Stabilizing Self-assembled Nano-objects Using Light Tetrazole Chemistry

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1. Materials

p-Anisidine (99%, *Sigma Aldrich*), 11-bromoundecan-1-ol (>97%, *TCI*), 2-cyano-2-propyl dodecyl trithiocarbonate (CPTCD, 97%, *Sigma Aldrich*), *N,N'*-dicyclohexylcarbodiimide (DCC, 99%, *Sigma Aldrich*), 4-dimethylaminopyridine (DMAP, ≥99%, *Sigma Aldrich*), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimid hydrochloride (EDC·HCl, ≥98%, *Carl Roth*), 4-formylbenzoic acid (97%, *Sigma Aldrich*), hydrochloric acid (37%, *Carl Roth*), magnesium sulfate ($MgSO_4$, 99 %, *Carl Roth*), 2-methacryloyloxyethyl hydrogen succinate (MMAES, *Sigma Aldrich*), 4-methylbenzenesulfonohydrazine (98%, *Alfa Aesar*), pyridine (≥99%, *Acros Organics*), silica gel (*Merck*), sodium chloride (NaCl, ≥99.8%, *Carl Roth*), sodium hydrogen carbonate ($NaHCO_3$, ≥99.5%, *Carl Roth*), sodium hydroxide (NaOH, ≥99%, *Carl Roth*), sodium nitrite ($NaNO_2$, 97%, *Acros Organics*), *tert*-butanol (*t*-BuOH, 99.5%, *Fluka*), trifluoroacetic acid (TFA, 99%, *Acros Organics)* were employed without further purification. 2,2′-Azobis(2-methylpropionitrile) (AIBN, >98%, *TCI*) was recrystallized before use. Benzyl methacrylate (BzMA, 98%, *Alfa Aesar*) and poly(ethylene glycol) methyl ether methacrylate (POEGMA M_n=300, *Sigma Aldrich*) were passed through a basic alumina column to remove inhibitor and stored at -20°C until use. Acetone, cyclohexane (CH), diethyl ether (Et_2O), ethyl acetate (EtOAc), acetonitrile and petroleum ether were used in p.a. degree. Dichloromethane (DCM), dimethylformamide (DMF) and dioxane were purchased from Acros organics and employed as dry solvents.

Ethanol (ROTISOLV HPLC ultra gradient grade, 99.8%, *Carl Roth*) and chloroform (for HPLC, 99.8%, *Sigma Aldrich*) were purchase as analytical grade and employed in the preparation of TEM samples.Chloroform-d ($CDCl_3$, 99.8%, EURISO-TOP) and dimethyl sulfoxide-d_6 (DMSO-d_6, 99.8%, EURISO-TOP) were utilized as solvent for NMR measurements.

2. Characterization

^{1}H-NMR (400 MHz) and ^{13}C NMR (100 MHz) were measured on a Brucker Avance III Microbay 400. All spectra were recorded at ambient temperature. Chemical shifts (δ) are referred to $CDCl_3$ signal and express in parts per million (ppm); coupling constants are expressed in Hertz (Hz).

Size exclusion chromatography (SEC) was performed on an Agilent 1220 system, comprising an auto-sampler, a PLgel 5 µm bead-size guard column (50 ×7.5 mm), two PLgel 5 µm Mixed C columns and a differential refractive index detector using *N,N*- dimethylacetamide (DMAc) containing 0.033 wt% LiBr as eluent at 50°C with a flow rate of 0.5 mL min^{-1}. The SEC system was calibrated using linear poly(styrene) standards with molecular weights ranging from 370 to 6 × 10^6 g mol^{-1}.

The UV-Vis spectra were recorded on a Varian Cary 300 UV-Visible Bio Spectrophotometer (Agilent Technologies, USA). Spectra were recorded in chloroform at 25°C between 250 and 800 nm. Samples were baseline corrected with respect to the pure solvent.

Dynamic Light Scattering (DLS) measurements were performed on a Malvern Zetasizer Nano ZS light scattering apparatus equipped with a He-Ne laser operating at a wavelength of 633 nm, 4 mW and an avalanche photodiode (APD) detector. Samples were measured at concentration between 0.5-1 mg mL^{-1} in either ethanol or ethanol/chloroform 1:1 v/v mixture. All samples were measured fivefold of which the average value was given. The dynamic viscosity, refractive index and dielectric constant of the dispersants employed in the measurements were reported below according to the literature.[1]

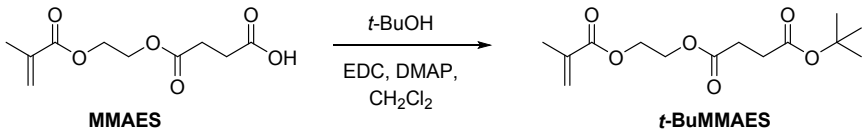
	Ethanol	Ethanol/chloroform 1:1 v/v
Viscosity, h (mPa×s)	1.083	0.7901
Refractive index, n	1.3594	1.401
Dielectric constant, e	24.55	8.899

Scanning electron microscopy (SEM) observations were performed on a Carl Zeiss LEO 1530 SEM and on a Zeiss Supra 55VP equipped with in-lens detector. The samples for SEM observations were prepared by depositing a drop of diluted dispersion solution (~1-5 mg mL^{-1}) on a glass slide, followed by drying under ambient conditions and gold sputtering coating.

Transmission Electron Microscopy (TEM) images of self-assembled block copolymers were recorded on a Tecnai F20 ST operated at an accelerating voltage of 200 kV. Triblock copolymer dispersions (~ 0.5-1.0 mg mL^{-1}) in either ethanol or ethanol/chloroform 1:1 v/v were deposited on carbon coated gold grids and stained with uranyl acetate solution (1.0 wt%).

3. Synthetic procedure

3.1 Synthesis of *tert*-butyl (2-(methacryloyloxy)ethyl) succinate (tBUMMAES)[2]



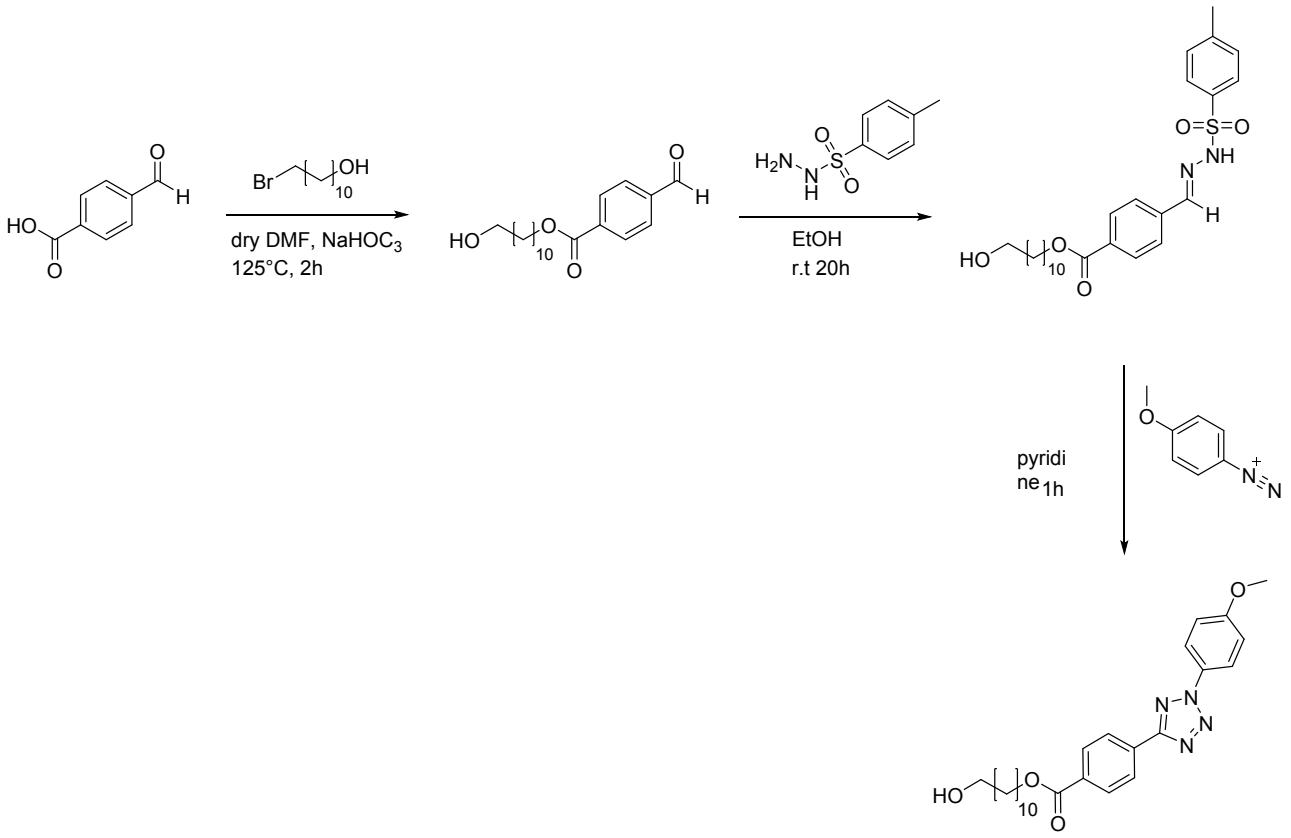
MMAES **t-BuMMAES**

The synthesis was adapted according to a literature procedure. 2-Methacryloyloxyethyl hydrogen succinate (15 g, 65.2 mmol, 1.0 eq) was dissolved in dry DCM (110 mL) under N_2 atmosphere and the solution cooled at 0 °C. Subsequently, *t*-BuOH (18.60 mL, 195.6 mmol, 3.0 eq), DMAP (0.800 g, 6.55 mmol, 0.1 eq) and DCC (17.4 g, 84.4 mmol, 1.3 eq) were added and the mixture was stirred overnight at room temperature. Then, the white precipitate was filtered off and washed with DCM. The combined organic layers were concentrated in vacuo and the crude product was dissolved in 150 mL EtOAc. The solution was washed with 0.5 M HCl solution, saturated solution of $NaHCO_3$ and brine. The organic layer was dried over magnesium sulfate and the solvent was evaporated. The crude product was purified by column chromatography (silica gel, cyclohexane/ethyl acetate, 20:1) to yield 16.6 g (89%) of a slightly yellowish oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 6.12 (m, 1H, =C*H*), 5.58 (m, 1H, =C*H*), 4.34 (s, 4H, (C=O)OCH_2), 2.57 (m, 4H, (C=O)CH_2), 1.94 (m, 3H, =CH_3), 1.43 (s, 9H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$): δ= 172.4, 171.5, 167.3, 136.0, 126.2, 80.9, 62.5, 62.4, 30.4, 29.3, 28.2, 18.4.

3.2. Synthesis of 11-hydroxyundecyl 4-(2-(4-methoxyphenyl)-2H-tetrazol-5-yl)benzoate (Tet 1)[3,4]



The three steps synthesis was performed according to a literature procedure.

4-formylbenzoic acid (4.02 g, 26.6 mmol, 1.0 eq), 11-bromoundecan-1-ol (8.70 g, 34.6 mmol, 1.3 eq) and $NaHCO_3$ (4.50 g, 53.3 mmol, 2.0 eq) were dissolved in 34 mL dry DMF under N_2 atmosphere. The solution was heated to 125 °C and stirred for 1h. After cooling down to room temperature, 100 mL ethyl acetate were added, the organic phase was washed with 1M HCl (3x30 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, cyclohexane/ethyl acetate 10:1) to yield 7.84 g of a white solid (92%).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 10.10 (s, 1H, C*H*O), 8.19 (d, 2H, Ar*H*, *J*= 8.2 Hz), 7.95 (d, 2H, Ar*H*, *J*= 8.5 Hz), 4.35 (t, 2H, (C=O)OCH_2, *J*= 6.6 Hz), 3.63 (t, 2H, HOCH_2, *J*= 6.7 Hz), 1.78 (m, 2H, CH_2), 1.55 (m, 2H, CH_2), 1.46-1.29 (m, 14H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ= 191.8, 165.8, 139.2, 135.6, 130.3, 129.6, 65.9, 63.2, 32.9, 29.7, 29.6, 29.6, 29.4, 28.7, 26.1, 25.9.

