Synthesis of bicyclo[3.1.1]heptanes and cyclopenta(e)nes by photocatalyzed cycloaddition of carbonyl cyclopropanes.

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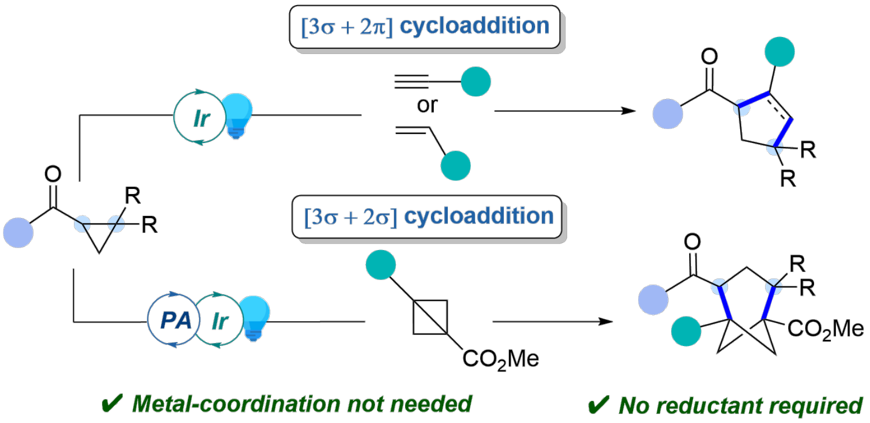
Cyclopropanes play a key role in synthetic chemistry, both as structural elements and reactive building blocks.[1] The studies of donor-acceptor cyclopropanes are well-established in synthetic chemistry to enable C-C bond cleavage and generate 1,3 dipole intermediate for further transformation.[1] However, it is usually required a diester group as an acceptor. Cyclopropanes bearing a single carbonyl group are usually not sufficient to promote ring opening under mild condition.



In this study, we report a photocatalyzed homolytic ring-opening of carbonyl cyclopropanes under mild conditions without the need for a metal co-catalyst or a strong reductant. The resulting intermediate can be used for cycloaddition with alkynes, alkenes, and bicyclo[1.1.0]butanes, yielding cyclopentenes, cyclopentanes, and bicyclo[3.1.1]heptanes (BCH) respectively.[2] In addition, bicyclo[3.1.1]heptanes have been recently studied as bioisosteres for *meta*-substituted aromatic rings.[3] Therefore, our protocol enables a convergent way to approach BCH scaffolds under mild and operationally simple conditions.

[1] (a) Schneider, T. F.; Kaschel, J.; Werz, D. B. A . *Angew. Chem., Int. Ed.* **2014**, *53*, 5504–5523. (b) Liu, J.; Liu, R.; Wei, Y.; Shi, M. *Trends Chem.* **2019**, *1*, 779–793.
[2] Nguyen, T. V. T.; Bossonnet, A.; Waser, J. *ChemRxiv* **2023**
[3] (a) Frank, N.; Nugent, J.; Shire, B. R.; Pickford, H. D.; Rabe, P.; Sterling, A. J.; Zarganes-Tzitzikas, T.; Grimes, T.; Thompson, A. L.; Smith, R. C.; Schofield, C. J.; Brennan, P. E.; Duarte, F.; Anderson, E. A. *Nature* **2022,** *611*, 721-726. (b) Iida, T.; Kanazawa, J.; Matsunaga, T.; Miyamoto, K.; Hirano, K.; Uchiyama, M**.** *J. Am. Chem. Soc.* **2022,** *144*, 21848–21852