Polymer Chemistry

Cite this: *Polym. Chem.*, 2011, **2**, 815

www.rsc.org/polymers

PAPER

View Online
Dynamic Article Links

# Synthesis and modification of thermoresponsive poly(oligo(ethylene glycol) methacrylate) *via* catalytic chain transfer polymerization and thiol–ene Michael addition†

**Alexander H. Soeriyadi,[a] Guang-Zhao Li,[bc] Stacy Slavin,[b] Mathew W. Jones,[b] Catherine M. Amos,[b] C. Remzi Becer,[b] Michael R. Whittaker,[a] David M. Haddleton,[b] Cyrille Boyer[a] and Thomas P. Davis*[a]**

***Received 16th November 2010, Accepted 15th December 2010***
**DOI: 10.1039/c0py00372g**

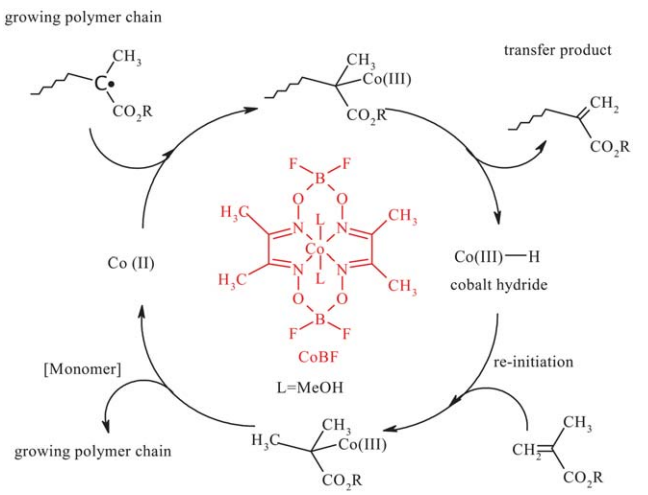
Downloaded on 21 March 2011
Published on 24 January 2011 on http://pubs.rsc.org | doi:10.1039/C0PY00372G

Various poly(oligo(ethylene glycol) methyl ether methacrylate)s (POEGMEMAs) have been prepared by Catalytic Chain Transfer Polymerization (CCTP) using a range of OEGMEMA monomers (molecular weight from 180 to 1100 g mol$^{-1}$). The chain transfer constants of bis(boron difluorodimethylglyoximate) cobalt(II) (CoBF) were determined and are reported for each monomer. The copolymerization of POEGMEMA ($M_n$ = 475 g mol$^{-1}$) with diethylene glycol methyl ether methacrylate (DEGMEMA) yielded thermoresponsive polymers. The lower critical solution temperatures (LCSTs) of the polymer chains can be tuned by the copolymer composition over the range 30 °C to 95 °C. In addition, the presence of the vinylic end-group, characteristic of CCT polymerization, provided further scope for post-synthetic modification *via* thiol–ene click chemistry, through nucleophilic Michael addition with various functional thiol compounds such as 2-mercaptoethanol, 3-mercaptopropionic acid, benzyl mercaptan and 1-dodecanethiol. The thiol–ene reaction was rigorously tested, optimized and characterized in this study in terms of solvents and most importantly the choice of the catalyst: dimethyl phenyl phosphine, tertiary amine or hexylamine. The optimum conditions reported allow near-quantitative functionalization of these macromonomers without significant side reactions. The effect of the end-group on the LCST has also been investigated, as well as thermal stability temperature of the copolymers.

This document is shared for only research purposes and cannot be distributed without the permission of the authors and the publisher.
Please visit WWW.BECERGROUP.SEMS.QMUL.AC.UK/PUBLICATIONS.HTML to get more info on our research interests!!!

## Introduction

Catalytic chain transfer polymerization is a very efficient and versatile free-radical polymerization technique for the synthesis of macromonomers with ω-unsaturated vinyl terminal groups.[1,2] It is used commercially by DSM and DuPont for the production of viscosity modifiers and engine additives for the automotive industry. The reaction is mediated by the ability of certain low-spin Co(II) complexes, such as cobaloximes, to efficiently catalyze the chain transfer to monomer reaction.[3] A widely investigated Co(II) transfer agent is bis(boron difluorodimethylglyoximate) cobalt(II) (CoBF).[1,2,4–6] The chain transfer constant of CoBF is typically $10^2$ to $10^4$ for monomers containing an α-methyl group, such as methacrylates. CCT occurs *via* a mechanism characterized by two consecutive steps:[3,7] firstly, the Co(II) complex abstracts a hydrogen from the propagating radical to form a dead polymer chain and a Co(III)–H complex; then this complex reacts with another monomer molecule to produce the original Co(II) complex and another propagating radical (Scheme 1). The Co(II)




**Scheme 1** General mechanism for Catalytic Chain Transfer Polymerization (CCTP).

[a]*Centre for Advanced Macromolecular Design (CAMD), School of Chemical Engineering, The University of New South Wales, Sydney, NSW, 2052, Australia. E-mail: t.davis@unsw.edu.au*
[b]*Department of Chemistry, University of Warwick, Coventry, CV4 7AL, UK. E-mail: d.m.haddleton@warwick.edu.uk*
[c]*Research Institute of Materials Science, South China University of Technology, Guangzhou, 510640, China*

† Electronic supplementary information (ESI) available: NMR spectra and MALDI-ToF spectra. See DOI: 10.1039/c0py00372g

View Online

Published on 24 January 2011 on http://pubs.rsc.org | doi:10.1039/C0PY00372G
Downloaded on 21 March 2011

complex acts in a catalytic fashion and therefore is not consumed in the process. CCT is a very powerful technique used to synthesize low molecular weight polymers/oligomers terminated by a vinyl end-group (macromonomers) with a large range of functional or non-functional monomers. CCT polymerization can be performed in a large range of solvents, ranging from aqueous to nonpolar organic media.[8,9]

Inspired by the work reported by Ishizone *et al.*[10] and later by Lutz and Hoth[11] and others, the preparation of thermoresponsive, antifouling PEG based polymers is of huge interest for the preparation of thermoresponsive micelles, hybrid organic/inorganic nanoparticles,[12–14] surface modification,[15–18] hyperbranched/nanogels and protein–polymer conjugates.[19–25] As illustrated by the recent publication of Dong and Matyjaszewski who describe the first preparation of thermally responsive poly(oligo(ethylene glycol) methyl ether methacrylate) *via* AGET ATRP in miniemulsion.[26] In this current study, the synthesis of thermoresponsive PEG based macromonomers by the copolymerization of OEGMEMA and DEGMEMA using CCT is described. The lower critical solution temperature (LCST) was tuned by the composition of these two monomers to yield thermoresponsive polymers with LCSTs ranging from 30 to 90 °C. To the best of our knowledge, this is the first preparation of thermally responsive poly(oligo(ethylene glycol) methyl ether methacrylate) *via* Catalytic Chain Transfer Polymerization. The advantage of CCT is that the resulting polymer chains have unsaturated vinylic end-groups (with very high chain-end fidelity; close to 100%) which create a large range of synthetic options for end-group modification with simple organic compounds. Over the last decade, "click" chemistry has opened new avenues for the design and creation of tailor-made macromolecules.[27–29] Thiol–ene "click" chemistry, in which thiols react quantitatively with double bonds, has been shown to be highly efficient in a large range of solvents, without the addition of metals, under mild conditions.[30–38] There are two types of thiol–ene reaction: (i) a base catalyzed Michael addition and (ii) the anti-Markovnikov radical UV initiated click. Both of these approaches have been used for the functionalization of polymers[31,39] or for the design of complex macromolecules.[40–45]

