Total Synthesis of (–)-Strictosidine

Anthony, S. M.; Tona, V.; Zou, Y.; Morrill, L. A.; Billingsley, J. M.; Lim, M.; Tang, Y.; Houk, K. N.; Garg, N. K.

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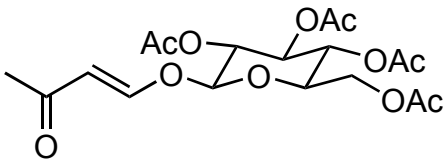
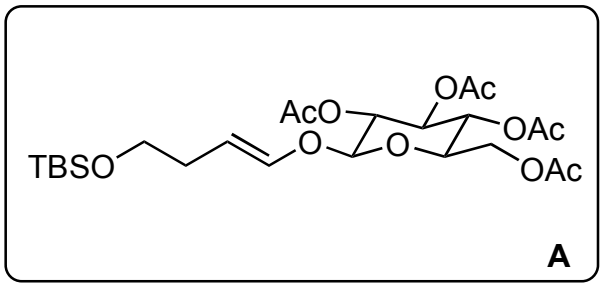


1-3

1) TBSOTf, NEt_3, THF, –78 °C
then m-CPBA
2) $CeCl_3 \cdot 7H_2O$, $NaBH_4$, MeOH
then Ac_2O, DMAP, THF
3) $NiCl_2$(DME) (3 mol%), $NaBH_4$, MeOH, THF

1) Name the reaction
2) Name the reaction
3) Propose a mechanism (FYI: the mechanism is still poorly understood)



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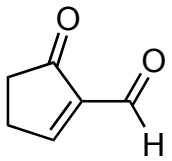
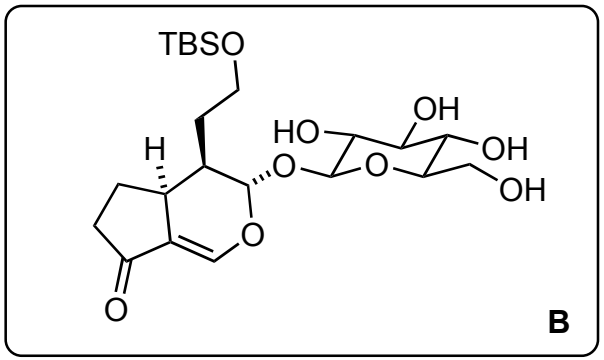


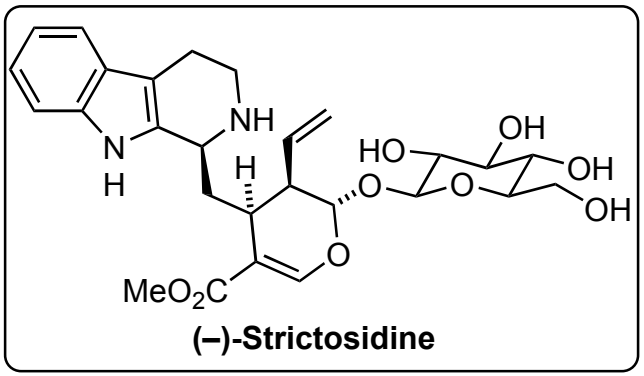
1

4) How would you prepare **1** in two steps starting from cyclopentenone?

4) **1**, 50 °C, HFIP

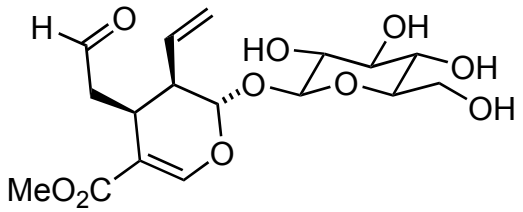
4) They obtained their product in 55% overall yield with a 1:1 dr





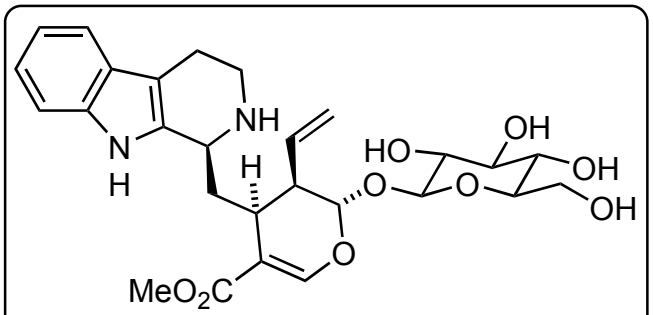
(–)-Strictosidine

5-9



(–)-Secologanin **C**

10

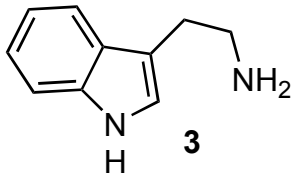


(–)-Strictosidine

5) TBAF, THF
6) **2**, P(*n*-Bu)$_3$, THF, *then* H_2O_2
7) TBSOTf, NEt_3, THF, –78 °C
then m-CPBA
8) Pb(OAc)4, –20 °C, MeOH
9) LiOMe, –20 °C, MeOH

