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Preparation and properties of optically active poly(*N*-methacryloyl L-leucine methyl ester)

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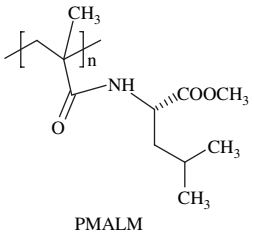
Abstract

Reported in this paper is the effect of varying initiator, catalyst, ligand, solvent, and temperature on atom transfer radical polymerization (ATRP) of *N*-methacryloyl L-leucine methyl ester (MALM). Optimized polymerization conditions involve tris[2-(dimethylamino)ethyl]amine (Me_6TREN) as ligand, CuBr as catalyst, methyl 2-bromopropionate as initiator, and toluene or benzene as solvent. Under these conditions the PMALM samples produced possess tunable molecular weight and low polydispersity. Also reported are results of PMALM characterization by differential scanning calorimetry (DSC), thermogravimetry, and polarimetry.

Keywords: Atom transfer radical polymerization; Chiral polymers; PMALM

1. Introduction

Chiral polymers including those bearing main- or side-chain amino acid units are used widely in the pharmaceutical industry for enantio-selective separation of drugs. This is achieved mainly via the use of chiral polymer membranes [1–3] or chromatography [4,5] and electrophoresis [6,7] involving chiral polymers as the stationary phase. Apart from chiral separations, biocompatible amino acid-containing polymers are used in dentistry [8], drug delivery [9–11], gene therapy [12], tissue engineering [13,14], etc. In some of these applications, control over the 3-d shape of the polymer is important. One such means to render shape control is to prepare block copolymers and to assemble the resultant block copolymers into nanostructures [15–19] with controlled shape, dimension, surface chemistry, etc. The preparation of block copolymers is normally achieved through living ionic and controlled free radical polymerization. While the use of amino acid-containing monomers to synthesize chiral polymers by conventional free radical polymerization dates back to the 1960s or earlier [20], only the groups of van Hest [21–23] and Mays [24] reported on the atom transfer radical polymerization (ATRP) [25,26] of peptide-containing vinyl monomers and acryloyl β-alanine, respectively. We report in this paper the ATRP of *N*-methacryloyl L-leucine methyl ester, MALM. We show that under optimized conditions ATRP yields PMALM with tunable molar mass and low polydispersity. We further show that ATRP can be used to yield block copolymers. Also reported in this paper are the thermal and optical properties of PMALM.



PMALM

While reports on ATRP of amino acid-based vinyl monomers are rare, there have been examples of ATRP of chiral

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monomers. Tsuji et al. [27] described the enantiomer-selective ATRP of a racemic bifunctional monomer *rac*-2,4-pentanediyl dimethacrylate. Angiolini et al. [28] reported ATRP of optically active photochromic methacrylic polymers. ATRP of (*R*)-2-methacryloyloxy-2′-methoxy-1,1′-binaphthalene ((*R*)-MAMBN) was reported by Xue et al. [29,30]. More recently, Wan and his coworkers [31] prepared helix-coil diblock copolymers based on poly(ethylene oxide) and optically active helical poly{(+)-2,5-bis[4′-((*S*)-2-methylbutoxy)-phenyl]styrene}.

2. Experimental section

2.1. Materials and reagents

Tris(2-aminoethyl)amine (96%), L-leucine (99%), calcium hydride (99.9%), methyl 2-bromopropionate (MBP, 98%), and thionyl chloride (99+%) were purchased from Aldrich. Formic acid [88 wt% solution in water] and formaldehyde (36 wt% solution in water) were products of Guangzhou Chemical Reagent Factory. *N*-(3-Dimethylaminopropyl)-*N*-ethylcarbodiimide hydrochloride (EDC·HCl, 98+%) was purchased from Acros. Deuterated toluene or toluene-d_8 (99.5%) and deuterated chloroform (99.8%) were from Cambridge Isotope Laboratories. Ethyl 2-chloropropionate (ECP, 99%) was obtained from Fluka. Reagents mentioned above were all used as received.

Triethylamine (99+%) and dichloromethane (99.5+%) were from Tianjing Chemical Reagent Developing Center and were freshly distilled over calcium hydride before use. CuBr (98+%, Fluka) and CuCl (99%, Aldrich) were purified by washing with glacial acetic acid 6 times and anhydrous ethanol three times. They were dried under vacuum at room temperature and stored under nitrogen atmosphere. Bipyridine (bpy) and *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine (PMDETA) were both purchased from Aldrich and were purified by distillation over calcium hydride. Methacrylic acid (99%, Aldrich) was distilled under vacuum just before use. Toluene (99%, Shanghai Chemical Reagent Co. Ltd) was refluxed with sodium and vacuum distilled. Isopropanol and *tert*-butyl alcohol were both purchased from Sinopharm Chemical Co. (Shanghai) and were distilled over CaO before use. Solvent 2,2,2-trifluoroethanol (99+%, Aldrich) was distilled before use. Initiator 2,2′-azobisisobutyronitrile (AIBN, +99.5%, purchased from Sinopharm Chemical Co. Ltd, Shanghai) was recrystallized from ethanol. Solvents and reagents not mentioned above were of analytical grade and were used as received.

