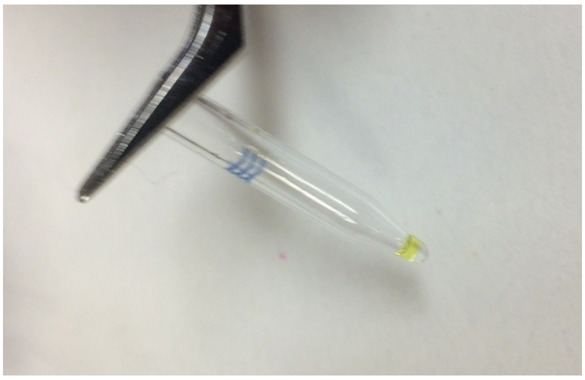
Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

Microscale Synthesis of Multiblock Copolymers Using Ultrafast RAFT Polymerization



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Materials:

2-((butylthio)-carbonothioyl) thio propanoic acid (PABTC) was synthesised according to the reported literature and recrystallized at least twice in hexane before use.[1] N-Acryloylmorpholine (NAM) N,N-Dimethylacrylamide (DMA) were filtered through a basic aluminium oxide (activated, basic, Brockman I, standard grade) to remove the radical inhibitor. 2,2′-azobis[2-(2-imidazolin-2yl)propane] dihydrochloride (VA-044, Wako), Dioxane (Sigma-Aldrich, >99%), HEAm (Sigma-Aldrich, > 97 %) and HPCL-grade H_2O (sigma-aldrich, > 99%) were used without further purification.

Instruments:

Nuclear Magnetic Resonance (NMR) spectroscopy (^1H NMR spectra) were recorded on a Bruker HD 400 spectrometer (400 MHz) at 27 °C using d_6-DMSO as solvent and the residual proton signal of the solvent (δ H = 2.50 ppm) was used as internal reference. Chemical shift values (δ) are reported in ppm. ACDLABS software was used to analyse the data obtained.

Number-average molar masses ($M_{n,SEC}$) and dispersity values ($Đ$) were determined using Size exclusion Chromatography (SEC) with THF or DMF as the eluent, depending on the composition of the copolymer. For conventional scale synthesis (for scales greater than 20 µL) polymer samples diluted with GPC eluent (1.5 ml) were filtered through a nylon membrane with 0.22 µm pore size before injection. For microscale synthesis with the microvolume inserts, the mixture was diluted with GPC eluent (200 µL) in the reaction vessels and were fitted inside a GPC sample vial. These were directly injected (80 µL) in to the SEC system. The THF system, Agilent 390-LC MDS instrument equipped with differential refractive index (DRI), viscometry (VS), dual angle light scatter (LS) and dual wavelength UV detectors. The system was equipped with 2 x PLgel Mixed C columns (300 x 7.5 mm) and a PLgel 5 µm guard column. The eluent is THF with 2 % TEA (triethylamine) and 0.01 % BHT (butylated hydroxytoluene) additives. Samples were run at 1ml/min at 30 °C. Poly(methyl methacrylate) (PMMA) standards (Agilent EasyVials) were used for calibration between 955,000 – 550 $gmol^{-1}$. The DMF system was operating on Agilent 390-LC MDS instrument, which was equipped with differential refractive index (DRI), viscometry (VS), dual angle light scatter (LS) and UV detectors. The system was equipped with 2 x PLgel Mixed D columns (300 x 7.5 mm) and a PLgel 5 µm guard column. The DMF eluent had 5 mmol NH_4BF_4 additive. Samples were run at 1 ml/min at 50 °C. PMMA were used for calibration. Both instruments were equipped with an autosampler. Experimental molar mass ($\boldsymbol{M_{n,SEC}}$) and dispersity ($\boldsymbol{Đ}$) values of synthesized polymers were determined based on PMMA calibration using Agilent GPC/SEC software.

Determination of monomer conversions.

Monomer conversion (ρ) were calculated from ^1H NMR sprectra using the following equation from Gody's protocol:[2]

$$\rho = \frac{[M]_0 - [M]_t}{[M]_0} = 1 - \frac{[M]_t}{[M]_0} = 1 - \frac{\int M_{5.5-7.00\,ppm} \Big/ \int CTA_{CH3}}{DP_{targeted}} \quad \text{(Eqn 1)}$$

Where $[M]_0$ is the initial monomer concentration and $[M]_t$ is the concentrations of the monomer at time t. ($\int M_{5.5\text{-}7.00\ ppm}$ / ($\int CTA_{CH3}$) is the corrected integrals for the vinylic protons of the monomer, $DP_{targeted}$ is the degree of the polymeirsation targeted and $\int_{CTA\text{-}CH3}$ is the integral of the 3 methyl protons belonging to the Z group of the RAFT agent (CH_2-CH_3) used as an internal reference. Note, the integral range for the vinylic protons is slightly wider than previously reported, this is to sufficiently cover all the vinylic protons.

Calculation of theoretical number average molar mass $M_{n,th}$

The theoretical number average molar mass ($M_{n,th}$) is calculated using equation (Eq 2).

$$M_{n,th} = \frac{[M]_0 \rho M_M}{[CTA]_0 + 2f[I]_0(1 - e^{-k_d t})\left(1 - \frac{f_c}{2}\right)} + M_{CTA} \qquad \text{(Eq 2)}$$

Where $[M]_0$, $[I]_0$and $[CTA]_0$ are the initial concentrations of the monomer, initiator and chain transfer agent respectively; ρ is the monomer conversion as determined by ^{1}H NMR (from Eqn 1), M_M and M_{CTA} are the molar molar masses (gmol^{-1}) of the monomer and chain transfer agent respectively. The factor "2" accounts for two radicals generated from one molecule of azoinitiator with efficiency f (assumed to be 0.5) to react with monomers to initiate propagating chains. The decomposition rate constant, k_d is calculated from the Arrhenius equation for a given temperature (Eqn 3). Time, t is polymerisation time (in seconds). The term ($1-f_c/2$) represents the number of chains produced in a radical-radical termination events. The coupling factor, f_c has a value between 1 (100% termination occur by bimolecular combination) and 0 (100% termination occurs by disproportionation). For simplicity in this study 100 % termination is assumed to be by disproportionation (fc = 0).

Calculation of the decomposition rate constant kd

$$k_d = Ae^{-E_A/RT} \qquad \text{(Eq 3)}$$

T is the temperature (in Kelvin). R is the molar gas constant (or universal gas constant) and has a value of 8.314 Jmol^{-1}. E_A is the activation energy, which is 10800 Jmol^{-1} for VA-044 (obtained from wako).[3] The Pre-exponential factor, A is determined using Eqn 4 shown below:

$$A = \frac{k_{d(317K)}}{e^{-Ea/RT_{317K}}} \qquad \text{(Eqn 4)}$$

Where $k_{d(317K)}$ is the decomposition rate when the initiator has a 10 hr half-life, at the specific temperature of the initiator. This temperature is 44 °C or 317 K for VA-044. The decomposition rate for a given half-life is a mathematical constant (for 10 hrs, it is 1.92 x 10^{-5} s^{-1}). In most cases,, where available, the 10 hr half-life temperature and activation energy of commercial thermal initiators can be obtained from the supplier (Wako).[3] From this the pre-exponential factor of VA-044 has a value of 1.18 x 10^{13}.

Calculation of the theoretical number fraction of living chains (livingness, L)

The number fraction of living chains is calculated using equation 5.

$$L = \frac{[CTA]_0}{([CTA]_0 + 2f[I]_0(1 - e^{-k_d t})\left(\frac{1 - f_c}{2}\right)} \qquad \text{(Eq5)}$$

All side reactions with oxygen is neglected.

General procedure for microscale polymerisation.

Master mix with CTA, Monomer, initiator and solvent (preparation of the master mix with CTA described below) is added into microvolume inserts using regular air displacement micropipettes (P10's for 1 - 10 µL reactions). The insert is heated for 3 mins at 100 °C in an oil bath. The insert is either directly diluted with GPC eluent and inserted into a GPC vial, directly used for SEC analysis or alternatively diluted with deuterated DMSO for ^{1}H NMR analysis. Duplicate reactions are required to achieve both analysis (one for each).

General Procedure for Conventional scale polymerisation (500 µL scale)

Master mix with CTA, Monomer, initiator and solvent (preparation of the master mix with CTA described below) is added into test tube (with or without stirrer) using a regular air displacement micropipettes (P1000) to pipette 500 µL. The test tube is heated for 3 mins at 100 °C in an oil bath. Approximately 10 µL is used for GPC and NMR analysis.

General procedure preparing the for master mix with CTA (with NAM, 3M, DPn = 25)

The RAFT agent PABTC (67.5 mg, 0.28 mmol, 1 eq), is weighed into a sealable vial. NAM is carefully weighed directly into the same vial (1000 mg, 7.1 mmol, 25 eq). Dioxane (294 µL) and water (1061 µL) is added and vortexed until the PABTC is completely dissolved. The solution was cooled in fridge or ice until the mixture is sufficiently below the room temperature before adding a stock solution of VA-044 (114.5 µL of 20 mg/ml stock solution) and vortex. Note, the solution may appear cloudy when chilled but will return back to clear solution at ambient temperatures.

In this study, a stock initiator solution is prepared and used to avoid weighing minute amount of initiator (2.29 mg). It is important to note that all initiator stock solution and master mix's once the initiator is added to be kept on ice or stored in the fridge to avoid decomposition of the initiator.

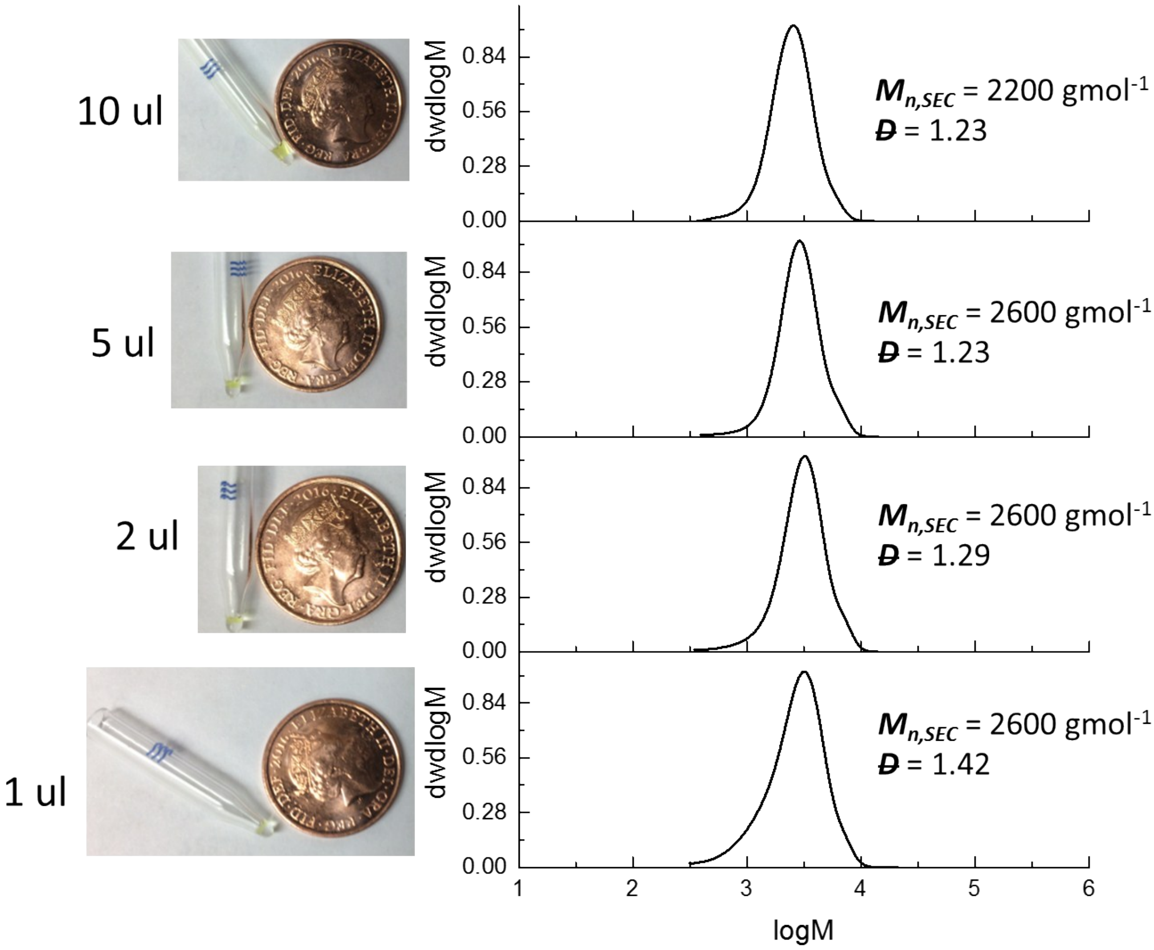


Figure S1: Polymerisation of P[NAM]25 carried out different scale inside microvolume inserts. At range of scales: 10 µL, 5 µL, 2 µL and 1 µL.

Table S1: The percentage of the weight loss of the reaction mixture in the microvolume inserts from evaporation.

Scale	Percentage of weight loss
10 µL	**14 %**
5 µL	**26 %**
2 µL	**43 %**
1 µL	**46 %**