11-hydroxyundecyl 4-formylbenzoate (3.65 g, 11.4 mmol, 1.0 eq) and 4-methylbenzenesulfonohydrazine (2.33 g, 12.5 mmol, 1.1 eq) were dissolved in 100 mL acetonitrile

and stirred at 50 °C for 40 h. Afterwards, the solvent was removed under reduced pressure. The product was used without further purification.

^{1}H NMR (400 MHz, Acetone-d_6): δ (ppm)= 10.39 (s, 1H, N*H*), 8.05 (s, 1H, (C=N)*H*), 8.02 (d, 2H, Ar*H*, *J*= 8.4 Hz), 7.85 (d, 2H, Ar*H*, *J*= 8.2 Hz), 7.74 (d, 2H, Ar*H*, *J*= 8.4 Hz), 7.40 (d, 2H, Ar*H*, *J*= 8.2 Hz), 4.30 (t, 2H, (C=O)OCH_2, *J*= 6.4Hz), 3.51 (t, 2H, HOCH_2, *J*= 7.2 Hz), 2.38 (s, 3H, Ar-CH_3), 1.77 (m, 2H, CH_2), 1.51-1.31 (m, 16H, CH_2).

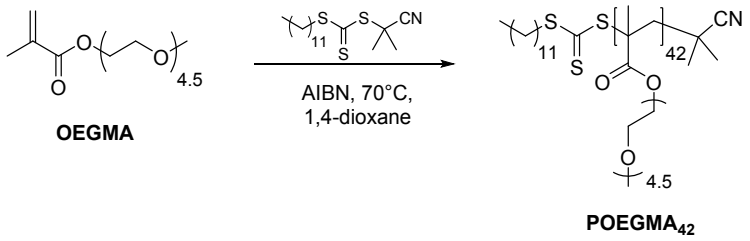
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)= 166.2, 146.5, 144.8, 139.2, 137.4, 132.4, 130.5, 130.4, 128.6, 127.8, 65.7, 62.4, 33.7, 27.6, 26.7, 21.4.

11-Hydroxyundecyl-4-((2-tosylhydrazineylidene) methyl)benzoate (5.57 g, 11.4 mmol, 1.3 eq) was dissolved in 55 mL pyridine and cooled to 0 °C. *p*-Anisidine (1.08 g, 8.8 mmol, 1.0 eq) was dissolved in 18.4 mL of a HCL/water/ethanol mixture (1:3:3) and cooled with an ice-bath. In parallel, sodium nitrite (0.60 g, 8.8 mmol, 1.0 eq) was dissolved in 4 mL of water and added dropwise to the *p*-anisidine solution. The resulting mixture was stirred for 30 minutes at 0 °C. Afterwards, the solution was allowed to reach room temperature and left to stir overnight. Then, 150 mL 10 vol% HCl-solution were added, and the resulting precipitate was filtered and washed with EtOH. The crude product was purified by column chromatography (silica gel, cyclohexane/ethyl acetate 5:1-2:1) and recrystallization from hexane/dichloromethane to yield 2.30 g of a slightly yellow solid (56%).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 8.32 (d, 2H, Ar*H*, *J*= 8.5 Hz), 8.19 (d, 2H, Ar*H*, *J*= 8.4 Hz), 8.12 (d, 2H, Ar*H*, *J*= 9.0 Hz), 7.07 (d, 2H, Ar*H*, *J*= 9.0 Hz), 4.36 (t, 2H, (C=O)OCH_2, *J*= 6.8 Hz), 3.90 (s, 3H, OCH_3), 3.51 (m, 2H, HOCH_2), 1.80 (m, 2H, CH_2), 1.55 (m, 2H, CH_2), 1.50-1.31 (m, 14H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)= 166.3, 164.3, 160.8, 132.2, 131.42, 130.5, 130.3, 127.0, 121.6, 114.9, 65.6, 63.2, 55.8, 32.9, 29.7, 29.6, 29.5, 29.4, 28.8, 26.2, 25.9.

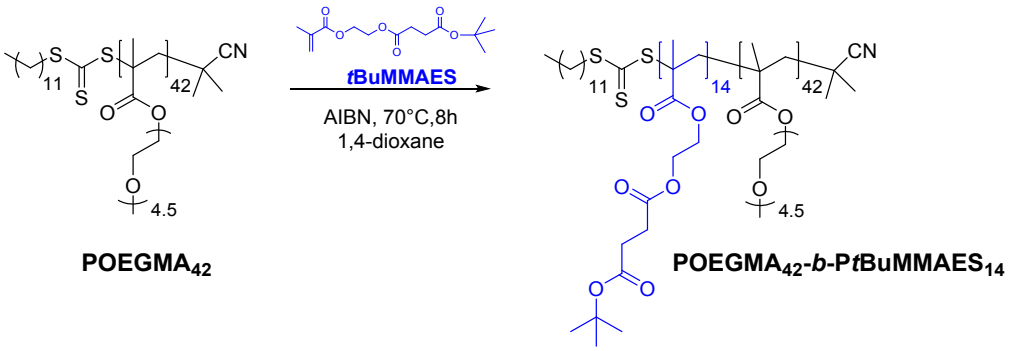
3.3 Synthesis of POEGMA macro-CTA



OEGMA (6.0 g, 20 mmol, 50 eq), CPTCD (0.138 g, 0.4 mmol, 1.0 eq) and AIBN (0.0132 g, 0.08 mmol, 0.2 eq) were dissolved in 19 mL dioxane in a 100 mL round bottom flask and sealed with a rubber septum. The resulting solution was purged for 30 minutes with nitrogen and placed in a preheated oil bath at 70 °C. After 5 h, the reaction mixture was cooled with an ice bath and exposed to air. Then, the reaction mixture was diluted with 18 mL DCM and precipitated in 400 mL petroleum ether. The precipitate was washed twice with 100 mL petroleum ether/diethyl ether (8:2 v/v) and dried under vacuum overnight to yield a yellow viscous liquid (4.7g, 76%).

Conversion (^{1}H-NMR): 78%. $M_{n,\ SEC}$: 13000 g mol^{-1}; $Đ$: 1.29; $M_{n,\ theo}$: 12 000 gmol^{-1}.

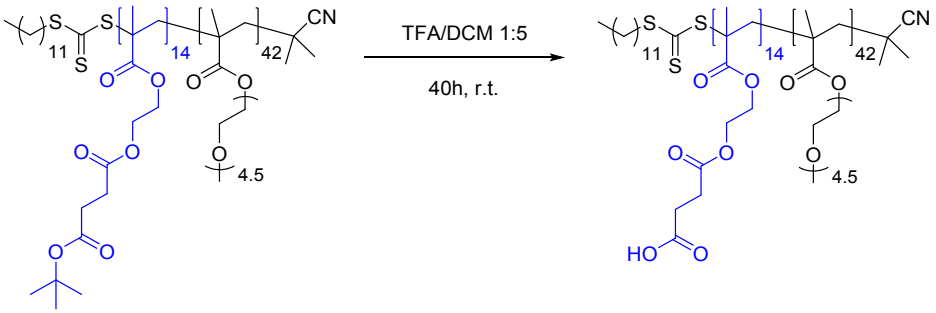
3.4 Synthesis of POEGMA-*b*-P*t*BuMMAES macro-CTA



POEGMA macro-CTA (4.0 g, 0.311 mmol, 1.0 eq), *t*BuMMAES (1.603 g, 5.60 mmol, 18 eq) and AIBN (0.0102 g, 0.0622 mmol, 0.2 eq) were dissolved in 22 mL dioxane in a 100 mL round bottom flask and sealed with a rubber septum. The resulting solution was purged for 30 minutes with nitrogen and placed overnight in a preheated oil bath at 70 °C. The resulting block copolymer was precipitated in 300 mL petroleum ether and washed twice with 100 mL petroleum ether/diethyl ether (8:2 v/v). The polymer was dried overnight to yield a yellow viscous liquid (5.3 g, 94%).

Conversion (^{1}H-NMR): 84%. $M_{n,\ SEC}$: 17000 gmol^{-1}; Đ: 1.28; $M_{n,\ theo}$: 17000 gmol^{-1}. The final composition of diblock copolymer is POEGMA$_{42}$-*b*-P*t*BuMMAES$_{14}$.

3.5 Synthesis of POEGMA-*b*-PMMAES macro-CTA



POEGMA$_{42}$-*b*-P*t*BuMMAES$_{14}$ **POEGMA$_{42}$-*b*-PMMAES$_{14}$**

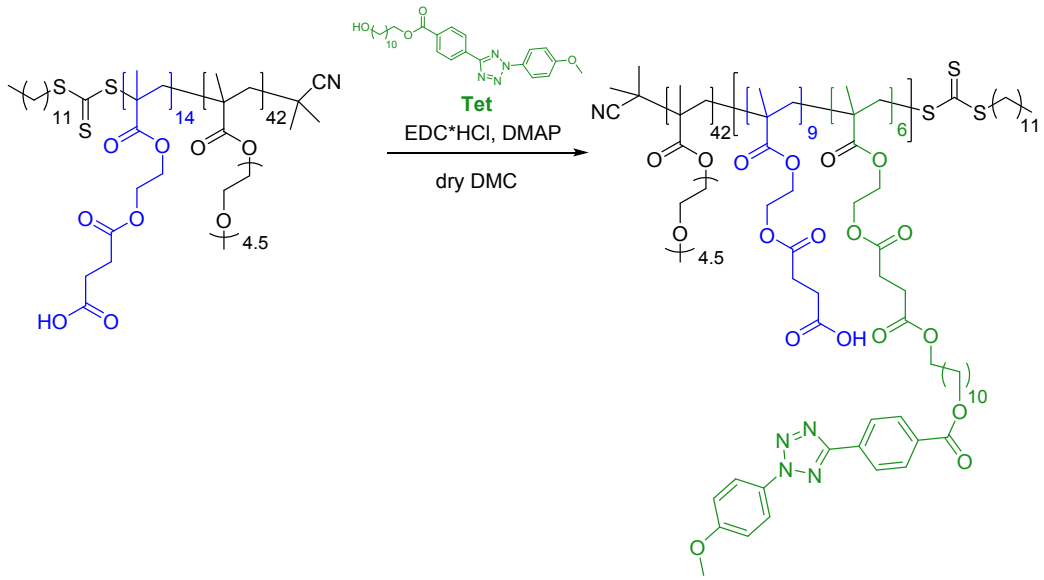
POEGMA$_{42}$-*b*-P*t*BuMMAES$_{14}$ copolymer (5.3 g, 0.310 mmol, 4.34 mmol COO-*t*Bu moieties) was dissolved in 40 mL DCM and TFA (8 mL, 104 mmol, 24 eq) was added. After stirring overnight, the resulting copolymer was precipitate in 400 mL petroleum ether/diethyl ether 1:1 (v/v) and reprecipitated in 400 mL petroleum ether. The polymer was dried overnight to obtain a yellow viscous liquid (4.9 g, 96%).

$M_{n,\,SEC}$: 13 500 gmol^{-1}; $Đ$: 1.73

The average molecular weight was calculated from $M_{n,\,SEC}$ of POEGMA$_{42}$-*b*-P*t*BuMMAES$_{14}$:

*t*BuMMAES repeating units: 14; M_n (*t*BuMMAES block) = 14* 286 g mol^{-1}= 4 089 g mol^{-1}; M_n (MMAES block) = 4 089* 230/286 g mol^{-1}= 3290 g mol^{-1}; M_n (POEGMA$_{42}$-*b*-PBuMMAES$_{14}$) = 17000-4090+3290= 16 200 g mol^{-1}.

