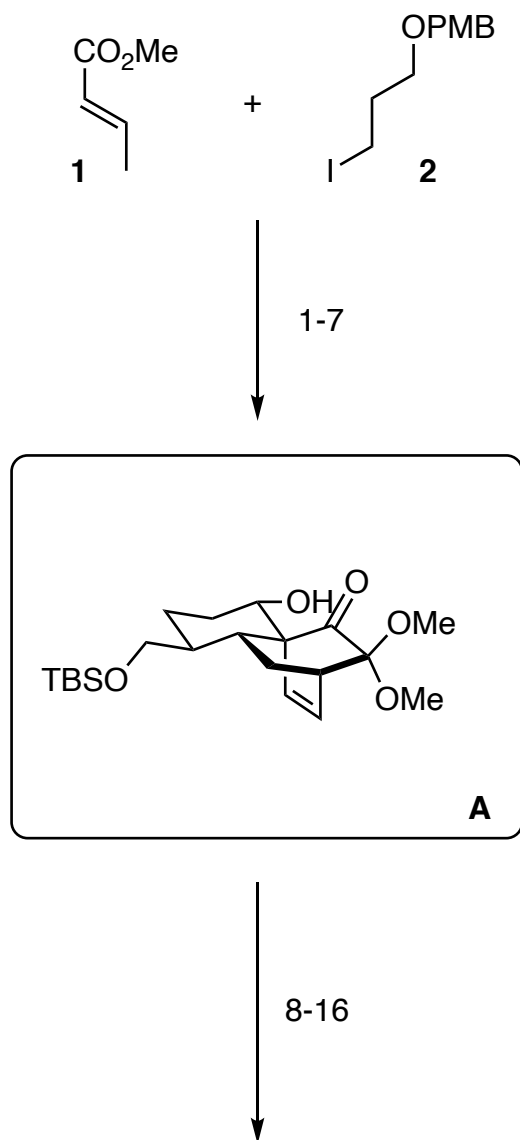
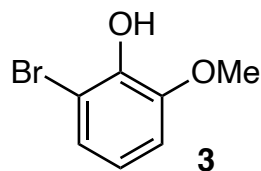


## Total Synthesis of Liangshanone

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 LiAlH<sub>4</sub>; then TBSCl, imidazole
- 2) DDQ
- 3) DMP, NaHCO<sub>3</sub>
- 4) **3**, *n*-BuLi; then product of step 3
- 5) PhI(OAc)<sub>2</sub>, NaHCO<sub>3</sub>, MeOH; then mesitylene, 180 °C
- 6) DMP, NaHCO<sub>3</sub>
- 7) NaBH(OMe)<sub>3</sub>, 7:1 d.r.



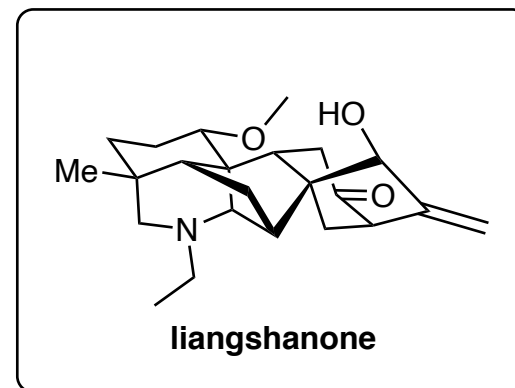
- 8) MeI, NaH
- 9) TBAF
- 10) DMP, NaHCO<sub>3</sub>
- 11) MeI, *t*-BuOK,
- 12) EtNH<sub>3</sub>Cl, Et<sub>3</sub>N, AcOH; then NaBH<sub>3</sub>CN
- 13) Sml<sub>2</sub> (5.0 equiv), MeOH
- 14) TFA, O<sub>3</sub>; then PPh<sub>3</sub>; then *t*-BuNH<sub>2</sub>
- 15) NaClO<sub>2</sub>, NaH<sub>2</sub>PO<sub>4</sub>, 2-methyl-2-butene
- 16) NHPI, DIC, DMAP; then Zn, NiCl<sub>2</sub>·6H<sub>2</sub>O, di-*t*-Bu-bipy, PhSiH<sub>3</sub>

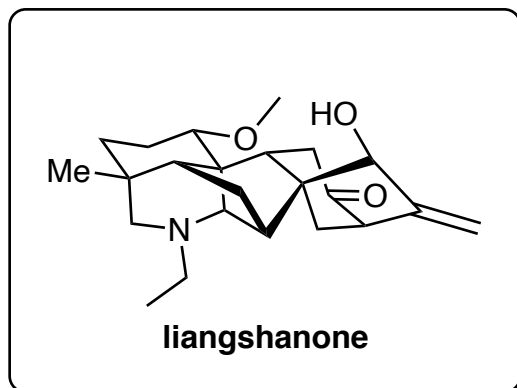
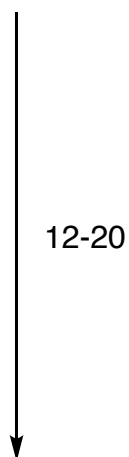
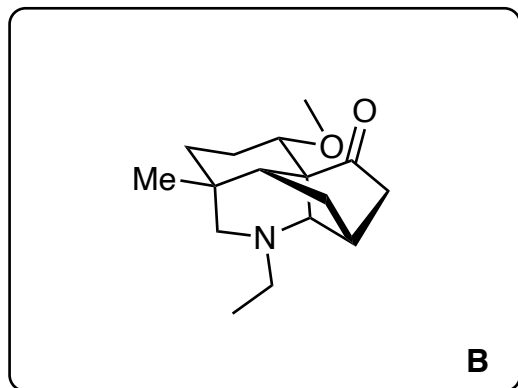
4) Hint: inseparable diastereoisomers in d.r. = 5:4