In this study, thermoresponsive PEG-based copolymers and homopolymers of OEGMEMA obtained by CCT were modified using thiol–ene click chemistry with a variety of different functional thiol compounds to yield functional thermoresponsive polymers in high yield. The optimal conditions for thiol–ene click chemistry to obtain a very high degree of functionality (solvent and nature of the catalyst) are reported. The polymers were rigorously characterized *via* electrospray mass spectrometry (ESI-MS), $^1$H NMR spectroscopy and MALDI-ToF MS analysis. In addition, the thermoresponsive properties (LCST) and thermal properties (glass transition and decomposition temperatures) of the copolymers were determined before and after thiol–ene modification.

## Experimental

### Materials

The CCT agent bis(methanol) complex, $(CH_3OH)_2Co$–$(dmgBF_2)_2$ (CoBF), was synthesized according to the method of Bakac *et al.*[46,47] The CTA transfer efficiency was checked by CCT polymerization of methyl methacrylate (MMA) which yielded a $C_S$ value = 25 000. The monomers, $OEGMEMA_{475}$ (Aldrich, 95%), DEGMEMA (Aldrich, 95%), and $OEGMEMA_{1100}$ (Aldrich, 95%), were used as received. The initiator 4,4′-azobis-(4-cyanovaleric acid) (ACVA) was used as received and 2,2′-azobisisobutyronitrile (AIBN) was purified by recrystallisation twice from methanol. The thiols, 2-mercaptoethanol (2-ME, 99%, Sigma-Aldrich), 1-dodecanethiol (DT, 98+%, Sigma-Aldrich), benzyl mercaptan (BM, 99%, Sigma-Aldrich), 3-mercaptopropionic acid (3-MPA, 99%, Sigma-Aldrich), triethylamine (TEA, 99%, Fisher Scientific UK Ltd.), hexylamine (HA, 99%, Sigma-Aldrich), and dimethylphenylphosphine (DMPP, 99%, Aldrich) were used as received.

### Catalytic chain transfer (CCT) homopolymerization

General catalytic chain transfer polymerizations (CCTPs) were performed as follows: monomers (DEGMEMA, $OEGMEMA_{475}$, and $OEGMEMA_{1100}$) and solvents (acetonitrile or water/methanol mixture) were purged with $N_2$ gas for at least an hour prior to use. Stock solutions of CoBF were also weighed and purged with $N_2$ prior to use. AIBN or CVA was weighed into Schlenk flasks. All reaction mixtures were then mixed under $N_2$ gas. To ensure the absence of $O_2$, the reaction mixtures were subjected to at least three freeze–pump–thaw cycles. Polymerizations were performed at a constant temperature of 70 °C. Polymerizations were stopped by cooling and subsequent exposure to air. Polymers were then purified by precipitation and dialysis. Poly(OEGMEMA) was precipitated in diethyl ether and poly(DEGMEMA) was precipitated in water or cold petroleum ether (40–60 °C).

For semi-batch polymerizations, the procedure was the same, however, the monomer and CoBF solutions were added at a rate of 1 mL min$^{-1}$ throughout the reactions.

### Catalytic chain transfer (CCT) copolymerization

General CCT copolymerization procedure was as follows: monomers $OEGMEMA_{475}$ and DEGMEMA with different compositions and solvents (acetonitrile or water/methanol mixture) were mixed with AIBN and purged with $N_2$ gas at least one hour before use. Stock solutions of CoBF were also prepared and purged before use. All reaction mixtures were then mixed under $N_2$ gas. To ensure the absence of $O_2$, the reaction mixtures were then subjected to at least three freeze–pump–thaw cycles. Polymerizations were performed at a constant temperature of 70 °C. Polymerizations were stopped by cooling and subsequent exposure to air. Copolymers were then purified by dialysis in water/acetone.

### Hexylamine or triethylamine catalyzed thio-click reactions

Poly(OEGMEMA) was mixed with hexylamine or triethylamine, water, acetone, acetonitrile or DMSO used as solvents, and thiol reagent. In a typical reaction, 1 eq. of poly(OEGMEMA) (100 mg), 2 eq. of thiol, and 3 eq. of hexylamine were added into a flask and then purged for 15 minutes with $N_2$. The vials were then placed at ambient temperature or in a 40 °C oil bath for 14 hours before the reaction was stopped. The reaction mixtures were purified *via* precipitation in cold petroleum ether or dialysis.

 This journal is © The Royal Society of Chemistry 2011

View Online

Published on 24 January 2011 on http://pubs.rsc.org | doi:10.1039/C0PY00372G
Downloaded on 21 March 2011

### DMPP catalyzed thio-click reactions

Polymers, thiols and DMPP were mixed in a NMR tube containing acetone-$d_6$, acetonitrile-$d_3$ or DMSO-$d_6$. The reactions were performed at room temperature and monitored by $^1$H NMR spectroscopy. In a typical reaction, 1 eq. of polymer (0.05 g), 1.5 eq. of thiol and 0.05 eq. (1.7 mg) of DMPP were added to a NMR tube containing 0.5 mL of deuterated solvent. The reaction was monitored by the disappearance of the vinyl bond seen at 5.5–6.0 ppm.

### Characterization

**Gel permeation chromatography (GPC).** THF GPC was performed on a Shimadzu modular system, comprised of an autoinjector and a Polymer Laboratories 5.0 μm bead-size guard column (50 × 7.5 mm), followed by three linear PL columns and a differential refractive index detector using THF as the eluent at 40 °C with a flow rate of 1 mL min$^{-1}$. The GPC system was calibrated using linear polystyrene standards. DMAc GPC analyses of the polymers were performed in *N*,*N*-dimethylacetamide [DMAc; 0.03% w/v LiBr, 0.05% 2,6-dibutyl-4-methylphenol (BHT)] at 50 °C (flow rate = 1 mL min$^{-1}$) using a Shimadzu modular system comprised of an SIL-10AD autoinjector, a PL 5.0 mm bead-size guard column (50 × 7.8 mm) followed by four linear PL (Styragel) columns ($10^5$, $10^4$, $10^3$, and 500 Å) and an RID-10A differential refractive-index detector. Calibration was achieved with commercial polystyrene standards ranging from 500 to $10^6$ g mol$^{-1}$.

**Nuclear magnetic resonance (NMR).** $^1$H NMR spectroscopy was used to determine the molecular weight and structural information for confirmation of thiol–ene click conjugation. NMR spectra were recorded on a Bruker DPX-300 MHz and Bruker DPX-400 MHz.

**UV-visible spectroscopy.** UV-visible spectra were recorded using a Cary 300 spectrophotometer (Bruker) equipped with a temperature controller.

