Computer-Aided Design of a Destabilized RAFT Adduct Radical: Toward Improved RAFT Agents for Styrene-*block*-Vinyl Acetate Copolymers

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ABSTRACT: High-level ab initio molecular orbital calculations indicate that a fluorine Z substituent significantly destabilizes the RAFT adduct radical, R′SC•(Z)SR, relative to known Z substituents. This destabilization of the RAFT adduct radical lowers the fragmentation enthalpy relative to normal dithioesters, but without stabilizing the C=S bond of the product RAFT agent, as in xanthate- or dithiocarbamate-mediated polymerization. On the basis of these calculations, it is predicted that, provided appropriate R groups are chosen, RAFT agents containing fluorine Z substituents (i.e., S=C(F)SR, fluorodithioformates, or “F-RAFT” agents) should provide a basis for improved control of monomers with reactive propagating radicals (such as vinyl acetate) and should have the advantage that their C=S bonds remain reactive enough for control of monomers with more stable propagating radicals (such as styrene) and hence the production of styrene−vinyl acetate copolymers.

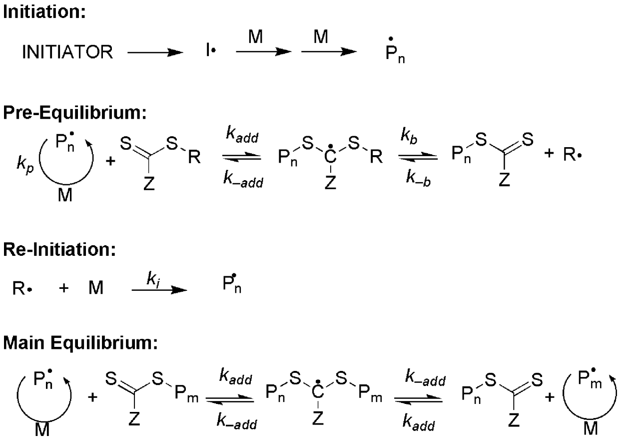
1. Introduction

Techniques for controlling free-radical polymerization are an important new development as they allow for the production of polymers with narrow molecular weight distributions, designer end groups, and novel architectures, such as star polymers and graft polymers.[1−3] Such polymers are useful in a range of bioengineering and nanotechnology applications, including as stabilizers for transition metal nanoparticles,[4] nanostructured carbon arrays,[5] and biocompatible nanocontainers for drug delivery applications.[6]

Among the most versatile of these new techniques is the reversible addition fragmentation chain-transfer “RAFT” process, which was developed by the CSIRO group[1,7] by combining their earlier work on addition−fragmentation reactions of macromonomers[8] with the small radical chemistry of Zard and co-workers.[9] A related process (termed “MADIX”), in which xanthates are used as the controlling agents, was independently developed by the Rhodia group and published shortly after.[10,11]

The basic principle of this process is to protect the majority of the propagating species from bimolecular termination reactions through their reversible trapping into a dormant thiocarbonyl compound via the degenerative transfer reaction shown in Scheme 1.[1] In this way, although the absolute rate of bimolecular termination is similar to that in conventional free-radical polymerization, the relative rate of termination is minimized with respect to the number of growing polymeric chains, and most of the chains bear the thiocarbonyl functionality and remain (potentially) active throughout the polymerization process. However, to achieve this, a delicate balance of the rate coefficients of the competing reactions within the process is required in order to ensure that the concentration of the dormant species is orders of magnitude greater than that of the active species, and the exchange between the two forms is rapid. Although the RAFT process has been successfully applied to a wide range of olefinic monomers,[12] the choice of RAFT agent substituents (i.e., R and Z) that strike this optimal balance is sometimes problematic.

