# Theoretical Prediction of the Stability and Intramolecular Rearrangement Reactions of Heteroanalogues of Cyclopropylcarbene: 2-Oxiranyl-, 2-Aziridinyl-, and 1-Aziridinylcarbene

Christian Mück-Lichtenfeld*

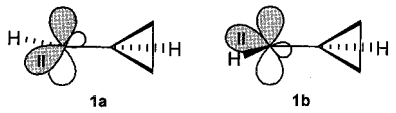
*Organisch-Chemisches Institut, Westfälische Wilhelms-Universität, Corrensstrasse 40, D-48149 Münster, Germany*

*Received September 8, 1999*

Ab initio studies have been carried out on the experimentally uncharacterized 2-oxiranyl- (**8**), fluoro-2-oxiranyl- (**15**), 2-aziridinyl- (**21**), and 1-aziridinylcarbene (**29**) on the B3LYP/6-31G(d) and CCSD-(T)/6-31G(d,p)//MP2/6-31G(d,p) levels of theory. Like the parent cyclopropylcarbene (**1**), the $\beta$-heterosubstituted carbenes **8** and **21**—intermediates in the Eschenmoser-Tanabe fragmentation—are predicted to give either ethyne extrusion or ring expansion reactions, depending on the initial conformation. The barriers for these reactions are low (<6 kcal mol$^{-1}$), while the interconversion of the carbene conformers requires higher energies. NBO analyses show that the donor−acceptor interactions between the carbene frontier orbitals and $\sigma$-bond orbitals in the oxiranyl and aziridinyl ring destabilize the compounds kinetically. 2-Oxiranyl- and 2-aziridinylcarbenes with a fixed cis (=exo) conformation are predicted to rearrange to the heteroanalogue derivatives of cyclobutene. The fluoro-substituted 2-oxiranylcarbene **15** is predicted to rearrange to the substituted oxete via one equilibrated conformer, due to the low barrier of the C−(CF)-rotation. 1-Aziridinylcarbene **29** is the thermodynamically most stable of the investigated carbenes; however, the fragmentation into HCN and ethene is a facile reaction with a calculated barrier of 15 kcal mol$^{-1}$, which confirms experiments.

## Introduction

Carbenes are highly reactive intermediates which have received attention from both experimental and theoretical chemists through many decades.[1] Derivatives of cyclopropylcarbene **1** have found widespread application in organic synthesis;[2] the first report of the generation of unsubstituted **1** by decomposing the sodium salt of the tosyl hydrazone dates back to 1960.[3] In this compound, the electron deficiency is stabilized by $\pi$ density donation from the cyclopropyl ring into the carbene p orbital. It may adopt two distinct conformations, *cis*-**1a** and *trans*-**1b**.[4] Computational studies have been performed on **1** on various theoretical levels.[5]




**1a** **1b**

**1** has also been prepared in the gas phase by flash vacuum pyrolysis and photolytically from cyclopropyl diazomethane.[6] The temperature-dependent product distribution has been explained by the different activation barriers leading to the two conformers **1a** and **1b** in the nitrogen elimination step. These CH-rotamers have a barrier of interconversion higher than the activation energies which lead to the respective products (Scheme 1). **1a** yields mainly cyclobutene **2**, and **1b** fragments to ethene and ethyne (**5** + **6**). Two other possible reaction products, bicyclo[1.1.0]butane **3** and methylenecyclopropane **4**, were not observed in these experiments.[7]

The sign of the singlet−triplet gap of **1** is controversial; earlier computational studies have concluded that $^3$**1** is the ground state, but more recent calculations favor the singlet by 2.15 kcal mol$^{-1}$.[8,9] Stereospecific fragmentation of 2,3-dimethylcyclopropylcarbene—even in the presence of triplet sensitizers—indicates the singlet nature of the intermediate,[10] even though reactions of cyclopropylcarbenes with vinylic substituents at the ring might involve triplet species.[11] Ring opening of $^3$**1** leads to a 1,4-diradical $^3$**7** (Scheme 2), with the configuration of the

* Fax: (+49) 251 8339772. E-mail: cml@uni-muenster.de.

(1) (a) Kirmse, W. *Carbene Chemistry*, 2nd ed.; Academic: New York, 1971. (b) Moss, R. A.; Jones, M., Jr. In *Reactive Intermediates*, Jones, M., Jr., Moss, R. A., Eds.; Wiley: New York, 1985; Vol. 3, pp 45−108 and cited references. (c) Wentrup, C. *Reactive Molecules*; Wiley: New York, 1984; pp 162−264.

(2) Arct, J.; Brinker, U. H. *Houben-Weyl, Methoden der Organischen Chemie*; Regitz, M., Ed.; Thieme: Stuttgart, 1995; Vol. E19b, pp 337−375.

(3) Friedman, L.; Shechter, H. *J. Am. Chem. Soc.* **1960**, *82*, 1002−1003.

(4) Hoffmann, R.; Zeiss, G. D.; Van Dine, G. W. *J. Am. Chem. Soc.* **1968**, *90*, 1485−1499.

(5) (a) Schoeller, W. W. *J. Org. Chem.* **1980**, *45*, 2161−2165. (b) Wang, B.; Deng, C. *Tetrahedron* **1988**, *44*, 7355−7362. (c) Shevlin, P. B.; McKee, M. L. *J. Am. Chem. Soc.* **1989**, *111*, 519−524.

(6) Chou, J.-H.; McKee, M. L.; Felippis, J. D.; Squillacote, M.; Shevlin, P. B. *J. Org. Chem.* **1990**, *55*, 3291−3295.

(7) The reaction of excited carbon atoms—generated in a carbon arc—with cyclopropane leads to **4** as the main product. This, however, may also be explained via formation of a cyclobutylidene by insertion of carbon in a C−C bond: Skell, P. S.; Engel, R. R. *J. Am. Chem. Soc.* **1966**, *88*, 4883−4890.

(8) Herges, R. *Angew. Chem.* **1994**, *106*, 261−283.

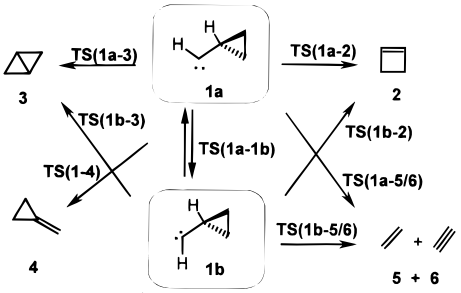
(9) To maintain lucidity throughout this work, only the multiplicities of triplet species are indicated by a superscript; all other structures referred to without superscript are singlet species.

(10) (a) Berson, J. A.; Bauer, W.; Campbell, M. M. *J. Am. Chem. Soc.* **1970**, *92*, 7515−7517. (b) Gallucci, R. R.; Jones, M., Jr. *J. Am. Chem. Soc.* **1976**, *98*, 7704−7711.

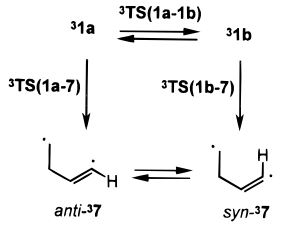
(11) Cummins, J. M.; Porter, T. A.; Jones, M., Jr. *J. Am. Chem. Soc.* **1998**, *120*, 6473−6476.

10.1021/jo991412x CCC: $19.00 
Published on Web 02/16/2000

**Scheme 1**

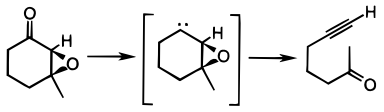



**Scheme 2**

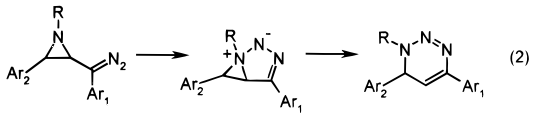



vinyl group being determined by the conformation of the carbene. Intersystem crossing to a singlet species is necessary to give either ring closure or fragmentation from $^3$**7**.

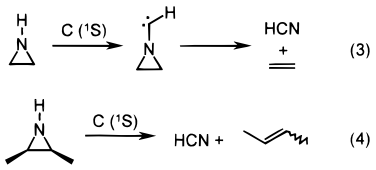
Oxygen-substituted three-membered rings adjacent to a carbenic center are formally involved in the fragmentation reaction of *N*-tosylhydrazones of cyclic 2,3-epoxyketones, first reported by Eschenmoser and Tanabe (eq 1).[12] The decomposition of the sodium salts of the *N*-tosylhydrazones (Bamford−Stevens reactions) or of oxadiazolinones[13] very likely involve concerted mechanisms, as can be concluded from a general discussion of the topological properties of the molecular orbitals involved in the fragmentation.[8] In contrast to this, the concerted pathway of the thermical fragmentation of diazirines[14] is forbidden and the free oxiranylcarbene is an intermediate. However, only 2,3-epoxy ketones with a trans conformation of the α-hydrogen and the carbene alkyl substituent gave uniform fragmentation products.[12c,13]


(1)

Information in the literature on "nitrogen-analogue" Eschenmoser reactions is sparse. Morioka and co-workers have investigated the potential precursor for a 2-aziridinylcarbene by applying Bamford−Stevens conditions to 2-aziridinyl-substituted *N*-tosylhydrazones. They observed a fast intramolecular cyclization of the diazo compound to dihydrotriazole, which isomerized to an *N*-alkylamino pyrazole (eq 2).[15] To our knowledge, no other approaches have been undertaken so far.


