Controlled/"Living" Radical Polymerization. Kinetics of the Homogeneous Atom Transfer Radical Polymerization of Styrene

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Abstract: The homogeneous atom transfer radical polymerization (ATRP) of styrene using solubilizing 4,4′-dialkyl substituted 2,2′-bipyridines yielded well-defined polymers with $M_w/M_n \leq 1.10$. The polymerizations exhibited an increase in molecular weight in direct proportion to the ratio of the monomer consumed to the initial initiator concentration and also exhibited internal first-order kinetics with respect to monomer concentration. The optimum ratio of ligand-to-copper(I) halide for these polymerizations was found to be 2:1, which tentatively indicates that the coordination sphere of the active copper(I) center contains two bipyridine ligands. The exclusive role for this copper-(I) complex in ATRP is atom transfer, since at typical concentrations that occur for these polymerizations ($\approx 10^{-7}$−10^{-8} M), polymeric radicals were found not to react with the copper(I) center in any manner that enhanced or detracted from the observed control. ATRP also exhibited first-order kinetics with respect to both initiator and copper(I) halide concentration; however, the polymerization kinetics were not simple inverse first-order with respect to the initial copper(II) halide concentration. The latter observation was found to be due to the persistent radical effect, which resulted in an increase in copper(II) concentration during the initial stages of the polymerization. This phenomenon also has the effect of regulating the polymerization by ensuring that the rate of radical combination and/or disproportionation is sufficiently less than the rate of propagation.
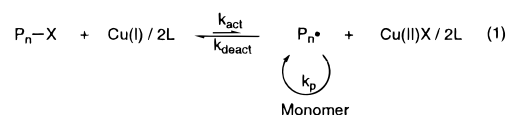
Introduction

Free-radical polymerization is one of the most important commercial processes leading to high molecular weight polymers, because a wide variety of monomers can be polymerized and copolymerized under relatively simple experimental conditions.[2] While free-radical polymerizations require the absence of oxygen, they can be conducted using water as a solvent or additive. A significant drawback to these polymerizations, however, is that they yield polymers with uncontrolled molecular weights and high polydispersities, which precludes the synthesis of well-defined polymers with low polydispersities and complex architectures.[3]

Termination by radical combination or disproportionation, which occurs at diffusion controlled rates, is unavoidable for radical chain reactions; however, the impact of this reaction upon the final product of radical polymerizations can be minimized. In analogy to controlled/"living" cationic polymerizations,[4] radical polymerizations can become controlled under conditions in which a low, stationary concentration of the active species is maintained and a fast, dynamic equilibrium is established between the active and dormant species.[5]

One such controlled/"living" radical polymerization is atom transfer radical polymerization (ATRP).[6,7] In this polymeriza-

tion a copper(I) complex, CuX/2L (X = Cl or Br, and L = 2,2′-bipyridine [bipy] or a 4,4′-disubstituted-2,2′-bipyridine) activates reversibly the dormant polymer chains via a halogen atom transfer reaction (eq 1), and it is this dynamic equilibrium which is responsible for the controlled behavior of the polymerizations. As reported, the homogeneous ATRP of styrene,

$$P_n\text{−}X \ + \ \text{Cu(I)} / 2L \ \underset{k_{deact}}{\overset{k_{act}}{\rightleftharpoons}} \ P_n{}^\bullet \ + \ \text{Cu(II)X} / 2L \quad (1)$$

$$\left(\downarrow k_p\right)$$
$$\text{Monomer}$$

acrylates, and methacrylates can yield polymers with predetermined degrees of polymerization up to DP ≈ 100 and polydispersities, M_w/M_n, as low as 1.04 and 1.05.[7] Other well-established, controlled radical polymerization systems include the following: TEMPO/nitroxyl radical-mediated polymerizations of styrenes,[8,9] ruthenium/aluminum-based polymerizations of methacrylates,[10] and cobalt-mediated polymerizations of acrylates.[11,12]

The remarkable results found for homogeneous ATRP prompted us to investigate the system further in order to understand the reasons for the high degree of control. Initial kinetic studies on the ATRP of styrene using heterogeneous conditions (CuBr/2bipy) showed that the rate law for the polymerization had kinetics orders of 1, 0.4, and 0.6 with respect to initiator, copper(I) catalyst, and ligand, respectively.[13] Most

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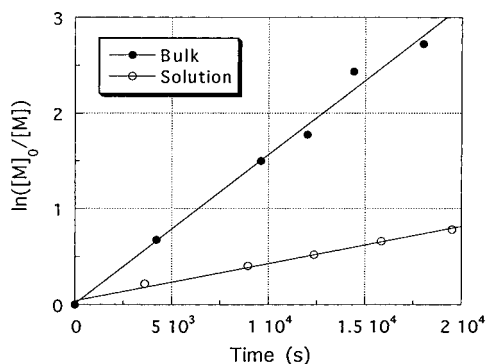(13) Wang, J. S.; Matyjaszewski, K. *Macromolecules* **1995**, *28*, 7901.

Figure 1. Semilogarithmic kinetic plots for the bulk and solution ATRPs of styrene at 110 °C. Bulk: $[\text{styrene}]_0 = 8.7$ M; $[\text{CuBr}]_0 = [\text{dNbipy}]_0/2 = 0.087$ M; $[\text{1-PEBr}]_0 = 0.087$ M. 50% (v/v) solution in diphenyl ether: $[\text{styrene}]_0 = 4.3$ M; $[\text{CuBr}]_0 = [\text{dNbipy}]_0/2 = 0.045$ M; $[\text{1-PEBr}]_0 = 0.045$ M. k_{app} (bulk) $= 1.6 \times 10^{-4}$ s^{-1}; k_{app} (solution) $= 3.9 \times 10^{-5}$ s^{-1}.
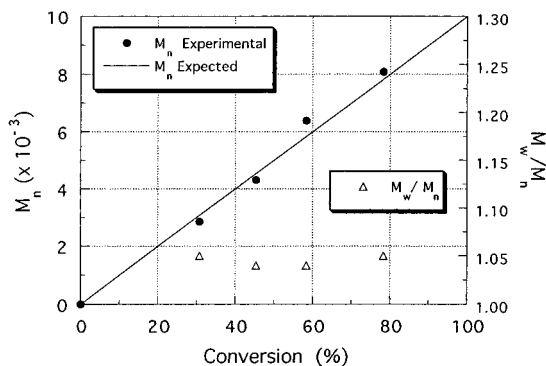

Figure 2. The dependence of molecular weight, M_n, and molecular weight distribution, M_w/M_n, upon monomer conversion for the bulk ATRP of styrene at 110 °C: $[\text{CuBr}]_0 = [\text{1-PEBr}]_0 = [\text{dNbipy}]_0/2 = 0.087$ M.

likely, the heterogeneity of the system was responsible for the fractional orders, and, therefore, it was difficult to explain their precise physical meanings. Here, we report a kinetic investigation of the homogeneous ATRP of styrene including the reaction orders of each component, the role of the deactivator in this system (Cu(II) halides), and the temperature dependence of the polymerization rate.

