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<td><strong>Author(s)</strong></td>
<td>Magee, Christopher</td>
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<tr>
<td><strong>Publication Date</strong></td>
<td>2014-12-11</td>
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<td><strong>Item record</strong></td>
<td><a href="http://hdl.handle.net/10379/4808">http://hdl.handle.net/10379/4808</a></td>
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Chain Transfer to Solvent in the Radical Polymerization of Acrylamide Monomers, Controlled/Living Radical Polymerizations, including in Supercritical Carbon Dioxide and Preparation of Carbon Dioxide Responsive Micelles

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Thesis presented for the qualification of Ph.D. degree to the National University of Ireland, Galway

School of Chemistry, National university of Ireland, Galway

September 2014

Supervisor: Dr. Fawaz Aldabbagh
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Acknowledgements

I would like to thank my supervisor Dr. Fawaz Aldabbagh for the opportunity to do this PhD and for all his advice and guidance throughout the course of the research.

I would also like to thank Prof Per B. Zetterlund for his contributions in Chapter 3, for providing PREDICI simulations of nitoxide partitioning.

I must also acknowledge Rebecca Braslau, Aruna Earla, Jennifer Petraitis and Chad Higa for the synthesis of the alkoxyamines that made the work in Chapter 3 possible.

I would also like to thank my friends and family for their support and invaluable advice throughout my PhD.

This thesis would not have been possible without the financial support from the Irish Research Council (formerly IRCSET) as part of the first IUPAC Transnational Call in Polymer Chemistry.

“Insanity: doing the same thing over and over again and expecting different results”

- Albert Einstein
Abstract

Chapter 1 provides a general introduction to radical polymerization, including chain transfer, and controlled/living radical polymerization. A review of the literature since 2009 on heterogeneous controlled/living radical polymerizations in supercritical carbon dioxide is provided.

Chapter 2 describes the work published in *Polymer Chemistry 2014*, 5, 2259-2265. Chain transfer to solvent in conventional radical polymerization of \( N\text{-}\text{tert-} \)butylacrylamide (TBAM) and \( N\text{-}(2\text{-morpholin-4-ylethyl})\text{acrylamide (MEA)} \) in a range of alcohol solvents at 120 °C was investigated. Mayo analysis of polymerizations of TBAM in linear alcohols (C\(_3\)–C\(_9\)) resulted in an approximately linear increase in chain transfer to solvent constant (\( C_{t,s} \)) with the number of methylene (CH\(_2\)) units in the solvent. The solvents with the lowest chain transfer to solvent constant (\( C_{t,s} \)) allowed the attainment of higher molecular weight (MWs) in both conventional and nitroxide-mediated radical polymerization (NMP) of TBAM. The first controlled/living polymerizations of MEA are detailed with chain transfer having a greater impact on maximum achievable MWs in NMP in comparison to TBAM.

Chapter 3 gives an account of work published in *Polymer Chemistry 2014*, 5, 5725-5733. The first alkoxyamine-initiated precipitation polymerization of styrene in supercritical carbon dioxide is provided. Reasonable controlled/living character using TIPNO-Alkoxyamine was possible in the absence of any excess free nitroxide. The analogous SG1-alkoxyamine gave inferior control under the same conditions. Nitroxide partitioning effects were investigated by comparing the relative performances of three novel fluorinated TIPNO based alkoxyamines. Despite increased steric bulk around the N-O bond, all polymerization using these three alkoxyamines proceeded at a similar rate and level of control to the TIPNO system in solution. These experiments were supported by PREDICI simulation of the partitioning effects of the styrene/TIPNO system in scCO\(_2\).

Chapter 4 describes the controlled/living reversible addition-fragmentation transfer (RAFT) polymerization of MEA. The morpholine moieties of the poly(MEA) were shown by \(^1\)H NMR spectroscopy to be reversibly protonated in aqueous solutions of CO\(_2\). Poly(MEA) was chain extended with \( N\text{-}N\text{-dimethylacrylamide and styrene to yield amphiphilic triblock copolymer, which self-assembled in water to form uniform spherical micelles of 25 nm in diameter. Colloidal aggregation was reduced by addition of CO}_2 \text{ in water with micelles appearing larger and more irregular in size.} \)
### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>AA</td>
<td>acrylic acid</td>
</tr>
<tr>
<td>ACN</td>
<td>1,1’-azobis(cyclohexanecarbonitrile)</td>
</tr>
<tr>
<td>AIBN</td>
<td>2,2’-azobisisobutyronitrile</td>
</tr>
<tr>
<td>AN</td>
<td>acrylonitrile</td>
</tr>
<tr>
<td>α</td>
<td>fractional monomer conversion</td>
</tr>
<tr>
<td>ATRP</td>
<td>atom transfer radical polymerization</td>
</tr>
<tr>
<td>b</td>
<td>block</td>
</tr>
<tr>
<td>b.p</td>
<td>boiling point</td>
</tr>
<tr>
<td>CLRIP</td>
<td>controlled/living radical polymerization</td>
</tr>
<tr>
<td>Conv.</td>
<td>conversion</td>
</tr>
<tr>
<td>$C_{tr}$</td>
<td>chain transfer constant</td>
</tr>
<tr>
<td>CTA</td>
<td>chain transfer agent</td>
</tr>
<tr>
<td>$C_{tr,M}$</td>
<td>chain transfer to monomer constant</td>
</tr>
<tr>
<td>$C_{tr,S}$</td>
<td>chain transfer to solvent constant</td>
</tr>
<tr>
<td>DCM</td>
<td>dichloromethane</td>
</tr>
<tr>
<td>DMA</td>
<td>$N,N$-dimethylacrylamide</td>
</tr>
<tr>
<td>DMF</td>
<td>$N,N$-dimethylformamide</td>
</tr>
<tr>
<td>$DP$</td>
<td>degree of polymerization</td>
</tr>
<tr>
<td>$DP_n$</td>
<td>number average degree of polymerization</td>
</tr>
<tr>
<td>Et</td>
<td>ethyl</td>
</tr>
<tr>
<td>$f$</td>
<td>initiator efficiency</td>
</tr>
<tr>
<td>g</td>
<td>gram</td>
</tr>
<tr>
<td>GPC</td>
<td>gel permeation chromatography</td>
</tr>
<tr>
<td>h</td>
<td>hour</td>
</tr>
<tr>
<td>Hz</td>
<td>hertz</td>
</tr>
<tr>
<td>[I]</td>
<td>initiator concentration</td>
</tr>
</tbody>
</table>
$J_{\text{crit}}$  
critical number-average degree of polymerization

$K$  
equilibrium constant

$k_{\text{act}}$  
rate coefficient for dissociation

$k_{\text{deact}}$  
rate coefficient for combination

$k_d$  
rate coefficient for decomposition of initiator

$k_i$  
rate coefficient for initiator radical addition

$k_{i,\text{th}}$  
rate coefficient for thermal self-initiation

$k_p$  
rate coefficient for propagation

$k_{ri}$  
rate coefficient for re-initiation

$k_t$  
total rate coefficient for termination

$k_{\text{tc}}$  
rate coefficient for termination by combination

$k_{\text{td}}$  
rate coefficient for termination by disproportionation

$k_{\text{tr}}$  
rate coefficient for chain transfer

$k_{\text{tr},S}$  
rate coefficient for chain transfer to solvent

$L$  
litre

LCST  
lower critical solution temperature

$[M]$  
monomer concentration

$M$  
molar

MA  
methyl acrylate

Me  
methyl

MEA  
$N$-(2-morpholin-4-ylethyl)acrylamide

mg  
milligram

MI  
macroinitiator

mL  
millilitre

µm  
micrometre

mmol  
millimole

$M_a$  
number-average molecular weight
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>$M_a$(GPC)</td>
<td>number average molecular weight estimated by GPC</td>
</tr>
<tr>
<td>$M_a$(NMR)</td>
<td>number average molecular weight estimated by NMR</td>
</tr>
<tr>
<td>$M_{n,th}$</td>
<td>theoretical number average molecular weight</td>
</tr>
<tr>
<td>mol</td>
<td>mole</td>
</tr>
<tr>
<td>m.p.</td>
<td>melting point</td>
</tr>
<tr>
<td>MPa</td>
<td>megapascal</td>
</tr>
<tr>
<td>MW</td>
<td>molecular weight</td>
</tr>
<tr>
<td>$M_w$</td>
<td>weight average molecular weight</td>
</tr>
<tr>
<td>MWD</td>
<td>molecular weight distribution</td>
</tr>
<tr>
<td>$M_w$/$M_n$</td>
<td>polydispersity</td>
</tr>
<tr>
<td>NIPAM</td>
<td>$N$-isopropylacrylamide</td>
</tr>
<tr>
<td>nm</td>
<td>nanometer</td>
</tr>
<tr>
<td>NMP</td>
<td>nitroxide-mediated polymerization</td>
</tr>
<tr>
<td>NMR</td>
<td>nuclear magnetic resonance</td>
</tr>
<tr>
<td>$P^*$</td>
<td>propagating radical</td>
</tr>
<tr>
<td>Ph</td>
<td>phenyl</td>
</tr>
<tr>
<td>$pK_{aH}$</td>
<td>conjugate acid strength</td>
</tr>
<tr>
<td>ppm</td>
<td>parts per million</td>
</tr>
<tr>
<td>P-T</td>
<td>polymeric alkoxyamine</td>
</tr>
<tr>
<td>$R^*$</td>
<td>radical</td>
</tr>
<tr>
<td>RAFT</td>
<td>reversible-addition fragmentation chain transfer</td>
</tr>
<tr>
<td>$R_{add}$</td>
<td>rate of initiator radical addition</td>
</tr>
<tr>
<td>$R_i$</td>
<td>rate of initiation</td>
</tr>
<tr>
<td>RI</td>
<td>refractive index</td>
</tr>
<tr>
<td>$R_{i,th}$</td>
<td>rate of thermal initiation</td>
</tr>
<tr>
<td>RP</td>
<td>radical polymerization</td>
</tr>
<tr>
<td>$R_p$</td>
<td>rate of polymerization</td>
</tr>
</tbody>
</table>
$R_{pr}$  rate of radical production
$R_t$  rate of termination
R-X  alkyl halide
s  second
scCO$_2$  supercritical carbon dioxide
SG1  $N$-tert-butyl-$N$-(1-diethylphosphono-2,2-dimethylpropyl) nitroxide
St  styrene
t  time
T*  nitroxide trap
$\Gamma$  partition coefficient
$t$-BA  $tert$-butyl acrylate
TBAM  $N$-tert-butylacrylamide
TBP  $tert$-butyl peroxide
$t$Bu  $tert$-butyl
TEM  transmission electron microscope
TEMPO  2,2,6,6-tetramethylpiperidinyl-1-oxy
THF  tetrahydrofuran
TIPNO  2,2,5-trimethyl-4-phenyl-3-azahexane-3-aminooxyl
VAc  vinyl acetate
VOC  volatile organic compound
wt. %  weight percentage
w/v  weight per volume
Chapter 1

General

Introduction
1.1 Introduction

1.1.1 Introduction to Radical Polymerization (RP)

Radical polymerization (RP) has advantages over other chain-growth (ionic or coordination polymerizations) and step-growth polymerizations as it can be carried out under less demanding conditions. Solvents and monomers do not require rigorous purification from trace amounts of water, oxygen and other impurities prior to polymerization. Unlike ionic polymerization, radical polymerization is compatible with both electron deficient and electron rich double bond monomers, and can be carried out in a large variety of reaction media, including: bulk (for liquid monomers), solution, emulsion (water), precipitation, dispersion and suspension polymerizations. A further significant advantage of radical polymerization over ionic polymerization is that it can be conducted in an aqueous medium (emulsion). An emulsion polymerization consists of water insoluble monomer dispersed in an aqueous medium, which can be used to produce polymer particles with diameters in the range of 10 nm to 100 µm.\[1\] Since radical polymerizations are tolerant to impurities in solvents and monomers, they can be applied to many different monomer classes, and can be carried out in various media (especially water). Radical polymerization accounts for approximately 50% of all commercially produced polymers.\[2\]

Many commercially important polymers are synthesized on a large scale via radical polymerization. Examples include low-density polyethylene (LDPE) (produced at high pressures), poly(vinylchloride) (PVC), poly(styrene), poly(methyl methacrylate), poly(vinyl acetate) and poly(tetrafluoroethylene) (PTFE).\[3\]
1.1.2 Conventional Radical Polymerization

A conventional radical polymerization mechanism consists of initiation, propagation, chain transfer events and termination (Scheme 1.01).

Initiation (e.g. using \(^{1}\text{BuO-OBu}^t\) as an initiator):

\[
\begin{align*}
^{1}\text{BuO} + \text{OBu}^t & \xrightarrow{\Delta} 2 \text{BuO}^* & \text{M} & \xrightarrow{k_i} \text{BuO-M}^* \\
\end{align*}
\]

Propagation:

\[
\begin{align*}
\text{BuO-M}^* & \xrightarrow{k_p} \text{P}_n^* & \text{M} & \xrightarrow{k_p} \text{P}_{n+1}^* \\
\end{align*}
\]

Chain transfer:

\[
\begin{align*}
\text{P}_n^* + \text{X-Y} & \xrightarrow{k_{tr}} \text{P}_n \text{X} + \text{Y}^* \\
\end{align*}
\]

Reinitiation:

\[
\begin{align*}
\text{Y}^* + \text{M} & \xrightarrow{k_{ri}} \text{P}_n^* \\
\end{align*}
\]

Termination:

\[
\begin{align*}
\text{P}_n^* + \text{P}_m^* & \xrightarrow{k_t} \text{P}_n \text{P}_m \\
\end{align*}
\]

Scheme 1.01 General conventional radical polymerization mechanism.

Initiation occurs in two steps; first the radical initiator (e.g. AIBN or a peroxide) decomposes thermally to give two initiating radicals, \(^1\text{BuO}^*\), with the rate coefficient for dissociation, \(k_d\). The rate of radical production \(R_{pr}\) is expressed by equation 1.01:

\[
R_{pr} = 2f k_d [\text{Initiator}] \quad (1.01)
\]

where \([\text{Initiator}]\) is the initiator concentration, the factor of 2 accounts for two initiating radicals produced during thermal initiation (e.g. using azo- and peroxide initiators) and \(f\) is the initiator efficiency which is less than 1 due to side reactions of the initiator derived radicals. For example, some of the 2-cyanoisopropyl radicals, \((\text{CH}_3)_2(\text{CN})\text{C}^*\), derived from
AIBN decomposition can disproportionate inside the solvent cage to give methacrylonitrile, CH$_2$=CCH$_3$(CN)$_2$. The second step involves the addition of the initiator radical, (tBuO$^\bullet$), onto the unsubstituted carbon atom (tail addition) of the monomer double bond.$^{[4]}$ Tail addition always occurs because of an increase in radical stability (tBuO−M$^\bullet$ Scheme 1.01) due to stabilization of the adduct radical. The addition step is not influenced by steric factors of the alkene substituents$^{[5]}$ resulting in fast rates of addition. The rate of initiator radical addition, $R_{add}$, is shown in equation 1.02:

$$R_{add} = k_i[R^\bullet][M]$$  (1.02)

Where $k_i$ is the rate coefficient for addition, $[R^\bullet]$ is the concentration of initiator radicals and [M] is the monomer concentration. The overall rate of initiation ($R_i$) is determined by the rate of initiator decomposition (equation 1.01) since the rate of addition ($R_{add}$) is much faster. i.e. $k_d << k_i$.

Propagation involves the successive addition of monomer units (M) to the propagating radical P$_n^\bullet$ with high regioselectivity (head to tail addition) which has a rate coefficient of propagation, $k_p$. The rate of monomer addition to the propagating radical is influenced by polar, resonance and steric effects resulting from the substituents bonded to the monomer double bond and the radical center.$^{[5]}$ For example, styrene has a relatively low $k_p$ (341 L mol$^{-1}$ s$^{-1}$ at 60 °C$^{[6]}$) in comparison to other monomer classes (e.g for MMA, $k_p$ = 833 L mol$^{-1}$ s$^{-1}$ at 60 °C$^{[7]}$) because the propagating radical is resonance stabilized by the adjacent phenyl group leading to slower monomer addition. $k_p$ is assumed to be independent of propagating radical chain length if the degree of polymerization ($DP$) is greater than 20.$^{[8]}$ $^{[9]}$The overall rate of propagation, $R_p$, can be expressed by equation 1.03:

$$R_p = \frac{-d[M]}{dt} = k_p[P_n^\bullet][M]$$  (1.03)

where $[P^\bullet]$ and [M] are propagating radical and monomer concentrations, respectively.

Chain transfer is the reaction of a propagating radical (P$_n^\bullet$) with a chain transfer agent (X−Y) to yield a dead polymer chain (P$_n$−X) and a small radical (Y$^\bullet$) which is capable of addition to monomer (M) to initiate a new propagating chain.$^{[5]}$ Further details on chain transfer are given below in section 1.1.3.

Termination is the reaction of two propagating radicals to produce a dead polymer chain. Termination can occur via combination (one dead polymer chain). Bimolecular
combination is the most common pathway for most vinyl monomers such as styrene,\textsuperscript{10} acrylonitrile\textsuperscript{11} and methyl acrylate.\textsuperscript{12} Alternately, termination can occur by disproportionation (hydrogen transfer from one propagating radical to another, producing a saturated and an unsaturated product). Disproportionation is more likely to occur for sterically hindered propagating radicals such as \( \alpha \)-methyl vinyl monomers (e.g. methyl methacrylate).\textsuperscript{10} The overall rate coefficient of termination (\( k_t \)) is the sum of rate coefficients of termination by combination (\( k_{tc} \)) and by disproportionation (\( k_{td} \)) (i.e. \( k_t = k_{tc} + k_{td} \)). The overall rate of termination, \( R_t \), is expressed by equation 1.04:

\[
R_t = \frac{-d[P^\bullet]}{dt} = 2k_t[P^\bullet]^2
\]  

(1.04)

where the factor of 2 accounts for the loss of two propagating radicals during bimolecular termination (combination or disproportionation).

At the beginning of a conventional radical polymerization the concentration of propagating radicals increases and reaches a steady state almost instantaneously (~1s). Initiation and termination are continuously occurring throughout the polymerization. The lifetime of a radical is in the order of 1s. The rate of initiation (\( R_i \)) is equal to the rate of termination (\( R_t \)) once the steady state is reached. This results in a constant propagating radical concentration. \( R_i = R_t \) as expressed by equation 1.05:

\[
R_t = R_i = 2k_t[P^\bullet]^2 = 2f k_d[I]
\]  

(1.05)

The propagating radical concentration can be determined by the rearrangement of equation 1.05 to give equation 1.06:

\[
[P^\bullet] = \sqrt{f k_d[I]/k_t}
\]  

(1.06)

Over the lifetime of a radical, propagation occurs hundreds to thousands of times while initiation only occurs once. Therefore the overall rate of polymerization is determined by the rate of propagation (\( R_p \)). Inserting \([P^\bullet]\) from equation 1.06 into the rate of propagation (equation 1.03) gives the rate of conventional radical polymerization under steady state kinetics, equation 1.07:

\[
R_p = k_p \sqrt{f k_d[I]/k_t} [M]
\]  

(1.07)
The rate of polymerization is first order with respect to monomer concentration, and half order with respect to initiator concentration.

### 1.1.3 Chain Transfer

A chain transfer agent (CTA) can be a specially designed small molecule (containing an easily abstractable atom) added to the polymerization to fulfil a specific purpose; to control the molecular weight (MW) by decreasing the MW of individual polymer chains by producing more polymer chains than would ordinarily occur in the absence of chain transfer where the combined length of all chains remains unchanged or to introduce specific end groups to polymers. For example, an ω-unsaturated end group can be introduced into a polymer by the use of addition fragmentation chain transfer (AFCT). Allylic CTAs (CH$_2$=C(CH$_2$-Y)(R)) containing double bonds with reactivity towards propagating radicals, and a suitable leaving group (Y) capable of reinitiation are used in AFCT. The addition of the CTA to a propagating radical is followed by β-fragmentation yielding a macromonomer, which contains the ω-unsaturated end group, and a small radical which initiates a new polymer chain.$^{[13]}$

Other reagents in a polymerization mixture; monomer, polymer, solvent, initiator etc. can act as CTAs that can undergo unwanted chain transfer reactions. Chain transfer to various species can occur with both conventional and controlled/living radical polymerization. Chain transfer to small molecules lowers the polymer chain length by premature termination of the propagating radical which results in a lower average MW than is theoretically expected in the absence of chain transfer. Chain transfer to polymer can result in midchain radicals which can lead to branching, resulting in higher average MWs than expected in the absence of chain transfer.

Ideally all chain transfer processes don’t influence the overall rate of polymerization ($R_p$) if the rate coefficient of reinitiation ($k_{ri}$) is greater than that of propagation ($k_p$) and the rate coefficient of chain transfer ($k_{tr}$) is significantly large.$^{[8]}$ The rate of polymerization is therefore unaffected because the concentration of propagating radicals remains unchanged since the radical centre is transferred from one polymer chain to another. Chain transfer results in an upper limit in accessible molecular weight (and corresponding degree of polymerization, $DP$) for both a conventional and controlled/living radical polymerization.$^{[14]}$ The magnitude of the extent of chain transfer is quantified by the ratio of $k_{tr}$ to $k_p$ ($C_{tr} = k_{tr}/k_p$).
\[
\frac{1}{\text{DP}}_n = \frac{1}{\text{DP}}_{n,0} + C_{tr} \frac{\text{[CTA]}}{\text{[M]}} \tag{1.08}
\]

The classical Mayo equation\textsuperscript{[15]} (equation 1.08) is used to determine the \( C_{tr} \) value of a CTA by relating the average degree of polymerization, \( \text{DP}_n \) to the ratio of CTA to monomer concentrations. \( \text{DP}_{n,0} \) denotes the average degree of polymerization in the absence of chain transfer. \([\text{CTA}]\) is the concentration of the chain transfer agent and \([\text{M}]\) is the monomer concentration. Chain transfer to solvent and monomer are investigated in Chapter 2 with details on determining \( C_{tr} \) values experimentally.

### 1.2 Controlled/Living Radical Polymerizations (CLRP)s

#### 1.2.1 Introduction to CLRP\( \text{s} \)

The term living polymerization can be defined as a chain growth polymerization in which chain termination and irreversible chain transfer are absent.\textsuperscript{[16]} The polymer chain will continue to grow provided sufficient monomer is available. The term living polymerization was first used to describe an anionic polymerization by Szwarc.\textsuperscript{[17]} Living polymerization refers to end-group preservation that allows the production of block copolymers by the addition of more monomer. A living polymerization does not specifically control the molecular weight (MW) or give narrow molecular weight distributions (MWD).

The term controlled polymerization is used to describe a radical polymerization in which reversible-deactivation of the chain carriers is an essential component of the mechanism, interrupting the propagation to secure control of one or more kinetic features (MW and polydispersities, \( M_w/M_n \)) of the polymerization or one or more structural aspects of the macromolecules formed, or both.\textsuperscript{[16]} The exchange between the active and dormant species allows slow but simultaneous growth of all chains while keeping the concentration of radicals low enough to minimize termination.\textsuperscript{[18]} The lifetime of propagating chains is extended from \( \sim 1s \) (Conventional RP) to \( \sim \)hours (CLRP).

A CLRP describes polymerizations that exhibit both living character through end-group preservation, and control over MW and MWD by minimizing unwanted termination and chain transfer events.
Scheme 1.02 equilibrium established between active and dormant states in a CLRP.\textsuperscript{[19]}

CLRP systems should obey the following criteria\textsuperscript{[18]}:

1. \textit{First order kinetics with respect to monomer:}

   A linear increase of \(\ln[M]_0/[M]\) vs conversion is observed if the polymerization is first-order with respect to monomer concentration. A straight line indicates only a constant number of propagating chains and will also be observed under the steady-state established during conventional RP.

2. \textit{Linear }\textit{M}_\text{w}/\textit{degree of polymerization (DP}_\text{n})\text{ with conversion.}

   A straight line indicates a constant number of propagating chains that all begin to grow simultaneously and continue to grow throughout the polymerization. Deviation from linearity indicates chain transfer or termination reactions.

3. \textit{Narrow polydispersities }\textit{(M}_\text{w}/\textit{M}_\text{n})\text{ with low polydispersities }\textit{(M}_\text{w}/\textit{M}_\text{n}<1.5)\text{ desirable for controlled/living systems. Provided that the rate of initiation is greater than that of propagation and all polymer chains grow at the same rate low MWDs will be achieved. The ratio of }\textit{M}_\text{w}/\textit{M}_\text{n}\text{ will remain narrow throughout the polymerization in the absence of unwanted chain transfer or termination.}

4. \textit{Preserved end-functionality.}

   Living polymer chains will be achieved in the absence of termination. End-group functionality allows the chain extension of the polymer with the introduction of additional monomer to form block copolymers.

   The pioneering work by Solomon and Rizzato\textsuperscript{[20]} in 1986 and Georges in 1993\textsuperscript{[21]} led to the development of nitroxide-mediated radical Polymerization (NMP). In 1995, Matyjaszewski\textsuperscript{[22]} and Sawamoto’s\textsuperscript{[23]} use of transition metal complexes to control polymerizations became known as atom transfer radical polymerization (ATRP). Reversible
Chain transfer agents were utilized by CSIRO\textsuperscript{[24]} in 1998 to establish reversible addition-fragmentation chain transfer (RAFT) polymerization. These are the three most commonly used CLRPs.

The use of alkyl iodides as chain transfer agents by Tatemoto in 1978 led to the development of iodine transfer radical polymerization (ITP)\textsuperscript{[25]} and more recently in 2002 Yamago\textsuperscript{[26]} reported organotellurium-mediated living radical polymerization (TERP). ITP and TERP are less commonly used.

Further details on these five CLRPs are discussed below.

### 1.2.2 Nitroxide-Mediated Radical Polymerization (NMP)

NMP\textsuperscript{[27]} is the simplest of the CLRPs discussed in this section. NMP is an example of a stable free radical polymerization and follows a reversible dissociation-combination mechanism\textsuperscript{[28]} (Scheme 1.03).

\[
\begin{align*}
P_n & \rightleftharpoons P_n^* + T^* \\
\text{"Dormant"} & \quad \text{"Active"} \\
\end{align*}
\]

**Scheme 1.03** General mechanism for an alkoxyamine initiated NMP.

Control is achieved by the addition of a stable free radical, (T\textsuperscript{*}), which reversibly traps propagating radicals, (P\textsubscript{n}\textsuperscript{*}), to extend its lifetime. The radical trap T\textsuperscript{*}, is a nitroxide (Scheme 1.04) which is a stable \textit{N,N}-disubstituted N-O persistent radical with a delocalised unpaired electron.

**Scheme 1.04** Nitroxides used in NMP.
At sufficiently high temperatures the dormant chain (alkoxyamine, $P_n^−-T$) is dissociated thermally back into a propagating polymer radical, $P_n\cdot$ and the stable free nitroxide $T\cdot$ with a rate coefficient for dissociation ($k_{act}$) and the stable free nitroxide $T\cdot$. In the presence of monomer $M$, $P_n\cdot$ undergoes propagation until it is deactivated to give back the dormant $P_n^−-T$ with a rate coefficient for combination ($k_{deact}$). The rate coefficient $k_{deact}$ is typically several orders of magnitude greater than that of $k_{act}$, which results in an equilibrium between active and dormant polymer chains that favours the dormant state. The equilibrium constant, $K$, establishes a relationship between $k_{act}$ and $k_{deact}$ (equation 1.09). The low concentration of active chains significantly reduces the chance of irreversible termination or chain transfer events. When the reversible activation-deactivation cycle occurs frequently enough over the course of the polymerization, every chain will have an approximately equal probability of growing; which leads to a low polydispersity polymer.

$$K = \frac{k_{act}}{k_{deact}} = \frac{[P\cdot][T\cdot]}{[P^−-T]}_0$$  (1.09)

TEMPO (Scheme 1.04) was the first nitroxide to successfully carry out a controlled/living NMP which was first described by the group of Georges at XEROX in 1993.\cite{21} In this early work low polydispersity polystyrene was achieved using a bimolecular system of benzyl peroxide with free TEMPO in bulk to control the polymerization. High temperatures ($125 − 145 \, ^\circ C$) and long polymerization times (up to 72 hrs) were required to achieve high conversions ($> 85\%$) with polydispersities of $M_w/M_n = 1.26$. TEMPO’s success in NMP is limited to controlling the polymerization of styrene and styrene derivatives.\cite{29} TEMPO is unable to control other vinyl monomer polymerizations such as acrylate and acrylamides because of the relatively strong Carbon−Oxygen bond in the formed alkoxyamine ($P_n^−-T$).

In order to polymerize a greater variety of monomer classes, new second generation asymmetric, acyclic nitroxides containing an $\alpha$-hydrogen were developed to control the polymerization of monomers such as acrylates and acrylamides. 2,2,5-Trimethyl-4-phenyl-3-azaheaxane-3-aminooxyl (TIPNO)\cite{30} and $N$-tert-butyl-$N$-[1-diethylphosphono-(2,2-dimethylpropyl)] nitoxide (SG1) (Scheme 1.04)\cite{31} are widely used acyclic nitroxides. TIPNO and SG1 are more sterically hindered than TEMPO which leads to a decreased Carbon−Oxygen bond strength in the alkoxyamine, resulting in higher $k_{act}$ and lower $k_{deact}$ relative to TEMPO at a given temperature. The presence of an $\alpha$-hydrogen makes TIPNO and
SG1 more unstable than TEMPO, resulting in nitroxide degradation during NMPs preventing the build-up of nitroxide. The large $K$ value of TIPNO and SG1 relative to TEMPO results in NMPs controlled by SG1 and TIPNO taking a longer time than TEMPO to reach a steady state. TIPNO, SG1 and analogues have been used to control the polymerization of a wide variety of monomers including; styrene,$^{[30]}$ acrylates,$^{[30]}$ acrylamides,$^{[30, 32-37]}$ acrylic acid,$^{[38]}$ 1,3-dienes,$^{[39]}$ and acrylonitrile.$^{[30, 40]}$ The NMP of methacrylates is problematic because of disproportionation between the propagating radical and the free nitroxide. It was shown by McHale that the addition of a large excess of SG1 did not help improve the control of the NMP of MMA. The abstraction from the $\alpha$-methyl hydrogen of poly(MMA) propagating radical by SG1 increases with SG1 concentration.$^{[31]}$ Charleux et al. controlled the NMP of MMA initiated with a SG1-based alkoxyamine in the presence a small amount (8.8 mol %) of a suitable co-monomer such as styrene$^{[41]}$ or acrylonitrile.$^{[42]}$ The co-monomer has a lower $K$ value which reduces the overall $K$ for the system, leading to a higher proportion of living polymers with MMA-comonomer-SG1 chain-ends.

### 1.2.3 Atom Transfer Radical Polymerization (ATRP)

ATRP is a CLRP technique that utilizes transition metal catalysts to form new carbon-carbon bonds during the polymerization. ATRP follows a reversible dissociation-combination mechanism as described in Scheme 1.05.$^{[43]}$ An ATRP is a multi-component system including monomer, initiator (containing a transferable halogen) and a catalyst (a transition metal species with a suitable ligand). An alkyl halide is typically used as the initiating species and will also determine the number of growing polymer chains.
Scheme 1.05 General mechanism for ATRP polymerization.

The initiator (R-X) undergoes fast homolytic fission upon reduction by the metal species (Mt⁰), which is capable of increasing its oxidation number and complexing with ligand (L). The metal complex (X-Mtⁿ⁺⁻¹-L) formed is reversibly deactivated upon reduction with R*. While the R* is in the active state it can react with monomer to form a propagating radical (Pⁿ●). Pⁿ● will propagate further until it is reversibly deactivated to form a dormant halide capped polymer chain (Pⁿ-X) and the original metal complex (Mt₀/L). Termination is minimized due to the persistent radical effect. Additional monomer can be added to form block copolymers. The theoretical MW $M_{n,th}$ is determined by the alkyl halide initiator to monomer ratio shown in equation 1.10.

$$M_{n,th} = \frac{\alpha[M] \cdot MW_{mono}}{[Alkyl \ halide]_0} + MW_{Alkyl \ halide}$$

Where $\alpha$ is the monomer conversion, $[M]_0$ is initial monomer concentration, $MW_{mono}$ is the molecular weight of monomer, $[Alkyl \ halide]_0$ is the initial concentration of the alkyl halide initiator. ATRP has been used to control many different monomers including; styrenes acrylates, methacrylate, acrylamides, methacrylamides, acrylonitrile and 1,3-dienes. Conventional radical initiators (e.g AIBN) can also be employed to initiate an ATRP alongside a transition metal complex in a higher oxidation state (e.g. CuBr₂(dNbpy)₂) This
has been named reverse ATRP\cite{44}. The mechanism for a reverse ATRP proceeds as shown in Scheme 1.06:

\[
\begin{align*}
I_2 & \rightarrow 2I^* \\
I^* + XM^{n+1/L} & \leftrightarrow I - X + M^n/L \\
\text{eqn. on M} & = \frac{k_i}{M} \\
P_n^* + XM^{n+1/L} & \leftrightarrow P_n - X + M^n/L
\end{align*}
\]

**Scheme 1.06** Initiation step for a reverse ATRP with conventional radical initiator.

### 1.2.4 Reversible Addition-Fragmentation Chain Transfer (RAFT)

RAFT\cite{45} polymerization was first developed and reported by CSIRO\cite{24} in 1998. At the same time, Zard et al.\cite{46} reported macromolecular design via interchange of xanthate (MADIX) which follows the same mechanism as RAFT. MADIX differs to RAFT only in that it uses xanthates as controlling agents. The concept of RAFT is similar to other CLRPs. It works on the principle of reversible reactivation of propagating radicals and the formation of an equilibrium between active and dormant states. Unlike NMP the mechanism operates under the degenerative chain transfer mechanism. Control is achieved by inclusion of a suitable thiocarbonylthio compound (RAFT agent Figure 1.01) into a conventional radical polymerization. Ideally the kinetics of a RAFT polymerization is identical to conventional radical polymerization if the selected RAFT agent behaves like an ideal chain transfer agent. (see section 1.1.3 on chain transfer). The rate of polymerization is therefore half order with respect to initiator concentration and independent of RAFT agent concentration.\cite{45} Steady state kinetics is established with a balance between initiation and termination. The RAFT mechanism proceeds as shown in Scheme 1.07.\cite{45}
Figure 1.01 Examples of different RAFT (and MADIX) agents and monomer classes they commonly control.

<table>
<thead>
<tr>
<th>RAFT Agent</th>
<th>Z</th>
<th>R</th>
<th>Monomers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dithioesters</td>
<td>Ph</td>
<td>C(Me)₂Ph</td>
<td>MA, methacrylamide</td>
</tr>
<tr>
<td>Trithiocarbonates</td>
<td>S(Me)</td>
<td>H(C(Ph)CO₂)H</td>
<td>St, acrylamide, acrylate</td>
</tr>
<tr>
<td>Dithiocarbamates</td>
<td>N(Et)₂</td>
<td>CH₂Ph</td>
<td>VAc, vinyl amide</td>
</tr>
<tr>
<td>Xanthate</td>
<td>OEt</td>
<td>C(Me)₂CN</td>
<td>VAc</td>
</tr>
</tbody>
</table>

**Scheme 1.07** General mechanism of RAFT Polymerization.⁴⁵
Initiation occurs in the same way as conventional radical polymerization. The initiator decomposes to give two initiating radicals, which subsequently adds to the monomer to give a propagating chain ($P_n^\cdot$). The $P_n^\cdot$ reversibly adds onto the RAFT agent (I) to form a RAFT intermediate radical (II), which is followed by fragmentation of intermediate radical (II) giving a polymeric RAFT (III) and a new radical ($R^\cdot$). The reaction of $R^\cdot$ radical with the monomer (M) initiates a new polymer chain ($P_n^\cdot$) which in turn adds onto the polymeric RAFT. Rapid equilibrium between the active propagating radicals, $P_n^\cdot$ and $P_m^\cdot$ and the dormant polymeric thiocarbonylthio (III) by way of the intermediate (IV) ensures that all chains have the same probability of growing, leading to a low polydispersity polymer. The theoretical MW ($M_{n,th}$) achieved can be calculated by equation 1.11:

$$M_{n,th} = \frac{\alpha[M]MW_{\text{mono}}}{[\text{RAFT}]} + MW_{\text{RAFT}}$$  \hspace{1cm} (1.11)

where $\alpha$ is monomer conversion, [M] is monomer concentration, $MW_{\text{mono}}$ is the molecular weight of the monomer, [RAFT] is the RAFT agent concentration and $MW_{\text{RAFT}}$ is the molecular weight of the RAFT agent.

The choice of RAFT agent (Figure 1.01) is important for the success of a RAFT polymerization. The initial RAFT agents (I) and the polymeric RAFT agent (III) should have a reactive C=S double bond (high rate coefficient for addition, $k_{\text{add}}$). The intermediate radicals (II) and (IV) should fragment rapidly (high rate coefficient of fragmentation, $k_{\beta}$). Z and R groups should be chosen that are compatible with the particular monomer class being polymerized. The R group must be a better leaving group than the incoming $P_n^\cdot$ ($k_{\beta} > k_{\text{add}}$) and must be able to rapidly initiate a new polymer chain as most polymer chains must originate from the R group of the RAFT agent. The Z group activates or deactivates the thiocarbonyl double bond to radical addition and modifies the stability of the intermediate radical. The rate of addition of $P_n^\cdot$ to RAFT agent is increased when $Z = \text{Ph}$ (dithioesters) or $Z = \text{S(Me)}$ (trithiocarbonates) making them suitable for RAFT polymerizations of more activated monomers (MAMs) such as styrenes, (meth)acrylates or meth(acrylamides). The rate of addition of $P_n^\cdot$ to RAFT agent is inhibited when $Z = \text{OEt}$ (xanthates or N(Et)$_2$ (dithiocarbamates) making them suitable for RAFT polymerizations of less activated monomers (LAMs) such as vinyl esters, vinyl amides or vinyl ethers (Figure 1.01). Resonance structures of xanthate and dithiocarbamates (Scheme 1.08) explain the lower
activity of the thiocarbonyl double bond, through delocalization of the lone pairs on oxygen and nitrogen. The stabilization reduces the rate of addition of LAMs to the RAFT agent.\textsuperscript{[47]}

\begin{equation}
\text{Scheme 1.08 Resonance structures of dithiocarbamate and xanthate.}
\end{equation}

A successful RAFT requires a continuous source of radicals being generated throughout the polymerization as initiation and termination continuously occur throughout unlike NMP which requires all radicals to be produces rapidly at the start. Living characteristics are observed if the MW of the polymer formed is substantially lower than that which would be formed under the same conditions but in the absence of a RAFT agent, and is such that the number of polymer chains with RAFT agent derived ends far exceeds the number formed as a consequence of termination.\textsuperscript{[45]} After the polymerization is completed, living macroRAFT end groups are retained. Additional initiator must be added in order to chain extend a macroRAFT with more monomer to form a block copolymer. In order to prepare block copolymers, the monomer with the highest rate of transfer towards the RAFT agent must be polymerized first, as this will favour fragmentation of the first block when the propagating radical of the second block is added to the C=S bond.\textsuperscript{[48]} e.g. to copolymerize MMA and St, the MMA block must be polymerized first.

1.2.5 Iodine Transfer Radical Polymerization (ITP)
ITP is another example of a degenerative transfer radical polymerization and utilizes alkyl iodides as chain transfer agents.\textsuperscript{[25]} ITP was used to give low polydispersities in the polymerization of fluoro-olefins.\textsuperscript{[49]} The mechanism described in Scheme 1.09 proceeds as follow.\textsuperscript{[50]}
An initiating radical is generated from a conventional radical initiator which adds to the monomer to form a propagating radical ($P_n^\bullet$). The propagating radical ($P_n^\bullet$) abstracts iodine from the chain transfer agent ($I-R$) to give a polymeric alkyl iodide ($P_n-I$), and a new radical ($R^\bullet$) capable of initiating a new chain. $R^\bullet$, generated from the alkyl iodide adds onto a monomer unit to form a new chain ($P_m^\bullet$). An equilibrium is established between active propagating $P_n/P_m$ radicals and the dormant polymeric alkyl iodide ($P_n-I$). As with all CLRPs, some termination inevitably occurs in ITP. The termination step is minimized in order to achieve good control.

The iodoalkyl compounds used as CTAs in ITP contain a weak Carbon–Iodine bond, which is advantageous for efficient iodine abstraction by $P_n^\bullet$, however these CTAs are unstable and prone to degradation. To overcome this limitation Lacroix-Desmazes et al. developed reversible iodine transfer polymerization (RITP). Molecular iodine is added, it reacts with radicals from the initiator to generate the reversible CTA in situ.
1.2.6 Organotellurium-Mediated Radical Polymerization (TERP)

Organotellurium-mediated living radical polymerization is the most recent type of CLRP. TERP was first proposed to mainly operate under a reversible chain transfer mechanism by homolytic substitution under thermal initiation followed by propagation similar to an alkoxyamine during the NMP process. The mediating agents (R-TeMe) was shown to homolytically cleave to give R● and ●TeMe radicals with bond dissociation energies comparable to a TEMPO alkoxyamine.

In a subsequent kinetic study it was found that TERP predominantly proceeds by degenerative transfer (similar to ITP) rather than dissociation combination. This LRP proceeds via two different competing pathways. The R● and ●TeMe radicals generated will act as a source of radicals to initiate the polymerization.

1.3 Radical Polymerization in Supercritical Carbon Dioxide (scCO₂)

1.3.1 Introduction

A supercritical fluid is a substance above a certain temperature and pressure, known as the critical point. As this critical temperature and pressure are approached, the liquid expands to form a vapour-like state above the surface of the liquid. Once the critical point is reached there is no interface between liquid or vapour phase, a single continuous phase exists and this is what is known as the supercritical state. Carbon dioxide has a readily accessible critical point of 31.1 °C and 7.38 MPa, which are relatively mild conditions compared to other supercritical fluids such as water (374.2 °C and 22.05 MPa). Above the critical point CO₂ exhibits liquid-like density and gas-like diffusivity. A CO₂ molecule is linear under normal conditions with a zero dipole moment, however, in the supercritical state it is slightly non-linear which induces a weak dipole. This gives scCO₂ the ability to dissolve a large number of organic molecules. The density of the supercritical fluid can be altered by small changes in temperature and pressure which leads to changes in solvating ability. CO₂ is an inert, non-toxic, non-flammable, cheap, commercially available gas which can also be easily recycled. CO₂ does not undergo chain transfer reactions with propagating radicals, making it an ideal medium for all radical polymerizations (both conventional and controlled/living). DeSimone et al. carried out the first homogeneous radical polymerization in scCO₂, which has led to scCO₂ being used industrially on a large scale. PTFE also known as TEFLON is commercially produced using scCO₂ as the reaction medium.
Many different types of conventional radical polymerization processes can be carried out in \( \text{scCO}_2 \); solution,\(^{[59]} \) suspension,\(^{[61, 62]} \) (mini)emulsion,\(^{[63-65]} \) precipitation\(^{[66, 67]} \) and dispersion\(^{[68]} \) polymerizations. Only fluoropolymers and polysiloxane polymers are completely soluble at the beginning and throughout the polymerization (solution polymerization).

### 1.3.2 Heterogeneous Controlled/Living Radical Polymerization in \( \text{scCO}_2 \)

Most polymerizations in \( \text{scCO}_2 \) are heterogeneous, where polymer formation does not occur in the continuous phase (\( \text{scCO}_2 \)). Suspension and emulsion polymerizations are heterogeneous from the offset. In a controlled/living precipitation polymerization\(^{[69, 70]} \) the monomer, initiator, controlling agent etc. are all soluble in the monomer/\( \text{scCO}_2 \) solution at the beginning of the polymerization. The polymer chains grow linearly up to a critical degree of polymerization (\( J_{\text{crit}} \))\(^{[71-74]} \) after this point the polymer chains are insoluble and the system becomes heterogeneous.Polymerization continues in the monomer rich particle phase. A dispersion polymerization\(^{[68, 75]} \) begins in the same way as a precipitation polymerization, with the addition of a colloidal stabilizer to prevent coagulation of particles after \( J_{\text{crit}} \).

In 2009, Zetterlund, Aldabbagh and Okubo\(^{[76]} \) published a review on heterogeneous controlled/living radical polymerizations in supercritical carbon dioxide. The review provides a detailed account of published precipitation and dispersion polymerizations using NMP, RAFT and ATRP in \( \text{scCO}_2 \). The following section is a literature review of heterogeneous CLRPs (including IRP) in \( \text{scCO}_2 \) that has been published since 2009.

### 1.3.3 Precipitation NMP

A model has been developed by O’Connor et al.\(^{[71]} \) that predicts \( J_{\text{crit}} \) as a function of both targeted molecular weight and initial monomer loading. \( J_{\text{crit}} \) values were obtained for NMP of styrene at 110 °C and \( \text{tert-} \)butylacrylate (\( \text{t-BA} \)) at 118 °C in \( \text{scCO}_2 \) mediated by SG1. \( J_{\text{crit}} \) increased close to linearly with increasing initial monomer loading and pressure for both monomers. \( J_{\text{crit}} \) values were found to be higher for \( \text{t-BA} \) than for St. Interestingly this approach can also be applied to other CLRPs like ATRP and RAFT as \( J_{\text{crit}} \) depends on polymer chain length only and is valid for dispersion polymerizations too.
1.3.4 Dispersion NMP

Block copolymers of poly(dimethylsiloxane-b-styrene) (PDMS) and poly(pentafluorostyrene-b-styrene) (PPFS) were prepared in scCO$_2$ for use as stabilizers during dispersion polymerizations.$^{[77]}$ Styrene was polymerized using TEMPO as nitroxide at 130 °C using PDMS and PPFS as surfactants. Conversions up to 35% in 4 hours were obtained with polydispersities in the range of 1.20 – 1.40.

Grignard and coworkers carried out a dispersion NMP of methyl methacrylate (MMA) in scCO$_2$. They used the method developed by Charleux, adding a small percentage of a comonomer (8.8 mol% styrene) to reduce the overall equilibrium constant, $K$ of the polymerization.$^{[41]}$ The polymerization was done in the presence of a CO$_2$-philic perfluorinated stabilizer (poly(heptadecafluorodecyl acrylate-b-methyl methacrylate) which was generated in situ during the dispersion NMP initiated by the commercially available SG1 based alkoxyamine, blockbuilder. Low polydispersities ($M_w/M_n = 1.26 – 1.31$) were achieved despite the lack of added excess free nitroxide.

1.3.5 Suspension NMP

The first stabilizer-free inverse suspension controlled/living polymerization in scCO$_2$ was reported by O’Connor in 2011.$^{[79]}$ The NMP of $N$-isopropylacrylamide (NIPAM), which is not initially soluble in scCO$_2$, proceeded to high conversion (80%) using SG1 as nitroxide. A linear increase of $M_n$ was observed with all $M_n$s close to $M_n,th$. The polymer was isolated as a dry polymer powder after purification using CO$_2$ until free from monomer (by $^1$H NMR) without using any VOCs in the workup.

Thermoresponsive block copolymers containing NIPAM were prepared by two successive heterogeneous NMPs in scCO$_2$ using SG1 as nitroxide (Scheme 1.10).$^{[80]}$ The first blocks of $N,N'$ dimethylacrylamide (DMA), tert-butyl acrylate (t-BA) and styrene (St) were prepared by precipitation and used as macrorinitiators. The macrorinitiators were chain extended with NIPAM to give various block copolymers (Scheme 1.10). Lower critical solution temperature (LCST) measurements were taken of the block copolymers. The LCSTs increased when NIPAM was copolymerized with hydrophilic monomer, DMA and decreased when copolymerized with hydrophobic monomers, t-BA and St.
Scheme 1.10 Preparation of thermoresponsive block copolymers containing NIPAM.

1.3.6 Heterogeneous ATRP
Minami et al.\textsuperscript{[81]} carried out precipitation reverse ATRP of acrylic acid in scCO\textsubscript{2} poor control was achieved with a $M_n$ and $M_w/M_n = 3 \times 10^4$ g mol\textsuperscript{-1} and 2.08 respectively after methyl esterification. Chains were shown to contain living ends by the chain extension of poly(methyl acrylate), (PMA)-Cl as a macroinitiator with styrene. Poly(acrylic acid-b-styrene) was also prepared directly in scCO\textsubscript{2} using precipitation ATRP of AA followed by the addition of styrene.

Poly(vinyl acetate) was synthesized in scCO\textsubscript{2} using the CuBr/2,2′:6′,2″-terpyridine (tPy) complex as a catalyst and ethyl 2-bromoisobutyrate (EBiB) as an initiator.\textsuperscript{[82]} A linear increase in $M_n$ with conversion was achieved for [VAc]$_0$ : [EBiB]$_0$ : [CuBr]$_0$ : [tPy]$_0$ = 600 : 1 : 1 : 1 at 65 °C and 310 bar. MWs were in the range of 20 – 40,000 with $M_w/M_n = 1.6 – 2.0$. Considering the high MWs achieved, it is likely that the polymerization was a precipitation.

1.3.7 Dispersion RAFT
The RAFT polymerizations of styrene in the presence of a poly(styrene-b-dimethylsiloxane) stabilizer using AIBN as initiator, S-(thiobenzoyl) thioglycolic acid, methyl naphthalene dithiobenzoate, 4-methyl allyl dithiobenzoate, and N,N-dimethyl benzyl dithiocarbamate as RAFT agents.\textsuperscript{[83]} Stabilizer concentrations of 3 – 7 wt.% were used which yielded particles in the 1 μm range. S-(thiobenzoyl) thioglycolic acid was shown to give the best control of the four RAFT agents tested.

