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Reliable Low-Cost Theoretical Procedures for Studying Addition−Fragmentation in RAFT Polymerization

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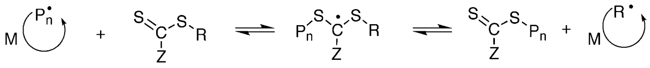
Enthalpies for the β-scission reactions, $R'SC^{\bullet}(Z)SR \rightarrow R'SC(Z){=}S + {}^{\bullet}R$ (for R, R′ = CH_3, CH_2CH_3, CH_2CN, $C(CH_3)_2CN$, CH_2COOCH_3, $CH(CH_3)COOCH_3$, CH_2OCOCH_3, CH_2Ph, $C(CH_3)_2Ph$, and $CH(CH_3)Ph$ and Z = CH_3, H, Cl, CN, CF_3, NH_2, Ph, CH_2Ph, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OC(CH_3)_3$, and F) have been calculated using a variety of DFT, MP2, and ONIOM-based methods, as well as G3(MP2)-RAD, with a view to identifying an accurate method that can be practically applied to larger systems. None of the DFT methods examined can reproduce the quantitative, nor qualitative, values of the fragmentation enthalpy; in most cases the relative errors are over 20 kJ mol^{-1} and in some cases as much as 55 kJ mol^{-1}. The ROMP2 methods fare much better, but fail when the leaving group radical ($R^{\bullet}$) is substituted with a group (such as phenyl or CN) that delocalizes the unpaired electron. However, provided the primary substituents on the leaving group radical are included in the core system, an ONIOM-based approach in which the full system is studied via ROMP2 (or SCS- or SOS-MP2) calculations with the 6-311+G(3df,2p) basis set and the core system is studied at G3(MP2)-RAD can reproduce the corresponding G3(MP2)-RAD values of the full systems within 5 kJ mol^{-1} and is a practical method for use on larger systems.

1. Introduction

The reversible-addition−fragmentation-transfer (RAFT) process is an important new method for controlling the molecular weight and architecture in free-radical polymerization.[1] The process can be used to generate complex macromolecular architectures such as comb, star, and block copolymers for use in bioengineering and nanotechnology applications.[2] Control is achieved by protecting the majority of the propagating species from bimolecular termination through their reversible trapping into a dormant thiocarbonyl compound as follows:



A delicate balance of the rates of these various reactions is required, so as to ensure that the dormant species is orders of magnitude greater in concentration than the active species, and the exchange between the two forms is rapid. The reactivity of the RAFT agent must thus be tailored to match the reactivity and stability of the polymeric propagating radical; information on the mechanism, kinetics, and thermodynamics of these individual steps can greatly assist in the design of optimal RAFT agents.

As in any complex multistep process, the kinetics and thermodynamics of the individual reactions are difficult to study via experimental approaches without recourse to kinetic model-based assumptions. This is because the experimentally observable properties of the process are not the rates and equilibrium constants of the individual reactions, but rather the overall polymerization rate, the average molecular weight distribution of the resulting polymer, and the concentrations of some of the major species. To infer the individual rate and equilibrium constants from these measured quantities, one has to assume a kinetic scheme and often make additional simplifying assumptions (such as the steady-state assumption), and these are a potentially large source of systematic error. For example, depending upon the type of data measured and the associated model-based assumptions used, alternative experimental values for the equilibrium constant in cumyl dithiobenzoate mediated polymerization of styrene at 60 °C differ by 6 orders of magnitude.[3,4] Computational chemistry offers an attractive solution to this problem, as it allows for the individual reactions to be studied directly, without recourse to kinetic model based assumptions. However, to study systems that are large enough to be of relevance to free-radical polymerization, reliable low cost theoretical procedures are required.

In an earlier study,[5] we examined the performance of a wide range of theoretical procedures for studying radical addition to C=S bonds. In general we found that low-cost methods, such as B3-LYP/6-31G(d), provided an excellent approximation to high-level CCSD(T)/6-311+G(d,p) geometries and frequencies, provided transition structures were corrected via an IRCmax approach. Indeed, provided the energies are calculated at a consistent level of theory and transition structures are corrected via IRCmax, the reaction barriers and enthalpies for ${}^{\bullet}CH_3 + S{=}CRR'$ (R, R′ = H, CH_3) vary by less than 1 kJ mol^{-1}, regardless of whether low levels such as B3-LYP/6-31G(d) or HF/6-31G(d) or higher levels such as CCSD(T)/6-311+G(d,p) are used for the geometry optimizations.[5] Likewise, provided the recommended scale factors are used,[6] the zero-point vibrational energy (and hence the frequency calculations) at these lower levels of theory agrees to within 1−2 kJ mol^{-1} of the CCSD(T)/6-311+G(d,p) calculations.[5] However, in contrast to geometries and frequencies, high-level composite methods were found to be necessary for accurate absolute barriers and enthalpies, with calculations at the ROMP2/6-311+G(3df,2p) level of theory offering reasonable performance for larger systems. However, this original assessment focused on the

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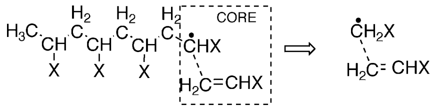
SCHEME 1



prototypical reactions, $^{\bullet}CH_3 + S{=}CRR'$ (for R, R′ = H, CH_3), so that the results could be benchmarked against both experiment and high levels of theory, such as W1.[7] In our more recent studies of practical RAFT-related systems,[8,9] we have noted that the ROMP2/6-311+G(3df,2p) method can suffer large errors for reactions involving delocalized radicals, such as $^{\bullet}CH_2Ph$ and $^{\bullet}C(CH_3)_2CN$. It is therefore necessary to find a more accurate low-cost method that remains suitable for these "problematic" systems.

