Ab Initio Molecular Orbital Calculations of Electronic Effects on the Kinetics of Cyclopropylcarbinyl Radical Ring Openings

Felix N. Martinez, H. Bernhard Schlegel,* and Martin Newcomb*

Department of Chemistry, Wayne State University, Detroit, Michigan 48202

Received December 15, 1997

Ab initio molecular orbital calculations have been performed on the ring-opening reactions of cyclopropylcarbinyl radical analogues containing vinyl and methoxy substituents on the ring and for vinyl, methoxy, and methyl substituents on the radical center. Barrier heights were calculated at the UHF/6-31G*, UMP2/6-31G*//UHF/6-31G*, and PMP2/6-31G*//UHF/6-31G* levels of theory. Substituent effects were analyzed using isodesmic reactions. Vinyl substituents on the ring reduce the barrier by 7−8 kcal/mol because of allylic conjugation stabilizing the transition state. Methoxy substituents on the ring reduce the barrier by ca. 2 kcal/mol, primarily as a result of hyperconjugation. Vinyl and methoxy substituents on the radical center raised the barrier 4.5 and 0.8 kcal/mol, respectively, because the stabilizing effects on the reactants are greater than the effects on the transition states. A methyl substituent decreased the barrier slightly in contrast to intuitive expectations. The computational results were compared to experimental thermochemical and kinetic data when available, and the agreements were good in an absolute sense and excellent in a relative sense. This work demonstrates that predictions of reactivity patterns and relative kinetics for radical reactions that do not involve polarized transition states can be computed without the use of supercomputers.

Reactions of radicals have attracted increased interest from organic chemists in recent years as radical-based synthetic methods have become more refined.[1] Because most radicals are destroyed in diffusion-controlled self-termination or cross-termination reactions and because most useful synthetic applications of radicals involve chain processes with several competing pathways available, knowledge of the kinetics of radical reactions is critical for experimental design. The requisite kinetic information usually has been derived from experimental results obtained in condensed phase. However, solvent effects have been shown to be small or nonexistent for cyclizations and ring openings of carbon-centered radicals when electron-withdrawing groups such as carbonyls are not conjugated to the radical centers of the reactant or product.[2,3] This raises the interesting possibility that radical kinetics could be determined computationally for gas phase reactions in many cases, a fact that should be of interest to synthetic chemists because relatively sophisticated computational methods are already available to research groups via powerful but inexpensive personal computers (PCs).

In a previous paper, we sought to determine what levels of ab initio theory were adequate for estimation of the activation barriers for ring opening of a series of methyl- and polymethyl-substituted cyclopropylcarbinyl radicals.[4] High-level G2 theory gives absolute results that are quite close to experimental values (calculated barrier of 7.9 kcal/mol vs 7.3 kcal/mol experimental, calculated heat of reaction of −3.5 vs −5.4 kcal/mol experimental),[5] but more importantly for organic chemists, even modest levels of theory were adequate for predicting relative rate constants and for determining the origins of the kinetic effects of methyl group substitution which derived primarily from steric interactions in the ground and transition states. In the present work, we have extended our computational studies to evaluate the effects of two substituents, a vinyl group and a methoxy group, that will have strong electronic interactions with a radical center. Comparison of the computational results obtained at a level of theory that can be achieved on a currently available PC with experimental thermochemical and kinetic data shows good absolute and excellent relative agreement.

Computational Methods

Ab initio molecular orbital calculations were performed using the Gaussian 94 series of programs.[6] Reactants and transition structures were optimized at the unrestricted Hartree−Fock (UHF)[7] level of theory using the 6-31G*[8] basis set.

(1) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon−Carbon Bonds*; Pergamon Press: Oxford, 1986. Curran, D. P. *Synthesis* **1988**, 417, 489. Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541.

(2) Maeda, Y.; Schmid, P.; Griller, D.; Ingold, K. U. *J. Chem. Soc., Chem. Commun.* **1978**, 525. Beckwith, A. L. J.; Bowry, V. W.; Ingold, K. U. *J. Am. Chem. Soc.* **1992**, *114*, 4983. Johnson, C. C.; Horner, J. H.; Tronche, C.; Newcomb, M. *J. Am. Chem. Soc.* **1995**, *117*, 1684. Tronche, C.; Martinez, F. N.; Horner, J. H.; Newcomb, M.; Senn, M.; Giese, B. *Tetrahedron Lett.* **1996**, *37*, 5845.

(3) Newcomb, M.; Horner, J. H.; Emanuel, C. J. *J. Am. Chem. Soc.* **1997**, *119*, 7147.

(4) Martinez, F. N.; Schlegel, H. B.; Newcomb, M. *J. Org. Chem.* **1996**, *61*, 8547.

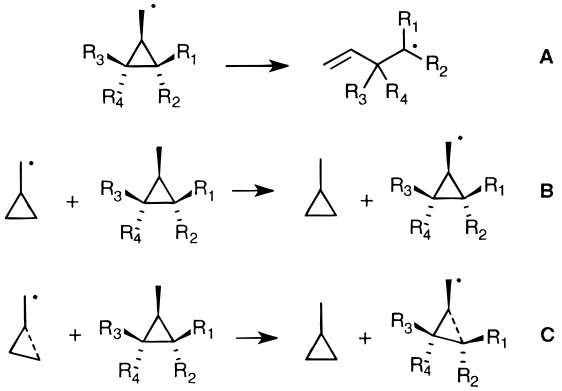
(5) Due to a clerical error, incorrect energies for the cyclopropylcarbinyl radical ring opening calculated at the G2 level were listed in ref 4. The correct values are −3.48 kcal/mol for the heat of reaction and 7.89 kcal/mol for the barrier. These values give Arrhenius parameters of log $A = 12.99$ for a reaction path degeneracy of 2 and $E_a = 8.17$ kcal/mol.

(6) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; and Pople, J. A. *GAUSSIAN 94*; Gaussian, Inc.: Pittsburgh, PA, 1995.

(7) Pople, J. A.; Nesbet, R. K. *J. Chem. Phys.* **1954**, *22*, 571.

S0022-3263(97)02272-X CCC: $15.00 © 1998 American Chemical Society
Published on Web 05/13/1998

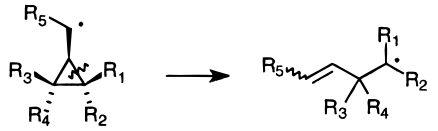
Scheme 1



Vibrational frequencies were calculated at the UHF/6-31G* level of theory to characterize the minima and transition states and to compute zero-point energies (ZPE). Barriers heights were calculated by second-order Møller−Plesset perturbation theory (UMP2/6-31G*) with spin projection (PMP2/6-31G*).[9]

Results and Discussion

We have computed the heats of reactions and barriers for ring opening of cyclopropylcarbinyl radicals with a vinyl and methoxy substituent at each possible position, that is each of the positions labeled with R_i below. The effects of methyl group substituents on the cyclopropane ring (R_1−R_4 = CH_3) were previously reported,[4] and the effect of a methyl substituent at the radical center (R_5 = CH_3) was determined in this work.



Most of the computations were performed at the UHF/6-31G*, MP2/6-31G*//UHF/6-31G*, and PMP2/6-31G*//UHF/6-31G* levels of theory. The UHF and single-point PMP2 calculations showed quite similar trends, but the single-point MP2 calculations appeared to be less reliable, apparently due to spin contamination.[9] Unless specifically stated otherwise, all of the computational results discussed herein are for the PMP2/6-31G*//UHF/6-31G* level.

We first consider the effects of the substituent on the ring of a cyclopropylcarbinyl radical. The calculated barriers for opening of the ring-substituted cyclopropylcarbinyl radicals (reaction A in Scheme 1) are collected in Table 1, and the calculated heats of the reactions for the vinyl and methoxy substituents are in Table 2. To understand the details of the reaction barriers, the energies of the isodesmic reactions for the ground states (reaction B in Scheme 1) and the transition states (reaction C in Scheme 1) were computed at the UHF/6-31G* level, and the results are collected in Table 3. In these tables, reaction 1 is the ring opening of the unsubstituted cyclopropylcarbinyl radical, reactions 2−5 are ring openings of vinyl-substituted radicals, reactions 6−9 are ring openings of methoxy-substituted radicals,

Table 1. Calculated Barriers for the Ring Opening of Cyclopropylcarbinyl Radicals with Substituents on the Ring[a]

reactn	R_1	R_2	R_3	R_4	HF/ 6-31G*	MP2/ 6-31G* [b]	PMP2/ 6-31G* [b]
1	H	H	H	H	10.57	15.43	8.31
2	Vi	H	H	H	3.30	12.39	1.20
3	H	Vi	H	H	3.05	10.96	0.52
4	H	H	Vi	H	11.31	15.54	8.70
5	H	H	H	Vi	11.98	15.72	10.00
6	OMe	H	H	H	9.80	13.35	6.53
7	H	OMe	H	H	9.77	12.96	6.20
8	H	H	OMe	H	9.02	14.07	7.01
9	H	H	H	OMe	8.81	13.76	6.84
10[c]	Me	H	H	H	9.47	13.84	6.91
11[c]	H	Me	H	H	10.40	15.08	7.97
12[c]	H	H	Me	H	9.95	14.53	7.45
13[c]	H	H	H	Me	9.86	14.62	7.51

[a] In kcal/mol with ZPE calculated at UHF/6-31G*; see Scheme 1 for placement of substituents. [b] Using the geometry optimized at the UHF/6-31G* level. [c] From ref 4.

Table 2. Calculated Heats of Reaction of the Ring Opening of Cyclopropylcarbinyl Radical with Substituents on the Ring[a]

reactn	R_1	R_2	R_3	R_4	UHF	MP2[b]	PMP2[b]
1[c]	H	H	H	H	−5.21	−8.74	−4.00
2	Vi	H	H	H	−23.79	−9.74	−17.02
3	H	Vi	H	H	−22.26	−9.51	−15.61
4	H	H	Vi	H	−3.08	1.79	1.81
5	H	H	H	Vi	−1.54	2.01	3.23
6	OMe	H	H	H	−8.56	−4.41	−4.12
7	H	OMe	H	H	−8.01	−4.83	−4.59
8	H	H	OMe	H	−5.07	0.86	0.27
9	H	H	H	OMe	−4.52	0.44	−0.20

[a] In kcal/mol with ZPE calculated at UHF/6-31G*; see Scheme 1 for placement of substituents. [b] Using the geometry optimized at the UHF/6-31G* level. [c] From ref 4.

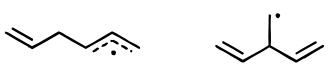
Table 3. Isodesmic Reactions for the Effects of Substituents on the Ring[a]

reactn	R_1	R_2	R_3	R_4	reactant	transition state
2	Vi	H	H	H	−0.43	−7.15
3	H	Vi	H	H	−0.31	−7.54
4	H	H	Vi	H	−0.43	0.50
5	H	H	H	Vi	−0.31	1.27
6	OMe	H	H	H	−0.67	−1.37
7	H	OMe	H	H	−0.33	−1.23
8	H	H	OMe	H	−0.67	−1.91
9	H	H	H	OMe	−0.33	−1.84
10	Me	H	H	H	−0.61	−1.61
11	H	Me	H	H	−0.18	−0.32
12	H	H	Me	H	−0.61	−0.97
13	H	H	H	Me	−0.18	−0.62

[a] In kcal/mol at the UHF/6-31G* level without ZPE; see Scheme 1 for the isodesmic reactions.

and reactions 10−13 are ring openings of methyl-substituted radicals.

Vinyl Substitution on the Ring. The *cis* and *trans* isomers of vinyl-substituted cyclopropylcarbinyl radicals can ring open to the give the allylic radical **1** (reactions 2 and 3) or the primary radical **2** (reactions 4 and 5). The



stabilities of the product radicals can be estimated from experimental bond dissociation energies of the respective hydrocarbon precursors (Figure 1). Radical **1** should be

(8) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.
(9) Schlegel, H. B. *J. Chem. Phys.* **1986**, *84*, 4530. Chen, W.; Schlegel, H. B. *J. Chem. Phys.* **1994**, 101, 5957.

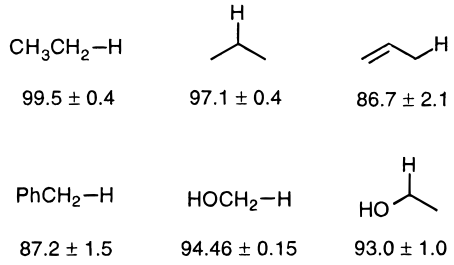
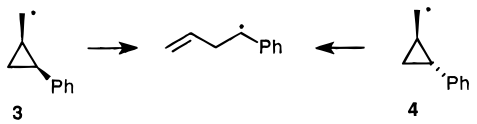


Figure 1. Experimental CH bond dissociation energies in kcal/mol from ref 12.