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

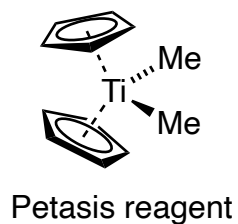
7) Hint: only one ketone reacts

16) Hint: NHPI = *N*-hydroxyphthalimide





- 17) LDA, NCCO<sub>2</sub>Me,
- 18) Cs<sub>2</sub>CO<sub>3</sub>, MVK
- 19) LDA
- 20) LiAlH<sub>4</sub>
- 21) AZADO, DMAP, bpy, CuCl, open to air
- 22) TMSOTf (4.0 equiv.), Et<sub>3</sub>N;  
then Ph<sub>3</sub>P=CHOMe
- 23) NaOH, MeOH
- 24) TfOH, 1:1.3 d.r.
- 25) Pd/C, H<sub>2</sub>, AcOH/EtOH
- 26) CH(OEt)<sub>3</sub>, *p*-TsOH, ethylene glycol
- 27) DMP, TFA
- 28) Petasis reagent
- 29) SeO<sub>2</sub>, *t*-BuOOH; then *p*-TsOH
- 30) DMP, TFA
- 31) NaBH(OMe)<sub>3</sub>



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

23) Hint: two transformations occur

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

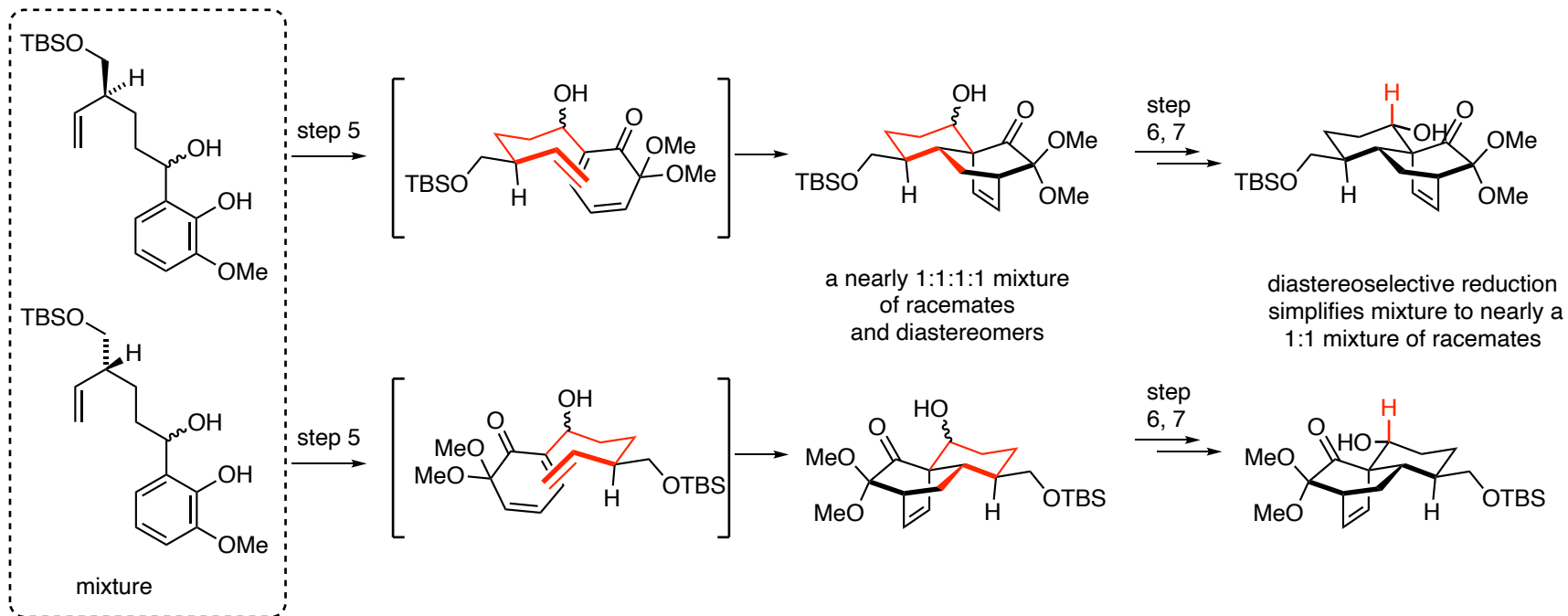
29) What stereoselectivity do you expect?

*Bonus:*

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

*Step 1; see the authors strategy below*

### solution to step 5-7:



### Bonus: Stereoselective Synthesis:

