

Aryl Nitrene Rearrangements: Spectroscopic Observation of a Benzazirine and Its Ring Expansion to a Ketenimine by Heavy-Atom Tunneling

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S Supporting Information

ABSTRACT: In the photodecompositions of 4-methoxyphenyl azide (**1**) and 4-methylthiophenyl azide (**5**) in argon matrixes at cryogenic temperatures, benzazirine intermediates were identified on the basis of IR spectra. As expected, the benzazirines photochemically rearranged to the corresponding ketenimines and triplet nitrenes. Interestingly, with the methylthio substituent, the rearrangement of benzazirine **8** to ketenimine **7** occurred at $1.49 \times 10^{-5} \text{ s}^{-1}$ even in the dark at 10 K, despite a computed activation barrier of 3.4 kcal mol⁻¹. Because this rate is 10^{57} times higher than that calculated for passing over the barrier and because it shows no temperature dependence, the rearrangement mechanism is interpreted in terms of heavy-atom tunneling.

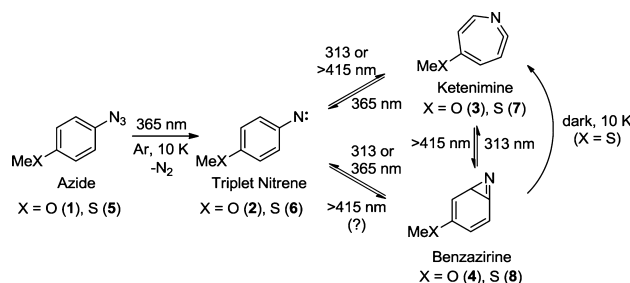
The photochemistry of aromatic azides has attracted wide interest for practical applications such as photoresists and biochemical affinity labeling.¹ To achieve the high efficiency needed for practical reactions, a detailed understanding of the reaction mechanism is imperative. Therefore, the mechanism has been extensively investigated by several groups using laser flash photolysis^{2,3} and matrix-isolation techniques.^{4–9} It is well-known that the irradiation of aromatic azides, including phenyl azide, in solution results in photodenitrogenation to give singlet nitrenes, which then undergo intersystem crossing to triplet nitrenes and ring expansion to ketenimines (Scheme 1).

Although the intermediates in the ring expansion are thought to be benzazirines, which can be trapped by ethanethiol to yield 2-ethylthioanilines, the direct observation of these species has been extremely rare.² For example, by means of laser flash

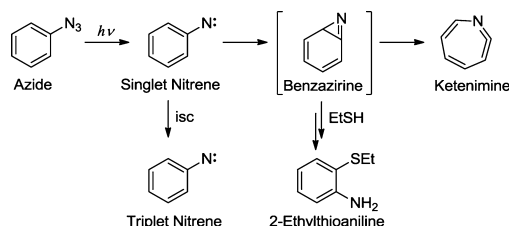
photolysis in solution at ambient temperature, Tsao and Platz³ detected *tert*-butyl-substituted benzazirine, which was identified by an absorption at 285 nm, as a transient precursor of the ketenimine, although the singlet nitrene was not observed in this case. Reports of the observation of benzazirines in matrixes at cryogenic temperatures have also been limited.^{6–9} In many studies on the photodecomposition of phenyl azide and its derivatives, only triplet nitrenes and ketenimines were observed.^{4,5} However, Morawietz and Sander⁶ found that when polyfluorinated phenyl azides such as 2,6-difluorophenyl azide were irradiated, the corresponding benzazirines (2*F*-type) were stabilized and observed. Moreover, Carra et al.⁷ monitored the reversible photoisomerization between this benzazirine and the corresponding ketenimine.

Herein we report an investigation of the photodecompositions of 4-methoxyphenyl azide (**1**) and 4-methylthiophenyl azide (**5**) via low-temperature matrix-isolation spectroscopy together with density functional theory (DFT) calculations.¹⁰ The direct observation of benzazirines (2*H*-type) was achieved on the basis of their clear-cut IR spectra, and new insights into the reactivity of benzazirines were obtained (Scheme 2).

