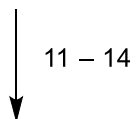
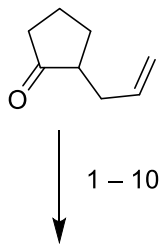


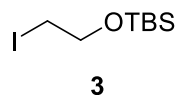
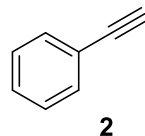
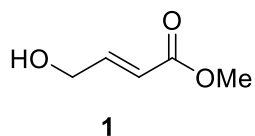
Total Synthesis of Ginkgolide C and Formal Syntheses of Ginkgolides A and B

Martin Hébert, Gabriel Bellavance, Louis Barriault

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1. Amberlyst 15, CH(OMe)₃, MeOH, reflux
2. Propionic acid (cat.), **1**, 150 °C
3. Grubbs II, CH₂Cl₂, reflux
4. DBU, PhMe, 80 °C
5. PhNTf₂, LHMDs, THF, -45 °C
6. Pd(PPh₃)₂Cl₂, **2**, CuI, Et₃N, 60 °C
7. KHMDS, 18-Crown-6, THF, -78 °C then **3**
8. *m*-CPBA, CH₂Cl₂, r.t.
9. Ac₂O, Et₃N, DMAP, CH₂Cl₂, r.t. then MeOH, TBAF, 65 °C
10. AcOK, DMSO, 145 °C



11. DMP, CH₂Cl₂, r.t.
12. Amberlyst 15, CH(OMe)₃, MeOH, CH₂Cl₂, 65 °C
13. DIBAL-H (5 eq.), THF, -78 °C → 0 °C
14. HCl (4M in dioxane), THF, r.t. then Et₃N, DMAP, Ac₂O, r.t.

Step 2: Please, name the reaction.

Step 3: Please, show the structure of Grubbs II catalyst.

Hint step 4: Isomerization.

Step 6: Please, name the reaction.

Hint step 8: Two products are formed. Step 9 converts one of them into **A** and step 10 converts the other into **A**.

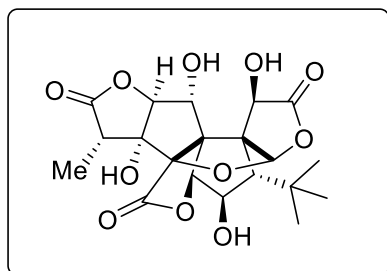
B

15 – 21



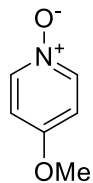
C

22 – 28

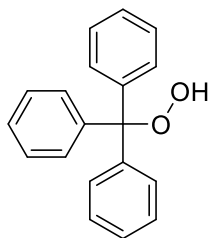


Ginkgolide C

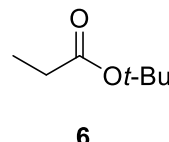
15. SeO_2 , 1,4-dioxane, 110 °C then DMP, CH_2Cl_2 , 60 °C
16. *t*-BuLi, CuCN, THF, -78 °C then TMSI, -78 °C then TBAF, r.t. then NaOH, MeOH, THF, H_2O , 75 °C
17. KHMDS, Davis' oxaziridine, THF, -78 °C → r.t.
18. MOMBr, DIPEA, TBAI, CH_2Cl_2 , 55 °C
19. RuCl_3 , NaIO_4 , CCl_4 , MeCN, H_2O , 50 °C
20. NaBH_4 , THF, H_2O , r.t. then NaOH, 50 °C then AcOH, r.t.
21. IBX (8 eq.), **4** (8 eq.), DMSO, 75 °C



4



5



6

22. PPTS, pyr, Ac_2O , PhCl, 135 °C
23. DBU, **5**, CH_2Cl_2 , -25 °C
24. LDA, **6** then SM, THF, HMPA, -78 °C → -30 °C
25. CSA, CH_2Cl_2 , r.t.
26. DMDO, acetone, r.t.
27. Br_2 , NaOAc, AcOH, H_2O , r.t.
28. K_2CO_3 , MeOH, r.t.

Step 15: Please name the first reaction which takes place and show the mechanism.

Step 16: Please, categorize the occurring cyclization according to the Baldwin rules.

Step 17: Please, show the structure of Davis' oxaziridine. How would you prepare this reagent?

Step 21: Please, show the structure of IBX.

Step 22: Same conditions without Ac_2O led only to several sideproducts and no desired product. Why is Ac_2O essential?

Step 25: Please, show the structure of CSA.

Step 26: How would you generate DMDO?