# Versatile Pathway to Functional Telechelics via RAFT Polymerization and Click Chemistry

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ABSTRACT: Two novel azidofunctionalized chain transfer agents (CTAs) were prepared and subsequently employed to mediate the reversible addition−fragmentation chain transfer (RAFT) polymerizations of styrene (Sty) and *N*,*N*-dimethylacrylamide (DMA) under a variety of conditions. Trithiocarbonate 2-dodecylsulfanylthiocarbonylsulfanyl-2-methyl-propionic acid 3-azido-propyl ester and dithioester 4-cyano-4-methyl-4-thiobenzoylsulfanyl-butyric acid 3-azido-propyl ester successfully mediated the polymerizations of Sty and DMA. Both RAFT polymerizations exhibited pseudo-first-order kinetics and a linear $M_n$ dependence with conversion. The resulting homopolymers ($M_n = 4 - 22 \times 10^3$ g/mol and $M_w/M_n \leq 1.33$) were demonstrated to have retained $\omega$ end group functionality, as evidenced by the successful formation of block copolymers. The α-azido terminal polymers and the azidofunctionalized CTAs were coupled with high efficiency by click chemistry to various alkynes (propargyl acrylate, propargyl methacrylate, and propargyl alcohol) in the presence of a Cu(I) catalyst, demonstrating the ability to prepare a range of functional telechelics and CTAs.

## Introduction

Controlled/living radical polymerization (CRP) techniques facilitate the preparation of (co)polymers with predetermined molecular weights, narrow molecular weight distributions, and high degrees of chain end functionalization.[1] While resulting in control comparable to living ionic polymerizations, CRP methods can be conducted under less stringent conditions and offer the additional advantage of enhanced functional group tolerance.[2−10] Despite the versatility of CRP techniques, post-polymerization modification is a viable means to incorporate functionality potentially incompatible with polymerization, characterization, or processing conditions.[11,12] In particular, functionalization of end groups retained during CRP is a potential method to prepare, for example, fluorescently labeled chains,[13,14] bioconjugates,[15,16] and surface-immobilized polymers.[17,18] However, because of the inherent low concentration of end groups and the possibility of side reactions with other functional groups within the polymer, reactions with high efficiency and fidelity are necessary for successful and specific polymer modification.

With the use of a Cu(I) catalyst, azide−alkyne coupling reactions result in highly specific and efficient preparation of 1,4-disubstituted 1,2,3-triazole products under moderate reaction conditions.[19,20] This particular coupling process can be conducted in aqueous or organic media, and little or no side reactions are observed. The practicality and versatility of the Cu(I)-catalyzed coupling reaction led to its inclusion in the class of efficient and specific organic reactions, commonly termed "click chemistry", as coined by Sharpless et al.[21]

Combining the synthetic techniques of CRP and click chemistry provides an efficient route to functional polymeric materials. Several groups reported the synthesis of (co)polymers via CRP and subsequent azide−alkyne coupling reactions, although the significant majority of these reports concern the modification of (co)polymers prepared by atom transfer radical polymerization (ATRP) or nitroxide-mediated polymerization.[14,22−37] For example, Lutz et al. demonstrated the preparation of $\omega$-functional telechelics from polymers prepared by ATRP via end group substitution with $NaN_3$ and subsequent coupling with various functional alkynes.[31] We reported the preparation of $\omega$-(meth)acryloyl macromonomers via ATRP and azide−alkyne coupling.[38] While this approach proved an efficient and specific means to prepare macromonomers with a high degree of end group functionalization from any monomer polymerizable by ATRP, we seek to expand the method to other radically polymerizable monomer classes.

Reversible addition−fragmentation chain transfer (RAFT) polymerization and macromolecular design via exchange of xanthates have emerged as some of the most promising CRP methods due to facile experimental setup and applicability to a wide range of monomers.[7−10] It is advantageous to extend the pairing of CRP and click chemistry to capitalize on the flexibility of RAFT polymerization and the efficiency and specificity of click chemistry to prepare functionalized materials. Previously, O'Reilly et al. reported the RAFT block copolymerization of a protected acetylene-containing monomer. After deprotection, the resulting block polymers were subsequently employed to prepare shell-crosslinked micelles with cores susceptible to functionalization with low-molecular-weight azides.[39] The same authors also reported alkynyl-functionalized RAFT agents being employed to prepare surface-decorated micelles capable of reaction with azido compounds.[40]

Herein, we describe the synthesis of azidofunctionalized RAFT chain transfer agents (CTAs), namely trithiocarbonate 2-dodecylsulfanylthiocarbonylsulfanyl-2-methyl-propionic acid 3-azido-propyl ester (**1**) and dithioester 4-cyano-4-methyl-4-thiobenzoylsulfanyl-butyric acid 3-azido-propyl ester (**2**). These novel CTAs were used to mediate RAFT polymerizations of styrene (Sty) and *N*,*N*-dimethylacrylamide (DMA) under conditions that provided kinetic and molecular weight control. The azidofunctionalized CTAs and the resulting α-azidoterminated polymers were reacted with various acetylene species, demonstrating the ability to prepare a range of telechelics and functional CTAs.

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**Table 1. Conditions for the RAFT Polymerizations of Styrene (Sty) and *N*,*N*-Dimethylacrylamide (DMA)**

| entry | monomer (concn) | CTA[a] | [M]:[CTA]:[I] | temp (°C) | time (h) | conv[b] (%) | $M_{n,theory}$ (g/mol) | $M_n$[c] (g/mol) | $M_w/M_n$[c] |
|---|---|---|---|---|---|---|---|---|---|
| **A** | Sty (4.0 M) | **1** | 200:1:0.2 | 70 | 31 | 40 | 8820 | 8580 | 1.18 |
| **B** | Sty (4.0 M) | **1** | 200:1:0.2 | 80 | 5 | 23 | 5270 | 5140 | 1.15 |
| **C** | Sty (4.0 M) | **1** | 200:1:0.5 | 80 | 5 | 37 | 8170 | 7490 | 1.19 |
| **D** | Sty (4.0 M) | **2** | 100:1:0.5 | 70 | 22 | 53 | 5840 | 5870 | 1.25 |
| **E** | Sty (2.7 M) | **2** | 200:1:0.5 | 70 | 23 | 40 | 8800 | 12 100 | 1.19 |
| **F** | Sty (4.0 M) | **2** | 200:1:0.25 | 70 | 22 | 32 | 6620 | 5510 | 1.21 |
| **G** | Sty (4.0 M) | **2** | 200:1:0.2 | 80 | 22 | 28 | 6200 | 5870 | 1.12 |
| **H** | DMA (4.7 M) | **1** | 100:1:0.1 | 70 | 1.3 | 87 | 9100 | 10 640 | 1.12 |
| **I** | DMA (4.7 M) | **1** | 50:1:0.1 | 70 | 1.5 | 94 | 5120 | 6300 | 1.13 |
| **J** | DMA (4.7 M) | **1** | 50:1:0.05 | 70 | 2.3 | 62 | 3510 | 4100 | 1.13 |
| **K** | DMA (4.7 M) | **1** | 100:1:0.05 | 80 | 1 | 98 | 10 100 | 10 400 | 1.11 |
| **L** | DMA (4.7 M) | **1** | 50:1:0.05 | 80 | 1 | 98 | 5120 | 6020 | 1.13 |
| **M** | DMA (4.0 M) | **2** | 100:1:0.5 | 70 | 41 | 94 | 9630 | 10 800 | 1.30 |
| **N** | DMA (4.0 M) | **2** | 200:1:0.5 | 70 | 41 | 94 | 20 000 | 21 800 | 1.33 |