Scheme 2



Scheme 1



Phenyl azides **1** and **5** were synthesized according to literature procedures¹¹ and purified using silica gel column chromatography with dichloromethane. The azides were stored at -20°C until immediately prior to use. When **1** was matrix-isolated in Ar at 10 K and irradiated with 365 nm light from a 250 W deep-UV lamp through a bandpass filter, a species having intense bands at

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1575, 1301, and 1272 cm^{-1} accumulated as the main product, accompanied by the disappearance of the bands for **1** [Figure S3 in the Supporting Information (SI)]. The IR peaks of the product were readily assigned to triplet nitrene **2** by comparison with an IR spectrum calculated using DFT at the B3LYP/6-31G(d) level. Subsequent irradiation at 313 or >415 nm for a few minutes resulted in a decrease in the intensities of the bands due to **2** and the appearance of a characteristically intense peak at 1894 cm^{-1} , indicating the formation of a product having a cumulenic double bond, which was identified as ketenimine **3** (Figure S4). Geometry optimization of **3** using DFT showed that two conformers, **3-a** and **3-b**, exist as true energy-minimum structures and that **3-a** is more stable than **3-b** by 2.2 kcal mol^{-1} . These conformers arise from the orientation of the methyl moiety of the methoxy substituent (Figure 1). The vibrational frequencies of **3-**

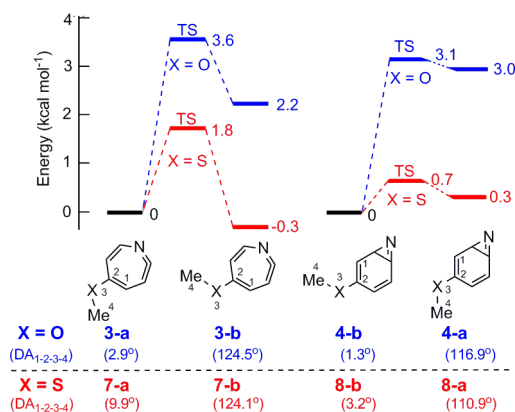


Figure 1. Optimized geometries and relative energies for (left) ketenimine and (right) benzazirine systems (blue, MeO; red, MeS) obtained from B3LYP/6-31G(d) calculations.¹⁰ Zero-point energies are included. TS = transition state; DA₁₋₂₋₃₋₄ = dihedral angle defined by atoms 1, 2, 3, and 4.

a and **3-b** were calculated, scaled by a factor of 0.9614,¹² and compared with the experimental values. Although the two conformers showed similar spectra, the spectrum calculated for the more stable conformer **3-a** reproduced the observed spectrum better than that for **3-b** in terms of the entire peak pattern, particularly in the region from 1100 to 1250 cm^{-1} , which is associated with C–O stretching vibrations (Figure 2a, down bands).

Ketenimine **3-a** could be changed back to nitrene **2** via irradiation at 365 nm. However, irradiation of a matrix containing almost exclusively **3-a** at >415 nm slowly yielded a different product exhibiting a weak but characteristic peak at 1717 cm^{-1} , which is in the region of C=N stretching vibrations reported in the literature (1680–1730 cm^{-1}) (Figures 2 and S16).^{6–9} Calculations on benzazirine **4** as a possible candidate with a C=N double bond showed that **4** could also exist as two conformers, **4-a** and **4-b**, with the latter being more stable by 3.0 kcal mol^{-1} . Similar to **3**, the dihedral angle formed by atoms 1–4, which specifies the orientation of the methoxy group with respect to the six-membered ring, is very small for **4-b** (DA₁₋₂₋₃₋₄ = 1.3°), while that for **4-a** is 116.9° (Figure 1). In addition to **4-a** and **4-b**, a conformer with DA₁₋₂₋₃₋₄ = 173.4° was also obtained; however, this conformer can isomerize to **4-a** without an activation barrier (Figure S21). The vibrational frequencies calculated for **4-b**, unlike those for **4-a**, were in excellent agreement with the experimental values, particularly with respect

