

Supporting Information: Photoresponsive Polymers for Carbodiimide-Fueled Transient Hydrogels

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Experimental

Materials

All starting materials, solvents, and reagents were purchased from commercial sources and used directly without further purification unless when otherwise stated. Thermal initiated azo-initiator azobisisobutyronitrile (AIBN) was obtained from Fisher Scientific. 2-nitrobenzylalcohol and methacrylic acid (99.5%, MA) were obtained from ACROS Organics. N,N-Dimethyl-acrylamide (99%, DMAm) was obtained from TCI. Acetonitrile (>99%) was obtained from Millipore-Sigma. 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (98%, EDC) was obtained from Carbosynth. 2-(((Ethylthio)carbonothioyl)thio)propanoic acid (PAETC) was synthesized as outlined in literature.¹

Monomer synthesis

Synthesis of 2-nitrobenzylmethacrylate (ONBM)

ONBM was synthesized by adapting a protocol in the literature.^{2,3} 2-nitrobenzylalcohol (10g, 0.065 mol) was added to a 500 mL round-bottom flask equipped with a magnetic stirrer bar containing (6.62g, 0.0542mol) 4-dimethylaminopyridine (DMAP), (8.39g, 0.0975 mol) methacrylic acid and 150 mL dichloromethane (DCM). The reaction solution was then cooled in an ice bath and (25.23g, 0.163 mol) EDC was added. The reaction mixture was capped and left to stir at room temperature for 24 hours. The DCM solution was washed three times with 0.2 M HCl solution, twice with 0.5 M NaOH solution, once with water, and twice with saturated brine solution. The combined organic layer was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. ¹H NMR was used to confirm the purified product.

Polymer synthesis

RAFT polymerization of poly(ONBM₁₅-DMAm₈₁)

AIBN (0.004 g, 0.024 mmol), PAETC (0.025 g, 0.019 mmol), 2-nitrobenzylmethacrylate (0.393 g, 1.78 mmol), N,N-Dimethyl-acrylamide (1.000 g, 10.00 mmol), and 1.5 g of acetonitrile were added to a 25 mL round button flask and capped with a rubber septum. The resulting reaction

mixture was purged with argon for 20 minutes to deoxygenate and then placed in an oil bath at 65 °C for 24 hours. ¹H NMR was used to determine the conversion of monomers to be >95%. The crude product was precipitated in hexane and dried under reduced pressure at 30 °C for 24 hours.

RAFT polymerization of poly(ONBM₁₅-DMAM₁₂₂)

AIBN (0.002 g, 0.015 mmol), PAETC (0.016 g, 0.075 mmol), 2-nitrobenzylmethacrylate (0.248 g, 1.120 mmol), N,N-Dimethyl-acrylamide (1.000 g, 10.00 mmol), and 1.65 g of acetonitrile were added to a 25 mL round bottom flask and capped with a rubber septum. The resulting reaction mixture was purged with argon for 20 minutes to deoxygenate and then placed in an oil bath at 65 °C for 24 hours. ¹H NMR was used to determine the conversion of monomers to be >95%. The crude product was precipitated in hexane and dried under reduced pressure at 30 °C for 24 hours.

RAFT polymerization of poly(ONBM₃₀-DMAM₁₅₅)

AIBN (0.002 g, 0.011 mmol), PAETC (0.012 g, 0.059 mmol), 2-nitrobenzylmethacrylate (0.393 g, 1.800 mmol), N,N-Dimethyl-acrylamide (1.000 g, 10.00 mmol), and acetonitrile were added to a 25 mL round bottom flask and capped with a rubber septum. The resulting reaction mixture was purged with argon for 20 minutes to deoxygenate and then placed in an oil bath at 65 °C for 24 hours. ¹H NMR was used to determine the conversion of monomers to be >95%. The crude product was precipitated in hexane and dried under reduced pressure at 30 °C for 24 hours.

Preparation of EDC stock solutions

Four different EDC solutions were used. EDC solution (0.50 M) was prepared by adding 0.096 g of EDC into a volumetric flask (1.00 mL), mixing, and topping up with water. EDC solution (1.00 M) was prepared by adding 0.192 g of EDC into a volumetric flask (1.00 mL), mixing, and topping up with water. EDC solution (1.50 M) was prepared by adding 0.288 g of EDC into a volumetric flask (1.00 mL), mixing, and topping up with water. EDC solution (2.00 M) was prepared by adding 0.384 g of EDC into a volumetric flask (1.00 mL), mixing, and topping up with water.

