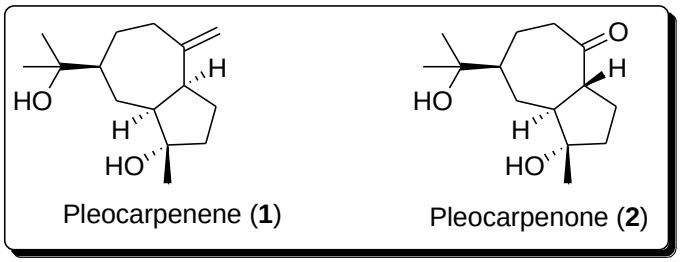
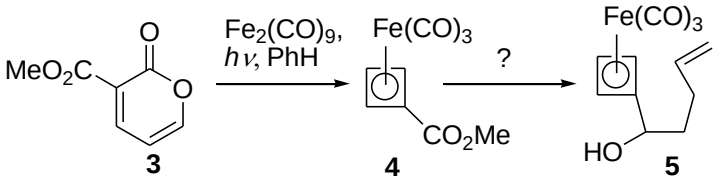
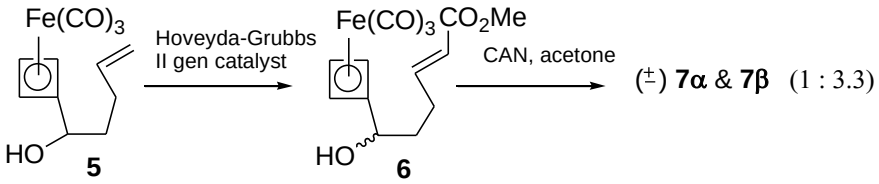
Total Syntheses of Pleocarpenene (1) and Pleocarpenone (2)



Pleocarpenene (**1**) and Pleocarpenone (**2**), two guaiane natural products, were isolated in 1976 from the *Pleocarphus revolutus*.
The synthetic route is as follows, starting from the commercially available α-pyrone **3**.



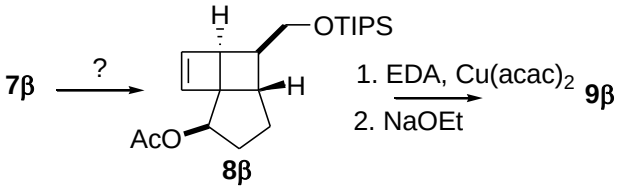
1) Which kind of reaction is the transformation of **3** to **4**? Provide a mechanism.
2) Transformation of **4** to **5** can be done in two or in three steps. Suggest conditions for both cases.



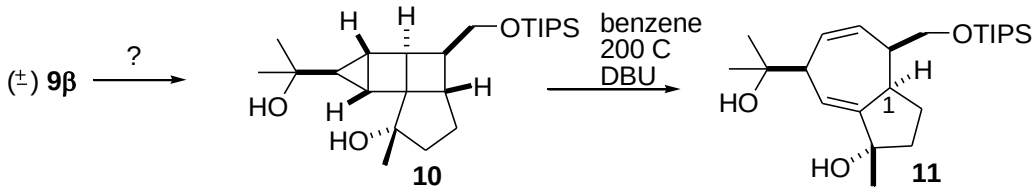
3) Provide the structure of the Hoveyda-Grubbs catalyst and the name and the mechanism of the transformation of **5** to **6**.

Alcohol **6** can be obtained enantioenriched (92% e.e., see below).

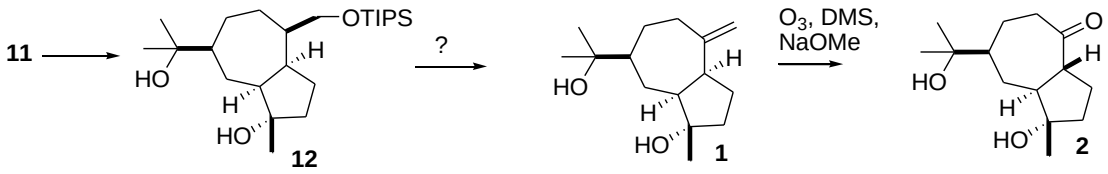
4) What are the structures of **7**? Discuss the stereoselectivity.



5) Suggest conditions for the transformation of **7β** to **8β**.
6) The transformation of **8β** to **9β** is catalysed by $Cu(acac)_2$. Provide structure and mechanism of formation of compound **9β**. The process presents a considerable stereochemical control. Try to explain why.

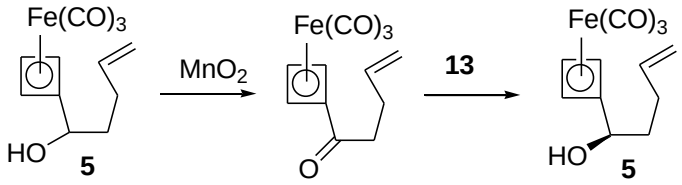


7) Provide conditions for the transformation of **9β** to **10**.
8) The transformation of **10** to **11** is a thermal rearrangement. Propose a mechanism and an explanation for the inversion of the configuration at the C-1.

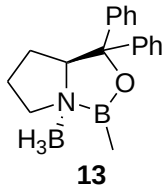


9) Hydrogenation of **11** to **12** occurs stereoselectively. What catalyst can be used?
10) The completion of the synthesis of **1** is achieved by FGI reactions. Give reagents.
11) Compound **1** is converted in **2** by ozonolysis. Give the mechanism of this reaction and explain as the right stereochemistry is obtained.

In the same paper, an enantioselective route for the synthesis of **1** and **2** is reported. The key step is the oxidation of racemic alcohol **5** and asymmetric reduction of the corresponding ketone.

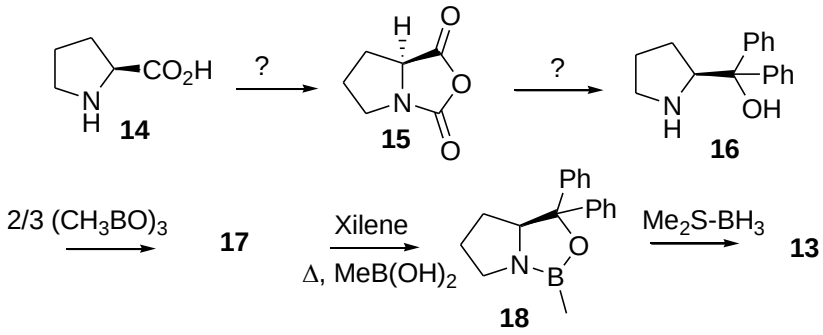


(**13**): cathecol borane, (3a*S*)-tetrahydro-1-methyl-3,3-diphenyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3,2]oxazaborole



13

The synthesis starts from proline (**14**).



12) Provide reagents for the transformation of **14** to **15**
13) Provide reagents for the transformation of **15** to **16**
14) What is the structure of **17**?