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Synthesis of Novel Architectures by Radical Polymerization with Reversible Addition Fragmentation Chain Transfer (RAFT Polymerization)

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Summary: Radical polymerization with **R**eversible **A**ddition-**F**ragmentation chain **T**ransfer - RAFT polymerization can be adapted to produce a wide variety of block copolymers and other polymers of complex architecture. Such polymerizations require use of a suitable compound [Z-(C=X)X-R], which is selected to have a very high transfer constants in radical polymerization of the desired monomers, and appropriate choice of reaction conditions. Block and multiblock polymers, stars and grafts are available through use of precursors containing multiple thiocarbonylthio groups. Stars and microgels are also available through self assembly and crosslinking of RAFT synthesized block copolymer micelles and by a varient of the 'arm-first' approach wherein of a diene monomer is (co)polymerized in the presence of a preformed RAFT-made polymer. This paper briefly reviews RAFT polymerization then examines the scope for utilizing the technology in the construction of novel architectures.

Introduction

In recent years, considerable effort has been expended to develop free radical processes that display the characteristics of a living polymerization.[1-6] Living polymerizations provide molecular weights that are predetermined by reagent concentrations and conversion, yield narrow molecular weight distributions and, most importantly, the polymer products can be reactivated for chain extension or block copolymer synthesis. Recently we have described a new method for achieving this end.[7-11] The key step in the process is **R**eversible **A**ddition-**F**ragmentation chain **T**ransfer. Accordingly, we designated the method **RAFT** polymerization.[11]

Some of the advantages of RAFT polymerization, over competing technologies [atom transfer radical polymerization (ATRP),[5,6] nitroxide mediated polymerization (NMP)[4]], stem from the fact that it is tolerant of a very wide range of functionality in monomer and solvent (*e.g.* -

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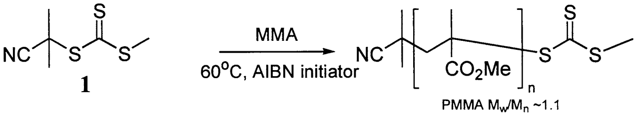
OH, -COOH, $CONR_2$, $-NR_2$, SO_3Na). This means that it is applicable to a vast range of monomer types and that polymerizations can be successfully carried out under a wide range of reaction conditions (bulk, solution, suspension, emulsion). The chain transfer process can be effective over a wide temperature range (>20-150°C). Indeed, with some limitations imposed by the need to limit termination reactions, the reaction conditions employed in RAFT polymerization are typical of those used for conventional free radical polymerization.

This paper will illustrate application of RAFT polymerization to the synthesis of polymers of various architectures (di-, tri-, multi-block, star, etc.). The aforementioned tolerance to functionality in the monomer means that there are tractable routes available to many structures that were previously not directly accessible. It is important to first consider the RAFT process to gain some understanding on how to select the RAFT agent appropriately so as to minimize side reactions and reaction times and maximize block purity

RAFT Polymerization



Scheme 1.

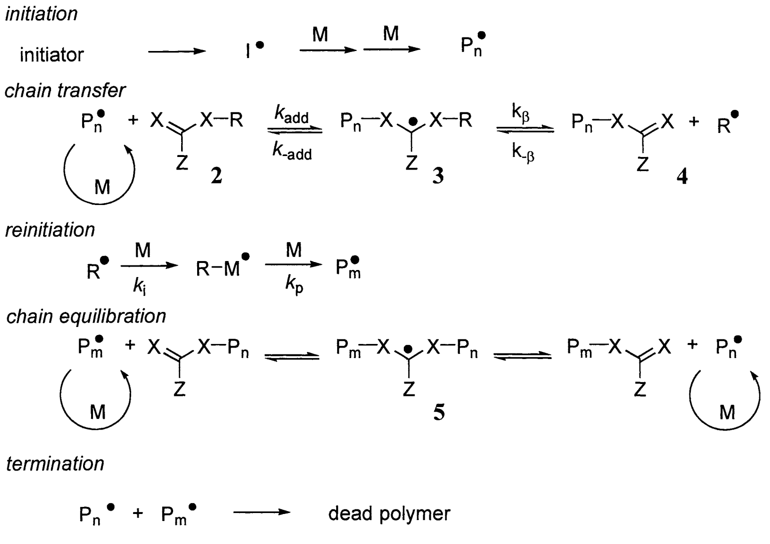
RAFT polymerization provides the characteristics usually associated with living polymerization. The overall process results in monomer units being inserted into RAFT agent structure as shown in Scheme 1. Reaction conditions should usually be chosen such that the fraction of initiator-derived chains (should be greater than or equal to the number of chains formed by radical-radical termination) is negligible. Molecular weights can then be estimated using the relationship (1):[12]

