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General Method for Determination of the Activation, Deactivation, and Initiation Rate Constants in Transition Metal-Catalyzed Atom Transfer Radical Processes

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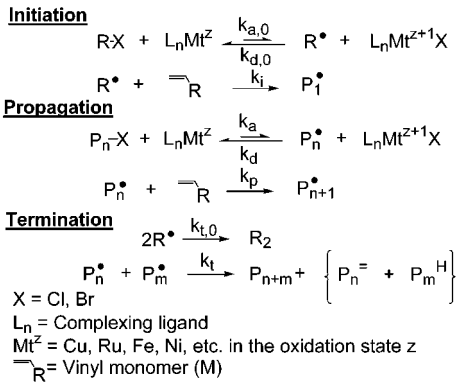
During the past few years, atom transfer radical polymerization (ATRP) has experienced a substantial progress and become one of the most powerful tools in obtaining well-defined polymers by radical means.[1] The catalytic cycle in ATRP involves reversible switching between two oxidation states of a transition metal complex as shown in Scheme 1.[2] It originates from atom transfer radical addition (ATRA), which is a well-known and widely used reaction in organic synthesis.[3]

Scheme 1



In the initiation process, the homolytic cleavage of the alkyl halogen bond by the transition metal (Cu,[4] Fe,[5] Ru,[6] Ni,[7] etc.) complex in the lower oxidation state (k_a) generates an alkyl radical and a transition metal complex in the higher oxidation state. The formed radicals can initiate the polymerization, by adding across the double bond of a vinyl monomer (k_i), propagate (k_p), terminate by either coupling or disproportionation (k_t), or be reversibly deactivated by the transition metal complex in the higher oxidation state (k_d). Since the ATRP equilibrium is strongly shifted toward the dormant species ($k_a \ll k_d$), proportion of the products formed by radical coupling or disproportionation is so small that it can be neglected. As a result of persistent radical effect,[8] polymers with predictable molecular weights, narrow molecular weight distributions, and high functionalities have been synthesized.[9]

The evaluation of the reaction parameters such as k_a, k_d, and k_i is crucial in further understanding of this catalytic system. Studies have thus far concentrated on measuring k_a for polymeric and monomeric systems using spectroscopy[10] and chromatography.[11,12] The deactivation (k_d)[11,13] and initiation (k_i) rate constants for alkyl halides commonly used in the ATRP[2] have been much less extensively studied. Detailed kinetic investigation of these reactions can provide much needed information as to how to correlate the catalyst structure with its reactivity, develop more active catalysts that can be used in smaller concentrations, extend the polymerization control to even higher-molecular weight polymers, and polymerize in a controlled fashion less reactive monomers (vinyl esters and olefins).

This article reports on the general method to determine k_a, k_d, and k_i in ATR processes by combining the analytical solution of the persistent radical effect and trapping of initiating radicals by monomer under polymerization conditions.

According to Scheme 1, the rate of disappearance of alkyl halide RX is given by the following equation:

$$\frac{d[RX]}{dt} = -k_a[L_nMt^z][RX] + k_d[L_nMt^{z+1}X][R^\bullet] \quad (1)$$

which under steady-state concentration of radicals and neglecting R$^\bullet$ termination can be rearranged to:

$$\frac{1}{k_{app}} = -\frac{dt}{d\ln[RX]} = \frac{1}{k_a[L_nMt^z]} + \frac{k_d[L_nMt^{z+1}X]}{k_a k_i[M][L_nMt^z]} \quad (2)$$

Similar derivations were already successfully applied in the determination of the kinetic parameters for transition-metal−alkyl bond homolysis, using TEMPO[14] and organotin compounds[15] as radical trapping agents. Under the pseudo-first-order conditions, plots of $1/k_{app}$ versus $1/[M]_0$ and $1/k_{app}$ versus $[L_nMt^{z+1}X]_0$ should yield straight lines with the y-intercept being equal to $1/k_a[L_nMt^z]_0$ and slopes $k_d[L_nMt^{z+1}X]/k_ak_i[L_nMt^z]_0$ and $k_d/k_ak_i[M][L_nMt^z]_0$, respectively. Large excess of the (de)activator ([L_nMt^z] or [$L_nMt^{z+1}X$]) relative to [RX] is not required since, due to the insignificant radical termination reactions,[8,16] their concentrations can be considered as being approximately constant. Equation 2 can be used only to determine k_a and k_d/k_i. However, in the absence of a radical trap, it has been shown that the concentration of deactivator [$L_nMt^{z+1}X$] should be proportional to $t^{1/3}$ according to the eq 3:[8]

