10. Aldeidi e Chetoni

(1) Reattività dei composti carbonilici.

(2) Addizione di nucleofili forti e deboli al carbonio carbonilico.

(3) Formazione di immine ed enammine.

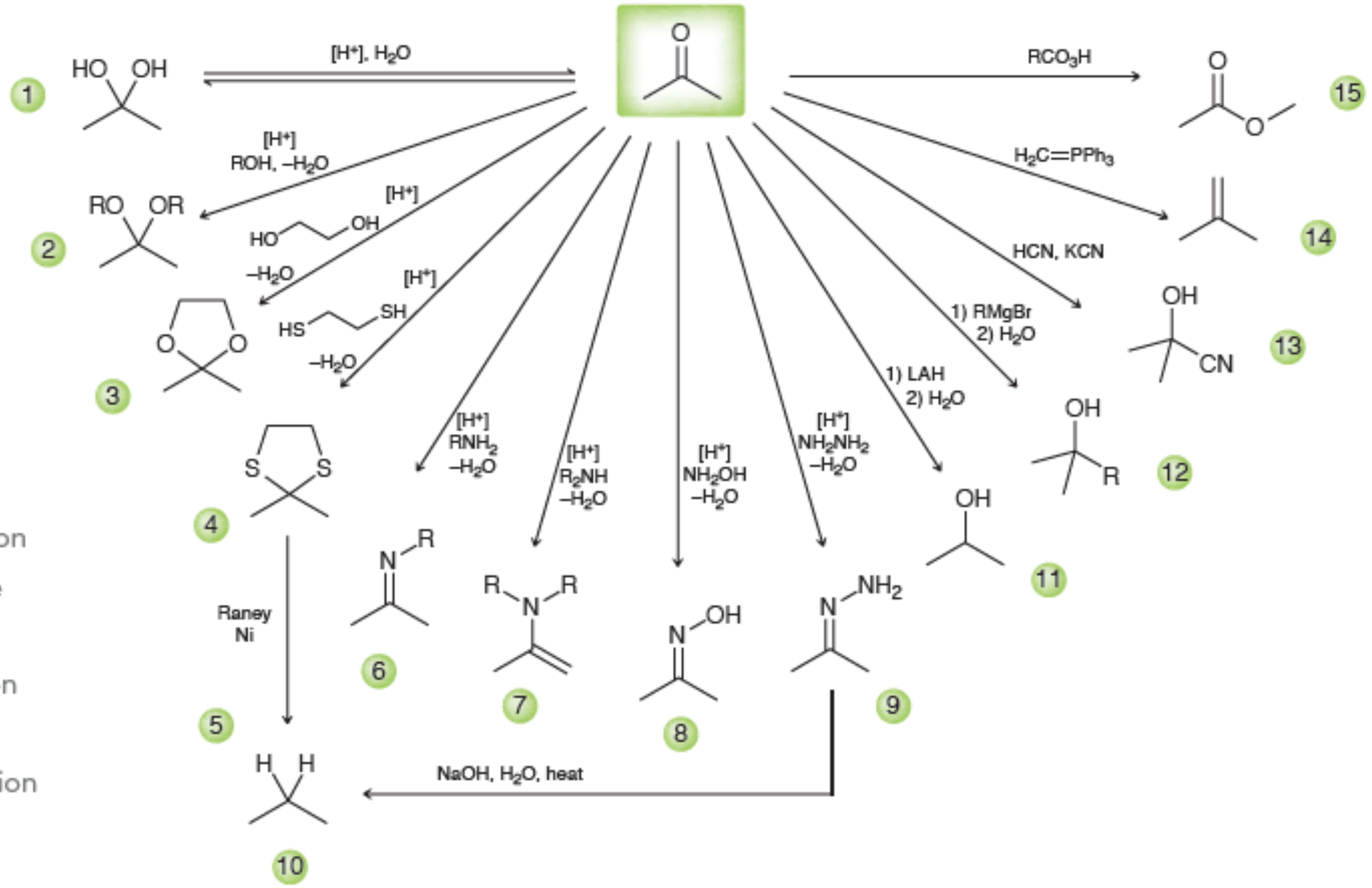
(4) Formazione di acetali e emiacetali come gruppi protettori del gruppo carbonilico.

(5) Reazione di Wittig.

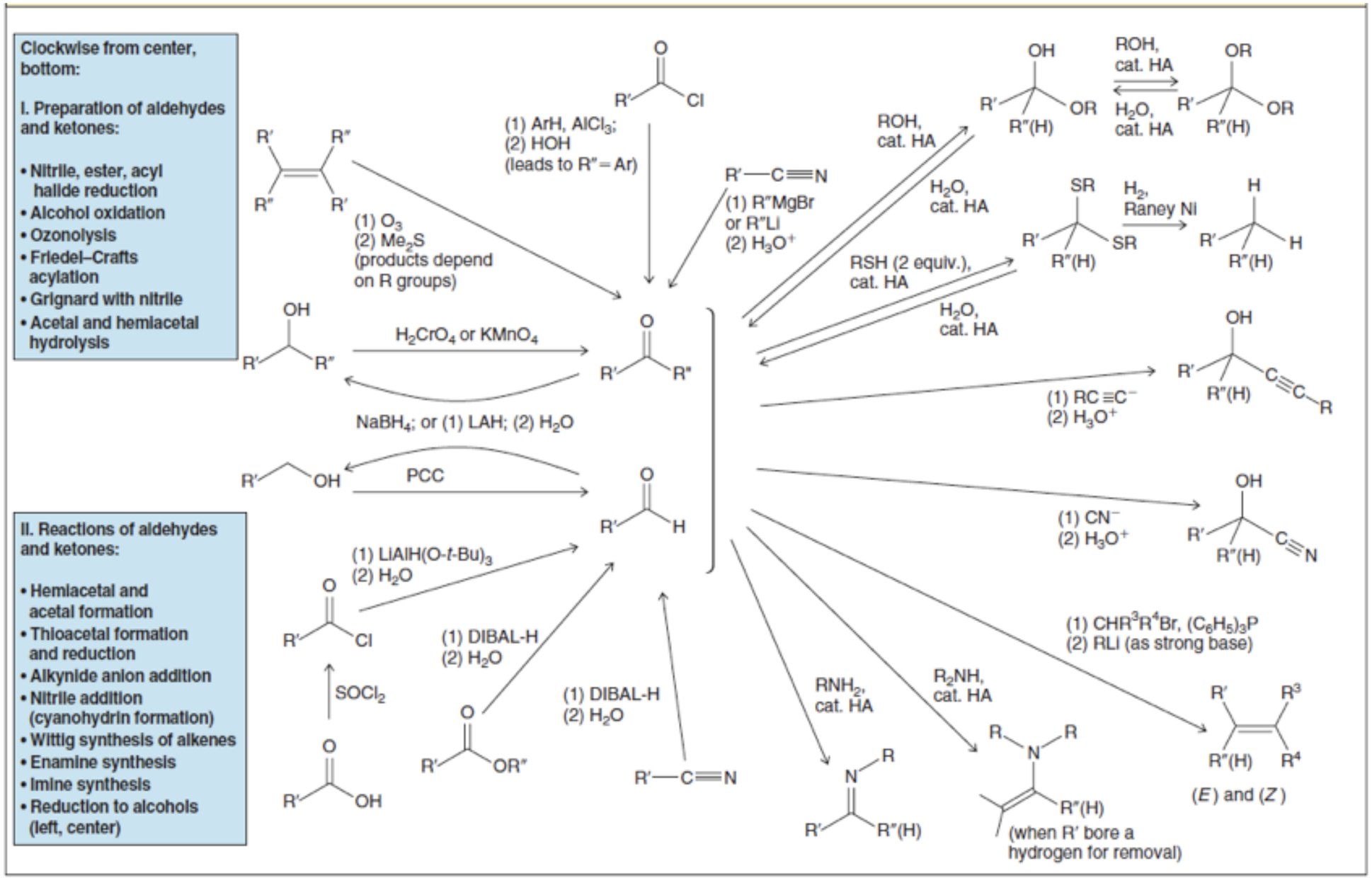
(6) ~~Addizione nucleofilica ad aldeidi e chetoni alfa,beta-insaturi in presenza di nucleofili deboli (addizione-1,4 coniugata) e forti (addizione-1,2 diretta).~~

Revisione delle reazioni di aldeidi e chetoni

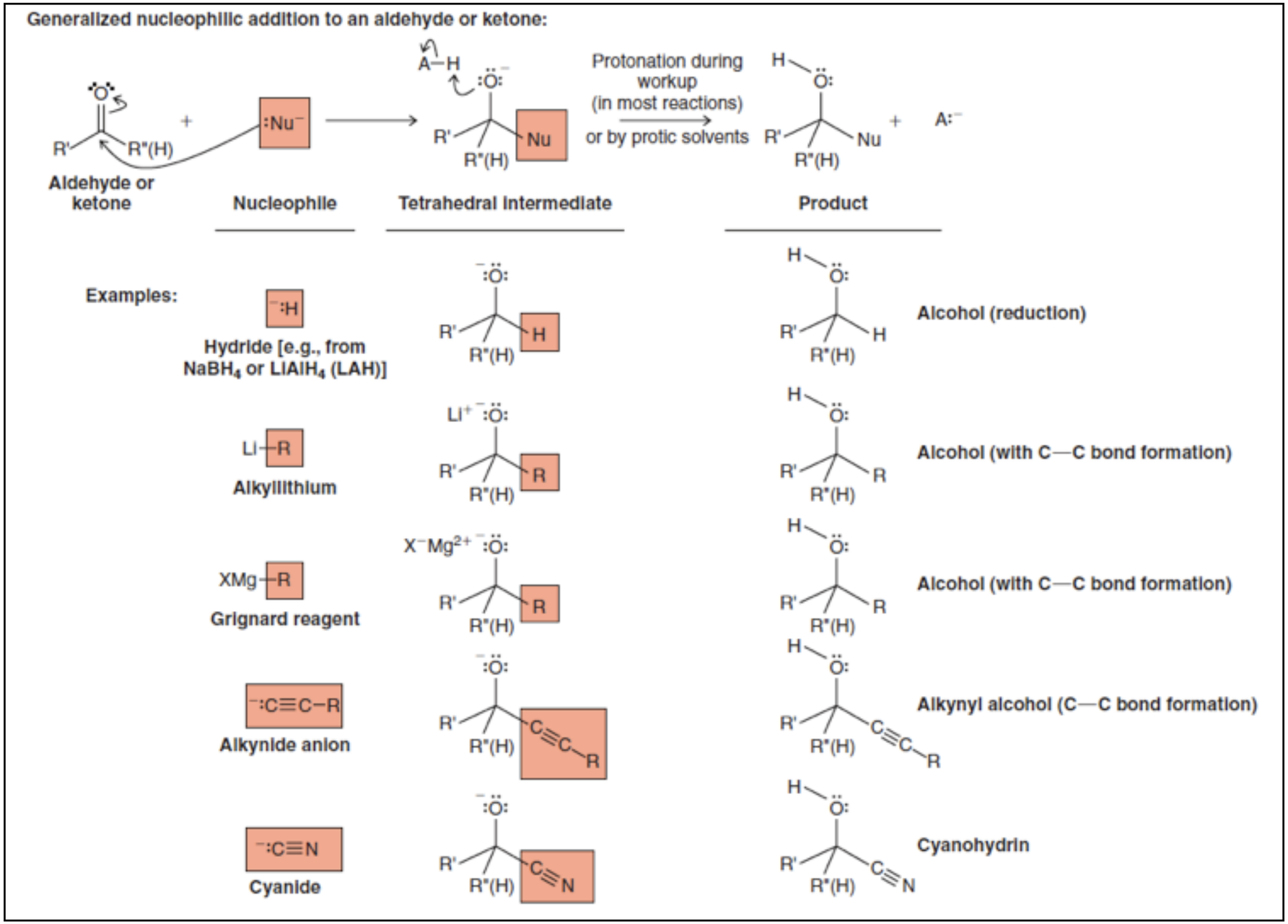
1. Hydrate Formation
2. Acetal Formation
3. Cyclic Acetal Formation
4. Cyclic Thioacetal Formation
5. Desulfurization
6. Imine Formation
7. Enamine Formation
8. Oxime Formation
9. Hydrazone Formation
10. Wolff-Kishner Reduction
11. Reduction of a Ketone
12. Grignard Reaction
13. Cyanohydrin Formation
14. Wittig Reaction
15. Baeyer-Villiger Oxidation



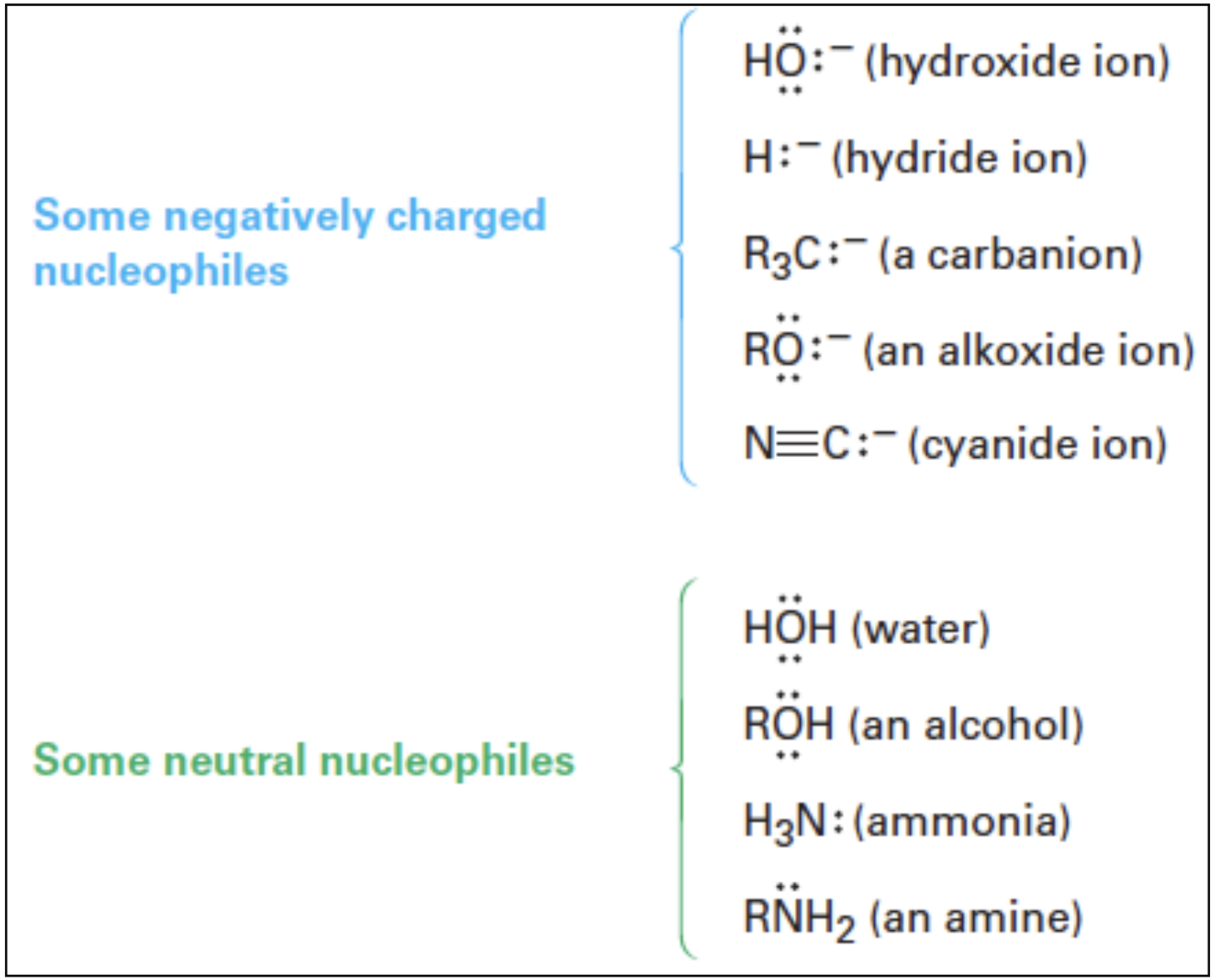
Connessioni sintetiche tra aldeidi, chetoni e altri gruppi funzionali



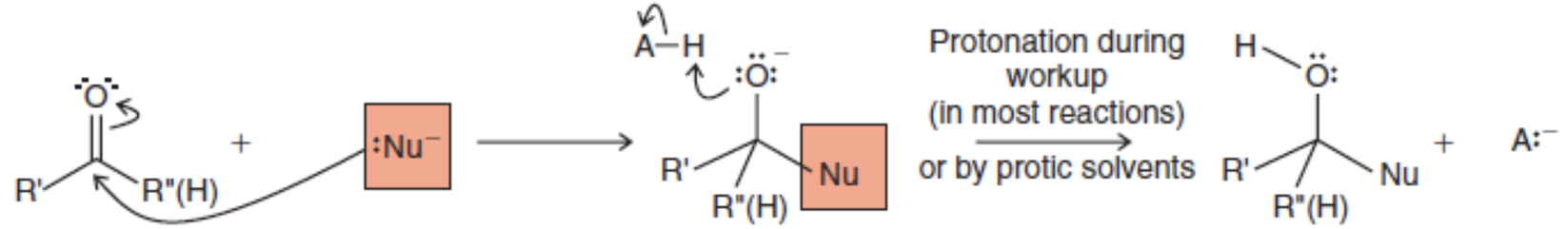
Reazione generale: Addizione nucleofila di aldeidi e chetoni in condizioni basiche



Addizione nucleofila di aldeidi e chetoni con Nucleofili forti e Deboli

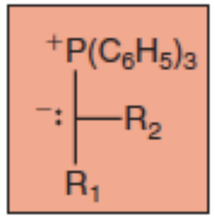


Generalized nucleophilic addition to an aldehyde or ketone:

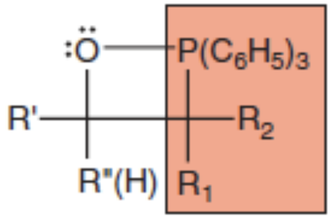


Aldehyde or ketone | **Nucleophile** | **Tetrahedral Intermediate** | **Product**

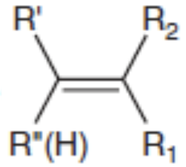
Examples (continued):



Phosphorus ylide

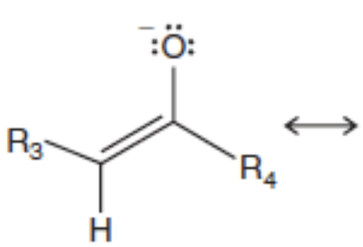


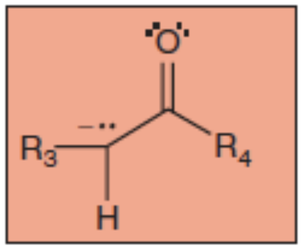
Oxaphosphetane intermediate



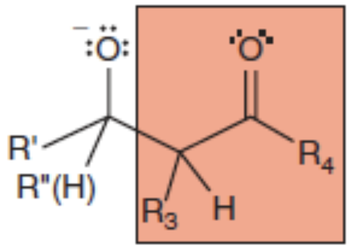
(plus diastereomer)

Wittig preparation of alkenes (with loss of triphenylphosphine oxide [$(C_6H_5)_3PO$])

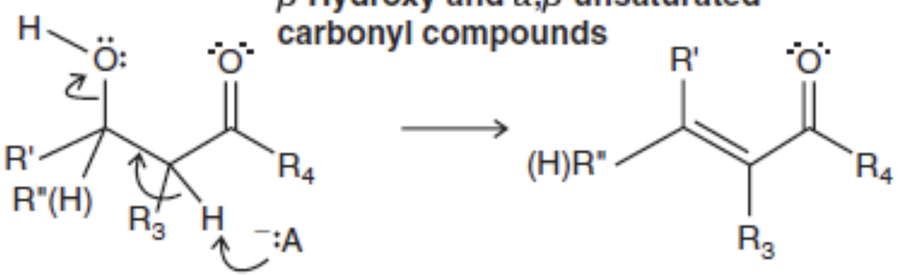


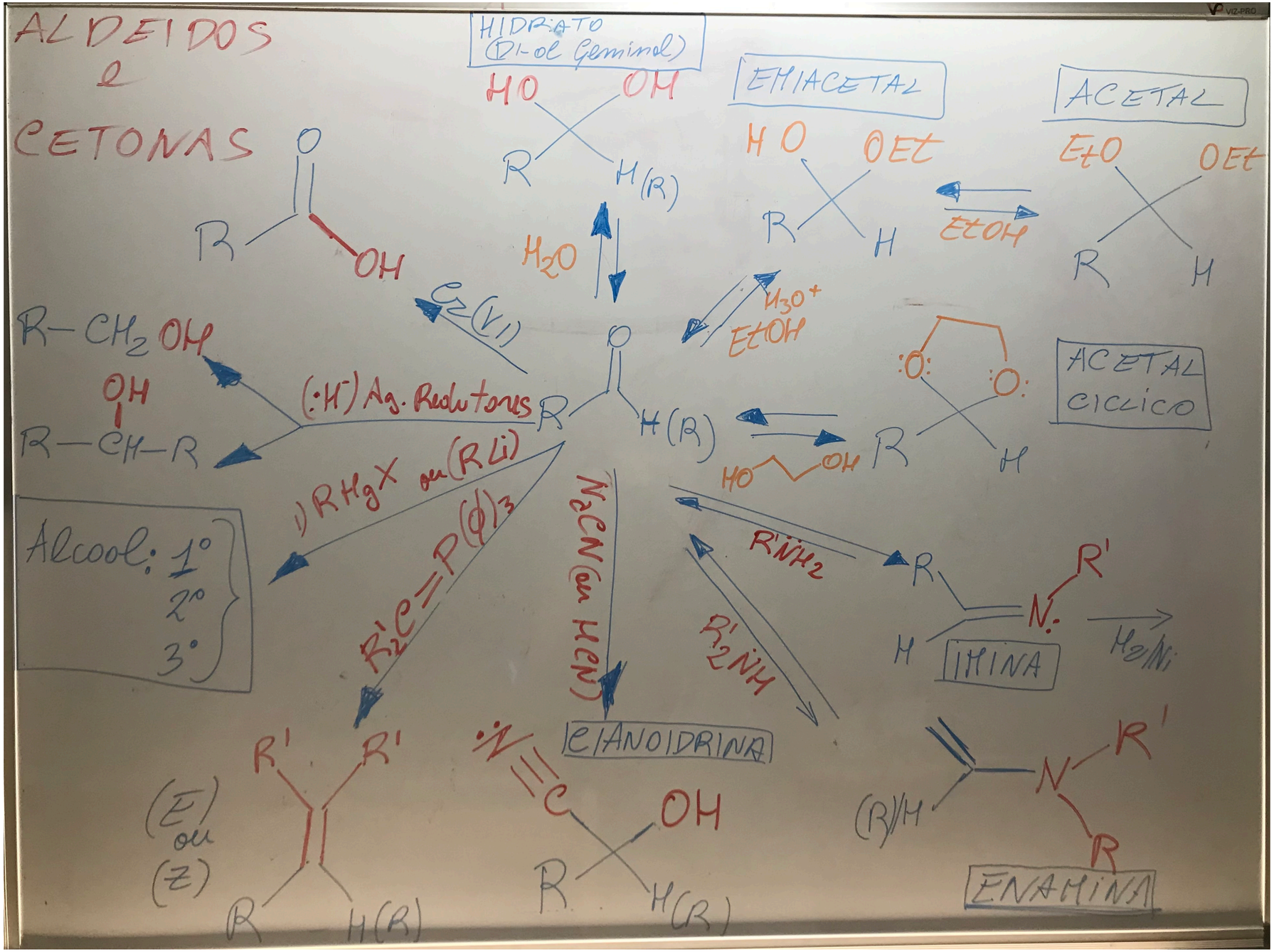


Enolate (see Chapter 18)

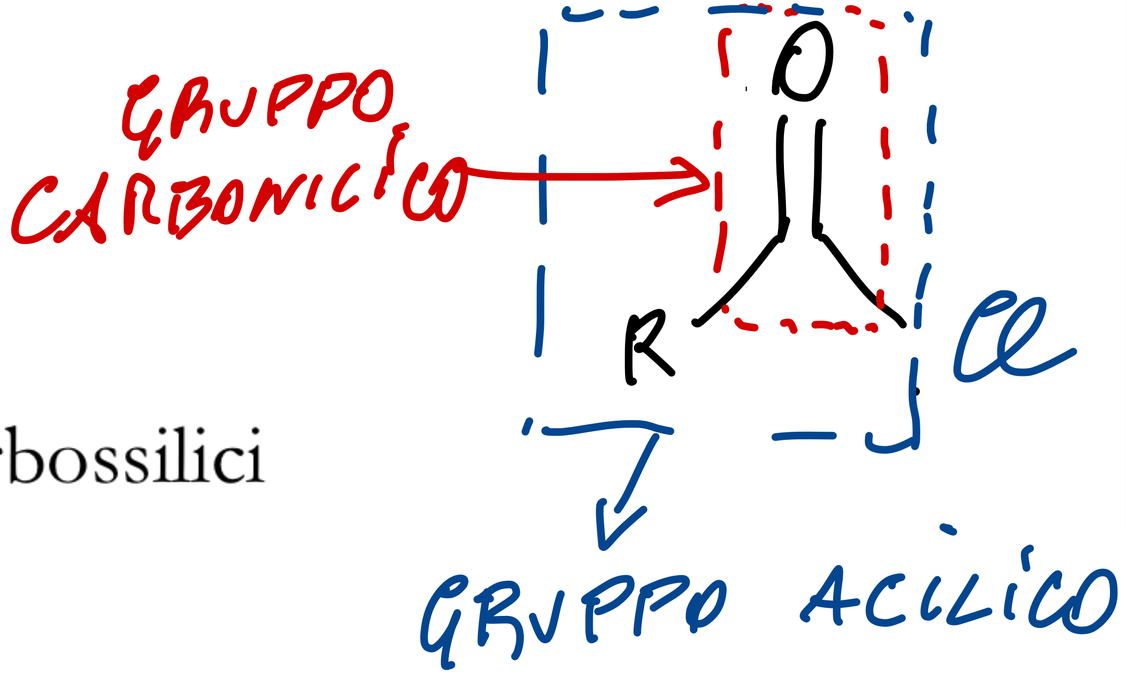


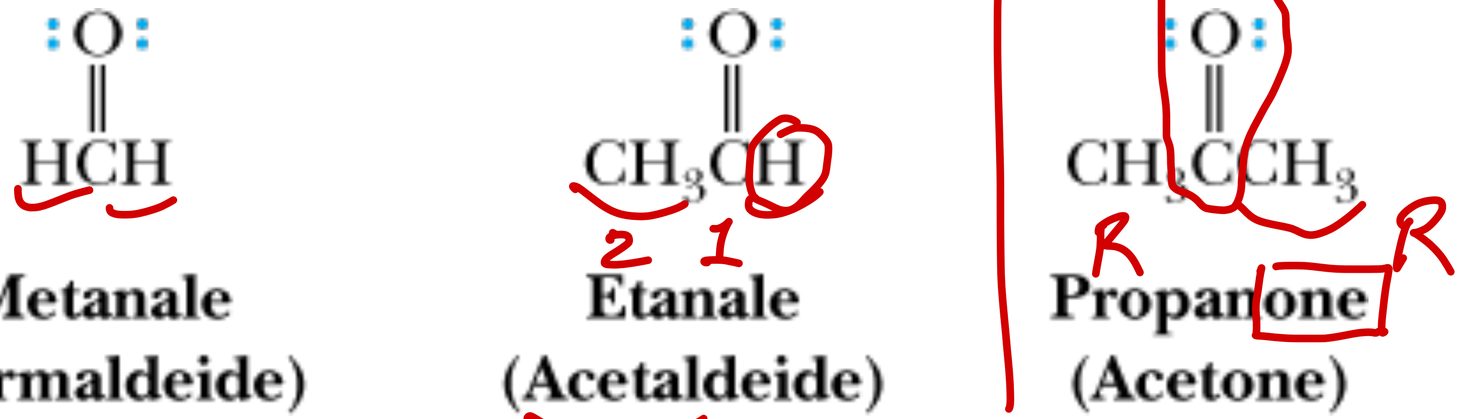
β-Hydroxy and α,β-unsaturated carbonyl compounds




ALDEIDOS
e
CETONAS
HIDRATO
(Di-ol Geminal)
HEMIACETAL
ACETAL
ACETAL
CICLICO
H_2O
H_3O^+
EtOH
$C_2(V_1)$
$R-CH_2OH$
OH
$R-CH-R$
(:H⁻) Ag. Redutores
1) $RMgX$ ou (RLi)
$R'_2C=P(\phi)_3$
N_2CN (ou HCN)
$R'NH_2$
R'_2NH
Alcool: 1°
2°
3°
CIANOIDRINA
IMINA
H_2/Ni
ENAMINA
(E)
ou
(Z)

- ✓ Gruppo carbonilico, C=O
  - Aldeidi e chetoni
  - Acidi carbossilici
  - Derivati funzionali degli acidi carbossilici
  - Enolati (?)

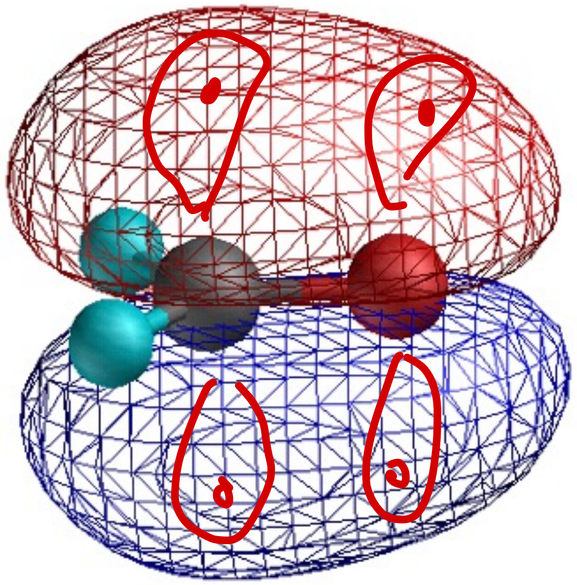




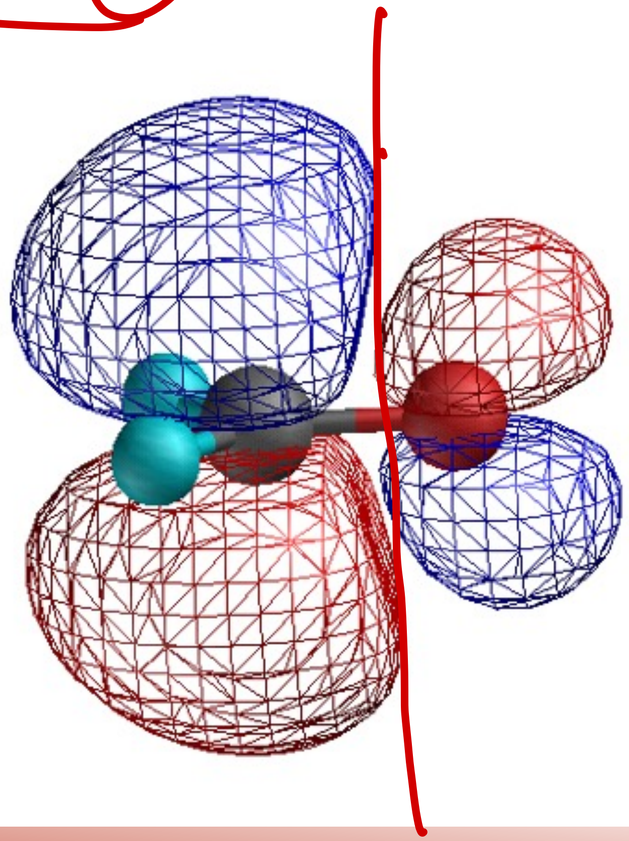
- **Metanale (Formaldeide)**
- **Etanale (Acetaldeide)**
- **Propanone (Acetone)**

- C=O
- Un legame sigma (sovrapposizione di orbitali sp^2) e un legame pi greco (sovrapposizione di orbitali paralleli $2p$)
- Es.: formaldeide:

Orbitale π

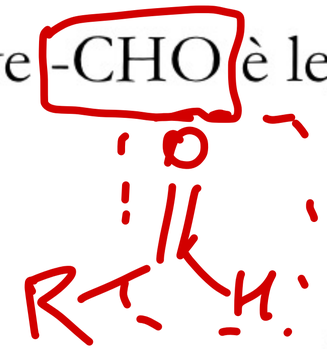


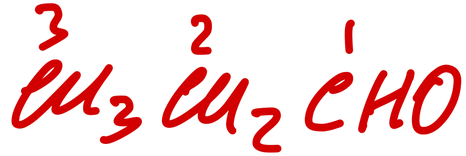
Orbitale π*



Nomenclatura: aldeidi

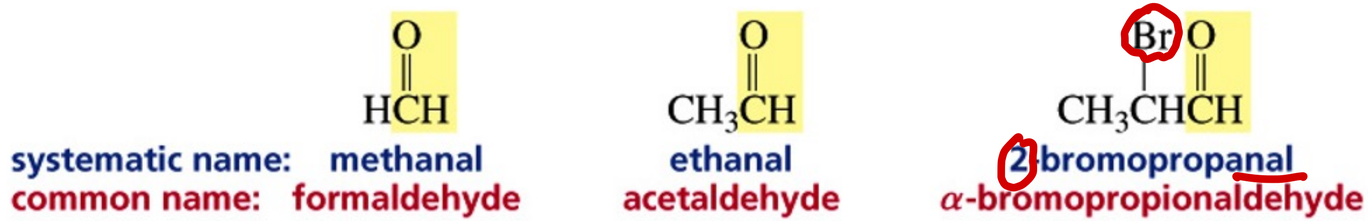
- ✓ IUPAC:
  - La catena base è la più lunga che contiene il gruppo funzionale
  - Cambiano il suffisso -o dell'alcano in -ale
  - Aldeidi insature: l'infisso -an- diventa -en-
  - Per molecole cicliche ove -CHO è legato all'anello si usa il suffisso –carbaldeide



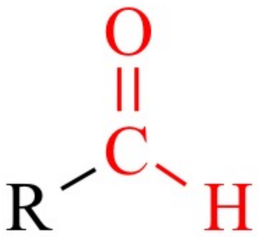


- ✓ Comune
  - for an aldehyde, the common name is derived from the common name of the corresponding carboxylic acid

Nomenclatura: aldeidi

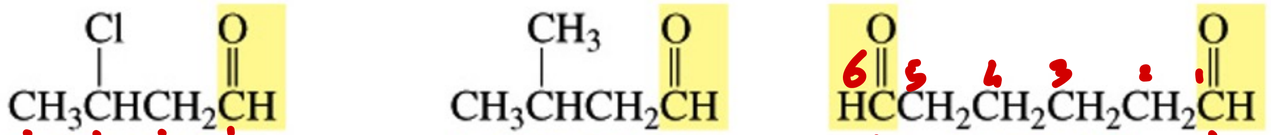


systematic name: methanal — ethanal — 2-bromopropanal
common name: formaldehyde — acetaldehyde — α-bromopropionaldehyde



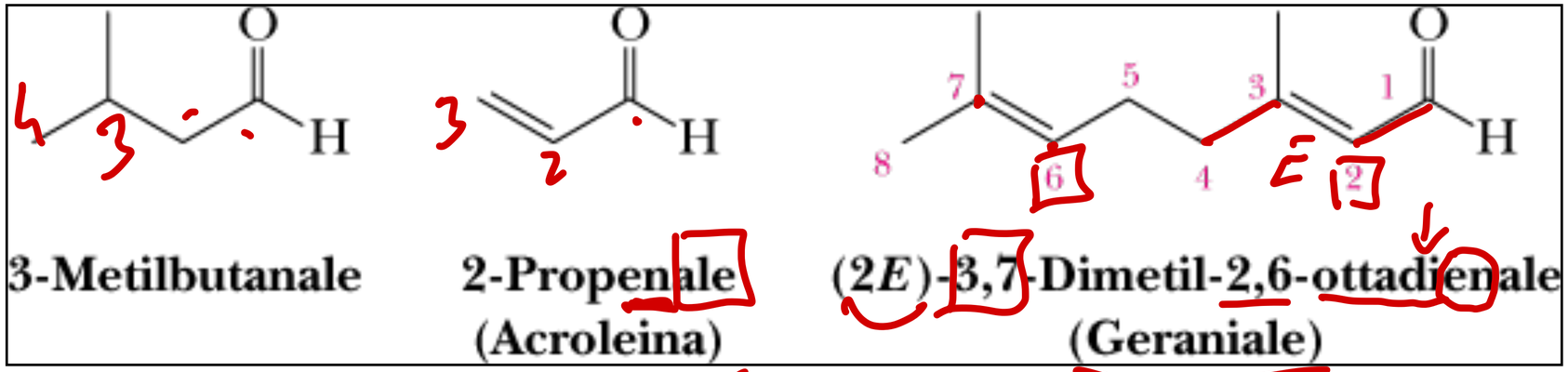
R—CHO

[R = R, Ar, H]



systematic name: 3-chlorobutanal — 3-methylbutanal — hexanedial
common name: β-chlorobutyraldehyde — isovaleraldehyde

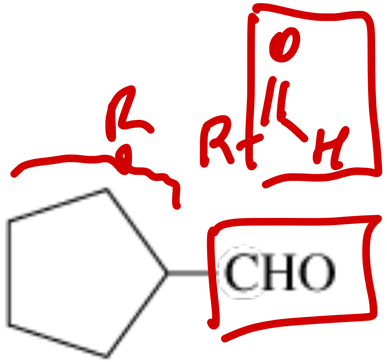
A. Nomenclatura IUPAC



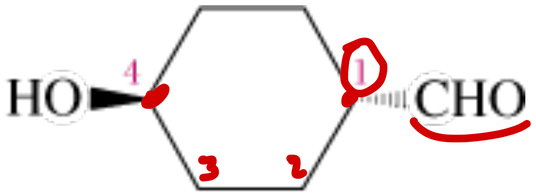
3-Metilbutanale

2-Propenale
(Acroleina)

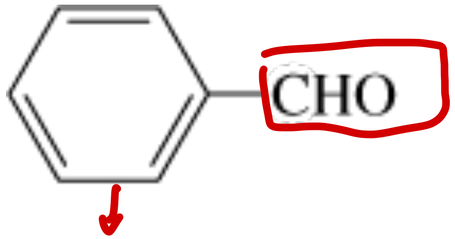
(2*E*)-3,7-Dimetil-2,6-ottadienale
(Geraniale)



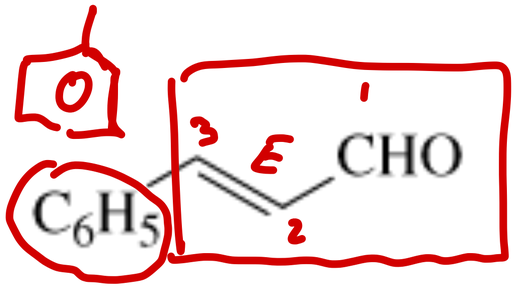
Ciclopentan-
carbaldeide



trans-4-Idrossi-
cicloesancarbaldeide



Benzaldeide

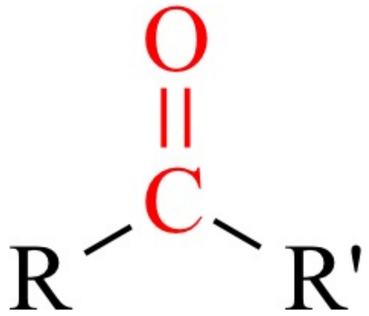


trans-3-Fenil-2-propenale
(Cinnamaldeide)

Nomenclatura: chetoni

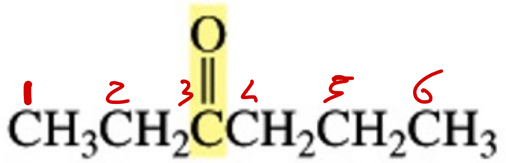
- ✓ IUPAC
  - Catena principale: la più lunga che contiene il carbonile
  - Il suffisso -o diventa -one
  - La catena si nulera dalla estremità che porta ad attribuire il numero più piccolo al C(=O)
- ✓ Comune
  - for a ketone, name the two alkyl or aryl groups bonded to the carbonyl carbon and add the word ketone

Nomenclatura: chetoni



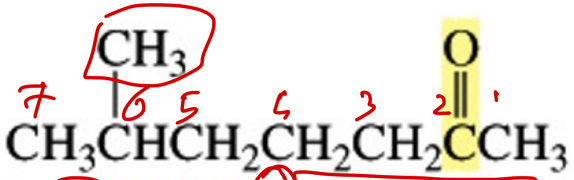
[R, R' = R, Ar]

systematic name: propanone
common name: acetone
derived name: dimethyl ketone



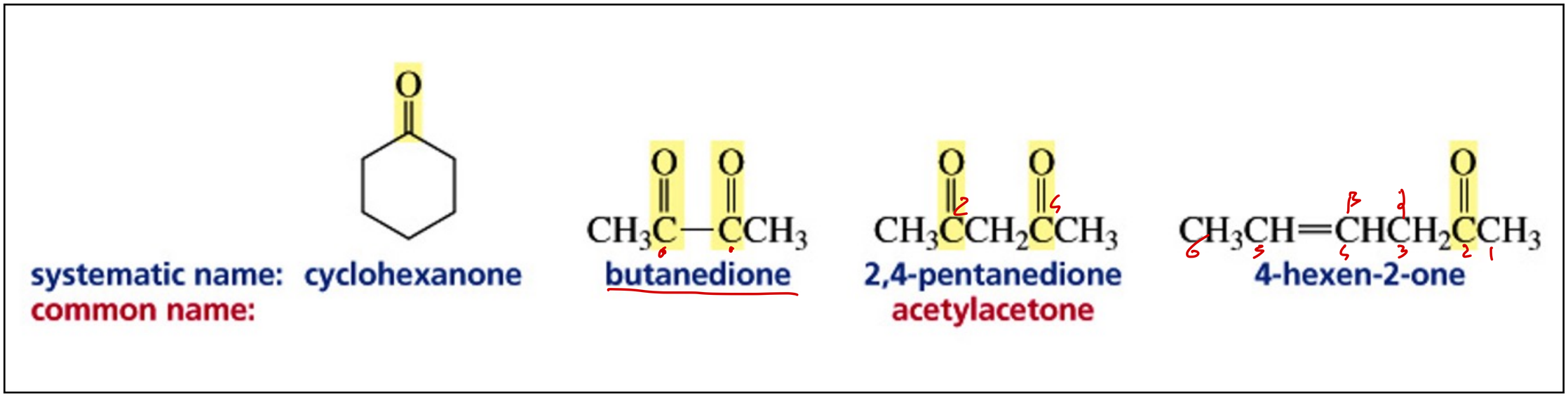
3-hexanone

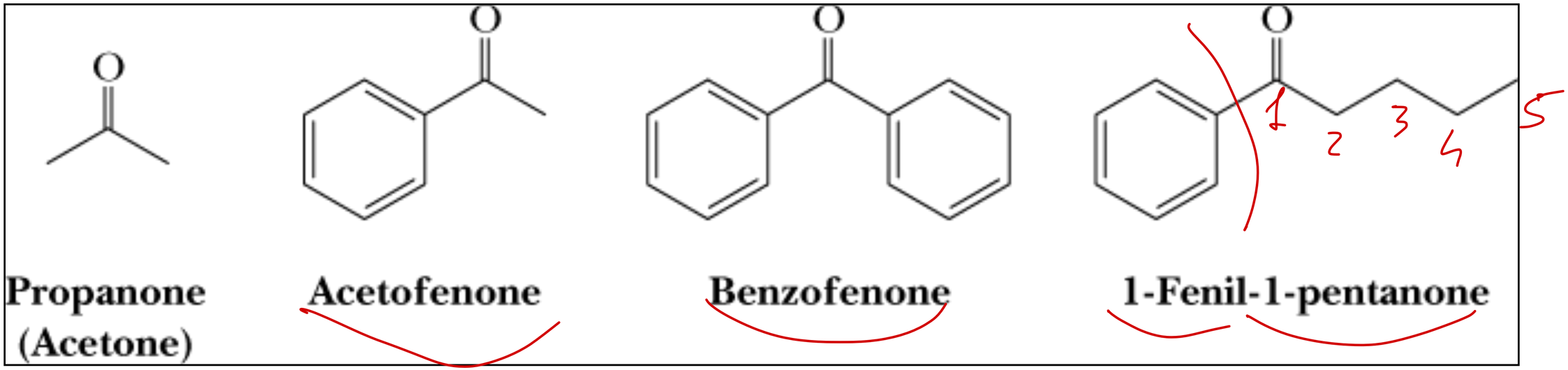
ethyl propyl ketone



6-methyl-2-heptanone

isohexyl methyl ketone

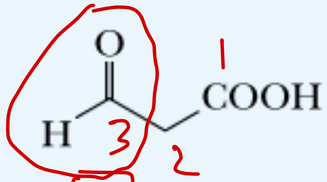
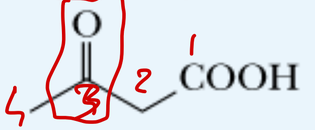
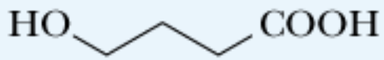
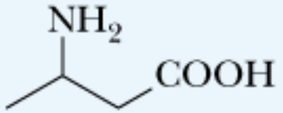
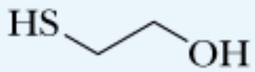

systematic name:
common name:
cyclohexanone
butanedione
2,4-pentanedione
acetylacetone
4-hexen-2-one


Propanone
(Acetone)
Acetofenone
Benzofenone
1-Fenil-1-pentanone

Nella denominazione di composti che contengono più di un gruppo funzionale che può essere indicato da un suffisso, il sistema IUPAC ha stabilito un ordine di priorità dei gruppi funzionali. L'ordine di priorità dei gruppi funzionali che abbiamo studiato finora è riportato nella Tabella

Tabella 13.1 Sei gruppi funzionali in ordine di priorità crescente

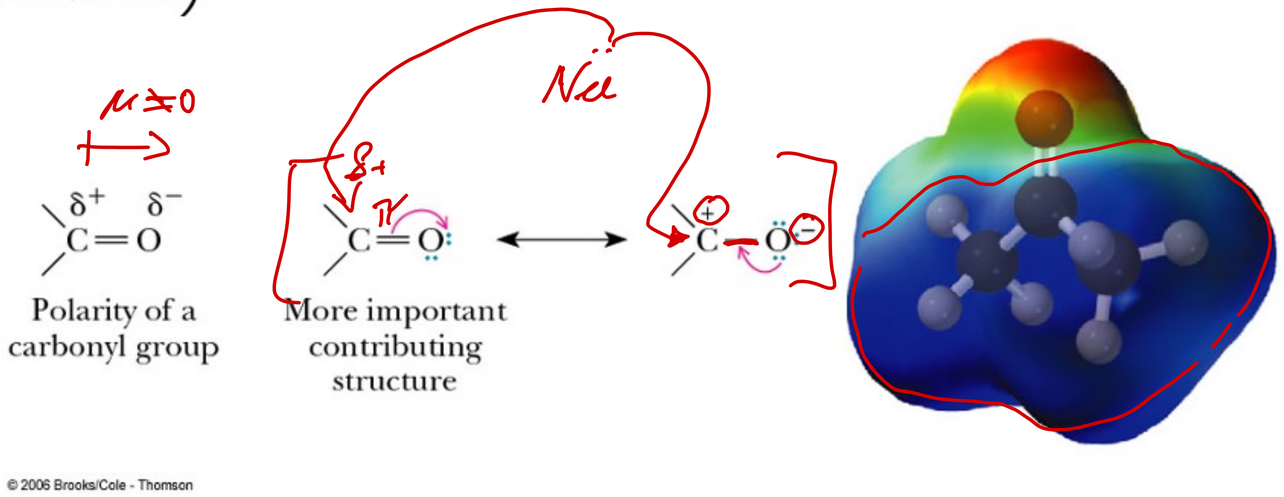
Priorità crescente

Gruppo funzionale	Suffisso se ha la priorità più alta	Prefisso se ha la priorità più bassa	Un esempio in cui il gruppo funzionale ha la priorità più bassa
Carbossile	acido -oico	—	
Aldeide	-ale	osso-	Acido 3-ossopropanoico 
Chetone	-one	osso-	Acido 3-ossobutanoico 
Alcol	-olo	idrossi-	Acido 4-idrossibutanoico 
Ammina	-ammina	ammino-	Acido 3-amminobutanoico 
Solfidrile	-tiolo	mercapto-	2-Mercaptoetanolo 


PRIORIDADE CRESCENTE
Função
Ácido carboxílico
Aldeído
Cetona
Álcool
Amina
Haleto orgânico
Sufixo
oico
al
ona
ol
amina
-
Prefixo (no caso da função não ser considerada a principal)
-
oxo ou formil
oxo
hidróxi
amino
nome do elemento

Proprietà fisiche

- ✓ L'ossigeno è più elettronegativo del carbonio (3.5 vs 2.5) e pertanto il gruppo C=O è polare (e polarizzabile)



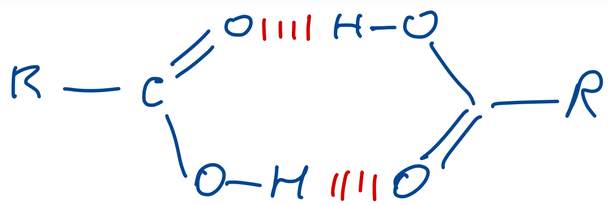
- ✓ interazioni dipolo-dipolo:
  - they have higher boiling points and are more soluble in water than nonpolar compounds of comparable molecular weight

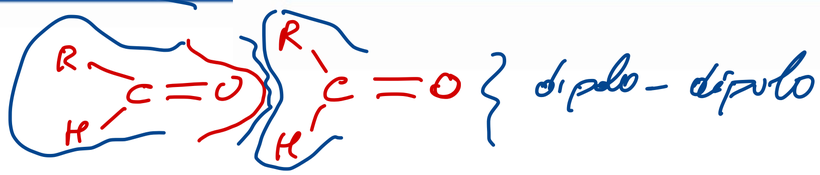
Tabella 16.2 Punti di ebollizione di sei composti di peso molecolare paragonabile

Nome	Formula di struttura	Peso molecolare (g/mole)	p.e. (°C)
Dietil etere	$CH_3CH_2OCH_2CH_3$	74	34
Pentano	$CH_3CH_2CH_2CH_2CH_3$	72	36
Butanale	$CH_3CH_2CH_2CHO$	72	76
2-Butanone	$CH_3COCH_2CH_3$	72	80
1-Butanolo	$CH_3CH_2CH_2CH_2OH$	74	117
Acido propanoico	$CH_3CH_2CO_2H$	74	141

Tabella 16.3 Proprietà fisiche di alcune aldeidi e di alcuni chetoni

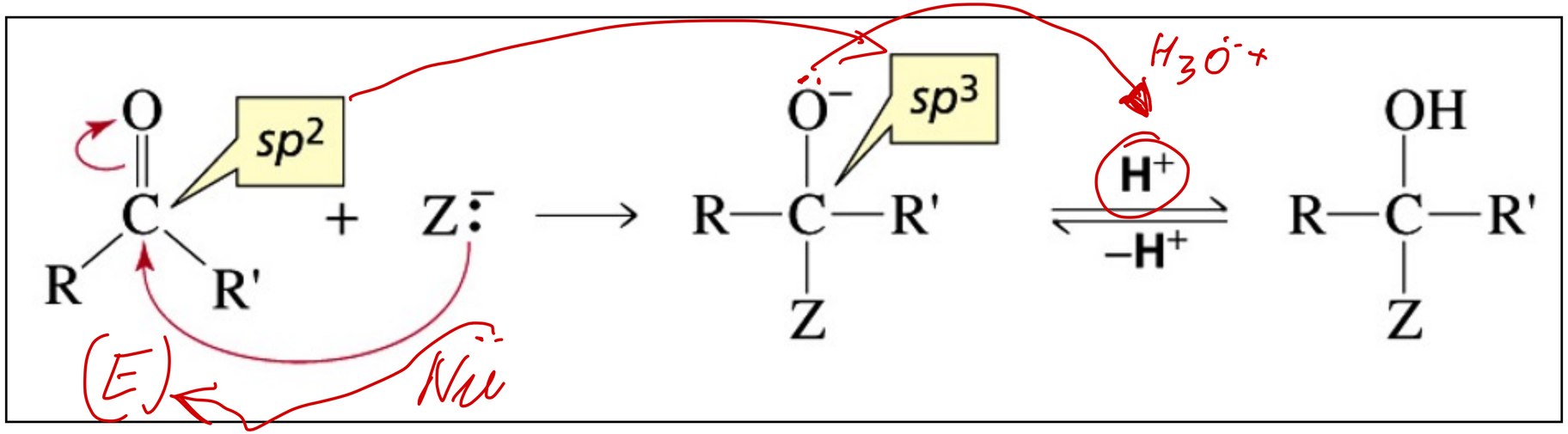
Nome IUPAC	Nome comune	Formula di struttura	p.e. (°C)	Solubilità (g/100 g acqua)
Metanale	Formaldeide	$HCHO$	−21	infinita
Etanale	Acetaldeide	CH_3CHO	20	infinita
Propanale	Propionaldeide	CH_3CH_2CHO	49	16
Butanale	Butirraldeide	$CH_3CH_2CH_2CHO$	76	7
Esanale	Caproaldeide	$CH_3(CH_2)_4CHO$	129	piccola
Propanone	Acetone	CH_3COCH_3	56	infinita
2-Butanone	Etil metil chetone	$CH_3COCH_2CH_3$	80	26
3-Pentanone	Dietil chetone	$CH_3CH_2COCH_2CH_3$	101	5

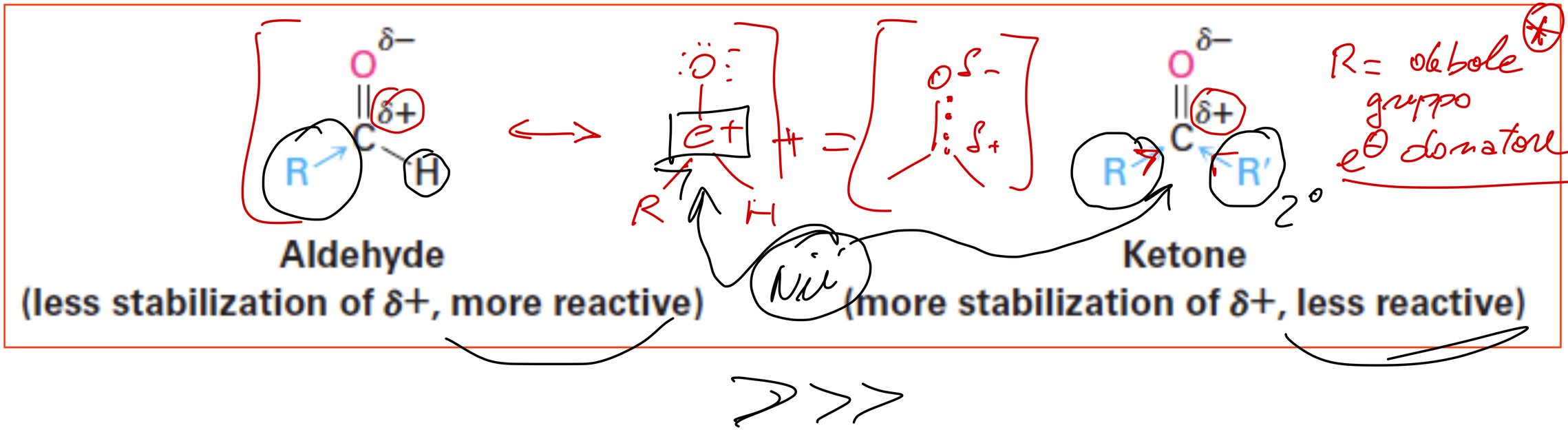




Reattività: ADDIZIONI NUCLEOFILE ACILICHE

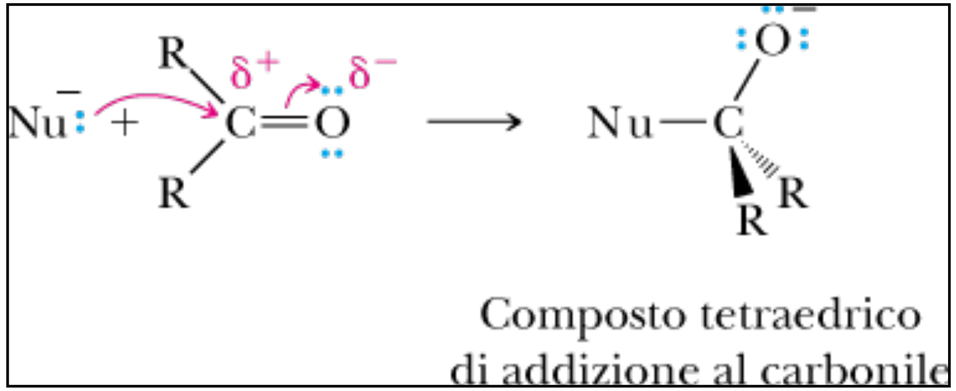
Addizione nucleofila al gruppo carbonile: addizione al doppio legame C=O

