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Comproportionation versus Disproportionation in the Initiation Step of Cu(0)-Mediated Living Radical Polymerization

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S *Supporting Information*

ABSTRACT: We present a study of the initiation step in copper(0)-mediated atom transfer radical polymerization (also known as SET-LRP or SARA ATRP), in which a nitroxide free radical, *N*-tert-butyl-*N*-[1-diethylphosphono-(2,2-dimethylpropyl)] nitroxide (SG1), is used to trap radicals derived from ethyl 2-bromoisobutyrate (EBiB), copper metal and pentamethyl diethylene triamine (PMDETA) ligand. A kinetic model was developed relating the rate of conversion of EBiB to the rate constants of activation by copper metal (k_{a0}) and comproportionation of Cu^0 and Cu^{II} (k_{comp}). This allowed the determination of these parameters in several solvents, including dimethyl sulfoxide (DMSO), dimethylformamide (DMF), ethanol (EtOH), and acetonitrile (MeCN), in which significant levels of comproportionation were observed, leading to autoacceleration of the reaction. A similar treatment of copper-mediated polymerization kinetics predicts 1/2 order dependence on initiator concentration and copper surface area, in accordance with previously published experimental data.
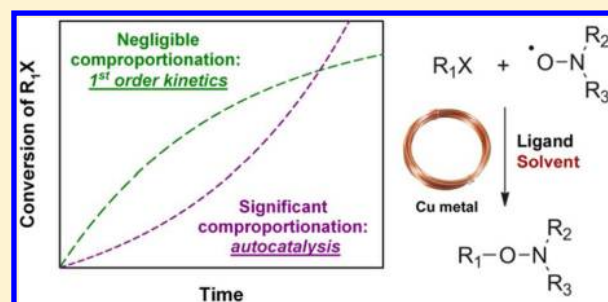
INTRODUCTION

Atom transfer radical polymerization (ATRP)[1,2] is one of the most commonly used techniques of controlled radical polymerization. The key step in this technique is the reversible reaction between an alkyl halide and a metal salt (or activator) to generate an alkyl radical (the propagating species) and a metal halide (or deactivator) (Scheme 1).[3,4]

Scheme 1. Reversible Activation in ATRP

$$RX + M^{n+} \underset{k_d}{\overset{k_{a1}}{\rightleftharpoons}} R^{\cdot} + [MX]^{(n+1)+}$$
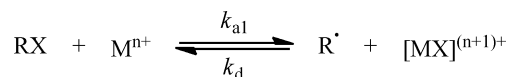
ATRP is compatible with many types of monomer and chemical functionalities but, in its original form, requires relatively high metal concentrations (typically Cu^I/Cu^{II}) to control the reaction. This is due to the persistent radical effect[5]—unavoidable termination of radicals during the polymerization results in a buildup of the deactivator, which in turn causes a reduction in the radical concentration, which is given by eq 1.[6] Unless the total metal concentration is of a similar magnitude to the initiator concentration, termination of a small fraction of the polymer chains will result in a large change in the activator/deactivator ratio and severely inhibit the polymerization.

$$[R^{\bullet}] = K_{ATRP} \frac{[RX][M^{n+}]}{[MX^{(n+1)+}]} \qquad (1)$$

In the years since its introduction, a number of variants of the technique have been developed to address this problem. One approach, pioneered by Matyjaszewski and co-workers, has been to provide an alternative route to convert the excess deactivator back to activator, for example, by using a reducing agent (ARGET,[7] AGET[8]), a secondary source of free radicals (ICAR[7]), or direct electrochemical reduction (eATRP[9]). A second approach, developed by Percec and co-workers,[10,11] is to use copper metal as the activator in solvents which favor the disproportionation of copper(I), such as dimethyl sulfoxide (DMSO). It is claimed that near-instantaneous disproportionation of copper(I) under the reaction conditions results in the simultaneous formation of copper(II) deactivator and highly reactive nanosized copper(0) species.[11] The high activity of the nanosized copper(0) activator leads to very rapid rates of reaction at low copper concentrations, while maintaining near-perfect control over chain-end fidelity, implying very low levels of termination.[12,13]

Percec's technique, termed SET-LRP, has gained in popularity as a synthetic technique,[14−18] due in part to the relative ease of handling copper metal as opposed to copper powder and rapid rates of reaction which can be achieved at room temperature.[19−21] The details of the mechanism have been subject to heated debate, however, with disagreement over the nature of electron transfer (outer sphere[22] versus inner

Scheme 2. Elementary Reactions in the Copper-Mediated Synthesis of Alkoxyamines

Step	Reaction	Rate
Activation ($Cu^0 \rightarrow Cu^I$)	$RBr + Cu^0 \rightarrow R^\bullet + CuBr$	$k_{a0}[RBr]$
Activation ($Cu^I \rightarrow Cu^{II}$)	$CuBr + RBr \rightarrow R^\bullet + CuBr_2$	$k_{a1}[CuBr][RBr]$
Deactivation ($Cu^{II} \rightarrow Cu^I$)	$R^\bullet + CuBr_2 \rightarrow CuBr + RBr$	$k_d[CuBr_2][R^\bullet]$
Coupling	$R^\bullet + NOx \rightarrow RNOx$	$k_c[R^\bullet][NOx]$
Comproportionation	$CuBr_2 + Cu^0 \rightarrow 2CuBr$	$k_{comp}[CuBr_2]$
Disproportionation	$CuBr + CuBr \rightarrow CuBr_2 + Cu^0$	$k_{disp}[CuBr]^2$
Net reaction	**$2.RBr + Cu^0 + 2.NOx \rightarrow 2RNOx + 2.CuBr$**	

sphere[23,24]) in the activation step and the extent to which disproportionation takes place.[25,26] Matyjaszewski has proposed an alternative explanation in which comproportionation dominates, the chief effect of the copper metal being to reduce copper(II) deactivator to copper(I). In this view, SET-LRP is best regarded as a form of ARGET ATRP[27,28] with the addition of a supplemental activation step (also known as SARA).[29,30] Other researchers have noted the similarities to ICAR, with the copper metal acting as a secondary source of radicals through its reaction with the alkyl halide initiator.[31]

There is a high degree of uncertainty regarding the actual extent of comproportionation and disproportionation reactions under polymerization conditions. Equilibrium values have been determined across a range of solvents, but the position of the equilibrium is dependent on the ligand, both explicitly (disproportionation of copper(I) releases one molecule of ligand) and implicitly by its effect on the relative energy levels of the copper species. Experiments using spectroscopic methods[25] to determine the extent of disproportionation of Cu^I in the presence of tris[2-(dimethylamino)ethyl]amine (Me_6TREN) in various solvents appear to show levels of disproportionation of 1−3 orders of magnitude greater than have been determined using electrochemical methods.[26] As a result, there is significant disagreement over whether SARA- or SET-type reactions take place under a given set of reaction conditions.

