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Regio- and Enantio-selective Chemo-Enzymatic C–H-Lactonization of Decanoic Acid to (*S*)-δ-Decalactone
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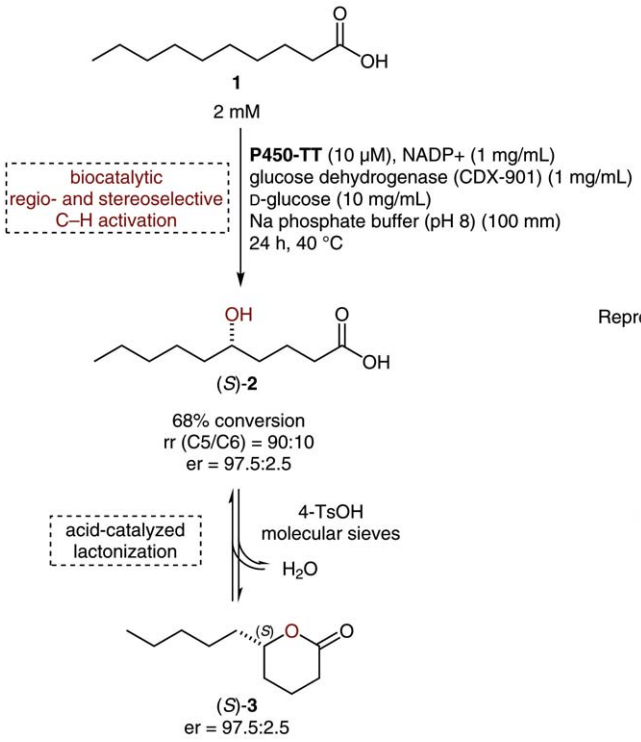
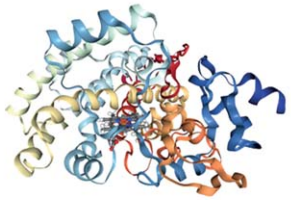
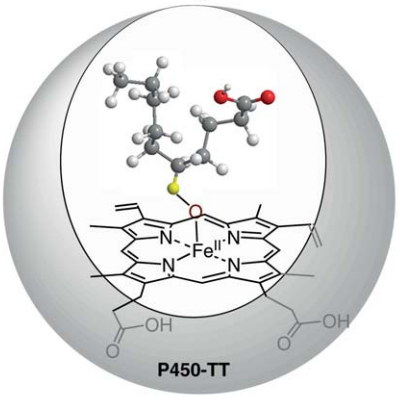
Valorization of a Saturated Fatty Acid to Enantioenriched (*S*)-δ-Decalactone





wild-type **P450-TT**
CYP116B46
from *Tepidiphilus thermophilus*

Representation of the docking structure of **1** in P450-TT:



Significance: Hydroxy fatty acids (HFAs) have a wide range of applications as fragrances, food supplements, and pharmaceuticals. The direct, regio- and enantioselective C–H hydroxylation of nonactivated fatty acids would provide an elegant and efficient approach toward HFAs. Flitsch and co-workers report the first example of a regio- and stereoselective C5 hydroxylation of decanoic acid (**1**) to give (*S*)-5-hydroxydecanoic acid (**2**), catalyzed by a wild-type cytochrome P450 monooxygenase (CYP116B46 from *Tepidiphilus thermophilus*). Acid-catalyzed cyclization of **2** gave access to the lactonization product (*S*)-δ-decalactone (**3**), a high-value fragrance compound.

Comment: Methodologies for the proximal α- and β-positions or the terminal ω-1, ω-2 and ω-3-hydroxy acids have been investigated in the past. The mid-chain γ- and δ-positions have previously been synthesized from functionalized materials. The authors explain the high enantioselectivity of the C–H oxyfunctionalization in terms of molecular docking of acid **1** with the active site of P450-TT. Accordingly, substrate **1** folds in a U-shaped conformation and is placed above the heme prosthetic group, permitting hydroxylation in the middle of the chain, giving access to the (*S*)-enantiomer at C5. It is noteworthy that further engineering of this protein family might enable utilization of a variety of nonactivated substrates.

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Category

Organo- and Biocatalysis

Key words

cytochrome P450 monooxygenase
decanoic acid
C–H activation
decalactones

Synfact of the Month