

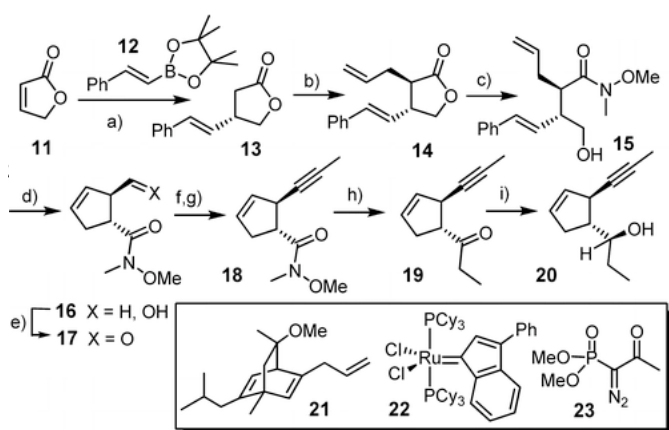
Problem Set Monday 29th November

The Fürstner synthesis of the Ecklonialactones

Please provide a route to Ecklonialactone A. Where appropriate provide a detailed rationale for any elements of stereochemistry that arise using clear chemical drawings. You should account for substrate, reagent and catalyst control in your answers.

Kickmann, V.; Alcarazo, M.; Fürstner, A. *J. Am. Chem. Soc.* **2010**, *132*, 11042.

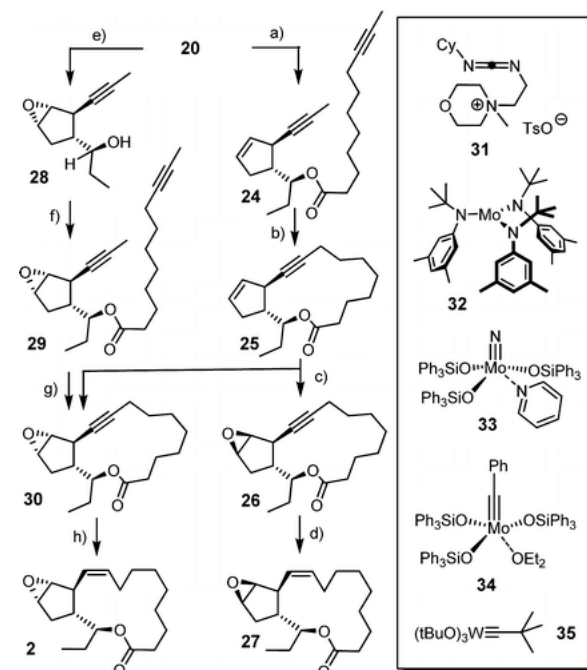
Scheme 1



^aReagents and conditions: (a) $[\text{Rh}(\text{C}_2\text{H}_4)_2\text{Cl}]_2$ (1.5 mol %), **21** (3.3 mol %), SiO_2 cat., 1,4-dioxane, aq. KOH, 52%, 80% ee (93% ee after recryst.); (b) LDA, THF, -78°C , then allyl iodide, 87%; (c) $\text{HN}(\text{OMe})\text{Me HCl}$, Me_3Al , CH_2Cl_2 , $0^\circ\text{C} \rightarrow \text{rt}$; (d) **22** (8 mol %), CH_2Cl_2 , 75% (over both steps); (e) Dess–Martin periodinane, NaHCO_3 , CH_2Cl_2 , 73%; (f) **23**, K_2CO_3 , MeOH, 75%; (g) LiHMDS, MeOTf, THF, -78°C , 80%; (h) EtMgBr , THF, 0°C , 93%; (i) $\text{LiBH}(\text{s-Bu})_3$, THF, -78°C .

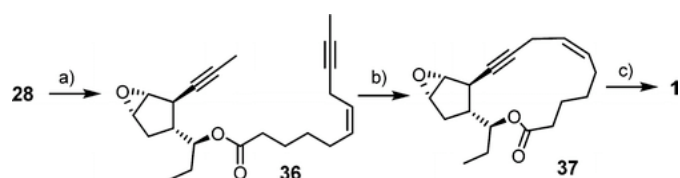
Scheme 2

Scheme 2



^aReagents and conditions: (a) 9-undecynoic acid, DMAP, CH_2Cl_2 , 70%; (b) **32** (20 mol %), toluene/ CH_2Cl_2 , 80°C , 71%; (c) dimethyl dioxirane, acetone/ CH_2Cl_2 , $-78^\circ\text{C} \rightarrow \text{rt}$, 75% (**26:30** = 3:1); (d) Lindlar catalyst, H_2 , CH_2Cl_2 , 80%; (e) $\text{VO}(\text{acac})_2$ (8 mol %), $t\text{-BuOOH}$, CH_2Cl_2 , 94%; (f) 9-undecynoic acid, **31**, DMAP, CH_2Cl_2 , 61%; (g) **34** (5 mol %), toluene, MS 5 Å, 80%; (h) Lindlar catalyst, H_2 , CH_2Cl_2 , 90%.

Scheme 3



^aReagents and conditions: (a) undec-6(Z)-en-9-ynoic acid, **31**, DMAP, CH_2Cl_2 , 65%; (b) **34** (5 mol %), MS 5 Å, toluene, 90%; (c) P_2Ni (25 mol %), H_2 , EtOH, 69%.

Points worth thinking about:

1. Transformation of **11** to **13**, how does this work? How does **21** induce asymmetry?
2. What is the mechanism for the formation of **18** from **17**?
3. What is the detailed mechanism for the formation of **19** from **18**?
4. Substrate control is relied upon in the formation of **28** (and **26**), if you wanted to do this reaction (epoxidation of a double bond) asymmetrically using reagent or catalyst control how would you do it?
5. The final step of the synthesis generates the Z-olefin using a Lindlar reduction, how would you get the E-olefin directly from an alkyne?