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Communication

Mild and Facile Synthesis of Multi-Functional RAFT Chain Transfer Agents

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Abstract: In this paper we will describe the synthesis and characterization of a series of novel chain transfer agents for application in reversible addition fragmentation chain transfer polymerization (RAFT). The facile and mild conditions used for the synthesis of these new chain transfer agents should allow for the application of these methods for the preparation of a wide range of multifunctional chain transfer agent species. Some initial polymerization data for these multifunctional chain transfer agents is also reported.

Keywords: RAFT; star polymers; multifunctional chain transfer agents

1. Introduction

Since being reported in 1998, reversible addition fragmentation chain transfer polymerization (RAFT) has been used to polymerize a wide range of monomers, some of which were previously inaccessible with other CRP techniques, whilst maintaining good control over the molecular weight and polydispersity of the resultant polymer [1-5]. There are four main families of RAFT chain transfer agents dithioesters, trithiocarbonates, dithiocarbamates and xanthates, each of which differ in the structure of the radical stabilizing group, Z. The key requirements for the design of effective RAFT chain transfer agents are that the C=S double bond is reactive and that the intermediate radicals fragment quickly. To avoid termination reactions and thus retain the *pseudo* living character of RAFT,

the leaving group, R, species must be a stable radical, and the fragmentation equilibrium must lie at the dormant species to keep the concentration of radicals low. This can be achieved by appropriate design of the RAFT chain transfer agent species [6,7]. Monomer insertion occurs between the CS_2 group and the R group in dithioesters, dithiocarbamates and xanthates, however for trithiocarbonates polymerization can occur on either side of the central CS_2 moiety, depending on which 'R' group generates the more stable radical. Recently, imidazole-based dithiocarbamates have been synthesized for use as a protecting group in organic synthesis, and also as chain transfer agents for RAFT[8,9]. In contrast to the air-sensitive routes which are conventionally used for the synthesis of RAFT chain transfer agents, the reported synthesis is tolerant to air and moisture, is high-yielding and can be carried out at room temperature. In addition, variation in both the alkyl halide and replacement of the imidazole with a thiol, amine or alkoxy group affords related trithiocarbonate, dithiocarbamate or xanthate RAFT agents. This synthetic strategy has recently been shown to be a facile route to a wide range of RAFT chain transfer agents in high yields [10].

Star polymers are characterized by several identical polymer chains emerging out of a single core functionality. Interest in star polymers compared to linear polymers is primarily due to the unique behavior that the viscosity increases exponentially as a function of molecular weight, instead of adhereing to a power law dependence which is observed for linear analogues [11,12]. With related 'families' of macromolecules such as dendrimers and hyperbranched polymers star polymers offer potential applications in areas such as encapsulation and drug delivery, biofunctionalized coatings, microelectronics and as stabilizers in emulsion polymerizations. There are two methods to synthesize star polymers; growing linear polymer chains and then utilizing functional end groups to graft the linear chains onto a multifunctional core [13,14], or synthesizing a core to grow the star polymer directly *via* living [15,16] or CRP polymerization methods [17-19]. The 'grafting to' methodology is useful since optimized conditions for the linear polymerization of many monomers have been reported in the literature using various different polymerization methods, making the arm synthesis relatively simple [20,21]. However, the coupling to the core often requires extensive reaction times, particularly with increasing molecular weight and number of arms, and fractionation is often required to separate the resultant star polymers from the unreacted polymer arms.

By first synthesizing the core and then carrying out polymerizations from this core (the 'grafting from' approach), the reaction times can be markedly reduced, and with careful core design and optimization of the polymerizations, formation of linear polymer can be avoided. Using a RAFT polymerization enables 2 distinct star polymer synthetic routes by the 'core-first' method - the Z and the R group approaches [22,23]. During propagation using the Z-group approach [24] the C=S moiety leaves the central core of the growing star in order for chain growth to continue, and hence propagation occurs exclusively in the solution surrounding the central core. This has implications for the potential synthesis of heteroarm or miktoarm star polymers, as the growing arms could potentially re-attach to the 'wrong' core functionality, potentially losing the targeted molecular architecture. Possible termination routes include the formation of linear polymers due to chain-chain coupling, this is the main disadvantage of the Z-group approach [25] as fractionation to separate the star polymer from the linear polymer has to be carried out. The accessibility of the RAFT functionality with increasing arm number and molecular weight can also be a problem, as the growing polymer arms can hinder the ability of the monomer to reach the RAFT moiety near the core of the star polymer [26]. In contrast,

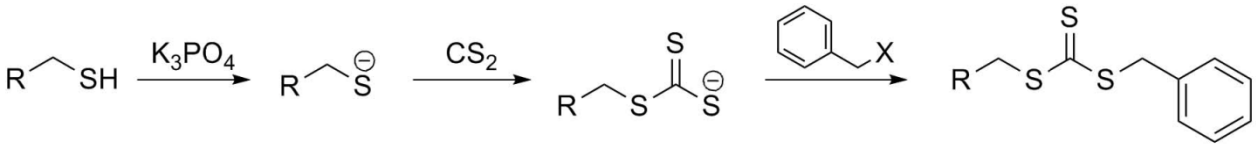
when using the R-group approach, the propagating radicals never leave the core, and thus instead of chain-chain coupling as a termination reaction, there is the possibility of star-star coupling as an unwanted side reaction, leading potentially to high molecular weight side products in the resulting star. The advantage of the R-group approach is that the thiocarbonyl functionalities are always on the chain ends, so there is no loss of accessibility with increasing molecular weight of polymer and it has been proposed that the polymerization is more likely to retain living characteristics than using the Z-group approach [27].

2. Results and Discussion

2.1. R group approach for multi functional chain transfer agent synthesis

The R- and Z-group approach to star polymer synthesis can be achieved using any of the RAFT chain transfer agent species, however we have chosen to focus on the trithiocarbonates as they have been used to polymerize the widest range of monomers and they are easily synthesized. Whether the star polymer grows in an R-group or Z-group manner is determined by variation of the groups either side of the central trithiocarbonate core unit. As a result the final polymer can have the CS_2 at the end of the arms (R-group approach) if the central core is better able at stabilizing radicals or with the CS_2 still near the central core (Z-group approach) if the core of the chain transfer agent is unable to stabilize radical species. The synthetic methods used in this paper are based on the reported facile trithiocarbonate synthesis (Scheme 1), and requires a displaceable halogen to be present on one of the starting materials for nucleophilic attack of the RCS group.

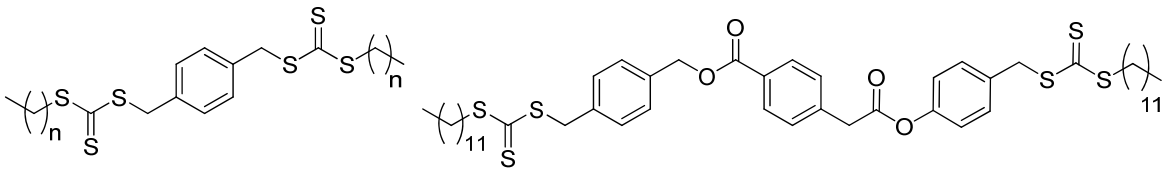
Scheme 1. General synthetic method for the RAFT chain transfer agent synthesis.



Our initial target was chain transfer agent **1**, which was prepared by reacting ethane thiol and carbon disulphide with α-α dichloro-*p*-xylene (Scheme 2). However, analysis by ^{1}H NMR indicated that both the *mono* and *bis* products formed in a 1:6 ratio (as determined by ^{1}H NMR analysis and examination of the methylene signals at 3.72 ppm for the chloro starting material and 4.60 ppm for the trithiocarbonate product). These 2 products were extremely difficult to separate by chromatography and subsequent attempts to push the reaction to completion by the addition of further reagents caused further purification difficulties. All attempts to purify this chain transfer agent from the excess starting materials were unsuccessful given their similar affinities in column chromatography in a wide range of solvents. In order to make the product easier to handle and purify, a similar synthesis using dodecane thiol was carried out, to afford chain transfer agent **2**. This was chosen as dodecane thiol has a number of advantages including the fact that it is less malodorous and also the long alkyl chains encourage the crystallization of the product and thus may enable more facile purification. Following overnight reaction at room temperature, in air, once again a mixture of *mono* and *bis* products were identified by TLC analysis however in this case product **2** could be readily isolated by recrystallization to yield a

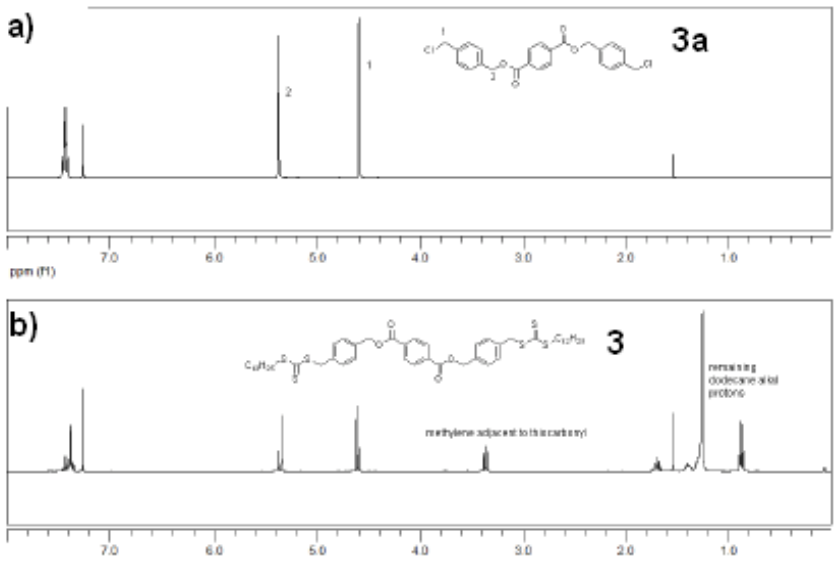
yellow solid in 62% yield. This compares very favorably with the previous literature report [28] of the synthesis of this chain transfer agent (in an 8 % yield) under harsher conditions. In the ^{13}C NMR spectrum the distinctive C=S signal was assigned at 223.6 ppm, which correlates well with the reported literature value.