Jennings et al.\textsuperscript{[84]} carried out a one-pot synthesis of nanostructured polymeric microparticles made from block copolymers via RAFT as a dispersion polymerization in
Block copolymers were prepared by sequential addition of monomer to the reaction vessel using poly(dimethylsiloxane monomethyl methacrylate) (PDMS-MA) as stabilizer. A poly(MMA) first block was prepared as macroinitiator and was then copolymerized with various monomer classes such as methacrylates, acrylamides, and styrenics. Block copolymers were isolated as free-flowing powders without the use of additional organic solvents.

A kinetics study of the first (RAFT) dispersion copolymerization with crosslinking of styrene where s-thiobenzoyl thioglycolic acid (TBTGA) and dibenzoyl peroxide were used as RAFT agent and initiator, respectively at 80 °C was presented by Jaramillo-Soto et al. The same author showed copolymerization of methyl methacrylate (MMA) and ethylene glycol dimethacrylate (EGDMA) where TBTGA and AIBN were used as RAFT agent and initiator respectively at 65 °C. The effect of RAFT agent concentration on polymerization rate, molecular weight development, gel fraction, swelling index, and particle morphology were analysed in both cases.

1.3.8 Dispersion ITP
Kuroda et al. achieved submicron-sized poly(St) particles obtained directly as a dry powder by dispersion iodine transfer radical polymerization (ITP) and reversible chain transfer catalyzed polymerization (RTCP) in scCO2 using a siloxane stabilizer. Conversions up to 80% after 21 hours were achieved in both cases. $M_N$S were higher than theoretical $M_N$ ($M_{N,th}$) with relatively narrow polydispersities ($M_{W}/M_N = 1.50 – 1.70$). The same group reported the ITP using CHI3 and RTCP using N-iodosuccinimide of methyl methacrylate (MMA) in scCO2. Polymerizations proceeded to 80 % conversion after 6 h again yielding a dry polymer powder. $M_n$ increased with conversion and low polydispersities were achieved ($M_{W}/M_n = 1.30 – 1.40$) for RTCP and ($M_{W}/M_n = 1.50 – 1.70$) for ITP.
1.4 Thesis Aims and Objectives

Chapter 2:

- To investigate the effect of chain transfer to solvent in the conventional radical polymerization of TBAM and MEA using various linear and branched alcohols as solvents.
- To investigate chain transfer to solvent and monomer in the NMP of TBAM and MEA.
- To achieve the first CLRPs of MEA.

Chapter 3:

- To carry out the first nitroxide-mediated precipitation polymerization of styrene in scCO₂ in the absence of any excess free nitroxide with reasonably good controlled/living character.
- To compare the relative performances of novel fluorinated alkoxyamines as initiators for the NMP of styrene in scCO₂ (precipitation polymerization) and in toluene (solution polymerization).

Chapter 4:

- To carry out the first RAFT polymerization of MEA at lower temperature to avoid chain transfer during polymerization.
- To investigate the CO₂ responsiveness of the morpholine group of MEA.
- To produce novel amphiphilic tri-block copolymers from a chain extension of MEA macroRAFT with N,N-dimethylacrylamide (DMA) and styrene (St) followed by self-assembly into polymer nanoparticles.
- To investigate the effect of the addition of CO₂ to the nanoparticles suspended in water by ¹H NMR and TEM analysis.
Chapter 2

Chain transfer to solvent in the radical polymerization of structurally diverse acrylamide monomers using straight-chain and branched alcohols as solvents
2.1 INTRODUCTION

Chain transfer to solvent or monomer is the abstraction of an atom by a propagating radical to give a dead polymer chain and a small radical capable of initiating a new chain. For a given set of conditions, chain transfer results in an upper limit in accessible molecular weight for both a conventional and controlled/living radical polymerization (CLRP). In a recent report, chain transfer to solvent was shown to be a significant end-forming reaction in the conventional and nitroxide-mediated polymerization (NMP) of N-isopropylacrylamide (NIPAM) in DMF at 120 °C. The same chain transfer to solvent constant \( C_{tr,S} = k_{tr,S}/k_p \), the ratio between the rate coefficients for chain transfer to solvent and propagation, was shown to account for experimental molecular weight (MW) data for both conventional radical polymerization and NMP. In the case of CLRP, chain transfer can compromise both control and livingness by generation of dead chains (loss of propagating radicals) and accumulation of short chains (due to reinitiation) that give low MW tailing or broadening in the MW distribution (MWD) with increasing conversion. In the case of chain transfer to solvent, it has been shown that, as a consequence of the total number of chains increasing, the number average molecular weight \( M_n \) deviates downwards from the theoretical value \( M_{n,th} \) and may even decrease with increasing conversion, which is distinctly different from chain transfer to monomer where theory dictates that \( M_n \) never goes through a maximum. The value of \( M_n \) going through a maximum with increasing conversion has also been observed in the NMP of acrylic acid using 1,4-dioxane as solvent at 120 °C. Chain transfer to solvent has been detected in other CLRPs, for example causing a limiting \( M_n \) in the reversible addition-fragmentation chain transfer (RAFT) polymerization of acrylic acid at 80 °C in ethanol, 2-propanol and 1,4-dioxane and RAFT of hydrophobic acrylamide monomers at 90 °C in DMF and 1,4-dioxane.

Chain transfer to solvent should be a fundamental consideration when polymerizing monomers that are solids, and thus are not polymerized in bulk, but rather in solutions of organic solvents. NIPAM is such a monomer (a solid with m.p. 60 – 63 °C), which is commonly polymerized in solution. The inverse suspension NMP of NIPAM in supercritical carbon dioxide has been reported, in which case \( M_n \) did not deviate significantly from \( M_{n,th} \) consistent with chain transfer to CO\(_2\) (as well as chain transfer to monomer) being negligible.
Scheme 2.1 Acrylamide monomers used: *N*-tert-butylacrylamide (TBAM) and *N*-(2-morpholin-4-ylethyl) acrylamide (MEA).

We now report on chain transfer to solvent in the conventional radical polymerization of two alternative solid acrylamide monomers (Scheme 2.1) using various straight chain and branched alcohol solvents. *N*-(2-morpholin-4-ylethyl)acrylamide (MEA; m.p. 114 °C) and *N*-tert-butylacrylamide (TBAM; m.p. 126 – 129 °C) have important biotechnological applications. TBAM is a hydrophobic monomer often used as a comonomer to reduce the lower critical solution temperature (LCST) of poly(NIPAM).\[33, 98, 99\] MEA is less exploited, but has an ionisable heterocyclic substituent, which as a polymer can be used to complex with biomolecules such as DNA in potential non-viral gene vectors.\[100, 101\] The first CLRP of MEA is disclosed, and we examine the significance of chain transfer in limiting the controlled/living character in the NMP of this monomer. TBAM is a good monomer for studying chain transfer to solvent since it contains no obvious abstractable hydrogens. Alcohols were chosen as solvents since there are no systematic studies reported comparing *C*\(_{tr,S}\) with incremental differences in solvent chemical structure. The relationship between the extent of chain transfer to solvent for these two diverse acrylamides and the chemical structure of the alcohol solvent is detailed with the magnitude of the *C*\(_{tr,S}\) related to solvent suitability for NMP. All molecular weight measurements were conducted relative to polystyrene standards, and as such the absolute *C*\(_{tr,S}\) values reported in this work should be treated with caution.
2.2 EXPERIMENTAL

2.2.1 Materials
tert-Butyl acrylate (t-BA, Aldrich, 98%) was purified by distillation under reduced pressure to remove inhibitors. N-tert-butylacrylamide (TBAM, TCI, 98%) was recrystallized from 1:1 benzene/acetone before use. 2,2’-Azobisisobutyronitrile and 1,1’-azobis(cyclohexanecarbonitrile) (AIBN and ACN, DuPont Chemical Solution Enterprise) were recrystallized from MeOH before use, and tert-butyl peroxide (TBP, Aldrich, 98%) was used as received. 1-Propanol (Aldrich, 99%), 1-butanol (TCI, 99%), 1-pentanol (Aldrich, 99%), 1-hexanol (Aldrich, 98%), 1-heptanol (Aldrich, 99%), 1-octanol (Aldrich, 99%), 1-nonanol (Aldrich, 99%), 2-ethylbutanol (Aldrich, 98%) and 3-methyl-3-pentanol (TCI, 98%) were used as received. N-tert-butyl-N-[1-diethylphosphono(2,2-dimethylpropyl)]oxy (SG1)[102] and N-(2-morpholin-4-ylethyl) acrylamide (MEA)[103] were prepared according to the literature by the reaction of acryloyl chloride (Aldrich, 97%) with 4-(2-aminoethyl)morpholine (MEA, Aldrich, 99%) in the presence of triethylamine (Aldrich 99%) with CHCl₃ as the reaction solvent. SG1 was purified by column chromatography with purity (95%) determined using ¹H NMR spectroscopy from reaction of SG1 radical with pentafluorophenylhydrazine (Aldrich, 97%).

2.2.2 Equipment and Measurements

Number-average molecular weight ($M_n$) and polydispersity ($M_w/M_n$) were determined using a gel permeation chromatography (GPC) system consisting of a Viscotek DM 400 data manager, a Viscotek VE 3580 refractive-index detector and two Viscotek Viscogel GMH₉₅-M columns. Measurements were carried out at 60 °C at a flow rate of 1.0 mL min⁻¹ using HPLC-grade DMF containing 0.01 M LiBr as the eluent. The columns were calibrated using twelve poly(styrene) standards ($M_n = 580 − 6,035,000$ g mol⁻¹). $M_n$ is given in g mol⁻¹ throughout. The use of poly(styrene) standards inevitably leads to an error in molecular weights – as such the $C_{tr,S}$ data reported also contains a comparable error. ¹H NMR spectra were recorded using a Joel GXFT 400 MHz instrument equipped with a DEC AXP 300 computer workstation. Using TBAM in 1-propanol or 1-hexanol as solvent, conversions were measured by GC using a Shimadzu GC-8A Gas Chromatograph. For all other polymerizations of TBAM, conversions were measured by gravimetry by removal of solvent under reduced pressure, dissolving the residue in a minimum amount of DMF, and precipitating the polymer from distilled water. Polymers were dried under vacuum for several
days at room temperature prior to conversion measurement. Conversions for both conventional radical polymerization and NMP of MEA were measured using $^1$H NMR by comparing the integral of the peak at 3.20-3.90 ppm (OCH$_2$, 1-CH$_2$, 6H), which contains both poly(MEA) and MEA monomer contributions with the vinyl peak of the monomer at 5.65 ppm (=CH-, 1H).

### 2.2.3 Synthesis of Macroinitiators

Macroinitiators were prepared by precipitation NMP in supercritical carbon dioxide.[104] Two batches of poly(t-BA)-SG1 ($M_n = 3,700$, $M_w/M_n = 1.20$; $M_n = 5,000$, $M_w/M_n = 1.18$) were used as macroinitiator for NMP of TBAM in various alcohols, and poly(t-BA)-SG1 with $M_n = 8,300$ and $M_w/M_n = 1.25$ was used for NMP of MEA in 3-methyl-3-pentanol. The $M_n$ and $M_w/M_n$ were measured using the above GPC conditions.

### 2.2.4 General Polymerization Procedure

All polymerization mixtures were added to Pyrex ampoules and subjected to several freeze-degas-thaw cycles to remove oxygen before sealing under vacuum. The ampoules were heated at a specific temperature in an aluminium heating block for various times. Polymerizations were stopped by placing ampoules in an ice-water bath.

### 2.2.5 Conventional Radical Polymerizations at Low Initiator Concentrations

A typical procedure is as follows: Stock solutions containing, 0.41, 1.4, 2.5 and 4.1 mM of TBP were made up in 1-propanol. Stock solution (1 mL) was added to MEA (0.3685 g, 2.00 mmol) in a Pyrex ampoule. Evacuated ampoules were heated at 120 °C for various times.

### 2.2.6 Estimating Chain Transfer Constants using Mayo Plots

A typical procedure is as follows: Stock solution of TBP (0.41 mM) in 1-hexanol (1 mL, 7.96 mmol) was added to MEA (0.293 g, 1.59 mmol; 0.147 g, 0.8 mmol; 0.098 g, 0.53 mmol and 0.073 g, 0.40 mmol to give [Solvent]$_0$/[Monomer]$_0$ = 5, 10, 15 and 20). Evacuated ampoules were heated at 120 °C for various times. Conversions were less than 10% in all cases.
2.2.7 Nitroxide-Mediated Polymerization (NMP) of TBAM using Macroinitiators

A typical procedure is as follows: The following NMPs were carried out using stock solutions of 1-hexanol and 3-methyl-3-pentanol containing SG1 (1.67 × 10^{-3} mM). Stock solutions (1 mL) were added to TBAM (0.2544 g, 2.00 mmol) and poly(t-BA)-SG1 (0.033 g, 6.67 × 10^{-3} mmol) to give [TBAM]₀/[poly(t-BA)-SG1]₀ = 300, and heated at 120 °C for various times.

2.2.8 NMP of MEA using SG1/AIBN and Macroinitiator Initiation Systems

NMP was carried out using a stock solution containing AIBN (9.03 × 10^{-3} mM) and SG1 (2.26 × 10^{-2} mM) in 1-propanol or 1-hexanol. Stock solution (1 mL) was added to MEA (0.3685 g, 2.00 mmol) to give [MEA]₀/[AIBN]₀ = 222, and heated at 120 °C for various times. For macroinitiator-initiated NMP, stock solution containing SG1 (2.25 × 10^{-3} mM) in 3-methyl-3-pentanol was prepared. Stock solution (1 mL) was added to MEA (0.3685 g, 2.00 mmol) and poly(t-BA)-SG1 (55.4 mg, 6.67 × 10^{-3} mmol) to give [MEA]₀/[poly(t-BA)-SG1]₀ = 300, and heated at 120 °C for various times.

2.2.9 Spontaneous Initiation of MEA in the Absence of Initiator or Nitroxide

Evacuated ampoules containing MEA (0.3685 g, 2.00 mmol) in 1-propanol (1 mL) were heated at 120 °C for various times
2.3 RESULTS AND DISCUSSION

2.3.1 Conventional Radical Polymerizations

Conventional radical polymerizations of TBAM were carried out using very low rates of initiation in 1-propanol at 120 °C. When the propagating radical concentration is sufficiently low, the rate of bimolecular termination is minimized to the extent that chain transfer to monomer or solvent becomes the main end-forming event.\[^{89}\] Figure 2.1a shows that the MWDs obtained for the three different initiator concentrations are essentially superimposed with $M_n = 36,900$ and $M_w/M_n = 1.69$ ([TBP]$_0$ = 4.1 mM), $M_n = 39,950$ and $M_w/M_n = 1.60$ ([TBP] = 1.4 mM), and $M_n = 41,400$ and $M_w/M_n = 1.68$ ([TBP] = 0.41 mM), consistent with chain transfer dictating the maximum attainable molecular weight. If chain transfer to a small molecule is the main end-forming event, theory dictates that $M_w/M_n = 2$,\[^{105}\] and as such it is surprising that $M_w/M_n < 2$ in these cases. However, it has been reported that GPC calibration error (i.e. use of inappropriate polymer standards) can cause artificial narrowing of the MWD.\[^{105, 106}\] Comparative polymerizations of MEA in 1-propanol at 120 °C were carried out, once again resulting in very similar MWDs (Figure 2.1b) with $M_n = 12,900$ and $M_w/M_n = 2.02$ ([TBP]$_0$ = 4.1 mM), $M_n = 13,900$ and $M_w/M_n = 2.03$ ([TBP]$_0$ = 2.5 mM), $M_n = 15,000$ and $M_w/M_n = 1.93$ ([TBP] = 1.4 mM), and $M_n = 14,700$ and $M_w/M_n = 2.04$ ([TBP] = 0.41 mM). The maximum $DP_n$ (< 82) reached is considerably less than for the analogous TBAM (< 326) polymerizations, indicating the poly(MEA) propagating radical is more susceptible to chain transfer (assuming similar $k_p$ values).
**Figure 2.1** MWDs for the conventional radical polymerizations of TBAM and MEA at 120 °C using the shown initiator (TBP) concentrations; (a) TBAM polymerizations in 1-propanol, 8 (0.41 mM), 21 (1.4 mM) and 32% (4.1 mM) conversion. (b) MEA polymerizations in 1-propanol, 5 (0.41 mM), 16 (1.4 mM), 14 (2.5 mM) and 10% (4.1 mM) conversion. (c) MEA polymerizations in 3-methyl-3-pentanol, 10 (0.41 mM), 6 (1.4 mM) and 20% (4.1 mM) conversion.
The value of $C_{tr,S}$ in the conventional radical polymerization of TBAM at 120 °C using a variety of alcohols as solvents was estimated based on the classical Mayo equation, equation 2.1:

$$\frac{1}{DP_n} = \frac{1}{DP_{n,0}} + C_{tr,S} \frac{[Solvent]}{[Monomer]}$$

(2.1)

where $DP_n$ denotes the number-average degree of polymerization and the subscript 0 denotes $DP_n$ in the absence of chain transfer agent (solvent). The value of $C_{tr,S}$ is obtained as the slope of a plot of $1/DP_n$ versus $[Solvent]/[Monomer]$ (Figure 2.2, Table 2.1).

The $C_{tr,S}$ values for TBAM from Figure 2.2a obtained for straight chain (linear) alcohols 1-propanol to 1-nonanol were then plotted versus the number of carbons ($n$) in the alcohol (Figure 2.3). An approximately linear increase in $C_{tr,S}$ is observed with the number of carbons in the linear alcohols $C_3 – C_9$. Since each alcohol differs from the next by a methylene unit ($CH_2$), the extent of chain transfer to solvent for TBAM is dictated by the relative number of $CH_2$ units in the alcohol solvent (assuming $k_p$ is not significantly influenced by the solvent). The $C_{tr,S}$ for TBAM increases approximately 3-fold from 1-propanol to 1-nonanol.

$C_{tr,S}$ in conventional radical polymerizations of MEA in various alcohol solvents at 120 °C were also estimated by Mayo analysis (Figure 2.2c), resulting in $C_{tr,S}$ values a factor of two or greater than for TBAM (Figure 2.3). The incremental increase in $C_{tr,S}$ for the straight chain alcohols is somewhat less pronounced for MEA than TBAM. $C_{tr,S}$ for MEA in straight chain alcohols was $1.4 \times 10^{-3}$, $1.5 \times 10^{-3}$ and $1.8 \times 10^{-3}$ compared to $C_{tr,S}$ for TBAM of $3.6 \times 10^{-4}$, $6.5 \times 10^{-4}$ and $9.3 \times 10^{-4}$ in 1-propanol, 1-hexanol and 1-octanol, respectively (Table 2.1).

The effect of branching in the alcohol solvent was next investigated by carrying out conventional radical polymerizations of TBAM in isomers of $C_6H_{13}OH$ (Scheme 2.2). $C_{tr,S}$ was estimated using the analogous Mayo conditions (Figure 2.2b), and again shown to increase with the number of methylene units; 3-methyl-3-pentanol ($2.2 \times 10^{-4}$), 2-ethyl-1-butanol ($5.7 \times 10^{-4}$) and 1-hexanol ($6.5 \times 10^{-4}$) (Table 2.1). The $C_{tr,S}$ in 2-ethyl-1-butanol is perhaps larger than expected by considering only the relative number of methylene units – this is due to the readily abstractable methine (CH) hydrogen, which would result in a stable
tertiary radical. Chain transfer to methyl isobutyrate, which also generates a tertiary radical, has previously been detected by mass spectrometry in the radical polymerization of methyl methacrylate.\textsuperscript{[107]}

\textbf{Scheme 2.2} Structural isomers of C$_6$H$_{13}$OH used as solvents.
Figure 2.2 Mayo plots for conventional radical polymerizations of TBAM and MEA initiated by TBP (0.41 mM) at 120 °C in various alcohols; (a) TBAM in 1-propanol (♦, solid line), 1-butanol (○, green line), 1-pentanol (Δ, brown line), 1-hexanol (■, short dashed line), 1-heptanol (□, red line), 1-octanol (▲, long dashed line) and 1-nonanol (●, purple line) as solvents (b) TBAM in isomers of C₆H₁₃OH; 1-hexanol (■, short dashed line), 2-ethyl-1-butanol (○, dashed-dotted line), and 3-methyl-3-pentanol (●, dotted line) as solvents (c) MEA in various alcohols; 1-propanol (♦, solid line), 1-hexanol (■, short dashed line), 1-octanol (▲, long dashed line) and 3-methyl-3-pentanol (●, dotted line) as solvents.
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Table 2.1 $C_{tr,S}$ coefficients obtained from the slope of Mayo plots (Fig. 2.2) for conventional radical polymerizations of TBAM and MEA in various alcohols as solvents at 120 °C (all $C_{tr,S}$ values are based on linear polystyrene standards)
Figure 2.3 Chain transfer to solvent constant ($C_{tr,S}$) (estimated from Mayo plots) plotted versus the number of carbons ($n$) in linear alcohols ($C_nH_{2n+1}OH$) used as solvent for conventional radical polymerizations of TBAM at 120 °C.\cite{37}
In order to investigate if significantly greater molecular weights could be achieved for the polymerization of MEA in 3-methyl-3-pentanol, the solvent that had the lowest $C_{tr,S}$ with TBAM, analogous conventional radical polymerizations at low radical concentrations were carried out (Figure 2.1c). The resulting overlapping MWDs are indicative of chain transfer being the main end-forming reaction, although higher $M_n$ values are indeed achieved (than for 1-propanol) because of the lower anticipated $C_{tr,S}$ with $M_n = 16,130$ and $M_w/M_n = 2.10$ ([TBP]$_0 = 4.1$ mM), $M_n = 17,990$ and $M_w/M_n = 2.09$ ([TBP] = 1.4 mM), and $M_n = 17,260$ and $M_w/M_n = 2.05$ ([TBP] = 0.41 mM).

Assuming that chain transfer to solvent is the sole chain end forming event and that the solvent concentration remains constant at its initial value, $DP_n$ (cumulative value) can be expressed as a function of conversion according to equation 2.2:

$$DP_n = \frac{[M]_0(2 - \alpha)}{2[S]_0C_{tr,S}}$$

where [M]$_0$ and [S]$_0$ represent initial monomer and solvent concentrations, and $\alpha$ denotes fractional monomer conversion. Fitting of equation 2.2 to a data set of $DP_n$ vs conversion for a system where chain transfer to solvent is not the sole end forming event leads to overestimation of $C_{tr,S}$. The $M_n$ data for the conventional radical polymerization of TBAM in 1-propanol at the three different (low) initiator concentrations in Figure 2.1a have been plotted versus conversion in Figure 2.4. The data were subsequently fitted to equation 2.2 resulting in $C_{tr,S} = 4.3 \times 10^{-4}$, which is close to the value of $C_{tr,S} = 3.6 \times 10^{-4}$ derived from the Mayo plot (Figure 2.3). The MWDs of Figure 2.1a may be influenced by chain transfer to solvent or monomer or both; however, the fact that the Mayo treatment (which gives $C_{tr,S}$) results in a value close to that from equation 2.2 is consistent with chain transfer to solvent being the main end-forming event under these conditions.
Figure 2.4 $M_n$ versus conversion for conventional radical polymerizations of TBAM in 1-propanol (□), MEA in 1-propanol (♢) and MEA in 3-methyl-3-pentanol (○) at 120 °C at different [TBP]$_0$ corresponding to Fig. 1 with full lines representing $M_n$ calculated using eq 2.2 with $C_{tr,S} = 4.3 \times 10^{-4}$, $1.9 \times 10^{-3}$ and $2.5 \times 10^{-3}$ respectively.
The $M_n$ data for the conventional radical polymerizations of MEA in 1-propanol (Figure 2.1b) and 3-methyl-3-pentanol (Figure 2.1c) at different (low) initiator concentrations were plotted versus conversion in Figure 2.4. Fitting with equation 2.2 resulted in $C_{tr,S} = 1.9 \times 10^{-3}$ in 1-propanol, in relatively good agreement with $C_{tr,S} = 1.4 \times 10^{-3}$ from the Mayo plot. In the case of 3-methyl-3-pentanol, $C_{tr,S} = 2.5 \times 10^{-3}$ is derived by fitting eq 2.2, which is more than six times greater than the $C_{tr,S} = 4.0 \times 10^{-4}$ obtained by Mayo analysis. This discrepancy may indicate that the conventional radical polymerization of MEA at low initiator concentrations (Figure 2.1c) is subject to chain transfer to monomer as well as to solvent (the Mayo plot is specifically designed to only “detect” chain transfer to solvent, whereas fitting of equation 2.2 “detects” chain transfer to all low MW species). The reason that chain transfer to monomer appears to be less significant for MEA in 1-propanol than 3-methyl-3-pentanol may be that $C_{tr,S}$(Mayo) is considerably higher (factor of 3.5) for MEA in 1-propanol than in 3-methyl-3-pentanol, thus reducing the relative impact of chain transfer to monomer (which impacts analysis using equation 2.2).

2.3.2 Nitroxide-Mediated Radical Polymerizations

NMP initiated by a macroinitiator of relatively high MW can be a useful tool for studying chain transfer processes because chain transfer to low MW species is readily detected in the MW distributions as low MW tailing. In the case of a sufficiently high level of chain transfer to solvent, $M_n$ may go through a maximum with increasing conversion.\[^{14}\] NMP of TBAM initiated by poly($t$-BA)-SG1 was carried out in the three different alcohol solvents: 3-methyl-3-pentanol, 1-propanol, and 1-hexanol possessing a range of $C_{tr,S}$ (Table 2.1). For all three solvents, $M_n$ initially increases with conversion indicative of a controlled/living system, but subsequently goes through a maximum at 60 – 75% conversion (depending on solvent), consistent with significant chain transfer to solvent (Figure 2.5 and 2.6). It is clear that the maximum attainable MW is dependent upon the magnitude of the $C_{tr,S}$ with the highest MW for the poly(TBAM) block achieved in 3-methyl-3-pentanol, which possesses the lowest $C_{tr,S}$. For all three solvents, the values of $M_w/M_n$ increase gradually with conversion, consistent with chain transfer to solvent occurring continuously (Figure 2.5).
Figure 2.5 (a) $M_w/M_n$ and (b) $M_n$ versus conversion plots of Poly (t-BA)-SG1-initiated NMP of TBAM at 120°C with 25 mol% excess free SG1 and $[\text{TBAM}]_0/[\text{poly(t-BA)-SG1}]_0 = 300$ in 3-methyl-3-pentanol (●), 1-propanol (♦) and 1-hexanol (□).
Figure 2.6 MWDs for poly(t-BA)-SG1-initiated NMP of TBAM with 25 mol% excess free SG1 and [TBAM]₀/[poly(t-BA)-SG1]₀ = 300 in (a) 1-propanol, (b) 1-hexanol and (c) 3-methyl-3-pentanol at 120 °C.
Figure 2.7 Conversion versus time for NMP of TBAM and MEA at 120 °C: Where (a) are polymerizations of TBAM initiated by poly(t-BA)-SG1, where [TBAM]₀/[poly(t-BA)-SG1]₀ = 300, and in the presence of 25 mol % free SG1 in 1-propanol (◊), 1-hexanol (□) and 3-methyl-3-pentanol (○), and (b) polymerizations of MEA using the bimolecular system of [SG1]₀/[AIBN]₀ = 2.5 and [MEA]₀/[AIBN]₀ = 222 (◊), 444 (Δ) in 1-propanol, and [MEA]₀/[AIBN]₀ = 444 in 1-hexanol (□), and poly(t-BA)-SG1-initiated system with 25 mol % free SG1 and [MEA]₀/[poly(t-BA)-SG1]₀ = 300 in 3-methyl-3-pentanol (○).
Rather significant differences in polymerization rate ($R_p$) can be observed between the solvents in the corresponding conversion versus time data (Figure 2.7) with the highest $R_p$ being obtained for 3-methyl-3-pentanol. It is well-known that the nature of the solvent can influence rate coefficients in radical polymerization\textsuperscript{[108]} - in the case of NMP the situation would be complex as solvent effects may be expected on both the fundamental rate coefficients of propagation and termination, as well as the rate coefficients associated with the NMP equilibrium\textsuperscript{[28]} – such a discussion goes beyond the scope of the present work. Suffice it to say that there is no correlation between $R_p$ and the $C_{tr,S}$ values.

We began by carrying out the NMP of MEA using the bimolecular AIBN/SG1 system in 1-propanol with $[\text{MEA}]_0/[\text{AIBN}]_0 = 222$ and 444 at 120 °C (Figures 2.8 – 2.10). Up to about 60% conversion, an increase in the initiator concentration by a factor of two (i.e. $[\text{MEA}]_0/[\text{AIBN}]_0 = 222$ vs 444 with constant $[\text{AIBN}]_0/[\text{SG1}]_0$) resulted in a decrease in $M_n$ by close to a factor of two. The higher the targeted $M_{n,th}$, the higher is the probability that a given chain will undergo chain transfer during the polymerization, and thus $M_n$ values begin to deviate from linearity at lower conversion (~60% vs ~70% conversion) and $M_w/M_n$ values are higher for the data set with the highest $M_{n,th}$. Replacing 1-propanol with 1-hexanol ($[\text{MEA}]_0/[\text{AIBN}]_0 = 444$) resulted in higher $M_w/M_n$ due to an increase in the size of the low MW tail (Figure 2.9), but $M_n$ remained approximately linear with conversion up to ~60% with a similar maximum $M_n$ as for 1-propanol (Figure 2.8). The similar maximum MW obtained in the two different linear alcohols supports the estimated similar $C_{tr,S}$ values from the above conventional radical polymerization Mayo data for MEA (Figure 2.3 and Table 2.1). NMP of MEA was also conducted using poly(t-BA)-SG1 as macroinitiator in 3-methyl-3-pentanol (Figure 2.8 and 2.10) using the same conditions as for the NMP of TBAM (including identical [monomer]/[macroinitiator] ratios, Figure 2.5). This resulted in significantly lower maximum $M_n$ in comparison to the NMP of TBAM in 3-methyl-3-pentanol, consistent with the higher $C_{tr,S}$ of MEA found using the above analysis of conventional radical polymerization data for this solvent. For both MEA and TBAM, there is an insignificant number of chains originating from spontaneous initiation in comparison to the number of chains from the macroinitiator or in situ generated alkoxyamine (previously reported for TBAM,\textsuperscript{[35]} and as verified for MEA in this work by heating MEA alone at 120 °C for various times (Figure 2.11)).
Figure 2.8 (a) $M_w/M_n$ and (b) $M_n$ versus conversion plots for NMP of MEA at 120 °C: Bimolecular systems used $[\text{SG}1]_0/[\text{AIBN}]_0 = 2.5$ and $[\text{MEA}]_0/[\text{AIBN}]_0 = 222$ (♦), 444 (▲) in 1-propanol, and $[\text{MEA}]_0/[\text{AIBN}]_0 = 444$ in 1-hexanol (□). Poly(t-BA)-SG1-initiated NMP (●) of MEA with 25 mol% excess free SG1 in 3-methyl-3-pentanol and $[\text{MEA}]_0/[\text{poly(t-BA)-SG1}]_0 = 300$. 

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Figure 2.9 MWDs for NMP of MEA at 120 °C using \([SG1]_0/[AIBN]_0 = 2.5\) and (a) \([MEA]_0/[AIBN]_0 = 222\) in 1-propanol (b) \([MEA]_0/[AIBN]_0 = 444\) in 1-propanol (c) \([MEA]_0/[AIBN]_0 = 444\) in 1-hexanol.
Figure 2.10 MWDs for poly(t-BA)-SG1-initiated NMP of MEA with 25 mol% excess free SG1 and [MEA]/[poly(t-Bu)-SG1]₀ = 300 in 3-methyl-3-pentanol at 120 °C.
Figure 2.11 First-order plot of the spontaneous polymerization (in the absence of initiator or nitroxide) of MEA in 1-propanol at 120 °C
2.4 CONCLUSIONS

Chain transfer to solvent is shown to strongly influence the maximum attainable molecular weight in the conventional radical polymerization and NMP of two structurally diverse acrylamide monomers in various alcohol solvents. For polymerizations of TBAM, the propensity for chain transfer to solvent or H-abstraction is shown to increase with the number of methylene units (CH$_2$) in the solvent with the highly branched alcohol, 3-methyl-3-pentanol (having fewer CH$_2$s) giving the smallest $C_{tr,S}$ values (using Mayo analysis). Among the solvents investigated, 3-methyl-3-pentanol is thus recommended for solution NMP, since it allows the attainment of higher molecular weights. $C_{tr,S}$ values obtained from Mayo analysis (detecting only chain transfer to solvent) and analyses of conventional radical polymerizations at low initiator concentrations (that account for chain transfer to all small molecules), suggest that chain transfer to monomer may also be a significant end forming event for the polymerization of MEA in 3-methyl-3-pentanol. This is perhaps not surprising given the high number of CH$_2$ units in this monomer (six saturated CH$_2$s versus two CH$_2$s in the alcohol solvent). Overall, the higher $C_{tr,S}$ values for MEA are consistent with the lower maximum $M_n$ values in NMP in comparison to TBAM.
Chapter 3

Alkoxyamine-initiated nitroxide-mediated precipitation polymerizations of styrene in supercritical carbon dioxide
3.1 INTRODUCTION

Supercritical carbon dioxide (scCO₂) is a benign solvent used to circumvent the requirement for environmentally damaging volatile organic solvents.⁷⁶, ¹⁰⁹, ¹¹⁰ Advantages include a readily accessible critical point (31 °C and 7.4 MPa),⁵⁵ variable solubility by subtle changes in pressure and temperature,¹¹¹ and the lack of chain transfer to solvent in radical polymerizations.¹⁴, ³⁷ It is particularly well-suited for heterogeneous radical polymerizations, since reagents such as the monomer, initiator and controlling agent are generally soluble in scCO₂, but the resultant polymer is insoluble and precipitates.⁷⁶, ¹¹⁰ If the precipitation system is carried out in the presence of a colloidal stabilizer to prevent coagulation of particles, then dispersion polymerization results giving polymer of narrow particle size distributions and well-defined particles (d ≈ 100 nm to 15 µm).⁷⁶, ¹⁰⁹, ¹¹⁰ The monomer is not always soluble in the reaction medium, such as in the controlled/living nitroxide-mediated radical polymerization (NMP) of N-isopropylacrylamide (NIPAM) in scCO₂, where an inverse suspension system is generated.⁸⁰, ⁹⁷ In recent years, there has been a proliferation in the numbers of reported controlled/living precipitation and dispersion polymerizations in scCO₂ with NMP,²⁸, ⁷¹, ⁷³, ⁷⁷, ⁷⁸, ⁸⁰, ⁹², ¹¹²-¹¹⁷ atom transfer radical polymerization (ATRP),⁸¹, ¹¹⁸-¹²⁴ reversible addition-fragmentation chain transfer (RAFT)⁴⁵, ⁸³-⁸⁶, ¹¹⁰, ¹²⁵-¹²⁹ and iodine transfer polymerization (ITP).⁸⁷, ⁸⁸ The slow build up in molecular weight (MW) in a controlled/living system by virtue of the equilibrium between active propagating radicals and dormant polymer chains allows measurement of the critical degree of polymerization ($J_{\text{crit}}$) before polymer chains precipitate from solution or the continuous phase (containing monomer and scCO₂). After $J_{\text{crit}}$, the polymerization continues in the monomer-rich particle phase. For controlled/living precipitation/dispersion polymerizations, $J_{\text{crit}}$ can be predicted as a function of targeted molecular weight and initial monomer loading.⁷¹ In contrast, in a non-living conventional radical polymerization, no single $J_{\text{crit}}$ value can be applied due to polymer chains instantaneously reaching high MW and continually precipitating. NMP of styrene in scCO₂ at high monomer loadings (70% w/v) is superior in terms of control over the molecular weight distribution (MWD) for the SG1 (N-tert-butyl-N-(1-diethylphosphono-2,2-dimethylpropyl) nitroxide) / AIBN (2,2'-azoisobutyronitrile) precipitation system in comparison to solution (toluene) polymerization carried out under analogous conditions.⁷³ The effect of nitroxide partitioning upon control was found to be extenuated at low styrene loadings,⁹² where the system becomes heterogeneous sooner due to a lower $J_{\text{crit}}$. In that work, the bimolecular nitroxide/AIBN system was used,⁷³, ⁹², ¹¹⁴, ¹¹⁶ leading to uncertainty in
initiator efficiencies due to unknown amounts of alkoxyamine generated in situ. Control was facilitated by using excess amounts of nitroxide relative to initiating AIBN-derived radicals in order to negate the loss of nitroxide from the locus of polymerization via partitioning, as well as side-reactions occurring at the initial stages of alkoxyamine formation and during polymerization. In the present chapter controlled/living precipitation NMP in scCO₂ has for the first time been achieved in the absence of excess free nitroxide. The effect of partitioning on nitroxide and styryl-initiating fragments (“foot” part of alkoxyamine) is examined by using three new alkoxyamine initiators.

Scheme 3.1 Chemical structures of styryl-alkoxyamine initiators 1a-1d with the four nitroxide fragments investigated.

Two alkoxyamines dissociate into scCO₂-phlic fluorinated TIPNO-nitroxide derivatives (F-TIPNO 1b and F-Si-TIPNO 1c, Scheme 3.1), while another contains a similar sized fluorinated “foot” (TIPNO alkoxyamine F-foot 2, Scheme 3.2), which will remain attached to the growing polymer chain. The performance of these fluorinated alkoxyamines in polymerizations of styrene in scCO₂ is compared with analogous polymerizations in solution, as well as, TIPNO and SG1-alkoxyamine 1a and 1d analogues.
Scheme 3.2 Chemical structure of TIPNO-alkoxyamine 2 containing fluorinated styryl “foot”

3.2  EXPERIMENTAL

3.2.1  Materials
Styrene monomer (St, Aldrich, >99%) was distilled under reduced pressure prior to use. Reagent grade toluene (Aldrich, >99.7%), THF (Aldrich >99%), MeOH (Aldrich, 99%) EtOH (Aldrich, 99%), CO₂ (BOC gases, 99.8%), trimethylacetaldehyde (Aldrich, 96%), diethyl phosphite (Aldrich, 98%), tert-butyl amine (Aldrich, 98%), ethylenediamine (Aldrich, 99%), salicylaldehyde (Aldrich, 98%), manganese (II) acetate tetrahydride (Aldrich, 99%), sodium chloride (Aldrich, 99%), sodium borohydride (Aldrich, 99%) and LiBr (Aldrich, 99%) were used as received. SG1₁³⁰ (N-tert-butyl-N-(1-diethylphosphono-2,2-dimethylpropyl) nitroxide) was prepared according to the literature. SG1 alkoxyamine (diethyl(1-[tert-butyl(1-phenylethoxy)amino]-2,2 dimethylpropyl)phosphonate) was prepared by reaction of the appropriate free nitrosoxide with styrene using a Mn(salen) catalyst.¹³¹ The preparations of F-TIPNO 1b, F-Si-TIPNO 1c and F-TIPNO-foot 2 alkoxyamines are described.¹³² The preparation of Mn(salen) catalyst and SG1 1d alkoxyamine are described in sections 3.2.4 and 3.2.5.¹³¹

3.2.2  Synthesis of Alkoxyamines
The following alkoxyamines: TIPNO 1a, F-TIPNO 1b, F-Si-TIPNO 1c and F-TIPNO-foot 2 were kindly synthesized¹³² and supplied by Aruna Earla, Jennifer Petraitis, Chad Higa, and Rebecca Braslau. SG1-Alkoxyamine 1d was synthesised by the author of this thesis.
3.2.3 Preparation of \(N,N'\)-ethylenebis(salicylimine) Ligand

Ethylenediamine (3.000 g, 49.92 mmol) was dissolved in 250 mL of absolute ethanol, and salicylaldehyde (12.191 g, 99.83 mmol) was added: a yellow precipitate formed. The mixture was heated to reflux for 30 minutes; all of the precipitate dissolved to form a yellow solution. Crystals formed upon cooling to room temperature. Additional cooling in an ice-water bath for 30 minutes followed by filtration resulted in 12.570 g (94% yield) of \(N,N'\)-ethylenebis(salicylimine) as large yellow flakes.

3.2.4 Preparation of Mn(salen) chloride oxo Catalyst (Jacobsens’s Catalyst)

To a 500 mL two-necked flask equipped with a reflux condenser; \(N,N'\)-ethylenebis(salicylimine) (12.570 g, 46.849 mmol), Mn(OAc)\(_2\)•4H\(_2\)O (22.970 g, 93.698 mmol) and 180 mL of methanol was added. Air was bubbled through the solution while being heated to reflux. After 3 hours, an aqueous solution of LiCl (9.930 g, 234.2 mmol in 70 mL of H\(_2\)O) was added to the refluxing solution. Reflux concurrent with air bubbling through the solution was continued for another 2 hours. After cooling to room temperature, the mixture was cooled with an ice water bath for 1 hour. The resulting precipitate was isolated by filtration. Additional crops of crystals were obtained by addition of water to the mother liquors and cooling in an ice bath to give a total of 12.728 g. The first batch of precipitate contains both an orange-brown clay-like material, and darker brown precipitate with a sand-like texture. The orange precipitate was not an effective catalyst for alkoxyamine formation. The later crops gave the darker brown precipitate. This is the active catalyst. The combined dark brown material was recrystallized once from boiling water including a hot filtration to give 7.898 g (45% yield) of black crystals (mp > 260 °C), which are a reliable catalyst for alkoxyamine formation.

3.2.5 Preparation of (diethyl(1-[tert-butyl(1-phenylethoxy)amino]-2,2-dimethylpropyl)phosphonate) Alkoxyamine SG1

SG1 nitroxide (1.350 g, 4.586 mmol) was dissolved in 2:3 v/v of toluene (12 mL) and ethanol (18 mL) followed by the addition of styrene (0.954 g, 9.160 mmol). Jacobsen’s catalyst (0.294 g, 0.695 mmol) was added slowly followed by sodium borohydride (0.519 g, 13.752 mmol) and the reaction was bubbled with air for 30 mins prior to stirring open to atmosphere overnight (>12 hours). The reaction mixture was concentrated and combined with diethyl ether (45 mL) and deionised water (45 mL) the aqueous layer was extracted with diethyl ether (4 x 45 mL). The combined organic layer was washed with saturated sodium
bicarbonate, dried over MgSO₄ and solvent removed under reduced pressure to give 1.652 g of dark brown oil. The oil was purified by silica gel column chromatography using a gradient eluent, starting with 100% petroleum ether changing to 1:1 petroleum ether/diethyl ether to give the alkoxyamine as a viscous oil with slight orange colour. Purity determined by ¹H NMR.

3.2.6 Equipment and Measurements for Polymerizations
All NMP in scCO₂ were conducted in a 25 ml stainless steel Parr reactor with a maximum operating pressure of 40 MPa and 130 °C. The pressure was achieved using a Thar P-50 series high pressure pump and temperature was monitored by a Thar CN6 controller. \( M_n \) and polydispersity (\( M_w/M_n \)) were determined using a gel permeation chromatography (GPC) system consisting of a Viscotek DM 400 data manager, a Viscotek VE 3580 refractive-index detector, and two Viscotek Viscogel GMH₄₅-M columns. Measurements were carried out at 60 °C at a flow rate of 1.0 mL min⁻¹ using HPLC-grade DMF containing 0.01 M LiBr as the eluent. The columns were calibrated using twelve polystyrene standards (\( M_n = 580 – 6,035,000 \) g mol⁻¹). \( M_n \) is given in g mol⁻¹ throughout. The theoretical value of \( M_n \) (\( M_{n,th} \)) is calculated using equation 3.1:

\[
M_{n,th} = \frac{\alpha [M]_0 MW_{mon}}{[Alkoxyamine]_0} + MW_{Alk}
\]  

(3.1)

where \( \alpha \) is fractional conversion of monomer, \([M]_0\) is the initial monomer concentration, \( MW_{mon} \) and \( MW_{Alk} \) are the molecular weights of monomer and alkoxyamine respectively. Reaction mixtures were added to a large excess of methanol to precipitate polystyrene. The polymer was filtered, dissolved in THF and re-precipitated from methanol. The polymer was dried under vacuum at room temperature for 24 hours before conversion was measured by gravimetry.

3.2.7 Solution Polymerizations
Styrene (2.0 g, 19.2 mmol), alkoxyamine (5.0 \( \times 10^{-5} \) mol) and toluene (1.8 ml) were added to a Pyrex ampoule, subjected to several freeze-degas-thaw cycles, and sealed under vacuum. Ampoules were heated at 110 °C for various times using an aluminium heating block. Reactions were quenched in an ice-water bath.
3.2.8 Precipitation Polymerizations in Supercritical Carbon Dioxide (ScCO₂)

The reactor (25 ml) was loaded with styrene (50% w/v loading, 12.5 g, 0.12 mol), alkoxyamine (3.125 × 10⁻⁴ mol) and a magnetic stirring bar and sealed. The reaction vessel was purged for 20 minutes by bubbling gaseous CO₂ through the reaction mixture. Liquid CO₂ (~5 MPa) was added and the reactor was immersed in an oil bath. The temperature was raised to the reaction temperature of 110 °C, followed by pressurizing the reaction vessel to 30 MPa by the addition of further CO₂. Reactions were quenched by submersion of the reactor in an ice-water bath.

3.3 RESULTS AND DISCUSSIONS

3.3.1 Solution Polymerizations

TIPNO 1a and TIPNO-derivative alkoxyamines 1b, 1c and alkoxyamine 2 all gave very similar rates of polymerization of styrene in toluene (50 % (w/v), Figure 3.1) at 110 °C, indicating that structural modifications to the nitroxide and styryl “foot” parts of the alkoxyamine have no significant effect on the equilibrium constant (K) for trapping and dissociation in organic solution.

As expected from the higher K for SG1, the SG1-alkoxyamine 1d-initiated polymerizations proceeded at a higher rate than TIPNO-derivatives 1a, 1b, 1c and 2. All alkoxyamine-initiated polymerizations in solution proceeded in a controlled/living manner with molecular weights close to theoretical values (equation 3.1) and only less than theoretical values beyond about 55% conversion, although in most cases M_w/M_n < 1.3 throughout (Figure 3.2). MWDs shown in Figures 3.3 – 3.7.
Figure 3.1 Conversion versus time plots for TIPNO-1a (circles), F-TIPNO-1b (squares), F-Si-TIPNO-1c (inverted triangle), SG1-1d (upright triangles) and TIPNO-F-Foot-2 (diamonds), styryl-alkoxyamine initiated NMP of styrene (50% w/v) at 110 °C using [Monomer]₀/[Alkoxyamine]₀ = 384. Open and closed symbols are respectively solution in toluene and precipitation in scCO₂ at 30 MPa polymerizations.
Figure 3.2 (a) Polydispersities \( (M_w/M_n) \) and (b) number-average molecular weights \( (M_n) \) versus conversion for TIPNO-1a (circles), F-TIPNO-1b (squares), F-Si-TIPNO-1c (inverted triangle), SG1-1d (upright triangles) and TIPNO-F-Foot-2 (diamonds) styryl-alkoxyamine initiated NMP of styrene (50% w/v) at 110 °C using \([\text{Monomer}]_0/[^{\text{Alkoxyamine}}]_0 = 384\). Open and closed symbols are respectively solution in toluene and precipitation in scCO_2 at 30 MPa polymerizations. The line represents theoretical MW \( (M_{n,\text{th}}) \) based on Equation 3.1.
Figure 3.3 MWDs for alkoxyamine 1a initiated NMP of styrene (50% w/v) at 110 °C using [Monomer]₀/[Alkoxyamine]₀ = 384: (a) Precipitation polymerizations in scCO₂ at 30 MPa; conversions are 23% (black), 42% (red) and 49% (green) and (b) solution polymerization in toluene; conversions are 27% (black), 40% (red), 55% (green), 63% (purple) and 72% (orange).
Figure 3.4 MWDs for alkoxyamine 1b initiated NMP of styrene (50% w/v) at 110 °C using [Monomer]₀/[Alkoxyamine]₀ = 384: (a) Precipitation polymerizations in scCO₂ at 30 MPa; conversions are 8 (black), 17 (red), 21 (green), 35 (purple) and 43% (orange) and (b) solution polymerizations in toluene; conversions are 13 (black), 33 (red), 51 (green), 63 (purple), 74% (orange) and 80% (blue).
Figure 3.5 MWDs for alkoxyamine 1c initiated solution NMP of styrene (50% w/v) at 110 °C in toluene using [Monomer]₀/[Alkoxyamine]₀ = 384: conversions are 24 (black), 44 (red), 65 (green) and 75% (purple).
Figure 3.6 MWDs for the alkoxyamine 1d initiated NMP of styrene (50% w/v) at 110 °C using $[\text{Monomer}]_0/[\text{Alkoxyamine}]_0 = 384$: (a) Precipitation polymerizations in scCO$_2$ at 30 MPa; conversions are 20 (black), 33 (red), 47 (green) and 62 (purple) and (b) solution polymerizations in toluene; conversions are 17 (black), 31 (red), 51 (green), 62 (purple) and 82% (orange).
Figure 3.7 MWDs for alkoxyamine 2 initiated solution NMPs of styrene (50% w/v) at 110 °C in toluene using [Monomer]₀/[Alkoxyamine]₀ = 384: conversions are 38 (black), 61 (red) and 78% (green).
Simulations using PREDICI for the partitioning effects of St/TIPNO in section 3.3.2 were conducted by Prof. Per B. Zetterlund at the University of New South Wales, Sydney, Australia.

