Total Synthesis of (-)-Batrachotoxinin A: A Local-Desymmetrization Approach

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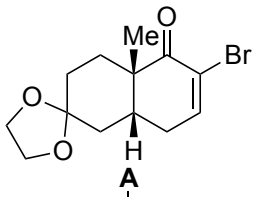
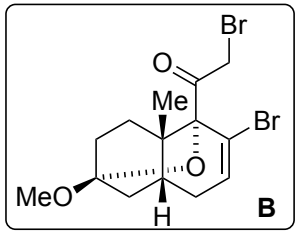


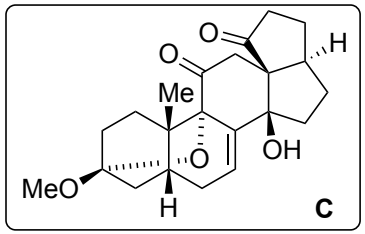
A

1 - 3



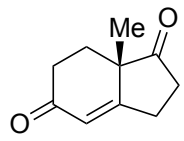
B

4/5

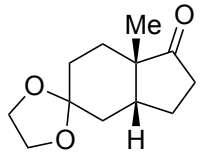


C

1) *t*-BuLi, ethyl vinyl ether,
then **A**, *then* aq. HCl
2) (+)-CSA, MeOH
3) TMSOTf, TEA, *then* NBS



Pd/C,
ethylene glycol



Hajos-Parrish ketone

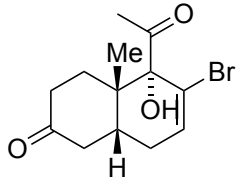
step 1: How would you prepare **A** from the Hajos-Parrish ketone?

Hint step 2: a 6-membered acetal is formed

1. TESMs, TEA
2. $CHBr_3$, KOtBu

A

A 1)



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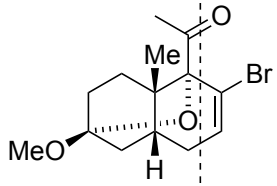
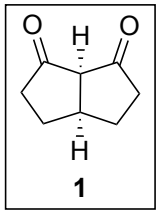
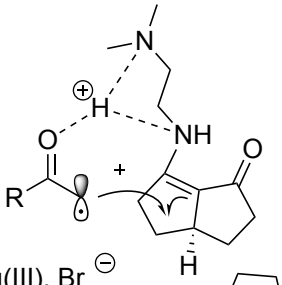


4) $Ru(bpy)_3Cl_2 \cdot 6H_2O$ (2 mol%),
$H_2NCH_2CH_2NMe_2 \cdot HOTf$, **1**,
$NaHCO_3$, 65W CFL
5) *t*-BuLi, *then* MeOH



1

4)
Ru(II)*, hν



Ru(III), Br ⊖

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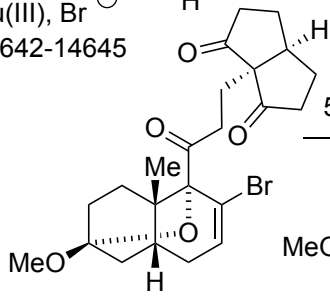
open-shell radical substitution



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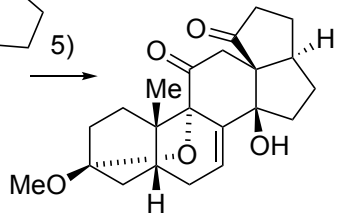
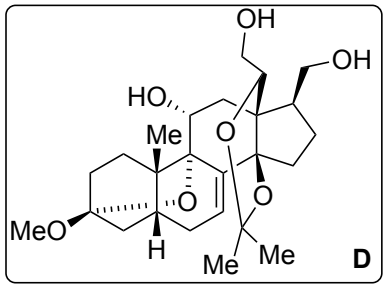
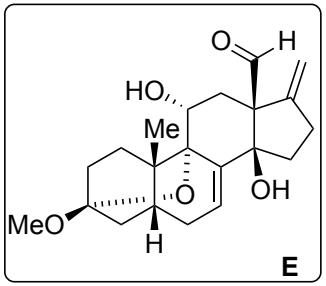


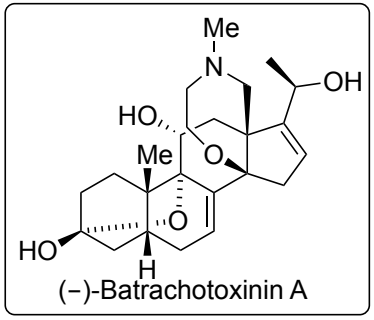
6 - 9



9 - 11

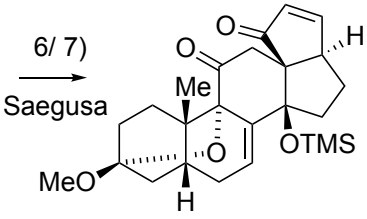


12 - 15



6) TMSOTf, TEA
7) $Pd(OAc)_2$
8) DIBAL, *then* LAH
9) *p*TsOH, $(MeO)_2CMe_2$, *then* O_3, MeOH *then* $NaBH_4$

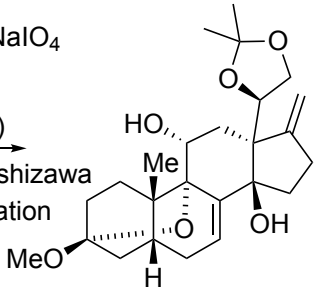
6/ 7) Saegusa



via TMS-enol ether

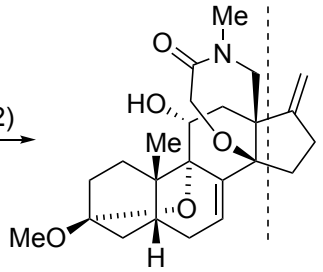
10) *p*TsOH (0.01 equiv), *then* *o*-$NO_2PhSeCN$, PBu_3, *then* H_2O_2
11) (+)-CSA, MeOH, *then* $NaIO_4$

10) Grieco-Nishizawa elimination



12) $NaBH(TFA)_3$, $MeNH_2$, $ClCH_2COCl$, *then* EtONa
13) $^1O_2$, *then* Ac_2O
14) MeMgBr
15) LAH, then aq. HCl

12)



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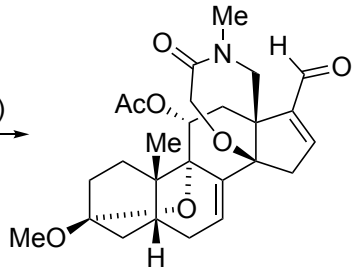

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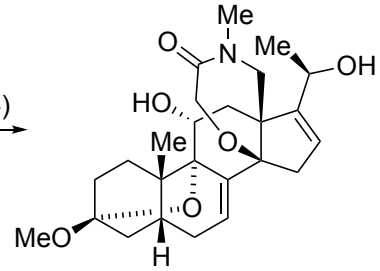
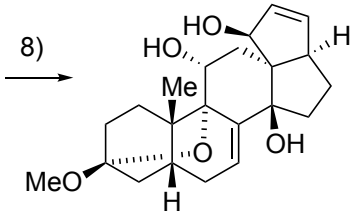


step 6/7: name reaction?
Hint step 8: a total of 2 [H] and 1 deprotection occur
Hint step 9: a 6-membered heterocycle forms

8)



step 10: name reaction?
Hint step 10: a re-acetalization occurs