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Graphical Abstract

Is methanol really a bad solvent for poly(*n*-butyl methacrylate)? Low dispersity and high molecular weight polymers of *n*-butyl methacrylate synthesised via ATRP in anhydrous methanol.

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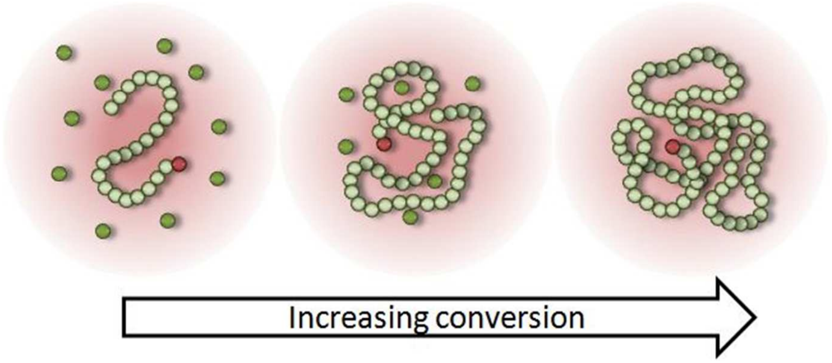
Anhydrous methanol, a traditional precipitant for poly(*n*-butyl methacrylate), has been shown to be an excellent synthesis solvent using ATRP. Polymerisations at 60 °C and 25 °C have generated high molecular weight samples (up to 76000 gmol^{-1}) with very low dispersities (as low as 1.02).



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Is methanol really a bad solvent for poly(*n*-butyl methacrylate)? Low dispersity and high molecular weight polymers of *n*-butyl methacrylate synthesised via ATRP in anhydrous methanol.

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Despite it being used widely as a precipitant for poly(*n*-butyl methacrylate), *p*(*n*BuMA), Cu-catalysed atom transfer radical polymerisation has been conducted in anhydrous methanol. Successful polymerisation (50 wt% monomer) was achieved at 60 °C and 25 °C, reaching high molecular weights (up to $M_n = 75880\ gmol^{-1}$), low dispersities (as low as Đ = 1.02) and high conversions without measureable molecular weight broadening. Cloud point behaviour (upper critical solution temperature) and the role of monomer co-solvency are studied and polymerisation comparisons are made with ATRP in isopropanol and in methanol with different ligands.

Introduction

Along with polymerisation techniques such as reversible addition-fragmentation chain-transfer (RAFT)[1] and nitroxide mediated polymerisation (NMP),[2] atom transfer radical polymerisation (ATRP)[3] has made a significant contribution to polymer synthesis and research globally. ATRP has been shown to controllably generate linear homopolymers and statistical copolymers,[4] segmented copolymers such as linear block copolymers, including peptide-based materials,[5] and graft copolymers,[6] and introduce complex architectures via branching to form stars[7] and hyperbranched polymers.[8] The observation that water[9-11] and protic solvents[12-14] may be used within ATRP without significant loss, and in some cases enhancement, of control has led to this technique being adopted by research groups around the world.

Homogeneous ATRP syntheses within mixed water/alcohol systems, especially when utilising Cu^I catalysis, has been shown to be beneficial in a number of cases. The monomers reported in such polymerisations are predominantly methacrylic hydrophilic compounds,[12,15] however, hydrophobic monomers such as methyl methacrylate[16] and *n*-butyl methacrylate (*n*BuMA)[17] have been polymerised within aqueous ethanol and aqueous isopropanol (IPA) respectively. In this latter case, IPA was used as it is a known theta solvent for *p*(*n*BuMA)[18] and IPA solutions of *p*(*n*BuMA) can tolerate up to approximately 10 vol% water before precipitation.

The ability to control the radical polymerisation of hydrophilic and hydrophobic monomers has allowed a range of polymers with responsive behaviour to be generated, such as: doubly-hydrophilic A-B block copolymers with triggered micelle formation when heating one block segment above its lower critical solution temperature (LCST);[19] heating above the LCST to stimulate micelle to vesicle transitions in chain-end, charge-carrying amphiphilic A-B block copolymers;[20] and reversible micelle switching through either heating above the LCST or cooling below the upper critical solution temperature (UCST) of individual block copolymer segments.[21]

A large number of reports of thermally sensitive, sometimes termed as ‘smart’, polymers describe LCST/UCST behaviour within aqueous[22] or alcohol/water solutions,[23] and rarely just within a non-aqueous environment.[24] LCST, observed when a polymer phase separates on *heating*, is well reported to be an entropically driven transition, however, the UCST of a polymer, observed as a precipitation on *cooling*, is dictated by the mixing enthalpy.[25] The UCST of a limited range of polymers in polar solvents has been described including micelle formation and crosslinking in octan-1-ol of linear di-block copolymers containing mixtures of oligoethylene glycol monomethacrylate, N-isopropyl acrylamide, pentafluorophenyl acrylate and N,N-diethylacrylamide.[24,26] Similarly, statistical copolymers of N-phenyl maleimide and *n*-octadecyl vinyl ether have been shown to exhibit UCST behavior in N,N-dimethylformamide and a range of alcohols such as *n*-butanol and *n*-hexanol[27] whilst *p*(*n*BuMA) and A-B block copolymers containing *p*(*n*BuMA) and poly(ethylene oxide) have been reported to exhibit LCST behaviour in ionic liquids.[28]

Poly(methyl methacrylate), *p*(MMA), and *p*(*n*BuMA) are both widely considered to be hydrophobic polymers with poor solubility in alcohols or water, however, *p*(MMA) has been known for some years to display UCST behaviour in a range of alcohol-water mixtures where the alcohol component of the mixture can be chosen from methanol (MeOH), ethanol, 1-propanol, IPA or 2-methyl-2-propanol (*t*-butanol).[23] Indeed, at specific ratios of 1-propanol or IPA with water, solvent mixtures can be found that reduce the UCST to below room temperature and form homogeneous solutions of *p*(MMA). The solubility in MeOH and ethanol has also been observed under controlled conditions at temperatures >65 °C, under pressure in thick pyrex tubes.[23]

Herein, we describe the previously unreported solubility of *p*(*n*BuMA) homopolymers in MeOH at elevated temperature and investigate the UCST behaviour of the polymer with respect to polymer concentration and water content within the organic solvent. We utilise this behaviour to conduct Cu-catalysed ATRP of *n*BuMA within MeOH and surprisingly show that this can be conducted across a range of temperatures to generate linear homopolymers with a wide range of molecular weights whilst maintaining very low dispersities and avoiding termination reactions that lead to increasing molecular weight at high monomer conversions. Mechanistic discussions consider the effects of monomer co-solvency, the impact of ligand chemistry and comparisons are made with polymerisations conducted in IPA.