3.3.2 Precipitation Polymerizations in Supercritical Carbon Dioxide (scCO₂)

For NMP of styrene (50% w/v) in scCO₂ at 110 °C and 30 MPa, the point of precipitation ($J_{\text{crit}}$) is predicted to occur at approximately $M_n = 3,450$ (~8.5% conv.) using the model developed by O’Connor et al.\(^{[71]}\) that can be used to estimate $J_{\text{crit}}$ as a function of initial monomer loading and targeted molecular weight. Since NMPs in scCO₂ in the present article go beyond this conversion, all are considered heterogeneous systems. The alkoxyamine TIPNO 1a-initiated styrene precipitation polymerization in scCO₂ proceeded at a similar rate to the analogous NMP carried out in the presence of a 5% excess of free TIPNO at lower conversions (23% conv. after 22 h as opposed to 19% conv. after 21 h, Figure 3.8), although the system containing an initial excess of free nitroxide reached a limiting conversion sooner (Figure 3.9). Moreover, controlled/living character was good without the 5% excess of free TIPNO ($M_n = 7,960$ and $M_w/M_n = 1.22$), with the presence of excess free nitroxide providing a marginally narrower MWD ($M_n = 9,000$ and $M_w/M_n = 1.14$, also see Figures 3.9 & 3.10 for additional data showing the effect of free TIPNO on control/living character). It was therefore evident that controlled/living character for alkoxyamine-initiated precipitation polymerizations in scCO₂ can be established without the requirement for excess free nitroxide. Thus all subsequent NMPs in scCO₂ were initiated by alkoxyamines without the addition of free nitroxide. As previously observed by Aldabbagh et al.\(^{[116]}\) for bimolecular nitroxide/AIBN systems, polymerization rates are lower for precipitation polymerizations in scCO₂ in comparison to analogous solution polymerizations of styrene (Figure 3.1). This has been attributed to monomer partitioning, i.e. some styrene residing in the continuous scCO₂ phase after particle formation, leading to a lower monomer concentration in the particles (the main locus of polymerization).
**Figure 3.8** Effect of free nitroxide on MWDs for the precipitation NMP of 50% (w/v) styrene at 30 MPa and 110 °C using $[\text{Monomer}]_0/[\text{Alkoxyamine}]_0 = 384$. $[\text{Free TIPNO}]_0/[\text{Alkoxyamine 1a}]_0 = 0.05$, dashed line is 19% conv. after 21 h, $M_n = 9,000$ and $M_w/M_n = 1.14$ and the solid line is 23% conv. after 22 h, $M_n = 7,960$ and $M_w/M_n = 1.22$. 
**Figure 3.9** The effect of free TIPNO on NMP in scCO$_2$ at 110 °C. (a) Conversion versus time and (b) $M_n$ (closed symbols) and $M_w/M_n$ (open symbols) vs conversion plots for TIPNO-$1a$ alkoxyamine initiated precipitation NMP of styrene (50% w/v) using $[\text{Monomer}]_0/[\text{Alkoxyamine}]_0 = 384$ with $[\text{Free TIPNO}]_0/[\text{Alkoxyamine}]_0 = 0.05$ (diamonds) and $[\text{Free TIPNO}]_0/[\text{Alkoxyamine}]_0 = 0$ (circles).
Figure 3.10 MWDs for alkoxyamine TIPNO-1a initiated precipitation NMP of styrene (50% w/v) at 110 °C in scCO₂ using [Monomer]₀/[Alkoxyamine]₀ = 384 with [Free TIPNO]₀/[Alkoxyamine]₀ = 0.05: conversions are 19% (black), 29% (red) and 34% (green).
Very significant differences in polymerization rate and control are observed in scCO\(_2\) between SG1-alkoxyamine \(1d\) and TIPNO-alkoxyamine \(1a\) with \(M_n\) \((1d) > M_n\) \((1a)\) and higher polydispersities for \(1d\) than \(1a\) \((1d: M_w/M_n = 1.25-1.57\) and \(1a: M_w/M_n = 1.22-1.36)\). The higher rate and inferior control for SG1 in scCO\(_2\) is due to a combination of higher \(K\)\([133, 134]\) and a higher solubility of SG1 in scCO\(_2\), leading to greater nitroxide partitioning away from the locus of polymerization after particle formation. Although there is no literature data available for nitroxide solubilities in scCO\(_2\), one may expect a greater solubility for TIPNO in the organic phase (particles) due to TIPNO’s organic nature in comparison to SG1, which contains heteroatoms (e.g. phosphorous). Poor control for SG1-mediated polymerizations in scCO\(_2\) were not previously observed in bimolecular nitroxide/AIBN systems in scCO\(_2\) because of the use of a high ratio of \([\text{SG1}]_0/[\text{AIBN}]_0\)\([73, 92, 114, 116]\). Despite TIPNO \(1a\) and fluorinated alkoxyamine F-TIPNO \(1b\)-initiated NMP exhibiting the same rate of polymerization in solution, unexpectedly the \(1a\)-initiated NMP was marginally faster in scCO\(_2\). The fluorinated nitroxide \(1b\) is more CO\(_2\)-philic than TIPNO \(1a\), and is expected to partition away from the locus of polymerization upon particle formation, which should lead to a higher rate rather than the observed lower rate of polymerization for \(1b\).

To understand the effects of nitroxide partitioning more quantitatively, modelling and simulations were conducted using PREDICI\([135]\) for the St/TIPNO system at 110 °C using a previously published approach\([136]\) (the model used here was identical, with the exception of the inclusion in this work of a reaction step for spontaneous (thermal) initiation of styrene according to: \(R_{i,\text{th}} = k_{i,\text{th}}[\text{St}]^3\)). Conditions and parameters: \([\text{St}]_0 = 8.7\) M, \([\text{alkoxyamine}]_0 = 0.0227\) M, propagation rate coeff. \((k_p)^{[6]} = 1580\) M\(^{-1}\)s\(^{-1}\), termination rate coeff. \((k_t)^{[137]} = 1.57 \times 10^8\) M\(^{-1}\)s\(^{-1}\) (combination only), activation rate coeff. \((k_{\text{act}})^{[133]} = 1.184 \times 10^{-3}\) s\(^{-1}\), deactivation rate coeff. \((k_{\text{deact}})^{[134]} = 8.2 \times 10^6\) M\(^{-1}\)s\(^{-1}\), thermal initiation of styrene \((k_{i,\text{th}})^{[138]} = 4.26 \times 10^{-11}\) M\(^{-1}\)s\(^{-1}\). The system modelled is a bulk polymerization with a fictitious nitroxide partitioning step into a continuous phase (i.e. the scCO\(_2\) phase) having the same volume as the organic phase, whereby a given fraction of free nitroxide is removed (equivalent to partitioning to the continuous phase) assuming phase transfer equilibrium. Figures 3.11 and 3.12 show conversion vs time data and MWDs obtained for different partition coefficients of \(\Gamma = [\text{nitroxide}]_{\text{org}}/[\text{nitroxide}]_{\text{CO2}} = \infty\) (no partitioning), 1 and 0.25. \(\Gamma = 1\) and 0.25 correspond to situations where 50% and 80% of free nitroxide, respectively, is located in the continuous phase. It is apparent that even if very extensive nitroxide partitioning occurs, the increase in rate of polymerization is relatively small. Figure 3.12 shows that as expected, there is a
broadening of the MWDs with increasing nitroxide partitioning, with the livingness (number fraction of chains with alkoxyamine-terminated α-ends at 48% conversion) decreasing according to 97.5, 96.8, 95.3% with increasing partitioning. Indeed the alkoxyamine-initiated polymerizations using fluorinated TIPNO derivative 1b ($M_\theta/M_n = 1.25-1.55$) proceeded with inferior control relative to TIPNO 1a, as demonstrated by $M_n$s higher than theoretical values and higher polydispersities (Figure 3.2).
Figure 3.11 Simulated conversion vs time data of the styrene/TIPNO system at 110 °C (see text for details). $\text{[nitroxide]}_{\text{org}}/\text{[nitroxide]}_{\text{CO2}} = \infty$ (dotted line), 1 (dashed line), and 0.25 (solid line). $\Gamma = \infty$, 1 and 0.25 correspond to situations where 0%, 50% and 80% of free nitroxide, respectively, is located in the continuous phase.
Figure 3.12 Simulated MWDs (at 48% conv.) of the styrene/TIPNO system at 110 °C. \([\text{nitroxide}]_{\text{org}}/[\text{nitroxide}]_{\text{CO2}} = \infty\) (dotted line), 1 (dashed line), and 0.25 (solid line). \(\Gamma = \infty\), 1 and 0.25 correspond to situations where 0%, 50% and 80% of free nitroxide, respectively, is located in the continuous phase.
If nitroxide partitioning is the main cause of inferior control for alkoxyamine 1b in scCO$_2$, it follows that the polymerization rate is quite insensitive to the degree of nitroxide partitioning, more so than one would have expected. As such it may be reasonable to argue that the relatively small difference in the rate of polymerization between TIPNO 1a and F-TIPNO 1b in scCO$_2$ is not necessarily inconsistent with F-TIPNO nitroxide partitioning away from the locus of polymerization resulting in wider MWDs.

Moreover similar to the simulated MWD overlays in Figure 3.12, nitroxide partitioning seems to give marginal broadening experimentally (Figure 3.13a), when comparing MWDs for TIPNO 1a with the F-TIPNO 1b-initiated polymerization at similar intermediate conversions.

Precipitation polymerizations of styrene in scCO$_2$ for fluorinated alkoxyamines F-Si-TIPNO 1c and TIPNO alkoxyamine F-foot 2 were carried out (Figures 3.13b and 3.13c). Broadening for 1c was analogous to F-TIPNO 1b-initiated polymerization in scCO$_2$ with the alkoxyamine 2 experiment also giving a high MW shoulder, in the case of 1c presumably due to nitroxide partitioning as discussed above for 1b. Again, contrary to expectation, the polymerization rate for 1c was somewhat lower than for 1a. Alkoxyamine 2 differs from the other fluorinated alkoxyamines 1b and 1c in that (non-fluorinated) TIPNO is the mediating nitroxide and a fluorinated initiating styryl “foot” radical is produced upon dissociation. As such, the extent of nitroxide partitioning would be expected to be the same as for 1a. One can speculate that the F-content in the propagating radical part of the alkoxyamine leads to an increase in $J_{\text{crit}}$ (due to increased solubility in the continuous phase), and thus later nucleation; it is possible that this is related to the partial loss of control. It is unlikely that a higher $k_d$ for TIPNO-F-foot 2 may be causing the observed MWD broadening in comparison to TIPNO-1a alkoxyamine, because rates and control are very similar in solution (toluene), assuming negligible solvent effects on activation-deactivation kinetics in scCO$_2$. 
Figure 3.13 Comparing the performance of fluorinated alkoxyamines 1b, 1c and 2 with the TIPNO analogue 1a in the precipitation NMP of styrene (50% w/v) at 110 °C using \([\text{Monomer}]_0/[\text{Alkoxyamine}]_0 = 384\). (a) TIPNO-1b, 43% after 98 h, \(M_n = 19,700\) and \(M_w/M_n = 1.55\) compared with TIPNO-1a initiated analogue, 49% after 72 h, \(M_n = 19,000\) and \(M_w/M_n = 1.36\) (b) TIPNO-1c, 39% conv. after 61 h, \(M_n = 20,000\) and \(M_w/M_n = 1.29\) compared with the TIPNO-1a initiated analogue, 42% conv. after 47 h, \(M_n = 17,400\) and \(M_w/M_n = 1.27\) (c) TIPNO-F-Foot-2, 38% conv. after 69 h, \(M_n = 19,500\) and \(M_w/M_n = 1.32\) compared with the TIPNO-1a initiated analogue, 42% conv. after 47 h, \(M_n = 17,400\) and \(M_w/M_n = 1.27\)
3.4 CONCLUSIONS

In the absence of excess free [nitroxide]₀, TIPNO alkoxyamine is found to give superior controlled/living character for precipitation NMP of styrene in scCO₂ compared to the SG1 analogue. In solution (toluene), the latter resulted in slightly less control and a higher rate of polymerization. Differences between TIPNO- and SG1-alkoxyamine can be rationalised in terms of the higher $K$ for SG1 and a greater level of nitroxide partitioning for SG1 in the heterogeneous system. Despite increased steric congestion about the alkoxyamine (N-O bond) in novel fluorinated TIPNO-alkoxyamine initiators, a similar equilibrium constant ($K$) to TIPNO for activation/deactivation in organic solution can be inferred. The greater partitioning of fluorinated TIPNO derivatives in scCO₂ impacts on the controlled/living character, broadening the molecular weight distributions.
Chapter 4

RAFT polymerizations to give CO₂-responsive triblock copolymer micelles containing CO₂-sensitive morpholine moieties
4.1 INTRODUCTION

The discovery of CO$_2$-switchable polymers originated from the introduction by Jessop et al. of switchable-hydrophilicity solvents (SHSs)\cite{139}. SHSs contain amidine and tertiary amine groups whose miscibility with water can be switched by addition or removal of CO$_2$ (Scheme 4.1)\cite{140}.

\begin{center}
\begin{tikzpicture}
\node (DBU) at (0,0) {\text{DBU}};
\node (ROH) at (2,0) {\text{ROH}};
\node (DBUH) at (4,0) {\text{DBUH}^+};
\node (RCO$_3^-$) at (6,0) {\text{RCO$_3^-$}};
\node (Decane) at (0,-2) {\text{Decane}};
\node (DBU) at (2,-2) {\text{DBU}};
\node (ROH) at (4,-2) {\text{ROH}};
\node (DBUH) at (6,-2) {\text{DBUH}^+};
\node (RCO$_3^-$) at (8,-2) {\text{RCO$_3^-$}};
\draw[->] (DBU) -- (ROH) node[midway,above] {CO$_2$} node[midway,below] {-CO$_2$};
\draw[->] (Decane) -- (DBU) node[midway,above] {CO$_2$} node[midway,below] {N$_2$};
\end{tikzpicture}
\end{center}

**Scheme 4.1** Reversible protonation of DBU (1,8-diazabicyclo-[5.4.0]-undec-7-ene) in the presence of an alcohol

Jessop with Cunningham and co-workers reported emulsion polymerizations of styrene (St) and methyl methacrylate (MMA) using CO$_2$-switchable cationic amidine and tertiary amine surfactants\cite{141-144}. Others have reported block copolymers whose micelle self-assembly and disassembly is CO$_2$-switchable due to the presence of amidine pendants\cite{145} or poly(N,N-dimethylaminoethyl methacrylate) (PDMAEMA) containing block copolymers that can react with CO$_2$ to drastically alter the lower critical solution temperature (LCST)\cite{146,147}. More recently, four-armed star-like hydrophobic associated polymer was reported containing PDMAEMA as the switchable hydrophobe, where reaction with CO$_2$ can reversibly alter viscosity in water\cite{148}. CO$_2$-responsivity is attractive due to its convenience, green credentials, low cost, and easy removal of the stimuli.

Morpholine moieties have thus far not been utilised as the CO$_2$-responsive part of the polymer, as is now disclosed. Notably, N-ethylmorpholine was reported as an unsuitable SHS because of its high initial water solubility and because of its relatively low conjugate acid strength ($pK_{aH} = 7.70$, while typical SHSs are in the range $pK_{aH} = 9.5 – 11.0$), making it less reactive towards carbonated water\cite{140}. The conventional and nitroxide-mediated polymerization (NMP) of N-(2-morpholin-4-ylethyl)acrylamide (MEA) has recently been reported\cite{37}, although the NMP allowed controlled/living character to be achieved, extensive
chain transfer at the polymerization temperature of 120 °C limited the achievable molecular weights (MWs). This led us to now report controlled/living polymerizations of MEA at the lower temperature of 60 °C using Reversible Addition Fragmentation Chain Transfer (RAFT) polymerization [45]. The living poly(MEA) macroRAFT agent is chain extended with \(N,N\text{-dimethylacrylamide (DMA)}\), followed by styrene (St) to give CO\(_2\)-responsive amphiphilic triblock copolymer micelles.

### 4.2 EXPERIMENTAL

#### 4.2.1 Materials

\(N,N\text{-Dimethylacrylamide (DMA, Aldrich, >99%) and styrene (St, Aldrich >99%)}\) were distilled under reduced pressure before use. 2,2’-Azobisisobutyronitrile (AIBN, DuPont Chemical Solution Enterprise) was recrystallized twice from MeOH (Aldrich, 99.8%) before use. \(N\text{-}(2\text{-morpholin-4-ylethyl) acrylamide (MEA)}\) was prepared by the reaction of acryloyl chloride (Aldrich, 97%) with 4-(2-aminoethyl)morpholine (Aldrich, 99%) in the presence of triethylamine (Aldrich 99%) with CHCl\(_3\) as the reaction solvent \([103]\) and was recrystallized from Et\(_2\)O. 2-(Dodecylthiocarbonothioylthio)-2-methylpropionic acid (TTCA, Aldrich, 98%), Et\(_2\)O (Aldrich, 99%), CHCl\(_3\) (Aldrich, 99%), CH\(_2\)Cl\(_2\) (Aldrich, 99%), petroleum ether (Aldrich, 40 – 60 °C), \(N,N\text{-dimethylformamide (DMF, Aldrich, 99.9%)}\), toluene (Aldrich, 99%), CDCl\(_3\) (Aldrich, 99.8 atom %), D\(_2\)O (Aldrich, 99.9 atom %) and LiBr (Aldrich, 99%) were used as received.

#### 4.2.2 Equipment and Measurements

\(M_n\) and polydispersity \((M_w/M_n)\) were determined using a gel permeation chromatography (GPC) system consisting of a Viscotek DM 400 data manager, a Viscotek VE 3580 refractive-index detector, and two Viscotek Viscogel GMH\(_{HR}\)-M columns. Measurements were carried out at 60 °C at a flow rate of 1.0 ml min\(^{-1}\) using HPLC-grade DMF containing 0.01 M LiBr as the eluent. The columns were calibrated using twelve poly(St) standards \((M_n = 580 – 6,035,000 \text{ g mol}^{-1}\)). \(M_n\) is given in g mol\(^{-1}\) throughout, and are not absolute, but relative to linear poly(St) standards. \(^1\text{H NMR} \) spectra were recorded using a Joel GXFT 400 MHz instrument equipped with a DEC AXP 300 computer workstation. The \(^1\text{H NMR of poly(MEA) macroRAFT and di-/tri block copolymers were obtained in CDCl}_3\). The \(^1\text{H NMR used to show the CO}_2\text{-responsiveness of poly(MEA) and triblock copolymer micelles were obtained in D}_2\text{O}.\)


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$M_n$(NMR) of purified block copolymers is calculated according to Equation 4.1:

$$M_n(NMR) = (DP_n(MacroRAFT))(X)(MW_{mono}) + M_n(MacroRAFT)$$  \hspace{1cm} (4.1)$$

where $DP_n(MacroRAFT)$ is the average degree of polymerization of the poly(MEA) obtained from $M_n(GPC)$. $X$ is the ratio of the poly(DMA) or poly(St) relative to poly(MEA) incorporated in the block copolymers obtained from the integration of poly(DMA) or poly(St) peaks relative to the integration of the poly(MEA) peaks. The poly(MEA), poly(DMA) and poly(St) peaks used are at 3.20 – 4.00 (OCH$_2$, NHCH$_2$, 6H), 2.70–3.10 (CH$_3$, 6H), and 6.25 – 7.24 (Ph–H, 5H) respectively of $^1$H NMR spectrum (Figure 4.6) chemical shift (in ppm). $MW_{mono}$ is the molecular weight of DMA or St. $M_n(MacroRAFT)$ is obtained from $M_n(GPC)$.

Conversions for the RAFT polymerizations of poly(MEA) were measured by gravimetry. Monomer conversion for the synthesis of poly(MEA-\textit{b}-DMA) block copolymer was measured by $^1$H NMR by comparing the integral of the polymer peak at 2.70 – 3.10 ppm (CH$_3$, 6H) with the DMA monomer vinyl peak at 6.56 ppm (=CH$_-$, 1H). Monomer conversion for the synthesis of poly(MEA-\textit{b}-DMA-\textit{b}-St) triblock copolymer was measured by $^1$H NMR by comparing the integral of the St polymer peak at 6.25 – 7.24 ppm (Ph–H, 5H), with the monomer vinyl peaks at 6.12 ppm (=CH$_-$, 1H).

TEM images were obtained using a Hitachi H7000 Transmission electron microscope using formvar/carbon 200 mesh Cu grids. One drop (~ 0.1 ml) of the micelle solution was placed on the copper grid and allowed to settle. After 10 minutes excess solution was absorbed with filter paper and allowed to dry for a further 30 minutes prior to TEM analysis.

### 4.2.3 General Polymerization Procedure

All polymerization reaction mixtures were added to Pyrex ampoules and subjected to several freeze-degas-thaw cycles to remove oxygen before sealing under vacuum. The ampoules were heated to the required temperature in an aluminium heating block for various times. Polymerizations were stopped by placing ampoules in an ice-water bath.

### 4.2.4 RAFT Polymerization of MEA

A stock solution containing TTCA (0.109 g, 0.30 mmol) and AIBN (9.85 mg, 0.06 mmol) in DMF (10 ml) was prepared, and 1 ml portions were added to MEA (0.461 g, 2.50 mmol) to give a 2.5 M solution of monomer with [MEA]$_0$/[TTCA]$_0$ = 83. The reaction mixture was sealed in a glass ampoule and heated at 60 °C for various times. The polymer was
precipitated by drop wise addition to an excess of diethyl ether, filtered and dried under vacuum for 24 hours at room temperature.

4.2.5 Synthesis of Poly(MEA-\textit{b}-DMA) Diblock Copolymer
Poly(MEA) macroRAFT ($\text{M}_n = 15,500$, $M_w/M_n = 1.35$; 0.320 g, $2.06 \times 10^{-2}$ mmol) and AIBN (0.67 mg, 4.12 $\times 10^{-3}$ mmol) were dissolved in DMA (0.408 g, 4.12 mmol) and toluene (0.39 mL) added. The reaction mixture was sealed in a glass ampoule and heated at 60 °C for 72 minutes. Conversion was measured by $^1\text{H}$ NMR. The block copolymer was isolated by direct precipitation of the reaction mixture from an excess of petroleum ether, dissolved in dichloromethane, and purified by further precipitation from an excess of petroleum ether, filtered, and dried at room temperature under vacuum for 24 hours.

4.2.6 Synthesis of Poly(MEA-\textit{b}-DMA-\textit{b}-St) Triblock Copolymer
Poly(MEA-\textit{b}-DMA) macroRAFT ($\text{M}_n = 20,000$, $M_w/M_n = 1.62$; 0.410 g, 2.05 $\times 10^{-2}$ mmol), AIBN (0.660 mg, 4.00 $\times 10^{-3}$ mmol) and St (0.960 g, 9.22 mmol) were added to DMF (0.86 mL). The reaction mixture was sealed in a glass ampoule and heated at 60 °C for 16 hours. Conversion was measured by $^1\text{H}$ NMR. The polymer was precipitated twice from an excess of petroleum ether, filtered, and dried at room temperature under vacuum for 24 hours prior to self-assembly. Note that this isolation procedure does not remove any non-extended (hydrophilic) polymers, which remain dissolved in D$_2$O or water, and therefore are not involved in micelle formation (see section 4.2.8).

4.2.7 CO$_2$-responsiveness of Polymers
A sample of poly (MEA) (~20 mg) or of the aqueous micelle solution of the triblock copolymer evaporated to dryness (~10 mg) was added to D$_2$O (~3 mL), and a $^1\text{H}$ NMR spectrum taken. CO$_2$ was bubbled through the solution for 10 minutes followed by the obtaining of a second $^1\text{H}$ NMR spectrum. The same solution was then subjected to N$_2$ bubbling for a further 10 minutes, and a third $^1\text{H}$ NMR spectrum was obtained.

4.2.8 Self-Assembly Procedure and Analysis
Self-assembly of the poly(MEA-\textit{b}-DMA-\textit{b}-St) ($\text{M}_n = 30,400$, $M_w/M_n = 1.80$) polymer was carried out using the method used by Zhang and Eisenberg $^{[149]}$. Non-purified (see section 4.2.6) poly(MEA-\textit{b}-DMA-\textit{b}-St) ($\text{M}_n = 30,400$, $M_w/M_n = 1.80$) (73.0 mg, $2.40 \times 10^{-3}$ mmol)
was dissolved in DMF (3.87 mL, 3.65 g), and distilled water (0.91 mL, 0.91 g) was added slowly with vigorous stirring at a rate of ~1 drop every 10 s. The resulting solution was placed in a dialysis bag (molecular weight cut-off, MWCO = 3000) and the DMF was exchanged (dialysis) with water (1 L) for 12 hours to exclude the organic solvent. The distilled water was replaced twice and dialyzed for a further 6 hours each time. Two samples of the purified micelle solution were retained for TEM analysis; a direct sample and ~3 mL of the micelle solution was placed in a glass vial and CO₂ bubbled through for 10 minutes, and stored under an atmosphere of CO₂ until required.

4.3 RESULTS AND DISCUSSIONS

4.3.1 RAFT Polymerization of MEA

The RAFT polymerization of 2.5 M MEA in DMF at 60 °C was carried out using two different [MEA]₀/[TTCA]₀ ratios with similar intermediate conversions (~50%) achieved after about 10 hours (Figure 4.1). Approximate linear first order plots were obtained indicative of a constant propagating radical concentration over time and steady state kinetics, although downward deviations from linearity were observed at higher conversions. The polymerization carried out with the higher initial RAFT agent concentration appeared marginally slower indicating some rate retardation.

