Supplementary Material (ESI) for Chemical Communications

Electronic Supporting Information

A facile route to end-functionalised polymers synthesised by SET-LRP *via* a one-pot reduction / thiol-ene Michael-type addition

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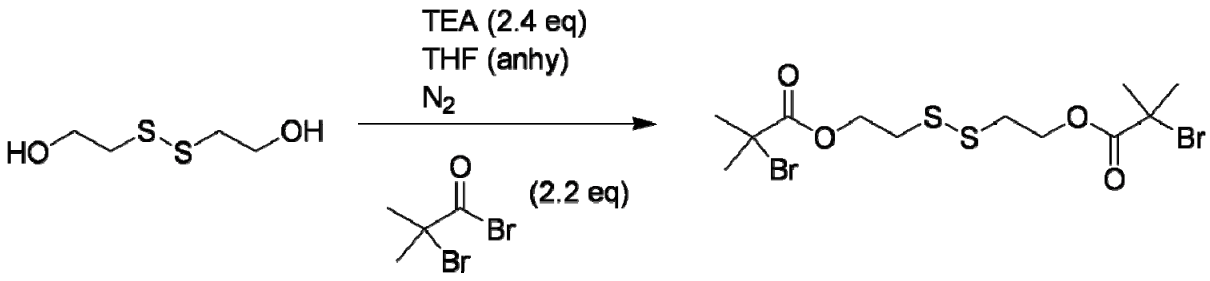
General Experimental

All chemicals were purchased from Sigma-Aldrich and used without further purification, unless otherwise stated. Size exclusion chromatography (SEC) was used to determinate the molecular weight averages and the polydispersity (M_w/M_n) with a 390-LC Varian MDS system equipped with a PL-AS RT/MT autosampler, a PL-gel 3 μm (50 × 7.5 mm) guard column, two PL-gel 5 μm (300 × 7.5 mm) mixed-D columns (suitable for separations up to MWt = 2.0×10^6 g mol^{-1}) equipped with a differential refractive index and a UV detector, using THF–triethylamine 95:5 (v/v) as eluent with a flow rate of 1.0 mL min^{-1}. Narrow molecular weight PMMA standards (1.0×10^6–200 g mol^{-1}) were used for calibration.

^{1}H-NMR spectroscopy was used to determine monomer conversion. ^{1}H NMR and ^{19}F NMR spectra were recorded on Bruker DPX300, Bruker DPX400 spectrometers as solutions in perdeuterated NMR solvents. FTIR was recorded using a VECTOR-22 Bruker spectrometer using a Golden Gate diamond attenuated total reflection cell to record the infrared absorption. All matrix assisted laser desorption ionisation time of flight (MALDI-ToF) were carried out on a Bruker Ultra FLEX ToF/ToF-MS utilizing MCP for ion detection. The instrument was equipped with a nitrogen laser emitting at 337 nm and ions were accelerated through an acceleration voltage of 25 kv. The spectra shown in this work have been accumulated from typically 300-500 laser shots. The extraction delay time needed to be adjusted for higher masses to obtain the best resolution. Typical pulse extraction delay time used was 90 ns. 2-(4-Hydroxyphenylazo)benzoic acid (20 mg/mL) as the matrix with NaI salt to aid ionisation (2 mg/mL) and analyte (5 mg/mL) with reflectron mode analysis was used for all analytes. All the MALDI spectra generated were analysed using Bruker Flex Analysis software.

(1) Synthesis of disulfide-based bifunctional initiator.

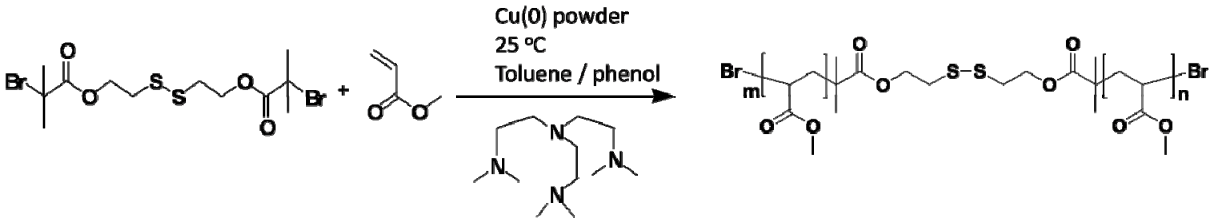
Bis[2-(2-bromoisobutyryloxy)ethyl] disulfide [DSDBr]



Bis(2-hydroxyethyl) disulfide (4.00 mL, 32.4 mmol) and an excess of triethylamine (9.90 mL, 71.3 mmol) was added to a 500 mL round bottom flask along with a stirrer bar, and was purged with nitrogen for 15 minutes on an ice bath. Anhydrous THF (150 mL) was canulated into the system, and allowed to cool to 0°C. 2-Bromoisobutyryl bromide (8.40 mL, 68.1 mmol) was added dropwise under a nitrogen atmosphere via a degassed syringe, dropwise addition is essential in order to minimise the exotherm. The solution was allowed to reach ambient temperature, and left to stir for 6 hours. The resulting triethylammonium bromide salt was removed by filtration, and volatiles removed by rotary evaporation. The resulting pale yellow solution was stirred with 0.10 M aqueous Na_2CO_3 to hydrolyze any residual 2-bromoisobutyryl bromide. The crude product was then extracted three times with dichloromethane using a separating funnel. The combined dichloromethane extracts were first dried with anhydrous magnesium sulphate, filtered, and the volatiles removed via rotary evaporation, yielding a yellow oil. The product was stored in a refrigerator. (10.1 g, 22.0 mmol, 74.1 %)

^{1}H NMR ($CDCl_3$): δ (ppm) 4.41 (t, 4H, *J* = 6.55), 2.95 (t, 4H, *J* = 6.55), 1.91 (s, 12H). ^{13}C NMR ($CDCl_3$): δ (ppm) 63.5, 55.5, 36.7, 30.7. FT-IR: 1731 cm^{-1}, 1268 cm^{-1}, 1153 cm^{-1}, 1105 cm^{-1} (ν*C=N*) MS (EI): m/z+1 = 451.91 Da

(2)Cu(0)/DSDBr catalysed polymerisation of methyl acrylate in toluene / phenol (*poly*[MA]-SS-*poly*[MA])



Cu(0) (0.28 g, 4.4 mmol), phenol (4.10 g, 44.0 mmol) and DSDBr (1.0 g, 2.2 mmol) was added to a clean, oven dried Schlenk tube, along with a magnetic follower. The Schlenk tube was sealed with a suba-seal, and purged with nitrogen several times. This was carried out by deoxygenating the tube via a high vacuum followed by flushing with nitrogen. Toluene (14.0 mL, 50% solids), MA (13.80 mL, 154.0 mmol) were added to the tube via a degassed syringe. Three freeze pump thaw cycles were then carried out using liquid nitrogen. The tube was placed in an oil bath at 25 ^{o}C (t = 0), and Me_6Tren (4.6 mL, 19.1 mmol) was added (T = 0) and samples were taken every 10 minutes via a degassed syringe for conversion and molecular weight analysis. The reaction mixture was washed with toluene and stirred with basic alumina for 2 hours in order to remove copper salts. The solution was then passed through a celite filter and the solvent was removed on a rotary evaporator and the resulting polymer dissolved in a minimum THF. A total of 1 L of methanol and 20 mL of water was measured into to a beaker and was left stirring in a dry ice/acetone bath. The polymer was then slowly dropped into the beaker with a pipette, and once completely added, was left to stand for 20 minutes. The solvent was decanted off and polymer was then dried in a vacuum oven at 45 ^{o}C.

Fig SI 2.1. (i) First order kinetic plot for polymerisation (1). Last time point at 40 minutes. **(ii)** Graph showing linear increase of molecular weight (M_n) against conversion, and molecular weight distribution (M_w/M_n).

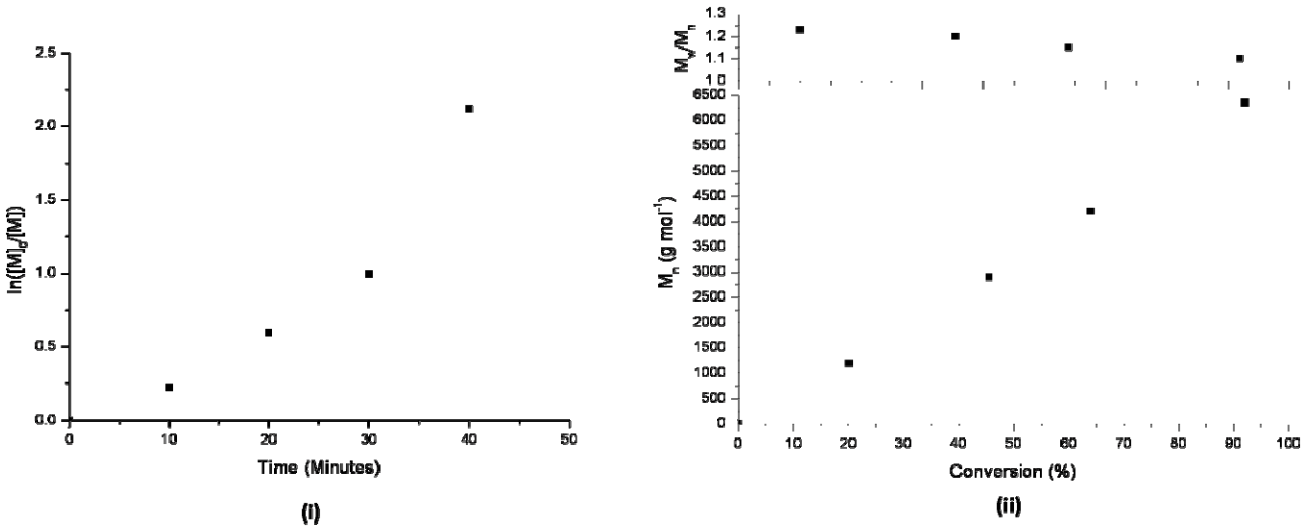


Fig SI 2.2. ^{1}H NMR of *poly*[MA]-SS-*poly*[MA], **(1)**.