Results and Discussion

When a solution of styrene and 1-phenylethyl bromide [1-PEBr] in a 100:1 mole ratio, 1 equiv of CuBr relative to initiator, and 2 equivs of 4,4′-di-(5-nonyl)-2,2′-bipyridine [dNbipy] per copper was heated at 110 °C, the solution progressively became viscous. The reaction mixture was homogeneous when the ligand used was dNbipy or 4,4′-di-*n*-heptyl-2,2′-bipyridine [dHbipy], and there was no quantitative difference between either of the two polymerizations. The polymerizations were heterogeneous, yet darkly colored, when the ligand used was 4,4′-di-*tert*-butyl-2,2′-bipyridine [dTbipy], which indicated appreciable solubility of the copper(I) complex in the polymerization medium. As shown in Figures 1 and 2, the polymerization rate for the example polymerization was first order with respect to monomer concentration, and the number-averaged molecular weight (M_n) of the polymer evolved linearly with conversion. Also from Figure 2, one observes that the experimentally determined molecular weights were very close to the expected molecular weights based upon $([\text{M}]_0 - [\text{M}]_t)/[\text{In}]_0$. Essentially identical behavior was observed when the same polymerization was conducted using a solvent such as

Table 1. ATRP with Different Additives[c]

additive[a]	time (h)	% conv	M_n expected	M_n GPC	M_w/M_n
none	7	70	7140	5900	1.07
ethylene carbonate	4	65	6520	7220	1.13
H$_2$O	6	60	5960	7740	1.09
CH$_3$OH	6	60	5950	7480	1.18
CH$_3$CN	6	63	6300	8430	1.12
pyridine	15	35	3480	5340	1.27
Ph$_3$P[b]	15	1	100	1710	1.34

[a] 5% (v/v) relative to styrene. [b] Two equivs relative to CuBr. [c] All of the polymerizations were conducted in sealed tubes with bulk styrene at 110 °C. $[\text{1-PEBr}]_0 = [\text{CuBr}]_0 = [\text{dNbipy}]_0/2 = 0.087$ M.

diphenyl ether (Figure 1), *p*-dimethoxybenzene, or benzophenone, although the observed rate was correspondingly slower than that of the bulk polymerization due to the lower concentration of the initiating system.[14] In 50% *p*-dimethoxybenzene solution, the ATRP of styrene using dTbipy ligand was homogeneous at 110 °C. In each of the homogeneous polymerizations the polydispersities remained remarkably low throughout the polymerization ($M_w/M_n \leq 1.10$).

In a previous report in which the ATRP of styrene was also conducted in various solvents, the conclusion was reached that no chain transfer-to-solvent occurs in ATRP.[15] However, the transfer constants for the solvents used in that study (as well as this one) are quite low,[16] and in the range of molecular weights studied one would not expect to observe transfer-to-solvent. Thus, the more appropriate conclusion is that the transfer coefficients for ATRP are not significantly higher than those found for conventional radical polymerization.

In order to assess the tolerance of ATRP toward functional groups, a series of polymerizations was performed in which equal amounts of various compounds were added to the polymerization mixture (Table 1). The resulting molecular weight and conversion data indicated that externally added polar protic and aprotic compounds, such as H$_2$O, CH$_3$OH, CH$_3$CN, and ethylene carbonate, had little effect upon the polymerization. When strongly coordinating compounds were used, such as pyridine and PPh$_3$, a large decrease in the polymerization rate and an increase in polydispersities was observed. Presumably these types of compounds can either saturate the coordination sphere of the copper(I) complex and render it inactive or bind to the copper(I) halide and form complexes that are not sufficiently active for atom transfer. Thus, a wide range of monomers with functional groups can be used in ATRP provided that the functional group is not a good ligand for copper(I).

Two equivs of ligand per copper center appears to be the kinetically optimum ratio for these polymerizations. As shown in Figure 3, when the concentration of ligand in a bulk polymerization was varied while the amounts of initiator and CuBr were kept constant, k_{app} (*vide infra*) did not reach an appreciable value until a ratio of approximately 1:1 (ligand-to-copper) was reached; at this ratio, the CuBr dissolved completely in the polymerization medium at 110 °C. Then, k_{app} increased until a ratio of 2:1 was reached, after which no increase in the apparent rate was observed.

These results were quite different from those found for heterogeneous ATRP, in which the polymerization rate was 0.6

(14) For polymerizations under dilute conditions when the observed rate is slower, we have directly observed a slow side reaction that may be responsible for the upper limit of molecular weights that can be achieved in the ATRP of styrene. This will be the subject of a subsequent paper.
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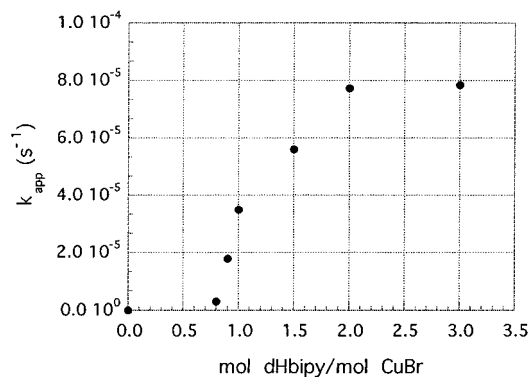
Figure 3. Plot of k_{app} as a function of increasing ligand concentration (dHbipy) at constant CuBr concentration for the bulk ATRP of styrene at 110 °C: $[1\text{-PEBr}]_0 = [\text{CuBr}]_0 = 0.087$ M.

order with respect to ligand concentration.[13] The difference was most likely due to the difference in solubilizing abilities of the ligands. In the case of bipy which poorly solubilizes copper(I) halides in nonpolar media, increasing the concentration of ligand solubilized more and more of the copper(I) halide. In the case of dNbipy, only enough ligand to saturate the coordination sphere of the copper(I) center or generate the active copper(I) species was necessary, because the ligand could make the copper halide completely soluble at this stoichiometry. These results were, however, similar to a previous report[15] on homogeneous ATRP using arenesulfonyl chlorides as initiators, in which a 2:1 stoichiometry of ligand-to-copper(I) chloride was used. The authors showed that at least a 1:1 stoichiometry of ligand-to-copper(I) chloride was needed to obtain polymers with M_w/M_n < 1.5, but no rate data as a function of the stoichiometry was provided so the kinetically optimum ratio was not found.