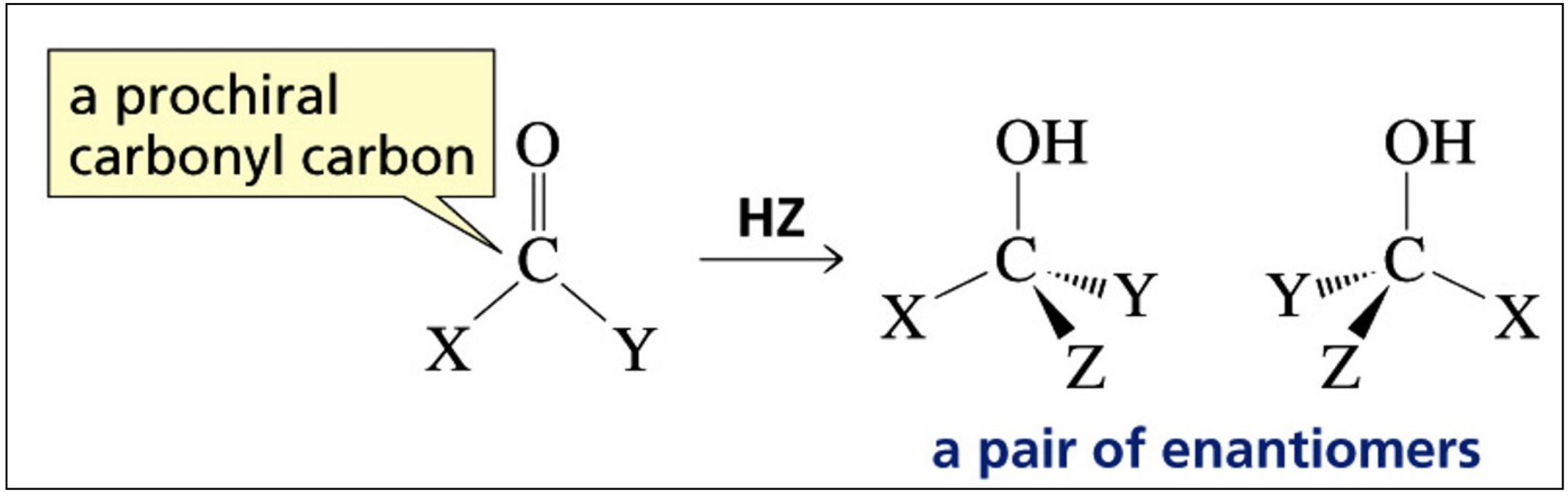




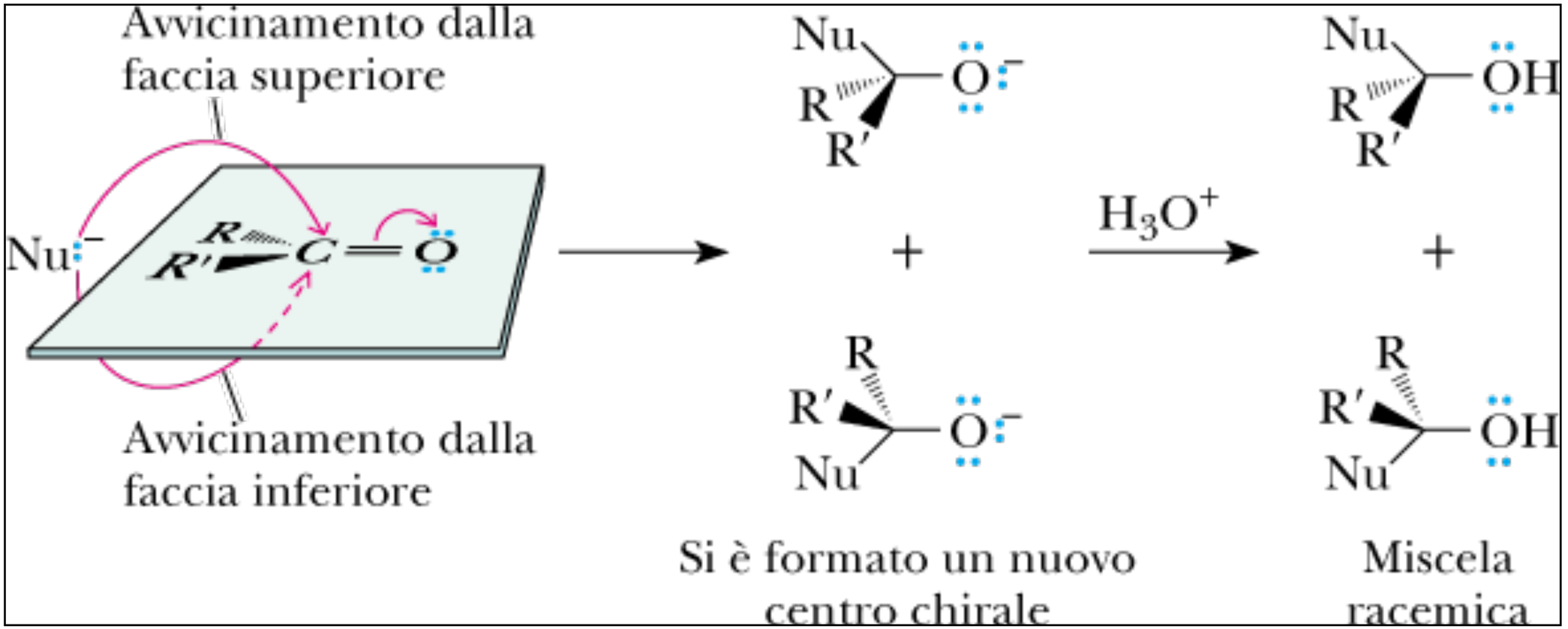
>>>

STEREOCHIMICA DELL'ADDIZIONE NUCLEOFILA





STEREOCHIMICA DELL'ADDIZIONE NUCLEOFILA



Addizione nucleofila al gruppo carbonile di Aldeidi e Chetoni

Some neutral nucleophiles

- HÖH (water)
- RÖH (an alcohol)
- H_3N: (ammonia)
- $R\ddot{N}H_2$ (an amine)

1°

R R' NH 2°

Some negatively charged nucleophiles

- $H\ddot{O}:^-$ (hydroxide ion)
- $H:^-$ (hydride ion)
- $R_3C:^-$ (a carbanion)
- $R\ddot{O}:^-$ (an alkoxide ion)
- $N\equiv C:^-$ (cyanide ion)

RMgX	RLi	$RC\equiv C:^-$	$:C\equiv N:^-$
Reattivo di Grignard	Composto di organolitio	Anione di un alchino terminale	Ione cianuro

Addizione nucleofila al gruppo carbonile di Aldeidi e Chetoni

Some neutral nucleophiles

- HÖH (water)
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- H_3N: (ammonia)
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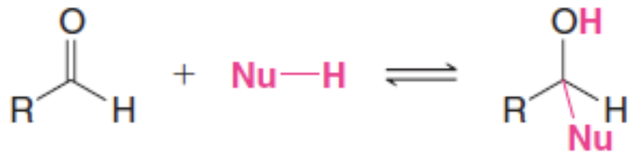
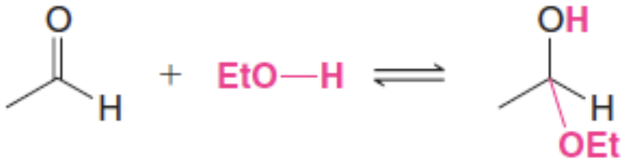
Some negatively charged nucleophiles

- HÖ:$^-$ (hydroxide ion)
- H:$^-$ (hydride ion)
- R_3C:$^-$ (a carbanion)
- RÖ:$^-$ (an alkoxide ion)
- N≡C:$^-$ (cyanide ion)

General Reaction

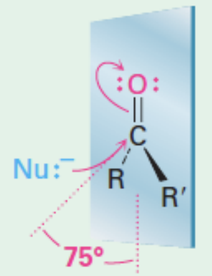


Specific Examples



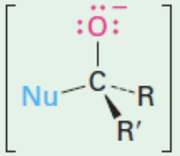
A hemiacetal (see Section 16.7)

A cyanohydrin (see Section 16.9)



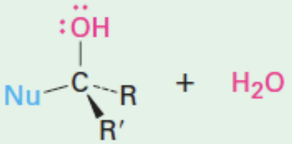
Aldehyde or ketone

1



Alkoxide ion

2 H_3O^+

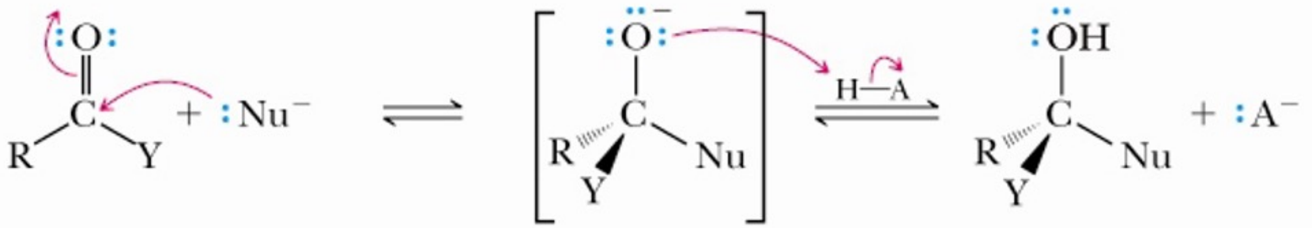


Alcohol

Reattività:

Addizione nucleofila al gruppo carbonile: base catalizzata e acido catalizzata

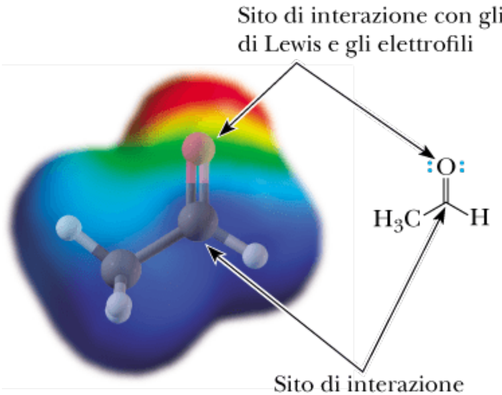
Addizione nucleofila (condizioni basiche):



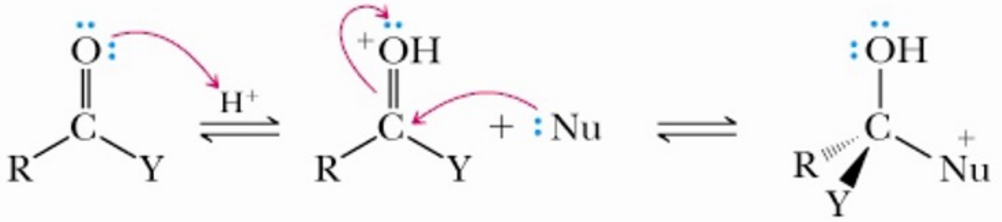
Un derivato di un acido carbossilico

Intermedio tetraedrico di addizione al carbonile

Prodotto di addizione



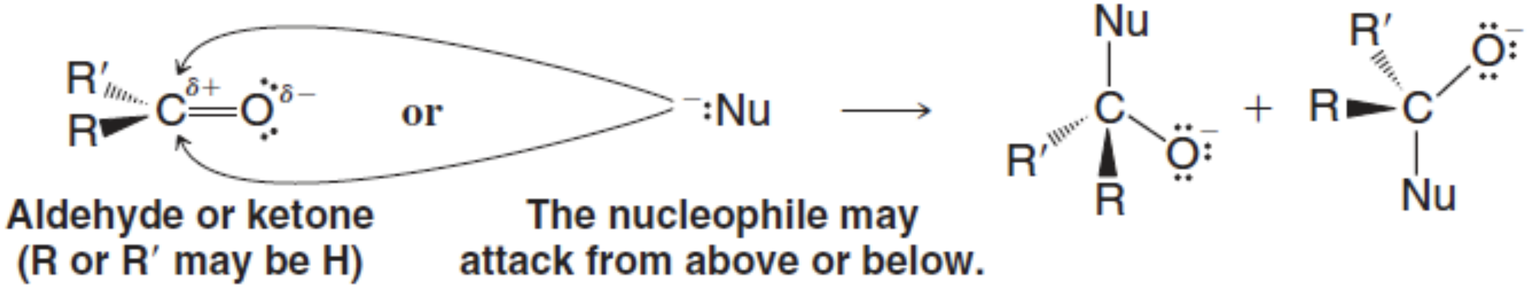
Addizione nucleofila (condizioni acide):

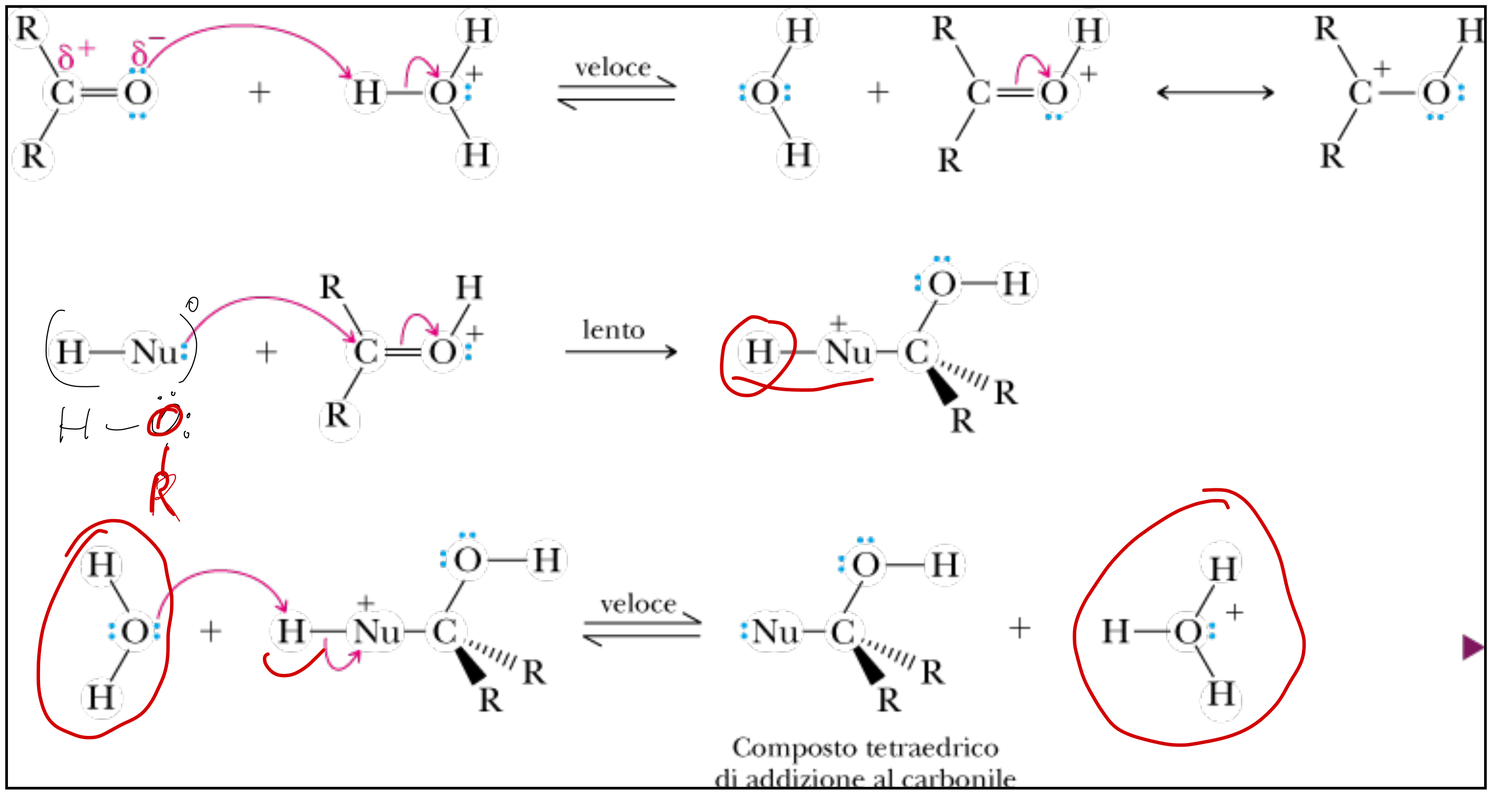


Un derivato di un acido carbossilico

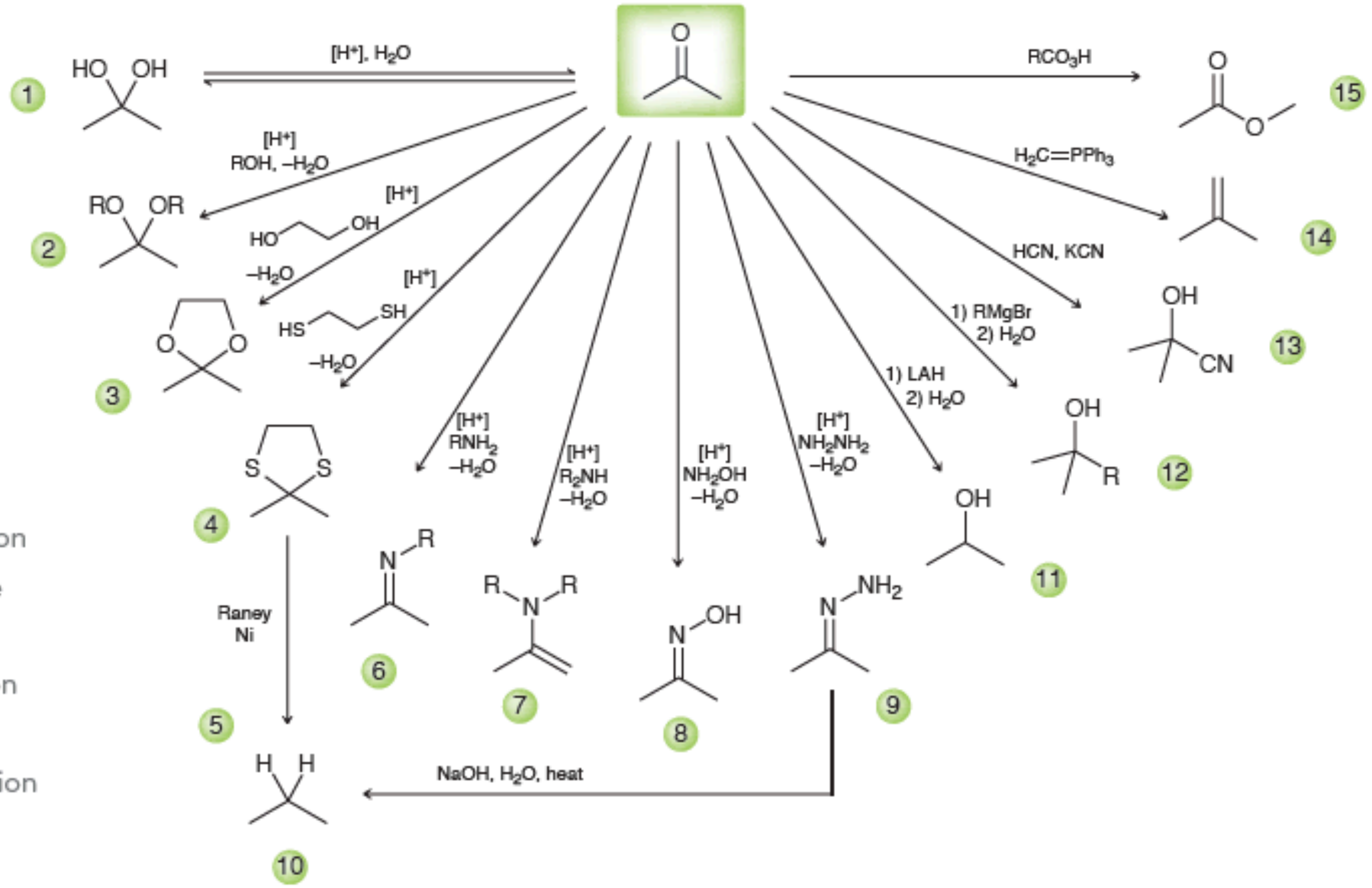
Intermedio tetraedrico di addizione al carbonile

STEREOCHIMICA DELL'ADDIZIONE NUCLEOFILA

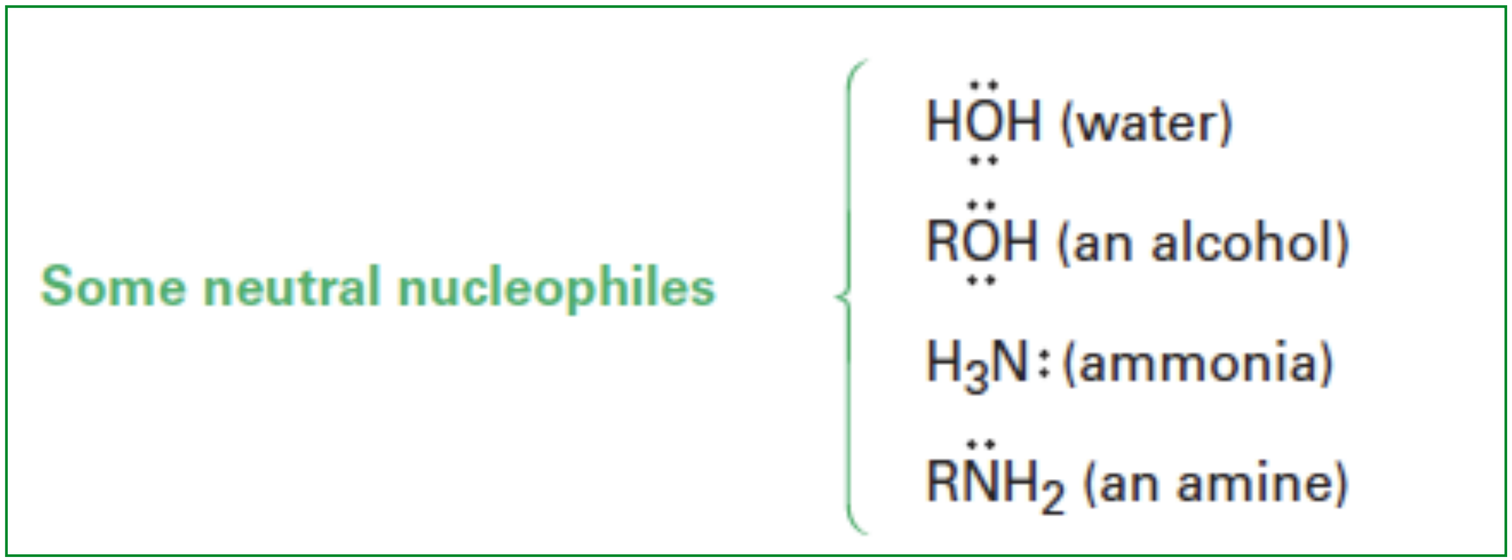




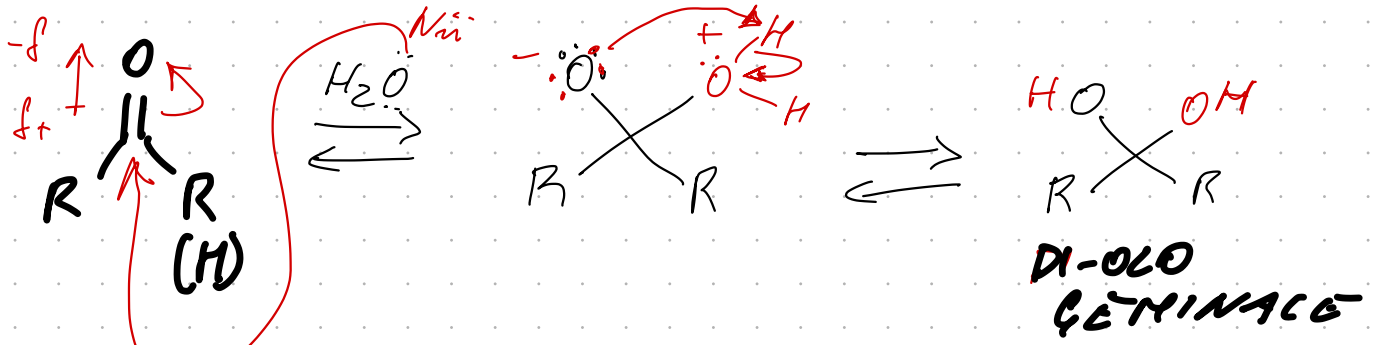
1. Hydrate Formation
2. Acetal Formation
3. Cyclic Acetal Formation
4. Cyclic Thioacetal Formation
5. Desulfurization
6. Imine Formation
7. Enamine Formation
8. Oxime Formation
9. Hydrazone Formation
10. Wolff-Kishner Reduction
11. Reduction of a Ketone
12. Grignard Reaction
13. Cyanohydrin Formation
14. Wittig Reaction
15. Baeyer-Villiger Oxidation

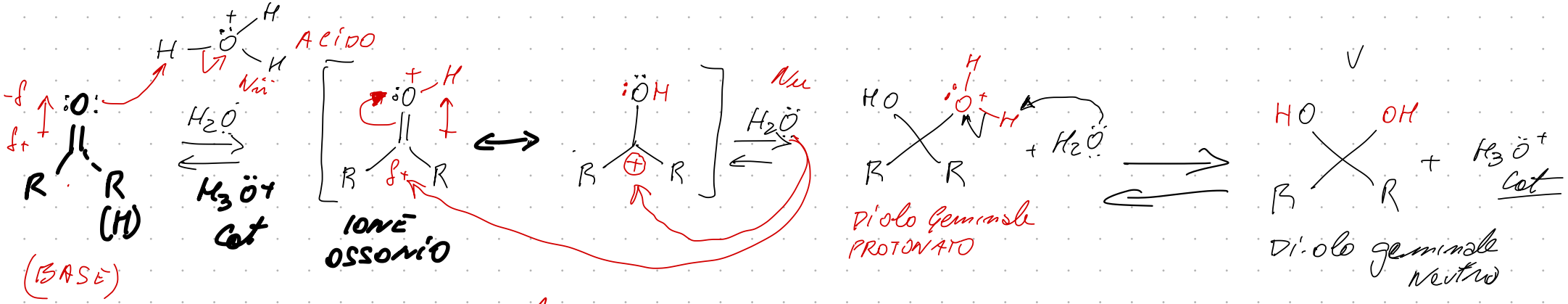


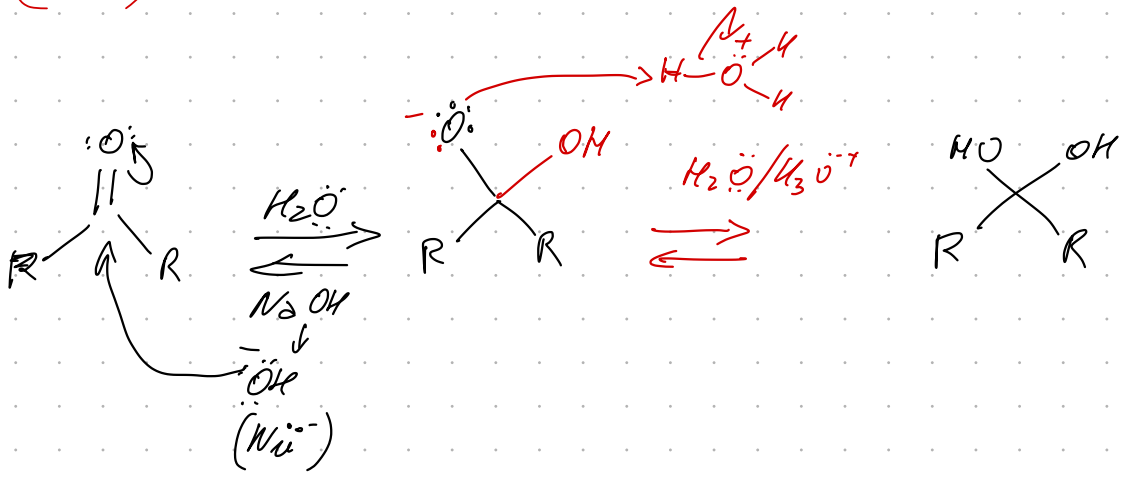
Reazioni di addizione nucleofila al gruppo carbonile
Con un nucleofilo debole (neutro)

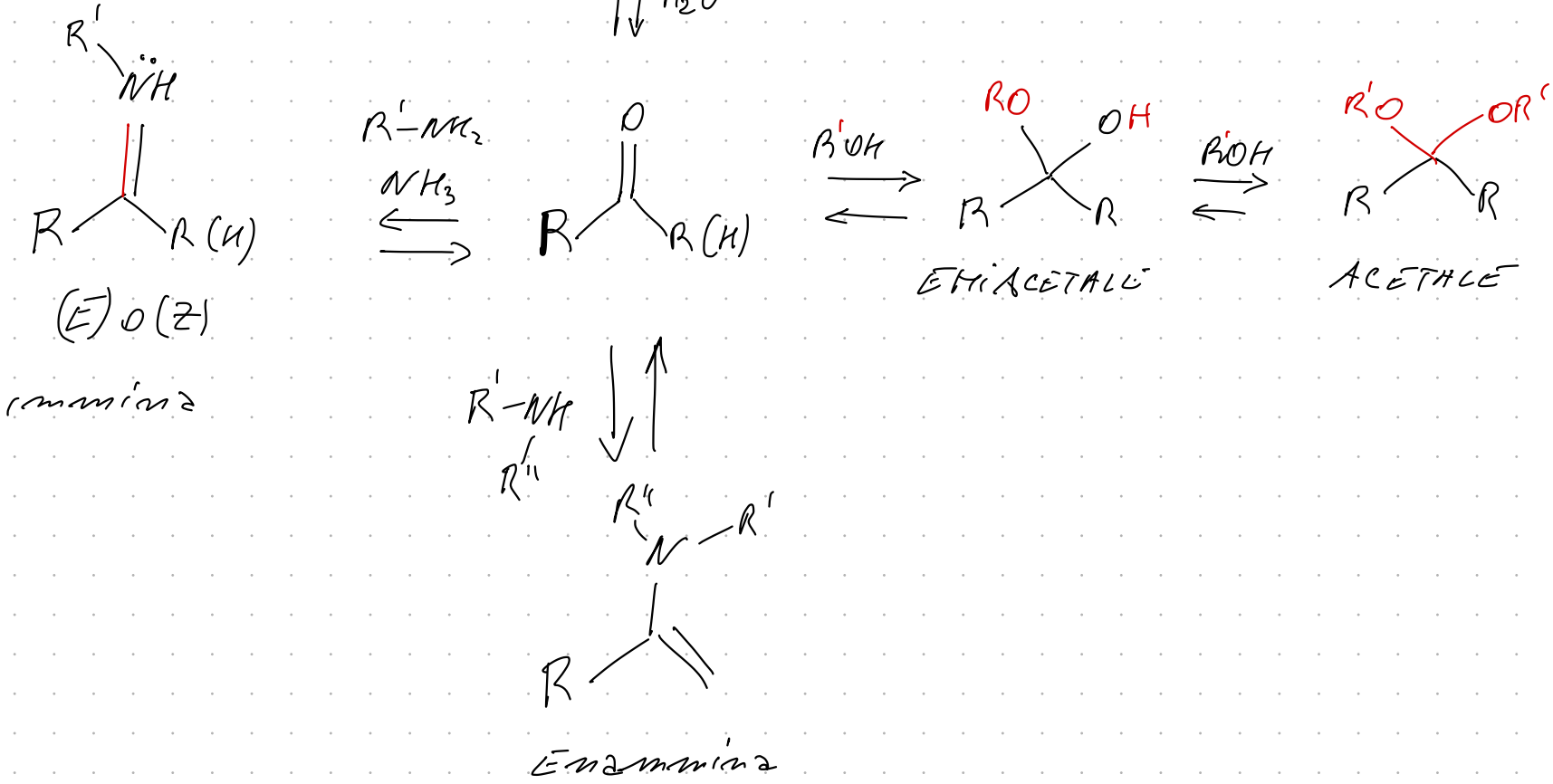


1) Aggiunta di acqua (idratazione): Di-ol geminale
2) Aggiunta di alcoli: emiacetali e acetali
3) Aggiunta di ammine: immine ed enamine


Nu
H_2O
DI-OLO GEMINALE

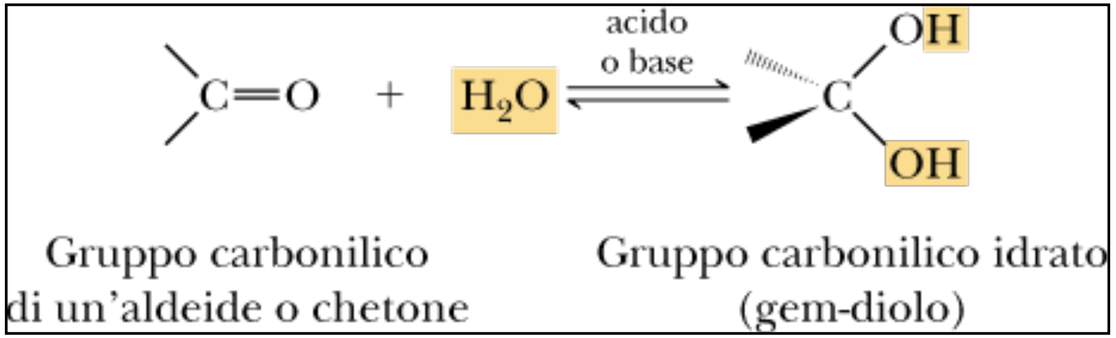

ACIDO
Nu
H_2O
H_3O^+ cat
(BASE)
IONE OSSONIO
Nu
H_2O
Diolo Geminale PROTONATO
+ H_2O
V
+ H_3O^+ cat
Diolo geminale Neutro

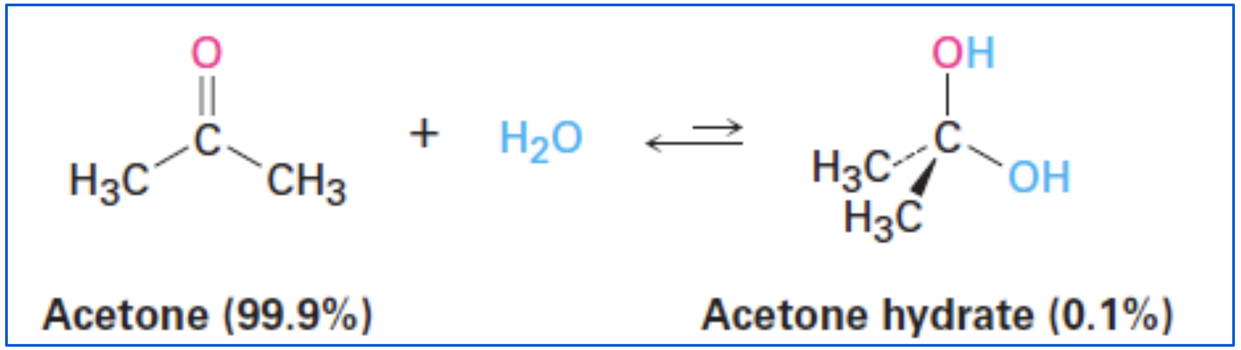

H_2O
$NaOH$
$(Nu^{:-})$
H_2O/H_3O^+

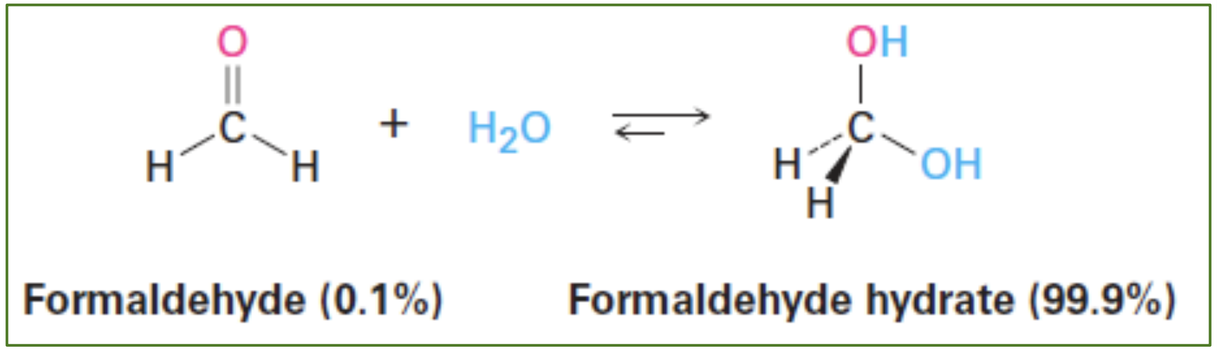

HO
OH
R
R(H)
DIOLO GEMINALE
H2O
R'
NH
R
R(H)
(E) o (Z)
enammina
R'-NH2
NH3
O
R
R(H)
R'OH
RO
OH
R
R
EMIACETALE
R'OH
R'O
OR'
R
R
ACETALE
R'-NH
R''
R''
N
R'
R
Enammina

(1) ADDIZIONE di H_2O: idratazione , Formazione di Carbonili idrati

Idrati di aldeidi 1,1-dioli (gem-Dios) derivanti da un'aggiunta nucleofila di acqua al gruppo carbonile dell'aldeide







(1) ADDIZIONE di H_2O: idratazione , Formazione di Carbonili idrati

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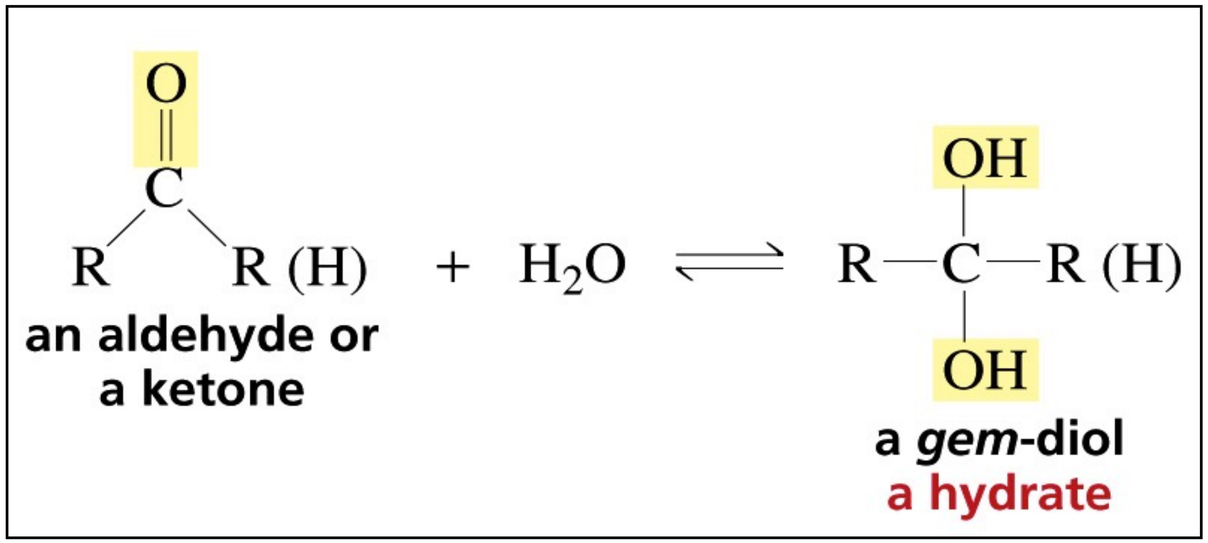
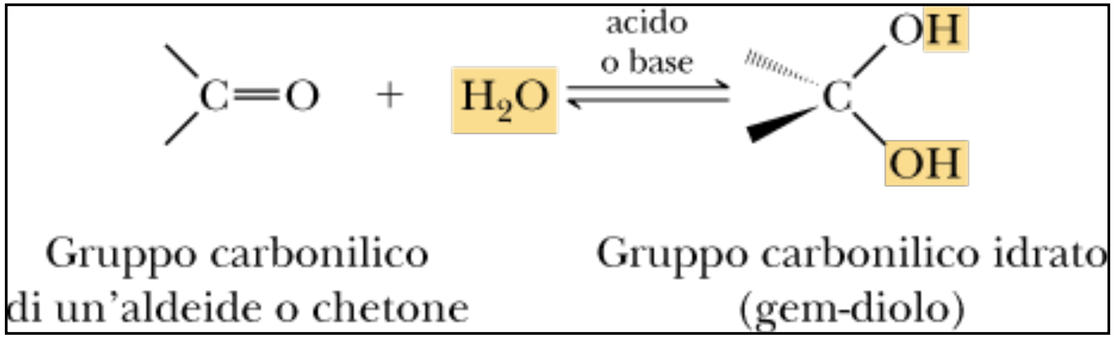
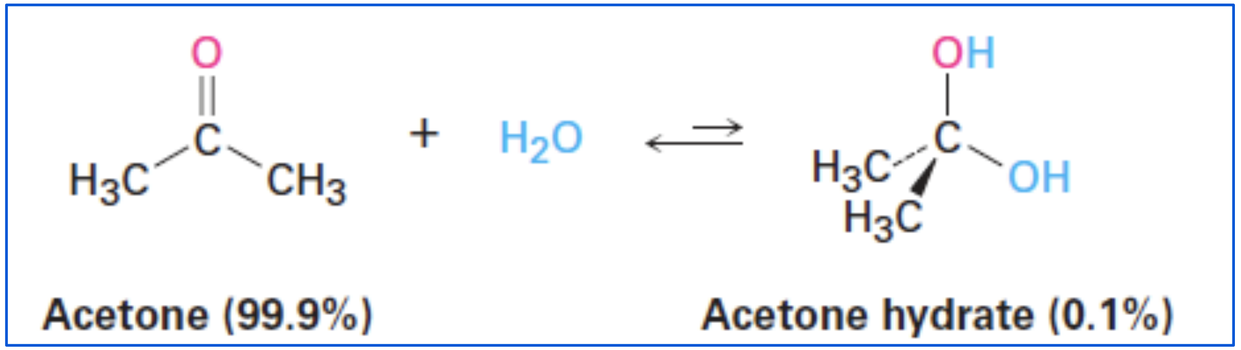
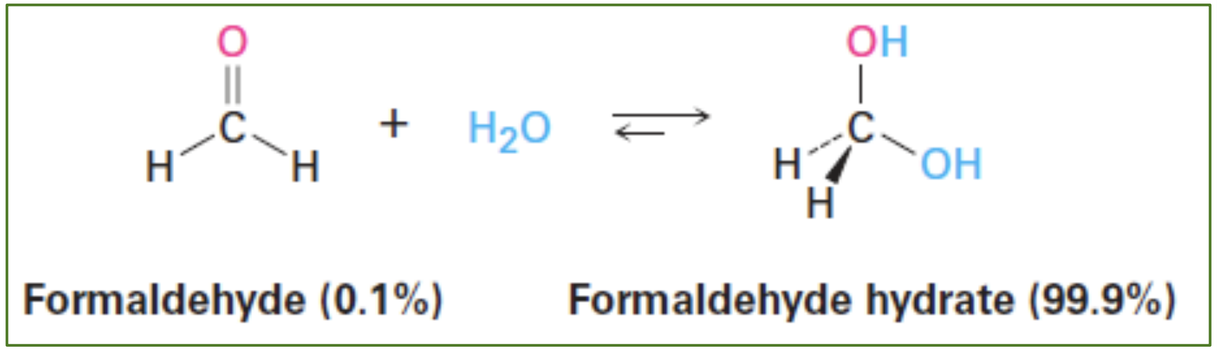
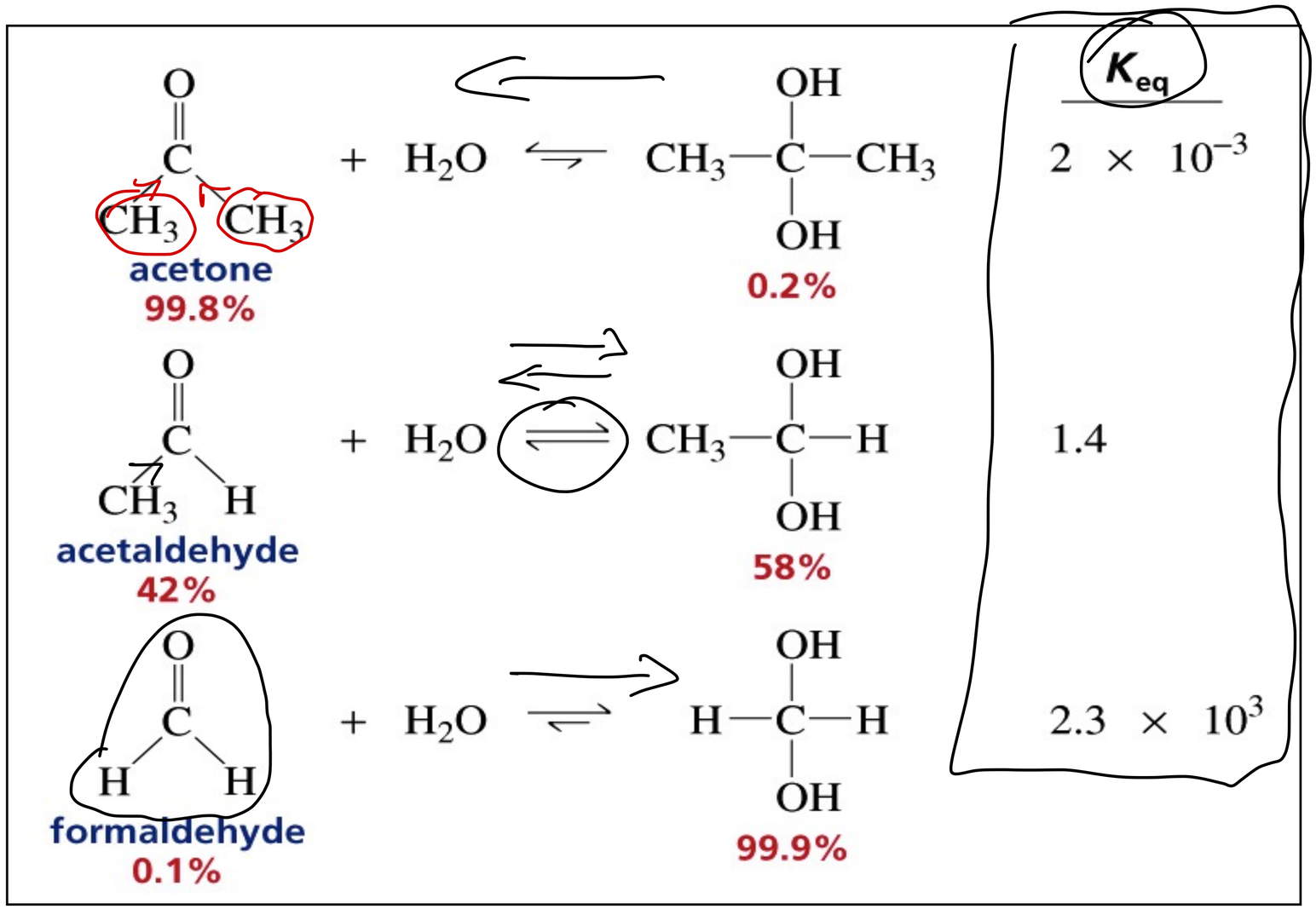






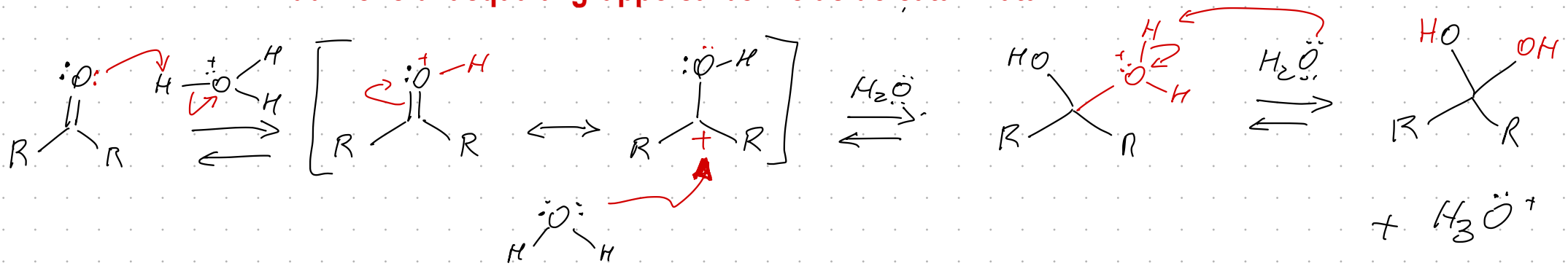


L'equilibrio in presenza di acqua: Il chetone è svantaggiato

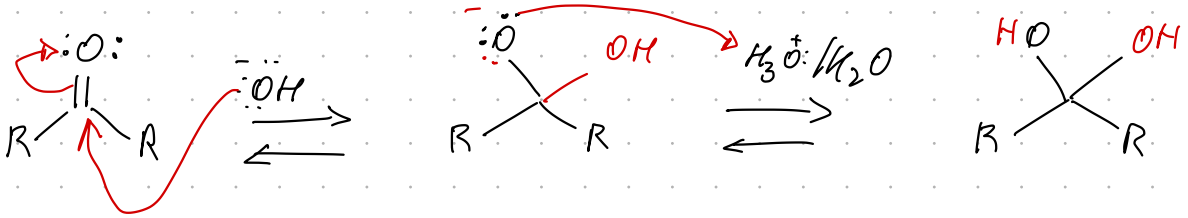


$$K_{eq} = \frac{[P]}{[R]}$$

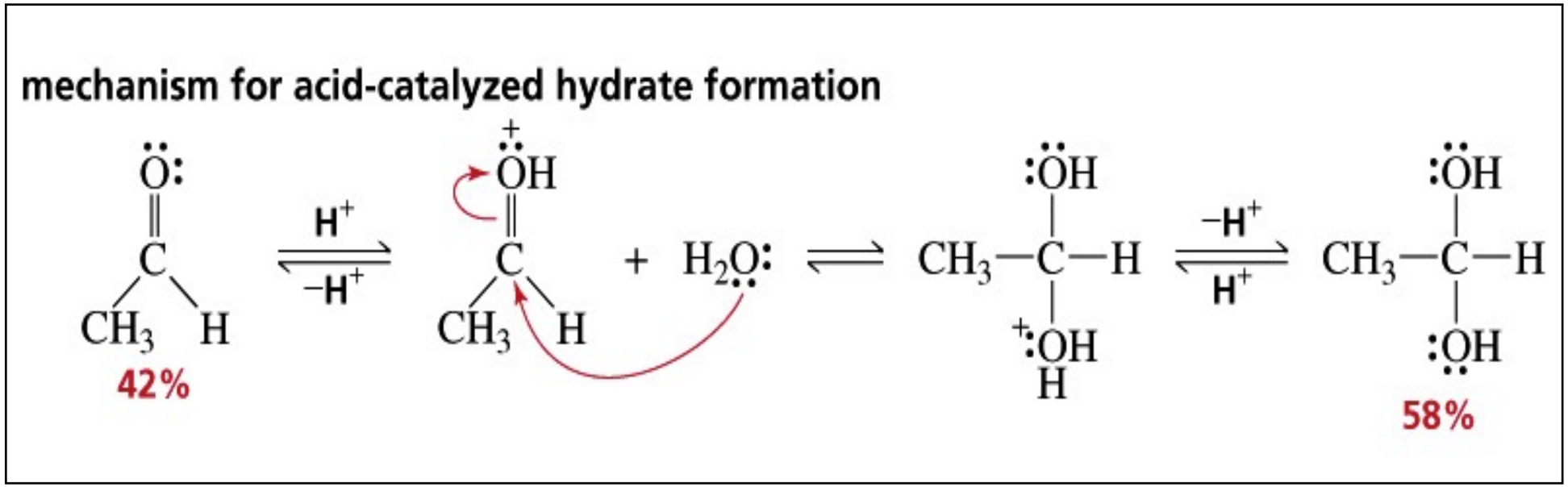
Addizione di acqua al gruppo carbonile acido catalizzata

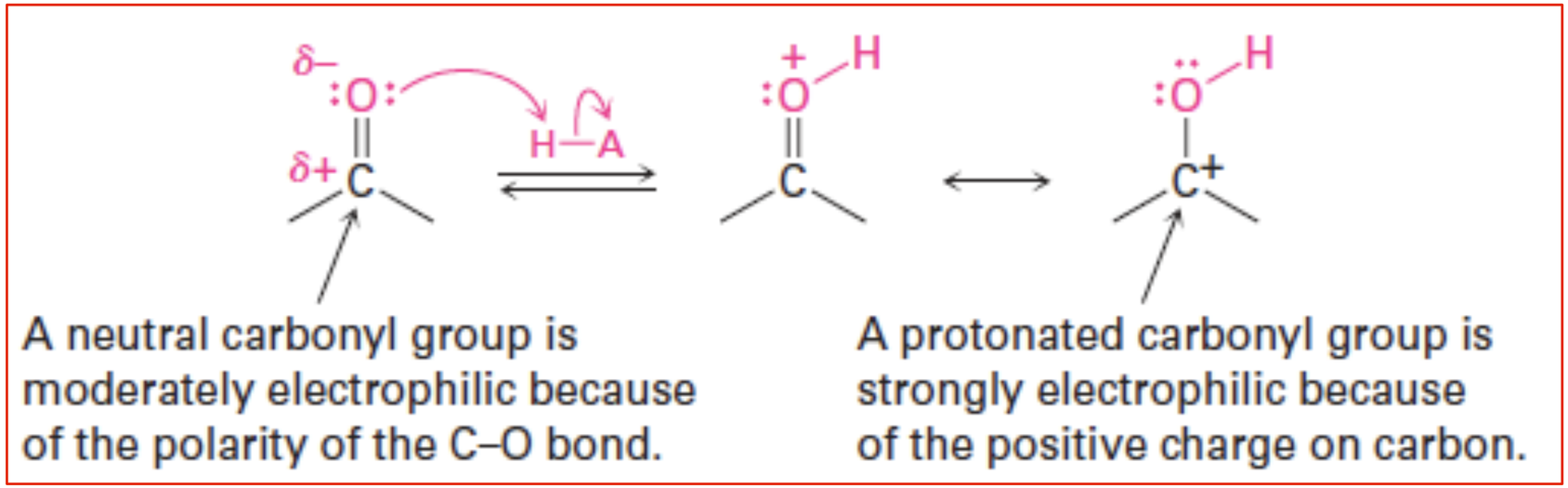


Addizione di acqua al gruppo carbonile base catalizzata



(1) Addizione di H_2O: Meccanismo di idratazione catalizzata dall'acido



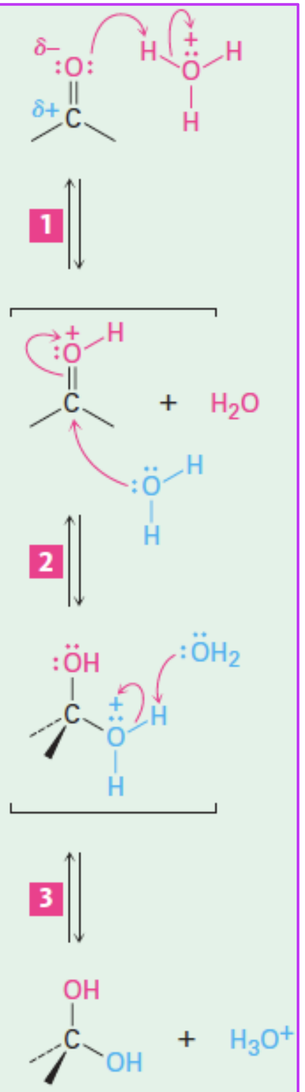


(1) Addizione di H_2O: Meccanismo di idratazione catalizzata da un acido o da una base

1 The carbonyl oxygen is protonated by acid H_3O^+, making the carbon more strongly electrophilic

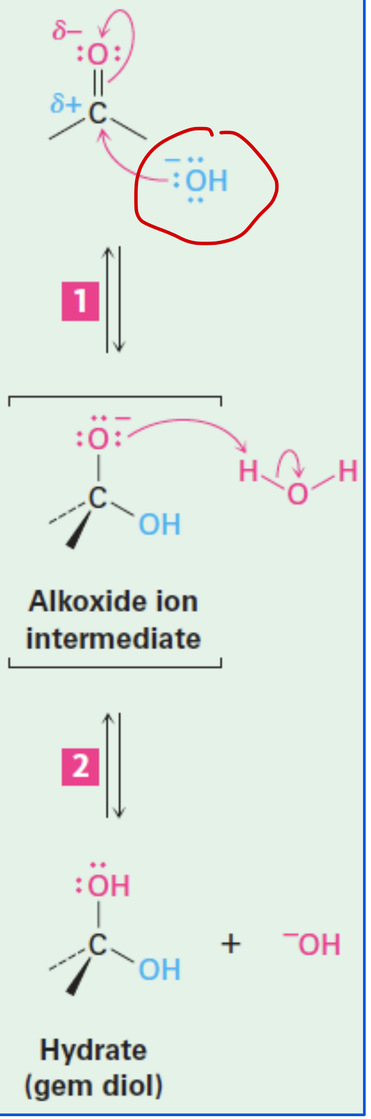
2 The neutral nucleophile $:\ddot{O}H_2$ adds to the electrophilic carbon, pushing the π electrons from the C=O onto oxygen. The oxygen becomes neutral, and the nucleophile gains the + charge.

3 Water deprotonates the intermediate, giving the neutral hydrate addition product and regenerating the acid catalyst H_3O^+.



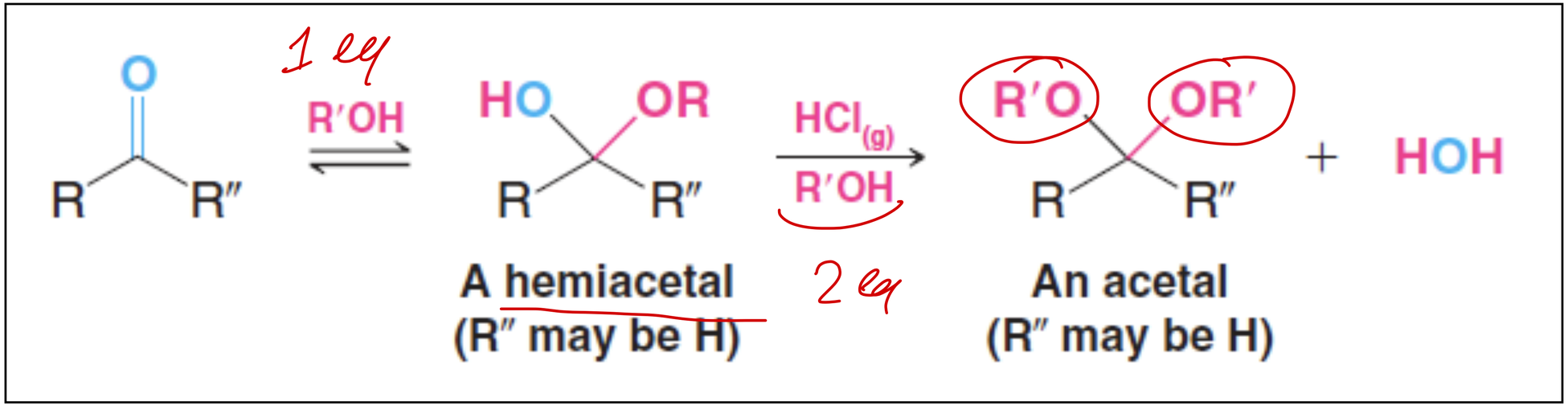
1 The negatively charged nucleophile OH^- adds to the electrophilic carbon and pushes π electrons from the C=O bond onto oxygen, giving an alkoxide ion.

2 The alkoxide ion is protonated by water to give the neutral hydrate as the addition product and regenerating OH^-.



(2) Addizione nucleofila degli alcoli al gruppo carbonile: Formazione di emiacetali e acetali

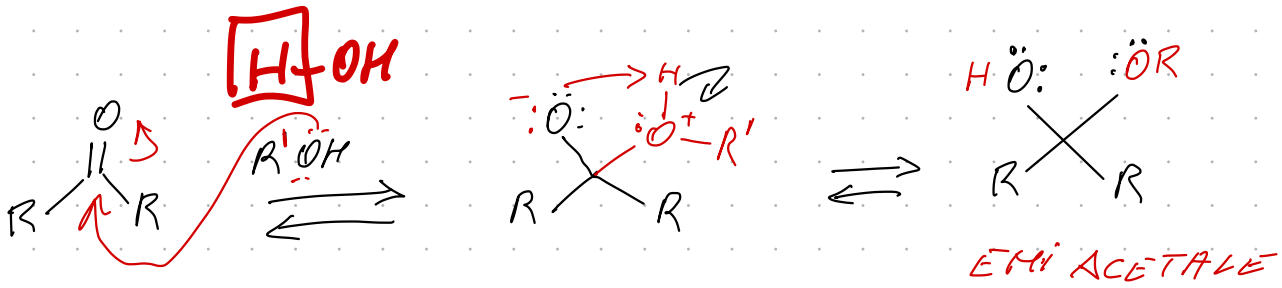
Gli aldeidi e i chetoni reagiscono reversibilmente con due equivalenti di un alcol in presenza di un catalizzatore acido per formare acetali

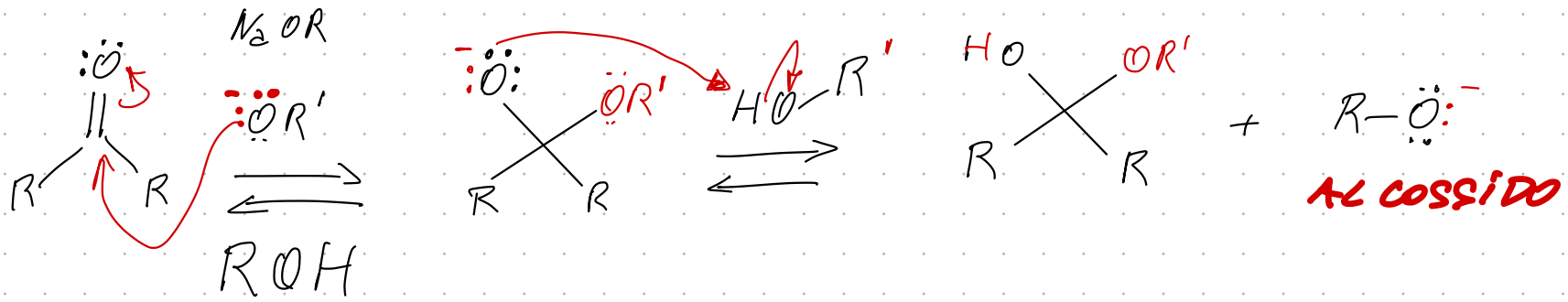


-Gli emiacetali hanno un gruppo -OH e un gruppo -OR legato allo stesso atomo di carbonio.

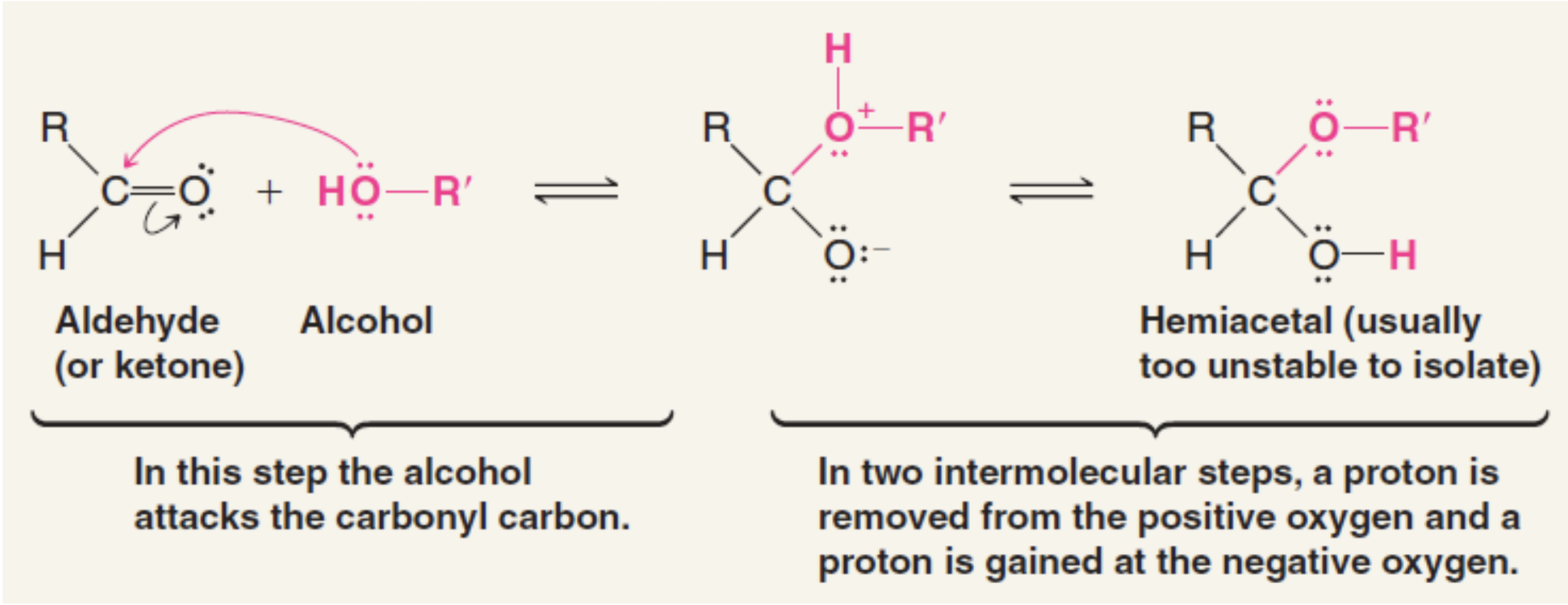
-Un acetale ha due gruppi -OR legati allo stesso atomo di C.

FORMAZIONE DI EMIACETALI Acido e base catalizzata





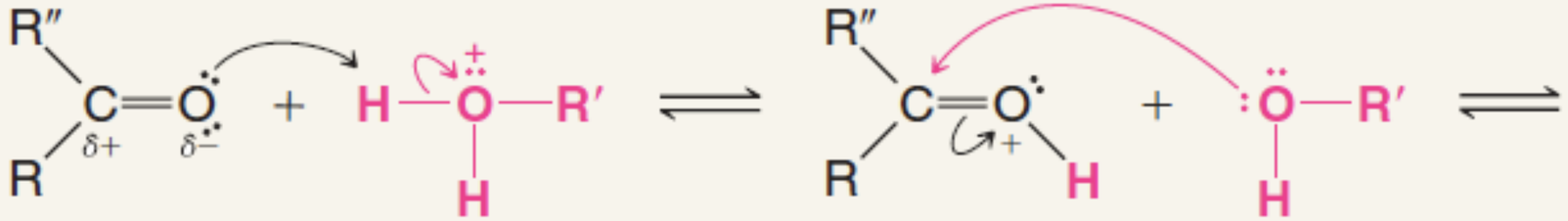
(2) Addizione nucleofila degli alcoli al gruppo carbonile: Formazione di emiacetali



Formazione di emiacetali:

Gli alcoli sono nucleofili deboli che si addizionano
Ad aldeidi e chetoni lentamente, in condizioni neutre.

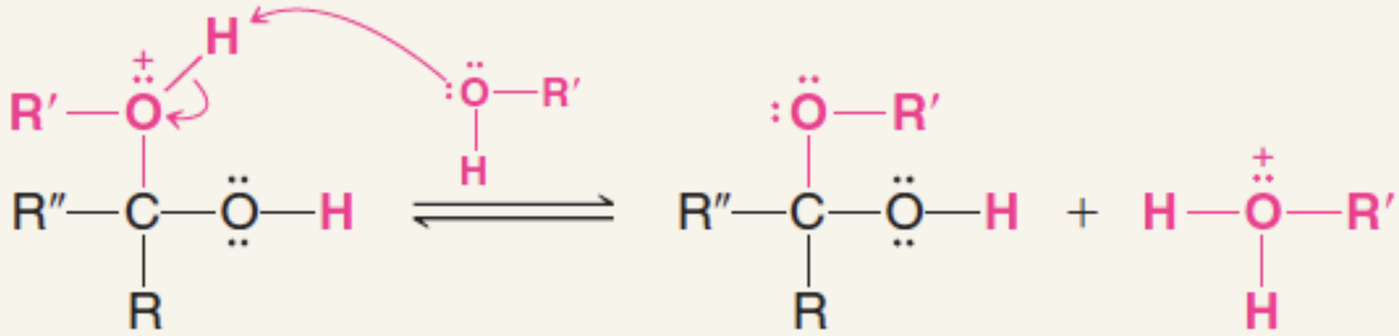
(2) Addizione nucleofila degli alcoli al gruppo carbonile: Formazione di emiacetali catalizzata da acidi



(R″ may be H)

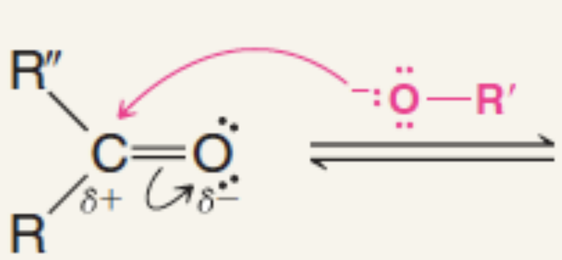
Protonation of the aldehyde or ketone oxygen atom makes the carbonyl carbon more susceptible to nucleophilic attack. [The protonated alcohol results from reaction of the alcohol (present in excess) with the acid catalyst, e.g., gaseous (anhydrous) HCl.]

An alcohol molecule adds to the carbon of the oxonium cation.



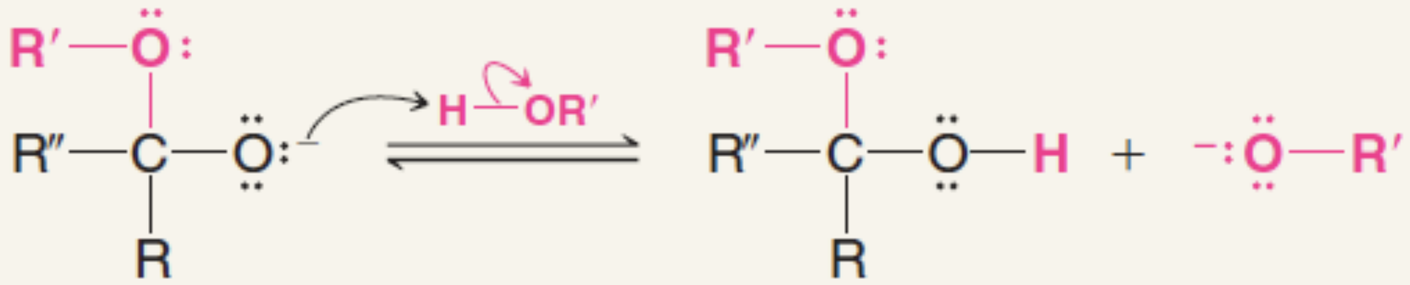
The transfer of a proton from the positive oxygen to another molecule of the alcohol leads to the hemiacetal.

(2) Addizione nucleofila degli alcoli al gruppo carbonile: Formazione di emiacetali catalizzata da basi



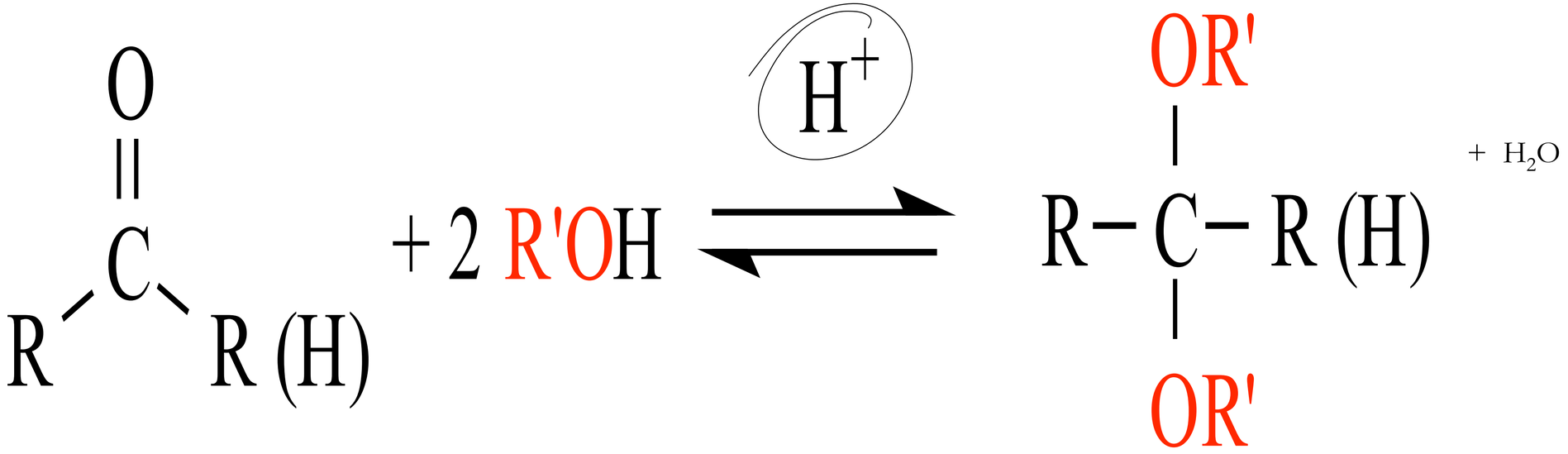
(R″ may be H)

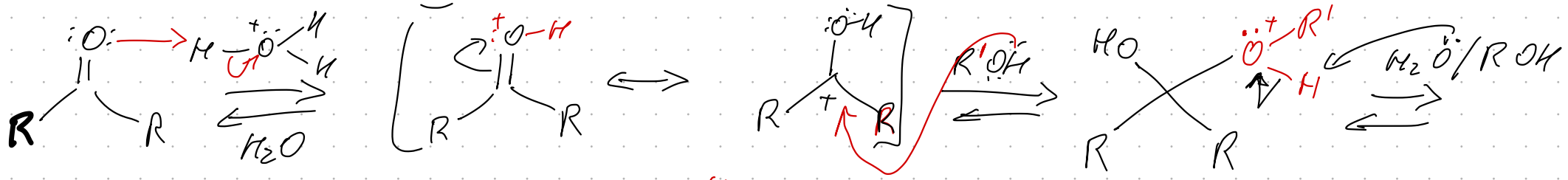
An alkoxide anion acting as a nucleophile attacks the carbonyl carbon atom. An electron pair shifts onto the oxygen atom, producing a new alkoxide anion.



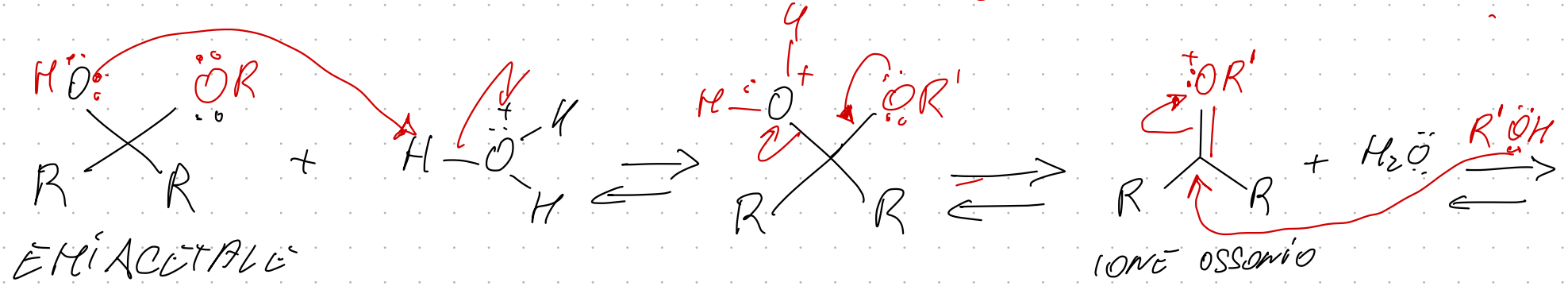
The alkoxide anion abstracts a proton from an alcohol molecule to produce the hemiacetal and regenerates an alkoxide anion.

(2) Addizione nucleofila degli alcoli al gruppo carbonile: Formazione di acetali





EMIACETALE

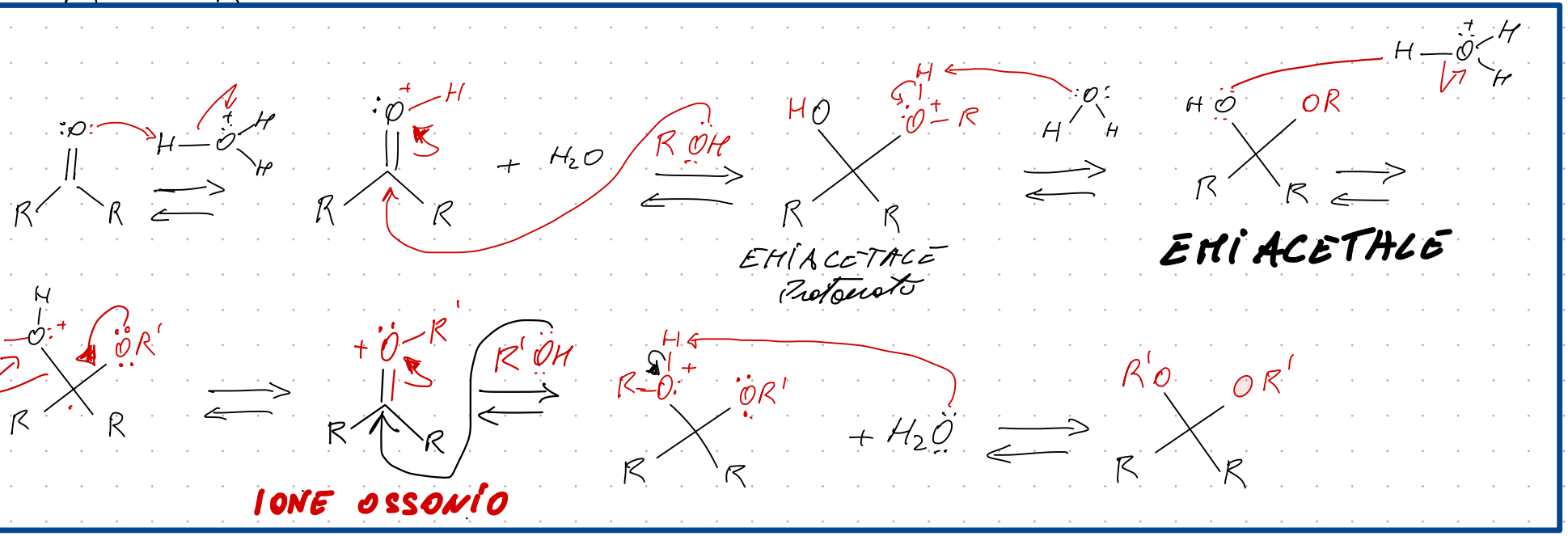


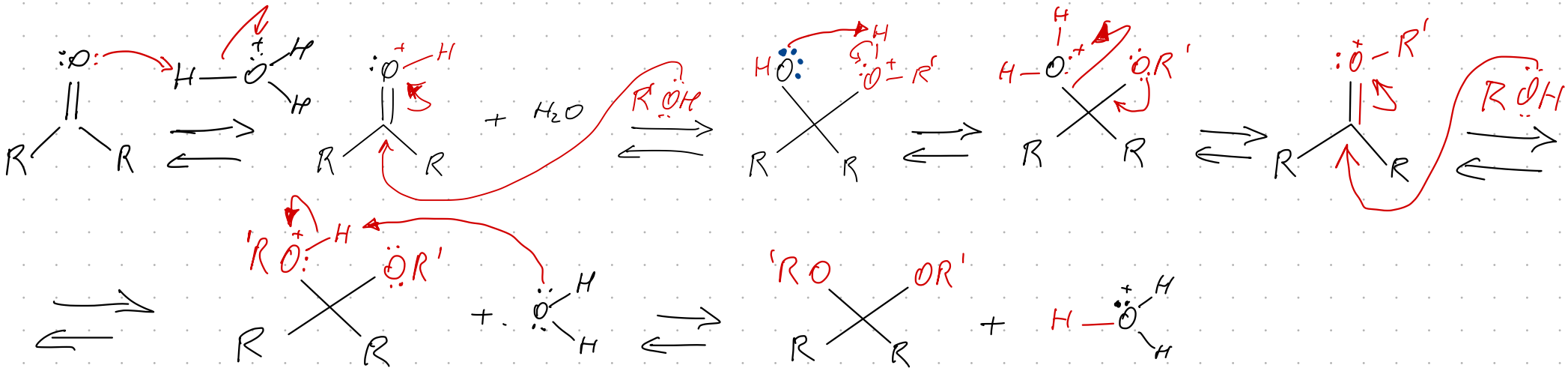
IONE OSSONIO

ACETALE PROTONATO

ACETALE

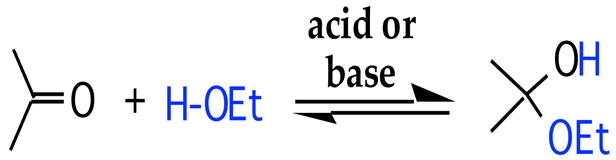
FORMAZIONE DI ACETALI Acido catalizzata





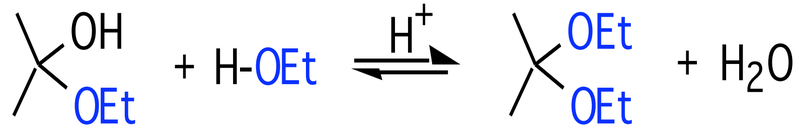
(2) Addizione nucleofila degli alcoli al gruppo carbonile: Formazione di acetali

1° STADIO:

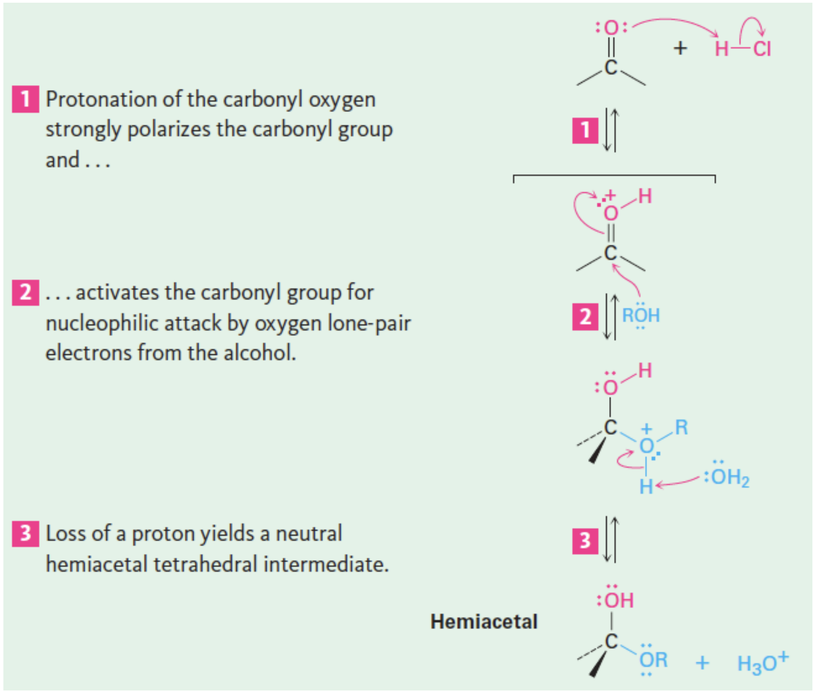


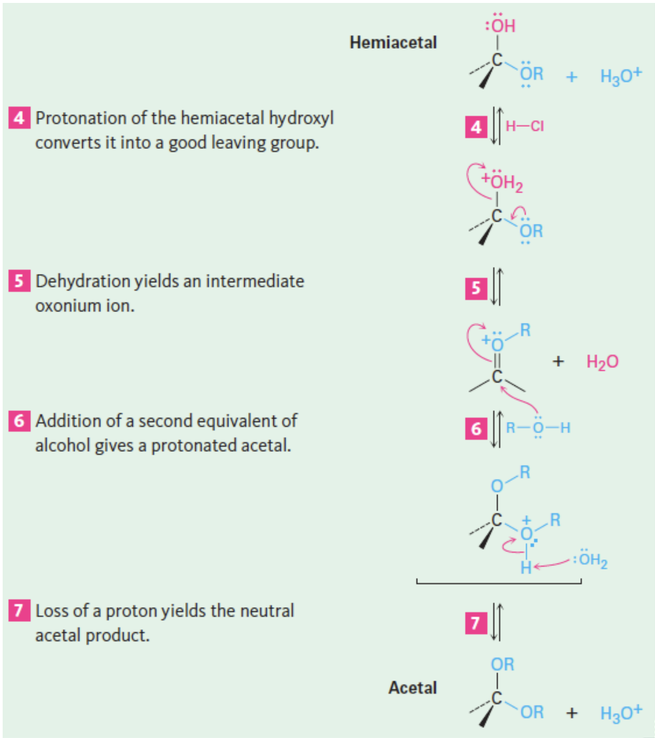
A hemiacetal

2° STADIO:

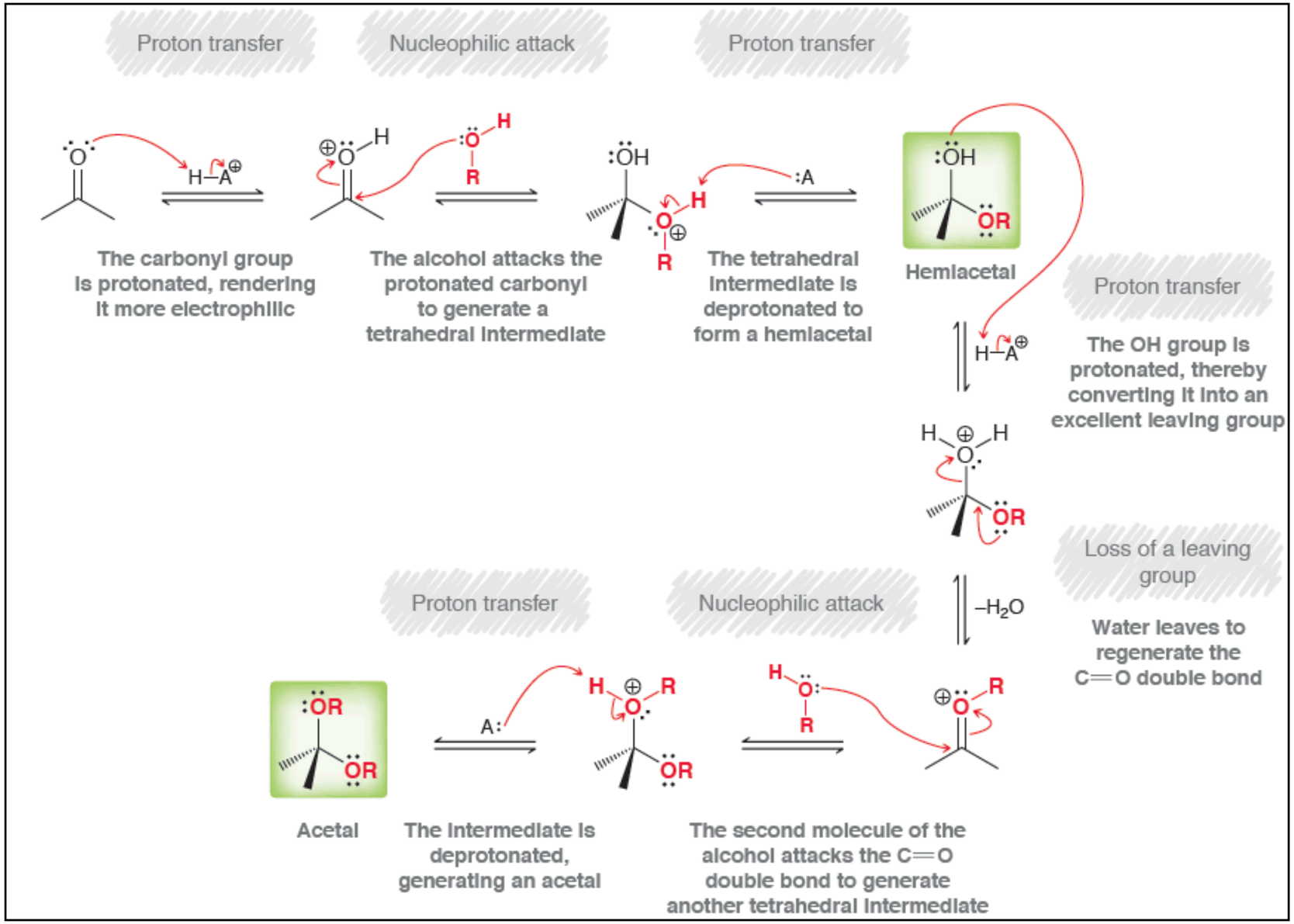


A hemiacetal A diethyl acetal

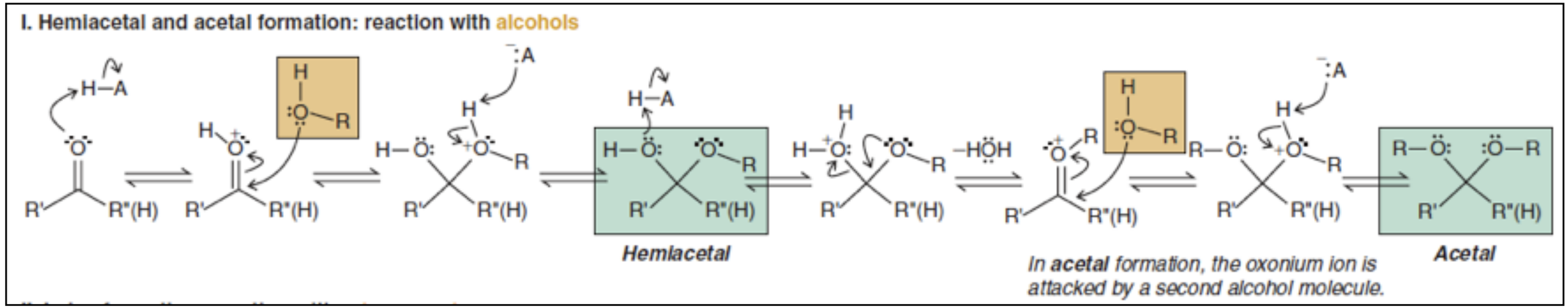


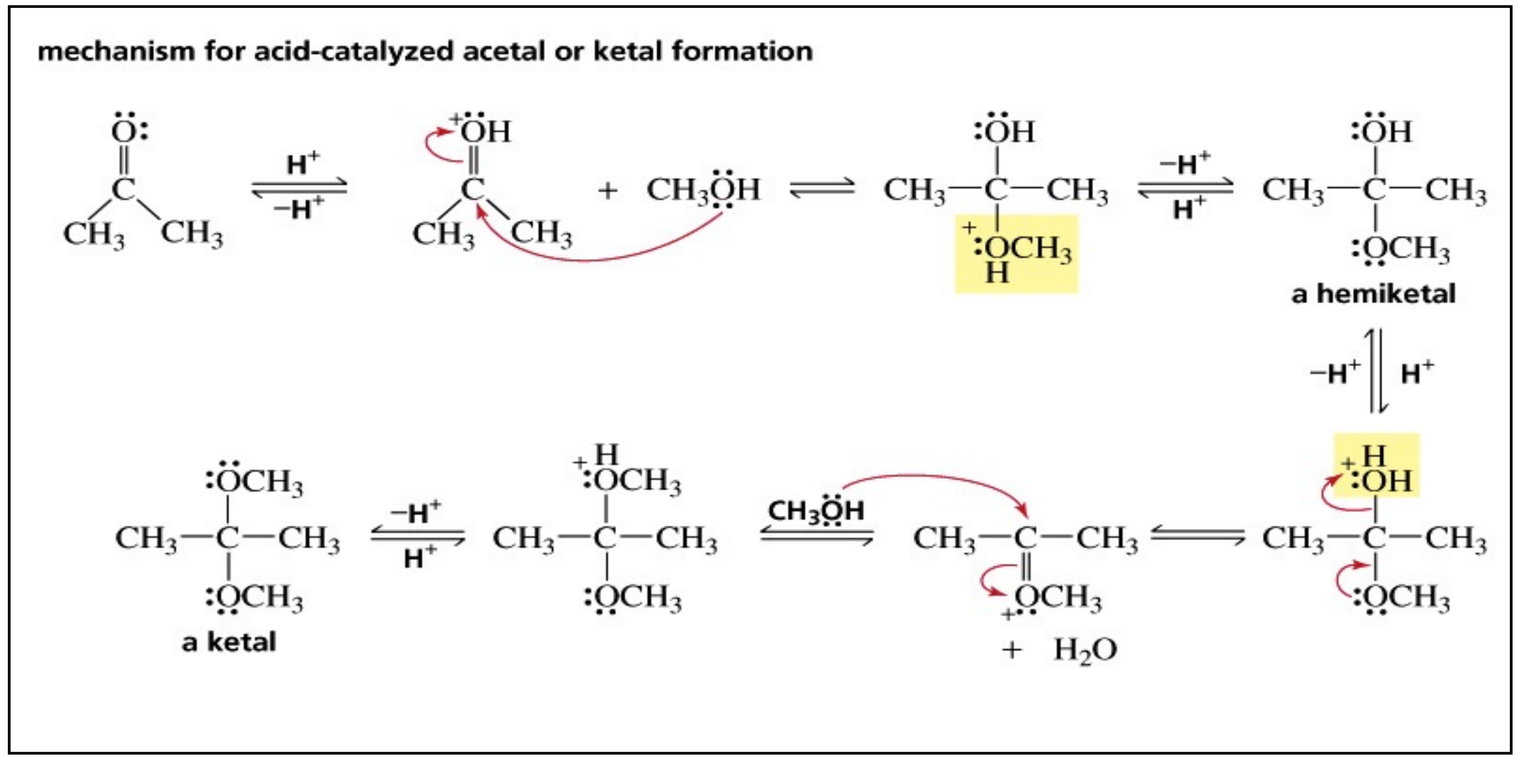


(2) Meccanismo per Formazione di acetali in ambiente acido

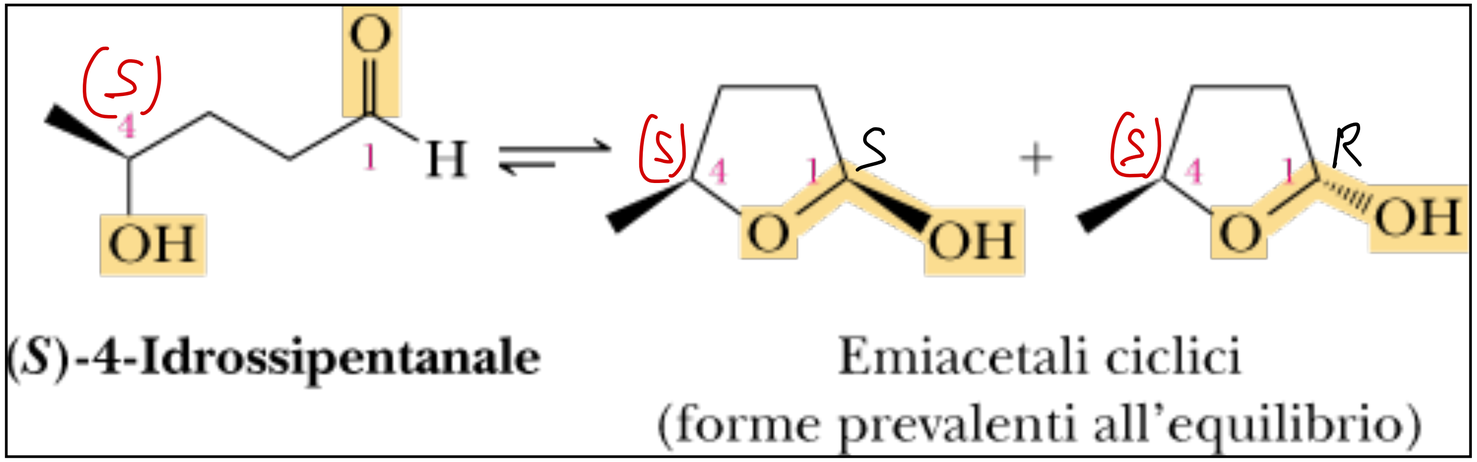


(2) Meccanismo per Formazione di acetali in ambiente acido

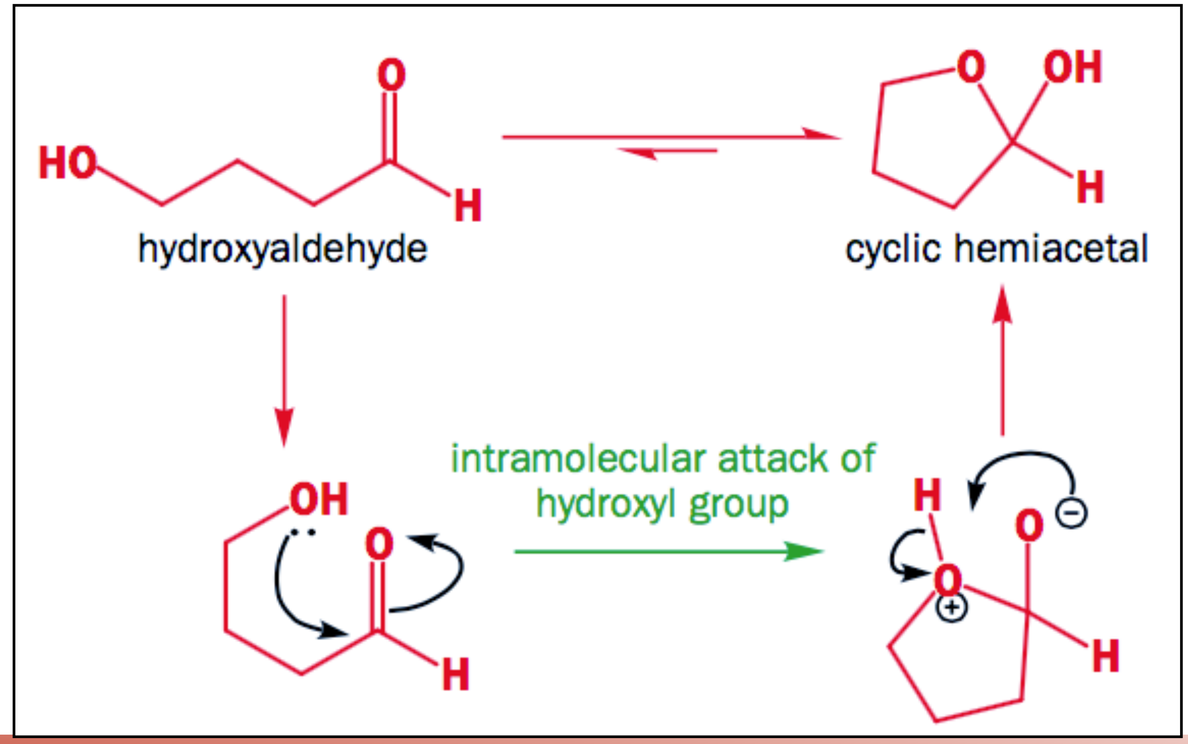




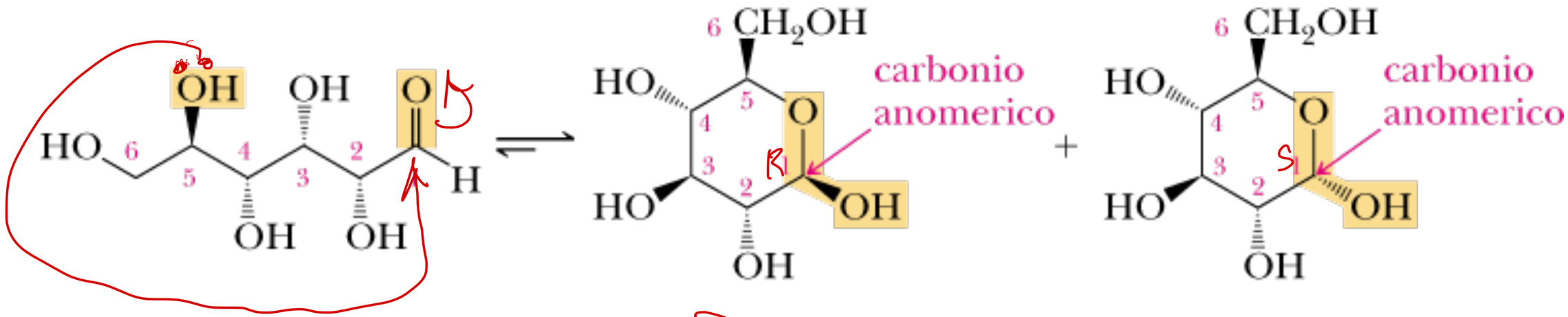
(2) Meccanismo per Formazione di emiacetali ciclici a 5 atomi



(*S*)-4-Idrossipentanale Emiacetali ciclici (forme prevalenti all'equilibrio)



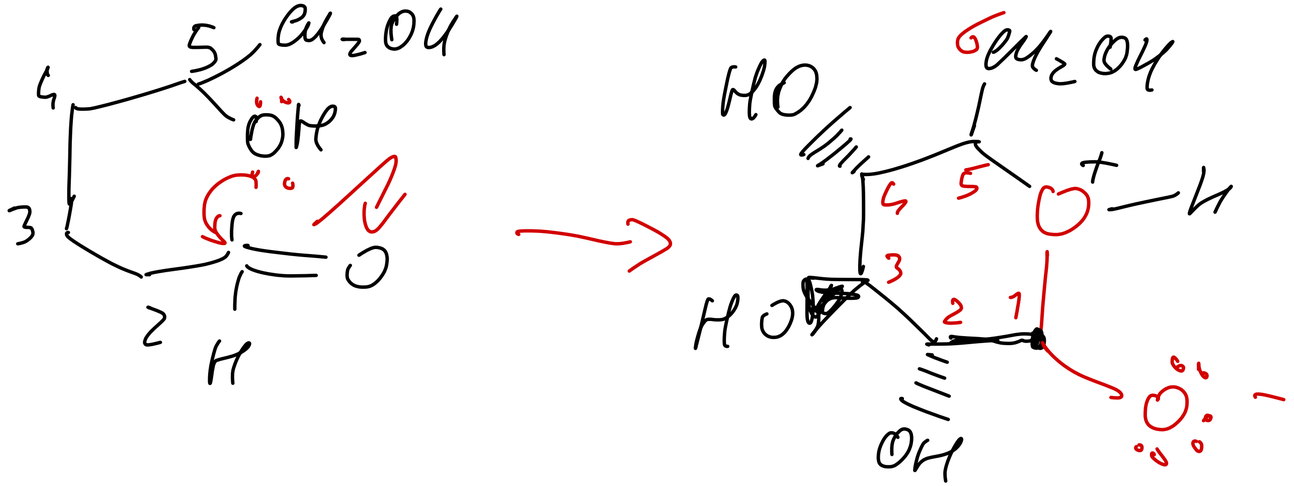
(2) Meccanismo per Formazione di emiacetali ciclici a 6 atomi



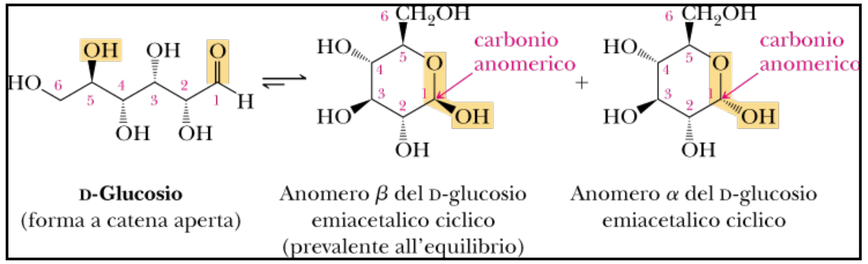
D-Glucosio
(forma a catena aperta)

Anomero β del D-glucosio
emiacetalico ciclico
(prevalente all'equilibrio)

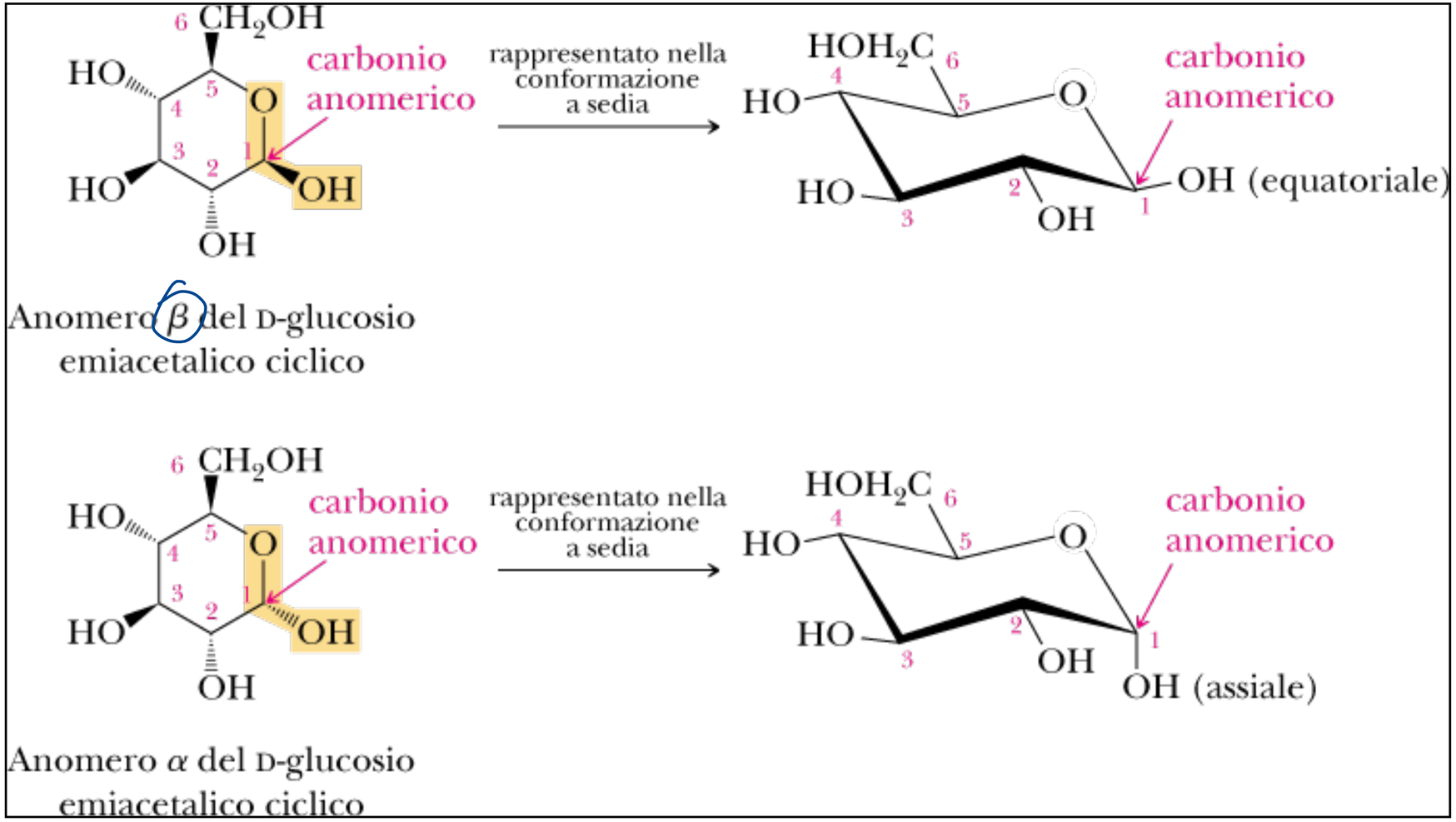
Anomero α del D-glucosio
emiacetalico ciclico

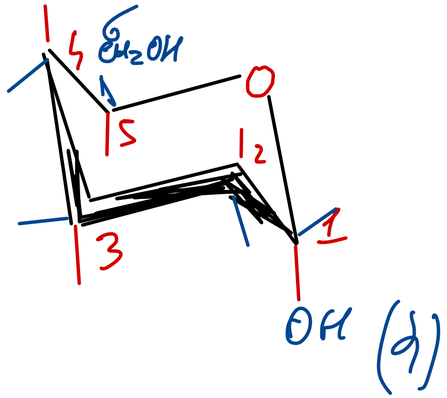


(2) Meccanismo per Formazione di emiacetali ciclici a 6 atomi

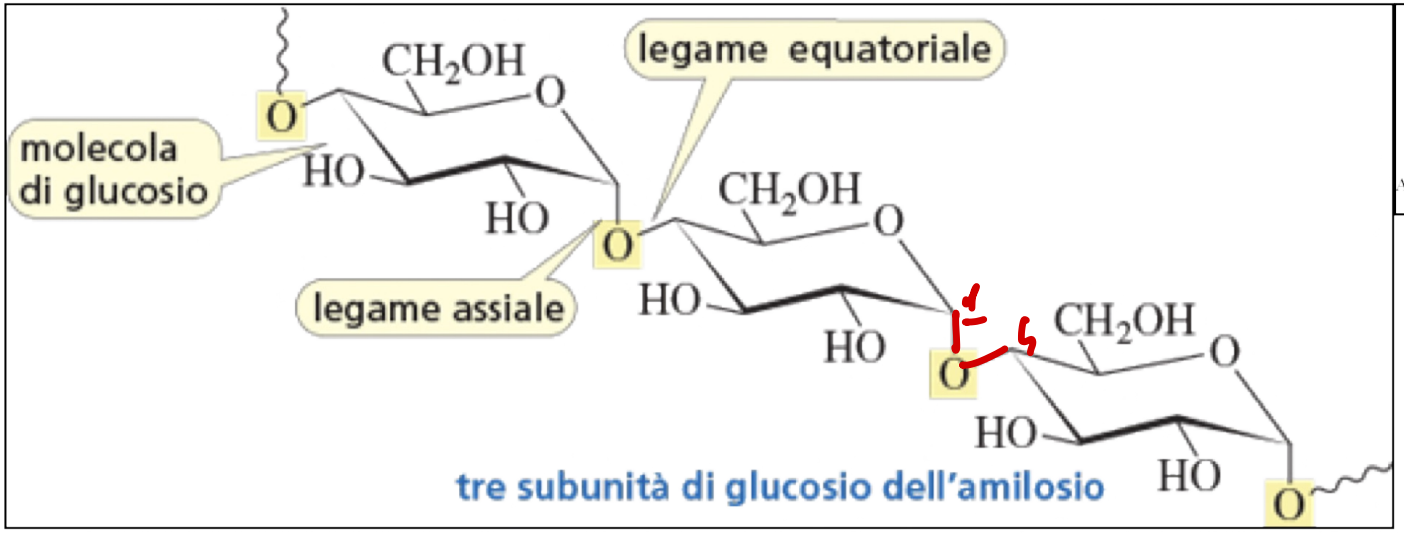


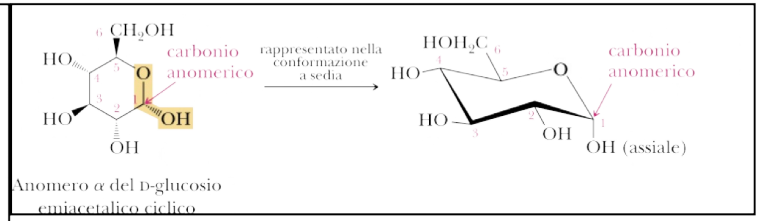
D-Glucosio (forma a catena aperta) ⇌ Anomero β del D-glucosio emiacetalico ciclico (prevalente all'equilibrio) + Anomero α del D-glucosio emiacetalico ciclico





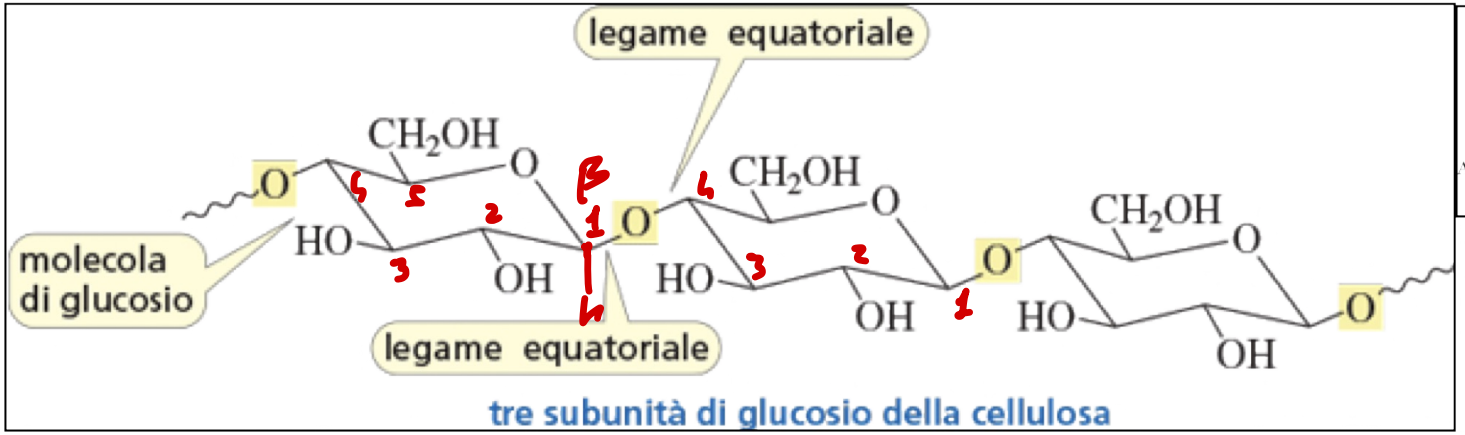
(2) alfa-glucosio nell'amilosio e beta-glucosio nella cellulosa

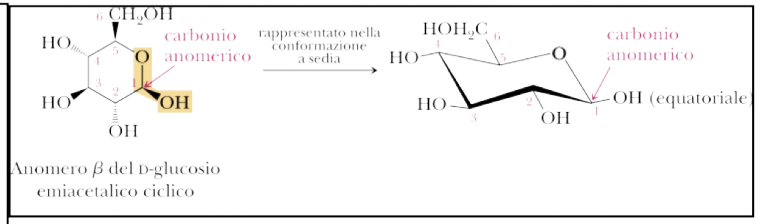




Anomero α del D-glucosio emiacetalico ciclico

α (1→4)





Anomero β del D-glucosio emiacetalico ciclico

β 1→4

I polisaccaridi di interesse biologico

L'**amido** e il **glicogeno** immagazzinano zuccheri di riserva
La **cellulosa** si trova nelle pareti delle cellule vegetali

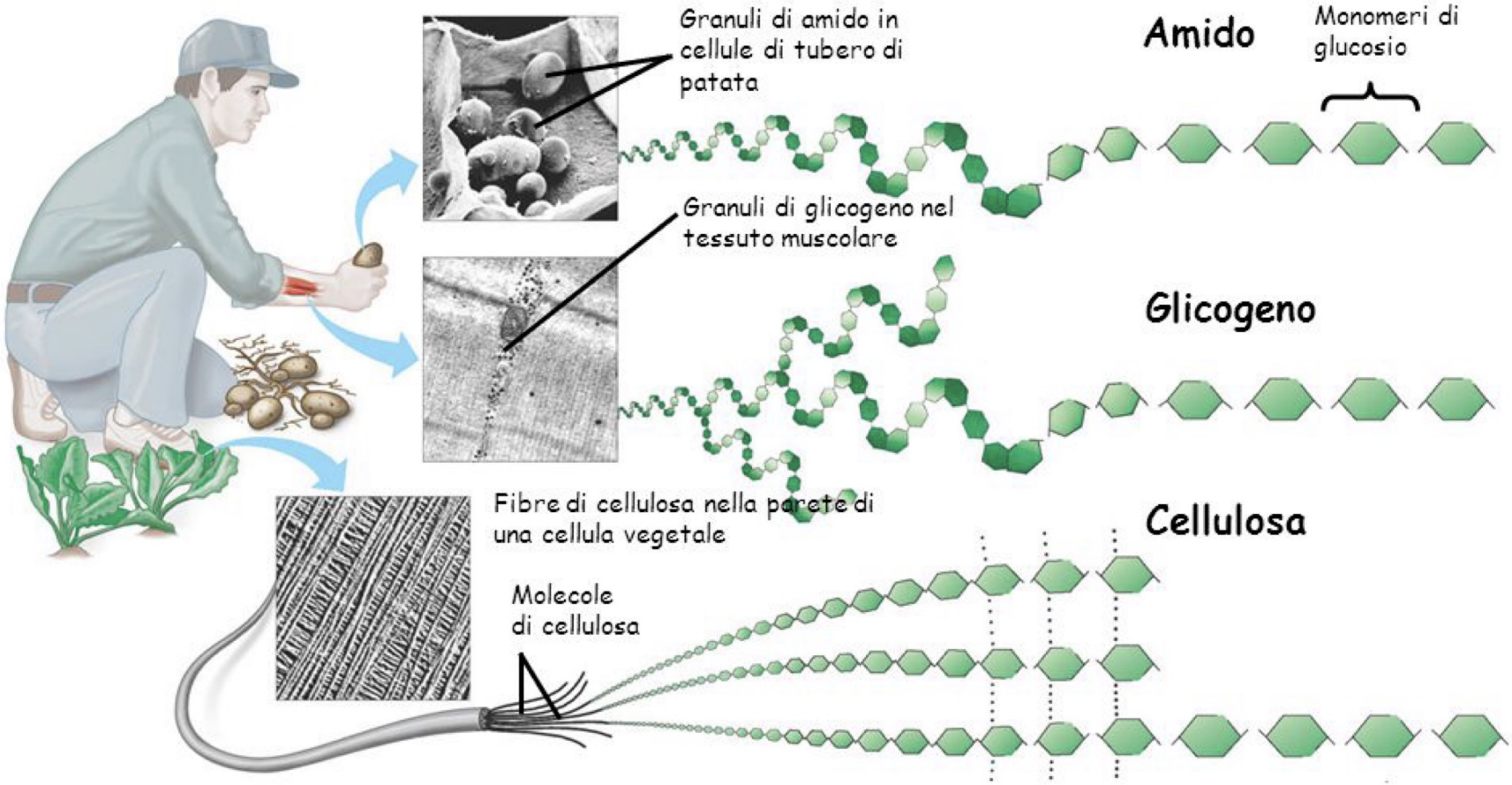
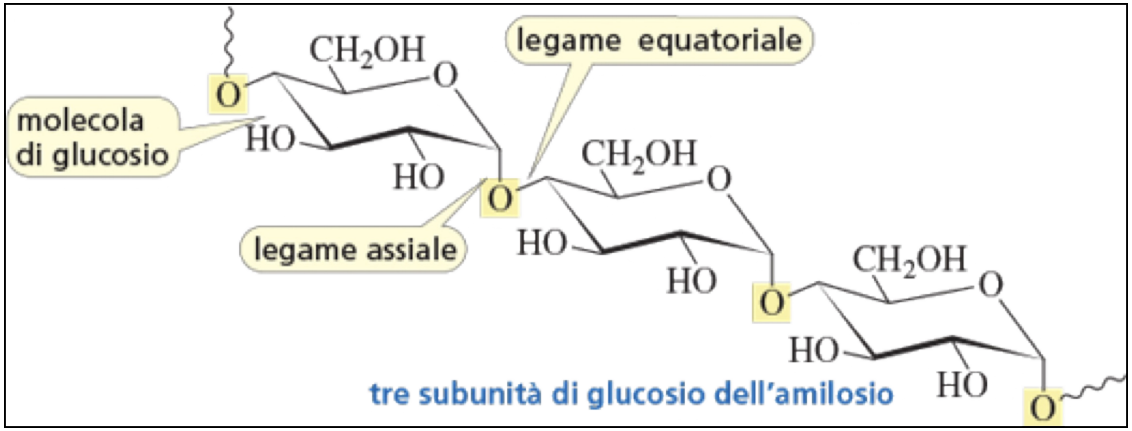
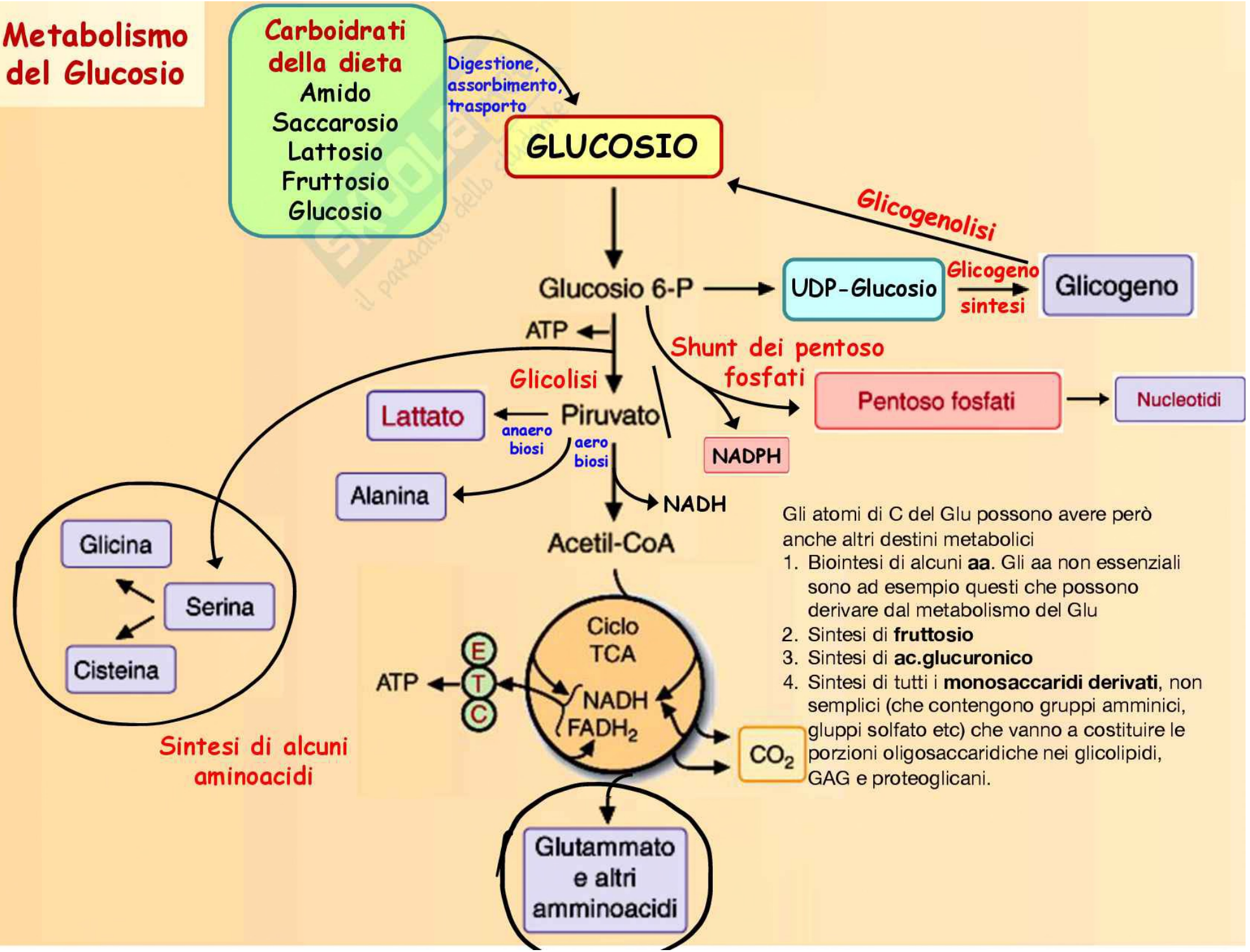


Illustrazione 3D dell amido, biomolecola elicoidale dell'amilosio,



Metabolismo del Glucosio



Gli atomi di C del Glu possono avere però anche altri destini metabolici

1. Biointesi di alcuni **aa**. Gli aa non essenziali sono ad esempio questi che possono derivare dal metabolismo del Glu
2. Sintesi di **fruttosio**
3. Sintesi di **ac.glucuronico**
4. Sintesi di tutti i **monosaccaridi derivati**, non semplici (che contengono gruppi amminici, gluppi solfato etc) che vanno a costituire le porzioni oligosaccaridiche nei glicolipidi, GAG e proteoglicani.

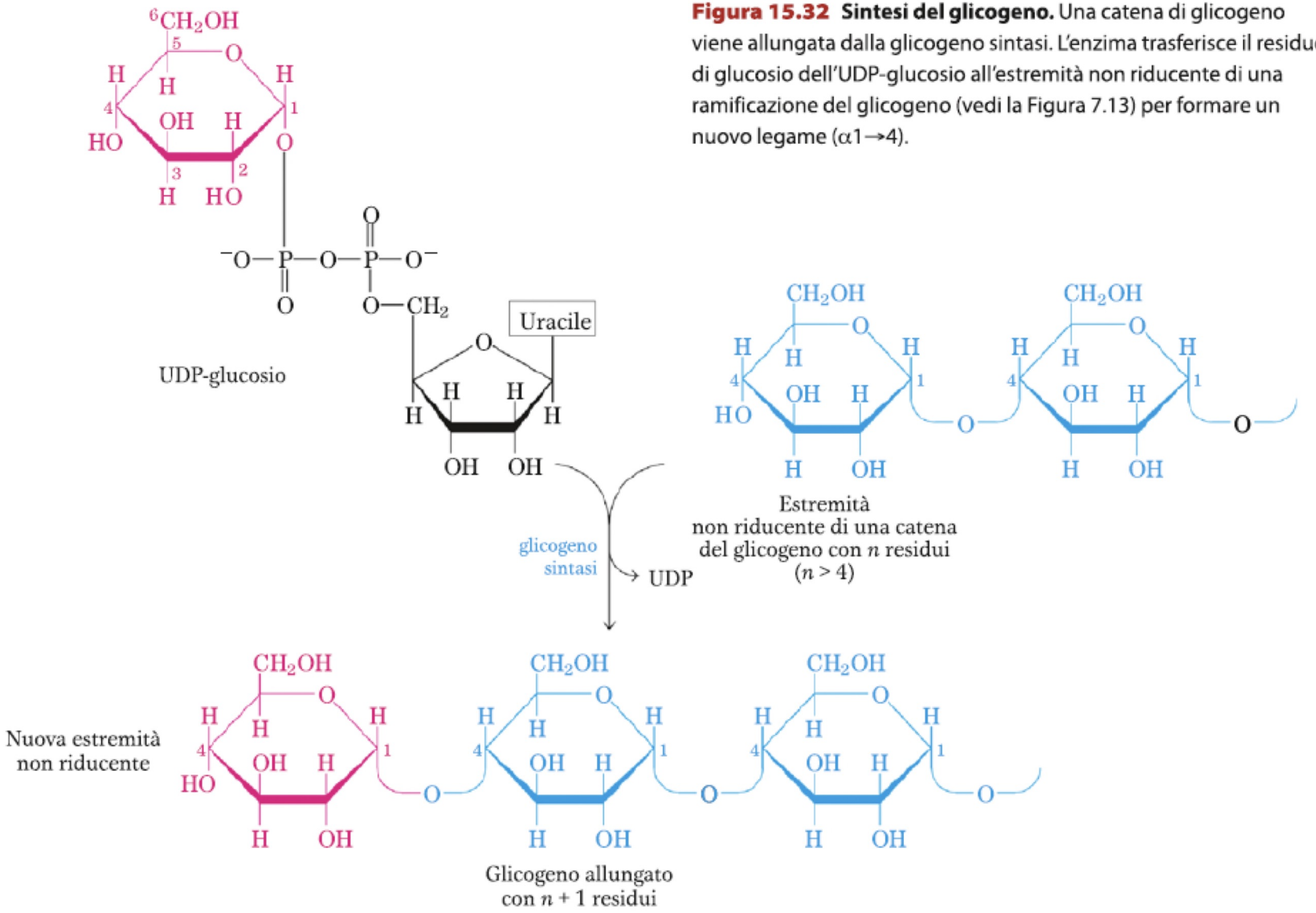
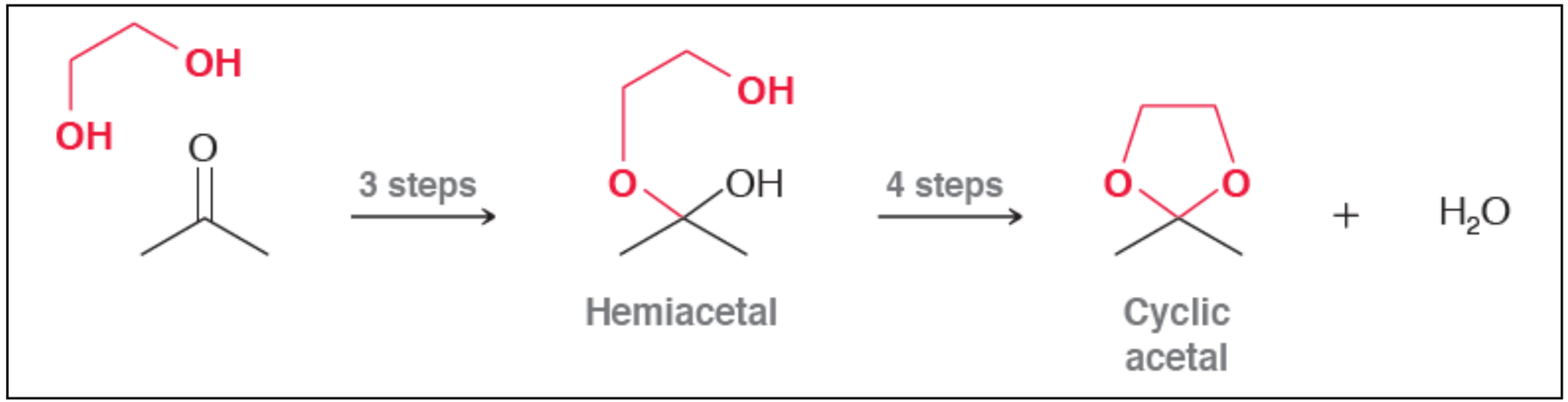
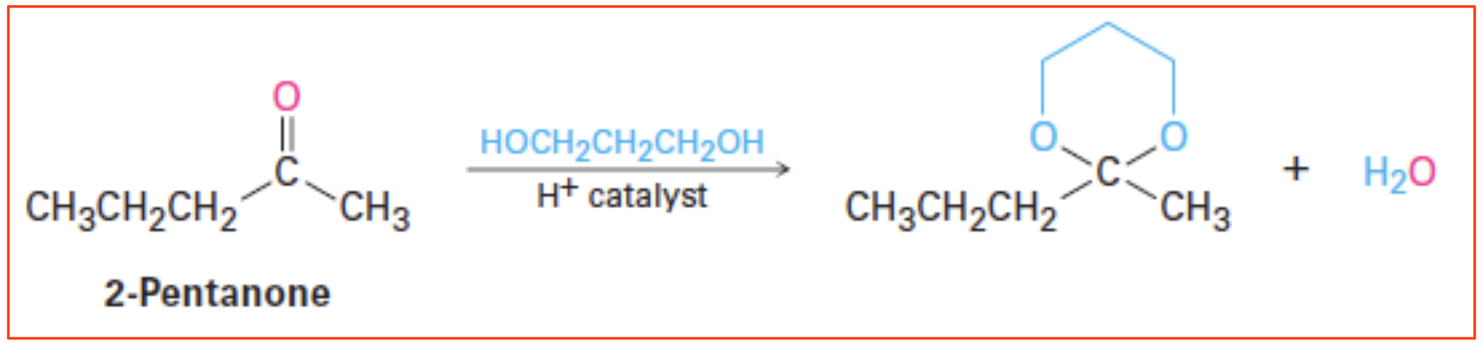
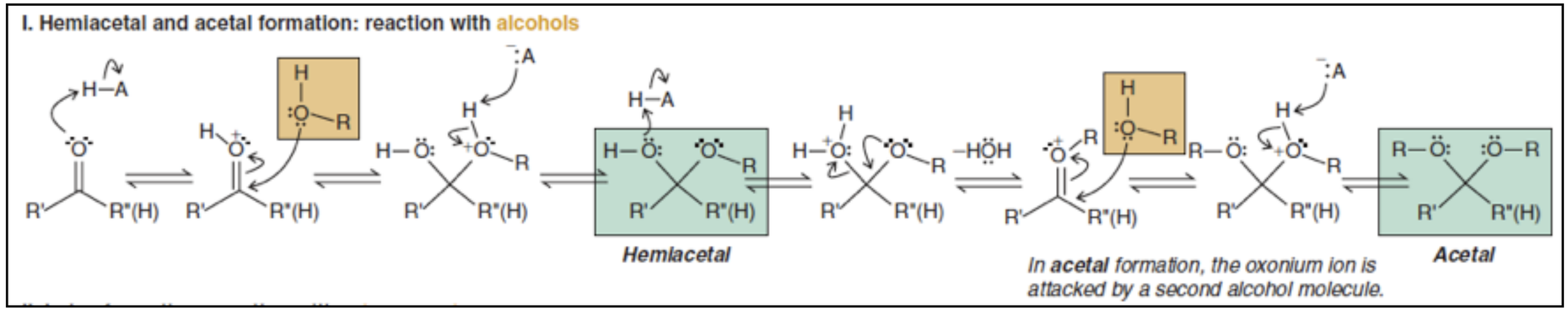


Figura 15.32 Sintesi del glicogeno. Una catena di glicogeno viene allungata dalla glicogeno sintasi. L'enzima trasferisce il residuo di glucosio dell'UDP-glucosio all'estremità non riducente di una ramificazione del glicogeno (vedi la Figura 7.13) per formare un nuovo legame (α1→4).

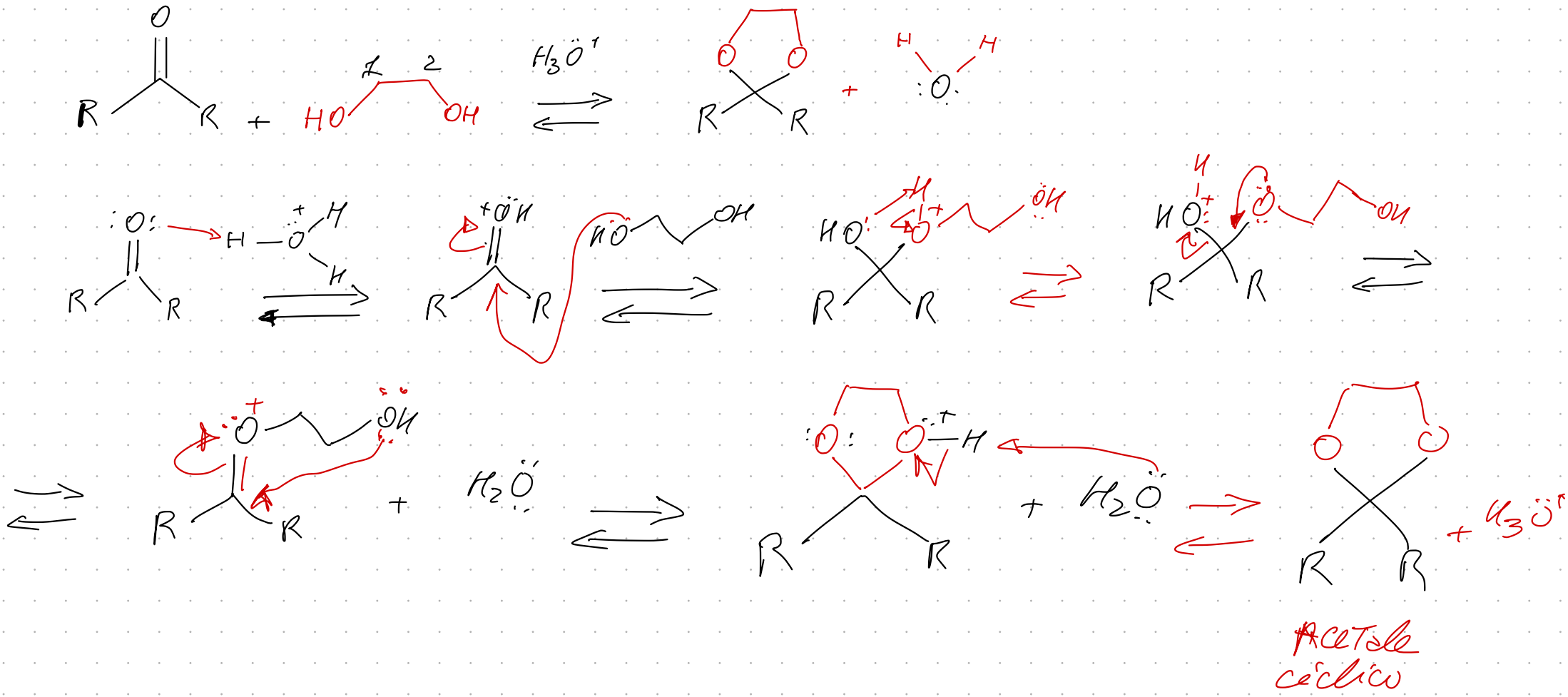
(2) Addizione nucleofila degli alcoli al gruppo carbonile: Formazione di acetali ciclico







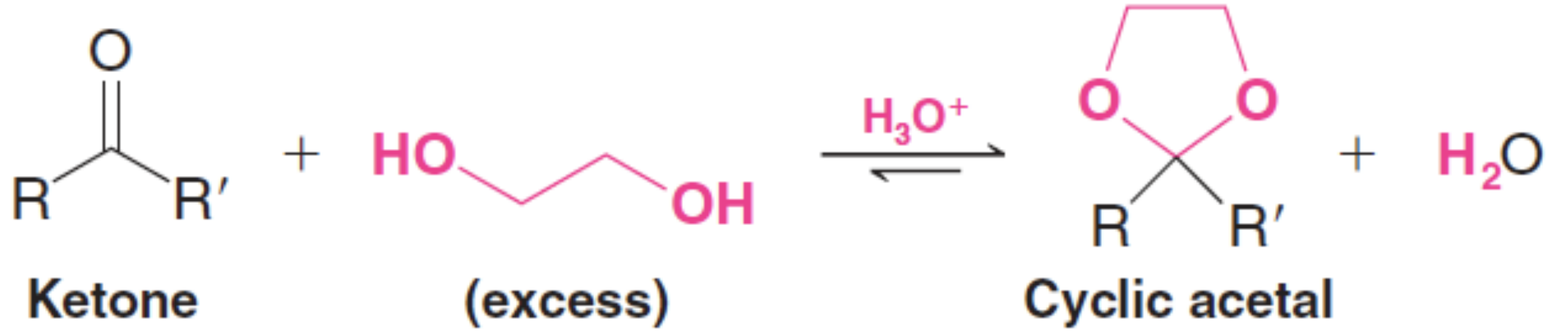
FORMAZIONE DI UN ACETALE CICLICO



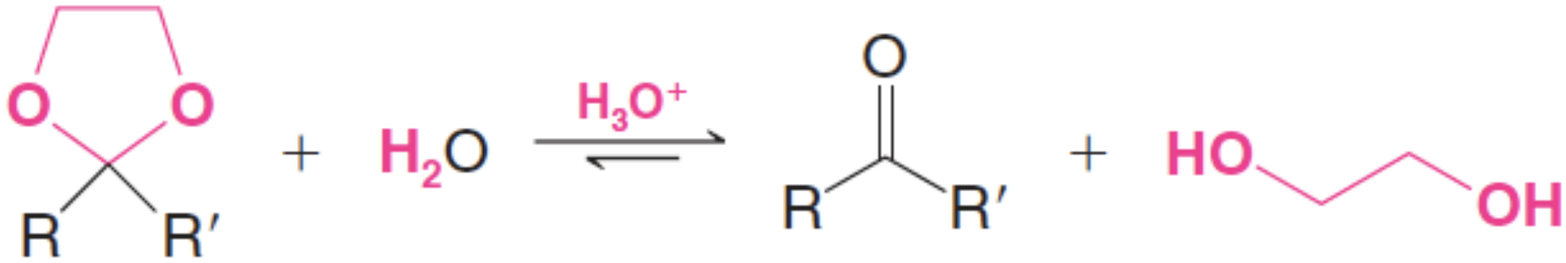
Acetali come gruppi di protezione del gruppo carbonile

Sebbene gli acetali siano idrolizzabili in aldeidi e chetoni in un ambiente acido acquoso, sono stabili nelle soluzioni di base.

PROTEZIONE

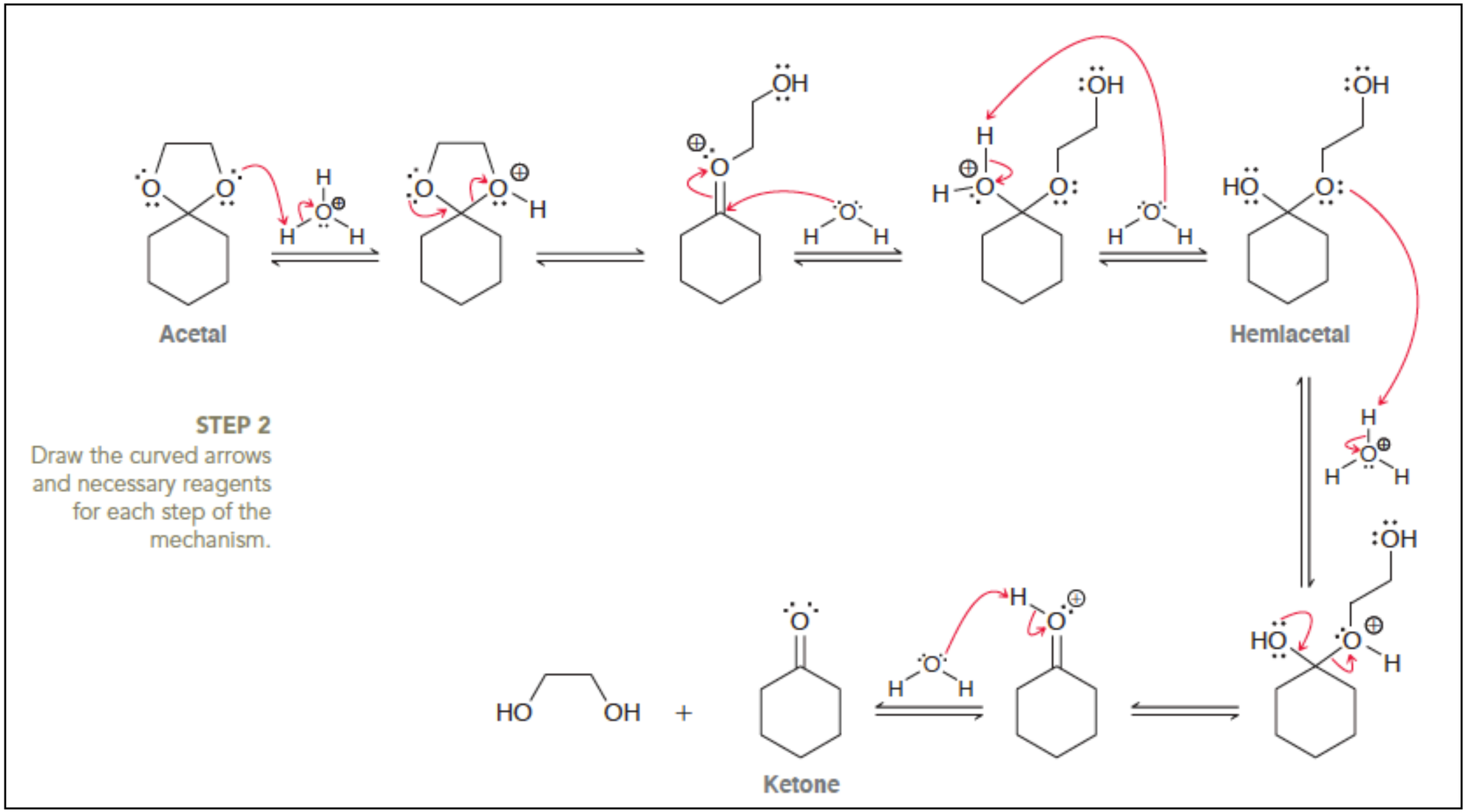


DEPROTEZIONE

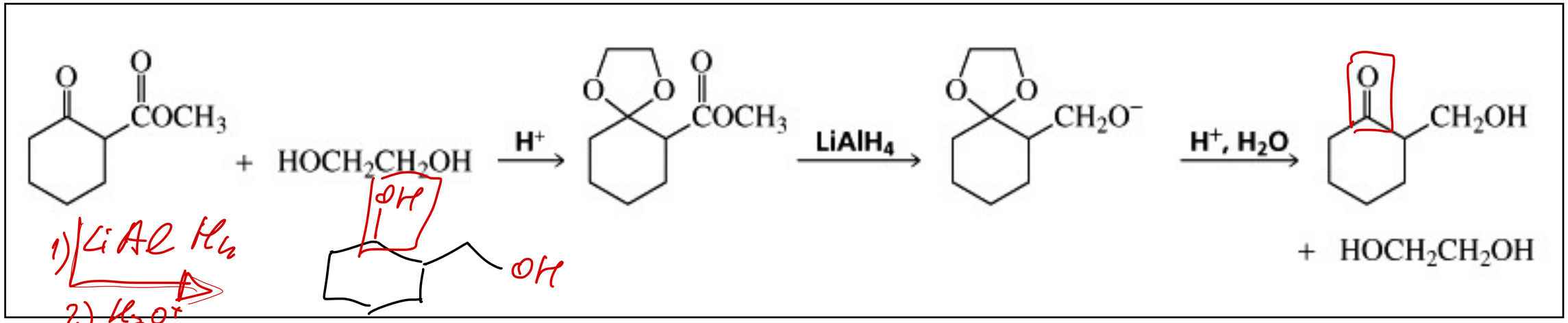


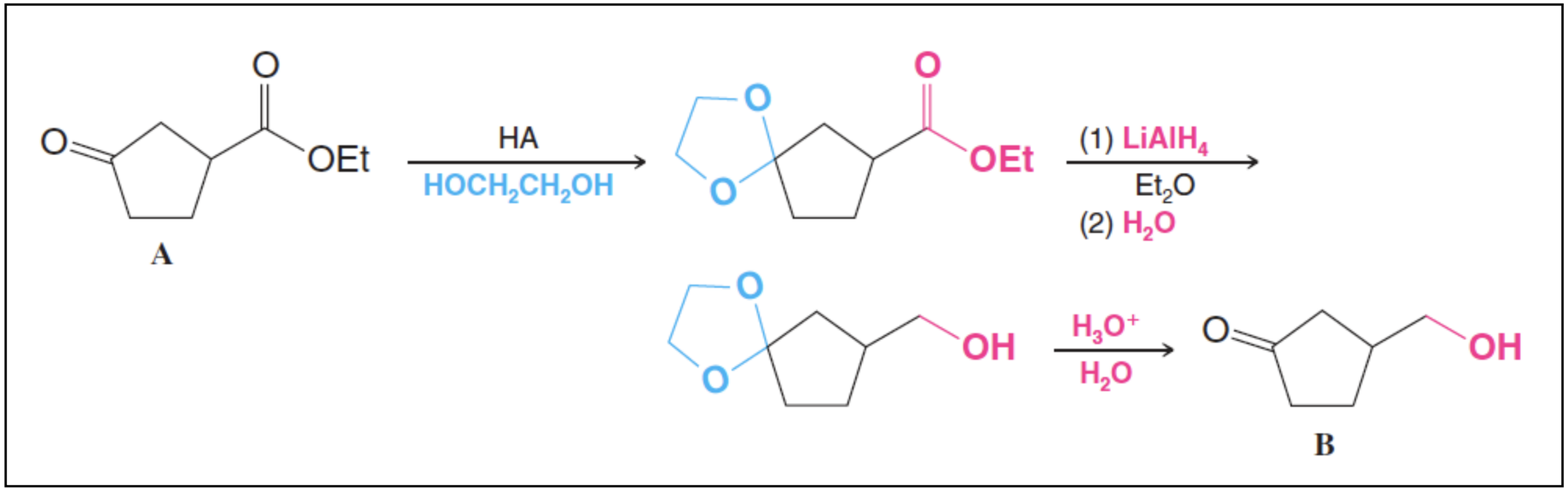
Gli acetali sono usati come gruppi protettori in un ambiente basico o nucleofilo

Idrolisi degli ACETALI in ambiente acido

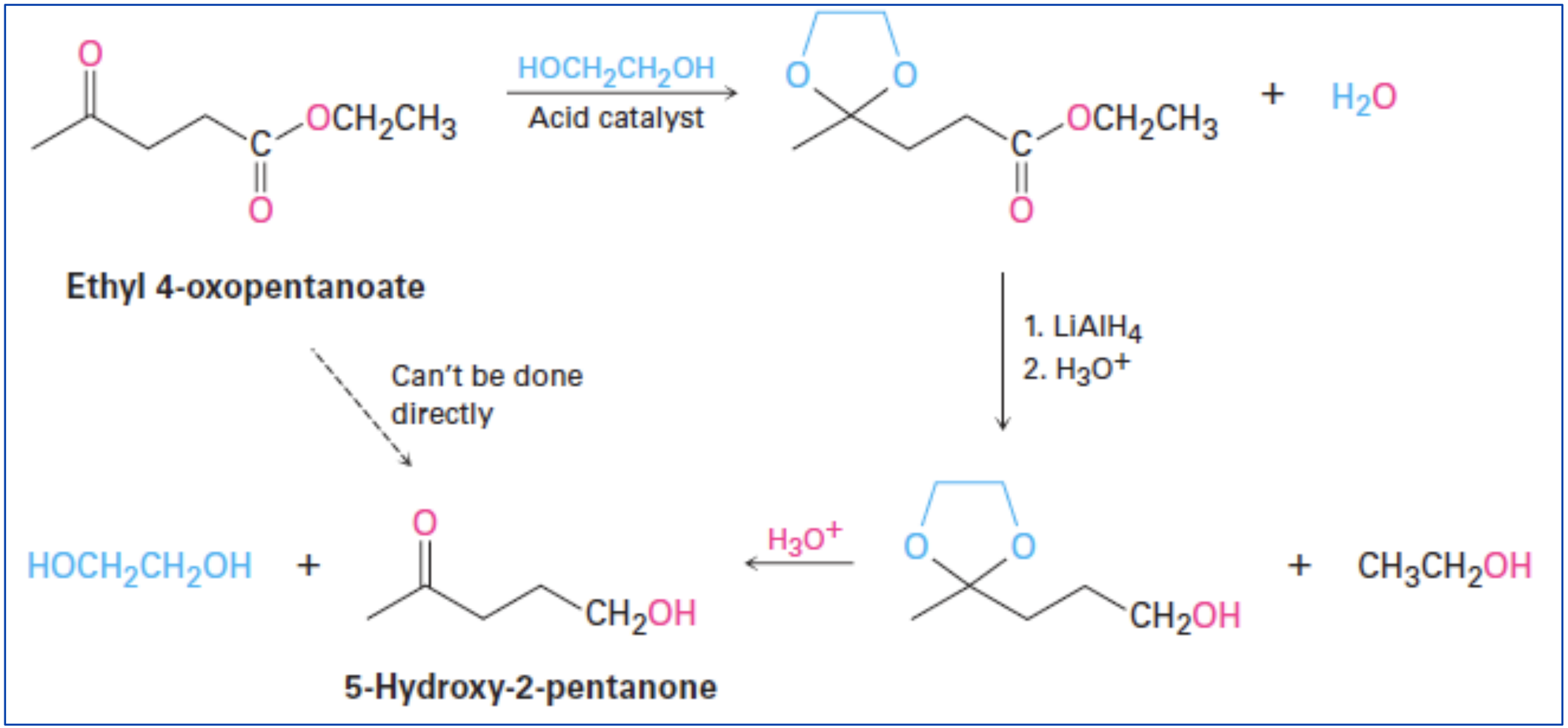


Acetali come gruppi protettori degli aldeidi e chetoni in soluzioni basiche

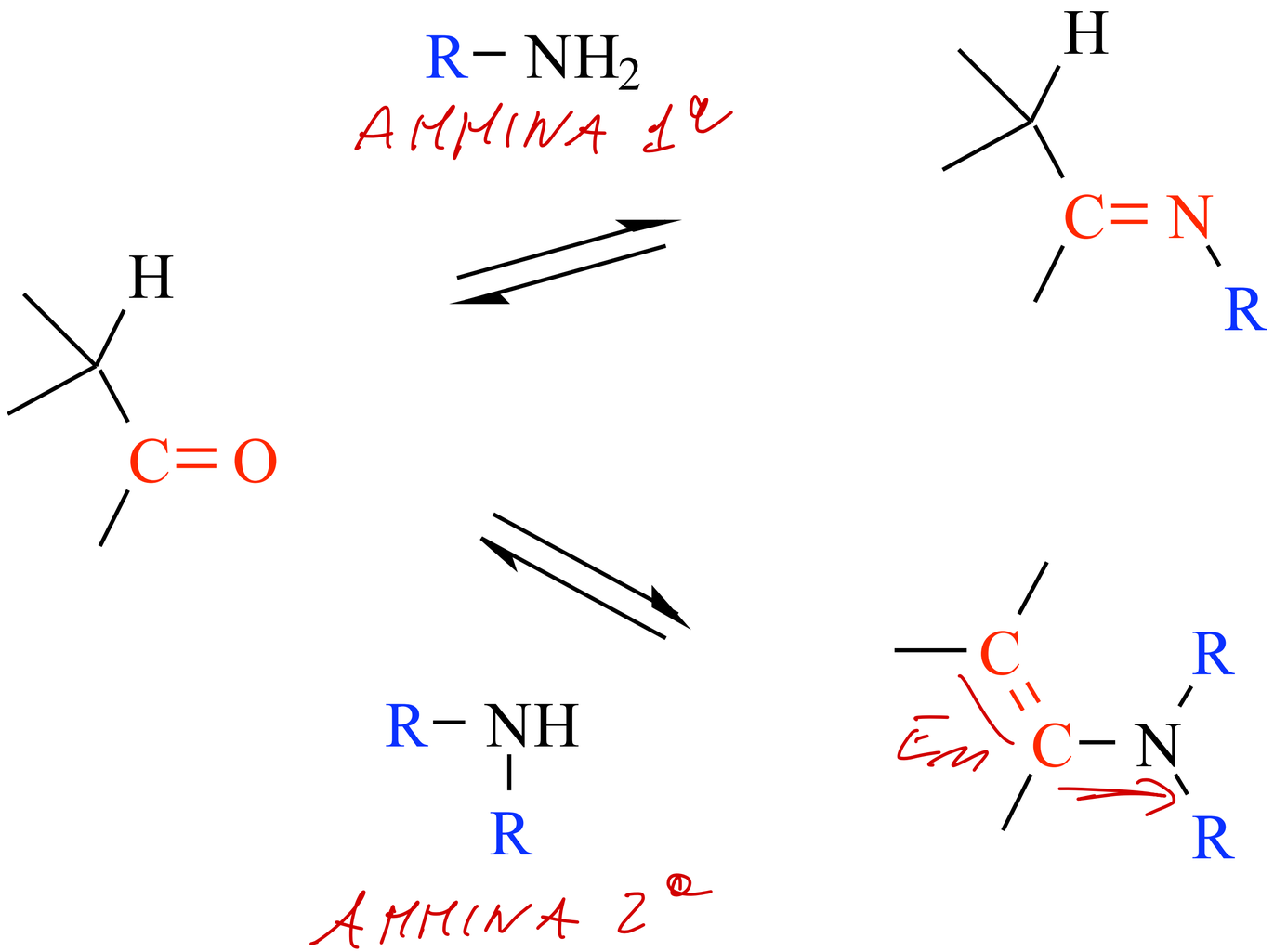




Acetali come gruppi protettori degli aldeidi e chetoni in soluzioni basiche



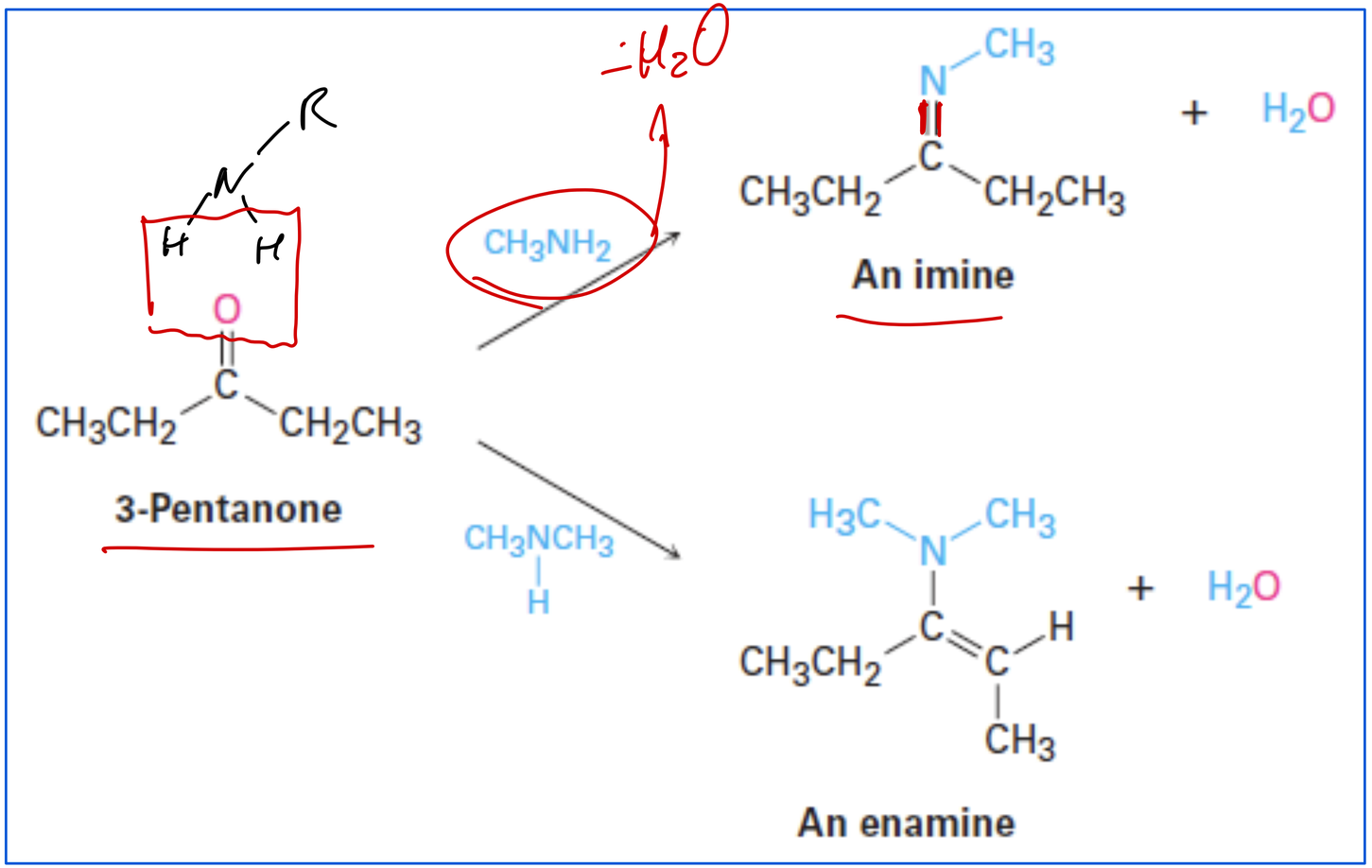
3) addizione Nucleofilica di ammine: Formazione di Immine e Enammine

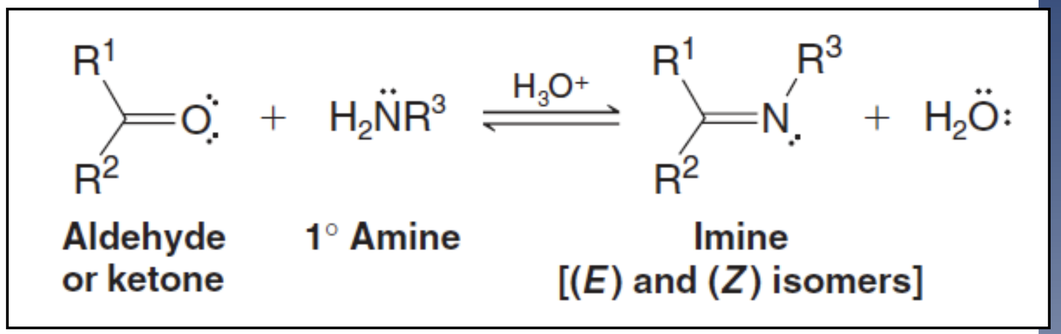


IMMINA
Doppio legame
C=N

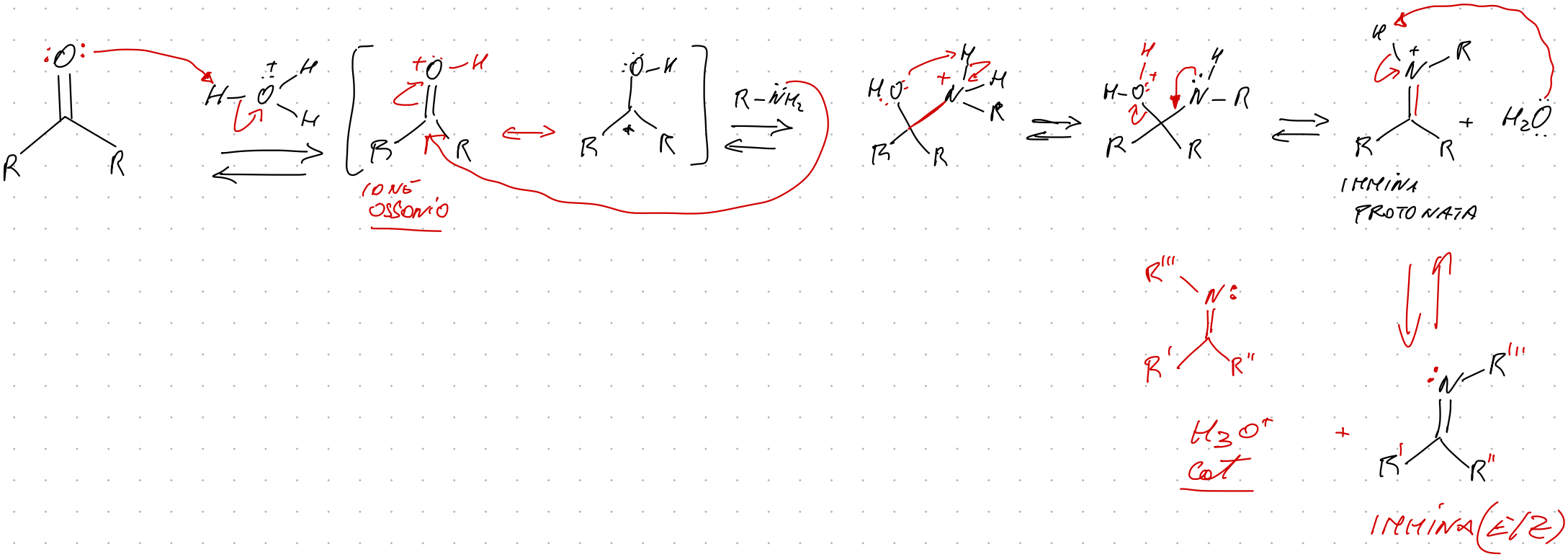
ENAMMINA
Doppio legame
C=C

3) addizione Nucleofilica di ammine: Formazione di Immine e Enammine



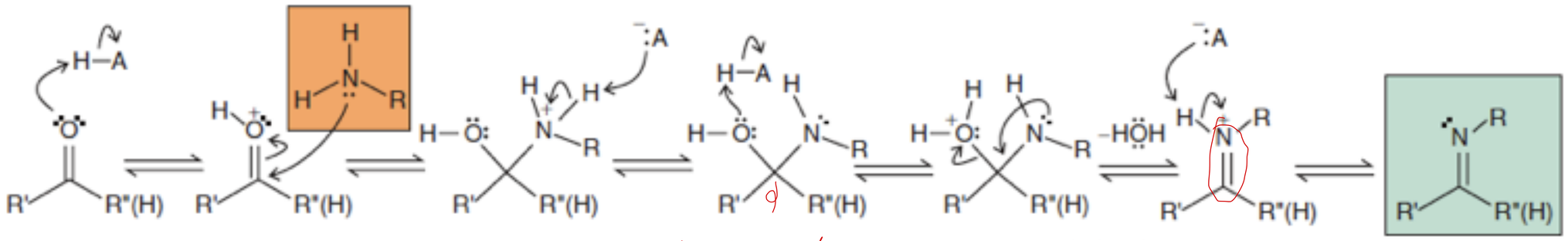


FORMAZIONE DI IMMINE:addizione di ammine primarie al gruppo carbonile



3) MECCANISMO addizione Nucleofilica di ammine: Formazione di Immine e Enammine

II. Imine formation: reaction with primary amines

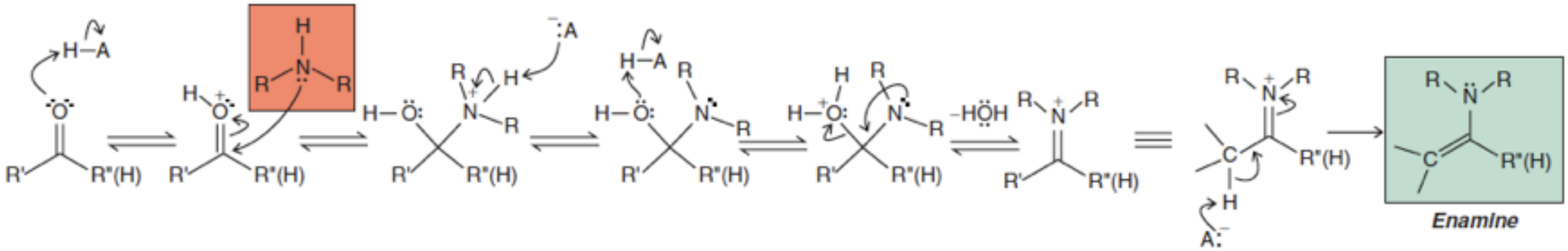


α-idrossi Ammina

*In **imine** formation, the proton on the initial iminium ion is removed, leading to the stable imine product.*

