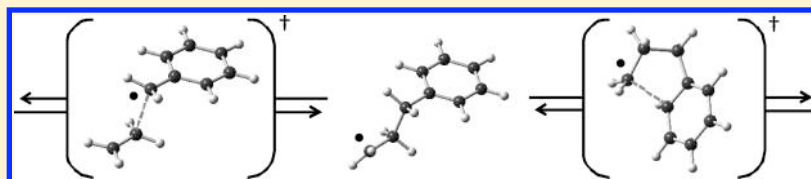


Hammett Correlations in the Chemistry of 3-Phenylpropyl Radicals

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S Supporting Information

ABSTRACT:



The energetics and kinetics of the reaction of variously substituted benzyl radicals with a model alkene were calculated at the G3(MP2)-RAD//B3-LYP/6-31G(d) level of theory to determine whether such reactions are amenable to Hammett analysis. The reactions were studied both in the gas phase and in toluene solution in the temperature range 298–353 K; calculations include 1D-hindered rotor corrections for low frequency torsional modes, and the solvation energies were calculated using COSMO-RS at the BP/TZP level of theory. The addition reaction was found to be dominated by radical stabilization effects, but under circumstances where olefin substituent effects were decoupled from aryl substituent effects, a modest polar effect comes into play, which is enhanced by solvation. Reasonable correlations with empirical substituent parameters such as Hammett σ and σ^* are observed for the enthalpy of activation, but additional entropic factors act to decrease the degree of correlation with respect to free energies and rate coefficients, confirming hypotheses from earlier experimental work. Substituent effects on the reverse β -fragmentation reaction, and potential cyclization of the 3-phenylpropyl radicals formed by addition are also discussed.

INTRODUCTION

Benzyl radical, as a useful computational and experimental analogue of styrene homo- and copolymerization, is known to add to olefins to generate substituted 3-phenylpropyl radical species. The kinetics and thermodynamics of the addition reaction have been studied both experimentally and computationally and interpreted in terms of FMO models that indicate the importance of polar effects in such reactions—reactions of this type have often been described in terms of a “complex interplay” of polar, steric, and thermodynamic (bond strength) effects.¹ In a polymerization reaction, the fate of these radicals appears to be dominated by the addition of further monomer to initiate chain growth. However, under conditions where additional monomer is (a) dilute or (b) absent, an alternative pathway involving cyclization into the aryl ring becomes possible. Zard and others have demonstrated the synthetic feasibility of cyclization of certain types of alkyl radicals into aryl rings,² and cyclization of aryl radicals into arenes is also a known reaction.³ Such reactions rely on an oxidant species (a peroxide, aminoxyl radical or the like) to remove hydrogen from the formed cyclohexadienyl radical and re-establish aromaticity.^{2–4}

In a previous contribution,⁵ we have studied the effect of chain functionalization on the reactivities of 3-phenylpropyl radicals with respect to fragmentation (and the reverse addition reaction) and cyclization of these species. We found that, in general, cyclization is a significantly more facile unimolecular reaction than fragmentation and, under dilute monomer conditions, may even

be competitive with subsequent addition reactions. In general terms, all three reactions (addition, fragmentation, cyclization), showed good adherence to Evans–Polanyi–Semenov behavior, and there was a reasonable correlation between the enthalpy of activation with the calculated radical stabilization energies (RSEs) of the substituted 3-phenylpropyl radicals in question. Heteroatom substitution in the chain (O, N) led to qualitatively similar behavior, although it should be noted that thia-substitution led to significant deviation from the remainder of the data set. Correlations with polarity indices (such as the SOMO–LUMO energy gaps used by Fischer and Radom), were somewhat weaker for fragmentation and cyclization reactions.

In this contribution, we report on our investigation of the effect of functionalization on the aryl ring on the reactivity of 3-phenylpropyl radicals with respect to fragmentation and cyclization reactions. Aryl ring functionalization is known to be amenable to the use of quantitative structure–reactivity relationships (QSAR), the simplest of which is the Hammett equation,⁶ which expresses reactivity (or equilibrium thermodynamics) in terms of a simple linear correlation,

$$\log(k_X/k_0) = \sigma_X \cdot \rho$$

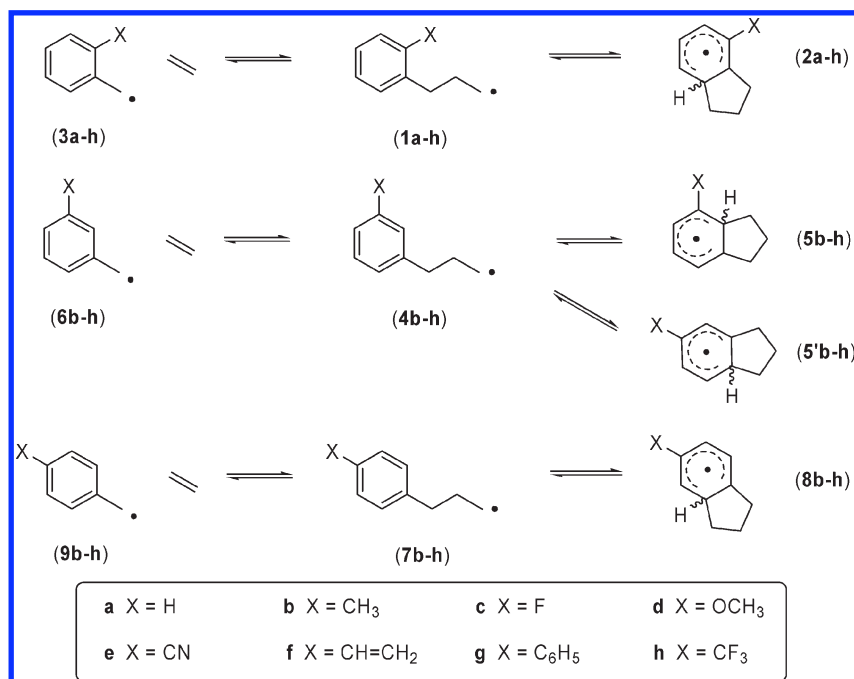
where σ_X represents a substituent ($-X$) parameter (parametrized originally from the acidity of substituted benzoic acids) and ρ a

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Scheme 1. Substituted 3-Phenylpropyl Radicals Used in This Study



so-called reactivity parameter or reaction constant, from which mechanistic information may be gleaned. k_X and k_0 are rate coefficients for the reaction of substituted and standard (typically $X = H$) systems, respectively. Most of the early σ -parameters and scales were primarily concerned with polar reactions, although there have been a number of experimental σ^\bullet scales published that are intended to apply specifically to free radical reactions.⁷

Previously, the applicability of the Hammett relationship to the description of para-substituent effects on the homopropagation rate coefficients, k_p , of para-substituted styrene monomers has been studied experimentally via pulsed laser polymerization.⁸ Although there was an apparent qualitative relationship between k_p and σ , the correlations with both the Hammett equation or the extended Hammett equation of Yamamoto,⁹ were poor. It was suggested that the substituents on the monomer and the attacking radical may affect the reaction in different ways (in effect, reactions with each monomer should require a separate reaction constant ρ); the effects of entropy and remote substituent effects may also play a role. To explain these results, it is necessary to decouple these effects through the study of simpler model reactions, which was not possible using the experimental techniques available at the time but is possible using accurate ab initio calculations.

