Scalable Total Synthesis of Portimine A and B Reveals the Basis of Their Potent and Selective Anti-cancer Activity


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1. HCHO, pyrrolidine, propionic acid, H₂O, i-PrOH
2. 1, [Co([t-Bu-Salen])SbF₆, 4Å MS, DCM, r.t.
3. NaBH₄, MeOH, DCM, 0 °C
4. TBAF, THF, r.t.
5. TEMPO, NaOCl, KBr, NaHCO₃, DCM, H₂O, 0 °C
6. 2, THF, –78 °C
7. DMP, NaHCO₃, DCM, 0 °C
8. TFA, DCM, r.t.
9. 3, t-BuLi, THF, –78 °C then 4, n-Bu₃P, THF, –78 °C then A, THF, –78 °C then Comins’ rgt., THF, 0 °C
10. TrocCl, DMAP, DCM, reflux
11. 5, 5Å MS, PhMe, 80 °C
12. PTSA, DCM, MeOH, H₂O, 50 °C
13. XPhosAuNTf₂, DCM, reflux
14. Ru(PPh₃)₃Cl₂, TBHP, TBAI, MeCN, PhMe, H₂O, r.t.

Step 2: Please, name the reaction, the reagent 1 and show structure of the salen ligand.

Step 5: Please, show the mechanism.

Step 11: Who developed this type of catalyst?

Hint step 12: Concomitant silyl deprotection.

Hint step 13: Three heterocycles are formed.
15. L-selectride, THF, –78 °C
16. NaBH₄, MeOH, 0 °C
17. TEMPO, NaOCl, KBr, NaHCO₃, DCM, H₂O, 0 °C
18. Zn, AcOH, H₂O, 70 °C
19. TBSOTf, Et₃N, DCM, reflux
20. DMDO (excess), acetone, DCM, 0 °C
21. Ac₂O (excess), Et₃N, DCM, 35 °C
22. LiOH, THF, H₂O, 0 °C
23. 6, Pd(dppf)Cl₂, Et₃N, n-PrOH, 90 °C
24. DMP, NaHCO₃, DCM, r.t.
25. NH₃, H₂O, MeOH

Step 18: Please, suggest a mechanism.

Hint step 20: Oxidation at 2 positions.

Step 21: Please, show the mechanism. Which analogous named rearrangement uses 2-alkylpyridine-N-oxides as substrates? Classify the rearrangement.

Hint step 22: Selective mono-deprotection.