

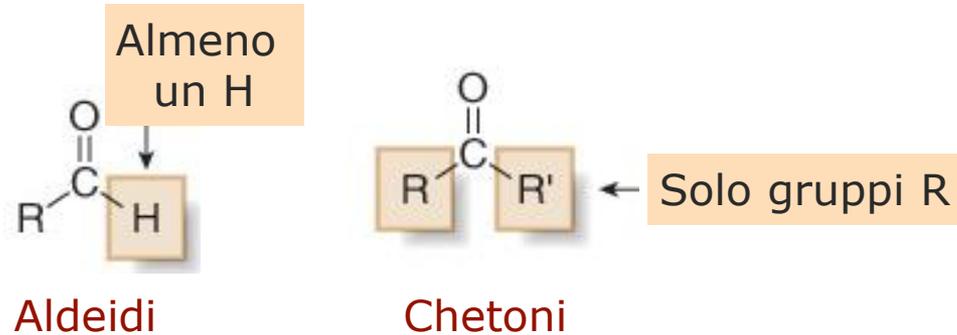
Composti carbonilici

Introduzione

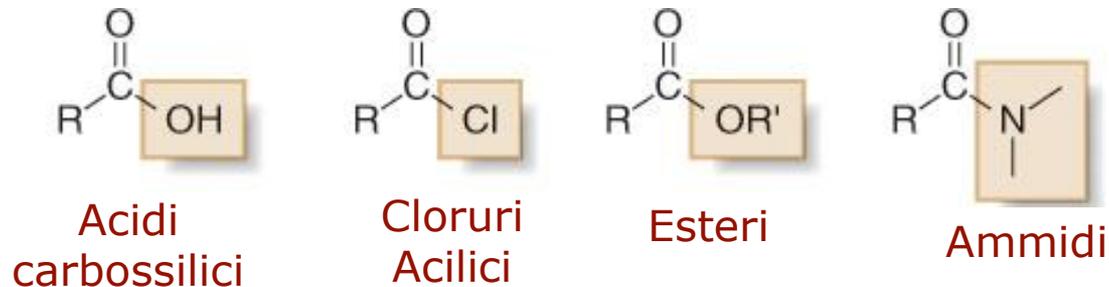
Introduzione

Ci sono due classi generali di composti che contengono il gruppo carbonilico C=O:

[1] Composti che hanno solo atomi di H e di C legati al carbonile

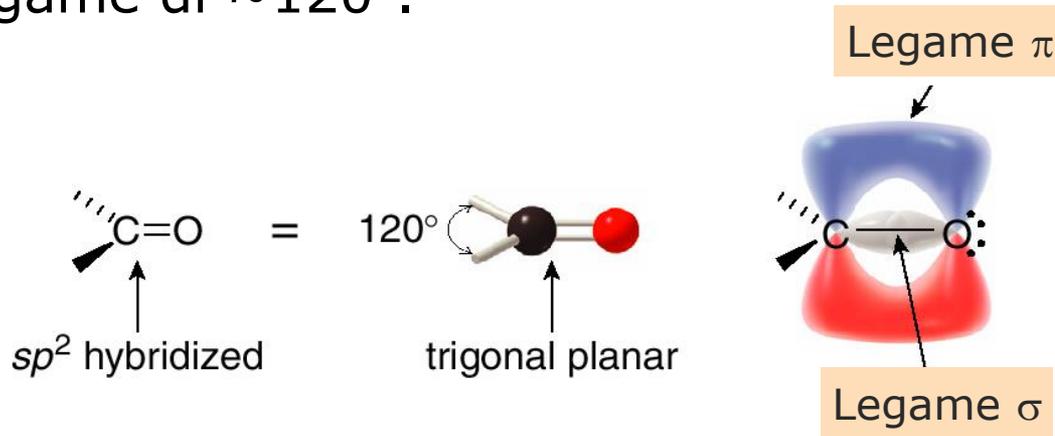


[2] Composti che contengono un eteroatomo (N, O, S, Cl) legato al carbonile

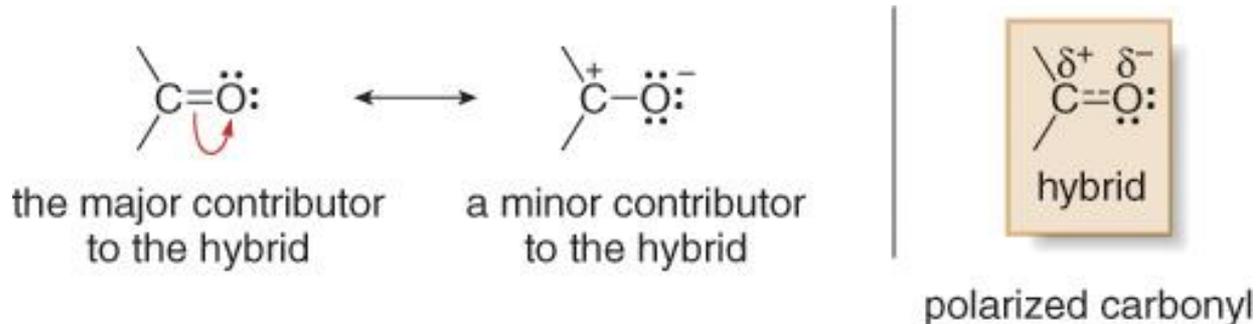


Introduzione

- Il carbonio carbonilico è ibridato sp^2 , trigonale planare, con angoli di legame di $\sim 120^\circ$.



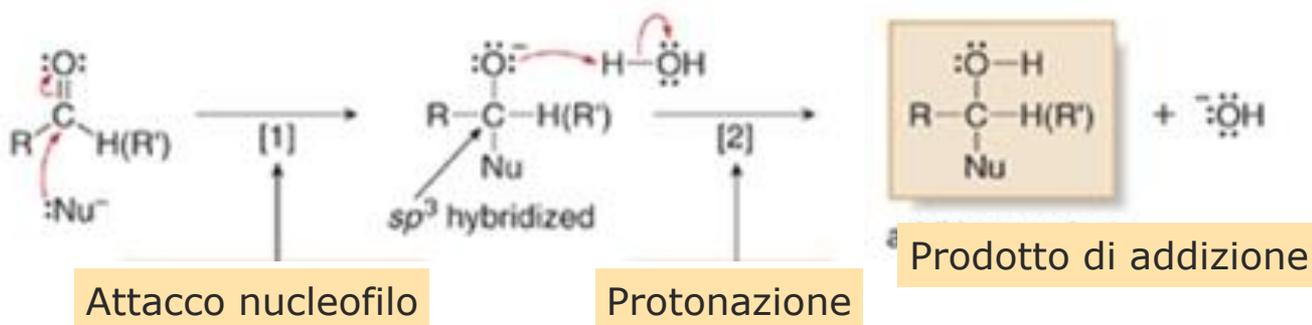
- Il legame carbonilico è polarizzato per la presenza dell'atomo elettronegativo di ossigeno. Questo rende il carbonio carbonilico povero di elettroni



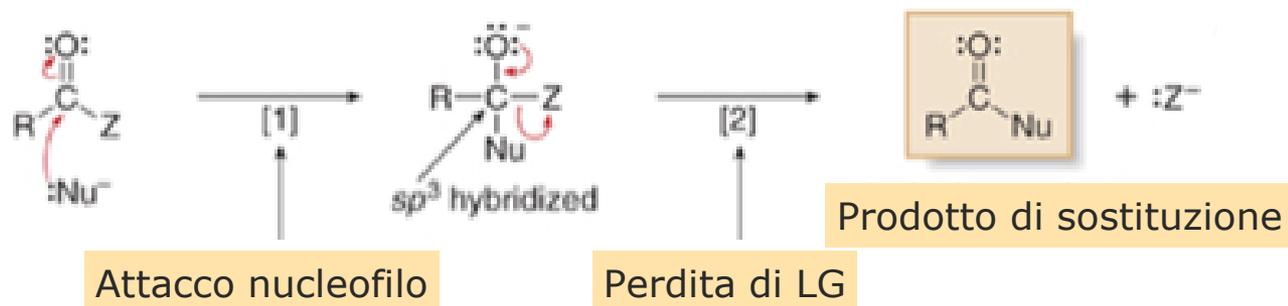
Reazioni generali dei composti carbonilici



Aldeidi e chetoni



Derivati acilici



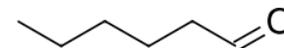
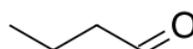
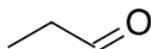
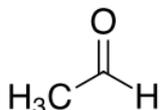
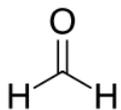
Aldeidi e Chetoni

Capitolo 19

Chimica Organica, *8^a Edizione*

John McMurry

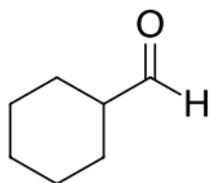
Nomenclatura delle aldeidi



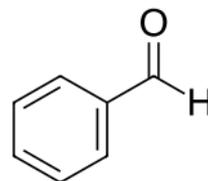
IUPAC	metanale	etanale	propanale	butanale	pentanale	esanale
COMUNE	(formaldeide)	(acetaldeide)	(propionaldeide)	(butirraldeide)	(valeraldeide)	(aldeide caproica)

IUPAC

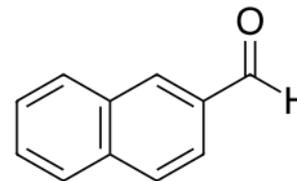
- Trovare la catena più lunga che contiene il gruppo CHO
- Cambiare il suffisso dell'alcano corrispondente in *-ale*.
- Se il gruppo CHO è legato ad un anello, aggiungere al nome del ciclo il suffisso *-carbaldeide*.



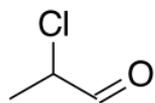
Cicloesancarbaldeide



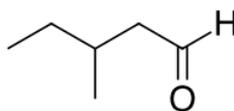
benzenecarbaldeide
(benzaldeide)



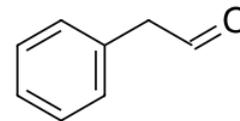
2-naftalenecarbaldeide



2-cloropropanale

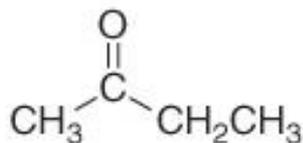


3-metilpentanale

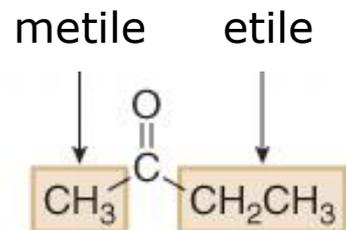


feniletanale

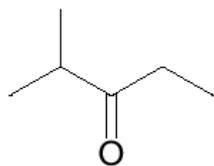
Nomenclatura dei chetoni



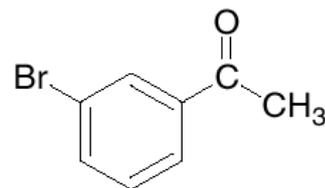
IUPAC 2-butanone



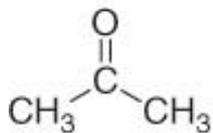
COMUNE etilmetilchetone



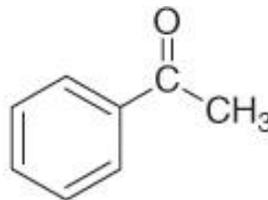
IUPAC 2-metil-3-pentanone
COMUNE etilisopropilchetone



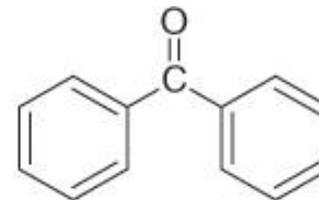
m-bromoacetofenone
3-bromoacetofenone



acetone
(2-propanone)

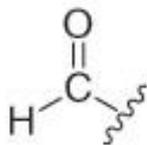


acetofenone

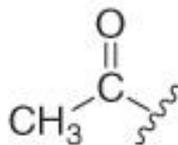


benzofenone

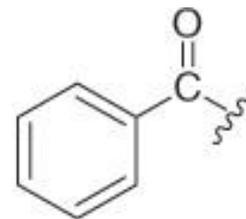
Nomenclatura di Aldeidi e Chetoni



gruppo formile

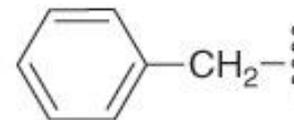


gruppo acetile



gruppo benzoile

Non confondere il gruppo benzoile con il benzile



gruppo benzile

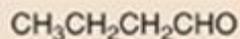
Proprietà Fisiche

Punti di ebollizione e di fusione

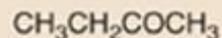
Confrontando composti di PM confrontabile, p.eb. e p.f. aumentano con la forza delle interazioni intermolecolari .



VDW
MW = 72
bp 36 °C



VDW, DD MW = 72
bp 76 °C

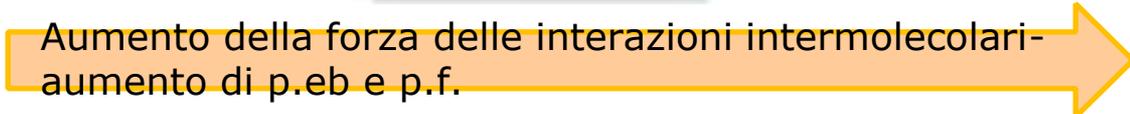


VDW, DD MW = 72
bp 80 °C



VDW, DD, HB
MW = 74
bp 118 °C

Aumento della forza delle interazioni intermolecolari-
aumento di p.eb e p.f.



Solubilità

- Aldeidi e chetoni con meno di 5 atomi di C sono solubili in H₂O, con cui formano legami H.
- Aldeidi e chetoni con più di 5 atomi sono insolubili in H₂O perchè prevale la parte alchilica idrofobica
- Aldeidi e chetoni di qualunque dimensione sono solubili in solventi organici

Aldeidi e chetoni di interesse



formaldeide
 $\text{CH}_2=\text{O}$

Annualmente si producono milioni di tonnellate di **formaldeide** per ossidazione del metanolo. E' venduta come soluzione al 37% in H_2O , chiamata formalina, che è usata come disinfettante, antisettico e conservante per campioni biologici. La formaldeide è il prodotto di combustione incompleta del carbone ed è responsabile dell'irritazione causata dallo smog.

