Notes

Effect of [Cu^{II}] on the Rate of Activation in ATRP

Krzysztof Matyjaszewski,*
Ajaya Kumar Nanda, and Wei Tang

Center for Macromolecular Engineering, Department of Chemistry, Carnegie Mellon University, 4400 Fifth Avenue, Pittsburgh, Pennsylvania 15213

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Among the controlled radical polymerizations (CRP),[1,2] atom transfer radical polymerization (ATRP) is the most frequently used process for making well-defined polymers under robust conditions.[3−7] ATRP is a catalyst-based process, and the catalytic cycle involves a reversible switching between two oxidation states of the transition metal complex as shown in Scheme 1. The activator is typically a Cu^{I} halide complexed by a nitrogen-based ligand.[8−18]

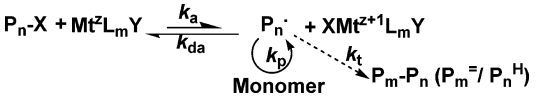
Homolytic cleavage of the alkyl−halogen bond (R−X) by the Cu^{I} complex generates an alkyl radical R• and the corresponding X−Cu^{II} complex. The radical R• can initiate and subsequently propagate with a propagation rate constant k_p. The radicals can either be terminated by coupling or disproportionation (k_t) or be reversibly deactivated by the X−Cu^{II} complex (k_{da}). As a result of the persistent radical effect,[19] the equilibrium is strongly shifted toward the dormant species ($k_a \ll k_{da}$); thus, radical concentration is low and termination is suppressed. Polymers with predictable molecular weights, narrow molecular weight distributions, and high functionalities were successfully synthesized.

The evaluation of all the reaction parameters such as k_a, k_{da}, and k_p (or k_i) is crucial for a comprehensive understanding of the process leading to better control over this catalytic system. Values of the activation rate constant, k_a, for polymeric and small molecule initiating systems were measured by suppressing the deactivation process in the presence of fast radical trapping agent (T• in Scheme 2) such as 2,2,6,6-tetramethylpiperidinyl-1-oxy (TEMPO).[20−29] We recently reported the effect of alkyl bromide, monomer, counterion, ligand, [ligand]/[Cu^{I}] ratio, solvent, and even the penultimate unit effect on the activation kinetics of ATRP.[26−29] The rate of consumption of alkyl halide in the presence of excess of Cu^{I} species follows pseudo-first-order kinetics:

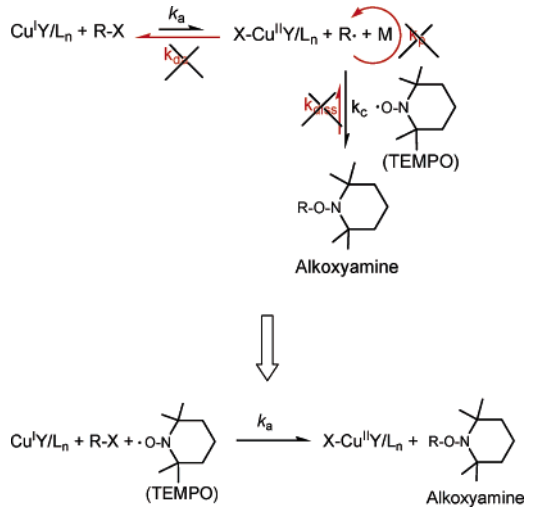
$$-\mathrm{d}\ln[\mathrm{RX}]/\mathrm{d}t = \text{slope} = k_{app}[\mathrm{Cu^I}]_0 = k_a[\mathrm{Cu^I}]_{act} \quad (1)$$

For the Cu^{I}/bpy (bpy: 2,2′-bipyridine) system with Br^- counterion the maximum slope and the highest values of k_{app} were observed at the $[bpy]_0/[Cu^I]_0 \approx 2/1$ and 1/1 in polar and less polar solvent mixtures, respectively.[26] This was attributed to the formation of $[Cu^I/bpy_2]^+[Br]^-$ and $[Cu^I/bpy_2]^+[CuBr_2]^-$ structures in different media.