UV Deprotection

Deprotection of 2-nitro benzyl group from poly(ONBM_x-DMAM_y)

1g of poly(ONBM_x-DMAM_y) was dissolved in the mixture of 1 mL of water and 1 mL of DMF and sonicated for 5 minutes at room temperature. Solution was irradiated with 360 nm light with intensity of 4.8 ± 0.5 mW/cm² in an NMR tube and upon irradiation NMR analysis was carried out at 0 h, 8 h, 16 h, and 24 h of irradiation times.

Characterization

Nuclear magnetic resonance (NMR) Spectroscopy

Nuclear magnetic resonance (NMR) measurements were carried out using Bruker 400 MHz spectrometers, calibrated using residual undeuterated solvent as an internal reference (CDCl₃, 7.26 ppm).

Size exclusion Chromatography (SEC)

Size exclusion chromatography (SEC) was performed on an Agilent SEC system (Waldbronn, Germany) comprised of an Agilent 1260 isocratic pump, an Agilent autosampler, 1 × Agilent Polar Gel-M-guard and 2 × Agilent Polar Gel-M analytical columns and an Agilent 1260 refractive index (RI) detector. N,N-Dimethylformamide (DMF) with 0.1 wt % LiBr was the eluent at a flow rate of 1 mL/min, maintained at 50 °C. The system was calibrated with poly(methyl methacrylate) (PMMA) standards with molecular weights the range of 617,500 to 1,010. Each sample was filtered through a PTFE 200 nm filter.

Rheology

All rheological time sweep experiments were carried out using a TA instrument (New Castle, DE) Discovery HR-1 rheometer with a 20 mm parallel plate geometry and a Peltier plate. All rheological time sweep experiments were performed at 1% applied strain at a frequency of 10 rad/s.

Rheological time sweep of poly(O_NB_M₁₅-DMAM₈₁)

The deprotected polymer solution (1g in 1 mL deionized water and 1 mL DMF) and 0.3 mL 1 M EDC solution were using a mixing syringe in a vial, and the mixture was injected onto the static Peltier plate of the rheometer. Storage and loss moduli during gelation and hydrolysis processes were monitored during time sweep experiments at 15 °C using an angular frequency of 10 Hz. The same procedure was followed for measurements of 0.5 M, 1.5 M, 2.0 M EDC solutions, 0 h, 8 h, 16 h and 24 h UV irradiation times and poly(O_NB_M₁₅-DMAM₁₂₂) and poly(O_NB_M₃₀-DMAM₁₅₅).

Inverted vial test

Inverted vial test for deprotected poly(O_NB_M₁₅-DMAM₈₁) with 1M EDC

1g of UV deprotected polymer poly(O_NB_M₁₅-DMAM_{80.8}) was dissolved in the mixture of 1 mL of water and 1 mL of DMF, and sonicated for 5 minutes at room temperature. The polymer solution was mixed with (0.3 mL) 1.0 M EDC solution in a 5 mL sample and the two mixtures were mixed using a mixing syringe. The vial was inverted, and visual changes observed over time were photographed and documented.

Inverted vial test for protected poly(O_NBM₁₅-DMAm₈₁) with 1M EDC

1g of protected polymer poly(O_NBM₁₅-DMAm₈₁) was dissolved in the mixture of 1 mL of water and 1 mL of DMF, and sonicated for 5 minutes at room temperature. The polymer solution was mixed with (0.3 mL) 1.0 M EDC solution in a 5 mL sample and the two mixtures were mixed using a mixing syringe. The vial was inverted, and visual changes observed over time were photographed and documented.

Inverted vial test for deprotected poly(O_NBM₁₅-DMAm₈₁) without EDC

1g of UV deprotected polymer poly(O_NBM₁₅-DMAm₈₁) was dissolved in the mixture of 1 mL of water and 1 mL of DMF, and sonicated for 5 minutes at room temperature. The polymer solution was transferred to a 5 mL sample vial. The vial was inverted, and visual changes observed over time were photographed and documented.

Inverted vial test for protected poly(O_NBM₁₅-DMAm₈₁) without EDC

1g of UV protected polymer poly(O_NBM₁₅-DMAm₈₁) was dissolved in the mixture of 1 mL of water and 1 mL of DMF, and sonicated for 5 minutes at room temperature. The polymer solution was transferred to a 5 mL sample vial. The vial was inverted, and visual changes observed over time were photographed and documented.

