Asymmetric Ring-Expansion of Activated Cyclopropanes *via* Peptide and Photoredox Catalysis

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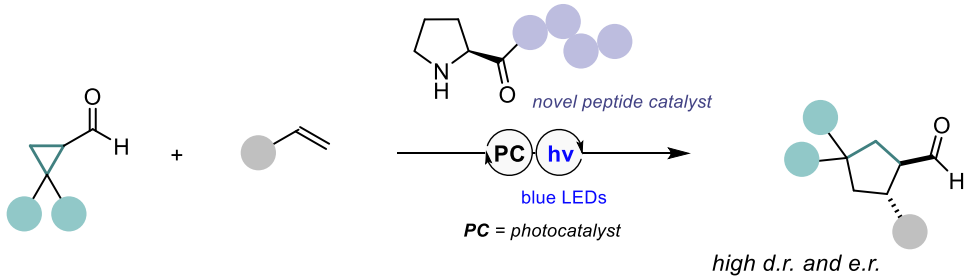
Peptides have been used as small chiral analogues of natural enzymes to catalyze asymmetric organic transformations for decades.[1] They have the advantage to be easily prepared via solid phase chemical synthesis, and their properties can be conveniently tuned with the incorporation of natural and non-canonical amino acids that greatly expand the chemical space available for catalyst design. Recently, cysteine-based peptide catalysts have been combined with more emergent photoredox methodologies and have found few applications in asymmetric radical transformations, such as deracemization of tailored substrates[2a-b] or hydrofunctionalization of alkenes[2c-d]. We envisaged that this dual catalytic approach has great potential to be applied in diverse asymmetric radical reactions. This would require the design of novel peptidic catalysts to unlock unexplored modes of activation under visible light irradiation. The strain-release activation of cyclopropane (CP) rings bearing an aldehydic functionality is well explored in classical polar chemistry.[3] Among the newest strategies, cyclopropane carbaldehydes were shown to undergo a ring-expansion reaction under photochemical conditions following a charge-transfer mechanism.[4] We noticed that asymmetric ring-expansion reactions of racemic CP carbaldahydes following a light-enabled radical mechanism are unprecedented.[5] Herein we disclose the combination of peptide and photoredox catalysis to enable a highly diastereo- and enantioselective [3+2] cycloaddition of cyclopropane carbaldehydes with alkene substrates. The design of a novel N-terminal proline peptide catalyst was crucial to enable the radical ring-expansion of acceptor-acceptor cyclopropanes through the formation of an iminium ion intermediate.



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