Scheme 1. RAFT Process



One type of polymerization for which optimal RAFT agent design can be difficult is for polymerizations in which the propagating radical is relatively unstable and is thus a poor leaving group from the RAFT adduct radical. In such situations, the fragmentation rate of the RAFT adduct radical is relatively slow, leading to rate retardation and (in the extreme case) total inhibition of the polymerization. Thus, for example, vinyl actetate has a relatively unstable propagating radical, and as a result, the normal dithioesters used to control monomers such as styrene or the acrylates completely inhibit its polymerization.[12] To date, the elegant solution to this problem has been to use xanthates[12,13] or dithiocarbamates as the controlling agents.[12,14,15] These are RAFT agents in which the Z group is an alkoxy or amino group that can stabilize the thiocarbonyl product

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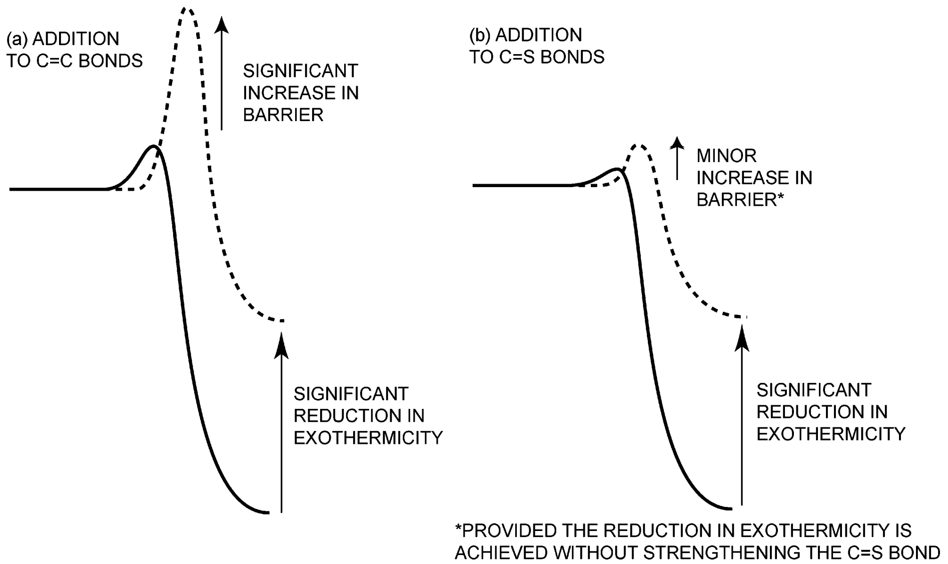
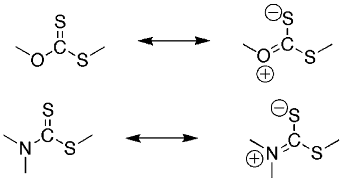


Figure 1. Schematic diagram of the minimum-energy path for radical addition to (a) C=C and (b) C=S bonds, showing the differing effects of reaction exothermicity on the barrier height.

of fragmentation via the following resonance contributions:[12,16]



(1)

In this way, the relative instability of the radical product of fragmentation is compensated for by an increased stability of the thiocarbonyl product, and the fragmentation reaction is promoted.

Although successful control of vinyl acetate polymerization has been achieved, this approach suffers from two disadvantages. By stabilizing the thiocarbonyl bond of the RAFT agent, its reactivity toward radical addition is reduced, and the agents are thus not sufficiently reactive for adequate control when the propagating radical is itself relatively stable (as in styrene polymerization, for example).[17] As a result, the xanthates and dithiocarbamates used to control vinyl acetate are not suitable for the production of well-defined styrene−vinyl acetate block copolymers. Moreover, even in vinyl acetate polymerization, the xanthates and dithiocarbamates do not appear to be as effective in controlling the polydispersity when compared with the best dithioesters in styrene or acrylate polymerizations. In the case of vinyl acetate polymerization narrow molecular weight distributions have only been reported for low to moderate molecular weights (up ca. 10^4 g mol^{-1}),[18] whereas for styrene and the acrylates, control can extend above 10^5 g mol^{-1}.[12]

