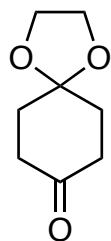


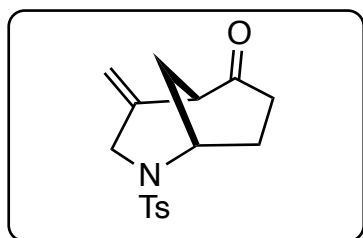
Enantioselective Total Synthesis of (–)-Himalensine A via a Palladium and 4-Hydroxyproline Co-catalyzed Desymmetrization of Vinyl-bromide-tethered Cyclohexanones.

Kučera, R.; Ellis, S. R.; Yamazaki, K.; Cook, J. H.; Chekshin, N.; Christensen, K. E.; Hamlin, T. A.; Dixon D. J.

J. Am. Chem. Soc. **2023**, *145*, 5422-5430.

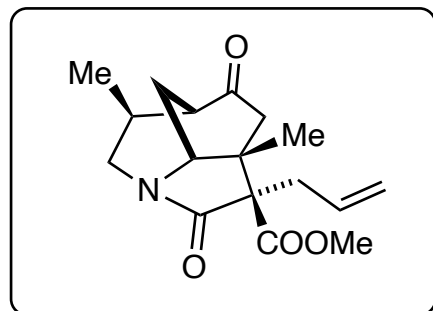


1-4

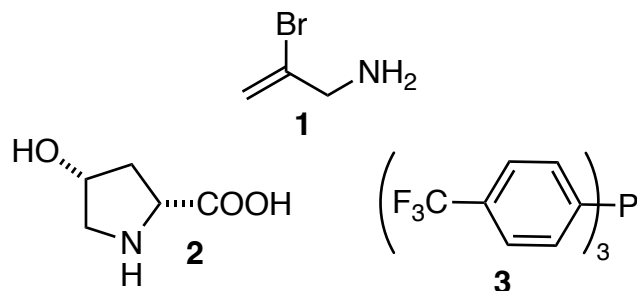


A

5-12

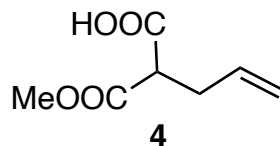


B

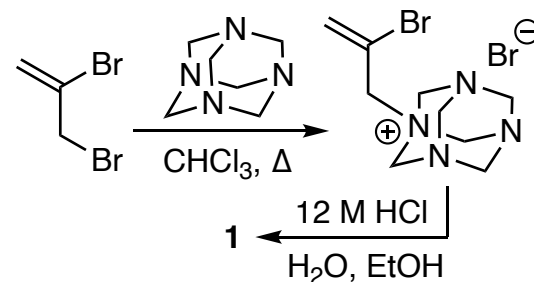


- 1) **1**, NaBH(OAc)₃
- 2) 3 M HCl, THF
- 3) TsCl, NEt₃, DMAP, DCM
- 4) **2** (20 mol%), **3** (15 mol%), Pd(OAc)₂ (5 mol%), K₂HPO₄, MeOH, 85 °C

- 5) Crabtree's catalyst (1.5 mol%), H₂ (58 bar)
- 6) Pd(TFA)₂, O₂, DMSO, AcOH, 80 °C
- 7) MeLi, CuI, THF *then* TMSCl, NEt₃
- 8) NBS, NaHCO₃, THF, -78 °C
- 9) Li₂CO₃, LiBr, DMF, 155 °C
- 10) NaHMDS, THF, 0 °C *then* Na-Nap
- 11) **4**, EDC·HCl, DMAP
- 12) K₂CO₃, MeCN, Δ

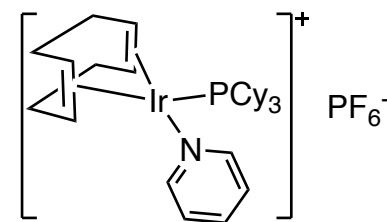


How would you make **1**? The authors employed the following route:



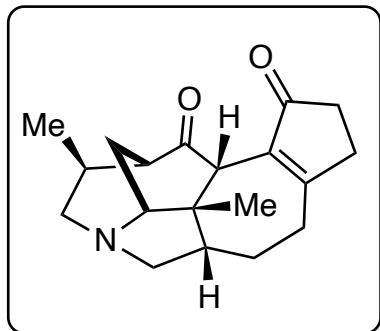
4) Propose a mechanism. *Hint*: Similar to Heck reaction but double bond at which migratory insertion takes place is generated *in situ*. See below for mechanism.

5) structure of Crabtree's catalyst?

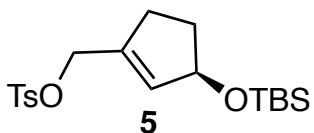


6) Who developed these conditions?
Shannon Stahl. See *J. Am. Chem. Soc.* **2011**, *133*, 14566-14569.

13-18

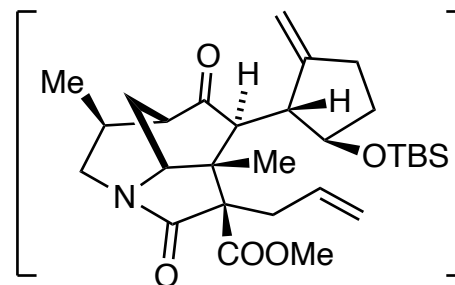


Himalensine A



- 13) KHMDS, **5**, 18-crown-6, THF, -78 °C
14) mesitylene, 200 °C *then* HG-II (2.5 mol%), PhMe, 125 °C
15) LiCl, DMSO, H₂O, 170 °C
16) KF, 4 M H₂SO₄, acetone
17) AZADO, PIDA
18) Vaska's catalyst, TMDS, PhMe *then* HCOOH, MeOH, 60 °C

14) An epimerization occurs during the second part of this step. What is the intermediate following heating in mesitylene?



Proposed mechanism of step 4 ($R = p\text{-CF}_3\text{C}_6\text{H}_4$)