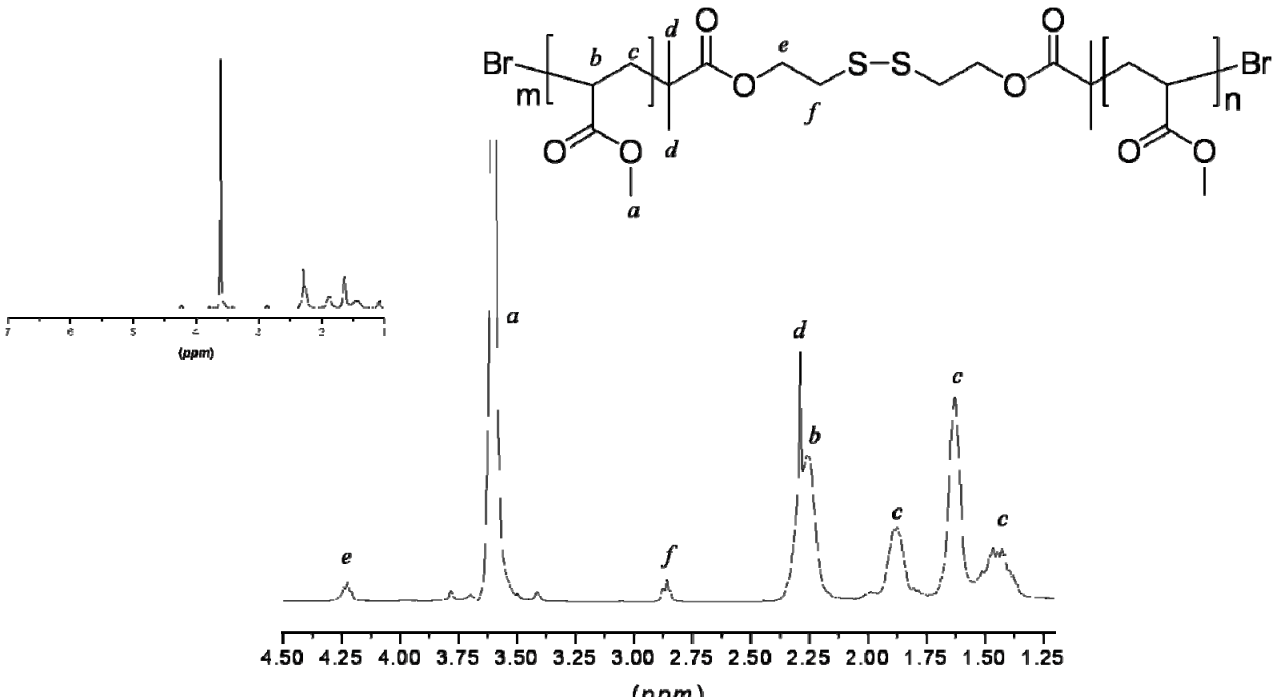


Fig SI 2.3. SEC trace of polymer **(1)** following precipitation, SEC conditions

described in general experimental section.

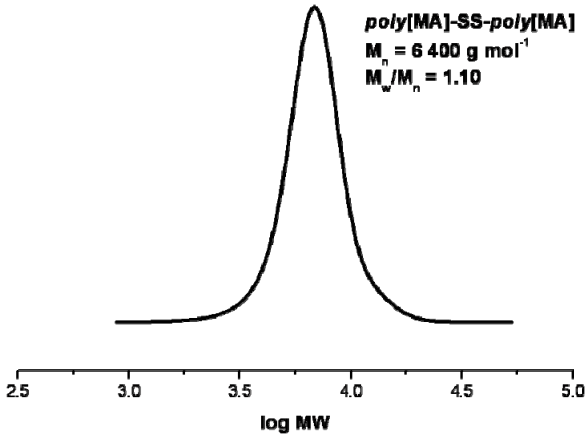
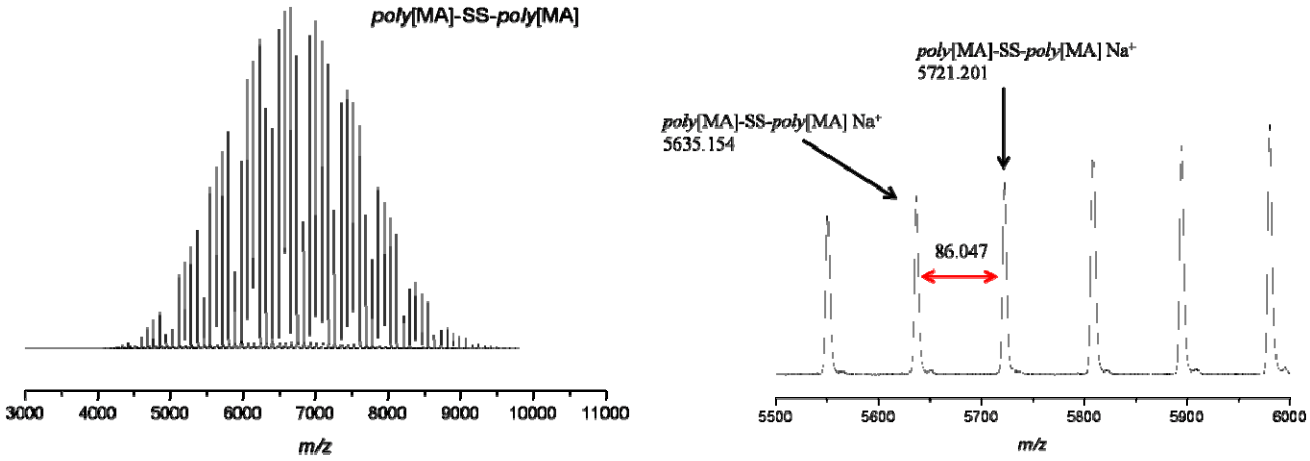


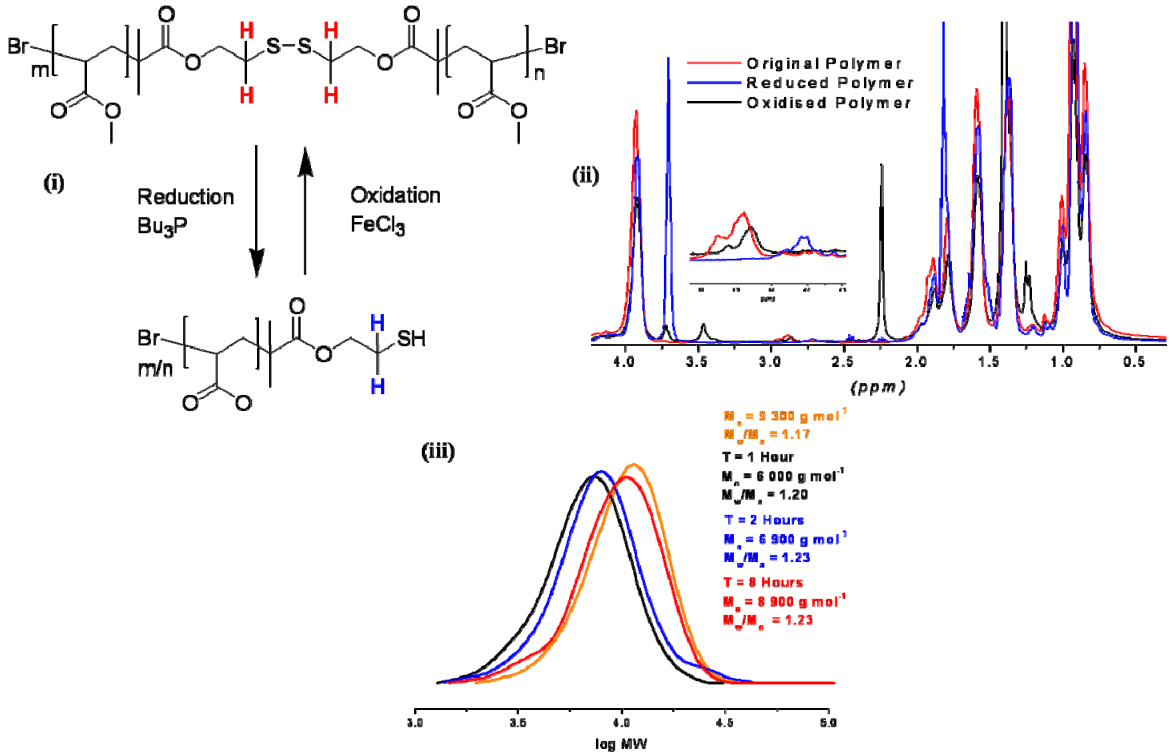
Fig SI 2.4. MALDI-ToF of polymer **(1)** conditions described in general experimental. Shown for degree of polymerisation DP 60 and DP 61



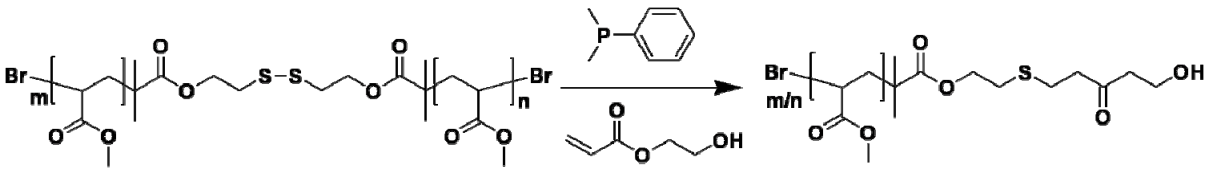
(3) One-pot reduction/oxidation reaction of *poly*[MA]-SS-*poly*[MA], (1).