Scheme 2. Schematic of chain transfer agents **1**, **2** and **3**.



We were also interested in exploring the introduction of a cleavable linker into the R-group approach chain transfer agents developed in this work. It was proposed that this would enable cleavage of the resultant polymer arms from the core and thus facilitate confirmation of a controlled polymerization mechanism and a uniform polymer arm growth. Hence an ester functionality was chosen as a robust yet readily cleavable unit in the multifunctional chain transfer agent synthesis. A new synthetic route was proposed and utilized to prepare chain transfer agent **3** in good yield. This method first utilized a Steglich esterification to afford **3a** in a 51% yield following column chromatography (Figure 1a). The successful synthesis of product **3a** was confirmed by IR analysis and loss of the characteristic hydroxy and acid signals and identification of a new signal at 1713 cm^{-1} attributable to the ester functionality. Following this, the reaction of **3a** with dodecane thiol under established RAFT chain transfer agent conditions and purification by column chromatography afforded **3** as a yellow solid in a 47% yield. The successful synthesis of chain transfer agent **3** was confirmed by ^{1}H NMR, ^{13}C NMR, IR spectroscopy and elemental analysis. The ^{1}H NMR spectrum for **3** is shown in Figure 1b.

Figure 1. ^{1}H NMR spectrum of **a) 3a** and **b) 3** both in $CDCl_3$.



This method was then utilized to prepare the three arm derivative of chain transfer agent **3**. This reaction proved more difficult and a number of coupling conditions were attempted to try to improve the overall yield of the reaction. In this case using EDCI as a coupling agent, along with excess 4-(chloromethyl) benzyl alcohol afforded the best results (38% yield) for the synthesis of **4a**. IR analysis of **4a** confirmed the presence of the ester functionality (strong signal at 1726 cm^{-1}) and this intermediate was then reacted under the conditions outlined in Scheme 3. Following column chromatography the 3 armed chain transfer agent **4** was isolated as a yellow crystalline solid in a 56% yield (Figure 2). The characteristic C=S peak in the ^{13}C NMR spectrum was present at 223.5 ppm, as were the characteristic signals in the ^{1}H NMR spectrum for the dodecane chain, in particular the methylene adjacent to the thiocarbonyl unit which appeared as a triplet at 3.41 ppm and the terminal methyl group which appeared at 0.92 ppm.

Scheme 3. Synthesis of chain transfer agent **4**.

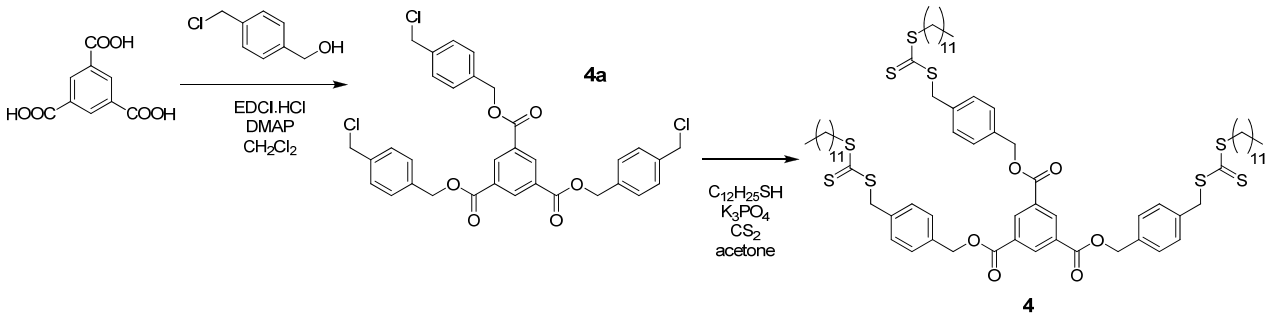
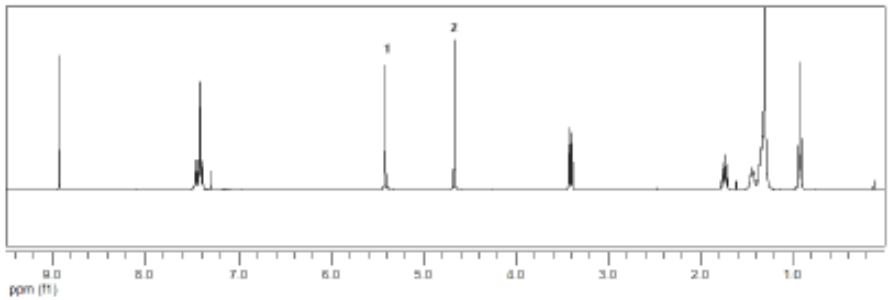