2.2. Synthesis of L-leucine methyl ester hydrochloride [32]

Dry methanol (90 mL or 2.2 mol) in a 250 mL reaction flask was cooled in an ice bath before 20 mL or 0.275 mol of thionyl chloride was dropped in slowly via a pre-dried syringe. After stirring for 15 min 12.0 g or 0.091 mol of L-leucine was added. The resultant mixture was stirred for 18 h. This was followed by rota-evaporation of the volatile components, washing the solid residue thrice with 30 mL of diethyl ether, and drying the solid under vacuum yielding needle-like crystals of L-leucine methyl ester hydrochloride at 15.5 g or a 93% yield. Proton NMR ($CDCl_3$): δ 0.98 [doublet (d), 6H, $CH(CH_3)_3$], 1.75–1.98 [multiplet (m), 3H, CH_2CH], 3.79 [s, 3H, $COOCH_3$], 3.98–4.15 (m, 1H, $CH(CH_2)COOCH_3$)), 8.82 (broad, s, 3H, $-NH_3^+$).

2.3. MALM synthesis [32]

L-Leucine methyl ester hydrochloride (6.50 g or 35.8 mmol), EDC·HCl (7.49 g or 39.07 mmol), and triethylamine (Et_3N, 3.63 g or 35.8 mmol) were mixed in 70 mL of dichloromethane at 0 °C before methacrylic acid (3.08 g or 35.8 mmol) was added dropwise. After stirring for 20 h at room temperature, the reaction mixture was washed twice by 100 mL of each of the following liquids: distilled water, 1.0 M hydrochloric acid, saturated aqueous sodium bicarbonate, and distilled water. The organic layer was then dried over anhydrous magnesium sulfate, filtered, and dried by rotary evaporation. After recrystallization from *n*-hexane/ethyl acetate at v/v = 5/1, 5.6 g of white fibrous solid was obtained at a 72.8% yield. Specific optical rotation measured for this sample at 16 °C, $[\alpha]_D^{16}$, was 5.3 deg dm^{-1} g^{-1} cm^3. Proton NMR ($CDCl_3$): δ 0.95 (d, 6H, $CH(CH_3)_2$), 1.513–1.641 (m, 1H, $CH(CH_3)_2$), 1.630–1.704 (m, 2H, $CH_2CH(CH_3)_2$), 1.958 (s, 3H, $COOCH_3$), 4.652–4.686 (m, 1H, $CH_2CHCOOCH_3$), 1.950 (s, 3H, $CH_2{=}CCH_3$), 5.720 (s, 1H, $CH(H){=}CCH_3$), 5.354 (s, 1H, $CH(H){=}CCH_3$.

2.4. Synthesis of tris[2-(dimethylamino)ethyl]amine (Me_6TREN)

A literature method [33] was followed to prepare Me_6TREN. To prepare the salt $(ClNH_3CH_2CH_2)_3NHCl$, 30 mL of 3.0 M HCl in methanol was added dropwise to 4.0 mL or 0.027 mol of tris(2-aminoethyl)amine in 50 mL of methanol. After stirring at room temperature for 1 h, the precipitate was filtered and washed with 50 mL methanol thrice to yield 6.72 g or 0.026 mol of product in 98% yield.

To prepare Me_6TREN, 6.72 g of $(ClNH_3CH_2CH_2)_3NHCl$, 10 mL of water, 50 mL of formic acid, and 46 mL of a formaldehyde aqueous solution were mixed. The mixture was heated under stirring in a 120 °C oil bath for 6 h before volatile components were removed by rota-evaporation. To the solid residue was then added 100 mL of 10 wt% NaOH aqueous solution. After shaking, the aqueous phase was extracted with diethyl ether at 100 mL each time for four times. The organic phase was combined, dried over anhydrous NaOH, and concentrated by rotary evaporation. After vacuum distillation at 62 °C and 133 Pa, 6.0 g of colorless oil was obtained with a yield of 89%. Proton NMR ($CDCl_3$): δ 2.198 (s, 18H, CH_3), 2.332–2.369 (m, 6H, CH_2), 2.560–2.597 (m, 6H, CH_2).

2.5. MALM ATRP

The preparation started with the addition of the solid reagents to a dry single-neck round-bottom flask containing a stirring bar before being sealed with a rubber septum. The flask was then evacuated and refilled with argon. This evacuation and argon refilling procedure was repeated thrice so as to remove oxygen. This was followed by the addition of liquid reagents via syringes which were pretreated in a desiccator containing P_2O_5 by evacuating and refilling the desiccator. All liquid reagents were degassed prior to use by bubbling argon through them for at least 30 min. The final polymerization mixture was further degassed via three freeze–evacuate–thaw–argon filling cycles before the initiator was added via a syringe. The reaction was carried out in an oil bath at a pre-designated temperature for a specific time before sample purification.

