Activators Regenerated by Electron Transfer for Atom Transfer Radical Polymerization of Styrene

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ABSTRACT: The amount of Cu-based catalysts in atom transfer radical polymerization (ATRP) of styrene has been reduced to a few ppm in the presence of the appropriate reducing agents such as FDA approved tin(II) 2-ethylhexanoate ($Sn(EH)_2$) or glucose. The reducing agents constantly regenerate ATRP activator, the Cu(I) species, from the Cu(II) species, formed during termination process, without directly or indirectly producing initiating species that generate new chains. Moreover, the reducing agents allow starting an ATRP with the oxidatively stable Cu(II) species. The reducing/reactivating cycle may also eliminate air or some other radical traps in the system. This new catalytic system is based on regeneration of the activators for an ATRP by electron transfer and therefore was named activators regenerated by electron transfer (ARGET) ATRP. The optimum amount of reducing agent and minimal amount of ATRP Cu catalyst depend on the particular system. For example, styrene was polymerized with 10 ppm of $CuCl_2$/Me_6TREN and 100 ppm of $Sn(EH)_2$ resulting in a polystyrene with $M_n = 63\,000$ ($M_{n,th} = 64\,000$) and $M_w/M_n = 1.17$.

Introduction

Atom transfer radical polymerization (ATRP)[1−3] is one of the most powerful controlled/living radical polymerization (CRP) techniques.[4,5] ATRP provides a very simple way to incorporate desired functionality to either end groups or distributed along a polymer backbone.[6−9] Many polymers with complex architecture, as well as hybrids with inorganic materials or bioconjugates, have been prepared by the introduction of haloesters, as ATRP initiators, via simple esterification reactions.[10−14] However, one of the disadvantages of ATRP, which limits its widespread industrial utilization, is that the transition metal complexes have to be removed from the reaction mixture and preferably recycled.[15] To reduce the residual transition metal in the final product, various techniques have been developed including adsorption, extraction, or immobilization.[15−22] However, the most attractive approach may simply be to decrease of the amount of the catalyst used in the reaction, providing that it has sufficient reactivity and imparts the desired level of control. Since CuBr/Me_6TREN complexes are ∼10 000 times more active than the originally used CuBr/bpy complexes, they allowed ATRP not only to be carried out at room temperature[23−25] but also to be conducted with much smaller amounts of copper.

A detailed inspection of the ATRP rate law (eq 1) indicates that the polymerization rate depends only on the ratio of concentrations of Cu(I) to X-Cu(II) and does *not* depend on the absolute concentration of the copper complexes.[26]

$$R_p = k_p[M][P^\bullet] = k_p[M]K_{eq}[I]_0\frac{[Cu^I]}{[X-Cu^{II}]} \qquad (1)$$

where k_p is the propagation rate constant; [M], [$P^\bullet$], and $[I]_0$ are concentrations of monomer, propagating species, and initiator, respectively; K_{eq} is the ATRP equilibrium constant; and $[Cu^I]/[X-Cu^{II}]$ is the molar ratio of activator to deactivator. Thus, in principle, one could reduce the absolute amount of copper complex to ppm or even ppb level, without affecting the polymerization rate.

However, a sufficient amount of deactivating species (i.e., X−Cu(II)) is always needed for well-controlled polymerization since both molecular weight distribution and initial molecular weight depend on the ratio of the propagation and deactivation rate constants and the concentration of deactivator, according to eq 2.

$$\frac{M_w}{M_n} = 1 + \frac{1}{DP_n} + \left(\frac{[R-X]_0 k_p}{k_{da}[X-Cu^{II}]}\right)\left(\frac{2}{p} - 1\right) \qquad (2)$$

where p is the conversion; $[R-X]_0$, and $[X-Cu^{II}]$ are the concentrations of initiator and deactivator, respectively; k_p and k_{da} are the propagation and deactivation rate constants; and DP_n is the degree of polymerization. To obtain polystyrene with $M_w/M_n \sim 1.2$ and DP ∼ 200 and 90% conversion at ∼100 °C, the amount of needed X−Cu(II) species is ∼2 ppm ($k_p \sim 10^3$ M^{-1} s^{-1} and $k_{da} \sim 10^7$ M^{-1} s^{-1}),[27,28] meaning that it could be reduced over 1000 times from a typical level.

However, one cannot just reduce the amount of Cu(I) 1000-fold because unavoidable radical termination reactions irreversibly consume activators, and reactions usually do not proceed to completion if the amount of Cu(I) initially added to the system is below 10 mol % of the initiator (i.e., all Cu(I) will be consumed if ∼10% of chains terminate). The amount of terminated chains depends on concentration of propagating radicals, $P^\bullet$, and the rate constant of termination, k_t, according to eq 3

$$-\Delta[Cu^I] = \Delta[P_t] = k_t[P^\bullet]^2 t \qquad (3)$$

where k_t is the termination rate constant, [$P^\bullet$] the concentration of propagating species, and t the time.

We have recently reported the development of a new efficient and convenient procedure for initiating an ATRP system where the activators are generated by electron transfer (AGET) ATRP. In this system, activating Cu(I) complexes are generated, in situ,

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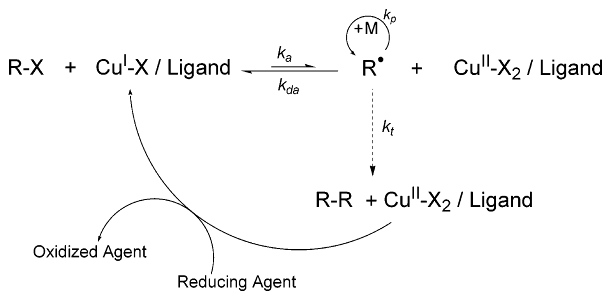
Scheme 1. Proposed Mechanism for Activators Regenerated by Electron Transfer for Atom Transfer Radical Polymerization (ARGET ATRP)



from oxidatively stable Cu(II) species by the action of reducing agents such as FDA approved tin(II) 2-ethylhexanoate[29] (Sn(EH)$_2$) or ascorbic acid.[30] These redox processes occur without formation of initiating radicals, or initiating species, and therefore pure copolymers with complex architecture (block, star, etc.) can be formed starting with the oxidatively stable catalyst precursor complex. AGET has therefore a strong advantage over simultaneous normal and reverse initiated ATRP (SR&NI ATRP), in which block copolymers are always contaminated by a fraction of homopolymers formed by direct initiation from the added free radical initiator.[30−32]

In this paper, we present a new technique for conducting ATRP, based on activators regenerated by electron transfer (ARGET). This method provides a continuous controlled polymerization with a significant reduction of the amount of copper based catalyst complex (down to ∼10 ppm) due to a constant regeneration of the Cu(I) activator species by environmentally acceptable reducing agents, which compensate for any loss of Cu(I) by termination (Scheme 1).

We report here the successful ARGET ATRP of styrene initiated by ethyl 2-bromoisobutyrate and catalyzed by minute amounts of CuCl/Me$_6$TREN complexes in the presence of FDA approved tin(II) 2-ethylhexanoate or glucose.

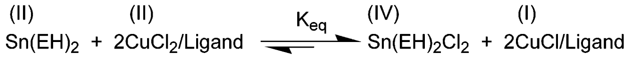
Experimental Section

Chemicals. Styrene (St) (Aldrich, 99%) and *n*-butyl acrylate (*n*BA) (Acros 99+%) were passed through a column filled with neutral alumina, dried over calcium hydride, and distilled under reduced pressure. Tris(2-(dimethylamino)ethyl)amine (Me$_6$TREN) was synthesized following the previously reported procedure.[23] Ethyl 2-bromoisobutyrate (EtBrIB) (Acros, 98%), copper(II) chloride (Acros, 99%), tin(II) 2-ethylhexanoate (Sn(EH)$_2$) (Aldrich), glucose (α-D-glucose, anhydrous, Aldrich, 96%), and anisole (Aldrich, 99%) were used as received.

General Procedure for ARGET ATRP of Styrene (Targeting Number-Average Degree of Polymerization (DP$_n$) of 200) with 50 ppm of Cu. Degassed styrene (5.0 mL, 44 mmol) and anisole (1.5 mL) were transferred via degassed syringes to a dry, thoroughly purged by flushing with nitrogen, Schlenk flask. Next, the CuCl$_2$ (0.29 mg, 0.22×10^{-2} mmol)/Me$_6$TREN (0.57 μL, 0.22×10^{-2} mmol)) complex in degassed anisole (0.5 mL) was added. The resulting mixture was stirred for 10 min, and then a purged solution of Sn(EH)$_2$ (7.0 μL, 2.2×10^{-2} mmol) and Me$_6$TREN (5.7 μL, 2.2×10^{-2} mmol) in anisole (0.5 mL) was added. Then EtBrIB (32.1 μL, 21.9×10^{-2} mmol) initiator was added to initiate the polymerization. An initial sample was taken, and the sealed flask was placed in thermostated oil bath at 110 °C. Samples were taken at timed intervals and analyzed by gas chromatography (GC) and gel permeation chromatography (GPC) to follow the progress of the reaction. The polymerization was stopped after 7.6 h ($M_{n,GPC} = 12700$, $M_w/M_n = 1.11$, conversion = 59%) by opening the flask and exposing the catalyst to air.

General Procedure for ARGET ATRP of Styrene under Limited Amount of Air (DP$_n$ = 200 and 50 ppm of Cu). Styrene (5.0 mL, 44 mmol) and anisole (1.5 mL) were added to an open Schlenk flask. Next, the CuCl$_2$ (0.29 mg, 0.22×10^{-2} mmol)/Me$_6$TREN (0.57 μL, 0.22×10^{-2} mmol) complex in anisole (0.5 mL) was added. The resulting mixture was stirred for 10 min, and then a solution of Sn(EH)$_2$ (7.0 μL, 2.2×10^{-2} mmol) and Me$_6$TREN (1.7 μL, 0.7×10^{-2} mmol) in anisole (0.5 mL) was added. Finally the initiator, EtBrIB (29.7 μL, 20.3×10^{-2} mmol), was added. The Schlenk flask was sealed and, after taking an initial sample, placed in thermostated oil bath at 110 °C. Samples were taken at timed intervals and analyzed by GC and GPC to follow the progress of the reaction. The polymerization was stopped after 20 h ($M_{n,GPC} = 15\,900$, $M_w/M_n = 1.28$, conversion = 76%) by opening the flask and exposing the catalyst to air.