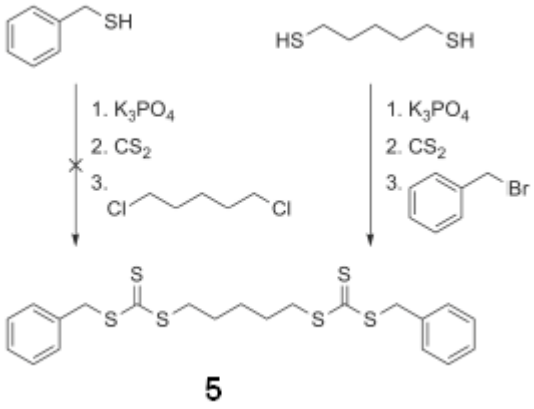
Figure 2. ^{1}H NMR spectrum of **4** in $CDCl_3$.



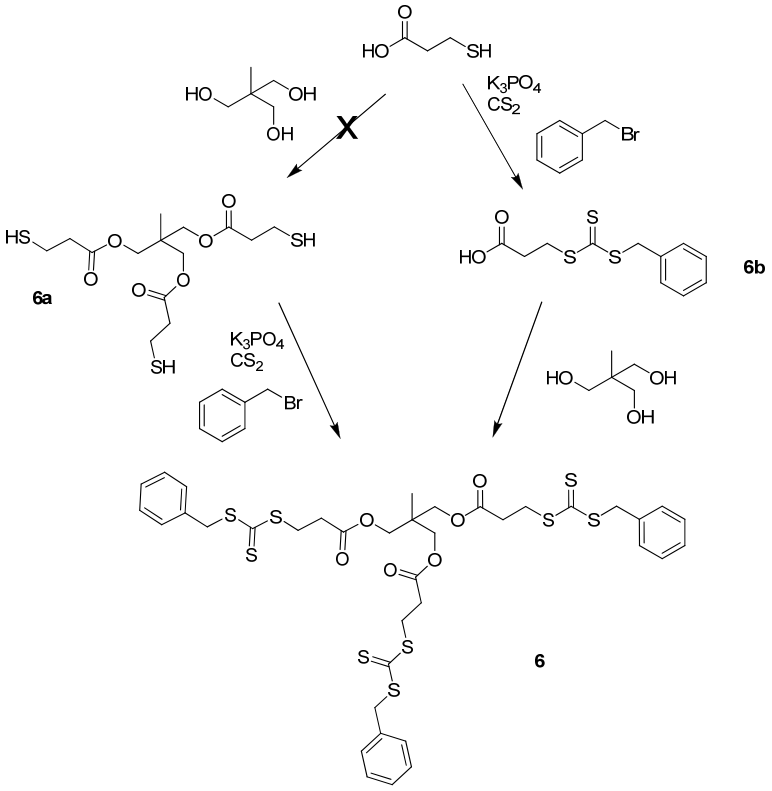
2.2. Z group approach for multi-functional chain transfer agent synthesis

To provide a comparison between the R-group and Z-group approach a series of related chain transfer agents to those already discussed in Section 2.1 were targeted. It is proposed that these bifunctional CTAs can be used as models for multifunctional CTAs which can provide access to star polymers. Once again our initial attempts to utilize an ethane bridge proved problematic as difficulties in purification resulted. Hence, our first target utilized a longer (pentane) alkyl chain and 2 complimentary reactions were attempted for the synthesis of chain transfer agent **5** (Scheme 4).

Scheme 4. Schematic of the 2 routes explored for the synthesis of chain transfer agent **5**.



Scheme 5. Schematic of the 2 routes explored for the synthesis of chain transfer agent **6**.



Route 1 provided unsuccessful with the symmetrical (*bis* (phenylmethyl) trithiocarbonate) chain transfer agent being isolated as the major product in a 46% yield (as confirmed by ^{1}H NMR analysis). However, the second route proved successful and enabled the isolation of chain transfer agent **5** as a bright yellow solid in a 62% yield following chromatography. Extension of this synthesis to allow for the preparation of a three-armed analogue, **6**, provided difficult, starting from commercially available 3-mercapto propionic acid. Once again 2 routes were attempted (Scheme 5). The first route first involved the esterification of the thiol acid with a trifunctional hydroxy core. This was successful by ^{1}H NMR analysis (by loss the distinctive signal at 3.68 ppm attributable to the methylene of the

hydroxy starting material), however the purification of the resultant trithiol, **6a** species proved very difficult. Given the low yield of the first step of this route (*ca*. 10%) a second route was investigated. This involved the synthesis of a previously reported acid functionalized trithiocarbonate chain transfer agent, **6b**, which was isolated in a 73% yield.[10] The coupling of this acid functionalized chain transfer agent to the trifunctional core, using EDCI, proceeded in good yield to afford the desired chain transfer agent in a 45% overall yield. This three-armed chain transfer agent **6** was characterized by ^{1}H and ^{13}C NMR as well as elemental analysis.

