Total Synthesis of Liangshanone

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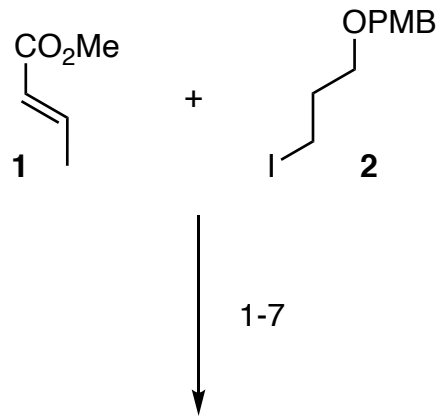
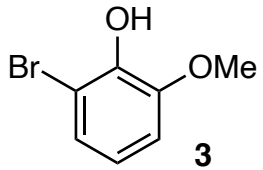
Angew. Chem. Int. Ed. **2020**, *early view*.



1) LDA/HPMA, **1**; *then* **2**; *then* $LiAlH_4$; *then* TBSCl, imidazole
2) DDQ
3) DMP, $NaHCO_3$
4) **3**, *n*-BuLi (2 equiv.); *then* product of step 3
5) $PhI(OAc)_2$, $NaHCO_3$, MeOH; *then* mesitylene, 180 °C
6) DMP, $NaHCO_3$
7) $NaBH(OMe)_3$



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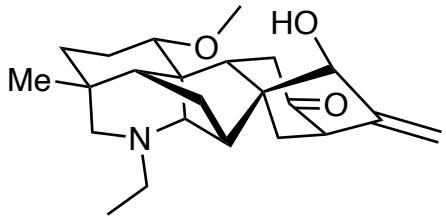
8) MeI, NaH
9) TBAF
10) DMP, $NaHCO_3$
11) MeI, *t*-BuOK,
12) $EtNH_3Cl$, Et_3N, AcOH; *then* $NaBH_3CN$
13) SmI_2 (5.0 equiv), MeOH
14) TFA, O_3; *then* PPh_3; *then* *t*-$BuNH_2$
15) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene
16) NHPI, DIC, DMAP; *then* Zn, $NiCl_2 \cdot 6H_2O$, di-*t*-Bu-bipy, $PhSiH_3$

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

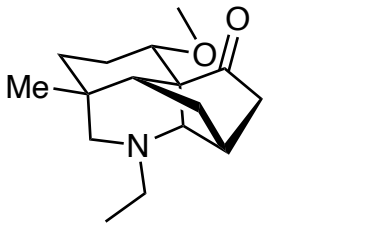
5-7) Rationalize the stereochemical outcome and why are step 6 & 7 performed? *see below*

7) Hint: only one ketone reacts

16) Hint: NHPI = *N*-hydroxyphthalimide



liangshanone



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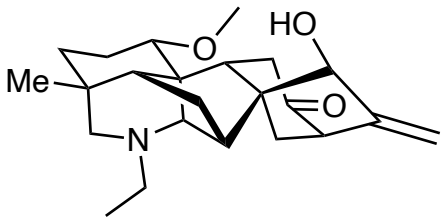
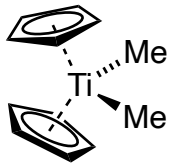


liangshanone

17) LDA, $NCCO_2Me$,
18) Cs_2CO_3, MVK
19) LDA
20) $LiAlH_4$
21) AZADO, DMAP, bpy, CuCl, open to air
22) TMSOTf (4.0 equiv.), Et_3N;
then $Ph_3P{=}CHOMe$
23) NaOH, MeOH
24) TfOH, 1:1.3 d.r.
25) Pd/C, H_2, AcOH/EtOH
26) $CH(OEt)_3$, *p*-TsOH, ethylene glycol
27) DMP, TFA
28) Petasis reagent
29) SeO_2, *t*-BuOOH; *then p*-TsOH
30) DMP, TFA
31) $NaBH(OMe)_3$



Petasis reagent

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

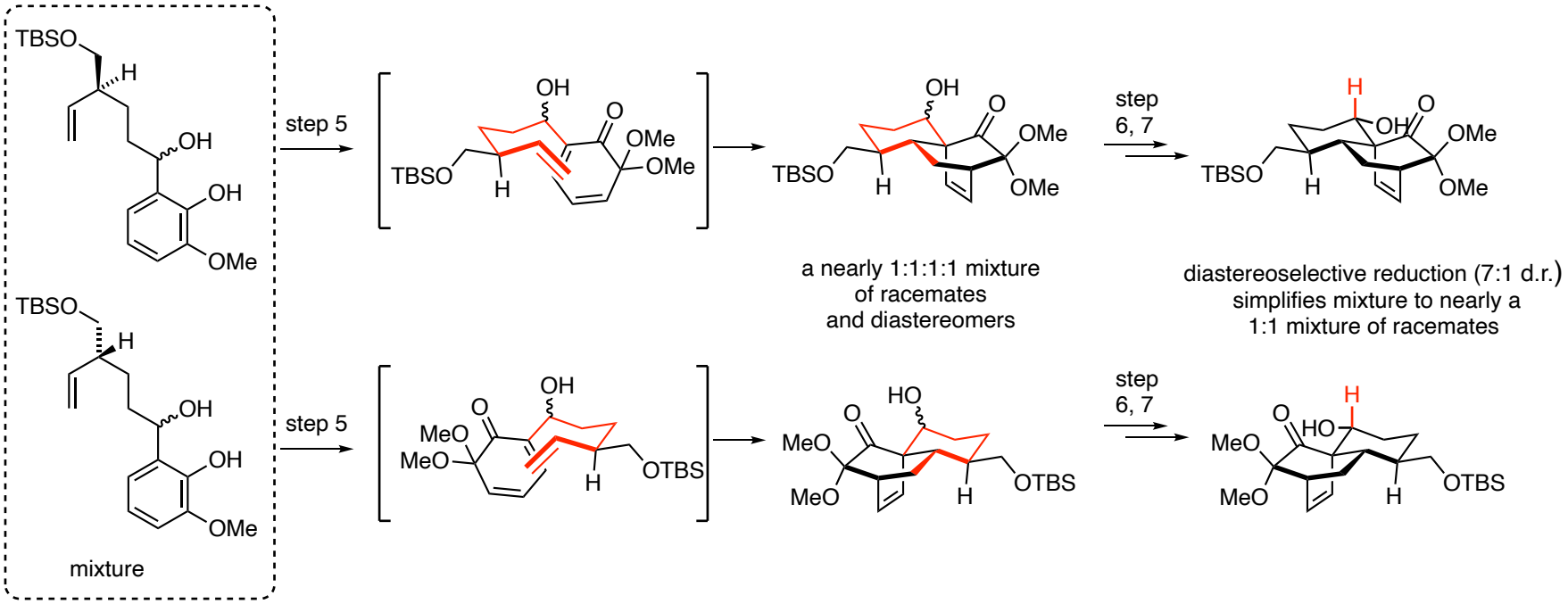
23) Hint: two transformations occur

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?

Step 1; see the authors strategy below

solution to step 5-7:



Bonus: Stereoselective Synthesis: