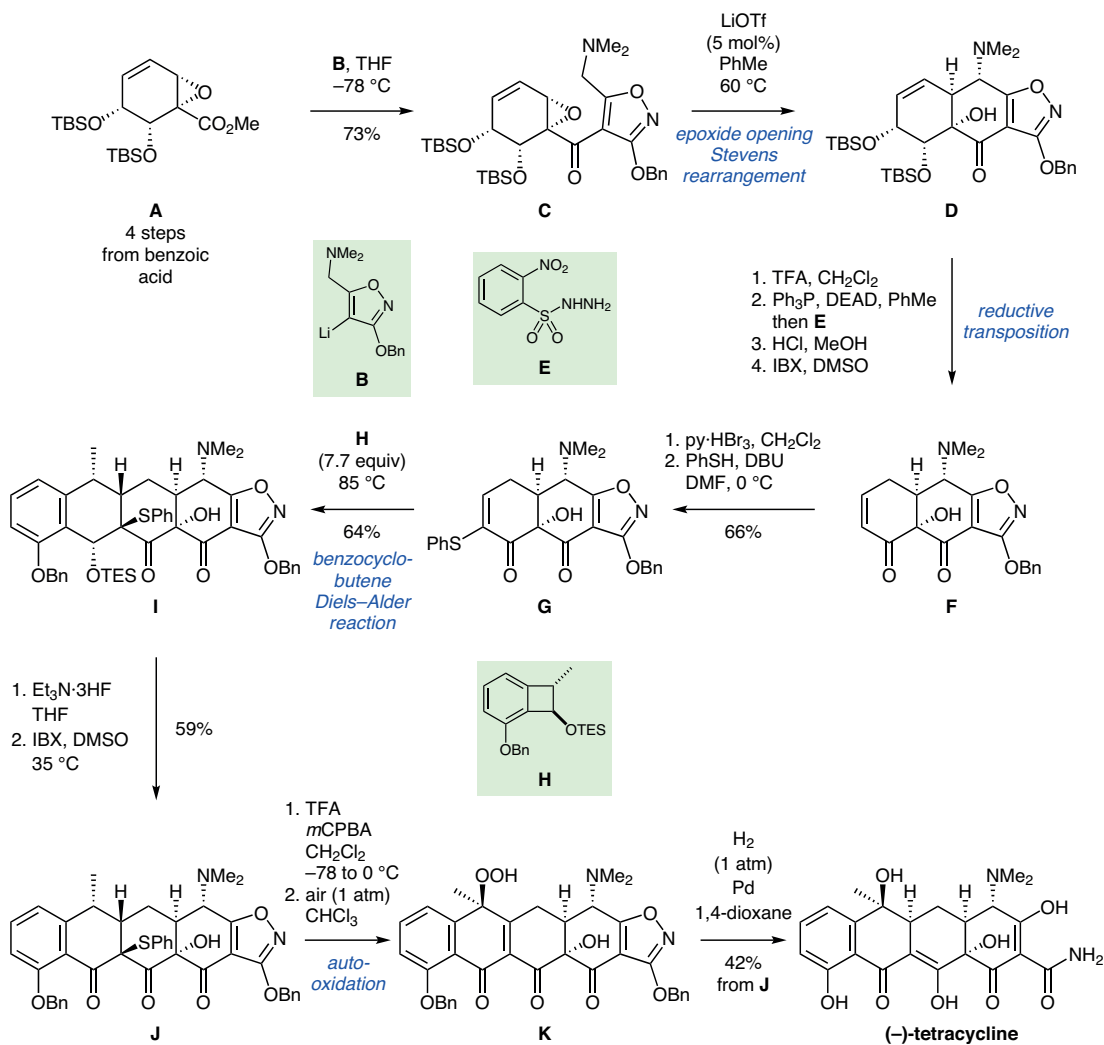


Total Synthesis of (–)-Tetracycline



Significance: The tetracyclines are a class of natural products and semisynthetic analogues that serve as antibiotics in human and veterinary medicine. Myers and co-workers describe a synthetic route to (–)-tetracycline. Their modular synthetic sequence allows for preparation of several 6-deoxytetracycline analogues, which culminated in development of the drug Eravacycline.

Comment: Ester **A**, accessed from benzoic acid in four steps, was converted into ketone **C** through 1,2-addition of heteroaryl anion **B**. The product was transformed into tricyclic ketone **D** by treatment with catalytic lithium triflate in toluene. The authors propose that the transformation proceeds through opening of the epoxide and subsequent Stevens rearrangement. Pentacycle **I** was accessed by a Diels–Alder reaction of enone **G** with benzocyclobutene **H**.