.

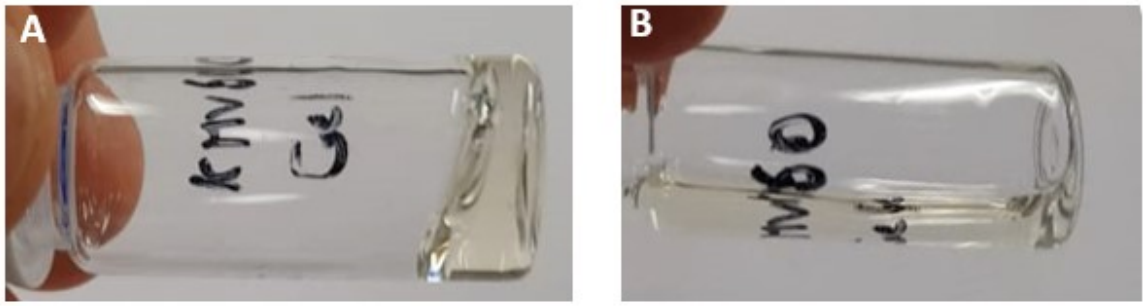


Figure S18. A) The 40 mM solution of **Cys-BTA** in MCH in presence of 4 eq. of 1-hexene and 0.3 eq. of DMPA. B) After 10 minutes of UV irradiation the solution of (A) showed a drastic decrease in viscosity resulting from the loss in polymers.

Depolymerization of inactive a-BTA polymers by competitive interactions.

Study of the copolymerization between **a-BTA** and **Cys-BTA** / **HexCys-BTA**:

Upon mixing **a-BTA** with **Cys-BTA** in a "sergeant-and-soldiers" experiments,[1] a complete helical sense bias was achieved from **Cys-BTA** added to **a-BTA** in 200 µM solution (Figure S19A), which points to the intercalation of **Cys-BTA** into **a-BTA** stacks. In contrary, addition of 4 mol% **HexCys-BTA** to **a-BTA** aggregates leads first to intercalation of **HexCys-BTA** into **a-BTA** stacks (below 50 mol% **HexCys-BTA** added, Figure S19B) and then to sequestration by formation of hetero- and homodimers (above 50 mol% **HexCys-BTA** added, Figure S19B). Comparing the SLS measurements of mixtures of 25 mol% of **Cys-BTA** or **HexCys-BTA** with **a-BTA** points to a change in morphology from elongated structures to short aggregates, confirming the ability of **HexCys-BTA** to act as a sequestrator of **a-BTA** by reducing the length of the assembly (Figure S20).[2] Figure S21 shows a similar result for the IR spectra of the **HexCys-BTA/a-BTA** mixtures, where > 50 mol% of **HexCys-BTA** is required to induce depolymerization of **a-BTA** stacks. In Figure S21B, the existence of the peak at ~3250 cm^{-1} suggests that more than 75% of **HexCys-BTA** is required for complete depolymerization of **a-BTA**.

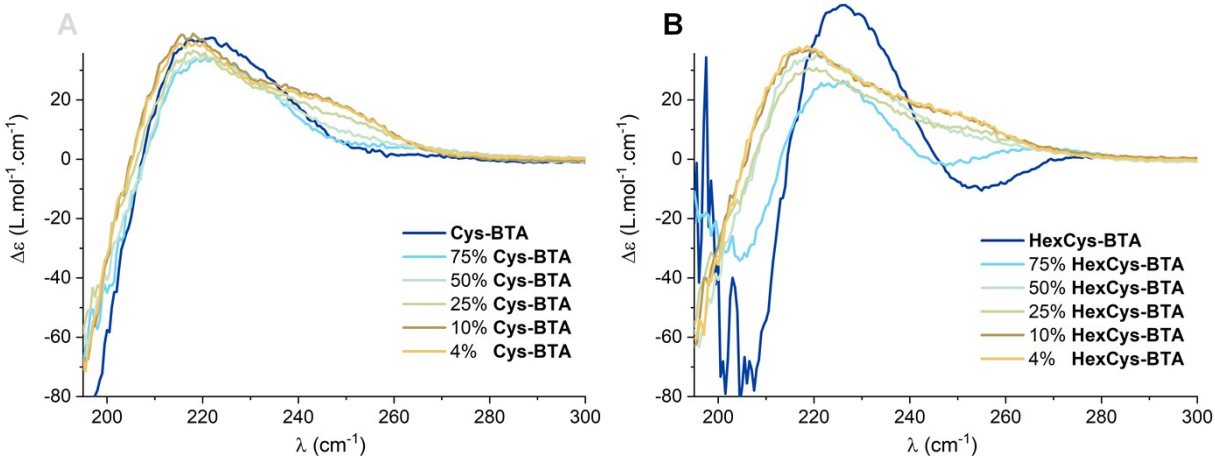


Figure S19. The CD spectra of (A) the **Cys-BTA/a-BTA** and (B) **HexCys-BTA/a-BTA** mixtures at c_{tot} = 0.2 mM in MCH at 20 °C. Percentages are given in moles of **HexCys-BTA** or **Cys-BTA** mixed with **a-BTA** in solution.