Supplemental Data

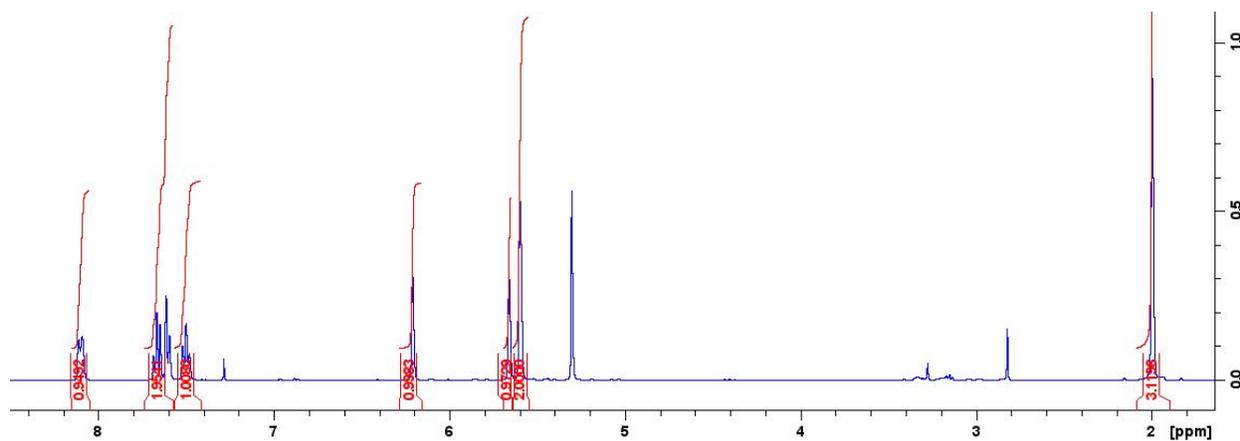


Figure S1. NMR spectrum for 2-nitrobenzylmethacrylate in CDCl₃

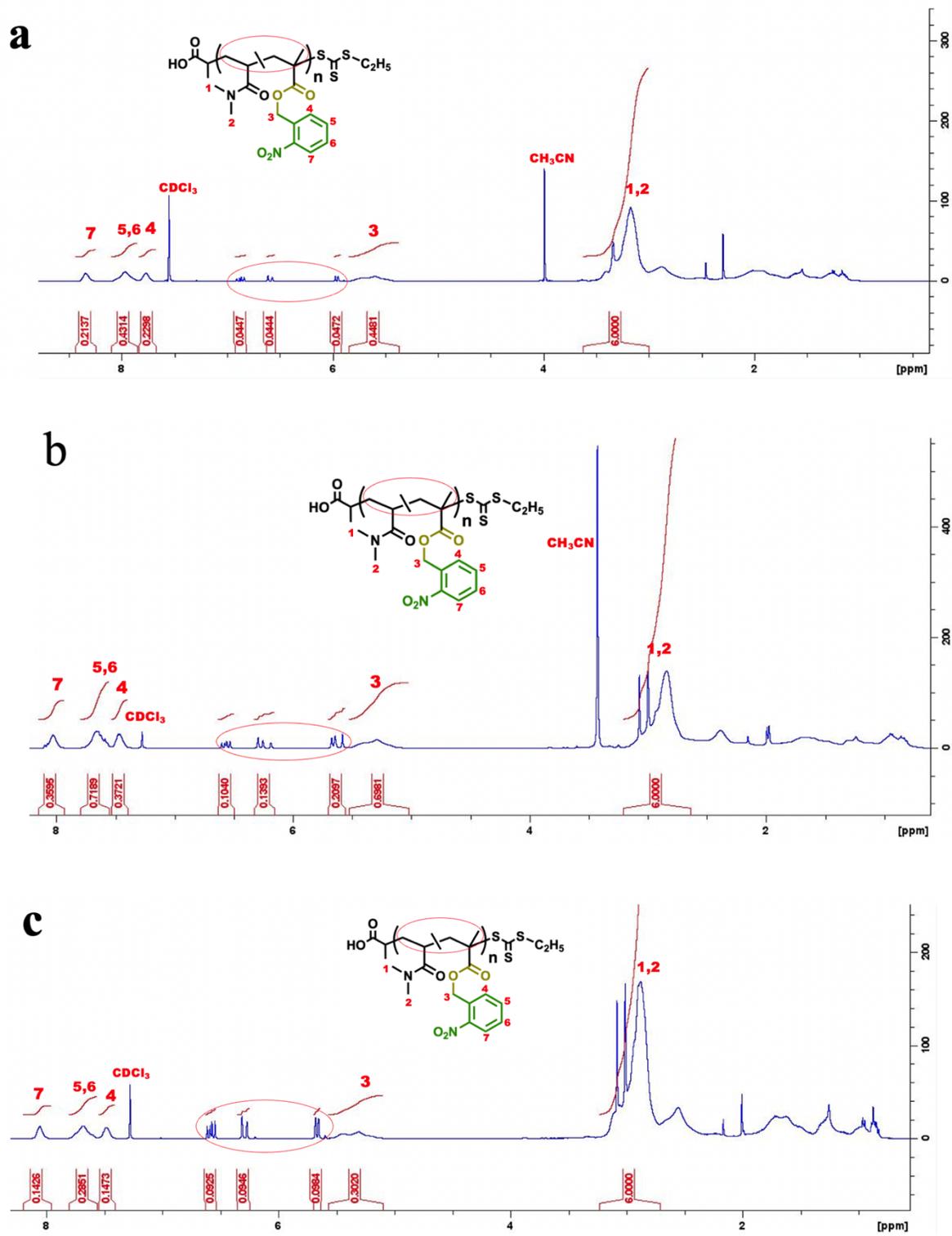


Figure S2. NMR spectra for (a) poly(ONBM₁₅-DMAm₈₁) (b) poly(ONBM₁₅-DMAm₁₂₂) and (c) poly(ONBM₃₀-DMAm₁₅₅) all in CDCl₃.

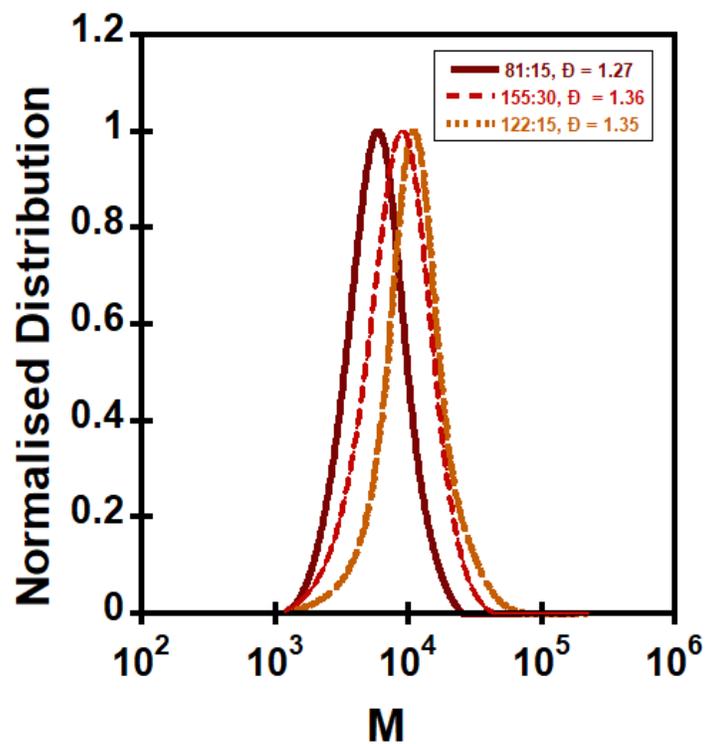
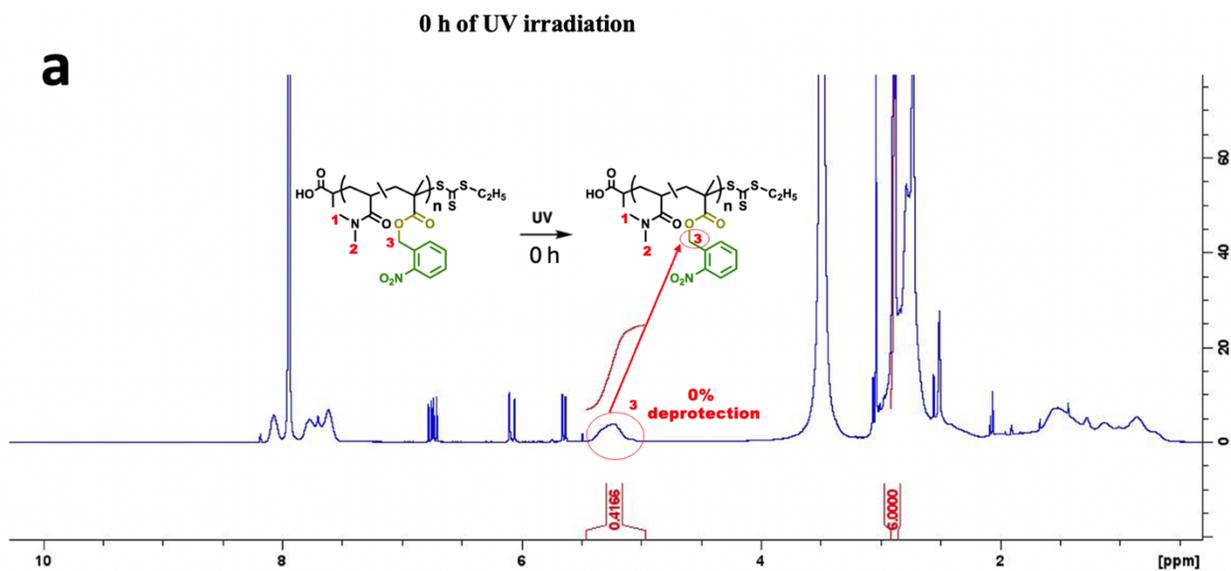
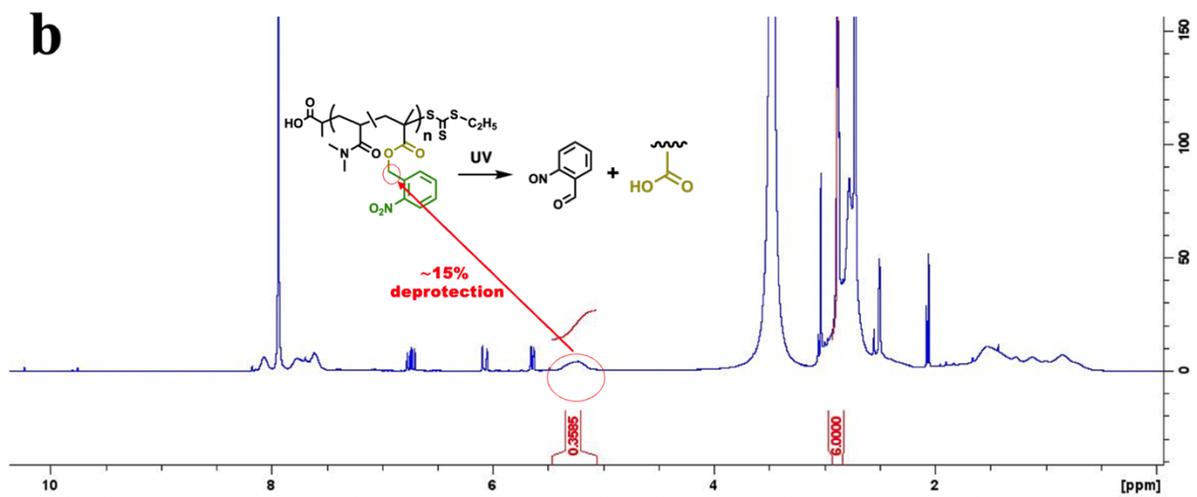