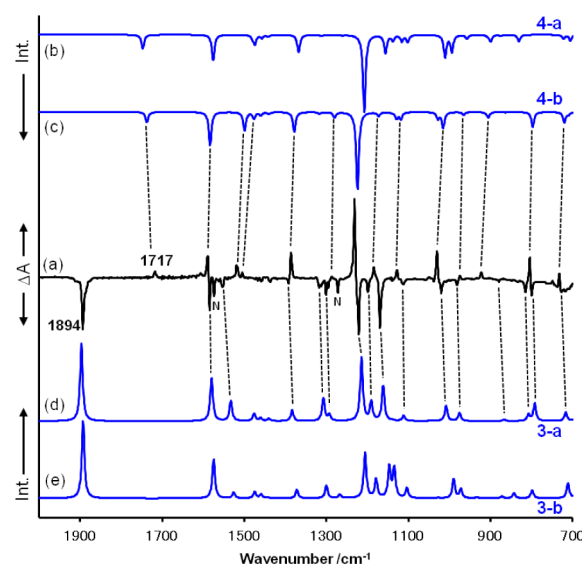


Figure 2. (a) Difference IR spectrum recorded after irradiation of ketenimine **3-a** (down bands) matrix-isolated in Ar at 10 K with >415 nm light. The bands labeled N were assigned to nitrene **2**. (b–e) B3LYP/6-31G(d)-calculated IR spectra (scaled by 0.9614¹²) of (b, c) benzazirines **4-a** and **4-b** and (d, e) ketenimines **3-a** and **3-b**, respectively.

to the following three features: (i) the peak observed at 1519 cm^{-1} was better reproduced by the peak at 1500 cm^{-1} calculated for **4-b** than that at 1474 cm^{-1} for **4-a**; (ii) the peak pattern observed at 900–1200 cm^{-1} completely agreed with that for **4-b** but not that for **4-a**; and (iii) the separation (Δ) of 73 cm^{-1} between the two peaks observed at 805 and 732 cm^{-1} in the region including the out-of-plane deformation of the ring C–H was well-reproduced (Δ = 77 cm^{-1}) for the peaks at 797 and 720 cm^{-1} calculated for **4-b**, compared with Δ = 109 cm^{-1} for the peaks at 831 and 722 cm^{-1} for **4-a** (Figure 2a, up bands). The rearrangement of **3-a** to **4-b** is at a structural disadvantage because of the orientation of the methoxy substituent. However, the calculated activation barrier for the reaction of **4-a** to give **4-b** is extremely low (0.1 kcal mol^{-1}) and should be overcome easily even at 10 K.¹³ Thus, it is concluded that irradiation of **3-a** at >415 nm produces **4-a**, which then undergoes thermal isomerization to give **4-b** via rotation of the methoxy group. Few reports of the direct observation of benzazirines, especially 2H-type ones, have been presented. Although Pritchina et al.⁹ observed an amino-substituted benzazirine in the photoreaction of 4-aminophenyl azide, no IR peaks were clearly observed except for a C=N stretching band at 1710 cm^{-1} .

Irradiation of benzazirine **4-b** at 365 nm gave mainly the triplet nitrene **2**, while irradiation at 313 nm resulted in a difference spectrum that showed a decrease in **4-b** and increases in **3-a** and **2** (Figure S6). The direct formation of **3-a** from **4-b** is thought to be difficult because the orientation of the methoxy group makes it structurally unfavorable, as in the case of the reaction above discussed. Furthermore, conformer **3-b**, which has a favorable geometry to be the reaction product from **4-b**, could not be detected, in spite of the modest activation barrier (1.4 kcal mol^{-1}) for the isomerization of **3-b** to **3-a** (Figure 1). It is highly probable that the ring-expansion of **4-b** to **3-a** proceeds by a consecutive mechanism via **2** or a mechanism involving rotation of the methoxy substituent utilizing the energy of the 313 nm light. At present, however, it was not determined whether one or both mechanisms participated in the reaction. Scheme 2

summarizes the observed interconversions among triplet nitrene 2, ketenimine 3, and benzazirine 4.

Next, the photolysis of 4-methylthiophenyl azide (5) was carried out in an Ar matrix at 10 K. Similar to the photolysis of 1, three important reactive species, triplet nitrene 6 (1551, 1434, 1313, 1080, 976, and 805 cm^{-1}), ketenimine 7 ($\nu_{\text{C}=\text{C}=\text{N}} = 1889 \text{ cm}^{-1}$), and benzazirine 8 ($\nu_{\text{C}=\text{N}} = 1716 \text{ cm}^{-1}$), were observed, depending on the irradiation wavelength (Figures S9–S15). That is, irradiation of nitrene 6 at 313 or $>415 \text{ nm}$ led to its ring expansion to ketenimine 7, and then subsequent irradiation of 7 at $>415 \text{ nm}$ slowly gave benzazirine 8. In addition, 7 and 8 were converted back to 6 upon irradiation at 365 nm. Keteneimine 7 also has conformational isomers because of the orientation of the methylthio substituent (Figure S22). In contrast to the conformers of methoxy-substituted ketenimine 3, however, conformers 7-a and 7-b have nearly the same energy (Figure 1) and similar IR spectra according to the DFT calculations (Figure 3a, up bands). Therefore, it cannot be determined

