

Directly Measured Activation Parameters for the Ring Expansions of Cyclopropylhalocarbenes

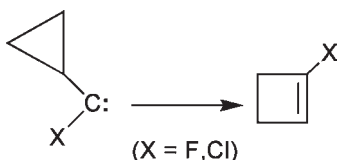
Yong-miao Shen, Robert A. Moss,* and Karsten Krogh-Jespersen*

Department of Chemistry and Chemical Biology, Rutgers, The State University of New Jersey, New Brunswick, New Jersey 08903, United States

moss@rutchem.rutgers.edu; krogh@rutchem.rutgers.edu

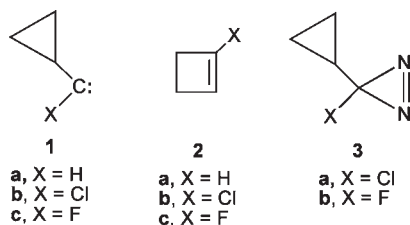
Received December 22, 2011

ABSTRACT



Activation parameters have been redetermined for the ring expansions of cyclopropylchlorocarbene and cyclopropylfluorocarbene; agreement between the experimental and computed activation parameters has been significantly improved.

The 1,2-C migration and ring expansion of cyclopropylcarbene (**1a**) to cyclobutene (**2a**) is the paradigmatic carbon shift among carbenic rearrangements.¹ The rate constant for this reaction has been estimated to be $\sim 4 \times 10^7 \text{ s}^{-1}$ in pentane at 25 °C,² but the associated activation parameters are unknown.



The analogous ring expansions of cyclopropylchlorocarbene (CyCCl, **1b**) and cyclopropylfluorocarbene

(CyCF, **1c**) to cyclobutenes **2b** and **2c** have been examined in greater detail.^{3,4} A compilation of kinetics data appears in Table 1, where it is seen that both CyCCl and CyCF ring expand with $10^5 < k < 10^6 \text{ s}^{-1}$.

However, the reported activation parameters are less certain: for both CyCCl and CyCF, we found low values of E_a ($\sim 3\text{--}4 \text{ kcal/mol}$) and $\log A$ ($\sim 8 \text{ s}^{-1}$), corresponding to $\Delta S^\ddagger \approx -22 \text{ eu}$.^{3d,e} For CyCCl, Bonneau and Liu reported higher values of the activation parameters: $E_a = 7.4 \text{ kcal/mol}$ and $\log A = 11.1 \text{ s}^{-1}$, corresponding to $\Delta S^\ddagger = -9.7 \text{ eu}$.^{3b} Both laboratories agreed that $\Delta G^\ddagger \approx 9\text{--}10 \text{ kcal/mol}$, but the contributions of ΔH^\ddagger and ΔS^\ddagger varied. In one report, $-T\Delta S^\ddagger$ was the major contributor to ΔG^\ddagger ,^{3d} whereas, in the other, ΔH^\ddagger was the principal component.^{3b}

(1) (a) Friedman, L.; Shechter, H. *J. Am. Chem. Soc.* **1960**, *82*, 1002. (b) Smith, J. A.; Shechter, H.; Bayless, J.; Friedman, L. *J. Am. Chem. Soc.* **1965**, *87*, 659.

(2) Modarelli, D. A.; Platz, M. S.; Sheridan, R. S.; Amann, J. R. *J. Am. Chem. Soc.* **1993**, *115*, 10440.

(3) (a) Bonneau, R.; Liu, M. T. H.; Rayez, M. T. *J. Am. Chem. Soc.* **1989**, *111*, 5973. (b) Liu, M. T. H.; Bonneau, R. *J. Phys. Chem.* **1989**, *93*, 7298. (c) Ho, G.-J.; Krogh-Jespersen, K.; Moss, R. A.; Shen, S.; Sheridan, R. S.; Subramanian, R. *J. Am. Chem. Soc.* **1989**, *111*, 6875. (d) Moss, R. A.; Ho, G.-J.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1990**, *112*, 1638. (e) Moss, R. A.; Ho, G.-J.; Liu, W. *J. Am. Chem. Soc.* **1992**, *114*, 959.

(4) Reviews: (a) Moss, R. A. *Adv. Carbene Chem.*; Brinker, U. H., Ed.; 1994, *1*, 59; see esp. pp 70f. (b) Merrer, D. C.; Moss, R. A. *Adv. Carbene Chem.*; Brinker, U. H., Ed.; 2001, *3*, 53; see esp. pp 95f.