Scheme 2. Reduction of Cu(II) to Cu(I) by Tin(II) 2-Ethylhexanoate



$$\overset{(II)}{\mathrm{Sn(EH)_2}} + \overset{(II)}{\mathrm{2CuCl_2/Ligand}} \underset{}{\overset{K_{eq}}{\rightleftharpoons}} \overset{(IV)}{\mathrm{Sn(EH)_2Cl_2}} + \overset{(I)}{\mathrm{2CuCl/Ligand}}$$

Extension of Polystyrene (PS) Macroinitiator with St by ARGET ATRP. A PS macroinitiator ($M_n = 16\,000$, PDI = 1.18) (2.0 g, 0.12 mmol), which was prepared by ARGET ATRP with 15 ppm of copper, was dissolved in styrene monomer (St, 5.72 mL, 49.9 mol) in a 25 mL Schlenk flask and bubbled with nitrogen for 15 min. Next, a solution of the CuCl$_2$ (10.1×10^{-2} mg, 0.75×10^{-3} mmol)/Me$_6$TREN (0.20 μL, 0.75×10^{-3} mmol) complex in degassed anisole (2.8 mL) was added. The resulting mixture was stirred for 10 min, and then 4.1 μL (1.2×10^{-2} mmol) of a purged solution of Sn(EH)$_2$ and Me$_6$TREN (3.3 μL, 1.2×10^{-2} mmol) in anisole (2.8 mL) was added. An initial sample was taken, and the sealed flask was placed in thermostated oil bath at 110 °C. Samples were taken at timed intervals and analyzed by GC and GPC. The polymerization was stopped after 42.3 h ($M_{n,GPC} = 54\,000$, $M_w/M_n = 1.22$, conversion = 81%) by opening the flask and exposing the catalyst to air.

Analysis. Molecular weight and polydispersity were determined by GPC, conducted with a Waters 515 pump and a Waters 2414 differential refractometer using PSS columns (Styrogel 10^5, 10^3, 10^2 Å) in THF as an eluent at 35 °C and at a flow rate of 1 mL/min. Linear polystyrene standards were used for calibration. Conversion of styrene was determined using a Shimadzu GC 14-A gas chromatograph equipped with a FID detector using a J&W Scientific 30 m DB WAX Megabore column with anisole as an internal standard. Injector and detector temperatures were kept constant at 250 °C. Analysis was carried out isothermally at 60 °C for 2 min followed by an increase of temperature to 140 °C at a heating rate of 40 °C/min and holding at 140 °C for 2 min. Conversion was calculated by detecting the decrease of the monomer peak area relative to the peak areas of the standards.

Results and Discussion

A new method has been developed that allows a homogeneous ATRP to be conducted with very low concentration of catalyst in the reaction. This new catalytic system is based on continuous regeneration of the activator by electron transfer (Scheme 1), which compensates for the loss of Cu(I) by termination reactions. This allows a significant reduction in the amount of copper species (down to ∼10 ppm from typically 1000 ppm), or any other catalyst complex, employed in ATRP. In our studies, tin(II) 2-ethylhexanoate (Sn(EH)$_2$) or glucose was used. Sn(EH)$_2$ and glucose are examples of several possible reducing agents which can be used for in-situ reduction of Cu(II) to Cu(I) (Scheme 2), without formation of radicals, or radical precursors, that can initiate new chains.[29,30]

The reducing agent also allows starting an ATRP with the oxidatively stable Cu(II) species. It may further allow to tolerate a limited amount of air or other radical traps in the system. This significantly simplifies the steps required for prepurification of ATRP systems.

Table 1. Experimental Conditions and Properties of PS Prepared by ARGET ATRP: Effect of Amount of Copper[a]

	molar ratios										
entry	St	EtBrIB	$CuCl_2$	Me_6TREN	$Sn(EH)_2$	Cu [ppm]	time (min)	conv (%)	$M_{n,theo}$[b]	$M_{n,GPC}$	M_w/M_n
1	200	1	0.1	0.1	0.1	500	1020	67	14 000	17 000	1.12
2	200	1	0.01	0.1	0.1	50	460	59	12 300	12 700	1.11
3	200	1	0.003	0.1	0.1	15	1830	90	18 700	20 600	1.15
4	200	1	0.001	0.03	0.1	5	1440	45	9 000	7 200	1.28
5	200	1	0.0002	0.1	0.1	1	1230	63	12 600	12 500	1.64
6	1000	1	0.1	0.1	0.1	100	2630	69	68 900	71 800	1.18
7	1000	1	0.01	0.1	0.1	10	1590	64	64 000	63 000	1.17

[a] $[St]_0 = 5.82$ M; $T = 110$ °C, in anisole (0.5 vol equiv vs monomer). [b] $M_{n,theo} = ([M]_0/[EtBrIB]_0) \times$ conversion.

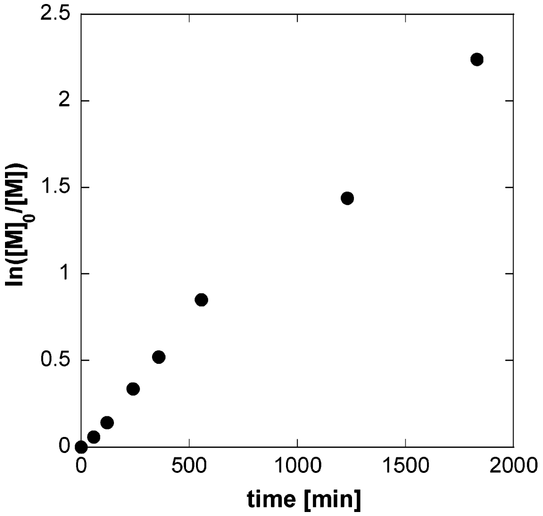


Figure 1. Kinetic plot for ARGET ATRP of styrene with 15 ppm of copper. Experimental conditions: $St/EtBrIB/Cu(II)/Me_6TREN/Sn(EH)_2 = 200/1/0.003/0.1/0.1$; $[St]_0 = 5.82$ M, $T = 110$ °C, in anisole (0.5 vol equiv vs monomer) (Table 1, entry 3).

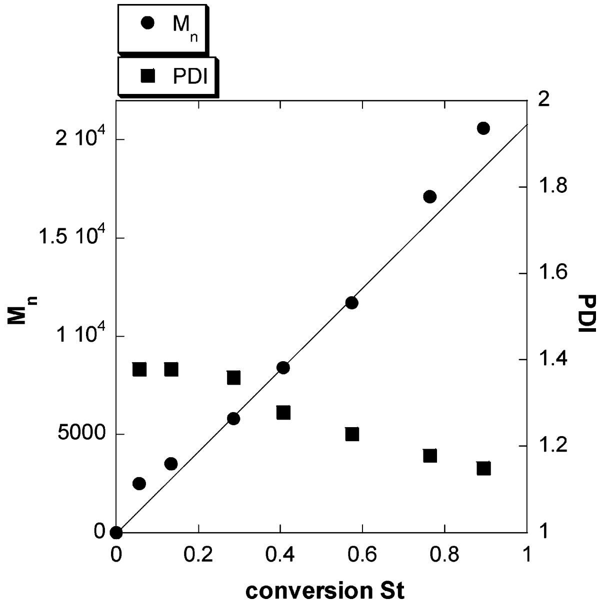


Figure 2. PS molecular weight and polydispersity as a function of conversion in ARGET ATRP of styrene with 15 ppm of copper. Experimental conditions: $St/EtBrIB/Cu(II)/Me_6TREN/Sn(EH)_2 = 200/1/0.003/0.1/0.1$; $[St]_0 = 5.82$ M, $T = 110$ °C, in anisole (0.5 vol equiv vs monomer) (Table 1, entry 3).

ARGET ATRP of styrene was initiated by ethyl 2-bromoisobutyrate and catalyzed by minute amounts of $CuCl/Me_6TREN$ complexes in the presence of FDA approved tin(II) 2-ethylhexanoate or glucose. The reduced levels of copper in the final polymer(s) could eliminate or significantly simplify postpolymerization purification of the products of the reactions. To investigate chain-end functionality of synthesized polymers, PS macroinitiator prepared by ARGET ATRP was extended with styrene under similar conditions. Additionally, to demonstrate the universality and simplicity of new catalytic system ARGET ATRP of styrene was carried out in the presence of limited amount of air.

Effect of the Amount of Added Copper Complex on ARGET ATRP of Styrene Targeting $DP_n = 200$ and $DP_n = 1000$. In first series of experiments, targeting a final $DP_n = 200$, styrene was polymerized in the presence of a constant amount of $Sn(EH)_2$, corresponding to 10 mol % of the initiator, in the presence of different concentrations of the Cu-based catalyst. The amount of copper was varied from a "high concentration" of 500 ppm down to 1 ppm vs monomer. The reaction conditions and results of these polymerizations are shown in Table 1 (entries 1−4). Figure 1 presents the kinetic plot for the polymerization of styrene with 15 ppm of copper (Table 1, entry 3, reported ppm values relate to the molar ratios and therefore 15 mol ppm corresponds to 9 ppm of Cu vs monomer by weight). According to the results shown in Table 1, the rate of polymerization decreased slightly with reduction in the concentration of the copper species. Figure 2 shows an excellent control over molecular weights and polydispersities in this system. Figure 3 shows a smooth shift of the entire molecular weight distribution toward higher molecular weights. With only 1 ppm of copper in the reaction medium, the molecular weight of the polymer was still well controlled, but a higher PDI (1.64) was observed (Table 1, entry 5).

One of the limitations of the preparation of high molecular weight polystyrene by ATRP was that the polystyryl radical could be oxidized to a carbocation by the Cu(II) species. This was proposed as the main side reaction limiting the formation of well-defined high molecular weight polystyrenes by ATRP.[33,34] However, ARGET can be run with very small amounts of Cu(II) species, and therefore the synthesis of high molecular weight polystyrenes is now more feasible. Therefore, styrene was polymerized with 10 ppm of copper vs monomer while targeting a final $DP_n = 1000$. Figures 4 and 5 demonstrate application of ARGET to formation of higher molecular weight polystyrenes. The amount of Cu can be reduced down to 10 ppm with preservation of an appropriate level of control (Table 1, entry 7).