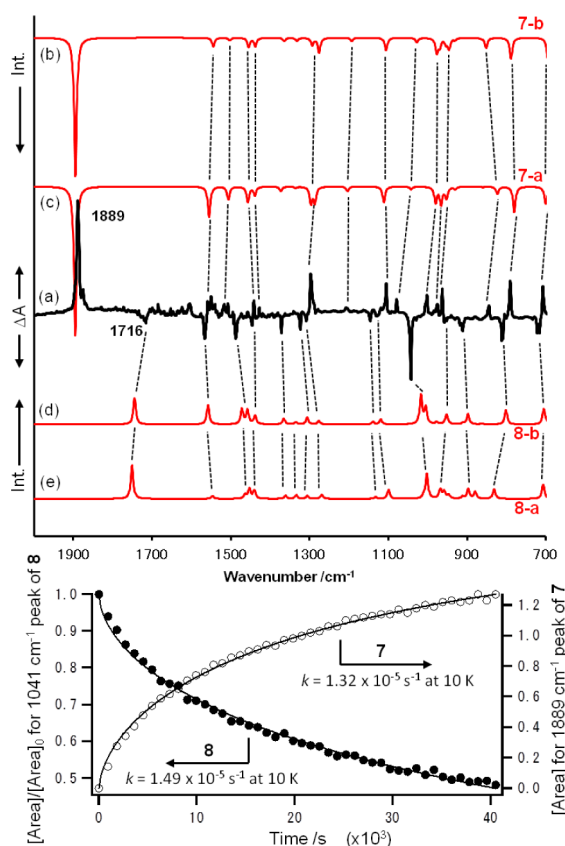
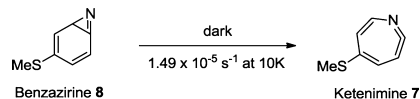


Figure 3. Top: (a) Difference IR spectrum recorded after an Ar matrix containing benzazirine 8 (down bands) was allowed to stand in the dark at 10 K for 10 h. (b–e) B3LYP/6-31G(d)-calculated IR spectra for (b, c) ketenimines 7-b and 7-a and (d, e) benzazirines 8-b and 8-a, respectively. Bottom: Plot showing the disappearance of the 1041 cm^{-1} peak of 8 (●) and the appearance of the 1889 cm^{-1} peak of 7 (○) in the dark at 10 K.

whether 7 exists only as the marginally more stable conformer 7-b. Also, the energy difference between the benzazirine conformers 8-a and 8-b is only 0.3 kcal mol^{-1} (Figures 1 and S22). Although the observed IR spectrum seems to be similar to that calculated for the marginally more stable conformer 8-b (Figure 3a, down bands), we again cannot conclude whether 8-b is the sole product.

As in the photoreaction of 4-b, irradiation of 8 at 313 nm also gave an IR spectrum that showed an increase in the bands for 7. Interestingly, however, the rearrangement from 8 to 7 proceeded even in the dark at 10 K (Scheme 3 and Figure 3). Such a reaction

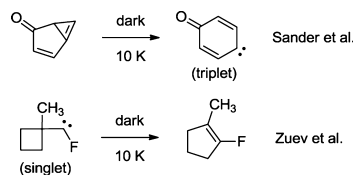
Scheme 3. Ring Expansion of 8 to 7 Observed in the Dark at 10 K



was not observed between the methoxy-substituted compounds 3 and 4. The B3LYP/6-31G(d)-calculated activation barrier for the reaction from 8 to 7 is 3.4 kcal mol^{-1} ,¹⁴ and the rate constant to surmount this barrier at 10 K is estimated to be $2.00 \times 10^{-63} \text{ s}^{-1}$ using the Eyring equation, indicating that this reaction will not occur as a thermally activated process at 10 K. However, the rate constants measured at 10 K for the decrease of 8 and the increase of 7 were 1.49×10^{-5} and $1.32 \times 10^{-5} \text{ s}^{-1}$, respectively (Figure 3 bottom).¹⁵ In addition, ~50% of 8 was converted to 7 during 10 h in the dark at 10 K. After 8 was regenerated from 7 with $>415 \text{ nm}$ light, the rate constants for the decrease of 8 were also determined at other matrix temperatures and found to be $1.46 \times 10^{-5} \text{ s}^{-1}$ at 15 K, $1.55 \times 10^{-5} \text{ s}^{-1}$ at 20 K, and $1.84 \times 10^{-5} \text{ s}^{-1}$ at 25 K (see section S-8 in the SI). Thus, this rearrangement barely showed any temperature dependence of the rate constant, although a small rate acceleration upon warming was observed because of matrix softening. These results suggest that the ring expansion reaction of 8 to 7 at cryogenic temperatures occurs via heavy-atom tunneling, as opposed to a thermally activated ('over the barrier') process.