Experimental details

Materials

n-Butyl methacrylate (*n*BuMA), ethyl α-bromoisobutyrate (97 %), copper (I) chloride (Cu(I)Cl, 99 %), $CDCl_3$ (99.8 atom % D), methanol-d_4 (99.8 atom % D), methanol (MeOH, anhydrous, 99.8 %) N,N,N',N'',N''-pentamethyl diethylene triamine (PMDETA, 99%), 2,2'-bipyridine (bpy, 99 %) were purchased from Aldrich. Tetrahydrofuran (THF, HPLC-grade), Propan-2-ol (IPA, HPLC-grade) and methanol (MeOH, analytical-grade) were purchased from Fisher. Tris(2-dimethyl aminoethyl)amine (Me_6TREN, 99+%) was purchased from Alfa Aesar. All materials were used as received.

Characterisation

^{1}H nuclear magnetic resonance (NMR) spectra were recorded in methanol-d_4 using a Bruker Avance spectrometer operating at 400 MHz. Triple detection gel permeation chromatography (GPC) was performed using a Malvern Viscotek instrument equipped with a GPCmax VE2001 auto-sampler, two Viscotek T6000 columns (and a guard column), a refractive index (RI) detector VE3580 and a 270 Dual Detector (light scattering and viscometer) with a mobile phase of THF containing 2 v/v % of triethylamine and a flow-rate of 1 mL min^{-1}.

Synthesis of *p*(*n*BuMA)$_x$ homopolymers in anhydrous methanol

In a typical synthesis, targeting a $DP_n = 60$ monomer units, *p*(*n*BuMA)$_{60}$, *n*BuMA (0.85 g, 6 mmol) and bpy (31.2 mg, 0.2 mmol) were added to a 15 mL round-bottomed flask equipped with a magnetic stirrer bar. MeOH (1.07 mL; 50 wt%) (deoxygenated via N_2 purge prior to use) was added and the resulting solution was sparged with N_2 for 10 minutes. Cu(I)Cl (9.9 mg, 0.1 mmol) was rapidly added to the flask, instantly forming a brown coloured mixture and purged with N_2 for a further 5 minutes. The flask was submerged into an oil bath pre-heated at 60 °C and ethyl α-bromoisobutyrate (14.7 µL, 0.1 mmol) was added under N_2 flow using a micro-syringe. The mixture was stirred at 60 °C for 24 hours before termination by dilution with MeOH until appearance of a blue/green colour. Upon cooling, the polymer precipitated and the supernatant containing the catalytic system was discarded. The polymer was dissolved in THF, passed though a neutral alumina column to remove residual catalyst and concentrated by rotary evaporation. The polymer was precipitated into cold MeOH to give a white solid.

Determination of *p*(*n*BuMA) UCST cloud point curves.

Cloud points where determined by visual observation. Different *p*(*n*BuMA) weight fractions in anhydrous MeOH (MeOH/H_2O or MeOH/*n*BuMA mixtures) were dissolved in test tubes under stirring/heating and cooled at a rate of approximately 0.5 °C min^{-1}. Cloud points were determined as the first visual indication of turbidity and were performed in triplicate. Errors values were determined by considering the difference between the highest and lowest values obtained. Typically, *p*(*n*BuMA)$_{60}$ (10 mg) and anhydrous MeOH (1.25 mL; 990 mg) was added to a test tube equipped with a magnetic flea and a rubber septum pierced with a long, small gauged, stainless steel needle. The tube was immersed in an oil bath fitted with a reference test tube containing pure methanol and equipped with a thermocouple. The temperature was increased until total dissolution of the polymer followed by switching off of the heating element. For this example, three cloud points measurements were recorded (using the reference tube) at 52.8 °C, 52.9 °C and 52.9 °C.

Determination of *p*(*n*BuMA) polymerisation kinetics.

Kinetic studies were performed by taking samples from the reaction medium under positive N2 pressure wih subsequent analysis by ^{1}H NMR in CDCl3 and triple detection GPC. Monomer conversion was determined by NMR spectroscopy using crude samples of the reaction medium. Integrals of the vinyl protons of the unreacted monomer (5.50 ppm and 6.05 ppm) were compared with integration of the CH_2 signal adjacent to the ester group of the both the polymer repeat units and the monomer (3.80 ppm and 4.30 ppm) to determine conversion. Catalyst was removed from the samples prior to GPC analysis by passing through a small alumina column.

Results and Discussion

Solubility of *p*(*n*BuMA) in methanol and cloud point measurements.

Methanol is considered a poor solvent for *p*(*n*BuMA) and is often used during workup at ambient temperature, or chilled, to precipitate the polymer after synthesis. During a study of *p*(*n*BuMA) (M_n = 13570 $gmol^{-1}$) in methanol, we warmed the precipitated polymer to temperatures approaching the boiling point of the solvent, and were surprised to find that the polymer dissolved fully to produce a clear solution which precipitated when the solution returned to ambient temperature. When a sample of *p*(*n*BuMA) was added to MeOH-d_4 within an nuclear magnetic resonance (NMR) spectroscopy sample tube (1 wt%), and warmed to 60 °C during an ^{1}H NMR experiment, the completely clear solution produced a well resolved NMR spectrum (Figure 1Ai & 1Bi) which integrated well and provided an excellent assignment of the polymer structure. On cooling to 25 °C, the polymer precipitated within the sample tube and a very weak ^{1}H NMR spectrum was generated (Figure 1Aii & 1Bii). An expansion of the regions between 0.50 – 2.00 ppm and 3.50 - 4.25 ppm provided a clear indication of the presence of the polymer resonances after cooling, suggesting residual solubility of the sample after the heating cycle (see Electronic Supplementary Information; ESI Figure S1). A shift of the water signal was also observed on heating and cooling as expected.[29]

