Polymer Architectures *via* Reversible Addition Fragmentation Chain Transfer (RAFT) Polymerization

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Summary: Various versatile chain transfer agents (CTAs) have been synthesized for reversible addition fragmentation chain transfer (RAFT) polymerzation. Such CTAs have been used to modify hydroxyl containing materials and produce well-controlled molecular architectures such as amphiphilic copolymer from poly (ethylene glycol), AB block copolymer consisting of a biodegradable segment, poly (*l*-lactic acid) (PLLA) and grafted copolymers of poly (styrene), poly (methyl methacrylate) and poly (methyl acrylate) from cellulose.

Keywords: block copolymers; cellulose graft polymer; functionalization of polymers; macromolecular architecture; reversible addition fragmentation chain transfer

Introduction

The study of molecular architecture design, resulting in the conception of many novel macromolecular structures such as di-block, grafted, dendrimeric, and hyperbranched polymers, with specific end group functionalities has been widely investigated by living ionic polymerization. However, this technique requires the use of protecting groups and has limited monomer selections.[1] The advantages of radical polymerization over ionic polymerization is the wide range of monomers that can be polymerized and the absence of protecting groups. Moreover, the ability to control polydispersities in a living free radical system makes it a powerful system for polymer synthesis. Living radical polymerization (LRP) techniques such as nitroxide mediated polymerization (NMP)[2], atom transfer radical polymerization (ATRP)[3,4], and reversible addition fragmentation chain transfer (RAFT) polymerization have been extensively studied.[5] RAFT[6,7] and macromolecular architecture design by interchange of xanthates (MADIX)[8,9] (scheme 1) are the newest of the living free radical techniques and one of

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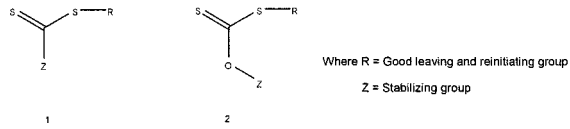
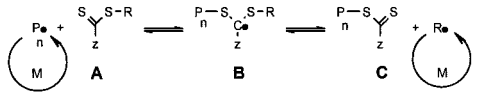
their most significant advantages over other techniques is the greater range of polymerizable monomers. The focus of much attention has been the use of both RAFT and MADIX on the key ancillary areas for the synthesis of specific functionalities on polymer backbones with particular chain ends and for the design of various polymeric architectures.



Scheme 1. Generic formula of RAFT (**1**) and MADIX (**2**) agent.

The use of LRP to synthesize block copolymers with unique properties to be used as compatibilizers or novel specific applications has been widely investigated.[10,11] Of special interest is the synthesis of ATRP initiators from hydroxyl group containing materials reported for the first time by Haddleton *et al.*[12,13] The study explored a new synthetic route for the preparation of copolymers with specific functionalities and properties which cannot be achieved via normal free radical polymerization methods. More recently, amphiphilic block copolymers of poly (ethylene oxide) with styrene (and other monomers) have been successfully prepared via either ATRP or nitroxide mediated polymerization (NMP) with narrow polydispersities.[11,14-16] In addition, the grafting from cellulose fibers via ATRP has been recently reported by Carlmark et al.[17]

RAFT and MADIX have appeared as the most versatile techniques for living free radical polymerization due to their wide range of polymerizable monomers and ease of scale-up. RAFT and MADIX are based on a similar process, the introduction of a small amount of dithioester of generic formula A, scheme 2 (chain transfer agent, CTA) in a classic free radical system (monomer and initiator). The transfer of the CTA between growing radical chains, present at very low concentration, and dormant polymer chains, present at higher concentration, will regulate the growth of the molecular weight, and limit termination reactions (Scheme 2).



Scheme 2. General accepted mechanism of RAFT.

Here, we report the syntheses of highly versatile CTAs by varying R group to polymeric chains (Scheme 2). The R groups are based on materials that are inexpensive, biodegradable, and renewable resources.

