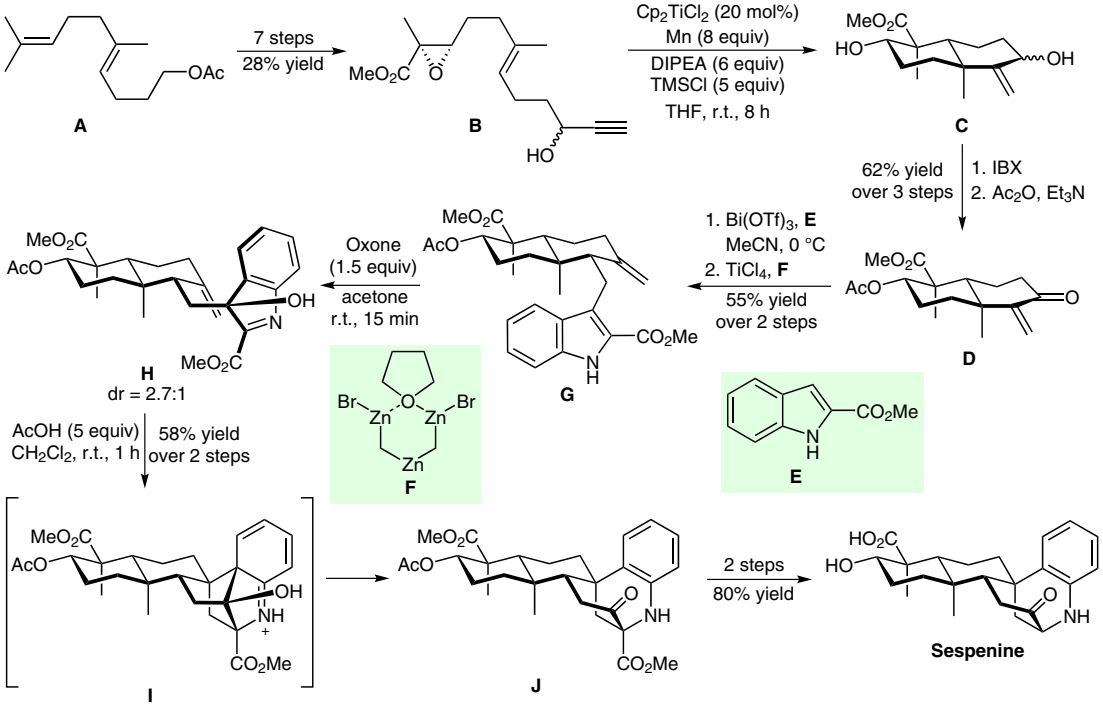
Y. SUN, P. CHEN, D. ZHANG, M. BAUNACH, C. HERTWECK, A. LI* (SHANGHAI INSTITUTE OF ORGANIC CHEMISTRY, P. R. OF CHINA AND LEIBNIZ INSTITUTE FOR NATURAL PRODUCT RESEARCH AND INFECTION BIOLOGY, JENA, GERMANY)

Bioinspired Total Synthesis of Sespenine
Angew. Chem. Int. Ed. **2014**, *53*, 9012–9016.

Total Synthesis of Sespenine



Significance: Sespenine is a rare and architecturally complex indole sesquiterpenoid that was isolated from an endophyte in 2011. Biosynthetically, sespenine may be formed from a structurally simpler indole precursor by oxidation of the indole C3 position followed by a cationic cascade involving an aza-Prins/Friedel–Crafts reaction and a subsequent fragmentation. Ang Li and co-workers now report the first total synthesis of sespenine. Their strategy relies on a titanium-mediated radical cascade for quick access to a key intermediate and an elegant implementation of the cationic cascade described above.

Comment: The synthesis commences with acetate **A**, which is converted into α,β-epoxy ester **B** in seven steps. Titanium(III)-mediated radical cyclization of **B** furnishes allylic alcohol **C**, which is oxidized and protected to give enone **D**. Key intermediate **G** is prepared via 1,4-addition of indole **E** and Nysted olefination using reagent **F**. Oxidation of **G** with Oxone affords **H** as a 2.7:1 mixture of epimers. The major and desired product undergoes the crucial sequence of aza-Prins/Friedel–Crafts reaction and fragmentation to give **J**, presumably via the intermediacy of **I**. Two additional steps then complete the synthesis of sespenine.

SYNFACTS Contributors: Erick M. Carreira, Simon Krautwald
Synfacts 2014, 10(9), 0895 Published online: 18.08.2014
DOI: 10.1055/s-0034-1378587; **Reg-No.:** C04414SF

Category
Synthesis of Natural Products and Potential Drugs

Key words
sespenine
indole sesquiterpenoids
aza-Prins recation
Friedel–Crafts reaction
radical cascades
Nysted olefination