2

10) **3**, strictosidine synthase,
100 mM NaH_2PO_4, 30 °C



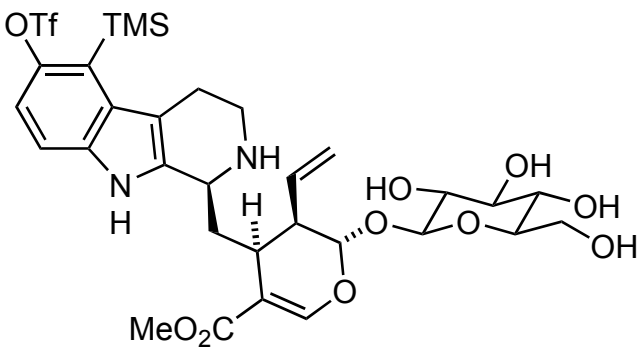
3

6) Name the reaction and show a mechanism

10) Name of this reaction

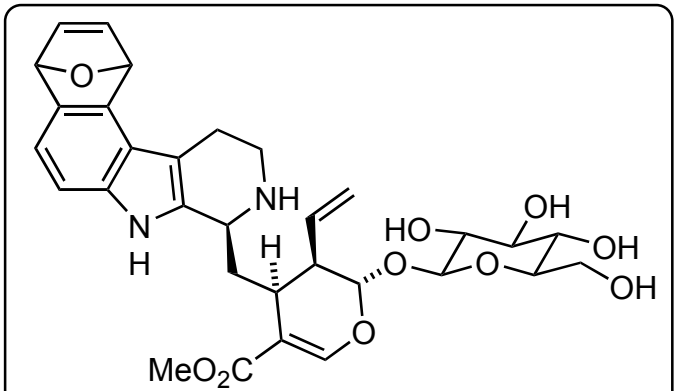
C

11

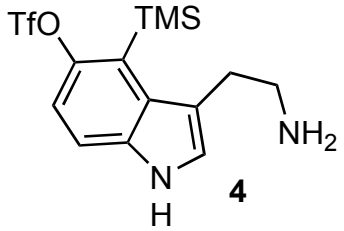


"Strictosidyne" precursor

12



Strictosidine analog



4

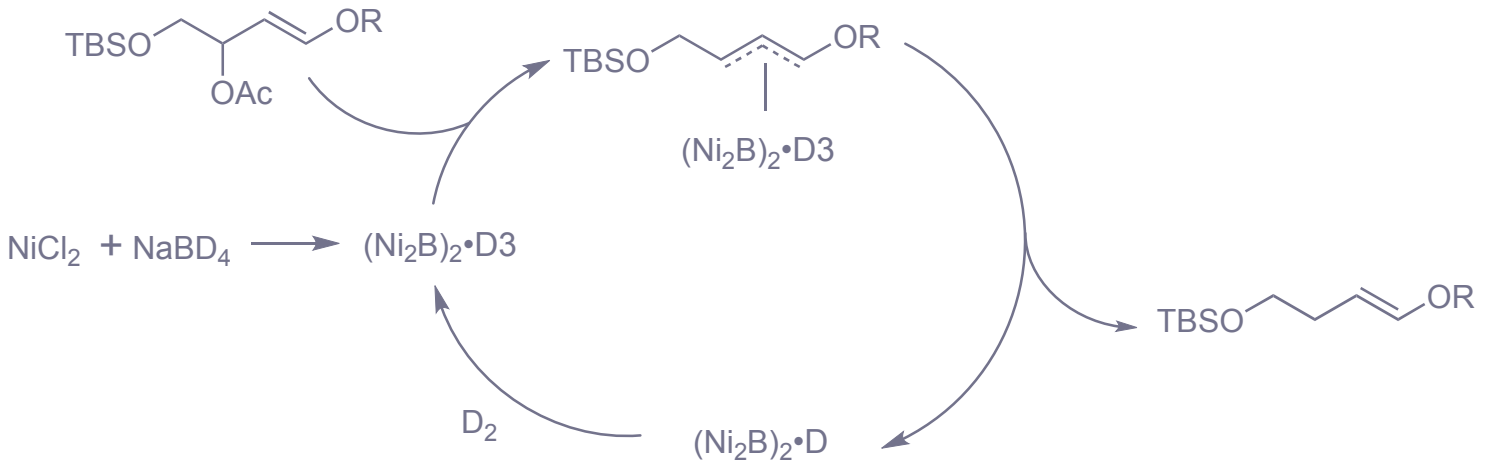
11) **4**, TFA, CH_2Cl_2, 0 to 23 °C

12) **5**, CsF, CH_3CN, 50 °C

5

1) Rubottom Oxidation
2) Luche reduction
4) Baylis–Hillman followed by DMP oxidation
6) Greico Elimination
10) Pictet–Spengler (enzyme mediated)

Mechanism for step 3 (suggested by Biao-Lin Yin group - DOI: 10.1002/adsc.201100612**)**



Mechanism for step 6