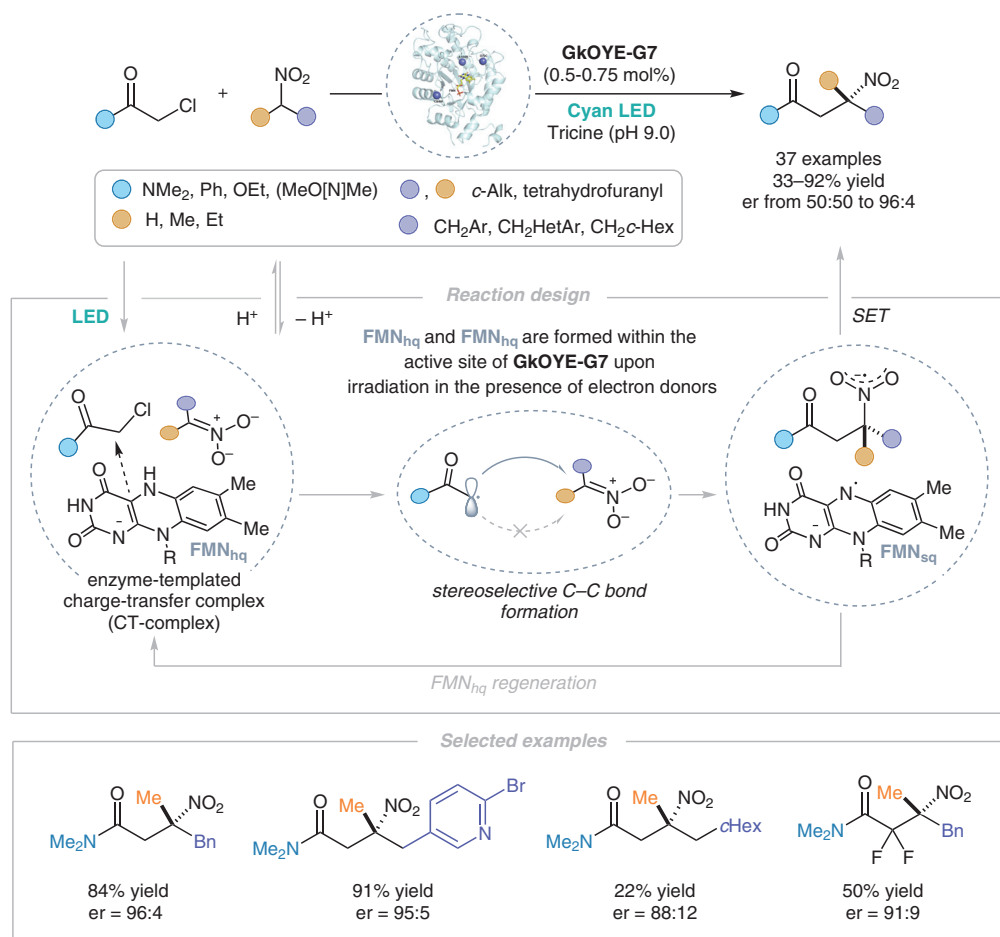


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Asymmetric C-Alkylation of Nitroalkanes via Enzymatic Photoredox Catalysis

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Enantioselective Synthesis of Tertiary Nitroalkanes Enabled by Enzyme Catalysis



Significance: Hyster and co-workers report a highly stereoselective C-alkylation of secondary nitronates with alkyl halides catalyzed by an engineered flavin-dependent ‘ene’-reductase (from *Geobacillus kaustophilus*, GkOYE-G7) under LED irradiation. The reported method provides straightforward access to tertiary nitroalkanes with moderate to high yields and generally high enantioselectivity. The obtained enantioenriched tertiary nitroalkanes can be reduced to the corresponding α -tertiary amines – important motifs in bioactive molecules and pharmaceuticals.

Comment: The high selectivity and evolvability of enzyme catalysis makes it an attractive solution for many synthetic challenges related to reactions’ chemo- and stereoselectivity. Although natural enzymes cannot catalyze the C-alkylation of nitronates with alkyl halides, the authors demonstrated that this non-natural mode of action can be evoked by photoirradiation and directed enzyme evolution. Such mechanism combining SET reduction, controlled radical addition and oxidation of nitro radical anion is enabled by an enzyme-templated CT complex, which was observed in mechanistic studies.

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