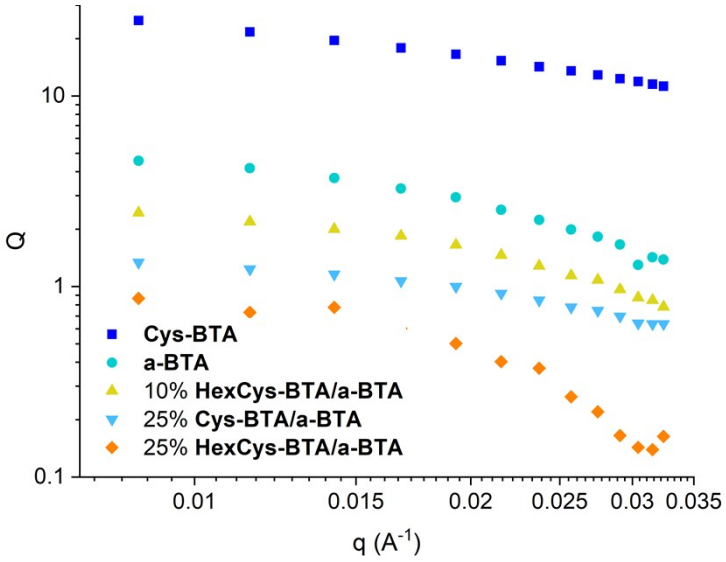


Figure S20. The SLS spectra of the mixtures of **Cys-BTA/HexCys-BTA/a-BTA** at c_{tot} = 0.2 mM in MCH at 20 °C. Percentages are given in moles of **HexCys-BTA** or **Cys-BTA** mixed with **a-BTA** in solution.

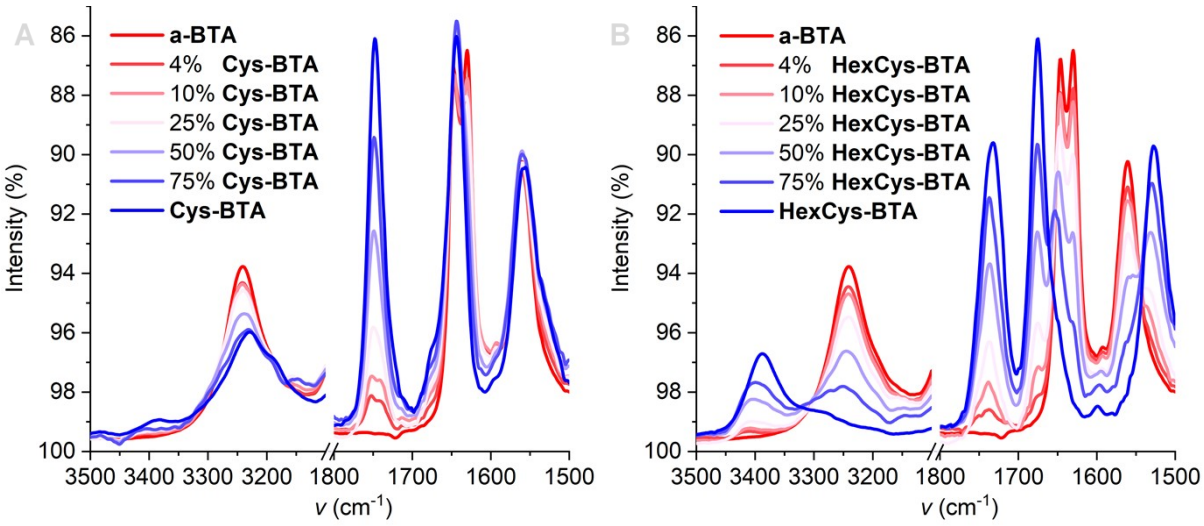


Figure S21. The IR spectra of the **Cys-BTA/a-BTA** (A) and the **HexCys-BTA/a-BTA** (B) mixtures at concentration of 1 mM in MCH at 20 °C. Percentages are given in moles of **HexCys-BTA** or **Cys-BTA** mixed with **a-BTA** in solution.

References

1 A. R. A. Palmans, J. A. J. M. Vekemans, E. E. Havinga and E. W. Meijer, *Angew. Chemie Int. Ed. English*, 1997, **36**, 2648–2651.

2 G. Vantomme, G. M. Ter Huurne, C. Kulkarni, H. M. M. Ten Eikelder, A. J. Markvoort, A. R. A. Palmans and E. W. Meijer, *J. Am. Chem. Soc.*, 2019, **141**, 18278–18285.