(2)

There is experimental evidence that decomposition to the olefin and HCN is the main reaction of 1-aziridinylcarbene, when generated from atomic carbon and aziridine (eq 3). The formation of 2-butene from *cis*-2,3-dimethylaziridine is not stereospecific (eq 4), thus suggesting a stepwise mechanism.[16]




A number of reports deal with the preparation and rearrangement reactions of 1-aziridinylcarbene complexes with transition metals, favorably tungsten.[17] These reactions do not involve uncomplexed carbene species and have to be considered as being irrelevant for explaining the reactivity of the free carbene.[18]

The intention of this computational study is to estimate the kinetic stability of cyclopropylcarbenes bearing a heterosubstituent (O,N) in the ring, assuming that the carbene can be generated as a distinct species. The conformational dependence of the reactivity is investigated. The thermodynamic stabilization exerted by the ring on the carbene is also estimated by choosing suitable reactions.

## Computational Methods

The initial geometry optimizations for ground state and transition structures (TS) were performed with semiempirical methods (AM1) using MOPAC93.[19] For the ab initio and DFT calculations of this study, the Gaussian 98 program was used.[20] The structures were optimized with the B3LYP hybrid density functional[21] using the standard 6-31G(d) basis set. Using the

(12) (a) Eschenmoser, A.; Felix, D.; Ohloff, G. *Helv. Chim. Acta* **1967**, *50*, 708−713. (b) Tanabe, M.; Crowe, D. F.; Dehn, R. L. *Tetrahedron Lett.* **1967**, 3943−3946. (c) Felix, D.; Müller, R. K.; Horn, U.; Joos, R.; Schreiber, J.; Eschenmoser, A. *Helv. Chim. Acta* **1972**, *55*, 1276−1319.

(13) MacAlpine, G. A.; Warkentin, J. *Can. J. Chem.* **1978**, *56*, 308−315.

(14) Borrevang, P.; Hjort, J.; Rapala, R. T.; Edie, R. *Tetrahedron Lett.* **1968**, *47*, 4905−4907.

(15) Morioka, M.; Kato, M.; Yoshida, H.; Ogata, T. *Heterocycles* **1996**, *43*, 1759−1765.

(16) Skell, P. S.; Havel, J. J.; McGlinchey, M. J. *Acc. Chem. Res.* **1973**, *6*, 97−105 and cited references.

(17) (a) Denise, B.; Parlier, A.; Rudler, H.; Vaissermann, J.; Daran, J. C. *J. Chem. Soc., Chem. Commun.* **1988**, 1303−1305. (b) Denise, B.; Massoud, A.; Parlier, A.; Rudler, H.; Daran, J. C.; Vaissermann, J.; Alvarez, C.; Patino, R.; Toscano, R. A. *J. Organomet. Chem.* **1990**, *386*, 51−62. (c) Denise, B.; Parlier, A.; Rudler, H.; Vaissermann, J. *J. Organomet. Chem.* **1995**, *494*, 43−51. (d) Lafollée-Bezzenine, S.; Parlier, A.; Rudler, H.; Vaissermann, J.; Daran, J. C. *J. Organomet. Chem.* **1998**, *567*, 83−100.

(18) In these cases, the fragmentation has been observed with chromium compounds and explained with a ring-expansion reaction. This reaction is equivalent to the ring expansion of *N*-acylaziridines to oxazolines.[17c]

(19) MOPAC93, Fujitsu Ltd. Stewart, J. J. P. MOPAC: A General Molecular Orbital Package. *Quantum Chem. Prog. Exch.* **1990**, *10*, 86.

(20) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A., Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr., Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; and Pople, J. A. Gaussian98, Revision A.5; Gaussian, Inc., Pittsburgh, PA, 1998.

(21) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652.

DFT structures, an MP2(fc)[22] optimization with the 6-31G-(d,p) basis set, which includes polarization functions, was then performed. For all triplet species unrestricted (UB3LYP and UMP2) wave functions were used. No symmetry restrictions were imposed at any point in the optimization procedures. Energies of the stationary points (obtained with MP2) were then recalculated using the coupled cluster approximation including single, double, and triple excitations (CCSD(T))[23] with the same basis set used for the optimization (6-31G(d,p)).

The stationary points were characterized by a frequency analysis at the level of geometry optimization, giving zero (minima) or exactly one (TS) imaginary vibrational frequency. The nature of the TS was verified in questionable cases by IRC path following on the B3LYP level.

Zero point vibrational energies (ZPE) were scaled with optimized scaling factors.[24] As no experimental data were available for comparison, it seemed legitimate to report no temperature correction. The relative energies discussed in the text are thus CCSD(T)/6-31G(d,p)//MP2/6-31G(d,p) + ΔZPE-(MP2/6-31G(d,p)) energies and are referenced to 0 K.

Spin contamination was negligible for UB3LYP but was notable for UMP2 wave functions of some species, which may be regarded as an example for the high sensitivity of this method.[25] On the other hand, the CCSD(T) energies can be regarded as reliable—especially when compared with the B3LYP/6-31G(d) energies.

NBO analyses were carried out with NBO 3.0 as implemented in Gaussian 98.[26] MP2 wave functions were used for the population analysis. In the NBO scheme, the molecular orbitals are transformed in the natural atomic orbitals basis, giving localized hybrid orbitals. These atomic orbitals are combined to form $\sigma$ and $\pi$ bonds and lone pairs which chemists are accustomed to dealing with.

## Results and Discussion

**Cyclopropylcarbene 1.** Cyclopropylcarbene **1** and its reactions (Scheme 1) have been recalculated on the theoretical levels of this study for purpose of comparison with the heteroanalogues. The two bisected conformers **1a** (cis) and **1b** (trans) are separated by 1.4 kcal mol$^{-1}$ on the CCSD(T) level of theory. The trans-triplet $^3$**1b** is found to be 1.7 kcal mol$^{-1}$ less stable than **1a**, contrary to the work of Shevlin and McKee,[5c] but in accordance with QCI results of Herges.[8]

The reactivity pattern of **1** has been discussed before, the results are confirmed in Table 1. Recently, DFT calculations have been published with relative energies for the two major reactions of **1** that are in good agreement with the CCSD(T) results of this work.[27]

Although the barrier of interconversion of **1a** and **1b** via **TS(1a-1b)** is low ($\Delta H^{\ddagger}$ = 14.5 kcal mol$^{-1}$) on the absolute scale, the rearrangement of the cis-conformer to give cyclobutene **(TS(1a-2)**; $\Delta H^{\ddagger}$ = 4.1 kcal mol$^{-1}$) has an even lower barrier. The fragmentation reaction of **1a** cannot compete **(TS(1a-5/6)**, $\Delta H^{\ddagger}$ = 19.0 kcal mol$^{-1}$) with the rearrangement. The trans-conformer has a higher activation energy toward ring expansion **(TS(1b-2)**, $\Delta H^{\ddagger}$ = 17.4 kcal mol$^{-1}$) than toward fragmentation **(TS(1b-5/6)**, $\Delta H^{\ddagger}$ = 13.2 kcal mol$^{-1}$). From these 0 K gas-phase barriers it might seem that the preferred reaction of **1b** is the rotation of the hydrogen atom to give **1a** ($\Delta H^{\ddagger}$ = 13.1 kcal mol$^{-1}$). However, upon adding the thermal corrections from the frequency analysis, $\Delta G^{\ddagger}$(298K) is lower for the fragmentation of **1b** (11.5 kcal mol$^{-1}$) than for the isomerization to **1a** (12.9 kcal mol$^{-1}$), indicating the larger positive entropy contribution to the free enthalpy of **TS(1b-5/6)**.

**Table 1. Energies of Stationary Points on the Cyclopropylcarbene Hypersurface in kcal mol$^{-1}$, Relative to the *cis*-Cyclopropylcarbene 1a in the Singlet State**

| structure | B3LYP[a] | CCSD(T)[b] | structure | B3LYP[a] | CCSD(T)[b] |
|---|---|---|---|---|---|
| **1a** | 0.0 | 0.0 | **TS(1a-1b)** | 15.4 | 14.5 |
| **1b** | 1.8 | 1.4 | **TS(1a-2)** | 3.5 | 4.1 |
| **2** | −63.9 | −66.2 | **TS(1b-2)** | 17.2 | 18.8 |
| **3** | −48.2 | −50.2 | **TS(1a-3)** | 15.5 | 14.0 |
| **4** | −58.1 | −58.4 | **TS(1b-3)** | 22.9 | 21.5 |
| **5 + 6** | −32.2 | −38.5 | **TS(1−4)** | 17.2 | 17.7 |
| $^3$**1a** | 3.8 | 2.3 | **TS(1a-5/6)** | 15.5 | 19.0 |
| $^3$**1b** | 3.7 | 1.7 | **TS(1b-5/6)** | 11.8 | 14.6 |
| ***anti*-$^3$7** | 2.0 | 3.9 | $^3$**TS(1a-7)** | 11.4 | 13.1 |
| ***syn*-$^3$7** | 2.4 | 4.2 | $^3$**TS(1b-7)** | 12.0 | 13.7 |

[a] B3LYP/6-31G(d)//B3LYP/6-31G(d) + ZPE (B3LYP/6-31G(d)). [b] CCSD(T)/6-31G(d,p)//MP2/6-31G(d,p) + ZPE (MP2/6-31G(d,p)).