Scheme 1. Proposed Mechanism for ATRP



Scheme 2. Determination of Activation Rate Constants



The observed approximately 2 times lower values of k_{app} with respect to k_a in less polar solvents were ascribed to the fact that only half of Cu^{I} species were in the form of the activating cationic complex ($[Cu^I]_{act} = [Cu^I/bpy_2]^+$; thus, $[Cu^I]_{act} = {}^1/_2[Cu^I]_0$). Similar effects were also observed for the Cu^{I}/PMDETA system.[27] Kinetics of the activation process was also studied for the polymeric systems.[21,22,30,31]

In ATRP, the presence of a X−Cu^{II}/ligand complex is necessary to reduce the concentration of radicals through a deactivation process in order to maintain the activation−deactivation equilibrium for the controlled growth of the polymer chains with conversion.[13,32,33,42] Therefore, the presence of Cu^{II} species reduces the overall rate of ATRP due to an increased rate of deactivation.[13,34,35] However, Cu^{II} should not formally affect the rate of the activation process, unless it would somehow interact with Cu^{I}. In this note, we report the influence of [Cu^{II}] on [Cu^{I}] at different [L] and in different solvents and how this affects the kinetics of the activation process in ATRP.

The activation process was studied using the TEMPO trapping methodology and chromatography described earlier.[23,24,26−28] Pseudo-first-order conditions were used, with an excess of the $Cu^{I}Br/L_n$ catalytic system, to simplify the kinetic analysis (Scheme 2).[21,26−28]

In the earlier studies, the activation rate constant (k_a) was calculated by dividing the slope of the semilogarithmic kinetic plot by total initial concentration of Cu^{I}, ($[Cu^I]_0$).[21−28] However, it was found that only $[Cu^I/L_n]^+$

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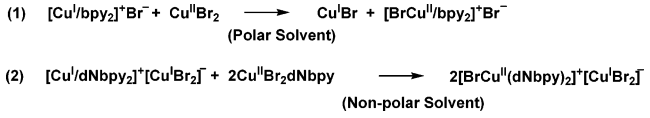
Table 1. Activation Rate Constants at 35 °C[a]

no.	L	$[L]_0$ (mM)	$[Cu^I]_0$ (mM)	$[Cu^{II}]_0$ (mM)	solvent	$[Cu^I]_{act}$ (mM)	k_{app} (M^{-1} s^{-1})	k_a[b] (M^{-1} s^{-1})
1	bpy	10	5	0	AN	5	0.066	0.066
2	bpy	15	5	2.5	AN	5	0.064	0.064
3	bpy	20	5	2.5	AN	5	0.064	0.064
4	bpy	10	5	2.5	AN	2.5	0.030	0.060
5	NPPMI	40	20	0	AN	20	0.0024	0.0024
6	NOPMI	40	20	0	AN	20	0.0021	0.0021
7	NPPMI	60	20	10	AN	20	0.0024	0.0024
8	NPPMI	40	20	10	AN	10	0.0014	0.0028
9	dNbpy	10	5	0	AN	5	0.44	0.44
10	dNbpy	10	5	0	THF	5	0.10	0.20
11	dNbpy	15	5	2.5	THF	2.5	0.05	0.20
12	dNbpy	20	5	5	THF	0	0	/
13	NOPMI	40	20	0	TOL	20	7.1×10^{-4}	1.4×10^{-3}
14	NOPMI	40	20	10	TOL	10	3.8×10^{-4}	1.5×10^{-4}

[a] $[Cu^I]_0 = 2[TEMPO] = 20[EtBriB]_0$; AN = acetonitrile; TOL = toluene; THF = tetrahydrofuran. [b] k_a values were determined by calculating the $[Cu^I]_{act}$ species as shown in Figure 2.

Scheme 3. Deactivation of [Cu^I] Active Species by [Cu^{II}] in Polar and Less Polar Solvents



participates in the activation process, whereas $[CuBr_2]^-$ does not. Therefore, the concentration of the true activator may be substantially lower than the initial $[Cu^I]_0$.[26,27] Hence, it is appropriate to distinguish the apparent rate constant from the true activation rate constant ($k_{app}[Cu^I]_0 = k_a[Cu^I]_{act}$). It should be noted that the activation rate constant (k_a) is independent of the concentration of the catalytic species.

