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Advances in RAFT polymerization: the synthesis of polymers with defined end-groups

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Abstract

This paper provides an overview and discusses some recent developments in radical polymerization with reversible addition–fragmentation chain transfer (RAFT polymerization). Guidelines for the selection of RAFT agents are presented. The utility of the RAFT process is then illustrated with several examples of the synthesis of polymers with reactive end-groups. Thus, RAFT polymerization with appropriately designed trithiocarbonate RAFT agents is successfully applied to the synthesis of narrow polydispersity carboxy-functional poly(methyl methacrylate) and primary amino-functional polystyrene. Methods for removing the thiocarbonylthio end-group by aminolysis, reduction and thermal elimination are discussed. It is shown that the thiocarbonylthio end-group can be cleanly cleaved by radical induced reduction with tri-*n*-butylstannane, to leave a saturated chain end, or by thermolysis, to leave an unsaturated chain end.

Keywords: RAFT polymerization; End-groups; Living radical polymerization

1. Introduction

Much work carried out in these laboratories [1–5] and elsewhere over the past few years has demonstrated that polymerization with reversible addition–fragmentation chain transfer (RAFT) is an extremely versatile process. It can be applied to form narrow polydispersity polymers or copolymers from most monomers amenable to radical polymerization. It is possible to take RAFT polymerizations to high conversion and achieve commercially acceptable polymerization rates. Polymerizations can be successfully carried out in heterogeneous media (emulsion, miniemulsion, suspension). There is compatibility with a wide range of functionality in monomers, solvents and initiators. Stars, blocks, microgel and hyperbranched structures, supramolecular assemblies and other complex architectures are accessible and can have high purity.

However, this outstanding versatility cannot be achieved without giving due thought to the choice of RAFT agent and reaction conditions. Reported difficulties with RAFT polymerization (retardation, poorer than expected control) are frequently attributable to inappropriate choice of RAFT agent for the monomer(s) and/or reaction conditions. RAFT agents that perform well under a given set of circumstances are not necessarily optimal for all circumstances.

This paper's main focus is the synthesis of end-functional polymers and in particular polymers with reactive functional groups. Living polymerization processes lend themselves to the synthesis of end-functional polymers and living radical processes are no exception. Nitroxide mediated polymerization (NMP) [6], atom transfer radical polymerization (ATRP) [7] and RAFT with macromonomers [8,9] or thiocarbonylthio compounds [10,11] have all been successfully adapted for the synthesis of end-functional polymers.

The overall RAFT process provides insertion of monomer units into the C–S bond of the RAFT agent structure (1) as shown in Scheme 1. Two direct approaches for making functional polymer are (a) to include the functionality in R (α-functionalization) and (b) to include the functionality in Z (ω-functionalization). There are some disadvantages in using the ω-functionalization approach in some applications because of the potential lability of the C–S bond in the RAFT end-group. Another method of achieving ω-functionalization involves making use of this lability to completely

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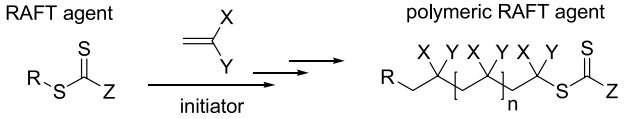

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Scheme 1.

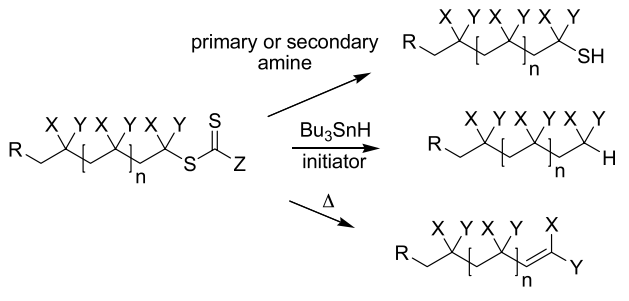
replace the RAFT functionality in a post polymerization reaction.

The aforementioned lability of the C–S bond in the RAFT end-group also means that, in some circumstances, the RAFT agent functionality which is retained in the polymer product can be an issue. A case in point involves the synthesis of primary or secondary amine end-functional polymers (primary or secondary amines are well-known to undergo facile reaction with RAFT end-groups) [1]. However, there are now a variety of methods available for replacing the RAFT end-group. Several approaches will be discussed with respect to the current application. These methods include: aminolysis, radical-induced reduction and thermal elimination (Scheme 2).

2. Experimental

2.1. General

Solvents were of AR grade and were distilled before use. Monomers, methyl methacrylate (MMA) and styrene, were obtained from Aldrich and were filtered through neutral alumina (70–230 mesh), fractionally distilled under reduced pressure, and redistilled under reduced pressure immediately before use. Nuclear magnetic resonance spectra (NMR) were obtained with a Bruker AC200, AC400 or DRX500 spectrometer. Chemical shifts are reported in ppm from external tetramethylsilane. Gel permeation chromatography (GPC) was performed on a Waters associates liquid chromatograph equipped with differential refractometer and $3\times$mixed C and 1 mixed E PLgel column (each 7.5×30 mm^2) from polymer laboratories. Tetrahydrofuran (flow rate of 1.0 mL/min) was used as eluent at 22 ± 2 °C. The columns were calibrated with narrow polydispersity



Scheme 2.

polystyrene standards (polymer laboratories). A third order polynomial was used to fit the $\log_{10}M$ vs. time calibration curve. PMMA molecular weights are based on use of a Universal calibration and Mark–Houwink–Sakaruda parameters of $K=11.4\times10^8$ g/L, $\alpha=0.716$ (PMMA) [12] and $K=9.44\times10^8$ g/L, $\alpha=0.719$ (polystyrene) [13]. These parameters have previously been shown to be applicable for accurately converting between PMMA and polystyrene molecular weights under our experimental conditions [8].

2.2. 4-Cyano-4-(dodecylsulfanylthiocarbonyl)sulfanyl pentanoic acid (*19*)

The general procedure described previously was used [14]. *n*-Dodecylthiol (15.4 g, 76 mmol) was added over 10 min to a stirred suspension of sodium hydride (60% in oil) (3.15 g, 79 mmol) in diethyl ether (150 mL) at a temperature between 5 and 10 °C. A vigorous evolution of hydrogen was observed and the greyish sodium hydride was transformed to a thick white slurry of sodium thiododecylate. The reaction mixture was cooled to 0 °C and carbon disulfide (6.0 g, 79 mmol) added to provide a thick yellow precipitate of sodium *S*-dodecyl trithiocarbonate which was collected by filtration and used in the next step without purification.

A suspension of sodium *S*-dodecyl trithiocarbonate (14.6 g, 0.049 mol) in diethyl ether (100 mL) was treated by portion-wise addition of solid iodine (6.3 g, 0.025 mol). The reaction mixture was then stirred at room temperature for 1 h when the white sodium iodide which settled was removed by filtration. The yellow–brown filtrate was washed with an aqueous solution of sodium thiosulfate to remove excess iodine and water and dried over sodium sulfate and evaporated to leave a residue of bis-(dodecylsulfanylthiocarbonyl) disulfide (13.6 g, quantitative), mp 33–35 °C. ^{1}H NMR ($CDCl_3$): δ 0.89, t, 6H; 1.30, br s, 36H; 1.71, m, 4H; 3.29, t, 4H.

A solution of 4,4′-azobis(4-cyanopentanoic acid) (2.10 g, 0.0075 mol) and the above bis-(dodecylsulfanylthiocarbonyl) disulfide (2.77 g, 0.005 mol) in ethyl acetate (50 mL) was heated at reflux for 18 h. After removal of the volatiles in vacuo, the crude product was extracted with water (5×100 mL) to afford 4-cyano-4-(dodecylsulfanylthiocarbonyl)sulfanyl pentanoic acid (**19**) as a pale yellow solid (3.65 g, 87% yield), mp 58–59 °C, after recrystallization from hexane. ^{1}H NMR ($CDCl_3$) δ 0.89 (t, 3H, CH_3); 1.28 (br s, 18H); 1.72 (m, 2H); 1.89 (s, 3H, CH_3); 2.40–2.80 (m, 4H, CH_2CH_2); 3.38 (t, 2H, CH_2S).

2.3. Phthalimidylmethyl trithiocarbonates (*26*–*28*)

The *n*-butyl phthalimidylmethyl trithiocarbonate (**26**) was prepared from *N*-bromomethylphthalimide, butanethiol and carbon disulfide in 96% overall yield using the general procedure described elsewhere [15]. Similarly, 1,4-bis-((phthalimidomethylsulfanylthiocarbonyl)sulfanyl)butane

Table 1
Molecular weights and polydispersities for PMMA formed by polymerization of MMA (6.55 M in benzene) with azobis(1-cyclohexanenitrile) (0.0018 M) as initiator and RAFT agent (**19**) for 6 h at 90 °C

Trace	$[RAFT]_0$ ($M\times10^2$)	$\bar{M}_n$[a] (g/mol)	$\bar{M}_w/\bar{M}_n$	$\bar{M}_n$ (calc)[b] (g/mol)	Conv (%)
1	19.92	2870	1.18	3000	80
2	9.96	5040	1.14	5600	80
3	4.95	9940	1.12	10,400	79
4	2.48	21,800	1.13	22,600	91
5	1.24	41,100	1.14	45,300	>99
6	0.61	80,900	1.13	80,100	>99
7	0.32	126,000	1.15	125,000	>99

[a] Values rounded off to three significant figures.
[b] Based Eq. (1) and an assumed cumulative initiator efficiency (f) of 0.3.

(**28**) was prepared using a similar procedure from *N*-bromomethylphthalimide, butane-1,4-dithiol and carbon disulfide in 31% yield after purification.

Bis-phthalimidomethyl-trithiocarbnonate (**27**) was prepared according to the general procedure of Leung et al. [16] from *N*-bromomethylphthalimide and carbon disulfide under phase transfer conditions in 43% overall yield.

Further details of the synthesis and characterization of these trithiocarbonates will be presented in a forthcoming publication [17].

2.4. Polymerization of methyl methacrylate in the presence of 4-cyano-4-(dodecylsulfanylthiocarbonyl)sulfanyl pentanoic acid (*19*)

An aliquot (2 mL) of a stock solution composed of MMA (14 mL), azobis-(1-cyclohexanenitrile) (9.8 mg), and benzene (6 mL) was added to each of a series of ampoules containing the weighed amounts of 4-cyano-4-(dodecylsulfanylthiocarbonyl)sulfanyl pentanoic acid (**19**). The contents were degassed by three freeze–evacuate–thaw cycles, the ampoules sealed and heated in a constant temperature bath at 90 °C for the times indicated. The polymer was isolated by exhaustive evaporation of monomer and conversions were determined gravimetrically. Molecular weight and conversion data are shown in Table 1 and in Figs. 2 and 3.

2.5. Polymerization of styrene in the presence of phthalimidomethyl RAFT agents (*26–28*)

Aliquots of a stock solution composed of styrene and the RAFT agent were added to a series of ampoules. The contents were degassed by three freeze–evacuate–thaw cycles, the ampoules sealed and heated in a constant temperature bath at 110 °C for 24 h. Conversions were determined by ^{1}H NMR analysis of the reaction mixtures. Molecular weight and conversion data are shown in Table 2.

2.6. Reduction of bis-polystyrene trithiocarbonate (*29*) with tri-n-butylstannane

Polystyrene (**29**) (51 mg, $M_n=51{,}100$ g/mol, $M_w/M_n=1.17$), tri-*n*-butylstannane (12 mg) and AIBN (0.3 mg) and benzene (800 mg) were placed in an argon flushed ampoule. The contents were degassed by three freeze–evacuate–thaw cycles, sealed and heated in a constant temperature bath at 70 °C for 3 h. Solution was observed to change from yellow to colourless. The product had $M_n=30{,}000$ g/mol, $M_w/M_n=1.11$. The GPC traces for the product and the precursor polystyrene are shown in Fig. 4(b).

