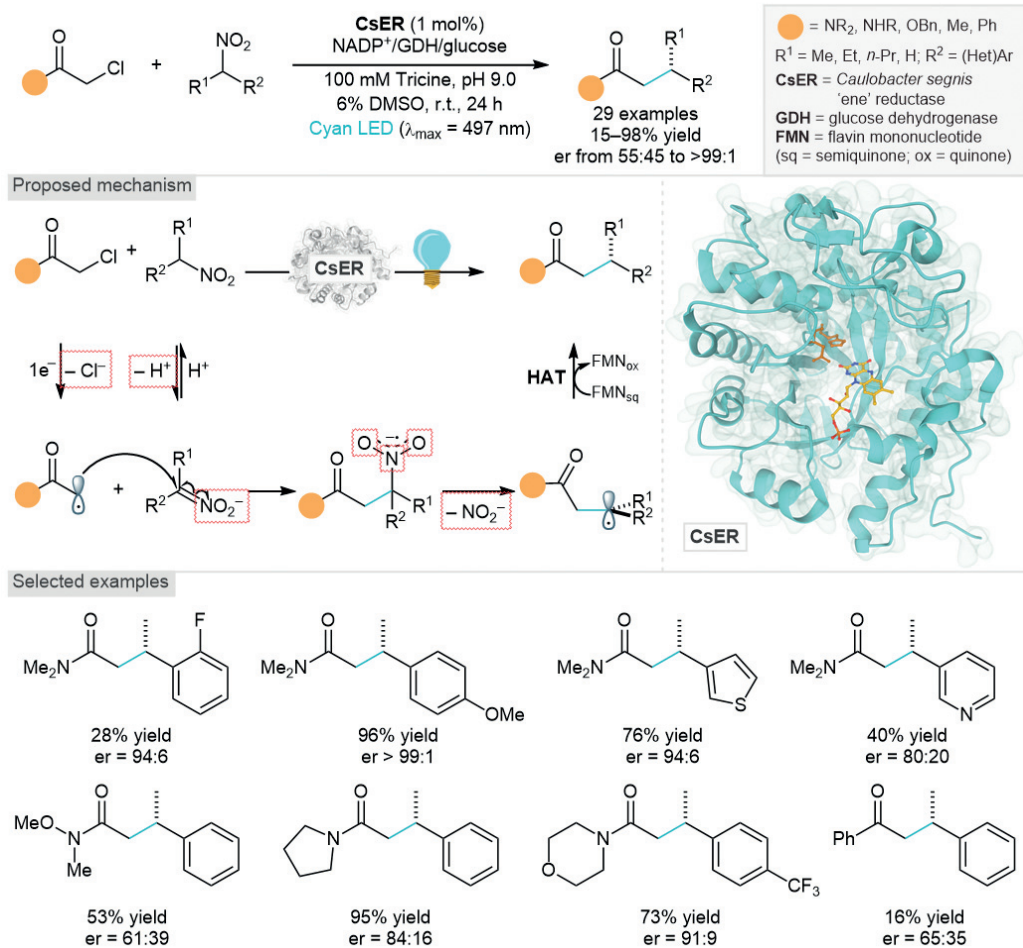


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An Asymmetric  $sp^3$ - $sp^3$  Cross-Electrophile Coupling Using 'Ene'-Reductases

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## Ene-Reductase Permits Cross-Electrophile Coupling of $\alpha$ -Chloro Carbonyls with $\alpha$ -Aryl Nitroalkanes



**Significance:** Hyster and co-workers describe a cross-electrophile coupling (XEC) between  $\alpha$ -aryl nitroalkanes and  $\alpha$ -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  $\beta$ -(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  $\alpha$ -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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