In an example run we started by charging 4.00 g (or 18.8 mmol) of MALM and 0.0270 g (0.188 mmol) of CuBr into a 100-mL flask. The flask was then evacuated and refilled with argon before 10 mL of degassed toluene and 53.3 μL (0.188 mmol) Me_6TREN were added via syringes. The mixture was further purged via three freeze–evacuate–thaw–argon filling cycles before 20.0 μL (0.188 mmol) of MBP was injected and the flask was immersed in a preheated oil bath at 70 ± 1 °C. The polymerization was left going for 61 h under stirring and was terminated by immersing the flask in an ice–water mixture and bubbling air through the liquid to oxidize CuBr. This was followed by the addition of 50 mL of THF/CH_2Cl_2 at v/v = 1/1 to the reaction mixture and the diluted sample was then filtered through a neutral alumina column to remove catalysts. The filtrate was concentrated by rotary evaporation to ~2 mL and added into 200 mL of hexane to precipitate the polymer. The product was further purified by re-dissolving it in THF and precipitating in hexane to yield 2.0 g of white solid PMALM at 50% yield.

2.6. MALM conventional free radical polymerization

MALM (0.64 g, 3 mmol), AIBN (9.8 mg, 0.06 mmol), and chlorobenzene (7 mL) were added in a 25 mL one-necked flask equipped with a stirring bar and septa. The flask was bubbled with argon for 50 min before heating for 15 h in an oil bath at 65 °C under stirring. The polymer was isolated by precipitation in hexane and further purified by dissolving in THF and precipitation into pentane. This re-dissolution and precipitation cycle was repeated thrice. The final polymer was dried to constant weight in a vacuum at ambient temperature to afford 0.55 g of PMALM at 85% yield.

2.7. Preparation of PMALM–PS

Procedures similar to MALM ATRP were used to perform ATRP of styrene (S) using PMALM as the macro-initiator to yield PMALM–PS, where PS denotes polystyrene. The recipe involved the use of 0.51 g of PMALM-Br with SEC $M_n = 8.4 \times 10^3$ and $M_w/M_n = 1.29$ as the macro-initiator. The amounts of styrene, anisole, CuBr, and Me_6TREN used were 1.53 g (15 mmol), 3.8 mL, 9.1 mg (0.063 mmol), and 17.8 μL (0.063 mmol), respectively. The polymerization was performed at 90 °C for 15 h. The resultant mixture was diluted by the addition of 100 mL of THF before filtration through a neutral alumina column to remove catalysts. The filtrate was concentrated by rota-evaporation to ~2 mL and added into 200 mL of hexane to precipitate the polymer. The product was further purified by re-dissolving it in THF and precipitation in hexane. After vacuum drying, 1.67 g of white solid was obtained.

2.8. Characterization techniques

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DMX-400 spectrometer with a Varian probe in deuterated chloroform or toluene. Size exclusion chromatography (SEC) was performed at 25 °C using a Waters 150C instrument equipped with a refractive index (RI) and UV–visible absorption detector. The eluant used was *N*,*N*-dimethylformamide containing LiBr at 3.0 mg/mL. The 5×10^4 Å, PSS 1000 Å and PSS 100 Å columns used were calibrated by monodisperse PS standards.

The glass transition temperature (T_g) was determined by a Perkin–Elmer Diamond differential scanning calorimeter (DSC) under nitrogen atmosphere. Samples, ~10 mg each, were subjected first to heating from 25 to 150 °C at 20 K/min, holding at 150 °C for 10 min, and then cooling to 25 °C at 20 K/min before the final thermoanalysis traces were obtained by heating samples to 210 °C at 10 K/min. Thermogravimetric analyses (TGA) were preformed on a Perkin–Elmer Pyris-1 instrument by heating samples up to 800 °C at 10 K/min under nitrogen flow at 20 mL/min. The sample sizes used ranged between 3 and 10 mg.

Optical activity measurements were performed at room temperature which changed between 16 and 19 °C on a WZZ-1 home-made digital polarimeter equipped with a sodium light bulb using a cell path length of 2.00 dm. The samples were prepared in $CHCl_3$ at 1.00 g/dL.