[a] **1**: 2-dodecylsulfanylthiocarbonylsulfanyl-2-methyl-propionic acid 3-azidopropyl ester; **2**: 4-cyano-4-methyl-4-thiobenzoylsulfanyl-butyric acid 3-azidopropyl ester. [b] Monomer conversion as determined by $^1$H NMR spectroscopy. [c] As determined by size exclusion chromatography in *N*,*N*-dimethylformamide by the triple detection method. CTA: chain transfer agent; M: monomer; I: initiator; $M_n$: number-average molecular weight; $M_{n,theory}$: theoretical $M_n$; $M_w$: weight-average molecular weight.

## Experimental

**Materials.** Styrene (Sty, Aldrich 99%) and *N*,*N*-dimethylacrylamide (DMA, Fluka, 98%) were passed through a small column of basic alumina for catalyst removal prior to polymerization. 2,2′-Azobisisobutyronitrile (AIBN, Sigma, 98%) was recrystallized from ethanol. 4-Cyano-4-((thiobenzoyl)sulfanyl)pentanoic acid (CTB) was prepared as previously reported.[41] *N*,*N*-Dimethylformamide (DMF, Aldrich 99.9%), 2-dodecylsulfanylthiocarbonylsulfanyl-2-methyl-propionic acid (DMP, Noveon >95%), 1-ethyl-3-(3′-dimethylaminopropyl)carbodiimide (EDC, Acros, 98%), 1-hydroxybenzotriaole (Chem-IPEX Intl., 99%), oxalyl chloride (Alfa Aesar, 98%), propargyl amine (TCI, 95%), potassium carbonate (Alfa Aesar, 99%), magnesium sulfate (EMD, 99%), sodium acetate (Alfa Aesar, 99%), acetic anhydride (Acros), methylene chloride (EMD, HPLC), triethylamine (Sigma, 99.5%), potassium bromide (EMD, 99%), sodium azide (Sigma, 99.5%), 3-chloro-1-propanol (Acros, 98%), propargyl alcohol (Aldrich, 99%), propargyl acrylate (Aldrich 98%), propargyl methacrylate (Alfa Aesar 98%), *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine (PMDETA, Aldrich, 99%), CuBr (Aldrich, 98%), $CDCl_3$ (Cambridge Isotope, 99% D), and dimethylsulfoxide-$d_6$ (DMSO-$d_6$, Cambridge Isotope, 99.9% D) were used as received.

**Synthesis of 3-Azidopropanol.** 3-Chloro-1-propanol (5.0 g, 53 mmol, 1.0 equiv) and sodium azide (8.59 g, 132 mmol, 2.5 equiv) were reacted in DMF (26.5 mL) at 100 °C for 48 h. The reaction mixture was cooled to room temperature, poured into ethyl ether (200 mL), and extracted with a saturated aqueous NaCl solution (500 mL). The organic layer was separated, dried over $MgSO_4$, and filtered. The supernatant was concentrated to obtain the product (5.1 g, 95% yield). $^1$H NMR ($\delta$, ppm): 3.76−3.73 (t, 2H, $J$ = 5.93 Hz, $-CH_2-CH_2$-OH), 3.46−3.43 (t, 2H, $J$ = 6.54 Hz, $-CH_2-CH_2-N_3$), 2.09 (br-s, 1H, OH), 1.86−1.80 (m, 2H, $HO-CH_2-CH_2-CH_2-N_3$). $^{13}$C NMR ($\delta$, ppm): 59.7 ($-CH_2-CH_2$-OH), 48.3 ($-CH_2-CH_2-N_3$), 31.3 ($HO-CH_2-CH_2-CH_2-N_3$). IR (KBr) (wavenumber, cm$^{-1}$): 3382 (br, s, OH); 2948 (C−C*s*), 2100 (C−N═N═N), 1266 and 738 (C−C*b*).

**Synthesis of 2-Dodecylsulfanylthiocarbonylsulfanyl-2-methyl-propionic Acid Chloride (DMP−Cl)**. DMP (1.0 g, 2.7 mmol, 1.0 equiv) was dissolved in methylene chloride (15 mL) in a 50 mL round-bottom flask, and the solution was cooled to approximately 0 °C. Oxalyl chloride (0.417 g, 3.3 mmol, 1.2 equiv) was added slowly under a nitrogen atmosphere, and the solution was allowed to reach room temperature and stirred for a total of 3 h. The resulting solution was concentrated under reduced pressure to yield the acid chloride product (1.0 g, 99% yield). Melting point = 63 °C. $^1$H NMR ($\delta$, ppm): 3.25−3.21 (t, 2H, $J$ = 7.4 Hz, $-CH_2-CH_2-S-C$═S), 1.77 (s, 6H, $-S-C(CH_3)_2-$COCl), 1.70−1.66 (t, 2H, $J$ = 7.3 Hz, $-CH_2-CH_2-S-C$═S), 1.39−1.25 (m, 18H, $CH_3-C_9H_{18}-CH_2-CH_2S-C$═S), 0.89−0.86 (t, 3H, $J$ = 6.2 Hz, $CH_3-C_9H_{18}-CH_2-CH_2S-C$═S). IR (KBr) (wavenumber, cm$^{-1}$): 2919 and 2851 (C−C*s*), 1717 (C═O), 1070 (C═S), 1281 and 815 (C−C*b*).

