Assessment of SET-LRP in DMSO using online monitoring and Rapid GPC†

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Online monitoring with *in situ* Fourier Transform Near Infra-Red (FT-NIR) spectroscopy and Rapid Gel Permeation Chromatography (Rapid GPC) coupled with light scattering detection are applied to monitor the single-electron transfer living radical polymerisation (SET-LRP) kinetics of methyl acrylate in DMSO. The reaction is catalyzed by copper wire and Me_6TREN ligand at 25 °C initiated by ethyl 2-bromoisobutyrate in the presence and absence of $CuBr_2$. The data are compared with that obtained from ^1H NMR and conventional GPC. The kinetic results demonstrate that both FT-NIR and Rapid GPC provide comparable conversion data with ^1H NMR and/or offline GPC. Furthermore, significant polymerisation exotherms were observed at the beginning of the reaction in DMSO under certain reaction conditions. In this study, we discuss the possible effect of these exotherms over the polymerization rate by taking into account that a period of slow rate is observed at the initial stage of polymerizations in all cases except where $CuBr_2$ is added to the reaction mixture.

Introduction

Controlling the molecular weight of synthetic polymers is one of the most important objectives of the polymer chemist. A commonly used way to achieve this is *via* living polymerization methods.[1] Several methods of radical and radical-type polymerization processes have emerged which all have their own particular advantages and disadvantages with regard to different monomers, catalysts and desired polymeric structures. In particular, it has been difficult to achieve controlled polymerization of monomers that generate very reactive radicals, such as vinyl chloride and vinyl acetate. In addition, polymers produced by these techniques can often be contaminated by catalyst and initiator residues which in turn give complications for product isolation and purification, which in turn has implication for applications.

An excellent method to achieve living/controlled radical polymerization of vinyl monomers is the use of transition metal based catalysts that can activate/deactivate appropriately terminated polymers, by a redox process, facilitated by the accessibility of different formal oxidation states for transition metals.[2] The most common method is based on the use of Cu(I) salts with ligands which facilitate the redox process whilst also enabling the catalyst to be soluble in the chosen reaction medium.[3–6] A number of variations on this have been well documented. For example, a Cu(II) salt can be utilized, often in conjunction with a reducing agent, which produces Cu(I) during the reaction.[7] Although this method is widespread and has considerable versatility and the mechanism is commonly thought to be well established, there have been several studies reported on critically questioning those inconsistent observations.

Percec *et al.* have reported a living polymerisation method based on Cu(0) as the source of the transition metal which has been termed "single-electron transfer living radical polymerization" (SET LRP).[8] This technique has many attributes in common with Atom Transfer Radical Polymerization[9–17] (ATRP), however, it uses Cu(0) metal in the absence of an inherent oxidising agent in place of Cu(I)[18,19] salts and mediates efficient polymerization of acrylates in a polar, or coordinating solvent. The use of Cu(0) is described to catalyse *via* outer sphere electron transfer to give Cu(I) which rapidly disproportionates to Cu(II) and Cu(0). This rapid disproportionation takes place in many coordinating solvents in the presence of *N*-donor ligands which are not efficient at stabilizing Cu(I) relative to Cu(II).[20] It is noted that when good π-acceptor ligands are utilized with low lying π anti bonding orbitals (π*) such as pyridine diimines and diazabutadienes, or when solvents that stabilize Cu(I) are used, such as acetonitrile, then this disproportionation does not occur on a timescale suitable for efficient SET LRP.

The use of SET LRP has been shown to be effective for amide functional monomers and initiators as well as alkenes that do not have electron withdrawing group adjacent to the propagating site.[21,22] Indeed, when Cu(I) salts have been used in polar/coordinating solvents, and with amide monomers, and practitioners have noticed a blue/green coloration to their reaction and a possible fine precipitate forming then it is quite likely that this disproportionation has indeed occurred.[23] The green/blue color is indicative of Cu(II) formation and the fine precipitate of Cu(0) metal.

It has been proposed that Cu(0) is the active species in the reaction, as opposed to Cu(I), and that disproportionation of Cu(I) in polar solvents generates nascent Cu(0) that activates alkyl halides to form the required radicals. Mechanistic discussions are currently ongoing,[24] although computational[25–28] and

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experimental[27,29–32] studies of SET-LRP kinetics have been reported. Moreover, the accelerating effect of Cu(0) on ATRP reactions has previously been described.[33–36]

As a synthetic method SET-LRP has potential advantages over ATRP as the reactions are reported to be "ultra-fast" with control over molecular weight, and facilitates product clean-up as copper wire could be used to mediate the reaction, lowering the quantity of the catalyst required. This current work reports the results of online monitoring SET-LRP polymerisations using *in situ* FT-NIR to obtain conversion, a thermocouple to record the reaction temperature, and using a series of pumps to continuously extract and dilute a polymerisation reaction solution for analysis by an instrument setup to perform rapid chromatography that provides molecular weight and conversion data.

Online monitoring refers to the concept that data regarding a polymerisation process may be obtained for a polymerisation process in "real-time" without the need for manual sampling of the reaction.[37–39] In recent years FT-NIR spectroscopy using *in situ* fibre-optic probes has been developed as a non-intrusive method of obtaining conversion and molecular weight data and has been applied to free-radical[40–44] and controlled radical[45] polymerisations. Whilst highly successful as a method of obtaining conversion data in a batch reactor, the drawback of this method has been the limitation on obtaining molecular weight and molecular weight distribution data for a propagating polymer chain as the instrumentation requires the use of mathematical models[46] to calibrate the instruments.