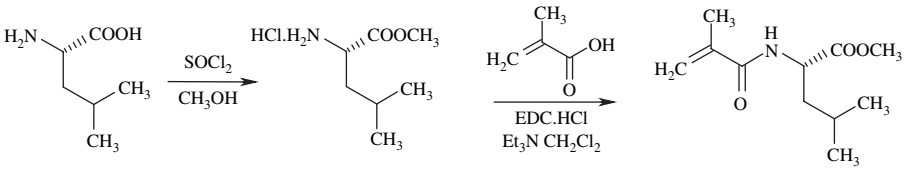
2.9. Kinetics of MALM ATRP

Kinetics of MALM ATRP were followed *in-situ* by ^{1}H NMR using a Bruker built-in kinetics software. A polymerization mixture was prepared in toluene-d_8 in a glove box before 2 mL of the mixture was dispensed into a Young's tap NMR tube. Timing started only after the sealed NMR tube was heated in the NMR sample holder to the desired polymerization temperature. MALM conversions were obtained by comparing the intensities of PMALM –CON*H*– peak at δ 8.0 and –NC*H*– peak at δ 4.6 with those of MALM vinyl proton peaks at δ 5.87 and δ 6.09.

3. Results and discussion

3.1. Monomer synthesis

L-Leucine methyl ester hydrochloride was prepared by reacting L-leucine with methanol in the presence of thionyl



Scheme 1. Reactions for the preparation of MALM.

chloride [32]. The optically active monomer MALM was synthesized by amidization of methacrylic acid with L-leucine methyl ester hydrochloride in dichloromethane using EDC·HCl as the coupling reagent and Et_3N as acid absorbent (Scheme 1) [32].

Our success in preparing pure MALM was confirmed by ^{1}H NMR analysis. We determined for MALM in chloroform also the specific optical rotation value $[\alpha]_D$ to be $+5.3\ \mathrm{deg\,dm^{-1}\,g^{-1}\,cm^3}$, which is higher than the values of 1.3 and $3.0\ \mathrm{deg\,dm^{-1}\,g^{-1}\,cm^3}$ reported by Sanda et al. [32,34] in different manuscripts. The difference might be due to difficulties associated with determining close to zero $[\alpha]_D$ values precisely.

3.2. Me_6TREN synthesis

The synthesis of Me_6TREN involved two steps [33]. First, tris(2-aminoethyl)amine was reacted with hydrochloric acid to produce the salt $(ClNH_3CH_2CH_2)_3NHCl$. The salt then underwent Eschweiler–Clarke reaction with formaldehyde and formic acid to yield Me_6TREN. Our success in the synthesis of clean Me_6TREN was confirmed by ^{1}H NMR analysis.

3.3. Overview of MALM ATRP

We performed MALM ATRP using different ligands (L), catalysts (CuX), initiator (I), solvents, and temperatures. Table 1 summarizes results for some runs, where MALM or monomer (M) conversions p was determined gravimetrically from the weight ratio of PMALM to MALM. Using p and the monomer to initiator feed molar ratio we calculated the conversion number-average molar mass M_n using:

$$M_n = p\frac{[M]_0}{[I]_0}M_u \quad (1)$$

where M_u is the molar mass of each MALM unit. The SEC M_n and M_w/M_n data were obtained based on PS standards. The fact that the M_n values determined from MALM conversion and SEC are close is only fortuitous because PMALM recovery may be incomplete and the use of PS rather than PMALM as SEC standards was not desirable.

A close examination of the results of Table 1 yields the following conclusions: (1) MALM ATRP does occur with reasonable conversion in most solvents when Me_6TREN was used as the ligand. (2) PMALM polydispersity M_w/M_n are

Table 1
Summary of conditions used for ATRP of MALM and properties of PMALM produced

Run	Ligand	Solvent	Molar ratio of M:I:CuX:L	T (°C)	Time (h)	Conv. (%)	Conv. $10^{-3}\times M_n$ (g/mol)	SEC $10^{-3}\times M_n$ (g/mol)	SEC M_w/M_n
Initiator = MBP; CuX = CuBr									
1	Bpy	Anisole	100:1:1:2	60	24	<5	–	–	–
2	PMDETA	Anisole	100:1:1:1	60	24	14	3.0	3.2	1.30
3	Me_6TREN	Anisole	100:1:1:1	60	24	43	9.2	10.4	1.26
4	Me_6TREN	Toluene	100:1:1:1	30	15	47	10.1	11.1	1.25
5	Me_6TREN	Toluene	100:1:1:1	40	48	52	11.1	11.0	1.22
6	Me_6TREN	Toluene	100:1:1:1	60	4	53	11.2	12.2	1.22
7	Me_6TREN	Toluene	100:1:1:1	70	61	49	10.0	10.0	1.20
8	Me_6TREN	Toluene	100:1:1:1	90	10	52	11.1	12.4	1.28
9	Me_6TREN	Benzene	100:1:1:1	30	15	47	10.0	11.1	1.25
10	Me_6TREN	THF	100:1:1:1	60	24	28	5.9	6.9	1.29
11	Me_6TREN	Butanone	100:1:1:1	60	48	17	3.6	3.9	1.31
12	Me_6TREN	Methanol	100:1:1:1	60	48	8	1.7	–	–
13	Me_6TREN	Toluene	75:1:1:1	60	24	44	7.1	8.4	1.29
14	Me_6TREN	Toluene	100:1:1:1	60	24	48	10.3	11.0	1.31
15	Me_6TREN	Toluene	120:1:1:1	60	24	46	11.8	13.4	1.21
16	Me_6TREN	Toluene	140:1:1:1	60	24	46	13.7	15.6	1.31
Initiator = ECP; CuX = CuCl									
17	Me_6TREN	Isopropanol	100:1:1:1	40	12	68	14.5	17.2	1.37
18	Me_6TREN	*tert*-Butyl alcohol	100:1:1:1	40	9	65	13.8	17.1	1.40
19	Me_6TREN	Toluene	100:1:1:1	40	12	54	11.5	13.2	1.33

