

Supporting Information for

**Divergent Photoiniferter Polymerization-Induced Self-Assembly**

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Small Molecule Synthesis and Characterization

Polymer Synthesis and Characterization

Photoreactor Setup and Characterization

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## **Materials and Instrumentation**

### **Materials**

All chemicals were used as received unless otherwise noted. 2-(((Ethylthio)carbonothioyl)thio)propanoic acid (ETPA) and 4-cyano-4-(((dodecylthio)carbonothioyl)thio)pentanoic acid (CDP) were synthesized following a previous report.<sup>1,2</sup> Benzyl methacrylate (BnMA, Sigma-Aldrich, 96%), oligo(ethylene glycol) methyl ether methacrylate (OEGMA, 500 g/mol, Sigma-Aldrich, 98%), *N,N*-dimethylacrylamide (DMA, TCI, 99%), and ethylene glycol dimethacrylate (EGDMA, Sigma-Aldrich, 98%) were passed through a column of neutral alumina to remove inhibitor prior to polymerization. 4-Dimethylaminopyridine (DMAP, >99%) was obtained from TCI, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC, 99%) was obtained from Ambeed, and 1,4-butanediol (ReagentPlus, 99%) was obtained from Sigma-Aldrich. Dimethyl sulfoxide (DMSO, ACS Grade), acetone (ACS Grade), ethyl acetate (EtOAc, ACS Grade), methanol (MeOH, anhydrous), hexanes (ACS Grade), tetrahydrofuran (THF, ACS Grade), and toluene (ACS Grade) were purchased from Fischer Scientific.

### **Instrumentation**

**Size Exclusion Chromatography (SEC).** Experiments were performed in *N,N*-dimethylacetamide (DMAc) with 50 mM LiCl at 50 °C at a flow rate of 1.0 mL/min (Agilent Infinity II isocratic pump, degasser, and autosampler). A ViscoGel I-series 5 µm guard column, Malvern I-MBLMW, and IMBHMW 3078 columns with an exclusion limit of 20,000 g/mol and  $1.0 \times 10^7$  g/mol, respectively, were used. A refractive index detector (Wyatt Optilab T-rEX) operating at 658 nm and a light scattering detector (Wyatt miniDAWN Treos) operating at 659 nm were used. Molecular weights and dispersities were calculated with Wyatt ASTRA software using multi-angler laser light scattering data. Polymer samples were dehydrated via lyophilization and dissolved in SEC solvent at a concentration of < 3 mg/mL.

**Dynamic Light Scattering (DLS).** DLS was performed with a non-invasive backscatter system (Malvern Zetasizer Nano ZS) with a measuring angle at 173° and adjustable focus. DLS was performed at 25 °C and 0.1% w/w of nanoparticles in a given solvent. The size distributions reported were averaged over five runs.

**NMR Spectroscopy.** Spectra were collected using a Magritek Spinsolve 60 ultra (60 MHz) or a Bruker 400 MHz spectrometer. Chemical shifts ( $\delta$ ) are reported in ppm, using residual solvent peak as a reference.

**Mass Spectrometry (MS).** Ionization Source: Electrospray ionization (ESI) (analyzed in positive mode), mid-mass optimized ( $m/z = 250 - 2000$ ). Mass Spectrometry: Bruker Daltonics, Impact II QTOF, drying gas (N<sub>2</sub>) – 4 L/min, gas temperature – 200 °C, capillary – 4500 V, nebulizer – 0.3 bar. Injection System: Thermo UltiMate 3000 series system, injection volume – 1 µL. Mobile Phase(s): 98% B (flow inject) (A) Water with 10mM ammonium formate and 0.1% formic acid (B)

acetonitrile with 0.1% formic acid. Flow Rate: Loading pump- 25  $\mu$ L/min. Sample Preparation: Sample (trace) was dissolved in 5-10  $\mu$ L chloroform and diluted in 1 mL methanol in a 1.5 mL glass autosample vial. Dilute sample was then analyzed by flow injection on the QTOF-MS. A plug of sodium formate was injected prior to the sample to allow re-calibration prior to analysis. Funding: NIH S10 OD021758-01A1 AND S10 OD030250-01A1

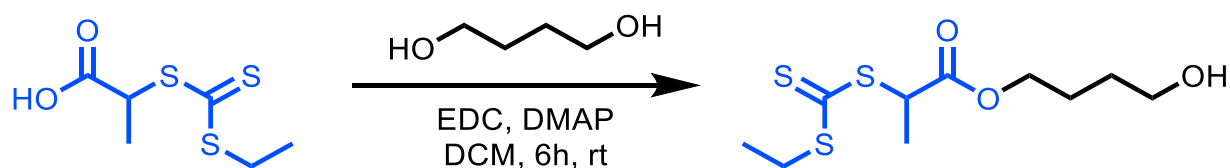
**Transmission electron microscopy (TEM).** TEM of crosslinked nanoparticles was conducted on a Thermo Scientific Talos L120C G2 (S)TEM operating at an accelerating voltage of 120 kV. Digital images were acquired with a 4K  $\times$  4K Thermo Scientific Ceta CMOS camera and Digital Micrograph 1.93 image acquisition software (Gatan Inc., Pleasanton, CA, USA.). Samples were prepared on Electron Microscopy Sciences Formvar Carbon Film on 400 mesh nickel grids (FCF400- Ni). 6  $\mu$ L of purified nanoparticle solution (1.0 mg/mL in DMSO) was spotted on the grid for 1 min. Afterwards, solvent was wicked off with filter paper. The grids were then stained with 1% w/w uranyl acetate solution for 30 s, and excess solution was again wicked off with filter paper.

**UV-Vis Spectroscopy.** All measurements were performed on a Molecular Devices SpectraMax 2 M2 Multimode Microplate Reader at 25  $^{\circ}$ C. Absorbance measurements were conducted with 150  $\mu$ L of sample on clear 96-well polystyrene microplates. Absorbances of iniferters were measured in DMSO at a concentration of approximately 1 mg/mL.

**Light reactor construction and characterization.** CHANZON High Power Led Chip 100W Green (3000mA / DC 30V - 34V / 100 Watt) and a CHANZON High Power Led Chip 10W Blue (900mA / DC 9V - 11V / 10 Watt) were purchased from Amazon. Green LED chips were attached to CPU coolers with thermal paste adhesive. The blue LED was adhered to a small aluminum heat sink. Emission intensities and spectra were measured using an International Light ILT350 Chroma Meter.

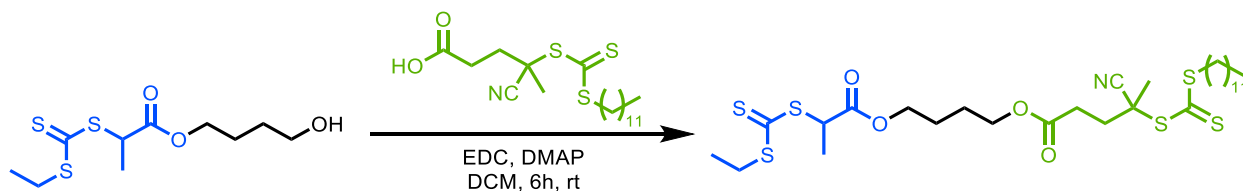
## Small Molecule Synthesis and Characterization:

### Synthesis of 4-hydroxybutyl 2-(ethyl sulfanylthiocarbonyl sulfanyl)-propanoate:

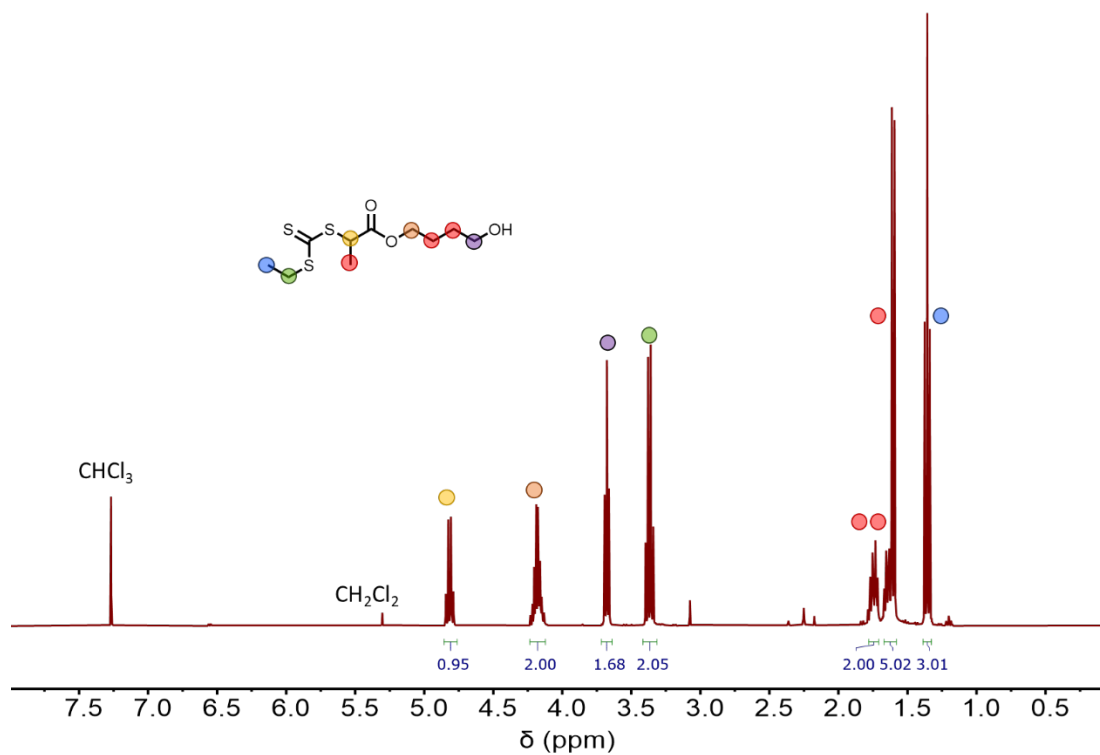


2-(Ethyl sulfanylthiocarbonyl sulfanyl)-propanoic acid (2.00 g, 9.51 mmol), DMAP (117 mg, 0.958 mmol), and 1,4 butanediol (8.4 mL, 95 mmol) were combined in a flame-dried round-bottom flask with a magnetic stir bar. EDC (1.63 g, 10.5 mmol) was dissolved in dry DCM (50 mL) and added slowly to the RBF while purging with argon. The reaction was left to stir at room temperature for 6 h. The crude mixture was diluted with water, and the organic layer was washed several times with water. The organic layer was further washed with saturated sodium bicarbonate before being dried with brine and then further dried over magnesium sulfate. A viscous orange oil was recovered after evaporation of the organic layer at reduced pressure (2.3 g, 86% yield) and used as is. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.81 (q, 1H), 4.18 (m, 2H), 3.68 (t, 2H), 3.37 (q, 2H), 1.69 (m, 4H), 1.60 (d, 3H), 1.36 (t, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 221.94, 171.22, 65.67, 65.19, 62.31, 47.91, 31.53, 29.05, 25.12, 24.98, 16.84, 12.98.

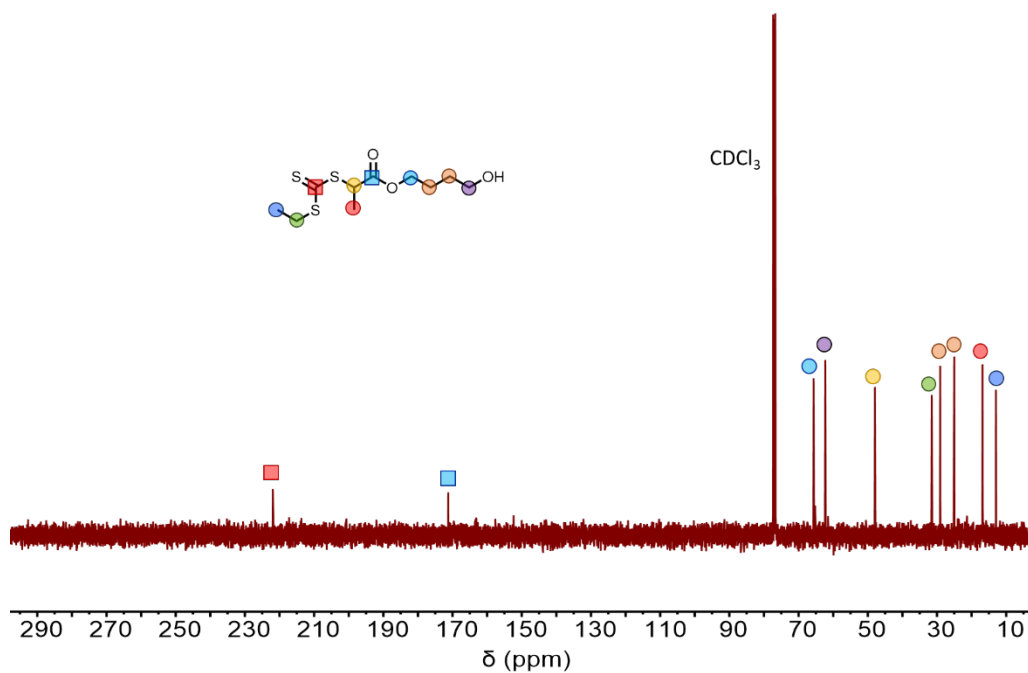
### Synthesis of 4-((2-(ethyl sulfanylthiocarbonyl sulfanyl)propanoyl)oxy)butyl 4-cyano-4-[(dodecylsulfanylthiocarbonyl)sulfanyl] pentanoate difunctional iniferter (ETPA-CDP):



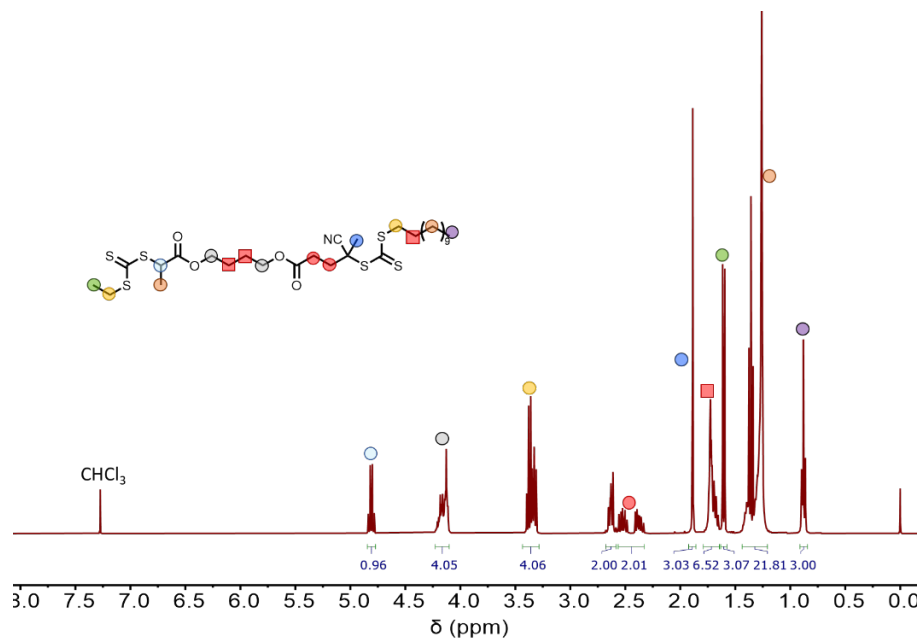
4-Hydroxybutyl 2-(ethyl sulfanylthiocarbonyl sulfanyl)-propanoate (2.3 g, 8.1 mmol, 1.0 equiv), DMAP (100 mg, 0.819 mmol, 0.1 equiv), CDP (3.2 g, 8.1 mmol, 1.0 equiv), and a stir bar were added to a round-bottom flask. EDC (1.4 g, 9.0 mmol, 1.1 equiv) was dissolved in 50 mL of dry DCM and slowly added to the RBF while purging with argon. The reaction was left to stir overnight. The crude reaction mixture was repeatedly washed with saturated sodium bicarbonate before being dried with MgSO<sub>4</sub> and concentrated under reduced pressure. Oil was further purified via auto-column chromatography using a gradient mobile phase, starting with hexanes and slowly transitioning to ethyl acetate. A viscous orange oil was recovered (3.207 g, 61% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.81 (q, 1H), 4.15 (m, 4H), 3.36 (m, 4.02H), 2.63 (m, 2H), 2.45 (m, 2H), 1.89 (s, 3H), 1.72 (m, 6H), 1.61 (d, 3H), 1.31 (m, 21H), 0.88 (t, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 221.87, 216.93, 171.45, 171.13, 119.01, 65.17, 64.48, 47.86, 46.36, 37.07, 33.87, 31.93, 31.55, 29.77, 29.64, 29.56, 29.44, 29.36, 29.09, 28.95, 27.69, 25.18, 25.14, 24.90, 22.71, 16.81, 14.16, 13.00.



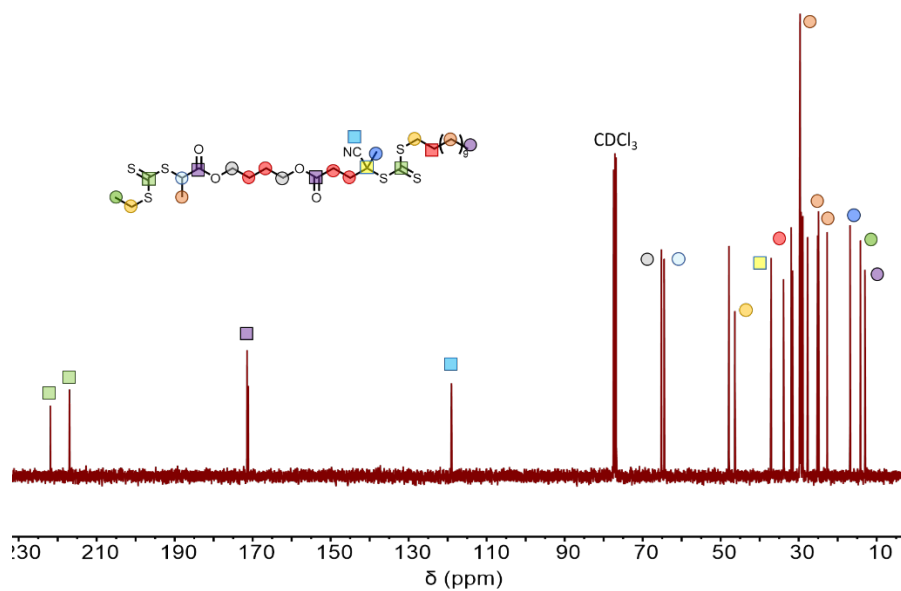
**Figure S1.** <sup>1</sup>H NMR spectrum of 4-hydroxybutyl 2-(ethyl sulfanylthiocarbonyl sulfanyl)propanoate (ETPA).



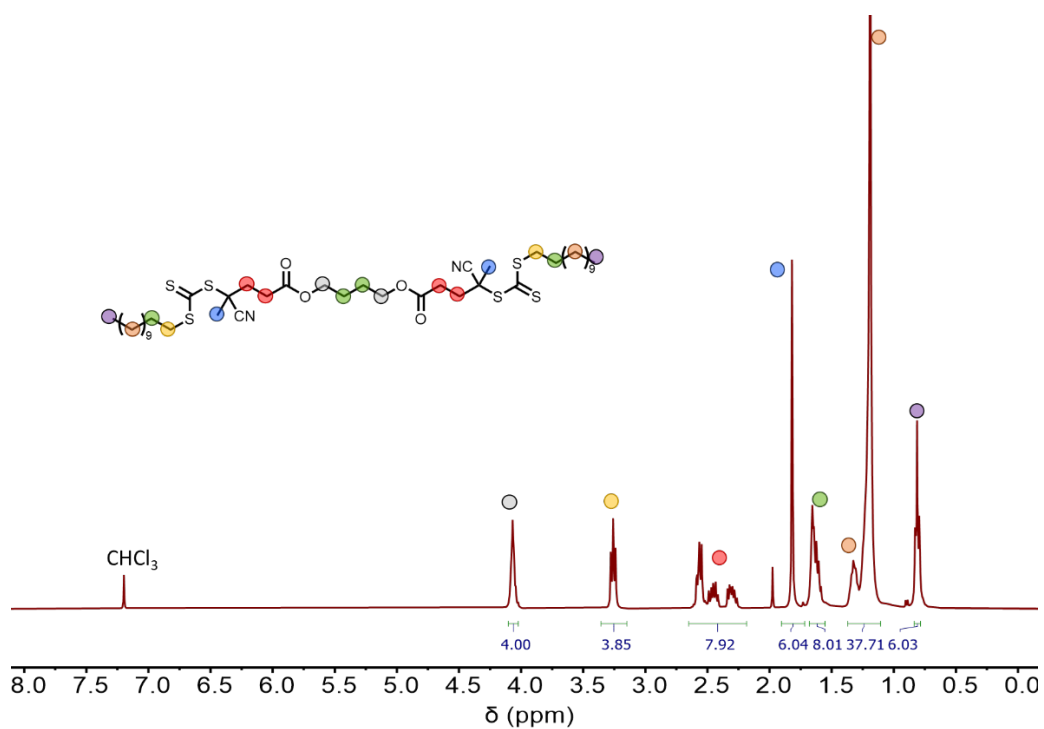
**Figure S2.** <sup>13</sup>C NMR spectrum of 4-hydroxybutyl 2-(ethyl sulfanylthiocarbonyl sulfanyl)propanoate (ETPA).



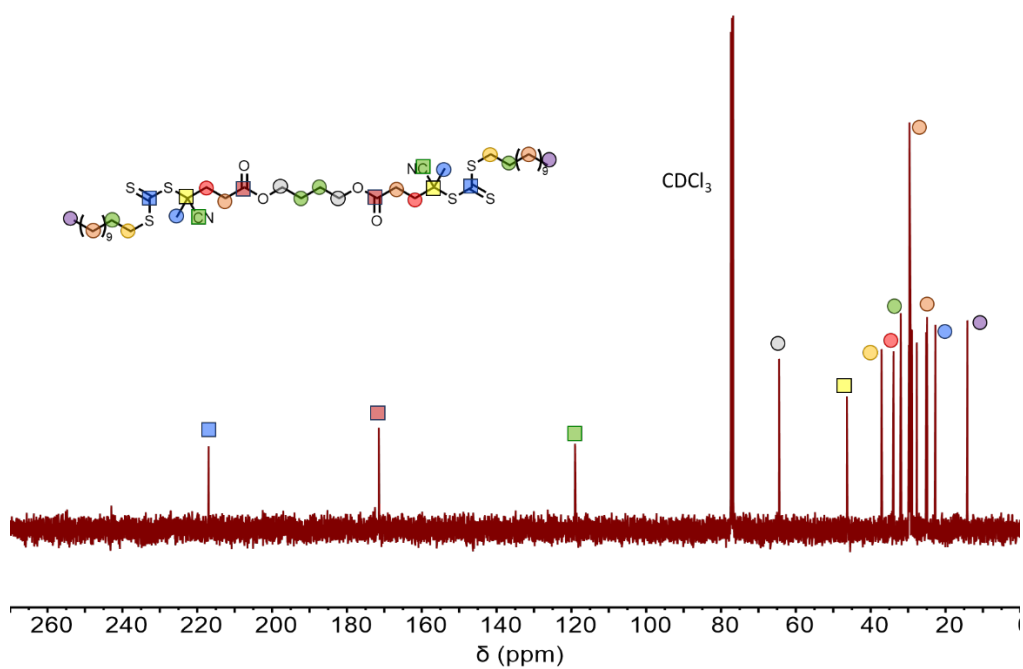
**Figure S3.**  $^1\text{H}$  NMR spectrum of 4-((2-(ethyl sulfanylthiocarbonyl sulfanyl)propanoyl)oxy)butyl 4-cyano-4-[(dodecylsulfanylthiocarbonyl)sulfanyl]pentanoate (ETPA-CDP).



**Figure S4.**  $^{13}\text{C}$  NMR spectrum of 4-((2-(ethyl sulfanylthiocarbonyl sulfanyl)propanoyl)oxy)butyl 4-cyano-4-[(dodecylsulfanylthiocarbonyl)sulfanyl]pentanoate (ETPA-CDP).

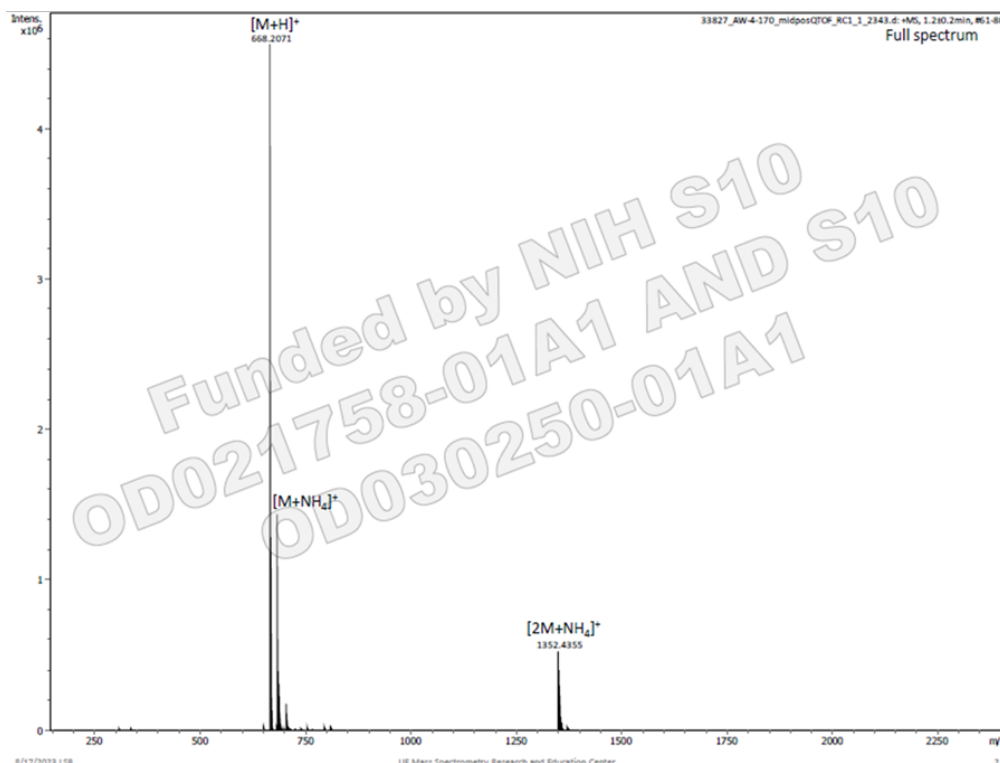


**Figure S5.** <sup>1</sup>H NMR spectrum of butane-1,4-diyl bis(4-cyano-4-((dodecylthio)carbonothioyl)thio)pentanoate) (diCDP).

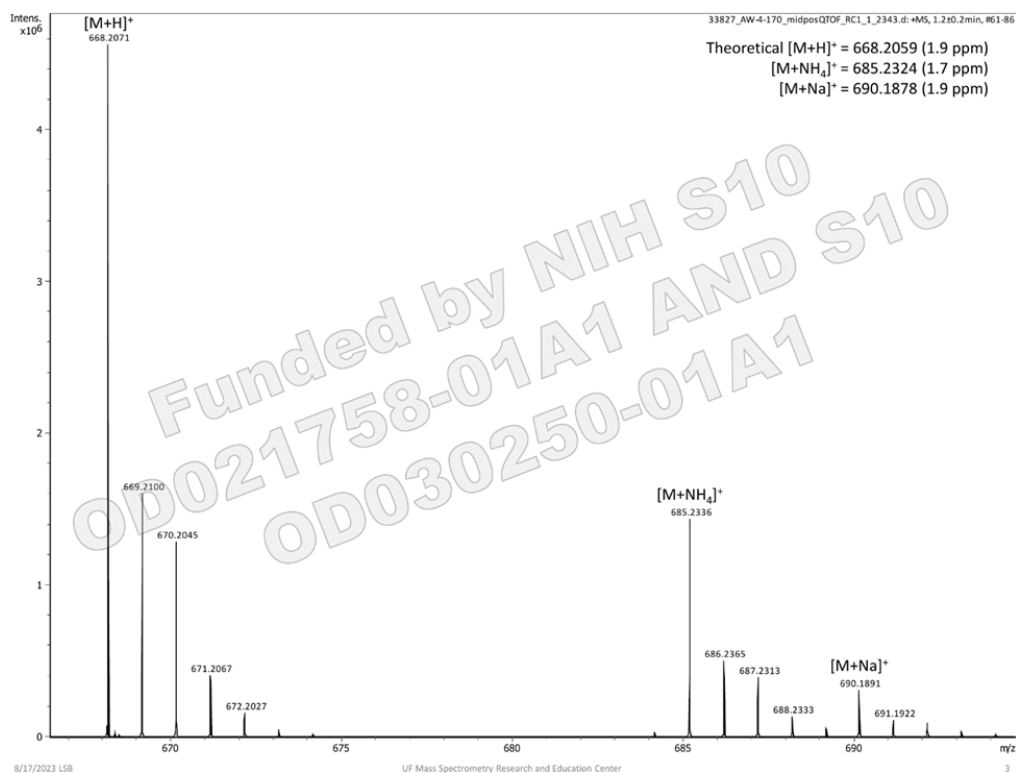


**Figure S6.** <sup>13</sup>C NMR spectrum of butane-1,4-diyl bis(4-cyano-4-((dodecylthio)carbonothioyl)thio)pentanoate) (diCDP).

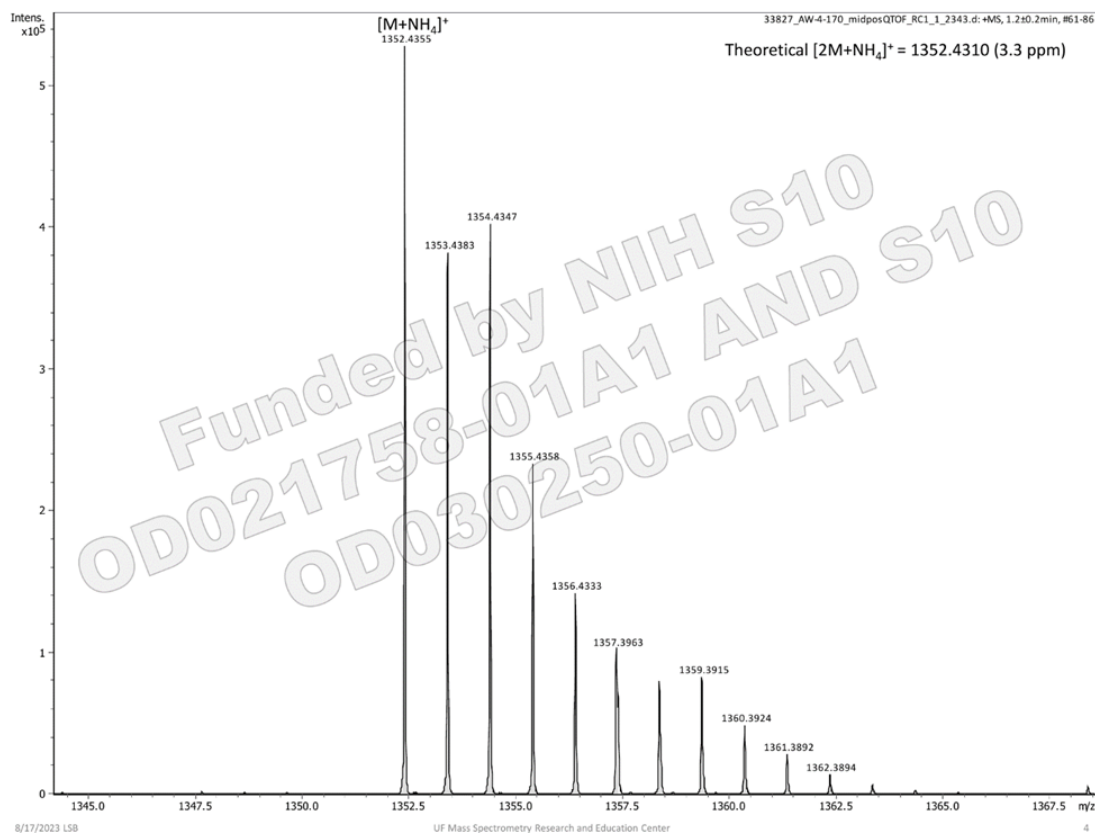




**Figure S7.** Mass spectrum of ETPA-CDP. Masses related to the sample were observed:  $[M+H]^+$ ,  $[M+NH_4]^+$ ,  $[M+Na]^+$ , and  $[2M+NH_4]^+$  and the observed isotope pattern matches theoretical.



**Figure S8.** Mass spectrum of ETPA-CDP, zoomed in to observe isotopes.



**Figure S9.** Mass spectrum of ETPA-CDP, zoomed in to the 2M isotope region.

## **Polymer Synthesis and Characterization**

### **Synthesis of ETPA-POEGMA macroiniferter:**

OEGMA (500 g/mol, 1.1 g, 1.11 mmol, 45 equiv) and ETPA-CDP (251 mg, 0.375 mmol, 1 equiv) were combined in a scintillation vial with 1,4-dioxane (9 mL) and a stir bar. *N,N*-Dimethylformamide (0.1 mL, DMF) was added as an internal standard for <sup>1</sup>H NMR analysis. The vial was sealed with a septum and sparged for 20 min with argon. The vial was placed on a gauge block that held the vial 1.5 cm from the green LED reactors (529 nm, 100 mW/cm<sup>2</sup>) for 3 h on a stir plate. The targeted degree of polymerization was 32, with overall monomer conversion of approximately 70% ( $M_{n,Theo} = 20.9$  kg/mol,  $M_{n,SEC} = 20.3$  kg/mol,  $\mathcal{D} = 1.14$ ). The polymer was purified by precipitation into a cold mixture of 50/50 hexanes/diethyl ether three times, then dried in vacuo overnight.

