Supplementary information

Materials

4-Acryloyl morpholine (NAM, 97%), *N,N*-dimethylacrylamide (DMA, >99%) and *N*-hydroxyethylacrylamide (HEA, >97%) were obtained from Sigma-Aldrich and used as received without removing the inhibitor. Deuterium oxide (99.9% D atom) was obtained from Sigma Aldrich and used for ^{1}H NMR spectroscopy. Thermal initiator 2,2'-Azobis[2-(2-imidazolin-2-yl)propane]dihydrochloride (VA-044, Wako-Chem). RAFT agent, 3-((((1-carboxyethyl)thio)carbonothioyl)thio)propanoic acid (CETCP, catalogue:BM1429) was kindly donated by Boron Molecular. Solvents were acquired from commercial sources.

Instrumentation and Analysis

NMR spectroscopy

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-250, DPX-300, or DPX-400 spectrometer using deuterated solvent (Materials section).

Size exclusion chromatography

An Agilent Infinity II MDS instrument equipped with differential refractive index (DRI), viscometry (VS), dual angle light scatter (LS) and multiple wavelength UV detectors was used for SEC analysis. The system was fitted with 2 x PLgel Mixed D columns (300 x 7.5 mm) and a PLgel 5 μm guard column. The eluent used was DMF with 5 mmol NH_4BH_4 additive. Samples were run at 1 ml min^{-1} at 50'C. Poly(methyl methacrylate) standards (Agilent EasyVials) were used for calibration between 955,500 – 550 g mol^{-1}. Analyte samples were filtered membrane with 0.22 μm pore size before injection. Respectively, experimental molar mass ($M_{n,SEC}$) and dispersity ($Đ$) values of synthesized polymers were determined by conventional calibration using Agilent GPC/SEC software.

High throughput size exclusion chromatography

A Polymer Labs PL50 MkII instrument equipped with differential refractive index (DRI) was used for high throughput SEC analysis. The system was fitted with a PL Rapide F column (100 x 10 mm) and a PL Rapide M column (100 x 10 mm). The eluent used was DMF with 1 wt% LiBr additive. Samples were run at 2 ml min^{-1} at 50'C. Poly(methyl methacrylate) standards (Agilent EasyVials) were used for calibration between 1,600,000 – 1,800 g mol^{-1}. Analyte samples were dissolved in plate, and then sampled directly from the plate without filtering. Respectively, experimental molar mass ($M_{n,SEC}$) and dispersity ($Đ$) values of synthesized polymers were determined by conventional calibration using Agilent GPC/SEC software.

Theoretical molar mass calculation

$$M_{n,th} = \frac{[M]_0 p M_M}{[CTA]_0} + M_{CTA}$$

Equation S1 Calculation of theoretical number average molar mass ($M_{n,th}$) where $[M]_0$ and $[CTA]_0$ are the initial concentrations (in mol dm-3) of monomer and chain transfer agent respectively. p is the monomer conversion as determined by ^{1}H NMR spectroscopy. M_M and M_{CTA} are the molar masses (g mol^{-1}) of the monomer and chain transfer agent respectively.

PCR-machine

A Techne-Prime (full size) PCR machine fitted with a 96 well heating block for 200 µL tubes was used for all PCR-RAFT polymerisations. The heating cycle was set to ramp at maximum heating rate to 100°C, hold for 5 mins, and return to 20°C at maximum rate and stop.

MALDI-TOF

MALDI-TOF was performed on a Bruker Daltonics Autoflex Speed, equipped with a 337 nm nitrogen laser and operating in reflectron positive mode. trans-2-[3-(4-tert-Butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB), was used as a matrix (20 mg mL^{-1} in Acetonitrile) without further purification. NaI salt was used as an ionization agent (10 mg mL^{-1} in Acetonitrile). Matrix, salts and polymer solution (10 mg mL^{-1} in Acetonitrile) were mixed in a 5 : 2 : 5 ratio, followed by deposition of 1 µL of the mixture onto the MALDI target before insertion into the ion source chamber.

Synthesis procedures

Preparation of CEPTC stock solution

200 mg of CEPTC was added to a 1.5 mL Eppendorf tube, and dissolved in 1 mL of a 50/50 DMSO/Water (v/v) ratio and then stored at 4°C.

Preparation of monomer + initiator mixtures

0.03 moles of monomer (4.23 g mass for NAM, 2.97 g for DMA and 3.45 g HEA) was added to a 10 mL volumetric flask and VA-044 (9.69 mg or 0.489 mL of a 20 mg mL^{-1} aqueous VA-044 stock solution) was added. The mixture was then topped up to 10 mL to make the final concentration of monomer 3 M and the [M]/[I] ratio = 500. These stock solutions were stored at 4°C.