There is considerable current interest in reactions that proceed via tunneling mechanisms,^{15–18} although there are few well-documented examples of organic reactions that proceed via heavy-atom tunneling.^{15–17} The ring expansions of 1H-bicyclo-[3.1.0]hexa-3,5-dien-2-one to triplet 4-oxocyclohexa-2,5-dienylidene (Scheme 4 top)^{15a} and methylcyclobutylfluoro-carbene

Scheme 4. Previously Reported Reactions Involving Carbon Tunneling^{15a,17a}



to 1-fluoro-2-methylcyclopentene¹⁷ (Scheme 4 bottom) involve carbon atom tunneling. In the latter reaction, for instance, Zuev et al.^{17a} measured a rate constant of $4 \times 10^{-5} \text{ s}^{-1}$ in Ar at 8 K, which is 10^{152} times greater than the rate would be if the system had to surmount the computed barrier of ca. 6.5 kcal mol^{-1} . Furthermore, they reported that the longest distance traveled by any of the carbon atoms during the tunneling is 0.44 Å. Intrinsic reaction coordinate (IRC) calculations at the B3LYP/6-31G(d) level for the transition state connecting the reactant 8-b and the product 7-b were used to compare the geometry of 8-b with that of the product having the same energy as 8 along the reaction pathway (Figure 4), and the maximum distance moved by any of the atoms was found to be only 0.33 Å for the carbon at the 2-position of the azirine ring. The fact that this value is smaller than

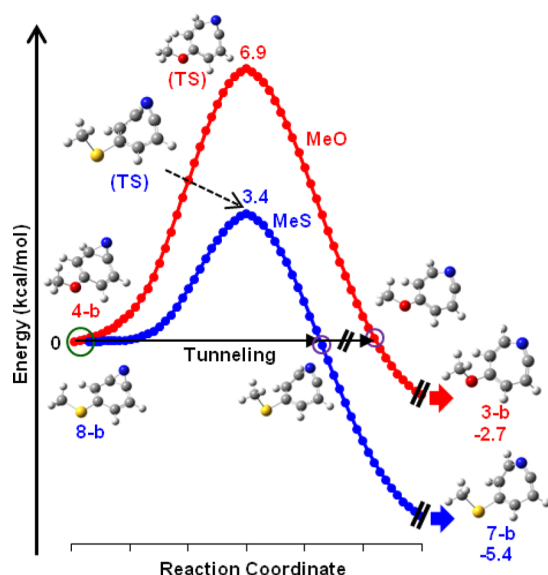


Figure 4. IRC calculations at the B3LYP/6-31G(d) level for the reactions of benzazirine 4-b to give ketenimine 3-b (red) and benzazirine 8-b to give ketenimine 7-b (blue). Comparisons of the geometries of the reactants (green circle) and the products having the same energies as the reactants along the reaction pathways (purple circles) are shown in section S-9 in the SI.

the previously reported results^{17a} also supports the conclusion that the ring expansion of 8 to 7 at cryogenic temperatures proceeds via carbon tunneling. As mentioned above, in the case of the reaction of methoxy-substituted 4 to give 3, no evidence for tunneling was obtained. This difference might be interpreted in terms of the calculated activation barrier and tunneling distance, which were found to be 6.9 kcal mol⁻¹ and 0.43 Å, respectively.

In this communication, we have described the direct observation of 2*H*-type benzazirines and details of their reactivity. In the case of methoxy substitution, the most stable benzazirine conformer, 4-b, was observed on the basis of a clear-cut IR spectrum, and the photoconversions to ketenimine 3-a and triplet nitrene 2 were monitored. By contrast, methylthio-substituted benzazirine 8 afforded ketenimine 7 even in the dark at 10 K. The measured rate constant was 10⁵⁷ times greater than the rate constant would have been if the system had to pass over the computed barrier of 3.4 kcal mol⁻¹ and showed little temperature dependence. On the basis of these results, we conclude that the ring expansion of 8 to give 7 proceeds via heavy-atom (carbon) tunneling.