2.3. Polymerization data for chain transfer agents 2-6

A selection of the chain transfer agents were also utilized in RAFT polymerizations to explore their effectiveness in mediating the controlled polymerization of both acrylate and styrenic monomers. Table 1 highlights the polymerization results for the difunctional chain transfer agents **2**, **3** and **5**. For the 2 armed chain transfer agents there appears to be little difference in polymerization control between the R and Z group approaches. The detailed kinetics for the polymerization of t-butyl acrylate with chain transfer agent **3** were determined using the conditions established in Table 1. The polymerization displayed linear kinetics (K_{papp} = 0.0114 min^{-1}) indicative of a constant concentration of radicals and a linear increase in polymer molecular weight with conversion which confirmed a controlled polymerization. It should be noted that AIBN is used as a radical initiator in all the reported polymerizations and this will lead to a minor fraction of linear chains in all of the polymerizations.

Table 1. Polymerization data for the dual functional chain transfer agents.

Chain transfer agent	Monomer	Time (hr)	Conv. (%)	M_n^{GPC} (Da)	M_w/M_n
2	St	2	76	24,600	1.09
2	*t*BuA	2	82	34,000	1.19
3	St	2	74	25,300	1.11
3	*t*BuA	1	65	27,900	1.17
5	St	3	79	30,200	1.12
5	*t*BuA	4	84	35,600	1.07

For styrene polymerizations, 85 ^{o}C, 300 eq. of monomer, 0.2 eq. AIBN, bulk and for *t*butyl acrylate polymerizations, 60 ^{o}C, 300 eq. of monomer, 0.2 eq. AIBN, bulk

Cleavage of the ester linkage was carried out according to a literature procedure *[29]*. The ester linkage of the 2-armed poly(tBuA) (Table 1, M_n^{GPC} = 27,900, M_w/M_n = 1.17) was cleaved by base hydrolysis (THF:H_2O 20:1 v/v, 50 ^{o}C, 46h). The resulting polymer had a polydispersity of 1.16 and molecular weight of 13,900 Da (determined by GPC) indicating successful cleavage of the ester linkage. As the polydispersity remained unchanged this indicated that the fidelity of the polymer backbone was unaffected by the hydrolysis conditions. A comparison of the ^{1}H NMR spectra of **3**, the resultant polymer and cleaved polymer shows evidence of the cleavage having occurred due to the disappearance of the peak from the central benzene core in the starting poly(tBuA) at 8.11 ppm in the cleaved polymer. Supporting evidence was also provided by FT-IR which showed the disappearance of

the carbonyl stretch (1713 cm^{-1}) originating from chain transfer agent **3**. The aqueous environment utilized for arm cleavage also hydrolyzed the active trithiocarbonate end group *[29]*, effectively rendering the arms 'dead' and unable to chain extend *[30]*. The ^{1}H NMR spectra of the polymers confirmed the hydrolysis of the trithiocarbonate to release the dodecane alkyl chain, as the signal at 3.37 ppm from the methyl unit adjacent to the trithiocarbonate functionality has disappeared in the cleaved polymer. The trifunctional RAFT chain transfer agents (**4** and **6**) were also explored for the polymerization of styrene (using the conditions outlined in Table 1). In the case of the trifunctional chain transfer agents it was evident that the R group approach afforded narrower polydispersities (M_w/M_n 1.21 versus 1.32) and also better control over molecular weight of the resultant polymer. Further work exploring the polymerization of these and higher functional chain transfer agents is currently underway.

3. Experimental Section

3.1. Materials and Instrumentation

AIBN (2,2'-Azobis(2-methylpropionitrile) was recrystallized twice from methanol and stored in the dark at 4 ◦C. t-Butyl acrylate and styrene were distilled over CaH_2 and stored at 4 ◦C. Dry dichloromethane was obtained by prolonged reflux over CaH_2. 3-(benzylthiocarbonothioylthio)propanoic acid CTA was synthesized as previously reported [10]. All other reagents were purchased from Sigma Aldrich and were used without further purification.