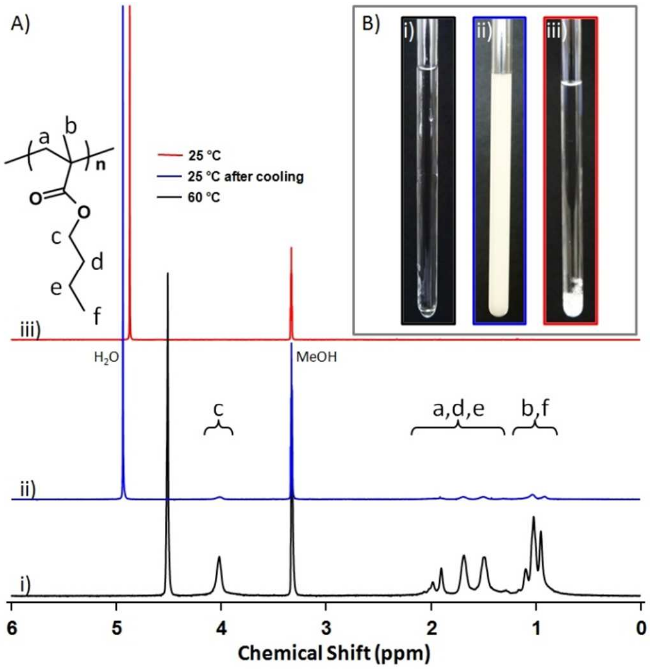

Figure 1: Studies of *p*(*n*BuMA) solubility in MeOH-d_4. A) ^{1}H NMR spectra of i) *p*(*n*BuMA) heated to 60 °C, ii) *p*(*n*BuMA) after heating and cooling to 25 °C, iii) *p*(*n*BuMA) at 25 °C before heating; B) Photographs of *p*(*n*BuMA) within the NMR tube at different temperatures – i) 60 °C, ii) after cooling to 25 °C, and iii) at 25 °C prior to heating.

To investigate the solubility of the *p*(*n*BuMA) sample without heating cycling, a ^{1}H NMR study was also undertaken by simply mixing the polymer with MeOH-d_4 at ambient temperature and obtaining a spectrum at 25 °C (Figure A1iii & 1Biii). As can be seen, no appreciable resonances were observed.

The cloud point behaviour of *p*(*n*BuMA) (M_n = 13,570 $gmol^{-1}$) in MeOH was evaluated by placing multiple tubes within a heated oil bath and repeatedly (3 repeats) observing the onset of precipitation during cooling at various concentrations (Figure 2). Initially, anhydrous MeOH was utilised (stated < 0.005 % H_2O) and cloud points were seen for polymer solutions up to 5 wt% *p*(*n*BuMA) across a wide range of temperatures (47.5 °C - 64.7 °C) with excellent reproducibility (see Table S1). When analytical grade MeOH (stated < 0.05 % H_2O) was utilised, a maximum polymer concentration that could be completely solvated decreased to 4.5 wt% (cloud point = 64.1 °C), with a further decrease to 2 wt% (cloud point = 63.7 °C) when the water content was increased to 1 wt% through controlled water addition to anhydrous MeOH (Figure 2 and Figure S2). As seen previously with 2-propanol/water mixtures at ambient temperature,[17] the addition of water to the methanolic solution inhibits solubility at elevated temperature which appears to be in stark contrast to the behaviour of *p*(MMA) when water is added at low ratios to alcoholic mixtures.[23]

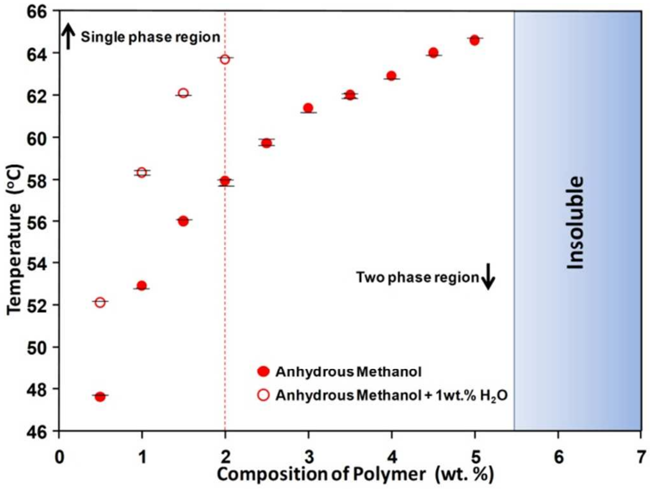

Figure 2: Cloud point behaviour for *p*(*n*BuMA) in MeOH with varying water content within the organic solvent. Maximum *p*(*n*BuMA) solubility in MeOH:H_2O (1 wt %) shown by red dashed line. Asymmetric error bars shown.

ATRP of *n*BuMA in MeOH at elevated temperature.

There is significant current interest in polymerisations that undergo phase separation during reaction, leading to colloidal structures at high conversion. This so-called polymerisation-induced self-assembly involves the initiation of polymerisation within a solvent environment that would normally lead to precipitation of the polymer at high chain length. Under conditions where oligomers stay dissolved, either as a function of their inherent solubility at low molecular weight or through co-solvency with unreacted monomer, the polymerisation proceeds in solution until a chain length is attained that leads to aggregation.[30] One of the earliest reports of such an approach involved a 'polymerisation induced micellar interconnection' during aqueous aniline polymerisation[31] and since this work, several groups have studied other techniques such as anionic polymerisation,[32] NMP[33] and RAFT.[34]

Despite the low concentration of polymer that was seen to undergo UCST behaviour in hot methanol (Figure 2), the homopolymerisation of *n*BuMA was attempted under conventional copper-catalysed (CuCl) ATRP conditions at 50 wt% in methanol at 60 °C using 2,2-bipyridine (bpy) as the ligand and using ethyl α-bromoisobutyrate as initiator. Number average degrees of polymerisation (DP_n) of 60, 80 and 100 monomer units were targeted initially, Table 1.

Table 1: Cu-catalysed methanolic ATRP of *n*BuMA at 60 °C

Target[a] DP_n	Conversion (%)	Time (hrs)	M_n Theory[b]	GPC (THF)[c] M_n (g/mol)	M_w (g/mol)	Đ
60	99	55	8640	13570	13950	1.03
80	96	55	11120	16700	17010	1.02
100[d]	95	79	13700	19690	20310	1.03
100[d]	93	25	13420	21830	22830	1.05
150	94	53	20250	26680	27650	1.04
200	87	46	24940	30150	33240	1.10
300	90	72	38590	52130	57260	1.10
400	74	100	42290	59200	64500	1.09
500	66	235	47120	55540	61950	1.12
1000	50	648	71300	75880	85500	1.13
p(styrene) Std.[e]	-	-	9200[e]	9310	9620	1.03

[a] Target DP_n calculated as [*n*BuMA]/[initiator]; [b] Theoretical M_n calculated as (Target DP_n x 142.2 $gmol^{-1}$)*actual fractional conversion achieved and includes initiator residue; [c] GPC utilising THF eluent and *dn*/*dc* = 0.0762 (averaged across 18 samples); [d] Repeat syntheses of *p*(*n*BuMA)$_{100}$; [e] *p*(styrene) GPC calibration standard (Polymer Laboratories Ltd)

The polymerisation reactions appeared to progress under controlled conditions with the characteristic dark brown opaque colour of the Cu-catalysed polymerisation being evident throughout (Figure 3Ai). On cooling, the reactions precipitated as the polymer solution passed through the cloud point temperature. This was difficult to assess initially as the highly coloured polymerisation was not transparent enough to see the onset of precipitation. To overcome this, a reaction was allowed to reach high conversion prior to the careful addition of air to the stirred reaction which led to oxidation of the Cu^I-based catalyst and the formation of a transparent blue/green, homogemeous solution at 60 °C (Figure 3Aii). When this solution was allowed to cool, the onset of precipitation was readily observed at 57 °C (Figure 3Aiii). This is highly surprising given the concentration of the polymer within the polymerisation and the observed inability to solvate powdered polymer in anhydrous MeOH at concentrations above 5 wt%. In all cases, the polymerisations targeting *p*(*n*BuMA)$_{60-100}$ reached high conversions (> 95%) and analysis by triple detection gel permeation chromatography (GPC) showed low dispersity polymers (Đ < 1.05) and number average molecular weight (M_n) values ranging from 1.06 - 1.58 fold higher than theoretical values (Table 1, Figure 3B).

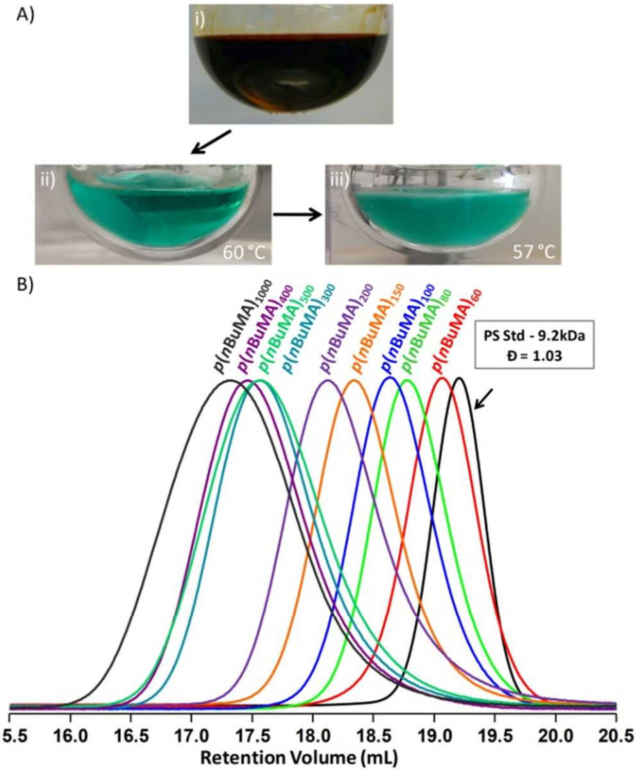

Figure 3: ATRP polymerisation of *n*BuMA in MeOH at 60 °C. A) Photographs of the polymerisation showing i) the strong dark brown catalyst complex during polymerisation, ii) the homogeneous polymerisation at 60 °C after oxygen allowed was into the reaction, and iii) precipitation of *p*(*n*BuMA) during cooling (57 °C); B) GPC chromatograms (RI) showing *p*(*n*BuMA) molecular weight distributions across targeted DP_n = 60 – 1000 monomer units – p(styrene) standard shown for comparison

Due to the success of the polymerisations and the very low dispersities obtained, a series of polymers with escalating target DP_n values, up to *p*(*n*BuMA)$_{1000}$, was conducted at 50 wt% monomer (Table 1). The time required to polymerise the increasingly longer targeted polymer chains increased considerably with the target *p*(*n*BuMA)$_{1000}$ achieving 50 % conversion in 27 days. Despite the achievement of reduced conversions and long reaction times, polymers with M_n values up to 76000 $gmol^{-1}$ were obtained with very low dispersities (Đ ≤ 1.13). The GPC chromatograms for all recovered polymers (Figure 3B) were monomodal and largely symmetrical, showing no significant loss of propagating chains during the polymerisation. As the targeted polymer chain lengths increased, the deviation from the theoretical M_n values (corrected for actual conversions in Table 1) reduced considerably to only a factor of 1.18 for p(nBuMA)$_{500}$ and 1.06 for p(nBuMA)$_{1000}$.

