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Kinetic Studies of the Cyclization of Singlet Vinylchlorocarbenes

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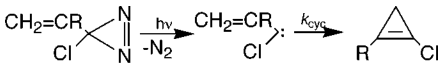
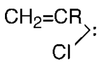
ABSTRACT



Vinylchlorocarbenes (R = Me or Cl) cyclize to cyclopropenes with k = (2.4–5.1) × 10^7 s^{-1} or (3.1–4.5) × 10^6 s^{-1}, respectively, in solution at room temperature. The corresponding E_a values are 6.6 and 5.7 kcal/mol. Excited diazirines are also likely precursors of the cyclopropenes.

Closs's discovery that vinylcarbenes and vinylcarbenoids cyclize to cyclopropenes[1] stimulated many subsequent studies of these highly reactive small ring compounds.[2] That cyclopropenes also undergo thermal reversion to their precursor vinylcarbenes greatly enhanced that interest.[3] Nevertheless, few direct characterizations of vinylcarbenes were available until recently. Several ground-state triplet vinylcarbenes had been examined by EPR[4] and IR[5] spectroscopy in cryogenic matrixes, but there were no comparable reports of singlet vinylcarbenes, the key reactive intermediates of the cyclopropene formation and reversion reactions.[1−3] In 2004, the first UV and IR studies were reported for several matrix-isolated singlet ground-state vinylchlorocarbenes (e.g., **1a**, **1b**), together with an account of their photochemically driven conversion to cyclopropenes **2a**,**2b** and allene **3a**.[6]

Here, we describe the first studies of the kinetics of singlet vinylcarbene to cyclopropene cyclization in solution. The subject carbenes are (1-methylvinyl)chlorocarbene (**1b**) and (1-chlorovinyl)chlorocarbene (**1c**), and the cyclization rate constants are accompanied by both experimentally determined and computed activation parameters. Moreover, we present compelling evidence that there is more than one direct precursor of the cyclopropenes formed in our reactions, with the excited diazirine precursors of carbenes **1b** and **1c** as the most likely second source.



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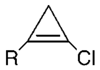

2

CH$_2$=C=CRCl

3

(**a**, R=H; **b**, R=CH$_3$; **c**, R=Cl)

Amidines **4b**[6] and **4c** were prepared from the corresponding nitriles by reaction with methylchloroaluminum amide[6−9] and then oxidized to the 3-chloro-3-vinyldiazirines **5b** and **5c** with hypochlorite.[6,9,10] In pentane solution, the diazirines display multiple UV absorptions in the 340−390 nm region. Laser flash photolysis (LFP)[11] at 351 nm of diazirines **5b** and **5c** in pentane afforded carbenes **1b** and **1c** with UV

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[1] (a) Closs, G. L.; Closs, L. E. *J. Am. Chem. Soc.* **1961**, *83*, 1003. (b) Closs, G. L.; Closs, L. E. *J. Am. Chem. Soc.* **1961**, *83*, 2015. (c) Closs, G. L.; Closs, L. E.; Böll, W. A. *J. Am. Chem. Soc.* **1963**, *85*, 3796.

[2] Misslitz, U.; de Meijere, A. In *Methoden der Organischen Chemie, Houben* Weyl *(Carbene Carbenoide)*; Georg Thieme Verlag: Stuttgart, Germany, 1989; Vol. E19b, pp 664f.

[3] Baird, M. S. *Chem. Rev.* **2003**, *103*, 1271.

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[7] (a) Garigipati, R. S. *Tetrahedron Lett.* **1990**, *31*, 1969. (b) Levin, J. I.; Turos, E.; Weinreb, S. M. *Synth. Commun.* **1982**, *12*, 989.

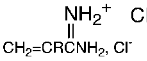
[8] Moss, R. A.; Ma, W.; Merrer, D. C.; Xue, S. *Tetrahedron Lett.* **1995**, *36*, 8761.

[9] See the Supporting Information for details.

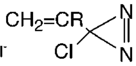
[10] Graham, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 4396.