The purpose of the present work is to identify and benchmark reliable low-cost theoretical procedures for studying the addition−fragmentation processes in RAFT polymerization. Three main classes of method are examined: DFT-based methods, MP2-based methods, and ONIOM-based methods. Density functional theory (DFT) is now widely used as a computational chemistry tool and is found to provide reasonable accuracy at modest computational cost for a wide range of chemical systems.[10] In our original study, we found that the popular hybrid DFT methods, B3-LYP and MPW1K, were *not* suitable for studying the energetics of these radical addition reactions.[5] However, a number of "new generation" functionals (including BB1K,[11] MPW1B95,[12] MPWB1K,[12] and BMK[13]) have since been developed, and appear to provide improved results for the kinetics and thermodynamics of other types of chemical reactions, though problems in their treatment of relative bond dissociation energies (and hence relative radical stabilities) and hydrogen abstraction barriers and enthalpies have been recently noted.[14,15] With the growing interest in applying DFT methods to problems in free-radical polymerization, it is of interest to evaluate their performance for the RAFT systems.

Second-order Møller−Plesset (MP2) theory offers an alternative low-cost approach to studying larger chemical systems. As noted above, in our previous studies of radical addition to C=S bonds,[5,8,9] standard (restricted open-shell) MP2 theory was found to provide the best low-cost performance, except when the reactions involved highly delocalized radicals. Recently, two modifications of MP2, namely spin-component-scaled MP2 (SCS-MP2)[16] and scaled-opposite-spin MP2 (SOS-MP2) have been introduced to provide an improvement over the performance of standard MP2.[17] Initial testing of these methods has produced very promising results,[16,17] and it is therefore of interest to evaluate their performance for the "problematic" RAFT systems.

The ONIOM method of Morokuma and co-workers[18] offers another possible strategy for obtaining accurate energetics at a modest computational cost. In this method, one first defines a "core" section of the reaction that includes all forming and breaking bonds, and the principal substituents attached to them. In forming the core system, deleted substituents are replaced with "link atoms" (typically hydrogens), chosen so that core system provides a good chemical model of the reaction center. For instance, in the oligomeric propagation reaction, CH_3-$CHXCH_2CHXCH_2CHXCH_2CHX^{\bullet} + CH_2{=}CHX$, the core could be modeled as $^{\bullet}CH_2X + CH_2{=}CHX$ (see Scheme 1). The core system is studied at both a high level of theory and also at a lower level, while the full system is studied only at the lower level of theory. The high-level barrier (or enthalpy) for the full system is then approximated as the sum of the high level barrier (or enthalpy) for the core system and the substituent effect, as measured at the lower level of theory.[19] This approximation is valid provided that the low level of theory measures the substituent effect accurately. We recently demonstrated that an ONIOM-based approach, in which the core system (as illustrated in Scheme 1) was studied at G3(MP2)-RAD and the substituent effect at ROMP2/6-311+G(3df,2p), provided an excellent approximation to standard G3(MP2)-RAD for the propagation reaction in radical polymerization.[20] In the present work, we design and evaluate an ONIOM-based method for studying RAFT polymerization.

In what follows, we calculate enthalpies for the β-scission reactions, $R'SC^{\bullet}(Z)SR \rightarrow R'SC(Z){=}S + {}^{\bullet}R$, using a variety of DFT, MP2, and ONIOM-based methods, as well as G3(MP2)-RAD, with a view to identifying an accurate method that can be practically applied to larger systems. To ensure a comprehensive testing of the various methods, a wide variety of substituents are considered, including combinations of R, R′ = CH_3, CH_2CH_3, CH_2CN, $C(CH_3)_2CN$, CH_2COOCH_3, $CH(CH_3)COOCH_3$, CH_2OCOCH_3, CH_2Ph, and $CH(CH_3)Ph$ and Z = CH_3, H, Cl, CN, CF_3, NH_2, Ph, CH_2Ph, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OC(CH_3)_3$, and F.

2. Theoretical Procedures

Standard ab initio molecular orbital theory and density functional theory (DFT) calculations were carried out mainly using the GAUSSIAN 03[21] software, though MOLPRO 2002.3[22] was utilized for restricted open-shell coupled cluster calculations. Enthalpies were calculated for the various β-scission reactions. To allow for a consistent comparison between the various methods, all geometries were optimized with B3-LYP/6-31G(d) and all corrections for the zero-point vibrational energies were calculated using scaled[23] B3-LYP/6-31G(d) frequencies. As noted above, our previous assessment studies (both for radical addition to C=S bonds[5] and for a range of other radical reactions[24,25]) indicate that, due to substantial systematic cancellation of error, low levels of theory such as this yield reliable geometries and frequencies, even when their predictions of the reaction energetics are poor. Improved relative energies were then calculated using a range of methods including various DFT, MP2, and ONIOM-based methods, as well as G3(MP2)-RAD.[26] For the open-shell species, all DFT calculations were carried out using unrestricted wave functions, whereas the ab initio calculations used restricted open-shell wave functions.

In the present work we treat G3(MP2)-RAD as our benchmark level of theory. This high-level composite procedure aims to approximate URCCSD(T) calculations with a large triple-ζ basis set via additivity approximations, and has been demonstrated to provide "chemical accuracy" (ca. 5 kJ mol^{-1}) when assessed against large test sets of thermochemical data.[26] We have previously assessed the performance of this method for studying the kinetics and thermodynamics of a variety of radical reactions, including radical addition to C=S double bonds,[5] radical addition to C=C bonds,[25] bond dissociation energies[15] and hydrogen abstraction.[24] In general, the errors in this method are small (usually less than 5 kJ mol^{-1}) when compared with both higher-level procedures (including G3X-RAD and W1) and also reliable gas-phase experimental data. For the specific case of radical addition to C=S bonds the errors are slightly larger (ca. 11 kJ mol^{-1}), but the relative errors are negligible (<0.5 kJ mol^{-1}). Thus, for accurate absolute values, the G3(MP2)-RAD values could themselves be corrected to "approximate" W1 values via an ONIOM-based approach (see below) in which W1 is used to study the reaction core (i.e., $^{\bullet}CH_3 + S{=}CH_2$) and G3(MP2)-RAD to study the substituent effects. We have recently shown that calculations at this “W1-ONIOM” level are capable of reproducing experimental equilibrium constants for radical addition to thioketones to within a factor of 2.[27] In the present work, we search for a low cost method that can be used as a substitute for the G3(MP2)-RAD component of this calculation for larger systems, either directly or in combination with G3(MP2)-RAD as an additional ONIOM layer. For the sake of clarity, in the present work we compare our results directly with the G3(MP2)-RAD values.

