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Universal (Switchable) RAFT Agents

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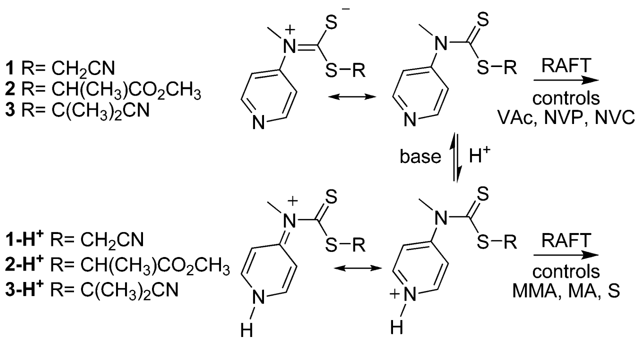
Radical polymerization with reversible addition−fragmentation chain transfer (RAFT polymerization) is a reversible deactivation polymerization and one of the most versatile processes for conferring living characteristics on radical polymerization.[1−4] The polymerization of most monomers that are polymerizable by radical polymerization can be controlled by the RAFT process. However, the RAFT agent [ZC(=S)S−R) must be selected according to the monomer(s) used. Thus, RAFT agents such as dithioesters (Z = aryl, alkyl) or trithiocarbonates (Z = alkylthio) suitable for controlling polymerization of "more-activated" monomers (MAMs), such as styrene, methyl acrylate (MA), and methyl methacrylate (MMA), inhibit or retard polymerizations of "less activated" monomers (LAMs), such as vinyl acetate (VAc), *N*-vinylpyrrolidone (NVP), and *N*-vinylcarbazole (NVC). Similarly RAFT agents suitable for controlling polymerizations of LAMs, such as *N*,*N*-dialkyl- or *N*-alkyl-*N*-aryldithiocarbamates and xanthates, tend to be ineffective with MAMs.

The reduced effectiveness of the dithiocarbamate RAFT agents with MAMs relates to their lower reactivity toward radical addition and consequent smaller transfer constants.[5] The double-bond character of the thiocarbonyl is reduced by the contribution of zwitterionic canonical forms that localize a positive charge on nitrogen and a negative charge on sulfur.[5,6] On the other hand, the tendency of dithioesters or trithiocarbonates to inhibit polymerization of LAMs stems from the poor radical leaving-group ability, with respect to the "R" radical, of propagating species with a terminal LAM unit. Dithiocarbamates that possess electron-withdrawing groups adjacent to nitrogen or where the nitrogen lone pair is part of an aromatic ring system are effective with MAMs[5,6] but inhibit polymerizations of LAMs. Fluorodithioformates have been proposed as universal RAFT agents, but their application has been tested with only a few monomers.[7] Thus, the synthesis of narrow-polydispersity poly(MAM)-*block*-poly(LAM) is difficult using conventional RAFT agents.

Several groups.[8,9] have reported processes where a first block comprising the MAM is prepared by atom-transfer radical polymerization (ATRP), after which the ATRP initiator functionality is converted to a xanthate end and the resultant macroRAFT agent is used in the synthesis of a poly(MAM)-*block*-poly(LAM) [e.g., poly(*tert*-butyl acrylate)-*block*-poly(VAc)[8]]. Compounds that combine RAFT agent and ATRP initiator functionality in one molecule have also been used to synthesize poly(MAM)-*block*-poly(LAM) [e.g., poly(MA)-*block*-poly(VAc)[10]].[10,11] Click chemistry has been used to link RAFT-synthesized poly(LAM) and poly(MAM) blocks.[12] There are reports of direct synthesis of poly(MAM)-*block*-poly(LAM) using other mechanisms. Cobalt-mediated polymerization was employed to synthesize polyacrylonitrile-*block*-poly-(VAc).[13] Stibine-mediated polymerization was used to synthesize polystyrene-*block*-poly(NVP).[14]

Scheme 1



We now report on a new class of stimuli-responsive RAFT agents that can be switched to offer good control over polymerization of both MAMs and LAMs and a route to poly(MAM)-*block*-poly(LAM), all with narrow molecular weight distributions. Our approach in developing switching mechanisms for such universal RAFT agents has been to identify chemistry to modify the electronic properties of the dithiocarbamate nitrogen that is simple, able to be performed in situ in a polymerization medium, rapid, and reversible. Protonation of (or interaction with a Lewis acid by) a conjugated nitrogen meets these criteria.

