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Spin-Selective Generation of Triplet Nitrenes: Olefin Aziridination through Visible-Light Photosensitization of Azidoformates

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Abstract: *Azidoformates are interesting potential nitrene precursors, but their direct photochemical activation can result in competitive formation of aziridination and allylic amination products. Herein, we show that visible-light-activated transition-metal complexes can be triplet sensitizers that selectively produce aziridines through the spin-selective photogeneration of triplet nitrenes from azidoformates. This approach enables the aziridination of a wide range of alkenes and the formal oxyamination of enol ethers using the alkene as the limiting reagent. Preparative-scale aziridinations can be easily achieved under continuous-flow conditions.*

This article begins drawing from the research done by outside sources in the very first sentence. Each of these first five sentences is informed by a large body of work that is recognized in the endnotes.

Aziridines are versatile intermediates for the synthesis of nitrogen-containing compounds.[1] Many important natural products also feature aziridines as their principal bioactive functionality.[2] However, methods for aziridine synthesis are somewhat underdeveloped,[3] particularly in comparison to the wealth of methods available for epoxide synthesis. The most widely utilized methods for alkene aziridination involve the generation of metallonitrenes from iminoiodinane reagents.[4] These methods, unfortunately, produce stoichiometric haloarene byproducts, and there has consequently been significant interest in the use of alternate nitrene precursors for aziridination reactions.[5] Organic azides appear particularly attractive in this regard because they generate nitrenes by expelling dinitrogen as the sole stoichiometric byproduct. Several laboratories, including notably the Zhang[6] and Katsuki[7] groups, have reported pioneering advances in catalytic aziridination with organoazides. Nevertheless, these processes often require a large excess of alkene, and many methods are limited to styrenic olefins. Thus, there remains a need for new approaches to aziridination that utilize organoazides as nitrene precursors.

In these sentences, the writers clearly establish what the field has done to explore these issues and then identify the limitations of these methods—limitations that are grounded in and recognized by the literature.

Photochemical activation offers one potential solution. Electronically excited organic azides rapidly decompose to form reactive free nitrenes.[8] However, attempts to perform intermolecular aziridination reactions by direct photolysis of azidoformates typically produce complex mixtures containing both aziridines and allylic amination products,[9] a result that has led to the pervasive notion that free nitrenes are too reactive to provide synthetically useful chemoselectivities.

Note that most of the time these writers are more interested in what the associated research has found than they are in who did this research. Notable exceptions to this are Zhang and Katsuki who lead laboratories that have explored aziridination through multiple studies.

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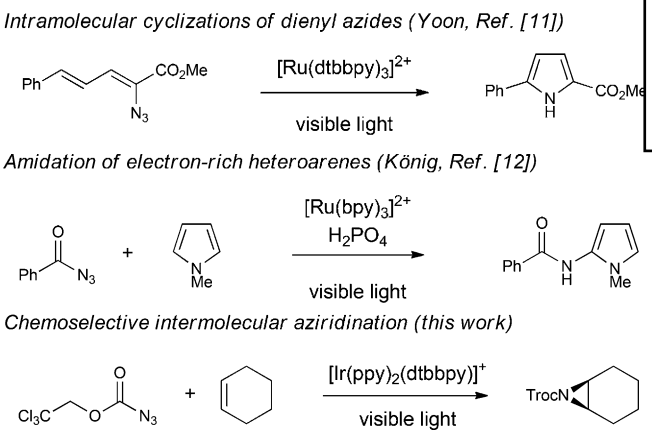
Seminal studies by Lwowski et al., however, demonstrated that while singlet carbethoxynitrenes competitively undergo both amination and aziridination reactions, triplet carbethoxynitrenes react selectively with alkenes to afford aziridines with comparatively slow reaction with allylic C–H bonds.[10] Thus the fundamental challenge in photochemical aziridination reactions appears not to be the absolute reactivity of free nitrenes but rather the unselective production of both singlet and triplet nitrenes from direct photolysis of azides.

We wondered if chemoselective photochemical aziridination reactions could be achieved through triplet sensitization, which would produce nitrenes selectively in the triplet state. Our laboratory previously studied the use of visible-light-absorbing transition-metal complexes to sensitize vinyl azides towards intramolecular heterocyclic ring-closing reactions (Scheme 1).[11] Quite recently, König and co-workers reported

As this paragraph exemplifies through its use of the Konig study, sometimes outside sources are important to reference because of the research methodology they employed.



Scheme 1. Photocatalytic activation of azides by visible-light triplet sensitization.

an intriguing method for photocatalytic amidation of electron-rich heterocycles, the key step of which was proposed to involve triplet sensitization of a benzoyl azide.[12] To the best of our knowledge, however, the use of triplet sensitizers to promote chemoselective intermolecular alkene aziridination reactions has not previously been described. Herein, we demonstrate that visible-light triplet sensitization of azidoformates enables the preparation of a range of structurally diverse aziridines. Notably, this method utilizes the alkene as the limiting reagent, provides high yields for both aliphatic and aromatic alkenes, and exhibits excellent selectivity for aziridination over allylic amination.

end of literature review/introduction

We elected to focus our investigations on azidoformates as nitrene precursors, based on several considerations. First,

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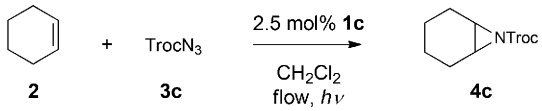

5.0 equiv. $TrocN_3$: 72% yield (t_R = 2.3 h)

2.0 equiv. $TrocN_3$: 70% yield (t_R = 8.0 h)

Scheme 4. Aziridination of **2** in flow.

absorbing transition-metal photosensitizer for the spin-selective generation of triplet nitrenes from azidoformates. A wide range of alkenes can be aziridinated or oxyaminated under operationally facile batch conditions, and the use of a flow reactor enables the reaction to be conducted on a preparative scale. Further efforts in our lab will continue to develop visible-light triplet sensitization as a general, conceptually novel strategy for C–N bond forming reactions using organoazides as the nitrene precursors.

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Keywords: azides · aziridination · chemoselectivity · nitrenes · photocatalysis

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[17] Organoazide compounds are potentially explosive, and proper safety procedures should always be used in their manipulation. However, samples of $TrocN_3$ stored at 0 °C in our laboratory show no signs of decomposition after several months, and DSC analysis indicates that $TrocN_3$ is stable to 157 °C. See: H. Lus, V. Subbarayan, J. Tao, X. P. Zhang, *Organometallics* **2010**, *29*, 389–393.

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[22] Addition of anthracene to an aziridination reaction completely inhibits consumption of the azidoformate, indicating that the excited Ir triplet complex reacts more rapidly with this triplet quencher than with azidoformate. This experiment, unfortunately, does not elucidate the mechanism by which azidoformate and the photocatalyst interact in the productive reaction.

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