$$\text{Calculated Degree of Polymerization} \sim [\text{monomer consumed}]/[\text{RAFT agent}] \qquad (1)$$

Positive deviations from equation (1) indicate incomplete usage of RAFT agent while negative deviations indicate that other sources of polymer chains are significant (*e.g.* the initiator). Polydispersities depend on the chain transfer constants associated with both the initial and the polymeric RAFT agent. The initial RAFT agent should be chosen such that is rapidly consumed during the initial stages of the polymerization. The rate of consumption of the RAFT agent can usually be predicted using the relationship (2).

$$-\frac{d[2]}{d[\mathrm{M}]} \approx C_{tr}\frac{[2]}{[\mathrm{M}]+C_{tr}[2]+C_{-tr}[4]} \qquad (2)$$

Where $C_{\mathrm{tr}} = k_{\mathrm{tr}}/k_{\mathrm{p}}$, $C_{\mathrm{-tr}} = k_{\mathrm{-tr}}/k_{\mathrm{i}}$, $k_{\mathrm{tr}} = k_{\mathrm{add}} \times \frac{k_\beta}{k_{-add}+k_\beta}$ and $k_{\mathrm{-tr}} = k_{-\beta} \times \frac{k_{-add}}{k_{-add}+k_\beta}$. Other parameters are defined in Scheme 2.

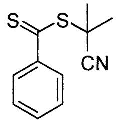


Scheme 2.

Or, with knowledge of the rate of consumption of RAFT agent this, equation (2) can be solved to provide transfer constants.[12] In this kinetic treatment it is assumed that the adduct species **3** and **5** give no chemistry other than fragmentation to give a radical and RAFT agent. Slow fragmentation or consumption of these species in side reactions will give retardation.[8,12-15] A fraction of dead chains determined by the number of chains formed from the initiator and the termination mechanism will always be formed. It is obviously important in block synthesis to maintain a very high fraction of living ends throughout the process. The common industrial practice of adding initiator or increasing initiation rate towards the end of a polymerization to drive the process towards 100% conversion should be avoided. This is particularly important in the intermediate stages of block syntheses involving sequential monomer addition.

RAFT Agents

A wide variety of reagents with the capacity to react by RAFT have now been reported. Examples of RAFT agents include macromonomers (*e.g.* **6** and **7**)[16-18] and thiocarbonylthio compounds (*e.g.* **1** and **8-14**).[8,9,11]



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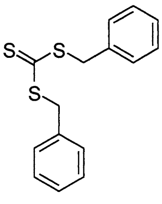

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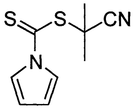

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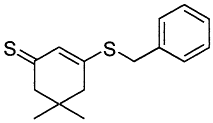

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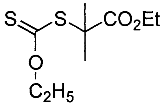

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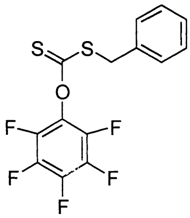

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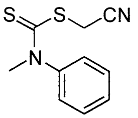

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The generic features common to all RAFT agents can be summarized as shown in Figure 1.

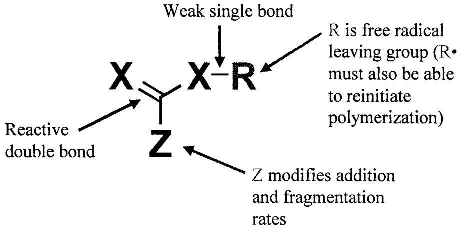


Figure 1. Generic RAFT Agent Structure.