$$[L_nMt^{z+1}X] = (3K_{EQ}^2k_t[RX]_0^2[L_nMt^z]_0^2)^{1/3}t^{1/3} \quad (3)$$

$$\frac{\sqrt{8k_t}K_{EQ}}{3[RX]_0k_a^{3/2}} < t < \frac{1}{3K_{EQ}^2k_t[RX]_0}$$

Therefore, in the time regime given above, a plot of [$L_nMt^{z+1}X$] versus $t^{1/3}$ can be used to determine $K_{EQ} = k_a/k_d$, provided that k_t for radical coupling reaction is known. Since the termination of two small radicals without an unusual steric effect is governed by diffusion limits ($2k_t = 5 \pm 1 \times 10^9$ M^{-1} s^{-1} at rt),[17] assumptions in k_t will introduce relatively small errors in the overall analysis.

Several rate constants of addition of small radicals to alkenes (k_i) are available from flash photolysis and time-resolved ESR

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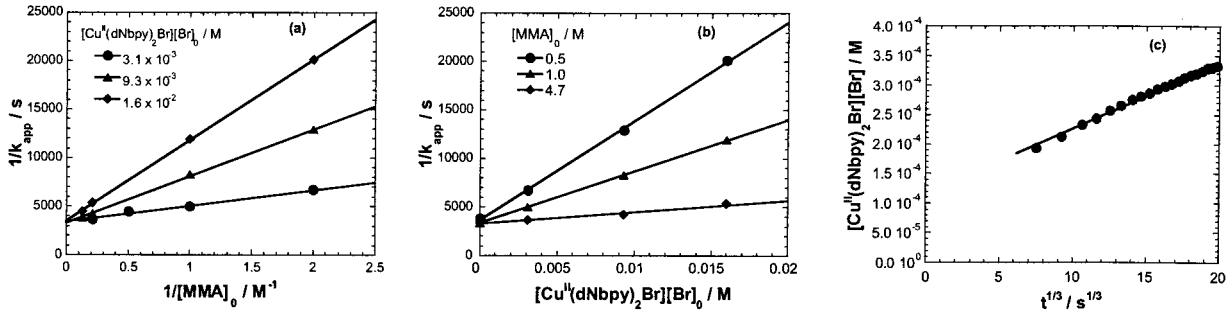

Figure 1. (a) $1/k_{app}$ vs $1/[MMA]_0$ at different concentrations of $[Cu^{II}(dNbpy)_2Br][Br]$, (b) $1/k_{app}$ vs $[Cu^{II}(dNbpy)_2Br][Br]_0$ at different concentrations of MMA $\{[t\text{BuBrP}]_0 = 3.1 \times 10^{-3}$ M, $[Cu^{I}(dNbpy)_2][Br]_0 = 3.1 \times 10^{-2}$ M$\}$, and (c) $[Cu^{II}(dNbpy)_2Br][Br]$ vs $t^{1/3}$ for $t >$ 120s $\{[t\text{BuBrP}]_0 = 4.0 \times 10^{-3}$ M, $[Cu^{I}(dNbpy)_2][Br]_0 = 0.10$ M$\}$, in CH_3CN at 22 ± 1 °C.

studies.[18,21] However, when k_i is not known, eq 3 can be used in conjunction with eq 2 to determine k_a, k_d, and k_i.

