Electronic Supplementary Material (ESI) for Polymer Chemistry.

Electronic Supplementary Information

of

The effect of ligand, solvent and Cu(0) source on the efficient polymerization of polyether acrylates and methacrylates in aqueous and organic media

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Materials

Poly(ethylene glycol) (PEG, av. M_n =1000 g.mol^{-1}, BioUltra, Sigma-Aldrich), poly(ethylene glycol) methyl ether acrylate (PEGA$_{480}$, 97%, Sigma-Aldrich, av. M_n = 480 g.mol^{-1}), poly(ethylene glycol) methyl ether methacrylate (PEGMA$_{475}$, 98%, Sigma-Aldrich, av. M_n = 475 g.mol^{-1}), copper(II)bromide (98%, Sigma-Aldrich), dimethyl sulfoxide (DMSO, reagent grade, Fisher Scientific), water (HPLC grade, VWR) were used as received without further purification. Cuprisorb™ resin was purchased from Seachem. Cu(I)Br (CuBr, 97%, Sigma-Aldrich) was washed sequentially with acetic acid glacial and ethanol and dried over reduced pressure. *N,N,N',N',N'',N''*-Hexamethyl-[tris(aminoethyl)amine] (Me_6-TREN) was synthesized according to a reported procedure[1], deoxygenated and stored at 4°C under nitrogen prior to use. *N,N,N',N',N''*-Pentamethyldiethylenetriamine (98%, Sigma-Aldrich) was distilled under reduced pressure (55°C, 10^{-1} mbar), deoxygenated and stored at 4°C under nitrogen prior to use. Copper(0) wire (Ø 0.25 mm) was pre-treated by washing in hydrochloric acid (35 %) for 10 minutes, then rinsed with acetone, dried under nitrogen and used immediately.

Instrument and analysis

^{1}H, ^{13}C NMR spectra were recorded on Bruker ACF-250 and DPX-300 spectrometers using deuterated solvents obtained from Sigma-Aldrich.

IR spectra were collected on a Bruker VECTOR-22 FT-IR spectrometer using a Golden Gate diamond attenuated reflection cell.

HRMS (ESI) data were collected in positive mode, using a Bruker HCT Ultra ESI spectrometer.

MALDI-ToF MS spectra were recorded in reflection mode on a Bruker Daltonics Ultraflex II MALDI-ToF mass spectrometer, equipped with a nitrogen LASER delivering 2 ns laser pulses at 337 nm with positive ion ToF detection performed using an accelerating voltage of 25 kV. The matrix solution was prepared by dissolving trans-2-[3-(4-tertbutylphenyl)-2-methyl-2-propenylidene] malononitrile (DCTB) in THF (200 mg/mL). Sodium iodide was dissolved in THF (2 mg/ mL). Polymer samples were dissolved in THF (1 to 5 mg/mL). Samples were prepared by mixing 5 μL of polymer solution, 5 μL of salt solution and 20 μL of matrix solution. Calibration was performed with a poly(ethylene glycol) methyl ether acrylate (M_w = 1100 g.mol^{-1}) standard. DMF SEC traces were obtained on a Varian 390-LC system using a DMF (5 mM NH_4BH_4) eluent at 50°C, equipped with refractive index, UV and viscometry detectors, 2 × PLgel 5 mm mixed D columns (300 × 7.5 mm), 1

× PLgel 5 mm guard column (50 × 7.5 mm) and autosampler. Narrow linear poly(methyl methacrylate) standards in range of 200 to 1.0 × 106 g·mol^{-1} were used to calibrate the system. All samples were passed through 0.45 μm PTFE filter before analysis.

Synthesis of initiators

Synthesis of poly(ethylene glycol) bis (2-bromoisobutyrate).

Poly(ethylene glycol) (av. M_n = 1000 g.mol^{-1}, 15 g, 15 mmol) was charged in a 500 mL three neck RB flask equipped with a dropping funnel, magnetic stirring bar and rubber septa and left to degas under nitrogen for 30 mins. Anhydrous toluene (300 mL) was canulated into the flask and the mixture left to stir for 5 mins. Subsequently, 50 mL of solvent was distilled under reduced pressure. Triethylamine (5.2 mL, 2.5 eq.) was added to the solution via a deoxygenated syringe and the mixture placed in an ice bath. α-bromoisobutyryl bromide (4.6 mL, 2.5 eq.) was added dropwise via the dropping funnel. Upon complete addition, the mixture was left to stir at 0°C for 30 minutes and at ambient temperature overnight.

The mixture was filtered to remove the amine salt and the volatiles removed by rotary evaporation. The solid was dissolved in dichloromethane (150 mL) and washed three times with a saturated solution of Na_2CO_3 (2* 75 mL). The organic phase was dried over $MgSO_4$ before the volatiles were removed by rotary evaporation to yield a light yellow liquid. The solid was dissolved in THF and precipitated twice in cold petroleum ether (60-80°C) to yield a light yellow solid (15.4 g, 84 % yield).

^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 4.33 (t, 4H, J_1=9.6 Hz, J_2=4.9Hz, CO-O-C$\boldsymbol{H}_2$-CH$_2$), 3.75 (t, 4H, J_1=9.6 Hz, J_2=4.9Hz, CO-O-CH$_2$-C$\boldsymbol{H}_2$), 3.65 (s, 74H, -O-C$\boldsymbol{H}_2$-C$\boldsymbol{H}_2$) and 1.95 (s, 12H, -(C$\boldsymbol{H}_3$)$_2$). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 70.5, 68.7, 65.1 and 30.7. FT-IR (ν, cm^{-1}): 3000 (C-H stretch) 1750 (O-CO-R), 1380 (-(CH$_3$)$_2$), 1300 (CH stretch), 1200 (CH stretch). HRMS (ESI, m/z, Da): [2M + Na$^+$] 621.9 (*DP$_n$* 18, *621.2 Th*).

