Macromolecules

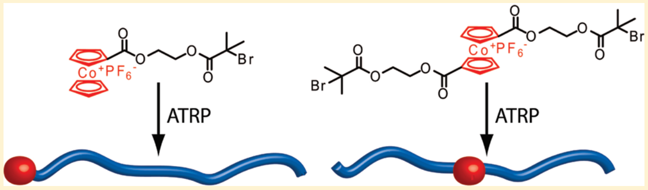
Article

pubs.acs.org/Macromolecules

Preparation of Cobaltocenium-Labeled Polymers by Atom Transfer Radical Polymerization

Lixia Ren, Jiuyang Zhang, Christopher G. Hardy, Deon Doxie, Barbara Fleming, and Chuanbing Tang*

Department of Chemistry and Biochemistry and USC Nanocenter, University of South Carolina, 631 Sumter Street, Columbia, South Carolina 29208, United States



ABSTRACT: Cobaltocenium-labeled polymers were prepared by atom transfer radical polymerization (ATRP) using cobaltocenium-containing α-haloesters as initiators. The locations of the cobaltocenium moiety in the polymer chains (either at the end or in the middle) were dictated by the chemical structures of initiators. Kinetic studies showed that polymerizations of styrene, tert-butyl acrylate, and methyl methacrylate monomers followed a controlled/living manner, except that polymerization of methyl methacrylate with the aid of cobaltocenium monoinitiator displayed significant termination. All resultant polymers were redox-active and exhibited characteristic UV−vis absorption from the cobaltocenium moiety.

■ INTRODUCTION

Labeled polymers are a class of important functional materials[1,2] which have found applications in molecular imaging,[3−6] (bio)sensing,[5,7−9] targeting,[10−14] electrode-decorating,[15−18] etc. Based on their specific applications, labeled polymers are designed to be optically active,[3,5,19−23] redox-active,[8,15,17,18,24−28] or radioactive.[29−31] By labeling the polymer chain with detectable probes, the study of polymer behavior in solution, especially single polymer chains, would be more accurate. For example, molecular weight of a chromophore-labeled polymer can be precisely determined by analyzing the chromophore probe using UV−vis spectroscopy.[23] Among diverse probes, redox-active probes have attracted special attention due to their high sensitivity, rapid response, and easy detection via appropriate analytical tools,[24] which can make them "visible" in solution. Metallocenes, which are widely used as sensors and catalysts,[8,32,33] are often used as redox probes due to their reversible electrochemical oxidation and reduction as well as their notable environmental stability.[27,34] Metallocenes have been used to label natural biopolymers including DNA,[35,36] proteins,[25] and drugs,[26] and synthetic polymers such as poly(ethylene oxide)[37] and polyamides.[27] Assembly of ferrocene-labeled streptavidin on biotinylated electrodes results in a reproducible unidirectional current flow in the presence of electron donors in solution.[15] Ferrocene-labeled polymers can be mapped via electrochemical atomic force microscopy.[18] A ferrocene-labeled poly(ethylene glycol) was used to study the chain dynamics of a poly(ethylene glycol) matrix via quantitative electrochemical diffusion measurements.[21,37,38] Recently, Zhu et al. prepared ferrocene-containing transfer agents for reversible addition−fragmentation transfer polymerization.[39]

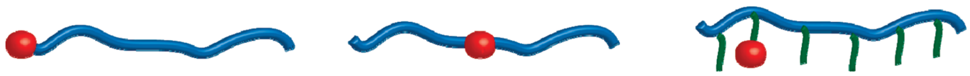
Cobaltocenium, an 18-electron cationic metallocene, has been used as a redox probe due to its one-electron reversible reduction (to cobaltocene) and high sensitivity (detection limit up to 10^{-8} M solution).[16] In addition, cobaltocenium has extremely high structure integrity stability toward oxidation (the half-wave potential ($E_{1/2}$) of the Co(III)/Co(IV) couple falling at ca. 2.7 V vs ferrocene).[16,26] These properties make cobaltocenium a desirable candidate as a redox-active probe for use in polymeric materials. In addition, cobaltocenium has characteristic optical absorption in the UV region. We have recently developed a class of side-chain cobaltocenium-containing polymers through both postpolymerization modification and direct polymerization.[40−44] A few other groups have developed cobaltocenium-containing dendrimers and main-chain cobaltocenium-containing polymers.[45−49] However, cobaltocenium-labeled polymers have not been reported in the literature.

There are three major pathways to prepare labeled polymers:[5] (1) Postpolymerization modification by labeling probes through covalent attachment[27] or supramolecular interactions.[50] However, this strategy requires highly efficient postpolymerization modification reactions. Additionally, the number of probe units is rather difficult to control. (2) Direct polymerization using a probe-labeled functional monomer as a comonomer.[51] However, the accurate position of probes is difficult to measure. (3) With the development of controlled and living polymerization,[52−56] probes can be also integrated into initiators,[13,57] transfer agents,[39] or mediating agents,[3,58] which can be used to prepare polymers with precise information about location and number of probes. These probes can be located at the end of or in the middle of polymer chain, or placed at the side chain or the backbone of polymers, as shown in Scheme 1.

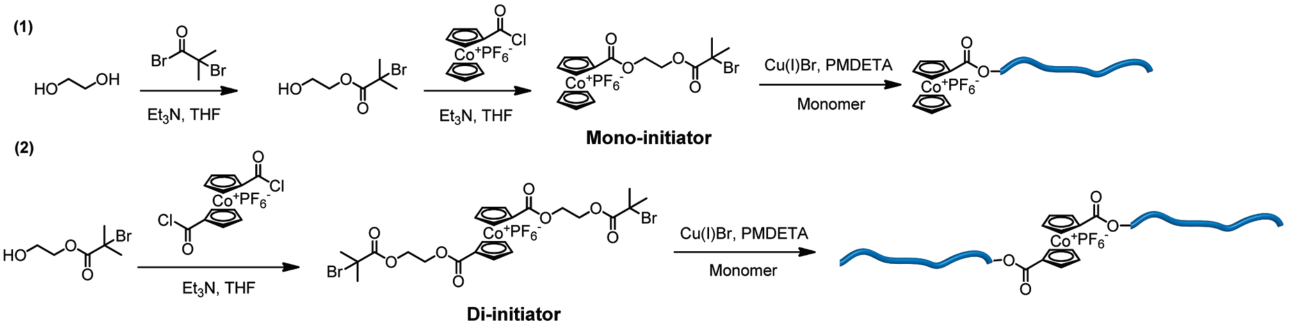
Herein, we report the preparation of novel cobaltocenium-labeled polymers by atom transfer radical polymerization (ATRP), one of the most widely used controlled radical

Received: December 16, 2011
Revised: February 7, 2012
Published: February 16, 2012

Scheme 1. Labeled Polymers with a Probe at Diverse Locations of Polymer Chains



Scheme 2. Synthesis of Cobaltocenium-Containing α-Haloesters and Their Use as Initiators To Prepare Cobaltocenium-Labeled Polymers by ATRP



polymerizations to prepare functional materials.[54,55,59−61] Specifically, we designed two cobaltocenium-based α-haloesters, monosubstituted and 1,1′-disubstituted bromoisobutyrate cobaltoceniumcarboxylate, which were used as ATRP initiators. With the aid of these initiators, polymers from three different classes of monomers (acrylate, methacrylate, and styrene) with cobaltocenium as the optically active redox-active probe were prepared. As shown in Scheme 2, all polymers have one cobaltocenium probe per chain with a predetermined location, either at the chain end or in the middle of chain. Kinetic studies using both initiators were conducted. The optical and redox properties of resultant cobaltocenium-containing polymers were studied by UV−vis spectroscopy and cyclic voltammetry, respectively.

