Ab Initio Molecular Orbital Calculations of Ring Opening of Cyclopropylcarbinyl Radicals

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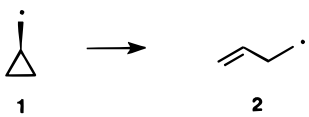
Ab initio molecular orbital calculations have been performed on the ring-opening reactions of the cyclopropylcarbinyl radical and analogs containing methyl substitution on the ring. The barrier height and heat of reaction for the cyclopropylcarbinyl radical ring opening calculated at the G2 level of theory are in good agreement with experiment. Barrier heights for the ring opening of substituted cyclopropylcarbinyl radicals and relative rate constants were computed at HF, UMP2, and PMP2 levels of theory using the 6-31G* basis set. The calculated relative rates are in good agreement with the experimental data available, and the trends in the kinetics can be explained primarily by steric interactions.

Introduction

Interest in organic radical reactions for synthesis has rapidly increased over the past several years due to the development of new synthetic methods and an increased understanding of radical kinetics. The kinetic information is critically important because most radical-based synthetic applications involve chain reactions in which undesired side reactions compete with desired conversions. Almost without exception, kinetic data for radical reactions derive from experimental results in the solution phase, which is often obtained with a great deal of effort. For the commonly employed cyclizations and ring openings of carbon-centered radical educts to carbon-centered radical products, however, only slight solvent effects (if any) are expected,[1,2] and it has been shown that heats of solvation of carbon-centered radicals and their hydrocarbon precursors are the same.[3] Therefore, in principle, gas-phase kinetic data and computationally derived activation energies can be employed to predict the kinetic behaviors of these radical reactions in solution. The primary question concerning the use of computational information for predicting radical kinetics involves the level of theory adequate for the estimation of useful relative activation energies. Is such an approach within the computational reach of most synthetic chemists?

In this paper, we describe detailed calculations of the transition states for the ring opening of the cyclopropylcarbinyl radical **1** and several methyl-substituted analogs. The results indicate that the activation energies and relative rate constants can be estimated with good accuracy at higher levels of theory, but, more importantly for organic chemists, even simple calculations at moderate levels of theory give useful relative rate constants.



1 **2** **(1)**

The cyclopropylcarbinyl radical ring opening is a linchpin reaction in a kinetic scale for carbon radical reactions that spans 8 orders of magnitude and is the most precisely calibrated radical reaction despite the fact that kinetic values have been obtained indirectly.[4] A number of synthetic applications involving this ring opening reaction have been reviewed by Clive.[5] Alkyl substitution of the cyclopropane ring in **1** has subtle influences on the kinetics of the two (now) nondegenerate channels for ring cleavage, and the origin of these kinetic effects is not clear. Given the small number of heavy atoms in **1** and its methyl-substituted analogs and the structural constraints of the cyclopropane ring, this family of reactions is well-suited for a computational study. Several low-level calculations had been performed on the cyclopropylcarbinyl ring opening. A calculated barrier of 21.6 kcal/mol was found by Hehre[6] when a partial UHF geometry optimization with a STO-3G basis set was used. Dewar and Olivella[7] calculated the reaction path using spin-unrestricted MINDO/3 and found a barrier of 12.5 kcal/mol and heat of reaction of −0.5 kcal/mol. Kochi[8] measured the ESR spectrum. The activation parameters measured by Newcomb and Glenn[9] are 12.85 for the log *A* and 7.0 kcal/mol for the activation energy (for cleavage of one bond). In the present work the ring opening of various methyl- or dimethylcyclopropylcarbinyl radicals has been calculated to investigate the nature of methyl substitution effects on the energetics and relative rates of the reaction.

