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Terminal Umpolung in Metal-Catalyzed Living Radical Polymerization: Quantitative End-Capping of Carbon−Halogen Bond via a Modifier Monomer

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Introduction. For their precision control, most of “modern” living polymerizations, in principle, depend on dormant species, metastable covalent precursors that are incapable of propagation per se but effectively serve as reservoirs for true growth-active species upon catalysis. This is particularly true for transition-metal-catalyzed living radical polymerization,[1] where halogen-capped polymers are dormant species to generate growing carbon radicals via transition-metal catalysis, reversibly, dynamically, and selectively to ensure efficient propagation, while thermodynamically favored enough to maintain a sufficiently low intermediate concentration so as to suppress bimolecular termination and other side reactions inherent to conventional radical polymerization (eq 1; X = halogen; R = ester):

$$\sim\!\!\sim \mathrm{CH_2{-}CHR{-}X}\ \text{(dormant)} \xrightarrow[\text{reversible}]{\text{metal catalyst}} \sim\!\!\sim \mathrm{CH_2{-}CHR}\ \text{(active radical)} \quad (1)$$

The fair stability of these alkyl halides imposes double-edged features: excellent for reaction control but excess for terminal functionalization. End-capping agents are indeed available, such as silyl enol ethers,[2] allyl compounds,[3] tin compounds,[4] and azides,[5] but in our view all these seem neither universal nor satisfactory one way or another, either exotic, expensive, or inefficient. The primary reason is that the dormant halide terminal should carry a conjugating, radical-stabilizing substituent, typically an ester (R in eq 1), which is in most cases also electron-withdrawing and thereby renders the halogen reluctant to ionically, albeit radically, dissociate and to undergo concerted nucleophilic or electrophilic substitution reactions. No doubt, efficient, selective, and quantitative terminal transformation has long been required, in part to eliminate the terminal halogen that potentially induce undesired reactions upon polymer processing and, more importantly, to expand the versatility in polymer synthesis directed to, for example, block, graft, telechelic, and other functionalized macromolecules.[6]

This work provides a novel method for an efficient transformation of the dormant species in metal-catalyzed living radical polymerization, taking notice that the terminal halogen is ambivalent and may be eligible not only to radical but also to ionic substitution depending on the electronic nature of its geminal substituent [R in $\sim\!\!\sim \mathrm{CH_2{-}CHR{-}X}$] (eq 1). In this regard we are particularly interested in “umpolung”[7] (unpoling) of the alkyl halide by replacing the original ester substituent (R) with a methoxy group, which may stabilize a radical through a mild conjugation and may simultaneously activate the precursor halide toward cationic dissociation (or electrophilic substitution), just as in the Lewis acid-catalyzed living cationic polymerization discovered by us (Scheme 1A).[8] For the umpolung we herein employ “modifier monomer”, an alkene suited for not only radical but cationic polymerizations as well (Scheme 1B). Namely, a modifier monomer should effectively add to a growing radical to form an “umpoled” dormant end that should be available for electrophilic substitution. The newly formed terminal now carries a halogen that is, in turn, readily substituted or quenched with suitable nucleophiles like an alcohol, as we have already demonstrated.

As illustrated more specifically in Scheme 1, we herein employed *p*-methoxystyrene (pMOS) and α-methoxystyrene (αMOS) as modifier monomers with an alkoxy group. These alkenes are active enough to react with the growing radicals due to the conjugated phenyl group, and the resulting alkoxystyryl halides may effectively be electrophilically quenched with an alcohol due to the high electron-donating alkoxy group. Given a large variety of alcohols with additional functionality, design of the alcohol quenchers will open a new route to replace the potentially noxious terminal halogen with a more useful terminal function.

Results and Discussion. Living Radical Polymerization. Methyl methacrylate (MMA) was polymerized with a ruthenium complex [$\mathrm{RuCl(Ind)(PPh_3)_2}$, Ind = η^5-$\mathrm{C_9H_7}$; RuCl(Ind)][9] as a catalyst in conjunction with ethyl 2-chloro-2-phenylacetate (ECPA; initiator)[10] and *n*-$\mathrm{Bu_3N}$ (cocatalyst or additive)[11] in toluene at 80 °C. Within 13 h, the MMA conversion reached 33%, and controlled polymers (PMMA) were obtained: the number-average molecular weight was close to the theoretical value ($M_\mathrm{n} = 4300$ vs $M_\mathrm{theor} = 3500$; the former by size-exclusion chromatography, SEC, and the latter based on $[\mathrm{MMA}]_0/[\mathrm{initiator}]_0$), and the molecular weight distribution (MWD) was narrow ($M_\mathrm{w}/M_\mathrm{n} = 1.25$) (Figure 1A-1). The fine controllability was also shown by structural analysis by MALDI-TOF-MS (Figure 1B-1) and ^{1}H NMR (see Supporting Information). Specifically important in this work is that these observations demonstrate the selective and quantitative formation of a chlorine-capped terminal originating from the initiator [$F_\mathrm{n}(\alpha) = 1.0$; $F_\mathrm{n}(\omega) = 0.95$; by ^{1}H NMR].

