

Bioinspired Synthesis of Tetraponerines and Analogues Thereof

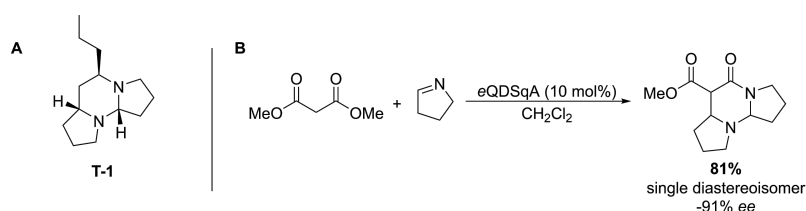
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Tetraponerines are natural alkaloids that occur in the smear venom of *Tetraponera* ants. Eight different members (T-1 to T-8) have been identified, with T-8 being the most abundant.^[1] All consist of a tricyclic aminal with a linear alkyl substituent (Figure 1). Tetraponerines inhibit non-competitively the nicotinic acetylcholine-receptor and thereby paralyze their enemy.^[1]

The Wennemers group has developed stereoselective (thio)acetate and (thio)malonate addition reactions by utilizing malonic acid-derived thioesters. These (thio)acetate equivalents react in the presence of catalytic amounts of cinchona alkaloid derivatives with a variety of different electrophiles, including aldehydes, nitroolefins, and imines.^[2]

Herein, we present the stereoselective addition of malonates to cyclic imines that yields the tricyclic core of tetraponerines (Figure 2). This organocatalytic addition reaction proceeds with high stereoselectivity (>90% ee). The synthesis of tetraponerines requires only four steps and is, thus, the shortest stereoselective synthesis of tetraponerines known to date.^{[3],[4]}



A: Structure of Tetraponerine T-1; B: Stereoselective addition of dimethyl malonate to Δ1-pyrroline as the key step.

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