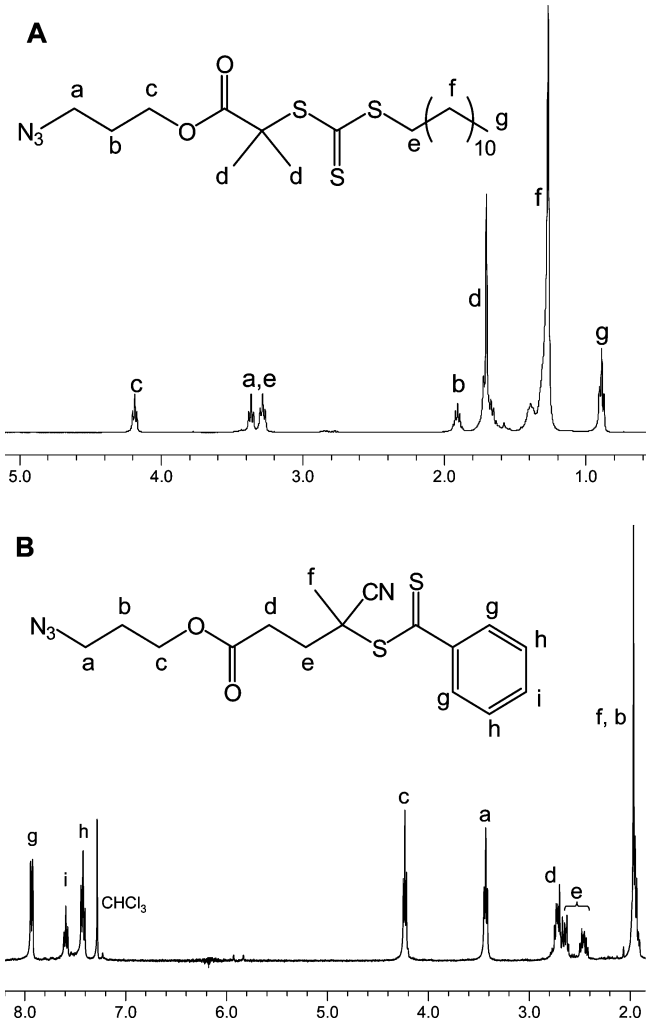
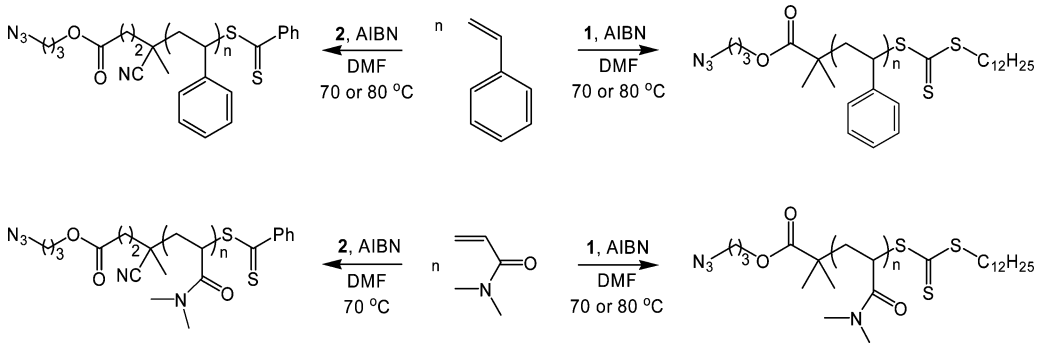



**Figure 1.** $^1$H NMR spectra and peak assignments for (A) 2-dodecylsulfanylthiocarbonylsulfanyl-2-methyl-propionic acid 3-azidopropyl ester (**1**) and (B) 4-cyano-4-methyl-4-thiobenzoylsulfanyl-butyric acid 3-azidopropyl ester (**2**).

**Synthesis of 2-Dodecylsulfanylthiocarbonylsulfanyl-2-methyl-propionic Acid 3-Azidopropyl Ester (1).** 3-Azidopropanol (265 mg, 2.62 mmol, 1.0 equiv) was dissolved in methylene chloride (5 mL) in a 50 mL round-bottom flask, and the solution was cooled to approximately 0 °C. A solution of triethylamine (0.73 mL) in

**Scheme 1. Reversible Addition−Fragmentation Chain Transfer Polymerizations of Styrene and *N*,*N*-Dimethylacrylamide with Azidofunctionalized Chain Transfer Agents (1: 2-Dodecylsulfanylthiocarbonylsulfanyl-2-Methyl-propionic Acid 3-Azidopropyl Ester and 2: 4-Cyano-4-methyl-4-thiobenzoylsulfanyl-butyric Acid 3-Azidopropyl Ester)**




DMF: *N*,*N*-Dimethylformamide. AIBN: 2,2′-Azobisisobutyronitrile.

