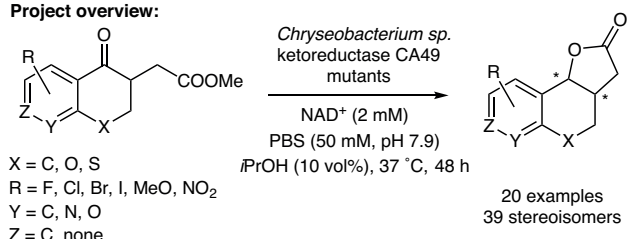
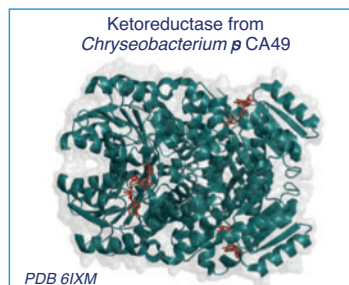


One Enzyme – Two Variants: Enantioselective Synthesis of Fused Lactones Giving Access to Two Enantiomers

Project overview:

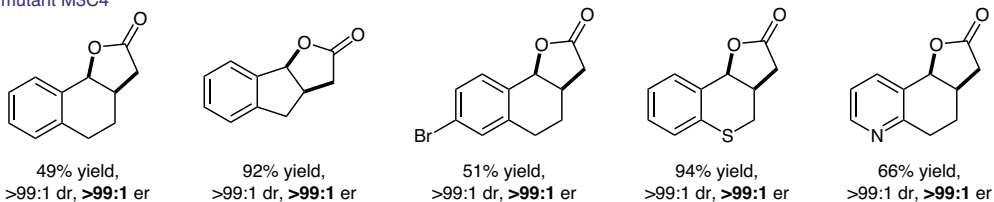


X = C, O, S
R = F, Cl, Br, I, MeO, NO₂
Y = C, N, O
Z = C, none

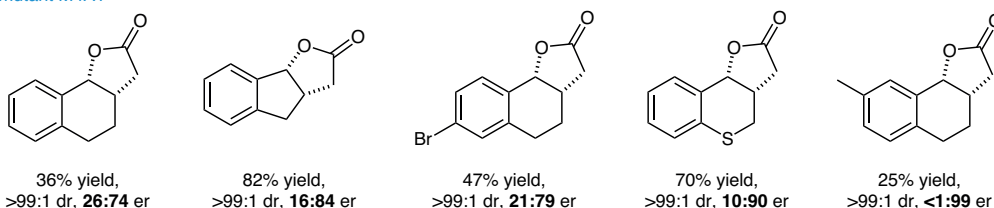


Selected scope examples:

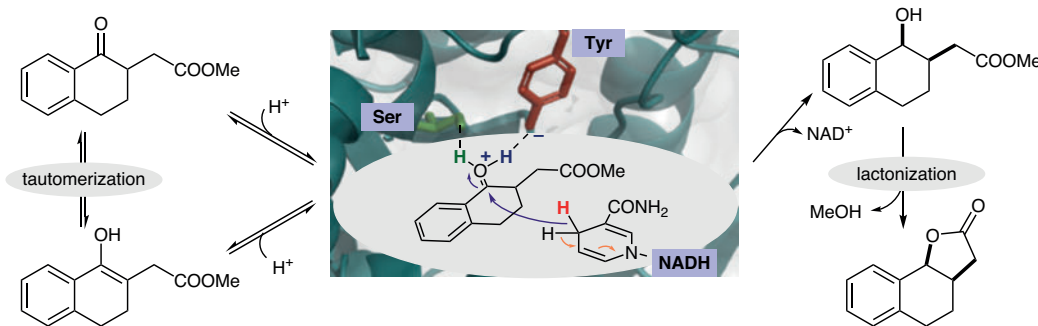
mutant M3C4



mutant M4A1



Mechanism:



Significance: The authors present the design of an enzyme – ketoreductase – used to obtain polycyclic lactones from β -ketoesters by dynamic kinetic resolution. The usefulness of the method was demonstrated on 20 examples, obtained diastereo- and enantioselectively. By changing the enzyme mutant, the stereoselectivity of the reaction can be reversed, maintaining decent enantioselectivity.

Comment: Since an enzyme is a complex biochemical structure, it is difficult to design it to work enantioselectively on enantiomers opposite to the natural one. Shi et al. overcame this limitation by developing a ketoreductase and presented two variants of the enzyme that process both enantiomers via enantioselective dynamic kinetic resolution.