Copper(I) complexes with bipy or phenanthroline [phen] ligands fall into two structural types depending upon the ligand-to-copper stoichiometry. Complexes of a 1:1 stoichiometry between bipy or phen and copper(I) halides are either halogen bridged dimers, $LCu(\mu\text{-X})_2CuL$, or 2:1 ligand-to-copper cations with a dihalocuprate counteranion, $L_2Cu^+ CuX_2^-$.[17] Complexes of a 2:1 stoichiometry between bipy or phen and copper(I) are monomeric complexes of the formula, $L_2Cu^+X^-$, where X^- can be Cl^-, Br^-, or PF_6^- among other counteranions.[18] Thus if the 2:1 stoichiometry necessary for the most active catalyst (as shown in Figure 3) indicates a 2:1 stoichiometry for bipy-to-copper, then the copper species most likely for the catalytic atom transfer activity in these polymerizations is $L_2Cu^+X^-$. However, the solution chemistry could be more complex and dynamic in that there could be several copper(I) species in rapid equilibria with varying ligand stoichiometries that average to CuBr/2dNbipy. For the purposes of the following discussion the active copper(I) catalyst shall be described generally by "Cu-(I)" or "Cu(I)/2L", and the corresponding copper(II) halide complex formed after atom transfer shall be described generally by "Cu(II)X" or "Cu(II)X/2L" (X = Cl, Br).

A proposed mechanism for ATRP is shown in Scheme 1, which contains eqs for the atom transfer equilibrium, the propagation step, and radical termination. The exclusive role for Cu(I) in these polymerizations is to abstract halogen atoms from the inactive chains. This was shown by an experiment in

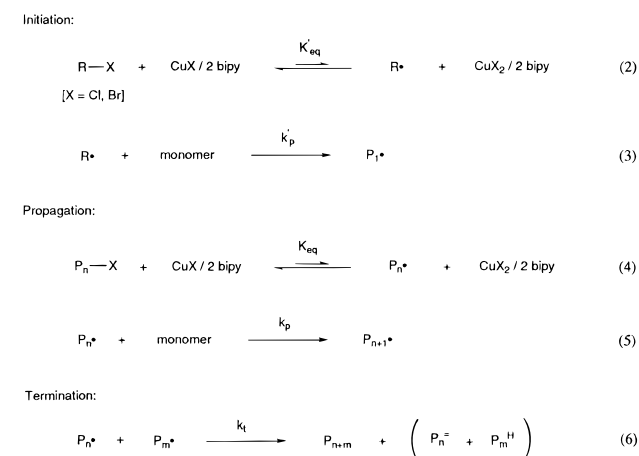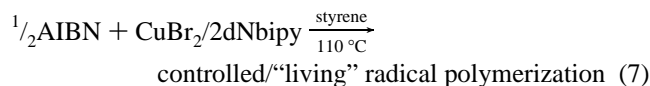(17) (a) Hathaway, B. J. In Comprehensive Inorganic Chemistry; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon: Oxford, 1987; Vol. 5, pp 533−593. (b) Healy, P. C.; Pakawatchai, C.; White, A. H. *J. Chem. Soc., Dalton. Trans.* **1985**, 2531. (c) Healy, P. C.; Englehart L. M.; Patrick, V. A.; White, A. H. *J. Chem. Soc., Dalton. Trans.* **1985**, 2541.

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Scheme 1

Initiation:

$$R\text{—}X \;+\; CuX / 2\,bipy \;\xrightleftharpoons{K'_{eq}}\; R\bullet \;+\; CuX_2 / 2\,bipy \qquad (2)$$

[X = Cl, Br]

$$R\bullet \;+\; monomer \;\xrightarrow{k'_p}\; P_1\bullet \qquad (3)$$

Propagation:

$$P_n\text{—}X \;+\; CuX / 2\,bipy \;\xrightleftharpoons{K_{eq}}\; P_n\bullet \;+\; CuX_2 / 2\,bipy \qquad (4)$$

$$P_n\bullet \;+\; monomer \;\xrightarrow{k_p}\; P_{n+1}\bullet \qquad (5)$$

Termination:

$$P_n\bullet \;+\; P_m\bullet \;\xrightarrow{k_t}\; P_{n+m} \;+\; \left(P_n^= \;+\; P_m^H \right) \qquad (6)$$

Table 2. Data for the "Reverse ATRP" of Bulk Styrene at 110 °C

time (s)	% conv	M_n GPC	M_n Expected	M_w/M_n
6 300	37	5620	3690	1.09
10 620	51	7460	5060	1.07
15 000	67	8330	6720	1.08
20 400	79	8860	7880	1.08
23 940	84	9330	8400	1.10

^{a} [Styrene]$_0$/2[AIBN]$_0$ = 96.

which CuBr/2dNbipy was added to free-radical polymerizations of styrene (dicumyl peroxide initiator at 110 °C). Within experimental error, no effect upon the kinetics or molecular weights of the polymerization was observed. Thus, at the radical concentrations of ATRP, Cu(I)/2L does not react with the intermediate radicals in such a way that contributes to or detracts from the observed control of the polymerization. One can also show that Cu(II)X/2L, the proposed species after atom transfer, does lie along the mechanistic pathway of the polymerization. When 1 equiv of CuBr$_2$/2dNbipy was added to bulk free-radical styrene polymerizations initiated by one-half an equiv of AIBN at 110 °C (essentially entering ATRP from the right side of the preequilibrium eq 2), controlled radical polymerization behavior was observed (eq 7). The observed polymerization rate was somewhat slower ($k_{app} = 7.7 \times 10^{-5}$ s^{-1}), and the resulting

$$^1\!/_2 \text{AIBN} + \text{CuBr}_2/2\text{dNbipy} \xrightarrow[\;110\,°C\;]{\text{styrene}}$$

controlled/"living" radical polymerization (7)

molecular weights were somewhat higher (Table 2) than found for the corresponding bulk styrene ATRP, which can be ascribed to the limited efficiency of radical generation from AIBN (f < 1). This "reverse ATRP" was also observed for heterogeneous systems using CuBr/2bipy catalyst.[19]