The formation of bicyclo[1.1.0]butane **3** and methylenecyclopropane **4**—despite the low absolute barriers of 14.0 and 17.7 kcal mol$^{-1}$, respectively—is less favored according to the findings in Table 1.

The triplet carbene $^3$**1** is not the preferred isomer of cyclopropylcarbene. Assuming it would be formed, ring opening to the butene-1,4-diyl diradical $^3$**7** would be a reaction with a barrier of only 10.8 kcal mol$^{-1}$ (from $^3$**1a**) or 12.0 kcal mol$^{-1}$ (from $^3$**1b**). Formation of *anti*-$^3$**7** from $^3$**1a** is less endothermic ($\Delta_R H$ = 1.6 kcal mol$^{-1}$) than opening of $^3$**1b** to *syn*-$^3$**7** ($\Delta_R H$ = 2.5 kcal mol$^{-1}$). This endothermicity contrasts with the negative ring opening enthalpy of the cyclopropylcarbinyl radical that has been calculated to be −3 kcal mol$^{-1}$ (on the G2 level) and measured experimentally to be −5.4 kcal mol$^{-1}$.[28]

**Oxiranylcarbene 8.** The electronegative $\beta$-heteroatom in **8** lowers the ring MO energies, thereby weakening the ability of the substituent to act as a $\pi$ donor. This can be demonstrated by calculating the energies of the natural bond orbitals involved in the stabilization in **8b** (trans) and comparing them with those of **1a** (Figure 1). The carbene lone pair sp$^2$(C1) and the empty p(C1) orbital remain unaltered by the oxiranyl substituent, but the $\sigma$ bond orbitals of the ring are lowered.

The unsymmetric splitting of the energies of the C2−O and C2−C3 bonds is important for the stabilization: the three-membered ring now acts as a donor solely through the C2−C3 bond. On the other hand, the lowering of the antibonding $\sigma$*(C2−O) orbital gives the ring more acceptor character. The resulting donor−acceptor interactions are revealed by the NBO analysis (Figure 2). Charge donation by the C2−C3 $\sigma$-orbital is operating in both isomers. In the *trans*-carbene, the C1 lone pair is

(22) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618.
(23) (a) Watts, J. D.; Bartlett, R. J. *Int. J. Quantum Chem.* **1993**, *S27*, 51. (b) Pople, J. A.; Head-Gordon, M.; Raghavachari, K. *J. Chem. Phys.* **1987**, *87*, 5968.
(24) Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502−16513. Scaling factors are 0.9806 (for B3LYP/6-31G(d)) and 0.9608 (for MP2/6-31G(d,p)).
(25) $\langle S^2 \rangle$ (UMP2) is in the range of 2.17−2.23 for triplet transition structures and diradicals, but smaller than 2.03 for all triplet carbenes. See Supporting Information for a table of calculated values. For a broader discussion of UMP2 calculations of open shell species see: Bally, T.; Borden, W. T. In *Reviews in Computational Chemistry*; Lipkovitz, K. B., Boyd, D. B., Eds.; VCH Publishers: New York, 1999; Vol. 13, pp 1−97.
(26) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899−926 and cited references.
(27) Thamattoor, D. M.; Snoonian, J. R.; Sulzbach, H. M.; Hadad, C. M. *J. Org. Chem.* **1999**, *64*, 5886−5895.
(28) Newcomb, M.; Glenn, A. G. *J. Am. Chem. Soc.* **1989**, *111*, 275−277.

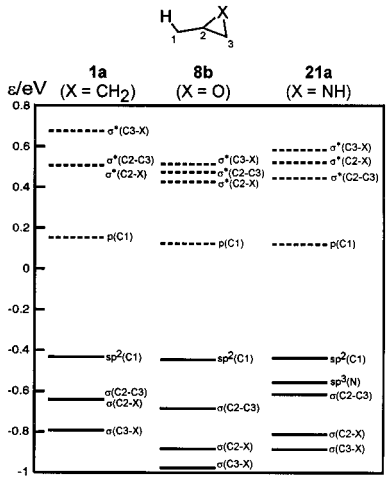



**Figure 1.** Natural bond orbitals of singlet cis cyclopropylcarbene **1a** and its heterosubstituted analogues **8b** (trans) and **21a** (cis): solid lines, occupied orbitals (population ca. 2 e); dashed lines, virtual orbitals (population ca. 0 e)

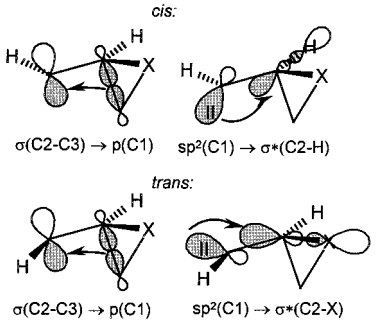



**Figure 2.** Donor−acceptor interactions in **8** (X = O) and **21** (X = NH), obtained from the NBO analysis.

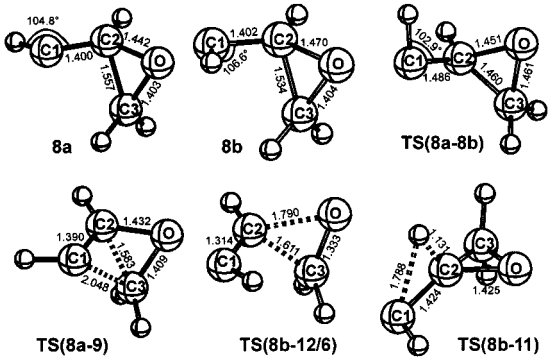



**Figure 3.** MP2/6-31G(d,p) geometries of singlet 2-oxiranylcarbene **8** and transition structures leading to the preferred reaction products. Bond lengths in Å.

interacting with the $\sigma^*$(C2−O) orbital, while in the cis isomer, the $\sigma^*$(C2−H) orbital is the (less stabilizing) acceptor.

Both interactions result in elongation of the C2 bonds in the ring and shortening of the C1−C2 bond and give rise to a peculiar geometry of carbon C2 in **8a** and **8b** (Figure 3). The substituted ring atom C2 is almost trigonally surrounded by C1, H and O, optimizing the orbital overlap of both interactions. The structural similarity with the 1-oxiranylethyl cation is notable, for which the according C2−C3 bond is even longer (1.583 Å, RHF/6-31G*).[29]

**Scheme 3**

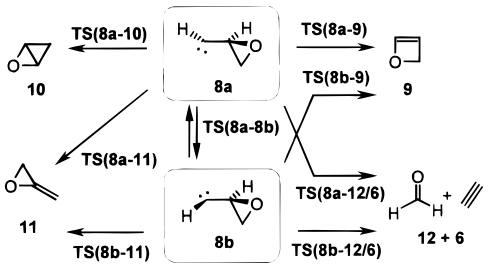



**Table 2. Energies of Stationary Points on the 2-Oxiranylcarbene Hypersurface in kcal mol$^{-1}$, Relative to the *trans*-2-Oxiridinylcarbene 8b in the Singlet State**

| structure | B3LYP[a] | CCSD(T)[b] | structure | B3LYP[a] | CCSD(T)[b] |
|---|---|---|---|---|---|
| **8a** | 0.9 | 1.5 | **TS(8a-9)** | 1.9 | 2.2 |
| **8b** | 0.0 | 0.0 | **TS(8b-9)** | 8.6 | 9.1 |
| **9** | −66.2 | −68.8 | **TS(8a-10)** | 23.9 | 22.6 |
| **10** | −37.8 | −40.1 | **TS(8a-11)** | 9.5 | 10.0 |
| **11** | −66.3 | −67.7 | **TS(8b-11)** | 8.6 | 8.8 |
| **12 + 6** | −48.4 | −56.5 | **TS(8a-12/6)** | 8.5 | 11.1 |
| $^3$**8a** | 0.1 | −2.3 | **TS(8b-12/6)** | 2.5 | 3.6 |
| $^3$**8b** | −0.1 | −2.3 | $^3$**TS(8a-8b)** | 0.8 | −1.7 |
| $^3$**13a** | −3.1 | −1.2 | $^3$**TS(8a-13a)** | 3.6 | 4.7 |
| $^3$**14a** | −3.4 | 0.2 | $^3$**TS(8a-14a)** | 13.5 | 15.5 |
| $^3$**13b** | −3.8 | −1.6 | $^3$**TS(8b-13b)** | 3.8 | 4.8 |
| $^3$**14b** | −2.2 | 1.2 | $^3$**TS(8b-14b)** | 13.5 | 15.4 |
| **TS(8a-8b)** | 13.7 | 10.9 | | | |

[a] B3LYP/6-31G(d)//B3LYP/6-31G(d) + ZPE (B3LYP/6-31G(d)). [b] CCSD(T)/6-31G(d,p)//MP2/6-31G(d,p) + ZPE (MP2/6-31G(d,p)).

**8a** and **8b** differ mainly in the relative bond lengths of the C2−C3 and C2−O bonds. The favorable overlap of the carbene lone pair with the $\sigma^*$(C2−O) orbital in **8b** gives rise to the longer C2−O bond (0.03 Å longer than in **8a**) and the higher stability of the trans conformer, contrary to the relative stabilities of the cyclopropylcarbene conformers.