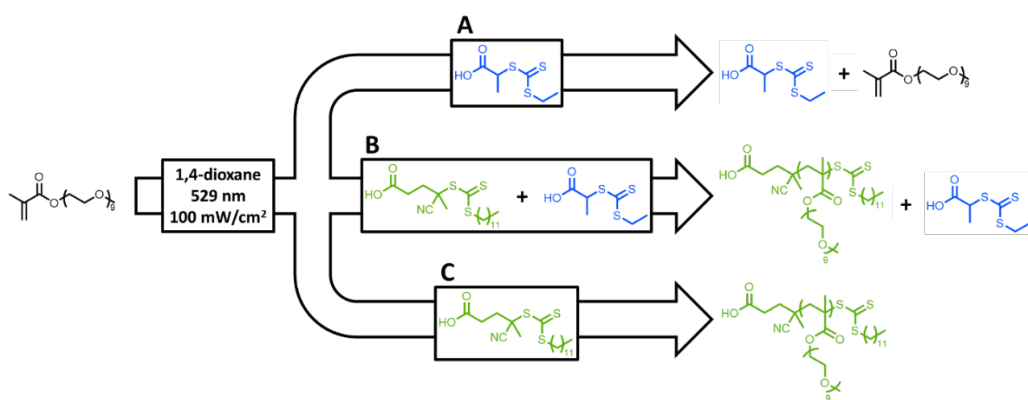
### **Synthesis of ETPA-POEGMA-*b*-PBnMA:**

ETPA-POEGMA macroiniferter ( $M_{n,SEC} = 20.3$  kg/mol, 177 mg, 0.00977 mmol, 1 equiv) was combined with BnMA (344 mg, 0.331 mL, 1.95 mmol, 200 equiv) in a scintillation vial with a stir bar, targeting a number average BnMA degree of polymerization of 200. Monomer and

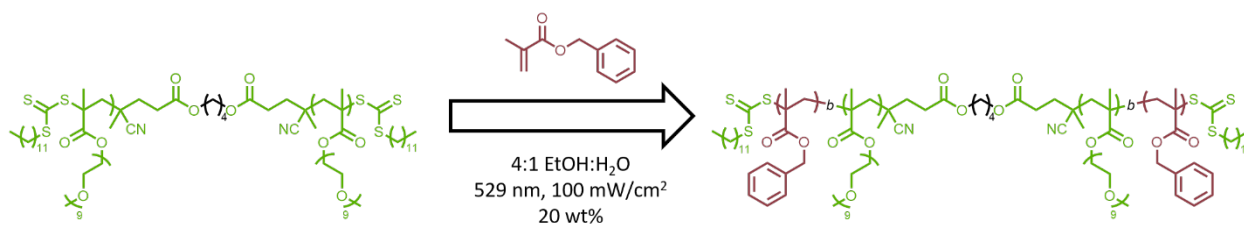
macroiniferter were dissolved in 4:1 w/w EtOH/H<sub>2</sub>O (2.12 mL EtOH, 0.417 mL H<sub>2</sub>O) at 20% w/w solids. DMF (0.1 mL) was added as an internal standard for <sup>1</sup>H NMR analysis. The solution was stirred to dissolve the macroiniferter at 400 RPM before being sparged for 20 min with argon in an ice bath. Post-sparging, the solution was warmed to room temperature and stirred at 400 RPM between the green LED reactors (529 nm, 100 mW/cm<sup>2</sup>) and irradiated for 2 h, reaching approximately 87% monomer conversion ( $M_{n,Theo} = 51.0$  kg/mol,  $M_{n,SEC} = 69.0$  kg/mol,  $\mathcal{D} = 1.44$ ). When synthesizing crosslinked particles, 1 mol% relative to BnMA of EGDMA was added before sparging. Crosslinked nanoparticles were precipitated into cold diethyl ether before being dried in vacuo.

### PDMA-*b*-POEGMA-*b*-PBnMA Synthesis (Coronal Chain Extension with DMA):

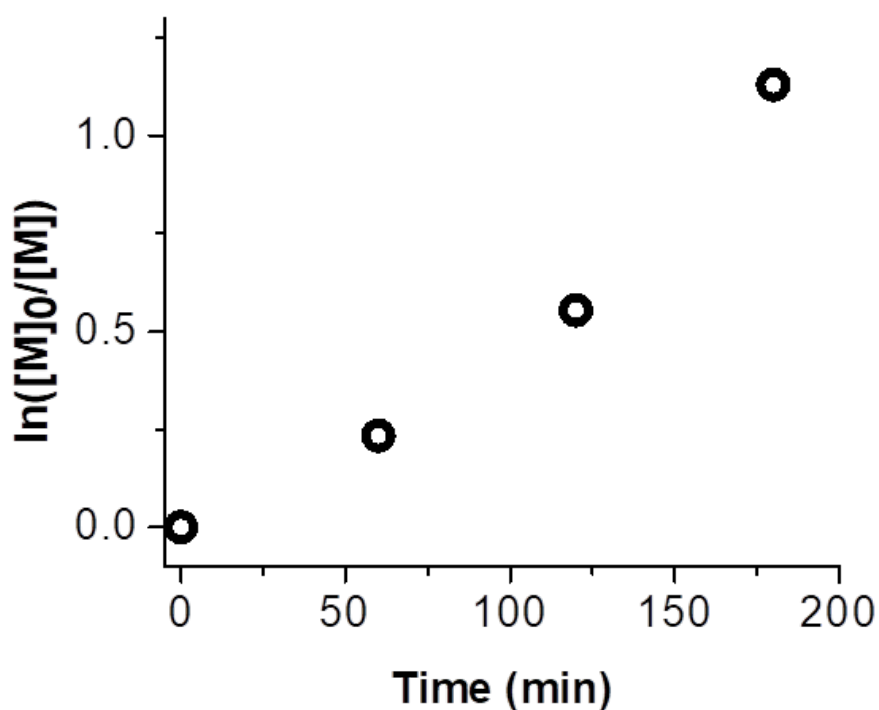
Uncrosslinked ETPA-POEGMA-*b*-PBnMA ( $M_{n,SEC} = 60.0$  kg/mol, 34.2 mg, 0.567  $\mu$ mol, 1 equiv) nanoiniferter particles were used from their native solution (0.2 mL); crosslinked particles were redispersed into DMSO at 20 wt% before being diluted with water. This crosslinked nanoiniferter solution (200  $\mu$ L, 20 wt% nanoiniferter) was diluted with water (0.5 mL). Nanoiniferter dispersions were sparged for 20 min at room temperature before DMA (0.1 mL, 0.970 mmol, 1200 equiv, 2 M in H<sub>2</sub>O, total volume of DMA/H<sub>2</sub>O solution added = 0.5 mL) was added. DMF (0.05 mL) was added as an internal standard for <sup>1</sup>H NMR analysis. Dispersions were sparged again at room temperature before being irradiated by blue light (452 nm, 8.5 mW/cm<sup>2</sup>) for 12 h, resulting in approximately 25% monomer conversion ( $M_{n,Theo} = 89.7$  kg/mol,  $M_{n,SEC} = 145.8$  kg/mol). Core-crosslinked PDMA-*b*-POEGMA-*b*-PBnMA nanoparticles were dialyzed against water to remove excess DMA and stored in an aqueous solution for subsequent TEM characterization. Uncrosslinked nanoparticles were analyzed immediately by DLS and SEC.



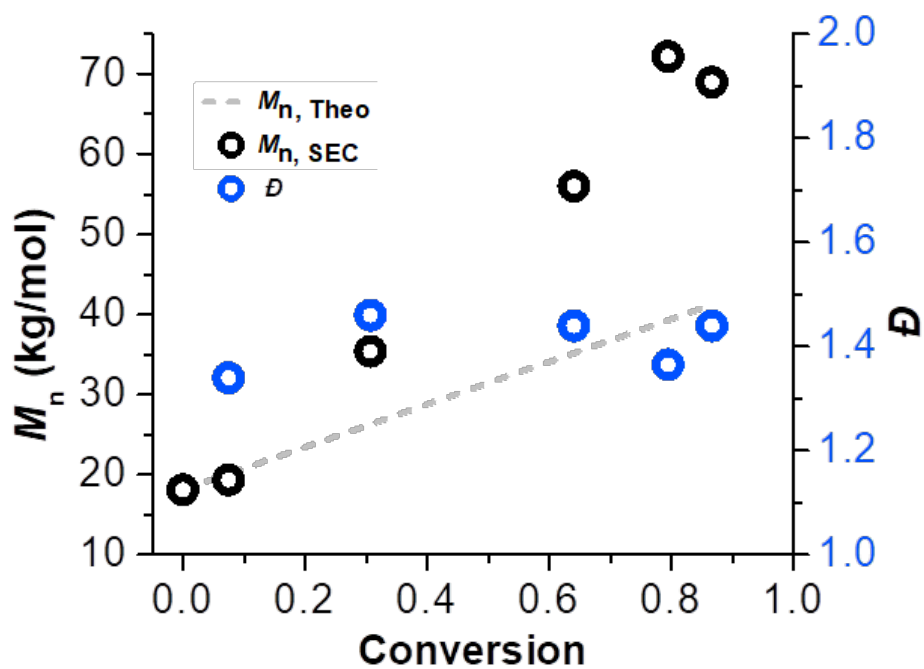
**Scheme S1.** Control experiments exposing 45 equiv oligoethylene glycol methacrylate (OEGMA) under green light (529 nm, 100 mW/cm<sup>2</sup>) in 1,4-dioxane to (A) 1 equiv ETPA (resulting in no observable polymerization), (B) 1 equiv CDP and 1 equiv ETPA (resulting in only OEGMA polymerization via CDP photoexcitation), and (C) 1 equiv CDP (resulting in poly(OEGMA) (POEGMA) synthesis).



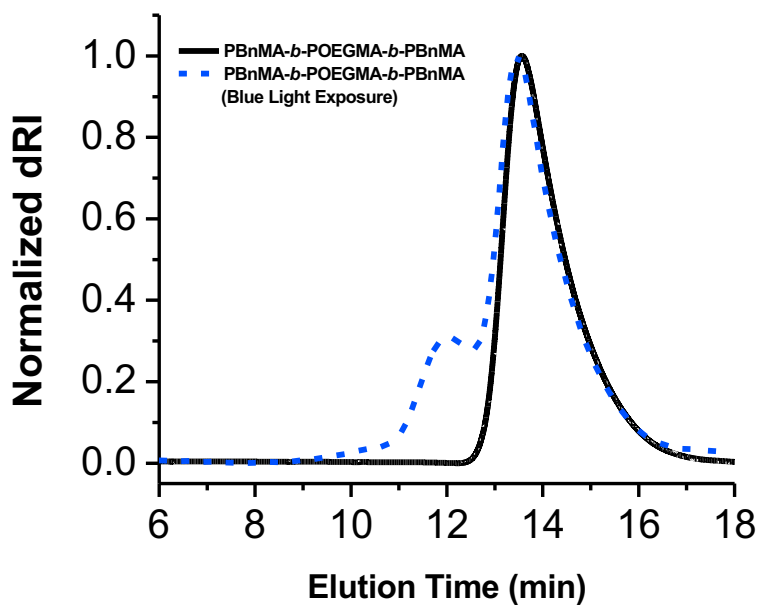
**Scheme S2.** Polymerization-induced self-assembly (PISA) chain extending diCDP-POEGMA with benzyl methacrylate (BnMA) in 4:1 EtOH:H<sub>2</sub>O under green light (529 nm, 100 mW/cm<sup>2</sup>) at 20% w/w solids content.



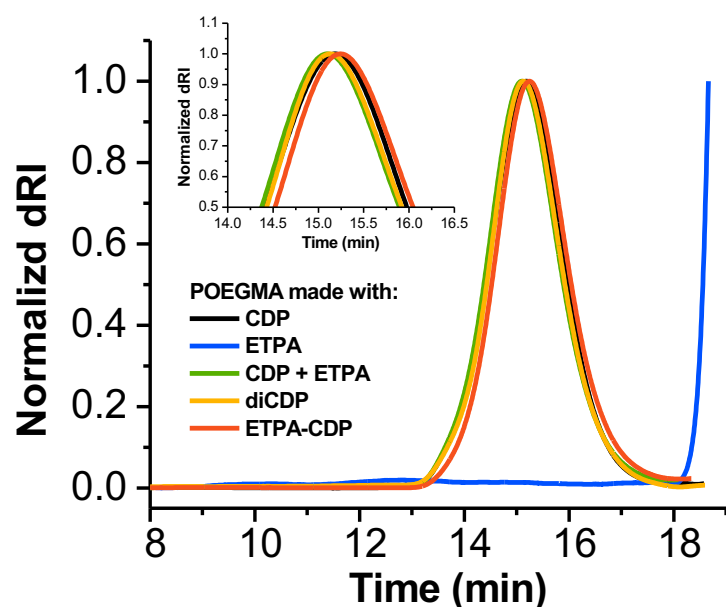
**Figure S10.** Pseudo-first-order kinetics of the polymerization of OEGMA with ETPA-CDP.



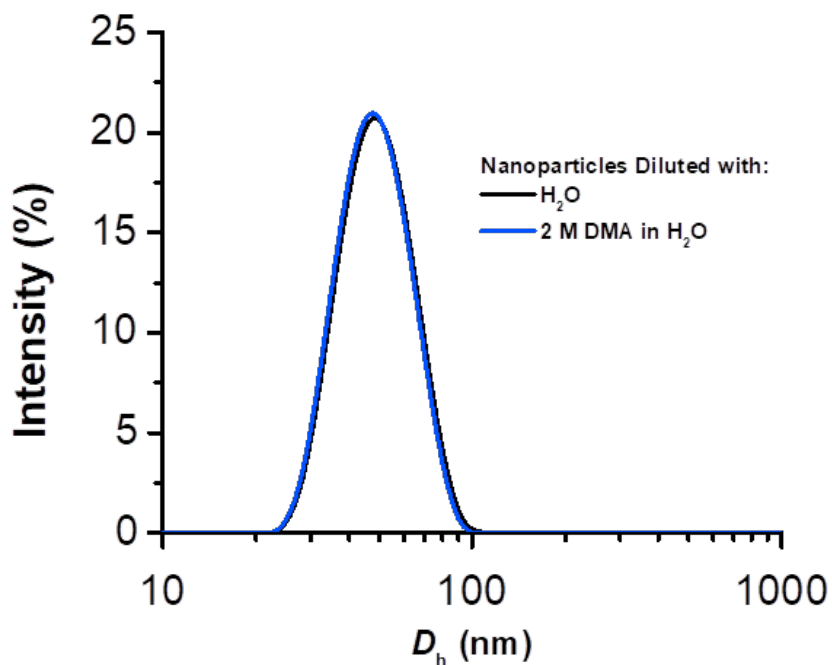
**Figure S11.** Molecular weight as a function of conversion for the green-light photoiniferter polymerization of BnMA by the POEGMA macroiniferter.



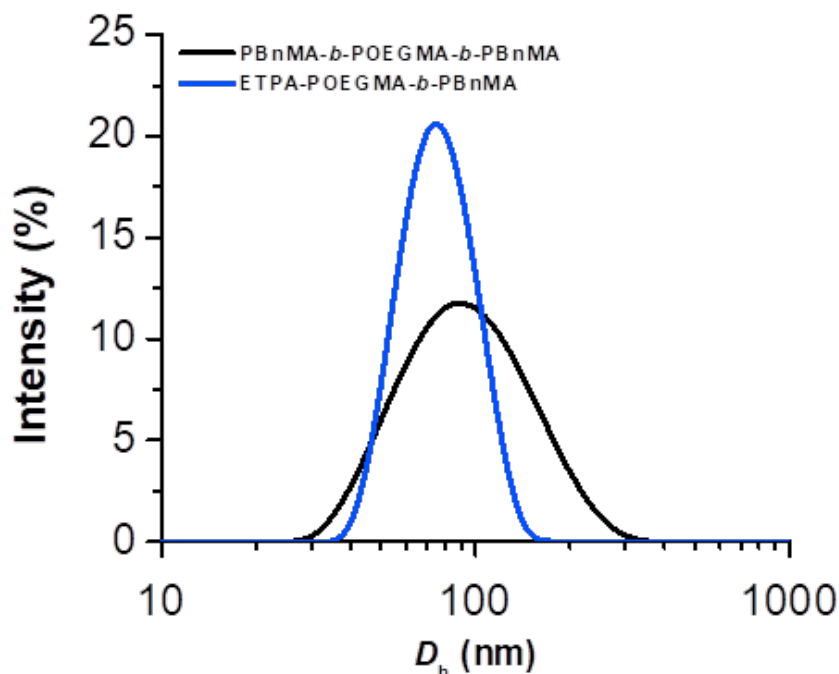
**Figure S12.** Size-exclusion chromatograms of the diCDP chain extension with DMA control experiment. Irradiation of the PBnMA-*b*-POEGMA-*b*-PBnMA (black) nanoparticles with blue light in the presence of DMA likely results in interchain coupling, resulting in a high MW shoulder (blue dash).



