Supplementary Information (SI) for Polymer Chemistry.
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Supplementary Information

Lipoic acid/ethyl lipoate as cleavable comonomers for synthesis of degradable polymer networks

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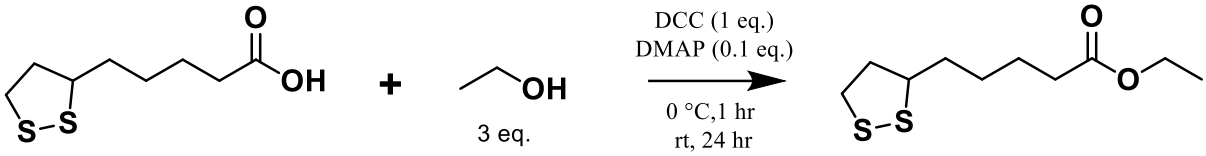
Experimental methods

Materials

n-Butyl acrylate (*n*-BA, 99%) and anisole (99%) were purchased from Acros Organics. Azobisisobutyronitrile (AIBN, 97%), α-lipoic acid (LA, ≥98%), 4-(dimethylamino)pyridine (DMAP, ≥99%), N,N-dimethylformamide (DMF, ≥99.9%), 2-(dodecylthiocarbonothioylthio)-2-methylpropionic acid (DDMAT, 98%), 2,2'-(ethylenedioxy)diethanethiol (EDDET, 95%), 1,8-diazabicyclo[5.4.0]undec-7- ene (DBU, 98%), pyridine (>99%), acetic acid (AcOH, 99.9-100%) and ethyl acetate (>99.5%) were purchased from Sigma-Aldrich. Tetrahydrofuran [THF, gel permeation chromatography (GPC) grade] was purchased from Fisher. 1,6-Hexanediol diacrylate (HDDA, 99%) was purchased from Alfa Aesar. N,N' dicyclohexylcarbodiimide (DCC, 99%) was purchased from Thermo Fisher Scientific. Ethanol absolute and dichloromethane (DCM) were purchased from VWR. All chemicals purchased from the manufacturers were stored at the recommended temperatures and used as received. n-BA and HDDA were passed basic alumina column to remove inhibitors before use.

Synthesis of ethyl lipoate (ELp)

Ethyl lipoate was synthesised from lipoic acid using a Steglich esterification method modified from published procedures.[1] In a 250 mL round bottomed flask, lipoic acid (5 g, 0.024 mol) and ethanol (4.2 mL, 0.073 mol) were dissolved in DCM (20 mL) over ice for 10 minutes. In a 50 mL beaker, DCC (5 g, 0.024 mol) was dissolved in DCM (20 mL) and this solution was then added to the lipoic acid/ethanol solution. The mixture was stirred for a further 10 minutes over ice. A solution of DMAP (0.2961 g, 0.0024 mol) in DCM (10 mL) was added dropwise to the round bottomed flask, resulting in precipitation. This mixture was stirred for a further 1 hour over ice, and then at room temperature for 24 hours. The white precipitate side product was removed by vacuum filtration and the yellow solution concentrated under vacuum. The crude product was then purified by silica column chromatography using ethyl acetate/hexane (5% v/v ethyl acetate) as the eluent. The product was isolated as a yellow oil with a yield of 4.42 g (78%).



Scheme 1: synthesis of ethyl lipoate (ELp) from Steglich esterification of lipoic acid (LA)

RAFT polymerisation of n-BA and lipoic acid/ethyl lipoate copolymer for kinetic studies

n-BA (1 mL, 70 mmol), AIBN (0.0038 g, 0.023 mmol), DDMAT (0.0212 g,0.05mmol), anisole (1 mL) and either ELp (0.355 mL, 1.7 mmol) or LA (0.360 g, 1.7 mmol) were added to a 25 mL vial and stirred. 5 drops of DMF were added as an NMR internal standard. The vial was sealed and degassed with nitrogen for 20 minutes before heating at 65 °C. Samples were taken at time intervals to monitor monomer conversion and polymer molecular weight. [*n*-BA]:[AIBN]:[DDMAT]:[ELp] or [LA] = 120:0.4:1:30.

Synthesis of PBA-lipoic acid/ethyl lipoate gels by RAFT polymerisation
n-BA (1 mL, 70 mmol), AIBN (0.0038 g, 0.023 mmol), DDMAT (0.0212 g,0.05 mmol), anisole (1 mL), HDDA (31.2 µL, 1.4 mmol and either ELp (0-25 mol%) or LA (0-30 mol%) were added to a 25 mL push top, neckless vial. 5 drops of DMF were added as an NMR internal standard and the mixture stirred until homogenous. The vial was sealed and degassed with nitrogen for 20 minutes before heating at 65 °C. Samples were taken at time intervals to monitor monomer conversion and polymer molecular weight. [*n*-BA]:[AIBN]:[DDMAT]:[HDDA]:[ELp]or [LA]=150-x:0.4:1:3:x

Synthesis of PBA-lipoic acid/ethyl lipoate gels by free radical polymerisation
Same procedure as described above for RAFT polymerisation was used to prepare FRP gels, but without the addition of the RAFT agent (DDMAT).

Equilibrium swelling ratio and gel fraction determination.
30-100 mg of a gel sample was placed into a pre-weighed vial and 4 mL THF added. This was left for 3-6 hours to wash and then the THF was transferred to another pre weighed vial to measure the polymer sol. This process was repeated 3 times so that the sample was immersed in THF for a total of at least 24 hours. The final THF wash was removed, and the mass of the swollen gel was recorded ($m_{swollen}$). Any excess surface solvent was removed before recording the mass of the swollen gel. The swollen gel and the THF washings were allowed to dry overnight, followed by 24 hours under vacuum. The mass of the dry gel (m_{dry}) and the mass of the remaining solids from the washings (m_{sol}) were recorded. The equilibrium swelling ratio (ESR) was calculated as ESR = $m_{swollen}/m_{dry}$. The gel fraction was calculated as % GF= $m_{dry}/(m_{dry}+m_{sol}) \times 100\%$. All measurements were performed in triplicate.

Degradation of PBA-lipoic acid/ethyl lipoate gels by thiol-disulfide exchange
50-120 mg of dried gel sample (1 equiv. ELp/ LA) was placed in a vial with THF (4 mL), EDDET (3 equiv.) and DBU (1 equiv.). The mixture was gently mixed, and the vial was sealed and degassed with nitrogen for 15 mins before being left at room temperature for 24 hours. If solid gel remained after degradation the sample was washed with 3 × 4 mL portions of THF over 24 hours. The swollen gel sample was weighed ($m_{swollen,deg}$) and allowed to dry overnight in air, followed by 24 hours under vacuum. The mass of the dry gel after degradation was recorded ($m_{dry,deg}$). The mass loss through degradation was calculated as % mass loss= $(m_{dry}-m_{dry,deg})/m_{dry} \times 100\%$. The ESR after degradation was calculated as $ESR_{deg}=m_{swollen,deg}/m_{dry,deg}$. All measurements were performed in triplicate.

Degradation of PBA-lipoic acid/ethyl lipoate gels by heating in DMF
50 - 120 mg of dried gel sample (1 equiv. ELp/ LA) was placed in a vial with 20 mL DMF. The vial was left open to air and heated at either 35 °C or 100 °C for 24 hours. If solid gel remained after degradation the sample was washed with 3 × 4 mL portions of THF over 24 hours .The swollen gel sample was weighed ($m_{swollen,deg}$) and allowed to dry overnight in air, followed by 24 hours under vacuum. The mass of the dry gel after degradation was recorded ($m_{dry,deg}$). The mass loss through degradation was calculated as % mass loss = $(m_{dry} - m_{dry,deg})/m_{dry} \times 100\%$. The ESR after degradation was calculated as $ESR_{deg} = m_{swollen,deg}/m_{dry,deg}$. All measurements were performed in triplicate.

Degradation-regelation of PBA-lipoic acid/ethyl lipoate gels

0.3-0.5g of dried gel sample ((1 equiv. ELp/ LA) was placed in a vial with THF (6 mL), EDDET (1.5 equiv.) and DBU(1 equiv.). The mixture was gently mixed and the vial was sealed and degassed with nitrogen for 15 mins before being left at room temperature for 24 hours. AcOH (1.5 equiv) was added to quench the thiols and the solution was concentrated by evaporating the THF under flowing nitrogen gas. The fragments were precipitated in cold methanol/water (90:10) and left overnight in the fridge. The fragments were removed from the methanol/water and mixed with 0.1 mL DMF or anisole, and pyridine (5 equiv.) in a small vial. The vial was heated at 35 °C with the vial open for 1 hour, then continued to be heated with the lid on for 24 hours. The vial was then left for 1 week at room temperature.

Self-healing

As synthesised gels were cut with a razor blade. The two halves were pressed together with 5 drops of DBU added to the cut surface. The samples were left with no external pressure for up to 2 weeks.