In every case the monomer weight (g) to solvent volume (mL) ratio used was 1.00/2.50.

lower than 1.40. (3) A limiting MALM conversion p_T appears to exist for a particular polymerization system in a particular solvent and one can increase the M_n of the resultant PMALM by increasing the monomer to initiator feed molar ratio $[M]_0/[I]_0$. (4) MALM p_T can be increased using different catalyst systems and solvents. Discussed below are these variation trends in some detail.

3.4. Polymerization of MALM by ATRP

The fact that MALM polymerized under our experimental conditions by ATRP can be appreciated from the following considerations. First, the ATRP product was PMALM derived from methacrylate double bond addition. Fig. 1 shows the ^{1}H and ^{13}C NMR spectra together with peak assignments for a PMALM sample denoted by entry 7 in Table 1. Both the peak positions and intensities are in agreement with those expected of PMALM. Second, the polydispersity indices M_w/M_n are in the range expected for ATRP. For confirmation purposes we performed also conventional free radical polymerization of MALM using AIBN as the initiator at 65 °C as described in Section 2. Such a polymerization yielded PMALM at a much higher 85% yield and a much higher M_w/M_n value of 2.02. Third, PMALM was produced under our experimental conditions at very low temperatures such as 40 °C at which conventional free radical polymerization occurs only slowly.

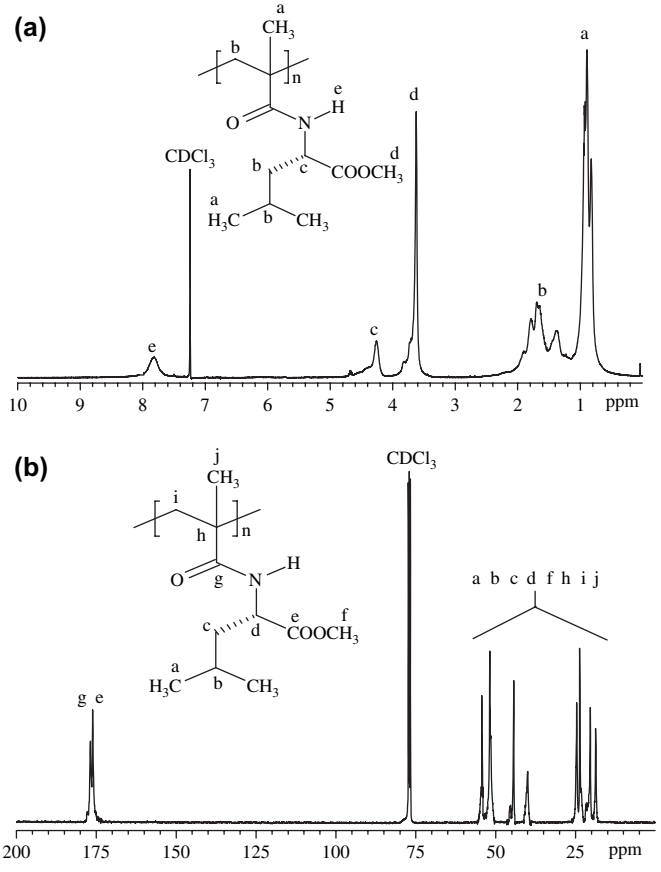


Fig. 1. ^{1}H NMR (a) and ^{13}C NMR (b) spectra of a PMALM sample in $CDCl_3$.