In this study we have utilized a series of substituents that cover a range of the traditional Hammett σ -values, and these are substituted in a number of different positions on the aromatic ring (Scheme 1), where they may exert primarily inductive or resonance effects, depending on their position on the ring. To explicitly study Hammett-type effects, the propyl chain remains unfunctionalized, although it is known that functionalization on the chain, particularly at the 1-position (the radical center), will affect the kinetics of these systems. In this way, we decouple the effects on the propagating radical in radical addition from effects on the monomer.

THEORETICAL MODELS

Energies. Geometry optimizations, single point energies, and frequency calculations were carried out using the GAUSSIAN 03 program suite.¹⁰ Calculated vibrational zero-point energies, and enthalpic corrections (ΔH_{vib}) at the B3LYP/6-31G(d) level of theory¹¹ were scaled using the scaling factors recommended by Scott and Radom.¹² All optimized stationary points were found to have the appropriate number of imaginary frequencies and in the case of transition states the imaginary modes corresponded to the correct reaction coordinates. Spin contamination at the B3LYP/6-31G(d) level of theory is significant in some cases, but not necessarily substantial. Typical values for the spin expectation value $\langle S^2 \rangle$ ranged between 0.75 and 0.80 at this level of theory, with greater spin contamination in the transition state geometries than in minima. We note that energy refinements at G3(MP2)-RAD use restricted open-shell wave functions for all component energy calculations.

Energies were refined using the G3(MP2)-RAD composite method,¹³ to achieve higher levels of accuracy. This method approximates URCCSD(T) calculations with the large triple- ζ basis set GTMP2large as the sum of the URCCSD(T)/6-31G(d) level energies and a basis set correction term evaluated at the R(O)MP2 level of theory. It has been shown to deliver "chemical accuracy" (ca. 1 kcal/mol) when assessed against a large test set of experimental thermochemical data¹³ and has recently been shown to deliver similar performance for a large test set of bond dissociation energies and associated radical stabilization energies for carbon-centered radicals.¹⁴ For the specific case of radical addition to C=C double bonds, and the corresponding β -scission processes, G3(MP2)-RAD was recently found to reproduce higher-level W1 calculations to within chemical accuracy¹⁵ and has been used successfully to reproduce experimental propagation rate coefficients in several free-radical polymerization processes.¹⁶

Table 1. Derived Kinetic Parameters for Solution Phase Reactions of Ortho-Substituted 3-Phenylpropyl Radicals at 298–353 K^a

	cyclization						β -fragmentation						addition				RSE	
	ΔH^\ddagger ^b	ΔS^\ddagger ^c	ΔH_R ^b	ΔS_R ^c	E_A ^b	$\log_{10} A$ ^d	ΔH^\ddagger ^b	ΔS^\ddagger ^c	ΔH_R ^b	ΔS_R ^c	E_A ^b	$\log_{10} A$ ^d	ΔH^\ddagger ^b	ΔS^\ddagger ^c	E_A ^b	$\log_{10} A$ ^d	3 ^b	2 ^b
1a	16.0	−10.4	−4.5	−12.2	16.6	11.0	20.4	−0.3	8.9	18.2	21.0	13.2	11.5	−18.5	12.2	9.2	0.0 ^e	0.0 ^e
1b	16.0	−5.4	−5.5	−6.8	16.7	12.1	19.9	1.1	8.3	22.2	20.6	13.5	11.6	−21.1	12.2	8.6	−0.2	0.0
1c	16.2	−11.3	−4.9	−12.9	16.8	10.8	20.7	−2.9	9.5	17.3	21.3	12.6	11.2	−20.1	11.9	8.9	0.6	−0.3
1d	17.1	−7.8	−3.6	−5.8	17.8	11.5	20.2	−0.1	8.6	22.2	20.8	13.2	11.5	−22.2	12.2	8.4	0.0	0.9
1e	14.7	−9.7	−6.4	−11.7	15.3	11.1	19.2	−3.7	8.4	18.7	19.9	12.4	10.8	−22.4	11.5	8.4	0.4	−0.3
1f	15.6	−6.4	−6.3	−7.2	16.2	11.8	19.9	1.8	8.6	22.9	20.6	13.7	11.3	−21.0	11.9	8.7	0.0	−0.5
1g	14.9	−9.5	−6.1	−9.0	15.6	11.2	19.9	−1.3	8.8	21.0	20.5	13.0	11.0	−22.3	11.7	8.4	−0.2	−0.8
1h	14.6	−7.7	−6.4	−6.5	15.2	11.6	20.2	−0.2	9.4	23.3	20.9	13.2	10.9	−23.5	11.5	8.1	0.8	0.2

^a Using in vacuo G3(MP2)-RAD energies and hindered rotor corrections for torsional modes. Solvation energies calculated by COSMO-RS using toluene as solvent. ^b kcal mol^{−1}. ^c cal mol^{−1} K^{−1}. ^d log₁₀(A.Ms) for addition, log₁₀(A.s) for cyclization and β -fragmentation. ^e Defined.

Kinetics. Rate coefficients for reaction at temperature T , $k(T)$ were estimated in the range 298–353 K using transition state theory:

$$k(T) = \frac{k_B T}{h} (c^\circ)^{1-m} e^{(-\Delta G^\ddagger/RT)} \quad (1)$$

where k_B and h are Boltzmann's and Planck's constants, respectively, R is the ideal gas constant, m is the molecularity of the reaction (unimolecular in the case of cyclization and fragmentation reactions; bimolecular for addition reactions), and ΔG^\ddagger is the free energy of activation for reaction. The concentration factor c° converts the gas phase ΔG^\ddagger from the standard state of 1 mol of ideal gas at the specified temperature and pressure (P at 1 atm) to standard concentration units of mol L^{−1} and is equal to $c^\circ = P/RT$. Equation 1 also typically includes a tunneling correction: given that all of the above reactions may be considered in terms of an attack of a radical species with spin density on a heavy atom on a similarly heavy atom involved in a double bond, we assume that such a correction will have minimal effect on the kinetics of reaction. Parameters such as enthalpies and entropies of activation (ΔH^\ddagger and ΔS^\ddagger), and the Arrhenius parameters E_A and A for reaction were determined from interpolation of $k(T)$ between 298 and 353 K. Enthalpies and entropies of reaction (ΔH_R and ΔS_R) were determined from calculated free energies in a similar manner.

