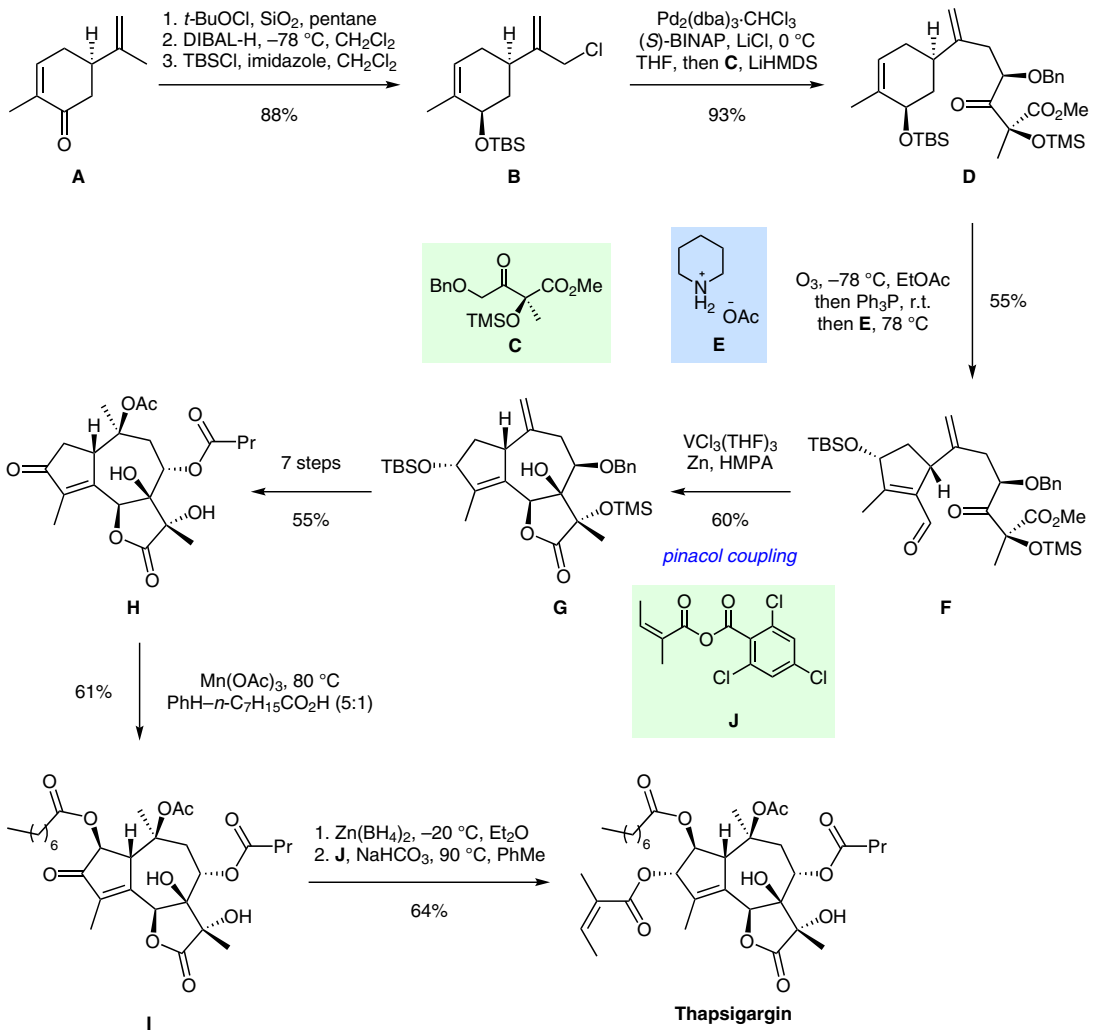
D. CHEN, P. A. EVANS* (QUEEN'S UNIVERSITY, KINGSTON, CANADA)
A Concise, Efficient and Scalable Total Synthesis of Thapsigargin and Nortrilobolide from (*R*)-(–)-Carvone
J. Am. Chem. Soc. **2017**, *139*, 6046–6049.

Total Synthesis of Thapsigargin and Nortrilobolide



Significance: Thapsigargin has attracted great interest over the past 40 years due to its highly oxygenated, complex framework combined with high biological activity. Thapsigargin inhibits intracellular calcium transport at picomolar concentrations. A closely related analogue is currently in phase II clinical trials against liver, brain, prostate, and kidney cancer.

Comment: (*R*)-(–)-Carvone is transformed into **D** through allylic chlorination and substitution. An ozonolysis–aldol sequence followed by a pinacol coupling delivers the characteristic 5-7-5 framework in **G**. Further redox manipulation and side-chain introductions then concisely deliver synthetic thapsigargin. Nortrilobolide lacking the α-acyloxy side chain at the ketone was similarly synthesized.

SYNFACTS Contributors: Erick M. Carreira, Philipp Sondermann
Synfacts 2017, 13(07), 0673 Published online: 19.06.2017
DOI: 10.1055/s-0036-1590515; **Reg-No.:** C02917SF

2017 © THIEME STUTTGART • NEW YORK

Category
Synthesis of Natural Products and Potential Drugs

Key words
thapsigargin
nortrilobolide
pinacol coupling
sesquiterpene lactone

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.