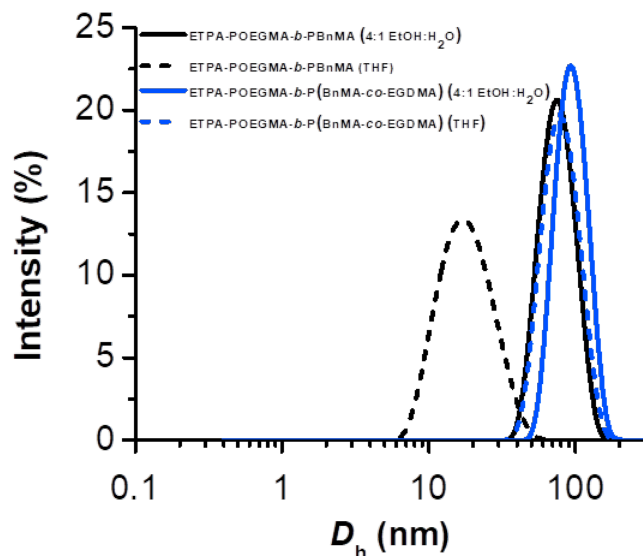
**Figure S13.** Size-exclusion chromatograms of POEGMA synthesized under green light (529 nm, 100 mW/cm<sup>2</sup>) in 1,4-dioxane with 60 equiv OEGMA and 1 equiv CDP (black), 1 equiv ETPA (blue), 1 equiv of CDP and 1 equiv of ETPA (green), 1 equiv of diCDP (yellow) and 1 equiv of the difunctional iniferter, ETPA-CDP (orange).



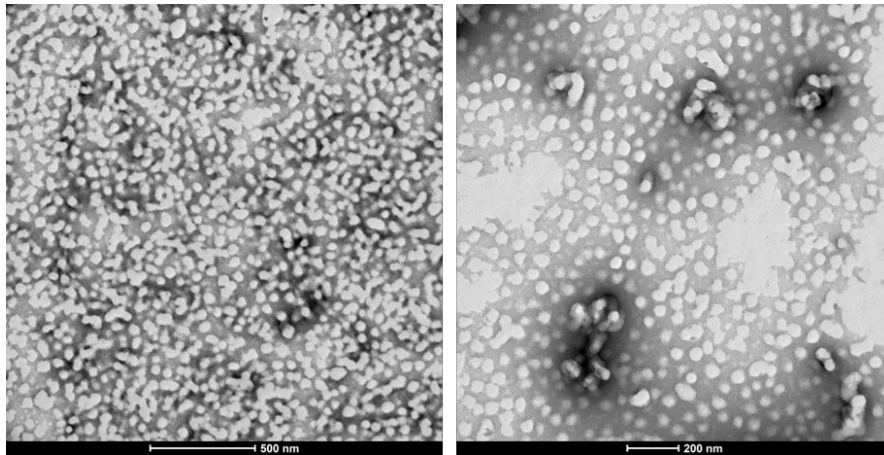
**Figure S14.** Dynamic light scattering (DLS) traces of ETPA-POEGMA-*b*-PBnMA nanoparticles diluted in H<sub>2</sub>O (black) and then a 2 M aqueous solution of DMA (blue).



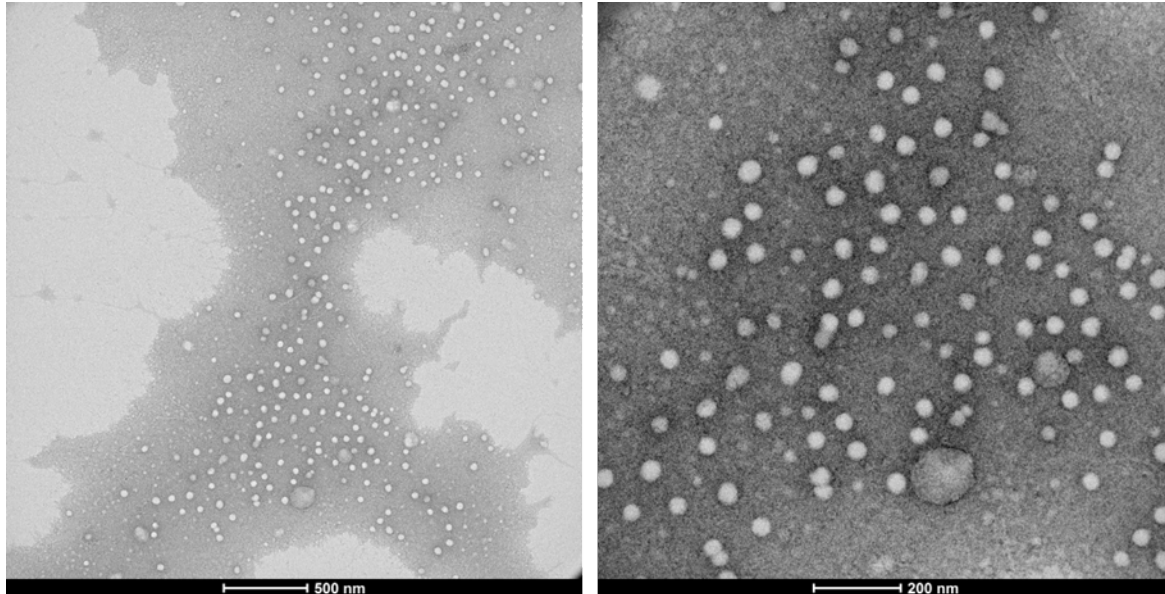
**Figure S15.** DLS traces of control nanoparticles synthesized with diCDP (black) or ETPA-CDP (blue) in 4:1 EtOH:H<sub>2</sub>O. Hydrodynamic diameters ( $D_h$ ) are similar to the ETPA-POEGMA-*b*-PBnMA nanoparticles. However, the diCDP particles have a higher PDI.



**Figure S16.** DLS traces of ETPA-POEGMA-*b*-PBnMA nanoparticles in 4:1 EtOH:H<sub>2</sub>O (black) and THF (black dashed), showing the disassembly of the nanoparticles in a good solvent for both blocks. DLS traces of core crosslinked nanoparticles (i.e., ETPA-POEGMA-*b*-P(BnMA-*co*-EGDMA)) in 4:1 EtOH:H<sub>2</sub>O (blue) and THF (blue dash) showing the tolerance of core crosslinked nanoparticles to dilution in a good solvent. Comparing non-crosslinked and core-crosslinked nanoparticles shows little difference in hydrodynamic diameter.