The DFT calculations were performed using the 6-311+G(3df,2p) basis set and a variety of hybrid functionals. These include the popular B3-LYP method,[28] and a number of relatively new functionals, including KMLYP,[29] BB1K,[11] MPW1B95,[12] MPWB1K,[12] and BMK.[13] These latter functionals have been specifically optimized to give improved performance for studying the thermodynamics and/or kinetics of chemical reactions. KMLYP is a hybrid 2-parameter functional in which the exchange functional is a mixture of Slater exchange and exact exchange (55.7%). This method differs from the other DFT methods in that it includes an additional empirical correction term, somewhat analogous to the higher-level correction (HLC) term in the G3-based methods, which depends on the number of unpaired electrons and the number of lone pairs. However, it should be noted that, unlike the G3-methods, this HLC term does not cancel from the fragmentation enthalpies, and makes a substantial contribution (32.3 kJ mol^{-1}) to the results. The other new functionals are hybrid meta-GGA functionals, which depend on the kinetic energy density. The BB1K[11] functional is based on a hybrid version (called B1B95) of Becke’s BB95 functional,[30] but with the fraction of HF exchange reoptimized for the prediction of kinetics. MPW1B95 and MPWB1K both comprise the modified Perdew and Wang 1991 exchange functional and Becke’s 1995 meta correlation functional, the difference being that the former was optimized for thermochemistry, whereas the latter was optimized for kinetics.[12] The BMK functional is somewhat different to the others, as it simulates a variable exact exchange. This is achieved by the combination of exact exchange (42%) and terms depending on the kinetic energy density. This combination is intended to lead to a “back-correction” for excessive HF exchange in systems where that would be undesirable.[13]

The ROMP2 relative energies were also computed with the 6-311+G(3df,2p) basis set. In addition to standard ROMP2, two recent modifications of second-order Møller−Plesset theory, namely spin-component-scaled MP2 (SCS-MP2)[16] and scaled-opposite-spin MP2 (SOS-MP2),[17] were also employed. Both methods are based on the idea that the correlation energy (E_c) can be split into two components:

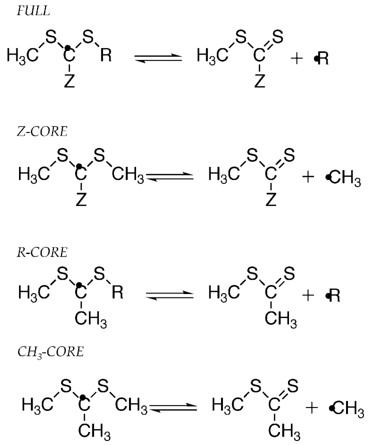
$$E_c = E_S + E_T \tag{1}$$

where E_S is the contribution from opposite-spin electron pairs, whereas same-spin electron pairs contribute to E_T. The original idea by Grimme[16] was to approximate the correlation energy by applying separate scaling factors for the two contributions:

$$E_c \approx p_S E_S + p_T E_T \tag{2}$$

The scaling factors ($p_S = {}^6/_5$ and $p_T = {}^1/_3$) were obtained through fitting to experimental enthalpies of formation but justified theoretically in a qualitative manner. The SOS-MP2 method of Head-Gordon and co-workers[17] simplifies the SCS-MP2 splitting scheme by including the opposite-spin components only. A slightly larger scaling factor $p_S = 1.3$ is used to compensate for the absence of explicit same-spin correlation. If implemented in an efficient way, SOS-MP2 offers the possibility of significantly reduced computational cost for larger systems (compared with standard MP2), as it is possible to formulate it as a fourth-order (rather than fifth-order) method.[17] Both modifications of the standard MP2 method have proven to work well for the prediction of enthalpies and barrier heights for a variety of chemical systems, and give accuracy comparable to that of QCISD(T).[16,17,31]

SCHEME 2



For the “disubstituted” systems (i.e., systems in which *both* Z and R are not CH_3), enthalpies were also calculated via ONIOM, using G3(MP2)-RAD for the core system and either ROMP2 or the various DFT methods for the full system. In the β-scission reaction, $CH_3SC^{\bullet}(Z)S{-}R \rightarrow CH_3SC(Z){=}S + {}^{\bullet}R$, the core system for the ONIOM calculation should ideally include the full Z-substituent (as this is typically a functional group such as phenyl) and all of the α-substituents on leaving $R^{\bullet}$ radical. However, for certain RAFT-agent substituents, such core systems are currently too large for practical G3(MP2)-RAD calculations. So two smaller core systems were designed, one (the “R-core”) in which all α-substituents on the leaving $R^{\bullet}$ radical are included but the Z-group is replaced with a CH_3 substituent, and one (the “Z-core”) which the leaving $R^{\bullet}$ radical is replaced with methyl but the Z-group is included in full (see Scheme 2). We also considered a simpler system (the “CH_3-core”) in which both the R- and Z-groups were replaced with methyl. For those systems for which full G3(MP2)-RAD calculations are possible, we compare the results obtained via ONIOM using the alternative core types, to establish whether any of them are suitable for the larger systems.

3. Results and Discussion

Fragmentation enthalpies for $R'SC^{\bullet}(Z)SR \rightarrow R'SC(Z){=}S + {}^{\bullet}R$ were calculated using a variety of DFT, MP2, and ONIOM-based methods, as well as G3(MP2)-RAD. Table 1 shows the enthalpies for systems in which the R-group is varied (R = CH_3, CH_2CH_3, CH_2CN, $C(CH_3)_2CN$, CH_2COOCH_3, $CH(CH_3)COOCH_3$, CH_2OCOCH_3, CH_2Ph, $C(CH_3)_2Ph$, and $CH(CH_3)Ph$), while R′ = Z = CH_3. Table 2 shows the enthalpies for systems in which the R′-group is varied (R′ = CH_3, CH_2CH_3, CH_2CN, $C(CH_3)_2CN$, CH_2COOCH_3, $CH(CH_3)COOCH_3$, CH_2OCOCH_3, CH_2Ph, and $CH(CH_3)Ph$), while R = Z = CH_3. Table 3 shows the enthalpies for systems in which the Z-group is varied (Z = CH_3, H, Cl, CN, CF_3, NH_2, Ph, CH_2Ph, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OC(CH_3)_3$, and F), while R = R′ = CH_3. Table 4 shows results for systems in which both R and Z are nonmethyl. It should be noted that the effects of these substituents on the kinetics and thermodynamics of the RAFT

