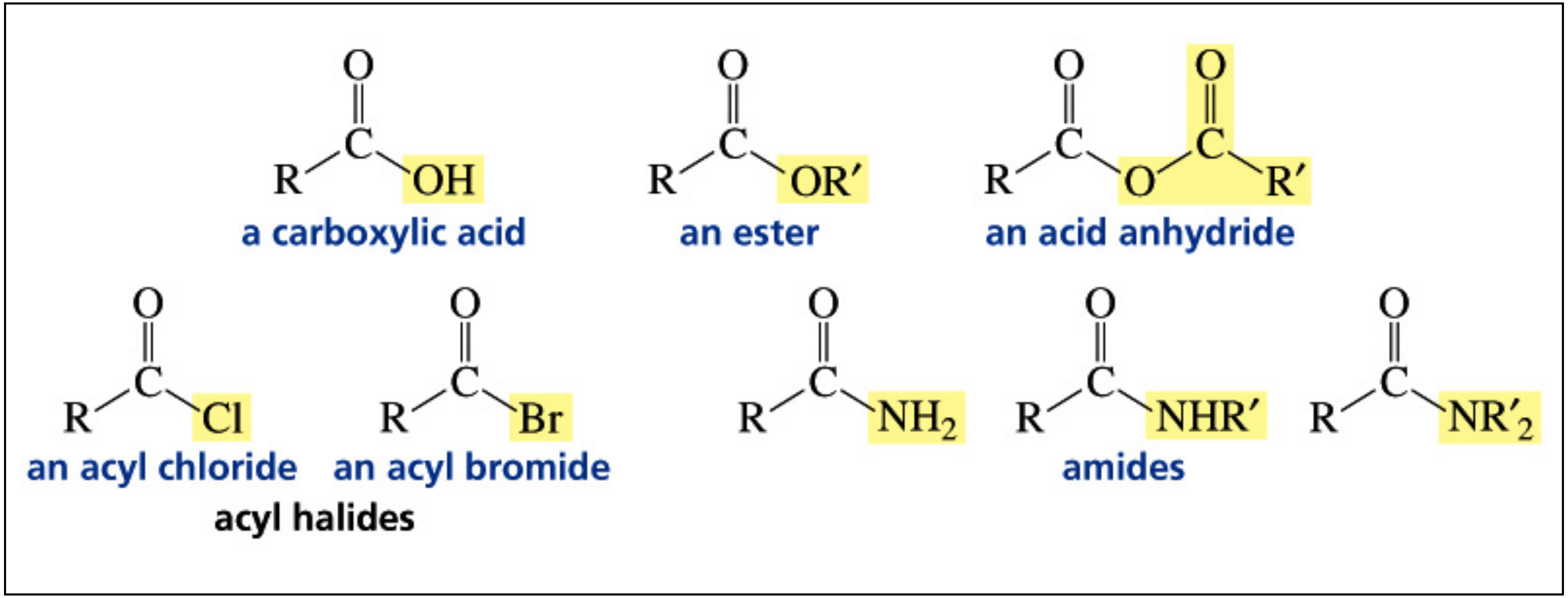
11. Reazioni degli acidi carbossilici e dei derivati degli acidi carbossilici

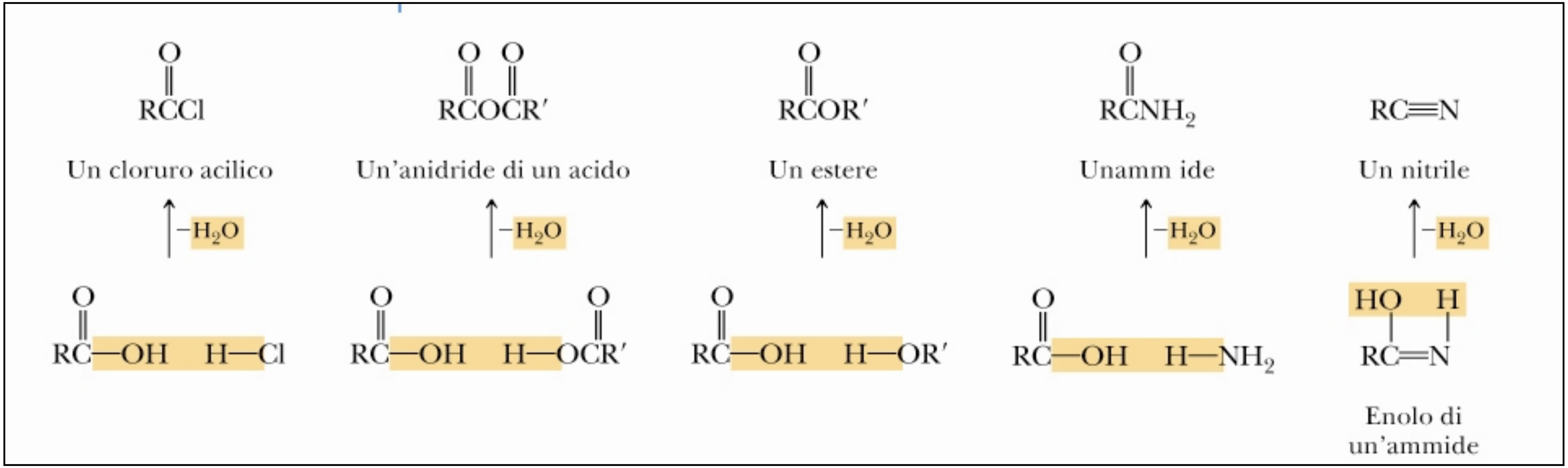
(1) Struttura, proprietà fisiche degli acidi carbossilici;

(2) Struttura e reattività dei derivati degli acidi carbossilici (cloruro acilico, anidride, estere e ammide).

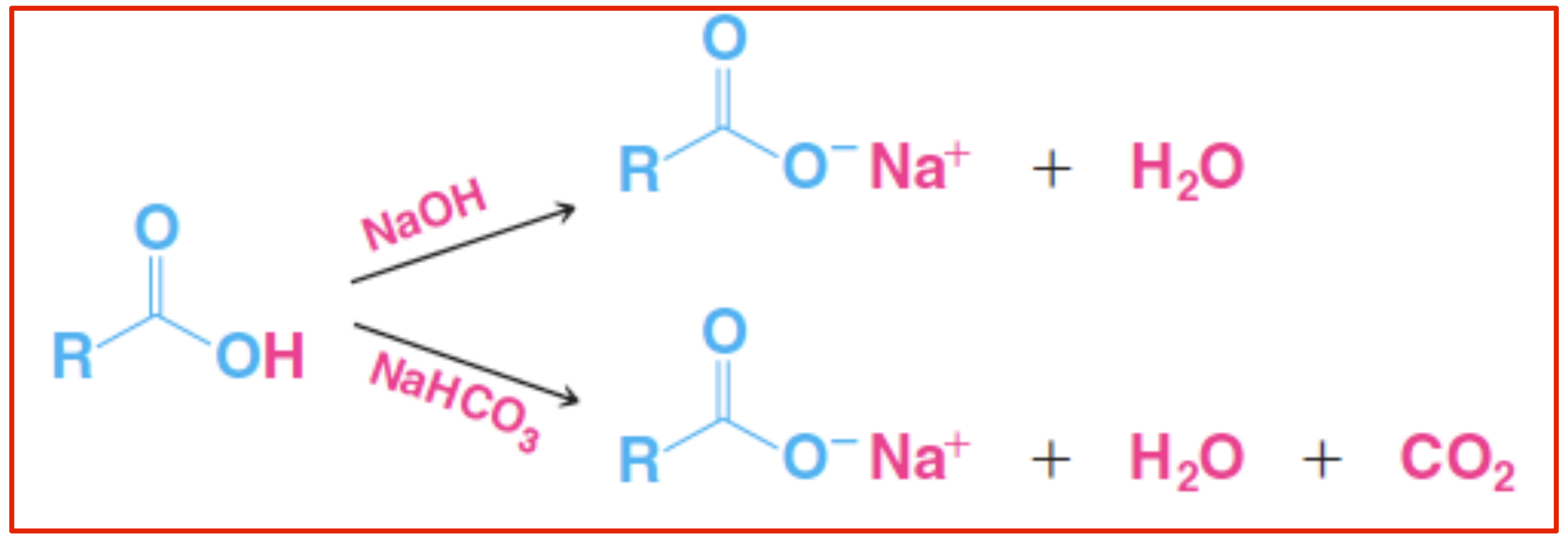
(3) Problemi

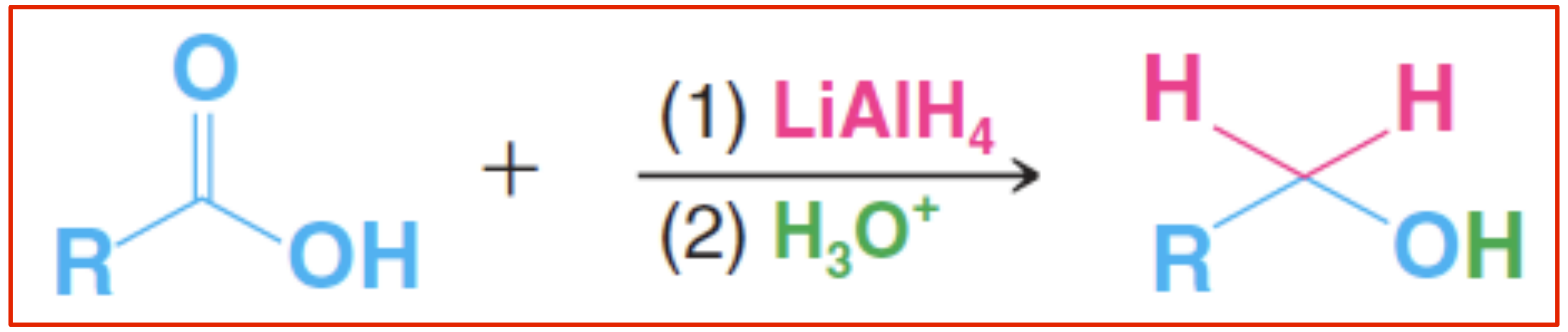


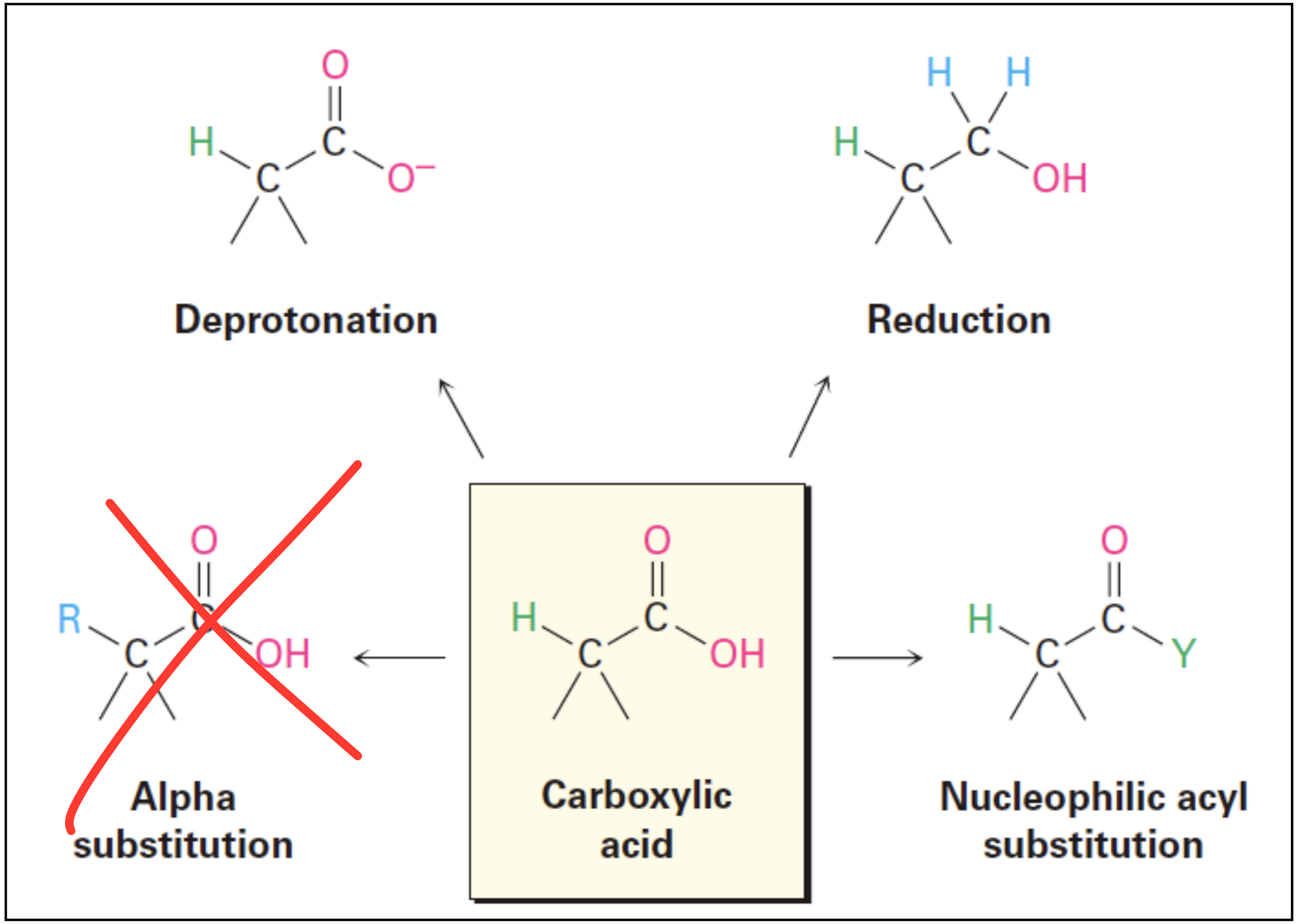
11. Reazioni degli acidi carbossilici e dei derivati degli acidi carbossilici



