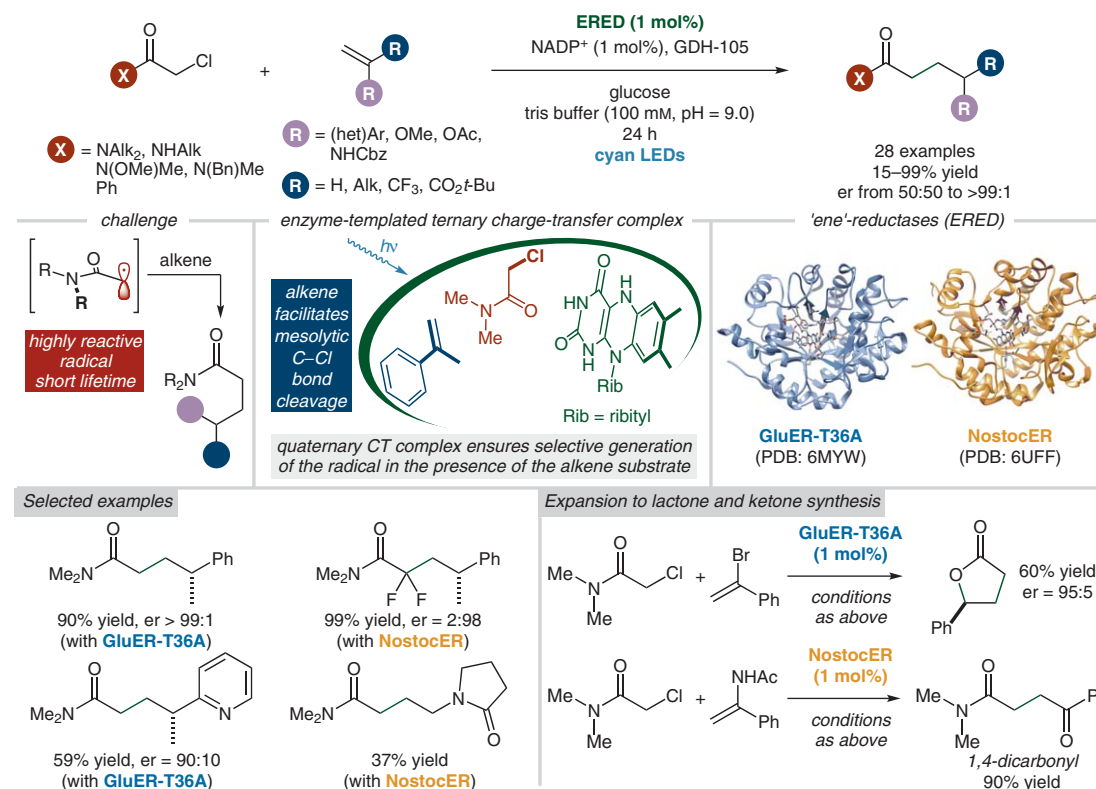


C. G. PAGE, S. J. COOPER, J. S. DEHOVITZ, D. G. OBLINSKY, K. F. BIEGASIEWICZ, A. H. ANTPOW, K. W. ARMBRUST, J. M. ELLIS, L. G. HAMANN, E. J. HORN, K. M. OBERG, G. D. SCHOLES, T. K. HYSTER\* (PRINCETON UNIVERSITY, USA)  
 Quaternary Charge-Transfer Complex Enables Photoenzymatic Intermolecular Hydroalkylation of Olefins  
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# Photoenzymatic Intermolecular Hydroalkylation of Alkenes



**Significance:** Hyster and co-workers report the application of flavin-dependent ene-reductases (EREDs) in a photoenzymatic intermolecular hydroalkylation of olefins with  $\alpha$ -chloro amides. A unique nonnatural mechanism, involving an enzyme-templated charge-transfer (CT) complex between the alkene,  $\alpha$ -chloro amide, and flavin hydroquinone cofactor, ensures that radical formation upon photoexcitation occurs exclusively when both substrates are bound within the active site. The radical-terminating hydrogen-atom transfer can be controlled by the active site of the ERED, thereby providing access to enantioenriched  $\gamma$ -stereogenic amides.

**Comment:** The authors previously discovered the formation of CT complexes when organohalides and the flavin hydroquinone cofactor within the active site of EREDs, and they applied these complexes in intramolecular C–C bond-forming reactions. The development of the corresponding intermolecular process (see X. Huang et al. *Nature* **2020**, *584*, 69 for a related approach) is a formidable challenge, as the transient radical is prone to undergo competing hydrodehalogenation in the absence of a coupling partner. In the present study, the authors discovered that a unique quaternary CT complex gates radical formation and suppresses hydrodehalogenation, permitting an intermolecular hydroalkylation of olefins.

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