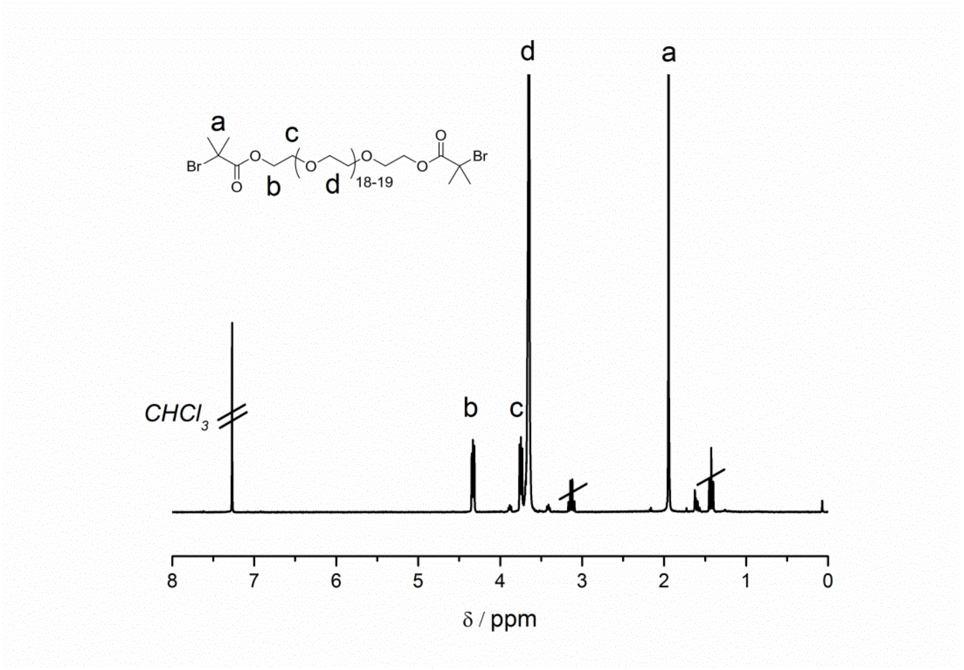

Figure S1. ^{1}H NMR (300 MHz, $CDCl_3$) spectrum of poly(ethylene glycol) bis(2-bromoisobutyrate).

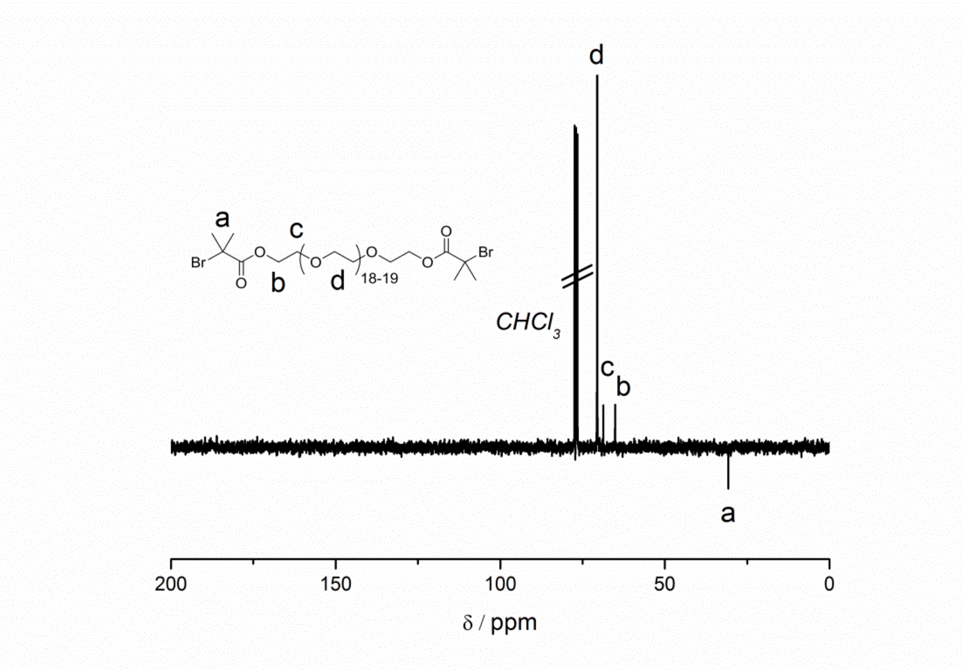

Figure S2. ^{13}C NMR (75 MHz, $CDCl_3$) spectrum of poly(ethylene glycol) bis(2-bromoisobutyrate).

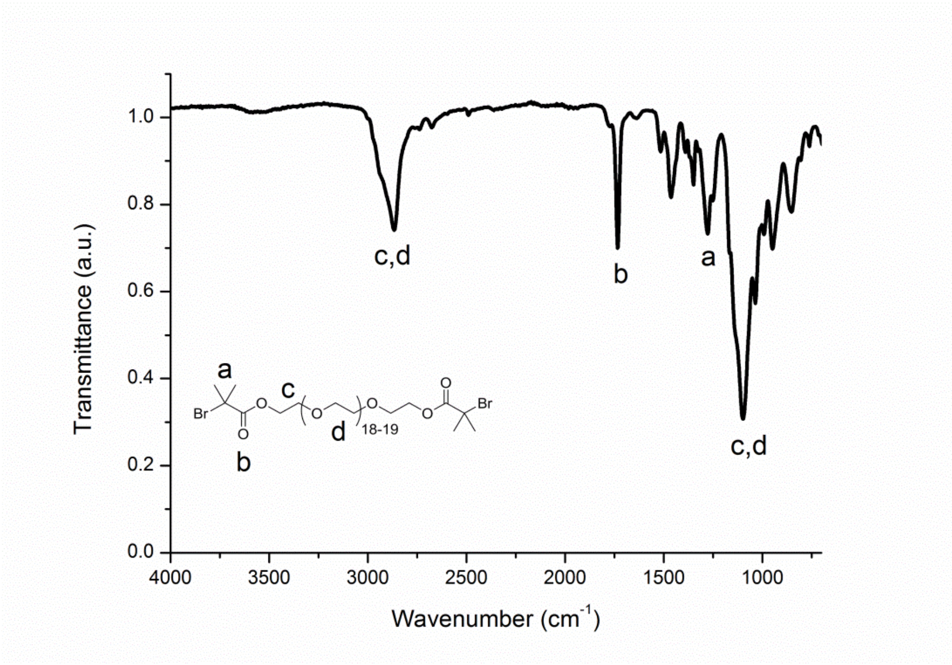

Figure S3. FT-IR spectrum of poly(ethylene glycol) bis(2-bromoisobutyrate).