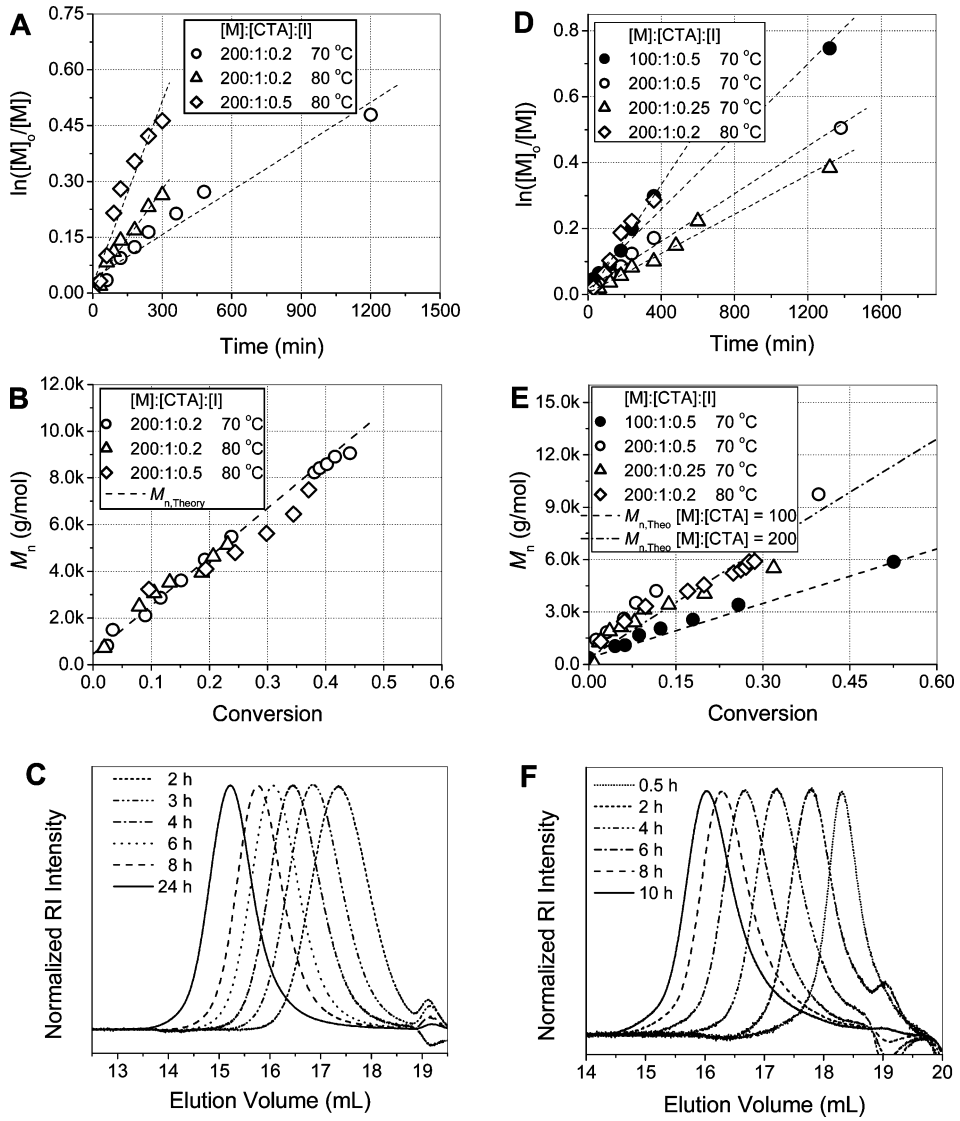



**Figure 2.** (A) Pseudo-first-order kinetic plot and (B) number-average molecular weight ($M_n$) vs monomer conversion for the reversible addition−fragmentation chain transfer (RAFT) polymerization of styrene (Sty) with 2-dodecylsulfanylthiocarbonylsulfanyl-2-methyl-propionic acid 3-azidopropyl ester (**1**). (C) Size exclusion chromatography (SEC) traces as a function of time for the RAFT polymerization of Sty with (**1**) (Table 1, Entry **A**: [Sty]:**[1]**:[2,2′-azobisisobutyronitrile (AIBN)] = 200:1:0.2; [Sty] = 4.0 M in *N*,*N*-dimethylformamide (DMF); $T$ = 70 °C). (D) Pseudo-first-order kinetic plot and (E) $M_n$ vs monomer conversion for the RAFT polymerization of Sty with 4-cyano-4-methyl-4-thiobenzoylsulfanyl-butyric acid 3-azidopropyl ester (**2**). (●: [Sty] = 4.0 M, ○: [Sty] = 2.7 M). (F) SEC traces as a function of time for the RAFT polymerization of Sty with **2** (Table 1, Entry **E**: [Sty]:**[2]**:[AIBN] = 200:1:0.5; [Sty] = 2.7 M in DMF; $T$ = 70 °C).

methylene chloride (5 mL) was added dropwise over 10 min. A solution of DMP−Cl (1.0 g, 2.6 mmol) in methylene chloride (5 mL) was added dropwise, and the solution was allowed to reach room temperature while stirring for 3 h. The solution was concentrated under reduced pressure, diluted with ethyl ether (100 mL), and washed with saturated aqueous sodium bicarbonate solution (50 mL), water (50 mL), and saturated NaCl solution (50 mL), successively. The organic layer was separated, dried over

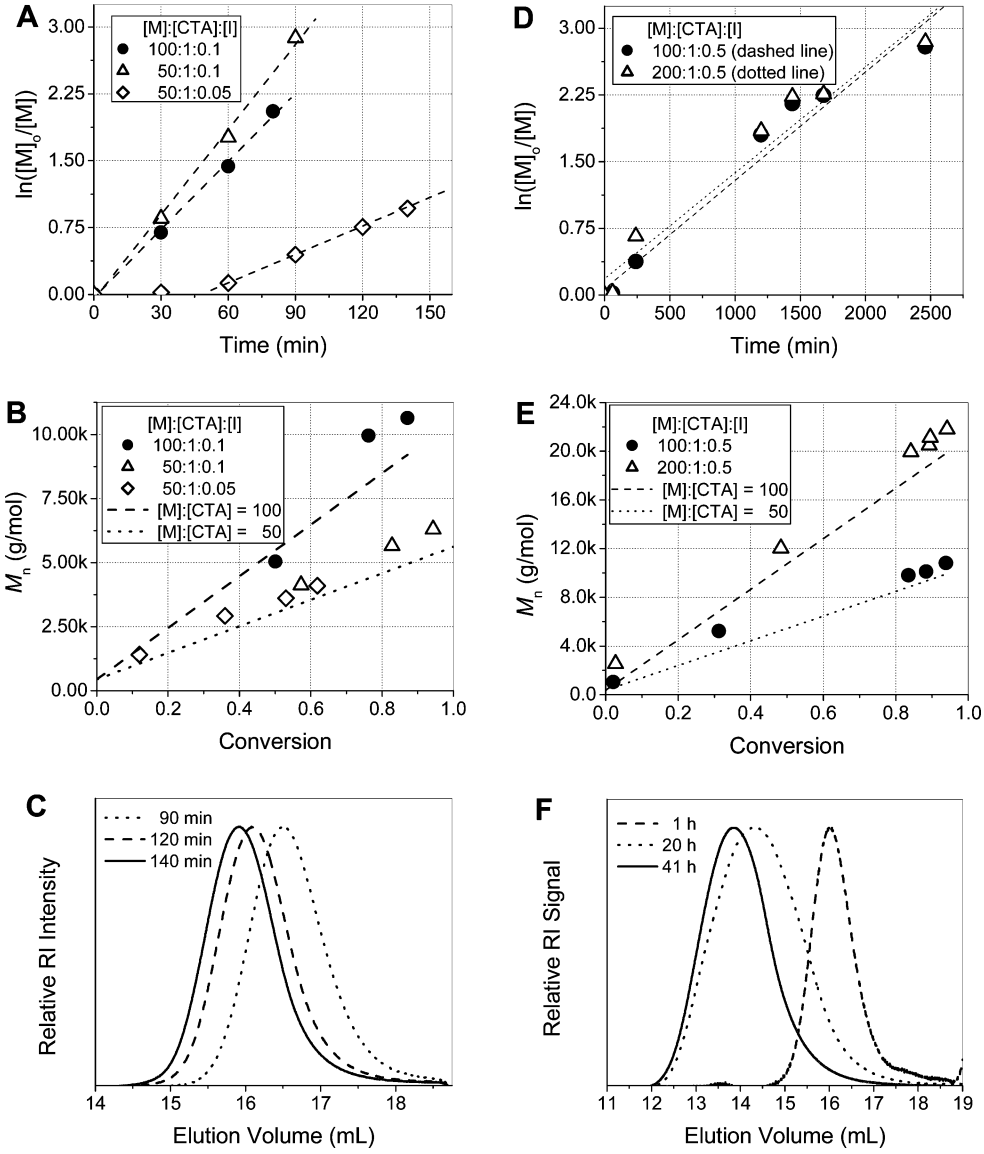



**Figure 3.** (A) Pseudo-first-order kinetic plot and (B) number-average molecular weight ($M_n$) vs monomer conversion for the reversible addition−fragmentation chain transfer (RAFT) polymerization of *N*,*N*-dimethylacrylamide (DMA) with 2-dodecylsulfanylthiocarbonylsulfanyl-2-methyl-propionic acid 3-azidopropyl ester (**1**). (C) Size exclusion chromatography (SEC) traces as a function of time for the RAFT polymerization of DMA with **1**. (Table 1, Entry **J**: [DMA]:**[1]**:[ 2,2′-azobisisobutyronitrile (AIBN)] = 50:1:0.05; [DMA] = 4.7 M in *N*,*N*-dimethylformamide (DMF); $T$ = 70 °C). (D) Pseudo-first-order kinetic plot and (E) $M_n$ vs monomer conversion for the RAFT polymerization of DMA with 4-cyano-4-methyl-4-thiobenzoylsulfanyl-butyric acid 3-azidopropyl ester (**2**) in DMF at 70 °C with [DMA] = 4 M. (F) SEC traces as a function of time for the RAFT polymerization of DMA with **2**. (Table 1, Entry **N**: [DMA]:**[2]**:[AIBN] = 200:1:0.5; [DMA] = 4 M in DMF; $T$ = 70 °C).