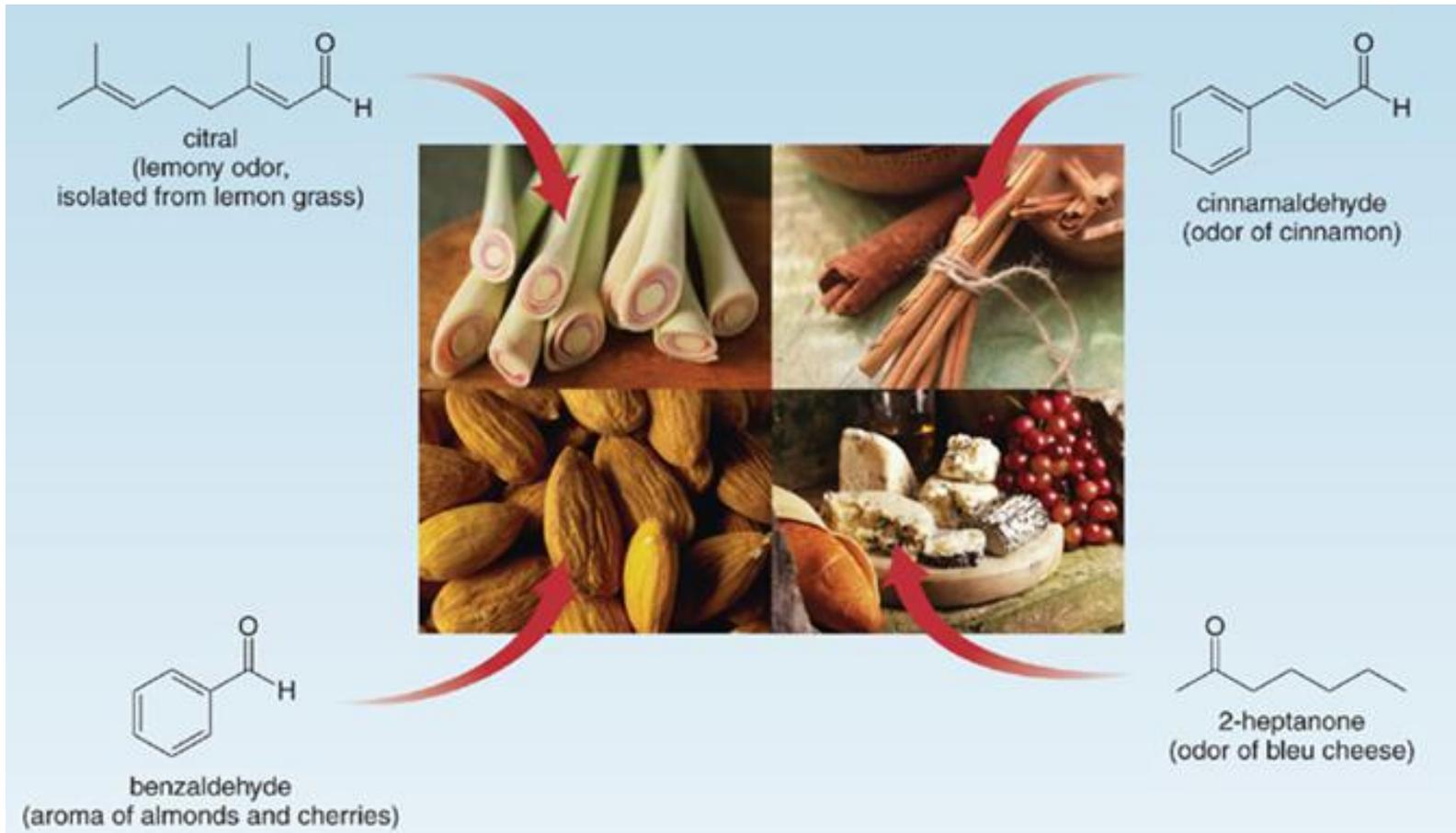


acetone
 $(\text{CH}_3)_2\text{C}=\text{O}$

L'**acetone** è un solvente industriale. E' anche prodotto *in vivo* nel metabolismo degli acidi grassi. I diabetici spesso hanno livelli inusualmente alti di acetone nel sangue.

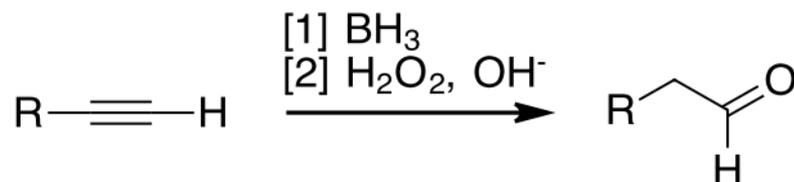
Aldeidi e chetoni di interesse

Molte aldeidi e chetoni sono aromi naturali.

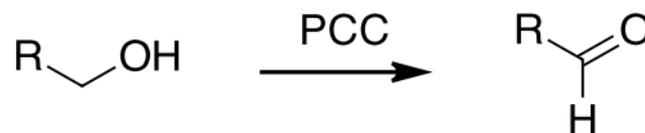


Preparazione di Aldeidi

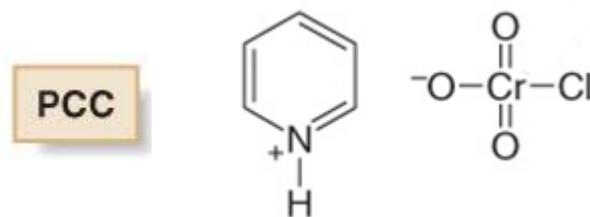
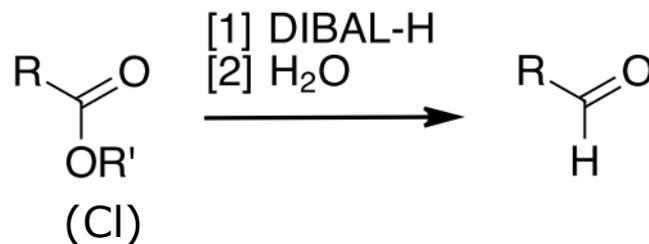
Idroborazione - ossidazione di alchini



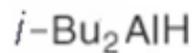
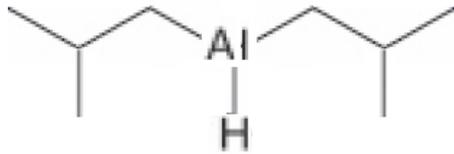
Ossidazione di alcoli primari



Riduzione di esteri e cloruri acilici

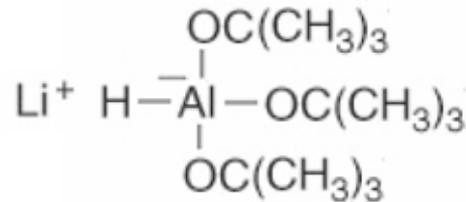


Preparazione di Aldeidi e Chetoni



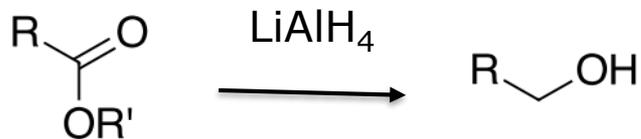
DIBAL-H

Diisobutilalluminio idruro



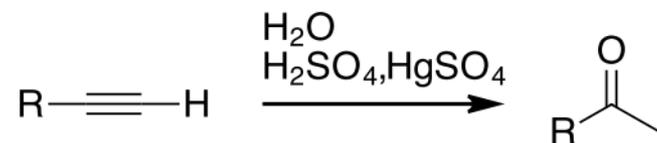
Litio tri-*tert*-butossialluminio idruro

Sono idruri ingombrati meno reattivi di LiAlH_4

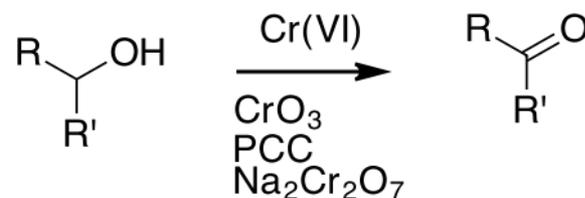


Preparazione di Chetoni

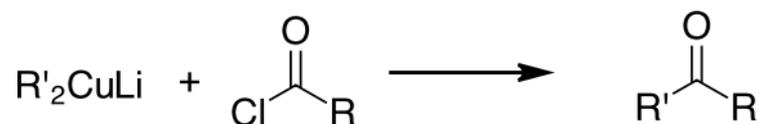
Idratazione di alchini



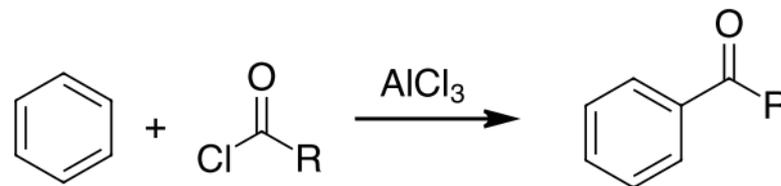
Ossidazione di alcoli secondari



Acilazione di organocuprati

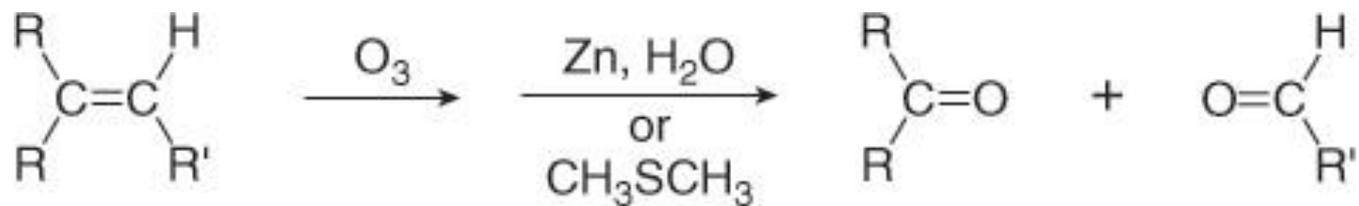


Acilazione di Friedel Crafts
(per chetoni aromatici)



Preparazione di Aldeidi e Chetoni

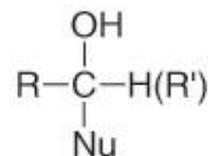
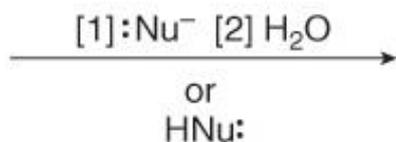
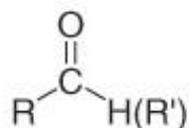
Scissione ossidativa di alcheni



Reazioni di Aldeidi e Chetoni — Generalità

[1] Addizione Nucleofila

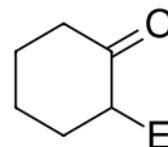
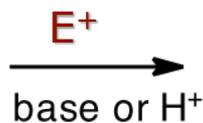
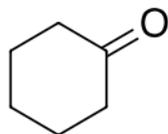
Reazione generale
Addizione nucleofila



Addizione
di H e Nu

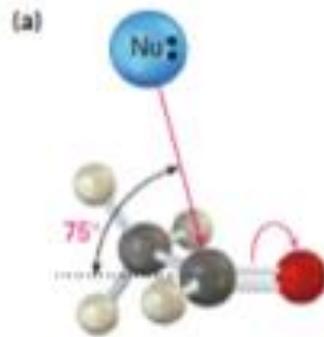
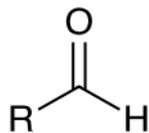
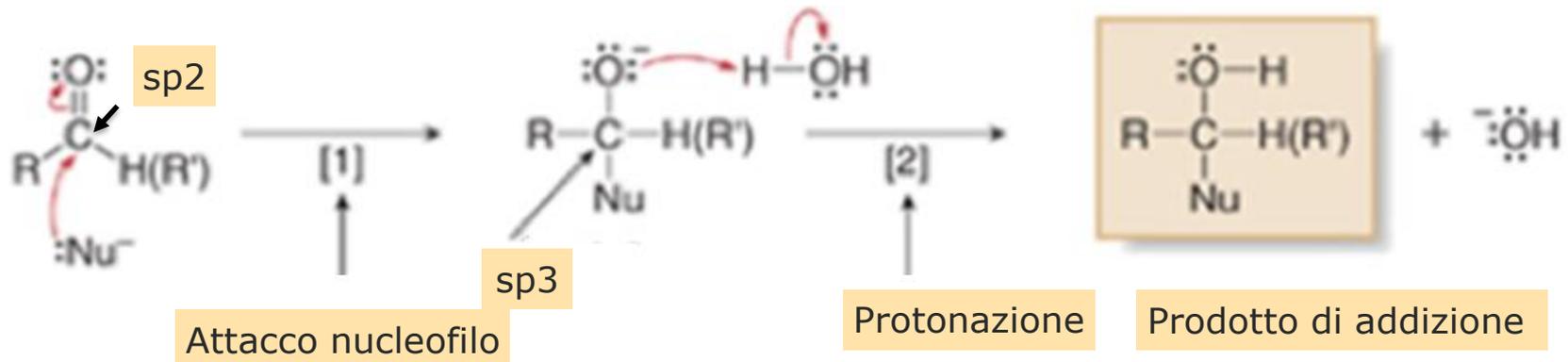
[2] Ossidazione (aldeidi)

[3] Reazioni al Carbonio α

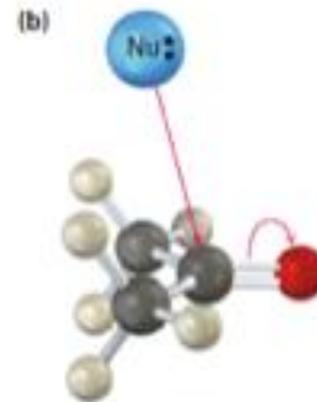


Addizione Nucleofila

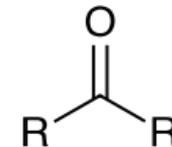
Si forma un alcolato come intermedio che viene poi protonato ad alcol



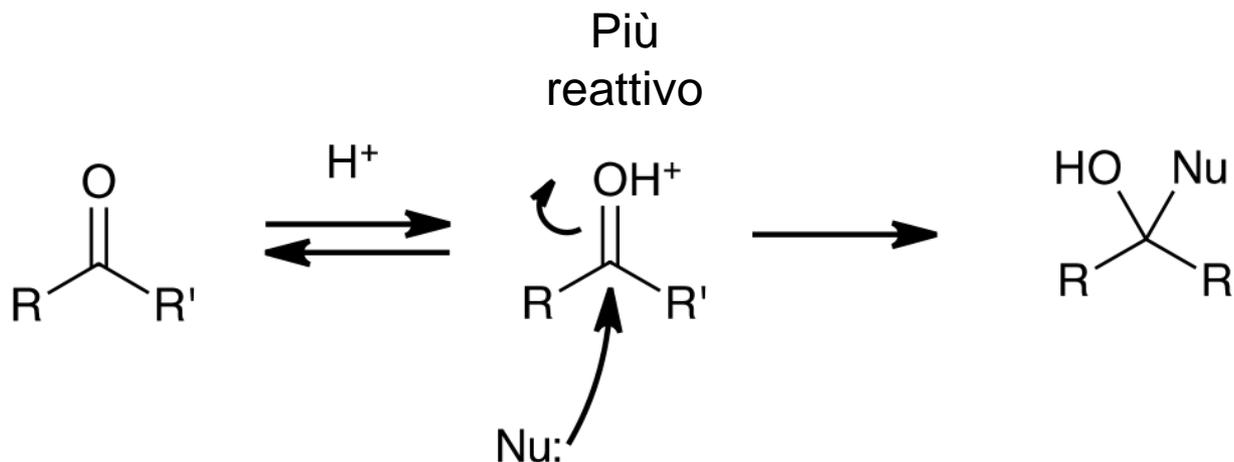
Aldeide:
Meno ingombrata
Più reattiva



Chetone
Più ingombrato
Meno reattivo



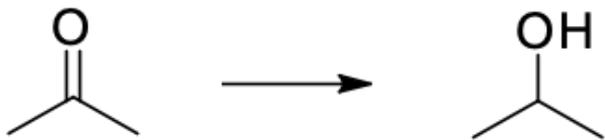
Catalisi Acida



E' necessaria con nucleofili deboli (H_2O , ROH , Ammine)