The calculated stationary points of the reactions of **8a** and **8b** are presented in Scheme 3 and Table 2. Lowering of $\sigma$ orbitals in the oxiranyl ring diminishes the barrier of interconversion of the rotamers **8a** and **8b** by 3.6 kcal mol$^{-1}$ compared to **1**. Since C2 is an asymmetric carbon atom, two transition states exist for the interconversion of the conformers. The more favorable **TS(8a-8b)** has the hydrogen substituent in the gauche position between hydrogen and oxygen at C2. The bond lengths and the tetrahedral shape of C2 indicate the reduced interaction between the C2−C3 $\sigma$ bond and the carbene p orbital.

The different elongations of the C2−O bond in **8a** and **8b** correspond to the main reaction paths. The C2−O bond is longer in the trans conformer: **8b** prefers the rupture of both C2 bonds ($\Delta H^{\ddagger} = 3.6$ kcal mol$^{-1}$), yielding formaldehyde (**12**) and ethyne. The transition structure **TS(8b-12/6)** reveals a simultaneous, although not symmetric, scission of the ring bonds. For **8a**, the barrier toward C2−C3 bond migration is vanishingly small ($\Delta H^{\ddagger} = 0.7$ kcal mol$^{-1}$) and leads to the formation of oxete **9** without a C2−O bond rupture. Migration of the oxygen atom of **8a** to give oxete **9** has a more than 12 kcal mol$^{-1}$ higher activation barrier; the transition structure is therefore not reported here.

$\beta$-CH insertion (via **TS(8a-10)**, $\Delta H^{\ddagger} = 21.1$ kcal mol$^{-1}$) leading to oxabicyclo[1.1.0]butane **10** is an insignificant

(29) Francl, M. M.; Hansell, G.; Patel, B. P.; Swindell, C. S. *J. Am. Chem. Soc.* **1990**, *111*, 3535−3539.

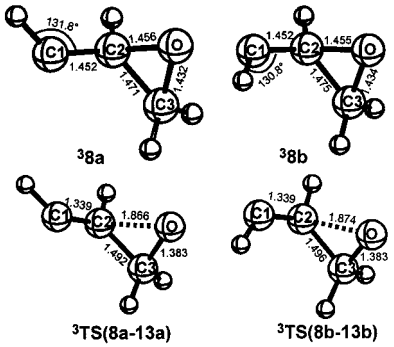


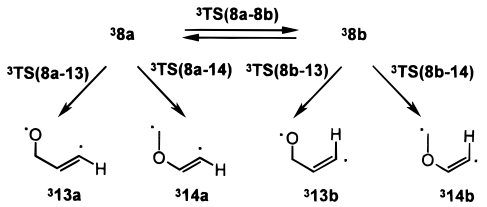

**Figure 4.** MP2/6-31G(d,p) geometries of triplet 2-oxiranylcarbene $^3$**8** and the two transition structures leading to the oxyallyl diradical $^3$**13**. Bond lengths in Å.

side reaction. The corresponding TS for the trans carbene **8b** could not be located; optimization lead to fragmentation. The 1,2-hydrogen shift reaction (via **TS(8b-11)**, $\Delta H^{\ddagger}$ = 8.8 kcal mol$^{-1}$), yielding methyleneoxirane **11**, has a significantly lower barrier than for the parent compound **1**. This can be interpreted as an accelerating "bystander" effect of oxygen over carbon.[30] The motion of the carbene to the transition state involves a C1−C2 bond rotation similar to transition state **TS(8a-8b)**. Since the barrier is lower for the hydrogen shift, this motion leads to **11** rather than formation of the other conformer.

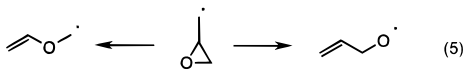
The very low barrier toward formation of acetylene and formaldehyde from *trans*-2-oxiranylcarbene **8b** makes it an undetectable intermediate in the Eschenmoser fragmentation reaction. The formation reaction of the carbene (e.g. by nitrogen extrusion from a diazirine precursor) will be accompanied by instantaneous ring opening even in a nonconcerted reaction. The complex product distribution observed with 2,3-epoxyhydrazones which are not fixed in a trans conformation like **8b** can thus be understood from the low barrier of rearrangement to the oxete, which is followed by consecutive ring opening or intermolecular reactions. Intermediate conformations between **8a** and **8b** might also be liable to hydrogen shift rearrangement, thus further complicating the product spectrum. Similar to the cyclopropylcarbene **1**, the initial conformation is decisive for the main rearrangement product.

According to the CCSD(T) energies, the triplet $^3$**8** is the preferred isomer of 2-oxiranylcarbene. The MP2-optimized structures (Figure 4) indicate the absence of the donor−acceptor interaction observed in the singlet; the geometry of the oxirane ring is not distorted that much. The C2−O and C2−C3 bond lengths differ only by ca. 0.02 Å and the C1−C2 bond is significantly longer (1.452 Å) than in the singlet. The relative DFT energies of the triplets are slightly higher and predict $^3$**8a** and $^3$**8b** to be isoenergetic with the singlet **8b**. Comparison with **1** gives a relative stabilization of the triplet by 4 kcal mol$^{-1}$ upon introduction of the heteroatom, presumably due to the weakened stability of the singlet state (see below). If the singlet 2-oxiranylcarbene had sufficient kinetic stability, intersystem crossing should be expected to occur, yielding $^3$**8a** and $^3$**8b** in equal amounts and in fast conformational interconversion ($\Delta H^{\ddagger}$ = 0.6 kcal mol$^{-1}$).

**Scheme 4**




The ring opening reaction of $^3$**8** (Scheme 4) resembles the corresponding reaction of oxiranyl radicals. Some experimental and theoretical interest has focused on the cyclopropyl carbinyl radical[31] and its heteroanalogues.[32] Due to the rapid ring opening reaction of these intermediates they can be utilized as "radical clocks".[33] The diradicaloid nature of $^3$**8** allows the comparison with the 2-oxiranyl methyl radical, which preferentially opens the C−O bond to give the oxyallyl radical in an exothermic reaction (eq 5). Theoretical studies agree over the kinetic preference of the C−O bond break, although the relative stabilities of the two radical products are controversial.[34]


(5)

In contrast to the radicals, the opening of the triplet carbene is slightly endothermic ($^3$**8a**→$^3$**13a**, $\Delta_R H$ = 1.1 kcal mol$^{-1}$; $^3$**8b**→$^3$**13b**, $\Delta_R H$ = 0.7 kcal mol$^{-1}$), which may be attributed to the formation of the vinylic radical center. The regioselectivity, however, is the same: The O,C diradicals $^3$**13a** ($\Delta H^{\ddagger}$ = 7.0 kcal mol$^{-1}$) and $^3$**13b** ($\Delta H^{\ddagger}$ = 7.1 kcal mol$^{-1}$) are formed with much lower barriers than the C,C diradicals $^3$**14a** ($\Delta H^{\ddagger}$ = 17.8 kcal mol$^{-1}$) and $^3$**14b** ($\Delta H^{\ddagger}$ = 17.7 kcal mol$^{-1}$), although their thermodynamic stabilities differ by only 1.4 and 2.8 kcal mol$^{-1}$ in favor of the former. With reference to $^3$**1**, oxygen in $^3$**8** lowers the barrier of ring opening by almost 4 kcal mol$^{-1}$, in accord with the observed acceleration in the ring opening of the oxiranylcarbinyl radical.[35]

The calculations show that the diradicals $^3$**13** and $^3$**14** prefer the planar endo conformation. The higher stability of an oxygen radical center in ($^3$**13**) compared to the O-substitued methyl radical center ($^3$**14**) may be due to the less stabilizing effect of the α-heteroatom on the carbon radical in $^3$**14**. Under equilibrating conditions, the triplet carbene $^3$**8** is expected to react nonstereospecifically in intermolecular olefin addition reactions as long as the diradicals $^3$**13** and $^3$**14** cyclize to form $^3$**8** faster than the ISC can convert them to singlet species.

(30) (a) Nickon, A. *Acc. Chem. Res.* **1993**, *26*, 84−89. (b) Keating, A. E.; Garcia-Garibay, M. A.; Houk, K. N. *J. Phys. Chem. A* **1998**, *102*, 8467−8476.

(31) (a) Martinez, F. N.; Schlegel, H. B.; Newcomb, M. *J. Org. Chem.* **1996**, *61*, 8547−8550. (b) Martinez, F. N.; Schlegel, H. B.; Newcomb, M. *J. Org. Chem.* **1998**, *63*, 3618−3623. (c) Horner, J. H.; Tanaka, N.; Newcomb, M. *J. Am. Chem. Soc.* **1998**, *120*, 10379−10390.

(32) (a) Pasto, D. J. J. *J. Org. Chem.* **1996**, *61*, 252−256. (b) Smith, D. M.; Nicolaides, A.; Golding, B. T.; Radom, L. *J. Am. Chem. Soc.* **1998**, *120*, 10223−10233.

(33) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317−323.