Partition functions for the evaluation of thermochemical data were based on standard rigid rotor models, and harmonic oscillator models for high frequency modes.^{16b} Low frequency torsional modes were treated as hindered internal rotations using the Truhlar CT- $C\omega$ method.¹⁷ There are a number of low frequency modes in the cyclized products and cyclization transition states that may be described as torsional (or pseudorotational) modes. A full 1-dimensional rotational potential cannot be constructed for these species without bond rupture; therefore, no hindered rotor corrections may be readily applied to these species.

Solvation Effects. Free energies of solvation in toluene were estimated for each species using the conductor-like screening model (COSMO-RS) were performed using the COSMO-RS module of the ADF program suite.¹⁸ Single point solvation energies are calculated using the BP/TZVP level because this was the level of theory for which it was parametrized. Geometries were not reoptimized in the solution phase. These solvation energies (ΔG_{solv}) are then combined with the accurate gas-phase energies (ΔG_{gas}) via a Hess cycle to obtain the solution free energies.

$$\Delta G_{\text{soln}} = \Delta G_{\text{gas}} + \Delta G_{\text{solv}} + \Delta G^{\text{latm} \rightarrow \text{1M}} \quad (2)$$

In this equation $\Delta G^{\text{latm} \rightarrow \text{1M}}$, is required for converting from the gas-phase standard state for an ideal gas (typically 1 atm) to 1 M in solution:

$$\Delta G^{\text{latm} \rightarrow \text{1M}} = \Delta n RT \ln(V) = \Delta n RT \ln\left(\frac{RT}{P}\right) \quad (3)$$

where Δn is the number of moles of gas change from reactants to products. Having made this correction for the change in state, the standard unit of concentration in the solution-phase rate constant expression, eq 1, becomes $c^\circ = 1 \text{ mol L}^{-1}$, rather than its value for an ideal gas (e.g., 0.0408 mol L^{−1} at room temperature and pressure).

RESULTS AND DISCUSSION

General Features. The general features of the transition states for fragmentation and cyclization have been discussed previously.⁵ To summarize the salient points, the transition state for cyclization broadly resembles the transition state of the addition/fragmentation reaction, with a generally shorter separation of atoms in the forming bond, and a more acute angle of approach. As would be expected, the spin density distribution in the cyclization transition state (calculated using NPA methods at B3LYP/6-31G*)¹⁹ is distributed on the attacking radical center and positions ortho- and para- with respect to the site of attack on the aromatic ring. There is relatively little evidence of a significant degree of charge transfer character in the transition states involved in this study, and so we would expect that the reaction would be governed by steric and radical stabilization phenomena. The kinetic and thermodynamic parameters for cyclization and β -fragmentation of compounds 1, 7, and 4 in toluene solution phase are summarized in Tables 1–3, respectively. Radical stabilization energies (RSE) included in these tables were estimated for free radicals by consideration of the isodesmic reactions in Scheme 2.

It is clear from the data in Tables 1–3 that the magnitude of the effects of substitution on the aryl ring are relatively small, on the order of 1–3 kcal/mol for each of the three reactions. Therefore, any attempts at correlation may be susceptible to distortion by minor conformational or steric effects. This is likely to be particularly true in the case of cyclization reactions, where a certain amount of steric congestion may become apparent in the transition state and even more so in the product. In addition, reactions involving ortho-substituted species are also likely to be susceptible to steric effects (this is true in the case of the classical Hammett correlations). The Evans–Polanyi–Semenov

Table 2. Derived Kinetic Parameters for Solution Phase Reactions of Para-Substituted 3-Phenylpropyl Radicals at 298–353 K^a

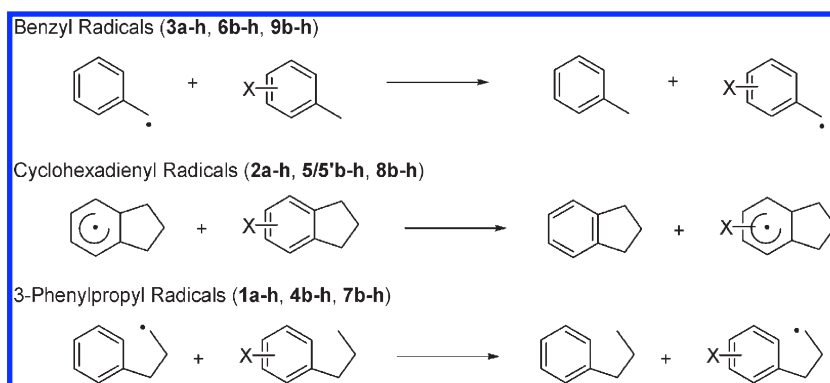
	cyclization						β -fragmentation						addition				RSE	
	$\Delta H^\ddagger{}^b$	$\Delta S^\ddagger{}^c$	$\Delta H_R{}^b$	$\Delta S_R{}^c$	$E_A{}^b$	$\log_{10} A{}^d$	$\Delta H^\ddagger{}^b$	$\Delta S^\ddagger{}^c$	$\Delta H_R{}^b$	$\Delta S_R{}^c$	$E_A{}^b$	$\log_{10} A{}^d$	$\Delta H^\ddagger{}^b$	$\Delta S^\ddagger{}^c$	$E_A{}^b$	$\log_{10} A{}^d$	9^b	8^b
7b	16.1	−7.4	−4.6	−9.6	16.7	11.6	20.3	−0.4	8.6	21.9	21.0	13.2	11.7	−22.3	12.4	8.4	−0.3	−0.3
7c	15.5	−7.0	−5.4	−8.8	16.1	11.7	20.6	−0.3	9.2	21.8	21.3	13.2	11.5	−22.1	12.1	8.4	0.2	−0.4
7d	16.0	−5.7	−5.3	−9.1	16.6	12.0	20.3	−0.4	8.4	21.7	21.0	13.2	11.9	−22.1	12.6	8.4	−0.5	−0.9
7e	15.2	−9.6	−5.1	−10.5	15.8	11.2	19.7	−2.4	8.6	19.8	20.3	12.7	11.1	−22.2	11.7	8.4	−0.2	0.2
7f	15.8	−8.1	−4.9	−9.8	16.4	11.5	19.8	−1.6	7.5	20.1	20.4	12.9	12.2	−21.7	12.9	8.5	−1.3	−0.5
7g	15.8	−7.4	−4.3	−9.0	16.4	11.6	20.1	−1.0	8.4	21.1	20.8	13.0	11.8	−22.2	12.4	8.4	−0.6	0.2
7h	15.4	−9.1	−5.3	−9.9	16.0	11.3	20.3	−0.9	9.3	21.1	21.0	13.1	11.0	−22.0	11.7	8.5	0.3	−0.2