From the initiation and propagation eqs in Scheme 1 the following rate laws were derived assuming a fast preequilibrium, a necessary condition to observe low M_w/M_ns in controlled/"living" free-radical polymerizations (eqs 8 and 9).[20]

$$K_{eq} = \frac{k_{act}}{k_{deact}} = \frac{[\text{P}^\bullet][\text{Cu(II)X}]}{[\text{Cu(I)}][\text{PX}]} \qquad (8)$$

$$R_p = k_{app}[\text{M}] = k_p[\text{P}^\bullet][\text{M}] = k_p K_{eq}[\text{In}]\frac{[\text{Cu(I)}]}{[\text{Cu(II)X}]}[\text{M}] \quad (9)$$

As shown before, plots of $\ln([\text{M}]_0/[\text{M}])$ versus time were linear, which confirmed that the polymerization rate was first-

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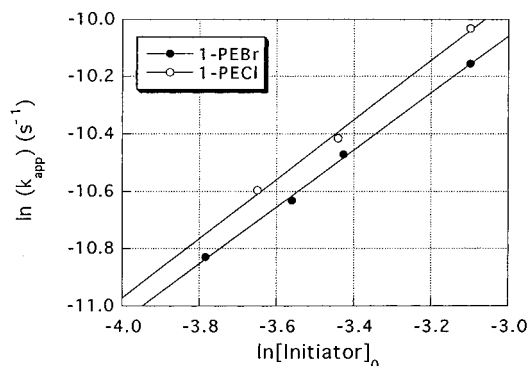(20) Greszta, D.; Matyjaszewski, K. *Macromolecules* **1996**, *29*, 7661.

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Figure 4. Reaction orders for the initiators, 1-PEBr (110 °C) and 1-PECl (130 °C), for the ATRP of styrene in diphenyl ether: $[styrene]_0$ = 4.34 M; $[CuX]_0 = [dNbipy]_0/2$ = 0.045 M. Slope (Br) = 0.99; Slope (Cl) = 1.04.
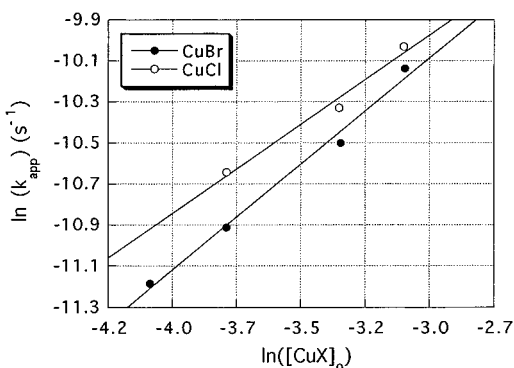

Figure 5. Reaction orders for CuBr (110 °C) and CuCl (130 °C) for the ATRP of styrene in diphenyl ether: $[styrene]_0$ = 4.34 M; $[1\text{-PEX}]_0$ = 0.045 M, $[CuX]_0 = [dNbipy]_0/2$. Slope (Cl) = 0.87; Slope (Br) = 1.03.

order with respect to monomer concentration and that the concentration of radicals was constant throughout the polymerization. Equation 9 in combination with the values of k_{app} from Figure 1 (bulk: 1.6×10^{-4} s^{-1}; solution: 3.9×10^{-5} s^{-1}) and the known rate constant of radical propagation for styrene ($k_p = 1.6 \times 10^3$ M^{-1} s^{-1} at 110 °C)[21] can be used to estimate the steady-state concentration of radicals in the polymerization. In this case, the calculated concentrations of radicals are 1.0×10^{-7} and 2.4×10^{-8} M, bulk and solution, respectively, which are sufficiently low for a minimal number of chains to undergo termination during the timespan in which the polymerization can go to high conversion. The bulk polymerization value (10^{-7} M at 110 °C) can be compared to that found for the corresponding TEMPO-mediated styrene polymerizations at 130 °C ($<10^{-8}$ M).[20,22]

A plot of $\ln(k_{app})$ versus $\ln[initiator]_0$ (for both 1-PEBr and 1-PECl, Figure 4) showed that the rate of polymerization was first-order with respect to the concentration of both initiators. A plot of $\ln(k_{app})$ versus $\ln[CuX]$ (for both CuBr and CuCl, Figure 5) showed that the rate of polymerization was first order with respect to the concentration of copper(I). This result is in contrast to a previous report[15] on ATRP using arenesulfonyl chlorides as initiators in which it was reported that the rate of polymerization decreased with an increase in soluble catalyst concentration. The authors used M_w/M_n as an indicator of catalyst efficiency; however, this parameter is mainly indicative

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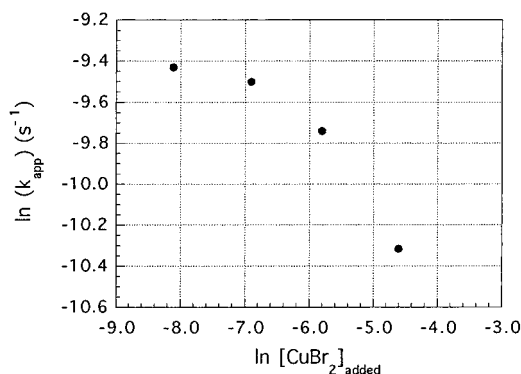(22) Veregin, R. P. N.; Georges, M. K.; Hamer, G. K.; Kazmaier, P. M. *Macromolecules* **1995**, *28*, 4391.

Figure 6. Plot of $\ln(k_{app})$ as a function of added CuBr$_2$ concentration (110 °C) for the bulk ATRP of styrene: $[1\text{-PEBr}]_0 = [CuBr]_0 = [dHbipy]_0/2$ = 0.087 M.

of the relative rate of exchange between dormant and active species in the polymerization. Information on the rates of polymerization and molecular weights in combination with the M_w/M_ns provides a better way to assess the efficiency of the catalyst system. The reaction orders thus determined help to explain why the observed rates of polymerization in bulk are approximately four times greater than those conducted in 50% monomer solution: a reduction in the concentration of both copper(I) and initiator by a factor of two should result in a reduction of the overall rate by a factor of four.

