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Photochemical Generation of Aziridinium Imides: Are AIs Bystanders or Perpetrators in the Ene Reaction?

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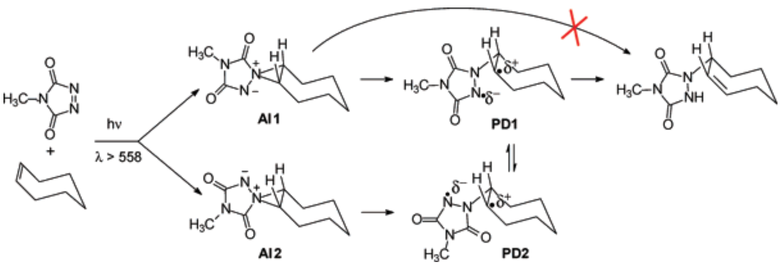
ABSTRACT



A non-equilibrating mixture of two aziridinium imides (AIs) resulting from the photoaddition of *N*-methyl-1,2,4-triazoline-3,5-dione and cycloheptene has been prepared. Warming the AIs produces only the product of the expected ene reaction with no back-reaction to starting materials. Even though one of the pair does not have the geometry necessary for hydrogen abstraction, both AIs disappear at essentially the same rate, showing that AIs cannot be the direct precursors of the ene product.

The mechanism of the ene reaction has generated interest because of this reaction's synthetic efficacy with its unique bond-making aspect.[1] It now appears that both concerted and stepwise routes exist for this reaction.[2] The mechanism of the ene reaction involving singlet oxygen, the isoelectronic *N*-alkyl-1,2,4-triazoline-3,5-diones (RTADs), and nitroso compounds appears to be a stepwise mechanism,[3] though a two-step no-intermediate mechanism has been calculated for the ene reaction involving singlet oxygen.[4] For the most part these enophiles react similarly, though some dissimilarities exist.[5] Because intramolecular kinetic isotope effects showed competition only between cis allylic hydrogens[6] a mechanism involving zwitterionic three-membered-ring intermediates

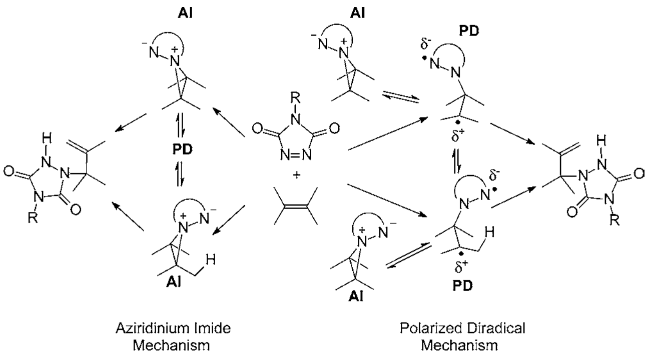


Figure 1. AI and PD mechanisms for the ene reaction.

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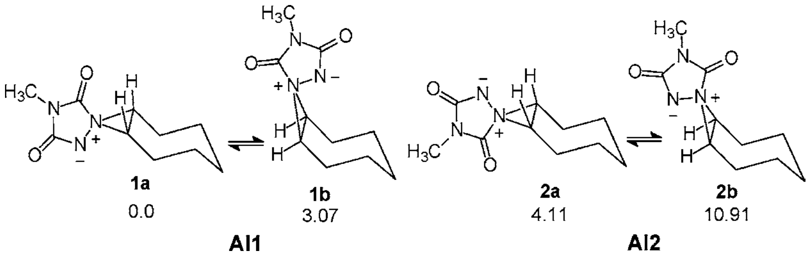

Figure 2. Two AIs from MTAD addition to *c*-CHP. Below each structure are the calculated (MP2/6-311+(2d,p)//B3LYP/6-31G(d) level) relative energies, in kcal/mol.

