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A Stereocontrolled Synthesis of (+)-Thienamycin
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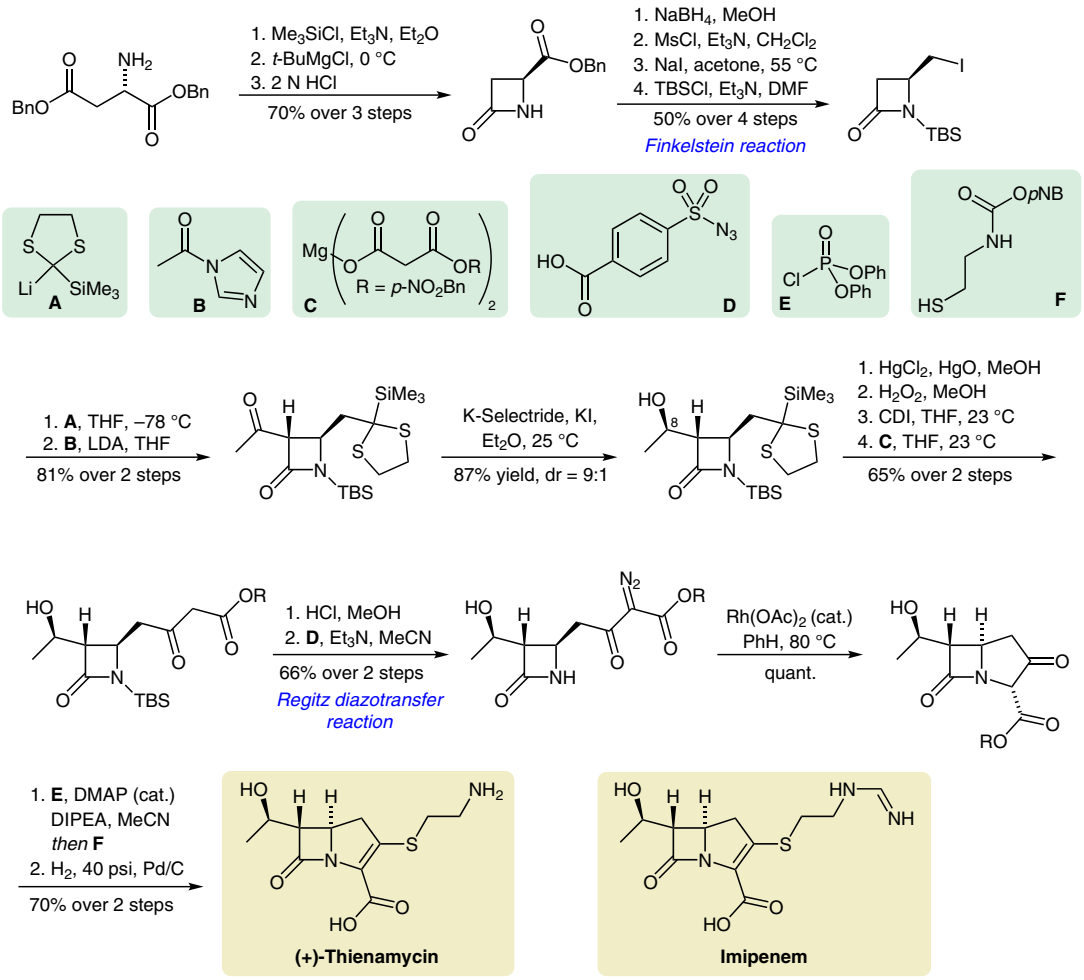
First Asymmetric Synthesis of (+)-Thienamycin



Significance: Thienamycin is a highly potent carbapenem antibiotic that demonstrates excellent activity against both Gram-positive and Gram-negative bacteria. It retains activity in the presence of β-lactamase enzymes and operates by inhibiting peptidoglycan biosynthesis. Because it decomposes when exposed to water, a more stable analogue (imipenem) was developed by Merck. In 1980, Salzmann and co-workers reported the first asymmetric total synthesis of thienamycin.

Comment: Starting from dibenzyl aspartate, a protection followed by cyclization afforded the desired azetidinone. To set the stereochemistry at C8, an acylation with *N*-acetylimidazole followed by reduction with K-Selectride was used. Key to the synthesis was a highly efficient carbene N–H insertion to form the sterically hindered bicyclic core of thienamycin. Finally, to complete the synthesis, a vinyl phosphate was displaced by **F** and a global deprotection gave thienamycin.

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