Determining the reaction order with respect to [Cu(II)X] was not as straightforward. A series of polymerizations was performed in which a known amount of CuBr$_2$/2dNbipy was added to the polymerization mixture. Plots of $\ln(k_{app})$ vs. $\ln[CuBr_2]_{added}$ (Figure 6) were not linear with a slope of -1 but instead reached a constant value of k_{app} at low added copper-(II) concentrations.[23] Evidently the reaction rate is not simple inverse first-order with respect to the initial, added CuBr$_2$ concentration. There are several possible explanations for this observation, but one that is borne out by experiment is that Cu-(II)X is formed irreversibly during the initial stages of the polymerization, and, therefore, the actual concentration of Cu-(II)X in the polymerization is not the same as the added concentration of Cu(II)X.

The rate law of the model mechanism (eq 9) is not consistent with the observations in this case, because in formulating the rate law, we explicitly omitted termination by radical coupling. It turns out that even though radical coupling is a negligible reaction during the majority of the polymerization and does not affect the controlled/"living" behavior, it plays a very important regulatory role during the very initial stages of the polymerization (cf. eq 12).

To investigate the incipient stage of the polymerization, we studied a model reaction between the initiator, 1-PEBr, and a well-defined copper(I) complex of the structural type that has been implicated in the catalytic activity of Cu(I)/2L catalyst mixture, $[(dNbipy)_2Cu]^+$ PF$_6^-$, **1**. When 2 equivs of 1-PEBr were heated with **1** at 110 °C in C$_6$D$_6$ and the reaction was monitored using ^{1}H NMR, in less than 30 min signals for the two diastereomers of 2,3-diphenylbutane were observed in the

(23) It was reported by Vofsi, Asscher, and Orochov (*J. Chem. Soc., Perkin II* **1973**, 1000) that CuBr$_2$ can react with styrene to form (1,2-dibromoethyl)-benzene and CuBr. The dihalide thus formed in ATRP could act as an initiator, and this reaction could account for the nonlinear behavior observed in Figure 8. However, when CuBr2/2dNbipy (or 2 bipy) and styrene were heated at reflux for 1 week and monitored using ^{1}H NMR spectroscopy, no formation of (1,2-dibromoethyl)benzene was observed. Furthermore, independently prepared (1,2-dibromoethyl)benzene was shown to be a very inefficient initiator for ATRP, presumably due to the deactivating effect of the β-bromo substituent.

spectrum (eq 10). The amount of 2,3-diphenylbutane formed

$$\text{(10)}$$
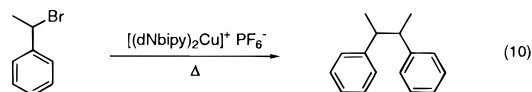
could not be quantitated due to overlap of the dNbipy ligand signals; however, the intensity of the signals did not appear to change with an increased time of heating.[24] The formation of this product was observed more clearly for the reaction between CuBr/2bipy and 1-PEBr under identical conditions, but the reaction proceeded at a much slower rate due to the insolubility of the copper complex. When a sample of the former NMR solution was analyzed using GC/MS, two signals with high retention times and equal integrations were observed. The molecular ion peaks were at $m/z = 210$, and the fragmentation patterns were identical, facts that are consistent with the formation of the two diastereomers of 2,3-diphenylbutane. Thus, the dimer of 1-phenylethyl radical clearly was formed during the initial stages of the reaction. According to the stoichiometry of the preequilibrium (Scheme 2), 2 equivs of Cu(II)X must be formed irreversibly along with the radical dimer. Due to the differences in extinction coefficients between

Scheme 2

$$\text{(11)}$$

$$\text{(12)}$$
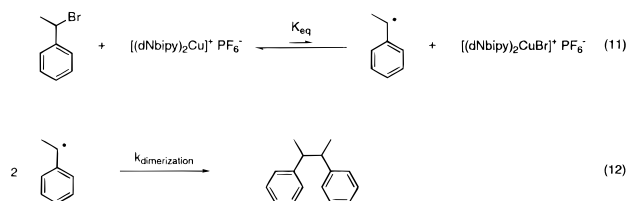
the corresponding copper(I) and (II) complexes (ϵ of $[(\text{dNbipy})_2\text{Cu}]^+ \text{PF}_6^- \approx 10$ times ϵ of $[(\text{dNbipy})_2\text{CuBr}]^+ \text{PF}_6^-$), it was difficult to detect the UV-visible spectrum of the few percent of the copper(II) complex formed in the presence of the copper(I) complex. However, when the above reaction was forced to completion by increasing the temperature to 130 °C and by increasing the heating time to 24 h, the UV-visible spectrum of the resulting solution showed an absorption at $\lambda = 750$ nm that matched the spectrum of an independently synthesized sample of $[(\text{dNbipy})_2\text{CuBr}]^+ \text{PF}_6^-$.

The above data suggest the following overall picture for the polymerization. At the start of the polymerization the concentrations of radicals and Cu(II)X are zero, and, as Cu(I) reacts with the initiator, the concentration of the former two species increases. Because of the form of the equilibrium expression (eq 8) and the fact that the concentrations of Cu(I) and R—X are constant to within a few percent, the product of the concentrations of Cu(II)X and R• should also be constant. Therefore, during the initial stages of the polymerization the concentration of radicals is sufficiently large that the rate at which the radicals revert to the dormant state (rate = k_{deact} * [Cu(II)X] [R•]) is much slower than the rate at which they undergo termination (rate = k_t * [R•]²). With each termination event, the concentration of Cu(II)X increases, and because the product [Cu(II)X][R•] is constant, the concentration of radicals decreases. Therefore, the rate at which the radicals terminate decreases until a sufficiently high concentration of Cu(II)X is formed, at which point the rate of termination is slow enough for a controlled/"living" polymerization to occur. This "self-adjustment" process during the initial stages of the polymeri-
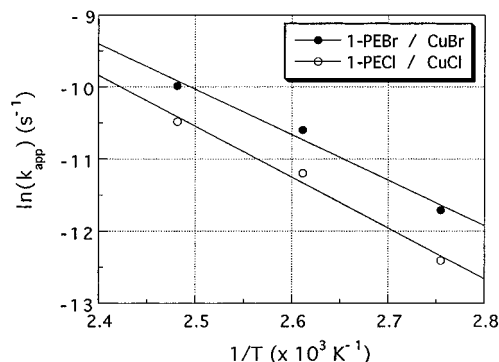

Figure 7. Temperature dependence plots for the 1-PEBr/CuBr- and 1-PECl/CuCl-mediated ATRPs of styrene in diphenyl ether at 110 °C: $[1\text{-PEX}]_0 = [\text{CuX}]_0 = [\text{dNbipy}]_0/2 = 0.045$ M. Slope (Br) = −6.31; Slope (Cl) = −7.05.