Table 1. Kinetics of Ring Expansions of CyCX^{a,b}

carbene	$10^{-5}k$	E_a	ΔH^\ddagger	ΔS^\ddagger	ref
CyCCl	6				3a
CyCCl	3.8	7.4	6.8	-9.7	3b
CyCCl	9				3c
CyCCl	8–8.5	3.0	2.4	-22 ^c	3d
CyCF	1.4	4.2	3.6	-22	3e

^a In hydrocarbon solvents; temperature 20–25 °C for k . ^b k in s^{-1} , E_a and ΔH^\ddagger in kcal/mol, ΔS^\ddagger in eu. ^c Range of -20 to -24 eu was reported.

Computational studies similarly implicated a dominant enthalpic contribution. Our early HF/6-311G(d) calculations gave $\Delta H^\ddagger = 8.2$ kcal/mol and $\Delta S^\ddagger = -2.7$ eu for the $\text{CyCCl} \rightarrow \mathbf{2b}$ rearrangement.^{3c} More recent studies, at the highly comprehensive [HDFT + SM] SM5.42R/HF/6-31G(d)//mPW1PW91/6-31+G(d,p) level, afforded very similar final values, $\Delta H^\ddagger = 7.9$ kcal/mol and $\Delta S^\ddagger = -2.8$ eu (in simulated isooctane).⁵

Borden highlighted the experimental/computational discordance in his recent “Perspective” and pointed out that high level gas phase calculations ((10,10)/CASPT2/cc-pVTZ) gave $\Delta H^\ddagger = 14.7$ kcal/mol and $\Delta S^\ddagger = -2.7$ eu for the rearrangement of CyCF to $\mathbf{2c}$,^{5,6} compared to experimental values of 3.6 kcal/mol and -22 eu.^{3c} At the HDFT+SM level referred to above, the computed values were $\Delta H^\ddagger = 11.3$ kcal/mol and $\Delta S^\ddagger = -2.8$ eu.⁵ Borden emphasized that “there was and there still is a major disagreement” between the experimental and computational results.⁶

An important new development since the foregoing experimental³ and theoretical studies⁵ is the direct spectroscopic monitoring of carbenic reactions via their “forbidden” $\sigma \rightarrow \text{p}$ absorptions,⁷ which provides a new opportunity for measurement of the activation parameters for the CyCCl and CyCF ring expansions. The new results, described herein, significantly narrow, but do not entirely eliminate, the gap between the measured and computed activation parameters.

CyCCl. The UV–vis spectrum of CyCCl in a nitrogen matrix at 14 K revealed a broad visible absorption centered at 460 nm, and a more intense UV absorption at 240 nm.^{3c} We can also observe the CyCCl spectrum by laser flash photolysis (LFP) of diazirine $\mathbf{3a}$ at ambient temperature in pentane (Figure 1), where these absorptions are at 244 and 476 nm.^{7,8} We compute transitions for singlet CyCCl (E conformation, see below) at 215 nm ($f = \text{oscillator strength} = 0.33$), 227 nm ($f = 0.089$), 243 nm ($f = 0.0054$) and 494 nm ($f = 0.0052$) at the TD-B3LYP/6-311+G(d,p)//CCSD/6-311+G(d,p) level of theory (in simulated pentane); see Supporting Information for details. The long wavelength feature represents the $\sigma \rightarrow \text{p}$ transition at the carbenic carbon atom, whereas the absorption observed at shorter wavelengths is dominated by transitions involving the Walsh-type cyclopropyl ring orbitals and the localized carbene center σ and p orbitals.

Although one can follow the $\text{CyCCl} \rightarrow \mathbf{2b}$ rearrangement at 240 nm,^{3b-d} the long wavelength absorption at 476 nm is more sensitive in our LFP system,⁹ and the

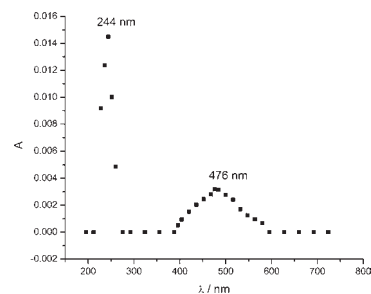


Figure 1. Calibrated UV–vis spectrum of CyCCl acquired 200 ns after LFP at 351 nm of diazirine $\mathbf{3a}$ ($A_{355} \approx 0.5$ in pentane).

analogous $\sigma \rightarrow \text{p}$ absorption can also be monitored for the CyCF rearrangement (see below).

In order to minimize competitive second order pathways for the disappearance of CyCCl by carbene dimerization^{3b} or the reaction of CyCCl with diazirine $\mathbf{3a}$, we carried out LFP of the diazirine at the lowest practical laser power (~ 62 mJ) and diazirine concentration ($A_{355} \sim 0.5$).¹⁰ These operational conditions were determined from correlations of k_{obs} for the disappearance of CyCCl at 476 nm vs laser power or diazirine concentration; see Figures S-2 and S-3 in the Supporting Information. Under the optimized conditions, we attribute the disappearance of CyCCl only to its rearrangement to $\mathbf{2b}$.¹¹

We measured the rate constant for the $\text{CyCCl} \rightarrow \mathbf{2b}$ rearrangement in pentane under the optimized LFP conditions at a series of temperatures between 261 and 310 K.¹² The resulting Arrhenius correlation of $\ln k$ vs $1/T$ appears in Figure 2, and affords $E_a = 5.9 \pm 0.09$ kcal/mol, $\ln A = 23.8 \pm 0.3 \text{ s}^{-1}$, and $\Delta S^\ddagger_{298} = -13.2 \pm 0.6$ eu.

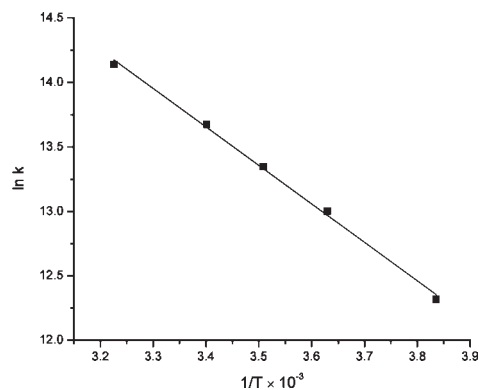


Figure 2. Arrhenius correlation for $\text{CyCCl} \rightarrow \mathbf{2b}$: $\ln k$ (s^{-1}) vs $1/T$ (K^{-1}); $E_a = 5.9$ kcal/mol, $\ln A = 23.8 \text{ s}^{-1}$, $r = -0.998$.

(5) Albu, T. V.; Lynch, B. J.; Truhlar, D. G.; Goren, A. C.; Hrovat, D. A.; Borden, W. T.; Moss, R. A. *J. Phys. Chem. A* **2002**, *106*, 5323.

(6) Borden, W. T. *J. Org. Chem.* **2011**, *76*, 2943.

(7) Moss, R. A.; Tian, J.; Sauers, R. R.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **2007**, *129*, 10019.

(8) LFP experiments employed a XeF_2 excimer laser emitting 42–56 ns light pulses at 351 nm with 52–65 mJ power.

(9) Our LFP detector system is more sensitive in the 400–500 nm region than it is at 200–300 nm; compare the calibrated Figure 1 with uncalibrated Figure S1 in the Supporting Information. Kinetics data were obtained by monitoring the uncalibrated CyCCl and CyCF spectra in the 400–500 nm region.

(10) For the preparation of diazirine $\mathbf{3a}$, see: (a) Graham, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 4396. See also: (b) Moss, R. A.; Fantina, M. E. *J. Am. Chem. Soc.* **1978**, *100*, 6788. (c) See reference 3e.

Two additional determinations gave $E_a = 5.9$ and 6.0 kcal/mol, and $\Delta S^\ddagger_{298} = -13.9$ eu and -13.1 eu; see Figures S4 and S5 in the Supporting Information. The average values of the activation parameters for 3 independent measurements are $E_a = 5.9 \pm 0.03$ kcal/mol and $\Delta S^\ddagger_{298} = -13.4 \pm 0.3$ eu. A more detailed error analysis (taking account of the maximum variance in each Arrhenius correlation) affords uncertainties of ± 0.4 kcal/mol in E_a and ± 1.4 eu in ΔS^\ddagger_{298} .

