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Conformational Product Control in the Low-Temperature Photochemistry of Cyclopropylcarbenes

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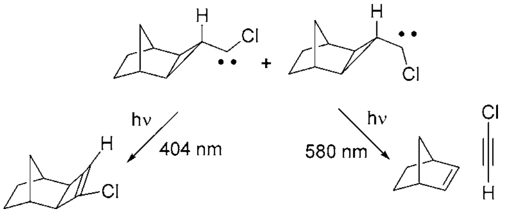
ABSTRACT



Different conformers of two fused-ring cyclopropylchlorocarbenes are shown to undergo distinct, wavelength-selectable, photochemistry in low-temperature matrixes. Conformers with H and Cl *syn* give ring expansion predominantly, whereas those with H and Cl *anti* mainly fragment.

Stereoelectronic effects in the intra- and intermolecular reactions of singlet carbenes have long been appreciated.[1] The coordinated participation of orthogonal electrophilic p and nucleophilic lone pair orbitals underlies a wide range of stereochemical consequences in concerted carbene reactions.[2] Nowhere, perhaps, is carbene stereoelectronic control demonstrated as vividly as in the reactions of cyclopropylcarbenes **1**.[3,4] In striking contrast to most carbenes that possess β-hydrogens, 1,2-H shifts in **1** to give methylenecyclopropanes **2** have never been detected. This unusual lack of reactivity has been attributed to the theoretical prediction that singlet **1** exists in two rotomeric forms, **1a** (*syn*) and **1b** (*anti*), which maximize overlap between the empty carbenic p-orbital and the electron-donating Walsh orbital on the ring.[4] In these conformational minima, the adjacent C−H is misaligned for migration toward the p-orbital. Moreover, the conformation with the carbene substituent and cyclopropyl-H aligned *syn* (**1a**) is considered to preferentially undergo C−C shift to give cyclobutene **3**. In contrast, the *anti* conformer **1b** favors a unique concerted fragmentation (termed a *coarctate* reaction by Herges[4e]) producing ethylene and acetylene. Although these geometric preferences in parent **1** and derivatives have been confirmed by theory,[4] and are

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(1) (a) Kirmse, W. *Carbene Chemistry*; Academic Press: New York, 1972. (b) *Carbenes*; Moss, R. A., Jones, M., Jr., Eds.; Wiley: New York, 1973; Vol. I; 1975; Vol. II.

(2) For examples of calculational treatments, see, e.g.: (a) Bettinger, H. F.; Schleyer, P. v. R.; Schreiner, P. R.; Schaefer, H. F. In *Modern Electronic Structure Theory and Applications in Organic Chemistry*; Davidson, E. R., Ed.; World Scientific Publishing: Hackensack, NJ, 1997; p 89. (b) Evanseck, J. D.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 9148. (c) Sulzbach, H. M.; Platz, M. S.; Schaefer, H. F.; Hadad, C. M. *J. Am. Chem. Soc.* **1997**, *119*, 5682.

(3) For leading references, see: Huang, H.; Platz, M. S. *J. Am. Chem. Soc.* **1998**, *120*, 5990. (b) Platz, M. S. *Adv. Carbene Chem.* (Brinker, U. H., Ed.) **1998**, *2*, 133.

(4) For theoretical examinations of cyclopropylcarbene rearrangements, see: (a) Hoffmann, R.; Zeiss, G. D.; Van Dine, G. W. *J. Am. Chem. Soc.* **1968**, *90*, 1485. (b) Schoeller, W. W. *J. Org. Chem.* **1980**, *45*, 2161. (c) Shevlin, P. B.; McKee, M. L. *J. Am. Chem. Soc.* **1989**, *111*, 519. (d) Choa, J.-H.; McKee, M. L.; DeFelppis, J.; Squillacote, M.; Shevlin, P. B. *J. Org. Chem.* **1990**, *55*, 3291. (e) Herges, R. *Angew. Chem., Int. Ed.* **1994**, *33*, 255. (f) Thamattoor, D. M.; Snoonian, J. R.; Sulzbach, H. M.; Hadad, C. M. *J. Org. Chem.* **1999**, *64*, 5886. (g) Muck-Lichtenfeld, C. *J. Org. Chem.* **2000**, *65*, 1366. (h) 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.