■ EXPERIMENTAL SECTION

Materials. Ethylene glycol (anhydrous, Aldrich), 2-bromoisobutyryl bromide (Aldrich), Cu(I)Br (99.999%, Aldrich), *N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDETA, Aldrich), sodium hexafluorophosphate ($NaPF_6$, 99%, Alfa Aesar), and tetra-*n*-butylammonium hexafluorophosphate ($TBAPF_6$, 98%, Acros) were used as received. Triethylamine (Et_3N, 99%, Aldrich) and tetrahydrofuran (THF, Alfa Aesar) were distilled before use. Cobaltocenium monoacyl chloride and diacyl chloride were synthesized according to our early reports.[40,41] Styrene (St, Aldrich), *tert*-butyl acrylate (tBA, Aldrich), and methyl methacrylate (MMA, Aldrich) were freshly distilled before use. All other chemicals were obtained from commercial sources and used as received unless otherwise mentioned.

Characterization. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian Mercury 400 spectrometer with tetramethylsilane (TMS) as an internal reference. Gel permeation chromatography (GPC) was performed in dimethylformamide (DMF, containing 0.1% LiBr) at a flow rate of 0.8 mL/min at 50 °C on a Varian system equipped with a ProStar 210 pump and a Varian 356-LC RI detector and three 5 μm phenogel columns (Phenomenex Co.) with narrow dispersed polystyrene as standards. High-resolution mass spectrometry (MS) was conducted on a Waters Micromass quadropole time-of-flight mass spectrometer, using electrospray ionization in a positive ion mode. UV−vis spectra were recorded on a Shimadzu UV 2450 spectrophotometer. Cyclic voltammetry (CV) characterization was carried on a BAS CV-50W voltametric analyzer. The samples were dissolved in 0.1 M $TBAPF_6$ solution in DMF at a concentration of 0.5 mM. The samples were then purged with nitrogen gas for 10 min before running CV. The samples were scanned at a rate of 100 mV/s at different potential ranges vs Ag/AgCl electrode.

Synthesis of 2-Hydroxyethyl 2-Bromoisobutyrate (HEBiB). HEBiB was synthesized following reported procedures.[62−64] Ethylene glycol (40.0 mL, 7.2×10^{-1} mol) and triethylamine (6.0 mL, 4.3×10^{-2} mol) were added into a dry flask followed by adding 2-bromoisobutyryl bromide (5.4 mL, 4.3×10^{-2} mol) dropwise over 1 h at 0 °C. The reaction mixture was kept at 60 °C overnight, followed by adding water (300 mL) and extracting with dichloromethane (3 × 200 mL). The organic layer was collected and dried over anhydrous magnesium sulfate. The product was purified by passing through a silica column with dichloromethane as eluent. Yield: 85%. ^1H NMR ($CDCl_3$) δ: 3.84 (t, 2H, $HOCH_2CH_2$); 4.30 (t, 2H, $HOCH_2CH_2$); 1.92 (s, 6H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 171.7 ($Br(CH_3)_2CCO$); 66.8 ($HOCH_2CH_2$); 60.1 ($HOCH_2CH_2$); 50.9 ($Br(CH_3)_2C$); 32.8 (CH_3).

Synthesis of Cobaltocenium Di-initiator. Freshly prepared cobaltocenium 1,1′-diacyl chloride (0.56 g, 1.2×10^{-3} mol) and HEBiB (1.50 g, 7.2×10^{-3} mol) were added into a dry round-bottom flask with 100 mL of dry THF. Triethylamine (1.0 mL, 7.4×10^{-3} mol) was added slowly. The reaction mixture was stirred at room temperature for 5 days. Afterward, solvents were evaporated and the crude product was dissolved in dichloromethane followed by sequential extraction with aqueous $NaPF_6$ solution and water. The organic layer was dried over anhydrous magnesium sulfate and precipitated from diethyl ether to give the product. Yield: 90%. ^1H NMR ($CDCl_3$) δ: 6.25 (broad, 4H, Cp); 6.15 (broad, 4H, Cp); 4.56 (dt, 8H, OCH_2CH_2O); 1.92 (s, 12H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 171.5 ($Br(CH_3)_2CCO$); 162.5 (CpCO); 85−89 (carbon from Cp ring); 64.2 and 65.0 (OCH_2CH_2O); 56.2 ($Br(CH_3)_2CCO$); 30.2 (CH_3). MS: theoretical *m/z* 569.94; found *m/z* 569.85.

Synthesis of Cobaltocenium Monoinitiator. The preparation was similar to the synthesis of cobaltocenium di-initiator. Cobaltocenium monoacyl chloride (0.48 g, 1.2×10^{-3} mol) and HEBiB (0.75 g, 3.6×10^{-3} mol) were mixed in a THF (100 mL) solution, followed by adding triethylamine (0.5 mL, 3.7×10^{-3} mol) slowly. The reaction mixture was stirred at room temperature for 5 days. The product was purified using the same procedure as the synthesis of cobaltocenium di-initiator. Yield: 90%. ^1H NMR ($CDCl_3$) δ: 6.20 (broad, 2H, Cp); 5.95 (broad, 2H, Cp); 5.82 (broad, Cp, 5H); 4.61 (d, broad, 4H, OCH_2CH_2O); 1.91 (s, 6H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 171.7 ($Br(CH_3)_2CCO$); 163.6 (CpCO); 85−89 (carbon from Cp ring); 62.9 and 65.0 (OCH_2CH_2O); 55.7 ($Br(CH_3)_2CCO$); 30.2 (CH_3). MS: theoretical *m/z* 424.98; found *m/z* 424.89.

Polymerization Procedure. The polymerization of all three monomers was very similar. A typical procedure was as follows. Cu(I)Br (2 equiv) and cobaltocenium monoinitiator (1 equiv) or cobaltocenium di-initiator (1 equiv of bromide) were charged into a Schlenk flask and degassed under nitrogen. Degassed monomer (400 equiv) and PMDETA (2 equiv) were then transferred into the Schlenk flask under the protection of nitrogen. The polymerization was conducted at 90 °C for St or tBA, while the polymerization of MMA was conducted at room temperature. Samples were taken out at predetermined intervals to monitor the reaction conversion before stopping the reaction. The final polymers were obtained by precipitation in methanol.

(1) Polymer PMMA-*Cc*-PMMA: ^{1}H NMR (CDCl$_3$, δ): 3.35–3.75 (broad, OCH_3), 2.15–2.40 (broad, CH_2–C(CH$_3$)), 1.20–1.95 (broad, CH$_2$–C(CH_3)). GPC M_n: 120 100 g/mol; PDI: 1.20.