Polymer **(1)** (1.0 g, 0.15 mmol) was placed in a Schlenk tube with 20 mL THF, a magnetic follower, tributylphosphine (Bu_3P, 1.10 g, 7.8 mmol), and iron(III) chloride ($FeCl_3$, 1.5g, 7.8 mmol). Samples were taken at various time points, outlined in the SEC traces below. Samples were passed through a small neutral alumina column prior to NMR and GPC analysis.

Fig SI 3.1. Data for a one pot reduction/oxidation reaction of the *poly*[MA]-SS-*poly*[MA]. **(i)** General reaction scheme for the one pot redox reaction, indicating the protons of interest in the ^{1}H NMR, α and β to the sulphur in the DSDBr initiator. **(ii)** ^{1}H NMR spectra of polymer (1) red, the reduced polymer (T = 1 hour) and the final polymer (T = 8 hours). We can follow the shift of the CH_2 α to the sulphur from a triplet at δ = 2.9 *ppm* to a multiplet at δ = 2.7 *ppm* in the reduced form, blue proton in **(i)**. The protons shift back to δ = 2.9 *ppm* in the oxidised polymer. **(iii)** SEC data to support the cleavage and reformation processes. Conditions used as described in general experimental.

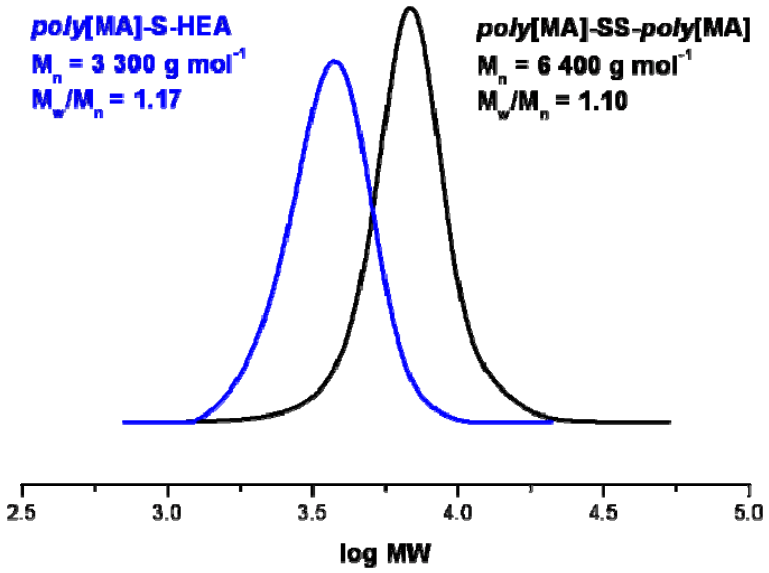


(4) General procedure, described for the conjugation of hydroxylethyl acrylate.

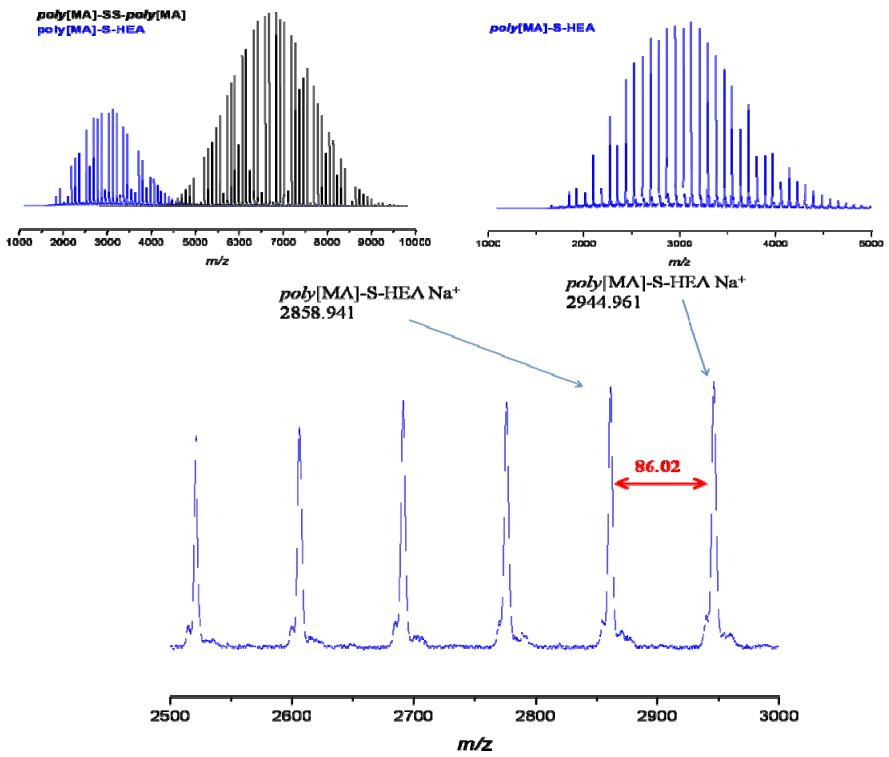


Poly[MA]-SS-*poly*[MA] (0.1 g, 0.015 mmol), 4.0 mL $CDCl_3$ and hydroxyethyl acrylate (3.8 mg, 0.033 mmol), were added to a Schlenk tube, and sealed with a suba seal and degassed, as described in **(1)**. A sample was taken via a degassed syringe for t = 0 analysis by ^{1}H NMR, SEC, and MALDI-TOF. Dimethylphenylphosphine (0.003 mL, 0.022 mmol) was added via a degassed syringe, and the reaction was left to stir at 25 °C for 12 hours, after which the remaining solution was analysed by ^{1}H NMR, SEC, and MALDI-TOF.

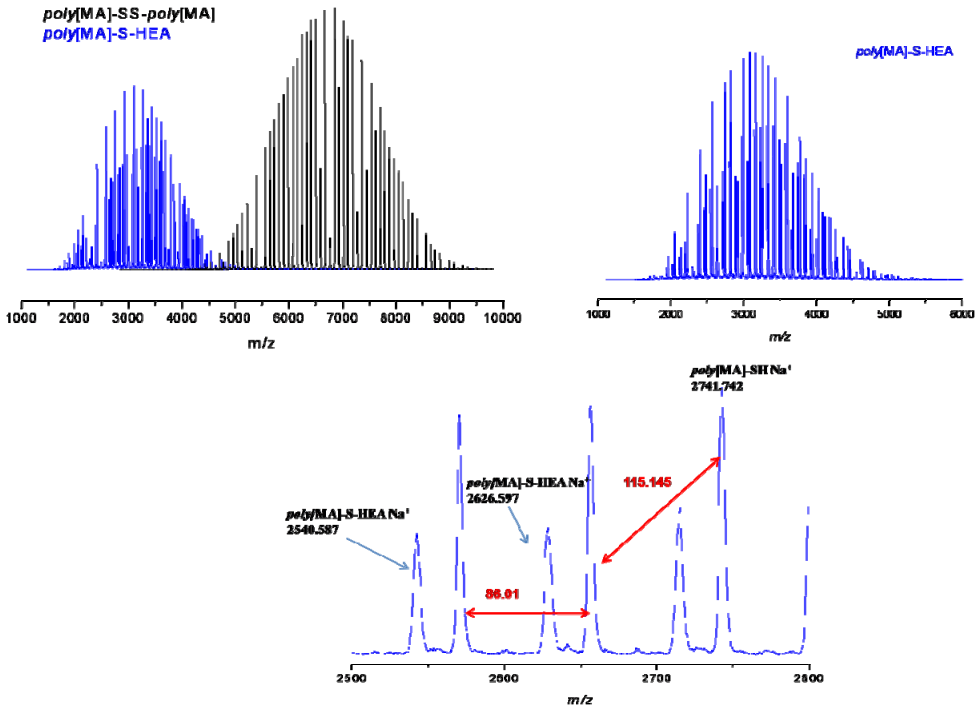
Fig SI 4.1. SEC analysis of polymer **(1)** in black, and the conjugate **(4),** the expected halving of molecular weight is observed.