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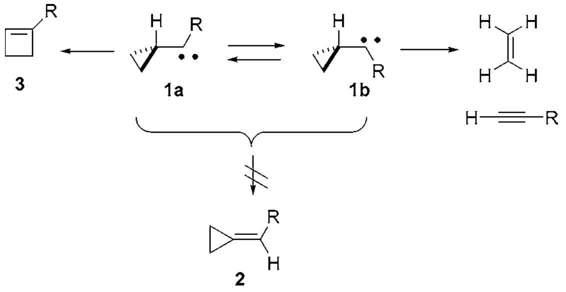
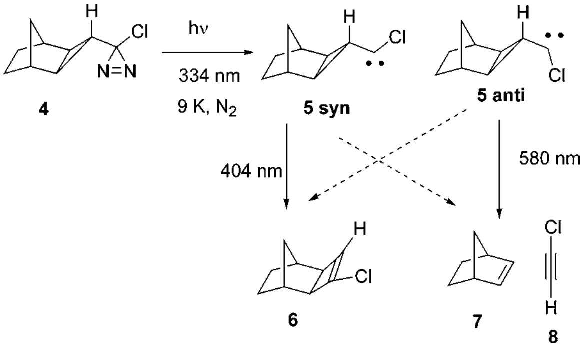
consistent with product analyses of conformationally locked derivatives,[3] there have been no *direct* observations of this stereoelectronic divergence of *syn* and *anti* conformers in a given carbene. We now report direct demonstration of these conformational preferences in the photochemistry of two bicyclic chlorocyclopropylcarbenes.



We previously reported preliminary investigations of the singlet cyclopropylchlorocarbenes **5** and **10** utilizing a combination of LFP and matrix isolation spectroscopy.[5] Ring expansion dominated the thermal reactions of these carbenes in solution at ambient temperatures, whereas mixtures of ring expansion and fragmentation products were generated photochemically at low temperatures. We have found, however, that careful control of irradiation wavelengths, together with close scrutiny of the resulting spectra, has permitted us to dissect divergent photochemical pathways resulting from distinct conformers of the carbenes.[6]



For example, 334 nm irradiation of diazirine **4** in a N_2 matrix (ca. 700:1) at 9 K produced mainly carbene **5**. Comparison to B3LYP/6-31+G**-calculated vibrational spectra[7−9] (vide infra) suggested the presence of a ca. 50:50 mixture of **5**-*syn* and **5**-*anti* carbenes. A broad absorption centered at 475 nm, ascribable likewise to carbene **5**, appeared concurrently in the visible spectrum.

Irradiation of the carbene mixture at ca. 500 nm caused all of the IR bands of **5** to disappear and absorptions of **6**, **7**, and **8** to grow.[10] However, irradiation of a fresh carbene mixture at 404 nm, near the short-wavelength edge of the visible absorption, caused selective destruction of one of two sets of IR bands corresponding to **5**, associated with major absorptions at 1125, 828, 822, 771, and 731 cm^{-1}, among others. Simultaneously, bands due to ring-expanded product **6**, and fragmentation products **7** and **8**, grew (Figure 1). Interestingly, cyclobutene **6** was clearly favored compared to product mixtures that resulted from destruction of both carbene isomers. Although the product ratios are difficult to determine precisely, comparison of several major product IR bands to intensities calculated at the B3LYP level suggests an approximate ratio of **6**/**7** > 2.

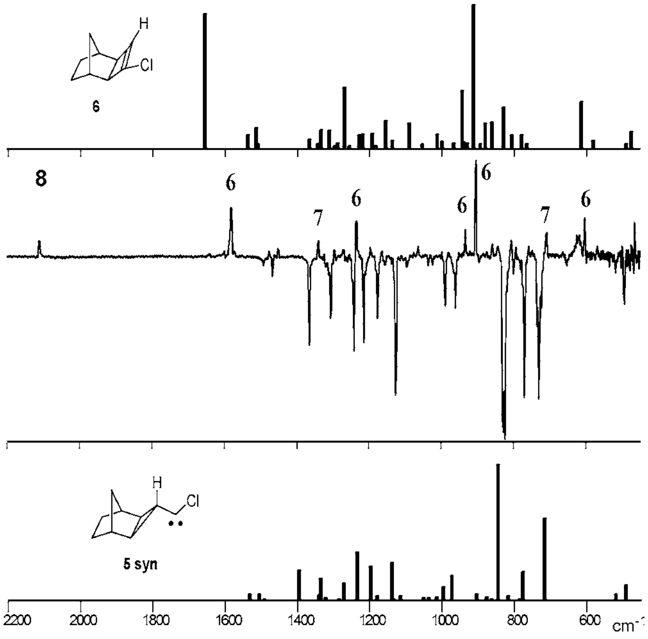


Figure 1. (a) IR difference spectra (arbitrary absorbance units) showing bleaching of carbene **5** *syn* ("down bands") on 1 h irradiation at 404 nm and formation of products **6** and **7** (prominent "up bands" labeled) from the matrix-isolated carbene mixture as described in the text. (b) B3LYP/6-31+G**-calculated IR spectrum for cyclobutene **6** (unscaled). (c) B3LYP/6-31+G**-calculated IR spectrum for carbene **5** *syn* (unscaled).