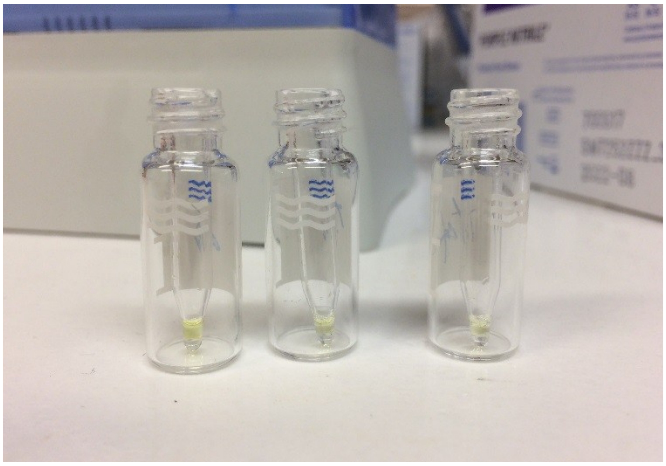
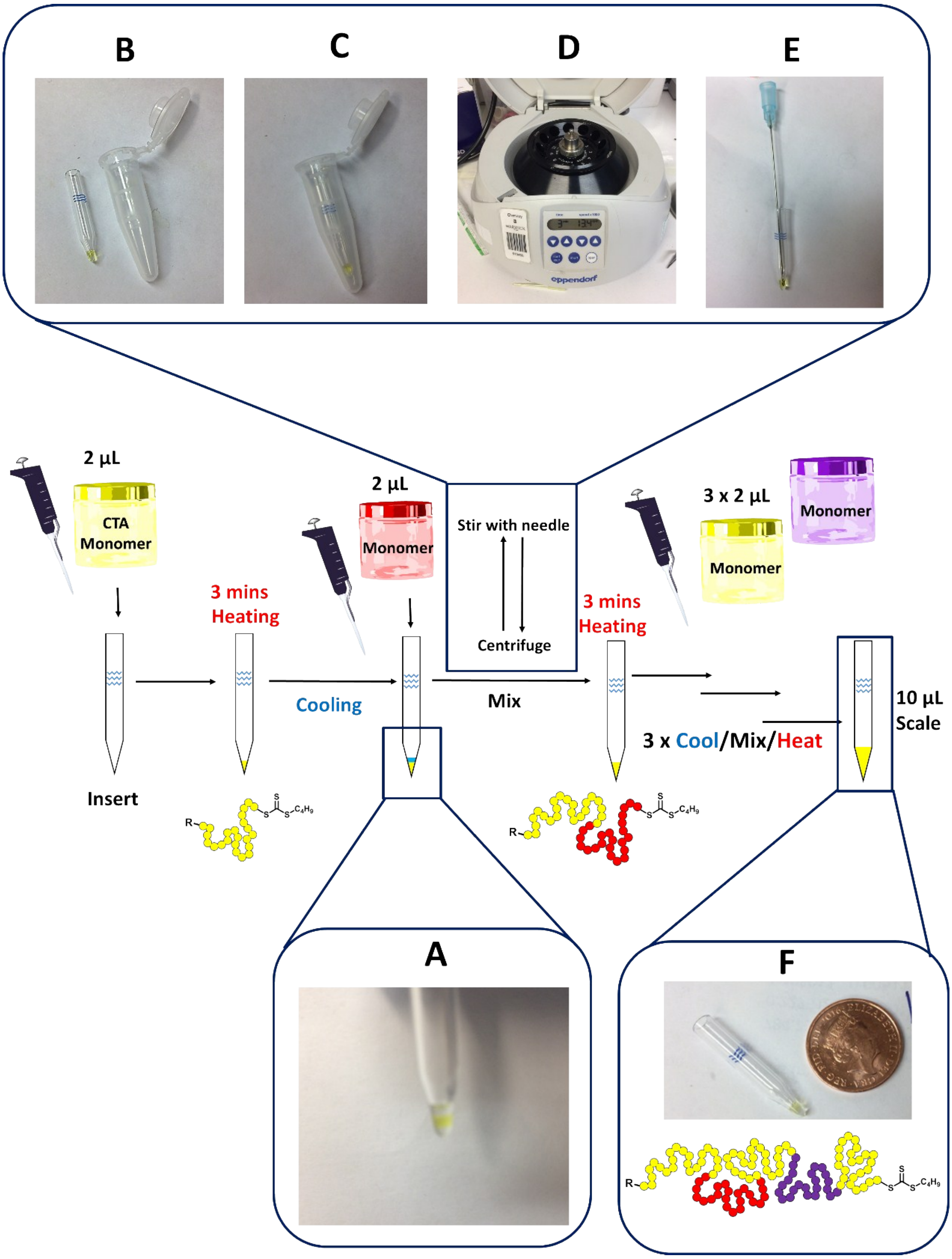


Figure S2: Photograph of the inserts in the GPC vials before dilution.



Scheme S1: Microscale synthesis of multiblock copolymers in 200 uL inserts.

General scheme: master mix with CTA, is added into insert using a regular air displacement micropipettes. After 3 mins of heating at 100 °C in an oil bath, the insert is cooled. For sequential chain extension, chain extension master mix is directly added into the inserts using the micropipette. **A** shows layers of macro CTA solution and newly added monomer layer. The mixture is mixed thoroughly by centrifuge and stirring: **B** and **C** photo showing the inserts next to and inside an Eppendorf tube. **D** photo of the centrifuge used in the study. **E** photo of a typical needle used to stir the reaction mixture inside the inserts. The resulting mixture is heated for additional 3 minutes. These processes are repeated until desired multiblock is obtained: **F** photo of the final (pentablock, 10 µL scale) next to a penny coin for a comparison in size. A detailed general procedure is described below.

General procedure for microscale multiblock synthesis

2 µL of the master mix with CTA (preparation of the CTA master mix described above) was added into the insert(s) using a regular air displacement micropipettes (P10's). After 3 mins of heating at 100 °C in an oil bath, the insert is cooled with liquid nitrogen until the insert is frozen (approximately 30 seconds). For sequential chain extension, 2 µL of a separate master mix with monomer (with identical Monomer concentration to previous block to target the same DP_n), initiator and solvent (no CTA) (preparation of chain extension master described below) was directly added using the micropipette. For thorough mixing, initially the inserts are placed inside an Eppendorf tube and centrifuged at 1.38 x 10^4 rpm for 1 minute to force the newly added monomer solution to bottom of the insert with the previous mixture. The mixtures were then crudely stirred with 23 gauge needle until the solution appeared homogenous and re-centrifuged (1.38 x 10^4 rpm for 1 minute). The mixture was then heated for 3 minutes 100 °C in an oil bath. This process was repeated for additional chain extensions. Tables S6, S7 has detailed conditions for specific multiblock described in the paper. For GPC and NMR analysis of each block see the **Scheme S2** for the analysis of the multiblock copolymers at microscale.

General procedure for conventional scale synthesis (done without a stirrer bar)

For comparison study with the microscale synthesis, conventional scale synthesis was carried without stirrer during polymerisation. Procedure follows: 500 µL of the master mix with CTA is added into insert using a regular air displacement micropipettes (P1000's). After 3 mins of heating at 100 °C in an oil bath, two aliquots of 10 µL of samples were taken out using P200's separately for GPC and NMR analysis. The reaction mixture was allowed to be cooled in ice, until the reaction mixture was sufficiently below room temperature. 500 µL of separate master mix (chain extension master described below) was directly added using the micropipette (P1000's). The layered mixture was carefully mixed thoroughly until the mixture was completely homogenous. Samples taken for GPC and NMR increased by additional 10 µL every 2 blocks i.e. 2 x 20 µL were taken 3rd and 4th block and 2 x 30 µL were taken for 5th (final) block. Multiblock obtained by this appeared identical to the multiblock made with stirring.

General procedure for preparing the chain extension master mix (NAM, 3M)

NAM is carefully weighed directly into the sealable vial (1000 mg, 7.1 mmol). Water (1061 µL) is added and then cool the solution in fridge or ice until the mixture is sufficiently below the room temperature. A stock solution of VA-044 (91.7 µL of 20 mg/ml stock solution) was added and vortexed. Note, combined with the initiator stock solution makes 3 M monomer concentration. The mixture can be used directly and should be stored in the fridge when not in use.