zation is also called the "persistent radical effect" and has been observed previously for organic radical reactions.[25]

The persistent radical effect accounts for the observed initial formation of 2,3-diphenylbutane under model reaction conditions, and because Cu(II)X was formed irreversibly along with the 2,3-diphenylbutane, this effect demonstrates why the actual concentration of Cu(II)X in the polymerization could not be predetermined (the effect as seen in Figure 6). If the amount of added Cu(II)X was not sufficient to ensure the proper steady-state concentration of radicals ($\approx 10^{-7} - 10^{-8}$ M), then more would be generated from Cu(I) and the initiator/dormant chains by radical coupling. The concentration of Cu(I) and the initiator/dormant chains in the polymerizations is always much greater than the concentration of Cu(II)X, so the decrease in the concentration of Cu(I) and the initiator/dormant chains upon the initial formation of Cu(II) is relatively small. Because this change is small, its effect upon the kinetics is not observed. Thus, radical coupling only shows an effect when determining the reaction order with respect to species that are present in low concentrations.

The temperature dependence of the rate of polymerization was studied using both the bromide- and chloride-mediated ATRP systems in which 10 mol % of CuX₂/2L (X = Br, Cl) was added (Figure 7).

The temperature dependence of the rate of polymerization was studied using both the bromide- and chloride-mediated ATRP systems in which 10 mol % of CuX2/2L (X = Br, Cl) was added. The excess of CuX2 was needed to ensure that its concentration remained constant to within a few percent error under different polymerization conditions. Otherwise, variations in the amount of CuX2 formed could have lead to variations in the determination of both k_{app} and the preequilibrium constant.

From the slopes of the plots, the apparent activation enthalpies ($\Delta H^{\ddagger}_{\text{app}}$) were measured at 11.9 kcal mol^{-1} for the bromide-mediated ATRP of styrene and 13.4 kcal mol^{-1} for the chloride-mediated ATRP of styrene. The activation enthalpy for styrene propagation is known ($\Delta H^{\ddagger}_{\text{prop}} = 7.1$ kcal mol^{-1}).[21] Equation 13 shows how the enthalpy of the preequilibrium and the activation enthalpy of propagation are related to the apparent

$$\Delta H^\circ = \Delta H^{\ddagger}_{\text{app}} - \Delta H^{\ddagger}_{\text{prop}} \qquad \text{(13)}$$

activation enthalpy, so we could calculate the the enthalpies of the preequilibrium: $\Delta H^\circ = 4.8$ kcal mol^{-1} and $\Delta H^\circ = 6.3$ kcal mol^{-1} for the ATRP of styrene initiated by 1-PEBr and 1-PECl, respectively.

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(24) Simultaneously, styrene formation was also observed (ref 14).

(25) Fisher, H. *J. Am. Chem. Soc.* **1986**, *108*, 3925.

The preequilibrium constants for both the 1-PEBr/CuBr- and 1-PECl/CuCl-initiated ATRPs of styrene at 110 °C were calculated using eq 9 and kinetic data from polymerizations in which 10 mol % of $CuX_2/2L$ (X = Br, Cl) was added initially. In these polymerizations, the amount of Cu(II) generated from the persistent radical effect would be small compared to the large added concentration of Cu(II) and therefore $[Cu(II)]_t \approx [Cu(II)]_0$. Thus, for 50% (v/v) styrene polymerizations performed using diphenyl ether solvent and with 1 mol % initiator and 1 mol % Cu(I)/2L, the apparent rate constants were 2.5×10^{-5} s^{-1} (X = Br) and 1.4×10^{-5} s^{-1} (X = Cl), and the calculated equilibrium constants were 3.9×10^{-8} (X = Br) and 2.1×10^{-8} (X = Cl). These values correspond to free energies of equilibrium ($\Delta G°$) at 110 °C of 13.0 kcal mol^{-1} (X = Br) and 13.5 kcal mol^{-1} (X = Cl). The differences in the equilibrium constants and free energies of polymerization for the bromide- and chloride-mediated ATRPs of styrene reflect the smaller difference in bond strengths between the carbon−bromine and copper(II)−bromine bonds relative to the carbon−chlorine and copper(II)−chlorine bonds.

With the free energies and enthalpies of the preequilibrium thus determined, we calculated the changes of entropy at equilibrium at 110 °C for both the bromide-mediated, $\Delta S° = -22$ cal mol^{-1} K^{-1}, and the chloride-mediated, $\Delta S° = -20$ cal mol^{-1} K^{-1}, ATRPs of styrene. Assuming that these calculations yielded the correct order of magnitude for $\Delta S°$, we find these strongly negative entropies of equilibrium quite surprising, because they are more typical of a 2:1 equilibria involving the loss of three degrees of translational freedom. A possible explanation for this large entropy change is the formation of a caged radical pair (Cu(II) and radical); however, this explanation is contradicted by the fact that the regio- and stereochemistries of polymerization for ATRP are identical to those typically found for free-radical polymerizations.[7,13] Furthermore, the proportion of caged radicals should be small relative to free radicals if the cage entry and exit rates are diffusion controlled ($k_1 = 10^9$ M^{-1} s^{-1} and $k_{-1} = 10^9$ s^{-1}). In ATRP there is no physical or chemical reason to expect otherwise. The concentration of growing radicals is approximately 10^{-8} M, and the concentration of Cu(II) species is less than 10^{-2} M. So, the concentration of caged radicals should be less than 10^{-10} M, which is less than 1% of the free radical concentration. Therefore, propagation should occur predominantly via free radicals.

An alternative explanation is that there is a large loss of conformational motion about the metal center upon atom transfer. For the copper(I/II) pair, [(dNbipy)$_2$Cu]$^+$ PF$_6^-$ and [(dNbipy)$_2$CuBr]$^+$ PF$_6^-$, the bipy ligands in the copper(I) complex show a great range of ligand motion about the metal center, as evidenced by the large variation in the ligand dihedral angle seen in the crystal structures of similar compounds.[17] In the copper(II) complex, the bromide ligand occupies a large volume of the ligand sphere,[26] and, therefore, the range of motions available to the bipy ligands is reduced. We are currently investigating the origin of the equilibrium entropy magnitude and possibility of variation of structures and activities of Cu(I) and Cu(II) species with temperature.