La protonazione dell'ossigeno aumenta l'elettrofilicità del C carbonilico

Riduzione



Alcoli secondari



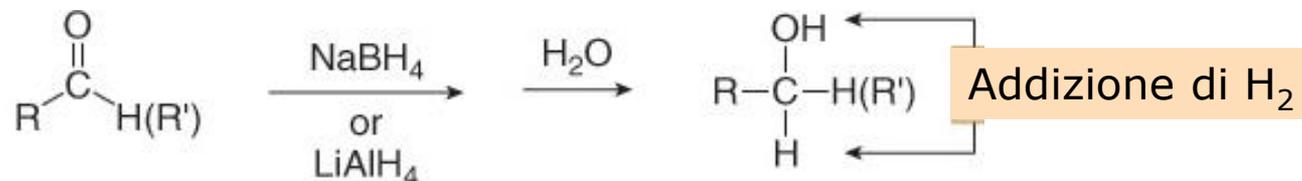
Alcoli primari



H_2/Pd riduce anche il $C=C$
 $NaBH_4, LiAlH_4$ selettivo per $C=O$

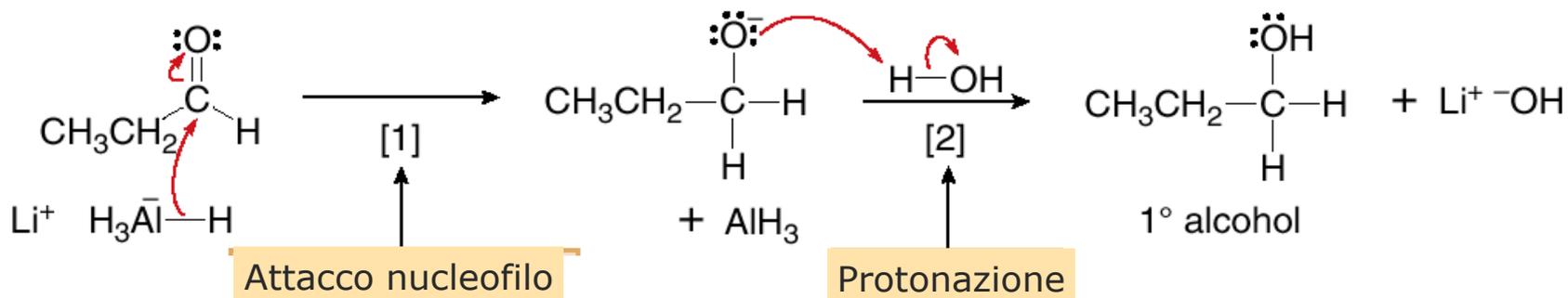
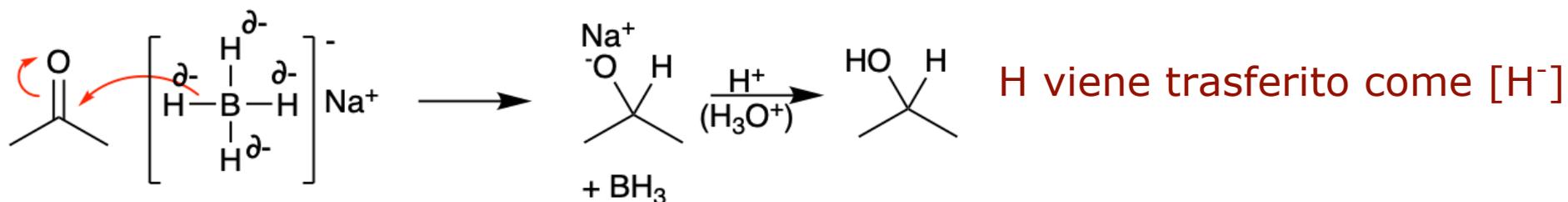
Riduzione

Reazione generale



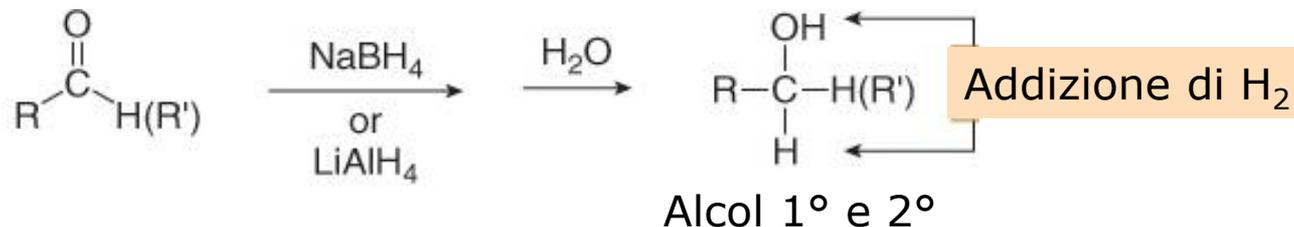
Alcol 1° e 2°

Meccanismo: **addizione nucleofila di H⁻ al C=O**



Riduzione

Reazione generale



Confronto NaBH₄ / LiAlH₄

LiAlH₄ (LAH) è più reattivo e meno selettivo di NaBH₄:

NaBH₄ riduce solo aldeidi e chetoni.

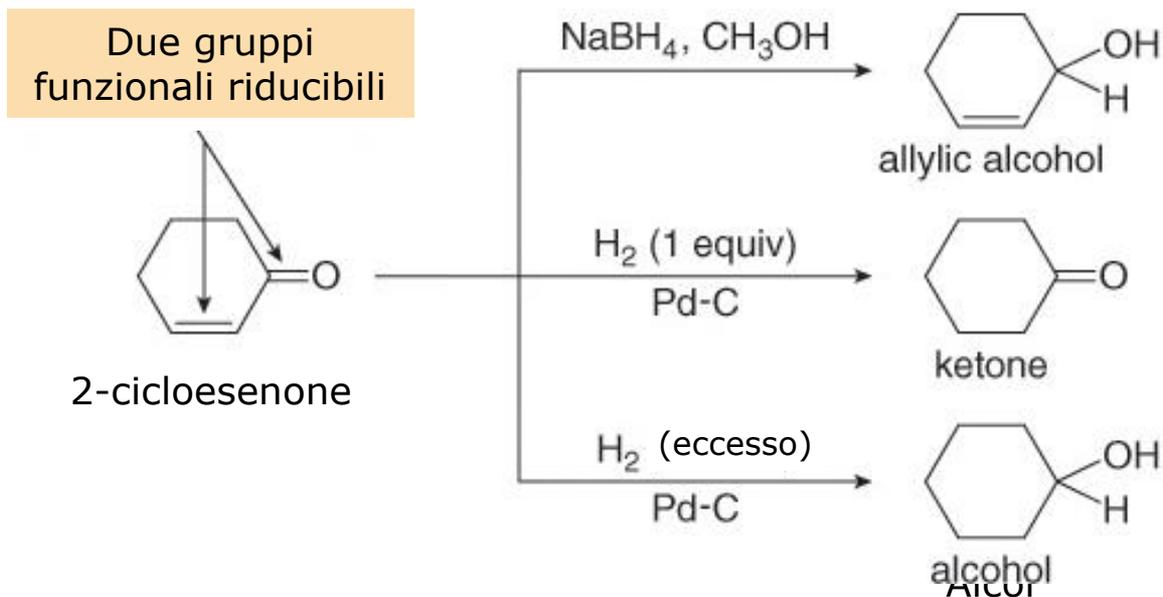
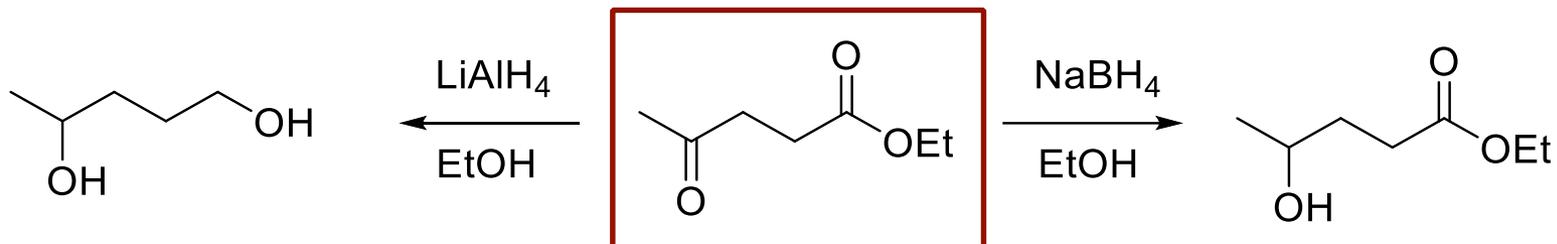
LAH riduce anche esteri, amidi e nitrili.

NaBH₄ può essere usato in solventi protici (alcoli e H₂O)

LAH deve essere usato in solventi non protici e anidri (EtOEt, THF) a causa della reazione di idrolisi:

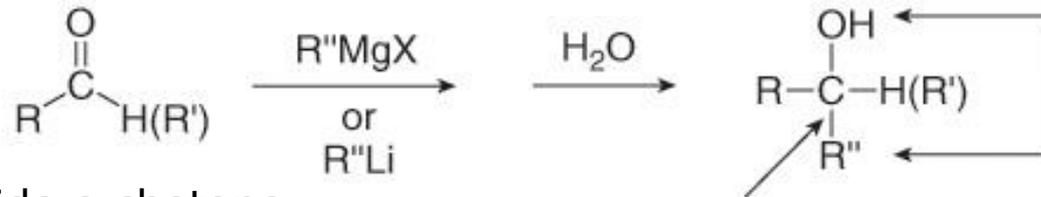


Riduzione - Selettività



Addizione Nucleofila di Reagenti Organometallici

Reazione generale

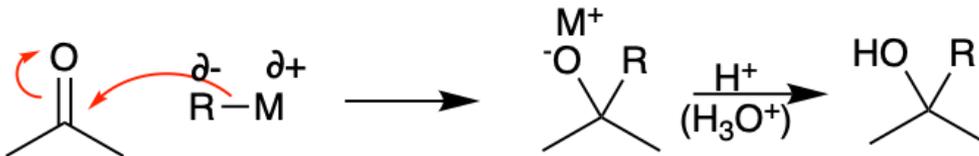


Aldeide o chetone

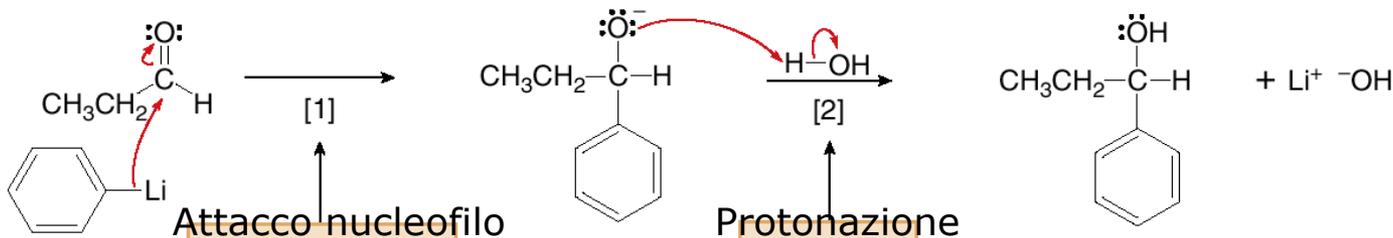
Addizione di R'' e H

Nuovo legame C-C
Alcol 1°, 2° e 3°

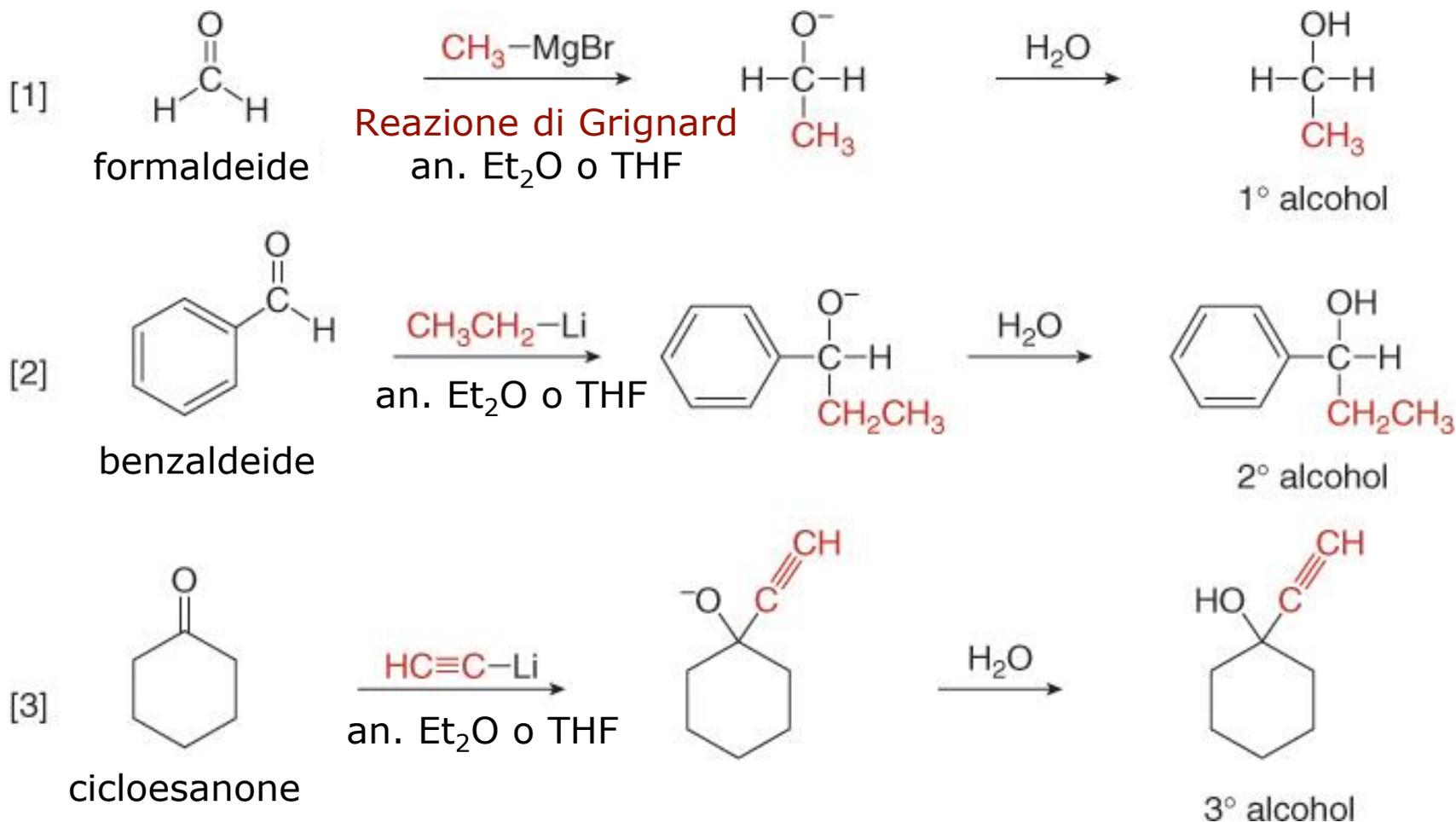
Meccanismo: **addizione nucleofila al C=O**



R viene trasferito come [R⁻]

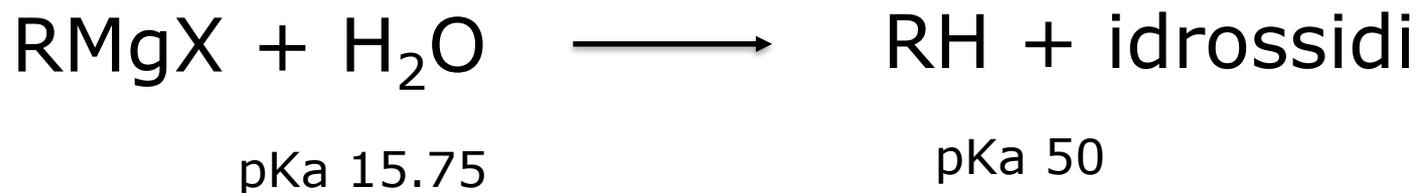


Reazione di composti carbonilici con reagenti organometallici.