Reattività degli acidi carbossilici

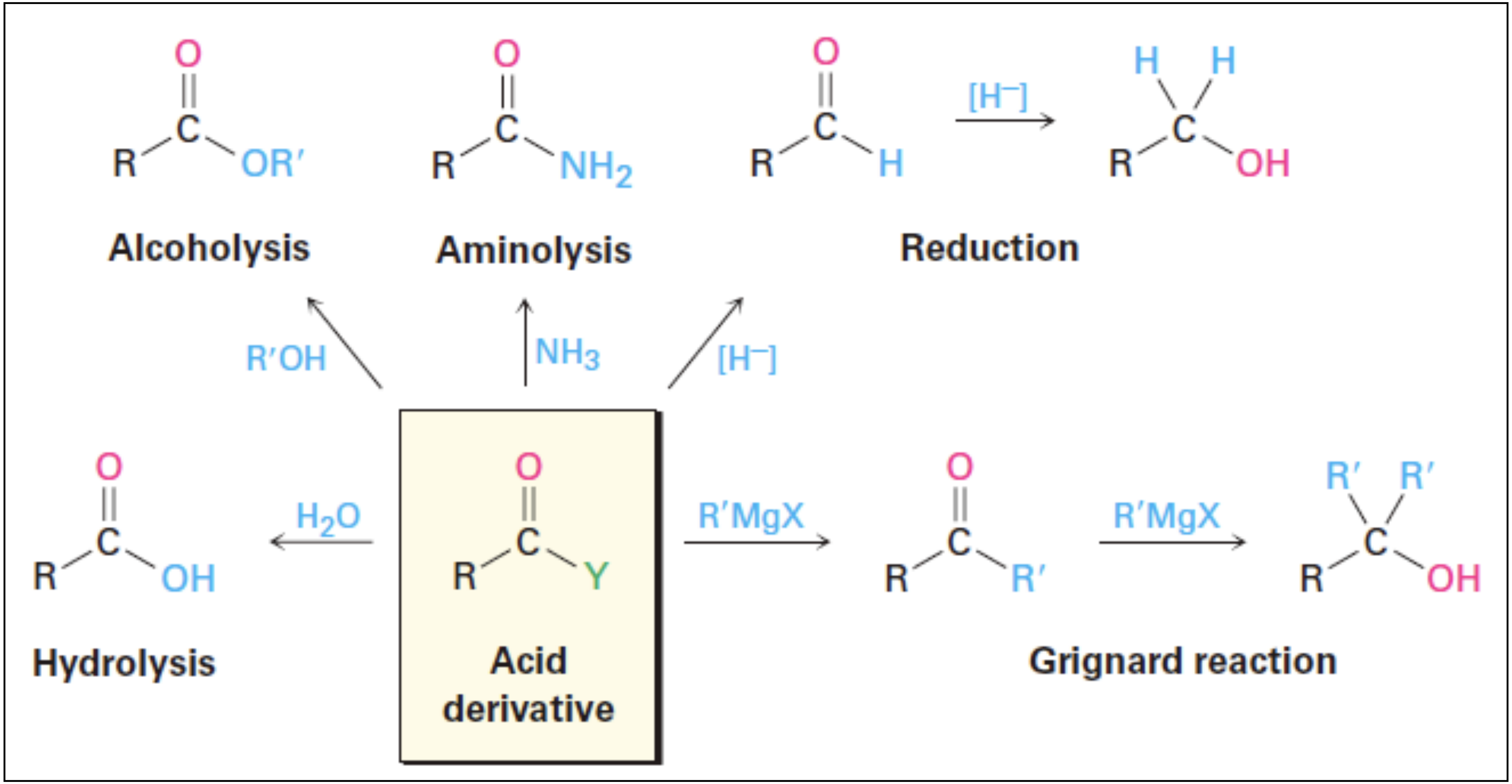




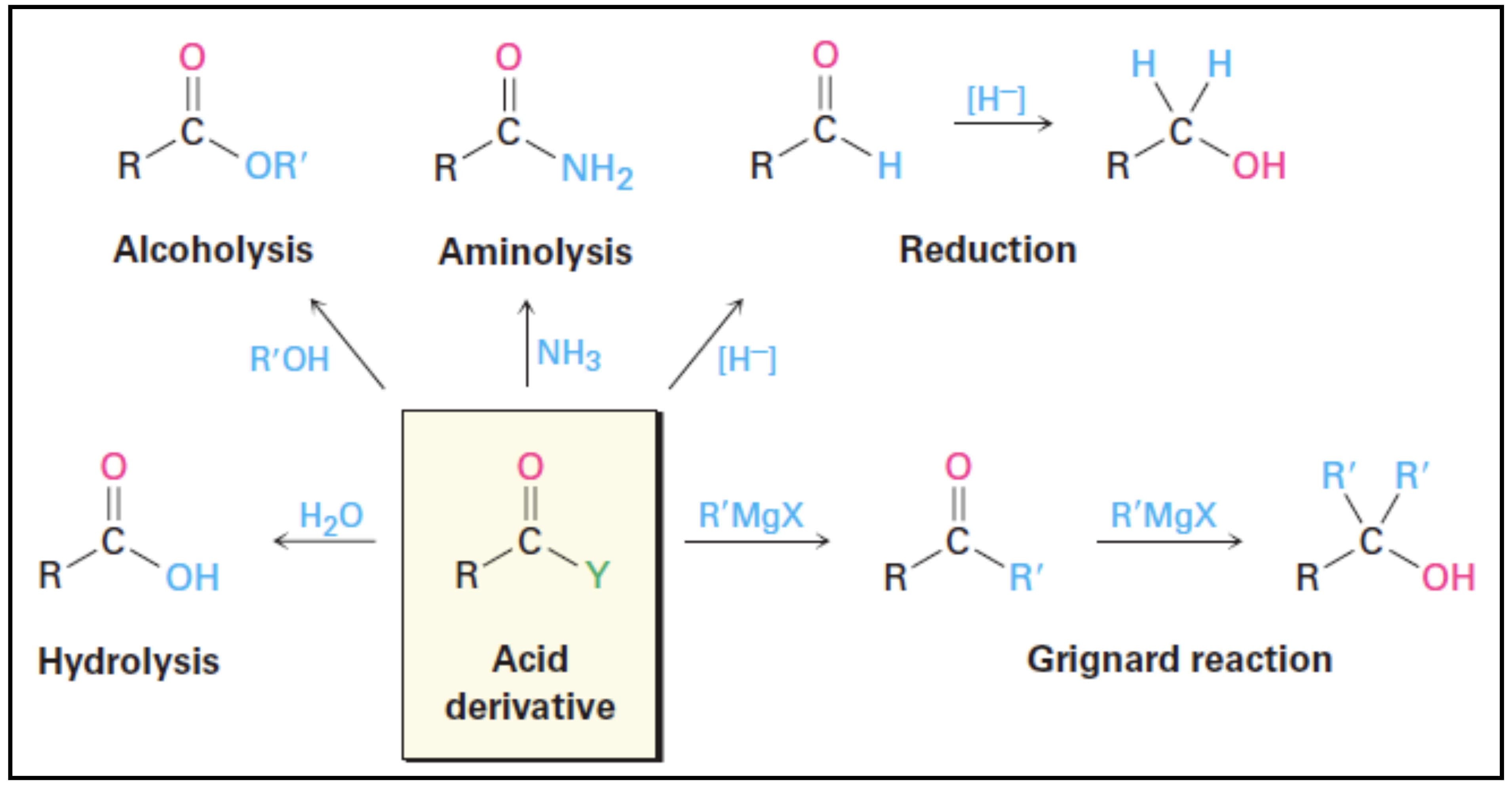


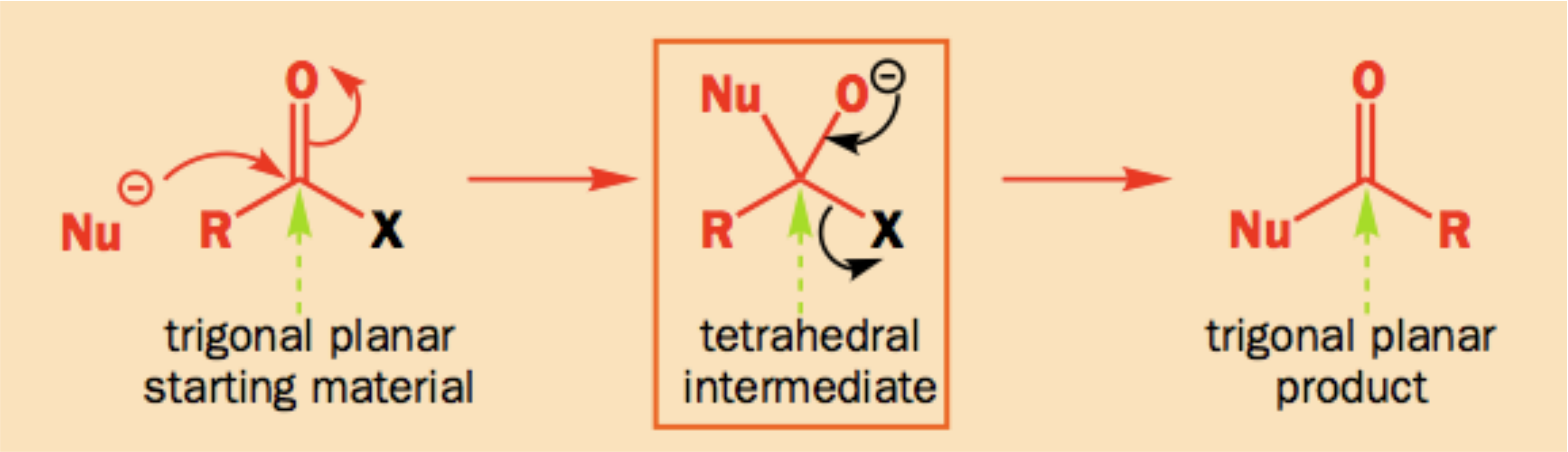
S_NAc

Addizione-eliminazione al carbonio acilico - Soztituzione Nucleofila Aciclica (S_NAc)



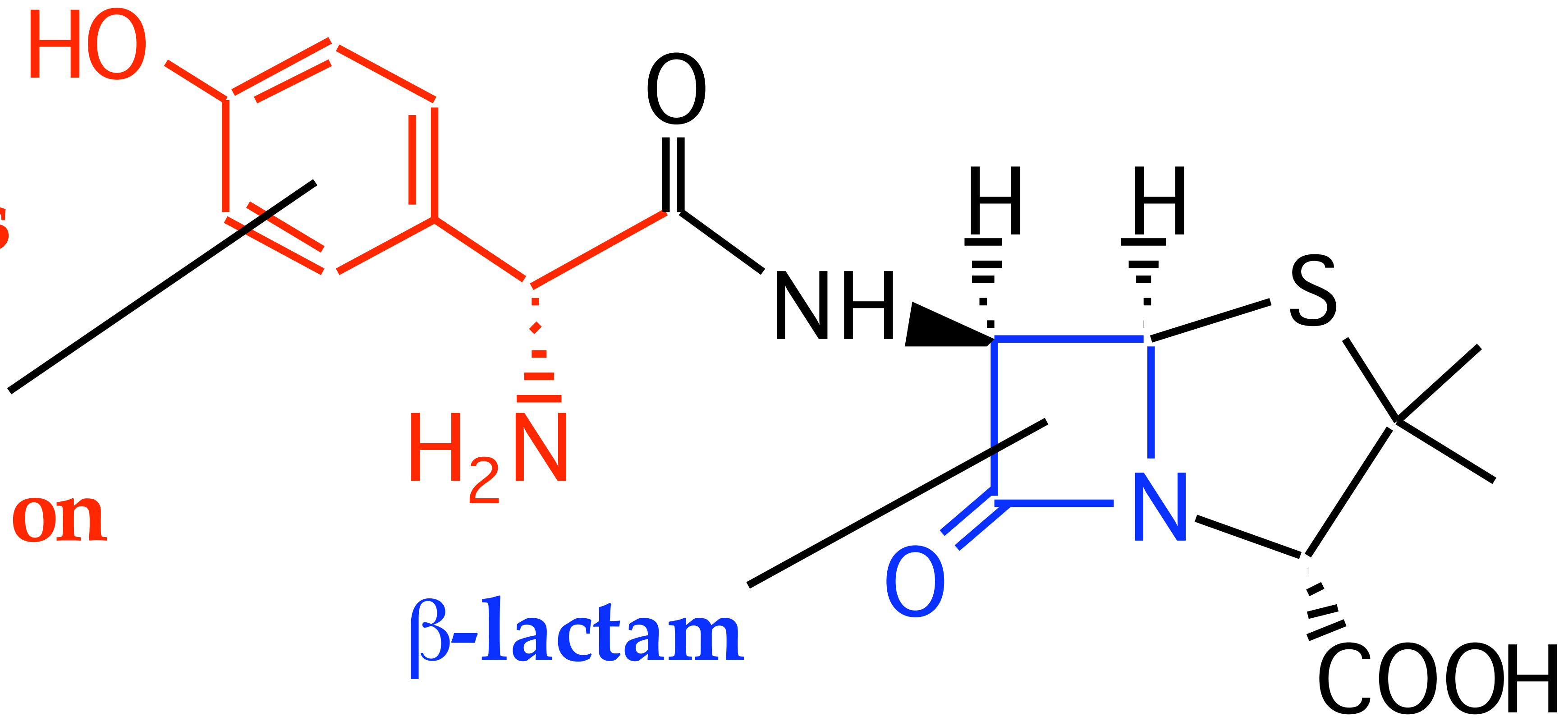
Addizione-eliminazione al carbonio acilico - Soztituzione Nucleofila Aciclica (S_NAc)