(34) The barrier of C−O ring opening has been calculated (QCISD/6-31G*) to be 9.0 kcal mol$^{-1}$, leading in an exothermic reaction ($\Delta_R H$ = −5.4 kcal mol$^{-1}$) to the oxyallyl radical.[32a] Using the CBS−RAD technique, which also makes use of CCSD(T) energies, the barrier has been determined to be 4.1 kcal mol$^{-1}$ ($\Delta_R$H = −1.2 kcal mol$^{-1}$), with the vinyloxymethyl radical as the thermodynamically preferred product ($\Delta_R H$ = −3.9 kcal mol$^{-1}$).[32b] The C2−O bond break is kinetically favored in both reports over the C2−C3 bond break by more than 10,[32a] respectively 7[32b] kcal mol$^{-1}$.

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

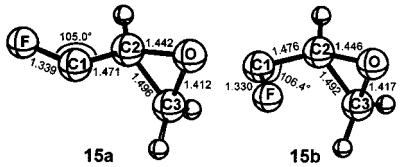



**Figure 5.** MP2/6-31G(d,p) geometries of singlet fluoro-2-oxiranylcarbene **15**. Bond lengths in Å.

**Scheme 5**

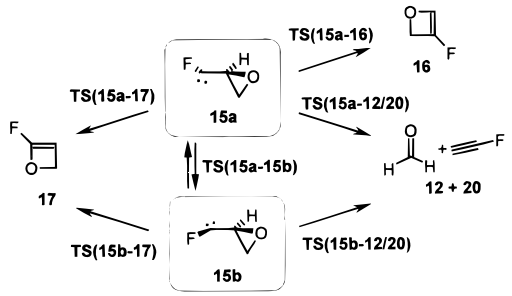



**Table 3. Energies of Stationary Points on the Fluoro-2-oxiranylcarbene Hypersurface in kcal mol$^{-1}$, Relative to the Singlet *cis*-Fluoro-2-oxiridinylcarbene 15a**

| structure | B3LYP[a] | CCSD(T)[b] | structure | B3LYP[a] | CCSD(T)[b] |
|---|---|---|---|---|---|
| **15a** | 0.0 | 0.0 | **TS(15a-15b)** | 8.1 | 6.6 |
| **15b** | 1.2 | 0.9 | **TS(15a-16)** | 13.2 | 15.4 |
| **16** | −44.4 | −44.1 | **TS(15a-17)** | 26.5 | 27.3 |
| **17** | −54.7 | −54.2 | **TS(15b-17)** | 32.7 | 24.6 |
| **18** | −18.5 | −19.2 | **TS(15a-18)** | 35.1 | 35.3 |
| **(E)-19** | −41.9 | −40.1 | **TS(15a-(E)-19)** | 22.9 | 24.9 |
| **(Z)-19** | −41.7 | −39.8 | **TS(15b-(Z)-19)** | 19.9 | 21.9 |
| **11 + 20** | −17.8 | −17.9 | **TS(15a-12/20)** | 32.8 | 35.6 |
| **$^3$15a** | 17.1 | 18.6 | **TS(15b-12/20)** | 18.6 | 19.6 |
| **$^3$15b** | 17.1 | 18.2 | | | |

[a] B3LYP/6-31G(d)//B3LYP/6-31G(d) + ZPE (B3LYP/6-31G(d)). [b] CCSD(T)/6-31G(d,p)//MP2/6-31G(d,p) + ZPE (MP2/6-31G(d,p)).

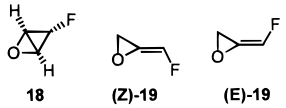
**Fluorooxiranylcarbene 15.** The kinetic and thermodynamic instability of 2-oxiranylcarbene **8** is expected to be altered by an electronegative and $\pi$-donating element, which replaces the hydrogen at the carbene carbon. The influence of a halogen substituent on the reactivity of **8** is evaluated with fluoro-2-oxiranylcarbene **15**. MP2-optimized geometries of the two singlet conformers are given in Figure 5.

The halogen substituent interacts with the carbene as $\pi$ donor and $\sigma$ acceptor. It increases the electron density in the p orbital at C1. The donation from the C2−C3 bond is less important. Concerning the hybridization at C1, the electronegative substituent increases the s character of the carbene lone pair, thus making it a less suitable donor for the C2−O $\sigma$* orbital. These effects are reflected in the notably longer C1−C2 bond, in the smaller elongation of the C2−C3 bond, and in the apparently more tetrahedral shape of C2. Both interactions, which are present in the oxiranylcarbene **8**, are dimished in **15**, making it kinetically more stable.

To test the implications of these structural findings, **15** has been investigated with regard to the same reactions as **8**. The relative energies of stationary points in the reaction scheme (Scheme 5) are given in Table 3.

The cis conformer **15a** is 0.9 kcal mol$^{-1}$ lower in energy than *trans*-**15b**, due to the diminished importance of the p(C1)−$\sigma$*(C2−O) interaction. The barrier of interconversion of **15b** to **15a** ($\Delta H^{\ddagger}$ = 5.8 kcal mol$^{-1}$) is lower than any activation energy for rearrangement or fragmentation. Consequently, the reactivity of **15** is *not* dependent on the initial conformation, in direct contrast to **1** and **8**. Moreover, all activation barriers are increased upon introduction of the halogen substituent.

The main deactivation path for the cis carbene is ring expansion via methylene migration (**15a**→**16**, $\Delta H^{\ddagger}$ = 15.4 kcal mol$^{-1}$) to form 2-fluorooxete **16**. Oxygen migration leads to 1-fluorooxete **17**. As with **8a**, the former pathway is preferred. Fragmentation to fluoroethyne (**20**) and formaldehyde (**12**) is as unfavorable for **15a** as is the formation of the *exo*-2-fluorooxabicyclo[1.1.0]butane **18** (both $\Delta H^{\ddagger}$ > 35 kcal mol$^{-1}$). The formation of the methyleneoxirane **(*E*)-19** is also less favorable ($\Delta H^{\ddagger}$ = 24.9 kcal mol$^{-1}$).




Fragmentation of the trans carbene is also very facile (**15b**→**12** + **20**, $\Delta H^{\ddagger}$ = 18.7 kcal mol$^{-1}$), but it has a considerably higher barrier than rotation of the C1−C2 bond, thus promoting ring expansion via **15a**. Other pathways, leading to **17** or **(Z)-19** from **15b** also require higher activation energies. The 1,2-hydrogen shift is the second most favorable reaction of the trans carbene (**15b**→**(Z)-19**, $\Delta H^{\ddagger}$ = 21.0 kcal mol$^{-1}$).

A 2-oxiranylcarbene substituted with an electronegative atom at C1 is therefore likely to form 2-substituted oxetes with a high selectivity in the absence of conformational restrictions. Experimentally, a longer lifetime has been determined for the chlorocyclopropylcarbene than for cyclopropylcarbene itself,[36] making even intermolecular reactions with substituted olefins feasible.[36a] A fluorine substituent increases the barrier toward ring expansion.[36e] A similar observation was made with chlorocyclopropylcarbene, which yields almost exclusively 1-chlorocyclobutene with an activation barrier higher than that of **1**.[36d,37] Ab initio calculations explained this with a similar effect of the halogen substituent on the relative barriers in the reactions scheme of the carbene.[36c]

The $\pi$-donor capability of fluorine stabilizes the singlet against the triplet $^3$**15** by more than 18 kcal mol$^{-1}$, according to the CCSD(T) energies in Table 3. The triplet of HCF has been calculated with density functional theory to be 13−14 kcal mol$^{-1}$ above the singlet,[38a] in accordance with the experimental value of 15.0 kcal mol$^{-1}$.[38b] The triplet reactions of **15** were therefore not considered in this study.

**2-Aziridinylcarbene 21.** Due to the relative electronegativities of C, N, and O, the ring orbital energies of aziridine are intermediate between those of cyclopro-

(36) (a) Moss; R. A.; Fantina, M. E. *J. Am. Chem. Soc.* **1978**, *100*, 6788−6790. (b) Bonneau, R.; Liu, M. T. H.; Rayez, M. T.; *J. Am. Chem. Soc.* **1989**, *111*, 5973−5974. (c) Ho, G.-J.; Krogh-Jespersen, K.; Moss, R. A.; Shen, S.; Sheridan, R. S.; Subramanian, R. *J. Am. Chem. Soc.* **1989**, *111*, 6875−6877. (d) Liu, M. T. H.; Bonneau, R. *J. Phys. Chem.* **1989**, *93*, 7298−7300. (e) Moss, R. A.; Ho, G.-J.; Liu, W. *J. Am. Chem. Soc.* **1992**, *114*, 959−963.

(37) (a) Liu, M. T. H.; Chien, D. H. T. *J. Chem. Soc., Perkin Trans. 2* **1974**, 937−941. (b) Moss, R. A.; Ho, G.-J.; Shen, S.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1990**, *112*, 1638−1640.

(38) (a) Worthington, S. E.; Cramer, C. J. *J. Phys. Org. Chem.* **1997**, *10*, 755−767. (b) Gilles, M. K.; Ervin, K. M.; Ho, J.; Lineberger, W. C. *J. Phys. Chem.* **1992**, *96*, 1130−1141.