**Cloud points measurements.** The transmittance of the solution was measured at $\lambda = 500$ nm through 10 mm path length cuvettes with a micro-stir bar and total volumes of 2 mL referenced against distilled water, using a PerkinElmer Lambda 35 UV-VIS spectrometer. The water-jacketed sample and reference cuvette holders were coupled with a Peltier PTP 1 + 1 Peltier temperature programmer adjusted at a heating rate of 1 °C min$^{-1}$. The cloud points (CP) were defined as the temperature corresponding to a 50% reduction in the original transmittance of the solution.

**Thermal gravimetric analysis (TGA).** TGA of polymers was performed using a Pyris 1 (PerkinElmer) with a rate of 5 °C min$^{-1}$ from ambient temperature to 500 °C. All the samples were preheated at 80 °C to remove any trace of water.

**Mass spectrometry (MALDI-ToF).** MALDI-ToF analysis was performed with a Bruker Ultraflex III equipped with a neodymium-doped yttrium aluminium garnet laser (Nd:YAG). The matrix solution was prepared by dissolving *trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) in a 1 mL mixture of acetone and water (equal volumes). Sodium iodide was added at 0.1% overall concentration and the polymer dissolved to a concentration of 10 mg cm$^{-3}$. The matrix solution (0.5 μL) was applied to the stainless steel side and the solvent allowed to evaporate. The same volume of the polymer sample solution was applied on top of the dried matrix, and the overall mixture allowed to dry. The sample was irradiated with 300–600 pulsed laser shots at a 1–10% laser power. Calibration was performed with various linear poly(ethylene glycol) methyl ether standards.

## Results and discussion

Catalytic chain transfer polymerizations of various oligo(ethylene glycol) methyl ether methacrylates were performed using 2,2′-azobisisobutyronitrile (AIBN) as the initiator, the bis(methanol) complex, $(CH_3OH)_2Co$–$(dmgBF_2)_2$ (CoBF), as a catalyst and acetonitrile as a solvent at 70 °C. The chain transfer constant of catalytic chain transfer polymerization can be easily calculated using the modified Mayo equation (eqn (1)),[1,2,48] provided the monomer conversion is maintained below 10%.

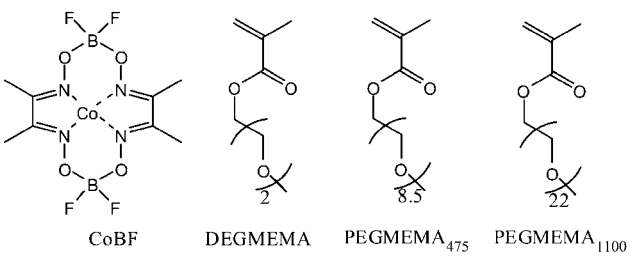
$$1/\mathrm{DP}_n = 2 + C_S \times ([C]/[M]) \quad (1)$$

where $\mathrm{DP}_n$ is the degree of polymerization, [*C*] is the concentration of the catalyst, and [*M*] is the initial monomer concentration. The monomers that were used in this study were diethylene glycol methyl ether methacrylate, oligo(ethylene glycol) methyl ether methacrylate (475), and oligo(ethylene glycol) methyl ether methacrylate (1100) as depicted in Scheme 2.

The polymer molecular weights were analyzed *via* GPC and $^1$H NMR spectroscopy. All the polymers exhibited monomodal distributions with PDI < 1.5. The polymers, after purification, were analyzed by $^1$H NMR and by MALDI-ToF (Fig. 1), and the molecular weights were calculated using the signal of the vinyl group at 5.5–6.0 ppm and eqn (2). It is noteworthy that the signals characteristic of the vinyl bond in the monomer and in the macromonomer are slightly different, *i.e.* 5.6–6.1 ppm and 5.5–6.0 ppm for monomer and macromonomer, respectively. This slight shift avoids any error in the molecular weight determination using NMR analyses (from traces of residual monomer).

$$M_{\mathrm{n,\ ^1H\ NMR}} = (\mathrm{I}^{\mathrm{CH_2OCO}}/\mathrm{I}^{\mathrm{CH=CH}}) \times M_{\mathrm{W}}^{\mathrm{OEGMEMA}} \quad (2)$$

where $M_{\mathrm{W}}^{\mathrm{OEGMEMA}}$, $\mathrm{I}^{\mathrm{CH_2OCO}}$ and $\mathrm{I}^{\mathrm{CH=CH}}$ correspond to the molar masses of OEGMEMA, integral of the signal at 4.1 ppm (attributed to $CH_2$ in the adjacent position of ester group) and of vinyl group, respectively. The molecular weights calculated by $^1$H NMR were in accordance with the molecular weights determined by MALDI-ToF.




**Scheme 2** Representation of CoBF and various oligo(ethylene glycol) monomers used in this study.

View Online

Published on 24 January 2011 on http://pubs.rsc.org | doi:10.1039/C0PY00372G
Downloaded on 21 March 2011

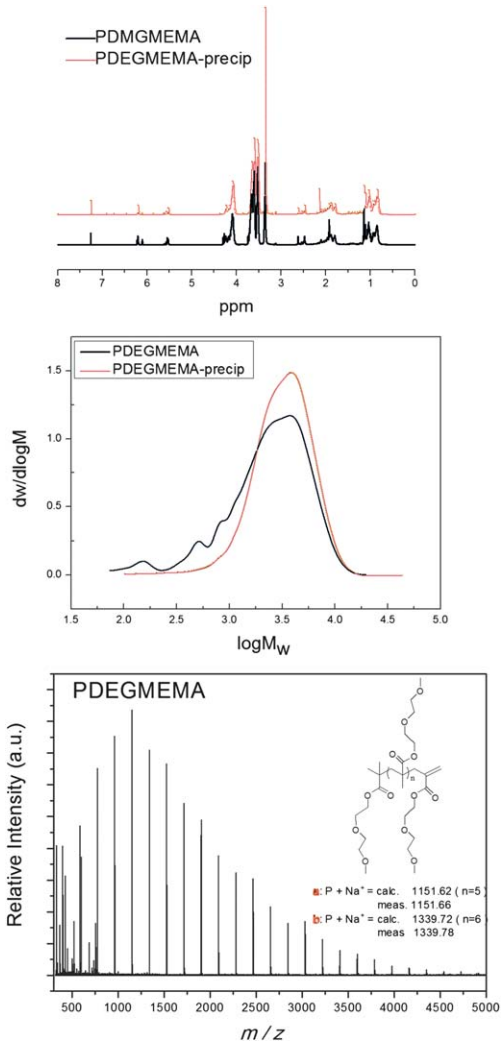



**Fig. 1** $^1$H NMR spectrum (top), GPC (middle) and MALDI-ToF MS (bottom) of poly(diethylene glycol) methyl ether methacrylate.

The plot of molecular weight *versus* the ratio of [CoBF]/[monomer] gives the chain transfer constant of CoBF for each monomer (Fig. 2).