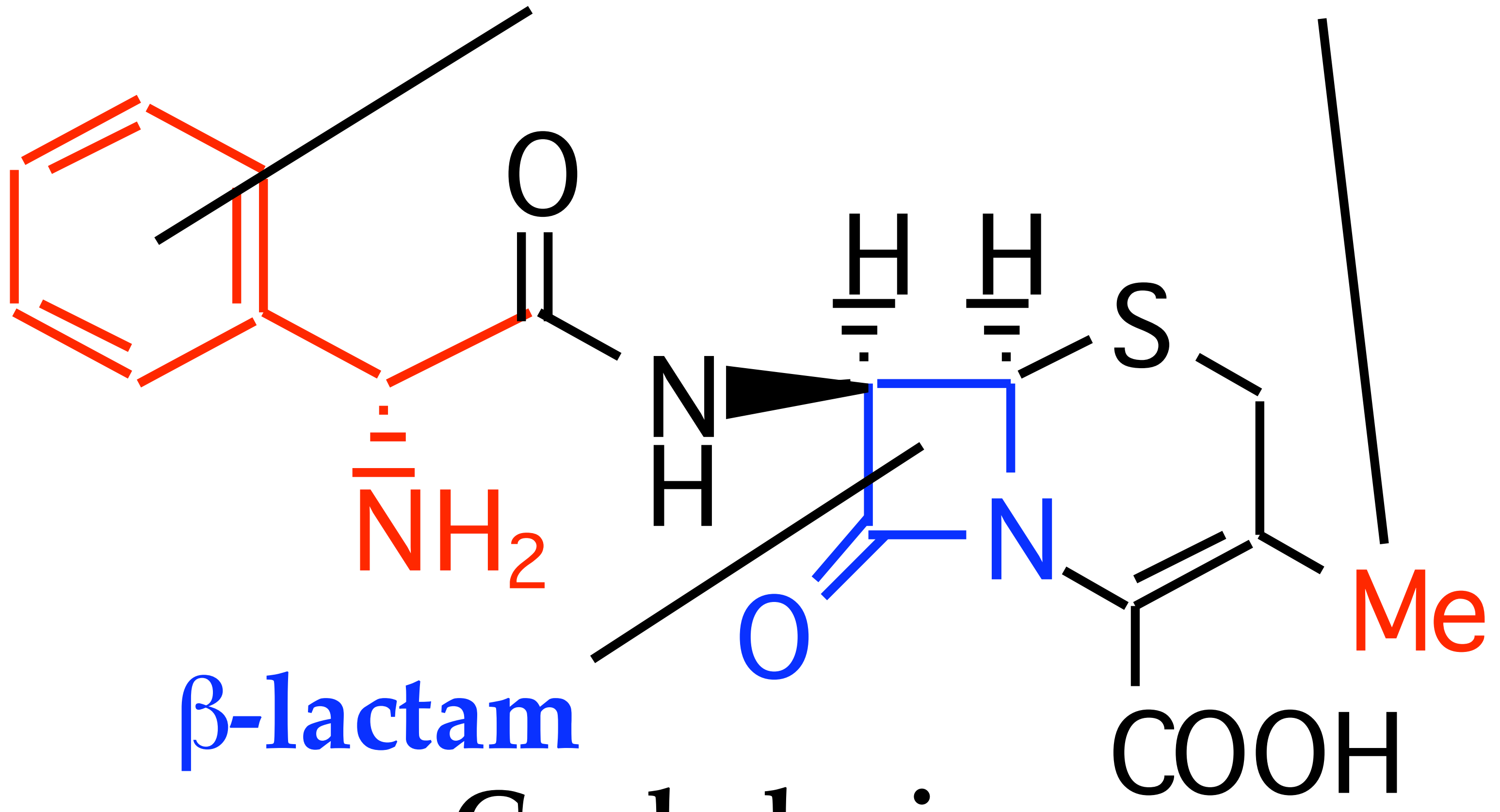
PENICILLINE e CEFALOSPORINE

The penicillins differ in the group bonded to the acyl carbon



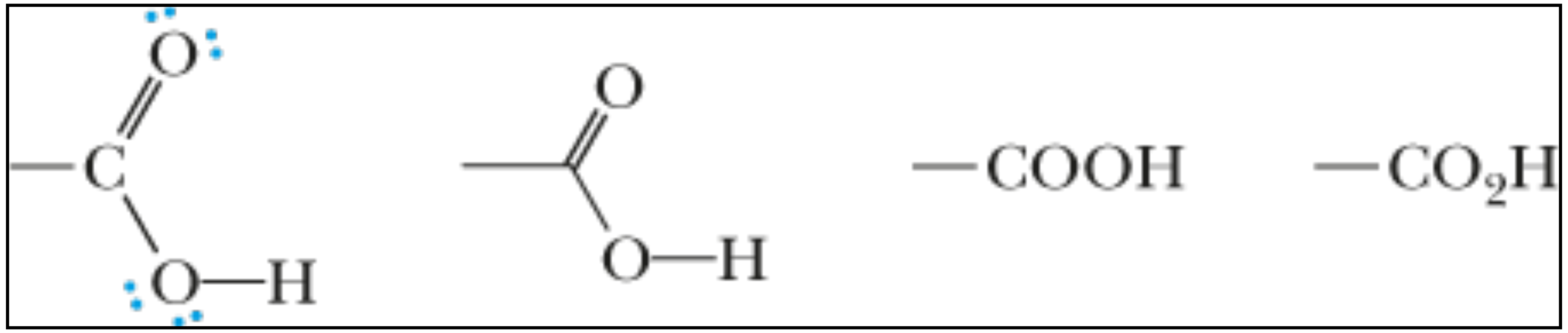
Amoxicillin
(a β-lactam antibiotic)

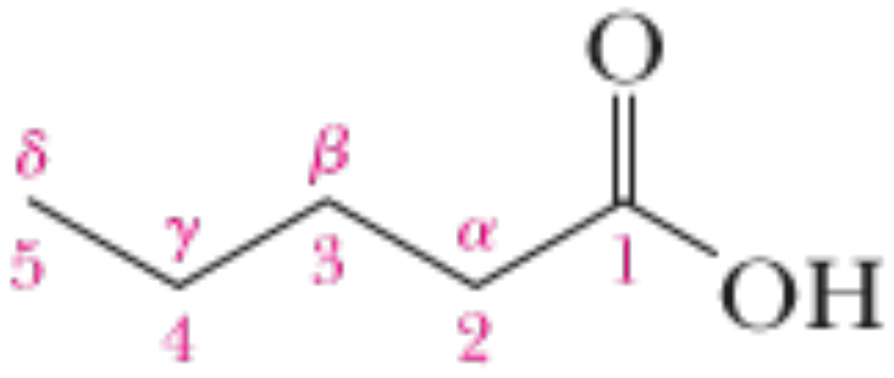
The cephalosporins differ in the group bonded to the acyl carbon and the side chain of the thiazine ring

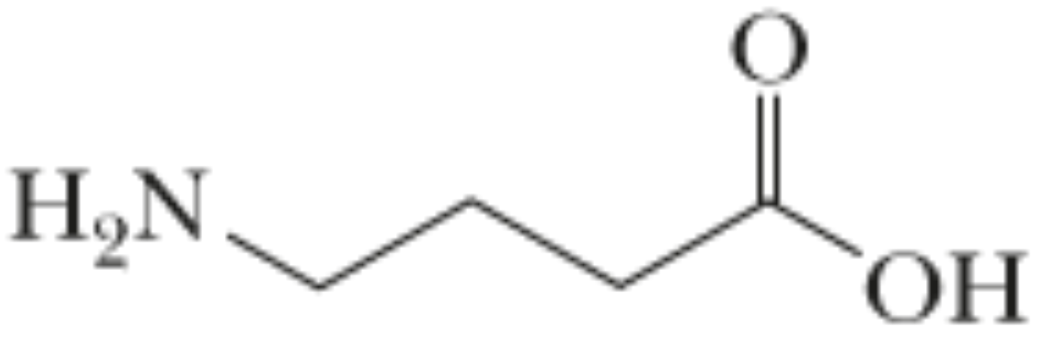


Cephalexin
(Keflex)

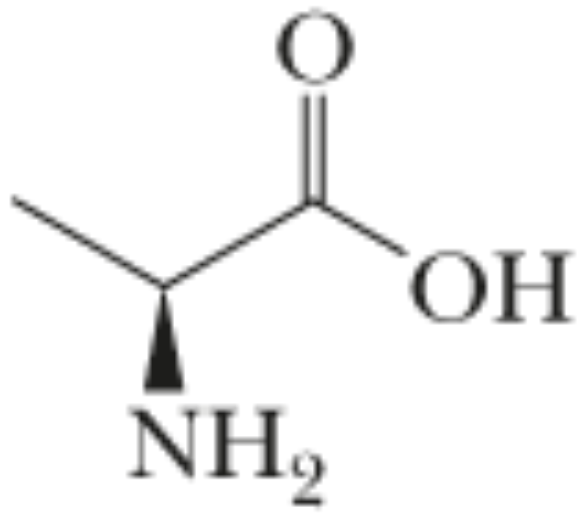
Struttura degli acidi carbossilici


$-COOH$ $-CO_2H$





Acido 4-amminobutanoico
(Acido γ-amminobutirrico,
GABA)



Acido (*S*)-2-amminopropanoico
[Acido (*S*)-α-amminopropionico;
L-Alanina]

Nomenclatura degli acidi carbossilici

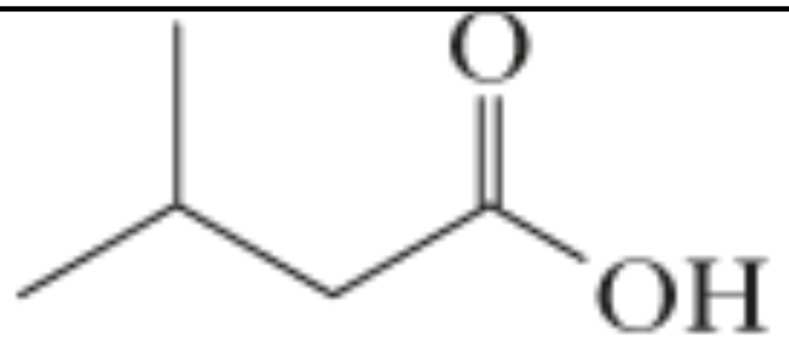
A. Sistema IUPAC

$HCOOH$

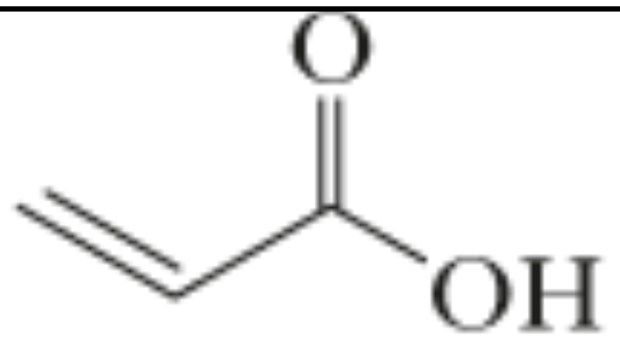
Acido metanoico
(Acido formico)

CH_3COOH

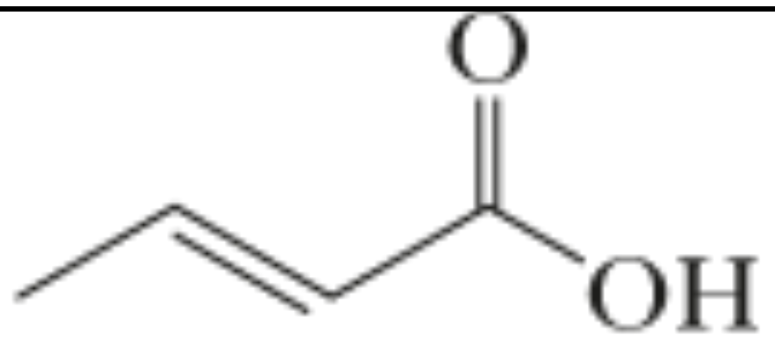
Acido etanoico
(Acido acetico)



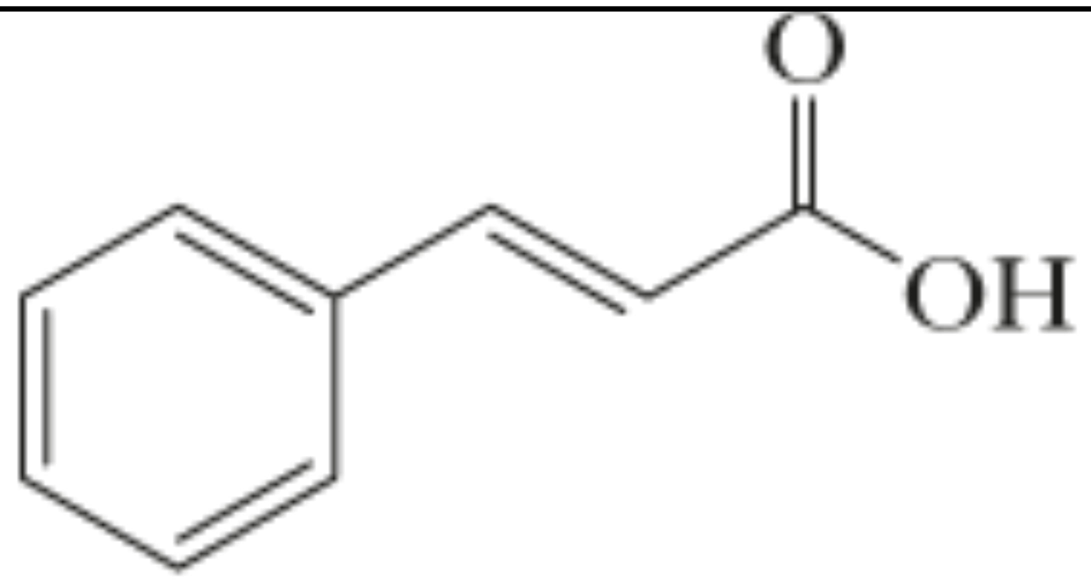
Acido 3-metilbutanoico
(Acido isovalerico)



Acido propenoico
(Acido acrilico)



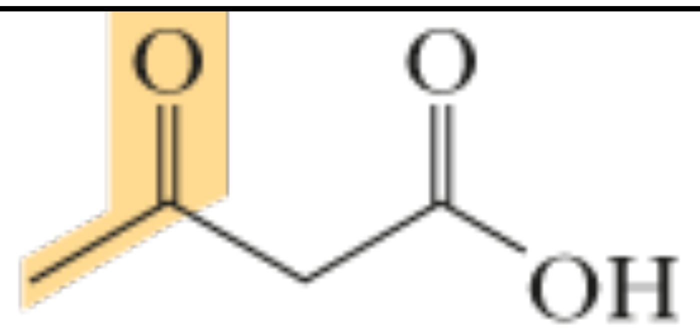
Acido *trans*-2-butenoico
(Acido crotonico)



Acido *trans*-3-fenilpropenoico
(Acido cinnamico)

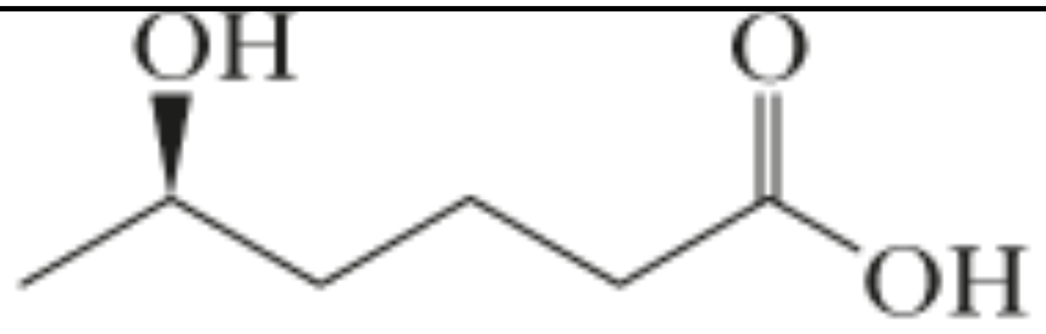
Nomenclatura degli acidi carbossilici

A. Sistema IUPAC

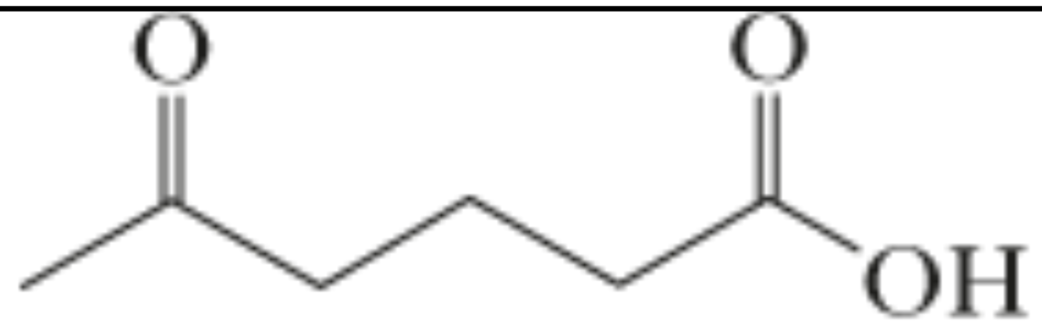


Acido 3-ossobutanoico
(Acido *β*-chetobutirrico;
Acido acetoacetico)

