J. Am. Chem. Soc. **1998,** *120,* 10223−10233

Ring Opening of the Cyclopropylcarbinyl Radical and Its *N*- and *O*-Substituted Analogues: A Theoretical Examination of Very Fast Unimolecular Reactions

David M. Smith,[1a] Athanassios Nicolaides,[1a,b] Bernard T. Golding,[1c] and Leo Radom*,[1a]

Contribution from the Research School of Chemistry, Australian National University, Canberra, ACT 0200, Australia, and Department of Chemistry, University of Newcastle upon Tyne, Newcastle upon Tyne NE1 7RU, UK

Received February 25, 1998

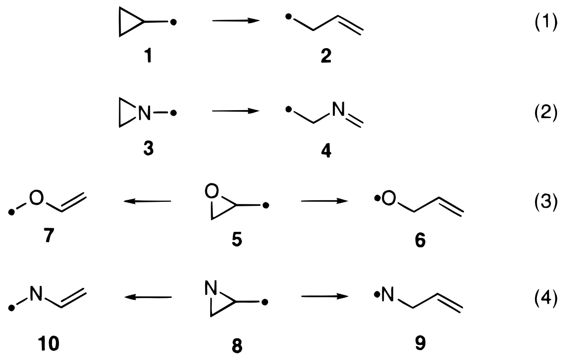
Abstract: High level ab initio molecular orbital calculations have been used to examine the ring opening of the cyclopropylcarbinyl radical and its heterosubstituted analogues. The applicability of various theoretical techniques to this ring-opening reaction has been investigated. A variant of the recently introduced CBS-RAD procedure is found to give good agreement with the experimental thermochemistry. The hybrid density functional method B3-LYP is found to perform well for various geometry- and frequency-dependent quantities and to provide a possible economical alternative for the reliable prediction of the energetics. We find that heterosubstitution by nitrogen at the 1-position has very little effect on the kinetics of ring opening. On the other hand, heterosubstitution by nitrogen or oxygen at the 2-position results in a significant rate enhancement for an already rapid reaction. In both these latter cases, the kinetically preferred ring-opening pathway is predicted not to lead to the thermodynamically preferred products.

Introduction

The ring opening of the cyclopropylcarbinyl radical (**1**) to the but-3-enyl (or homoallyl) radical (**2**) (Scheme 1, reaction 1) is one of the fastest unimolecular reactions known, with a rate constant at 353 K of 6.1×10^8 s^{-1}.[2] A popular application has been to use the ring opening as a probe for the intermediacy of radicals in both chemical[3,4] and biochemical[3,5] processes. It has also been widely used as a "radical clock", enabling the rate constants of some exceptionally fast bimolecular reactions to be estimated.[6]

Many important biochemical processes have been suggested to involve rearrangements of the type shown in reaction 1. For example, the interconversion of a substituted cyclopropylcarbinyl radical with isomeric but-3-enyl radicals has been proposed for the coenzyme-B_{12}-dependent enzyme, 2-methyleneglutarate mutase, during its catalysis of the rearrangement of 2-methyleneglutarate to 3-methylitaconate.[7] A 1-aziridinylcarbinyl species (**3**) (Scheme 1, reaction 2) has been suggested as an intermediate in the equilibration of 3,5-diaminohexanoate with the 3,6-isomer catalyzed by β-lysine aminomutase.[8] Closely related ring openings are also thought to be involved in the biosynthesis of ethylene[9] and the inhibition of monoamine oxidase-B.[10] A good understanding of the fundamental electronic structure aspects of these reactions is therefore important and may provide valuable insights.

Scheme 1. The Ring-Opening Reactions of the Cyclopropylcarbinyl Radical and Three of Its Heterosubstituted Analogues



In this paper, we present results of ab initio molecular orbital calculations on the ring opening of the cyclopropylcarbinyl radical and three of its heterosubstituted analogues (see Scheme 1, reactions 1−4). Previous theoretical studies of radical reactions have indicated that the results are sensitive to the level of theory used.[11] An assessment of the performance of the various methods is therefore desirable in the first instance. To this end, we have performed extensive analyses of the impact of the chosen theoretical method on properties such as geometry,

---

[1] (a) Australian National University. (b) Present address: Chemistry Department for Materials, Faculty of Engineering, Mie University, Tsu, Mie 514, Japan. (c) University of Newcastle upon Tyne.

[2] Beckwith, A. L. J.; Bowry, V. *J. Am. Chem. Soc.* **1994**, *116*, 2710−2716.

[3] For a recent review, see: Nonhebel, D. C. *Chem. Soc. Rev.* **1993**, 347−359.

[4] See, for example: He, M.; Dowd, P. *J. Am. Chem. Soc.* **1996**, *118*, 711.

[5] See, for example: Newcomb, M.; Le Tadic-Biadatti, M.; Chestney, D. L.; Roberts, E. S.; Hollenberg, P. F. *J. Am. Chem. Soc.* **1995**, *117*, 12085−12091.

[6] For a recent review, see: Newcomb, M. *Tetrahedron* **1993**, *49*, 1151−1176.

[7] Buckel, W.; Golding, B. T. *Chem. Soc. Rev.* **1996**, 329−337.

[8] Ballinger, M. D.; Frey, P. A.; Reed, G. H.; LoBrutto, R. *Biochemistry* **1995**, *34*, 10086−10093.

[9] Baldwin, J. E.; Adlington, R. M.; Lajoie, G. A.; Lowe, C.; Baird, P. D. *J. Chem. Soc., Chem. Commun.* **1988**, 775.

[10] Silverman, R. B.; Cesarone, J. M.; Xingliang, L. *J. Am. Chem. Soc.* **1993**, *115*, 4955−4961.

S0002-7863(98)00635-0 CCC: $15.00

activation energy, zero-point vibrational energy, the Arrhenius frequency factor, and reaction thermochemistry for reaction 1 of Scheme 1. As a result of the assessment study, we are able to select levels of theory that are suitably reliable. In the second part of this study, we apply these levels of theory in a uniform treatment of the other ring-opening reactions (Scheme 1, reactions 2−4).

Theoretical Procedures

Standard ab initio molecular orbital calculations[12] were performed with GAUSSIAN 94,[13] MOLPRO 96,[14] and ACES II.[15,16] As part of the assessment study, geometries were optimized with the UHF, UMP2(full), RMP2,[11b] B3-LYP,[17] and QCISD[18] procedures, all in conjunction with the 6-31G(d) basis set. Vibrational frequencies were calculated for the subset of these methods for which analytic second derivatives of the energy with respect to the nuclear displacements are readily available (UHF, UMP2(full), and B3-LYP). The frequencies thus obtained were used in conjunction with appropriate scaling factors[19] for the calculation of various frequency-dependent quantities.

Improved relative energies for the species involved in the ring opening of the cyclopropylcarbinyl radical were obtained from single-point calculations with use of the UMP2, PMP2, RMP2, and B3-LYP techniques with a variety of basis sets. Additional single-point energies were provided by several variants of the G2[20] and CBS[21] procedures. Both these procedures have been designed with the aim of predicting thermochemical quantities to chemical accuracy (~10 kJ mol^{-1}). A subset of the best of the theoretical procedures described above was then applied to the heterosubstituted ring openings (Scheme 1, reactions 2−4). Of particular note is a recently introduced variation of the CBS-Q[21] technique denoted CBS-RAD, which employs CCSD(T) in place of QCISD(T) and uses B3-LYP/6-31G(d) geometries and zero-point vibrational energies.[11e] The CBS-RAD procedure has been shown to perform well in predicting the heats of formation of a small set of organic radicals.[11e] Of more relevance to the current work is the recent application of CBS-RAD to a large number of reactions involving radical addition to alkenes[11f] where a mean absolute deviation from experiment of 1.4 kJ mol^{-1} was found. Because the ring-opening reactions of the type investigated in the current work are simply the reverse of intramolecular additions to double bonds, the CBS-RAD technique can reasonably be expected to perform well in the present context. However, as has been mentioned elsewhere,[11f] we note that the CBS-RAD technique when applied to radicals should not generally be expected to perform better than the parent CBS-Q procedure performs for closed-shell systems. Calculated CBS-RAD total energies are presented in Table S1 of the Supporting Information.

Results and Discussion

A. The Ring Opening of the Cyclopropylcarbinyl Radical. (1) Previous Experimental Studies. The ring opening of the cyclopropylcarbinyl radical provides an ideal starting point for our assessment study. This reaction has been widely studied experimentally and has been described as “the most precisely calibrated radical reaction”.[22a] A combination of direct and indirect experimental methods such as low-temperature EPR spectroscopy[23] and competitive trapping techniques[24,25] in the temperature range 128−398 K have given a well-established Arrhenius function of $\log(k/\mathrm{s}^{-1}) = (13.15) - (29.50)/\theta$,[25] where $\theta = 2.3RT$ kJ mol^{-1}.

While the activation energy and Arrhenius frequency factor have been accurately measured and a consensus on their values has been reached, the same cannot be said for the reaction enthalpy and the heats of formation of the reactant and product. One estimate of the enthalpy change for the ring opening is $\Delta H_{298} = -13.2$ kJ mol^{-1}. This value originates from kinetic studies of the reverse reaction ($\log(k/\mathrm{s}^{-1}) = (10.3 \pm 0.5) - (38.0 \pm 2.1)/\theta$),[26] used in combination with earlier data pertaining to the forward reaction.[23] The above description of the reverse reaction, when combined with the currently accepted Arrhenius function for the ring opening,[25] results in a ΔH_{298} value of −8.5 kJ mol^{-1}. An alternative value for the enthalpy of ring opening at 0 K is given in ref 22a as −22.6 kJ mol^{-1}, reportedly calculated from the data in ref 25.