A better approach to the problem of RAFT agent design in polymerizations involving relatively unstable propagating radicals would be to promote fragmentation by destabilizing the RAFT adduct radical, rather than by stabilizing the thiocarbonyl product. If this could be achieved without concurrently stabilizing the C=S bond of the RAFT agent, fragmentation could be made sufficiently fast for vinyl acetate polymerization using RAFT agents that also are sufficiently reactive to control monomers such as styrene. In this regard it should be noted that, unlike addition to C=C bonds, it should be possible to engineer RAFT agents with both fast addition and fast fragmentation rates. As shown previously, the π bond in C=S compounds is considerably weaker than in C=C bonds (owing to poorer overlap), and the transition state for addition is considerably earlier.[19,20] As a result, in the addition direction, the barrier height is only weakly affected by the overall exothermicity and is instead dominated by the strength of the C=S π bond (as measured by its singlet−triplet gap).[21] Conversely, in the reverse direction, the transition state is very late and almost completely dominated by the reaction exothermicity. Thus, if one could make the addition reaction less exothermic without strengthening the π bond (i.e., by destabilizing the product radical), then the fragmentation rate would increase considerably, but the addition rate should only be marginally reduced. This is in contrast to radical addition to C=C bonds, for which reductions in the reaction exothermicity are generally accompanied by significant increases in the barrier height.[22] These contrasting cases are illustrated schematically in Figure 1.

In the present work we use high-level ab initio calculations to design a new class of RAFT agent in which the RAFT adduct radical is significantly destabilized relative to the radicals based upon all existing RAFT agents. Provided the RAFT adduct radical is destabilized sufficiently, this should allow for the control of polymerizations involving relatively unstable propagating radicals (such as vinyl acetate). We aim to destabilize the RAFT adduct radical without stabilizing the C=S bond of the RAFT agent, so that the resulting RAFT agents can remain sufficiently reactive to control monomers with less stable propagating radicals, such as styrene. Provided appropriate R groups are chosen, such agents should not only improve upon the existing control in vinyl acetate polymerization but also allow for the production of styrene−vinyl acetate block copolymers.

2. Theoretical Design Strategy

Destabilizing the RAFT adduct radical (R′SC•(Z)SR) is somewhat of a challenge. As demonstrated in a recent high-level ab initio study of radical stability in RAFT

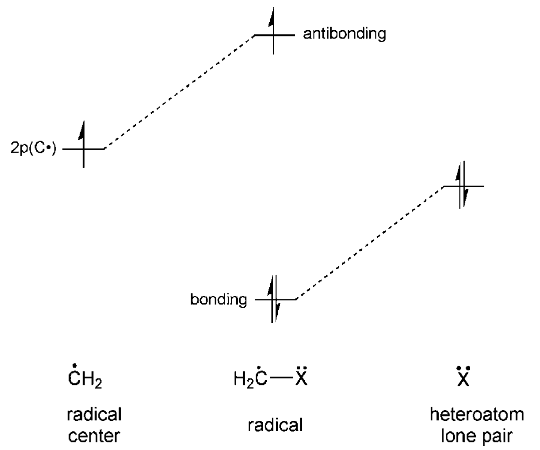


Figure 2. Orbital interaction diagram showing the three-electron interaction between the lone pair of a heteroatom and the unpaired electron at a carbon radical center.[24,25]

polymerization,[23] existing RAFT adduct radicals are relatively stable species due to the necessary presence of two thiyl substituents (i.e., SR′ and SR). These are known to be strong radical stabilizing substituents due to lone pair donation from the sulfur atoms adjacent to the radical center (see Figure 2).[24,25] As a result of this effect, even when the Z group is not a good radical stabilizer itself (e.g., Z = H, CH_3, or CH_2Ph), the radical stabilization energy (RSE) is at least 60 kJ mol^{-1} (which is equivalent to that of the benzyl radical).[23] Moreover, when Z is a strong π-accepting substituent (such as phenyl or CN), RSEs in excess of 100 kJ mol^{-1} are possible.[23] Clearly, one cannot remove these thiyl substituents—if this were to happen, one would no longer have a RAFT process. Instead, one must find a Z group that destabilizes the radical center and thereby counteracts some of the stabilization from the thiyl substituents.