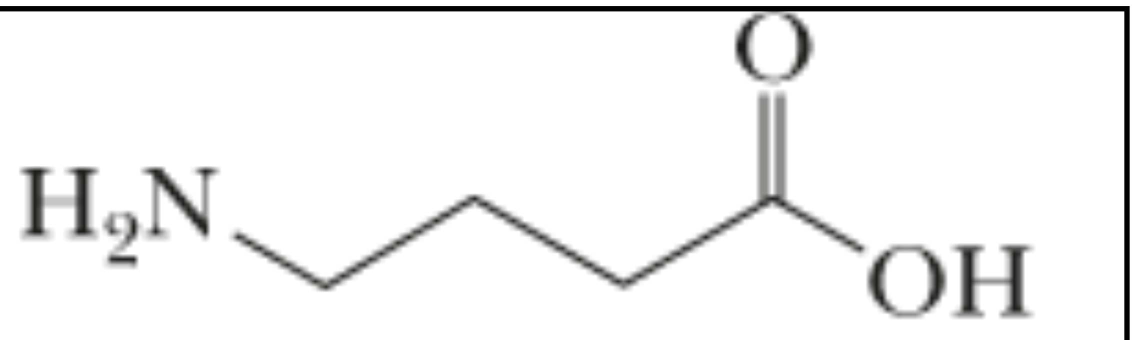
Gruppo acetilico



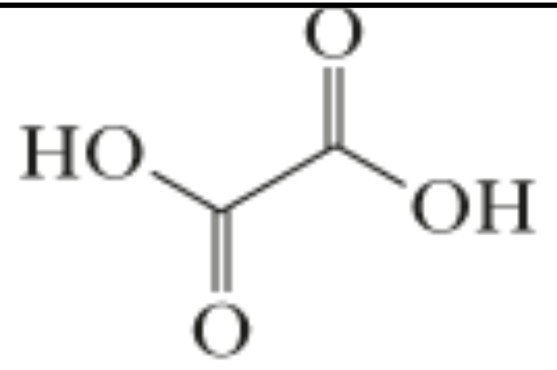
Acido (*R*)-5-idrossiesanoico



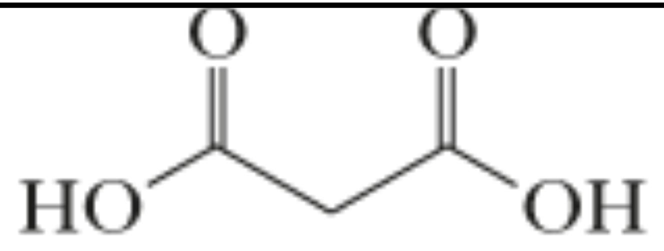
Acido 5-ossoesanoico



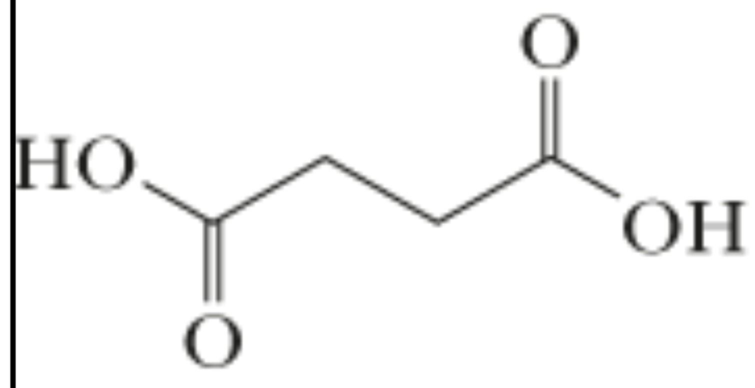
Acido 4-amminobutanoico



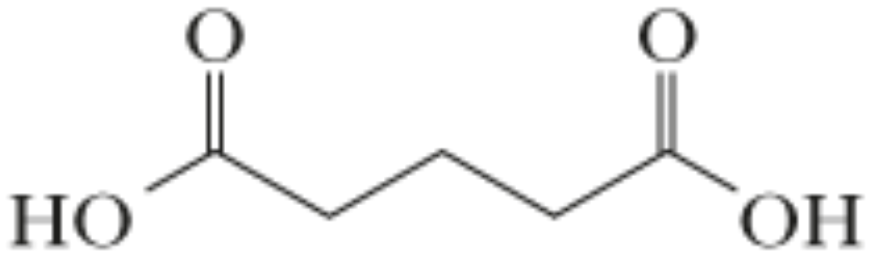
Acido etandioico
(Acido ossalico)



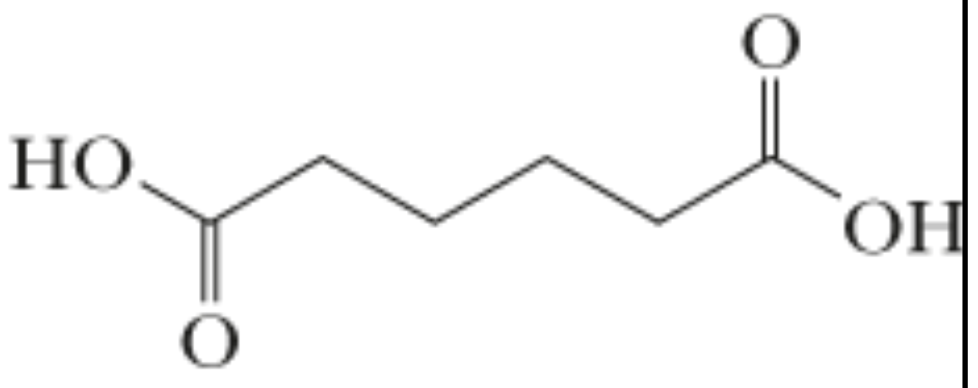
Acido propandioico
(Acido malonico)



Acido butandioico
(Acido succinico)



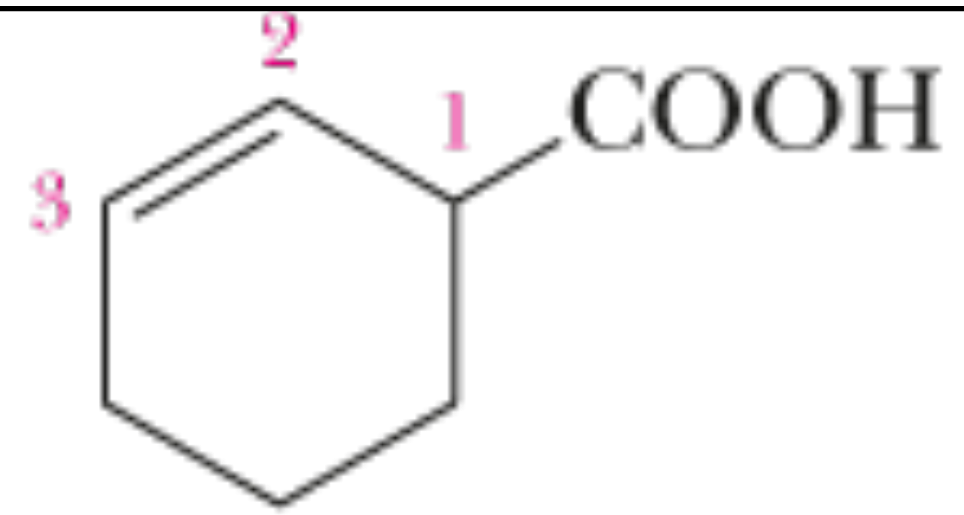
Acido petandioico
(Acido glutarico)



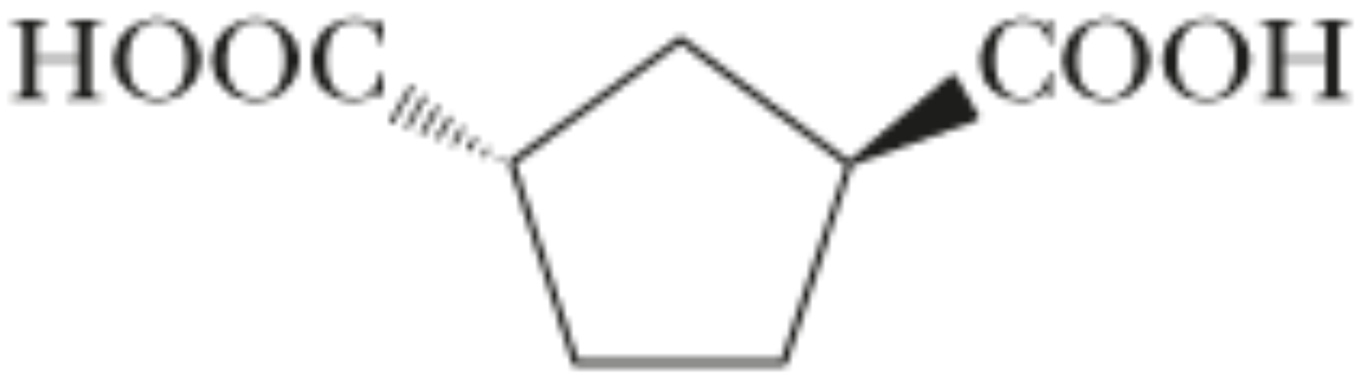
Acido esandioico
(Acido adipico)

Nomenclatura degli acidi carbossilici

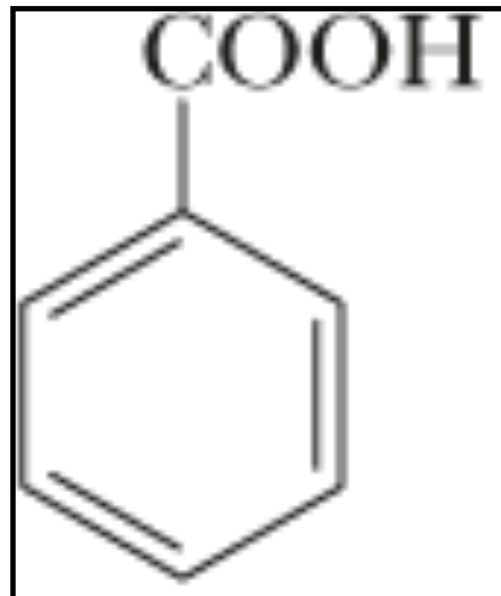
A. Sistema IUPAC



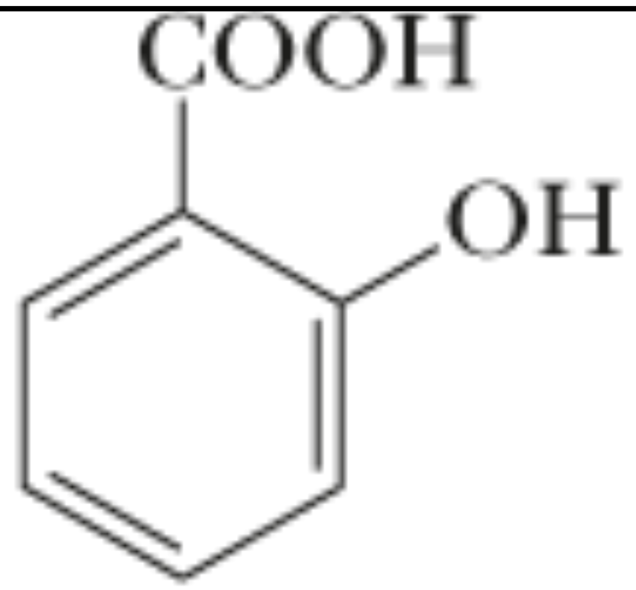
Acido
2-cicloesencarbossilico



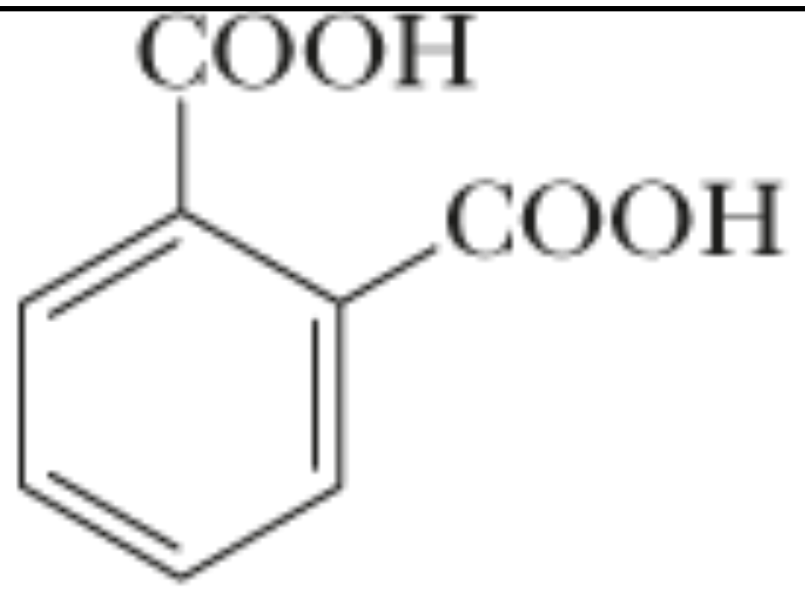
Acido
***trans*-1,3-ciclopentandicarbossilico**



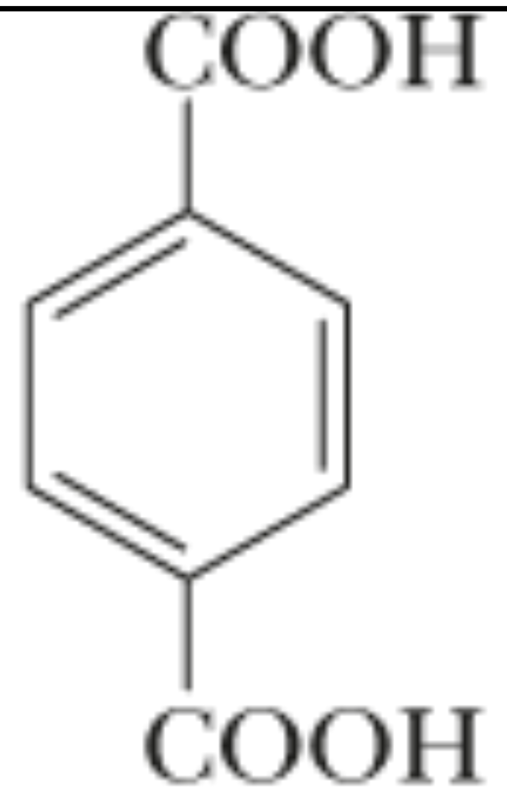
Acido
benzoico



Acido
2-idrossibenzoico
(Acido salicilico)



Acido
1,2-benzendicarbossilico
(Acido ftalico)



Acido
1,4-benzendicarbossilico
(Acido tereftalico)

