USA) Total Synthesis of (±)-Actinophyllic Acid

J. Am. Chem. Soc. 2008, 130, 7568-7569.

Synthesis of (±)-Actinophyllic Acid

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Significance: (±)-Actinophyllic acid was isolated from the leaves of the tree Alstonia actinophylla. It is an inhibitor of carboxypeptidase U, an endogenous inhibitor of the process the body uses to clear fibrin clots. This synthesis proceeds in only eight stages all but one of which construct C-C or C-N bonds.

Comment: The oxidative coupling $(\mathbf{C} \to \mathbf{D})$ of the piperidinone and malonate enolates by an iron(III) oxidant is believed to be the first intramolecular example. The bulky tert-butyl ester groups blocked one face of the ketone towards nucleophilic attack ($\mathbf{D} \to \mathbf{E}$) resulting in a single isomer.

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