2.7. Thermolysis of bis-polystyrene trithiocarbonate (*29*)

Polystyrene (**29**) (19 mg, $M_n=51{,}100$ g/mol, $M_w/M_n=1.17$) was weighed into in an alumina crucible and placed in

Table 2
Molecular weights and polydispersities for polystyrene obtained in thermal polymerizations of styrene in the presence of RAFT agents (**26–28**) at 110 °C [17]

RAFT agent	Time (h)	$[M]/[RAFT]_0$ ($M\times10^2$)	M_n (calc)[a,b] (g/mol)	M_n[a] (g/mol)	M_w/M_n	Conv (%)
Control	24	–	–	288,000	1.95	77
26	24	0.20	1680	1460	1.21	65
26	24	1.00	7400	6800	1.16	68
26	24	6.04	42,400	43,200	1.16	67
27	32	5.92	47,700	50,600	1.14	77
28	24	0.20	1610	1470	1.25	57
28	24	1.00	6730	6650	1.14	59
28	24	3.00	19,300	19,800	1.12	60
28	24	5.94	41,400	38,100	1.15	66

[a] Values rounded off to three significant figures.
[b] $\bar{M}_n(\text{calc}) \sim [M]/[RAFT]_0 \times \text{Conv} \times 104 + (\text{molecular weight of RAFT agent})$.

the sample furnace of a Mettler TGA/SDTA521 thermobalance. The sample was heated dynamically at 10 °C/min under nitrogen to 300 °C. The colourless residue had $\bar{M}_n$ = 27,100 g/mol, $\bar{M}_w/\bar{M}_n$ = 1.17. GPC traces for the product and the precursor polystyrene are shown in Fig. 4(a). The thermogram indicated an onset of weight loss at ~200 °C and a maximum rate of weight loss at ~220 °C.

2.8. Aminolysis with piperidine of bis-polystyrene trithiocarbonate (29)

Polystyrene (**29**) (50 mg, $\bar{M}_n$ = 51,100 g/mol, $\bar{M}_n/\bar{M}_n$ = 1.17) was dissolved in dry THF (10 mL) in a 25 mL round-bottomed flask. The solution was flushed with argon for 10 min prior to the addition of an excess of piperidine (1 mL). The stirred reaction mixture was heated and maintained under reflux for 1 h during which time the initially yellow solution became colourless. The product had $\bar{M}_n$ = 29,700 g/mol, $\bar{M}_w/\bar{M}_n$ = 1.24. GPC traces for the product and the precursor polystyrene is shown in Fig. 4(c).

The above polystyrene (51 mg) was redissolved in THF (3 mL) and the solution was flushed with argon for 10 min. Glacial acetic acid (1 mL) and zinc powder (0.5 g) were added and the stirred reaction mixture was warmed to 40 °C and maintained at that temperature under argon for 12 h. The product had $\bar{M}_n$ = 27,800 g/mol, $\bar{M}_w/\bar{M}_n$ = 1.28. The GPC trace for the product is shown in Fig. 4(c).

2.9. Deprotection-conversion of phthalimido group to amino group

Sufficient ethanol (ca. 1 mL) was added to a two phase mixture of a solution of the end-functional polystyrene (0.8 g) in THF (10 mL) and hydrazine monohydrate (0.5 mL) to give a homogeneous solution which was then heated under reflux overnight (16 h). The solution was observed to turn yellow after ca. 2 h due to formation of phthalyl hydrazide. The polystyrene was isolated by precipitation into methanol and filtration and air dried.

2.10. Polymer derivitization with trichloromethyl isocyanate [18]

A sample of polymer [carboxy end functional PMMA (Scheme 4) or amino end function polystyrene (Scheme 11)] (~40 mg) was dissolved in $CDCl_3$ (0.5 mL) and the solution transferred to a 5 mm NMR tube. An excess of trichloroacetyl isocyanate (10 μL, 6.3 mg, 33.4 μmol) was then added and the ^{1}H NMR spectrum obtained. The derivitization reaction was complete within the time taken to place the tube in the spectrometer (< 10 min).

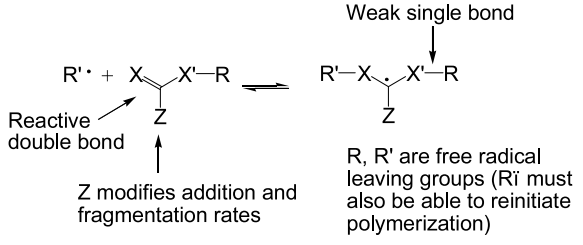


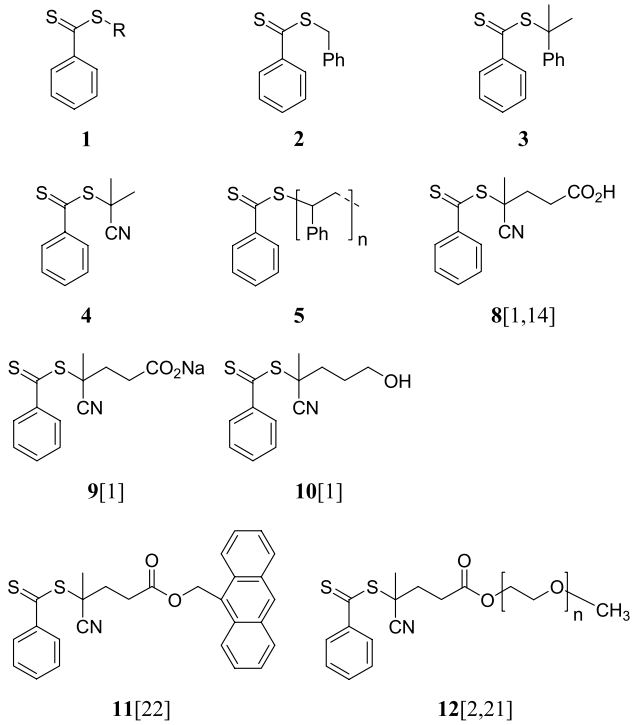
Fig. 1. R,R′ are propagating radicals, initiator derived radicals, etc.