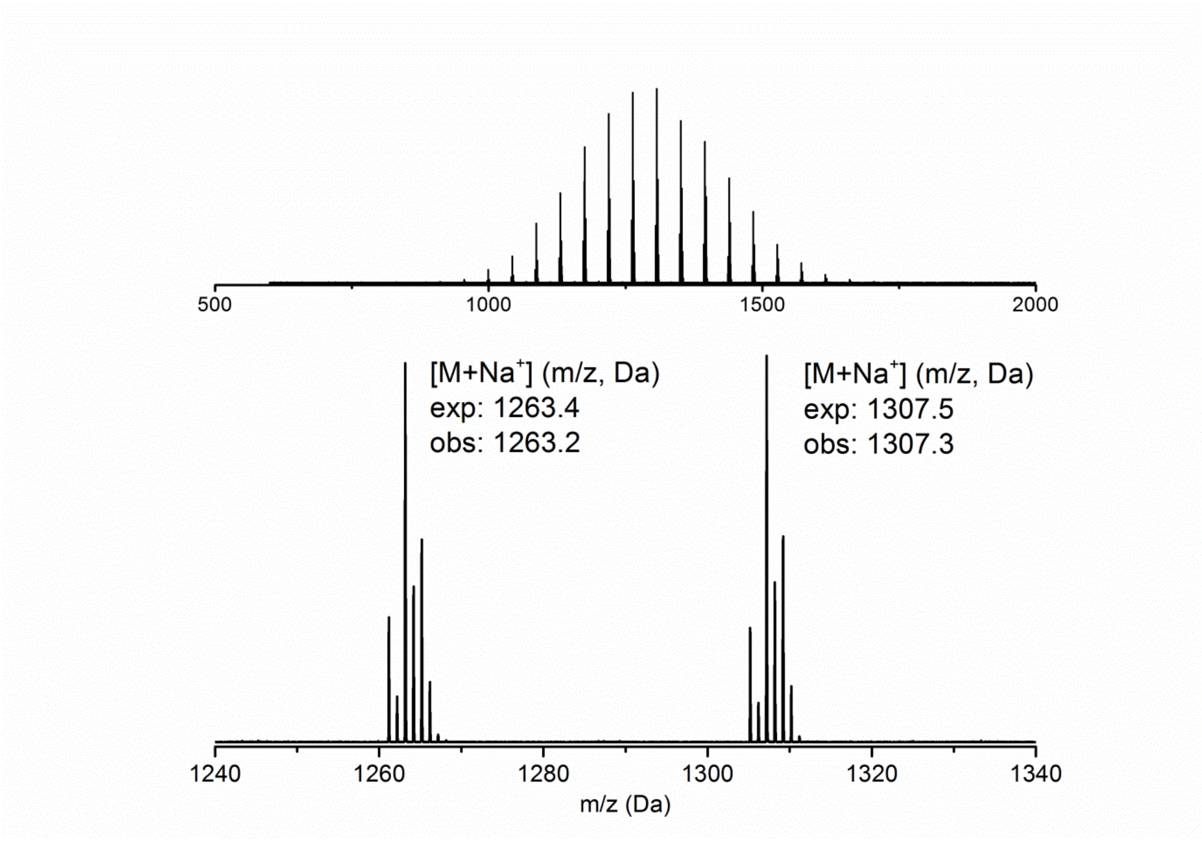

Figure S4. MALDI-ToF spectrum of poly(ethylene glycol) bis(2-bromoisobutyrate).

Disproportionation and polymerization experiments

Cu(0)-mediated polymerization of PEGA$_{480}$ DP_n=20 using Me$_6$-TREN ligand in DMSO.

In an oven dried Schlenk tube were added poly(ethylene glycol) bis(2-bromoisobutyrate) (0.7 g, 0.57 mmol), copper(II) bromide (6.4 mg, 0.05 eq.), PEGA$_{480}$ (5.0 mL, 20 eq.), DMSO (5 mL). The stirring bar with the pre-activated copper wire was then added and the Schlenk tube was sealed with a rubber septum. The reaction was kept stirring and degassed with nitrogen for 10 min. Me$_6$-TREN (27.5 µL, 0.18 eq.) was injected via a degassed microsyringe and the reaction was left to polymerize at 25°C.

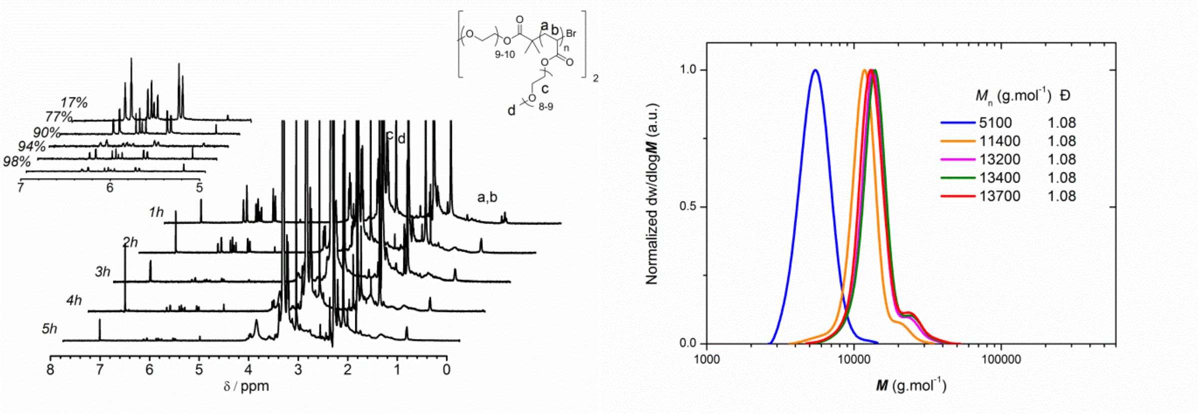

Figure S5. Monitoring the polymerization of poly(ethylene glycol) methyl ether acrylate (av. M_n=480 g.mol^{-1}) in DMSO with Me$_6$-TREN ligand at 25°C, by ^{1}H NMR (CDCl$_3$, 250 MHz, left) and SEC (DMF eluent, right).

Cu(0)-mediated polymerization of PEGMA$_{475}$ DP_n=20 using Me$_6$-TREN ligand in DMSO.

In an oven dried Schlenk tube were added poly(ethylene glycol) bis(2-bromoisobutyrate) (0.7 g, 0.57 mmol), copper(II) bromide (6.4 mg, 0.05 eq.), PEGMA$_{475}$ (5.0 mL, 20 eq.), DMSO (5 mL). The stirring bar with the pre-activated copper wire was then added and the Schlenk tube was sealed with a rubber septum. The reaction was kept stirring and degassed with nitrogen for 10 min. Me$_6$-TREN

(27.5 µL, 0.18 eq.) was injected via a degassed microsyringe and the reaction was left to polymerize at 25°C.

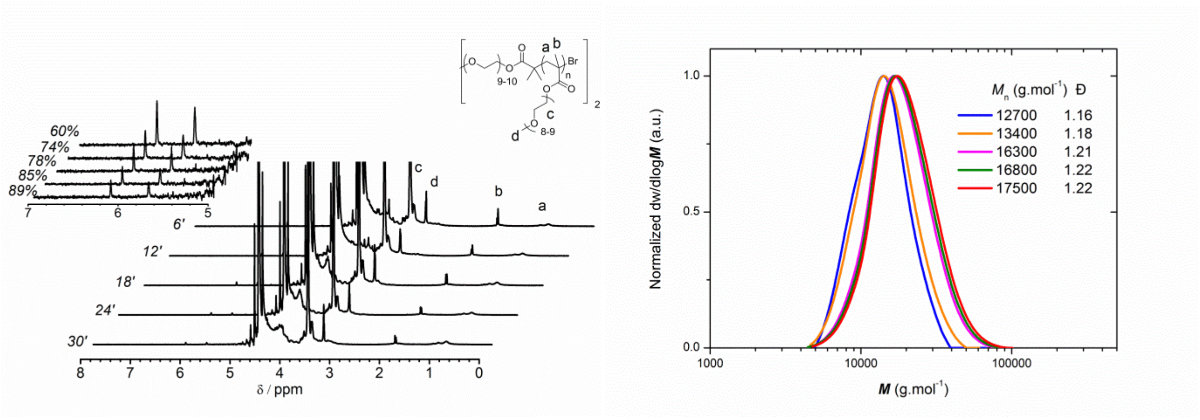

Figure S6. Monitoring the polymerization of poly(ethylene glycol) methyl ether methacrylate (av. M_n=475 g.mol^{-1}) in DMSO with Me$_6$-TREN ligand at 25°C, by ^{1}H NMR (CDCl$_3$, 250 MHz) and SEC (DMF eluent).

Monitoring the disproportionation of Cu(I)Br in the presence of PMDETA in DMSO.

The theoretical disproportionation curve was obtained by preparing a solution of Cu(II)Br$_2$ (10.8 mg, 4.8 10^{-5} mol) in the presence of PMDETA (11.5 µL) in DMSO. Disproportionation was performed by adding Cu(I)Br (14 mg, 9.7 10^{-5} mol) to a solution of solvent (2 mL) and PMDETA (11.5 µL, 0.75 eq.), which was left to stir and deoxygenate with nitrogen for 15 minutes. Subsequently, the solution was filtered under nitrogen to remove any Cu(0) particles. UV-Vis spectrum was recorded using a quartz cuvette (path length 1 cm).

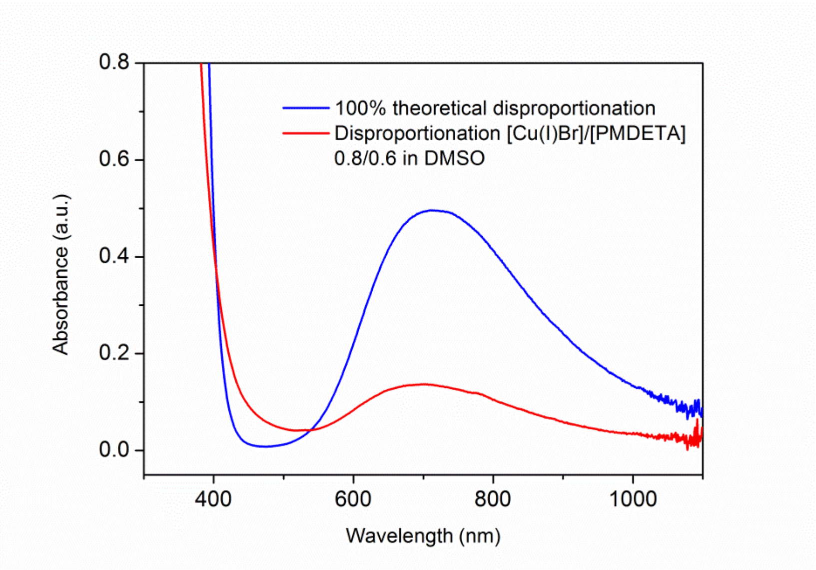

Figure S7. Monitoring the disproportionation of Cu(I)Br in the presence of PMDETA in DMSO.

Cu(0)-mediated polymerization of PEGA$_{480}$ DP_n=20 using PMDETA ligand in DMSO.

In an oven dried Schlenk tube were added poly(ethylene glycol) bis(2-bromoisobutyrate) (0.7 g, 0.57 mmol), copper(II) bromide (6.4 mg, 0.05 eq.), PEGA$_{480}$ (5.0 mL, 20 eq.), DMSO (5 mL). The stirring bar with the pre-activated copper wire was then added and the Schlenk tube was sealed with a rubber septum. The reaction was kept stirring and degassed with nitrogen for 10 min. PMDETA (21.5 µL, 0.18 eq.) was injected via a degassed microsyringe and the reaction was left to polymerize at 25°C.

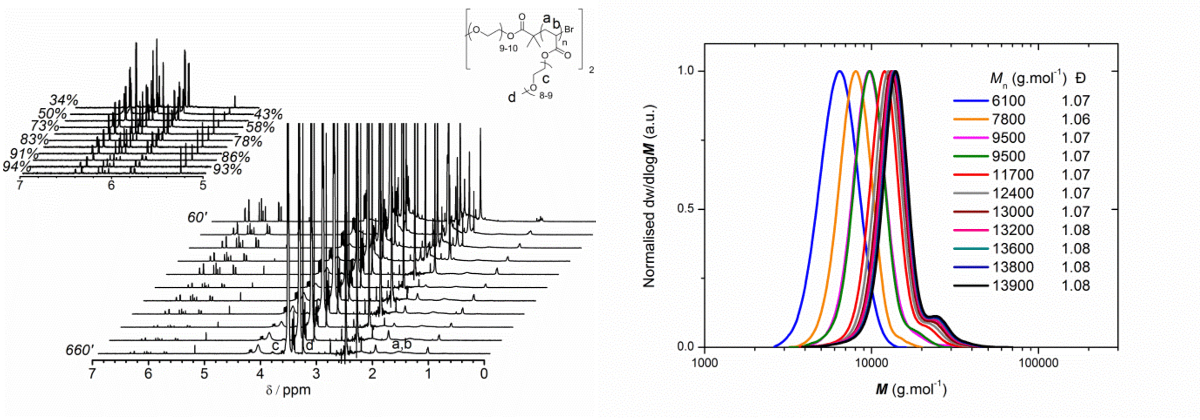

Figure S8. Monitoring the polymerization of poly(ethylene glycol) methyl ether acrylate (av. M_n = 480 g.mol^{-1}) in DMSO with PMDETA ligand at 25°C, by ^{1}H NMR ($CDCl_3$, 250 MHz, left) and SEC (DMF eluent, right).

Cu(0)-mediated polymerization of PEGMA$_{475}$ DP_n=20 using PMDETA ligand in DMSO.

In an oven dried Schlenk tube were added poly(ethylene glycol) bis(2-bromoisobutyrate) (0.7 g, 0.57 mmol), copper(II) bromide (6.4 mg, 0.05 eq.), PEGMA$_{475}$ (5.0 mL, 20 eq.), DMSO (5 mL). The stirring bar with the pre-activated copper wire was then added and the Schlenk tube was sealed with a rubber septum. The reaction was kept stirring and degassed with nitrogen for 10 min. Me$_6$-TREN (27.5 µL, 0.18 eq.) was injected via a degassed microsyringe and the reaction was left to polymerize at 25°C.

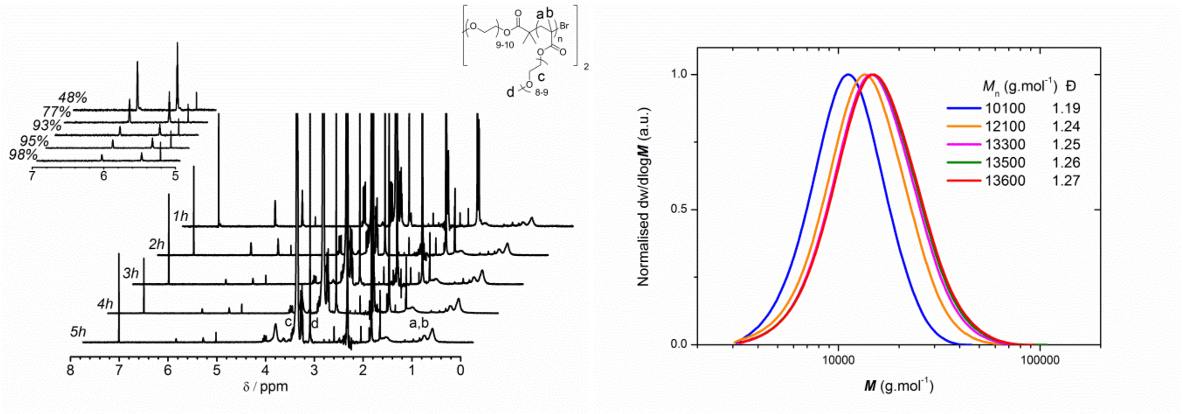

Figure S9. Monitoring the polymerization of poly(ethylene glycol) methyl ether methacrylate (av. M_n=475 g.mol^{-1}) in DMSO with PMDETA ligand at 25°C, by ^{1}H NMR ($CDCl_3$, 250 MHz, left) and SEC (DMF eluent, right).

Cu(0)-mediated polymerization of PEGA$_{480}$ DP_n=20 using Cu(0)-wire, Me$_6$-TREN ligand in H$_2$O.

In an oven dried Schlenk tube were added poly(ethylene glycol) bis(2-bromoisobutyrate) (0.7 g, 0.57 mmol), copper(II) bromide (6.4 mg, 0.05 eq.), $PEGA_{480}$ (5.0 mL, 20 eq.), H_2O (5 mL). The stirring bar with the pre-activated copper wire was then added and the Schlenk tube was sealed with a rubber septum. The reaction was kept stirring and degassed with nitrogen for 10 min. Me_6-TREN (27.5 µL, 0.18 eq.) was injected via a degassed microsyringe and the reaction was left to polymerize at 25°C.

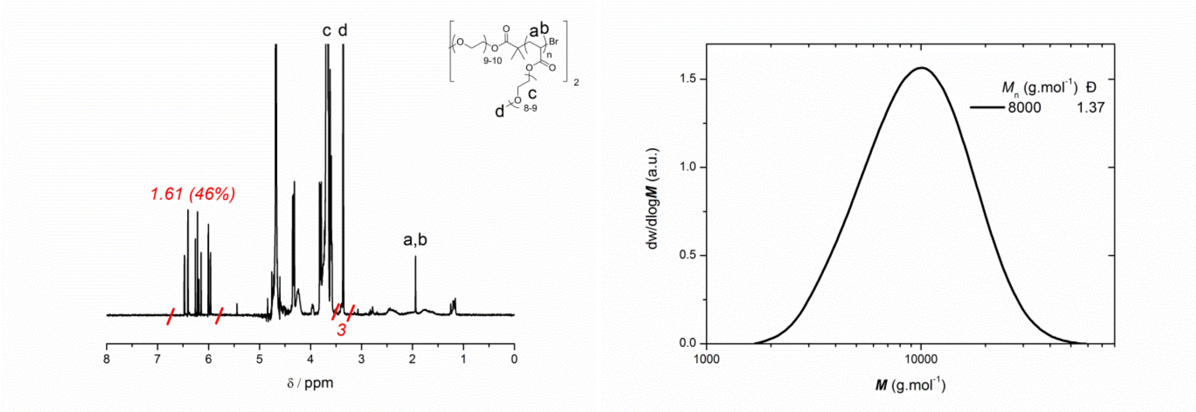

Figure S10. Monitoring the polymerization of poly(ethylene glycol) methyl ether acrylate (av. M_n = 480 $g.mol^{-1}$) in H_2O with Me_6-TREN ligand after 300 minutes at 25°C, by ^1H NMR (D_2O, 250 MHz, left) and SEC (DMF eluent, right).

Disproportionation of Cu(I)Br in the presence of Me_6-TREN to catalyse the polymerization of $PEGA_{480}$ DP_n=20 in H_2O.

