Enantioselective Photocatalyzed [3+2] Cycloaddition of Cyclopropylimines

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"Escape from the Flatland" is a well-recognized goal in medicinal chemistry as sp^3 hybridized carbon centers and chiral motifs correlate positively with the success of drug candidates. Stephenson's group published an elegant method for synthesizing cyclopentanes starting from cyclopropylimines. Direct irradiation generates an N-centered radical which, due to its electrophilicity and suitable geometry, leads to the homolysis of the cyclopropyl moiety. This is followed by intra- or intermolecular cyclization of the formed radical, resulting in the formation of the cyclopentane ring.[1]

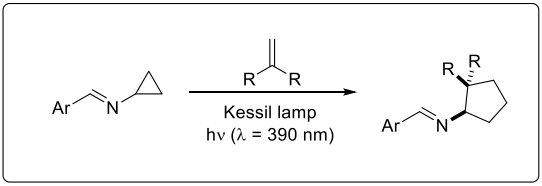

Figure 1: Intermolecular [3+2]-Cycloaddition of Cyclopropylamin with an Olefin.[1]

In enantioselective reactions, suppressing the background reaction is crucial. One method to achieve this is by shifting the absorption of the reactant upon coordination to a longer wavelength, allowing only the activated substrate-catalyst complex to be selectively excited. This technique, known as chromophore activation, can be achieved by Brønsted acids or Lewis acids.[2] UV/Vis experiments on various substituted imines and their iminium perchlorate salts demonstrated the desired bathochromic shift for the un- and methoxy-substituted imine upon activation with the Brønsted acid. In contrast, Stephenson's Nitro-imine exhibited a hypsochromic shift, making it unsuitable for potential enantioselective reactions.

[1] D. Staveness, J. L. Collins III, R. C. McAtee, C. R. Stephenson, *Angew. Chem. Int. Ed,.* 2019, **58**, 19000-19006, https://doi.org/10.1002/anie.201909492.

[2] J. Großkopf, T. Kratz, T. Rigotti, T. Bach, *Chem. Rev.*, 2022, *122*, 1626-1653, doi.org/10.1021/acs.chemrev.1c00272.