3. Results and discussion

3.1. Selection of RAFT agents

Notwithstanding the fact that currently RAFT agents are generally not commercially available, RAFT polymerizations should, in principle, be no more difficult to conduct than conventional free radical polymerizations. The same apparatus (reactor), solvents, initiators and temperatures are applicable. There is a need to rigorously exclude oxygen to obtain optimal results. A generic description of thiocarbonylthio RAFT agents is shown in Fig. 1. Our initial communication on this form of RAFT polymerization [1] focussed on the utility of dithiobenzoate (**3**, including **4**–**10**) and other dithioesters as RAFT agents. Our patents [19,20] and the subsequent papers show that a wide range of compounds that contain the thiocarbonylthio group can be used. The effectiveness of RAFT agents has been shown to depend strongly on the properties of the free radical leaving group R [4] and the activating group Z (Fig. 1) [3].

Many functional RAFT agents are also described in the literature (e.g. **8**–**10**) [1]. These RAFT agents have also been modified to form other functional RAFT agents (e.g. **11**–**12**) [2,21–23].



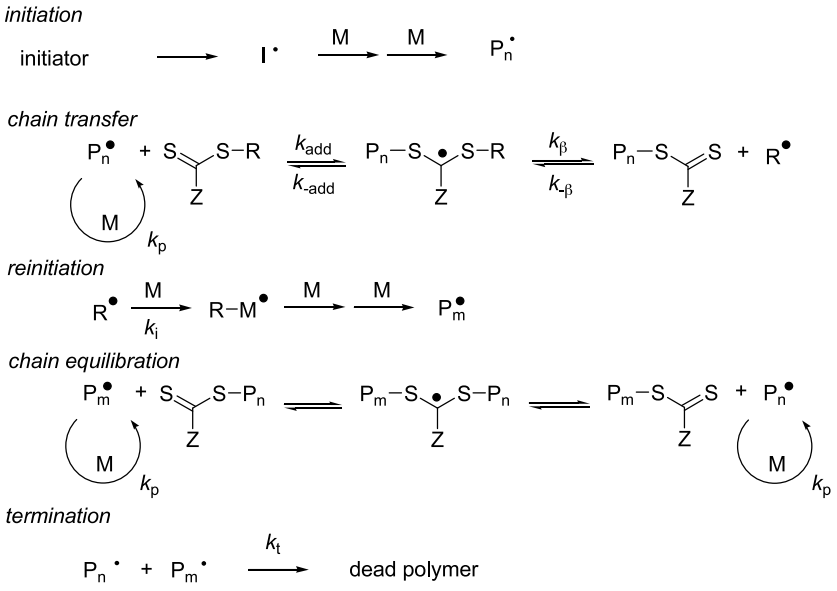
For low conversions, or for polymerization in solution,

the rates of RAFT polymerization are often similar to those observed for similar conventional polymerizations [3,11,24]. Moreover, slower rates of polymerization observed for higher conversions can often be attributed to the elimination or reduction of the gel effect. However, it is nonetheless clear that retardation is present with certain RAFT agent/monomer combinations. Thus, we [4,25] and others [26,27] have shown that the polymerization of acrylates in the presence of dithiobenzoate RAFT agents (**3**) is subject to marked retardation. The polymerization of methacrylates and styrene may also show substantial retardation when high concentrations of dithiobenzoate RAFT agents, in particular, cumyl dithiobenzoate (**5**), are used [4,25]. With lower concentrations of RAFT agent, an inhibition period may sometimes be observed which corresponds to the time taken for consumption of the initial RAFT agent [4,25]. Not surprisingly, this inhibition period is most notable with dithiobenzoates with lower transfer constants such as benzyl dithiobenzoate [4]. The mechanisms of retardation in RAFT polymerization have been a subject for many recent papers [28–36].

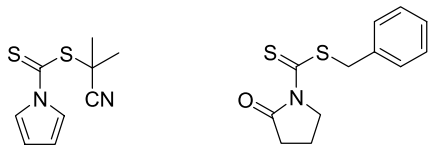
A variety of experimental findings indicate that fragmentation of radical adducts to dithiobenzoate RAFT agents is slow with reference to the rate of fragmentation of analogous trithiocarbonate, aliphatic dithioester, xanthate and dithiocarbamate RAFT agents. However, there is controversy as to whether this, in itself, might be wholly responsible for the marked retardation seen when high concentrations of dithiobenzoate RAFT agent are used or whether any retardation might instead be due to the consumption of the adduct radical in side reactions (such as coupling with other radical species) or other causes. Our data shows that polymerizations of MMA or styrene carried out with lower concentrations of dithiobenzoate RAFT agents (such as cumyl dithiobenzoate (**5**)) need not be significantly retarded beyond that caused by a reduction in the gel or Trommsdorf effect [3,11,24]. That other experimental data suggests more substantial retardation under comparable experimental conditions suggests that, in some cases, the retardation observed is due to extraneous factors such as impurities in the RAFT agent or the polymerization medium or poor degassing. Potential contaminants in cumyl dithiobenzoate which are know to cause an inhibition period include dithiobenzoic acid and bis-(thiobenzoyl)disulfide.

The mechanism of exchange between dormant and active species involves a series of linked equilibria as shown in Scheme 3 [1]. To this scheme various side reactions can be added such as coupling with the adduct radicals. The activity of RAFT agents, rate and retardation, and the appearance of molecular weight distributions can be understood in these terms. It is particularly important to take into account the very different reactivities of the initial and final RAFT agent and the reversibility of the initial chain transfer step [4].

A wide range of compounds containing the thiocarbonylthio group and which are known to be effective as RAFT agents are described in patents [19,37] and in recent publications. They include certain dithiocarbamates (e.g. **13**, **14**) [3,38,39], xanthates (**15**, **16**) [3,40–42], trithiocarbonates (e.g. **17**–**19**) [3,43] and other compounds [3]. The key structural features of all thiocarbonylthio based RAFT agents are a reactive C=S double bond and a weak S–R single bond (Fig. 1).



Scheme 3.



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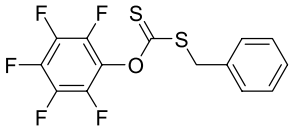

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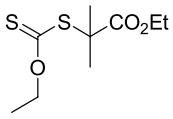

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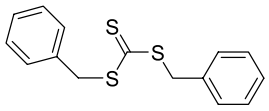

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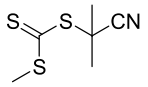

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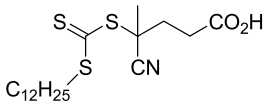

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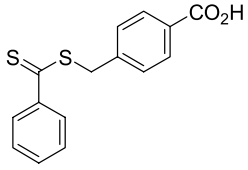
The choice of the groups Z and R is important in determining both addition and fragmentation rates and thus the effectiveness of the RAFT agent [3,4,44]. Radicals, including propagating species, partition between reacting with monomer and reacting with RAFT agent. With the more reactive RAFT agents, the number of propagation events per transfer event is less than unity. Transfer constants exceeding 6000 (styrene polymerization with polystyryl dithiobenzoate (**7**)) have been reported [45]. Rapid chain transfer ensures the chain equilibration required for narrow polydispersities. It is also important that the initial RAFT agent be chosen such that it is rapidly consumed during the initial stages of the polymerization. Like most free radical reactions, RAFT agent activity is controlled by a complex interplay of polar, steric, bond strength and stereoelectronic effects.

The dependence of RAFT agent activity on Z can be qualitatively predicted using low level molecular orbital calculations and these also provide a guide to the relative importance of the various factors [3,4,46]. There appears to be good prospects for more quantitative predictions using high level ab initio calculations [3,47,48]. These studies are able to predict trends of RAFT agent activity with the Z and R substituents and by providing some understanding of the reason for these trends may prove an extremely useful tool for RAFT agent design. However, this work is still in its infancy and the use of these methods to predict absolute values of rate constants or equilibrium constants associated with RAFT must still be treated circumspectly.

The choice of RAFT agent is of particular importance in synthesis of end-functional, block and star copolymers. Incorrect choice can lead to non-functional polymers, homopolymer impurity, or less than the desired number of arms, respectively. In the case of block copolymers, the RAFT agent and/or reaction conditions must be chosen to be suitable for each of the monomers used [4,21,44].

3.2. Carboxy end-functional poly(methyl methacrylate)

The carboxy end-functional dithiobenzoate RAFT agent (**8**) or derived salts have been widely used to prepare carboxy functional polymer and more generally as water soluble RAFT agents [49]. Recently, another carboxy end-functional dithiobenzoate RAFT agent (**20**) has been described [50]. There are some issues associated with the use of the dithiobenzoate RAFT agents in aqueous media related to their hydrolytic instability [49,51]. Another, more general, concern is the extent of retardation that may be observed when high concentrations of dithiobenzoate RAFT agents are used to prepare low molecular weight polymers (see above). Aliphatic dithioester and trithiocarbonate RAFT agents have greater hydrolytic stability and are also known give less retardation [3,25,52].



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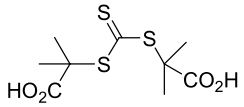

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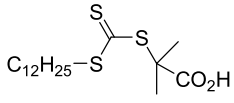

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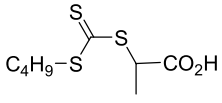

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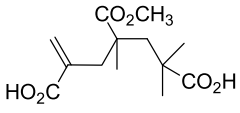

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Carboxy functional trithiocarbonates have been reported by Lai et al. (**21** and **22**) [53] and Ferguson et al. (**23**) [54]. The RAFT agents (**21** and **22**) appear effective with styrene, acrylates and acrylamides [53] but do not yield narrow polydispersity polymers with methacrylates [53] which is attributed to the 2-carboxy-2-propyl radical, like the corresponding ester (2-ethoxycarbonyl-2-propyl radical [4]), being a poor radical leaving group with respect to the PMMA propagating radical. For similar reasons, the RAFT agent (**23**) is also unlikely to be effective with methacrylates.

The macromonomer RAFT agent (**24**) and related species could, in principle, be used to synthesize carboxy end functional PMMA [8]. However, the transfer constant

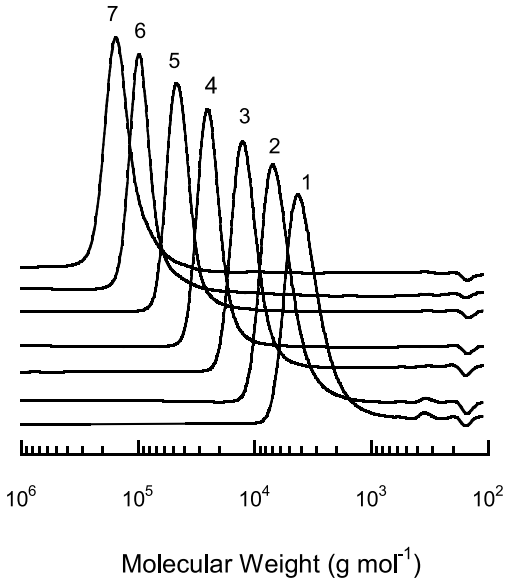


Fig. 2. GPC traces of PMMA formed by polymerization of MMA (6.55 M in benzene) with azobis(1-cyclohexanenitrile) (0.0018 M) as initiator and RAFT agent (**19**) (Table 1) for 6 h at 90 °C.

