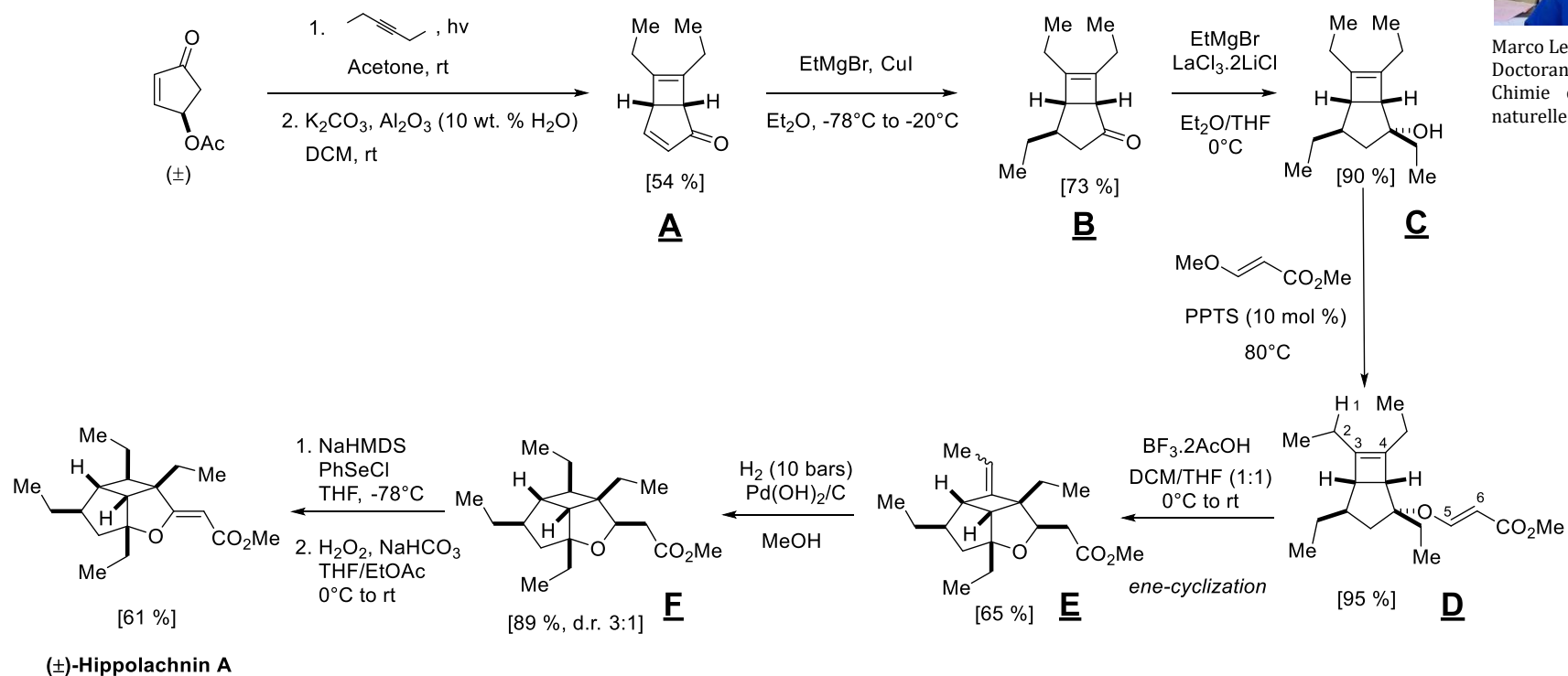




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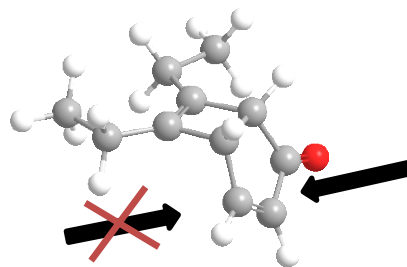
## Total synthesis of ( $\pm$ )-Hippolachnin A



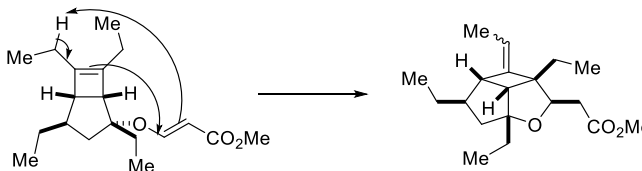
Ruider *et al.*, *Angewandte Chemie*, 2014, 127 (8), 2408

1. Explain the diastereoselectivity from **A** to **B**.
2. Explain the roles played by  $\text{LaCl}_3 \cdot 2\text{LiCl}$  during the transformation of **B** to **C**.
3. What are the reactions involved in the transformation of **C** to **D**?
4. Give the mechanism of the ene reaction involved in the cyclization of **D**.  
(Ene reaction on Organic Chemistry Portal: <http://www.organic-chemistry.org/namedreactions/alder-ene-reaction.shtml>)
5. Explain the diastereoselectivity from **E** to **F**.
6. Give the mechanism of the selenoxide *syn*-elimination which gives ( $\pm$ )-Hippolachnin A.

- The organocuprate reagent attacks the less sterically hindered face of **A**. **A** is concave, as shown hereafter, so the nucleophile attacks the “open” face of the compound.



- $\text{LaCl}_3 \cdot 2\text{LiCl}$  serves as a Lewis acid to complex and activates the carbonyl oxygen. It can also be hypothesized that  $\text{LiCl}$  helps creating *in situ* “Turbo-Grignards” to enhance Grignard’s reagent nucleophilicity.
- Reaction involves an addition/elimination sequence catalysed by PPTS. The alcohol nucleophile adds to the electrophilic compound through a Michael addition giving the ketene hemiacetal which interconverts into the  $\alpha,\beta$ -unsaturated ester by elimination of methanol.
- The “ene-reaction” is a cycloaddition reaction analogous to the Diels-Alder one.



- Hydrogenation reactions are very sterically sensitive. Therefore, they attack the less hindered side of the molecule. It is also possible that the intracyclic oxygen orientates the Pd for the hydrogenation.

6.