about 15 kcal/mol more stable than radical **2** on the basis of 12 kcal/mol stabilization of the allylic radical relative to the ethyl radical and an additional 3 kcal/mol stabilization for a secondary radical. Computationally, radical **1** is found to be 18 kcal/mol more stable than radical **2**, an energy difference in reasonable agreement with experiment considering the level of theory. The heats of the ring-opening reactions listed in Table 2 are also in reasonable agreement with experiment although it appears that the computed total energy for the vinyl-substituted cyclopropylcarbinyl radicals are slightly low. For example, ring opening of the unsubstituted cyclopropylcarbinyl radical is exothermic by about 5 kcal/mol[10] and the calculated value for reaction 1 is quite similar, but the ring-opening reaction 3 would be estimated to be exothermic by about 20 kcal/mol instead of the 15 kcal/mol found computationally. The computational error can be attributed to difficulties in handling the allyl radical and related species at this level of theory because of artifactual symmetry breaking problems.[11]

The barriers for ring opening also are in reasonable agreement with experimental results.[12] The unsubstituted cyclopropylcarbinyl radical ring opens with an activation energy of 7.0 kcal/mol.[13] On the basis of the similar stabilization energies of a vinyl group and a phenyl group (Figure 1), the ring-opening reactions of the phenyl-substituted cyclopropylcarbinyl radicals **3** and **4** should be good models for comparisons to the vinyl-substituted radicals. Radicals **3** and **4** ring open more than 3 orders of magnitude faster than the parent cyclopropylcarbinyl radical, and the only observed product is 4-phenyl-1-butene from trapping of the benzylic radical product shown. The experimentally determined activation energy for ring opening of the cis-substituted radical **3** is 3.1 kcal/mol, and that for the trans-substituted radical **4** is 3.3 kcal/mol.[14]



The isodesmic reactions (**B** and **C** in Scheme 1) provide a more detailed understanding of the barrier heights. In isodesmic reactions, where reactants and products have

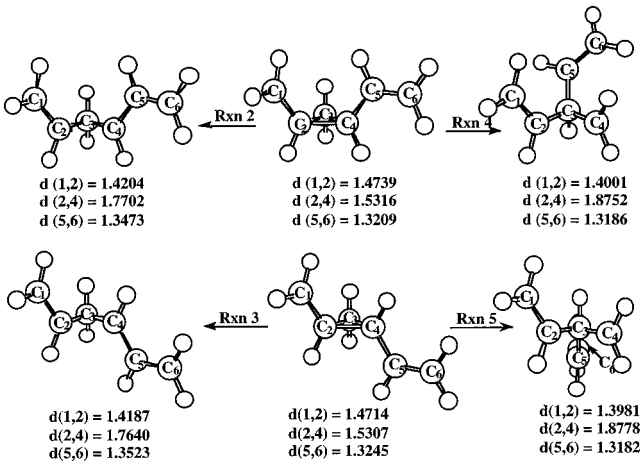


Figure 2. Selected bond distances (in Å) for the reactant and transition structures of reactions 2−4 optimized at the UHF/6-31G* level of theory.

the same number of each type of bond, errors in the computational results cancel, and the energy differences are more reliable. As shown in Table 3, the addition of a vinyl substituent does not produce a significant stabilization of the ground states (i.e. < 0.5 kcal/mol) and the small stabilization is independent of the substituent position. However, vinyl substitution in the transition states giving the allyl radical products results in 7.2 and 7.5 kcal/mol stabilization for reactions 2 and 3, respectively, primarily due to conjugation. The transition states for reactions 4 and 5 are destabilized by a small amount.

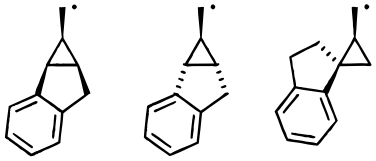
The exothermicity of the reaction should affect the geometry of the transition state. Figure 2 shows the key parameters for reactions 2−5. Both of the transition states leading to the more stable allylic radical product **1** (reactions 2 and 3) have C−C bond lengths for the breaking bonds that are about 0.11 Å shorter than those for the transition states leading to the less stable primary radical product **2**. Thus as expected from Hammond's postulate, the transition states for reactions 2 and 3 are earlier along the reaction path than those for reactions 4 and 5 as a consequence of the allylic conjugation stabilization.