Imine

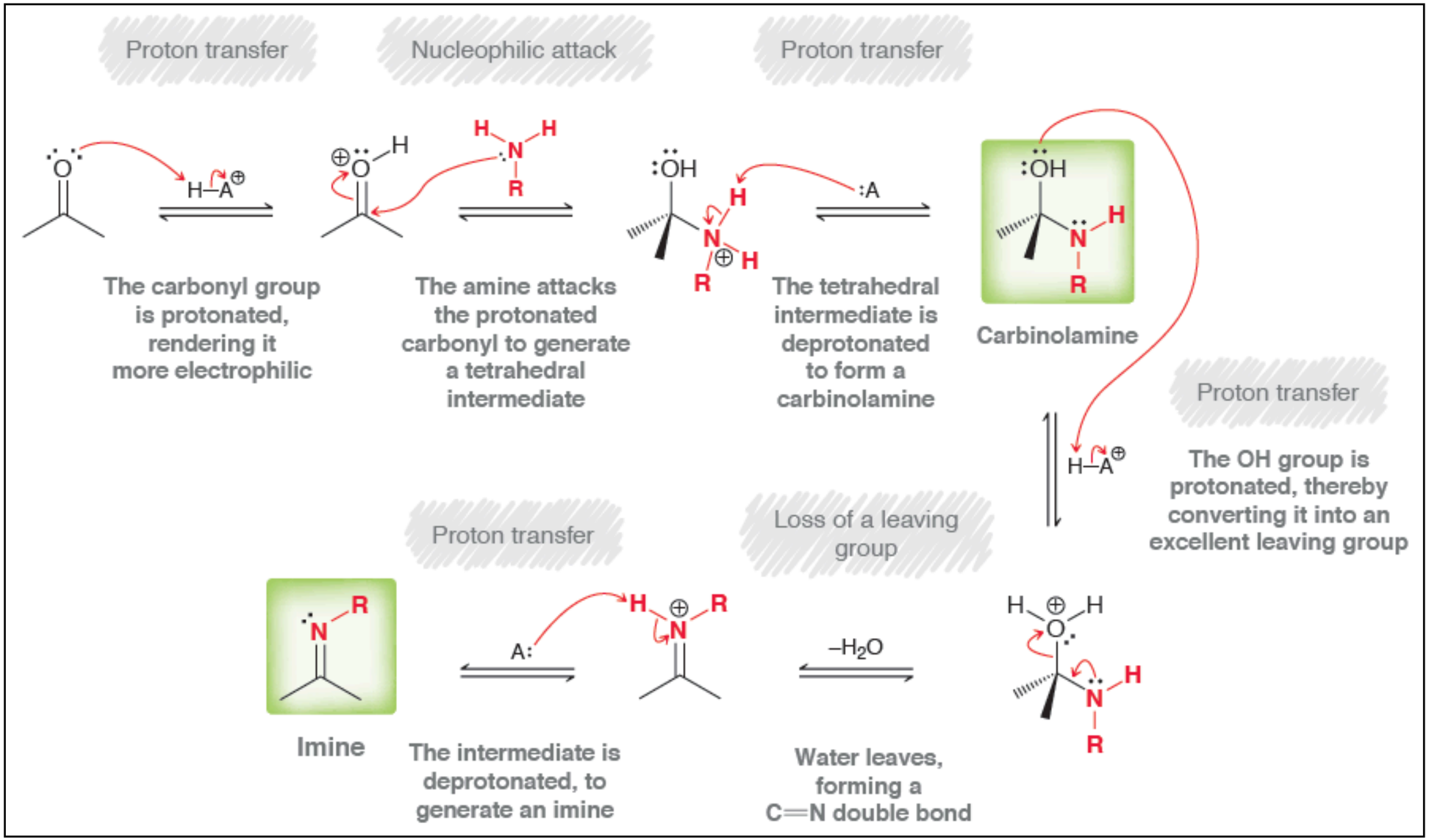
III. Enamine formation: reaction with secondary amines



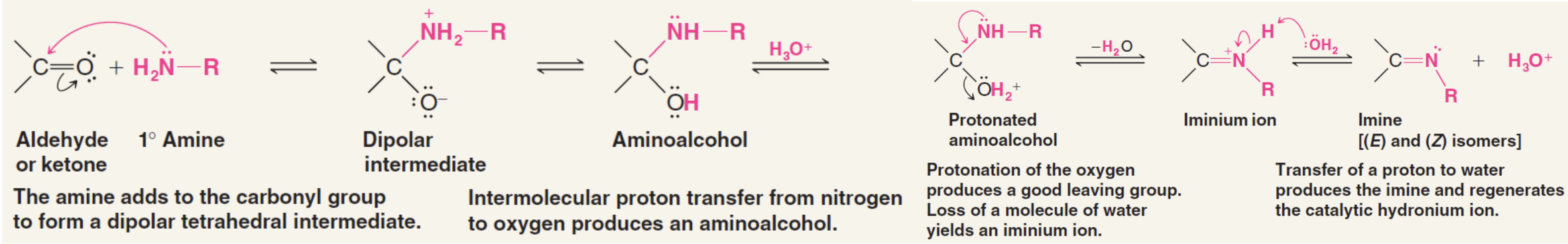
Enamine

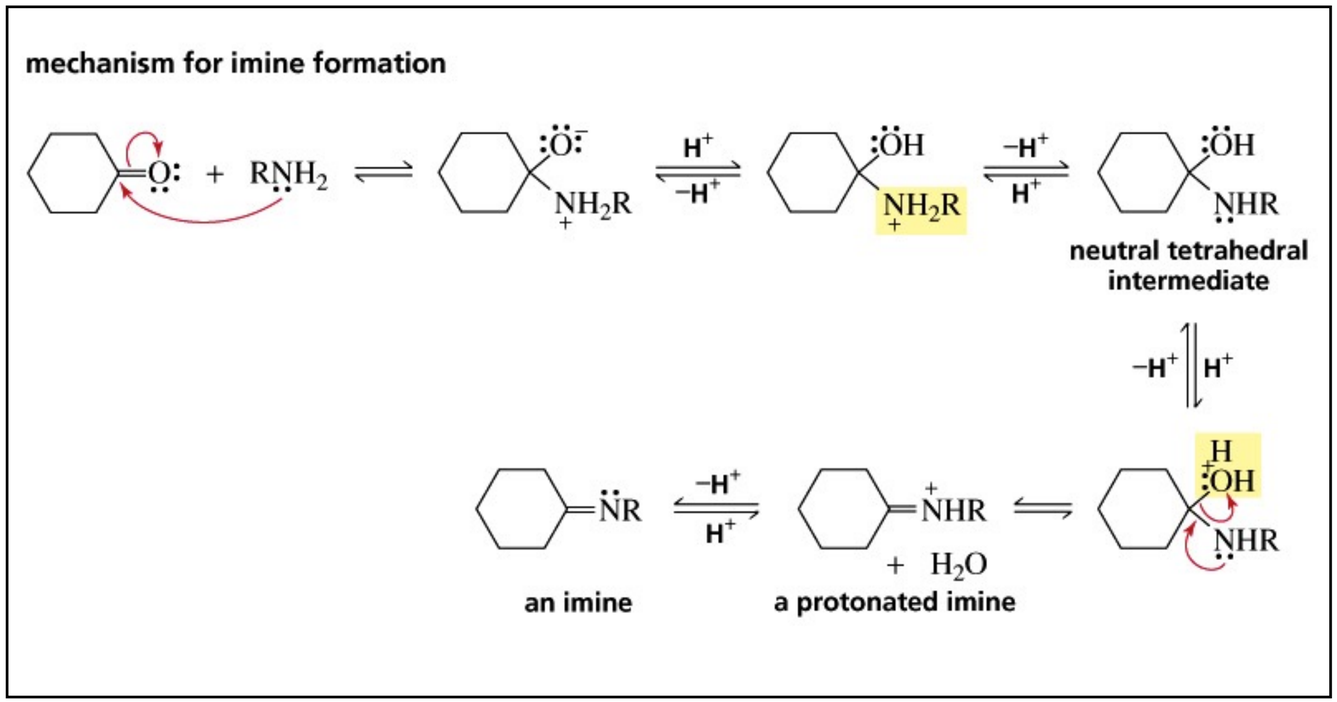
*In **enamine** formation, a proton is removed from a carbon adjacent to the iminium carbon (because no proton is available for removal from the nitrogen).*

3) MECCANISMO addizione Nucleofilica di ammine: Formazione di Immine

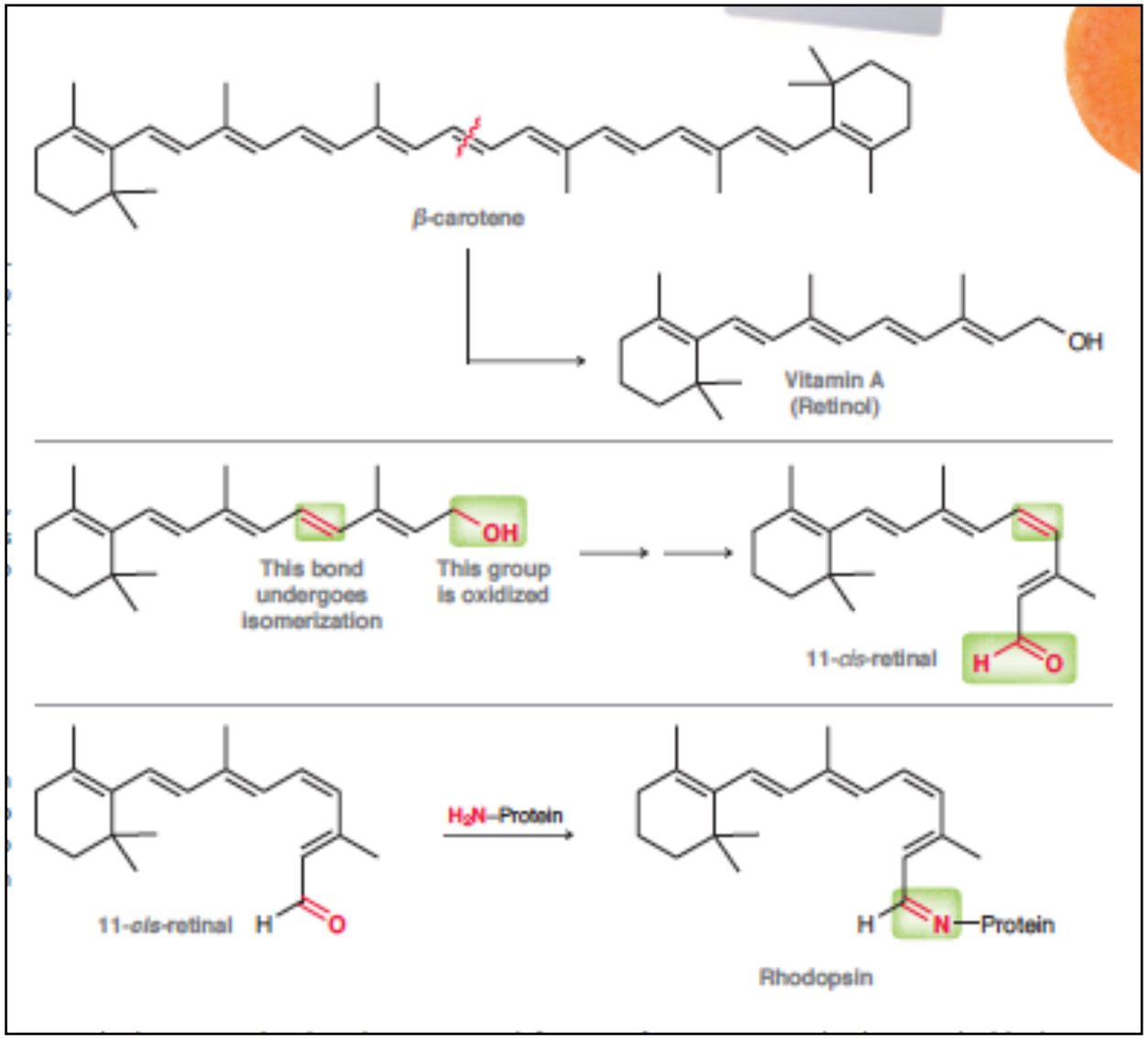


3) MECCANISMO addizione Nucleofilica di ammine: Formazione di Immine (miscela di isomeri E e Z)

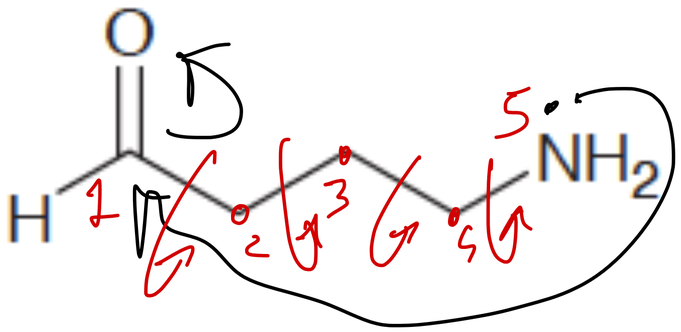


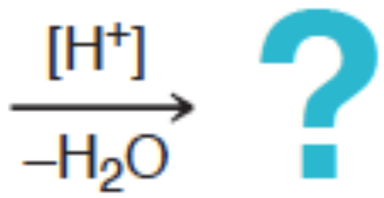


Beta-carotene e la vista



PROBLEMA: Prevedere il prodotto principale della seguente reazione intramolecolare





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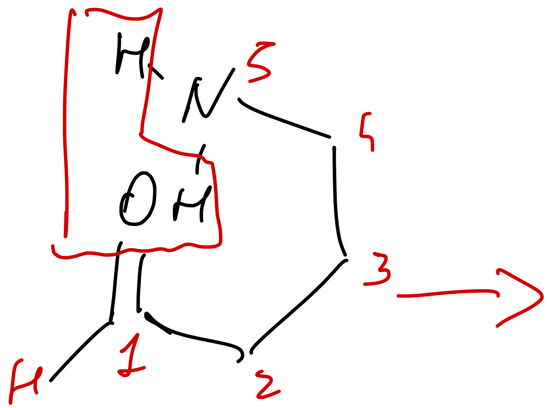
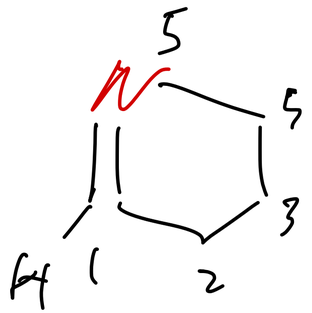
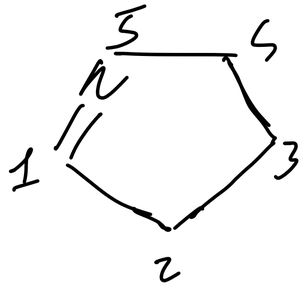
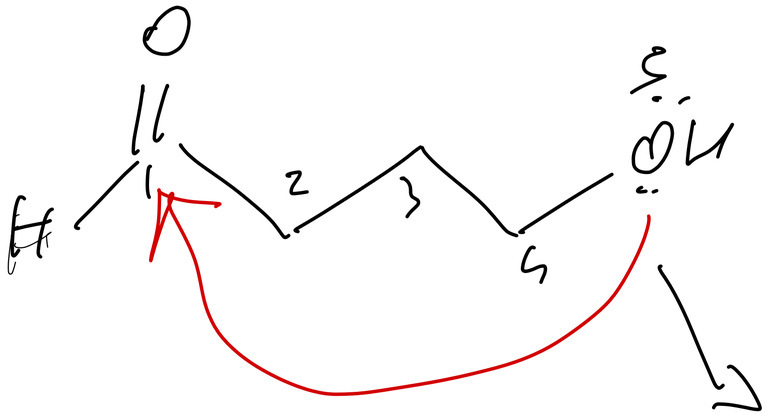
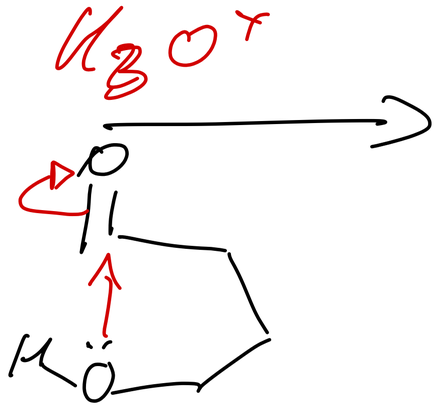
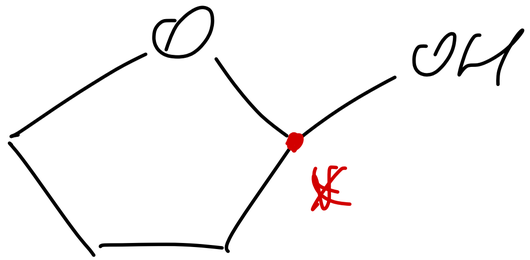






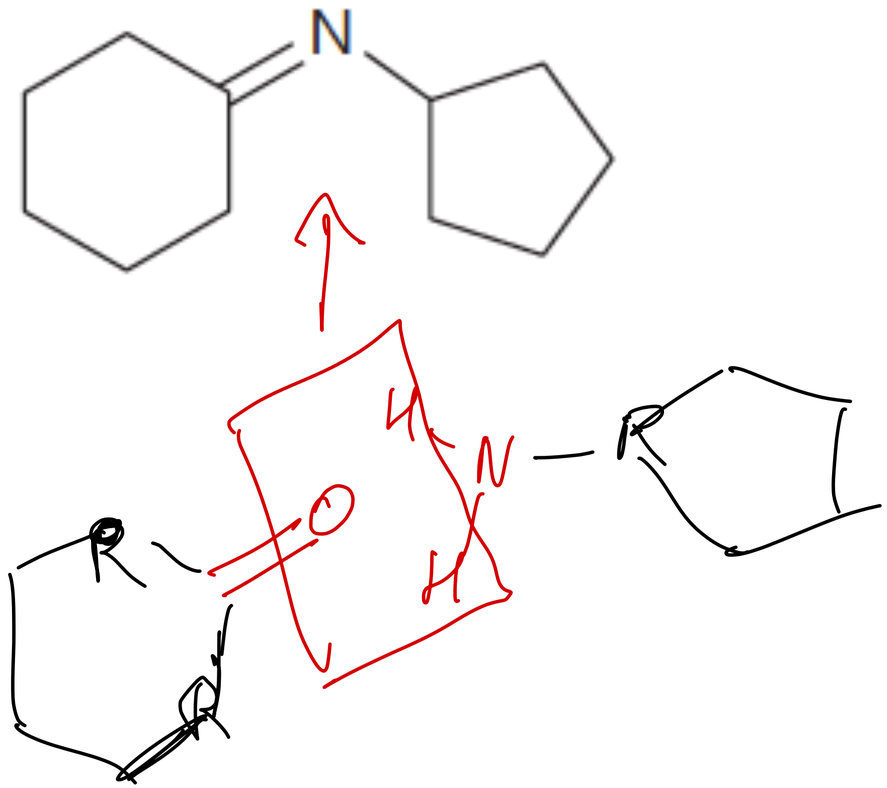


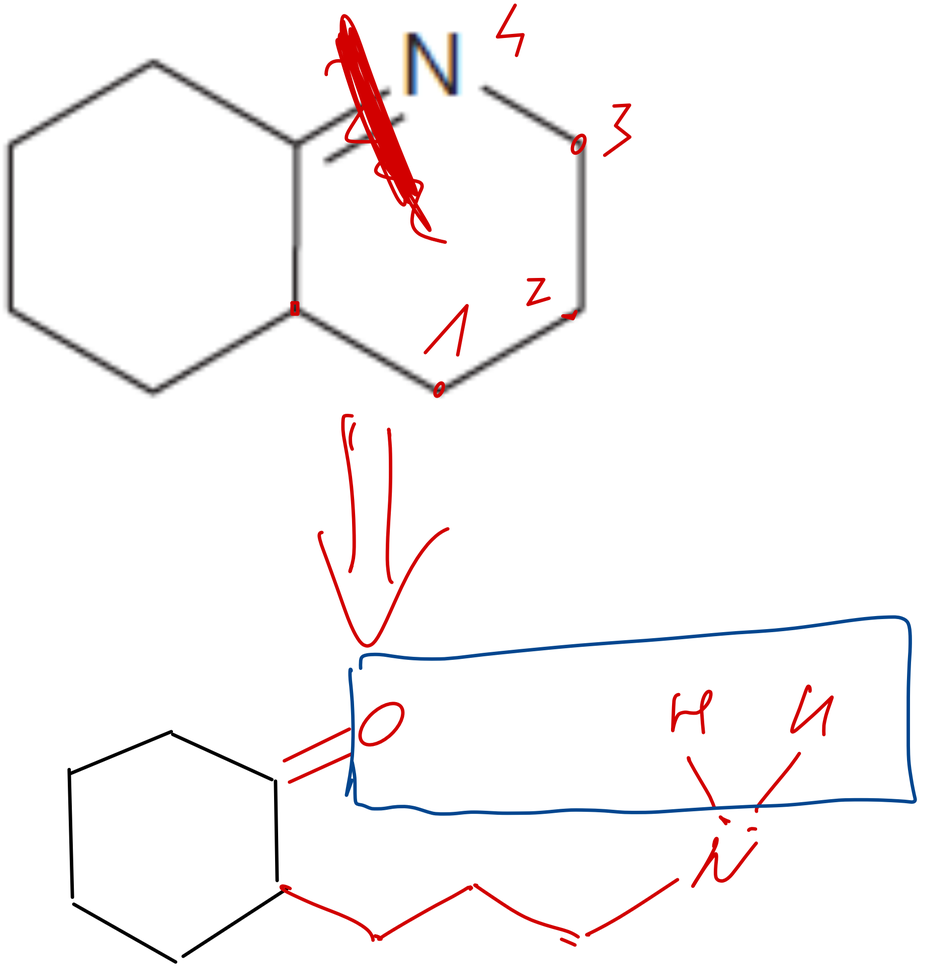




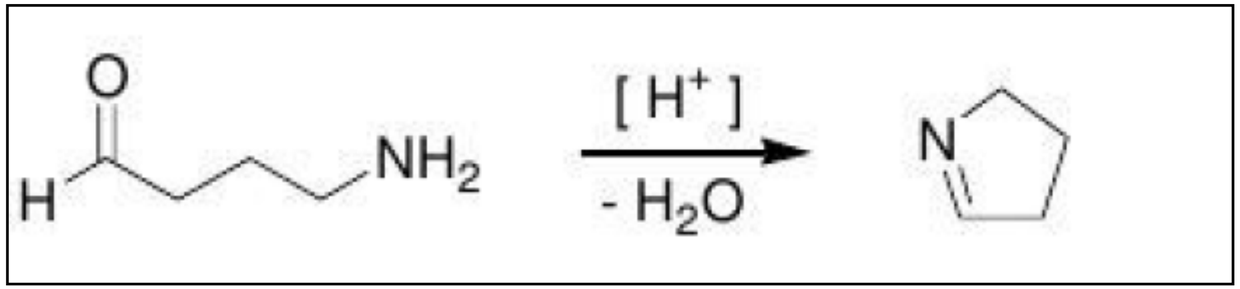
EMIACETALICO

PROBLEMA: Indica i reagenti che useresti per ottenere ciascuna delle seguenti imine.

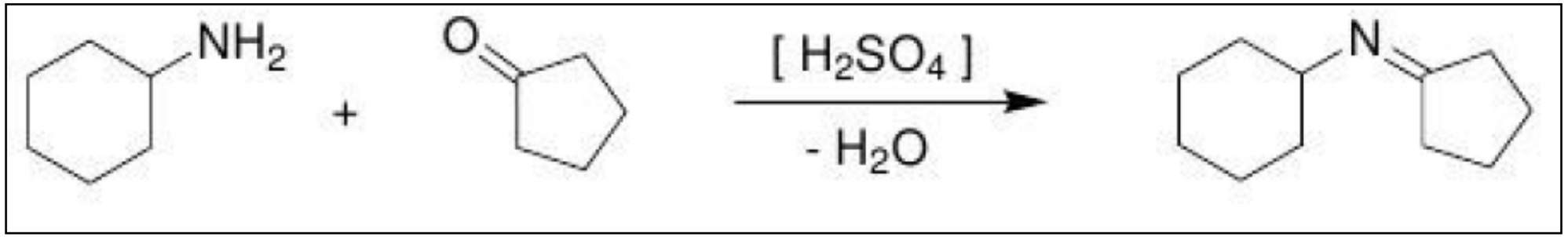


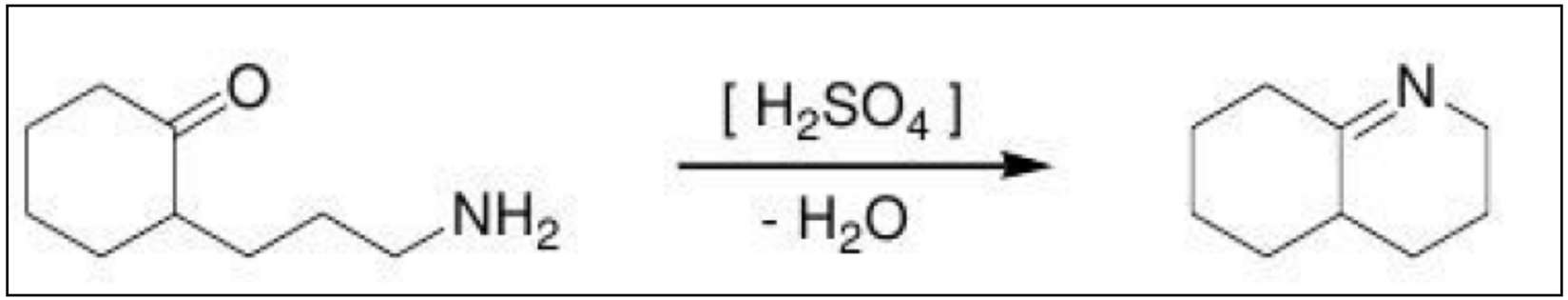


PROBLEMA: Prevedere il prodotto principale della seguente reazione intramolecolare

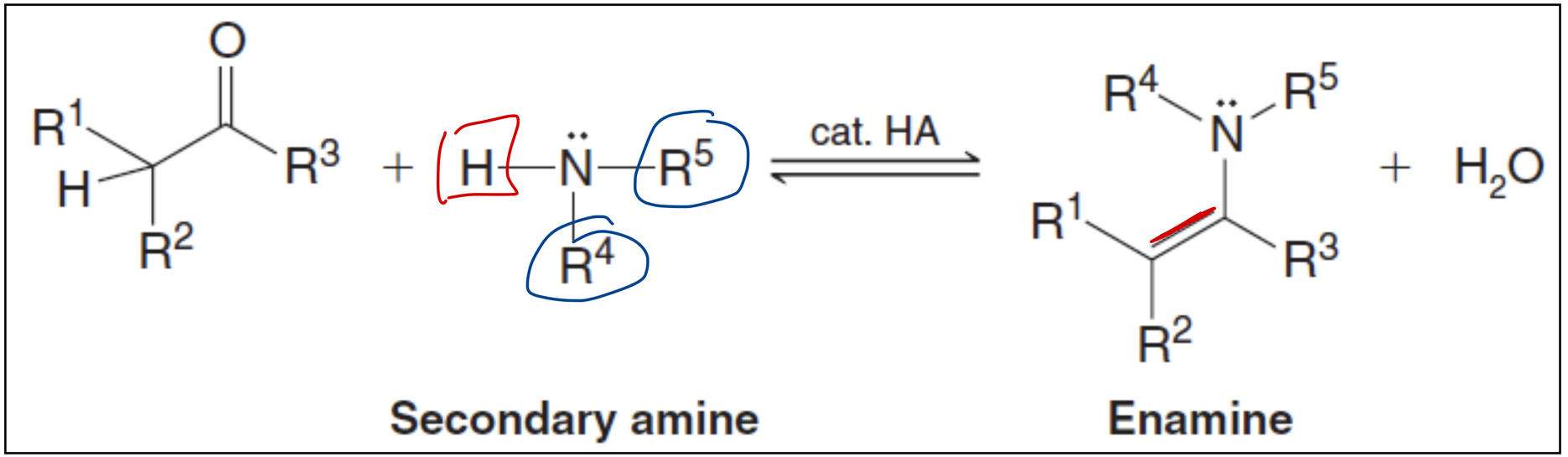


PROBLEMA: Indica i reagenti che useresti per ottenere ciascuna delle seguenti imine.



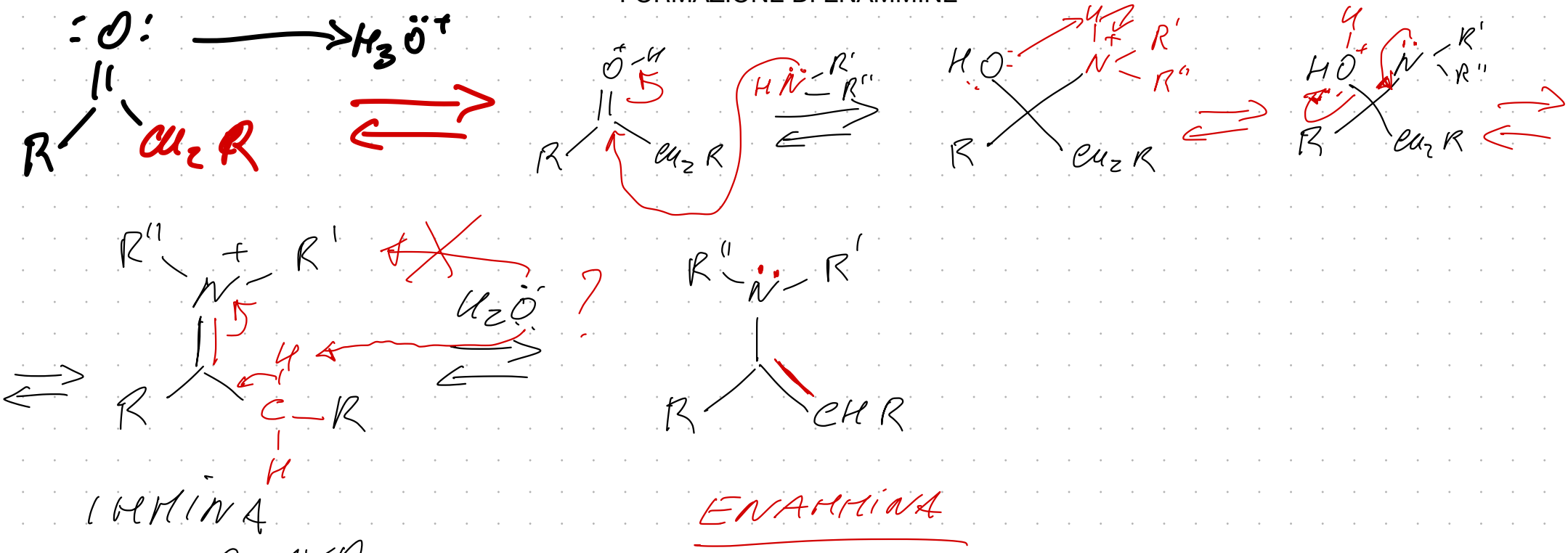


3) addizione Nucleofilica di ammine: Formazione di Enammine

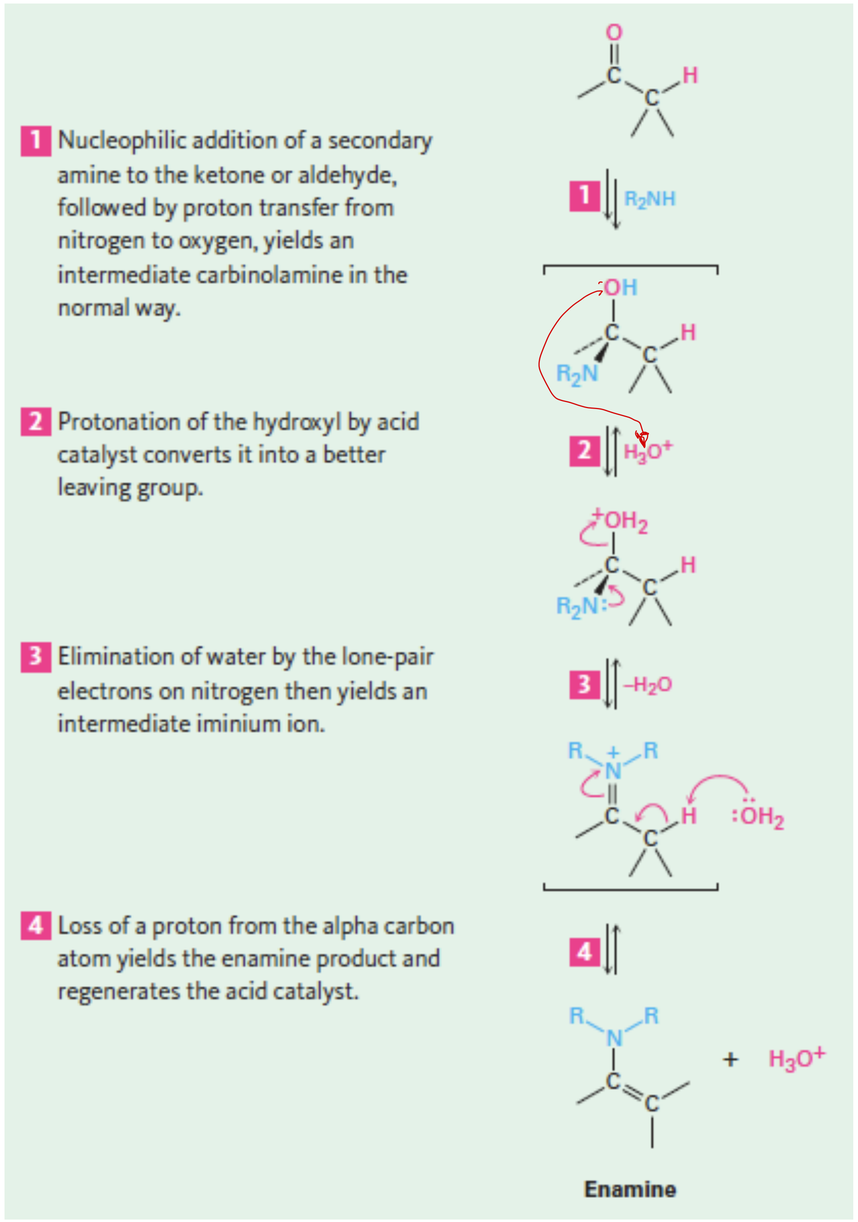


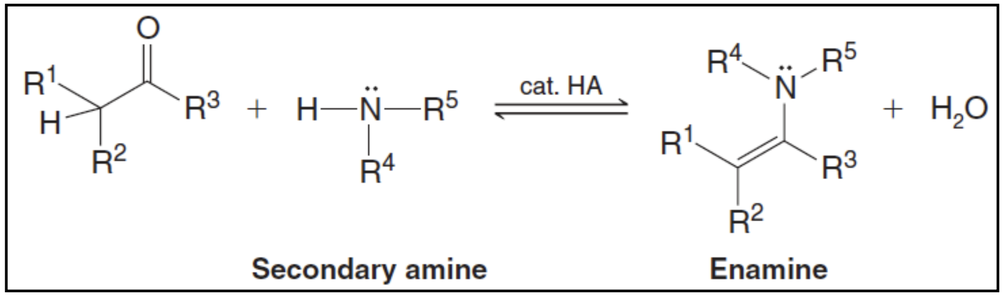
Aldeidi e chetoni reagiscono. Con ammine secondarie per forme ENAMINE

FORMAZIONE DI ENAMMINE

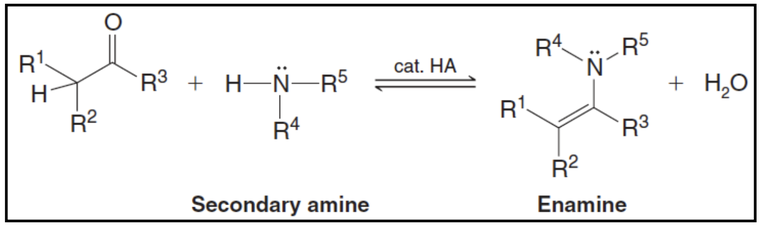


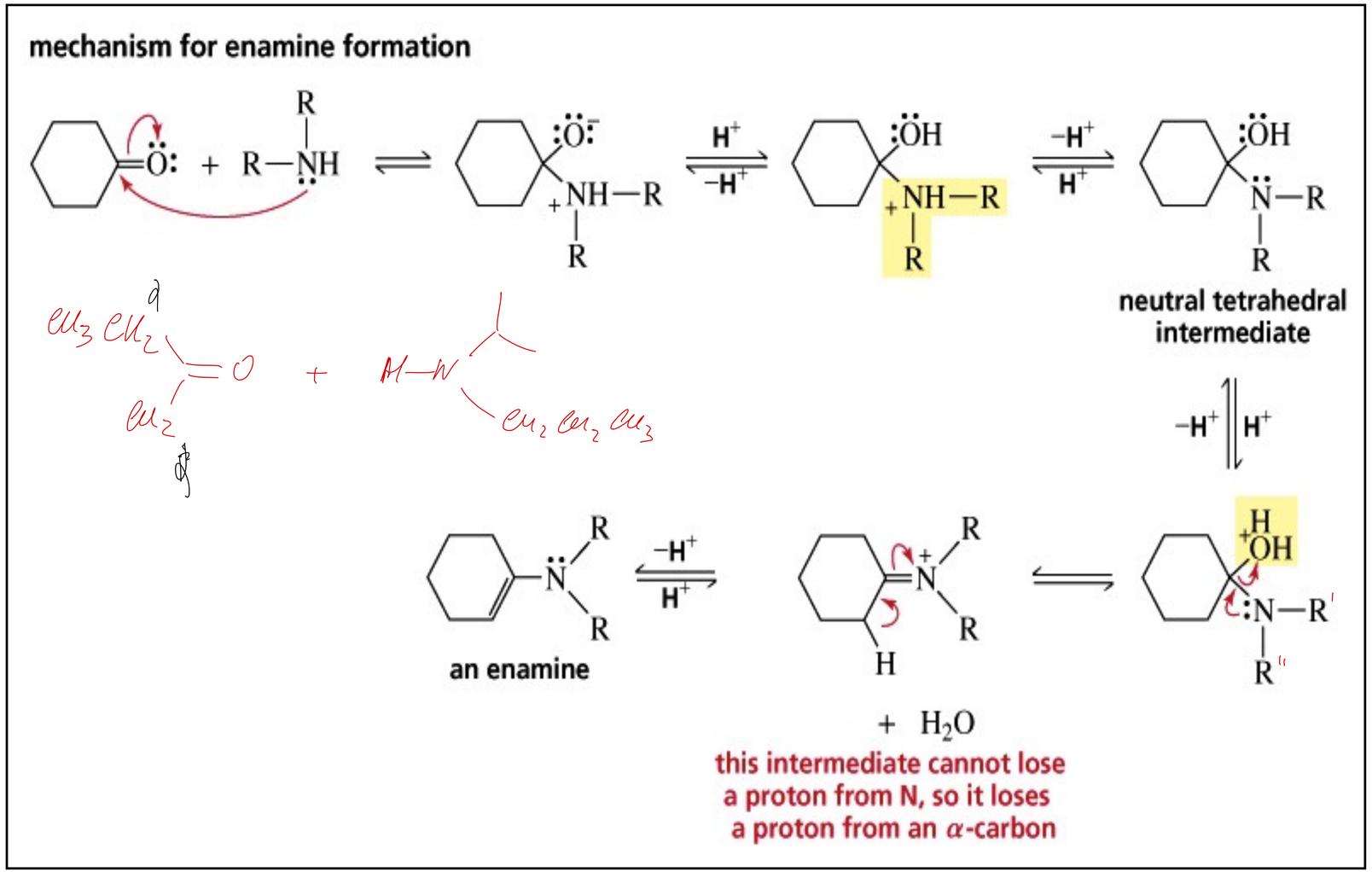
3) MECCANISMO: addizione Nucleofilica di ammine per la Formazione di Enammine



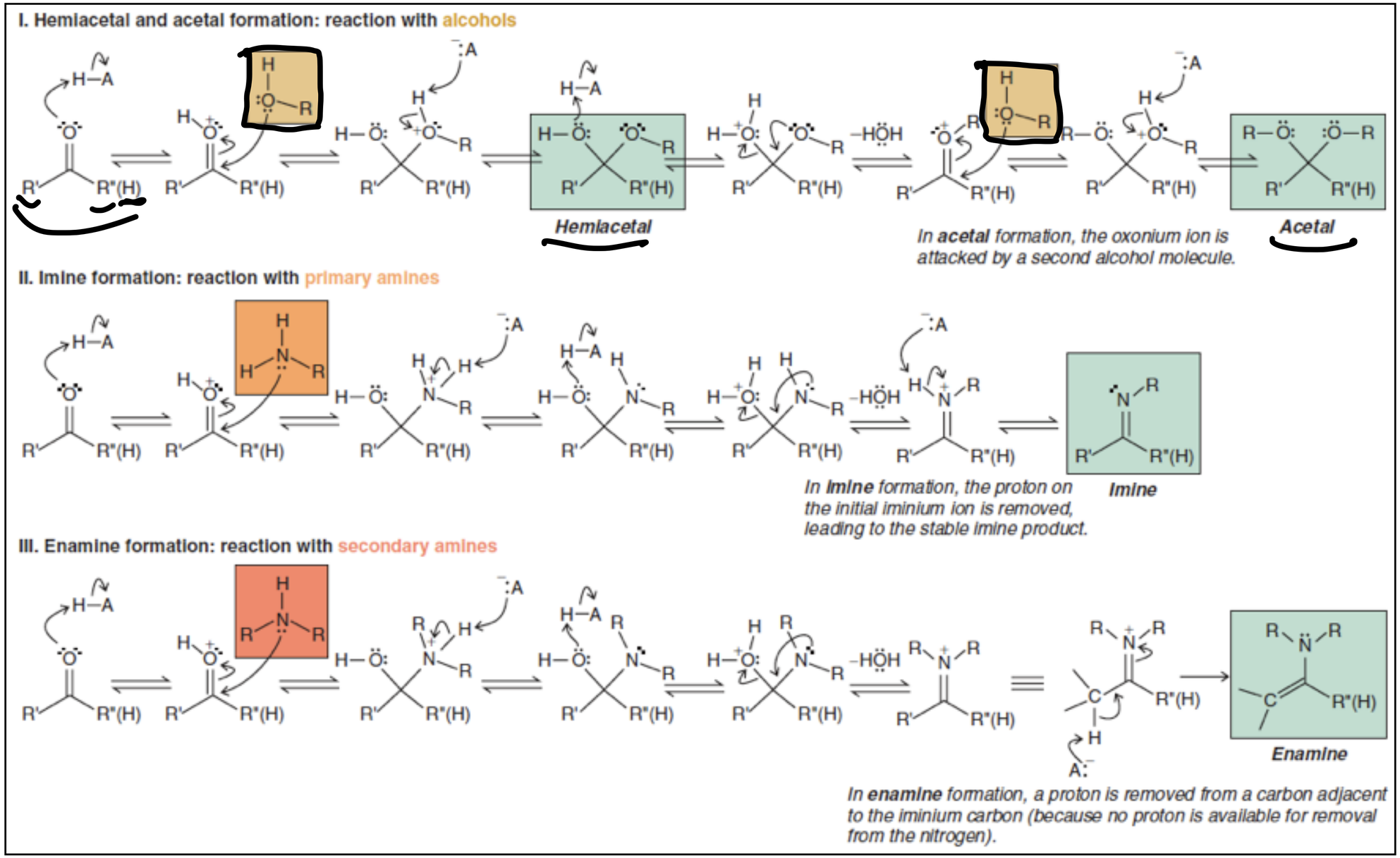


3) MECCANISMO: addizione Nucleofilica di ammine per la Formazione di Enammine

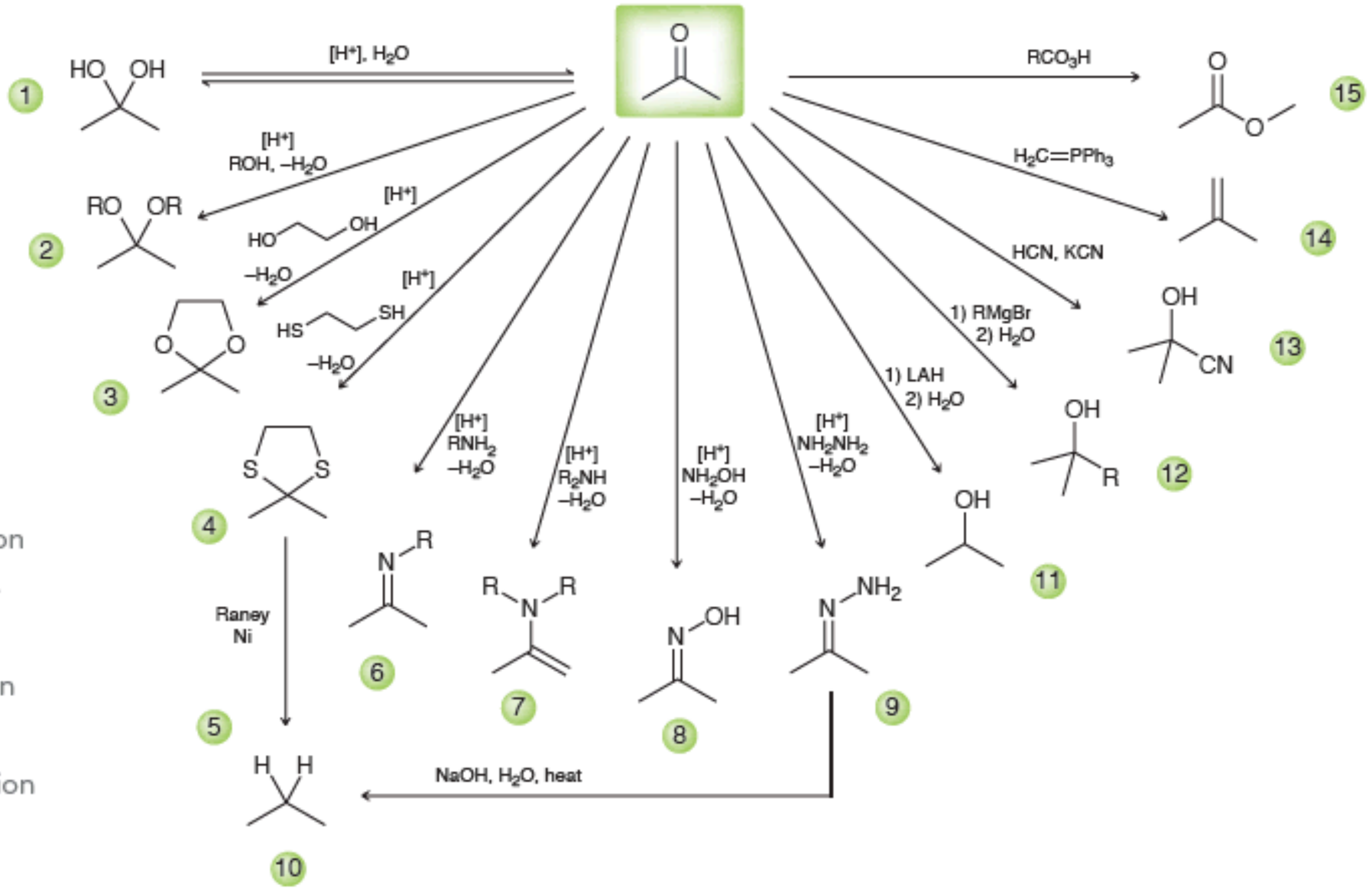


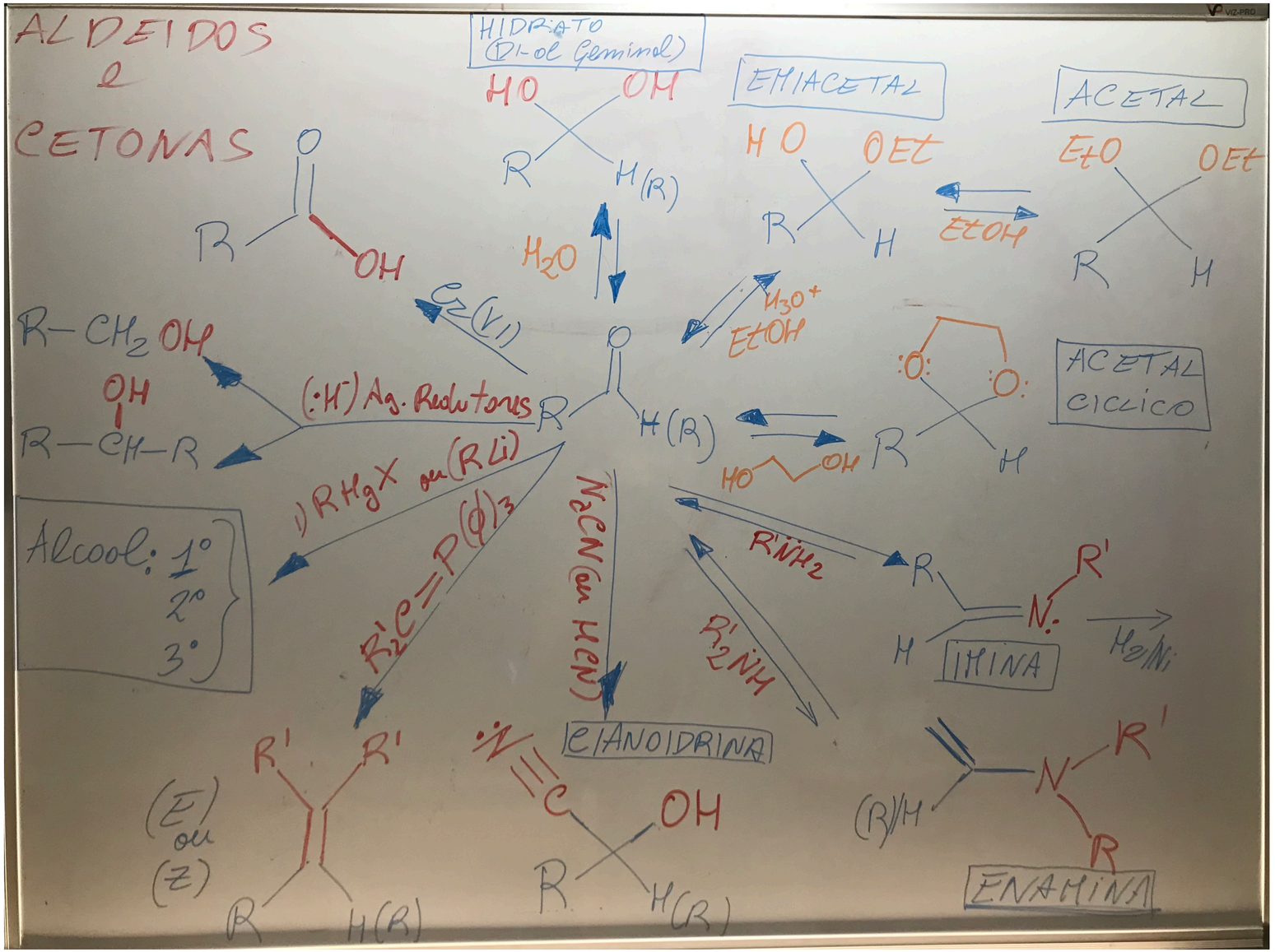


3) MECCANISMi per la formazione di Emiacetali, Acetali, Immine ed enammine



1. Hydrate Formation
2. Acetal Formation
3. Cyclic Acetal Formation
4. Cyclic Thioacetal Formation
5. Desulfurization
6. Imine Formation
7. Enamine Formation
8. Oxime Formation
9. Hydrazone Formation
10. Wolff-Kishner Reduction
11. Reduction of a Ketone
12. Grignard Reaction
13. Cyanohydrin Formation
14. Wittig Reaction
15. Baeyer-Villiger Oxidation



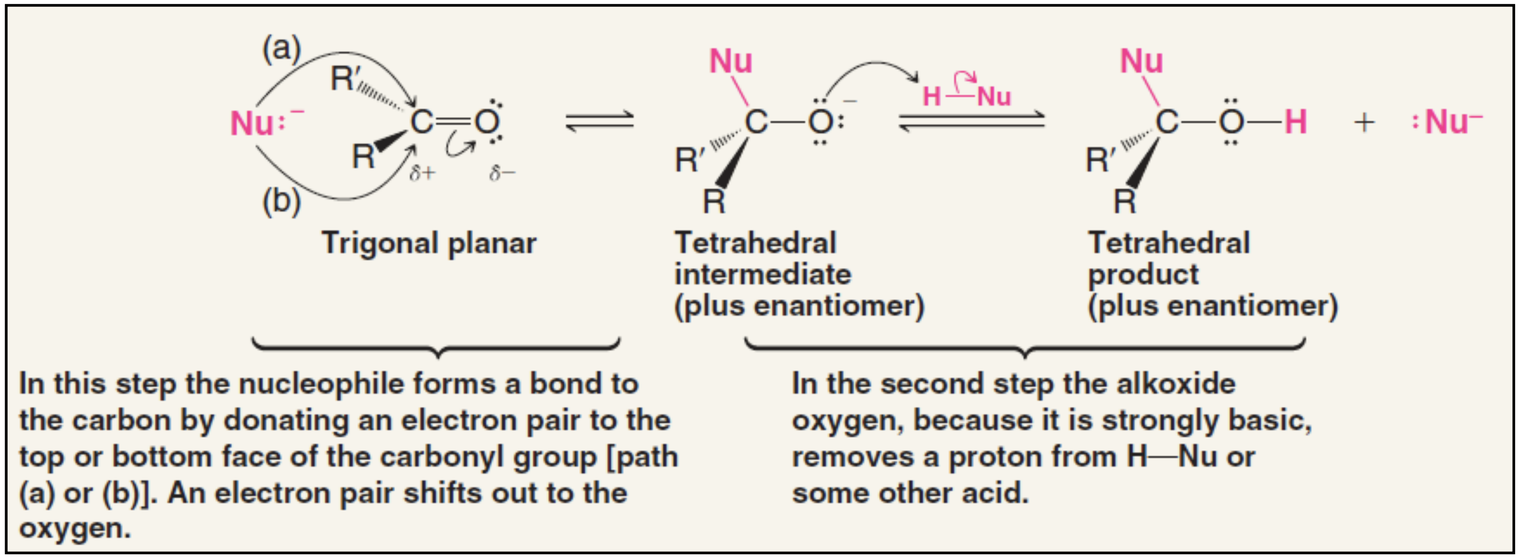

ALDEIDOS
e
CETONAS
HIDRATO
(Di-ol Geminal)
HEMIACETAL
ACETAL
ACETAL
CICLICO
(:H⁻) Ag. Redutores
1) RMgX ou (RLi)
Alcool: 1°
2°
3°
N≡CN (ou HCN)
CIANOIDRINA
IMINA
ENAMINA
(E)
ou
(Z)

Reazioni di addizione nucleofila al gruppo carbonile
Con un nucleofilo FORTE (Carico negativamente)

Some negatively charged nucleophiles

- $HO:^-$ (hydroxide ion)
- $H:^-$ (hydride ion)
- $R_3C:^-$ (a carbanion)
- $RO:^-$ (an alkoxide ion)
- $N{\equiv}C:^-$ (cyanide ion)

$R:^- MgX$ / $R:^- Li^+$



Reazioni di addizione nucleofila al gruppo carbonile
Con un nucleofilo FORTE (Carico negativamente)

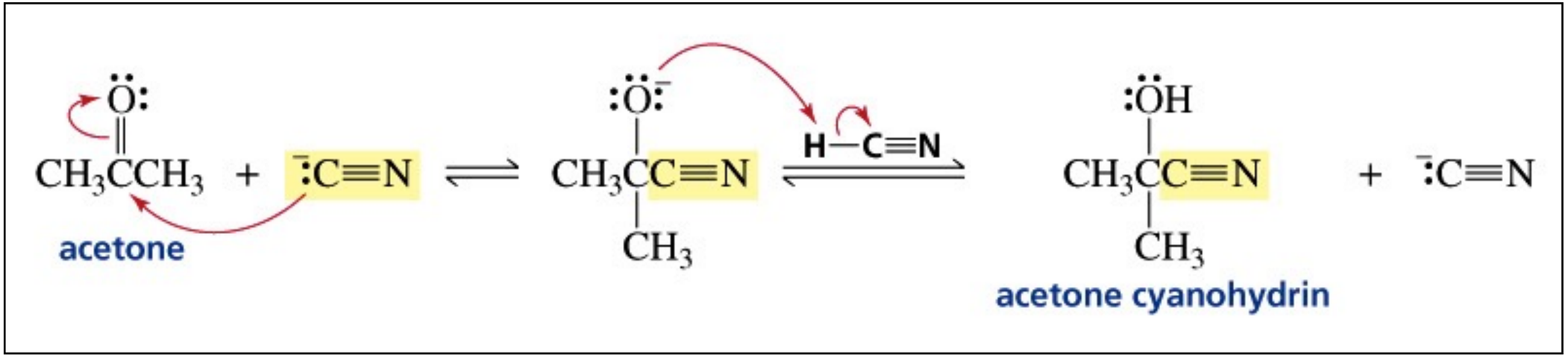
4) Reazione con cianuro di idrogeno (HCN) o NaCN

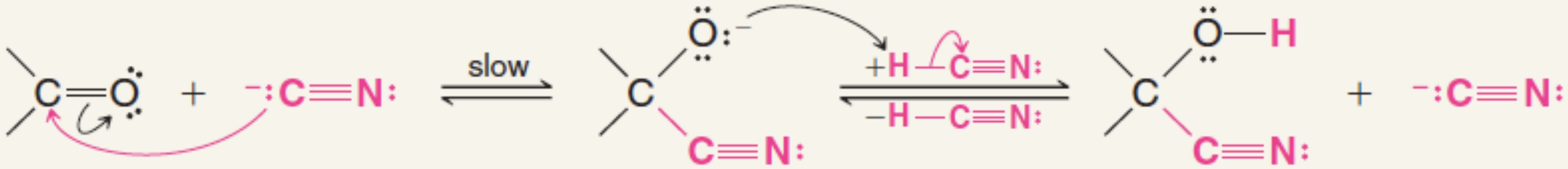
5) Reazione di Wittig: $R_2C=P(Ph)_3$

6) Aggiunta di un reagente Grignard: RMgX o RLi

7) Reazione dell'anione acetiluro (base coniugata dell'acetilene): $RCC:^- Na^+$

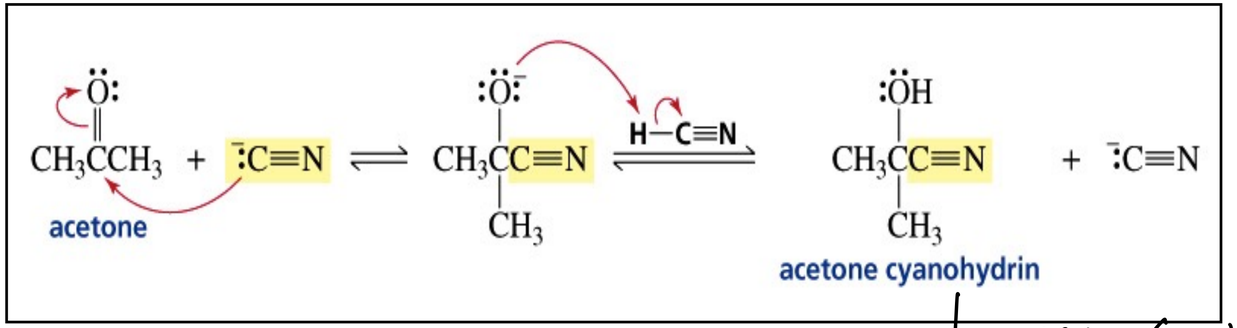
FORMAZIONE DELLA CIANOIDRINA

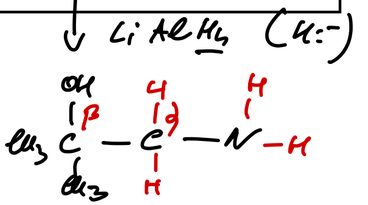




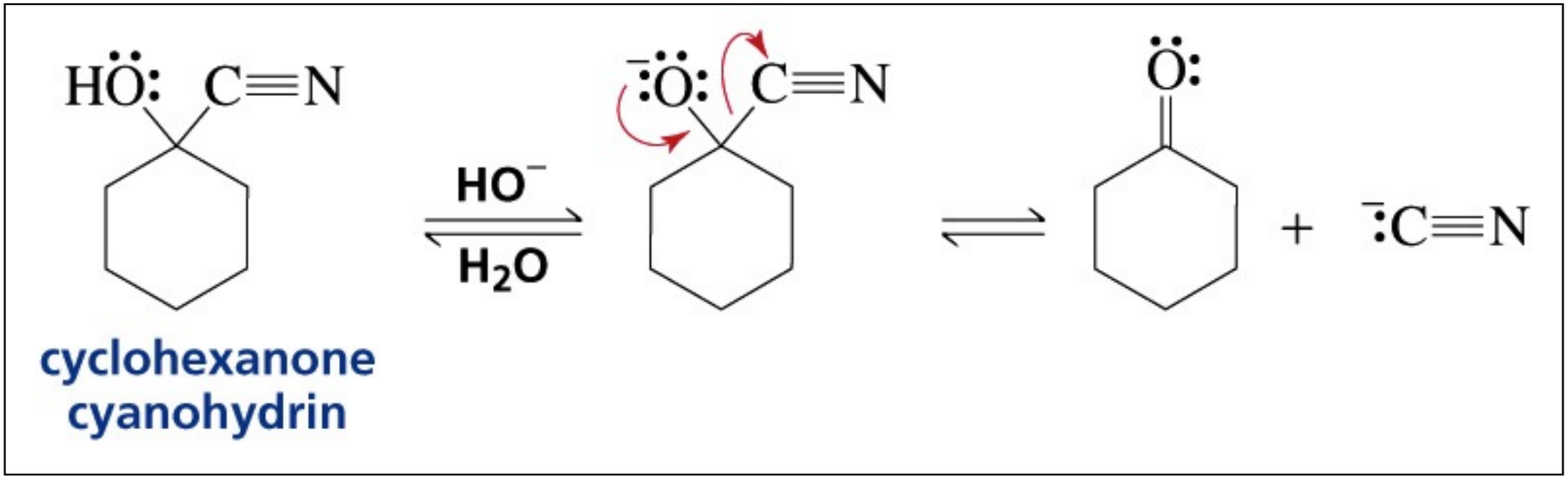
Great care must be taken when working with hydrogen cyanide due to its high toxicity and volatility. Reactions involving HCN must be conducted in an efficient fume hood.