TABLE 1: Effect of Level of Theory on the Calculated Enthalpies[a] for $\mathrm{CH_3SC^{\bullet}(CH_3)S{-}R \rightarrow CH_3SC(CH_3){=}S + {}^{\bullet}R}$

R	CH$_3$	CH$_2$CH$_3$	CH$_2$CN	C(CH$_3$)$_2$CN	CH$_2$COOCH$_3$	CH(CH$_3$)COOCH$_3$	CH$_2$OCOCH$_3$	CH$_2$Ph	CH(CH$_3$)Ph	C(CH$_3$)$_2$Ph	MAX	MIN	MAD
B3LYP	56.8	46.1	13.7	−18.4	28.9	7.8	43.9	−0.3	−11.0	−26.9	−7.4	−62.1	36.2
KMLYP	68.1	60.8	28.2	4.8	48.1	30.8	64.5	17.2	9.1	−0.8	3.9	−36.0	17.9
MPW1B95	77.5	67.4	36.0	8.8	53.7	35.4	67.8	25.3	15.6	4.8	13.3	−30.4	13.7
BB1K	77.4	68.1	36.0	9.4	53.4	34.9	68.0	25.7	15.7	4.9	13.2	−30.3	13.5
MPWB1K	82.1	73.2	41.4	16.1	59.6	42.1	74.6	31.7	22.3	12.3	17.9	−22.9	9.6
BMK	76.3	69.3	40.8	18.1	55.7	40.4	66.7	29.2	20.5	11.7	12.1	−23.5	10.0
ROMP2	65.5	77.9	42.1	40.1	59.0	62.1	76.9	47.5	51.9	51.7	16.5	0.9	7.2
SCS-MP2	61.6	71.9	37.0	31.7	51.9	51.8	69.9	39.3	41.4	38.6	5.5	−6.2	3.9
SOS-MP2	59.7	68.9	34.5	27.5	48.3	46.7	66.4	35.3	36.1	32.1	1.1	−9.8	5.0
G3(MP2)-RAD	64.2	69.9	39.7	33.9	58.1	55.9	75.4	34.2	35.9	35.2	0	0	0

[a] Enthalpies (0 K, kJ mol^{-1}) were calculated using B3-LYP/6-31G(d) optimized geometries and include scaled B3-LYP/6-31G(d) zero-point vibrational energy. With the exception of the composite procedure, G3(MP2)-RAD, all energy calculations were performed using the 6-311+G(3df,2p) basis set. Here "min" and "max" refer to the minimum and maximum deviations from G3(MP2)-RAD, while "MAD" is the mean absolute deviation.

TABLE 2: Effect of Level of Theory on the Calculated Enthalpies[a] for $\mathrm{R'SC^{\bullet}(CH_3)S{-}CH_3 \rightarrow R'SC(CH_3){=}S + {}^{\bullet}CH_3}$

R′	CH$_3$	CH$_2$CH$_3$	CH$_2$CN	C(CH$_3$)$_2$CN	CH$_2$COOCH$_3$	CH(CH$_3$)COOCH$_3$	CH$_2$OCOCH$_3$	CH$_2$Ph	CH(CH$_3$)Ph	C(CH$_3$)$_2$Ph	max	min	MAD
B3LYP	56.8	57.7	72.9	85.4	66.7	68.6	66.5	60.0	63.3	77.2	−5.1	−18.8	11.9
KMLYP	68.1	68.6	84.1	97.2	79.0	85.3	82.8	74.5	76.8	92.2	6.7	−2.5	2.6
MPW1B95	77.5	77.7	94.6	107.4	88.5	94.6	91.6	84.7	86.8	102.7	16.9	6.3	11.2
BB1K	77.4	77.9	92.9	106.6	86.8	93.0	90.3	83.6	85.5	101.7	16.1	5.0	10.2
MPWB1K	82.1	82.4	98.1	111.5	92.4	99.2	96.3	89.2	91.0	107.3	21.0	11.0	15.6
BMK	76.3	76.1	92.7	103.8	87.6	91.9	87.7	82.9	83.8	98.6	13.3	2.4	8.7
ROMP2	65.5	69.9	83.6	91.4	79.6	83.2	88.2	78.0	77.7	92.5	3.0	−0.4	1.7
SCS−MP2	61.6	65.8	77.0	86.0	73.6	76.3	81.0	71.4	71.1	85.9	−2.2	−7.0	4.4
SOS−MP2	59.7	63.7	73.8	83.3	70.6	72.9	77.4	68.0	67.8	82.6	−4.3	−10.3	7.4
G3(MP2)-RAD	64.2	68.0	81.0	90.5	78.1	80.2	85.3	75.9	78.1	92.7	0	0	0

[a] Enthalpies (0 K, kJ mol^{-1}) were calculated using B3-LYP/6-31G(d) optimized geometries and include scaled B3-LYP/6-31G(d) zero-point vibrational energy. With the exception of the composite procedure, G3(MP2)-RAD, all energy calculations were performed using the 6-311+G(3df,2p) basis set. Here, "min" and "max" refer to the minimum and maximum deviations from G3(MP2)-RAD, while "MAD" is the mean absolute deviation.

