Synthesis of Scopadulic Acid A

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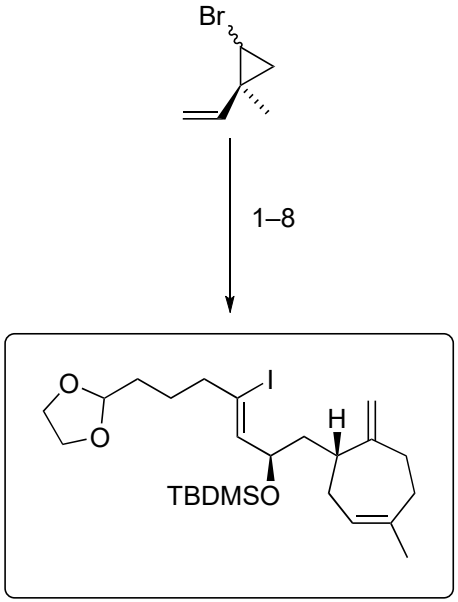
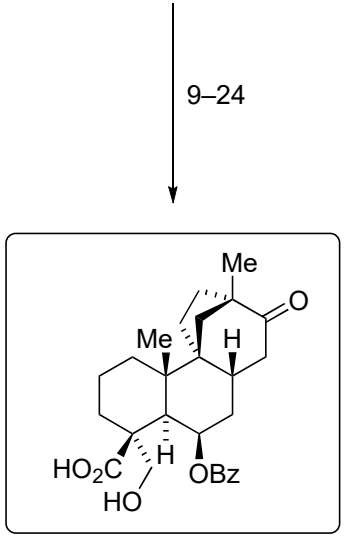
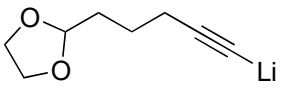


A



Scopadulic Acid A

1) *t*-BuLi, –78 °C *then* $TBSO(CH_2)_3CHO$
2) $(COCl)_2$, DMSO, NEt_3
3) TMSOTf, NEt_3
4) PhH, 110 °C *then*, PPTS, *i*-PrOH/H_2O, 23 °C
5) Ph_3PMeBr, base
6) $(COCl)_2$, DMSO, NEt_3
7) **1**, –78 °C to 0 °C
8) RedAl, 23 °C *then* NIS, –78 °C to 23 °C *then* TBDMSCl, ImH, DMF



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9) $Pd(OAc)_2$, PPh_3, Ag_2CO_3, 90 °C *then* TBAF
10) TPAP, NMO
11) Me_2Zn, LiBr, $Ni(acac)_2$
12) $(CH_2OH)_2$, Amberlyst 15
13) *m*-CPBA, $NaHCO_3$ *then* $LiAlH_4$
14) 20% aq. HCl, MeOH, 65 °C
15) MOMCl, $(i\text{-}Pr)_2NEt$
16) Et_2AlCN, TMSCl, NEt_3 *then* HCl
17) $LiAlH_4$ *then* TMSCl, DMAP, py
18) LDA, $BnOCH_2Br$, –78 °C to 0 °C
19) KOH, K_2CO_3, 140 °C *then* CH_2N_2
20) BzCl, DMAP, py, 100 °C
21) HCl, MeOH, 70 °C
22) PCC, CH_2Cl_2, 23 °C
23) *n*-PrSLi, DMPU, 23 °C
24) Pd/C, H_2, MeOH

4) What is the name of the reaction? Only one of the TMS enol ethers reacts as desired; the other is recovered as the hydrolyzed product. The desired product has (R) stereochemistry.

Cope Rearrangment

5) Name two alternative methods to perform this reaction.

Tebbe Olefination, Lebel Olefination, Peterson

7) The product is a mixture of diastereoisomers. How can the undesired isomer be converted into the desired one? What is the approximate pKa of the shown anion, and why is it less basic than n-BuLi?

Mitsunobu, $pK_A = 25$, hybridization $sp^3 < sp^2 < sp$

8) Hint: A hydroxy group is required in this reaction — it results in formation of the Z-isomer.

9) Draw the full mechanism.

14) Hint: This step involves more than just deprotection.

16) What is the name of the reagent used here?

Nagats's reagent

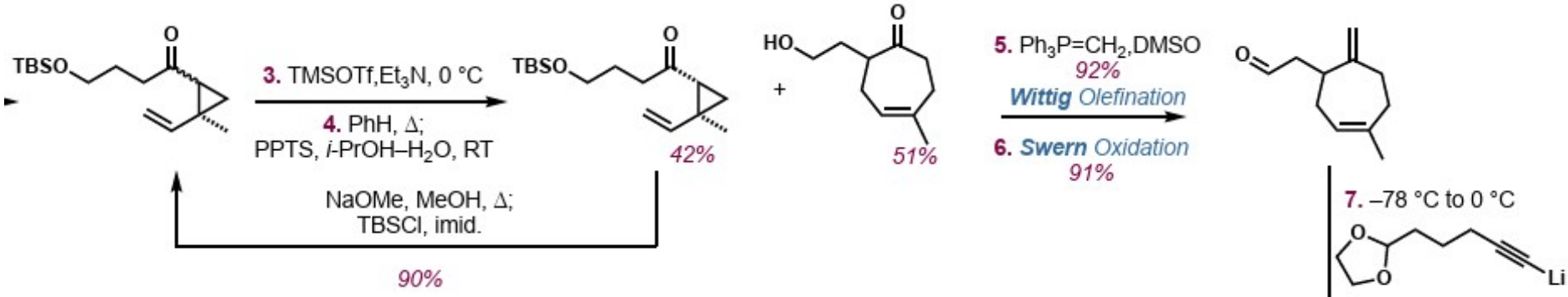
17) The nitrile group remains after this step.

19) How can CH_2N_2 be generated in situ?

Diazald + base, MNU + base, MNNG

22) What is the name of the reagent?

Corey's reagent



Diastereoselectivity of Intramolecular Heck Cascade.