Reagenti Organometallici

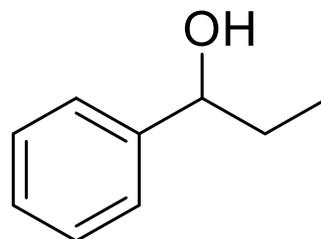
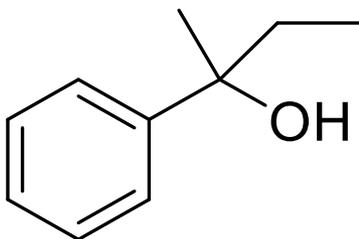
I reagenti organometallici devono essere preparati e usati in solventi aprotici anidri (EtOEt, THF)



H₂O (pKa 16), alcoli (pKa 16 -18), ammine (pKa 35) distruggono i reattivi di Grignard e litioorganici che sono basi molto forti, Protonandoli e convertendoli nei corrispondenti alcani.

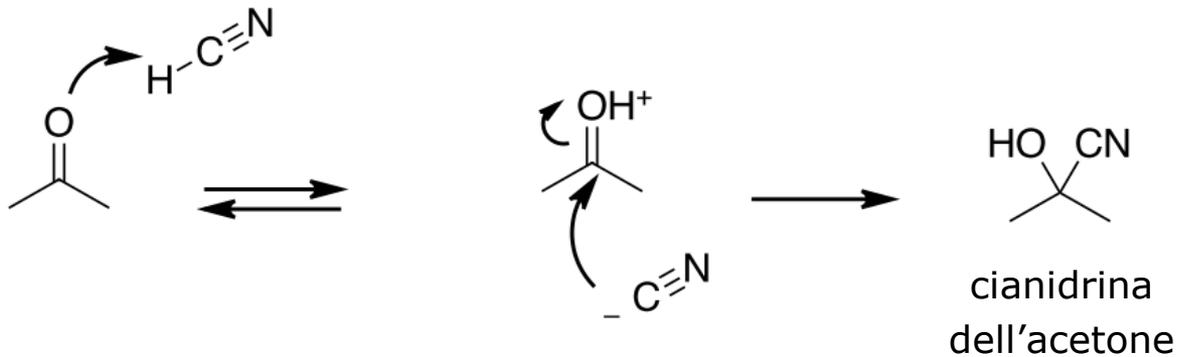
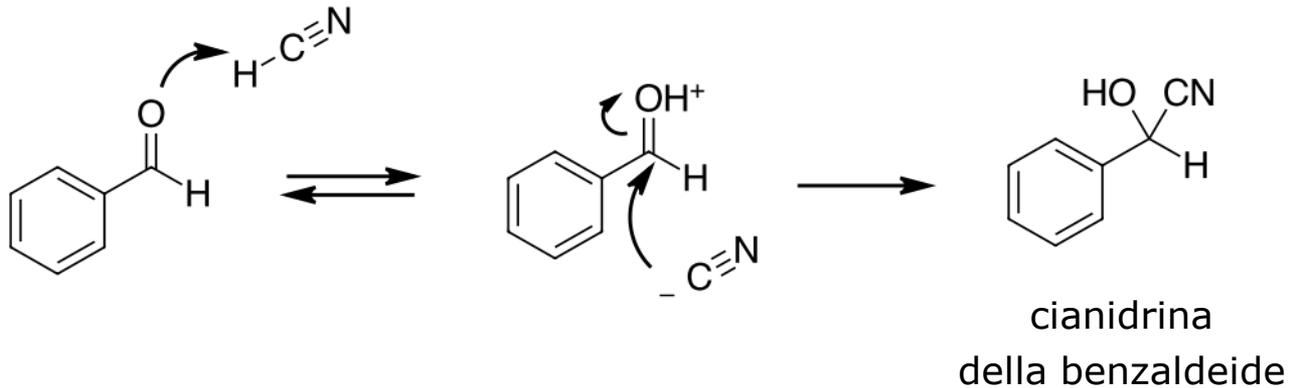
Esercizi

Sintesi dei seguenti alcoli



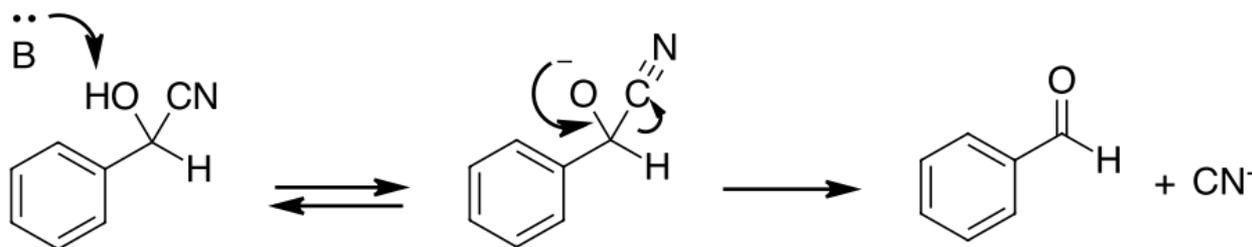
Addizione Nucleofila di CN^-

- Il trattamento di un'aldeide o chetone con HCN dà una cianidrina.



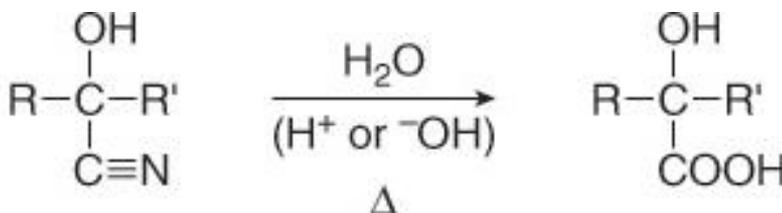
Addizione Nucleofila di CN⁻

- Le **cianidrine** possono essere riconvertite nei composti carbonilici di partenza per trattamento con una base. Questo è il processo esattamente inverso dell'addizione di HCN: deprotonazione dell'OH seguita da eliminazione di ⁻CN.



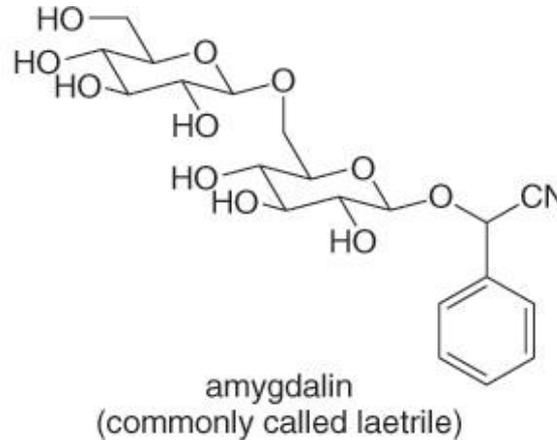
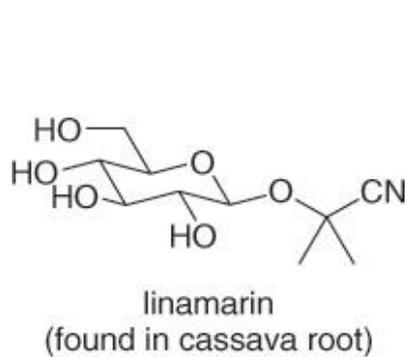
- Il gruppo ciano di una cianidrina è facilmente idrolizzabile a gruppo carbossilico per riscaldamento con una soluzione acquosa acida o basica.

Idrolisi di cianidrine



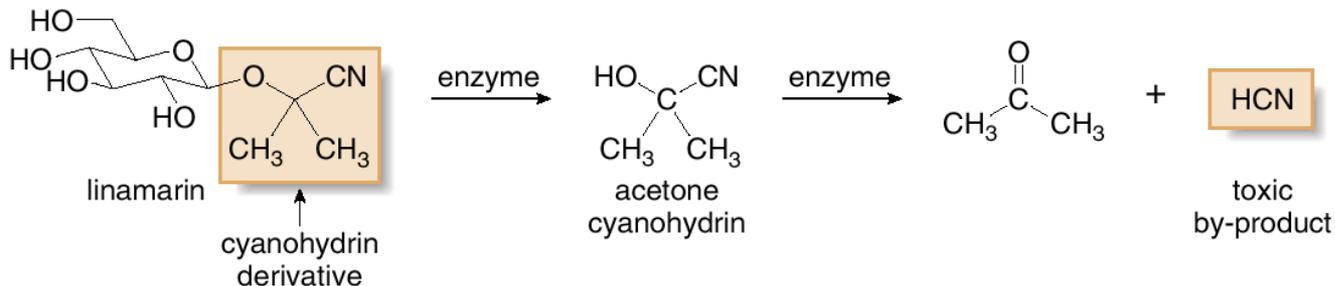
Addizione Nucleofila di CN⁻

- Linamarina e Amigdalina sono due cianidrine naturali



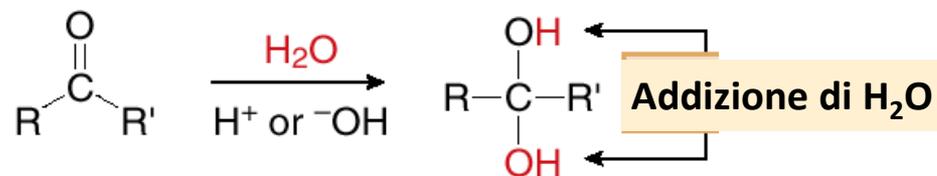
- Entrambi questi composti sono tossici perché vengono metabolizzati a cianidrine semplici che vengono a loro volta idrolizzate a composti carbonilici e HCN.

The breakdown of linamarin to HCN



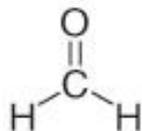
Addizione di H₂O — Idratazione

Addizione nucleofila di H₂O

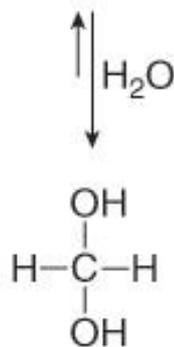


R' = H o alchile

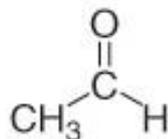
Diolo geminale
(idrato)



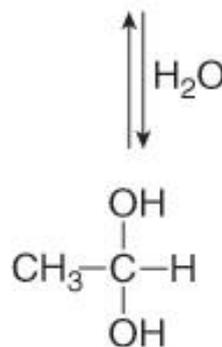
Formaldeide



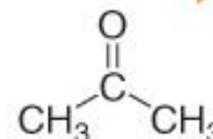
99%



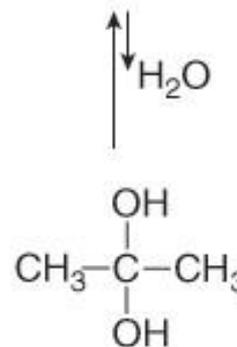
Acetaldeide



58%



Acetone

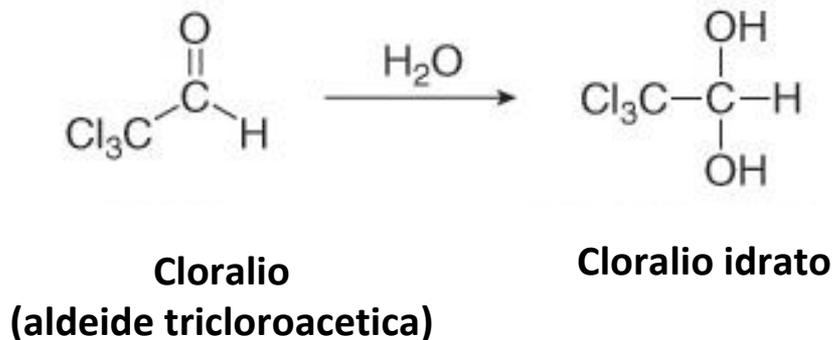
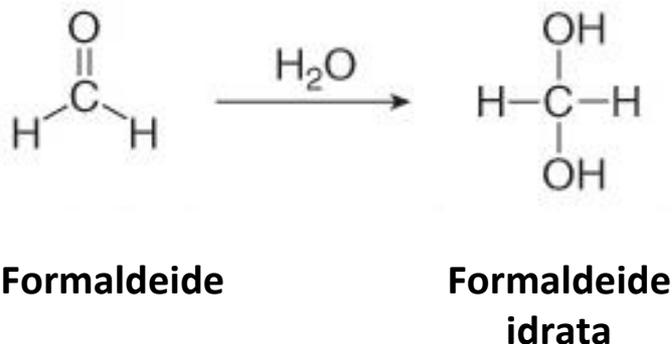


0.2%

Addizione di H₂O — Idratazione

Gem-dioli si formano con buone rese solo con aldeidi **non ingombrate** (formaldeide) o aldeidi con gruppi fortemente elettronattrattori vicini.

