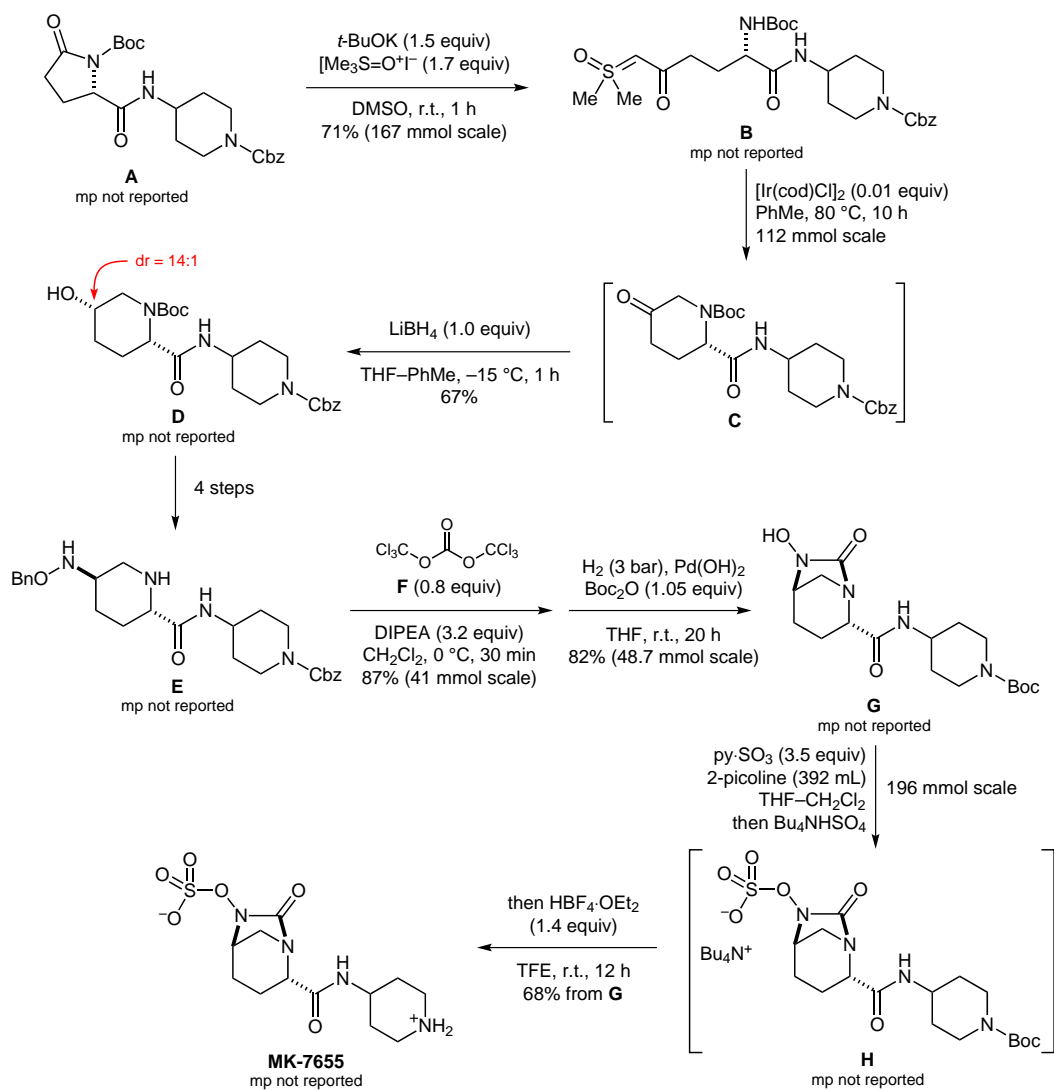


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A Concise Synthesis of a β -Lactamase Inhibitor

Org. Lett. **2011**, *13*, 5480–5483.

Synthesis of MK-7655



Significance: MK-7655 is a potent β -lactamase inhibitor. It is in clinical trials for the treatment of bacterial infections in conjunction with β -lactam antibiotics. The bicyclic urea is highly reactive and a major challenge was to find conditions for its formation and preservation during the construction of the aminoxy sulfate. This work features the first practical application of the N–H insertion of a sulfoxonium ylide (**D** \rightarrow **E**) in a complex synthesis.

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Comment: The synthesis depicted delivered multikilogram quantities of API in twelve steps and 10% overall yield. MK-7655 is only stable in the pH range of 4–8; therefore, removal of the Boc group in the final step cannot be achieved under the usual acidic conditions. After extensive experiments, 1.4 equivalents of $\text{HBF}_4\cdot\text{OEt}_2$ in trifluoroethanol successfully removed the Boc group.

Category

Synthesis of Natural Products and Potential Drugs

Key words

MK-7655

β -lactamase inhibitors

iridium-catalyzed N–H insertion

sulfoxonium ylides

SYNFACTS
of the month

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