General procedure for conventional scale RAFT polymerisation

Conventional RAFT polymerisation was performed as follows, NAM_{25} is given as an example. 72 µL of a CETCP (14.4 mg, 5.67 x 10^{-5} mol) stock solution in DMSO/Water (50/50, v/v, 200 mg mL^{-1}), was added into a 4 mL test tube without a stirrer bar. 472 µL volume of the NAM (3 M) + VA-044 ([M]/[I] = 500) aqueous mixture in water was added to the test tube, deoxygenated for 10 minutes by bubbling N_2 and immersed in a preheated oil bath at 70°C for 2 h. 20 µL samples were taken for ^1H NMR and SEC analysis.

General procedure for RAFT polymerisation in PCR machine (PCR-RAFT)

PCR-RAFT was performed as follows, NAM_{25} is given as an example. 7.2 µL volume of a CETCP (1.44 mg, 5.67 x 10^{-5} mol) stock solution in DMSO/Water (50/50, v/v, 200 mg mL^{-1}), was pipetted into a 200 µL PCR tube and 47.2 µL of a NAM (3 M) and VA-044 ([M]/[I] = 500) aqueous mixture was added. The tube was vortexed thoroughly and centrifuged such that all of the liquid was at the bottom of the tube. The tube was then placed into a position within the PCR machine and heated to 100°C for 5 mins using the method described above (instrumentation section). Different chain lengths were targeted by adding different volumes of CETCP stock solution.

Kinetic profile of PCR-RAFT polymerisation

50 µL of the NAM_{25} polymerisation mixture prepared for conventional scale RAFT polymerisation was added into eight separate PCR-tubes and seven placed in the PCR-machine and heated using the method described above

(instrumentation section). One tube was held for the t = 0 measurement. After 15, 30, 45, 60, 75, 90 and 120 s, a sample was removed by quickly opening the lid, taking a sample and immediately immersing it in liquid N_2 to stop further polymerisation. Samples were then analysed with ^{1}H NMR spectroscopy to determine monomer conversion.

Reproducibility study

Reproducibility of heating position

50 µL of a NAM_{50} polymerisation mixture prepared at conventional scale was added into six separate PCR-tubes and placed in the PCR-machine at positions chosen by a third party (A4, F4, D6, E8, F8, D10) and heated using the method described above (instrumentation section).

Reproducibility of PCR-RAFT polymerisation mixture preparation

Six individual tubes were prepared with 3.6 µL of the CEPTC stock solution in DMSO/Water (50/50, v/v, 200 mg mL^{-1}), and 47.2 µL volume of NAM (3 M) and VA-044 ([M]/[I] = 500) aqueous mixture. These were then placed in the same positions as above and heated using the method described above (instrumentation section).

Variation in target chain length

To prepare different chain length polymers in increments of DP25, 100 µL of the NAM (3M) and VA-044 ([M]/[I] = 500) was added to 200 µL PCR tubes containing different volumes of CEPTC stock solution in DMSO/Water (50/50, v/v, 200 mg mL^{-1}; DP25 = 15.24 µL, DP50 = 7.62 µL, DP75 = 5.08 µL, DP100 = 3.81 µL, DP125 =3.05 µL, DP150 =2.54 µL, DP175 =2.18 µL, DP200 =1.91 µL). These were then mixed, centrifuged and heated within the PCR-machine as described above.

Preparation of triblock copolymers

Six triblock copolymers (1) $pNAM_{25}$-*b*-$pDMA_{25}$-*b*-$pHEA_{25}$, (2) $pNAM_{25}$-*b*-$pHEA_{25}$-*b*-$pDMA_{25}$, (3) $pHEA_{25}$-*b*-$pDMA_{25}$-*b*-$pNAM_{25}$, (4) $pHEA_{25}$-*b*-$pNAM_{25}$-*b*-$pDMA_{25}$, (5) $pDMA_{25}$-*b*-$pNAM_{25}$-*b*-$pHEA_{25}$, (6) $pDMA_{25}$-*b*-$pHEA_{25}$-*b*-$pNAM_{25}$) were prepared using PCR-RAFT. As an example $pNAM_{25}$-*b*-$pDMA_{25}$-*b*-$pHEA_{25}$ is described. 7.2 µL of CEPTC stock solution in DMSO/Water (50/50, v/v, 200 mg mL^{-1}) and 47.2 µL of NAM (3M) + VA-044 aqueous mixture were added to three separate PCR tubes. These were then mixed, centrifuged and heated within the PCR-machine as described above. The first tube was removed and 47.2 µL of the DMA + VA-044 aqueous mixture was added to the remaining two tubes and the mixing, centrifugation and heating cycle repeated. The second tube was subsequently removed, and 47.2 µL volume of the HEA + VA-044 aqueous mixture was added to the final tube and the mixing, centrifugation and heating cycle repeated. For a more detailed explanation please see **Figure S4**. All three tubes (tube 1 = $pNAM_{25}$, tube 2 = $pNAM_{25}$-*b*-$pDMA_{25}$, tube 3 = $pNAM_{25}$-*b*-$pDMA_{25}$-*b*-$pHEA_{25}$) were taken for ^{1}H NMR and SEC analysis.

Preparation of binary statistical copolymers

Three sets of binary statistic copolymers ($pHEA_n$-*co*-$pNAM_m$, $pDMA_n$-*co*-$pNAM_m$, $pDMA_n$-*co*-$pHEA_m$) with varying amount of *n* (0-100%) and *m* (100-0%) were prepared targeting a total DP of 50 using the PCR-RAFT method described. As an example HEA_n-*co*-NAM_m is described. 3.6 µL of CEPTC stock solution in DMSO/Water (50/50, v/v, 200 mg mL^{-1}) was added to 11 separate PCR-tubes. (100-0 µL, tube 1- 11 in increments of 10 µL) of HEA + VA-044 aqueous solution and (0-100 µL, tube 1-11 in increments of 10 µL) of NAM + VA-044 aqueous solution were pipetted into the 11 separate tubes. The tubes were then mixed, centrifuged and heated as described in the general procedure. All 11 tubes (tube 1 = $pHEA_{100\%}$, tube 2 = $pHEA_{90\%}$-*co*-$pNAM_{10\%}$, tube 3 = $pHEA_{80\%}$-*co*-$pNAM_{20\%}$, tube 4 = $pHEA_{70\%}$-*co*-$pNAM_{30\%}$, tube 5 = $pHEA_{60\%}$-*co*-$pNAM_{40\%}$, tube 6 = $pHEA_{50\%}$-*co*-$pNAM_{50\%}$, tube 7 = $pHEA_{40\%}$-*co*-$pNAM_{60\%}$, tube 8 = $pHEA_{30\%}$-*co*-$pNAM_{70\%}$, tube 9 = $pHEA_{20\%}$-*co*-$pNAM_{80\%}$, tube 10 = $pHEA_{10\%}$-*co*-$pNAM_{90\%}$, tube 11 = $pNAM_{100\%}$, were taken for ^1H NMR and SEC analysis.

Supplementary data

Table S1. Comparison of PCR machine heating and conventional RAFT polymerisation.

Heating	Conversion (%)[a]	$M_{n,th}$[b]	$M_{n,SEC}$[c]	$Đ$[c]
PCR machine	>99	3800	4300	1.16
Conventional	>99	3800	4000	1.14

[a]Determined using ^{1}H NMR spectroscopy, [b]Calculated using Equation 1, [c]Determined using DMF-SEC.

