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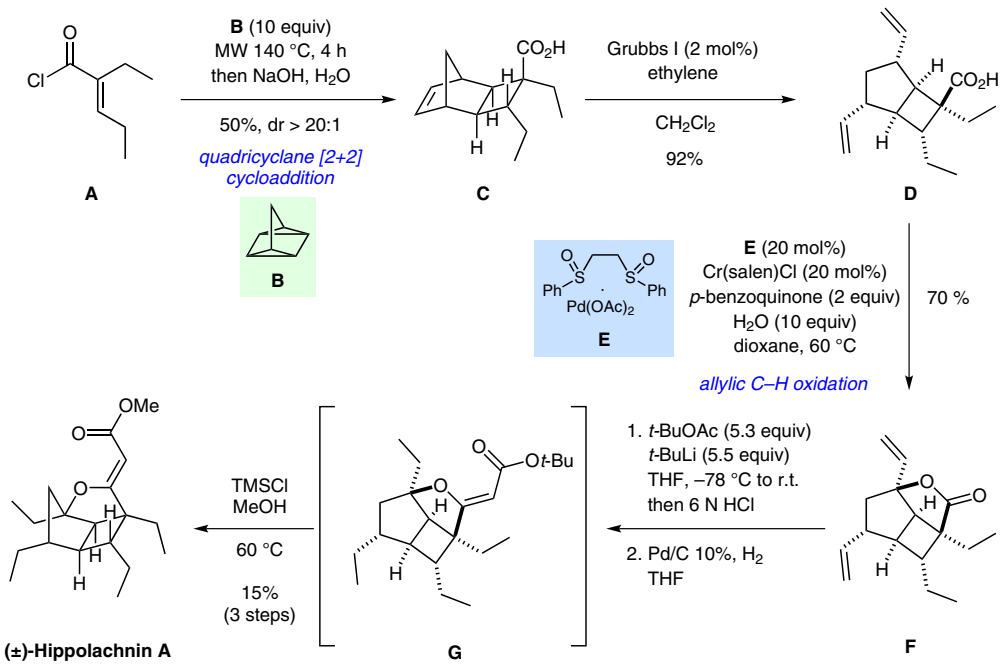
Collaborative Total Synthesis: Routes to (±)-Hippolachnin A Enabled by Quadricyclane Cycloaddition and Late-Stage C–H Oxidation

J. Am. Chem. Soc. **2016**, *138*, 2437–2442.

Synthesis of (±)-Hippolachnin A



Significance: In this work, the authors combine their independently elaborated routes into a unique collaborative total synthesis of (±)-hippolachnin A. The convergent synthesis relies on a [2+2] quadricyclane cycloaddition, followed by ring-opening metathesis and allylic C–H oxidation.

Comment: Thermal [2+2] cycloaddition of acyl chloride **A** and quadricyclane **B** generated cyclobutane **C** after treatment with sodium hydroxide in moderate yield and excellent diastereoselectivity. Ring-opening metathesis catalyzed by Grubbs I under an ethylene atmosphere gave carboxylic acid **D**. A late stage C–H oxidation of bicycle **D** gave lactone **F**, which was converted in three further steps into (±)-hippolachnin A.

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Synfacts 2016, 12(5), 0441 Published online: 18.04.2016
DOI: 10.1055/s-0035-1562026; **Reg-No.:** C01616SF