The RAFT agent should to be chosen with attention to the particular polymerization process (the monomers and the reaction conditions) and according to required end group functionality.[9]

Design feature to take into account are:

(a) The RAFT agent (**2**, **4**) should have a high transfer constant in the monomers to be polymerized.

(b) The intermediates (**3** and **5**) should fragment rapidly and give no side reactions.

(c) The expelled radicals (R•) should efficiently reinitiate polymerization.

The magnitude and origin of the substituent effects on the rates of addition and fragmentation are discussed in detail elsewhere. Macromonomers ($X=CH_2$ *e.g.* **6**, **7**) are suited to the synthesis of methacrylic and similar polymers and copolymers. However, transfer constants are generally <1.0 and narrow polydispersities can only be achieved using feed addition protocol.[18-20]

As a general guideline, dithioesters (*e.g.* **8**)[11] and trithiocarbonates (*e.g.* **1**, **9**)[9,21] and certain dithiocarbamates[22,23] (*e.g.* **10**) are the preferred RAFT agents for (meth)acrylic and styrenic monomers in that their use affords narrow polydispersity polymers in a batch polymerization process. When the monomer is vinyl acetate, N-vinyl pyrrolidone[9,23] or similar Z is chosen to give a less stable intermediate (less side reactions, less retardation). Xanthates (*e.g.* **12**) and dithiocarbamates such as **14** are preferred. Within each class of thiocarbonylthio compound it is possible to tune the activity through the choice of substituents on Z.[22-25]

Blocks by Sequential Monomer Addition

In its simplest form, block synthesis simply requires sequential addition of monomers in a polymerization process.[22,26-28] The reaction scheme is then identical to that shown in Scheme 2 where R is a preformed polymer chain. Di-, tri- and multiblock polymers can be formed in this way. Block copolymers based on non radically polymerized chains can be formed by appropriate functionalization of a chain end.[26,29]

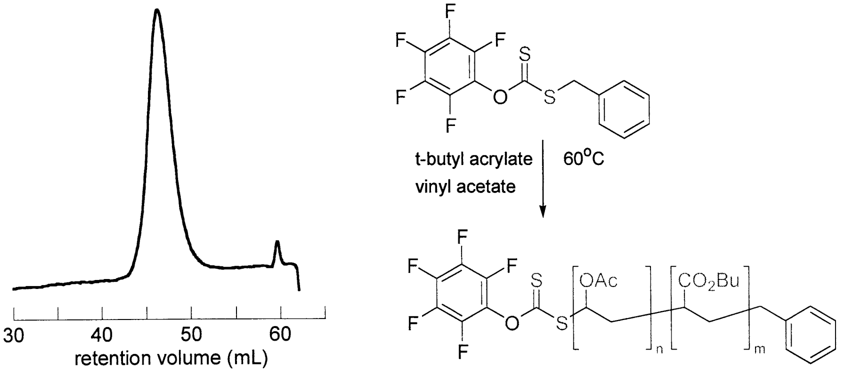


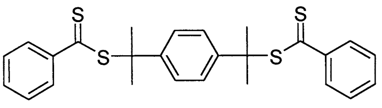
Figure 2. GPC trace showing poly(*t*-butyl acrylate-*co*-vinyl acetate-*block*-poly(vinyl acetate) (M_n16500 M_w/M_n 1.31) prepared by batch gradient copolymerization at 60°C with AIBN initiator.

