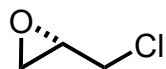
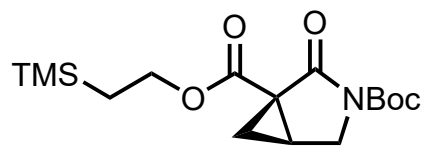


Total Synthesis of (+)-Fastigiatine

Brian B. Liao and Matthew D. Shair*
J. Am. Chem. Soc. **2010**, 132, 9594–9595.



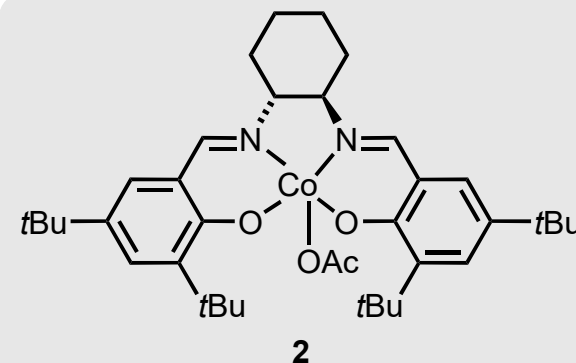
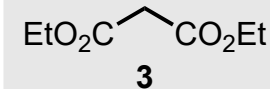
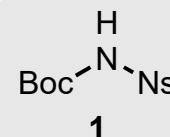
- 1) **1**, **2** (2 mol%)
- 2) TFA, CH₂Cl₂
- 3) Ms₂O, 4-DMAP, pyridine
- 4) Cs₂CO₃
- 5) **3**, Cs₂CO₃
- 6) PhSH, K₂CO₃
- 7) TMSCH₂CH₂OH, KH
- 8) Boc₂O



A

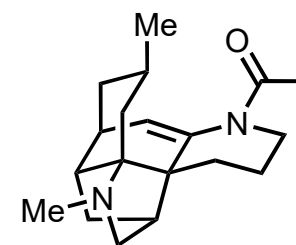
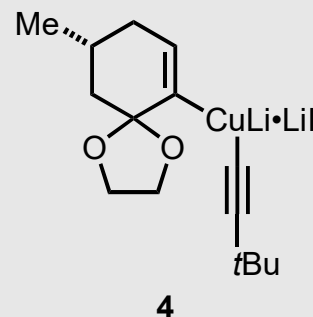
- 9) **4**
- 10) I(CH₂)₃Cl, Cs₂CO₃
- 11) NaN₃, NaI
- 12) TBAF, DBU
- 13) cat. Mg(ClO₄)₂
- 14) LiHMDS, NsCl

Name of starting material?
 (S)-epichlorohydrin

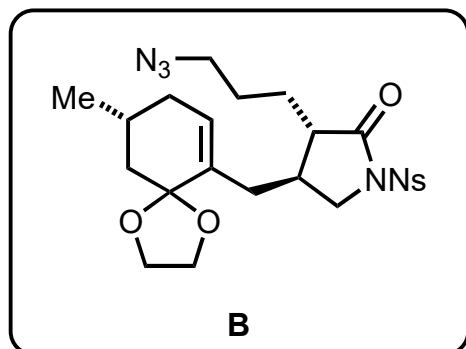


- 5) *Hint*: A small ring is broken and a new one is formed.
 6) *Hint*: Lactam formation.

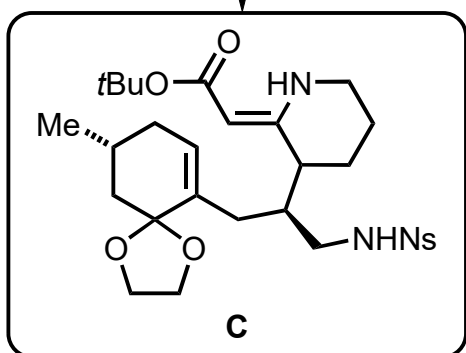
13–14) *Hint*: Protecting group swap.



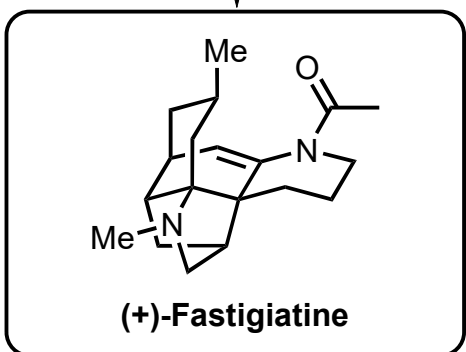
(+)-Fastigiatine



15) *t*BuOAc, LDA; then **B**
 16) PPh₃



17) HCl, THF/H₂O
 18) K₂CO₃, MeI; then PhSH
 19) TFE, 80 °C
 20) TsOH·H₂O, 80 °C
 21) Ac₂O, Et₃N



16) Name the reactions (two consecutive ones).

Hint: A piperidine is formed.

Staudinger reaction & aza-Wittig reaction

17) *Hint:* Key step: the ketal is cleaved first, then a new ring is formed.

Afterward, it is best to draw the intermediates in the same style as the natural product.

Write a stepwise mechanism.

19) *Hint:* A pyrrolidine is formed under these *solvolytic* conditions.

20) *Hint:* CO₂ is liberated.

Mechanism of the Michael Addition–Aldol Reaction Cascade (Step 17)