10.1021/ol051743y CCC: $30.25

absorptions at λ_{max} 270 nm (**1b**) and 290 nm (**1c**), as illustrated in Figures S1[9] and S2,[9] respectively. We did not observe the weak long wavelength absorption at 680 nm that was reported for matrix-isolated **1b**.[6] In pentane solutions containing 50 mM of pyridine, LFP provided absorptions at 460 and 450 nm, respectively, for the pyridinium ylides[12] of carbenes **1b** (Figure S3)[9] and **1c** (Figure S4).[9]


$\overset{NH_2^+}{\overset{\|}{CH_2{=}CRCNH_2}}$, Cl^-

4



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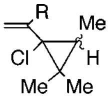

6

Conventional photolysis of diazirines **5b** and **5c** in $CDCl_3$ at 350 nm afforded cyclopropenes **2b**[6] and **2c**, identified by NMR and GC−MS. Cyclopropene **2b** was formed cleanly, but **2c** was accompanied by small quantities of several unidentified impurities. We attribute the cyclopropene formation (in part) to the intermediacy of carbenes **1b** and **1c**, which are expected to cyclize.[1−3] The carbenes could also be competitively intercepted by addition to an olefin: photolysis of diazirines **5b** and **5c** in the presence of trimethylethylene (TME, 2-methyl-2-butene) gave cyclopropane adducts **6b** and **6c** in 50% yields, each as a mixture of stereoisomers. The adducts were characterized by ^{1}H and ^{13}C NMR spectroscopy and GC−MS.[9]

Absolute rate constants for cyclizations of carbenes **1b** and **1c** to cyclopropenes **2b** and **2c** were determined by LFP. We first used the pyridine ylide method.[12] LFP at 351 nm and 25 °C of a pentane solution of diazirine **5b** ($A_{370} = 0.5$) in the presence of pyridine afforded an absorption for the pyridinium ylide derived from carbene **1b** at 460 nm (Figure S3, Supporting Information). A correlation of the apparent rate constants for ylide formation (5.2×10^7−6.5×10^7 s^{-1}) vs pyridine concentration (0.46−3.5 mM) was linear (8 points, $r = 0.996$) with a slope of 4.1×10^9 M^{-1} s^{-1}, equivalent to the rate constant for ylide formation, and a *Y*-intercept of 5.1×10^7 s^{-1} (see Figure S5, Supporting Information). The latter value can be equated with k_{cyc} for **1b** → **2b**, the process that destroys >90% of carbene **1b** in the absence of pyridine.

An alternative LFP determination of k_{cyc} employed TME rather than pyridine as the carbene trap and directly monitored the quenching of the carbene's UV absorption at 270 nm (Figure S1, Supporting Information). A correlation of the apparent rate constants for carbene quenching (2.5×10^7−5.2×10^7 s^{-1}) vs the concentration of TME in pentane (0.0−0.16 M) was linear (6 points, $r = 0.998$) with a slope of 1.7×10^8 M^{-1} s^{-1}, which we take as the rate constant for addition of **1b** to TME, and a *Y*-intercept of 2.4×10^7 s^{-1} (see Figure S6, Supporting Information). The latter value can be taken as k_{cyc} for **1b** → **2b**. From the pyridine- and TME-quenching experiments, we conclude that the cyclization of **1b** to **2b** occurs with a rate constant of (2.4−5.1) × 10^7 s^{-1}.

A parallel series of pyridine and TME LFP quenching experiments were carried out with diazirine **5c** (carbene **1c**). The results are shown in Figures S7 and S8 (Supporting Information) and led to $k_{cyc} = (3.1{-}4.5) \times 10^6$ s^{-1} for the cyclization of carbene **1c** to cyclopropene **2c**, about 10 times slower than the cyclization of **1b** to **2b**. For perspective, we note that these cyclization rate constants are comparable to the rate constants characterizing the 1,2-H shifts which convert alkylchlorocarbenes to chloroalkenes.[13]

LFP determinations of k_{cyc} at various temperatures afforded activation parameters for the carbene cyclizations. Thus, k_{cyc} was determined for carbene **1b** using the pyridine method at seven temperatures ranging from −30 °C ($k_{cyc} = 4.42 \times 10^6$ s^{-1}) to 28.1 °C ($k_{cyc} = 6.16 \times 10^7$ s^{-1}). An Arrhenius correlation of ln k_{cyc} vs $1/T$, shown in Figure S9,[9] is reasonably linear ($r = 0.991$) and gives $E_a = 6.6$ kcal/mol, ln $A = 29.1$ s^{-1}, and $\Delta S^* = -2.6$ eu. Analogous experiments for the cyclization of carbene **1c** lead to the Arrhenius correlation shown in Figure S10 (Supporting Information), from which we derive $E_a = 5.7$ kcal/mol, ln $A = 25.2$ s^{-1}, and $\Delta S^* = -10.5$ eu.

Most intriguingly, carbenes **1b** and **1c** cannot be the sole precursors of cyclopropenes **2b** and **2c**. Consider the photolysis of diazirine **5b** to generate carbene **1b** in TME. The carbene partitions between intramolecular addition, affording cyclopropene **2b**, and intermolecular addition yielding adducts **6b**. If the carbene were the only precursor of **2b** and **6b**, then a plot of the product ratio **6b**/**2b** vs [TME] would be linear. As illustrated in Figure 1, however, this correlation is distinctly curved.[14] Very similar results were obtained for the intermolecular/intramolecular partitioning of **1c**, as shown in Figure S11 and Table S2 (Supporting Information).

