Electronic Supporting information

Degradable thiomethacrylate core-crosslinked star-shaped polymers

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Experimental procedures

Materials

Methacryloyl chloride was purchased from Merck, 2-cyanoprop-2-yl-dithiobenzoate was purchased from Strem Chemicals, *para*-methoxyphenol was purchased from Fluka. All other chemicals, including tetrabutylammonium bromide, methyl methacrylate, 4,4'-thiobisbenzenethiol, ethylene glycol dimethacrylate, AIBN, hexylamine, benzylamine, ethanolamine and 3-amino-1-propanol were purchased from Sigma.

Instrumental conditions

Nuclear magnetic resonance (NMR) spectroscopy

NMR spectra (^{1}H and ^{13}C NMR) were recorded on a Bruker Avance III HD 300 MHz, III HD 400 MHz, or 500 MHz. $CDCl_3$ was used as solvent and the signal of the residual $CHCl_3$ served as reference for the chemical shift δ expressed in ppm. The data analysis was performed using TopSpin 3.2 software.

Gel permeation chromatography (GPC)

GPC measurements were performed using different eluents depending on the solubility of the samples and on the type of analysis, being either:

- THF with 2% triethyl amine. The Agilent Technologies 1260 Infinity instrument was equipped with a refractive index (RI) and 308 nm UV detectors, a PLgel 5 µm guard column, and a PLgel 5 µm mixed D column (300 × 7.5 mm). Samples were run at 1 mL min^{-1} at 40 °C. Poly(methyl methacrylate) standards (Agilent PMMA calibration kits, M-M-10 and M-L-10) were used for the calibration. Before injection (100 µL), the samples were filtered through a PTFE membrane with 0.2 µL pore size.

- $CHCl_3$ with 2% TEA. The Agilent Infinity II MDS instrument was equipped with differential refractive index (DRI), viscometry (VS), dual angle light scatter (LS) and multiple wavelength UV detectors, 2× PLgel Mixed C columns (300 × 7.5 mm) and a PLgel 5 µm guard column. Samples were run at 1 mL min^{-1} at 30 °C. Poly(methyl methacrylate) and polystyrene standards (Agilent EasiVials) were used for the calibration. Ethanol was added as a flow rate marker. The samples were filtered through a GVHP membrane with 0.22 µm pore size before injection (100 µL).

Microwave reactor

Degradation experiments of **D1-D8** were carried out in a Biotage initiator + microwave reactor utilising capped reaction vials.

Experimental methods

Synthesis of the bifunctional thiomethacrylate crosslinker, S,S'-(thiobis(4,1-phenylene)) bis(2-methylprop-2-enethioate), bis-TMA

A solution of 4,4′-thiobisbenzenethiol (13.96 g, 250.40 g mol^{-1}, 0.0558 mol) in 10% aqueous potassium hydroxide (75 g) was added simultaneously to tetrabutylammonium bromide (1.35 g, 322.37 g mol^{-1}, 0.00419 mol) and *para*-methoxyphenol (0.50 g, 124.14 g mol^{-1}, 0.00403 mol) in dichloromethane (70 mL) and was cooled in an ice bath. Methacryloyl chloride (11.98 mL, 1.07 g cm^{-3}, 104.53 g mol^{-1}, 0.123 mol) was then added dropwise. Upon completion, the reaction mixture was stirred in the ice bath for a further 90 minutes. The organic layer was separated and washed with a saturated aqueous sodium hydrogen carbonate solution. More *para*-methoxyphenol inhibitor (0.22 g) was added to the product, which was dried over magnesium sulfate. Filtration followed by removal of the dichloromethane by rotary evaporation to give the viscous yellow liquid product (15.13 g, yield 70.1%). ^{1}H NMR ($CDCl_3$, δ ppm, 300 MHz) 7.44-7.26 (m, 10H, Ar**H**), 6.20 (s, 2H, **H**C=C), 5.71 (s, 2H, **H**C=C), 2.01 (s, 6H, C-C**H$_3$**).

Typical polymer synthesis procedure

Typical RAFT core-crosslinked polymer formation by addition of the ethylene glycol dimethacrylate crosslinker

The monomers MMA and ethylene glycol dimethacrylate were filtered through basic alumina columns to remove the inhibitor. For a targeted DP60 PMMA polymer, a solution of MMA (1 mL, 0.940 g cm^{-3}, 100.12 g mol^{-1}, 9.39 mmol, 60 eq.), 2-cyanoprop-2-yl-dithiobenzoate (0.035 g, 221.34 g mol^{-1}, 0.156 mmol, 1 eq.), AIBN (0.0026 g, 164.21 g mol^{-1}, 0.0156 mmol, 0.1 eq.) and dioxane (2 mL) was degassed for 20 minutes. The vial was then heated in an oil bath at 70 °C for 24 hours. In a next step, a solution of the ethylene glycol dimethacrylate (0.148 mL, 1.051 g cm^{-3}, 198.22 g mol^{-1}, 0.782 mmol, 5 eq.), AIBN (0.0026 g, 164.21 g mol^{-1}, 0.0156 mmol, 0.1 eq.) and dioxane (2.5 mL) was degassed for 15 minutes before the solution was added to the polymerisation mixture. The temperature of the reaction was maintained at 70 °C and the reaction was left stirring for a further 24 h. Samples were collected for ^{1}H NMR and THF GPC analysis at t_0, after 24 hours (before the crosslinker addition), just after the crosslinker addition and once the reaction had finished (after 48 h). ^{1}H NMR and GPC (in THF) were recorded to determine monomer conversions and molecular weights. Variables that were altered for different reactions include the crosslinker equivalents, the concentration of crosslinker added, the solvent and the reaction times.

After 48 h, the reaction mixture was precipitated in methanol and dried open to air. A 15 mg sample was dissolved in 5 mL and allowed to stir overnight. The sample was then run on the advanced chloroform viscometry GPC to collect the viscosity data.