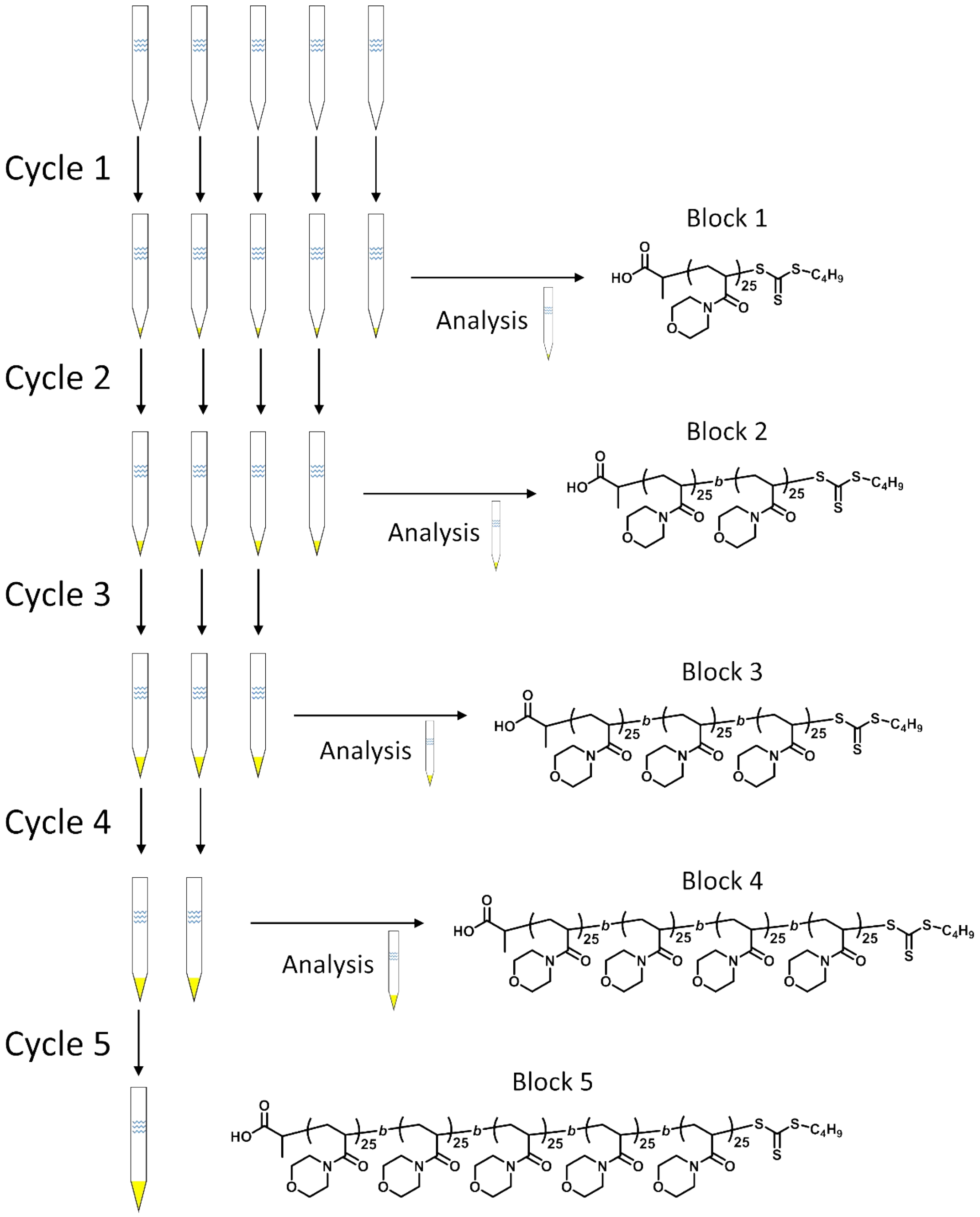
General procedure for preparing the chain extension master mix (DMA, 3M)

DMA is carefully weighed directly into the sealable vial (702 mg, 7.1 mmol). Water (1540 µL) is added and the solution was then cooled in fridge or ice until the mixture is sufficiently below the room temperature. A stock solution of VA-044 (91.7 µL of 20 mg/ml stock solution) was added and vortex.

Note, combined with the initiator stock solution makes 3 M monomer concentration. The mixture can be used directly and should be stored in the fridge when not in use.

General procedure for preparing the chain extension master mix (HEAm, 3M)

HEAm is carefully weighed directly into the sealable vial (816 mg, 7.1 mmol). Water (1535 µL) is added and then cool the solution in fridge or ice until the mixture is sufficiently below the room temperature. A stock solution of VA-044 (91.7 µL of 20 mg/ml stock solution) and vortex. Note, combined with the initiator stock solution makes 3 M monomer concentration. The mixture can be used directly and should be stored in the fridge when not in use.



Scheme S2: the method for analysis of the multiblock copolymers at microscale

Twice as many reactions are prepared as number of blocks and polymerised simultaneously. After each block cycle a whole insert is taken as a representative sample. Two separate samples per block are required to enable both GPC and NMR analysis.

Table S2: The percentage of the weight loss for each block extension during the preparation of P(NAM$_{25}$)$_5$.

	Percentage of weight loss[a]	
	2 µL per block[b]	500 µL per block[c]
Block 1	**43 %**	**3.7 %**
Block 2	**39 %**	**3.6 %**
Block 3	**40 %**	**3.6 %**
Block 4	**44 %**	**3.3 %**
Block 5	**28 %**	**2.7 %**

[a] Non-cumulative relative percentage weight loss per block before and after the reaction (3 mins heating at 100 °C). Calculated on the bases of the weight of the reaction mixture reaction added for the individual blocks.

[b] Reaction was carried out in a 200 µL microvolume insert vials

[c] Reaction was carried out in a conventional test tube (5.4 mL)

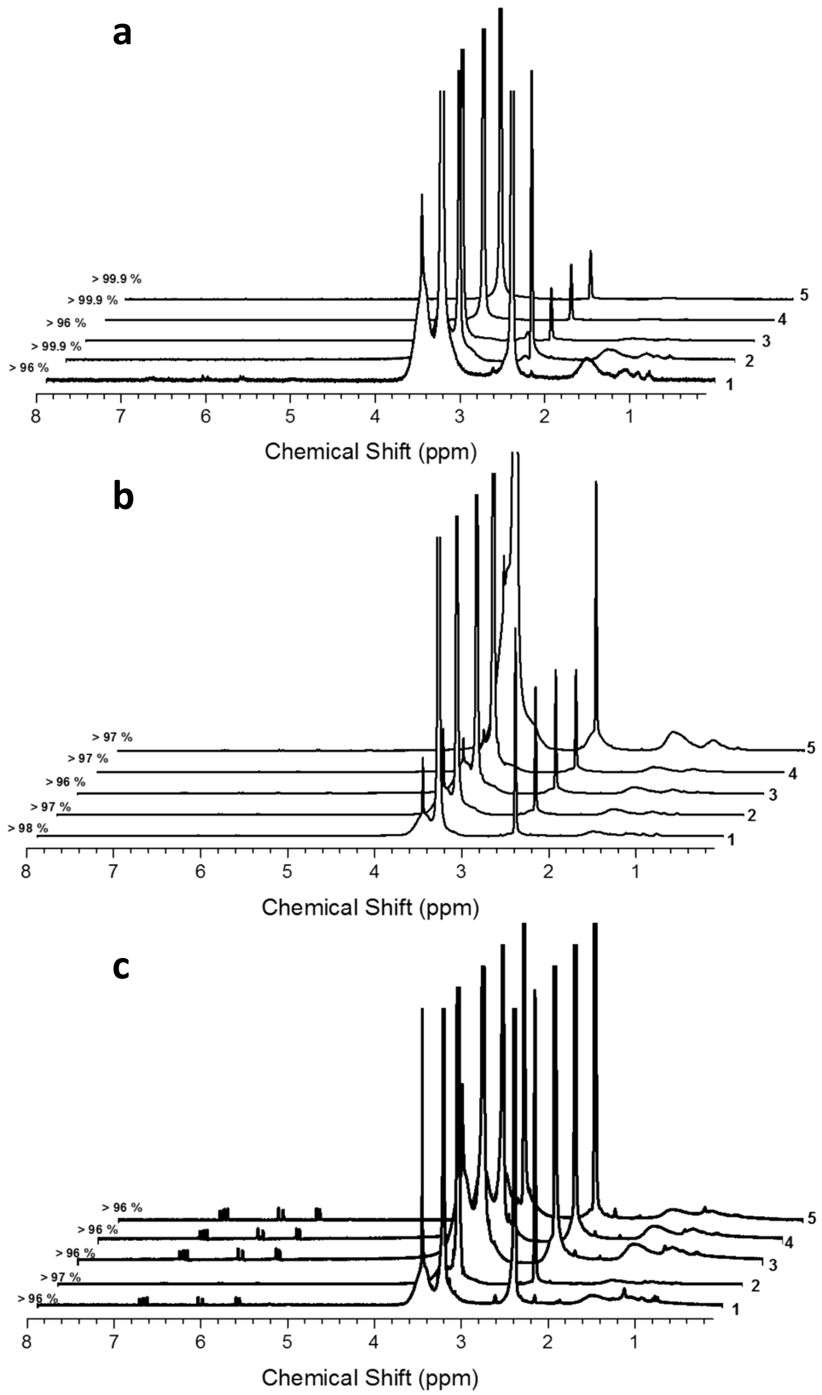


Figure S3 ^{1}H NMR spectra (DMSO, 400 MHz) showing the conversion of NAM for each new block during the multichain extension to generate P(NAM$_{25}$)$_5$, after 3 mins per block. Scale of the reaction: a) 500 µL per block, b) 5 µL per block, c) 2 µL per block.