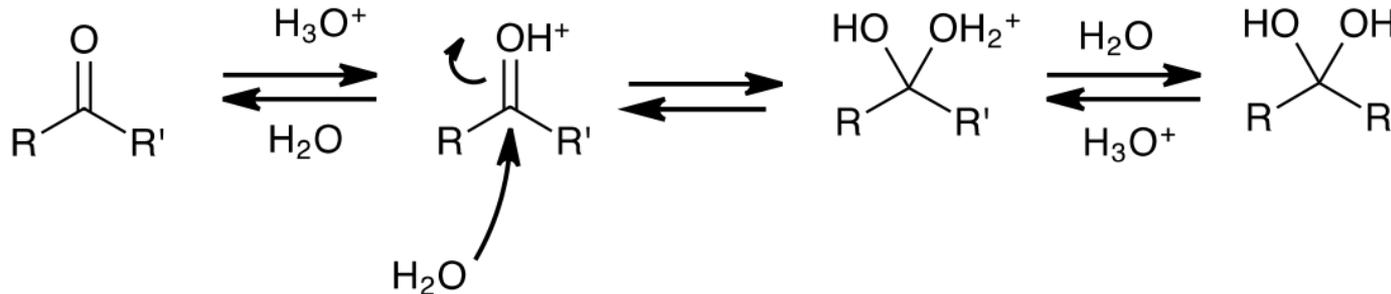
Esempi



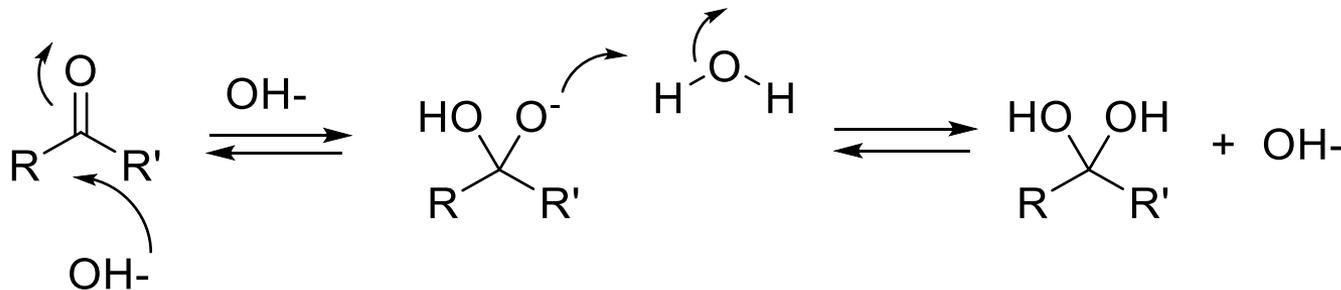
Addizione di H₂O — Idratazione

L'addizione di H₂O è generalmente lenta ma può essere catalizzata da OH⁻ e H⁺

Catalisi acida:

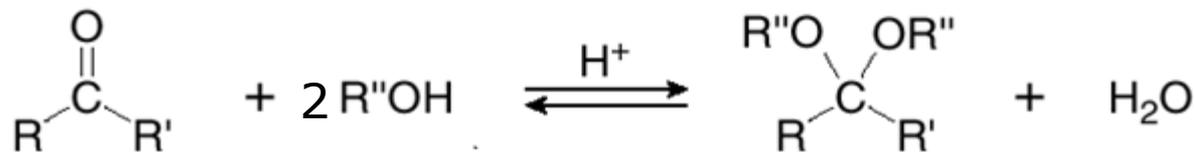


Catalisi basica:



Addizione di Alcoli — Formazione di Acetali

Formazione di acetali

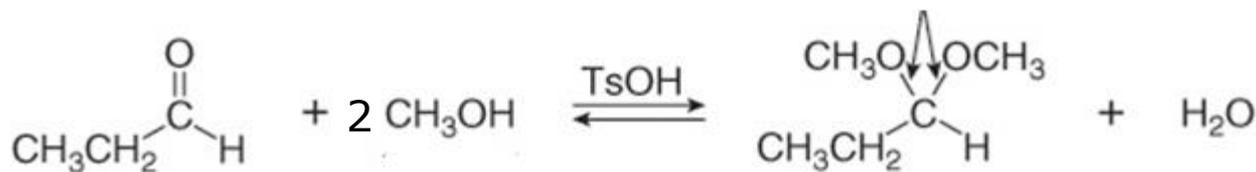


R' = H o alchile

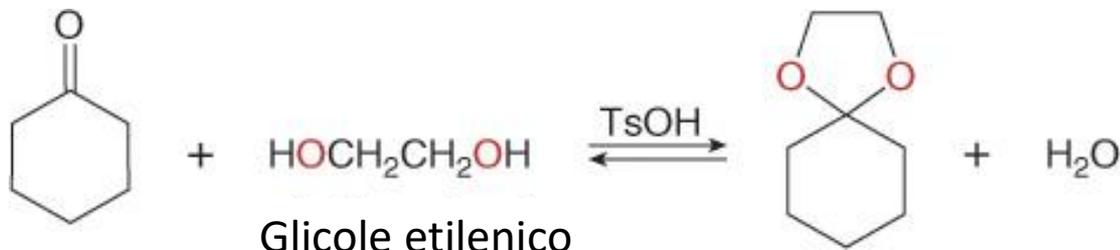
Acetale

L'equilibrio viene spostato a destra con un eccesso di alcol o rimuovendo l'H₂O

Esempi



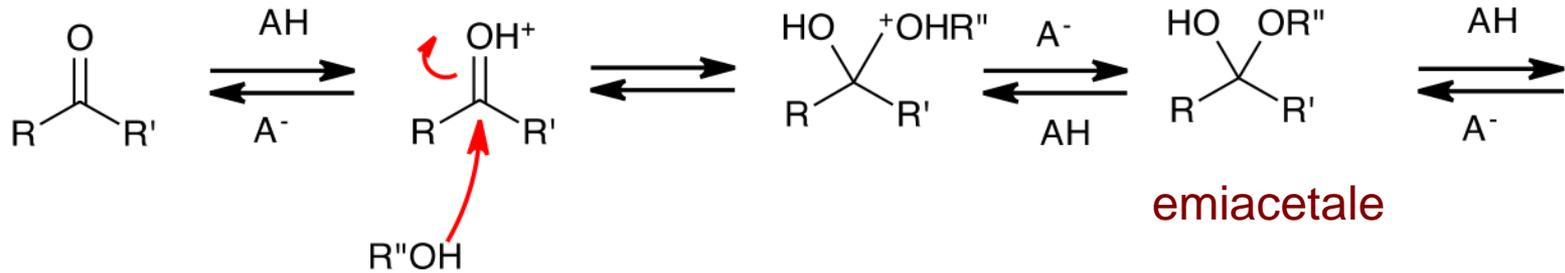
Acetale



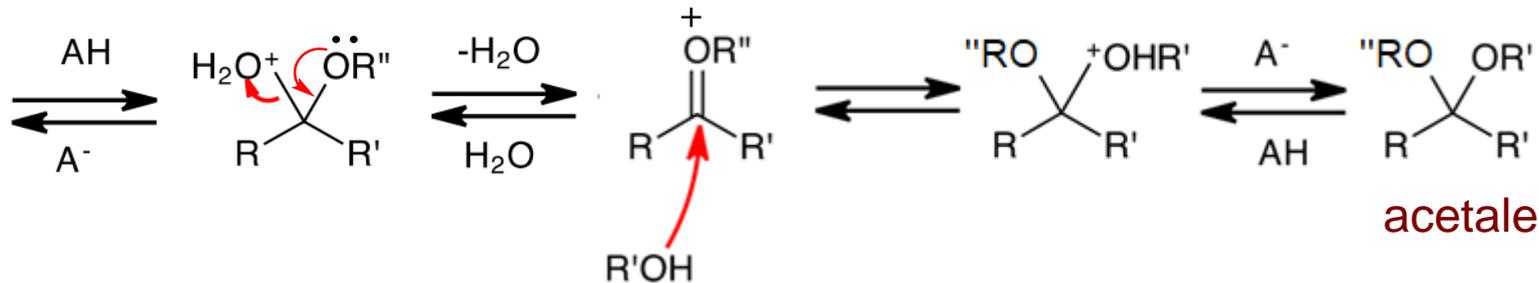
Glicole etilenico

Acetale ciclico

Addizione di Alcoli — Formazione di Acetali



emiacetale

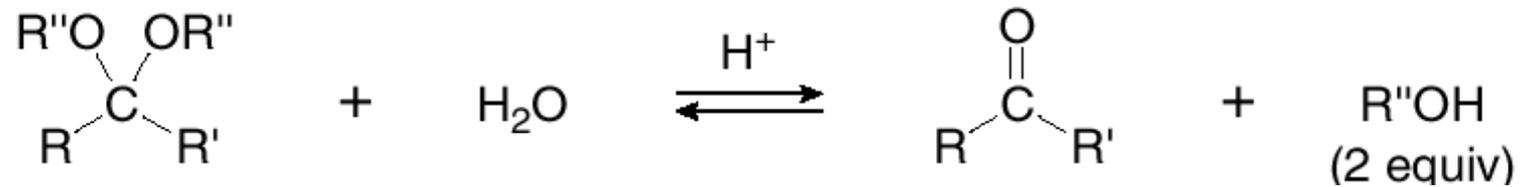


acetale

Formalmente si ha sostituzione dell'OH dell emiacetale con il gruppo R'O (attraverso uno step di eliminazione di H₂O e addizione di R'OH)

AH = HCl (g), PTSA (acido p-toluensolfonico)...

Idrolisi di Acetali

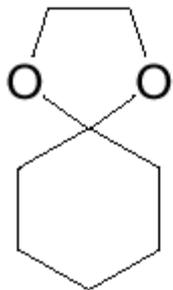


Acetale

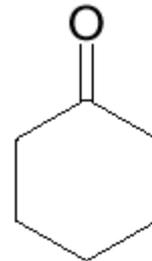
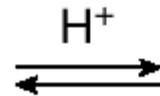
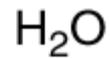
R' = H o alchile

Largo

eccesso



+

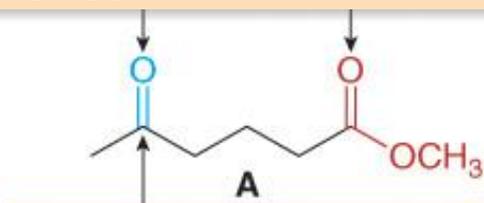


+

HOCH₂CH₂OH
Glicole etilenico

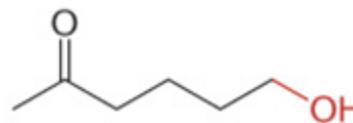
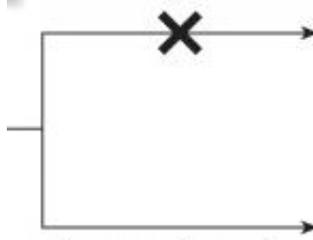
Acetali come Gruppi Proteggenti

Due gruppi funzionali riducibili



Il C=O è più reattivo

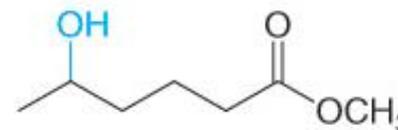
Reazione desiderata



6-idrossi-2-esanone

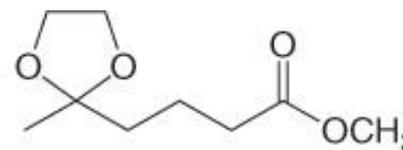
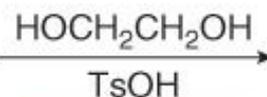
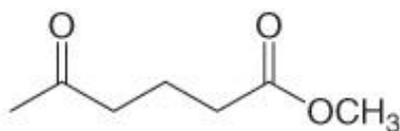
Riduzione selettiva dell'estere

Reazione osservata



Metil 5-idrossiesanoato

Riduzione selettiva del chetone



Step [1]
Protezione

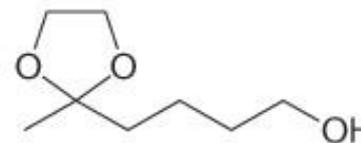
[1] LiAlH_4
[2] H_2O Step [2]
Riduzione



Prodotto desiderato
+ $\text{HOCH}_2\text{CH}_2\text{OH}$

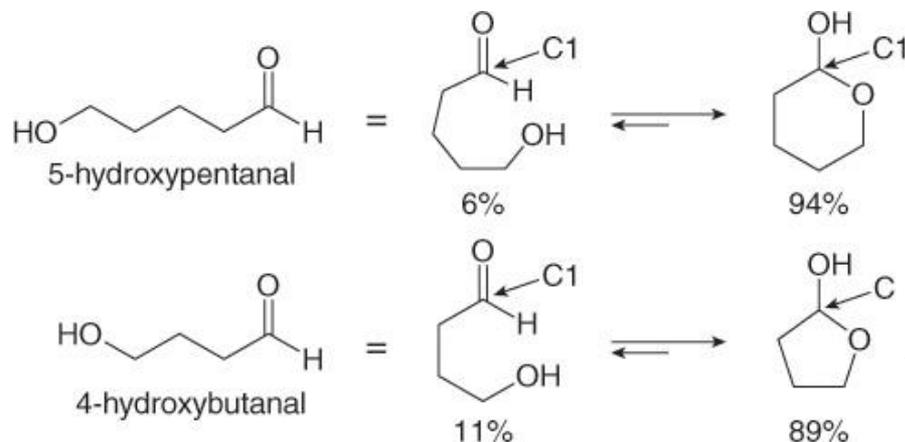


Step [3]
Deprotezione

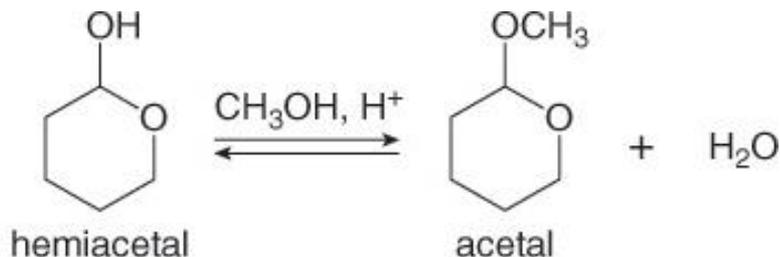


Emiacetali Ciclici ed Acetali

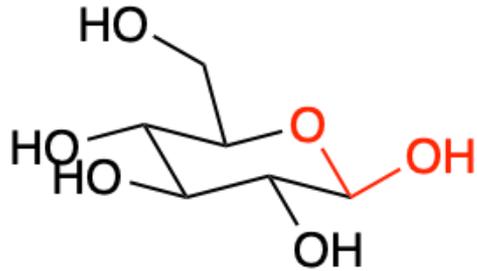
Emiacetali ciclici si formano per ciclizzazione intramolecolare di idrossialdeidi



Emiacetali ciclici possono essere convertiti in acetali per trattamento con un alcol e un acido.



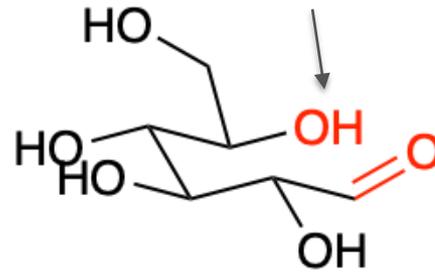
Equilibrio fra forma ciclica emiacetale e forma aperta del glucosio



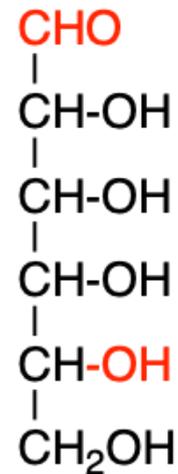
Forma ciclica del glucosio



Questo gruppo OH è usato per formare l'emiacetale

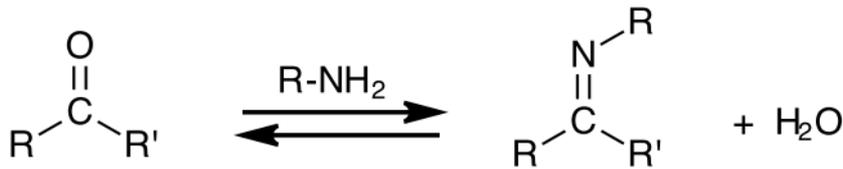


Forma aperta del glucosio
(Polidrossialdeide)



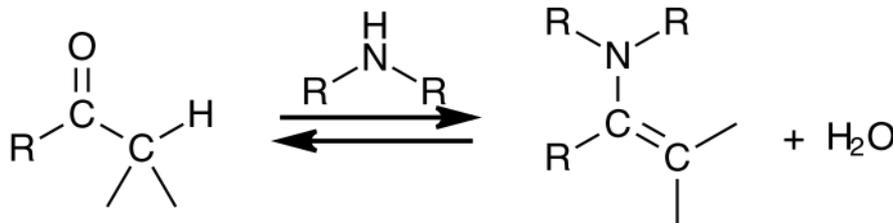
Addizione di Ammine

- Il trattamento di un'aldeide o di un chetone con un'ammina primaria produce un'immina (chiamata anche **base di Schiff**).