Typical RAFT core-crosslinked polymer formation by addition of the bis-TMA crosslinker

The monomers MMA and bis-TMA were filtered through basic alumina columns to remove the inhibitor. For a targeted DP60 PMMA polymer, a solution of MMA (1 mL, 0.940 g cm^{-3}, 100.12 g mol^{-1}, 9.39 mmol, 60 eq.), 2-cyanoprop-2-yl-dithiobenzoate (0.035 g, 221.34 g mol^{-1}, 0.156 mmol, 1 eq.), AIBN (0.0026 g, 164.21 g mol^{-1}, 0.0156 mmol, 0.1 eq.) and dioxane (2 mL) was degassed for 20 minutes. The vial was then heated in an oil bath at 70 °C for 24 hours. A solution of the bis-TMA (0.3024 g, 386.54 g mol^{-1}, 0.782 mmol, 5 eq.), AIBN (0.0026 g, 164.21 g mol^{-1}, 0.0156 mmol, 0.1 eq.) and dioxane (2.5 mL) was degassed for 15 minutes before the solution was added to the polymerisation mixture. The temperature of the reaction was maintained at 70 °C and the reaction was left stirring for a further 24 h. Samples were collected for ^{1}H NMR and THF GPC analysis at t_0, after 24 hours (before the crosslinker addition), just after the crosslinker addition and once the reaction had finished (after 48 h). ^{1}H NMR and GPC (in THF) were recorded to determine monomer conversions and molecular weights. Variables that were altered for different reactions include the crosslinker equivalents, the concentration of crosslinker added, the solvent and the reaction times.

After 48 h, the solution was precipitated in methanol and dried open to air. A 15 mg sample was dissolved in 5 mL and allowed to stir overnight. The sample was then run on the advanced chloroform viscometry GPC to collect the viscosity data.

Typical amidation of thioester core-crosslinked polymers in a microwave reactor

A core-crosslinked polymer (0.02 g) was dissolved in a THF:water (4:1, 1 mL) solvent mixture in a Biotage 2-5 mL microwave vial. Hexylamine (19.2 µL, 0.77 g cm^{-3}, 101.19 $gmol^{-1}$, 0.146 mmol) was added, the vial was sealed with a PTFE lined butyl rubber septum and aluminium crimp cap, and placed in the microwave reactor and subjected to 150 °C for 4 h. After 4 h, the crude reaction mixture was subjected to THF GPC analysis to monitor the progress of degradation. The degraded polymers were then precipitated in methanol and dried before ^{1}H NMR and IR spectroscopy were conducted.

Typical amidation of thioester core-crosslinked polymers in an oil bath

A core-crosslinked polymer (0.02 g) was dissolved in a THF (1 mL) solvent mixture in a Biotage 2-5 mL microwave vial. Hexylamine (19.2 µL, 0.77 g cm^{-3}, 101.19 g mol^{-1}, 0.146 mmol) was added, the vial was sealed with a PTFE lined butyl rubber septum and aluminium crimp cap, and the resulting mixture was placed in a pre-heated oil bath at 150 °C for 4 hours. Samples of the crude reaction mixture were collected after 0.5, 1, 2, 3 and 4 h and THF GPC was run to monitor the progress of degradation. The degraded polymers were then precipitated in methanol and dried before ^{1}H NMR and IR spectroscopy were conducted.

Method for calculating the amine equivalents

The number of amine equivalents was calculated based on the equivalents of thiomethacrylate crosslinker incorporated into the star polymer. The proportion of thiomethacrylate to methacrylate was calculated by comparing the integrals of the methyl protons. In an example where the ratio of thiomethacrylate to methacrylate is 0.15

$M_{n,star} = 38,000$

n (thioester) = $0.02/(38,000 \times 0.15) = 3.51 \times 10^{-6}$ mol

The volume of amine required was then calculated using the above value and the number of equivalents needed.

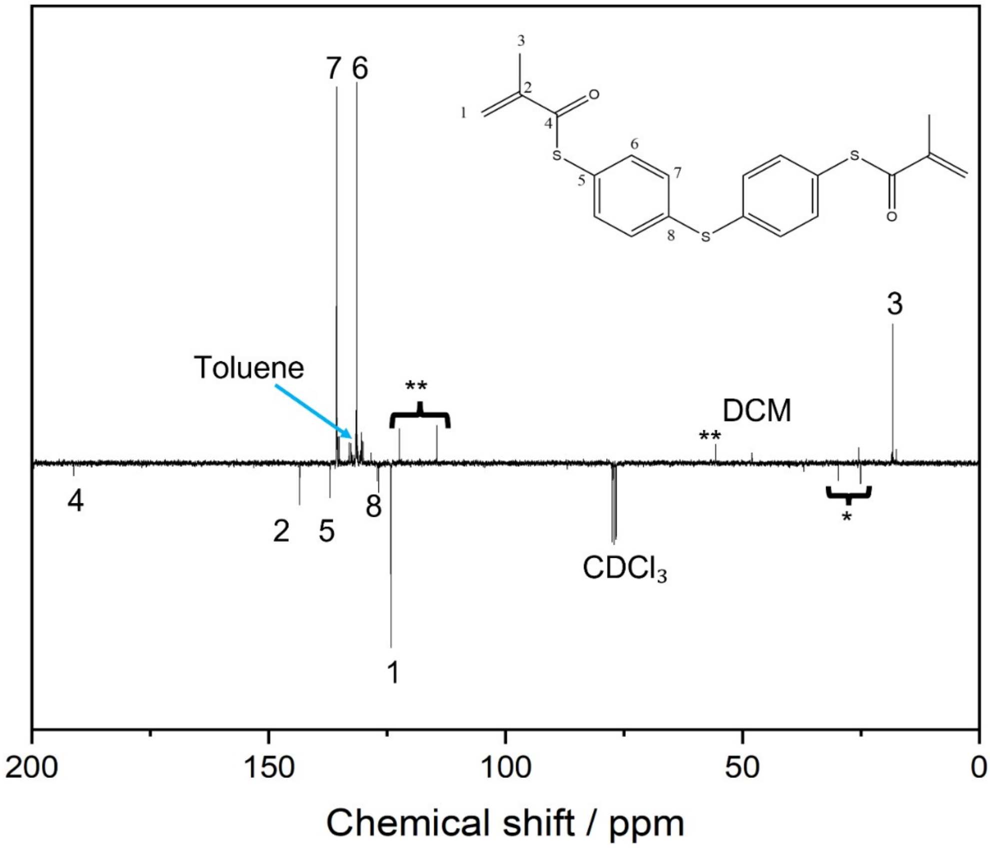

Figure S1- ^{13}C NMR spectrum (CDCl$_3$) for the crude bifunctional thiomethacrylate crosslinker. Peaks corresponding to tetrabutylammonium bromide (*), para-methoxyphenol (**), DCM and toluene were also observed.

^{1}H NMR spectra to obtain conversions:

All monomer conversions during the polymerisation reactions were obtained from ^{1}H NMR integration. Figures S2-S5 show examples of how the conversion values were obtained for the bis-MA core-crosslinked polymer in toluene, the bis-MA core-crosslinked polymer in 1,4-dioxane, the bis-TMA core-crosslinked polymer in toluene and the bis-TMA core-crosslinked polymer in 1,4-dioxane, respectively. The determination of the conversion values for these examples are detailed below. Conversions of other polymerisations were obtained using the same method.

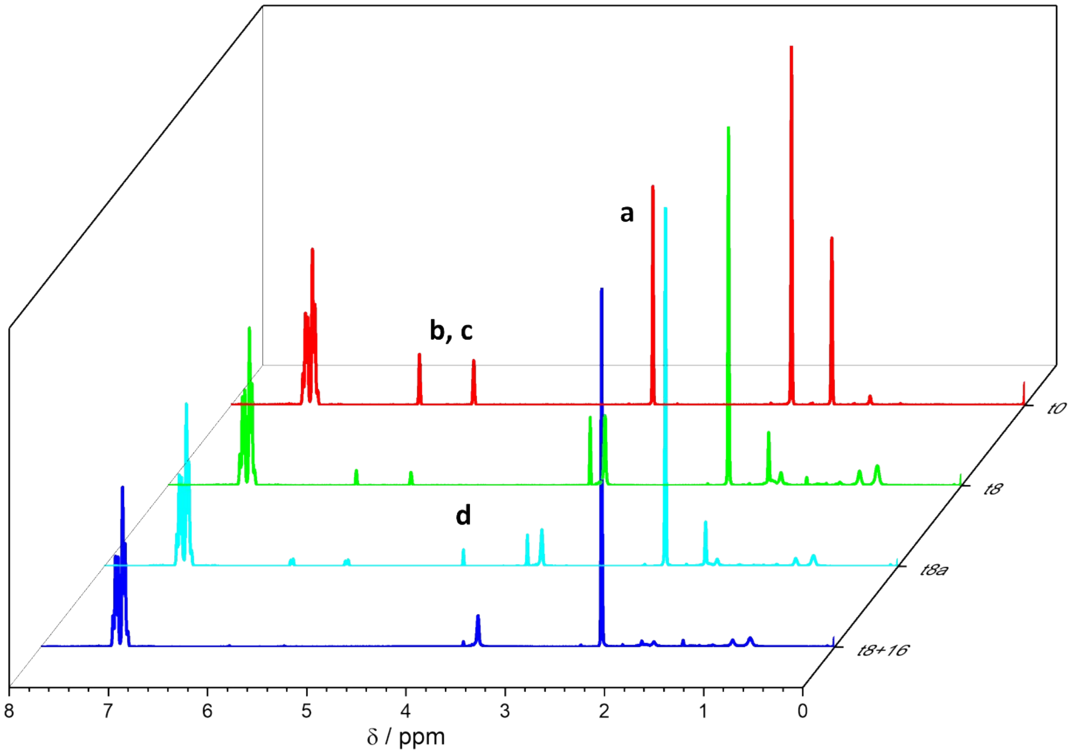

Figure S2- ^{1}H NMRs used to obtain the conversion for bis-MA core-crosslinked polymer S2.

For polymerisations conducted in toluene, the integral of the methyl protons from the methyl methacrylate (**a**) was set to 3 (Figure S2).

The integrals of b, c and d were reported.

% conversion MMA= $(1 - \text{integral}_{\text{b,c t8+16}}) \times 100$

% conversion (XL) crosslinker = $[1 - (\text{Integral}_{\text{d, t8+16}} / \text{integral}_{\text{d, t8a}})] \times 100$

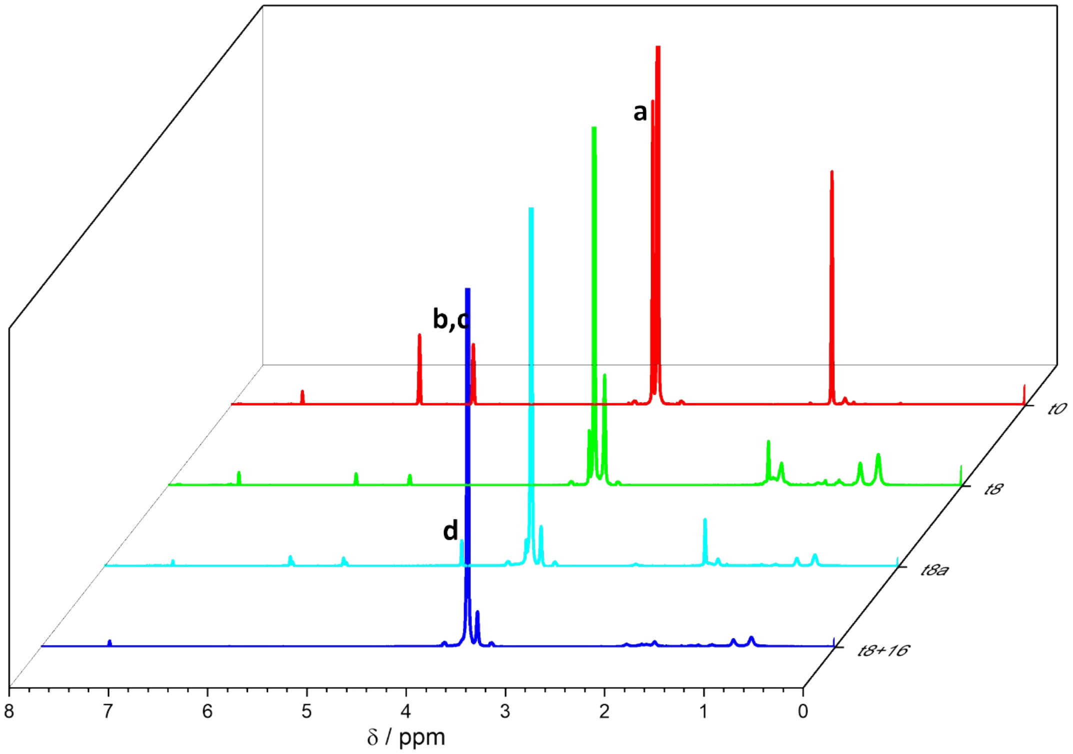

Figure S3- ^{1}H NMR used to calculate the conversion for the bis-MA core-crosslinked polymer S3.

