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

Lian-Dong Guo, Jingping Hu, Yan Zhang, Wentong Tu, Yue Zhang, Fan Pu, and Jing Xu


1) MVK, NEt₃, *then* L-Prolinamide, HOAc
2) CH(OMe)₃, PTSA, *then* HCHO, X
3) 1,3-Dimethylbarbituric acid, Pd(Ph₃)₄ *then* NaHCO₃, TsCl
4) ZnMe₂, LiBr, Ni(acac)₂
5) LiHMDS, Y
6) CAN

Step 7: How do you prepare Davis’ oxaziridine?

Step 2: Methyl enol ether formation, *then* vinologous Mannich

Step 4: Conjugate addition under Luche’s conditions

Step 5: Name and mechanism?

Mukaiyama dehydrogenation

Hint: The (R)-enatiomer is formed in step 1.
Step 18 - KEY STEP: Please provide a mechanism and classify each of the three steps happening in this cyclization cascade.

5-exo-trig, 1,5-HAT, 5-exo-trig, mechanism below

12) I₂, PPh₃, imidazole
13) LDA
14) 9-BBN, NaOMe, I₂
15) SmI₂, Fe(dbm)₃

16) SOCl₂, pyridine
17) Na-naph
then propargyl bromide
18) n-Bu₃SnH, AIBN
then p-TsOH

19) (COCl)₂, DMSO, TEA
20) n-BuLi, Z
then p-TsOH
then NaOMe
21) H₂, 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?

Kagan Molander coupling

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

5-exo-trig, 1,5-HAT, 5-exo-trig, mechanism below

(-)-Caldaphnidine O
Mechanism of step 18

[Diagram showing the chemical reactions and structural changes involving SnBu₃ groups, 5-exo-trig addition, and 1,5-HAT processes.]