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

Spencer O. Scholz, Elliot P. Farney, Sangyun Kim, Desiree M. Bates, and Tehshik P. Yoon*

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 oxamination of enol ethers using the alkene as the limiting reagent. Preparative-scale aziridinations can be readily achieved under continuous-flow conditions.

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 used methods for alkene aziridination involve the generation of metallonitrenes from iminoiodinane reagents.[4] These methods, unfortunately, produce stoichiometric halocarbon 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 aziridinations 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.

Photochemical activation offers one potential solution. Electronically excited organic azides rapidly decompose to form reactive free nitrenes.[8] However, attempts to perform intermolecular aziridinations 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.

Semininal 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 toward intramolecular heterocyclic ring-closing reactions (Scheme 1).[11] Quite recently, König and co-workers reported

Intramolecular cyclizations of diaryl azides (Yoon, Ref. [11])

Amidation of electron-rich heteroarenes (König, Ref. [12])

Chemoselective intermolecular aziridination (this work)

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 olefins, and exhibits excellent selectivity for aziridination over allylic amination.

We elected to focus our investigations on azidoformates as nitrene precursors, based on several considerations. First,
absorbing transition-metal photosensitizer for the spin-selective generation of triplet nitrenes from azidoformates. A wide range of alkenes can be azidinated or oxaminated 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.

Acknowledgements

We are grateful to Dale Kreitler and Prof. Sam Gellman for the loan of the HPLC pump used in all flow experiments. We thank Yuliya Preger for helpful discussions. We gratefully acknowledge the NIH NIGMS for financial support (GM095666) and Sigma–Aldrich for a generous gift of iridium(III) chloride.

Keywords: azides – azidination – chemoselectivity – nitrenes – photocatalysis

How to cite: Angew. Chem. Int. Ed. 2016, 55, 2239–2242
Angew. Chem. 2016, 128, 2279–2282


[15] See the Supporting Information for further information regarding the molecular energies and coordinates of these computational studies.


[17] Organoazide compounds are potentially explosive, and proper safety procedures should always be used in their manipulation. However, samples of TrocN2 stored at 0°C in our laboratory show no signs of decomposition after several months, and DSC analysis indicates that TrocN2 is stable at 157°C. See: H. Lus, V. Subbarayan, J. Tao, X. P. Zhang, Organometalics 2010, 29, 389–393.


[19] See the Supporting Information for details of these experiments.


[21] König et al. reported the formation of an analogous oxazole product in two examples. In the reaction of benzyl azide with benzoforman, the oxazole is produced as a 2:1 mixture with the C–H amination product in 50% overall yield. See Ref. [12].

[22] Addition of anthracene to an azidination 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.


Received: November 23, 2015
Published online: January 6, 2016