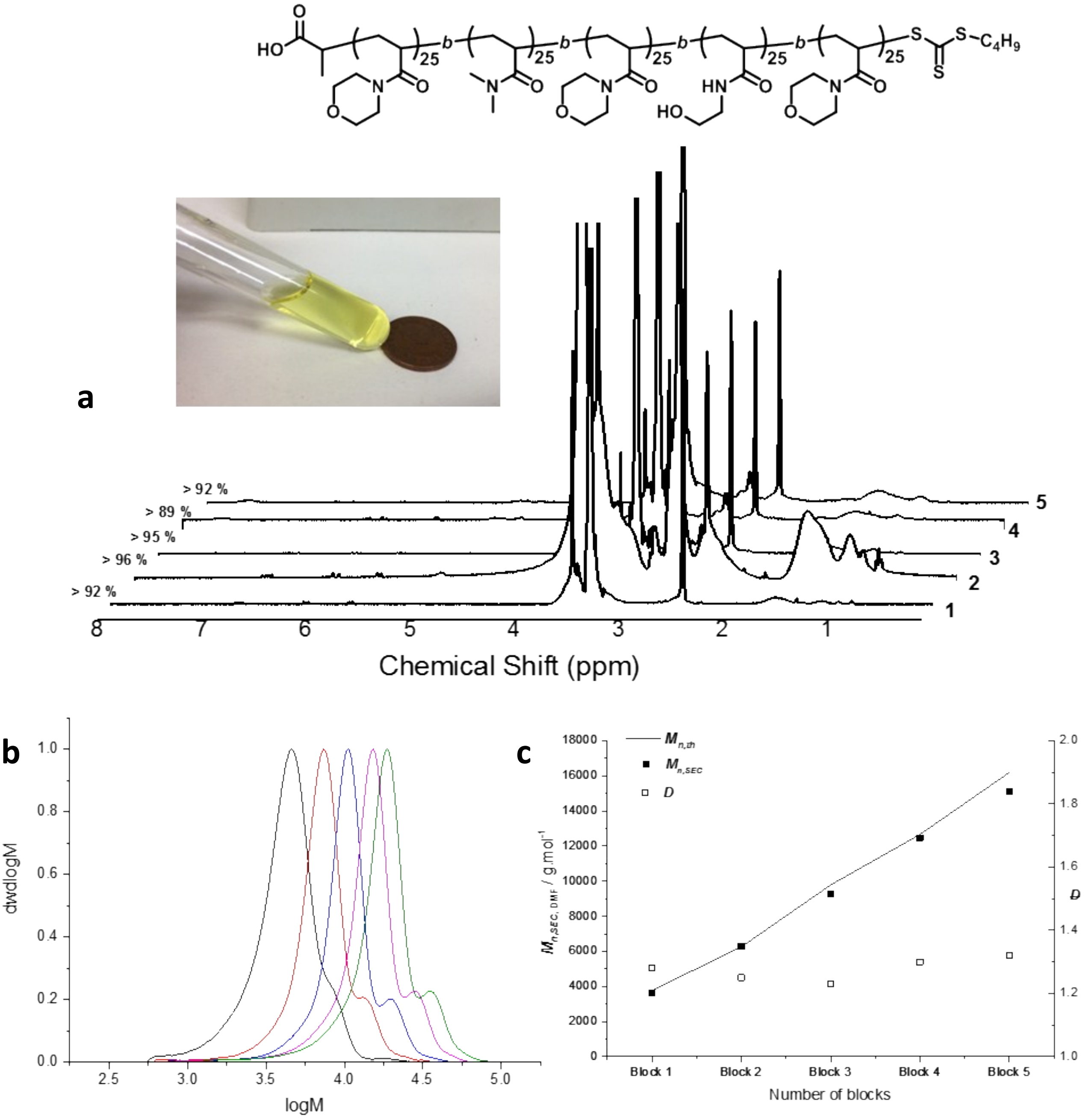


Figure S4. (a) ^1H NMR spectra (DMSO, 400 MHz) showing the monomer conversion for each new block PNAM$_{25}$-*b*-PDMA$_{25}$-*b*-PNAM$_{25}$-*b*-PHEAm$_{25}$-*b*-PNAM$_{25}$, after 3 mins of iterative RAFT polymerisation at conventional scale (scale = 0.5 ml per each block). (b) SEC chromatograms for successive chain extensions. (c) Evolution of number-average molar masses and dispersity values with the number of blocks during the preparation of the pentablock copolymer. The black line represents the theoretical molar mass calculated from equation 2. The filled squares represents the experimental molar mass and empty squares represents the dispersity values, both as determined by DMF SEC.

