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A Concise, Efficient and Scalable Total Synthesis of Thapsigargin and Nortrilobolide from (R)-(−)-Carvone

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**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-acyl-oxy side chain at the ketone was similarly synthesized.

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