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

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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, 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.

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.

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.
15. \( \text{SeO}_2, \text{1,4-dioxane, 110 °C then DMP, CH}_2\text{Cl}_2, 60 \text{ °C} \)
16. \( \text{t-BuLi, CuCN, THF, −78 °C then TMSI, −78 °C then TBAF, r.t. then NaOH, MeOH, THF, H}_2\text{O, 75 °C} \)
17. KHMDS, Davis’ oxaziridine, THF, −78 °C → r.t.
18. MOMBr, DIPEA, TBAI, CH\(_2\)Cl\(_2\), 55 °C
19. RuCl\(_3\), NaIO\(_4\), CCl\(_4\), MeCN, H\(_2\)O, 50 °C
20. NaBH\(_4\), THF, H\(_2\)O, 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.

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\(_2\)O led only to several sideproducts and no desired product. Why is Ac\(_2\)O essential?

Step 25: Please, show the structure of CSA.

Step 26: How would you generate DMDO?

Ginkgolide C