In copolymerization of monomers with disparate reactivity ratios compositional drift with conversion will necessarily provide a gradient copolymer. Use of monomers with appropriately disparate reactivity ratios enables synthesis of block copolymers in a one step batch polymerization. In copolymerization of vinyl acetate and *t*-butyl acrylate all propagating radicals prefer to add *t*-butyl acrylate (r_{VAc}~0.026, r_{nBA}~5.93). Thus, the first formed polymer is predominantly composed of *t*-butyl acrylate units and the product following exhaustion of this monomer is poly(*t*-butyl acrylate-*co*-vinyl acetate-*block*-poly(vinyl acetate).[24] It is important in this experiment to chose a RAFT agent which is compatible with both the acrylate ester and vinyl acetate. The xanthate **10** was used in this case to provide a block copolymer with polydispersity ~1.3 (see Figure 2). The blocky structure of the product was immediately apparent from the ^{1}H NMR spectrum. Styrene and maleic anhydride show a strong tendency to alternate in the chain. Copolymerizations with excess styrene yield poly(styrene-*co*-maleic anhydride)-*block*-poly(styrene).[29,30]

Multiarm Polymer Synthesis

Triblocks from Difunctional RAFT Agents

Triblocks can also be made using difunctional RAFT agent (for example compounds **15, 16**).[21,26,31] Possibly the simplest compounds of this class are the trithiocarbonates.[21] The use of a difunctional RAFT agent as a triblock precursor helps ensure that both arms are of the same length and composition.



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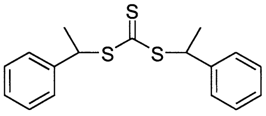

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Some recent work has been orientated towards using this strategy for the synthesis of triblocks intended as thermoplastic elastomers based on a „soft“ acrylate mid section and „hard“ styrene or styrene-co acrylonitrile outer blocks (Scheme 3). The RAFT agent was chosen such that the thiocarbonylthio functions would remain at the chain ends (note that methyl is a poor free radical leaving group). In the case shown (Scheme 3), an α,ω-bis(methylsulfanylthiocarbonylsulfanyl)-poly(butyl acrylate) M_n=77000, M_w/M_n=1.05 was successfully converted to a triblock copolymer M_n=171000, M_w/M_n=1.12. A series of such block copolymers has been made to enable a full structure property correlation. It was found that narrow polydispersities for both the mid- and end blocks were critical to achieving good mechanical properties.

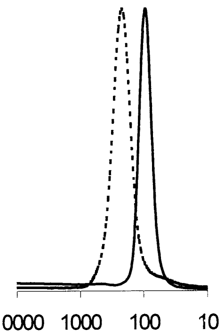
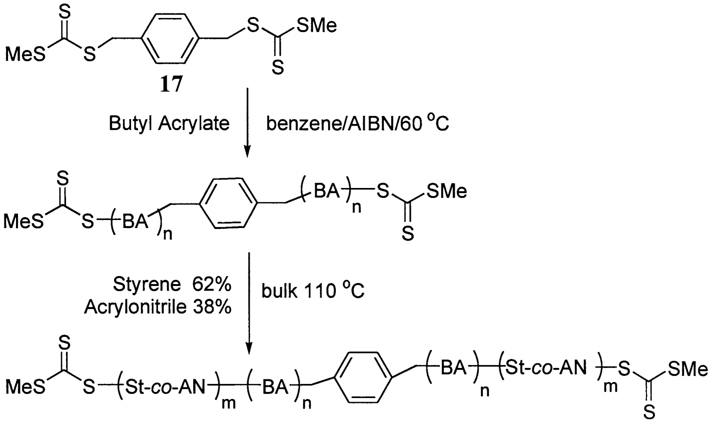
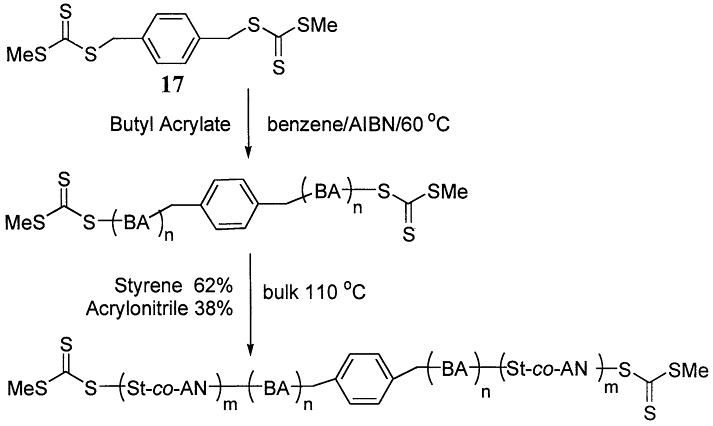


Figure 3. Molecular weight weight distributions for poly(butyl acrylate (—) and derived triblock copolymer (- - -).





