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Effect of Penultimate Unit on the Activation Process in ATRP

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Atom transfer radical polymerization (ATRP) is among the most successful processes for controlled radical polymerization.[1−5] The catalytic cycle in ATRP involves a transition metal complex reversible switching between two oxidation states as shown in Scheme 1. The activator is typically a copper(I) halide complex formed with a nitrogen-based ligand.[6−15]

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 by adding across the double bond of a vinyl monomer. The radicals can either terminate by coupling or disproportionation (k_t) or be reversibly deactivated by the $X-Cu^{II}$ complex (k_{deact}). Since the equilibrium is strongly shifted toward the dormant species ($k_{act} \ll k_{deact}$), radical concentration is low and termination is suppressed. As a result of the persistent radical effect,[16] polymers with predictable molecular weights, narrow molecular weight distributions, and high functionalities have been synthesized.

The evaluation of all the reaction parameters such as k_{act}, k_{dact}, and k_p (or k_i) are crucial for development of a deeper understanding of the process leading to better control over this catalytic system. Values of the rate constant of activation, k_{act}, for polymeric and monomeric systems can be measured by suppressing the deactivation process in the presence of fast radical traps ($T^•$ in Scheme 1) such as 2,2,6,6-tetramethylpiperidinyl-1-oxy (TEMPO).[17−24] We recently reported that for both Cu(I)/bpy[23] and Cu(I)/PMDETA[24] catalysts reactivity of *tert*-butyl 2-bromopropionate (H-tBA-Br) is 3.4 times smaller than that of either ethyl or methyl 2-bromopropionate (H-MA-Br) and 45 times smaller than that of ethyl 2-bromoisobutyrate (H-EMA-Br, where H represents a hydrogen atom). These compounds could be considered as models of dormant species present in the ATRP homopolymerization of *tert*-butyl acrylate (tBA), methyl acrylate (MA), and methyl methacrylate (MMA). However, it was reported earlier that although H-MA-Br or H-tBA-Br is a good initiator for ATRP of MA and tBA, H-EMA-Br is a rather poor initiator for ATRP of MMA, plausibly due to the higher reactivity of the dormant polymeric species, ascribed to the B-strain effect.[25−27] Thus, it is of interest to compare activation rate constants for the "monomeric" and "dimeric" dormant species and expand these studies to mixed dimeric species which will model copolymerization systems.[2,28−30] Figure S-12 in the Supporting Information illustrates the structures of all studied monomeric, dimeric, and the related dormant polymeric species.

The activation process was studied using the TEMPO trapping methodology and chromatography described earlier.[20−24] Pseudo-first-order conditions were used, with an excess of the CuBr/2bpy catalytic system, to simplify the kinetic analysis.[18,23,24]

Scheme 1. Proposed Mechanism for ATRP

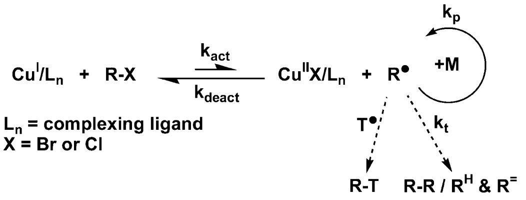

Table 1 presents the values of the rate constants of activation for the model monomeric and dimeric species measured in acetonitrile solution at 35 °C. They demonstrate that structural effects have a very large influence on k_{act}, H-MMA-MMA-Br being 355 times more reactive than H-tBA-Br (Table 2).

Table 2 presents the relative values of k_{act} obtained in this study and allows for a better comparison of the effects of the terminal and penultimate units on the activation process. These results can be summarized in the following way:

1. The reactivities of methyl and ethyl bromoesters (Table 1) are similar. This is the case for both 2-bromoisobutyrates and 2-bromopropionates. However, *tert*-butyl esters are 3.4 times less reactive than primary methyl and ethyl species, presumably due to steric effects.