Coupling GPC instrumentation to a batch reactor for online analysis of molecular weight distribution has been attempted since the 1970's, with the most successful results coming from Kiparissides *et al.*[47] in the 1980's. In these experiments a series of pumps were used to continuously extract a stream of reaction solution from the batch reactor and dilute it for the analysis *via* GPC, with a programmed injection sequence automatically injecting samples. Long analysis times and corrosion of the components of the extraction system of the instrument limited the success of this setup. In recent years, the development of rapid gel permeation chromatography (GPC) utilizing columns of smaller dimensions has facilitated the high-throughput screening of polymer samples and process monitoring.[48,49]

In this work, we utilized the online monitoring techniques of *in situ* Fourier Transform Near Infra-Red (FT-NIR) spectroscopy and Rapid Gel Permeation Chromatography (Rapid GPC) coupled with light scattering detection applied to the single-electron transfer living radical polymerisation (SET-LRP) kinetics of methyl acrylate. The reaction was carried out in DMSO as solvent catalyzed by copper wire and Me$_6$TREN as ligand at 25 °C initiated by ethyl 2-bromoisobutyrate in the presence and absence of CuBr$_2$. The data are compared with that obtained from ^{1}H NMR and conventional GPC. Finally, we examined the effect of Cu(II) on the inhibition time by taking into account the exotherm of the reaction.

Experimental

Materials

Methyl acrylate (MA, Aldrich, ≥99%), CuBr (Aldrich, ≥99.999%), CuBr$_2$ (Aldrich, ≥99.0%) and ethyl 2-bromoisobutyrate (EBrB, Aldrich, 98%) were used as received without further purification. DMSO was purchased from Fisher and used as received without further purification. Copper wire with a diameter of 0.25 mm was obtained from Comax. Copper powder (particle size of 1–5 μm) was obtained from Aldrich. Tris(2-(dimethylamino)ethyl)amine (Me$_6$TREN) was synthesized according to literature procedure and stored under nitrogen prior to use.[50] Tris(2-aminoethyl)amine (TREN), formaldehyde and formic acid used in the synthesis of Me$_6$TREN were purchased from Aldrich and used without further purification.

Instrumentation

Offline ^{1}H NMR analysis to determine conversion performed on a Bruker DPX 300 MHz spectrometer at 25 °C using deuterated chloroform as a solvent. Offline GPC analysis performed on an ambient temperature system fitted with 2 × PL Mixed D (300 × 7.5 mm) columns and a 5 μm guard column with chloroform as eluent. GPC analysis for reaction in the absence of initiator performed on an ambient temperature system fitted with 2 × PL Mixed C (300 × 7.5 mm) columns and a 5 μm guard column with THF as eluent. Both GPC systems were equipped with a differential refractive index (DRI) detector and calibrated with linear narrow molecular weight PMMA standards ranging from a dimer (200 Da) up to 772 000 Da using a second order polynomial fit.

Online monitoring *via* FT-NIR was performed on a Bruker Vector22/N-F equipped with a HELLMA fibre-optic probe (3 mm) for remote sampling immersed in the solution mixture. Spectra were obtained by accumulating sixteen spectra every two minutes. Online GPC was performed on a Polymer Laboratories PL50 instrument fitted with a PL-Rapide M (100 × 10 mm) column and refractometer, UV detector and dual angle (45° and 90°) light scattering detector with THF as eluent at a flow rate of 3 mL min^{-1}. The light scattering detector was calibrated with a single standard of polystyrene at a known concentration, whilst the rapid GPC was calibrated by linear narrow molecular weight PMMA standards ranging from 772 000 Da to 625 Da. A Shimadzu LC10 pump was used to continuously extract the solution from the reactor and direct it to a mixing tee, where it was diluted with incoming THF. The diluted mixture passed to the 100 μL injection loop of the online GPC instrument where an automated injection sequence was programmed to inject a sample for analysis every three minutes. Extraction rate was set to 0.05 mL min^{-1} and dilution rate set to 2.2 mL min^{-1}.

Synthesis

Online monitoring of SET-LRP *via* FT-NIR in the absence of CuBr$_2$ (T1). Methyl acrylate (15 mL, 166 mmol, 100 eq), copper wire (8 cm), Me$_6$TREN (0.25 mL, 0.94 mmol, 0.57 eq) and a magnetic stir bar were charged to a Schlenk tube fitted with a rubber septum and the mixture degassed *via* four freeze–pump–thaw cycles. The copper wire was wrapped around the stir bar. When all of the air had been removed and replaced with nitrogen degassed DMSO (15 mL) was added to the Schlenk tube *via* gas-tight syringe. A slight positive pressure of nitrogen was applied and the reaction solution placed in a thermoset oil bath at 25 °C,

until thermal equilibrium had been reached. The FT-NIR fibre optic probe was placed through the rubber septum.

As soon as thermal equilibrium had been reached a quantity of EBrB (0.24 mL, 1.64 mmol, 1 eq, degassed by bubbling with nitrogen) was injected into the Schlenk tube to initiate polymerisation. The introduction of the initiator defines $t = 0$. Recording the FT-NIR was started simultaneously and data collected every two minutes. Samples were periodically withdrawn manually using a degassed syringe, passed through a short column of neutral alumina to remove dissolved copper salts and the aliquot was dissolved in $CDCl_3$ for analysis *via* ^{1}H NMR and GPC.

Online monitoring of SET-LRP *via* FT-NIR in the presence of $CuBr_2$/CuBr (T2–T5). Methyl acrylate (15 mL, 166 mmol, 100 eq), copper wire (5 cm, 24 mg), $CuBr_2$ at varying amounts ((7.3 mg, 0.03 mmol, 0.020 eq), (9.4 mg, 0.04 mmol, 0.026 eq), (18.6 mg, 0.08 mmol, 0.052 eq)) and Me_6TREN (0.25 mL, 0.94 mmol, 0.57 eq) were added to a Schlenk tube and the reaction mixture was prepared as above. The effect of Cu(I) was examined using CuBr (11.9 mg, 0.05 eq) and Me_6TREN (0.37 mL, 1.4 mmol, 0.85 eq). When thermal equilibrium had been reached a quantity of EBrB (0.24 mL, 1.64 mmol, 1 eq) that had been degassed separately by bubbling with nitrogen was injected into the Schlenk tube to initiate polymerisation. Analysis was performed as described above.