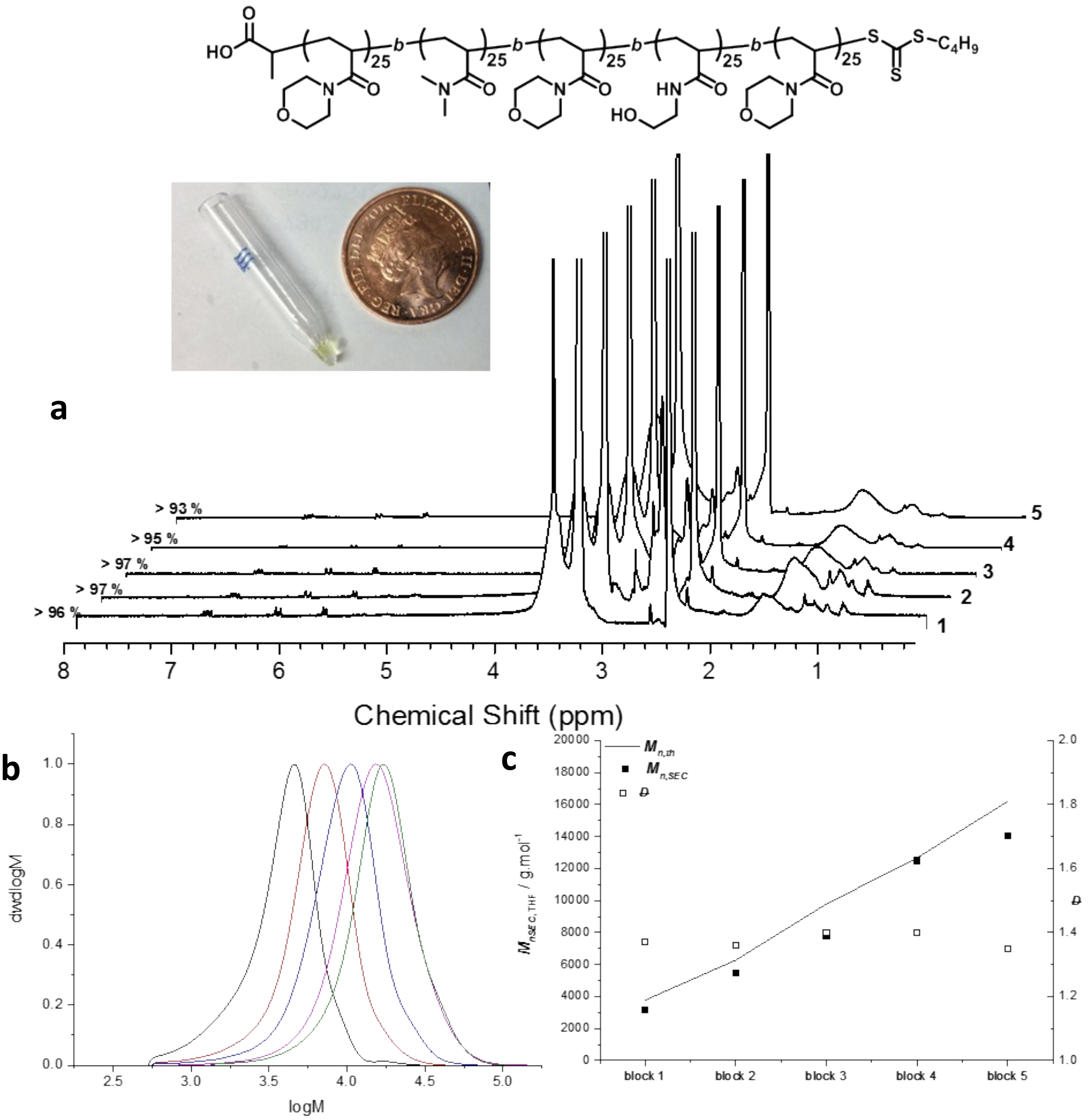


Figure S5. (a) ^{1}H NMR spectra (DMSO, 400 MHz) showing the monomer conversion for each new block PNAM$_{25}$-*b*-PDMA$_{25}$-*b*-PNAM$_{25}$-*b*-PHEAm$_{25}$-*b*-PNAM$_{25}$ after 3 mins of iterative RAFT polymerisation inside microvolume inserts (scale = 2 µL per each block). (b) SEC chromatograms for successive chain extensions. (c) Evolution of number-average molar masses and dispersity values with the number of blocks during the preparation of the pentablock copolymer. The black line represents the theoretical molar mass calculated from equation 2. The filled squares represents the experimental molar mass and empty squares represents the dispersity values, both as determined by DMF SEC.

Table S3. Experimental conditions for the preparation of $PNAM_{25}$ at range of scales in H_2O/dioxane at 100 °C with VA-044 as initiator (3 mins per reaction, in presence of air an without degassing).

Scale	**500 µL**[a]	**10 µL**[b]	**5 µL**[b]	**2 µL**[b]	**1 µL**[b]
Monomer	NAM	NAM	NAM	NAM	NAM
$DP_{targeted}$	25	25	25	25	25
$m_{monomer\ added}$ (mg)	211.7	4.24	2.12	0.848	0.424
$m_{CTA\ added}$ (mg)	14.3	0.286	0.143	5.73×10^{-2}	2.86×10^{-2}
$m_{VA\text{-}044\ added}$ (mg)	0.48	9.71×10^{-3}	4.86×10^{-3}	1.94×10^{-3}	9.71×10^{-4}
$V_{water\ added}$ (µL)	249	4.986	2.493	0.997	0.499
$V_{dioxane\ added}$ (µL)	62	1.247	0.623	0.249	0.125
$[VA\text{-}044]_{0\ Master\ mix}$ (moldm^{-3}) [c]	3.00×10^{-3}	3.00×10^{-3}	3.00×10^{-3}	3.00×10^{-3}	3.00×10^{-3}
$[NAM]_{0\ Master\ mix}$ (moldm^{-3}) [c]	3.00	3.00	3.00	3.00	3.00
Water/Dioxane ratio $_{master\ mix}$	80:20	100:0	100:0	100:0	100:0
$V_{master\ mix\ added}$ (µL) [d]	500	10	5	2	1
% H_2O[e]	80 %	80 %	80 %	80 %	80 %
V_{total} (µL)	0.500	0.010	0.005	0.002	0.001
Overall $[VA\text{-}044]_0$ (moldm^{-3})	3.00×10^{-3}	3.00×10^{-3}	3.00×10^{-3}	3.00×10^{-3}	3.00×10^{-3}
Overall $[NAM]_0$ (moldm^{-3})	3	3	3	3	3
$[CTA]_0/[VA\text{-}044]_0$	40	40	40	40	40
L[f] (%)	98.04	98.04	98.04	98.04	98.04

[a] Reaction carried out in a conventional X ml test tube. [b] Reaction carried out in a 200 µL inserts [c] Overall concentration of the master mix (monomer, initiator and solvent), CTA added in the cycle 1 master mix. For subsequent chain extensions (cycles = 2, 3, 4 and 5) the same master mix was used. [d] Volume of the master mix added into the reaction vessel using an air displacement micropipette. [e] The amount of water as a percentage of the total solvent. [f] Theoretical estimation of the fraction of living chains per block (e.g. extendable chains having the Z group).

Table S4. Experimental conditions for the preparation of $PNAM_{100}$ at range of scales in H_2O/dioxane at 100 °C with VA-044 as initiator (3 mins per reaction, consuming 80% of initiator; in presence of air and without degassing).

Scale	**500 µL**[a]	**2 µL**[b]
Monomer	NAM	NAM
$DP_{targeted}$	100	100
$m_{monomer\ added}$ (mg)	211.7	0.848
$m_{CTA\ added}$ (mg)	35.7	1.43×10^{-2}
$m_{VA\text{-}044\ added}$ (mg)	0.36	6.5×10^{-4}
$V_{water\ added}$ (µL)	280	1.122
$V_{dioxane\ added}$ (µL)	311	0.125
$[VA\text{-}044]_{0\ Master\ mix}$ ($moldm^{-3}$) [c]	1.00×10^{-3}	1.00×10^{-3}
$[NAM]_{0\ Master\ mix}$ ($moldm^{-3}$) [c]	3.00	3.00
Water/Dioxane ratio $_{master\ mix}$	90:10	90:10
$V_{master\ mix\ added}$ (µL) [d]	500	2
% H_2O[e]	90 %	90 %
V_{total} (µL)	500	2
Overall $[VA\text{-}044]_0$ ($moldm^{-3}$)	1.00×10^{-3}	1.00×10^{-3}
Overall $[NAM]_0$ ($moldm^{-3}$)	3.00	3.00
$[CTA]_0/[VA\text{-}044]_0$	30	30
L[f] (%)	97.40	97.40

[a] Reaction carried out in a conventional X ml test tube. [b] Reaction carried out in a 200 µL inserts [c] Overall concentration of the master mix (monomer, initiator and solvent), CTA added in the cycle 1 master mix. For subsequent chain extensions (cycles = 2, 3, 4 and 5) the same master mix was used. [d] Volume of the master mix added into the reaction vessel using an air displacement micropipette. [e] The amount of water as a percentage of the total solvent. [f] Theoretical estimation of the fraction of living chains per block (e.g. extendable chains having the Z group).

Table S5. Experimental conditions for the preparation of $PNAM_{200}$ at range of scales in H_2O/dioxane at 100 °C with VA-044 as initiator (3 mins per reaction, consuming 80% of initiator; in presence of air and without degassing).

Scale	**500 µL**[a]	**2 µL**[b]
Monomer	NAM	NAM
DP_{targeted}	200	200
$m_{\text{monomer added}}$ (mg)	211.7	0.848
$m_{\text{CTA added}}$ (mg)	1.79	7.2×10^{-3}
$m_{\text{VA-044 added}}$ (mg)	0.121	4.9×10^{-4}
$V_{\text{water added}}$ (µL)	296	1.184
$V_{\text{dioxane added}}$ (µL)	156	0.062
$[\text{VA-044}]_{0\ \text{Master mix}}$ (moldm^{-3}) [c]	7.50×10^{-4}	7.50×10^{-4}
$[\text{NAM}]_{0\ \text{Master mix}}$ (moldm^{-3}) [c]	3.00	3.00
Water/Dioxane ratio $_{\text{master mix}}$	95:05	95:05
$V_{\text{master mix added}}$ (µL) [d]	500	2
% H_2O[e]	95 %	95 %
V_{total} (µL)	500	2
Overall $[\text{VA-044}]_0$ (moldm^{-3})	7.5×10^{-4}	7.5×10^{-4}
Overall $[\text{NAM}]_0$ (moldm^{-3})	3.00	3.00
$[\text{CTA}]_0/[\text{VA-044}]_0$	20	20
L[f] (%)	96.15	96.15

[a] Reaction carried out in a conventional X ml test tube. [b] Reaction carried out in a 200 µL inserts [c] Overall concentration of the master mix (monomer, initiator and solvent), CTA added in the cycle 1 master mix. For subsequent chain extensions (cycles = 2, 3, 4 and 5) the same master mix was used. [d] Volume of the master mix added into the reaction vessel using an air displacement micropipette. [e] The amount of water as a percentage of the total solvent. [f] Theoretical estimation of the fraction of living chains per block (e.g. extendable chains having the Z group).

