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Enantioselective Synthesis of (+)-Peganumine A
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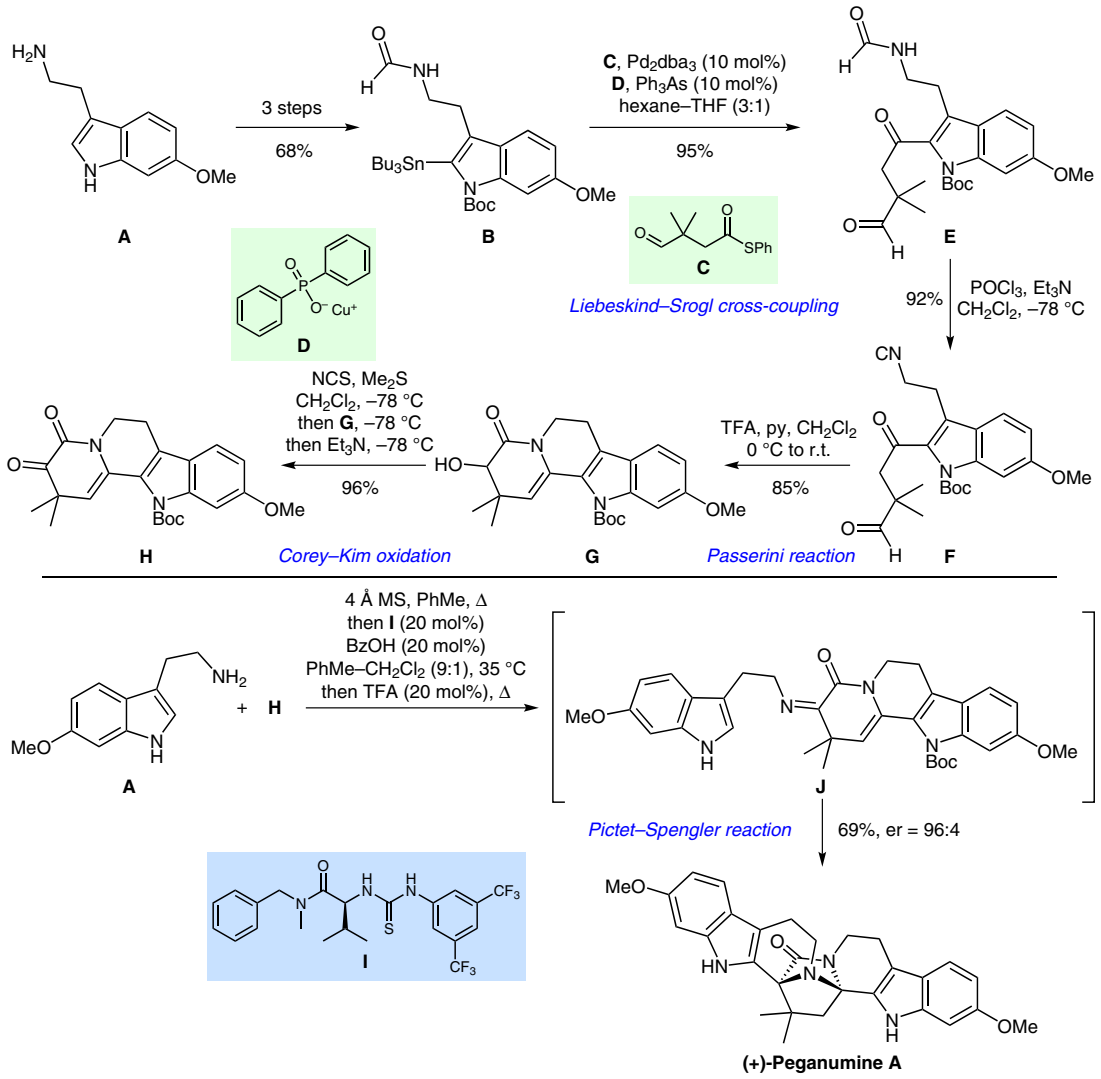
Total Synthesis of (+)-Peganumine A



Significance: (+)-Peganumine A, isolated from the seeds of *Peganum harmala L.*, is a dimeric tetrahydro-β-carboline alkaloid displaying significant selective cytotoxic activity against HL-60 cells (IC_{50} = 5.8 μM). The first enantioselective synthesis by Zhu and co-workers relies on an early Liebeskind–Srogl cross-coupling and a thiourea-catalyzed Pictet–Spengler reaction to form the unprecedented octacyclic scaffold.

Comment: Liebeskind–Srogl cross-coupling of stannane **B** and thioester **C** provided *N*-formamide **E** in 95% yield. After dehydration, a three-center-two-component Passerini reaction followed by oxidation furnished tetracycle **H**. The synthesis was completed by an enantioselective Pictet–Spengler reaction of **H** and 6-methoxytryptamine (**A**) to give (+)-peganumine A in a total of 7 steps and 33% overall yield.

SYNFACTS Contributors: Erick M. Carreira, Marco Brandstätter
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