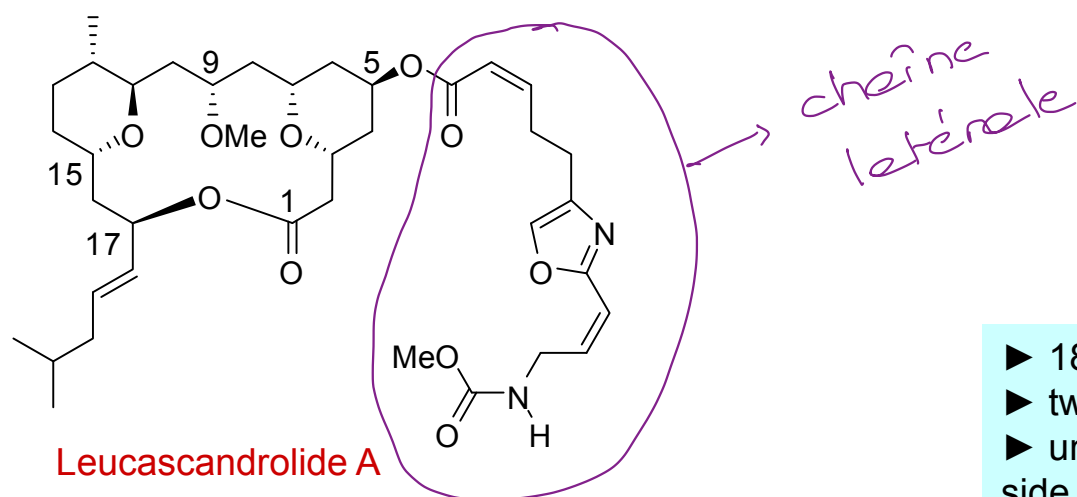


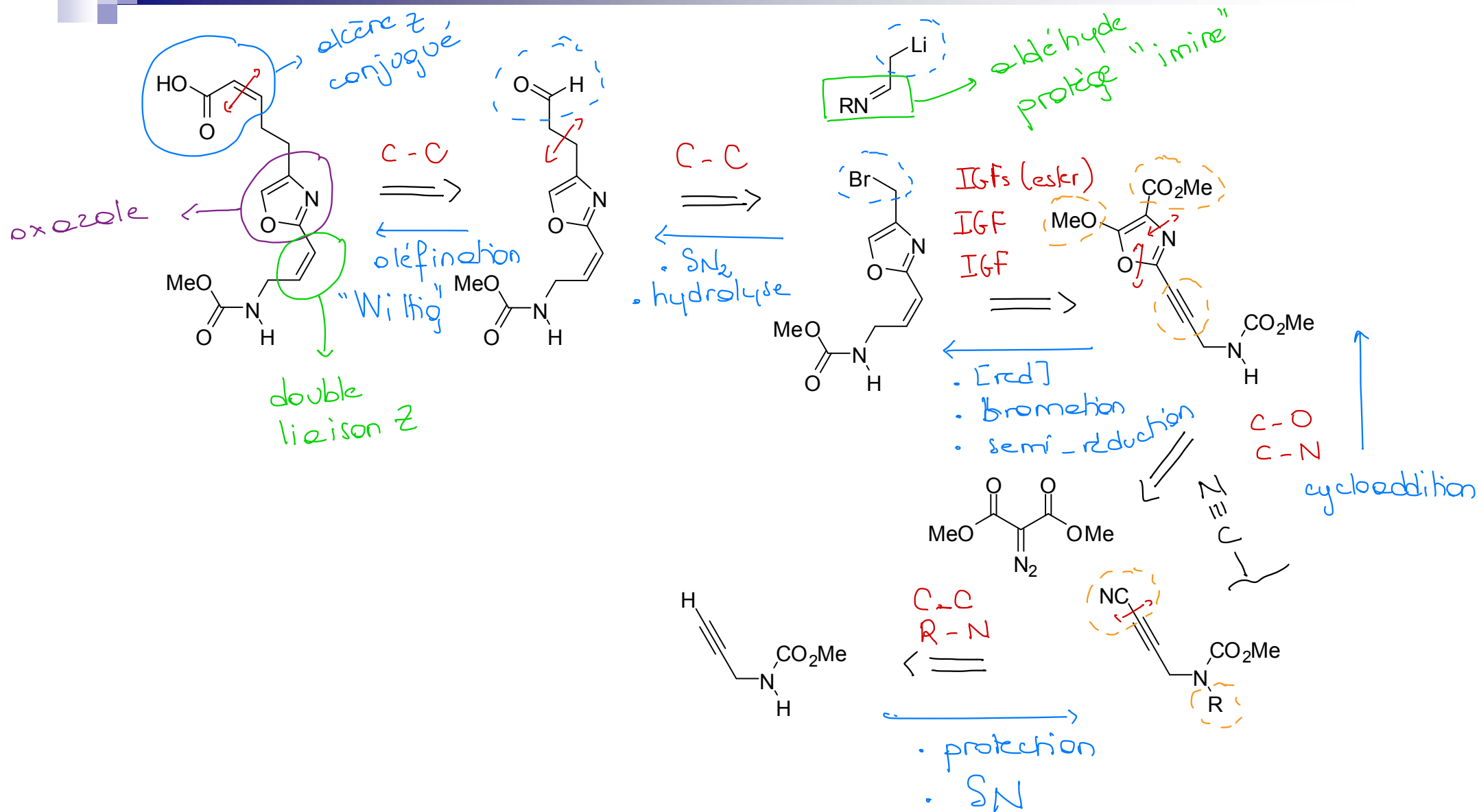


- 18-membered macrolide ring
- two substituted tetrahydropyran rings
- unsaturated oxazole containing side chain

- Extracted in 1996 from sponges of the genus *Leucascandra caveolata*
- Potent cytotoxicity against KB and P388 tumor cell lines
- Strong inhibition of the pathogenic yeast *Candida albicans*

Kozmin, S.A. *Org. Lett.* **2001**, 3, 755-758. Wang, Y.; Janjic, J.; Kozmin, S.A. *J. Am. Chem. Soc.* 2002, 124, 13670-13671. Su, Q.; Panek, J.S. *Angew. Chem. Int. Ed.* **2005**, 44, 1223-1225.

Leucascandrolide A - Retrosynthesis



$\sqrt[3]{}$

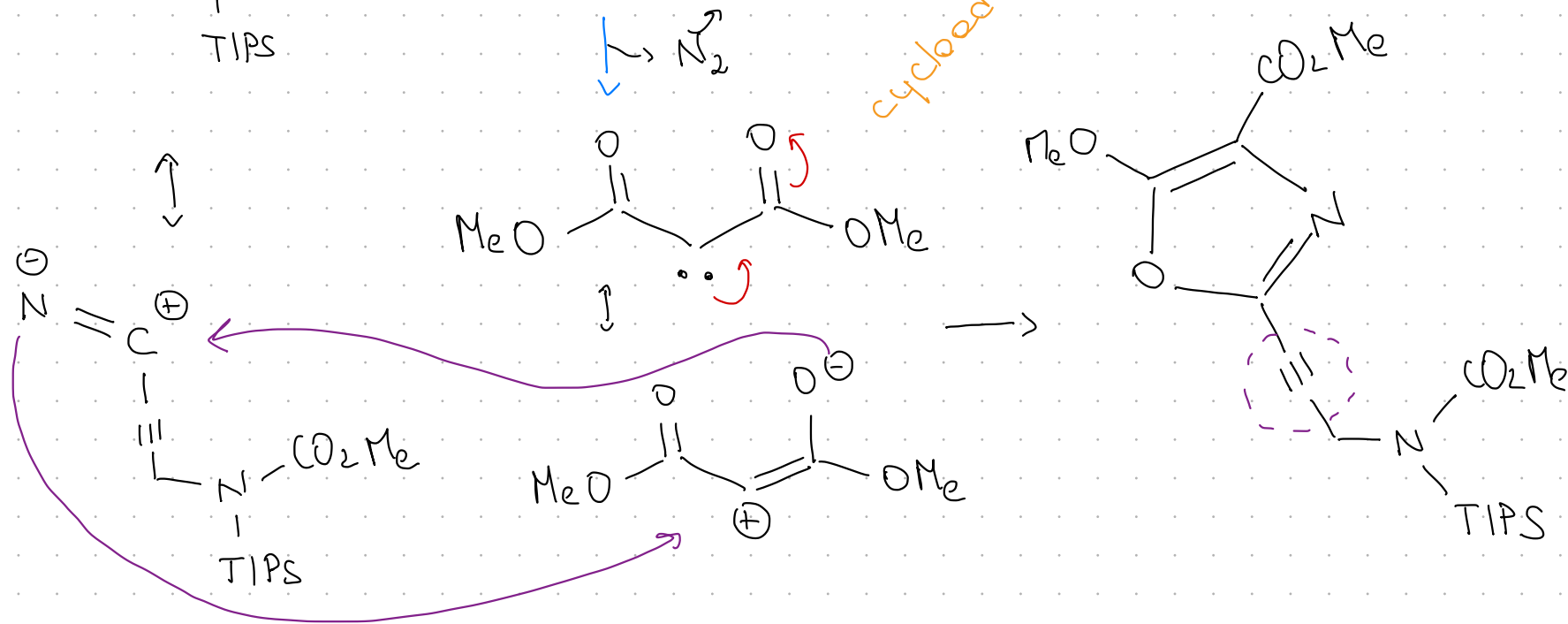
CC(=O)N(C)C

 H pKa v 2S

H
|
||
I—N—CO₂Me
|
TIPS

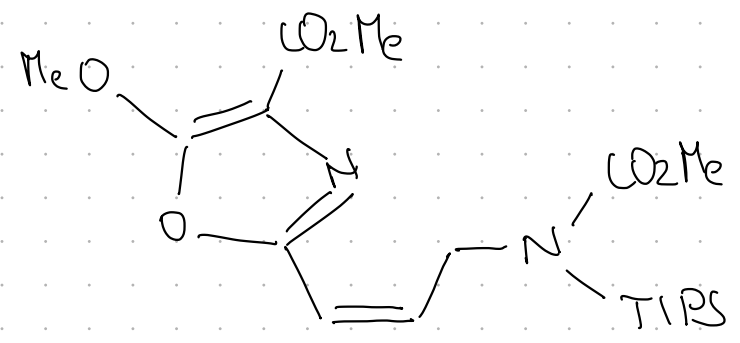
1. LiN⁻L
—————>
-78°C
deprotonation

2. TsCN
←—————>
substitution

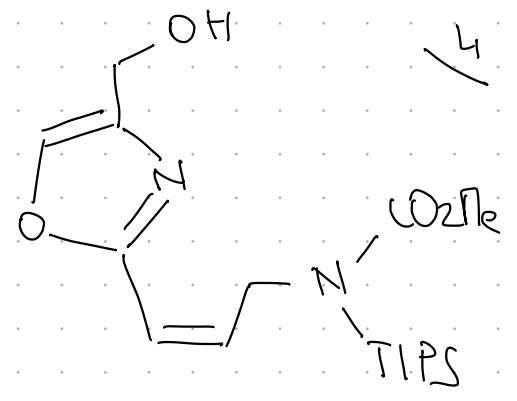


H₂
Pd Lindlar cat.
→

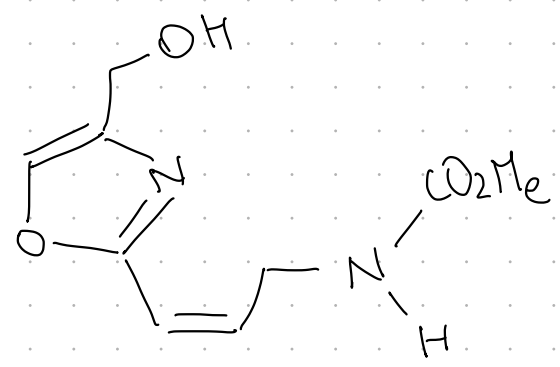
semi-reduction
stereoselective



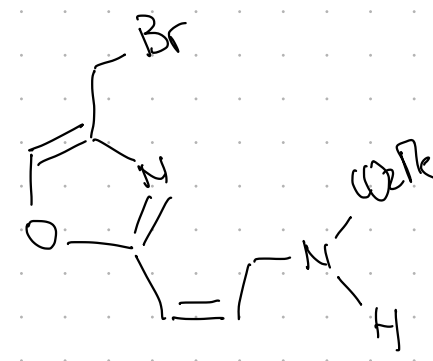
Et₂BH Li
[red]
fort
→



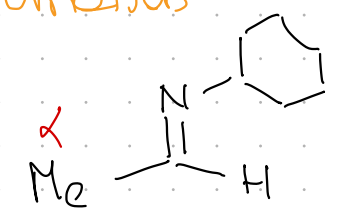
Bu₄NF
couper groupe
protecteur
→



CBr₄ ; PPh₃
bromation
→



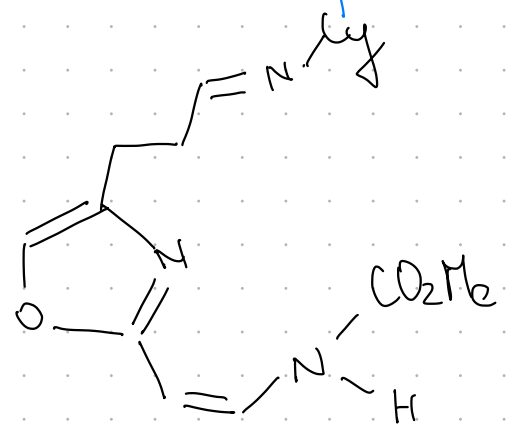
Me-C(=O)-H
[]-NH₂
p-TsOH cat.
→



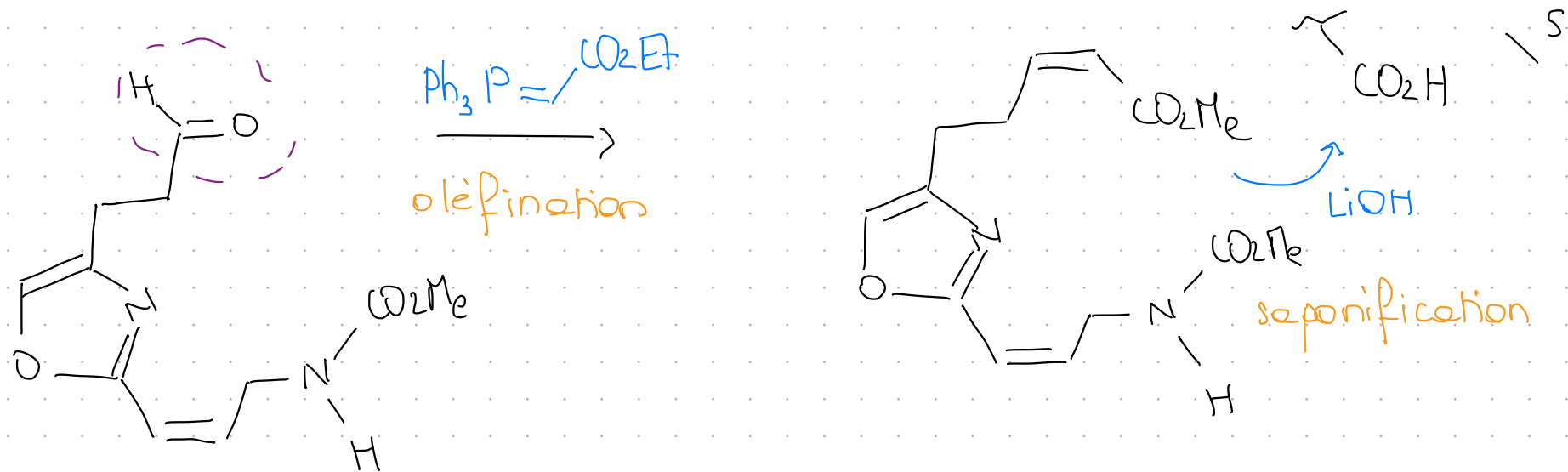
Et₂NLi
→



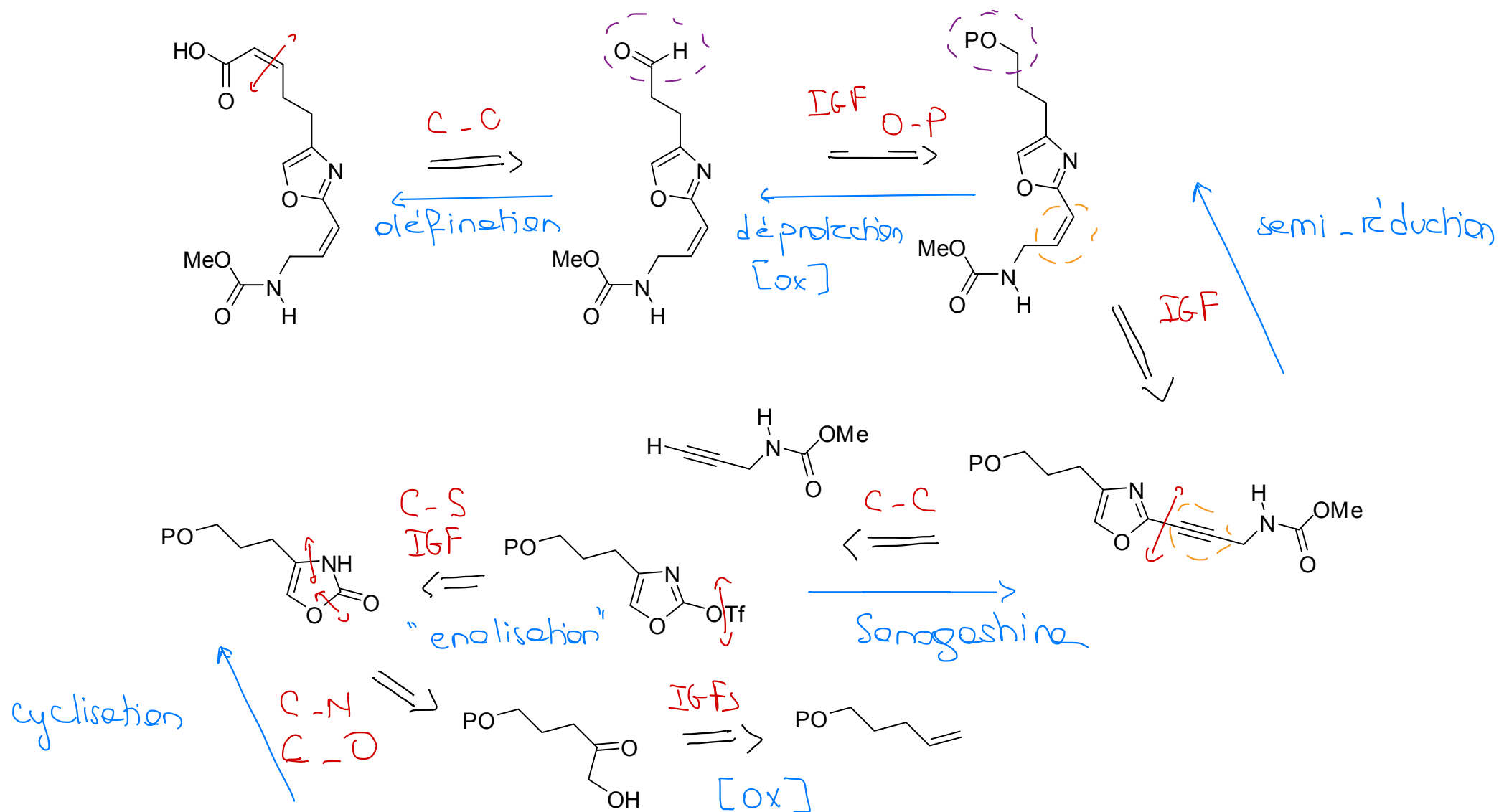
H₂O, H⁺ cat.
hydrolyse
↓

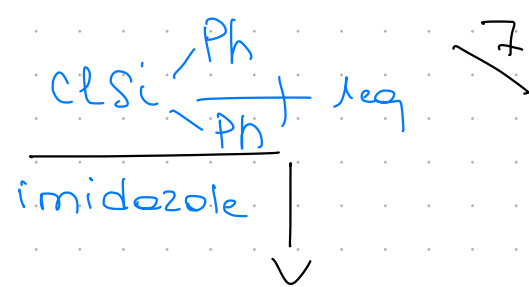
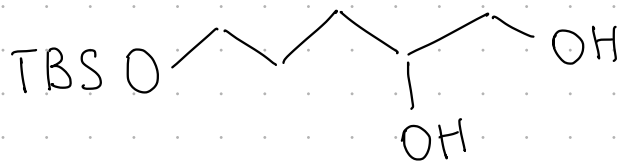
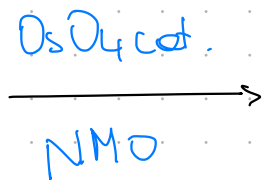
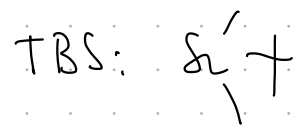
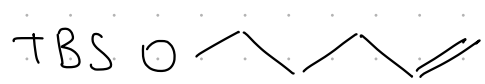


"S_N2"
←

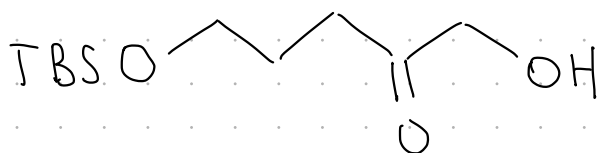
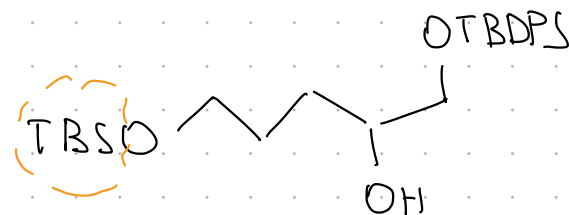
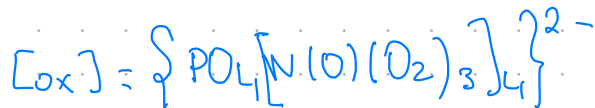


- 8 étapes linéaires
- 13% rendement global

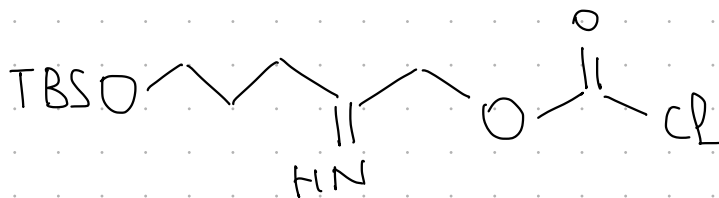
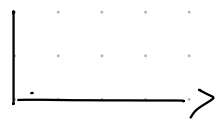
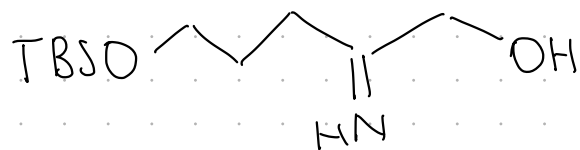
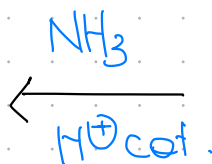




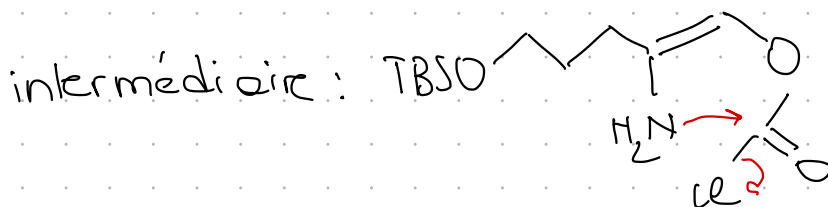
oxydation
selective

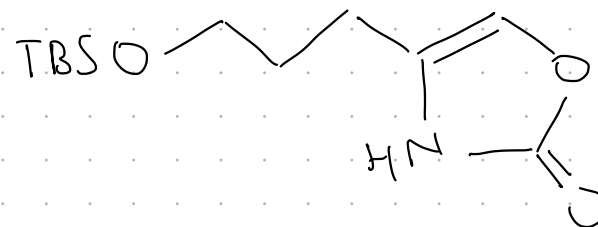
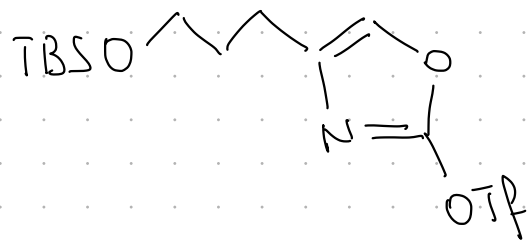


1. Swern
2. BO_4NF

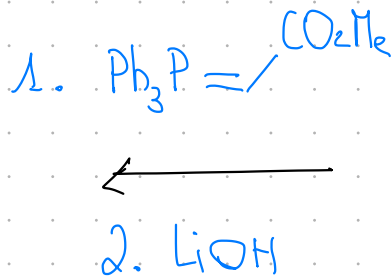
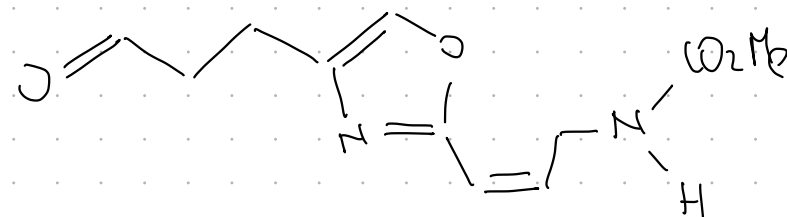
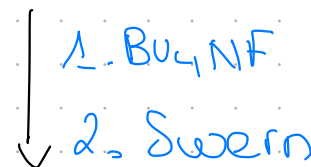
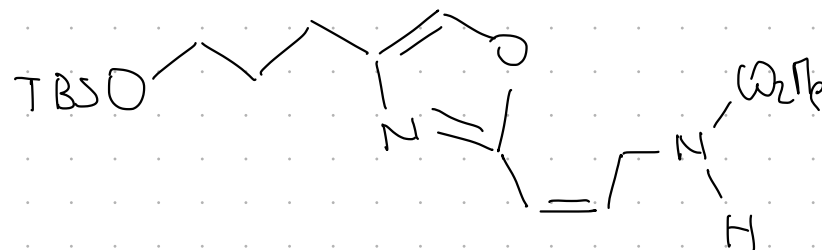
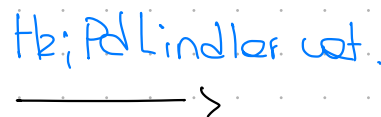
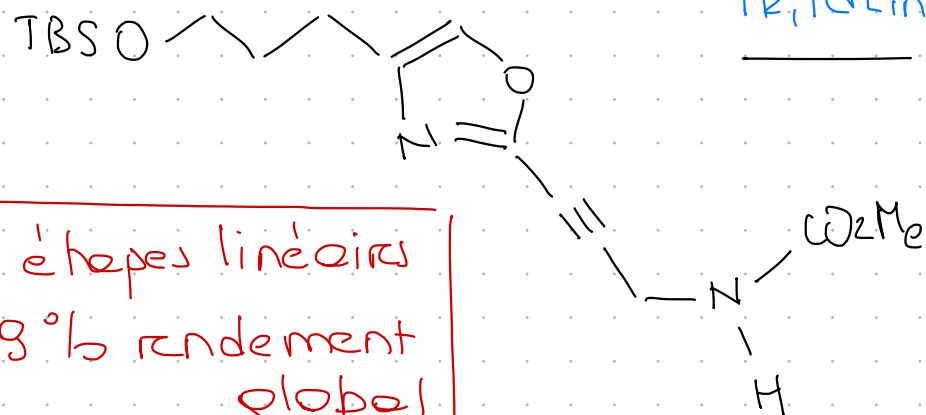
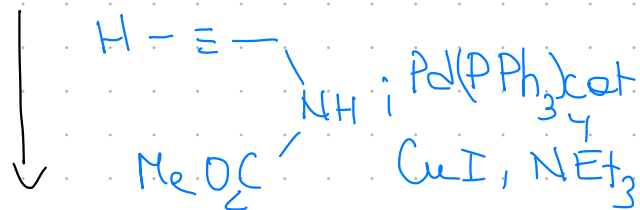


$\xrightarrow[\text{isom\`erisation cyclisation}]{\text{H}_2\text{SO}_4 \text{ cat.}}$





couplage de
Sonogashira



Moécule cible

12 étapes linéaires
29% rendement global