The kinetics of the *n*BuMA polymerisation at 60 °C was studied for the targeted *p*(*n*BuMA)$_{80}$ synthesis and linear relationships were seen for the semi-logarithmic plot of $\ln([M_o]/[M])$ *vs.* time (Figure 4A) and an M_n *vs.* conversion analysis (Figure 4B), confirming controlled polymerisation conditions. Low dispersities (Đ < 1.10) were also maintained throughout the reaction.

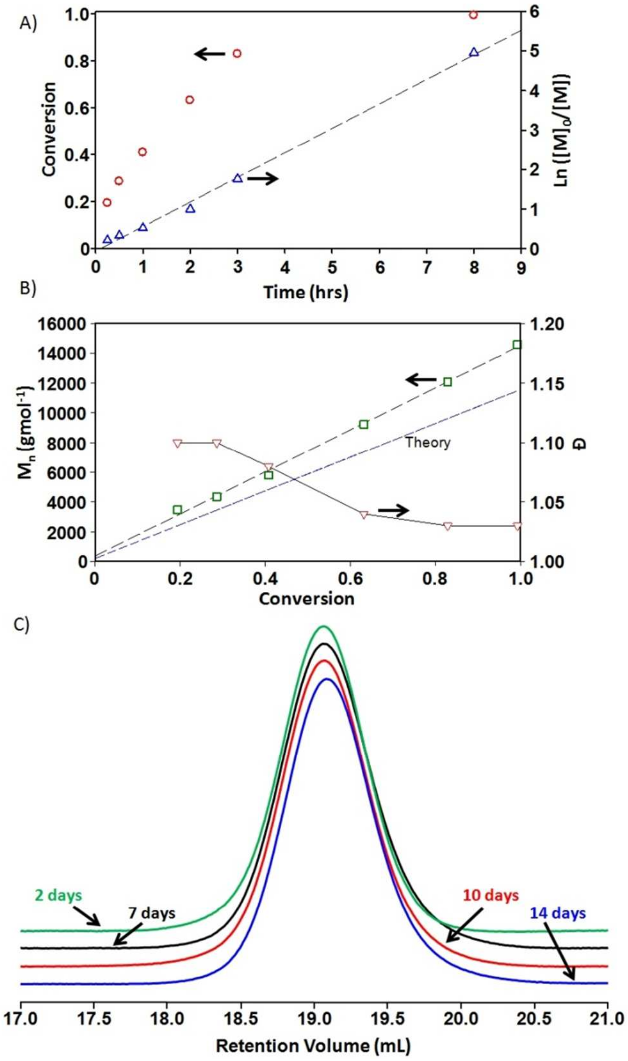

Figure 4: Studies of the ATRP polymerisation of *n*BuMA in MeOH at 60 °C. Kinetic studies of $p(n\text{BuMA})_{80}$ synthesis A) Conversion and semilogarithmic plots *vs.* time; B) Evolution of M_n and dispersity with conversion; C) GPC (RI) chromatograms of $p(n\text{BuMA})_{60}$ synthesis left to stir (heated) for 14 days at high conversion.

It is well known that ATRP polymerisations that reach very high conversion have the potential to undergo termination by combination and/or disproportionation (more likely for methacrylate monomers) due to the equilibrium of radical formation and capping occurring in the absence of monomer.[35] Either case will lead to broadening of the molecular weight distribution. Many of the polymerisations outlined in Table 1 were left to react for extended periods and the potential for termination within the methanolic polymerisation was studied. A series of polymerisations with a target $p(n\text{BuMA})_{60}$ were left to stir at 60 °C for 14 days and terminated at varying intervals to monitor the molecular weight distribution by GPC (Figure 4C). The reactions had achieved near complete conversion within the first 24 hours reaction time, however, samples taken after 2 days, 7 days, 10 days and finally after 14 days showed no appreciable broadening of the molecular weight distribution or movement of the distribution towards lower retention times.

Contribution of monomer co-solvency within the ATRP of *n*BuMA in MeOH.

In the initial stages of the polymerisation, it is reasonable to assume that the presence of unreacted *n*BuMA may be acting as a co-solvent, however, at high conversions the polymer can only be solvated by the hot methanol. The synthesis of the polymer within the MeOH environment appears to generate a relatively weak interaction between the solvent and the $p(n\text{BuMA})$ chains. This interaction appears to not be able to overcome interchain interactions within the dried purified polymer; no purified samples were able to be re-solvated at high concentrations above the cloud point curves (Figure 2).

The impact of co-solvency from unreacted monomer was studied by determining the cloud points of products of the targeted $p(n\text{BuMA})_{60}$, $p(n\text{BuMA})_{200}$ and $p(n\text{BuMA})_{300}$ polymerisations in MeOH at varying concentrations of *n*BuMA monomer. MeOH/polymer mixtures (50 wt % $p(n\text{BuMA})_x$) were prepared and subsequently cycled in temperature prior to addition of more unreacted monomer and further heat cycling; observation of dissolution on heating led to measurement of the cloud point temperatures on cooling. The experiment can be considered from several viewpoints; the concentration of added monomer can be viewed as a single timepoint within a polymerisation reaction, where the polymer present represents the conversion of the polymerisation and the monomer present represents the *n*(BuMA) left to react. As such, each cloud point measurement would represent a polymerisation with a subtly different, and systematically increasing, target DP_n (Figure S4 and Table S2). Alternatively, the cloud point data may be assessed as the number of polymer repeat units per monomer (unreacted) co-solvent molecule that generates a particular cloud point temperature (Figure 5).

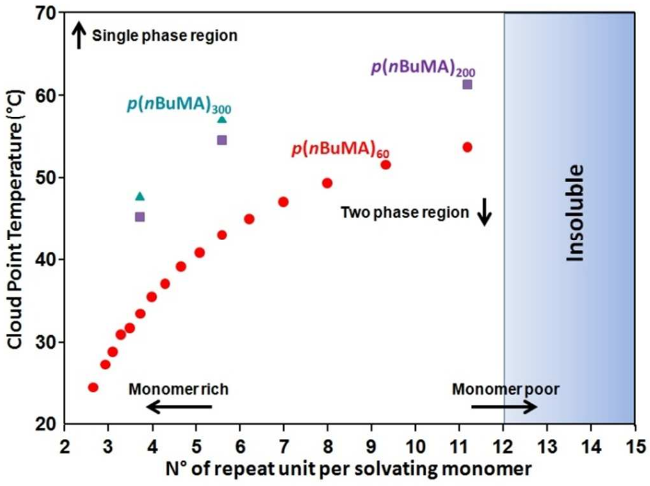

Figure 5: Cloud point measurement of $p(n\text{BuMA})_x$ in MeOH with increasing concentrations of $n(\text{BuMA})$ monomer.