Experimental

Materials

Scoured and bleached, fluorescent brightener-free, woven cotton was used throughout the work. The cotton fabric was dried in a vacuum oven overnight before use. All solvents, monomers and other reagents were purchased from Aldrich Chemical and used as received unless otherwise stated. Tetrahydrofuran (THF), triethylamine and dimethylformamide (DMF) were dried over molecular sieved 4 A. All monomers were purified by passing through aluminium oxide, activated basic Brockmann I. Air and moisture sensitive compounds were manipulated using standard Schlenk techniques under a nitrogen atmosphere.

Characterizations

1. Size exclusion chromatography

Molecular weight distributions were determined using size exclusion chromatography (SEC) at ambient temperature using a system equipped with a guard column and two mixed columns (Polymer Laboratories) with a differential refractive index detector. Tetrahydrofuran was used as an eluent unless otherwise stated at a flow rate of 1 mL min^{-1} with toluene as a flow rate marker. Both poly (styrene) in the range of 7,500,000 and 580 g mol^{-1} and poly (methyl methacrylate) in the range of 1,944,000 – 1,020 g mol^{-1} were used for calibrations.

2. ^{1}H- NMR

^{1}H-NMR spectra were recorded on a Bruker 400 MHz spectrometer with d^{3}-chloroform as solvent.

3. ATR-FTIR and Raman

IR analysis of cotton was carried out using a Perkin Elmer 1740 Fourier Transform Infrared Spectrometer. The contact sampler used was a horizontal internal reflectance accessory (ATR). One hundred scans were carried out over 222 seconds to produce the final spectrum.

Synthesis and use of Novel Chain Transfer Agents (CTAs)

Preparation of S-Methoxycarbonylphenylmethyl dithiobenzoate (MCPDB) CTA (Scheme 3, CTA 1).

Phenyl magnesium bromide was prepared from bromobenzene (3.14g, 20.0 mmols) and magnesium turning (0.50g, 21.0 mmols) in dry THF. The solution was heated to 40 °C and carbon disulphide (1.525g, 20.0 mmols) was added and a dark brown solution was obtained. Methyl-α-bromophenylacetate (5.00g, 21.8 mmols) was then transferred to the solution. The reaction temperature was raised to 80 °C and maintained for 24 hrs under reflux. Ice water was then added to the solution, before extracting three times the organic products with diethylether. The combined organic extracts were rinsed with saturated sodium hydrogen carbonate and dried over anhydrous magnesium sulphate. After solvent removal, flash column chromatography was undertaken using diethylether:n-hexane (1:9) as eluent.

Preparation of S-methoxycarbonylphenylmethyl methyltrithiocarbonate (MCPMT) CTA (Scheme 3, CTA 2).

The method proposed by CSIRO base on similar Z and R group for the preparation of multi-arm functionalization was used to synthesize MCPMT.[18]

Preparation of S-diethylcarbamoylphenylmethyl dithiobenzoate (DCPDB) CTA (Scheme 3, CTA 3).

α-Chlorophenyl acetyl chloride (8.241g, 0.044 mmols) was added to a round bottom flask containing dry THF and connected to a reflux condenser. 4,4 Dimethyl amino pyridine (DMAP) (0.004 mmols) was then put into the solution. Diethylene amine (0.060 mmols) was then transferred and the solution was allowed to reflux over night. THF was removed and the resultant compound was used without purification.

Phenyl magnesium bromide was prepared as mentioned above in a 3-neck round bottom flask. Carbon disulphide (1.525g, 20.0 mmols) was added dropwise for approximately 15 min and the temperature was increased to 40 °C. 2-Chloro-N,N-diethyl-2phenyl acetamide (4.52 g) that was prepared in the previous step in 20 mL of THF were added to the flask. The orange solid was recrystalized by diethyl ether. The product was dried under vacuum and analyzed with FTIR, Raman and ^{1}H-NMR.[19]

Polymerization sing CTA 1, CTA 2 and CTA 3

The kinetic studies of MCPDB, MCPMT and DCPDB CTAs were processed in bulk systems.[19,20] The ratio of monomer (styrene (Sty), methyl methacrylate (MMA), methyl acrylate (MA) or dimethyl acrylamide (DMA)), CTA and α,α'-azoisobutyronitrile (AIBN) was 5000:10:1 respectively. 1 mL of the solution was transferred in a different ampoule and nitrogen gas was flowed through the solutions for 5 min. The ampoules were placed in a water bath pre-heated to 60°C. Each ampoule was taken out at various times and placed into an ice bath to quench the reaction. The percentage conversions were measured by ^{1}H-NMR. Molecular weights and PDIs were recorded by SEC.