The situation is analogous to the 1,2-H shift rearrangements of, e.g., methylchlorocarbene[15] and benzylchlorocarbene[16] (also generated by diazirine photolysis), where correlations of (carbene−alkene trapping/carbene rearrange-

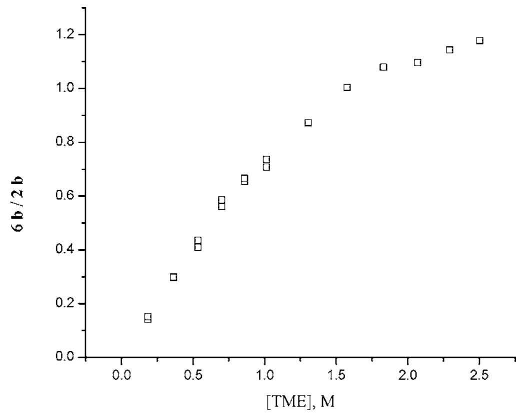

Figure 1. Product ratio **6b**/**2b** vs [TME] (M).

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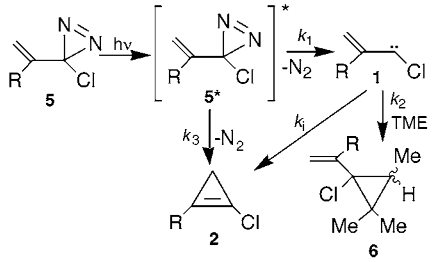
[11] For a description of our LFP system, see: Moss, R. A.; Johnson, L. A.; Merrer, D. C.; Lee, G. E., Jr. *J. Am. Chem. Soc.* **1999**, *121*, 5940. The 1000 W Xe monitoring lamp has been replaced by a 150 W pulsed Xe lamp.

[12] (a) Jackson, J. E.; Soundararajan, N.; Platz, M. S.; Liu, M. T. H. *J. Am. Chem. Soc.* **1988**, *110*, 5595. (b) Platz, M. S.; Modarelli, D. A.; Morgan, S.; White, W. R.; Mullins, M.; Celebi, S.; Toscano, J. P. *Prog. React. Kinet.* **1994**, *19*, 93.

ment) vs alkene concentration are also curved. It is accepted that this curvature implicates a second reactive intermediate (besides the carbene) as a precursor of the rearrangement product,[15,16] and after much consideration,[17] the most likely candidate appears to be an excited state of the diazirine which can directly yield the same intramolecular product as the carbene.[18]

If this is also true for the photolytic decompositions of diazirines **5b** and **5c**, then we can represent these reactions with Scheme 1.[15−17] Here, excited diazirine **5*** can lose nitrogen (k_1), affording carbene **1**, which can either add to TME (k_2) or cyclize (k_i) to cyclopropene **2**. However, **5*** can also give the cyclopropene *directly* (k_3).[19] From Scheme 1, we obtain eq 1,[15,17] which predicts that an inverse correlation of **2**/**6** vs 1/[TME] will be linear.

Scheme 1



$$\mathbf{2/6} = k_3/k_1 + k_i(k_1 + k_3)/k_1k_2[\mathrm{TME}] \qquad (1)$$

As shown in Figure 2, the appropriate plot of the **2b**/**6b** product ratio for the photolysis of diazirine **5b** in TME−pentane is indeed linear. The analogous inverse correlation of the **2c**/**6c** product ratio for photolysis of diazirine **5c** is also linear; see Figure S12 (Supporting Information).

From Figure 1 (and Table S1, Supporting Information), we estimate that about 40% of cyclopropene **2b** forms even in the presence of excess TME and can be attributed to a noncarbenic origin. In the case of diazirine **5c**, we estimate that about 50−55% of cyclopropene **2c** is formed in this manner.[20]

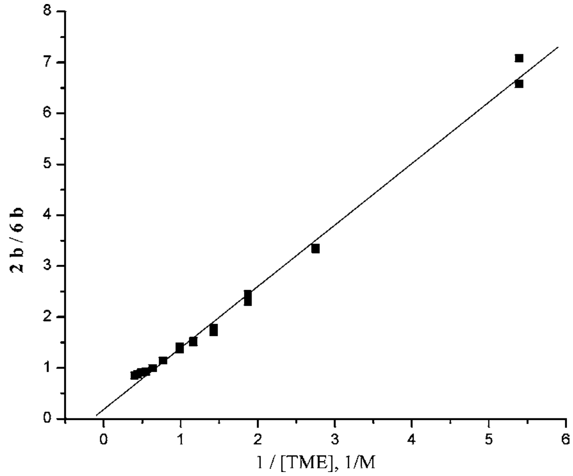
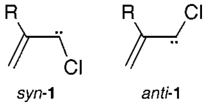


Figure 2. Product ratio **2b**/**6b** vs 1/[TME] (M^{-1}).

