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

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1. Amberlyst 15, CH(O Me)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, Cul, 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

Step 2: Please, name the reaction.

Claisen rearrangement

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

Step 6: Please, name the reaction.

Sonogashira cross-coupling

Hint step 8: Two products are formed. Step 9 converts one of them into A and step 10 converts the other into A.
15. SeO₂, 1,4-dioxane, 110 °C then DMP, CH₂Cl₂, 60 °C
16. t-BuLi, CuCN, THF, −78 °C then TMSI, −78 °C then TBAF, r.t. then NaOH, MeOH, THF, H₂O, 75 °C
17. KHMS, Davis’ oxaziridine, THF, −78 °C → r.t.
18. MOMBr, DIPEA, TBAI, CH₂Cl₂, 55 °C
19. RuCl₃, NaIO₄, CCl₄, MeCN, H₂O, 50 °C
20. NaBH₄, THF, H₂O, r.t. then NaOH, 50 °C then AcOH, r.t.
21. IBX (8 eq.), 4 (8 eq.), DMSO, 75 °C

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

Riley oxidation

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

5-endo-dig

22. PPTS, pyr, Ac₂O, PhCl, 135 °C
23. DBU, 5, CH₂Cl₂, −25 °C
24. LDA, 6 then SM, THF, HMPA, −78 °C → −30 °C
25. CSA, CH₂Cl₂, r.t.
26. DMD, acetone, r.t.
27. Br₂, NaOAc, AcOH, H₂O, r.t.
28. K₂CO₃, MeOH, r.t.
Step 17: Please, show the structure of Davis’ oxaziridine. How would you prepare this reagent?

\[
\text{PhCHO} + \text{PhSO}_2\text{NH}_2 \xrightarrow{\text{H}^+} \text{Ph-N=S-Ph} \xrightarrow{m\text{-CPBA}} \text{Ph-NO-SO}_2\text{Ph}
\]

Step 21: Please, show the structure of IBX.

Step 22: Same conditions without Ac\(_2\)O led only to several sideproducts and no desired product. Why is Ac\(_2\)O essential?

MOM-group is cleaved under reaction conditions which leads to formation of several acetals. Ac\(_2\)O replaces the MOM-group which prevents formation of undesired acetals.

Step 25: Please, show the structure of CSA.

Step 26: How would you generate DMDO?

\[
\text{O} \xrightarrow{\text{Oxone}} \text{O-O} \quad \text{Dilute solution in acetone after distillation}
\]