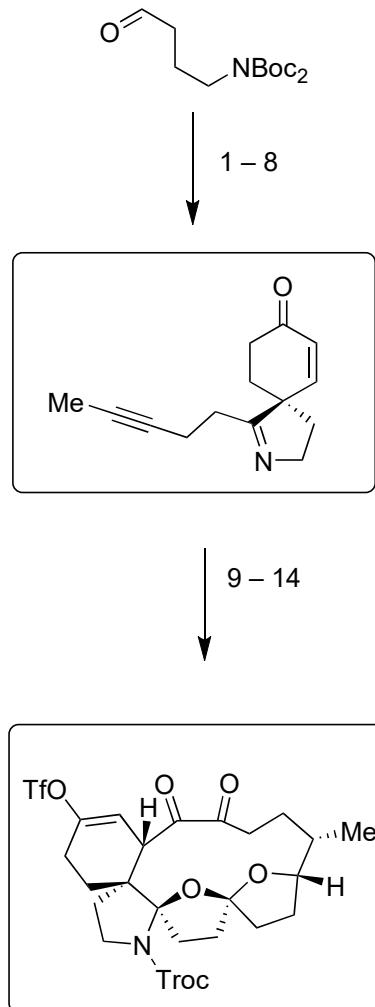


Scalable Total Synthesis of Portimine A and B Reveals the Basis of Their Potent and Selective Anti-cancer Acitivity

J. Tang, W. Li, T.-Y. Chiu, Z. Luo, C. T. Chong, Q. Wei, F. Martinez-Peña, N. Gazaniga, Y. Y. See, L. L. Lairson, C. G. Parker, P. S. Baran

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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

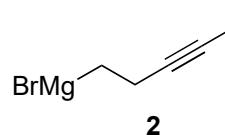
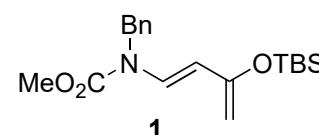
4. TBAF, THF, r.t.

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

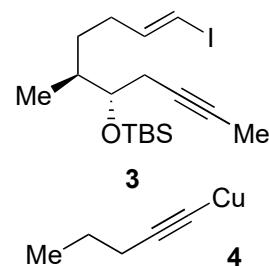
10. TrocCl, DMAP, DCM, reflux

11. **5**, 5Å MS, PhMe, 80 °C

12. PTSA, DCM, MeOH, H₂O, 50 °C

13. XPhosAuNTf₂, DCM, reflux

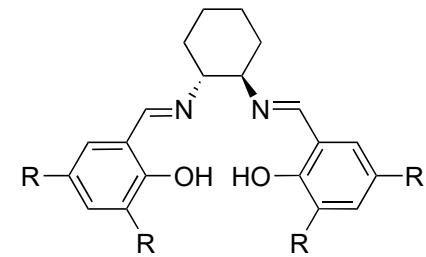
14. Ru(PPh₃)₂Cl₂, TBHP, TBAI, MeCN, PhMe, H₂O, r.t.



Hint step 1: Formation of terminal alkene

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

Diels-Alder, Rawal's diene



Hint step 4: E1cb reaction occurs

Step 5: Please, show the mechanism.

Hint step 8: Loss of water

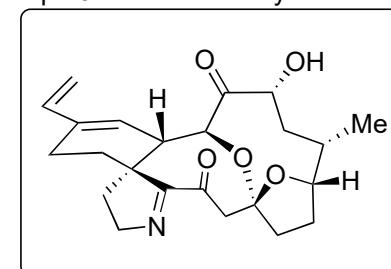
Hint Step 9: Formation of reactive organocuprate

Step 11: Who developed this type of catalyst?

Alois Fürstner et al.

Hint step 12: Concomitant silyl deprotection.

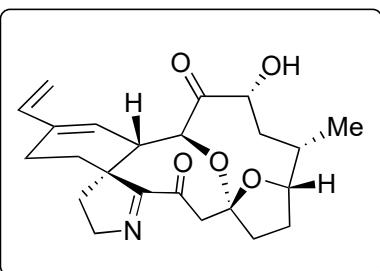
Hint step 13: Three heterocycles are formed.



Portimine B

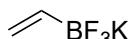
B

15 – 25



Portimine B

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



6

Step 18: Please, suggest a mechanism.

