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Time-Resolved IR Detection and Study of an Iminooxirane Intermediate

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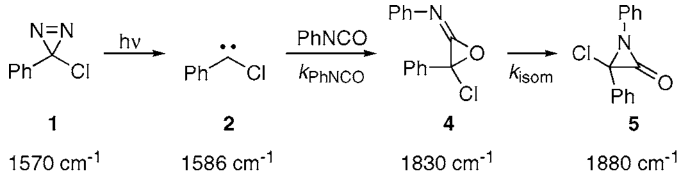
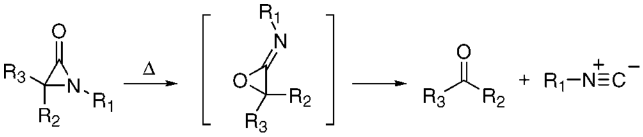
ABSTRACT



Iminooxirane 4 has been generated by the reaction of phenylchlorocarbene (2) with phenyl isocyanate (3) and studied by nanosecond time-resolved infrared spectroscopy. Iminooxirane 4 (1830 cm^{-1}) isomerizes to α-lactam 5 (1880 cm^{-1}) at an observed rate of 3 × 10^4 s^{-1}. Peak assignments were confirmed by a combination of B3LYP calculations and isotopic labeling. An acyclic transition state was found computationally for the isomerization reaction.

Iminooxiranes are three-membered heterocyclic isomers of α-lactams. Their existence was first postulated to explain the formation of isocyanide products in the thermal decomposition of α-lactams (Scheme 1).[1−3] Scrimin et al. postulate an iminooxirane intermediate in an attempted formation of an α-lactam from 2-bromo-*N*-alkylisobutyramides.[4] An iminooxirane intermediate was proposed to explain the products of the Lewis acid-catalyzed reaction of a carbonyl compound with an isocyanide.[5] In addition, iminooxirane-derived products were also observed in both the thermal and photochemical decomposition of 3,5,5-trialkyl-3,5-dihydro-4*H*-1,2,3-triazol-4-ones.[6,7] Quast and co-workers have also reported a comprehensive experimental and computational study of the thermal reorganization and cycloaddition reactions of a stable nonracemic chiral α-lactam, in which they observe iminooxirane-derived products.[8] Using ab initio quantum mechanical calculations of the C_2H_3NO potential energy surface, they find that the parent α-lactam is approximately 7 kcal/mol lower in energy than the isomeric iminoxirane. Additionally, they estimate an activation barrier to ring opening of approximately 40 kcal/mol. To our knowledge, the direct spectroscopic observation of an iminooxirane intermediate has not been reported.

Scheme 1. Proposed Mechanism for Thermal Decomposition of Stable α-Lactams



We are pleased to report herein the first direct detection of this elusive reactive intermediate by nanosecond time-resolved infrared (TRIR) spectroscopy, as well as computational evidence for a concerted reaction path connecting iminooxiranes with α-lactams. Analogous to corresponding

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[3] L'Abbe, G. *Angew. Chem., Int. Ed. Engl.* **1980**, *92*, 277−290.
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[8] Quast, H.; Leybach, H.; Wuerthwein, E. U. *Chem. Ber.* **1992**, *125*, 1249−1262.

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experiments on α-lactones,[9] we set out to generate α-lactams by the reaction of a singlet carbene with an isocyanate and to examine their chemistry using TRIR spectroscopy.

Upon 355 nm laser photolysis of diazirine **1** in the presence of phenyl isocyanate (**3**), we observe the TRIR difference spectra shown in Figure 1. The relevant kinetic traces are shown in Figure 2. Similar spectra were observed in both dichloromethane and acetonitrile. The absorbance at 1586 cm^{-1} is due to phenylchlorocarbene (**2**), in good agreement with previous low-temperature matrix IR studies.[10] The carbene is formed faster than the time resolution of our instrument and is efficiently quenched by **3** with a second-order rate constant (k_{PhNCO}) of 1.5×10^6 M^{-1} s^{-1} (see the Supporting Information). In the presence of **3** (84 mM), the band at 1586 cm^{-1} decays at the same rate within experimental error (±10%) as the growth of a new band at 1830 cm^{-1} (Figure 2a). The band at 1830 cm^{-1} decays ($k_{obsd} = 2.9 \times 10^4$ s^{-1}) at the same rate as the growth of a band at 1880 cm^{-1} ($k_{obsd} = 3.3 \times 10^4$ s^{-1}) that is stable for at least 180 μs (Figure 2b).