Instrumentation

^{1}H NMR measurements were performed on a 400 MHz Bruker Neo in $CDCl_3$. DMF (δH = 8.0ppm) was used as an internal reference in kinetic experiments. GPC analysis was conducted using a 1260 Infinity Multi-Detector GPC/SEC System manufactured by Agilent. The system uses three columns, two identical PLgel 5 μm Mixed-D columns (300 × 7.5 mm) and a guard column, PLgel 5 μm Mixed Guard (50 × 7.5 mm). All GPC analyses were conducted at 35 °C using THF as the mobile phase; each sample injection was 100 μL, with a run time of 40 min and 1 mL/min flow rate. Data acquisition was performed using linear polystyrene calibration standards. Oscillatory rheology measurements were carried out using a TA Instruments Discovery HR-30 rheometer fitted with a 20 mm crosshatched parallel plate geometry and a crosshatched base plate. As-synthesized disc-shaped gel samples with a thickness of 2.5-4 mm were assessed under a constant axial force of 0.35N. Frequency sweeps were carried out at 25°C over a range of 0.01–100 rad s^{-1} at a constant strain of 0.1%. Amplitude sweeps were carried out at 25 °C over a range of 0.01%-1% strain at 0.1 rad s^{-1} angular frequency. Differential scanning calorimetry (DSC) experiments were carried out on dry gel networks using a TA Instruments Q20, in the temperature range of −80 to 150 °C with a heating/cooling rate of 10 °C/min under nitrogen (flow rate 20 mL/min). Data analysis was conducted using Q Series software and always using the second thermal cycle. Thermogravimetric analysis (TGA) was carried out on a Setaram Setsys Evolution TGA 16/18. Samples were heated from 45 to 600 °C with a heating rate of 10 °C/min under argon (flow rate 20 mL/min). The onset temperatures were measured by recording the temperature at 5% mass loss.

Supplementary Data

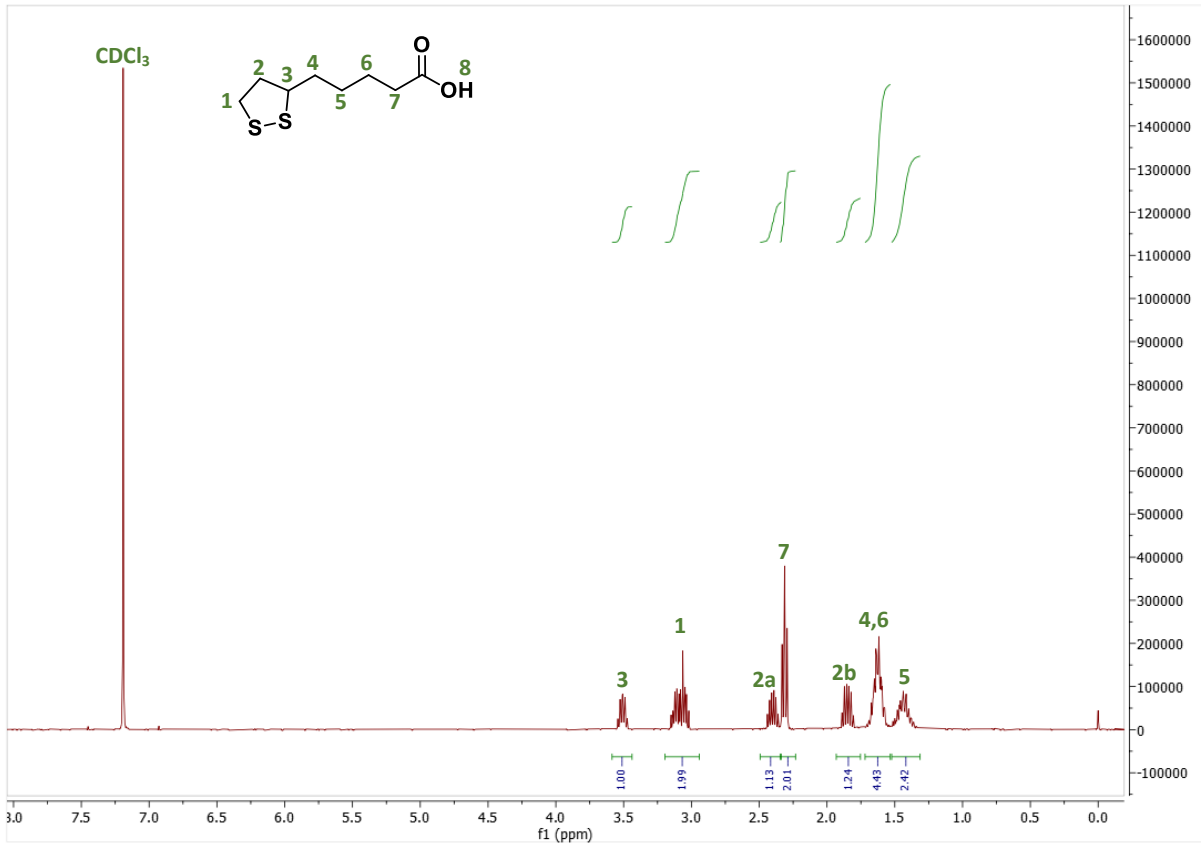


Figure S1: ^{1}H NMR spectrum of α-lipoic acid (LA) in $CDCl_3$. Carboxylic acid proton (8) presents as very broad low intensity peak at 11 ppm, but not visible at this resolution.

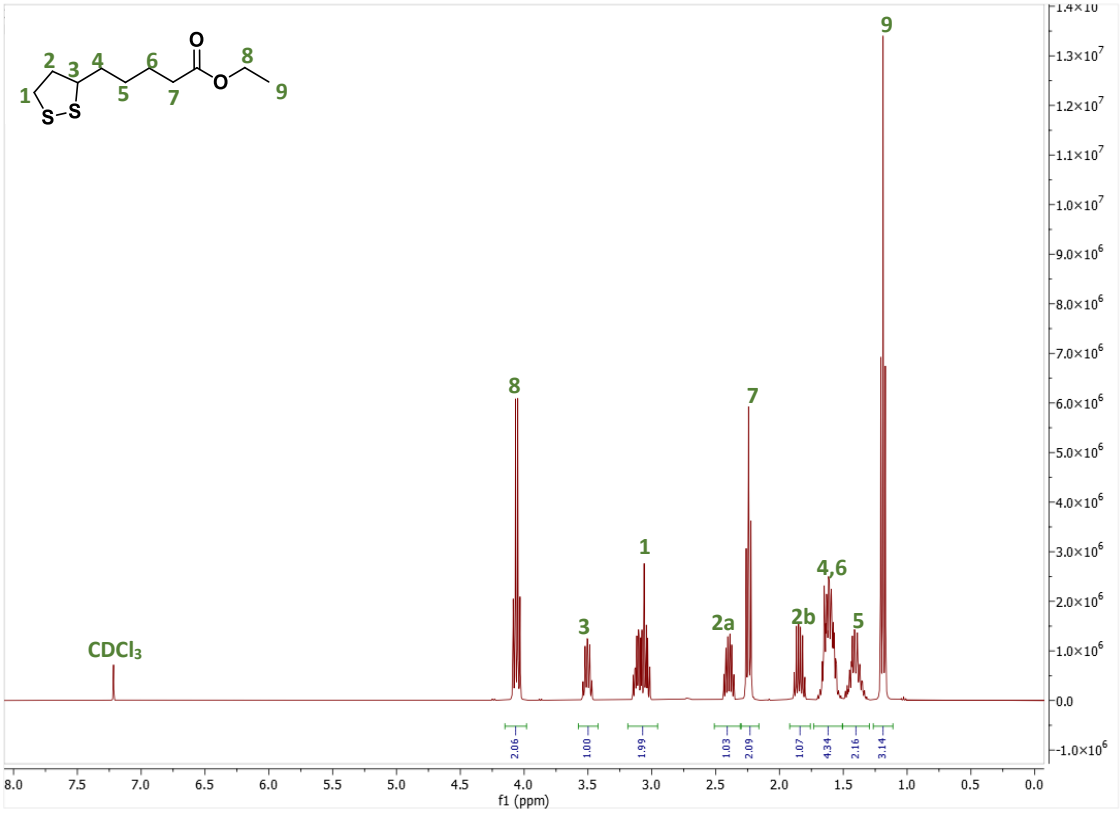


Figure S2: ^{1}H NMR spectrum of ethyl lipoate (ELp) in $CDCl_3$.

