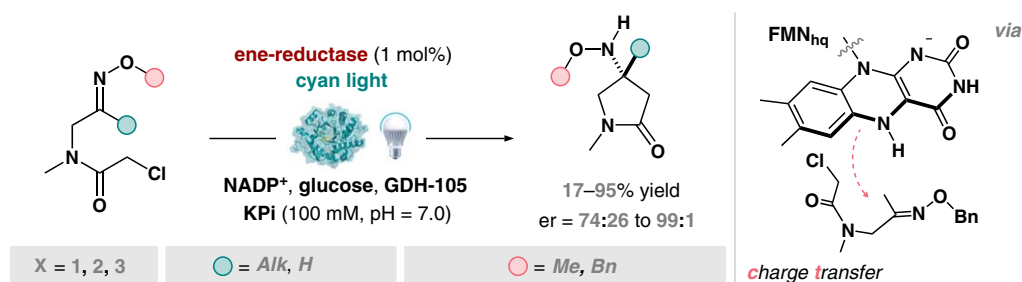


X. GAO, J. R. TUREK-HERMAN, Y. J. CHOI, R. D. COHEN, T. K. HYSTER* (PRINCETON UNIVERSITY AND CORNELL UNIVERSITY, ITHACA, USA)

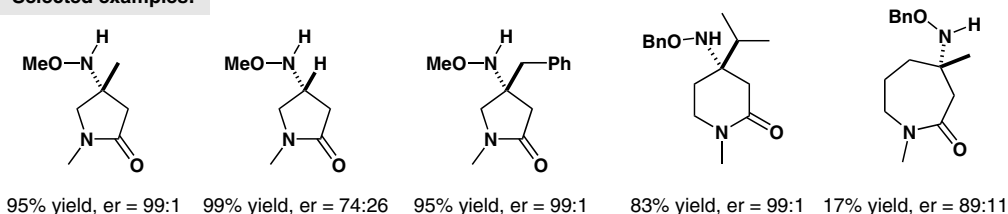
Photoenzymatic Synthesis of α -Tertiary Amines by Engineered Flavin-Dependent "Ene"-Reductases

J. Am. Chem. Soc. **2021**, *143*, 19643–19647, DOI: 10.1021/jacs.1c09828.

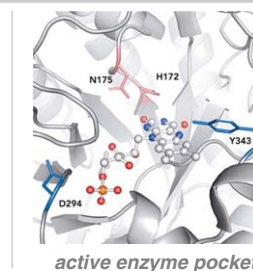
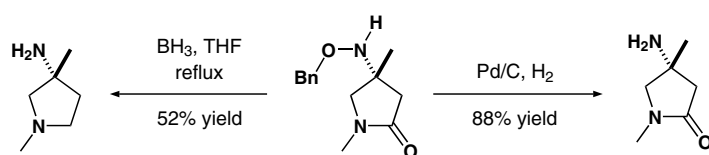
Photoenzymatic Catalysis Paves the Way for the Synthesis of Enantioenriched Tertiary Amines



Selected examples:



Follow-up transformations:



Significance: Hyster and co-workers disclose a photoenzymatic synthesis of enantioenriched α -tertiary amines starting from *O*-alkyloximes, which readily act as electron donors for the formation of charge-transfer (CT) complexes with flavoenzymes. Photoexcitation then leads to radical formation, which subsequently enables the intramolecular addition to the oxime, generating the desired tertiary amine products. Generally, very high enantiomeric ratios were observed by using engineered versions of GluEr-T36A- and NCR-enzymes, obtained by site-saturation mutagenesis. The resulting hydroxylamine products could, furthermore, be converted into useful compounds in follow-up transformations, giving reduced or ring-opened derivatives.

Comment: Building on their pioneering work (*Science* **2019**, *364*, 1166; *J. Am. Chem. Soc.* **2020**, *142*, 15673), the authors expand the scope of photoinduced enzyme-catalyzed radical cyclizations to chloro-*O*-alkyloximes. UV/Vis experiments carried out by the authors indicate that the substrate's oxime moiety is crucial for CT complex-formation, enabling radical generation. Whereas generally excellent enantiomeric ratios are obtained under mild reaction conditions, the reaction's scope seems to be limited, as only substrates bearing alkyl residues attached to the oxime carbon gave the corresponding products with high selectivity.

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