Computational Methods

Ab initio molecular orbital calculations for the reactions in Scheme 1 were performed using the Gaussian 94 series of programs.[10] Reactants, transition-state structures, and prod-

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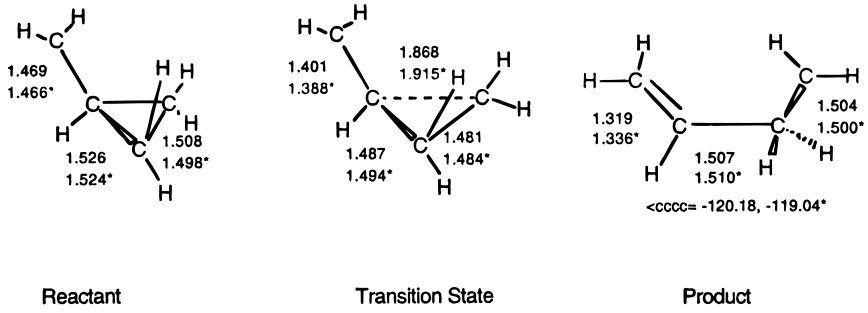
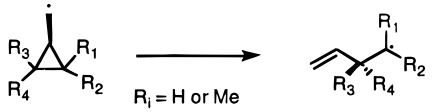


Figure 1. Comparison of the optimized geometries of the reactant, transition state, and product for the ring opening of the unsubstituted cyclopropylcarbinyl radical: UHF/6-31G* optimized (no asterisk), QCISD/6-31G* optimized (asterisk).

Scheme 1



ucts were optimized at the unrestricted Hartree−Fock[11] (UHF) level of theory using the 6-31G*[12] basis set. 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. Barrier heights and heats of reaction were calculated by second-order Møller−Plesset perturbation theory (UMP2) with spin projection[13] (PMP2/6-31G*). The relative reaction rates for the substituted ring openings were computed by conventional transition-state theory[14] using the UHF/6-31G* geometries, the UHF/6-31G* frequencies, and the PMP2/6-31G* relative energies.

To probe whether or not the quality of HF/6-31G* geometry optimizations was sufficiently accurate, the unsubstituted cyclopropylcarbinyl ring opening was also optimized at the QCISD/6-31G* level of theory,[15] which is less susceptible to spin contamination than the UMP2 level.[16] For the energetics, the G2 level of theory[17] was used to calculate the barrier height and heat of reaction for the unsubstituted ring opening. The G2 level of theory combines higher order correlation effects, diffuse functions, and multiple polarization functions to obtain accurate energetics and has a mean absolute error of 1.3 kcal/mol for 125 well-characterized energy differences.[17]

Results and Discussion

Figure 1 compares the geometries of the ring opening of unsubstituted cyclopropylcarbinyl radical optimized at different levels of theory. The UHF/6-31G* and QCISD/6-31G* geometries are very similar, justifying the use of the UHF/6-31G* geometries for the substituted cyclopropylcarbinyl radical reactions. The QCISD/6-31G*-optimized transition state is slightly later along the reaction path as judged by the C_1-C_2 and C_2-C_3 bond distances. Because the potential energy surface is fairly flat in the region of the transition state, the effect the geometry difference on the barrier is very small (*i.e.*, −0.42 kcal/mol at the UHF/6-31G* level).

Table 1 lists the heats of reaction and barrier heights for the unsubstituted ring-opening reaction. Even though there is significant change in the bonding, the heat of reaction is relatively insensitive to the level of theory for this system. The absolute barrier height, however, does vary considerably. The UMP2 barrier is 7 kcal/mol higher than the PMP2 barrier because of spin contamination. The UHF, PMP2, and QCISD barriers agree well with each other but are 1−3 kcal/mol higher than the experimental barrier, 7.3 kcal/mol.[9] The G2 level of theory, which used higher order correlation corrections and larger basis sets, compares well with the experimental data. The Arrhenius parameters, calculated by conventional transition state theory, log (k·s) = 12.92−9.25/2.3RT in kcal/mol, are in good agreement with the values measured by Newcomb and Glenn,[9] (log (k·s) = 12.85−7.05/2.3RT in kcal/mol yielding a barrier of ca. 7.3 kcal/mol).

Experimentally, alkyl substitution on the ring increases the rate constant for ring opening of a cyclopropylcarbinyl radical.[18] Table 2 summarizes the barriers

Table 1. Calculated Barrier Heights and Heats of Reaction at Different Levels of Theory for the Unsubstituted Cyclopropylcarbinyl Ring Opening[a]

	UHF	UMP2	PMP2	QCISD	G2	exptl[b]
heat of reaction	−5.21	−8.74	−4.00	−3.06	−2.96	−5.4 ± 0.1
barrier	10.60	15.45	8.34	10.41	9.53	7.3 ± 0.1

[a] Energies are in kcal/mol. The UMP2 and PMP2 values are single point energy calculations at HF/6-31G* geometries. The 6-31G* basis set was used for HF, MP2, and QCISD calculations. [b] The experimental heat of reaction and barrier are calculated from ref 9.

Table 2. Calculated Reaction Barriers for Ring Opening of Methyl Substituted Cyclopropylcarbinyl Radicals[a,b]

reaction no.	R_1	R_2	R_3	R_4	HF/6-31G*	MP2/6-31G*	PMP2 6-31G*
0	H	H	H	H	10.60	15.45	8.34
1	Me	H	H	H	9.47	13.84	6.91
2	H	Me	H	H	10.40	15.07	7.97
3	H	H	Me	H	9.94	14.53	7.45
4	H	H	H	Me	9.86	14.62	7.51
5	Me	Me	H	H	9.15	13.46	6.64
6	H	H	Me	Me	9.75	14.20	7.01
7	H	Me	Me	H	10.04	14.41	7.40
8	Me	H	H	Me	9.01	13.25	6.38
9	Me	H	Me	H	9.30	13.41	6.62
10	H	Me	H	Me	10.17	14.72	7.71

[a] In kcal/mol with ZPE calculated at HF/6-31G*; see Scheme 1 for placement of substituents for R_1-R_4. [b] $<S^2>$ for the reactants were 0.76−0.78 and between 0.93−0.95 for transition states at the HF/6-31G* level of theory.

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Table 3. Energetics for the Isodesmic Reactions[a]

ground state	R_1	R_2	R_3	R_4	kcal/mol	transition state	R_1	R_2	R_3	R_4	kcal/mol
1	Me	H	H	H	0.97	11	Me	H	H	H	−0.03
2	H	Me	H	H	−0.08	12	H	Me	H	H	−0.22
3	H	H	Me	H	0.97	13	H	H	Me	H	0.60
4	H	H	H	Me	−0.08	14	H	H	H	Me	−0.52
5	Me	Me	H	H	1.21	15	Me	Me	H	H	−0.29
6	H	H	Me	Me	1.21	16	H	H	Me	Me	0.65
7	H	Me	Me	H	0.96	17	H	Me	Me	H	0.46
8	Me	H	H	Me	0.96	18	Me	H	H	Me	−0.49
9	Me	H	Me	H	3.41	19	Me	H	Me	H	1.95
10	H	Me	H	Me	1.40	20	H	Me	H	Me	0.78

[a] In kcal/mol, with ZPE calculated at HF/6-31G*; see Scheme 2 for placement for substituents R_1−R_4.

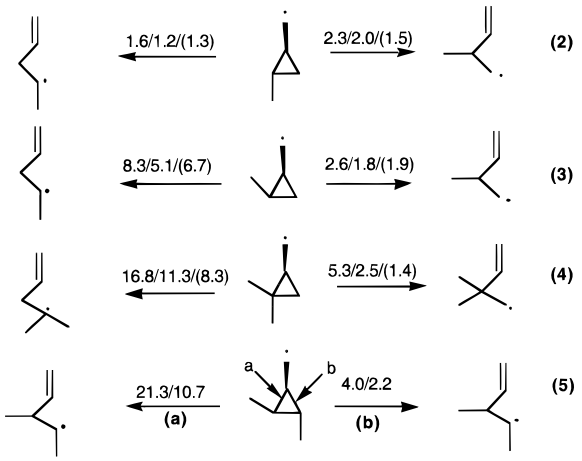
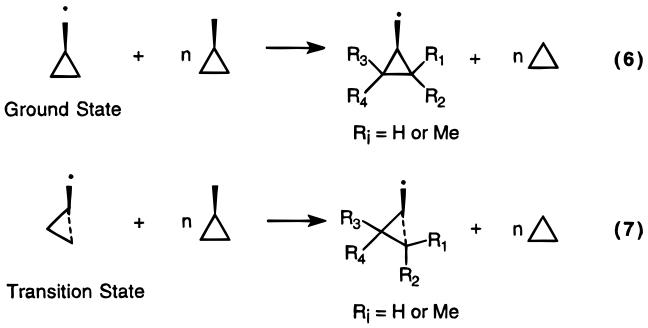


Figure 2. Relative rates for ring opening of methyl-substituted cyclopropylcarbinyl radical compared to the unsubstituted radical: HF/6-31G* (no superscript), PMP2/6-31G* (asterisk), experimental[18] (parentheses).

at different levels of theory for mono- and dimethyl-substituted cyclopropylcarbinyl radicals. Methyl substitution decreases the barriers by 0.2−1.3 kcal/mol per methyl group, depending on the position. The effects are nearly additive; the barriers for dimethyl-substituted systems are given to within 0.2 kcal/mol by summing the monomethyl barriers. Substituents that end up in the α-position in the products have a greater effect that those that end up in the *β*-position. Substituents that are *cis* to the carbinyl group in the reactants lower the barrier more than those that are *trans*. There is a good correlation between the UHF/6-31G* and PMP2/6-31G* barriers ($r^2 = 0.977$). The monomethyl substitutent effect at the PMP2/6-31G* and QCISD/6-31G* levels are very similar ($\Delta\Delta H^{\ddagger} = 0.30$ vs 0.43 kcal/mol for R_2 = Me, respectively; $\Delta\Delta H^{\ddagger} = 0.52$ vs 0.49 kcal/mol for R_4 = Me). This suggests that the trends in the barrier heights are well reproduced at the PMP2/6-31G* or even the UHF/6-31G* level.

Figure 2 compares the calculated and experimental relative rate constants for a series of ring openings. The relative rates do not depend on the heat of reaction. For example, in reaction 2 the ring opening of *trans*-(2-methylcyclopropyl)carbinyl radical to the primary homoallylic radical is slightly favored over opening to the secondary radical counterpart, even though secondary radicals are more stable than primary radicals (calculated $\Delta H°_r = -3.4$ and −6.0 kcal/mol for the primary and secondary radicals, respectively). Reaction 5 provides another example; the heats of reactions are the same since the products of both reactions are the same, but breaking the C−C bond next to the *cis*-methyl group is predicted to occur five times faster than breaking the bond next to the *trans*-methyl group. Mariano rationalized these results using frontier molecular orbital theory,[19] but the kinetics can be explained solely by steric effects, as shown below.

Scheme 2



To dissect the effects of substituents, isodesmic reactions (*i.e.*, reactions in which the reactants and products have the same number of each type of bond) are very convenient since many sources of error cancel. Reactions 6 and 7 in Scheme 2 examine the interactions of methyl groups in the ground states and transition states for openings of cyclopropylcarbinyl radicals. The results are collected in Table 3. For the reactant, *cis*-methyl substitution (*i.e.*, R_1 or R_3 = Me) destabilizes the reactant by about 1 kcal/mol, due to the interaction between the methylene and the methyl in the R_1 or R_3 position. However, a single methyl substitution in the R_2 or R_4 does not produce any significant destabilization or stabilization (0.1 kcal/mol). For geminal substitution (*i.e.*, R_1 = R_2 = Me or R_3 = R_4 = Me) and for the *trans* disubstitution, the destabilization is about the same as for the single substitution at R_1 or R_3. *cis*-Dimethyl substitution (R_1 = R_3 = Me, entry 9 in Table 3) is destabilizing by 3.4 kcal/mol; the interactions are additive with 1 kcal/mol coming from each methylene−methyl interaction and the 1.4 kcal/mol interaction from the methyl−methyl interactions (*e.g.*, entry 10 in Table 3). The relative rates for reactions 3−5 in Figure 2 can be understood in terms of relief of *cis*-methyl−methylene steric interactions in the reactants.

To explain the relative rates for reaction 2, the substituent effects in the transition state must be examined. The ring opening of the substituted side is stabilized by about 0.2 kcal/mol compared to 0.5 kcal/mol for ring opening of the unsubstituted (entries 12 and 14 in Table 3, respectively).

The *destabilizing* interactions in Table 3 are readily understood in terms of steric repulsion. It would be tempting to ascribe the *stabilizing* effects to specific electronic interactions. However, the isodesmic reactions

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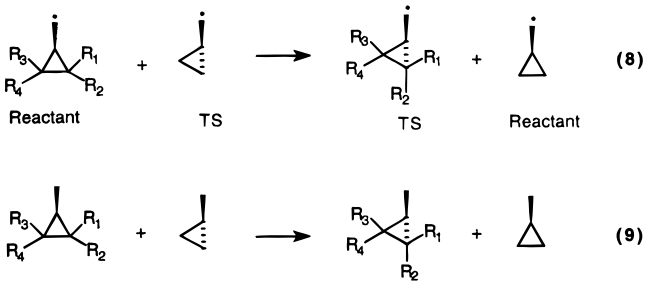
Scheme 3



in eqs 8 qnd 9 (Scheme 3) show that these effects are also due to relief of steric interactions that can be modeled by substituted cyclopropanes.

Reaction 8 is the difference in the barrier height for the substituted and the unsubstituted cyclopropylcarbinyl ring opening, $\Delta\Delta E^{\ddagger}$. Reaction 9 is the effect of methyl substitution on the difference in the steric energy of the ground state and distorted methyl cyclopropane, ΔE(steric). In the distorted structure, the ∠CCC angle in the ring has been opened to 80.0° to mimic the geometries in the transition state. There is a good correlation between the change in the barrier heights and the change in the steric energy of substituted methyl cyclopropane ($r^2 = 0.952$). Thus, there is no need to invoke any additional electronic interactions to explain the changes in the barrier heights. Steric effects found in substituted cyclopropane are quite sufficient to account for the changes in the barrier heights of cyclopropylcarbinyl ring openings caused by simple alkyl substituents.

In summary, the calculated barrier heights and relative rates are in good agreement with the experimental data available. Substituent effects were analyzed using isodesmic reactions. Steric effects are found to explain the alkyl substituent effects for the cyclopropylcarbinyl radical ring opening; it is not necessary to invoke electronic effects. One of our goals was to evaluate what levels of computational theory are needed to provide useful relative rate constants for radical reactions; the HF/6-31G*and PMP2/6-31G* levels of theory are quite adequate to describe the relative rate constants for alkyl substituents. An optimization at the HF/6-31G* level of theory for the unsubstituted cyclopropylcarbinyl radical starting at the HF/3-21G geometry takes 49 min on a 200 MHz Pentium PC with 64 MB of RAM using Gaussian 94 for Windows. A single point energy calculation at the MP2/6-31G* level on the same computer takes about 22 min of cpu time.

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Supporting Information Available: Cartesian Coordinates of all molecules; computed total energies are available (29 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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