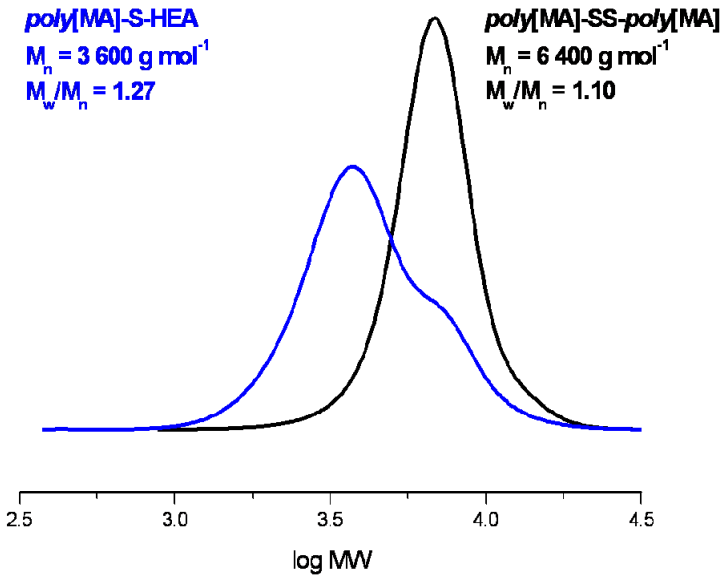
SI FIG 4.2. MALDI-TOF analysis of conjugate **(4)**, shown for DP 30 and 31. Conditions used as described in general experimental.



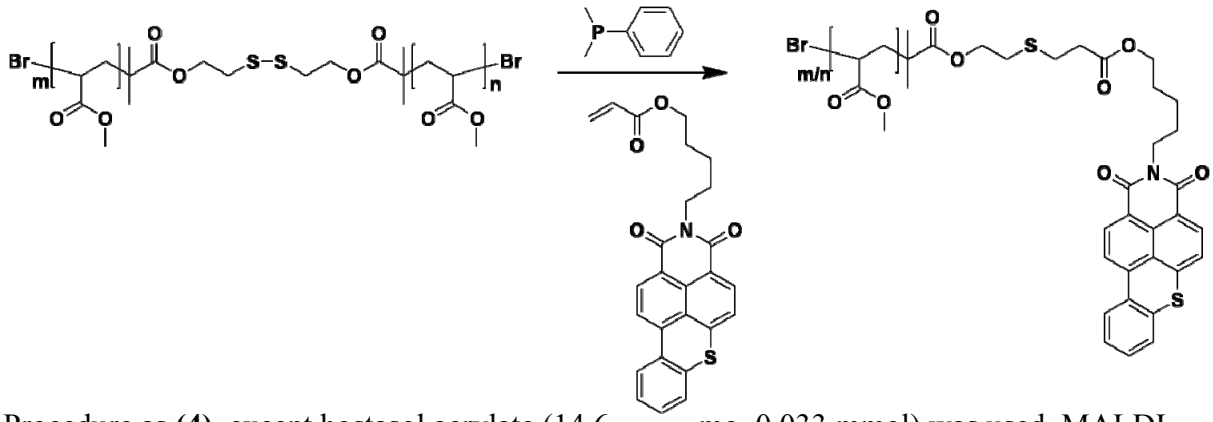
SI FIG 4.3. MALDI-ToF analysis of the conjugate **(4),** initial attempt. Conditions used as described in general experimental. Two distributions as not all the free thiol reacted. This is what you would expect to see if 100% conjugation was not achieved. We did not observe this for any other MALDI-TOF spectra.



SI FIG 4.4 GPC analysis of conjugate with some free thiol, bimodal distribution showing there is not 100% conjugation.

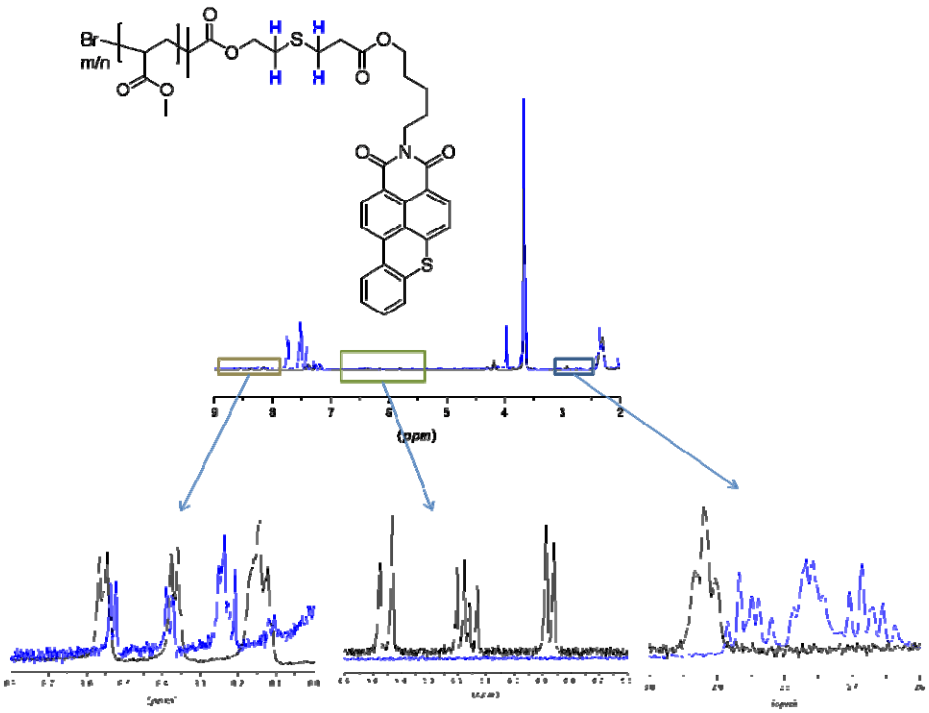


(5) Conjugation of hostasol acrylate

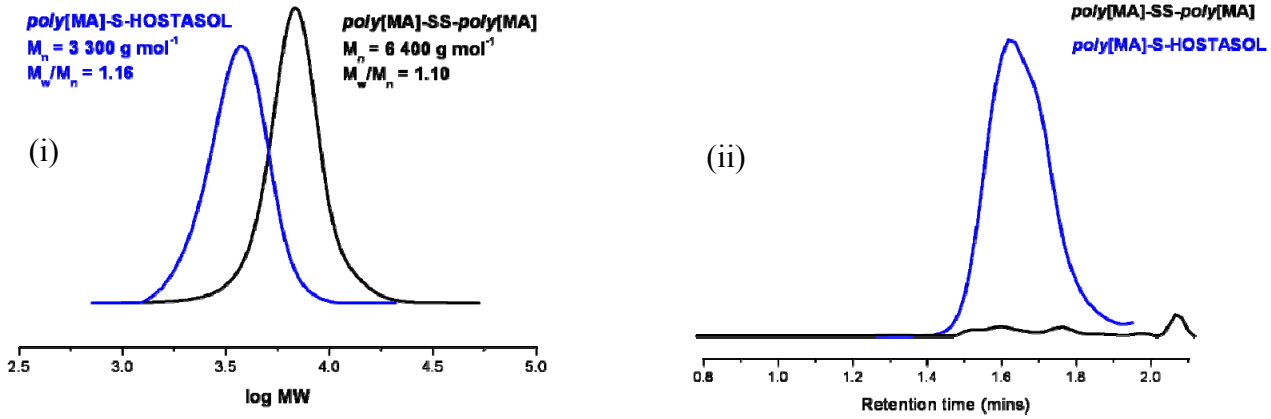


Procedure as **(4)**, except hostasol acrylate (14.6 mg, 0.033 mmol) was used. MALDI-TOF data is reported in the main body of the publication.

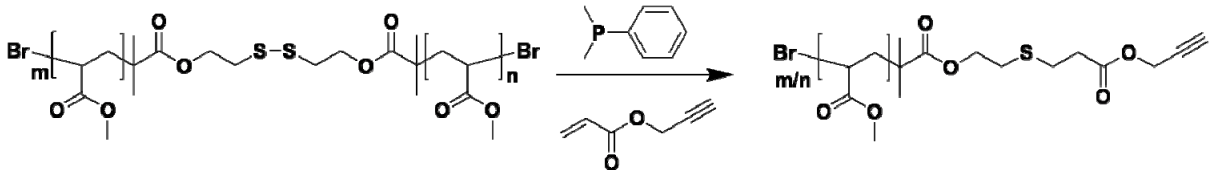
SI Fig 5.1 ^{1}H NMR indicates that complete conjugation has occurred, as previously described. Complete disappearance of the acrylate peaks post purification δ = 6.45 (d, 1H), 6.15 (m, 1H), 5.85 (d, 1H), whist the hostasol aromatic protons remain at δ = 8.55 – 8.20 *ppm*. The CH_2 alpha to the sulphur in the original polymer shifts from δ = 2.9 *ppm* to a multiplet down field at δ = 2.7 *ppm*, from the chiral coupling of the CH_2's either side of the sulphur.



SI Fig 5.2. **(i)** SEC analysis of polymer **(1)** in black, and the conjugate **(5)**. The expected halving of molecular weight is observed. **(ii)** UV SEC trace, run at 460 nm, showing further evidence that the conjugation was successful and the polymer is now fluorescently tagged.