The preparation of alkoxyamines by reaction with copper metal[32] may serve as a useful model for SARA- or SET-type reactions, as this reaction incorporates the radical-generating reactions of these polymerizations, without the complication of polymerization. A similar approach has been used to determine rate constants (k_{a1}) for the activation of alkyl halides (RX) in classical ATRP.[33] In the copper(0)-mediated synthesis of alkoxyamines, an activated alkyl bromide (RBr:e.g., ethyl 2-bromoisobutyrate, EBiB) reacts with copper metal to produce copper(I) bromide and an alkyl radical. This radical then couples with free nitroxide radical (NOx: e.g., SG1, TEMPO) to produce the desired alkoxyamine. The copper(I) bromide produced may react either by abstracting a bromine atom from a second molecule of alkyl bromide to produce copper(II) bromide and an alkyl radical (SARA-type mechanism) or by disproportionating with a second molecule of copper(I) bromide to produce copper(0) and copper(II) bromide (SET-type mechanism). The copper(II) bromide thus formed may react by comproportionation with copper metal to generate more copper(I) bromide (ARGET) or transfer a

bromine atom to a radical, regenerating copper(I) bromide and alkyl bromide (both SET and SARA). These reactions are summarized in Scheme 2.

In this paper, we present an analysis of the kinetics of this reaction in several different solvents, including DMSO, the most commonly reported solvent for SET;[11] acetonitrile (MeCN), which strongly stabilizes copper(I) species and should favor comproportionation;[26] and toluene, a nonpolar solvent which has been used for the copper(0)-mediated polymerization of methyl methacrylate,[34] styrene,[35] and methyl acrylate.[31,36] Other solvents investigated include ethanol (EtOH), dimethylformamide (DMF), and a 1:1 mixture of $EtOH/H_2O$ (solvents with high equilibrium constants of disproportionation which have been used for SET polymerizations)[37,38] as well as ethyl acetate (EtOAc), a moderately polar solvent which was used in the first report of an ARGET-based synthesis of alkoxyamines.[39] The ligand employed was N,N,N',N'',N''-pentamethyldiethylenetriamine (PMDETA), a ligand of moderate activity in ATRP.

This paper represents the first attempt to quantify rates of activation by copper metal and comproportionation of copper(II) and copper(0) under ATRP conditions. The methodology presented here could easily be extended to further solvents, ligands, and initiators.

■ EXPERIMENTAL SECTION

Materials. All materials were used without further purification. *N*-*tert*-Butyl-*N*-(1-diethylphosphono-2,2-dimethylpropyl)-*N*-oxyl nitroxide (SG1, 85%) was kindly supplied by Arkema. Copper wire (0.25 mm diameter, 99.999%), copper(I) bromide (98%), copper(II) bromide (99%), ethyl-2-bromo-2-methylpropionate (EBiB, 98%), N,N,N',N'',N''-pentamethyldiethylenetriamine (PMDETA, 99%), and dimethyl sulfoxide (DMSO, 99.9%) were obtained from Sigma-Aldrich. The solvents N,N-dimethylformamide (DMF, 99.9%), ethanol (EtOH, 99.9%), ethyl acetate (EtOAc, 99.9%), acetonitrile (MeCN, 99.9%), and toluene (99.5%) were obtained from Carlo Erba Reagents.

Instrumentation. ^1H NMR spectroscopy was performed in 5 mm diameter tubes in $CDCl_3$ on a Bruker Avance-300 (300 MHz) spectrometer. The chemical shift scale was calibrated on the basis of the solvent peak ($\delta = 7.26$ ppm).

Kinetic Experiments to Determine the Effect of Solvent on the Rate of Formation of Ethyl 2-Methyl-2-[*N*-*tert*-butyl-*N*-(1-diethoxyphosphoryl-2,2-dimethylpropyl)aminoxy]propionate. *General Method.* SG1 (0.94 g, 2.7 mmol), copper wire (80 mg, 1.25 mmol), EBiB (0.49 g, 2.5 mmol), and solvent (DMSO, DMF, EtOH, 1:1 EtOH:H₂O, EtOAc, MeCN, or toluene, 5 mL) were added to a 25 mL round-bottomed flask with magnetic stirrer bar. The flask was sealed with a rubber septum, placed in an oil bath at 30 °C, and degassed by bubbling with Ar for 10 min while stirring. PMDETA (0.3

mL, 0.25 g, 1.5 mmol) was added by syringe. This was considered to be the start of the reaction. Samples were removed by syringe at regular intervals. The samples were immediately diluted with CDCl₃, and ¹H NMR spectra were obtained. Conversion was calculated by comparing the area under the peak at 1.91 ppm (EBiB, (C$\underline{\text{H}}_3$)$_2$CBr, 6H) with the sum of the areas under the peaks at 1.57 and 1.67 ppm (SG1 adduct, (C$\underline{\text{H}}_3$)$_2$CON⟨, 2 × 3H).

Kinetic Experiment Using Activated Copper Wire. SG1 (0.94 g, 2.7 mmol), copper wire (80 mg, 1.25 mmol), EBiB (0.49 g, 2.5 mmol), and MeCN (5 mL) were added to a 25 mL round-bottomed flask with magnetic stirrer bar. The flask was sealed with a rubber septum, placed in an oil bath at 30 °C, and degassed by bubbling with Ar for 10 min while stirring. PMDETA (0.3 mL, 0.25 g, 1.5 mmol) was added by syringe. After 20 min, the flask was opened, the wire was removed, quickly rinsed with MeCN, and placed in a second 25 mL round-bottomed flask which contained identical quantities of SG1, EBiB, and MeCN. This was degassed by bubbling with Ar for 10 min, and an identical quantity of PMDETA was added. Subsequent sampling of the reaction and kinetic analysis was carried out as for the general method.

Experiment with Added CuBr or CuBr₂ (0.05 equiv). These experiments were carried out using the general method, with the exception that CuBr (9 mg, 0.25 mmol, 0.05 equiv relative to EBiB) or CuBr₂ (14 mg, 0.25 mmol, 0.05 equiv relative to EBiB) was added to the reaction prior to degassing.

Experiment with Added CuBr₂ (0.25 equiv). SG1 (0.94 g, 2.7 mmol), copper wire (80 mg, 1.25 mmol), EBiB (0.49 g, 2.5 mmol), CuBr₂ (70 mg, 0.25 mmol, 0.25 equiv relative to EBiB), and MeCN (5 mL) were added to a 25 mL round-bottomed flask with magnetic stirrer bar. The flask was sealed with a rubber septum, placed in an oil bath at 30 °C, and degassed by bubbling with Ar for 10 min while stirring. PMDETA (0.3 mL, 0.25 g, 1.5 mmol) was added by syringe. Subsequent sampling of the reaction and kinetic analysis was carried out as for the general method.

■ RESULTS AND DISCUSSION

Solvent Effects on Preparation. The copper-mediated reaction between EBiB and SG1 free nitroxide was carried out in several solvents which favor comproportionation or disproportionation of copper to varying degrees: toluene, EtOAc, EtOH, 1:1 EtOH/H₂O, DMSO, DMF, and MeCN. The kinetics of the reaction are shown in Figure 1. The solvents fall into two groups. The first group, consisting of toluene, EtOAc, and EtOH/H₂O, show first-order dependence on the concentration of EBiB (Figure 1a). By contrast, the remaining solvents exhibit sigmoidal reaction profiles, characterized by an accelerating rate of reaction in the early stages of the reaction (Figure 1b).

The kinetics of the reactions in EtOAc, 1:1 EtOH:H₂O, and toluene are readily explained with reference to the elementary reactions of Scheme 1 (excluding comproportionation and disproportionation reactions), if it is assumed that the rate-limiting step is reaction of EBiB with Cu (e.g., $k_{a0} \ll k_{a1}, k_c$). This assumption is justified by the relatively low surface area of the copper wire and by thermodynamic calculations which indicate that Cu^I is generally several orders of magnitude more active as an initiating species than Cu^0 in solvent/ligand systems which do not strongly favor comproportionation.[40] In this case, the rate of reaction is proportional to [EBiB]. As copper is not a soluble species, its concentration does not appear in the rate equation. The surface area of the copper is assumed to remain approximately constant throughout the reaction. The rates of change in concentration of EBiB and CuBr are given by eqs 2 and 3.
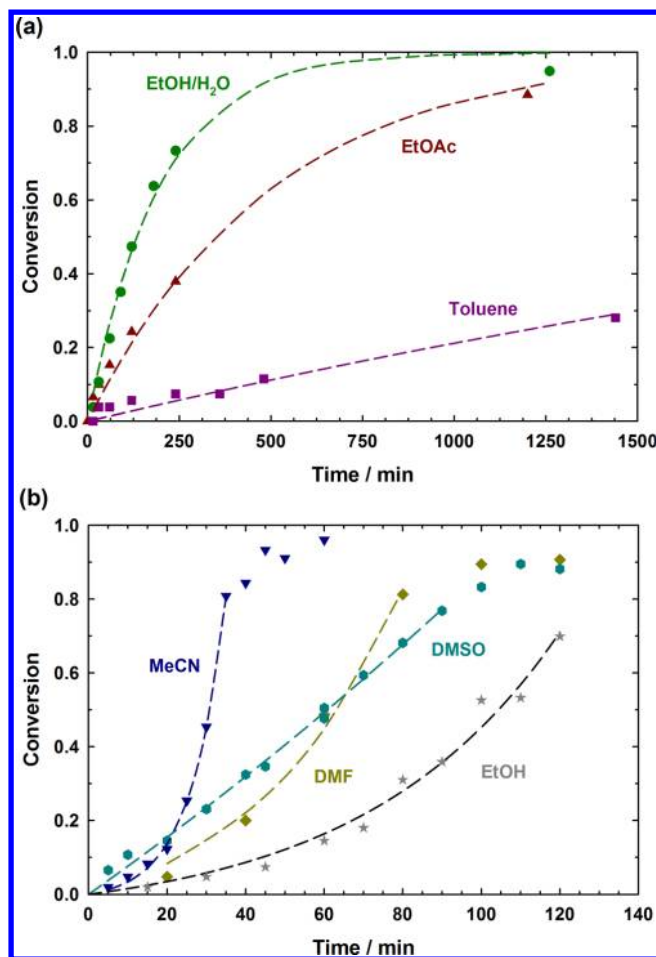
Figure 1. (a) Kinetic plot of reaction of EBiB in EtOAc, 1:1 EtOH:H₂O, and toluene, showing fit to first-order kinetics (conversion = $(1 - \exp\{-2k_{a0}t\})$). (b) Kinetic plot of reactions of EBiB in MeCN, EtOH, DMSO, and DMF, showing fit to autocatalytic reaction kinetics (conversion = $2k_{a0}/(k_{comp} - 2k_{a0})(\exp[(k_{comp} - 2k_{a0})t] - 1)$, see eq 7).

$$-\frac{d[\text{EBiB}]}{dt} = k_{a0}[\text{EBiB}] + k_{a1}[\text{EBiB}][\text{CuBr}]$$
$$- k_d[\text{CuBr}_2][\text{R}^\bullet] \tag{2}$$

$$\frac{d[\text{CuBr}]}{dt} = k_{a0}[\text{EBiB}] - k_{a1}[\text{EBiB}][\text{CuBr}]$$
$$+ k_d[\text{CuBr}_2][\text{R}^\bullet] \tag{3}$$

The concentration of [CuBr] will approach a steady state, equal to $(k_{a0}[\text{EBiB}] + k_d[\text{CuBr}_2][\text{R}^\bullet])/(k_{a1}[\text{EBiB}])$—approximately k_{a0}/k_{a1} if it is assumed that the rate of deactivation is negligible. At this concentration, $d[\text{CuBr}]/dt = 0$, and $-d[\text{EBiB}]/dt = 2k_{a0}[\text{EBiB}]$. If it is assumed that the steady-state concentration of [CuBr] is reached rapidly, the conversion of EBiB is given by eq 4 (see Supporting Information for derivation).

$$\frac{[\text{EBiB}]_0 - [\text{EBiB}]}{[\text{EBiB}]_0} = 1 - e^{-2k_{a0}t} \tag{4}$$

The rate constant of the reaction between copper and EBiB, k_{a0}, varies between 2×10^{-6} s^{-1} (toluene) and 4×10^{-5} s^{-1} (EtOH:H₂O). Activation rate constants (k_{a1}) for Cu^I/PMDETA have been measured in several solvents and range

from 0.4 M^{-1} s^{-1} (toluene) to 2 M^{-1} s^{-1} (acetonitrile).[33] If it is assumed that the rate of deactivation is negligible (efficient trapping of radicals by SG1), this suggests a steady-state concentration of CuBr of around 10^{-5}–10^{-6} M. The steady-state concentration of CuBr will be higher if significant deactivation takes place, but once it is established, the overall rate of reaction will still be determined by k_{a0}.

The second group of solvents (MeCN, DMSO, DMF, EtOH) present unusual kinetic profiles, in which the rate of reaction accelerates as the reaction proceeds (Figure 1b). The observed acceleration may be the result of an induction period (due, for instance, to the slow dissolution of a passivating layer), or autocatalysis, in which the reaction is catalyzed by one of its products.

The first possibility is an induction period caused by the slow dissolution of a passivating layer (e.g., copper oxide)[41] or an increase in the surface area of the copper wire caused by pitting as copper is dissolved. This was tested by repeating the reaction using an "activated" length of copper wire. Activation was carried out by exposing the wire to a degassed MeCN solution of EBiB, SG1, and ligand for a period of 20 min (the length of the induction period in MeCN), briefly rinsing with MeCN, and transferring the wire to a freshly degassed solution of EBiB, SG1, and ligand. Nearly identical kinetics were observed using activated and nonactivated wires (Figure 2). Most importantly, the length of the induction period was unchanged at 20 min.
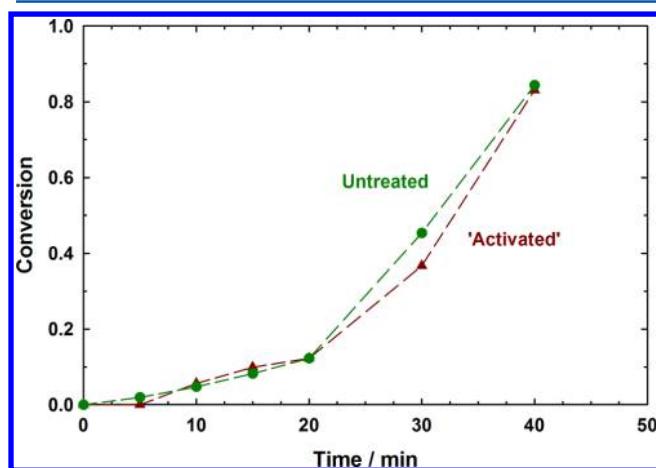
Figure 2. Kinetic plots of reaction of EBiB in MeCN using untreated vs "activated" copper wire.

This result indicates that the observed kinetics are due to autocatalysis: catalysis of the reaction by one of the reaction products. The most likely catalysts are the copper species (Cu^I and Cu^{II}) which are produced during the reaction. Copper(I) may have a catalytic effect on the reaction as a result of disproportionation to copper(II) and highly reactive nanosized copper(0) (i.e., Cu^{0*}), as proposed by Percec.[19] Alternatively, copper(II) may undergo comproportionation with copper metal to form 2 equiv of copper(I), which subsequently react with alkyl halide. The catalytic effect of copper(II) would stem from its ability to increase the rate of conversion of copper metal to copper(I).

As an explanation for the observed autocatalysis, disproportionation suffers from the following problems: (i) It plays no role in the initial, rate-determining step of the reaction, reaction of copper metal with EBiB. (ii) The effect is self-limiting: the rate of disproportionation increases with the square of the CuBr concentration, while the rate of CuBr production is proportional to [EBiB] and is gradually decreasing; thus, a point will be reached at which CuBr is consumed as fast as it is produced, after which no further increase in the rate of reaction is possible. (iii) The strongest autocatalytic effect is observed in MeCN, a solvent which strongly favors comproportionation over disproportionation.

If it is assumed that the nanosized copper(0) is consumed through reaction with EBiB as quickly as it is formed and that [CuBr] reaches a steady state in which the rate at which CuBr is consumed balances the rate at which it is formed (by reaction with macroscopic copper), the system of kinetic equations can be solved to give eq 5, describing the conversion of EBiB as a function of time (see Supporting Information for a full derivation).

$$\frac{[EBiB]_0 - [EBiB]}{[EBiB]_0} = 1 - e^{-2k_{a0}t} \tag{5}$$

This is identical to the expression derived in the absence of disproportionation, indicating that disproportionation cannot have a catalytic effect on the rate of conversion, even under the optimal condition of maximally reactive nanosized copper(0). By contrast, comproportionation increases the overall rate of conversion of copper(0) to copper(I), thus affecting the initial step of the reaction. As the reaction proceeds, and $[CuBr_2]$ increases, the rate of comproportionation will increase as well. No steady state is possible, and the rate of reaction is limited only by the availability of the EBiB and copper metal substrates.

The resulting reaction kinetics are complex, but can be solved if it is assumed that the concentration of CuBr reaches a steady state. Solution of the resulting system of differential equations (see Supporting Information for derivation) gives the conversion of EBiB (eq 6).

$$\frac{[EBiB]_0 - [EBiB]}{[EBiB]_0} =$$
$$\begin{cases} \dfrac{2k_{comp}\frac{[CuBr_2]_0}{[EBiB]_0} + 2k_{a0}}{k_{comp} - 2k_{a0}}(e^{(k_{comp}-2k_{a0})t} - 1) & k_{comp} \neq 2k_{a0} \\ 2k_{a0}\left(1 + \dfrac{[CuBr_2]_0}{[EBiB]_0}\right)t & k_{comp} = 2k_{a0} \end{cases} \tag{6}$$

If no dissolved copper is present at the beginning of the reaction, eq 6 reduces to eq 7.

$$\frac{[EBiB]_0 - [EBiB]}{[EBiB]_0} =$$
$$\begin{cases} \dfrac{2k_{a0}}{k_{comp} - 2k_{a0}}(e^{(k_{comp}-2k_{a0})t} - 1) & k_{comp} \neq 2k_{a0} \\ 2k_{a0}t & k_{comp} = 2k_{a0} \end{cases} \tag{7}$$

Indeed, the observed reaction kinetics (for conversion <80%) are well described by an equation of the form $A(e^{kt} - 1)$ (Figure 1). In the case of negligible comproportionation ($k_{comp} \ll 2k_{a0}$), the conversion approximates eq 5, which describes the kinetics in solvents which do not show autoacceleration.
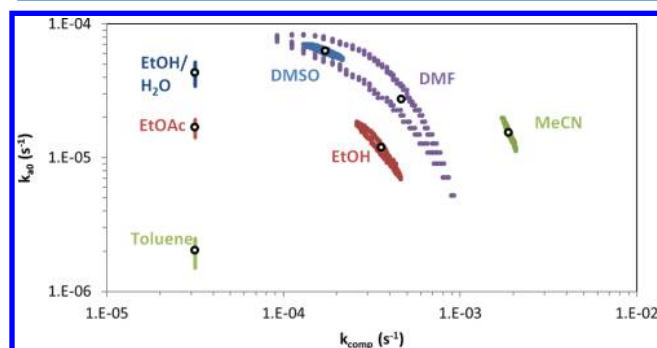
The rate constants k_{a0} and k_{comp} (for solvents showing autoacceleration) were determined by nonlinear least-squared fitting of eq 5 or eq 7 to the conversion vs time data. Point estimates are given in Table 1, while 95% confidence intervals

and joint confidence regions (determined by visualization of the sum of squared residuals space[42]) are given in Figure 3.

Table 1. Rate Constants for Activation by Copper Metal (k_{a0}) and Comproportionation (k_{comp})

| solvent	k_{a0} ($\times 10^6$ s^{-1})	k_{a0} (relative to MeCN)	k_{comp} ($\times 10^6$ s^{-1})	k_{comp}/k_{a0}
toluene	2.0	0.1	<2[a]	
EtOH	12	0.8	360	30
MeCN	15	1	1900	124
EtOAc	17	1.1	<20[a]	
DMF	27	1.8	470	18
EtOH/H$_2$O	43	2.9	<40[a]	
DMSO	63	4.2	170	2.8

[a]Negligible relative to k_{a0}.

Figure 3. 95% confidence intervals (EtOH/H$_2$O, EtOAc, and toluene) and 95% joint confidence regions (DMSO, EtOH, MeCN, and DMF) for rate constants k_{a0} (all solvents) and k_{comp} (DMSO, EtOH, MeCN, and DMF only). Point estimates are marked by black circles.

Measured rate constants for activation by copper metal (k_{a0}) range from 2.0×10^{-6} s^{-1} (toluene) to 6.3×10^{-5} s^{-1} (DMSO). These values are dependent on the surface area of copper, and so values relative to MeCN have also been presented in Table 1, which are independent of the copper surface area. The most polar solvents (DMSO, EtOH/H$_2$O, and DMF) have the highest values, but k_{a0} of EtOH is lower than EtOAc and MeCN, indicating that solvent polarity is not the sole determining factor. Rate constants of comproportionation (k_{comp}) vary widely from 1.9×10^{-3} s^{-1} (MeCN) to $< 2 \times 10^{-6}$ s^{-1} (toluene). The less polar solvents generally have lower k_{comp} than more polar solvents, but relative stability of Cu^{I} and Cu^{II} species plays an important role. MeCN, which strongly stabilizes Cu^{I} has the highest k_{comp}, while comproportionation is negligible ($k_{comp} \ll 4 \times 10^{-5}$ s^{-1}) in the EtOH/H$_2$O mixture, which most strongly stabilizes Cu^{II} species.

