M. G. CHAREST, C. D. LERNER, J. D. BRUBAKER, D. R. SIEGEL, A. G. MYERS* (HARVARD UNIVERSITY, CAMBRIDGE, USA)

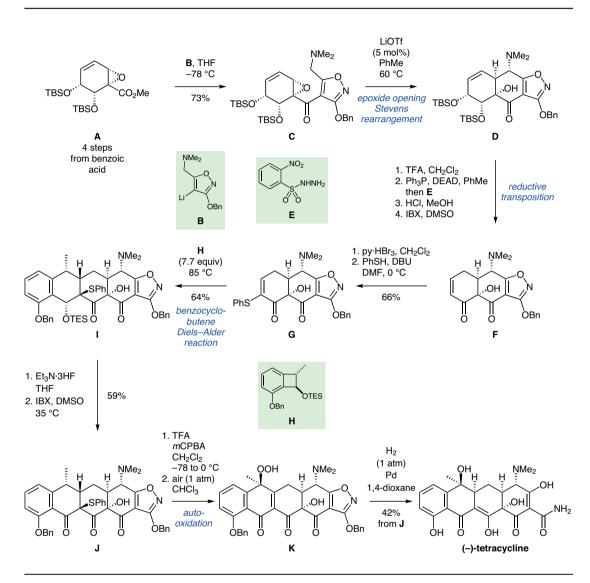
A Convergent Enantioselective Route to Structurally Diverse 6-Deoxytetracycline Antibiotics

Science 2005, 308, 395–398, DOI: 10.1126/science.1109755

M. G. CHAREST, D. R. SIEGEL, A. G. MYERS* (HARVARD UNIVERSITY, CAMBRIDGE, USA) Synthesis of (-)-Tetracycline

J. Am. Chem. Soc. 2005, 127, 8292-8293, DOI: 10.1021/ja052151d

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**.

SYNFACTS Contributors: Erick M. Carreira ⁹, Lukas J. Sprenger Synfacts 2024; 20(12), 1239

 $\textbf{DOI:}\ \ 10.1055/a-2439-7100; \ \textbf{Reg-No.:}\ \ C08424SF$

Category

Synthesis of Natural Products

Key words

(-)-tetracycline
tetracycline antibiotics
epoxide opening
Stevens rearrangement
reductive transposition

benzocyclobutene Diels-Alder reaction

auto-oxidation