In the case of MCPDB mediated polymerizations, the reactions with each monomer follow pseudo first order rate plot with time and the molecular weight values increase linearly with conversion, following theoretical values, as expected from living polymerization systems.[20] MCPDB gives good control over styrene, MMA, MA, and DMA. Whereas MCPMT and DCPDB also show good control over styrene, MA, and DMA but not for MMA.[19, 20]

Poly(methyl methacrylate)-*block*-Poly(styrene) (PMMA-*b*-PS) was prepared by further reacting a PMMA macro CTA with MCPDB (PMMA-MCPDB) by addition of styrene monomers. The

clean conversion of PMMA into block copolymer was confirmed by SEC. The initial PMMA macro CTA (M_n^{SEC} = 13,400 g/mol; PDI = 1.18) was transferred into a PMMA-*b*-PS (M_n^{SEC} = 63,600 g/mol; PDI = 1.27). Whereas the AB block copolymer of PS-*b*-PMA was prepared by the addition of MA monomers into a PS Macro CTA with DCPDB (PS-DCPDB). The chromatograms (Figure 1) show the formation of a PMA second block to form a PS-*b*-PMA (M_n^{SEC} = 42,000 g/mol; PDI = 1.27). This was achieved by addition of MA monomers to the initial PS-DCPDB (M_n^{SEC} = 25,450 g/mol; PDI = 1.23).

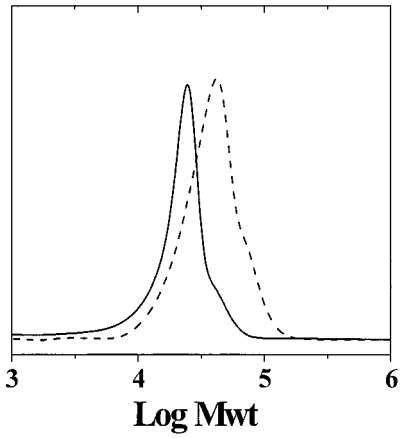
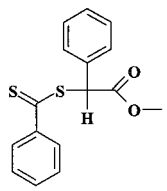


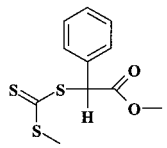
Figure 1. SEC traces of PS (-) and PS-*b*-PMA (- -) mediated by DCPDB.

Syntheses and Use of Macro CTAs (MCPDB analogues)

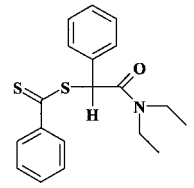
As living radical polymerizations mediated by MCPDB[20] have shown a better degree of control over molecular weight than those mediated by MCPMT[20] and DCPDB[19], analogues of MCPDB, scheme 3, were synthesized and subsequently tested in polymerization systems.



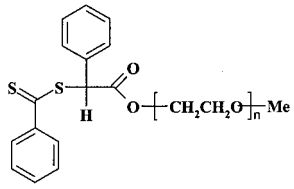
CTA1, MCPDB



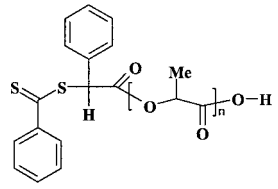
CTA2, MCPMT



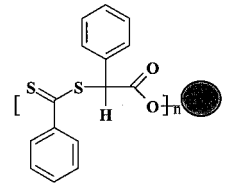
CTA3, DCPDB



MacroCTA4, MeOPEG-MCPDB



MacroCTA5, PLLA-MCPDB



MacroCTA6, Cotton-MCPDB

Scheme 3. MCPDB, MCPMT, DCPDB and CTA analogues of MCPDB used in this study.