## CCTP of OEGMEMA

The chain transfer constants ($C_S$) of CoBF to DEGMEMA, POEGMEMA$_{475}$, and POEGMEMA$_{1100}$ have been calculated as 7600, 1800, and 180, respectively (in acetonitrile at 70 °C). The $C_S$ values decrease proportionally with the chain length of the side chain (in this case, oligo(ethylene glycol)). A similar result was obtained by Forster and co-workers[5,49] for alkyl methacrylate (methyl methacrylate, ethyl methacrylate, and butyl methacrylate). The end-group fidelity of the polymers was well maintained as confirmed by MALDI-ToF for all monomers examined. According to the concentration of CoBF, it is possible to synthesize polymer with a DP$_n$ from 7 to 50 in acetonitrile with a PDI less than 1.5 (see earlier comments on PDI veracity).

As OEGMEMA and CoBF are water soluble, it was decided to investigate the polymerization of these monomers in water at 80 °C. The addition of methanol (50 v%), as a co-solvent, was successful for the polymerization of DEGMEMA {LCST ≈ 26 °C}. Table 1 shows the evolution of the molecular weights and PDI obtained for the polymerizations of OEGMEMA and DEGMEMA in water or water/methanol. For polymerization of OEGMEMA in water, poor control of the polymerization was observed as shown by a broadening of the molecular weight distributions. In comparison when acetonitrile was used as a solvent, narrower distributions were obtained. In addition, the molecular weights obtained in acetonitrile were usually lower than the molecular weights obtained in water, showing a better efficiency of transfer. It is possible that this difference in transfer efficiency could be attributed to the slight difference of temperature. However, Davis and Kukulj[50] and Heuts *et al.*[51] show that the efficiency of CoBF (or the transfer constant) is relatively unaffected by temperature. An increase in the temperature causes an increase in propagation rate ($k_p$) as well as an increase in transfer rate ($k_{tr}$), resulting in a null effect on the $C_S$ ($C_S = k_p/k_{tr}$). Another possible explanation is that the differences reported here are attributable to solvent effects. Haddleton and co-workers[52] have previously reported that CoBF can be degraded in water at elevated temperatures (~70 °C) and that the kinetics of the degradation process can be accelerated at low pH values. The degradation of CoBF causes a decrease in efficiency of the catalyst, inducing significant increases in the PDI during the polymerization. In the case of polymerization with CoBF in water, a semi-batch approach is necessary to keep the concentration of the CoBF constant thereby maintaining lower PDI.[52] As expected, improved PDIs and control of molecular weights

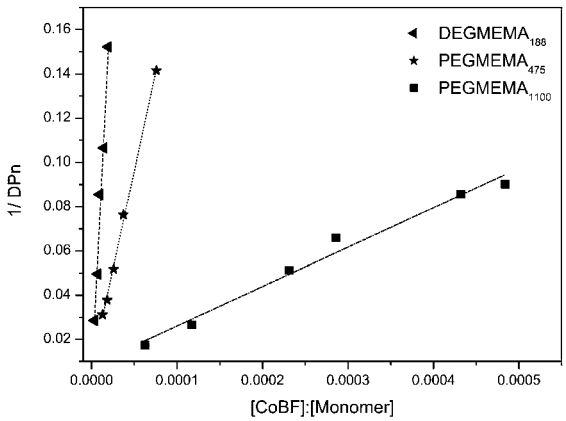



**Fig. 2** Mayo plot for chain transfer coefficient ($C_S$) of CoBF in catalytic chain transfer polymerization of various oligo(ethylene glycol) methyl ether methacrylates.

**Table 1** Catalytic chain transfer polymerization of diethylene glycol methyl ether methacrylate and oligo(ethylene glycol) methyl ether methacrylate using feed and batch techniques

| Run | Monomer | CoBF/ppm | Technique | $M_{n,\ GPC}$/g mol$^{-1}$ | PDI |
|---|---|---|---|---|---|
| P1[a] | DEGMEMA | 50 | Feed | 11 000 | 1.39 |
| P2[a] | DEGMEMA | 100 | Feed | 4600 | 1.31 |
| P3[a] | DEGMEMA | 100 | Batch | 4600 | 1.32 |
| P4 | OEGMEMA$_{475}$ | 50 | Feed | 3200 | 1.68 |
| P5 | OEGMEMA$_{475}$ | 100 | Feed | 2600 | 1.31 |
| P6 | OEGMEMA$_{475}$ | 50 | Batch | 2300 | 1.85 |
| P7 | OEGMEMA$_{475}$ | 100 | Batch | 4500 | 2.03 |

[a] Polymerization was carried out in mixture solvents: methanol/water (50/50 v%).

 This journal is © The Royal Society of Chemistry 2011

View Online

Published on 24 January 2011 on http://pubs.rsc.org | doi:10.1039/C0PY00372G
Downloaded on 21 March 2011

were observed for polymers obtained using a feed methodology compared to a batch approach (Table 1, runs P4–P7). In the batch approach, the CoBF is degraded during the polymerization, resulting in a change of the [*M*]/[CoBF] ratio and a subsequent drift in the polymer chain distribution.

### Copolymers of OEGMEMA

Inspired by the work of Lutz *et al.*[11,53] and Ishizone *et al.*,[10] the copolymerization of oligo(ethylene glycol) methyl ether methacrylate ($OEGMEMA_{475}$) with diethylene glycol methyl ether methacrylate (DEGMEMA) using CCT to yield thermo-responsive macromonomers was investigated. Copolymerizations were performed in acetonitrile at 70 °C for 14 hours. The feed compositions of these monomers were varied from 50/50 to 90/10 mol% of OEGMEMA/DEGEMMA. The final composition of these copolymers was calculated from $^1$H NMR using the ratio between $-OCH_2$ (ether group of OEG or DEG chains) and $OCH_3$ (from end-group). Table 2 shows the final composition of each copolymer (F). It is interesting to note that the monomer feed ratio and the final copolymer composition do not differ significantly at low conversion indicative that the reactivity ratios of the monomers are similar, implying that compositional drift is not a major factor in the reactions. The presence of composition drift during copolymerization can result in the synthesis of gradient copolymers, when a living radical polymerization is used,[54] or in the synthesis of heterogeneous copolymers, when a non-living free-radical polymerization is employed (such as CCTP).[55]

The copolymer composition of DEGMEMA and OEGMEMA allows tuning of the lower critical solution temperatures (LCSTs) from 30 to 90 °C as determined by turbidimetry measurements. Fig. 3 shows the evolution of LCST with copolymer composition. An increase of DEGMEMA in the copolymers causes a decrease in the LCST. For all copolymers, a very sharp transition (when heated) was observed (see Fig. 3). A relatively small hysteresis (5 °C) on heating and cooling was observed, comparable with the hysteresis obtained for copolymers synthesized by ATRP.[11]

### Thiol–ene "click" of OEGMEMA oligomers

Catalytic chain transfer polymerization yields oligomers with terminal vinyl end-groups at high efficiency (almost 100%). This vinyl-functionalization is not possible to achieve by other common radical polymerization techniques, such as ATRP,[56] NMP[57] or RAFT.[58] Since the introduction of the "click" concept by Sharpless *et al.*,[27] there have been a number of efficient conjugation reactions designated as "click" reactions. Recently, Hawker *et al.*[40] re-introduced an old but very efficient reaction,

