Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting information

Synthesis of Asymmetric Star Polymers by Post-polymerisation Modification and Photomediated Polymerisation

Yichuan Zhang, Mark Bradley and Jin Geng*

Supporting Figures and Tables

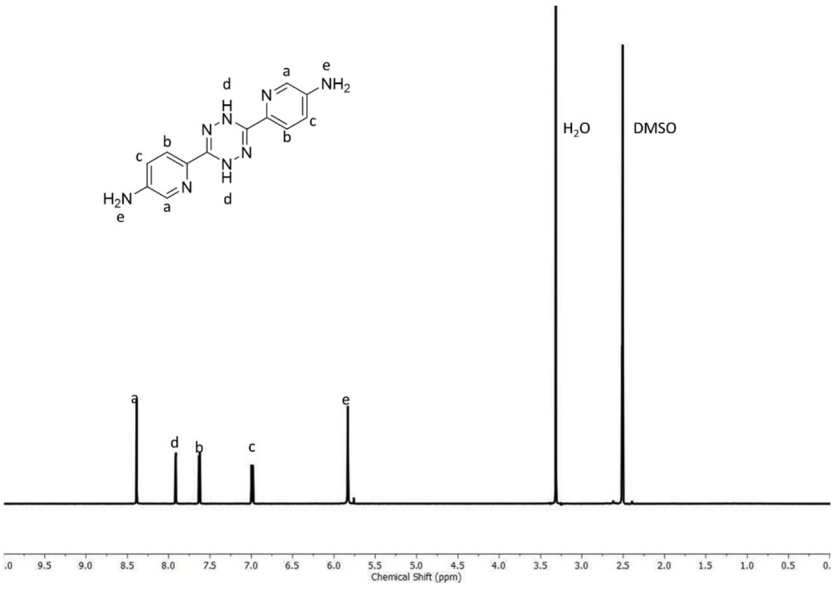

Fig. S1 ^{1}H NMR of 3,6-bis(5-amino-2-pyridyl)-1,2-dihydro-1,2,4,5-tetrazine **S1** in d_6-DMSO.

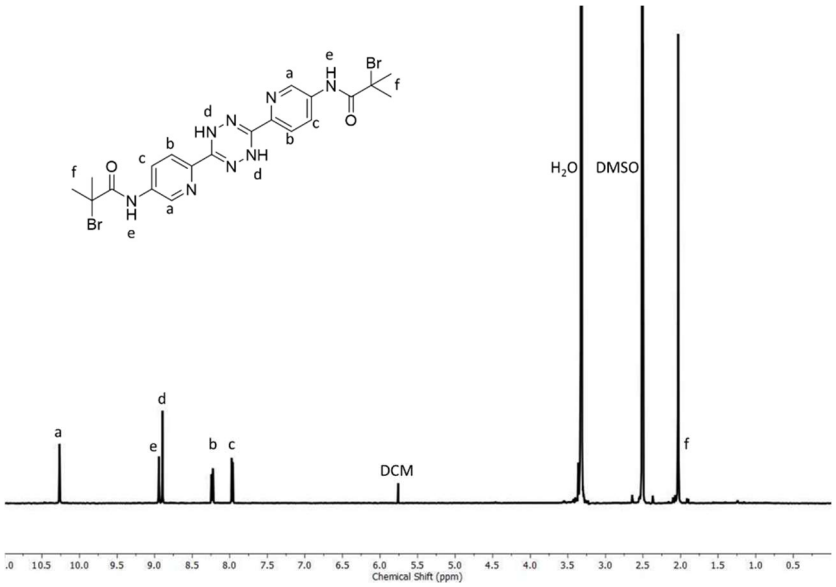

Fig. S2 ^{1}H NMR of bromine functionalised dihydrotetrazine **1** in d_6-DMSO.

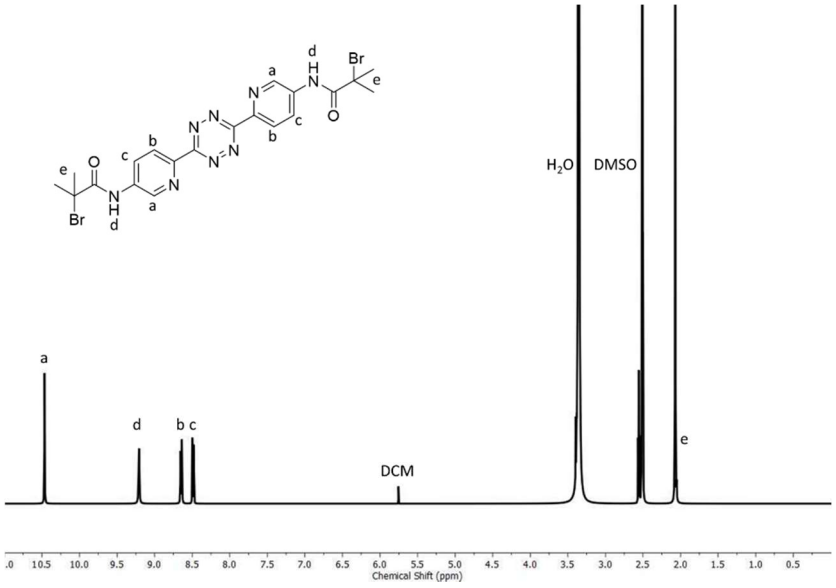

Fig. S3 ^{1}H NMR of bromine functionalised tetrazine **2** in d_6-DMSO.

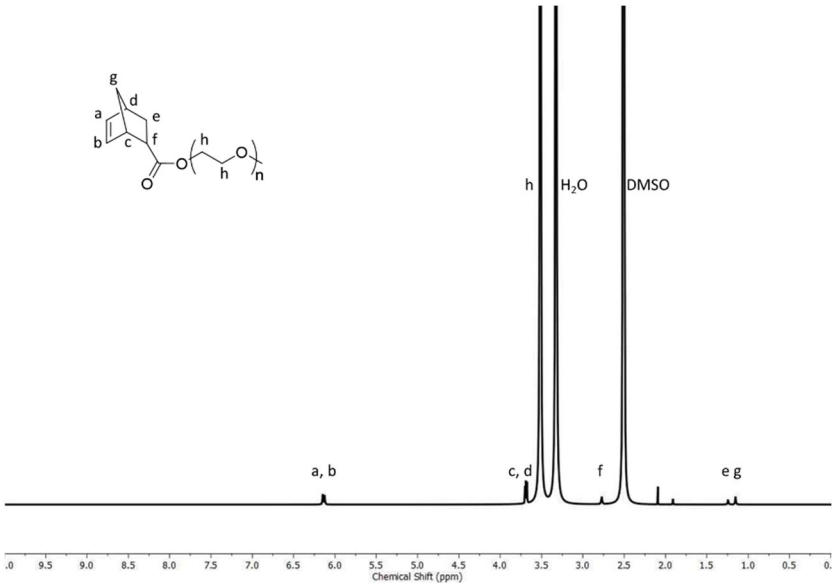

Fig. S4 ^{1}H NMR of norbornene terminated PEG initiator precursor **IP2** in d_6-DMSO.

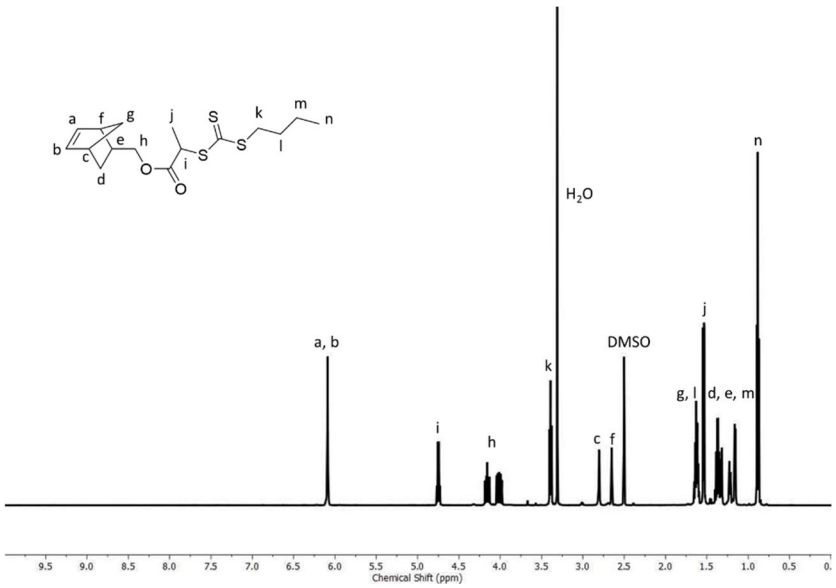

Fig. S5 ^{1}H NMR of norbornene trithiocarbonate initiator precursor **IP3** in d_6-DMSO.

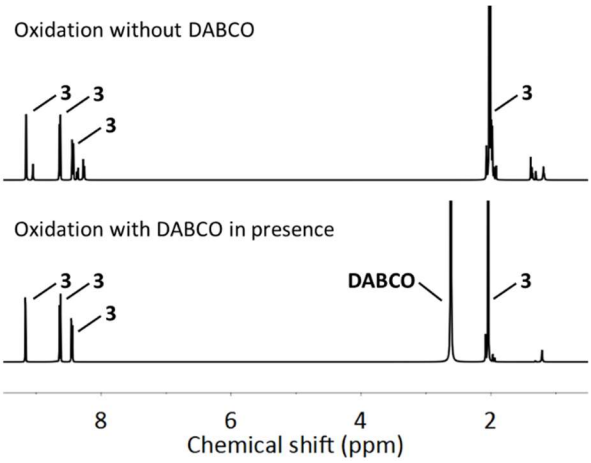

Fig. S6 ^{1}H NMR spectra (in d_6-DMSO) of the dihydrotetrazine **1** oxidised by molecular oxygen aided with methylene blue (0.2 eq to dihydrotetrazine) and light irradiation (630 nm, 4.0mW/cm^2), with and without DABCO in presence.

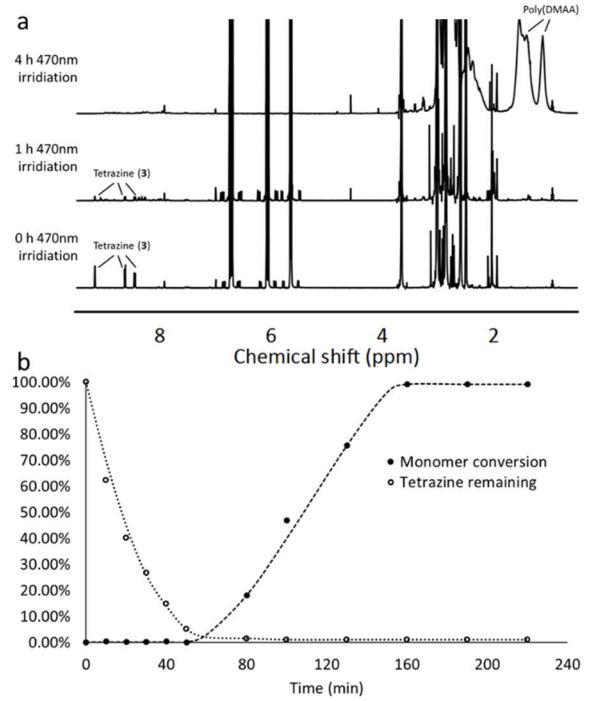

Fig. S7 (a) ^{1}H NMR spectra (in d_6-DMSO) of the polymerisation of DMAA in presence of tetrazine **2**, DABCO and Eosin Y with 470 nm irradiation. (b) Plot of DMAA conversion and tetrazine **2** amount at the polymerisation condition with different irradiation time.

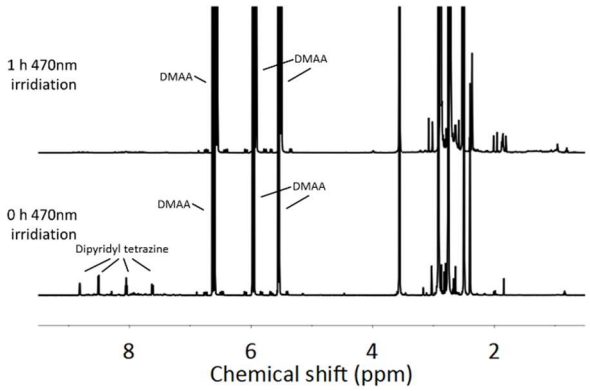

Fig. S8 ^{1}H NMR spectra (in d_6-DMSO) of the polymerisation of DMAA in presence of 3,6-di-2-pyridyl-1,2,4,5-tetrazine, macro initiator **3**, DABCO and Eosin Y with 0 h and 1 h 470 nm light irradiation.

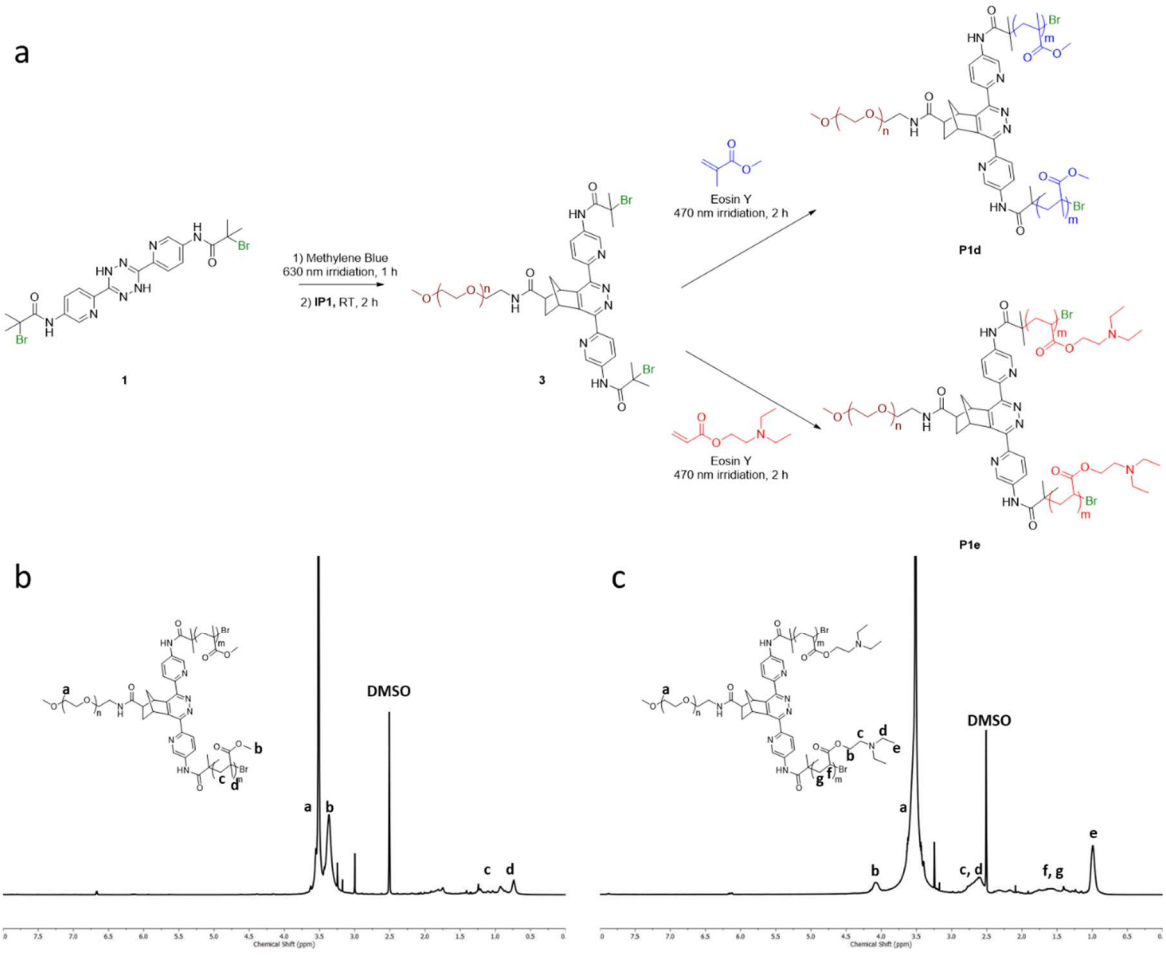

Fig. S9 (a) Synthesis of star polymer **P1d** and **P1e** using methyl methacrylate and 2-(diethylamino)ethyl acrylate as monomers; (b) and (c) ^{1}H NMR spectra (in d_6-DMSO) of **P1d** and **P1e** (polymer isolated by precipitation from ether and dialysis against water, MWCO = 7000).

Table S1 Evaluation of individual reactions. [**1**]:[Methylene blue]:[DABCO]:[Eosin Y]:[DMAA]:[**IP1**] = 1.05:0.2:17:0.1:1000:1. Observations were evidenced by ^{1}H NMR.

Entry	**1**	Methylene blue	DABCO	Eosin Y	DMAA	**IP1**	Reaction conditions	Observation
1	✓	✓	✓	✕	✕	✕	630 nm 1 h	Oxidation of 1; Conversion >99% *
2	✓	✓	✕	✕	✕	✕	630 nm 1 h	Oxidation of 1; Conversion ~80% *
3	✓	✓	✓	✕	✕	✓	630 nm 1 h + RT 2 h	Obtain 3
4	✓	✓	✓	✓	✓	✓	630 nm 1 h + RT 2 h + 470 nm 2 h	Polymerisation; Obtain **P1b**
5	✓	✓	✓	✕	✓	✓	630 nm 1 h + RT 2 h + 470 nm 2 h	No polymerisation; Obtain 3
6	✕	✓	✓	✓	✓	✓	630 nm 1 h + RT 2 h + 470 nm 2 h	No polymerisation
7	✕	✕	✓	✓	✓	✓	630 nm 1 h + RT 2 h + 470 nm 2 h	No polymerisation
8	✓	✕	✓	✓	✓	✓	630 nm 1 h + RT 2 h + 470 nm 2 h	Polymerisation; Aromatic peak shift
9	✓	✕	✓	✓	✓	✕	630 nm 1 h + RT 2 h + 470 nm 2 h	Polymerisation; Aromatic peak shift
10	✓	✓	✓	✓	✓	✕	630 nm 1 h + RT 2 h + 470 nm 4 h	Polymerisation after tetrazine fully reacted

* Conversions of dihydrotetrazines were quantified by ^{1}H NMR.

Table S2 Characterisation of the asymmetric star polymers using methyl methacrylate and 2-(diethylamino)ethyl acrylate as monomers with **IP1** as the initiator precursor.

Polymer entry	Monomer	[DMAA] / [macro-initiator precursor]	Conversion[a] (%)	M_n[b] (kDa)	Đ[b]
P1d	methyl methacrylate	200/1	71	34	1.46
P1e	2-(diethylamino)ethyl acrylate	200/1	73	43	1.31

[a]: determined by by ^{1}H NMR; [b]: determined by GPC (eluting with DMF with 1% LiBr at 60 ^{o}C, calibrated with PMMA standards).

Experimental

General

All chemicals were purchased from Acros Organics, Alfa Aesar, Fisher Scientific or Sigma Aldrich and used as received. LED lights (470 nm, 4.0mW/cm^2 and 630 nm, 4.0mW/cm^2) were purchased from THORLABS. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVA-500 (at 500 and 125 MHz, respectively) at 298 K in the solvents indicated (with resonances shown in ppm). Low resolution mass spectroscopy (LRMS) were carried out using an Agilent LCMS 1100 ChemStation with a G1946B quadrupole mass detector. High Resolution Mass Spectra (HRMS) were performed on a Bruker 3.0 T Apex II spectrometer. UV-*vis* spectroscopy was performed on a Shimadzu UV-1800 spectrometer. Molecular weights of polymers were determined by a Agilent 1100 GPC equipped with 2 × PLgel MIXED-C columns (2 × 10^2 - 2 × 10^6 g/mol, 5 µm) and an RI detector, eluting with DMF containing 0.1 % *w*/*v* LiBr at 60 °C at 1 mL/min flow rate. Molecular weights obtained were relative to narrow dispersity poly(methyl methacrylate) standards.

Synthesis

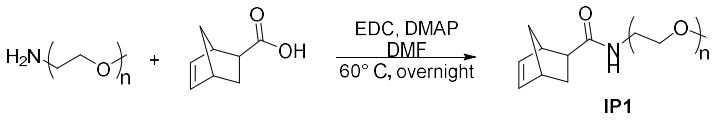

Fig. S10 Synthesis of norbornene terminated PEG initiator precursor **IP1**.

Norbornene terminated PEG initiator precursor IP1

Commercial poly(ethylene glycol) methyl ether amine (1.0 g, 0.20 mmol, M_n = 5000 (M_n = 16 kDa with Đ = 1.22 when analysed by GPC using PMMA as the standard)), 5-norbornene-2-carboxylic acid (138.2 mg, 1.0 mmol) were pre-mixed in DMF (25 mL), *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (191.7 mg, 1.0 mmol) was added to the solution in one portion and stirred at 60 °C overnight. The solvent was removed *in vacuo* and the crude product was redissolved in deionised water, dialysed against deionised water for 72 h (water changed every 12 h) and freeze dried, yielding the title polymer as a white powder (700 mg, 68%). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 6.20 – 6.07 (m), 3.76 – 3.64 (s), 3.51 (m), 2.98 (m), 2.18 (m), 1.82 (m). GPC (DMF) M_n = 16 kDa, Đ = 1.21.

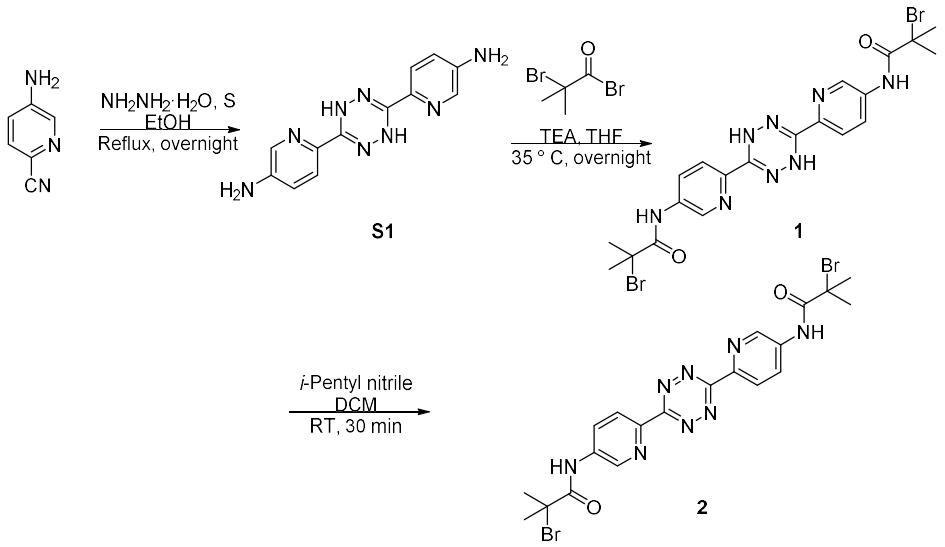

Fig. S11 Synthesis of bromine functionalised dihydrotetrazine **1** and the corresponding tetrazine **2**.

3,6-Bis(5-amino-2-pyridyl)-1,2-dihydro-1,2,4,5-tetrazine S1[1]

5-Amino-2-pyridinecarbonitrile (236.3 mg, 2.00 mmol) and elemental sulfur (128 mg, 4.00 mmol) was dissolved in anhydrous EtOH (6 mL) in a flask, degassed and refilled with argon before cooled down to 0 °C in an ice bath. Hydrazine monohydratre (500 µL, 16.0 mmol) was slowly syringed into the mixture and the resulting mixture was heated at 70 °C under argon for 18 h behind a blast shield. The crude product was precipitated from water, redissolved in DCM and concentrated on silica gel and was further purified by silica gel chromatography (eluting with 0% to 2% MeOH in DCM) as an orange solid (72 mg, 13%). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 8.39 (s, 2H), 7.91 (d, J = 2.6 Hz, 2H), 7.63 (d, J = 8.5 Hz, 2H), 6.99 (dd, J = 8.5, 2.6 Hz, 2H), 5.83 (s, 4H). ^{13}C NMR (125 MHz, DMSO-d6) δ = 147.53, 146.96, 135.04, 134.49, 122.03, 120.78. LRMS (m/z): $[M+H]^+$ calcd. for $C_{12}H_{13}N_8$, 269.1; found, 269.1.

Bromine functionalised dihydrotetrazine 1

Amine terminated dihydrotetrazine **1** (70 mg, 0.263 mmol) and triethylamine (110 µL, 0.789 mmol) were dissolved in pre-degassed anhydrous THF (5 mL) and heated to 35 °C. A solution of α-bromoisobutyryl bromide (71.45 µL, 0.579 mmol) in pre-degassed anhydrous THF was added at a rate of 1 drop per second. The resulting cloudy mixture was allowed to stir under argon at 35 °C overnight and cooled to room temperature. The crude produce was precipitated from water and redissolved in warm DMF, concentrated onto silica gel and purified by silica gel chromatography (eluting with DCM) as orange solid (103 mg, 69%). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 10.26 (s, 2H), 8.95 (dd, *J* = 2.5, 0.7 Hz, 2H), 8.90 (s, 2H), 8.23 (dd, *J* = 8.8, 2.5 Hz, 2H), 7.97 (dd, *J* = 8.7, 0.7 Hz, 2H), 2.03 (s, 12H). ^{13}C NMR (125

MHz, DMSO-d_6) δ = 170.84, 163.04, 145.25, 142.90, 138.44, 128.14, 124.97, 60.55, 31.01. HRMS (m/z): $[M+H]^+$ calcd. for $C_{20}H_{22}{}^{79}Br_2N_8O_2$, 565.03052; found, 565.0304.

Bromine functionalised tetrazine 2

To a solution of bromine terminated dihydrotetrazine **2** (62 mg, 0.109 mmol) in DMSO (10 mL) was added isopentyl nitrite (48 µL, 0.350 mmol). After 30 min, the reaction solution was poured in ice cooled water and the precipitation was collected by filtration yielding the title product as purple solid (55 mg, 89%). ^{1}H NMR = (500 MHz, DMSO-d_6) δ 10.47 (s, 2H), 9.21 (d, *J* = 2.3 Hz, 2H), 8.65 (d, *J* = 8.7 Hz, 2H), 8.49 (dd, *J* = 8.7, 2.5 Hz, 2H), 2.07 (s, 12H). ^{13}C NMR = (125 MHz, DMSO-d_6) δ 170.84, 162.80, 145.25, 142.90, 138.45, 128.16, 124.98, 60.55, 31.01. HRMS (m/z): $[M+H]^+$ calcd. for $C_{20}H_{20}{}^{79}Br_2N_8O_2$, 563.0149; found, 563.0158.

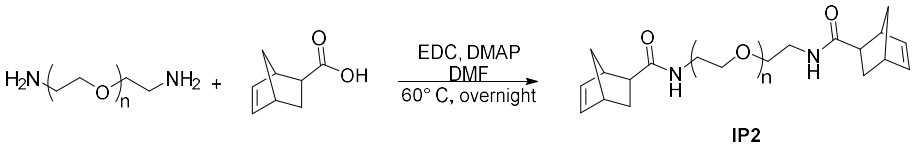

Fig. S12 Synthesis of norbornene terminated PEG initiator precursor **IP2**.

Norbornene terminated PEG initiator precursor IP2

Commercial poly(ethylene glycol) bis(amine) (240 mg, 30 µmol, M_n = 8000 (M_n = 58 kDa with Đ = 1.82 when analysed by GPC using PMMA as the standard)), 5-norbornene-2-carboxylic acid (20.7 mg, 150 µmol) were premixed in DMF (5 mL), *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (28.8 mg, 150 µmol) was added to the solution in one portion and stirred at 60 °C overnight. The solvent was removed *in vacuo* and the crude product was redissolved in deionised water, dialyse against deionised water for 72 h and freeze dried, yielding the title polymer as white powder (230 mg, 95%). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 6.14 (d), 3.74 – 3.65 (s), 3.42 (m), 2.77 (s), 2.09 (s), 1.91 (s). GPC (DMF) M_n = 58 kDa, Đ = 1.80.

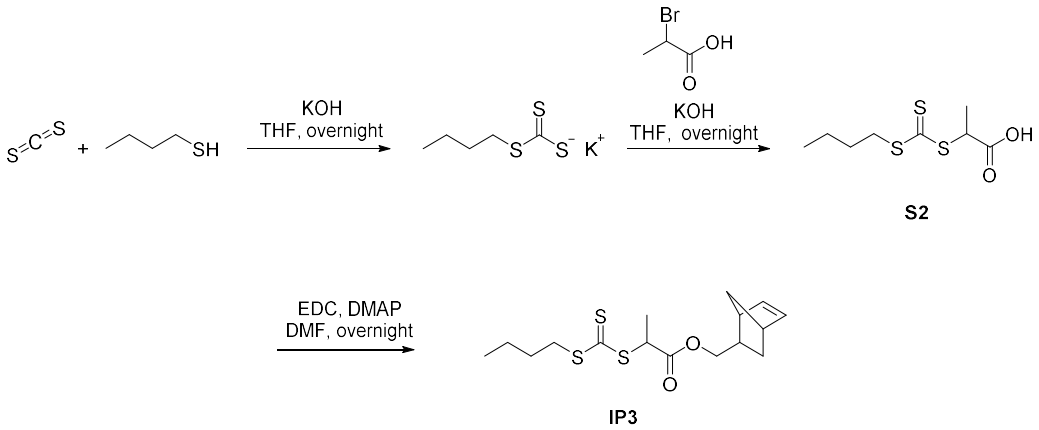

Fig. S13 Synthesis of norbornene trithiocarbonate initiator precursor **IP3**.

Norbornene trithiocarbonate initiator precursor IP3

The carboxylic acid functional RAFT agent, **2-{[(butylsulfanyl)carbonothioyl]sulfanyl} propanoic acid**[2], was firstly synthesized as follows. To a suspension of KOH (9.0 g, 0.16 mol) in THF (150 mL), a solution of 1-butanethiol (16.0 g, 0.18 mol) in THF (50 mL) was added and stirred at RT for 30 min followed by addition of CS_2 (17.0 g, 0.23 mol) in THF (50 mL). The resulting mixture was stirred at RT overnight and concentrated to 50 mL. A solution of tetrapropylammonium bromide (22.4 g, 0.15 mol) in THF (50 mL) was added dropwise and the resulting solution was stirred at RT for 24 h before concentrated onto silica gel and purified by silica gel chromatography (eluting with DCM) as a bright yellow solid (22 g, 63%). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 13.16 (s, 1H), 4.69 (q, J = 7.4 Hz, 1H), 3.40 (t, J = 6.8 Hz, 2H), 1.64 (tt, J = 8.6, 6.8 Hz, 2H), 1.52 (d, J = 7.4 Hz, 3H), 1.46–1.31 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H).^{13}C NMR (125 MHz, DMSO-d_6) δ = 222.94, 172.00, 48.59, 36.68, 30.06, 21.88, 17.24, 13.89. HRMS (m/z): $[M+H]^+$ calcd. for $C_8H_{14}O_2S_3$, 239.0229; found, 239.0242.

To a solution of 2-{[(butylsulfanyl)carbonothioyl]sulfanyl} propanoic acid (650 mg, 2.7 mmol), 5-norbornene-2-methanol (340 mg, 2.7 mmol) and 4-(dimethylamino)pyridine (36.7 mg, 0.30 mmol) in anhydrous DMF (10 mL), *N*-(3-dimethylamino propyl)-*N*'-ethylcarbodiimide hydrochloride (575 mg, 3.0 mmol) was added in one portion and the solution was stirred for 6 h at RT. The solvent was removed *in vacuo* and the crude product was redissolved in DCM and concentrated onto silica gel and purified by silica gel chromatography (eluting with 10% ethyl acetate in hexane) as bright yellow liquid (430 mg, 67%). ^{1}H NMR (500 MHz, DMSO-d_6) δ = 6.09 (d, J = 1.8 Hz, 2H), 4.75 (q, J = 7.4 Hz, 1H), 4.23 – 3.94 (m, 2H), 3.39 (t, J = 7.3 Hz, 2H), 2.84 – 2.77 (m, 1H), 2.71 – 2.63 (m, 1H), 1.68 – 1.58 (m, 4H), 1.54 (d, J = 7.4, 3H), 1.45 – 1.29 (m, 4H), 1.26 – 1.20 (m, 1H), 1.19 – 1.13 (m, 2H), 0.88 (t, J = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 227.43, 175.41, 142.09, 141.30, 74.36, 52.88, 49.79, 48.35,

46.33, 42.80, 41.49, 34.83, 34.08, 26.60, 21.45, 18.64. HRMS (m/z): $[M+H]^+$ calcd. for $C_{16}H_{24}O_2S_3$, 345.1011; found, 345.0993.

Norbornene-tetrazine coupling and PET-ATRP polymerisation.

DMAA based star polymers

Dihydrotetrazine **1** (2.1 mM), methylene blue (0.4 mM), DABCO (34 mM), Eoisin Y (0.2 mM), DMAA (200, 1000 or 2000 mM, for **P1a**, **P1b** and **P1c**, respectively), ω-norbornene-PEG **IP1** (2.0 mM) were prepared in 9:1 (*v*/*v*) DMSO-d_6/D_2O in a glass vial and transferred to an NMR tube.

These concentrations were used for all the reactions described unless otherwise specified. The NMR tubes were irradiated with a 630 nm LED (4.0mW/cm^2) located 1 cm above the NMR tubes for 1 hour. The NMR spectra were taken directly after irradiation. The reaction mixtures in the NMR tubes were left at ambient conditions for another 2 h to allow completion of the norbornene-tetrazine IEDDA reaction. Following NMR analysis, the reaction mixtures (in the NMR tubes) were subsequently irradiated with a 470 nm LED (4.0 mW/cm^2) located 1 cm above the NMR tubes for 2 h. The reaction mixtures were poured into diethyl ether (50 mL), the precipitate was collected by centrifugation and re-dissolved in a minimum amount of methanol and re-precipitated from diethyl ether (50 mL) (x2). The resulting polymers were collected by centrifugation and further purified by dialysis (molecular weight cut off 7 kDa) against deionized water for 72 h and freeze-dried. The same procedure was applied to **IP2** and **IP3** at the same scale. The resulting star polymers were purified by precipitation from ether (3 times) and dialysis (molecular weight cut off 7 kDa) against deionised water for 72 h and freeze-dried.

Methyl methacrylate and 2-(diethylamino)ethyl acrylate based star polymers

Dihydrotetrazine **1** (2.1 mM), methylene blue (0.4 mM), DABCO (34 mM), Eoisin Y (0.2 mM), methyl methacrylate (give **P1d**) or 2-(diethylamino)ethyl acrylate (give **P1e**) (200 mM), ω-norbornene-PEG **IP1** (2.0 mM) were prepared in 9:1 (*v*/*v*) DMSO-d_6/D_2O in a glass vial and transferred to an NMR tube.

The PET polymerisation and purifications followed the same method as for DMAA as described above.

References

1. J. Yuasa, A. Mitsui and T. Kawai, *Chem. Commun.*, 2011, **47** (20), 5807-5809.
2. C. J. Ferguson, R. J. Hughes, B. T. Pham, B. S. Hawkett, R. G. Gilbert, A. K. Serelis and C. H. Such, *Macromolecules*, 2002, **35** (25), 9243-9245.