^a Using in vacuo G3(MP2)-RAD energies and hindered rotor corrections for torsional modes. Solvation energies calculated by COSMO-RS using toluene as solvent. ^b kcal mol^{−1}. ^c cal mol^{−1} K^{−1}. ^d log₁₀(A, ms) for addition, log₁₀(A, s) for cyclization and β -fragmentation.

Table 3. Derived Kinetic Parameters for Solution Phase Reactions of Meta-Substituted 3-Phenylpropyl Radicals at 298–353 K^a

	cyclization						β -fragmentation						addition				RSE	
	$\Delta H^\ddagger{}^b$	$\Delta S^\ddagger{}^c$	$\Delta H_R{}^b$	$\Delta S_R{}^c$	$E_A{}^b$	$\log_{10} A{}^d$	$\Delta H^\ddagger{}^b$	$\Delta S^\ddagger{}^c$	$\Delta H_R{}^b$	$\Delta S_R{}^c$	$E_A{}^b$	$\log_{10} A{}^d$	$\Delta H^\ddagger{}^b$	$\Delta S^\ddagger{}^c$	$E_A{}^b$	$\log_{10} A{}^d$	6^b	$5/5^b$
4b (2')	15.4	−8.1	−5.7	−10.7	16.0	11.5	20.5	−0.8	8.9	21.1	21.1	13.1	11.6	−21.9	12.2	8.5	−0.2	−0.9
(6')	16.2	−7.3	−4.2	−8.9	16.9	11.7												−0.1
4c (2')	15.5	−7.5	−5.5	−9.1	16.1	11.6	20.5	−1.2	9.3	21.1	21.1	13.0	11.2	−22.3	11.8	8.4	0.3	−0.8
(6')	16.4	−7.4	−3.6	−8.7	17.0	11.6												0.6
4d (2')	15.0	−7.2	−7.1	−10.9	15.6	11.7	20.6	−0.5	9.5	21.7	21.3	13.1	11.2	−22.2	11.8	8.4	0.5	−2.4
(6')	16.4	−7.7	−3.7	−8.3	17.0	11.6												0.1
4e (2')	13.8	−8.4	−8.6	−10.4	14.4	11.4	20.6	−1.5	9.7	20.5	21.2	12.9	10.9	−22.0	11.6	8.4	0.7	−2.5
(6')	13.9	−8.3	−8.5	−10.4	14.6	11.4												−2.7
4f (2')	14.6	−6.8	−6.7	−7.1	15.3	11.8	20.4	0.0	9.0	21.4	21.0	13.3	11.4	−21.4	12.0	8.6	0.1	−2.7
(6')	14.7	−7.5	−9.6	−10.6	15.3	11.6												−4.9
4g (2')	14.3	−7.6	−4.5	−9.0	14.9	11.6	20.4	−0.6	9.2	21.5	21.1	13.1	11.3	−22.1	11.9	8.4	0.2	−0.6
(6')	15.1	−9.3	−7.0	−9.4	15.7	11.2												−2.3
4h (2')	14.2	−9.0	−7.0	−11.2	14.9	11.3	20.6	−1.3	9.5	21.3	21.2	13.0	11.1	−22.6	11.8	8.3	0.4	−1.6
(6')	15.0	−9.4	−5.7	−9.1	15.7	11.2												−0.4

^a Using in vacuo G3(MP2)-RAD energies and hindered rotor corrections for torsional modes. Solvation energies calculated by COSMO-RS using toluene as solvent. ^b kcal mol^{−1}. ^c cal mol^{−1} K^{−1}. ^d log₁₀(A, ms) for addition, log₁₀(A, s) for cyclization and β -fragmentation.

Scheme 2. Estimation of Stabilization Energies for Substituted Free Radicals

correlations for these systems are less marked than for substituents, which have large effects on the radical kinetics (i.e., on the propyl chain).

Addition Reactions. Correlations observed in our previous study indicate that the addition reactions of benzyl radicals to

alkenes are dominated by radical stability/thermochemistry effects, with some degree of correlation with polar effects with regard to addition in the “tail” mode. Typically, the regioselectivity for “tail” addition is believed to be due to a combination of polar and steric factors. In this case, because our alkene is

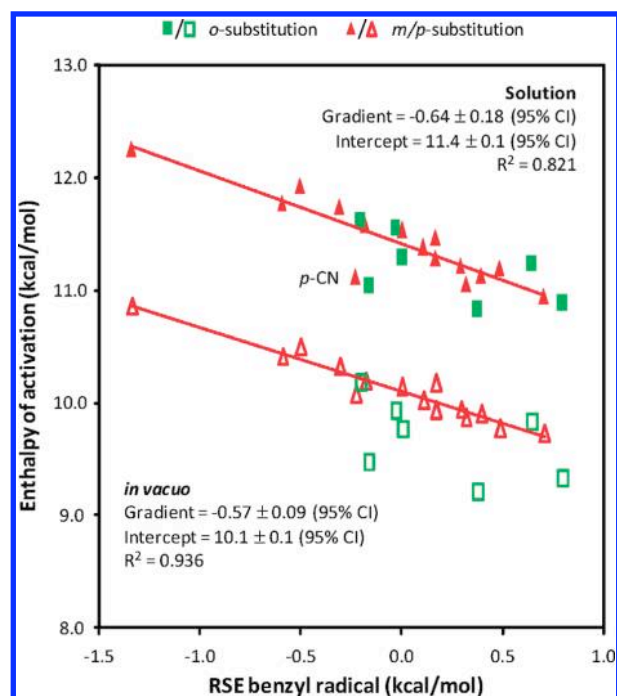


Figure 1. Correlation for enthalpy of activation for addition of benzyl radicals to ethylene in vacuo (open symbols) and in toluene solution (closed symbols) with the calculated radical stabilization energy of the attacking benzyl radical. Lines of best fit data are for meta-/para-substituted species; all quantities were computed at the G3(MP2)-RAD level of theory.

ethylene in all cases (i.e., nonpolar and with no regiochemical preference), we would expect radical stabilization effects to dominate, with the possibility of complexity due to the steric proximity of ortho-substituents to the active site.