**Table 2** Copolymerization results of oligo(ethylene glycol) methyl ether methacrylate ($OEGMEMA_{475}$) with diethylene glycol methyl ether methacrylate (DEGEMEMA). $M_n$ was calculated by GPC and NMR. Composition of polymer (F) was calculated from $^1$H NMR

| Run | *f* (initial feed) | *F* (final composition) | $M_{n,\,GPC}$/ g mol$^{-1}$ | $M_{n,\,NMR}$/ g mol$^{-1}$ |
|---|---|---|---|---|
| CP1 | 50 : 50 | 48 : 52 | 2800 | 3000 |
| CP2 | 70 : 30 | 69 : 31 | 2600 | 2700 |
| CP3 | 80 : 20 | 76 : 24 | 2600 | 3200 |
| CP4 | 90 : 10 | 92 : 8 | 3000 | 3400 |

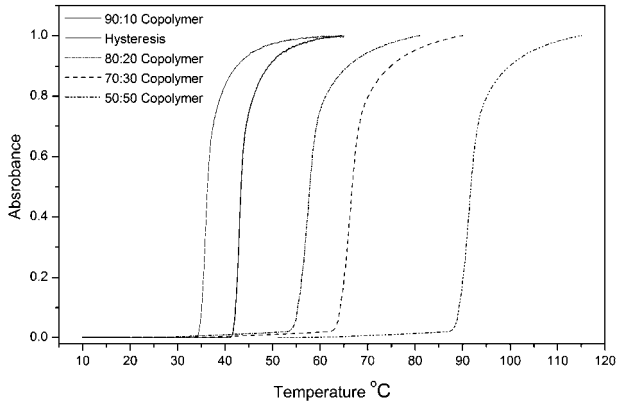



**Fig. 3** UV-Vis plot of various copolymers to show the lower critical solution temperature (LCST) behavior in water.

thiol–ene reactions, as a potential "click" reaction. Thiol–ene reactions embrace two types of mechanism: (i) anti-Markovnikov radical addition and (ii) base or nucleophile catalyzed Michael addition reaction.[27,29,40,43,59–61] Thiol–ene reactions can be performed in different solvents and are tolerant of a large range of functionalities. Recent work has been performed on the nature of thiol–ene reaction conditions by Davis and Haddleton and Lowe and co-workers[59] where it was reported that primary amines are more effective catalysts than secondary or tertiary amines, as well as significant reductions in the reactivity of methacrylates attributable to a combination of steric hindrance and inductive effects. The structure of the thiol compound also affects the efficiency of thiol–ene reactions, for example, alkyl thiols are less reactive than functional thiols, such as 2-mercaptoethanol or 1-thioglycerol. However, the previously reported studies were focused mainly on small molecules (monomers) or very short oligomers (dimers, trimers). In this current work it was necessary to optimize the thiol–ene Michael addition, as the "ene" components were methacrylate polymers to ensure high conversion and purity of the final product.

Poly(DEGMEMA) polymer was used to optimize the thiol–ene Michael addition of 2-mercaptoethanol. To establish the best solvent, the thiol–ene reactions were performed in a range of solvents: acetone, acetonitrile, and dimethyl sulfoxide (DMSO).

The following order of reactivity was established: DMSO > acetonitrile > acetone. The reaction carried out in DMSO reaches a very high yield at ambient temperature after 10 hours, while in acetone, yields superior to 30% could not be achieved. It

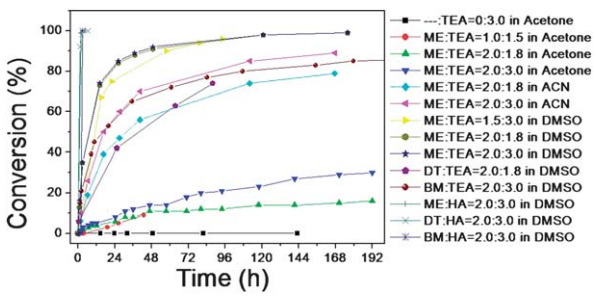



**Fig. 4** Vinyl conversion *versus* time plot for thiol-Michael addition of PDEGMEMA and different thiols in the presence of triethylamine or hexylamine in different solvents in order to study the solvents effect.

View Online

Published on 24 January 2011 on http://pubs.rsc.org | doi:10.1039/C0PY00372G
Downloaded on 21 March 2011

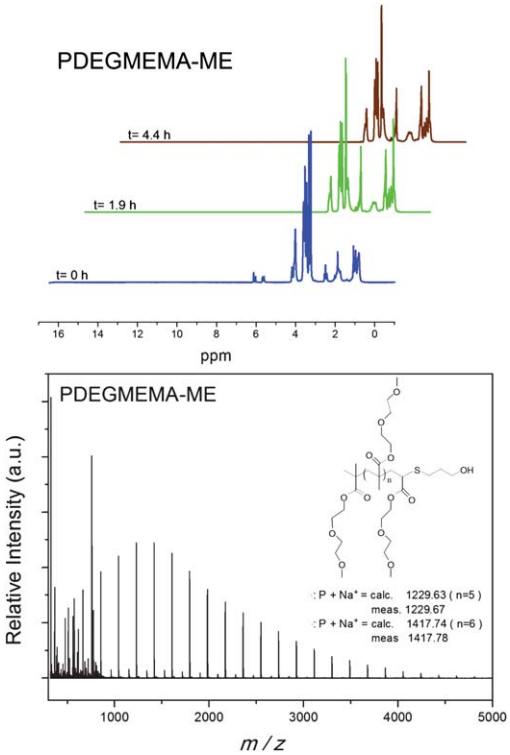



**Fig. 5** [1]H NMR spectrum (top) and MALDI-ToF MS (bottom) of 2-mercaptoethanol conjugated poly(diethylene glycol) methyl ether methacrylate catalyzed with hexylamine.

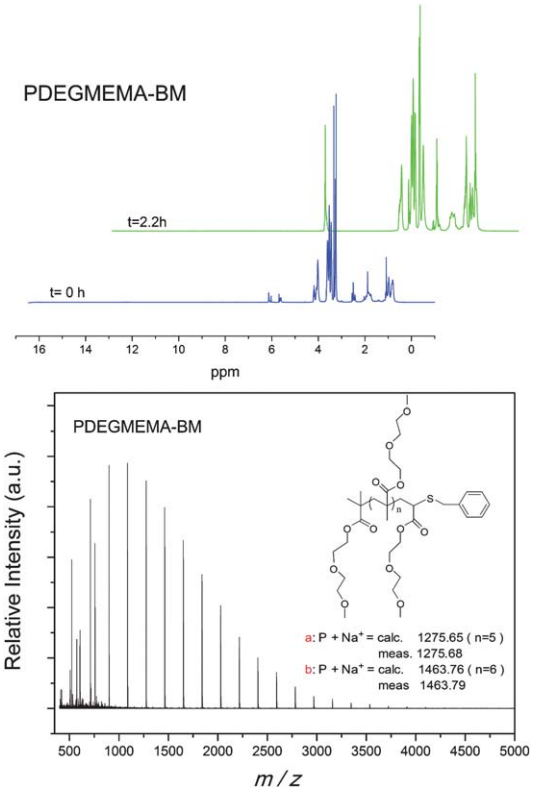



**Fig. 7** [1]H NMR spectrum (top) and MALDI-ToF MS (bottom) of benzyl mercaptan conjugated poly(diethylene glycol) methyl ether methacrylate catalyzed with hexylamine.

