**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 heteromeric 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.

**Selected examples:**

- 8200 TTN 72% yield dr and er > 99:1 (wild-type PfTrpB: 66 TTN)
- 220 TTN 17% yield
- 500 TTN 33% yield
- 1300 TTN 14% yield (N-Boc derivative, over two steps)

**Key words**

- tryptophan
- genetic engineering
- threonine
- directed evolution

**Category**

- Organo- and Biocatalysis