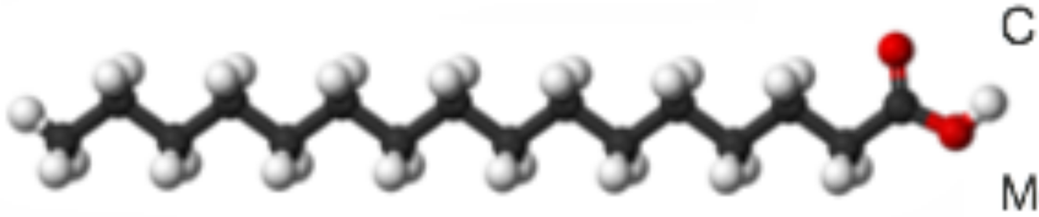
B. Nomi comuni

Tabella 14.1 **Alcuni acidi carbossilici alifatici, nomi comuni e derivazioni**

Struttura	Nome IUPAC	Nome comune	Derivazione
$HCOOH$	**Acido metanoico**	**Acido formico**	dal latino *formica*, formica
CH_3COOH	**Acido etanoico**	**Acido acetico**	dal latino *acetum*, aceto
CH_3CH_2COOH	**Acido propanoico**	**Acido propionico**	dal greco *propion*, primo grasso
$CH_3(CH_2)_2COOH$	**Acido butanoico**	**Acido butirrico**	dal latino *butyrum*, burro
$CH_3(CH_2)_3COOH$	**Acido pentanoico**	**Acido valerico**	dal latino *valeriana*, una pianta da fiore
$CH_3(CH_2)_4COOH$	**Acido esanoico**	**Acido caproico**	dal latino *caper*, capra
$CH_3(CH_2)_6COOH$	**Acido ottanoico**	**Acido caprilico**	dal latino *caper*, capra
$CH_3(CH_2)_8COOH$	**Acido decanoico**	**Acido caprico**	dal latino *caper*, capra
$CH_3(CH_2)_{10}COOH$	**Acido dodecanoico**	**Acido laurico**	dal latino *laurus*, lauro

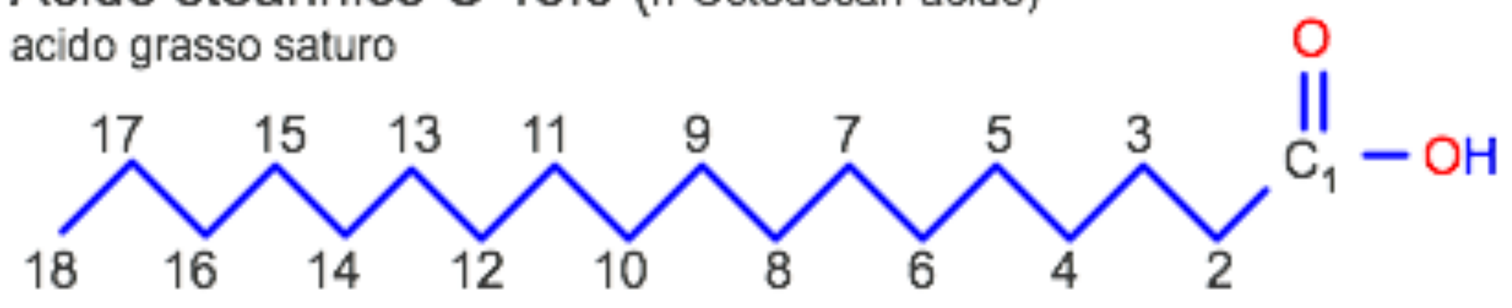
Acido palmitico C 16:0
acido grasso saturo

n-Esadecan-acido
$CH_3(CH_2)_{14}COOH$
C 16:0 (ionizzato)

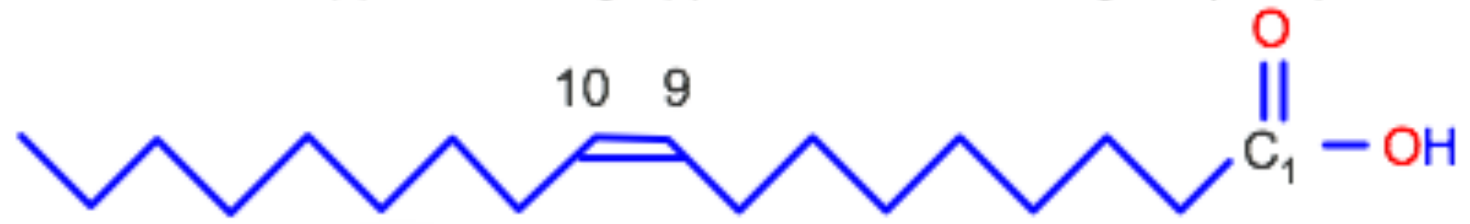


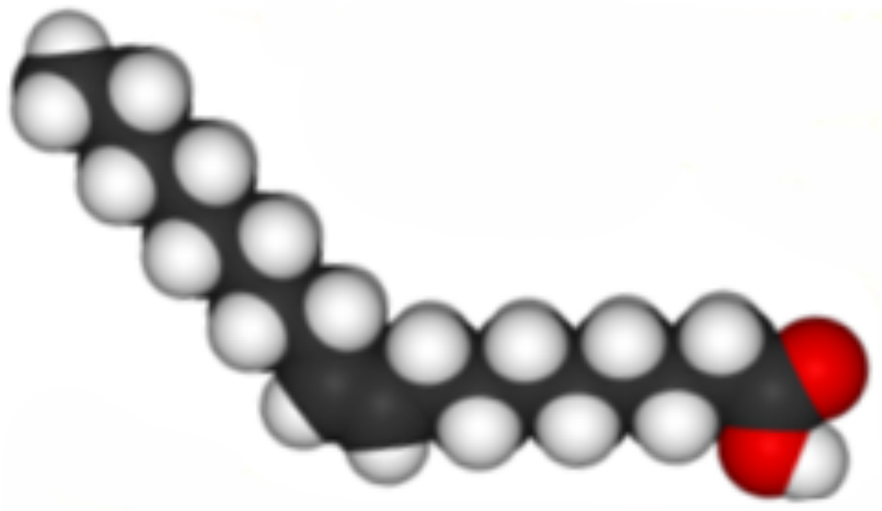
Modello a calotta

Acido stearinico C 18:0 (n-Octodecan-acido)
acido grasso saturo



Acido oleico C 18:1, Δ^9
monoinsaturo: appartiene al gruppo metabolico omega-9 (18-9)

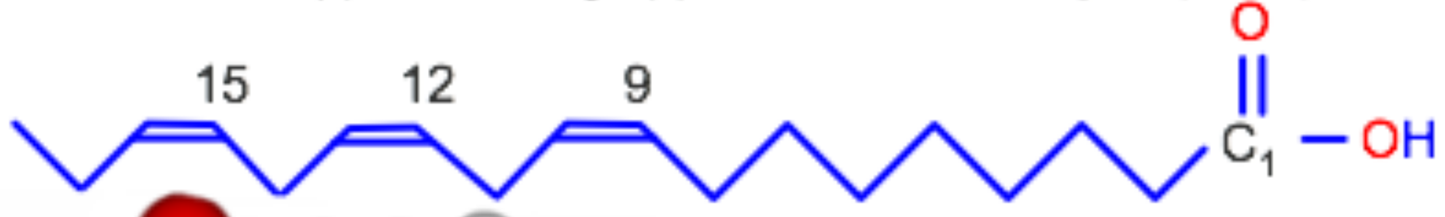


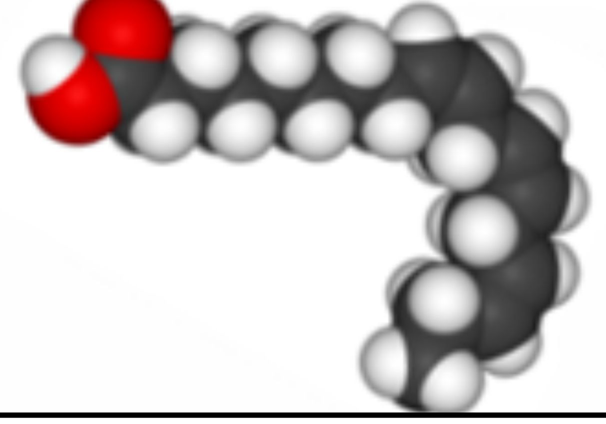


cis-9-Octodecen-acido
$CH_3(CH_2)_7CH{=}CH(CH_2)_7COO^-$
C 18:1, Δ^9 (ionizzato)

Modello a calotta

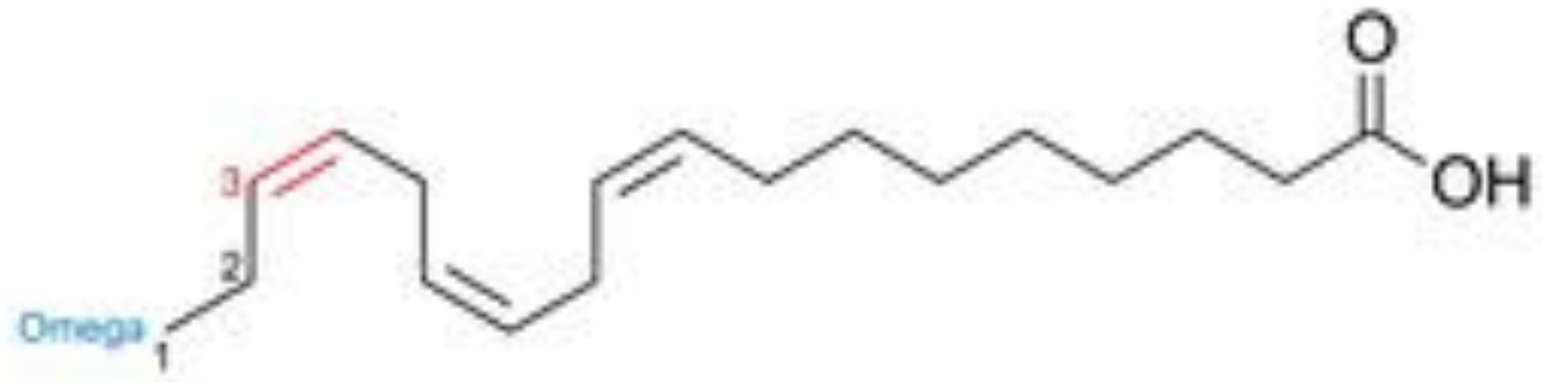
Acido linolenico C 18:3, $\Delta^{9, 12, 15}$
triplice insaturo: appartiene al gruppo metabolico omega-3 (18-15)



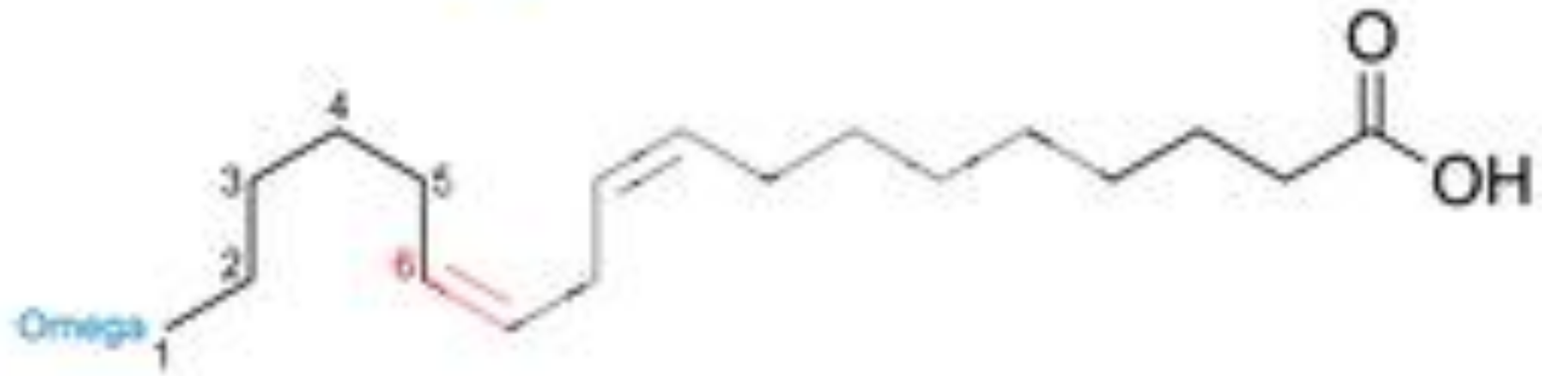


Z,Z,Z-9,12,15-
Octadecatrien-acido
C 18:3, $\Delta^{9, 12, 15}$

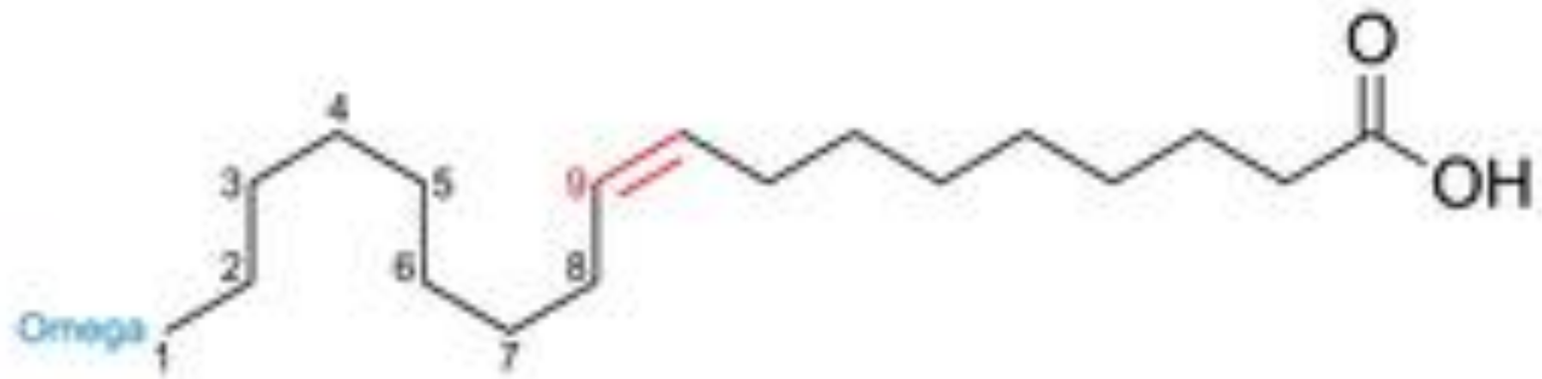
Modello a calotta



Omega-3 (Linolenic acid)



Omega-6 (Linoleic acid)



Omega-9 (Oleic acid)

Recomendación de consumo:
Adultos, tomar 2 softgels al día repartidas en las comidas con abundante agua.