$MgSO_4$ (1.0 g), and filtered. The supernatant was concentrated under reduced pressure to yield the product (1.05 g, 90% yield) as a residual oil. $^1$H NMR ($\delta$, ppm): 4.19−4.16 (t, 2H, $J$ = 6.0 Hz, $-CH_2-CH_2-O-C(=O)$), 3.37−3.33 (t, 2H, $J$ = 6.9 Hz, $-CH_2-CH_2-N_3$), 3.29−3.25 (t, 2H, $J$ = 7.6 Hz, $-CH_2-CH_2-S-C(=S)$), 1.91−1.88 (t, 2H, $J$ = 6.3 Hz, $-CH_2-CH_2-N_3$), 1.71−1.62 (m, 8H, $-CH_2-CH_2-S-C(=S)$ and $-S-C(CH_3)_2-CO$), 1.38−1.25 (m, 18H, $CH_3-C_9H_{18}-CH_2-CH_2S-C(=S)$), 0.89−0.86 (t, 3H, $J$ = 5.9 Hz, $CH_3-C_9H_{18}-CH_2-CH_2S-C(=S)$). $^{13}$C NMR ($\delta$, ppm): 172.7 (C=O), 62.6 ($-CH_2-CH_2-O-C(=O)$), 55.8 ($-S-C(CH_3)_2-CO$), 48.1 ($-CH_2-CH_2-N_3$), 36.8 ($-CH_2-CH_2-S-C(=S)$), 31.8 ($-CH_2-CH_2-N_3$), 29.6 ($-C(3)H_2-CH_2-S$), 29.5 ($-C(4)H_2-CH_2-S$), 29.4 ($-C(5)H_2-CH_2-S$), 29.3 ($-C(6)H_2-CH_2-S$), 29.0($-C(7)H_2-CH_2-S$), 28.9 ($-C(8)H_2-CH_2-S$), 27.9 ($-C(9)H_2-CH_2-S$), 27.8 ($-C(10)H_2-CH_2-S$), 25.2 ($-S-C(CH_3)_2-CO$), 22.6 ($-C(11)H_2-CH_2-S$), 14.0 ($CH_3-C_9H_{18}-CH_2-CH_2S-C(=S)$). IR (KBr) (wavenumber, cm$^{-1}$): 2929 and 2853 (C−C*s*), 2098 (C−N=N=N), 1735 (C=O), 1066 (C=S), 1156 and 815 (C−C*b*). Elemental Analysis. Calcd: C = 53.65%, H = 8.33%, N = 9.39%. Found: C = 53.98%, H = 8.33%, N = 7.84%.

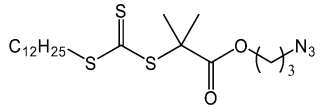
**Synthesis of 4-Cyano-4-methyl-4-thiobenzoylsulfanyl-butyric Acid 3-Azidopropyl Ester (2).** CTP (1.0 g, 3.5 mmol, 1.0 equiv) was dissolved in methylene chloride (10 mL) in a 100 mL round-bottom flask and cooled to approximately 0 °C. 1-Hydroxybenzotriazole (530 mg, 3.9 mmol, 1.1 equiv) and EDC (753 mg, 3.9 mmol, 1.1 equiv) were added, and the solution was allowed to stir at 0 °C for 30 min. A solution of 3-azidopropanol (362 mg, 3.5 mol, 1.0 equiv) in methylene chloride (5 mL) was added dropwise, and the reaction mixture was allowed to warm to room temperature and stir for 48 h. The reaction mixture was poured into a 10% aqueous sodium bicarbonate solution and stirred for 30 min. The mixture was extracted with methylene chloride (50 mL × 2), and the organic layer was washed with a 10% sodium bicarbonate solution (100 mL), water (100 mL), and a saturated NaCl solution (100 mL), successively. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting oily residue was purified by column chromatography (silica gel, eluent: ethyl acetate/hexane (2:8)) to give the product (440 mg, 34% yield). $^1$H NMR ($\delta$, ppm): 7.91−7.89 (d, 2H, $J$ = 7.5 Hz, Ph−$C_2$ and $C_6$), 7.58−7.54 (t, 1H, $J$ = 7.3 Hz, Ph−$C_4$), 7.41−

**Table 2. Block Copolymerizations of Styrene and *N,N*-Dimethylacrylamide with α-Azido Macro Chain Transfer Agents**

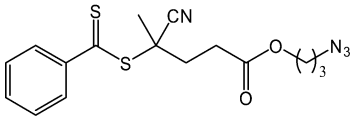
| homopolymer[a] | $M_n$[b] (g/mol) | $M_w/M_n$[b] | block copolymer | $M_n$[c] (g/mol) | $M_w/M_n$[c] |
|---|---|---|---|---|---|
| $N_3-$PS (**1**)[d] | 5100 | 1.15 | $N_3-$PS-*b*-PDMA | 14 200 | 1.17 |
| $N_3-$PS (**2**)[e] | 6600 | 1.21 | $N_3-$PS-*b*-PDMA | 10 800 | 1.24 |
| $N_3-$PDMA (**1**)[f] | 3500 | 1.20 | $N_3-$PDMA-*b*-PS | 10 720 | 1.27 |
| $N_3-$PDMA (**2**)[g] | 9660 | 1.26 | $N_3-$PDMA-*b*-PS | 12 000 | 1.26 |

[a] Homopolymer macro chain transfer agent (macroCTA) employed for block copolymerization with [monomer] = 2 M in *N,N*-dimethylformamide (DMF). The chain transfer agent (CTA) from which each homopolymer was derived is given in parentheses after each polymer (**1**: 2-dodecylsulfanylthiocarbonylsulfanyl-2-methyl-propionic acid 3-azidopropyl ester; **2**: 4-cyano-4-methyl-4-thiobenzoylsulfanyl-butyric acid 3-azidopropyl ester). [b] Determined by size exclusion chromatography (SEC) with the triple detection method. [c] Determine by SEC with conventional calibration based on polystyrene (PS) standards. [d] [*N,N*-Dimethylacrylamide (DMA)]:[PS-macroCTA]:[ 2,2′-azobisisobutyronitrile (AIBN)] = 200:1:0.05; $T$ = 80 °C. [e] [DMA]:[PS-macroCTA]:[AIBN] = 100:1:0.5; $T$ = 70 °C. [f] [Styrene]:[poly(*N,N*-dimethylacrylamide macroCTA (PDMA-macroCTA)]:[AIBN] = 200:1:0.5; $T$ = 80 °C. [g] [Styrene]:[PDMA-macroCTA]:[AIBN] = 100:1:0.5; $T$ = 70 °C.