Effect of Added Copper Salts. The mechanism described above, in which the reaction of alkyl bromide is catalyzed by CuBr$_2$ via comproportionation with Cu^0, intuitively suggests that addition of a small amount of CuBr$_2$ should increase the rate of reaction. In fact, the opposite is observed. Addition of 0.05 equiv of CuBr$_2$ with respect to EBiB was found to slow the reaction in MeCN and EtOAc and had no effect on the reaction in EtOH (Figure 4). This may be due to competition between CuBr$_2$ and SG1 as radical scavengers. If this is the case, addition of CuBr$_2$ in the early stages of the reaction would cause a larger fraction of radicals to be deactivated by CuBr$_2$ rather than trapped by SG1. The effect would be an induction period in which the rate of conversion of EBiB is reduced while a steady-
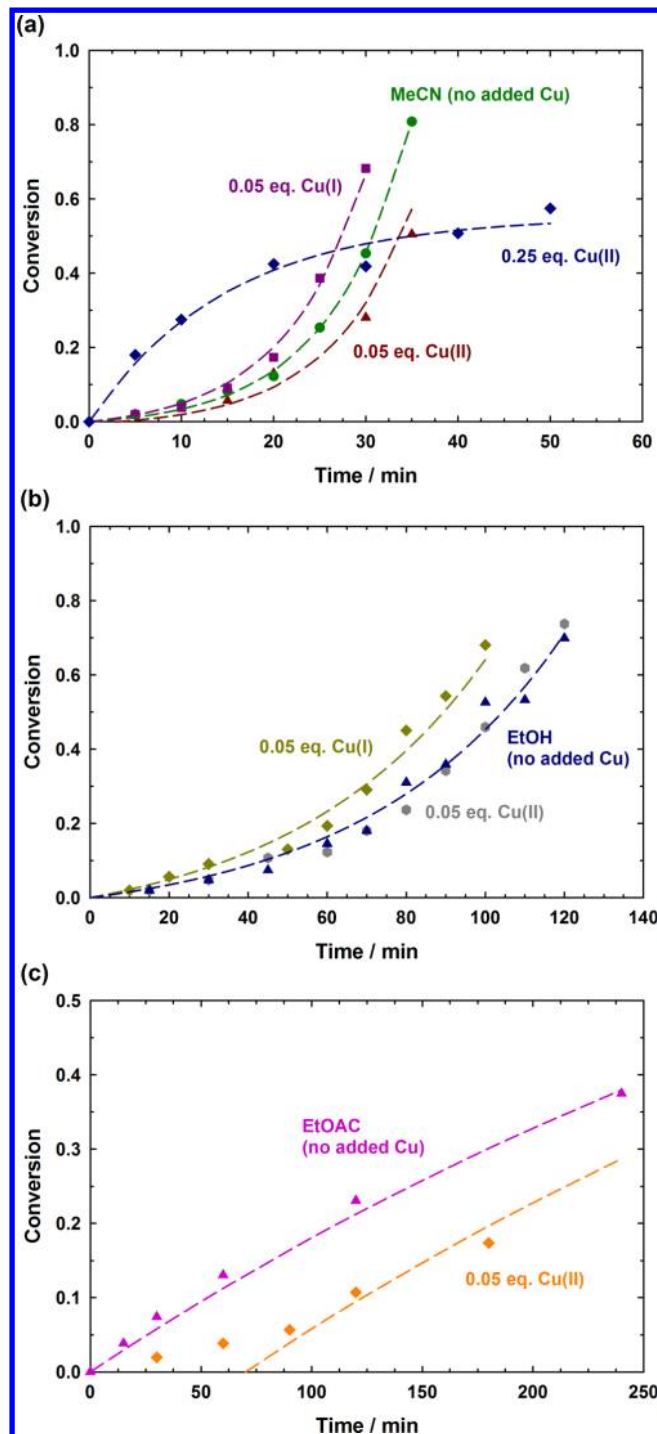
Figure 4. Effect of addition of dissolved copper species on reaction kinetics. (a) Reaction in MeCN, without additional soluble copper, with 0.05 or 0.25 equiv of CuBr$_2$ or with 0.05 equiv of CuBr. (b) Reaction in EtOH, without additional soluble copper, with 0.05 equiv of CuBr$_2$ or CuBr. (c) Reaction in EtOAc, without additional soluble copper, with 0.05 equiv of CuBr$_2$. Reactions in the presence of 0.05 equiv of CuBr are fitted to equations of the form $A(e^{kt} - 1)$, where k represents $k_{comp} - 2k_{a0}$ (values from Table 1). Reactions in the presence of 0.05 equiv of CuBr$_2$ are fitted to equations of the form $A(e^{k(t - t_0)} - 1)$, where A and k are best fit parameters for the reaction without additional soluble copper. The line connecting data for the reaction in MeCN in the presence of 0.25 equiv of CuBr is a guide to the eye only.

state concentration of CuBr is established. This hypothesis is in agreement with the experimental data for the reactions, which can be fitted using parameters established for reactions without additional Cu^{II} by the addition of an induction time, t_0, of 70 min for EtOAc, 3 min for AN, or negligible in the case of EtOH (Figure 4).

Addition of a relatively large amount of copper(II) (0.25 equiv) to the reaction in MeCN did however result in a significant increase in the initial rate of reaction, although a limiting conversion of 50% was obtained, possibly due to formation of an equilibrium between EBiB and RSG1 driven by thermal dissociation of the alkoxyamine.

Addition of a small amount (0.05 equiv) of CuBr to reactions in EtOH and MeCN had a catalytic effect on the reaction. CuBr present at the beginning of the reaction will rapidly react with EBiB to form $CuBr_2$. Once the steady-state condition has been established, the reaction kinetics are given by eq 3. The effective initial concentration of $CuBr_2$ is > 0, as a result of the initial conversion of CuBr to $CuBr_2$. The kinetics are fitted by an equation of the form $y = A(e^{kt} - 1)$, in which $k = k_{comp} - 2k_{a0}$, as for the reactions without initial dissolved copper (Figure 4). The pre-exponential term is dependent on k_{comp}, k_{a0}, and the effective initial ratio of $[CuBr_2]/[EBiB]$. Using values for k_{comp} and k_{a0} derived from reactions without copper, $[CuBr_2]_0/[EBiB]_0$ is determined to be 0.004 and 0.014 for MeCN and EtOH, respectively. These values are significantly lower than the amount of added CuBr (0.05 equiv relative to EBiB), indicating that steady-state conditions are established when $[CuBr_2]/[CuBr]$ is approximately $0.004/(0.05 - 0.004) = 0.08$ (in MeCN) or $0.014/(0.05 - 0.014) = 0.39$ (in EtOH). This accords with the expectation that a lower concentration of $CuBr_2$ is required to balance activation in MeCN, which stabilizes Cu^I complexes, than in EtOH, which does not.