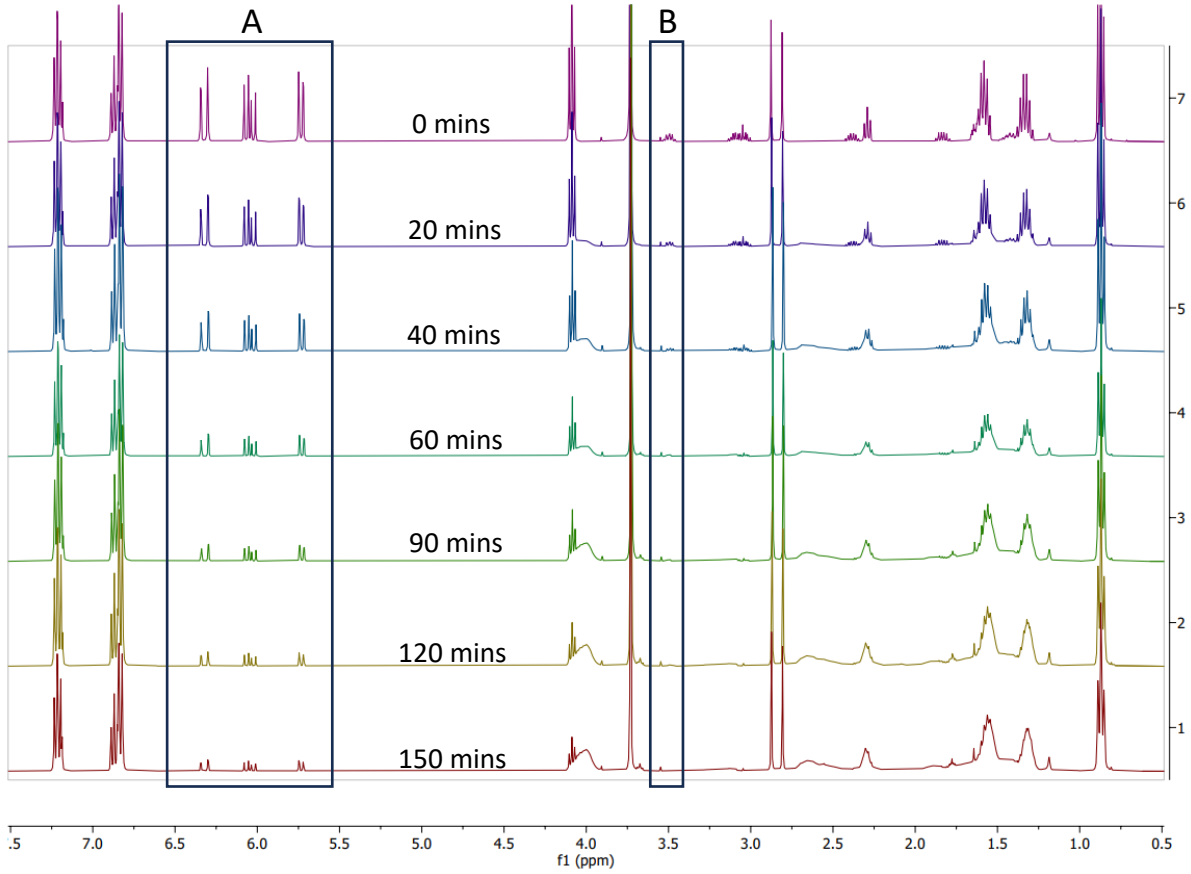


Figure S3: ^{1}HNMR spectra in $CDCl_3$ for kinetic measurements of PBA-20%LA-RAFT copolymerisation with no crosslinker. Conversion of butyl acrylate measured by decrease in integral of vinyl protons' peaks (A, 5.6 ppm-6.4 ppm) and conversion of lipoic acid measured though decrease in integral of proton within dithiolane ring (B, 3.5 ppm). Peak integrals measured with reference to DMF proton peak at 8.02 ppm.

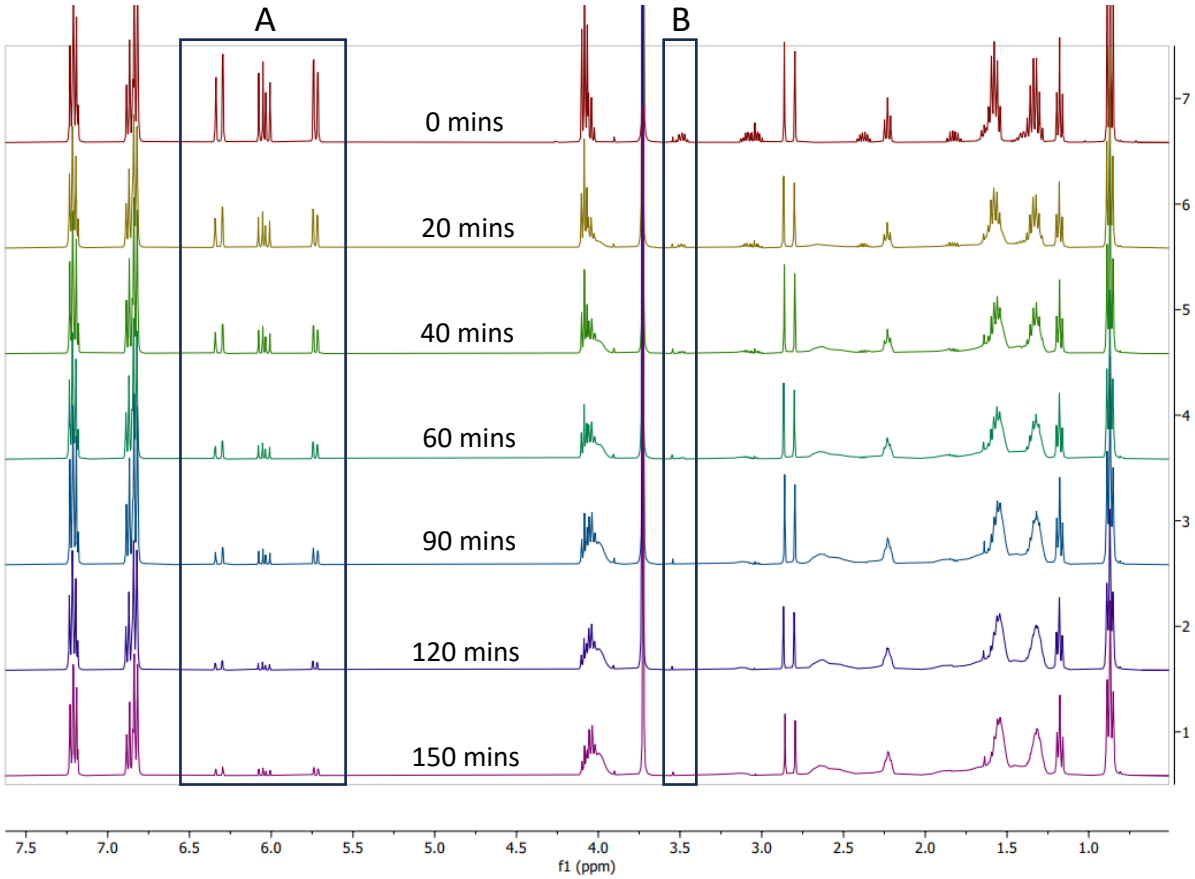


Figure S4: ^{1}HNMR spectra in $CDCl_3$ for kinetic measurements of PBA-20%ELp-RAFT copolymerisation with no crosslinker. Conversion of butyl acrylate measured by decrease in integral of vinyl protons' peaks (A, 5.6 ppm-6.4 ppm) and conversion of ethyl lipoate measured though decrease in integral of proton within dithiolane ring (B, 3.5 ppm). Peak integrals measured with reference to DMF proton peak at 8.02 ppm.

