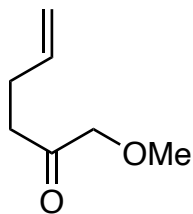


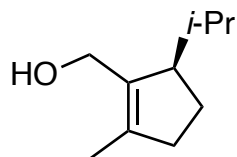
Synthesis of (–)-Cotylenol, a 14-3-3 Molecular Glue Component

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

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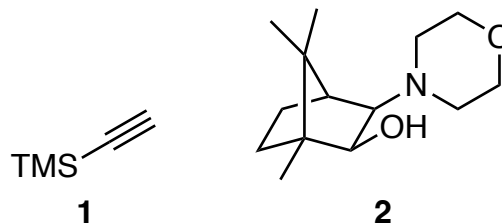
1-4



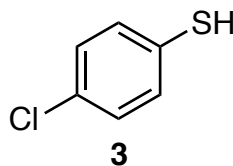
5, 6



- 1) **1**, Et_2Zn , **2** (cat.)
- 2) TBAF
- 3) B_2pin_2 , CuCl (cat.), $\text{P}(t\text{-Bu})_3$ (cat.)
 $\text{LiO}t\text{-Bu}$ (cat.), MeOH , PhMe
- 4) HG-II (cat.)

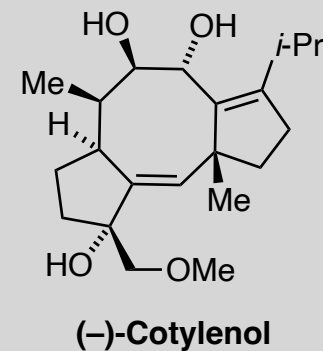


- 5) **3**, $\text{BF}_3 \cdot \text{OEt}_2$
- 6) CHCl_3 , $\text{NaO}t\text{-Bu}$, THF then SiO_2 , H_2O



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

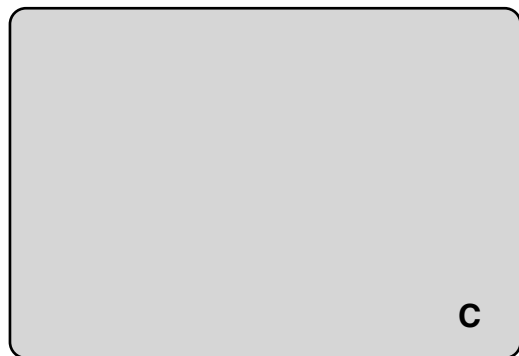
6) Propose a reasonable mechanism for this transformation. *Hint*: $:\text{CCl}_2$ is generated *in situ*.



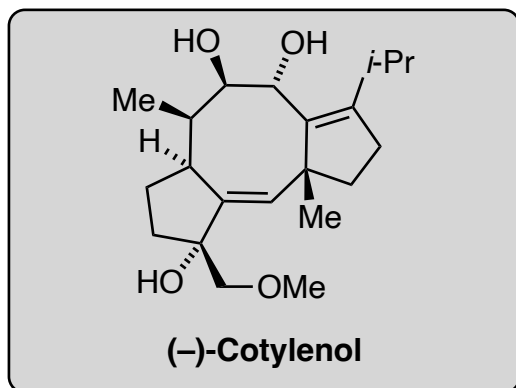
(–)-Cotylenol

A + B

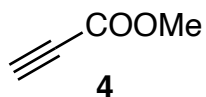
7-10



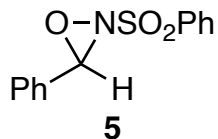
11-16



- 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) TrisNHNH₂, NaHCO_3 , MeOH
- 16) $[\text{NMe}_4]^+[\text{BH}(\textit{i}\text{-PrCOO})_3]^-$



7) Name this reaction.

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*.