Visible Light-Driven Reductive Amination and a Cyclic Reaction Network for Enantioselective Synthesis of Amines

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Photoredox catalysis and enzymatic catalysis represent two powerful strategies for molecule activation by enabling energetically demanding transformations with light as an input[1] and by providing access to highly efficient substrate-specific enantioselective biochemical synthesis,[2, 3] respectively. Excitation of a new water-soluble variant of the widely used [Ir(ppy)$_3$] (ppy = 2-phenylpyridine) photosensitizer in the presence of a cyclic imine affords a highly reactive α-amino alkyl radical that is intercepted by hydrogen atom transfer (HAT) from ascorbate or thiol donors to afford the corresponding amine. The enzyme monoamine oxidase (MAO-N-9) selectively catalyzes the oxidation of one of the enantiomers to the corresponding imine. Upon combining the photoredox and biocatalytic processes under continuous photo-irradiation, enantioenriched amines are obtained in excellent yields.

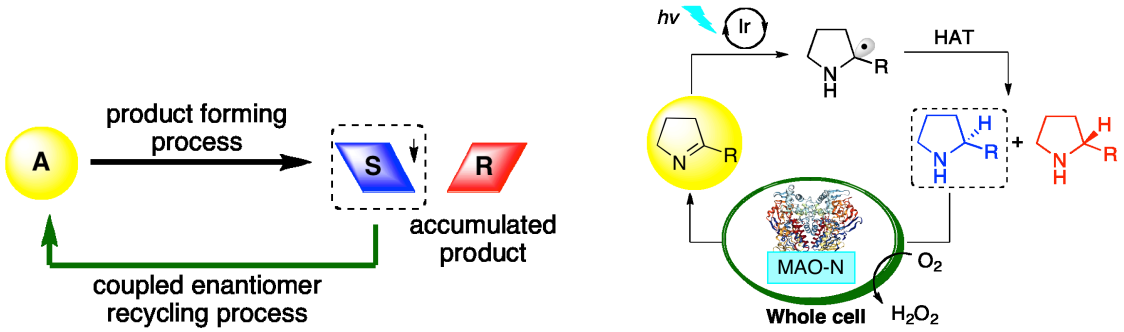

Figure 1. The cyclic reaction network. Sulfonated Ir(ppy)$_3$ complexes catalyze imine reduction to form racemic products, then (S)-selective monoamine oxidase selectively oxidize (S)-amine back to imine, finally the (R)-amine is accumulated as the only product after several iterations.

[1] a) X. Guo, O.S. Wenger, *Angew. Chem. Int. Ed.*, **2018**, *57*, 2469-2473; b) X. Guo. Y. Okamoto, M. R. Schreier, T. R. Ward, O. S. Wenger *Chem. Sci.*, **2018**, *9*, 5052-5056.
[2] V. Köhler, Y. M. Wilson, M. Dürrenberger, D. Ghislieri, E. Churakova, T. Quinto, L. Könrr, D. Häussinger, F. Hollmann, N. J. Turner and T. R. Ward, *Nat. Chem.*, **2013**, *5*, 93-99.
[3] Y. Okamoto, V. Köhler, T.R. Ward, *J. Am. Chem. Soc.*, **2016**, *138*, 5781-5784.