Effect of the Amount of Ligand on ARGET ATRP of Styrene. Styrene was polymerized with the same amounts of initiator, reducing agent, and 50 ppm of copper but different amounts of Me_6TREN. When 10-fold excess of ligand was used (Table 2, entry 1), polymerization was well controlled resulting in a polystyrene with $M_n = 12\,700$ ($M_{n,th} = 12\,300$) and $M_w/M_n = 1.11$. When amount of ligand was decreased to 3-fold excess over Cu (Table 2, entry 2), molecular weight was still well controlled forming a polymer with a $M_n = 6900$ ($M_{n,th} =$

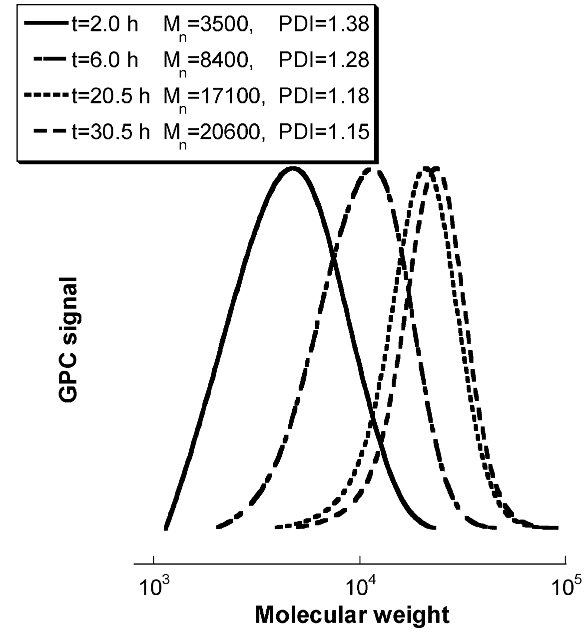


Figure 3. Evolution of molecular weight distribution during ARGET ATRP of styrene with 15 ppm of copper. Experimental conditions: St/EtBrIB/Cu(II)/Me_6TREN/$Sn(EH)_2$ = 200/1/0.003/0.1/0.1; $[St]_0$ = 5.82 M, T = 110 °C, in anisole (0.5 vol equiv vs monomer) (Table 1, entry 3).

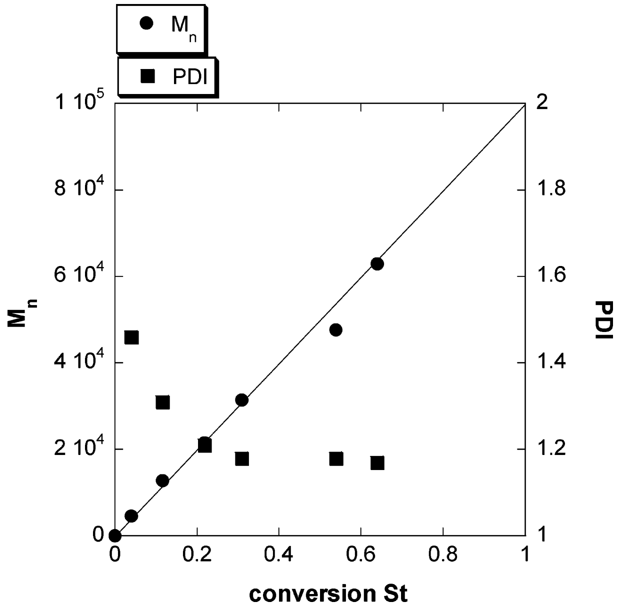


Figure 4. PS molecular weight and polydispersity as a function of conversion in ARGET ATRP of styrene with 10 ppm of copper. Experimental conditions: St/EtBrIB/Cu(II)/Me_6TREN/$Sn(EH)_2$ = 1000/1/0.003/0.1/0.1; $[St]_0$ = 5.82 M, T = 110 °C, in anisole (0.5 vol equiv vs monomer) (Table 1, entry 7).

7100), but polydispersities were slightly higher, M_w/M_n = 1.20. When a stoichiometric amount of Me_6TREN to Cu was used (Table 2, entry 3) in the ARGET ATRP reactions, low molecular weight oligomers were formed. This loss of the control was probably due to complexation of Cu(I) with excess styrene.[35,36] Loss of the complex, $CuBr_n$/Me_6TREN, can be also due to a competitive complexation of Me_6TREN with the stronger Lewis acids, $SnCl_2(EH)_2$, formed in the reactivation process (Scheme 2). Therefore, an excess ligand was used in all experiments to provide a sufficient control.

Effect of Temperature on ARGET ATRP of Styrene. Figure 6 presents the kinetic plot for a polymerization of styrene with 15 ppm of copper complex targeting DP = 200 at two different temperatures, 60 and 110 °C (Table 2, entries 4 and 5). The rate of polymerization is faster at 110 °C, although both reactions are well controlled, yielding polymer with precisely controlled molecular weight and low PDI (1.18).

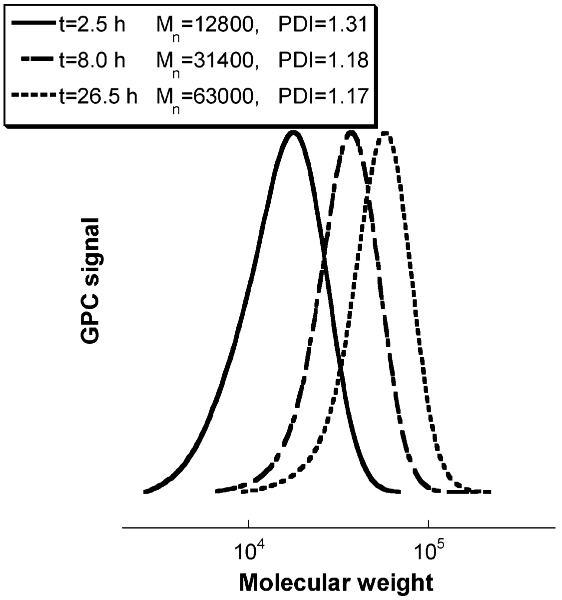


Figure 5. Evolution of molecular weight distribution during ARGET ATRP of styrene with 10 ppm of copper. Experimental conditions: St/EtBrIB/Cu(II)/Me_6TREN/$Sn(EH)_2$ = 1000/1/0.003/0.1/0.1; $[St]_0$ = 5.82 M, T = 110 °C, in anisole (0.5 vol equiv vs monomer) (Table 1, entry 7).

Polymerization in the Presence of a Limited Amount of Air. Cu(I)/Me_6TREN complexes are very active ATRP catalysts and therefore are easily oxidized by air. However, the resulting Cu(II) species can still be regenerated to the activating Cu(I) state by the action of $Sn(EH)_2$. Thus, in one experiment (Table 2, entry 6), no nitrogen purging was applied to the reaction medium, but reducing agent, $Sn(EH)_2$, was used to compensate for the presence of any oxygen impurities. As shown in Figure 7, a short induction period was observed, but then polymerization started and good control over molecular weight and polydispersities (PDI = 1.28) was observed (Figure 8).

Extension of PS Macroinitiator with St by ARGET ATRP. To investigate chain-end functionality, PS macroinitiator was prepared and then extended, using similar conditions, with styrene by the ARGET ATRP method. Both polymerizations were carried out with 15 ppm of copper catalyst. All the experimental conditions and properties of synthesized polymers are shown in Table 3. Chain extension of the PS macroinitiator with styrene using ARGET ATRP with 15 ppm of copper was very efficient ($M_{n,GPC}$ = 54 000, $M_{n,th}$ = 47 500 M_w/M_n = 1.22). Figure 9 presents the SEC chromatograms recorded after each step of synthesis. The reactions were well controlled, as evidenced by the monomodal GPC traces.

ARGET ATRP of Styrene in the Presence of Glucose as a Reducing Agent. ARGET ATRP of styrene was also carried out in the presence of glucose as a reducing agent. The amount of ligand, Me_6TREN, was constant (10 mol % vs initiator), but the amount of copper was varied from 10 to 250 ppm vs monomer. The reaction conditions and final results of these polymerizations are shown in Table 4 (entries 1−3). According to the results shown in Table 4, the rate of polymerization decreased as the amount of copper increased, plausibly because glucose, as a relatively weak reducing agent, could not convert all Cu(II) species to Cu(I) state. Both Table 4 and Figure 10

Table 2. Experimental Conditions and Properties of PS Prepared by ARGET ATRP: Effect of Ligand, Temperature, and Air

	molar ratios										
entry	M	EtBrIB	$CuCl_2$	Me_6TREN	$Sn(EH)_2$	Cu [ppm]	time (min)	conv (%)	$M_{n,theo}$[d]	$M_{n,GPC}$	M_w/M_n
1[a]	200	1	0.01	0.1	0.1	50	460	59	12 300	12 700	1.11
2[a]	200	1	0.01	0.03	0.1	50	460	34	7 100	6 900	1.20
3[a]	200	1	0.01	0.01	0.1	50	1000	44	9 200	*e*	
4[a]	200	1	0.003	0.1	0.1	15	1230	76	15 300	17 100	1.18
5[b]	200	1	0.003	0.1	0.1	15	3150	24	4 800	4 500	1.18
6[c]	200	1	0.01	0.03	0.1	50	1415	76	15 200	15 900	1.28

[a] $[St]_0 = 5.82$ M; $T = 110$ °C, in anisole (0.5 vol equiv vs monomer). [b] $[St]_0 = 5.82$ M; $T = 60$ °C, in anisole (0.5 vol equiv vs monomer). [c] $[St]_0 = 5.82$ M; $T = 110$ °C, in anisole (0.5 vol equiv vs monomer), reaction under limited amount of air. [d] $M_{n,\ theo} = ([M]_0/[EtBrIB]_0) \times$ conversion. [e] Oligomers.

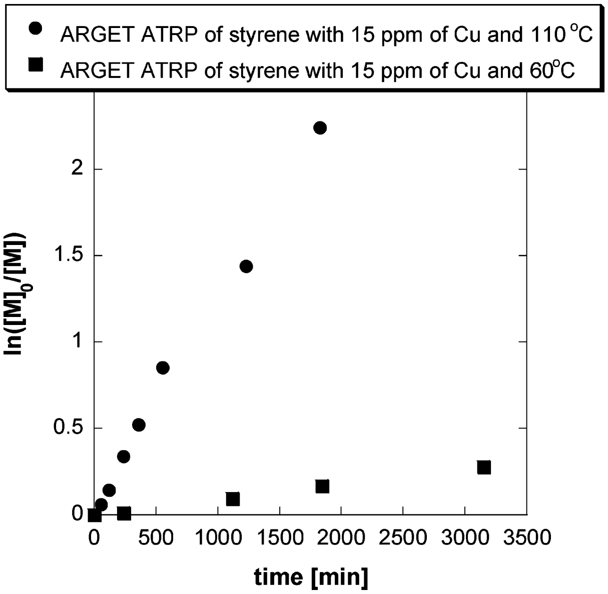


Figure 6. Kinetic plot for ARGET ATRP of styrene with 15 ppm of copper and two different temperatures 60 and 110 °C. Experimental conditions: $St/EtBrIB/Cu(II)/Me_6TREN/Sn(EH)_2 = 200/1/0.003/0.1/0.1$; $[St]_0 = 5.82$ M in anisole (0.5 vol equiv vs monomer) (Table 2, entries 4 and 5).

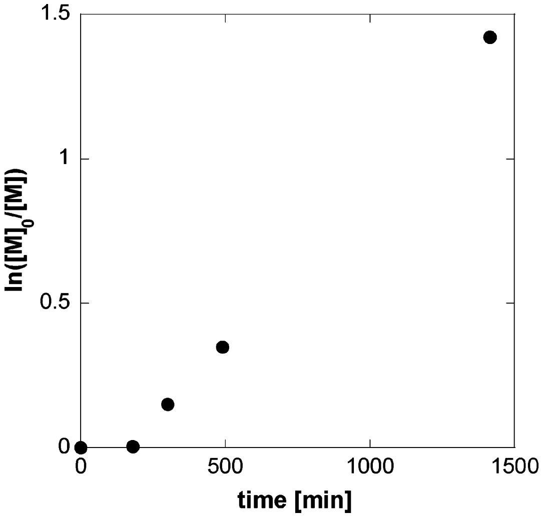


Figure 7. Kinetic plot for ARGET ATRP of styrene with 50 ppm of copper in the presence of limited amount of air. Experimental conditions: $St/EtBrIB/Cu(II)/Me_6TREN/Sn(EH)_2 = 200/1/0.01/0.1/0.1$; $[St]_0 = 5.82$ M, $T = 110$ °C, in anisole (0.5 vol equiv vs monomer) (Table 2, entry 6).

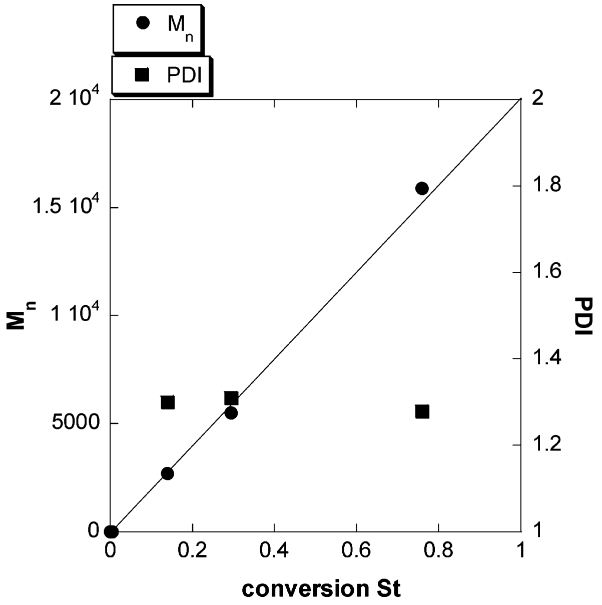


Figure 8. PS molecular weight and polydispersity as a function of conversion in ARGET ATRP of styrene with 50 ppm of copper in the presence of limited amount of air. Experimental conditions: $St/EtBrIB/Cu(II)/Me_6TREN/Sn(EH)_2 = 200/1/0.01/0.1/0.1$; $[St]_0 = 5.82$ M, $T = 110$ °C, in anisole (0.5 vol equiv vs monomer) (Table 2, entry 6).

show excellent control over molecular weight and molecular weight distribution.

Conclusions

It has been demonstrated that in ARGET ATRP the amount of Cu species in ATRP can be reduced down to a few ppm without losing control over the polymerization, if an appropriate amount of an additional reducing agent is used to account for catalyst oxidation by termination. There are several requirements for an efficient ARGET ATRP.

- The redox process should occur without generation of initiating radicals.
- While the reducing agent may also be involved in an atom transfer process (this would generate a dual catalytic system, e.g., bimetallic catalysis), a sufficient amount of deactivating species (i.e., X−Cu(II)) is needed for control. The final molecular weight distribution and initial molecular weight both depend on the ratio of propagation to deactivation rate constants, according to eqs 1 and 2.
- The position of the equilibrium between the reducing species and the true ATRP catalyst should allow for the continued presence of a sufficient amount of Cu(II) species. This sets the overall rate of ATRP.
- The concentration of reducing agent added to the reaction should account for the sum of the amount of the Cu(II) species to be activated, the amount of air or other radical traps present in the system, and the amount of terminated chains generated during the polymerization reaction.
- The minimal amount of active ATRP catalyst depends on the particular system and can be less than 10 ppm, significantly lower than in any other reported ATRP polymerizations.

Table 3. Experimental Conditions and Properties of PS Macroinitiator and after Extension with St Using ARGET ATRP

		molar ratios										
entry		M	initiator	$CuCl_2$	Me_6TREN	$Sn(EH)_2$	Cu [ppm]	time (min)	conv (%)	$M_{n,theo}$[c]	$M_{n,GPC}$	M_w/M_n
1	PS[a]	200	1	0.003	0.1	0.1	15	1180	80	16 600	16 000	1.18
2	PS-*b*-PS[b]	400	1	0.006	0.1	0.1	15	2540	81	47 500	54 000	1.22

[a] Initiator: EtBrIB; $[St]_0 = 5.82$ M; $T = 110$ °C, in anisole (0.5 vol equiv vs monomer). [b] Initiator: PS (entry 1); $[St]_0 = 4.80$ M; $T = 110$ °C, in anisole (1 vol equiv vs monomer). [c] $M_{n,\ theo} = ([M]_0/[initiator]_0) \times$ conversion.

Table 4. Experimental Conditions and Properties of PS Prepared by ARGET ATRP in the Presence of Glucose[a]

	molar ratios										
entry	St	EtBrIB	$CuCl_2$	Me_6TREN	glucose	Cu [ppm]	time (min)	conv (%)	$M_{n,theo}$[b]	$M_{n,GPC}$	M_w/M_n
1	200	1	0.05	0.1	0.1	250	1245	65	13 500	13 700	1.18
2	200	1	0.01	0.1	0.1	50	1350	80	16 600	18 000	1.23
3	200	1	0.002	0.1	0.1	10	1320	80	16 600	17 500	1.27

[a] $[St]_0 = 5.82$ M; $T = 110$ °C, in anisole (0.5 vol equiv vs monomer). [b] $M_{n,theo} = ([M]_0/[EtBrIB]_0) \times$ conversion.

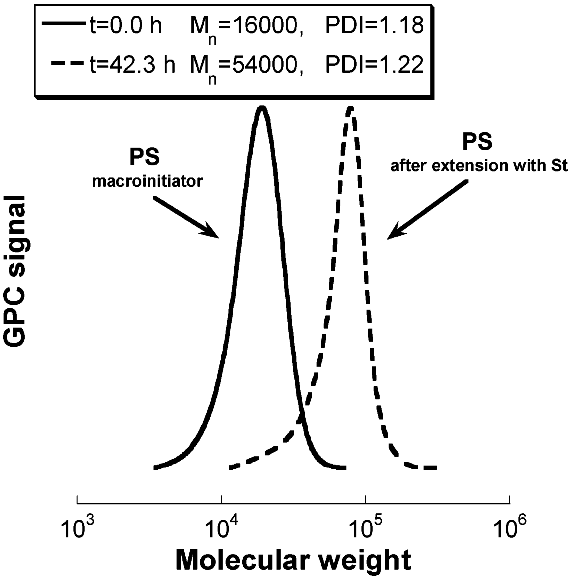


Figure 9. GPC traces of PS macroinitiator before and after chain extension with St. Experimental conditions for preparation of PS macroinitiator: $St/EtBrIB/Cu(II)/Me_6TREN/Sn(EH)_2 = 200/1/0.003/0.1/0.1$; $[St]_0 = 5.82$ M, $T = 110$ °C, in anisole (0.5 vol equiv vs monomer) and for extension with styrene: $St/PS/Cu(II)/Me_6TREN/Sn(EH)_2 = 400/1/0.006/0.1/0.1$; $[St]_0 = 4.80$ M, $T = 110$ °C, in anisole (1.0 vol equiv vs monomer) (Table 3, entries 1 and 2).

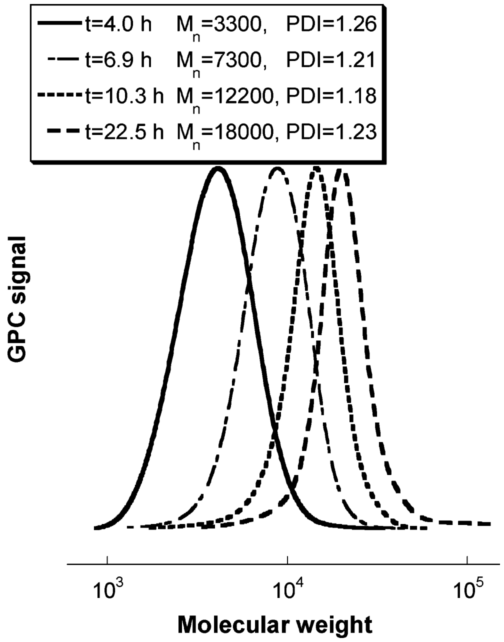


Figure 10. Evolution of molecular weight distribution during ARGET ATRP of styrene with 50 ppm of copper in the presence of glucose. Experimental conditions: $St/EtBrIB/Cu(II)/Me_6TREN/glucose = 200/1/0.01/0.1/0.1$; $[St]_0 = 5.82$ M, $T = 110$ °C, in anisole (0.5 vol equiv vs monomer) (Table 4, entry 2).

ARGET ATRP is a significant improvement over traditional ATRP, since it can be carried out with a drastically reduced amount of the transition metal catalyst in the reaction medium. FDA approved $Sn(EH)_2$ and other environmentally benign reducing agents, such as sugars (e.g., glucose), allow continuous reactivation of the ATRP catalyst complex. In this report, the simplicity of ARGET ATRP was illustrated by applying the new catalytic system to the polymerization of styrene. Polymerization of styrene, with catalyst concentration as low as 5 ppm of Cu, resulted in the formation of well-defined polymers with controlled degree of polymerization and narrow molecular weight distribution. Polymerization conducted with only 1 ppm of Cu was still well controlled, but higher polydispersities were observed. Chain extension using PS macroinitiator, prepared by ARGET ATRP, was efficient, demonstrating that ARGET ATRP can be applied to a successful synthesis of block copolymers (will be presented in another report). The use of reducing agents allows starting ATRP with the oxidatively stable Cu(II) species; it may also compensate for the presence of air or some other radical traps in the system. The development of this new catalytic system, ARGET ATRP, is a huge step toward development of a viable process for industrial scale production, since it uses a drastically reduced amount of Cu species in its oxidatively stable form, environmentally friendly reducing agents and can be performed in the presence of limited amounts of air.

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