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.

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**Category**
- Synthesis of Natural Products and Potential Drugs

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

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Synfacts 2013, 9(9), 0915 Published online: 19.08.2013

DOI: 10.1055/s-0033-1339553; Reg-No.: C04513SF

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