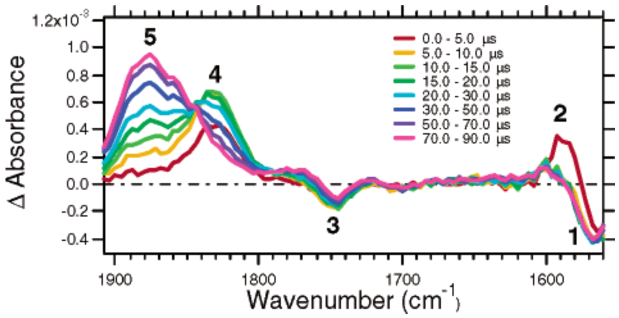

Figure 1. TRIR difference spectra averaged over the time scales indicated following laser photolysis (355 nm, 90 ns, 0.7 mJ) of a solution of diazirine **1** (66 mM) and **3** (84 mM) in dichloromethane. Negative signals are due to depletion of the reactants in solution, and positive signals are due to new transients or products.

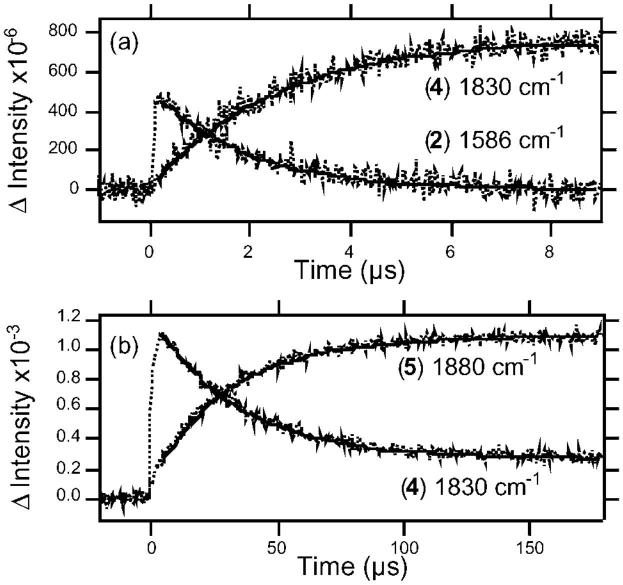

Figure 2. Kinetic traces observed following laser photolysis (355 nm, 90 ns, 0.7 mJ) of a solution of diazirine **1** (66 mM) and **3** (84 mM) in dichloromethane. The dotted curves are experimental data; the solid curves are best fits to a single-exponential function.

To aid in the assignments of the bands above 1800 cm^{-1}, we performed an identical trapping experiment with ^{15}*N*-phenyl isocyanate (**^{15}N-3**). The TRIR difference spectra observed following photolysis of **1** in the presence of either **3** or **^{15}N-3** are shown in Figure 3. The absorbance at 1830 cm^{-1} is shifted to a lower frequency by approximately 20 cm^{-1}, while the 1880 cm^{-1} band shifts only negligibly.

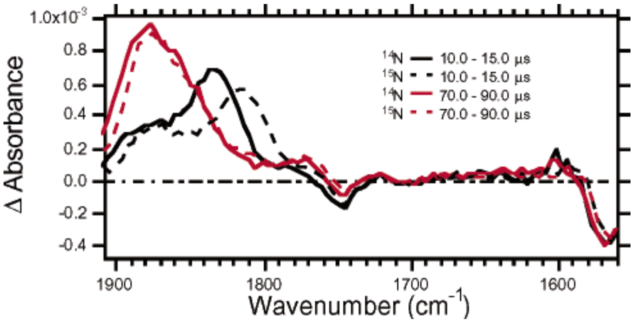

Figure 3. TRIR difference spectra averaged over the time scales indicated following laser photolysis (355 nm, 90 ns, 0.7 mJ) of a solution of diazirine **1** (66 mM) and either **3** or **^{15}N-3** (84 mM) in dichloromethane.

To gain additional insight into the origin of these new bands, we performed density functional theory geometry optimizations and vibrational analyses at the B3LYP/6-31G* level of theory on the two most likely candidates, iminooxirane **4** and α-lactam **5**, and their ^{15}N-labeled isotopomers (see the Supporting Information for a full listing of calculated vibrational frequencies and intensities). The most intense vibrational mode (scaled by 0.96)[11] of iminooxirane **4** is the C−N stretch, calculated at 1848 cm^{-1} for the natural isotope and 1831 cm^{-1} for the ^{15}N isotopomer. In the case of α-lactam **5**, the most intense vibrational mode is the C−O stretch, predicted at 1896 cm^{-1} for the natural isotope, and 1893 cm^{-1} for the ^{15}N isotopomer. Therefore, based on both the labeling experiment and the calculations, we assign the band at 1830 cm^{-1} to iminooxirane **4** and the band at 1880 cm^{-1} to α-lactam **5**.