Conclusions

The homogeneous atom transfer radical polymerization (ATRP) of styrene using solubilizing 4,4′-dialkyl substituted 2,2′-bipyridines yielded well-defined polymers with $M_w/M_n \leq$

1.10. The polymerizations exhibited an increase in molecular weight in direct proportion to the ratio of the monomer consumed to the initial initiator concentration and also exhibited internal first-order kinetics with respect to monomer concentration. The kinetically optimum ratio of ligand-to-copper(I) halide for these polymerizations was found to be 2:1, which tentatively indicates that the coordination sphere of the active copper(I) center contains two bipyridine ligands. The exclusive role for this copper(I) complex in ATRP is atom transfer, since at typical concentrations that occur for these polymerizations ($\approx 10^{-7}-10^{-8}$ M), polymeric radicals were found not to react with the copper(I) center in any manner that enhanced or detracted from the observed control. ATRP also exhibited first-order kinetics with respect to both initiator and copper(I) halide concentration; however, the polymerization kinetics were not simple inverse first-order with respect to the initial copper(II) halide concentration. The latter observation was found to be due to the persistent radical effect, which resulted in an increase in copper(II) concentration during the initial stages of the polymerization. This phenomenon also has the effect of regulating the polymerization by ensuring that the rate of radical combination and/or disproportionation is sufficiently less than the rate of propagation. The temperature dependence of the rate of ATRP was measured, and the apparent activation enthalpies were found to be $\Delta H^{\ddagger}_{app} = 11.9$ kcal mol^{-1} for the bromide-mediated ATRP of styrene and $\Delta H^{\ddagger}_{app} = 13.4$ kcal mol^{-1} for the chloride-mediated ATRP of styrene. Estimates of the enthalpies and entropies of equilibrium for the preequilibrium step were calculated at $\Delta H° = 4.8$ and $\Delta H° = 6.3$ kcal mol^{-1} for the ATRP of styrene initiated by 1-PEBr and 1-PECl, respectively, and $\Delta S° = -22$ and $\Delta S° = -20$ cal mol^{-1} K^{-1} for the ATRP of styrene initiated by 1-PEBr and 1-PECl, respectively.

Experimental Section

Materials. Styrene was stirred over CaH$_2$ overnight and vacuum distilled before use. CuBr (98%, Aldrich) and CuCl (98%, Aldrich) were purified according to the procedure of Keller and Wycoff.[27] The initiators, 1-phenylethyl bromide and 1-phenylethyl chloride, were distilled from CaSO$_4$ before use. Diphenyl ether (ACROS) was purged with argon for 15 min before use. Acetonitrile (CH$_3$CN) was stirred over anhydrous CuSO$_4$ for 24 h and then distilled onto P$_4$O$_{10}$. The CH$_3$CN was stirred over the P$_4$O$_{10}$ for 24 h, after which time it was distilled and stored under argon. Tetrahydrofuran (THF) and toluene were distilled from Na/benzophenone before use. Diisopropylamine was distilled from CaH$_2$ before use. dTbipy, 4,4′-di-*tert*-butyl-2,2′-bipyridine, was prepared according to the procedure of Hadda and Bozec.[28] Unless specified, all other reagents were purchased from commercial sources and used without further purification.

General Procedures and Characterizations. Monomer conversion was determined by GC using THF or diphenyl ether (when present) as an internal standard. Molecular weights and molecular weight distributions were measured using a Waters 712 WISP autosampler and the following Phenogel GPC columns: guard, linear, 1000 Å and 100 Å. Molecular weights were calibrated using polystyrene standards. Experiments requiring an inert atmosphere were performed using standard Schlenk and drybox techniques.

4,4′-Di-*n*-heptyl-2,2′-bipyridine [dHbipy].[29] To a stirred solution of dry THF (70 mL) and diisopropylamine (7.36 mL, 52.1 mmol) under Ar at −78 °C was added dropwise *n*-butyllithium (2.3 M in THF, 21.6 mL, 49.6 mmol). After 15 min, the solution was warmed to 0 °C and allowed to stir for 15 min. The mixture was cooled to −78 °C again, and a solution of 4,4′-dimethyl-2,2′-bipyridine (4.00 g, 21.7 mmol) in dry THF (120 mL) was added slowly via cannula. After 3 h,

(26) For the crystal structure of several halide derivatives, see: Tyagi, S.; Hathaway, B. J.; Kremer, S.; Stratemeier, H.; Reinen, D. *J. Chem. Soc., Dalton Trans.* **1984**, 2087.

(27) Keller, R. N.; Wycoff, H. D. *Inorg. Synth.* **1946**, *2*, 1.

(28) Hadda, T. B.; Bozec, H. L. *Polyhedron* **1988**, *7*, 575.

(29) This synthesis is a modification of the following procedure: Kramer, R.; Lehn, J. M.; Cian, A. D.; Fisher, J. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 703.

1-bromohexane (9.2 ml, 65.5 mmol) was added. The mixture was allowed to warm to room temperature overnight and was then poured into cold brine (250 mL). The aqueous phase was extracted with 2 × 50 mL EtOAc (ether may also be used). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. Purification by activated neutral aluminum oxide chromatography (ether/hexane, 1/12, $R_f = 0.29$) afforded 4.00 g (75% combined yield) of a white solid. Further purification can be achieved by recrystallization in acetonitrile to give white needles: mp 52.0−53.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.5 (d, 2H), 8.2 (s, 2H), 7.1 (d, 2H), 2.6 (t, 4H), 1.6 (m, 4H), 1.2 (m, 20H), 0.8 (t, 6H).

4,4′-Di-(5-nonyl)-2,2′-bipyridine [dNbipy]. Dry 4-(5-nonyl)pyridine (200 mL), distilled from CaH_2) and 17 g of Pd/C were stirred and heated under an argon atmosphere at 190−200 °C for 7 days. After, the mixture was filtered through regular filter paper to remove most of the Pd/C (it can be recycled for later preparations of this ligand) and then filtered through 2 cm of Celite to remove the rest of the Pd/C suspended in the solution. For both filtrations Et_2O was used as a wash solvent. The Et_2O was removed from the filtrate by rotary evaporation, and then the starting pyridine was removed from the residue by dynamic vacuum distillation. The yellow oil was then transferred into a Kugelrhor distillation apparatus and distilled at 190−200 °C and 1 × 10^{-6} Torr, yielding a clear, colorless oil that slowly crystallized at room temperature (37.6 g); ^{1}H NMR (C_6D_6, 300 MHz) δ (ppm): 8.86 (s, 2H); 8.59 (d, 2H, J = 4.9 Hz); 6.77 (d, 2H, J = 4.8 Hz); 2.40 (m, 2H); 1.46 (m, 8H); 1.10 (m, 16H); 0.76 (m, 12H).