FORMAZIONE DELLA CIANOIDRINA





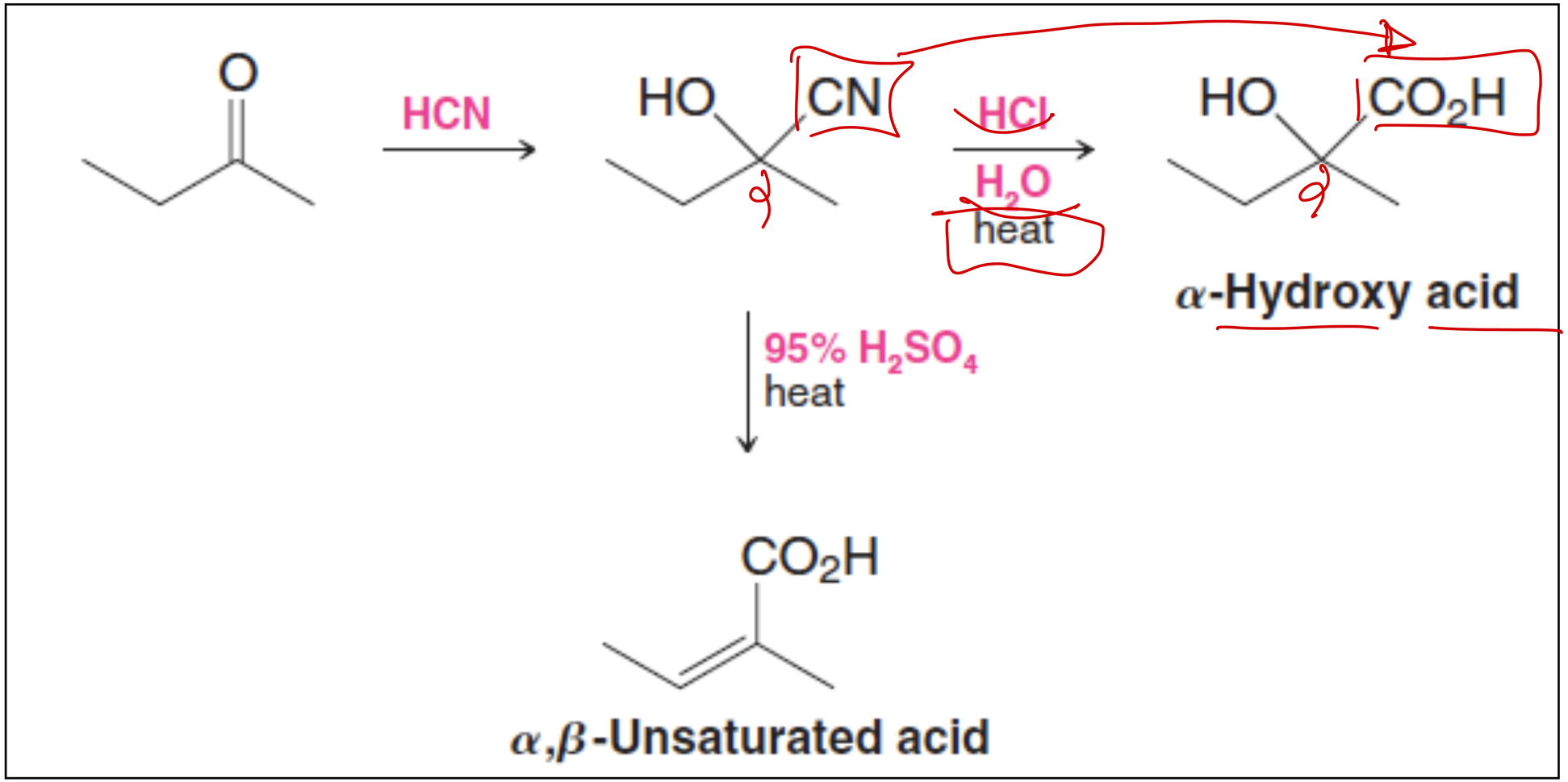
In un ambiente basico , una cianidrina viene trasformata in un composto carbonilico



FORMAZIONE DELLA CIANOIDRINA E TRASFORMAZIONE DELLA CIANOIDRINA

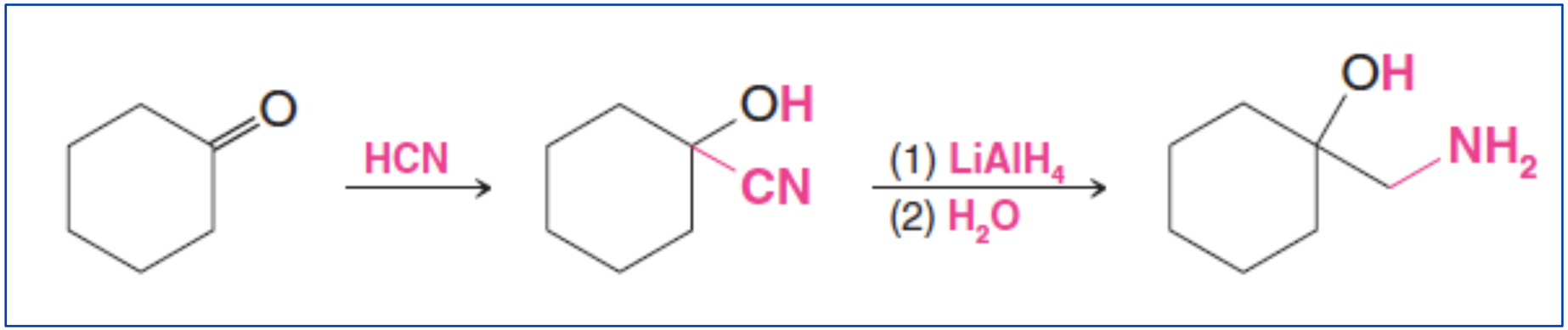
Reazione con cianuro di idrogeno (HCN) o NaCN: ADDIZIONE NUCLEOFILA DI HCN

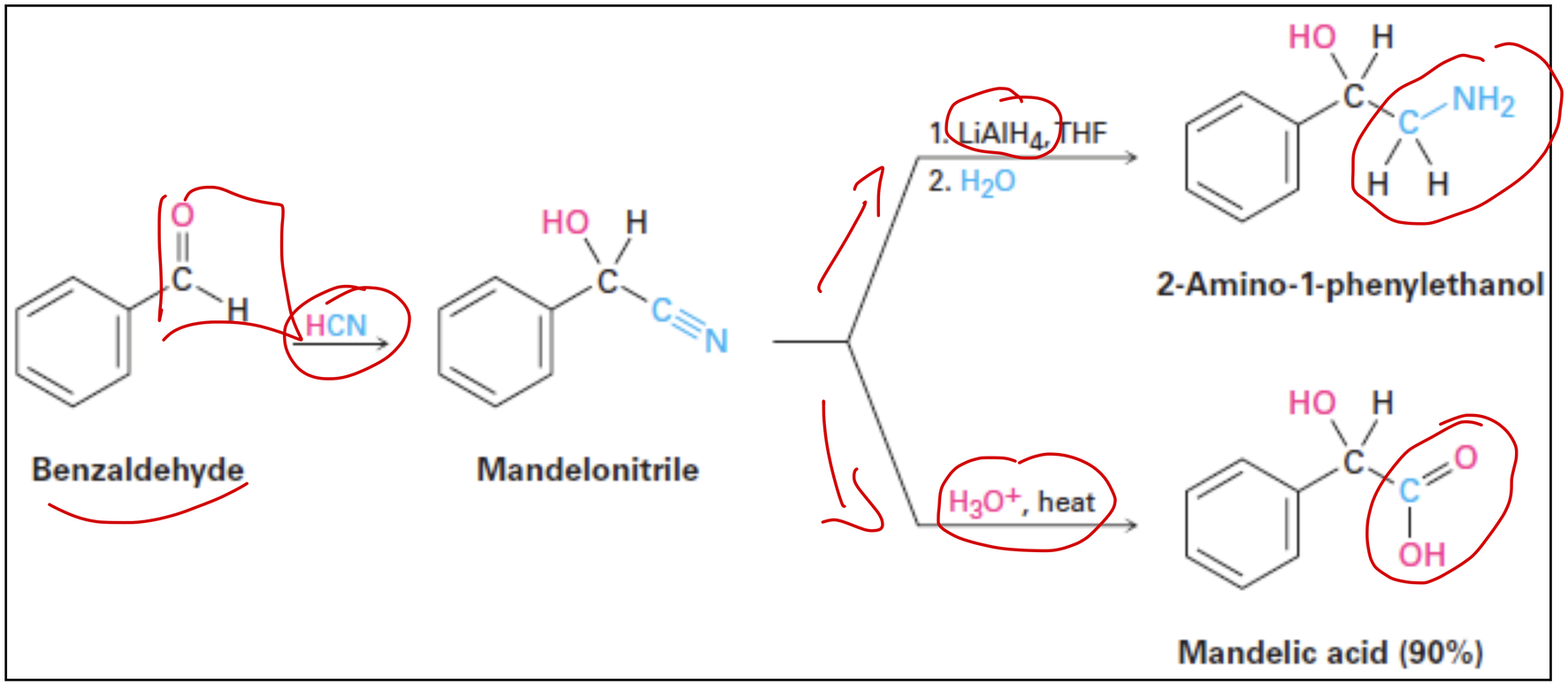
L'IDROLISI ACIDA DELLA CIANOIDRINA PERMETTE LA FORMAZIONE DI ALFA-IDROSSI ACIDI E ALFA-BETA-INSATURI



FORMAZIONE DELLA CIANOIDRINA E TRASFORMAZIONE DELLA CIANOIDRINA

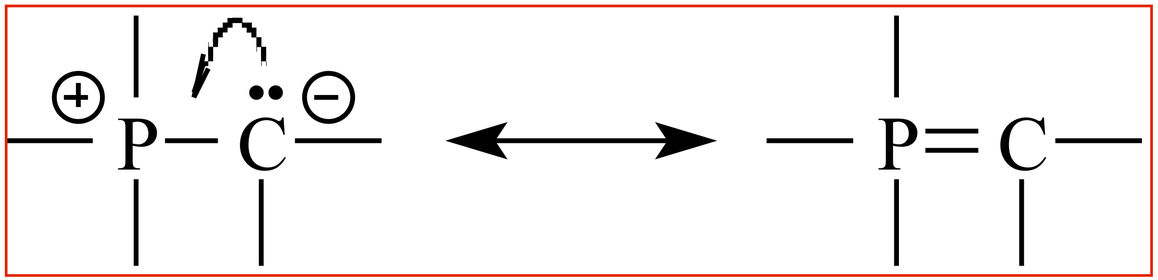
Riduzione della cianoidrina con Litio Alluminio idruro (LAH) per fornire beta-amminoalcoli

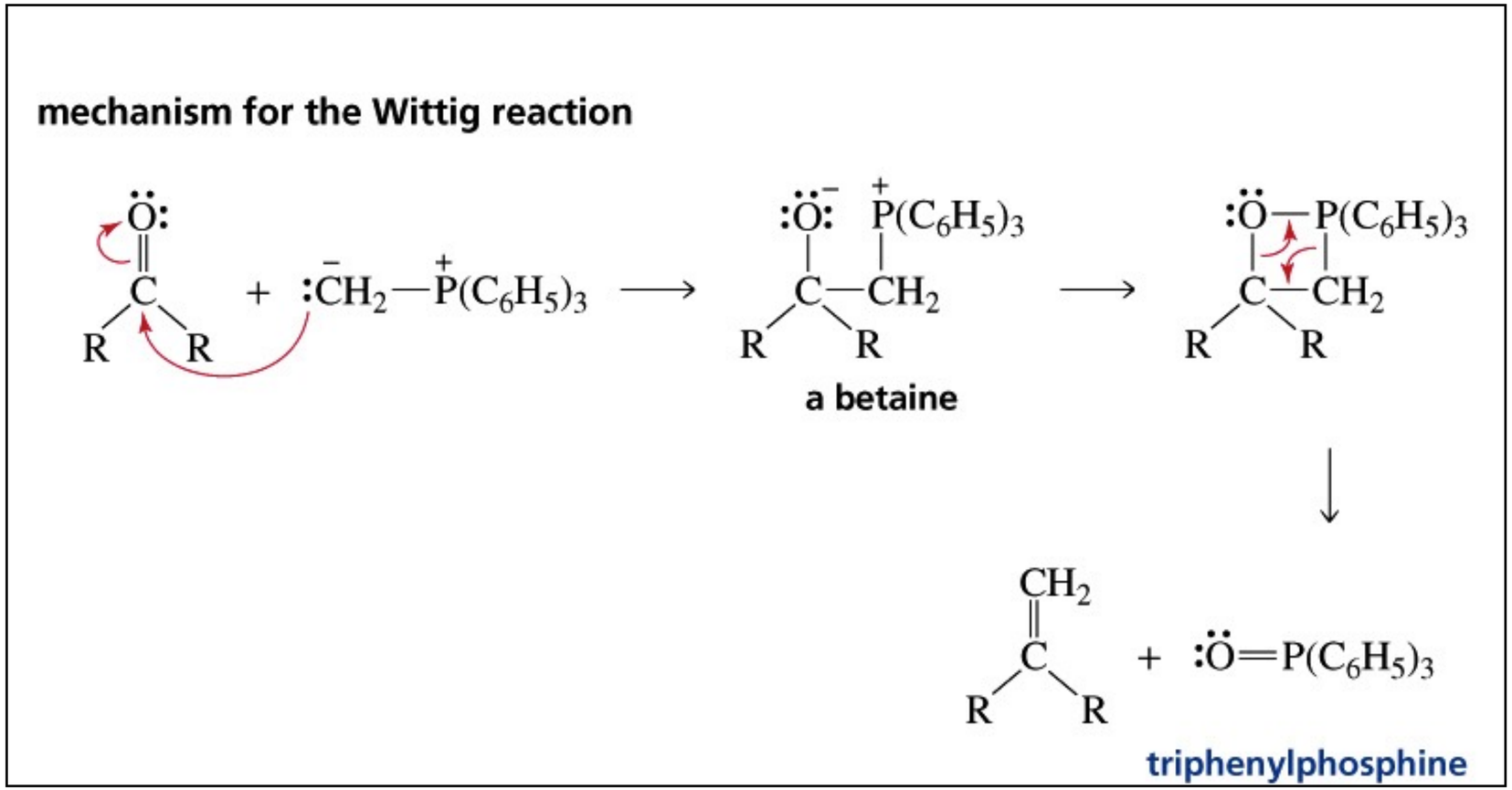




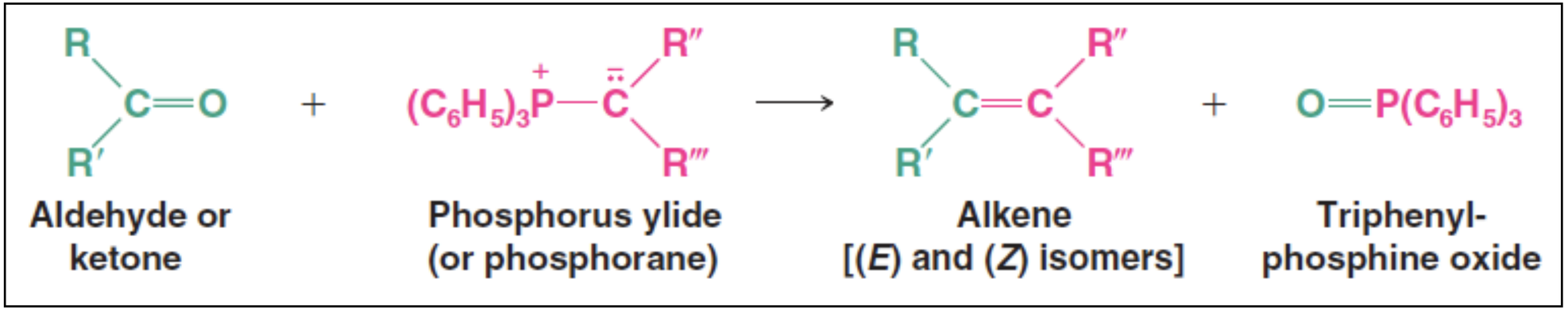
(5) Reazione di Wittig: Addizione nucleofila di ileto i fosforo $R_2C=P(C_6H_5)_3$

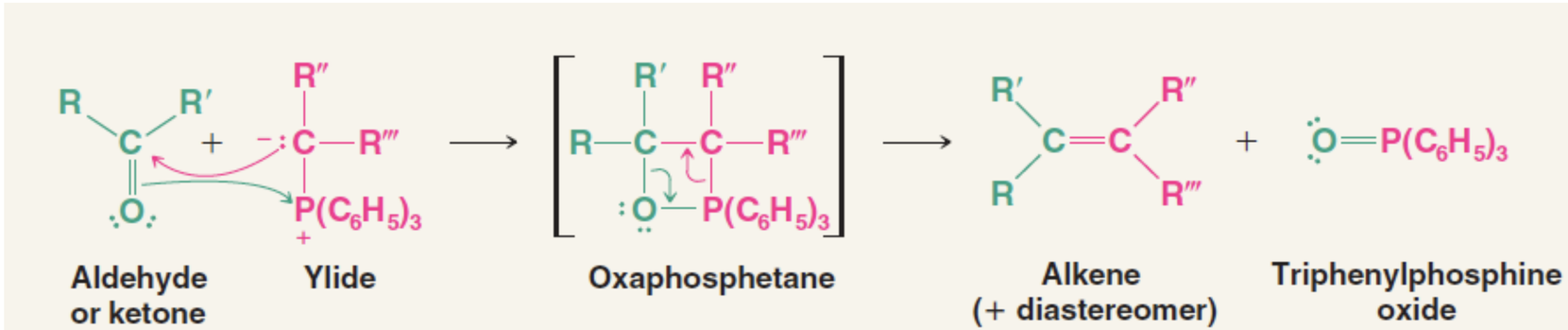
Un ilide è un composto dipolare neutro



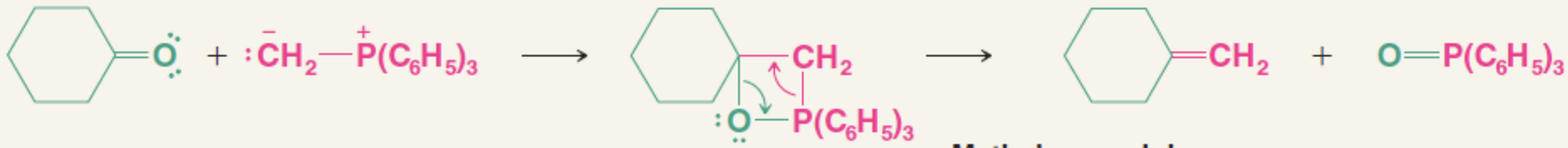


(5) Reazione di Wittig: aldeidi e chetoni reagiscono con le ilidi del fosforo per produrre alcheni e ossido di trifenil fosfina

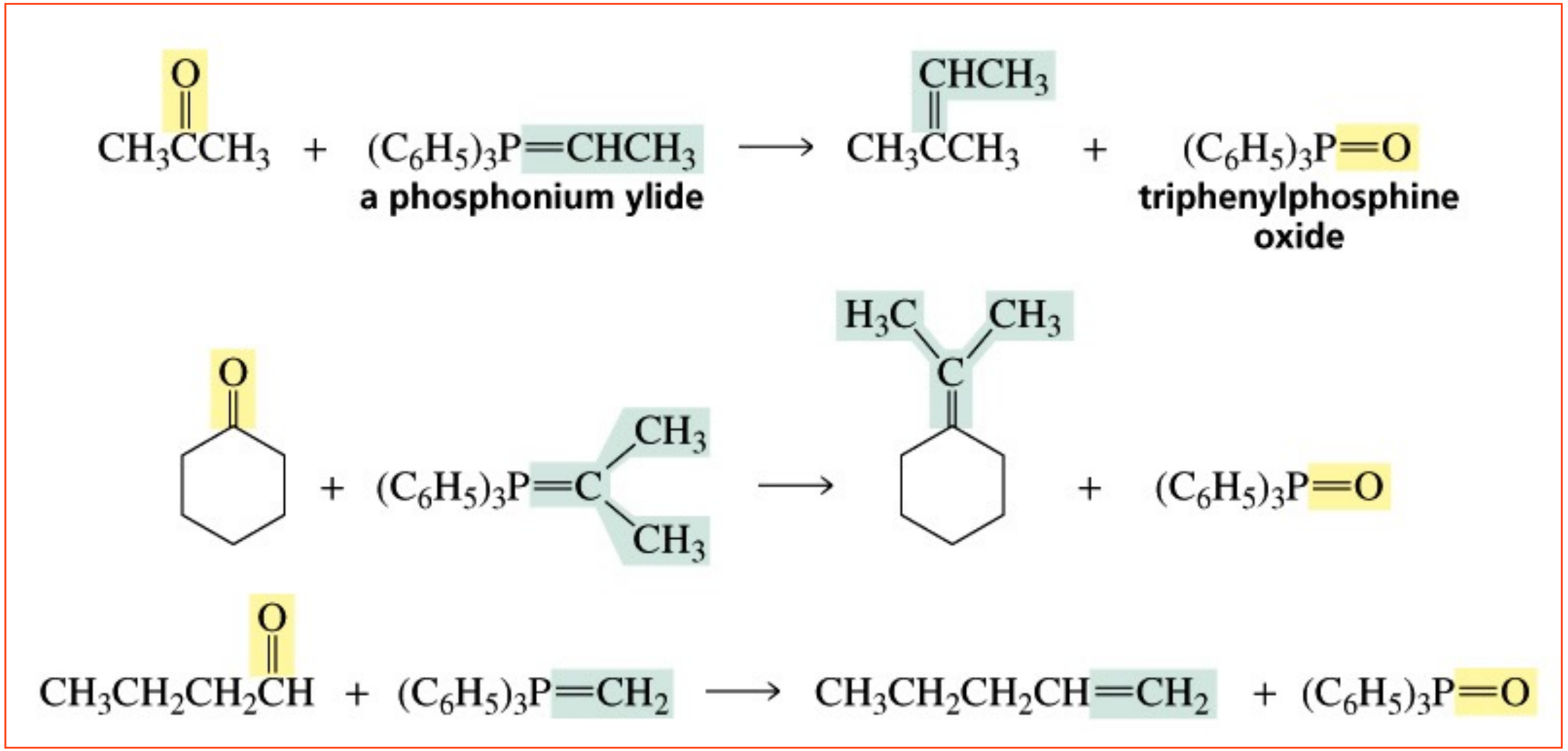




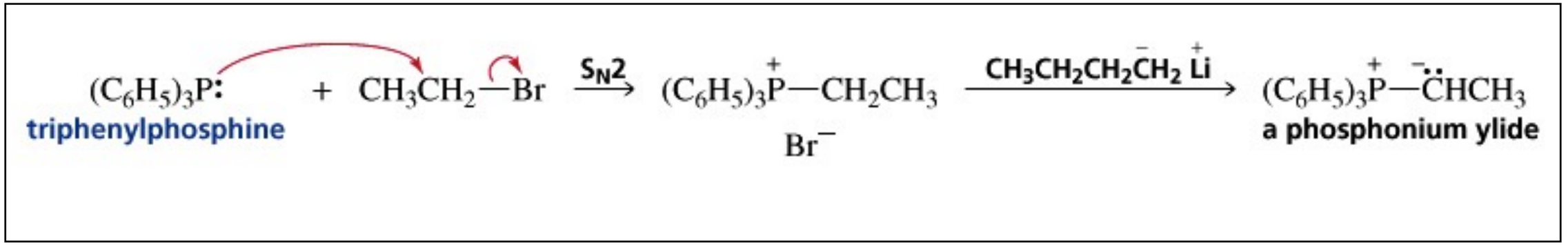
Specific Example

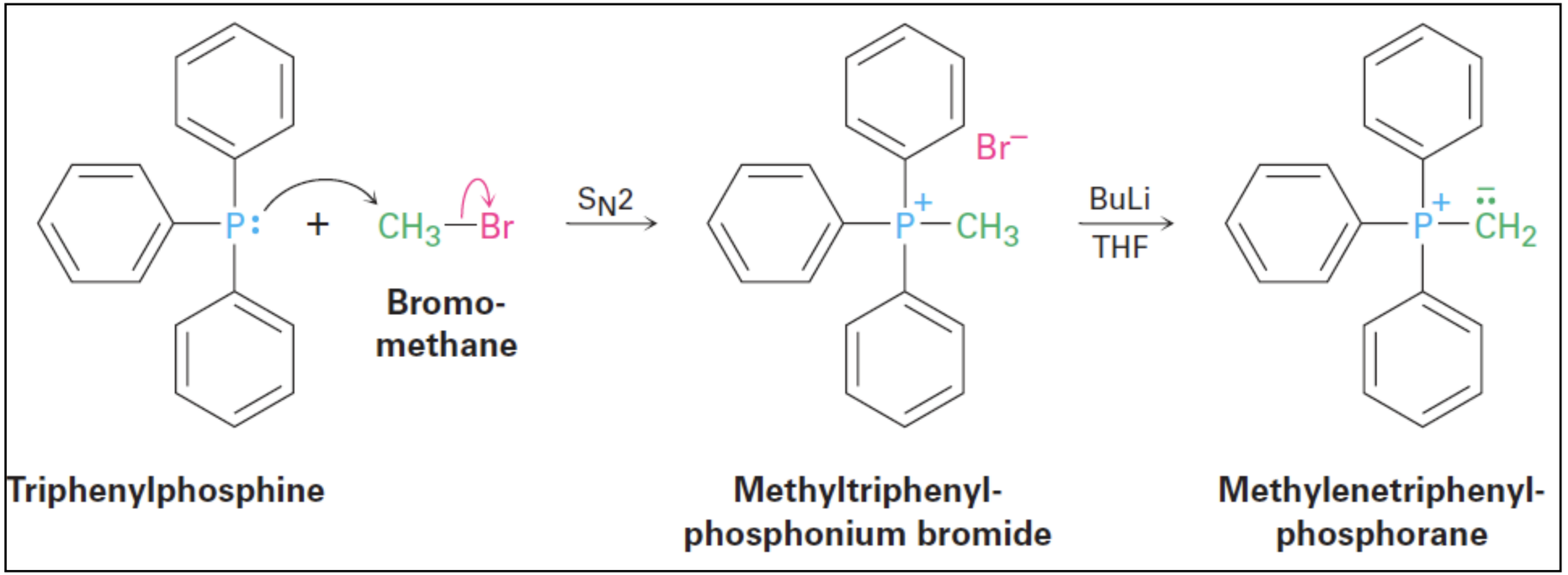


(5) Reazione di Wittig: aldeidi e chetoni reagiscono con le ilidi del fosforo per produrre alcheni e ossido di trifenil fosfina

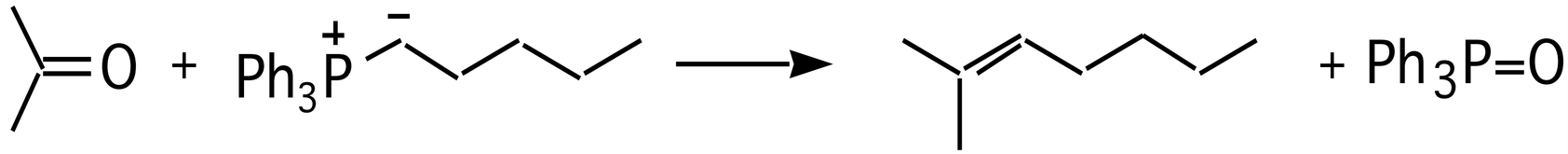


Preparazione degli ilidi di fosforo:
Sono facilmente preparati da trifenil fosfine e alogenuri alchilici primari o secondari

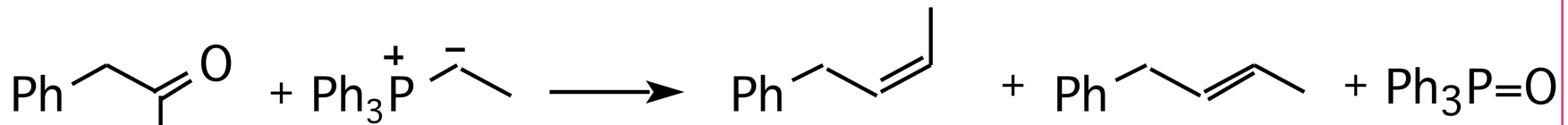




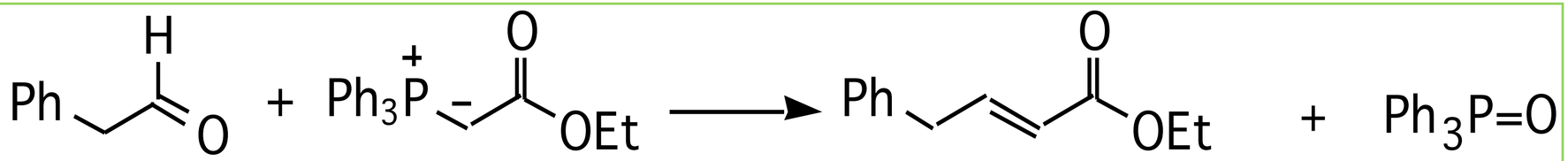
ESEMPI: sintesi di alcheni attraverso la reazione di Wittig



Acetone **2-Methyl-2-heptene**



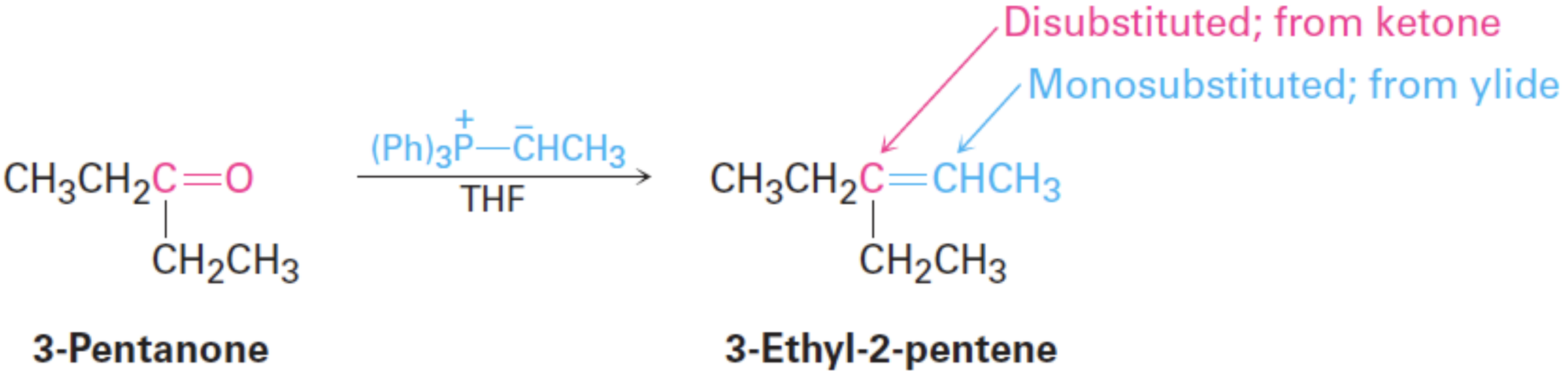
Phenyl-acetaldehyde **(*Z*)-1-Phenyl-2-butene (87%)** **(*E*)-1-Phenyl-2-butene (13%)**



Phenyl-acetaldehyde **Ethyl (*E*)-4-phenyl-2-butenoate (only the E isomer is formed)**

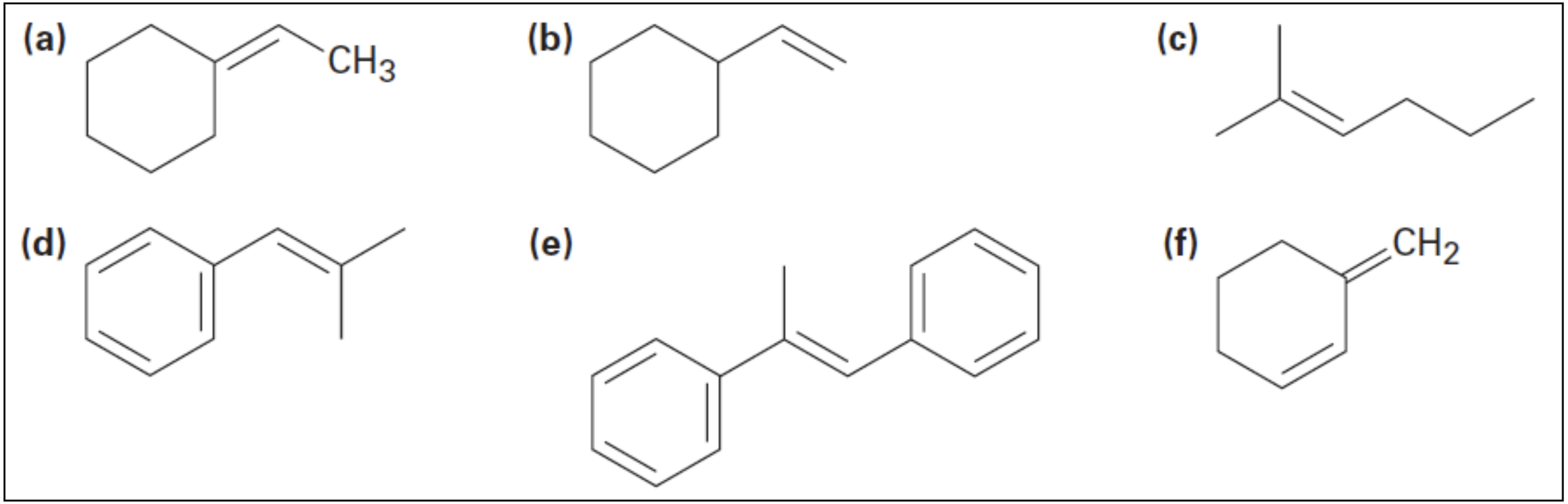
- **Problema: Sintetizzare gli alcheni usando una reazione di Wittig .**
- **Quale composto di carbonile e quale ileto di fosforo puoi usare per preparare 3-etil-2-pentene?**

- **Problema: Sintetizzare gli alcheni usando una reazione di Wittig .**
- **Quale composto di carbonile e quale ileto di fosforo puoi usare per preparare 3-etil-2-pentene?**



- **Problema: Sintetizzare gli alcheni usando una reazione di Wittig.**

- **Quale composto di carbonile e quale ileto di fosforo dovresti usare per preparare ciascuno dei seguenti composti?**

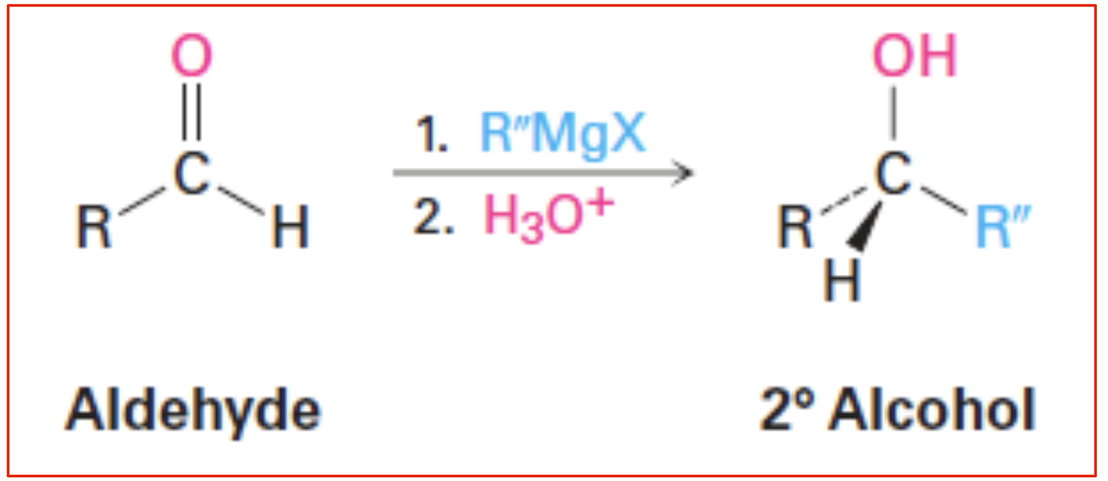


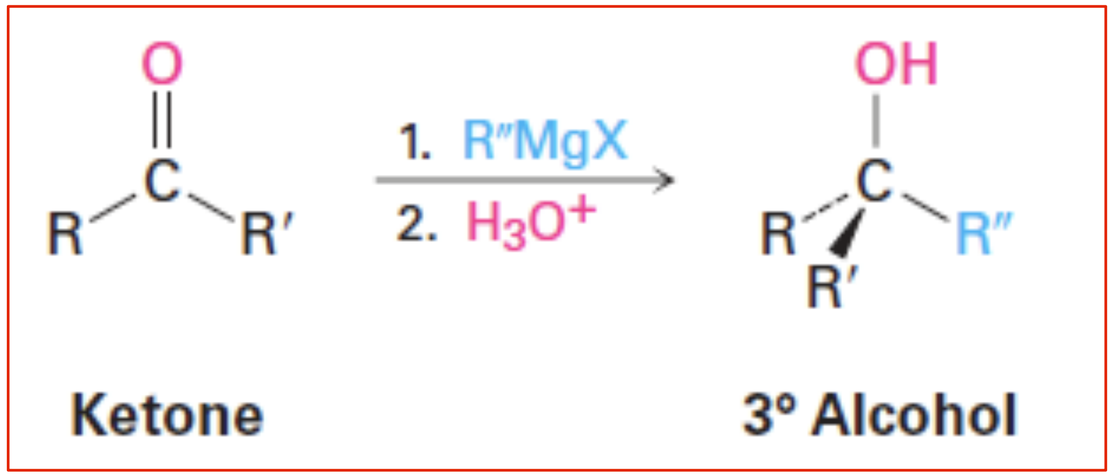
(6) Addizione nucleofila dei reagenti di Grignard:

Formazione di alcoli

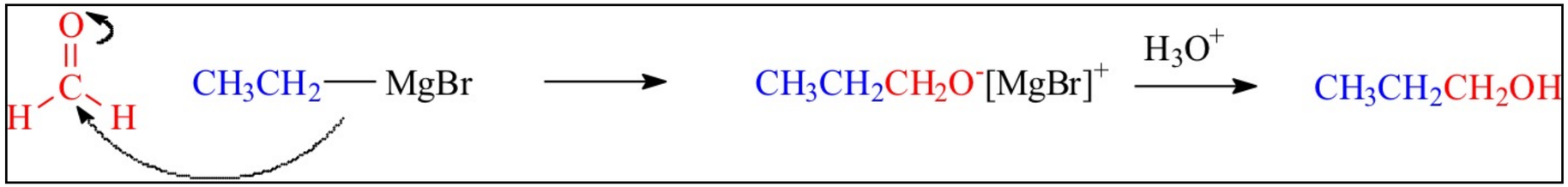
$$CH_3CH_2Br \xrightarrow[Et_2O]{Mg} CH_3CH_2MgBr$$

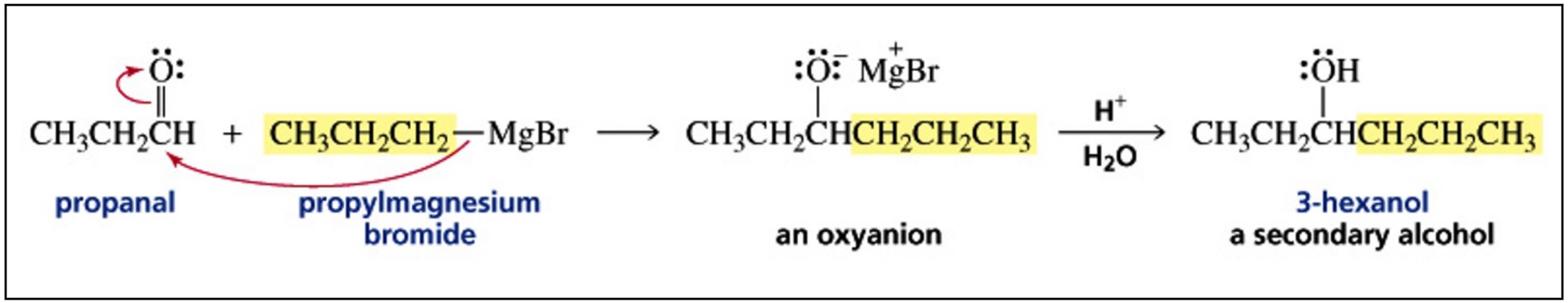
CH_3CH_2MgBr reacts as if it were $CH_3\ddot{C}H_2$ $\overset{+}{M}gBr$

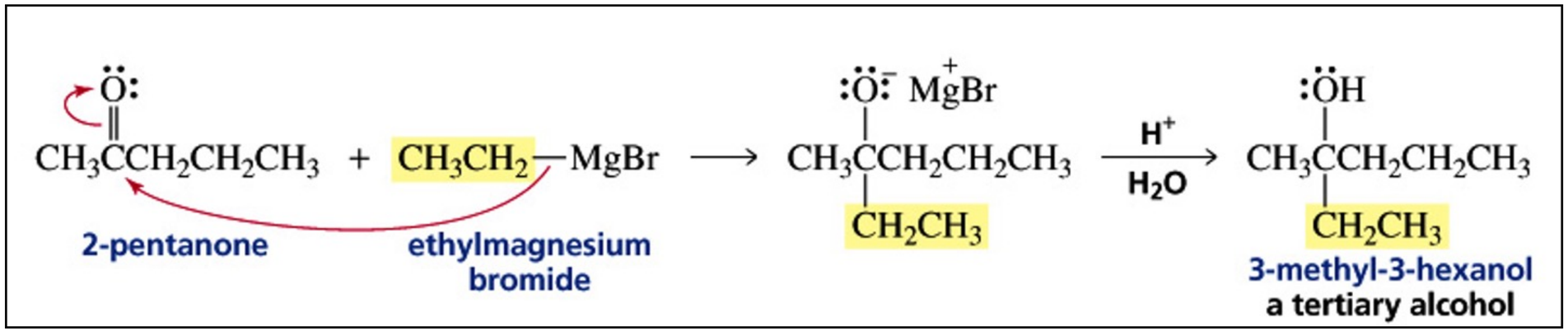




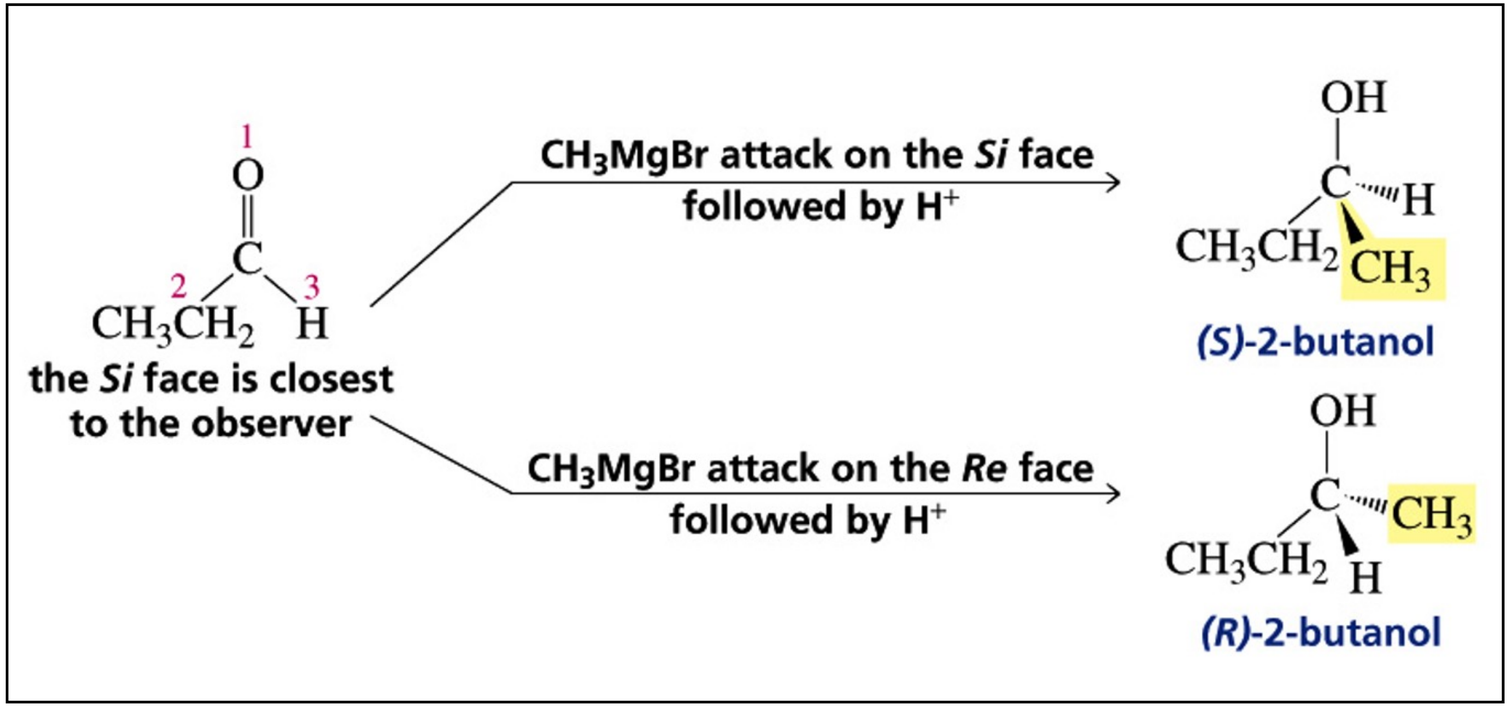
(6) Meccanismo dell'aggiunta nucleofilica di RMgX al gruppo carbonile, seguita dalla protonazione di un alcossido intermedio, producendo un alcol

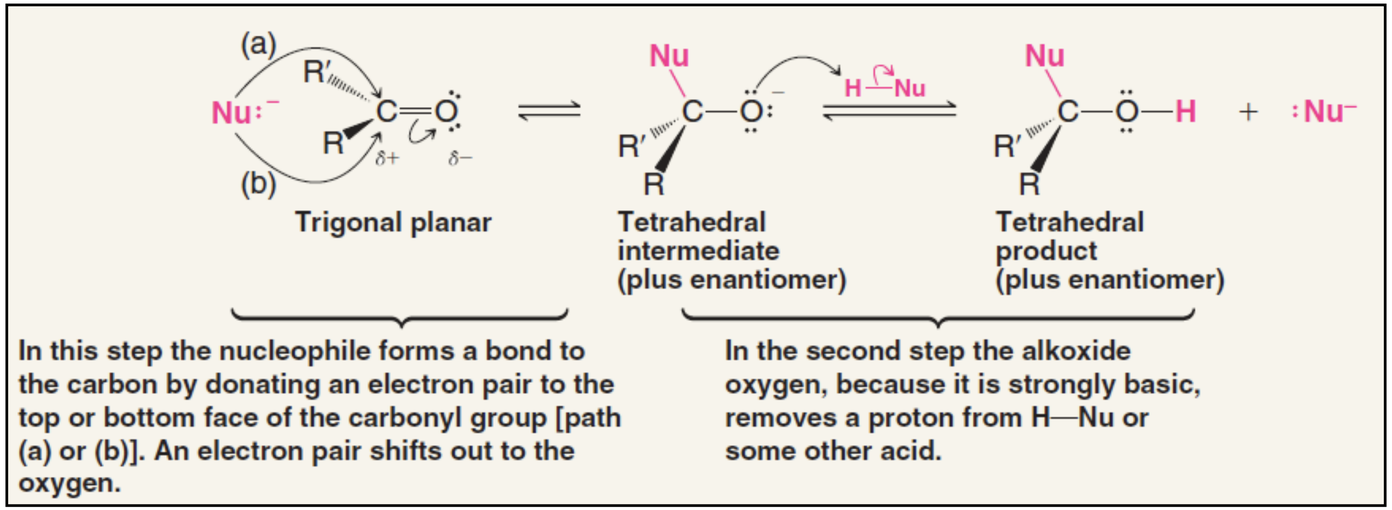




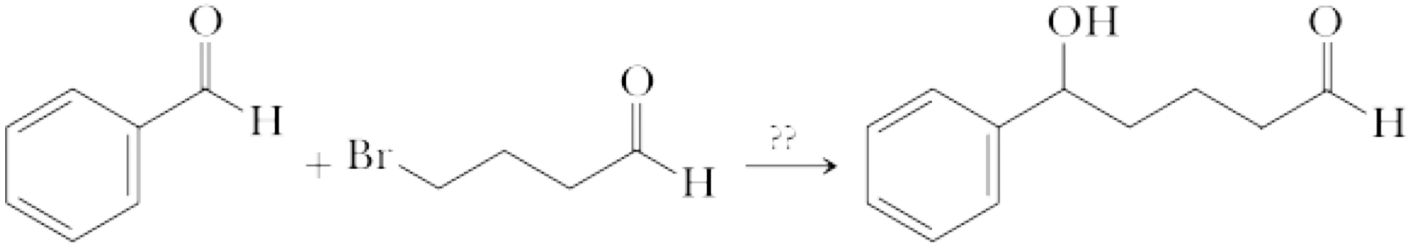


(6) Stereochimica dell'addizione nucleofila di RMgX al gruppo carbonile

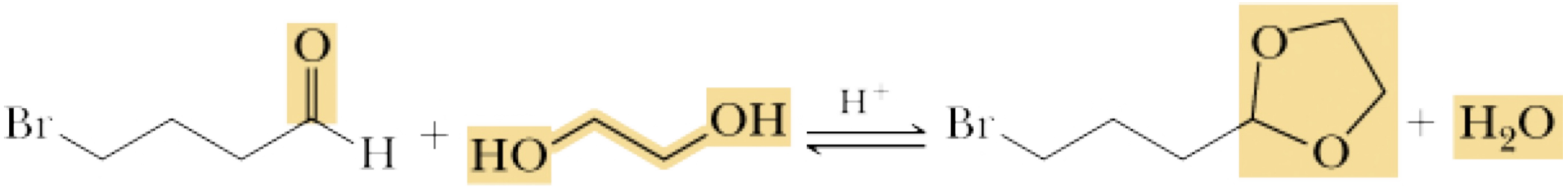




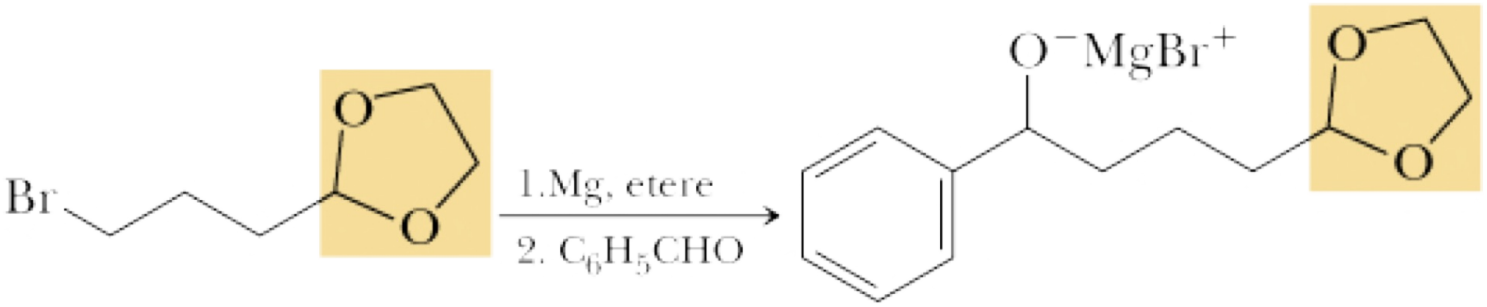
Acetali come gruppi protettori del carbonile