Monitoring Cu(0) powder mediated polymerisations in DMSO *via* thermocouple (T6–T7). Methyl acrylate (15 mL, 166 mmol, 100 eq), copper powder (103 mg, 1.6 mmol, 1 eq), Me_6TREN (0.32 mL, 1.2 mmol, 0.72 eq) and a magnetic stir bar were charged to a Schlenk tube fitted with a rubber septum and the mixture degassed *via* four freeze–pump–thaw cycles in liquid nitrogen. The same procedure was applied to investigate the effect of $CuBr_2$ by addition of $CuBr_2$ (18.9 mg, 0.085 mmol, 0.053 eq) into the Schlenk tube in a separate experiment. Copper wire was wrapped around the magnetic stir bar. When all the air had been removed degassed DMSO (7.5 mL) was added to the Schlenk tube using a degassed syringe under a slight positive pressure of nitrogen and the reaction solution placed in a thermoset oil bath operating at 25 °C until thermal equilibrium had been reached. When thermal equilibrium had been reached a quantity of degassed EBrB (0.24 mL, 1.64 mmol, 1 eq) was injected into the Schlenk tube to initiate the polymerisation. Analysis was performed as described above.

Typical SET-LRP procedure using copper wire monitored *via* thermocouple (L1–L4). Methyl acrylate (20 mL, 221 mmol, 100 eq), Me_6TREN (0.5 mL, 1.89 mmol, 0.85 eq), copper wire (0.25 mm diameter) at varying lengths (2.5 cm (10.7 mg), 5.0 cm (22.1 mg), 15.0 cm (68.0 mg), 30.0 cm (133.4 mg)) and a magnetic stir bar were charged to a Schlenk tube fitted with a rubber septum and the mixture degassed *via* four freeze–pump–thaw cycles in liquid nitrogen. The copper wire was wrapped around the magnetic stir bar. When all the air had been removed degassed DMSO (20 mL) was added to the Schlenk tube using degassed syringe under a slight positive pressure of nitrogen and the reaction solution placed in a thermoset oil bath at 25 °C until thermal equilibrium had been reached. When thermal

equilibrium had been reached a quantity of degassed EBrB (0.32 mL, 2.2 mmol, 1 eq) was injected into the Schlenk tube to initiate the polymerisation. The temperature was manually recorded every two minutes. Samples were periodically withdrawn manually using a degassed syringe, passed through a short column of neutral alumina to remove copper salts and diluted with $CDCl_3$ for analysis *via* ^{1}H NMR and GPC.

Online monitoring of SET-LRP *via* Rapid GPC (D2). Copper wire (8 cm, 36 mg) was wrapped around a magnetic follower and charged to a Schlenk tube along with methyl acrylate (15 mL, 166 mmol, 100 eq) and Me_6TREN (0.32 mL, 1.2 mmol, 0.73 eq) and the mixture degassed *via* four freeze–pump–thaw cycles. DMSO (15 mL) was purged of oxygen prior to reaction setup by bubbling with nitrogen overnight and added to the Schenk tube, and the mixture placed into a thermoset oil bath maintained at 25 °C. A tube connected to the extraction pump was passed through the rubber septum into the reaction solution to remove a continuous stream of material from the reactor. EBrB was degassed by bubbling with N_2 and a measured quantity (0.24 mL, 1.64 mmol, 1 eq) injected into the Schlenk tube as initiator ($t = 0$). The extraction pump removed a continued stream at reaction mixture from the reactor at 0.05 mL min^{-1} and the solution passed to a mixing tee for dilution with THF pumped at 2.2 mL min^{-1}. The diluted reaction mixture was transported to the injection loop of the online GPC programmed to inject a sample onto the column every four minutes. Samples were manually extracted from the reactor using a degassed gas-tight syringe to obtain reference data *via* ^{1}H NMR and conventional GPC. When targeting different molecular weights a different amount of initiator is used and all other parameters were kept the same.

Results and discussion

Monitoring the conversion of a SET-LRP reaction online *via* FT-NIR

An immersion dip probe was used to monitor the polymerisation in the Cu(0) wire/Me_6TREN catalysed reaction, Scheme 1.

Monomer conversion to polymer with time is seen by the decrease in the peak at 6180 cm^{-1}, the overtone of the vinyl stretch in the monomer, with time, Fig. 1. The SET-LRP reaction particularly lends itself to *in situ* monitoring with a transmission dip probe as the use of copper wire to mediate the reaction (as opposed to Cu(I) salts or copper(0) powder) greatly reduces fouling of the optics and ensures a good signal-to-noise ratio and minimises baseline drift throughout the reaction.

The proportion of monomer remaining in the system can be determined from the integral at time t by taking it as a function of the integral at time $t = 0$. The integrals calculated at the start of
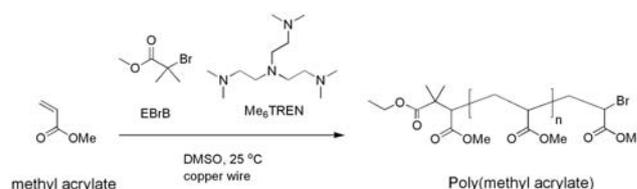
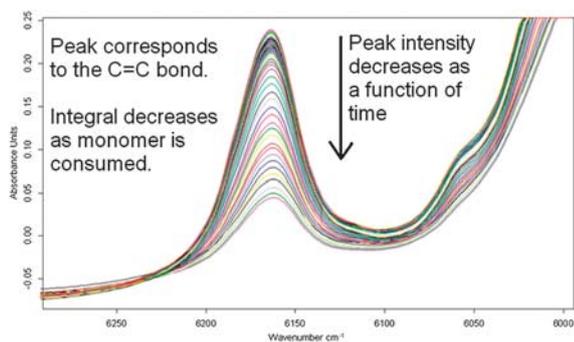**Scheme 1** SET-LRP of methyl acrylate in DMSO.