^{1}H and ^{13}C NMR spectra were obtained at 400 or 500 MHz with Bruker DPX-400/DPX-500 spectrometer using $CDCl_3$. Chemical shifts are reported in ppm (δ) relative to $CHCl_3$ (7.26 ppm for 1H and 77.2 ppm for ^{13}C) as an internal reference. Gel Permeation Chromatography (GPC) data for polymers was obtained in THF (Shimadzu UFLC autosampler with Polymer Laboratories gel 5 m Mixed C column) at room temperature with PS standards at a flow rate of 1 $mlmin^{-1}$. IR spectra were obtained on Perkin-Elmer Spectrum 100 ATR FT-IR Spectrometer. Elemental analyses were run by Alan Dickerson at the University of Cambridge.

3.2. Methods

3.2.1. General polymerization method

The requisite concentrations of RAFT agent (chain transfer agent), monomer and radical chain transfer agent (AIBN) were placed in a sealed ampoule with a stirrer bar and thoroughly degassed *via* at least 4 freeze-pump-thaw cycles. The temperature was controlled by an isothermal oil bath and the polymerizations were stirred throughout. Polymers were precipitated into cold methanol:water (10:1 v/v) solutions and the polymer isolated by filtration, dried over $MgSO_4$ and the residual solvent was removed in *vacuo*.

3.2.2. Attempted synthesis of **1** - 1,4-phenylenebis(methylene) diethyl dicarbonotrithiocarbonate

To a stirred suspension of potassium phosphate (1.21 g, 5.71 mmol) in acetone (20 ml) was added ethane thiol (0.423 ml, 0.354 g, 5.71 mmol). After 5 minutes carbon disulfide (1.03 ml, 1.30 g,

17.1 mmol) was added, followed by α-α dichloro-*p*-xylene (0.500 g, 2.86 mmol) after a further 10 minutes. The reaction was monitored by TLC. The acetone was removed in *vacuo* and the mixture taken into dichloromethane (20 ml), extracted with water (20 ml) and dried over $MgSO_4$. The reaction mixture was analyzed by TLC and showed evidence of both *mono*- and *bis*-substituted product, running at very similar R_f values in a wide range of solvent systems. They proved impossible to separate from either each other or the α,α dichloro-*p*-xylene starting material.

3.2.3. Synthesis of **2** - 1,4-phenylenebis(methylene) didodecyl dicarbonotrithiocarbonate

Potassium phosphate (1.21 g, 5.71 mmol) was stirred in acetone (20 ml), dodecane thiol (1.37 ml, 1.15 g, 5.71 mmol) added and the reaction mixture stirred for 20 minutes. Carbon disulfide (1.03 ml, 1.30 g, 17.1 mmol) was added, the mixture stirred for 20 minutes and α,α dichloro-*p*-xylene added. The reaction was monitored by TLC and after 30 minutes was filtered. The solvent was removed in *vacuo* and the product, **2**, was isolated *via* hot filtration and recrystallization from ethyl acetate as a yellow crystalline solid (1.16 g, 1.76 mmol, 62% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28 (s, aryl, 4H), 4.59 (s, benzylCH_2, 4H), 3.37 (t, SCSCH_2, 4H), 1.70 (m, CH_2, 4H), 1.40 (m, CH_2, 4H), 1.26-1.36 (m, alkyl, 32H), 0.88 (t, CH_3, 6H). ^{13}C NMR δ 223.6 (C=S), 134.8, 129.5, 40.8, 37.1, 31.9, 29.6, 29.6, 29.5, 29.4, 29.3, 29.1, 28.9, 27.9, 22.7, 14.1. FT-IR: 2916, 2848 (C-H stretch), 1511, 1469, 1396, 1237, 1083, 1061, 1033, 980, 836, 819,718, 670 cm^{-1}. Elemental analysis calcd. for $C_{34}H_{58}S_6$ C 61.45; H 8.87. Found C 60.96; H 8.75.

3.2.4. Synthesis of **3a**

Terephthalic acid (0.579 g, 3.49 mmol), 4-(chloromethyl) benzyl alcohol (0.900 g, 6.34 mmol) and *N*,*N*-dimethyl aminopyridine (0.077 g, 0.630 mmol) were dissolved in dry dichloromethane (25 ml). DCC (1.95 g, 9.51 mmol) was added and the mixture stirred overnight. The product **3a** was purified by column chromatography in neat dichloromethane, dried in *vacuo* and isolated as a white solid (0.790 g, 1.78 mmol, 51% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12 (s, aryl, 4H), 7.45 (d, aryl, 4H), 7.42 (d, aryl, 4H), 5.38 (s, CO_2CH_2, 4H), 4.60 (s, CH_2Cl, 4H). ^{13}C NMR δ 165.5, 137.7, 135.9, 133.9, 129.7, 128.9, 128.6, 66.6, 45.7. FT-IR: 2964 (C-H stretch), 1917, 1713 (C=O stretch), 1674, 1616, 1504, 1449, 1422, 1407, 1370, 1328, 1302, 1248, 1215, 1116, 1095, 1017, 917, 854, 834 cm^{-1}. Elemental analysis calcd. for $C_{24}H_{20}Cl_2O_4$ C 65.02; H 4.55. Found C 64.91; H 4.57.

