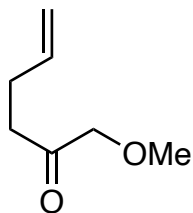


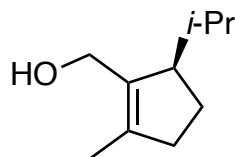
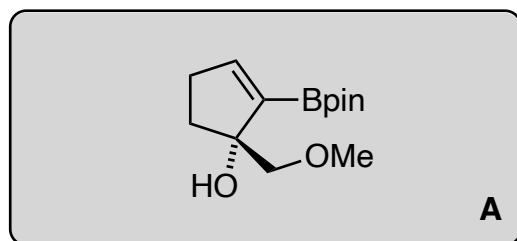
Synthesis of (–)-Cotylenol, a 14-3-3 Molecular Glue Component

Ting, S. I.; Snelson, D. W.; Huffman, T. R.; Kuroo, A.; Sato, R.; Shenvi, R. A.

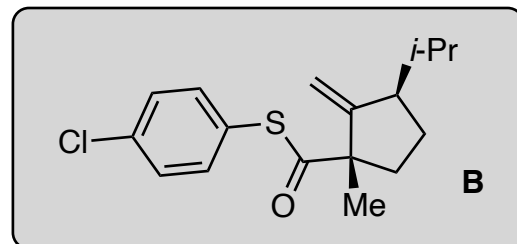
J. Am. Chem. Soc. **2023**, *145*, 20634-20645.



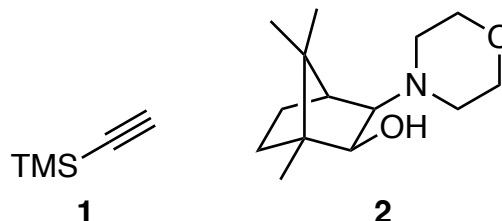
1-4



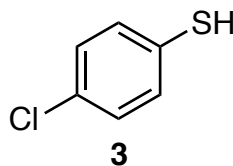
5, 6



- 1) **1**, Et₂Zn, **2** (cat.)
- 2) TBAF
- 3) B₂pin₂, CuCl (cat.), P(*t*-Bu)₃ (cat.)
LiO*t*-Bu (cat.), MeOH, PhMe
- 4) HG-II (cat.)

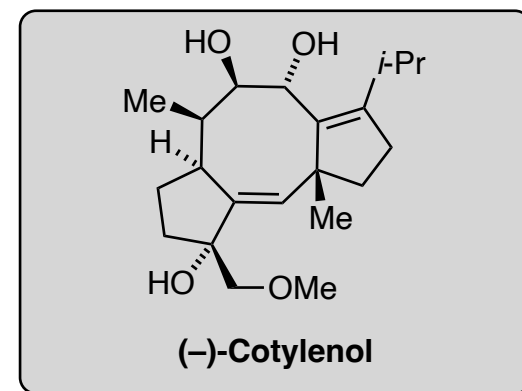


- 5) **3**, BF₃•OEt₂
- 6) CHCl₃, NaO*t*-Bu, THF then SiO₂, H₂O



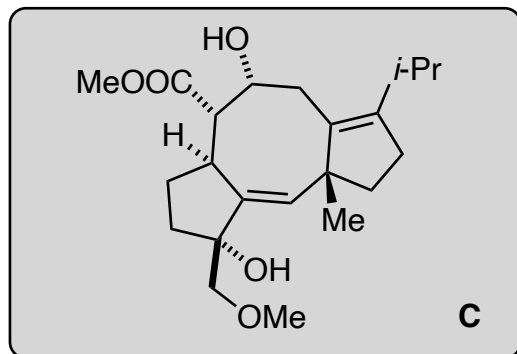
3) *Hint*: product has 5 ¹H NMR peaks from 4.8 to 6.5 ppm, two of which have a 17 Hz coupling constant.

6) Propose a reasonable mechanism for this transformation. *Hint*: :CCl₂ is generated *in situ*.

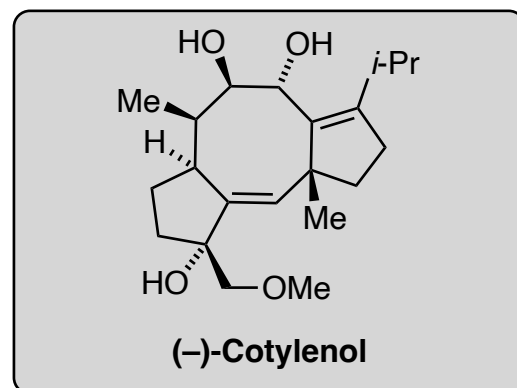


A + B

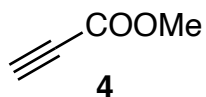
7-10



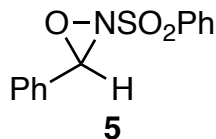
11-16



- 7) $\text{Pd}_2(\text{dba})_3$ (cat.), $\text{P}(2\text{-furyl})_3$ (cat.), CuTC , $\text{B}(\text{OH})_3$, acetone/EtOAc, rt
- 8) NaBH_4 , $\text{CeCl}_3 \cdot \text{H}_2\text{O}$, MeOH, -78°C
- 9) **4**, NMM
- 10) mesitylene, 160°C



- 11) DMP
- 12) KOH , CH_2O (aq.)
- 13) MsCl , NEt_3 then DBU
- 14) KHMDs , **5**
- 15) TrisNHNH_2 , NaHCO_3 , MeOH
- 16) $[\text{NMe}_4]^+[\text{BH}(\text{i-PrCOO})_3]^-$



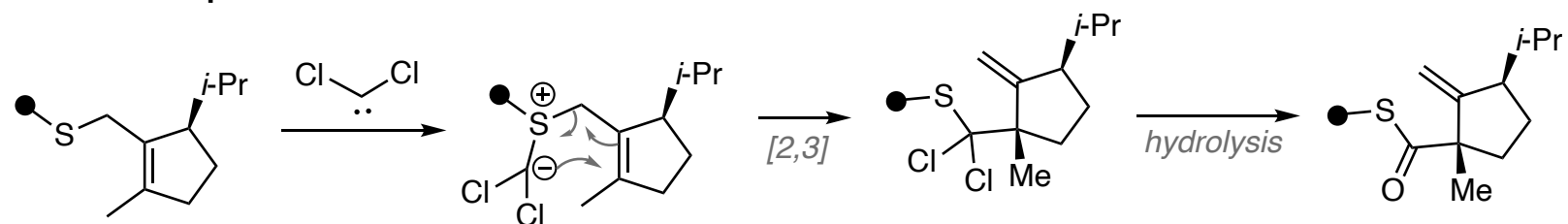
7) Name this reaction. *Liebeskind-Srogl coupling*.

8) *Hint*: reaction proceeds with 20:1 dr.

10) Propose a reasonable mechanism.
Hint: two pericyclic reactions complete the 5/8/5 scaffold; the product of the first rearrangement would be expected to have a ^1H NMR peak around 9.8 ppm.

12) *Hint*: 1 eq CO_2 generated *in situ*.

solution to step 6:



solution to step 10:

