

Supporting Information

Combining Enzymatic Monomer Transformation with Photoinduced Electron Transfer – Reversible Addition-Fragmentation Chain Transfer (PET-RAFT) for the Synthesis of Complex Multiblock Copolymers

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Experimental section

Materials: 2,2,2-Trifluoroethyl acrylate (TFEA, 98%), methanol (99%), ethanol (99%), *n*-propanol (99%), *n*-butanol (99%), *n*-pentanol (99%), *n*-hexanol (99%), 4-hydroxybutan-2-one (98%) and 3-(trimethylsilyl)prop-2-yn-1-ol (98%), tris[2-phenylpyridinato-C2,N]iridium(III) (*fac*-[Ir(ppy)₃], 99%) were all purchased from Sigma Aldrich and used as received. Immobilized CLAB (Novozym 435) was purchased from Beijing Cliscent Science and Technology Co., LTD with enzyme activity of 10800 PLU/g. The RAFT agent 3-benzylsulfanylthiocarbonylsulfanyl propionic acid (BSTP) was synthesized according to previous literature.¹

Instrumentation

Gel permeation chromatography (GPC) was performed using *N,N'*-dimethylacetamide (DMAc) as the eluent.

The GPC system was a Shimadzu modular system comprising an auto injector, a Phenomenex 5.0 μm bead-size guard column (50×7.5 mm) followed by four Phenomenex 5.0 μm bead-size columns (10^5 , 10^4 , 10^3 and 10^2 Å) for DMAc system and a differential refractive-index detector and a UV detector. The system was calibrated with narrow molecular weight distribution polystyrene standards with molecular weights of 200 to 10^6 g mol⁻¹. The molecular weight of poly(HA-*b*-HA-*b*-HA-*b*-HA-*b*-HA) pentablock homopolymer was recalculated using the Mark-Houwink constant of poly(HA) homopolymer.

GPC-LS analysis was carried out using two PLgel columns, 5 μm , 1000 Å, 300×7.5 mm (Polymer Labs), using DMF as solvent, 1.0 mL/min at 40 °C. The sample was detected using a refractive index detector (Viscostar-II viscometer, available from Wyatt Technology Co.), and the molar mass was measured using a multiple-angle light scattering detector (miniDAWN available from Wyatt Technology Co.). This technology determines accurate molecular weight distributions without using calibration standards. The processing parameters that were used for the molar mass calculation included an exponential first-order molar mass fit and a zero detector fit degree. The calculation method included using a measured AUX calibration constant for the refractive index detector and assumed 100% mass recovery. The total injected mass was for poly(MA-*b*-EA-*b*-PA-*b*-BA-*b*-P'A) and poly(OBA-*b*-MA-*b*-TMSPA) were 5.75×10^{-4} g and 5.35×10^{-4} g, respectively, and the refractive index increment (dn/dc) was calculated to be 0.0363 and 0.0446.

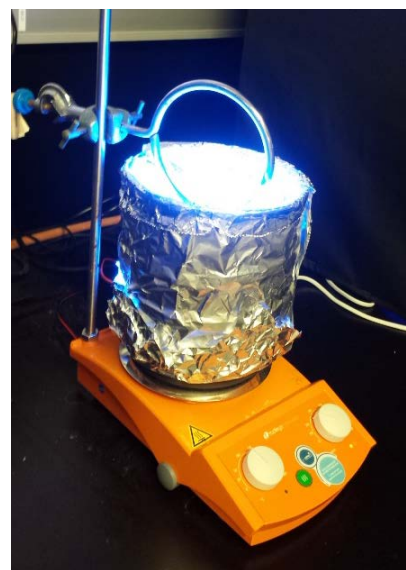
Nuclear magnetic resonance (NMR) spectroscopy was carried out on a Bruker DPX 300 spectrometer operating at 400 MHz for ¹H and 100 MHz for ¹³C using CDCl₃ as solvents and tetramethylsilane (TMS) as a reference. Data were reported as follows: chemical shift (δ) measured in ppm downfield from TMS.

On-line Fourier Transform Near-Infrared (FTNIR) spectroscopy was used to determine the monomer conversions by following the decrease of the vinylic C-H stretching overtone of the monomer at ~ 6200 cm⁻¹.

A Bruker IFS 66/S Fourier transform spectrometer equipped with a tungsten halogen lamp, a CaF₂ beam splitter and liquid nitrogen cooled InSb detector was used. The sample was placed in a FT-NIR quartz cuvette (1 cm × 2 mm) and polymerised under blue LED light irradiation. Every 10 min, the sample was put into holder manually and each spectrum in the spectral region of 7000-4000 cm⁻¹ was constructed from 32 scans with a resolution of 4 cm⁻¹. The total collection time per spectrum was about 15 s. Spectra were analysed with OPUS software.

UV-vis Spectroscopy. UV-vis spectra were recorded using a CARY 300 spectrophotometer (Varian) equipped with a temperature controller.