Comproportionation vs Disporportionation in Copper(0)-Mediated LRP. These results show that comproportionation, not disproportionation, is dominant in copper(0)-mediated living radical polymerizations in MeCN, EtOH, DMF, and DMSO if PMDETA is used as ligand, while negligible rates of comproportionation occur in toluene, EtOAc, and EtOH:H_2O mixtures. As comproportionation leads to an autocatalytic reaction with exponentially increasing copper concentrations, radical concentrations must rise exponentially in response, and significant termination will follow. Significant levels of comproportionation will lead to a rapid but poorly controlled reaction, as observed in polymerizations in MeCN.[43] Comproportionation is negligible in toluene, but activation is also very slow, leading to slow polymerizations.[31,34−36]

DMSO is unusual among the solvents investigated in that it combines a relatively high k_{a0} with a low k_{comp}. Under polymerization conditions, which are typically characterized by $CuBr_2$/initiator ratios of ≤0.05, the rate of comproportionation will be much smaller than the rate of activation by copper metal. This allows rapid polymerization without loss of control over the polymerization. Other solvents which exhibit rapid activation combined with negligible comproportionation are EtOH:H_2O and EtOAc, with k_{a0} of 2/3 and 1/3 that of DMSO, respectively. These solvents may be good alternatives to DMSO for copper(0)-mediated polymerizations.

While PMDETA is a commonly used ligand for ATRP, Me_6TREN is generally preferred in copper(0)-mediated polymerizations.[11] This ligand is orders of magnitude more active than PMDETA with respect to both ATRP and disproportionation,[26] thus favoring activation (k_{a1}) over

deactivation (k_d) and disproportionation (k_{disp}) over comproportionation (k_{comp}) relative to PMDETA. Use of Me_6TREN in place of PMDETA should result in a reduced rate of comproportionation, improving the control over polymerization in all solvents. Further experiments on the effect of ligand on k_{a0} and k_{comp} should be carried out to test this proposal.

It should be noted that the dominance of comproportionation over disproportionation under polymerization conditions does not imply that the disproportionation equilibrium favors Cu^I over Cu^{II}. During polymerization, the $CuBr_2$/CuBr ratio approaches the ATRP equilibrium ratio[31] ($[CuBr_2]/[CuBr] = k_{a1}[EBiB]/k_d[R^\bullet] = K_{ATRP}[EBiB]/[R^\bullet]$), which may be far from the disproportionation equilibrium ratio ($[CuBr_2]/[CuBr] = K_{disp}[CuBr]$). Furthermore, the rate of disproportionation is proportional to the square of the copper(I) concentration and hence becomes very slow at low copper(I) concentrations. If a high value of K_{ATRP} causes a buildup of copper(II) species relative to copper(I), comproportionation may dominate disproportionation even when K_{disp} is large.

Kinetics of Copper(0)-Mediated Living Radical Polymerization. A similar treatment of the differential equations governing copper(0)-mediated polymerization allows the generation of equations describing the rate of polymerization in terms of the elementary rate constants. During polymerization, copper(I) is continually converted to copper(II) by reaction with initiator or dormant polymer (both represented as RBr in the following equations) and regenerated by the deactivation reaction between polymeric radicals and copper-(II) as well as by the supplemental activation reaction between initiator/dormant polymer and copper metal.

If comproportionation is negligible, the reaction will reach a steady state in which the ratio of $[CuBr_2]/[CuBr]$ approaches $k_{a1}[RBr]/k_d[R^\bullet]$.[31] This implies that

$$\frac{d[CuBr_2]}{dt} = \varphi \frac{d[\sum Cu]}{dt} \tag{8}$$

where $[\sum Cu]$ represents the total concentration of copper(I) and copper(II) species and

$$\varphi = \frac{k_{a1}[RBr]}{k_d[R^\bullet] + k_{a1}[RBr]}, \quad 0 < \varphi < 1 \tag{9}$$

If it is further assumed that the amount of termination is negligible ($d[RBr]/dt = 0$), the steady-state radical concentration is given by eq 10.

$$[R^\bullet] = \sqrt{\frac{(1 + \varphi)k_{a0}[RBr]}{2k_t}} \tag{10}$$

The parameter φ is strongly dependent on the ATRP equilibrium constant, being close to zero for low values of K_{ATRP} (e.g., PMDETA, $K_{ATRP} \sim 10^{-7}$), but close to 1 for ligands such as Me_6TREN which have high K_{ATRP} values ($\sim 10^{-4}$).[26] As $0 < \varphi < 1$, the overall contribution of φ to the radical concentration, and hence the rate of polymerization is relatively small: increasing φ from 0 to 1 leads to an increase in $[R^\bullet]$ of a factor of $\sqrt{2}$.

Rate Dependence on Copper Concentration. The rate of polymerization in copper(0)-mediated polymerization has been reported to be proportional to either the square root[19,29] or the 0.44th power of the surface area of copper.[44] This fractional dependence of polymerization rate on copper surface area has

been attributed to Langmuir−Hinshelwood kinetics involving coadsorption of the ligand and initiator on the copper surface.[11,19] The bimolecular Langmuir−Hinshelwood model describes a complex rate dependence on initiator concentration and copper surface area, given by eq 11, in which K_{RBr} and K_L represent the adsorption/desorption equilibria of initiator, RBr, and ligand, L, respectively, k is the rate of reaction, and N_{RBr} and N_L are the number of adsorption sites for RBr and L, which are each proportional to the surface area of copper.[45]

$$-\frac{d[RBr]}{dt} = kN_{RBr}N_L$$

$$\frac{K_{RBr}K_L[RBr][L]}{1 + K_{RBr}[RBr] + K_L[L] + K_{RBr}K_L[RBr][L]} \quad (11)$$

While the external rate dependence on initiator and ligand is complex, the dependence on copper surface area is second order. An alternative proposal was also advanced, involving only adsorption of ligand, with activation of alkyl halide occurring via proximity but not binding to the metal surface.[11] This corresponds to the Eley−Rideal mechanism, which predicts first-order dependence on copper surface area, according to eq 12. Neither explanation by itself can account for the observed fractional rate dependence on copper surface area.

$$-\frac{d[RBr]}{dt} = kN_L[RBr]\frac{K_{RBr}[L]}{1 + K_L[L]} \quad (12)$$

The model developed here, however, predicts that the rate of polymerization will be proportional to $k_{a0}^{0.5}$ (eq 11). As k_{a0} is itself proportional to the surface area of copper, an overall 1/2-order dependence of rate of polymerization on copper surface area is predicted, in accordance with experimental observations. This treatment of the rate of activation as first order in [RBr] is compatible with the Eley−Rideal model of eq 13.

Rate Dependence on Initiator Concentration. A 1/2-order rate dependence is also predicted for the initiator concentration: to our knowledge, however, no experimental determination of the external order of initiator concentration on the rate of SET-LRP has been carried out.