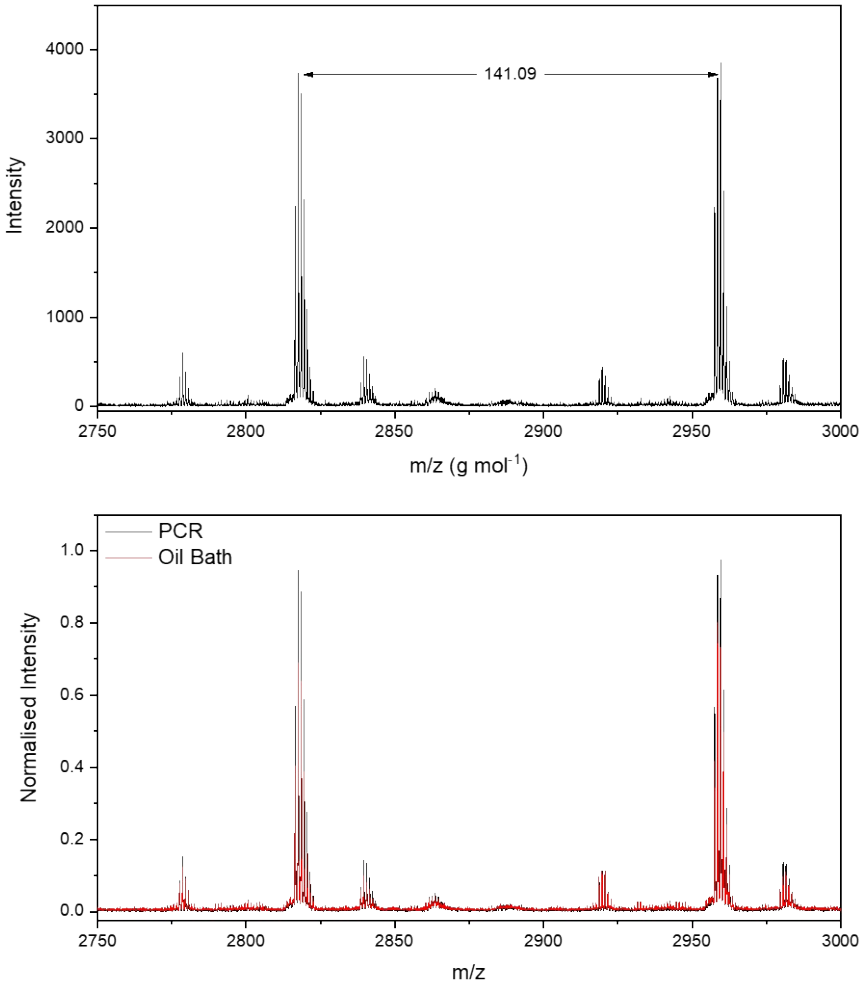

Figure S1. MALDI-TOF spectra of $pNAM_{25}$ synthesised by ultrafast PCR-RAFT (top), and overlay with the oil bath conventional RAFT polymerisation (bottom).

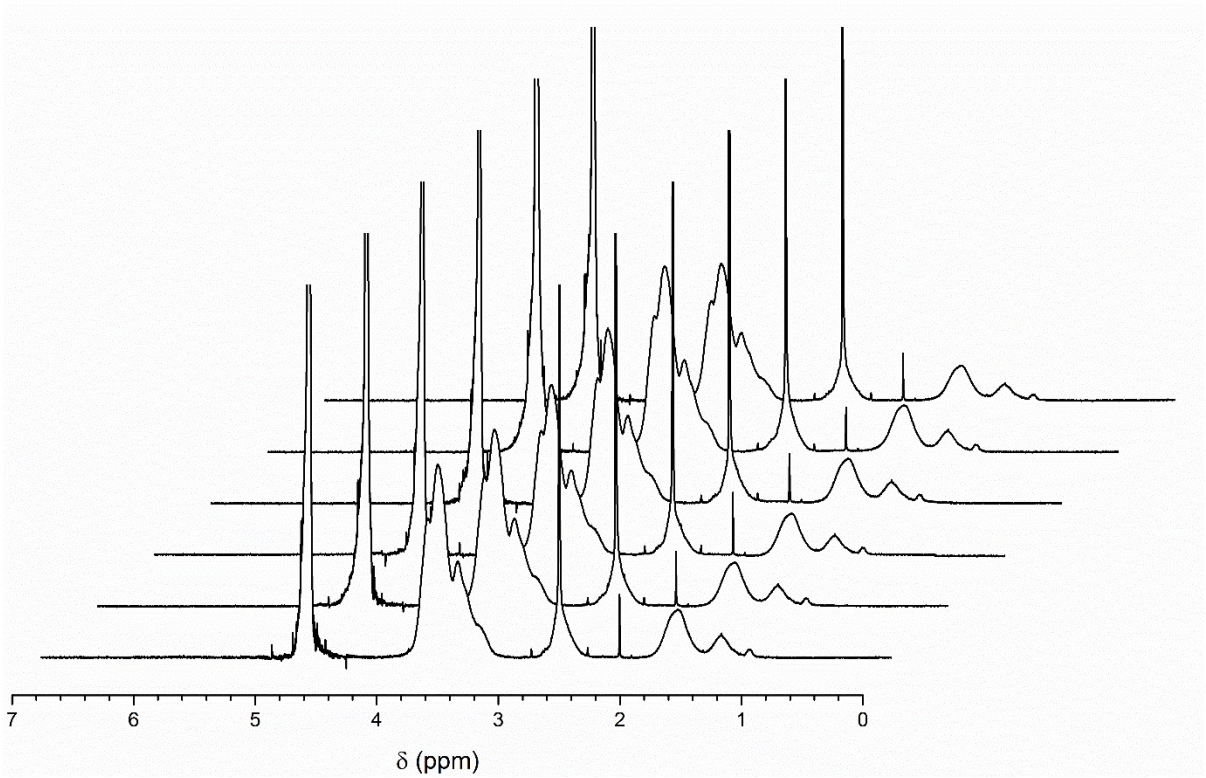

Figure S2. ^{1}H NMR spectra in D_2O of the six $pNAM_{50}$ prepared from same mother solution, aliquoted and heated in different wells of the 96 well thermocycler.