The correlation plot for addition reactions (Figure 1) shows a reasonable correlation between the activation enthalpy of addition with the computed radical stabilization energy (RSE) for the attacking benzyl radical, particularly in vacuo. The inclusion of solvation effects reduces the degree of correlation somewhat ($R^2 = 0.821$); this is not unexpected given that RSE was calculated in vacuo. In that regard, we note that the only major outlier is the *p*-cyano-substituted species, which, due to its greater polarity, would be affected to be solvation to a greater extent than the other species. In both the gas phase and solution, correlations were determined using only meta- and para-substituted radicals, where the steric impact of the substituent remains minimal. It is clearly seen that the inclusion of ortho-substituents reduces the degree of correlation dramatically, more so in vacuo than in solution.

In our previous report,⁵ we found a significant degree of correlation between the RSE for benzylic radicals with the degree of spin density at the benzylic position (the active site for addition) calculated using NPA methods; we have also reported similar correlations for other test sets of carbon centered radicals.¹⁴ The correlation for benzyl radicals with substituents on aryl sites broadly conforms to the previously established correlation for α -substituted species. Combination of the data for all substituents (o/m/p/ α) yields the following relationship:

$$\text{RSE} = (50.6 \pm 5.7) - (36.2 \pm 4.0) \cdot \rho_{\text{Bz}}$$

In this equation, RSE has units of kcal/mol and is interpolated from values calculated at the G3(MP2)-RAD level of theory, and

ρ_{Bz} is the NPA spin density at the benzylic position, calculated at the B3LYP/6-31G* level of theory ($R^2 = 0.927$); the uncertainties correspond to the 95% confidence interval on the line of best fit. The correlation between enthalpy of activation with spin density at the benzylic position is moderate for meta-/para-substituted systems, and better in vacuo than in solution. As with the correlation with RSE, the outlier is the *p*-cyano species, which due to its greater polarity is affected by solvation to a greater extent than the others (Figure 2a). It appears that solvation effects, which are often overlooked for radical reactions, may play a crucial role in structure–reactivity relationships and can lead to additional indirect effects of polarity on the barriers and other properties.

We may use the charge density on the benzylic carbon, determined from NPA calculations at the B3LYP/6-31G* level of theory as a measure of polar (ionic) character in the reacting benzyl radical. Alternatively, one may utilize a frontier molecular orbital approach: in radical additions where the attacking radical is viewed as being nucleophilic (such as benzyl), the primary polar interaction (having $\text{Bz}^+/\text{alkene}^{\bullet-}$ character) should be well described by the magnitude of the SOMO(Bz^{\bullet})–LUMO(alkene) energy gap. Because the LUMO(ethylene) remains constant throughout this study, it is the SOMO(Bz^{\bullet}) that is critical, and experimentally, these energies are approximated by the relevant ionization potentials (IP). In this study, vertical (nonadiabatic) IP energies were estimated at the G3(MP2)-RAD level of theory. Correlation with either parameter gives similar degrees of correlation, and the correlation with IP(benzyl) is shown in Figure 2b. It is noteworthy that significantly better correlation with polarity parameters is obtained in solution, rather than in vacuo and that even solution data for ortho-substituents is consistent: the two noteworthy outliers are the *p*-vinyl substituent (larger RSE) and *o*-phenyl substituent (sterically bulky).

Clearly both radical stabilization and polar effects are important in these systems, with the latter playing an increasingly important role in solution. In the broader context of our previous work,⁵ it is perhaps fairer to state that the range of radical stabilization energies exhibited by these systems is sufficiently small that the effects of polarity become more apparent than before. In any case, quantities such as charge density and IP are not completely separable from phenomena such as spin density.

With respect to correlations with empirical substituent parameters, one might anticipate that solution phase data may show correlations with Hammett-type parameters (which are typically formulated with polar reactions in mind) but that such behavior would not be shared in the gas phase. Hansch et al. have provided an extensive tabulation of Hammett substituent parameters for meta- and para-substituents, σ_m and σ_p , respectively.²⁰ Formulation of σ_o parameters is hampered by the differing steric demands of ortho-substituents. In recognition of the relative importance of polar effects and the nucleophilicity of the benzyl radical, we may also consider the use of substituent parameters σ_p^+ ,²¹ which are intended to model the ability of para-substituents to delocalize positive charge by resonance interactions. Clearly the latter scale offers a more limited data set.

With respect to radical stabilization effects, there are a number of possible scales in the literature based either on intrinsic radical properties, often spectroscopic, or on observed reactivities. Here we opt to use the σ_a^{\bullet} scale of Arnold et al.,^{7a} based on observed EPR hyperfine coupling of benzyl radicals, and the σ^{\bullet} scale of Creary et al., based on the observed kinetics of rearrangement of methylenecyclopropane systems.^{7b} The latter scale provides a

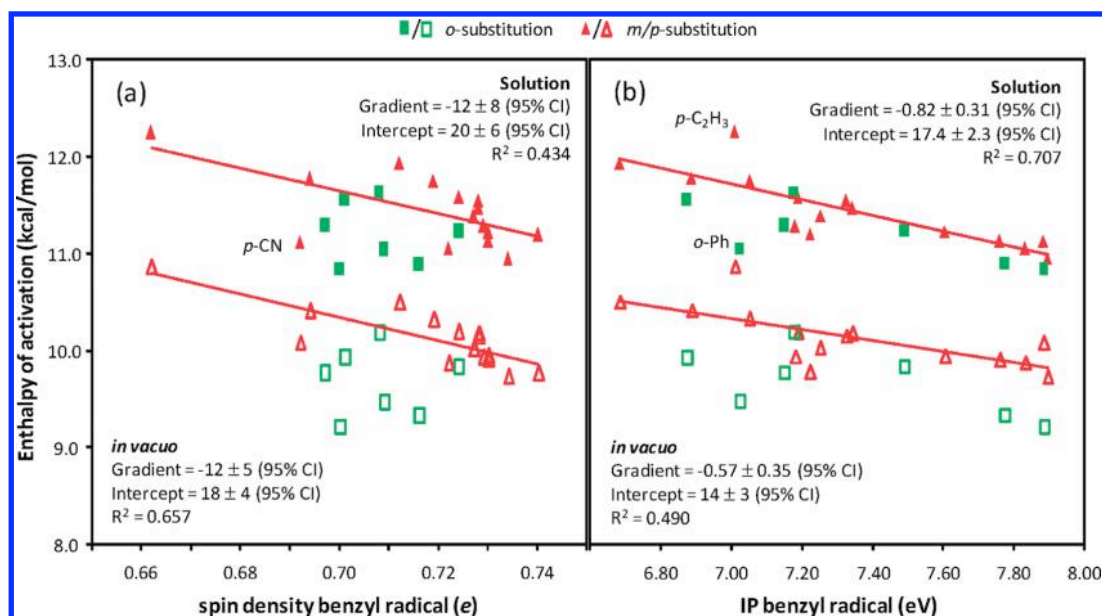


Figure 2. Correlation for enthalpy of activation for addition of benzyl radicals to ethylene in vacuo (open symbols) and in toluene solution (closed symbols) with (a) the calculated benzylic spin density (NPA B3LYP/6-31G*) and (b) vertical ionization energy (G3(MP2)-RAD) of the attacking benzyl radical. Lines of best fit data are for meta/para-substituted species.

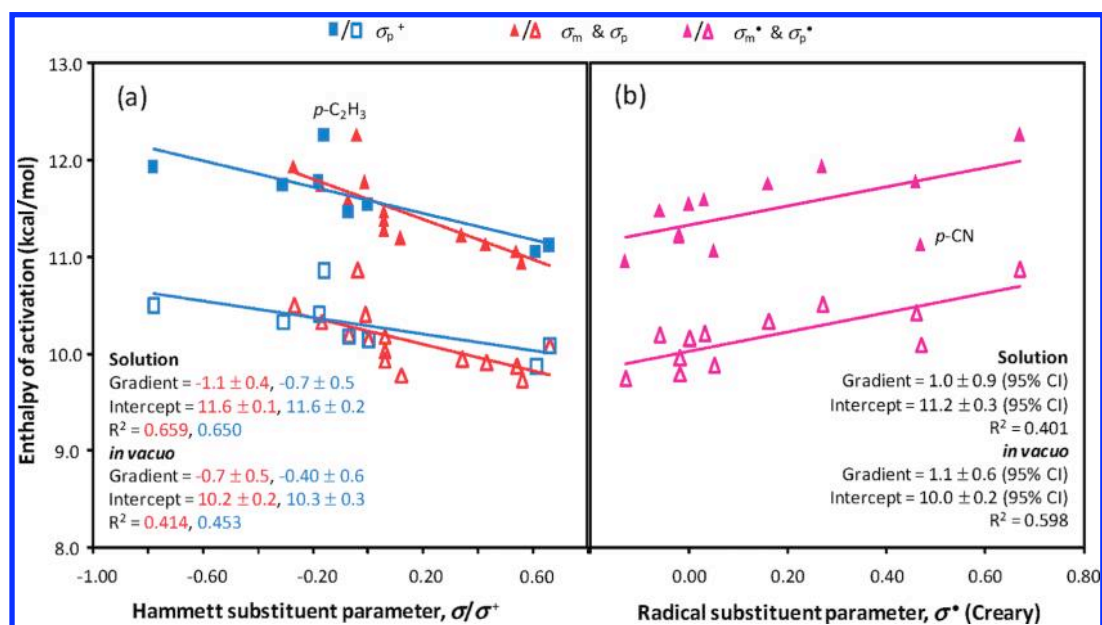


Figure 3. Correlation for enthalpy of activation for addition of benzyl radicals to ethylene in vacuo (open symbols) and in toluene solution (closed symbols) with empirical substituent parameters: (a) Hammett and (b) radical substituent parameters.

slightly larger data set of substituent parameters for this study, and on the basis of previous correlations, one would anticipate a higher degree of correlation of σ^* in the gas phase data.

In general terms, the anticipated behavior is observed, although none of the correlations with empirical substituent parameters are particularly strong (Figure 3). The σ^* scale of Creary provides clearer correlations than the σ_p^+ scale, which is not shown in Figure 3. The Hammett correlations have relatively shallow slopes of the correlation curves yield a reaction constant ρ in the range of $-1 \leq \rho \leq -0.5$, consistent with benzyl radical behaving as a weak nucleophilic species.

The correlations of ΔH^\ddagger and activation energy E_A with empirical substituent parameters are similar, which is consistent with the relationship between the two; that is

$$E_A = \Delta H^\ddagger + RT$$

As we consider the effects of entropy by calculating the free energy of activation at 298 K, we find that the degree of correlation is compromised. However, unlike the previous examples, it is the unsubstituted species that represents outlier data, and the difference is largely entropic in origin: the Arrhenius

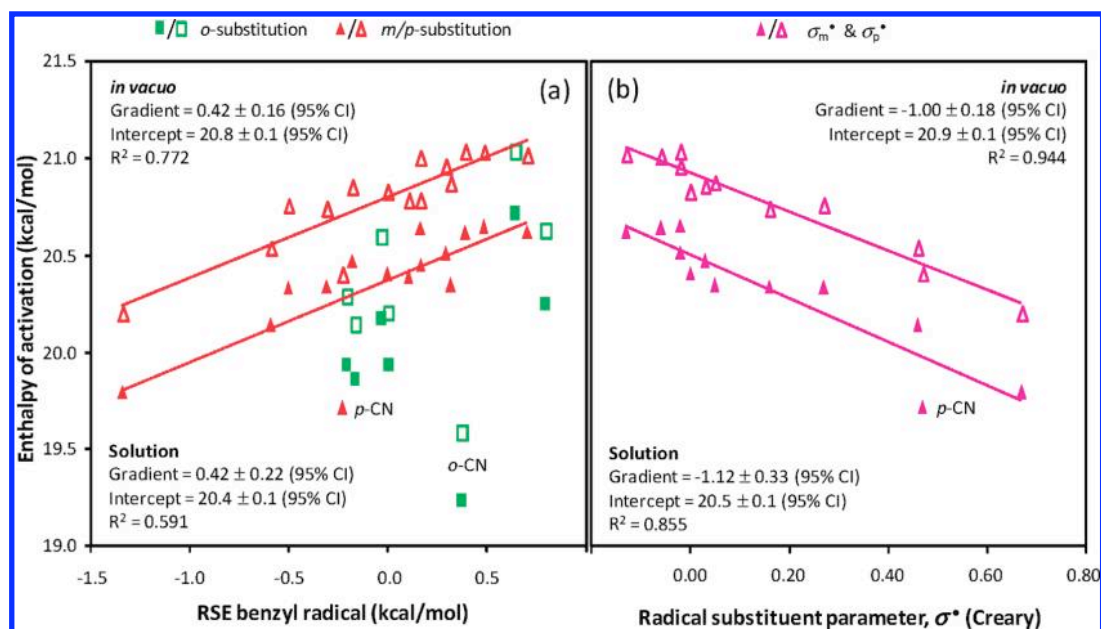


Figure 4. Correlation for enthalpy of activation for β -fragmentation of 3-phenylpropyl radicals in *vacuo* (open symbols) and in toluene solution (closed symbols) with (a) calculated radical stabilization energies of the benzyl radical fragments (G3(MP2)-RAD) and (b) radical substituent parameters σ^* (Creary, ref 7b).

