Enantioselective Total Synthesis of (−)-Caldaphnidine O via a Radical Cyclization Cascade

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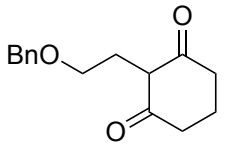


1 – 6

A

7 – 11

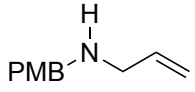
B

1) MVK, NEt_3,
then L-Prolinamide, HOAc
2) $CH(OMe)_3$, PTSA,
then HCHO, **X**
3) 1,3-Dimethylbarbituric acid, $Pd(Ph_3)_4$
then $NAHCO_3$, TsCl
4) $ZnMe_2$, LiBr, $Ni(acac)_2$
5) LiHMDS, **Y**
6) CAN

7) KHMDS, $PhNTf_2$,
then KHMDS, Davis' oxaziridine
8) $Pd(OAc)_2$, PPh_3, HCOOH, DIPEA
9) 3-butenylmagnisum bromide, $CeCl_3$
10) $Pb(OAc)_4$
11) $NaBH_4$

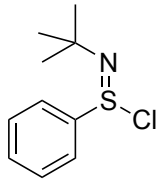
Hint: The (*R*)-enatiomer is formed in step 1.

X =

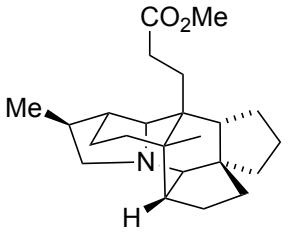


Step 5: Name and mechanism?

Y =



Step 7: How do you prepare Davis' oxaziridine?



(−)-Caldaphnidine O

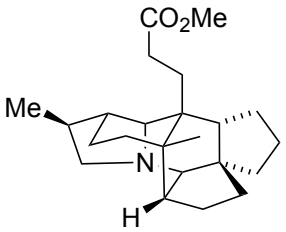
12 – 15

C

16 – 18

E

19 – 21



(−)-Caldaphnidine O

12) I_2, PPh_3, imidazole
13) LDA
14) 9-BBN, NaOMe, I_2
15) SmI_2, $Fe(dbm)_3$

16) $SOCl_2$, pyridine
17) Na-naph
then propargyl bromide
18) *n*-Bu_3SnH, AIBN
then p-TsOH

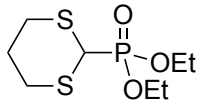
19) $(COCl)_2$, DMSO, TEA
20) *n*-BuLi, **Z**
then p-TsOH
then NaOMe
21) H_2, Pt/C

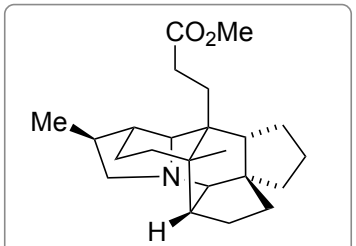
Hint for step 13: A 2:1 mixture of diastereomers is formed. It ultimately (step 16) converges back into the same intermediate.

Step 15: What are the names associated with and the mechanism of this reaction?

Step 18 - KEY STEP: Please provide a mechanism and classify each of the three steps happening in this cyclization cascade.

Z =





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