Terminal “Umpolung” with Modifier Monomer pMOS. The polymerization solution, thus obtained at a 33% conversion, was evaporated under an inert and air-free atmosphere to remove the remaining MMA.[12] The reaction mixture now consisted of the Cl-capped PMMA, the ruthenium catalyst, and *n*-$\mathrm{Bu_3N}$,[13] with toluene and *n*-octane (internal standard for gas chromatography) removed. To this oily mixture was added pMOS (10 equiv to PMMA or the terminal chlorine), excess methanol (MeOH; 8 vol %), and toluene (84 vol %), and the solution was heated at 80 °C for 8 h. Upon a dual mode-detection SEC analysis, the isolated products (Figure 1A-3) exhibited an intense UV response at 250 nm that was virtually absent in a control product (Figure 1A-2) obtained under the same conditions but without pMOS treatment, while both samples had nearly identical narrow and unimodal MWDs under refractive index (RI) detection. These results show that a pMOS unit(s) was introduced into the PMMA terminal without further propagation and undesirable side reactions. The terminally modified products were further analyzed by MALDI-TOF-MS (Figure 1B, 1−3). The peak pattern was quite different from that for the corresponding controls, PMMAs one directly obtained just after the living radical polymerization and the other treated with MeOH

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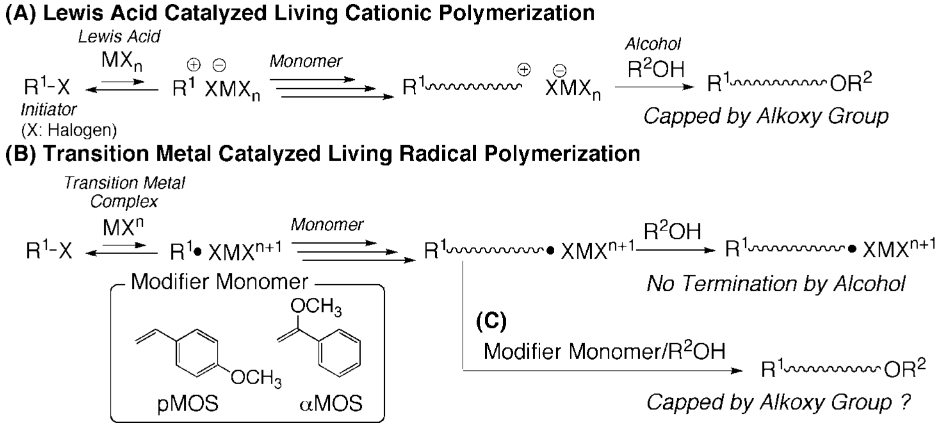
Scheme 1



alone (traces 3 vs 1 and 2). The spectrum for the modified products (Figure 1B-3) consisted of one major (with circles) and two minor series (with triangles and squares) of peaks, all separated by the 100.1 mass unit of MMA but clearly differing from the single array of both chlorine-capped PMMA signals expected for the living radical polymerization[14] for both control samples (Figure 1B, 1 and 2). The major series turned out to be separated from the chlorine-capped PMMA series by a mass unit of 129.6, close to the value (129.7) for a single pMOS unit with a methoxy terminal but without a chlorine, as indicated in trace 3 [$\sim$(MMA)$_n$−(pMOS)$_m$−OCH$_3$; $m = 1$]. The main array was further separated from another minor series (with triangles) by a mass difference indicative of the same structure but doubled pMOS units ($m = 2$). These results therefore show the formation

