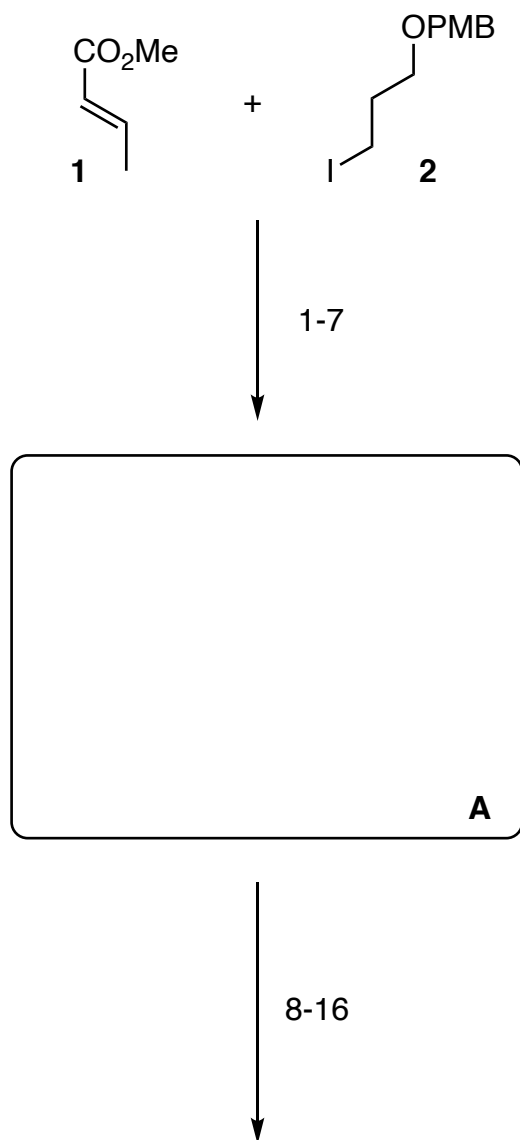
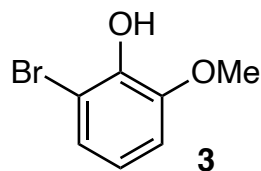


Total Synthesis of Liangshanone

Huang, H.-X.; Mi, F.; Li, C.; He, H.; Wang, F.-P.; Liu, X.-Y.; Qin, Y.
Angew. Chem. Int. Ed. **2020**, early view.



- 1) LDA/HPMA, **1**; then **2**; then LiAlH₄; then TBSCl, imidazole
- 2) DDQ
- 3) DMP, NaHCO₃
- 4) **3**, *n*-BuLi (2 equiv.); then product of step 3
- 5) PhI(OAc)₂, NaHCO₃, MeOH; then mesitylene, 180 °C
- 6) DMP, NaHCO₃
- 7) NaBH(OMe)₃



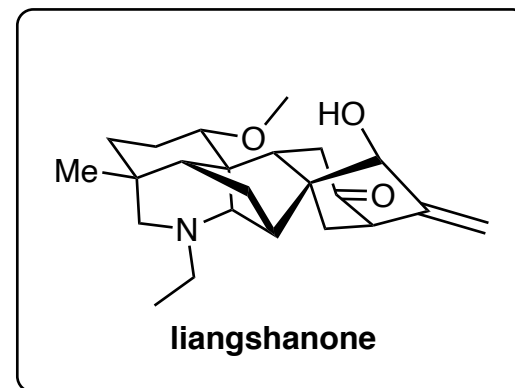
- 8) MeI, NaH
- 9) TBAF
- 10) DMP, NaHCO₃
- 11) MeI, *t*-BuOK,
- 12) EtNH₃Cl, Et₃N, AcOH; then NaBH₃CN
- 13) Sml₂ (5.0 equiv), MeOH
- 14) TFA, O₃; then PPh₃; then *t*-BuNH₂
- 15) NaClO₂, NaH₂PO₄, 2-methyl-2-butene
- 16) NHPI, DIC, DMAP; then Zn, NiCl₂·6H₂O, di-*t*-Bu-bipy, PhSiH₃

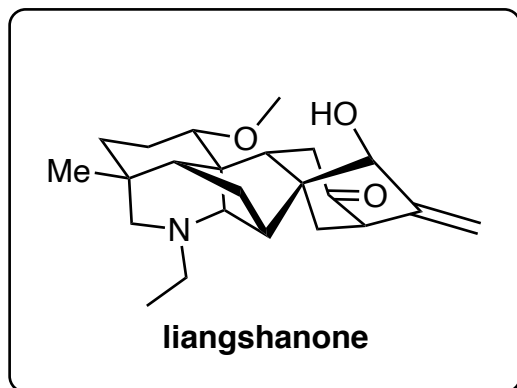
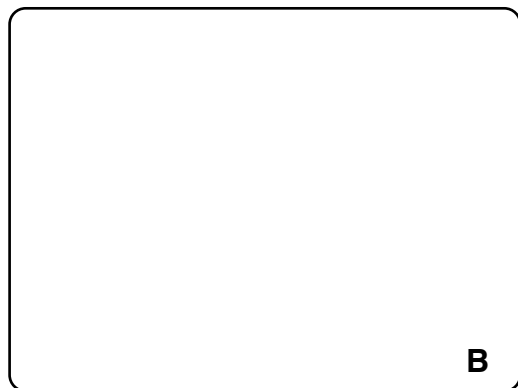
4) Hint: inseparable diastereoisomers in d.r. = 5:4

5-7) Rationalize the stereochemical outcome and why are step 6 & 7 performed?

7) Hint: only one ketone reacts

16) Hint: NHPI = *N*-hydroxyphthalimide





- 17) LDA, NCCO₂Me,
- 18) Cs₂CO₃, MVK
- 19) LDA
- 20) LiAlH₄
- 21) AZADO, DMAP, bpy, CuCl, open to air
- 22) TMSOTf (4.0 equiv.), Et₃N;
then Ph₃P=CHOMe
- 23) NaOH, MeOH
- 24) TfOH, 1:1.3 d.r.
- 25) Pd/C, H₂, AcOH/EtOH
- 26) CH(OEt)₃, *p*-TsOH, ethylene glycol
- 27) DMP, TFA
- 28) Petasis reagent
- 29) SeO₂, *t*-BuOOH; then *p*-TsOH
- 30) DMP, TFA
- 31) NaBH(OMe)₃

17) Hint: d.r. of 5:4 carried through to step 18 where product is isolated as a single diastereomer.

19) Hint: only the addition takes place

23) Hint: two transformations occur

28) What is the molecular structure of the Petasis reagent?

Bonus:

To access a stereoselective synthesis of liangshanone which step do you need to modify? What strategy would you choose?