3.6 Synthesis of POEGMA-*b*-P(MMAES-*co*-TetMA) macro-CTA[3]



POEGMA$_{42}$-*b*-PMMAES$_{14}$ **POEGMA$_{42}$-*b*-P(MMAES$_{14}$-*co*-TetMA$_6$)**

The synthesis was adapted according to a literature procedure. Under nitrogen atmosphere, POEGMA$_{42}$-*b*-PBUMMAES$_{14}$ (1.8 g, 0.1117 mmol, 1.59 mmol COOH moieties), DMAP (0.039 g, 0.3194 mmol, 0.2 eq COOH moieties) and **Tet 1**(0.299 g, 0.640 mmol, 0.4 eq COOH moieties) were dissolved in 80 mL DCM. The reaction mixture was cooled with an ice-bath and EDC*HCl was added (0.612 g, 3.19 mmol, 2.0 eq COOH moieties). The reaction was allowed to reach room temperature and stirred overnight. The resulting polymer was dialyzed against ethanol and precipitated in 200 mL petroleum ether. The final precipitate was washed twice with 40 mL petroleum ether/diethyl ether 8:2 (v/v) and dried overnight to obtain a yellow viscous liquid (2.09 g, 99%).

$M_{n,\,SEC}$: 12 500 gmol^{-1}; $Đ$: 1.50

The ratio between OEGMA/MMAES/**Tet 1**was determined via ^{1}H-NMR measurements and the average molecular weight was calculated starting from $M_{n,\,SEC}$ of POEGMA$_{42}$-*b*-P*t*BuMMAES$_{14}$:

OEGMA/MMAES/Tet = 1: 0.199: 0.134 (75%, 15%, 10%)

*t*BuMMAES repeating units (POEGMA$_{42}$-*b*-P*t*BuMMAES$_{14}$): 14; M_n (*t*BuMMAES block) = 14* 286 g mol^{-1}= 4089 g mol^{-1}; MMAES repeating units: 8.6, **Tet 1** repeating units: 5.7.

M_n (MMAES block) = 8.6* 230 g mol^{-1}= 1978 g mol^{-1}; M_n (**Tet 1** block) = 5.7* 679 g mol^{-1}= 3870 g mol^{-1}; M_n (POEGMA-*b*-P(MMAES-*co*-TetMA)) = 17000-4090+3870+1978= 18760 g mol^{-1}.

3.7 RAFT dispersion polymerization of POEGMA-*b*-PMMAES-*b*-PBzMA

Nanoparticles of POEGMA-*b*-PMMAES-*b*-PBzMA were prepared by RAFT dispersion polymerization with different target benzyl methacrylate DP and solids contents. Here follows the standard protocol for the synthesis of POEGMA-*b*-PMMAES-*b*-PBzMA particles at 20 wt% solid in ethanol/dioxane 8:2 v/v mixture as an example. POEGMA-*b*-PMMAES macroCTA (0.030 g, 0.00186 mmol, 1.0 eq) was dissolved in 0.075 mL dioxane in a 2 mL vial. Subsequently, 0.280 mL ethanol, BzMA (0.055 g, 0.312 mmol, 168 eq) and 0.020 mL of AIBN stock solution in ethanol (10.2* 10^{-4} g, 0.00062 mmol, 0.33 eq) were added. The vial was sealed and the mixture was purged with nitrogen for 10 minutes at 0 °C. Afterwards, the vial was immersed in a preheated bath at 65 °C for 24h and quenched by exposure to air. The monomer conversion was determined via ^{1}H-NMR according to the equation $x(\%)=[I^{4.90\ ppm} /(I^{4.90\ ppm} + I^{5.20\ ppm})*100]$, where 4.90 ppm and 5.20 are the O$\underline{CH_2}$-Ph signals corresponding to the polymer and the monomer, respectively. The samples were characterized by ^{1}H-NMR, SEC, DLS and SEM.

3.8 RAFT dispersion polymerization of POEGMA-*b*-P(MMAES-*co*-TetMA)-*b*-PBzMA

Nanoparticles of POEGMA-b-P(MMAES-*co*-TetMA)-b-PBzMA were prepared by RAFT dispersion polymerization with different target benzyl methacrylate DP and solids contents. Here follows the standard protocol for the synthesis of POEGMA-b-P(MMAES-*co*-TetMA)-b-PBzMA particles at 20% w/w solid in ethanol/dioxane 8:2 v/v mixture as an example. POEGMA-*b*-PMMAES macroCTA (0.025 g, 0.001339 mmol, 1.0 eq) was dissolved in 0.064 mL dioxane in a 2 mL vial. Subsequently, 0.220 mL ethanol, BzMA (0.042 g, 0.240 mmol, 150 eq) and 0.030 mL of AIBN stock solution in ethanol (7.32* 10^{-4} g, 0.000446 mmol, 0.33 eq) were added. The vial was sealed and the mixture was purged with nitrogen for 10 minutes at 0 °C. Afterwards, the vial was immersed in a preheated bath at 65 °C for 24h and quenched by exposure to air. The monomer conversion was determined via ^{1}H-NMR according to the equation $x(\%)=[I^{4.90\ ppm} /(I^{4.90\ ppm} + I^{5.20\ ppm})*100]$. The samples were characterized by ^{1}H-NMR, SEC, DLS and SEM.

4. Irradiation tests

4.1 Irradiation on the model system

Tet 1 (16.6 mg, 0.0356 mmol, 1.0 eq) was dissolved in 5 mL ethanol and acetic acid (3.05 μL, 0.0533 mmol, 1.5 eq) was added. The resulting solution was irradiated for 4 h in a custom build photoreactor with a 36 W compact low-pressure UV-A fluorescent lamp emitting at 320 nm (Arimed B6). During the irradiation, samples of 50 μL were taken at fixed time intervals and diluted in 2 mL $CHCl_3$ for UV-visible measurements.

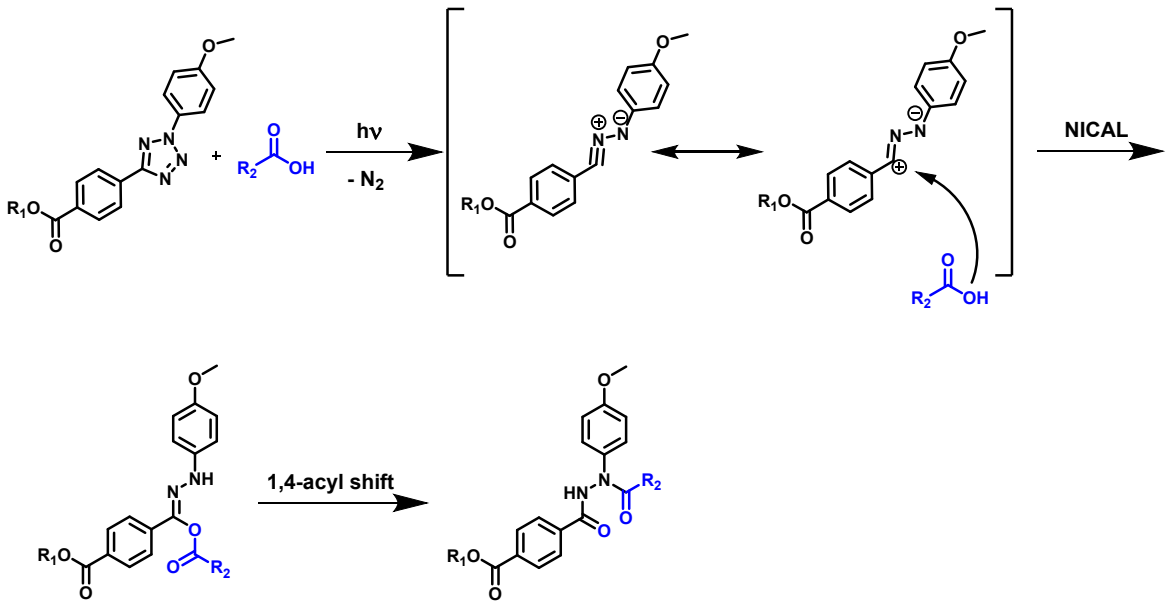
4.2 Photo-crosslinking of self-assembled POEGMA-*b*-P(MMAES-*co*-TetMA)-*b*-PBzMA nanoparticles

A typical procedure for the photo-crosslinking was described as follows: 1.0 mL ethanol were added to a 0.5 mL of 15 wt% dispersion of POEGMA-*b*-P(MMAES-*co*-TetMA)-*b*-PBzMA nanoparticles to give a 5 wt% nanoparticles concentration. The resulting dispersion was dialyzed against ethanol to remove the unreacted BzMA and then irradiated for 4 h in a custom build photoreactor with a 36 W compact low-pressure UV-A fluorescent lamp emitting at 320 nm (Arimed B6). During the reaction, samples of 50 μL were taken at fixed time intervals and diluted in 2 mL $CHCl_3$ for UV-Visible and in EtOH/$CHCl_3$ 1:1 v/v mixture for DLS measurements.

4.3 Irradiation of POEGMA-*b*-PMMAES-*b*-PBzMA self-assembled nanoparticles

1.0 mL ethanol were added to a 0.5 mL of 15 wt% dispersion of POEGMA-*b*-PMMAES-*b*-PBzMA nanoparticles to give a 5 wt% nanoparticles concentration. The resulting dispersion was dialyzed against ethanol to remove the unreacted BzMA and then irradiated for 3 hcoco in a custom build photoreactor with a 36 W compact low-pressure UV-A fluorescent lamp emitting at 320 nm (Arimed B6). Samples of 50 μL were taken before irradiation and at the end of reaction and diluted in 2 mL EtOH/$CHCl_3$ 1:1 v/v mixture for DLS measurements.

5. Scheme



Scheme S1. Mechanism of nitrile imine carboxylic acid ligation (NICAL).

6. Figures

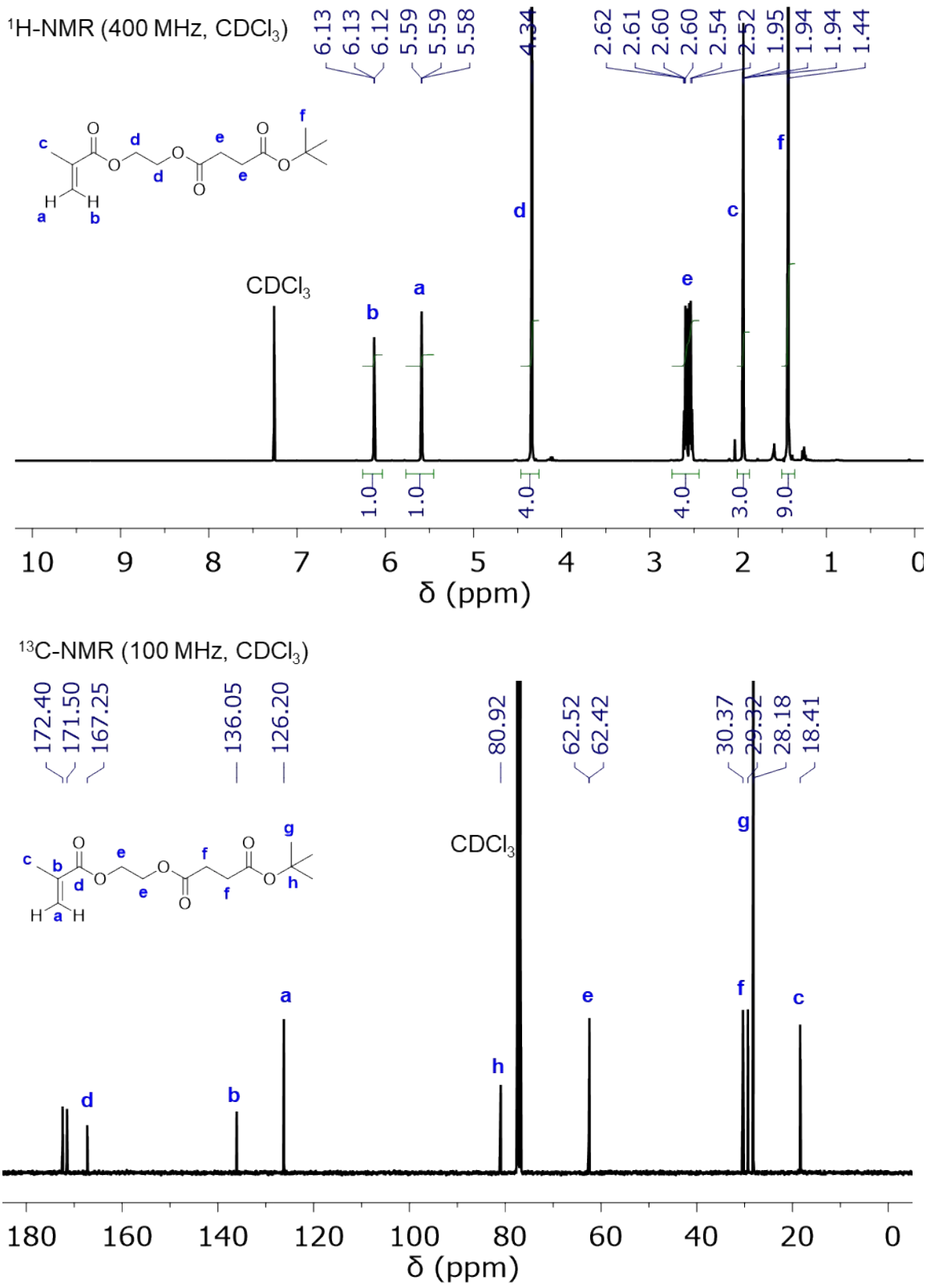


Figure S1. ^{1}H NMR and ^{13}C NMR spectra of *tert*-butyl (2-(methacryloyloxy)ethyl) succinate (*t*BuMMAES)

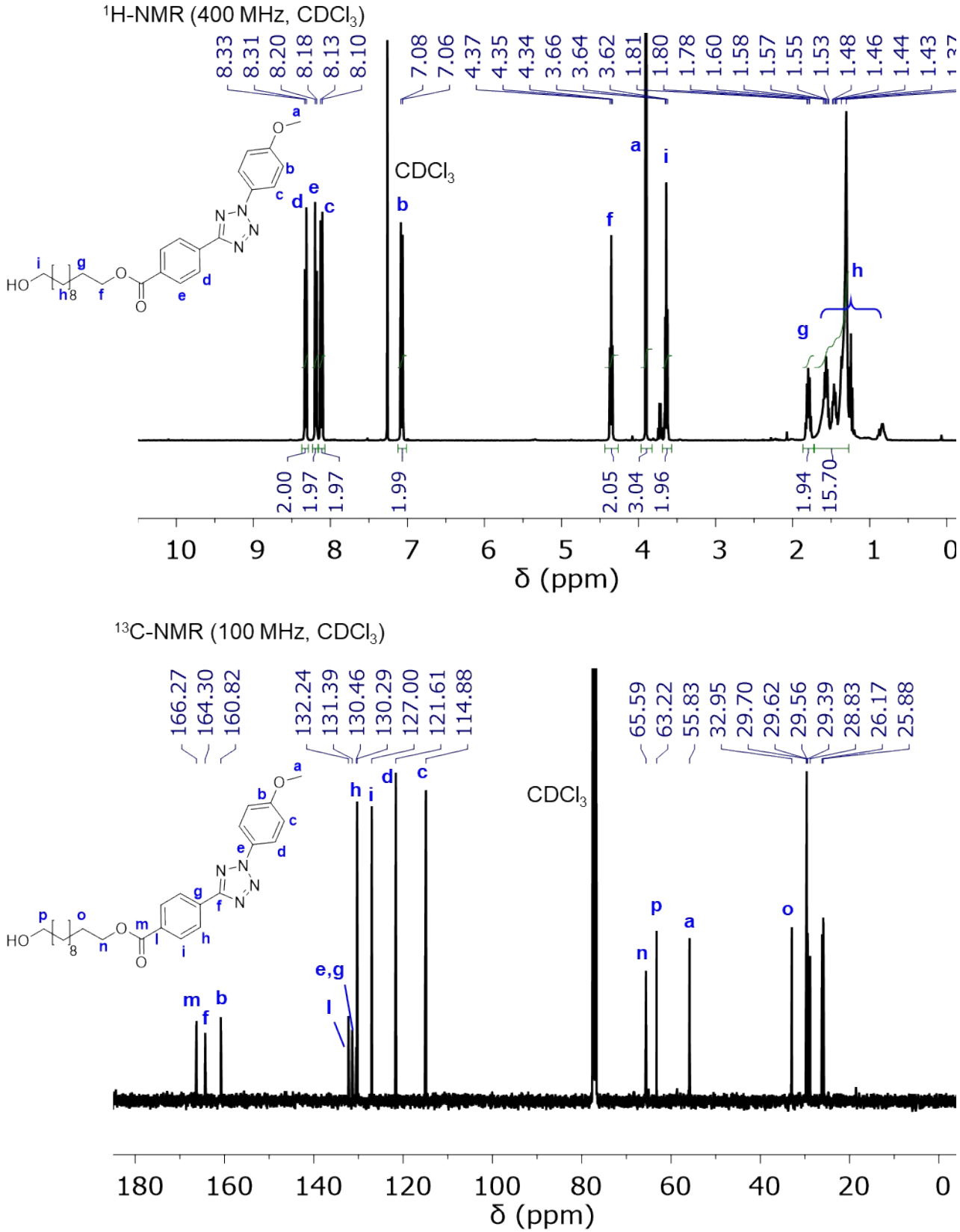


Figure S2. ^{1}H NMR and ^{13}C NMR spectra of 11-hydroxyundecyl 4-(2-(4-methoxyphenyl)-2H-tetrazol-5-yl)benzoate (**Tet 1**).

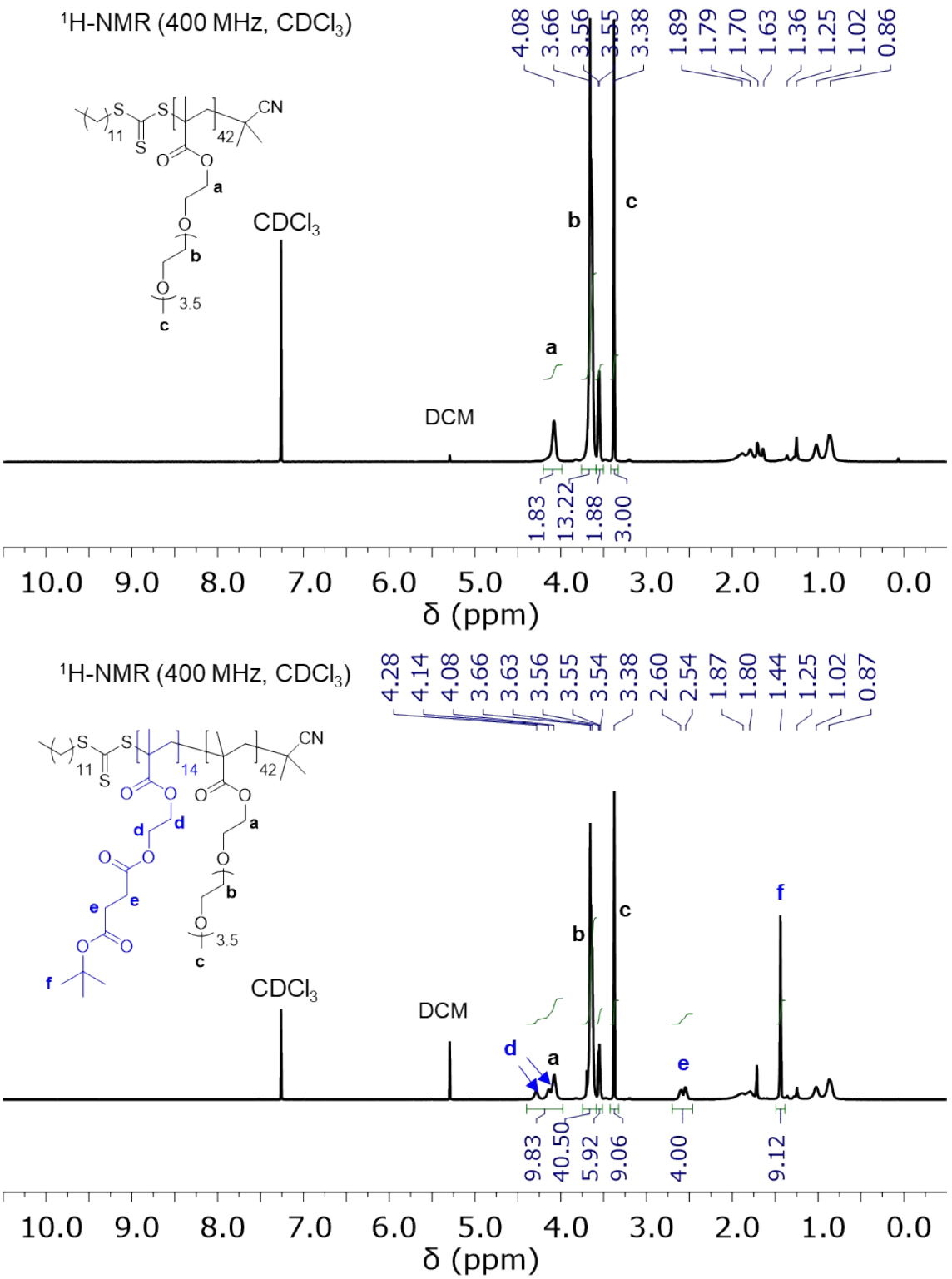


Figure S3. [1]H NMR spectra of POEGMA and POEGMA-*b*-P*t*BuMMAES

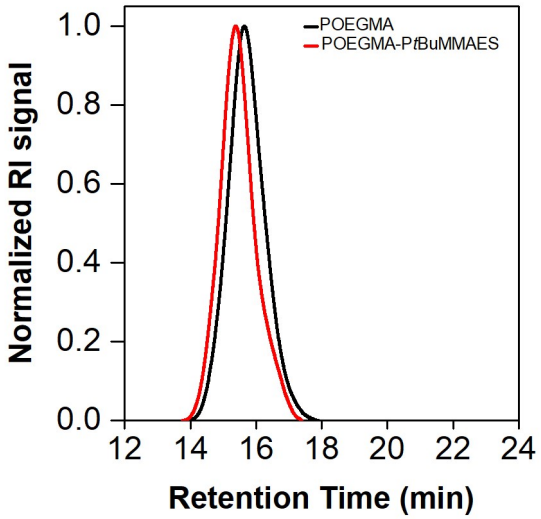


Figure S4. SEC traces of POEGMA and POEGMA-*b*-P*t*BuMMAES

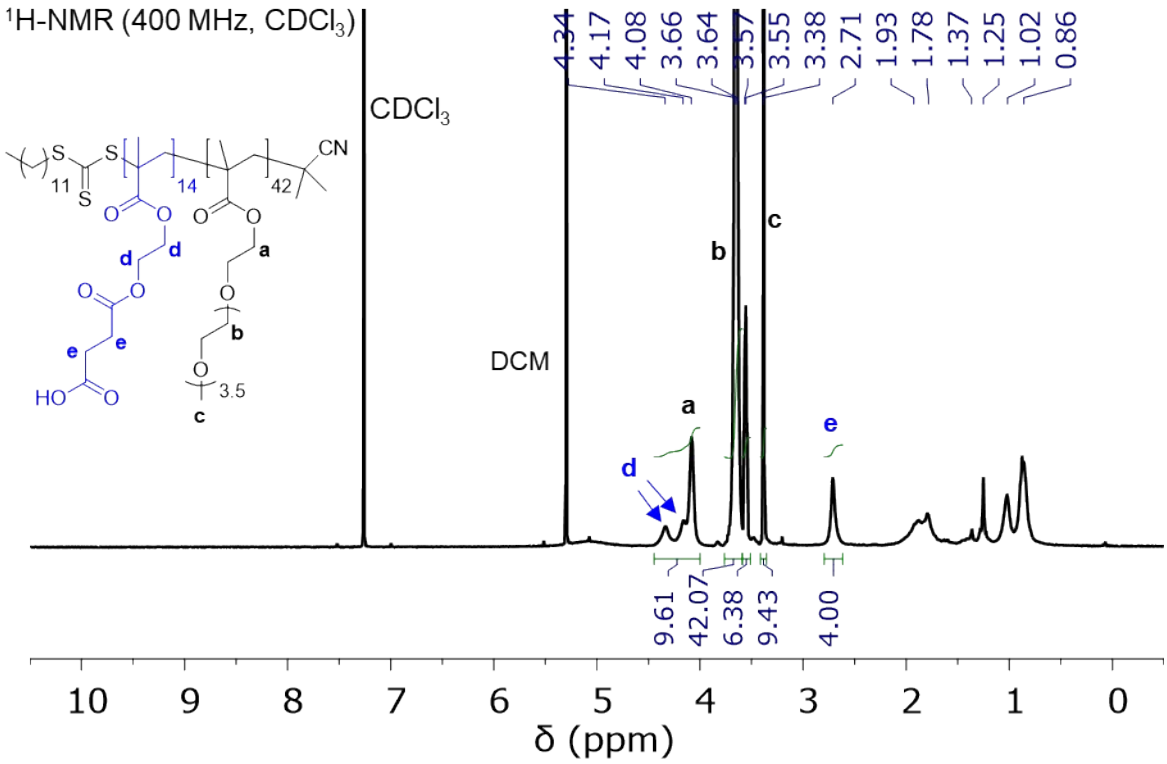


Figure S5. ^{1}H NMR spectra of POEGMA-*b*-PMMAES

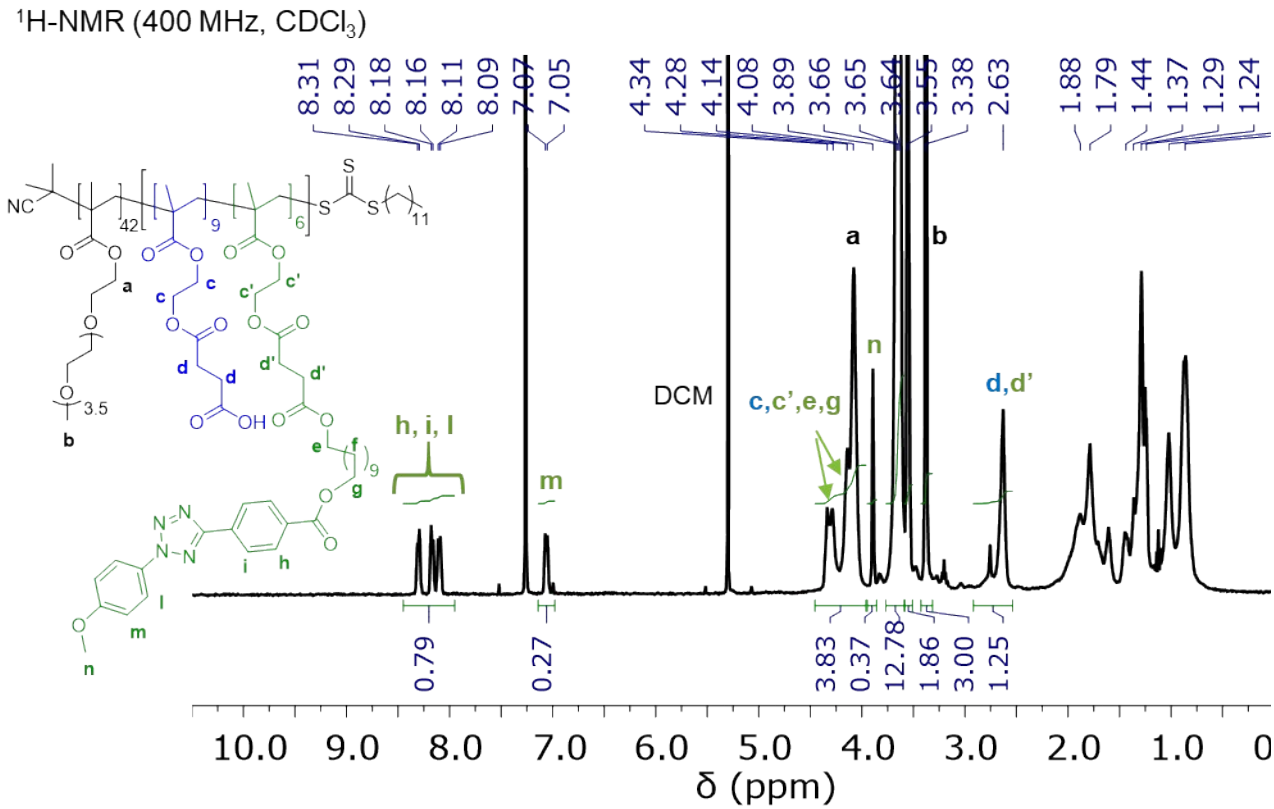


Figure S6. ^{1}H NMR spectra of POEGMA-*b*-P(MMAES-*co*-TetMA) macroCTA

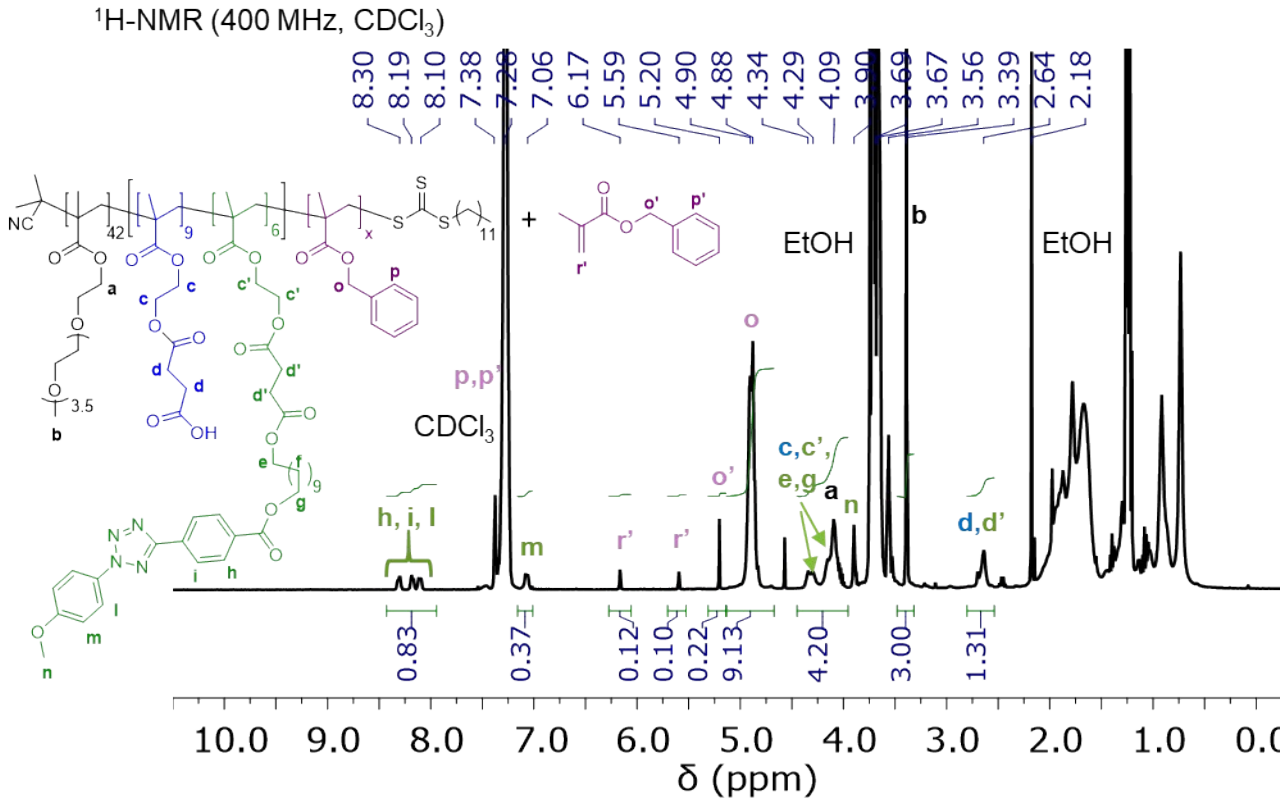


Figure S7. ^{1}H NMR spectra of POEGMA-*b*-P(MMAES-*co*-TetMA)-b-PBzMA crude mixture, as an example.

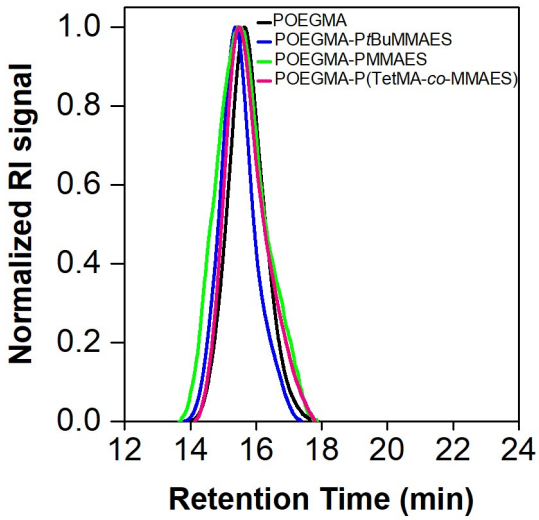


Figure S8. SEC traces of POEGMA, POEGMA-*b*-P*t*BuMMAES, POEGMA-*b*-PMMAES and POEGMA-*b*-P(MMAES-*co*-TetMA) macroCTA.

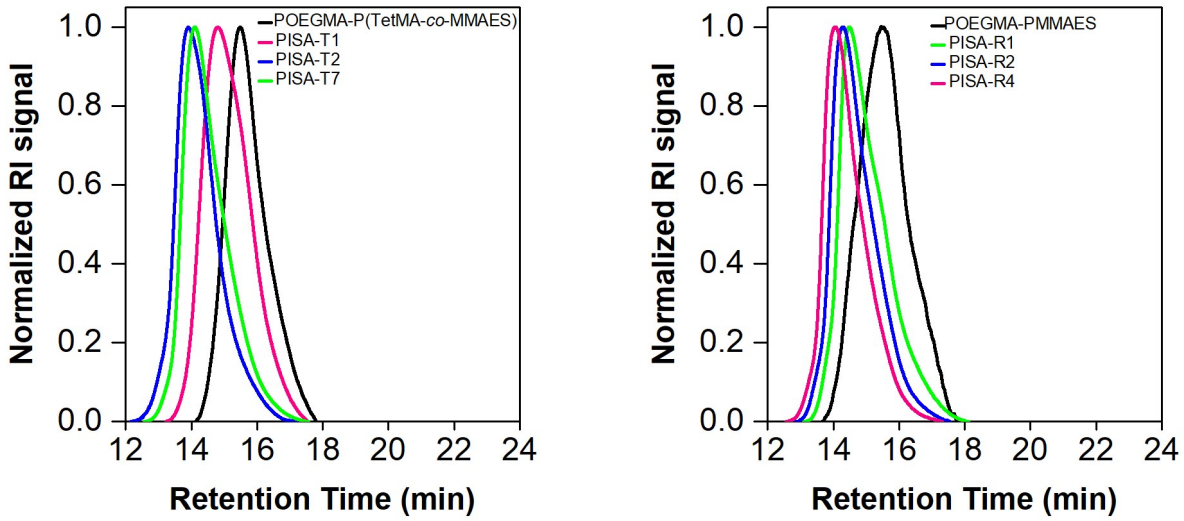


Figure S9. Left: SEC traces of POEGMA-*b*-P(MMAES-*co*-TetMA) macroCTA and selected POEGMA-*b*-P(MMAES-*co*-TetMA)-*b*-PBzMA triblock copolymers. Right: SEC traces of POEGMA-*b*-PMMAES macroCTA and selected POEGMA-*b*-PMMAES-*b*-PBzMA triblock copolymers.

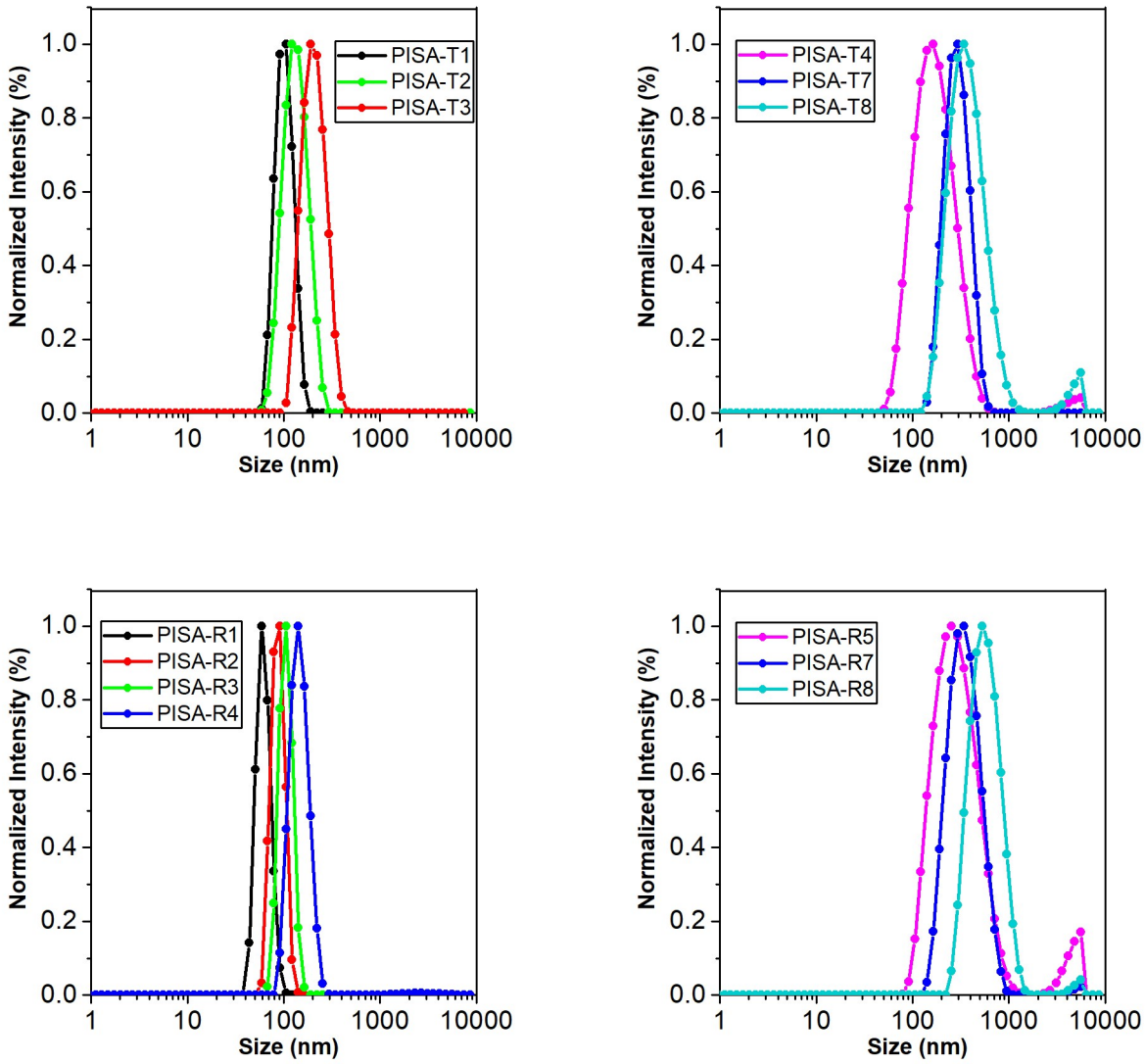


Figure S10. Intensity-weighted size (D_h) distributions of POEGMA-*b*-P(MMAES-*co*-TetMA)-*b*-PBzMA (above) and POEGMA-*b*-PMMAES-*b*-PBzMA (below) nano-objects obtained by DLS (c= 1 mg mL^{-1} in ethanol).

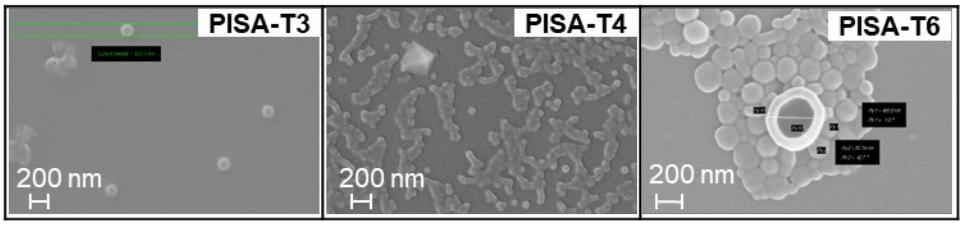


Figure S11. Additional SEM images of various POEGMA-*b*-P(MMAES-*co*-TetMA)-*b*-PBzMA triblock copolymer nano-objects.

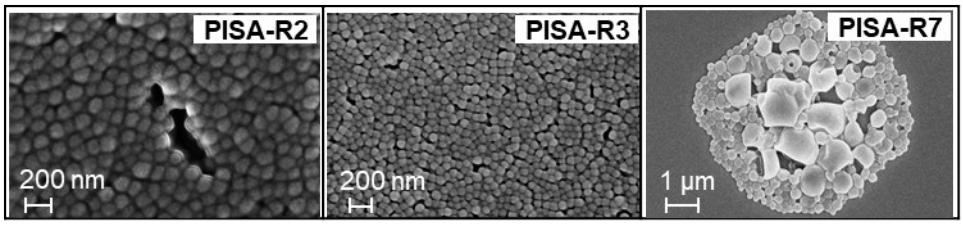
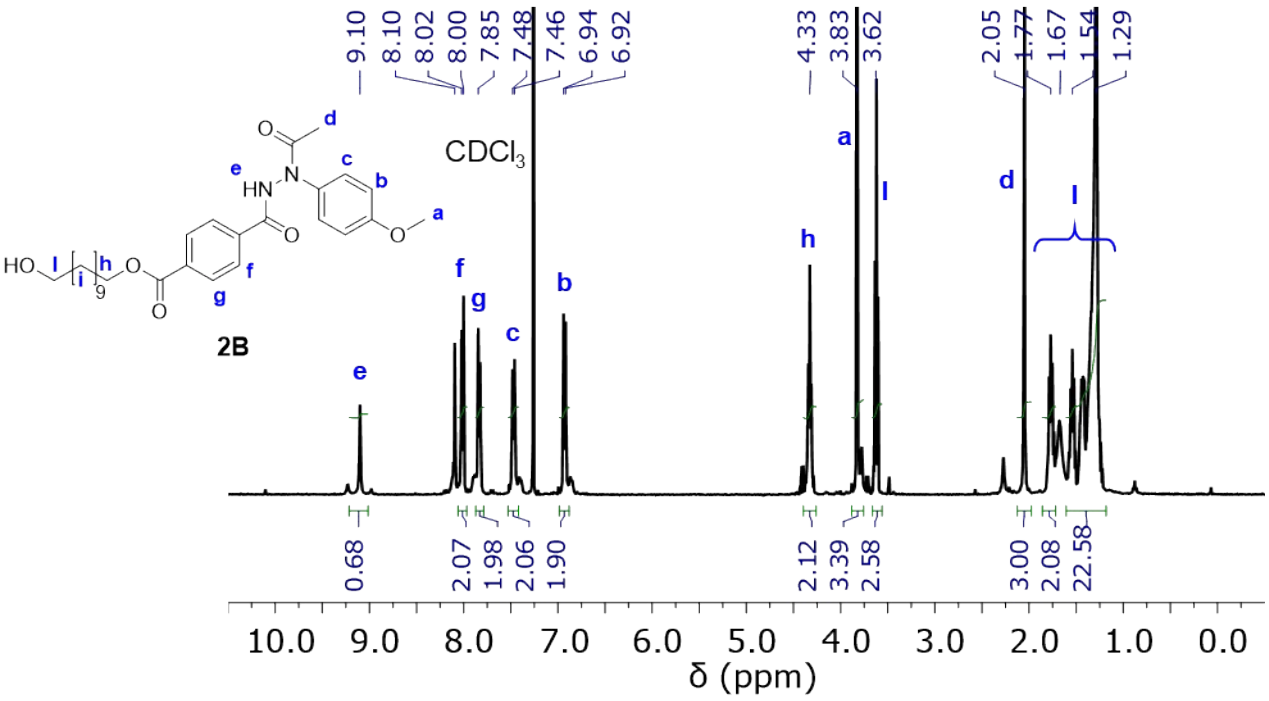
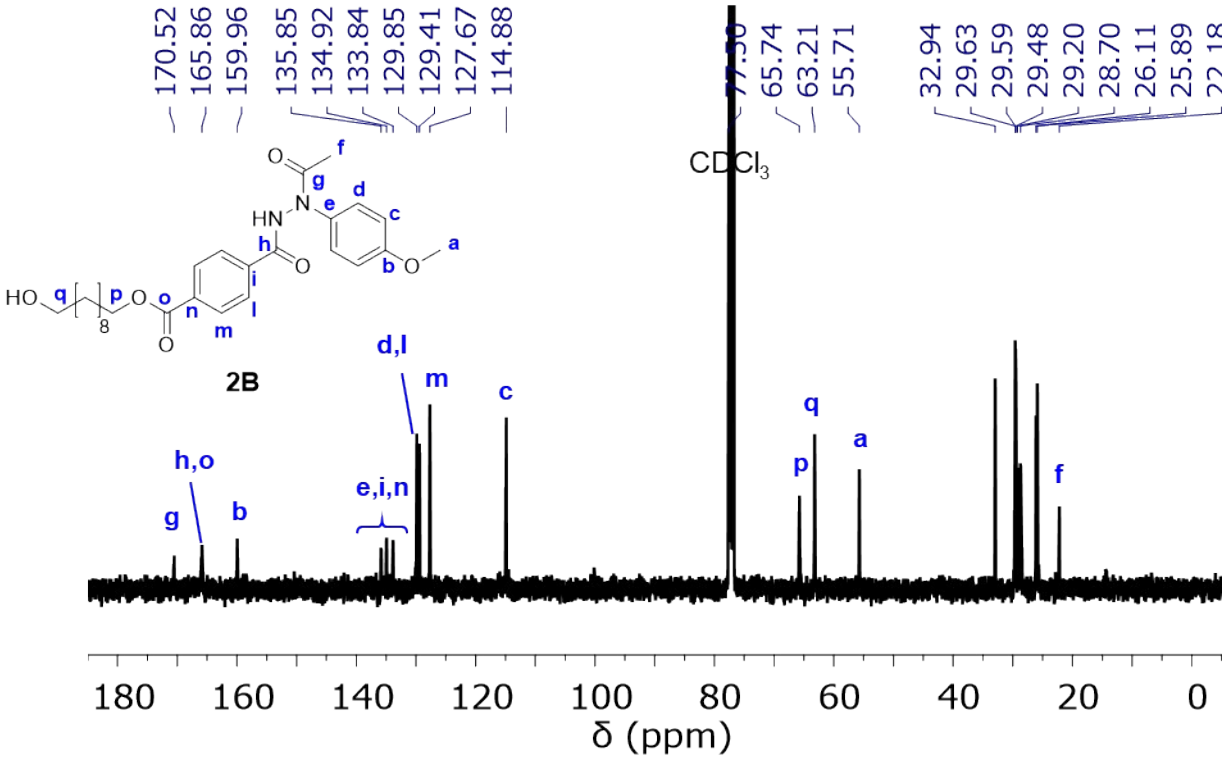


Figure S12. Additional SEM images of various POEGMA-*b*-PMMAES-*b*-PBzMA triblock copolymer nano-objects.

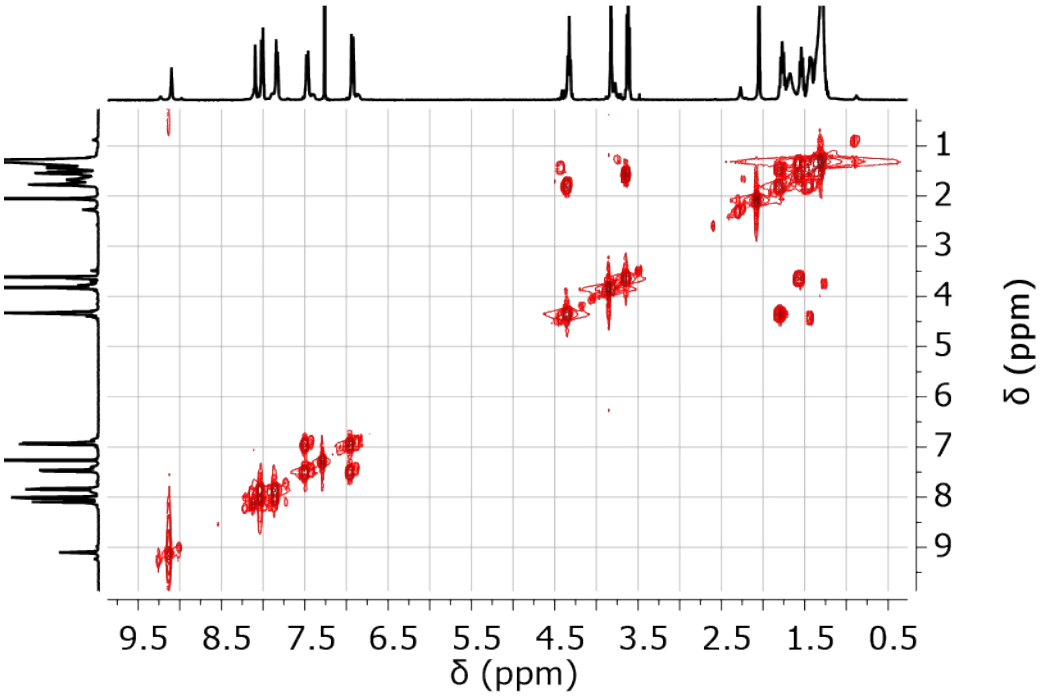
^{1}H-NMR (400 MHz, $CDCl_3$)



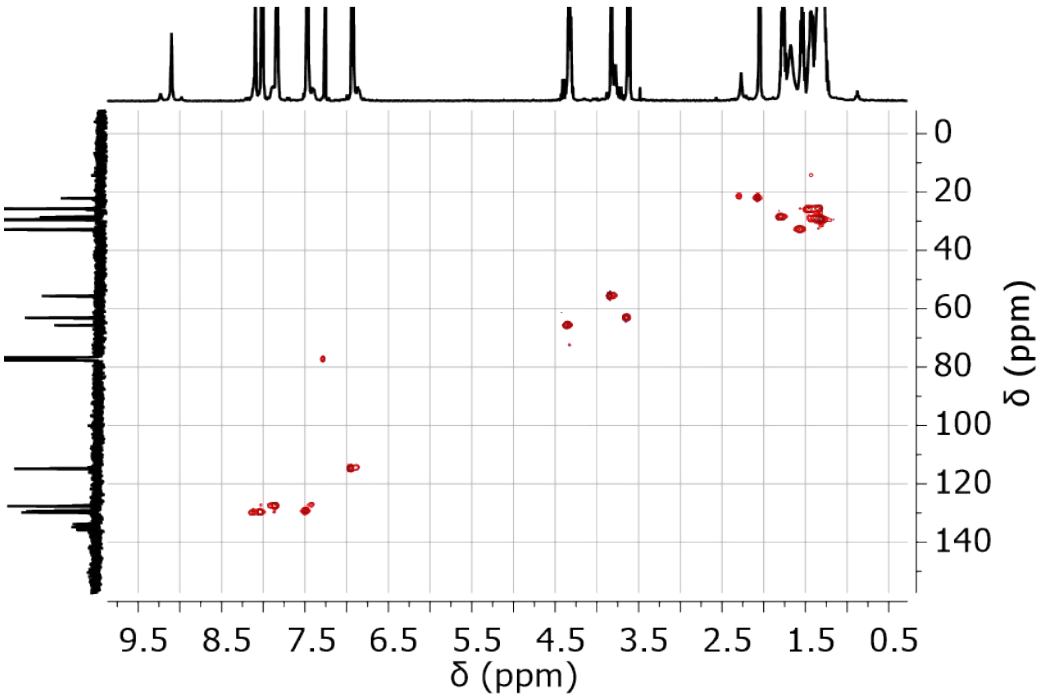
^{13}C-NMR (100 MHz, $CDCl_3$)



COSY (400 MHz, $CDCl_3$)



HSQC (400 MHz, $CDCl_3$)



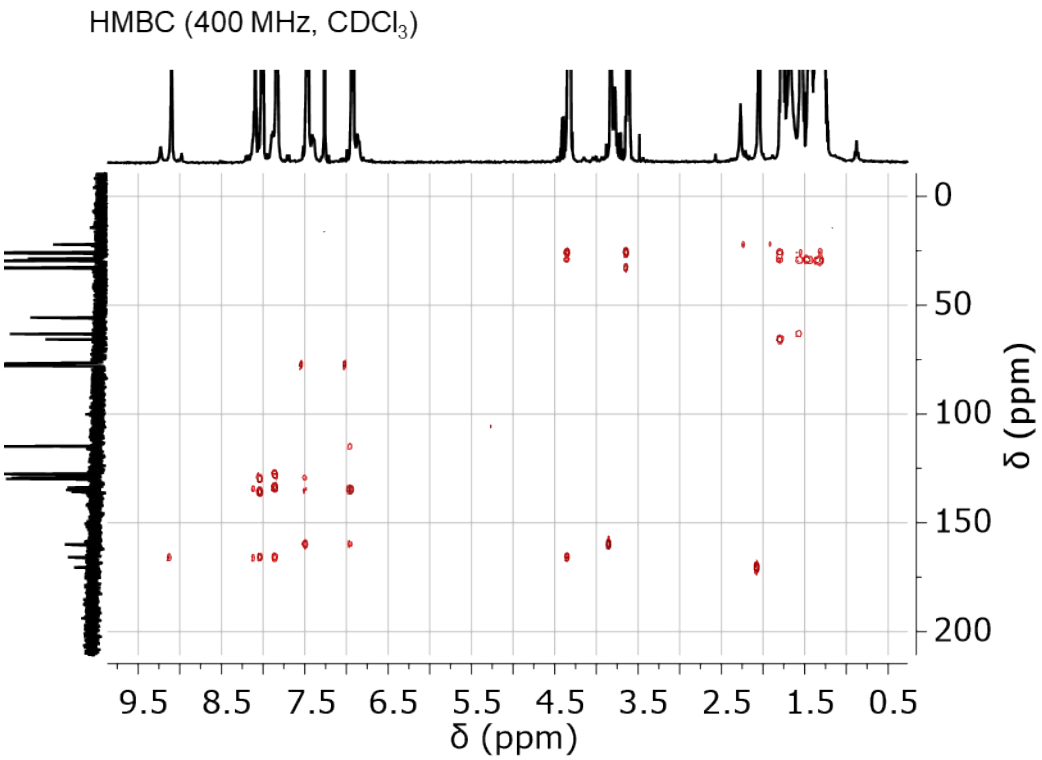


Figure S13. ^{1}H NMR, ^{13}C NMR and 2D spectra of 11-hydroxyundecyl 4-(2-(4-methoxyphenyl)-2H-tetrazol-5-yl)benzoate (**Tet 1**)/acetic acid adduct derived from 1,4 acyl shift formed after 4 h irradiation.

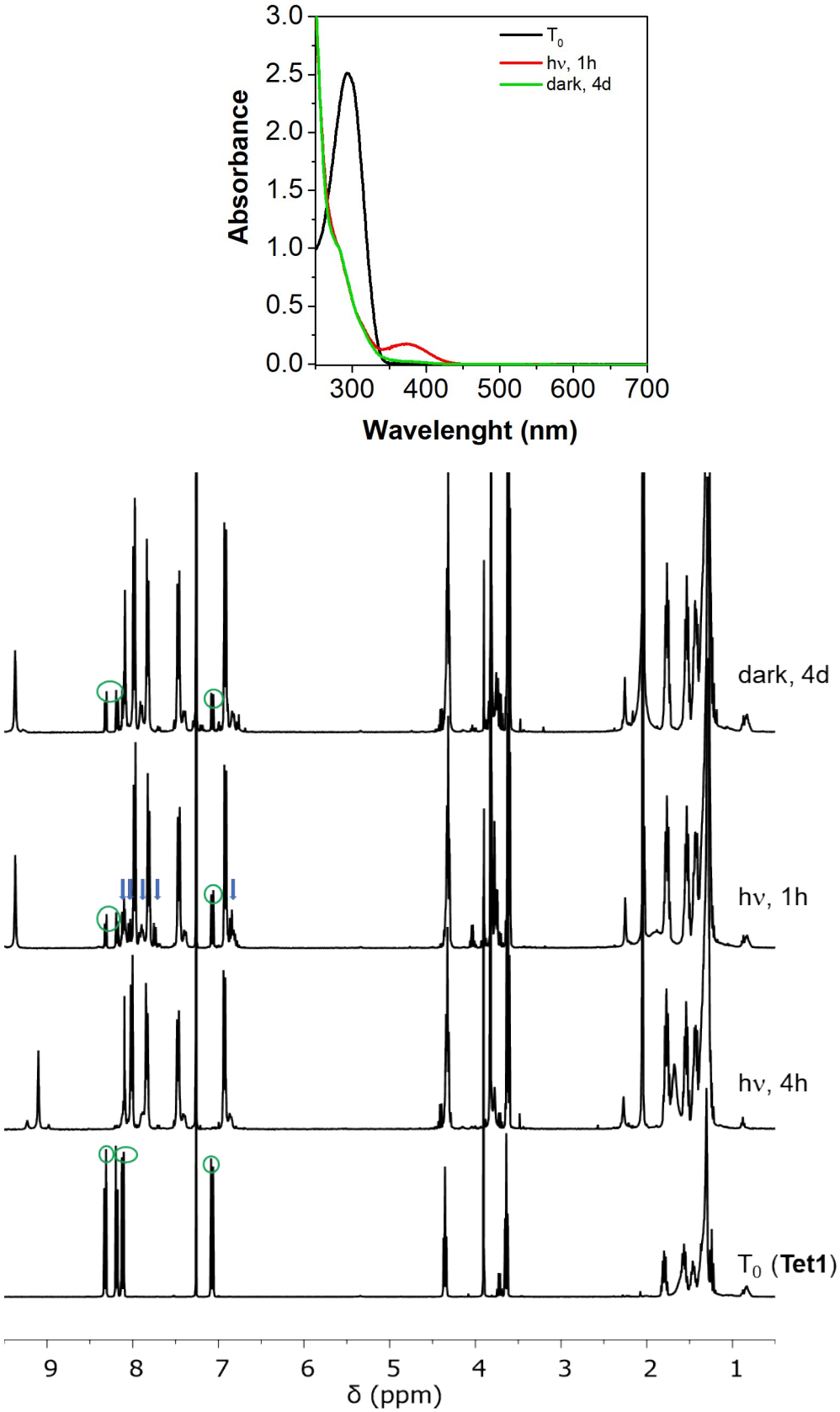


Figure S14. UV-vis absorbance spectrum (above) and ^{1}H NMR spectrum (below) of the 11-hydroxyundecyl 4-(2-(4-methoxyphenyl)-2H-tetrazol-5-yl)benzoate (**Tet 1**)/acetic acid reaction mixture obtained after 1h irradiation and after the following 4 d equilibration in the dark.

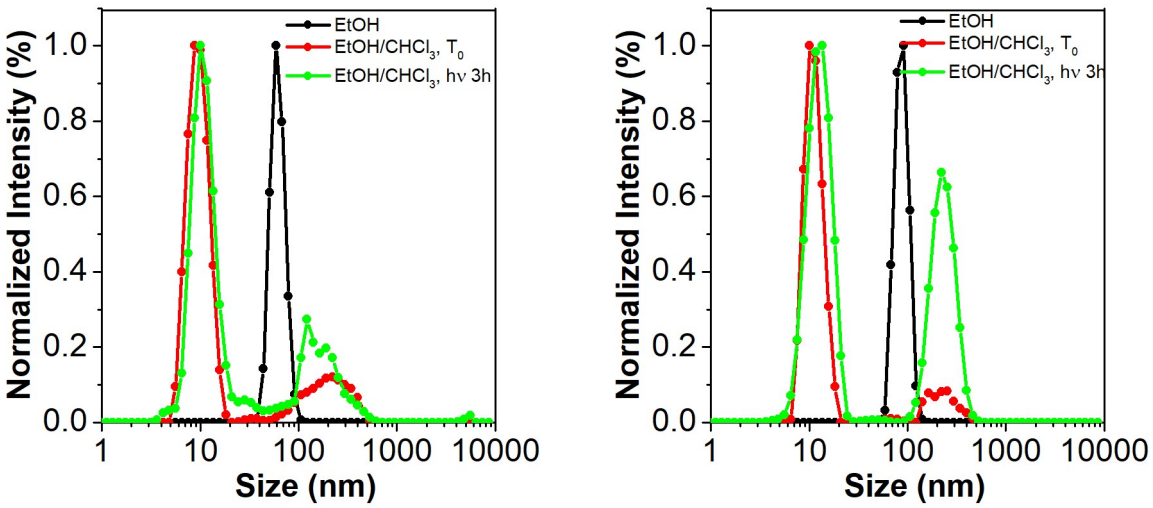


Figure S15. Intensity-weighted size (D_h) distributions obtained by DLS (c= 0.6 mg mL^{-1} in ethanol/chloroform 1:1 v/v) of self-assembled POEGMA-*b*-PMMAES-*b*-BzMA triblock copolymer nanospheres before and after 3h irradiation time (PISA R1 left and PISA R2 right).

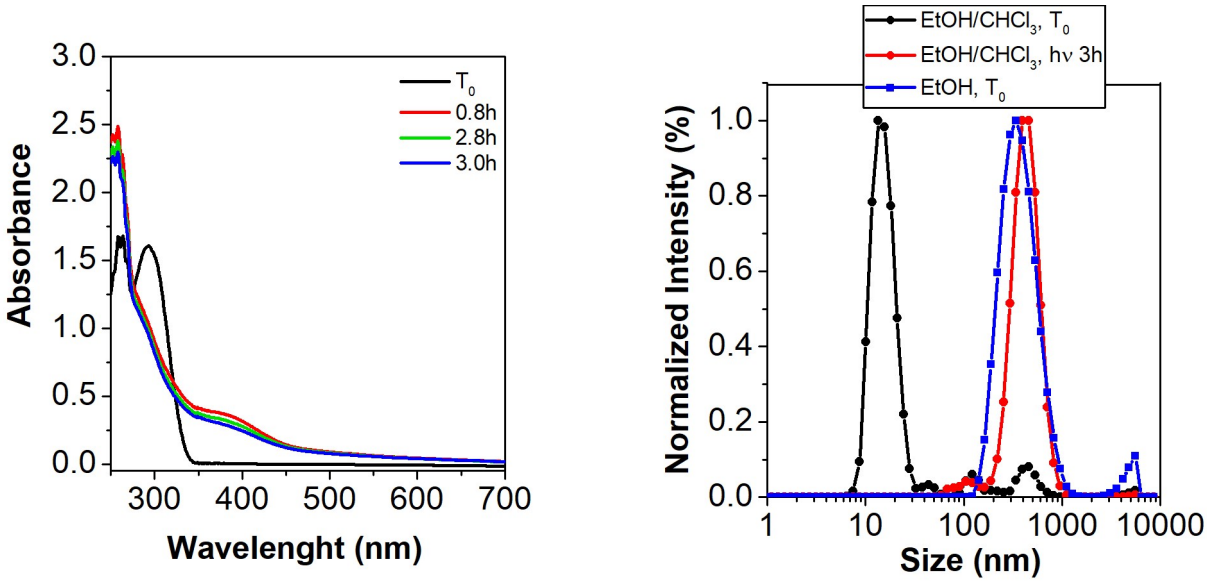


Figure S16. UV−vis absorbance spectra (c= 0.6 mg mL^{-1} in chloroform) of reaction mixture at different irradiation time (left) and intensity-weighted size (D_h) distributions obtained by DLS (c= 0.6 mg mL^{-1}) of worm-like nanoparticles (PISA-T8) in ethanol/chloroform 1:1 v/v before and after 3h irradiation and in ethanol before irradiation (right).

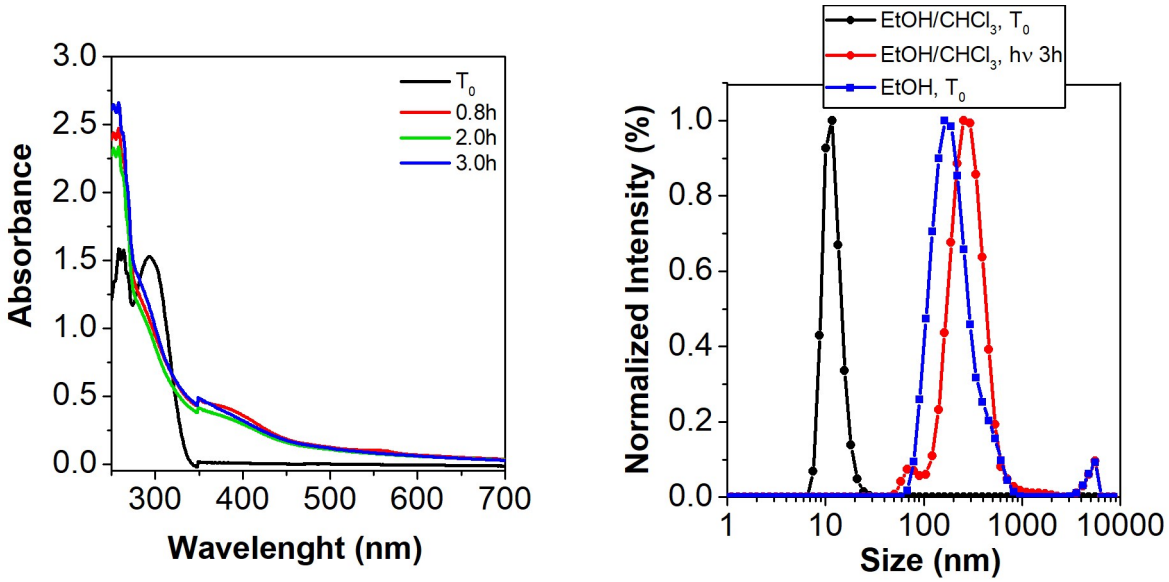


Figure S17 UV−vis absorbance spectra (c= 0.6 mg mL^{-1} in chloroform) of reaction mixture at different irradiation time (left) and intensity-weighted size (D_h) distributions obtained by DLS (c= 0.6 mg mL^{-1}) of vesicles nanoparticles (PISA-T7) in ethanol/chloroform 1:1 v/v before and after 3h irradiation and in ethanol before irradiation (right).

7. Tables

Table S1. Summary of thermally initiated RAFT dispersion polymerization of BzMA using POEGMA-*b*-P(MMAES-*co*-TetMA) at 65°C.

Entry	*DP* [a] (PBzMA)	Solid Content (*wt%*)	*Time* (h)	*Conv.* (%)	$M_{n,SEC}$ (g mol^{-1})	*Đ*	D_h (nm) (*PDI*) [d]	Morphology [e]
PISA-T1	148	15 [b]	24	90	21230	1.72	100.1 (0.071)	S
PISA-T2	373	15 [b]	24	80	39620	1.88	127.5 (0.095)	S
PISA-T3	515	15 [b]	24	86	47015	1.82	196.1 (0.065)	S
PISA-T4	171	21 [b]	24	98	26250	1.67	153.0 (0.205)	S+short W
PISA-T5	163	26 [b]	24	98	27480	1.63	255.8 (0.371)	S+short W
PISA-T6	436	29 [b]	24	98	50030	1.85	187.2 (0.083)	S+V
PISA-T7	418	30 [b]	44	99	53720	1.88	276.2 (0.056)	V+S
PISA-T8	421	30 [c]	44	98	44420	1.92	361.7 (0.225)	W+S

[a] *DP*= [target DP (PBzMA)]*[conv. (^{1}H-NMR)] [b] Ethanol/dioxane 8:2 v/v. [c] Ethanol/dioxane 7:3 v/v. [d] Hydrodynamic diameter D_h and polydispersity index (*PDI*) determined by DLS. [e] Morphology of nano-objects evaluated from SEM and TEM analysis.

Table S2. Summary of thermally initiated RAFT dispersion polymerization of BzMA using POEGMA-*b*-PMMAES at 65°C (Reference System).

Entry	*DP* [a] (PBzMA)	Solid Content (*wt%*)	*Time* (h)	*Conv.* (%)	$M_{n,SEC}$ (g mol^{-1})	*Đ*	D_h (nm) (*PDI*) [d]	Morphology [e]
PISA-R1	130	15 [b]	24	82	23880	1.82	67.66 (0.013)	S
PISA-R2	230	15 [b]	24	78	33977	1.76	85.66 (0.019)	S
PISA-R3	336	15 [b]	24	75	46790	1.70	103.0 (0.025)	S
PISA-R4	457	15 [b]	24	75	59550	1.67	147.0 (0.129)	S
PISA-R5	172	30 [b]	24	99	32220	1.70	276.2 (0.283)	S+ short W
PISA-R6	400	30 [b]	24	90	54050	1.67	243.0 (0.062)	S+V
PISA-R7	434	30 [b]	44	99	61710	1.63	226.8 (0.075)	S+V
PISA-R8	418	30 [c]	44	96	55800	1.64	226.8 (0.075)	W+V

[a] *DP*= [target DP (PBzMA)]*[conv. (^{1}H-NMR)] [b] Ethanol/dioxane 8:2 v/v. [c] Ethanol/dioxane 7:3 v/v. [d] Hydrodynamic diameter D_h and polydispersity index (*PDI*) determined by DLS. [e] Morphology of nano-objects evaluated from SEM and TEM analysis.

8. References

1. N. Busatto, V. Stolojan, M. Shaw, J. L. Keddie and P. J. Roth, *Macromol. Rapid Commun*. 2019, **40** (2), 1800346.
2. C. Moreno-Yruela and C. A. Olsen, *Synth.* 2018, **50** (20), 4037-4046.
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4. W.; Konrad, C.; Fengler, S.; Putwa and C. Barner-Kowollik, *Angew. Chemie - Int. Ed.*, 2019, **58**, 7133-7137.