■ ASSOCIATED CONTENT

Supporting Information

Methods and additional results. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

- (1) (a) Morishita, H.; Ito, M.; Hayashi, N.; Nonogaki, S. *J. Photopolym. Sci. Technol.* **1994**, 7, 59. (b) Platz, M. S. *Photochem. Photobiol.* **1997**, 65, 193 and references cited therein.
- (2) (a) Borden, W. T.; Gritsan, N. P.; Hadad, C. M.; Karney, W. L.; Kemnitz, C. R.; Platz, M. S. *Acc. Chem. Res.* **2000**, 33, 765. (b) Platz, M. S.; Gritsan, N. P. *Chem. Rev.* **2006**, 106, 3844.
- (3) Tsao, M.-L.; Platz, M. S. *J. Am. Chem. Soc.* **2003**, 125, 12014.
- (4) Chapman, O. L.; LeRoux, J.-P. *J. Am. Chem. Soc.* **1978**, 100, 282.
- (5) Hayes, J. C.; Sheridan, R. S. *J. Am. Chem. Soc.* **1990**, 112, 5879.
- (6) Morawietz, J.; Sander, W. *J. Org. Chem.* **1996**, 61, 4351.
- (7) Carra, C.; Nussbaum, R.; Bally, T. *ChemPhysChem* **2006**, 7, 1268.
- (8) Grote, D.; Sander, W. *J. Org. Chem.* **2009**, 74, 7370.
- (9) Pritchina, E. A.; Gritsan, N. P.; Bally, T. *Phys. Chem. Chem. Phys.* **2006**, 8, 719.
- (10) The geometry optimizations, energy calculations, and calculations of vibrational frequencies and intensities were performed using DFT at the restricted or unrestricted B3LYP level with the 6-31G(d) basis set. The energies include zero-point energy scaled by 0.9806. The DFT calculations were carried out using Gaussian 03. See: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision A.1; Gaussian, Inc.: Pittsburgh, PA, 2003.
- (11) Hu, M.; Li, J.; Yao, S. Q. *Org. Lett.* **2008**, 10, 5529.
- (12) Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, 100, 16502.
- (13) *Matrix Isolation Spectroscopy*; Barnes, A. J., Orville-Thomas, W. J., Müller, A., Gaufrès, R., Eds.; D. Reidel: Dordrecht, The Netherlands, 1981; Chapter 23, pp 531–549.
- (14) This activation barrier was calculated to be 3.4 kcal mol⁻¹ at the MP2/6-31+G(d,p) level and 4.8 kcal mol⁻¹ at the CCSD(T)/6-311+G(d,p) level using the MP2/6-31+G(d,p)-optimized geometries (Figure S18).
- (15) (a) Sander, W.; Bucher, G.; Reichel, F.; Cremer, D. *J. Am. Chem. Soc.* **1991**, 113, 5311. (b) McMahon, R. J.; Chapman, O. L. *J. Am. Chem. Soc.* **1987**, 109, 683. According to the above papers, in glassy matrices with multiple sites, the concentration of a reactant [A] normally depends on $t^{1/2}$. In this study, $\alpha = 0.50$ – 0.57 was used for $[A] = [A]_0 \exp[-(kt)^\alpha]$.
- (16) McMahon, R. J. *Science* **2003**, 299, 833–834.
- (17) (a) Zuev, P. S.; Sheridan, R. S.; Albu, T. V.; Truhlar, D. G.; Hrovat, D. A.; Borden, W. T. *Science* **2003**, 299, 867. (b) Moss, R. A.; Sauers, R. R.; Sheridan, R. S.; Tian, J.; Zuev, P. S. *J. Am. Chem. Soc.* **2004**, 126, 10196.
- (18) (a) Ley, D.; Gerbig, D.; Schreiner, P. R. *Chem. Sci.* **2013**, 4, 677. (b) Ley, D.; Gerbig, D.; Wagner, J. P.; Reisenauer, H. P.; Schreiner, P. R. *J. Am. Chem. Soc.* **2011**, 133, 13614. (c) Schreiner, P. R.; Reisenauer, H. P.; Pickard, F. C., IV; Simmonett, A. C.; Allen, W. D.; Mátyus, E.; Császár, A. G. *Nature* **2008**, 453, 906–909.