One of the major attractions of the computational approach is that it can provide energies that are quite difficult, if not impossible, to measure experimentally. We investigated the conjugation effects of the vinyl groups by rotating them ±90° from their minimum energy positions in the reactants and transition structures and re-optimizing the remaining coordinates. The energies of the reactants changed by only ca. 0.7 kcal/mol, but the barriers for reactions 2 and 3 increased by an average of 4.0 kcal/mol. For reactions 4 and 5 where allylic conjugation is not an issue, the reaction barriers increased by 0.4 and 1.7 kcal/mol apparently as a result of steric effects. A net increase in the barrier heights for reactions 2 and 3 of about 3 kcal/mol represents the effect of elimination of conjugation, and the remaining differences in the barrier heights for reactions 2 and 3 in comparison to reaction 1 reflect an inductive effect of the vinyl substituent.

The above analysis has an important ramification for practical applications of aryl-substituted cyclopropylcarbinyl radical ring openings. These reactions have

(10) Newcomb, M. *Tetrahedron* **1993**, *49*, 1151.
(11) Palduo, J.; Veillard, A. *Mol. Phys.* **1978**, *35*, 445. Ayala, P. Y.; Schlegel, H. B., submitted for publication.
(12) Berkowitz, J.; Ellison, G. B.; Gutman, D. *J. Phys. Chem.* **1994**, *98*, 2744.
(13) Newcomb, M.; Glenn, A. G. *J. Am. Chem. Soc.* **1989**, *111*, 275.
(14) Newcomb, M.; Johnson, C. C.; Manek, M. B.; Varick, T. R. *J. Am. Chem. Soc.* **1992**, *114*, 10915.

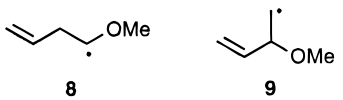
been employed in "hypersensitive" radical probes in mechanistic studies of enzyme-catalyzed oxidation reactions.[15] One can question the possible effect an enzyme could exert on the kinetics of the radical ring-opening reactions by sterically constraining the aryl group from optimal overlap with the forming radical center and thus reducing conjugation. The results with the vinyl substituent suggest that even complete elimination of the conjugation should not reduce the rate constant for radical ring opening by more than a factor of 100. This prediction was essentially verified experimentally; the rate constants for ring openings of structurally constrained, aryl-substituted cyclopropylcarbinyl radicals **5**−**7** were effectively unchanged from those for the unconstrained analogues **3** and **4**.[16]



5 **6** **7**

Methoxy Substitution on the Ring. The methoxy substituent resulted in an average decrease in barrier height of about 1.6 kcal/mol for reactions 6−9 in comparison to that for the unsubstituted case, reaction 1. Although the barriers for the methoxy-substituted radicals are lower than those for the methyl-substituted radicals (reactions 10−13), they are less sensitive to the position of the substituent. This results because the major influences of methyl substitution were steric in origin,[4] and those for the (smaller) methoxy group are electronic.

Intuitively, one would expect that the reactions 6 and 7 would have lower barrier heights than reactions 8 and 9 because the former produce the α-methoxy secondary radical **8** which will be more stable than the *β*-methoxy primary radical **9** produced in the latter reactions. Computationally, radical **8** is 4.4 kcal/mol more stable than radical **9** at the PMP2/6-31G*//UHF/6-31G* level in good agreement with experimental results in Figure 1. The anticipated reduction in the barrier for ring opening of cyclopropylcarbinyl radicals due to transition state energetic effects is supported by the calculations, but the differences in the barrier heights for reactions 6 and 7 in comparison to those for reactions 8 and 9 are small.



8 **9**

For the series of isodesmic reactions (Table 3), the ground state stabilization of the methoxy substituent in the *cis* position is 0.7 kcal/mol and that in the *trans* position is 0.3 kcal/mol, and similar ground state stabilizations were found for methyl group substitution. In

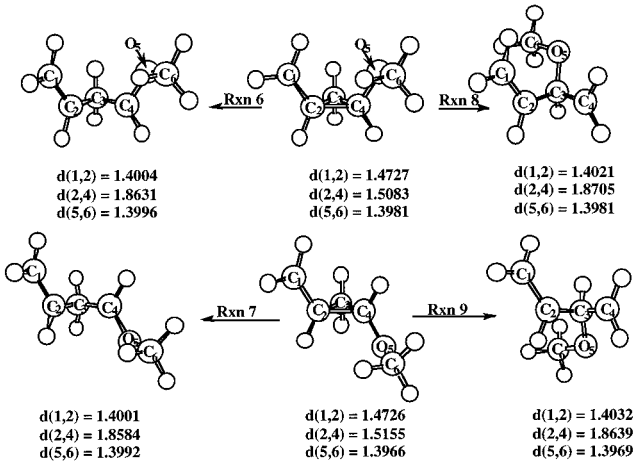


Figure 3. Selected bond distances (in Å) for the reactant and transition structures of reactions 6−8 optimized at the UHF/6-31G* level of theory.