To an oven dried Schlenk tube fitted with a magnetic stirring bar and rubber septum was added H_2O (2 mL), Me_6-TREN (52 µL, 0.6 eq.) and Cu(I)Br (37.5 mg, 0.8 eq.). The solution was left to degas for 20 minutes and to stir for an extra 10 minutes. A vial fitted with a rubber septum and magnetic stirring bar was charged with poly(ethylene glycol) bis(2-bromoisobutyrate) (400 mg, 0.33 mmol), $PEGA_{480}$ (2.87 mL, 20 eq.) and H_2O (10 mL). The mixture was left to stir until complete dissolution of the monomer (typically 2 minutes) and deoxygenated with nitrogen for 10 minutes. The solution was cannulated into the Schlenk tube and the reaction was left to polymerize at 0°C.

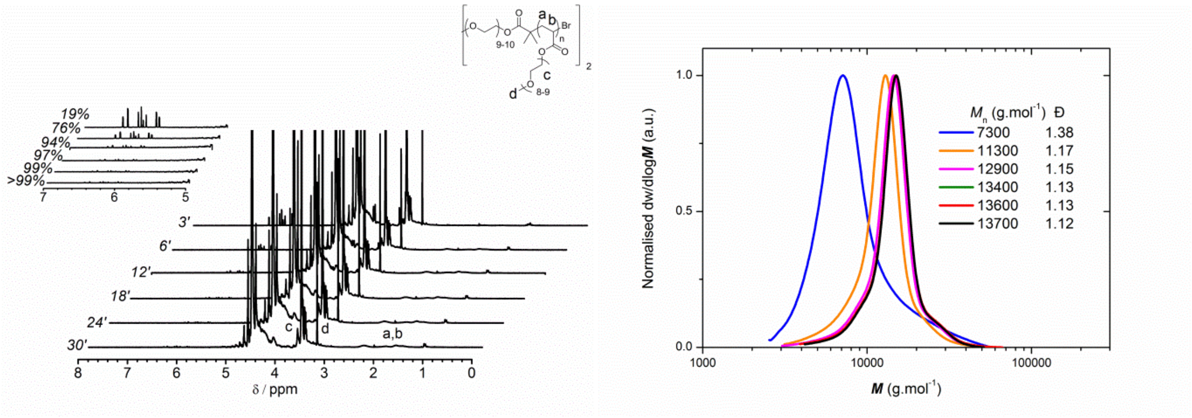

Figure S11. Monitoring the polymerization of poly(ethylene glycol) methyl ether acrylate (av. M_n=480 g.mol^{-1}) in H_2O with Me_6-TREN ligand at 0°C, by ^{1}H NMR (D_2O, 250 MHz) (left) and SEC (DMF eluent, right).

Disproportionation of Cu(I)Br in the presence of Me_6-TREN to catalyse the polymerization of PEGMA$_{475}$ DP_n=20 in H_2O.

To an oven dried Schlenk tube fitted with a magnetic stirring bar and rubber septum was added H_2O (2 mL), Me_6-TREN (52 µL, 0.6 eq.) and Cu(I)Br (37.5 mg, 0.8 eq.). The solution was left to degas for 20 minutes and to stir for an extra 10 minutes. A vial fitted with a rubber septum and magnetic stirring bar was charged with poly(ethylene glycol) bis(2-bromoisobutyrate) (400 mg, 0.33 mmol), PEGMA$_{475}$ (2.87 mL, 20 eq.) and H_2O (10 mL). The mixture was left to stir until complete dissolution of the monomer (typically 2 minutes) and deoxygenated with nitrogen for 10 minutes. The solution was cannulated into the Schlenk tube and the reaction was left to polymerize at 0°C.

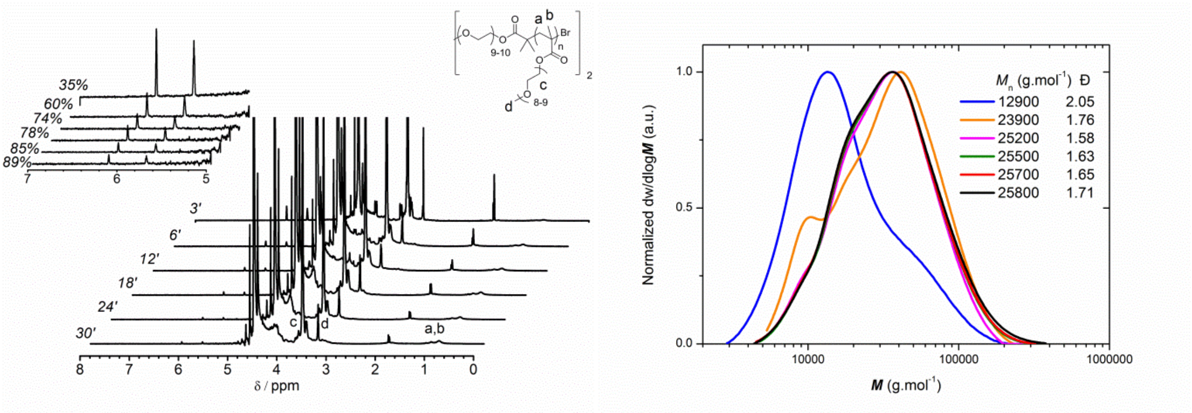

Figure S12. Monitoring the polymerization of poly(ethylene glycol) methyl ether methacrylate (av. M_n = 475 g.mol^{-1}) in H_2O with Me_6-TREN ligand at 0°C, by ^{1}H NMR (D_2O, 250 MHz, left) and SEC (DMF eluent, right).

Monitoring the disproportionation of Cu(I)Br in the presence of PMDETA in water

The theoretical disproportionation curve was obtained by preparing a solution of Cu(II)Br_2 (10.8 mg, 4.8 10^{-5} mol) in the presence of PMDETA (11.5 μL) in H_2O. Disproportionation was performed by adding Cu(I)Br (14 mg, 9.7 10^{-5} mol) to a solution of solvent (2 mL) and PMDETA (11.5 μL, 0.75 eq.), which was left to stir and deoxygenate with nitrogen for 15 minutes. Subsequently, the solution was filtered under nitrogen to remove any Cu(0) particles. UV-Vis spectrum was recorded using a quartz cuvette (path length 1 cm).

