

# ASYMMETRIC PHOTOCATALYTIC C-H FUNCTIONALIZATION OF TOLUENE AND DERIVATIVES

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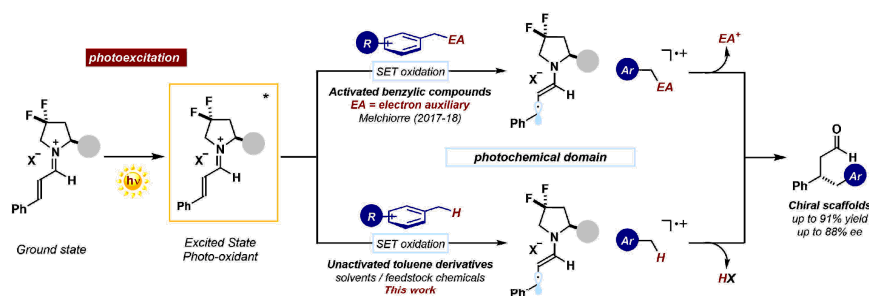
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The emerging field of photoredox catalysis has led to the development of new transformations due to the ability to generate radical intermediates under mild conditions.<sup>1</sup> Traditionally, this relies on a photocatalyst which efficiently absorbs light and induces a single electron transfer (SET). Recently, our group proved that a SET event can be triggered by the direct visible-light excitation of organocatalytic intermediates, unlocking reaction manifolds that are unavailable to conventional ground-state organocatalytic pathways.<sup>2</sup> In particular, we demonstrated that photolytically generated excited-state chiral iminium ions act as strong SET oxidants, enabling the enantioselective  $\beta$ -functionalization of enals in combination with reaction partners bearing suitable electron-auxiliary functionalities.<sup>2c,d,e</sup>

To further expand the synthetic potential of this reactivity, we wondered whether this could be applied to the direct asymmetric C-H functionalization of simple toluene derivatives. This strategy is attractive as it utilizes highly available feedstock chemicals and visible-light for making chiral molecules. While the use of toluene has already been reported in photoredox processes,<sup>3</sup> its employment in asymmetric catalysis has remained elusive.

This reactivity has been achieved by coupling the enhanced oxidizing capability of excited-state iminium ion with the basic character of its counter-anion to trigger a proton-coupled electron transfer pathway. This generates reactive benzylic radicals directly from the corresponding unfunctionalized precursors. The transformation proceeds under mild conditions and delivers the desired  $\beta$ -alkylated products generally in high yield and with good enantioselectivity.<sup>4</sup>



[1] M. H. Shaw, J. Twilton, D. W. C. MacMillan *J. Org. Chem.* 2016, 81, 6898.

[2] Selected contributions by Melchiorre and co-workers: a) *J. Am. Chem. Soc.* 2015, 137, 6120; b) *Nat. Chem.* 2017, 9, 868; c) *Angew. Chem. Int. Ed.* 2017, 56, 4447; d) *Angew. Chem. Int. Ed.* 2018, 57, 1068; e) *ACS Catal.* 2018, 8, 1062.

[3] a) K. Ohkubo, K. Mizushima, R. Iwata, K. Souma, N. Suzuki, S. Fukuzumi *Chem. Commun.* 2010, 46, 601; b) R. Zhuo, H. Liu, H. Tao, X. Yu, J. Wu *Chem. Sci.* 2017, 8, 4654.

[4] D. Mazzarella, G. E. M. Crisenza, P. Melchiorre *J. Am. Chem. Soc.* 2018, 140, 8439.