Kinetic data are available, however, for polymerizations in which the monomer:initiator ratio and monomer:copper ratio have been varied simultaneously while keeping the copper:ligand ratio and monomer concentration constant.[37,46] Data are also available for SET-RAFT of MMA using 2-cyanoprop-2-yl 1-dithionaphthalate (CPDN) as initiator/chain transfer agent for varying CPDN concentrations, while all other parameters were kept constant.[47] The apparent rate constants derived from these data, normalized by dividing by the square root of the copper concentration, are plotted in Figure 5.

The combined data were fitted to a model of the form $k_{p,app}$(normalized) $= A_i[I]^n$, in which n was assumed to be constant, while a different pre-exponential factor, A_i, was fitted to each of the three sets of data. This process resulted in a best fit value of 0.33 for n, with a 95% confidence interval of [0.20, 0.47]. This value is heavily influenced by a single data point, however. When the point corresponding to the lowest initiator concentration evaluated in ref 37 (marked by an open triangle in Figure 5) is excluded, a value of 0.45 is obtained for n (95% confidence interval [0.37, 0.52]), and the quality of the fit is significantly improved (sum of squared residuals decreases from 0.19 to 0.026). The excluded point was obtained using an extremely small quantity of copper powder (0.19 mg) and
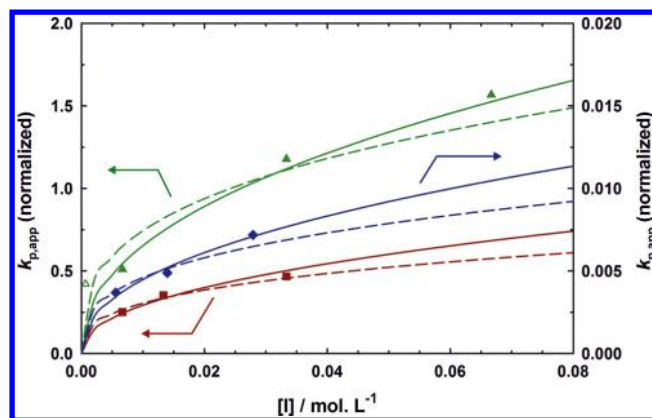
Figure 5. Apparent rate constants for SET and SET-RAFT polymerizations, normalized by dividing by $[Cu]^{1/2}$. The data were fitted to an equation of the form $k_{p,app} = A[I]^n$, in which n was assumed to be constant across all data sets. Dashed lines show best fit to the full data set ($n = 0.33$); solid lines show best fit to the data set, excluding the outlying data point marked with an open triangle ($n = 0.45$). Original data may be found in Figure 5, ref 46 (red squares), and Figures 2−4, ref 37 (green triangles) and ref 47 (blue diamonds).

hence may be subject to greater than normal error. In either case, the data are broadly consistent with a 1/2-order rate dependence on initiator concentration.

Effect of Comproportionation on Polymerization Kinetics. In the case of non-negligible comproportionation, a similar treatment gives

$$[R^\bullet] \approx \sqrt{\frac{(1 + \varphi)(k_{comp}\varphi[CuBr_2]_0 + k_{a0}[RBr])}{2k_t}} e^{k_{comp}\varphi t/2} \quad (13)$$

Note that in this case the radical concentration increases exponentially, a situation which will lead to significant levels of termination, loss of end-group fidelity, and an initially rapid rate of polymerization which slows dramatically as the dormant polymer is consumed via irreversible termination reactions.

Effect of Disproportionation on Polymerization Kinetics. If disproportionation of CuBr to form Cu^0 and $CuBr_2$ is significant, [CuBr] will reach a steady state in which the rate of consumption through activation and disproportionation matches its rate of generation through deactivation and reaction of initiator/dormant polymer with copper(0). If it is assumed that all copper(0) generated by disproportionation is in the form of highly reactive nanosized copper(0) which reacts instantaneously with initiator/dormant polymer to generate a radical and CuBr, the steady-state radical concentration will be given by

$$[R^\bullet] = \sqrt{\frac{k_{a0}[RBr]}{k_t}} \quad (14)$$

This is equivalent to the case where no disproportionation or comproportionation takes place and $\varphi = 1$. As before, the rate of polymerization is proportional to $k_{a0}^{0.5}$. This rate constant, in turn, is proportional to the surface area of copper, and thus the overall rate of polymerization will be proportional to the square root of the surface area of copper.

■ CONCLUSIONS

The preparation of alkoxyamines by reaction of EBiB with copper in the presence of a nitroxide free radical presents

interesting autocatalytic reaction kinetics in a number of solvents, including MeCN, EtOH, DMF, and DMSO. These kinetics can be explained by a reaction mechanism in which $CuBr_2$, a reaction product, is reduced by comproportionation with metallic copper to give 2 equiv of CuBr. As dissolved CuBr reacts more quickly with EBiB than does solid copper, the result is that the rate of reaction increases as the reaction proceeds. For conversions < 80%, good agreement is obtained between experimental data and a simple kinetic model, allowing the calculation of rate constants for activation by metallic copper (k_{a0}) and comproportionation (k_{comp}) for each solvent. While the values shown for each rate constant are dependent on the surface area of the copper, the ratio k_{comp}/k_{a0} will be invariable. This ratio varies across 3 orders of magnitude, ranging from 3 (DMSO) to 120 (MeCN). The solvents toluene, EtOAc, and a 1:1 mixture of EtOH and H_2O were also investigated. In these solvents, no effect of comproportionation was observed on the reaction kinetics ($k_{comp} \ll k_{a0}$), while k_{a0} varied across an order of magnitude from toluene (2×10^{-6} s^{-1}) to $EtOH/H_2O$ (43×10^{-6} s^{-1}). Effects of the addition of small amounts of soluble copper were also investigated: addition of CuBr caused acceleration of the rate of reaction, while addition of a small amount of $CuBr_2$ resulted in an induction time of slow conversion of EBiB during which a steady-state concentration of CuBr was established.

Finally, a kinetic treatment of copper(0)-mediated living radical polymerization has been developed, which predicts that the rate of polymerization will be proportional to the square root of the copper surface area and initiator concentration, in accordance with previously published experimental data. When significant levels of comproportionation take place, an exponential increase in radical concentration is predicted, which will result in higher levels of termination and ultimately loss of control over the polymerization.

These results demonstrate that comproportionation is dominant over disproportionation in copper(0)-mediated polymerization reactions using PMDETA as ligand in MeCN, EtOH, DMF, and, significantly, DMSO, the most widely used solvent for this reaction. DMSO, however, is characterized by a relatively high k_{a0} and low k_{comp}, which means that under polymerization conditions ($[CuBr_2] \ll [RBr]$) the extent of comproportionation will be low relative to the extent of supplemental activation by copper metal. This may explain the improved control over polymerization obtained in DMSO relative to MeCN, in which the rate of comproportionation is much greater than the rate of supplemental activation. So long as the rate of comproportionation is low compared to the rate of supplemental activation, and regardless of the rate of disproportionation, the overall rate of polymerization is proportional to the square root of the rate of supplemental activation, with radical concentrations given by eq 10 (negligible disproportionation) or eq 14 (significant disproportionation with highly reactive nanosized copper(0)). Significant levels of comproportionation will lead to an exponentially increasing radical concentration which is incompatible with a well-controlled polymerization.