Table 1 presents the values of slope, the apparent (k_{app}), and true (k_a) rate constants of the activation process for EtBriB and Cu^IBr complexed by bpy (2,2′-bipyridine), dNbpy (4,4′-di(5-nonyl)-2,2′-bipyridine), NPPMI (*N*-(*n*-propyl)pyridylmethanimine), and NOPMI (*N*-(*n*-octyl)pyridylmethanimine) measured at 35 °C in the absence and presence of Cu^{II} for various systems. The true activation rate constants were calculated on the basis of the the fact that ligands complex stronger with Cu^{II} than with Cu^I (in aqueous media, for bidendate ligand bpy, $\beta_2([Cu^I/bpy_2]^+) = 1.51 \times 10^{13}$, $\beta_2([Cu^{II}/bpy_2]^{2+}) = 4.46 \times 10^{13}$; for tridendate ligand PMDETA (*N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine), $\beta_2([Cu^I/PMDETA]^+) < 10^8$, $\beta_2([Cu^{II}/PMDETA]^{2+}) = 1.45 \times 10^{12}$)[40,41] and that in a polar solvent $[Cu^I/L_2]^+[Br]^-$ and $[BrCu^{II}/L_2]^+[Br]^-$ species dominate, whereas in nonpolar solvents $[Cu^I/L_2]^+[Cu^IBr_2]^-$ and $[BrCu^{II}/L_2]^+[Cu^IBr_2]^-$ species dominate (vide infra and Scheme 3).[39]

In a polar solvent, acetonitrile, the value for k_{app} for the bpy system decreased slightly with the addition of Cu^{II} (entries 1 and 2 in Table 1). In these reactions, bpy was kept at a concentration 2 times higher than the total amount of $[Cu^I]$ and $[Cu^{II}]$. Excess of bpy has no further effect on the rate of the activation (entry 3 in Table 1). In contrast, when the amount of bpy was less than 2 times (required by complex stoichiometry), the total concentration of both Cu^I and Cu^{II} (10 mM vs 5 + 2.5 mM, respectively), the value of k_{app} decreased by half (entry 4). The value of k_a, calculated from the available $[Cu^I/L_2]^+$ species, since bpy complexes stronger to Cu^{II} species than Cu^I (Scheme 3), remains nearly the same. This is in agreement with an earlier observation that in polar solvents the rate of activation was 2 times lower at $[bpy]/[Cu^I] \sim 1$ in comparison with $[bpy]/[Cu^I] > 2$.[26] Hence, 2.5 mM of Cu^{II} consumes 5 mM of bpy for the formation of the $[Cu^{II}/(bpy)_2]^+$ complex, leaving the remaining 5 mM of bpy available for complex formation with 5 mM of Cu^I. Therefore, only 2.5 mM of $[Cu^I/bpy_2]^+$-$[Br]^-$ can be formed for the activation process out of 5 mM of Cu^I present in the reaction mixture. Hence, the k_{app} is reduced by half.

Similar behavior was observed for another class of bidentate ligands based on pyridylmethanimines: NPPMI and NOPMI.[18,36−38] The resulting copper complexes are approximately 30 times less active than complexes with bpy (entries 5 and 6). When the concentration of added ligand was 2 times higher than combined $[Cu^I]$ and $[Cu^{II}]$ species, no effect on the rate of activation was noticed in acetonitrile (entry 7). However, the value for k_{app} was reduced by half when 40 mM of NPPMI was used for complex formation with 20 mM of Cu^I and 10 mM of Cu^{II}, which can be attributed to the formation of only half of $[Cu^I/L_2]^+$ activating species, as seen for the Cu^I/bpy system (entry 8). The color of the solution was dark brown for both Cu^I/bpy and Cu^I/NPPMI systems.

