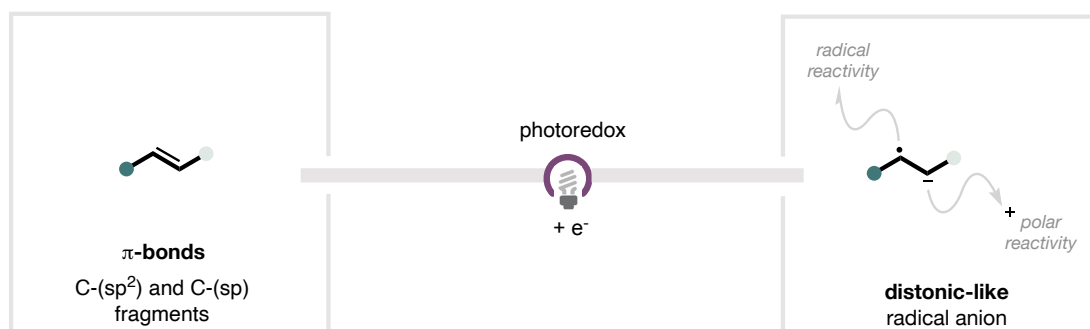


Multiphoton Photoredox Strategies for the Generation and Elaboration of Radical Intermediates

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Organometallic reagents are routinely used as fundamental building blocks in organic chemistry to rapidly diversify molecular fragments via carbanion intermediates. However, the catalytic generation of carbanion equivalents, particularly from sp^3 -hybridized alkyl scaffolds, remains an underdeveloped goal in chemical synthesis. Here we disclose an approach for the generation of alkyl carbanions via single electron reduction of aryl alkenes and radical polar crossover of alkyl radicals, enabled by multiphoton photoredox catalysis¹. We demonstrate that photocatalytically induced alkyl carbanions engage in intermolecular C-C bond-forming reactions with carbonyl electrophiles. Central to this method is controlled formation of an alkene radical anion intermediate² that undergoes nucleophilic addition, followed by a kinetically favoured reductive polar crossover to produce a second carbanion available for further diversification. This versatility of this protocol was illustrated by the development of four distinct intermolecular C-C bond forming reactions with aromatic alkenes: hydroalkoxylation, hydroamidation, aminoalkylation and carboxyaminoalkylation to generate a range of valuable, and complex scaffolds³.



1. J. A. Forni, N. Micic, T. U. Connell, G. K. Weragoda, A. Polyzos, *Angew. Chem. Int. Ed.* (2020), 132, 2-11.
2. M. L. Czyz, M. S. Taylor, T. H. Horngren, A. Polyzos, *ACS Catalysis* (2021) 11, 5472-5480.
3. L. J. Franov, T. L. Wilsdon, M. L. Czyz, A. Polyzos, *J. Am. Chem. Soc.* (2024), 146, 29450-29461.
4. M. L. Czyz, T. H. Horngren, A. Kondopoulos, L. J. Franov, J. A. Forni, L. N. Pham, M. L. Coote, A. Polyzos, *Nat. Catal.* (2024), 7, 1316-1329.