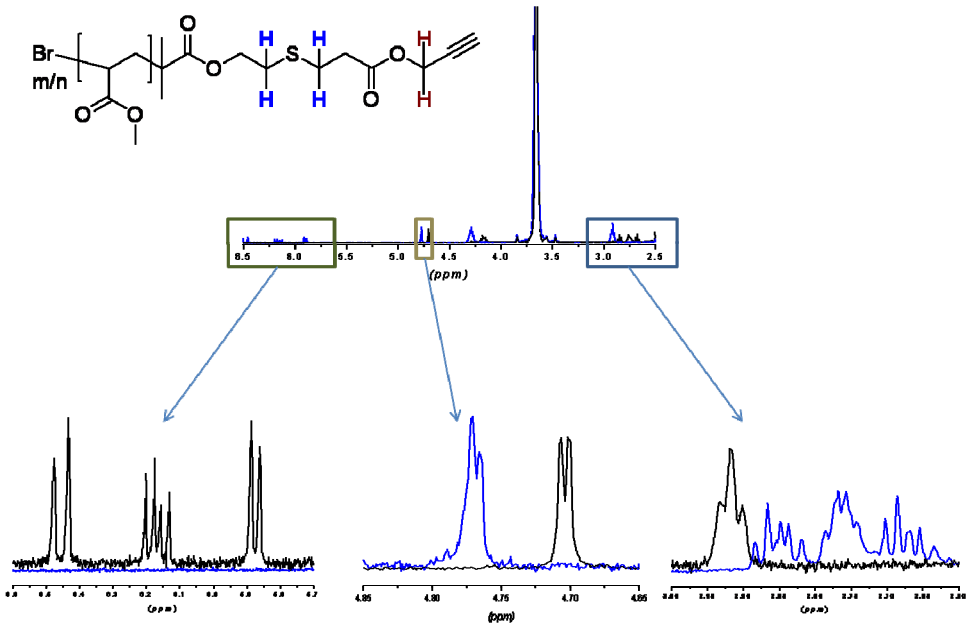


(6) Conjugation of propargyl acrylate.

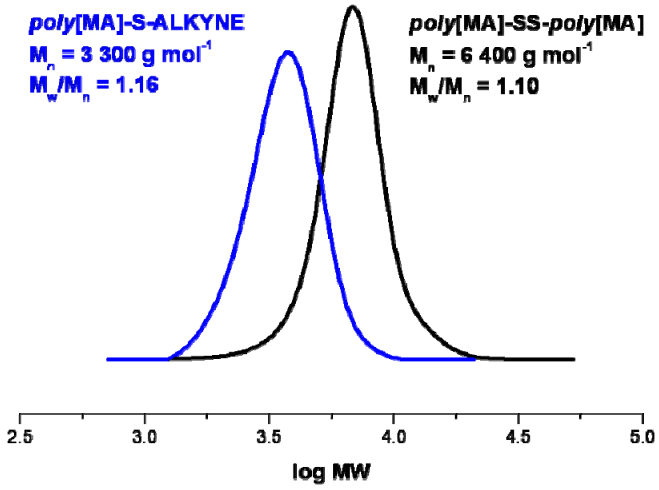


Procedure as **(4)**, except propargyl acrylate (3.1 mg, 0.033 mmol) was used.

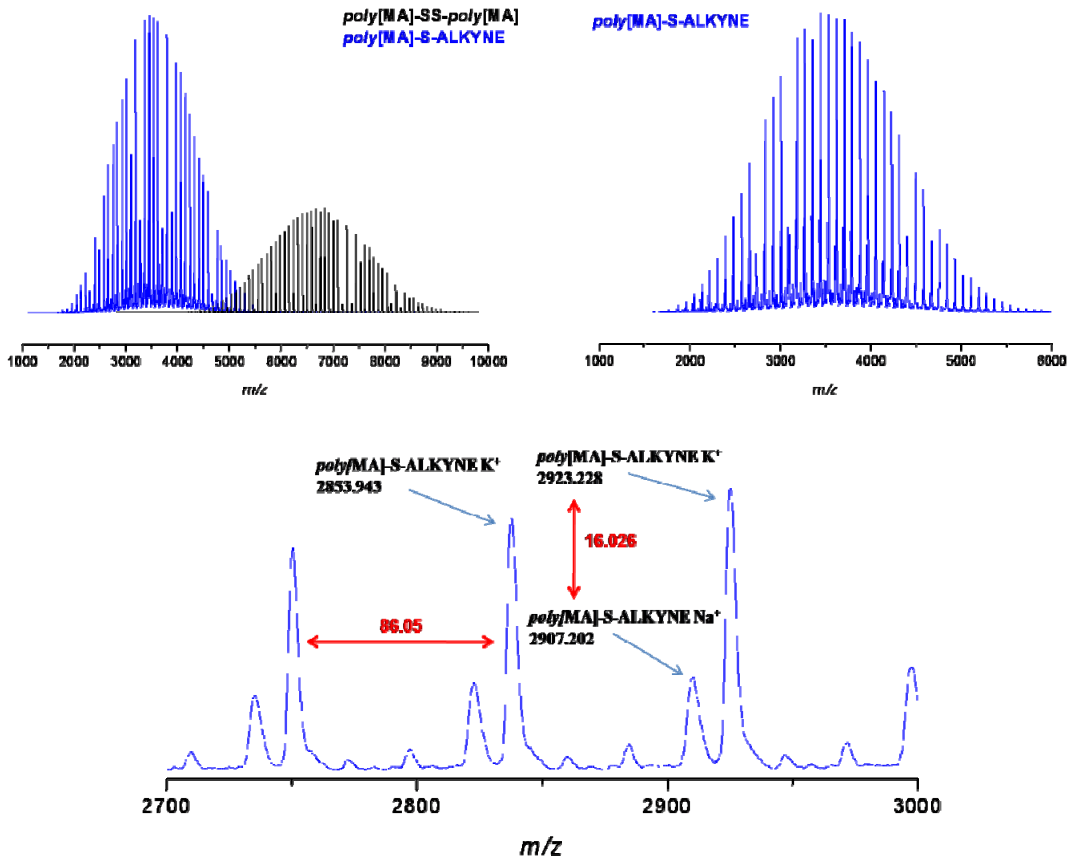
SI Fig 6.1. ^{1}H NMR indicates that complete conjugation has occurred, as previously described. Complete disappearance of the acrylate peaks post purification δ = 6.45 (d, 1H), 6.15 (m, 1H), 5.85 (d, 1H), whist the propargyl CH_2 α to the ester remains but shifts to δ = 4.75 *ppm* from δ = 4.70 *ppm*. The CH_2 α to the sulphur in the original polymer shifts from δ = 2.9 *ppm* to a multiplet down field at δ = 2.7 *ppm*, from the chiral coupling of the CH_2 groups either side of the sulphur.



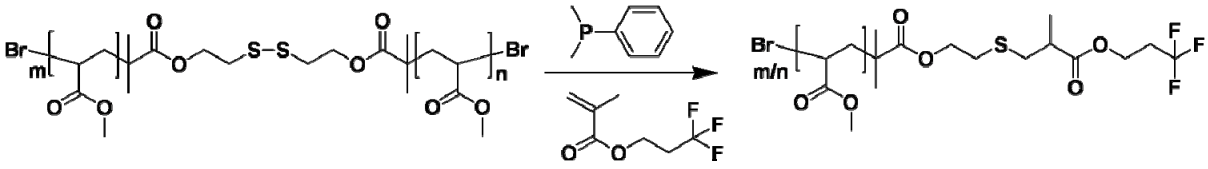
SI Fig 6.2. SEC analysis of polymer **(1)** in black, and the conjugate **(6)**. The expected halving of molecular weight is observed.



SI Fig 6.3. MALDI-ToF analysis of the conjugate **(6)**, shown for DP 30 and 31. Both potassium and sodiated distributions observed. Conditions used as described in general experimental.

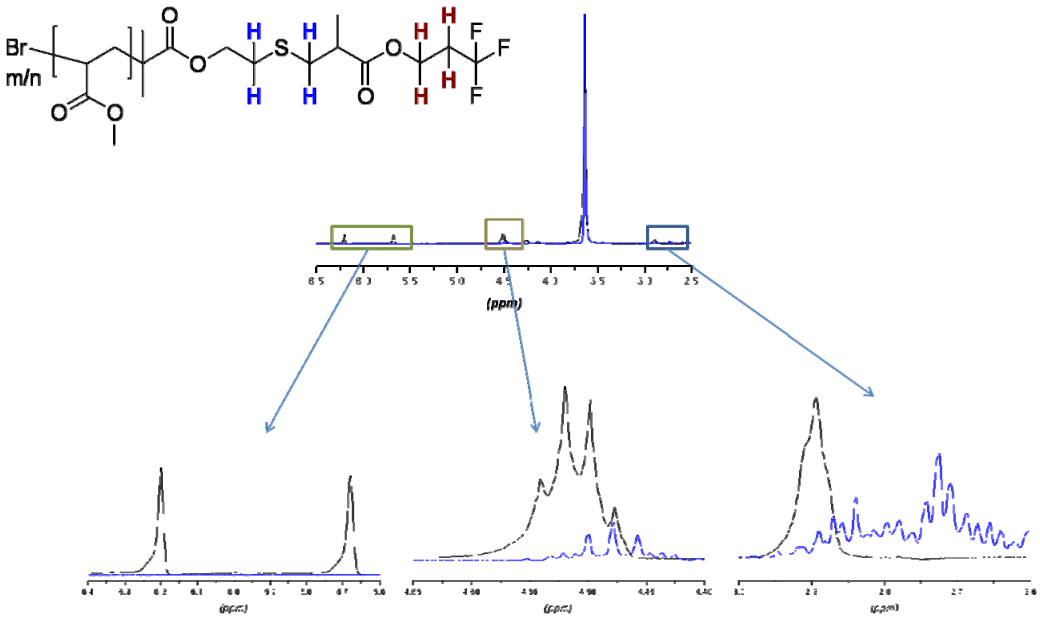


(7) Conjugation of trifluroethyl methacrylate

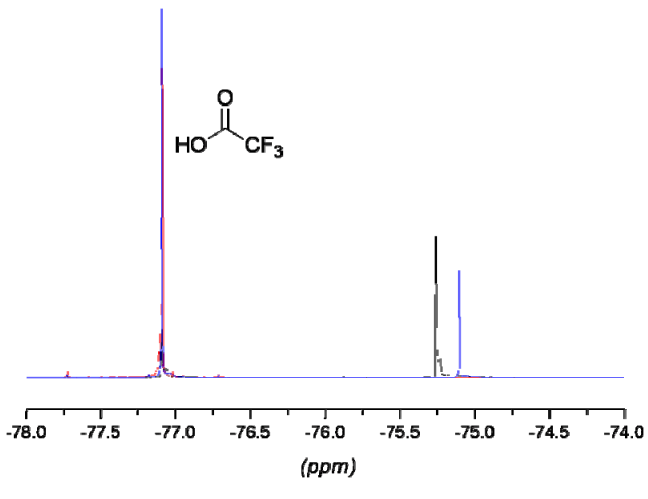


Procedure as **(4)**, except trifluroethyl methacrylate (6.0 mg, 0.033 mmol) was used