Table S2. Characterisation data for the six $pNAM_{50}$ prepared in the reproducibility study from the same mother solution and heated in different wells of the 96 well thermocycler.

Position	Conversion (%)[a]	$M_{n,SEC}$[b]	$M_{w,SEC}$[c]	$Đ$[c]
A4	>99	7300	8200	1.14
F4	>99	7400	8300	1.13
D6	>99	7300	8300	1.13
E8	>99	7400	8300	1.12
F8	>99	7200	8300	1.15
D10	>99	7300	8300	1.14

[a]Determined using ^{1}H NMR spectroscopy, [b]Calculated using Equation S1, [c]Determined using DMF-SEC using PMMA calibration.

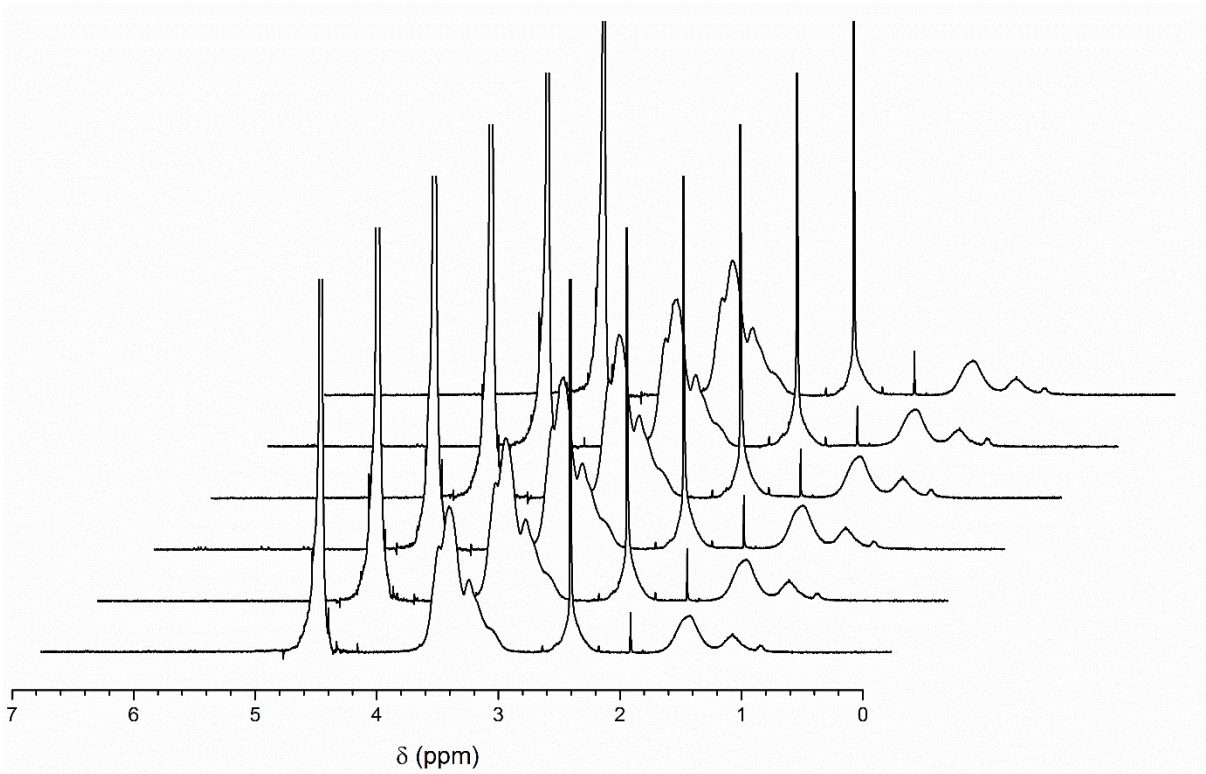

Figure S3. ^{1}H NMR spectra in D_2O of the six $pNAM_{50}$ prepared individually and heated in different wells of the 96 well thermocycler.

Table S3. Characterisation data for the six $pNAM_{50}$ in the reproducibility study prepared individually and heated in different wells of the 96 well thermocycler.

Position	Conversion (%)[a]	$M_{n,th}$[b]	$M_{n,SEC}$[c]	$Đ$[c]
A4	>99	7200	8200	1.15
F4	>99	6800	7700	1.14
D6	>99	7400	8300	1.13
E8	>99	7800	9000	1.15
F8	>99	7300	8400	1.14
D10	>99	6800	7800	1.16

[a]Determined using ^{1}H NMR spectroscopy, [b]Calculated using Equation S1, [c]Determined using DMF-SEC using PMMA calibration.