For the cyclopropylcarbinyl radical, the heat of formation has been determined from a spectrometric investigation of the reaction of cyclopropylcarbinyl iodide with hydrogen iodide and is given as $\Delta H_{\mathrm{f}\ 298} = 213.8 \pm 25$ kJ mol^{-1}.[27] The heat of formation of the but-3-enyl radical has been estimated from the heat of formation of 1-butene (−0.4 ± 0.4 kJ mol^{-1})[28] and the *n*-propyl C−H bond dissociation energy (409.6 ± 4 kJ mol^{-1}).[29] This procedure gives[30] $\Delta H_{\mathrm{f}\ 298} = 190.8 \pm 4$ kJ mol^{-1} which, when combined with the cyclopropylcarbinyl radical heat of formation, gives $\Delta H_{298} = -23.0 \pm 25$ kJ mol^{-1} for the ring-opening reaction. A more recent determination[31] of the *n*-propyl

---

(11) (a) Schlegel, H. B. *J. Chem. Phys.* **1986**, *84*, 4530. (b) Knowles, P. J.; Andrews, S. J.; Amos, R. D.; Handy, N. C.; Pople, J. A. *Chem. Phys. Lett.* **1991**, *186*, 130−136. (c) Stanton, J. F. *J. Chem. Phys.* **1994**, *101*, 371−374. (d) Wong, M. W.; Radom, L. *J. Phys. Chem.* **1995**, *99*, 8582−8588. (e) Mayer, P. M.; Parkinson, C. J.; Smith, D. M.; Radom, L. *J. Chem. Phys.* **1998**, *108*, 604−615. (f) Wong, M. W.; Radom, L. *J. Phys. Chem.* **1998**, *102*, 2237−2245.

(12) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

(13) 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.; Pople, J. A. GAUSSIAN 94 (Rev. E.2); Gaussian, Inc.: Pittsburgh, 1995.

(14) MOLPRO 96 is a package of ab initio programs written by H.-J. Werner and P. J. Knowles with contributions from J. Almlof, R. D. Amos, M. J. O. Deegan, S. T. Elbert, C. Hampel, W. Meyer, K. Peterson, R. Pitzer, A. J. Stone, P. R. Taylor, and R. Lindh.

(15) Stanton, J. F.; Gauss, J.; Watts, J. D.; Lauderdale, W. J.; Bartlett, R. J. ACES II; Quantum Theory Project, Departments of Chemistry and Physics, University of Florida, Gainsville, 1992.

(16) Stanton, J. F.; Gauss, J.; Watts, J. D.; Lauderdale, W. J.; Bartlett, R. J. *Int. J. Quantum Chem. Symp.* **1992**, *26*, 879.

(17) (a) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785. (c) Johnson, B. G.; Gill, P. M. W.; Pople, J. A. *J. Chem. Phys.* **1993**, *98*, 5612. (d) Stephens, P. J.; Devlin, F. J.; Chablowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623.

(18) Pople, J. A.; Head-Gordon, M.; Raghavachari, K. *J. Chem. Phys.* **1987**, *87*, 5968.

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

(20) Curtiss, L. A.; Raghavachari, K.; Trucks, G. W.; Pople, J. A. *J. Chem. Phys.* **1991**, *94*, 7221−7230.

(21) Ochterski, J. W.; Petersson, G. A.; Montgomery, J. A. *J. Chem. Phys.* **1996**, *104*, 2598−2619.

(22) (a) Martinez, F. N.; Schlegel, H. B.; Newcomb, M. *J. Org. Chem.* **1996**, *61*, 8547−8550. (b) Due to a clerical error, incorrect values of the activation energy (38.7 kJ mol^{-1}) and reaction enthalpy (−12.4 kJ mol^{-1}) were reported in ref 22a. The correct values are given in the text. See also: Martinez, F. N.; Schlegel, H. B.; Newcomb, M. *J. Org. Chem.* In press. We thank Professor Newcomb for bringing the above discrepancy to our attention.

(23) Maillard, B.; Forrest, D.; Ingold, K. U. *J. Am. Chem. Soc.* **1976**, *98*, 7024−7026.

(24) Beckwith, A. L.; Bowry, V. W.; Moad, G. J. *J. Org. Chem.* **1988**, *53*, 1632−1641.

(25) Newcomb, M.; Glenn, A. G. *J. Am. Chem. Soc.* **1989**, *111*, 275−277.

(26) Effio, A.; Griller, D.; Ingold, K. U.; Beckwith, A. L. J.; Serelis, A. K. *J. Am. Chem. Soc.* **1980**, *102*, 1734−1736.

(27) McMillen, D. F.; Golden, D. M.; Benson, S. W. *Int. J. Chem. Kinet.* **1971**, *3*, 358−374.

(28) Cox, J. D.; Pilcher, G. *Thermochemistry of Organic and Organometallic Compounds*; Academic Press: New York, 1970.

(29) McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493.

(30) Schultz, J. C.; Houle, F. A.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 7336−7347.

(31) Tsang, W. *J. Am. Chem. Soc.* **1985**, *107*, 2872−2880.

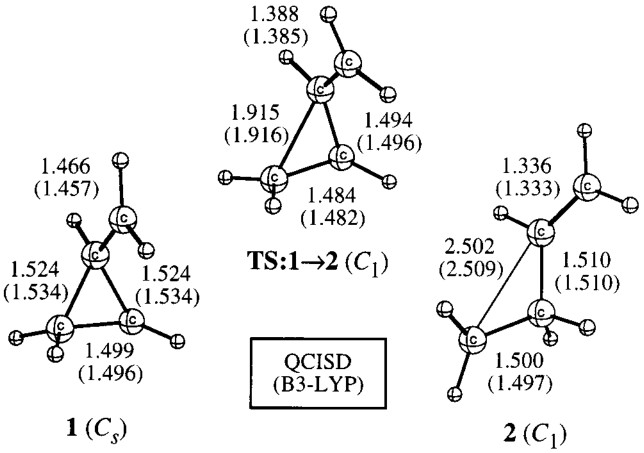


Figure 1. Bond lengths (Å) for the cyclopropylcarbinyl radical (**1**), the ring-opening transition structure (**TS:1→2**), and the but-3-enyl radical (**2**) at the QCISD and B3-LYP (in parentheses) levels of theory with the 6-31G(d) basis set.

C−H bond dissociation energy of 422.6 ± 2.1 kJ mol^{-1} leads to $\Delta H_{f\ 298} = 204.2 \pm 2.3$ kJ mol^{-1} for the but-3-enyl radical. This new heat of formation for the but-3-enyl radical yields a new enthalpy associated with the ring opening of the cyclopropylcarbinyl radical of $\Delta H_{298} = -9.6 \pm 25$ kJ mol^{-1}.

In summary, the experimental Arrhenius activation energy (E_a) of the ring opening of the cyclopropylcarbinyl radical at 298 K is 29.5 kJ mol^{-1}. The reaction enthalpy is less well established with estimates for ΔH_{298} of −8.5, −9.6, and −13.2 kJ mol^{-1} and for ΔH_0 of −22.6 kJ mol^{-1}. The latter value corresponds to a ΔH_{298} of −21.0 kJ mol^{-1}.

(2) Previous Theoretical Studies. Earlier, lower-level theoretical estimates of the activation energy of the ring opening of the cyclopropylcarbinyl radical range from 15.1[32] to 54.0 kJ mol^{-1},[33] with calculated reaction enthalpies ranging from −2.1[33] to −36.0 kJ mol^{-1}.[34] More recent calculations, including the effects of electron correlation, give predictions for the activation energy of 55.6[35] and 38.5 kJ mol^{-1},[36] with associated reaction enthalpies of −6.7[35] and −15.5 kJ mol^{-1}.[36] G2 theory (using HF/6-31G(d) geometries) gives an activation energy of 33.0 kJ mol^{-1} and an enthalpy of reaction of −14.6 kJ mol^{-1} for the ring-opening reaction.[22]

The observation that the previous theoretical predictions of the activation energy vary so greatly suggests that a systematic study would be desirable. In addition, because there are significant uncertainties associated with the enthalpy of the ring-opening reaction and with the heats of formation of both the reactant and the product, clarification of these issues is also desirable.

In the following sections, we discuss the influence of various factors involved in the theoretical treatment of the ring opening of the cyclopropylcarbinyl radical.

(3) Geometry Effects. Figure 1 shows the lowest energy conformations of the cyclopropylcarbinyl radical (**1**), the but-3-enyl radical (**2**), and the ring-opening transition structure (**TS: 1→2**), calculated at the QCISD/6-31G(d) level of theory (the B3-LYP/6-31G(d) bond lengths are given in parentheses). We expect the QCISD/6-31G(d) geometries to be of high quality and will therefore assess the other methods based on comparisons with this level of theory.

The cyclopropylcarbinyl radical has C_s symmetry, with a plane of symmetry dividing the ring, and the bonds at the planar radical center oriented so as to "bisect" the adjacent ring.[37] This conformation allows maximum overlap of the orbital containing the unpaired electron with the C−C bonds of the ring and leads to a shortened exocyclic C−C bond (1.466 Å) in **1**. For the other methods examined, the geometry that most closely resembles the QCISD/6-31G(d) structure for this species is obtained with B3-LYP/6-31G(d) (see Figure 1 and Table S2 of the Supporting Information).

The QCISD/6-31G(d) transition structure for ring opening predicts a length for the breaking C- - -C bond of 1.915 Å, approximately midway between the appropriate values for the reactant (1.524 Å) and product (2.502 Å). This bond length shows a significant dependence on the level of theory in that it ranges from 1.869 (UHF) to 1.951 Å (RMP2) although the energetic consequences of the changes in the length of this extended bond are likely to be small. The B3-LYP prediction of 1.916 Å is in very good agreement with the QCISD length (see Figure 1 and Table S2 of the Supporting Information).

