

M. LI, W. HARRISON, Z. ZHANG, Y. YUAN, H. ZHAO\* (UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN, USA)

Remote Stereocontrol with Azaarenes via Enzymatic Hydrogen Atom Transfer

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# Enzymatic Hydrogen Atom Transfer Allows for Remote Stereocontrol Using Aza-arenes

Category

Organo- and Biocatalysis

Key words

asymmetric catalysis

organocatalysis

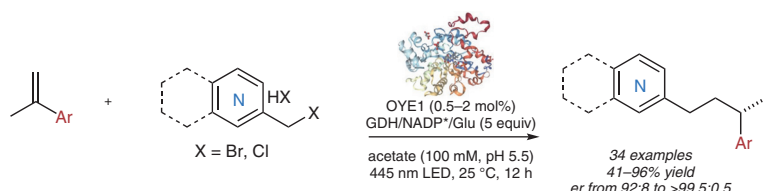
remote stereocontrol

ene-reductase

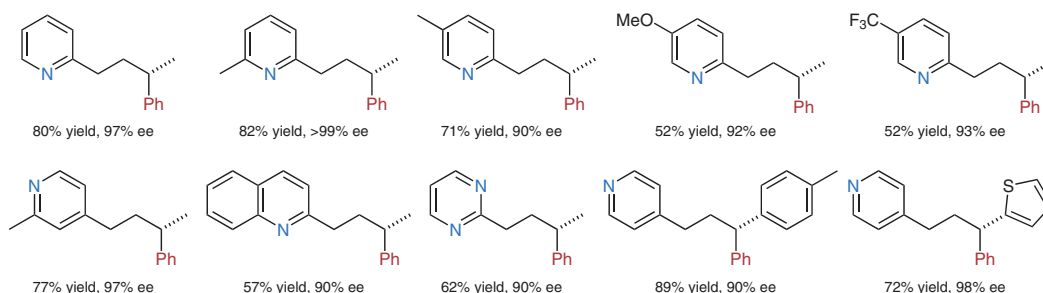
photoenzyme

radical hydroalkylation

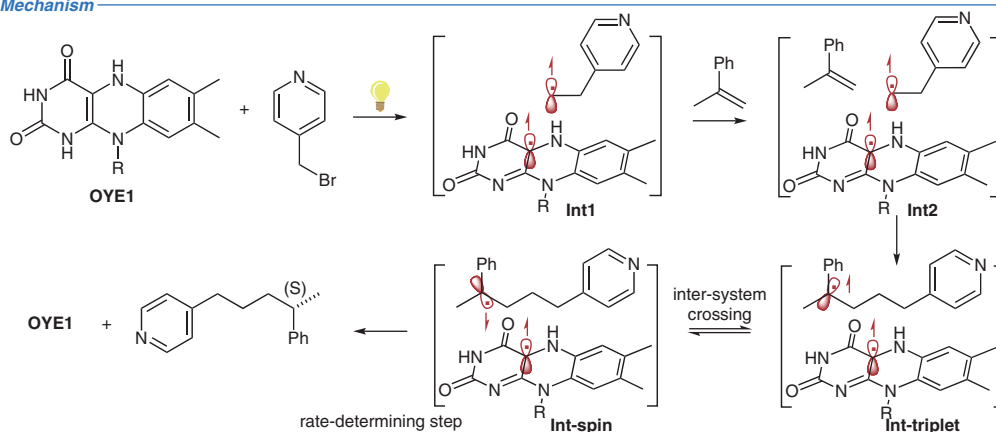
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of the Month



## Selected examples



## Mechanism



**Significance:** The Zhao group describes a radical hydroalkylation reaction in which the ene-reductase system modulates the enantioselectivity of remote carbon-centered radicals on aza-arenes. Their computational and experimental analysis highlights the importance of hydrogen bonding and steric effects of critical amino acid residues in generating such high stereoselectivities. They also offer a plausible technique for inserting an aza-arene pharmacophore into 'ene'-containing molecules, thus opening new pathways for the creation of value-added products from styrenes.

**Comment:** The decreasing control provided by the catalyst's chiral environment with increasing distance to the reaction site makes remote stereocontrol a challenging task in chemical synthesis. The authors show how to use a flavin mononucleotide (FMN)-dependent ene-reductase for an enantioselective radical hydroalkylation process. DFT calculations show that Int1 serves as the initiating intermediate and that the product formation involves an electron-spin-state transition from triplet (Int-triplet) to singlet (Int-spin) process. This paper tackles a long-standing problem in asymmetric catalysis by proposing a feasible technique for remote stereocontrol using a single functional group.

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