Table S4. Characterisation data for pNAM of varying chain length (DP25 – DP200)

DP_{target}	Conversion (%)[a]	$M_{n,th}$[b]	$M_{n,SEC}$[c]	$Đ$[c]
25	>99	3800	4000	1.16
50	>99	7300	7200	1.19
75	>99	10800	9400	1.18
100	>99	14400	11900	1.19
125	>99	17900	14300	1.22
150	>99	21400	16300	1.23
175	>99	25900	19100	1.21
200	>99	28400	26700	1.30

[a]Determined using ^{1}H NMR spectroscopy, [b]Calculated using Equation S1, [c]Determined using DMF-SEC using PMMA calibration.

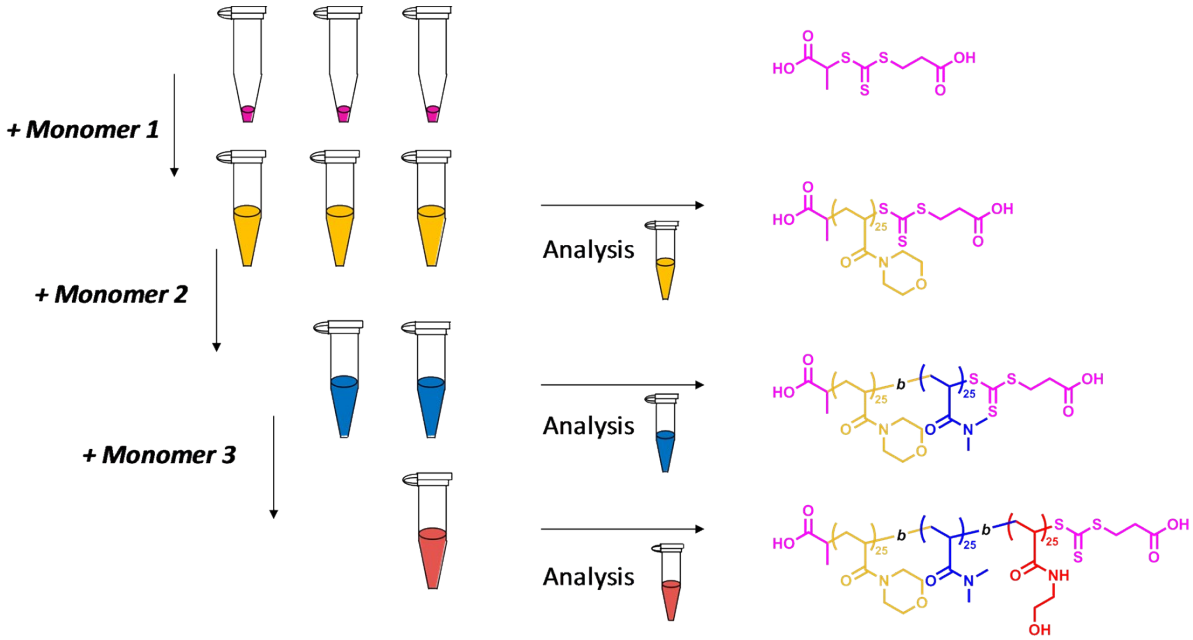

Figure S4. Schematic representation of the analysis method for preparing triblock copolymers via PCR-RAFT by removing a sample after each heating cycle.

Table S5. Characterisation data for the 6 triblock copolymers and their preceding diblock and homopolymers prepared via PCR-RAFT.

Structure	Conversion (%)[a]	$M_{n,th}$[b]	$M_{n,SEC}$[c]	$Đ$[c]
$pNAM_{25}$	>99	3800	4800	1.15
$pNAM_{25}$-$pDMA_{25}$	97	6300	7200	1.21
$pNAM_{25}$-$pDMA_{25}$-$pHEA_{25}$	98	9200	10000	1.25
$pNAM_{25}$	99	3800	4200	1.16
$pNAM_{25}$-$pHEA_{25}$	>99	6700	8200	1.22
$pNAM_{25}$-$pHEA_{25}$-$pDMA_{25}$	97	9200	11400	1.26
$pHEAm_{25}$	97	3100	5700	1.17
$pHEAm_{25}$-$pDMA_{25}$	97	5600	8100	1.19
$pHEAm_{25}$-$pDMA_{25}$-$pNAM_{25}$	>99	9200	11200	1.22
$pHEAm_{25}$	97	3100	5500	1.16
$pHEAm_{25}$-$pNAM_{25}$	97	6700	8500	1.20
$pHEAm_{25}$-$pNAM_{25}$-$pDMA_{25}$	98	9200	10700	1.20
$pDMA_{25}$	98	2800	4200	1.15
$pDMA_{25}$-$pNAM_{25}$	99	6300	7800	1.14
$pDMA_{25}$-$pNAM_{25}$-$pHEA_{25}$	98	9200	11300	1.16
$pDMA_{25}$	98	2800	4400	1.15
$pDMA_{25}$-$pHEA_{25}$	98	5600	8200	1.18
$pDMA_{25}$-$pHEA_{25}$-$pNAM_{25}$	98	9200	11700	1.22