ASSOCIATED CONTENT

S **Supporting Information**

Semilogarithmic plot of kinetic data from Figure 1 and derivation of reaction kinetics. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

REFERENCES

(1) Kato, M.; Kamigaito, M.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1995**, *28*, 1721.

(2) Wang, J. S.; Matyjaszewski, K. *J. Am. Chem. Soc.* **1995**, *117*, 5614.

(3) Ayres, N. *Polym. Rev.* **2011**, *51*, 138.

(4) Sawamoto, M.; Ouchi, M.; Terashima, T. *Chem. Rev.* **2009**, *109*, 4963.

(5) Fischer, H. *Macromolecules* **1997**, *30*, 5666.

(6) Matyjaszewski, K.; Patten, T. E.; Xia, J. *J. Am. Chem. Soc.* **1997**, *119*, 674.

(7) Matyjaszewski, K.; Jakubowski, W.; Min, K.; Tang, W.; Huang, J. Y.; Braunecker, W. A.; Tsarevsky, N. V. *Proc. Natl. Acad. Sci. U. S. A.* **2006**, *103*, 15309.

(8) Matyjaszewski, K.; Jakubowski, W. *Macromolecules* **2005**, *38*, 4139.

(9) Magenau, A. J. D.; Strandwitz, N. C.; Gennaro, A.; Matyjaszewski, K. *Science* **2011**, *332*, 81.

(10) Percec, V.; Guliashvili, T.; Ladislaw, J. S.; Wistrand, A.; Stjerndahl, A.; Sienkowska, M. J.; Monteiro, M. J.; Sahoo, S. *J. Am. Chem. Soc.* **2006**, *128*, 14156.

(11) Percec, V.; Rosen, B. M. *Chem. Rev.* **2009**, *109*, 5069.

(12) Lligadas, G.; Percec, V. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 6880.

(13) Nguyen, N. H.; Levere, M. E.; Percec, V. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 860.

(14) Boyer, C.; Soeriyadi, A. H.; Zetterlund, P. B.; Whittaker, M. R. *Macromolecules* **2011**, *44*, 8028.

(15) Soeriyadi, A. H.; Boyer, C.; Nystrom, F.; Zetterlund, P. B.; Whittaker, M. R. *J. Am. Chem. Soc.* **2011**, *133*, 11128.

(16) Sundaram, H. S.; Raghavachari, D. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 996.

(17) Wang, W. X.; Zhang, Z. B.; Wu, Y.; Zhu, J.; Cheng, Z. P.; Zhou, N. C.; Zhang, W.; Zhu, X. L. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 711.

(18) Zhai, S. J.; Shang, J.; Yang, D.; Wang, S. Y.; Hu, J. H.; Lu, G. L.; Huang, X. Y. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 811.

(19) Lligadas, G.; Rosen, B. M.; Bell, C. A.; Monteiro, M. J.; Percec, V. *Macromolecules* **2008**, *41*, 8365.

(20) Nguyen, N. H.; Rosen, B. M.; Lligadas, G.; Percec, V. *Macromolecules* **2009**, *42*, 2379.

(21) Percec, V.; Jiang, X.; Rosen, B. M. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, *48*, 403.

(22) Rosen, B. M.; Percec, V. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 5663.

(23) Lin, C. Y.; Coote, M. L.; Gennaro, A.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2008**, *130*, 12762.

(24) Isse, A. A.; Gennaro, A.; Lin, C. Y.; Hodgson, J. L.; Coote, M. L.; Guliashvili, T. *J. Am. Chem. Soc.* **2011**, *133*, 6254.

(25) Percec, V.; Rosen, B. M.; Jiang, X.; Wilson, C. J.; Nguyen, N. H.; Monteiro, M. J. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 5606.

(26) Tsarevsky, N. V.; Braunecker, W. A.; Matyjaszewski, K. *J. Organomet. Chem.* **2007**, *692*, 3212.

(27) Matyjaszewski, K.; Coca, S.; Gaynor, S. G.; Wei, M. L.; Woodworth, B. E. *Macromolecules* **1997**, *30*, 7348.

(28) Matyjaszewski, K.; Tsarevsky, N. V.; Braunecker, W. A.; Dong, H.; Huang, J.; Jakubowski, W.; Kwak, Y.; Nicolay, R.; Tang, W.; Yoon, J. A. *Macromolecules* **2007**, *40*, 7795.

(29) Zhang, Y.; Wang, Y.; Peng, C.-h.; Zhong, M.; Zhu, W.; Konkolewicz, D.; Matyjaszewski, K. *Macromolecules* **2012**, *45*, 78.

(30) Guliashvili, T.; Mendonça, P. V.; Serra, A. C.; Popov, A. V.; Coelho, J. F. J. *Chem.—Eur. J.* **2012**, *18*, 4607.

(31) West, A. G.; Hornby, B.; Tom, J.; Ladmiral, V.; Harrisson, S.; Perrier, S. *Macromolecules* **2011**, *44*, 8034.

(32) Harrisson, S.; Couvreur, P.; Nicolas, J. *Polym. Chem.* **2011**, *2*, 1859.

(33) Nanda, A. K.; Matyjaszewski, K. *Macromolecules* **2003**, *36*, 1487.

(34) Hornby, B. D.; West, A. G.; Tom, J. C.; Waterson, C.; Harrisson, S.; Perrier, S. *Macromol. Rapid Commun.* **2010**, *31*, 1276.

(35) Tom, J.; Hornby, B.; West, A.; Harrisson, S.; Perrier, S. *Polym. Chem.* **2010**, *1*, 420.

(36) Wright, P. M.; Mantovani, G.; Haddleton, D. M. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 7376.

(37) Lligadas, G.; Percec, V. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 2745.

(38) Percec, V.; Nguyen, N. H.; Rosen, B. M.; Jiang, X.; Fleischmann, S. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 5577.

(39) Matyjaszewski, K.; Woodworth, B. E.; Zhang, X.; Gaynor, S. G.; Metzner, Z. *Macromolecules* **1998**, *31*, 5955.

(40) Tsarevsky, N. *Isr. J. Chem.* **2012**, *52*, 276.

(41) Nguyen, N. H.; Percec, V. *J. Polym. Sci., Part A: Polym. Chem.* **2011**, *49*, 4241.

(42) Van den Brink, M.; Van Herk, A. M.; German, A. L. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 3793.

(43) Lligadas, G.; Rosen, B. M.; Monteiro, M. J.; Percec, V. *Macromolecules* **2008**, *41*, 8360.

(44) Percec, V.; Nguyen, N. H.; Rosen, B. M.; Lligadas, G. *Macromolecules* **2009**, *42*, 2379.

(45) Egorov, A. M.; Matyukhova, S. A. *Int. J. Chem. Kinet.* **2007**, *39*, 546.

(46) Lligadas, G.; Ladislaw, J. S.; Guliashvili, T.; Percec, V. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 278.

(47) Zhang, Z.; Wang, W.; Xia, H.; Zhu, J.; Zhang, W.; Zhu, X. *Macromolecules* **2009**, *42*, 7360.

■ NOTE ADDED AFTER ASAP PUBLICATION

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