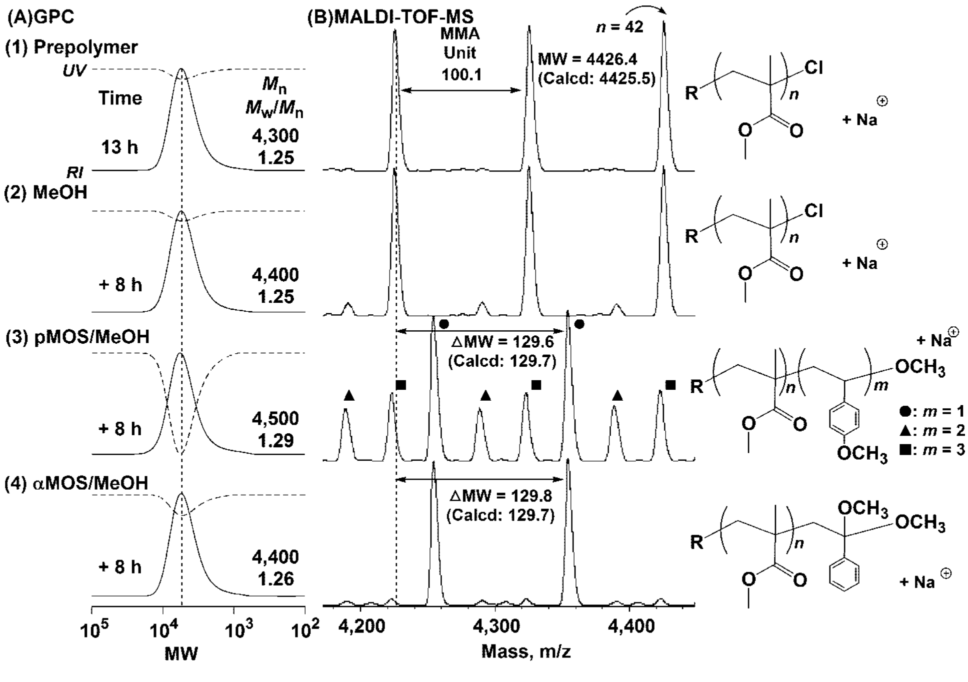
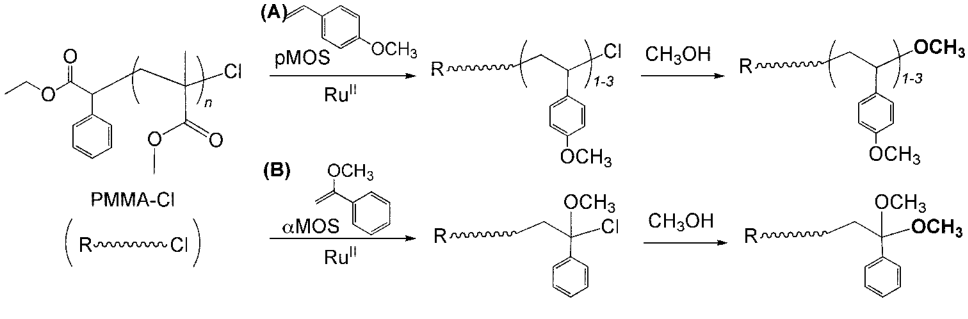


Figure 1. (A) SEC curves and (B) MALDI-TOF-MS spectra of PMMA obtained with ruthenium-catalyzed living radical polymerization and sequential end-capping reaction with modifier monomer and methanol in toluene at 80 °C. Polymerization: [MMA]$_0$ = 2.0 M; [ECPA]$_0$ = 20 mM; [Ru(Ind)Cl(PPh$_3$)$_2$]$_0$ = 2.0 mM; [nBu$_3$N]$_0$ = 20 mM. End-capping reaction: [modifier monomer]$_{add}$ = 200 mM; [MeOH]$_{add}$ = 2.0 M; [nBu$_3$N]$_{add}$ = 20 mM. (1) Polymerization in 13 h. (2) Control experiment for end-capping without modifier monomer. (3) End-capping with pMOS. (4) End-capping with αMOS. Reaction time for end-capping is 8 h.

Scheme 2



of PMMA carrying an extended short segment with one and two (and possibly three) pMOS units and also capped with a methoxy group from MeOH. The conclusion was corroborated by ^{1}H NMR analysis (see Supporting Information). Thus, a few pMOS monomers polymerized from the Cl-capped dormant PMMA, radically under the ruthenium catalysis, to form a new chloride terminal now attached to a pMOS unit and was thereby umpoled and activated to readily react with added MeOH to eventually give a methoxy terminal (Scheme 2A). The results therefore demonstrate that our "umpolung" strategy works but that the use of pMOS as a modifier monomer is not perfectly suited, albeit effective, by giving mixed products with varying length of the terminal pMOS segments.

