Supporting Information for

Preparation of 1:1 alternating, nucleobase-containing copolymers for use in sequence-controlled polymerization

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Materials. Maleic anhydride (MAh) was obtained from Sigma Aldrich and used as received. 5-Methyl-1-(4-vinylbenzyl)pyrimidine-2,4(1H,3H)-dione (StyThy) was synthesised from vinylbenzyl chloride according to literature procedures.¹ All solvents were analytical grade (AR) unless otherwise stated. Azobisisobutylonitrile (AIBN) was obtained from TCI Chemicals and recrystallised from chloroform and stored in the freezer at -10°C. 2,2'-Azobis(4-methoxy-2.4-dimethyl valeronitrile) (V70) was purchased from Wako and used as received. All other materials were obtained from commercial sources and used as received. (*S*)-4-Cyano-4-(dodecylthiocarbonothioylthio)pentanoic acid (1) was prepared according to a literature procedure described previously.² Analytical thin layer chromatography (TLC) was performed on Merck Silica Gel 60 (70–230 mesh). Purification of polymers was completed using Spectra/Por 6 Standard RC pre-wetted dialysis tubing (0.05 % sodium azide aqueous solution) with a 1kD molecular weight cut-off (MWCO) regenerated cellulose (RC) dialysis tubing purchased from VWR.

Characterisation. Standard ¹H NMR spectra were obtained with a Bruker Avance 400 MHz spectrometer (¹H 400.1 MHz, ¹³C 100.6 MHz). HSQC and DEPT 45° were performed on a Bruker Avance 600 MHz spectrometer (¹H 600.1 MHz, ¹³C 151.0 MHz). Size exclusion chromatography (SEC) was performed on a Shimadzu system equipped with a CMB-20A controller system, a SIL-20A HT autosampler, a LC-20AT tandem pump system, a DGU-20A degasser unit, a CTO-20AC column oven, a RDI-10A refractive index detector, and four Waters Styragel columns (HT2, HT3, HT4, HT5 each 300 mm × 7.8 mm, providing an effective molar mass range of 100 to 4 × 10⁶). This SEC system uses *N*,*N*-dimethylacetamide (DMAc) (with 2.1 g·L⁻¹ of lithium chloride (LiCl)) as eluent with a flow rate of 1 mL.min⁻¹ at 80 °C. The molar mass of the samples was obtained from a calibration curve constructed with PMMA standards (Polymer Laboratories) of low dispersity (*D*) value. A third order

polynomial was used to fit the log M_p vs time calibration curve, which was linear across the molar mass ranges.

Representative procedure for the polymerisation of MAh and StyThy

StyThy (100 mg, 0.413 mmol) and MAh (40.5 mg, 0.413 mmol) were dissolved in HFIP (0.3 mL). CTA **1** (3.3 mg, 0.008 mmol) and 10 μ L of a stock solution of AIBN initiator (3 mg in 100 μ L HFIP, 0.002 mmol, [Initiator]:[CTA] = 1:5) was added to the reaction mixture. Oxygen was removed from the reaction by freeze-thaw degassing three times. The reaction was then placed in an oil bath at 60 °C for 2.5 h (or for a length of time as specified for desired DP). After 2.5 h the reaction vessel was cooled and opened to air. The crude reaction mixture was purified by dialysis from H₂O using 1kD MWCO RC dialysis tubing, stirred for 16 h. Pure polymer was isolated as a yellow oil after lyophilisation. Note that [CTA]₀/[AIBN]₀ was kept constant at 1:5 for all polymerisations.

Data



Fig S1: ¹H NMR spectrum of StyThy-alt-MAh copolymer in DMSO-d₆

Molecular Weight

Fig S2: GPC curves for StyThy-*alt*-MAh copolymerisations at different concentrations (0.6 M and 1.2 M) taken at T = 1h and T = 6h (Table 4)

Initial Monomer Feed Ratio Experiments

Monomer feed ratios of StyThy:MAh at 1:7, 1:3 and 1:1 were chosen to understand the effect of monomer feed ratio on the alternating composition of the polymer. Polymers were analysed by ^{13}C DEPT NMR experiments to identify CH₂ subunit distinctive triad resonances and therefore identify the sequential nature of the resulting polymer.

Polymers were prepared as follows:

StyThy:MAh 1:1 monomer feed ratio = 100 mg, 0.413 mmol StyThy : 40.5 mg, 0.413 mmol MAh

StyThy:MAh 1:3 monomer feed ratio = 100 mg, 0.413 mmol StyThy : 121.4 mg, 1.238 mmol MAh

StyThy:MAh 1:7 monomer feed ratio = 100 mg, 0.413 mmol StyThy : 283.3 mg, 2.889 mmol MAh

Required amounts of StyThy and MAh were dissolved in HFIP (0.3 mL). CTA **1** (3.3 mg, 0.008 mmol) and 10 μ L of a stock solution of AIBN initiator (3 mg in 100 μ L HFIP, 0.002 mmol, [Initiator]:[CTA] = 1:5) was added to the reaction mixture. Oxygen was removed from the reaction by freeze-thaw degassing three times. The reaction was then placed in an oil bath at 60 °C for 2.5 h (or for a length of time as specified for desired DP). After 2.5 h the reaction vessel was cooled and opened to air. The crude reaction mixture was purified by dialysis from H₂O using 1kD MWCO RC dialysis tubing, stirred for 16 h. Pure polymer was isolated as a yellow oil after lyophilisation. Polymer was submitted for ¹³C DEPT NMR characterisation.