Scheme 3.

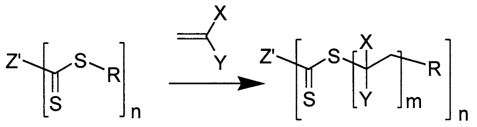
Star Synthesis

Stars from Multifunctional RAFT Agents

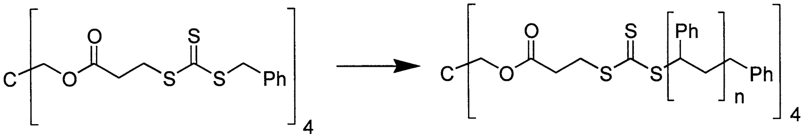
This form of star synthesis can be seen as an extension of triblock syntheses described above where the number of thiocarbonylthio groups exceeds two.[8,9,32-34] The multifunctional compound may be a small organic compound, a macromolecular species, a dendrimer, a particle, or indeed, any object possessing multiple thiocarbonylthio groups (though here the distinction between star and graft and other copolymers may become blurred). We can envisage two limiting forms of star growth depending on the orientation of the thiocarbonylthio group with respect to the core.[8,9]

Away from Process

In this case the thiocarbonylthio groups remain attached to the core (Z’) (see Scheme 4). All propagating radicals are linear chains detached from the core. No radical centers are at any stage attached to the core.



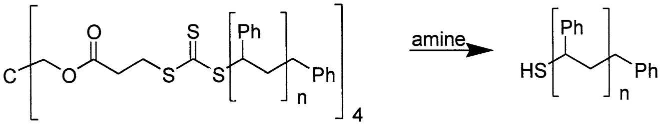
example



Scheme 4.

Advantages: no star-star coupling.

Disadvantages: cleavage of thiocarbonylthio group results in destruction of the star. This property may be turned to an advantage in some circumstances. For example, polymer supported polymer synthesis.



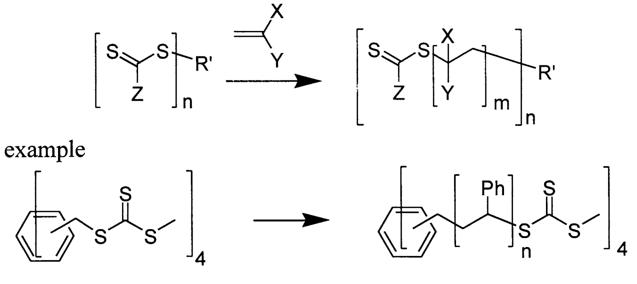
Scheme 5.

Thus, the four-arm star shown in Scheme 4 is cleaved by treatment with a primary or secondary amine to provide a narrow polydispersity linear polymer (Scheme 5).

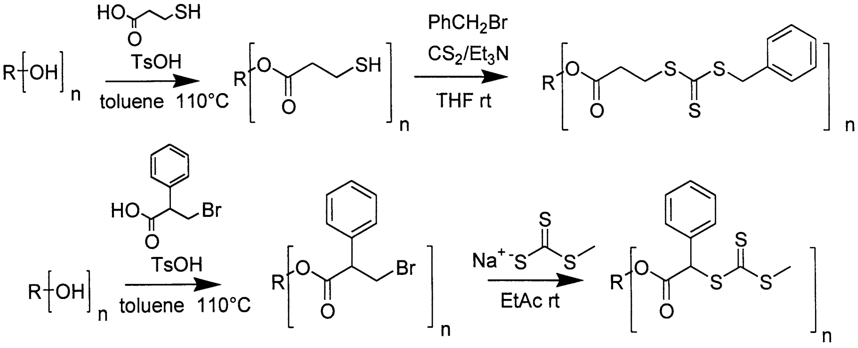
Attached to Process

In this case, most thiocarbonylthio groups remain attached to the periphery of the star. (Scheme 6). Most propagating radicals (other than initiator-derived chains) remain attached to the core (R’).