The data reveal that carbene **2** reacts preferentially with the C−O bond of phenyl isocyanate to form iminooxirane **4** (Scheme 2) and *not* the C−N bond to form α-lactam **5**. The

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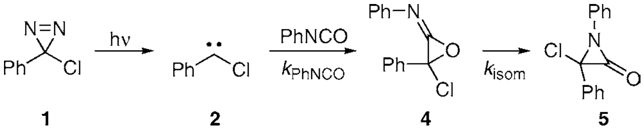
Scheme 2



observed rate of insertion of carbene **2** into the C−O bonds of both **3** (1.5×10^6 M^{-1} s^{-1}) and carbon dioxide (1.0×10^6 M^{-1} s^{-1})[9] are comparable. Interestingly, the kinetically favored iminooxirane is calculated to be higher in energy than **5** by about 7 kcal/mol (the same energy difference calculated by Quast and co-workers[8] for the parent system). Indeed, for a variety of iminoxirane/α-lactam pairs examined computationally, all α-lactams are predicted to be lower in energy by 4−9 kcal/mol (see the Supporting Information). Although the kinetic data are consistent with a concerted cycloaddition, we cannot rule out the formation of a short-lived *O*-ylide intermediate. We are currently examining this possibility by computational techniques.

The rate of isomerization of **4** to **5** (k_{isom}) is observed by TRIR spectroscopy to be 3.0×10^4 s^{-1} (Figure 2b) and is unaffected by varying the concentrations of either **1** or **3**. Based on the data, we cannot rule out a short-lived intermediate, though calculations suggest this process to be concerted (see below). This isomerization is the reverse of the reaction shown in Scheme 1, the mechanism proposed to explain the products of thermal decomposition of many α-lactams. Interestingly, we observe no signals due the formation of either benzoyl chloride (1776 cm^{-1}) or phenyl isocyanide (2130 cm^{-1}) from iminooxirane **4**. These data imply that in this particular system the activation barrier to fragmentation of **4** must be higher than the barrier of isomerization to **5**.

To understand this isomerization further, we attempted to calculate a transition state structure for the model system illustrated in Figure 4. A transition state was found and confirmed by the calculation of only one imaginary vibrational mode. The atomic displacements of this imaginary mode suggest that the methylene group is "transferring" from oxygen to nitrogen in a concerted fashion. The structure is exactly as one might predict for a concerted isomerization; the central carbon is nearly planar, the central angles are all nearly 120°, and the C−O and C−N bond lengths are intermediate to those of the α-lactam and iminooxirane (see the Supporting Information). This structure is quite analogous to a transition state structure found computationally by Skancke et al. for the methylenecyclopropane rearrangement.[12] Given that the calculations were performed in the gas phase on a model system that has different steric and electronic features, the actual activation barrier for the isomerization of **4** to **5** is likely less than the calculated 22.7 kcal/mol (Figure 4). In addition, the relatively fast rate of isomerization observed for **4** (τ = 33 μs) also suggests that the true activation barrier must be relatively small.

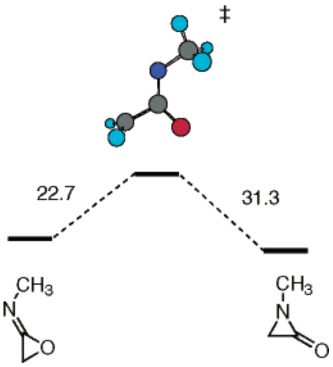


Figure 4. Relative energetics (in kcal/mol) with zero-point and thermal corrections included and optimized structure of the acyclic transition state for a model iminooxirane/α-lactam isomerization calculated at the B3LYP/6-31+G* level of theory.

In summary, we have generated and characterized by TRIR spectroscopy iminooxirane **4** from the reaction of phenylchlorocarbene (**2**) and phenyl isocyanate (**3**). This constitutes the first direct observation of an iminooxirane. Additionally, we observe the isomerization of iminooxirane **4** to α-lactam **5**, the reverse of the reaction proposed in the literature to explain α-lactam decomposition. We have also been able to identify a transition state structure for this isomerization by B3LYP calculations.

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Supporting Information Available: Experimental details, derivation of second-order rate constant for trapping of **2** by **3**, and computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

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