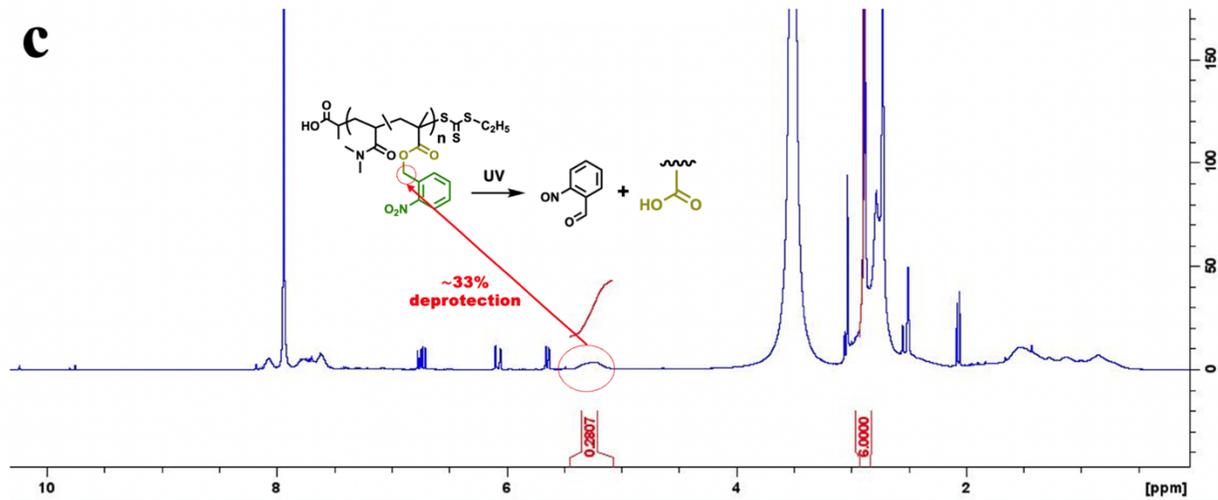
Figure S3. Normalized gel permeation chromatography plot for (a) poly(ONBM₁₅-DMAm₈₁) (b) poly(ONBM₁₅-DMAm₁₂₂) and (c) poly(ONBM₃₀-DMAm₁₅₅).



8 h of UV irradiation



16 h of UV irradiation



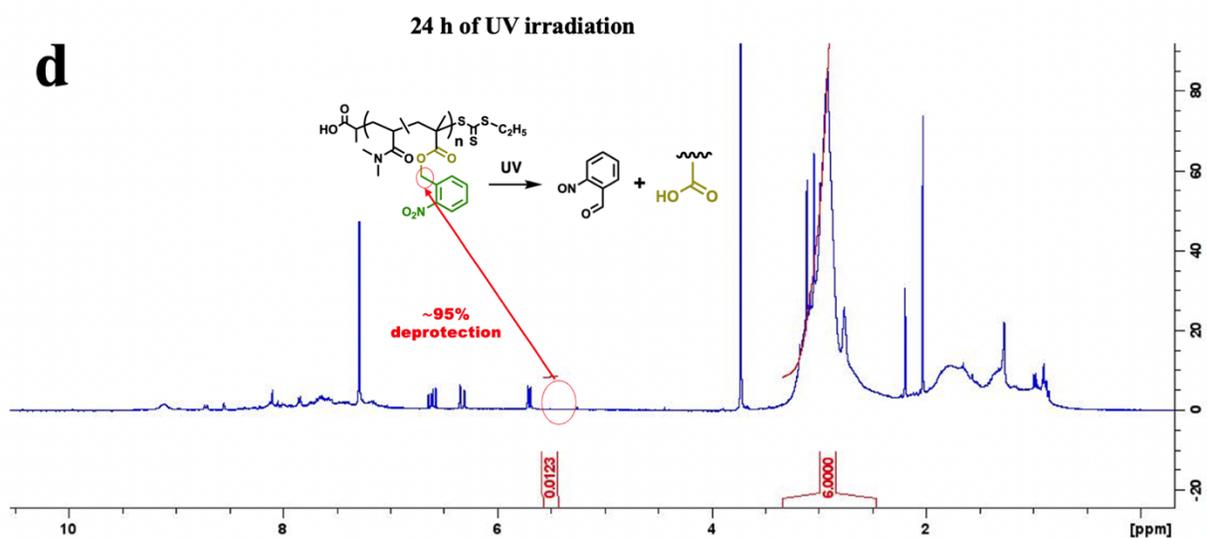


Figure S4. NMR spectra for poly(ONBM₁₅-DMAM₈₁) with UV irradiation at (a) 0 h (b) 8 h (c) 16 h (d) 24 h all in DMSO

