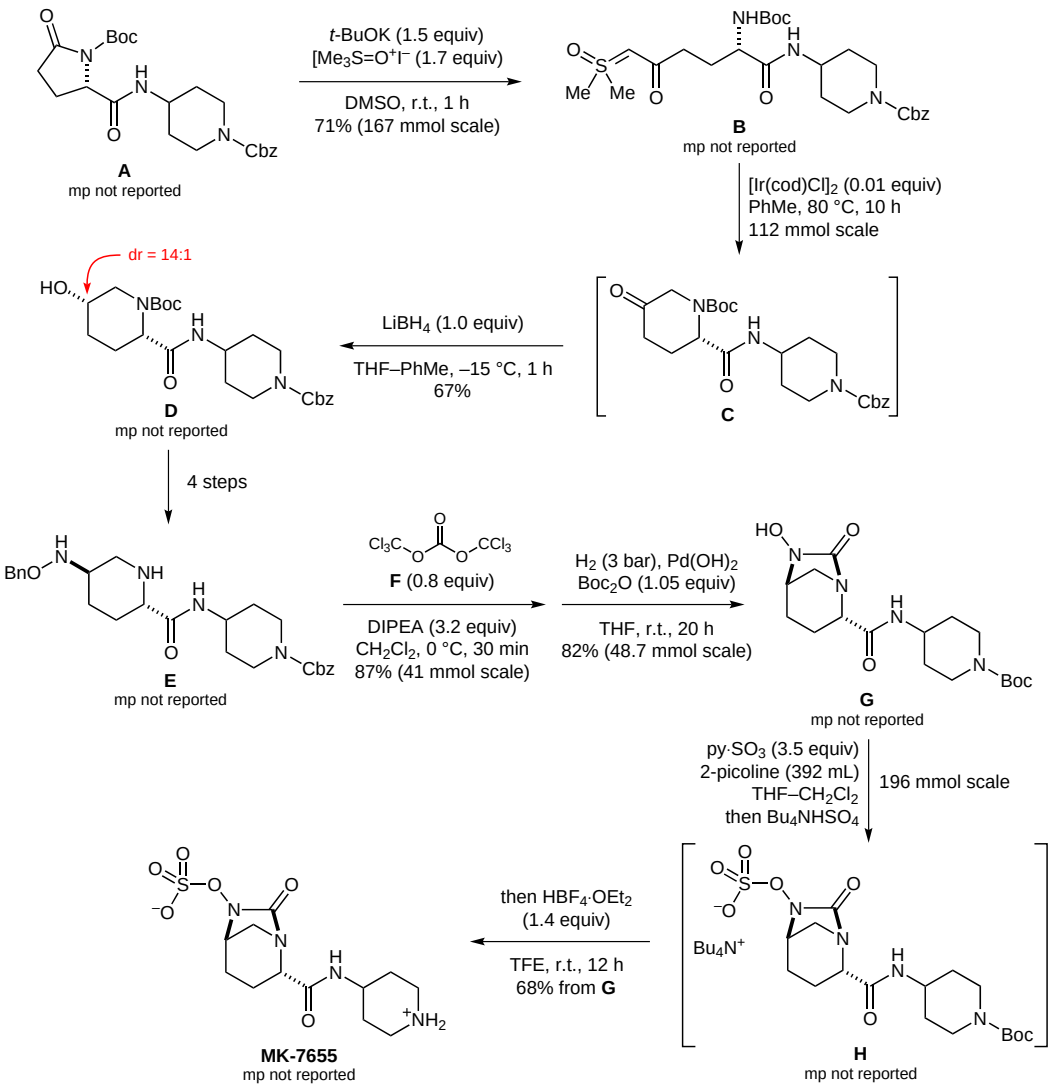
I. K. MANGION,* R. T. RUCK, N. RIVERA, M. A. HUFFMAN, M. SHEVLIN (MERCK AND CO., INC., RAHWAY, USA)

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** → **E**) in a complex synthesis.

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 $HBF_4{\cdot}OEt_2$ in trifluoroethanol successfully removed the Boc group.

SYNFACTS Contributors: Philip Kocienski
Synfacts 2012, 8(1), 0001 Published online: 19.12.2011
DOI: 10.1055/s-0031-1289917; **Reg-No.:** K07011SF

Category

Synthesis of Natural Products and Potential Drugs

Key words

MK-7655

β-lactamase inhibitors

iridium-catalyzed N–H insertion

sulfoxonium ylides