Bis-(4,4′-di-(5-nonyl)-2,2′-bipyridine)copper(I) hexafluorophosphate. To a 50 mL Schlenk flask, 0.500 g (1.34 mmol) of [Cu(CH_3CN)_4]^+ PF_6^− [30] and 1.10 g (2.69 mmol) of dNbipy were added, and then 20 mL of CH_3CN was added. The solution immediately turned dark brown-red, and the dNbipy slowly dissolved over a period of 1 h. After the mixture became homogeneous, volatile materials were removed under vacuum. The flask with the remaining brown-red solid (1.16 g crude) was taken into the drybox, and the solid was recrystallized from a minimum amount (∼5−10 mL) of toluene. The recrystallization left 1.02 g (78% yield) of brown needles: ^{1}H NMR (300 MHz, C_6D_6) δ (ppm): 8.71 (s, 4 H); 8.13 (d, J = 5.4 Hz, 4 H); 6.98 (d, J = 5.1 Hz, 4 H); 2.97 (m, 4 H); 1.68 (m, 16 H); 1.23 (m, 32 H), 0.88 (t, J = 6.57 Hz, 24 H); UV-vis (toluene): 455 nm (ε 3630 M^{-1} cm^{-1}). Anal. Calcd for $C_{56}H_{88}CuF_6N_4P$: C, 65.57; H, 8.65; N, 5.46. Found: C, 65.33; H, 8.66; N, 5.58.

Bromobis-(4,4′-di-(5-nonyl)-2,2′-bipyridine)copper(II) Hexfluorophosphate. To a 50 mL Schlenk flask, 0.500 g (1.34 mmol) of [Cu(CH_3CN)_4]^+PF_6^− [29] and 1.10 g (2.69 mmol) of dNbipy were added, and then 10 mL of CH_3CN was added. The solution immediately turned dark brown-red, and the dNbipy slowly dissolved over a period of 1 h. The solution was stirred overnight, and then the next day $CHBr_3$ (0.120 mL, 1.34 mmol) was added via syringe. The solution turned dark green and was allowed to stir for several hours. Next, volatile materials were removed under vacuum. The flask with the remaining dark green solid was taken into the drybox, and the solid was recrystallized from a minimum amount (∼5−10 mL) of toluene. The recrystallization yielded 0.472 g (32%) of emerald green crystals: UV-vis (toluene): 750 nm (ε 370 M^{-1} cm^{-1}). Anal. Calcd for $C_{56}H_{88}BrCuF_6N_4P$: C, 60.83; H, 8.02; N, 5.07. Found: C, 60.96; H, 8.11; N, 4.92.

(30) Hathaway, B. J.; Holah, D. G.; Postlethwaite, J. D. *J. Chem. Soc.* **1961**, 3215.

General Procedures for the Homogeneous ATRP of Styrene. In bulk. The following reagents were weighed into glass tubes under ambient atmosphere: 12.0 mg (8.37 × 10^{-2} mmol) of CuBr. For polymerizations using dTbipy 47.0 mg (0.175 mmol) of the ligand was added, for polymerizations using dHbipy 62.0 mg (0.175 mmol) of the ligand was added, and for polymerizations using dNbipy 71.0 mg (0.175 mmol) of the ligand was added. Next, 1.00 mL (0.909 g, 8.73 mmol) of styrene and the amount of 1-PEBr necessary to give the desired monomer-to-initiator ratio were added quickly, and the tube was attached to a vacuum line. Two "freeze−pump−thaw" cycles were performed to remove any oxygen from the polymerization solution. Each tube was sealed under vacuum. The tubes were placed in an oil bath thermostatted at 110 ± 1°C. At timed intervals, the tubes were removed from the oil bath and cooled to room temperature by washing the tube with hexanes. Afterwards, the individual tubes were broken and the contents were dissolved in 10.0 mL of THF.

In Solution. A 25 mL Schlenk flask was charged with solvent and the appropriate copper compound/ligands. The flask was sealed with a glass stopper and cycled between vacuum and argon three times in order to remove all oxygen. Next, initiator and styrene were added via syringe, and the flask was immersed in an oil bath at 110 ± 1 °C, and when all solids had dissolved a time = 0 data point was taken. At timed intervals, a 1.00 mL sample of the solution was withdrawn using a purged syringe and added to 5.00 mL of THF.

The THF solutions were injected into the GC, and percent conversions were calculated relative to the time = 0 data points. The samples were then filtered through a small column of alumina and a 0.2 micron filter and then injected into the GPC for analysis.

Procedure for Conducting Free-Radical Polymerizations in the Presence of Copper Compounds. Under an inert atmosphere, the following stock solutions were prepared: (1) blank: 13 mg (3.8 mM) of dicumyl peroxide in 10.00 mL of styrene; (2) well-defined copper-(I) compound: 0.894 g (87.0 mM) of [(dNbipy)_2Cu]^+ PF_6^− and 13 mg (3.8 mM) of dicumyl peroxide in 10.00 mL of styrene; (3) ATRP copper(I) catalyst: 0.125 g (87.0 mM) of CuBr, 0.721 g (176 mM) of dNbipy, and 13 mg (3.8 mM) of dicumyl peroxide in 10.00 mL of styrene. Several samples (1.00 mL) of each solution were added to individual glass tubes. While maintained under an inert atmosphere, each tube was attached to the vacuum line, "freeze−pump−thaw" degassed once, and sealed under vacuum. The tubes were placed in an oil bath thermostatted at 110 ± 1 °C. At timed intervals, the tubes were removed from the oil bath and cooled to room temperature by washing the tube with hexanes. Afterwards, the individual tubes were broken, and the contents were dissolved in 10.0 mL of THF. The polymer solutions were analyzed as described above.

Procedure for Homogeneous "Reverse ATRP". The procedure used here was the same as that used for the bulk ATRP of styrene. The quantities of reagents used for each glass tube were as follows: 3.7 mg (2.3 × 10^{-2} mmol) of AIBN, 10.1 mg (4.5 × 10^{-2} mmol) of $CuBr_2$, 37.1 mg (9.1 × 10^{-2} mmol) of dNbipy, and 0.500 mL (0.454 g, 4.4 mmol) of styrene. After polymerization, the contents of each tube were dissolved in 5.0 mL of THF, and the polymer solutions were analyzed as described above.

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