Synthesis of Poly (l-lactic acid) and Poly (ethylene glycol) methyl ester macroCTAs (Scheme 3, CTA 4 and 5)

Poly (*l*-lactic acid) (PLLA)[21] or Poly (ethylene glycol) methyl ester (MeOPEG) (1.81 mmol) was placed in a 3-necked round bottom flask with dry tetrahydrofuran (THF). Triethylamine (2.5 mmols) and 2-chloro-2-phenylacetyl chloride, (CPAC) (2.2 mmols) were added in the flask and the solution was refluxed for 2 days. The solvent was then removed *in vacuo* and dichloromethane was added. The resulting solution was washed with saturated sodium hydrogen carbonate and the yellow organic phase was dried over anhydrous magnesium sulphate. The product was reprecipitated in cold diethyl ether.

The Grignard reaction with carbon disulfide was prepared for the synthesis of MCPDB. However, the 2-chloro-2-phenylacetyl chloride ester of PLLA or MeOPEG synthesised above (21.8 mmols) was then added to the solution instead of methyl-α-bromophenylacetate. The reaction temperature was raised to 80 °C and maintained for 24 hrs. The products were reprecipated in cold diethyl ether.

Preparation of Cotton-MCPDB (Scheme 3, CTA6)

Cotton (4.255 g) was suspended and stirred in a THF solution with triethylamine (72.4 mmols) at 60 °C. CPAC (53 mmols) was added. The reaction was then refluxed for few hours and then cooled down. The light yellow fabric was washed with THF and rinsed thoroughly with deionised water. The treated cotton was oven-dried under vacuum to give the chloro-phenyl-acetic acid cotton ester (cotton-CPA). The degree of substitution (D.S.) was calculated to be 0.53. The cotton CTA was anlyzed by FTIR and Raman. Raman spectroscopy (Figure 2, spectrum A) illustrates the successful reaction of CPAC with the cotton hydroxyl groups by incorporation of the mono-substituted phenyl (1602, 1583 and 1004 cm^{-1}) and the C-Cl bond (617 cm^{-1}) of the acid chloride. Further confirmation was also obtained from FTIR spectroscopy, Figure 3, with stretches at 1736 cm^{-1} and 1187 cm^{-1}, characteristic of C=O and C-O, respectively.

The Grignard reaction with CS_2 was prepared as mentioned in the MCPDB preparation. The solution was transferred to another flask containing cotton-CPA (1.923 g). The reaction temperature was then increased to 80 °C and left overnight. The resulting fabric, with a characteristic orange colour, was washed with THF (3 x 20 mL) and then rinsed thoroughly with deionised water. The CTA cotton was then oven-dried under vacuum. D.S. was calculated to be 0.45.

The alteration into dithioester moiety is also described in Figure 3, where the strong Raman bands at 1236 cm^{-1} and 651 cm^{-1} (top spectrum) are accredited to the C=S and C-S bonds, respectively. The characteristic peaks of aromatic structure are still observed at 1602 and 1001 cm^{-1}, demonstrating the incorporation of an extra phenyl ring. The degree of substitution of the hydroxyl groups of the cotton fabric was estimated to be 14% by gravimetric method. The reactions were therefore prepared aiming for a degree of polymerization DP = [M] / [CTA], with [CTA] obtained from the degree of substitution. D.S. is calculated from the number of substituted hydroxyl groups per repeating unit, with a $D.S._{max} = 3$.