CyCF. LFP at 351 nm of diazirine **3b**^{3c} in pentane gives the spectrum shown in Figure 3, where the carbenic transition of CyCF appears at 404 nm. For the singlet *E* CyCF conformer, the computed wavelength for this transition is 412 nm ($f = 0.011$) at the TD-B3LYP/6-311+G(d,p)//CCSD/6-311+G(d,p) level of theory (in simulated pentane). We did not observe the short wavelength transitions computed just below 200 nm (see Supporting Information).

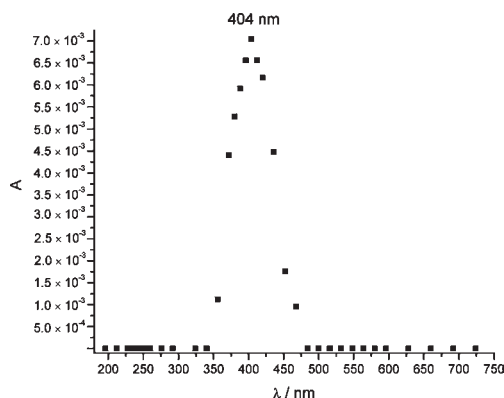


Figure 3. UV-vis spectrum of CyCF acquired 200 ns after LFP at 351 nm of diazirine **3b** ($A_{354} \approx 0.3$ in pentane).

LFP conditions for diazirine **3b** were optimized to employ the minimum practical laser power (52 mJ) and diazirine concentration ($A_{354} \approx 0.3$); see Figures S6 and S7 in the Supporting Information. We then determined the rate constants for the decay of CyCF at 404 nm in pentane, under the optimized LFP conditions, at a series of 5 temperatures between 264 and 308 K.¹³ The resulting Arrhenius correlation for the $\text{CyCF} \rightarrow \mathbf{2c}$ rearrangement

(11) Even at higher diazirine concentration ($A \approx 1.0$) and laser power (70–80 mJ), product analyses revealed 85–92% yields of **2b**, with no evidence of carbene dimer, although some carbene-diazirine ylide might have formed.^{3d} Capillary GC analysis confirmed 85–92% yields of **2b**, with no evidence of carbene dimer.^{3d}

(12) (a) At 295 K, the directly measured rate constant at 476 nm for the $\text{CyCCl} \rightarrow \mathbf{2b}$ rearrangement was $8.5 \times 10^5 \text{ s}^{-1}$ in good agreement with previous values (see Table 1), and with $k = 6.2 \times 10^5 \text{ s}^{-1}$ measured by the (indirect) pyridine ylide method at 372 nm. Pyridine ylide method: (b) Jackson, J. E.; Soundararajan, N.; Platz, M. S.; Liu, M. T. H. *J. Am. Chem. Soc.* **1988**, *110*, 5595.

(13) At 295 K, the directly measured rate constant at 404 nm for the $\text{CyCF} \rightarrow \mathbf{2c}$ rearrangement was $5.8 \times 10^5 \text{ s}^{-1}$, somewhat faster than the old pyridine ylide-determined^{12b} rate constant ($1.4 \times 10^5 \text{ s}^{-1}$),^{3e} but in reasonable agreement with a newly measured pyridine ylide value, $k = 4.1 \times 10^5 \text{ s}^{-1}$ at 364 nm.

appears in Figure 4, where $E_a = 7.8 \pm 0.2$ kcal/mol and $\ln A = 26.6 \pm 0.7 \text{ s}^{-1}$, corresponding to $\Delta S^\ddagger_{298} = -7.8 \pm 1.4$ eu.

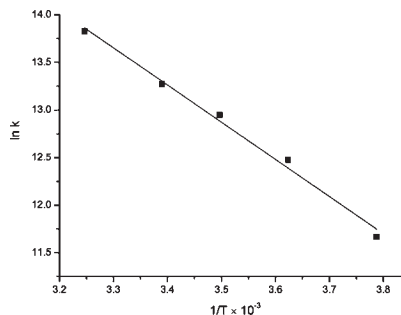


Figure 4. Arrhenius correlation for $\text{CyCF} \rightarrow \mathbf{2c}$: $\ln k (\text{s}^{-1})$ vs $1/T (\text{K}^{-1})$; $E_a = 7.8$ kcal/mol, $\ln A = 26.6 \text{ s}^{-1}$, $r = -0.996$.

Two additional determinations led to $E_a = 7.6$ and 8.2 kcal/mol, and $\Delta S^\ddagger_{298} = -7.8$ eu and -6.4 eu; see Figures S-8 and S-9 in the Supporting Information. The average values of the activation parameters for 3 independent measurements are $E_a = 7.9 \pm 0.2$ kcal/mol and $\Delta S^\ddagger_{298} = -7.3 \pm 0.6$ eu. A more detailed analysis affords uncertainties of ± 0.5 kcal/mol in E_a and ± 2.0 eu in ΔS^\ddagger_{298} .

Computations. Cyclopropylcarbenes **1** may exist as *E* and *Z* conformers [dihedral angle $\text{H-C}(\text{Cy})\text{-C}(\text{carbene})\text{-Cl}(\text{F}, \text{H}) = 0^\circ$ or 180° , respectively].^{3c} On the singlet potential energy surface at the CCSD/6-311+G(d,p)//CCSD/6-311+G(d,p) level, *E*-CyCCl is found to be 3.3 kcal/mol lower in free energy than *Z*-CyCCl, and the potential energy barrier to $Z \rightarrow E$ interconversion is 9.1 kcal/mol. Internal rotation thus presents the lowest energy reaction pathway for *Z*-CyCCl, since the 1,2-C migration has been computed to be opposed by a barrier of more than 20 kcal/mol.^{3c} The adiabatic singlet-triplet separation in *E*-CyCCl is 13.8 kcal/mol in favor of the singlet. For CyCF, we find a *E-Z* free energy difference of 1.9 kcal/mol and a potential energy barrier to $Z \rightarrow E$ interconversion of 8.9 kcal/mol; the adiabatic singlet-triplet separation in CyCF is computed at 23.1 kcal/mol. Thus, the ring expansions observed here undoubtedly involve *E*-cyclopropylhalocarbenes reacting in their *singlet* states.¹⁴

A comparison of our new, directly measured activation parameters for the CyCCl and CyCF rearrangements with the analogous computed values from the thorough study of Albu et al.⁵ appears in Table 2. Also included in Table 2 are results from our new calculations, which apply coupled-cluster (CC) electronic structure methods to account for electron correlation effects.¹⁵ Our results largely confirm those of the previous work⁵ and will

(14) For the parent cyclopropylcarbene, CyCH, we find an *E-Z* free energy difference of only 0.9 kcal/mol but a potential energy barrier to $Z \rightarrow E$ interconversion of 14.7 kcal/mol. The adiabatic singlet-triplet separation is only 2.3 kcal/mol but remains in favor of the singlet state.

(15) Shavitt, I.; Bartlett, R. J. *Many-Body Methods in Chemistry and Physics: MBPT and Coupled-Cluster Theory*; Cambridge University Press: New York, 2009.

therefore be described only briefly (a full description is available in the Supporting Information).

From geometry optimizations and normal-mode analysis of CyCCl, CyCF, and the TS's for ring expansion at the CCSD/6-311+G(d,p) level we derive $\Delta S^\ddagger_{298} = -3.0$ and -2.9 eu for CyCCl and CyCF, respectively (Table 2). From CCSD(T)/cc-pVQZ//CCSD/cc-pVQZ calculations, we obtain gas phase electronic barrier heights $\Delta E^\ddagger = 11.2$ and 15.8 kcal/mol for CyCCl and CyCF, respectively. We estimate the effect of adding diffuse basis functions to the cc-pVQZ basis set from comparative CCSD(T) calculations with aug-cc-pVTZ/cc-pVTZ basis sets and employ zero-point vibrational and thermal energy corrections from the CCSD/6-311+G(d,p) calculations to arrive at gas phase activation enthalpy values $\Delta H^\ddagger_{298} = 9.6$ and 13.6 kcal/mol for CyCCl and CyCF, respectively. Finally, including bulk solvation effects via a dielectric continuum model reduces the barriers by $0.8 - 0.9$ kcal/mol and leads to values of $\Delta H^\ddagger_{298} = 8.8$ and 12.7 kcal/mol for CyCCl and CyCF, respectively, in simulated pentane solution (Table 2).

The new experimental values for CyCCl in Table 2 are in reasonable agreement with the Bonneau-Liu data^{3b} in Table 1. Our new computed values for ΔH^\ddagger in the gas phase are slightly smaller ($\sim 0.5 - 1.0$ kcal/mol) than those calculated by Albu et al.,⁵ whereas the ΔS^\ddagger values are virtually identical. The more elaborate solvation model applied by Albu et al.⁵ (SM5.2R) generates larger reductions in activation enthalpies ($2.2 - 2.7$ kcal/mol) than the solvation model applied by us (CPCM). In fact, if we appropriate the differential solvation energy values of Albu et al.⁵ and apply them to our gas phase activation enthalpies, we arrive at "best values" of $\Delta H^\ddagger_{298} = 7.4$ and 10.9 kcal/mol for CyCCl and CyCF, respectively (Table 2). Disparities between the newly measured experimental data and the older or newly computed parameters are thus significantly reduced: differences between measured and computed values are now $\sim 2 - 4$ kcal/mol in E_a or ΔH^\ddagger , and $\sim 4 - 11$ eu in ΔS^\ddagger . Taking account of the uncertainties in the measured values further narrows the differences. Previously, the gaps between our experimental data (Table 1) and the computed parameters were $5 - 8$ kcal/mol in E_a or ΔH^\ddagger , and ~ 19 eu in ΔS^\ddagger .¹⁶

The present differences of $2 - 4$ kcal/mol between measured and computed values of E_a or ΔH^\ddagger are not egregious; future applications of even higher levels of correlation energy treatments than CCSD(T) are likely to further reduce the activation energies. The disparities of $4 - 11$ eu in ΔS^\ddagger may be of greater concern. However, the experimental ΔS^\ddagger is inherently less accurate than ΔH^\ddagger , because the former derives from the extrapolated

(16) It is difficult to account for discrepancies between the newly determined activation parameters and our older data.^{3d} However, the new values stem from optimized experimental conditions using the most direct and sensitive spectroscopic measurements yet employed.

Table 2. Experimental and Computed Activation Parameters^a

carbene	E_a	ΔH^\ddagger_{298}	ΔS^\ddagger_{298}	ref
CyCCl	5.9 (0.4)	5.3 (0.4)	-13.4 (1.4)	^b (exp)
CyCCl	10.2	9.6	-3.0	^c (comp)
CyCCl	9.4	8.8	-3.0	^d (comp)
CyCCl	8.0	7.4	-3.0	^e (comp)
CyCCl	8.5	7.9	-2.8	^f (comp)
CyCF	7.9 (0.5)	7.3 (0.5)	-7.3 (2.0)	^b (exp)
CyCF	14.2	13.6	-2.9	^c (comp)
CyCF	13.3	12.7	-2.9	^d (comp)
CyCF	11.5	10.9	-2.9	^e (comp)
CyCF	11.9	11.3	-2.8	^f (comp)

^a E_a and ΔH^\ddagger_{298} in kcal/mol; ΔS^\ddagger_{298} in eu. Uncertainties are shown in parentheses. ^b This work, experimental values in pentane. ^c This work, idealized gas phase. ^d This work, in simulated pentane. ^e Our best gas phase results combined with solvation energies from ref 5, see text. ^f Reference 5, in simulated isooctane.

intercept, rather than the measured slope, of the Arrhenius correlation. Electronic structure calculations on a solitary cyclopropylhalocarbene, whether carried out in idealized gas phase or solution phase simulated as a continuum, inevitably converge on a TS for ring expansion with $\Delta S^\ddagger \approx -3$ eu, as found in the present work and previously published in the literature.^{3c,5} Consequently, location of a qualitatively different TS is required to obtain different (more negative) computed ΔS^\ddagger values. Explicit consideration of discrete solvent molecules in addition to a dielectric continuum, perhaps within a combined quantum-classical mechanical dynamics simulation framework (QM/MM), could conceivably improve upon the estimates of *both* ΔS^\ddagger and ΔH^\ddagger , even in a hydrocarbon solvent, because the TS's for ring expansion show an increase in polarity relative to the carbene ground states.

It seems fair to conclude that the new direct measurements of the activation parameters for the CyCX rearrangements, at their $\sigma \rightarrow p$ carbenic absorptions, have eliminated "major disagreement"⁶ between experimental and computational results. Moreover, there may still be room for improvement in our detailed physical understanding of this seemingly "simple" intramolecular rearrangement.

Acknowledgment. We are grateful to the National Science Foundation and the Petroleum Research Fund for financial support.

Supporting Information Available. Figures S1–S9, computational details, and optimized geometries, absolute energies, electronic excitation energies and oscillator strengths of all relevant species. This material is available free of charge via the Internet at <http://pubs.acs.org>.

The authors declare no competing financial interest.