Table S6. Experimental conditions for the preparation of multichain extension to generate $P(NAM_{25})_5$ at 25 µL scale (5 µL per block) in H_2O/dioxane at 100 °C with VA-044 as initiator (3 mins per block, consuming 80% of initiator; per block in presence of air an without degassing).

Cycles	**1**	**2**	**3**	**4**	**5**
Monomer	NAM	NAM	NAM	NAM	NAM
$DP_{targeted}$	25	25	25	25	25
$m_{monomer\ added}$ (mg)	2.117	2.117	2.117	2.117	2.117
$m_{CTA\ added}$ (mg)	0.143	-	-	-	-
$m_{VA\text{-}044\ added}$ (mg)	4.85×10^{-3}	3.88×10^{-3}	3.88×10^{-3}	3.88×10^{-3}	3.88×10^{-3}
$V_{water\ added}$ (µL)	0.997	1.247	1.247	1.247	1.247
$V_{dioxane\ added}$ (µL)	0.249	-	-	-	-
$[VA\text{-}044]_{0\ Master\ mix}$ ($moldm^{-3}$) [a]	3.00×10^{-3}	2.37×10^{-3}	2.37×10^{-3}	2.37×10^{-3}	2.37×10^{-3}
$[NAM]_{0\ Master\ mix}$ ($moldm^{-3}$) [a]	3.00	3.00	3.00	3.00	3.00
Water/Dioxane ratio $_{master\ mix}$	80:20	100:0	100:0	100:0	100:0
$V_{master\ mix\ added}$ (µL) [b]	5.00	5.00	5.00	5.00	5.00
% H_2O[c]	80 %	90 %	93 %	95 %	96 %
V_{total}[d] (µL)	5.00	10.00	15.00	20.00	25.00
Overall $[VA\text{-}044]_0$ ($moldm^{-3}$) [e]	3.00×10^{-3}	1.50×10^{-3}	1.00×10^{-3}	7.5×10^{-4}	6.0×10^{-4}
Overall $[NAM]_0$ ($moldm^{-3}$)	3.00	1.50	1.00	0.75	0.60
$[CTA]_0/[VA\text{-}044]_0$	40	40	40	40	40
L[f] (%)	98.04	98.04	98.04	98.04	98.04
Cumulative L[g] (%)	98.04	96.11	94.23	92.38	90.56

[a] Overall concentration of the master mix (monomer, initiator and solvent), CTA added in the cycle 1 master mix. For subsequent chain extensions (cycles = 2, 3, 4 and 5) the same master mix was used. [b] Volume of the master mix added into the reaction vessel using an air displacement micropipette. [c] The amount of water as a percentage of the total solvent. [d] The sum of volume of the solvent added + volume of monomer + V_{total} previous block. [e] Takes into the account the theoretical initiator remaining from the previous block (using the Arrhenius equation). [f] Theoretical estimation of the fraction of living chains per block (e.g. extendable chains having the Z group). [g] Theoretical estimation of the cumulated fraction of living chains.

Table S7. Experimental conditions for the preparation of multichain extension to generate P(NAM$_{25}$)$_5$ at 10 µL scale (2 µL per block) in H_2O/dioxane at 100 °C with VA-044 as initiator (3 mins per block, consuming 80% of initiator; per block in presence of air an without degassing).

Cycles	**1**	**2**	**3**	**4**	**5**
Monomer	NAM	NAM	NAM	NAM	NAM
$DP_{targeted}$	25	25	25	25	25
$m_{monomer\ added}$ (mg)	0.847	0.847	0.847	0.847	0.847
$m_{CTA\ added}$ (mg)	5.73×10^{-2}	-	-	-	-
$m_{VA\text{-}044\ added}$ (mg)	1.94×10^{-3}	1.55×10^{-3}	1.55×10^{-3}	1.55×10^{-3}	1.55×10^{-3}
$V_{water\ added}$ (µL)	0.996	1.247	1.247	1.247	1.247
$V_{dioxane\ added}$ (µL)	0.249	-	-	-	-
$[VA\text{-}044]_{0\ Master\ mix}$ (moldm^{-3}) [a]	3.00×10^{-3}	2.37×10^{-3}	2.37×10^{-3}	2.37×10^{-3}	2.37×10^{-3}
$[NAM]_{0\ Master\ mix}$ (moldm^{-3}) [a]	3.00	3.00	3.00	3.00	3.00
Water/Dioxane ratio $_{master\ mix}$	80:20	100:0	100:0	100:0	100:0
$V_{master\ mix\ added}$ (µL) [b]	2.00	2.00	2.00	2.00	2.00
% H_2O[c]	80 %	90 %	93 %	95 %	96 %
V_{total}[d] (µL)	2.00	4.00	6.00	8.00	10.00
Overall $[VA\text{-}044]_0$ (moldm^{-3}) [e]	3.00×10^{-3}	1.50×10^{-3}	1.00×10^{-3}	7.5×10^{-4}	6.0×10^{-4}
Overall $[NAM]_0$ (moldm^{-3})	3.00	1.50	1.00	0.75	0.60
$[CTA]_0/[VA\text{-}044]_0$	40	40	40	40	40
L[f] (%)	98.04	98.04	98.04	98.04	98.04
Cumulative L[g] (%)	98.04	96.11	94.23	92.38	90.56

[a] Overall concentration of the master mix (monomer, initiator and solvent), CTA added in the cycle 1 master mix. For subsequent chain extensions (cycles = 2, 3, 4 and 5) the same master mix was used. [b] Volume of the master mix added into the reaction vessel using an air displacement micropipette. [c] The amount of water as a percentage of the total solvent. [d] The sum of volume of the solvent added + volume of monomer + V_{total} previous block. [e] Takes into the account the theoretical initiator remaining from the previous block (using the Arrhenius equation). [f] Theoretical estimation of the fraction of living chains per block (e.g. extendable chains having the Z group). [g] Theoretical estimation of the cumulated fraction of living chains.

Table S8. Experimental conditions for the preparation of multichain extension to generate $P(NAM_{25})_5$ at 2.5 ml scale in H_2O/dioxane at 100 °C with VA-044 as initiator (3 mins per block, consuming 80% of initiator; per block in presence of air an without degassing).