(2) Polymer PtBA-*Cc*-PtBA: ^{1}H NMR (CDCl$_3$, δ): 2.00–2.35 (broad, CH_2–CH), 1.65–1.80 (broad, CH$_2$–CH), 1.00–1.65 (broad, –C(CH_3)$_3$). GPC M_n: 22 500 g/mol; PDI: 1.45.

(3) Polymer PSt-*Cc*-PSt: ^{1}H NMR (CDCl$_3$, δ): 6.00–7.2 (broad, aromatic), 0.80–2.00 (broad, CH_2–CH). GPC M_n: 123 000 g/mol; PDI: 1.20.

(4) Polymer *Cc*-PMMA: ^{1}H NMR (CDCl$_3$, δ): 3.35–3.75 (broad, OCH_3), 2.15–2.40 (broad, CH_2–C(CH$_3$)), 1.20–1.95 (broad, CH$_2$–C(CH_3)).

(5) Polymer *Cc*-PtBA: ^{1}H NMR (CDCl$_3$, δ): 2.00–2.35 (broad, CH_2–CH), 1.65–1.80 (broad, CH$_2$–CH), 1.00–1.65 (broad, –C(CH_3)$_3$). GPC M_n: 135 000 g/mol; PDI: 1.18.

(6) Polymer *Cc*-PSt: ^{1}H NMR (CDCl$_3$, δ): 6.00–7.2 (broad, aromatic), 0.80–2.00 (broad, CH_2–CH). GPC M_n: 134 200 g/mol; PDI: 1.35.

Kinetic Study of Monomers Initiated by Cobaltocenium Di-initiator and Monoinitiator. All kinetic studies were conducted similarly as aforementioned. Here, the St polymerization is described as an example. Cobaltocenium di-initiator (4.1 mg, 5.0 × 10^{-6} mol) and Cu(I)Br (2.8 mg, 2.0 × 10^{-5} mol) were charged into a Schlenk flask and purged with nitrogen for 30 min. Degassed St (0.9 mL, 9.0 × 10^{-3} mol) and PMDETA (5 μL, 2.0 × 10^{-5} mol) were transferred into the Schlenk flask. The flask was placed in an oil bath set at 90 °C. Samples were taken at different intervals under the protection of nitrogen. The conversion of the monomers was calculated by ^{1}H NMR analyses. The kinetic studies of all three monomers initiated by cobaltocenium monoinitiator were also conducted similarly to those using the cobaltocenium di-initiator. It should be noted that the kinetic studies of MMA monomers were conducted at room temperature.

RESULTS AND DISCUSSION

Synthesis of Cobaltocenium-Ended and Cobaltocenium-Centered Polymers by ATRP. As shown in Scheme 2, cobaltocenium-containing ATRP initiators were synthesized via esterification reactions between cobaltocenium acyl chloride and 2-hydroxyethyl 2-bromoisobutyrate (HEBiB), in the presence of triethylamine. The use of 1,1′-diacyl chloride and monoacyl chloride produced cobaltocenium di-initiator and monoinitiator respectively, with yields at ~90%. Both initiators were characterized by proton and carbon NMR. As shown in Figure 1A, the ^{1}H NMR spectrum of the di-initiator showed peaks at 5.97–6.33, 4.37–4.73, and 1.75–2.10 ppm, corresponding to characteristic Cp protons, ethylene protons, and methyl protons, respectively. The integration ratios of each group were in great agreement with theoretical ones. ^{13}C NMR agreed very well with the ^{1}H NMR result, and each signal was clearly assigned (Figure 1B). The identity of di-initiator was further confirmed by high-resolution MS, which showed a mass/charge (m/z) ratio of 569.85, consistent with the theoretical m/z of 569.94. Compared to the di-initiator, monoinitiator showed slight shift to the lower field for both the Cp protons (5.75–6.25 ppm) and the ethylene protons (4.50–4.70 ppm), as shown in Figure 2A. Three distinct peaks were observed for the Cp protons. The ^{13}C NMR spectrum showed similar chemical shifts for all characteristic protons to those of the di-initiator (Figure 2B). High-resolution MS showed that the m/z ratio was 424.89, in a good agreement with the theoretical ratio of 424.98. Therefore, both cobaltocenium-containing ATRP initiators were successfully synthesized by simple esterification reactions with high yields.

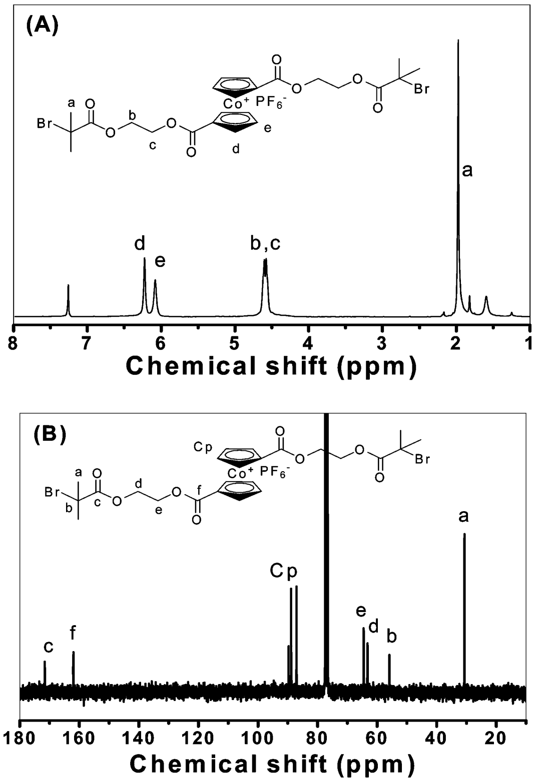


Figure 1. (A) ^{1}H NMR and (B) ^{13}C NMR spectra of cobaltocenium di-initiator in CDCl$_3$.

We first conducted polymerization of tBA in solution. However, the polymerization was very slow, as only 30% conversion was reached after 24 h. Hence, bulk polymerization was carried out for all monomers initiated by cobaltocenium-containing initiators reported in this paper. Both tBA and St polymerizations were carried out at 90 °C, while MMA polymerization was employed at room temperature. Bulk polymerizations of monomers including tBA, St, and MMA were first carried out with the aid of cobaltocenium-containing di-initiator. The catalyst system consisted of copper(I) bromide and PMDETA. The molar ratio of catalyst to initiator was 4:1 (2:1 for copper bromide to the bromide in the initiator). As reactions continued, all reaction mixtures clearly turned more viscous. Figure 3A shows the ^{1}H NMR spectrum of PMMA polymers initiated by the di-initiator. The vinyl protons (5.0–6.0 ppm) from the monomers disappeared completely, while broad peaks from 1.0 to 2.5 ppm appeared, corresponding to protons from the PMMA backbone. More importantly, for a polymer with relatively lower molecular weight, two peaks were clearly observed at lower field from 6.05 to 6.23 ppm, which originated from Cp protons of the cobaltocenium moiety from the initiator in the middle of polymer chain. Similarly, PtBA and PSt prepared by ATRP with the cobaltocenium di-initiator showed their respective signals in the NMR spectra (Figure 3B,C). Figure 4 shows the GPC traces of the polymers, PtBA-*Cc*-PtBA, PSt-*Cc*-PSt, and PMMA-*Cc*-PMMA, synthesized using the cobaltocenium di-initiator. In all cases, symmetric monomodal peaks were observed. The polydispersity indexes (PDI) of PSt-*Cc*-PSt and PMMA-*Cc*-PMMA were ~1.20 while the PtBA-*Cc*-PtBA had a higher PDI of 1.45.