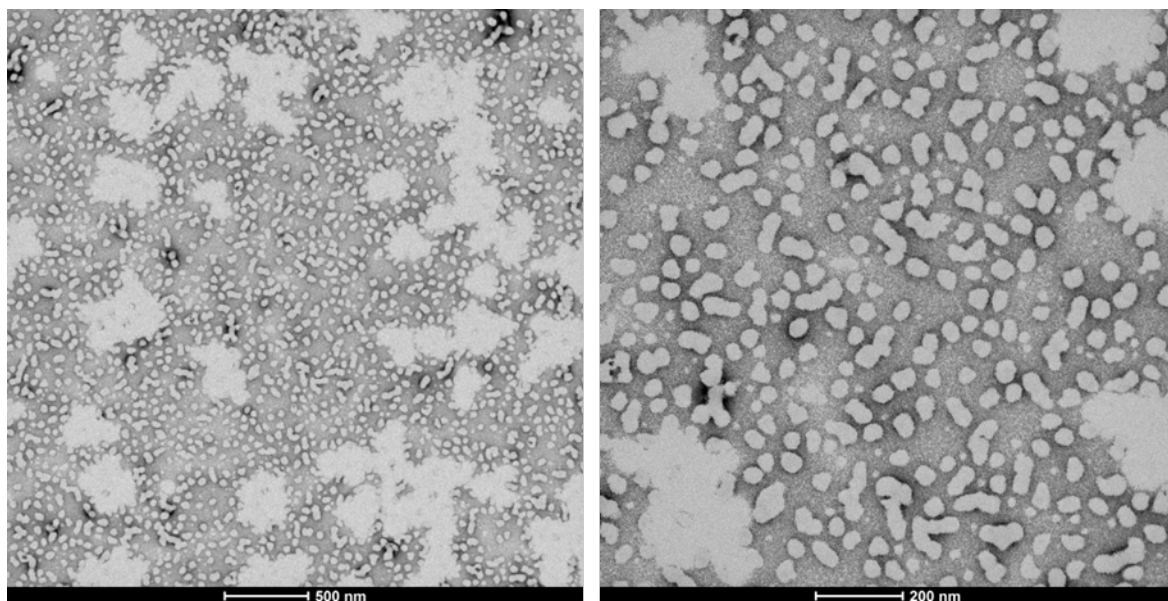


**Figure S17.** Transmission electron micrographs of ETPA-POEGMA-*b*-PBnMA nanoparticles.

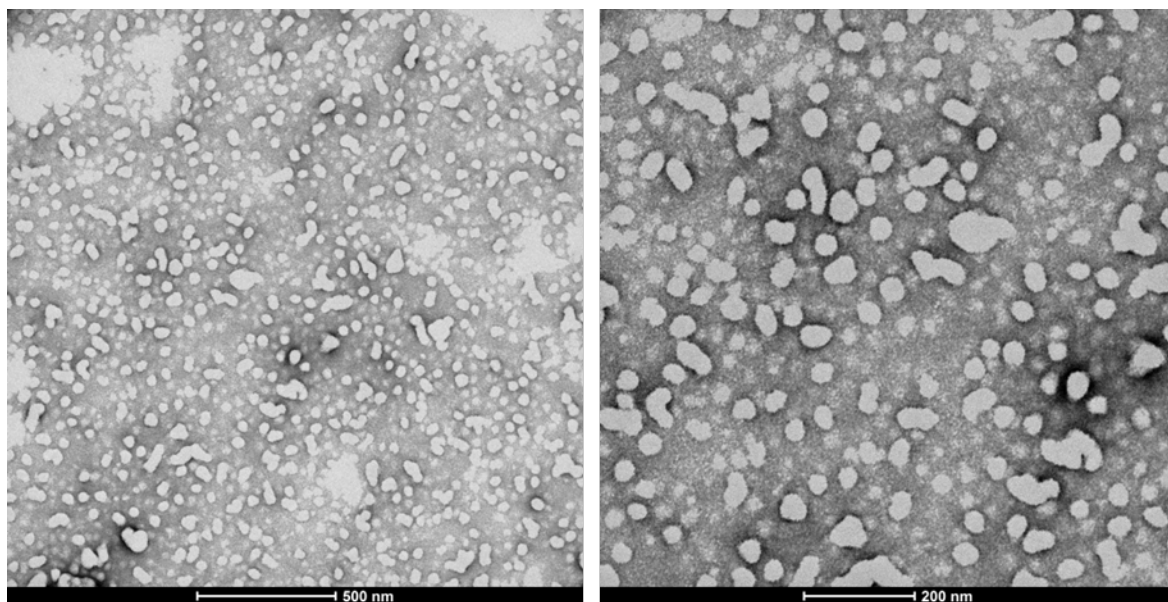


**Figure S18.** Transmission electron micrographs of PDMA-*b*-PPEGMA-*b*-PBnMA nanoparticles.

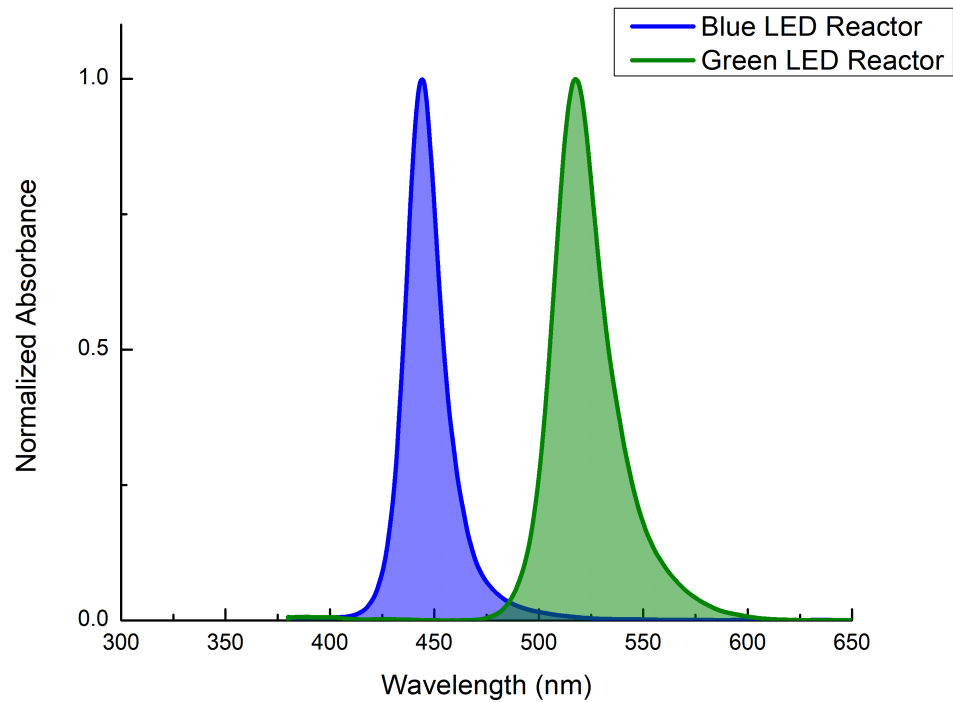




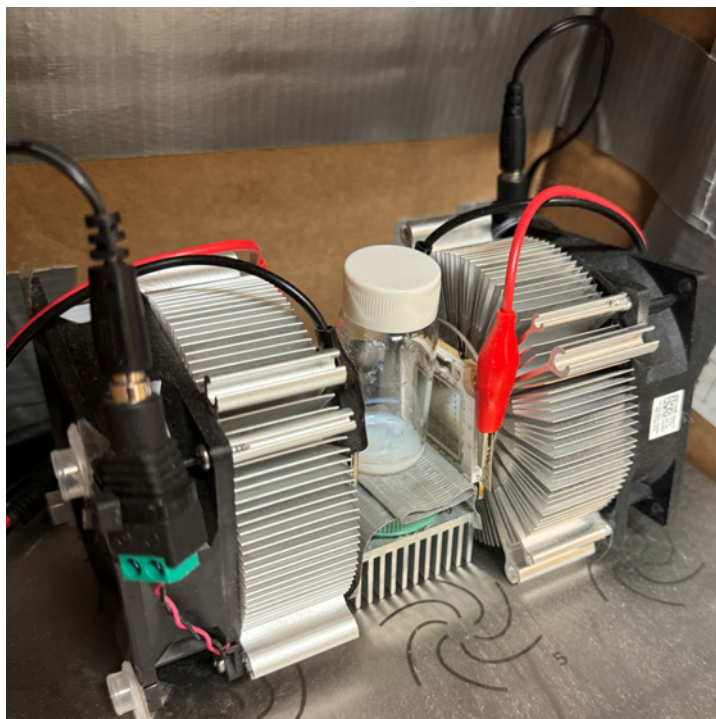
**Figure S19.** Transmission electron micrographs of POEGMA-*b*-PBnMA nanoparticles synthesized with CDP.



**Figure S20.** Transmission electron micrographs of PBnMA-*b*-POEGMA-*b*-PBnMA nanoparticles synthesized with diCDP.



**Figure S21.** Photoreactor characterization spectra. Blue LED intensity was measured at 8.5 mW/cm<sup>2</sup>, and the green LED intensity was measured at 100 mW/cm<sup>2</sup>.



**Figure S22.** Green LED photoreactor with gauge block and vial containing nanoparticles.

#### References

1. X. Cao, D. Horák, Z. An and Z. Plichta, *J. Polym. Sci., Part A: Polym. Chem.* 2016, **54**, 1036-1043.
2. G. Moad, Y.K. Chong, A. Postma, E. Rizzardo, and S.H. Thang, *Polymer.* 2005, **46**, 8458– 8468.