Fig. 1 Expansion of the near IR spectrum between 6000 and 6300 cm^{-1} showing the disappearance of the overtone of the vinyl bond of methyl acrylate for the Cu(0) wire (8 cm)/Me$_6$TREN catalysed polymerisation of MA in DMSO initiated by EBrB at 25 °C; [M]/[I]/[L] = 100/1/0.57, at 50% solids (**T1**).

the reaction and at time t of the reaction are represented by A_0 and A, respectively. Conversion of monomer to polymer is given by the expression:

$$\text{Monomer conversion} = 100 - [(A/A_0) \times 100]$$

An apparent period of slow rate is observed at the start of the polymerisation where there is a small conversion from monomer to polymer. After approximately 30 minutes there is a more rapid polymerisation. The reaction reaches to 83% conversion after 2 hours, Fig. 2, left. The conversion data from online monitoring are in excellent agreement with that obtained via manually sampling the reaction and determining the conversion from ^{1}H NMR. The polymerisation proceeds in a living manner, although slight termination reactions were observed. The number average molecular weight (M_n) of the polymer (obtained from the manually sampling of the reaction) increases and the polydispersity index (PDI) decreases with conversion, Fig. 2, right, to form a polymer with $M_{n,exp}$ = 7710 g mol^{-1} and PDI = 1.08 at 83% conversion. The experimentally determined molecular weight is in agreement with $M_{n,theo}$ = 7333 g mol^{-1}, an indication of high initiation efficiency. A first order semi-logarithmic kinetic plot is not shown for this reaction as there is an
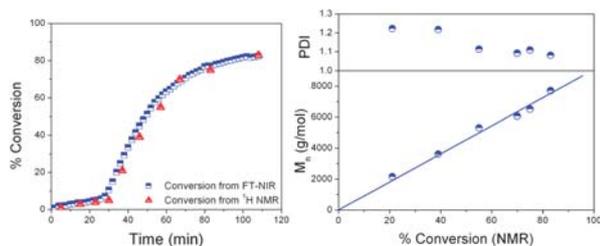
exotherm, removing the appropriateness of this analysis. This observation is discussed in more detail in the following section.

Exotherms for the SET-LRP of MA in DMSO

An exotherm is observed for the SET-LRP of methyl acrylate in DMSO under these conditions, Fig. 3. This is important as most studies in living radical polymerization assume reactions to be isothermal due to the timescale reactions are carried out. This allows for first order plots to be utilised to give a measure/indication of termination reactions. The temperature profile mirrors the conversion profile as the polymerisation starts at 25 °C, the temperature of the oil bath, and there is a very slight temperature rise during the period of slow rate at the start of the polymerisation, and a very rapid rise in temperature during the period where there is significant conversion from monomer to polymer ($\Delta H = -54.415$ kJ).[51,52] As such the usual first order kinetic plot is not shown as the reaction is not isothermal. It is noted that in a first order plot the gradient is directly proportional to the rate constant and as the rate constant is temperature dependent this type of plot is not appropriate unless the reaction is carried out isothermally. In addition the temperature rise cannot be used as a measure of rate in these experiments as the reaction is not carried out adiabatically and the heat lost to the surroundings occurs at different rates depending on the reactor parameters.

The sigmoidal shape of the conversion versus time plot is due to the heat generated by the exothermic nature of polymerisation. Besides, the heat is not removed from the reaction vessel in a controlled way. This leads to a temperature increase which in turn accelerates the reaction until a critical point is reached where the temperature is at its peak as the rate slows due to monomer consumption and the rate thus slows, $R_p = k_p[M]$.

Varying the length of copper wire affects the rate of polymerisation and the subsequent observed exotherm. Polymerisations carried out using longer lengths of copper wire lead to a shorter period of slow rate and a faster rate of polymerisation as the polymerisation starts whilst polymerisations performed using shorter lengths of copper wire have longer periods of slow rate, and the rate of polymerisation is slower, Fig. 4. When a large surface area of wire is used there is a greater rate of
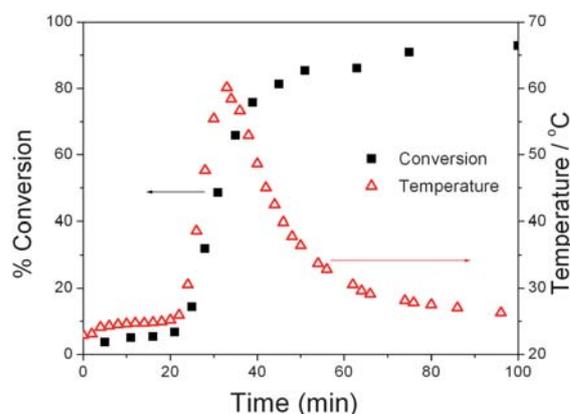

Fig. 2 Conversion vs. time plot and M_n and PDI vs. conversion for the Cu(0) wire/Me$_6$TREN catalysed polymerization of MA as monitored by FT-NIR and ^{1}H NMR. The reaction was carried out at 25 °C at 50% solids in DMSO initiated with EBrB and mediated by 8 cm Cu wire; [M]/[I]/[L] = 100/1/0.57 (**T1**). The line is the line at best fit through the data (R^2 = 0.9934).