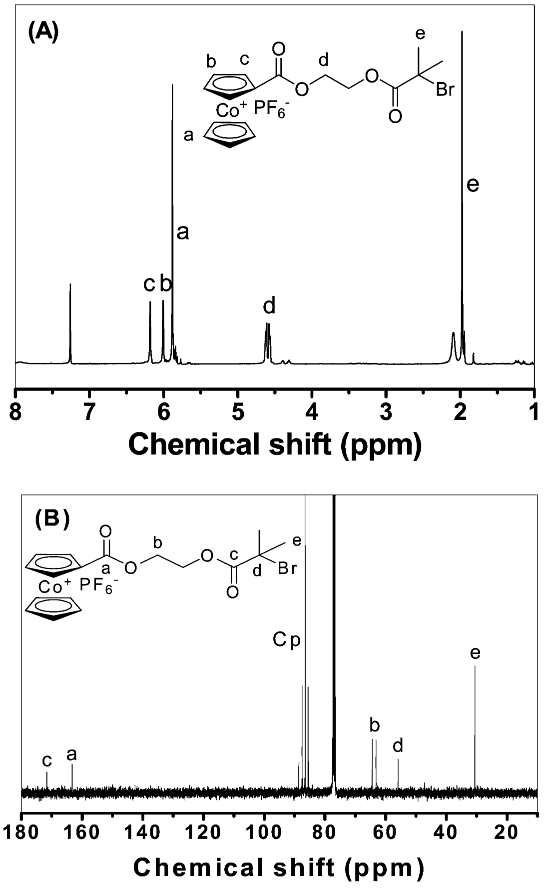


Figure 2. (A) ^{1}H NMR and (B) ^{13}C NMR spectra of cobaltocenium monoinitiator in $CDCl_3$.

In order to verify whether the polymerization was living and controlled, kinetic studies of all monomer polymerization were carried out. The conversion was determined from in situ ^{1}H NMR analysis by comparing the integration areas between the monomers and polymers in the reaction system. Figure 5A shows the semilogarithmic plots of $\ln([M_0]/[M])$ vs reaction time for polymerization of monomers initiated by the cobaltocenium di-initiator. These plots exhibited linear kinetics, indicating that all polymerizations followed a controlled and living manner. While the rates of polymerization of St and tBA were very close, the polymerization of MMA was much faster. The conversion of MMA reached 50% within 2.5 h, while it took 10 h for St to reach a comparable conversion. The evolution of molecular weight vs conversion was also monitored in the polymerizations of tBA, St, and MMA. Clearly the molecular weight increased linearly with the conversion, another signature of controlled and living polymerizations (Figure 5B).

The cobaltocenium monoinitiator was then used to conduct ATRP of tBA, St, and MMA under similar conditions. Figure 6 shows the ^{1}H NMR spectra of *Cc*-PtBA, *Cc*-PSt, and *Cc*-PMMA polymers, which showed similar characteristic peaks to those observed from polymers prepared by the cobaltocenium di-initiator. A representative ^{1}H NMR spectrum of *Cc*-PtBA with relatively lower molecular weight clearly showed typical signals in the range of 5.85−6.45 ppm, corresponding to the Cp protons from the ended cobaltocenium moiety. Figure 7 shows the GPC traces of the polymers synthesized using the cobaltocenium monoinitiator. *Cc*-PtBA had a symmetric trace with the PDI as low as 1.18. Although *Cc*-PSt had a PDI of 1.35, a shoulder appeared at the higher molecular weight end, suggesting that some bimolecular termination may occur. The *Cc*-PMMA polymer exhibited an asymmetrical trace with a rough baseline, indicating the polymerization was not controlled.

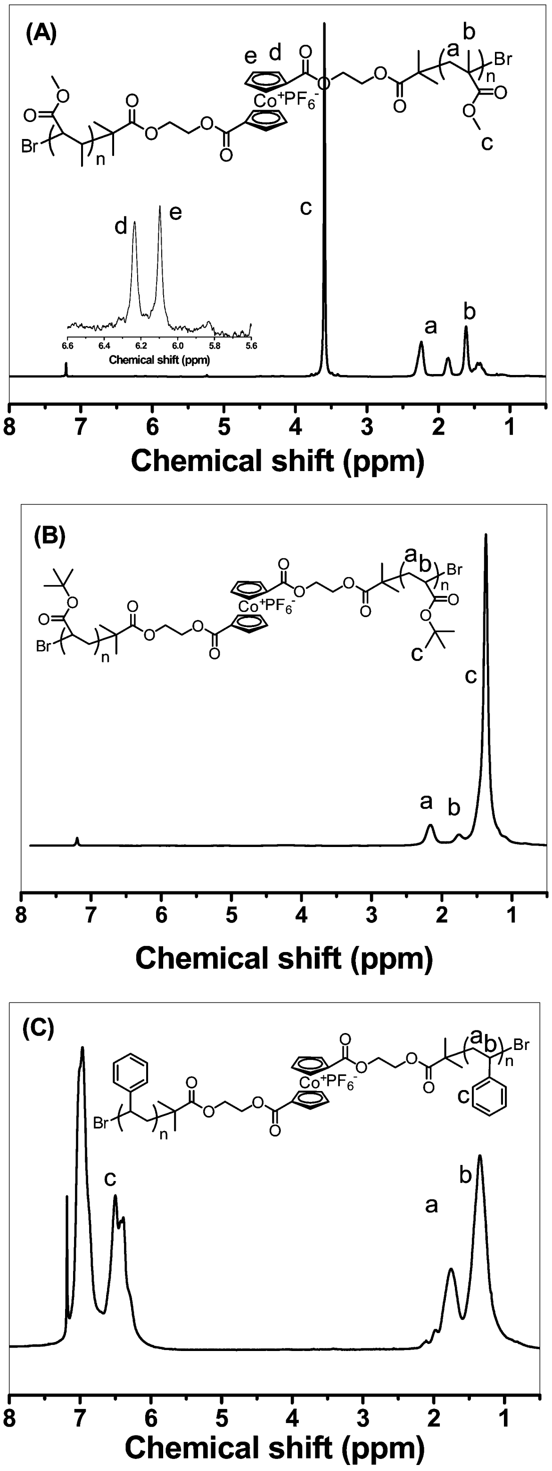


Figure 3. ^{1}H NMR spectra of (A) PMMA, (B) PtBA, and (C) PSt prepared by ATRP with the use of cobaltocenium di-initiator in $CDCl_3$.

Kinetic studies were conducted using the cobaltocenium monoinitiator and the same procedures as those with the

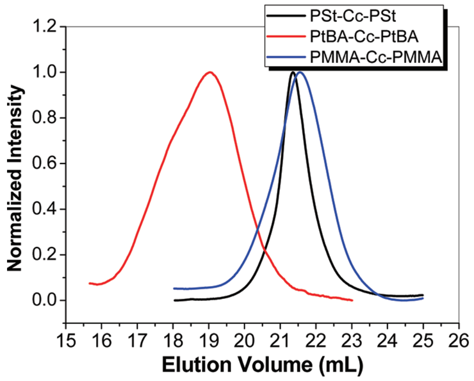


Figure 4. GPC traces of PtBA-*Cc*-PtBA, PSt-*Cc*-PSt, and PMMA-*Cc*-PMMA prepared by ATRP with the use of cobaltocenium di-initiator.