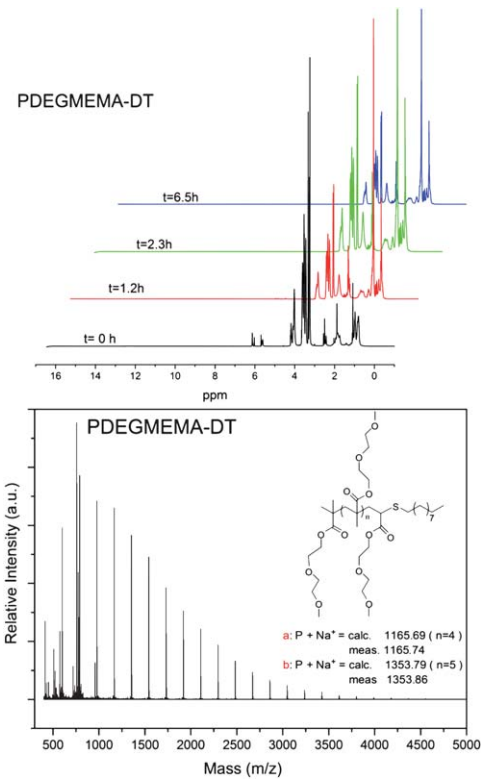



**Fig. 6** [1]H NMR spectrum (top) and MALDI-ToF MS (bottom) of 1-dodecanethiol conjugated poly(diethylene glycol) methyl ether methacrylate catalyzed with hexylamine.

is well known that polar solvents, such as DMSO, are good solvents for nucleophilic reactions.[59b] The efficacy of the catalyst used in these reactions, either phosphine or amine, was then examined. It has been highlighted previously that phosphine (*e.g.* dimethyl phenyl phosphine) is an effective catalyst[30,59b] at concentrations less than 0.05 mol% of the "ene" to prevent the side reaction of the conjugation of DMPP to the double bond.[59a] In this study, thiol–ene Michael reactions were initially performed and catalyzed by a combination of DMPP and TEA (the concentration of DMPP was maintained at less than 0.1 mol%),

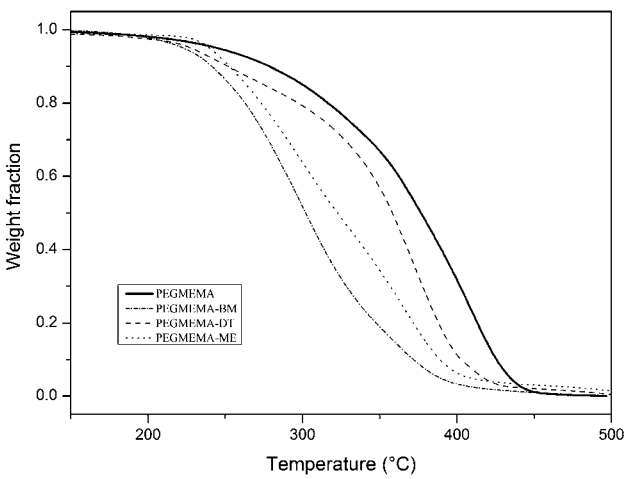



**Fig. 8** TGA curve for PEGMEMA after thiol–ene end-group modification.

 This journal is © The Royal Society of Chemistry 2011

View Online

Published on 24 January 2011 on http://pubs.rsc.org | doi:10.1039/C0PY00372G
Downloaded on 21 March 2011

**Table 3** Common bonds that can be found in the polymers with its corresponding enthalpy[64]

| Bond | Enthalpy $\Delta H$ (kJ mol$^{-1}$) at 25 °C |
|---|---|
| C–C | 346 |
| C–H | 414 |
| C–O | 358 |
| C–S | 289 |
| C=C | 614 |

in which side reactions of DMPP conjugated to the vinyl end-group of poly(DEGMEMA) were observed (Fig. S2–S7, ESI†).

Subsequently, to minimize the formation of by-products, it was decided to use amine catalysts. Two different amines were compared: triethylene amine (TEA) (tertiary) and hexylamine (HA) (primary). The TEA catalyst ensured a full conversion of the vinyl end-group of poly(DEGMEMA), without the formation of by-products, when the reaction was performed with 2-mercaptoethanol at ambient temperature.[59a]

However, the efficiency of this TEA-catalyzed reaction drops when an aliphatic or aromatic thiol is used, such as benzyl mercaptan. (TEA can only drive the reaction to a maximum of 70% after 3 days with benzyl mercaptan at ambient temperature, Fig. 4.) Quantitative conversion could only be attained when the reaction was performed at 40 °C for 14 hours. In order to accelerate the rate and increase the conversion of the thiol-Michael addition reaction, HA was used as a catalyst.

Thus, it was possible to functionalize different homopolymers of DEGMEMA and $OEGMEMA_{475}$ with different functional thiols, such as benzyl mercaptan, 1-dodecanethiol, and 2-mercaptoethanol with a high efficiency. The detailed characterization of the "clicked" polymers was performed using $^1$H NMR, GPC as well as MALDI-ToF MS. The characterization data are presented in Fig. 5, 6 and 7 for 2-mercaptoethanol, 1-dodecanthiol and benzyl mercaptan, respectively.

### Thermal analyses of post-functionalized poly(OEGMEMA)

TGA and DSC of poly(OEGMEMA) were performed to show the influence of thiol–ene "click" products on the thermal properties of the polymers. The thermal gravimetry analysis data, as shown in Fig. 8, indicates that all thiol–ene modified poly(OEGMEMA) have lower thermal stability than poly(-OEGMEMA) before modification (terminated by vinyl end-groups), regardless of the type of functional group. This result can be explained by the presence of the C–S bond, more unstable at high temperature than a C–C bond as indicated by the enthalpy of dissociation (Table 3).[62,64]

### Catalytic chain transfer copolymerization and thiol–ene modification

Further thiol–ene 'click' chemistry was performed on the copolymers of $OEGMEMA_{475}$ and DEGMEMA to investigate the effect of different end-groups on their thermoresponsive behavior (LCST), Table 4. Recently Theato's group investigated copolymers made with various RAFT agents giving rise to a range of end-group functionalities and they investigated the influence of end-groups on LCST behavior.[63] Homopolymers and copolymers functionalized by 1-dodecanethiol, benzyl mercaptan and 2-mercaptoethanol gave significantly different LCST temperatures attributable to hydrophobic and hydrophilic effects, Table 4. As expected, the thiol–ene "click" reaction of the hydrophobic end-group caused an LCST decrease while "click" reaction of the hydrophilic end-group lead the LCST to increase.