StyThy:MAh 1:1 monomer feed ratio = 99 mg in DMSO- d_6

StyThy:MAh 1:3 monomer feed ratio = 92 mg in DMSO- d_6





Fig S3: DEPT ¹³C NMR CH₂ subspectra data for different monomer feed ratio polymers showing MSM repeating triad diagnostic peaks at 32-37 ppm in DMSO-*d*₆

End Group Fidelity: OEGMA block extension of [StyThy-alt-MAh]₄₉ macroRAFT agent

StyThy-*alt*-MAh copolymer (19.6 mg, 16.7 x10⁻³ kg/mol, 1.153 μ mol, 1 eq.) was dissolved in DMF (0.23 mL). OEGMA₈₋₉ (57.6 mg, 115.3 μ mol, 10 eq.) and 10 μ L of a stock solution of AIBN initiator (40 mg in 100 μ L DMF, 0.231 μ mol, [Initiator]:[macroCTA]:[OEGMA₈₋₉] = 1:5:500) was added to the reaction mixture. Oxygen was removed from the reaction by freeze-thaw degassing three times. The reaction was then placed in an oil bath at 60 °C for 7 h. After 7 h the reaction vessel was cooled and opened to air. The crude reaction mixture was purified by dialysis from H₂O using 25 kD MWCO RC dialysis tubing, stirred for 16 h. Pure polymer was isolated as a pale yellow sticky solid after lyophilisation.

[M]/ [CTA]	Conversion OEGMA/% ^a	Calc. DP ^b	M ^b _n POEGMA block x10 ⁻³	$M_{\rm n}{}^b$ Polymer x10 ⁻³	$M_{\rm n}{}^c$ x10 ⁻³	$M_{\rm w}{}^c { m x10^{-3}}$	Đ
100	82	82	40.8	57.5	37.4	44.7	1.20

^a Conversion based upon ¹H NMR data: comparison of 1H aromatic peak at 9.11 ppm of 3,5-dichloronitrobenzene standard with 1H olefin peak at 6.11 ppm of OEGMA₈₋₉ monomer ^b DP/M_n calculated from ¹H NMR conversions of OEGMA monomer where M_n = M(macroRAFT) + (conv.*M(monomer)). All M_n and M_w values are kg/mol. ^c M_n values from DMAc GPC data and are based upon PMMA calibration curves.

Controlled block extension to high conversion evidences end group fidelity of macroRAFT trithiocarbonate group.



Fig S4: ¹H NMR spectrum of [StyThy-alt-MAh]₄₉-co-[OEGMA]₈₂ copolymer in DMSO-d₆

DEPT 45 procedure and analysis

¹³C DEPT experiments were performed on a Bruker Avance 600 NMR spectrometer with a 5 mm TCI 1 H/²H-¹³C/¹⁵N cryoprobe. DEPT experiments were collected with 45, 90 and 135° ¹H pulses, each with the same number of scans. The individual subspectra were obtained during processing: CH signals are provided by the DEPT90; CH₂ signals are obtained by subtracting 1.0× the DEPT135 spectrum from the DEPT45 spectrum; CH₃ signals are obtained by adding 1.0× the DEPT135 spectrum and -1.414× the DEPT90 spectrum to the DEPT45 spectrum. The 1.0 and -1.414 factors are adjusted for each calculation to minimise the residual nulled signals.

Polymer was prepared as described above with a [StyThy]/[MAh]/[CTA]/[AIBN] ratio of 25/25/1/0.2. After 2.5 h at 60 °C, (91% StyThy conversion) polymer was isolated with $M_n = 9.6 \times 10^{-3} \text{ kg/mol}$ (calculated from $M_n = M(RAFT) + (\text{conv.*}M(\text{monomer}))$ and a D = 1.17 (GPC data determined by PMMA calibration curves in DMAc solvent).

NMR Samples: StyThy-*alt*-MAh: 45 mg/mL; Styrene homopolymer: 50 mg/mL; StyThy homopolymer: 95 mg/mL; StyThy-*alt*-MAh (initial feed ratio 1:7): 99 mg/mL; StyThy-*alt*-MAh (initial feed ratio 1:3): 92 mg/mL; StyThy-*alt*-MAh (initial feed ratio 1:1): 75 mg/mL all in DMSO-*d*₆



Fig S5: DEPT 45° ¹³C NMR spectrum of StyThy-alt-MAh copolymer in DMSO-d₆



Fig S6: DEPT CH₂ only ¹³C NMR Spectrum of StyThy-alt-MAh copolymer in DMSO-d₆



Fig S7: DEPT CH₃ only ¹³C NMR Spectrum of StyThy-alt-MAh copolymer in DMSO-d₆



Fig S8: DEPT 90° ¹³C NMR Spectrum of StyThy-alt-MAh copolymer in DMSO-d₆



Fig S9: HSQC NMR Spectrum of StyThy-*alt*-MAh copolymer in DMSO-*d*₆ (CH₂ groups are depicted as red spots; CH and CH₃ groups as blue spots)

References:

- 1. Yang, X.; Xu, P.; Ding, S.; Radosz, M.; Shen, Y. Polym. Preprints, 2004, 45, 1061.
- 2. Moad, G.; Chong, Y. K.; Rizzardo, E.; Postma, A.; Thang, S. H. Polymer, 2005, 46, 8458.