For polymerisations conducted in dioxane, the integral of the methyl protons from the dioxane solvent peak (**a**) was set to 30000 (Figure S3).

The integrals of b, c and d were reported.

% conversion MMA= [1 - (integral$_{b,c\ t8+16}$ / integral$_{b,c\ t0}$)] x 100

% conversion (XL) crosslinker = [1 - (integral$_{d,\ t8+16}$ / integral$_{d,\ t8a}$) x 100

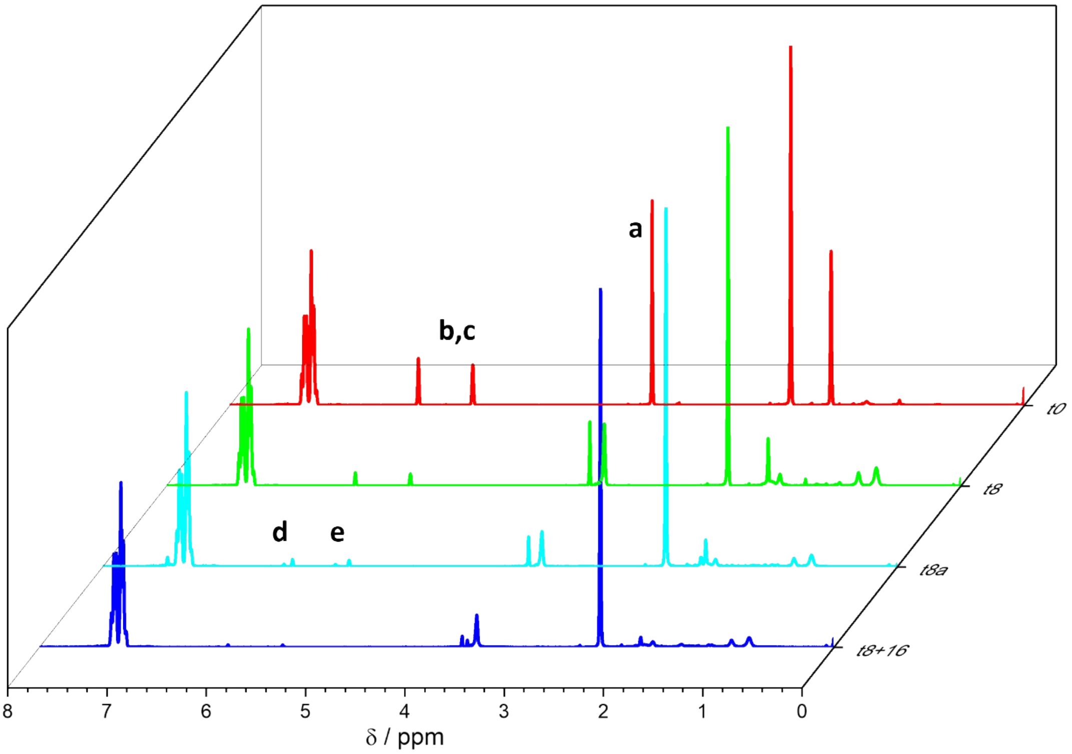

Figure S4- ^{1}H NMR used to calculate the conversion for the bis-TMA core-crosslinked polymer S9.

For polymerisations conducted in toluene, the integral of the methyl protons from the methyl methacrylate (**a**) was set to 3 (Figure S4).

The integrals of b, c, d and e were reported.

% conversion MMA= $(1 - \text{integral}_{b,c,\ t8+16}) \times 100$

% conversion (XL) crosslinker = $[1 - (\text{Integral}_{d,e,\ t8+16} / \text{integral}_{d,\ t8a})] \times 100$

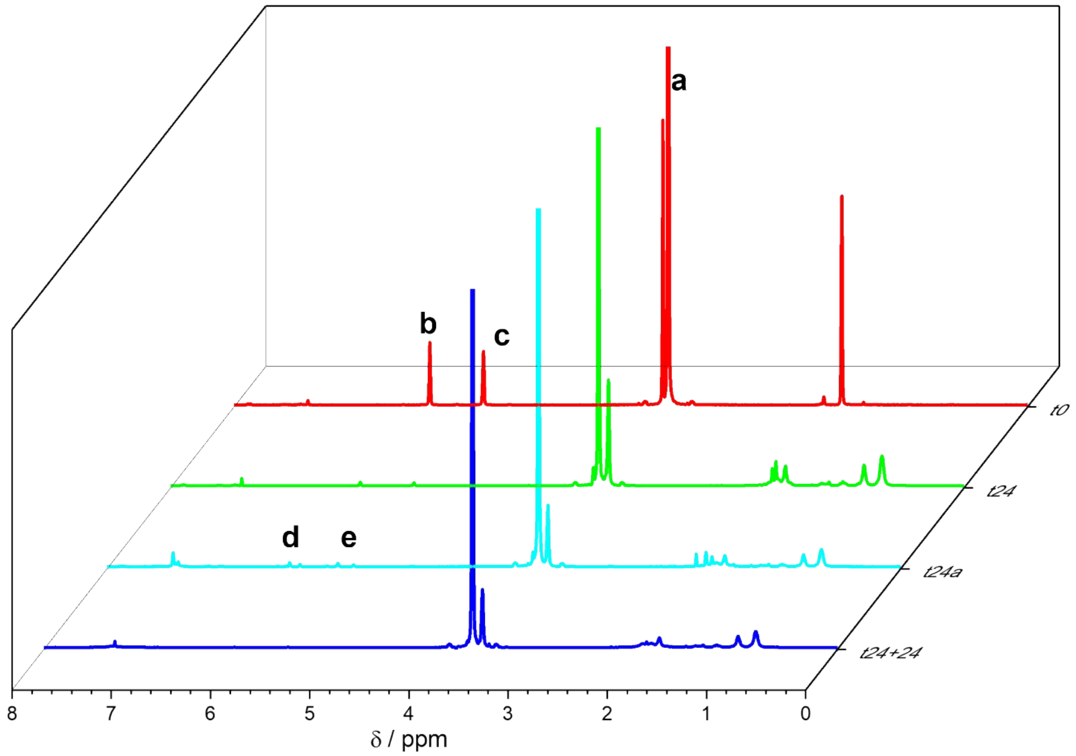

Figure S5- ^{1}H NMR used to calculate the conversion for the bis-TMA core-crosslinked polymer S10.