It is well-known that carbon-centered radicals are destabilized by sigma withdrawal. Unfortunately, sigma-withdrawing substituents typically have (radical-stabilizing) lone pair donating or π (or pseudo-π) accepting properties that counteract their radical destabilizing effects. It is thus necessary to find a Z group for which the sigma-withdrawal effect outweighs the radical stabilization effect. For example, in carbon-centered radicals of the form $^{\bullet}CH_2X$, the X substituents CF_3 and CF_2CF_3 are net destabilizers because the destabilizing effect of sigma withdrawal outweighs the stabilizing effect of pseudo-π acceptance (via hyperconjugation with the β-C−F bonds). Unfortunately, in RAFT adduct radicals such substituents are net stabilizers because their pseudo-π acceptance is enhanced (via captodative interactions with the lone pair donating thiyl substituents).[23]

However, another class of sigma-withdrawing substituents may be more promising. Lone-pair donor/sigma-acceptor substituents such as amino, alkoxy, and halogen substituents normally stabilize a carbon-centered radical (such as $^{\bullet}CH_2X$) because the lone-pair donation effect outweighs the sigma-withdrawal effect.[25] However, it was recently demonstrated that in RAFT adduct radicals the effect of lone pair donation on the radical center is dramatically reduced by the presence of the thiyl substituents.[23] This is because the interaction of the sulfur lone pairs with the radical center, though stabilizing, results in the unpaired electron occupying an orbital higher in energy than $2p(C^{\bullet})$ (see Figure 2).[24,25] As a result, the energy gap between the unpaired electron and a second lone pair donor is larger, and the stabilizing interaction is weaker. Thus, for example, the radical stabilization associated with a single thiyl substituent (as in $^{\bullet}CH_2SCH_3$) is ≈40 kJ mol^{-1}, and that of two substituents together (as in the model RAFT adduct $CH_3SC{\bullet}(H)SCH_3$) is only 60 kJ mol^{-1}, the second substituent effectively contributing only half of the stabilization effect it would in isolation.[23] By the time a third lone-pair donor substituent is included, its stabilization effect is usually negligible. Thus, for example, when Z = NH_2, Cl, or OCH_3, the RSEs are either equal to or just less than the stabilizing effects of two out of the three lone-pair donor substituents.[23] These results suggest that in the RAFT adduct radical, provided we could find a substituent for which the sigma-withdrawal effect was large enough, the balance between lone-pair donation and sigma withdrawal could be tipped in favor of the latter effect, and the radical could be destabilized.

Of the known lone-pair-donor/sigma-acceptor substituents, one of the strongest sigma-acceptor substituents is of course fluorine. In carbon-centered radicals of the form $^{\bullet}CH_2X$, this X substituent is nonetheless a net stabilizer (by 12.4 kJ mol^{-1})[25] because lone-pair donation outweighs sigma acceptance. However, in the RAFT adduct radicals the diminished role of lone pair donation may be sufficient to tip the balance in favor of sigma withdrawal. In the present work we use ab initio calculations to explore this possibility. To this end, we calculate the radical stabilization energies (RSEs) of the model RAFT adduct radicals ($CH_3SC{\bullet}(F)SR$) and the enthalpies and equilibrium constants associated with their fragmentation reactions ($CH_3SC{\bullet}(F)SR \rightarrow CH_3SC(F){=}S + {}^{\bullet}R$), for R = CH_3 (as a reference) and CH_2OCOCH_3 (as a small model of the propagating radical in vinyl acetate polymerization). The results are compared with the corresponding values for $CH_3SC{\bullet}(CH_3)SR$ (as a prototypical dithioester) and $CH_3SC{\bullet}(OCH_3)SR$ (as a prototypical xanthate), as taken from earlier studies.[23,26−28]

