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Merrifield Resin-Supported Chain Transfer Agents, Precursors for RAFT Polymerization

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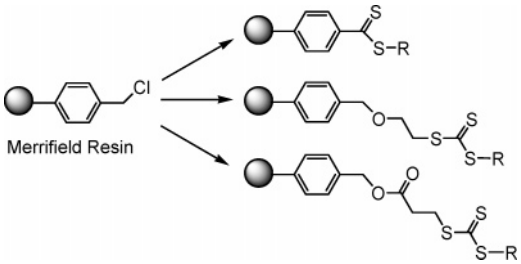
ABSTRACT



The modification of Merrifield resins to form chain transfer agent (CTA) precursors for reversible addition fragmentation chain transfer (RAFT) polymerization is investigated. A series of CTA precursor resins were prepared and characterized by FTIR and elemental analysis (EA).

Reversible addition chain transfer (RAFT) polymerization is among the most versatile of all the controlled/living radical polymerization techniques used to date due to its compatibility with a wide range of monomers and reaction conditions.[1] The RAFT polymerization process and chain transfer agents (CTAs) used have been extensively studied and prepared over the past few years.[2] However, the process is not industrially viable due to the presence of impurities trapped in the final polymer, including uncontrolled polymeric chains, monomer, and unrecoverable CTA. One of the most successful methods for removing a catalyst from a reaction is to attach it to a solid support.[3] Among the range of solid supports currently available, resins are one of the most commonly used due to their commercial accessibility, with a variety of end group functionalities and loadings, and solvent resistance compared to other solid supports.[4] There are a number of commercially available resins, including Merrifield,[5] Wang,[6] and JandaJel,[7] all of which have been used for combinatorial chemistry and solid-phase (supported) organic syntheses.[8] Several solid-supported CTAs have been reported previously, but all are linked to the support via the leaving and reinitiating group (R group)[9] of the thiocarbonylthio compound (Scheme 1), which results in the final polymer

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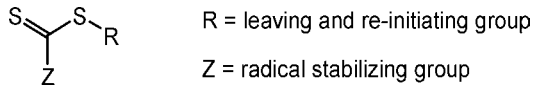
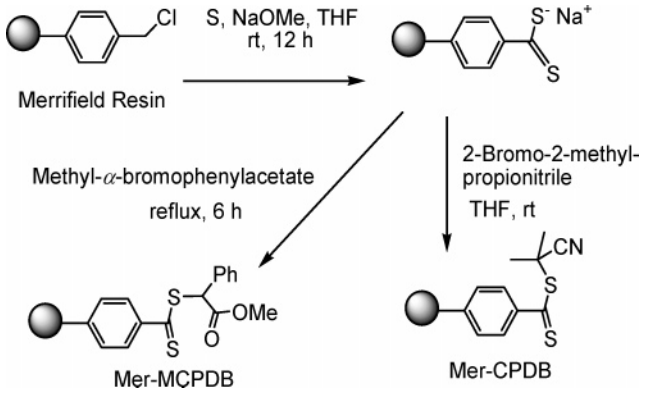
Scheme 1. Generic Structure of RAFT Chain Transfer Agents



being attached to the solid support. We report in this communication the first known immobilized thiocarbonylthio compounds attached to a resin though the radical stabilizing group (Z group).

We initially attempted the synthesis of a Merrifield resin-supported analogue (Mer-MCPDB) of the previously reported *S*-methoxycarbonylphenylmethyl dithiobenzoate (MCPDB),[10] shown in Scheme 2.

Scheme 2. Schematic Representation of the Synthesis of Merrifield Resin-Supported Dithiobenzoate Derivatives



The two-step synthesis involves the formation of the sodium dithiobenzoate salt[11] on Merrifield resin via the reaction of the resin with sodium methoxide and elemental sulfur. The sodium dithiobenzoate salt was then converted to (Mer-MCPDB) by the addition of methyl-α-bromophenylacetate.[10] The resin was purified by washing with copious amounts of a range of solvents to remove any unreacted starting reagents, byproducts, and salts. Resin-supported compounds are usually characterized by infrared and elemental analysis (EA).[8] In our case, the FT-IR of the final product showed the expected stretches characteristic of C═O at 1720 cm^{-1} and C−O at 1277 cm^{-1}. Elemental analyses allowed us to quantify the amount of sulfur introduced on the support, and we deduced the percentage substitution of Cl by thiocarbonyl-thio group (40% substitution from S content).[12]

In addition to the synthesis of a Merrifield resin-supported MCPDB, a Merrifield resin-supported cyanoisopropyl dithiobenzoate (CPDB)[2b,11] analogue, Mer-CPDB, was also prepared (see Scheme 2). The reaction was similar to that of Mer-MCPDB, with the methyl-α-bromophenylacetate-substituted by α-bromoisobutyronitrile[13] to give the corresponding Mer-CPDB, which was characterized by FT-IR and EA. This new compound allowed us to quantify the conversion from thiocarbonyl-thio salt to chain transfer agent by EA, by comparing the percentage substitution based on N content to S content. The conversion to the salt was assessed to be 67% (S content),[12] while the conversion to the product (N content) was much lower (10%). This low conversion was attributed to the difficulty for the reactants to diffuse to the reactive sites on the resin, due to the differences in swelling of the unreacted resin, the dithiobenzoate salt resin, and the final product.[14] Although the results indicated that both the Mer-MCPDB and Mer-CPDB had been formed, the carbon/nitrogen to sulfur content from elemental analysis was not consistent with complete conversion of the dithiobenzoate salt to the corresponding supported CTA. We therefore concluded that the S content established from elemental analysis was not representative of the CTA content on the resin and were unable to quantify the amount of supported chain transfer agent.