[a]Determined using ^{1}H NMR spectroscopy, [b]Calculated using Equation S1, [c]Determined using DMF-SEC using PMMA calibration.

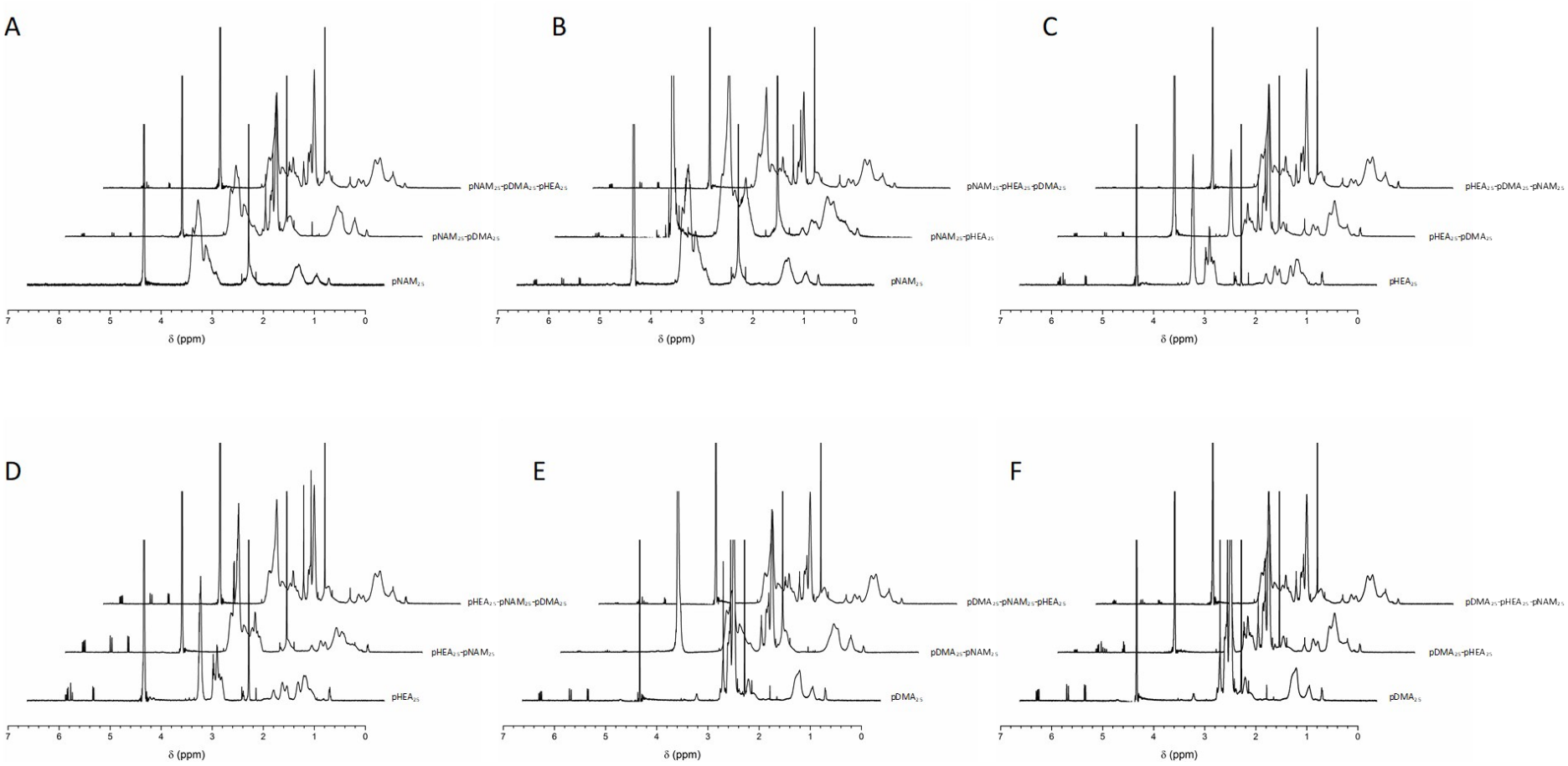

Figure S5. ^{1}H NMR spectra in D_2O of the each block for the six triblocks prepared using 3 heating cycles (A) $pNAM_{25}$-$pDMA_{25}$-$pHEA_{25}$ (B) $pNAM_{25}$-$pHEA_{25}$-$pDMA_{25}$ (C) $pHEAm_{25}$-$pDMA_{25}$-$pNAM_{25}$ (D) $pHEAm_{25}$-$pNAM_{25}$-$pDMA_{25}$ (E) $pDMA_{25}$-$pNAM_{25}$-$pHEA_{25}$ (F) $pDMA_{25}$-$pHEA_{25}$-$pNAM_{25}$ using PCR-RAFT.

Table S6. Characterisation data for the five binary copolymers analysed by both the rapid-SEC and conventional SEC and their relative positions.

				Rapid-SEC		Conventional SEC	
Position	Co-monomer ratio (%)		$M_{n,th}$ (g mol^{-1})^a	$M_{n,SEC}$ (g mol^{-1})^b	$Đ^b$	$M_{n,SEC}$ (g mol^{-1})^b	$Đ^b$