3. Computational Procedures

The radical stabilization energies (RSEs) and β-scission enthalpies were calculated at 0 K, using standard ab initio molecular orbital theory[29] and density functional theory[30] calculations, carried out using GAUSSIAN 98,[31] GAUSSIAN 03,[32] and MOLPRO 2000.6.[33] The RSE of a radical $R^{\bullet}$ is defined as the energy change of the reaction:[25]

$$R^{\bullet} + H{-}CH_3 \rightarrow R{-}H + {}^{\bullet}CH_3 \qquad (2)$$

The geometries of the reactants and products were optimized at the B3-LYP/6-31G(d) level of theory, while improved energies were calculated at the G3(MP2)-RAD[34] level of theory. It has previously been shown that G3(MP2)-RAD provides accurate absolute values for the enthalpies of radical addition to C=S double bonds[35] and the RSEs of carbon-centered radicals.[25] Having obtained the G3(MP2)-RAD barriers at 0 K, approximate gas-phase equilibrium constants for the fragmentation reactions were calculated at 60 °C using standard formulas based on the statistical thermodynamics of an ideal gas under the rigid rotor/harmonic oscillator approximation.[36,37]

For each radical and thiocarbonyl compound considered, care was taken to ensure that the optimized

Table 1. Stabilities of $CH_3SC(Z){=}S$ and Radical Stabilization Energies (RSEs) and Fragmentation Enthalpies (ΔH) of $CH_3SC{\cdot}(Z)SR$, for Z = F, CH_3, and OCH_3 and R = CH_3 and CH_2OCOCH_3[a]

	Z = F	Z = CH_3[b]	Z = OCH_3[b]
stability	43.5	35.1	85.9
R = CH_3			
RSE	46.5	59.9	58.5
ΔH	50.2	64.2	29.2
R = CH_2OCOCH_3			
RSE	42.7	63.7	50.5[c]
ΔH	50.9	75.4	36.1[c]

[a] Energies (0 K, kJ mol^{-1}) were calculated at the G3(MP2)-RAD level of theory using B3-LYP/6-31G(d) geometries and include scaled B3-LYP/6-31G(d) zero-point vibrational energy. The RSE is defined as the energy change of reaction 2. The fragmentation enthalpy of the radical $CH_3SC{\cdot}(Z)SR$ is defined as the energy change of the reaction $CH_3SC{\cdot}(Z)SR \rightarrow CH_3SC(Z){=}S + {}^{\bullet}R$. The stability of the RAFT agent is defined as the energy change of reaction 3. [b] Taken from ref 23 and references therein. [c] Approximate G3(MP2)-RAD value calculated via the ONIOM method using G3(MP2)-RAD values for the $CH_3SC{\cdot}(OCH_3)SCH_3$ system and RMP2/6-311+G(3df,2p) values for the R group effect.

structure was the global (rather than merely local) minimum-energy structure by first performing extensive conformational searches at the B3-LYP/6-31G(d) level of theory. In calculating the radical stabilization energies, however, the minimum-energy conformation of the radical was used as a basis for selecting the conformation of the corresponding alkane. The geometry of the alkane was then fully optimized to a (local) minimum-energy structure within that conformation. In this way, the RSE is calculated for the most stable conformation of the RAFT adduct radical (which is the species that is relevant to the polymerization system), but any possible contribution to the RSE arising from conformational changes between the radical and alkane is minimized.

