Single-Step Enzymatic Synthesis of β-Methyltryptophans

Significance: Arnold and co-workers report an enzymatic single-step synthesis of β-methyltryptophan analogues from various nucleophiles and L-threonine by using a mutant β-subunit of the tryptophan synthase from Pyrococcus furiosus (PfTrpB). This subunit, derived from directed evolution, proved to be significantly more active than the wild-type subunit.

Comment: By employing directed evolution, the authors have previously achieved the restoration of activity of the sole β-subunit of the heteromeric tryptophan synthase from Pyrococcus furiosus, which facilitates applications outside the cell (Proc. Natl. Acad. Sci. U.S.A. 2015, 112, 14599). The current work is an intriguing extension that permits the efficient transformation of threonine instead of serine. The resulting β-methyltryptophans are valuable precursors to a variety of natural products and could previously be only accessed by several chemical or enzymatic steps.