What other explanations can be considered for these results? The "second intermediate" of Scheme 1 and eq 1 could be an excited carbene[21] rather than an excited diazirine. However, the work of Platz et al. strongly suggests that excited diazirines are most reasonably associated with the curvature of correlations such as those in Figures 1 and S11 (Supporting Information).[18] Similarly, carbene−alkene complexes are kinetically competent but mechanistically unlikely second intermediates.[17,18]

Another alternative involves the syn and anti conformations of carbene **1**, which have been identified in the matrix IR spectra of **1b**.[6] If one conformer cyclized too rapidly to be captured by an added alkene while the other conformer was more readily trapped, one could explain the curvature in Figure 1 and the linearity in Figure 2. To examine this possibility, we subjected the carbenes to B3LYP/6-31+G-(d,p) computational studies.[22−24] Results for carbene **1b** appear in Figure 3, where it is seen that *anti*-**1b** is more stable than *syn*-**1b** by 3.7 kcal/mol. Cyclization of *syn*-**1b** to **2b** is opposed by a large enthalpic barrier (15 kcal/mol), but its isomerization to *anti*-**1b** requires only 4.3 kcal/mol. Thus, syn-**1b** is predicted to isomerize to *anti*-**1b**, whose cyclization



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(13) Merrer, D. C.; Moss, R. A. *Adv. Carbene Chem.* Brinker, U. H., Ed. **2001**, *3*, 53f.

(14) The product ratios were determined by capillary GC on a 30 m 5% phenylmethylsiloxane column. The product distributions appear in Table S1 (Supporting Information).

(15) LaVilla, J. A.; Goodman, J. L. *Tetrahedron Lett.* **1990**, *31*, 5109.

(16) (a) Tomioka, H.; Hayashi, N.; Izawa, Y.; Liu, M. T. H. *J. Am. Chem. Soc.* **1984**, *106*, 454. (b) Liu, M. T. H.; Subramanian, R. *Tetrahedron Lett.* **1985**, *26*, 3071. (c) Bonneau, R.; Liu, M. T. H.; Kim, K. C.; Goodman, J. L. *J. Am. Chem. Soc.* **1996**, *118*, 3829.

(17) Reviews: (a) Liu, M. T. H. *Acc. Chem. Res.* **1994**, *27*, 287. (b) Moss, R. A. *Adv. Carbene Chem.* Brinker, U. H., Ed. **1994**, *1*, 59. (c) Platz, M. S. *Adv. Carbene Chem.* Brinker, U. H., Ed. **1998**, *2*, 133. (d) Reference 13.

(18) (a) Robert, M.; Likhotvorik, I. R.; Platz, M. S.; Abbot, S. C.; Kirchoff, M. M.; Johnson, R. *J. Phys. Chem.* **1998**, *120*, 1507. (b) Nigam, M.; Platz, M. S.; Showalter, B. M.; Toscano, J. P.; Johnson, R.; Abbot, S. C.; Kirchoff, M. M. *J. Am. Chem. Soc.* **1998**, *120*, 8055.

(19) More likely the proximate intermediate is actually the 1,3-carbon−nitrogen diradical obtained by a single C−N homolysis of **5***; cf. ref 17c, pp 165f.

(20) See Table S2 and Figure S11 (Supporting Information).

(21) Warner, P. M. *Tetrahedron Lett.* **1984**, *25*, 4211.

(22) All structures were fully optimized by analytical gradient methods using the Gaussian 03 suite[23] and density functional (DFT) calculations at the 6-31+G(d, p) level, the exchange potentials of Becke,[24a] and the correlation functional of Lee, Yang, and Parr.[24b] Activation energies were corrected for zero-point energy differences (ZPVE) (unscaled) and thermal effects at 298.150 K. Vibrational analyses established the nature of all stationary points as either energy minima (no imaginary frequencies) or first-order saddle points (one imaginary frequency).