Fig. 3 Profile of monomer conversion and temperature with respect to time for the Cu(0) wire (8 cm)/Me$_6$TREN catalysed polymerisation of MA at 50% solids in DMSO initiated by EBrB; [M]/[I]/[L] = 100/1/0.85 (**L1**).
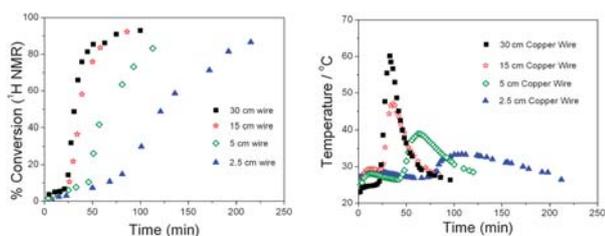
Fig. 4 Plots of conversion *versus* time (left) and temperature profiles *versus* time (right) for Cu(0) wire/Me$_6$TREN catalysed polymerisation of MA using 30 cm, 15 cm, 5 cm and 2.5 cm of copper wire; polymerisations at 25 °C at 50% solids in DMSO initiated by EBrB; [M]/[I]/[L] = 100/1/0.85 (**L1–L4**).
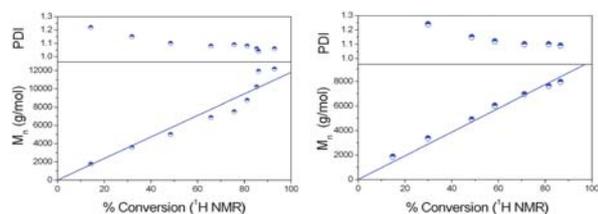

Fig. 5 Plots of M_n and PDI against conversion for the Cu(0)/Me$_6$TREN catalysed polymerisation of MA at 50% solids in DMSO, initiated by EBrB and mediated by 30 cm (left) and 2.5 cm (right) Cu wire. Reactions performed at 25 °C with [M]/[I]/[L] = 100/1/0.85 (**L1, L4**). The lines are the lines at the best fit through the data (R^2 = 0.9607 and 0.9974 for the left and right plots, respectively).

activation, leading to a higher concentration of propagating radicals in the reactor.

The observed temperature rise is dependent on the length of copper wire used (which is proportional to the surface area). The rate of heat removal across the wall of the Schlenk tube is similar under all conditions. When a larger amount of heat is produced from polymerization with a longer length of copper wire heat removal is inefficient, leading to a temperature rise which in turn increases the rate of polymerisation. The rate and the maximum temperature reached are dependent on the length of wire used, Fig. 4.

The rise to higher temperatures can lead to a loss of control over the M_n of the polymer formed. Increased termination is ascribed to radical–radical coupling that occur between growing radical chains and results in a rapid increase in molecular weight (approximately doubling) at high conversion values, Fig. 5. By contrast, better control is obtained with shorter lengths of copper

Table 1 Exotherm data for the Cu(0) wire/Me$_6$TREN catalysed polymerisation of MA in DMSO initiated by EBrB in the presence of differing lengths of copper wire. Reaction is 50% solids, ratio [M]/[I] = 100

Run	Length of wire/cm	Exotherm start time/min	Exotherm end time/min	Exotherm peak temp./°C	Reaction time/min
L1	30	18	30	67.4	12
L2	15	26	40	47.1	14
L3	5	50	62	39.0	12
L4	2.5	82	108	33.3	26

Table 2 Data summarising the change in mass of copper wire after the Cu(0)/Me$_6$TREN catalysed polymerisation of MA in DMSO initiated by EBrB at 50% solids. Polymerisations are carried out in the presence of varying lengths of copper wire, ratio [M]/[I] = 100

Run	Length/cm	Cu consumed/mg	Cu consumed/mol	Consumed wt initiator (%)
L1	30	9.1	1.4×10^{-4}	14
L2	15	6.0	9.4×10^{-5}	9
L3	5	1.4	2.2×10^{-5}	2
L4	2.5	0.8	1.3×10^{-5}	1

wire when the temperature of the exotherm is lower and more controlled, Fig. 5. The exotherm data are collected in Table 1.

Copper wire is observed to be consumed during the polymerisations, Table 2. Eventually, the reaction solution turns a yellow/green colour with the formation of Cu(II) salts during the polymerisations according to the SET-LRP mechanism.

The effect of CuBr$_2$ and CuBr on the period of slow rate of the SET-LRP of MA

CuBr$_2$ is a deactivator in ATRP and has been reported to reduce the rate of SET-LRP reactions if the ratio of [Cu(II)]/[Cu(I)] increases. Polymerisation of methyl acrylate in DMSO at 25 °C mediated by 5 cm copper wire and Me$_6$TREN consistently features an initial period of slow rate in the absence of CuBr$_2$. However, when a small quantity of CuBr$_2$ is added to the reaction mixture the period of slow rate is reduced, Fig. 6. Polymerisation occurs from $t = 0$, although there is a slight delay at the very start of the reaction. The final polymers have relatively narrow PDIs ranging from 1.07 to 1.04, Table 3, entries T1–T5.