Photopolymerization reactions. The reactions were carried out under visible light irradiation by a 1 m blue LED strip ($\lambda_{\text{max}} = 435$ nm, 4.8 Watts) surrounding the reaction vessels.



Monomer transformation via enzymatic transacylation was performed as follow: TFEA (1.0 g, 6.5 mmol), methanol (0.208 g, 6.5 mmol), CALB (100 mg) were mixed together under gentle stirring in round bottom flask at 40 °C. The monomer mixture was used directly for the polymerization after removal of enzyme by centrifugation. The conversion of TFEA can be calculated as follow: $\alpha = \left(1 - \frac{I_t}{I_0}\right) * 100\%$, I_t and I_0 represent the integration of ester bond (CH₂O) of TFEA at 4.55 ppm at time t and 0, respectively.

Homopolymerization of *n*-hexyl acrylate mixture: 5 mL glass vial was equipped with a rubber septum and charged with DMSO (0.5 mL), *n*-hexyl acrylate mixture (1.67 g, 6.5mmol), BSTP (8.8 mg, 0.032mmol), Ir(ppy)₃ (2.2×10^{-2} mg, 3.2×10^{-5} mmol). The mixture was covered in aluminum foil and degassed by N₂ for 20 minutes. The mixture was then irradiated by a blue LED strip (4.8 Watts) as light source at room temperature. Aliquots were withdrawn periodically for ¹H NMR and GPC measurements.

Synthesis P(HA-*b*-HA-*b*-HA-*b*-HA-*b*-HA) pentablock homopolymer: a 25 mL glass flask was equipped with a rubber septum and charged with DMSO (0.5 mL), *n*-hexyl acrylate mixture (0.5 g, 2.0 mmol), BSTP (17.6 mg, 0.065 mmol), Ir(ppy)₃ (1.3×10^{-2} mg, 2.0×10^{-5} mmol). The mixture was covered in aluminum foil and degassed by N₂ for 20 minutes. The mixture was then irradiated by a blue LED strip ($\lambda_{\text{max}} = 435$ nm, 4.8 Watts) as light source at room temperature for predetermined time (24 hours for the first 3 chain extensions and 48 hours for the #4 and #5 chain extensions). Then the polymerization was stopped by covered by aluminum foil and an aliquot of the reaction mixture was withdrawn for ¹H NMR and GPC analyses. For the iterative chain extensions, a further 0.5 g of *n*-hexyl acrylate mixture was added into the flask. After degassed by N₂ for 20 minutes, the polymerization was then irradiated by a blue LED light ($\lambda_{\text{max}} = 435$ nm, 4.8 Watts). The monomer addition and polymerization was repeated as required to produce the multiblock copolymers. The polymer was precipitated 3 times in methanol. The molecular weight of polymer was calculated by ¹H NMR by comparing the integration of ester group of polymer with phenyl group in BSTP, using $M_{n, \text{NMR}} = [I_{4.0\text{ppm}}/2]/[I_{7.2-7.4\text{ppm}}/5] \times \text{MW}^{\text{Monomer}} + \text{MW}^{\text{BSTP}}$, where $I_{4.0\text{ppm}}$ and $I_{7.2-7.4\text{ppm}}$ correspond to the integral of signal at 4.0ppm (CH₂O) and at 7.2-7.4ppm (CH, benzyl group).

The theoretical molecular weight was calculated using the following equation: $M_{n, \text{theo}} = ([M]_0/[RAFT]_0) \times \text{MW}^{\text{Monomer}} + \text{MW}^{\text{BSTP}}$, where $[M]_0$ and $[RAFT]_0$ correspond to the initial monomer and RAFT concentration, respectively.

The end group functionality was calculated by UV-vis using the following equation: End group functionality

$(\%) = ((\text{Abs}^{305\text{nm}}/\epsilon) / [\text{polymer}]) \times 100$, with $\text{Abs}^{305\text{nm}}$, ϵ and $[\text{polymer}]$ correspond to the absorbance at 305 nm (attributed to trithiocarbonate group), extension coefficient of trithiocarbonate² ($\epsilon = 14\,500\text{ mol}^{-1}\text{ cm}^{-1}\text{ l}^{-1}$) and polymer concentration (in mol/l), respectively; by NMR: $f(\%) = [I_{3.4\text{ppm}}/2]/[I_{7.2-7.4\text{ppm}}/5] \times 100$, where $I_{3.4\text{ppm}}$ and $I_{7.2-7.4\text{ppm}}$ correspond to the integration of signal at 3.4ppm and at 7.2-7.4ppm, respectively.

For different catalyst amounts, the polymerization condition was kept at the same. The polymerization time was 24 hours for the first 3 chain extensions and 48 hours for the last two chain extensions.

