Chemoenzymatic Distal C–H Hydroxylation

Significance: Zwick and Renata report the chemoenzymatic hydroxylation of the δ-position of aliphatic amino acids. By using an α-ketoglutarate-dependent dioxygenase, the desired products could usually be obtained in high yield and with high selectivity. This novel methodology was applied to the formal total synthesis of manzacidin C and proline analogues.

Comment: C–H bond functionalization of distal bonds within amino acids represents a major challenge in organic synthesis. Transition-metal-catalyzed systems are typically limited to functionalization of the β-position whereas the δ-position can be functionalized by Hofmann–Löffler–Freytag-type reactions.