Controlled/living character was established up to high conversions (70 – 75%) for the RAFT polymerizations of MEA at two different [MEA]₀/[TTCA]₀ ratios with molecular weight distributions (MWDs) shifting to higher MW and remaining relatively narrow throughout (Figure 4.2). As expected for a controlled/living polymerization, there is a linear increase of $M_n$ with conversion, and increasing the [MEA]₀/[TTCA]₀ from 83 to 150 leads to an approximate doubling in $M_n$ at similar conversions (Figure 4.3). There was no discernible trend in polydispersities, which remained reasonably low throughout ($M_w/M_n = 1.34 – 1.55$). Unlike the reported NMP of MEAⁿ, the lower polymerization temperature facilitated controlled/living character with no maximum for the attainable polymer MW.
Figure 4.1 (a) Conversion vs time and (b) first order plot for the RAFT polymerization of 2.5 M MEA in DMF at 60 °C using TTCA as the RAFT agent, where [MEA]₀/[TTCA]₀ = 83 (circles, solid line of best fit) and 150 (squares, dashed line of best fit) respectively.
Figure 4.2 MWDs for the RAFT polymerization of 2.5 M MEA in DMF at 60 °C; (a) \([\text{MEA}]_0/\text{TTCA}_0 = 83\) (conversions are 11% (black), 27% (red), 50% (green), 60% (purple), and 78% (yellow)) and (b) \([\text{MEA}]_0/\text{TTCA}_0 = 150\) (conversions are 20% (black), 31% (red), 48% (green) and 70% (purple)). GPC traces are prior to polymer isolation via precipitation.
Figure 4.3 (a) $M_w/M_n$ (open symbols) and (b) $M_n$ (closed symbols) versus conversion plots for the RAFT polymerization of 2.5 M MEA in DMF at 60 °C using TTCA as the RAFT agent, where [MEA]$_0$/[TTCA]$_0$ = 83 (red circles) and 150 (black square), respectively.
### 4.3.2 CO\textsubscript{2}-Responsiveness of Poly(MEA)

The CO\textsubscript{2}-sensitivity of morpholine moieties of poly(MEA) were revealed using $^1$H NMR spectroscopy by using a dilute solution in D\textsubscript{2}O (Figure 4.4). After bubbling CO\textsubscript{2} through the poly(MEA) solution, the morpholine moieties reacted with the acidic solution (Scheme 4.2), and a downfield shift was observed for the 3,5-methylene groups of morpholine and immediate attached ethyl CH\textsubscript{2} to the morpholine from $\delta_H = 2.30 - 2.65$ (6 H) to $\delta_H = 2.45 - 2.80$ (6 H) in the salt.

![Scheme 4.2. CO\textsubscript{2}-responsive moieties of poly(MEA)](image)

The CO\textsubscript{2}-response of poly(MEA) was found to be switchable, since passing N\textsubscript{2} through the CO\textsubscript{2}-enriched polymer solution resulted in the chemical shift of the methylene groups adjacent to the morpholine nitrogen in D\textsubscript{2}O reverting up field to the original value of $\delta_H = 2.30 - 2.65$. A less significant but discernible downfield shift was observed from $\delta_H = 3.50 - 3.70$ to $3.55 - 3.75$ for (6H) OCH\textsubscript{2} and NHCH\textsubscript{2} of poly(MEA) with addition of CO\textsubscript{2} to D\textsubscript{2}O.
Figure 4.4 $^1$H NMR spectrum of (a) poly(MEA) in D$_2$O, (b) poly(MEA) in D$_2$O after the addition of CO$_2$, and (c) poly(MEA) in D$_2$O after the removal of CO$_2$ by addition of N$_2$. 
4.3.3 Synthesis of Triblock Copolymer Micelles

Poly(MEA) macroRAFT ($M_n = 15,500, M_w/M_n = 1.35$) was chain extended with DMA in toluene at 60 °C to give water soluble poly(MEA-b-DMA) ($M_n = 20,000, M_w/M_n = 1.62$, Figure 4.5). The latter living copolymer was isolated by precipitation from petroleum ether, and chain extended with styrene in DMF at 60 °C to give poly(MEA-b-DMA-b-St) ($M_n = 30,400, M_w/M_n = 1.80$). The precipitation procedure used to isolate the amphiphilic triblock copolymer also resulted in dead non-extended poly(MEA) and poly(MEA-b-DMA) recovery, however these chains are water soluble, and do not self-assemble upon preparation of micelles. $^1$H NMR was used to estimate the relative size of blocks and molecular weight of isolated (non-purified) polymer (see Experimental and Figure 4.6) with $M_n$(NMR) values proving to be close to $M_n$(GPC), which are based on linear poly(St) standards (Table 4.1). Thus, despite GPC calibration error, good livingness is indicated upon comparison with $M_n$(NMR).

The method used by Zhang and Eisenberg [149] was used to produce the micelles of poly(MEA-b-DMA-b-St) at a critical aggregation concentration of approximately 0.60 mmol L$^{-1}$. The aggregation was detected using $^1$H NMR spectroscopy, where the spectrum in CDCl$_3$ displayed peaks from both the hydrophobic (St) and hydrophilic (MEA and DMA) parts of the polymer (Figure 4.7a), while in D$_2$O the hydrophobic poly(St) part disappeared from the spectrum (Figure 4.7b). Thus in CDCl$_3$ all three blocks are soluble, while in D$_2$O the self-assembly leads to suppression of the poly(St) block, which evidently gives the hydrophobic core of micelles.

TEM micrograph from the aqueous solution shows the poly(MEA-b-DMA-b-St) gives uniform spherical micelles of an average diameter of 25 nm (Figure 4.8a).
Figure 4.5 MWDs for (a) poly(MEA) macroRAFT (black line, $M_n = 15,500, M_w/M_n = 1.35$) chain extended with DMA at 60 °C to give poly(MEA-b-DMA) (red line, $M_n = 20,000, M_w/M_n = 1.62$, 24% conversion), which was chain extended with St at 60 °C to give poly(MEA-b-DMA-b-St) (green line, $M_n = 30,400, M_w/M_n = 1.80$, 32% conversion). GPC traces are prior to polymer isolation via precipitation.
Figure 4.6 $^1$H NMR spectrum of precipitated polymers: (a) poly(MEA$_{83}$), (b) poly(MEA$_{83}$-$b$-DMA$_{45}$) and (c) poly(MEA$_{83}$-$b$-DMA$_{45}$-$b$-St$_{99}$).
Figure 4.7 $^1$H NMR spectrum for the poly(MEA-b-DMA-b-St) polymer in (a) CDCl$_3$ and (b) D$_2$O
Table 1
Estimated molecular weights based on GPC and NMR (in CDCl$_3$)

<table>
<thead>
<tr>
<th>Polymer</th>
<th>$M_n$(GPC)</th>
<th>$M_n$ (NMR)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poly(MEA$_{83}$)</td>
<td>15500</td>
<td>–</td>
</tr>
<tr>
<td>Poly(MEA$<em>{83}$-b-DMA$</em>{45}$)</td>
<td>20000</td>
<td>21500</td>
</tr>
<tr>
<td>Poly(MEA$<em>{83}$-b-DMA$</em>{45}$-b-St$_{99}$)</td>
<td>30400</td>
<td>30000</td>
</tr>
</tbody>
</table>

$^aM_n$ (NMR) is calculated according to equation 4.1.

4.3.4 CO$_2$-Responsive Micelles
A TEM micrograph was obtained for the micelles after the addition of CO$_2$ in water (Figure 4.8b). There is now significantly less aggregation, and noticeable irregularity in the size and shape of the nanoparticles. The significant increase in size of the micelles to ~30 – 45 nm, is expected since overall water solubility of the triblock copolymer will increase upon salt formation at the tertiary amine of morpholine units. Upon protonation, there is a downfield chemical shift of the 3,5-methylene groups of morpholine and immediate attached ethyl CH$_2$ to the morpholine from $\delta_H = 2.30 – 2.65$ (6H) (Figure 4.9a) to $\delta_H = 2.45 – 2.80$ (6H) in D$_2$O (Figure 9b). The DMA peak $\delta_H = 2.70 – 2.85$ (CH$_3$, 6H) is overlapping with the MEA peaks ($\delta_H = 2.45 – 2.80$) upon addition of CO$_2$. 
Figure 4.8 TEM of poly(MEA-b-DMA-b-St) after self-assembly in water, (a) before the addition of CO\(_2\) and (b) after the addition of CO\(_2\).
Figure 4.9 $^1$H NMR spectrum of (a) poly(MEA-$b$-DMA-$b$-St) in D$_2$O and (b) poly(MEA-$b$-DMA-$b$-St) in D$_2$O after the addition of CO$_2$. 
4.4. CONCLUSIONS

RAFT achieved controlled/living polymerizations of MEA at 60 °C with no limiting MW observed. $^1$H NMR spectroscopy is used to show a CO$_2$-switchable response for the morpholine units of poly(MEA). This represents the first time morpholine containing polymers have shown CO$_2$ response. RAFT allowed the preparation of the amphiphilic poly(MEA-$b$-DMA-$b$-St) triblock copolymer, which self-assembled in water to give aggregates of uniform spherical nanoparticles. These micelles are CO$_2$-responsive with aggregation reduced, and particles less regular and larger in size upon application of CO$_2$ in water.
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**Peer-Reviewed Publications**

Chain Transfer to Solvent in the Radical Polymerization of Structurally Diverse Acrylamide Monomers using Straight-Chain and Branched Alcohols as Solvents.

Synthesis of Fluorinated Alkoxyamines and Alkoxyamine-Initiated Nitroxide-Mediated Precipitation Polymerizations of Styrene in Supercritical Carbon Dioxide.

RAFT Polymerizations to Give CO₂-Responsive Triblock Copolymer Micelles Containing CO₂-Sensitive Morpholine Moieties.
Christopher Magee and Fawaz Aldabbagh.

Submitted for peer-review.

**Conference Proceedings**

*Chain Transfer to Solvent in the Radical Polymerization of N-tert-Butylacrylamide (TBAM)*

Christopher Magee, Per B. Zetterlund and Fawaz Aldabbagh. *Irish Polymer and Materials Conference, 30th April – 1st May 2014, University College Dublin (UCD)*
Chain Transfer to Solvent in the Radical Polymerization of N-tert-Butylacrylamide (TBAM)

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Introduction

TBAM is a hydrophobic monomer often used as a comonomer to reduce the lower critical solution temperature (LCST) of polyanisopropylacrylamide. TBAM is a solid at room temperature and can only be polymerized in organic solvents. Thus the importance of studying chain transfer to solvent.

\[ \text{TBAM} \]

\[ P_\cdot + S-H \rightarrow P\cdot-S + H^+ \] hydrogen abstraction

\[ S^\cdot + M \rightarrow S-M^\cdot \] initiation

\[ S-M^\cdot + M \rightarrow P\cdot^\cdot + S \] propagation

Chain transfer to solvent (S-H) or monomer (M) is the abstraction of an atom (hydrogen) by a propagating radical (P\cdot) to give a dead polymer chain (P\cdot-S) and a small radical (S\cdot or M\cdot) capable of initiating a new chain. Chain transfer results in an upper limit in accessible molecular weight for both a conventional and controlled/living radical polymerization.[1,2]

MWDs obtained for conventional radical polymerizations of TBAM at low initiator concentrations are superimposable, thus chain transfer is the main end forming event.

Measuring \( C_{tr,S} \) using the Mayo Equation

The extent that chain transfer to solvent occurs can be estimated using the classical Mayo equation from the slope of a plot of inverse \( DP_n \) vs [Solvent]/[Monomer]. This is the chain transfer to solvent constant \( \{C_{tr,S}\} \).

\[ \frac{1}{DP_n} = \frac{1}{DP_n^{0}} + \frac{C_{tr,S}}{[\text{Solvent}]/[\text{Monomer}]} \]

Mayo plots for conventional radical polymerizations of TBAM in isomers of \( C_6H_{13}OH \). The \( C_{tr,S} \) increases with the number of methylene units. (2)

1-hexanol (\( C_{tr,S} = 6.5 \times 10^{-4} \))

2-ethyl-1-butanol (\( C_{tr,S} = 5.7 \times 10^{-4} \))

3-methyl-3-pentanol (\( C_{tr,S} = 2.2 \times 10^{-4} \))

3-Methyl-3-pentanol contains the fewest methylene units.

Conclusions

Chain transfer to solvent is shown to strongly influence the maximum attainable molecular weight in both the conventional radical polymerization and NMP of TBAM in various alcohol solvents. Chain transfer to solvent is shown to increase with the number of methylene units (\( CH_2 \)) in the solvent with the highly branched alcohol, 3-methyl-3-pentanol (having fewer \( CH_3\)) giving the smallest \( C_{tr,S} \) values (using Mayo analysis). Among the solvents investigated, 3-methyl-3-pentanol is thus recommended for solution NMP, since it allows the attainment of higher molecular weights.

References


Acknowledgements

 IRC for funding as part of the First IUPAC Transnational call in Polymer Chemistry.
Chain transfer to solvent in the radical polymerization of structurally diverse acrylamide monomers using straight-chain and branched alcohols as solvents†

Christopher Magee, Yusuke Sugihara, Per B. Zetterlund and Fawaz Aldabbagh

Chain transfer to solvent in conventional radical polymerizations of N-tert-butylacrylamide (TBAM) and N-(2-morpholin-4-yl)ethylacrylamide (MEA) in a range of alcohol solvents is investigated. Mayo analysis of polymerization of TBAM in linear alcohols (C3–C10) resulted in an approximately linear increase in chain transfer to solvent constant (C_{tr,S}) with the number of methylene (CH2) units in the solvent. The branched alcohol 3-methyl-3-pentanol gave the smallest C_{tr,S} (using Mayo analysis), and thus allowed attainment of higher molecular weights (MWs) in the nitroxide-mediated polymerizations (NMP) of TBAM. Overall, the data show that MEA is more prone to chain transfer to solvent than TBAM (higher C_{tr,S}), and further analysis of the conventional radical polymerization of MEA in 3-methyl-3-pentanol indicate chain transfer to monomer may also be occurring. The first controlled/living polymerizations of MEA are detailed with chain transfer having a greater impact on maximum achievable MWs in NMP in comparison to TBAM.

Introduction

Chain transfer to solvent or monomer is the abstraction of an atom by a propagating radical to give a dead polymer chain and a small radical capable of initiating a new chain. For a given set of conditions, chain transfer results in an upper limit in accessible molecular weight for both a conventional and controlled/living radical polymerization (CLRP). In a recent report, chain transfer to solvent was shown to be a significant end-forming reaction in the conventional and nitroxide-mediated polymerization [NMP] of N-isopropylacrylamide (NIPAM) in DMF at 120 °C. The same chain transfer to solvent constant (C_{tr,S} = k_{tr,S}/k_p, the ratio between the rate coefficients for chain transfer to solvent and propagation), within experimental error, was shown to account for experimental molecular weight (MW) data for both conventional radical polymerization and NMP. In the case of CLRP, chain transfer can compromise both control and livingness by generation of dead chains (loss of propagating radicals) and accumulation of short chains (due to reinitiation) that give low M_n tailing or broadening in the MW distribution (MWD) with increasing conversion. In the case of chain transfer to solvent, it has been shown that as a consequence of the total number of chains increasing, the number-average molecular weight (M_n) deviates downwards from the theoretical value (M_{n,th}) and may even decrease with increasing conversion, which is distinctly different from chain transfer to monomer where theory dictates that M_n never goes through a maximum. The value of M_n going through a maximum with increasing conversion has also been observed in the NMP of acrylic acid using 1,4-dioxane as solvent at 120 °C. Chain transfer to solvent has been detected in other CRPs, for example causing a limiting M_n in the reversible addition–fragmentation chain transfer (RAFT) polymerization of acrylic acid at 80 °C in ethanol, 2-propanol and 1,4-dioxane and RAFT of hydrophobic acrylamide monomers at 90 °C in DMF and 1,4-dioxane.

Chain transfer to solvent should be a fundamental consideration when polymerizing monomers that are solids, and thus are not polymerized in bulk, but rather in solutions of organic solvents. NIPAM is such a monomer (a solid with m.p. 60–63 °C), which is commonly polymerized in solution. The inverse suspension NMP of NIPAM in supercritical carbon dioxide has been reported, in which case M_n did not deviate significantly from M_{n,th} consistent with chain transfer to CO2 (as well as chain transfer to monomer) being negligible.

We now report on chain transfer to solvent in the conventional radical polymerization of two alternative solid acrylamide monomers (Scheme 1) using various straight chain and branched alcohols as solvents.
Experimental

Materials

tert-Butyl acrylate (t-BA, Aldrich, 98%) was purified by distillation under reduced pressure to remove inhibitors. N-tert-butylacrylamide (TBAM, TCI, 98%) was recrystallized from 1:1 benzene/acetonitrile before use. 2,2′-Azobisisobutyronitrile and 1,1′-azobis(cyclohexane-1-carbonyl) diimide (AIBN and ACN, DuPont Chemical Solution Enterprise) were recrystallized from MeOH before use, and tert-butyl peroxide (TBP, Aldrich, 98%) was used as received. 1-Propanol (Aldrich, 99%), 1-butanol (TCI, 99%), 1-pentanol (Aldrich, 99%), 1-hexanol (Aldrich, 98%), 1-heptanol (Aldrich, 99%), 1-octanol (Aldrich, 99%), 1-nonanol (Aldrich, 99%), 2-ethylbutanol (Aldrich, 98%) and 3-methyl-3-pentanol (TCI, 98%) were used as received. N-tert-butyl-N-(1-diethylphosphono(2,2-dimethylpropyl))oxo (SG1) and N-(2-morpholin-4-ylethyl)acrylamide (MEA) were prepared according to the literature, and SG1 was purified by column chromatography with purity (95%) determined using 1H NMR spectroscopy from reaction of SG1 radical with perfluorophenylethylamine (Aldrich, 97%).

Measurements

Number-average molecular weight ($M_n$) and polydispersity ($M_w/M_n$) were determined using a gel permeation chromatography (GPC) system consisting of a Viscotek DM 400 data manager, a Viscotek VE 3580 refractive-index detector and two Viscotek Viscogel GMH4HR-M columns. Measurements were carried out at 60 °C at a flow rate of 1.0 mL min$^{-1}$ using HPLC-grade DMF containing 0.01 M LiBr as the eluent. The columns were calibrated using twelve poly(styrene) standards ($M_n$ = 580–6 035 000 g mol$^{-1}$). $M_n$ is given in g mol$^{-1}$ throughout. The use of poly(styrene) standards inevitably leads to an error in molecular weights – as such the $C_{tr,s}$ data reported also contains a comparable error. 1H NMR spectra were recorded using a JEOL GXFT 400 MHz instrument equipped with a DEC AXP 300 computer workstation. For conversion measurement each spectrum received a total of 16 scans with relaxation delay of 1 s and repetition time of 3.18 s. The signal to noise is higher than 1000:1 with integration errors of less than 1%. Using TBAM in 1-propanol or 1-hexanol as solvent, conversions were measured by GC using a Shimadzu GC-8A Gas Chromatograph. For all other polymerizations of TBAM, conversions were measured by gravimetry by removal of solvent under reduced pressure, dissolving the residue in a minimum amount of DMF, and precipitating the polymer from distilled water. Polymers were dried under vacuum for several days at room temperature prior to conversion measurement. Conversions for both conventional radical polymerization and NMP of MEA were measured using 1H NMR by comparing the integral of the peak at 3.20 ppm (OCH$_2$, 1-CH$_2$, 6H), which contains both poly(MEA) and MEA monomer contributions with the vinyl peak of the monomer at 5.65 ppm (=CH=C=, 1H).

Synthesis of macroinitiators

Macroinitiators were prepared by precipitation NMP in supercritical carbon dioxide.$^{22}$ Two batches of poly(t-BA)-SG1 ($M_n$ = 3,700, $M_w/M_n$ = 1.20; $M_n$ = 5,000, $M_w/M_n$ = 1.18) were used as macroinitiator for NMP of TBAM in various alcohols, and poly(t-BA)-SG1 with $M_n$ = 8,300 and $M_w/M_n$ = 1.25 was used for NMP of MEA in 3-methyl-3-pentanol. The $M_n$ and $M_w/M_n$ were measured using the above GPC conditions.

General polymerization procedure

All polymerization mixtures were added to Pyrex ampoules and subjected to several freeze–degas–thaw cycles to remove oxygen before sealing under vacuum. The ampoules were heated at a specific temperature in an aluminium heating block for various times. Polymerizations were stopped by placing ampoules in an ice-water bath.

Conventional radical polymerizations at low initiator concentrations

A typical procedure is as follows: Stock solutions containing, 0.41, 1.4, 2.5 and 4.1 mM of TBP were made up in 1-propanol. Stock solution (1 mL) was added to MEA (0.3685 g, 2.00 mmol)
in a Pyrex ampoule. Evacuated ampoules were heated at 120 °C for various times.

Estimating chain transfer constants using Mayo plots
A typical procedure is as follows: Stock solution of TBP (0.41 mM) in 1-hexanol (1 mL, 7.96 mmol) was added to MEA (0.293 g, 1.59 mmol; 0.147 g, 0.8 mmol; 0.098 g, 0.53 mmol and 0.073 g, 0.40 mmol to give [solvent]/[monomer] = 5, 10, 15 and 20). Evacuated ampoules were heated at 120 °C for various times. Conversions were less than 10% in all cases.

Nitroxide-mediated polymerization (NMP) of TBAM using macroinitiators
A typical procedure is as follows: The following NMPs were carried out using stock solutions of 1-hexanol and 3-methyl-3-pentanol containing SG1 (1.67 × 10⁻³ mM). Stock solutions (1 mL) were added to TBAM (0.2544 g, 2.00 mmol) and poly-(t-BA)-SG1 (55.4 mg, 6.67 × 10⁻³ mmol) to give [TBAM]/[poly-(t-BA)-SG1]₀ = 300, and heated at 120 °C for various times.

NMP of MEA using SG1/AIBN and Macroinitiator initiation systems
NMP was carried out using a stock solution containing AIBN (9.03 × 10⁻³ mM) and SG1 (2.26 × 10⁻² mM) in 1-propanol or 1-hexanol. Stock solution (1 mL) was added to MEA (0.3685 g, 2.00 mmol) to give [MEA]/[AIBN]₀ = 222, and heated at 120 °C for various times. For macroinitiator-initiated NMP, stock solution containing SG1 (1.67 × 10⁻³ mM) in 3-methyl-3-pentanol was prepared. Stock solution (1 mL) was added to MEA (0.3685 g, 2.00 mmol) and poly-(t-BA)-SG1 (55.4 mg, 6.67 × 10⁻³ mmol) to give [MEA]/[poly-(t-BA)-SG1]₀ = 300, and heated at 120 °C for various times.

Spontaneous initiation of MEA in the absence of initiator or nitroxide
Evacuated ampoules containing MEA (0.3685 g, 2.00 mmol) in 1-propanol (1 mL) were heated at 120 °C for various times.

Results and discussion
Conventional radical polymerizations
Conventional radical polymerizations of TBAM were carried out using very low rates of initiation in 1-propanol at 120 °C. When the propagating radical concentration is sufficiently low, the rate of bimolecular termination is minimized to the extent that chain transfer to monomer or solvent becomes the main end-forming event. Fig. 1a shows that the MWDs obtained for the three different initiator concentrations are essentially superimposed with Mₙ = 36,900 and Mₘ/Mₙ = 1.69 ([TBP]₀ = 4.1 mM), Mₙ = 39,950 and Mₘ/Mₙ = 1.60 ([TBP]₀ = 1.4 mM), and Mₙ = 41,400 and Mₘ/Mₙ = 1.68 ([TBP]₀ = 0.41 mM), consistent with chain transfer dictating the maximum attainable molecular weight. If chain transfer to a small molecule is the main end-forming event, theory dictates that Mₘ/Mₙ = 2, and as such it is surprising that Mₘ/Mₙ < 2 in these cases. However, it has been reported that GPC calibration error (i.e. use of inappropriate polymer standards) can cause artificial narrowing of the MWD. Comparative polymerizations of MEA in 1-propanol at 120 °C were carried out, once again resulting in very similar MWDs (Fig. 1b) with Mₙ = 12,900 and Mₘ/Mₙ = 2.02 ([TBP]₀ = 4.1 mM), Mₙ = 13,900 and Mₘ/Mₙ = 2.03 ([TBP]₀ = 2.5 mM), Mₙ = 15,000 and Mₘ/Mₙ = 1.93 ([TBP]₀ = 1.4 mM), and Mₙ = 14,700 and Mₘ/Mₙ = 2.04 ([TBP]₀ = 0.41 mM). The maximum Dₚₙ (282) reached is considerably less than for the analogous

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Fig. 1 MWDs for the conventional radical polymerizations of 2 M TBAM and MEA at 120 °C using the shown initiator (TBP) concentrations: (a) TBAM polymerizations in 1-propanol, 8 (0.41 mM), 21 (1.4 mM) and 32% (4.1 mM) conversion. (b) MEA polymerizations in 1-propanol, 5 (0.41 mM), 16 (1.4 mM), 14 (2.5 mM) and 10% (4.1 mM) conversion. (c) MEA polymerizations in 3-methyl-3-pentanol, 10 (0.41 mM), 6 (1.4 mM) and 20% (4.1 mM) conversion.
TBAM (<326) polymerizations, indicating the poly(MEA) propagating radical is more susceptible to chain transfer (assuming similar $k_p$ values).

