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

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 sulf oxonium 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 HBF₄·OEt₂ in trifluoroethanol successfully removed the Boc group.

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**Key words**
MK-7655
β-lactamase inhibitors
iridium-catalyzed N–H insertion
sulf oxonium ylides