	HEA	NAM					
A1	100	0	6000	4000	1.41	7600	1.37
A6	50	50	6700	7700	1.28	8100	1.29
	DMA	NAM					
B1	100	0	5300	3800	1.28	6700	1.23
B7	40	60	6500	4800	1.26	6800	1.23
	DMA	HEA					
C1	100	0	5300	7900	1.35	7000	1.24

^{a}Calculated using Equation S1, ^{b}Determined using DMF-SEC using PMMA calibration.

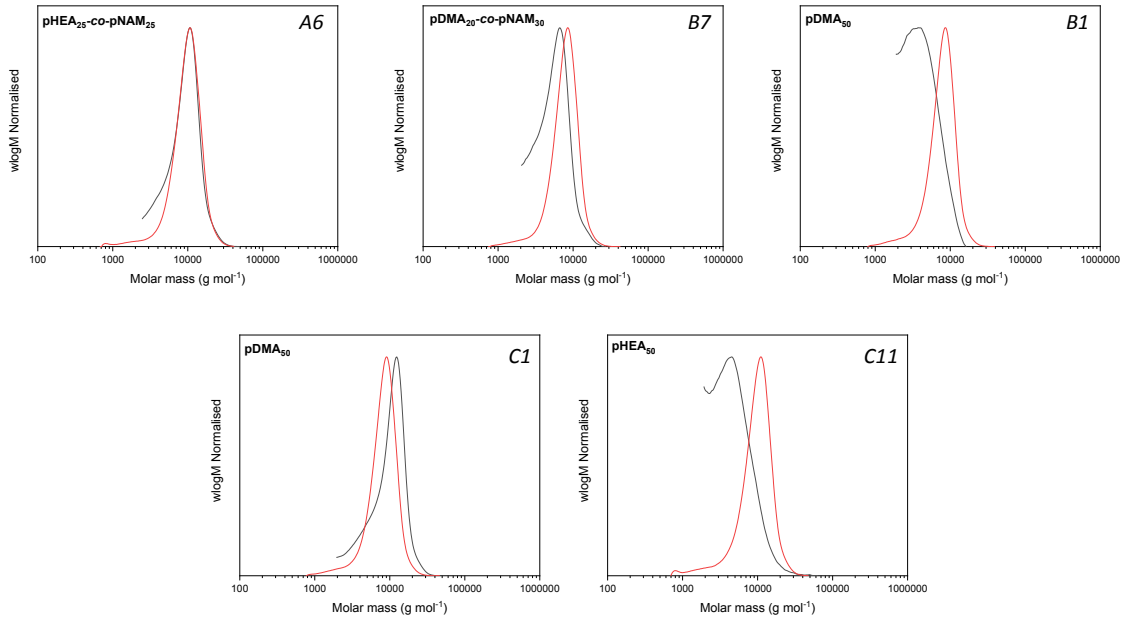

Figure S6. SEC chromatograms of pHEA$_{25}$-*co*-pNAM$_{25}$ (Position A6), pDMA$_{20}$-*co*-pNAM$_{30}$ (Position B7), pDMA$_{50}$ (Position B1), pDMA$_{50}$ (Position C1), pHEA$_{50}$ (Position C11) comparing the rapid-SEC (grey line) and conventional SEC (red line).

Figure S7. Digital photograph of the equipment required for the experiments in this study, excluding reagents.