Subsequent irradiation of the matrix at 580 nm resulted in disappearance of the remaining set of carbene IR absorptions, showing most intense bands at 1135, 819, and 653 cm^{-1}. Disappearance of these carbene absorptions was accompanied by formation of fragmentation products **7** and

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(5) Chu, G.; Moss, R. A.; Sauers, R. R.; Sheridan, R. S.; Zuev, P. S. *Tetrahedron Lett.* **2005**, *46*, 4137.

(6) For a general description of the matrix isolation instrumentation, see: Sheridan, R. S.; Zuev, P. S. *J. Am. Chem. Soc.* **2004**, *126*, 12220 and references therein.

(7) All structures were fully optimized by analytical gradient methods using the Gaussian03 suite[8] and density functional calculations with the exchange functional of Becke[9a,b] and the correlation functional of Lee, Yang, and Parr.[9c] The BH&HLYP functional with a 6-31G(d) basis set was used for enegetics and the B3LYP functional with a 6-31+G(dp) basis set was used for vibrational and TD calculations. Vibrational analyses established the nature of all stationary points as either energy minima (no imaginary frequencies) or first-order saddle points (one imaginary frequency).

(8) Gaussian 03, Revision B.02; Gaussian, Inc.; Pittsburgh, PA, 2003. See the Supporting Information for the entire reference.

(9) (a) Becke, A. D. *J. Chem. Phys.* **1992**, *98*, 1372. (b) Miehlich, B.; Savin, A.; Stoll, H.; Pruess, H. *Chem. Phys. Lett.* **1989**, *157*, 200. (c) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(10) The IR spectra of **6** and **11** were predicted by calculation and those of **7**, **8**, and **12** by comparison to authentic samples.

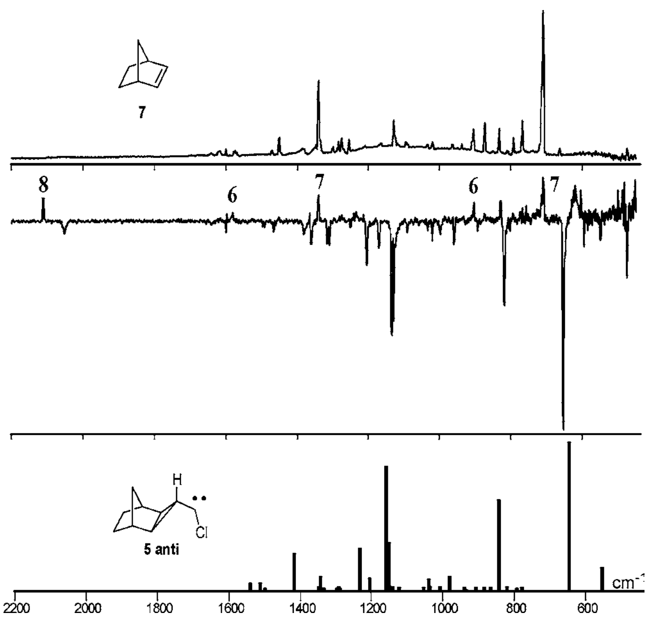
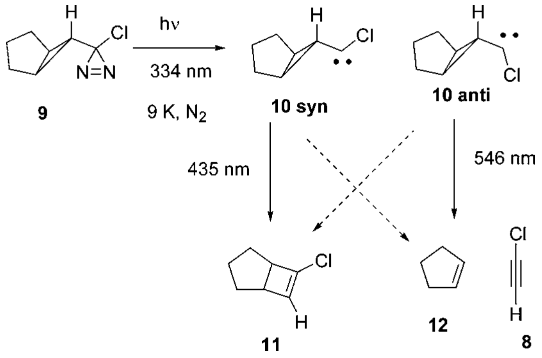


Figure 2. (a) IR difference spectra (arbitrary absorbance units) showing bleaching of carbene **5** *anti* ("down bands") on 1 h irradiation of matrix shown in Figure 1 at 580 nm and formation of products **6**−**8** (prominent "up bands" labeled). (b) IR spectrum of N_2 matrix isolated **7**. (c) B3LYP/6-31+G**.calculated IR spectrum for carbene **5** *anti* (unscaled).

