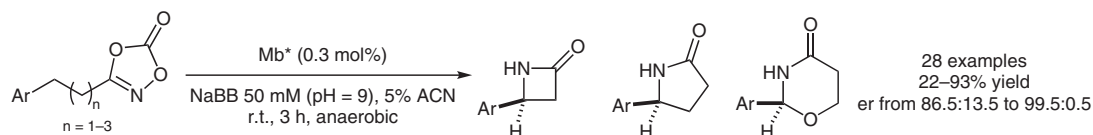


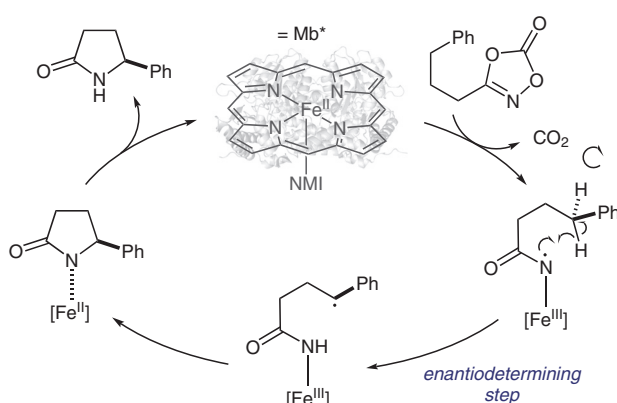
S. ROY, D. A. VARGAS, P. MA, A. SENGUPTA, L. ZHU, K. N. HOUK*, R. FASAN*
(UNIVERSITY OF ROCHESTER, UNIVERSITY OF TEXAS AT DALLAS AND UNIVERSITY OF CALIFORNIA, LOS ANGELES, USA)

Stereoselective Construction of β -, γ - and δ -Lactam Rings via Enzymatic C–H Amidation
Nat. Catal. **2024**, *7*, 65–76, DOI: 10.1038/s41929-023-01068-2.

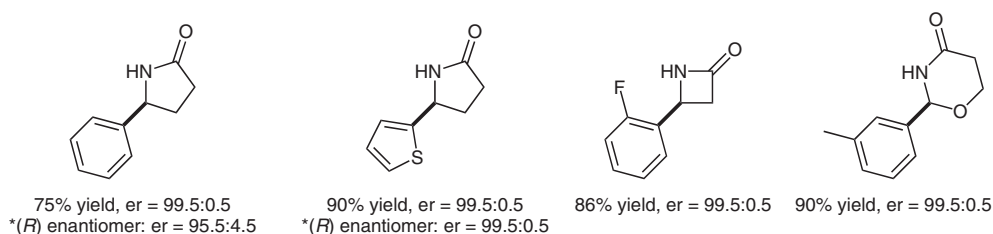
Enzymatic C–H Amidation toward Stereoselective Construction of β -, γ - and δ -Lactams



Proposed mechanism for catalyzed C–H amidation



Selected examples



Significance: Houk, Fasan, and co-workers disclose the haemoprotein-catalysed intramolecular C–H amidation of dioxazolone reagents toward the asymmetric synthesis of β -, γ - and δ -lactams with good to excellent enantioselectivity. Mechanistic studies suggest that the protein-mediated enantioinduction in the C–N bond-forming process occurs in the radical rebound step. Furthermore, an alkaloid natural product and a drug molecule were synthesized in a reduced number of steps (7–8 versus 11–12) compared to previous reports.

Comment: Enantiodivergent biocatalysts are highly desirable for medicinal chemistry and other synthetic applications, yet their development is often challenging. Notably, examination of the primary myoglobin (Mb) active-site mutant library uncovered a variant, Mb(L29T,H64V,V68L), which induces the cyclization with opposite enantioselectivity to that of Mb*, resulting in the production of the *R*-configured γ -lactam product.

SYNFACTS Contributors: Benjamin List, Marian Guillén
Synfacts 2024, 20(03), 0299 Published online: 14.02.2024
DOI: 10.1055/s-0043-1773112; Reg-No.: B02124SF

© 2024, Thieme. All rights reserved.
Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Category

Organo- and Biocatalysis

Key words

C–H amidation

myoglobin

dioxazolones

enantiodivergence

nitrene transfer

Synfact
of the
Month

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.