To overcome both the synthetic and analytical problems resulting from the stepwise synthesis of the on-the-solid support, we designed a second synthetic approach, which involved the preparation of the thiocarbonylthio ester, followed by attachment of the CTA to the resin. Three different trithiocarbonate CTAs were synthesized, *S*-methoxycarbonylphenylmethyl 2-hydroxyethyltrithiocarbonate (MCPHT), 3-(methoxycarbonylphenylmethylsulfanylthiocarbonylsulfanyl) propionic acid (MPPA), and 3-(benzylsulfanylthiocarbonylsulfanyl) propionic acid (BSPA).[15] Note that in this case, the CTAs belong to the family of trithioesters, which have been widely used to mediate RAFT polymerization.[1]

MCPHT was synthesized from 2-mercaptoethanol in the solution of potassium hydroxide and followed by the addition of carbon disulfide at room temperature. The solution was stirred for 5 h; then, methyl-α-bromophenylacetate was added, and the reaction was heated to 80 °C for 12 h (see Scheme 3).

MPPA was prepared from the potassium salt of 3-mercaptopropionic acid with an excess of carbon disulfide,[13] followed by the addition of methyl-α-bromophenylacetate.

(10) (a) Perrier, S.; Takolpuckdee, P.; Westwood, J.; Lewis, D. M. *Macromolecules* **2004**, *37*, 2709. (b) Takolpuckdee, P.; Westwood, J.; Lewis, D. M.; Perrier, S. *Macromol. Symp.* **2004**, *216*, 23.

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(12) Calculated using the following equation:

$$S_{theo}\,(\%) = \frac{s \times M_s}{m_{Mer} - n_{Cl} \times (M_{Cl} + 2M_H) + n_{Cl} \times M_{thio}} \times 100$$

where S_{theo} (%) is the theoretical sulfur content of the resin in weight %, s is the number of sulfur atoms per thiocarbonates, M_s is the molar mass of sulfur, m_{Mer} is the mass of the Merrifield resin used for the synthesis, n_{Cl} is the number of moles of chlorine in the resin, M_{Cl} is the molar mass of chlorine, M_H is the molar mass of hydrogen, and M_{thio} is the molar mass of the thiocarbonate substituting the chlorine atom.

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(14) See Supporting Information.

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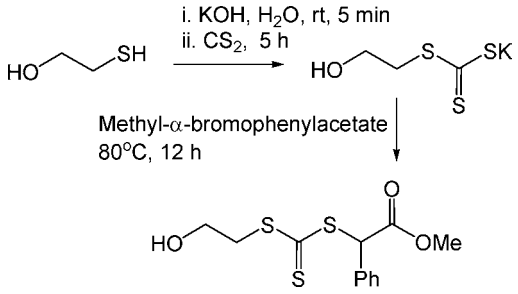
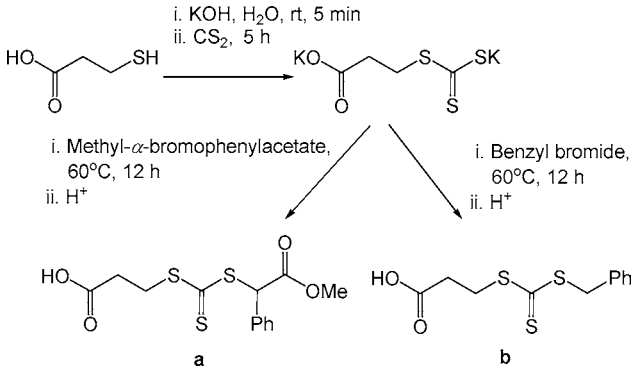
Scheme 3. Preparation Methodology of *S*-Methoxycarbonyl-phenylmethyl 2-Hydroxyethyl Trithiocarbonate (MCPHT)



The product was isolated by acidification of the solution with hydrochloric acid to give a yellow solid. BSPA was synthesized using the same procedure as MPPA, but with the addition of benzyl bromide in place of methyl-α-bromophenylacetate (see Scheme 4).

