

Ab Initio Evidence for Slow Fragmentation in RAFT Polymerization

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In recent years, the field of free-radical polymerization has been revolutionized by the development of techniques for controlling the molecular weight and architecture of the resulting polymer. One of the most versatile is the reversible-addition-fragmentation-transfer (RAFT) process in which thiocarbonyl compounds (known as RAFT agents, **2**) reversibly react with the growing polymeric radical (**1**) via the chain-transfer reaction shown in Scheme 1.¹ Ideally, this process should be fast, and the intermediate RAFT adduct radical (**3**) should be short-lived. In this way, the rapid transfer of the growing polymeric radicals between their "free" (**1** and **5**) and corresponding "dormant" (**2** and **4**) forms minimizes unwanted radical-radical termination processes without significantly reducing the propagation and hence polymerization rates.

The stability (and fate) of the RAFT adduct radical (**3**) has attracted considerable controversy. It is well-known that the RAFT agents cumyl or 1-phenylethyl dithiobenzoate (**2**; Z = phenyl, R = C(CH₃)₂C₆H₅ or CH(CH₃)C₆H₅) significantly retard the polymerization rate for styrene,²⁻⁶ methyl methacrylate,⁷ butyl acrylate,² and methyl acrylate.^{5,8,9} This retardation effect can be relieved through either a reduction in the RAFT agent concentration, an increase in polymerization temperature, or the use of alternative RAFT agents containing a benzyl or methyl (rather than phenyl) group in the Z-position.^{2,8,10} The effect of the R-group on retardation is more variable. Changing the R-group to 2-cyanopropyl was found to relieve retardation in styrene² and methyl methacrylate⁷ polymerization, but not in methyl acrylate polymerization.⁹ However, it was found that the initial inhibition period was relieved in the latter case.⁹

The main point of controversy concerns the interpretation of the above results. Some workers^{2,5-10} argue that the rate retardation is due to the slow fragmentation of the RAFT adduct radical (**3**) when the highly stabilizing phenyl substituent is attached to the radical center. Others^{3,4} suggest that the fragmentation rate of the phenyl-substituted RAFT adduct could not be slow enough to account for the retardation in the polymerization rates. Instead, they suggest that termination side reactions involving the RAFT adduct must be responsible.

At the center of the controversy are alternative experimental estimates of the fragmentation rate of the cumyl dithiobenzoate adduct, which differ by 6 orders of magnitude.^{3,4,10} This enormous discrepancy reflects the difficulty in using conventional kinetic experiments to study the rates of the individual steps in the RAFT process. Such quantities cannot be measured directly and must instead be inferred from related quantities (such as the overall rate of polymerization, and either the total radical concentration or the molecular weight distribution of the resulting polymer) by first assuming a specific kinetic model and values for some of the individual rate coefficients. Depending on the method used, estimates^{4,6} of the fragmentation rate coefficient of the cumyl dithiobenzoate adduct in styrene polymerization at 60 °C range from 10⁴ to 10⁻² s⁻¹. Only with the latter (lower) value is it possible

Scheme 1. RAFT Process

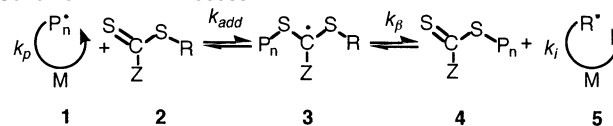


Table 1. Calculated Barriers and Enthalpies (G3(MP2)-RAD, 0 K, kJ mol⁻¹) for R'SC•(Z)SR ⇌ R'SC(Z)=S + R•

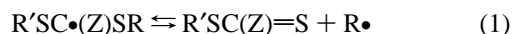
Z	R'	R	ΔH [‡]	ΔH
CH ₃	CH ₃	CH ₃	74.8	64.2
phenyl	CH ₃	CH ₃	100.7	95.2
benzyl	CH ₃	CH ₃	78.0	72.3
CH ₃	CH ₂ CO ₂ CH ₃	CH ₃	88.1	78.1
CH ₃	C(CH ₃) ₂ CN	CH ₃	92.1	90.5
CH ₃	CH ₃	CH ₂ CO ₂ CH ₃	58.1 ^a	58.1
CH ₃	CH ₃	C(CH ₃) ₂ CN	33.9 ^a	33.9

^a The reverse (i.e., addition) reactions are barrierless at this level of theory.

to explain the rate retardation without invoking some form of self-termination.¹⁰

In contrast to experiment, ab initio molecular orbital calculations offer *direct* access to barriers, enthalpies, and rate coefficients for the individual reactions and should provide a powerful tool for probing the reaction mechanism. In the present work we use this approach to calculate the fragmentation enthalpies and barriers for a selection of model RAFT adduct radicals and thereby determine whether the rate retardation in certain RAFT systems may be attributable to slow fragmentation.

Barriers and enthalpies were calculated¹¹⁻¹⁶ for fragmentation of the RAFT adduct radical in the prototype system:



The substituents considered include CH₃, phenyl, and benzyl in the Z-position and CH₃, CH₂COOCH₃, and C(CH₃)₂CN in the R- and R'-positions (Table 1).

It can be seen from Table 1 that the RAFT adduct radical containing a phenyl Z-substituent has a fragmentation barrier that is considerably larger (by 23 kJ mol⁻¹) than that with the corresponding benzyl Z-substituent. This would contribute a difference of 4 orders of magnitude to the fragmentation rates at room temperature. In other words, the presence of a phenyl substituent at the radical center in **3** *does significantly retard the fragmentation rate* compared with the corresponding benzyl substituent. This result is not surprising since the phenyl substituent allows delocalization of the unpaired electron onto the aromatic ring, while for the benzyl substituent this effect is inhibited via the insulating CH₂ group. A measure of the relative stabilizing effects of the phenyl and benzyl substituents on the radical center can also be seen in a comparison of the radical stabilization energies of PhCH₂• and PhCH₂CH₂• which, at the G3(MP2)-RAD level of theory, are 58.9¹⁷ and 10.6 kJ mol⁻¹, respectively.

The present results show that changing from a benzyl to a phenyl Z-substituent should significantly retard the fragmentation rate of

the RAFT adduct radical. However, the key question is: does this retardation in the *fragmentation* rate explain the observed retardation in the *polymerization* rate? To answer this, we must examine the relative rate coefficients for the addition and fragmentation reactions. A recent detailed kinetic analysis of RAFT polymerization¹⁸ showed that, in the absence of self-termination, significant rate retardation occurs if the ratio (denoted K_{eq}) of the addition and fragmentation rate coefficients exceeds 10^6 – 10^7 . For our model RAFT systems, we calculate¹⁹ approximate gas-phase K_{eq} values at 333 K of 7.6×10^6 L mol⁻¹ for the benzyl-substituted system, and 5.4×10^9 L mol⁻¹ for the phenyl-substituted system. These values would therefore place the phenyl- but not the benzyl-substituted system in the region where *slow fragmentation does cause rate retardation*. While the K_{eq} values are only approximate—having been calculated for a model system in the gas-phase—the errors are not likely to exceed an order of magnitude and are much smaller than the 6 orders of magnitude discrepancy between the alternative experimental estimates. Our present results thus support the large values of K_{eq} (1.6×10^7 L mol⁻¹)⁶ required to fit the 333 K experimental data for the retarded cumyl dithiobenzoate system in the absence of self-termination.

The present calculations thus indicate that it is possible to account for rate retardation in certain RAFT polymerizations solely through the slow fragmentation of the RAFT adduct radical. However, this result does not necessarily preclude the occurrence of side-reactions such as self-termination. Indeed, the slow fragmentation rate of the RAFT adduct serves to greatly increase its concentration, and could thus make such reactions more likely than in the corresponding nonretarded systems. Thus, we would argue that such side-reactions, if they do occur, are a consequence of slow fragmentation, rather than its primary cause.

The results in Table 1 also show that substitution of a model methyl acrylate leaving group ($R = \text{CH}_2\text{COOCH}_3$) by 2-cyanopropyl leads to a decrease in the fragmentation barrier by 24 kJ mol⁻¹. This result is also not surprising since the $\bullet\text{C}(\text{CH}_3)_2\text{CN}$ radical is much more stable than the $\bullet\text{CH}_2\text{COOCH}_3$ radical, the radical stabilization energies being 59.0 and 21.5¹⁷ kJ mol⁻¹, respectively. What is interesting about the results is that they predict that the presence of the $\text{C}(\text{CH}_3)_2\text{CN}$ leaving group should lower the barrier (relative to $R = \text{CH}_2\text{COOCH}_3$) by about as much as the phenyl Z-substituent raises the barrier (relative to $Z = \text{benzyl}$). In other words, it would appear that the fragmentation of the *polymeric* RAFT adduct radical (modeled by $R = \text{CH}_2\text{CO}_2\text{CH}_3$) may be retarded in methyl acrylate polymerization with 2-cyanopropyl dithiobenzoate RAFT agent, while the *initial* RAFT adduct (modeled by $R = \text{C}(\text{CH}_3)_2\text{CN}$) is not.

The present calculations are therefore consistent with the recent experimental observation⁹ that rate retardation occurs in methyl acrylate polymerization in the presence of either 2-cyanopropyl dithiobenzoate or 1-phenylethyl dithiobenzoate but an initial inhibition period occurs only for the latter agent. Thus, for 2-cyanopropyl dithiobenzoate, the fragmentation of the initial adduct is not significantly retarded (and hence there is no inhibition period). However, the overall polymerization is retarded since the only leaving groups available on the RAFT adducts once the initial agent is consumed are methyl acrylate polymers that, as the present calculations predict, should retard the fragmentation rate. Calculations using the 1-phenylethyl leaving group are currently under way to examine whether the theoretical results can also explain the inhibition period observed in this system. In addition, we are currently examining the effect of Z- and R-substituents acting in combination. The preliminary indications are that this does not

significantly affect our conclusions drawn on the basis of the isolated effects of Z and R.

In conclusion, we show via high-level ab initio molecular orbital calculations that the presence of a phenyl substituent at the radical center of the RAFT adduct radical significantly retards the fragmentation rate compared with the corresponding benzyl-substituted adduct. Our results for model RAFT systems place the phenyl- but not the benzyl-substituted system in the region where *slow fragmentation causes retardation to the rate of polymerization*. Our calculations also predict that in methyl acrylate polymerization using the RAFT agent 2-cyanopropyl dithiobenzoate it is the fragmentation of the *polymeric* agent rather than the *initial* agent that is retarded, which is in accord with recent experimental evidence for this system.⁹

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Supporting Information Available: Tables containing B3-LYP/6-31G(d) geometries (in the form of GAUSSIAN archive entries) and G3(MP2)-RAD total energies (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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