To test the applicability of eqs 2 and 3, a system was chosen which consisted of *tert*-butyl 2-bromopropionate (*t*BuBrP) as the alkyl halide, $Cu^{I}Br$ and $Cu^{II}Br_2$ complexes with 2 equiv of 4,4′-di(5-nonyl)-2,2′-bipyridine ligand (dNbpy) as the activator and deactivator, respectively, and methyl methacrylate (MMA) as the monomer. In polar solvents such as CH_3CN, $Cu^{I}Br$/2dNbpy and $Cu^{II}Br_2$/2dNbpy predominantly exist as $[Cu^{I}(dNbpy)_2][Br]$[19] and $[Cu^{II}(dNbpy)_2Br][Br]$,[20] respectively. The rate of the addition of *t*BuP radicals ($CH_3C^{\bullet}HCOOC(CH_3)_3$) to MMA, $k_i = 6.0 \times 10^4$ M^{-1} s^{-1}, and the rate of radical coupling, $2k_t = 4.1 \times 10^9$ M^{-1} s^{-1} in CH_3CN at 22 °C, have been recently reported.[21]

In Figure 1 (a and b) are shown the plots of $1/k_{app}$ versus $1/[MMA]_0$ and versus $[Cu^{II}(dNbpy)_2Br][Br]_0$ at different concentrations of $[Cu^{II}(dNbpy)_2Br][Br]$ and [MMA], respectively. In both cases, the linearity was observed, which confirms that the decomposition kinetics of *t*BuBrP given by eq 2 is consistent with the mechanism underlined in Scheme 1. The activation rate constant was calculated from the *y*-intercept. Similarly, the ratio of the deactivation to the initiation rate constant (k_d/k_i) was determined from the slope. Results are summarized in Table 1.

Table 1. Summary of Kinetic Parameters for *t*BuBrP and MBrP Using $[Cu^{I}(dNbpy)_2][Br]$ Catalyst in CH_3CN at 22 ± 1 °C

initiator	$k_a \times 10^3/M^{-1}$ s^{-1}	$k_d \times 10^{-6}/M^{-1}$ s^{-1} [a]	$k_{i,MMA} \times 10^{-4}/M^{-1}$ s^{-1} [b]	
*t*BuBrP	9.4 ± 0.6	8.5 ± 1.2	5.5 ± 0.9	6.0 ± 0.3[c]
MBrP	26 ± 5.9	29 ± 7.3	5.7 ± 1.6	

[a] k_d for *t*BuBrP and MBrP was calculated using k_a and $K_{EQ} = (1.1 \pm 0.18) \times 10^{-9}$ and $(9.0 \pm 1.0) \times 10^{-10}$, respectively. [b] $k_{i,MMA}$ for *t*BuBrP and MBrP was calculated using $k_d/k_i = 155 \pm 14$ and 506 ± 55, respectively. [c] Determined using time-resolved ESR spectroscopy (ref 21).

Figure 1c shows the concentration of $[Cu^{II}(dNbpy)_2Br][Br]$, generated by the reaction of $[Cu^{I}(dNbpy)_2][Br]$ with *t*BuBrP in the absence of MMA, as a function of $t^{1/3}$ for $t >$ 120s due to eq 3. Excess of $[Cu^{I}(dNbpy)_2][Br]$ was used in order to shift K_{EQ} (Scheme 1) to the right-hand side. Using eq 3 and the rate of radical termination $2k_t = 4.1 \times 10^9$ M^{-1} s^{-1},[21] the equilibrium constant $K_{EQ} = k_a/k_d$ for the atom transfer was calculated. The value of K_{EQ} in conjunction with k_a and k_d/k_i was then used to determine k_d and k_i (Table 1). The initiation rate constant determined using this methodology is in good agreement with the literature value,[21] confirming the validity of the proposed approach.

Methyl 2-bromopropionate (MBrP) is a commonly used initiator in copper-catalyzed ATRP of acrylates.[22] The above methodology was used to determine the previously unknown k_a, k_d, and $k_{i,MMA}$, assuming the rate constant of radical termination $2k_t = 4.0 \times 10^9$ M^{-1} s^{-1}. Results are shown in Table 1. The rate constants for MBrP are higher than for *t*BuBrP, which can be tentatively attributed to steric effects; however, more detailed investigation is required.

In summary, a general method to determine the activation (k_a), deactivation (k_d), and initiation (k_i) rate constants by monomer trapping of the initiating radicals and the analytical solution of the persistent radical effect in ATR processes has been reported. This method opens a new way to systemically evaluate the efficiency of the catalyst in the polymerization. Subject to future investigation is determination of the kinetic and thermodynamic parameters for other catalytic systems used in the ATRP.

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Supporting Information Available: Experimental procedures, derivation of eq 2, and kinetic plots for the determination of k_a, k_d, and $k_{i,MMA}$ for MBrP in CH_3CN at 22 °C (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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