

Remote Stereocontrol with Azaarenes via Enzymatic Hydrogen Atom Transfer

Background/Objective

Azaarenes are ring-like, nitrogen-containing molecules essential in creating agrochemicals and other specialized chemical products. Achieving “remote stereocontrol,” or manipulating the spatial arrangement of atoms in far-reaching parts of azaarene molecules relative to the catalyst’s reaction site, allows for crafting more effective bioactive compounds but is hindered by the azaarene ring’s rigid structure. This structure difficulty impacts the consistent creation of molecules with specific orientations, or enantiomers. In this study, we present a method to overcome this, catalyzing remote stereocontrol reactions with high enantioselectivity in azaarenes.

Approach

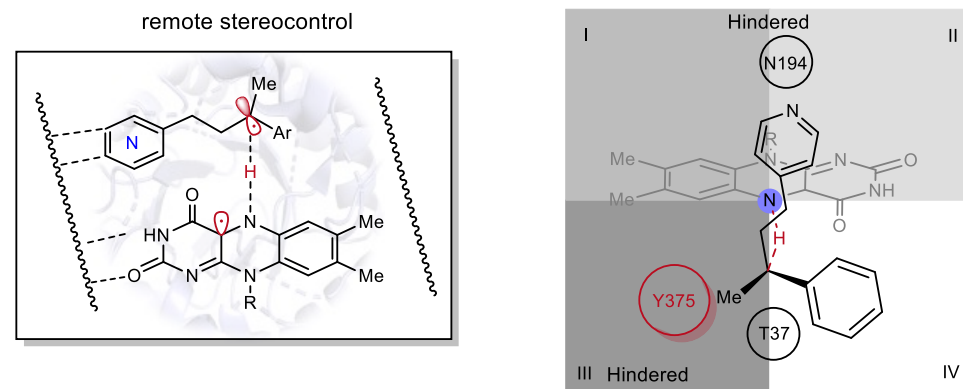
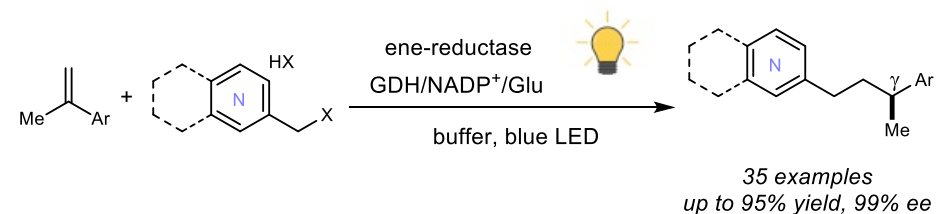
We developed an “ene-reductase” system to alter the arrangement of chemical groups attached to carbon atoms on distant parts of azaarenes. This system, through an enzymatic hydrogen atom transfer process, selectively transfers hydrogen atoms to carbon radicals, influencing their spatial arrangement. This guides the formation of unique azaarenes with distinctive γ -stereocenters, broadening the spectrum and versatility of azaarenes we can produce.

Results

We discovered that the amino acid residues T37, N194, and Y375, through their hydrogen bonding and spatial roles, are central to achieving high levels of enantioselectivity, which is crucial for synthesizing more specialized chemical products.

Significance/Impacts

This ene-reductase system addresses a key challenge in biocatalysis by achieving remote stereocontrol with azaarene groups and would enable the transformation of biomass-derived alcohols into high-value compounds using a more efficient process.



The photoenzymatic process produces azaarenes with unique γ -stereocenters.

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