3.2.5. Synthesis of **3** - bis(4-((dodecylthiocarbonothioylthio)methyl)benzyl) terephthalate

Potassium phosphate (0.287 g, 1.35 mmol) was stirred in acetone (25 ml), dodecane thiol (0.324 ml, 0.270 g, 1.35 mmol) added after 10 minutes and stirred for a further 60 minutes, and carbon disulfide (0.245 ml, 0.308 g, 4.05 mmol) added, after which the reaction mixture turned from colorless to a bright yellow. **3a** (0.300 g, 0.670 mmol) was dissolved in 150 ml acetone, added to the reaction mixture over a period of 60 minutes and stirred overnight. The resulting solids were filtered off and the filtrate washed with water (2 x 50 ml) and brine (50 ml) and dried over $MgSO_4$. The product, **3**, was purified by column chromatography (3:1 chloroform:petroleum ether 40-60), dried in *vacuo* and isolated as a yellow solid (0.29 g, 0.310 mmol, 47% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.11 (s, aryl,

4H), 7.26-7.46 (m, aryl, 8H), 5.36 (d, CH_2SCS, 4H), 4.61 (d, CO_2CH_2, 4H), 3.37 (t, $SCSCH_2$, 4H), 1.70 (m, alkyl, 4H), 1.40 (m, alkyl, 4H), 1.25-1.32 (m, alkyl, 32H), 0.88 (t, CH_3, 6H). ^{13}C NMR δ 223.6, 165.5, 135.6, 135.2, 134.0, 129.6, 128.9, 128.6, 66.7, 45.8, 40.8, 37.1, 31.9, 29.6, 239.5, 29.4, 29.3, 29.1, 28.9, 29.0, 28.9, 28.0, 22.7, 14.1. FT-IR: 2956, 2916, 2850 (C-H stretch), 1713 (C=O stretch), 1514, 1470, 1453, 1423, 1408, 1397, 1375, 1269, 1213, 1114, 1110, 1063, 1018, 929, 871, 853, 820, 771, 724, 667 cm^{-1}. Elemental analysis calcd. for $C_{50}H_{70}O_4S_6$ C 64.75; H 7.61. Found C 64.64; H 7.45.

3.2.6. Synthesis of **4a** - tris(4-(chloromethyl)benzyl) benzene-1,3,5-tricarboxylate

Trimesic acid (0.179 g, 0.850 mmol), 4-(chloromethyl) benzyl alcohol (1.20 g, 7.67 mmol) and *N*,*N*-dimethyl aminopyridine (0.0312 g, 0.255 mmol) were dried in *vacuo* before being dissolved in dry dichloromethane (25 ml). EDCI.HCl (0.538 g, 2.81 mmol) in 15 ml dichloromethane was added dropwise at 0 ◦C over 30 minutes, and the reaction mixture was stirred at room temperature for 24h. The reaction mixture was washed with 1M HCl (2 x 50 ml), and the aqueous layers extracted with dichloromethane (2 x 50 ml). The organic extracts were combined and dried over $MgSO_4$, and the product isolated by column chromatography (neat dichloromethane). The product was a white solid (0.158 g, 0.253 mmol, 38% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.82 (s, aryl, 3H), 7.39 (d, aryl, 6H), 7.37 (d, aryl, 6H), 5.33 (s, CO_2CH_2, 6H), 4.52 (s, CH_2Cl, 6H). ^{13}C NMR δ 164.7, 137.8, 135.7, 134.9, 131.2, 128.9, 128.7, 66.9, 45.7. FT-IR: 2964 (C-H stretch), 1735, 1726 (C=O stretch), 1607, 1514, 1447, 1424, 1384, 1369, 1331, 1249, 1225, 1139, 1109, 1099, 965, 834 cm^{-1}. Elemental analysis calcd for $C_{30}H_{27}Cl_3O_6$ C 63.32; H 4.35. Found C 63.11; H 4.33.

3.2.7. Synthesis of **4** - 1-(3-((dodecylthiocarbonothioylthio)methyl)benzyl) 3,5-bis(4-((dodecylthiocarbonothioylthio)methyl)benzyl) benzene-1,3,5-tricarboxylate

