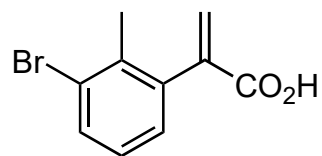


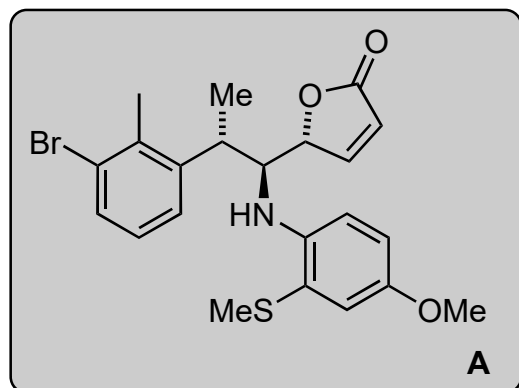
Asymmetric Synthesis of Cyclopamine, a Hedgehog (Hh) Signaling Pathway Inhibitor

Shao, A.; Liu, W.; Liu, M.; He, H.; Zhou, Q.-L.; Zhu, S.-F.; Gao, S.

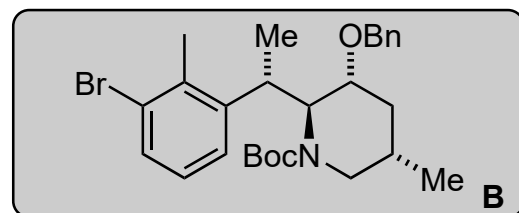
J. Am. Chem. Soc. **2023**. DOI:10.1021/jacs.3c10362



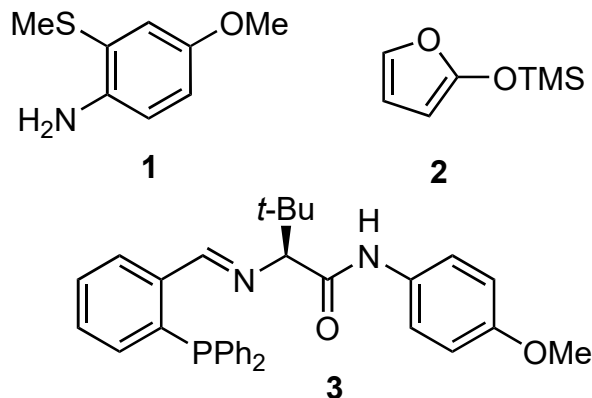
1-3



4-9



- 1) H₂, [Ir-SpiroBAP]⁺, Cs₂CO₃
- 2) TMSCHN₂, DIBALH *then* DMP
- 3) **1**, **2**, **3**, *i*-PrOH, AgOAc

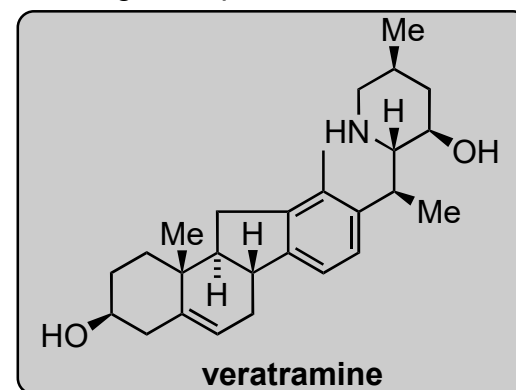


- 4) Cu(OAc)₂, PhSiH₃
- 5) LiHMDS, MeI, 1,3-dimethyl-2-imidazolidinone
- 6) CAN *then* HCl
- 7) NaOH
- 8) BH₃·SMe₂ *then* Boc₂O, Na₂CO₃
- 9) NaH, BnBr, TBAI

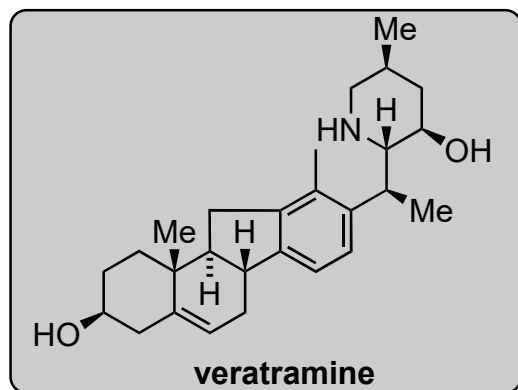
1) HINT: Stereochem. maps onto natural product

3) HINT: Product has ¹³C signal at 173.5 ppm, 8 ¹H signals >6 ppm

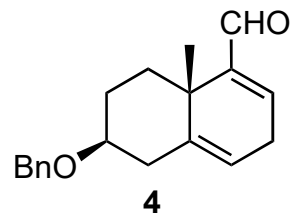
7) HINT: Product has two exchangeable protons



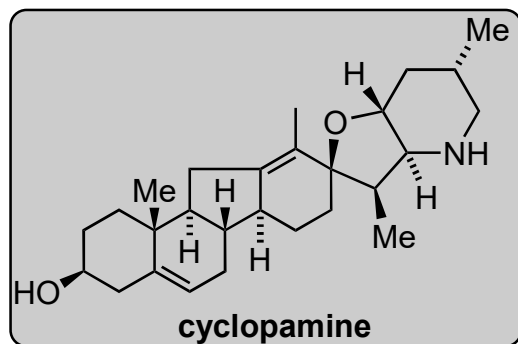
10-14



- 10) *t*-BuLi then **4**
- 11) DMP
- 12) *hν* (366 nm)
- 13) LAH, AlCl₃
- 14) Na, NH₃ then HCl



15-20



- 15) Li, NH₃ then PtO₂, H₂
- 16) Fmoc-OSu
- 17) *m*-CPBA
- 18) HCl (aq.)
- 19) TMSOTf
- 20) Et₂NH

15) HINT: ¹³C signals at 143.1, 134.8, 132.0, 123.2