TABLE 3: Effect of Level of Theory on the Calculated Enthalpies[a] for $\mathrm{CH_3SC^{\bullet}(Z)S{-}CH_3 \rightarrow CH_3SC(Z){=}S + {}^{\bullet}CH_3}$

Z	CH$_3$	H	F	Cl	CN	CF$_3$	NH$_2$	Ph	CH$_2$Ph	OMe	OEt	OPr	OBu	max	min	MAD
B3LYP	56.8	68.9	47.5	67.5	120.0	88.1	24.5	83.2	59.5	23.7	23.5	24.8	29.3	−2.7	−12.8	7.1
KMLYP	68.1	80.9	56.7	83.1	137.6	101.1	28.7	98.4	74.1	28.2	28.3	30.9	36.4	14.7	−7.0	5.3
MPW1B95	77.5	89.3	65.5	89.2	142.8	109.3	42.4	106.4	83.0	39.4	39.4	41.6	46.6	19.9	6.7	12.6
BB1K	77.4	89.7	65.6	90.1	143.4	108.8	41.1	106.1	82.6	38.2	38.0	40.1	45.8	20.5	5.4	12.1
MPWB1K	82.1	94.2	70.2	94.9	148.4	114.2	45.4	111.0	87.9	42.7	42.6	45.0	50.6	25.5	9.7	16.9
BMK	76.3	88.2	64.0	87.1	139.9	106.1	39.6	104.3	81.1	37.1	36.6	39.1	44.9	17.0	3.9	10.4
ROMP2	65.5	77.0	44.8	71.5	128.1	89.5	36.4	94.3	72.6	26.7	27.6	31.0	35.2	5.2	−5.4	2.3
SCS-MP2	61.6	72.6	42.7	68.3	120.7	85.0	32.7	88.4	67.6	24.3	24.9	28.1	32.6	−1.6	−7.5	4.6
SOS-MP2	59.7	70.4	41.7	66.7	117.0	82.8	30.9	85.5	65.1	23.1	23.6	26.6	31.2	−3.8	−9.7	6.5
G3(MP2)-RAD	64.2	74.2	50.2	72.9	122.9	92.0	35.7	95.2	72.3	29.2	29.8	33.4	37.1	0	0	0

[a] Enthalpies (0 K, kJ mol^{-1}) were calculated using B3-LYP/6-31G(d) optimized geometries and include scaled B3-LYP/6-31G(d) zero-point vibrational energy. With the exception of the composite procedure, G3(MP2)-RAD, all energy calculations were performed using the 6-311+G(3df,2p) basis set. Here "min" and "max" refer to the minimum and maximum deviations from G3(MP2)-RAD, while "MAD" is the mean absolute deviation.

process have been discussed elsewhere;[8,9,32−36] in the present work we are concerned solely with the effect of level of theory on the accuracy of the results. In what follows we compare the performance of the DFT, MP2, and ONIOM-based procedures against our benchmark level of theory, G3(MP2)-RAD.

Performance of DFT. On the basis of the results in Tables 1−4, none of the DFT procedures examined provide an adequate substitute for G3(MP2)-RAD. For example, in Table 1 it is seen that the mean absolute deviations (MADs) exceed 8 kJ mol^{-1} for all of the methods examined (B3-LYP, KMLYP, MPW1B95, BB1K, MPWB1K, and BMK), and for the popular B3-LYP method, the error is as much as 36 kJ mol^{-1}. Of even greater concern is the fact that the errors in all of the DFT methods are highly nonsystematic, spanning ranges of greater than 25 kJ mol^{-1} in all cases (and as much as 55 kJ mol^{-1} in the case of B3-LYP). In other words, these procedures cannot be used to study the effect of substituents (in this case the leaving group R) on the fragmentation reaction. In Table 2, which shows the effects of the more remote R′ substituent, the errors are generally smaller, but the MADs still exceed 9 kJ mol^{-1} for all of the methods except KMLYP. In this case the MAD is just 2.6 kJ mol^{-1} but the errors remain nonsystematic and span a range of nearly 10 kJ mol^{-1}. Likewise in Table 3, which shows the effects of the Z-group, the MADs are greater than 10 kJ mol^{-1} for most of the DFT methods and for those having lower MADs, the errors still span a range of over 10 kJ mol^{-1}. Not surprisingly, when the R and Z groups are both varied (Table 4), an even larger range of errors are observed (ca. 20−30 kJ mol^{-1}).

It is difficult to identify which of the DFT methods tested shows the "best" performance. KMLYP shows the smallest MADs for the systems in which R′ or Z are varied, but still has errors that span a range of more than 20 kJ mol^{-1} in the latter case, and over 30 kJ mol^{-1} when R is varied. The newer DFT methods (MPW1B95, BB1K, MPWB1K, and BMK) have better "all-round" performance, but still have MADs over 10 kJ mol^{-1} in most cases, and relative errors of the order of 20−30 kJ mol^{-1}. For the toughest systems, those in which both R and Z are nonmethyl, BMK tends to perform slightly better than the other DFT methods, having an MAD of 7.8 kJ mol^{-1}, but even in this case the errors span a range of 20 kJ mol^{-1}. The main conclusion that may be drawn from these data is that all of the

TABLE 4: Effect of Level of Theory on the Calculated Enthalpies[a] for $CH_3SC^{\bullet}(Z)S{-}R \rightarrow CH_3SC(Z){=}S + {}^{\bullet}R$ for R = CH_2Ph (Bz), CH_2OCOCH_3 (VAc), and $(CH_3)_2CN$ and Z = CN, F,and OCH_3

	Z = F			Z = CN			Z = OCH_3					
method	R = VAc	R = $C(CH_3)_2CN$	R = Bz	R = VAc	R = $C(CH_3)_2CN$	R = Bz	R = VAc	R = $C(CH_3)_2CN$	R = Bz	max	min	MAD
B3LYP	31.3	−29.0	−11.2	102.8	32.4	61.8	8.5	−46.7	−32.3	−19.6	−50.1	33.0
KMLYP	45.4	−9.1	3.0	124.9	61.6	84.4	21.3	−34.4	−21.9	1.3	−36.0	15.7
MPW1B95	49.0	−4.1	10.2	124.9	60.5	87.8	25.3	−25.1	−11.1	1.3	−26.7	11.1
BB1K	50.6	−4.7	11.1	127.1	62.4	89.3	24.8	−27.6	−12.3	3.5	−29.2	11.3
MPWB1K	55.8	2.1	16.6	132.8	69.4	95.3	30.9	−21.2	−6.5	9.2	−22.8	9.6
BMK	49.2	3.7	13.0	124.1	69.5	90.4	25.1	−17.5	−9.2	1.5	−19.1	7.8
ROMP2	47.8	21.2	22.5	127.7	93.8	106.1	30.4	3.5	10.2	17.2	−3.8	7.0
SCS-MP2	45.3	13.0	17.5	119.8	82.4	95.2	26.2	−5.2	3.0	6.3	−8.0	4.8
SOS-MP2	44.1	8.9	15.0	115.8	76.6	89.8	24.6	−9.5	−0.5	1.5	−11.1	6.0
ONIOM (CH_3-core)												
B3LYP	38.6	−21.6	−3.8	110.1	39.8	69.1	15.9	−39.4	−24.9	−12.3	−42.7	25.6
KMLYP	41.4	−13.0	−0.9	120.9	57.7	80.5	17.4	−38.3	−25.8	−2.7	−39.9	19.4
MPW1B95	35.6	−17.4	−3.1	111.6	47.2	74.5	11.9	−38.5	−24.4	−12.0	−40.1	24.1
BB1K	37.3	−18.0	−2.1	113.8	49.1	76.0	11.5	−40.9	−25.6	−9.8	−42.5	23.7
MPWB1K	37.9	−15.9	−1.3	114.8	51.4	77.4	13.0	−39.2	−24.4	−8.8	−40.8	22.3
BMK	37.2	−8.3	1.0	112.1	57.5	78.4	13.1	−29.5	−21.2	−10.5	−31.1	19.3
ROMP2	49.7	23.1	24.3	129.6	95.7	108.0	32.3	5.4	12.0	19.1	−1.9	8.0
SCS-MP2	51.1	18.8	23.3	125.6	88.1	101.0	32.0	0.6	8.8	12.1	−2.2	4.6
SOS-MP2	51.8	16.6	22.8	123.5	84.3	97.5	31.9	−1.8	7.2	9.3	−3.4	4.0
ONIOM (Z-core)												
B3LYP	33.9	−26.3	−8.5	105.7	35.4	64.7	14.0	−41.2	−26.8	−17.0	−47.1	29.3
KMLYP	38.8	−15.7	−3.5	110.2	47.0	69.7	22.3	−33.4	−20.9	−11.9	−35.5	22.2
MPW1B95	33.6	−19.5	−5.1	105.1	40.7	68.0	15.0	−35.4	−21.3	−17.3	−41.8	25.9
BB1K	35.2	−20.2	−4.3	106.6	41.9	68.8	15.8	−36.6	−21.3	−15.7	−40.6	25.4
MPWB1K	35.8	−17.9	−3.4	107.2	43.9	69.8	17.5	−34.7	−19.9	−15.1	−38.6	24.0
BMK	35.4	−10.1	−0.8	107.1	52.5	73.4	17.2	−25.5	−17.1	−14.3	−30.0	20.2
ROMP2	53.2	26.6	27.8	125.8	91.9	104.1	36.1	9.2	15.8	15.6	1.9	8.5
SCS-MP2	52.7	20.4	24.9	125.2	87.8	100.6	34.4	3.0	11.1	11.7	0.2	5.1
SOS-MP2	52.5	17.3	23.5	124.9	85.7	98.9	33.5	−0.2	8.8	10.0	−1.8	4.3
ONIOM (R-core)												
B3LYP	62.8	23.3	23.4	134.3	84.8	96.3	40.0	5.6	2.2	11.9	2.0	6.5
KMLYP	56.3	20.0	20.0	135.8	90.7	101.4	32.2	−5.3	−4.9	12.5	−6.9	6.7
MPW1B95	56.6	21.0	19.2	132.6	85.6	96.8	32.9	0.0	−2.1	9.0	−2.3	4.3
BB1K	58.1	19.8	19.6	134.5	87.0	97.8	32.3	−3.1	−3.8	10.9	−4.7	5.5
MPWB1K	56.6	19.9	19.1	133.6	87.2	97.8	31.7	−3.4	−3.9	10.0	−5.0	5.3
BMK	57.9	19.5	18.0	132.7	85.3	95.4	33.8	−1.7	−4.2	9.1	−4.4	4.3
ROMP2	46.2	15.0	9.2	126.2	87.6	92.8	28.8	−2.7	−3.1	5.1	−5.4	4.2
SCS-MP2	50.8	15.2	12.4	125.3	84.5	90.1	31.7	−3.0	−2.1	2.0	−4.6	2.1
SOS-MP2	53.1	15.3	14.0	124.8	83.0	88.7	33.2	−3.1	−1.6	2.2	−4.7	1.7
G3(MP2)-RAD	50.9	18.9	13.5	123.6	82.5	88.9	34.2	1.6	0.2	0	0	0

[a] Enthalpies (0 K, kJ mol^{-1}) were calculated using B3-LYP/6-31G(d) optimized geometries and include scaled B3-LYP/6-31G(d) zero-point vibrational energy. With the exception of the composite procedure, G3(MP2)-RAD, all energy calculations were performed using the 6-311+G(3df,2p) basis set. In the ONIOM based procedures, G3(MP2)-RAD was used for the core system, and various levels of theory were adopted for the substituent effect. For definition of the R-core, Z-core, and CH_3-core, see Scheme 2. Here "min" and "max" refer to the minimum and maximum deviations from G3(MP2)-RAD, while "MAD" is the mean absolute deviation.

DFT methods tested fail to model the absolute and relative values of the β-scission enthalpies, and new functionals would be desirable for this class of reactions.

Performance of MP2. In general terms, ROMP2 and its variants, SCS-MP2 and SOS-MP2, perform much better than the DFT methods. In particular when the leaving group (R) is held constant (as in Tables 2 and 3), the MADs for standard ROMP2 are of the order of 2 kJ mol^{-1}. However, when the leaving group is varied (Tables 1 and 4), the MADs rise to 7 kJ mol^{-1}; although lower than their DFT counterparts, these errors are still unacceptably high. Closer examination of the results confirms that in fact ROMP2 generally shows excellent agreement with G3(MP2)-RAD but breaks down when the radical leaving group is substituted with groups such as phenyl or CN that delocalize the unpaired electron. Interestingly, the accuracy is less affected when such groups are included at the radical center of the RAFT-adduct radical. For example, the error for the phenyl-substituted RAFT-adduct is just 0.4 kJ mol^{-1}, compared with 16.0 kJ mol^{-1} when it is on the leaving group. This is probably related to that fact that all of the RAFT adduct radicals have two thiyl substituents that dominate their stabilities, and delocalize the unpaired electron regardless of whether there is an additional phenyl substituent at the radical center. Indeed, it is the Z-substituents that have the strongest electron withdrawing capabilities that also show the largest errors, possibly because they interfere with the stabilizing effect of the sulfurs. More specifically, the CN Z-substituent, which interacts captodatively and is a strong radical stabilizer has an error of 5.2 kJ mol^{-1}, while fluorine, which is a strong sigma withdrawer and destabilizer of the RAFT adduct radical has an error of −5.4 kJ mol^{-1}. Nonetheless, in general, ROMP2 provides an excellent substitute for G3(MP2)-RAD, except when the leaving group is substituted with groups that delocalize the unpaired electron.