7.37 (d, 2H, $J$ = 7.6 Hz, Ph−$C_3$ and $C_5$), 4.22−4.19 (t, 2H, $J$ = 6.2 Hz, $-CH_2-CH_2-O-C=O$), 3.42−3.38 (t, 2H, $J$ = 6.5 Hz, $-CH_2-CH_2-N_3$), 2.72−2.59 (m, 3H, $-CH_1-CH_2-$COOR), 2.45−2.43 (m, 1H, $-CH_1-CH_2-$COOR), 1.95−1.90 (m, 5H, $CH_2-CH_2-N_3$ and S−C($CH_3$)−CN). $^{13}$C NMR ($\delta$, ppm): 171.2 (C=O), 144.4 (Ph−$C_1$), 132.9 (Ph−$C_4$), 128.4 (Ph−$C_2$ and $C_6$), 126.5 (Ph−$C_3$ and $C_5$), 118.3 (S−C($CH_3$)−*C*N), 61.9 $-CH_2-CH_2-O-C=O$), 48.0 ($-CH_2-CH_2-N_3$), 45.6 (S−*C*($CH_3$)−CN), 33.2 ($-CH_2-CH_2-$COOR), 29.6 ($CH_2-CH_2-N_3$), 27.9 ($-CH_2-CH_2-$COOR), 24.0 S−C($CH_3$)−CN). IR (KBr) (wavenumber, cm$^{-1}$): 2933 (C−C*s*), 2098 (C−N=N=N), 1735 (C=O), 1445 (C=C*s*), 1047 (C=S), 1181 and 867 (C−C*b*). Elemental Analysis. Calcd: $C$ = 53.02%, $H$ = 5.01%, $N$ = 15.46%. Found: $C$ = 53.07%, $H$ = 5.29%, $N$ = 12.90%.




**1**




**2**

**RAFT Polymerizations of Sty and DMA with Azidofunctionalized CTAs.** An example RAFT polymerization procedure was as follows. DMA (0.795 g, 8.00 mmol), CTA **2** (29 mg, 0.081 mmol), trioxane (83 mg, 0.92 mmol), and DMF (1.0 mL) were sealed in a 20 mL vial and purged with nitrogen for 30 min. A concentrated and nitrogen-purged solution of AIBN (6.5 mg, 0.040 mmol) in DMF (0.1 mL) was added via syringe, and the reaction vial was placed in a preheated reaction block at 70 °C. Samples were removed periodically by syringe to determine molecular weight and polydispersity index by size exclusion chromatography (SEC) and monomer conversion by $^1$H NMR spectroscopy. The polymerization was quenched after 41 h by freezing the polymerization solution in liquid nitrogen and exposing to air. The resulting poly(*N,N*-dimethylacrylamide) (PDMA, 94% conversion; $M_n$ = 10 800 g/mol; $M_w/M_n$ = 1.30) was isolated by precipitating into hexanes and drying under vacuum. Specific reaction conditions for all polymerizations are given in Table 1.

**Click Reactions of Azido CTAs and α-Azidoterminated Polymers with Acetylene Species.** The low-molecular-weight azido CTAs and azidoterminated polymers were reacted with alkynes in a manner analogous to the following example procedure. A solution of α-azidoterminated polystyrene (PS; $M_n$ = 2960 g/mol; 0.236 g, 0.0797 mmol) in DMF (4.0 mL), propargyl alcohol (9.3 μL, 0.16 mmol), and PMDETA (3.3 μL, 0.016 mmol) was purged with nitrogen and transferred via cannula to a vial containing CuBr (2.3 mg, 0.016 mmol) under a nitrogen environment. The reaction mixture stirred at room temperature in the absence of oxygen for 24 h. The reaction mixture was exposed to air, and the solution was passed through a column of neutral alumina. The polymer was precipitated into hexanes and dried under vacuum. Reaction conversion was 94%, as determined with $^1$H NMR spectroscopy by observing the disappearance of the methylene protons adjacent to the azido group ($N_3-CH_2CH_2CH_2-$) at $\delta \approx 3.4$ ppm and the appearance of the new methylene protons adjacent to the triazole ring at $\delta \approx 4.4$ ppm (HO−$CH_2-$triazole−$CH_2CH_2CH_2-$) and $\delta \approx 4.8$ ppm (HO−$CH_2-$triazole−$CH_2CH_2CH_2-$). The low-molecular-weight CTA products were reacted with equimolar alkyne-containing species and isolated by evaporation of excess solvent.

**Analyses.** SEC was conducted in DMF at 50 °C with a flow rate of 1.0 mL/min (Viscotek GPC pump; columns: ViscoGel I-series G3000 and G4000 mixed bed columns: molecular weight range $0-60 \times 10^3$ and $0-400 \times 10^3$ g/mol, respectively). Detection consisted of a Viscotek refractive index detector operating at $\lambda$ = 660 nm, a Viscotek UV−vis detector operating at $\lambda$ = 254 nm, and a Viscotek model 270 series platform, consisting of a laser light scattering detector (operating at 3 mW, $\lambda$ = 670 nm with detection angles of 7° and 90°) and a four-capillary viscometer. Molecular weights were determined by conventional calibration based on polystyrene standards or triple detection method. $^1$H and $^{13}$C NMR spectroscopy was conducted in $CDCl_3$ or DMSO-$d_6$ with a Bruker Avance 400 spectrometer operating at 400 and 100 MHz, respectively. The sample was analyzed on a ThermoFinnigan CE Elantech model Flash EA1112 elemental analyzer, which was initially five-point calibrated against atropine, acetanilide, nicatinamide, and cyclohexanone-2,4-dinitrophenylhydrazine. Samples were run in duplicate or triplicate.

