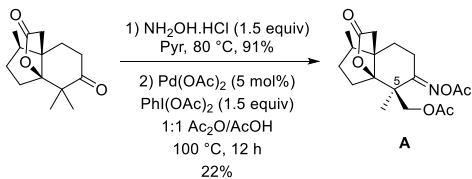


Exercise session: Solutions– 11.04.2019 – Alexandre Leclair

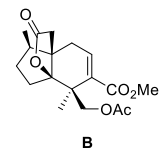
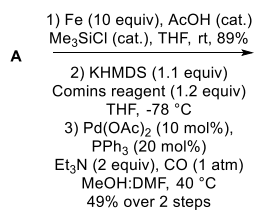
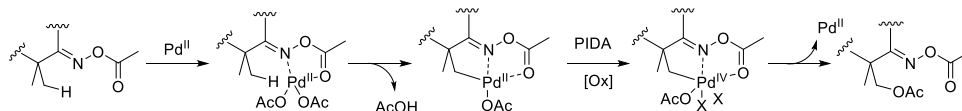
Exercise 1 Sorensen *et al.*, *Angew. Chem. Int. Ed.* **2014**, 53, 5332–5335



C-H activation using Sanford's methodology
(*J. Am. Chem. Soc.* **2004**, 126, 9542–9543;
Org. Lett. **2010**, 12, 532–535)
Bad yield due to the C-H activation of the diastereotopic CH_3
(Epimeric at C_5) + small amount of the double C-H activated product

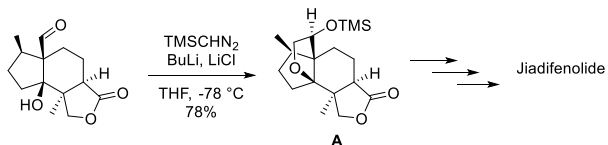
Mechanism ?

Possible mechanism:



1) Oxime hydrolysis to the ketone via Weinreb's method
(*Tetrahedron Lett.* **2010**, 51, 3555–3557)
2) Vinyl triflate formation
3) Methyl ester formation via Pd-cat. alkoxyacylation

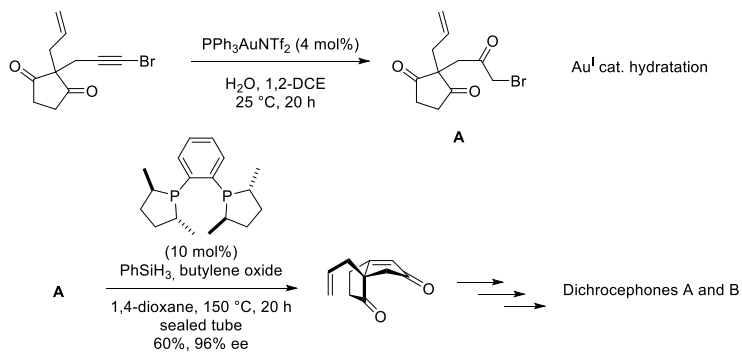
Exercise 2 Zhang *et al.*, *Org.Lett.* **2015**, 17, 5480-548



Mechanism: See paper for detailed mechanism

- 1) Deprotonation of the TMSCHN_2 with BuLi
- 2) Chelation of the aldehyde + alcohol with LiCl
- 3) Addition to the aldehyde
- 4) 1,2-Brook rearrangement
- 5) Proton transfer
- 6) Addition of the alkoxide to the carbene followed by protonation OR O-H insertion after protonation

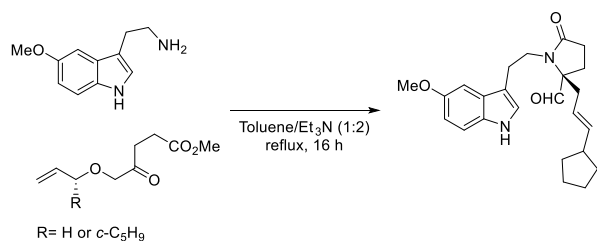
Exercise 3 Tantillo, Christmann *et al.*, *Angew. Chem. Int. Ed.* **2018**, *57*, 2419–2422



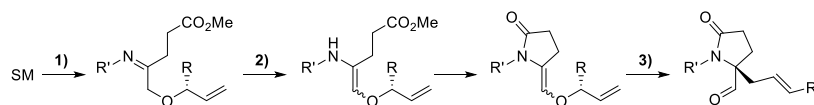
Mechanism: Enantioselective catalytic Wittig reaction using Werner's methodology
(*Eur. J. Org. Chem.* 2014, 6630–6633)

- [(S,S)-Me-DuPhos]: gave the best ee
- PhSiH₃: used to regenerate the phosphine
- butylene oxide: used as a masked base: after substitution of the bromide by the phosphine, opening of the epoxide by the bromide, generate an alkoxide which acts as a base to deprotonate the phosphonium

Exercise 4 Echevarren *et al.*, *J. Am. Chem. Soc.* **2016**, *138*, 3671-367



Mechanism: For detail mechanism see the publication

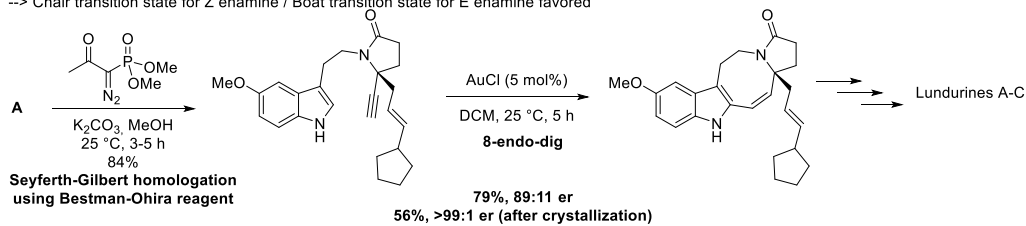


- 1) Condensation of the amine with the ketone
- 2) Tautomerization imine/enamine and cyclization on the methyl ester to form the pyrrolidinone
- 3) Claisen rearrangement with transfer of chirality from the R group

Basic conditions important to avoid Pictet-Spengler pathway

Mixture of Z/E enamine (in favor of E) but to explain the good er authors proposed:

--> Chair transition state for Z enamine / Boat transition state for E enamine favored



Exercise 5 Maimone *et al.*, *Science* 2016, 352, 1078-1082