Similar results were obtained by carrying out the reaction in the presence of Cu(I). Prior to initiation, a slight green colour formed in the Schlenk tube, suggesting rapid disproportionation to Cu(0) and Cu(II). Polymerization occurs from $t = 0$ and was monitored online with FT-NIR and offline with NMR, Fig. 7.
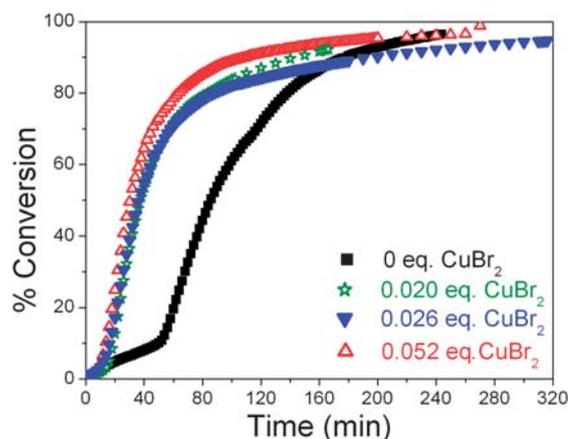

Fig. 6 Overlaid plots of conversion *versus* Cu(0)/Me$_6$TREN catalysed polymerisations of methyl acrylate in DMSO in the presence of 0 eq, 0.020 eq, 0.026 eq, and 0.052 eq of CuBr$_2$. Reactions at 50% solids with t_0 = 25 °C, initiated by EBrB with [M]/[I] = 100/1. Conversion data obtained by monitoring the loss of the peak at 6120 cm^{-1} *in situ*, by FT-NIR (**T1–T4**).

Table 3 Characterisation of the Cu(0)/Me$_6$TREN catalysed polymerisations of MA in DMSO initiated by EBrB in the presence of various amounts of CuBr or CuBr$_2$. Reaction performed at 25 °C, [M]/[I] = 100/1

Run	Cu(0) (type)	CuBr (eq)	CuBr$_2$ (eq)	Me$_6$Tren (eq)	Time/min	Conv. (^{1}H NMR) (%)	$M_{n,theo}$/g mol^{-1}	$M_{n,exp}$/g mol^{-1}	PDI
T1	Wire	—	—	0.57	246	98	8632	11 200	1.07
T2	Wire	—	0.02	0.94	168	95	8374	9600	1.05
T3	Wire	—	0.026	0.94	163	93	8201	10 500	1.04
T4	Wire	—	0.052	0.94	220	98	8632	8810	1.06
T5	Wire	0.5	—	0.85	130	93	8201	8470	1.06
T6	Powder	—	0.053	0.72	31	96	8460	11 800	1.19
T7	Powder	—	—	0.72	36	90	7943	12 100	1.18
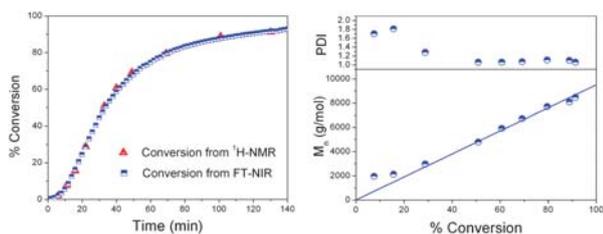
Fig. 7 Conversion *vs.* time (left) and M_n and PDI *vs.* conversion (right) plots for the Cu(0) wire/Me$_6$TREN catalysed polymerisation of MA in DMSO in the presence of Cu(I). $t_0 = 25$ °C, 50% solids, initiated by EBrB with [M]/[I]/[L]/[CuBr] = 100/1/0.85/0.5 (**T5**).
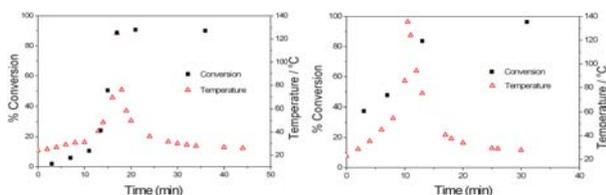
Fig. 8 Plots of conversion and temperature *versus* time for the Cu(0) powder/Me$_6$TREN catalysed polymerisation of MA in DMSO in the absence (left) and presence 0.053 eq of Cu(II) (right). Reaction is 66% solids initiated by EBrB with [M]/[I]/[L] = 100/1/0.72 (**T6, T7**).

The polymerisation gives good control, Fig. 7 (*right*), with M_n increasing and PDI decreasing with conversion to give a polymer with a narrow PDI. Initiation efficiency is close to 1. $M_{n,exp} = 8470$ g mol^{-1} and PDI = 1.06 were obtained at 93% conversion, in good agreement with $M_{n,theo} = 8201$ g mol^{-1}.

Polymerisation of methyl acrylate may be mediated by copper powder in the presence of Me$_6$TREN ligand with an alkyl halide initiator in DMSO solvent. The reaction is rapid, reaching 90% conversion in 35 minutes in the absence of Cu(II). There is a period of slow rate lasting for approximately 12 minutes at the start of the polymerisation, and a rise in temperature occurs as the reaction proceeds, Fig. 8. When the reaction is performed in the presence of Cu(II) salts (**T7**) there is no period of slow rate observed and the polymerisation occurs from $t = 0$, Fig. 8. Both polymerisations have exotherms reaching temperatures as high as 125 °C. Reactions mediated by Cu(0) powder in DMSO proceed faster than those mediated by Cu(0) wire due to the larger surface area of the powder, and result in larger exotherms due to inefficient heat transfer. The PDI of the product is broader when powder is used in place of wire.

Online monitoring of molecular weight distribution *via* Rapid GPC

The setup for the system for rapid GPC analysis is shown schematically in Fig. 9. Label (1) is the reactor, a Schlenk tube. Label (2) is THF used to dilute the reaction mixture in order to allow analysis. Labels (3) are Shimadzu HPLC pumps that continuously extract reaction solution and dilute it to an appropriate concentration for analysis. The solution is sent to the injection loop of a GPC (4) where a programmed sequence injects a sample every 4 minutes for analysis. Analysis was carried out on using a Rapide M column (Varian) with a three minute runtime, and detection with DRI and dual angle LALS (5). Excess reaction solution from the injection loop and from the column was diverted to (6), waste.