3.5. Effect of ligand variation

Entries 1–3 in Table 1 compare results of MALM polymerization under otherwise identical conditions except L differences. As L changed from Bpy to PMDETA and Me_6TREN, the MALM conversion increased. Our further study demonstrated that the conversions under a given set of conditions did not increase with polymerization time. Thus, these conversions were terminal conversions p_T under a set of polymerization conditions. Such a p_T variation trend is similar to what has been observed by Teodorescu and Matyjaszewski for ATRP of other methacrylamides and acrylamides or, in general, (meth)acrylamides [35]. An accepted explanation for such an observed trend involved the following. First, (meth)acrylamide ATRP is plagued by side reactions [35,36]. These side reactions include the complexation and deactivation of Cu by the amide units of the forming (meth)acrylamide chains and also possibly the nucleophilic displacement of the terminal bromine atom by the amide group. Second, as the ligating power increases in the order Bpy < PMDETA < Me_6TREN, the following equilibrium shifts increasingly towards the right and thus polymerization rate increases.

$$\text{P-Br} + \text{CuBr/L} \underset{k_b}{\overset{k_f}{\rightleftharpoons}} \text{P}\cdot + \text{CuBr}_2\text{/L} \qquad \text{P}\cdot \xrightarrow{k_p} \text{M} \tag{2}$$

In Eq. (2) P and M denote polymer and monomer, respectively, and the ks are the respective rate constants. Since p_T is governed by the rate of polymer chain propagation relative to those of side reactions, an increase in ligating power of L thus lead to increases in p_T. Me_6TREN has been used in all subsequent polymerizations because of the decent p_T that it helps afford.

3.6. Terminal MALM conversion

Regardless of the temperature or time used, polymerization in toluene as denoted by entries 4–8 seems to give a constant final MALM conversion of ~50%. This suggests the presence of a terminal conversion p_T for MALM. To confirm this, we followed MALM polymerization at 60 °C initiated by MBP/CuBr/Me_6TREN in toluene-d_8 by *in-situ* ^{1}H NMR. Fig. 2 shows the MALM conversion data plotted in the form of $\ln\{[M]_0/[M]\}$ vs. t. The data show that the polymerization was fast initially and a linear relationship existed between $\ln\{[M]_0/[M]\}$ and t in the first hour. After ~4 h, the conversion leveled off at 46% or $\ln\{[M]_0/[M]\} = 0.78$. This confirms unambiguously the existence of a terminal conversion p_T.

To know properties of the polymers produced at various stages, we polymerized MALM for different times using conditions identical to those mentioned above except the replacement of toluene-d_8 by toluene as solvent and analyzed the resultant polymers gravimetrically for MALM conversion and by SEC for PMALM M_n and M_w/M_n. Shown in the right

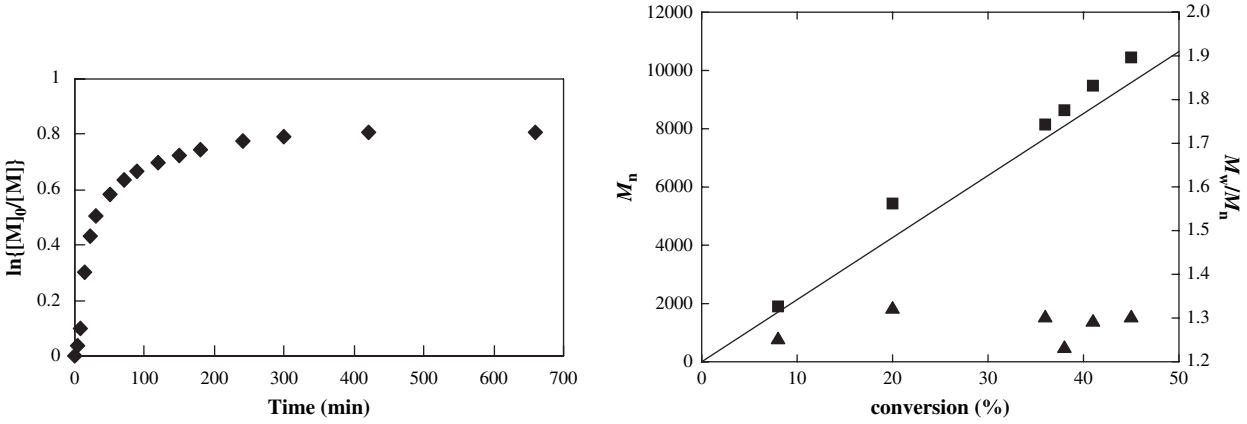


Fig. 2. Right: plot of $\ln\{[M]_0/[M]\}$ vs. t for MALM ATRP in toluene-d_8 at 60 °C initiated by MBP/CuBr/Me_6TREN. Left: variation in SEC M_n and M_w/M_n as a function of MALM conversion.

panel of Fig. 2 is variation of PMALM SEC M_n and M_w/M_n with MALM conversion. The fact that the SEC M_n values are always higher than those calculated from monomer conversions as denoted by the solid line in the figure might be caused by intrinsic errors of the SEC technique. The general trend that the SEC M_n increased linearly with conversion below $p \approx 50\%$ is in agreement with a living polymerization process. The living character below $p \approx 50\%$ is also supported by the invariably low M_w/M_n values throughout the polymerization process.