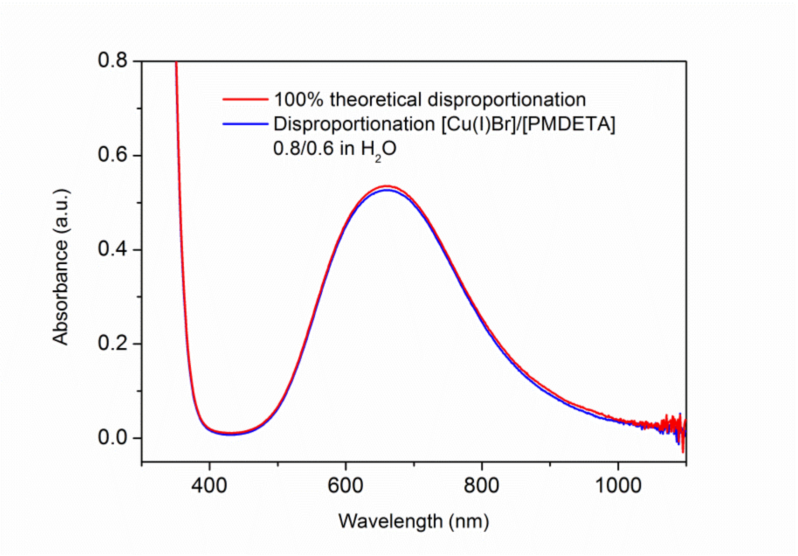

Figure S13. Monitoring the disproportionation of Cu(I)Br in the presence of PMDETA in water.

Disproportionation of Cu(I)Br in the presence of PMDETA to catalyse the polymerization of $PEGA_{480}$ DP_n=20 in H_2O.

To an oven dried Schlenk tube fitted with a magnetic stirring bar and rubber septum was added H_2O (2 mL), PMDETA (41 μL, 0.6 eq.) and Cu(I)Br (37.5 mg, 0.8 eq.). The solution was left to degas for 20 minutes and to stir for an extra 10 minutes. A vial fitted with a rubber septum and magnetic stirring bar was charged with poly(ethylene glycol) bis(2-bromoisobutyrate) (400 mg, 0.33 mmol), $PEGA_{480}$ (2.87 mL, 20 eq.) and H_2O (10 mL). The mixture was left to stir until complete dissolution of the monomer (typically 2 minutes) and deoxygenated with nitrogen for 10 minutes. The solution was cannulated into the Schlenk tube and the reaction was left to polymerize at 0°C.

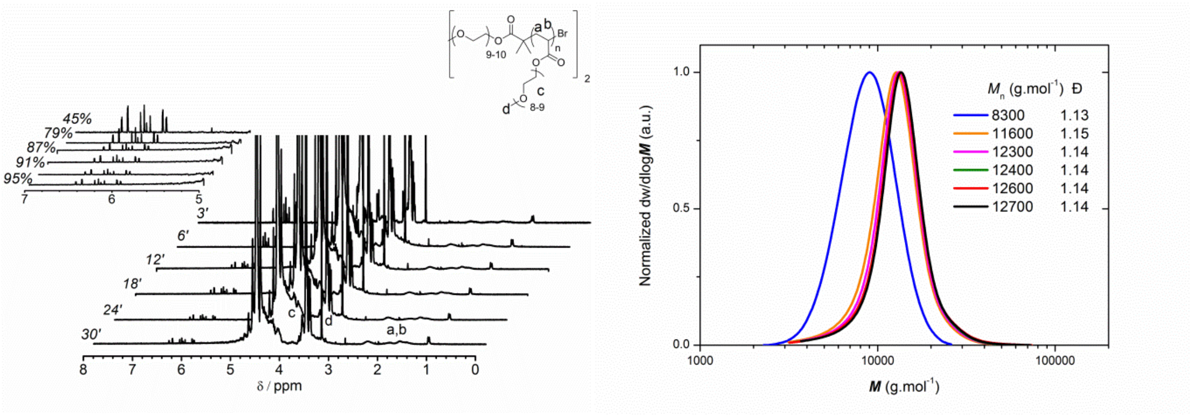

Figure S14. Monitoring the polymerization of poly(ethylene glycol) methyl ether acrylate (av. M_n = 480 g.mol^{-1}) in H_2O with PMDETA ligand at 0°C, by ^{1}H NMR (D_2O, 250 MHz, left) and SEC (DMF eluent, right) .

Disproportionation of Cu(I)Br in the presence of PMDETA to catalyse the polymerization of PEGMA$_{475}$ DP_n=20 in H_2O.

To an oven dried Schlenk tube fitted with a magnetic stirring bar and rubber septum was added H_2O (2 mL), PMDETA (41 μL, 0.6 eq.) and Cu(I)Br (37.5 mg, 0.8 eq.). The solution was left to degas for 20 minutes and to stir for an extra 10 minutes. A vial fitted with a rubber septum and magnetic stirring bar was charged with poly(ethylene glycol) bis(2-bromoisobutyrate) (400 mg, 0.33 mmol), PEGMA$_{475}$ (2.87 mL, 20 eq.) and H_2O (10 mL). The mixture was left to stir until complete dissolution of the monomer (typically 2 minutes) and deoxygenated with nitrogen for 10 minutes. The solution was cannulated into the Schlenk tube and the reaction was left to polymerize at 0°C.

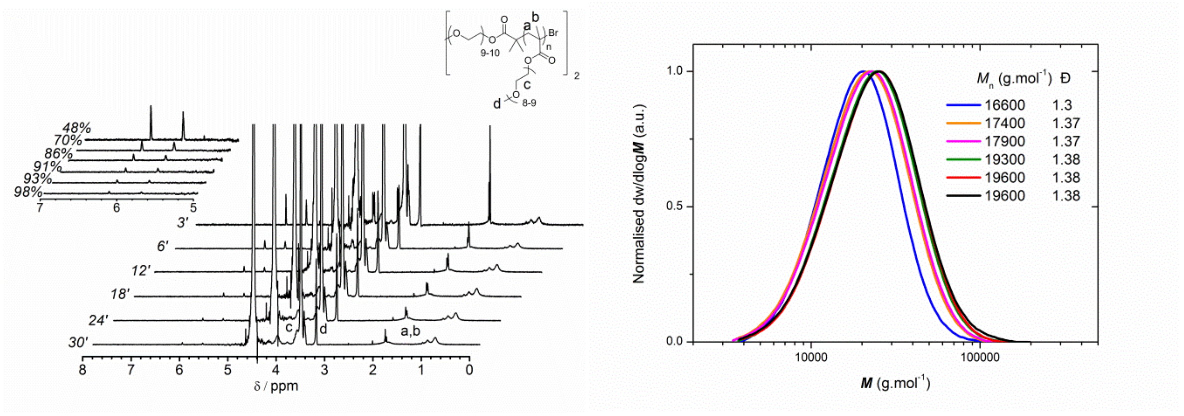

Figure S15. Monitoring the polymerization of poly(ethylene glycol) methyl ether methacrylate (av. M_n=475 g.mol^{-1}) in H_2O with PMDETA ligand at 0°C, by ^{1}H NMR (D_2O, 250 MHz, left) and SEC (DMF eluent, right).