Polymerisation of MA catalyzed with Cu(0) wire/Me$_6$TREN may be monitored from the increasing integral of the polymer peak on the refractometer (DRI) detector. The integral response of the detector is given by the relationship: Integral$_{RI}$ = K_{RI} × (dn/dc) × concentration. Thus, the detector response is directly proportional to the concentration of the polymer in solution. By calculating a maximum hypothetical integral (corresponding to the integral response if all the monomer was converted to polymer and assuming that the refractive index is chain length independent) the conversion may be calculated from the integral response. In these experiments the hypothetical maximum response was determined experimentally by pumping a solution of poly(methyl acrylate) at 95% conversion through the injection loop under experimental conditions and measuring the detector response.

The concentration of polymer builds up in solution as monomer is converted to polymer, Fig. 10. As the polymer increases in
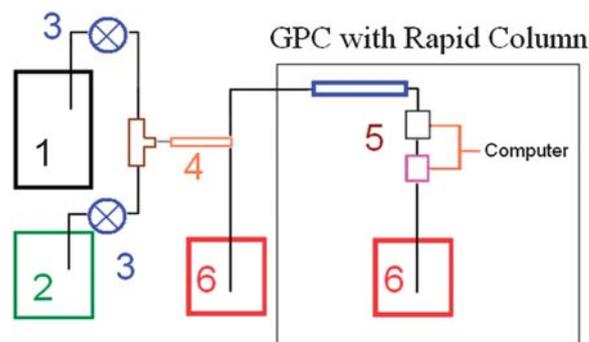
Fig. 9 Setup of instrumentation used to monitor polymerisation reactions online *via* Rapid GPC.
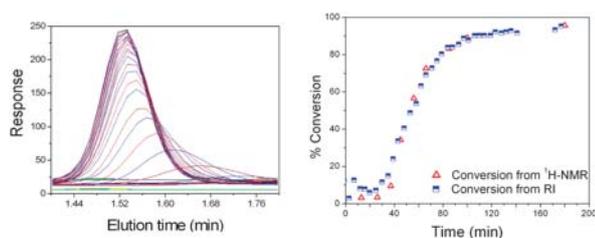
Fig. 10 Overlaid chromatograms from Rapid GPC (left) and conversion *vs.* time (right) plots for Cu(0)/Me$_6$TREN catalysed polymerisation initiated by EBrB. Reaction carried out at 25 °C, 50% solids in DMSO, ratio [M]/[I] = 100/1, mediated by 8 cm copper wire (**D2**).

Fig. 12 Overlaid plots of dW/dlog$M$ from rapid GPC (left) and conventional GPC (right) showing evolution of molecular weight distribution for the Cu(0) (8 cm)/Me$_6$TREN catalysed polymerisation of MA in DMSO initiated at 25 °C by EBrB; 50% solids, [M]/[I] = 100.

chain length the peak moves to earlier retention times, reflecting the larger hydrodynamic volume. There is a period of slow growth rate at the start of the reaction but there is rapid propagation after 30 minutes (Fig. 10, right). The polymerisation has the conversion profile expected for a SET-LRP reaction performed in the absence of CuBr$_2$.

The number average molecular weight increases and the PDI narrows with conversion indicative at controlled radical polymerisation, Fig. 11. The molecular weights calculated from rapid GPC are in good agreement with those calculated from more conventional GPC. The PDI of the final polymer from rapid GPC is broader (1.20) than that from conventional GPC (1.08), confirming that there is little termination. The number average molecular weight of the polymer is 7190 g mol^{-1} at 96% conversion, rapid chromatography, and 8060 g mol^{-1} at 96% conversion from offline monitoring. Initiation efficiency was found to be high as these numbers are in good agreement with the theoretical value of 8451 g mol^{-1} at 96% conversion.

Termination is evident at the start of the reaction but as the polymerisation proceeds the reaction becomes better behaved. The evolution of the molecular weight distribution with conversion (Fig. 12) shows a broad peak at low conversions which narrows as the reaction reaches higher conversions. The distribution shifts to higher molecular weights as the chains grow and the peak shape is symmetrical. The molecular weight
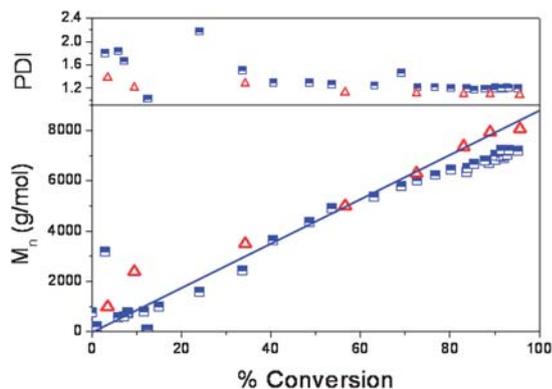
distribution from rapid GPC compares favourably with that from conventional GPC, Fig. 12.

Different molecular weights can be targeted by varying the ratio of [monomer] to [initiator], Fig. 13. Poly(methyl acrylate) with targeted DP$_n$ = 50, 100 and 200 was monitored online. Initiation is efficient in these reactions, with the experimentally determined molecular weights from rapid GPC, conventional GPC and from Low Angle Laser Light Scattering (LALS) detection all in agreement with the theoretical values. The analysis of the final molecular weights is summarised in Table 4.

Analysis of polymer samples by GPC can reveal the presence of a high molecular weight contaminants in the reaction, shown in the raw chromatogram, Fig. 14. This peak is observed to form before the desired polymer product during the period of slow rate and could easily be missed or ignored during a conventional GPC analysis. This became obvious when the reaction is monitored online with a LALS detector (Fig. S5†). The raw chromatogram is taken from a reaction where the final M_n of the polymer = 5980 g mol^{-1} at 92% conversion from rapid GPC and 6600 g mol^{-1} at 95% conversion from conventional GPC, considerably lower than the theoretical M_n of 8110 g mol^{-1}. By contrast the polymerisation **D2** described in the previous section does not feature the appearance of this high molecular weight species on

Fig. 11 Evolution of M_n and PDI with conversion for the Cu(0) wire/Me$_6$TREN catalysed polymerization of MA initiated by EBrB. Reaction at 25 °C, 50% solids in DMSO, [M]/[I] = 100, 8 cm Cu wire. Data from online methods (blue squares) and offline methods (red triangles) are overlaid to allow comparison of the two methods (**D2**).
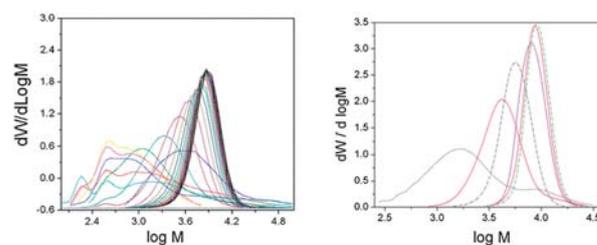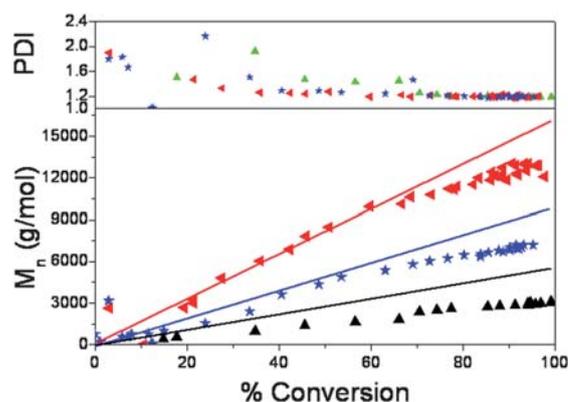

Fig. 13 Evolution of M_n and PDI against conversion from the online monitoring *via* an automated rapid GPC system for the Cu(0) wire/Me$_6$TREN catalysed polymerisation of MA in DMSO initiated by EBrB at 25 °C. Reactions performed at 50% solids, mediated by 8 cm copper wire, [M]/[I] = 200 (red triangles), 100 (blue stars) and 50 (green triangles). The lines show theoretical molecular weight.
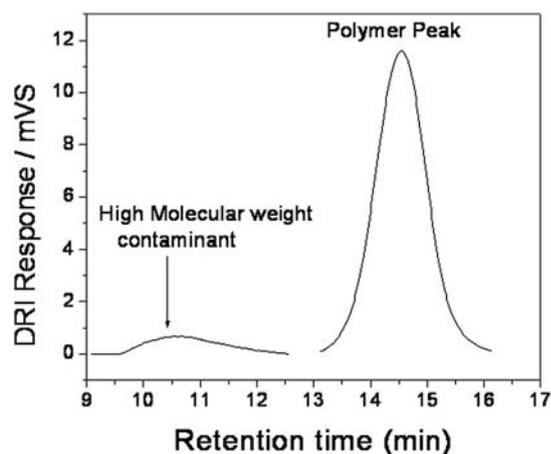
Fig. 14 Raw GPC chromatogram for the Cu(0) (15 cm)/Me$_6$TREN catalysed polymerisation of MA in DMSO initiated by EBrB at 25 °C, showing the presence of a high molecular weight distribution contaminant in the chromatogram.

Table 4 Comparison between LALS data and rapid GPC data for poly(methyl acrylate) of varying molecular weights synthesised *via* Cu(0) wire/Me$_6$TREN catalysed polymerisation and initiated by EBrB in DMSO at 25 °C

Run	[M]/[I]	$M_{n,theo}$/g mol^{-1}	Conv. (%)	$M_{n,LALS}$/g mol^{-1}	PDI (LALS)	$M_{n,GPC}$/g mol^{-1}	PDI (GPC)
D1	50	4295	97	3120	1.16	4880	1.06
D2	100	8795	95	8570	1.13	8060	1.08
D3	200	17 395	95	17 400	1.15	15 600	1.08

the LALS analysis, Fig. S6† and the molecular weight is in closer agreement to the theoretical value.

Conclusions

The SET-LRP of methyl acrylate in DSMO mediated by Cu(0) wire has been monitored online using *in situ* FT-NIR, thermocouple and rapid GPC and some common deviations from non-ideal behaviour observed that have not previously been described in the literature. SET-LRP is an excellent controlled radical method for synthesising end-functional PMA with targeted molecular weight. The polymerisations are relatively rapid at ambient temperature, with M_n increasing and PDI decreasing with conversion. Monitoring conversion online with FT-NIR revealed the presence of a period of slow rate at the start of the polymerisation reaction that could be removed with the addition of a small quantity of CuBr$_2$. Monitoring the temperature shows that the reaction exotherms in DMSO under the conditions used and that control over the molecular weight of the polymer can be lost if an excessive amount of copper wire is used. Polymerisations using copper wire form polymers with narrower PDI than using copper powder. The evolution of molecular weight and molecular weight distribution with increasing conversion has been monitored using an automated rapid chromatographic instrument fitted with LALS detector, obtaining a data point every 4 minutes and potentially removing the need for manually sampling the reaction mixture. These experiments have shown the evolution of molecular weight distribution in

a SET-LRP reaction, with M_n increasing with conversion. Comparison with offline analysis has shown that the molecular weight data provided by this instrument are valid. Online monitoring with LALS has revealed the presence of a high molecular weight contaminant that can form in the initial stages of the reaction that can led to lower molecular weights than those targeted.

Acknowledgements

Notes and references

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