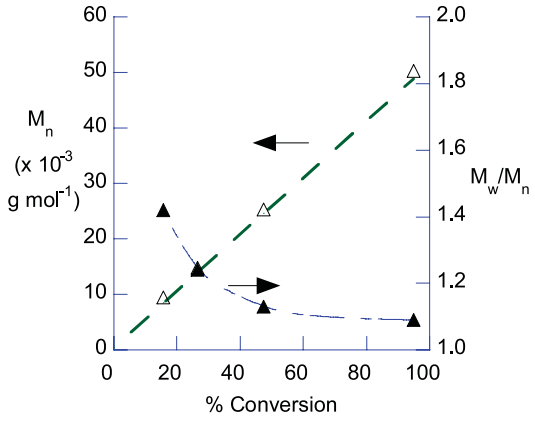


Fig. 3. Molecular weight/conversion data for the polymerisation of MMA (6.55 M) at 90 °C with azobis(1-cyclohexanenitrite) (0.0018 M) as initiator in the presence of RAFT agent (**19**) (0.0113 M). The plot shows: experimental $\bar{M}_n$ (△); $\bar{M}_n$ calculated with Eq. (1) and with $f=0.5$, $d=1.67$ and $k_d=2.54\times10^{-5}$ M^{-1}/s (—); experimental (▲); line of best fit (- - - -).

of such macromonomers is relatively low (~0.3 at 60 °C) [8] and they are not generally useful for forming narrow polydispersity polymers in a batch process [9,55].

We, therefore, designed a new acid end-functional trithiocarbonate RAFT agent (**19**) which has a tertiary cyanoalkyl 'R' group. Tertiary cyanoalkyl radicals are known to be good radical leaving groups [4]. The data in Table 1, Figs. 2 and 3 shows the synthesis of acid end-functional poly(methyl methacrylate) with this RAFT agent (**19**). PMMA of narrow polydispersity (PD < 1.2) with predictable molecular weights and little retardation can be attained over a ca. 50-fold range of RAFT agent concentrations. High conversions (80–100%) are achieved within a relatively short reaction time (6 h). Conversions for the higher RAFT agent concentrations are lower, but it is nonetheless clear that there is no marked retardation. The conversion-time-molecular weight dependence was only examined for one RAFT agent concentration (Fig. 3). Molecular weights calculated with Eq. (1) are slightly lower than calculated at the highest conversion probably due to a reduction in the initiator efficiency with conversion.

The carboxy group functionality was confirmed by derivitization with trichloroacetyl isocyanate (Schemes 4 and 5) and ^{1}H NMR [18]. Signals attributed to the diastereomeric imidic hydrogens of (**25**) appear at δ 9.3 (singlet) and 9.4 (broad singlet) in the ^{1}H NMR spectrum enabling the end group to be readily quantitated. The carboxy end groups were quantitatively determined for the lowest molecular weight PMMA by integration of the ^{1}H NMR spectrum and their amount was consistent with the GPC determined molecular weight within experimental error. The number of carboxy groups per molecule for higher molecular weight polymers will be lower because of a higher proportion of initiator derived chains. A higher degree of functionality could be achieved by use of a functional initiator.

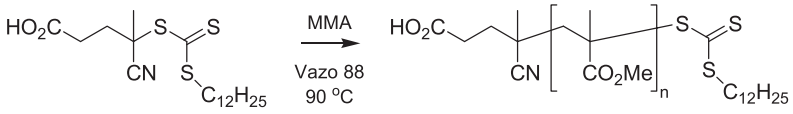
Calculated molecular weights shown in Table 1 and Fig. 3 were determined using the relationship [4]

$$\bar{M}_n(\text{calc}) = \frac{[M]_0 - [M]_f}{[RAFT]_0 + df([I]_0 - [I]_t)} m_M + m_{RAFT} \qquad (1)$$

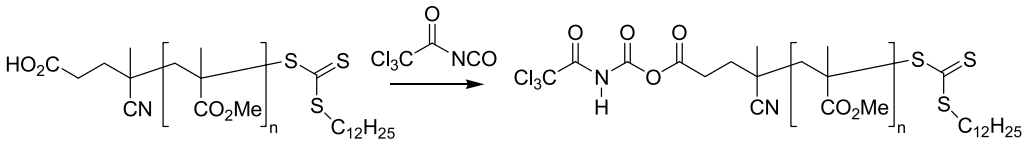
where m_M and m_{RAFT} are molecular weights of the monomer and the RAFT agent, respectively, d is the number of radicals formed from the initiator ($d=1.67$ for PMMA with azobis(1-cyclohexanenitrile)) [4] and f is the initiator efficiency (taken as 0.5). $[I]_t$ was calculated from the known value of k_d ($k_d=2.5368\times10^{-5}$ M^{-1}/s at 90 °C for azobis(1-cyclohexanenitrile)) [56,57].

3.3. Primary phthalimido end-functional polystyrene

There have been a number of papers on the synthesis of polymers with primary amine end-groups [58–63]. The



Scheme 4.



25

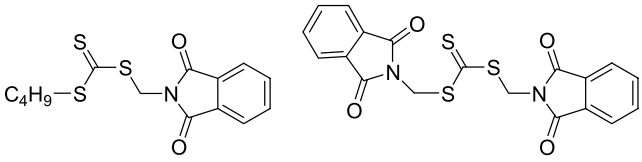
Scheme 5.

polymers have a range of applications in biomedical and materials science. Our interest was the synthesis of block and graft copolymers with well defined segment lengths [58,59,64]. Primary amino-functional polymers have previously been prepared by anionic polymerization [58–62] and by ATRP [63,65–69]. They have also been prepared by conventional radical polymerization with use of a functional iniferter [70], functional transfer agents [71,72] or functional initiators [73,74]. Most processes have required the primary amine group to be protected during the polymerization process.