the transition states, however, the average stabilization of a methoxy group was 1.6 kcal/mol, whereas that for a methyl group was 0.9 kcal/mol. These results suggest a small conjugation effect of the methoxy group in the transition states. However, when the methoxy groups were rotated ±90° from their minimum energy positions in the transition states and the remaining coordinates were re-optimized, the energies of the transition states for reactions 6 and 7 increased by 2.9 and 2.4 kcal/mol, respectively, whereas those for reactions 8 and 9 increased by significantly less (ca. 0.6 kcal/mol). The hyperconjugation stabilization in the transition states for reactions 6 and 7 apparently reduces the barrier heights by about 2 kcal/mol. The transition structures for reactions 6−9 are shown in Figure 3. Since reactions 6 and 7 are 4−5 kcal/mol more exothermic, the C−C bond lengths for the breaking bonds are slightly shorter, but the effect is much smaller than that found for the vinyl substituent.

The computational results are again in excellent agreement with limited experimental results on related systems. The kinetics of ring openings of alkoxy-substituted cyclopropylcarbinyl radicals have not been studied extensively, but the rate constants for ring openings of radicals **10** and **11** have been reported.[17] As in the case of other aryl-substituted cyclopropylcarbinyl radicals, radicals **10** and **11** fragment very rapidly giving mainly benzylic radical products. However, unlike the case with radicals **3** and **4**, fragmentation to give the less stable products, the alkoxy-substituted radicals, is observed for both **10** and **11**. That is, the ring openings of **10** and **11** to give the less stable products are appreciably faster than ring openings of unsubstituted cyclopropylcarbinyl radicals. Specifically, at ambient temperature, ring opening of **10** to give the α-methoxy radical was 100 times faster than ring opening of the unsubstituted parent when corrected for the statistical effect in the parent radical, and ring opening of **11** to give the α-*tert*-butoxy radical was even faster. The steric effects in the transition states for fragmentations of radicals **10** and **11** obviously will be different than those in reactions 6 and 7, but nevertheless, the net transition state stabilization effects of the alkoxy groups in **10** and **11** of 2.5−3

(15) See, for example: Liu, K. E.; Johnson, C. C.; Newcomb, M.; Lippard, S. J. *J. Am. Chem. Soc.* **1993**, *115*, 939. Newcomb, M.; Le Tadic-Biadatti, M.-H.; Chestney, D. L.; Roberts, E. S.; Hollenberg, P. F. *J. Am. Chem. Soc.* **1995**, *117*, 12085.

(16) Martin-Esker, A. A.; Johnson, C. C.; Horner, J. H.; Newcomb, M. *J. Am. Chem. Soc.* **1994**, *116*, 9174.

(17) Le Tadic-Biadatti, M.-H.; Newcomb, M. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1467.

Scheme 2

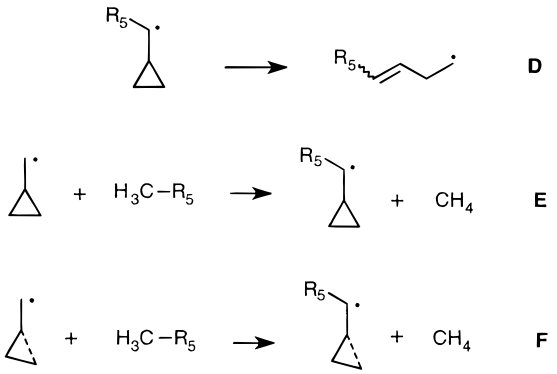


Table 4. Calculated Barriers for the Ring Opening of Cyclopropylcarbinyl Radicals with Substituents at the Radical Center[a]

reactn	R_5	UHF	MP2[b]	PMP2[b]
1	H	10.57	15.43	8.31
14	Vi	14.41	22.43	12.81
15	OMe	11.61	17.07	9.14
16	Me	10.16	14.77	7.47

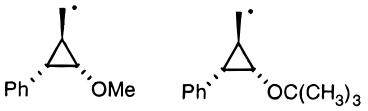
[a] In kcal/mol with ZPE calculated at UHF/6-31G*; see Scheme 2. [b] Using the geometry optimized at the UHF/6-31G* level.