Benzaldeide **4-Bromobutanale** **5-Idrossi-5-fenilpentanale**
(miscela racemica)

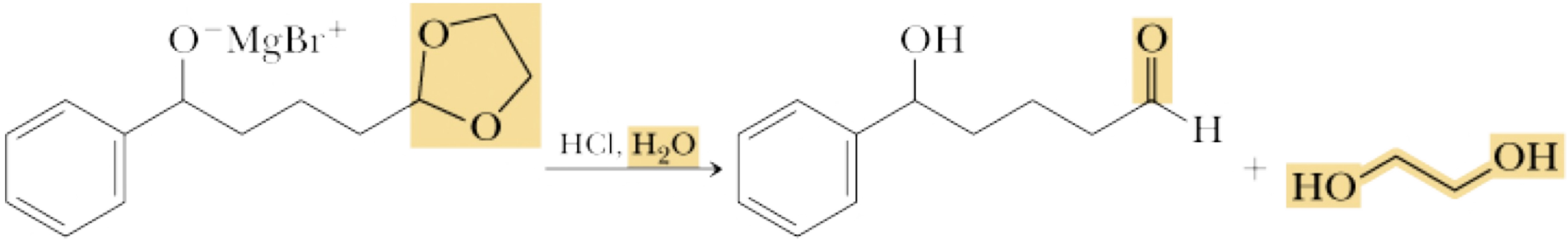


Acetale ciclico



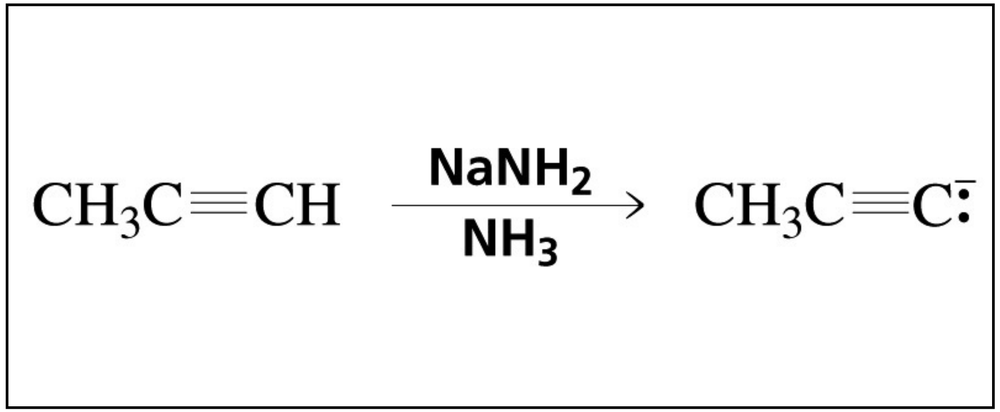
Acetale ciclico

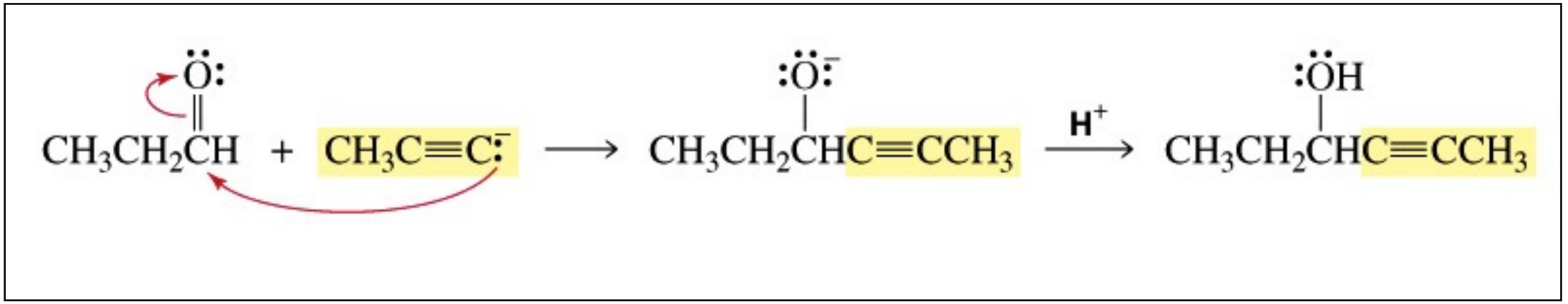
Alcossido di magnesio chirale
(miscela racemica)



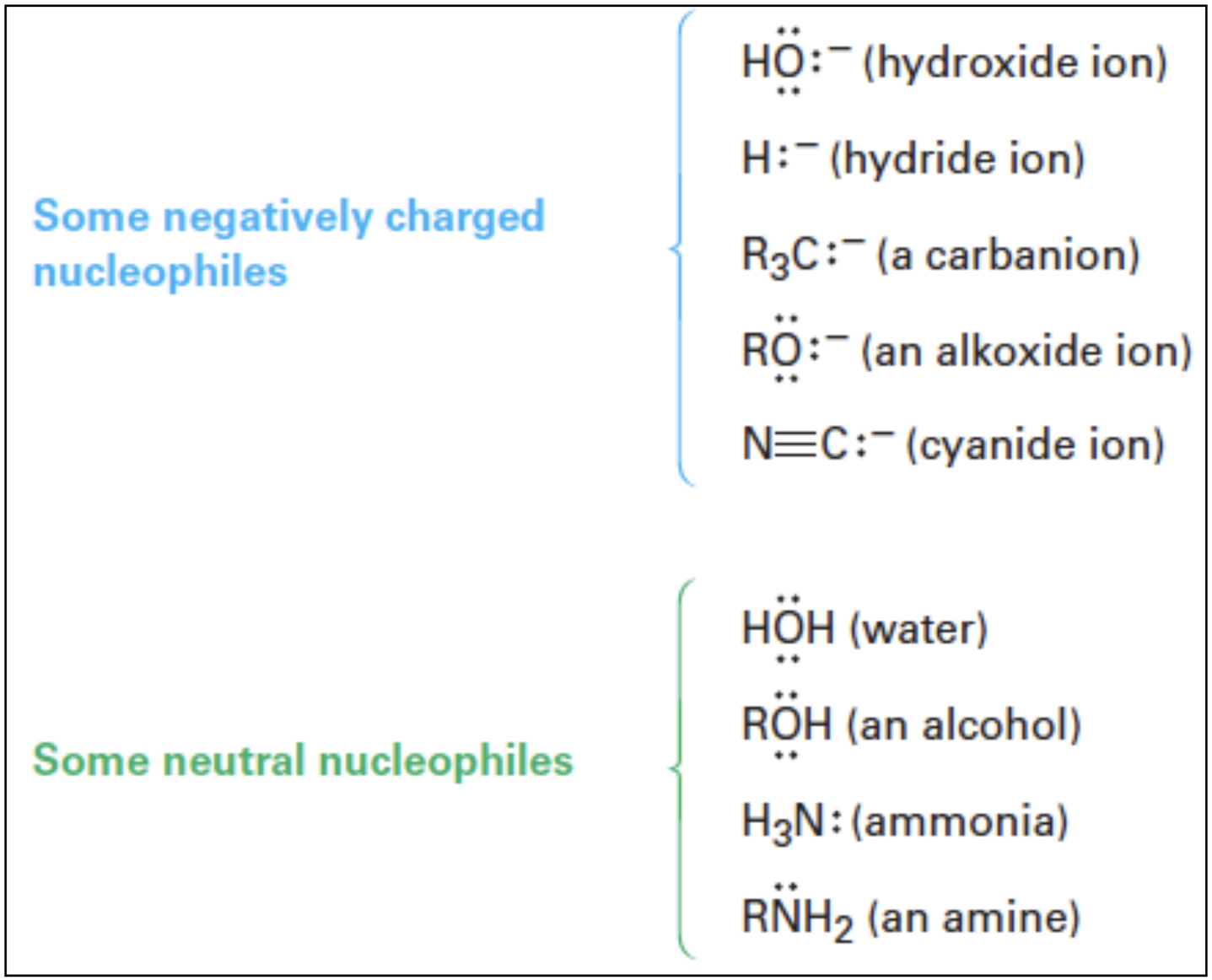
5-Idrossi-5-fenilpentanale
(miscela racemica)

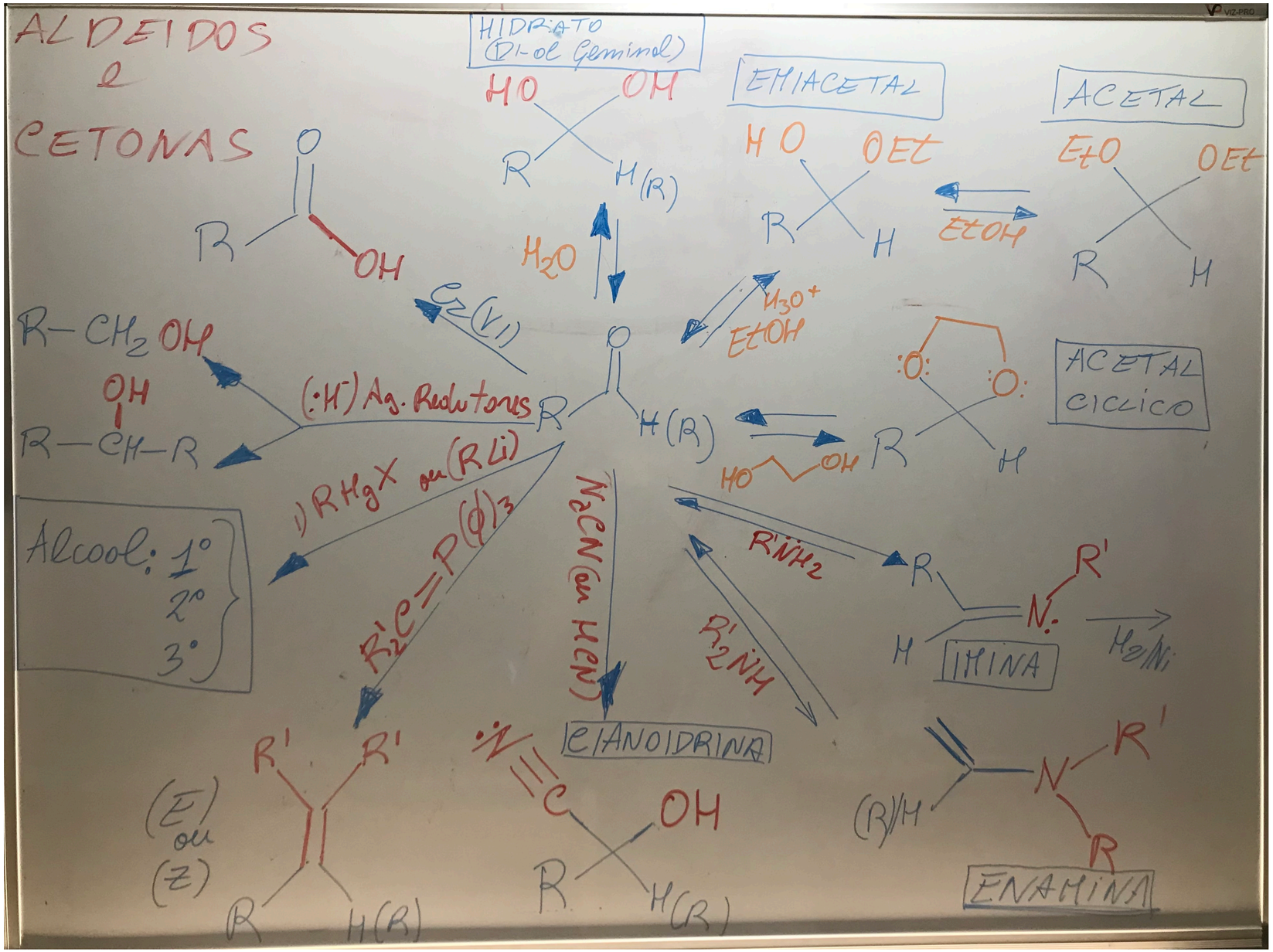
7) Reazione dell'anione acetiluro (base coniugata dell'acetilene): RCC:$^-$ Na$^+$



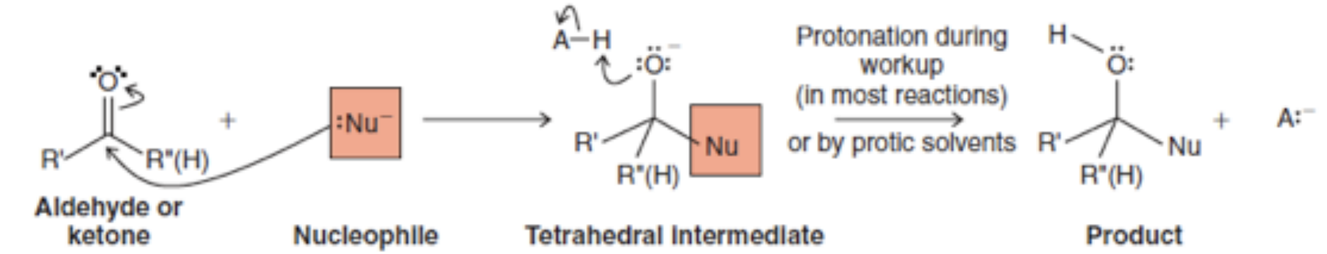


Reazioni di addizione nucleofila di aldeidi e chetoni




ALDEIDOS
e
CETONAS
HIDRATO
(Di-ol Geminal)
HEMIACETAL
ACETAL
ACETAL
CICLICO
Alcool: 1°
2°
3°
(:H⁻) Ag. Redutores
1) RMgX ou (RLi)
R'₂C=P(Φ)₃
N₂CN(ou HCN)
R'NH₂
R'₂NH
CIANOIDRINA
IMINA
ENAMINA
(E)
ou
(Z)

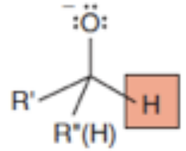
Generalized nucleophilic addition to an aldehyde or ketone:

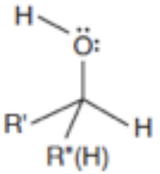


Aldehyde or ketone | Nucleophile | Tetrahedral intermediate | Product

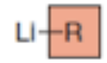
Examples:

Hydride [e.g., from $NaBH_4$ or $LiAlH_4$ (LAH)]

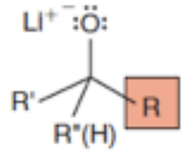


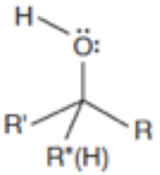


Alcohol (reduction)

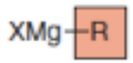


Alkyllithium

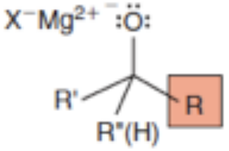


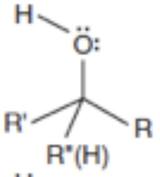


Alcohol (with C—C bond formation)

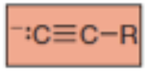


Grignard reagent

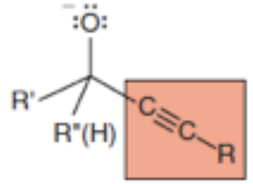


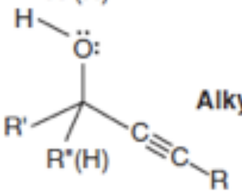


Alcohol (with C—C bond formation)

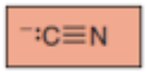


Alkynide anion

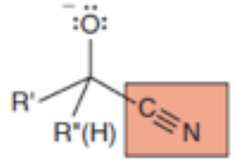


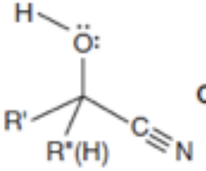


Alkynyl alcohol (C—C bond formation)



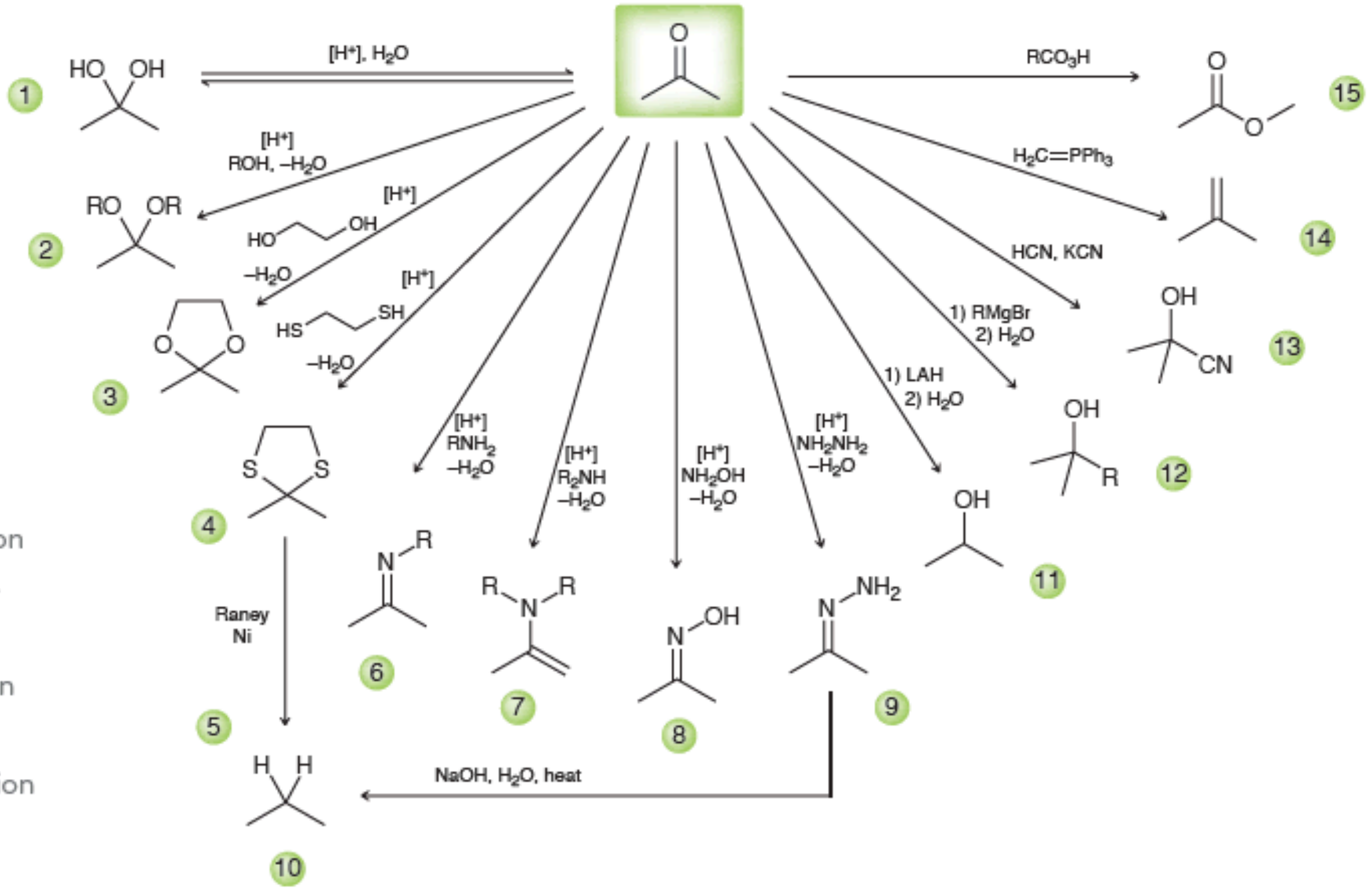
Cyanide

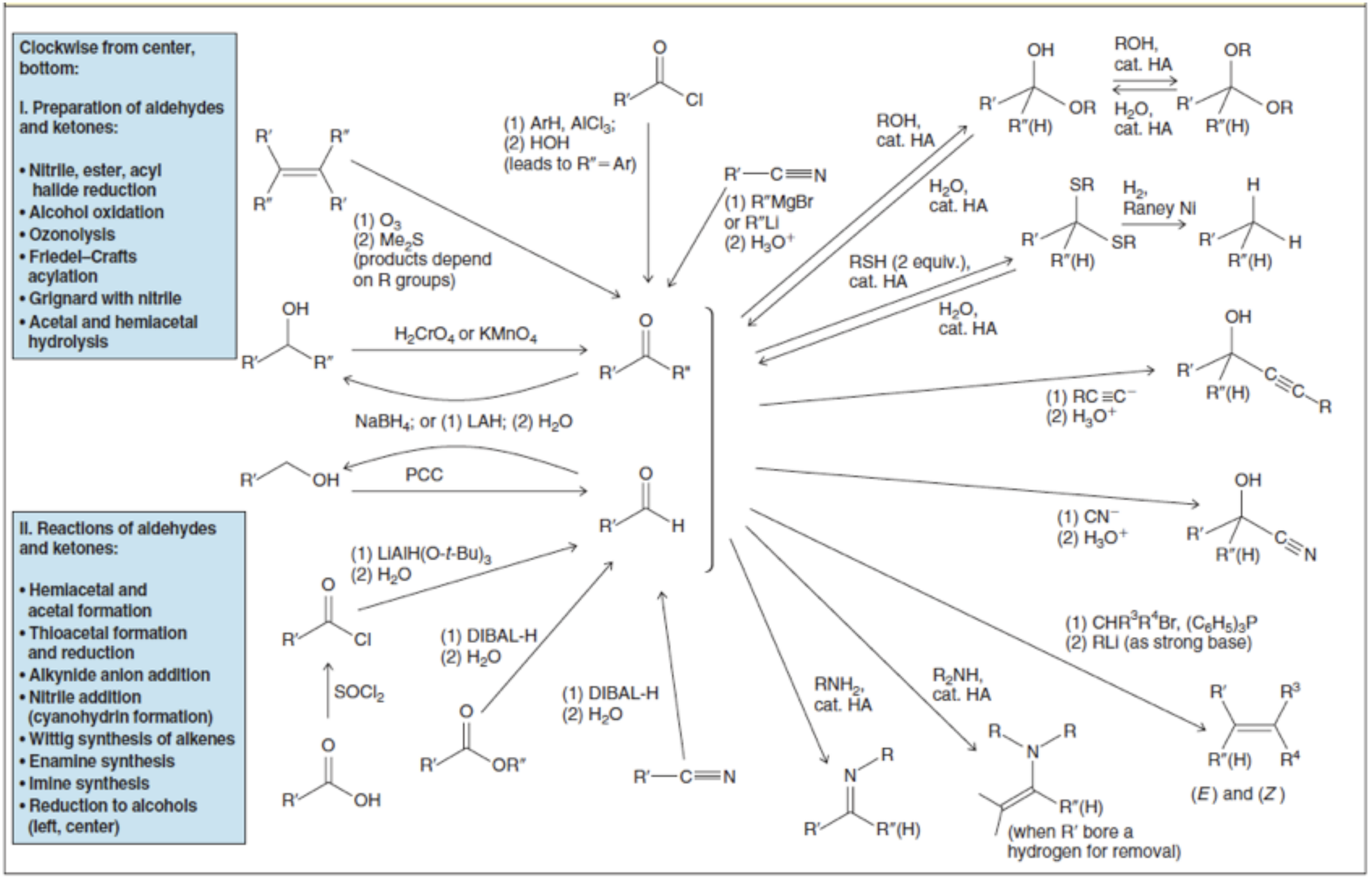




Cyanohydrin

1. Hydrate Formation
2. Acetal Formation
3. Cyclic Acetal Formation
4. Cyclic Thioacetal Formation
5. Desulfurization
6. Imine Formation
7. Enamine Formation
8. Oxime Formation
9. Hydrazone Formation
10. Wolff-Kishner Reduction
11. Reduction of a Ketone
12. Grignard Reaction
13. Cyanohydrin Formation
14. Wittig Reaction
15. Baeyer-Villiger Oxidation




Clockwise from center, bottom:
I. Preparation of aldehydes and ketones:
• Nitrile, ester, acyl halide reduction
• Alcohol oxidation
• Ozonolysis
• Friedel–Crafts acylation
• Grignard with nitrile
• Acetal and hemiacetal hydrolysis
II. Reactions of aldehydes and ketones:
• Hemiacetal and acetal formation
• Thioacetal formation and reduction
• Alkynide anion addition
• Nitrile addition (cyanohydrin formation)
• Wittig synthesis of alkenes
• Enamine synthesis
• Imine synthesis
• Reduction to alcohols (left, center)
(1) ArH, AlCl3; (2) HOH (leads to R″ = Ar)
(1) O3 (2) Me2S (products depend on R groups)
R′—C≡N (1) R″MgBr or R″Li (2) H3O+
ROH, cat. HA
H2O, cat. HA
RSH (2 equiv.), cat. HA
H2, Raney Ni
H2CrO4 or KMnO4
NaBH4; or (1) LAH; (2) H2O
PCC
(1) RC≡C− (2) H3O+
(1) CN− (2) H3O+
(1) LiAlH(O-t-Bu)3 (2) H2O
SOCl2
(1) DIBAL-H (2) H2O
RNH2, cat. HA
R2NH, cat. HA
(1) CHR3R4Br, (C6H5)3P (2) RLi (as strong base)
(E) and (Z)
(when R′ bore a hydrogen for removal)

Preparazione

Di aldeidi e chetoni

Riduzione e ossidazione di aldeidi e chetoni

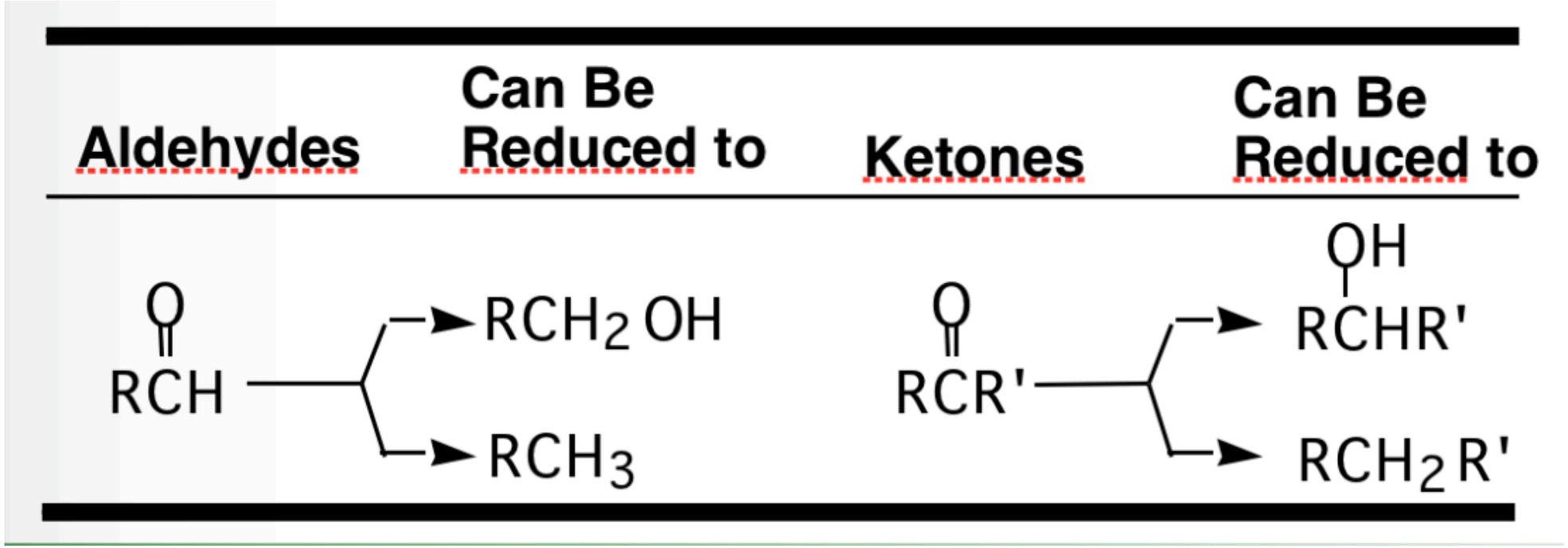
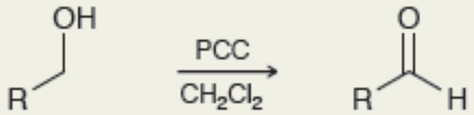


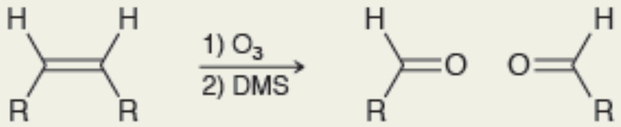
TABLE 20.1 A SUMMARY OF ALDEHYDE PREPARATION METHODS COVERED IN PREVIOUS CHAPTERS

REACTION	SECTION
Oxidation of Primary Alcohols	13.10



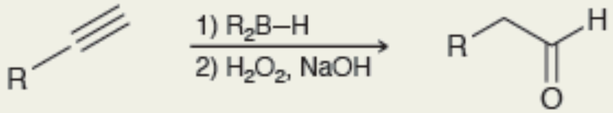
When treated with a strong oxidizing agent, primary alcohols are oxidized to carboxylic acids. Formation of an aldehyde requires an oxidizing agent, such as PCC, that will not further oxidize the resulting aldehyde.

Ozonolysis of Alkenes	9.11



Ozonolysis will cleave a C═C double bond. If either carbon atom bears a hydrogen atom, an aldehyde will be formed.

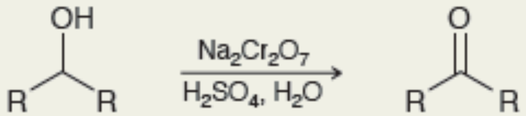
Hydroboration-Oxidation of Terminal Alkynes	10.7



Hydroboration-oxidation results in an anti-Markovnikov addition of water across a π bond, followed by tautomerization of the resulting enol to form an aldehyde.

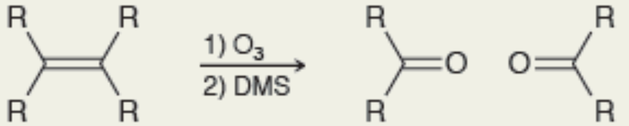
TABLE 20.2 A SUMMARY OF KETONE PREPARATION METHODS COVERED IN PREVIOUS CHAPTERS

REACTION	SECTION
Oxidation of Secondary Alcohols	13.10



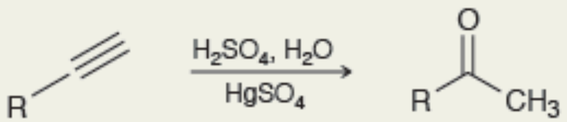
A variety of strong or mild oxidizing agents can be used to oxidize secondary alcohols. The resulting ketone does not undergo further oxidation.

Ozonolysis of Alkenes	9.11



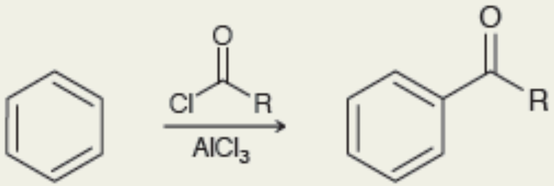
Tetrasubstituted alkenes are cleaved to form ketones.

Acid-Catalyzed Hydration of Terminal Alkynes	10.7



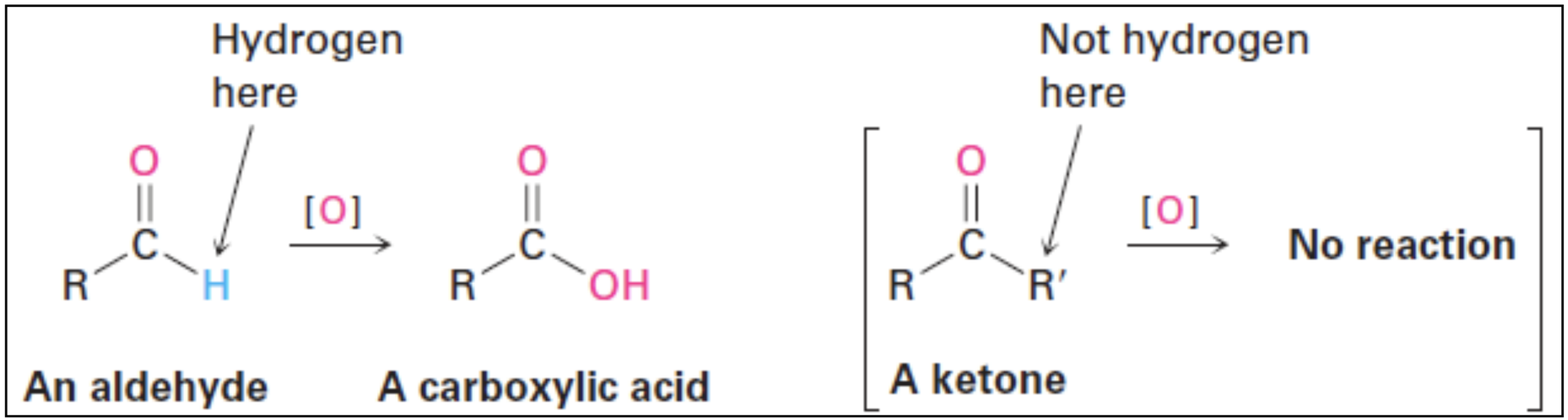
This procedure results in a Markovnikov addition of water across the π bond, followed by tautomerization to form a methyl ketone.

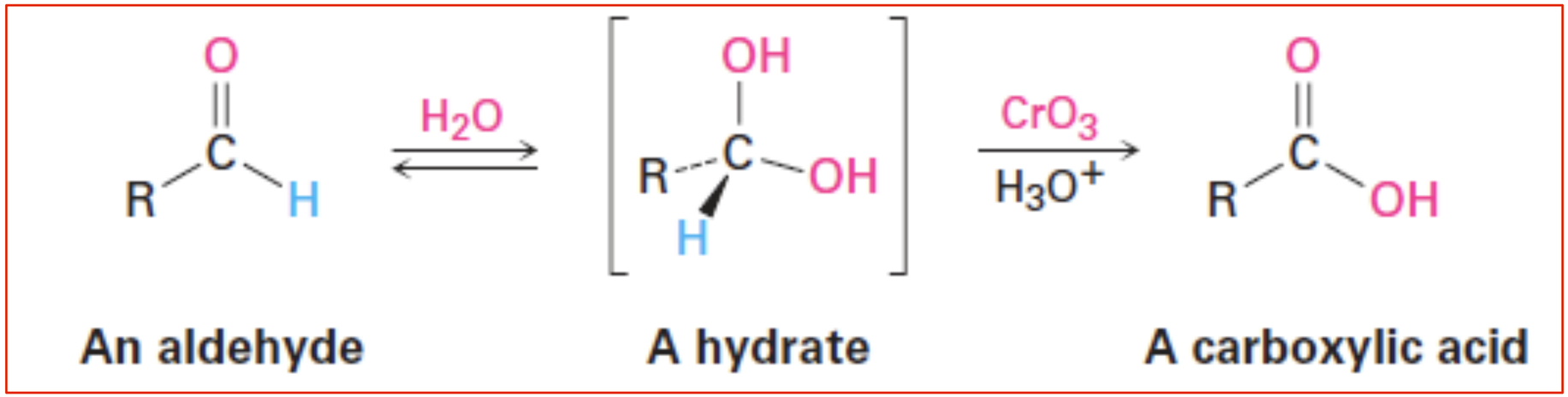
Friedel-Crafts Acylation	19.6



Aromatic rings that are not too strongly deactivated will react with an acid halide in the presence of a Lewis acid to produce an aryl ketone.

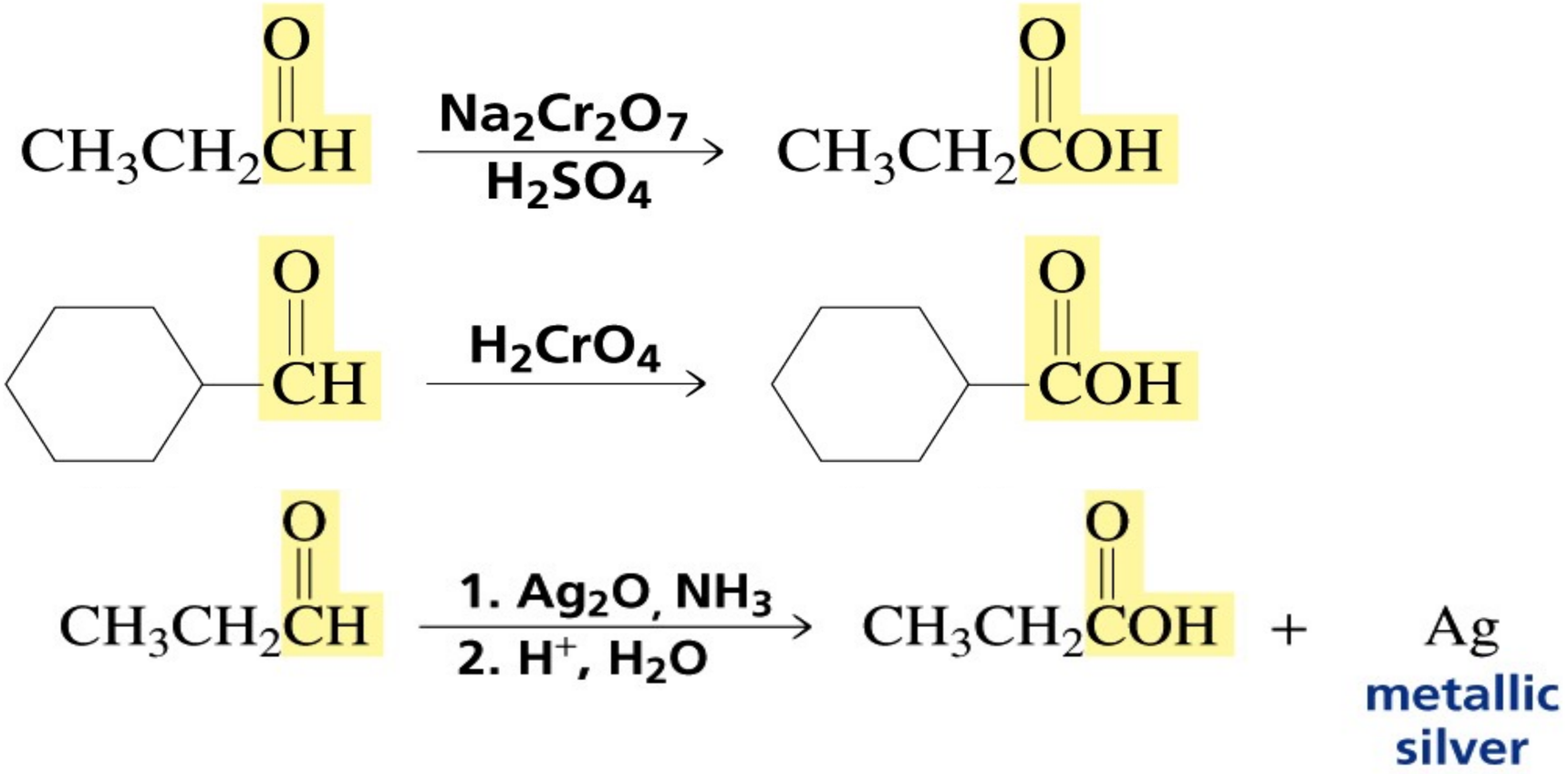
Ossidazione delle aldeidi



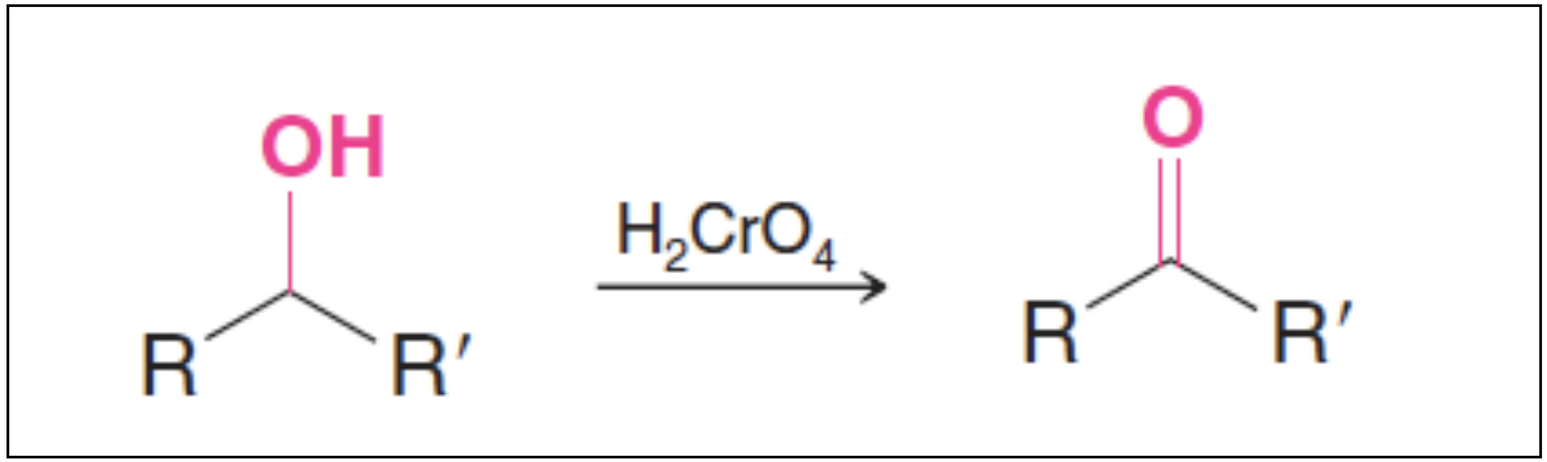


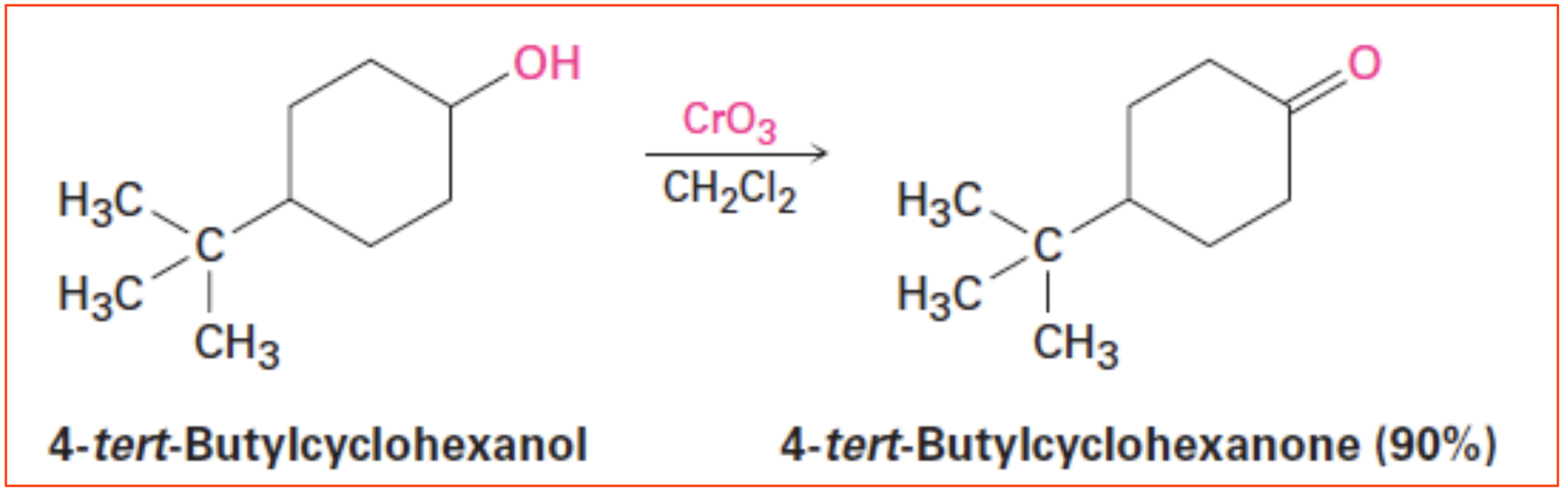
Ossidazione degli aldeidi in acidi carbossilici

✓ Gli aldeidi sono ossidati da Cr(VI) o Ag(I) ad acidi carbossilici

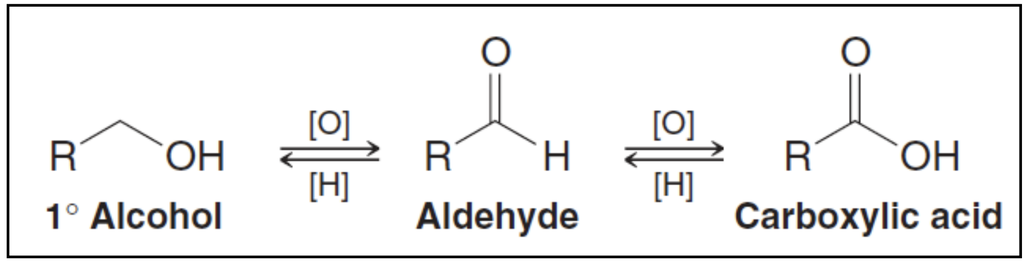


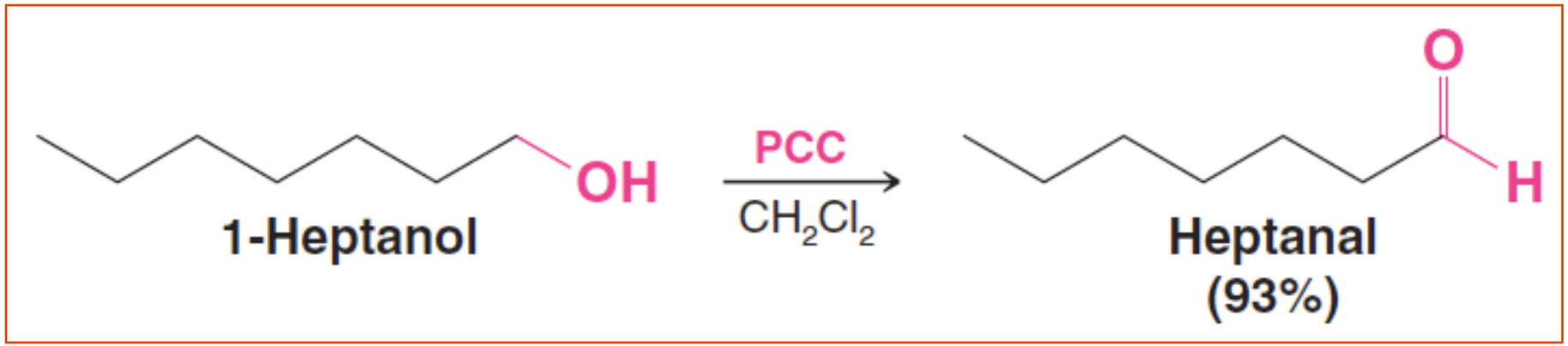
Ossidazione dei chetoni ad alcoli secondari

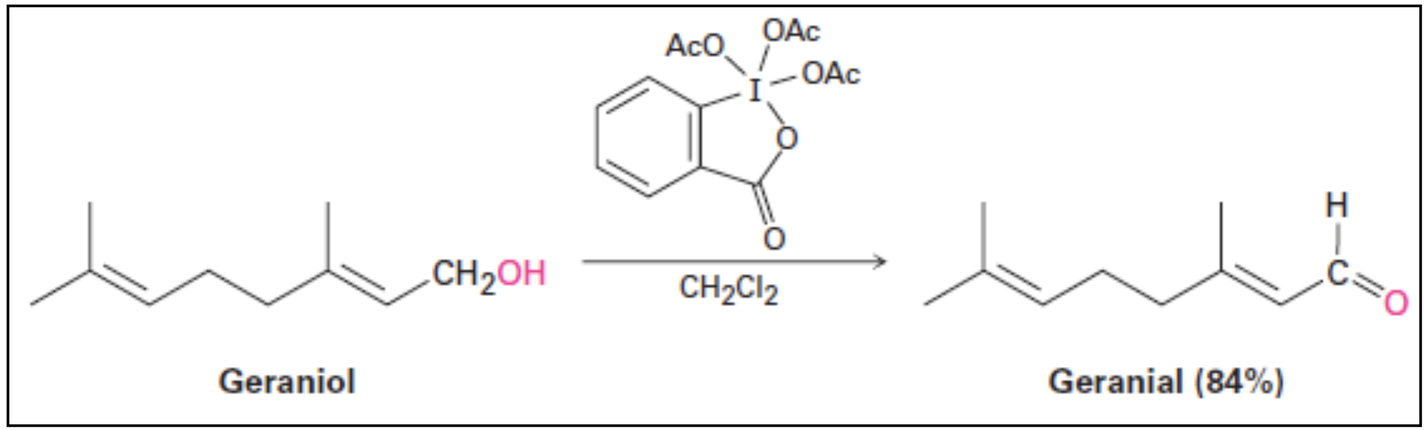




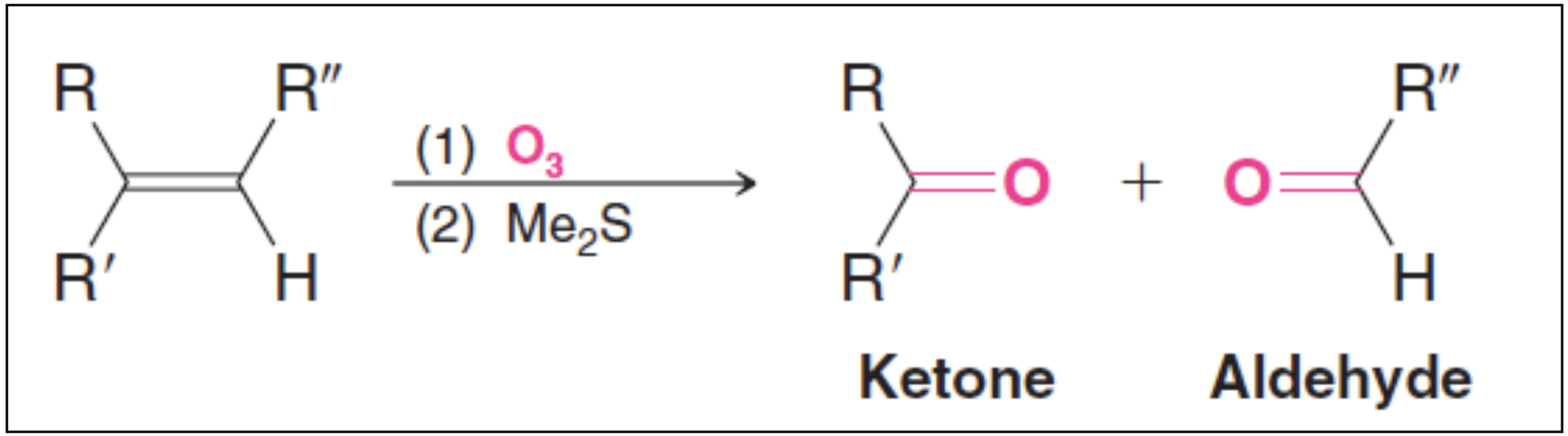
Ossidazione delle aldeidi ad alcoli primari