had become accepted. In the case of RTADs this intermediate, an aziridinium imide (AI), has been observed spectroscopically,[7] and this AI mechanism is shown on the left in Figure 1. More recently, a study combining experimental ^{13}C isotope effects with ab initio calculations suggested that AIs are "innocent bystanders", and that a polarized diradical (PD) intermediate is responsible for the abstraction of the allylic hydrogen. This PD mechanism is shown on the right in Figure 1.[8] A polarized biradical intermediate has also been suggested as the source of the ene product in the reaction of nitroso compounds with alkenes.[9] Both of these conclusions have been called into question.[10]

We reported the first observation of an AI that decayed upon warming to produce the ene product.[11] This AI (**AI1** in Figure 2) was produced from the reaction of *trans*-cycloheptene (*t*-CHP) and *N*-methyl-1,2,4-triazoline-3,5-dione (MTAD) at low temperatures. However, this method of AI production can be accomplished only with very strained alkenes.[12] We now wish to report a general method for photochemically generating AIs in high yields at temperatures low enough to permit spectroscopic observation. Further, the subsequent decay of isomeric AIs so produced suggests that they cannot be responsible for abstracting the allylic hydrogen of the alkene, and are, in fact, bystanders in the ene reaction.

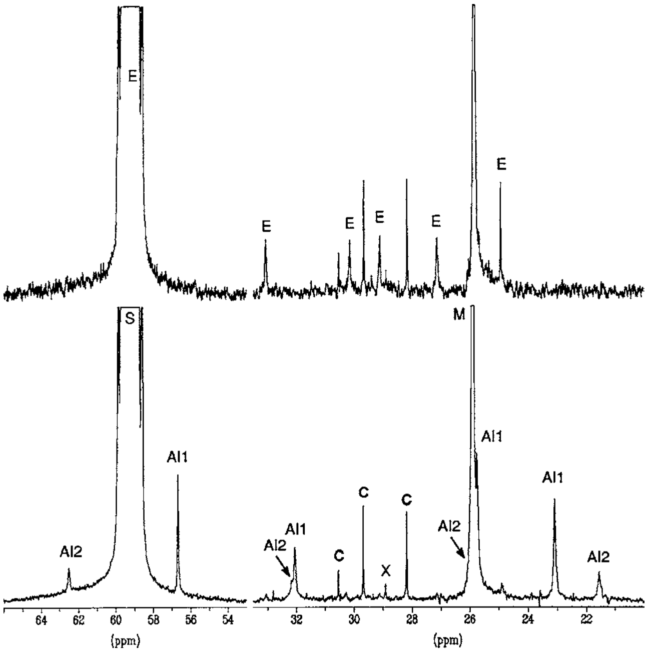

Figure 3. Bottom: Upfield portion of the ^{13}C NMR spectrum at −110 °C of the photolyzed MTAD:*c*-CHP mixture with **AI1** and **AI2** peaks indicated. The MTAD, solvent impurity, remaining *c*-CHP, and solvent peaks are labeled as M, X, C, and S, respectively. Top: Same sample warmed to −60 °C for 15 min and recooled. Ene products peaks are labeled as E.

When a dimethyl ether-d_6 solution 0.06 M in *cis*-cycloheptene (*c*-CHP) and 0.3 M in MTAD is photolyzed with $\lambda > 558$ nm at −125 °C with a 1000 W Hg lamp, the red solution becomes orange-red and the bottom 100 MHz ^{13}C NMR spectrum shown in Figure 3 results. The peaks labeled **AI1** in this spectrum are identical with those of the AI intermediate formed from the thermal reaction of *t*-CHP and MTAD.[11] Photolysis of MTAD is known to produce an uncharacterized polymer,[13] but while some polymer is produced here, and reduces resolution, AI production proceeds more efficiently than polymer formation in this solvent. An excess of MTAD must be used for the substantial conversion of *c*-CHP shown in the bottom spectrum of Figure 3, and some care must be taken not to over-photolyze because

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the AI produced can be photochemically destroyed. We have also demonstrated that this photochemical method produces the aziridinium imide from the addition of MTAD to *trans*-2-butene. Finally we have attempted this photochemical reaction in other solvents but have successfully produced high yields of AIs only in dimethyl ether. This may be due to a solvent dependence in polymer formation. More intriguingly, recently, a solvent dependence on the mechanism of the PTAD/alkene ene reaction has been observed, which may be caused by a change in the relative stability of the AIs and PDs induced by the changing polarity of the solvents,[14] which could also explain our photochemical solvent effect.