pre-exponential for addition of **3a** to ethylene is $10^{9.2} \text{ M}^{-1} \text{ s}^{-1}$; for the meta- and para-substituted species **6b–h** and **9b–h** it is $10^{(8.5 \pm 0.2)} \text{ M}^{-1} \text{ s}^{-1}$. This is largely a consequence of the additional degenerate reaction pathway available for the C_{2v} benzyl radical addition; for the lower symmetry attacking radicals this additional pathway constitutes a distinct higher-barrier reaction that is not considered in the calculation.

The impact of entropic and solvation effects may go some way to explaining the previously reported⁸ failure of the Hammett equation for the homopropagation rate coefficients in free-radical polymerization; however, the observed polar effects may also play a crucial role. When polar effects are significant, as indicated by the present work, one would expect the reaction constant to vary with the nature of the monomer. In the present work the monomer is held constant but in a homopropagation reaction this is varied simultaneously with the attacking radical, and this would lead to an apparent breakdown in the Hammett correlation.

Fragmentation. The calculated radical stabilization energies for the various 3-phenylpropyl systems in this study are small, as would be expected given the remoteness of the aryl substituents from the radical center, and the intervening alkyl chain: for meta- and para-substituents, calculated RSEs lie within ± 0.1 kcal/mol, with the single exception of the *o*-cyano substituent (0.5 kcal/mol), which may be due to a weak interaction between the coplanar π -bond and benzylic hydrogen. Thus, the only readily available structure–reactivity correlation involves the stability of the fragmentation products (i.e., the benzyl radical). Our attempts to find correlations for meta- and para-substituted species indicate that the activation enthalpy for fragmentation shows a weak dependence on the radical stabilization energy (Figure 4a) and the spin density at the benzylic site of the formed benzyl radical. There is a significant degree of correlation between ΔH^\ddagger and the Creary substituent parameter σ^* , consistent with the fact that the substituent scale is based on fragmentation of a C–C bond at a benzylic position, similar to the reaction being investigated in this study (Figure 4b).

Unlike the addition reaction, there is no apparent correlation between the enthalpy of activation and the charge density or ionization potential (the activation enthalpy appears to be effectively independent of these parameters). As would be expected, the activation barriers for the fragmentation of ortho-substituted systems is significantly influenced by steric effects—by and large the relaxation of steric compression from reactant to transition state leads to lower barriers, and only the sterically undemanding fluoro group shows behavior consistent with that of the meta- and para-substituted systems. As before, of the meta- and para-substituents, only the *p*-cyano group is a significant outlier, and the effect is exacerbated as solvation effects are included. The effect of ortho-substituents is less easily described: there is a weak qualitative correlation with radical stabilization energy, broken by the *o*-cyano group.

The plots in Figure 4 indicate a degree of correlation between the enthalpy of activation for fragmentation and the stabilization of the formed benzyl radical, as would be expected, and the relative magnitudes of the effect (indicated by the gradients of the linear correlations: -0.64 for addition in solution, and 0.42 for fragmentation) are consistent with a system where (a) the forward (in this case addition) reaction is not greatly exothermic and (b) the transition state for the forward reaction is relatively “early”. Radical addition/ β -fragmentation reactions are known to exhibit these qualities. The nucleophilicity of the formed benzyl radical does not play a significant role in determining the magnitude of the reaction barrier, and there is no correlation between the enthalpy of activation for fragmentation and the Hammett substituent parameters σ or σ^+ . Once again, the cyano-substituted species are the main outliers, due mainly to the larger effects of solvation on these polar species.

Cyclization. Correlations for cyclization reactions are difficult to determine under many circumstances, because they are the reactions most susceptible to steric factors. The cyclizations **1** \rightarrow **2** and **4** \rightarrow **6** yield sterically congested 1,2,3-trisubstituted aryl systems, where two (nonseparable) steric interactions must be

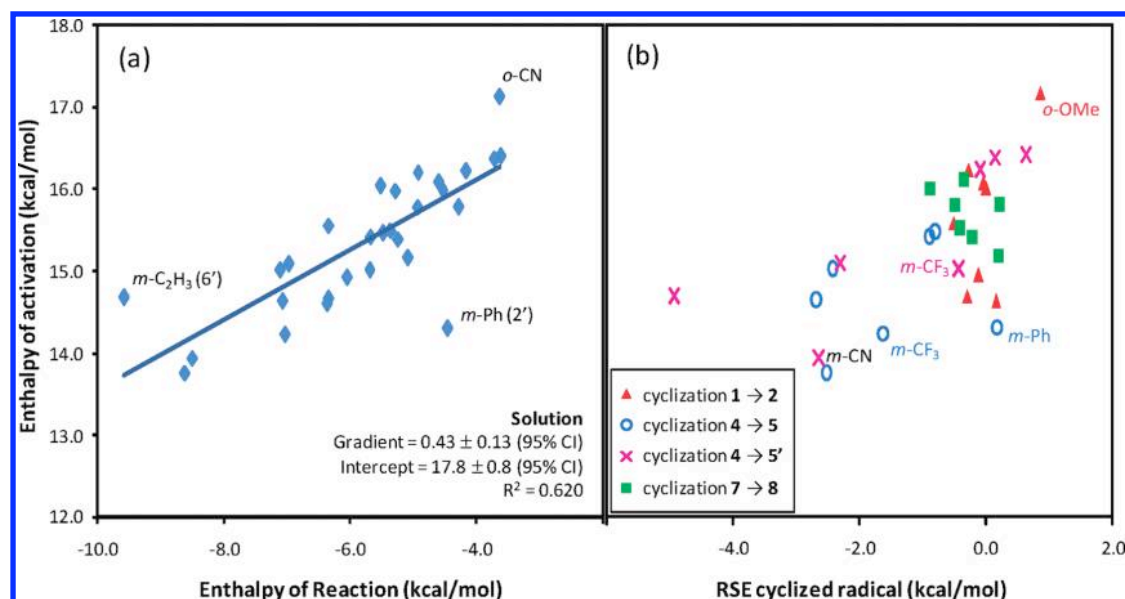
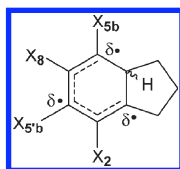