Synthesis of P(MA-*b*-EA-*b*-PA-*b*-BA-*b*-P'A) pentablock copolymer: a 25 mL glass flask was equipped with a rubber septum and charged with DMSO (0.5 mL), methyl acrylate mixture (0.6 g, 3.2 mmol), BSTP (17.6 mg, 0.065 mmol), Ir(ppy)₃ (2.08×10^{-2} mg, 3.2×10^{-5} mmol). The mixture was covered in aluminum foil and degassed by N₂ for 20 minutes. The mixture was then irradiated by a blue LED strip (4.8 Watts) as light source at room temperature for predetermined time (24 hours for the first 3 chain extensions and 48 hours for the #4 and #5 chain extensions). Then the polymerization was stopped by covered by aluminum foil and an aliquot of the reaction mixture was withdrawn for ¹H NMR and GPC characterization. For the iterative chain extensions, 0.65 g of ethyl acrylate mixture was added into the flask. After degassed by N₂ for 20 minutes, the polymerization was then irradiated by a blue light. The monomer addition and polymerization was repeated as required to produce the multiblock copolymers. The polymer was precipitated 3 times in *n*-hexane.

Synthesis of P(OBA-*b*-MA-*b*-TMSPA) triblock copolymer: a 25 mL glass flask was equipped with a rubber septum and charged with DMSO (0.5 mL), 3-oxobutyl acrylate mixture (0.47 g, 2 mmol), BSTP (17.6 mg, 0.065 mmol), Ir(ppy)₃ (1.3×10^{-2} mg, 2×10^{-5} mmol). The mixture was covered in aluminum foil

and degassed by N₂ for 20 minutes. The mixture was then irradiated by a blue LED strip (4.8 Watts) as light source at room temperature for predetermined time (24 hours for each chain extensions). Then the polymerization was stopped by covered by aluminum foil and an aliquot of the reaction mixture was withdrawn for ¹H NMR and GPC characterization. For the 2nd chain extension, 0.36 g of methyl acrylate mixture was added into the flask. After degassed by N₂ for 20 minutes, the polymerization was then irradiated by a blue light. Then the polymerization was stopped by covered by aluminum foil and an aliquot of the reaction mixture was withdrawn for ¹H NMR and GPC characterization. For the 3rd chain extension, 0.55 g 3-(trimethylsilyl)prop -2-yn-1-yl acrylate mixture was added into the flask to produce the multiblock copolymers. The conversions in the synthesis of functional triblock copolymer were 98%, 95%, 60% for 1st, 2nd, 3rd chain extension, respectively. The polymer was precipitated 3 times in *n*-hexane.

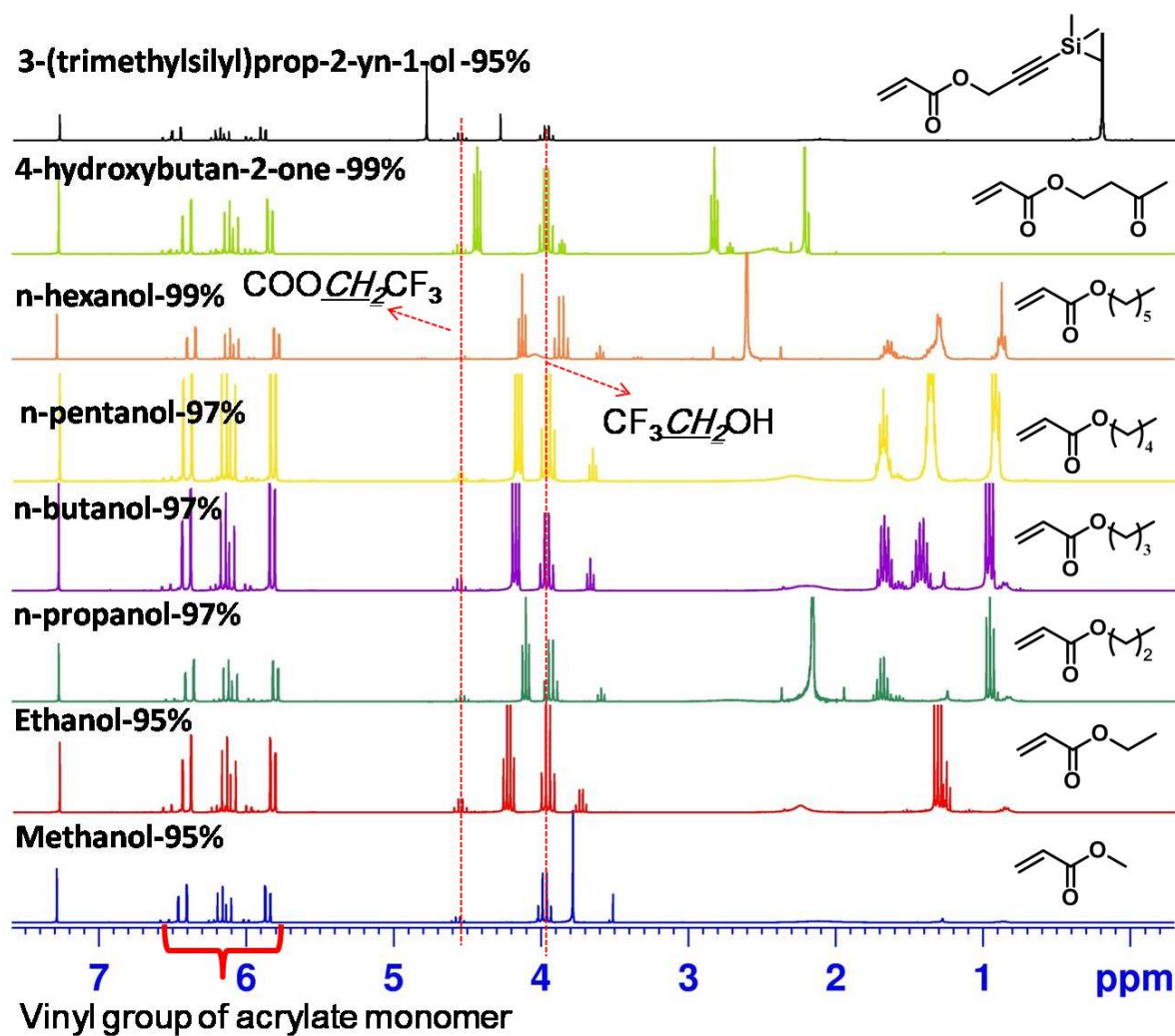


Figure S1. ^1H NMR spectra of enzymatic transacylation reaction mixture using different alcohols in the presence of CALB at 40 °C in 12 hours (recorded in CDCl_3).

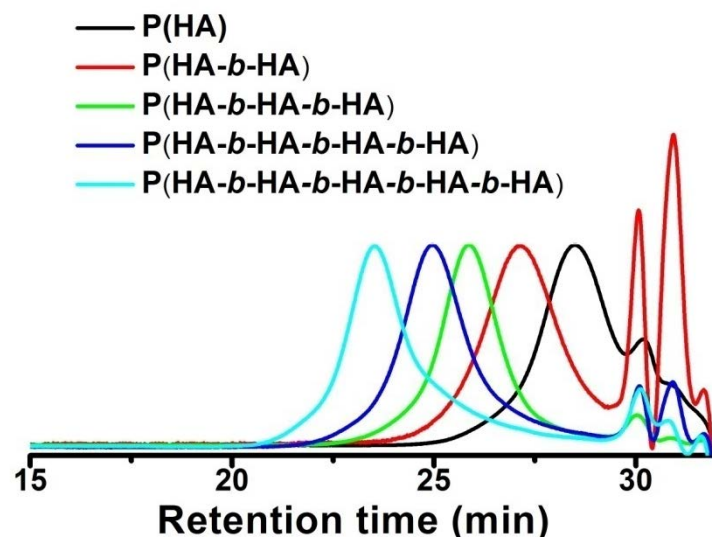


Figure S2. GPC traces of each block using 5 ppm of Ir-based photocatalyst in the synthesis of multiblock poly(P(HA-*b*-HA-*b*-HA-*b*-HA)) homopolymer. *Note: The peaks at 30 min correspond to the trace of solvents (outside calibration range, 200-2 000 000 g/mol).*

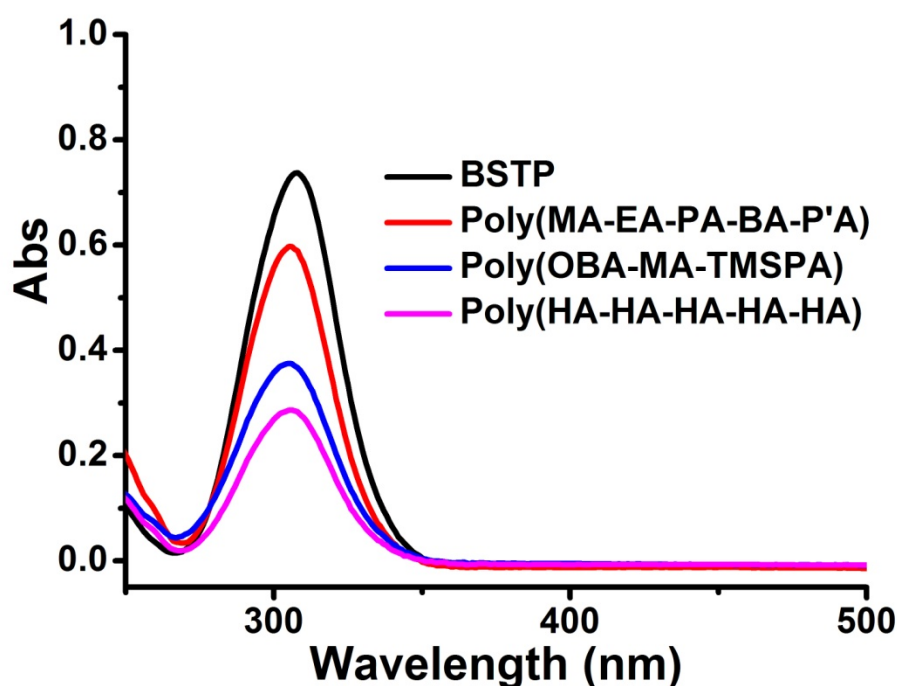


Figure S3. UV-vis spectra of BSTP, poly(HA-*b*-HA-*b*-HA-*b*-HA-*b*-HA), poly(MA-*b*-EA-*b*-PA-*b*-BA-*b*-P'A) and poly(OBA-*b*-MA-*b*-TMSPA) in THF.