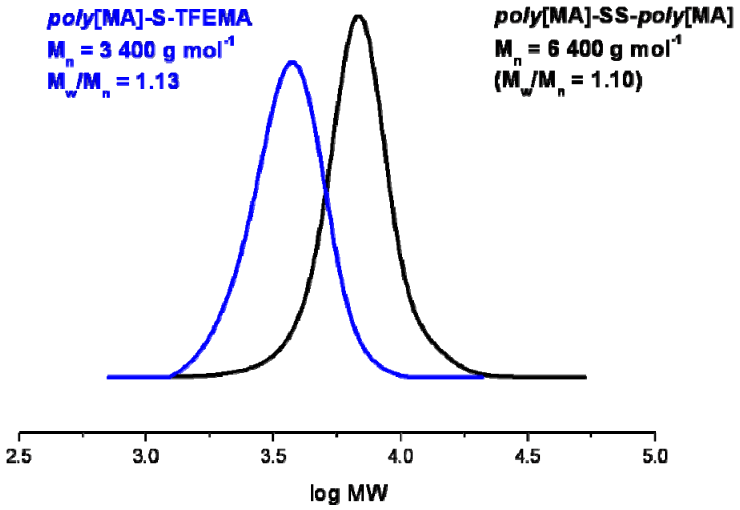
SI Fig 7.1. ^{1}H NMR indicates that complete conjugation has occurred, as previously described. Complete disappearance of the methacrylate peaks post purification δ = 6.19 (d, 1H), 5.67 (d, 1H), whist the CH_2 α to the ester remain at δ = 4.51 *ppm*. The CH_2 α to the sulphur in the original polymer shifts from δ = 2.9 *ppm* to a multiplet down field at δ = 2.7 *ppm*, from the chiral coupling of the CH_2's either side of the sulphur atom.



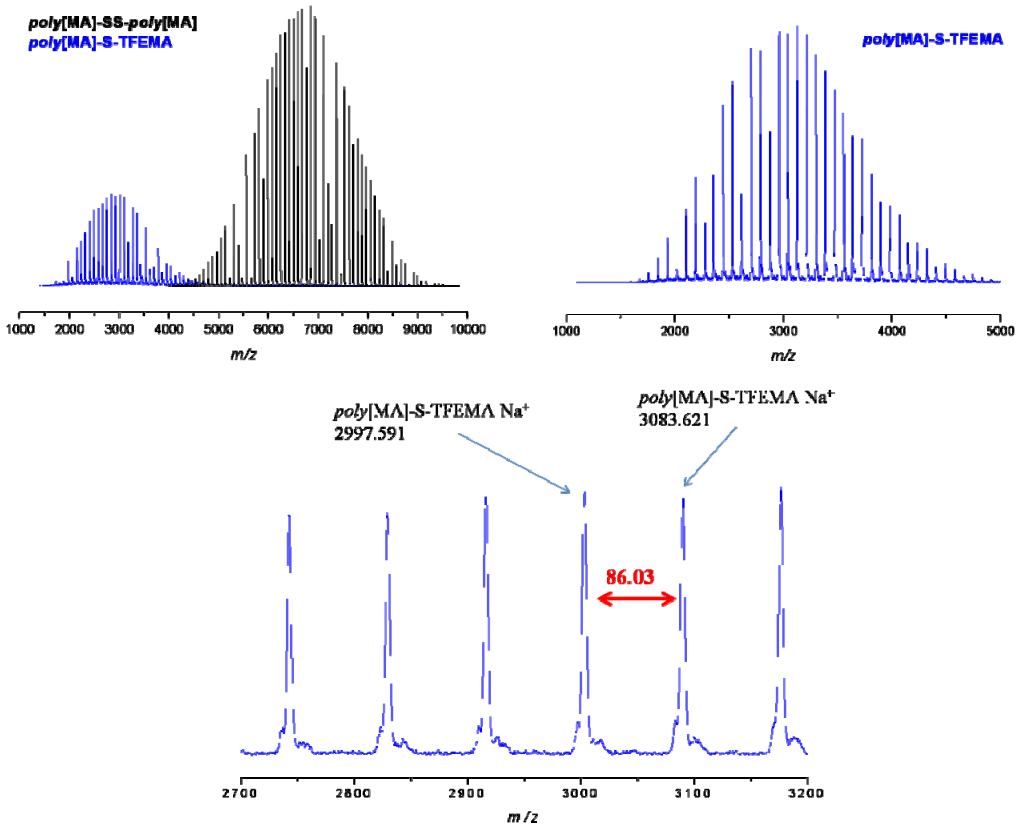
SI Fig 7.2. ^{19}F NMR, calibrated to trifluroacetic acid. A shift is seen in the ^{19}F signal from δ = -75.10 to δ = -75.28 in the conjugate species.



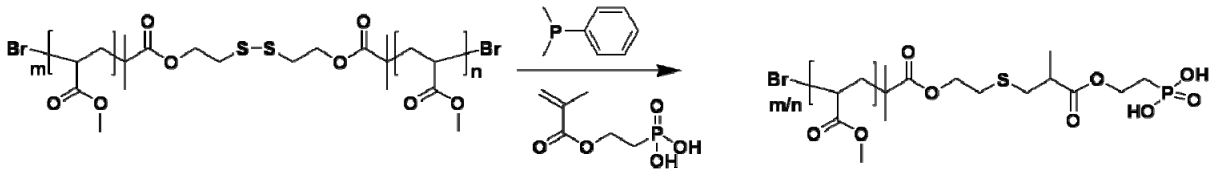
SI Fig 7.3. SEC analysis of polymer **(1)** in black, and the conjugate **(7)**. The expected halving of molecular weight is observed



SI Fig 7.4. MALDI-ToF analysis of the conjugate **(7)**, shown for DP 32 and 33.

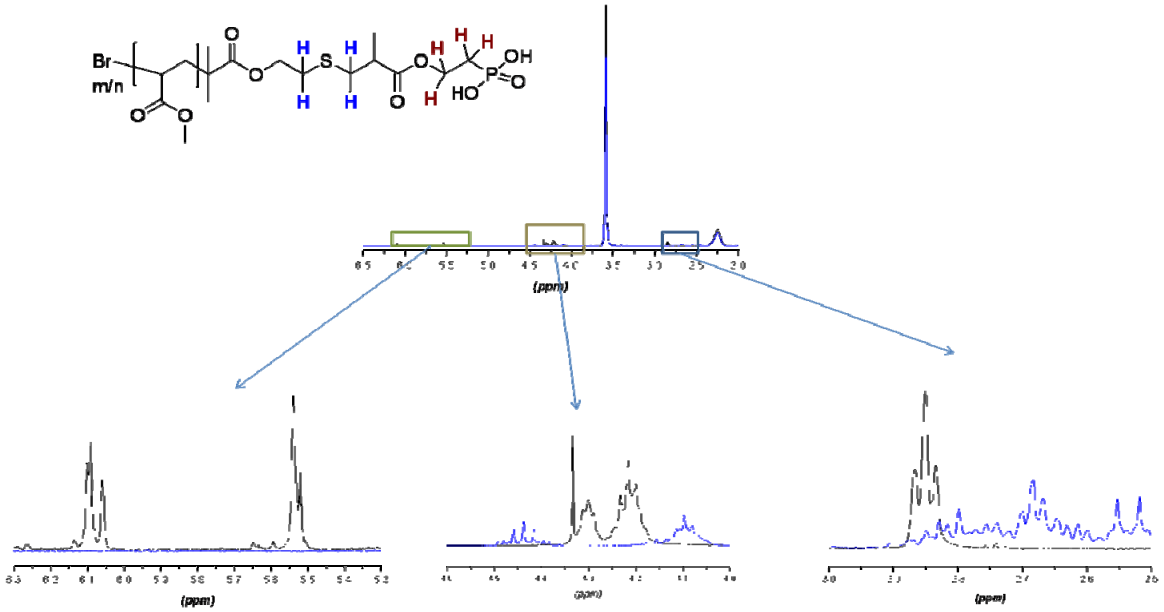


(8) Conjugation on ethylene glycol methacrylate phosphate.