Cycles	**1**	**2**	**3**	**4**	**5**
Monomer	NAM	NAM	NAM	NAM	NAM
$DP_{targeted}$	25	25	25	25	25
$m_{monomer\ added}$ (mg)	211.7	211.7	211.7	211.7	211.7
$m_{CTA\ added}$ (mg)	14.3	-	-	-	-
$m_{VA\text{-}044\ added}$ (mg)	0.48	0.39	0.39	0.39	0.39
$V_{water\ added}$ (μL)	249	311	311	311	311
$V_{dioxane\ added}$ (μL)	62	-	-	-	-
$[VA\text{-}044]_{0\ Master\ mix}$ (moldm^{-3}) [a]	3.00×10^{-3}	2.37×10^{-3}	2.37×10^{-3}	2.37×10^{-3}	2.37×10^{-3}
$[NAM]_{0\ Master\ mix}$ (moldm^{-3}) [a]	3.00	3.00	3.00	3.00	3.00
Water/Dioxane ratio $_{master\ mix}$	80:20	100:0	100:0	100:0	100:0
$V_{master\ mix\ added}$ (μL) [b]	500	500	500	500	500
% H_2O[c]	80 %	90 %	93 %	95 %	96 %
V_{total}[d] (μL)	500	1000	1500	2000	2500
Overall $[VA\text{-}044]_0$ (moldm^{-3}) [e]	3.00×10^{-3}	1.50×10^{-3}	1.00×10^{-3}	7.5×10^{-4}	6.0×10^{-4}
Overall $[NAM]_0$ (moldm^{-3})	3.00	1.50	1.00	0.75	0.60
$[CTA]_0/[VA\text{-}044]_0$	40	40	40	40	40
L[f] (%)	98.04	98.04	98.04	98.04	98.04
Cumulative L[g] (%)	98.04	96.11	94.23	92.38	90.56

[a] Overall concentration of the master mix (monomer, initiator and solvent), CTA added in the cycle 1 master mix. For subsequent chain extensions (cycles = 2, 3, 4 and 5) the same master mix was used. [b] Volume of the master mix added into the reaction vessel using an air displacement micropipette. [c] The amount of water as a percentage of the total solvent. [d] The sum of volume of the solvent added + volume of monomer + V_{total} previous block. [d] Takes into the account the theoretical initiator remaining from the previous block (using the Arrhenius equation). [e] Theoretical estimation of the fraction of living chains per block (e.g. extendable chains having the Z group). [f] Theoretical estimation of the cumulated fraction of living chains.

Table S9. Experimental conditions for the preparation of the pentablock copolymer PNAM$_{25}$-*b*-PDMA$_{25}$-*b*-PNAM$_{25}$-*b*-PHEAm$_{25}$-*b*-PNAM$_{25}$ at 10 µL scale (2 µL per block)scale in H_2O/dioxane at 100 °C with VA-044 as initiator (3 mins per block, consuming 80% of initiator; per block in presence of air an without degassing).

Cycles	**1**	**2**	**3**	**4**	**5**
Monomer	NAM	DMA	NAM	HEAm	NAM
$DP_{targeted}$	25	25	25	25	25
$m_{monomer\ added}$ (mg)	0.848	0.595	0.848	0.691	0.848
$m_{CTA\ added}$ (mg)	5.72×10^{-2}	-	-	-	-
$m_{VA\text{-}044\ added}$ (mg)	1.94×10^{-3}	1.55×10^{-3}	1.55×10^{-3}	1.55×10^{-3}	1.55×10^{-3}
$V_{water\ added}$ (µL)	0.996	1.382	1.245	1.378	1.245
$V_{dioxane\ added}$ (µL)	0.249	-	-	-	-
$[VA\text{-}044]_{0\ Master\ mix}$ (moldm^{-3}) [a]	3.00×10^{-3}	2.37×10^{-3}	2.37×10^{-3}	2.37×10^{-3}	2.37×10^{-3}
$[M]_{0\ Master\ mix}$ (moldm^{-3}) [a]	3.00	3.00	3.00	3.00	3.00
Water/Dioxane ratio $_{master\ mix}$	80:20	100:0	100:0	100:0	100:0
$V_{master\ mix\ added}$ (µL) [b]	2.00	2.00	2.00	2.00	2.00
% H_2O[c]	80 %	90 %	93 %	95 %	96 %
V_{total}[d] (µL)	2.00	4.00	6.00	8.00	10.00
Overall $[VA\text{-}044]_0$ (moldm^{-3}) [e]	3.00×10^{-3}	1.50×10^{-3}	1.00×10^{-3}	7.5×10^{-4}	6.0×10^{-4}
Overall $[M]_0$ (moldm^{-3})	3.00	1.50	1.00	0.75	0.60
$[CTA]_0/[VA\text{-}044]_0$	40	40	40	40	40
L[f] (%)	98.04	98.04	98.04	98.04	98.04
Cumulative L[g] (%)	98.04	96.11	94.23	92.38	90.56

[a] Overall concentration of the master mix (monomer, initiator and solvent), CTA added in the cycle 1 master mix. For subsequent chain extensions (cycles = 2, 3, 4 and 5) the same master mix was used. [b] Volume of the master mix added into the reaction vessel using an air displacement micropipette. [c] The amount of water as a percentage of the total solvent. [d] The sum of volume of the solvent added + volume of monomer + V_{total} previous block. [e] Takes into the account the theoretical initiator remaining from the previous block (using the Arrhenius equation). [f] Theoretical estimation of the fraction of living chains per block (e.g. extendable chains having the Z group). [g] Theoretical estimation of the cumulated fraction of living chains.

Table S10. Experimental conditions for the preparation of the pentablock copolymer PNAM$_{25}$-*b*-PDMA$_{25}$-*b*-PNAM$_{25}$-*b*-PHEAm$_{25}$-*b*-PNAM$_{25}$ at 2.5 ml scale (500 µL per block)scale in H_2O/dioxane at 100 °C with VA-044 as initiator (3 mins per block, consuming 80% of initiator; per block in presence of air an without degassing).

Cycles	**1**	**2**	**3**	**4**	**5**
Monomer	NAM	DMA	NAM	HEAm	NAM
$DP_{targeted}$	25	25	25	25	25
$m_{monomer\ added}$ (mg)	212	149	212	173	212
$m_{CTA\ added}$ (mg)	14.3	-	-	-	-
$m_{VA\text{-}044\ added}$ (mg)	0.49	0.39	0.39	0.39	0.39
$V_{water\ added}$ (µL)	249.0	345.5	311.3	344.6	311.3
$V_{dioxane\ added}$ (µL)	62	-	-	-	-
$[VA\text{-}044]_{0\ Master\ mix}$ ($moldm^{-3}$) [a]	3.00×10^{-3}	2.37×10^{-3}	2.37×10^{-3}	2.37×10^{-3}	2.37×10^{-3}
$[M]_{0\ Master\ mix}$ ($moldm^{-3}$) [a]	3.00	3.00	3.00	3.00	3.00
Water/Dioxane ratio $_{master\ mix}$	80:20	100:0	100:0	100:0	100:0
$V_{master\ mix\ added}$ (µL) [b]	500	500	500	500	500
% H_2O[c]	80 %	90 %	93 %	95 %	96 %
V_{total}[d] (µL)	2.00	4.00	6.00	8.00	10.00
Overall $[VA\text{-}044]_0$ ($moldm^{-3}$) [e]	3.00×10^{-3}	1.50×10^{-3}	1.00×10^{-3}	7.5×10^{-4}	6.0×10^{-4}
Overall $[M]_0$ ($moldm^{-3}$)	3.00	1.50	1.00	0.75	0.60
$[CTA]_0/[VA\text{-}044]_0$	40	40	40	40	40
L[f] (%)	98.04	98.04	98.04	98.04	98.04
Cumulative L[g] (%)	98.04	96.11	94.23	92.38	90.56

[a] Overall concentration of the master mix (monomer, initiator and solvent), CTA added in the cycle 1 master mix. For subsequent chain extensions (cycles = 2, 3, 4 and 5) the same master mix was used. [b] Volume of the master mix added into the reaction vessel using an air displacement micropipette. [c] The amount of water as a percentage of the total solvent. [d] The sum of volume of the solvent added + volume of monomer + V_{total} previous block. [d] Takes into the account the theoretical initiator remaining from the previous block (using the Arrhenius equation). [e] Theoretical estimation of the fraction of living chains per block (e.g. extendable chains having the Z group). [f] Theoretical estimation of the cumulated fraction of living chains.

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