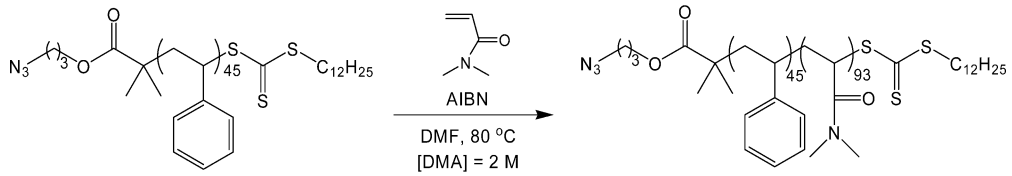
## Results and Discussion

**CTA Syntheses.** The versatility and functional group tolerance of both RAFT and copper-catalyzed azide−alkyne coupling facilitate the preparation of a wide range of diverse (co)polymers with potentially useful terminal functionality. To this end, we synthesized two novel azidofunctional RAFT CTAs by esterification of carboxyl-containing CTA precursors with 3-azidopropanol. A trithiocarbonate CTA, DMP, was converted to an acid chloride and reacted with 3-azidopropanol to yield CTA **1**. Similarly, the dithioester, CTB, was functionalized by carbodiimide-promoted esterification with 3-azidopropanol to yield CTA **2**. FTIR spectroscopy of the products revealed strong absorbance bands at 1735 and 2098 cm$^{-1}$ for the C=O stretch and the N=N=N stretch, respectively. The $^1$H NMR spectra and peak assignments for the resulting azidofunctionalized CTAs are given in Figure 1.

**RAFT Polymerizations.** Polymerizations of styrene and DMA, mediated by RAFT CTAs **1** and **2**, resulted in α-azidofunctionalized polymers (Scheme 1). Because of the versatility of RAFT, controlled polymerization of an acrylamido monomer was successful. A range of polymerization conditions were used to efficiently prepare well-defined polymers of predetermined molecular weight (Table 1).

Pseudo-first-order rate plots and plots of molecular weight versus conversion for styrene polymerizations mediated by CTAs **1** and **2** are shown in Figure 2. The relative linearity of the kinetic plots (Figure 2A,D) is indicative of a constant concentration of radicals throughout each polymerization. As expected, faster rates of polymerization were observed with increasing temperature. Ratios of [CTA]:[AIBN] were in the range of 5:1 to 2:1. Higher concentrations of AIBN resulted in

**Scheme 2. Reversible Addition−Fragmentation Chain Transfer Block Copolymerization of *N,N*-Dimethylacrylamide (DMA) with a Polystyrene Macro Chain Transfer Agent (PS-macroCTA) ([DMA]:[PS-macroCTA]:[2,2′-Azobisisobutyronitrile] = 200:1:0.05; $T$ = 80 °C)**




DMF: *N,N*-Dimethylformamide.

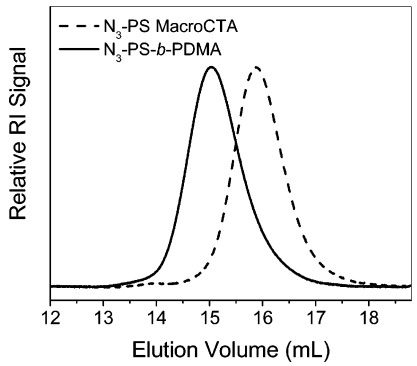



**Figure 4.** Size exclusion chromatography traces of an α-azido polystyrene ($N_3$−PS) macro chain transfer agent (macroCTA) and the resulting $N_3$−PS-*b*-poly(*N,N*-dimethylacrylamide) after block copolymerization with *N,N*-dimethylacrylamide (DMA) ([DMA]:[$N_3$−PS-macroCTA]:[ 2,2′-azobisisobutyronitrile] = 200:1:0.05 at 80 °C in *N,N*-dimethylformamide).

faster polymerizations with no observable deleterious effect on molecular weight control. Molecular weights were in the range of 5−12 × $10^3$ g/mol, and as expected for a controlled polymerization, narrow and unimodal molecular weight distributions ($M_w/M_n$ < 1.25) were observed. As seen in Figure 2B,E, all polymerizations of styrene mediated with CTAs **1** and **2** resulted in a linear increase in $M_n$ with conversion, and the correlation between theoretical and experimental values was excellent throughout the conversion ranges. The traces for polymerization **A** (Table 1) are given in Figure 2C and those for polymerization **E** in Figure 2F. No evidence of bimodality or termination products was observed, and elution volumes shifted to lower values as a function of polymerization time, which is a qualitative indication of increasing molecular weight with monomer conversion. A small amount of low-molecular-weight tailing in polymerizations with CTA **2** is most likely the result of background initiation resulting from the higher concentration of AIBN.

Polymerization of the acrylamido monomer, DMA, was also mediated by the azidofunctional RAFT CTAs **1** and **2**. A significant advantage of RAFT is the ability to control polymerizations of most vinyl monomers. While ATRP has benefited from significant advances that enable its application with functional monomers, RAFT is generally considered most attractive for controlling the polymerization of acrylamides. By employing CTAs **1** and **2**, DMA was polymerized to yield azidoterminated PDMA.

The polymerizations of DMA with CTAs **1** and **2** were similarly well-controlled (Figure 3). For instance, ratios of [DMA]:**[1]**:[AIBN] = 100:1:0.1 and 50:1:0.1 resulted in conversions of approximately 90% and $M_w/M_n$ < 1.13 in less than 1.5 h at 70 °C. While ratios of [CTA]:[AIBN] = 10:1 and 20:1 both led to the preparation of well-defined PDMA with CTA **1**, the initiator concentrations for polymerizations mediated with CTA **2** were increased, with [CTA]:[AIBN] = 2:1, in order to impart sufficiently fast polymerization rates. RAFT polymerizations of acrylamido monomers mediated with dithioester CTAs are generally slower than those mediated with trithiocarbonate CTAs under a given general set of conditions.[42−44] When the ratio of [CTA]:[AIBN] was 20:1 with CTA **1**, an inhibition period of approximately 1 h was observed, after which controlled polymerization occurred. For all cases, no significant reduction in radical concentration was observed during the polymerizations of DMA, despite the relatively high rates of polymerization. Target molecular weight was controlled by varying the ratio of [DMA]:[CTA], although in some cases, experimental values of higher molecular weight polymers deviated slightly from theory with CTA **1**. Nevertheless, in all cases, the molecular weight distributions were unimodal and molecular weight increased with monomer conversion (Figure 3C,E).

To demonstrate ω-chain end retention during polymerization, block copolymers were prepared by chain extension with a second monomer (Table 2). For example, $N_3$−PS ($M_n$ = 5100 g/mol, $M_w/M_n$ = 1.15) prepared with CTA **1** was employed as macroCTA for polymerization of DMA with [DMA]:[PS-macroCTA]:[AIBN] = 200:1:0.05 at 80 °C in DMF (Scheme 2). A conversion of 62% was obtained in 2 h, resulting in a $N_3$−PS-*b*-PDMA block copolymer with $M_n$ = 14 200 g/mol and $M_w/M_n$ = 1.17. SEC analysis of the product demonstrated high CTA efficiency with no evidence of unreacted macroCTA (Figure 4).

