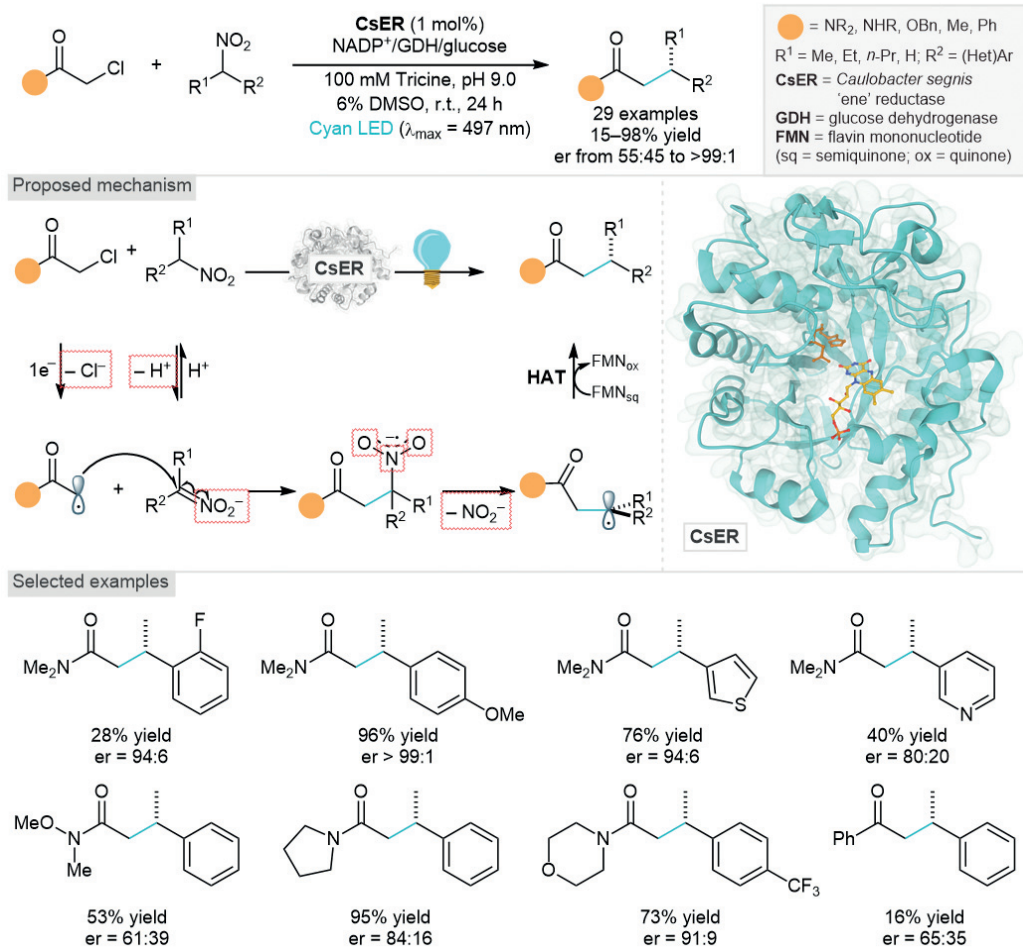


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An Asymmetric sp^3 - sp^3 Cross-Electrophile Coupling Using 'Ene'-Reductases

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Ene-Reductase Permits Cross-Electrophile Coupling of α -Chloro Carbonyls with α -Aryl Nitroalkanes



Significance: Hyster and co-workers describe a cross-electrophile coupling (XEC) between α -aryl nitroalkanes and α -chloro carbonyl compounds catalyzed by a flavin-dependent ene-reductase from *Caulobacter segnis* (CsER). Unnatural reactivity of the enzyme permits the formation of a new C–C bond through an unprecedented mechanistic pathway. The resulting β -(hetero)aryl carbonyl compounds are obtained in modest to excellent yields with poor to excellent enantioselectivities.

Comment: Mechanistic investigations showed that a charge-transfer complex between flavin hydroquinone and the α -chloro carbonyl substrate favors the reduction of the less oxidizing coupling partner. In contrast, conventional transition-metal-based XEC strategies afford dimerized byproducts due to the inability of organometallic catalysts to differentiate between two C(sp^3) electrophiles. The reported approach underlines the potential of exploiting the unique selectivity of enzymes in challenging radical-based C–C bond-forming transformations.

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