4. Results and Discussion

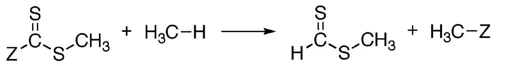
Radical stabilization energies (RSEs) of the model RAFT adduct radicals ($CH_3SC{\cdot}(F)SR$) and the enthalpies of their fragmentation reactions ($CH_3SC{\cdot}(F)SR \rightarrow CH_3SC(F){=}S + {}^{\bullet}R$) are provided in Table 1 for R = CH_3 and CH_2OCOCH_3. The corresponding values for $CH_3SC{\cdot}(CH_3)SR$ (as a prototypical dithioester) and $CH_3SC{\cdot}(OCH_3)SR$ (as a prototypical xanthate), as taken from earlier studies,[23,26–28] are included in Table 1 for purposes of comparison. The geometries of the RAFT adduct radicals are shown in Figure 3; complete geometries for all species are provided in the Supporting Information.

The results clearly indicate that the fluorine Z substituent does destabilize the RAFT adduct radical ($CH_3SC{\cdot}(Z)SR$) relative to those based on common dithioesters, xanthates, and dithiocarbamates. When R = CH_3, the RSE of $CH_3SC{\cdot}(F)SCH_3$ is just 46.5 kJ mol^{-1} at the G3(MP2)-RAD level of theory. The lowest value of all other reported RSEs for RAFT adduct radicals of the form $CH_3SC{\cdot}(Z)SCH_3$ (including those for Z = H, CH_3, CF_3, CH_2Ph, Ph, naphthyl, C≡CH, CH=CH_2, CN, Cl, NH_2, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OC(CH_3)_3$) is 58.5 kJ mol^{-1}.[23] As discussed above, a fluorine substituent normally stabilizes a carbon-centered radical (such as ${}^{\bullet}CH_2F$) because the stabilizing effect of lone-pair donation counteracts the destabilizing influence of sigma withdrawal. However, in the RAFT adduct radicals, the presence of the lone-pair-donating thiyl substituents diminishes the radical-stabilizing effect of additional lone-pair donor substituents. As a result, the destabilizing effect of sigma withdrawal dominates, and the radical is destabilized.

It is also clear that the fluorine Z substituent significantly destabilizes RAFT adduct radicals bearing model vinyl acetate leaving groups (i.e., $CH_3SC{\cdot}(Z)SCH_2OCOCH_3$). It was previously shown that in such systems even alkoxy Z groups (such as OCH_3) destabilize the RAFT adduct relative to those bearing normal alkyl substituents (CH_3). It should be remembered that the alkoxy groups are also lone-pair donor/sigma acceptor substituents, though the sigma-withdrawal effect is weaker than in fluorine. It was suggested that the presence of the sigma-withdrawing CH_2OCOCH_3 group enhances the destabilizing effect of sigma withdrawal, leading to the reduced RSEs in the xanthate systems. The present results indicate that this enhanced destabilization is also experienced in the fluorine-substituted radicals. For Z = F, the RSE is just 42.7 kJ mol^{-1}—8 kJ mol^{-1} lower than the corresponding value for the model xanthate radical (i.e., Z = OCH_3)[38] and more than 20 kJ mol^{-1} less than those with alkyl substituents such as Z = CH_3 (see Table 1).[23] In short, it is clear that a fluorine Z substituent significantly destabilizes the RAFT adduct radical relative to those derived from normal dithioesters and xanthates, and this destabilization is further enhanced when the leaving group is a model of the vinyl acetate propagating radical.

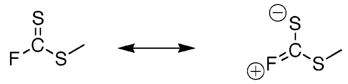
The results also indicate that this radical destabilization effect is translated into a lower fragmentation enthalpy, when compared with dithioesters. The fragmentation enthalpy for the $CH_3SC{\cdot}(F)SCH_2OCOCH_3$ is 50.9 kJ mol^{-1}, ≈25 kJ mol^{-1} lower than that of the corresponding $CH_3SC{\cdot}(CH_3)SCH_2OCOCH_3$ radical. However, the fragmentation enthalpy is not as low as that of the corresponding xanthate-derived adduct $CH_3SC{\cdot}(OCH_3)SCH_2OCOCH_3$ (36.1 kJ mol^{-1}). Thus, fragmentation of $CH_3SC{\cdot}(F)SCH_2OCOCH_3$ is preferred over $CH_3SC{\cdot}(CH_3)SCH_2OCOCH_3$ due to the reduced stability of the RAFT adduct radical in the former case. However, fragmentation of $CH_3SC{\cdot}(OCH_3)SCH_2OCOCH_3$ is preferred over $CH_3SC{\cdot}(F)SCH_2OCOCH_3$, despite the greater stability of the $CH_3SC{\cdot}(OCH_3)SCH_2OCOCH_3$ radical, due to the greater stability of the C=S bond in the xanthate agents.