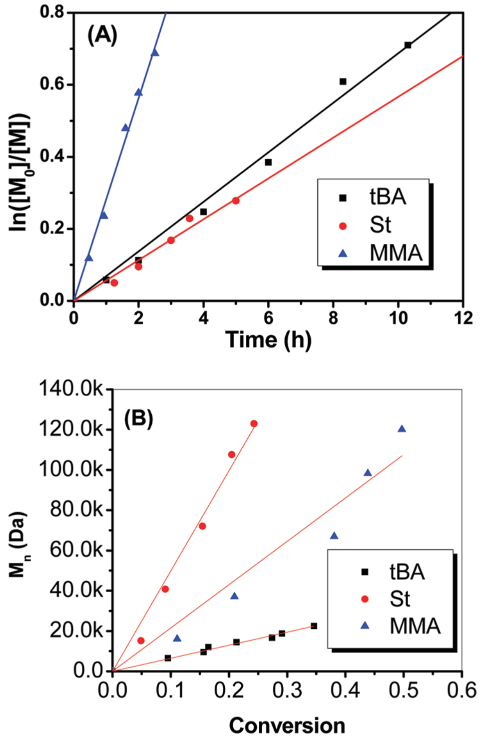


Figure 5. (A) Semilogarithmic plots and (B) number-average molecular weight vs conversion for bulk polymerizations of tBA, St, and MMA initiated by the cobaltocenium di-initiator.

cobaltocenium di-initiator. As shown in Figure 8, bulk polymerizations of both St and tBA exhibited linear kinetics, while the molecular weight had a linear relationship with conversion. All these results indicated the polymerizations of tBA and St were controlled and living. In addition, the rates of polymerization for tBA and St were also comparable. However, the kinetic plot of polymerization of MMA showed a distinct curvature, a signature of significant termination. Nevertheless, at conversions below 50% the polymerization of MMA was still much faster than that of St and tBA. Repeated experiments showed similar kinetics. This is in sharp contrast with the living characteristics of MMA initiated by the cobaltocenium di-initiator. Given that both initiators have similar functionalities, this behavior was quite peculiar. It is not very clear at this stage what could induce the significant termination reactions.

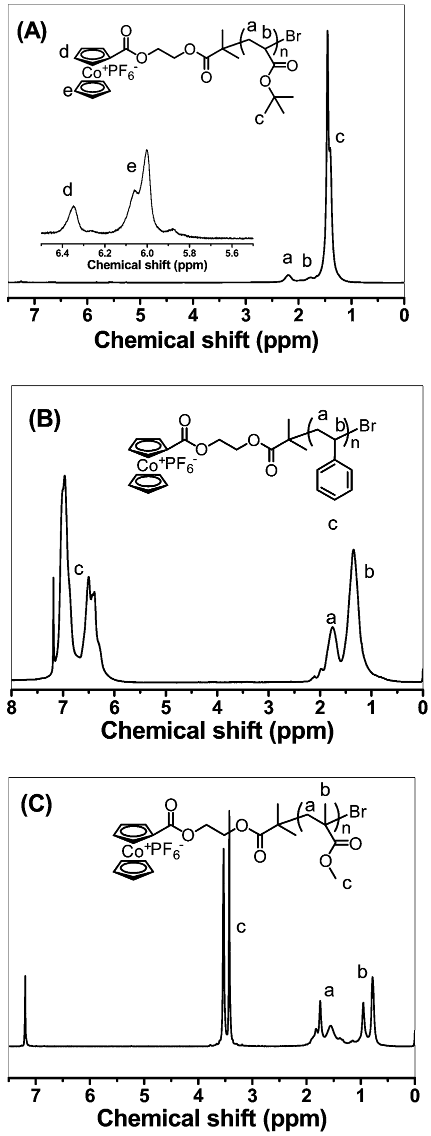


Figure 6. ^{1}H NMR spectra of (A) PtBA, (B) PSt, and (C) PMMA prepared by ATRP with the use of the cobaltocenium monoinitiator.

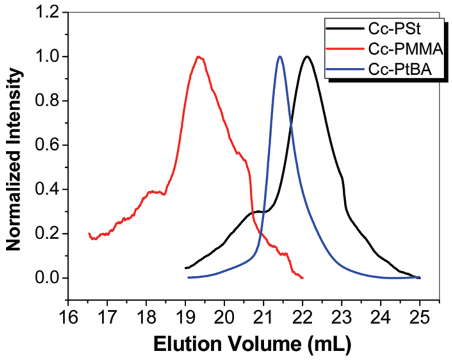


Figure 7. GPC traces of *Cc*-PtBA, *Cc*-PSt, and *Cc*-PMMA prepared by ATRP with the use of the cobaltocenium monoinitiator.

Ion-Exchange Effect on the Polymerization. In our early study,[41,43] we have demonstrated that the counterions of cobaltocenium can undergo exchange with other anions. With the use of chloride-based anionic exchange resin, hexafluorophosphate ions can be readily exchanged to chloride ions. This early work indicated that a similar ion exchange between hexafluorophosphate ions in the cobaltocenium initiators and

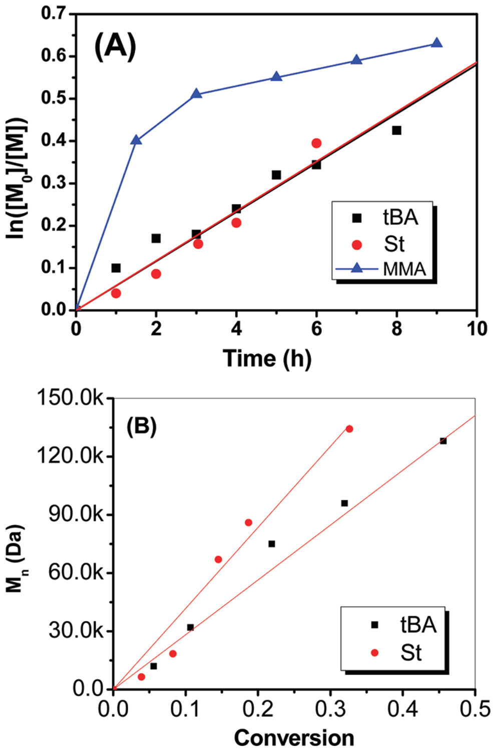


Figure 8. (A) Semilogarithmic plots of bulk polymerization of tBA, St, and MMA initiated by cobaltocenium monoinitiator. (B) number-average molecular weight vs conversion for bulk polymerizations of tBA and St initiated by cobaltocenium monoinitiator (due to the nonliving behavior of MMA polymerization, M_n vs conversion was not monitored).