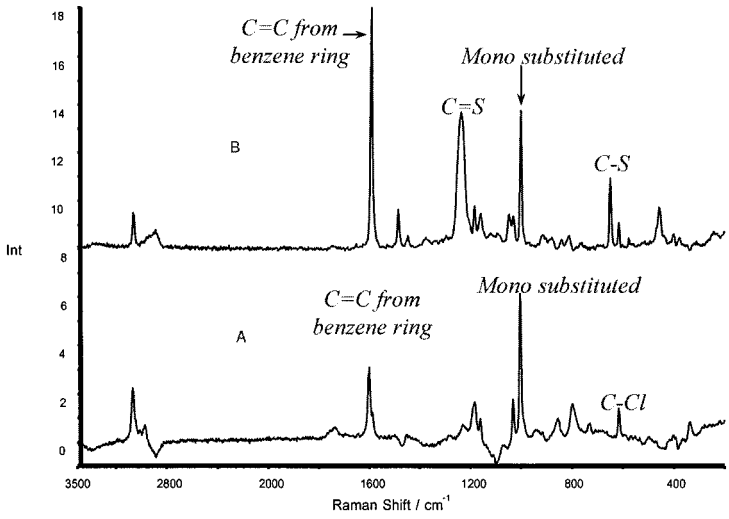


Figure 2. Subtraction of Raman spectra showing [(cotton-CPA) - cotton] (bottom spectrum) and [(cotton-MCPDB) – (cotton-CPA)] (top spectrum).

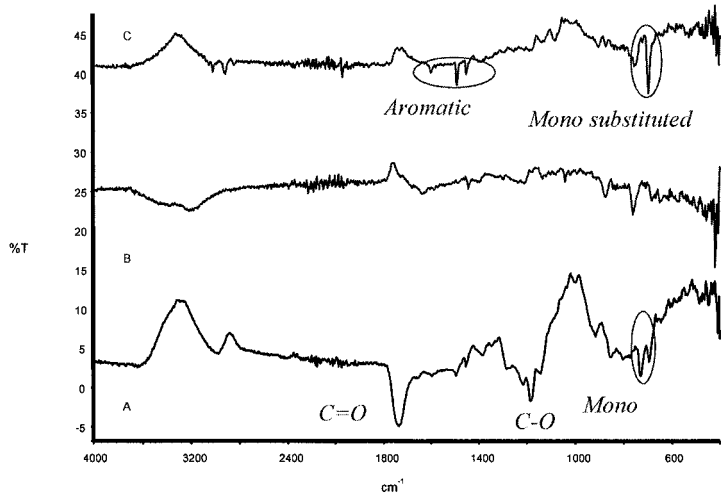


Figure 3. Subtraction of FTIR spectra showing [(cotton-CPA) – cotton].

Polymerizations *via* Macro CTAs

MMA, macro-RAFT agent, and α,α'-azobisisobutyronitrile (AIBN) were added to ampoules in various ratios; 5000:10:1 for PLLA-MCPDB and MeOPEG-MCPDB and 10000:10:1 for cotton MCPDB. Toluene (6 mL) was added to the ampoules. The clinched ampoules were deoxygenated by flushing out with nitrogen for approximately 10 min and placed in a pre-heated oil bath at 60°C. The reactions were stopped at the appropriate times by cooling the reaction tubes in an ice bath. Poly (ethylene glycol) methyl ester-*block*-poly (methyl methacrylate) and poly (*l*-lactic acid)-*block*-poly (methyl methacrylate) were reprecipitated in cold diethyl ether. GPC traces of the initial peaks of PLLA and MeOPEG macro CTAs were shifted after adding MMA, good indication that the second block copolymer is formed.

Table 1. Molecular weight data for AB diblock copolymers and graft copolymers.

Entry	Monomer A	M_n[a]	*PDI*[b]	Monomer B	M_n[a,c]	M_n[b,c]	*PDI* (copolymer)[b]
1	Ethylene oxide	5,000	1.12	MMA	43,700	44,150	1.28
2	l-lactic acid	4,800	1.50	MMA	96,300	98,950	1.33
3	Cellulose	-	-	Styrene	-	106,900[d]	1.35
4	Cellulose	-	-	MA	-	84,850	1.38
5	Cellulose	-	-	MMA	-	60,500	2.22

[a] Determined by ^{1}H NMR using $CDCl_3$ as solvent. [b] Determined by SEC using THF as an eluent and PMMA standards. [c] M_n of the copolymer. [d] PS as SEC standards.

^{1}H-NMR spectrum of the final product, shown in Figure 4, displayed the chemical shift signals of both PMMA and MeOPEG macro CTA. The degree of polymerization in this copolymer, estimated from the calculation of methylene protons of PMMA, between 0.5 and 1.3 ppm, with a proton on the phenyl acetyl linkage at 5.24 ppm, correlated well with the GPC results (see in Table 1).