Terminal "Umpolung" with Modifier Monomer α*MOS.* In an effort to obtain a more uniform structure of the methoxy-capped polymer, we employed an α-substituted methoxystyrene (αMOS) in place of pMOS as a modifier monomer because αMOS, a sterically hindered α,α-disubstituted alkene, is less favorable for radical polymerization.[15] Upon a treatment identical with the procedures with pMOS except for the use of αMOS, the products led to SEC traces with weaker UV intensity, consistent with an αMOS-capped structure with a weaker aromatic chromophore (Figure 1A-4). A single peak-series with the MMA mass difference was observed in MALDI-TOF-MS spectrum (Figure 1B-4). The observed absolute mass values agreed with the calculated ones for the expected structure with a single αMOS unit and a methoxy terminal (from MeOH) attached to a PMMA chain. Thus, we achieved quantitative methoxy-capping for one series of PMMA (Scheme 2B). Such a selective methoxy-capping via a single αMOS extension was also possible even when a mixture of αMOS and MeOH was directly added into a polymerization solution without the evaporation of remaining MMA. This result will be reported in the coming paper in future.

In conclusion, we demonstrated a novel method for a quantitative substitution of a terminal halogen in PMMA obtained with ruthenium-catalyzed living radical polymerization. The crucial point is a modification of the terminal carbon−halogen bond to be polarized for an acceptance of ionic substitution by alcohol, which was brought about by attaching a modifier monomer with conjugated and electron-donating substituents, such as pMOS and αMOS. This method would be developed for various functionalizations at terminal with use of the corresponding alcohols, which is now under investigation. For example, the acetal terminal, generated with αMOS/MeOH, can readily be converted, by a simple acidic transformation, into the corresponding ketone that will be useful for further modifications including conjugation with peptides and other biologically important molecules.

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Supporting Information Available: Experimental details, data for the polymers, and ^{1}H NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) For reviews on metal-catalyzed living radical polymerization, see: (a) Kamigaito, M.; Ando, T.; Sawamoto, M. *Chem. Rev.* **2001**, *101*, 3689–3745. (b) Kamigaito, M.; Ando, T.; Sawamoto, M. *Chem. Rec.* **2004**, *4*, 159–175. (c) Matyjaszewski, K.; Xia, J. *Chem. Rev.* **2001**, *101*, 2921–2990.

(2) Ando, T.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **1998**, *31*, 6708–6711.

(3) Coessens, V.; Pyun, J.; Miller, P. J.; Gaynor, S. G.; Matyjaszewski, K. *Macromol. Rapid Commun.* **2000**, *21*, 103–109.

(4) Coessens, V.; Matyjaszewski, K. *Macromol. Rapid Commun.* **1999**, *20*, 66–70.

(5) Matyjaszewski, K.; Nakagawa, Y.; Gaynor, S. G. *Macromol. Rapid Commun.* **1997**, *18*, 1057–1066.

(6) (a) Yagci, Y.; Tasdelen, M. A. *Prog. Polym. Sci.* **2006**, *31*, 1133–1170. (b) Toman, L.; Janata, M.; Spevacek, J.; Vlcek, P.; Latalova, P.; Masar, B.; Sikora, A. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 6098–6108. (c) Francis, R.; Taton, D.; Logan, J. L.; Masse, P.; Gnanou, Y.; Duran, R. S. *Macromolecules* **2003**, *36*, 8253–8259.

(7) Seebach, D. *Angew. Chem., Int. Ed.* **1979**, *18*, 239–258.

(8) Sawamoto, M. *Prog. Polym. Sci.* **1991**, *16*, 111–172.

(9) Takahashi, H.; Ando, T.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **1999**, *32*, 3820–3823.

(10) Baek, K.-Y.; Kamigaito, M.; Sawamoto, M. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 1937–1944.

(11) Hamasaki, S.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **2002**, *35*, 2934–2940.

(12) We also examined direct addition of a pMOS/MeOH mixture without the evaporation procedure described in the text. However, the more the MMA residue, the more pMOS was needed for the modification, which in turn resulted in higher polymeric byproducts most likely due to spontaneous radical polymerization of pMOS.

(13) Note that the amine cocatalyst remaining in the mixture now serves as a base (proton trap) in the methoxy-capping.

(14) Terashima, T.; Ouchi, M.; Ando, T.; Sawamoto, M. *J. Am. Chem. Soc.* **2006**, *128*, 11014–11015.

(15) Lüssi, V. H. *Makromol. Chem.* **1967**, *103*, 68–73.

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