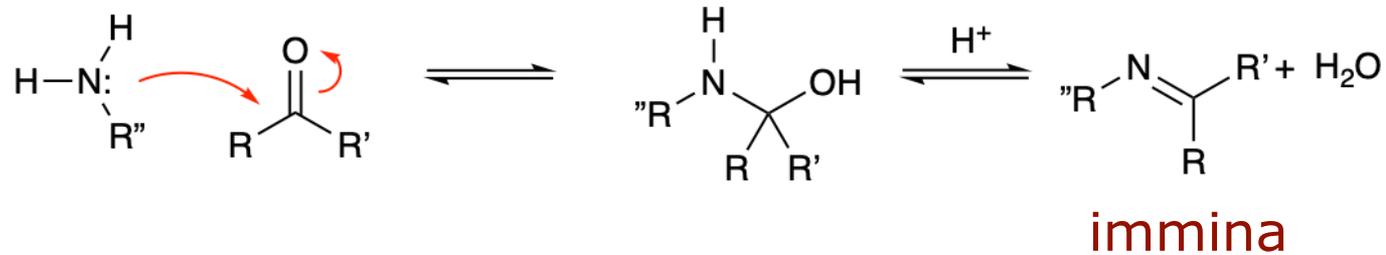
L'atomo di N di un'immina è ibridizzato sp^2 , e l'angolo C—N—R è quindi di 120° (non 180°).

- Il trattamento di un aldeide o di un chetone con un'ammina secondaria produce un'enammina.

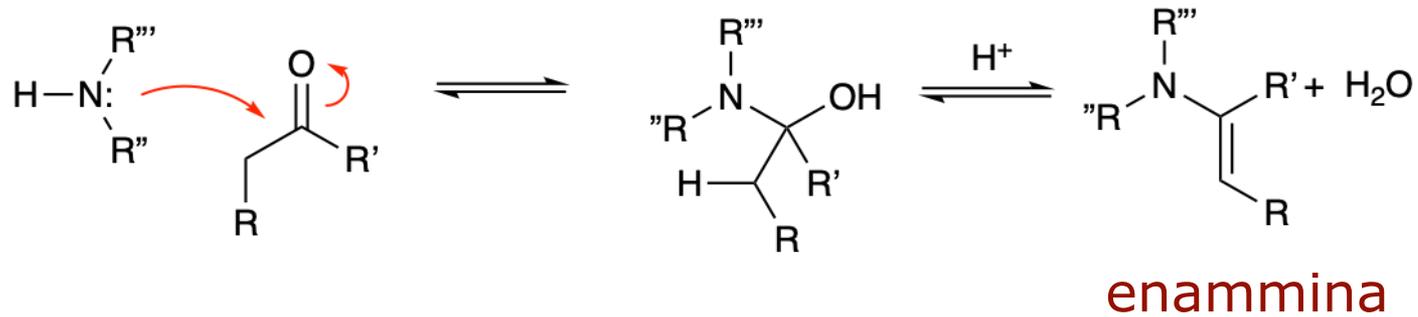


Immine ed Enammine: Meccanismo Semplificato

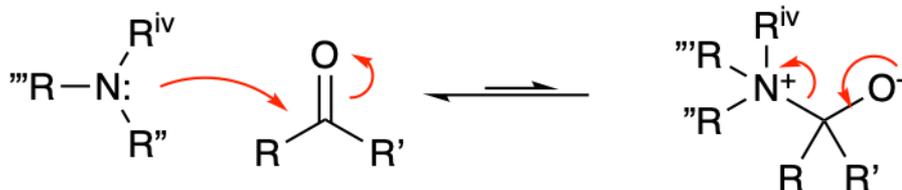
Ammine primarie:



Ammine secondarie:

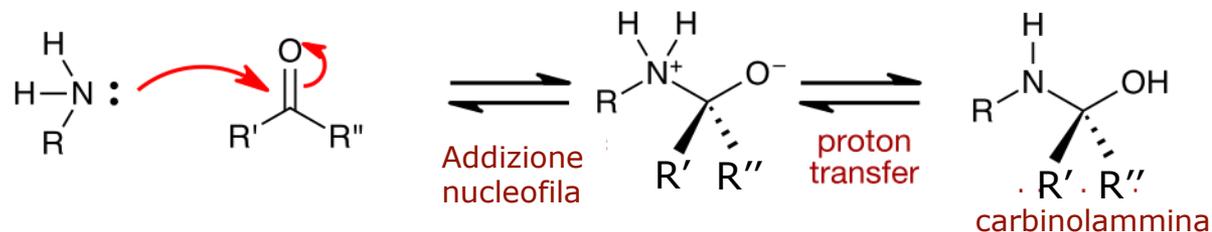


Ammine terziarie:

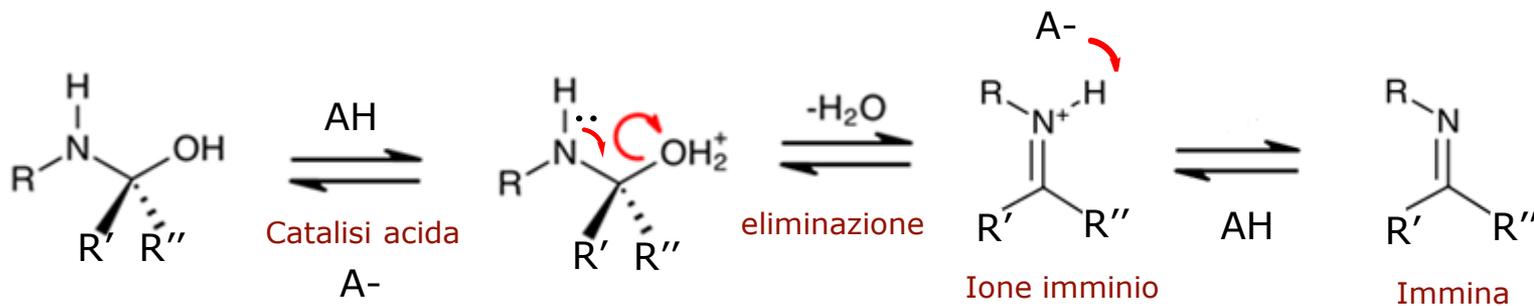


Ammine Primarie: Meccanismo Completo

1. Addizione dell'ammina



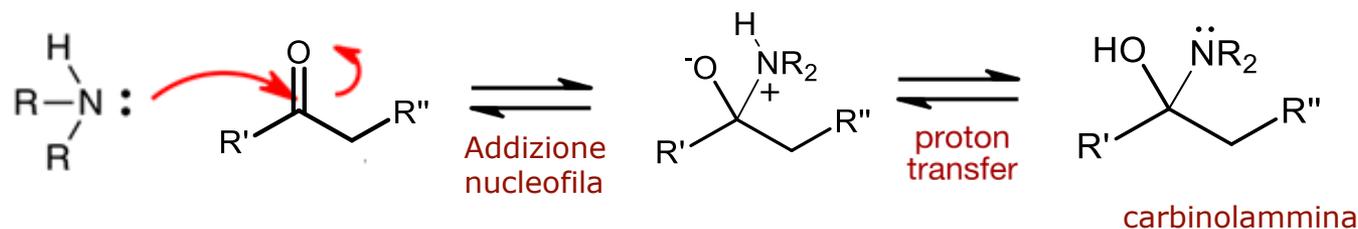
2. Eliminazione di acqua acido catalizzata (E1)



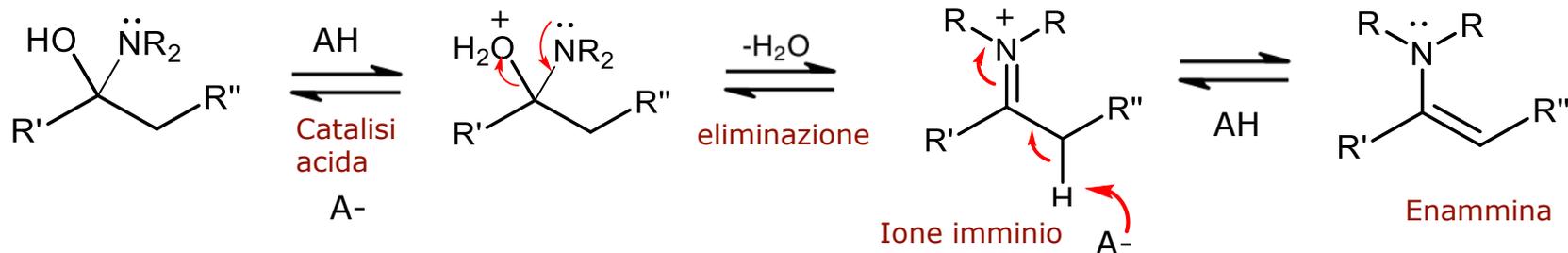
AH = PTSA (acido p-toluensolfonico)...

Ammine Secondarie: Meccanismo Completo

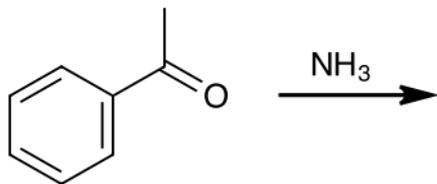
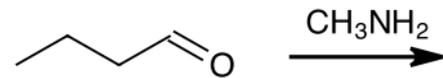
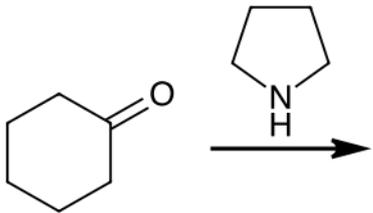
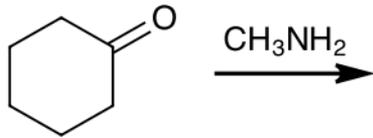
1. Addizione dell'ammina



2. Eliminazione di acqua (E1)



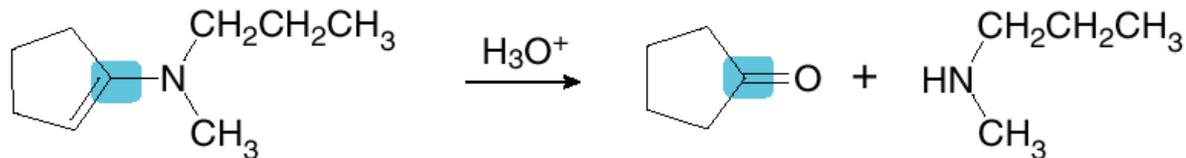
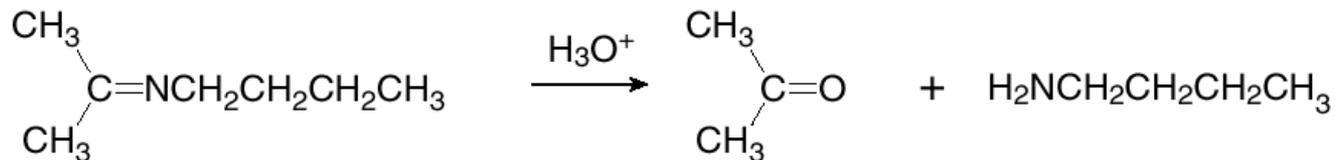
Addizione di Ammine



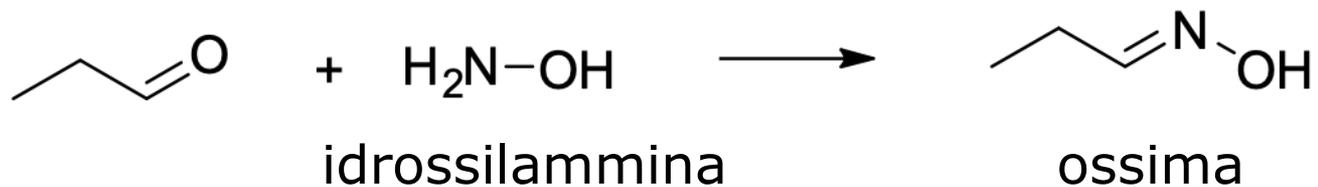
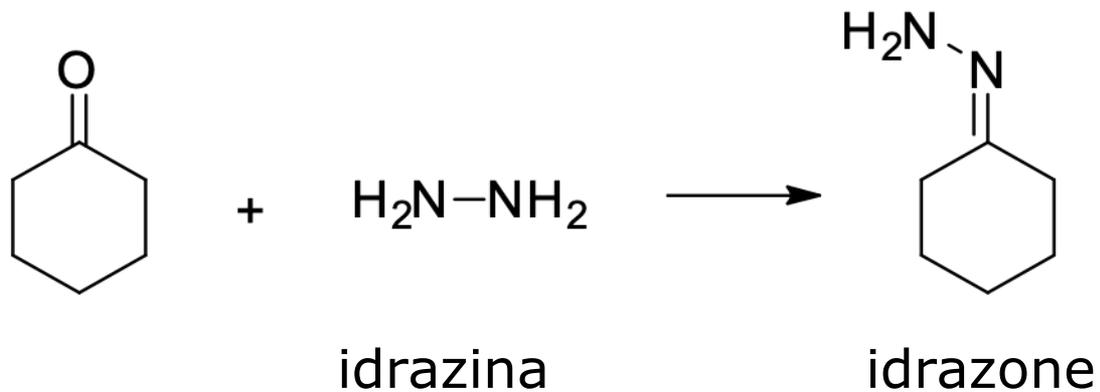
Idrolisi di Immine ed Enammine

- Siccome le immine e le enammine si formano attraverso una serie di step reversibili, entrambe possono essere convertite in composti carbonilici per **idrolisi** con acidi deboli.
- Il meccanismo dell'idrolisi di immine ed enammine è esattamente l'inverso di quello della loro formazione.

