Photocatalyzed Azidofunctionalization of Alkenes via Radical-Polar Crossover

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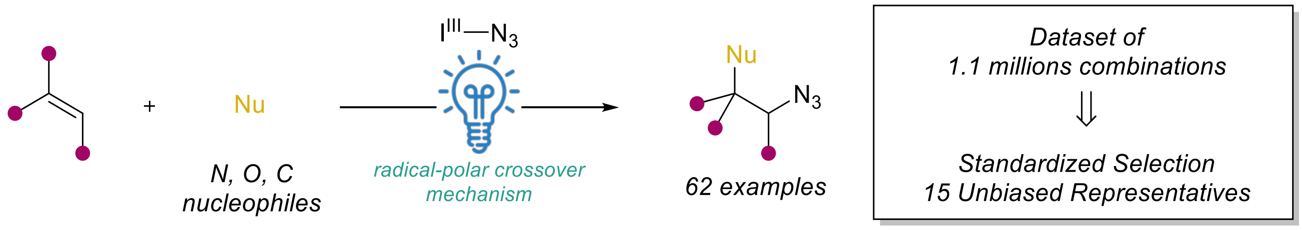
The difunctionalization of alkene is among the most efficient methods for introducing diverse functional groups in a single step. Azides, in particular, are recognized as highly versatile and have found broad applications in synthetic chemistry and the pharmaceutical industry.[1] As precursors of various functionalities such as triazoles, they are also widely considered as protected amines and have been used as such as key intermediates. In recent years, a variety of functional groups have been introduced alongside an azide in a single step.[2] Upon azide radical addition to the double bond, an efficient strategy enabling the addition of a nucleophile is the oxidation of the formed alkyl radical to a carbocation – a strategy coined as radical-polar crossover.[3] When considering limitations of the current state-of the art in the radical-polar crossover azidofunctionalization of alkenes, a range of nucleophiles, such as azole derivatives, carboxylic acids, alcohols, phosphoric acids, oximes or phenols have still not been introduced. The azidofunctionalization of alkene is also mainly reported on the use of styrene and other π-systems have not been explored.

In this context, we developed a general azidofunctionalization of alkenes, enabling the introduction of a wide range of commercially available nucleophiles across diverse alkenes without changes in reaction conditions (Scheme 1).[4] This transformation allows access to a variety of azidofunctionalized products, with the potential of accessing more than one million compounds considering only easily available reaction partners. It represents a significant advancement in efficiency for the synthesis of azidoazoles, azidoesters, and azidoethers, while also allowing the formation of novel, unprecedented scaffolds. Investigations of the generality and limitations of the scope was performed through a standard unbiased selection of 15 substrates using a clustering technique. The methodology was subsequently applied in the synthesis of key pharmaceutical intermediates, demonstrating a marked improvement in efficiency, with reduced step counts and enhanced yields.



Scheme 1: Photocatalyzed azidofunctionalization of alkenes

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