2. The reactivity of tertiary alkyl halides is much higher than that of secondary alkyl halides due to better stabilization of the radicals derived from the former species and a lower C−Br bond dissociation energy. They are 19 and 21 times respectively more reactive for both H-MA and H-EMA penultimate units. However, a smaller value of 13 was noted for H as the penultimate unit, i.e., monomeric species. The overall ratio of reactivity of tBA-Br to MMA-Br terminal ranges from 45 to 77, depending further on the penultimate unit.

3. There is an essentially negligible penultimate unit effect of H, H-tBA, or H-MA on the reactivity of secondary bromoesters. However, the presence of a bulky H-EMA as the penultimate unit increases the reactivity 4.6 times for tBA-Br and MA-Br terminal units.

4. The MMA-Br terminal unit is most sensitive to the structure of the penultimate unit. There is already 1.6 times the effect on the rate of activation for H vs H-MA and an additional 5.1 times the effect on activation for H-MA vs H-EMA/H-MMA.

5. Thus, reactivities of monomeric and dimeric acrylates are essentially identical, meaning that both species are good initiators for ATRP of the corresponding monomers. However, H-EMA-Br/H-MMA-Br is 8 times less reactive than H-MMA−MMA-Br, indicating lower reactivity and plausibly slower initiation.

6. In the MMA−MA copolymerization, the reactivity of the tertiary bromoesters is ~20 times higher than that of secondary bromoesters with the same penultimate units. The presence of the EMA/MMA penultimate unit in comparison with a MA penultimate unit increases the reactivity of the MA-Br or MMA-Br terminal units ~5 times. Thus, pMMA-Br is activated ~100 times faster than pMA-Br.

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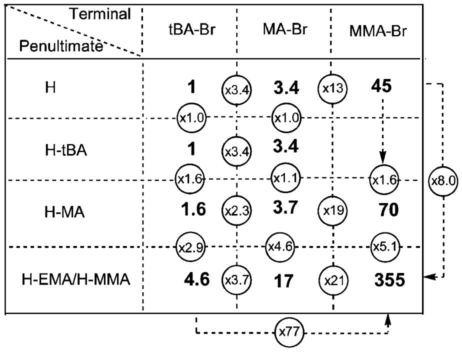
Table 1. Activation Rate Constants for Model Monomeric and Dimeric Species in Acetonitrile at 35 °C with $[bpy]_0/[Cu(I)Br]_0 = 2/1$[a]

model monomer and dimer	k_{act} ($M^{-1}\,s^{-1}$)
H-tBA-Br	0.0054
H-MA-Br	0.018
H-EA-Br	0.017
H-MMA-Br	0.26
H-EMA-Br	0.24
H-tBA−tBA-Br	0.0053[b] (0.0048, 0.0057)
H-MA−tBA-Br	0.0088[b] (0.0077, 0.010)
H-EMA−tBA-Br	0.025
H-MA−MA-Br	0.020[b] (0.020, 0.020)
H-EMA−MA-Br	0.091
H-MA−MMA-Br	0.38[b] (0.38, 0.38)
H-MMA−MMA-Br	1.92

[a] Temperature = 35 °C, $[Cu(I)Br]_0 = [bpy]_0/2 = 0.02$ mol/L, $[TEMPO]_0 = 0.01$ mol/L, $[R{-}X]_0 = 0.001$ mol/L. [b] Average values of the k_{act} for the diastereomers.

Table 2. Relative Values (Bold) and Their Ratios (Inside Circles) of Activation Rate Constants of Model Monomeric and Dimeric Species in Acetonitrile at 35 °C with $[bpy]_0/[Cu(I)Br]_0 = 2/1$



Terminal / Penultimate	tBA-Br		MA-Br		MMA-Br
H	**1**	x3.4	**3.4**	x13	**45**
	x1.0		x1.0		
H-tBA	**1**	x3.4	**3.4**		
	x1.6		x1.1		x1.6
H-MA	**1.6**	x2.3	**3.7**	x19	**70**
	x2.9		x4.6		x5.1
H-EMA/H-MMA	**4.6**	x3.7	**17**	x21	**355**

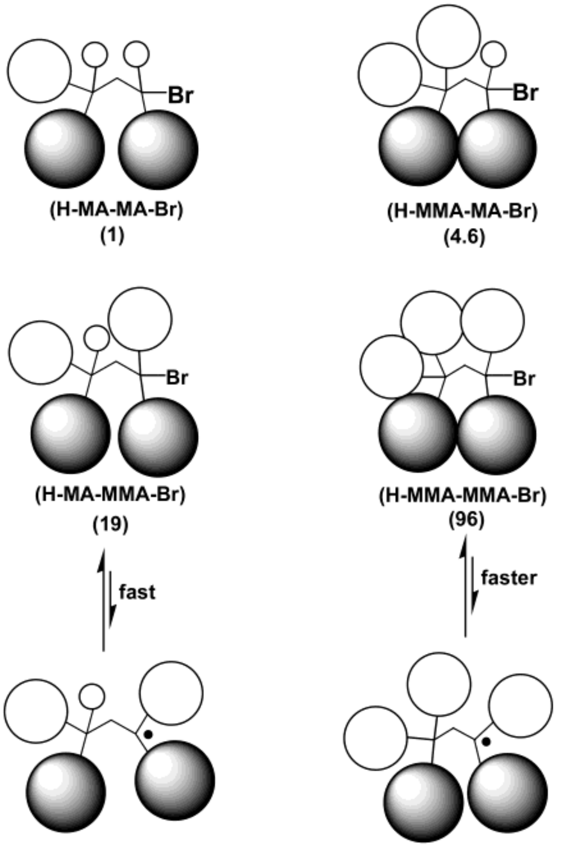


Figure 1. Structural comparison of dimeric species with their relative values of activation rate constants: ○, H; ◯, CH_3; ●, $COOCH_3$.

It must be noted that for the dimers H-MA−MA-Br, H-MA−MMA-Br, H-MA−tBA-Br, and H-tBA−tBA-Br two diastereomers were observed by ^{1}H NMR and GC at the corresponding ratios: 50:50, 49:51, 47:53, and 44:56 (cf. Supporting Information). Reactivities of the diastereomers were very similar for H-MA−MA-Br and H-MA−MMA-Br; however for H-MA−tBA-Br and H-tBA−tBA-Br one of the isomers was 1.3 and 1.2 times, respectively, more reactive than the other one (Table 1).

Figure 1 illustrates the structures of the corresponding dimeric species. The bulky MMA penultimate unit destabilizes the dormant alkyl bromide, reduces the bond dissociation energy, and presumably stabilizes the resulting sp^2-hybridized radical species. As a result of this B-strain effect, H-MMA−MA-Br is ∼5 times more active than H-MA−MA-Br. The rate of activation of a dormant chain end with a MMA-Br terminal unit is ∼20 times faster than with a MA terminal unit with the same penultimate unit. This is attributed to the formation of thermodynamically more stable 3° radical from the former species when compared to the less stable 2° radical from the latter species. The combined effects of B-strain and generation of stable 3° radical result in a ∼100 fold increase of k_{act} for H-MMA−MMA-Br. Similar effects were previously reported on the solvolysis of alkyl halides and ionization of alkyl halides to sp^2-hybridized carbocations.[31,32]

The presence of a penultimate unit effect was reported earlier in propagation studies. At 60 °C, the rate constant of addition of the H-MMA$^\bullet$ radical (i.e., methyl isobutyryl radical) to MMA was 3.9 times higher than that of the H-MMA−MMA$^\bullet$ dimeric radical and 17 times higher than a value of k_p from PLP measurements.[33,34] A similar effect was reported for a disubstituted monomer, methacrylonitrile (6 times),[33] but a much weaker dependence for monosubstituted acrylonitrile (<2 times).[35]

It will be very interesting to determine the effect of penultimate units on deactivation rate constants, i.e., on the equilibrium constant, and perhaps also extend these studies to longer oligomers and compare them with the rate constants obtained for polymeric species.

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Supporting Information Available: Synthesis of dimers, coupling patterns of individual diastereomers in ^{1}H NMR, ^{1}H−^{1}H COSY spectra and kinetic procedures for activation rate constant measurements, first-order kinetic plots of the activation process, and structures of model monomeric, polymeric, and dimeric analogues. This material is available free of charge via the Internet at http://pubs.acs.org.

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