As can be seen in Figure 5, *n*BuMA has a considerable effect on the observed cloud points of *p*(*n*BuMA)$_x$ within a methanolic environment. Cloud points as low as 24.5 °C were observed for *p*(*n*BuMA)$_{60}$ within a monomer-rich environment. A very noticeable effect was seen as the length of the dissolved polymer chains increased, and an increased number of solvating monomers was required to impact the cloud point of the dissolved polymer from *p*(*n*BuMA)$_{60}$ through *p*(*n*BuMA)$_{200}$ to *p*(*n*BuMA)$_{300}$; *p*(*n*BuMA)$_{300}$ could only be induced to show measureable UCST behaviour in monomer rich environments whilst *p*(*n*BuMA)$_{200}$ and *p*(*n*BuMA)$_{60}$ both exhibited cloud point behaviour across the range of monomer concentrations studied.

This observation underlines the complex behaviour of the *n*(BuMA) ATRP in MeOH. The lowest chain length polymer studied, *p*(*n*BuMA)$_{60}$, showed a cloud point of 53.6 °C in a solvent environment representing 11 repeat units per monomer co-solvent molecule or, alternatively, at a model polymerisation conversion of approximately 92 % for a targeted DP$_n$ = 65 *n*BuMA units (calculated as (1-[(60/11)/((60/11)+60)])*100%). At lower monomer concentrations, the powdered polymer cannot be solvated below the boiling point of the monomer/MeOH mixture; however, we were able to maintain a homogeneous *p*(*n*BuMA)$_{60}$ at 60 °C for 14 days (Figure 4). Additionally, the longer *p*(*n*BuMA)$_x$ chains appear to require considerable monomer concentrations to reduce the UCST to temperatures below the boiling point of MeOH and therefore would only be expected to polymerise to relatively low conversions before precipitation. The presence of unreacted *n*(BuMA) is clearly not the only factor allowing the reaction to proceed with the observed success.

Cu-catalysed ATRP of *n*BuMA in MeOH at low temperature.

The study of monomer co-solvency showed the potential to maintain *p*(*n*BuMA) in solution at much lower temperatures than our initial studies. In principle, a methanolic ATRP of *n*BuMA may be able to be initiated at low temperature and lead to polymerisation induced phase separation during the consumption of monomer. This opportunity was studied by conducting three polymerisations to target *p*(*n*BuMA)$_{60}$, *p*(*n*BuMA)$_{100}$ and *p*(*n*BuMA)$_{200}$ in MeOH whilst maintaining the temperature at 25 °C. As can be seen from Table 2, surprisingly the polymerisations underwent homogeneous and controlled polymerisation to high conversion yielding narrow dispersity products and without observable precipitation.

The GPC analysis of the products showed monomodal and symmetrical molecular weight distributions (Figure S5) that closely resembled the products from the polymerisations at elevated temperature. The ability to conduct the polymerisation successfully without the need for higher temperatures again suggests a more complicated polymerisation mechanism than simple co-solvency from the unreacted monomer.

Table 2 does also indicate better targeting of theoretical molecular weights at this lower temperature than equivalent polymerisations at 60 °C and across the chain lengths studied: *p*(*n*BuMA)$_{60}$ varies from the theoretical M$_n$ value by a factor of 1.43; *p*(*n*BuMA)$_{100}$ by a factor of 1.19 and *p*(*n*BuMA)$_{200}$ by a factor of 1.08.

Table 2: Cu-catalysed methanolic ATRP of *n*BuMA at 25 °C

Target^a DP$_n$	Conversion (%)	Time (hrs)	M$_n$ Theory^b	GPC (THF)^c M$_n$ (g/mol)	M$_w$ (g/mol)	Đ
60	95	24	8300	11810	12100	1.03
100	97	74	13990	16660	17150	1.03
200	97	122	27780	29960	30830	1.03

^{a} Target DP$_n$ calculated as [*n*BuMA]/[initiator]; ^{b} Theoretical M$_n$ calculated as (Target DP$_n$ x 142.2 gmol^{-1})*actual fractional conversion achieved and includes initiator residue; ^{c} GPC utilising THF eluent and *dn*/*dc* = 0.0762 (averaged across 18 samples).

Comparative Cu-catalysed ATRP of *n*BuMA in IPA and using different ligands in anhydrous MeOH.

As mentioned previously, the ambient temperature polymerisation of *n*BuMA has been reported in IPA in the presence an absence of water.[17] As IPA is a theta solvent for *p*(*n*BuMA), a series of polymerisations were conducted to compare against the methanolic ATRP syntheses described above. *p*(*n*BuMA)$_{60}$, *p*(*n*BuMA)$_{100}$ and *p*(*n*BuMA)$_{200}$ were targeted using IPA at 60 °C and *p*(*n*BuMA)$_{60}$ and *p*(*n*BuMA)$_{200}$ were also targeted in identical polymerisations at 25 °C (Table 3). Each polymerisation was able to achieve high conversion of monomer at both temperatures. A direct comparison of *p*(*n*BuMA) synthesised under identical conditions but within either IPA or MeOH was readily achieved by overlaying the GPC refractive index chromatograms (Figure 5).

