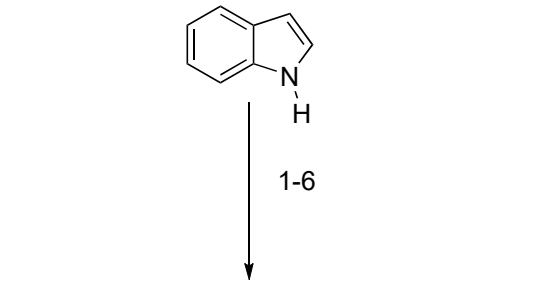
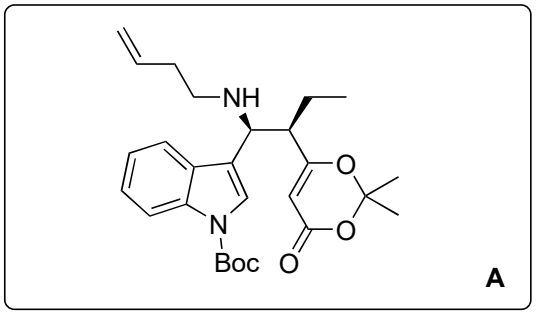
Total Synthesis of (–)-Vindorosine

W. Chen, X.-D. Yang, W.-Y. Tan, X.-Y. Zhang, X.-L. Liao, H. Zhang

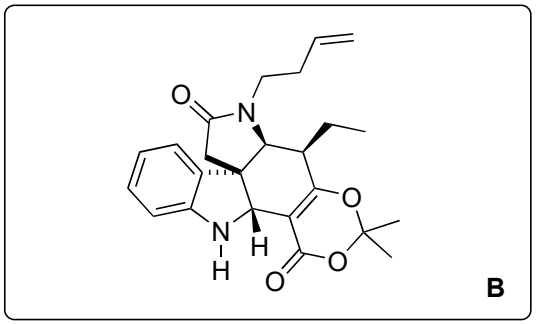
Angew. Chem. Int. Ed. **2017**, *56*, 12327-12331.



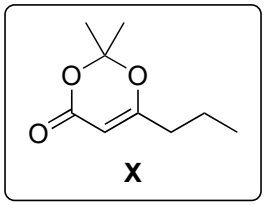
1-6



7-10



1) $POCl_3$, DMF
2) Boc_2O
3) *(S)-tert*-butylsulfinamide, $Ti(OEt)_4$
4) **X**, LiHMDS, BF_3•OEt_2
5) I_2 (0.2 equiv), THF/H_2O
6) K_2CO_3, NaI, 4-bromo-1-butene



7) TFA
8) $CH_2ClCOCl$
9) NaI
10) AgOTf

Which named reaction takes place in step 1?
Vilsmeier-Haack reaction

Step 4 involves a named reaction.
Which one?
(vinylogous) Mannich addition

How would you synthesise **X** from Meldrum's acid? What's the pK_a of Meldrum's acid?
see below, $pK_a \sim 5$

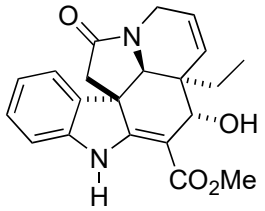
Please give a plausible mechanism for step 5.
See below

Step 10 involves a named reaction. Please provide name and mechanism.
Heathcock-aza-Prins, mechanism see below

11-18

11) $ClCO_2Me$, Na_2CO_3
12) OsO_4, NMO
13) $NaIO_4$
14) DBU
15) $SOCl_2$, py, 90 °C
16) NaOMe, MeOH
17) $CeCl_3 \cdot 7H_2O$, O_2
18) $CeCl_3 \cdot 7H_2O$, $NaBH_4$

Step 12 involves a named reaction. Please provide the name. Which Nobel prize laureate developed an asymmetric variant?
Upjohn dihydroxylation, Barry Sharpless

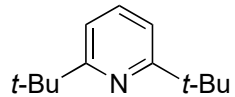


C

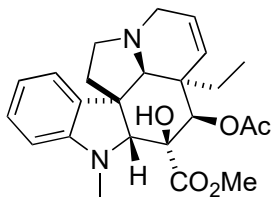
19-24

19) CBr_4, Ph_3P *then* THF/aq. $NaHCO_3$
20) *m*-CPBA, CH_2Cl_2/MeOH
21) HCHO, $NaBH_3CN$
22) Ac_2O, py, DMAP
23) MeOTf, **Y**
24) $NaBH_4$, MeOH

Please provide the name for the reaction used in Step 19.
Appel reaction

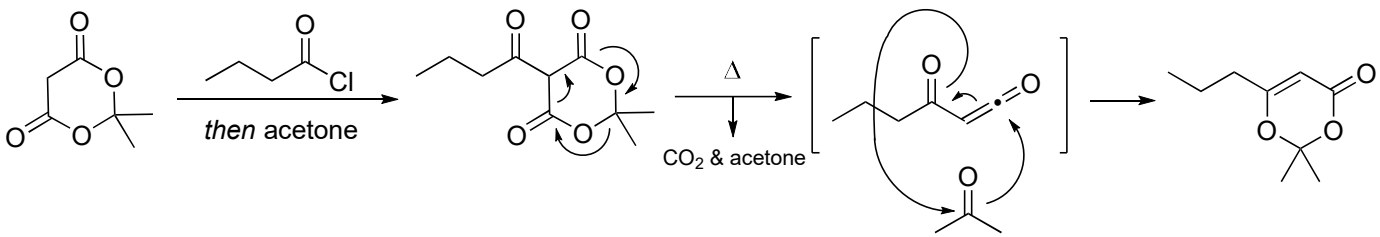


Y

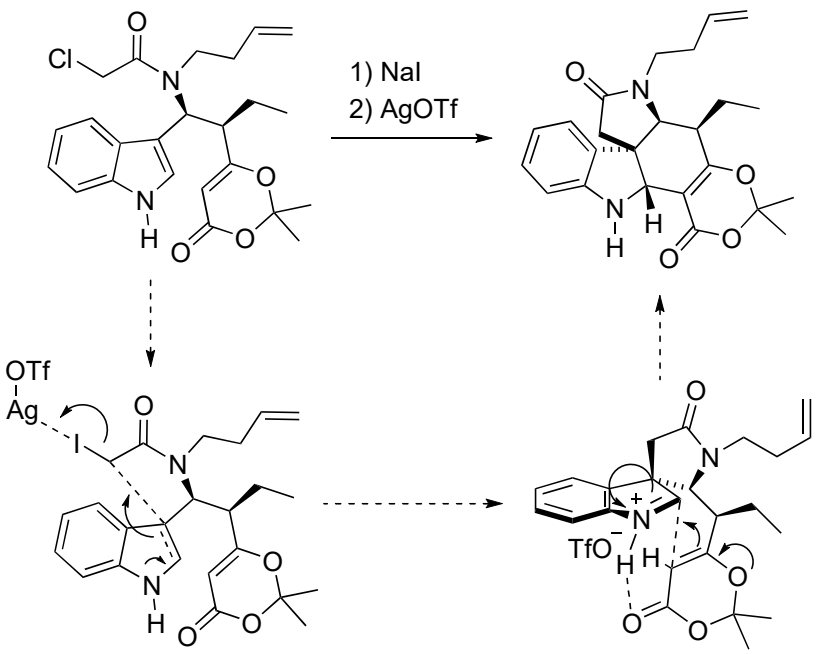


(–)-Vindorosine

Synthesis of X from Meldrum's acid



Mechanism of step 10



Sulfinamide deprotection