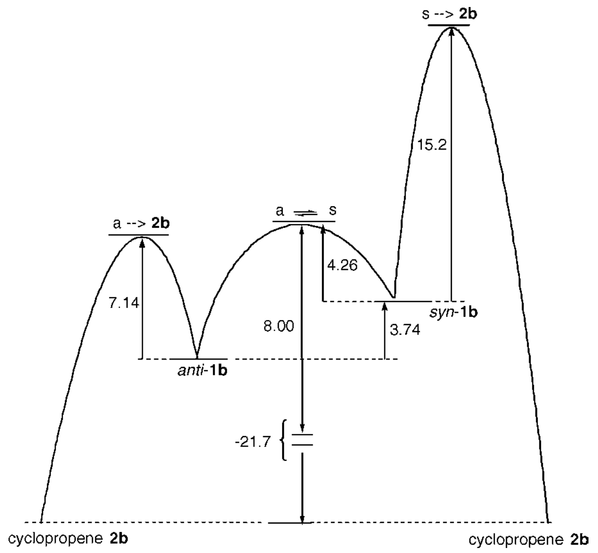

Figure 3. Computed enthalpies for conformers of **1b** and transition states for their interconversion and cyclization to **2b** (energies in kcal/mol).

to **2b** has $\Delta H^* = 7.1$ kcal/mol, in good agreement with the experimentally determined $E_a = 6.6$ kcal/mol for cyclization of carbene **1b** (see above). *anti*-**1b** is therefore the likely source of cyclopropene **2b** and, as the rate constant for cyclization ($2.4-5.1 \times 10^7$ s^{-1}) is *smaller* than the rate constant for addition to TME (1.7×10^8 M^{-1} s^{-1}), *anti*-**1b** should be efficiently trapped by added alkene. It thus seems unlikely that an explanation based on carbene conformers can account for the duality of paths to cyclopropene **2b** or the failure of added TME to fully prevent its formation. Computational studies of carbene **1c** parallel those of **1b** and lead to similar conclusions;[25] see Figure S13 (Supporting Information).

The direct path from excited diazirines **5a**,**b** to the corresponding cyclopropenes also operates at very low temperatures. Previously,[6] irradiation of matrix isolated **5b** produced a significant amount of cyclopropene **2b** together with carbene **1b**. Comparison of the experimental IR spectra with DFT calculated intensities suggests direct formation of ~30−50% of cyclopropene (although some of the **2b** likely arose from adventitious irradiation of the carbene). Subsequent irradiation at wavelengths absorbed by **1b** converted the carbene to additional **2b**.

In the present study, we explored the photochemistry of diazirine **5c** at 10 K.[26] Irradiation of N_2 matrix isolated **5c** with 375 nm light produced a mixture of carbene *anti*-**1c** and cyclopropene **2c** in a ratio of ~3:2, judging by comparison of the observed and calculated IR spectra. No evidence was obtained for *syn*-**1c**, which is predicted to have a distinct IR spectrum.[27] The new IR spectrum was accompanied by a strong UV absorption at 290 nm, and a very broad weak absorption centered at 750 nm in the visible spectrum. Strikingly, irradiation of **1c** at 480 nm for 1 h led to some additional **2c**, but mainly to a new product whose IR fits that calculated for 1,1-dichloroallene **3c** (see Figures S14 and S15).[9] Taken together, the matrix results suggest that excited diazirine **5c*** leads *directly* to cyclopropene **2c**, and not to an excited state of carbene **1c**.

Acknowledgment. We thank the National Science Foundation (Rutgers and Nevada) and the donors of the Petroleum Research Fund (Nevada) for financial support. We acknowledge the National Center for Computer Applications for time on the IBM P Series 690 (to R.R.S.).

Supporting Information Available: UV spectra of carbenes and ylides, determinations of rate constants, preparative procedures, and products. This material is available free of charge via the Internet at http://pubs.acs.org.

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[23] *Gaussian 03*, revision B.03; Gaussian, Inc.; Pittsburgh, PA, 2003. See the Supporting Information for the full reference.

[24] (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B.* **1988**, *37*, 785.

[25] *anti*-**1c** is computed to be 5.8 kcal/mol more stable than *syn*-**1c** and to face a barrier of 8.3 kcal/mol for cyclization to **2c**. *syn*-**1c** requires 4.9 kcal/mol to isomerize to *anti*-**1c**, but 13 kcal/mol to cyclize to **2c**.[9]

[26] See ref 6 for matrix isolation methodology and instrumentation.

[27] TD-B3LYP/6-31+G** calculations predict UV/vis absorptions at 777 ($f = 0.0015$) and 303 nm ($f = 0.084$) for *anti*-**1c** vs 719 ($f = 0.006$) and 338 nm ($f = 0.045$) for *syn*-**1c**, consistent with detection of the former isomer both in solution and in matrixes.