La dosis diaria expresamente recomendada no debe ser sobrepasada. Los complementos alimenticios no deben utilizarse como sustituto de una dieta equilibrada. Mantenga este producto fuera del alcance de los niños más pequeños. **No apto para mujeres embarazadas o en periodo de lactancia.**

Ingredientes:
Aceite de linaza (prensado en frío, contiene 52,6% de ácido alfalinolénico), agente de recubrimiento gelatina (bovino, cubierto de la cápsula), agente humectante glicerina (cubierta de la cápsula), acetato de D-alfa-Tocoferola (vitamina E)

fairvital
Sustancias Vitales Bioactivas

Sin Gluten, Lactosa ni Fructosa

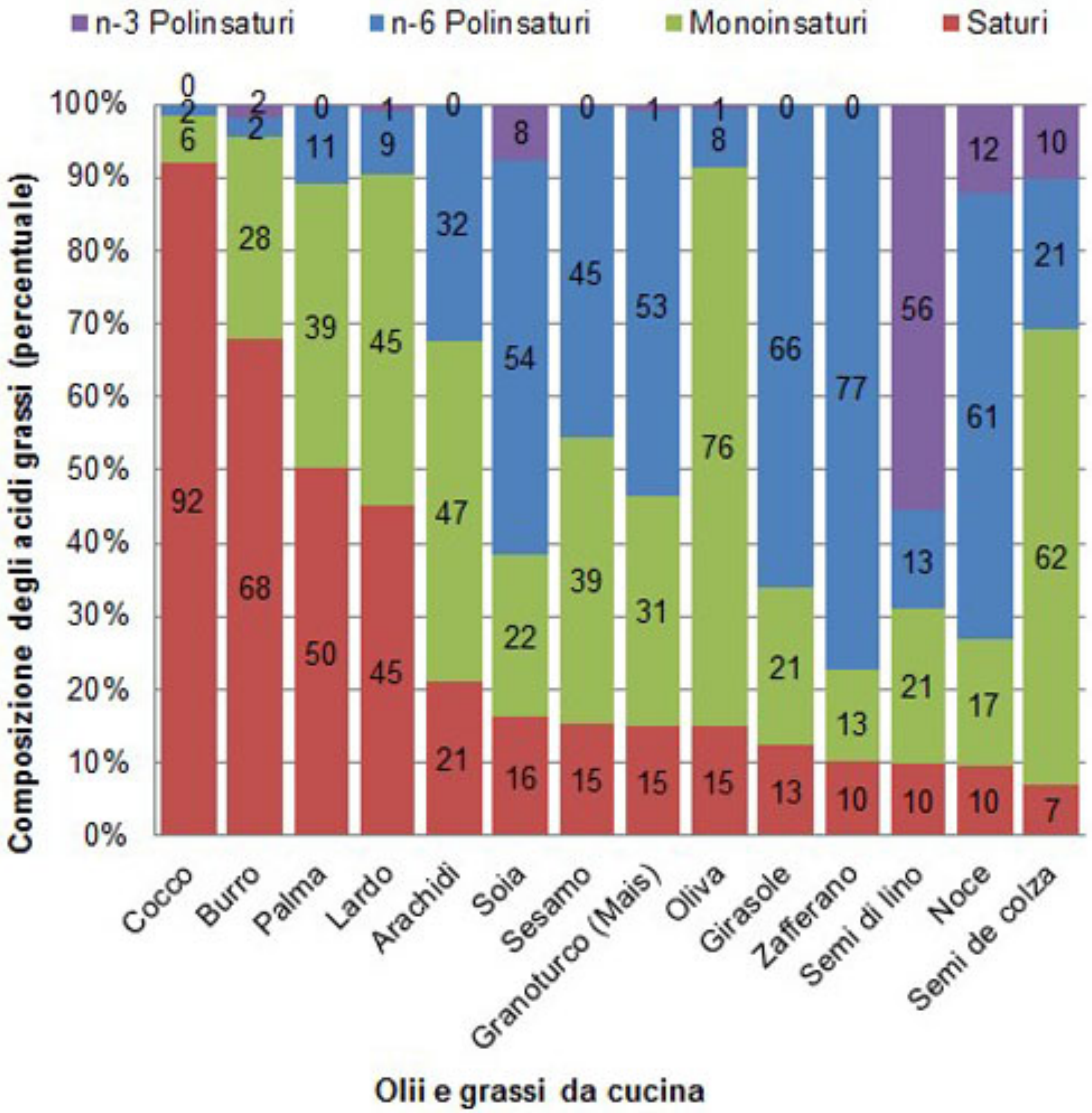
Aceite de Linaza
Omega 3-6-9
1000mg
Complemento Alimenticio
120 Softgels

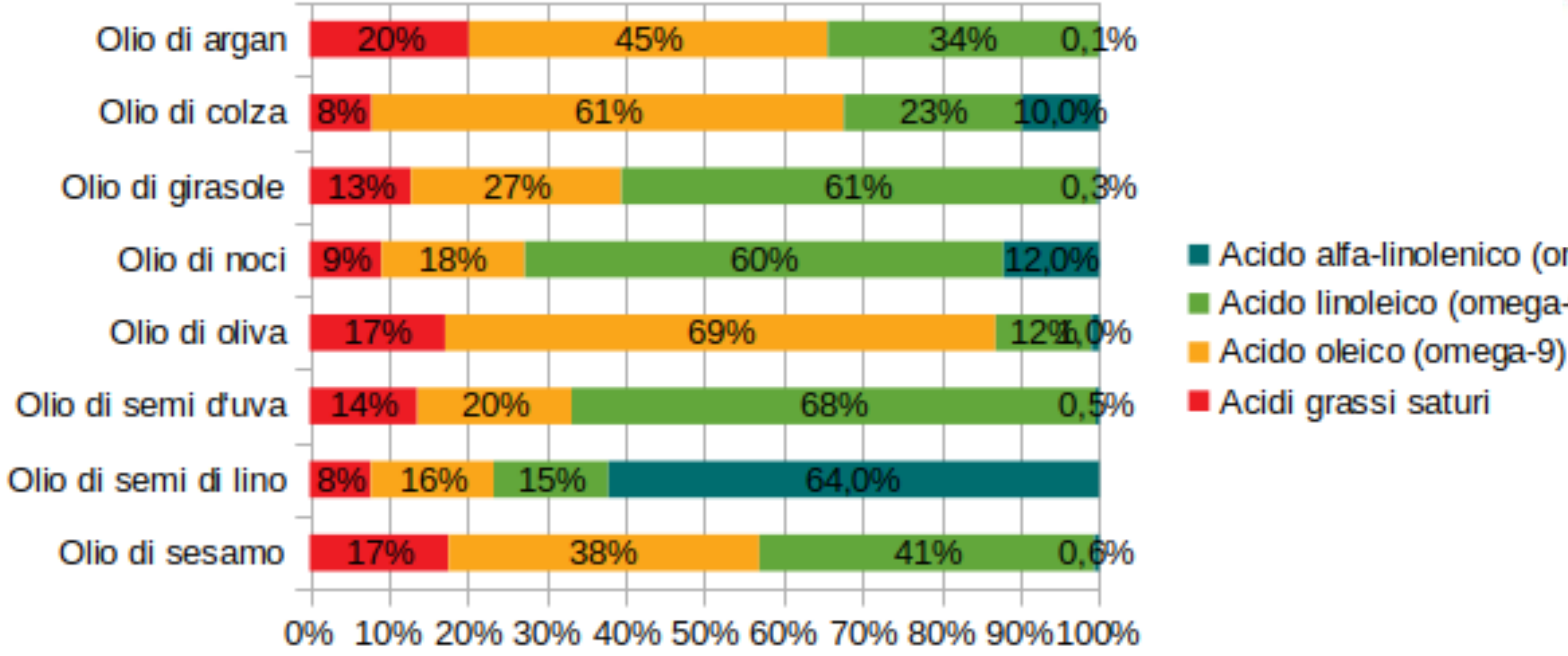
Información Nutricional	por 2 Softgels	%VRN*
Aceite de linaza	2000mg	
de los cuales		
Ácido alfa-Linolénico (Omega-3)	1052mg	-
Ácido Linoleico (Omega-6)	336mg	-
Ácido Oleico (Omega-9)	442mg	-
Vitamina E (alpha-TE)	20mg	167

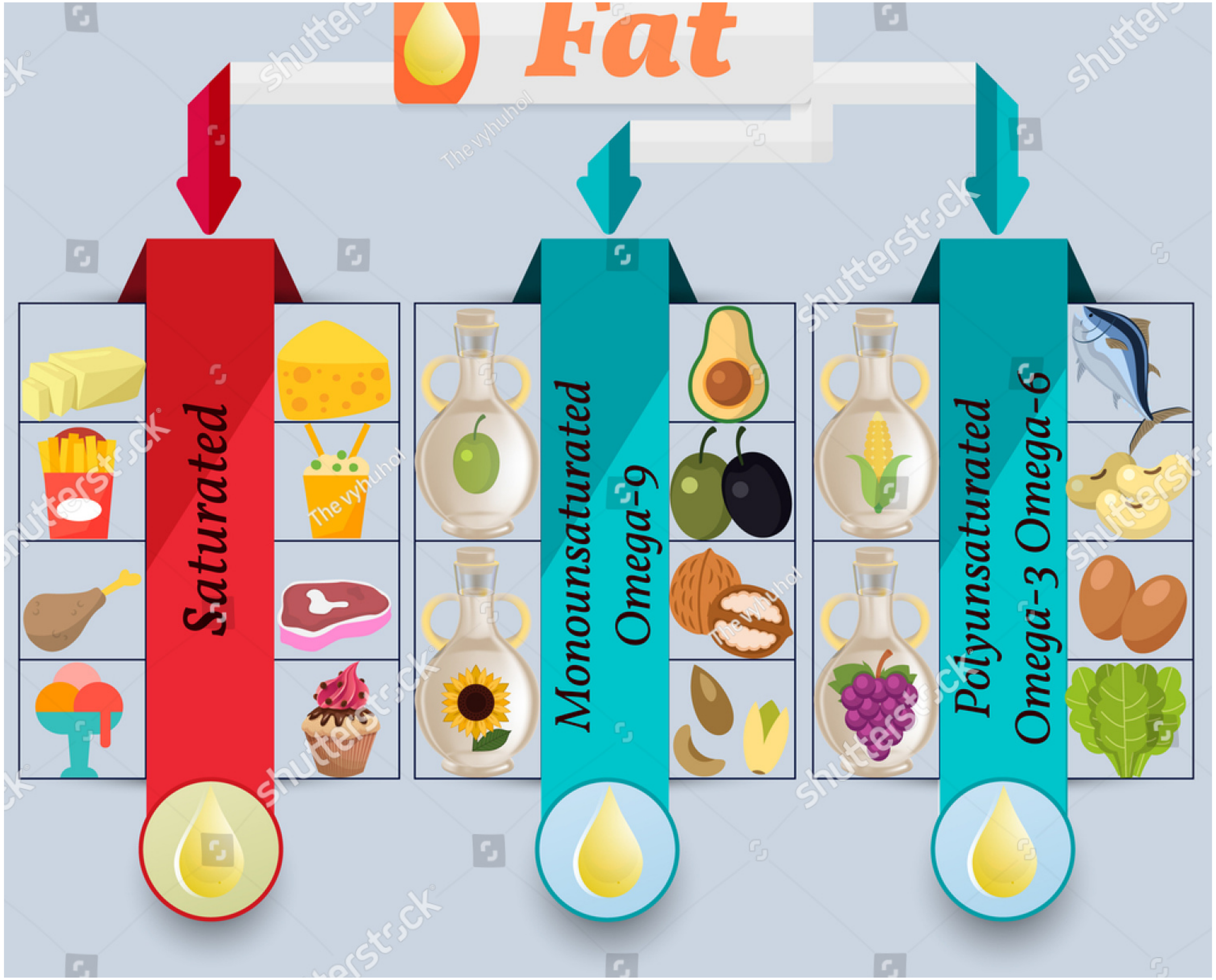
*Valores de referencia de nutrientes según el Reglamento (UE) nº 1169/2011

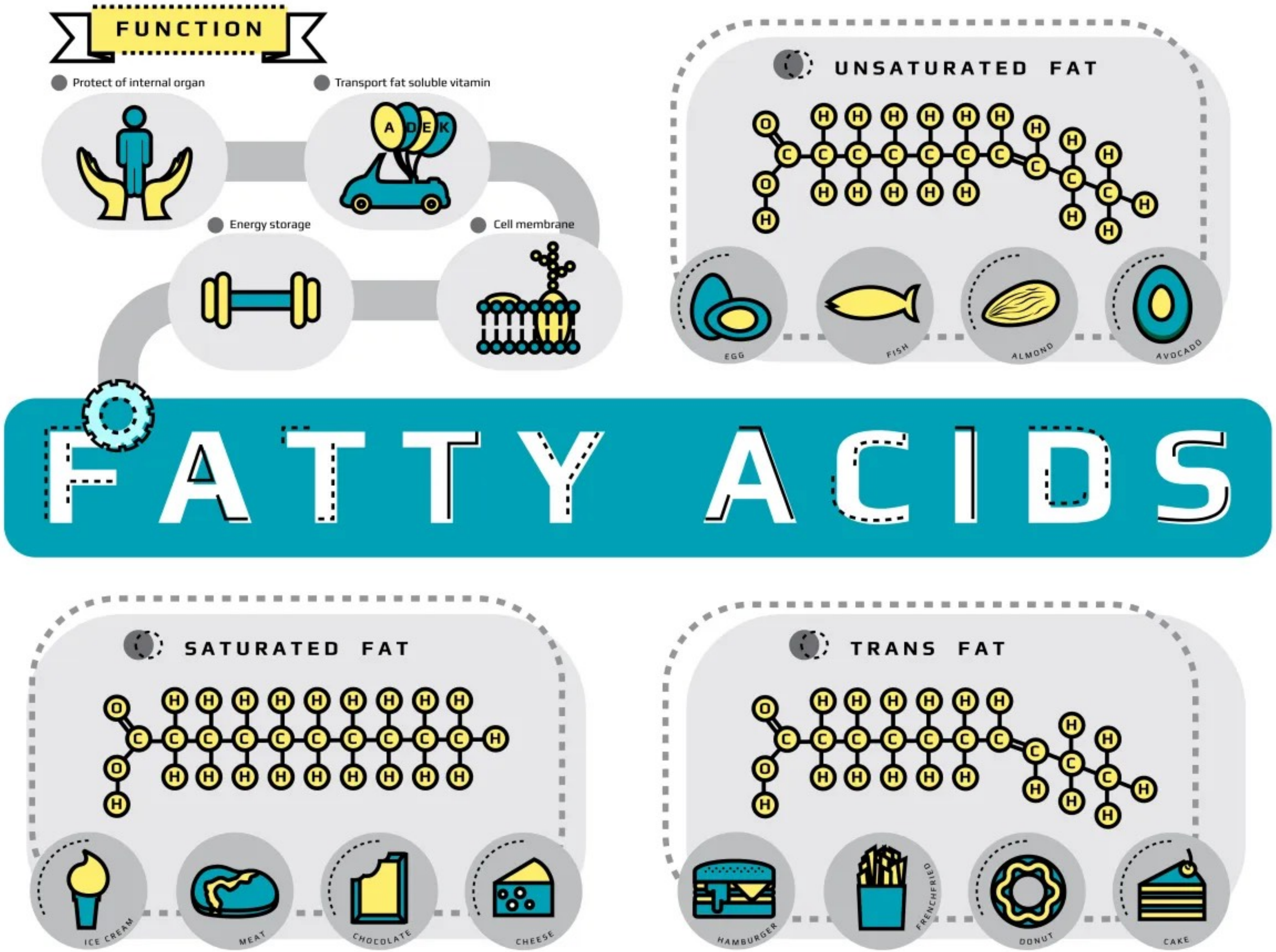
Cantidad neta: 166g (120 Softgels)
Núm. de art°: 73412

fairvital b.v., Postbus 31119, NL-6370 AC Landgraaf, Tel: 020 60 05 47, info@fairvital.com, www.fairvital.com