Table 5. Isodesmic Reactions for the Effects of Substituents at the Radical Center[a]

R_5	ground state	transition state
Vi	−21.26	−17.42
OMe	−7.22	−6.15
Me	−3.34	−3.74

[a] In kcal/mol with ZPE at UHF/6-31G*; see Scheme 2.

kcal/mol agrees with the computational results.



10 **11**

Substituents at the Radical Center. To study the effects of the vinyl, methoxy, and methyl substituents at the radical center, we computed the barriers for the ring-opening reactions D and the energies of the isodesmic reactions E and F (Scheme 2). The results are given in Tables 4 and 5. As was the case for substituents on the ring, the barriers computed at the MP2/6-31G*//UHF/6-31G* level were higher than those at the UHF/G-31G* and PMP2/6-31G*//UHF/6-31G* levels due to problems with spin contamination. Nevertheless, the trends were the same at all levels of theory.

Vinyl substitution at the radical center raises the barrier for ring opening (reaction 14) by 4.5 kcal/mol compared to that of the unsubstituted cyclopropylcarbinyl radical ring opening (reaction 1). The bond broken in the transition state is 0.06 Å longer than that in the unsubstituted case (Figure 4). From the bond dissociation energies in Figure 1, the vinyl group should stabilize the ground state by ca. 12 kcal/mol, and a portion of this stabilization is lost in the transition state for ring opening. The results of the isodesmic reaction calculations (Table 5) indicate that the vinyl-substituted ground state is stabilized by 21.3 kcal/mol whereas the transition state is stabilized by 17.4 kcal/mol, resulting in the net increase in the reaction barrier. When the vinyl conjugation effect was "turned off" by rotating the group ±90° from the optimal position and re-optimizing the remaining structure at the HF/3-21G level, the ground state energy increased by 18.0 kcal/mol, and the transition state energy increased by 13.2 kcal/mol; the difference compares well with that found for the barrier heights calculated at the PMP2/6-31G* level.

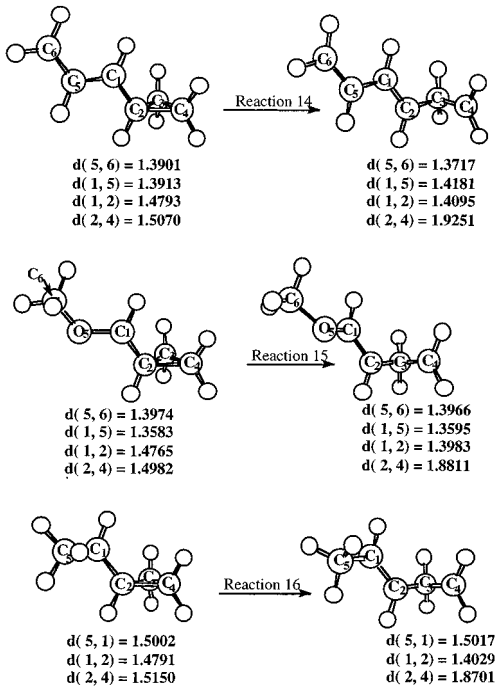


Figure 4. Selected bond distances (in Å) for the reactant and transition structures of reactions 14−16 optimized at the UHF/6-31G* level of theory.

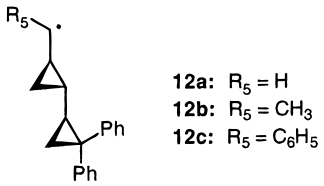
Methoxy substitution at the radical center (reaction 15) resulted in an increase in the barrier height of 0.8 kcal/mol. One might have expected a larger increase in the barrier height because the hydroxy group in the hydroxymethyl radical leads to 4−5 kcal/mol stabilization as judged from bond dissociation energies (Figure 1), but the calculations of the isodesmic reactions indicate that the ground state is stabilized by only 1 kcal/mol more than the transition state. Rotation of the methoxy group by ±90° had little effect on the energies, indicating that the methoxy stabilization is primarily inductive.

Computations of the kinetic effect of methyl group substitution at the radical center (reaction 16) give a counterintuitive result in that the substituted radical has a slightly lower barrier for ring opening than that of the unsubstituted parent (reaction 1). The results from the isodesmic reactions confirm that this effect arises because the transition state is slightly more stabilized by methyl substitution than the ground state.