End group fidelity was calculated by the following equation: End group functionality (%) = $((\text{Abs}^{305\text{nm}}/\epsilon) / [\text{polymer}]) \times 100$, with $\text{Abs}^{305\text{nm}}$, ϵ and $[\text{polymer}]$ correspond to the absorbance at 305 nm (attributed to

trithiocarbonate group), extension coefficient of trithiocarbonate² ($\epsilon = 14\,500\text{ mol}^{-1}\text{ cm}^{-1}\text{ l}^{-1}$) and polymer concentration (in mol/l), respectively.

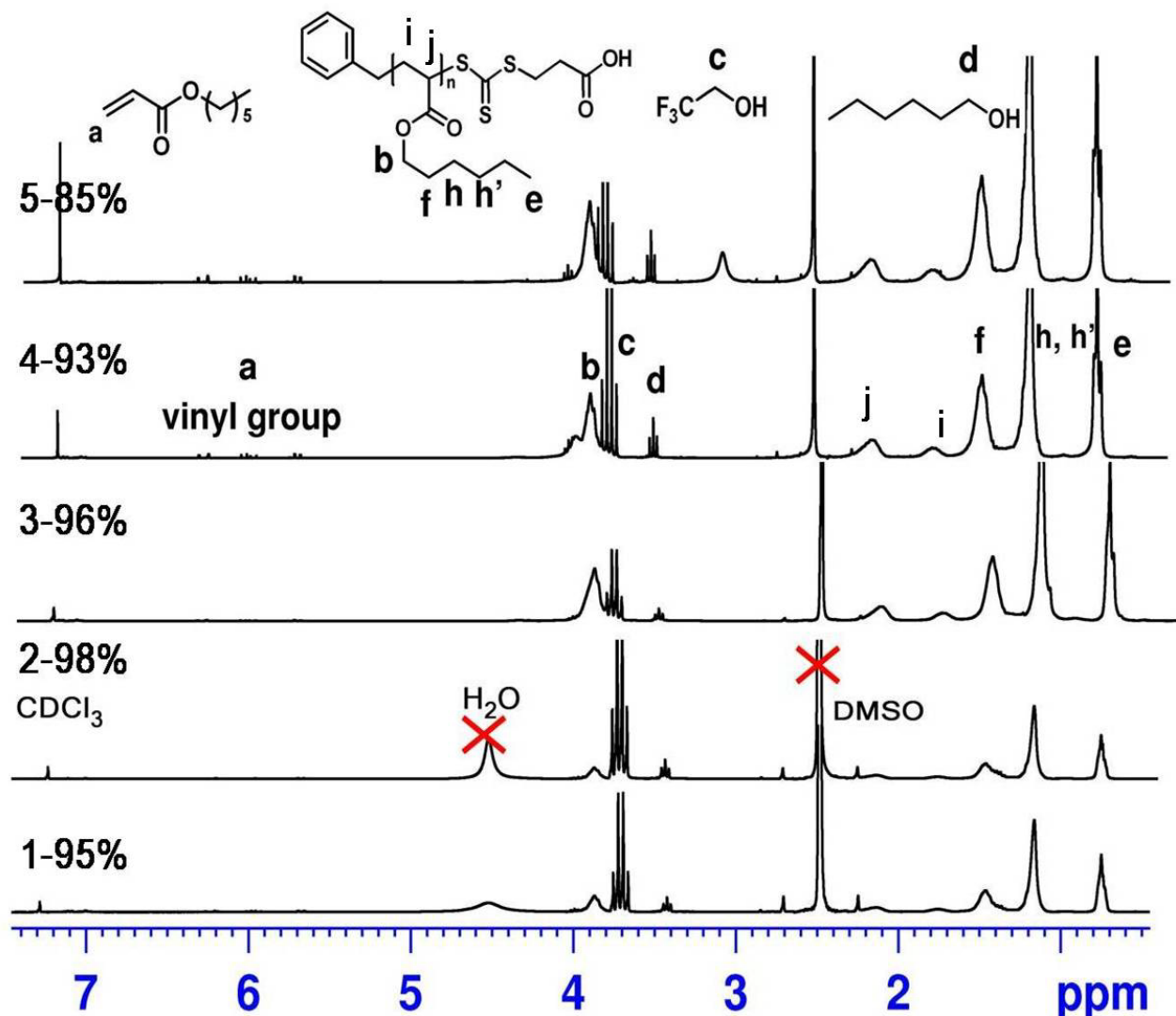


Figure S4. ^1H NMR spectra of poly(HA) reaction mixtures after different chain extensions.