The gradual termination of polymerization above $p \approx 50\%$ may be due to the slow deactivation of the catalyst CuBr/Me_6TREN or displacement of the polymer terminal Br atom or a combination of the two. Xia et al. [37] have recently argued based on experimental evidence for Cu deactivation as the main cause. Based on the low M_w/M_n values of Table 1 we believe that Cu deactivation should be the main cause in our system as well. This conclusion is unambiguously substantiated by our ability to use PMALM prepared from ATRP as a macro-initiator to synthesize a diblock copolymer PMALM–PS with 180 styrene units at a styrene conversion of 76% and SEC M_w/M_n of 1.34.

3.7. Ethyl 2-chloropropionate as the initiator

The use of Cl-containing initiators and thus the formation of polymer chains with terminal Cl groups are believed to reduce the chances of X group displacement by nucleophilic substitution [38]. Ethyl 2-chloropropionate (ECP) and CuCl complexed with Me_6TREN have been used recently to polymerize *N*-isopropylacrylamide [37] with essentially quantitative conversion in isopropanol and *tert*-butanol. Based on these results, we tested out ECP/CuCl/Me_6TREN as an initiating system.

The use of this initiating system in alcohols (entries 17 and 18) seemed to speed up MALM polymerization as we noticed that the viscosity of such a polymerization solution turned high ~5 min after ECP addition. The apparently faster polymerization led to higher p_T values as expected. We did not see, however, any signs for a sped-up MALM polymerization in toluene at 40 °C (entry 19) and interestingly the p_T value of 54% for entry 19 is comparable to 52% determined for entry 5. These results suggest that the apparently enhanced polymerization rates in the alcohols were probably caused by a medium effect rather than by ECP/CuCl because use of ECP/CuCl rather than MBP/CuBr as the former initiating system should slow down the polymerization for the stronger C–Cl bonds formed at the chain termini.

Despite the higher p_T values in alcohols when ECP/CuCl/Me_6TREN was used as the initiating system, the resultant polymers have slightly higher M_w/M_n values than those obtained when MBP/CuBr/Me_6TREN was used. Because of this, we prepared most of our polymers using MBP/CuBr/Me_6TREN as the initiating system.

3.8. Effect of solvent

Surprisingly, polymerization initiated by MBP/CuBr/Me_6TREN proceeded better in less polar solvents including toluene and benzene than in more polar solvents such as methanol and butanone. This trend is in agreement with what was observed by Teodorescu and Matyjaszewski [38] for ATRP of some (meth)acrylamides but is different from that observed by other researchers [23,24,37], who worked on the premise that a hydrogen-bonding solvent could bind to the amide groups of both monomer and polymer and showed that the use of polar solvents led to well-defined polymers containing amide side groups. This trend is also contradictory to what we have observed visually for polymerizations carried out in different solvents using ECP/CuCl/Me_6TREN as the initiating system. We are not certain of the reason for this observation.

3.9. Preparation of PMALM with different M_n

Data of Fig. 2 show that one can tune the M_n of PMALM by changing the polymerization time from minutes to 1 h. Alternatively, one can change M_n also by changing monomer to

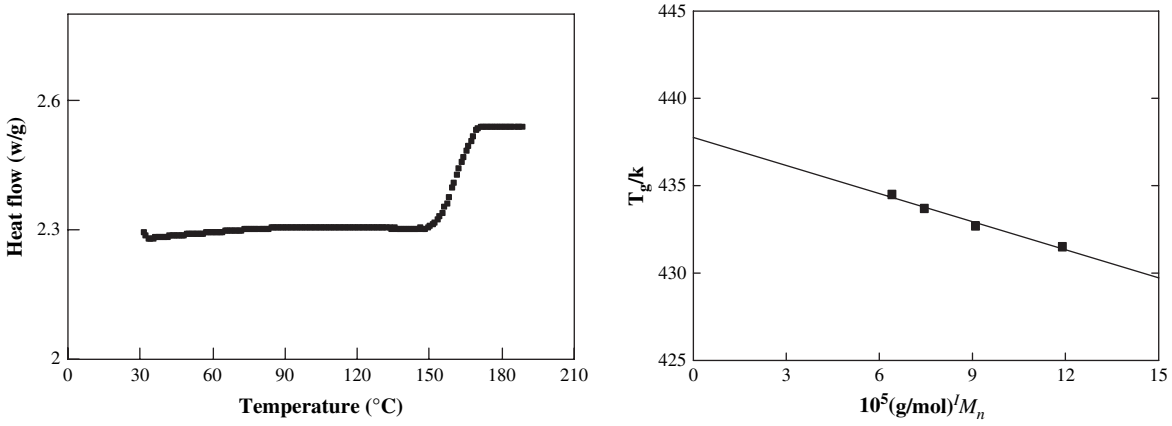


Fig. 3. Left: DSC curve of PMALM sample with SEC $M_n = 1.1 \times 10^4$ g/mol. Right: variation of PMALM T_g as a function of their SEC M_n.