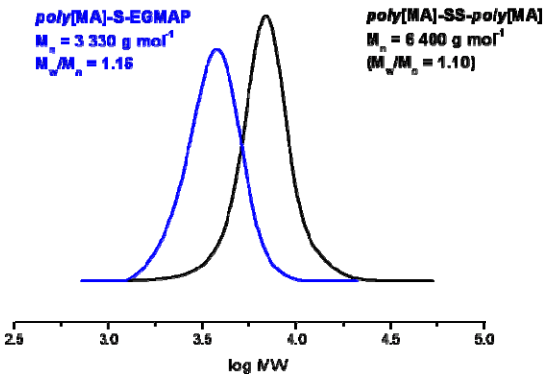


Procedure as **(4)**, except ethylene glycol methacrylate phosphate (6.4 mg, 0.033 mmol) was used.

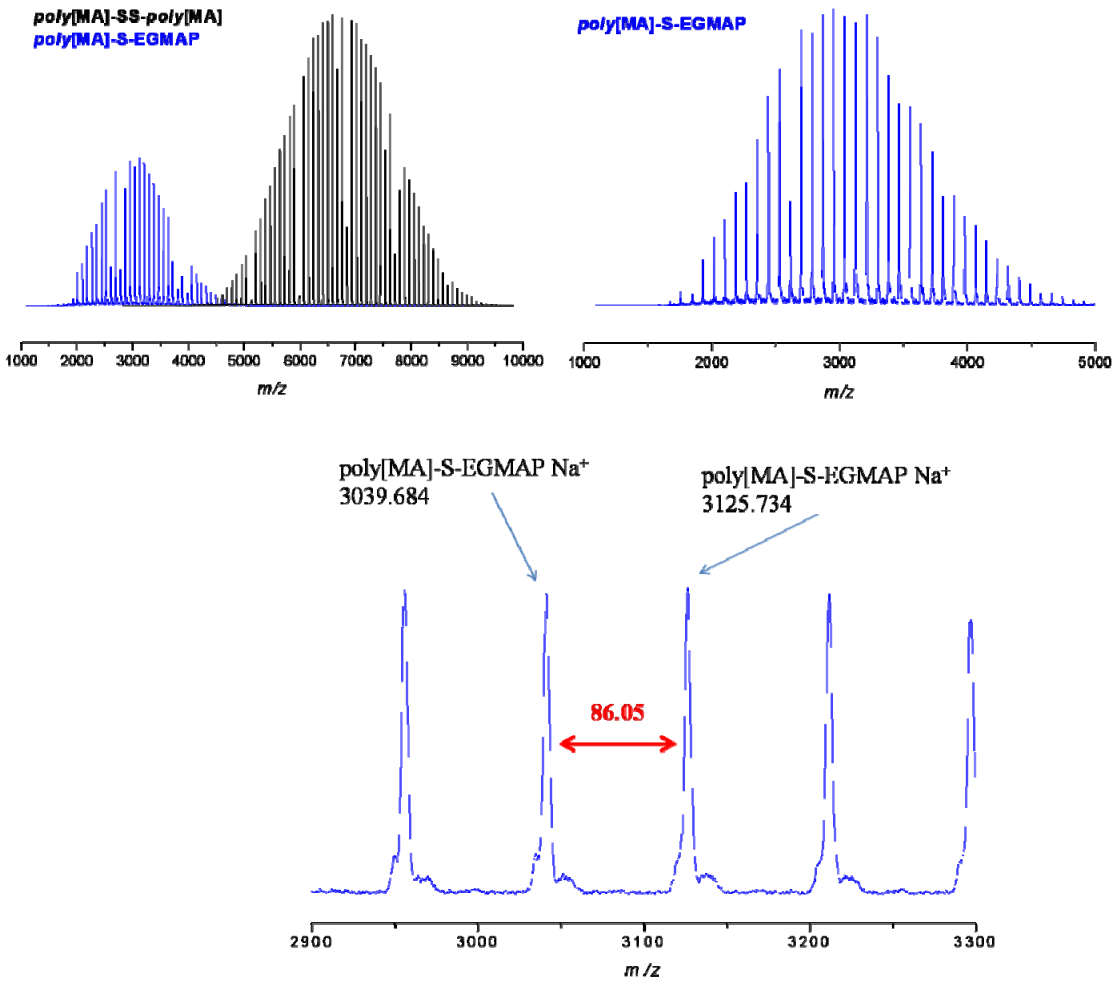
SI Fig 8.1. ^{1}H NMR indicates that complete conjugation has occurred, as previously described. Complete disappearance of the methacrylate peaks post purification δ = 6.19 (d, 1H), 5.67 (d, 1H), whist the CH_2 α to the ester remains but shifts from at δ = 4.3 *ppm* to δ = 4.5 *ppm*. The CH_2 α to the sulphur in the original polymer shifts from δ = 2.9 *ppm* to a multiplet down field at δ = 2.7 *ppm*, from the chiral coupling of the CH_2's either side of the sulphur.



SI Fig 8.2. SEC analysis of polymer **(1)** in black, and the conjugate **(8)**. The expected halving of molecular weight is observed

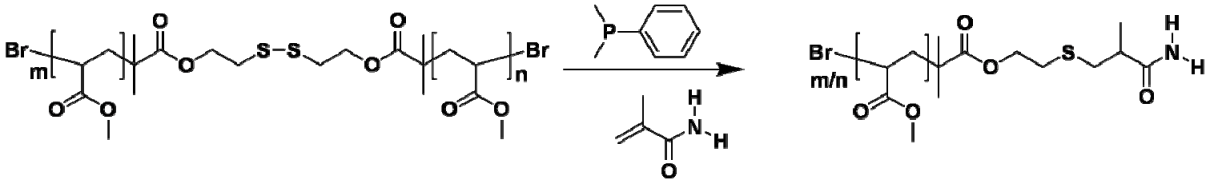


SI fig 8.3. MALDI-ToF analysis of the conjugate **(8)**, shown for DP 32 and 34.

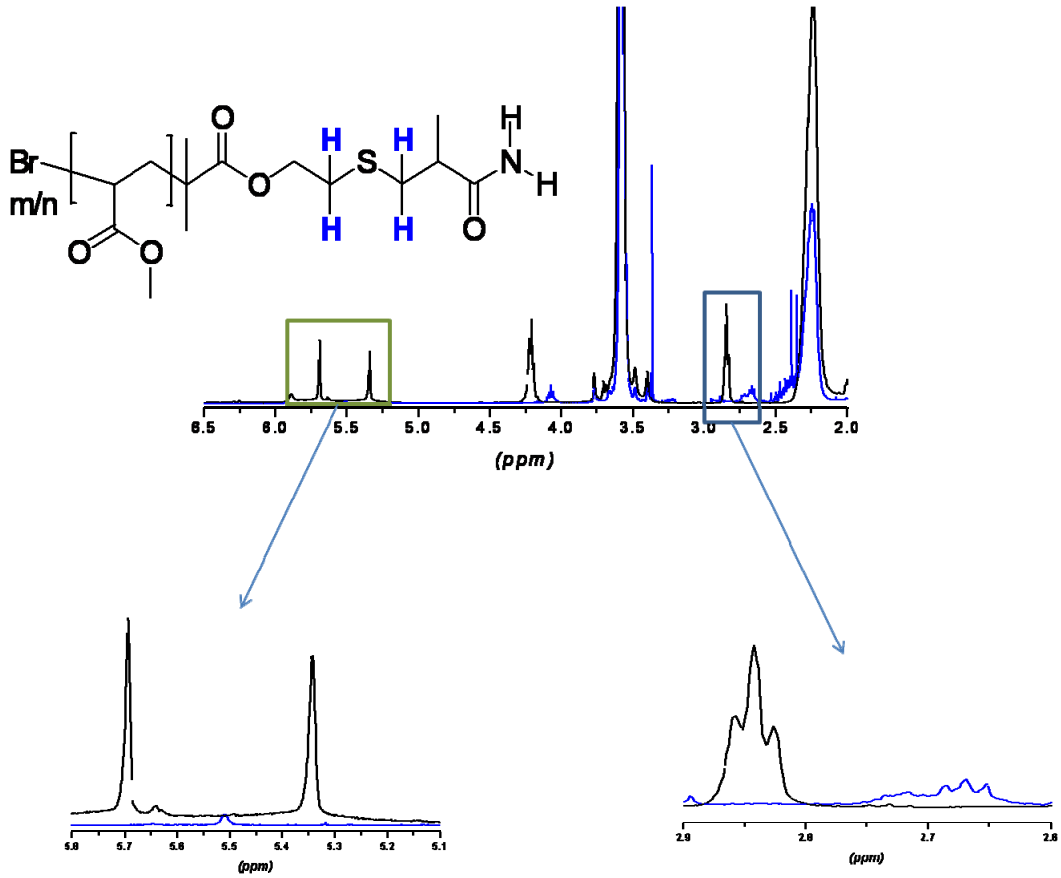


(9) Conjugation of methacrylamide

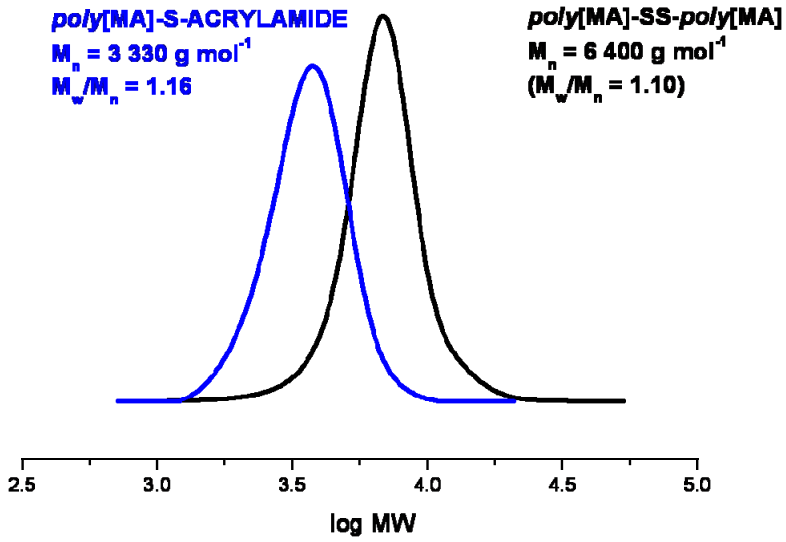
Procedure as **(4)**, except methacrylamide (2.8 mg, 0.033 mmol) was used.