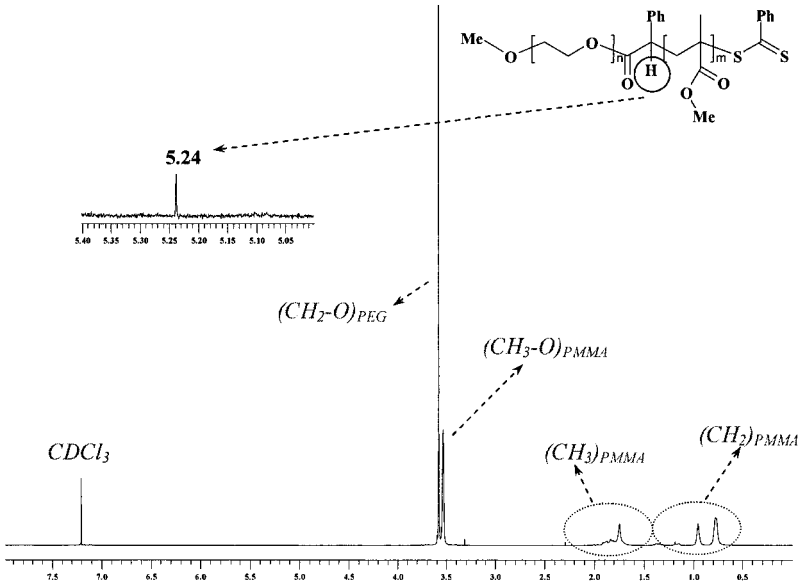
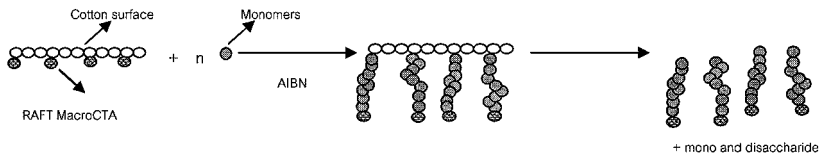


Figure 4. ^{1}H NMR spectrum for diblock MeOPEG-b-PMMA synthesized from CTA2.

In the cases of cotton polymerizations, after reaction, the grafted cotton substrate was washed 3 times with toluene and twice with THF (while stirring overnight) to remove non-grafted polymeric chains. The grafted cotton sample was hydrolyzed to acidic condition in THF, using 35% hydrochloric acid, to isolate the grafted polymer chains. The solvents were removed in vacuum and water was added to the product to precipitate the polymeric chains. The cotton supported polymerizations of MMA, MA and Styrene were undertaken in bulk up to full conversion. After polymerization, a sample of cotton was hydrolyzed in acidic conditions to yield the grafted PMMA, PS and PMA chains which were then analyzed by SEC. Table 1 exemplifies the remarkable control obtained during polymerization. PS and PMA (entry 3 and 4) exhibit a molecular weight very near to the expected one ($M_{n,\ theo}$ = 104,200 and 99,100 g mol^{-1}, respectively) with polydispersities as low as 1.3. In the case of PMMA (entry 5), a higher molecular weight than anticipated was obtained ($M_{n,\ theo}$ = 100,100 g mol^{-1}), with higher PDI. Therefore, an easy process for supported polymerization was demonstrated, which leads to a remarkable control of the polymeric chains molecular weight. Furthermore, this technique brings

new scope in the grafting and functionalization of natural textiles. Additional studies to improve the current technique are currently undertaken in our laboratories.



Scheme 4. Hydrolyzed the graft copolymer on the cotton fabric.

Conclusions

We have described the facile synthesis of highly versatile CTAs that can produce an extensive range of polymers with predictable M_n and low PDI and that allow the easy incorporation of any molecules containing a hydroxy group at the end of a polymeric chain. We believe this technique will bring new opportunities in the synthesis of functional polymers, so far dominated by atom transfer radical polymerization. The major advantage of RAFT over ATRP is that potential pollution of the final product by the catalyst is avoided. In addition the process is easier to undertake, with a wider range of monomers.

Acknowledgements

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