Category

Organo- and Biocatalysis

Key words

enzyme catalysis

C–H amination

regiodivergency

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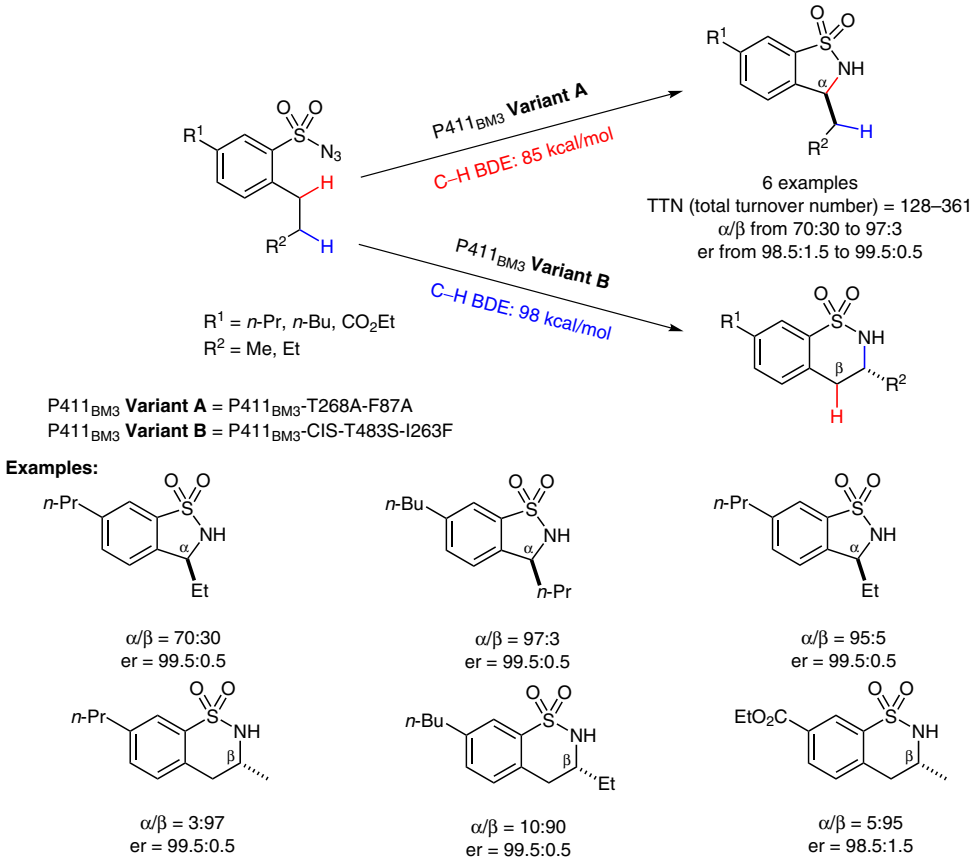
Enzyme-Controlled Nitrogen-Atom Transfer Enables Regiodivergent C–H Amination
J. Am. Chem. Soc. **2014**, *136*, 15505–15508.

Enzyme-Controlled Regiodivergent C–H Amination



Significance: Arnold and co-workers report an enzyme-catalyzed asymmetric and regiodivergent C–H amination. By modifying the active site of $P411_{BM3}$, a cytochrome $P450_{BM3}$ variant in which the axial position of the iron-heme prosthetic group is ligated by serine instead of cysteine, two variants enabling different regioselectivity were obtained. One allowed the selective amination of the energetically more favored benzylic position, while the other was selective for the homobenzylic position of 2,5-disubstituted benzenesulfonyl azides.

Comment: Due to the availability of a weaker benzylic C–H bond, direct C–H amination of homobenzylic positions are a challenge in small-molecule catalysis. Breaking the C–H bond is kinetically controlled, and therefore, this can in some cases be overcome by variation of the steric properties of the used ligands. However, genetically engineered enzymes are an attractive alternative for regiodivergent C–H amination, enabling access to the desired products in good to excellent regio- and enantioselectivities.

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Synfacts 2015, 11(1), 0090 Published online: 15.12.2014
DOI: 10.1055/s-0034-1379624; **Reg-No.:** B12714SF

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