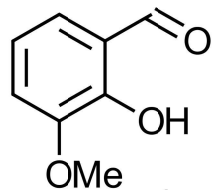


## Synthesis Challenge #77

### A Nine-Step Formal Synthesis of (±)-Morphine

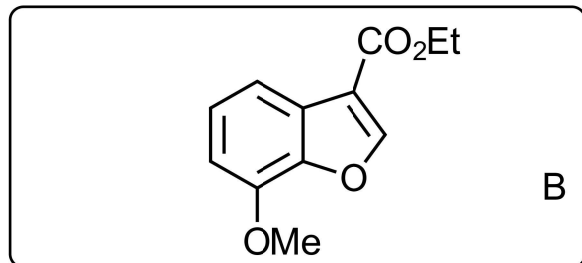
J. Brousseau, A. Xolin, L. Barriault, *Org. Lett.* **2019**, *21*, 1347–1349.

14.03.2019



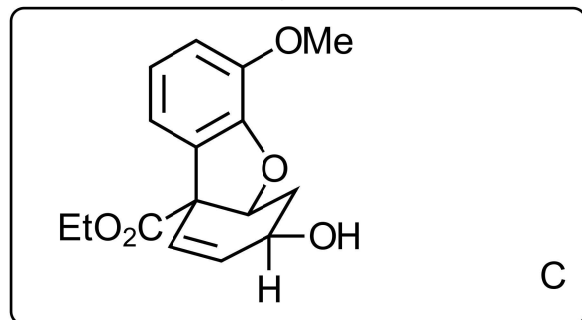
↓ 1

A



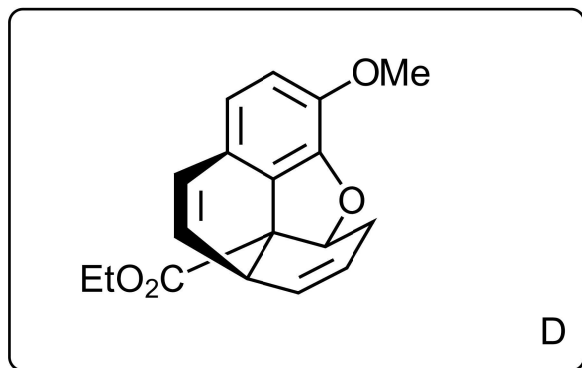
B

↓ 2, 3



C

↓ 4,5

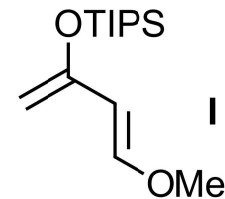


D

1)  $\text{HBF}_4 \cdot \text{Et}_2\text{O}$  (10 mol%),  $\text{N}_2\text{CHCO}_2\text{Et}$ ,  
DCM, then  $\text{H}_2\text{SO}_4$

2) I,  $160^\circ\text{C}$   
then PTSA, toluene  
3) L-Selectride, THF

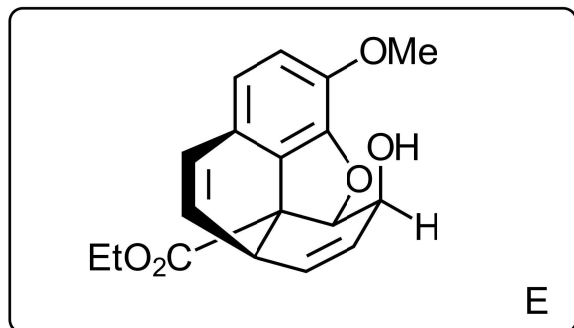
4)  $\text{Pd}(\text{TFA})_2$  (2mol%),  
1,10-phenanthroline (2mol%),  $\text{Et}_3\text{N}$ ,  
ethyl vinyl ether,  $50^\circ\text{C}$   
5) 2,6-lutidine, xylene,  $160^\circ\text{C}$ ,  
then PTSA



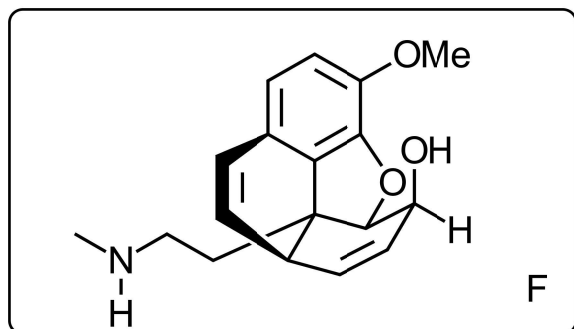
I

Claisen-rearrangement/  
Friedel-Crafts

↓ 6,7

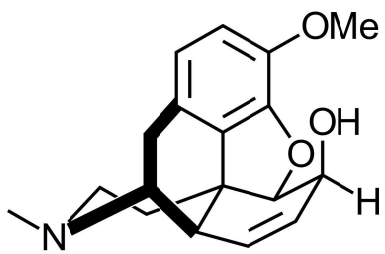


↓ 8,9



↓ 2-3 steps

(+/-)-Morphine



6)  $\text{SeO}_2$ , 1,4-dioxane, then DMP, DCM  
7) DIBAL-H, THF,  $-78^\circ\text{C}$

8)  $\text{Ph}_3\text{PCH}_2\text{OMeCl}$ , tBuOK, THF,  
then HCl (12 M)  
9)  $\text{MeNH}_2$ , MeOH, rt, then  $\text{NaBH}_4$

Step 1: *p*-TsCl, DMAP, pyridine  
Step 2: Li,  $\text{NH}_3$  (l), tBuOH, THF,  $-78^\circ\text{C}$

Please, provide reagents  
for the last transformation

Li, Q.; Zhang, H. *Chem. - Eur. J.*  
**2015**, 21, 16379–16382