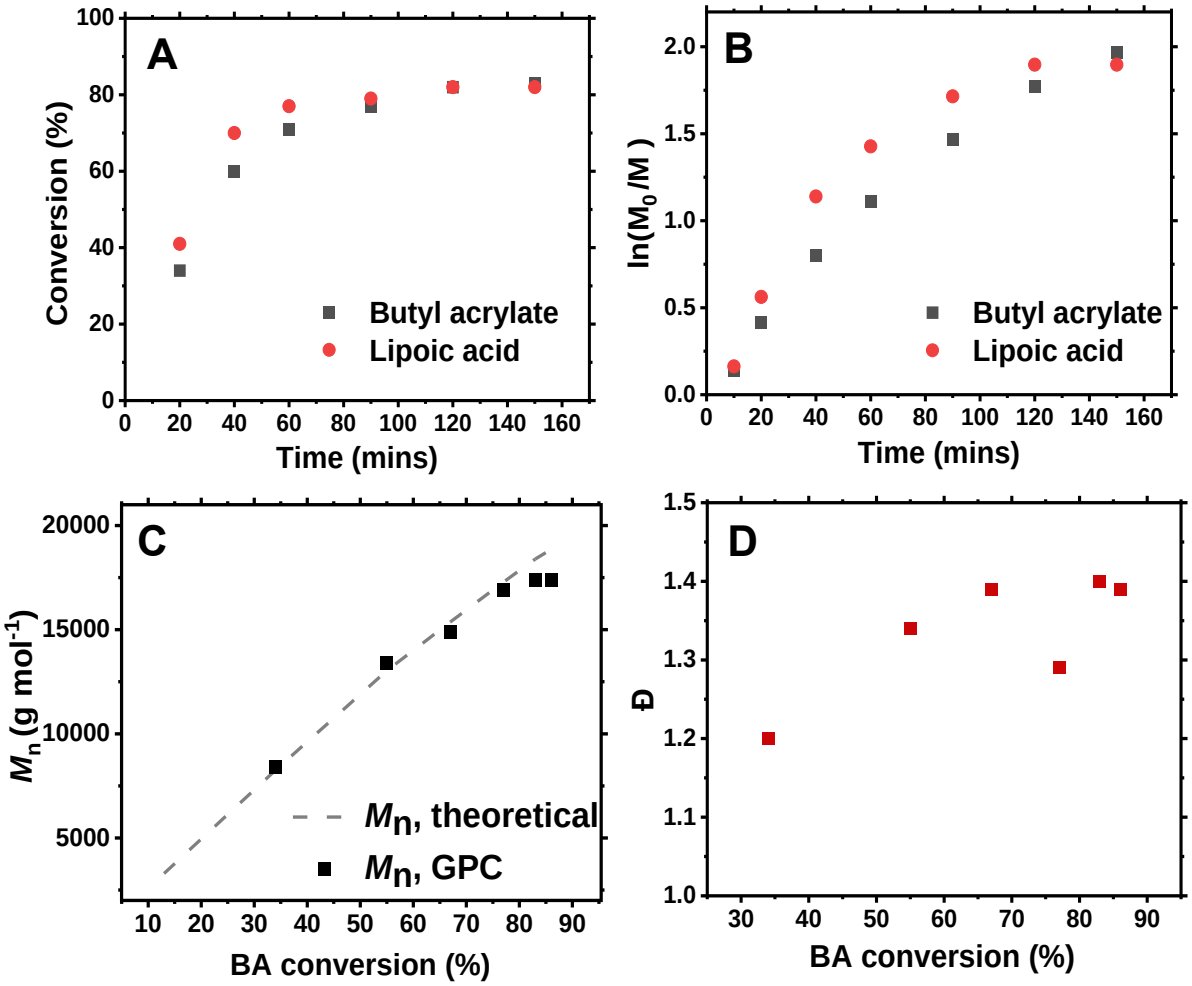


Figure S5: Conversion plots (A) and first-order semi-logarithmic kinetic plots (B) for RAFT copolymerisation of *n*-butyl acrylate with lipoic acid comonomer. [BA]:[LA]:[AIBN]:[CTA] 120:30:0.4:1. BA:anisole 1:1 v/v, T = 65 °C. M_n (C) and $Đ$ (D) measured by THF GPC, and monomer conversions and theoretical M_n measured from ^{1}H NMR.

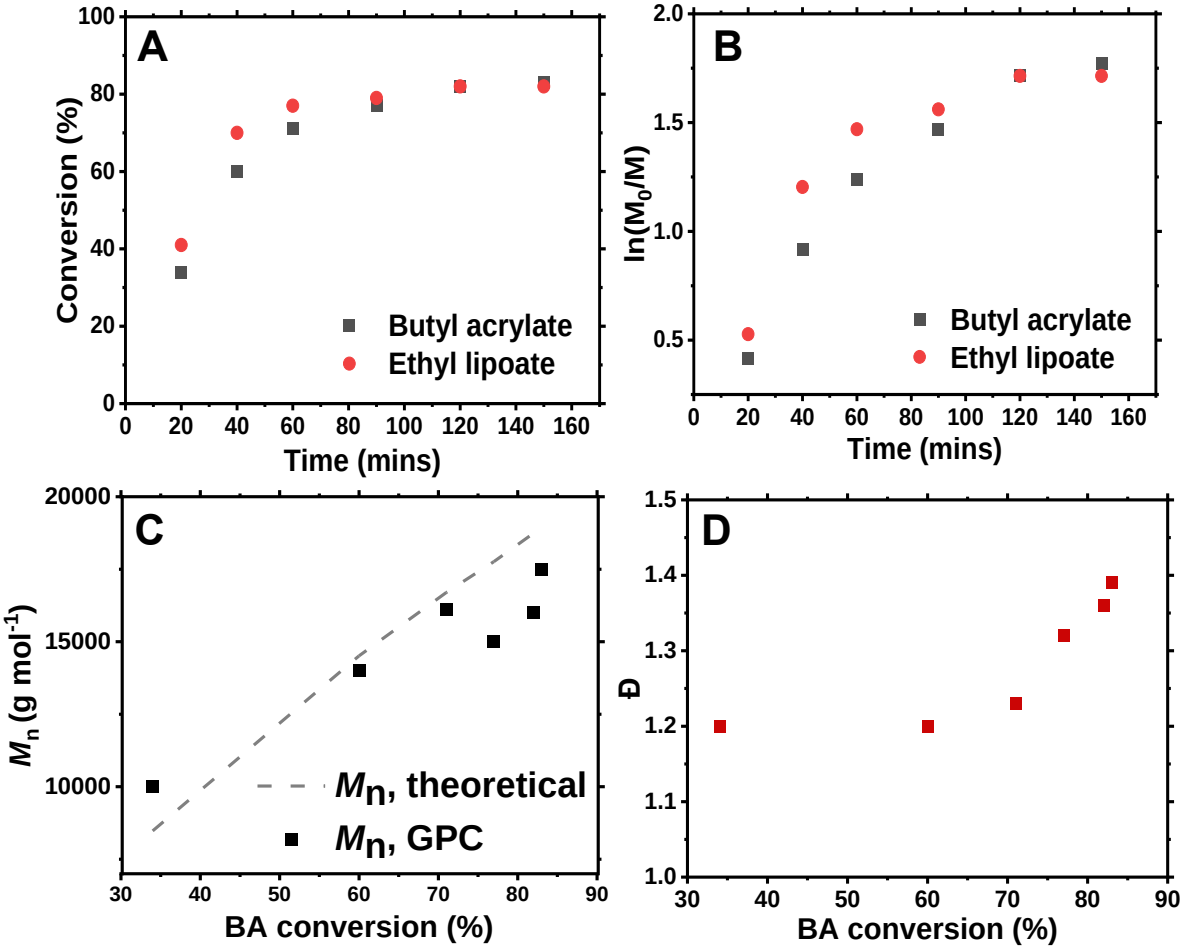


Figure S6: Conversion plots (A) and first-order semi-logarithmic kinetic plots (B) for RAFT copolymerisation of *n*-butyl acrylate with ELp comonomer. [BA]:[ELp]:[AIBN]:[CTA] 120:30:0.4:1. BA:anisole 1:1 v/v, T = 65 °C. M_n (C) and $Đ$ (D) measured by THF GPC. Monomer conversions and theoretical M_n measured from ^{1}H NMR.

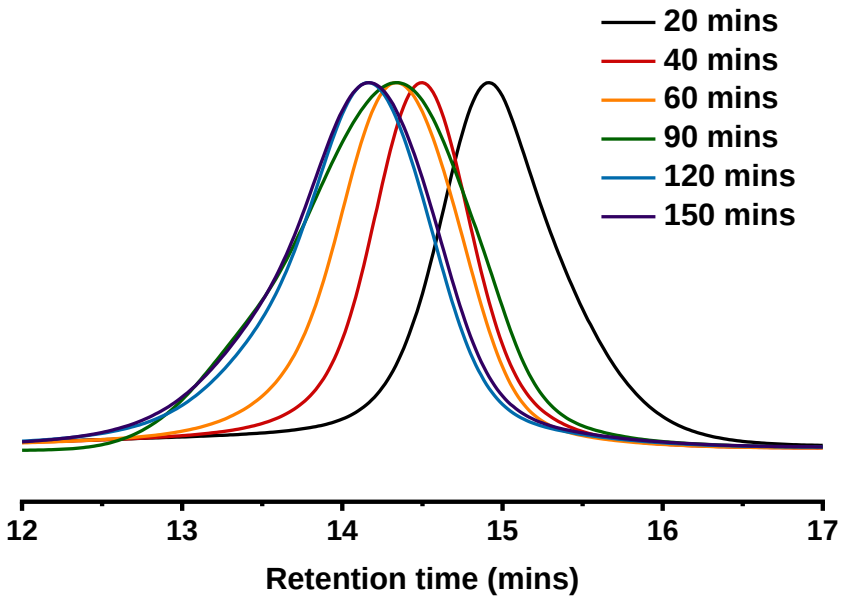


Figure S7: GPC traces for RAFT copolymerisation of *n*-BA and LA. [BA]:[LA]:[AIBN]:[CTA] 120:30:0.4:1. BA:anisole 1:1 v/v, T = 65 °C.

Table S1: Theoretical and measured M_n for RAFT copolymerisation of *n*-BA and LA.

Reaction time (mins)	$M_{n,theory}$ (g mol^{-1})	$M_{n,GPC}$ (g mol^{-1})	$Đ$
20	8300	8400	1.20
40	13000	13400	1.34
60	15400	14900	1.39
90	17300	16900	1.29
120	18400	17400	1.40
150	18900	17400	1.39

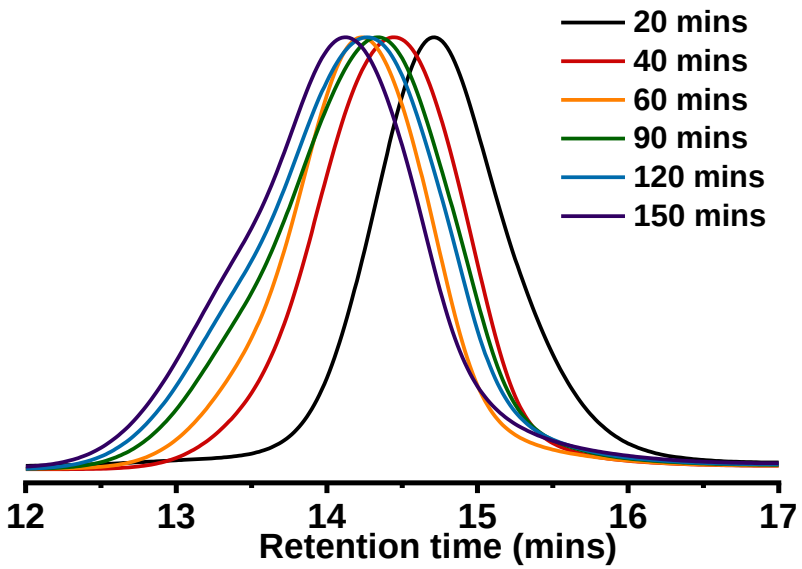


Figure S8: GPC traces for RAFT copolymerisation of *n*-BA and ELp. [BA]:[ELp]:[AIBN]:[CTA] 120:30:0.4:1. BA:anisole 1:1 v/v, T = 65 °C.

Table S2: Theoretical and measured M_n for RAFT copolymerisation of *n*-BA and ELp.

Reaction time (mins)	$M_{n,theory}$ (g mol^{-1})	$M_{n,GPC}$ (g mol^{-1})	$Đ$
20	8400	10000	1.20
40	14500	14000	1.20
60	16700	16100	1.23
90	17800	15000	1.32
120	18700	16000	1.36
150	18900	17500	1.39

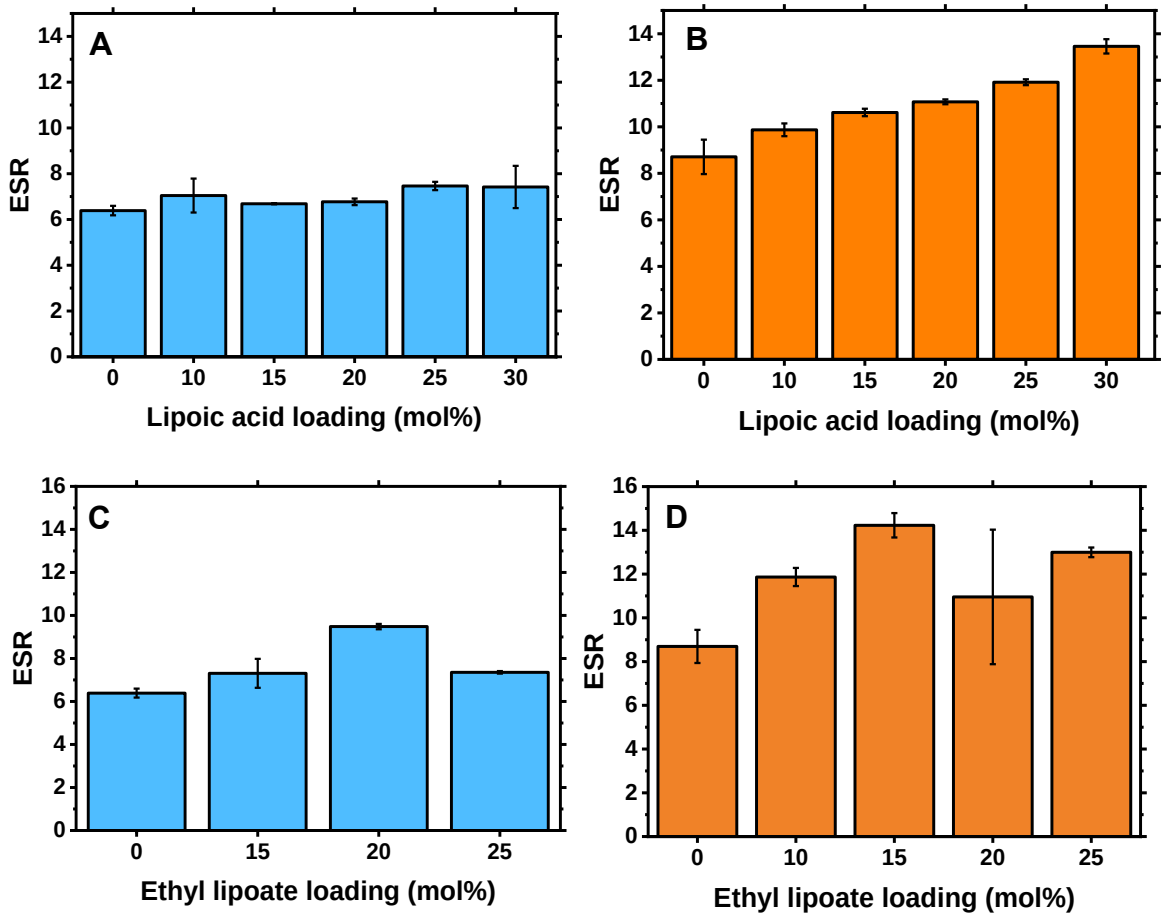


Figure S9: Equilibrium swelling ratio (ESR) in THF for PBA-LA and PBA-ELp gels synthesised by FRP and RAFT polymerisation. ESR = $m_{swollen}/m_{dry}$

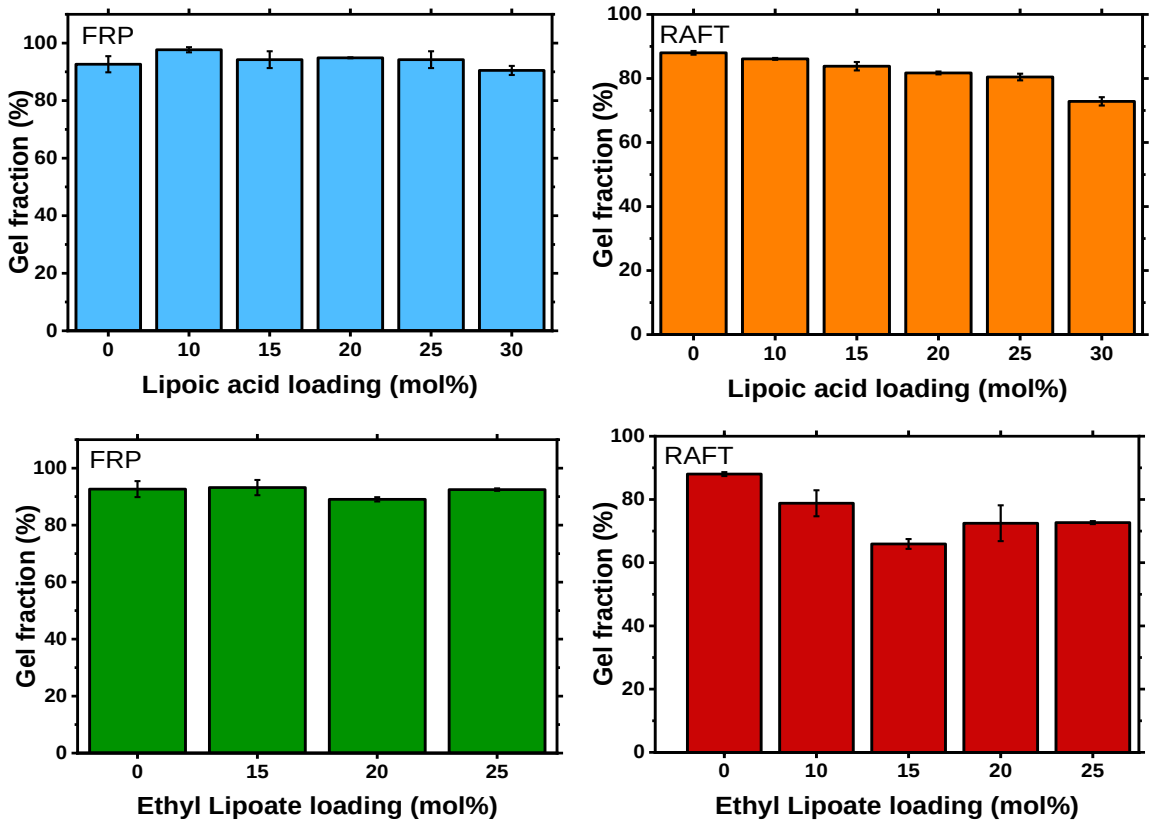


Figure S10: Gel fraction measurements PBA-LA and PBA-ELp gels synthesised by FRP and RAFT polymerisation. % GF = $m_{dry}/(m_{dry}+m_{sol})$ ×100%.

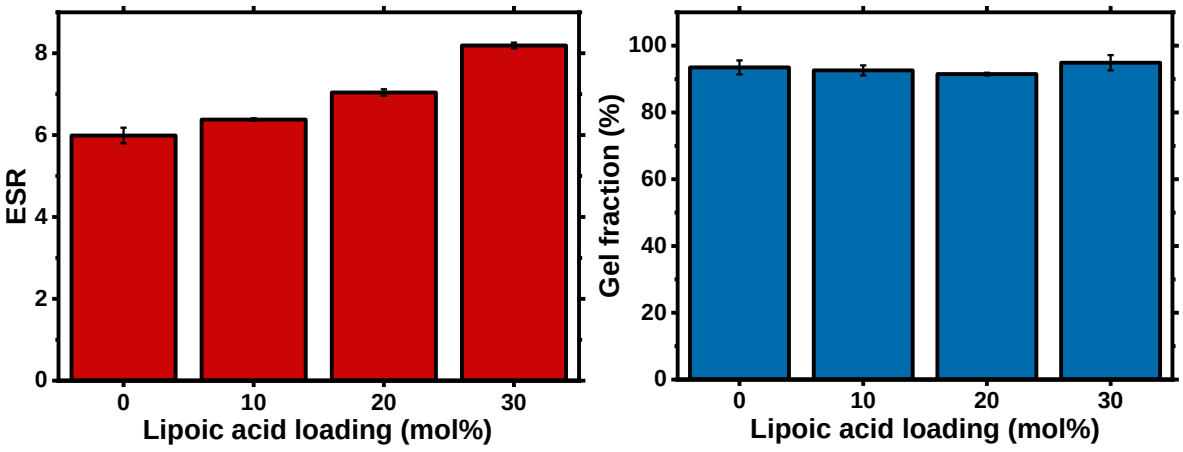


Figure S11: (A) Equilibrium swelling ratio (ESR) in THF and (B) gel fraction measurements for PBA-LA gels synthesised by RAFT polymerisation with higher crosslink density (**Table 1**, entries 13-15). [BA]:[DDMAT]:[LA]:[AIBN]:[HDDA]=150-x:1:x:0.4:5. ESR = $m_{swollen}/m_{dry}$, gel fraction = $m_{dry}/(m_{dry}+m_{sol})$ × 100%.

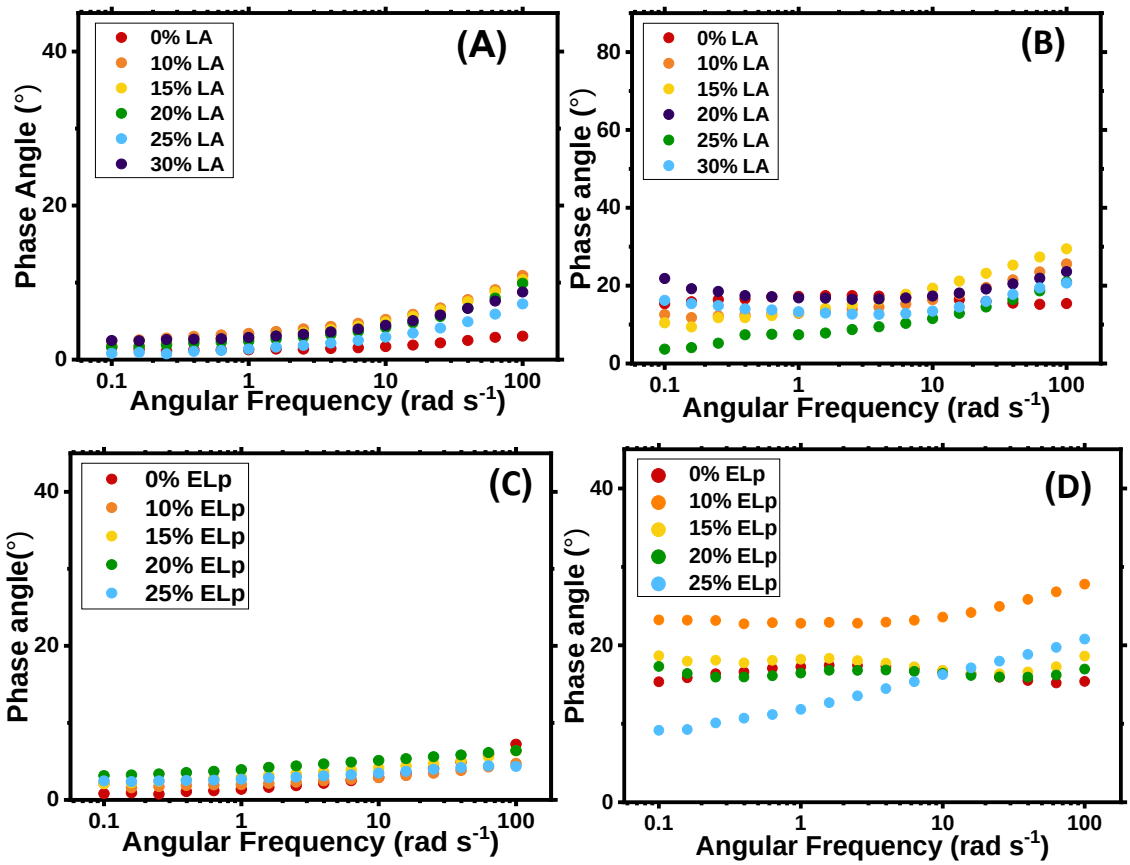


Figure S12: Oscillatory rheology frequency sweep of as-synthesised PBA-LA (A,B) and PBA-ELp gels (C,D) synthesised by FRP (A,C) and RAFT (B,D). Phase angle, δ, given by tanδ = *G"/G'*, indicates contribution of viscous flow/elastic deformation to complex modulus.

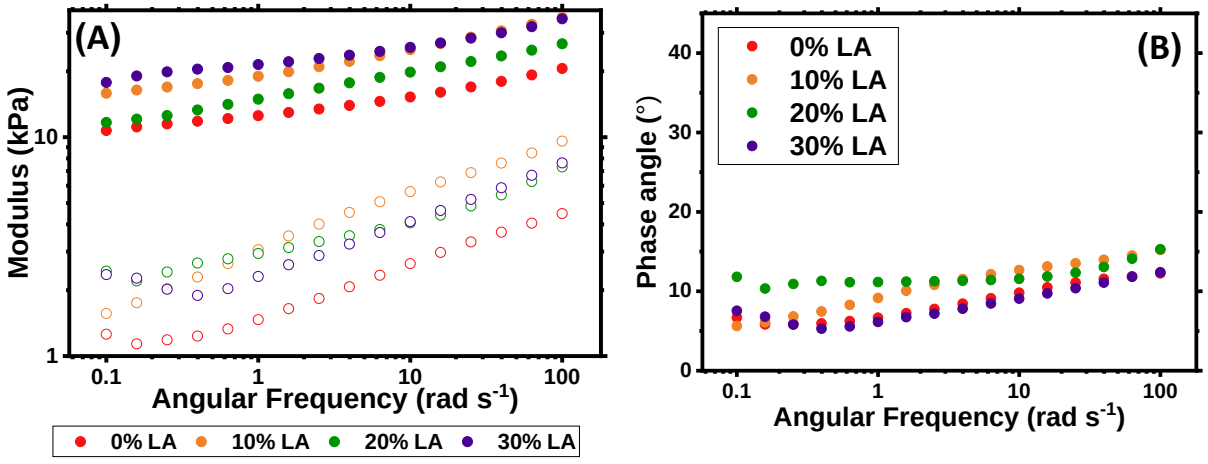


Figure S13: Oscillatory rheology frequency sweeps for PBA-LA gels synthesised by RAFT polymerisation with higher crosslink density (**Table 1**, entries 13-15). **(A)** Storage modulus (*G'*) indicated by closed symbols ● and loss modulus (*G"*) indicated by open symbols ○. **(B)** Phase angle, δ, given by tanδ = *G"/G'*, indicates contribution of viscous flow/elastic deformation to complex modulus. Gels measured as synthesised. [BA]:[DDMAT]:[LA]:[AIBN]:[HDDA]=150-x:1:x:0.4:5

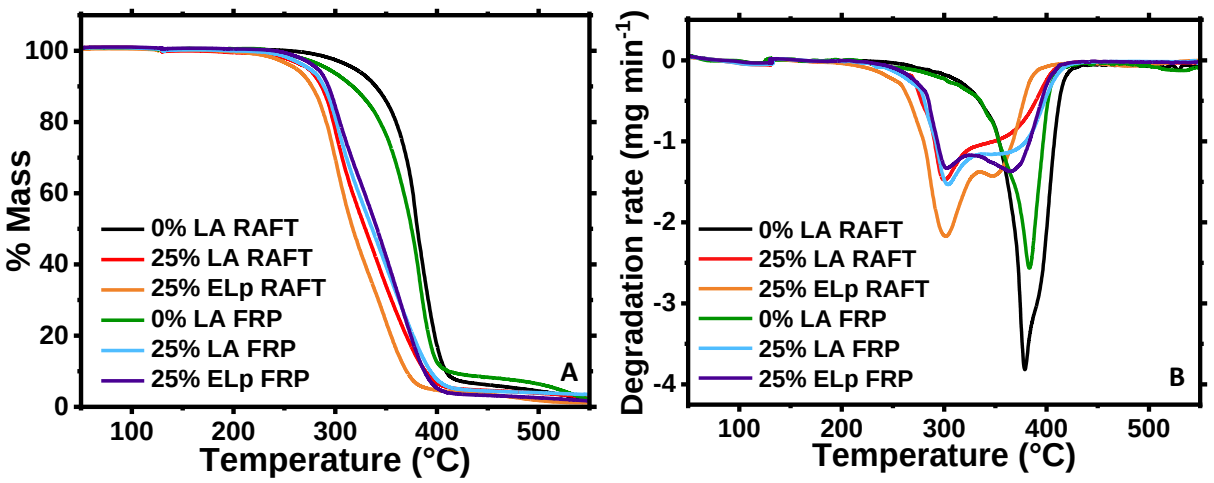


Figure S14: Thermogravimetric data for dry PBA gel networks containing no comonomer, 25% ELp or 25% LA. (A) Normalised mass loss data. (B) 1st differential of mass loss data.

Table S3: Onset and peak degradation temperatures for PBA, PBA-LA and PBA-ELp networks measured by thermogravimetric analysis.

Sample	Degradation onset temperature, T_{onset} (°C)	Peak rate of degradation temperature (°C)
PBA-0% LA-RAFT	319	379
PBA-25% LA-RAFT	274	300
PBA-25% ELp-RAFT	261	302
PBA-0% LA-FRP	293	383
PBA-25% LA- FRP	274	304
PBA-25% ELp- FRP	282	303, 365

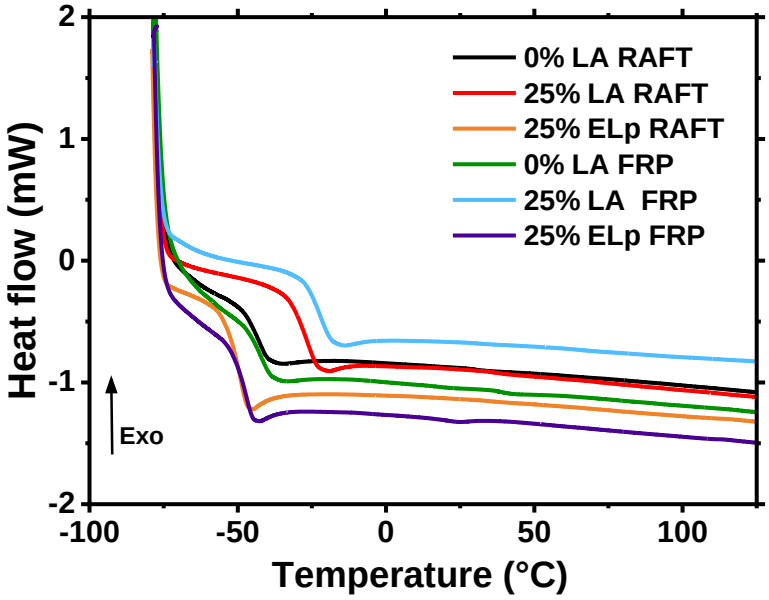


Figure S15: Differential scanning calorimetry data for PBA, PBA-LA and PBA-ELp networks. Data collected from second heating cycle.

Table S4: Glass transition temperature (T_g) values measured by DSC for dry PBA gel samples. T_g taken from the midpoint between the onset and endset temperatures of the glass transition region.

Sample	T_g (°C)
PBA-0% LA-RAFT	−40.0
PBA-25% LA-RAFT	−22.7
PBA-25% ELp-RAFT	−46.5
PBA-0% LA-FRP	−38.5
PBA-25% LA- FRP	−18.1
PBA-25% ELp- FRP	−44.6

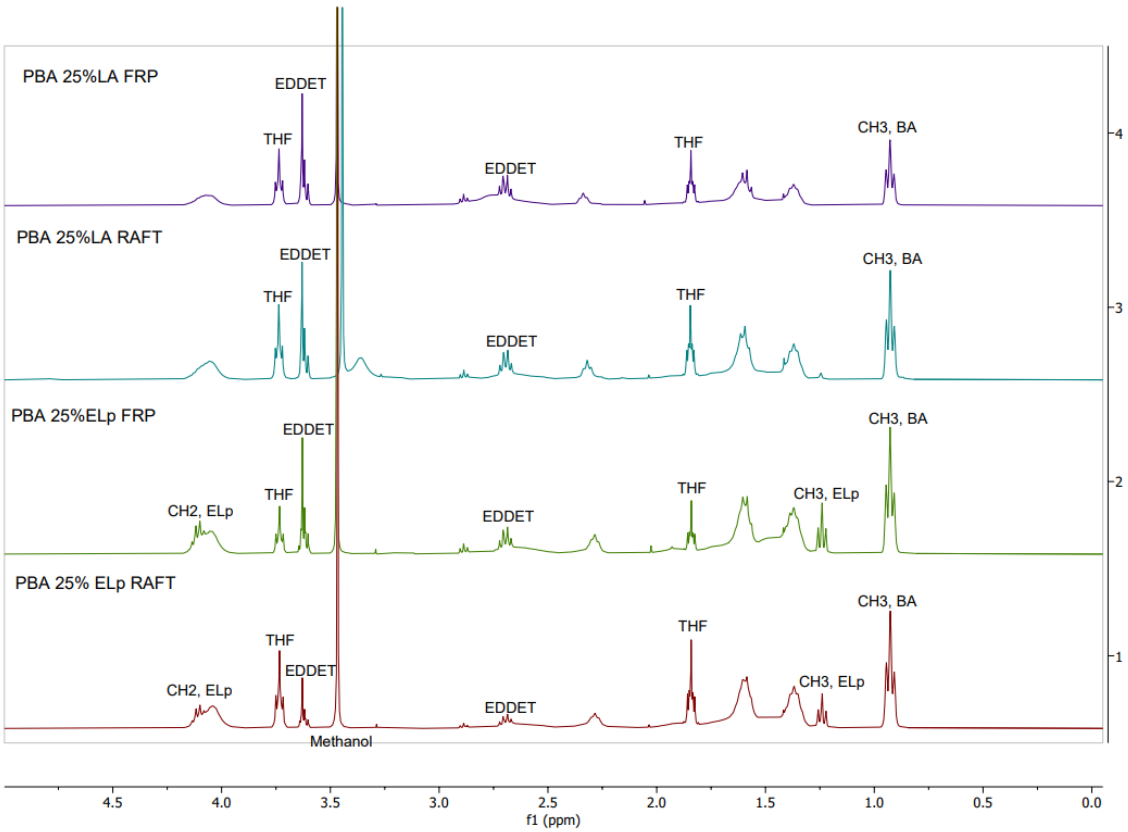


Figure S16: ^{1}H NMR of fragments of PBA-LA and PBA-ELp networks degraded by treatment with EDDET/DBU in THF at room temperature. Fragments precipitated in methanol/water before analysis.

Table S5: Degradation of dried PBA-LA gels heated at 100 °C in excess DMF in vial open to air for 24 hours.

Sample	Macroscopic degradation? [a]	Mass loss (%) [b]	ESR before degradation[c]	ESR after degradation[c]
PBA-0%LA-RAFT	No	3.9 ±0.2	8.7±0.7	9.4 ±0.3
PBA-10% LA-RAFT	Yes**	86.1 ±24.1	9.9 ±0.3	22.9
PBA-15% LA-RAFT	Yes	100	10.6 ±0.2	-
PBA-20% LA-RAFT	Yes	97.8 ±24.1	11.1±0.1	37.5
PBA-25% LA-RAFT	Yes	100	11.9±0.1	-
PBA-30% LA-RAFT	Yes**	94.7 ±24.1	13.5±0.3	30.2
PBA-0%LA-FRP	No	2.3 ±2.5	6.4 ±0.2	6.5 ±0.2

PBA-10% LA-FRP	No*	82.4 ±21.6	7.0 ±0.74	30.0 ±10.9
PBA-15% LA-FRP	No*	85.3 ±15.2	6.7 ±0.3	27 ±10.5
PBA-20% LA-FRP	Yes**	96.2 ±6.6	6.8±0.1	34.3
PBA-25% LA-FRP	Yes	100	7.5±0.2	-
PBA-30% LA-FRP	Yes**	98.4 ±2.8	7.4±0.9	40

[a] Macroscopic degradation determined visually when no solids remain. 3 replicate samples taken from 1 gel for each comonomer loading. [b] Measured gravimetrically by washing and drying remaining solids after degradation. When full macroscopic degradation was observed, the mass loss was assumed to be 100%. [c] Determined gravimetrically by swelling in excess THF, average over 3 replicates (if applicable). *1 sample out of 3 replicates macroscopically degraded ** 2 replicates out of 3 did macroscopically degrade.

Table S6: Degradation of dried PBA-ELp gels heated at 100 °C in excess DMF in vial open to air for 24 hours.

Sample	Macroscopic degradation? [a]	Mass loss (%) [b]	ESR before degradation[c]	ESR after degradation[c]
PBA-0%ELp-RAFT	No	3.9 ±0.2	8.7 ±0.7	9.4 ±0.3
PBA-10% ELp-RAFT	No	48.1 ± 3.6	11.9±0.4	16.0 ±3.6
PBA-15% ELp-RAFT	No	11.7 ±3.5	14.2±0.6	11.3 ±1.1
PBA-20% ELp-RAFT	No	50.0 ±25.3	12.3±1.23	17.2 ±2.6
PBA-25% ELp-RAFT	Yes	100	13.0±0.2	-
PBA-0%ELp-FRP	No	2.3 ±2.5	6.4±0.2	6.5 ±0.2
PBA-10% ELp-FRP	No	4.4 ±0.1	6.1±0.2	6.4 ±0.3
PBA-15% ELp-FRP	No	5.7 ±0.5	7.3±0.7	7.5±0.5
PBA-20% ELp-FRP	No	13.3 ±6.7	9.5±0.1	8.7 ±0.8
PBA-25% ELp-FRP	No	34 ±5.0	7.4±0.1	15.1 ±1.5

[a] Macroscopic degradation determined visually when no solids remain. 3 replicate samples taken from 1 gel for each comonomer loading. [b] Measured gravimetrically by washing and drying remaining solids after degradation. When full macroscopic degradation was observed, the mass loss was assumed to be 100%. [c] Determined gravimetrically by swelling in excess THF, average over 3 replicates.

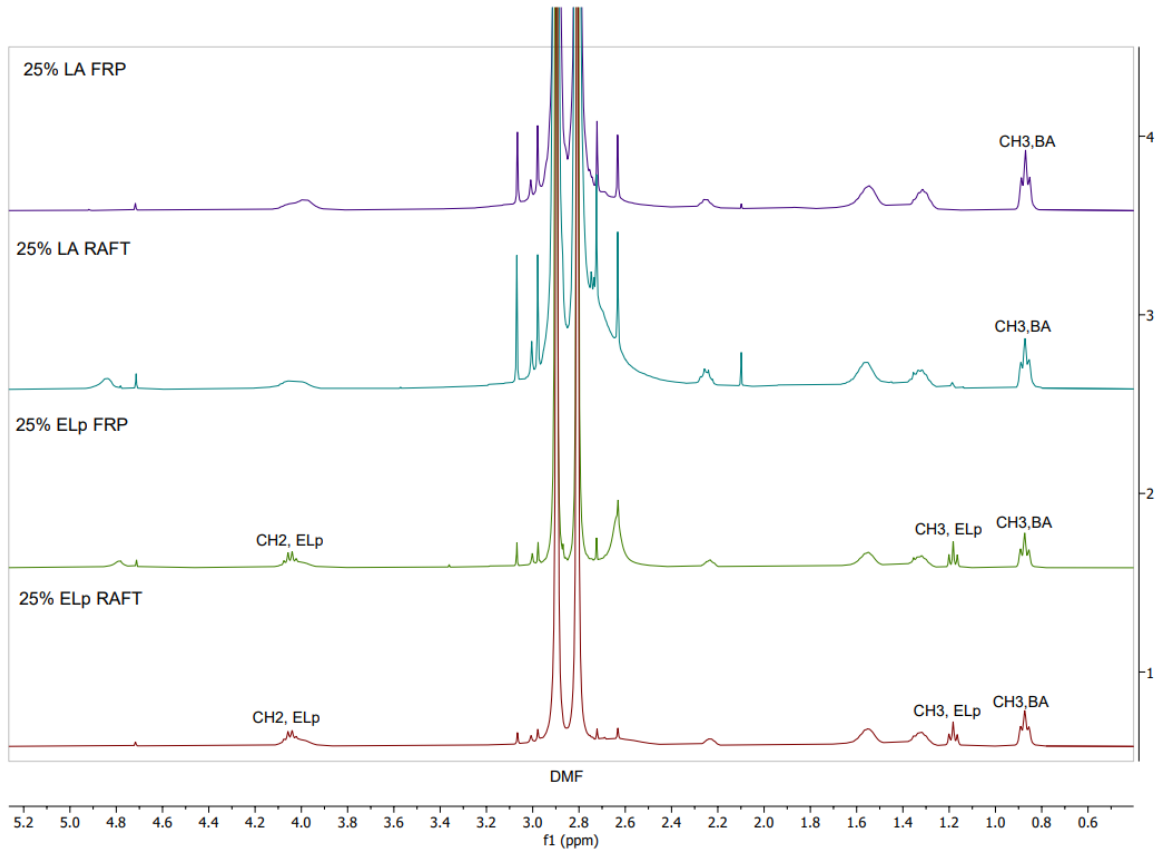


Figure S17: ^{1}H NMR of fragments of PBA-LA and PBA-ELp networks degraded by treatment with DMF at 100 °C.

Table S7: Degradation of dried PBA-LA and PBA-ELp gels heated at 35°C in excess DMF in vial open to air for 24 hours.

Sample	Macroscopic degradation? [a]	Mass loss (%) [b]	ESR before degradation[c]	ESR after degradation[c]
0% FRP	No	1.3 ±0.5	6.4±0.2	6.4 ±0.03
25%LA FRP	No	-2.6 ±1.7	7.5±0.2	7.5 ±0.3
25%ELp FRP	No	-0.4 ±1.3	7.4±0.1	7.4 ±0.1
0% RAFT	No	0.1 ±0.1	8.7±0.7	8.8 ±0.9
25%LA RAFT	No	-1.5 ± 1.2	11.9±0.1	12.0 ±0.2
25%ELp RAFT	No	15.6 ±2.1	13.0±0.2	29.2 ±1.1

[a] Macroscopic degradation determined visually when no solids remain. [b] Measured gravimetrically by washing and drying remaining solids after degradation. When full macroscopic degradation was observed, the mass loss was assumed to be 100%. [c] Determined gravimetrically by swelling in excess THF, average over 3 replicates.

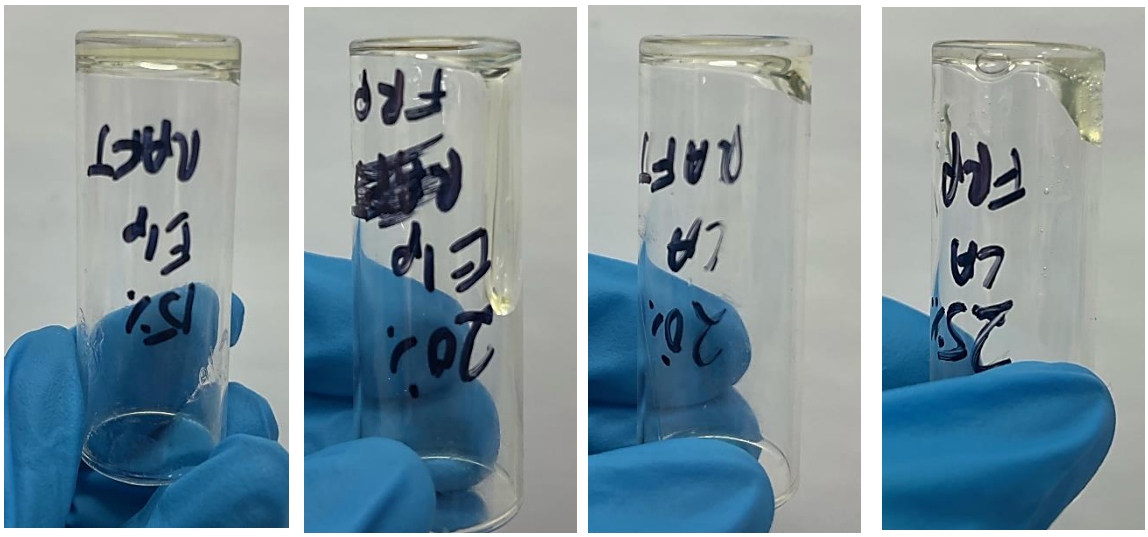


Figure S18: Samples after 1 week of regelation process. Left to right: 15% ELp RAFT, 20% ELp FRP, 20% LA RAFT, 25% LA FRP. Sample vials were held horizontally for 30 minutes prior to taking pictures. 15% ELp RAFT was the only sample to pass inverted vial test. All attempts led to an increase in fragment viscosity to varying extents.

References

1 M. Raeisi and N. V. Tsarevsky, *J. Polym. Sci.*, 2021, **59**, 675–684.