The other variants of MP2 show similar performance to standard MP2. They show slightly smaller errors in the "problem" systems, but at the cost of slightly worse performance overall. Since SOS-MP2 can be potentially framed as a fourth order method, it shows some promise as a lower-cost substitute for ROMP2 in larger systems. However, it is clear that none of the methods provide a sufficiently accurate substitute for G3-(MP2)-RAD for the chemically accurate treatment of larger systems.

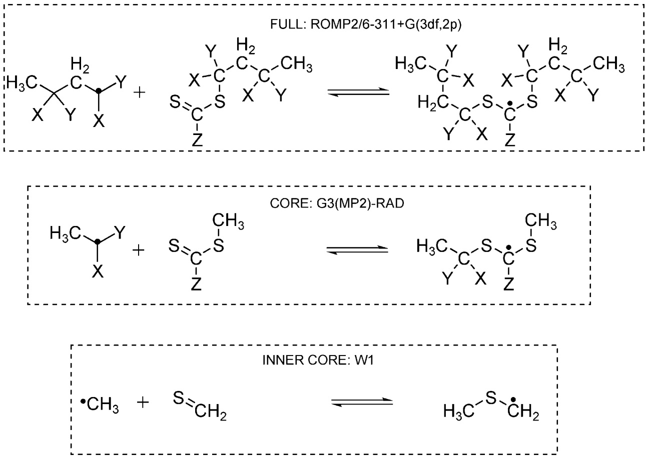
Performance of ONIOM. For a number of RAFT systems, including those with “problem” Z-groups (F and CN) and R-groups ($C(CH_3)_2CN$ and CH_2Ph) it was possible to calculate systems in which both R and Z were nonmethyl groups at the G3(MP2)-RAD level of theory. These were then compared with ONIOM values constructed using either the CH_3-core, Z-core, or R-core approach (see Scheme 2) in conjunction with various levels of theory for the substituent effect. Not surprisingly, the ONIOM values calculated using the CH_3-core and Z-core approaches had very large errors because the problem R-substituents were not treated at the high level of theory. However, the R-core approach fared better, particularly when used in conjunction with the MP2-based methods. For example, using ROMP2/6-311+G(3df,2p) to measure the substituent effect, the MAD was just 4.2 kJ mol^{-1}, with maximum deviations of around ±5 kJ mol^{-1}. Moreover, in practice the errors might be expected to be smaller than this because the problem Z-groups (CN and F) are small enough to be included in the core system, and the effects of the larger substituents (such as phenyl and benzyl) appear to be well described at the ROMP2 level of theory.

The SCS- and SOS-MP2 methods are also appear to be appropriate for measuring the substituent effect in the R-core ONIOM method. In these cases, the maximum absolute deviations were similar to those obtained using ROMP2, and the MADs (1.7 and 2.1 kJ mol^{-1}, respectively) were actually slightly smaller, though this is possibly because the Z-groups that showed the largest errors with these methods (such as phenyl and benzyl) were unable to be included in the analysis. Overall, there does not appear to be any significant differences in the performances of SCS-MP2, SOS-MP2, and standard ROMP2 (either in isolation or as part of the ONIOM method) and hence the standard method might be preferred on the basis that it does not depend on empirically optimized parameters. However, as noted above, if coded efficiently, the SOS-MP2 method is less computationally intensive than either SCS-MP2 or standard ROMP2, and might be attractive as a substitute for standard ROMP2 for larger systems.

Despite their problems in modeling the effects of substituents on these reactions, the DFT methods also fare remarkably well when used to correct for the substituent effect in the R-core ONIOM method. Indeed for the best DFT methods (MPW1B95 and BMK), the MADs and range of errors are only marginally larger than those with ROMP2. As in the case of ROMP2, the worst errors are obtained when the leaving group (R) is varied and once this is included in the core, much of the error cancels. However, for modeling more general addition−fragmentation reactions (such as in Scheme 3), one might expect the errors in the DFT-procedures to be considerably larger. This is because in those situations a typical core system would replace the R′-group with methyl, and would include only the α-substituents on the leaving R-group. As we saw from Table 2, whereas the ROMP2 method can model the R′-substituent effect accurately, the DFT methods cannot. Moreover, on the basis of studies of related systems, such as radical addition to C═C double bonds[20] and bond dissociation energies,[15] current DFT methods appear to be generally less reliable than ROMP2 in modeling substituent effects on radical stability and thus less suitable for use in ONIOM-based procedures.

Practical Recommendations. It is clear that the addition−fragmentation reaction in the RAFT polymerization process is a difficult system to model computationally, with lower cost procedures, such as ROMP2 and particularly DFT, having large absolute and relative errors for the thermodynamics of some systems. Ideally, one should use a very high-level composite procedure such as W1 for the entire system; however, since this is currently impractical, a lower-cost strategy is needed. On the basis of the current assessment and our earlier higher-level study of prototypical systems,[5] it appears reasonable to study the addition−fragmentation reaction via a 3-layer ONIOM method as depicted in Scheme 3. The full system is first calculated at the ROMP2/6-311+G(3df,2p) level of theory (or its SCS or SOS variants) and then corrected to G3(MP2)-RAD using a core reaction that includes the α-substituents on the leaving group but replaces the R′-group with a CH_3 substituent. The Z-group should preferably be included in full in the core, but for larger groups such as phenyl and benzyl it can be replaced with a CH_3 group without significant additional error. Finally, the G3(MP2)-RAD value for the core is itself corrected to W1, using an “inner core” that includes the principal forming and breaking bonds (i.e., $^{\bullet}CH_3 + S{=}CH_2$). Although it is currently impossible to validate this approach fully (as this would entail the use of W1 calculations on the full systems), our stepwise study of the substituent effects in these reactions suggests that this approach should reproduce the W1 values for these reactions within an uncertainty of approximately 5 kJ mol^{-1}, with the accuracy expected to improve further as larger core sizes become practical.