## Conclusions

In conclusion, we report on the catalytic chain transfer polymerizations of oligo(ethylene glycol) methyl ether methacrylates using CoBF as a catalyst. The chain transfer values were measured to be similar with other (larger) methacrylates and also exhibit the same trends with the ester chain length. Moreover, copolymers of $OEGMEMA_{475}$ and DEGMEMA have been synthesized and characterized in terms of thermal behavior and the lower critical solution temperature (LCST) in water. The terminal vinyl functionality of the oligomers has been exploited in thiol–ene reactions to make a range of functional oligomers.

## Acknowledgements

CB and TPD thank ARC and UNSW for funding and for fellowship (CB and TPD: APD and Federation Fellow,

**Table 4** List of polymers synthesized in this study using catalytic chain transfer polymerization and further modification by thiol-Michael addition to give an LCST library[a]

| Run | Structure | $M_{n,\ GPC}$/g mol$^{-1}$ | PDI | LCST/°C |
|---|---|---|---|---|
| A1 | DEGMEMA | 2500 | 1.53 | 47.2 |
| A2 | DEGMEMA–ME | 1100 | 2.91 | 52 |
| A3 | DEGMEMA–DT | 3200 | 1.50 | 16 |
| A4 | DEGMEMA–BM | 2200 | 1.61 | 32 |
| A5 | PEGMEMA | 6000 | 1.40 | >100 |
| CP1 | DEGMEMA–PEGMEMA (50 : 50) | 2800 | 1.55 | 95 |
| CP2 | DEGMEMA–PEGMEMA (70 : 30) | 2600 | 1.45 | 65 |
| CP3 | DEGMEMA–PEGMEMA (80 : 20) | 2600 | 1.56 | 58 |
| CP4 | DEGMEMA–PEGMEMA (90 : 10) | 3000 | 1.52 | 43 |
| A12 | DEGMEMA–PEGMEMA (90 : 10)–DT | 3100 | 1.56 | 35 |
| A13 | DEGMEMA–PEGMEMA (90 : 10)–ME | 3050 | 1.54 | 42 |

[a] A2–A4 were obtained after thiol–ene modification with 2-mercaptoethanol, 1-dodecanethiol and benzyl mercaptan. A12 and A13 were obtained after thiol–ene modification with 1-dodecanethiol and 2-mercaptoethanol.

View Online

respectively). DMH thanks CSC and UoW for funding (GL) and the EU MC fellowship (235999) (CRB). Equipment used in part was supported by the Innovative Uses for Advanced Materials in the Modern World (AM2), with support from Advantage West Midlands (AWM) and part funded by the European Regional Development Fund (ERDF).