8, predominantly, with significantly less **6** produced (**7**/**6** approximately > 4, Figure 2).

Quite similar results were obtained in the selective photochemistry of carbene **10**. Irradiation of N_2 matrix isolated diazirine **9** at 9 K with 334 nm light produced a mixture of **10**-*syn* and **10**-*anti* carbenes in the IR spectrum, together with a broad visible absorbance with $\lambda_{max} = 490$ nm. Irradiation of the matrix at 546 nm caused the destruction of all carbene IR bands and associated growth of absorptions due to **8**, **11**, and **12**. Irradiation of the carbene mixture at 435 nm, however, destroyed one set of carbene IR bands mainly and favored generation of ring-expanded product **11** compared to fragmentation (see the Supporting Information). Subsequent irradiation of the remaining carbene at 546 nm led to fragmentation products **12** and **8** predominantly.

Several pieces of information indicate that the carbene conformers having *syn* alignment of H and Cl, **5**-*syn* and **10**-*syn*, were those observed to undergo photochemistry selectively at shorter wavelengths; **5**-*anti* and **10**-*anti* reacted at longer wavelengths. B3LYP/6-31+G** calculations indicate that the two conformers in each system should have significantly different IR spectra. In particular, analysis of the calculated normal modes suggests that the very strong C−Cl stretching vibrations of **5**-*syn* and **10**-*syn* are relatively localized and are predicted to appear at 720 and 727 cm^{-1}, respectively, compared to experiment at 731 and 735 cm^{-1}. In contrast, the C−Cl stretches in **5**-*anti* and **10**-*anti* are coupled significantly to ring-breathing in the adjacent cyclopropane and should be observed at significantly lower frequencies of 638 and 630 cm^{-1}, respectively, close to the observed 653 and 646 cm^{-1} bands. Overall, the good agreement between calculated and experimental IR frequencies and intensities for both **5** and **10** confirm the structural assignments (Figures 1 and 2).



The theoretically predicted lowest energy electronic transitions for the two conformers of **5** and **10** also parallel the wavelength dependencies of their photochemical reactivity. TD B3LYP/6-31+G** calculations predict shorter wavelength σ-p transitions for **5**-*syn* and **10**-*syn* (489 and 488 nm, respectively) than for the *anti* conformers (555 and 553 nm for **5**-*anti* and **10**-*anti*, respectively). Examination of the carbene geometries suggests a reason for the lower energy *anti* transitions. As noted previously,[11] σ−p transitions for singlet carbenes depend sensitively on the carbenic angle. Smaller angles correspond to greater s-character in the in-plane σ orbital, lowering its energy and correspondingly increasing the σ−p energy gap. The calculated geometries (B3LYP/6-31+G**) indicate somewhat larger bond angles for **5**-*anti* and **10**-*anti* (111.9° and 112.2°) compared to **5**-*syn* and **10**-*syn* (109.2° and 109.7°). The larger angles in the *anti* isomers may reflect steric repulsion between Cl and the endocyclic cyclopropyl bridgehead CH bonds. Although the absorptions of the carbene conformers cannot be resolved in the UV/vis spectra, selective destruction of the *syn* conformations by ca. 400 nm irradiation leads to a noticeable shift of the visible band maximum to longer wavelengths (see the Supporting Information). Irradiation of conformational mixtures of **5** and **10** at the longer wavelength edge, e.g., 580 nm, is not as selective and shows only a small preference for destruction of the *anti* isomers.

The spectral evidence thus indicates that the *syn*-conformers of the cyclopropylcarbenes on low temperature irradiation undergo ring expansion preferentially compared to the *anti*-conformers, which give mainly fragmentation on photolysis. For comparison, the corresponding ground-state energetics were explored calculationally. Interestingly, the most popular B3LYP methodology predicted very unsymmetric transition states for fragmentation, with unstable wave functions, irrespective of basis set; efforts to constrain the reactions to C_S symmetry failed.[12] However, we found that the BH&HLYP

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[11] Matsumura, M.; Ammann, J. R.; Sheridan, R. S. *Tetrahedron Lett.* **1992**, *33*, 1843.