Along with **AI1** a small amount of another species (~20% of **AI1**) is produced. This species shows a partial ^{13}C NMR spectrum with peaks at 21.5, 32.2, 62.5, 157.5, and 160.3 ppm. Of particular interest is the peak at 62.5 ppm, which appears as a 174 Hz doublet in the coupled ^{13}C spectrum. This second species is also observed in the ^{1}H spectrum, showing a broad triplet at 3.92 ppm, a multiplet at 2.45 ppm, and other multiplets at higher field, which are obscured by the resonances of the known AI.

As was critical in the identification of **AI1**[11] the large C−H coupling of the 62.5 ppm resonance for the second species suggests that it also contains a 3-membered nitrogen-containing ring. As seen in Figure 2, two ring-flip isomeric pairs of AIs are possible in this system, **AI1** (**1a** $\rightleftharpoons$ **1b**), which has allylic hydrogens available to the nitrogen for direct abstraction, and **AI2** (**2a** $\rightleftharpoons$ **2b**), which does not. The identity of this second AI is confirmed by the excellent fit (see Table 1) between the experimental carbon shifts and those calculated by using the GIAO approach at the MP2/6-311+(2d,p)//B3LYP/6-31G(d) level.[16]

Table 1. Experimental and Calculated ^{13}C NMR Shifts of **AI1-a** and **AI2-a**

	AI1-a		**AI2-a**	
carbon	exptl[a]	calcd[b]	exptl[a]	calcd[b]
C1,7	56.00	54.49	62.5	62.36
C2,6	23.16	23.91	21.5	21.82
C3,5	25.79	29.45	*c*	29.23
C4	32.45	34.00	32.2	33.92
C10	160.52	158.90	160.3	157.75
C12	159.42	155.79	157.5	155.26
C13	25.79	22.01	*c*	21.94

[a] Observed ^{13}C chemical shifts in dimethyl ether-d_6. Assignments were based the observed multiplicity in the gated coupled spectrum, the relative intensities of the peaks (C4), and the known assignments for cycloheptene oxide.[15] [b] Computational method used was GIAO at the MP2/6-311+(2d,p)//B3LYP/6-31G(d) level. [c] Some of **AI2**'s ^{13}C resonances are obscured by the 26 ppm peaks of the known **AI1** and the excess MTAD.

The relative energies of the AIs were calculated at the MP2/6-311+(2d,p)//B3LYP/6-31G(d) level,[17] and are indicated in Figure 2. **AI1-a** and **AI2-a** are substantially lower in energy than their ring-flip isomers and **AI1-a** is shown to be much more stable than **AI2-a**.

Warming the solution to −60 °C and recooling produces the top spectrum in Figure 3. Only the previously identified ene product[11] is produced with neither AI remaining. Further, the unreacted *c*-CHP does not increase. Therefore cleavage of the AIs to *c*-CHP and MTAD does not occur here.

At lower decay temperatures (−90 °C) the ene product is formed gradually and during its formation the ratio of the two AIs remains essentially constant. This result leads to two important conclusions. First, there is at no time a rapid equilibration of the AIs as this would result in the disappearance of **AI2** in favor of the more stable **AI1**. Second, monitoring the ^{1}H NMR spectra of the two AIs shows that their decays occur at indistinguishable rates with a free energy of activation of 13.4 kcal/mol as seen previously.[11] Because the amount of **AI2** is significantly less than that of **AI1**, the precision of this measurement for **AI2** is certainly less, but we see no indication that any species other than the expected ene product is produced upon the decay of the AIs.

