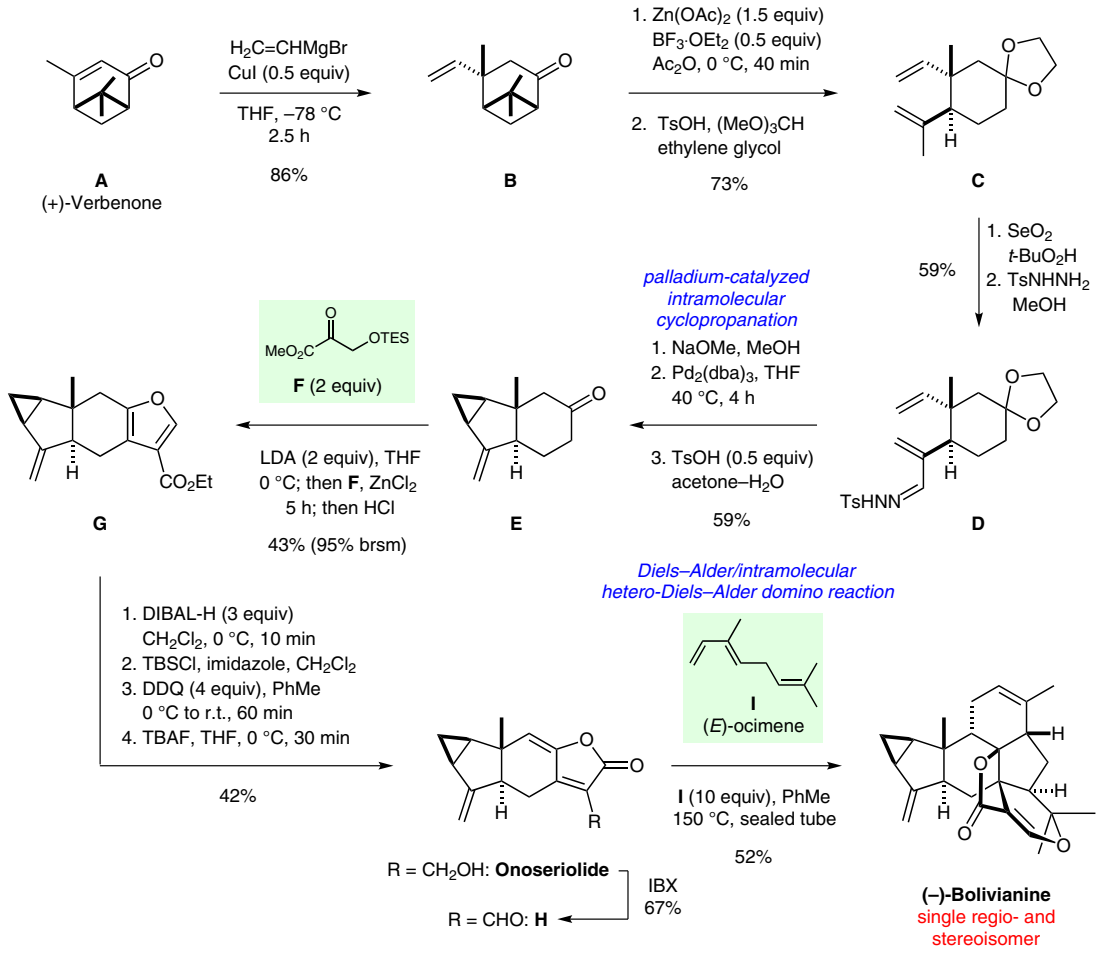
C. YUAN, B. DU, L. YANG, B. LIU* (SICHUAN UNIVERSITY, CHENGDU AND SHANGHAI INSTITUTE OF ORGANIC CHEMISTRY, P. R. OF CHINA)

Bioinspired Total Synthesis of Bolivianine: A Diels–Alder/Intramolecular Hetero-Diels–Alder Cascade Approach
J. Am. Chem. Soc. **2013**, *135*, 9291–9294.

Total Synthesis of (–)-Bolivianine



Significance: The first total synthesis of (–)-bolivianine, a sesquiterpenoid isolated from the trunk bark of the Andean forest tree *Hedyosmum angustifolium*, is reported together with some interesting preliminary experiments on possible biosynthetic pathways. The synthetic route devised towards this natural product which harbors nine contiguous stereogenic centers within a complex heptacyclic scaffold thereby affords the target molecule in only 15 steps from commercially available (+)-verbenone.

Comment: The synthetic strategy is based on the insight that (–)-bolivianine could be biosynthetically derived from onoseriolide and (*E*)-ocimene (**I**), both of which are constituents of *Hedyosmum angustifolium* as well. While onoseriolide itself did not react with diene **I** even at elevated temperatures, the oxidized derivative **H** was found to undergo the desired Diels–Alder/hetero-Diels–Alder domino reaction to afford the targeted natural product as a single regio- and diastereoisomer. Another salient feature of the synthesis is the palladium-catalyzed intramolecular cyclopropanation.

SYNFACTS Contributors: Erick M. Carreira, Nikolas Huwyler
Synfacts 2013, 9(9), 0915 Published online: 19.08.2013
DOI: 10.1055/s-0033-1339553; **Reg-No.:** C04513SF

Category
Synthesis of Natural Products and Potential Drugs

Key words
bolivianine
onoseriolide
intramolecular cyclopropanation
Diels–Alder reaction
hetero-Diels–Alder reaction
domino reaction