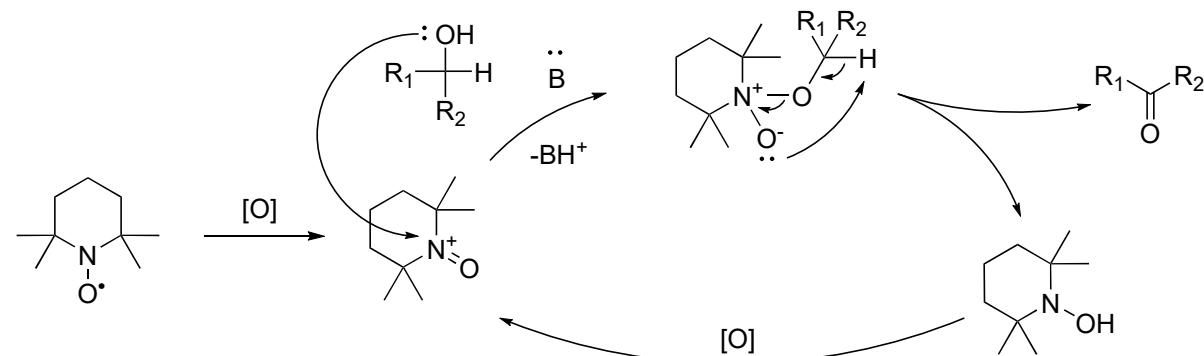
Hint step 20: Oxidation at 2 positions.

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

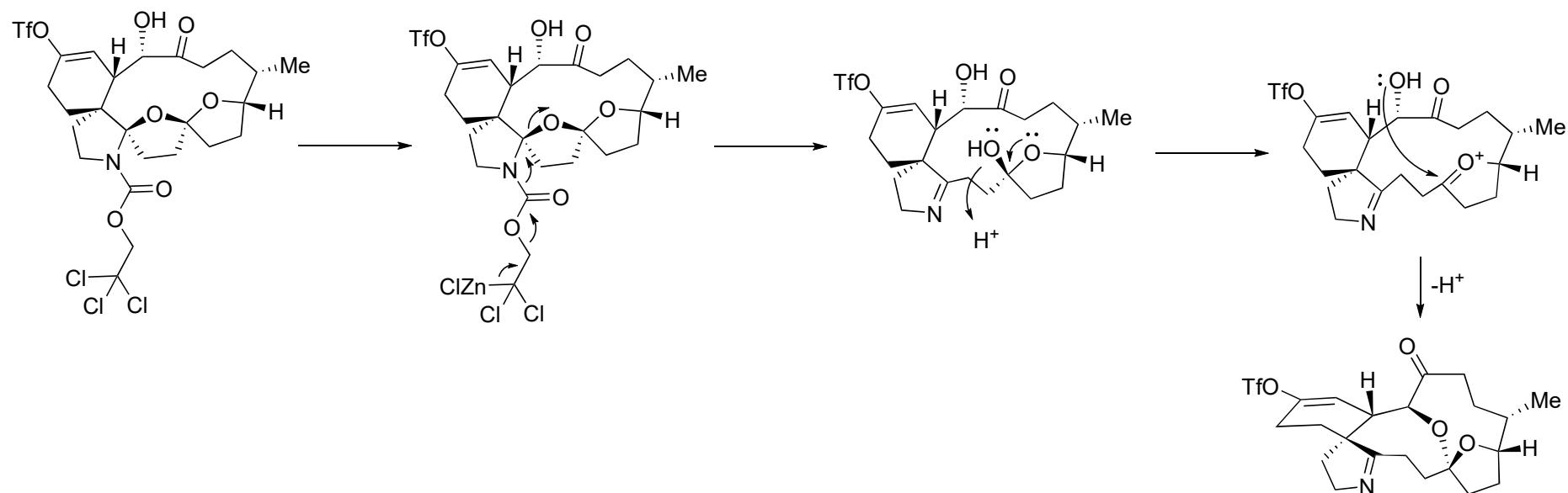
Boekelheide rearrangement, [3,3]sigmatropic

Hint step 22: Selective mono-deprotection.

Step 5: Please, show the mechanism.



Step 18: Please, suggest a mechanism



Step 21: Please, show the mechanism.