Sequential addition of a second monomer aliquot *in situ.*

A vial fitted with a rubber septum and magnetic stirring bar was charged with monomer (PEGA$_{480}$ or PEGMA$_{475}$ respectively, 20 eq.) and H_2O (10 mL). The mixture was left to stir until complete dissolution of the monomer (typically 1 minutes) and deoxygenated with nitrogen for 10 minutes. The solution was cannulated into the reaction vessel upon 30 minutes of polymerization and the reaction was left to stir at 0°C.

Disproportionation of Cu(I)Br in the presence of Me$_6$-TREN in DMSO

The theoretical disproportionation curve was obtained by preparing a solution of Cu(II)Br$_2$ (10.8 mg, 4.8 10^{-5} mol) in the presence of Me$_6$-TREN (20 μL) in DMSO. Disproportionation was performed by adding Cu(I)Br (14 mg, 9.7 10^{-5} mol) to a solution of solvent (2 mL) and Me$_6$-TREN (20 μL, 0.75 eq.), which was left to stir and deoxygenate with nitrogen for 15 minutes. Subsequently, the solution was filtered under nitrogen to remove any Cu(0) particles. UV-Vis spectrum was recorded using a quartz cuvette (path length 1 cm).

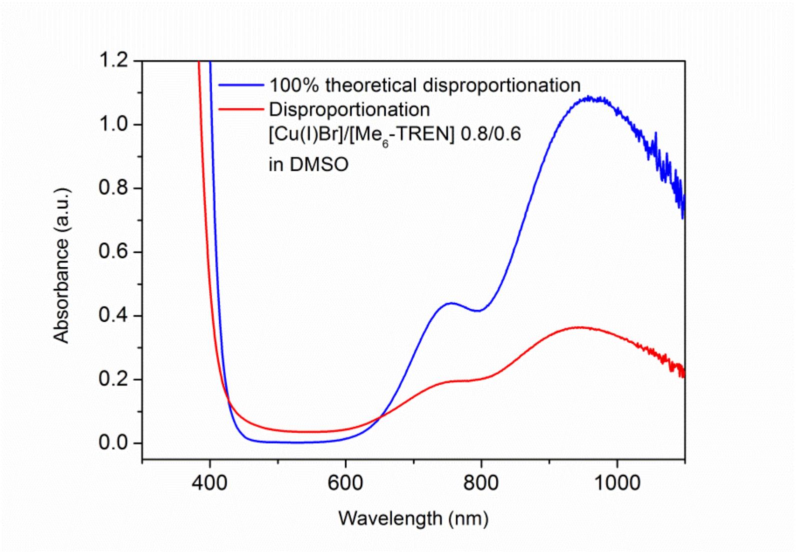

Figure S16. Monitoring the disproportionation of Cu(I)Br in the presence of Me$_6$-TREN in DMSO.

Disproportionation of Cu(I)Br in the presence of Me$_6$-TREN to catalyse the polymerization of PEGA$_{480}$ DP_n=20 in DMSO.

To an oven dried Schlenk tube fitted with a magnetic stirring bar and rubber septum was added DMSO (2 mL), Me$_6$-TREN (52 µL, 0.6 eq.) and Cu(I)Br (37.5 mg, 0.8 eq.). The solution was left to degas for 20 minutes and to stir for an extra 10 minutes. A vial fitted with a rubber septum and magnetic stirring bar was charged with poly(ethylene glycol) bis(2-bromoisobutyrate) (400 mg, 0.33 mmol), PEGA$_{480}$ (2.87 mL, 20 eq.) and DMSO (10 mL). The mixture was left to stir until complete dissolution of the monomer (typically 2 minutes) and deoxygenated with nitrogen for 10 minutes. The solution was cannulated into the Schlenk tube and the reaction was left to polymerize at 0°C.

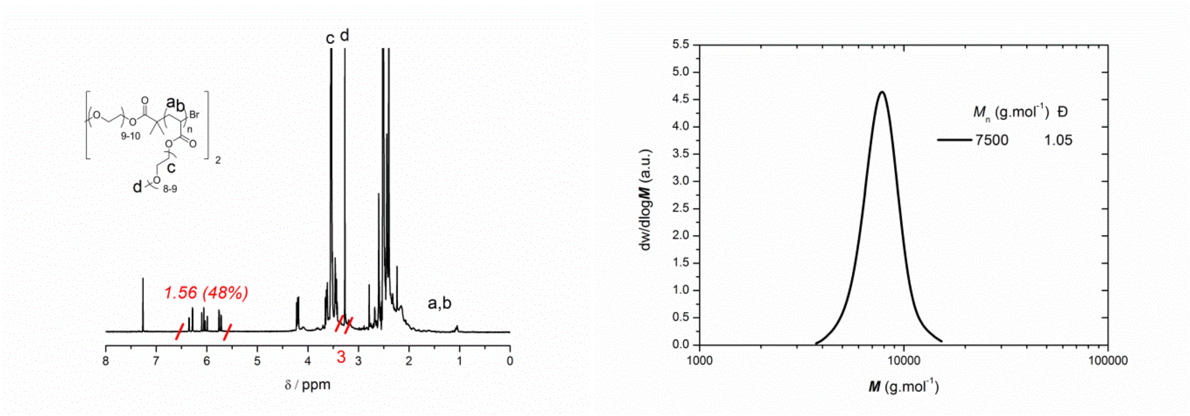

Figure S17. Monitoring the polymerization of poly(ethylene glycol) methyl ether methacrylate (av. M_n=475 g.mol^{-1}) in DMSO with Me$_6$-TREN ligand after 30 minutes at 0°C, by ^{1}H NMR (CDCl$_3$, 250 MHz) and SEC (DMF eluent).

References

1. M. Ciampolini and N. Nardi, *Inorg. Chem.*, 1966, **5**, 41-44.