No conformation of **AI2** has the geometry necessary for abstraction of the allylic hydrogen. Thus if the AI mechanism is operative **AI1** must produce the ene product (Figure 4), and **AI2**'s lifetime would be determined by the highest barrier along the route to **AI1**, i.e., the barrier to either **AI2** ring opening to **PD2** (or zwitterion), k_{O2}, the rotation of the C−N bond of the PD, k_{rot}, or the closure of **PD1** to **AI1**, k_{C1}. Further, to explain the fact that the decay of the two AIs is so similar the highest of these three barriers would have to be exactly equal to the activation energy for hydrogen abstraction by **AI1**, $k_{AI\rightarrow ene}$. Note that at −90 °C even a 0.2 kcal/mol difference in the activation energies for the decays of **AI1** and **AI2** would give an easily discernible difference in the decay rates. Finally, calculations at the UMP2/6-31G-(d) level (see the Supporting Information) give energies for **PD1** and **PD2** lower than that for **AI2**. However, neither PD is seen during the decays of the AIs, so no preequilibrium of **AI2** occurs with the PDs nor, as mentioned above, with

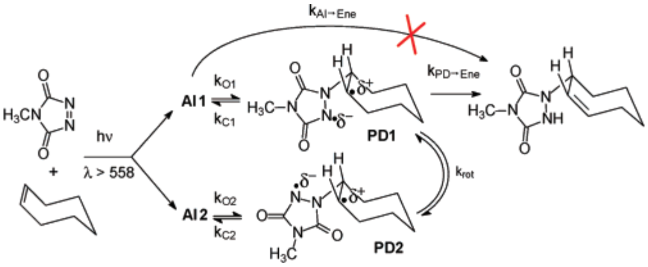

Figure 4. Photochemically generated AIs as bystanders in the ene reaction.

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AI1. Thus, the only way our results are consistent with the AI mechanism is if there is a fortuitous equality of $k_{AI \rightarrow ene}$ with k_{O2}, and given the disparity of these reaction types this seems extremely unlikely.

On the other hand, with the PD mechanism operative (Figure 4) the simultaneous decay and non-equilibration of **AI1** and **AI2** and the lack of any buildup of **PD1** or **PD2** are easy to explain. A rate-controlling ring opening of **AI1** and **AI2** to **PD1** and **PD2**, respectively, should proceed with nearly identical barriers. A rapid hydrogen abstraction by **PD1** would follow, with a less rapid, but still fast, rotation of **PD2** to **PD1** completing the route of **AI2** decay, i.e., $k_{O1} \approx k_{O2} < k_{rot} < k_{PD \rightarrow ene}$.

These relative rates would explain our results and the known isotope effects found in the ene reaction. These include, as has been pointed out by Singleton and Hang,[8] the usual "cis" effect and the significant intramolecular isotope effect found for *trans*-d_3-2-butene by Foote et al.[18] This latter isotope effect is not caused by reversion of formation of the AI intermediate[19] since no *c*-CHP is formed during the decay of the AIs.

The observed free energy of activation for ene formation in this case is substantially higher than the barrier calculated for the 2-butene system at the B3LYP/6-31G(d) level,[8] though the considerable stabilization of the polar AIs by a high dielectric solvent like dimethyl ether was not included in these calculations. Additionally, as others have pointed out, these results are relevant to this system and may not be relevant to all systems.[10b] These stipulations aside, our results are best explained by the PD mechanism. We believe this is the most direct evidence available to date showing that an open intermediate must be responsible for hydrogen abstraction in the ene reaction.

Acknowledgment. Computer time was provided by the Alabama Supercomputer Network. This paper is dedicated to the memory of Professor Christopher Foote in appreciation for his kindness and admiration for his work.

Supporting Information Available: Calculated geometries, energies, copies of NMR spectra of a sample before and after decay of AIs, and complete ref 17. This material is available free of charge via the Internet at http://pubs.acs.org.

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