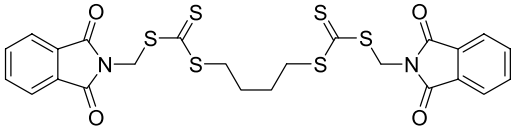
The trithiocarbonate group reacts rapidly with primary and secondary amines to form, in the first instance, a thiol and a dithiocarbamate derivative. It was, therefore, necessary to protect such amine end-groups during polymerization. For the present work, a variant of the Gabriel/Ing–Manske procedure [75] was adopted which involved introducing a latent primary amine group as a phthalimidomethyl residue. A related protection strategy was used by Clouet and Juhl [70] who made use of a phthalimido functional iniferter in the synthesis of α,ω-primary amino-functional polyisoprene. The trithiocarbonate RAFT agents (**26**–**28**) were synthesized from *N*-bromomethylphthalimide. The overall process for synthesis of α-phthalimidomethylpolystyrene is shown in Scheme 6. RAFT agents **26** and **28** proved to be effective and provided molecular weights close to those expected as well as narrow polydispersities ($M_w/M_n < 1.2$—Table 2). The RAFT agent (**27**) also gave good control but its use was complicated by its very low solubility in styrene at room temperature. The rate of polydispersity narrowing achieved suggests a transfer constant similar to that of dibenzyl trithiocarbonate (**17**) [3]. Further details of these polymerizations will be reported elsewhere [17]. The use phthalimidomethyl dithiobenzoate and related RAFT agents is described in a recent patent [76] though its use as a precursor of amine-functional polymers is not mentioned.

Analogous chemistry (Scheme 7) making use of ATRP with *N*-bromomethylphthalimide as initiator and copper (I) bromide, 4,4′-di(5-nonyl)-2,2′-bipyridine (dNbpy) as catalyst also gave a narrow polydispersity polymer but was complicated by the poor organic solubility of the initiator [77].

The conversion of the α-phthalimidomethylpolystyrene to α-aminomethylpolystyrene required removal of the RAFT end-group.



26 27



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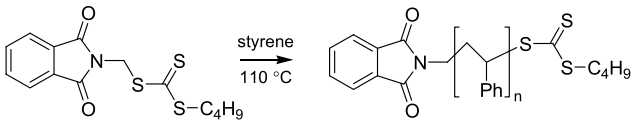
3.4. Removal of RAFT end groups

In some circumstances, depending on the application, the residual RAFT agent functionality can be an issue. A variety of methods are available for cleaving the thiocarbonylthio group [79,80]. These include radical induced reduction (to provide a hydrocarbon end-group), thermal elimination (to provide an unsaturated end-group) and reaction with a nucleophile (e.g. amine [1,5,43,81–83], hydroxide [84], borohydride [49,85]—to provide a thiol end-group). These processes are summarized in Scheme 2.

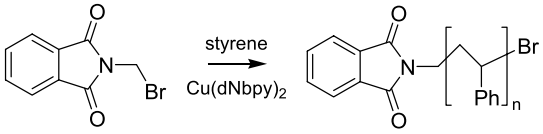
In the present work, we required a primary amino-functional polymer. Since, primary and secondary amines are known to react with thiocarbonylthio groups, it was important that we removed the RAFT functionality prior to deprotection of the amine group.

For lower molecular weight polymers, the end-group transformations can be conveniently followed by ^{1}H NMR. The polystyryl methine hydrogen adjacent to the thiocarbonylthio appears as a broad 'doublet' at $\delta = 4.7$ in the ^{1}H NMR spectrum of the polystyrenes formed with (**26**–**28**). However, for the case of the polymers formed with the bis-RAFT agent (**28**), it is also possible to follow the process by GPC since removal of the RAFT agent functionality cleaves the polymer in half. Before/after GPC traces for the processes investigated are shown in Fig. 4.

Small scale thermolysis was carried out using a thermogravimetric balance. Thermolysis at 210–250 °C appears to cleanly cleave the polymer in half (Fig. 4(a)). This experiment also shows that the two polystyrene chains of (**29**) are equivalent and, therefore, that the two trithiocarbonate groups of the bis-RAFT agent (**28**) have reacted equally during polymerization. ^{1}H NMR demonstrates the disappearance of



Scheme 6.



Scheme 7.

the thiocarbonylthio group, the formation of the olefinic end-group and the retention of the phthalimido end-group. The data is consistent with the product being α-phthalimidopolystyrene (**30**) (Scheme 8).

Chen et al. [86] have shown that tri-*n*-butylstannane reduces dithiobenzoate end groups It is also possible to cleave trithiocarbonate groups quantitatively by reduction with tri-*n*-butylstannane (Fig. 4(b)). The ^{1}H NMR demonstrates the removal of the thiocarbonylthio group and the retention of the phthalimido end-group group. The data is consistent with reduction providing α-phthalimidopolystyrene (**31**) as shown in Scheme 9. Removal of excess tri-*n*-butylstannane and derived by-products from the reduction proved, however, problematical. Even after several precipitations the NMR spectrum demonstrated the presence of tri-*n*-butylstannane derived by-products.

Reaction of (**29**) with piperidine was also examined. This reaction was expected to produce polystyrene with a thiol chain end (**32**) (Scheme 10). Even though the product was colourless, indicating loss of the thiocarbonylthio end-group, the reaction product had a bimodal distribution

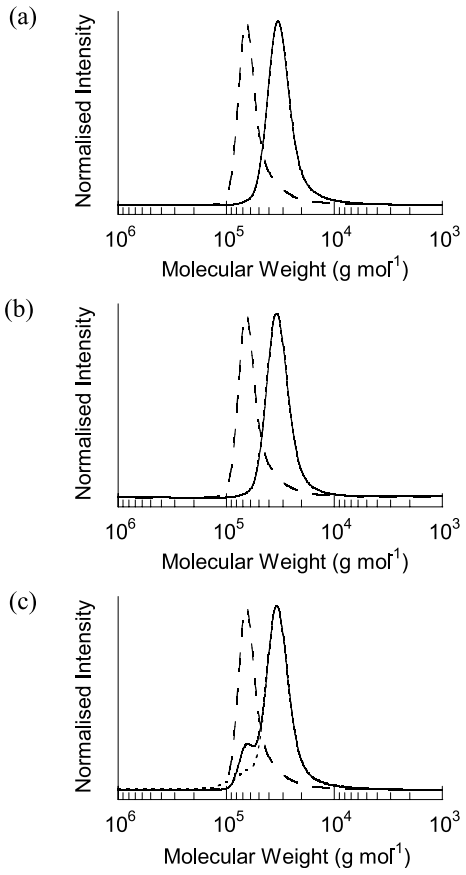
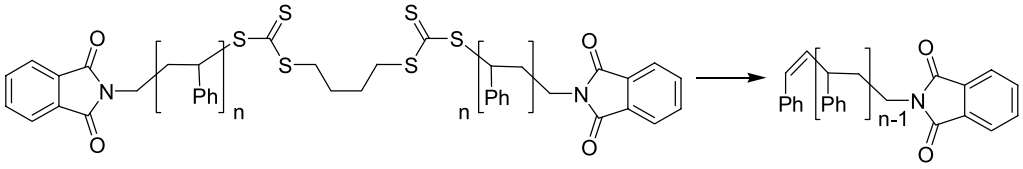
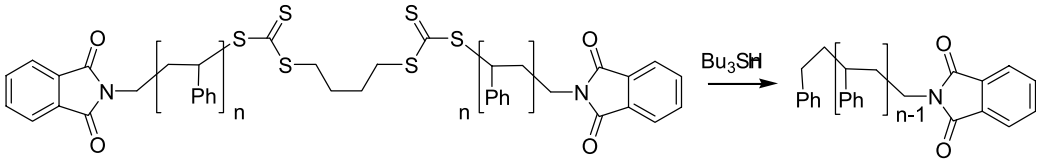


Fig. 4. GPC traces for the precursor polystyrene and reaction products which arise from the bis-polystyrene trithiocarbonate (**29**) (– – –) with (a) after treatment with tri-*n*-butylstannane (Scheme 8) (—), (b) by thermolysis (Scheme 9) (—) and (c) after treatment with piperidine (Scheme 10) (—) and Zn/CH_3COOH reduction (- - -). For details see Section 2.



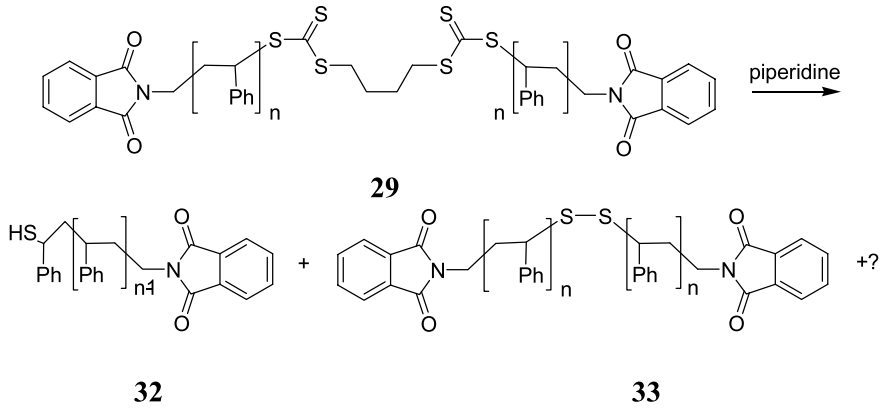
29 **30**

Scheme 8.



29 **31**

Scheme 9.



Scheme 10.

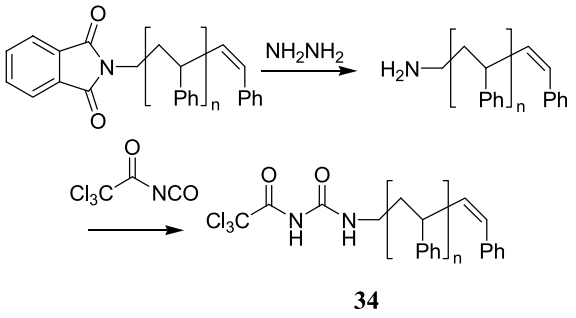
(Fig. 4(c)). It is possible that if air was not completely excluded from the reaction, the initially formed thiol may have undergone oxidative coupling to give the disulfide (**33**). Further treatment with Zn/acetic acid to reduce any disulfide by-product diminished but did not eliminate the high molecular weight shoulder in the molecular weight distribution (Fig. 4(c)).

3.5. Primary amino end-functional polystyrene

Hydrazinolysis of the phthalimido end-group in α-phthalimidopolystyrene (**30**) or (**31**) afforded a polystyrene with the desired ω-monoamino functionality (Scheme 11). The deprotection step was realized by treatment with hydrazine either in DMF at 80 °C for 12 h or in refluxing THF/ethanol for 2 h [87]. The presence of the primary amino group was confirmed by derivitization with trichloroacetyl isocyanate (Scheme 11) and ^{1}H NMR [18]. The amidic and imidic hydrogens of (**34**) are diagnostic and appear in a clear region of the ^{1}H NMR spectrum at $\delta = 7.5$ (multiplet) and 8.2 (broad "doublet").

4. Conclusions

RAFT polymerization has been successfully applied to the synthesis of carboxy-functional poly(methyl methacrylate) and primary amino-functional polystyrene through the use of appropriately designed trithiocarbonate RAFT agents. Several methods removing the thiocarbonylthio end-group of RAFT-made polymers have been explored. It is shown that the thiocarbonylthio end-group can be cleanly cleaved by radical induced reduction with tri-*n*-butylstannane, to leave a saturated chain end, or by thermolysis, to leave an unsaturated chain end.



Scheme 11.

Acknowledgements

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