For polymerisations conducted in dioxane, the integral of the dioxane solvent peak(**a**) was set to 30,000 (Figure S5).

The integrals of b, c, d and e were reported.

% conversion MMA= [1- (integral$_{b,c\ t24+24}$ / integral$_{b,c\ t0}$)] x 100

% conversion (XL) crosslinker = (Integral$_{d,e,\ t24+24}$ / integral$_{d,e,\ t24a}$) x 100

Estimation of the percentage of leftover arms:

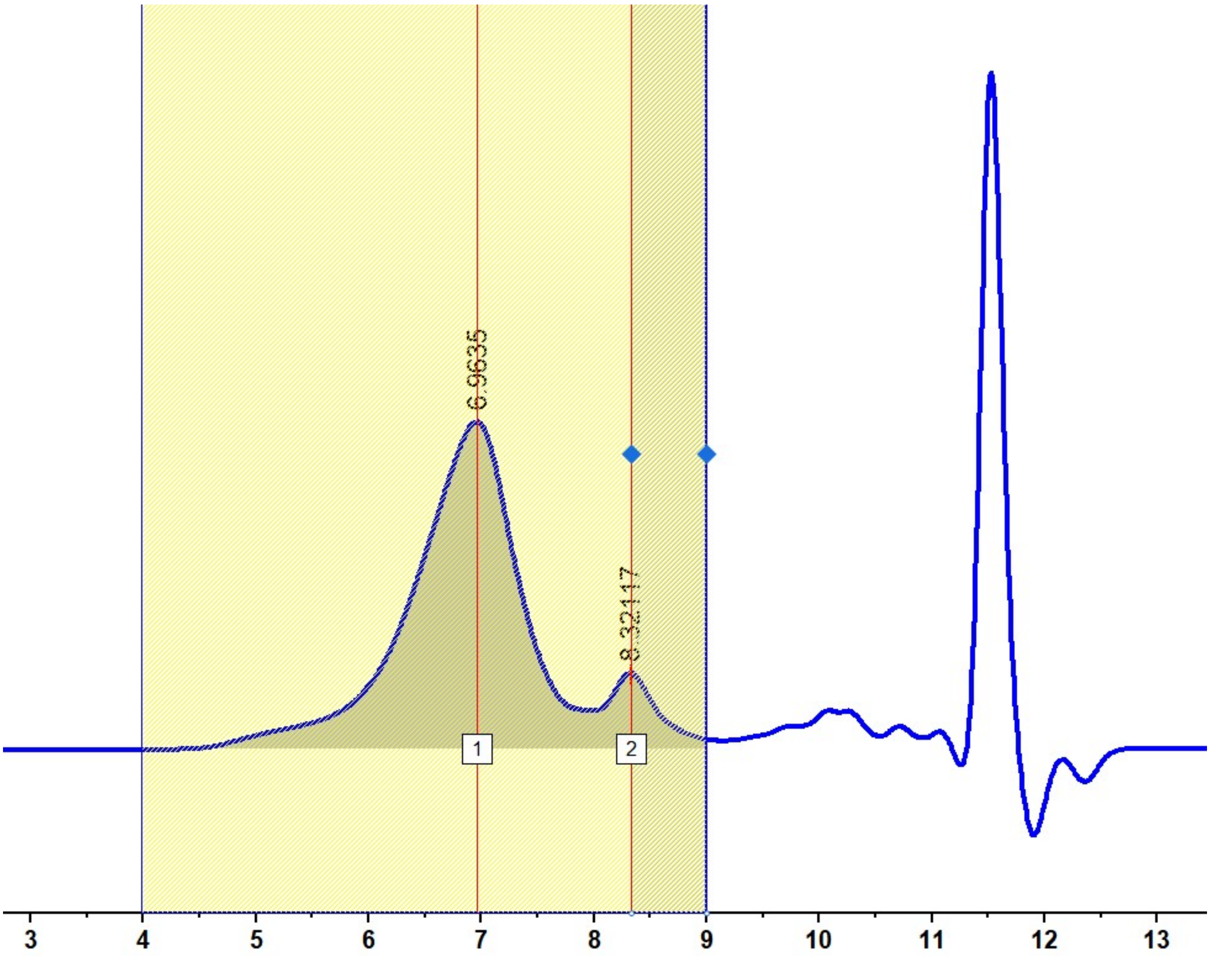

Figure S6- Illustration of the GPC integration used to estimate the percentage of leftover arms for S16.

Area 1 = total area of the star + arm peak

Area 2= Half of the arm peak

% arms = 100 x (2 x area 2)/area 1

<u>Advanced GPC analysis:</u> Advanced GPC can be used to measure the viscosity and the data can be used in mathematical models to allow for conclusions to be drawn about the degree of branching in the star-shaped polymers. By measuring samples of known concentration, information on the concentration and specific viscosity at different molecular weights can be obtained from the RI and VS detectors respectively.[1, 2] When combined, the intrinsic viscosity at each molecular weight can be calculated using **Equation S1**, where [η] is the intrinsic viscosity, η_{sp} is the specific viscosity and C is the concentration.[2]

$$[\eta]=\lim_{C\to 0}\left(\frac{\eta_{sp}}{C}\right)$$

(**Equation S1**)

The branching factor, g′, was calculated with **Equation S2**.[2] The intrinsic viscosity of the branched polymer is divided by the intrinsic viscosity of the linear reference at each molecular weight.

$$g' = \left(\frac{IV\ (Branched)}{IV\ (linear)}\right)_{\mathrm{MW}}$$

(**Equation S2**)

The contraction factor, g, was calculated with **Equation S3,** where the structural factor, ε, had a value of 0.75**.**[2] It is noteworthy that this value for ε is an assumption based on literature data rather than being an accurate value.[2]

$$g = g'^{\left(\frac{1}{\varepsilon}\right)}$$

(**Equation S3**)

The number of arms, f, was then calculated using **Equation S4** and the assumption that the star polymers were polydisperse.[2]

$$g = \frac{3f}{(f+1)^2}$$

(Equation S4)

The average number of arms, f $_{(n)}$, was calculated by averaging the number of arms for all of the molecular weight values. These values are displayed below in **Table S1.**

Table S1- Advanced viscometry GPC data for the core-crosslinked branched polymers formed with a bis-methacrylate and a bis-thiomethacrylate crosslinker along with the calculated average branching factor, g' and the average number of arms, $f_{(n)}$.

Label	**$M_{p,\mathrm{GPC}}$ Da)**	**$M_{p,VS}$ (*Da*)**	**Đ**	**$g'_{(n)}$**[a]	**$f_{(n)}$**[b]
S1	45,900	70,900	1.91	0.43	77
S2	63,700	117,600	2.66	0.34	208
S3	63,700	129,900	2.63	0.29	290
S4	55,400	93,000	1.52	0.46	101
S5	47,600	96,600	2.05	0.37	120
S6	41,200	76,200	1.93	0.32	237
S7	65,600	152,900	1.56	0.28	248
S8	102,000	216,900	3.44	0.23	497
S9	58,600	155,200	2.31	0.30	248
S10	55,700	124,300	2.66	0.33	388
S11	56,400	135,500	2.17	0.31	302
S12	57,500	148,200	2.35	0.30	480
S13	-[c]	-[c]	-[c]	-[c]	-[c]
S14	67,000	166,000	2.56	0.25	720
S15	67,300	163,400	2.06	0.26	453
S16	77,100	229,300	2.79	0.22	956

[a] Calculated using Equations S1 and S2; [b] Calculated using a polydisperse star model with an ε value of 0.75; [c] Advanced GPC analysis could not be carried out on **S13** due to gelation.

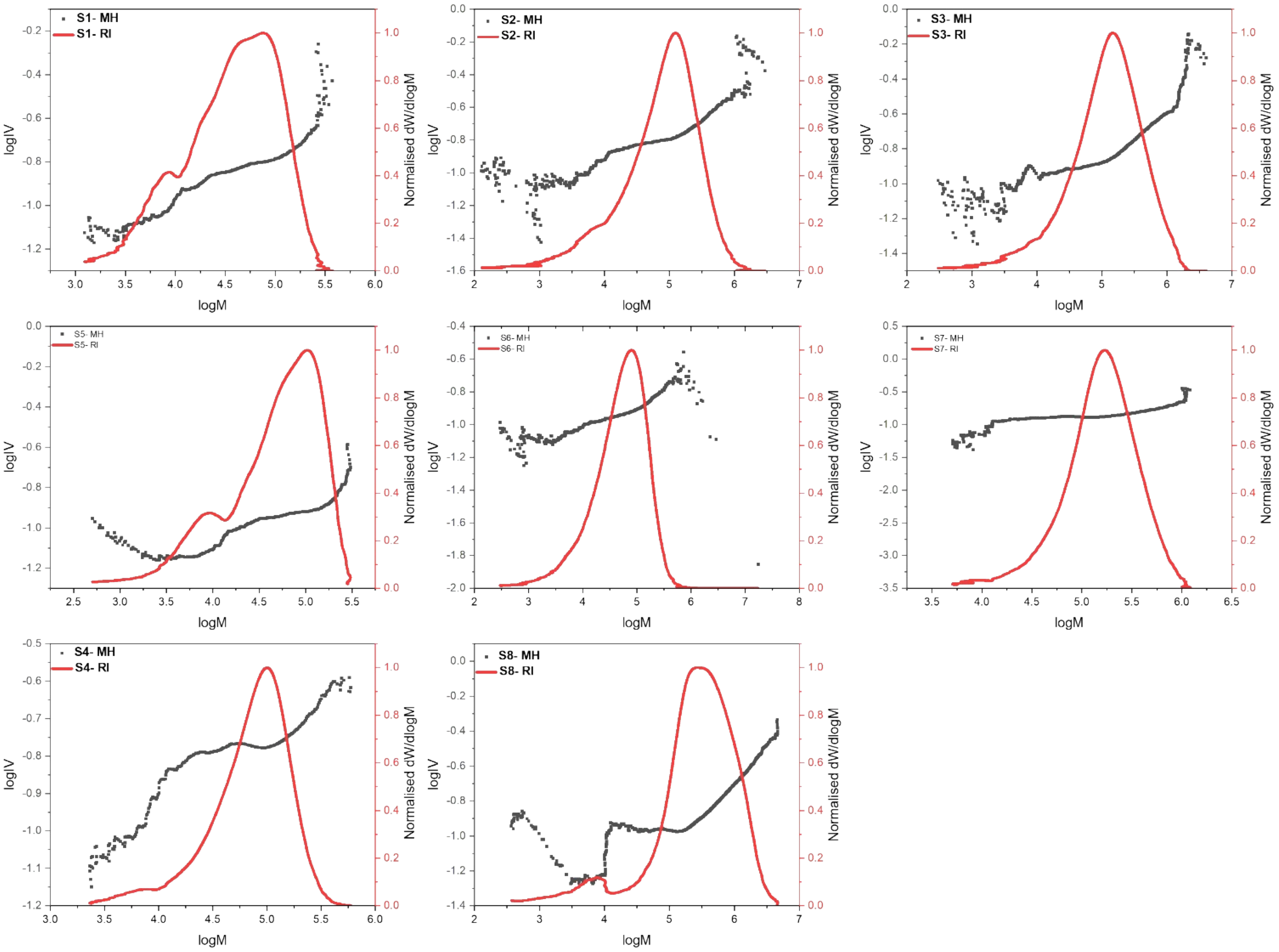

Figure S7- Mark-Houwink plots overlaid with the RI traces for S1-S8.

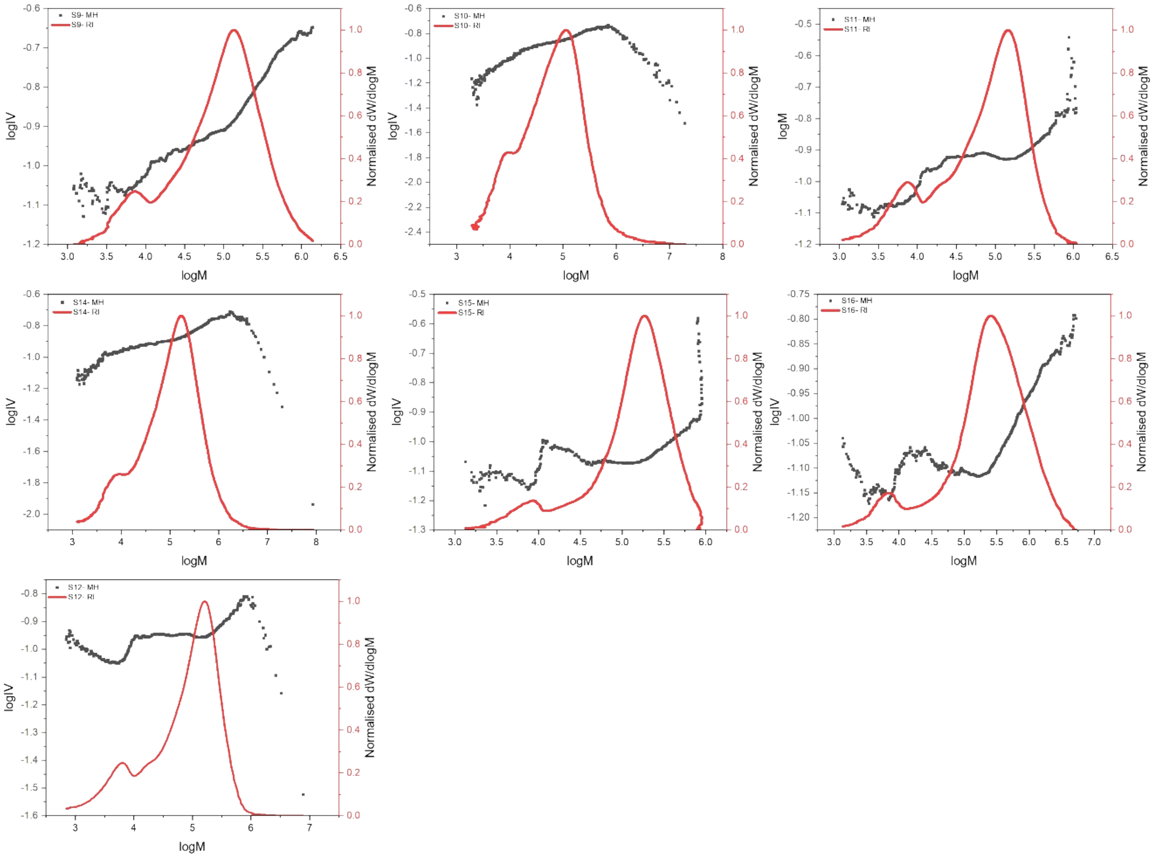

Figure S8- Mark-Houwink plots overlaid with the RI traces for S9-S12 and S14-16. Advanced GPC was not measured for S13 due to gelation.

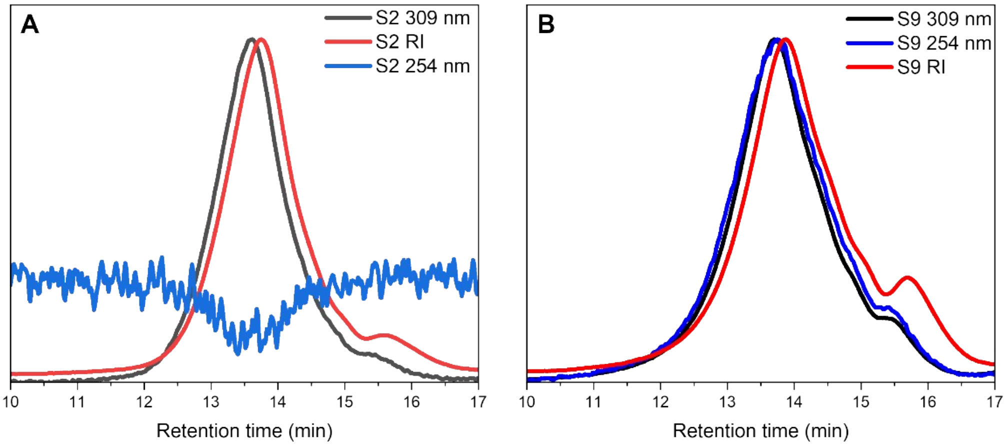

Figure S9- The UV GPC traces at 309 nm and 254 nm for a bis-methacrylate crosslinked star-shaped polymer (A) and a bis-thiomethacrylate crosslinked star-shape polymer (B). The RI traces have also been overlaid.

GPC traces, ^{1}H NMR and IR spectra from the degradation studies:

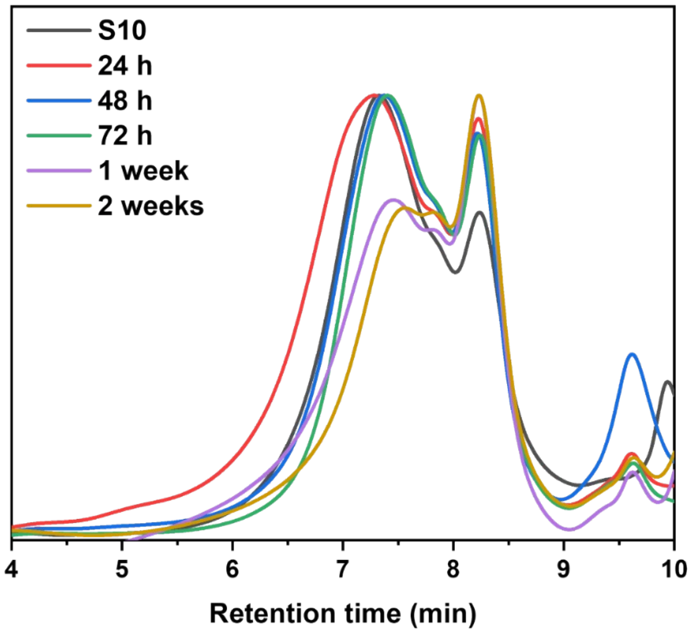

Figure S10- GPC traces for the room temperature degradation of polymer S10 with 10 eq. hexylamine at 25 °C.

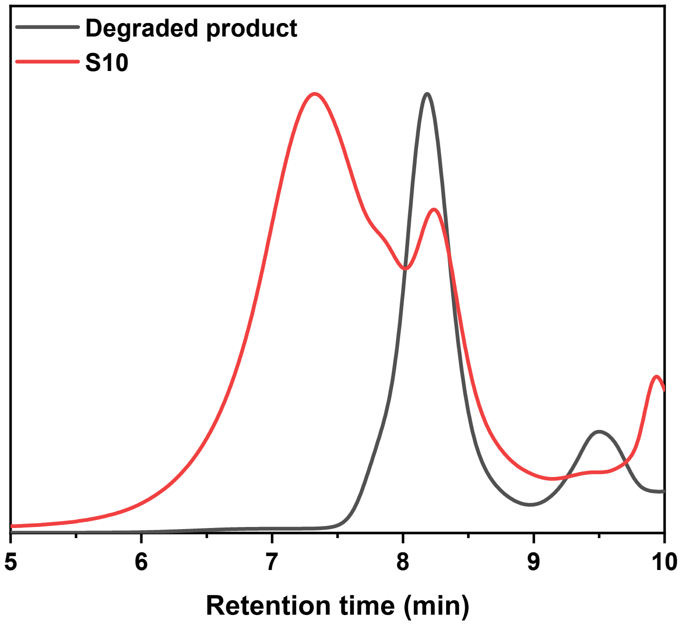

Figure S11- GPC traces for the starting material and degraded product of S10 with 10 eq. hexylamine kept at 70 °C for 9 days.

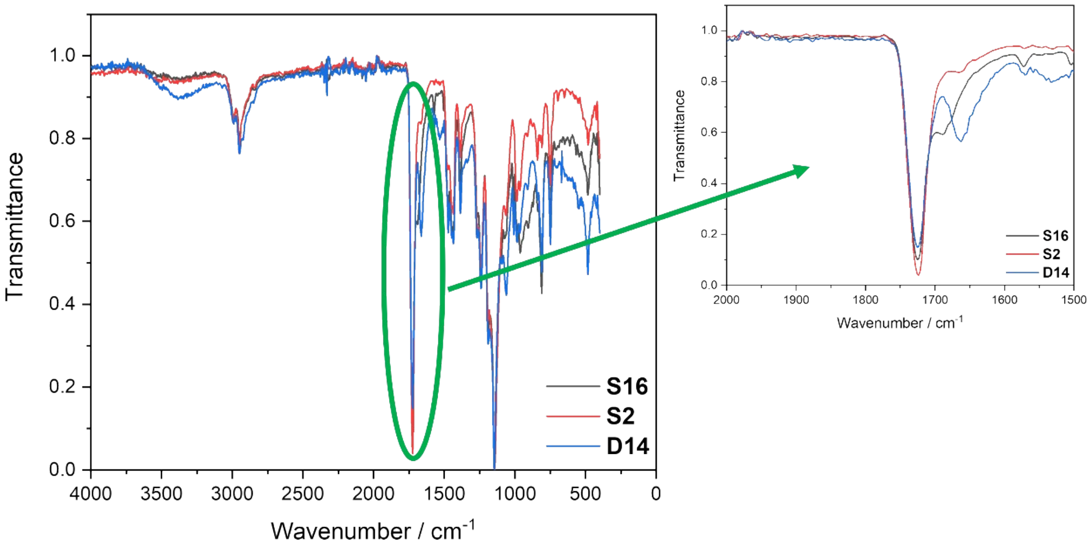

Figure S12- IR spectra of S16, S2 and the degraded product D14. The carbonyl stretch region between 1500-2000 cm^{-1} (right) shows the shift from the thioester carbonyl stretch in S16 to an amide carbonyl stretch in D14.

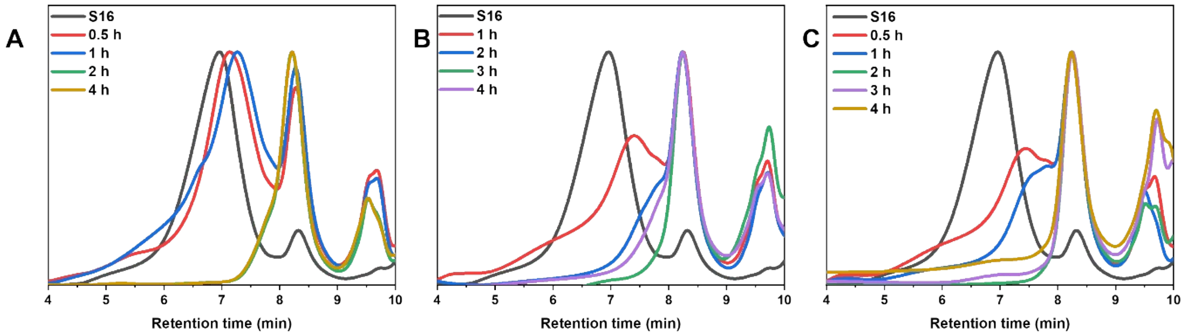

Figure S13- GPC traces for the degradation kinetics using benzylamine (A), ethanolamine (B) and 3-amino-1-propanol (C).

References:

1. G. Hayes, B. Drain and C. R. Becer, *Macromolecules,* 2021***, 55*** (1), 146-155.
2. A. Monaco, B. Drain and C. R. Becer, *Polym. Chem.,* 2021***, 12*** (36), 5229-5238.