Our previous work has shown that *S*-cyanomethyl-*N*-phenyl-*N*-methyldithiocarbamate is a very effective RAFT agent for controlling the polymerization of VAc.[3,15] We have found that *N*-(4-pyridinyl)-*N*-methyldithiocarbamates (e.g., **1**−**3**) are similarly effective with VAc and other LAMs (NVP, NVC; see Table 1), whereas in the presence of a strong acid, the protonated form of the *N*-(4-pyridinyl)-*N*-methyldithiocarbamates (e.g., **1-H**$^+$−**3-H**$^+$) provide excellent control over the polymerization of MAMs (MA, BA, MMA, styrene; see Table 1). These protonated RAFT agents were ineffective in controlling polymerization of LAMs.

The efficiency of the protonated dithiocarbamate in controlling MAM polymerization suggests the importance of the canonical form with the charge on the dithiocarbamate nitrogen (Scheme 1). Molecular orbital calculations (AM1) provided support for this hypothesis, showing a decrease in C=S bond length for the protonated RAFT agents: in **1**, the C=S bond length is 1.578 Å, while in **1-H**$^+$ it is 1.560 Å. The reversibility of protonation was demonstrated by ^{1}H NMR (see the Supporting Information).

The acid used to form the protonated RAFT agent should be a strong acid (e.g., 4-toluenesulfonic acid, trifluoromethanesulfonic acid), and the acid should be added in a stoichiometric amount. The use of less than a stoichiometric amount of acid or of a weaker acid (e.g., acetic acid) was found to provide poorer control. Nonprotic Lewis acids such as aluminum triflate were also effective (see Table 1).

Propagating species with a terminal LAM are poor radical leaving groups relative to those with a terminal MAM. Thus, in the synthesis

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Table 1. Details of Polymer Syntheses

RAFT agent	conc (10^{-2} M)	acid[a]	M1[a]	conc (M)	*T* (°C)	solvent[a]	initiator[a]	conc (10^{-2} M)	$10^{-3}M_n$[b]	M_w/M_n[c]	time (h)	conv (%)
2	2.47		**NVC**	3.45	60	dioxane	AIBN	1.62	15.8	1.09	20	80
2-H$^+$	2.47		**NVC**	3.45	60	dioxane	AIBN	1.62	oligomeric product			
2	1.25		**NVP**	4.68	60	CH_3CN	AIBN	0.30	29.4	1.19	16	83
1	5.23		**VAc**	7.21	75	EtAc	ACHN	0.28	8.9	1.24	72	54
2-H$^+$	1.41	TsOH	**MA**	4.44	70	CH_3CN	AIBN	0.04	31.1	1.08[d]	7	87
1	0.80[f]		**BA**	2.79	70	CH_3CN	AIBN	0.04	51.4	1.88	6	85
1-Al(OTf)$_3$	0.80	Al(OTf)$_3$	**BA**	2.79	70	CH_3CN	AIBN	0.04	47.0	1.14	6	85
1	1.35[f]		**BA**	2.79	70	CH_3CN	AIBN	0.04	21.3	1.57	6	84
1-H$^+$	1.35	TsOH	**BA**	2.79	70	CH_3CN	AIBN	0.04	24.1	1.12	6	91
3-H^{+c}	1.99	TfOH	**MMA**	6.55	60	CH_3CN	AIBN	0.61	33.0	1.25[e]	16	98
2-H$^+$	7.0	TfOH	**S**	8.75	90	bulk	ACHN	0.99	10.5	1.06	12	82