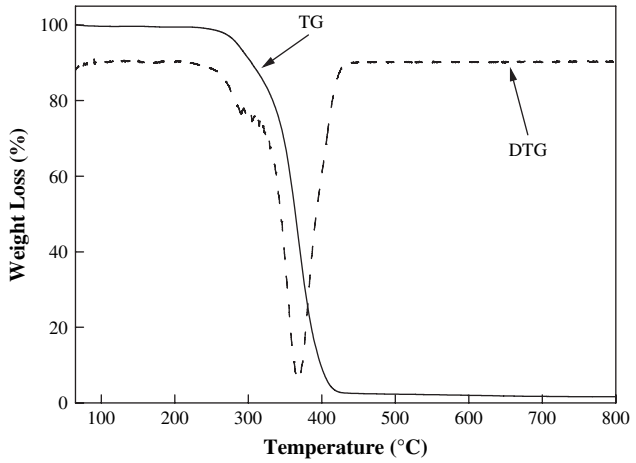


Fig. 4. TGA and DTGA curves of a PMALM sample with SEC $M_n = 1.1 \times 10^4$ g/mol.

initiator molar feed ratio $[M]_0/[I]_0$. Entries 13–16 in Table 1 show effectiveness of this strategy.

3.10. Thermal properties of the PMALM

Fig. 3 shows a DSC curve for a PMALM sample (entry 14 in Table 1). The glass transition temperature T_g determined for this sample is 160.5 °C. We have obtained similar curves for samples with other M_n values. Plotted in the right panel of Fig. 3 is T_g vs. $1/M_n$ for 4 PMALM samples (entries 13–16 of Table 1). The data are best fitted by $T_g = T_{g\infty} - (\alpha/\overline{M}_n)$ with $T_{g\infty} = 437.8$ K and $\alpha = 5.36 \times 10^4$ K g/mol. The $T_{g\infty}$ value of 437.8 K or 164.6 °C compares well with a T_g value of 165 °C determined for a PMALM sample with $M_n = 4.9 \times 10^4$ g/mol prepared from traditional free radical polymerization by Sanda et al. [39].

Fig. 4 shows a thermogravimetric analysis (TGA) curve of a PMALM sample with SEC $M_n = 1.1 \times 10^4$ g/mol. Also shown is a differential TGA or DTGA curve of the sample. The DTGA curve clearly show two degradation steps for the sample with one starting at 240 °C the other at 317 °C. By 430 °C, 98.5% of the polymer decomposed into volatile components. Such two-step decomposition phenomenon is in agreement with that observed by Silva et al. [40] for polyacrylamide which was stable up to 285 °C and decomposed in two distinctive steps with liberation of ammonia. It is also analogous to the decomposition behavior of poly(*N-tert*-butylacrylamide).

Table 2
Specific optical rotation values of several PMALM samples measured at 19 °C in $CHCl_3$

Sample entry in Table 1	$[\alpha]_D^{19}$ (deg dm^{-1} g^{-1} cm^3)
13	−42.2
14	−38.5
15	−37.1
16	−35.1

3.11. Optical properties of the polymers

The specific optical rotation values $[\alpha]_D^{19}$ determined in $CHCl_3$ at 19 °C for four PMALM samples (entries 13–16 of Table 1) are shown in Table 2. The polymer $[\alpha]_D^{19}$ values are between −35.1 and −42.2 deg dm^{-1} g^{-1} cm^3, which are comparable to those obtained by Sanda et al. [39] for PMALM prepared by conventional free radical polymerization. We also note that $[\alpha]_D^{19}$ increased from more negative to less negative values as PMALM molecular weight increased. This is again in agreement with the trend seen by Sanda et al. The large negative $[\alpha]_D^{19}$ values suggest the optical activities of the polymers and their possible future use in chiral separations.

4. Conclusions

MALM has been shown to undergo ATRP with reasonable conversion when ECP/CuCl/Me_6TREN or MBP/CuBr/Me_6TREN was used as the initiating system. In less polar solvents like toluene, PMALM produced using MBP/CuBr/Me_6TREN as the initiating system possessed low polydispersity and contained terminal Br atoms that can initiate

polymerization of other monomers to yield block copolymers. Polymerization initiated by ECP/CuCl/Me_6TREN was seen to be faster in alcohols than that initiated by MBP/CuBr/Me_6TREN and produced PMALM with slightly higher polydispersity. MALM polymerization in toluene using MBP/CuBr/Me_6TREN as the initiating system at 60 °C was shown to be living in the initial hour and changing polymerization time can be used to tune the molecular weight of PMALM produced. Another viable strategy to produce PMALM with different molecular weights is to change the monomer to initiator molar feed ratio. Study of PMALM samples of different molecular weights showed that the glass transition temperature of infinitely long PMALM is 437.8 K. The PMALM samples are sufficiently stable thermally below 240 °C and are optically active. Such polymers when incorporated into block copolymers may assemble into different 3-d nanostructures and may be useful in chiral separations.

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