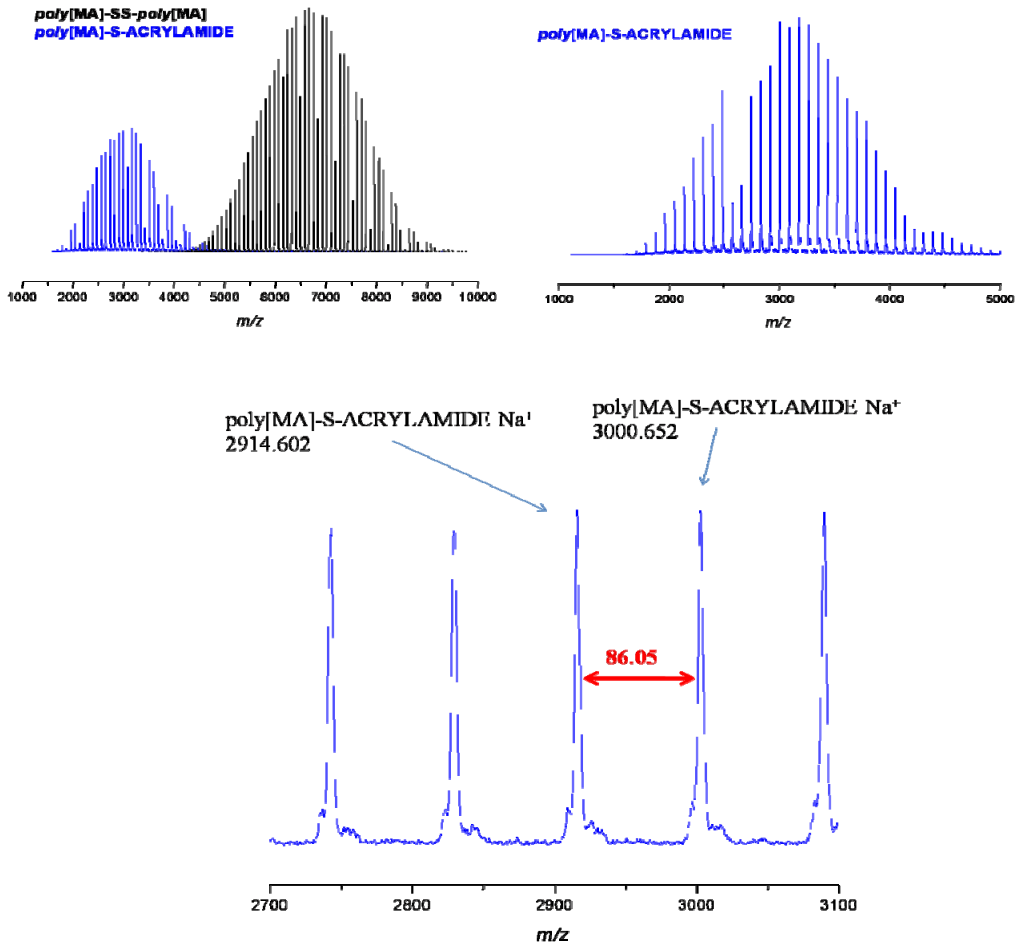
SI Fig 9.1 ^{1}H NMR indicates that complete conjugation has occurred, as previously described. Complete disappearance of the methacrylate peaks post purification δ = 6.19 (d, 1H), 5.67 (d, 1H). The CH_2 α to the sulphur in the original polymer shifts from δ = 2.9 *ppm* to a multiplet down field at δ = 2.7 *ppm*, from the chiral coupling of the CH_2's either side of the sulphur. No detectable end groups are available in the functional end group.



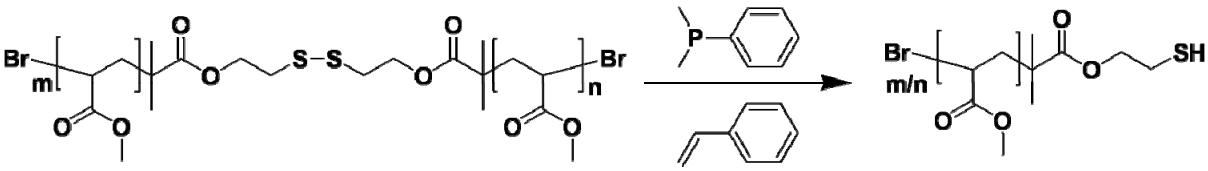
SI Fig 9.2. SEC analysis of polymer **(1)** in black, and the conjugate **(9)**. The expected halving of molecular weight is observed



SI Fig 9.3. MALDI-ToF analysis of the conjugate **(9)**, shown for DP 31 and 32.

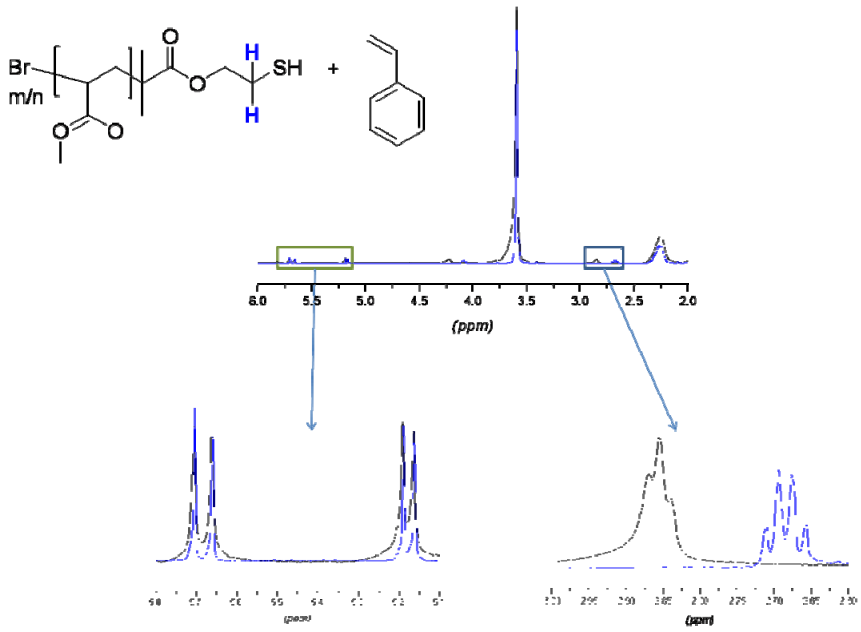


(10) Conjugation of styrene

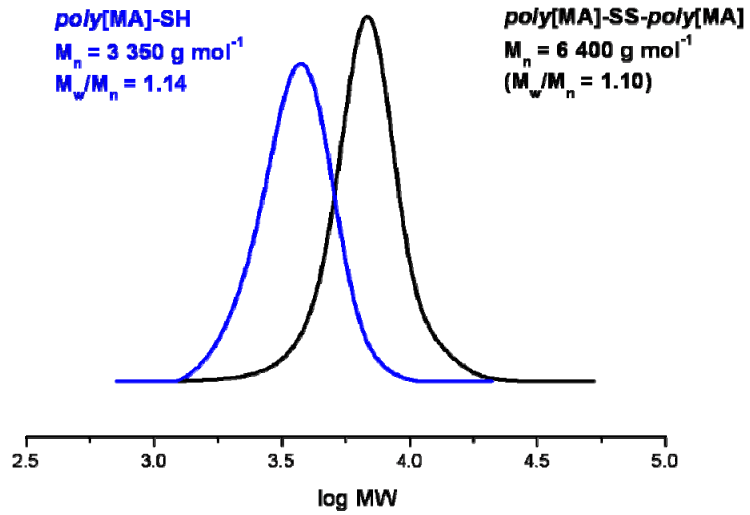


Procedure as **(4)**, except styrene (3.4 mg, 0.033 mmol) was used.

SI Fig 10.1. ^{1}H NMR indicates that no conjugation occurred. The vinyl peaks post purification δ = 5.15 and δ = 2.7 remain. The CH_2 α to the sulphur in the original polymer shifts from δ = 2.9 *ppm* to a multiplet down field at δ = 2.7 *ppm*, from the chiral coupling of the CH_2's either side of the sulphur, which shows the polymer has reduced, but no conjugation has proceeded.



SI Fig 10.2. SEC analysis of polymer **(1)** in black, and the reduced polymer **(10)**. The expected halving of molecular weight is observed



SI Fig 10.3. MALDI-ToF analysis of the reduced poly[MA]-SS-poly[MA], shown for DP 29 and 30.