Potassium phosphate (0.163 g, 0.770 mmol) was stirred in acetone (25 ml), dodecane thiol (0.183 ml, 0.154 g, 0.770 mmol) added after 10 minutes and stirred for a further 1 h, and carbon disulfide (0.139 ml, 0.174 g, 2.30 mmol) added, after which the reaction mixture slowly turned to a bright yellow color. **4a** (0.120 g, 0.190 mmol) was dissolved in 30 ml acetone, added to the reaction mixture over a period of 45 minutes and stirred overnight. The resulting solids were filtered off, and the product purified by column chromatography (petroleum ether 40-60:dichloromethane gradient), dried in *vacuo* and isolated as a yellow solid (0.689 g, 0.51 mmol, 56% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.91 (s, aryl, 3H), 7.39-7.45 (m, aryl, 12H), 5.41 (s, CO_2CH_2, 6H), 4.66 (s, aryl-CH_2S, 6H), 3.41 (t, $SCSCH_2$, 6H), 1.74 (m, alkyl, 6H), 1.44 (m, alkyl, 6H), 1.30-1.47 (m, alkyl, 48H), 0.92 (t, CH_3, 9H). ^{13}C NMR δ 164.6, 137.8, 135.6, 134.9, 131.2, 128.9, 128.7, 66.9, 45.7. FT-IR: 2917, 2850 (C-H stretch), 1728 (C=O stretch), 1516, 1469, 1333, 1261, 1232, 1188, 1061, 999, 859, 811, 737, 718, 677 cm^{-1}. Elemental analysis calcd for $C_{72}H_{102}O_6S_9$ C 63.95; H 7.60, Found C 63.89; H 7.42.

3.2.8. Synthesis of **5** - benzyl pentane-1,5-diyl dicarbonotrithiocarbonate

To a suspension of potassium phosphate (2.34 g, 11.0 mmol) in acetone (20 ml) was added pentane dithiol (0.492 ml, 0.500 g, 3.68 mmol), carbon disulfide (1.33 ml, 1.68 g, 22.1 mmol) after 20 minutes

and benzyl bromide (1.31 ml, 1.89 g, 11.0 mmol) after a further 60 minutes. The reaction mixture was stirred overnight and the product purified by column chromatography (neat petroleum ether 40-60). The product was isolated as a dark yellow oil (1.06 g, 2.27 mmol, 62% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34 (m, aryl, 10H), 4.65 (s, benzylCH_2, 4H), 3.42 (t, SCSCH_2, 4H), 1.78 (m, alkyl, 4H), 1.58 (m, alkyl, 2H). ^{13}C NMR δ 223.5, 135.0, 129.2, 128.7, 127.7, 41.4, 36.5, 27.7, 27.6. FT-IR: 3060, 3027, 2927, 2852 (C-H stretch); 1600, (aromatic C=C); 1493, 1452, 1419, 1396, 1267, 1234, 1194, 1060, 1028 (C=S stretch), 914, 877, 798, 768, 694 cm^{-1}. Elemental analysis calcd. for $C_{21}H_{24}S_6$ C 53.80; H 5.16. Found C 54.13; H 5.29.

3.2.9. Synthesis of **6**

3-(benzylthiocarbonothioylthio)propanoic acid (0.272 g, 1.0 mmol), 1,1,1-*tris*(hydroxymethyl) ethane (0.036 g, 0.3 mmol) and *N*,*N*-dimethyl aminopyridine (0.027 g, 0.33 mmol) were dried in *vacuo* before being dissolved in dry dichloromethane (20 ml). EDCI.HCl (0.63 g, 3.3 mmol) in 15 ml dichloromethane was added dropwise at 0 ◦C over 30 minutes, and the reaction mixture was stirred at room temperature for 24h. The reaction mixture was washed with 1M HCl (2 x 50 ml), and the aqueous layers extracted with dichloromethane (2 x 50 ml). The organic extracts were combined and dried over $MgSO_4$, and the product isolated by column chromatography (4:1 petroleum ether 40-60:dichloromethane). The product was a yellow solid (0.119 g, 0.135 mmol, 45% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38-7.20 (d, aryl, 15H), 4.52 (s, CH_2, 6H), 3.55 (s, CO_2CH_2, 6H), 3.25 (s, CH_2, 6H), 2.80 (t, CH_2, 6H), 0.79 (s, CH_3, 3H). ^{13}C NMR δ 219.6 (C=S), 131.2, 129.9, 128.7, 128.2, 53.0, 42.1, 37.2, 33.6, 32.0, 19.0. FT-IR: 2962, 2862 (C-H stretch), 1730 (C=O stretch), 1613, 1516, 1449, 1428, 1379, 1364, 1333, 1261, 1229, 1141, 1111, 1099, 966, 835, cm^{-1}. Elemental analysis calcd for $C_{38}H_{42}O_6S_9$ C 51.67; H 4.79. Found C 52.02; H 4.53.

4. Conclusions

In this work we have applied recently developed mild and effective synthetic methods for the preparation of chain transfer agents for the synthesis of multifunctional RAFT chain transfer agents. This has proven difficult given the challenging purification procedures required. However, a number of different multifunctional RAFT chain transfer agents have been reported and tested for the polymerization of a range of vinyl monomers. Further work will explore extending these results to the synthesis of higher order star structures and also introducing functionality into the multifunctional materials which can be prepared by this method.

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