Previously, it was shown that the effect of Z on the stability of the C=S bond in the RAFT agent could be quantified via the following isodesmic reaction:[23]

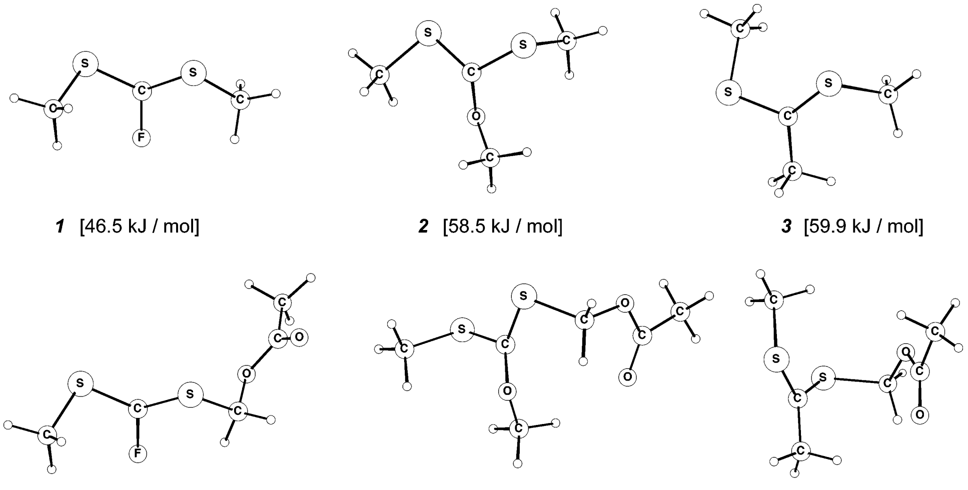


$$\mathrm{Z{-}C({=}S){-}S{-}CH_3 + H_3C{-}H \longrightarrow H{-}C({=}S){-}S{-}CH_3 + H_3C{-}Z} \quad (3)$$

Under such measures, the stabilities of the model xanthates and dithiocarbamates (Z = OCH_3, OCH_2CH_3, $OCH(CH_3)_2$ $OC(CH_3)_3$, and NH_2) fall into the range 81.0−92.8 kJ mol^{-1}, while those for "typical" dithioester (such as Z = CH_3, CH_2Ph, and Ph) are of the order 35.1−41.2 kJ mol^{-1}.[23] The calculated value for the fluorine-substituted RAFT is similar to that of dithioesters (43.5 kJ mol^{-1}) and much lower than those for the xanthates. One may well ask why the lone-pair-donating F substituent does not itself stabilize the C=S bond of the RAFT agent via resonance as follows:



$$\mathrm{F{-}C({=}S){-}S{-} \longleftrightarrow {}^{\oplus}F{=}C(S^{\ominus}){-}S{-}} \quad (4)$$



1 [46.5 kJ / mol] *2* [58.5 kJ / mol] *3* [59.9 kJ / mol]

4 [42.7 kJ / mol] *5* [50.5 kJ / mol] *6* [63.7 kJ / mol]

Figure 3. B3-LYP/6-31G(d) optimized geometries of the RAFT adduct radicals and corresponding radical stabilization energies.

As in the case of the radicals, it is a question of competing lone-pair donation and sigma-withdrawal effects, the latter effect destabilizing the C=S bond.[23] The alkoxy substituents are strong lone-pair donors and weak sigma acceptors, and hence the stabilizing effect dominates. In contrast, the fluorine subsituent is a weaker lone-pair donor and a stronger sigma acceptor, and as a result, the destabilizing effect dominates.

Thus far, we have demonstrated that a fluorine Z substituent is capable of destabilizing a RAFT adduct radical, relative to other known Z substituents. We have also shown that this destabilization of the radical helps to promote fragmentation, relative to normal dithioesters, without significantly stabilizing the C=S bond of the RAFT agent. However, it is clear the calculated fragmentation enthalpies are not as low as those of the xanthates or dithiocarbamates, and so the question arises as to whether the fragmentation enthalpies are low enough for non-rate-retarded polymerization of vinyl acetate. Previously, it has been shown that rate retardation occurs when the equilibrium constant of the addition reaction exceeds 10^6-10^7 L mol^{-1}.[39] To explore whether RAFT agents with fluorine Z substituents would be non-rate-retarding in vinyl acetate polymerization, an approximate equilibrium constant was calculated for the reaction

$$\mathrm{CH_3SC(F){=}S + {}^{\bullet}CH_2OCOCH_3 \rightarrow CH_3SC{\cdot}(F)SCH_2OCOCH_3} \quad (5)$$

The value obtained was 3.1×10^1 L mol^{-1} at 60 °C, much lower than the calculated equilibrium constants for known rate retarded systems, such as cumyl dithiobenzoate-mediated polymerization of styrene or methyl acrylate.[26,40] The possible sources of error in such calculations (solvent effects, chain length effects, and the treatment of hindered internal rotations) have been discussed previously,[26] and within the possible uncertainty of the calculations this value is significantly lower than what would be required to induce rate retardation. Although careful design of the initial leaving group in the RAFT agent (i.e., R in S=C(F)SR) is still required in order to avoid inhibition effects and hybrid behavior, it nonetheless appears that fluorine-substituted RAFT agents (which we denote as "F-RAFT" agents) should provide a basis for improved control of vinyl acetate, and the production of well-defined styrene−vinyl acetate block copolymers. Experiments to evaluate these F-RAFT agents are currently underway.

5. Conclusions

In the present work, we have used a combination of theoretical molecular orbital arguments and high-level ab initio molecular orbital calculations to design a Z group that significantly destabilizes the RAFT adduct radical (R′SC·(Z)SR), relative to those based on all currently known RAFT agents. This Z group is fluorine, and the RAFT agents based on this group (i.e., fluorodithioformates, S=C(F)SR) are denoted as F-RAFT agents. On the basis of these calculations, we predict that, provided appropriate R groups are chosen, F-RAFT agents should provide a basis for improved control of monomers with reactive propagating radicals (such as vinyl acetate) and should have the advantage that their C=S bonds remain reactive enough for control of monomers with more stable propagating radicals (such as styrene) and hence the production of styrene−vinyl acetate copolymers.

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Supporting Information Available: Tables S1 showing the B3-LYP/6-31G(d) optimized geometries (in the form of GAUSSIAN archive entries). This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) It should be noted that xanthates and dithiocarbamates can be used to control monomers such as styrene, provided the alkoxy or amino Z group is designed so as to minimize the resonance stabilization of the C═S bond. For example, xanthates, in which the alkoxy group is substituted with strong electron-withdrawing groups that reduce the lone-pair-donating ability of the oxygen (see for example ref 13) or dithiocarbamates in which the lone pair of the nitrogen in the dithiocarbamates is included as part of an aromatic system (see for example ref 14), can control styrene. However, when modified in this way, such agents do not appear to be suitable for controlling vinyl acetate.

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(21) Obviously, the overall exothermicity is also affected by the π bond strength, but it also depends on other factors (such as the strength of the forming C−S bond and the stabilities of the reactant and product radicals). By manipulating these other factors (in this case the stability of the product radical), it may be possible make the addition reaction less exothermic without making the addition reaction significantly less reactive.

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