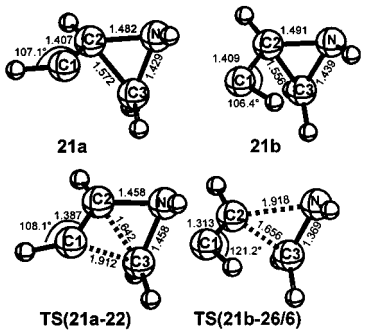
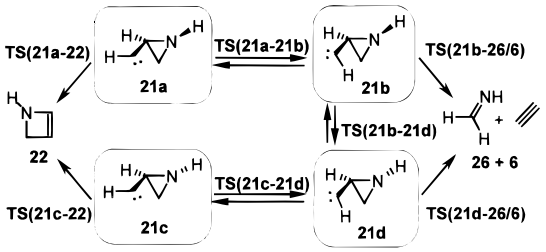


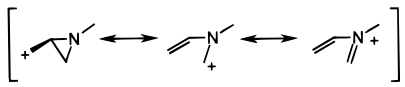

**Figure 6.** MP2/6-31G(d,p) geometries of prevailing conformers of singlet 2-aziridinylcarbene **21** and transitions structures leading to the preferred products. Bond lengths in Å.

**Scheme 6**




pane and oxirane. This can be seen from the NBOs of *cis*,(NH)*cis*-2-aziridinylcarbene **21a** (right column of Figure 1). The C2−N and C3−N $\sigma$ orbitals are higher in energy than the C−O orbitals in **8b**, but the C2−C3 bond is an even better donor than in **1a**, similar in energy with the nitrogen lone pair. The C−N $\sigma$* orbitals are worse acceptor orbitals than the C−O $\sigma$* orbitals in **8b**. That leaves $\sigma$*(C2−C3) to be the best acceptor in **21a**. However, the geometry does not allow efficient overlap with the lone pair at C1. The MP2 geometries of the CH rotamers **21a** and **21b** (Figure 6) show that $\sigma$*(C2−N) is less important as an acceptor orbital since the C2−N distance varies by only 0.01 Å. The C2−C3 distance is ca. 0.02 Å longer than in **8a** and **8b**, but this may be due to the increased size of the aziridine ring as compared with the oxiranyl system. As a second consequence, the relative energies of the conformers have changed and the *cis*-carbene **21a** is the global minimum of **21**.

A similar geometry has been found and discussed in a study of 2-aziridinyl methyl cations in which the C2−C3 bonds were even more elongated (1.713 Å for the cation corresponding to **21**, RHF/6-311G**). The explanation has been given by the resonance structures, which also account for the short (1.369 Å) N−C3 bond:[39]



The MP2 structures of **21a** and **21b** indicate no similar—ylidic—stabilization in the carbenes. The N−C3 bonds do not possess a double bond character. (1.429 and 1.439 Å, respectively).

The main pathways of conformational interconversion and reactions of **21** are depicted in Scheme 6, the energies are given in Table 4. The two (NH)trans isomers **21c** and **21d** are less stable than the (NH)cis conformers, probably due to the steric repulsion between the nitrogen lone pair and the CH moeity. The comparatively high inversion barrier of nitrogen (**21b**→**21d**, $\Delta H^{\ddagger}$ = 22.3 kcal mol$^{-1}$) is typical for aziridines.[40] Attempts to locate the corresponding transition state of the cis carbene (**21a**→**21c**) ended with the rearrangement saddle point **TS(21a-22)**. The angle widening in the inversion process facilitates the rearrangement when the carbene lone pair is directed toward nitrogen.

**Table 4. Energies of Stationary Points on the 2-Aziridinylcarbene Hypersurface in kcal mol$^{-1}$, Relative to the Singlet *cis*,(NH)*cis*-2-Aziridinylcarbene 21a**

| structure | B3LYP[a] | CCSD(T)[b] | structure | B3LYP[a] | CCSD(T)[b] |
|---|---|---|---|---|---|
| **21a** | 0.0 | 0.0 | **TS(21b-26/6)** | 9.1 | 8.5 |
| **21b** | 3.3 | 2.6 | **TS(21d-26/6)** | 11.7 | 10.8 |
| **21c** | 6.7 | 6.4 | $^3$**21a** | 4.0 | 1.6 |
| **21d** | 5.6 | 4.7 | $^3$**21b** | 4.9 | 2.2 |
| **22** | −61.9 | −64.4 | $^3$**21c** | 6.6 | 3.3 |
| **23** | −52.1 | −55.0 | $^3$**21d** | 6.3 | 3.1 |
| ***endo*-24** | −41.5 | −44.5 | $^3$**TS(21a-27a)** | 14.8 | 16.4 |
| ***exo*-24** | −36.4 | −39.7 | $^3$**TS(21a-28a)** | 7.9 | 8.0 |
| **25** | −59.1 | −59.8 | $^3$**27a** | −8.9 | −4.2 |
| **26 + 6** | −39.1 | −47.3 | $^3$**27b** | −7.8 | −3.0 |
| **TS(21a-21b)** | 18.3 | 15.7 | $^3$**28a** | −1.6 | −0.7 |
| **TS(21c-21d)** | 18.4 | 15.3 | $^3$**28b** | −1.1[c] | −0.2[c] |
| **TS(21b-21d)** | 23.5 | 24.9 | $^3$**28c** | −1.7 | −0.7 |
| **TS(21a-22)** | 3.9 | 3.6 | $^3$**28d** | −1.6 | −0.3 |
| **TS(21c-22)** | 7.7 | 7.2 | | | |

[a] B3LYP/6-31G(d)//B3LYP/6-31G(d) + ZPE (B3LYP/6-31G(d)). [b] CCSD(T)/6-31G(d,p)//MP2/6-31G(d,p) + ZPE (MP2/6-31G(d,p)). [c] The *endo*-conformer is more stable: $E_{rel}$ = −1.3 (B3LYP), −0.6 (CCSD(T)).

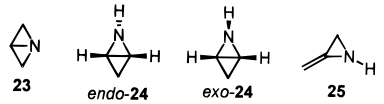
**21a**→**21c**) ended with the rearrangement saddle point **TS(21a-22)**. The angle widening in the inversion process facilitates the rearrangement when the carbene lone pair is directed toward nitrogen.

Rotation of the −CH group requires 15.7 kcal mol$^{-1}$ for the (NH)cis diastereomers (**21a**→**21b**), whereas the process has a lower barrier for the (NH)trans conformers (**21d**→**21c**, $\Delta H^{\ddagger}$ = 10.6 kcal mol$^{-1}$) due to the higher ground-state energies of **21c** and **21d**.

2-Aziridinylcarbene is expected to react similar to 2-oxiranylcarbene **8**. The barriers of interconversion via CH rotation or nitrogen inversion are higher than for the respective major rearrangement or fragmentation reaction, thus making the initial conformation decisive for the reaction pathway.

The cis carbenes **21a** and **21c** prefer $CH_2$ over NH migration and yield 2-azetine **22** as the major product. The activation enthalpy of 3.6 kcal mol$^{-1}$ for **21a**→**22** implies a very short lifetime of **21** when formed in the cis,(NH)cis conformation. **21c** has an even lower barrier of 0.8 kcal mol$^{-1}$ toward rearrangement. The fragmentation of **21b** and **21d** to yield ethyne and formimine (**26**) is also a very facile process ($\Delta H^{\ddagger}$ = 5.9 kcal mol$^{-1}$ for **21b** and 6.1 kcal mol$^{-1}$ for **21d**). If an Eschenmoser-type reaction was attempted with an α-acylaziridine in the fixed trans conformation, ring scission would be the immediate result.

Formation of 1-azabicyclo[1.1.0]butane (**23**), 2-azabicyclo[1.1.0]butane (*endo*- and *exo*-**24**), and methyleneaziridine (**25**) have also been investigated. These pathways all afford higher activation energies than the reactions presented above and are not reported in detail.




The triplet 2-aziridinyl carbene is not the preferred isomer since all four conformers of $^3$**21** are endothermic

(39) Higgins, R. H.; Kidd, B. *J. Phys. Org. Chem.* **1998**, *11*, 763−773.

**Scheme 7**

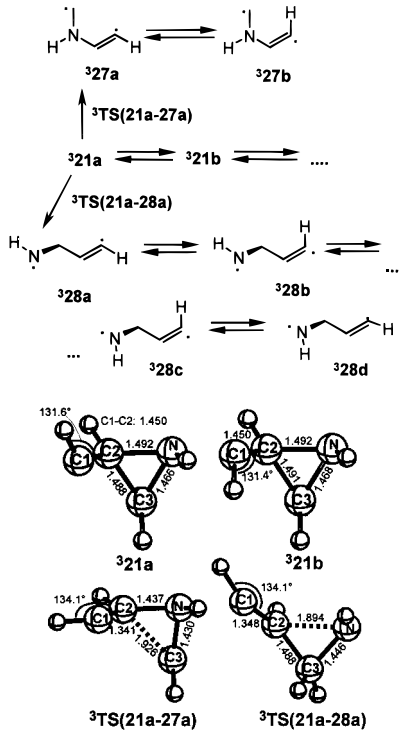



**Figure 7.** MP2/6-31G(d,p) geometries of prevailing conformers of triplet 2-aziridinylcarbene $^3$**21** and TS for ring opening of the dominant conformer $^3$**21a**. Bond lengths in Å.

compared with **21a** on both the CCSD(T) and the B3LYP level. Nevertheless, the triplet—once formed—is expected to undergo a fast exothermic ring opening reaction (Scheme 7). Figure 7 presents the MP2 geometries of the two lowest triplet carbenes and the transition structures for the C,N and C,C bond cleavage.

