Total Synthesis of ( $\pm$ )-Actinophyllic Acid
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## Gategory

Synthesis of Natural

## Products and

## Potential Drugs

## Key words

actinophyllic acid
aza-Cope
rearrangement
Mannich reaction
oxidative enolate coupling

Significance: $( \pm)$-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 $\mathrm{C}-\mathrm{C}$ or $\mathrm{C}-\mathrm{N}$ bonds.

Comment: The oxidative coupling ( $\mathbf{C} \rightarrow \mathbf{D}$ ) 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 $(\mathbf{D} \rightarrow \mathbf{E})$ resulting in a single isomer.

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[^0]:    synfacts Contributors: Philip Kocienski, Stewart Eccles
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