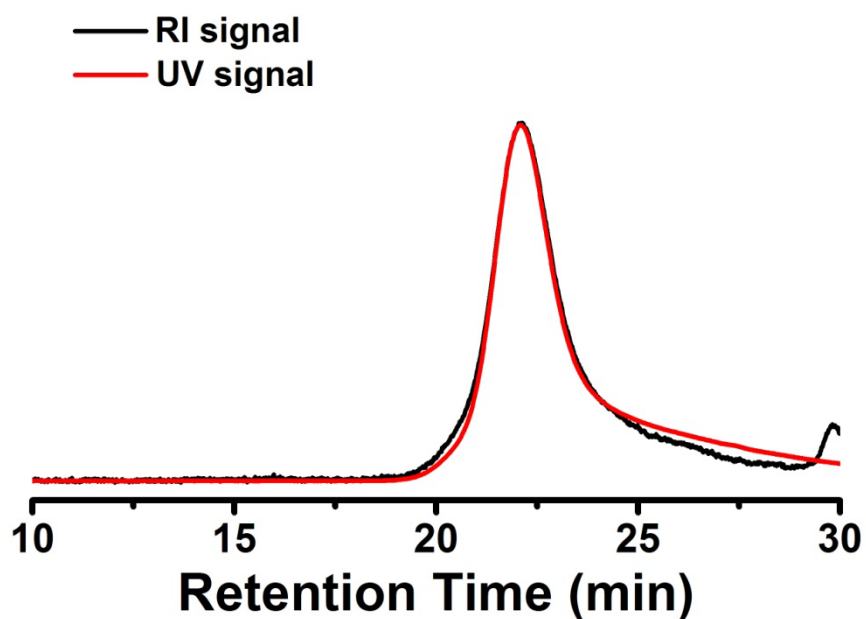


Figure S5. GPC curves using a RI and UV ($\lambda = 305$ nm) detector for pentablock poly(HA-*b*-HA-*b*-HA-*b*-HA-*b*-HA) homopolymer. *Note: The wavelength at 305 nm corresponds to the maximum absorption of trithiocarbonate. As a control experiment, we removed the trithiocarbonate by aminolysis and re-analyzed by GPC using UV detector. No signal was observed after aminolysis.*

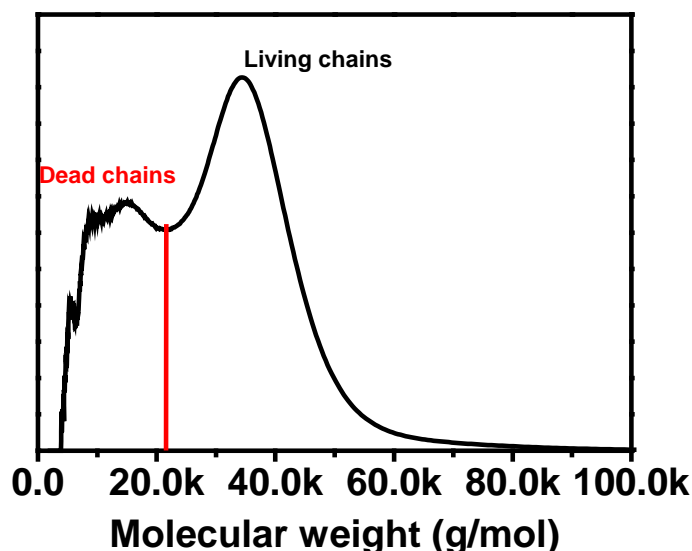


Figure S6. Number of chains versus molecular weight obtained by photoinduced living polymerization after 5 chain extensions of poly(HA-*b*-HA-*b*-HA-*b*-HA-*b*-HA) homopolymer. The end group fidelity was determined to be 85% after 5 chain extensions.

Note: To estimate the livingness according to GPC data, we first converted the molecular weight distributions to the corresponding number distributions.³ The y-axis values in the GPC distributions (normally what is given by the GPC software) are proportional to nM^2 , where n is the number of chains and M is the molecular weight. It follows that the number distribution, where the y-axis values are proportional to the number of chains, is given by $w(\log M)/M^2$. Thus, if one plots $w(\log M)/M^2$ vs M , the area under the curve between two given values of M is proportional to the number of chains within that range of M values. Note: This calculation is estimated using the following hypothesis: the low molecular weight tails is attributed to dead polymers.⁴⁻⁵