The value of $C_{tr,S}$ in the conventional radical polymerization of TBAM at 120 °C using a variety of alcohols as solvents was estimated based on the classical Mayo equation:

$$\frac{1}{DP_n} = \frac{1}{DP_{n,0}} + C_{tr,S} \frac{[\text{Solvent}]}{[\text{Monomer}]}$$

where $DP_n$ denotes the number-average degree of polymerization and the subscript 0 denotes $DP_n$ in the absence of chain transfer agent (solvent). The value of $C_{tr,S}$ is obtained as the slope of a plot of $1/DP_n$ versus [solvent]/[monomer] (Fig. 2, Table 1).

The $C_{tr,S}$ values for TBAM from Fig. 2a obtained for straight chain (linear) alcohols 1-propanol to 1-nonanol were then plotted versus the number of carbons ($n$) in the alcohol (Fig. 3). An approximately linear increase in $C_{tr,S}$ is observed with the number of carbons in the linear alcohols $C_3$ – $C_9$. Since each alcohol differs from the next by a methylene unit (CH$_2$), the extent of chain transfer to solvent for TBAM is dictated by the relative number of CH$_2$ units in the alcohol solvent (assuming $k_p$ is not significantly influenced by the solvent). The $C_{tr,S}$ for TBAM increases approximately 3-fold from 1-propanol to 1-nonanol.

### Table 1

<table>
<thead>
<tr>
<th>Monomer</th>
<th>Solvent</th>
<th>$C_{tr,S}$ from Mayo plot (conv. rad. polym.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBAM</td>
<td>1-Propanol</td>
<td>3.6 x 10$^{-4}$</td>
</tr>
<tr>
<td>TBAM</td>
<td>1-Butanol</td>
<td>4.7 x 10$^{-4}$</td>
</tr>
<tr>
<td>TBAM</td>
<td>1-Pentanol</td>
<td>6.1 x 10$^{-4}$</td>
</tr>
<tr>
<td>TBAM</td>
<td>1-Hexanol</td>
<td>6.5 x 10$^{-4}$</td>
</tr>
<tr>
<td>TBAM</td>
<td>1-Heptanol</td>
<td>7.9 x 10$^{-4}$</td>
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<tr>
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<td>1-Nonanol</td>
<td>11.0 x 10$^{-4}$</td>
</tr>
<tr>
<td>TBAM</td>
<td>2-Ethyl-1-butanol</td>
<td>5.7 x 10$^{-4}$</td>
</tr>
<tr>
<td>TBAM</td>
<td>3-Methyl-3-pentanol</td>
<td>2.2 x 10$^{-4}$</td>
</tr>
<tr>
<td>MEA</td>
<td>1-Propanol</td>
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</tr>
<tr>
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<td>1-Hexanol</td>
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</tr>
<tr>
<td>MEA</td>
<td>1-Octanol</td>
<td>18.0 x 10$^{-4}$</td>
</tr>
<tr>
<td>MEA</td>
<td>3-Methyl-3-pentanol</td>
<td>4.0 x 10$^{-4}$</td>
</tr>
</tbody>
</table>
$C_{tr,S}$ in conventional radical polymerizations of MEA in various alcohol solvents at 120 °C were also estimated by Mayo analysis (Fig. 2c), resulting in $C_{tr,S}$ values a factor of two or greater than for TBAM (Fig. 3). The incremental increase in $C_{tr,S}$ for the straight chain alcohols is somewhat less pronounced for MEA than TBAM. $C_{tr,S}$ for MEA in straight chain alcohols was $1.4 \times 10^{-3}$, $1.5 \times 10^{-3}$ and $1.8 \times 10^{-3}$ compared to $C_{tr,S}$ for TBAM of $3.6 \times 10^{-4}$, $6.5 \times 10^{-4}$ and $9.3 \times 10^{-4}$ in 1-propanol, 1-hexanol and 1-octanol, respectively (Table 1).

The effect of branching in the alcohol solvent was next investigated by carrying out conventional radical polymerizations of TBAM in isomers of C₆H₁₃OH (Scheme 2). $C_{tr,S}$ was estimated using the analogous Mayo conditions (Fig. 2b), and again shown to increase with the number of methylene units; 3-methyl-3-pentanol ($2.2 \times 10^{-4}$), 2-ethyl-1-butanol ($5.7 \times 10^{-4}$) and 1-hexanol ($6.5 \times 10^{-4}$) (Table 1). The $C_{tr,S}$ in 2-ethyl-1-butanol is perhaps larger than expected by considering only the relative number of methylene units – this is due to the readily abstractable methine (CH) hydrogen, which would result in a stable tertiary radical. Chain transfer to methyl isobutyrate, which also generates a tertiary radical, has previously been shown to increase with the number of methylene units; 3-methyl-3-pentanol ($2.2 \times 10^{-4}$), 2-ethyl-1-butanol ($5.7 \times 10^{-4}$) and 1-hexanol ($6.5 \times 10^{-4}$) (Table 1).

In order to investigate if significantly greater molecular weights could be achieved for the polymerization of MEA in 3-methyl-3-pentanol, the solvent that had the lowest $C_{tr,S}$ with TBAM, analogous conventional radical polymerizations at low radical concentrations were carried out (Fig. 1c). The resulting overlapping MWDs are indicative of chain transfer being the main end-forming reaction, although higher $M_n$ values are indeed achieved (than for 1-propanol) because of the lower anticipated $C_{tr,S}$ with $M_n = 16,130$ and $M_n/M_n = 2.10$ ([TBP]₀ = 4.1 mM), $M_n = 17,990$ and $M_n/M_n = 2.09$ ([TBP] = 1.4 mM), and $M_n = 17,260$ and $M_n/M_n = 2.05$ ([TBP] = 0.41 mM).

Assuming that chain transfer to solvent is the sole chain end forming event and that the solvent concentration remains constant at its initial value, $DP_n$ (cumulative value) can be expressed as a function of conversion according to eqn (2):¹³

$$DP_n = \frac{[M]_0(2 - \alpha)}{2[S]_0 C_{tr,S}}$$

where $[M]_0$ and $[S]_0$ represent initial monomer and solvent concentrations, and $\alpha$ denotes fractional monomer conversion. Fitting of eqn (2) to a data set of $DP_n$ vs. conversion for a system where chain transfer to solvent is not the sole end forming event leads to overestimation of $C_{tr,S}$. The $M_n$ data for the conventional radical polymerization of TBAM in 1-propanol at the three different (low) initiator concentrations in Fig. 1a have been plotted versus conversion in Fig. 4. The data were subsequently fitted to eqn (2) resulting in $C_{tr,S} = 4.3 \times 10^{-4}$, which is close to the value of $C_{tr,S} = 3.6 \times 10^{-4}$ derived from the Mayo plot (Fig. 3 and Table 1). The MWDs of Fig. 1a may be influenced by chain transfer to solvent or monomer or both; however, the fact that the Mayo treatment (which gives $C_{tr,S}$) results in a value close to that from eqn (2) is consistent with chain transfer to solvent being the main end-forming event under these conditions.

The $M_n$ data for the conventional radical polymerizations of MEA in 1-propanol (Fig. 1b) and 3-methyl-3-pentanol (Fig. 1c) at different (low) initiator concentrations were plotted versus conversion in Fig. 4. Fitting with eqn (2) resulted in $C_{tr,S} = 1.9 \times 10^{-3}$ in 1-propanol, in relatively good agreement with $C_{tr,S} = 1.4 \times 10^{-3}$ obtained by Mayo analysis. In the case of 3-methyl-3-pentanol, $C_{tr,S} = 2.5 \times 10^{-3}$ is derived by fitting eqn (2), which is more than six times greater than the $C_{tr,S} = 4.0 \times 10^{-4}$ obtained by Mayo analysis. This discrepancy may indicate that the conventional radical polymerization of MEA at low initiator concentrations (Fig. 1c) is subject to chain transfer to monomer as well as to solvent (the Mayo plot is specifically designed to only “detect” chain transfer to solvent, whereas fitting of eqn (2) “detects” chain transfer to all low MW species). The reason that chain transfer to monomer appears to be less significant for MEA in 1-propanol than 3-methyl-3-pentanol may be that $C_{tr,S}$(Mayo) is considerably higher (factor of 3.5) for MEA in 1-propanol than in 3-methyl-3-pentanol, thus reducing the relative impact of chain transfer to monomer (which impacts analysis using eqn (2)).

**Nitroxide-Mediated radical polymerizations**

NMP initiated by a macroinitiator of relatively high MW can be a useful tool for studying chain transfer processes because chain

![Scheme 2: Structural isomers of C₆H₁₃OH used as solvents.](image)

![Fig. 4: $M_n$ versus conversion for conventional radical polymerizations of 2 M TBAM in 1-propanol (□), MEA in 1-propanol (○) and MEA in 3-methyl-3-pentanol (○) at 120 °C at different [TBP]₀ corresponding to Fig. 1 with full lines representing $M_n$ calculated using eqn (2) with $C_{tr,S} = 4.3 \times 10^{-4}$, $1.9 \times 10^{-3}$ and $2.5 \times 10^{-3}$ respectively.](image)
transfer to low MW species is readily detected in the MWDs as low MW tailing. In the case of a sufficiently high level of chain transfer to solvent, $M_n$ may go through a maximum with increasing conversion.\(^2\) NMP of TBAM initiated by poly(t-BA)-SG1 was carried out in the three different alcohol solvents: 3-methyl-3-pentanol, 1-propanol, and 1-hexanol possessing a range of $C_{tr,S}$ (Table 1). For all three alcohols, $M_n$ initially increases with conversion indicative of a controlled/living system, but subsequently goes through a maximum at 60–75\% conversion (depending on solvent), consistent with significant chain transfer to solvent (Fig. 5). It is clear that the maximum attainable MW is dependent upon the magnitude of the $C_{tr,S}$ with the highest MW for the poly(TBAM) block achieved in 3-methyl-3-pentanol, which possesses the lowest $C_{tr,S}$. For all three solvents, the values of $M_w/M_n$ increase gradually with conversion, consistent with chain transfer to solvent occurring continuously (Fig. 5).

Rather significant differences in polymerization rate ($R_p$) can be observed between the solvents in the corresponding conversion versus time data (Fig. S1†) with the highest $R_p$ being obtained for 3-methyl-3-pentanol. It is well-known that the nature of the solvent can influence rate coefficients in radical polymerization\(^26\)– such a discussion goes beyond the scope of the present work. Suffice it to say that there is no correlation between $R_p$ and the $C_{tr,S}$ values.

We began by carrying out the NMP of MEA using the bimolecular AIBN/SG1 system in 1-propanol with $[MEA]_0/[AIBN]_0 = 222$ and 444 at 120 °C (Fig. 6). Up to about 60\% conversion, an increase in the initiator concentration by a factor of two (i.e. $[MEA]_0/[AIBN]_0 = 222$ vs. 444 with constant $[AIBN]_0/[SG1]_0$) resulted in a decrease in $M_n$ by close to a factor of two. The higher the targeted $M_{n,th}$, the higher is the probability that a given chain will undergo chain transfer during the polymerization, and thus $M_n$ values begin to deviate from linearity at lower conversion (~60 vs. ~70\% conversion) and $M_w/M_n$ values are higher for the data set with the highest $M_{n,th}$. Replacing 1-propanol with 1-hexanol ($[MEA]_0/[AIBN]_0 = 444$) resulted in higher $M_w/M_n$ due to an increase in the size of the low MW tail (Fig. S3†), but $M_n$ remained approximately linear with conversion up to ~60\% with a similar maximum $M_n$ as for 1-propanol (Fig. 6). The similar maximum MW obtained in the two different

![Fig. 5](a) $M_w/M_n$ and (b) $M_n$ versus conversion plots of poly(t-BA)-SG1-initiated NMP of 2 M TBAM at 120 °C with 25 mol\% excess free SG1 and [TBAM]$_0$/[poly(t-BA)-SG1]$_0 = 300$ in 3-methyl-3-pentanol (●), 1-propanol (▲) and 1-hexanol (□).

![Fig. 6](a) $M_w/M_n$ and (b) $M_n$ versus conversion plots for NMP of 2 M MEA at 120 °C: Bimolecular systems used [SG1]$_0$/[AIBN]$_0 = 2.5$ and [MEA]$_0$/[AIBN]$_0 = 222$ (●), 444 (▲) in 1-propanol, and [MEA]$_0$/[AIBN]$_0 = 444$ in 1-hexanol (□). Poly(t-BA)-SG1-initiated NMP (●) of MEA with 25 mol\% excess free SG1 in 3-methyl-3-pentanol and [MEA]$_0$/[poly(t-BA)-SG1]$_0 = 300$. 

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linear alcohols supports the estimated similar $C_{tr,S}$ values from the above conventional radical polymerization Mayo data for MEA (Fig. 3 & Table 1). NMP of MEA was also conducted using poly(r-Ba)-SG1 as macroinitiator in 3-methyl-3-pentanol (Fig. 6) using the same conditions as for the NMP of TBAM (including identical [monomer]/[macroinitiator] ratios, Fig. 5). This resulted in significantly lower maximum $M_n$ in comparison to TBAM. For both MEA and TBAM, there is an insignificant number of chains originating from spontaneous initiation in comparison to the number of chains from the macroinitiator or in situ generated alkoxyamine (previously reported for TBAM,7 and as verified for MEA in this work by heating MEA alone at 120 °C for various times (Fig. S5†)).

Conclusions

Chain transfer to solvent is shown to strongly influence the maximum attainable molecular weight in the conventional radical polymerization and NMP of two structurally diverse acrylamide monomers in various alcohol solvents. For polymerizations of TBAM, the propensity for chain transfer to solvent is shown to increase with the number of methylene units (CH$_2$) in the solvent with the highly branched alcohol, 3-methyl-3-pentanol (having fewer CH$_2$S) giving the smallest $C_{tr,S}$ values (using Mayo analysis). Among the solvents investigated, 3-methyl-3-pentanol is thus recommended for solution NMP, since it allows the attainment of higher molecular weights. $C_{tr,S}$ values obtained from Mayo analysis (detecting only chain transfer to solvent) and analyses of conventional radical polymerizations at low initiator concentrations (that account for chain transfer to all small molecules), suggest that chain transfer to monomer may also be a significant end forming event for the polymerization of MEA in 3-methyl-3-pentanol. This is perhaps not surprising given the high number of CH$_2$ units in this monomer (six saturated CH$_2$s versus two CH$_2$s in the alcohol solvent). Overall, the higher $C_{tr,S}$ values for MEA are consistent with the lower maximum $M_n$ values in NMP in comparison to TBAM.

Acknowledgements

The authors are grateful to the Irish Research Council (formerly IRCSET) for a postgraduate scholarship award to C. Magee, as part of the first IUPAC Transnational Call in Polymer Chemistry, which was co-ordinated by F. Aldabagh. The authors are grateful to C. Elvira and M. Nash (CSIC, Madrid, Spain) for supplying MEA monomer.

Notes and references

Synthesis of fluorinated alkoxyamines and alkoxyamine-initiated nitroxide-mediated precipitation polymerizations of styrene in supercritical carbon dioxide†

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TIPNO (2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide)-alkoxyamine was found to give reasonably controlled/living nitroxide-mediated (NMP) precipitation polymerizations of styrene in supercritical carbon dioxide (scCO2). In contrast under the same conditions, the analogous SG1 (N-tert-butyl-N′-(1-diethylphosphono-2,2-dimethylpropyl)nitroxide)-alkoxyamine gave higher rates of polymerization and inferior controlled/living character. The circumvention of the requirement for excess free [nitroxide]0 allowed the study of nitroxide partitioning effects in scCO2 for three newly synthesized fluorinated alkoxyamines. Two alkoxyamines dissociated into scCO2-philic fluorinated TIPNO-nitroxide derivatives, while another contains a similar sized fluorinated "foot". Despite the increased steric bulk about the N–O bond for the novel fluorinated alkoxyamines, all polymerizations proceeded at a similar rate and level of control to the TIPNO system in solution (toluene). PREDICI simulations for the styrene/TIPNO system are used to support extensive partitioning effects observed in scCO2 for the fluorinated alkoxyamines.

Introduction

Supercritical carbon dioxide (scCO2) is a benign solvent used to circumvent the requirement for environmentally damaging volatile organic solvents.1–3 Advantages include a readily accessible critical point (31 °C and 7.4 MPa),4 variable solubility by subtle changes in pressure and temperature,5 and the lack of chain transfer to solvent in radical polymerizations.6,7 It is particularly well-suited for heterogeneous radical polymerizations, since reagents such as the monomer, initiator and controlling agent are generally soluble in scCO2, but the resultant polymer is insoluble and precipitates.5,1

If the precipitation system is carried out in the presence of a colloidal stabilizer to prevent coagulation of particles, then dispersion polymerization results giving polymer of narrow particle size distributions and well-defined particles (d ≈ 100 nm to 15 μm).1–3 The monomer is not always soluble in the reaction medium, such as in the controlled/living nitroxide-mediated radical polymerization (NMP) of N-isopropylacrylamide (NIPAM) in scCO2, where an inverse suspension system is generated.8,9 In recent years, there has been a proliferation in the numbers of reported controlled/living precipitation and dispersion polymerizations in scCO2 with NMP,9–11 atom transfer radical polymerization (ATRP),12–19 reversible addition-fragmentation chain transfer (RAFT),15–19 and iodine transfer polymerization (ITP).16–20 The slow build up in molecular weight (MW) in a controlled/living system by virtue of the equilibrium between active propagating radicals and dormant polymer chains allows measurement of the critical degree of polymerization (Jcrit) before polymer chains precipitate from solution or the continuous phase (containing monomer and scCO2). After Jcrit, the polymerization continues in the monomer-rich particle phase. For controlled/living precipitation/dispersion polymerizations, Jcrit can be predicted as a function of targeted molecular weight and initial monomer loading.10 In contrast, in a non-living conventional radical polymerization, no single Jcrit value can be applied due to polymer chains instantaneously reaching high MW and continually precipitating. NMP of styrene in scCO2 at high monomer loadings (70% w/w) is superior in terms of control over the molecular weight distribution (MWD) for the SG1 (N-tert-butyl-N′-(1-diethylphosphono-2,2-dimethylpropyl)nitroxide)/AIBN (2,2′-azoisobutyronitrile) precipitation system in comparison to solution (toluene) polymerization carried out.
under analogous conditions.\textsuperscript{47} The effect of nitroxide partitioning upon control was found to be extenuated at low styrene loadings,\textsuperscript{15} where the system becomes heterogeneous sooner due to a lower $f_{\text{eq}}$. In that work, the bimolecular nitroxide/AIBN system was used,\textsuperscript{14,23} leading to uncertainty in initiator efficiencies due to unknown amounts of alkoxyamine generated in situ. Control was facilitated by using excess amounts of nitroxide relative to initiating AIBN-derived radicals in order to negate the loss of nitroxide from the locus of polymerization via partitioning, as well as side-reactions occurring at the initial stages of alkoxyamine formation and during polymerization. In the present article controlled/living precipitation NMP in scCO$_2$ has for the first time been achieved in the absence of excess free nitroxide. The effect of partitioning on nitroxide and styryl-initiating fragments ("foot" part of alkoxyamine) is examined by preparing and using three new alkoxyamine initiators. Preparation of the fluorous-labeled nitroxides required incorporation of functional handles in the TIPNO (2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide)nitroxide (either on the phenyl position, or the $t$-butyl fragment), whereas introduction of a fluorous-labelled foot was easily accomplished by modification of the popular benzyl chloride alkoxyamine\textsuperscript{42} prepared with regular TIPNO.

Two alkoxyamines dissociate into scCO$_2$-philic fluorinated TIPNO-nitroxide derivatives (F-TIPNO 1b and F-Si-TIPNO 1c, Scheme 1), while another contains a similar sized fluorinated "foot" (TIPNO alkoxyamine F-foot 2, Scheme 2), which will remain attached to the growing polymer chain. The performance of these fluorinated alkoxyamines in polymerizations of styrene in scCO$_2$ is compared with analogous polymerizations in solution, as well as TIPNO and SG1-alkoxyamine 1a and 1d analogues.

## Experimental

### Materials

Styrene monomer (Aldrich, >99%) was distilled under reduced pressure prior to use. Reagent grade toluene (Aldrich, >99.7%), THF (Aldrich >99%), methanol, ethanol, CO$_2$ (BOC gases, 99.8%), trimethylacetaldehyde (Aldrich, 96%), diethyl phosphate (Aldrich, 98%), tert-butyl amine (Aldrich, 98%), ethylenediamine (Aldrich, 99%), salicylaldehyde (Aldrich, 98%), sodium chloride (Aldrich, 99%), sodium borohydride (Aldrich, 99%), 4,4,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecanoyl chloride (Santa Cruz Biotechnology), triethylamine (Aldrich), ethylenediamine (Aldrich), Mn(OAc)$_2$•4H$_2$O (Acros Organics), pyridine (Acros Organics), diisopropyl(1H,1H,2H,2H-perfluorodecyl) silane (Fluorous Technologies Inc.), trifluoromethanesulfonic acid (TCI America), 1H,1H,2H,2H-perfluorodecanol (Matrix Scientific), tetrabutylammonium hydrogen sulfate (TCI America), 2-hydroxybenzaldehyde (EMD), and sodium hydroxide (Fisher Scientific) were used as received. Dichloromethane (Fisher Scientific) was dried over calcium hydride (Fisher Scientific) when anhydrous conditions were required. NMR solvents CDCl$_3$ and C$_6$F$_6$ were obtained from Cambridge Isotope Laboratories and used as received. TIPNO \textsuperscript{41} (2,5,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide) and SG1 \textsuperscript{44} (N-tert-butyl-N\{(1-diethylphosphono-2,2-dimethylpropyl)nitroxide\}) were prepared according to the literature. TIPNO alkoxyamine (2,2,5-trimethyl-3-(1-phenylethoxy)-4-phenyl-3-azahexane) and SG1 alkoxyamine (diethyl-[1-[tert-butyl(1-phenylethoxy)amino]-2,2-dimethylpropyl]phosphonate) were prepared by reaction of the appropriate free nitroxide with styrene using a Mn(salen) catalyst.\textsuperscript{43} The preparations of F-TIPNO 1b, F-Si-TIPNO 1c and F-TIPNO-foot 2 alkoxyamines and the Mn(salen) catalyst are described below.

### Characterization of alkoxyamines

NMR spectra were recorded at ambient temperature on a Varian 500 MHz spectrometer in CDCl$_3$, as solvent unless otherwise noted. C$_6$F$_6$ ($\delta$ = 164.9 ppm) was used as reference for $^{19}$F NMR. FTIR spectra were recorded on a Perkin-Elmer spectrometer as a neat film on a KBr cell. High resolution mass spectra (HRMS) were recorded on a benchtop Mariner electrospray ionization time-of-flight (ESITOF) mass spectrometer.

### Synthesis of alkoxyamines

#### Preparation of N,N'-ethylenbis(salicylimine) ligand

Ethylene diamine (3.000 g, 49.92 mmol) was dissolved in 250 mL of absolute ethanol, and 2-hydroxybenzaldehyde (12.191 g, 99.83 mmol) was added: a yellow precipitate formed. The mixture was heated to reflux for 30 minutes; all of the precipitate dissolved to form a yellow solution. Crystals formed upon cooling to room temperature. Additional cooling in an ice-water bath for 30
Preparation of Mn(salen) chloride o xo catalyst. To a 500 mL two-necked flask equipped with a reflux condenser was added N,N'-ethylenebis(salicylimine) (12.570 g, 46.849 mmol), Mn(OAc)\textsubscript{2} - 4H\textsubscript{2}O (22.970 g, 93.698 mmol) and 180 mL of methanol. Air was bubbled through the solution while being heated to reflux. After 3 hours, an aqueous solution of LiCl (9.930 g, 234.2 mmol in 70 mL of H\textsubscript{2}O) was added to the refluxing solution. Reflux concurrent with air bubbling through the solution was continued for another 2 hours. After cooling to room temperature, the mixture was cooled with an ice water bath for 1 hour. The resulting precipitate was isolated by filtration. Additional crops of crystals were obtained by addition of water to the mother liquors and cooling in an ice bath to give a total of 12.728 g. The first batch of precipitate contains both an orange-brown clay-like material, and darker brown precipitate with a sand-like texture. The orange precipitate was not an effective catalyst for alkoxamine formation. The later crops gave the darker brown precipitate. This is the active catalyst. The combined dark brown material was recrystallized once from boiling water including a hot filtration to give 7.989 g (45% yield) of black crystals (mp > 260 °C), which are a reliable catalyst for alkoxamine formation.