Scheme 4. Preparation Methodology of (a) 3-(Methoxycarbonyl phenylmethylsulfanylthiocarbonylsulfanyl) Propionic Acid (MPPA) and (b) 3-(Benzylsulfanylthiocarbonylsulfanyl) Propionic Acid (BSPA)



The modification of the chloromethylphenyl group of Merrifield resin with MPPA and BSPA was achieved by the addition of MPPA or BSPA to a suspension of Merrifield resin in tetrahydrofuran in the presence of potassium carbonate and tetra-*n*-butylammonium iodide and heated to 60 °C for 12 h.[16]

The solid was filtered and washed extensively with THF and then a mixture of water and THF (1:1), H_2O, acetone, toluene, and acetone to give a deep yellow solid material. The product was characterized by FTIR and EA to confirm the formation of MPPA and BSPA on the resins (Mer-MPPA and Mer-BSPA, respectively). Elemental analysis (EA) shows that the S content in Mer-MPPA and Mer-BSPA is 0.48 and 0.7 mmol/g (equivalent to 68 and 86% conversion of the active sites[12]), respectively. Indeed, in this case, the measured S content is representative of the CTA content on the resin.

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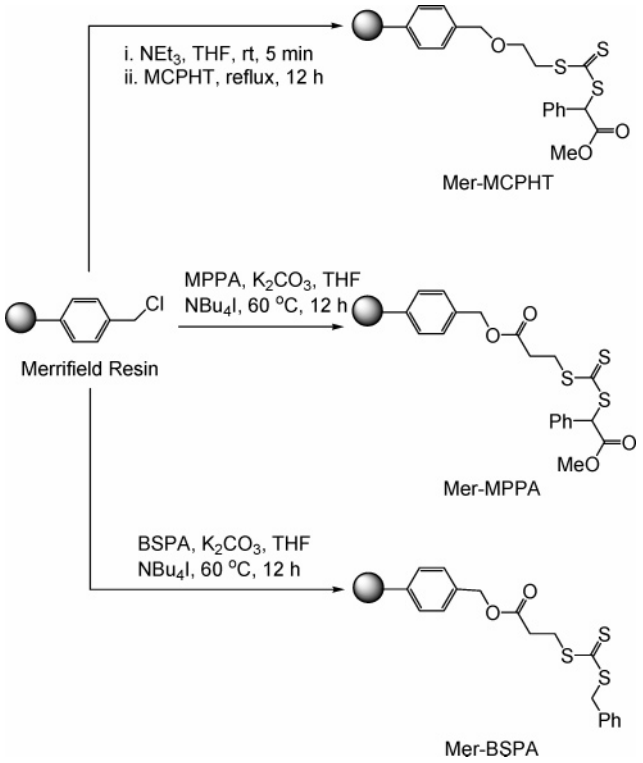
The modification of the chloromethylphenyl group of Merrifield resin with MCPHT was achieved by the addition of MCPHT to a suspension of Merrifield resin in tetrahydrofuran in the presence of triethylamine and heated to reflux for 12 h. The solid was filtered and washed extensively as previously reported to give a light yellow solid material. The product was also characterized by FT-IR and EA (16% conversion of the active sites[12]).

Scheme 5. Schematic Representation of the Synthesis of Merrifield Resin-Supported Trithiocarbonate Derivatives



In RAFT polymerization mediated by these supported CTAs, the polymeric chains grow away from the resin support, before reacting back on the C=S bond to trigger the chain transfer reaction.[1] A direct outcome of such process is that the products from termination reactions remain in solution, while the living chains are attached to the support. Therefore, supported chain transfer agent offers the great advantage of allowing separation by filtration between pure living polymeric chains, which are attached to the support, from nonliving chains, nonreacted monomers, and other side-products from the reaction, which remain free in solution. To illustrate the principle, we used Mer-MCPDB and Mer-BSPA to mediate the polymerization of methyl acrylate and styrene (Table 1). All polymerizations were performed in toluene (1:1 v/v to monomer). After polymerization, the polymeric chains attached to the beads were recovered by filtration and cleaved from the support by reaction with an excess of AIBN at 80 °C in toluene, following a procedure recently reported by our group.[17] The cleaved polymeric chains were analyzed by size exclusion chromatography. Table 1 illustrates the results and shows that a variety of

Table 1. Examples of Polymers Produced via Merrifield-Supported RAFT Polymerization

CTA	monomer[a]	$M_{n,\text{theo}}$[b] (conversion)	M_n[c]	PDI[c]
Mer-MCPDB[d]	MA	14 800 (69%)	13 950	1.24
Mer-BSPA[e]	MA	2100 (24%)	1800	1.21
Mer-BSPA[e]	S	2600 (25%)	2200	1.32

[a] MA: methyl acrylate. S: styrene. [b] Units: g/mol. [c] Units: g/mol. Determined by size exclusion chromatography, using THF as an eluent, toluene as a flow rate marker, and PS as standards. [d] Ratio of monomer:CTA:AIBN = 250:1:0.1. [e] Ratio of monomer:CTA:AIBN = 100:1:0.1.

molecular weights can be achieved via RAFT-supported polymerization mediated by the CTAs reported in this study, with polydispersities ranging from 1.2−1.3. Further work is being conducted in our laboratories in order to improve the control over such polymerizations.

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Supporting Information Available: All experimental procedures and analyses data. This material is available free of charge via the Internet at http://pubs.acs.org.

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