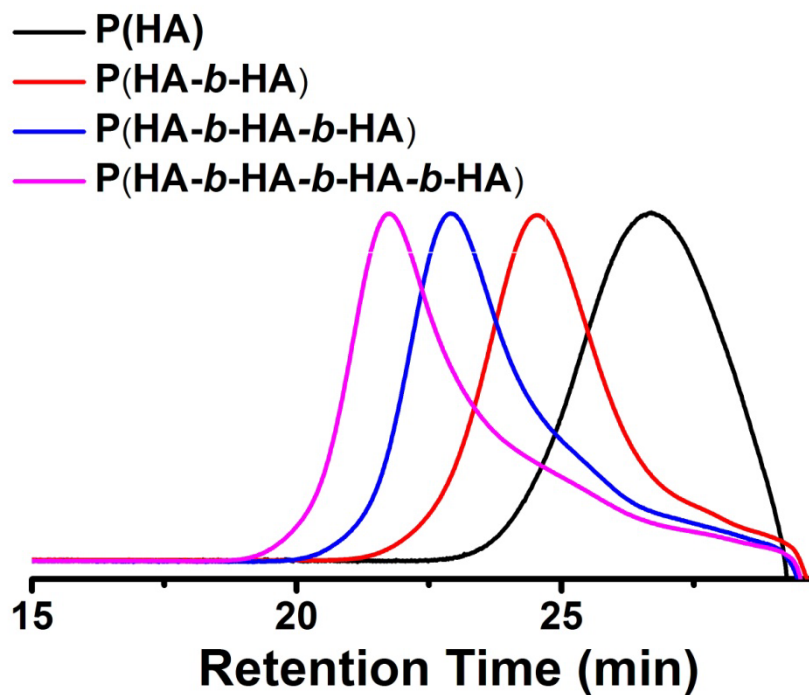


Figure S7. GPC traces of each block using 15 ppm of Ir-based photocatalyst in the synthesis of poly(P(HA-*b*-HA-*b*-HA-*b*-HA)) multiblock homopolymer. The end group fidelity after 4 chain extensions was calculated by GPC deconvolution to be close to 45%.

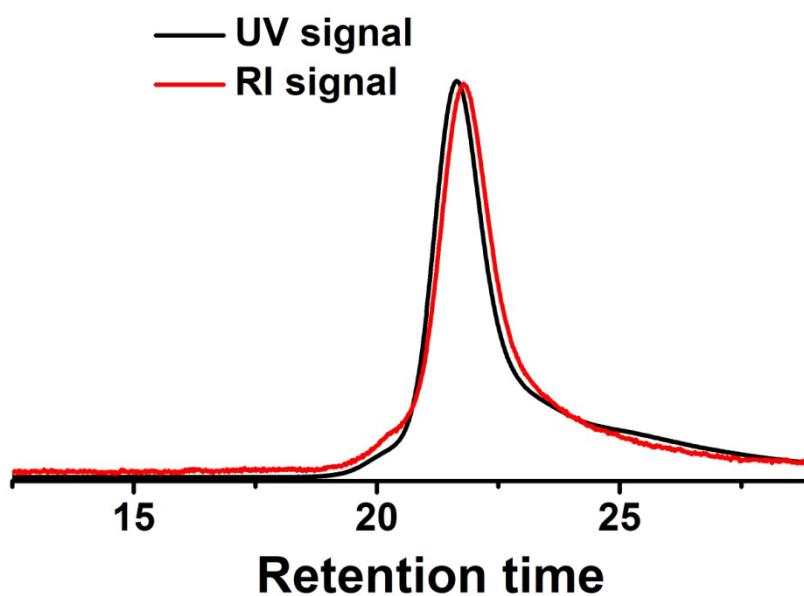


Figure S8. GPC curves using a RI and UV ($\lambda = 305$ nm) detector for pentablock poly(MA-*b*-EA-*b*-PA-*b*-BA-*b*-P'A) copolymer.