SCHEME 3



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Supporting Information Available: GAUSSIAN archive entries for UB3-LYP/6-31G(d) equilibrium structures (Tables S1−S4). This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Le, T. P. T.; Moad, G.; Rizzardo, E.; Thang, S. H. PCT Int. Appl. WO 9801478 A1 980115 1998; *Chem. Abstr.* **1998** *128*, 115390. (b) Charmot, D.; Corpart, P.; Michelet, D. Zard, S. Z.; Biadatti, T. PCT Int. Appl. WO 9858974, 1998; *Chem Abstr.* **1999**, *130*, 82018.

(2) Moad, G.; Rizzardo, E.; Thang, S. H. *Aust. J. Chem.* **2005**, *58*, 379−410.

(3) Feldermann, A.; Coote, M. L.; Stenzel, M. H.; Davis, T. P.; Barner-Kowollik, C. *J. Am. Chem. Soc.* **2004**, *126*, 15915−15923.

(4) Kwak, Y.; Goto, A.; Fukuda, T. *Macromolecules* **2004**, *37*, 1219−1225.

(5) Coote, M. L.; Wood, G. P. F.; Radom, L. *J. Phys. Chem. A* **2002**, *106*, 12124−12138.

(6) Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502−16513.

(7) Martin, J. M. L.; Parthiban, S. In *Quantum Mechanical Prediction of Thermochemical Data*; Cioslowski, J., Ed.; Kluwer-Academic: Dordrecht, The Netherlands, 2001; pp 31−65.

(8) Coote, M. L.; Henry, D. J. *Macromolecules* **2005**, *38*, 1415−1433.

(9) Coote, M. L. *J. Phys. Chem. A* **2005**, *109*, 1230−1239.

(10) (a) Kohn, W.; Becke, A. D.; Parr, R. G. *J. Phys. Chem.* **1996**, *100*, 12974−12980. (b) Koch, W.; Holthausen, M. C. *A Chemist's Guide to Density Functional Theory*; Wiley-VCH: Weinheim, Germany, 2000.

(11) See for example: Zhao, Y.; Lynch, B. J.; Truhlar, D. G. *J. Phys. Chem. A* **2004**, *108*, 2715−2719 and references therein.

(12) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2004**, *108*, 6908−6918.

(13) Boese, A. D.; Martin, J. M. L. *J. Chem. Phys.* **2004**, *121*, 3405−3416.

(14) Dybala-Defratyka, A.; Paneth, P.; Pu, J.; Truhlar, D. G. *J. Phys. Chem. A* **2004**, *108*, 2475−2486.

(15) Izgorodina, E. I.; Coote, M. L.; Radom, L. *J. Phys. Chem. A* **2005**, *109*, 7558−7566.

(16) Grimme, S. *J. Chem. Phys.* **2003**, *118*, 9095−9102.

(17) Jung, Y.; Lochan, C.; Dutoi, A. D.; Head-Gordon, M. *J. Chem. Phys.* **2004**, *121*, 9793−9802.

(18) Vreven, T.; Morokuma, K. *Theor. Chem. Acc.* **2003**, *109*, 125−132.

(19) Note that the ONIOM approach can also be applied to the calculation of geometries and frequencies. However, in the present work, we are able to perform all geometry optimizations and frequency calculations on the full systems, and merely use ONIOM to correct the energetics of the reaction.

(20) Izgorodina, E. I.; Coote, M. L. *Chem. Phys.* **2006**, in press; (available online Oct 25, 2005).

(21) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision C.02. Gaussian, Inc.: Wallingford, CT, 2004.

(22) Werner, H.-J.; Knowles, P. J.; Lindh, R.; Schütz, M.; Celani, P.; Korona, T.; Manby, F. R.; Rauhut, G.; Amos, R. D.; Bernhardsson, A.; Berning, A.; Cooper, D. L.; Deegan, M. J. O.; Dobbyn, A. J.; Eckert, F.; Hampel, C.; Hetzer, G.; Lloyd, A. W.; McNicholas, S. J.; Meyer, W.; Mura, M. E.; Nicklass, A.; Palmieri, P.; Pitzer, R.; Schumann, U.; Stoll, H.; Stone, A. J.; Tarroni, R.; Thorsteinsson, T. *MOLPRO* 2002.6, *a package of ab initio programs*; University of Birmingham: Birmingham, U.K., 2003.

(23) Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502−16513.

(24) Coote, M. L. *J. Phys. Chem. A* **2004**, *108*, 3865−3872.

(25) Gómez-Balderas, R.; Coote, M. L.; Henry, D. J.; Radom, L. *J. Phys. Chem. A* **2004**, *108*, 2874−2883.

(26) Henry, D. J.; Sullivan, M. B.; Radom, L. *J. Chem. Phys.* **2003**, *118*, 4849−4860.

(27) Ah Toy, A.; Chaffey-Millar, H.; Davis, T. P.; Stenzel, M. H.; Izgorodina, E. I.; Coote, M. L.; Barner-Kowollik, C. *Chem. Commun.* **2006**, in press; (DOI: 10.1039/b515561d; available online Jan 20, 2006).

(28) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(29) Kang, J. K.; Musgrave, C. B. *J. Chem. Phys.* **2001**, *115*, 11040−11051.

(30) Becke, A. D. *J. Chem. Phys.* **1996**, *104*, 1040−1046.

(31) (a) Piacenza, M.; Grimme, S. *J. Comput. Chem.* **2003**, *25*, 83−98. (b) Grimme, S. *J. Phys. Chem. A* **2005**, *109*, 3067−3077.

(32) Coote, M. L.; Radom, L. *J. Am. Chem. Soc.* **2003**, *125*, 1490−1491.

(33) Coote, M. L.; Radom, L. *Macromolecules* **2004**, *37*, 590−596.

(34) Coote, M. L. *Macromolecules* **2004**, *37*, 5023−5031.

(35) Coote, M. L. *Aust. J. Chem.* **2004**, *57*, 1125−1132.

(36) Coote, M. L.; Henry, D. J. *Macromolecules* **2005**, *38*, 5774−5779.