[12] It is unclear whether the failure of B3LYP methodology in this case represents an atypical pathology or if it suggests a stepwise fragmentation pathway. Shevlin and McKee[4c] have proposed that a diradical mechanism may have a lower energy transition state in the cleavage of **1**.

functional, which has been successfully applied to simpler cyclopropylcarbene (**1**),[4f] and other carbene,[2c] rearrangements, predicted C_s fragmentation transition states for **5**-*syn*, **10**-*syn*, and **10**-*anti*, though unsymmetric for **5**-*anti*, with stable wave functions. The resulting theoretical ground-state energy barriers parallel the photochemical results, as summarized in Figure 3.

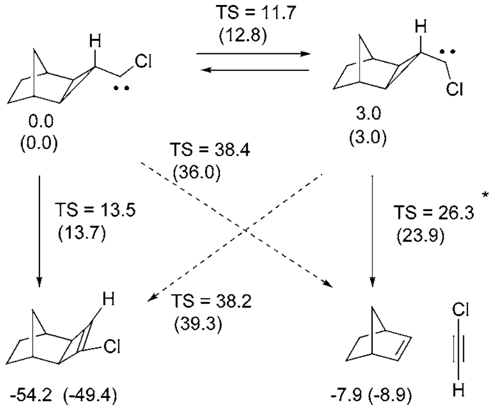

Figure 3. Relative energies at BH&HLYP/6-31G* level, corrected for zero-point vibrations, in kcal/mol (corresponding energies for carbene **10** in parentheses). *Unsymmetrical transition state (see text).

In both **5** and **10**, the *syn* conformations are calculated to be slightly lower in energy than the *anti* geometries (3.0 kcal/mol for both) and are separated from the *anti* conformers by barriers of 11.7 and 12.8 kcal/mol, respectively. As recognized by others, the *syn* cyclopropylcarbenes can undergo 1,2-C shift to cyclobutenes straightforwardly (transition state energies 13.5 and 13.7 kcal/mol relative to **5**-*syn* and **10**-*syn*, respectively). The *anti* conformers would transform to extremely strained *trans*-cyclobutenes, and thus, we located considerably higher energy ring-expansion transition states for **5**-*anti* and **10**-*anti* (38.2 and 39.3 kcal/mol, respectively). On the other hand, the barriers for fragmentation of the *anti*-conformers (26.3 and 23.9 kcal/mol, for **5**-*anti* and **10**-*anti*) are considerably lower in energy than for the *syn* species (38.4 and 36.0 kcal/mol, for **5**-*syn* and **10**-*syn*). Previous authors have noted this conformational preference and have ascribed it to four-electron repulsion between the developing ethylenic π-bond and the carbene σ-lone pair in the *syn* isomers and/or better overlap in the *anti* isomers between the carbenic σ-orbital and the cleaving cyclopropyl bonds.[4]

In conclusion, we have directly observed divergent product pathways in the two conformational isomers of singlet cyclopropylcarbenes. In solution, the *syn* and *anti* conformations of chlorocyclopropylcarbenes **5** and **10** likely can equilibrate prior to reaction, which we have previously shown is dominated by the globally lowest energy route, ring expansion from the *syn* isomers. At low temperatures, however, the carbenes cannot surmount the significant rotational barrier, and a static conformational mix can be prepared and scrutinized spectroscopically. The difference in $\lambda_{\max}$ allows us to selectively probe the photochemistry of the *syn* conformers, which favor ring expansion, and the *anti* conformers, which mainly fragment. The exact details of the photochemical mechanisms are unknown. It is clear from the divergent products that the *syn* and *anti* carbenes retain their stereochemical integrity in the electronic excited state.[13] However, whether the reaction products arise directly from electronically excited singlet carbenes, or alternatively from vibrationally excited ground state carbenes, is an open question. Although geometry dependent photolability in carbenes has been previously described,[6,14] we believe this is the first detection of the generation of different product mixtures from different carbene conformers.

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Supporting Information Available: Calculated geometries, energies, and IR spectra of species described in text, matrix experimental spectra of **10**, UV/vis spectra of **5**, and ^{13}C and ^{1}H NMR spectra of **4** and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) We detect no photochemical *syn*−*anti* interconversion in the carbenes.[14] Calculations suggest the barrier for *triplet* **1a**/**1b** interconversion to be <1.0 kcal/mol.[4c] If similar barriers exist for excited *singlet* **5** and **10**, rearrangement and fragmentation are likely highly efficient.

(14) See, for example: (a) Khasanova, T.; Sheridan, R. S. *J. Am. Chem. Soc.* **1998**, *120*, 233. (b) Khasanova, T.; Sheridan, R. S. *Org. Lett.* **1999**, *1*, 1091.