Table 3: Cu-catalysed ATRP of *n*BuMA in IPA

Target^a DP$_n$	Conversion (%)	Time (hrs)	M$_n$ Theory^b	GPC (THF)^c M$_n$ (g/mol)	M$_w$ (g/mol)	Đ
60 °C						
60	99	47	8640	11850	13500	1.14
100	99	68	14270	17900	20740	1.16
200	99	68	28350	33770	38900	1.15
25 °C						
60	99	68	8640	14190	16400	1.16
200	97	100	27780	32830	37980	1.16

^{a} Target DP$_n$ calculated as [*n*BuMA]/[initiator]; ^{b} Theoretical M$_n$ calculated as (Target DP$_n$ x 142.2 gmol^{-1})*actual fractional conversion achieved and includes initiator residue; ^{c} GPC utilising THF eluent and *dn*/*dc* = 0.0762 (averaged across 18 samples).

The samples of *p*(*n*BuMA)$_{60}$, *p*(*n*BuMA)$_{100}$ and *p*(*n*BuMA)$_{200}$ synthesised in MeOH all displayed molecular weight distributions that were entirely encapsulated within the distributions of the equivalent samples synthesised in IPA (Figure 5A and Figure S8), demonstrating the increased control when utilising MeOH. Also, a *p*(*n*BuMA)$_{60}$ polymerisation in IPA was left to stir at 60 °C at high conversion for 7 days; unlike the reaction conducted in MeOH, a broadening of the distribution towards lower retention times was observed (Figure 5B).

In a separate study, three syntheses of $p(n\text{BuMA})_{60}$ were conducted under identical conditions in MeOH using Cu(I)Cl but employing either the bpy ligand, tris[2-(dimethylamino) ethyl]amine (often referred to as Me_6TREN) or N,N,N′,N′,N″-pentamethyldiethylenetriamine (also referred to as PMDETA). Despite all polymerisations achieving relatively high conversions, PMDETA and Me_6TREN polymerisations under these conditions produced polymers with asymmetric molecular weight distributions (Figure 5C) and much higher M_n and M_w values (Table S4) than seen with the bpy ligand ($M_{nPMDETA}$ = 20360 $gmol^{-1}$; $M_{nMe6TREN}$ = 38550 $gmol^{-1}$).

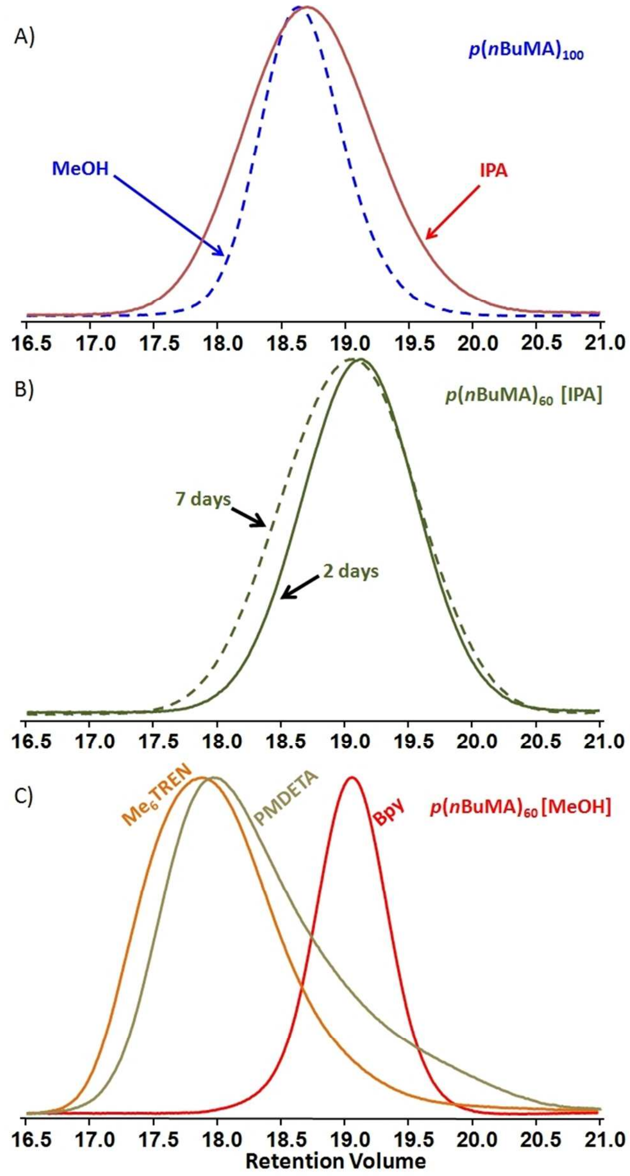

Figure 5: GPC comparison of $p(n\text{BuMA})$ synthesised under different conditions. A) Overlaid molecular weight distributions of $p(n\text{BuMA})_{100}$ polymerised in MeOH (blue dotted line) and IPA (red solid line) at 60 °C; B) Extended heating of $p(n\text{BuMA})_{60}$ at high conversion in IPA, showing increase in sample dispersity over 7 days; C) Synthesis of $p(n\text{BuMA})_{60}$ in MeOH using different catalyst ligands.

To rule out any potential solubility issues that may arise within the different catalyst systems, mixtures of Cu(I)Cl and either bpy, PMDETA or Me_6TREN were prepared within bulk *n*BuMA and an *n*BuMA/MeOH mixture. It was clear that the Cu/bpy complex was not particularly soluble in bulk monomer at ambient temperature but the other Cu/ligand complexes showed appreciable solubility (Figure S9); addition of MeOH led to a clearly soluble complex for each system studied. Whether this difference plays a role in the monomer-depleted or monomer-swollen stages of the polymerisation is unclear.

Potential rationale for successful ATRP of *n*BuMA in MeOH.

There have been many reports of the details of the mechanism of ATRP in polar and protic solvents with advances in the understanding leading to the development of single-electron transfer living radical polymerization (SET-LRP)[36] and supplemental activator and reducing agent ATRP (SARA ATRP).[37] The role of Cu(0) within these polymerisations has been demonstrated by the direct addition of solid copper wire to reactions containing Cu(II) compounds[38] and studies of the disproportionation of Cu(I) halides under varying ligand and solvent conditions.[39] These latter studies have very recently reported the direct formation of Cu(0) nanoparticles in MeOH systems containing a 1:1 molar ratio of bpy and Cu(I)Br. SET-LRP has also been reported to provide "ultrafast" polymerisation and "ultrahigh" molecular weight methacrylates at 25 °C in dimethyl sulphoxide (DMSO).[40]

The methanolic polymerisation of *n*BuMA reported herein utilises a 2:1 bpy:Cu(I)Cl molar ratio and generates polymers of high molecular weight over long timescales that are typical of wide reports of ATRP (Table 1). As mentioned above, the solubility of the Me_6TREN and PMDETA complexes with Cu(I)Cl was considered to be a potential issue contributing to the observed lack of success in these cases. It is important to note, however, that PMDETA and Me_6TREN mediated systems did polymerise the monomer to high conversions and Me_6TREN is a very common ligand for reports of SET-LRP. To study the potential for Cu(0) formation within the successful methanolic bpy:Cu(I)Cl conditions used here, a qualitative comparison of Cu(I) disproportionation to Cu(O) and Cu(II) was conducted between bpy:Cu(I)Cl mixtures at either 2:1 and 1:1 molar ratios; considerably less solid material was evident under the 2:1 catalyst ratio (Figure S10). This appears to correlate well with recent reports showing that higher ratios of Me_6TREN in the presence of Cu(I)Br, leads to lower levels of observable Cu(0) formation in DMSO.[39]

Irrespective of the exact mechanism, the successful bpy:Cu(I)Cl mediated polymerisation of *n*BuMA in MeOH over a wide range of temperatures, and the comparison to the results across the same temperature range and target polymer chain lengths, suggests a polymerisation enhanced by the specific solvent conditions. The very narrow dispersities and lack of broadening at high conversions, high temperatures and long timescales may also be indicative of a propagating chain end that is sterically hidden from other active chain ends, thereby restricting the proximity of active radicals and/or the addition of polymer chain ends with vinyl functionality (formed by termination by disproportionation) to active propagating centres.

It is reasonable to envisage a methanolic polymerisation that is initiated in a very good solvent environment, enhanced by unreacted monomer, which progressively changes to an increasingly poor environment as the monomer is depleted. As the concentration of monomer decreases, the polymer chains will, therefore, adopt more densely coiled structures than an equivalent polymerisation within a good (or theta) solvent (Figure 6). It is possible that unreacted monomer interacts with longer polymer chains in the later polymerisation stages; however, phase separation is not seen at very high conversions. The different behaviour of the Me_6TREN and PMDETA mediated reactions also suggest an increased initiating efficiency for the bpy/Cu(I)Cl system under these conditions.

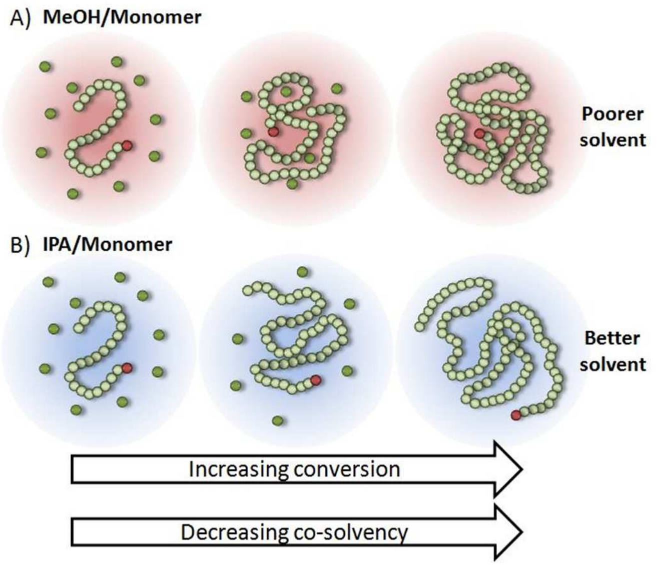

Figure 6: Schematic representation of proposed *n*BuMA polymerisation in MeOH and IPA: A) Monomer/MeOH acts a good solvent for growing oligomers but larger polymer chains in monomer depleted environments adopt collapsed coils with hidden chain ends; B) Monomer/IPA mixtures act as a good solvent environment and monomer depletion does not generate a poor solvent system at high conversion, leading to more expanded coils and available chain ends. Key: Red background = MeOH solvent, blue background = IPA solvent, dark green spheres represent unreacted *n*BuMA, red sphere represents active chain end.

Unreacted monomer clearly has a role to play in aiding the solvation of the propagating chains, however, the ability to produce very long chains with such narrow dispersity within a solvent that is conventionally used as a precipitant is highly surprising, especially at low temperatures. It is important to note that experimentally the polymerisations were easy to conduct but a number of polymerisations precipitated if samples were taken during the polymerisation timescales. Detailed kinetic studies at higher conversions were therefore not conducted broadly. The reaction mixtures appear to be quite sensitive to any perturbation, again suggesting that the balance of solvent interaction and polymer-polymer interactions is indeed very fine. For example, attempts to conduct self-blocking experiments at high conversion often led to precipitation despite considerable effort to add pre-heated monomer to ongoing polymerisations at 60 °C by cannula needle techniques.

Conclusions

The previously unreported UCST behaviour of *p*(*n*BuMA) in MeOH has been studied and a clear relationship between the presence of water and reduced cloud point temperatures was seen. The considerable success of *n*BuMA ATRP conducted in MeOH (using bpy as the ligand) was initially confusing, as completely homogeneous solutions and very controlled reactions to significant chain lengths were achievable, even at low temperatures. The observed dispersity values are comparable to those typically associated with anionic polymerisation and the lack of chain termination by combination offers a relatively easy route to the production of uniform molecular weight distributions. The presented rationale for the observed behaviour requires further detailed study to fully ascertain the actual factors controlling and influencing the synthesis of *p*(*n*BuMA) in MeOH. Further syntheses are underway to utilise the benefits of this route to introduce complex architecture and amphiphilicity whilst maintaining low dispersity polymers.

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Notes and references

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Electronic Supplementary Information (ESI) available: Additional experimental details, NMR spectra, UCST cloud point data and additional GPC chromatograms. Molecular weight data tables, tabulated data from graphical presentations, photographic images of catalyst solubility within *n*BuMA monomer. See DOI: 10.1039/b000000x/

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