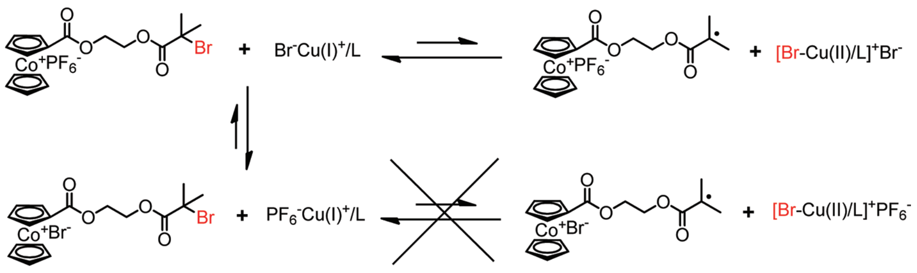
bromide ions in the copper catalysts should occur. Such exchange could induce significant undesirable effects on the activation and deactivation equilibrium of the ATRP process. This hypothesis was confirmed with the following experiments, in which the 1:1 molar ratio of the bromide in the initiators and copper(I) bromide led to the formation of uncontrolled polymers with very low molecular weight. As shown in Scheme 3, the exchange between hexafluorophosphate ions and copper(I) bromide would significantly alter the activation and deactivation equilibrium, as copper hexafluorophosphate is a very poor catalyst. Therefore, all the reaction systems were intentionally designed with the 1:2 molar ratio of the bromide in the initiators and copper(I) bromide. The 1 equiv of excess of copper(I) bromide would be used as a "buffer reagent" to digest the hexafluorophosphate ions and therefore minimize the ion-exchange effect on the control of polymerization. Another possible strategy is to prepare cobaltocenium initiators with halide as the counterions. However, our preliminary study indicated that these initiators were somehow not stable, ultimately leading to the decomposition of the cobaltocenium moiety. More investigations on this matter are currently in progress.

The ion-exchange process was further confirmed with ATRP experiments on cobaltocenium-containing monomers. We have failed to polymerize any cobaltocenium hexafluorophosphate-containing vinyl monomers by ATRP. Most likely, the reaction system was involved with the ion-exchange process between cobaltocenium hexafluorophosphate in the vinyl monomers and catalyst copper(I) bromide, as shown in Scheme 4. Since the molar ratio of monomer to catalyst is usually very high (i.e., 100:1), even a small fraction of monomers (i.e., 1%) participating the ion exchange would cause all catalysts to lose activity.

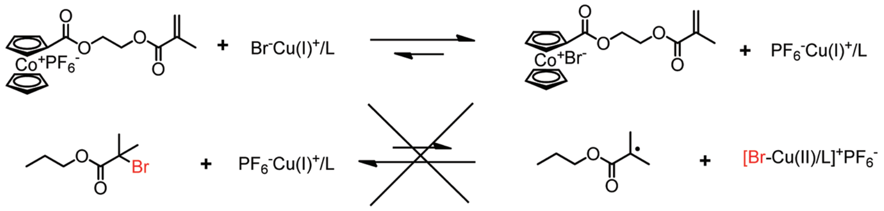
Optical and Redox Properties. Using the cobaltocenium-containing ATRP initiators, single cobaltocenium-labeled polymers PtBA, PSt, and PMMA were obtained. The presence of cobaltocenium was quantitatively verified from ^{1}H NMR analysis discussed above. In our early report,[41] we have shown that side-chain cobaltocenium-containing polymers exhibited characteristic UV–vis absorption from their cobaltocenium units. Therefore, UV–vis spectroscopy was first used to monitor the cobaltocenium moiety in these labeled polymers prepared by ATRP. Figure 9 showed the representative UV–vis absorption spectra of cobaltocenium-containing initiators and their polymers. Both cobaltocenium mono- and di-initiators exhibited two characteristic absorptions at 229 and 276 nm, which were assigned to $\pi-\pi^*$ or $n-\pi^*$ transitions of cobaltocenium, very similar to transitions in ferrocene studied by Scott and Becker.[65] A weak absorption at 410 nm corresponded to the d–d* transition of cobaltocenium. All cobaltocenium-labeled polymers showed a typical absorption at ca. 230 nm, similar to the initiators. In addition, these polymers also showed an absorption peak in the range of 260–300 nm. The peak at ~400 nm was much weaker in most cobaltocenium-labeled polymers. The change of peak intensity and the variation of peak positions were most likely related with the change of surroundings of cobaltocenium, as these polymer chains have different diffusion dynamics. In contrast, no distinct UV–vis absorptions were observed from polymers synthesized via ATRP without the cobaltocenium moiety, further confirming the presence of cobaltocenium group in the polymers.

Redox properties of cobaltocenium initiators and cobaltocenium-labeled polymers were investigated with the aid of cyclic voltammetry.[40,41] As shown in Figure 10, the redox process of cobaltocenium mono- and di-initiators was not reversible. The oxidation peak current was much higher than the reduction peak current. The irreversibility was likely due to solubility

Scheme 3. Possible Side Effects of Ion-Exchange between Initiators and Catalysts



Scheme 4. Possible Side Effects of Ion-Exchange between Monomers and Catalysts



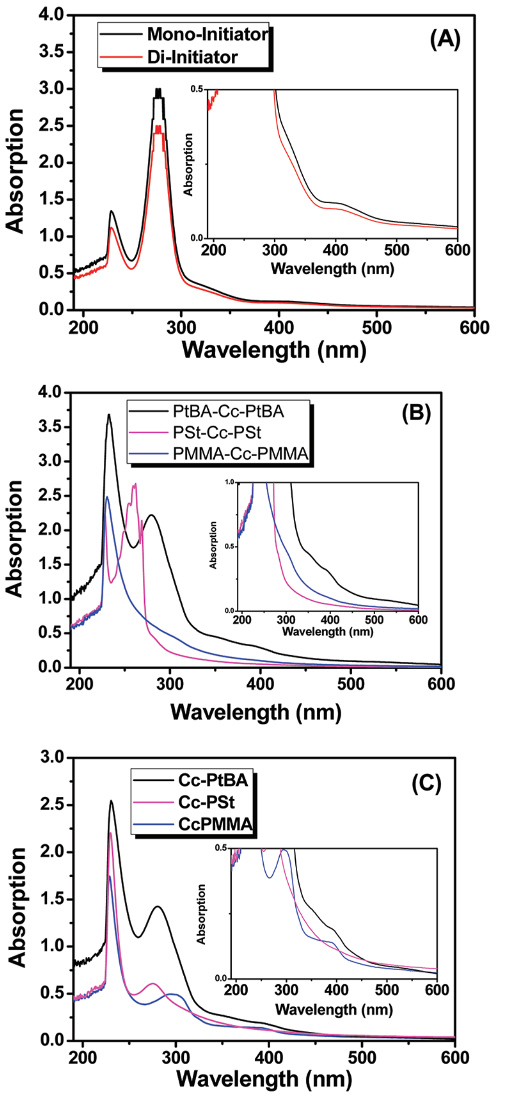


Figure 9. UV−vis absorption spectra of (A) cobaltocenium monoinitiator and di-initiator, (B) polymers prepared by di-initiator, and (C) polymers prepared by monoinitiator (solvent: dichloromethane).

change of cobaltocenium mono- and di-initiators under redox process. Although cobaltocenium mono- and di-initiators are soluble in DMF, the reduced cobaltocenium-labeled polymers (cobaltocene-containing mono- and di-initiators) might have different solubility in DMF. The styrene-based polymers (*Cc*-PSt and PS-*Cc*-PSt) had the similar redox process to the initiators, while the acrylate polymers showed different redox behaviors between end- and centered cobaltocenium-labeled polymers. Both PMMA polymers (*Cc*-PMMA and PMMA-*Cc*-PMMA) exhibited a much more reversible redox process. Nevertheless, all polymers exhibited redox-active properties.