Preparation of F-TIPNO 1b. To a solution of TIPNO-OH alkoxamine\textsuperscript{40} (0.6962 g, 1.961 mmol) and 4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecanoyl chloride (1.001 g, 1.961 mmol) in 30 mL of anhydrous dichloromethane was added triethylamine (0.1997 g, 1.961 mmol) at room temperature, the mixture was stirred for 1 hour, then 50 mL of dichloromethane and 50 mL of H\textsubscript{2}O were added. The layers were separated; the organic layer was washed two times with 30 mL of brine, dried over MgSO\textsubscript{4}, and concentrated in vacuo.

The resulting crude oil (2.136 g) was purified by silica gel column chromatography using 95 : 5 hexanes/ethyl acetate, to give the title compound as a colorless oil, 1.445 g, (87% yield) of black crystals (mp > 260 °C), which are a reliable catalyst for alkoxamine formation.

Preparation of F-Si-TIPNO 1c. TIPNO-neopentyl-OH alkoxamine was synthesized as previously described.\textsuperscript{47} Following the procedure of Crich et al.\textsuperscript{48} a mixture of di-isopropyl-(1H,1H,2H,2H-perfluorododecyl)silane (0.3012 g, 0.4549 mmol) and trifluoromethanesulfonic acid (0.6827 g, 0.4549 mmol) was added to a flame-dried round bottom flask and stirred under nitrogen for 48 hours. The reaction mixture was diluted with 1 mL of dichloromethane and a solution of TIPNO-neopentyl-OH alkoxamine (0.1032 g, 0.3026 mmol), and pyridine (0.036 mL, 0.455 mmol) in 1 mL of dichloromethane was added at 0 °C. The reaction mixture was stirred at 0 °C for 1 hour, diluted with 15 mL of dichloromethane, washed sequentially with H\textsubscript{2}O (10 mL), sat. NH\textsubscript{4}Cl solution (10 mL), brine (10 mL), dried over MgSO\textsubscript{4}, and concentrated in vacuo. The resulting crude oil (0.3503 g) was purified by silica gel column chromatography with 90 : 10 hexanes/ethyl acetate as eluent to give 0.1081 g (36% yield) of the title compound 1c as a colorless viscous oil as a 1 : 1 mixture of diastereomers.

TLC: 90 : 10 hexanes/ethyl acetate, UV, p-anisaldehyde, R\textsubscript{f}: 0.62.\textsuperscript{4} H NMR (500 MHz, CDCl\textsubscript{3}, both diastereomers): 7.54–7.15 (m, 18H), 5.18 (s, 2H), 5.11 (s, 2H), 4.95–4.90 (m, 2H), 3.45 (d, J = 10.6 Hz, 1H), 3.33 (d, J = 10.6 Hz, 1H), 2.73–2.67 (m, 4H), 2.55–2.45 (m, 4H), 2.36–2.31 (m, 1H), 1.64 (d, J = 6.6 Hz, 3H), 1.56 (d, J = 6.6 Hz, 3H), 1.43–1.35 (m, 1H), 1.32 (d, J = 6.4 Hz, 3H), 1.06 (s, 9H), 0.94 (d, J = 6.4 Hz, 3H), 0.79 (s, 9H), 0.55 (d, J = 6.6 Hz, 3H), 0.22 (d, J = 6.6 Hz, 3H) ppm.

\textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}, DEPT, both diastereomers): δ 171.15, 148.27, 145.76, 142.97, 142.77, 133.34, 133.26, 131.30 (CH), 128.21 (CH), 127.51 (CH), 127.37 (CH), 127.15 (CH), 126.82 (CH), 126.32 (CH), 83.65 (CH), 83.02 (CH), 71.99 (CH), 71.87 (CH), 67.06 (CH\textsubscript{2}), 60.58, 60.45, 32.08 (CH), 31.68 (CH), 28.44 (CH\textsubscript{3}), 28.26 (CH\textsubscript{2}), 26.82 (CH\textsubscript{3}), 26.65 (CH\textsubscript{2}), 25.67 (CH\textsubscript{3}), 25.67 (CH\textsubscript{3}), 24.59 (CH\textsubscript{2}), 23.05 (CH\textsubscript{3}), 22.09 (CH\textsubscript{3}), 21.94 (CH\textsubscript{3}), 21.13 (CH\textsubscript{3}), 21.01 (CH\textsubscript{2}) ppm. \textsuperscript{19}F NMR (470 MHz, CDCl\textsubscript{3}): δ = −82.9 (t, J = 9.9 Hz, 4F), −116.9 to −117.0 (m, 4F), −123.7 to −123.9 (m, 4F), −123.8 to −123.9 (m, 4F), −124.0 to −124.1 (m, 4F), −124.8 to −124.9 (m, 4F), −125.6 (t, J = 14.6 Hz, 6F), −128.2 to −128.3 (m, 4F) ppm. FTIR: 3075 (aromatic C–H stretch), 2969 (benzyl C–H stretch), 1744 (C=O stretch), 1449 and 1365 (N–O stretch), 1428 (aromatic C–C stretch), 1204 (C–O stretch), 815 (p-substituted benzene), 699 (mono substituted benzene) cm\textsuperscript{-1}. HRMS: calcd for C\textsubscript{14}H\textsubscript{16}F\textsubscript{2}NO\textsubscript{3} [M + H]\textsuperscript{+}: 830.2486: found 830.2502.

Preparation of F-Si-TIPNO 1c. TIPNO-neopentyl-OH alkoxamine was synthesized as previously described.\textsuperscript{47} Following the procedure of Deni et al.,\textsuperscript{48} a solution of 1H, 1H, 2H, 2H-perfluorododecyl (8.715 g, 18.77 mmol) and tetrabutylammonium hydrogen sulfate (TBAH) (1.912 g, 5.633 mmol) in 44 mL of 50% aqueous NaOH and 45 mL of dichloromethane
was stirred vigorously for 10 minutes. A solution of TIPNO-benzyl Cl alkoxyamine (1.752 g, 4.694 mmol) in 45 mL of dichloromethane was added and the reaction mixture was heated to 40 °C for 2.5 hours. After cooling to room temperature, the layers were separated, and the aqueous layer was extracted three times with 50 mL of dichloromethane. The organic layers were combined, washed three times with 50 mL of 0.1 M hydrochloric acid, dried over MgSO₄, and concentrated in vacuo. The resulting crude oil (3.527 g) was purified by silica gel column chromatography with 98 : 2 hexanes/ethyl acetate as the eluent to give 2.353 g (63% yield) of the title compound as pale yellow oil as a 2.7 : 1 mixture of diastereomers. 1H NMR (500 MHz, CDCl₃, both diastereomers): δ 7.57–7.09 (m, 18H), 4.93 (m, 2H), 4.55 (s, 2H), 4.51 (s, 2H), 3.75 (m, 4H), 3.43 (d, J = 10.4 Hz, 1H), 3.31 (d, J = 10.4 Hz, 1H), 2.43–2.38 (m, 4H), 2.36–2.28 (m, 1H), 1.62 (d, J = 6.6 Hz, 3H), 1.32 (d, J = 6.6 Hz, 3H), 1.30 (d, J = 6.3 Hz, 3H), 1.05 (s, 9H), 1.02–0.96 (m, 1H), 0.92 (d, J = 6.3 Hz, 3H), 0.78 (s, 9H), 0.54 (d, J = 6.6 Hz, 3H), 0.21 (d, J = 6.6 Hz, 3H) ppm. 13C NMR (125 MHz, CDCl₃, DEPT, both diastereomers): δ 145.67, 144.91, 136.59, 135.95, 131.11 (CH), 131.02 (CH), 127.69 (CH), 127.63 (CH), 127.49 (CH), 127.27 (CH), 126.45 (CH), 126.31 (CH), 83.38 (CH), 82.57 (CH), 73.27 (CH₂), 73.19 (CH), 72.24 (CH), 72.19 (CH), 62.10 (CH₂), 61.91 (CH₂), 59.66, 59.63, 32.03 (CH), 31.68 (CH₂-CH₂), 31.63 (CH₂-CH₂), 31.63 (CH), 28.36 (CH₃), 28.17 (CH₃), 24.66 (CH₃), 23.15 (CH₃), 22.11 (CH₃), 21.94 (CH₃), 21.11 (CH₃), 20.96 (CH₃) ppm. 19F NMR (470 MHz, CDCl₃, both diastereomers): δ –82.9 (t, J = 10 Hz, 2F), –83.1 (t, J = 10 Hz, 2F), –115.5 to –115.7 (m, 2F), –115.7 to –115.8 (m, 2F) –123.8 to –124.0 (m, 4F), –124.1 to –124.0 (m, 8F), –124.8 to –124.9 (m, 4F), 125.8 to –125.9 (m, 4F), –128.3 to –128.4 (m, 6F) ppm. FTIR: 3034 (aromatic C–H stretch), 2934 (benzyllic C–H stretch), 1492 and 1365 (CH₂–CH₂), 1152 (CH₂–CH₂), 882 (p–substituted benzene) cm⁻¹. HRMS: calcd for C₃₃H₃₆F₁₇NO₂ [M + H]⁺: 5728.2381; found 5732.2381. This journal is © The Royal Society of Chemistry 2014

Solution polymerizations

Styrene (2.0 g, 19.2 mmol), alkoxyamine (5.0 × 10⁻⁵ mol) and toluene (1.8 mL) were added to a Pyrex ampoule, subjected to several freeze–degass–thaw cycles, and sealed under vacuum. Ampoules were heated at 110 °C for various times using an aluminium heating block. Reactions were quenched in an ice-water bath.

Precipitation polymerizations in supercritical carbon dioxide

The reactor (25 mL) was loaded with styrene (50%) w/v loading, 12.5 g, 0.12 mol, alkoxyamine (3.125 × 10⁻⁴ mol) and a magnetic stirring bar and sealed. The reaction vessel was purged for 20 minutes by bubbling gaseous CO₂ through the reaction mixture. Liquid CO₂ (~5 MPa) was added and the reactor was immersed in an oil bath. The temperature was raised to the reaction temperature of 110 °C, followed by pressurizing the reaction vessel to 30 MPa by the addition of further CO₂. Reactions were quenched by submersion of the reactor in an ice-water bath.

Results and discussion

Synthesis of fluorinated alkoxyamine initiators

Three TIPNO-based alkoxyamine initiators were prepared for this study: F-TIPNO 1b and F-Si-TIPNO 1c, in which a fluorous fragment was attached to the nitroxide TIPNO, and TIPNO alkoxyamine F-foot 2 in which the phenethyl “foot” of the alkoxyamine was labelled with a fluorous segment.

For the preparation of F-TIPNO 1b (Scheme 3), 4-bromo-benzyl alcohol was protected using THP, and the Grignard

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**Scheme 3** Preparation of F-TIPNO alkoxyamine 1b.
reagent was prepared. The latter was a challenging reaction: the key to success was the use of 1,2-dibromoethane to enhance formation of the Grignard species. Following the standard TIPNO synthesis of addition to the nitro oxide and Cu-catalyzed oxidation to the nitro oxide, treatment with styrene and Mn(salen) gave the THP-protected alkoxyamine. The synthetic technique required to make reliable Mn(salen) catalyst required careful air oxidation of the Mn-species while preparing the salen chloride complex, presumably forming the oxo species. Hot recrystallization, and discarding the orange portion of precipitate (the non-oxo species) gave a Mn(salen)Cl-oxo catalyst that was extremely effective in the styrene/nitro oxide coupling reaction. Although the formation of this catalyst has been published previously,43 this detailed experimental is included to ensure the repeatability of the alkoxyamine synthesis. Acid-mediated deprotection followed by esterification with the fluoroalkane acid chloride provided F-TIPNO alkoxyamine 1b bearing a tag containing 17 fluorine atoms.

F-Si-TIPNO 1c was prepared starting with THP-protection of 2-methy1-2-nitropropan-1-ol (Scheme 4), followed by reductive condensation with isobutyl aldehyde to give the THP protected nitrone. Addition of phenyl Grignard, oxidation and coupling with styrene using the Mn(salen) protocol afforded THP-protected alkoxyamine. Acidic removal of the protecting group, followed by silylation using the procedure of Crich48 gave F-Si-TIPNO alkoxyamine 1c bearing 21 fluorine atoms on the fluorous unit.

The synthesis of the alkoxyamine containing a fluorourous-tagged phenethyl “foot” portion proceeded by the normal synthesis of TIPNO,49 coupling with styrene benzyl chloride, and etherification to provide TIPNO alkoxyamine F-foot 2 (Scheme 5). This alkoxyamine contains a fluoruous fragment consisting of a 17-fluorine atom segment on the portion of the initiator, which dissociates to become the first carbon radical of the polymerization sequence. Consequently, the fluoruous tag is covalently attached to the growing polymer on the end distal to the nitro oxide cap.

Solution polymerizations

TIPNO 1a and TIPNO-derivative alkoxyamines 1b, 1c and alkoxyamine 2 all gave very similar rates of polymerization of styrene in toluene (50% (w/v), Fig. 1) at 110 °C, indicating that structural modifications to the nitro oxide and styryl “foot” parts of the alkoxyamine have no significant effect on the equilibrium constant (K) for trapping and dissociation in organic solution.

As expected from the higher K for SG1,30,31 the SG1-alkoxyamine 1d-initiated polymerizations proceeded at a higher rate than TIPNO-derivatives 1a, 1b, 1c and 2. All alkoxyamine-initiated polymerizations in solution proceeded in a controlled/living manner with molecular weights close to theoretical values (eqn (1)) and only less than theoretical values beyond about 55% conversion, although in most cases \( M_n/M_\infty < 1.3 \) throughout (Fig. 2).

Precipitation polymerizations in supercritical carbon dioxide (scCO2)

For NMP of styrene (50% w/v) in scCO2 at 110 °C and 30 MPa, the point of precipitation \( J_{\text{crit}} \) is predicted to occur at approximately \( M_n = 3,450 (\sim 8.5\% \text{ conv.}) \) using the model developed by O’Connor et al.,19 that can be used to estimate \( J_{\text{crit}} \) as a function of initial monomer loading and targeted molecular weight.

![Scheme 4 Preparation of F-Si-TIPNO alkoxyamine 1c.](image)

Fig. 1 Conversion versus time plots for TIPNO-1a (circles), F-TIPNO-1b (squares), F-Si-TIPNO-1c (inverted triangle), SG1-1d (upright triangles) and TIPNO-F-foot-2 (diamonds). styryl-alkoxyamine initiated NMP of styrene (50% w/v) at 110 °C using \([\text{monomer}]_0/\text{alkoxyamine}_0 = 384\). Open and closed symbols are respectively solution in toluene and precipitation in scCO2 at 30 MPa polymerizations.
Since NMPs in scCO₂ in the present article go beyond this conversion, all are considered heterogeneous systems. The alkoxyamine TIPNO 1a-initiated styrene precipitation polymerization in scCO₂ proceeded at a similar rate to the analogous NMP carried out in the presence of a 5% excess of free TIPNO at lower conversions (23% conv. after 22 h as opposed to 19% conv. after 21 h, Fig. 3), although the system containing an initial excess of free nitroxide reached a limiting conversion sooner (Fig. S18a†). Moreover, controlled/living character was good without the 5% excess of free TIPNO (M_n = 7960 and M_w/M_n = 1.22), with the presence of excess free nitroxide providing a marginally narrower MWD (M_n = 9000 and M_w/M_n = 1.14, also see Fig. S18b† for additional data showing the effect of free TIPNO on control/living character). It was therefore evident that controlled/living character for alkoxyamine-initiated precipitation polymerizations in scCO₂ can be established without the requirement for excess free nitroxide. Thus all subsequent NMPs in scCO₂ were initiated by alkoxyamines without the addition of free nitroxide. As previously observed by Aldabbagh et al.¹⁶ for bimolecular nitroxide/AIBN systems, polymerization rates are lower for precipitation polymerizations in scCO₂ in comparison to analogous solution polymerizations of styrene (Fig. 1). This has been attributed to monomer partitioning, i.e. some styrene residing in the continuous scCO₂ phase after particle formation, leading to a lower monomer concentration in the particles (the main locus of polymerization).

Very significant differences in polymerization rate and control are observed in scCO₂ between SG1-alkoxyamine 1d and TIPNO-alkoxyamine 1a with M_n (1d) > M_n (1a) and higher polydispersities for 1d than 1a (1d: M_w/M_n = 1.25–1.57 and 1a: M_w/M_n = 1.22–1.36). The higher rate and inferior control for SG1 in scCO₂ is due to a combination of higher K_{i,th}²⁰,²¹ and a higher solubility of SG1 in scCO₂, leading to greater nitroxide partitioning away from the locus of polymerization after particle formation. Although there is no literature data available for nitroxide solubilities in scCO₂, one may expect a greater solubility for TIPNO in the organic phase (particles) due to TIPNO’s organic nature in comparison to SG1, which contains heteroatoms (e.g. phosphorous). Poor control for SG1-mediated polymerizations in scCO₂ were not previously observed in bimolecular nitroxide/AIBN systems in scCO₂ because of the use of a high ratio of [SG1]_0/[AIBN]_{0,53}²³–²⁵ Despite TIPNO 1a and fluorinated alkoxyamine F-TIPNO 1b-initiated NMP exhibiting the same rate of polymerization in solution, unexpectedly the 1a-initiated NMP was marginally faster in scCO₂. The fluorinated nitroxide 1b is more CO₂philic than TIPNO 1a, and is expected to partition away from the locus of polymerization upon particle formation, which should lead to a higher rate rather than the observed lower rate of polymerization for 1b.

To understand the effects of nitroxide partitioning more quantitatively, modelling and simulations were conducted using PREDICI²⁵ for the St/TIPNO system at 110 °C using a previously published approach²⁵ (the model used here was identical, with the exception of the inclusion in this work of a reaction step for spontaneous (thermal) initiation of styrene according to: R_{nth} = k_{nth}[St]^3). Conditions and parameters: [St]_0 = 8.7 M, [alkoxyamine]_0 = 0.0227 M, propagation rate coeff. (k_p)²⁴ = 1580 M⁻¹ s⁻¹, termination rate coeff. (k_t)²⁵ = 1.57 × 10⁸ M⁻¹ s⁻¹ (combination only), activation rate coeff.
\( k_{\text{act}} = 1.184 \times 10^{-3} \text{ s}^{-1} \), deactivation rate coeff. \( k_{\text{deact}} = 8.2 \times 10^2 \text{ M}^{-1} \text{ s}^{-1} \), thermal initiation of styrene \( k_{\text{i,th}} = 4.26 \times 10^{-11} \text{ M}^{-1} \text{ s}^{-1} \). The system modelled is a bulk polymerization with a fictitious nitroxide partitioning step into a continuous phase (i.e. the scCO\(_2\) phase) having the same volume as the organic phase, whereby a given fraction of free nitroxide is removed (equivalent to partitioning to the continuous phase) assuming phase transfer equilibrium. Fig. 4 and 5 show conversion vs. time data and MWDs obtained for different partition coefficients of \( \Gamma = [\text{nitroxide}]_{\text{org}}/[\text{nitroxide}]_{\text{CO}_2} = \infty \) (no partitioning), 1 and 0.25. \( \Gamma = 1 \) and 0.25 correspond to situations where 50% and 80% of free nitroxide, respectively, is located in the continuous phase. It is apparent that even if very extensive nitroxide partitioning occurs, the increase in rate of polymerization is relatively small. Fig. 5 shows that as expected, there is a broadening of the MWDs with increasing nitroxide.

![Fig. 4](image1)

**Fig. 4** Simulated conversion vs. time data of the styrene/TIPNO system at 110 °C (see text for details). [Nitroxide]\(_{\text{org}}\)/[Nitroxide]\(_{\text{CO}_2}\) = \( \infty \) (dotted line), 1 (dashed line), and 0.25 (solid line). \( \Gamma = \infty \), 1 and 0.25 correspond to situations where 0, 50 and 80% of free nitroxide, respectively, is located in the continuous phase.

![Fig. 5](image2)

**Fig. 5** Simulated MWDs (at 48% conv.) of the styrene/TIPNO system at 110 °C. [Nitroxide]\(_{\text{org}}\)/[Nitroxide]\(_{\text{CO}_2}\) = \( \infty \) (dotted line), 1 (dashed line), and 0.25 (solid line). \( \Gamma = \infty \), 1 and 0.25 correspond to situations where 0, 50 and 80% of free nitroxide, respectively, is located in the continuous phase.

![Fig. 6](image3)

**Fig. 6** Comparing the performance of fluorinated alkoxyamines 1b, 1c and 2 with the TIPNO analogue 1a in the precipitation NMP of styrene (50% w/v) at 110 °C using [monomer]\(_0\)/[alkoxyamine]\(_0\) = 384. (a) TIPNO-1b, 43% after 98 h, \( M_n = 19700 \) and \( M_w/M_n = 1.55 \) compared with TIPNO-1a initiated analogue, 49% after 72 h, \( M_n = 19000 \) and \( M_w/M_n = 1.36 \). (b) TIPNO-1c, 39% conv. after 61 h, \( M_n = 20000 \) and \( M_w/M_n = 1.29 \) compared with the TIPNO-1a initiated analogue, 42% conv. after 47 h, \( M_n = 17400 \) and \( M_w/M_n = 1.27 \). (c) TIPNO-F-Foot-2, 38% conv. after 69 h, \( M_n = 19500 \) and \( M_w/M_n = 1.32 \) compared with the TIPNO-1a initiated analogue, 42% conv. after 47 h, \( M_n = 17400 \) and \( M_w/M_n = 1.27 \).
partitioning, with the livingness (number fraction of chains with alkoxyamine-terminated z-ends at 48% conversion) decreasing according to 97.5, 96.8, 95.3% with increasing partitioning. Indeed the alkoxyamine-initiated polymerizations using fluorinated TIPNO derivative 1b ($M_n/M_w = 1.25–1.55$) proceeded with inferior control relative to TIPNO 1a, as demonstrated by $M_w$ higher than theoretical values and higher polydispersities (Fig. 2).

If nitroxide partitioning is the main cause of inferior control for alkoxyamine 1b in scCO$_2$, it follows that the polymerization rate is quite insensitive to the degree of nitroxide partitioning, more so than one would have expected. As such it may be reasonable to argue that the relatively small difference in the rate of polymerization between TIPNO 1a and F-TIPNO 1b in scCO$_2$ is not necessarily inconsistent with F-TIPNO nitroxide partitioning away from the locus of polymerization resulting in wider MWDs. Moreover similar to the simulated MWD overlays in Fig. 5, nitroxide partitioning seems to give marginal broadening experimentally (Fig. 6a), when comparing MWDs for TIPNO 1a with the F-TIPNO 1b-initiated polymerization at similar intermediate conversions.

Precipitation polymerizations of styrene in scCO$_2$ for fluorinated alkoxyamines F-Si-TIPNO 1c and TIPNO alkoxyamine F-foot 2 were carried out (Fig. 6b and c). Broadening for 1c was analogous to F-TIPNO 1b-initiated polymerization in scCO$_2$ with the alkoxyamine 2 experiment also giving a high $M_w$ shoulder, in the case of 1c presumably due to nitroxide partitioning as discussed above for 1b. Again, contrary to expectation, the polymerization rate for 1c was somewhat lower than for 1a. Alkoxyamine 2 differs from the other fluorinated alkoxyamines 1b and 1c in that (non-fluorinated) TIPNO is the mediating nitroxide and a fluorinated initiating styryl “foot” radical is produced upon dissociation. As such, the extent of nitroxide partitioning would be expected to be the same as for 1a. One can speculate that the F-content in the propagating radical part of the alkoxyamine leads to an increase in $k_{act}$ (due to increased solubility in the continuous phase), and thus later nucleation; it is possible that this is related to the partial loss of control. It is unlikely that a higher $k_d$ for TIPNO-F-foot 2 is causing the observed MWD broadening in comparison to TIPNO-1a alkoxyamine, because rates and control are very similar in solution (toluene), assuming negligible solvent effects on activation-deactivation kinetics in scCO$_2$.

Conclusions

In the absence of excess free [nitroxide]$_0$, TIPNO alkoxyamine is found to give superior controlled/living character for precipitation NMP of styrene in scCO$_2$ compared to the SG1 analogue. In solution (toluene), the latter system resulted in slightly less control and a higher rate of polymerization. Differences between TIPNO- and SG1-alkoxyamine can be rationalised in terms of the higher $K$ for SG1 and a greater level of nitroxide partitioning for SG1 in the heterogeneous system. Despite increased steric congestion about the alkoxyamine (N-O bond) in novel fluorinorated TIPNO-alkoxyamine initiators, a similar equilibrium constant ($K$) to TIPNO for activation/deactivation in organic solution can be inferred. The greater partitioning of fluorinated TIPNO derivatives in scCO$_2$ impacts on the controlled/living character, broadening the molecular weight distributions.

Acknowledgements

This work received financial support as part of the first IUPAC Transnational Call in Polymer Chemistry funded by awards from the Irish Research Council (formerly IRCSET) to F. Aldabbagh and the National Science Foundation (NSF CHE-1057927, USA) to R. Braslav.

Notes and references