The effect of $[Cu^{II}]$ on the activation rate in a less polar solvent, toluene or THF, is different from acetonitrile. To obtain homogeneous solutions, Cu^I/dNbpy and Cu^I/NOPMI were used as ligands instead of Cu^I/bpy and Cu^I/NPPMI systems, which have limited solubility in toluene or THF. The values of activation rate constants were lower than in acetonitrile (entry 6 vs 13 and entry 9 vs 10). This is partially due to solvent effects.[26] In addition, in less polar solvents the maximum value of the apparent rate constant is already obtained at $[bpy]/[Cu^I] \sim 1/1$, which is ~2 times smaller than its k_a in less polar solvent and thus ~4 times smaller than its k_a in AN.[26] This is due to the formation of half of active $[Cu^I/bpy_2]^+$ cation and half of inactive $[CuBr_2]^-$ anion. In the case of dNbpy in THF, the presence of 2.5 mM of Cu^{II} reduced the value of k_{app} by a factor of 2 (entry 10) with respect to k_{app} in AN (entry 11). However, the introduction of 5 mM of Cu^{II} completely consumed all the Cu^I presented in the catalytic system, leading to 0 for the rate of activation (entry 12). This indicated that $Cu^{II}Br_2$ converts the active $[Cu^I/dNbpy_2]^+$ cation to an inactive $[Cu^IBr_2]^-$ species, which serves as a counterion to the $[BrCu^{II}/dNbpy_2]^+$ cation. Such a conclusion was also reached from ESR studies of similar copper complexes.[39] The NOPMI system in toluene behaves in a manner similar to dNbpy in THF. Values of k_{app} are smaller in toluene than in acetonitrile, and Cu^{II} reduces concentration of active Cu^I species (entries 13 and 14).

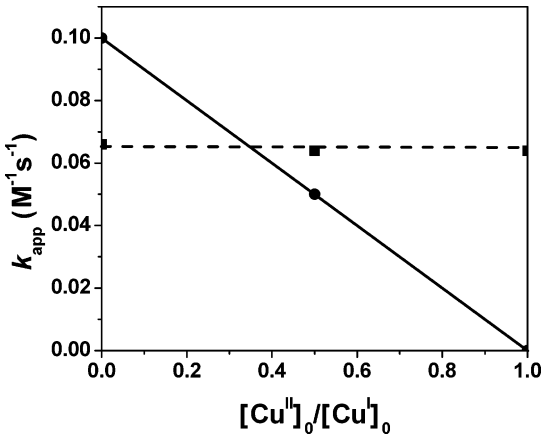


Figure 1. Calculation of $[Cu^I]_{act}$ in (—) polar and (· · ·) less polar solvents.

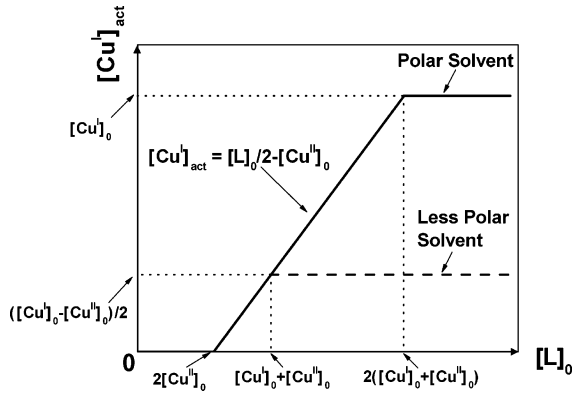


Figure 2. Dependence of k_{app} on $[Cu^{II}]/[Cu^I]$ ratio for (■) bpy with EtBriB in acetonitrile and (●) dNbpy with EtBriB in THF at 35 °C. $[TEMPO]_0 = 10\ [EtBriB]_0$. (—) [dNbpy] = $[Cu^I]$ + $[Cu^{II}]$. (· · ·) [bpy] = 2($[Cu^I]$ + $[Cu^{II}]$).

Figure 1 presents detailed studies of the effect of $[Cu^{II}]$ on the vales of k_{app} in the presence of excess of dNbpy and bpy ligands for EtBriB. In THF, vales of k_{app} decrease linearly with the increase in $[Cu^{II}]_0/[Cu^I]_0$ ratio. In acetonitrile, the effect is negligible.

The relevant reactions were presented in Scheme 3. In polar solvents, ligands complex stronger to Cu^{II} than to Cu^I. In the presence of excess ligands, Cu^{II} should not affect the rate of activation process, and the true values of activation rate constants are similar to the apparent values. For [L] > 2$[Cu^I]$, all Cu^I species are complexed by bidentate ligands and activate ATRP. If the amount of ligand is not sufficient to form a complex with all Cu species, then the presence of Cu^{II} reduces the concentration of activating Cu^I species. In a less polar solvent, like toluene or THF, Cu^I forms a $[Cu^I/L_2]^+[Cu^IBr_2]^-$ complex, where only half of the Cu^I participates in the activation process. Under these conditions, $k_{app} = {}^1/_2 k_a$. In the presence of Cu^{II}, even if excess ligand is used, $Cu^{II}Br_2$(dNbpy) reacts with $[Cu^I/dNbpy_2]^+$ and converts it to its inactive counterion, i.e., forms a $[BrCu^{II}/dNbpy_2]^+\ [Cu^IBr_2]^-$ complex (Scheme 3). Therefore, with the continued addition of Cu^{II}, there is a progressive decrease in the active $[Cu^I(dNbpy)_2]^+$ in the reaction mixture. Consequently, k_{app} decreases with an increase of the ratio of $[Cu^{II}]/[Cu^I]$. The value for k_{app} becomes zero at $[Cu^{II}] \sim [Cu^I]$ (Figure 1). Hence, with an increase of $[Cu^{II}]$ in less polar solvent, the rate of ATRP will decrease, not only due to the increase in the rate of deactivation but also due to the decrease of the rate of activation caused by depletion of the concentration of the active species, $[Cu^I/L_2]^+$. It should be noted that although k_{app} is quite strongly affected by the amount of Cu^{II} present in the system, k_a remains nearly constant for the same ligand and solvent (cf. Table 1).

The detailed calculations of active catalytic species $[Cu^I]_{act}$ in the presence of Cu^{II} are shown in Figure 2. In both polar and less polar solvents, bidendate ligand should be present at a concentration at least 2 times higher than $[Cu^{II}]_0$ to start polymerization. After this point, the $[Cu^I]_{act}$ depends both on $[Cu^{II}]_0$ and also on $[L]_0$. The $[Cu^I]_{act}$ in both polar and less polar solvents could be calculated from the same equation, i.e., $[Cu^I]_{act} = [L]_0/2 - [Cu^{II}]_0$. A lower amount of ligand is needed to reach maximal rate and maximal $[Cu^I]_{act}$ in less polar solvent ($[L]_0 = [Cu^I]_0 + [Cu^{II}]_0$) than in polar solvent ($[L]_0 = 2([Cu^I]_0 + [Cu^{II}]_0)$). Once there is enough ligand present in the system, all the Cu^I species will be active in polar solvent. However, a smaller amount of Cu^I species is active in less polar solvent ($[Cu^I]_{act} = ([Cu^I]_0 - [Cu^{II}]_0)/2$). In this case Cu^I also serves as a counterion ($Cu^IBr_2^-$) for both Cu^{II} and Cu^I complexes (Scheme 3).

Thus, some earlier reported values of k_a for ATRP systems even with a sufficient amount of bidentate ligands measured in less polar media, especially in the presence of Cu^{II} species, should be recalculated. True values of the activation rate constants for systems with bpy and pyridylmethanimine ligands used as complexing agents for Cu^IBr and Cu^ICl in less polar media without added Cu^{II} are 2 times larger than reported, since only half of the added Cu^I species activates the atom transfer process.[26] Moreover, addition of Cu^{II} species in less polar media reduces the concentration of active Cu^I species and results in a decrease of the apparent rate constant of activation[31] and may also dramatically reduce the overall rate of ATRP.[13] Therefore, the calculation of true rate constants of activation and true ATRP equilibrium constants should not be based on the concentration of the added Cu^I species. They should take into account only truly activating Cu^I cationic species, i.e., $[Cu^I]_{act} = ([Cu^I]_0 - [Cu^{II}]_0)/2$, since the remaining Cu^I species act as counteranions to both Cu^I and Cu^{II} cations and cannot activate the atom transfer process.

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Supporting Information Available: Experimental procedure and examples of kinetic measurements. This material is available free of charge via the Internet at http://pubs.acs.org.

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