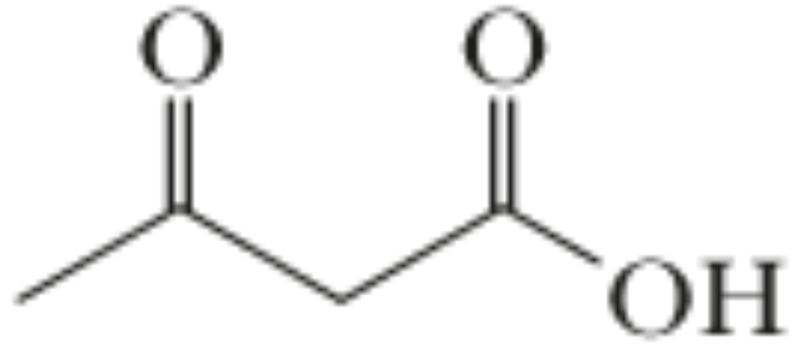


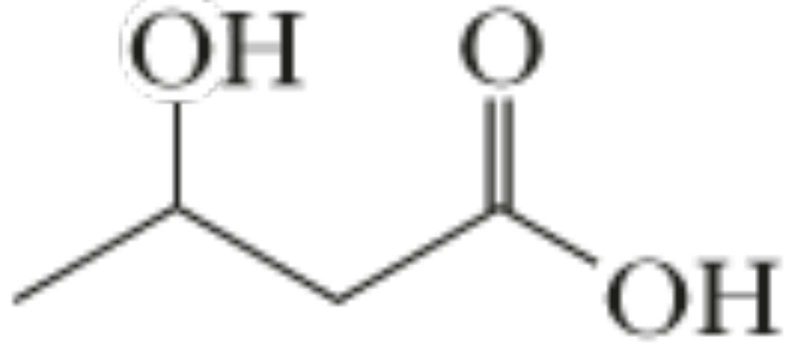

Fat
Saturated
Monounsaturated
Omega-9
Polyunsaturated
Omega-3 Omega-6

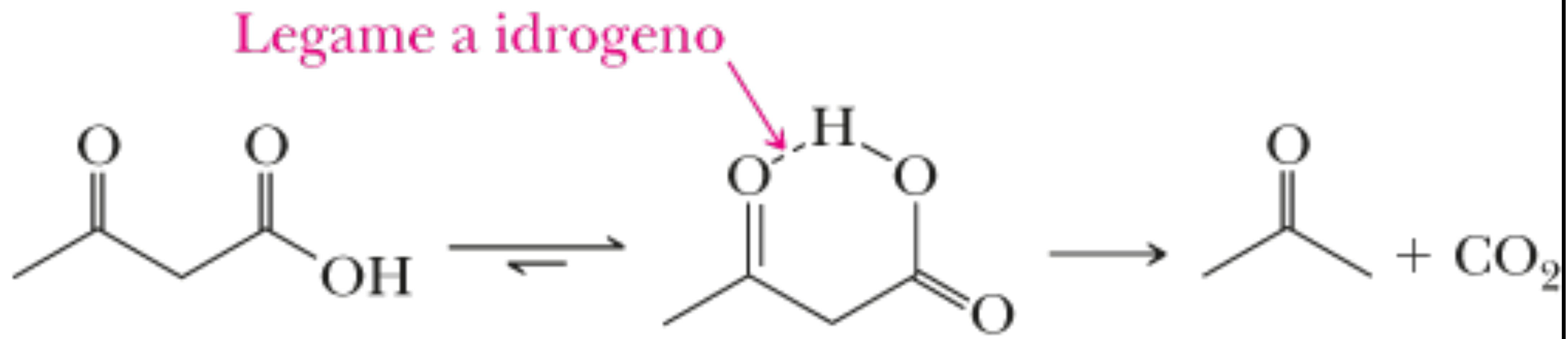

FUNCTION
Protect of internal organ
Transport fat soluble vitamin
A D E K
Energy storage
Cell membrane
UNSATURATED FAT
EGG
FISH
ALMOND
AVOCADO
FATTY ACIDS
SATURATED FAT
ICE CREAM
MEAT
CHOCOLATE
CHEESE
TRANS FAT
HAMBURGER
FRENCHFRIED
DONUT
CAKE

Corpi chetonici e diabete mellito

L'acido 3-ossobutanoico (acido acetoacetico) e il suo prodotto di riduzione, l'acido 3-idrossibutanoico, sono sintetizzati nel fegato dall'acetil-CoA, un prodotto del metabolismo degli acidi grassi e di alcuni amminoacidi. L'acido 3-idrossibutanoico e l'acido 3-ossobutanoico sono comunemente noti come corpi chetonici.

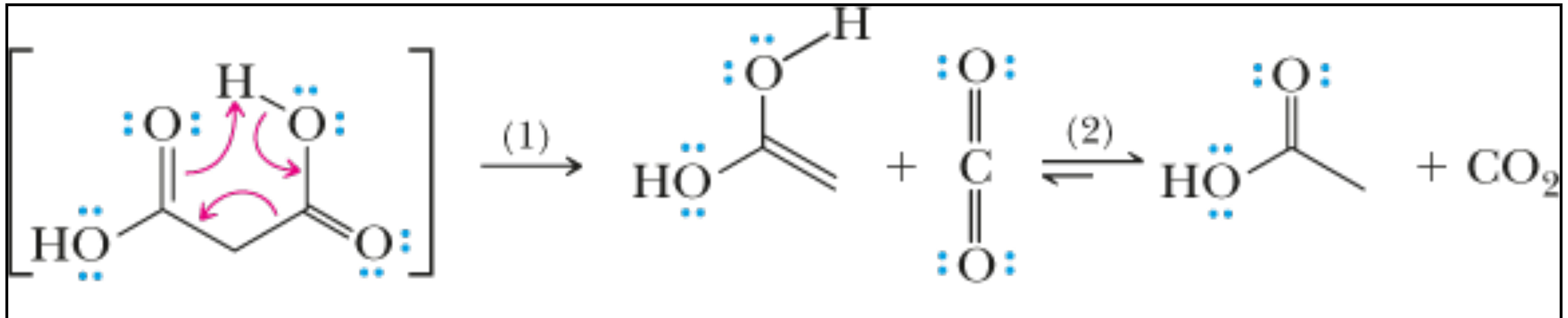

Acido 3-ossobutanoico
(Acido acetoacetico)


Acido 3-idrossibutanoico
(Acido β-idrossibutirrico)



Conformazione reattiva

La concentrazione dei corpi chetonici nel sangue delle persone sane e ben nutrite è circa 0.01 mmol/L. Invece, nelle persone sofferenti per fame o per diabete mellito, la concentrazione dei corpi chetonici può aumentare sino a 500 volte rispetto ai valori normali. In queste condizioni, la concentrazione dell'acido acetoacetico aumenta fino al punto in cui esso subisce decarbossilazione spontanea, dando acetone e diossido di carbonio. L'acetone non viene metabolizzato nell'uomo e viene eliminato attraverso i reni e i polmoni. L'odore di acetone è responsabile del caratteristico "odore dolce" dell'alito dei pazienti diabetici gravi.



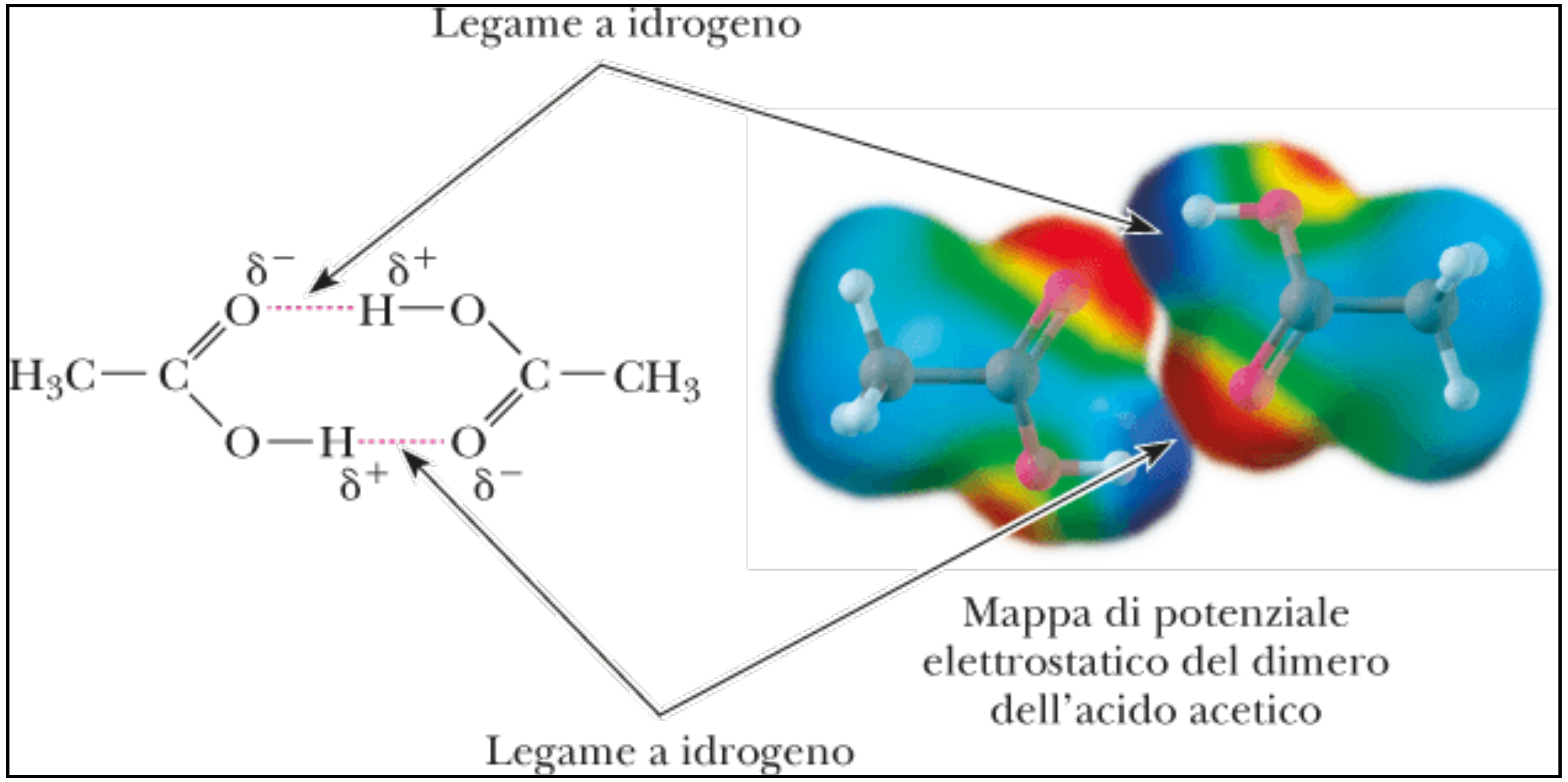
Stato di transizione ciclico a sei termini

Enolo di un acido carbossilico

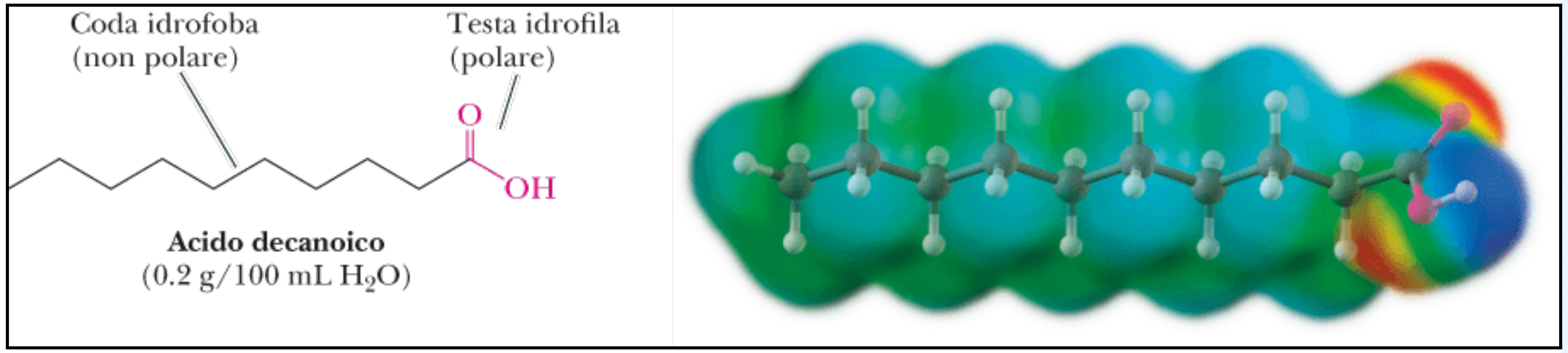
Acido carbossilico

Proprietà fisiche

Allo stato liquido e solido, gli acidi carbossilici si associano mediante legami a idrogeno in strutture dimeriche, come viene mostrato di seguito per l'acido acetico allo stato liquido



Mappa di potenziale elettrostatico del dimero dell'acido acetico



Acido decanoico
(0.2 g/100 mL H_2O)