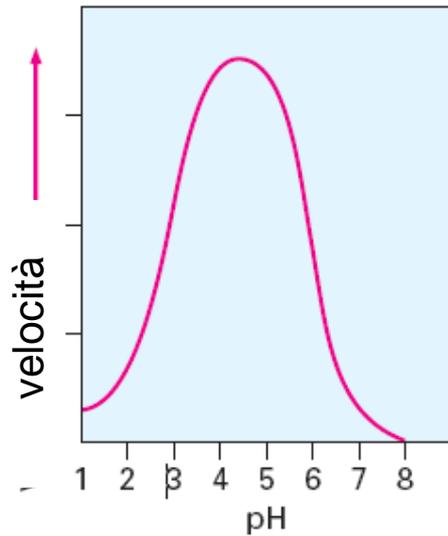
L'Idrolisi di immine ed enammine forma aldeidi e chetoni



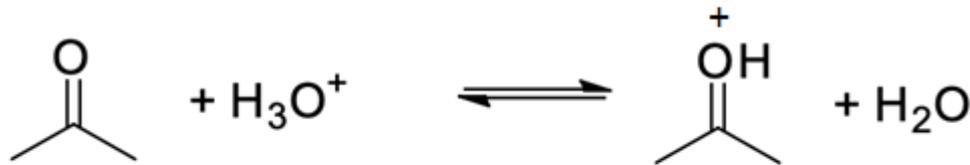
Altre Ammine



Addizione di Ammine – Effetto del pH



Profilo generale pH vs velocità di reazione
per l'addizione di ammine a composti
carbonilici

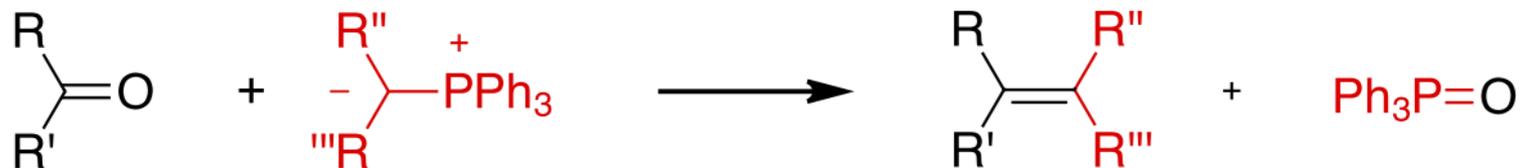


La protonazione attiva
l'elettrofilo



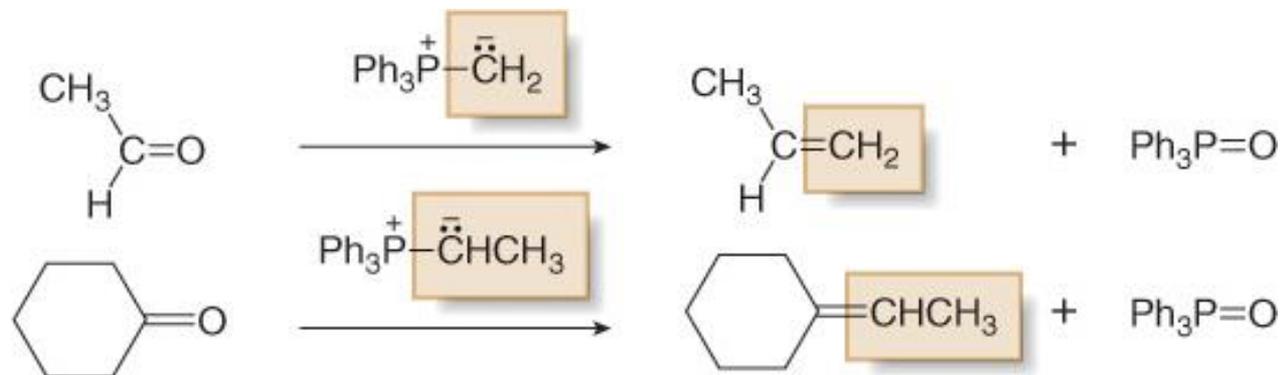
La protonazione disattiva
il nucleofilo

La Reazione di Wittig



Ilide di fosfonio
(Reagente di Wittig)

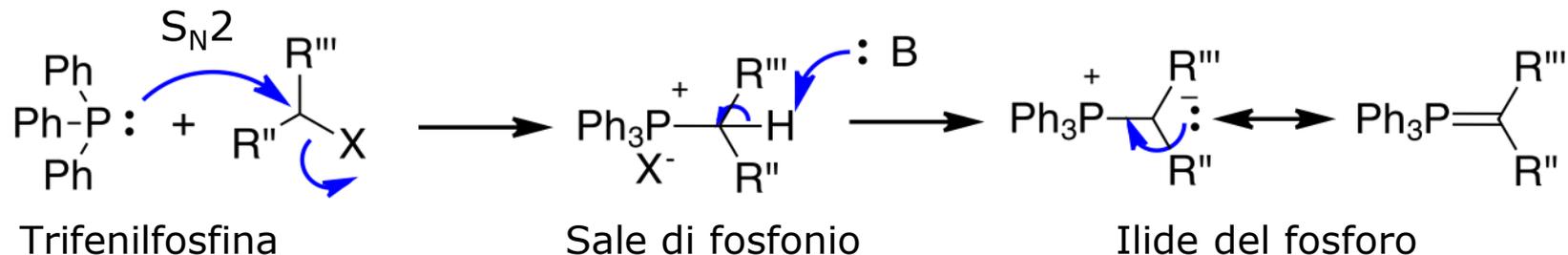
Esempi



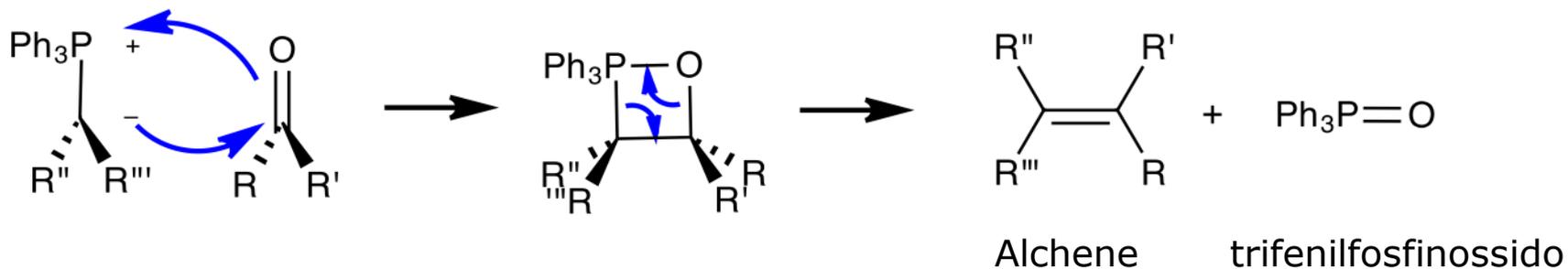
La Reazione di Wittig

Preparazione dell'ilide del fosforo (fosforano)

B: nBuLi, NaNH₂, NaH

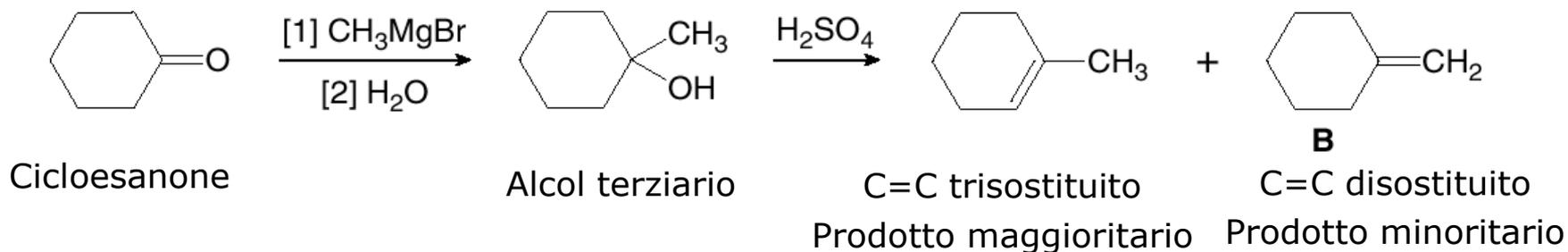
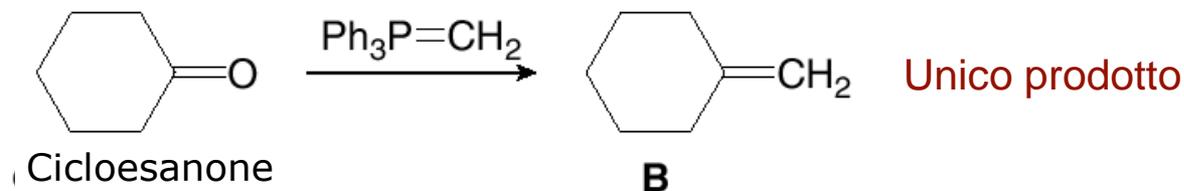


Reazione delle ilidi del fosforo con un composto carbonilico

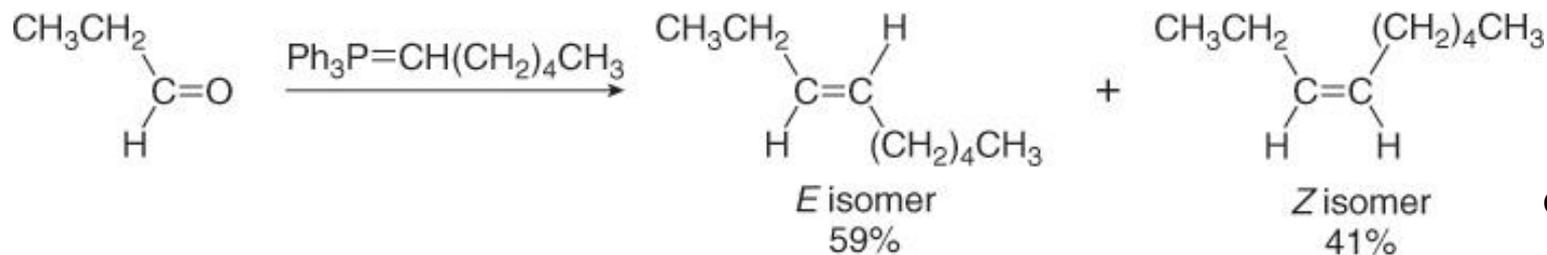


La Reazione di Wittig

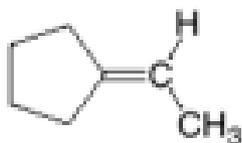
Vantaggio: La reazione di Wittig produce sempre un unico isomero costituzionale dell'alchene

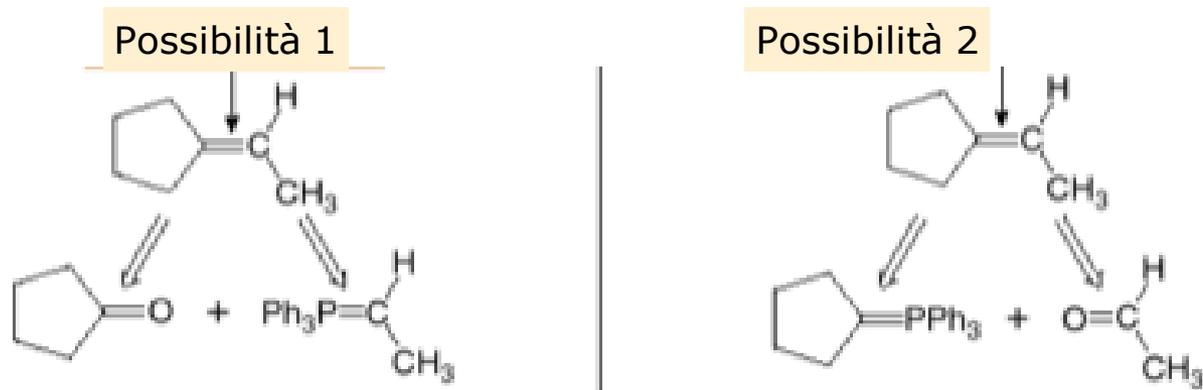


Limitazione: talvolta si formano miscele di stereoisomeri E e Z

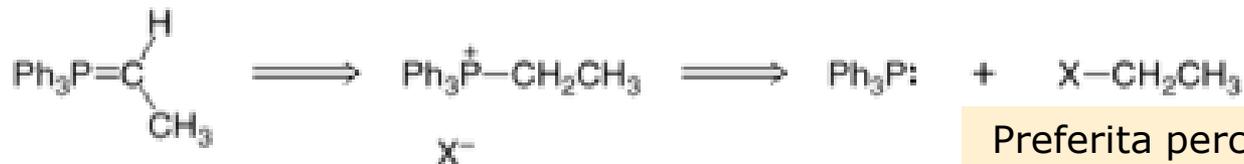


La Reazione di Wittig

Sintesi di:  mediante reazione di Wittig

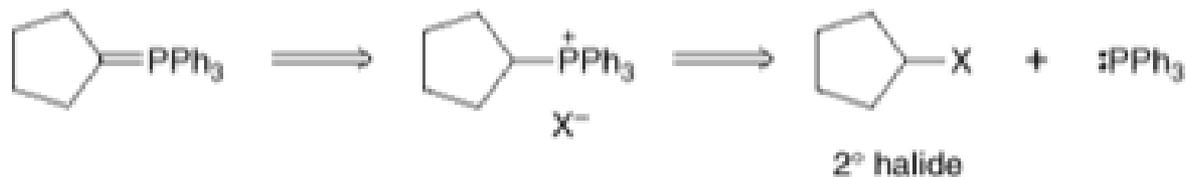


Possibilità 1

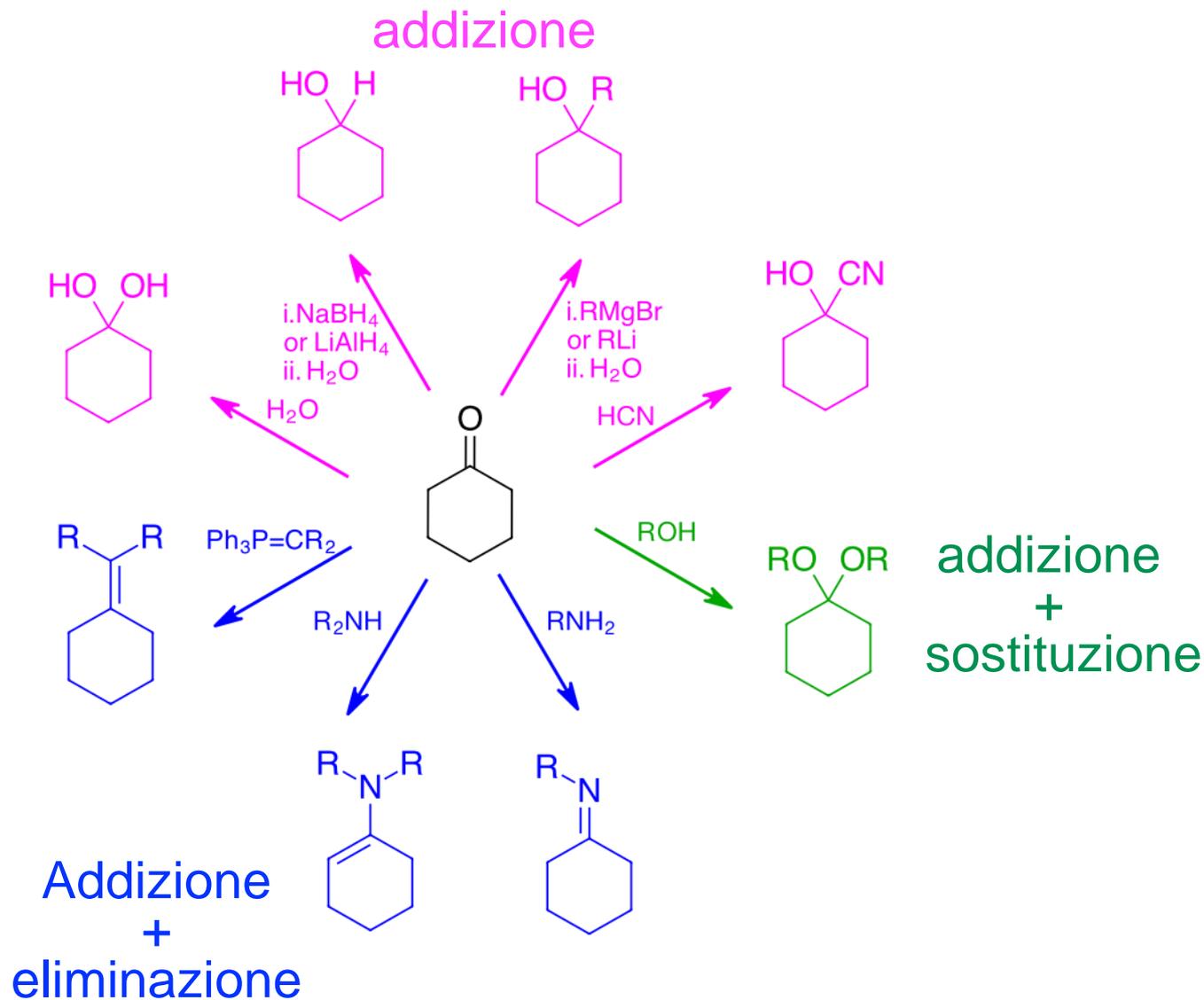


Preferita perché SN2
su alogenuro primario

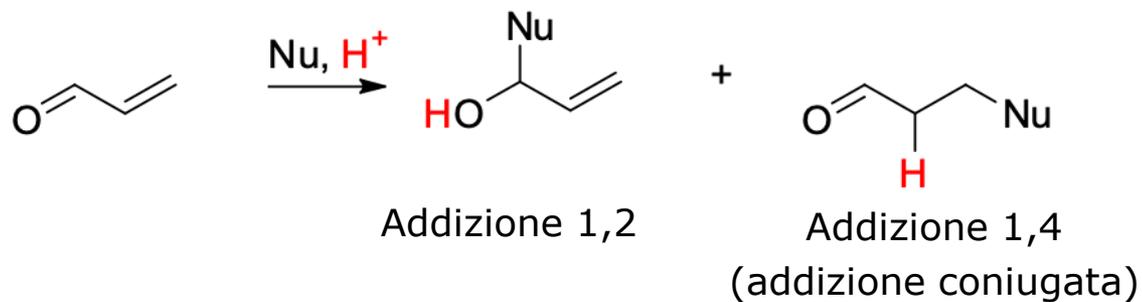
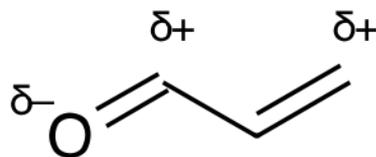
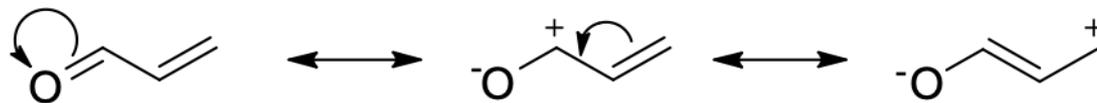
Possibilità 2