Although no multi-RAFT agents are commercially available, precursor species are readily obtained. The RAFT agents shown in Schemes 5 and 6 were prepared from commercially available thiols and halo-compounds respectively. We have recently reported[35] methods to quantitatively (>95% overall yield) convert (more readily available) multi-hydroxy compounds to both types of multi-RAFT agents (Scheme 7). These methods have been successfully applied to make (n=) 3,4,6 and 8-armed stars of narrow polydispersity. Star blocks are also possible.



Scheme 6.

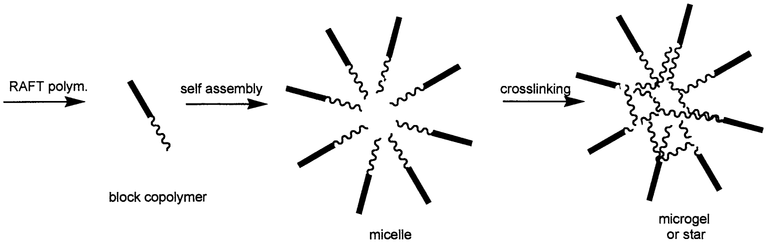


Scheme 7.

In the above-mentioned approaches to stars, the core has been synthesized first. There are a number of alternative strategies available whereby the arms of the star are synthesized first. The arm length and polydispersity are determined by the properties of that precursor polymer.

Stars by Self-Assembly of Block Copolymers

Suitably constructed hydrophilic-hydrophobic (or solvophilic-solvophobic) block copolymers possess the ability to self-assemble to form micelles (or other supramolecular structures). Such supramolecular assemblies may only be stable in a particular medium and/or over a specific concentration range. Various crosslinking mechanisms can be used to stitch these structures together to form a stable star polymer, microgel (or other structure). The core, the shell or mid block section of the micelle may be crosslinked to stabilize the structure.[36-38] Star synthesis would usually require crosslinking of the micelle's core (cf. Scheme 8). Care is needed in selecting reaction conditions so as to avoid intermicelle crosslinking and gel formation.



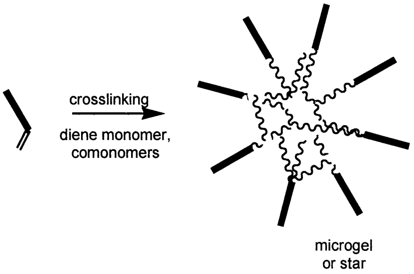
Scheme 8.

In this application, RAFT polymerization opens new possibilities, over more conventional strategies, mainly because of the much wider range of monomers that can be polymerized.[39] For example, monomers with unprotected acid functionality (methacrylic acid, acrylic acid) can be successfully converted to narrow polydispersity blocks. We have applied this approach to create novel encapsulants for dyes and rheology control agents. Many other applications are possible.[39] Since it is possible to maintain the thiocarbonyl thio groups during the crosslinking step further elaboration of the supramolecular structures by RAFT polymerization is also possible.

Stars by Copolymerization of Multifunctional Monomers

The so called 'arm-first' process involves making a living polymer then using this to initiate (co)polymerization of a di (or higher) functional monomer which forms a crosslinked core (Scheme 9). The methodology has been used to make star shaped molecules using NMP[40-44] or ATRP.[45-47]

Again RAFT polymerization offers new scope to this process.[48] The RAFT process involves (co)polymerization of an appropriate diene monomer (*e.g.* divinylbenzene) in the presence of a polymer formed by RAFT polymerization.



Scheme 9.

Conclusions

Living radical polymerization provides ready access a wide variety of polymer architectures. RAFT polymerization significantly extends the scope of existing methods allowing the synthesis of novel structures and compositions.

Acknowledgements

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