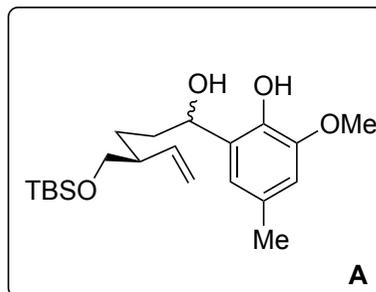
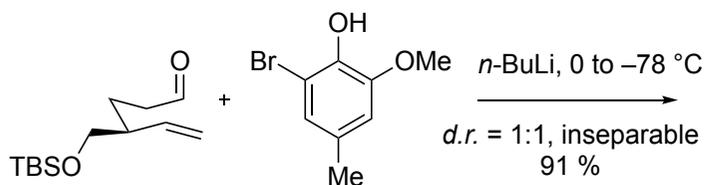




Total synthesis of Vilmoraconitine

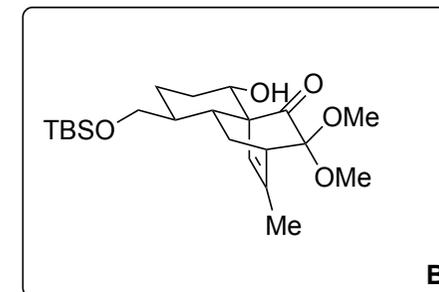
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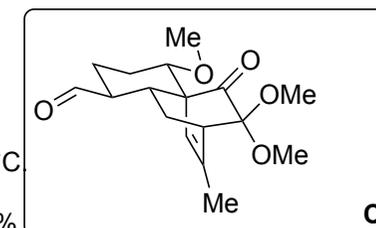
1. $\text{PhI}(\text{OAc})_2$, MeOH, NaHCO_3 , 23 °C
2. Mesitylene, 180 °C
62% overall yield of the desired α -isomer based on recycling of the other one

How would you recycle?

1. NaH, MeI, THF, 0 to 30 °C, 85%
2. TBAF, THF, 23 °C, 93%
3. IBX, DMSO, 23 °C, 90%

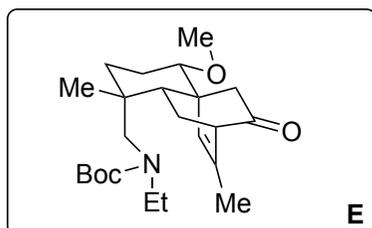
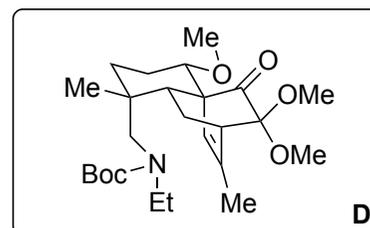


1. *t*-BuOK, MeI, THF, -10 °C, 89%
2. EtNH_2HCl , TEA, HOAc, ACN, 23 °C, then NaBH_3CN , 23 °C, then aq. NaOH, $(\text{Boc})_2\text{O}$, 23 °C, 90%

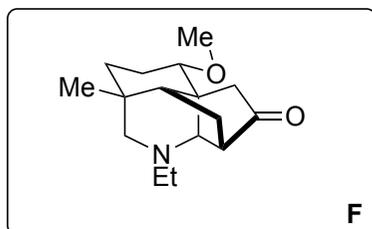


1. LAH, THF, 23 °C
2. *p*TSA, MeOH/ H_2O (10:1), 23 °C
3. Sml_2 , MeOH, 0 °C to 23 °C

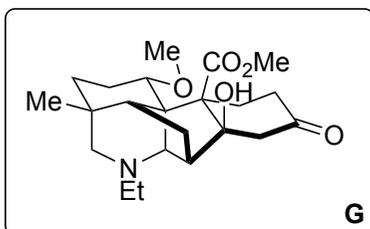
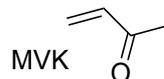
62%
Mechanism for Sml_2



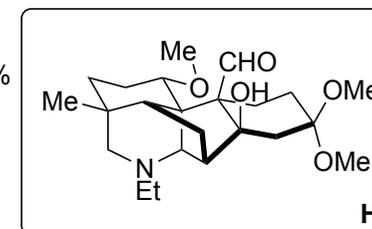
1. O_3 , MeOH, -78 °C, then $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$, 4-methoxybenzenethiol, -78 °C to 23 °C, 77%
2. TFA, DCM, 40 °C, 90%

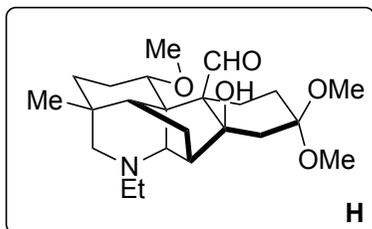


1. LDA, NCCO_2Me , -78 °C
2. Cs_2CO_3 , MVK, THF, 0 to 23 °C, 62% (over 2 steps)
3. KHMDs , THF, -78 °C, 85%

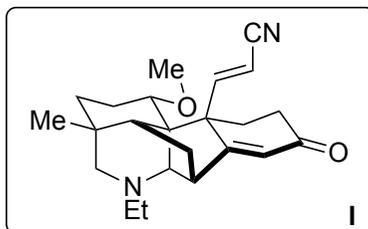


1. TiCl_4 , MeOH, TEA, 23 °C, 80%
2. LAH, THF, 23 °C,
3. AZADO, CuCl, bpy, DMAP, ACN/DCM (10:1), air, 23 °C, 88%
over 2 steps

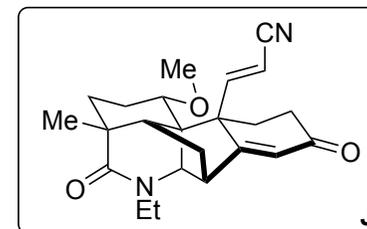




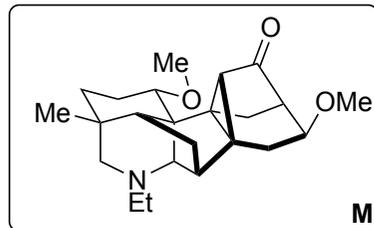
1. LDA, (EtO)₂P(O)CH₂CN
THF, 23 °C to 50 °C, 93%
2. TMSOTf, DCM, 23 °C, 92%



I₂, NaHCO₃, THF/H₂O
(2:1), 0 °C to 23 °C, 80%



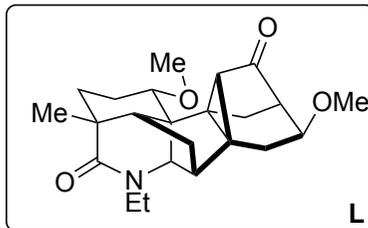
TMP, TBSOTf, THF, -78 °C,
then mesitylene, 150 °C,
then *p*TSA, DCM, 23 °C, 75%



Vilmoraconitine

1. LAH, THF, 70 °C
2. AZADO, CuCl, bpy, DMAP,
ACN/DCM (10:1), air, 23 °C
68% over 2 steps

Vaska's catalyst/TMDS protocol
or Rh(H)(CO)(PPh₃)₃/PhSiH₃ did
not work



1. NaBH₄, MeOH/THF (1:1),
0 °C
2. *t*-BuOK, MeI, THF, -20 °C
67% over 2 steps
3. LDA, O₂, THF, -78 °C,
then SnCl₂, H₂O, aq.
Na₂CO₃, 23 °C, 80%