The barriers of interconversion of the 2-aziridinyl carbenes $^3$**21a**−**d** are expected to be as low as those calculated for $^3$**8a**−**b** and were not explicitely determined. $^3$**21a** is the reactive conformation for ring opening. Analogue to the opening of the 2-aziridinylcarbinyl radical, openings under kinetic and thermodynamic control give different products (Scheme 7): Scission of the C2−N bond in $^3$**21a** to give the C,N diradical $^3$**28a** is less exothermic ($\Delta_R H = -2.3$ kcal mol$^{-1}$) than formation of the C,C diradical $^3$**27a** ($\Delta_R H = -5.8$ kcal mol$^{-1}$). The preference for the vinylaminomethyl over the allylaminyl diradical—contrary to the preference of $^3$**13** over $^3$**14**—can be rationalized by the greater radical stabilization energy of the amino over the alkoxy substituent.[41]

On the other hand, $\Delta H^{\ddagger}$ for the ring-opening reaction is less than half as large via $^3$**TS(21a-28a)** (6.5 kcal mol$^{-1}$) than it is via $^3$**TS(21a-27a)** (14.9 kcal mol$^{-1}$). $^3$**21a** exhibits the lowest activation energies of all conformers with regard to both bond-breaking processes. The barrier is larger than for the according radical. Compared with the geometries of the radical transition structures, which possess a smaller elongation of the breaking bond, the carbene has the "later" TS, in accord with the higher barrier.[42]

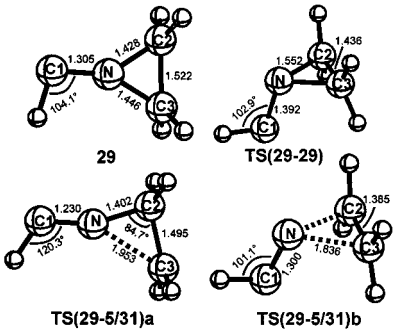
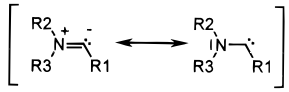



**Figure 8.** MP2/6-31G(d,p) geometries of singlet 1-aziridinylcarbene **29** and transitions structures. Bond lengths in Å.

In contrast to the oxygen diradicals, the exothermicity of the reactions $^3$**21**→$^3$**27** and $^3$**21**→$^3$**28** increases the probability for pathways involving diradicals, as they are more stable than the singlet carbene **21a**. Ring closure or fragmentation products are then expected to originate from the intermediates **27** or **28** after ISC.

**1-Aziridinylcarbene 29.** α-Heterosubstituted carbenes are stabilized by the interaction of the heteroatom lone pair with the vacant carbene p orbital. For instance, this $p_\pi-p_\pi$ delocalization has been found for aminomethylene H−C−$NH_2$.[43] The NBO analysis of **29** attributes double bond character to the C−N bond with a Wiberg bond index[44] of 1.44, the $\pi$ orbital being polarized toward the heteroatom. The short C1−N bond (1.305 Å) can be considered a C=N double bond. 1,2-Ylides derived from iminium ions[45] have been discussed in terms of a partially polar resonance structure:[46]




However, an NBO analysis shows that such a charge distribution is not present for 1-aziridinylcarbene. The N bears a negative charge (−0.545 e) and the carbene moiety bears a positive (+0.105 e) charge in **29**. This polarity observed is a consequence of the polarization of the $\sigma$ bonds which opposes and exceeds the $\pi$ interaction. Furthermore, the carbene lone pair of **29** is interacting with the antibonding C3−N $\sigma^*$ orbital, elongating the bond (1.446 Å). MP2-optimized geometries of **29** and its transition structures are given in Figure 8.

From the electronic structure of **29**, it is expected that it is less prone to fast deactivation processes than **8** and **21**. The three reaction pathways are given in Scheme 8; relative energies are listed in Table 5.

One transition state could be located for the double bond isomerization (identity) reaction **29**→**29** ($\Delta H^{\ddagger} = 25.3$ kcal mol$^{-1}$). The CH rotation is coupled with a pyramidalization of nitrogen as the $p_\pi-p_\pi$ interaction disappears. Ring strain is relieved in **TS(29-29)** with a C2−

(40) see for example: (a) Armarego, W. L. F. *Stereochemistry of Heterocyclic Compounds*; Wiley: New York, 1977; Part 1, Chapter 2. (b) Lehn, J. M. *Fortschr. Chem. Forsch.* **1970**, *15*, 311−377.

(41) Pasto, D. J.; Krasnansky, R.; Zercher, C. *J. Org. Chem.* **1987**, *52*, 3062−3072.

(42) Depending on the method used, the C−N ring-opening barrier is calculated to be between 3.7 and 3.9 kcal mol$^{-1}$, the C−C bond break requires 9.7−12.3 kcal mol$^{-1}$.[32]

(43) Boehme, C.; Frenking, G. *J. Am. Chem. Soc.* **1996**, *118*, 2039−2046.

(44) Wiberg, K. B. *Tetrahedron* **1968**, *24*, 1083−1096.

(45) (a) Aly, M. F.; Grigg, R. *J. Chem. Soc., Chem. Commun.* **1985**, 1523−1524. (b) Aly, M. F.; Grigg, R. *Tetrahedron* **1988**, *44*, 7271−7282.

(46) Grigg, R.; Wallace, L.; Morley, J. O. *J. Chem. Soc., Perkin Trans. 2* **1990**, 51−56.

**Scheme 8**

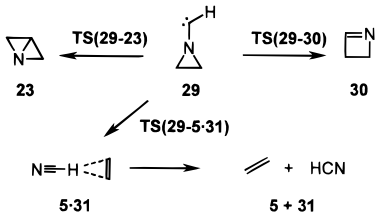



**Table 5. Energies of Stationary Points on the 1-Aziridinylcarbene Hypersurface in kcal mol$^{-1}$, Relative to the 1-Aziridinylcarbene 29 in the Singlet State**

| structure | B3LYP[a] | CCSD(T)[b] | structure | B3LYP[a] | CCSD(T)[b] |
|---|---|---|---|---|---|
| **29** | 0.0 | 0.0 | **$^3$29b** | 27.5 | 26.6 |
| **30** | −52.3 | −56.8 | **TS(29-29)** | 27.4 | 25.3 |
| **23** | −30.6 | −35.0 | **TS(29-23)** | 35.1 | 31.5 |
| **5·31** | −54.5 | −64.6 | **TS(29-30)** | 30.6 | 29.4 |
| **5 + 31** | −53.6 | −63.5 | **TS(29-5/31)a** | 17.1 | 14.9 |
| **$^3$29a** | 24.3 | 23.6 | **TS(29-5/31)b** | 29.7 | 29.2 |

[a] B3LYP/6-31G(d)//B3LYP/6-31G(d) + ZPE (B3LYP/6-31G(d)). [b] CCSD(T)/6-31G(d,p)//MP2/6-31G(d,p) + ZPE (MP2/6-31G(d,p)).

N−C3 angle of 55.1° (63.9° in **29**), thus allowing for longer N−C2/C3 bonds and a shorter C2−C3 distance than in **29**.

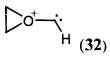
There are two transition states for decomposition to ethylene and HCN. The $C_s$-symmetric **TS(29-5/31)b** is geometrically very similar to **TS(29-29)**, but the barrier ($\Delta H^{\ddagger} = 29.2$ kcal mol$^{-1}$) is too high to compete with the ring-opening reaction via **TS(29-5/31)a** ($\Delta H^{\ddagger} = 14.9$ kcal mol$^{-1}$). In this preferred saddle point, the $p_\pi-p_\pi$ interaction is retained. The latter structure is peculiar as the N−C2 distance is shorter than in the carbene **29** itself. Nevertheless, following the IRC on the UB3LYP level beginning from **TS(29-5/31)a**, the reaction path leads to the carbene on the one side and the fragmentation products in loose contact with each other on the other side. Further optimization yields a weakly bound complex between ethylene and HCN (**5·31**), which is only 1.1 kcal mol$^{-1}$ lower in energy than the separated reactants.

The symmetric fragmentation is favored by 0.2 kcal mol$^{-1}$ over the methylene migration rearrangement to 1-azetine **30**. Formation of bicyclic 1-azabicyclo[1.1.0]-butane **23** (via $\beta$-CH-insertion, $\Delta H^{\ddagger} = 31.5$ kcal mol$^{-1}$) is predicted to be less favorable, although the barrier is only 2.1 kcal mol$^{-1}$ higher than toward ring expansion to **30**.

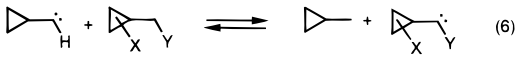
From these energies, fragmentation is the preferred reaction of **29**, confirming the results of the carbon arc reaction of aziridine.[16] From the CCSD(T) energies, **$^3$29** is by almost 24 kcal mol$^{-1}$ less stable than the singlet. Triplet pathways are therefore unlikely to occur for the ground states and have not been investigated in this study. To explain the unspecific fragmentation in the carbon arc generation of 2,3-dimethylaziridine (eq 4), the unsymmetric transition structure **TS(29-5/31)a** would have to allow a C2−C3 bond rotation during the ring opening. A similar explanation has been given for the stereochemical scrambling in vinylcyclopropane−cyclopentene rearrangements, which involves diradicaloid reaction paths with low barriers of $\sigma$ bond rotation.[47]

**Isodesmic Reactions.** To compare the relative intrinsic thermodynamic substituent effects of the oxirane and aziridine rings on the stability of methylene, isodesmic reactions have been calculated, which represent a dihydrogen transfer from the methyl or fluoromethyl substituent of a heterosubstituted ring to cyclopropylcarbene, yielding methylcyclopropane and the respective carbene (eq 6, Table 6).

