10. Aldeidi e Chetoni

(1) Reattività dei composti carbonilici.

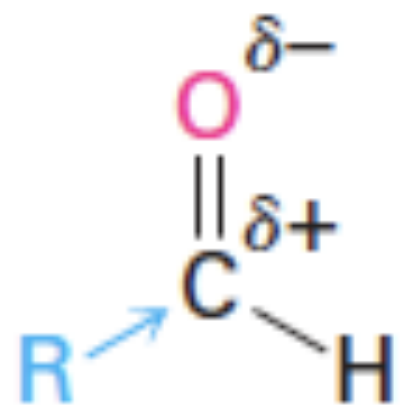
(2) Addizione di nucleofili forti e deboli al carbonio carbonilico.

(3) Formazione di immine ed enammine.

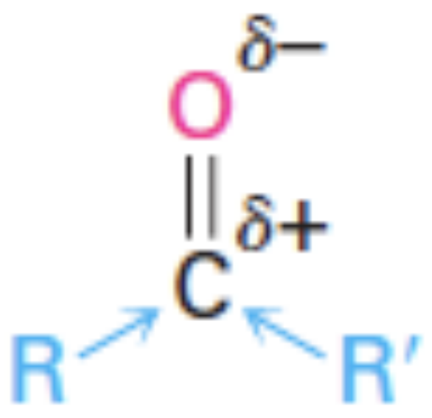
(4) Formazione di acetali e emiacetali come gruppi protettori del gruppo carbonilico.

(5) Reazione di Wittig.

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



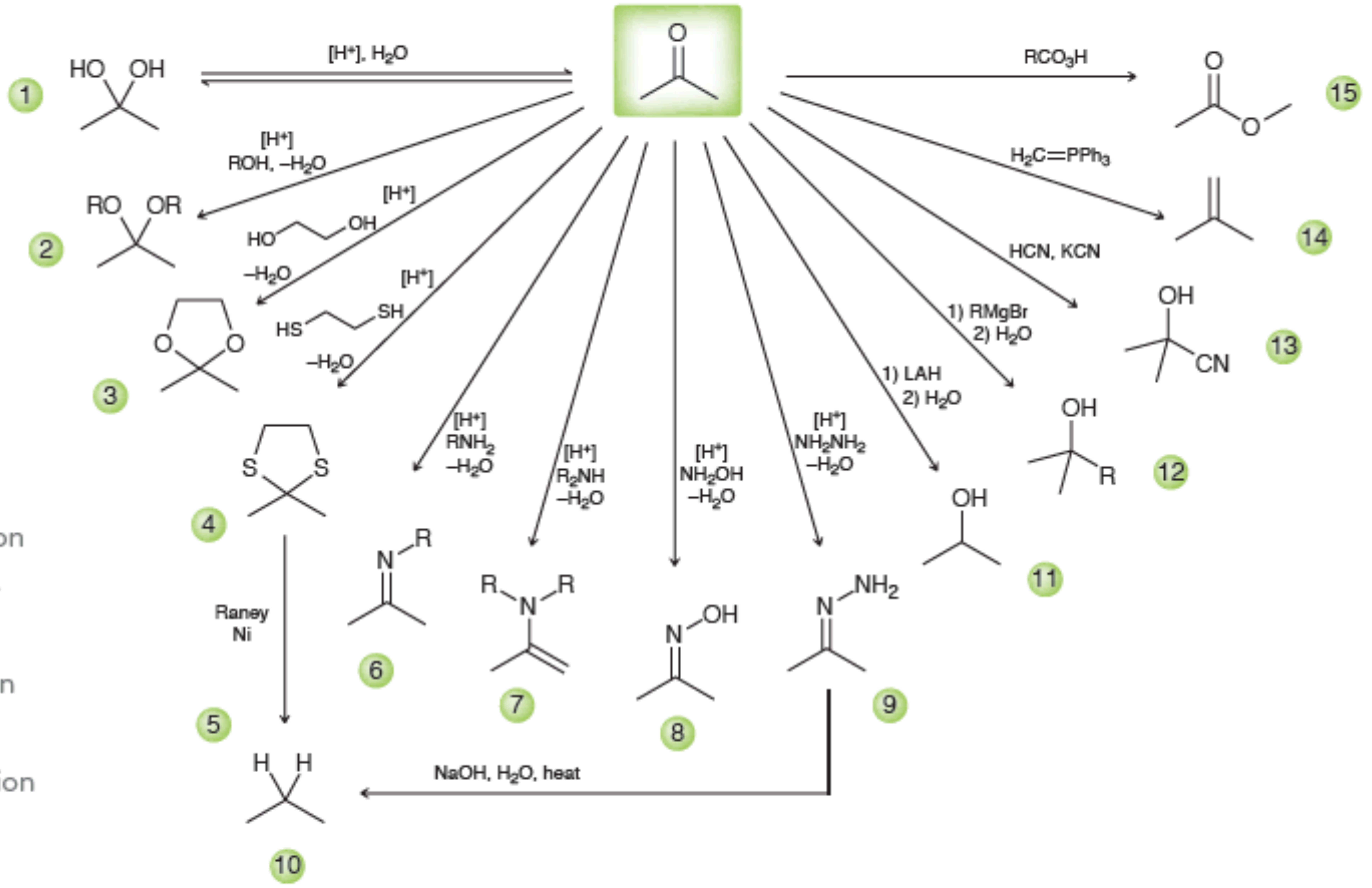
Aldehyde
(less stabilization of δ+, more reactive)



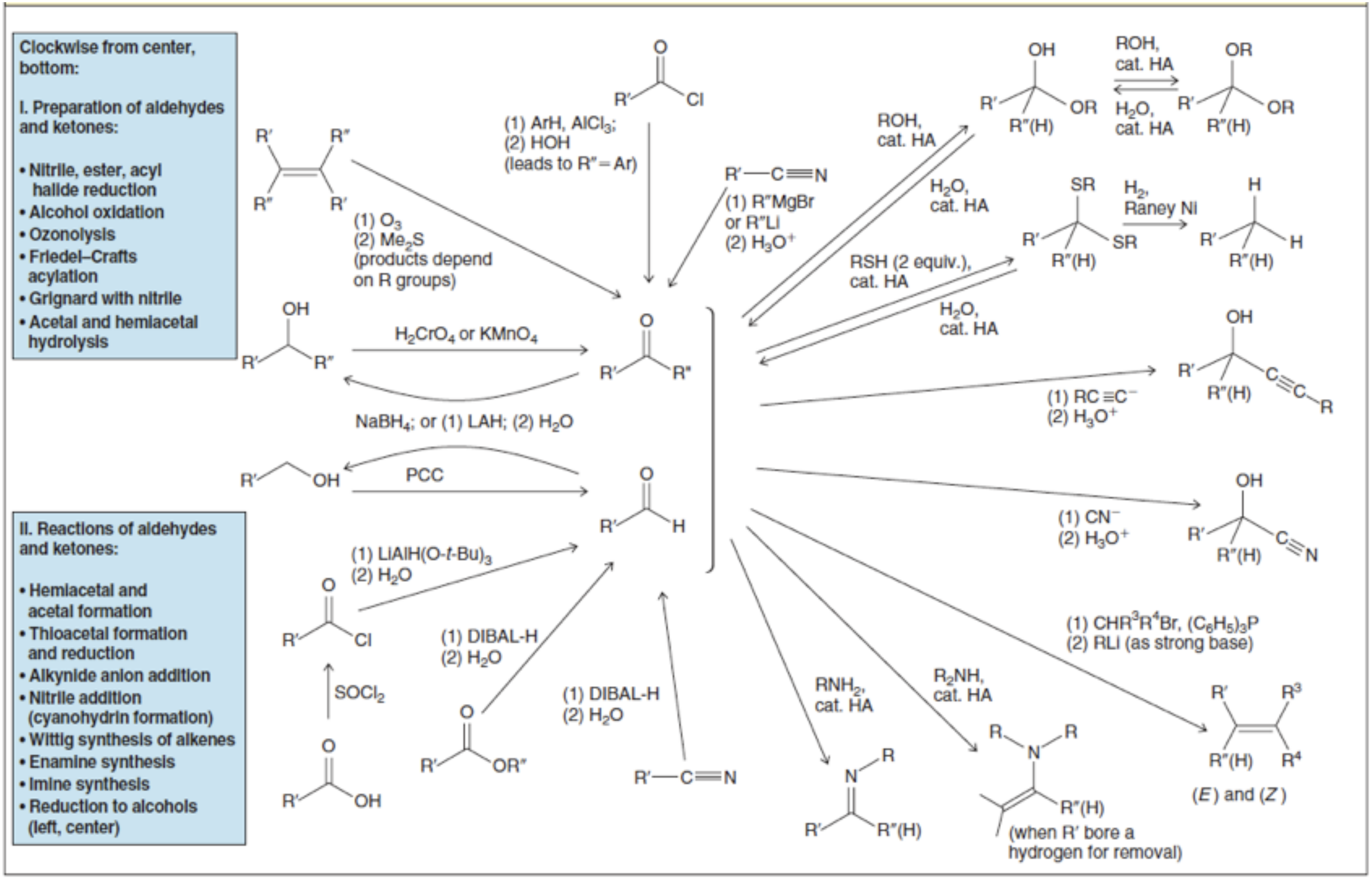
Ketone
(more stabilization of δ+, less reactive)

Revisione delle reazioni egli 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



Clockwise from center, bottom:

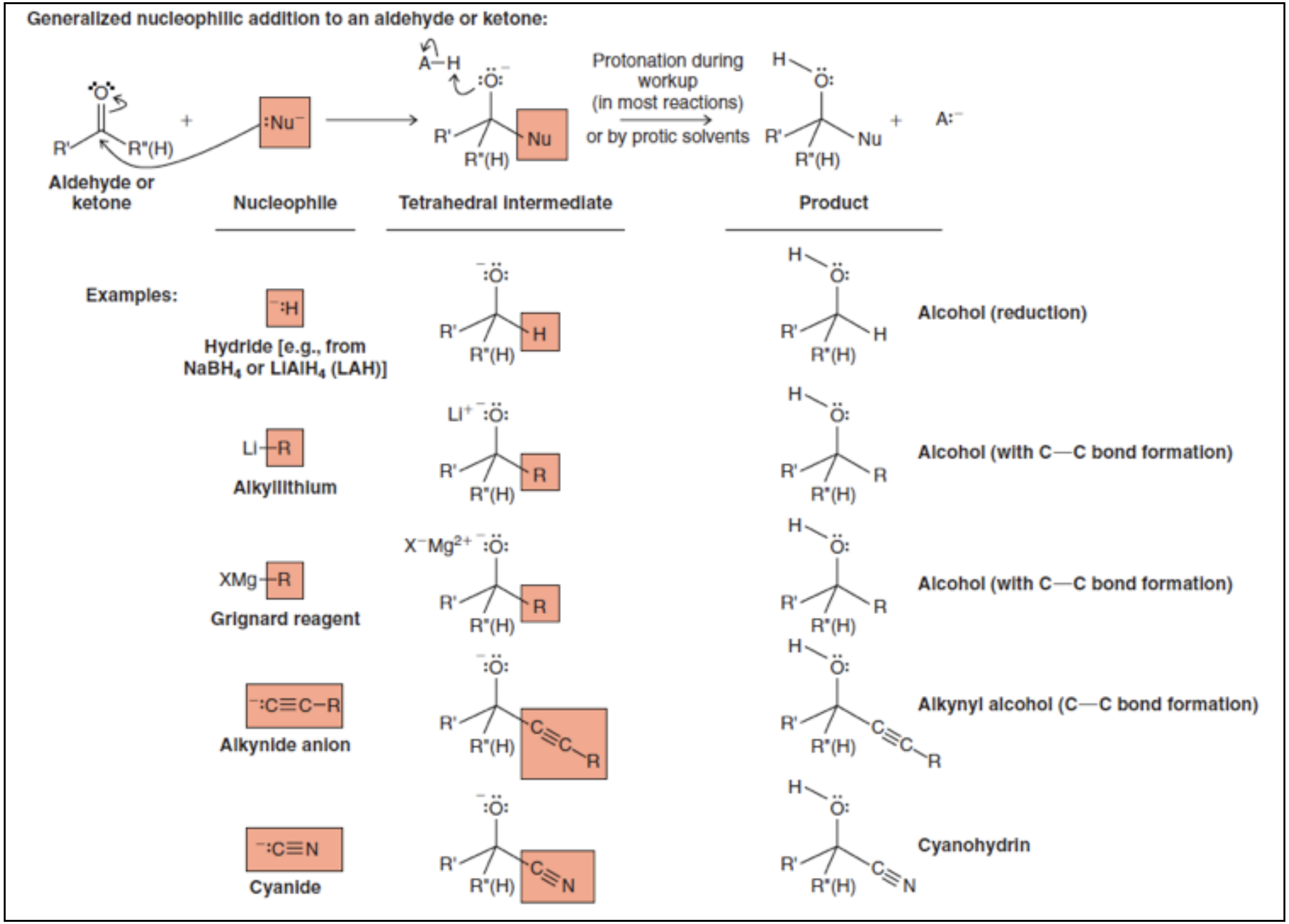
I. Preparation of aldehydes and ketones:

- Nitrile, ester, acyl halide reduction
- Alcohol oxidation
- Ozonolysis
- Friedel–Crafts acylation
- Grignard with nitrile
- Acetal and hemiacetal hydrolysis

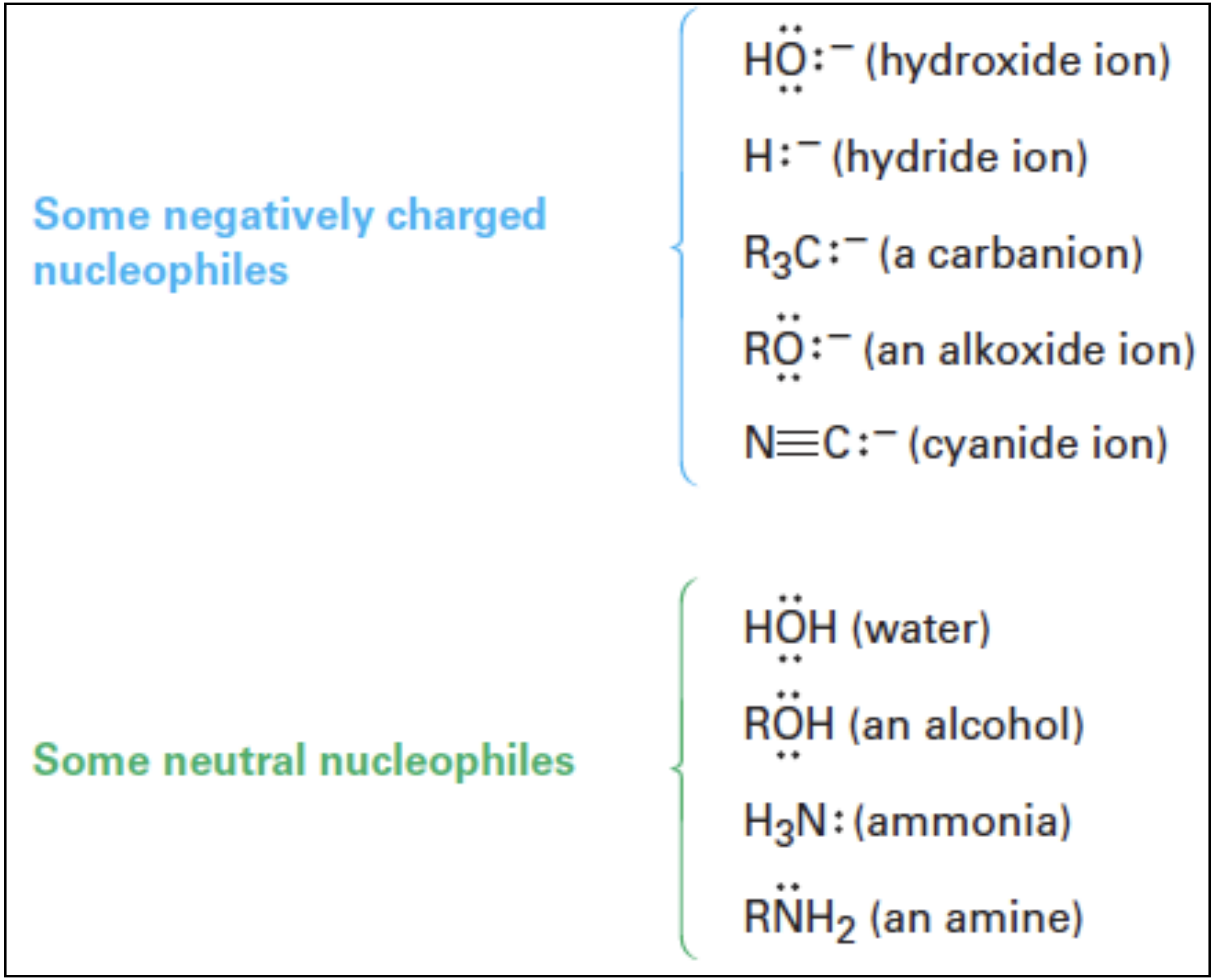
II. Reactions of aldehydes and ketones:

- 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)

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



Addizione nucleofila ad aldeidi e chetoni con Nucleofili forti e Deboli



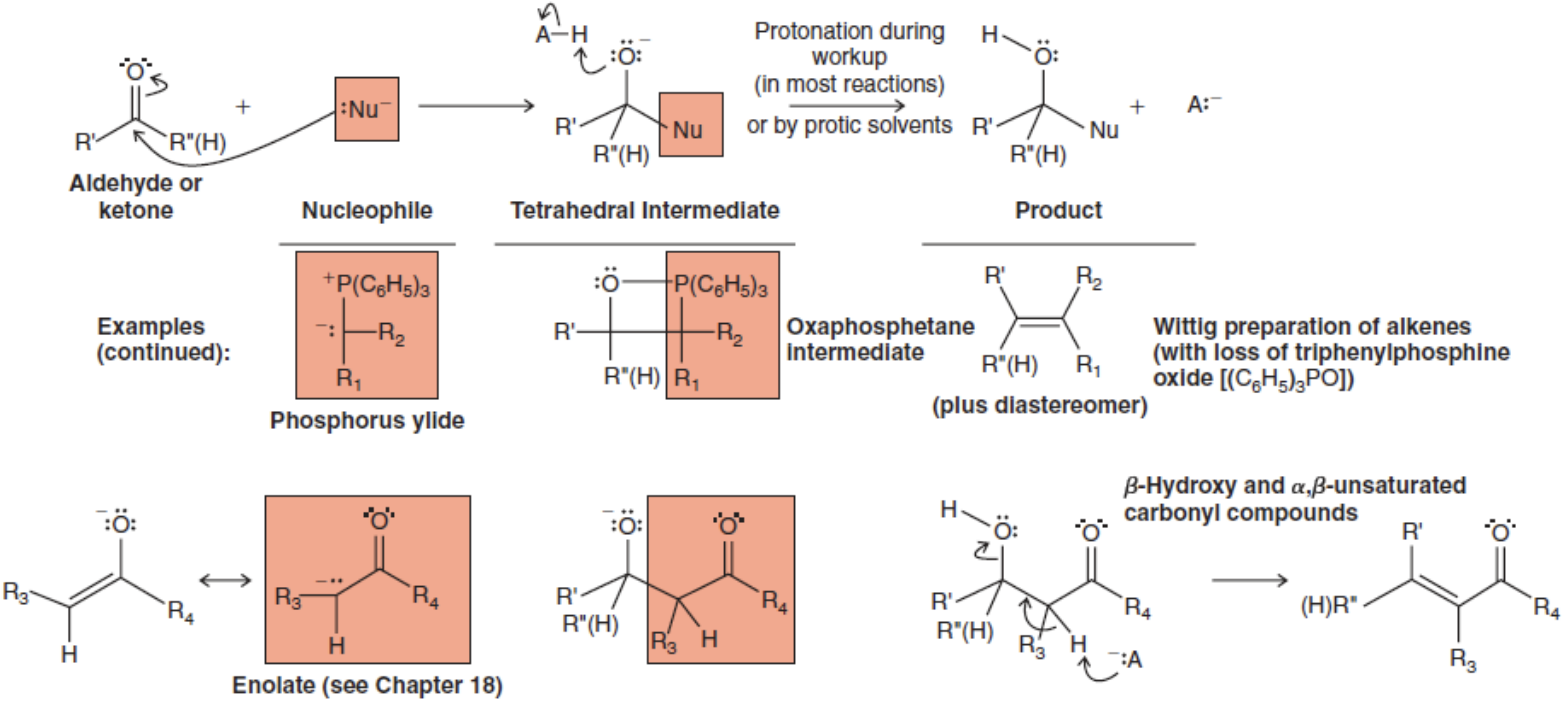
Some negatively charged nucleophiles

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

Some neutral nucleophiles

- $\mathrm{H}\underset{\cdot\cdot}{\overset{\cdot\cdot}{\mathrm{O}}}\mathrm{H}$ (water)
- $\mathrm{R}\underset{\cdot\cdot}{\overset{\cdot\cdot}{\mathrm{O}}}\mathrm{H}$ (an alcohol)
- $\mathrm{H_3N}:$ (ammonia)
- $\mathrm{R}\overset{\cdot\cdot}{\mathrm{N}}\mathrm{H_2}$ (an amine)

Generalized nucleophilic addition to an aldehyde or ketone:



Aldehyde or ketone

Nucleophile

Tetrahedral Intermediate

Protonation during workup (in most reactions)

or by protic solvents

Product

Examples (continued):

Phosphorus ylide

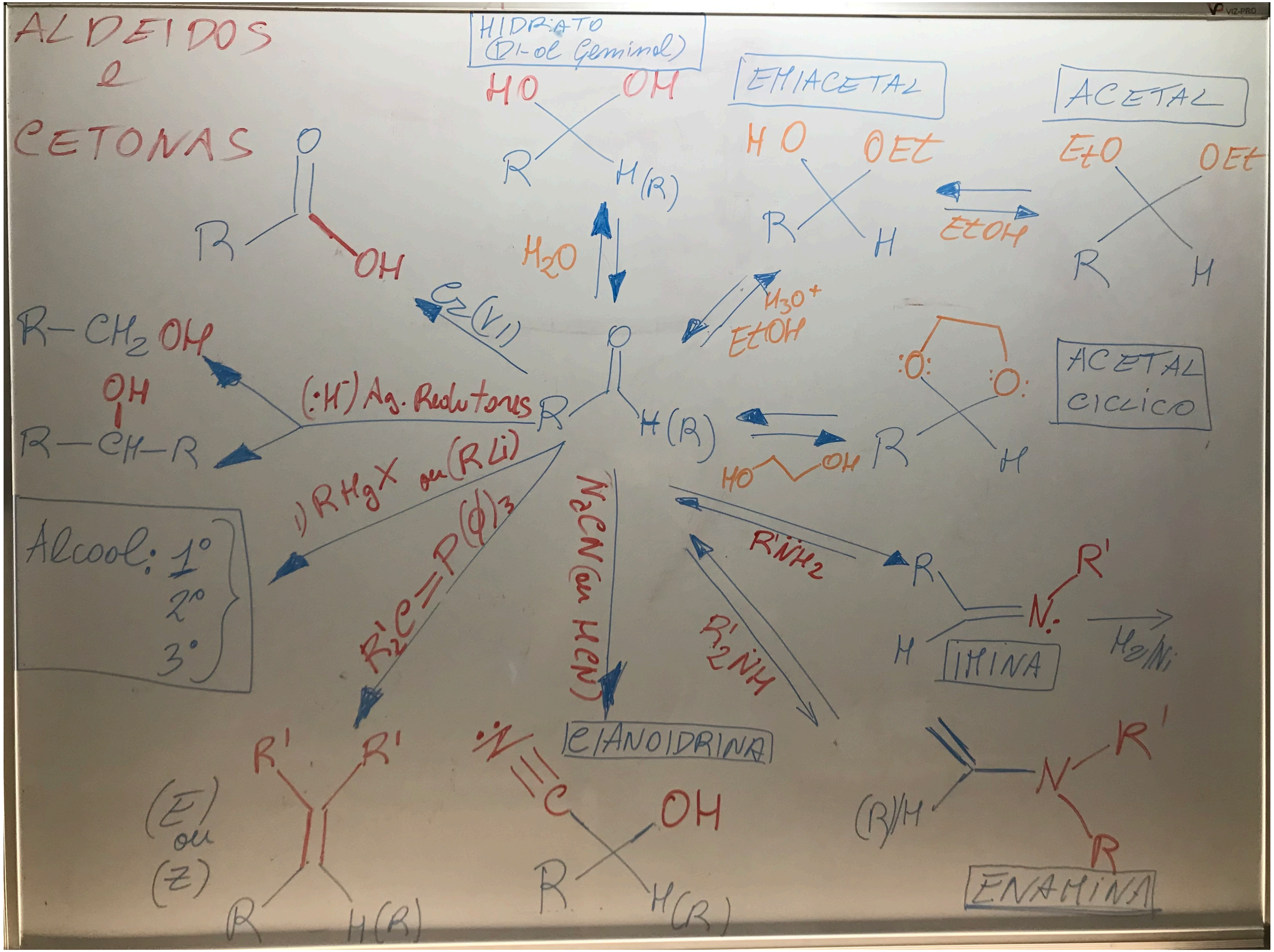
Oxaphosphetane intermediate

(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

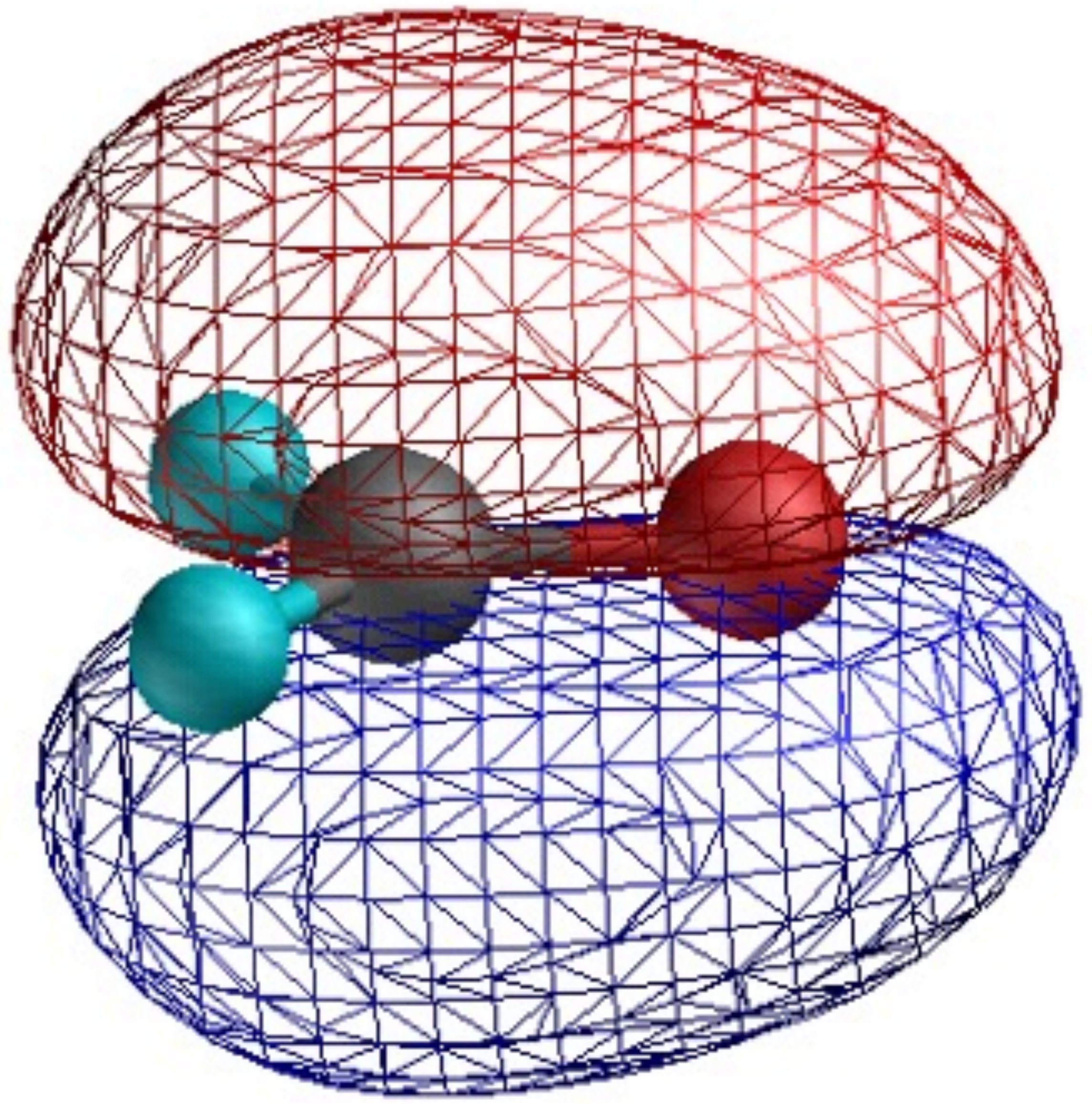

ALDEIDOS
e
CETONAS
HIDRATO
(DI-ol Geminal)
HO OH
R H(R)
H2O
EMIACETAL
HO OEt
R H
EtOH
ACETAL
EtO OEt
R H
H3O+
EtOH
O
R OH
Cr(VI)
R—CH2OH
OH
R—CH—R
(:H-) Ag. Redutores
O
R H(R)
1) RMgX ou (RLi)
Alcool: 1°
2°
3°
R'2C=P(ϕ)3
N2CN(ou HCN)
:O: :O:
R H
HO OH
ACETAL ciclico
R'NH2
R R'
N:
H
IMINA
H2/Ni
R'2NH
CIANOIDRINA
R' R'
(E) ou (Z)
R H(R)
:N≡C OH
R H(R)
R'
N
(R)/H
R
ENAMINA

✓ Gruppo carbonilico, C=O

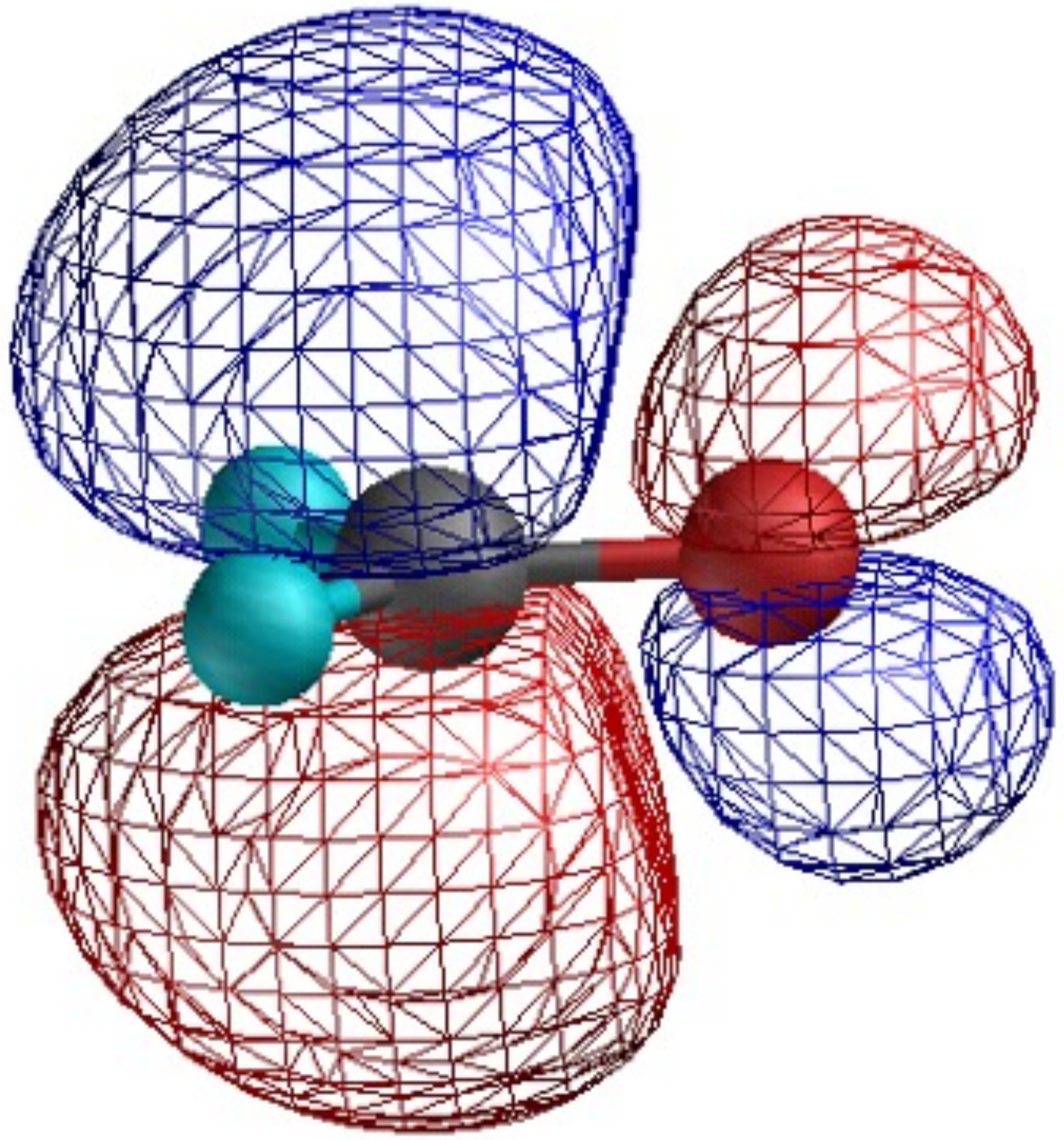
- Aldeidi e chetoni
- Acidi carbossilici
- Derivati funzionali degli acidi carbossilici
- Enolati

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

Orbitale π



Orbitale π*

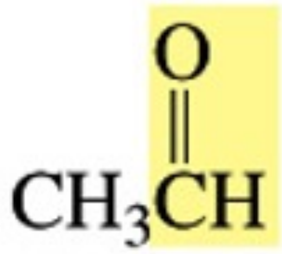


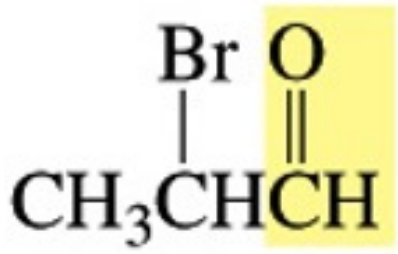
Nomenclatura: aldeidi

- ✓ 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

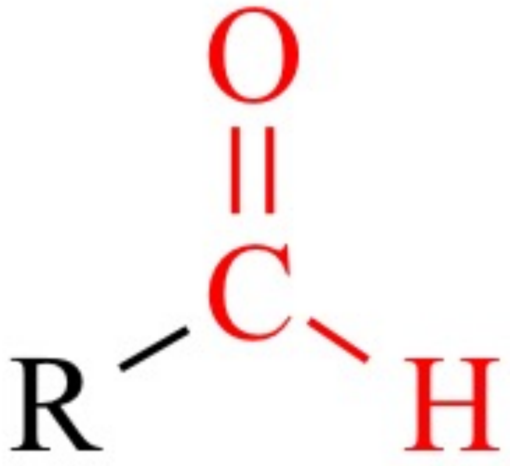
Nomenclatura: aldeidi


$HC(=O)H$


$CH_3C(=O)H$


$CH_3CH(Br)C(=O)H$

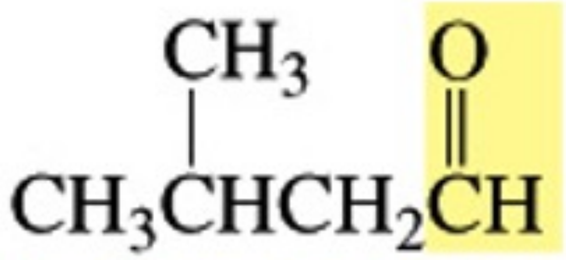
systematic name:	methanal	ethanal	2-bromopropanal
common name:	formaldehyde	acetaldehyde	α-bromopropionaldehyde

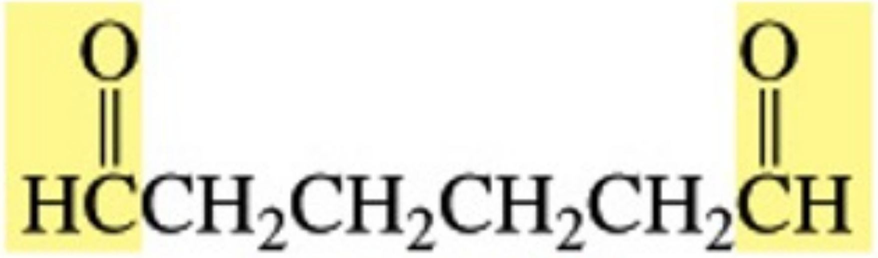


R−CHO

[R = R, Ar, H]


$CH_3CH(Cl)CH_2C(=O)H$


$CH_3CH(CH_3)CH_2C(=O)H$


$HC(=O)CH_2CH_2CH_2CH_2C(=O)H$

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

Nomenclatura: chetoni

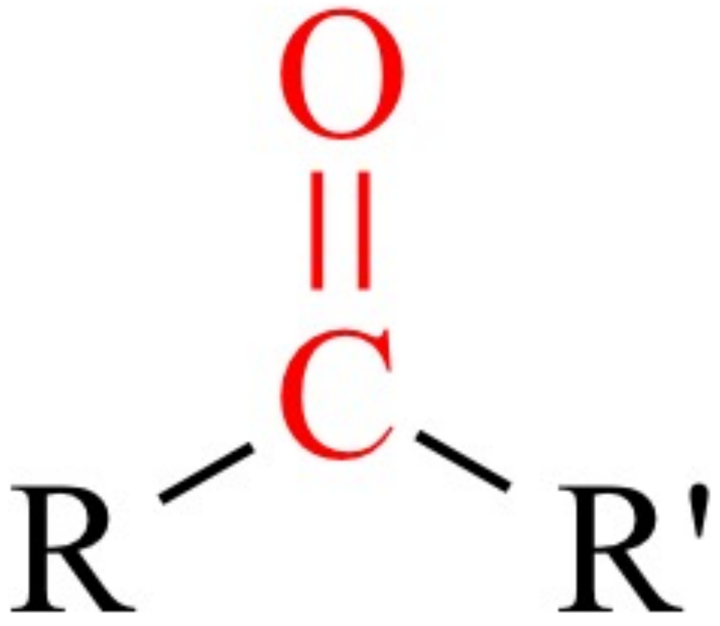
✓ IUPAC

- 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)

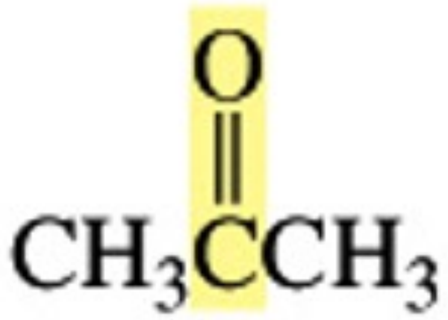
✓ Comune

- for a ketone, name the two alkyl or aryl groups bonded to the carbonyl carbon and add the word ketone

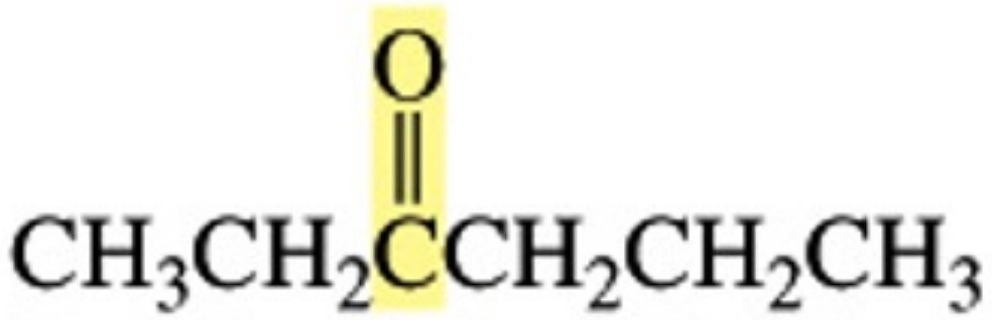
Nomenclatura: chetoni



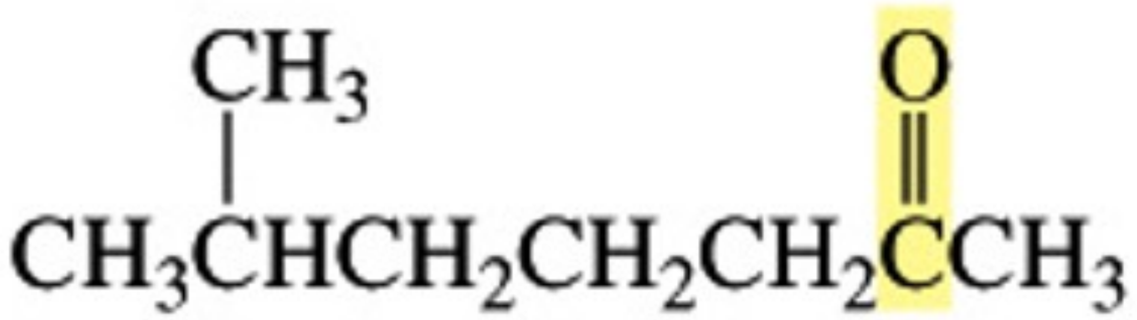
[R, R' = R, Ar]



$CH_3\overset{O}{\overset{\|}{C}}CH_3$

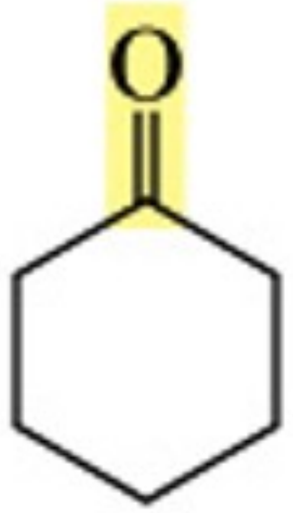
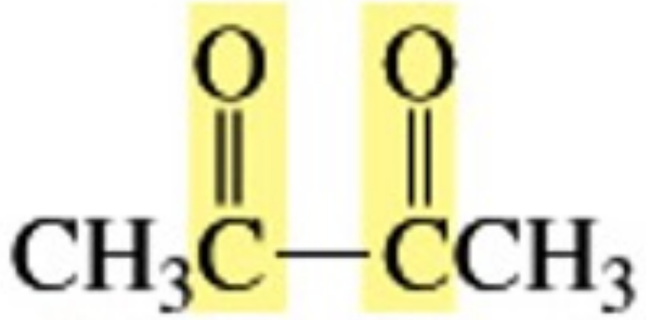
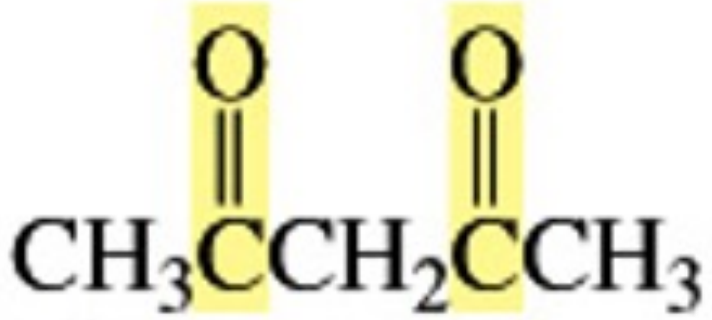
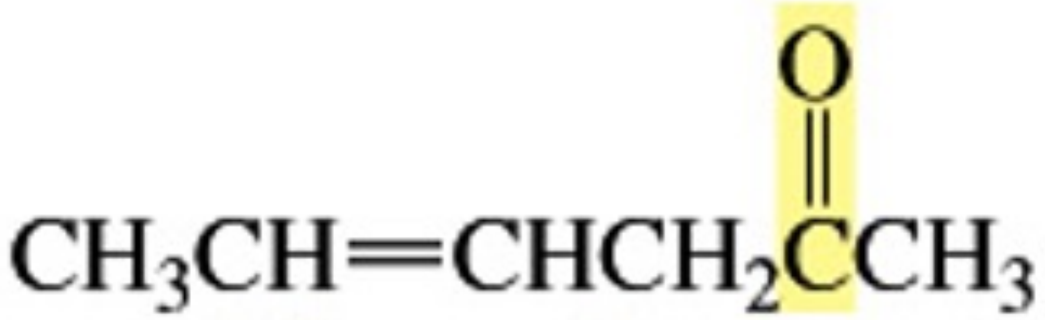


$CH_3CH_2\overset{O}{\overset{\|}{C}}CH_2CH_2CH_3$



$CH_3\overset{CH_3}{\overset{|}{C}}HCH_2CH_2CH_2\overset{O}{\overset{\|}{C}}CH_3$

systematic name:	propanone	3-hexanone	6-methyl-2-heptanone
common name:	acetone		
derived name:	dimethyl ketone	ethyl propyl ketone	isohexyl methyl ketone

		 $\mathrm{CH_3}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_3}$	 $\mathrm{CH_3}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_3}$	 $\mathrm{CH_3CH{=}CHCH_2}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_3}$
systematic name:	**cyclohexanone**	**butanedione**	**2,4-pentanedione**	**4-hexen-2-one**
common name:			**acetylacetone**	

- Se sono presenti due (o più) gruppi funzionali, quello a priorità più alta è indicato con il suffisso, mentre l'altro (gli altri) con un prefisso.

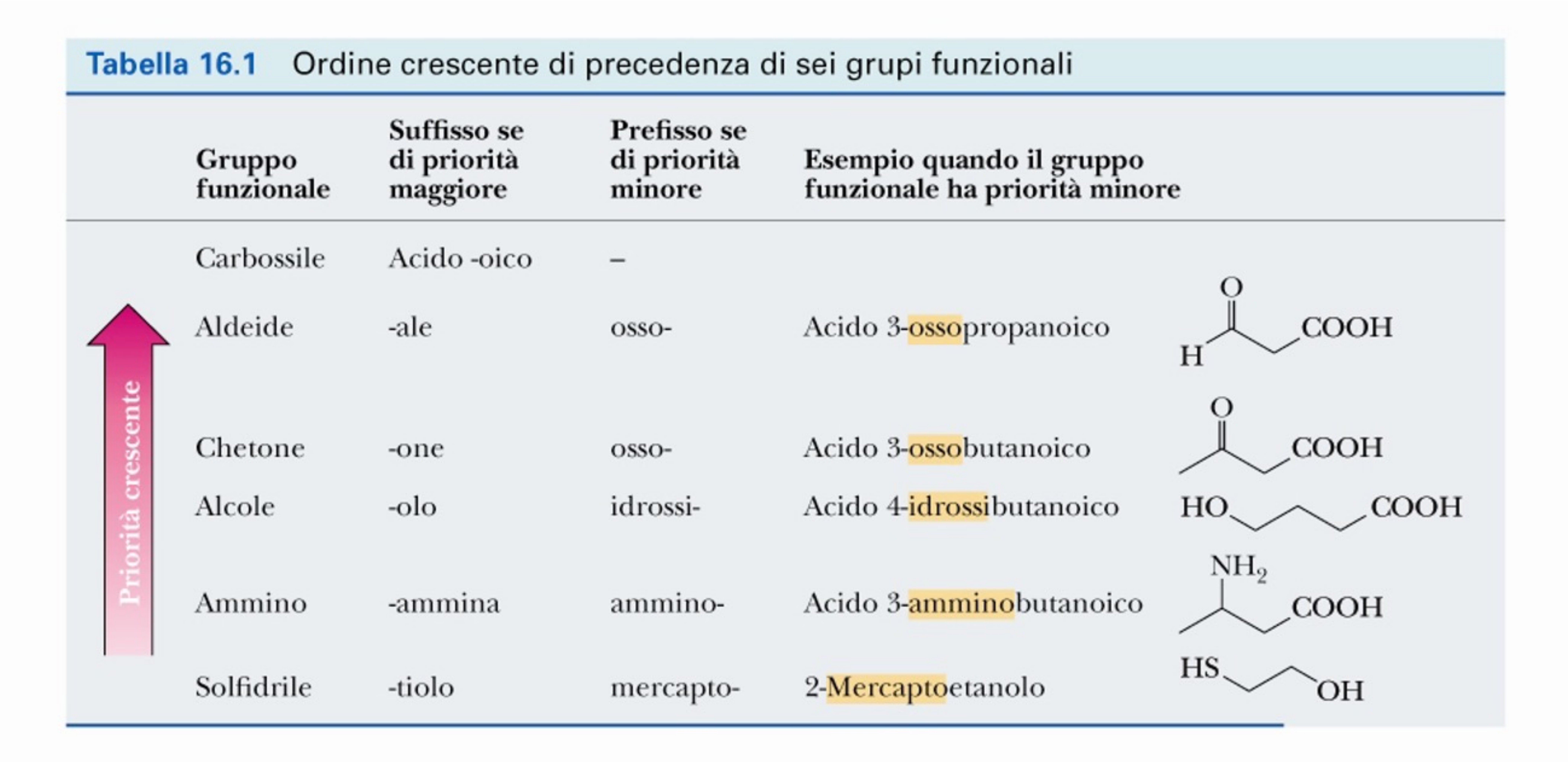


Tabella 16.1 Ordine crescente di precedenza di sei grupi funzionali

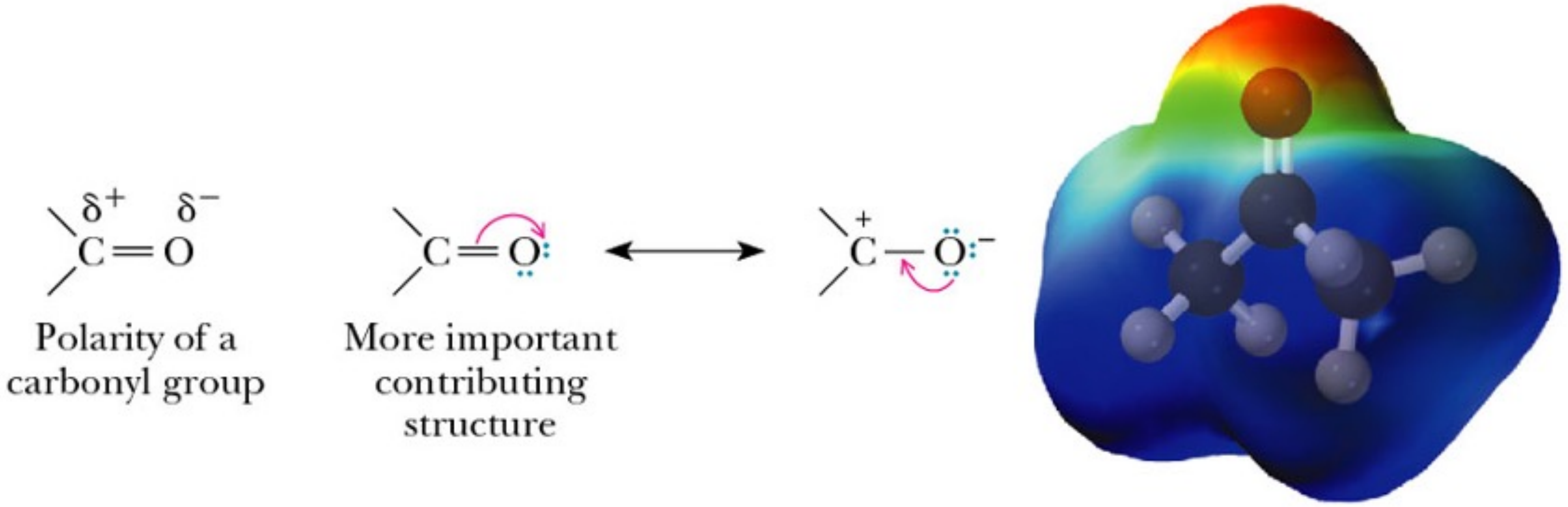
Gruppo funzionale	Suffisso se di priorità maggiore	Prefisso se di priorità minore	Esempio quando il gruppo funzionale ha priorità minore
Carbossile	Acido -oico	–	
Aldeide	-ale	osso-	Acido 3-ossopropanoico
Chetone	-one	osso-	Acido 3-ossobutanoico
Alcole	-olo	idrossi-	Acido 4-idrossibutanoico
Ammino	-ammina	ammino-	Acido 3-amminobutanoico
Solfidrile	-tiolo	mercapto-	2-Mercaptoetanolo

PRIORIDADE CRESCENTE

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



Polarity of a carbonyl group

More important contributing structure

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

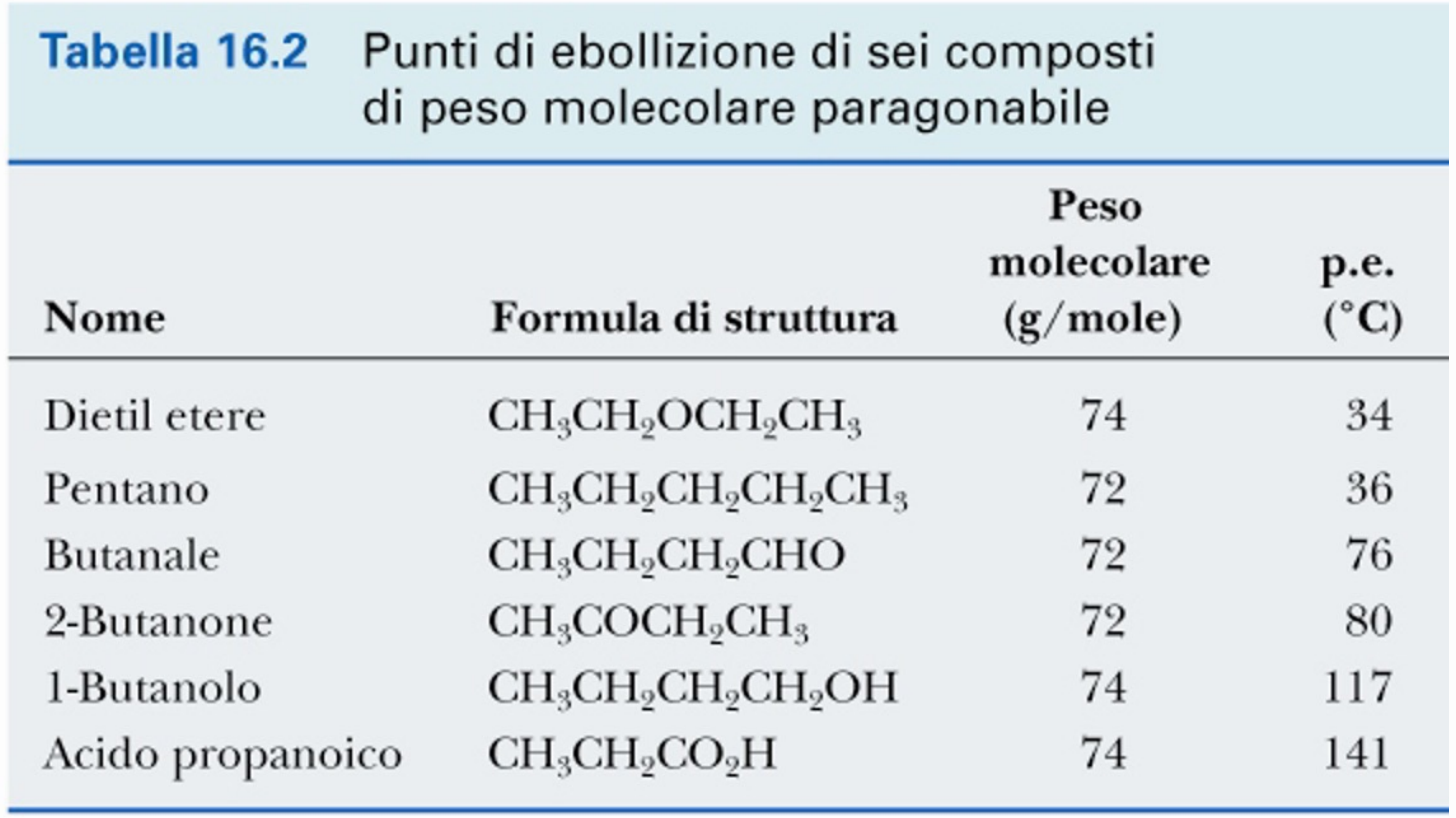


Tabella 16.2 Punti di ebollizione di sei composti di peso molecolare paragonabile

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

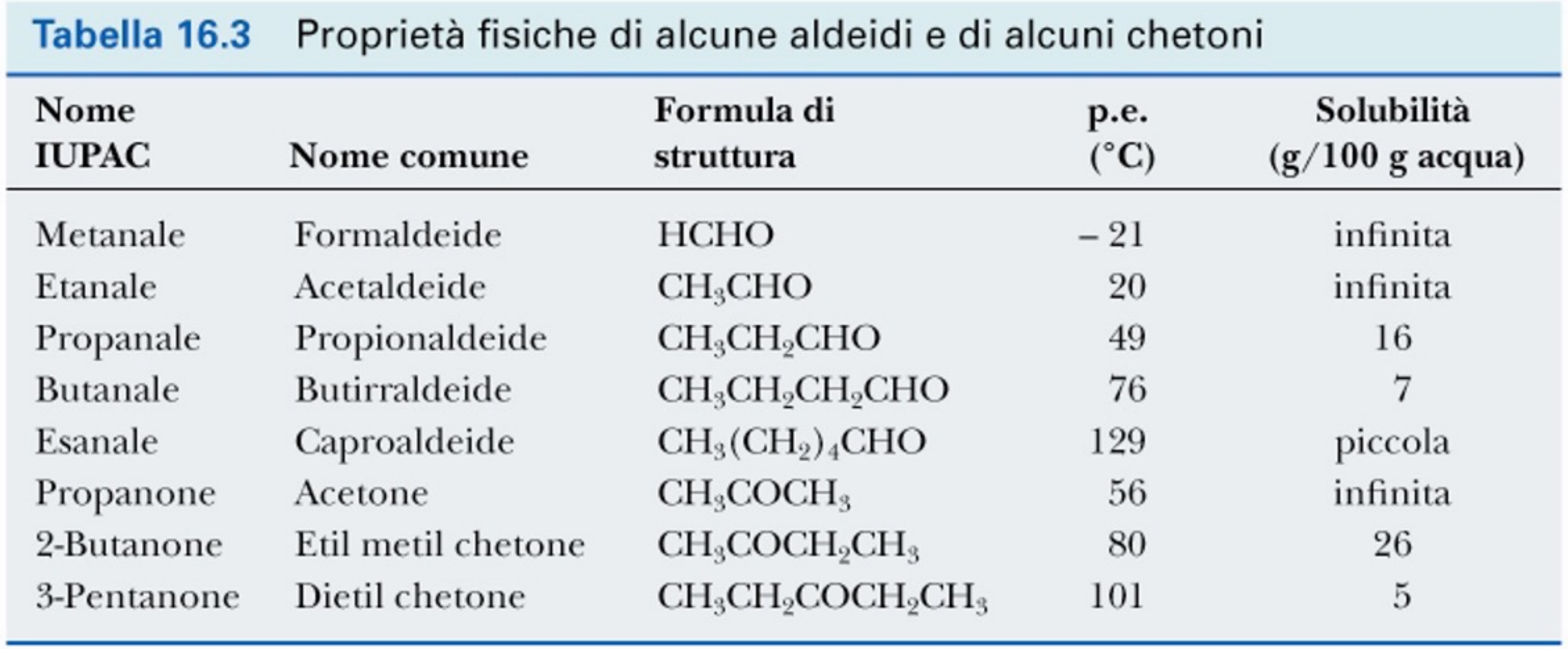
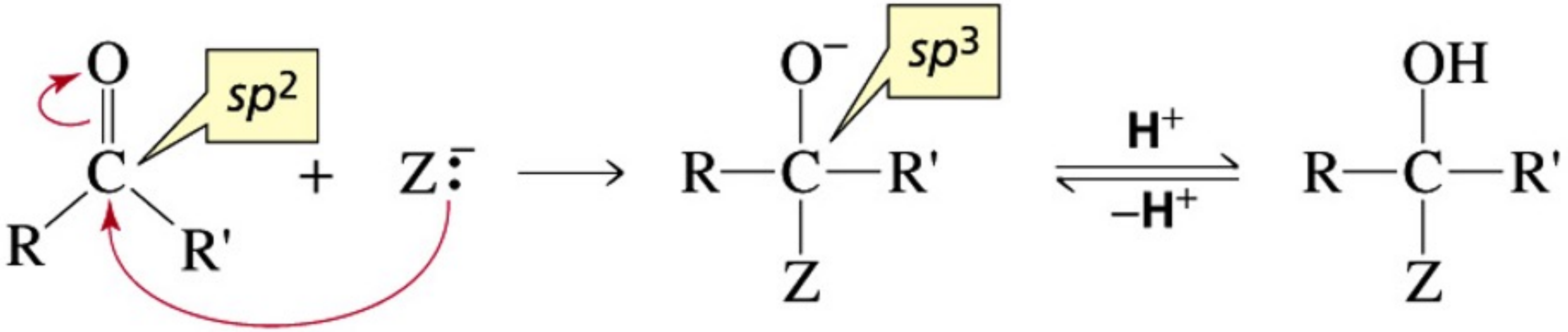


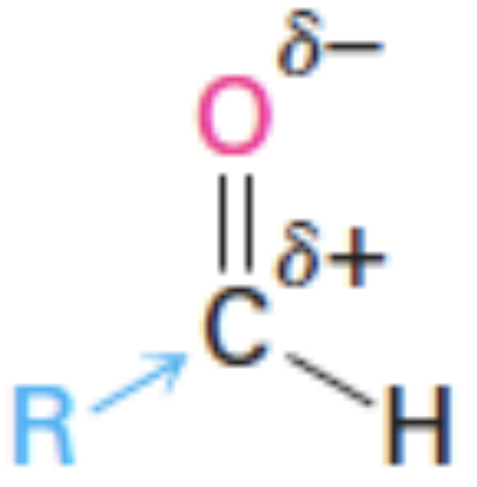
Tabella 16.3 Proprietà fisiche di alcune aldeidi e di alcuni chetoni

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:

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

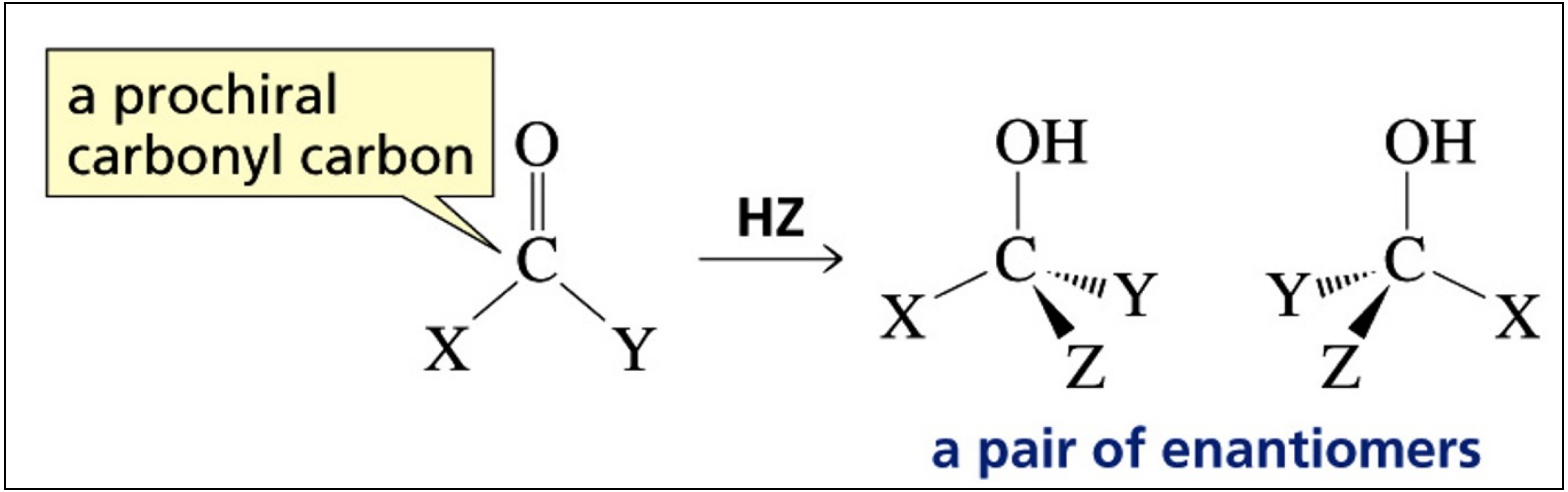




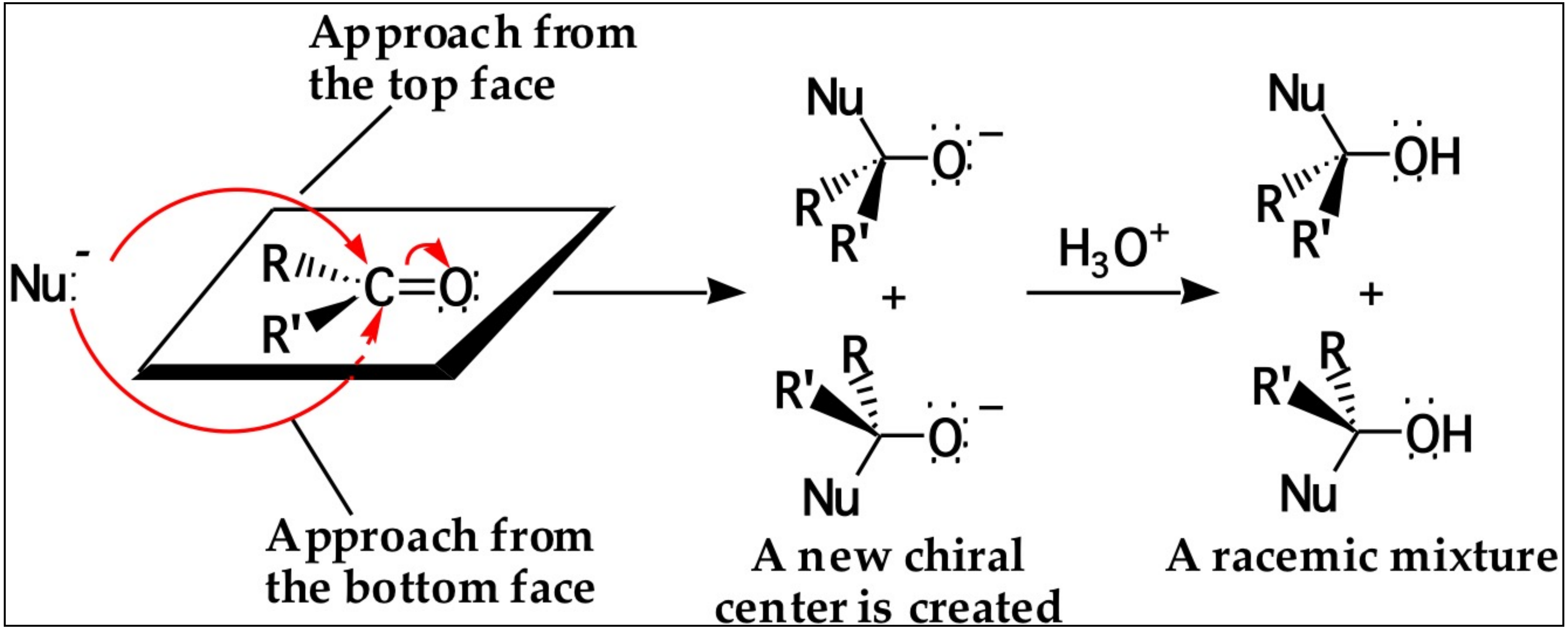
Aldehyde
(less stabilization of δ+, more reactive)