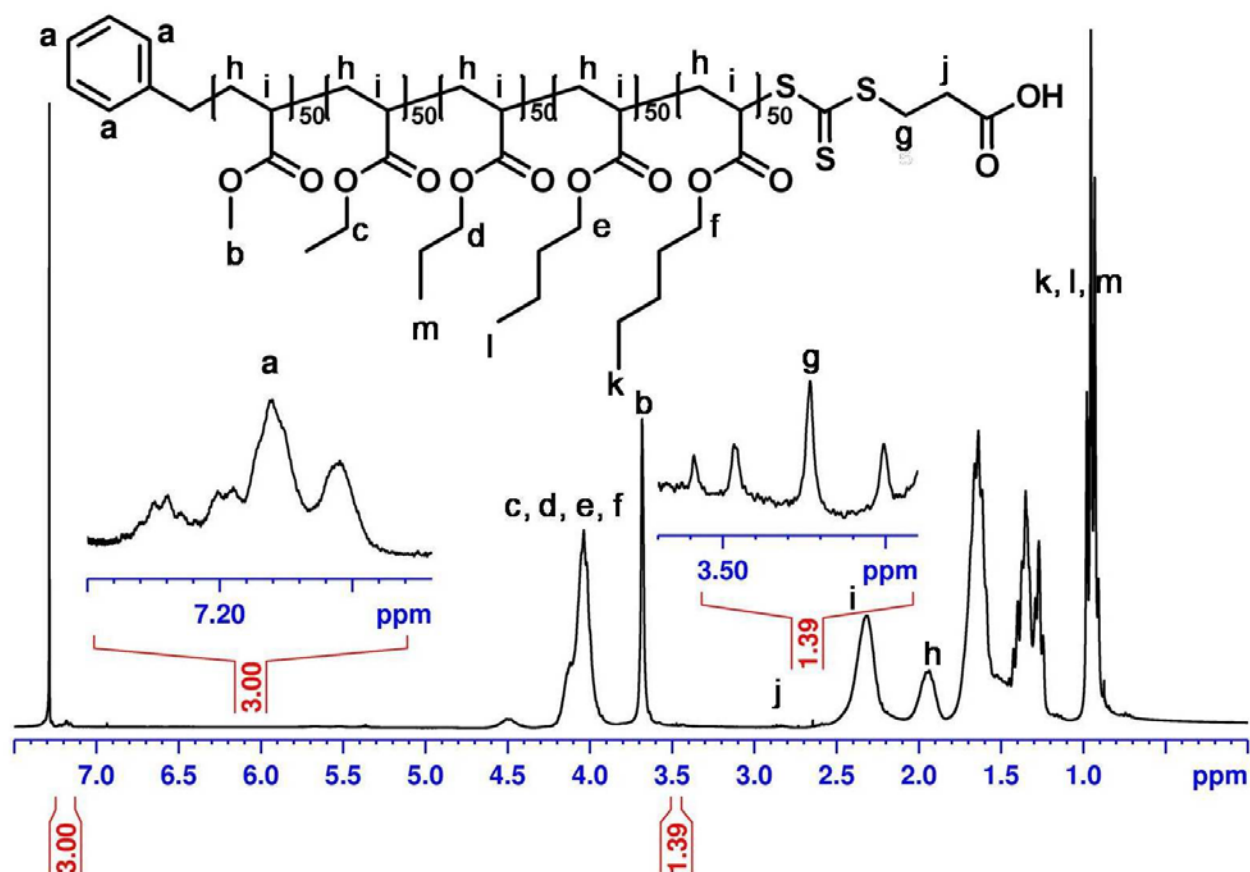


Figure S9. ^1H NMR spectrum of pentablock P(MA-*b*-EA-*b*-PA-*b*-BA-*b*-P'A) copolymer (recorded in CDCl_3). (End group functionality is equal to ~70%)

End group functionality was calculated using the following equation: $f(\%) = [I_{3.4\text{ppm}}/2]/[I_{7.2-7.4\text{ppm}}/5] \times 100$,

where $I_{3.4\text{ppm}}$ and $I_{7.2-7.4\text{ppm}}$ correspond to the integration of signal at 3.4ppm and at 7.2-7.4ppm, respectively.

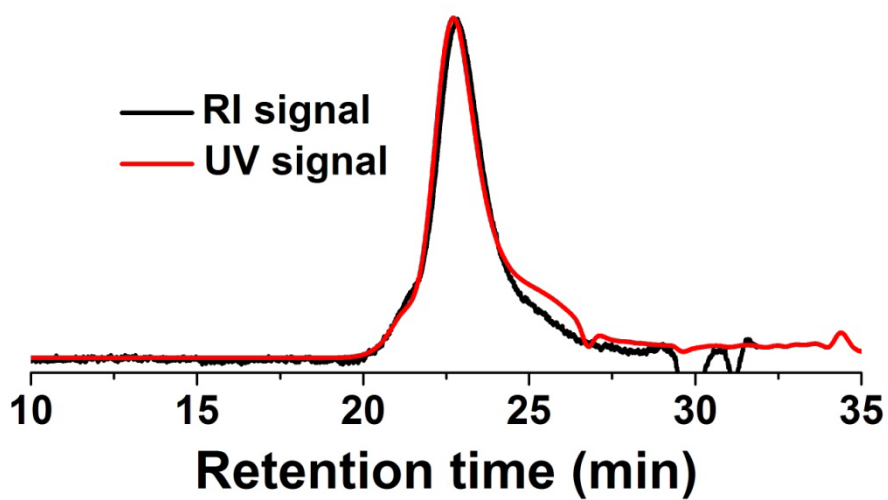


Figure S10. GPC curves using a RI and UV ($\lambda = 305$ nm) detector for functional triblock poly(OBA-*b*-MA-*b*-TMSPA) copolymer.

Additional References

- (1) Boyer, C. and Davis, T. P. *Chem. Commun.* **2009**, 40, 6029-6031.
- (2) Boyer, C.; Liu, J.; Bulmus, V.; Davis, T. P. *Aust. J. Chem.* **2009**, 62, 830-847.
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- (4) Boyer, C.; Soeriyadi, A. H.; Zetterlund, P. B.; Whittaker, M. R. *Macromolecules* **2011**, 44, 8028.
- (5) Gody, G.; Maschmeyer, T.; Zetterlund, P. B.; Perrier, S. *Macromolecules* **2014**.