Addizione Nucleofila

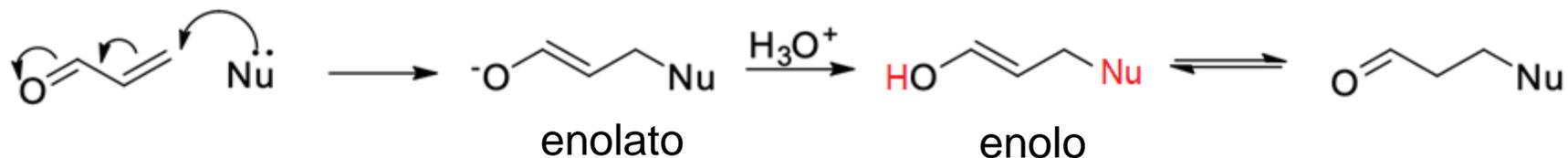


Composti Carbonilici α,β -insaturi

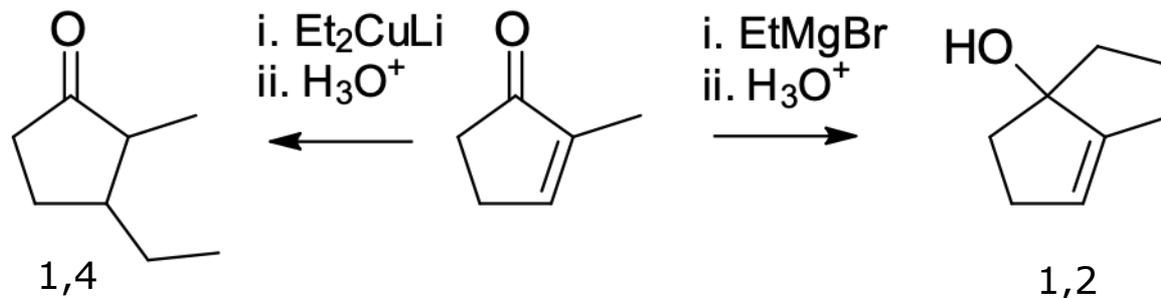
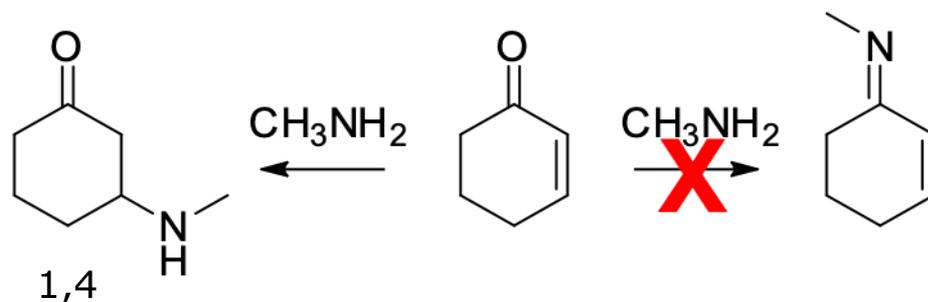


Addizione Coniugata

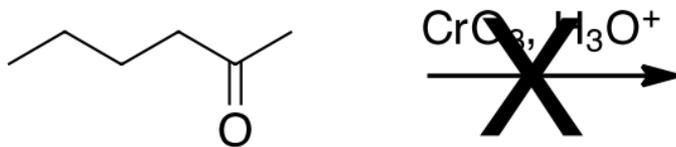
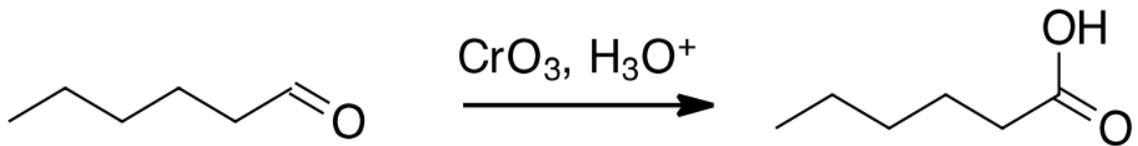
Meccanismo generale:



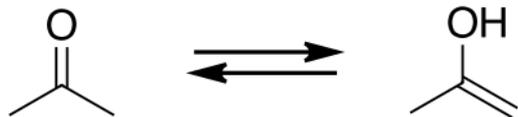
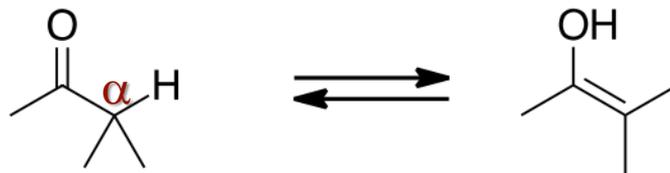
Esempi:



Ossidazione

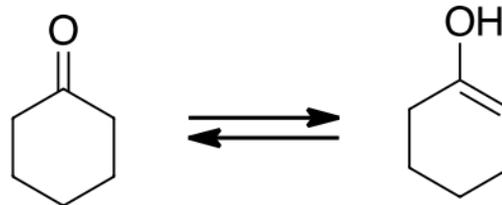


Tautomeria Cheto-Enolica



99,9999999%

0,0000001%

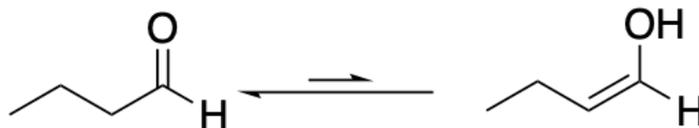


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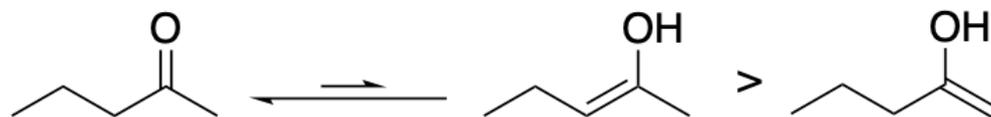
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Tautomeria Cheto-Enolica

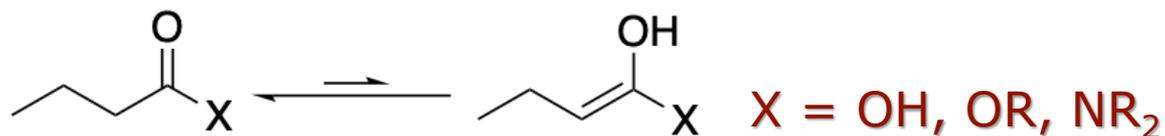
Aldeidi: 1 enolo



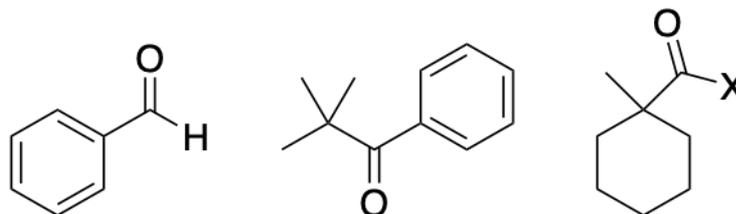
Chetoni non simmetrici:
2 enoli



Derivati degli acidi:
1 enolo

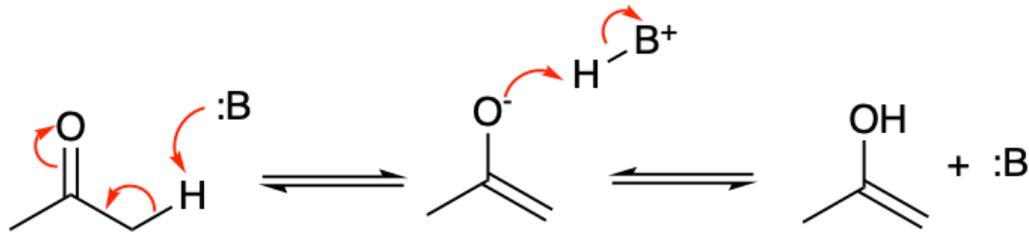
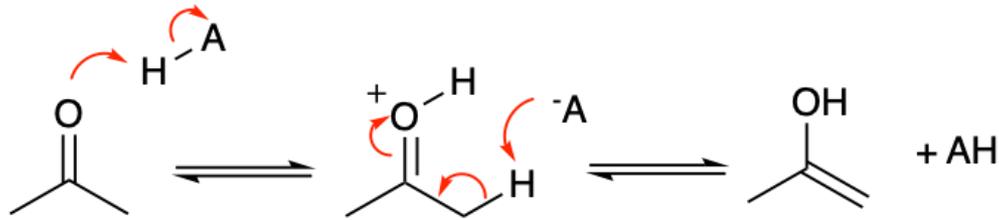


Non-enolizzabili



Tautomeria Cheto-Enolica

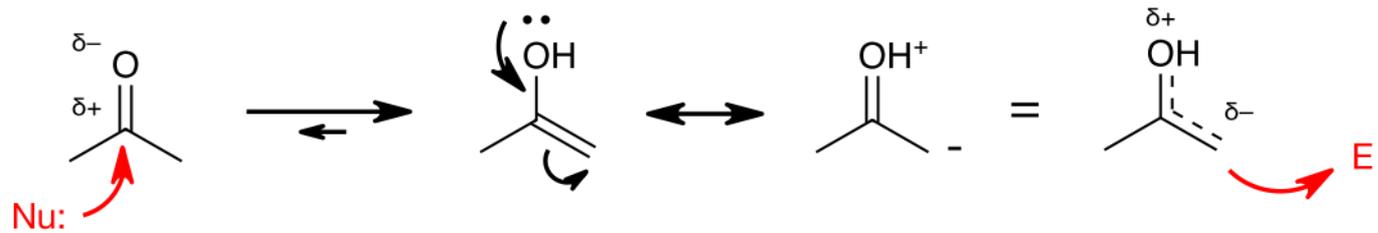
L'enolizzazione è catalizzata sia da acidi che da basi.



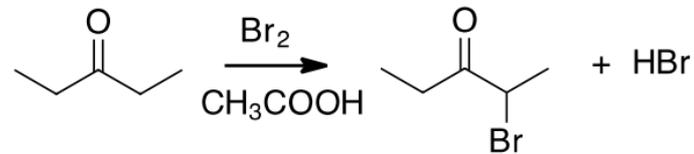
Il catalizzatore accelera l'equilibrio ma non influenza la sua posizione

Tautomeria Cheto-Enolica.

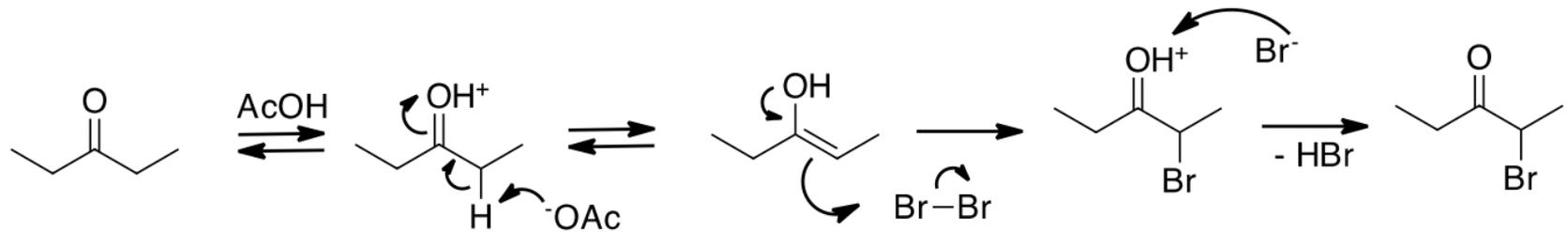
Reazione al Carbonio α



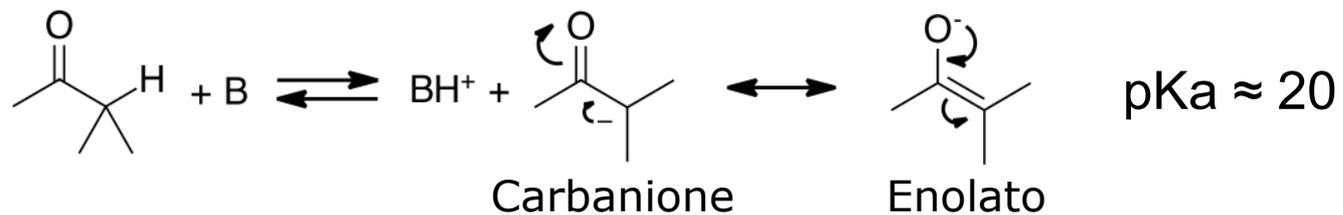
α -alogenazione:



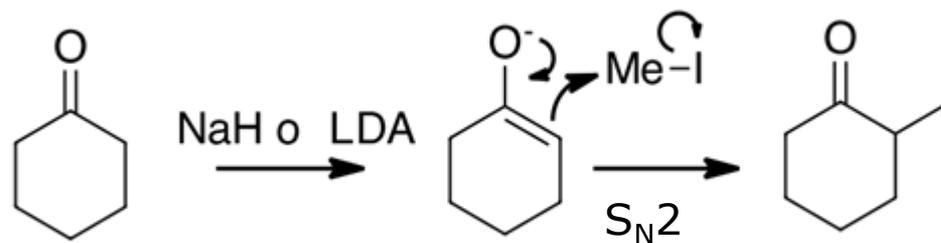
meccanismo



Enolati. Reazione al Carbonio α



Esempio: alchilazione del 2-metilcicloesano



con R-X primari