[a] Abbreviations: TsOH, 4-toluenesulfonic acid; TfOH, trifluoromethanesulfonic acid; Al(OTf)$_3$, aluminum trifluoromethanesulfonate; **MA**, methyl acrylate; **MMA**, methyl methacrylate; **S**, styrene; **VAc**, vinyl acetate; **NVC**, *N*-vinylcarbazole; **NVP**, *N*-vinylpyrrolidone; EtAc, ethyl acetate; AIBN, azobis(isobutyronitrile); ACHN, azobis(1-cyclohexanenitrile). [b] Number-average molecular weight in polystyrene equivalents. [c] Ratio of weight-average to number-average molecular weight. [d] See Figure 1b. [e] See Figure 1a. [f] In the absence of acid, there is control over the molecular weight at high monomer conversion, but the molecular weight distributions are broad.

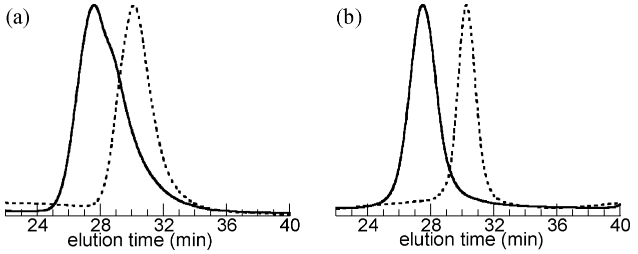
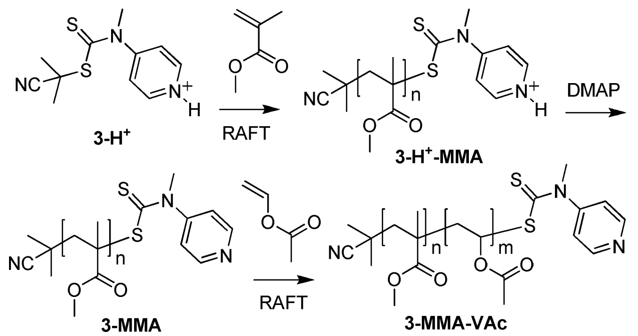


Figure 1. GPC chromatograms of (a) poly(MMA) **3-H**$^+$**−MMA** (M_n = 33 000, M_w/M_n = 1.25) prepared with **3-H**$^+$ (dashed curve) and poly(MMA)-*block*-poly(VAc) **3−MMA−VAc** (M_n = 55 900, M_w/M_n = 1.39) (solid curve) (see Scheme 2) and (b) poly(MA) (M_n = 31 100, M_w/M_n = 1.08) prepared with **2-H**$^+$ (dashed curve) and poly(MA)-*block*-poly(NVC) (M_n = 48 000, M_w/M_n = 1.33) (solid curve).

Scheme 2



of a diblock where one block is composed of MAMs and another block is based on LAMs, the block comprising MAMs should be synthesized first, as illustrated in Scheme 2 for poly(MMA)-*block*-poly(VAc) (Figure 1a).

Thus, in the first step, the protonated RAFT agent **3-H**$^+$ (formed from **3** by adding 1 equiv of 4-toluenesulfonic acid) was used to control the polymerization of MMA to form poly(MMA) (**3-H**$^+$**−MMA**). This macroRAFT agent was then neutralized in situ by adding a stoichiometric amount of *N*,*N*-dimethylaminopyridine (DMAP), forming **3−MMA.** RAFT polymerization of VAc then provided the desired poly(MMA)-*block*-poly(VAc) (**3−MMA−VAc**). The same strategy was used to synthesize poly(MA)-*block*-poly(NVC) (Figure 1b).

In conclusion, we have discovered a new class of "switchable" RAFT agents, *N*-(4-pyridinyl)-*N*-methyldithiocarbamates, that provide excellent control over polymerization of LAMs and, after addition of 1 equiv of a protic or Lewis acid, become effective in controlling polymerization of MAMs, allowing the synthesis of poly(MAM)-*block*-poly(LAM) with narrow molecular weight distributions. Further examples and application of a similar strategy with appropriate xanthate RAFT agents to improve their effectiveness with MAMs will be reported in a forthcoming paper.

Supporting Information Available: Experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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