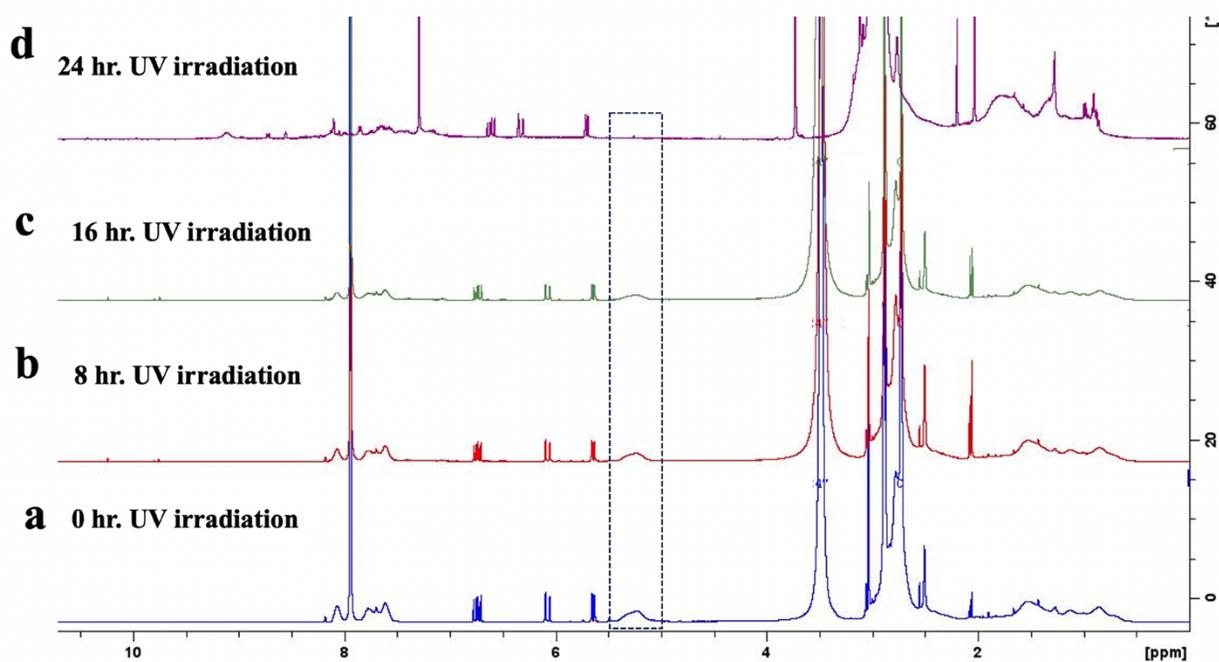


Figure S5. Stacked NMR spectra for poly(ONBM₁₅-DMAM₈₁) with UV irradiation at (a) 0 h (b) 8 h (c) 16 h (d) 24 h all in DMSO

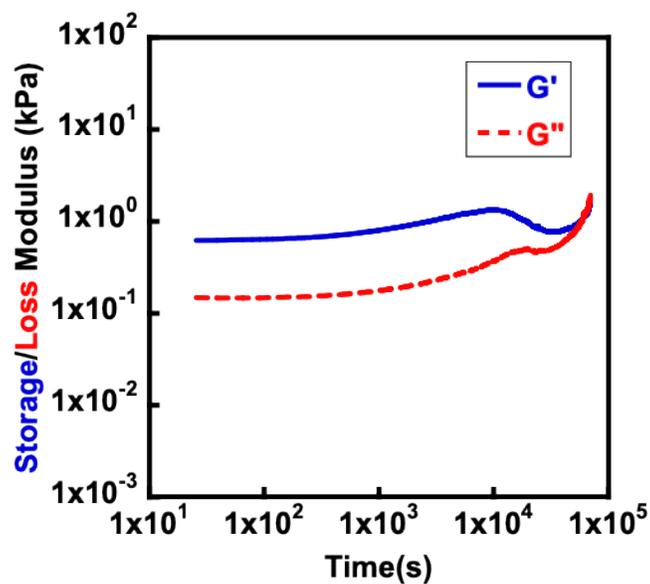


Figure S6. Typical rheology time sweeps at 15 °C using 1 M EDC for deprotected poly(OONBM₃₀-DMAM₁₅₅)

References

- 1 R. Falatach, C. McGlone, M. S. Al-Abdul-Wahid, S. Averick, R. C. Page, J. A. Berberich and D. Konkolewicz, *Chemical Communications*, 2015, **51**, 5343–5346.
- 2 O. J. Dodo, L. Petit, D. Dunn, C. P. Myers and D. Konkolewicz, *ACS Appl Polym Mater*, 2022, **4**, 6850–6862.
- 3 J.-M. Schumers, C.-A. Fustin, A. Can, R. Hoogenboom, U. S. Schubert and J.-F. Gohy, *J Polym Sci A Polym Chem*, 2009, **47**, 6504–6513.