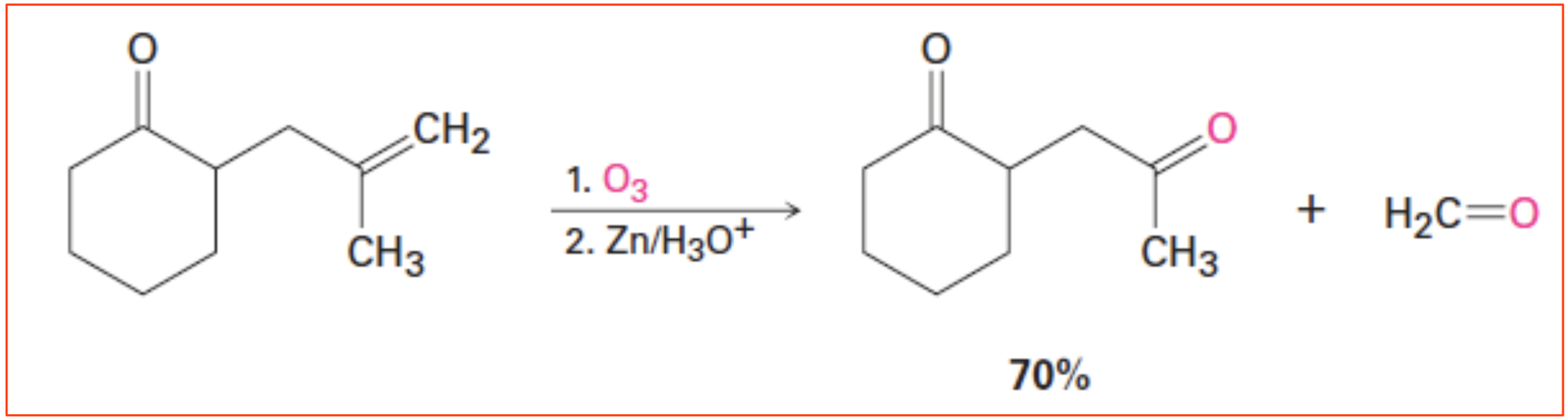




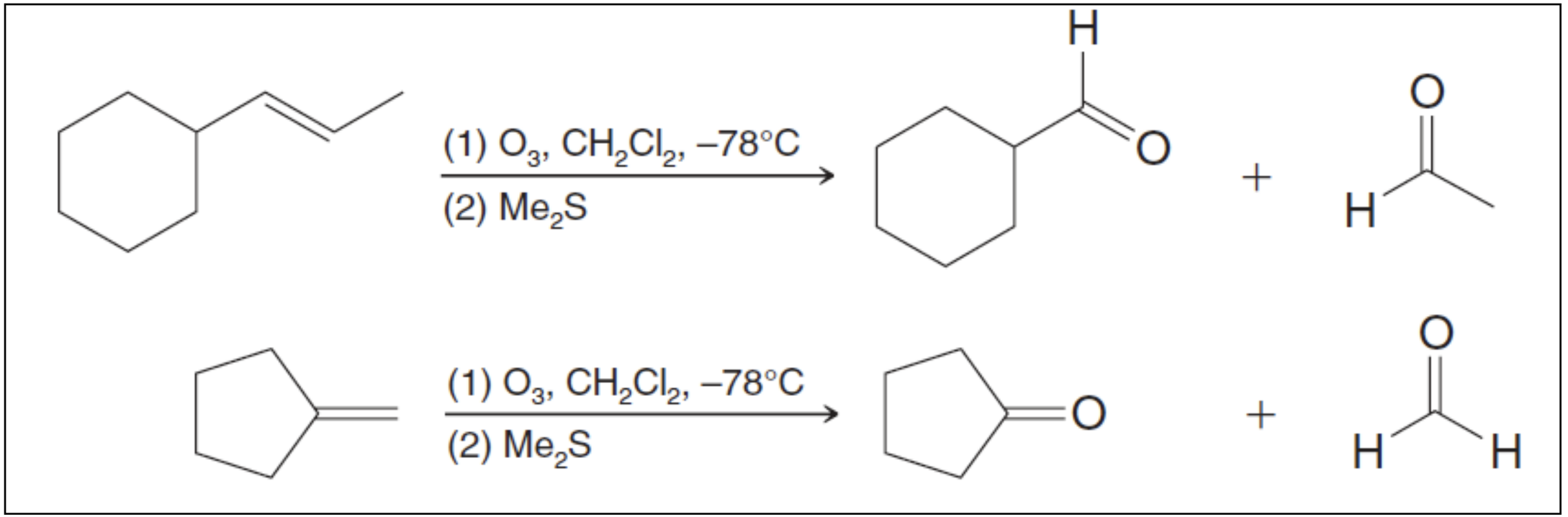


Sintesi di aldeidi e chetoni
Ozonolisi degli alcheni

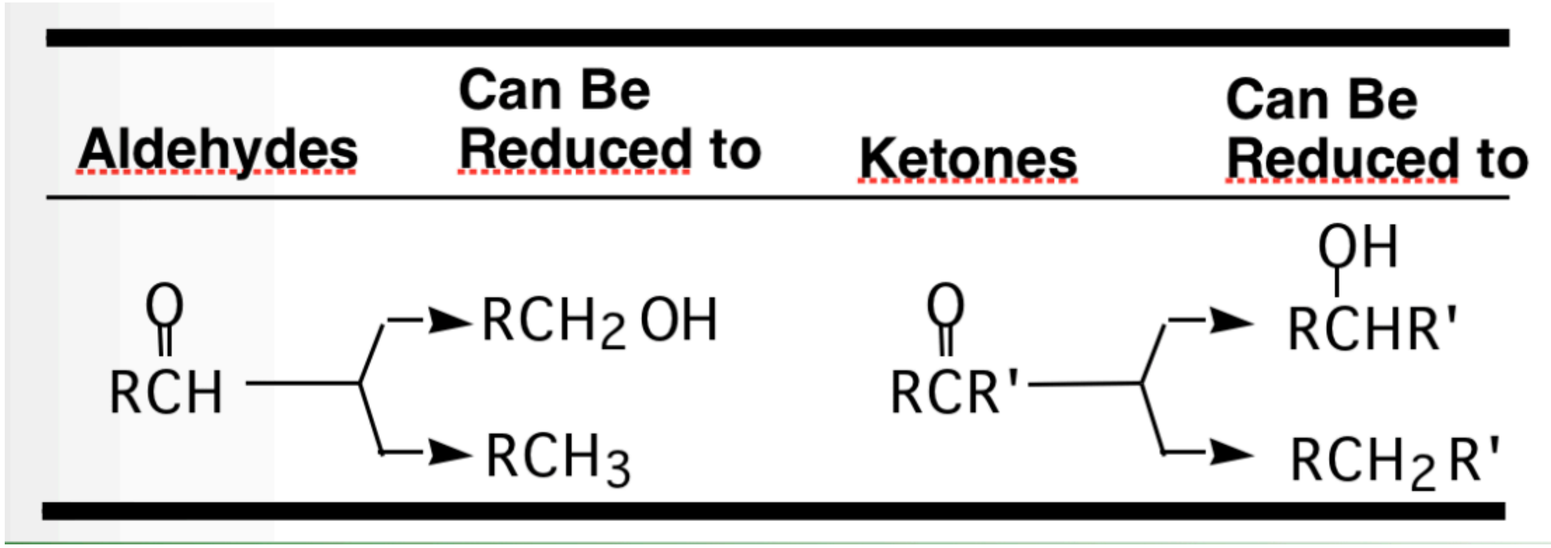


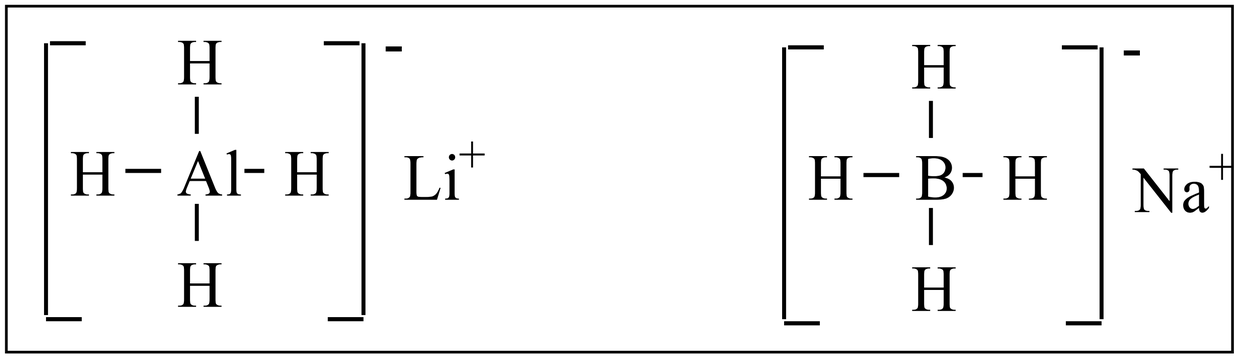


Sintesi di aldeidi e chetoni
Ozonolisi degli alcheni



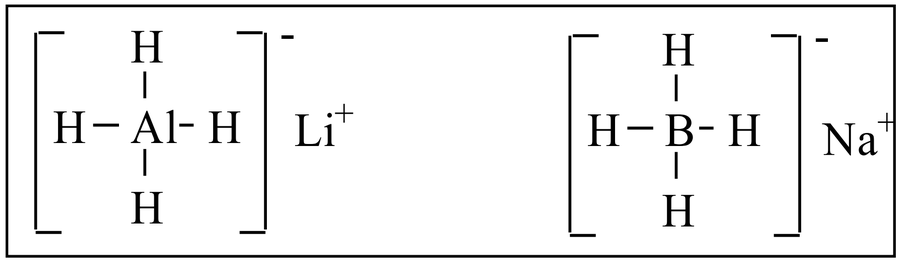
Riduzione con ione idruro ($H:^-$)

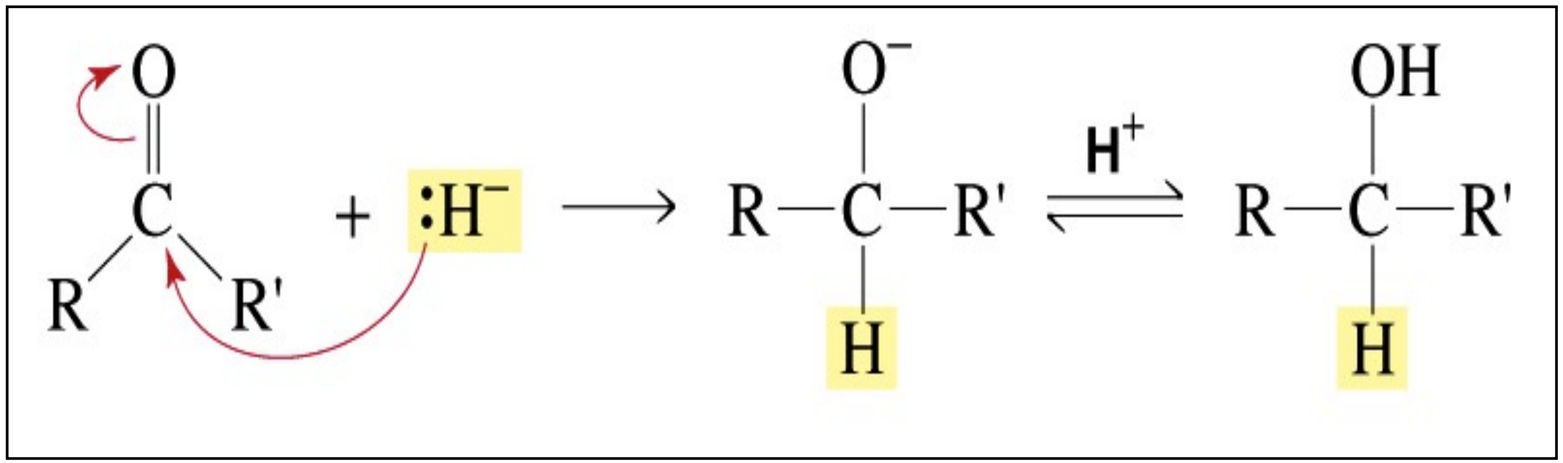


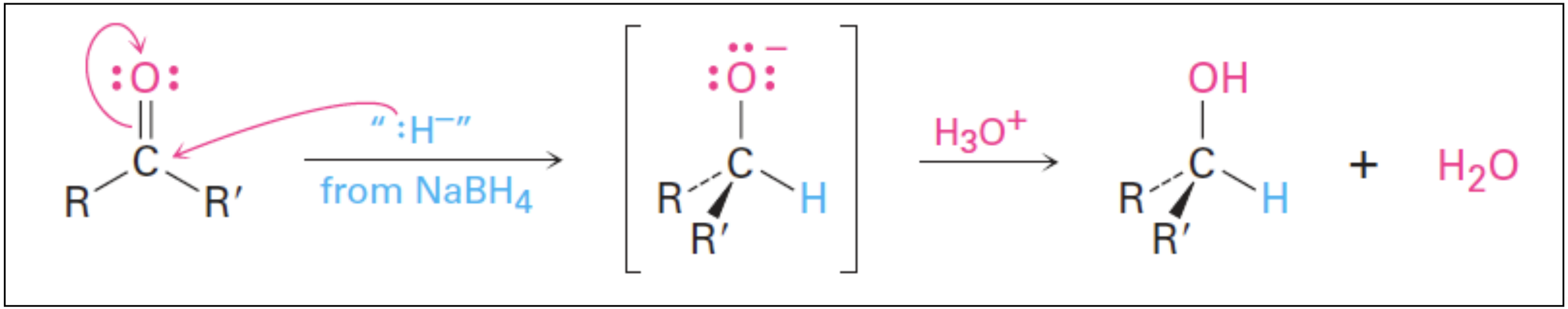


- ✓$NaBH_4$ (**Sodio Boro Idruro**) e
- ✓$LiAlH_4$ (**Litio Aluminio Idruro**, LAH)
  - Fonte di ioni idruro $H:^-$,
  - eccelente nucleofilo

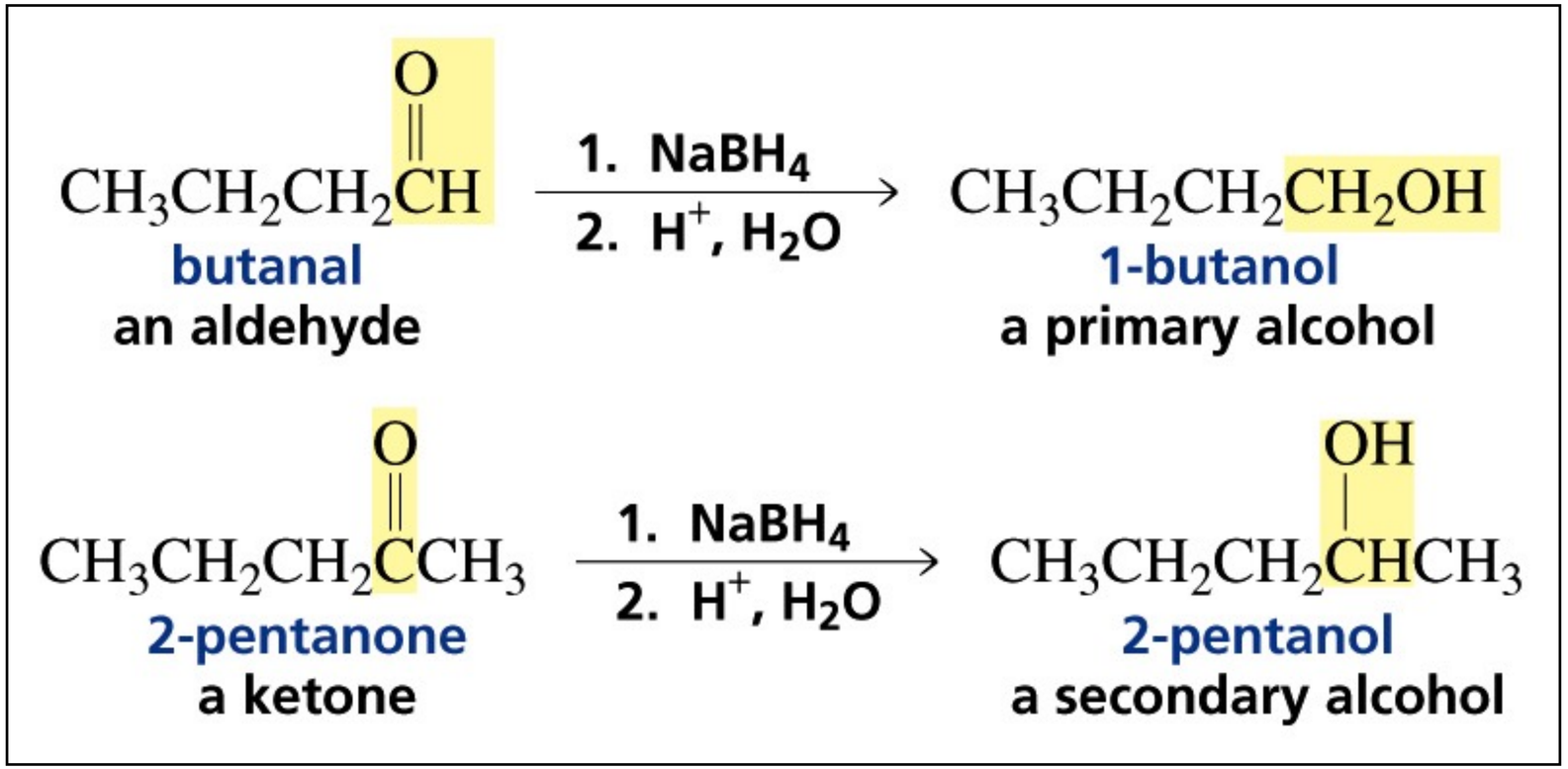
Riduzione con ione idruro (H:⁻)

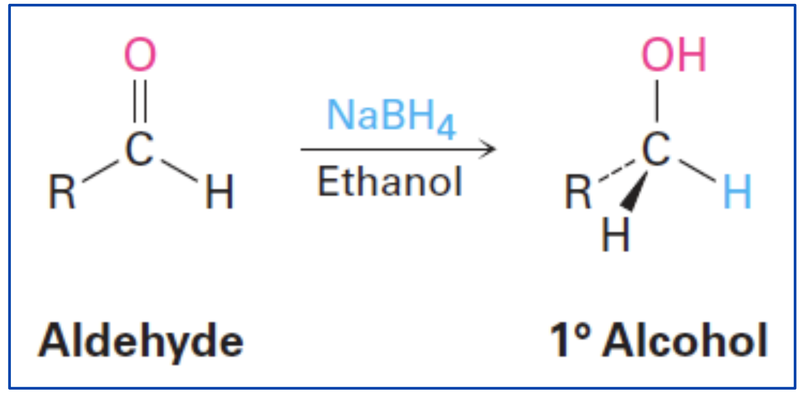


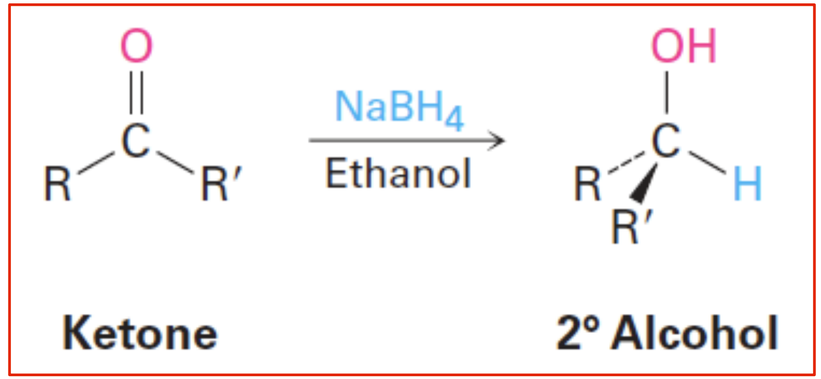




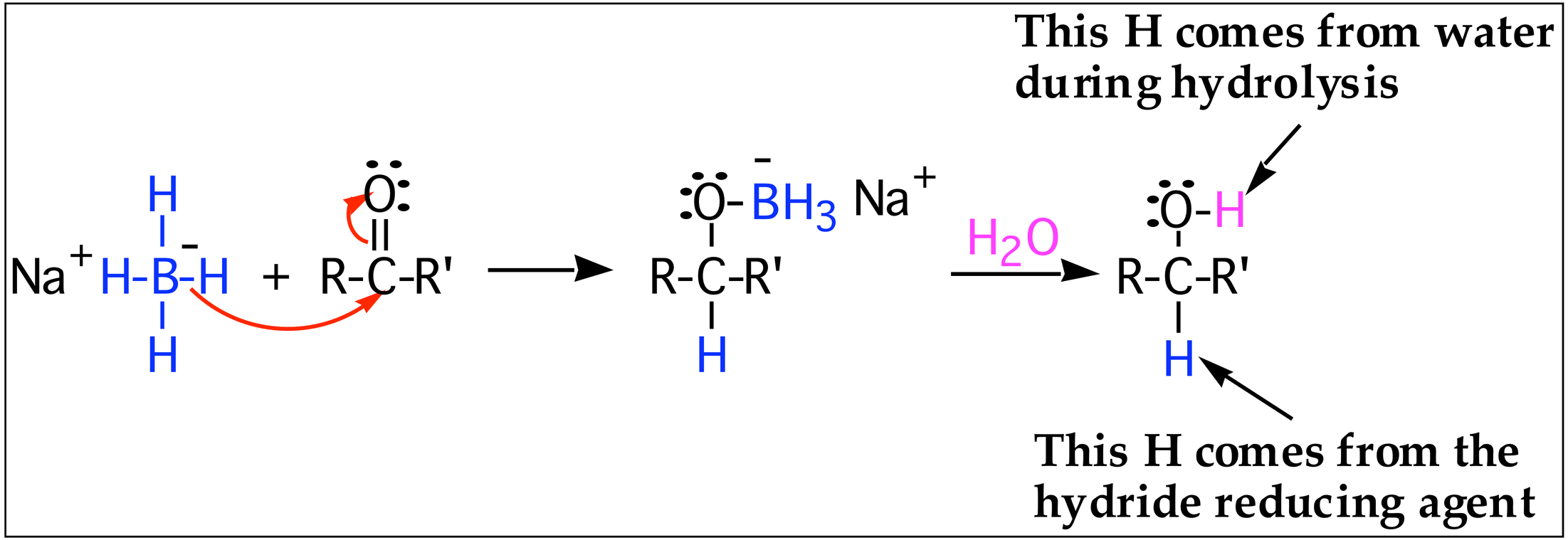
Riduzione con $NaBH_4$ fonte di ($H:^-$)





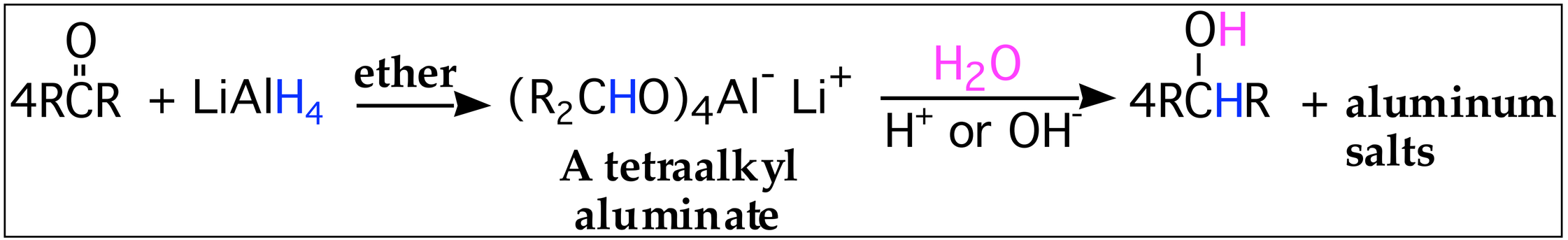


Meccanismo di Riduzione del $NaBH_4$ fonte di ($H:^-$)

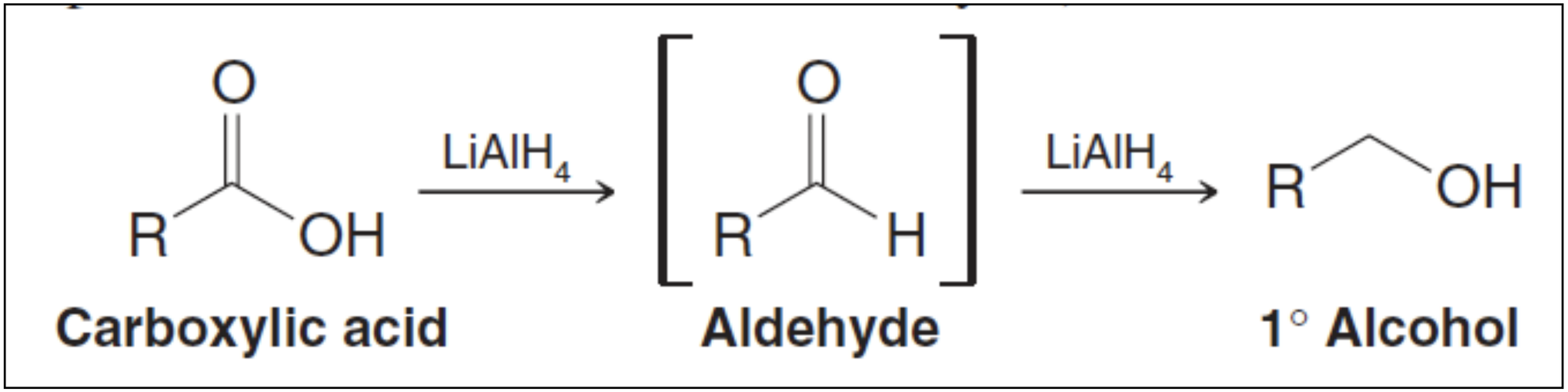


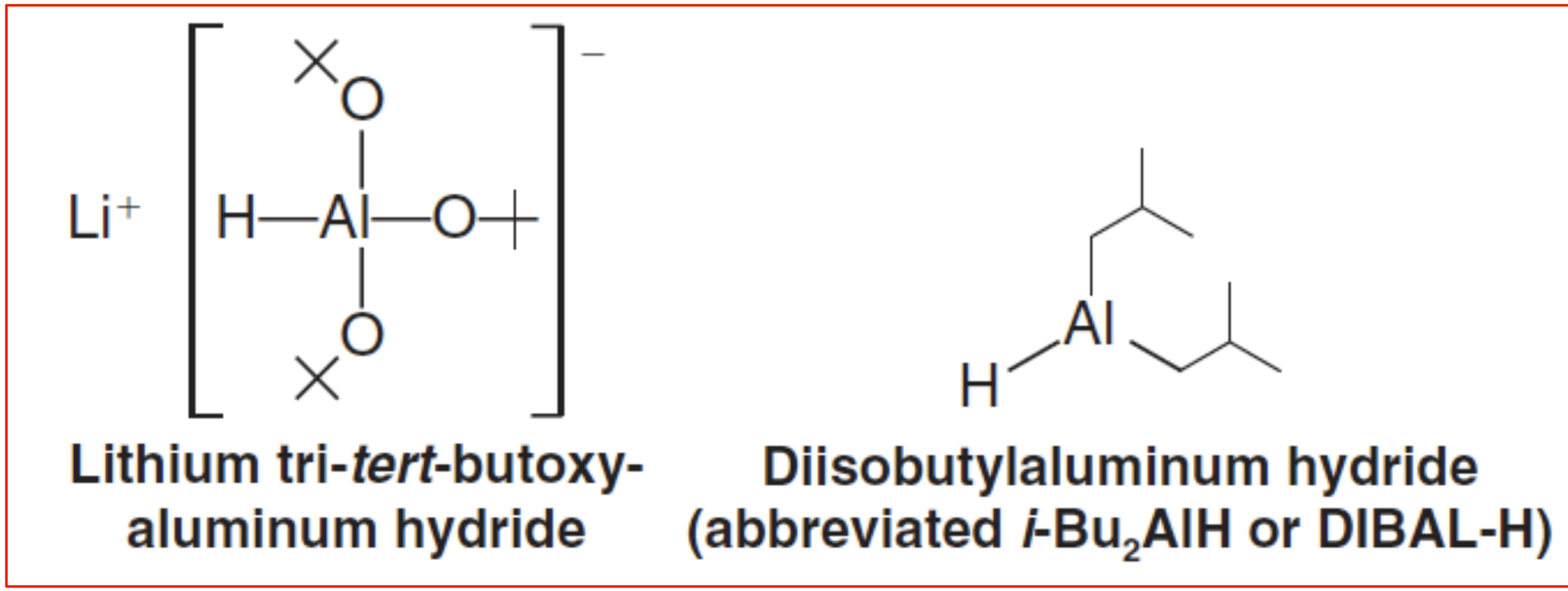
Riduzione dei chetoni con $LiAlH_4$ fonte di ($H:^-$)

- A differenza di $NaBH_4$, $LiAlH_4$ reagisce violentemente con acqua, alcol e altri solventi protici
- La riduzione deve avvenire in etere

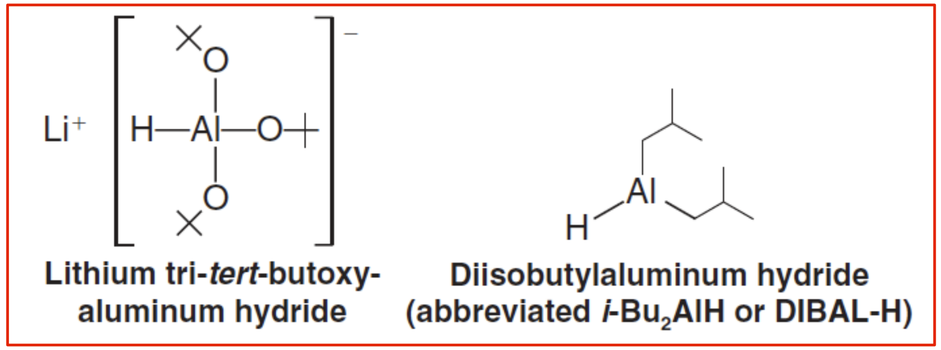


Riduzione degli acidi carbossilici e aldeidi con $LiAlH_4$ fonte di ($H:^-$)



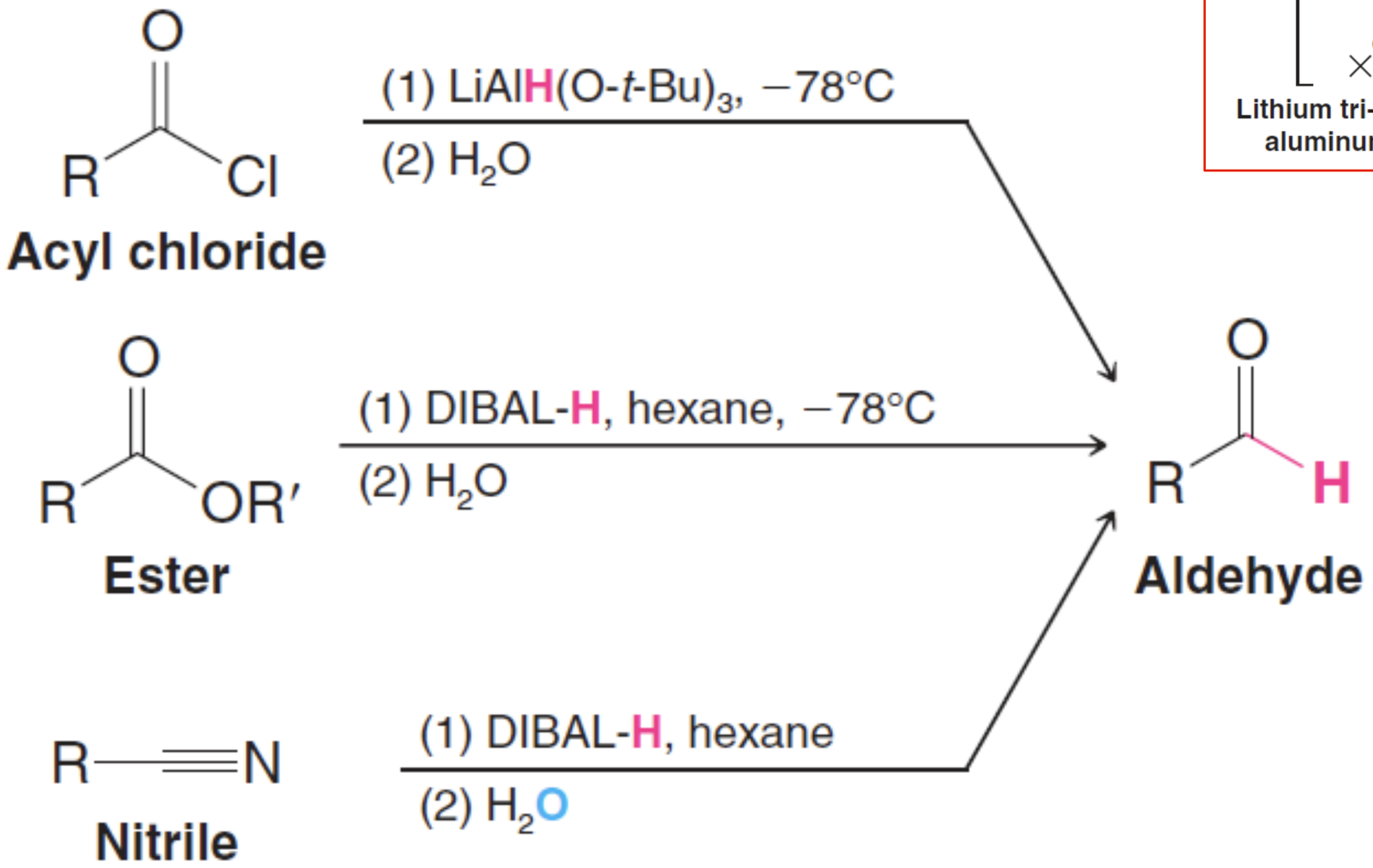


Formazioni delle delle aldeidi con riduttori deboli (DIBAL) in presenza di cloruro acilico, estere e nitrile.

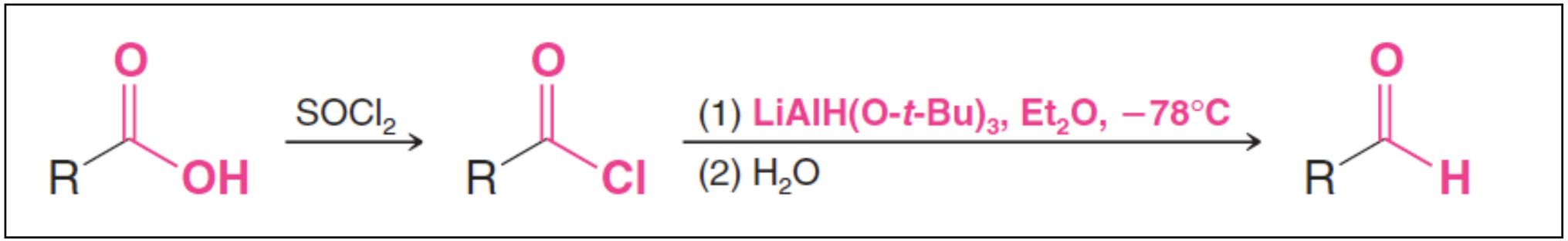


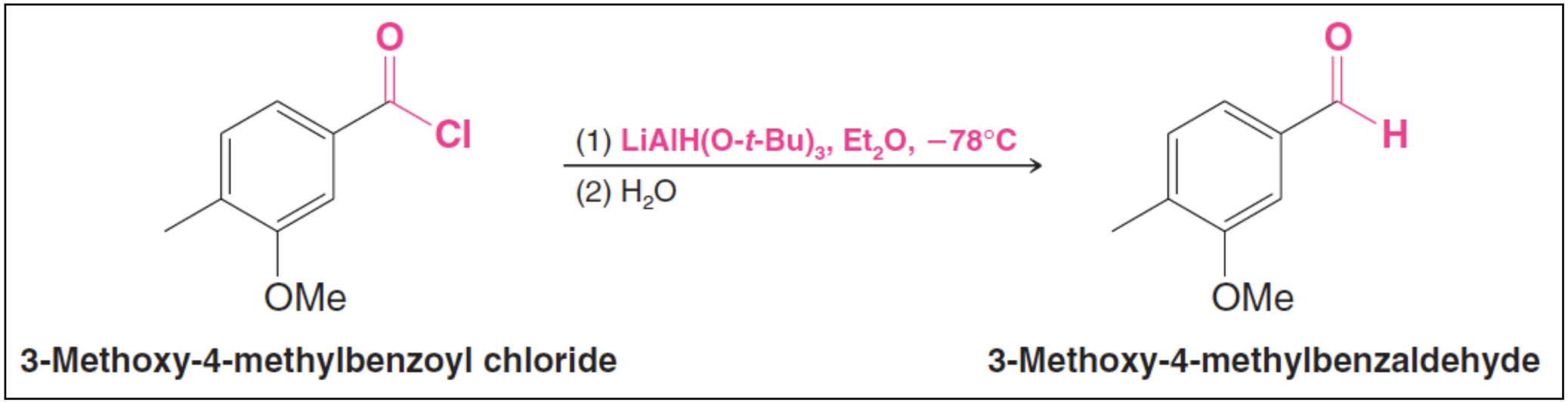
Lithium tri-*tert*-butoxy-aluminum hydride

Diisobutylaluminum hydride (abbreviated *i*-Bu_2AlH or DIBAL-H)



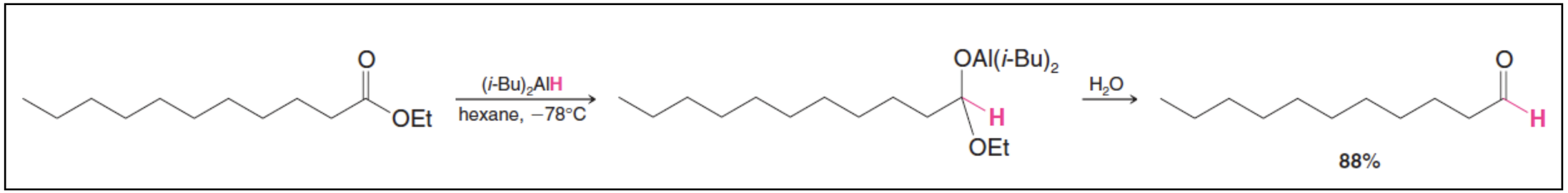
Sintesi di aldeidi da acidi e derivati carbossilici (Cloruro acilico)

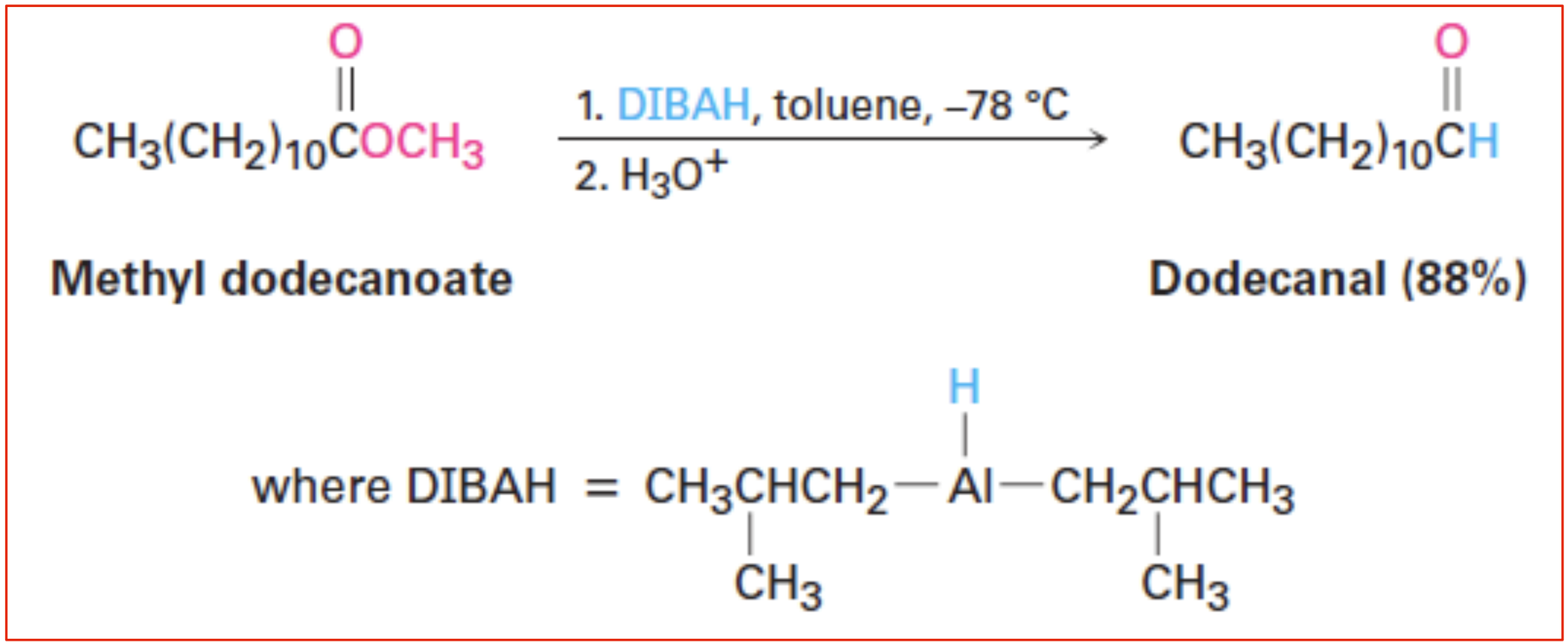




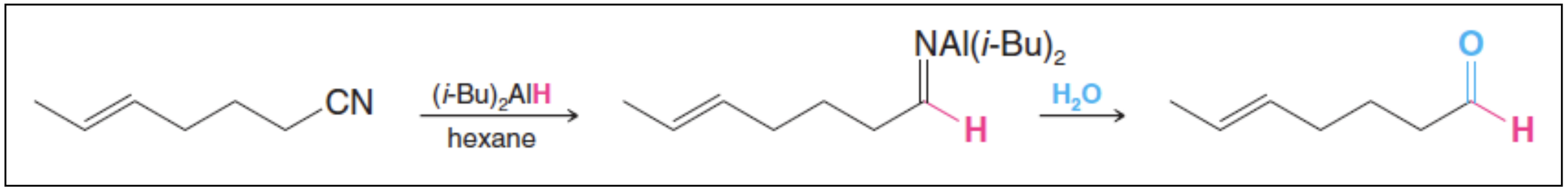
3-Methoxy-4-methylbenzoyl chloride **3-Methoxy-4-methylbenzaldehyde**

Sintesi di aldeidi da acidi e derivati carbossilici (Esteri)

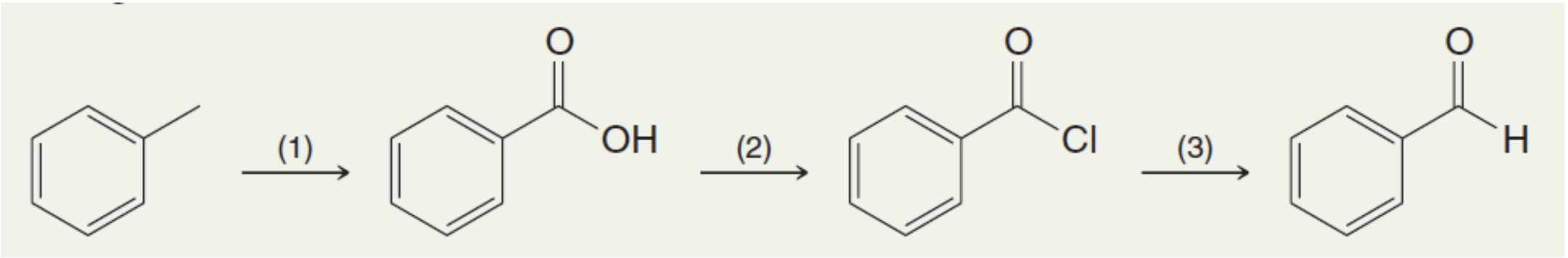




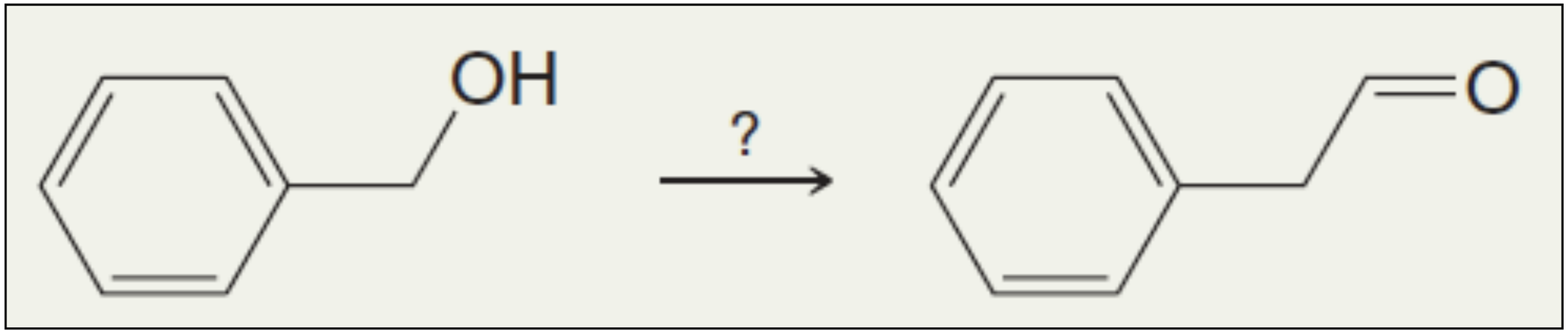
Sintesi di aldeidi da acidi e derivati carbossilici (Nitrili)



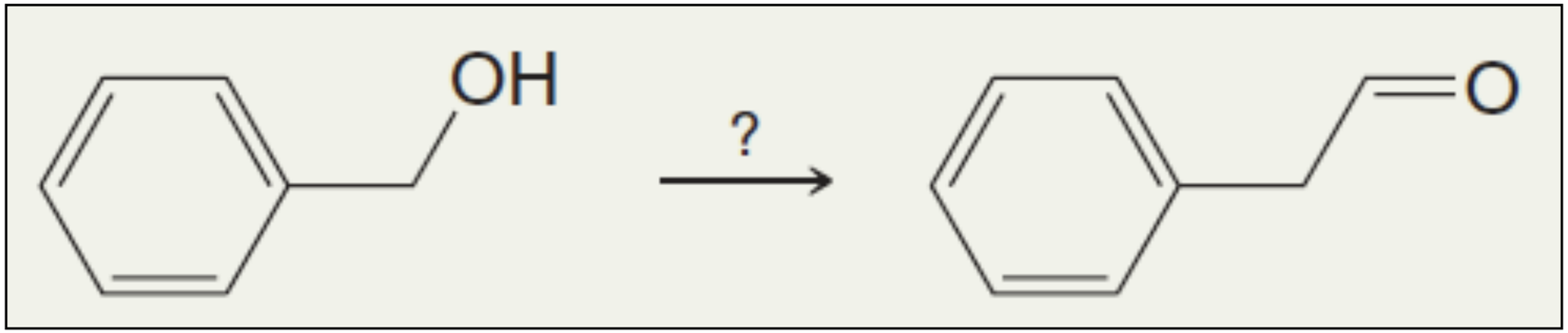
ESERCIZIO: FORNIRE i REAGENTI PER LE SEGUENTI TRASFORMAZIONI

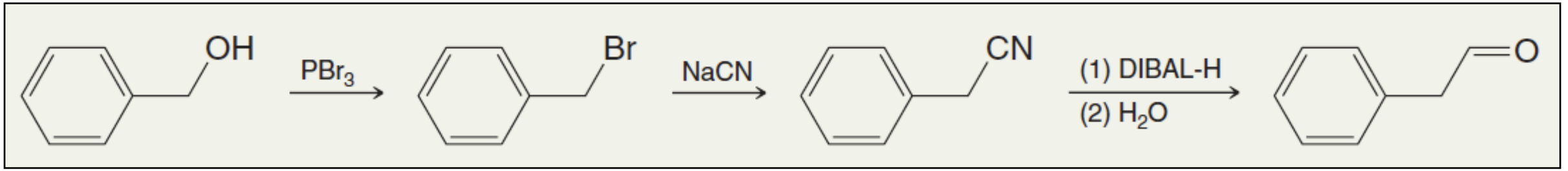


ESERCIZIO: PARTENDO DALL'ALCOL BENZILICO , PROPONETE UNA SINTESI PER IL FENILETANO

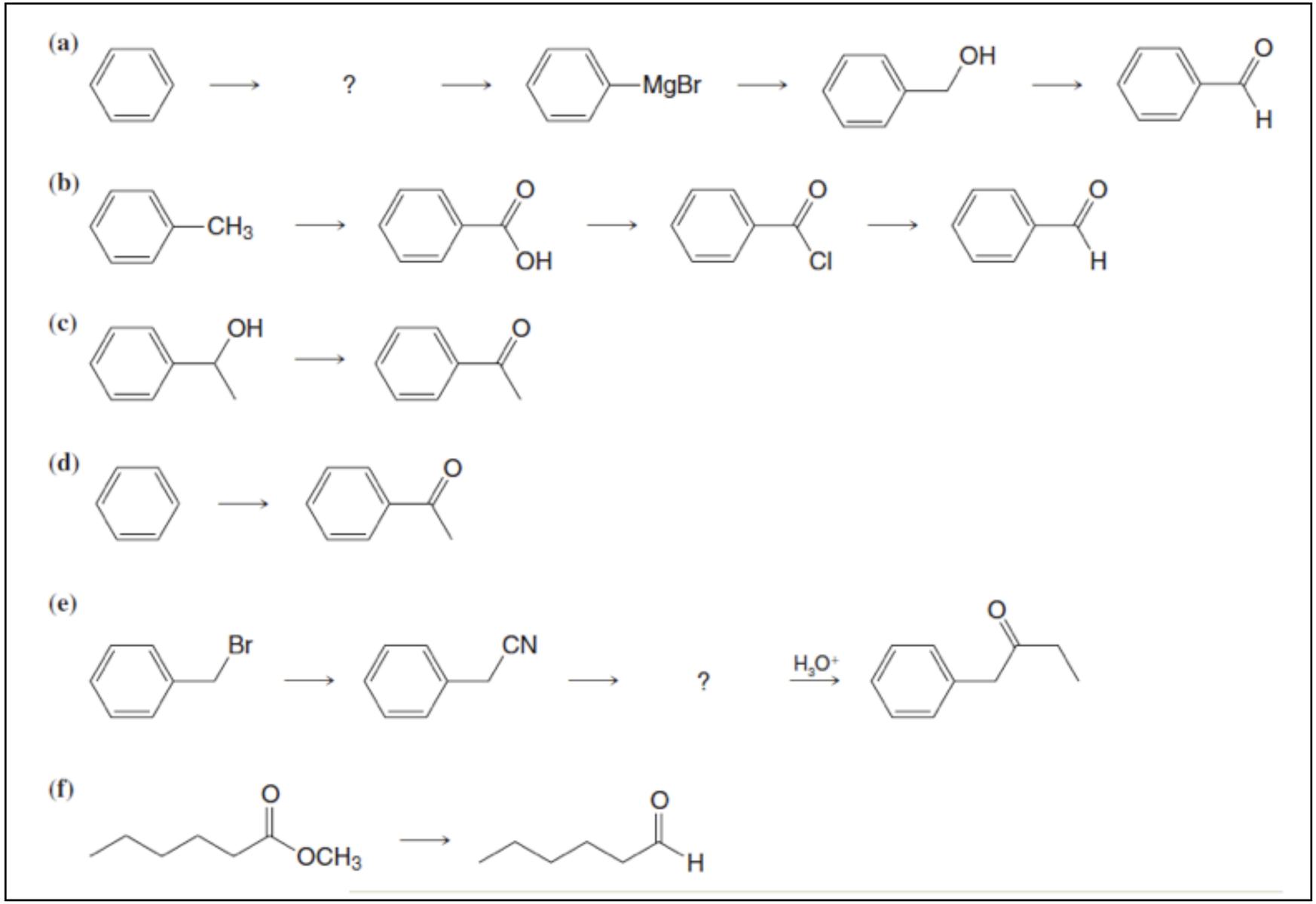


ESERCIZIO: PARTENDO DALL'ALCOL BENZILICO , PROPONETE UNA SINTESI PER IL FENILETANO

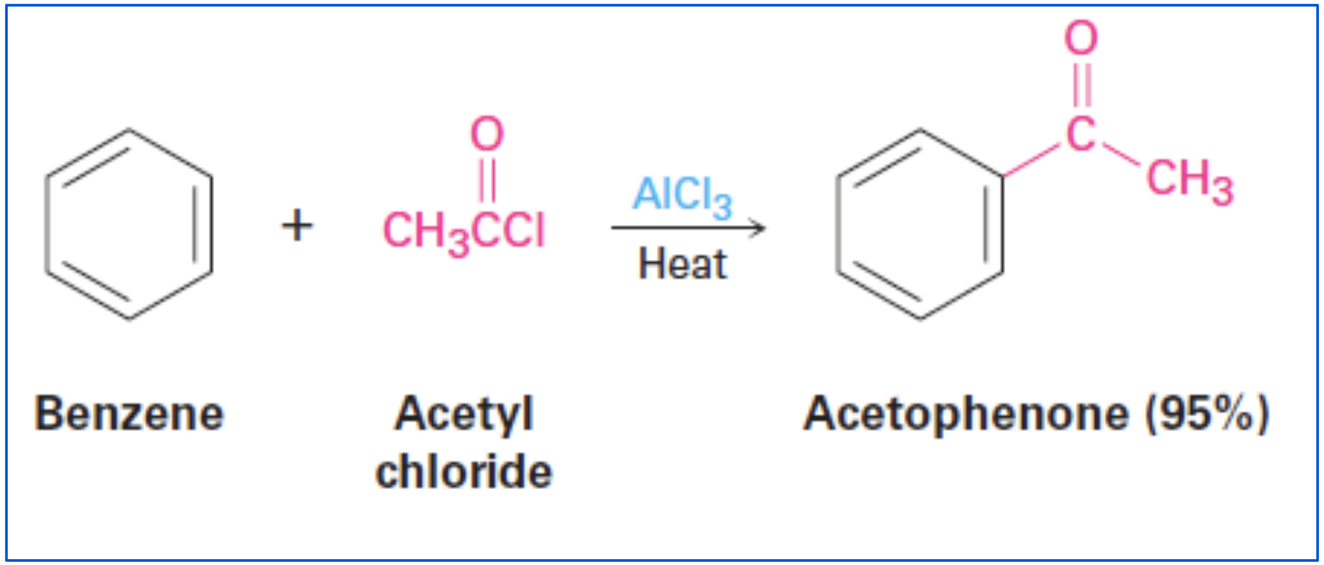


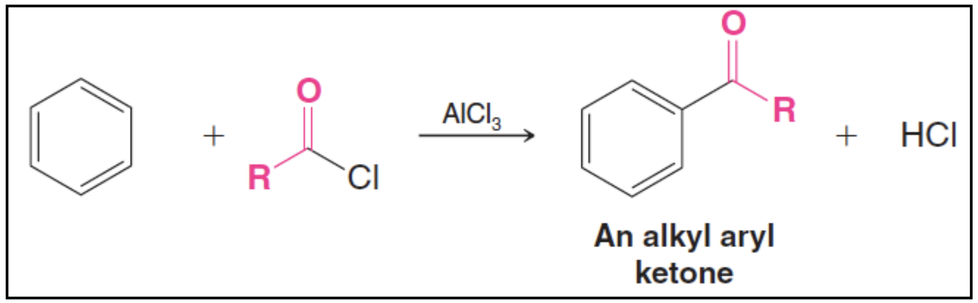


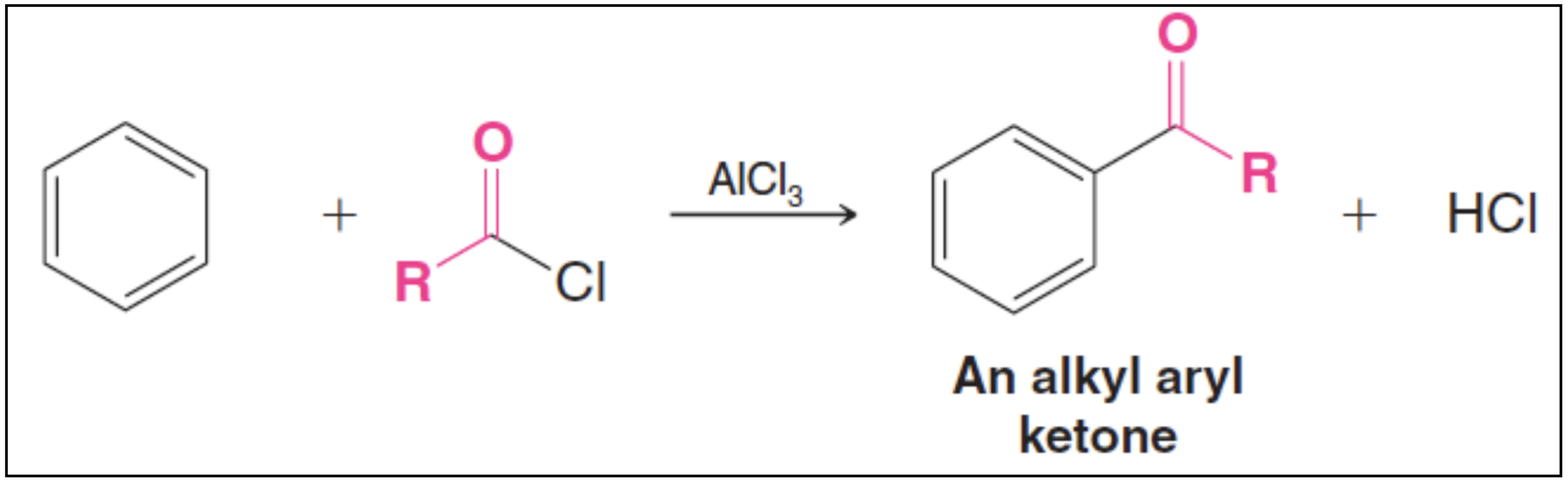
Problema: fornire i reagenti e indicare gli intermediari per ciascuna delle seguenti sintesi



Sintesi dei chetoni a partire dai benzeni: REAZIONI DI FRIEDEL CRAFT







10. Aldeidi e Chetoni

(1) Reattività dei composti carbonilici.

(2) Addizione di nucleofili forti e deboli al carbonio carbonilico.

(3) Formazione di immine ed enammine.

(4) Formazione di acetali e emiacetali come gruppi protettori del gruppo carbonilico.

(5) Reazione di Wittig.

(6) ~~Addizione nucleofilica ad aldeidi e chetoni alfa,beta-insaturi in presenza di nucleofili deboli (addizione-1,4 coniugata) e forti (addizione-1,2 diretta).~~