Enzymatic Nitrene Transfer/Sigmatropic Rearrangement to Access Allylic Amines

Significance: Arnold and co-workers report an enzymatic synthesis of allylic amines through a sulfimidation/[2,3]-sigmatropic rearrangement of phenyl allyl sulfides with tosyl azide. A mutant variant of cytochrome P411 from Bacillus megaterium efficiently catalyzes a highly enantioselective nitrene transfer to the sulfides, and permits a subsequent rearrangement with partial retention of the stereochemical information. In a scale-up experiment with reduced catalyst loading, 0.1 mmol of substrate was converted into the corresponding allylic amine in 71% yield and a remarkable total turnover number of 6100.

Comment: The authors have successfully employed directed evolution to achieve a chemoselective nitrene transfer over the competing reduction. Furthermore, they achieved a sigmatropic rearrangement of the intermediate allylic sulfimides, a process unknown in wild-type biological systems.

Selected examples:

- 86% yield, TTN = 2200, er = 94:6
- 48% yield, TTN = 1100, er = 96:1
- 71% yield, TTN = 6100, er = 85.5:14.5
- 68% yield, TTN = 1500
- 36% yield, TTN = 1000