Ketone
(more stabilization of δ+, less reactive)

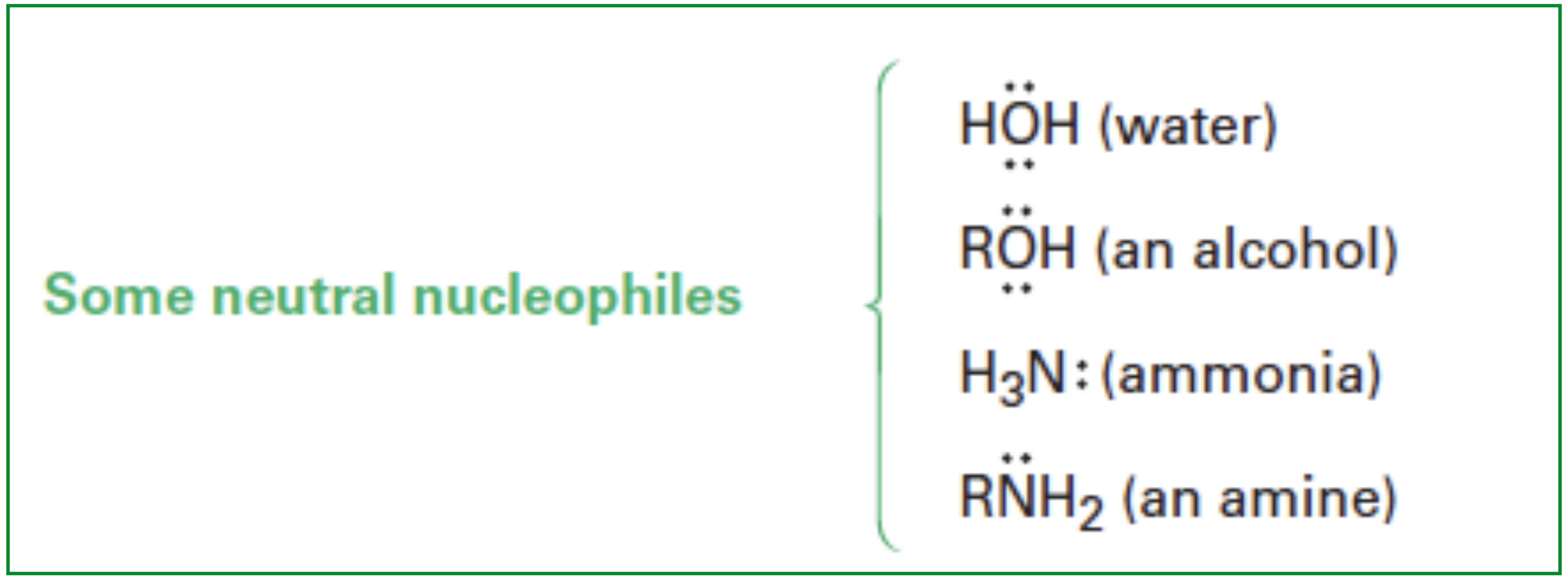
STEREOCHIMICA DELL'ADDIZIONE NUCLEOFILA



STEREOCHIMICA DELL'ADDIZIONE NUCLEOFILA

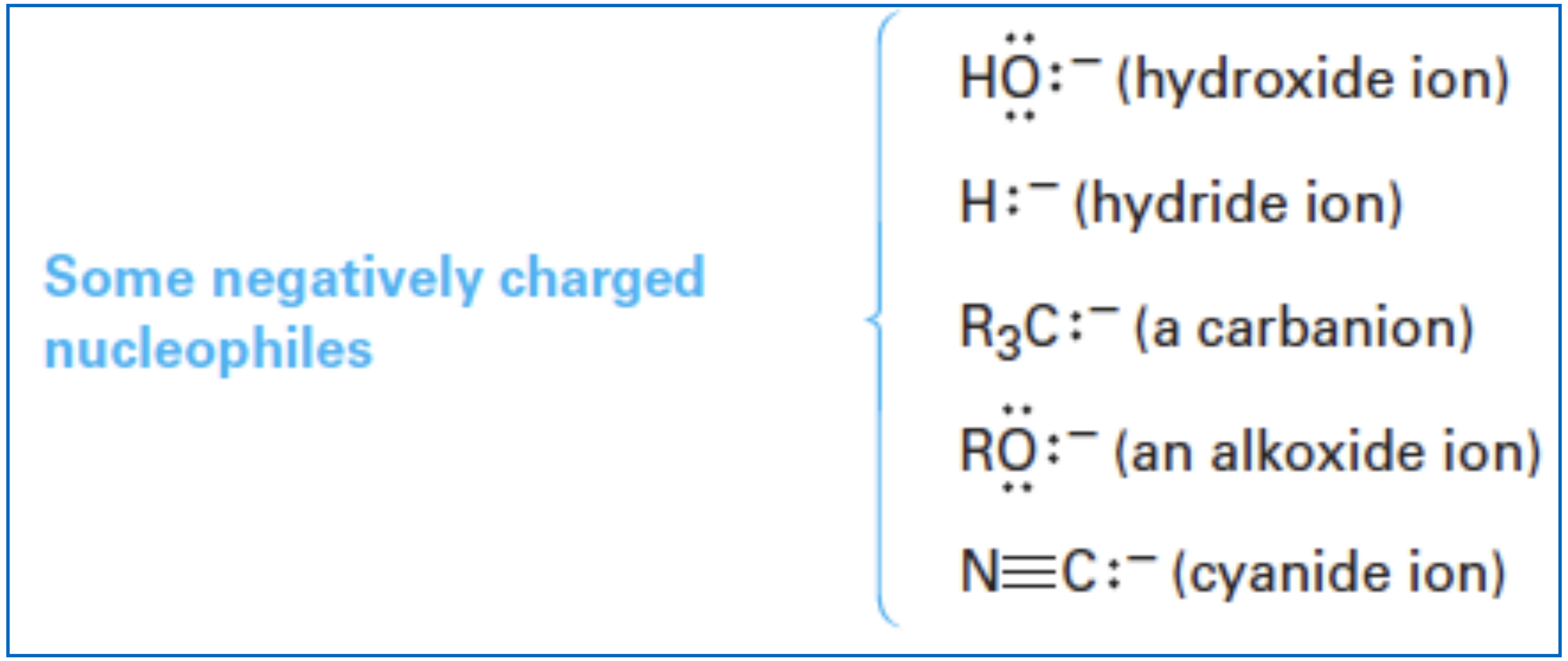


Addizione nucleofila al gruppo carbonile di Aldeidi e Chetoni



Some neutral nucleophiles

- $H\overset{\cdot\cdot}{\underset{\cdot\cdot}{O}}H$ (water)
- $R\overset{\cdot\cdot}{\underset{\cdot\cdot}{O}}H$ (an alcohol)
- $H_3N{:}$ (ammonia)
- $R\overset{\cdot\cdot}{N}H_2$ (an amine)



Some negatively charged nucleophiles

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

Addizione nucleofila al gruppo carbonile di Aldeidi e Chetoni

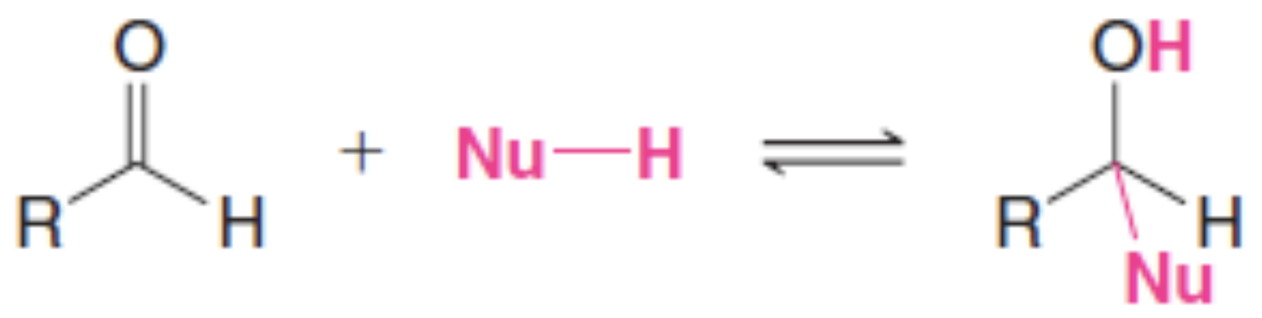
Some neutral nucleophiles

- $H\ddot{\underset{..}{O}}H$ (water)
- $R\ddot{\underset{..}{O}}H$ (an alcohol)
- $H_3N{:}$ (ammonia)
- $R\ddot{N}H_2$ (an amine)

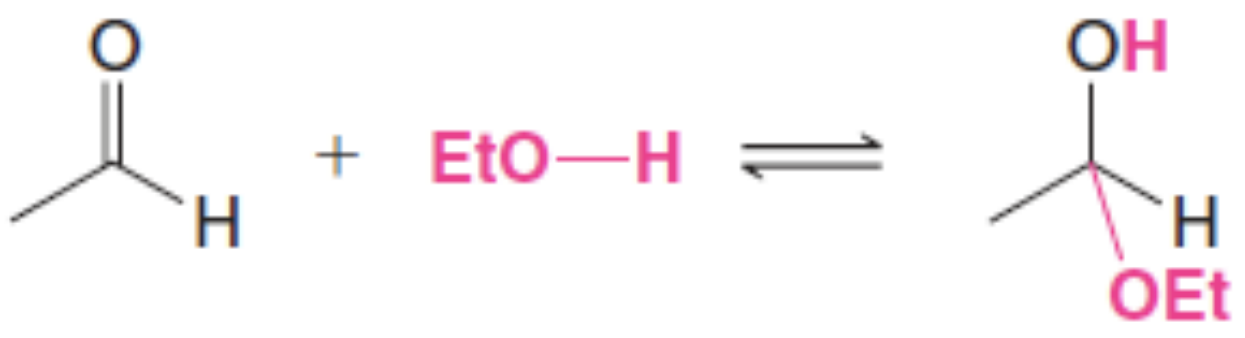
Some negatively charged nucleophiles

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

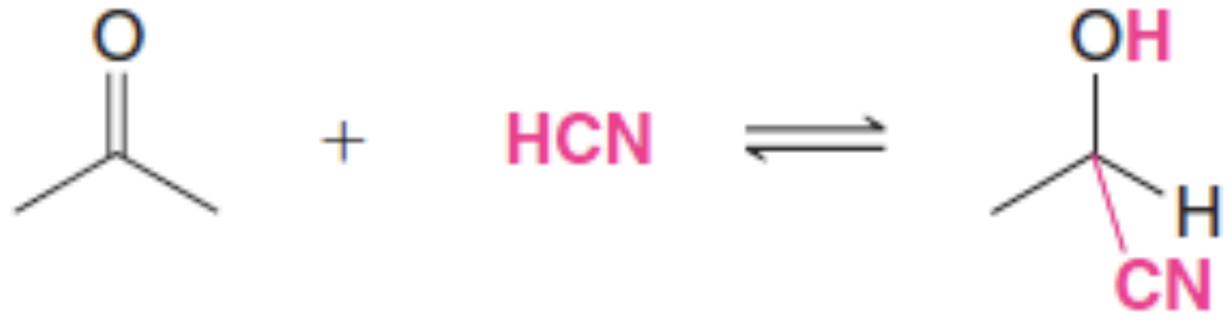
General Reaction



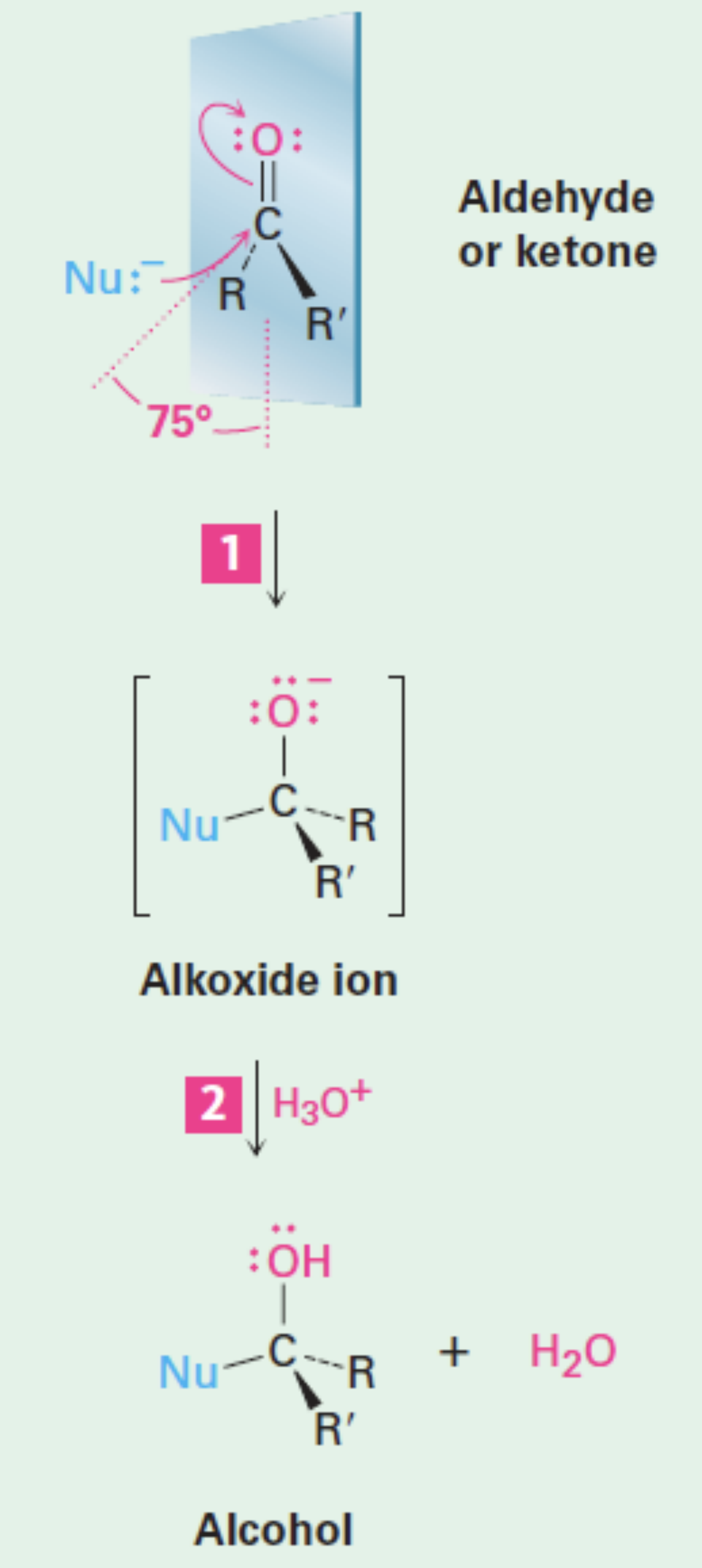
Specific Examples



A hemiacetal
(see Section 16.7)

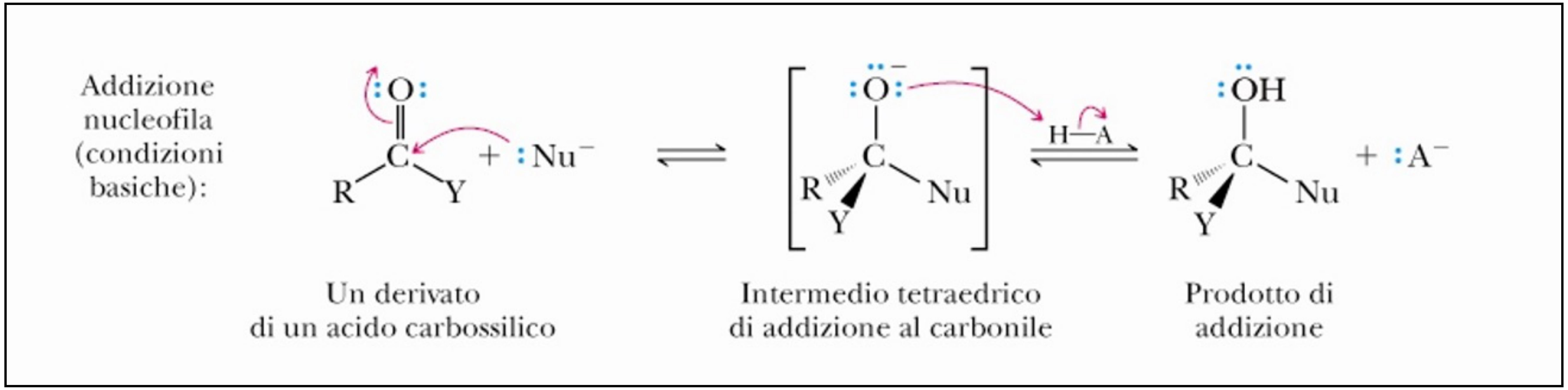


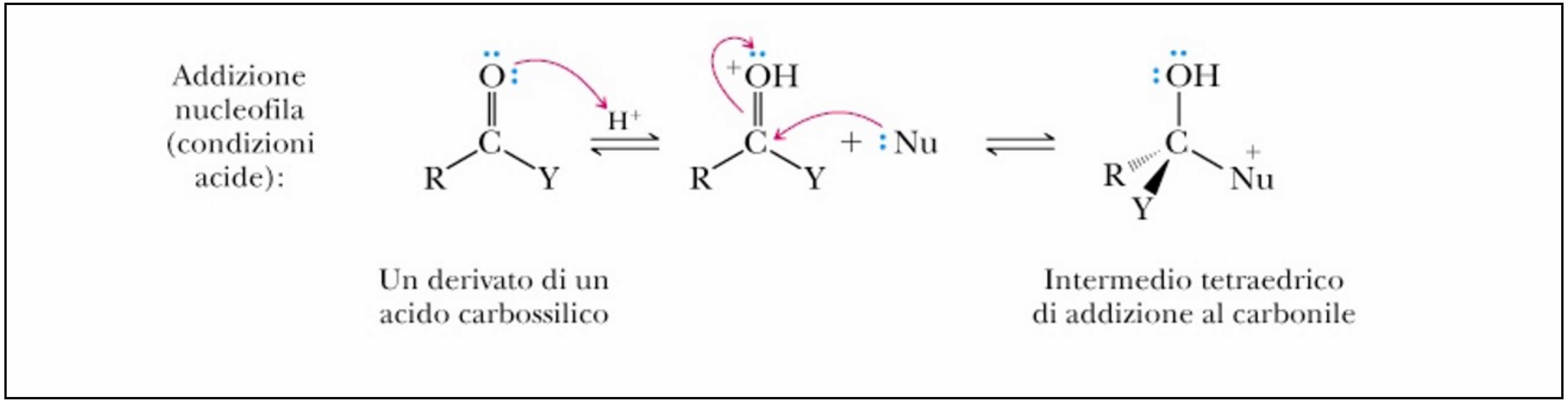
A cyanohydrin
(see Section 16.9)



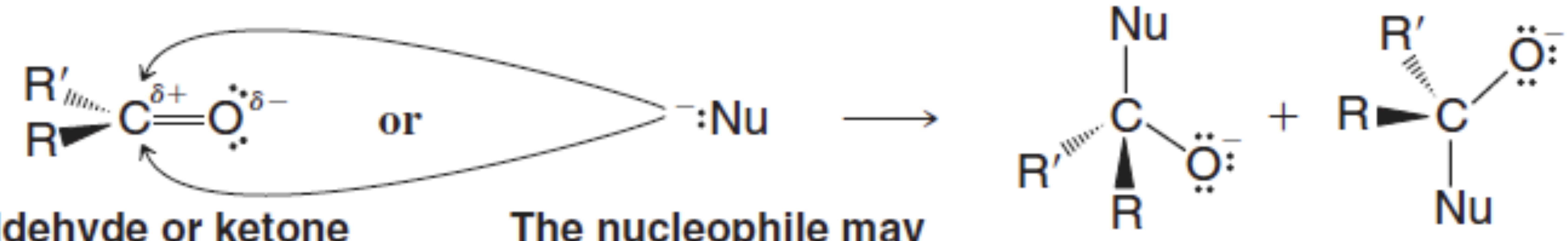
Reattività:

Addizione nucleofila al gruppo carbonile: base catalizzata e acido catalizzata



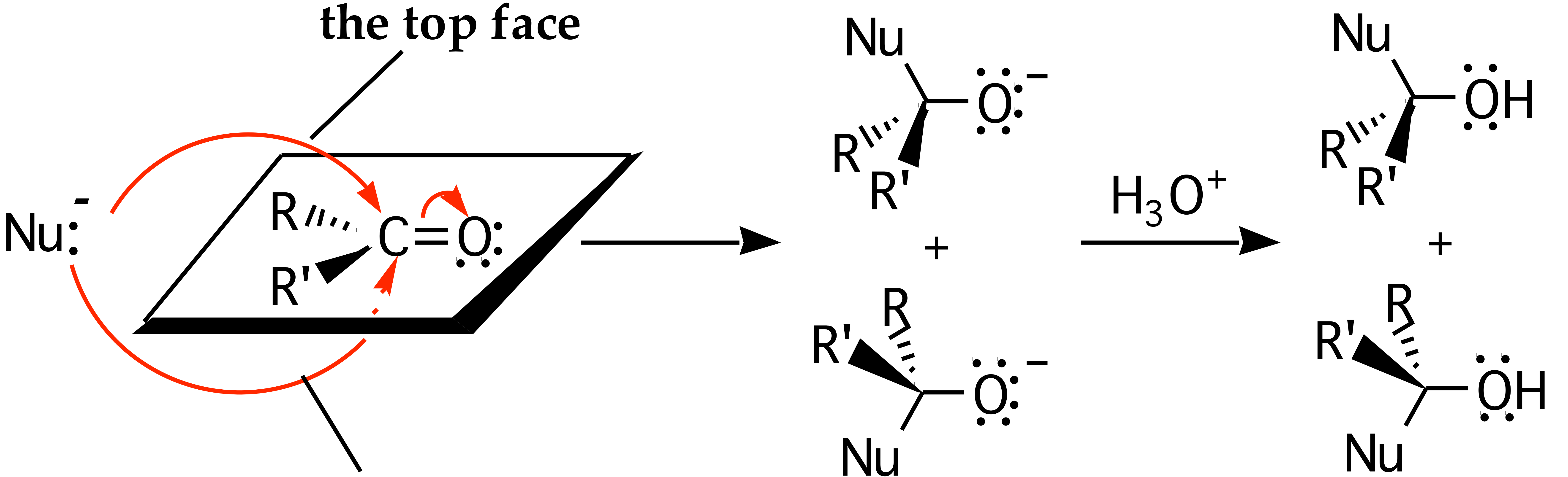


STEREOCHIMICA DELL'ADDIZIONE NUCLEOFILA



Aldehyde or ketone
(R or R′ may be H)

The nucleophile may
attack from above or below.



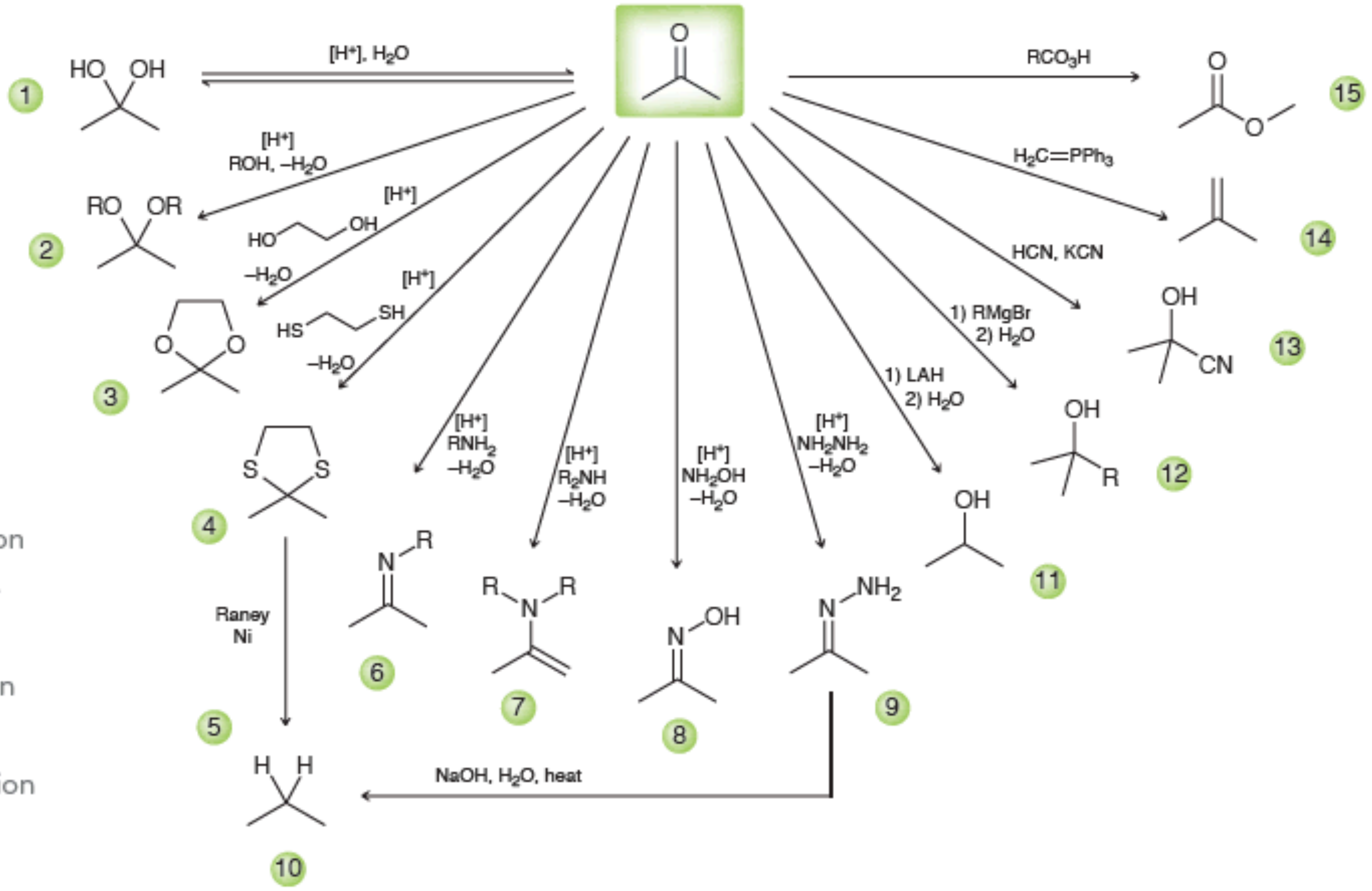
Approach from
the top face

Approach from
the bottom face

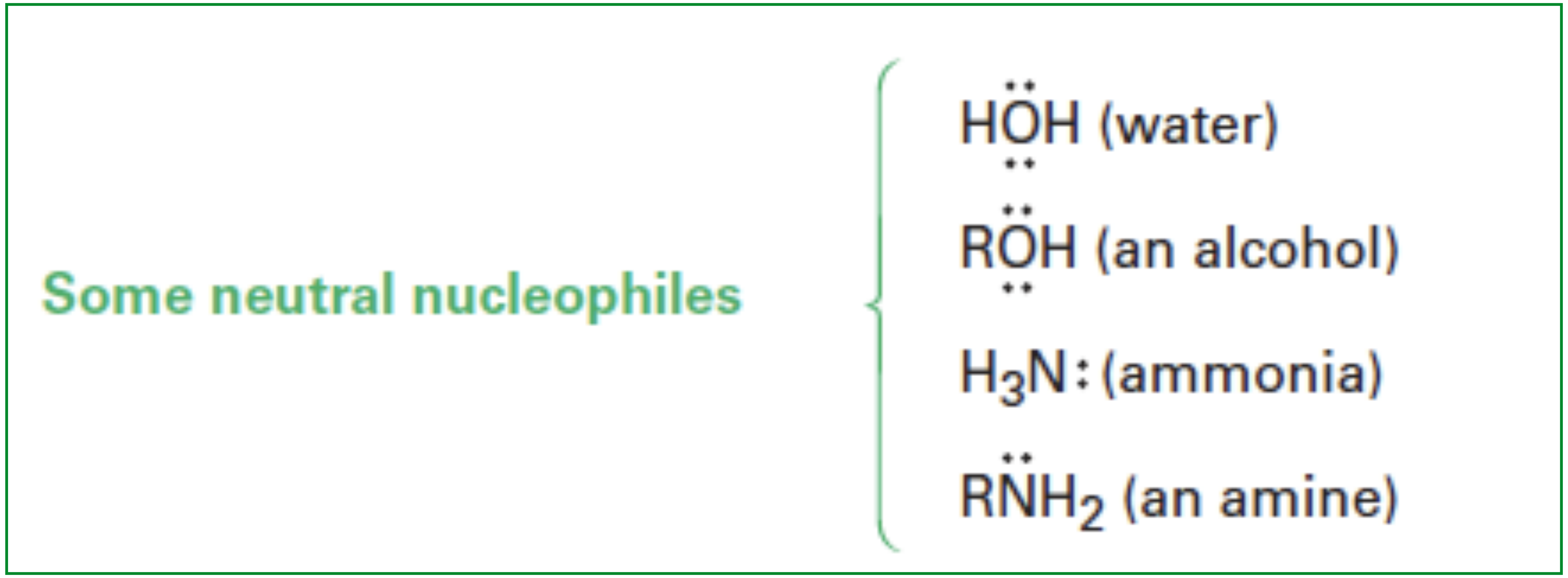
A new chiral
center is created

A racemic mixture

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)



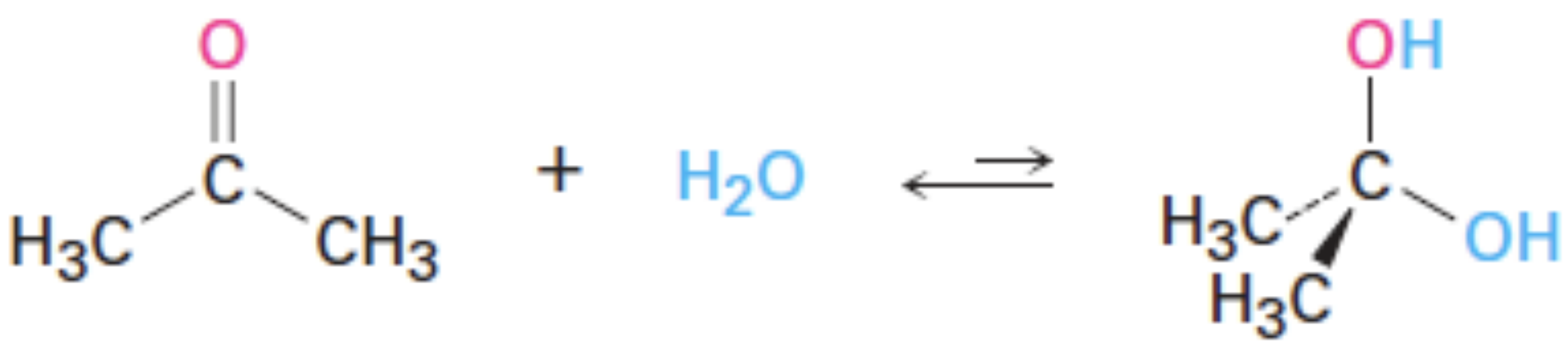
Some neutral nucleophiles

- $\mathrm{H\ddot{\underset{\cdot\cdot}{O}}H}$ (water)
- $\mathrm{R\ddot{\underset{\cdot\cdot}{O}}H}$ (an alcohol)
- $H_3N:$ (ammonia)
- $\mathrm{R\ddot{N}H_2}$ (an amine)

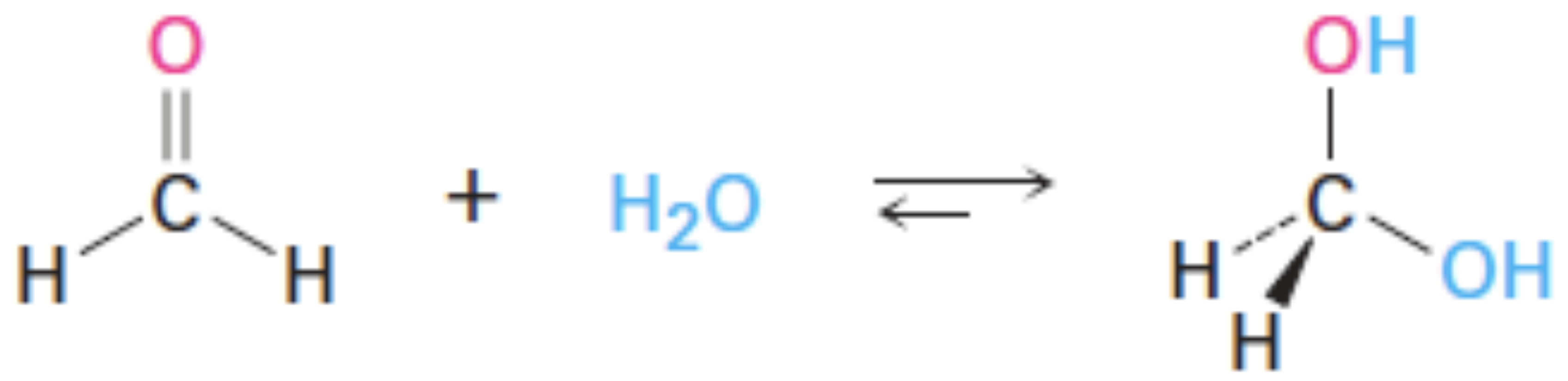
1) Aggiunta di acqua (idratazione): Di-ol geminale
2) Aggiunta di alcoli: emiacetali e acetali
3) Aggiunta di ammine: immine ed enamine

(1) Aggiunta di H2O: idratazione

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



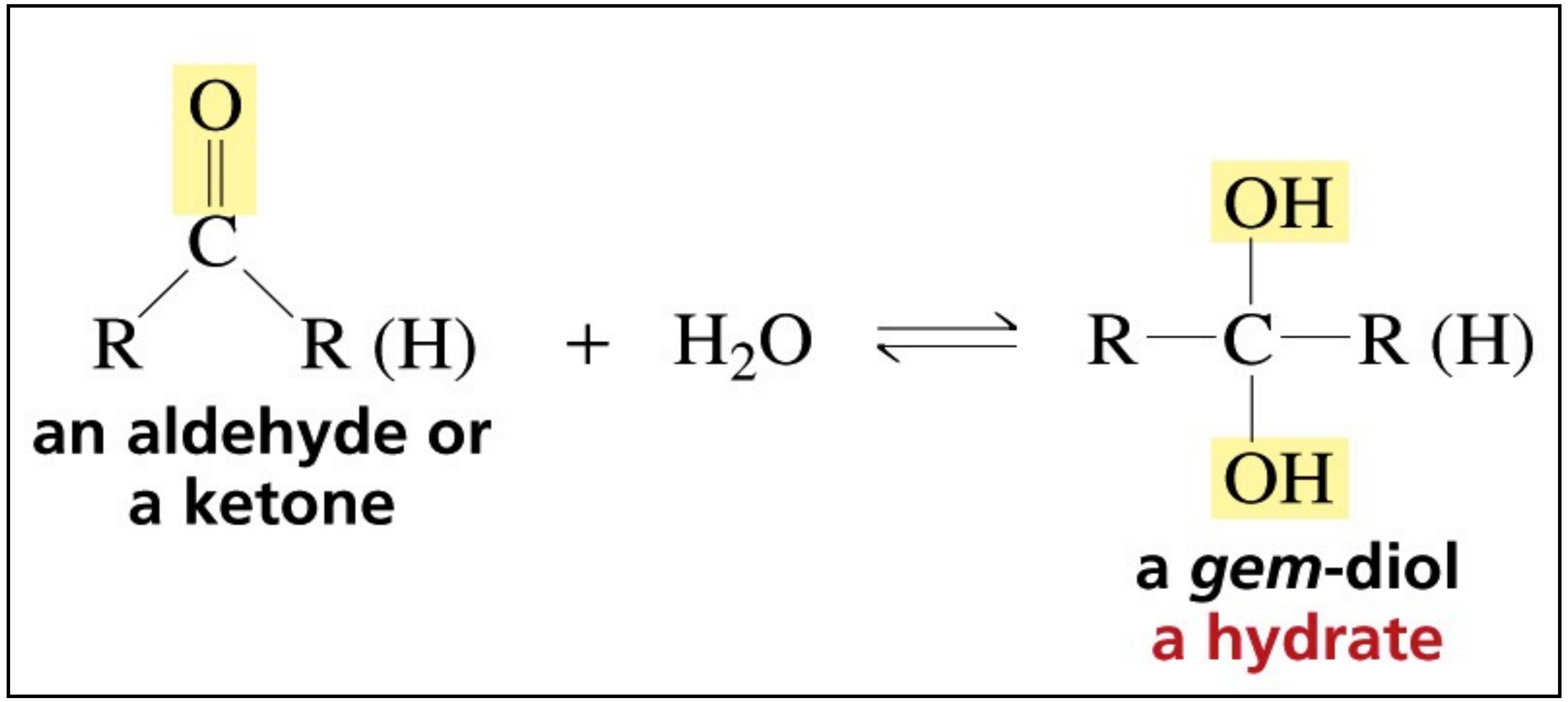
Acetone (99.9%) **Acetone hydrate (0.1%)**

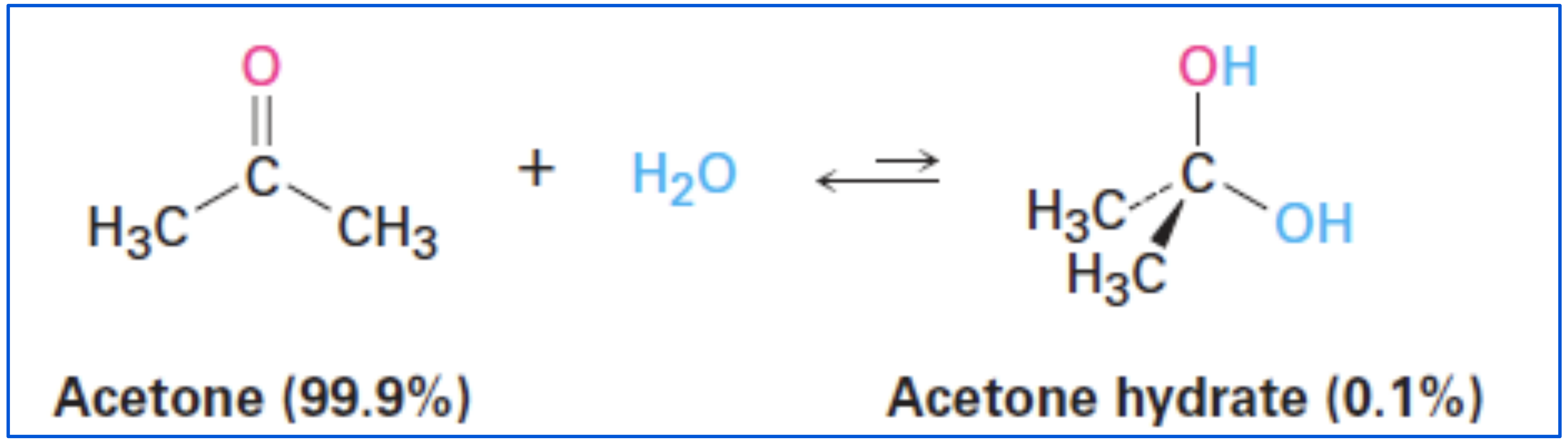


Formaldehyde (0.1%) **Formaldehyde hydrate (99.9%)**

(1) Aggiunta di H2O: idratazione

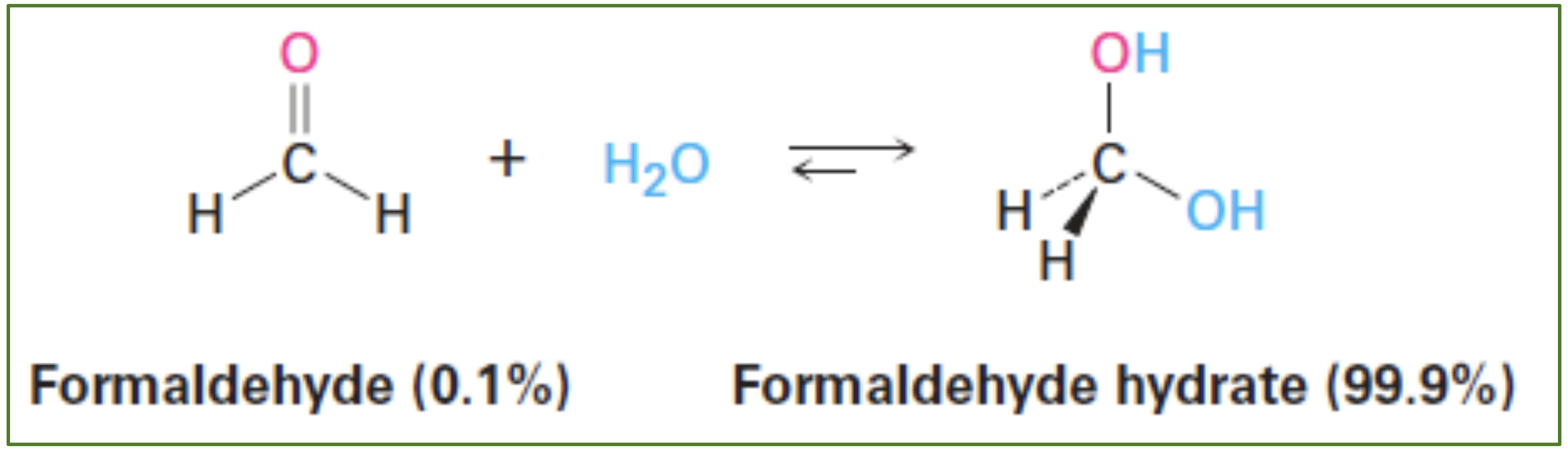
Idrati di aldeidi 1,1-dioli (gem-Dios) derivanti da un'aggiunta nucleofila di acqua al gruppo carbonile dell'aldeide





Acetone (99.9%)

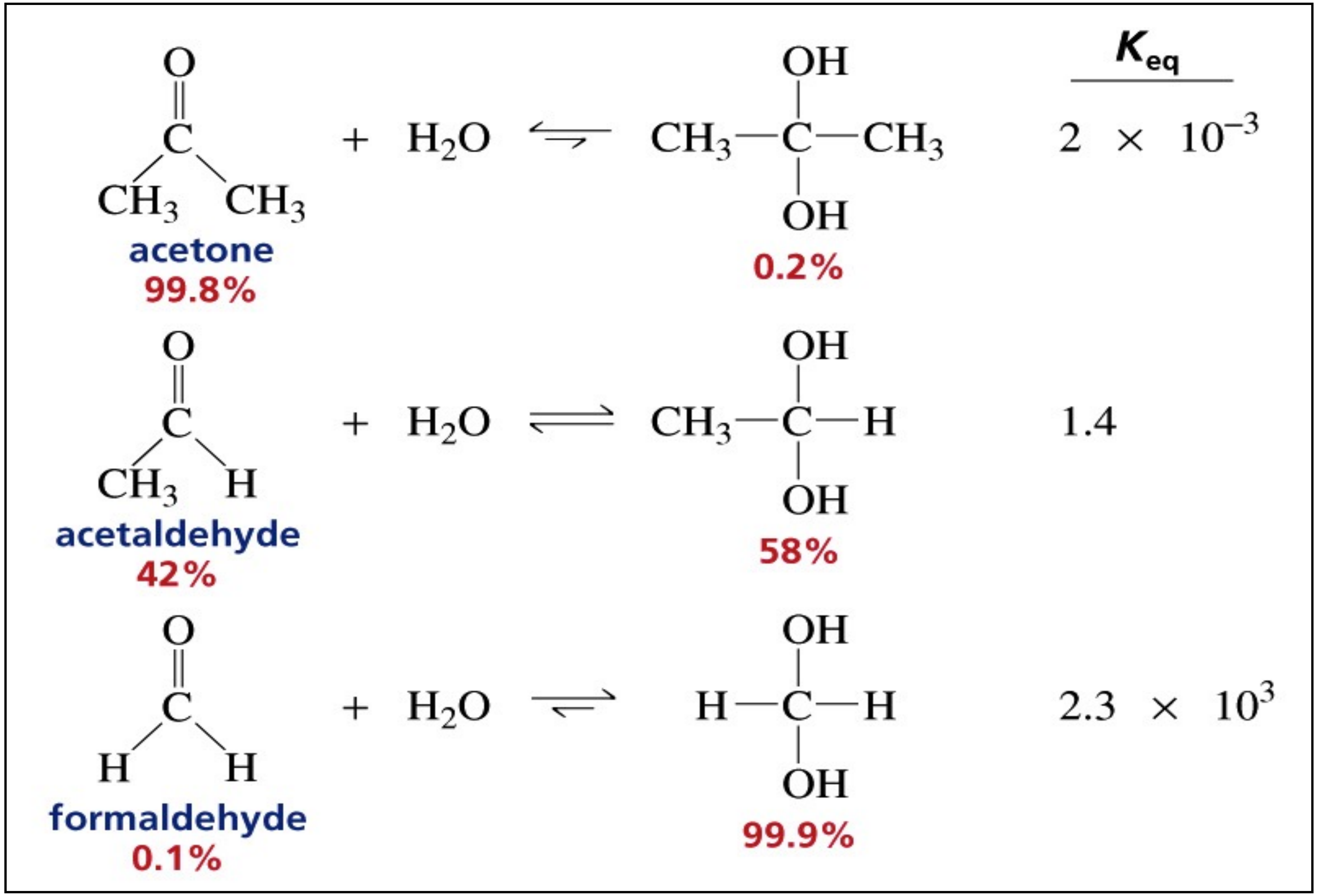
Acetone hydrate (0.1%)



Formaldehyde (0.1%)

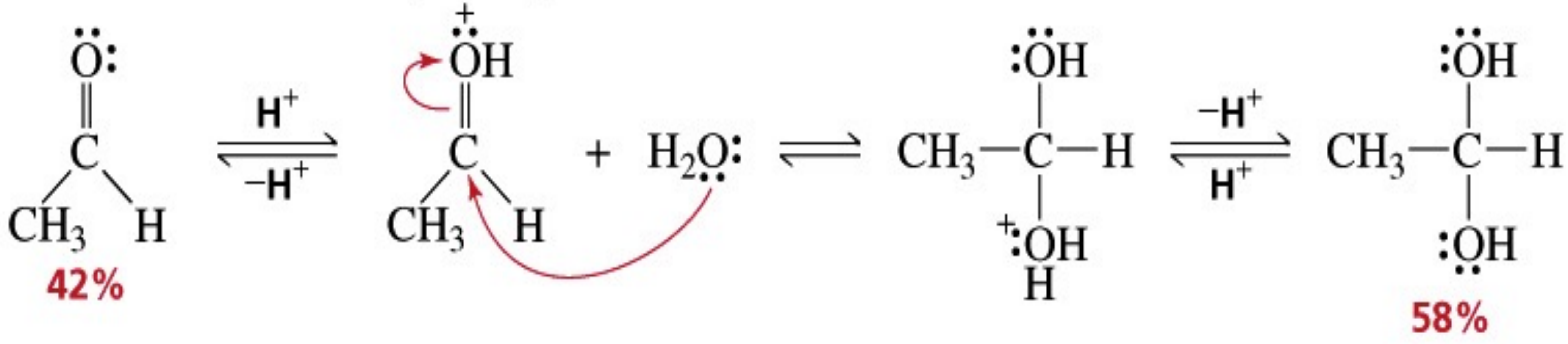
Formaldehyde hydrate (99.9%)

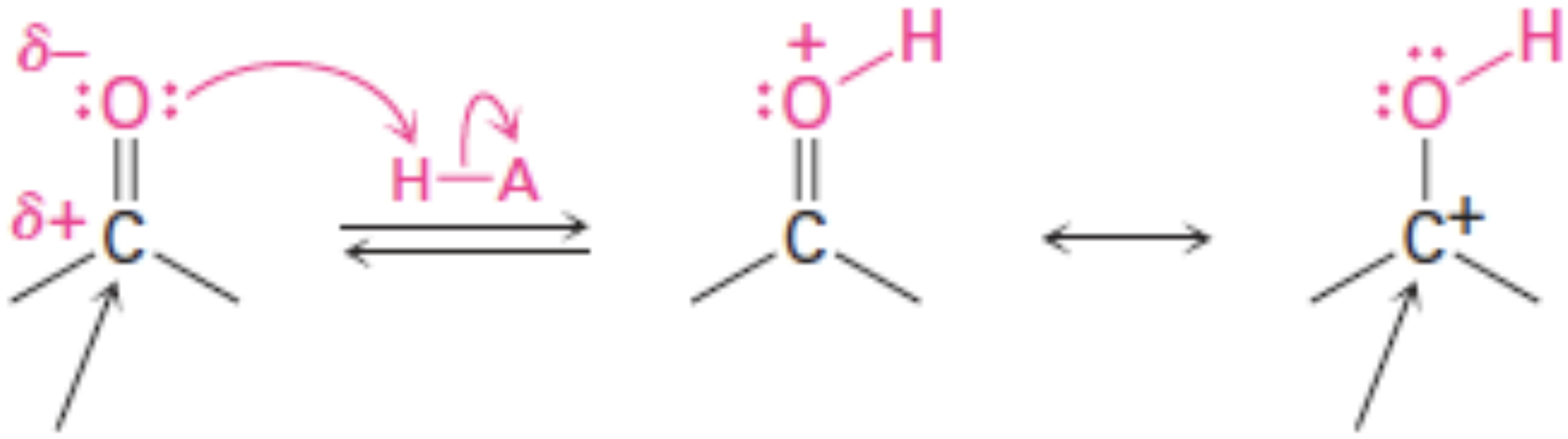
L'equilibrio in presenza di acqua: Il chetone è svantaggiato



(1) Aggiunta di H2O: Meccanismo di idratazione catalizzata dall'acido

mechanism for acid-catalyzed hydrate formation

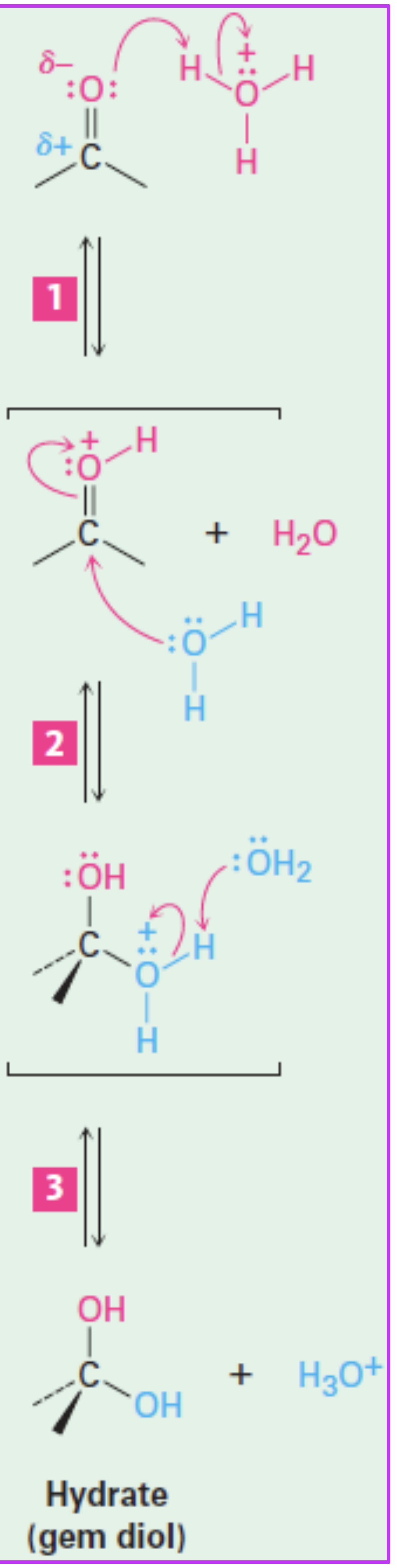




A neutral carbonyl group is moderately electrophilic because of the polarity of the C–O bond.

A protonated carbonyl group is strongly electrophilic because of the positive charge on carbon.

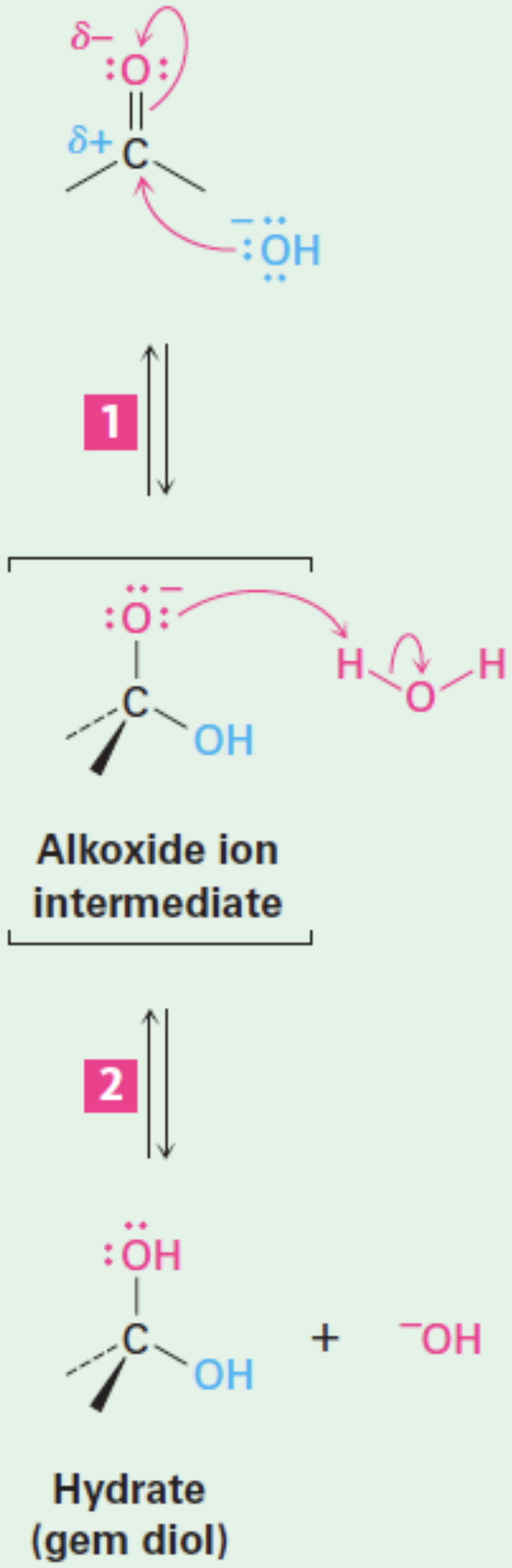
(1) Aggiunta di H2O: Meccanismo di idratazione catalizzata da un acido o da una base



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^+.

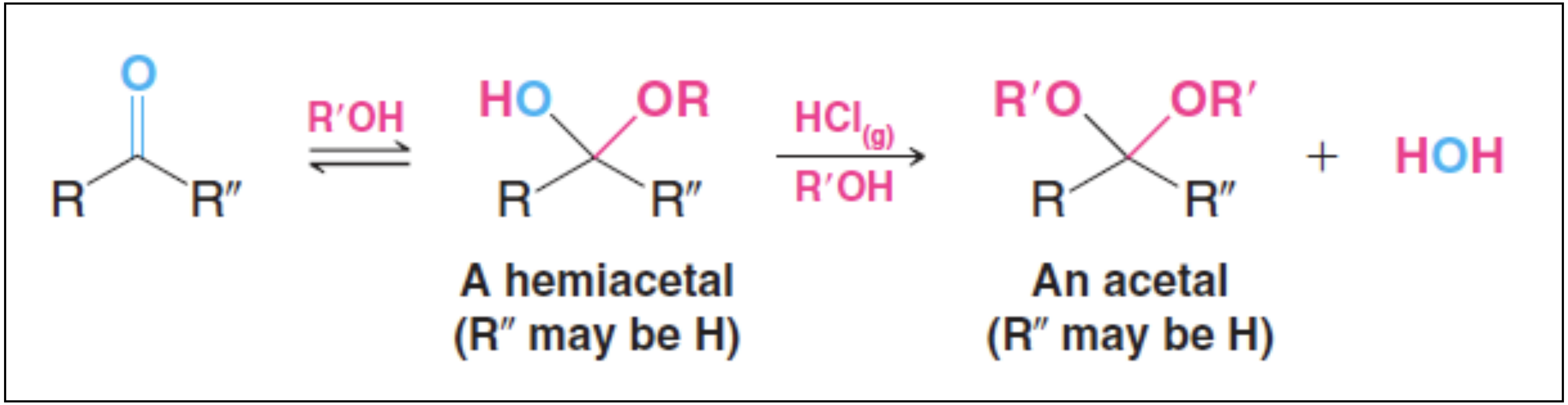


1 The negatively charged nucleophile OH^- adds to the electrophilic carbon and pushes π electrons from the C=O bond onto oxygen, giving an alkoxide ion.

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

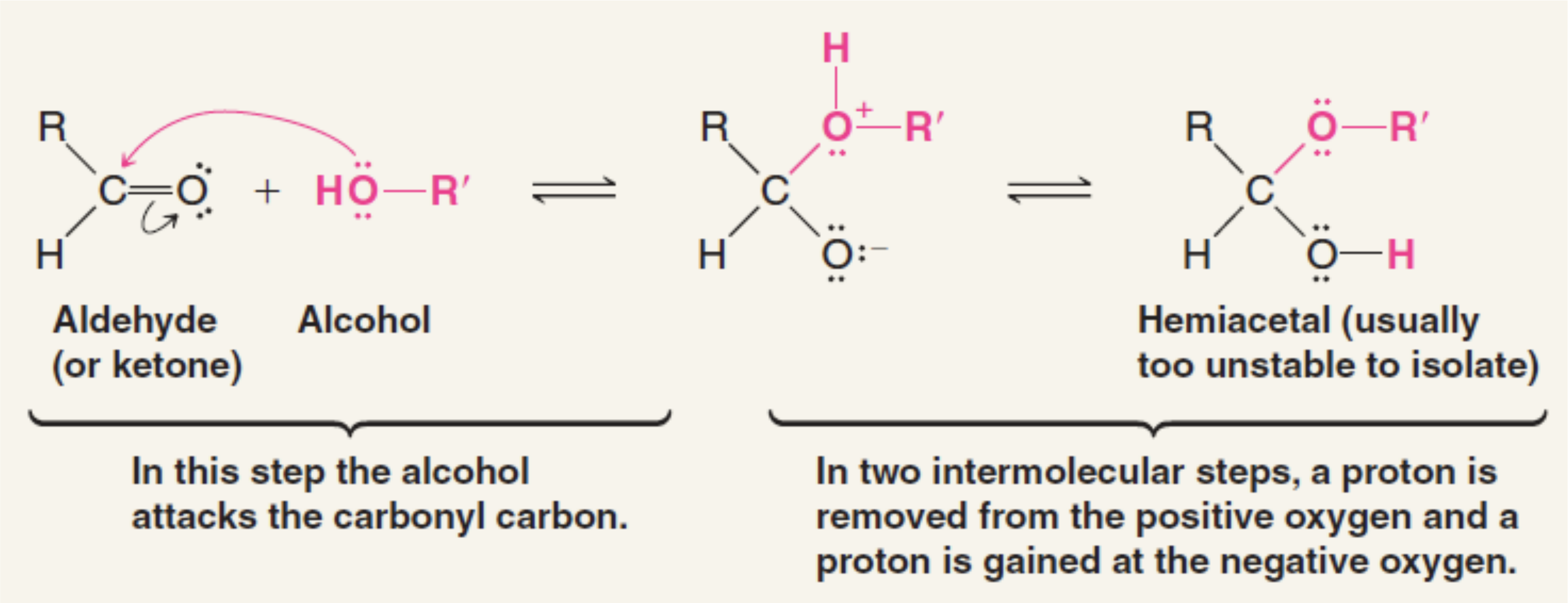
Gli aldeidi e i chetoni reagiscono reversibilmente con due equivalenti di un alcol in presenza di un catalizzatore acido per formare acetali



-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.

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



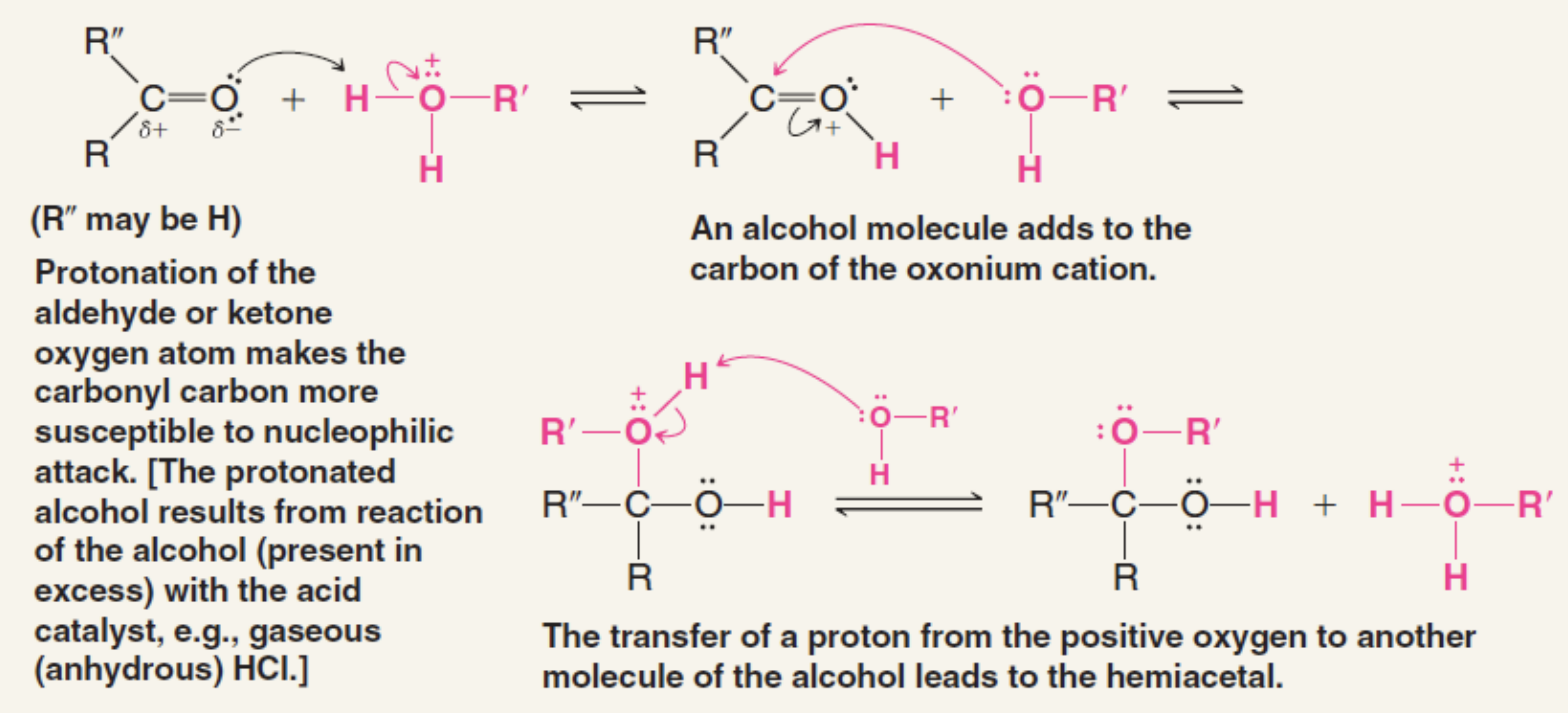
In this step the alcohol attacks the carbonyl carbon.

In two intermolecular steps, a proton is removed from the positive oxygen and a proton is gained at the negative oxygen.

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



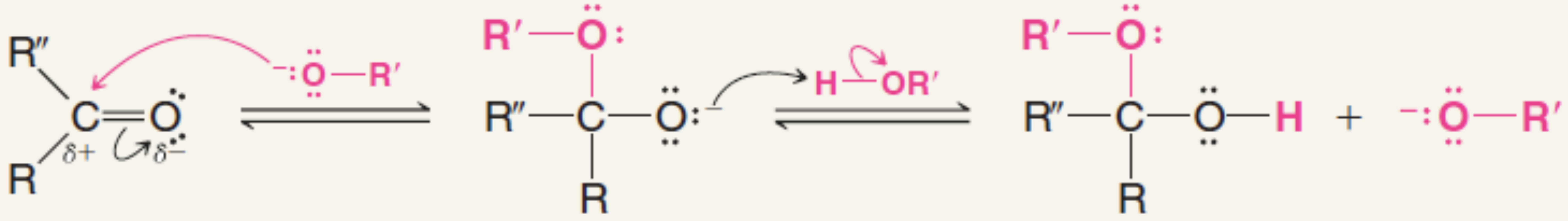
(R″ may be H)

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

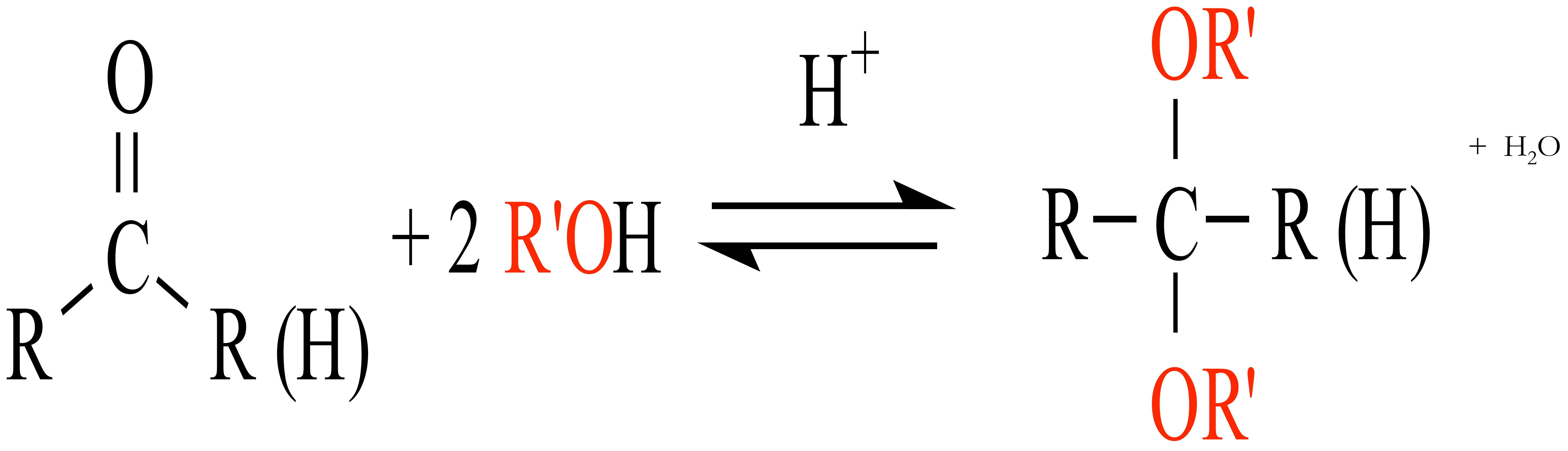


(R″ may be H)

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.

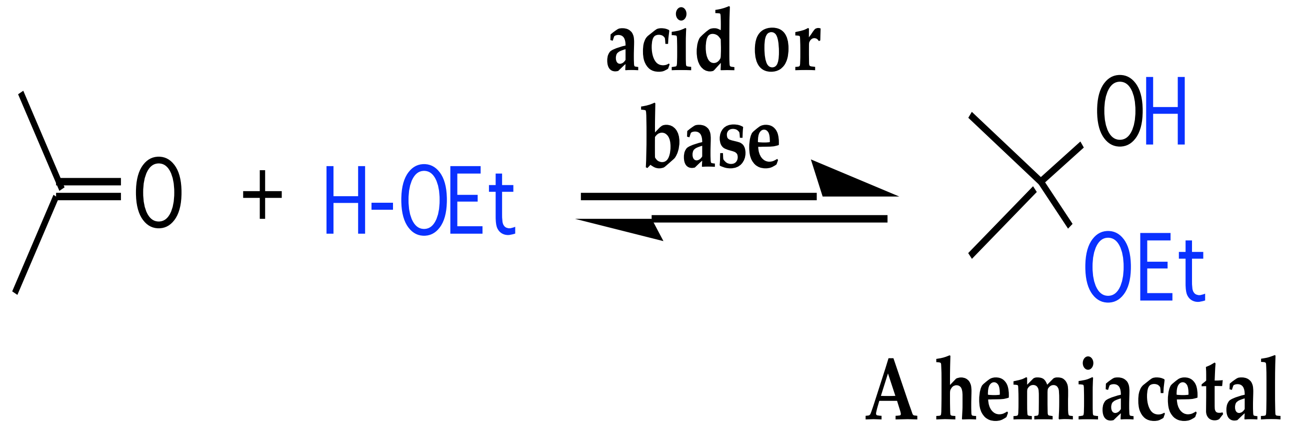
The alkoxide anion abstracts a proton from an alcohol molecule to produce the hemiacetal and regenerates an alkoxide anion.

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

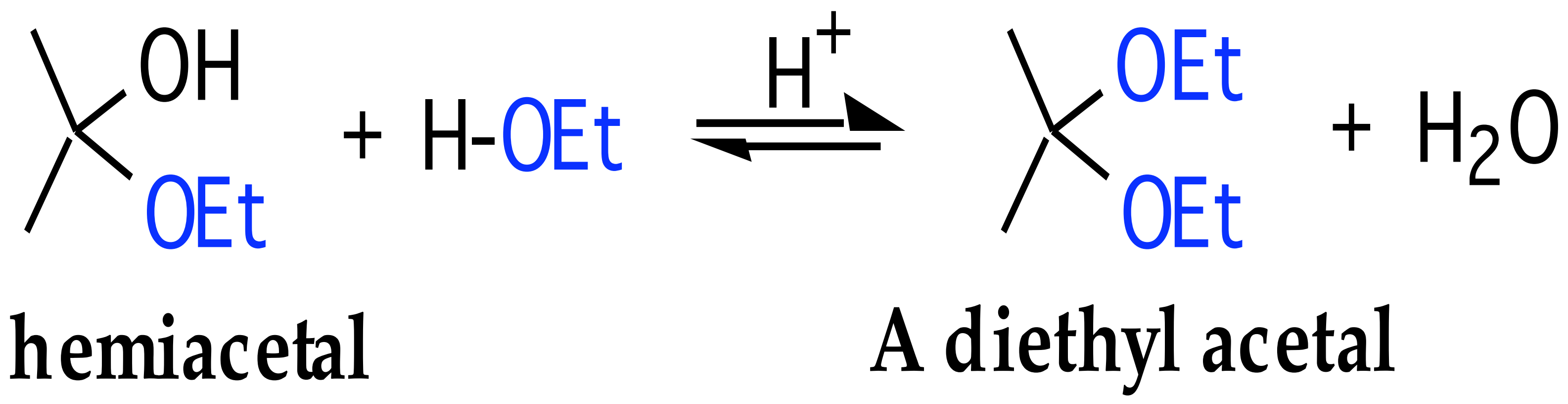


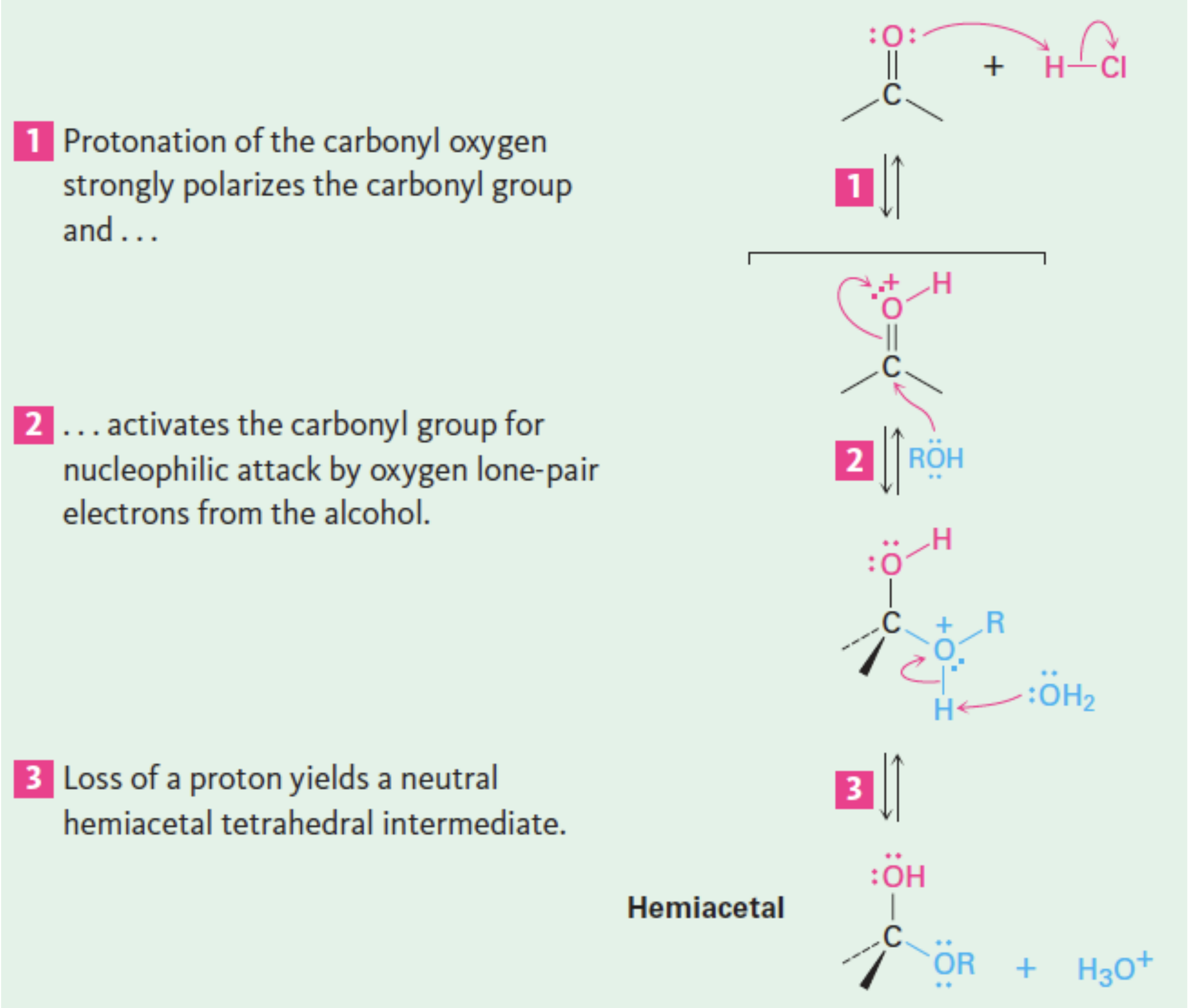
(2) Addizione nucleofila degli alcoli al gruppo carbonile: Formazione di acetali

1° STADIO:



2° STADIO:

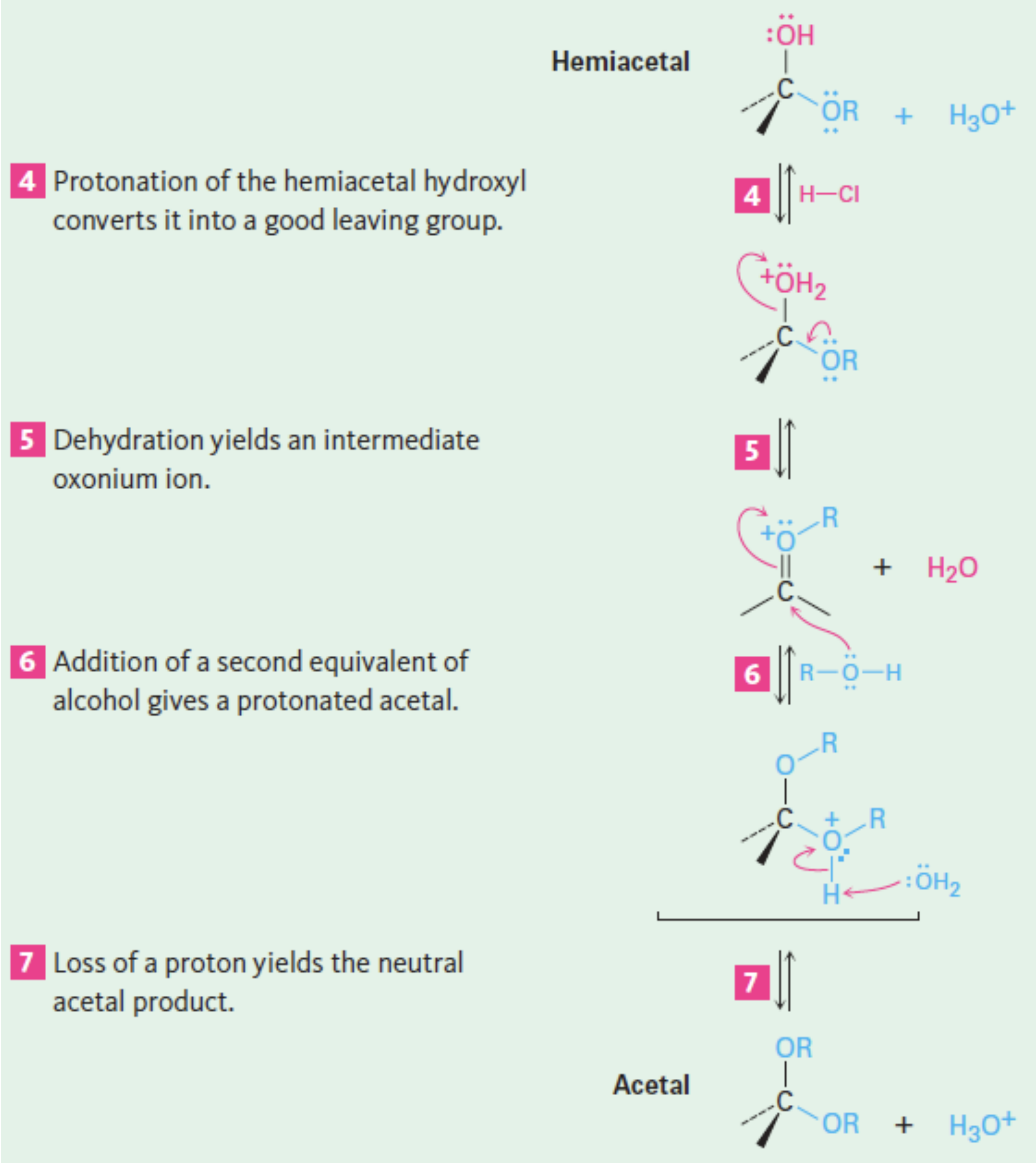




1 Protonation of the carbonyl oxygen strongly polarizes the carbonyl group and . . .

2 . . . activates the carbonyl group for nucleophilic attack by oxygen lone-pair electrons from the alcohol.

3 Loss of a proton yields a neutral hemiacetal tetrahedral intermediate.



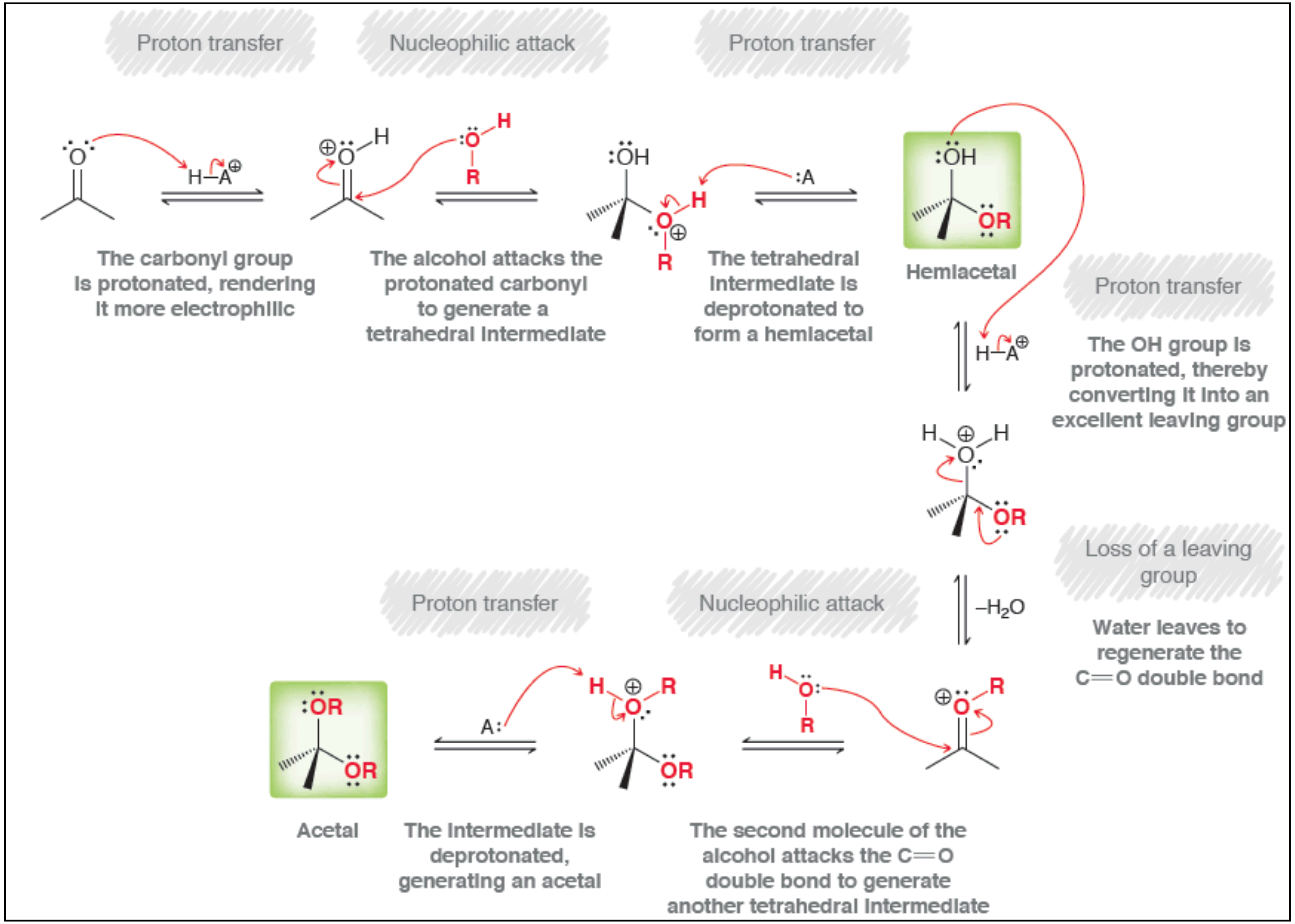
4 Protonation of the hemiacetal hydroxyl converts it into a good leaving group.

5 Dehydration yields an intermediate oxonium ion.

6 Addition of a second equivalent of alcohol gives a protonated acetal.

7 Loss of a proton yields the neutral acetal product.

(2) Meccanismo per Formazione di acetali in ambiente acido



Proton transfer

The carbonyl group is protonated, rendering it more electrophilic

Nucleophilic attack

The alcohol attacks the protonated carbonyl to generate a tetrahedral intermediate

Proton transfer

The tetrahedral intermediate is deprotonated to form a hemiacetal

Proton transfer

The OH group is protonated, thereby converting it into an excellent leaving group

Loss of a leaving group

Water leaves to regenerate the C═O double bond

Nucleophilic attack

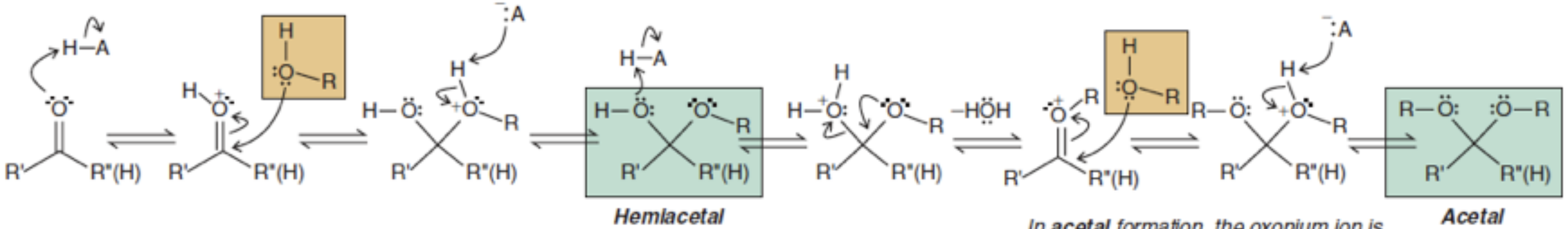
The second molecule of the alcohol attacks the C═O double bond to generate another tetrahedral intermediate

Proton transfer

The intermediate is deprotonated, generating an acetal

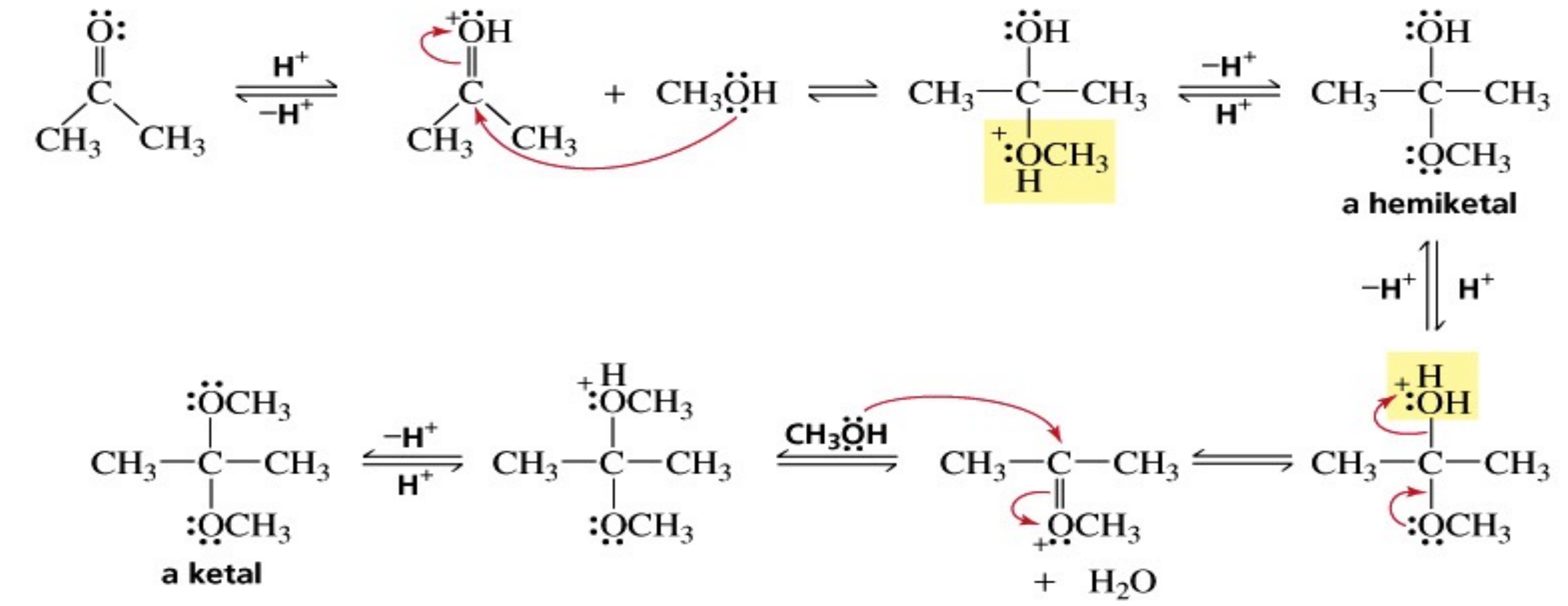
(2) Meccanismo per Formazione di acetali in ambiente acido

I. Hemiacetal and acetal formation: reaction with alcohols

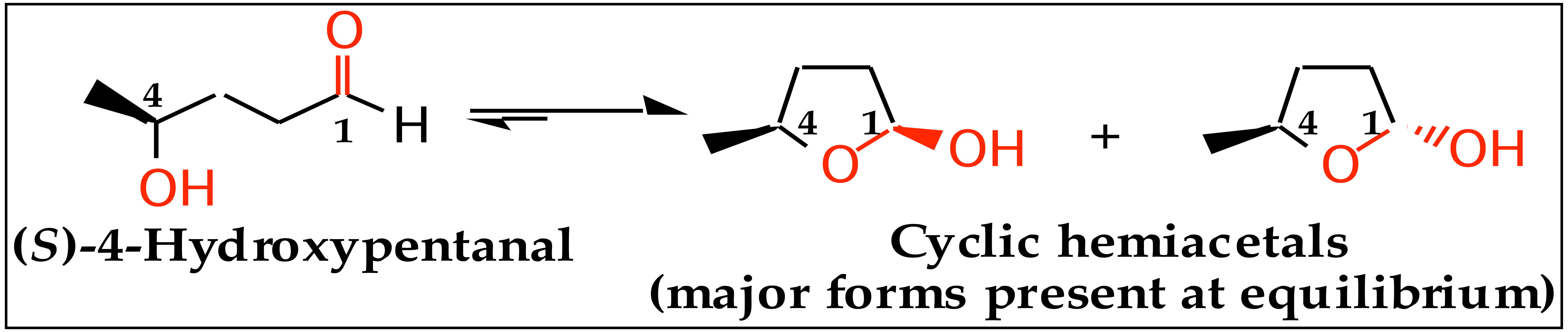


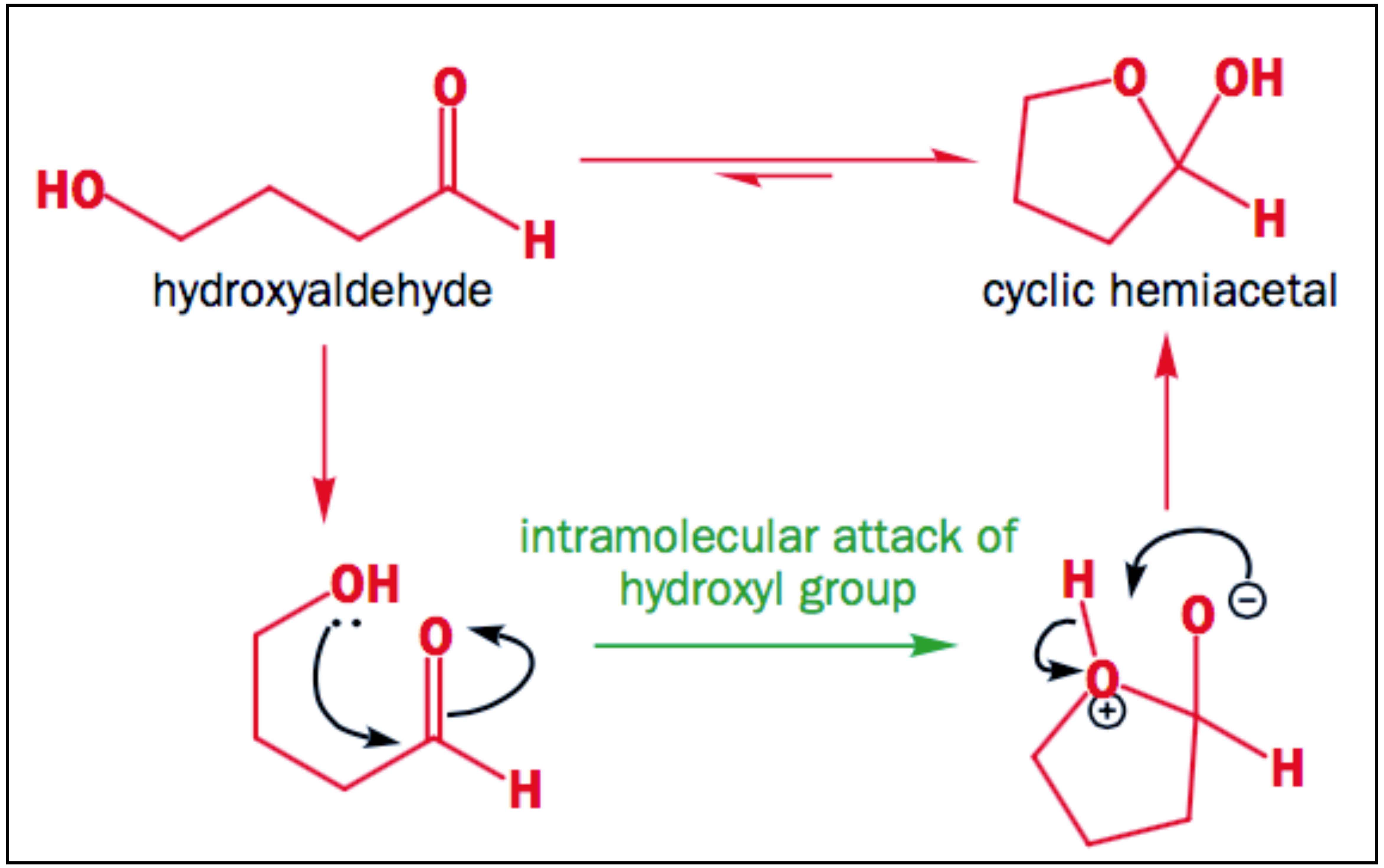
In acetal formation, the oxonium ion is attacked by a second alcohol molecule.

mechanism for acid-catalyzed acetal or ketal formation

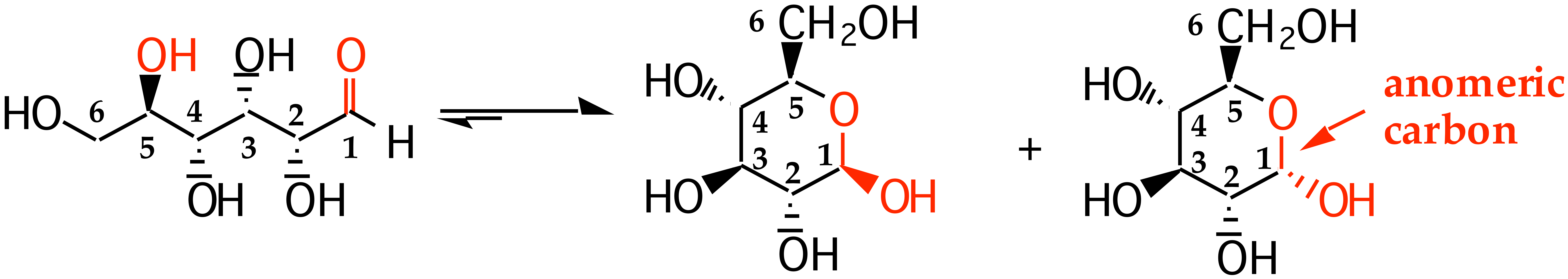


(2) Meccanismo per Formazione di emiacetali ciclici a 5 atomi





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

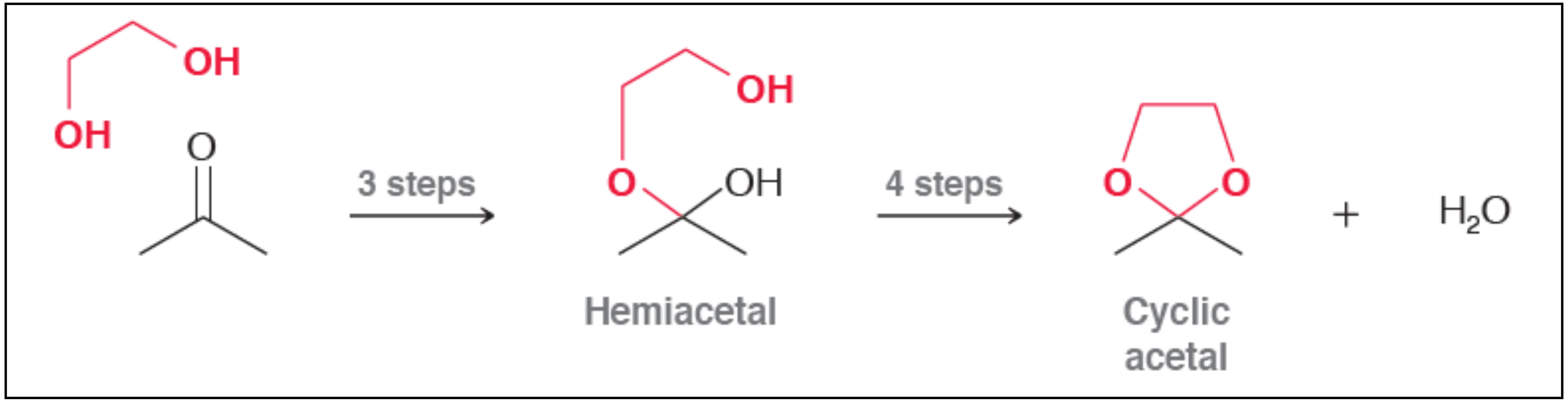


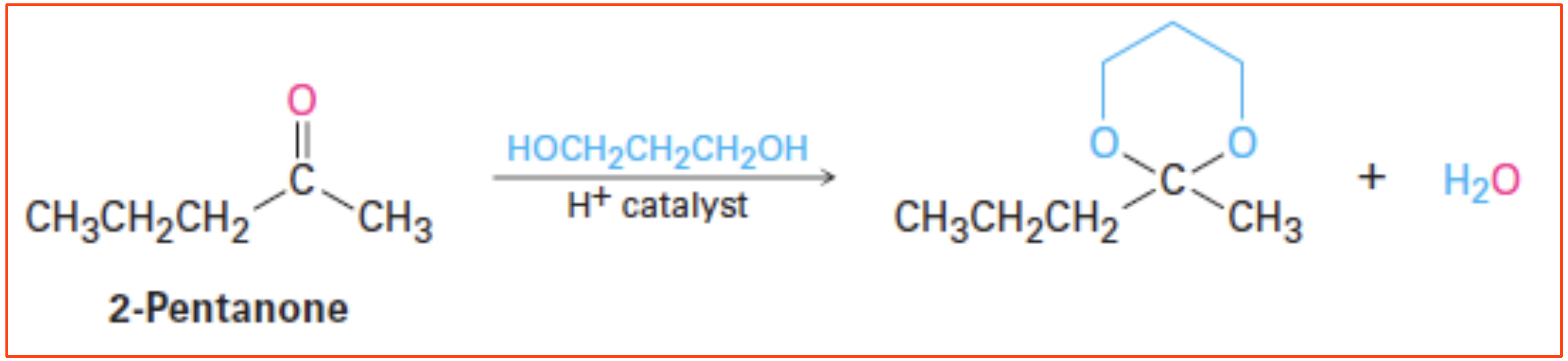
D-Glucose (open chain form)

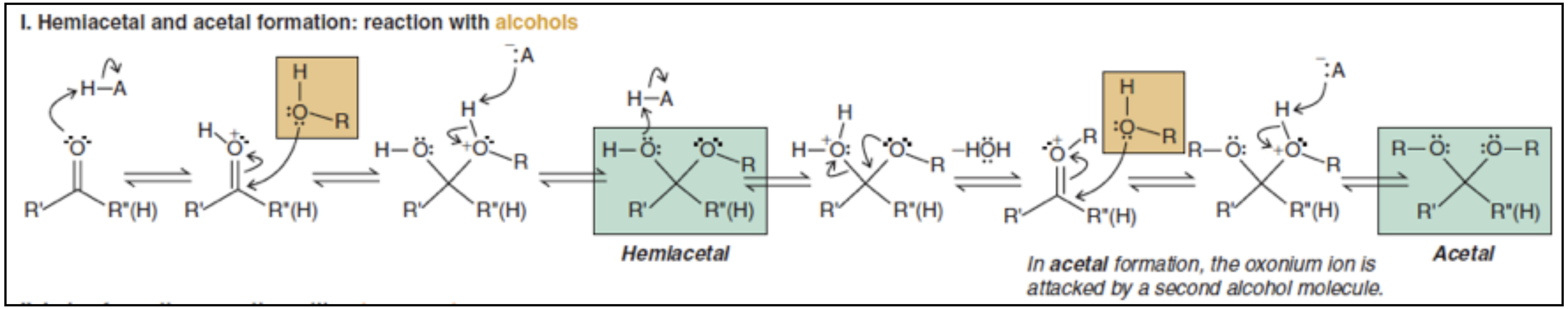
β Anomer of D-glucose cyclic hemiacetal (predominates at equilibrium)

α Anomer of D-glucose cyclic hemiacetal

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

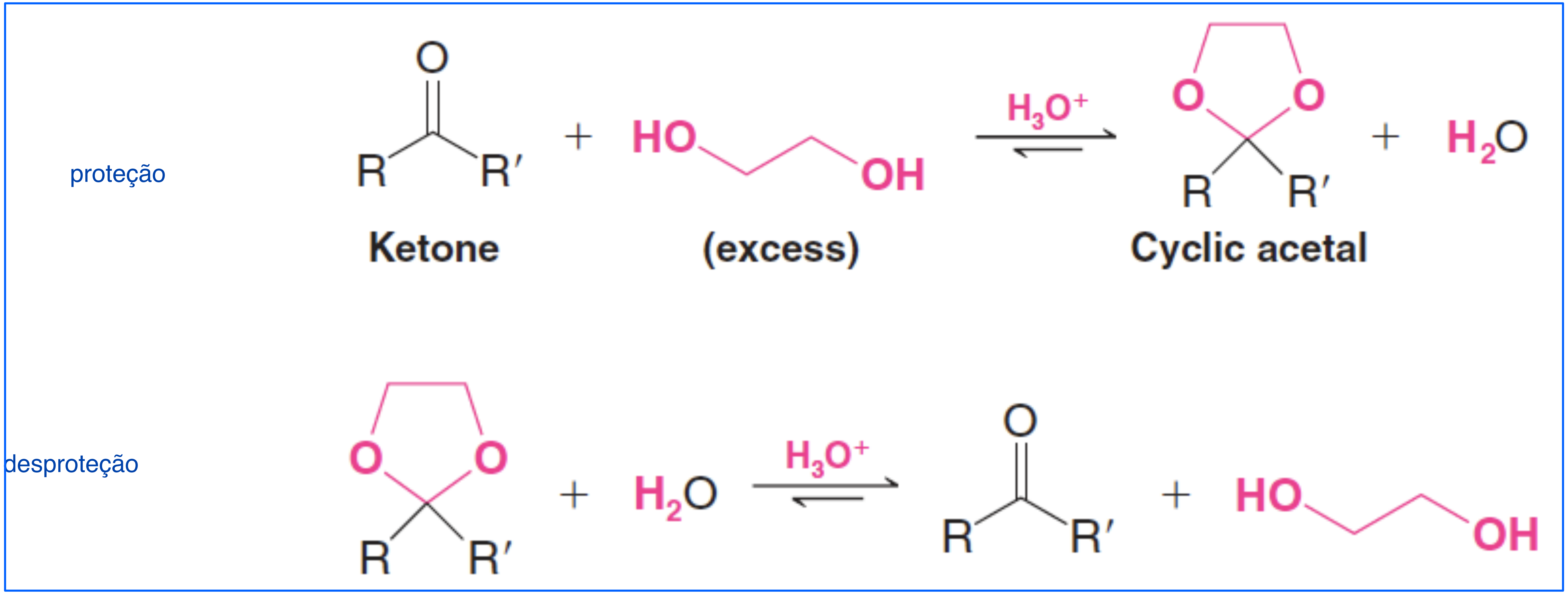






Acetali come gruppi di protezione del gruppo carbonile

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

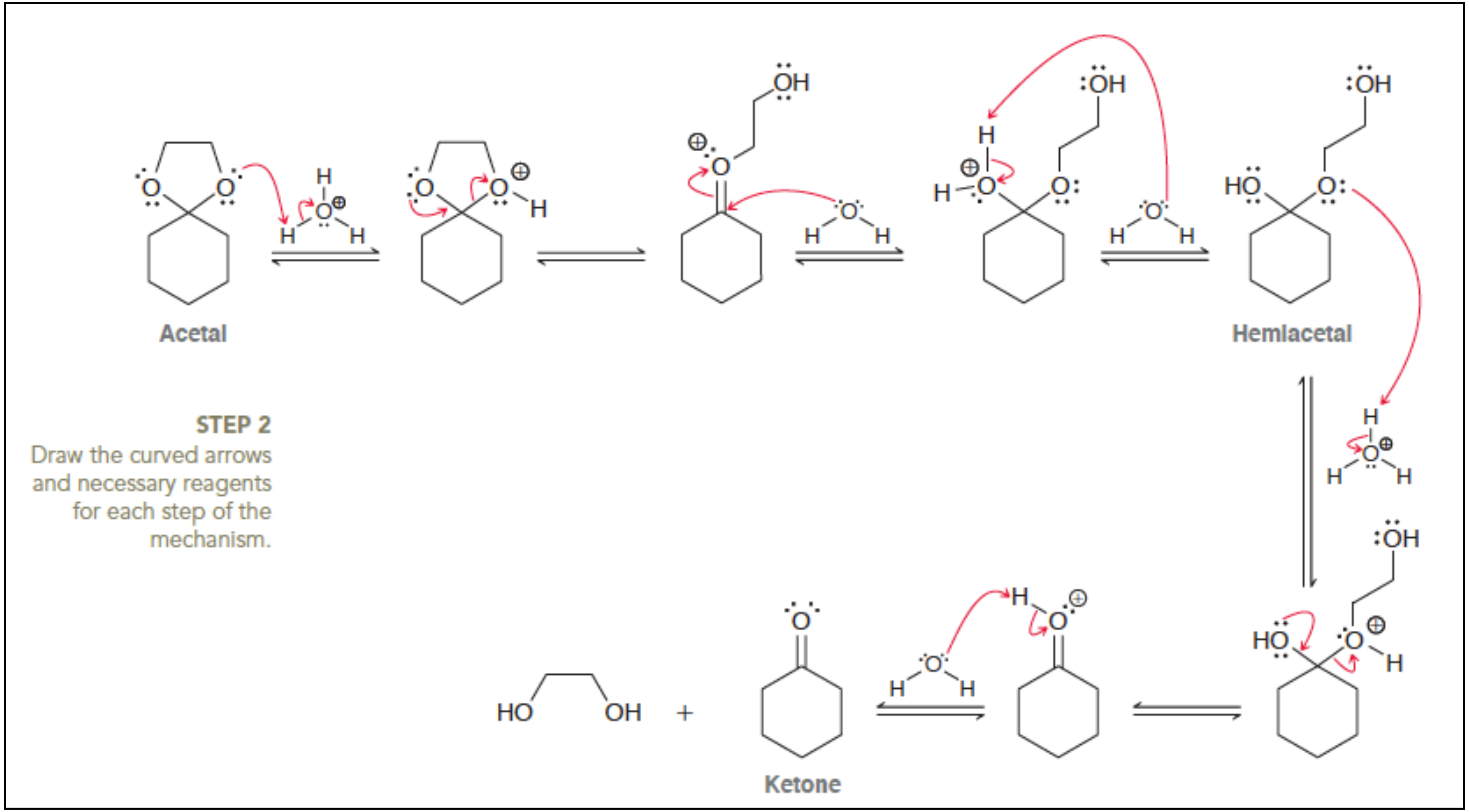


proteção

desproteção

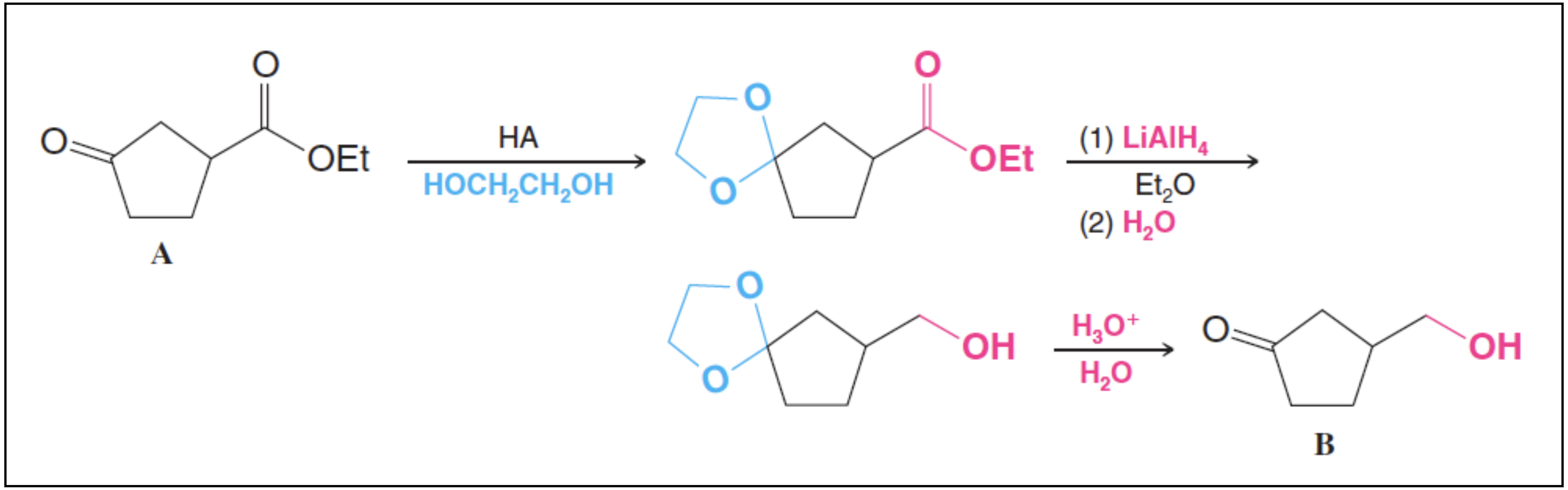
Gli acetali sono usati come gruppi protettori in un ambiente basico o nucleofilo

Idrolisi degli ACETI in ambiente acido

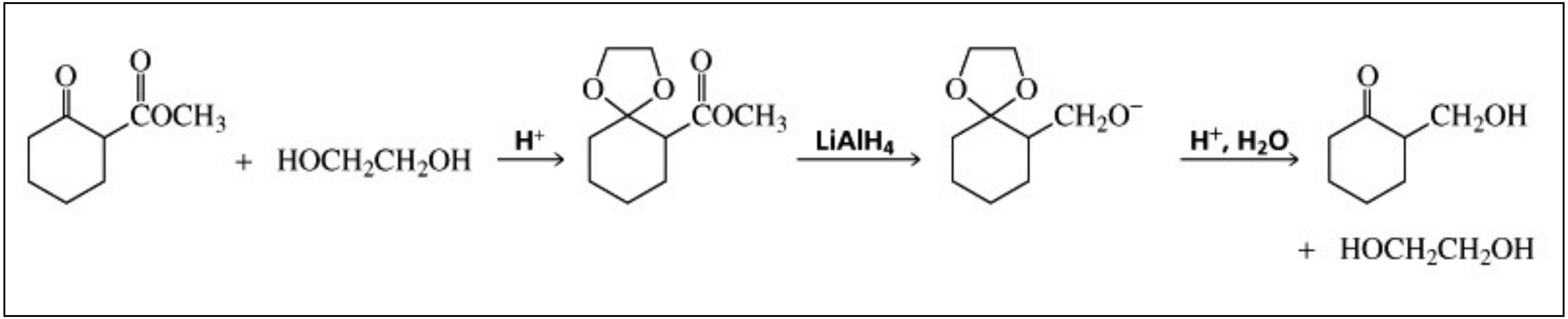


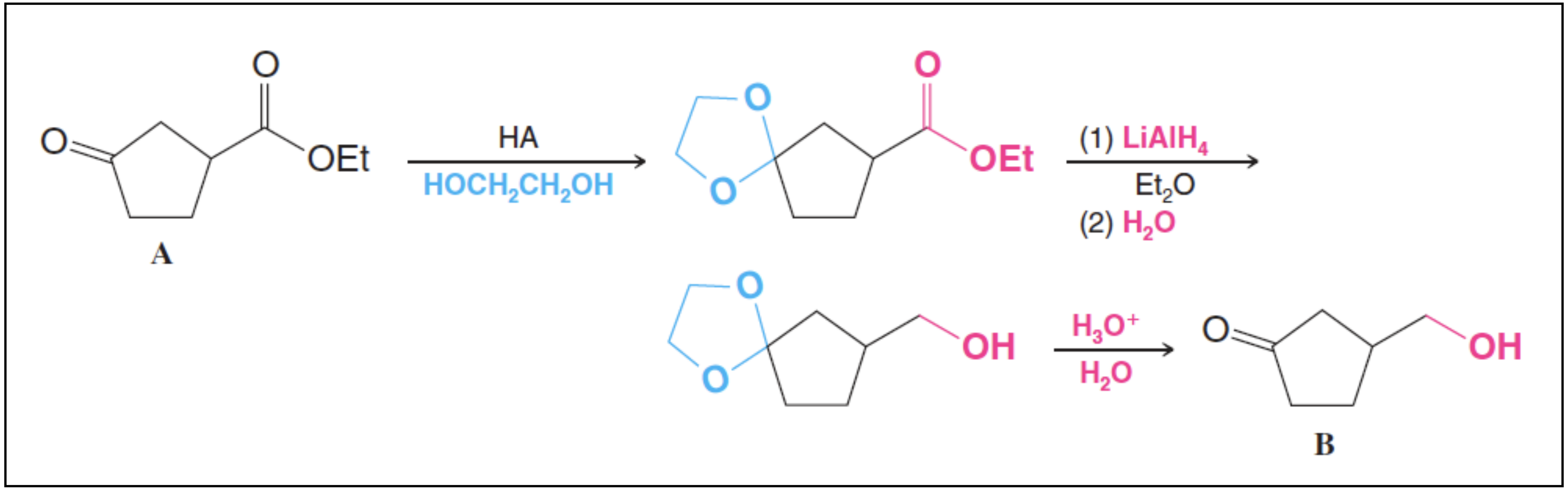
STEP 2
Draw the curved arrows and necessary reagents for each step of the mechanism.

Acetali come gruppi protettori degli aldeidi e chetoni in soluzioni basiche

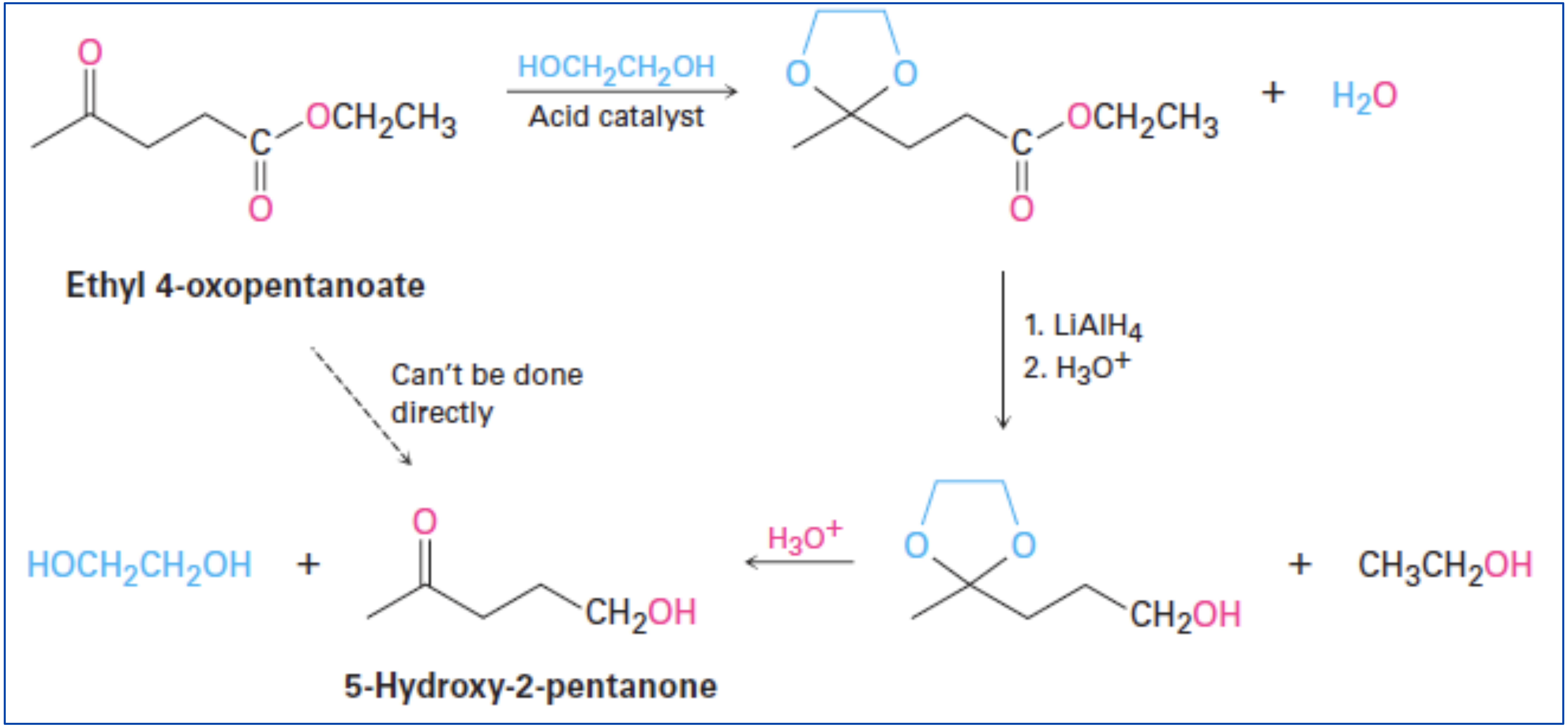


Acetali come gruppi protettori degli aldeidi e chetoni in soluzioni basiche

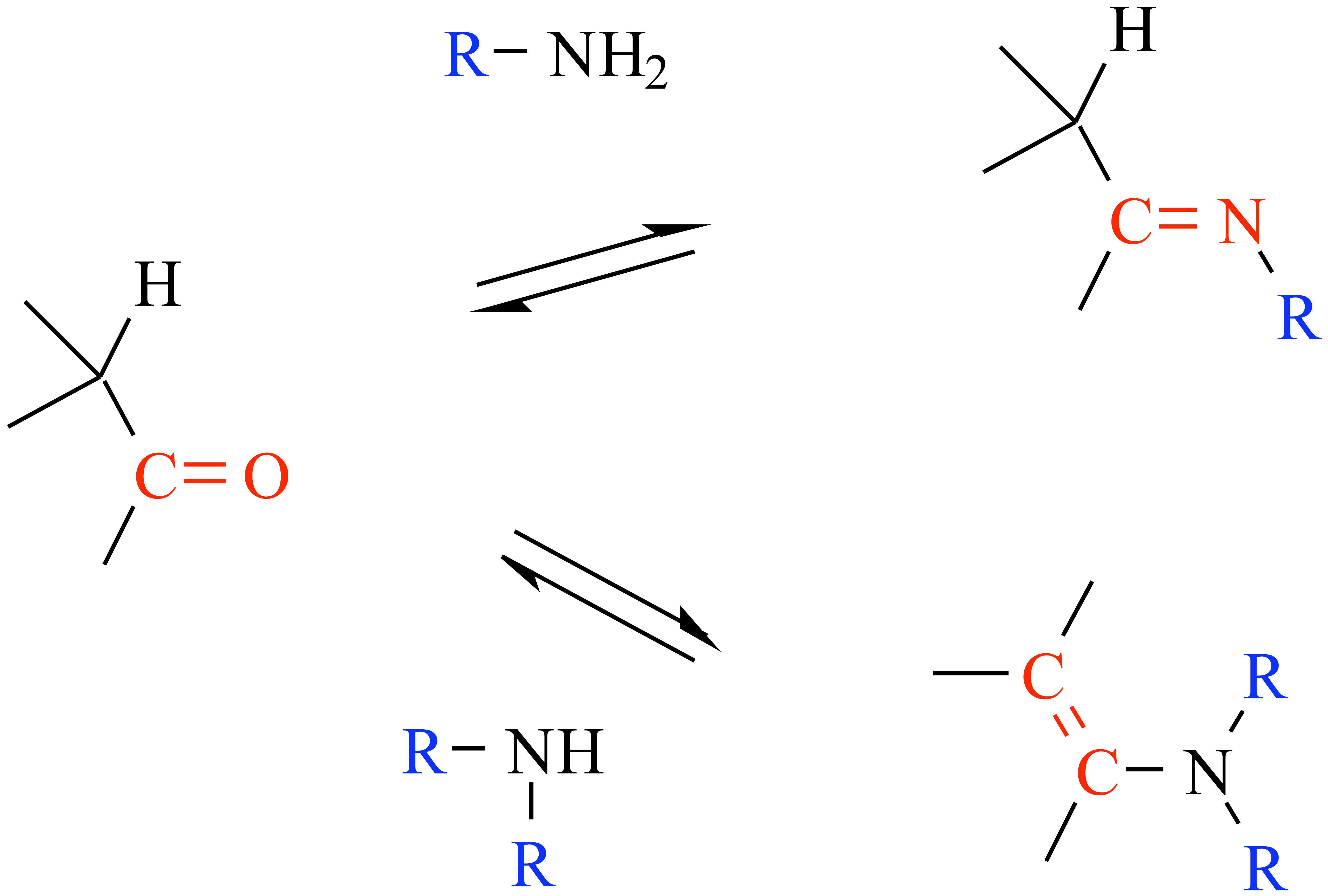




Acetali come gruppi protettori degli aldeidi e chetoni in soluzioni basiche



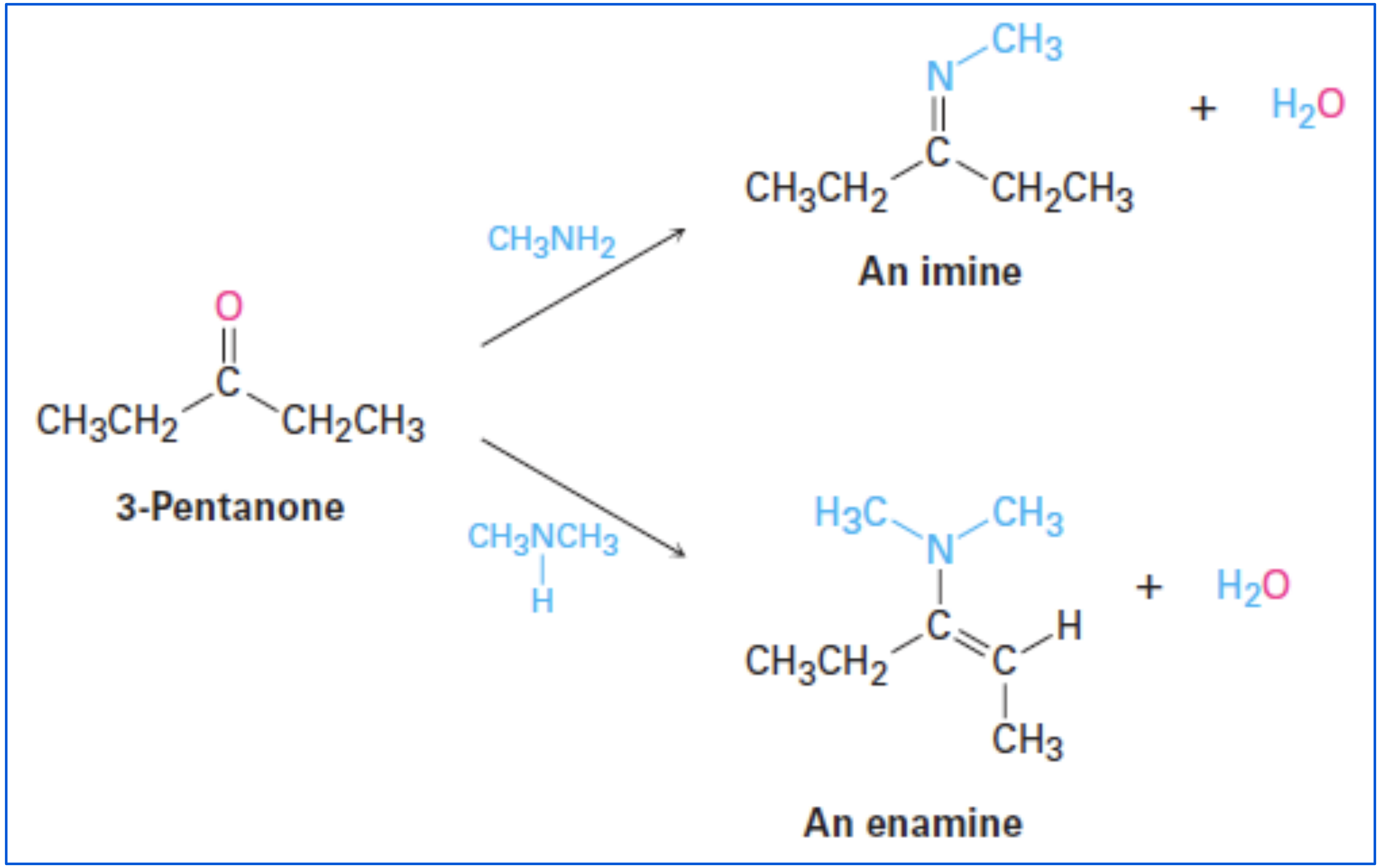
3) addizione Nucleofilica di ammine: Formazione di Immine e Enammine

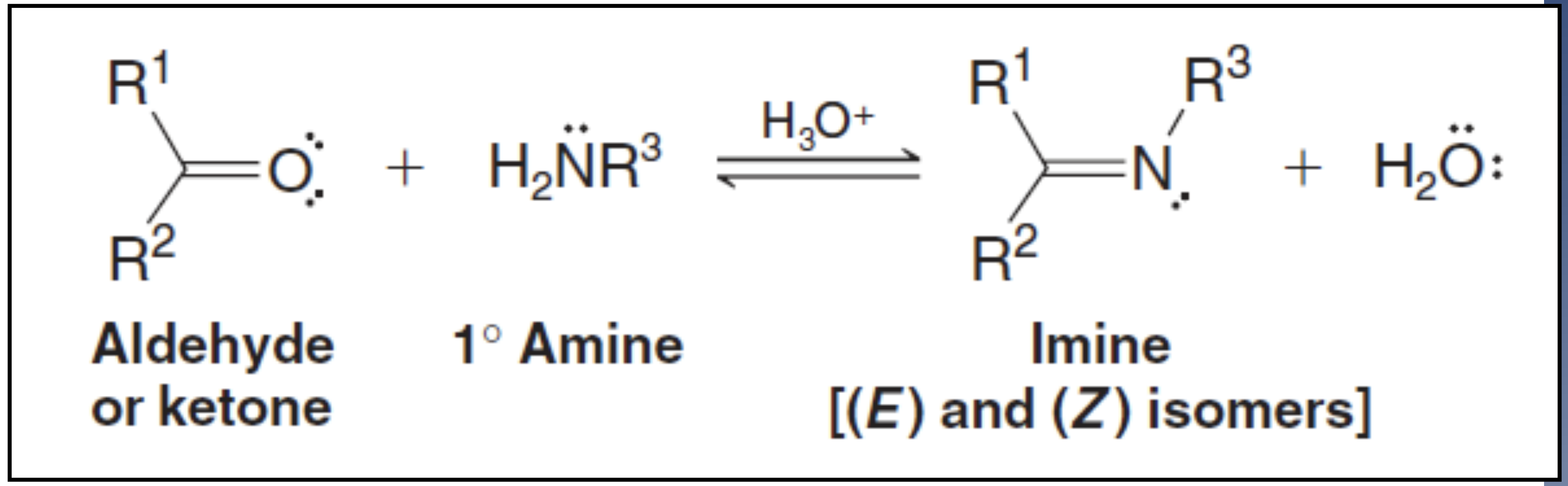


IMMINA
Doppio legame
C=N

ENAMMINA
Doppio legame
C=C

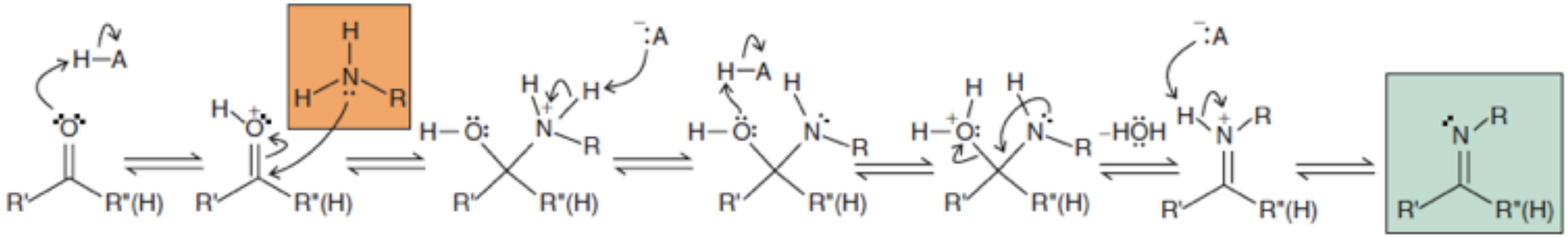
3) addizione Nucleofilica di ammine: Formazione di Immine e Enammine





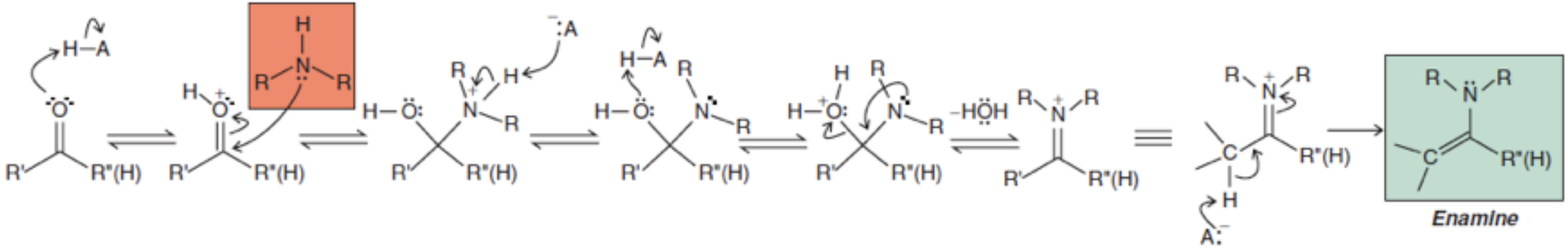
3) MECCANISMO addizione Nucleofilica di ammine: Formazione di Immine e Enammine

II. Imine formation: reaction with primary amines



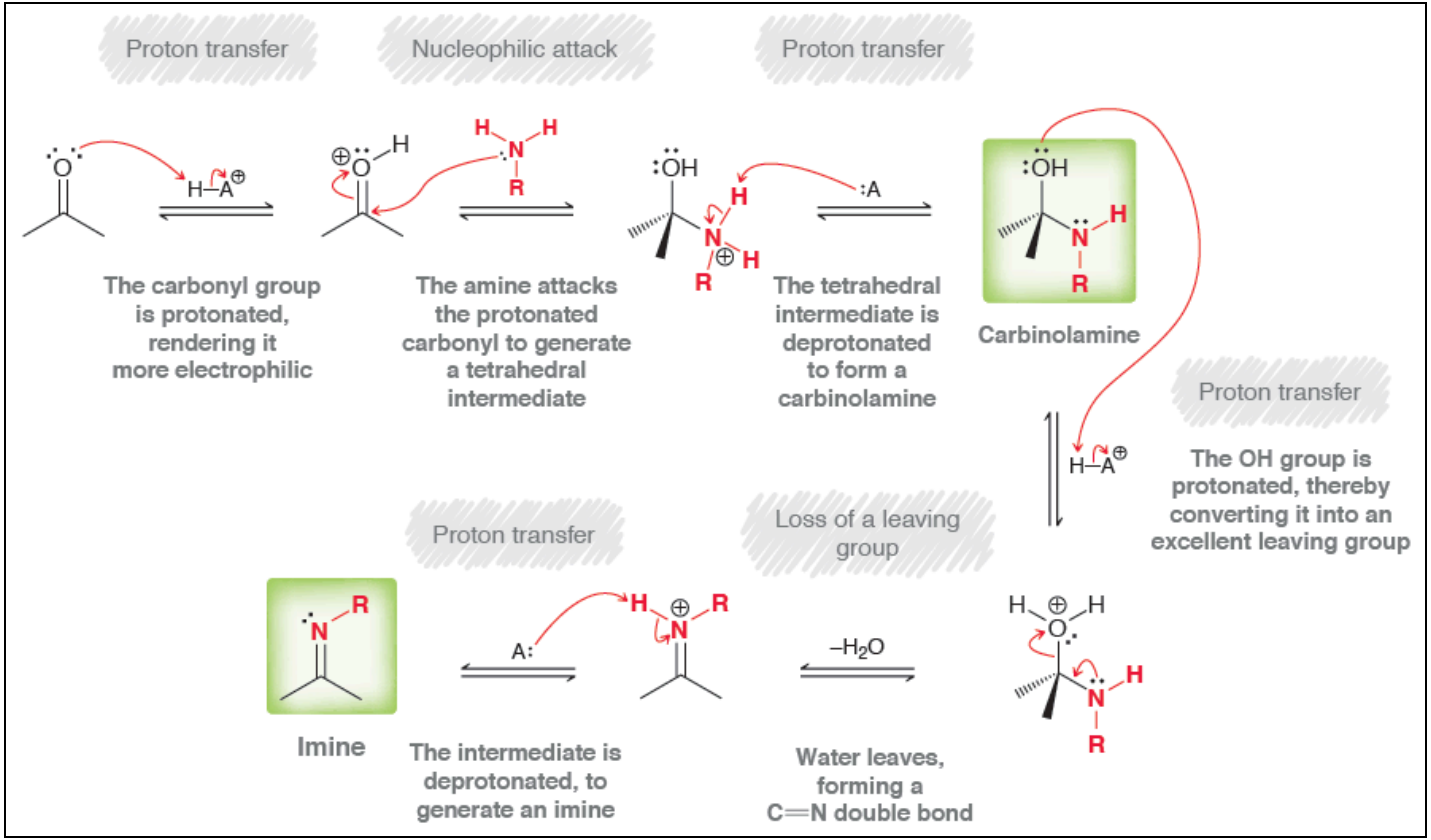
In ***imine*** *formation, the proton on the initial iminium ion is removed, leading to the stable imine product.*

III. Enamine formation: reaction with secondary amines



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



Proton transfer

The carbonyl group is protonated, rendering it more electrophilic

Nucleophilic attack

The amine attacks the protonated carbonyl to generate a tetrahedral intermediate

Proton transfer

The tetrahedral intermediate is deprotonated to form a carbinolamine

Carbinolamine

Proton transfer

The OH group is protonated, thereby converting it into an excellent leaving group

Loss of a leaving group

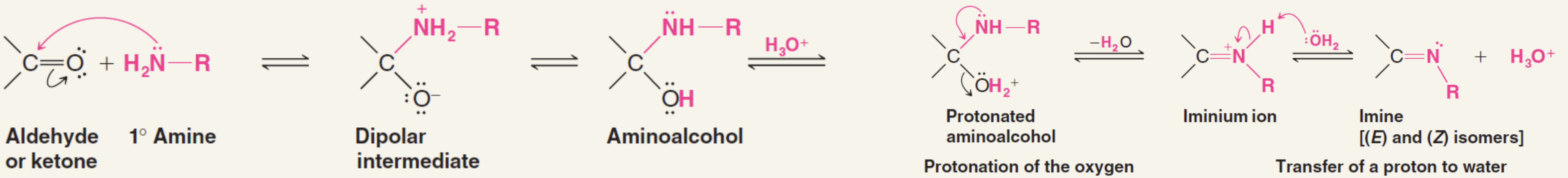
Water leaves, forming a C═N double bond

Proton transfer

The intermediate is deprotonated, to generate an imine

Imine

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



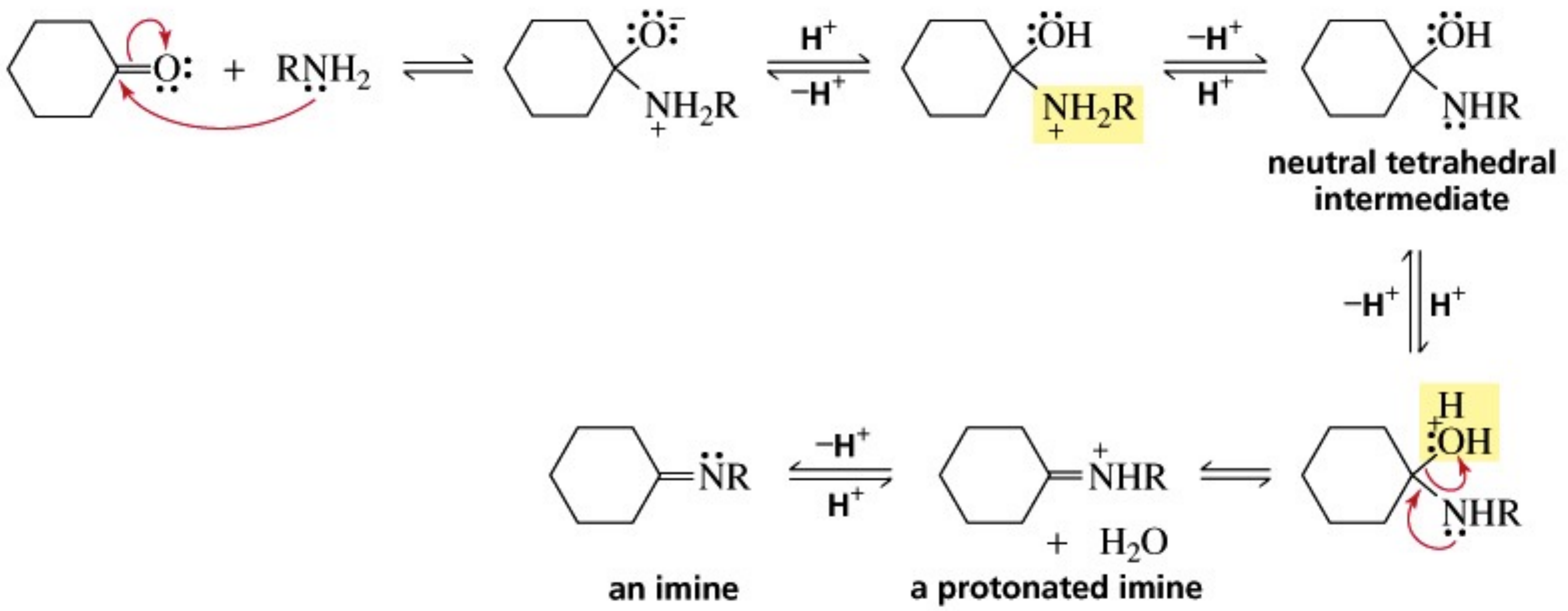
The amine adds to the carbonyl group to form a dipolar tetrahedral intermediate.

Intermolecular proton transfer from nitrogen to oxygen produces an aminoalcohol.

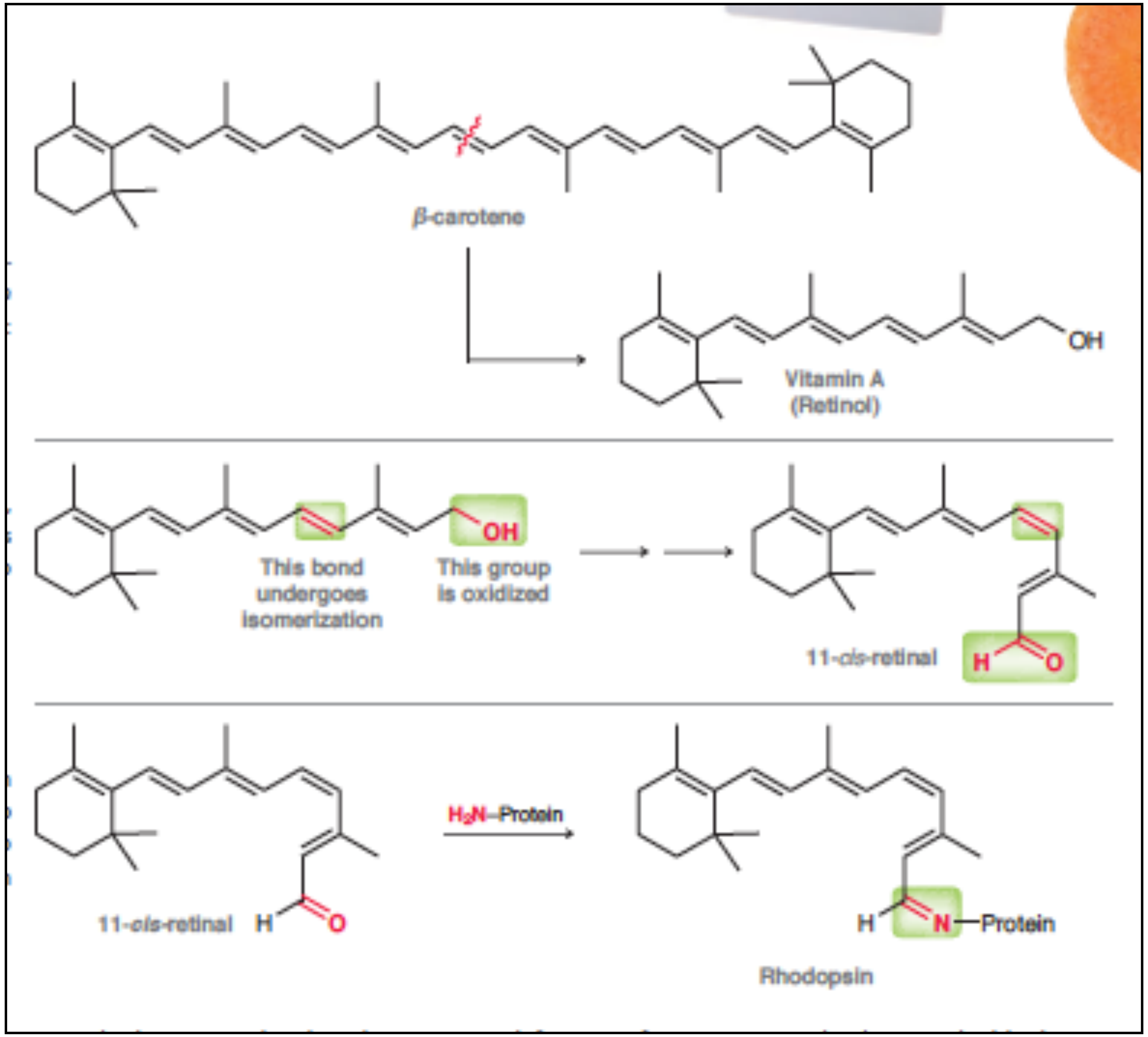
Protonation of the oxygen produces a good leaving group. Loss of a molecule of water yields an iminium ion.

Transfer of a proton to water produces the imine and regenerates the catalytic hydronium ion.

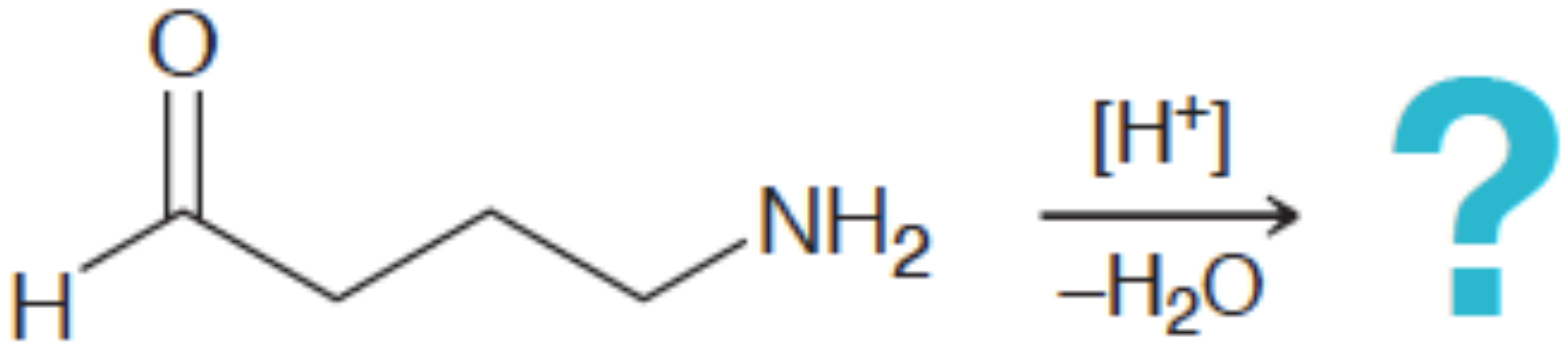
mechanism for imine formation



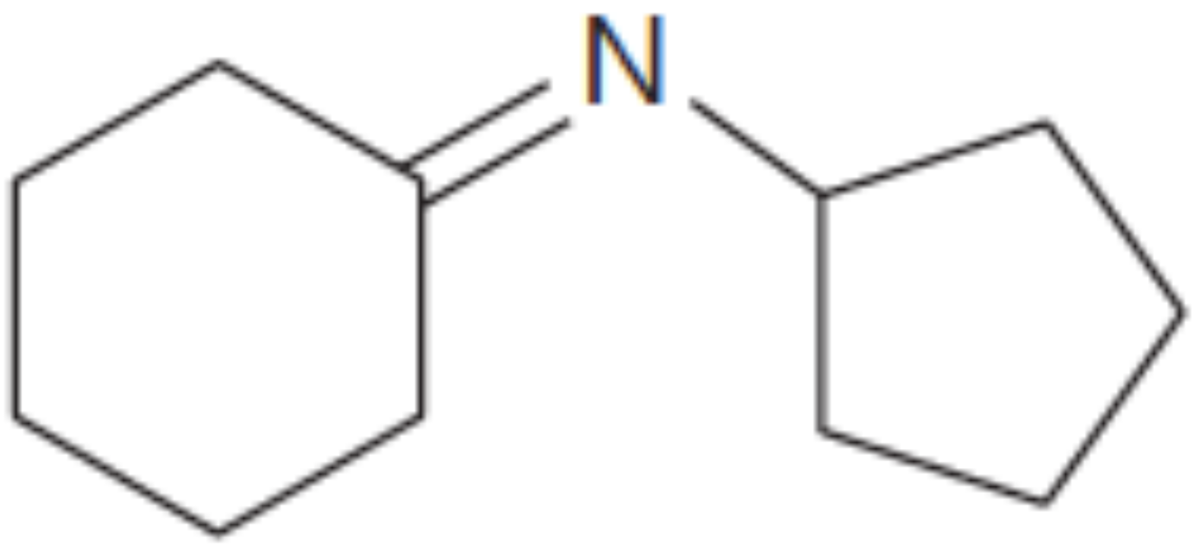
Beta-carotene e la vista

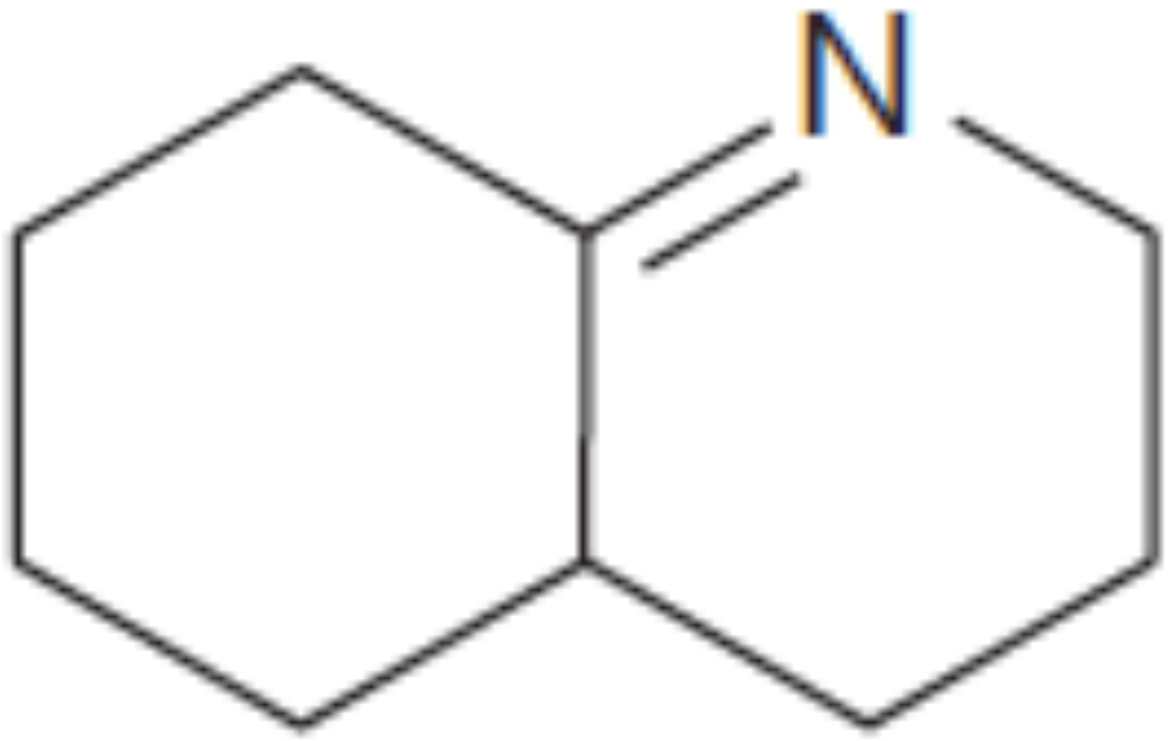


PROBLEMA: Prevedere il prodotto principale della seguente reazione intramolecolare

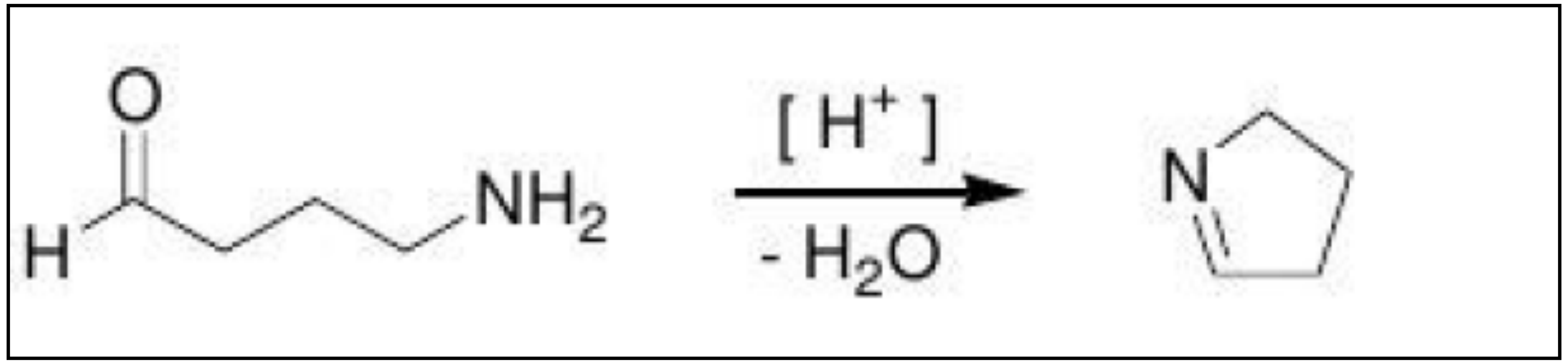


PROBLEMA: Indica i reagenti che useresti per ottenere ciascuna delle seguenti imine.

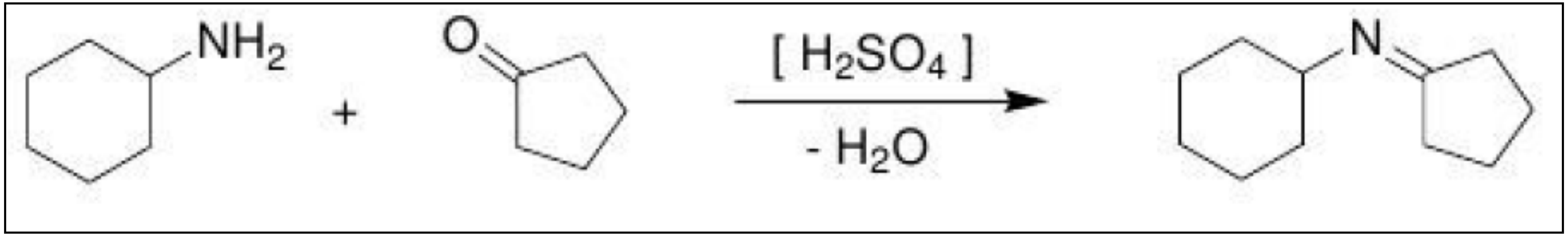


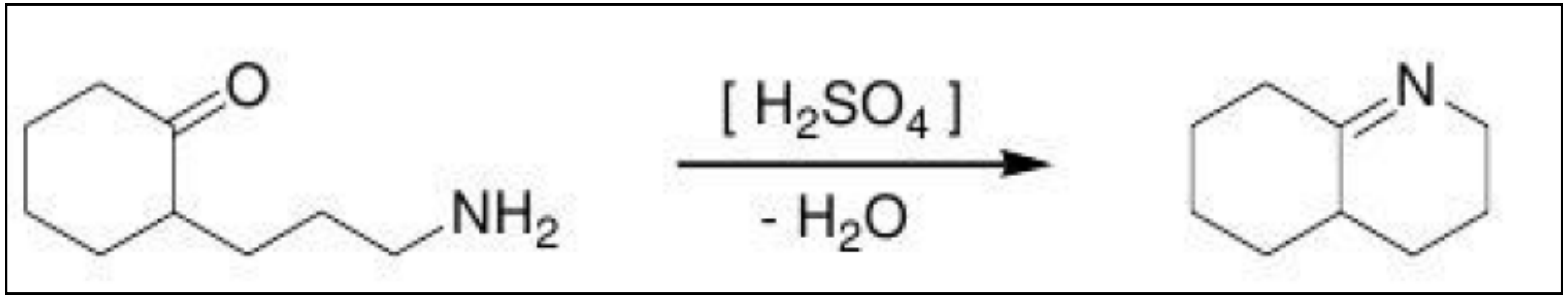


PROBLEMA: Prevedere il prodotto principale della seguente reazione intramolecolare

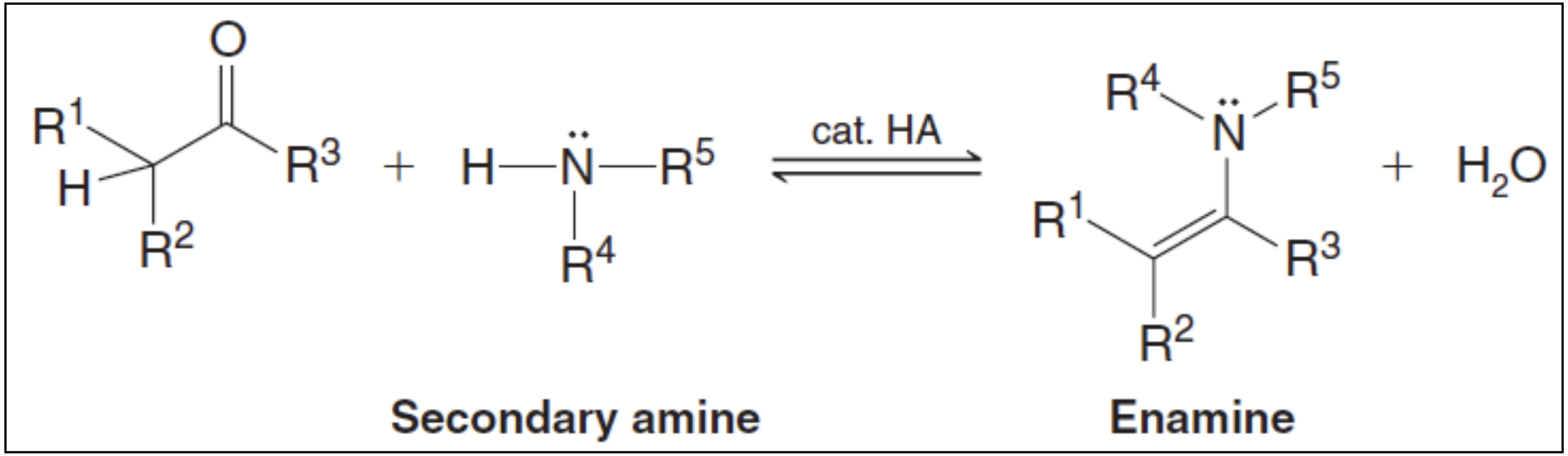


PROBLEMA: Indica i reagenti che useresti per ottenere ciascuna delle seguenti imine.



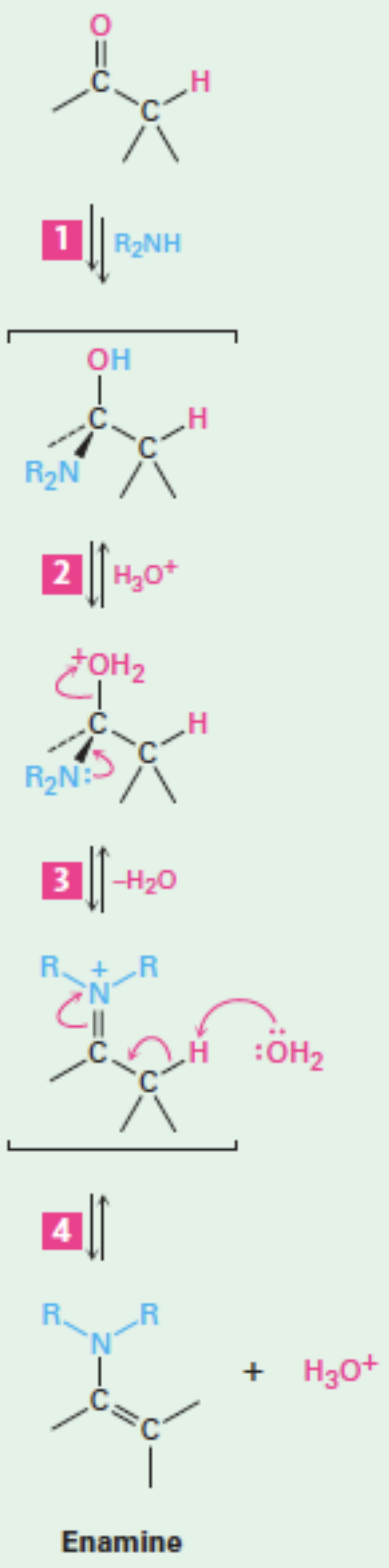


3) addizione Nucleofilica di ammine: Formazione di Enammine



Aldeidi e chetoni reagiscono. Con ammine secondarie per forme ENAMINE

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

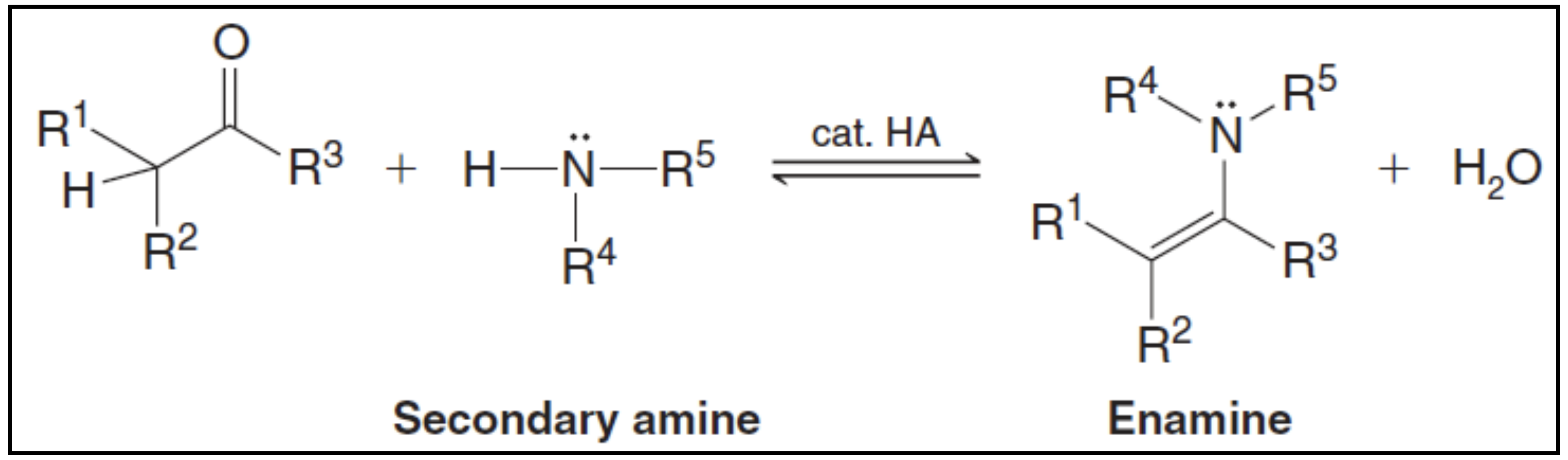


1 Nucleophilic addition of a secondary amine to the ketone or aldehyde, followed by proton transfer from nitrogen to oxygen, yields an intermediate carbinolamine in the normal way.

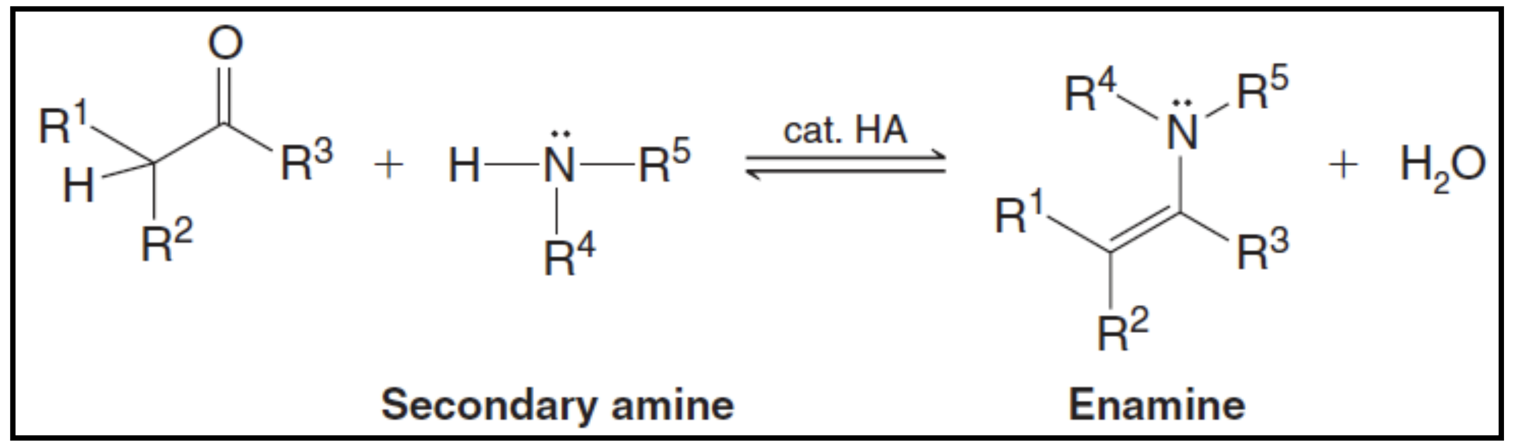
2 Protonation of the hydroxyl by acid catalyst converts it into a better leaving group.

3 Elimination of water by the lone-pair electrons on nitrogen then yields an intermediate iminium ion.

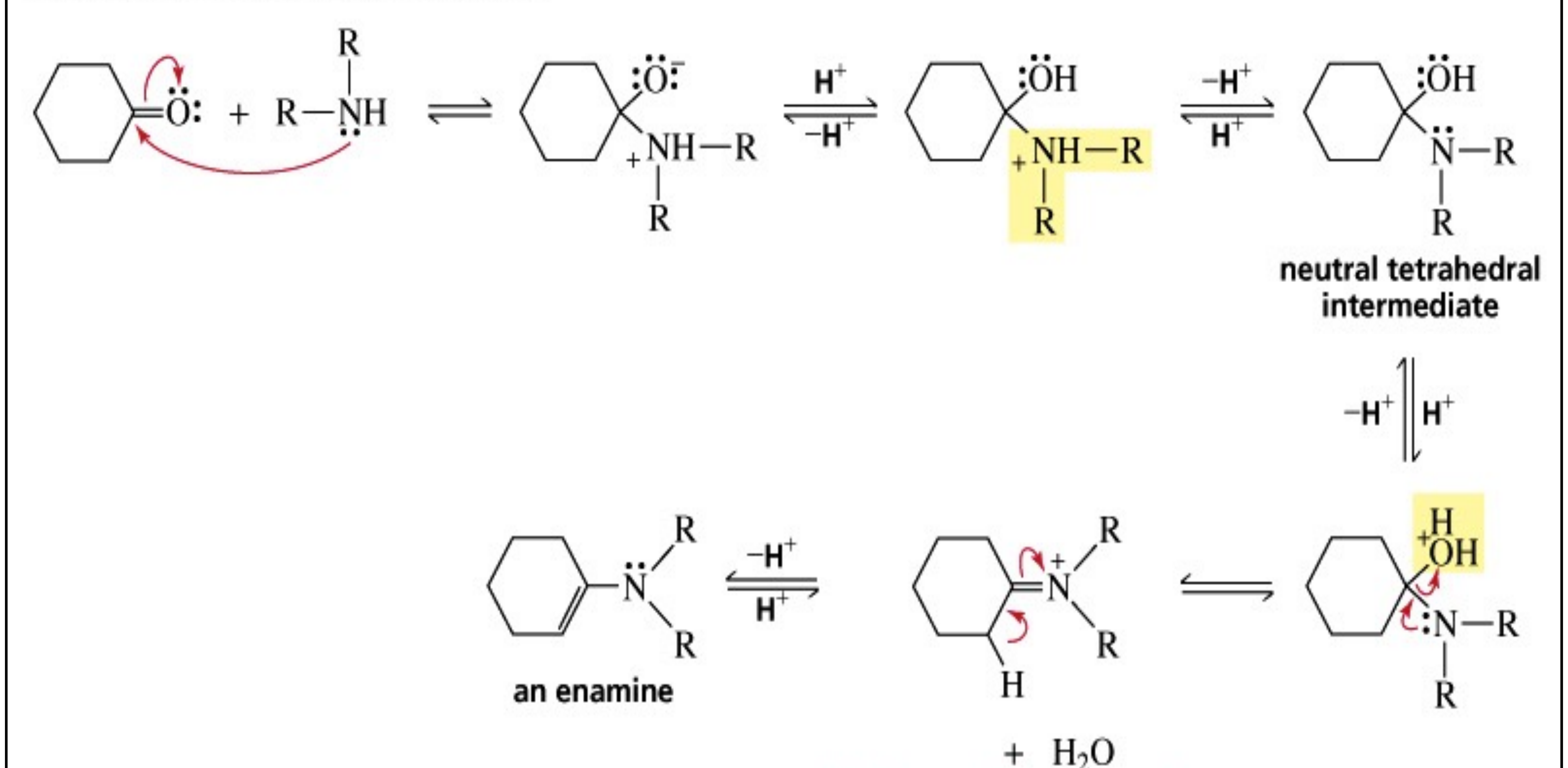
4 Loss of a proton from the alpha carbon atom yields the enamine product and regenerates the acid catalyst.



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

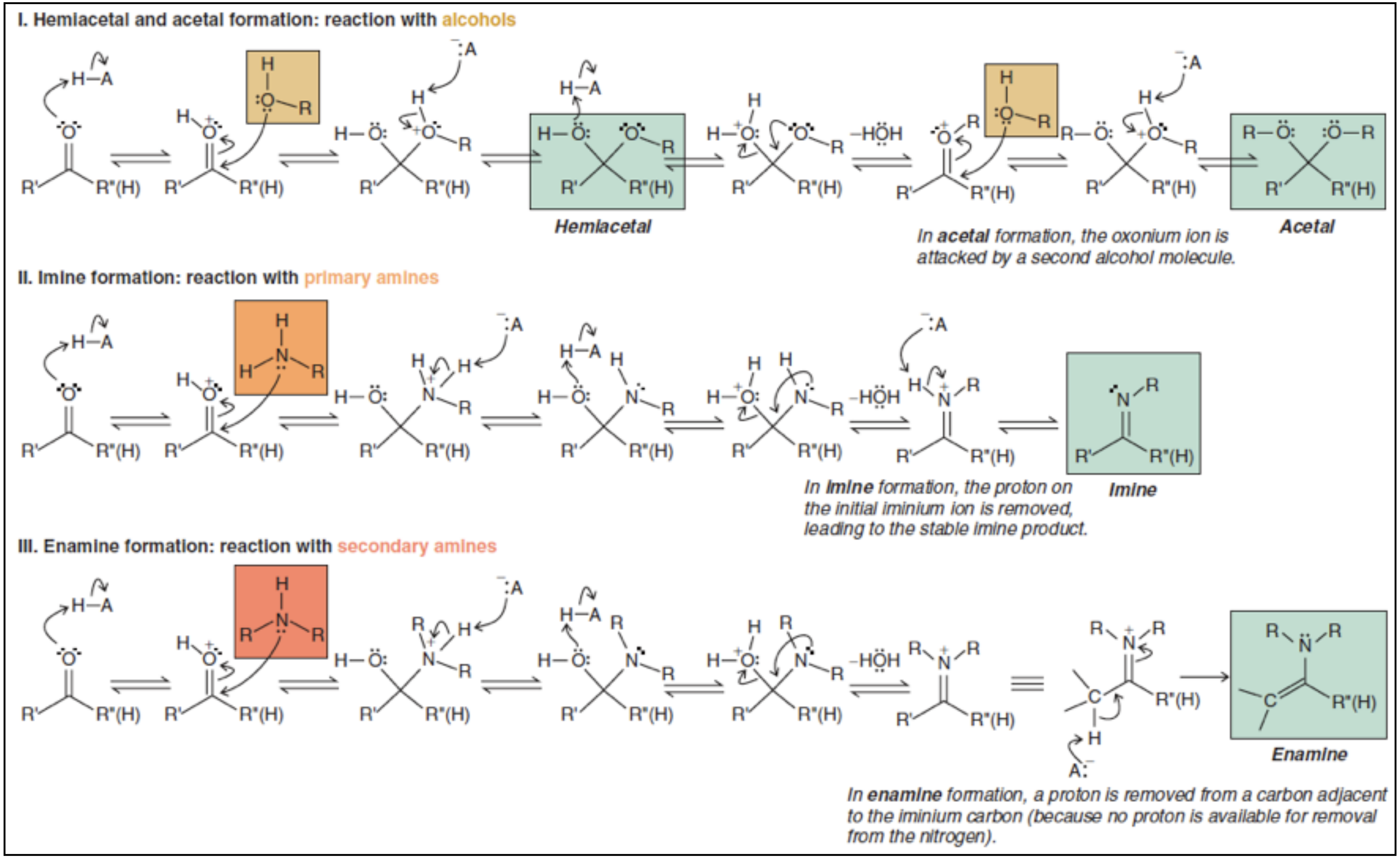


mechanism for enamine formation



this intermediate cannot lose a proton from N, so it loses a proton from an α-carbon

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


I. Hemiacetal and acetal formation: reaction with alcohols

Hemiacetal

Acetal

*In **acetal** formation, the oxonium ion is attacked by a second alcohol molecule.*

II. Imine formation: reaction with primary amines

Imine

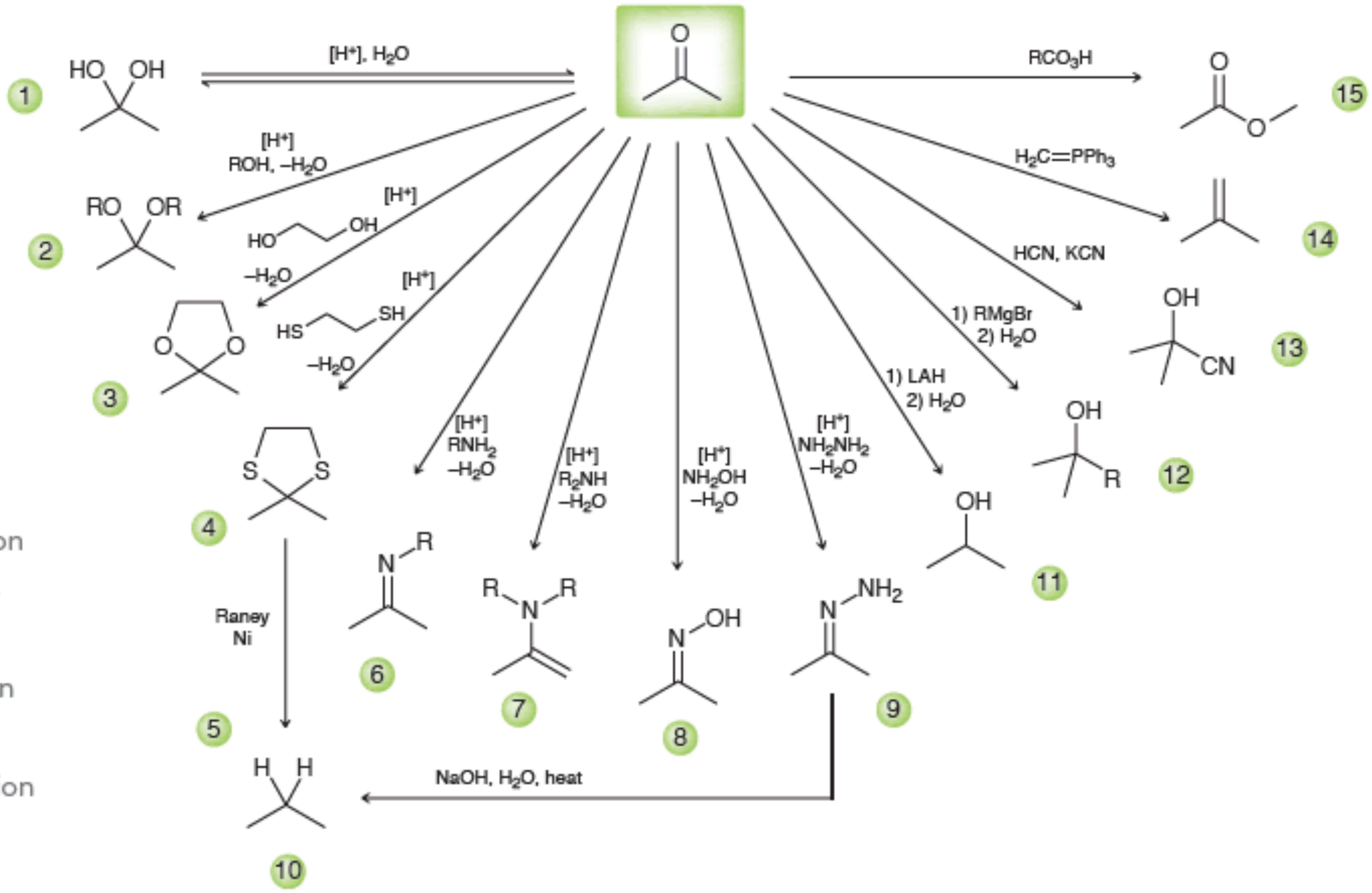
*In **imine** formation, the proton on the initial iminium ion is removed, leading to the stable imine product.*

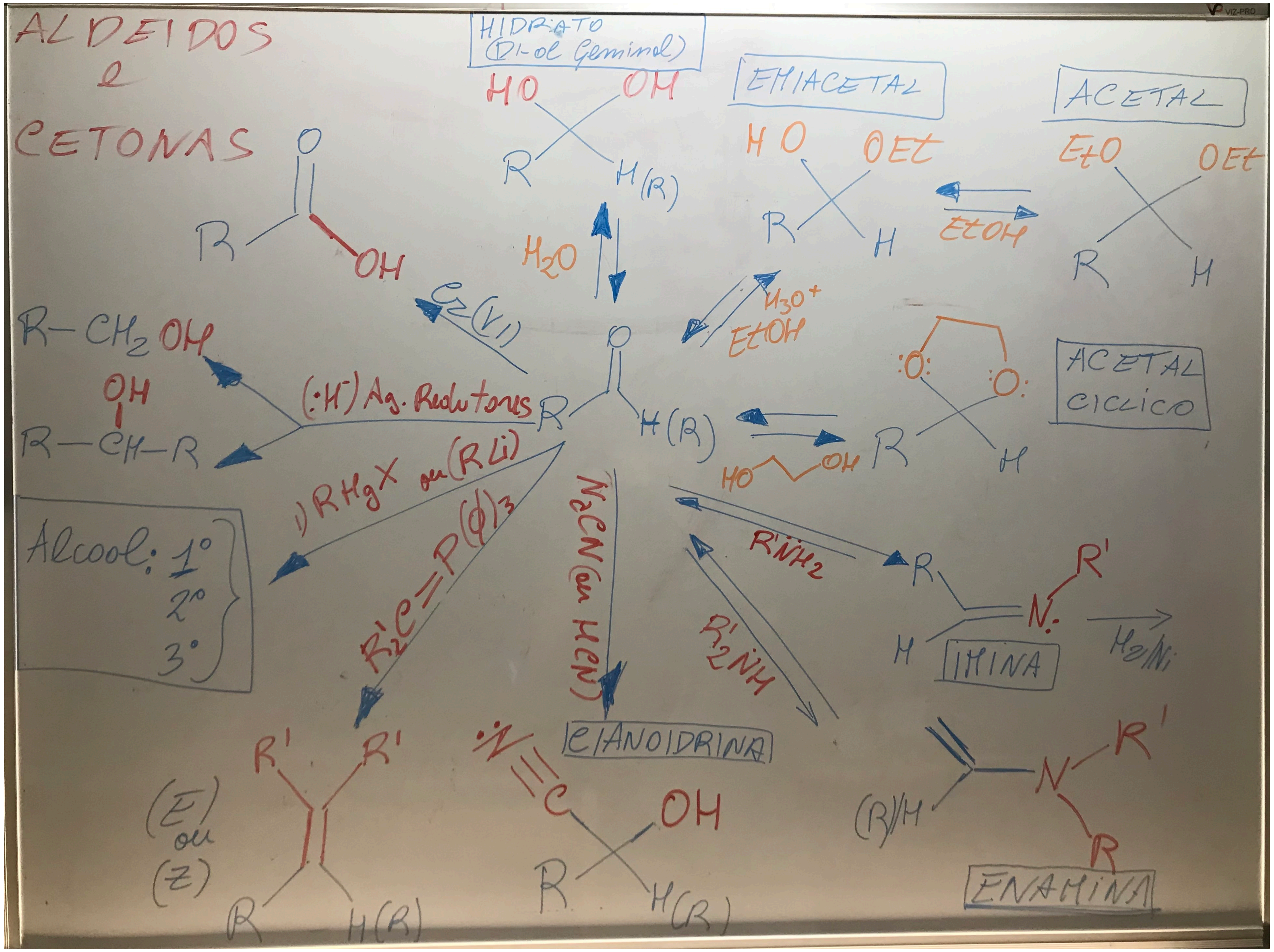
III. Enamine formation: reaction with secondary amines

Enamine

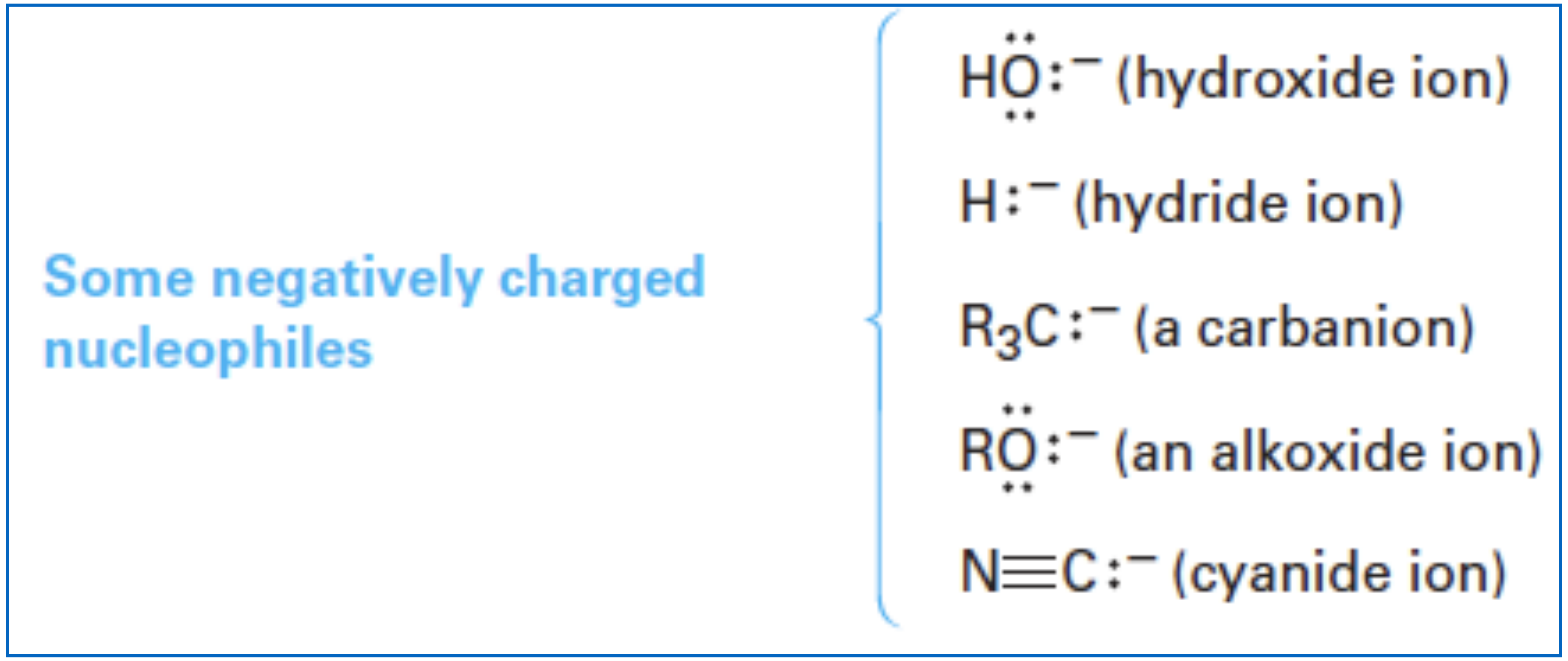
*In **enamine** formation, a proton is removed from a carbon adjacent to the iminium carbon (because no proton is available for removal from the nitrogen).*

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



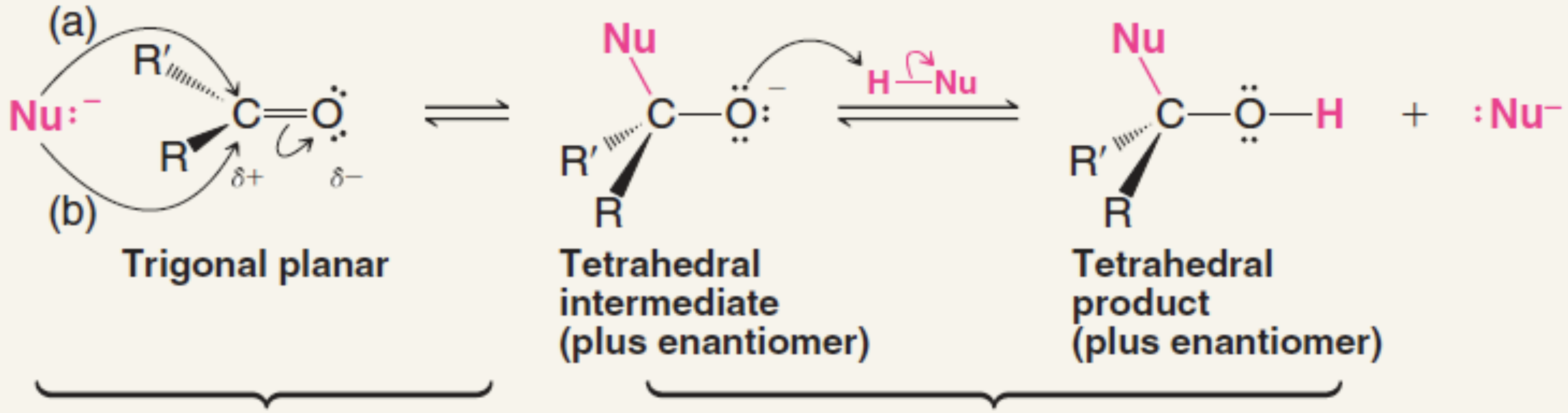

ALDEIDOS
e
CETONAS
O
R
OH
HIDRATO
(Di-ol Geminal)
HO
OH
R
H(R)
EMIACETAL
HO
OEt
R
H
ACETAL
EtO
OEt
R
H
EtOH
H2O
Cr(VI)
H3O+
EtOH
O
R
H(R)
R–CH2OH
OH
R–CH–R
(:H⁻) Ag. Redutores
:O:
:O:
R
H
HO
OH
ACETAL
CICLICO
1) RMgX ou (RLi)
Alcool: 1°
2°
3°
R'2C=P(φ)3
NaCN(ou HCN)
R'NH2
R'2NH
R
N:
R'
H
IMINA
H2/Ni
CIANOIDRINA
:N≡C
OH
R
H(R)
R'
R'
(E)
ou
(Z)
R
H(R)
(R)/H
N
R'
R
ENAMINA

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)



In this step the nucleophile forms a bond to the carbon by donating an electron pair to the top or bottom face of the carbonyl group [path (a) or (b)]. An electron pair shifts out to the oxygen.

In the second step the alkoxide oxygen, because it is strongly basic, removes a proton from H—Nu or some other acid.

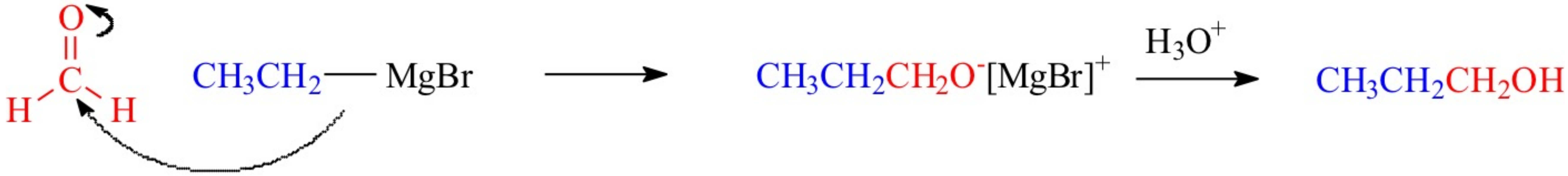
Reazioni di addizione nucleofila al gruppo carbonile
Con un nucleofilo FORTE (Carico negativamente)

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

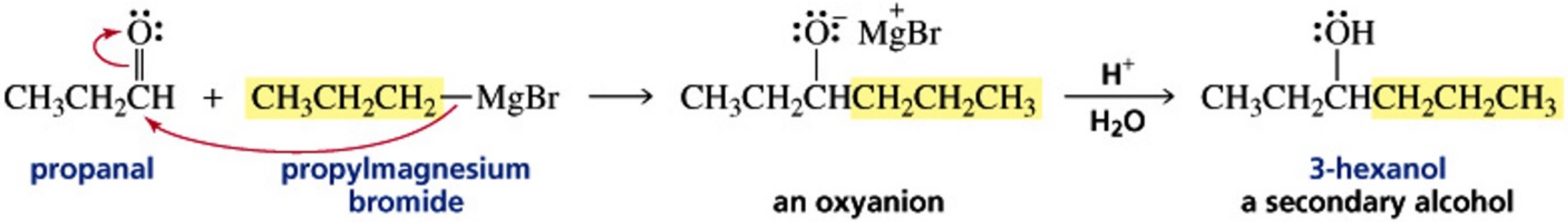
5) Reazione di Wittig: R2C=P(Ph)3

6) Aggiunta di un reagente Grignard: RMgX o RLi

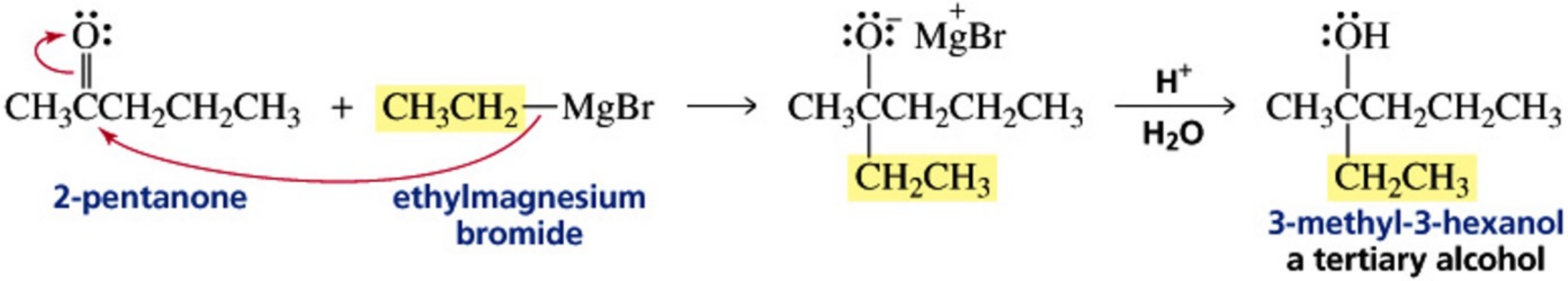
7) Reazione dello ione acetilene: RCC:- Na+



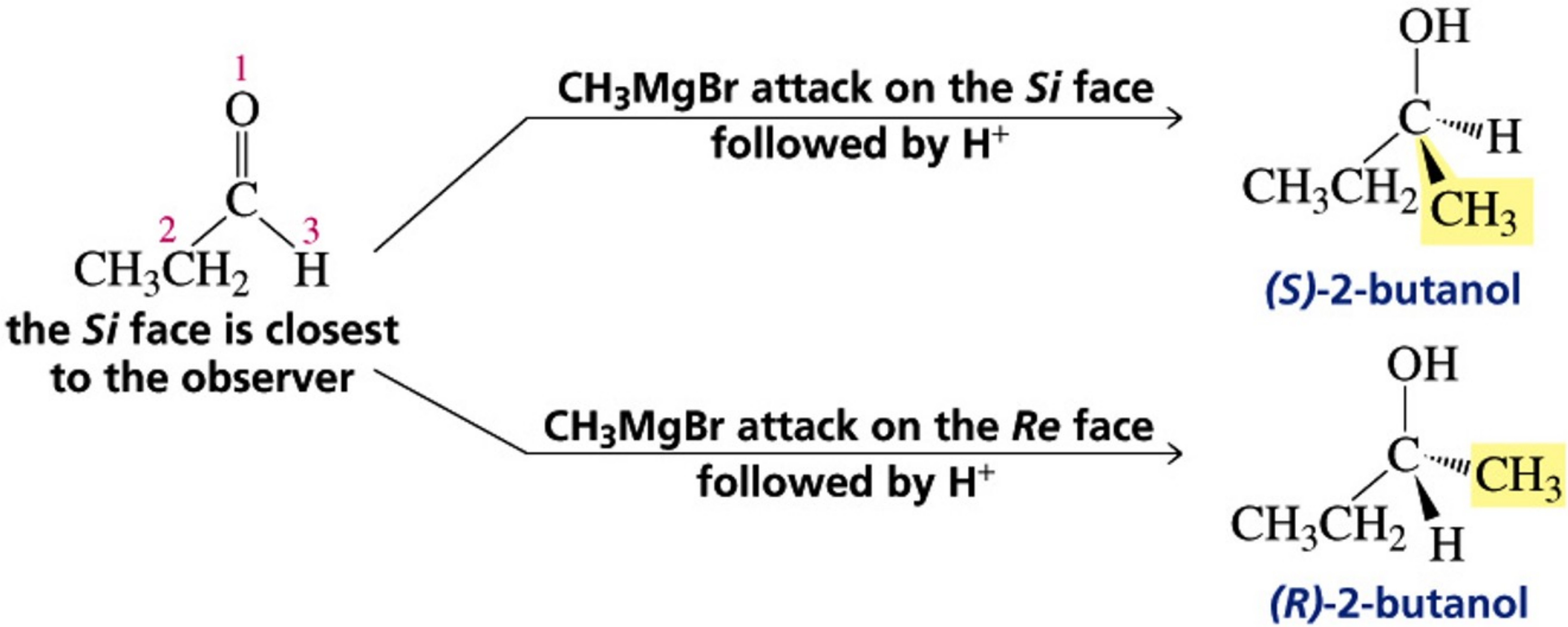
$$HCHO + CH_3CH_2{-}MgBr \longrightarrow CH_3CH_2CH_2O^-[MgBr]^+ \xrightarrow{H_3O^+} CH_3CH_2CH_2OH$$



$$CH_3CH_2CH{=}O + CH_3CH_2CH_2{-}MgBr \longrightarrow CH_3CH_2CH(O^-\,\overset{+}{Mg}Br)CH_2CH_2CH_3 \xrightarrow[H_2O]{H^+} CH_3CH_2CH(OH)CH_2CH_2CH_3$$



$$CH_3C(=O)CH_2CH_2CH_3 + CH_3CH_2{-}MgBr \longrightarrow CH_3C(O^-\,\overset{+}{Mg}Br)(CH_2CH_3)CH_2CH_2CH_3 \xrightarrow[H_2O]{H^+} CH_3C(OH)(CH_2CH_3)CH_2CH_2CH_3$$



the *Si* face is closest to the observer

CH_3MgBr attack on the *Si* face followed by H^+

(S)-2-butanol

CH_3MgBr attack on the *Re* face followed by H^+

(R)-2-butanol

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 ⍰,⍰-insaturi in presenza di nucleofili deboli (addizione-1,4 coniugata) e forti (addizione-1,2 diretta).