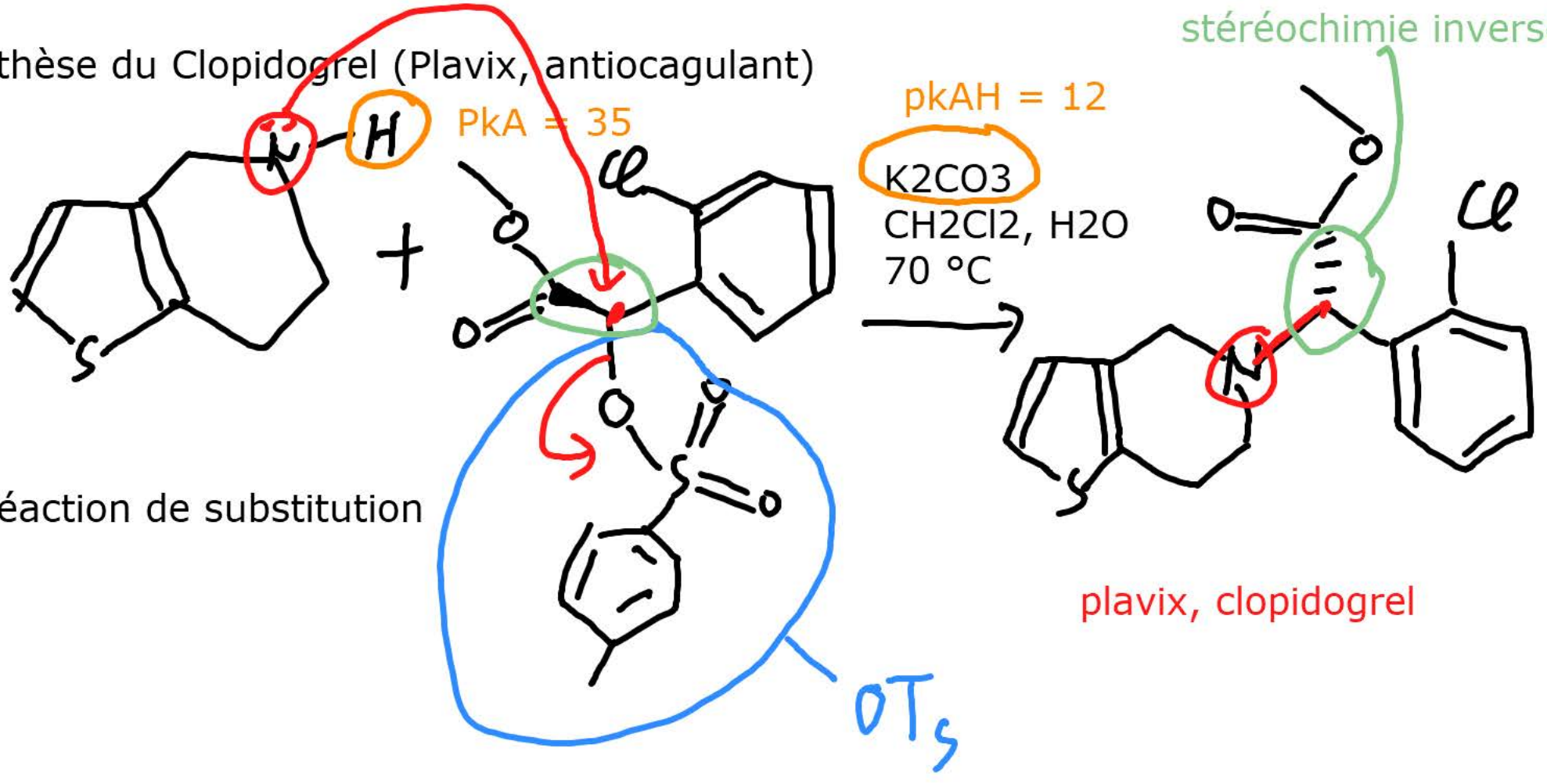
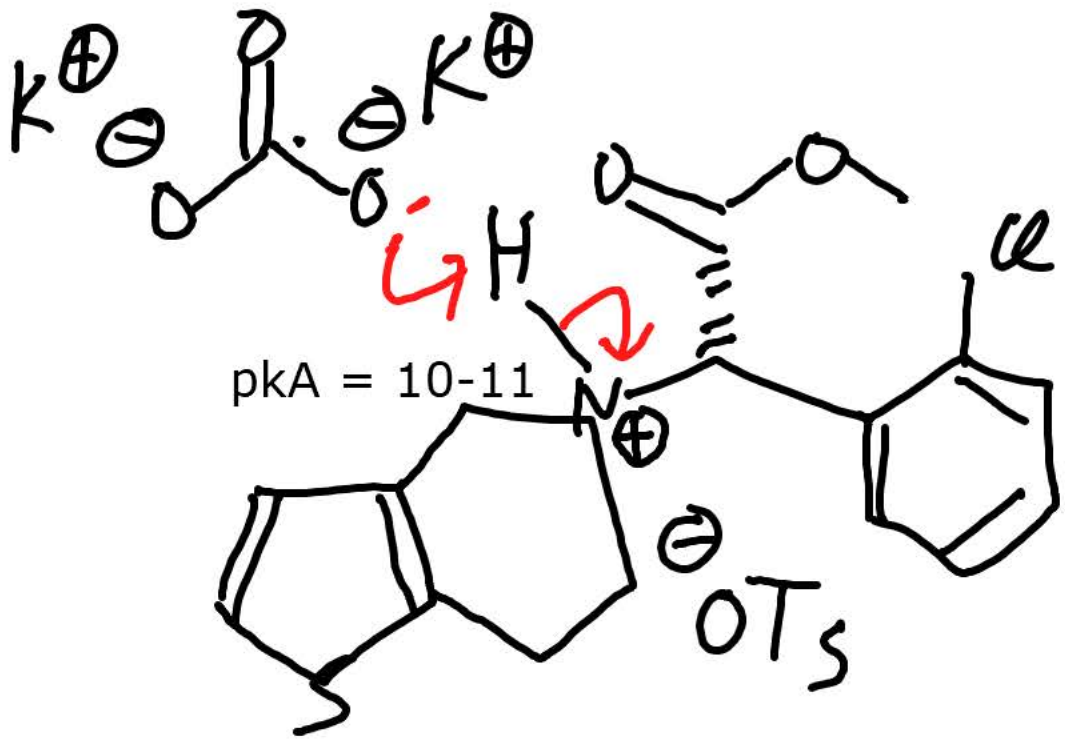
synthèse du Clopidogrel (Plavix, antiocagulant)



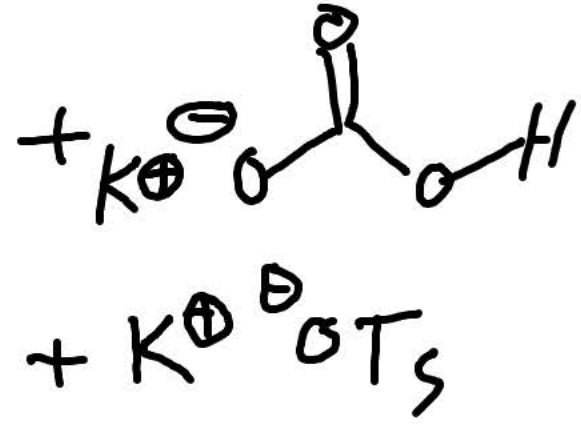
réaction de substitution

plavix, clopidogrel

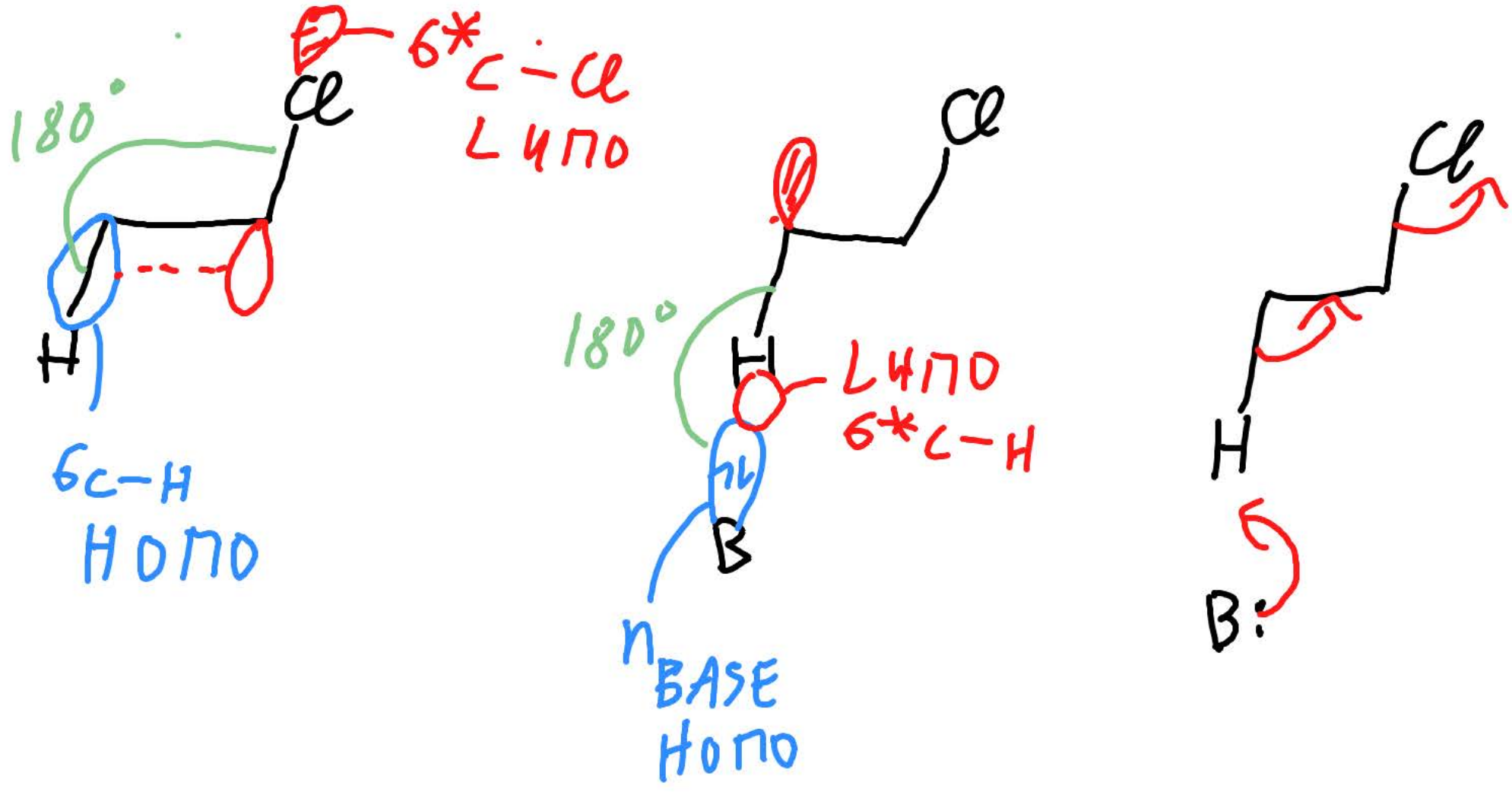
OTs: bon group partant (nucléofuge)

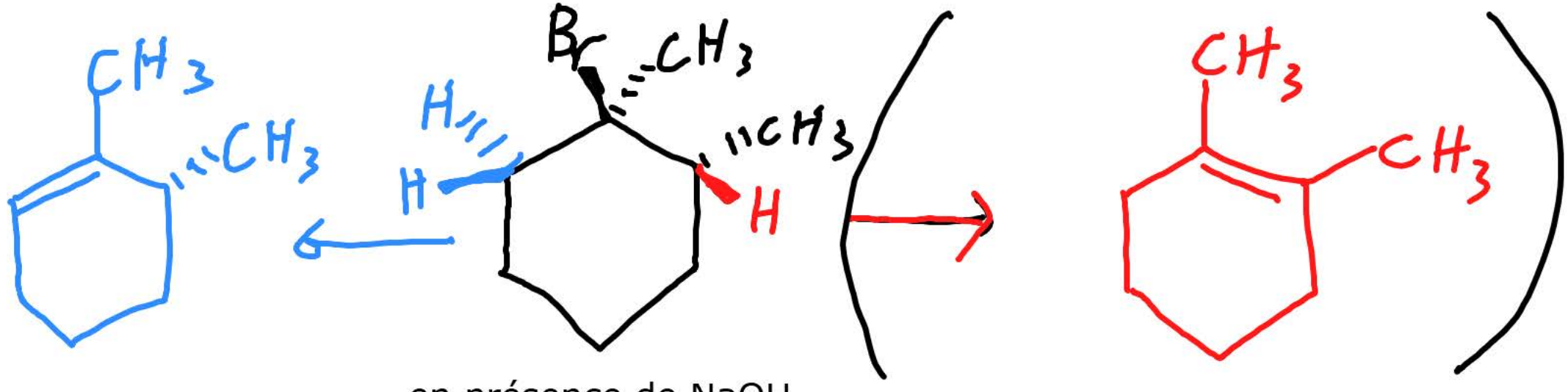


clopidogrel



élimination E2, orbitales moléculaires

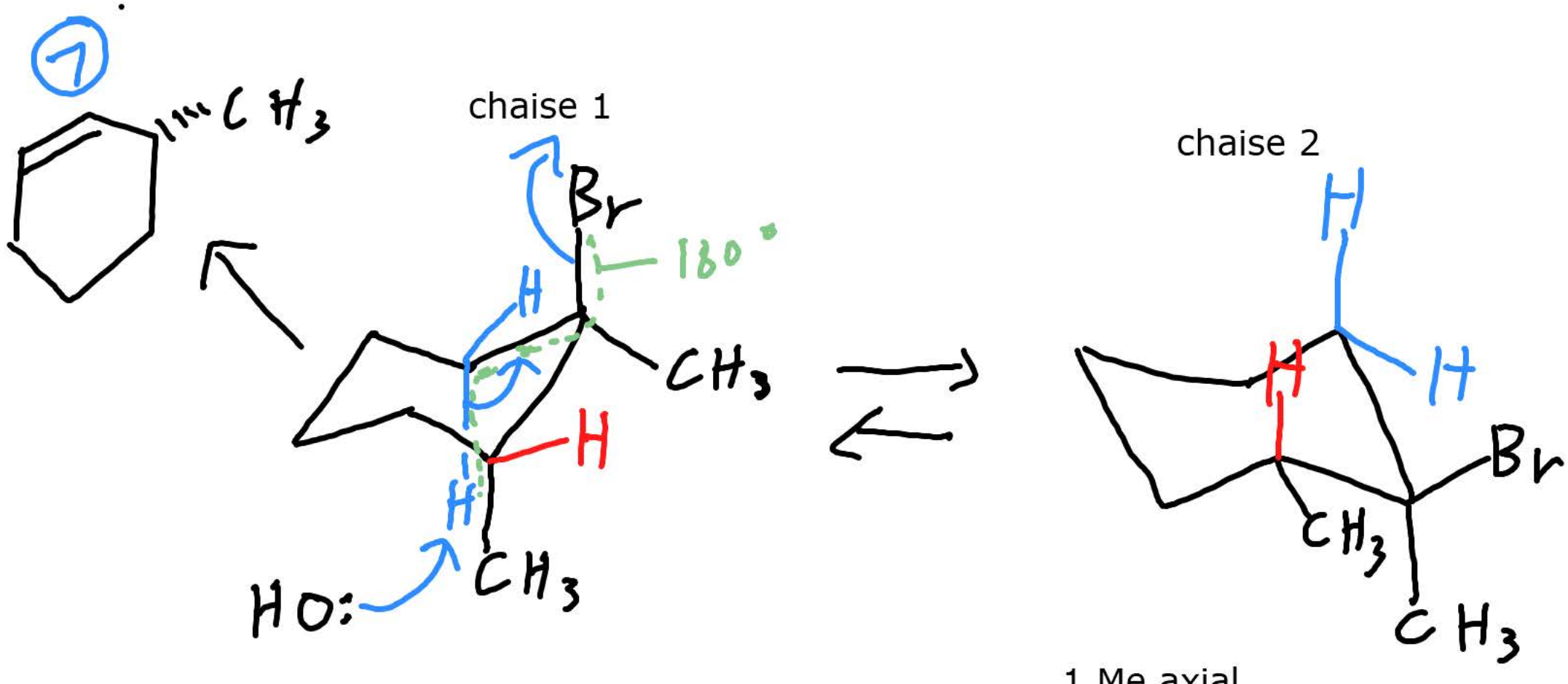




en présence de NaOH

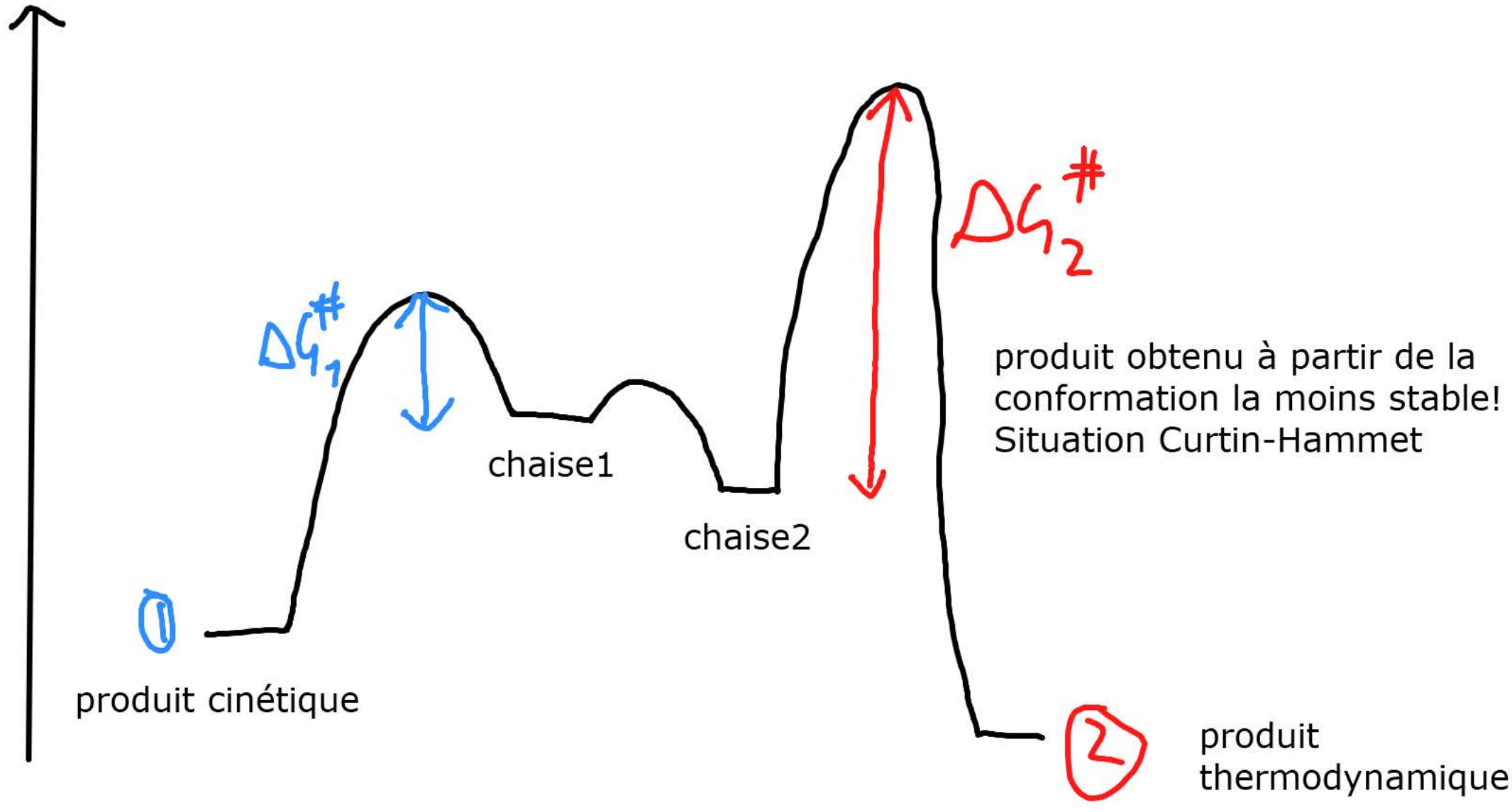
alcène trisubstitué
moins stable
produit observé!
Produit cinétique.

alcène tétrasubstitué
plus stable
produit thermodynamique

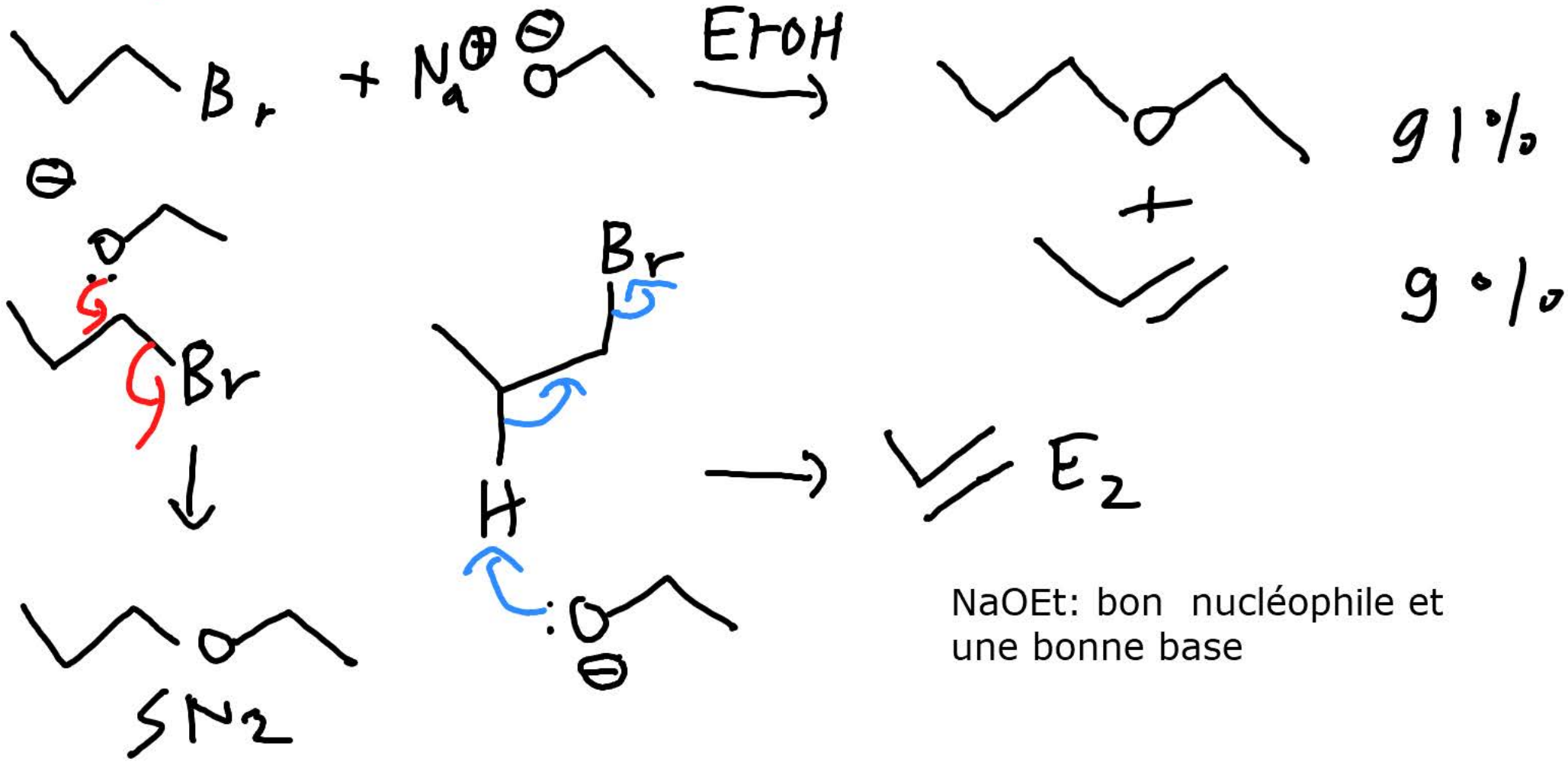


1 Me, 1 Br axial
1 Me équatorial

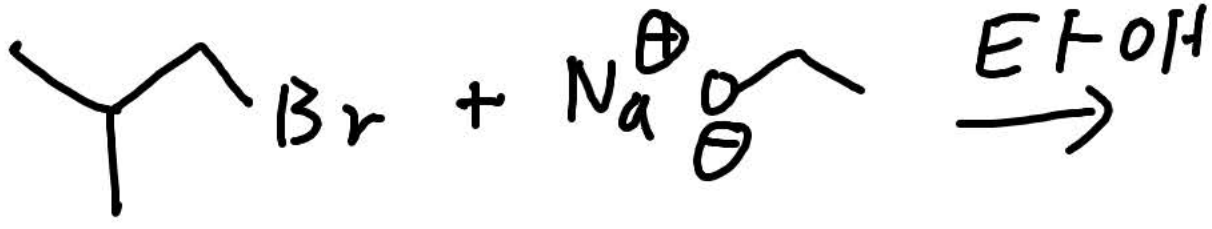
1 Me axial
1 Me et 1 Br équatorial
plus stable!


$\Delta G_1^{\#}$
$\Delta G_2^{\#}$
chaise1
chaise2
1
2
produit cinétique
produit obtenu à partir de la conformation la moins stable! Situation Curtin-Hammet
produit thermodynamique

Sn vs E: influence du substrat: position primaire: plutôt SN2/E2



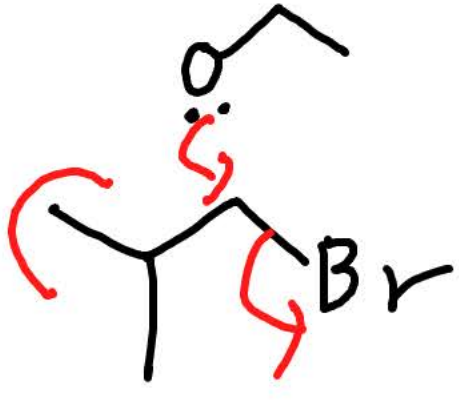
NaOEt: bon nucléophile et une bonne base



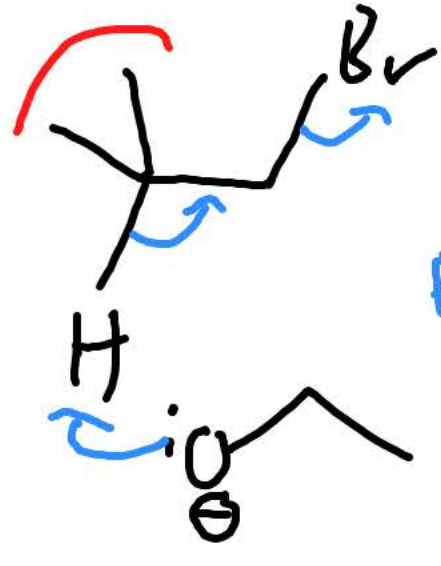
S_N2 40%

+

E_2 60%



S_N2



E_2

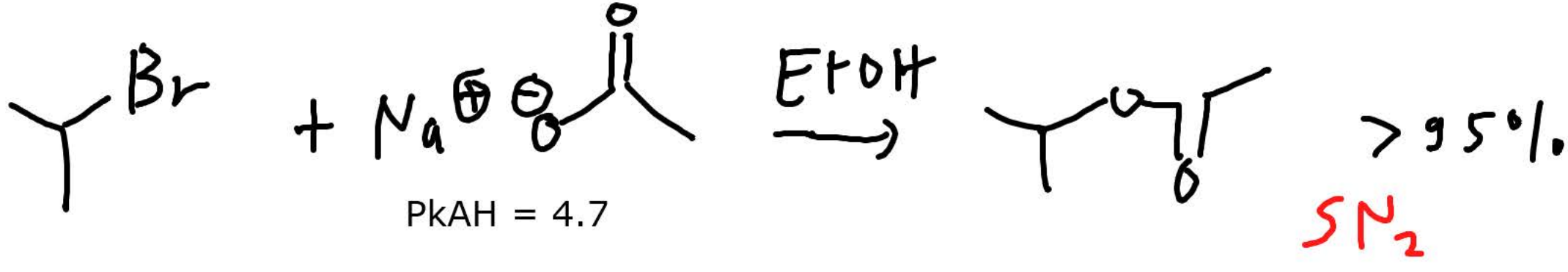
Sn est plus sensible à l'effet du group stérique que E! on devrait augmenter la proportion d'E2.

position secondaire

PkAH = 16

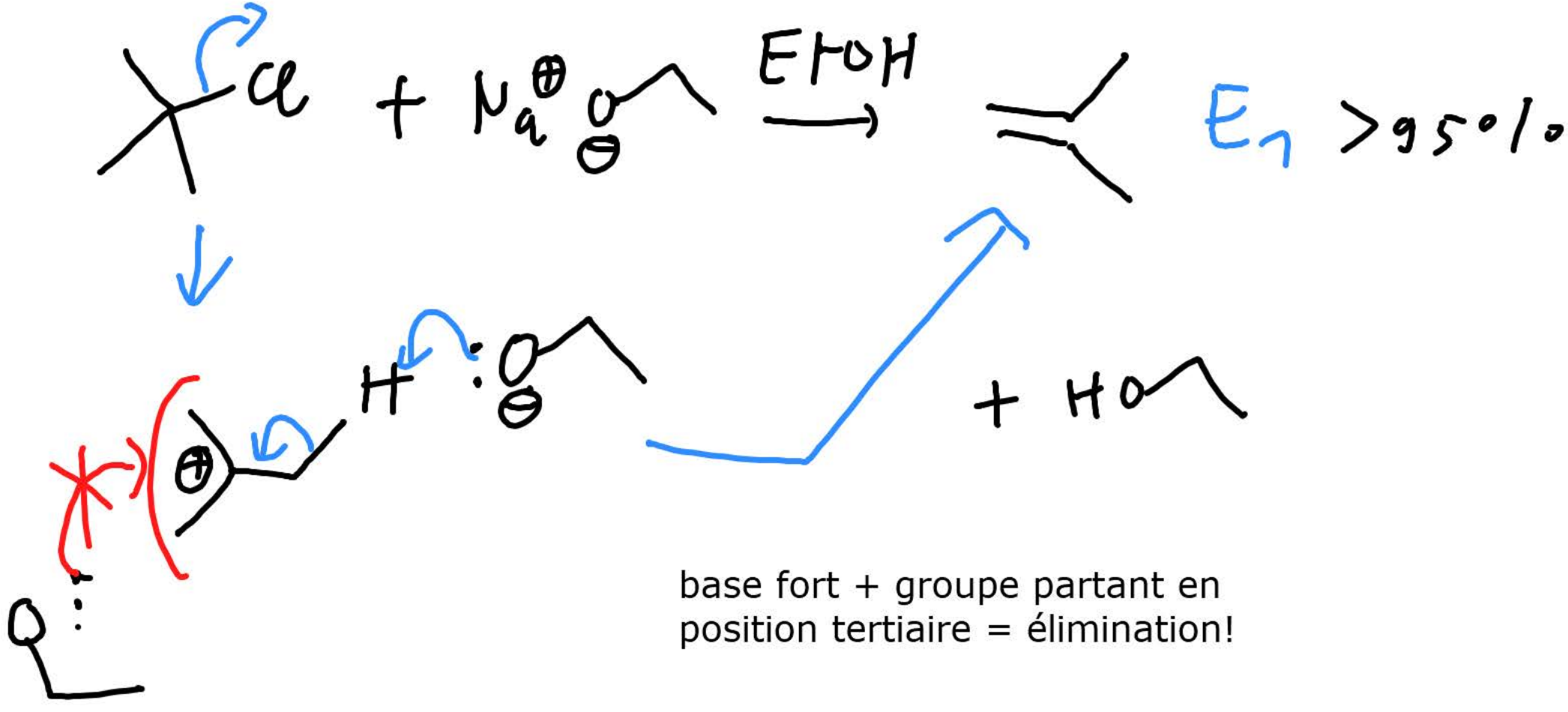
secondaire avec forte base:
E1/2 domine!

pour favoriser SN: il faut diminuer la basicité!

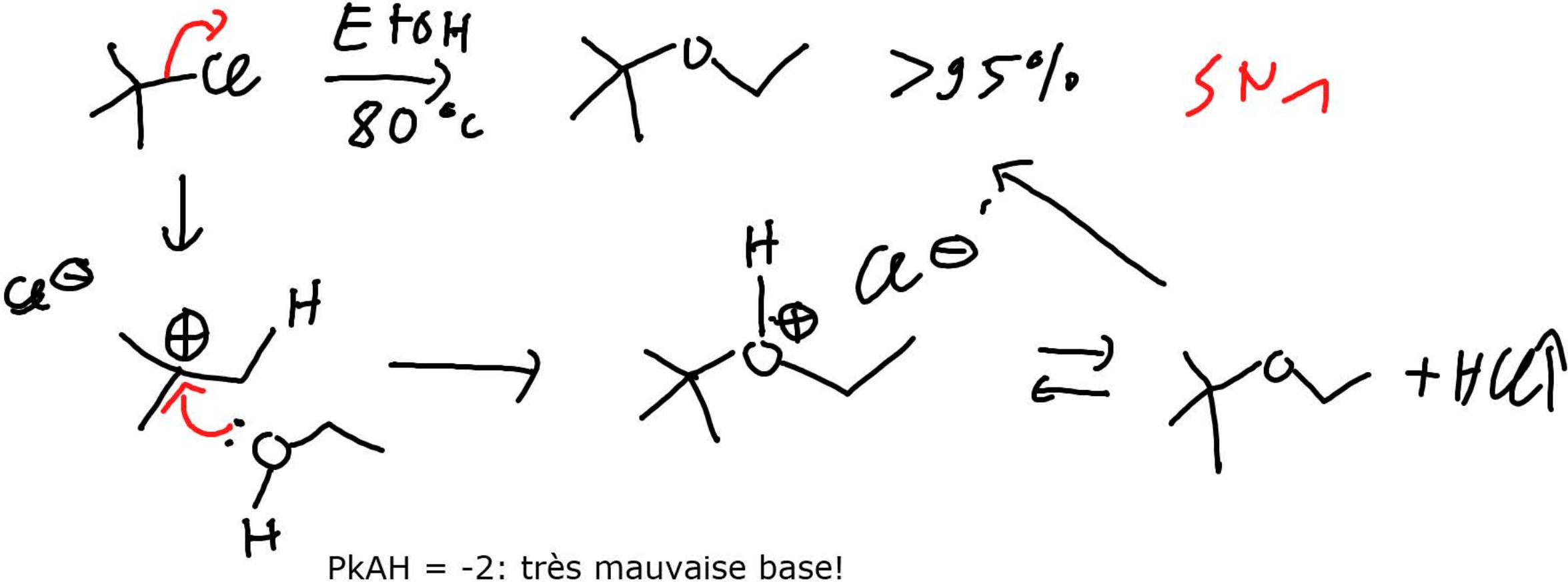


PkAH = 4.7

position tertiaire: E1 our SN1

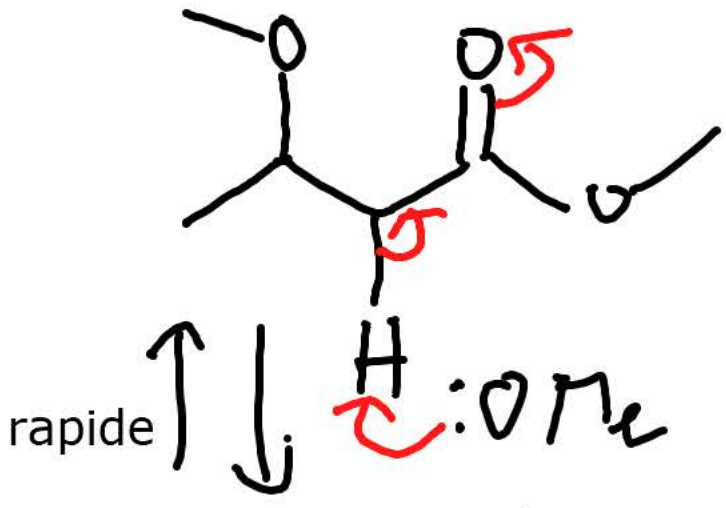


Pour SN1: réaction en absence de base

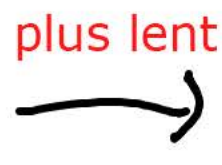


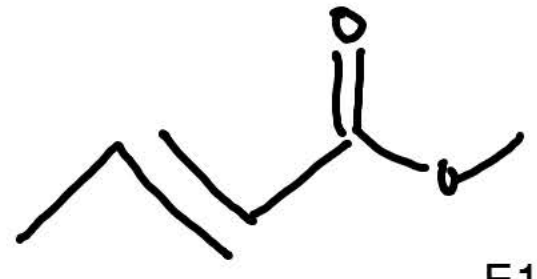
PkAH = -2: très mauvaise base!

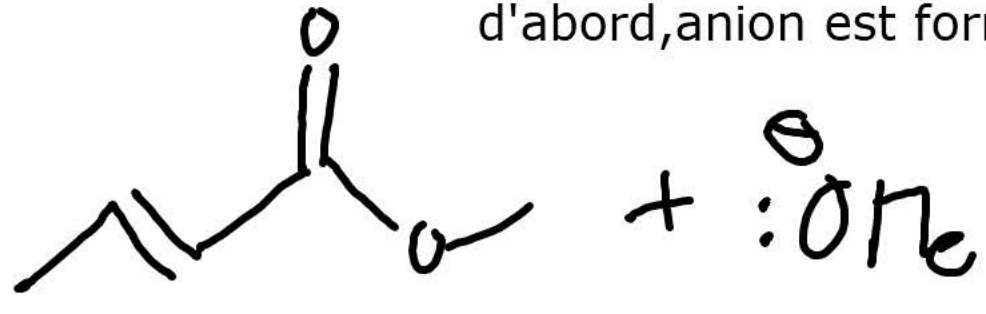
"5ème mécanisme" cas particulier E1cb des protons acides



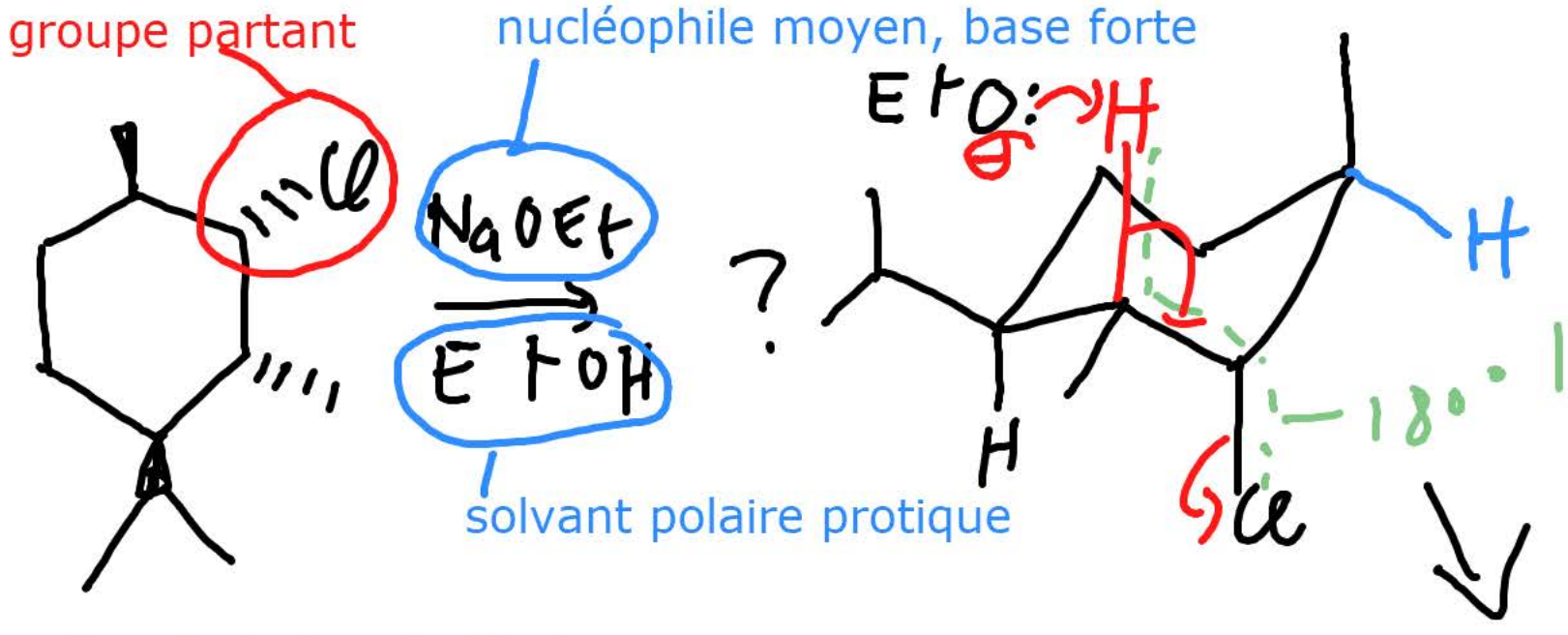
anion comme intermédiaire







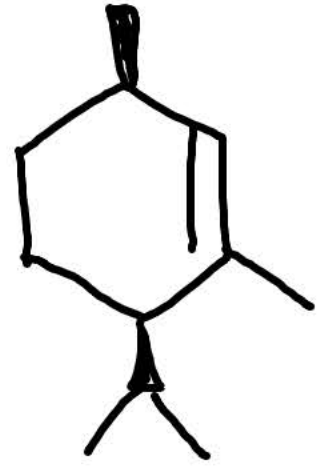
E1 : group partant d'abord, cation est formé
E1cb: déprotonation d'abord,anion est formé



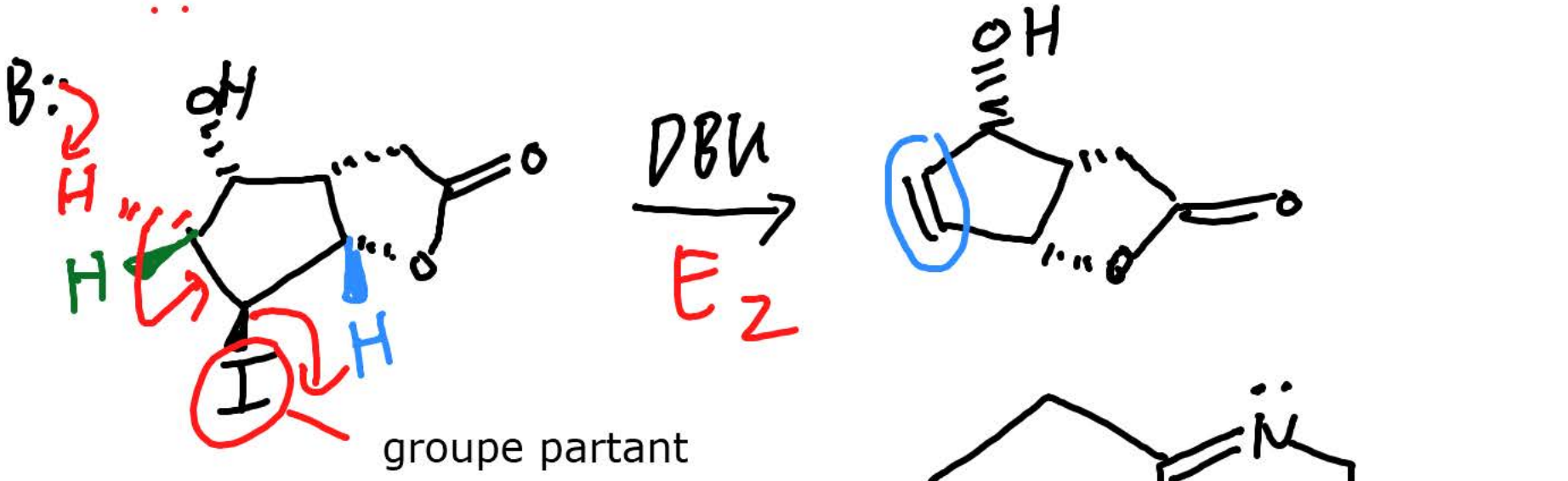
1) analyser le substrat: substitution ou élimination? position secondaire: les 2 possibles

2) conditions: forte base, solvent polaire protique: favorisent élimination: E2 si on peut atteindre l'angle idéal de 180°, sinon plutôt E1: on doit dessiner en 3D!

produit principal

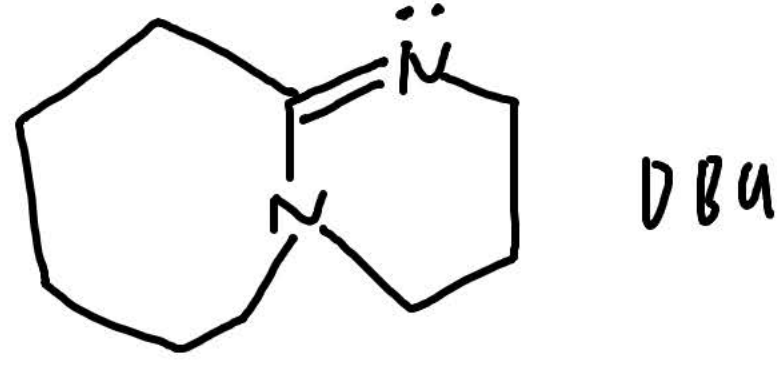


synthèse de produit naturel: prostaglandines (hormones naturelles)



groupe partant

cycle à 5 presque "plat", seul l'hydrogène rouge en trans/anti à le bon angle pour réagir.



DBU

bonne base, acide stabilisé par résonance, PkaH = 14