## References


1 A. A. Gridnev, *J. Polym. Sci., Part A: Polym. Chem.*, 2000, **38**, 1753–1766.
2 A. A. Gridnev and S. D. Ittel, *Chem. Rev.*, 2001, **101**, 3611–3659.
3 (*a*) J. P. A. Heuts, G. E. Roberts and J. D. Biasutti, *Aust. J. Chem.*, 2002, **55**, 381–398; (*b*) T. P. Davis, D. M. Haddleton and S. N. Richards, *J. Macromol. Sci., Rev. Macromol. Chem. Phys.*, 1994, **C34**, 243–324.
4 T. P. Davis, D. Kukulj, D. M. Haddleton and D. R. Maloney, *Trends Polym. Sci.*, 1995, **3**, 365–373.
5 J. P. A. Heuts, D. J. Forster and T. P. Davis, *Macromolecules*, 1999, **32**, 3907–3912.
6 C. Kowollik and T. P. Davis, *J. Polym. Sci., Part A: Polym. Chem.*, 2000, **38**, 3303–3312.
7 A. Debuigne, R. Poli, C. Jérôme and C. Detrembleur, *Prog. Polym. Sci.*, 2009, **34**, 211–239.
8 D. M. Haddleton, E. Depaquis, E. J. Kelly, D. Kukulj, S. R. Morsley, S. A. F. Bon, M. D. Eason and A. G. Steward, *J. Polym. Sci., Part A: Polym. Chem.*, 2001, **39**, 2378–2384.
9 M. E. Thomson, N. M. B. Smeets, J. P. A. Heuts, J. Meuldijk and M. F. Cunningham, *Macromolecules*, 2010, **43**, 5647–5658.
10 S. Han, M. Hagiwara and T. Ishizone, *Macromolecules*, 2003, **36**, 8312–8319.
11 J.-F. Lutz and A. Hoth, *Macromolecules*, 2005, **39**, 893–896.
12 C. Boyer, M. R. Whittaker, M. Luzon and T. P. Davis, *Macromolecules*, 2009, **42**, 6917–6926; C. Boyer, M. R. Whittaker, K. Chuah, J. Liu and T. P. Davis, *Langmuir*, 2010, **26**, 2721–2730.
13 S. A. Meenach, K. W. Anderson and J. Z. Hilt, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 3229–3235.
14 M. Chanana, S. Jahn, R. Georgieva, J.-F. Lutz, H. Bäumler and D. Wang, *Chem. Mater.*, 2009, **21**, 1906–1914.
15 S. Kessel, S. Schmidt, R. Müller, E. Wischerhoff, A. Laschewsky, J.-F. Lutz, K. Uhlig, A. Lankenau, C. Duschl and A. Fery, *Langmuir*, 2009, **26**, 3462–3467.
16 H. M. Zareie, C. Boyer, V. Bulmus, E. Nateghi and T. P. Davis, *ACS Nano*, 2008, **2**, 757–765.
17 E. Wischerhoff, S. Glatzel, K. Uhlig, A. Lankenau, J.-F. o. Lutz and A. Laschewsky, *Langmuir*, 2009, **25**, 5949–5956.
18 E. Wischerhoff, N. Badi, J.-F. Lutz and A. Laschewsky, *Soft Matter*, 2010, **6**, 705–713.
19 Z. Zarafshani, T. Obata and J.-F. Lutz, *Biomacromolecules*, 2010, **11**, 2130–2135.
20 C. R. Becer, S. Hahn, M. W. M. Fijten, H. M. L. Thijs, R. Hoogenboom and U. S. Schubert, *J. Polym. Sci., Part A: Polym. Chem.*, 2008, **46**, 7138–7147.
21 T. M. Eggenhuisen, C. R. Becer, M. W. M. Fijten, R. Eckardt, R. Hoogenboom and U. S. Schubert, *Macromolecules*, 2008, **41**, 5132–5140.
22 H. M. L. Thijs, C. R. Becer, C. Guerrero-Sanchez, D. Fournier, R. Hoogenboom and U. S. Schubert, *J. Mater. Chem.*, 2007, **17**, 4864–4871.
23 C. Weber, C. R. Becer, W. Guenther, R. Hoogenboom and U. S. Schubert, *Macromolecules*, 2010, **43**, 160–167.
24 C. Weber, C. R. Becer, R. Hoogenboom and U. S. Schubertt, *Macromolecules*, 2009, **42**, 2965–2971.
25 C. R. Becer, K. Kokado, C. Weber, A. Can, Y. Chujo and U. S. Schubert, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 1278–1286.
26 H. Dong and K. Matyjaszewski, *Macromolecules*, 2010, **43**, 4623–4628.
27 H. C. Kolb, M. G. Finn and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2001, **40**, 2004–2021.
28 R. K. Iha, K. L. Wooley, A. M. Nystrom, D. J. Burke, M. J. Kade and C. J. Hawker, *Chem. Rev.*, 2009, **109**, 5620–5686.
29 C. R. Becer, R. Hoogenboom and U. S. Schubert, *Angew. Chem., Int. Ed.*, 2009, **48**, 4900–4908.
30 J. W. Chan, B. Yu, C. E. Hoyle and A. B. Lowe, *Polymer*, 2009, **50**, 3158–3168.
31 L. Nurmi, J. Lindqvist, R. Randev, J. Syrett and D. M. Haddleton, *Chem. Commun.*, 2009, 2727–2729.
32 B. Yu, J. W. Chan, C. E. Hoyle and A. B. Lowe, *J. Polym. Sci., Part A: Polym. Chem.*, 2009, **47**, 3544–3557.
33 L. M. Campos, K. L. Killops, R. Sakai, J. M. J. Paulusse, D. Damiron, E. Drockenmuller, B. W. Messmore and C. J. Hawker, *Macromolecules*, 2008, **41**, 7063–7070.
34 D. Valade, C. Boyer, T. P. Davis and V. Bulmus, *Aust. J. Chem.*, 2009, **62**, 1344–1350.
35 (*a*) C. Boyer, A. Granville, T. P. Davis and V. Bulmus, *J. Polym. Sci., Part A: Polym. Chem.*, 2009, **47**, 3773–3794; (*b*) C. Boyer and T. P. Davis, *Chem. Commun.*, 2009, 6029–6031.
36 G. Chen, S. Amajjahe and M. H. Stenzel, *Chem. Commun.*, 2009, 1198–1200.
37 A. B. Lowe, C. E. Hoyle and C. N. Bowman, *J. Mater. Sci.*, 2010, **20**, 4745–4750.
38 A. B. Lowe, *Polym. Chem.*, 2010, **1**, 17–36.
39 M. W. Jones, G. Mantovani, S. M. Ryan, X. Wang, D. J. Brayden and D. M. Haddleton, *Chem. Commun.*, 2009, 5272–5274.
40 L. M. Campos, K. L. Killops, R. Sakai, J. M. J. Paulusse, D. Damiron, E. Drockenmuller, B. W. Messmore and C. J. Hawker, *Macromolecules*, 2008, **41**, 7063–7070.
41 N. Gupta, B. F. Lin, L. M. Campos, M. D. Dimitriou, S. T. Hikita, N. D. Treat, M. V. Tirrell, D. O. Clegg, E. J. Kramer and C. J. Hawker, *Nat. Chem.*, 2010, **2**, 138–145.
42 C. J. Hawker and K. L. Wooley, *Science*, 2005, **309**, 1200–1205.
43 M. J. Kade, D. J. Burke and C. J. Hawker, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 743–750.
44 K. L. Killops, L. M. Campos and C. J. Hawker, *J. Am. Chem. Soc.*, 2008, **130**, 5062–5064.
45 F. A. Leibfarth, M. Kang, M. Ham, J. Kim, L. M. Campos, N. Gupta, B. Moon and C. J. Hawker, *Nat. Chem.*, 2010, **2**, 207–212.
46 A. Bakac, M. E. Brynildson and J. H. Espenson, *Inorg. Chem.*, 1986, **25**, 4108–4114.
47 A. Bakac and J. H. Espenson, *J. Am. Chem. Soc.*, 1984, **106**, 5197–5202.
48 A. A. Gridnev, *J. Polym. Sci., Part A: Polym. Chem.*, 2002, **40**, 1366–1376.
49 R. A. Sanayei and K. F. O'Driscoll, *J. Macromol. Sci. Part A*, 1989, **26**, 1137–1149.
50 T. P. Davis and D. Kukuly, *Macromol. Chem. Phys.*, 1998, **199**, 1697–1708.
51 J. P. A. Heuts, L. M. Muratore and T. P. Davis, *Macromol. Chem. Phys.*, 2000, **201**, 2780–2788.
52 D. M. Haddleton, E. Depaquis, E. J. Kelly, D. Kukulj, S. R. Morsley, S. A. F. Bon, M. D. Eason and A. G. Steward, *J. Polym. Sci., Part A: Polym. Chem.*, 2001, **39**, 2378–2384.
53 J.-F. Lutz, Ö. Akdemir and A. Hoth, *J. Am. Chem. Soc.*, 2006, **128**, 13046–13047.
54 S. Harrison, F. Ercole and B. Muir, *Polym. Chem.*, 2010, **1**, 326–332.
55 J. P. A. Heuts, D. Kukulj, D. J. Forster and T. P. Davis, *Macromolecules*, 1998, **31**, 2894–2905.
56 J. F. Lutz and K. Matyjaszewski, *J. Polym. Sci., Part A: Polym. Chem.*, 2005, **43**, 897–910.
57 C. J. Hawker, A. W. Bosman and E. Harth, *Chem. Rev.*, 2001, **101**, 3661–3688.
58 C. Boyer, V. Bulmus, T. P. Davis, V. Ladmiral, J. Liu and S. Perrier, *Chem. Rev.*, 2009, **109**, 5402–5436; C. Boyer, M. H. Stenzel and T. P. Davis, *J. Polym. Sci., Part A: Polym. Chem.*, 2011, **49**, 551–595.
59 (*a*) G.-Z. Li, R. K. Randev, A. H. Soeriyadi, G. Rees, C. Boyer, Z. Tong, T. P. Davis, C. R. Becer and D. M. Haddleton, *Polym. Chem.*, 2010, **1**, 1196–1204; (*b*) J. W. Chan, C. E. Hoyle, A. B. Lowe and M. Bowman, *Macromolecules*, 2010, **43**, 6381–6388.
60 A. B. Lowe, *Polym. Chem.*, 2010, **1**, 17–36.
61 (*a*) C. Boyer, C. Loubat, J. J. Robin and B. Boutevin, *J. Polym. Sci., Part A: Polym. Chem.*, 2004, **42**, 5146–5160; (*b*) C. Boyer, G. Boutevin, J. J. Robin and B. Boutevin, *Polymer*, 2004, **45**, 7863–7876; (*c*) B. Boutevin, *J. Polym. Sci., Part A: Polym. Chem.*, 2000, **38**, 3235–3243; (*d*) C. Boyer, G. Boutevin, J.-J. Robin and B. Boutevin, *Macromol. Chem. Phys.*, 2004, **205**, 645–655.
62 J. D. Coyle, *Tetrahedron*, 1985, **41**, 5393–5425.
63 P. J. Roth, F. D. Jochum, F. R. Forst, R. Zentel and P. Theato, *Macromolecules*, 2010, **43**, 4638–4645.
64 G. Aylward and T. Findlay, *SI Chemical Data*, John Wiley & Sons, Milton, QLD, 5th edn, 2002, p. 121.


Published on 24 January 2011 on http://pubs.rsc.org | doi:10.1039/C0PY00372G
Downloaded on 21 March 2011

 This journal is © The Royal Society of Chemistry 2011