A representative geometrical parameter for the but-3-enyl radical is the ∠CCCC dihedral angle. The predictions of this angle lie in a narrow range from 118.1° (RMP2) to 120.2° (UHF), with continued good agreement between B3-LYP (119.4°) and QCISD (119.0°). Figure 1 also demonstrates the good agreement obtained between these two levels of theory with respect to the bond lengths for this species. The optimization of the geometry of the but-3-enyl radical at the UMP2-(full)/6-31G(d) level of theory presents some difficulties. This issue has been discussed previously by Bauschlicher,[38] who noted that numerical problems in the optimization prevent ultimate convergence. We have adopted the same strategy as Bauschlicher by taking the B3-LYP/6-31G(d) optimized geometry as our best approximation to the UMP2(full)/6-31G(d) optimum geometry for the but-3-enyl radical for use in the appropriate calculations of the enthalpy of reaction.

(4) Effects of Geometry on Calculated Thermochemistry. Table 1 shows the CBS-RAD thermochemical properties for the ring-opening reaction, calculated at several different geometries. For this comparison, we have chosen to present the barriers ($\Delta H^{\ddagger}$) and reaction enthalpies (ΔH) at 0 K and to exclude the zero-point vibrational energy. To make a meaningful comparison with experiment, the experimental activation energy and enthalpy of reaction must be back-corrected accordingly.[39] We have accomplished these corrections by using zero-point vibrational energies and temperature corrections calculated at the B3-LYP/6-31G(d) level. This leads to an experimental vibrationless $\Delta H^{\ddagger}$ at 0 K of 31.2 kJ mol^{-1} and, depending on which experimental value is used,[22,25−28,31] vibrationless enthalpies of reaction at 0 K (ΔH) of −6.9, −8.0, −11.6, or −19.4 kJ mol^{-1} are obtained.

The effect of the chosen geometry on the calculated thermochemical parameters can be seen to be very small (Table 1), a

---

[32] Delbecq, F. *J. Mol. Struct. (THEOCHEM)* **1986**, *136*, 65−75.

[33] Dewar, M. J. S.; Olivella, S. *J. Am. Chem. Soc.* **1979**, *101*, 4958−4962.

[34] Hehre, W. J. *J. Am. Chem. Soc.* **1973**, *95*, 2643−2646.

[35] Giese, B.; Heinrich, N.; Horler, H.; Koch, W.; Schwarz, H. *Chem. Ber.* **1986**, *119*, 3528−3535.

[36] Quenemoen, K.; Borden, W. T.; Davidson, E. R.; Feller, D. *J. Am. Chem. Soc.* **1985**, *107*, 5054−5059.

[37] The lowest energy conformer of the cyclopropylcarbinyl radical at the UHF/6-31G(d) level has C_1 symmetry. This lack of symmetry is associated with the pyramidalization of the radical center at this level of theory. However, the UHF/6-31G(d) energy difference between the C_1 and C_s structures is only 0.1 kJ mol^{-1}, so this factor will not have a significant impact on the overall thermochemistry. All correlated levels of theory predict a C_s structure.

[38] Bauschlicher, C. W. *Chem. Phys. Lett.* **1995**, *293*, 252−257.

[39] It should be noted that the relationship between the activation energy (E_a) and the reaction barrier ($\Delta H^{\ddagger}$) for a unimolecular reaction is $E_a(T) = \Delta H^{\ddagger}(T) + RT$.

Table 1. Effect of Geometry on the Calculated (CBS−RAD) Barrier ($\Delta H^{\ddagger}$) and Reaction Enthalpy (ΔH)[a] (kJ mol^{-1}) for the Ring Opening of the Cyclopropylcarbinyl Radical

	$\Delta H^{\ddagger}$	ΔH
CBS-RAD//QCISD[b]	33.0	−9.4
CBS-RAD//UHF[b]	31.6	−8.9
CBS-RAD//UMP2(full)[b]	33.2	−8.8[c]
CBS-RAD//RMP2[b]	32.2	−9.2
CBS-RAD//B3-LYP[b]	32.9	−9.1
experimental[d]	31.2[e]	−6.9,[f] −8.0,[g] −11.6,[h] −19.4[i]

[a] $\Delta H^{\ddagger}$ and ΔH are the calculated barrier and reaction enthalpy, respectively, at 0 K and without zero-point vibrational energy contributions. [b] Geometries obtained with the 6-31G(d) basis set. [c] Calculated with use of the B3-LYP/6-31G(d) geometry for the but-3-enyl radical. Use of the RMP2/6-31G(d) geometry for the but-3-enyl radical gives $\Delta H = -9.4$ kJ mol^{-1}. See text. [d] Experimental results have been corrected to 0 K and the zero-point energy contribution has been removed. See text. [e] From ref 25. See text. [f] From refs 25 and 26. See text. [g] From references 23 and 26. See text. [h] From experimental heats of formation of reactant and product. See text. [i] From reference 22. See text.

Table 2. Calculated Barriers ($\Delta H^{\ddagger}$) and Reaction Enthalpies (ΔH) (kJ mol^{-1}) for the Ring Opening of the Cyclopropylcarbinyl Radical[a]

	$\Delta H^{\ddagger}$	ΔH
CBS-RAD	32.9	−9.1
CBS-Q	32.1	−9.1
G2	37.5	−11.3
G2(MP2)	38.2	−11.2
G2M(RCC)[b]	41.3	−10.7
G2(MP2)-RAD	35.5	−10.1
B3-LYP/6-31G(d)	35.0	−9.5
B3-LYP/6-311+G(d,p)	30.3	−15.6
B3-LYP/6-311+G(3df,2p)	30.7	−14.1
UMP2/6-311+G(d,p)	66.5	−0.2
UMP2/6-311+G(3df,2p)	66.6	1.0
PMP2/6-311+G(d,p)	36.2	−0.1
PMP2/6-311+G(3df,2p)	36.3	1.3
RMP2/6-311+G(d,p)	43.0	−0.7
RMP2/6-311+G(3df,2p)	41.4	0.8
experimental[c]	31.2[d]	−6.9,[e] −8.0,[f] −11.6,[g] −19.4[h]

[a] Unless otherwise specified, all values have been calculated with use of B3-LYP/6-31G(d) geometries and are without zero-point vibrational energies. [b] Calculated at B3-LYP/6-311G(d,p) geometries. [c] Experimental results have been corrected to 0 K and the zero-point energy contribution has been removed. See text. [d] From ref 25. See text. [e] From refs 25 and 26. See text. [f] From refs 23 and 26. See text. [g] From experimental heats of formation of reactant and product. See text. [h] From refs 22. See text.

result that could not be assumed prior to the present analysis. For example, a recent study of radical additions to alkenes[11f] found geometry effects as large as 14 kJ mol^{-1}. There is very good agreement between the $\Delta H^{\ddagger}$ calculated by all the CBS-RAD variants and the adjusted experimental value. The CBS-RAD ΔH values are close to the cluster of experimental results corresponding to lower exothermicities. Owing to its excellent agreement with the computationally demanding QCISD method, the B3-LYP technique appears to be the best alternative to QCISD for the calculation of geometry in the current application. However, any of the theoretical methods presented in the above discussion should be adequate for geometry optimization of this and closely related systems.

(5) Higher Level Energy Calculations. Once the geometry has been selected, it is necessary to determine the best method for the calculation of the total energy (Table 2). We continue to use the vibrationless quantities $\Delta H^{\ddagger}$ and ΔH to assess the impact of different techniques.

The first row of entries in Table 2 is reproduced from Table 1 and corresponds to the calculation of the thermochemical quantities $\Delta H^{\ddagger}$ and ΔH, using the CBS-RAD technique with B3-LYP/6-31G(d) geometries. The entries in the second row (CBS-Q on B3-LYP/6-31G(d) geometries) are aimed at demonstrating the effect of changing the high-level calculation from CCSD(T) to QCISD(T). Although there exist many situations where there is a nontrivial difference between CCSD(T) and QCISD(T),[11e] this appears not to be one of them, as the barrier is reduced by just 0.8 kJ mol^{-1} and the enthalpy of reaction is changed by less than 0.1 kJ mol^{-1}.

The third row in Table 2 is obtained by applying the G2 methodology to the B3-LYP/6-31G(d) geometries of the stationary points of the ring-opening reaction. It can be seen that this alteration does produce a relatively large change in the enthalpy of activation in a direction away from the experimental value, accompanied by a smaller change in the reaction enthalpy.

There are several possible reasons for the discrepancy between the G2 and CBS activation energies, but the one that we deem to be dominant arises from the inclusion of the ΔE(spin) term in the CBS procedures. This term attempts to correct for spin contamination[40] and in the current case lowers the barrier by approximately 5 kJ mol^{-1}. The present result is consistent with previous findings that G2 and related methods overestimate the barriers for radical addition reactions by about 5 kJ mol^{-1}.[11d,f] The most likely reason for this is that the spin contamination inherent in the transition structure (e.g. $\langle S^2 \rangle = 0.95$ for the transition structure in the cyclopropylcarbinyl ring-opening reaction) causes the energy for this species to be artificially high. A correction such as ΔE(spin) seems to be able to account satisfactorily for this deficiency.

A modification of the G2 method (G2M(RCC)) has been proposed by Mebel et al.[41] for use with open-shell systems. The G2M(RCC) technique uses geometries and zero-point energies calculated at the B3-LYP/6-311G(d,p) level. A restricted open-shell coupled-cluster calculation (RRCCSD(T)/6-311G(d,p))[42] is used to estimate the major part of the correlation energy and the basis set extension is performed with spin-projected (PMP) perturbation theory. The calculated G2M(RCC) barrier (Table 2) is actually slightly worse than that obtained with the standard G2 or CBS techniques.

Recent work has indicated that a modified G2(MP2) procedure (denoted G2(MP2)-RAD in Table 2) gives reliable results when applied to open-shell systems.[43] This technique is a variant of G2(MP2) in which a restricted open-shell coupled-cluster calculation (URCCSD(T)/6-311G(d,p))[42] replaces the standard UQCISD(T)/6-311G(d,p), and the basis set extension is calculated by using restricted open-shell perturbation theory (RMP2) instead of UMP2. B3-LYP/6-31G(d) geometries are used. The results in Table 2 show that G2(MP2)-RAD offers a small improvement over standard G2(MP2) in the present situation.

The B3-LYP technique has been shown to perform reasonably well for the heats of formation of the molecules in the G2 test

---

(40) For the CBS-Q and CBS-RAD procedures, this factor is evaluated as $\Delta E(\mathrm{spin}) = -9.20\ mE_{\mathrm{h}} \times \Delta\langle S^2 \rangle$ where $\Delta\langle S^2 \rangle$ is the difference between $S(S+1)$ (0.75 for a pure doublet state) and the calculated expectation value of the S^2 operator for the species being examined.[21.]

(41) Mebel, A. M.; Morokuma, K.; Lin, M. C. *J. Chem. Phys.* **1995**, *103*, 7414−7421.

(42) MOLPRO 96 offers two types of open-shell coupled cluster calculations, referred to by us as RRCCCSD(T) and URCCSD(T). Both techniques employ a restricted open-shell Hartree−Fock (ROHF) reference function. The URCCSD(T) procedure is virtually identical to performing a CCSD(T) calculation with an ROHF reference in ACES II. The RRCCSD(T) technique introduces additional constraints so that the linear part of the wave function becomes a spin eigenfunction. See: Knowles, P. J.; Hampel, C.; Werner, H.-J. *J. Chem. Phys.* **1993**, *99*, 5219.

(43) Parkinson, C. J.; Radom, L. Work in progress.

Table 3. Calculated Zero-Point Vibrational Energies (kJ mol^{-1}) and Their Impact on the Barrier ($\Delta H^{\ddagger}$) and Reaction Enthalpy (ΔH) for the Ring Opening of the Cyclopropylcarbinyl Radical[a]

	1	**TS:1→2**	**2**	$\Delta\Delta H^{\ddagger}$	$\Delta\Delta H$
UHF[b]	242.6	237.9	239.7	−4.7	−2.9
B3-LYP[b]	244.4	241.5	241.2	−2.9	−3.2
UMP2(full)[b]	246.3	244.6		−1.7	

[a] 6-31G(d) basis set used throughout. [b] Scaled by the optimum zero-point vibrational energy scale factors of 0.9135 (UHF), 0.9661 (UMP2(full)), and 0.9806 (B3-LYP). Scaling factors from ref 19.

set.[44] We have therefore performed B3-LYP single-point energy calculations with the 6-311+G(d,p) and 6-311+G(3df,2p) basis sets using the B3-LYP/6-31G(d) optimized geometry. We also include the B3-LYP/6-31G(d) energies for comparison. The B3-LYP barriers (Table 2) are in impressive agreement with experiment, particularly considering the relatively inexpensive nature of such calculations. Such results are very encouraging for the chemist with limited computational resources or with potential application to larger, related systems in mind. The B3-LYP reaction enthalpies are quite close to those obtained with the CBS or G2 procedures.

We have also calculated the reaction thermochemistry at the MP2 level of theory with unrestricted (UMP), projected (PMP), and restricted (RMP) approaches. The 6-311+G(d,p) and 6-311+G(3df,2p) basis sets were used for these calculations. UMP2 performs quite poorly, overestimating the barrier by some 35 kJ mol^{-1}. Projecting out the first spin contaminant (PMP2) remedies the situation somewhat, lowering the activation energy by approximately 30 kJ mol^{-1}. The RMP2 results, which correspond to pure doublet states, also constitute a significant improvement to the UMP2 barriers. These results suggest that the large degree of spin contamination in the transition structure is the major contributor to the poor UMP2 result. The MP2 reaction enthalpies are essentially the same within each basis set, regardless of which approach is used. This result is consistent with the small degree of spin contamination found in the reactant and product (both having $<S^2> \approx 0.77$). The MP2 enthalpies deviate by around 10 kJ mol^{-1} from the higher-level results, predicting the ring opening to be essentially thermoneutral.

It is of interest to compare briefly the barriers for the reverse reaction (easily obtainable from Table 2 as $\Delta H^{\ddagger} - \Delta H$), which corresponds to an intramolecular radical addition, with results for the intermolecular addition of the methyl radical to ethylene. On the basis of our best calculations (Table 2) the true reverse barrier is around 42 kJ mol^{-1}. G2 (48.8 kJ mol^{-1}), G2(MP2) (49.4 kJ mol^{-1}), and UMP2/6-311+G(3df,2p) (67.6 kJ mol^{-1}) all overestimate this quantity by amounts similar to those observed in the intermolecular case.[11d] Similarly, the PMP2 values (36.3 and 37.6 kJ mol^{-1}) can be seen to underestimate the reverse barrier just as they do in the case of the addition of the methyl radical to ethylene.[11d] The remainder of the methods in Table 2 (including G2(MP2)-RAD) are all found to predict the reverse barrier for reaction 1 (Scheme 1) to lie in the narrow range of 41−46 kJ mol^{-1}.

(6) Zero-Point Vibrational Energy. Zero-point energies have been calculated for the species involved in the ring-opening reaction at the UHF, B3-LYP, and UMP2(full) levels of theory with use of the 6-31G(d) basis set. Table 3 shows the appropriately scaled[19] zero-point energies and their contribution to the thermochemical parameters.

Table 4. Calculated Temperature Corrections, $H_{298} - H_0$ (kJ mol^{-1}), and Their Impact on the Barrier ($\Delta H^{\ddagger}$) and Reaction Enthalpy (ΔH) for the Ring Opening of the Cyclopropylcarbinyl Radical[a]

	1	**TS:1→2**	**2**	$\Delta\Delta H^{\ddagger}$	$\Delta\Delta H$
UHF[b]	16.2	14.9	17.5	−1.3	1.3
B3-LYP[b]	15.6	14.3	17.2	−1.3	1.6
UMP2(full)[b]	15.9	13.5		−2.0	

[a] 6-31G(d) basis set used throughout. [b] Scaled by optimum $\Delta H_{\mathrm{vib}}(T)$ scale factors of 0.8905 (UHF), 1.0084 (UMP2(full)), and 0.9989 (B3-LYP), respectively. Scaling factors from ref 19.

The B3-LYP procedure has been shown previously to perform well in the calculation of zero-point energies,[11f,19,45,46] and the results in Table 3 show that the B3-LYP zero-point energies lie between the UHF and UMP2 values in the current context. Using UMP2 or UHF zero-point vibrational energies could result in an error as large as 4 kJ mol^{-1} with respect to the B3-LYP *absolute* values. However, the effect is reduced when calculating *relative* energies such as the reaction barrier or enthalpy. Although the differences between the various methods are small, we recommend the use of B3-LYP/6-31G(d) zero-point vibrational energies here.

(7) Temperature Correction. Calculated temperature corrections ($H_{298} - H_0$) are shown in Table 4 for the species involved in the ring opening of the cyclopropylcarbinyl radical. The vibrational contribution has been evaluated by using the harmonic approximation and scaled[19] frequencies calculated at three different levels of theory (UHF, B3-LYP, and UMP2(full)) in conjunction with the 6-31G(d) basis set. It can be seen from Table 4 that the temperature corrections are relatively insensitive to the choice of vibrational frequencies, with a maximum variation within any one species of 1.4 kJ mol^{-1}. The largest difference in relative thermochemical quantities obtained with the various levels of theory is 0.7 kJ mol^{-1}. We can therefore conclude that any of the treatments is adequate for the evaluation of the temperature correction for this reaction. As we recommend B3-LYP/6-31G(d) for the calculation of geometry and zero-point vibrational energy, we also recommend it for the calculation of $H_{298} - H_0$.

(8) Frequency Factor. To obtain the rate constant for the ring opening of the cyclopropylcarbinyl radical requires the calculation of the Arrhenius frequency factor (A) in addition to the barrier or activation energy. A popular way to do this has been to use partition functions obtained from ab initio molecular orbital calculations in the rate constant expression of transition state theory.[47]

Table 5 shows the log A values calculated at three different levels of theory (UHF, B3-LYP, and UMP2(full), each with the 6-31G(d) basis set), along with the experimental value. All but one of the vibrational partition functions were obtained with use of scaled[19] harmonic frequencies. The motion for which the harmonic approximation becomes suspect corresponds to the rotation of the *exo*-methylene group in the cyclopropylcarbinyl radical. This motion is better described as a hindered rotor and we have therefore employed Truhlar's approximation[48] to obtain the partition function for this mode. The calculated frequency factors have been multiplied by a factor of 2 to account for the fact that either of the two equivalent bonds of

---

(44) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Pople, J. A. *J. Chem. Phys.* **1997**, *106*, 1063−1079.

(45) Bauschlicher, C. W.; Partridge, H. J. *J. Chem. Phys.* **1995**, *103*, 1788.

(46) Rauhut, G.; Pulay, R. *J. Phys. Chem.* **1995**, *99*, 3093.

(47) See, for example: Heuts, J. P. A.; Gilbert, R. G.; Radom, L. *Macromolecules* **1995**, *28*, 8771−8781 and references therein.

(48) Truhlar, D. G. *J. Comput. Chem.* **1991**, *12*, 266−270.

Table 5. Calculated Arrhenius Frequency Factors ($\log(A/\mathrm{s}^{-1})$) for the Ring Opening of the Cyclopropylcarbinyl Radical[a]

	$\log(A/\mathrm{s}^{-1})$
UHF[b]	13.14
B3-LYP[b]	13.16
UMP2(full)[b]	12.99
experimental	13.15[c]

[a] 6-31G(d) basis set used throughout. [b] Values obtained with Truhlar's hindered rotor approximation[48] for the $^\bullet CH_2$ torsion in the cyclopropylcarbinyl radical and scaled harmonic frequencies for all other modes. Optimum low-frequency scale factors from ref 19 of 0.9061 (UHF), 1.0013 (B3-LYP), and 1.0214 (UMP2(full)), respectively, are used. [c] From ref 25.

the cyclopropylcarbinyl radical may fragment in the ring-opening reaction.

The B3-LYP/6-31G(d) and UHF/6-31G(d) methods both give frequency factors that are in very good agreement with experiment while the UMP2(full)/6-31G(d) frequency factor is somewhat lower. This discrepancy can be traced to the unusually low frequency ($\nu = 50.4$ cm^{-1}) calculated by UMP2-(full)/6-31(d) for the methylene torsion in the cyclopropylcarbinyl radical. The UHF ($\nu = 123.9$ cm^{-1}) and B3-LYP/6-31G(d) ($\nu = 142.1$ cm^{-1}) frequencies for this mode are significantly higher, resulting in larger Arrhenius frequency factors. We note that the Truhlar approximation[48] improves the standard harmonic oscillator results for all three methods but particularly so for the otherwise poor UMP2 quantity, with the resulting UMP2 frequency factor now differing from those of the other two methods (and experiment) by a factor of just 1.5. Owing to the good agreement with experiment obtained with B3-LYP/6-31G(d) and our selection previously of B3-LYP for geometries and frequencies, we recommend use of this method (in combination with Truhlar's approximation for the $^\bullet CH_2$ torsion) in the calculation of the Arrhenius frequency factors for this and closely related reactions.

(9) Recommended Procedure. On the basis of the above analysis, we are able to select a procedure for the calculation of the energy profile and rate constants for the ring opening of the cyclopropylcarbinyl radical and related reactions, and the conclusions are summarized here. The CBS-RAD method is chosen for the calculation of energies and the B3-LYP/6-31G-(d) technique is chosen for the evaluation of geometries and vibrational frequencies. The scaled B3-LYP frequencies in conjunction with the Truhlar approximation[48] for the $^\bullet CH_2$ torsion are used to evaluate the Arrhenius frequency factors. The combination of B3-LYP/6-31G(d) geometries and frequencies with CBS-RAD energies has been previously referred to as CBS-RAD(B3-LYP,B3-LYP),[11e] and it is this technique that is now applied to all of the ring-opening reactions investigated in the present work. In the interests of simplicity, this level of theory will be referred to as CBS-RAD in the following sections.

We note that not only does B3-LYP perform well for geometries and frequencies but it also performs quite well for the barrier and reaction enthalpy, giving results to within approximately 5 kJ mol^{-1} of CBS-RAD values. We submit that, in cases where computational resources are modest or the system of interest is large so that CBS-RAD is not practical, B3-LYP provides a viable alternative. Although the uncertainty is a little larger than that for CBS-RAD, it appears that B3-LYP, particularly with a larger basis set, provides a good description of the ring opening of the cyclopropylcarbinyl radical and it should therefore be applicable to closely related systems.

(10) Application of the Recommended Procedure to the Ring Opening of the Cyclopropylcarbinyl Radical. Inclusion of zero-point vibrational and temperature effects leads to the CBS-RAD results shown in Table 6. The theoretical Arrhenius function for the ring opening of the cyclopropylcarbinyl radical is $\log(k/\mathrm{s}^{-1}) = (13.16) - (31.2)/\theta$ ($\theta = 2.3RT$ kJ mol^{-1}). This function leads to a rate constant at 298 K of $k = 4.9 \times 10^7$ s^{-1}. These results are in very good agreement with the experimental Arrhenius function ($\log(k/\mathrm{s}^{-1}) = (13.15) - (29.5)/\theta$), which corresponds to a rate constant at 298 K of $k = 9.6 \times 10^7$ s^{-1}.

Table 6. Comparison of Experimental and Best Theoretical[a] Parameters for the Ring Opening of the Cyclopropylcarbinyl Radical[b]

	theory	experiment
E_a (kJ mol^{-1})	31.2[c]	29.5[d]
ΔH (kJ mol^{-1})	−10.8[e]	−8.5,[f] −9.6,[g] −13.2,[h] −21.0[i]
$\log(A/\mathrm{s}^{-1})$	13.16	13.15[j]
k (s^{-1})	4.9×10^7 [k]	9.6×10^7 [k]

[a] CBS-RAD values obtained with use of B3-LYP/6-31G(d) geometries and frequencies (see text), i.e., CBS-RAD(B3-LYP,B3-LYP). [b] At 298 K. [c] At 0 K, $E_a = \Delta H^{\ddagger}(0) = 30.0$ kJ mol^{-1}. [d] From ref 25. [e] At 0 K, $\Delta H(0) = -12.4$ kJ mol^{-1}. [f] From refs 25 and 26. See text. [g] From experimental heats of formation of reactant and product. See text. [h] From refs 23 and 26. [i] From ref 22, corrected to 298 K. [j] From ref 25. [k] Calculated from Arrhenius parameters.

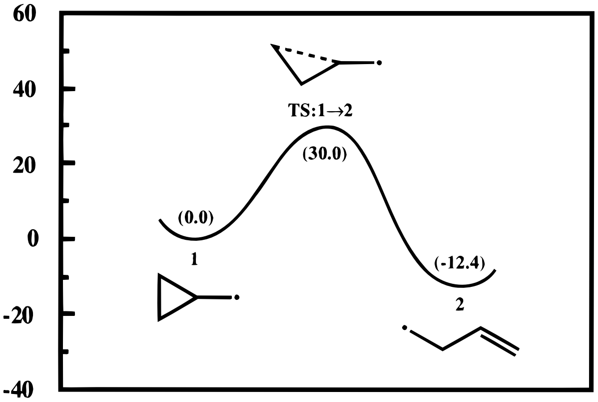
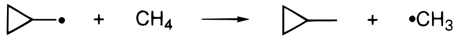


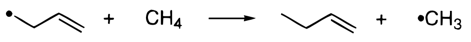
Figure 2. Schematic CBS-RAD energy profile for the ring opening of the cyclopropylcarbinyl radical (**1**). Relative energies (kJ mol^{-1}) are given in parentheses.

We predict an exothermicity for the ring-opening reaction of 10.8 kJ mol^{-1} at 298 K. This supports the lower experimental estimates (8.5, 9.6, and 13.2 kJ mol^{-1}) of the exothermicity. The calculated reaction profile for the ring opening of the cyclopropylcarbinyl radical is shown in Figure 2.

As previously mentioned, there is considerable uncertainty in the experimental heats of formation of the species involved in the ring-opening reaction. We have calculated these heats of formation in two separate ways and the results are presented in Table 7. First, we have evaluated the heats of formation at 298 K from atomization reactions.[49] Second we have employed the isodesmic reactions[50,51] shown in reactions 5 and 6:



(5)



(6)

With the latter procedure, the heat of formation of the cyclopropylcarbinyl radical is obtained by combining the

---

(49) See, for example: Nicolaides, A.; Rauk, A.; Glukhovtsev, M. N.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 17460−17464.

(50) Raghavachari, K.; Stefanov, B. B.; Curtiss, L. A. *J. Chem. Phys.* **1997**, *106*, 6764.

(51) Nicolaides, A.; Radom, L. *Mol. Phys.* **1996**, *88*, 759.

Table 7. Calculated and Experimental Heats of Formation ($\Delta H_{f\ 298}$, kJ mol^{-1}) of the Species Involved in the Ring Opening of the Cyclopropylcarbinyl Radical

	calcd		
	atomization	isodesmic	exptl
1	229.1[a]	218.5[b]	213.8 ± 25[d]
2	218.4[a]	209.2[c]	204.2 ± 2.3[e]

[a] Calculated from atomization reactions[49] with use of the CBS-RAD(B3-LYP,B3-LYP) reaction enthalpies. [b] Calculated from the isodesmic reaction 5 with use of the CBS-RAD(B3-LYP,B3-LYP) reaction enthalpies. [c] Calculated from the isodesmic reaction 6 with use of the CBS-RAD(B3-LYP,B3-LYP) reaction enthalpies. [d] From ref 27. [e] Calculated from the heat of formation of 1-butene and the bond dissociation energy of the *n*-propyl radical. See text.

theoretical (CBS-RAD) enthalpy of reaction 5 with the experimental heats of formation of the methyl radical, methane, and methylcyclopropane.[52] The heat of formation of the but-3-enyl radical is obtained in an analogous way, using 1-butene in place of methylcyclopropane (see reaction 6). The heats of formation obtained by the two different methods differ by about 10 kJ mol^{-1}. The difference can be traced to an overestimation by the atomization method of the heats of formation of 1-butene and methylcyclopropane by approximately this amount. The isodesmic method is aimed at correcting any such problems and therefore should generally give the more reliable heats of formation. Although the experimental results have significant uncertainties, they are closer to the isodesmic heats of formation than to those calculated from atomization reactions.

The enthalpies of reactions 5 and 6 are equivalent to the radical stabilization energies of the cyclopropylcarbinyl and but-3-enyl radicals, respectively. The CBS-RAD radical stabilization energy for the cyclopropylcarbinyl radical at 298 K is 26.0 kJ mol^{-1}, indicating significant stabilization of the radical center by the cyclopropyl group. The but-3-enyl radical is calculated to have a somewhat smaller radical stabilization energy at 298 K of 12.3 kJ mol^{-1}.

One further property of interest is the barrier to rotation of the methylene group bearing the unpaired electron in the cyclopropylcarbinyl radical. The Arrhenius activation energy for this process has been measured[53] as 11.3 ± 0.8 kJ mol^{-1} between 125 and 155 K. The CBS-RAD procedure predicts a barrier at 0 K of 13.4 kJ mol^{-1}, corresponding to an Arrhenius activation energy at 140 K of 14.6 kJ mol^{-1}. The B3-LYP Arrhenius activation energies at 140 K are 12.4 (6-31G(d)), 14.0 (6-311+G(d,p)), and 14.5 (6-311+G(3df,2p)) kJ mol^{-1}. These results indicate that both CBS-RAD and B3-LYP can prove useful in the calculation of such rotational barriers.

We are now in a position to apply our best levels of theory to the heterosubstituted cyclopropylcarbinyl radical ring openings. The good agreement obtained between CBS-RAD and experiment for the unsubstituted ring opening lends confidence to the proposal that it is a suitable theoretical method for application to slightly modified systems. Bearing in mind that there are sometimes systems of interest for which CBS-RAD is not a practical technique, either because the system is large or the resources available are limited, we continue to present the B3-LYP results to demonstrate the performance of this computationally less demanding method. The following sections aim to compare and contrast the various systems using uniform treatments and to examine some of the indicated trends.

B. The Ring Opening of the 1-Aziridinylcarbinyl Radical. Nitrogen substitution of the cyclopropylcarbinyl radical at the 1-position affords the 1-aziridinylcarbinyl radical (**3**). As shown in reaction 2 (Scheme 1), homolysis of either C−N bond results in the formation of the 2-(*N*-methylidene)ethyl radical (**4**). A substituted version of this rearrangement has been suggested to be involved in the 1,2-amino shift effected by β-lysine aminomutase.[8] Both the forward (ring-opening) and reverse (ring-closure) reactions have been implicated in this process.

The lowest energy conformers (B3-LYP/6-31G(d)) of the reactant (**3**), transition structure (**TS:3→4**), and product (**4**) are shown in Figure 3. The calculations predict that, in contrast to the cyclopropylcarbinyl radical, the 1-aziridinylcarbinyl radical prefers a "perpendicular" conformation so that the singly occupied orbital at the radical center is oriented to permit maximum interaction with the nitrogen lone pair, leading to a quite short exocyclic C−N bond (1.393 Å). This conformational preference is in agreement with observed hyperfine couplings obtained from a low-temperature ESR study.[54] The CBS-RAD barrier to rotation about the N−CH$_2^{\bullet}$ bond is calculated to be 14.4 kJ mol^{-1} at 0 K. Rotation about the N−CH$_2^{\bullet}$ bond during the course of the reaction results in the conformations of the product and transition structure being similar to those found in the case of the ring opening of the cyclopropylcarbinyl radical (Figure 1).

Table 8 shows calculated thermochemical parameters for the ring opening of the 1-azirdinylcarbinyl radical at 0 K. An energy profile for this reaction is included in Figure 4. The barrier for the bond fission is very close to that predicted (and observed) for the cyclopropylcarbinyl radical. The B3-LYP results can be seen to provide a useful alternative to the more expensive CBS-RAD technique. However, increasing the size of the basis set with B3-LYP does not result in smooth convergence of properties such as the barrier and reaction enthalpy. Indeed, for the majority of the B3-LYP results presented in this study, the large (6-311+G(3df,2p) and small (6-31G(d)) basis sets tend to be in good agreement with one another while the intermediate basis set (6-311+G(d,p)) often exhibits a small but noticeable deviation.

Table 9 contains the calculated Arrhenius parameters, the reaction enthalpy, and the rate constant at 298 K. The Arrhenius frequency factor in this case is approximately double that calculated for the ring opening of the cyclopropylcarbinyl radical. This difference is almost solely responsible for the approximately 2-fold increase in rate predicted to accompany nitrogen substitution. We are not aware of any experimental determination of the rate constant for the ring opening of the 1-aziridinylcarbinyl radical.

C. The Ring Opening of the Oxiranylcarbinyl Radical. Heterosubstitution of the cyclopropylcarbinyl radical in the 2-position reduces the symmetry of the cyclic structure in a way that allows two distinct ring-opening reactions. This situation is exemplified by the ring opening of the oxiranylcarbinyl radical (**5**) (Scheme 1, reaction 3). Cleavage of the C−O bond affords the allyloxy radical (**6**), whereas C−C cleavage leads to the vinyloxymethyl radical (**7**). Experimentally, ring opening of simple alkyl-substituted oxiranylcarbinyl radicals proceeds with exclusive formation of substituted allyloxy radicals,[55] although appropriate substitution of the parent oxirane can cause C−C cleavage to occur.[56]

---

[52] Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Ref. Data* **1988**, *17* (Suppl. 1).

[53] Walton, J. C. *Magn. Reson. Chem.* **1987**, *25*, 998−1000.

[54] Danen, W. C.; West, C. T. *J. Am. Chem. Soc.* **1974**, *96*, 2447−2453.

[55] See, for example: (a) Davies, A. G.; Muggleton, B. *J. Chem. Soc., Perkin Trans. 2* **1979**, 589. (b) Barton, D. H. R.; Motherwell, R. S. H.; Motherwell, W. B. *J. Chem. Soc., Perkin. Trans. 1* **1981**, 2363.

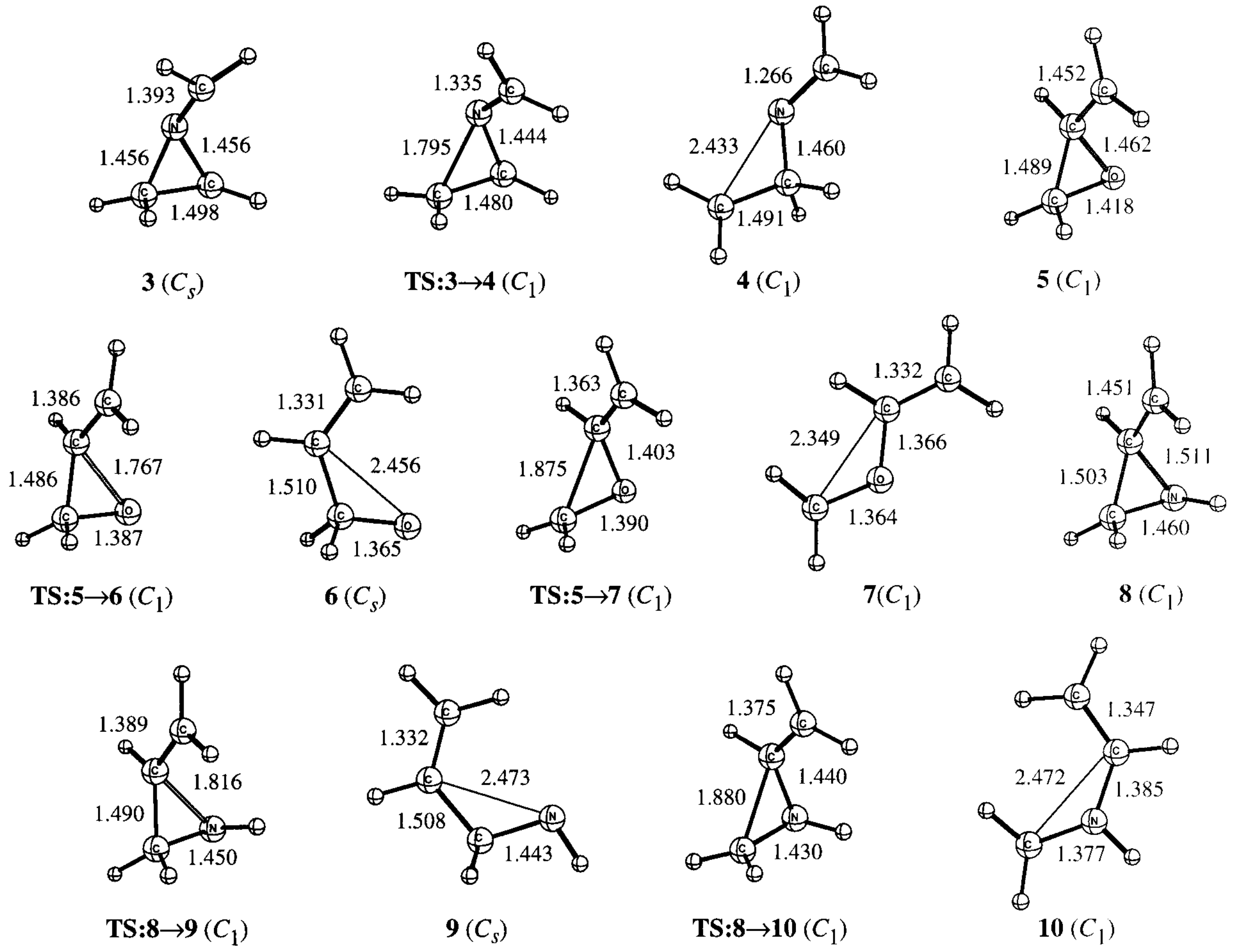


Figure 3. B3-LYP/6-31G(d) bond lengths (Å) for the structures involved in various heterosubstituted analogues of the ring opening of the cyclopropylcarbinyl radical.

Table 8. Calculated Thermochemical Parameters (kJ mol^{-1}) for the Ring Opening of the 1-Aziridinylcarbinyl Radical

	$\Delta H^{\ddagger}$(0 K)	ΔH(0 K)
CBS-RAD	29.0	−46.4
B3-LYP/6-31G(d)	30.3	−45.4
B3-LYP/6-311+G(d,p)	28.9	−48.4
B3-LYP/6-311+G(3df,2p)	29.5	−45.7

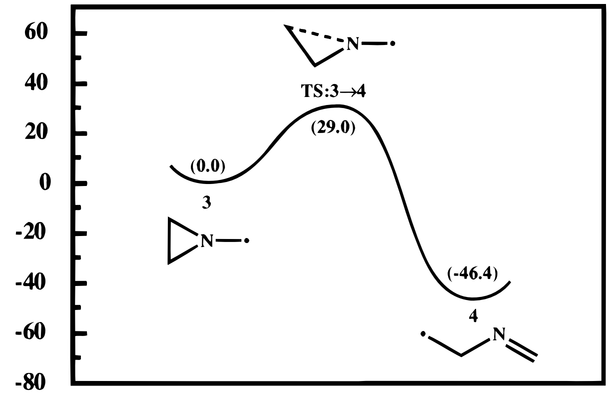


Figure 4. Schematic CBS-RAD energy profile for the ring opening of the 1-aziridinylcarbinyl radical (**3**). Relative energies (kJ mol^{-1}) are given in parentheses.

For many years, attempts to observe the oxiranylcarbinyl radical or to measure the rate of C−O bond cleavage had proved unsuccessful.[57] Recently, however, the oxiranylcarbinyl radical has been reportedly trapped with use of the alkyl nitrate method,[58] and an approximate rate constant for the ring opening to the allyloxy radical has been measured.[59] This rate constant was derived for a cyclohexyl-substituted oxiranylcarbinyl radical by using competition between the unimolecular rearrangement and bimolecular trapping with 5 M thiophenol at 298−303 K.

Table 9. Calculated Arrhenius Parameters for the Ring Opening of the 1-Aziridinylcarbinyl Radical[a]

	theory
E_a (kJ mol^{-1})	31.1
ΔH (kJ mol^{-1})	−44.1
log(A/s^{-1})	13.43
k(s^{-1})	9.5 × 10^{7} [b]

[a] At 298 K. [b] Calculated from theoretical Arrhenius parameters.

---

(56) See, for example: (a) Stogryn, E. L.; Gianni, M. H. *Tetrahedron Lett.* **1970**, 3025. (b) Cook, M.; Hares, O.; Johns, A.; Murphy, J. A.; Patterson, C. W. *J. Chem. Soc., Chem. Commun.* **1986**, 1419.

(57) (a) Laurie, D.; Nonhebel, D. C.; Suckling, C. J.; Walton, J. C. *Tetrahedron* **1993**, *49*, 5869−5872. (b) Dickinson, J. M.; Murphy, J. A.; Patterson, C. W.; Wooster, N. F. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1179−1184.

(58) Grossi, L.; Strazzari, S. *J. Chem. Soc., Chem. Commun.* **1997**, 917−918.

(59) Krishnamurthy, V.; Rawal, V. H. *J. Org. Chem.* **1997**, *62*, 1572−1573.

(60) The reported rate constant of 3.2 × 10^{10} s^{-1} was derived assuming a negliglible rate for ring closure of the allyloxy radical. Our calculations indicate that the reaction of **5**→**7** is only midly exothermic and that the rate constant for the reverse reaction is 3.9 × 10^{8} s^{-1}, suggesting that the reported ring-opening rate constant is a lower bound. Detailed analysis of the kinetic implications of the trapping experiment will be published elsewhere. See also: Ziegler, F. E.; Petersen, A. K. *J. Org. Chem.* **1995**, *60*, 2666−2667.

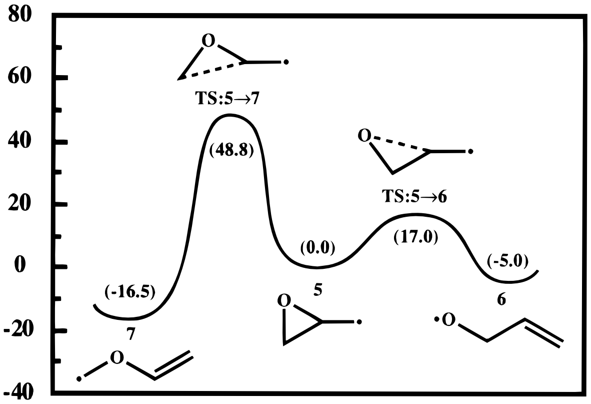


Figure 5. Schematic CBS-RAD energy profile for the ring openings of the oxiranylcarbinyl radical (**5**). Relative energies (kJ mol^{-1}) are given in parentheses.

Table 10. Calculated Thermochemical Parameters (kJ mol^{-1}) for the Ring Opening of the Oxiranylcarbinyl Radical

	C−O cleavage		C−C cleavage	
	$\Delta H^{\ddagger}$(0 K)	ΔH(0 K)^a	$\Delta H^{\ddagger}$(0 K)	ΔH(0 K)^a
CBS-RAD	17.0	−5.0	48.8	−16.5
B3-LYP/6-31G(d)	16.6	−19.1	50.8	−20.0
B3-LYP/6-311+G(d,p)	12.4	−25.8	46.3	−27.3
B3-LYP/6-311+G(3df,2p)	14.3	−19.9	45.9	−29.3

[a] Energy difference between the oxiranylcarbinyl radical and the lowest energy conformer of the ring-opened product.

Table 11. Calculated Arrhenius Parameters for the Ring Opening of the Oxiranylcarbinyl Radical[a]

	C−O cleavage	C−C cleavage
E_a (kJ mol^{-1})	18.3	50.7
ΔH (kJ mol^{-1})	−4.5	−16.0
log(A/s^{-1})	12.92	13.06
k(s^{-1})	$5.2 \times 10^{9\ b}$	$1.5 \times 10^{4\ b}$

[a] At 298 K. [b] Calculated from theoretical Arrhenius parameters.

A ratio of trapped, unrearranged to rearranged products of 57.5:1 along with some kinetic assumptions[60] results in an approximate rate constant for C−O cleavage of 3.2×10^{10} s^{-1}.[59]

The system shown in reaction 3 has been investigated previously with ab initio techniques.[61] This study has considered many of the finer details involved in the rearrangements and the reader is referred to that work for a thorough discussion of some important aspects of the ring openings. In the current work, we wish to provide more definitive values for the reaction barriers, enthalpies, and rate constants, with our uniform high level treatment allowing meaningful comparisons with the other ring openings.

Figure 5 shows the calculated CBS-RAD reaction profile for the two possible ring-opening modes of the oxiranylcarbinyl radical. The calculated thermochemical parameters may be found in Tables 10 and 11. The lowest energy conformers (B3-LYP/6-31G(d)) of the species involved in the reaction are shown in Figure 3. There are two stable conformers for each of the product radicals (**6** and **7**), but in the current discussion only the lowest energy conformations will be discussed.[62]

In agreement with all previous work on this system, we find the barrier for C−O bond cleavage (producing the allyloxy radical **6**) to be significantly lower than that associated with C−C cleavage (producing the vinyloxymethyl radical **7**). Although the calculated rate constant for C−O cleavage of 5.2×10^9 s^{-1} is approximately an order of magnitude less than the approximate experimental rate constant of 3.2×10^{10} s^{-1},[59] it should be noted that the activation energy need only be lowered by 5 kJ mol^{-1} to remove this discrepancy,[60] suggesting continued good agreement between CBS-RAD and experiment. It is unlikely that experimental information for C−C cleavage in the unsubstituted system will ever be obtained, but the calculations suggest a barrier of around 50 kJ mol^{-1} with an associated rate constant of 1.5×10^4 s^{-1}. The CBS-RAD barrier (0 K) to methylene rotation about the exocyclic C−C bond in **5** is calculated to be 16.3 kJ mol^{-1}.

The relative stability of the two possible products (**6** and **7**) is a matter of some contention. Previous small basis set, high level calculations have indicated that the allyloxy radical (**6**) is lower in energy than the vinyloxymethyl radical (**7**). For example, QCISD(T)/6-31G(d) predicts an energy difference of 7.9 kJ mol^{-1} in favor of the allyloxy radical.[61,63] This is in agreement with the CCSD(T)/6-31+G† component of the present CBS-RAD calculation, which has the allyloxy radical 5.3 kJ mol^{-1} below the vinyloxymethyl radical. On the other hand, the best results in our present study, which correspond to correlated *large* basis set calculations, all predict that the vinyloxymethyl radical (**7**) is favored over the allyloxy radical (**6**). The CBS-RAD estimate of the energy difference is 11.5 kJ mol^{-1}. Such a preference would be consistent with stabilization of the vinyloxymethyl radical arising from interaction of the singly occupied orbital with a p-type lone pair on oxygen or interaction of the oxygen lone pair with the C═C double bond. Interactions of this type cannot take place in the allyloxy radical.

Calculations in the current work indicate that the relative energies of **6** and **7** are subject to a significant basis set effect at the MP2, MP4, QCISD(T), and B3-LYP levels of theory. This contrasts with the results of an investigation at the SCF level,[63] which showed the energy difference between **6** and **7** to be relatively insensitive to the size of the basis set. At the MP2 level, the effect of increasing the basis set from 6−311G(d,p) to 6-311+G(3df,2p) is to lower the energy of the vinyloxymethyl radical, with respect to the allyloxy radical, by 16.8 kJ mol^{-1}. The basis set effects at MP4 and QCISD(T) are in the same direction but with slightly smaller magnitudes. The B3-LYP results in Table 10 also follow the same trend, with an 8.5 kJ mol^{-1} increase in the stability of **7** with respect to **6** accompanying the change in basis set from 6-31G(d) to 6-311+G(3df,2p). We conclude that use of a large basis set is essential for the reliable estimation of the relative stabilities of the two possible ring-opened products.

As noted above, the CBS-RAD technique predicts the vinyloxymethyl radical to be 11.5 kJ mol^{-1} more stable than the allyloxy radical. The large-basis-set B3-LYP results are in agreement with these relative energies, giving an energy difference of 9.4 kJ mol^{-1} in favor of **7** over **6**. There is less good agreement between the B3-LYP values and the CBS-RAD predictions regarding the positioning of the cyclic structure (**5**) with respect to the ring-opened products. Both ring openings are more exothermic with B3-LYP than with CBS-RAD. Evaluation of the relative energies of **5**, **6**, and **7** at the G2 level of theory[64] supports the CBS-RAD results.

We find that the thermodynamically preferred product of the

---

(61) Pasto, D. J. *J. Org. Chem.* **1996**, *61*, 252−256.

(62) For more information concerning the conformational aspects of this system, see Tables S1 and S2 of the Supporting Information or ref 61.

(63) Pasto, D. J.; Cottard, F.; Picconato, C. *J. Org. Chem.* **1994**, *59*, 7172−7177.

(64) G2 calculations carried out with use of B3-LYP/6-31G(d) geometries and frequencies predict the enthalpies of C−O and C−C cleavage to be −6.7 and −17.0 kJ mol^{-1}, respectively.

Table 12. Calculated Thermochemical Parameters (kJ mol^{-1}) for the Ring Opening of *cis*- and *trans*-2-Aziridinylcarbinyl Radical

	C−N cleavage			C−C cleavage		
	ΔH‡(0 K)		Δ*H*(0 K)^c	ΔH‡(0 K)		Δ*H*(0 K)^c
CBS-RAD	15.4^a	16.6^b	−23.7	40.8^a	38.0^b	−61.8
B3-LYP/6-31G(d)	15.4^a	18.6^b	−30.8	40.9^a	37.8^b	−63.3
B3-LYP/6-311+G(d,p)	13.0^a	15.9^b	−36.6	35.3^a	32.8^b	−79.0
B3-LYP/6-311+G(3df,2p)	13.8^a	16.2^b	−33.5	35.7^a	33.5^b	−79.4

[a] Energy difference between the *cis*-2-aziridinylcarbinyl radical and the cis−transition structure. [b] Energy difference between the *trans*-2-aziridinylcarbinyl radical and the trans-transition structure. [c] Energy difference between the *cis*-2-aziridinylcarbinyl radical and the lowest energy conformer of the ring-opened product.

Table 13. Calculated Arrhenius Parameters for the Ring Opening of *cis*-2-Aziridinylcarbinyl Radical[a]

	C−N cleavage	C−C cleavage
E_a (kJ mol^{-1})	16.7	42.8
Δ*H* (kJ mol^{-1})	−23.7	−63.2
log(*A*/s^{-1})	12.92	13.03
k(s^{-1})	9.8×10^9 [b]	3.4×10^5 [b]

[a] At 298 K. [b] Calculated from theoretical Arrhenius parameters.

ring opening is the vinyloxymethyl radical (**7**) whereas the kinetically preferred pathway leads to the allyloxy radical (**6**). Thus the ring opening of the oxiranylcarbinyl radical (**5**) is an example of a reaction in which kinetics does not follow thermodynamics. A possible rationalization of this finding comes from noting that the atomic arrangement required for the stabilizing interactions of the oxygen lone pair with the radical center and/or the C=C double bond of the vinyloxymethyl radical (**7**) is not yet present in the ring-opening transition structure **TS:5→7** (Figure 3).

D. The Ring Opening of the 2-Aziridinylcarbinyl Radical. The ring opening of the 2-aziridinylcarbinyl radical (**8**) (Scheme 1, reaction 4) bears similarities to that of the oxiranylcarbinyl radical discussed above. There are two possible ring-opened products, namely the allylaza radical (**9**) resulting from C−N cleavage, and the vinylazamethyl radical (**10**) derived from homolysis of the C−C bond. Experimentally, C−N homolysis is preferred[65] but appropriate substitution can favor C−C cleavage.[66] This system has also received some previous theoretical attention[61] and, as with the ring opening of the oxiranylcarbinyl radical, the reader is referred to that work for a thorough discussion. We are unaware of any experimental determination of rate constants involved in the ring opening of the 2-aziridinylcarbinyl radical.

An additional degree of complexity is introduced into this ring opening because of the possibility of cis and trans isomers of the 2-aziridinylcarbinyl radical. The CBS-RAD barriers to methylene torsion for the two isomers at 0 K are 18.6 (cis) and 13.3 (trans) kJ mol^{-1}, respectively. Table 12 shows the barriers for the ring opening of both isomers. For the reaction enthalpies in Table 12, the summary information in Table 13, the structures shown in Figure 3, and the reaction profile depicted in Figure 6, we have only included results for the ring opening of the *cis*-2-aziridinylcarbinyl radical (**8**) to the lowest energy conformations of the product radicals (**9** and **10**).[67]

The cleavage of the C−N bond is predicted to be a low-energy process and is therefore expected to proceed rapidly. Our best estimate of the rate constant is 9.8×10^9 s^{-1}.

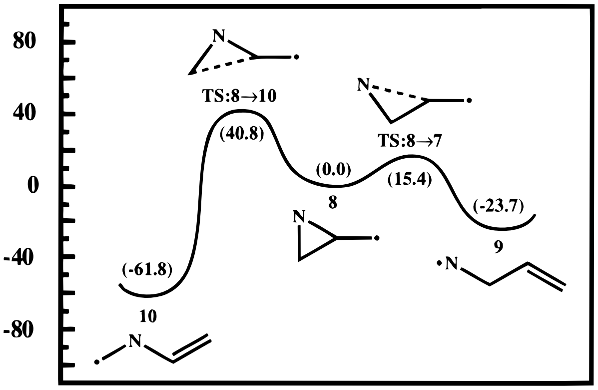


Figure 6. Schematic CBS-RAD energy profile for the ring openings of the *cis*-2-aziridinylcarbinyl radical (**8**). Relative energies (kJ mol^{-1}) are given in parentheses.

Formation of the vinylazamethyl radical (**10**) by way of C−C bond cleavage is predicted to be several orders of magnitude slower, with an activation energy (42.8 kJ mol^{-1}) more than twice that calculated (16.7 kJ mol^{-1}) for the formation of the allylaza radical (**9**).

The relative stabilities of the ring-opened products are quite clear-cut. The allylaza radical, resulting from the kinetically favored pathway (C−N cleavage), is predicted to lie approximately 40 kJ mol^{-1} higher in energy than the vinylazamethyl radical, which results from the slower C−C cleavage. Thus, as for the ring opening of the oxiranylcarbinyl radical, kinetics does not follow thermodynamics. The absolute discrepancies between B3-LYP and CBS-RAD are somewhat larger in this case than in the ring opening of the oxiranylcarbinyl radical, but each of these techniques predicts both modes of ring opening of the 2-aziridinylcarbinyl radical to be quite exothermic, a situation reminiscent of the ring opening of the 1-aziridinylcarbinyl radical.

Concluding Remarks

The theoretical aspects of ring opening of the cyclopropylcarbinyl radical have been thoroughly investigated in this study. We find that B3-LYP/6-31G(d) performs well for geometries, zero-point vibrational energies, temperature corrections, and the Arrhenius frequency factor. The use of the CBS-RAD(B3-LYP,B3-LYP) procedure to calculate activation energies and reaction exothermicities gives results in good agreement with experiment. The B3-LYP method when used in conjunction with an adequate basis set also proves useful for the calculation of energies, and may provide a viable alternative in cases where CBS-RAD is computationally too expensive.

The good performance of the CBS-RAD procedure in describing the ring opening of the cyclopropylcarbinyl radical lends confidence to its ability to predict the effects of heterosubstitution on this ring opening. Nitrogen substitution at the 1-position leaves the kinetics of the ring opening virtually

---

(65) See, for example: (a) Dickinson, J. M.; Murphy, J. A. *J. Chem. Soc., Chem. Commun.* **1990**, 434−436. (b) Dickinson, J. M.; Murphy, J. A. *Tetrahedron* **1992**, *48*, 1317−1326.

(66) Schwan, A. L.; Refvik, M. D. *Tetrahedron Lett.* **1993**, *34*, 4901−4904.

(67) For further information on the various conformational possibilities, see Tables S1 and S2 of the Supporting Information or ref 61.

unaltered. However, the ring opening of the 1-aziridinylcarbinyl radical is found to be significantly more exothermic than its hydrocarbon analogue. There is good agreement between the B3-LYP and CBS-RAD results for this system.

Oxygen substitution at the 2-position results in two ring-opening possibilities. Cleavage of the C−O bond is found to dominate the kinetics and is predicted to be at least an order of magnitude faster than the ring opening for the parent cyclopropylcarbinyl radical. The CBS-RAD activation energy is in good agreement with a recent experimental estimate. Homolysis of the C−C bond of the oxiranylcarbinyl radical is predicted to be significantly slower than the ring opening in the unsubstituted parent.

We find the vinyloxymethyl radical to lie lower in energy than the allyloxy radical, making the ring opening of the oxiranylcarbinyl radical an example of a system where the kinetics does not follow the thermodynamics. The calculated relative energies of the two possible ring-opened products are found to be sensitive to the size of the basis set and to the theoretical procedure used.

C−N bond fission in the 2-aziridinylcarbinyl radical is predicted to be slightly faster than C−O cleavage in the oxiranylcarbinyl radical and in fact is the fastest of all the ring openings investigated in this study. C−C cleavage in the 2-aziridinylcarbinyl radical is predicted to be slower than the analogous process in the cyclopropylcarbinyl radical but faster than C−C cleavage in the oxiranylcarbinyl radical. As found for the oxiranylcarbinyl radical, the kinetically favored product of the ring opening of the 2-aziridinylcarbinyl radical is not thermodynamically favored.

Overall, heterosubstution in the 1-position has little effect on the kinetics of ring opening. Heterosubstitution in the 2-position has the effect of slowing C−C cleavage with respect to the unsubstituted system while accelerating the C−X bond fission. In addition, we find that heterosubstitution in the 2-position produces a situation where the kinetically and thermodynamically favored products are not the same.

Acknowledgment. We gratefully acknowledge generous allocations of time on the Fujitsu VPP300 and SGI Power Challenge computers of the Australian National University Supercomputing Facility. We would also like to thank the British Council for awarding D.M.S a Partnerships for Excellence Postgraduate Bursary to study at the University of Newcastle upon Tyne.

Supporting Information Available: Total CBS-RAD energies (Table S1) and GAUSSIAN 94 archive entries for the MP2/CbsB3 calculation for all relevant structures (Table S2) (13 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

JA980635M