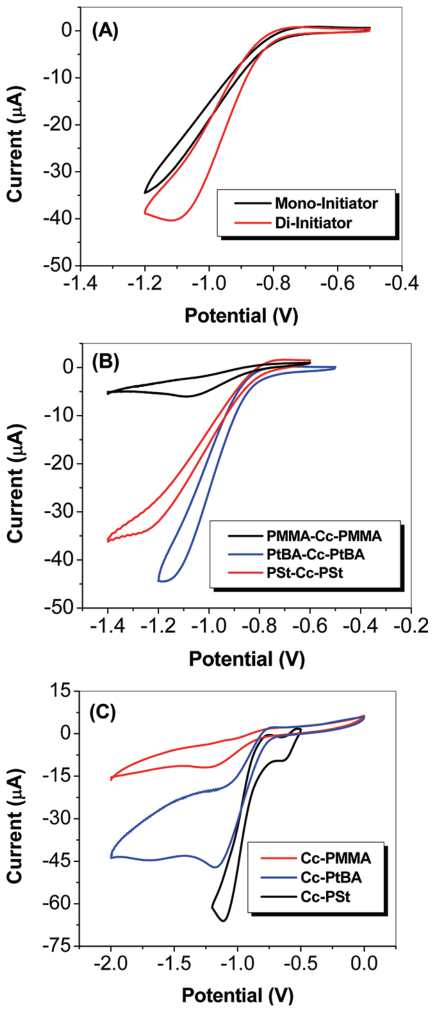


Figure 10. Cyclic voltammetry curves of (A) cobaltocenium monoinitiator and cobaltocenium di-initiator, (B) polymers prepared by di-initiator, and (C) polymers prepared by monoinitiator.

■ CONCLUSIONS

In conclusion, we synthesized cobaltocenium-containing mono- and dihaloesters, which were used as initiators to prepare cobaltocenium-labeled polymers by atom transfer radical polymerization. Three different classes of monomers including styrene, acrylate, and methacrylate were polymerized by ATRP. Because of the potential ion exchange between copper catalysts and counterions of cobaltocenium moiety, excess copper catalysts (compared to initiators) were used. Most polymerization systems exhibited a living and control kinetics, while polymerization of MMA by the monoinitiator showed significant termination. Both cobaltocenium-ended and centered-polymers showed characteristic UV−vis absorption of cobaltocenium. All polymers exhibited redox-active behaviors, indicating the retention of cobaltocenium moiety although the redox process was not reversible. These optically active and redox-active cobaltocenium-labeled polymers may find applications in the field such as sensing, imaging, etc.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: tang4@mailbox.sc.edu.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We acknowledge the University of South Carolina for financial support.

■ REFERENCES

(1) Bellan, L. M.; Wu, D.; Langer, R. S. *WIRES Nanomed. Nanobi.* **2011**, *3*, 229−246.

(2) Bonanni, B.; Andolfi, L.; Bizzarri, A. R.; Cannistraro, S. *J. Phys. Chem. B* **2007**, *111*, 5062−5075.

(3) Bowden, N. B.; Willets, K. A.; Moerner, W. E.; Waymouth, R. M. *Macromolecules* **2002**, *35*, 8122−8125.

(4) Haley, J. C.; Liu, Y.; Winnik, M. A.; Demmer, D.; Haslett, T.; Lau, W. *Rev. Sci. Instrum.* **2007**, *78*, 084101−084101−084105.

(5) Beija, M.; Charreyre, M.-T.; Martinho, J. M. G. *Prog. Polym. Sci.* **2010**, *36*, 568−602.

(6) Malpei, F.; Andreoni, V.; Daffonchio, D.; Rozzi, A. *Biores. Technol.* **1998**, *63*, 49−56.

(7) Isaad, J.; Salaun, F. *Sens. Actuator, B* **2011**, *157*, 26−33.

(8) Chen, Y.-f.; Banerjee, I. A.; Yu, L.; Djalali, R.; Matsui, H. *Langmuir* **2004**, *20*, 8409−8413.

(9) Li, F.; Westphal, A. H.; Marcelis, A. T. M.; Sudholter, E. J. R.; Cohen Stuart, M. A.; Leermakers, F. A. M. *Soft Matter* **2011**, *7*, 1214−1218.

(10) Kim, J.; Nam, H. Y.; Kim, T. I.; Kim, P. H.; Ryu, J.; Yun, C. O.; Kim, S. W. *Biomaterials* **2011**, *32*, 5158−5166.

(11) De Koker, S.; De Cock, L. J.; Rivera-Gil, P.; Parak, W. J.; Auzéy Velty, R.; Vervaet, C.; Remon, J. P.; Grooten, J.; De Geest, B. G. *Adv. Drug Delivery Rev.* **2011**, *63*, 748−761.

(12) Cortez, C.; Tomaskovic-Crook, E.; Johnston, A. P. R.; Radt, B.; Cody, S. H.; Scott, A. M.; Nice, E. C.; Heath, J. K.; Caruso, F. *Adv. Mater.* **2006**, *18*, 1998−2003.

(13) Bathfield, M.; D'Agosto, F.; Spitz, R.; Charreyre, M.-T.; Delair, T. *J. Am. Chem. Soc.* **2006**, *128*, 2546−2547.

(14) Callahan, J.; Kopecek, J. *Biomacromolecules* **2006**, *7*, 2347−2356.

(15) Azzaroni, O.; Mir, M.; Alvarez, M.; Tiefenauer, L.; Knoll, W. *Langmuir* **2008**, *24*, 2878−2883.

(16) Degrand, C.; Limoges, B.; Gautier, A.; Blankespoor, R. L. *Appl. Organomet. Chem.* **1993**, *7*, 233−241.

(17) Yang, X.-Q.; Guo, L.-H. *Anal. Chim. Acta* **2009**, *632*, 15−20.

(18) Anne, A.; Cambril, E.; Chovin, A.; Demaille, C. *Anal. Chem.* **2010**, *82*, 6353−6362.

(19) Chen, M.; Ghiggino, K. P.; Mau, A. W. H.; Rizzardo, E.; Thang, S. H.; Wilson, G. J. *Chem. Commun.* **2002**, 2276−2277.

(20) Pietsch, C.; Vollrath, A.; Hoogenboom, R.; Schubert, U. S. *Sensors* **2010**, *10*, 7979−7990.

(21) Duhamel, J. *Acc. Chem. Res.* **2006**, *39*, 953−960.

(22) Hu, J. M.; Li, C. H.; Cui, Y.; Liu, S. Y. *Macromol. Rapid Commun.* **2011**, *32*, 610−615.

(23) Tillman, E. S.; Roof, A. C.; Palmer, S. M.; Zarko, B. A.; Goodman, C. C.; Roland, A. M. *J. Chem. Educ.* **2006**, *83*, 1215−null.

(24) Bier, F. F.; Ehrentreich-Forster, E.; Dolling, R.; Eremenko, A. V.; Scheller, F. W. *Anal. Chim. Acta* **1997**, *344*, 119−124.

(25) Hromadov, M.; Salmain, M.; Sokolov, R.; Pospsil, L.; Jaouen, G. *J. Organomet. Chem.* **2003**, *668*, 17−24.

(26) Limoges, B.; Degrand, C.; Brossier, P. *J. Electroanal. Chem.* **1996**, *402*, 175−187.

(27) Meirim, M. G.; Neuse, E. W.; Caldwell, G. *J. Inorg. Organomet. Polym.* **1998**, *8*, 225−236.

(28) Nakadan, N.; Imabayashi, S.-i.; Watanabe, M. *Langmuir* **2004**, *20*, 8786−8791.

(29) Sun, G.; Xu, J.; Hagooly, A.; Rossin, R.; Li, Z.; Moore, D. A.; Hawker, C. J.; Welch, M. J.; Wooley, K. L. *Adv. Mater.* **2007**, *19*, 3157−3162.

(30) Fukukawa, K.-i.; Rossin, R.; Hagooly, A.; Pressly, E. D.; Hunt, J. N.; Messmore, B. W.; Wooley, K. L.; Welch, M. J.; Hawker, C. J. *Biomacromolecules* **2008**, *9*, 1329−1339.

(31) Welch, M. J.; Hawker, C. J.; Wooley, K. L. *J. Nucl. Med.* **2009**, *50*, 1743−1746.

(32) Wollenberger, U. *Biotechnol. Genet. Eng. Rev.* **1996**, *13*, 237−266.

(33) Kawahara, N.; Saito, J.; Matsuo, S.; Kaneko, H.; Matsugi, T.; Kashiwa, N. In *New Frontiers in Polymer Synthesis*; Springer-Verlag: Berlin, 2008; Vol. *217*, pp 79−119.

(34) Nishihara, H.; Murata, M. *J. Inorg. Organomet. Polym. Mater.* **2005**, *15*, 147−156.

(35) Ricci, F.; Lai, R. Y.; Plaxco, K. W. *Chem. Commun.* **2007**, 3768−3770.

(36) Wlassoff, W. A.; King, G. C. *Nucleic Acids Res.* **2002**, *30*, e58.

(37) Haas, O.; Velazquez, C. S.; Porat, Z. e.; Murray, R. W. *J. Phys. Chem.* **1995**, *99*, 15279−15284.

(38) Teertstra, S. J.; Lin, W. Y.; Gauthier, M.; Ingratta, M.; Duhamel, J. *Polymer* **2009**, *50*, 5456−5466.

(39) Zhou, N.; Zhang, Z.; Zhu, J.; Cheng, Z.; Zhu, X. *Macromolecules* **2009**, *42*, 3898−3905.

(40) Ren, L.; Hardy, C. G.; Tang, C. *J. Am. Chem. Soc.* **2010**, *132*, 8874−8875.

(41) Ren, L.; Hardy, C. G.; Tang, S.; Doxie, D. B.; Hamidi, N.; Tang, C. *Macromolecules* **2010**, *43*, 9304−9310.

(42) Ren, L.; Zhang, J.; Bai, X.; Hardy, C. G.; Shimizu, K. D.; Tang, C. *Chem. Sci.* **2012**, *3*, 580−583.

(43) Ren, L.; Zhang, J.; Hardy, C. G.; Tang, C. *Macromol. Rapid Commun.* **2012**, DOI: 10.1002/marc.201100732.

(44) Hardy, C. G.; Ren, L.; Zhang, J.; Tang, C. *Isr. J. Chem.* **2012**, DOI: 10.1002/ijch.201100110.

(45) Astruc, D.; Ornelas, C.; Ruiz, J. *Acc. Chem. Res.* **2008**, *41*, 841−856.

(46) Casado, C. M.; Gonzalez, B.; Cuadrado, I.; Alonso, B.; Moran, M.; Losada, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2135−2138.

(47) Cuadrado, I.; Casado, C. M.; Lobete, F.; Alonso, B.; Gonzalez, B.; Losada, J.; Amador, U. *Organometallics* **1999**, *18*, 4960−6969.

(48) Mayer, U. F. J.; Gilroy, J. B.; O'Hare, D.; Manners, I. *J. Am. Chem. Soc.* **2009**, *131*, 10382−10383.

(49) Gilroy, J. B.; Patra, S. K.; Mitchels, J. M.; Winnik, M. A.; Manners, I. *Angew. Chem., Int. Ed.* **2011**, *50*, 5851−5855.

(50) Horikoshi, R.; Mochida, T. *Eur. J. Inorg. Chem.* **2010**, *2010*, 5355−5371.

(51) Winnik, F. M.; Ottaviani, M. F.; Bossman, S. H.; Pan, W.; Garcia-Garibay, M.; Turro, N. J. *J. Phys. Chem.* **1993**, *97*, 12998−13005.

(52) Hawker, C. J.; Bosman, A. W.; Harth, E. *Chem. Rev.* **2001**, *101*, 3661−3688.

(53) Kamigaito, M.; Ando, T.; Sawamoto, M. *Chem. Rev.* **2001**, *101*, 3689−3745.

(54) Matyjaszewski, K., Ed. *Controlled/Living Radical Polymerization. From Synthesis to Materials*; American Chemical Society: Washington, DC, 2006; Vol. *944*.

(55) Matyjaszewski, K.; Xia, J. *Chem. Rev.* **2001**, *101*, 2921−2990.

(56) Moad, G.; Rizzardo, E.; Thang, S. H. *Aust. J. Chem.* **2005**, *58*, 379−410.

(57) High, L. R. H.; Holder, S. J.; Penfold, H. V. *Macromolecules* **2007**, *40*, 7157−7165.

(58) Turro, N. J.; Lem, G.; Zavarine, I. S. *Macromolecules* **2000**, *33*, 9782−9785.

(59) Hardy, C. G.; Ren, L.; Tamboue, T. C.; Tang, C. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, *49*, 1409−1420.

(60) Zheng, Y.; Yao, K.; Lee, J.; Chandler, D.; Wang, J.-F.; Wang, C.-P.; Chu, F.-X.; Tang, C. *Macromolecules* **2010**, *43*, 5922−5924.

(61) Dufour, B.; Tang, C.; Koynov, K.; Zhang, Y.; Pakula, T.; Matyjaszewski, K. *Macromolecules* **2008**, *41*, 2451−2458.

(62) Xia, J.; Gaynor, S. G.; Matyjaszewski, K. *Macromolecules* **1998**, *31*, 5958−5959.

(63) Wilbon, P. A.; Zheng, Y.; Yao, K.; Tang, C. *Macromolecules* **2010**, *43*, 8747−8754.

(64) Yao, K.; Wang, J.; Zhang, W.; Lee, J. S.; Wang, C.; Chu, F.; He, X.; Tang, C. *Biomacromolecules* **2011**, *12*, 2171−2177.

(65) Scott, D. R.; Becker, R. S. *J. Chem. Phys.* **1961**, *35*, 516−531.