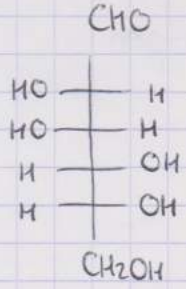
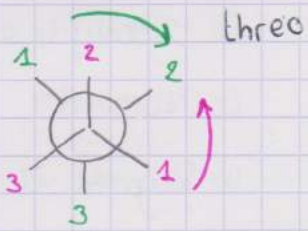
Fiche révision Stéréochimie I.

- Modèle Fisher : (par sucres)

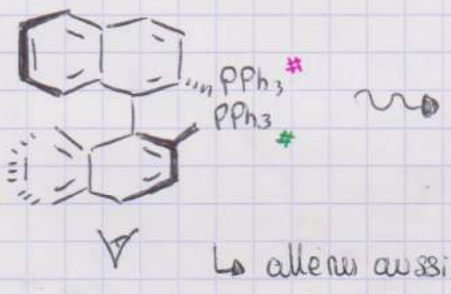


- OH du bas à { droite => (D) / gauche => (L) }

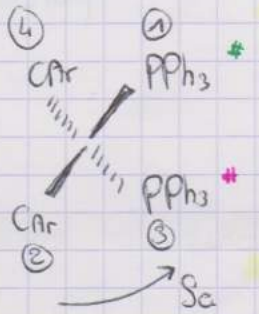


- 2OH du bas { même côté => erythro <= même sens Newman / côté opp => threo <= sans opp Newman }

- Chiralité axiale :



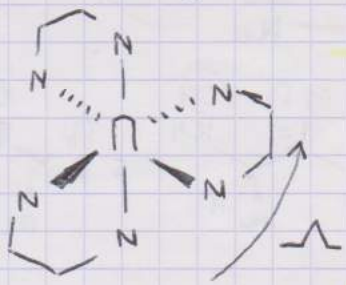
↳ allènes aussi



tourne de 2 → 3
- horaire => Ra
- trigo => Sa

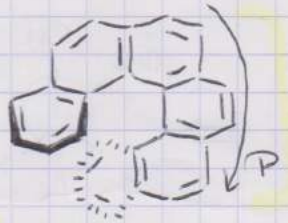
Atropoisomère : rotation autour liaison simple impossible

- Octaédrique tournante



tourne avant → arrière
- horaire : Δ (Delta) Droite
- trigo : Λ (Lambda) Left

- Hélicoïdale



tourne avant → arrière
- horaire : (P) : plus
- trigo : (M) : moins

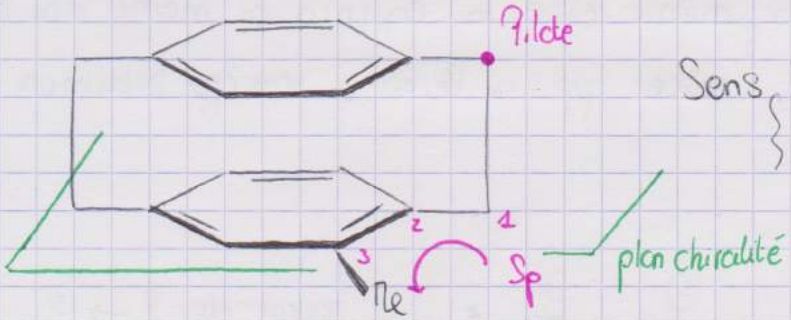
- Chiralité planaire :

① Déterminer plan chiralité (celui avec ⊕ atomes)

② Identifier atome (1er hors plan, directement lié au plan, ⊕ proche atome prio plan)

③ Numéroter : 1 : lié atome pilote, dans plan, 2 et 3 vers atome prioplan

④ Regarde depuis pilote :

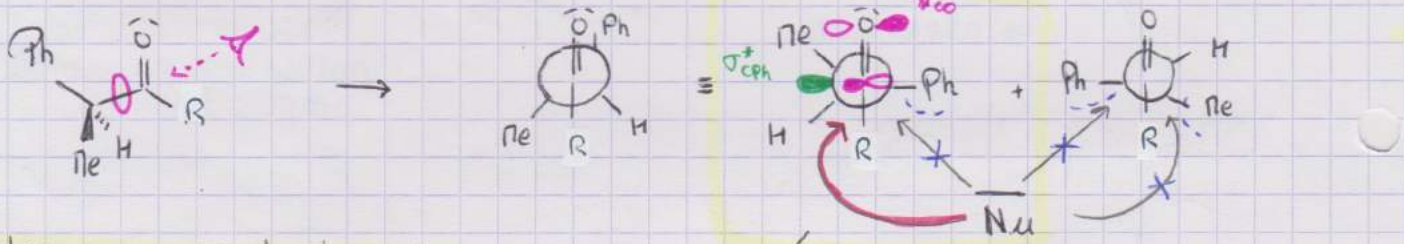


Sens { horaire : Rp
trigo : Sp

- Modèle Felkin - Ahn

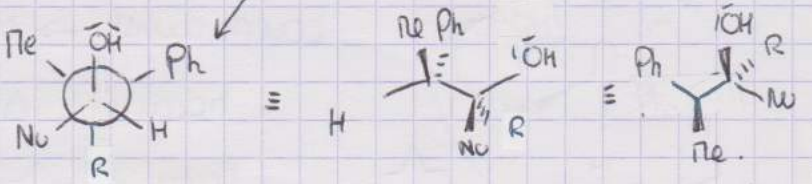
Gros orthogonal ⇒ ⊕ réactif

• Attaque d'un nucléophile sur un carbonyle



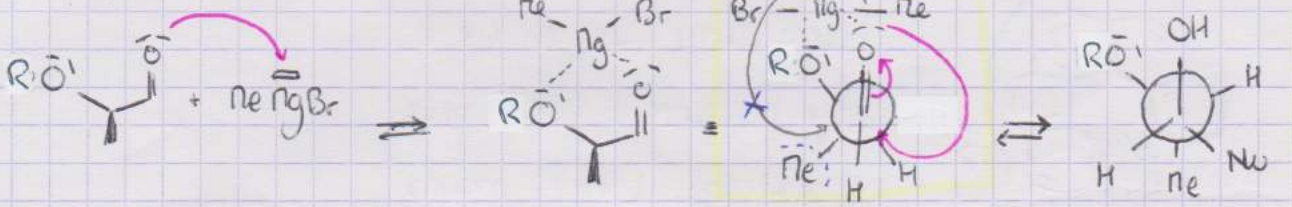
⚠ Hétéroatome prend place du gros groupe ± (orbitales)

⊕ R gros ⊕ Sélectif



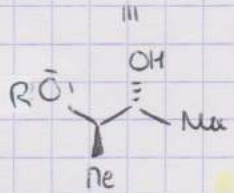
- Modèle Cram chelaté

• Si possibilité chélation Nu - carbonyle - autre groupe



⚠ Si R est trop gros : chélation impossible

↳ Felkin - Ahn

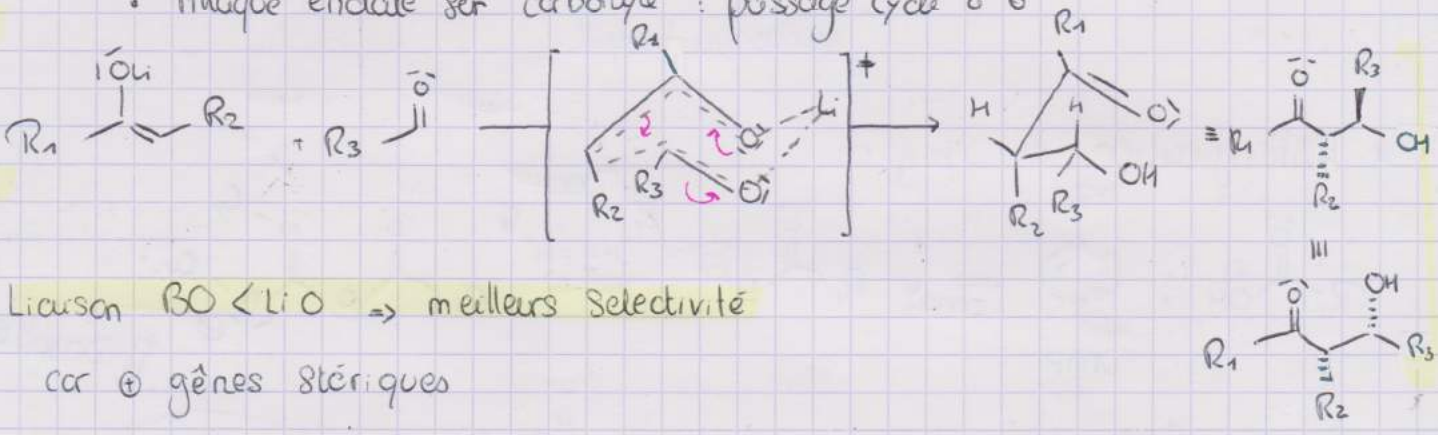


• Les contre-ions sont ± libre en fonction solvant

Fiche révision Stéréochimie II

- Modèle Zimmerman - Traxler

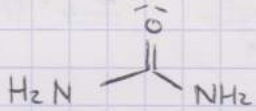
• Attaque enolate sur carbonyle : passage cycle à 6

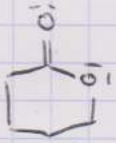


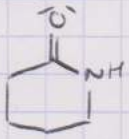
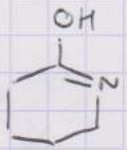
• Liaison BO < Li O => meilleurs sélectivité

car ⊕ gênes stériques

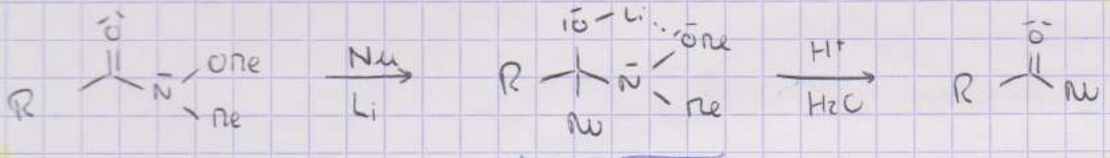
- Nomenclature:

• Urée : 

• Lactone 

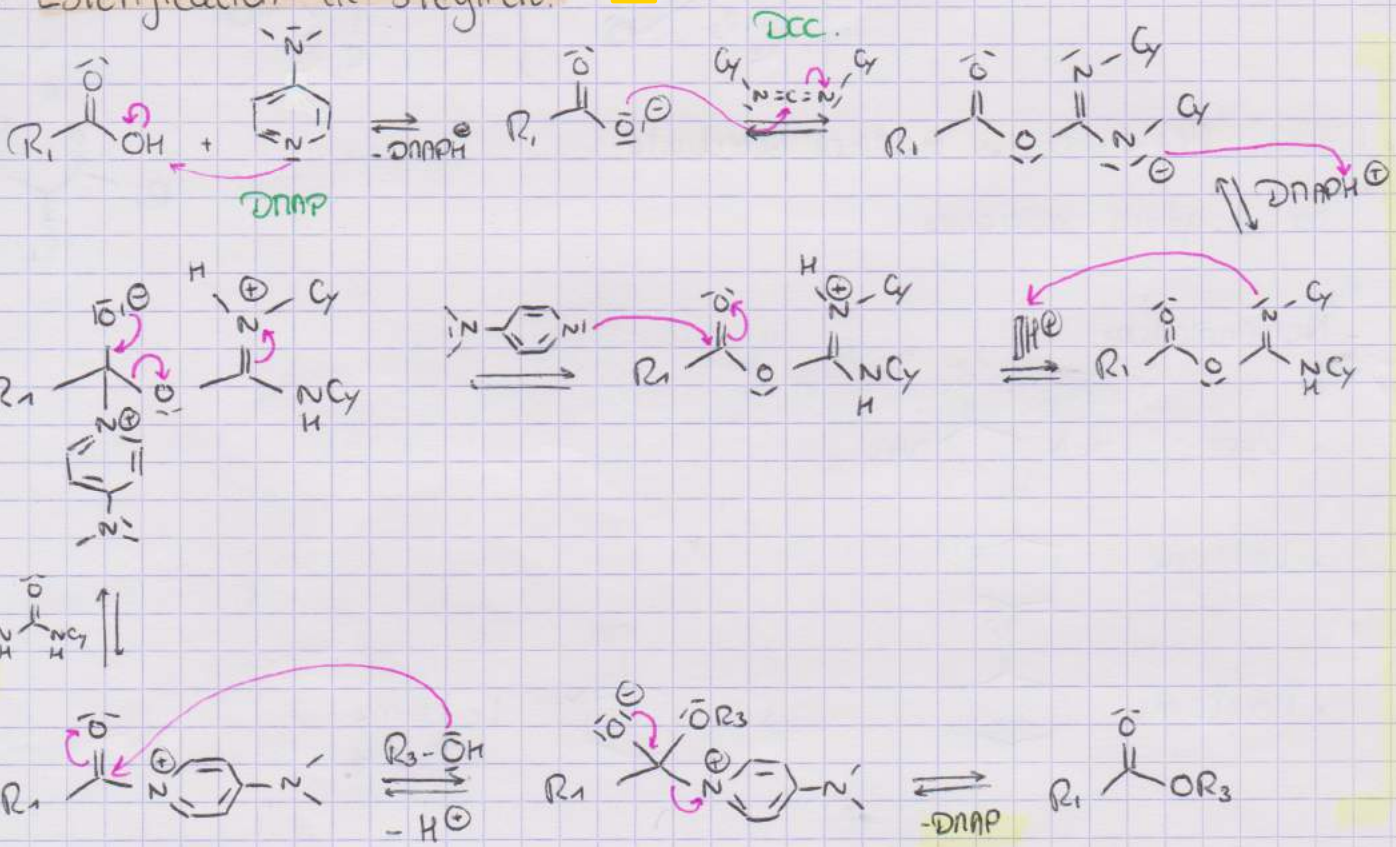
• Lactame  ⟷  Lactime

- Amine Weinreb: Permet de s'arreter à une unique addition



carbonyle bloqué

* Estérification de Steglich:

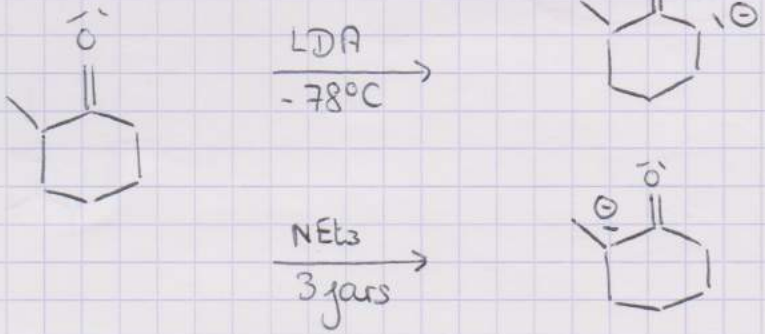


La fonctionne aussi par formation amide

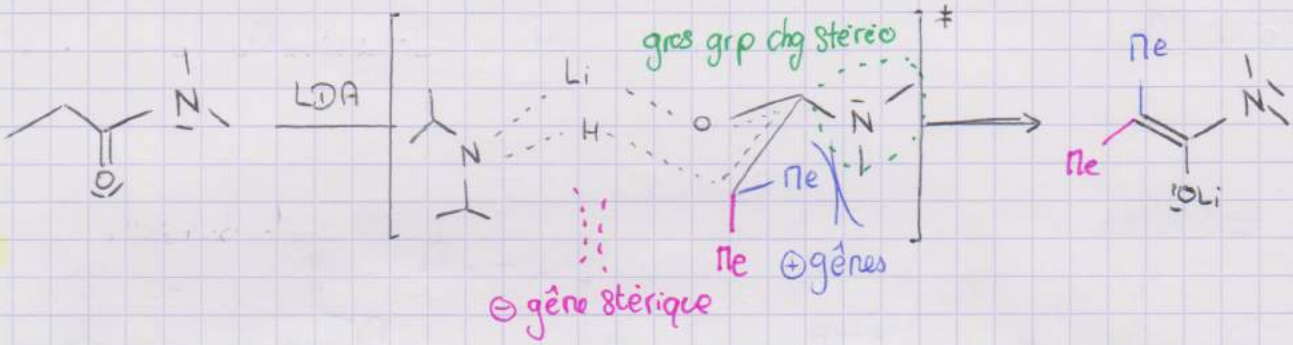
La DMAP est catalyseur nucléophile

Fiche Chimie Organique I.

- Chimie des énolates

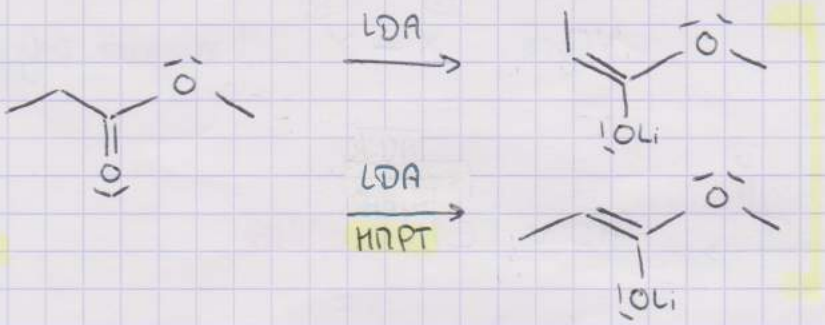


• Formation des énolates : modèle de Ireland (cycle à 6)



⚠ Si on ajoute un complexant type HMPT, on n'a plus Li => plus cycle à 6

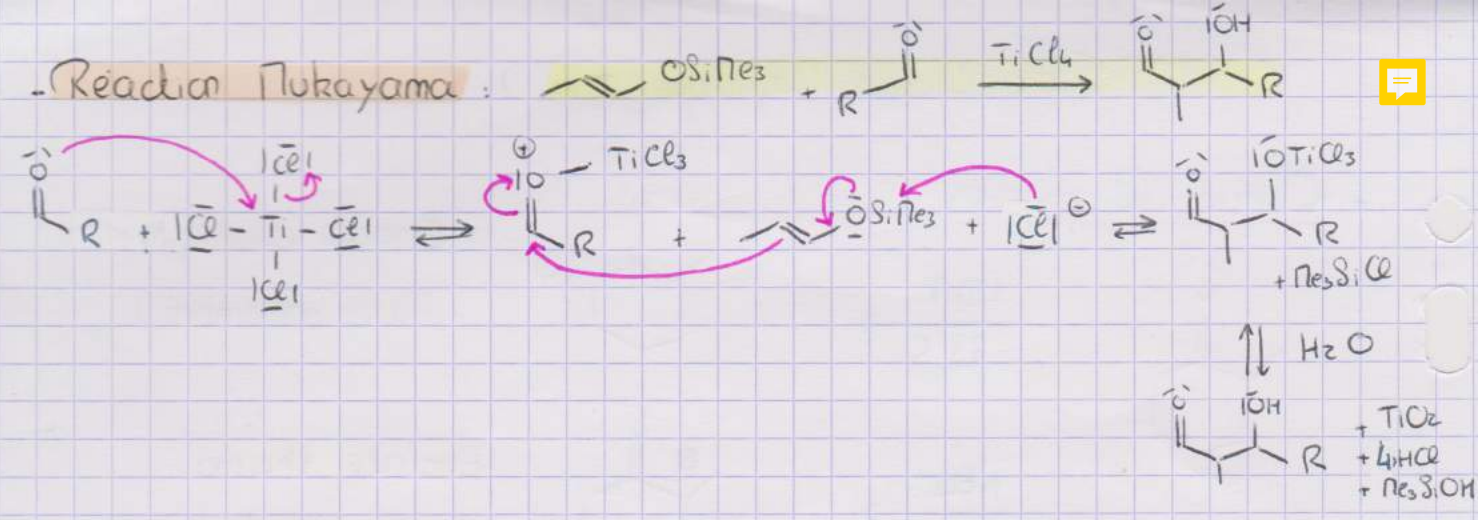
La formation enolate thermo (gros groupe ± en anti)



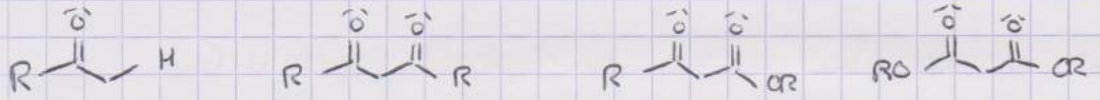
• C alkylation Vs O-alkylation

- Solvant dissociant favorise O-alkylation
- Solvant protique => liaison H avec O => C-alkylation
- Contre ion mou => interaction avec C => O-alkylation ($K^{\oplus}$)
- Contre ion dur => interaction avec O => C-alkylation ($Li^{\oplus}$, $Na^{\oplus}$)
- Nucléofuge dur => réaction en O-alkylation.

- Réaction Mukayama :

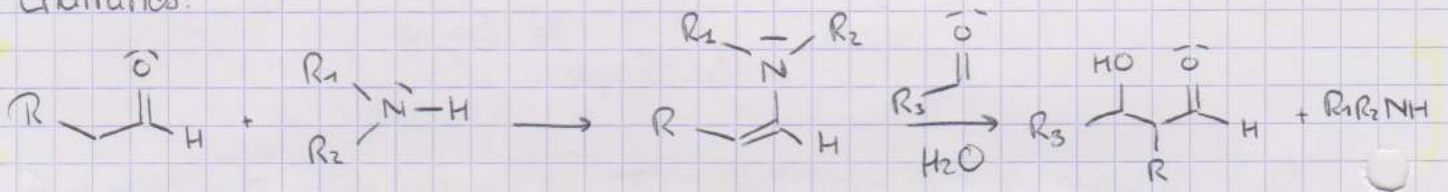


- pKa composés enolisables :



pKa ~ 20 | 9 | 11 | 13

- Enamines :

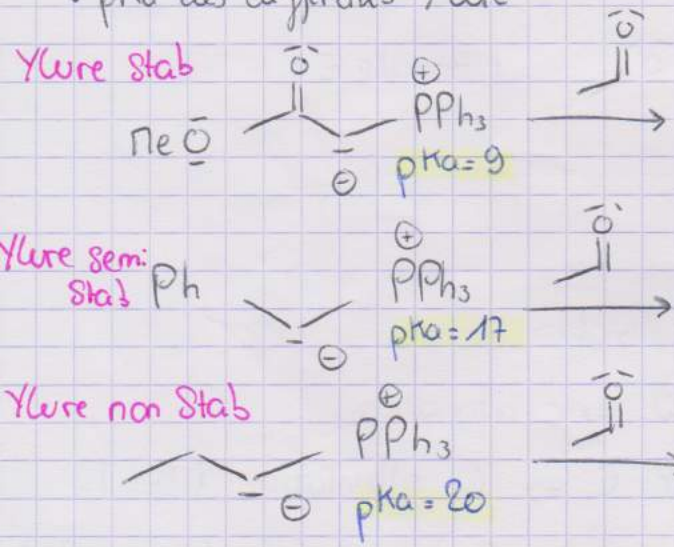


↳ moins d'autocondensation qu'avec les enolates (⊖ electrophiles)

- Wittig et apparentées

Ylure : $X^{\ominus}-Y^{\oplus}$ (zwitterion adjacent)

• pKa des différents Ylure



Ylure Stab → Alcène (E) : Stabilisé

Ylure semi-Stab → Alcène (Z) + (E)

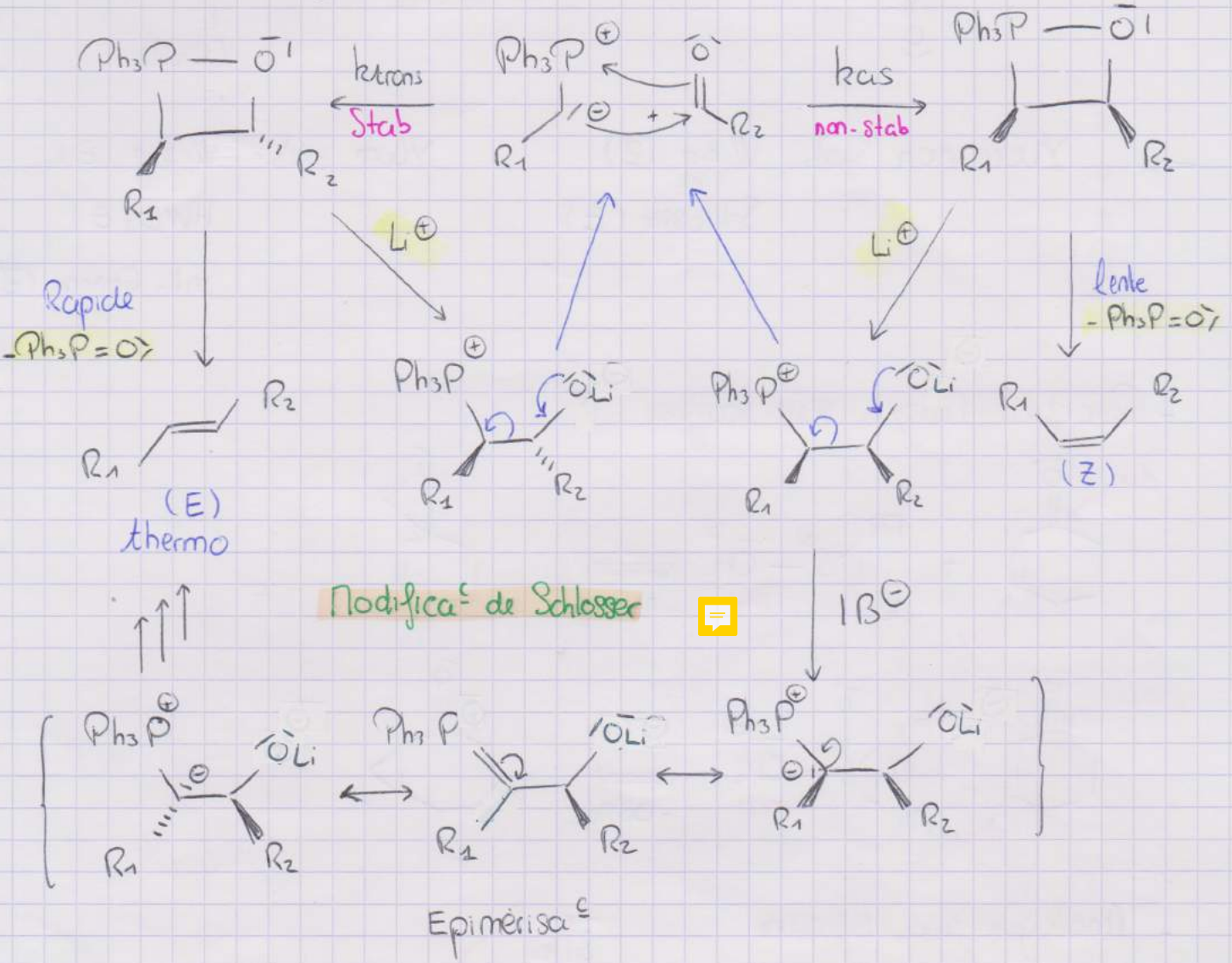
Ylure non Stab → Alcène (Z) : non Stabilisé

↳ Ylure Stabilisés approchent en Supra-Supra => contrôle thermo

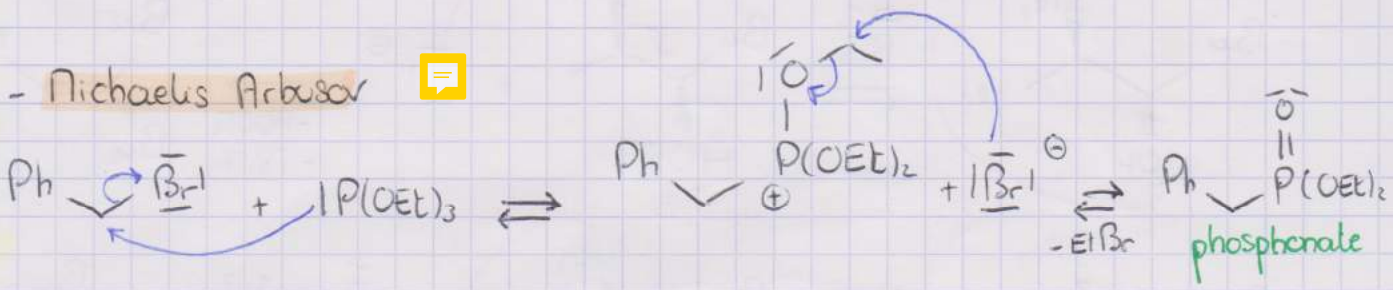
↳ Ylure non Stab = anthara-Supra => = cinétique

Fiche chimie Organique II

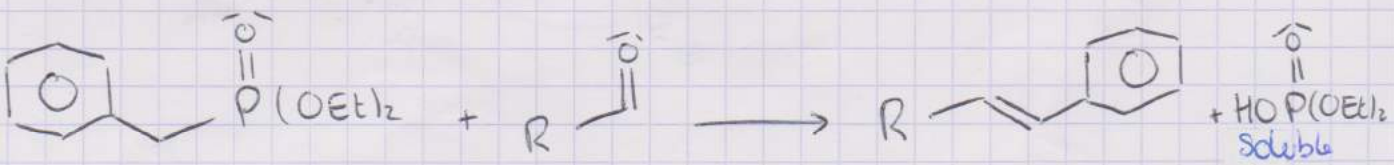
- Mecanismes généraux



- Michaelis Arbusov



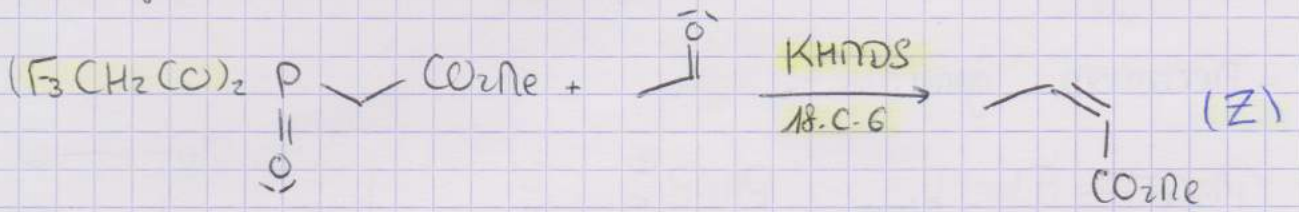
- Horner-Wadsworth. Emmons



⇒ Obtention alcène (E)

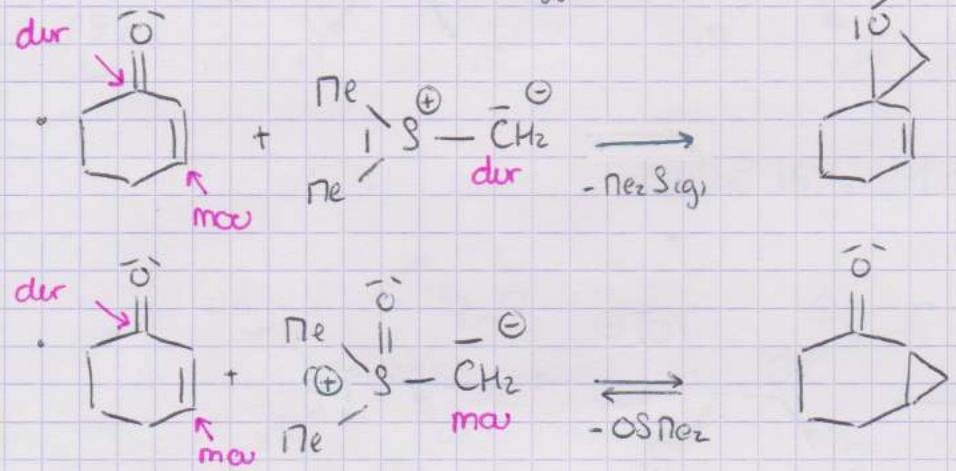
→ Noter réa°: formation liaison P=O : E ≃ 800 kJ/mol

- Modification Still - Gennari

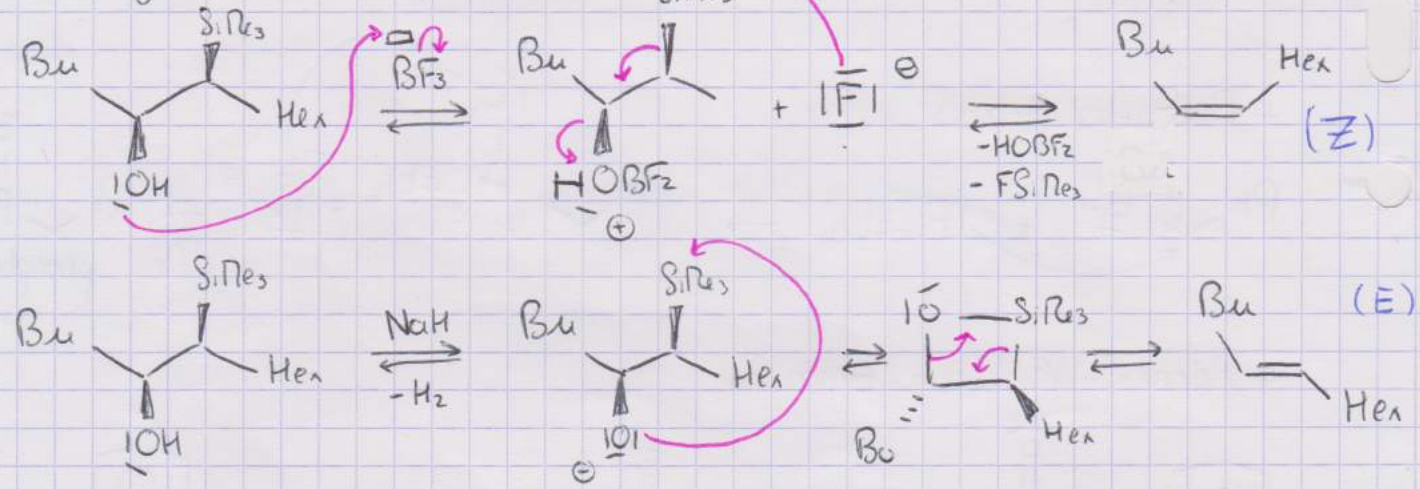


→ Ylure non stab : Wittig (Z) Ylure stab. : Wittig (E)
Schlosser (E) HWE (E)
Still-Gennari (Z)

- Réaction Corey : Ylure soufré :



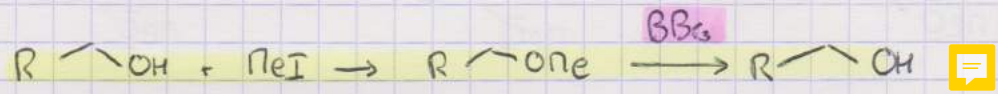
- Analogue avec silicium



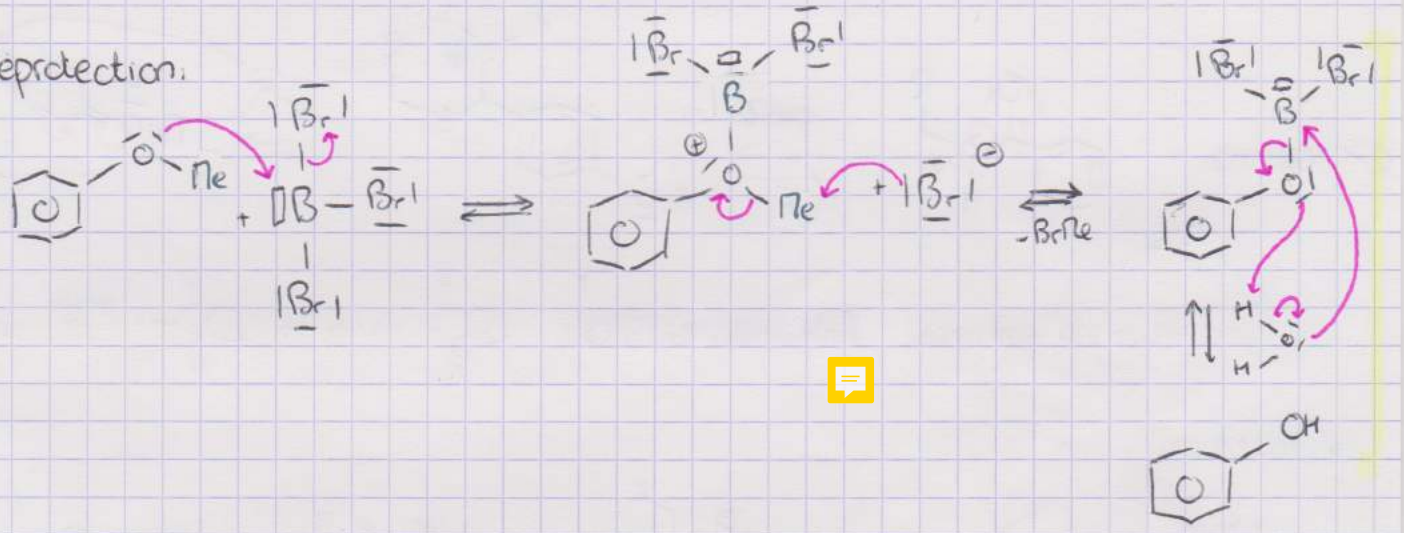
Fiche Chimie Organique III

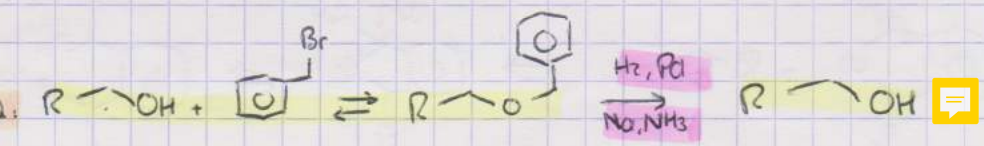
- Protection de fonctions

- Groupe protecteur doit être
  - Introduit selectivement et efficacement
  - Insensible à la suit et aux purif
  - Facilement caractérisable
  - Déprotec simple

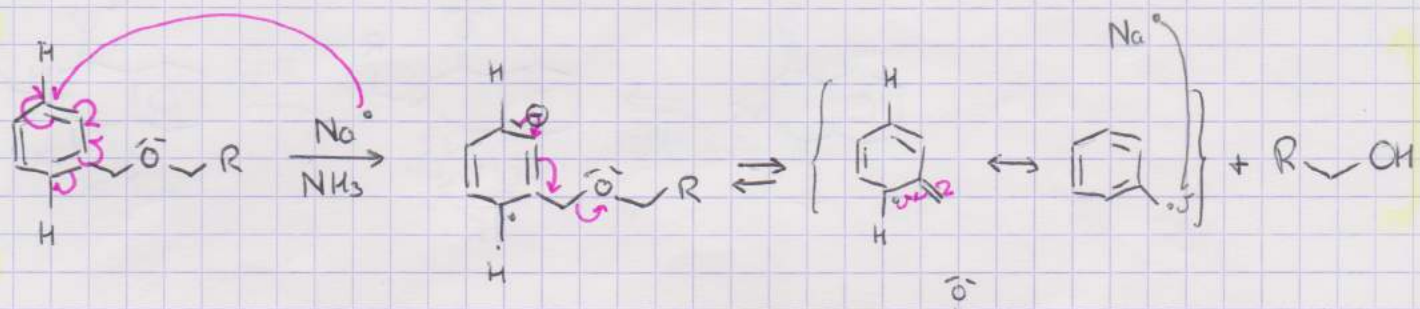
- Estérification : 

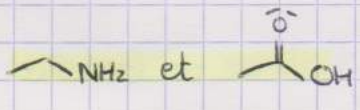
× Déprotection.

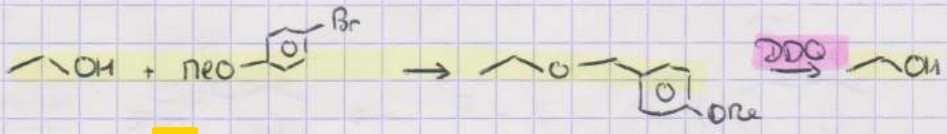


- Estérificat° aromatiq. 

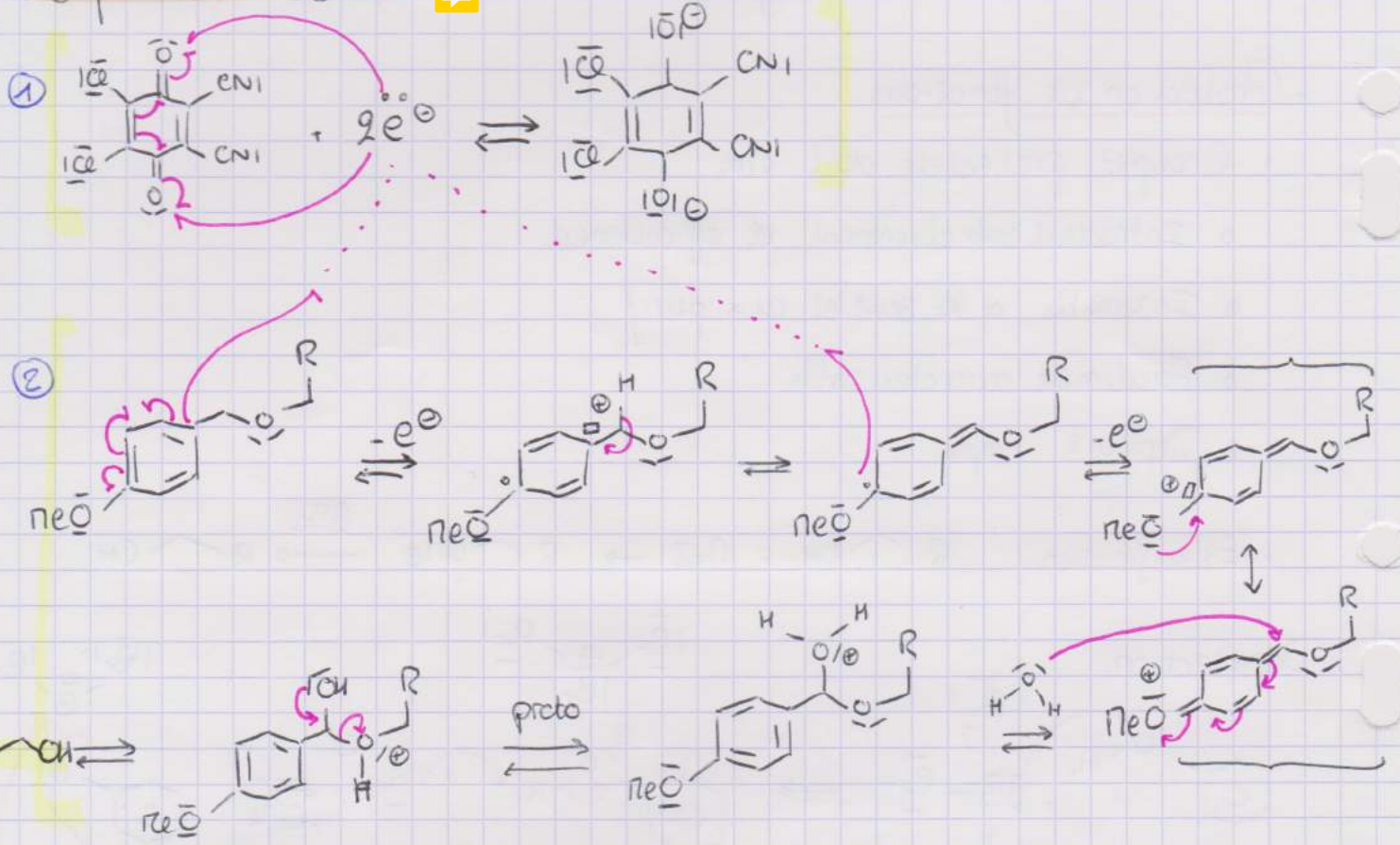
* Mécanisme condition de Birch : Na, NH3



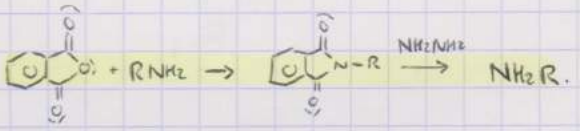
↳ Aussi un groupement protecteur 

- Estérificat° MeOBz : 

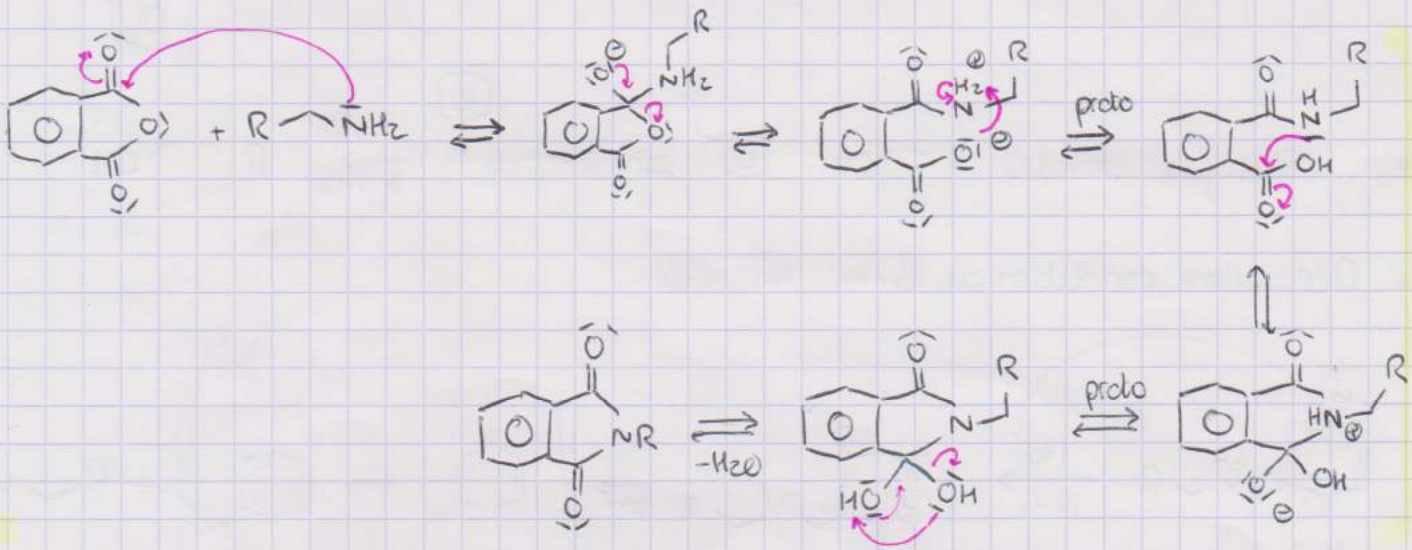
* Deprotection DDQ.



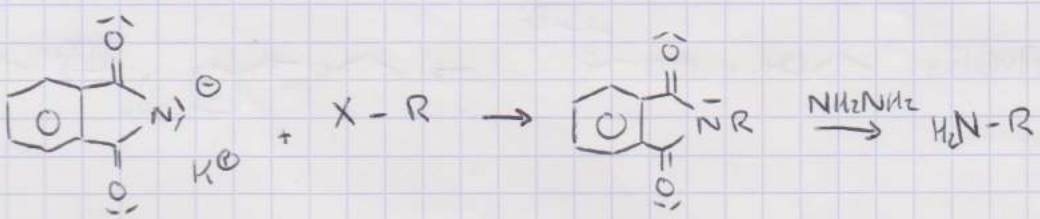
. Protection d'amines : Anhydride phtalique



* Protection :

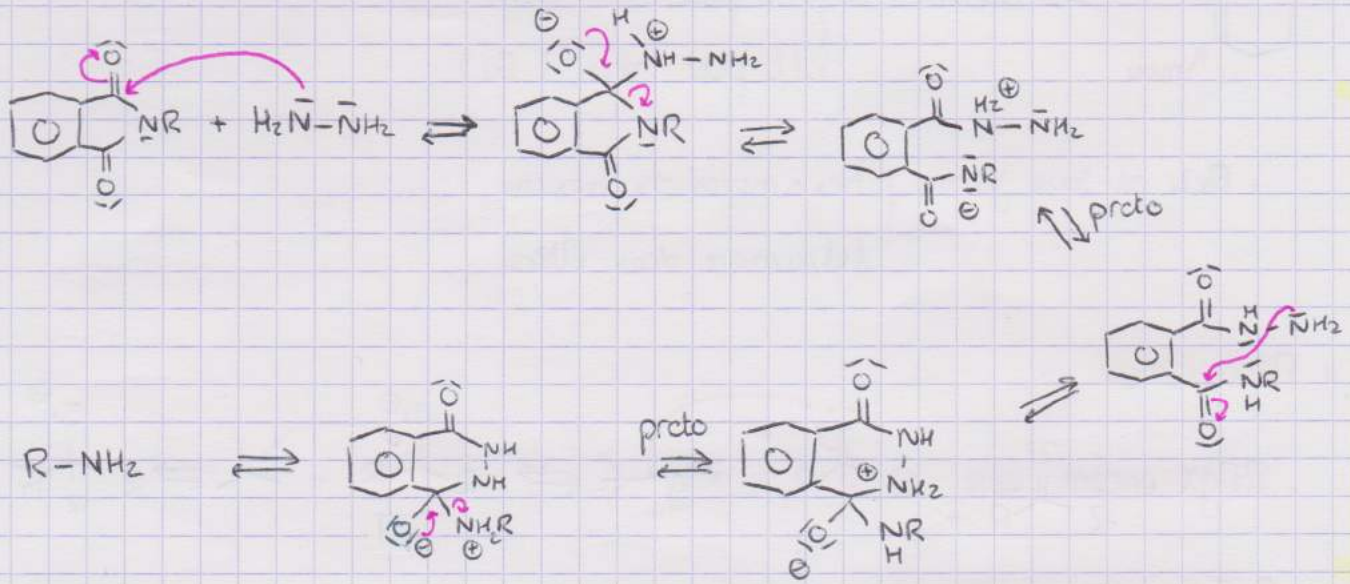


↳ Utilisation : Synthèse de Gabriel

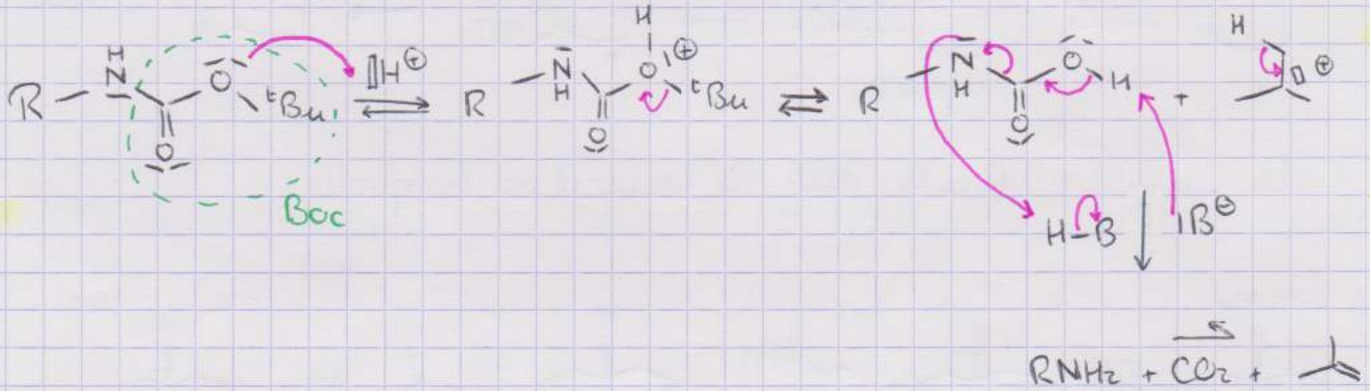


Fiche Chimie Organique IV

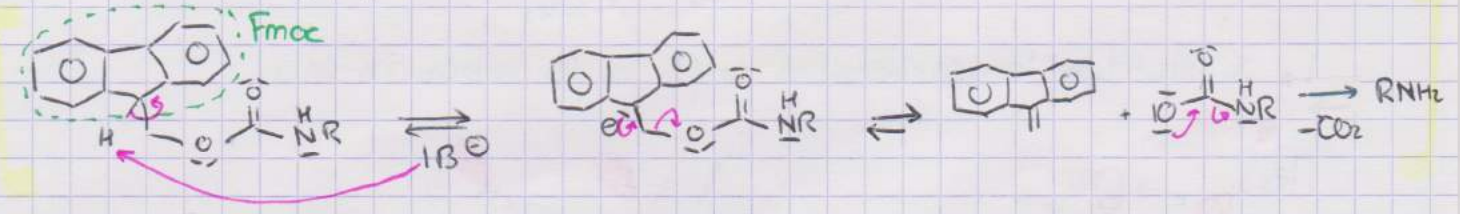
* Déprotection hydrazines H_2N-NH_2



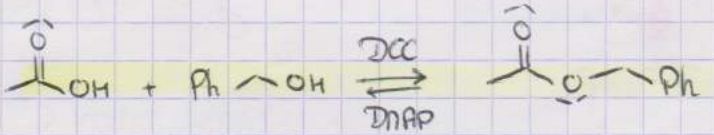
* Déprotection du groupe Boc RN^H-Boc.



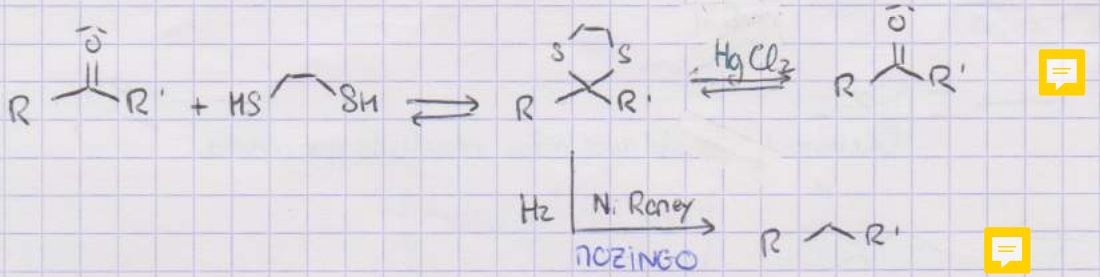
* Déprotection grape Fmoc : RN^H-Fmoc.



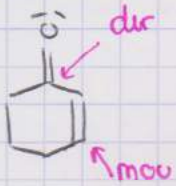
. Protection Acide Carbo :



. Protection avec ethane-1,2-thiol :



- Organométalliques

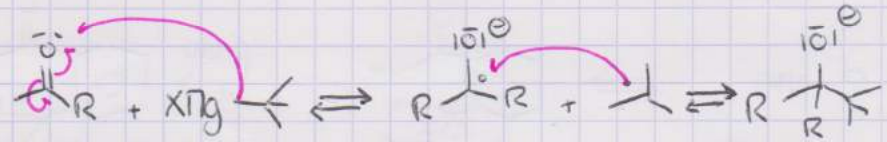


=> Addition en { 1.2 par dur (Li)
1.4 par mou (Cu)

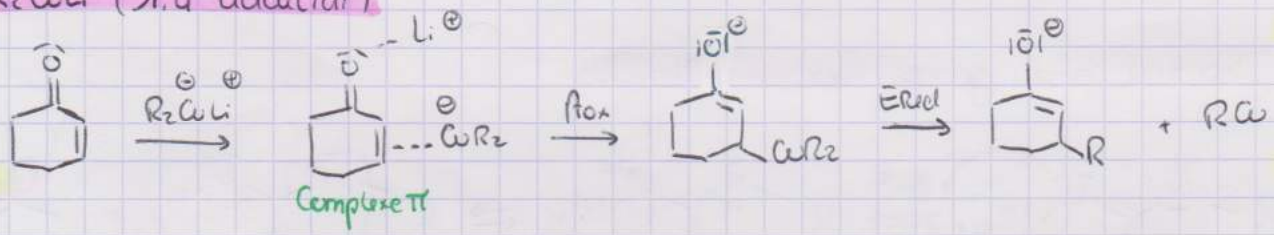
. MeLi est sous forme { hexamères ds hexane
tétramère dans éthers

* Mécanismes

. RMgX : encombrées :

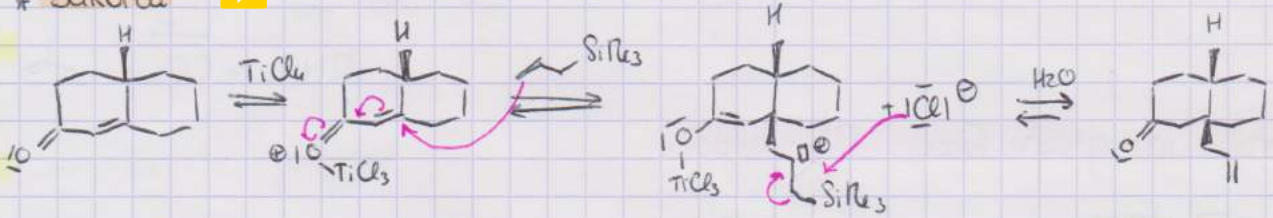


. R_2CuLi (1,4 addition)

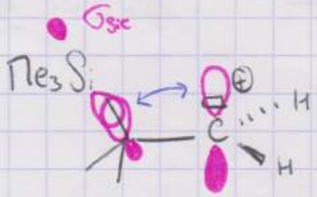


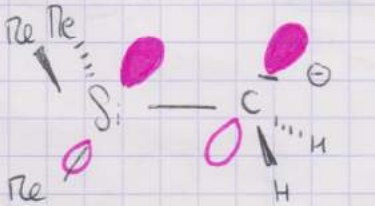
↳ On utilise R_1CuR_2 avec R_1 inutile et non transférable

* Sakurai



↳ Si stabilise les carbocation en β et les carbanions en α

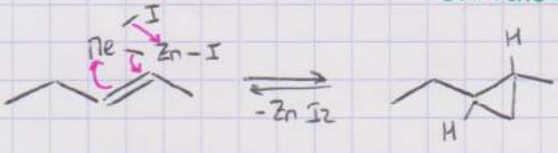




* Simmons - Smith (1958)

. $MeI_2 + Zn \longrightarrow IMeZnI$

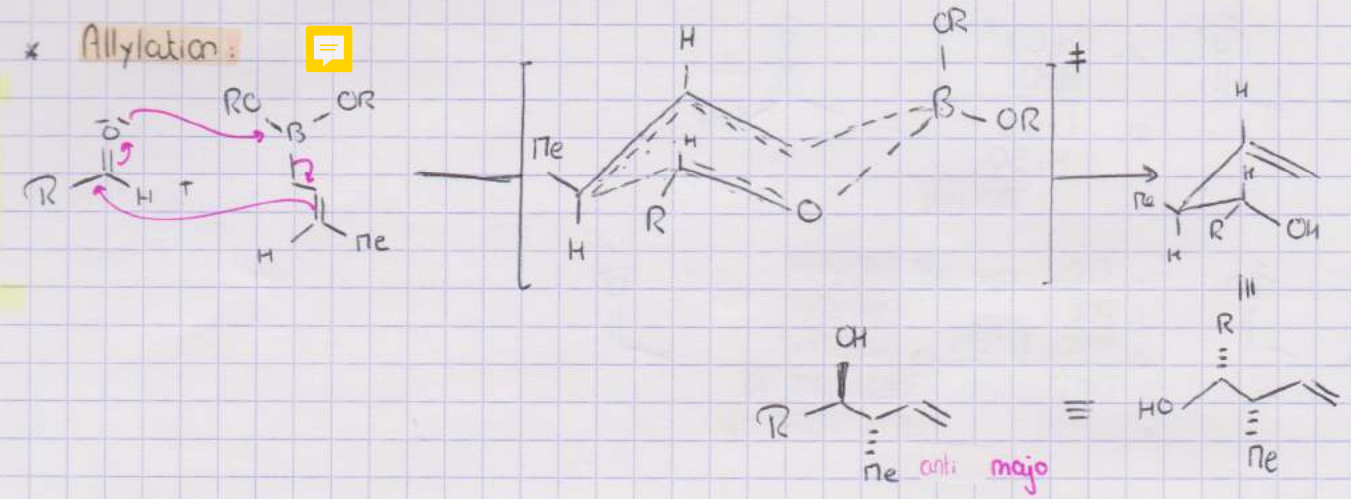
Carbenoïde : entité avec même réactivité que carbène



} diastéréosélectif
diastéréospécifique

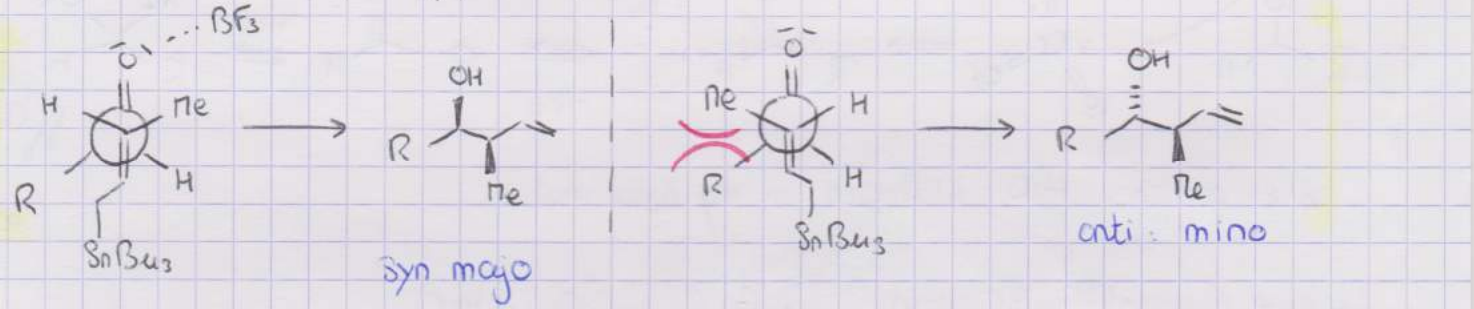
Fiche Chimie Organique V.

* **Allylation :**



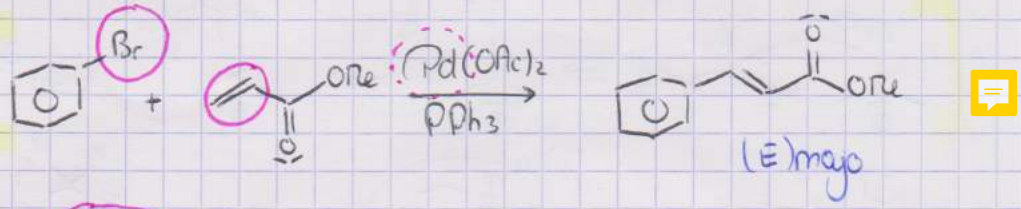
↳ Même réaction si on prend $SnBu_3$ au lieu $RB(OR)_2$

⚠ Avec acide Lewis on perd le cycle à 6 centres

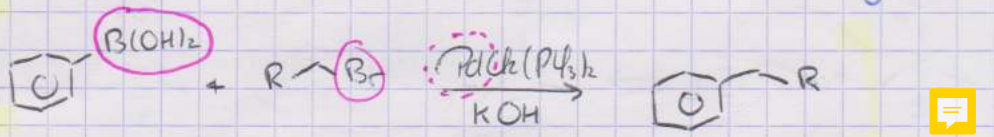


- **Couplage avec Palladium.**

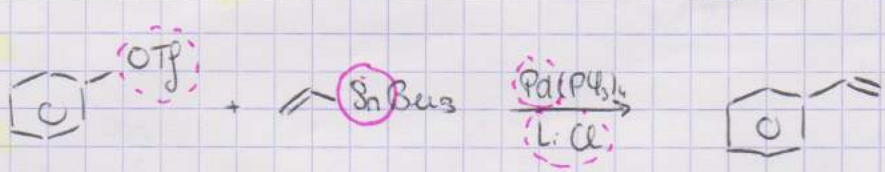
. **Heck** (1972 ; PN 2010)



. **Suzuki** (1979 ; PN 2010)



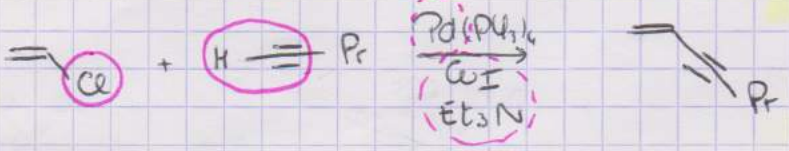
. **Stille**



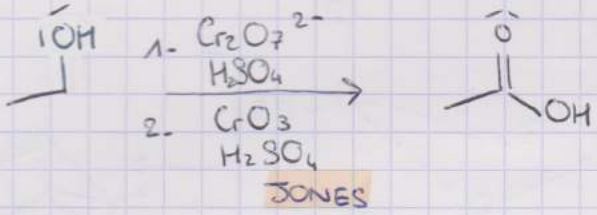
↳ Avec Zn Negishi

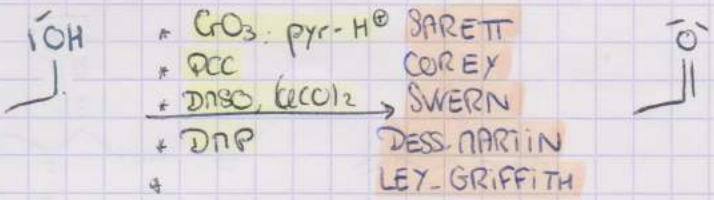
↳ Avec Mg Kumada

. **Sonogashura :**

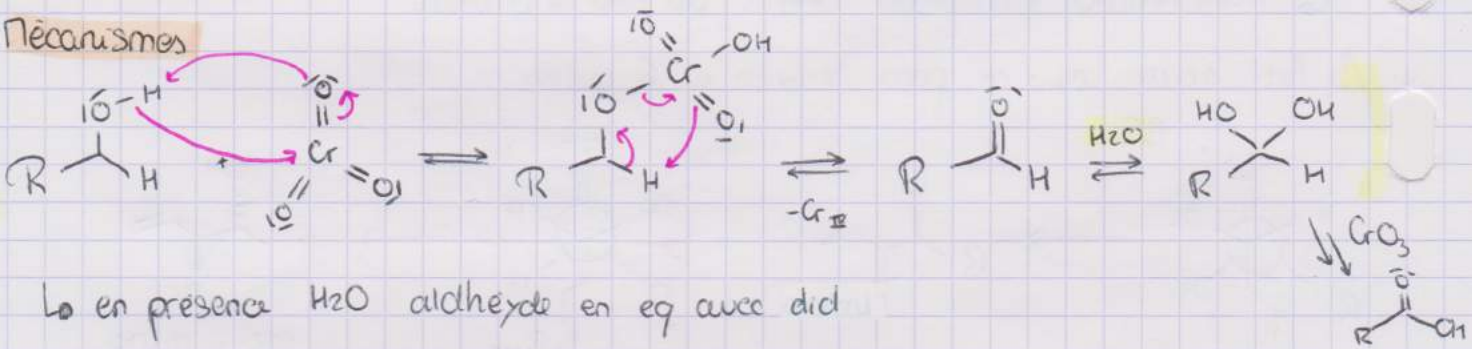


- Oxydations





* Mécanismes

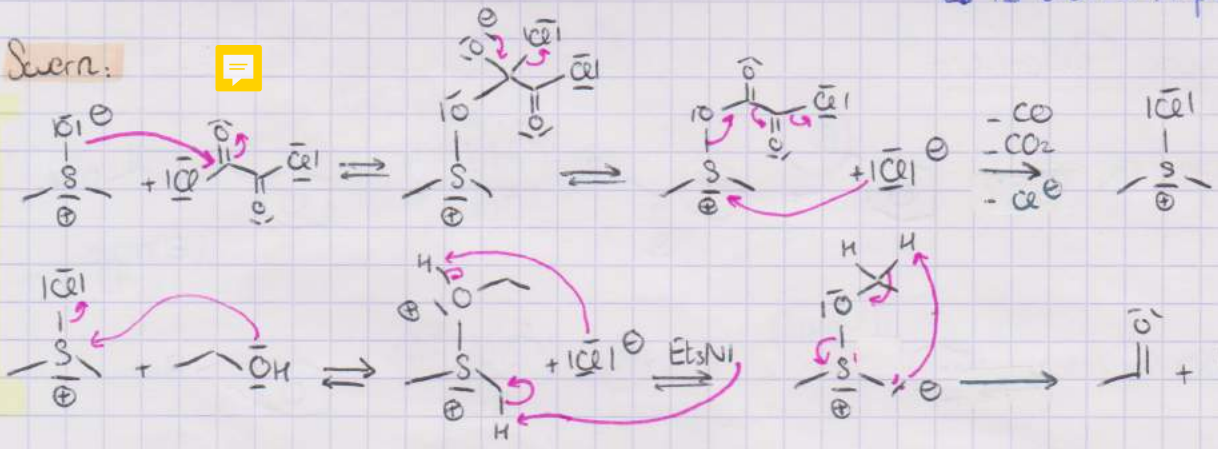


↳ en présence H_2O aldhéyde en eq avec diol

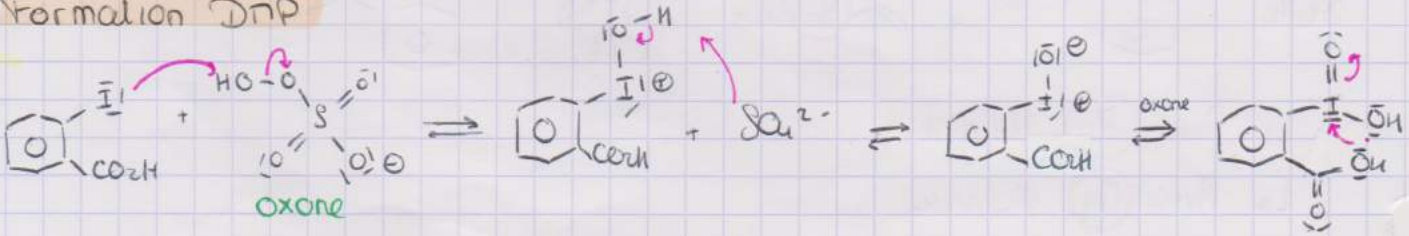
↳ Cr_{IV} non stable $3CrO(OH)_2 \rightarrow Cr_2O_3 + CrO_3 + H_2O$

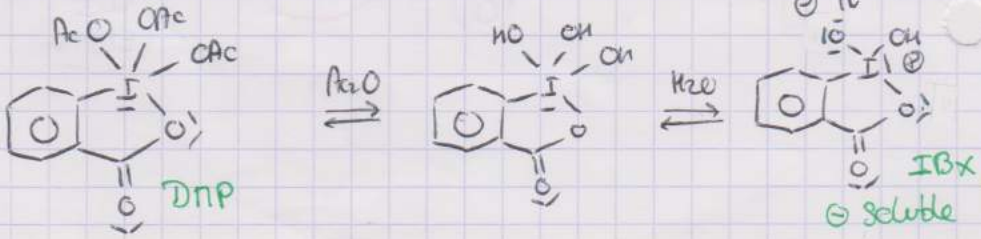
↳ Δ cinétiq importante ici

• Swern:



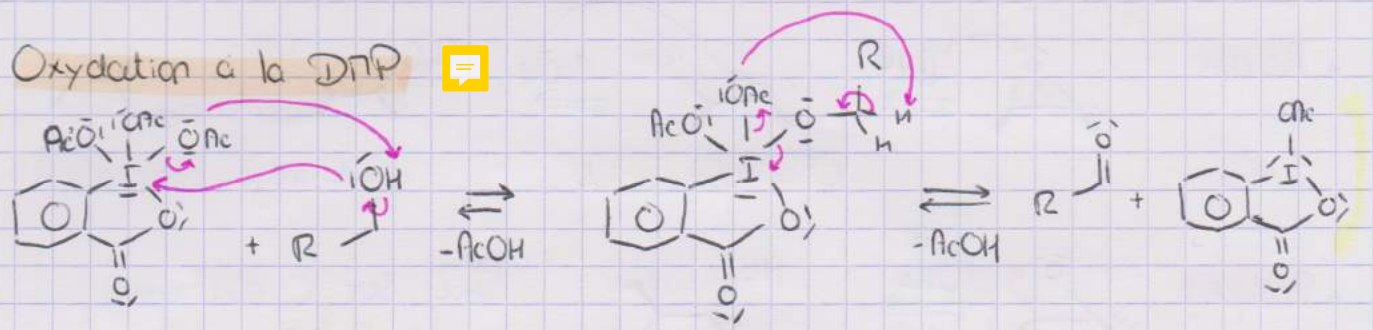
• Formation DNP





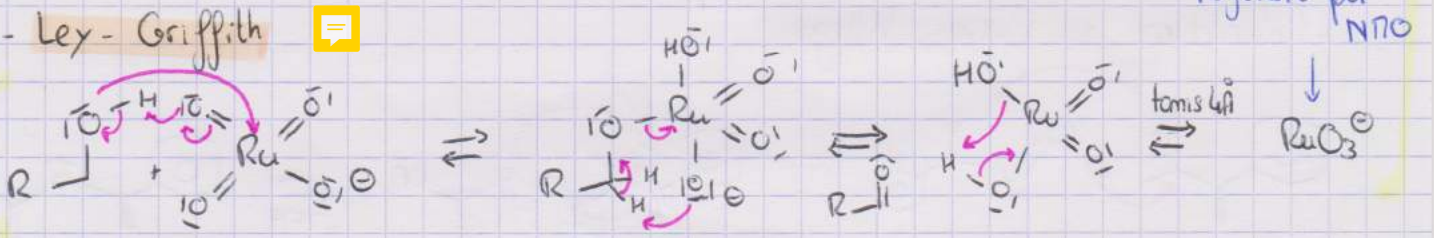
Fiche Chimie Organique VI

- Oxydation à la DMP

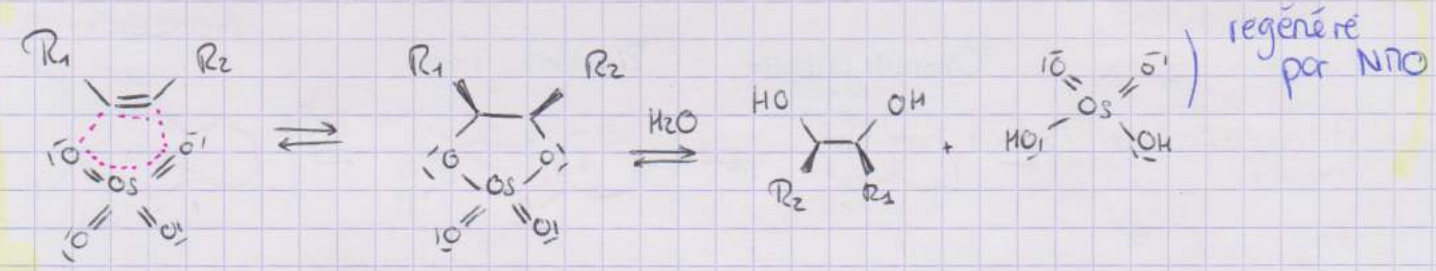


↳ Formation aldehyde uniquement

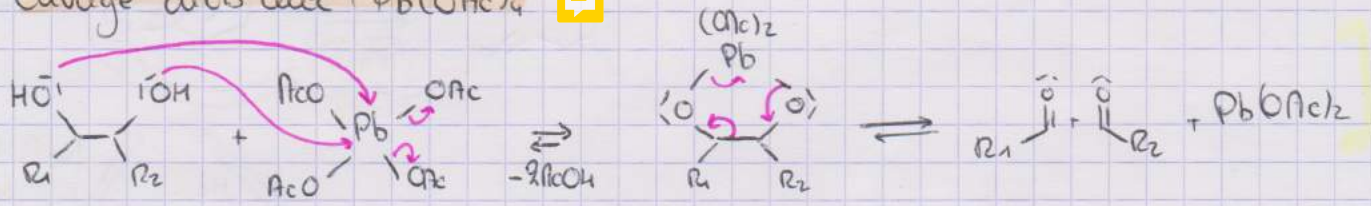
- Ley - Griffith



- Dihydroxylation de Upjonn :

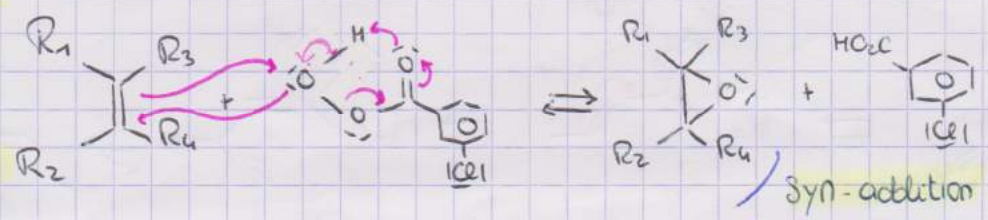


- Clivage diols avec $Pb(OAc)_4$

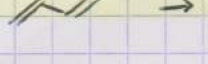


↳ Fonctionne aussi avec $NaIO_4$ => OsO_4 (cat) + $NaIO_4$ (2eq) Lemieux-Johnson

- Epoxydation de Prilezhaev

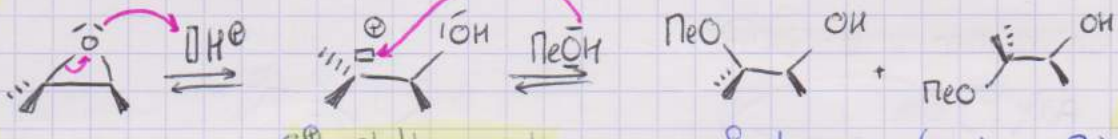


↳ attaque la double liaison la ⊕ riche (la ⊕ substituée)

↳ par enone : peroxo basique ($HO_2^{\ominus}$ + )

- Ouverture d'époxydes

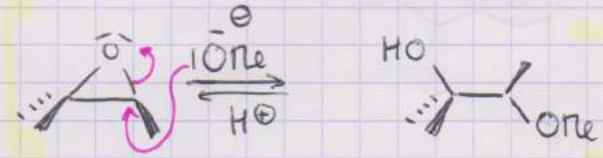
* Acide :



$C^{\oplus}$ ⊕ stable = ⊕ sub

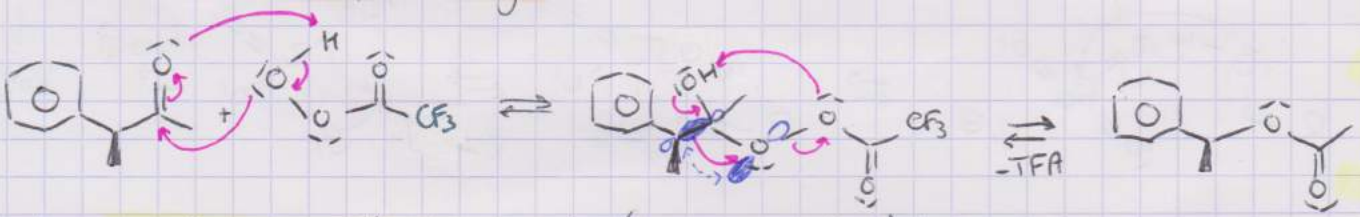
S_N1 majo (peut dép R)

* Basique :



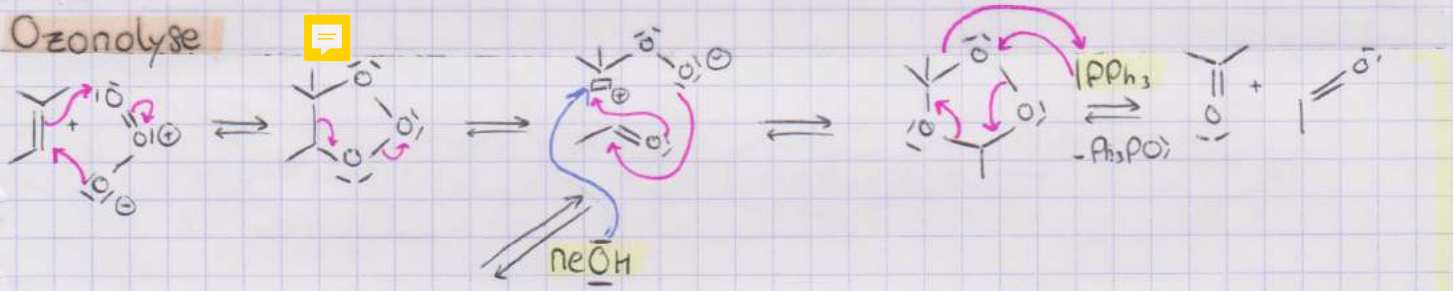
S_N2 sur C électrophile
↳ ⊖ sub.

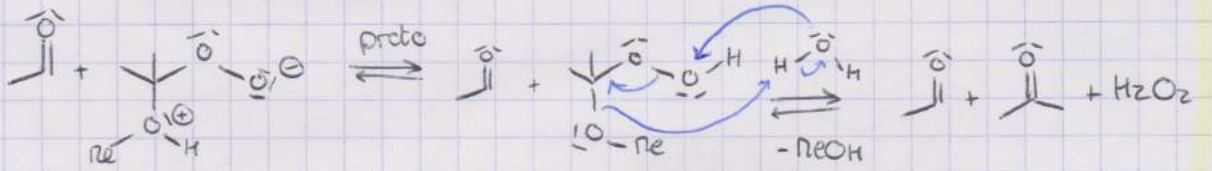
- Réaction de Bayer-Villiger

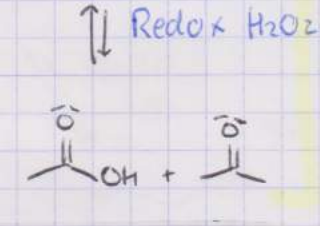


↳ Insertion du côté le ⊕ sub (recouvrement orbitales)

- Ozonolyse

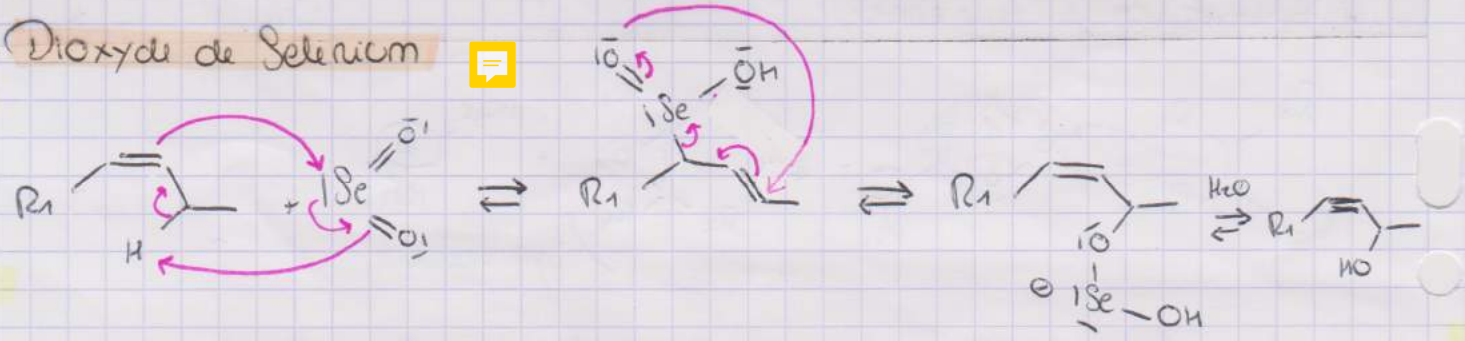






- Différent produits en milieu Red, Ox, protique

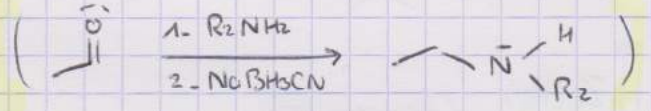
- Dioxyde de Sélénium



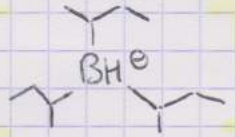
Fiche revision Chimie Organique VII

- Reductions

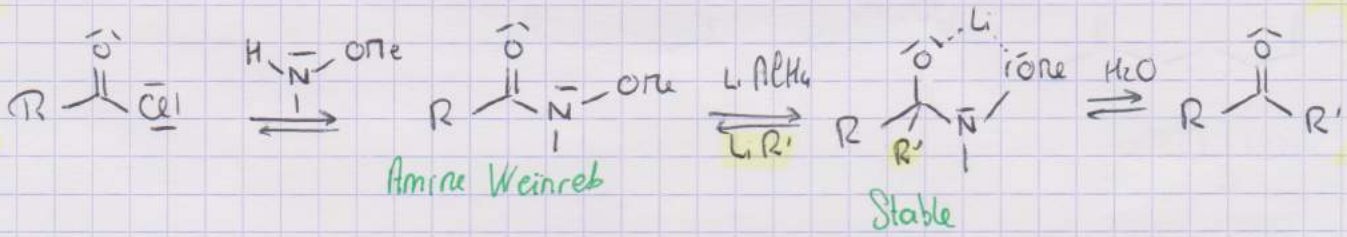
- $NaBH_3CN$ selectif des imines



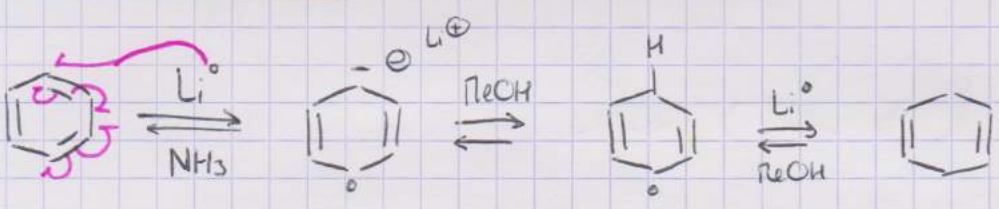
- BH_3 selectif des acides % autres carbonyles
- Selectride : encombré :



- Amine Weinreb

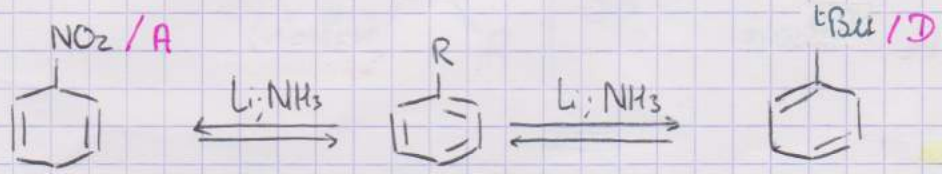


- Reduction Birch : (Li, NH_3 donne un $e^{\ominus}$)

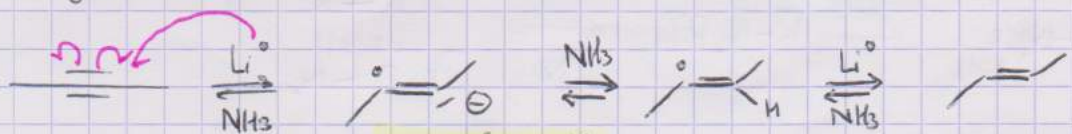


- grpment attracteur stab par densité $e^{\ominus}$ en ipso/para
- grpment donneur - - " meta/ortho

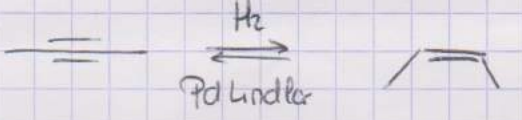
$\Rightarrow$



- Hydrogenation catalytique des alcènes

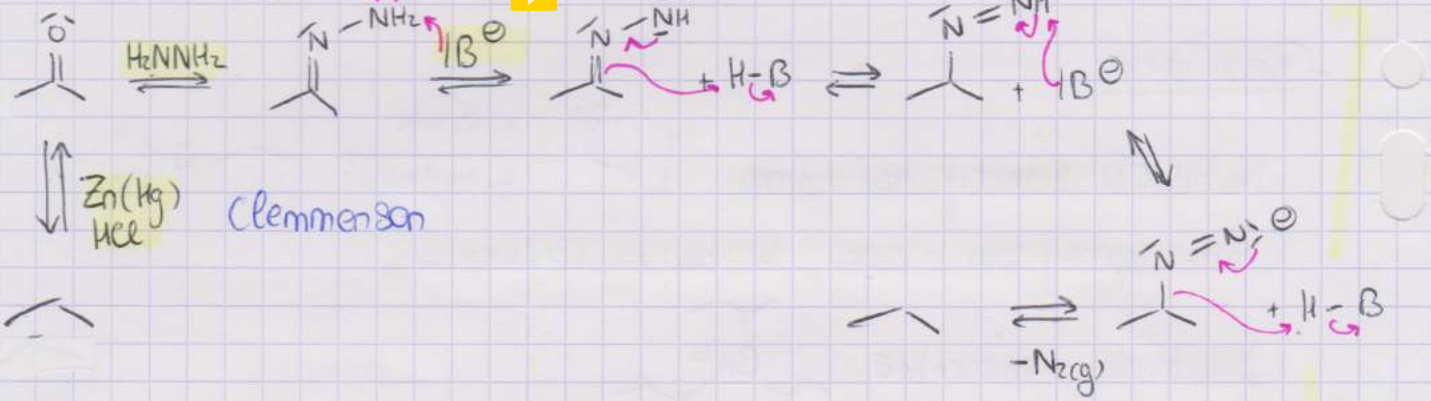


isomerisation possible

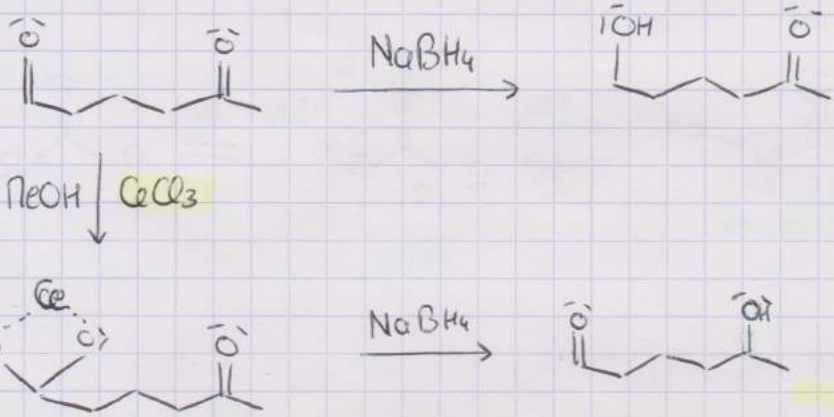


Pd Lindlar = Pd sur $CaCO_3$ avec { $Pb(OAc)_2$ (poison), quinoléine, Ba_2SO_4

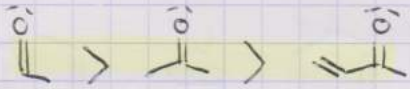
- Reduction Wolf-Kishner :



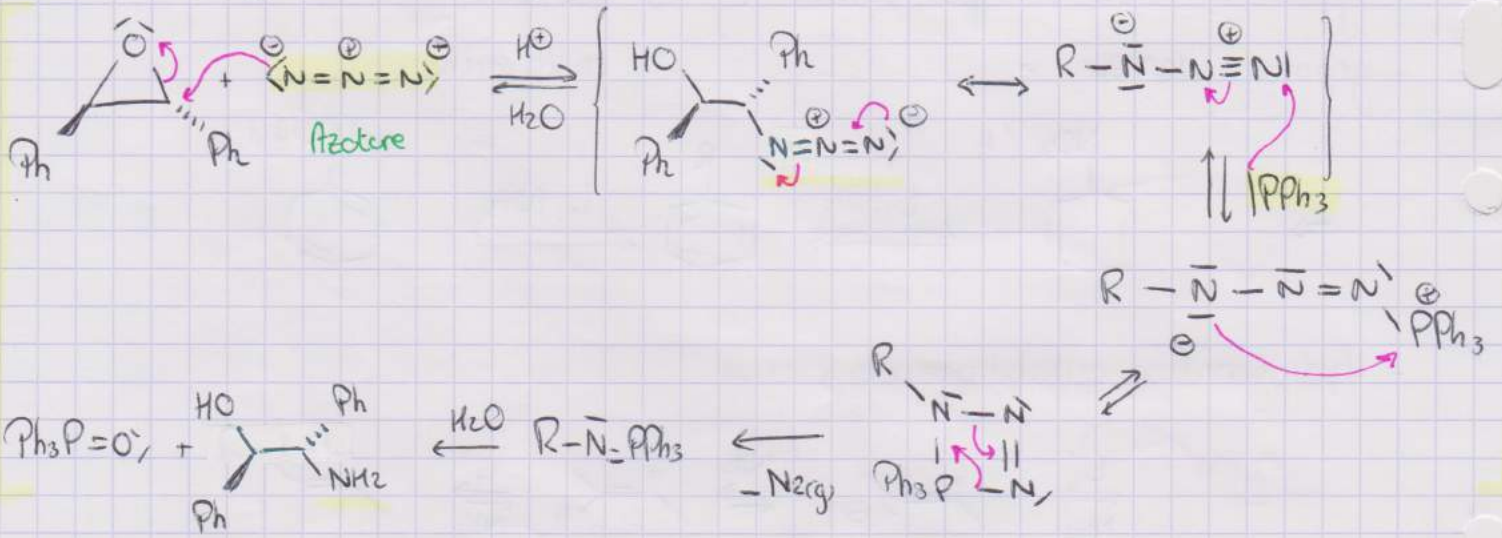
- Réduction sous conditions de Luche



Bloque reactivité

La Réactivile : 

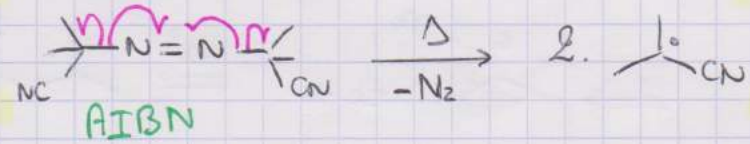
- Staudinger / aza Wittig



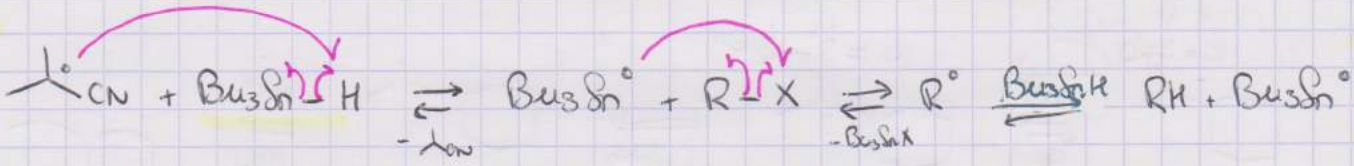
Fiche révision Chimie Organique VIII

- Réaction radicalaires

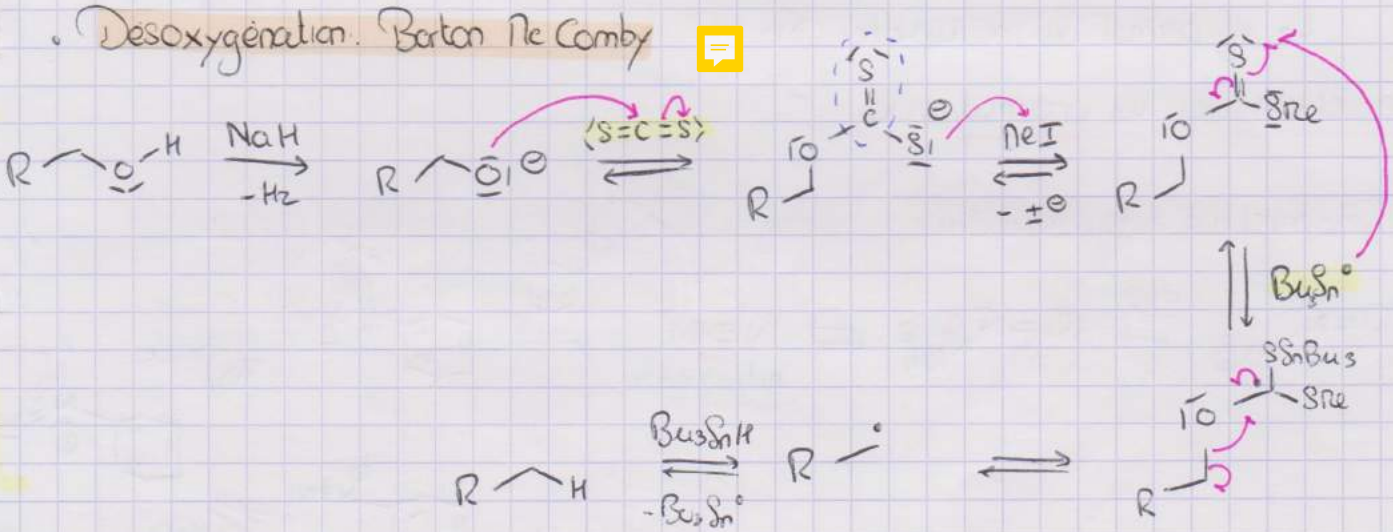
• Formation radicaux



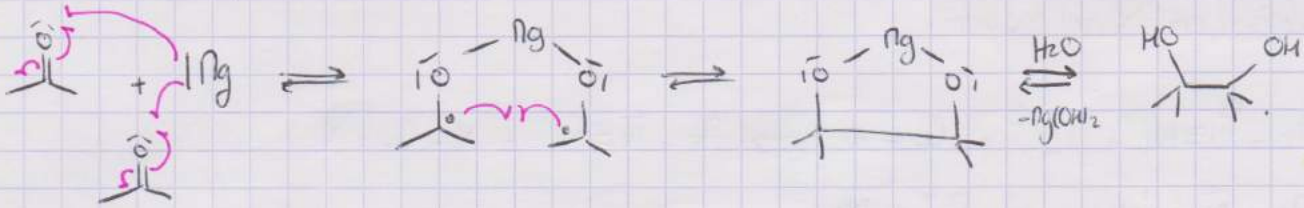
• Déshalogénation :



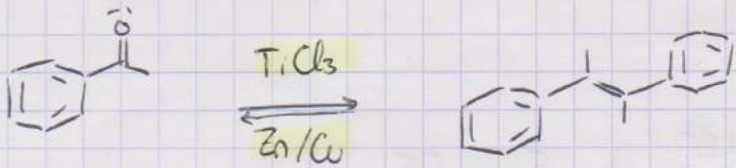
• Désoxygénation : Barton Mc Comby



• Couplage pinacolique :



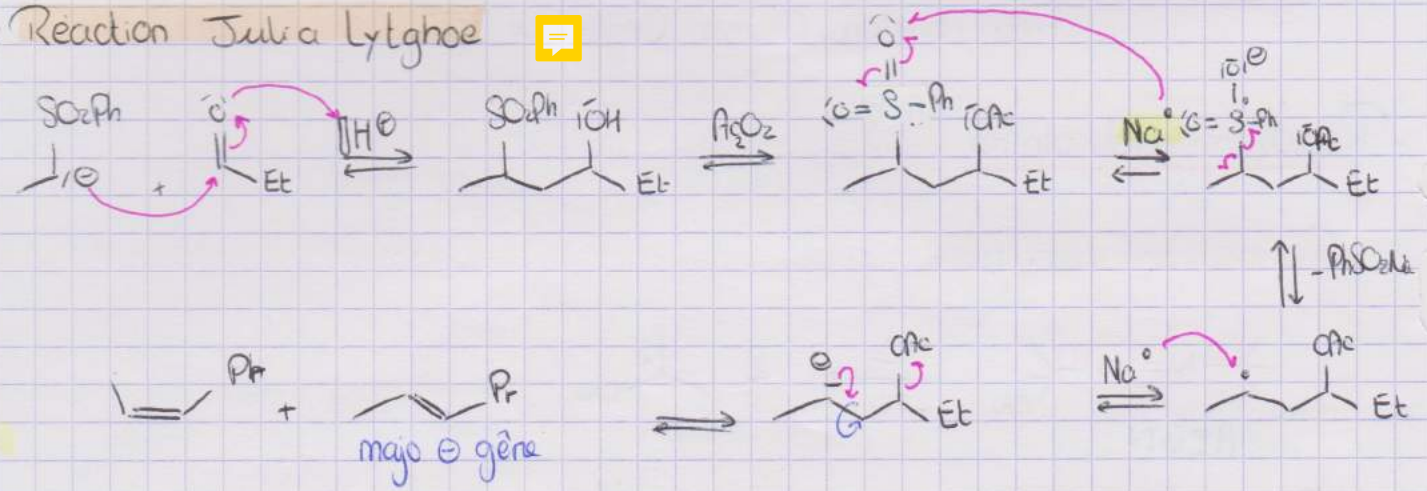
• Couplage Mc Murry



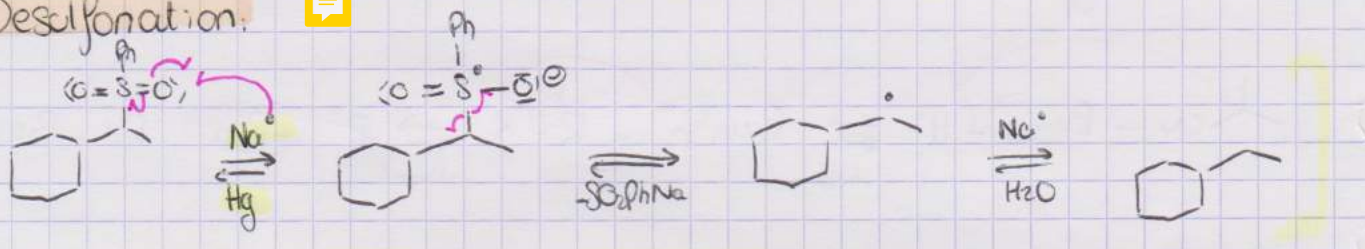
Z / E variable

Mécanisme mal connu

Réaction Julia Lythoe



majo ⊖ gêne

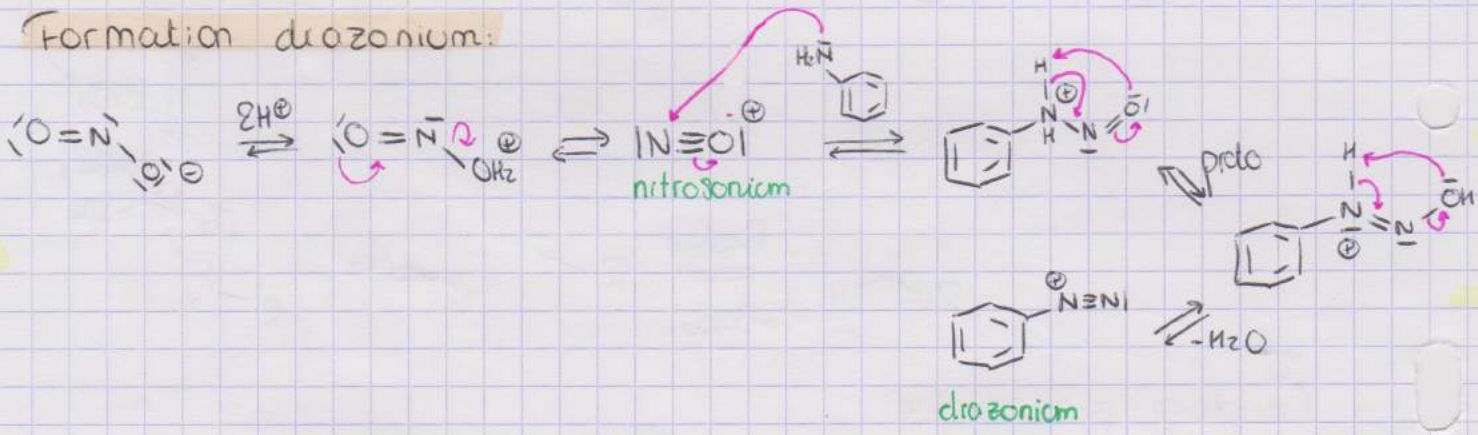


Desulfonation:

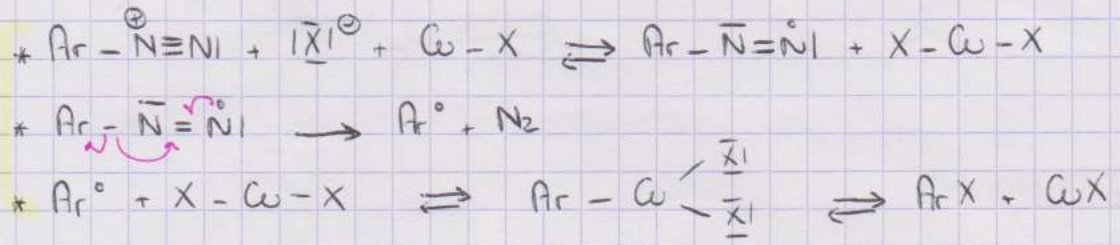
↳ Hg permet de manipuler Na dans H_2O

Réaction sur les aromatiques

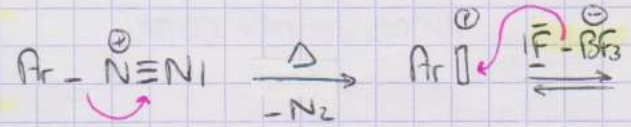
Formation diazonium:



Réaction Sandmeyer

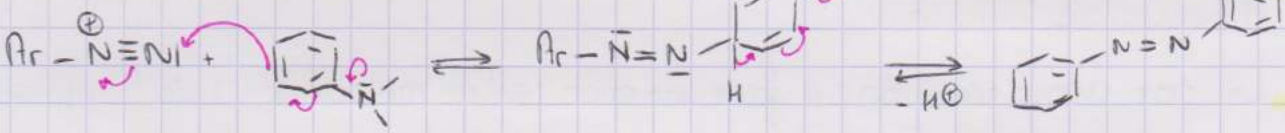


Réaction Schiemann:

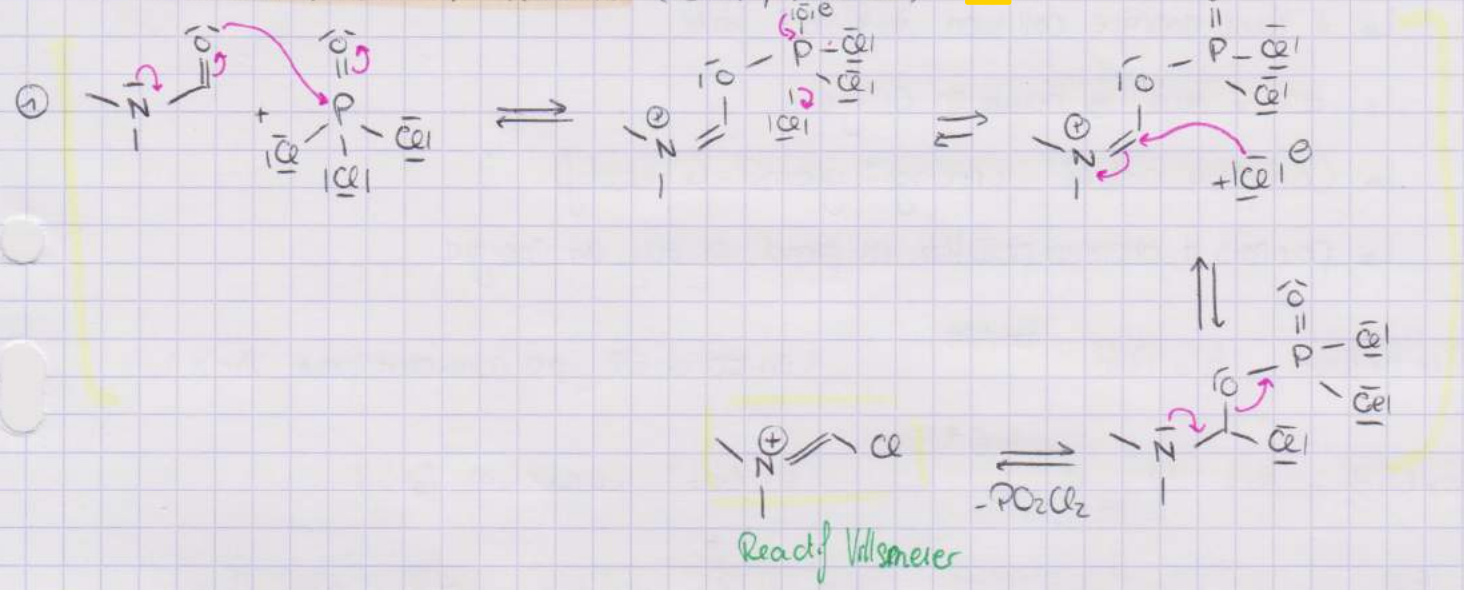


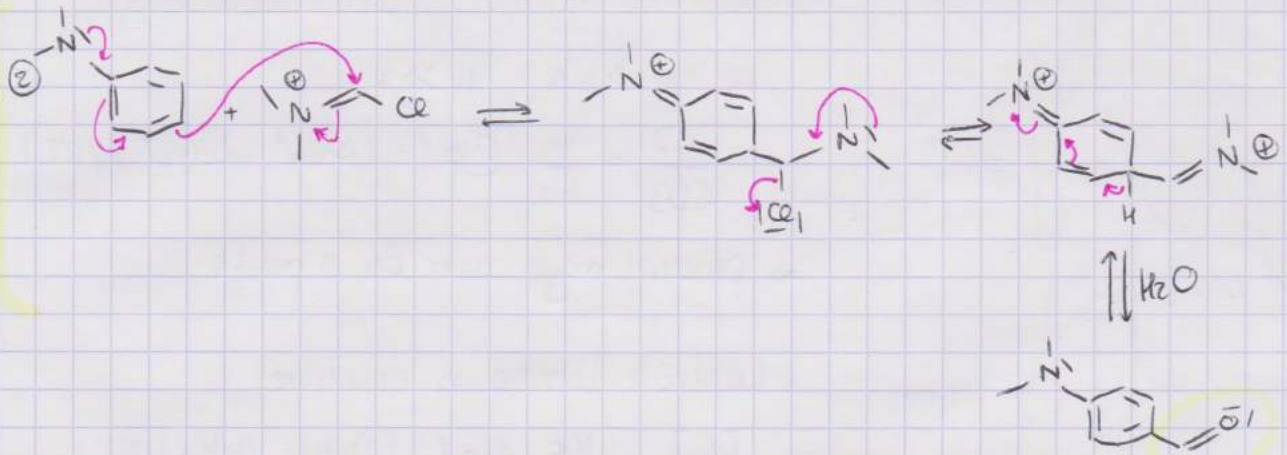
Fiche revision Chimie Organique IX

• Couplage diazoïque

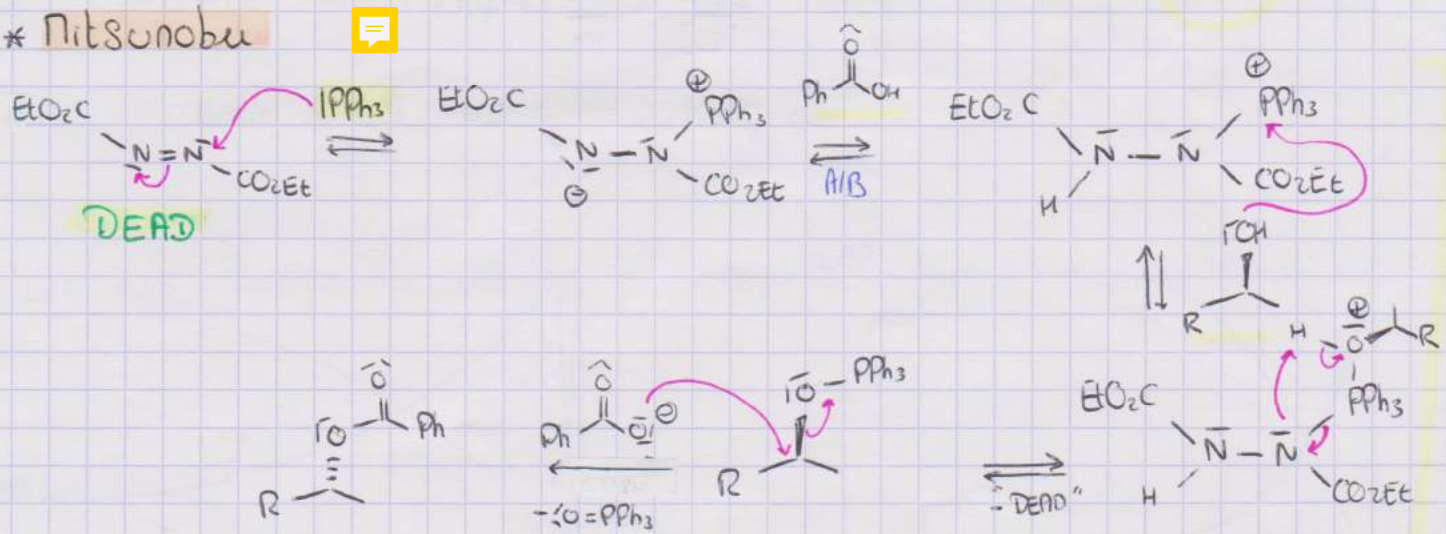


• Réaction Villsmeier - Haack (DMF, $POCl_3$)





* Mitsunobu



- Contrôle cinétique - Contrôle thermodynamique

. Par avoir une réaction il faut une cinétique et une thermo favorable

. Théorie des collisions

↳ par avoir réaction il faut un choc entre molécules (10^{-15} efficaces)

. Théorie état transition

↳ il faut énergie collision suffisa^{t} forte

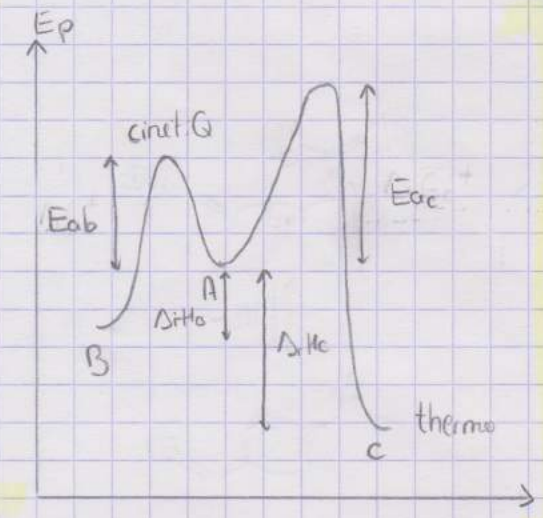
↳ ET = état ⊕ haute en énergie

↳ Complexe activé : arrange^{t} géométri Q réactifs

↳ parmis tt chemins possibles on prend ⊖ bas en énergie.

Arrhénius : $k = A e^{-Ea/RT}$ (en Ep et CR ne considère pas $\Delta_r S$)

Eyring : $k = \frac{k_B T}{h} e^{-\Delta G^{\ddagger}/RT}$ (en $\Delta_r G°$: considère $\Delta_r S$)



. Contrôle cinétique : pas d'équilibres

↳ $k_B \gg k_{-B}$; $k_C \gg k_{-C}$

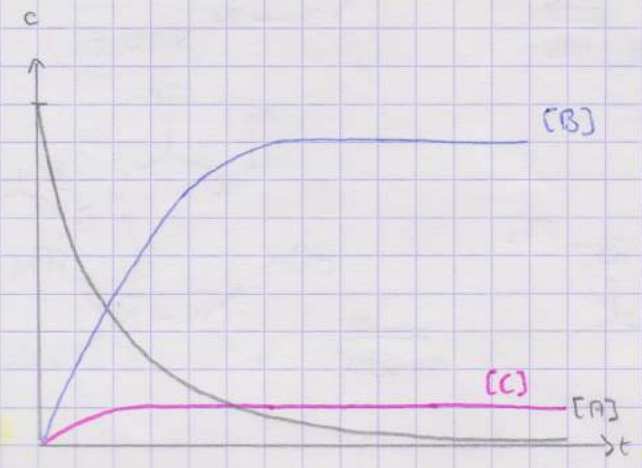
$$\frac{[C]}{[B]} = \frac{k_C}{k_B} \exp(-(Eac - Eab)/RT)$$

⇒ produit majo avec Ea ⊖ petite

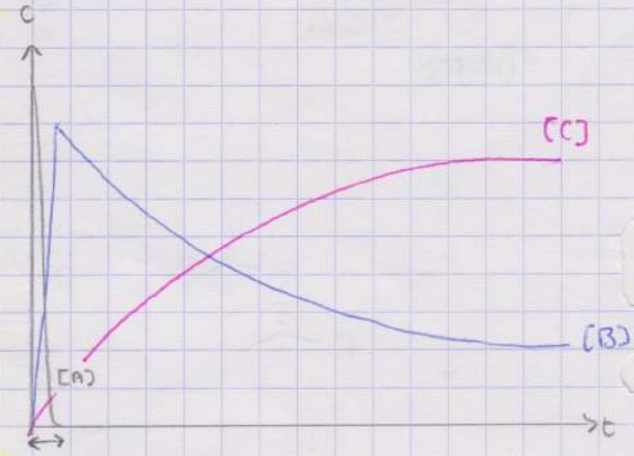
. Contrôle thermo ⇒ équilibre

$$\frac{[C]}{[B]} = \frac{K_C}{K_B} \exp(-(\Delta_r H_c - \Delta_r H_a)/RT)$$

⇒ produit majo avec $\Delta_r H$ ⊖ grand.



Contrôle cinétique : t ~ min



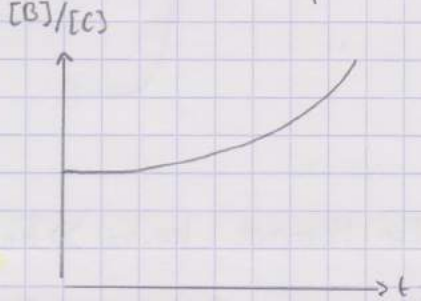
cinétique Contrôle thermo : t ~ h

Fiche revision Chimie Organique X

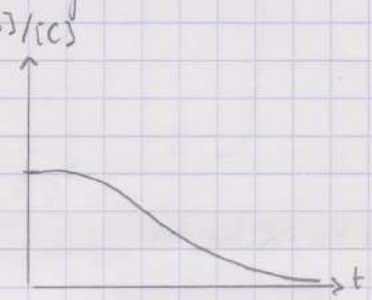
* Loi d'Arrhenius

$$\frac{d\ln(k)}{dT} = \frac{Ea}{RT^2}$$: k_A et k_{-A} augmente avec T

⚠ Pour avoir compet cinetiQ / thermo il faut des reactions renversables



$C \rightleftarrows A \rightarrow B$

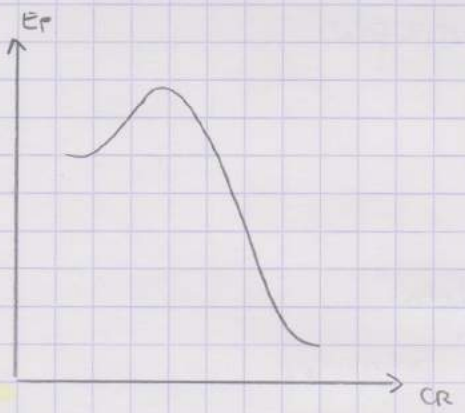


$C \leftarrow A \rightleftarrows B$

=> Deplacement d'équilibres

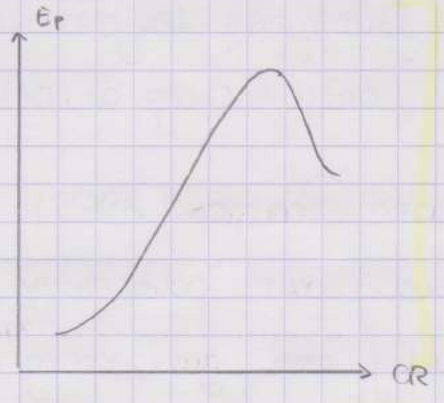
* Postulat de Hammond (⚠ Contrôle cinetique)

  ◦ Deux etats proches en énergie sont structurellements proches



ET precoce : etudie reactif

↳ exothermique

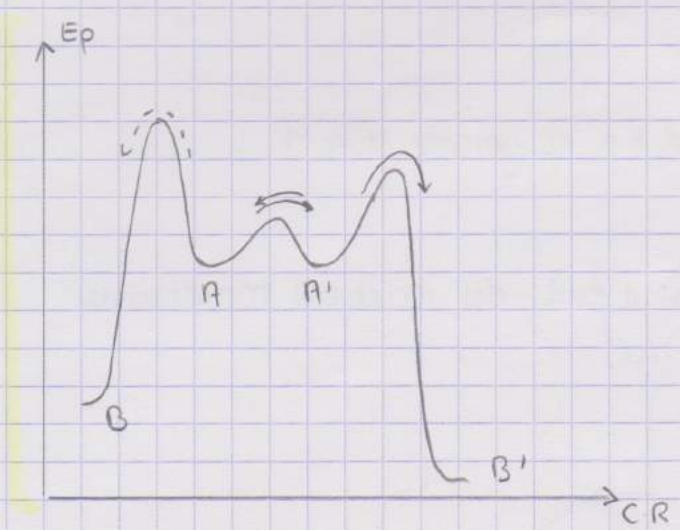


ET tardif : etudie produits

↳ endothermique

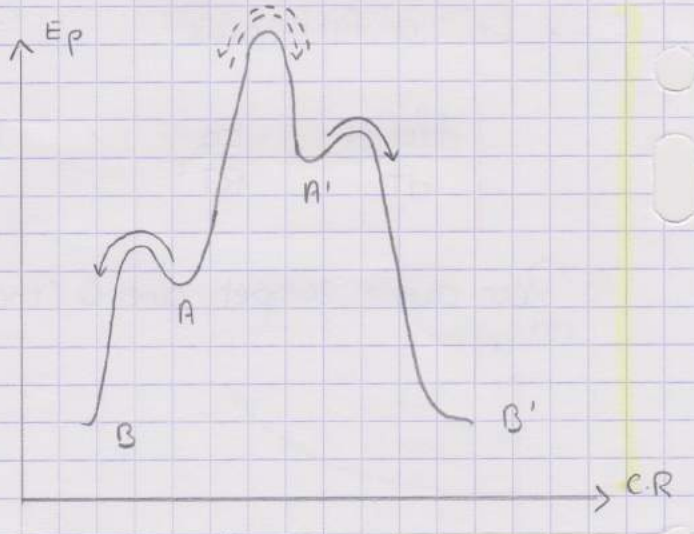
* Etape cinetique ± determinante (Ea ⊕ grand) impose sa vitesse

* Principe de Curtin-Hammet (conformères)



Curtin Hammet $k_A, k_{A'} \ll k_B, k_{B'}$

↳ produit majo : E_{a_B} ⊖ faible



Anti Curtin-Hammet : $k_A, k_{A'} \gg k_B\ k_{B'}$

↳ produit majo : conformère ⊖ stable

* Equation Klopman-Salem

$$\Delta E = \Delta E_{ster.a} + \Delta E_{orb} + \Delta E_{elec}$$

↳ Quasiment toujours ster. G, mais varie peu.

↳ Contrôle charge ou orbitalaire

* Théorie Pearson (1963)

- réactif dur : petit, chargé, ON contractées
- réactif mou : gros, charge diffuse, ON polarisée

=> Contrôle de charge : dur-dur

=> Contrôle orbitalaire : mou-mou

* Approximation de Fukui

- Contrôle orbitalaire : interaction entre HO et BV ⇒ de réactivité

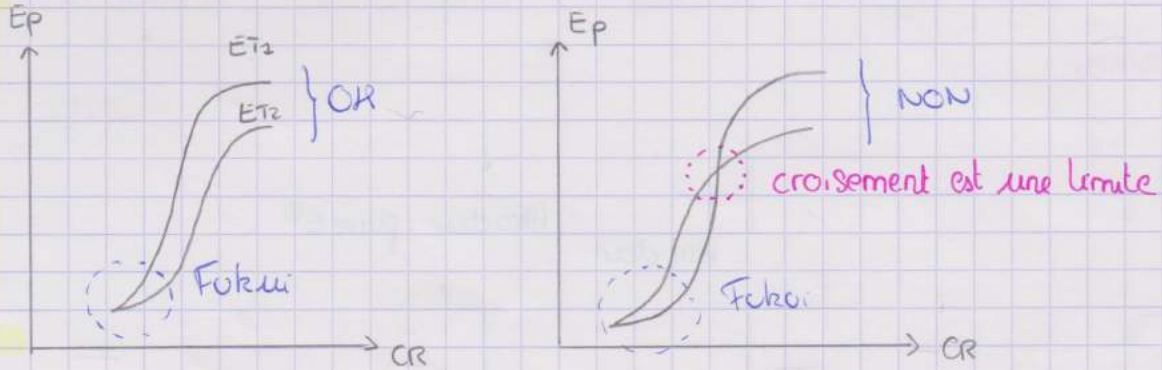
↳ Il faut proche en énergie et gros recouvrement : $E \propto S^2/\Delta E$

⚠ ne s'intéresse qu'au réactif => faux si croisement

Fiche révision Chimie Organique XI

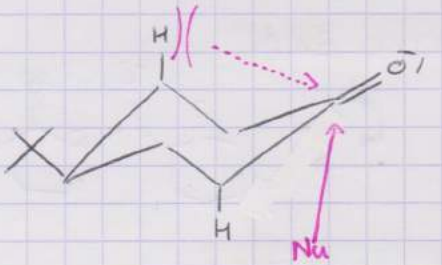
- Limite au modèle de Fukui

  - ne s'intéresse qu'aux réactifs

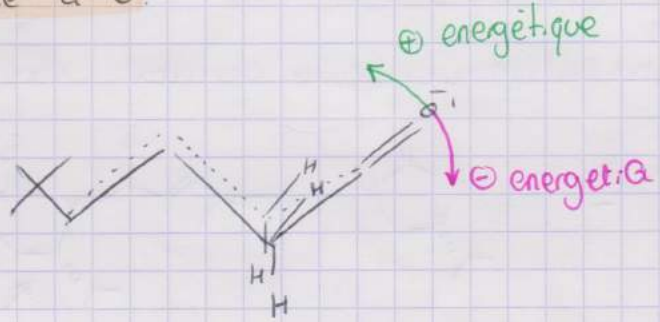


  - Si HO-1 est proche HO => intéract° à 3 on
  - Si recouvrement HO-BV faible => contrôle charge.

- Méthode approche Scr cycle à 6



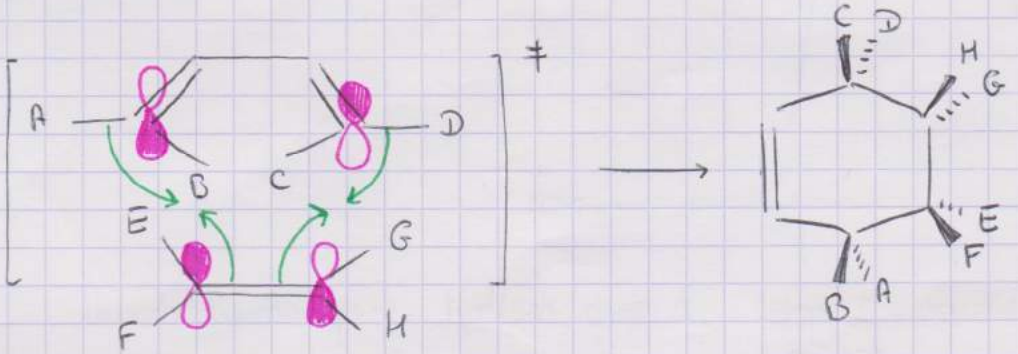
  - Si substituant gros



  - gêne des H par orienta° ○
  - pris en compte si substituant petit

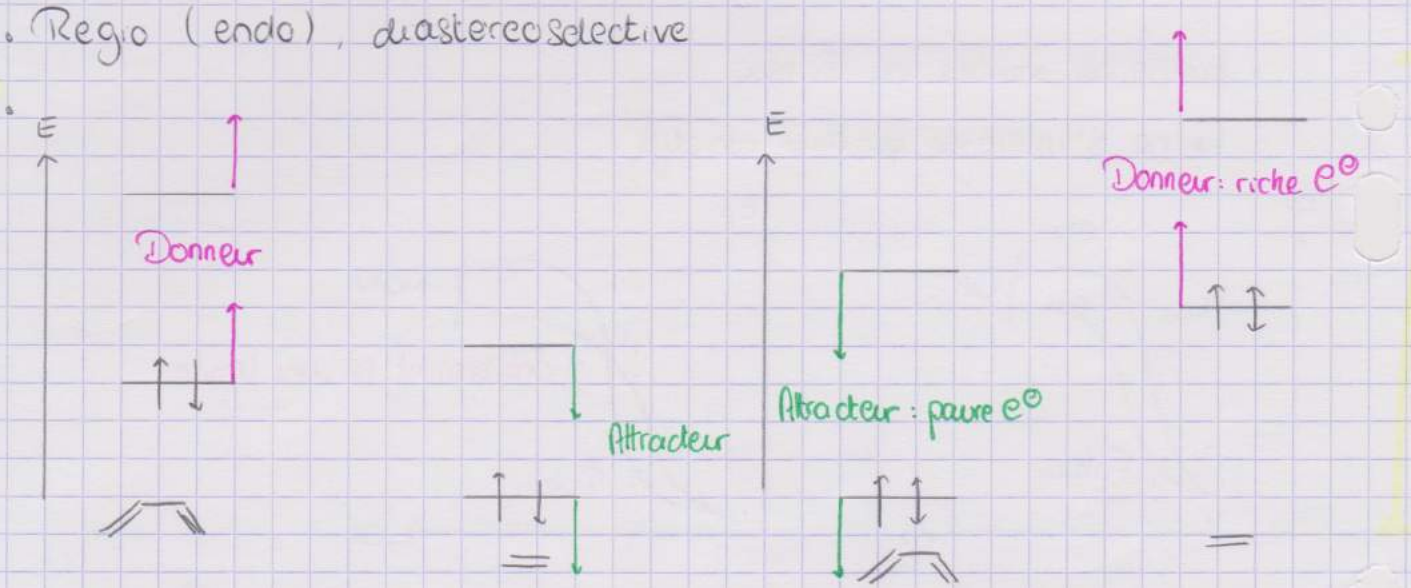
- Excès énantiomérique : $ee = \frac{|n(1) - n(2)|}{n(1) + n(2)}$

- Réaction Diels-Alder



- Diels-Alder (1928, PN 1950)

. Rego (endo), diastereoselective

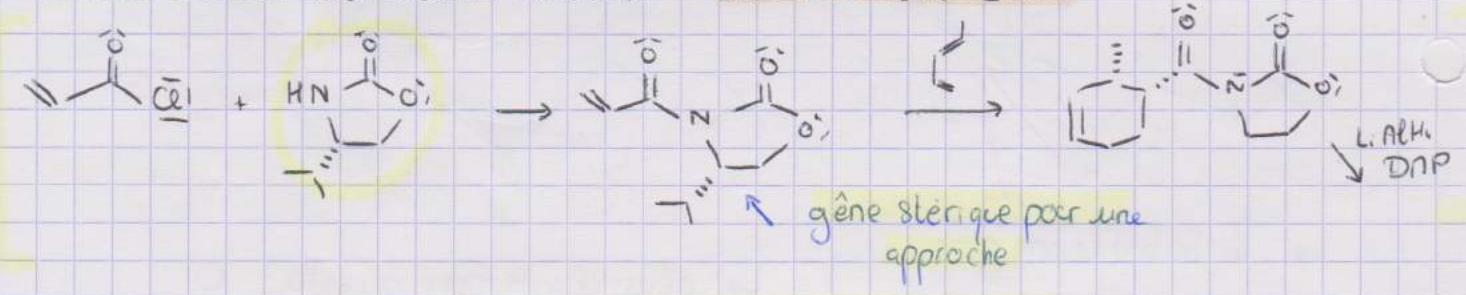


↳ Demande normale: diène = Nu ↳ Demande inverse: dienophile Nu

=> Reagit sur les atomes avec les ⊖ gros coeff dans la bonne OM

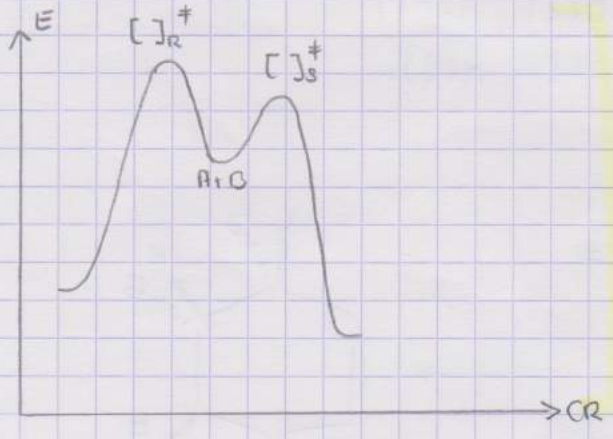
* Enantioselectivité

↳ utilisation auxiliaires chiraux : oxazolidinones Evans



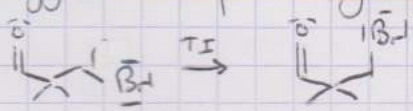
↳ On sépare les diastéréoisomères et on enlève la copule

. Utilisation catalyseurs chiraux



=> Obtention majoritaire d'un énantiomère.

. Effet Thorpe-Ingold : 2 grp methyl => repliement chaîne



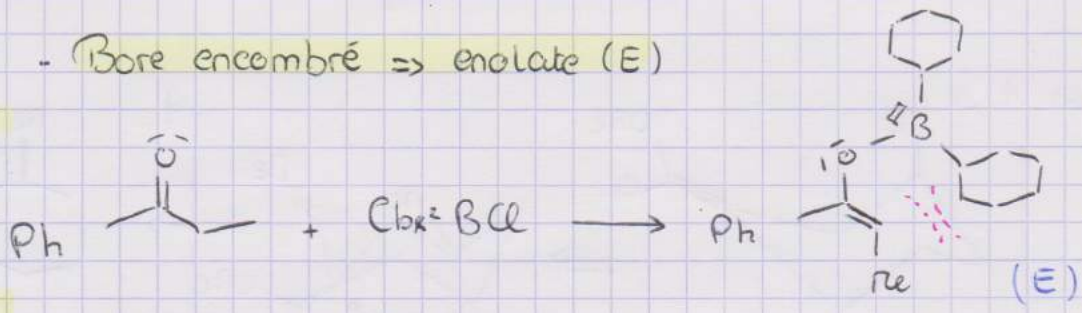
Fiche Chimie Organique XII

- Chimie des enolates

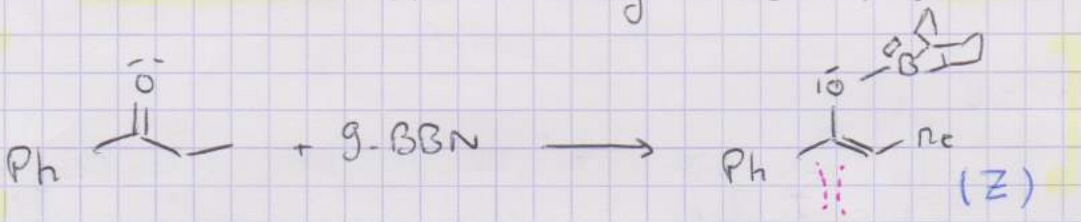
• Enolates de Bore : ⚠ Pas ET cylique : ≠ Ireland

↳ Stabilité finale uniquement

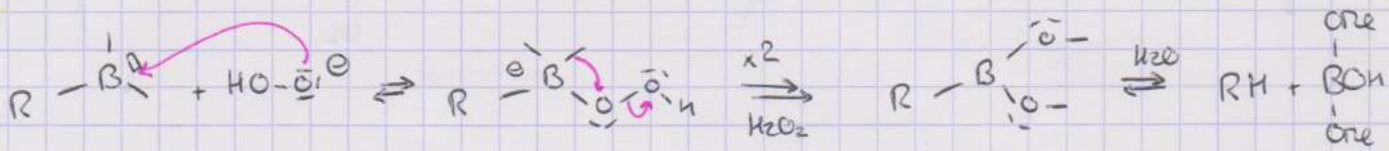
- Bore encombré => enolate (E)



- Bore ⊖ encombré (tt sauf $Chex_2BCl$) => Enolate (Z)

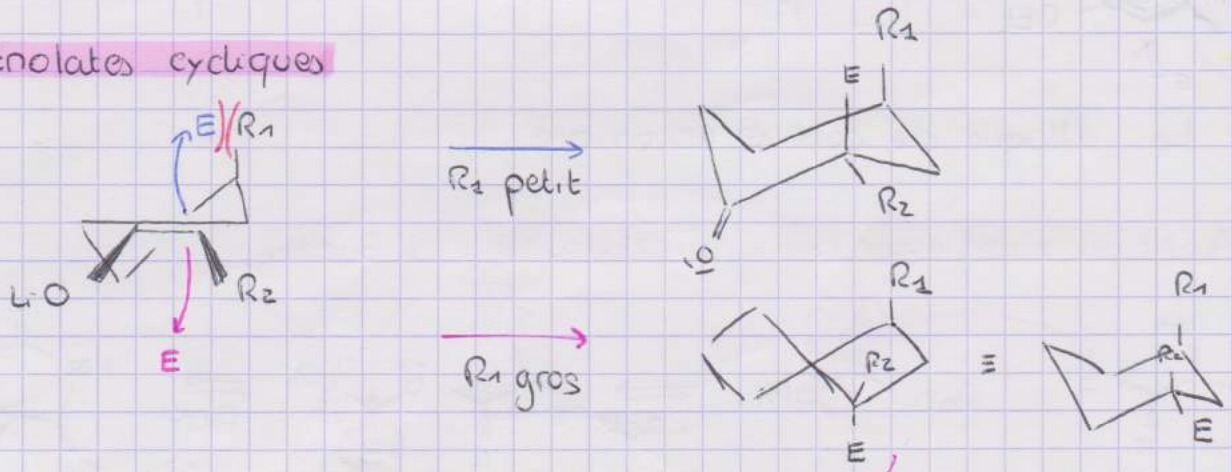


⚠ Necessite H_2O_2 par hydrolise $O-BR_2 \rightarrow HO$



• Alkylation des enolates

- Enolates cycliques

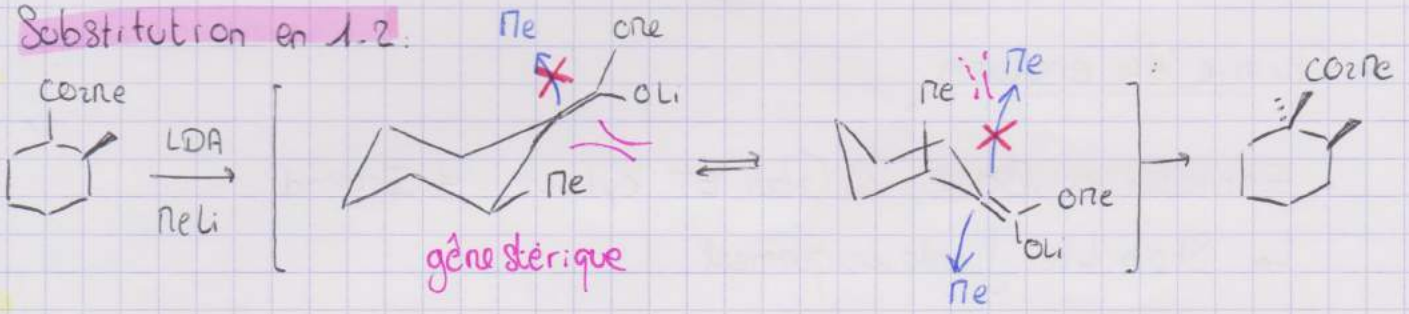


Conformation (geometrie) plus favorable

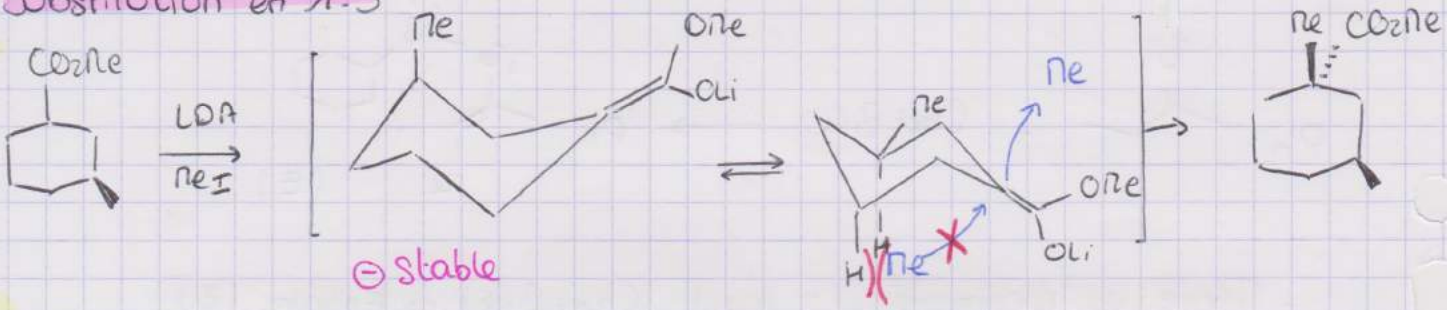
Favorisé si groupement R_1 est gros

- Enolates exocycliques

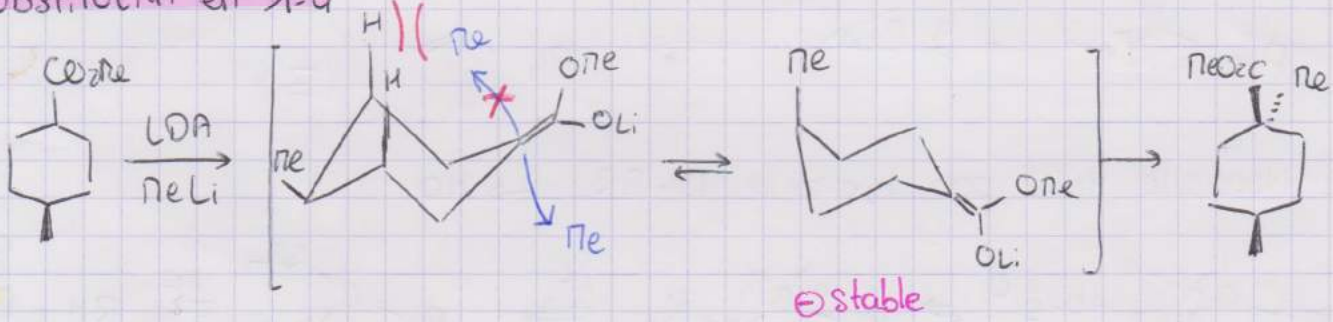
* Substitution en 1-2 :



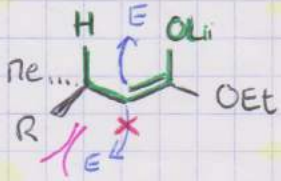
* Substitution en 1-3



* Substitution en 1-4



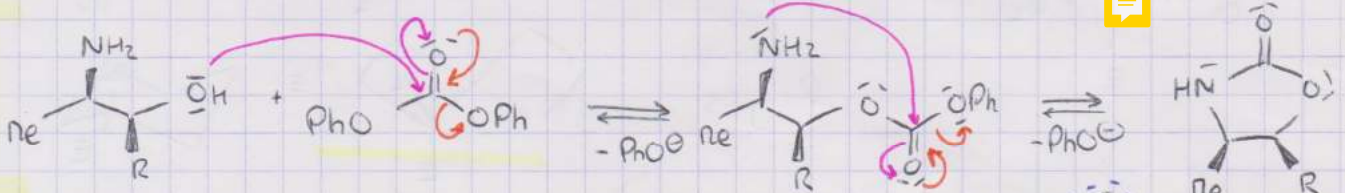
- Modèle de Hook (C* en β enolate)

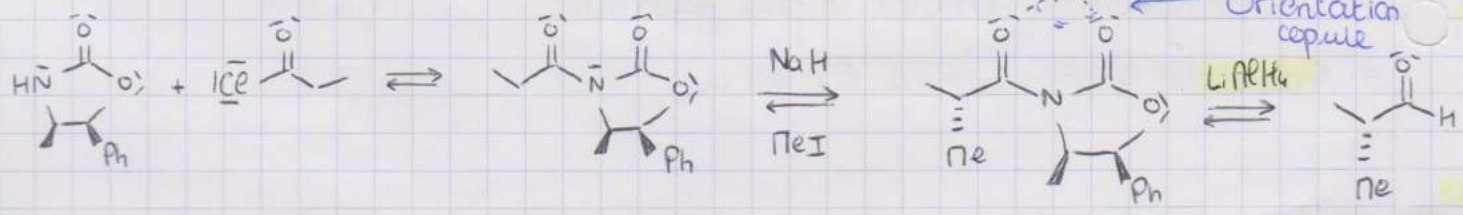


} Conformᵗ ⊕ reactive : H et Li eclipsés

↳ attaque du côté ⊖ encombré

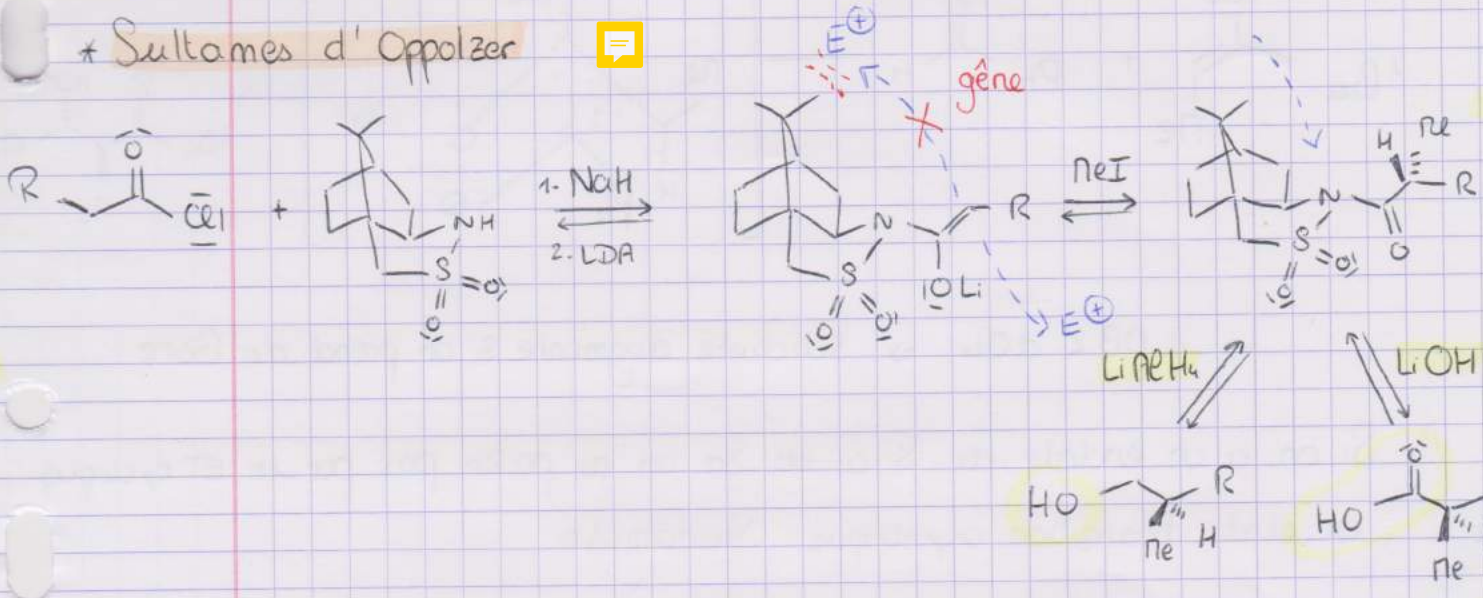
- Addition enantioselective : oxazolidinones d'Evans





Fiche Chimie Organique XIII

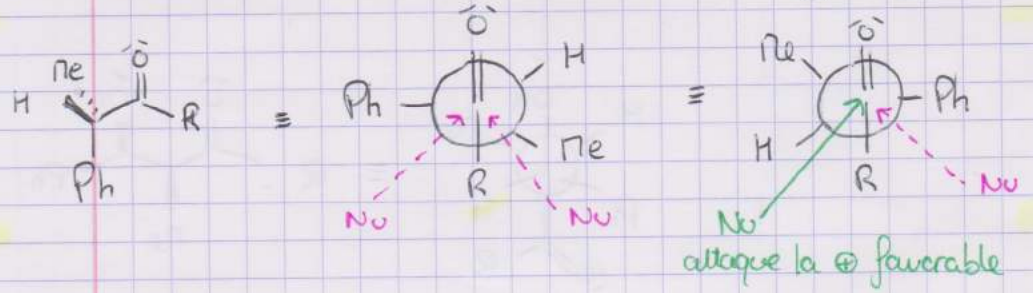
* Sultames d'Oppolzer



◦ Addition Nucleophile sur carbonylés.

* Felkin-Ahn

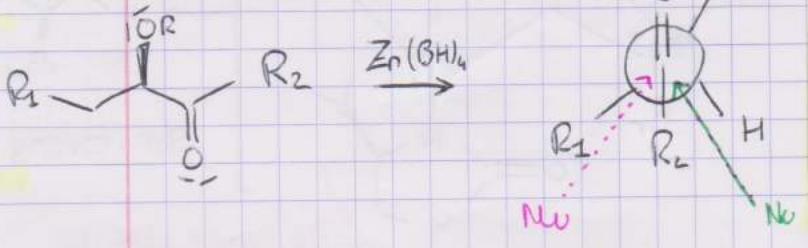
↳ Conformation la ⊕ reactive avec gros grp ⊥ O=C (orbitales)



↳ Groupement R gros => bonne selectivité

⚠ Heteroatome : { Avec metal => modele Cram chelate
Sinon prend place gros grapement.

* Modele Cram chelate

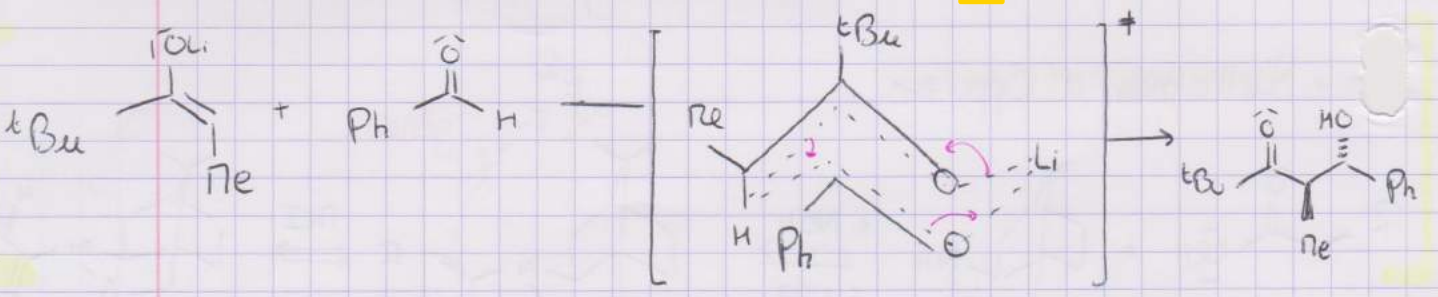


⚠ Si R est très gros on n'aura pas chelation => F-A

attaque ⊕ favorable

↳ $Li^{\oplus}$, $Na^{\oplus}$ et $K^{\oplus}$ ne permettent pas souvent la chelation

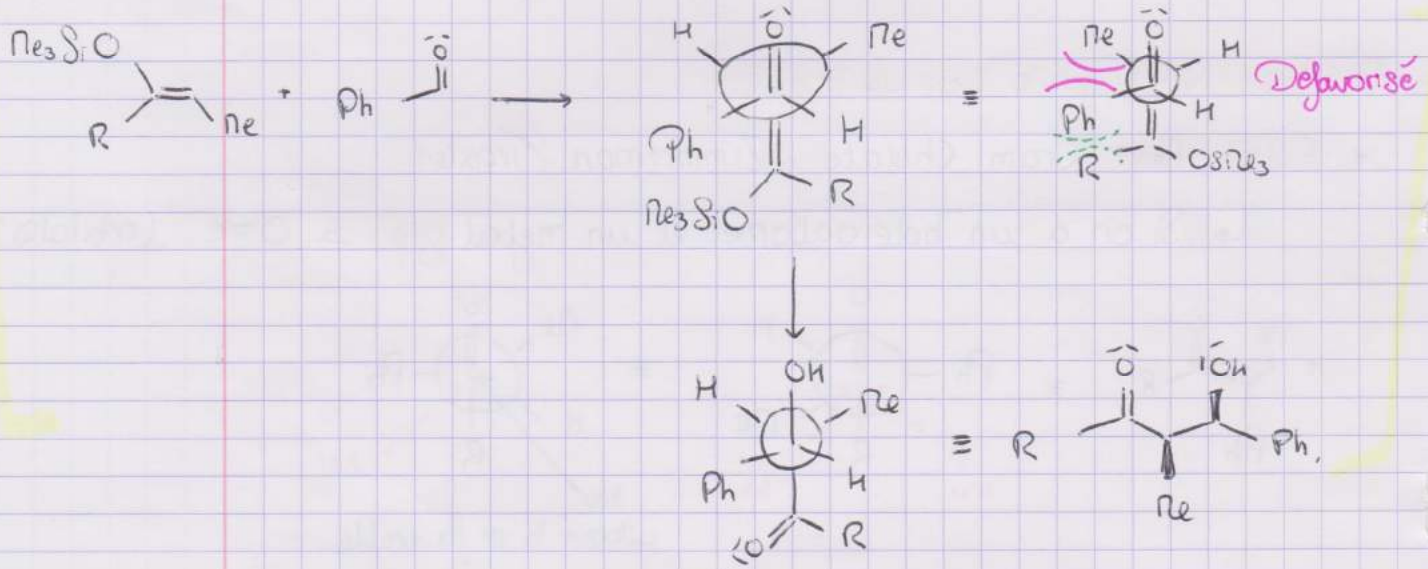
* Aldolisation : modèle Zimmerman - Traxler



↳ d OB < d OLi => Sélectivité augmente si on prend du Bore

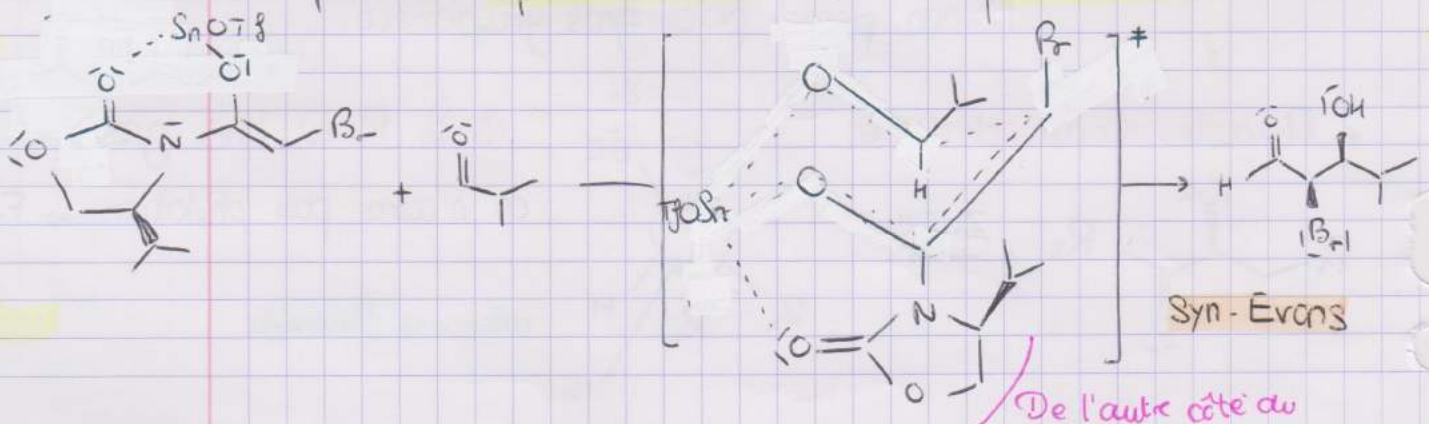
⚠ Si on a un enolate de Si ou de Sn on ne passe pas par un ET cyclique

↳ état transition acyclique Yamamoto



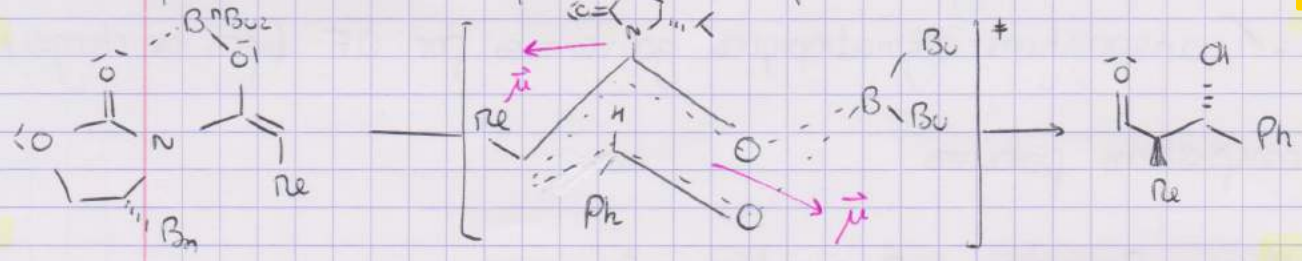
⚠ Si groupe R est très encombrant on peut avoir intera° avec Ph #

. Si on a en plus une copule chirale : Sn, Zr, Ti permettent coordination

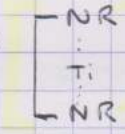


Fiche Chimie Organique XIV

⚠ Si Copule chirale mais pas de metal pour coordiner (B,)



les moments dipolaires en opposé

- Crimmins : même copule chirale mais énantiomères diff en fct° condi°
  - ↳ Sparteine :  : bloque la coordination avec copule chirale

* Addition crotyle metallé

↳ Organoboranes Roush

gêne avec aldehyde même côté que grp⁺ boo

⚠ Si on a des Si ou Sn encombrés passage par etats transition non cycliques ⇒ Yamamoto : Syn majo

⇒ Si effet metal, copule et groupement aldehyde

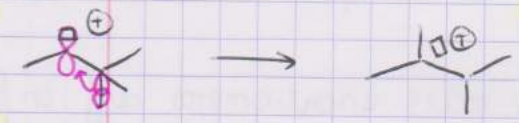
↳ { même sens : MATCH
  { sens opposé : MISMATCH

Transposition en chimie organique

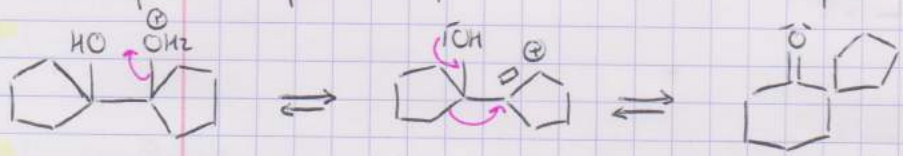
- Transpositions polaires : défaut ou excès $e^{\ominus}$ sur un atome
- Transpositions sigmatropiques gouvernées par OF (pas de charges)

* Transpositions polaires

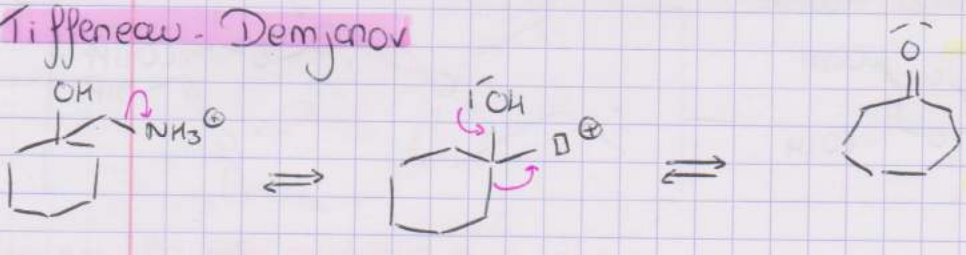
• Wagner Meerwein : ON orientées même sens



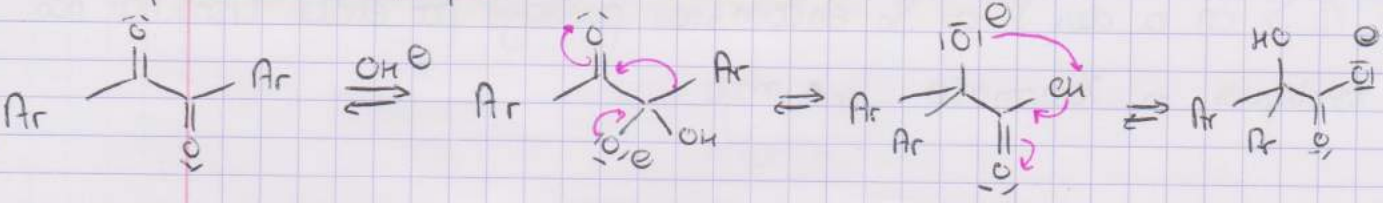
• Transposition pinacolique : Obtention composés spiro



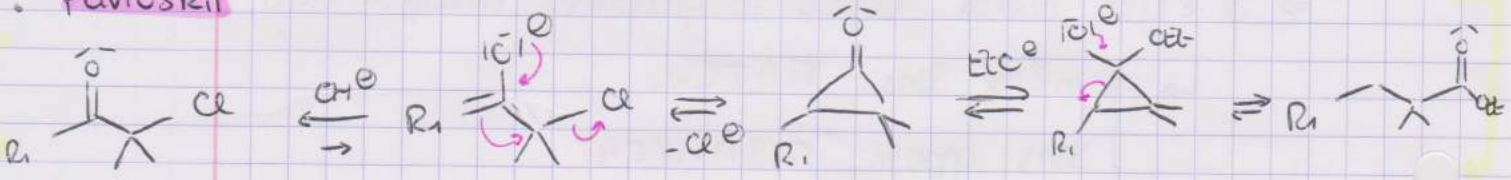
• Tiffeneau - Demjanov



• Transposition benzylique :



• Favroskii



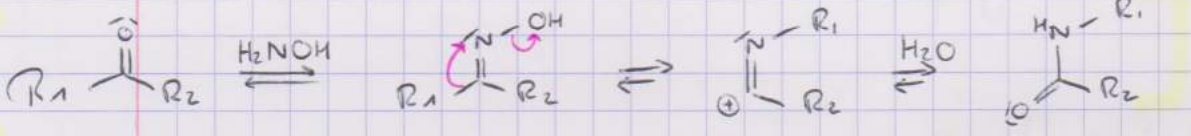
Fiche Chimie Organique XV

• Bayer - Villiger

- La aptitude migratoire $\overline{III}^{aire} > \overline{II}^{aire} > \overline{I}^{aire}$
- La Retention configuration

⚠ Avec m-CPBA risque epoxydation et inversement.

• Transposition de Beckman



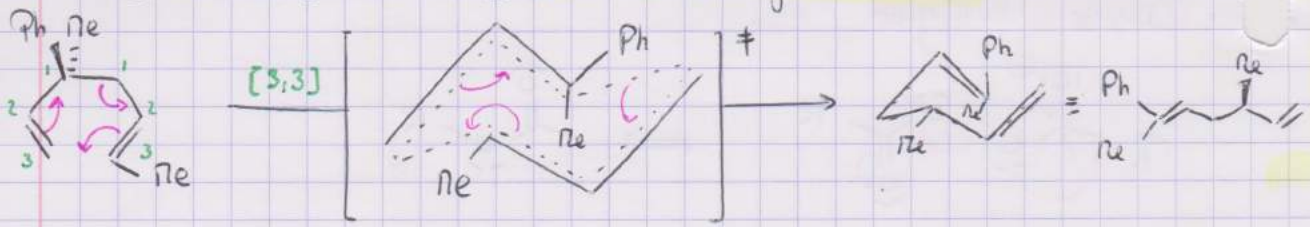
- La groupe en anti de OH qui migre
- La diminue les tensions de cycle

✱ Transposition Sigmatropiques

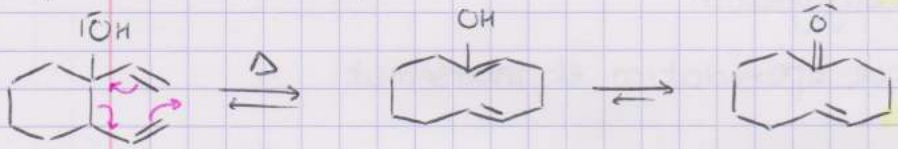
- Gouverné par les OF ; processus concertés
  - Cycloaddition : $\Delta\sigma = \pm 2$
  - Electrocyclisation : $\Delta\sigma = \pm 1$
  - Sigmatropiques $\Delta\sigma = 0$

- Transposition de Cope :

• Etat transition 6 centres ⇒ transfert chiralité

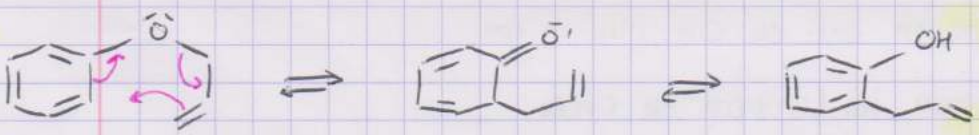


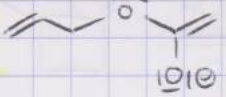
- Transposition oxy - Cope



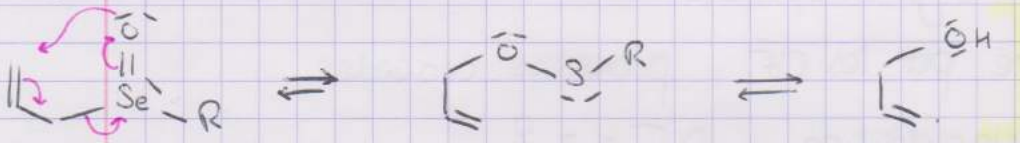
↳ Passage par alcoolate ↗ réac (encore ⊕ si $O^{\ominus}$ libre)

- Transposition Claisen

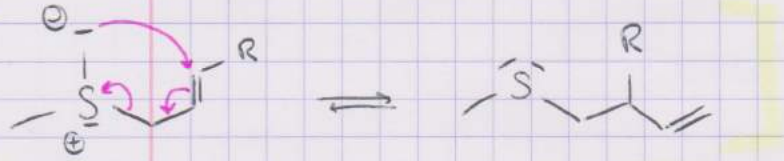


↳ possible avec enolates esthers  (+ TNS par prdé)

- Rearangement Sulfoxydes / Selenoxydes



- Rearangement Ylures de Soufre

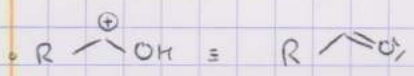
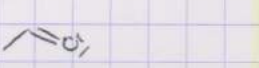


Fiche révision Chimie organique XVI

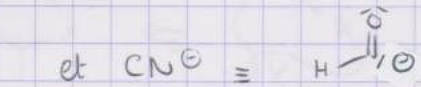
Retrosynthese :

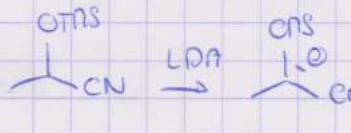
- Privilegier Synthèse convergente
- Interconversion groupes fonctionnels peut donner nouvelles possibilités
- Obtenir Synthons lineaires et de même taille

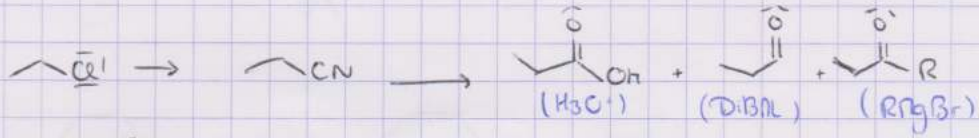
* Equivalent Synthetiques

- $R^{\oplus}$ ≡ R-Br ; ROTs | $R^{\ominus}$ ≡ RMgBr - RCuLi
-  ≡ 
- 
- 

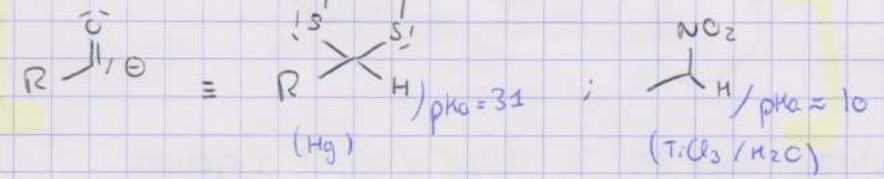
* Synthons à polarité inversée = "Umpolung"

- $CN^{\ominus}$ est très Nu et $CN^{\ominus}$ ≡ 



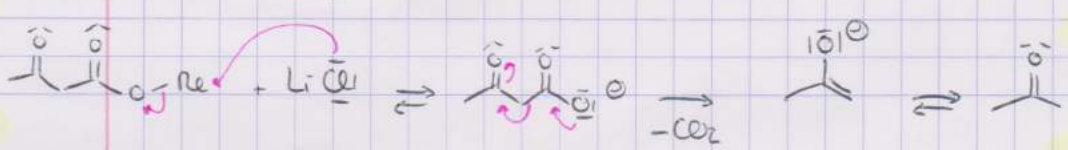
↳ $INCl^{\ominus}$ + 

(H₃O⁺) (DiBAL) (RMgBr)

- 

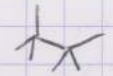
(Hg) pKa = 31 ; pKa ≈ 10 ($TiCl_3$ / H_2O)

* Decarboxylation Krapcho



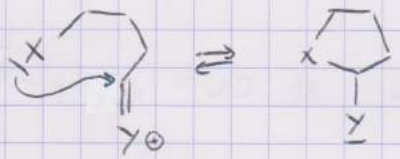
Formation de cycles

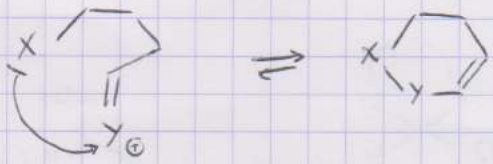
- Effet entropique : probabilité de rencontre
- Effet enthalpique : dépend de la tension des cycles

- Effet Thorp-Ingold favorise cyclisation 
  ↳ diminue nb conforma° / rapproche extrémités

* Règle de Baldwin :

- Expérimental

↳ endo 

↳ exo : 

- Cyclisation favorisée si diluée / goutte à goutte
- Effet template