As was the case for the ring-substituted radicals, some experimental kinetic data for methyl- and phenyl-substituted cyclopropylcarbinyl radicals is available that can be compared with the computational results for the methyl and vinyl substituents. One group of cyclopropylcarbinyl radicals that are especially useful for comparison of the kinetic effects of substituents at the radical position are radicals **12** that contain a UV-detectable "reporter group".[3,18] After the initial fragmentation of

(18) Horner, J. H.; Tanaka, N.; Newcomb. Unpublished results.

these radicals, a second and much faster ring cleavage occurs, leading to a diphenylalkyl radical that can be monitored by its UV absorbance, and precise kinetics of ring openings of radicals **12** have been measured by laser flash photolysis methods. At 20 °C, the parent radical **12a** rearranges with a rate constant of 4.0×10^8 s^{-1}, the methyl-substituted radical **12b** rearranges with a rate constant of 1.5×10^8 s^{-1}, and the phenyl-substituted radical **12c** rearranges with a rate constant of 5.4×10^5 s^{-1}.[3,18]



12a: $R_5 = H$
12b: $R_5 = CH_3$
12c: $R_5 = C_6H_5$

The activation energies for ring opening of **12a** and **12b** differ by only 0.3 kcal/mol, with that for **12a** slightly smaller. Most of the difference in rate constants for fragmentation of these two radicals derives from a difference in the entropies of activation and not from one in the reaction barriers. Specifically, the log *A* term in the Arrhenius function for radical **12a** is 0.3 (or log 2) greater than that for radical **12b**.[3,18] In the transition state for ring opening of cyclopropylcarbinyl at the QCISD level of theory, one of the hydrogen atoms at the radical center eclipses a ring carbon atom.[4] Therefore, radical **12a** has two equal energy reactive conformations, but one of the reactive conformations in radical **12b** is unfavorable due to an eclipsing interaction of the methyl group with the cyclopropyl ring that amounts to about 0.7 kcal/mol at the B3LYP/6-31G level.[18] Thus, in excellent agreement with the computational results of this work, the difference in the barriers for ring opening of **12a** and **12b** determined experimentally is only 1 kcal/mol greater than the computed value. A similar conclusion is reached from comparison of kinetics of fragmentation of the cyclopropylcarbinyl radical with that of the methylcyclopropylcarbinyl radical; the methyl-substituted radical reacts 0.5 times as fast as the parent, suggesting nearly equal inherent energy barriers and a slightly increased barrier for one reactive conformation of the methyl-substituted case.[13,19]

The phenyl-substituted radical **12c** will also have one reactive conformation, and the ring opening of **12a** at 20 °C is about 400 times faster than ring opening of **12c** when one applies the statistical correction. Thus, the experimental barrier for **12c** is 3.5 kcal/mol greater than that for **12a**. The computational results were that the barrier for ring opening of vinylcyclopropylcarbinyl radical is 4.5 kcal/mol greater than that for the parent. Again one sees excellent agreement between theory and experiment.

Conclusion

In this work and our earlier study,[4] we have evaluated the nature of electronic effects on the ring openings of cyclopropylcarbinyl radicals containing substituents on the ring and at the radical center. The computational approach is possible for these reactions because the solvation energies of radicals are similar to those of hydrocarbons and the transition states for the reactions studied here are not polarized. The results provide a quantitative evaluation of the origins of effects that would be predicted qualitatively without theory, the major conjugative interactions for substituents on the ring are in the transition states and the major effects for substituents at the radical center are in the ground states. The results of methyl substitution are perhaps counterintuitive in that methyl groups substituted on the ring have slight electronic effects and influence kinetics more by steric compression effects,[4] and methyl substitution at the radical center has little effect on the barrier for ring opening for one reactive conformation in the parent while raising the barrier for the other conformation.

An overriding theme in the computational work has been to evaluate what level of theory is adequate for useful kinetic predictions of radical reactions. In this work, we employed methods that are available to any scientist with access to a contemporary PC. Very good agreement between experiment and theory at the PMP2/6-31G* level was found, but it is important to note that accurate relative predictions of reactivity patterns were provided even at the UHF/6-31G* level. We evaluated rather simple systems, substituted cyclopropylcarbinyl radicals, but the rapidly increasing computational capabilities available at affordable prices suggest that larger systems soon can be addressed at high levels of accuracy without supercomputers.

Acknowledgment. We thank the National Science Foundation for support of this work (CHE-9400678 to H.B.S. and CHE-9614968 to M.N.).

JO972272Z

(19) Bowry, V. W.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1991**, *113*, 5687.