**Table 6. Reaction Energies Including ZPE Corrections ($\Delta_R H$ (0 K))[a] for the Isodesmic Reaction Depicted in eq 6 in kcal mol$^{-1}$**

| | | | $\Delta_R H$ (0 K)[a] | | |
|---|---|---|---|---|---|
| carbene | X | Y | singlet | triplet | $E(S_0) - E(T_1)$[a,b,d] |
| **8b**; **$^3$8b** | 2-O | H | +5.9 | +2.0 | +2.3 |
| **15a**; **$^3$15b** | 2-O | F | −17.4 | −0.9 | −18.2 |
| **21a**; **$^3$21a** | 2-NH | H | +0.2 | +0.1 | −1.6 |
| **29**, **$^3$29a** | 1-N | H | −26.6 | −4.7 | −23.6 |
|  (32) | 1-O$^+$ | H | +11.3 | *c* | *c* |

[a] CCSD(T)/6-31G(d,p)//MP2/6-31G(d,p) + ZPE(MP2/6-31G(d,p)). [b] $E(S_0) - E(T_1)$ for **1**: −1.7 kcal mol$^{-1}$. [c] Not determined. [d] Singlet−Triplet splitting for the heterosubstituted carbenes in kcal mol$^{-1}$.



(6)

The positive enthalpies for the reactions leading to the formation of the 2-heterosubstituted singlet cyclopropylcarbenes **8b** and **21a** demonstrate the destabilizing effect exerted by the oxygen and nitrogen substituent in the ring. The $\pi$ donor effect from the substituent to the carbene is reduced by the lowering of the donor orbital energies in these rings, with the more electronegative oxygen leading to the larger effect. The larger acceptor capability of the $\sigma^*$(C2-X) orbital of the oxiranyl *vs* the 2-aziridinyl substituent cannot compensate this. The 2-aziridinyl carbene **21a** is almost isoenergetic to **1**, due to the comparable donor capability of the C2−C3 bond in **21a** and the cyclopropyl ring.

α-Fluorine substitution in the oxiranyl compound (**15a**) leads to an overall stabilization of 23.3 kcal mol$^{-1}$ as compared to **8b**. The replacement of both hydrogens in $^1CH_2$ with fluorine has been estimated to give a stabilizing energy of 54 kcal mol$^{-1}$, roughly consistent with this value.[1c]

As expected, the 1-aziridinylcarbene **29**, with the α-heteroatom directly interacting with the carbene center, is thermodynamically favored over **1**. The isoelectronic oxonium ion **32** (Table 6) might be expected to stabilize the carbene via a similar mechanism. This, however, is not found in the isodesmic reaction: Compared with the neutral nitrogen analogue, **32** is disfavored over **29** by more than 37 kcal mol$^{-1}$. The MP2 structure reveals no $\pi$ bond between C1 and O; the heteroatom has a pyramidal and not a planar geometry.[48] $O^+$ is too electronegative to share its lone pair as a $\pi$ donor.

The effect of the heteroatom on the reaction enthalpies in the triplet reactions is less pronounced for the four neutral carbenes. The compounds with strong $p_\pi-p_\pi$ interactions between the empty carbene p orbital and the substituent in the singlet state (**15**, **29**) show a much lower exothermicity in the triplet reaction.[6] This is due

(47) Houk, K. N.; Nendel, M.; Wiest, O.; Storer, J. W. *J. Am. Chem. Soc.* **1997**, *119*, 10545−10546.

(48) The B3LYP geometry (planar, $C_s$) differs from the MP2 structure.

to the singlet−triplet gap which reflects the loss of $\pi$-dative stabilization in the triplet.[49] $E(S_0) - E(T_1)$ for the $\beta$-heterosubstituted carbenes **8** and **21** is 1 order of magnitude smaller. The $\sigma-p_\pi$ donation mechanism is less effective than the former stabilization. The enthalpies for the reaction (eq 6) are still both positive, but within a smaller margin. The cyclopropyl substituent and its 2-heterosubstituted analogues do not differ much in their influence on a triplet carbene center.

## Conclusions

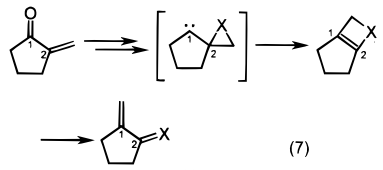
DFT and ab initio calculations have been used to explore the stability and intramolecular reactivity of carbenes bearing oxiranyl and aziridinyl subtituents. The "cheaper" DFT results are in good qualitative and sufficient quantitative agreement with the conclusions drawn from CCSD(T) calculations. For computational studies of similar, larger compounds this method can be highly recommended. Other groups have come to the same conclusion in theoretical studies of carbene reactions, although other basis sets and functionals were used.[50]

Unsubstituted 2-oxiranylcarbene **8** and 2-aziridinylcarbene **21** are predicted to have very low barriers toward rearrangement and fragmentation and are therefore difficult to be detected experimentally. The dependence of the main reaction pathways (ethyne extrusion *vs* ring expansion) on the initial conformation of these two intermediates is predicted to be the same as for cyclopropylcarbene **1**.

2-Oxiranylcarbene **8** is the simplest model for the intermediate formed in the fragmentation reactions of 2,3-epoxyhydrazones and related compounds. The results of this study explain the experimentally observed reaction with the very low barrier of the conformationally restricted *trans*-carbene. Two explanations for the nonuniform product distribution found in the reaction involving noncyclic 2,3-epoxycarbenes might be given which have not been investigated in terms of suitable experiments: (a) The triplet carbene ($^3$**8**) is predicted by theory as being preferred over the singlet and could open alternative pathways leading to more diverse and unselectively formed products. (b) The cis conformer of singlet **8**, after being generated from an open chain precursor, rearranges to oxete **9** before it can equilibrate with *trans*-**8b**. **9** reacts to completely different products in the following steps via ring opening or intermolecular reactions.

2-Aziridinylcarbenes derived from **21**, although not yet reported in the literature, are expected to behave very similar to the oxygen compounds. However, the singlet carbene will be preferred, since the aziridine ring in **21** has better $\pi$-donating (singlet-stabilizing) properties than the oxirane ring.

To find experimental evidence for the theoretical predictions, the investigation of heterocyclic spiro compounds is suggested as shown in eq 7. The conditions of the Eschenmoser−Tanabe fragmentation reaction have not yet been applied systematically to such precursors. The restricted cis conformation of a singlet oxiranyl- or aziridinylcarbene would favor the methylene migration to give a strained bicylic intermediate, which yields an $\alpha,\beta$-unsaturated ketone or imine in an electrocyclic ring opening reaction.




(7)

A fluorine substituent at the divalent carbon atom increases the kinetic and thermodynamic stability of 2-oxiranyl carbene. This opens new perspectives for the preparation of carbenes substituted with a heterosubstituted three-membered ring. Fluoro-2-oxiranylcarbene **15** is predicted to have a prolonged lifetime and to show selective reactions independent from the initial conformation. Similar effects may be expected for chlorine- or alkoxy-substituted 2-oxiranylcarbenes.

1-Aziridinylcarbene **29**, although kinetically and thermodynamically more stable than **8** and **21**, is predicted to fragment, in accord with the experimental observations. The asymmetric geometry of the transition structure accounts for the observed nonstereospecific reaction.

**Acknowledgment.** The author thanks the Deutsche Forschungsgemeinschaft (DFG) for a postdoc scholarship in the Graduiertenkolleg "Hochreaktive Mehrfachbindungssysteme" and Prof. E.-U. Würthwein for valuable discussions. The support of the computational centers at Münster (Universitätsrechenzentrum) and Köln (Rechenzentrum der Universität Köln) was highly appreciated.

**Supporting Information Available:** Calculated total energies (B3LYP and CCSD(T)) of the reported structures **1**−**32**, cartesian coordinates (MP2) for these compounds, vibrational frequencies for the major isomers of the investigated carbenes and $\langle S^2 \rangle$ values for the triplet species discussed in this work. This material is available free of charge via the Internet at http://pubs.acs.org.

JO991412X

(49) (a) Baird, N. C.; Taylor, K. F. *J. Am. Chem. Soc.* **1978**, *100*, 1333−1338. (b) Feller, D.; Borden, W. T.; Davidson, E. R. *Chem. Phys. Lett.* **1980**, *71*, 22−26. (c) Mueller, P. H.; Rondan, N. G.; Houk, K. N.; Harrison, J. F.; Hooper, D.; Willen, B. H.; Liebman, J. F. *J. Am. Chem. Soc.* **1981**, *103*, 5049−5052.

(50) Sulzbach, H. M.; Platz, M. S.; Schaefer, H. F., III.; Hadad, C. M. *J. Am. Chem. Soc.* **1997**, *119*, 5682−5689.