**Click Reactions.** Because of the efficiency and fidelity of copper-catalyzed azide−alkyne coupling, azidofunctionalized polymer end groups undergo facile modification with a variety of acetylene species. We considered three specific alkynes as models for preparing telechelics by this method. Reaction with propargyl alcohol yields polymers with α-hydroxy groups that could modify solubility or be utilized for further functionalization. Clicking azidoterminal polymers with propargyl acrylate or propargyl methacrylate leads to (meth)acryloyl macromonomers, as we previously reported.[38] By capitalizing on the versatility of RAFT using azidofunctionalized CTAs, we are now able to employ click chemistry to prepare functional telechelics from a wider range of monomers, including acrylamides.

The α-azidoterminated polymers prepared with either CTA **1** or **2** were dissolved in DMF or DMSO-$d_6$ and reacted with various propargyl species (R−$CH_2$−≡) in the presence of CuBr at room temperature. Although a ligand is not necessary for sufficient solubility of the copper catalyst in DMF,[45,46] PMDETA was employed to ensure enhanced reaction rates and increased end group functionalization. After catalyst removal, the resulting polymers were precipitated and dried under vacuum. The extent of conversion of the terminal azido moieties was monitored by $^1$H NMR spectroscopy by observing the disappearance of the methylene protons adjacent to the azido group ($N_3$−C$H_2$$CH_2$$CH_2$−) at $\delta \approx 3.4$ ppm and the appearance of the new methylene protons adjacent to the triazole ring at $\delta \approx 4.4$ ppm (R−$CH_2$−triazole−C$H_2$$CH_2$$CH_2$−) and $\delta \approx 4.8$−5.2 ppm (R−C$H_2$−triazole−$CH_2$$CH_2$$CH_2$−) (Figure 5). The end group click reactions were efficient, as evidenced by near-

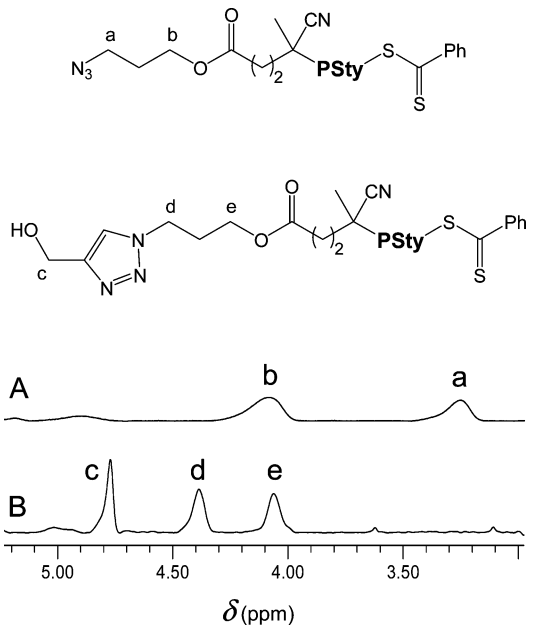



**Figure 5.** $^1$H NMR spectra and peak assignments for (A) polystyrene (PSty) prepared with 4-cyano-4-methyl-4-thiobenzoylsulfanyl-butyric acid 3-azidopropyl ester (CTA **2**) and (B) the product after coupling with propargyl alcohol.

**Table 3. Azide−Alkyne Coupling Reactions between α-Azidoterminated Polymers and Azido Chain Transfer Agents**

| reaction[a] | conv[b] (%) |
|---|---|
| $N_3$−PDMA (**1**) + PgMA | >95 |
| $N_3$−PS (**2**) + PgOH | 94 |
| **1** + PgMA | 92 |
| **1** + PgA | 84 |
| **1** + PgOH | 92 |
| **2** + PgOH | 95 |

[a] PgMA: propargyl methacrylate; PgA: propargyl acrylate; PgOH: propargyl alcohol. [b] Determined by $^1$H NMR spectroscopy. **1**: 2-dodecylsulfanylthiocarbonylsulfanyl-2-methyl-propionic acid 3-azidopropyl ester; **2**: 4-cyano-4-methyl-4-thiobenzoylsulfanyl-butyric acid 3-azidopropyl ester. Reactions of polymers were conducted at room temperature for 24 h in *N*,*N*-dimethylformamide (DMF) with 0.02 M $-N_3$, propargyl species (2.0 equiv), CuBr (0.2 equiv), *N*,*N*,*N*′,*N*″,*N*′-pentamethyldiethylenetriamine (0.2 equiv). Reactions of low-molecular-weight chain transfer agents were conducted in a similar manner with an equimolar amount of propargyl species.

quantitative functionalization (Table 3). For example, $N_3$-PDMA ($M_n$ = 4800 g/mol) prepared with CTA **1** resulted in 96% functionalization with propargyl methacrylate to yield the corresponding α-methacryloyl macromonomer. $N_3$-PS ($M_n$ = 2960 g/mol) prepared with CTA **2** was reacted with propargyl alcohol to yield hydroxyterminated polymer with 94% end group functionalization. General agreement between the molecular weight of the clicked polymer obtained by SEC with that calculated from $^1$H NMR spectroscopy, using the signals adjacent to the triazole functionality, confirms efficient coupling and retention of the azido functionality during polymerization.

Azidofunctionalized CTAs **1** and **2** can similarly be modified by coupling with acetylenes prior to polymerization, yielding a plethora of available structures from a single thiocarbonylthio compound. For example, CTAs **1** and **2** were reacted with propargyl alcohol to yield CTAs with 92% and >95% hydroxyl functionality, respectively. Coupling CTA **1** with propargyl acrylate and propargyl methacrylate resulted in the preparation of CTA-functional monomers that can subsequently be used to prepare well-defined hyperbranched polymers. Whereas other methods of CTA modification are limited because of potential side reactions with the thiocarbonyl or other susceptible moieties, the orthogonal nature of click chemistry facilitates specific CTA functionalization in a highly efficient manner.

## Conclusions

The particular combination of RAFT and click chemistry is a promising strategy to synthesize functional telechelics due to efficient postpolymerization modification afforded by $Cu^I$-catalyzed azide−alkyne coupling. Two novel azido RAFT CTAs were prepared and subsequently employed to mediate the polymerizations of Sty and DMA under a variety of reaction conditions. Characteristics of controlled polymerization were observed, and the resulting homopolymers retained end group functionality, as evidenced by the successful formation of block copolymers. Coupling reactions of the α-azidoterminated polymers and the azidofunctionalized CTAs with various acetylene species proved a successful means to efficiently modify polymer chain ends and low-molecular-weight CTAs.

Preparing end-functional polymers or functional CTAs by modification via other reaction pathways could have limited applicability due to potential side reactions with functional groups contained along the polymer backbone or within the CTA structure. However, the fidelity associated with click chemistry facilitates employing this method to prepare macromonomers and other telechelics from essentially any monomer polymerizable by RAFT.

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