Figure 5. (a) Evans–Polanyi–Semenov correlation for cyclization reactions in toluene solution. (b) Correlation for enthalpy of activation for cyclization reactions in solution with calculated radical stabilization energies for the formed cyclohexadienyl radicals (G3(MP2)-RAD).

considered. In addition, it is not clear whether the calculation of radical stabilization energy for **2** and **6** (where the attacking moiety sits above the plane of the ring), based as it is on the oxidized products (where all groups are approximately coplanar), accurately captures the degree of steric congestion in such systems. The Evans–Polanyi–Semenov correlation for these reactions is reasonable, but the degree of correlation with calculated RSE is poor (Figure 5). Figure 5b suggests that the data for $4 \rightarrow 5/5'$ has some degree of correlation, with large deviations for the electron-withdrawing groups $-\text{CN}$ and CF_3 ; and the large phenyl group in the case of cyclization to the $2'$ position. This may indicate that polar effects are relatively significant in these cyclization reactions as well.

Attempts to determine structure–reactivity correlations with empirical parameters is limited by the fact that the cyclization transition state corresponds to an incipient cyclohexadienyl radical, and it is not clear whether resonance and inductive effects are transmitted through such a system in a way that is analogous to an arene ring. As a first approximation, we may utilize σ_p parameters to describe substituents in a position to interact with formed radical centers by means of both inductive and resonance effects, and σ_m parameters to describe substituents in position to interact with formed radical centers only (in principle) by means of inductive effects. Given the structure of the product radical,



we assign σ_p for the systems **5b** and **5'a**, and σ_m for the systems **2** and **8**. There is no evidence of any significant correlation between the enthalpy of activation and the corresponding radical substituent parameters σ^\bullet for any of the cyclization parameters. However, there is some evidence of correlation with the Hammett substituent parameters (in this particular case, we use only σ_p and

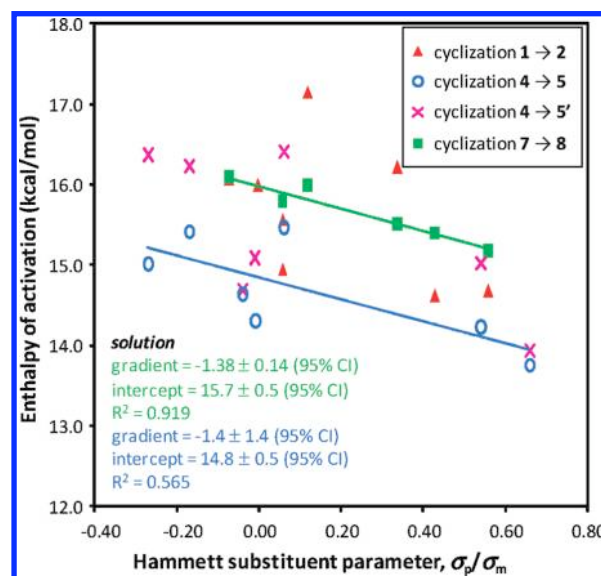


Figure 6. Correlation for enthalpy of activation for cyclization of 3-phenylpropyl radicals in toluene solution with empirical Hammett parameters σ_p/σ_m .

σ_m but not σ_p^\bullet , Figure 6). As expected, the cyclization $1 \rightarrow 2$ exhibits little correlation, which is not unexpected, given the steric demands on the system. Cyclization $7 \rightarrow 8$ is relatively sterically undemanding and is expected to only depend on inductive effects (the correlation with σ_m is relatively strong). Surprisingly, the reaction $4 \rightarrow 5$ shows marginally better correlation than $4 \rightarrow 5'$, despite the fact that the latter is less susceptible to steric congestion. It is not clear why this might be so; the admittedly limited data set for $4 \rightarrow 5'$ indicates that the activation energies for systems with π -bonded resonance stabilizing groups ($-\text{CN}$, $-\text{Ph}$, and $-\text{C}_2\text{H}_3$) are consistently below those for non π -containing groups with similar values of σ_p . This suggests that σ_p may not provide an accurate representation of the π -resonance stabilization of the cyclohexadienyl radical.

Whether the better performance for $4 \rightarrow 5$ derives from fortuitous cancellation of errors cannot be established from the data available.

CONCLUSIONS

A study of remote substituent effects on the rate of benzyl free radical addition to olefins, β -fragmentation, and cyclization of formed 3-phenylpropyl radicals has been carried out on systems where the effect of monomer (olefin) are decoupled from the substituent effects on the benzyl radical. We draw the following conclusions:

- As with other benzyl radical/olefin systems, the addition reaction is dominated by radical stability effects that can be illustrated by strong correlations with computed parameters such as the radical stabilization energy (RSE), or with empirical radical stabilization scales.
- In these particular systems, where a single monomer is used, leading to a narrow range of activation energies, evidence of a dependence on polar effects becomes apparent, and correlations with polar substituent parameters such as the classical Hammett parameters may be observed. These effects are enhanced by solvation.
- As indicated by previous experimental studies, attempts to find Hammett correlations based on rate coefficients rather than derived thermochemical properties such as E_A or ΔH^\ddagger have been unsuccessful. Calculations indicate that entropic considerations play an important role, though for the meta- and para-substituted reactions of the present work this is largely due to differences in reaction path degeneracy. In addition, ortho-substituted systems give poor correlations due to steric congestion effects.
- Fragmentation reactions are similarly dominated by radical stabilization/bond strength terms, and there is no evidence of correlation with parameters describing polar interactions, even in solution.
- Cyclization reactions show a strong dependence on thermochemical factors, and exhibit Evans–Polanyi–Semenov behavior. There is no clear correlation with radical stabilization terms, which is in all likelihood due to steric compression factors that become important with cyclization, particularly those involving 1,2,3-trisubstituted systems. There is, however, evidence to suggest that polar interactions do play a role in these cyclization reactions.

Our conclusions regarding cyclization reactions must be considered with the proviso that we are using parameters that describe the propagation of resonance and inductive effects through an aromatic ring, but that the system under consideration, though delocalized, is by no means aromatic. The correlations observed with σ_p and σ_m should be considered indicative, rather than quantitative. Given the experimental difficulty in isolating cyclohexadienyl systems, it seems likely that the best description for propagation of resonance/inductive effects in cyclohexadienyl systems will arise from direct computational study.

ASSOCIATED CONTENT

S Supporting Information. Computational output in the form of optimized geometries, energies, and vibrational/ZPE corrections for species relevant to this study. This information is available free of charge via the Internet at <http://pubs.acs.org>.

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