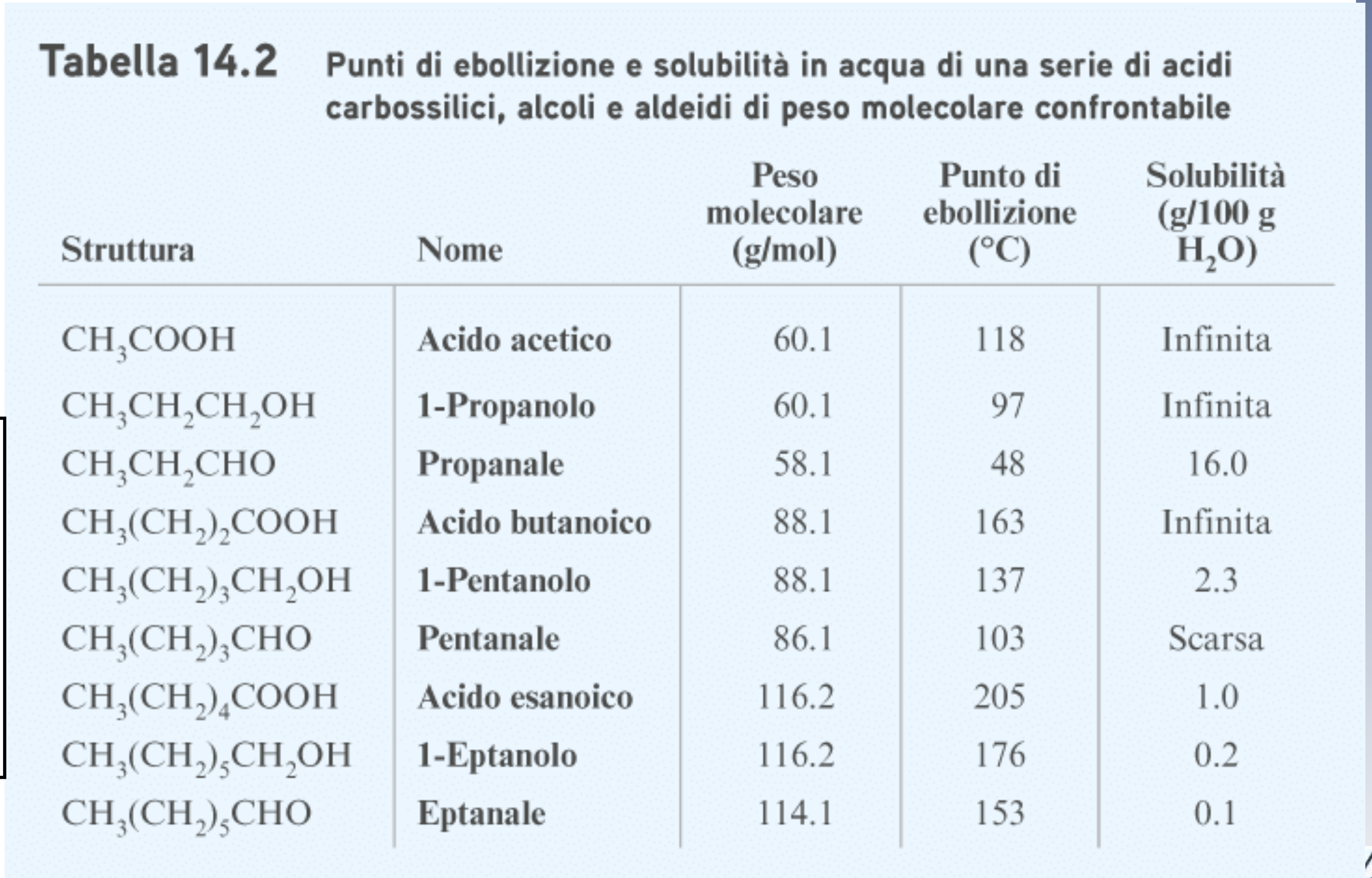
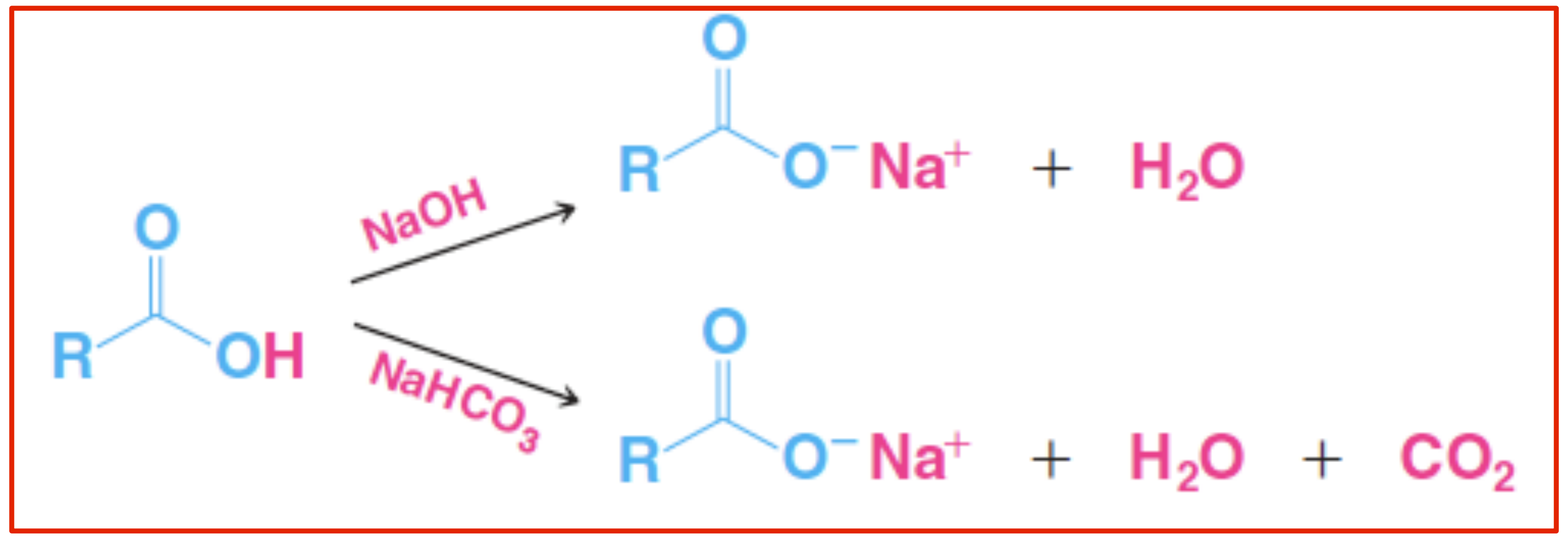
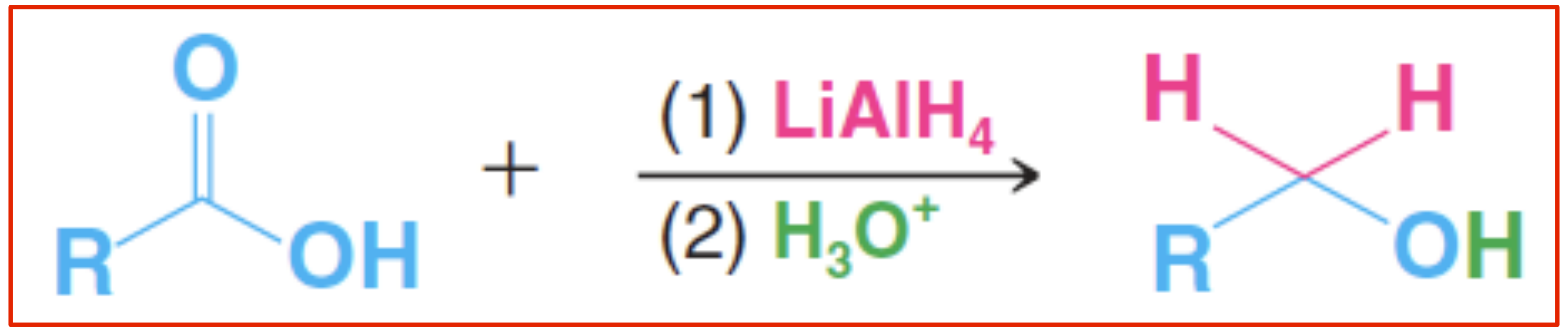


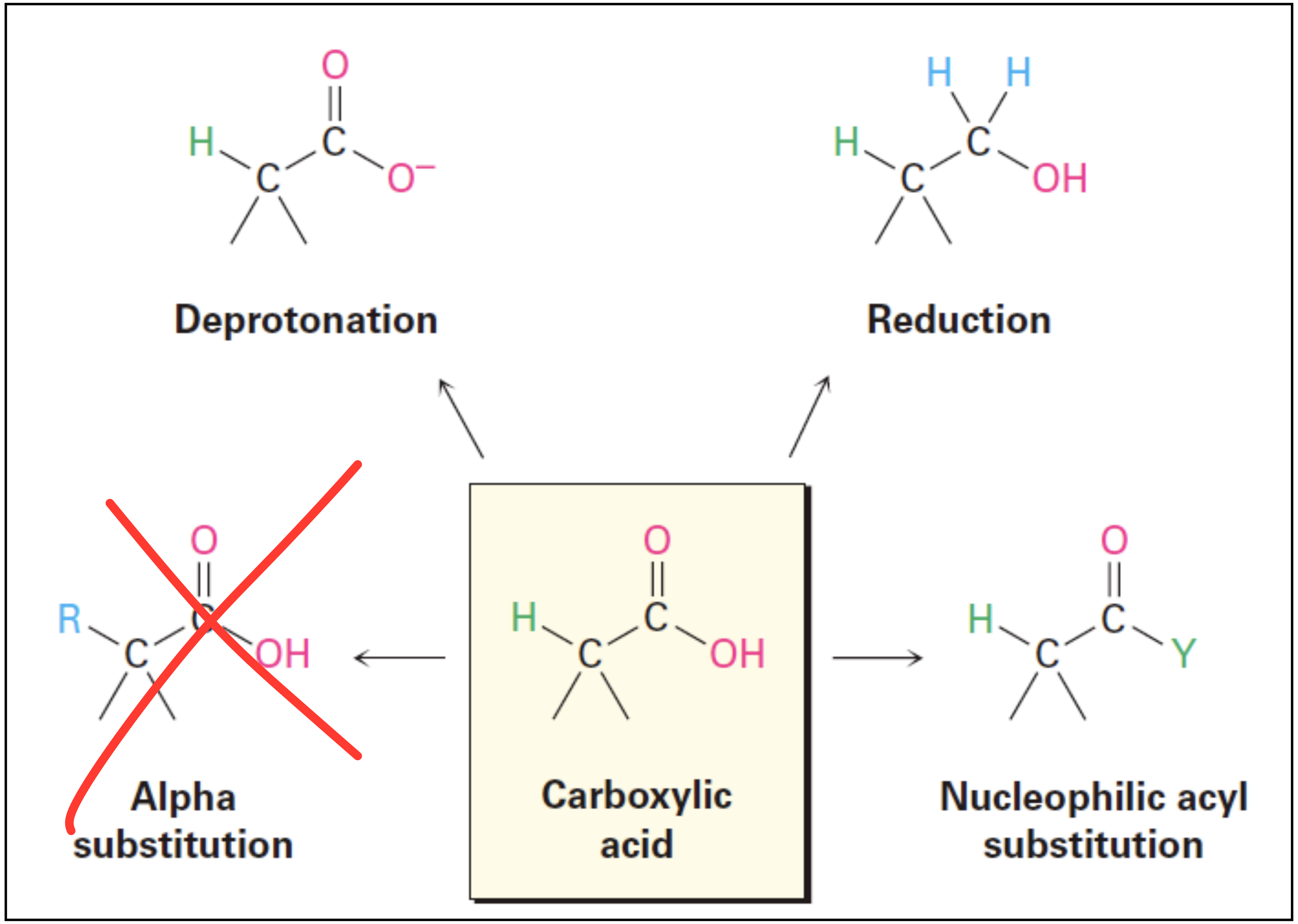
Tabella 14.2 Punti di ebollizione e solubilità in acqua di una serie di acidi carbossilici, alcoli e aldeidi di peso molecolare confrontabile

Struttura	Nome	Peso molecolare (g/mol)	Punto di ebollizione (°C)	Solubilità (g/100 g H_2O)
CH_3COOH	**Acido acetico**	60.1	118	Infinita
$CH_3CH_2CH_2OH$	**1-Propanolo**	60.1	97	Infinita
CH_3CH_2CHO	**Propanale**	58.1	48	16.0
$CH_3(CH_2)_2COOH$	**Acido butanoico**	88.1	163	Infinita
$CH_3(CH_2)_3CH_2OH$	**1-Pentanolo**	88.1	137	2.3
$CH_3(CH_2)_3CHO$	**Pentanale**	86.1	103	Scarsa
$CH_3(CH_2)_4COOH$	**Acido esanoico**	116.2	205	1.0
$CH_3(CH_2)_5CH_2OH$	**1-Eptanolo**	116.2	176	0.2
$CH_3(CH_2)_5CHO$	**Eptanale**	114.1	153	0.1

Reattività degli acidi carbossilici





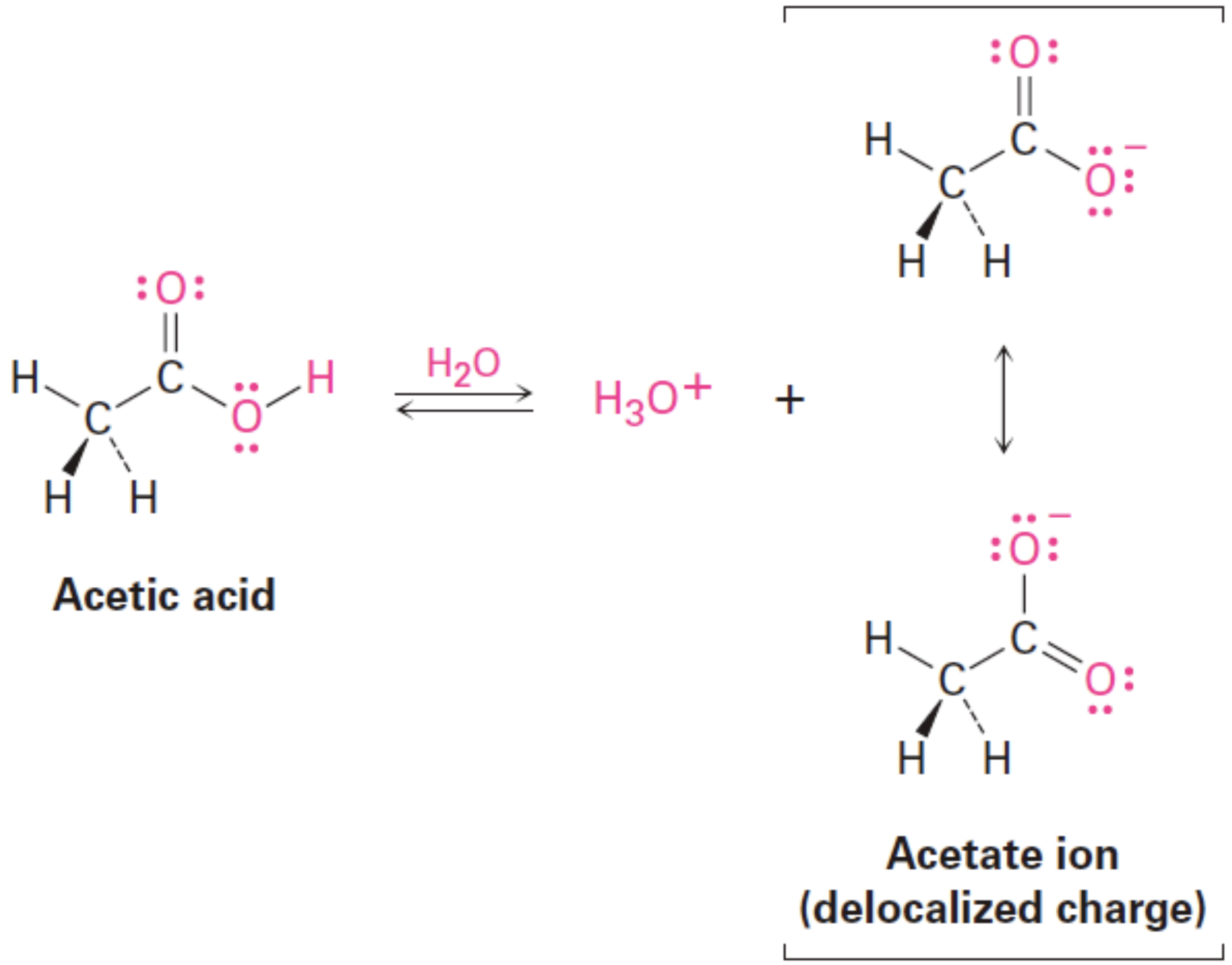


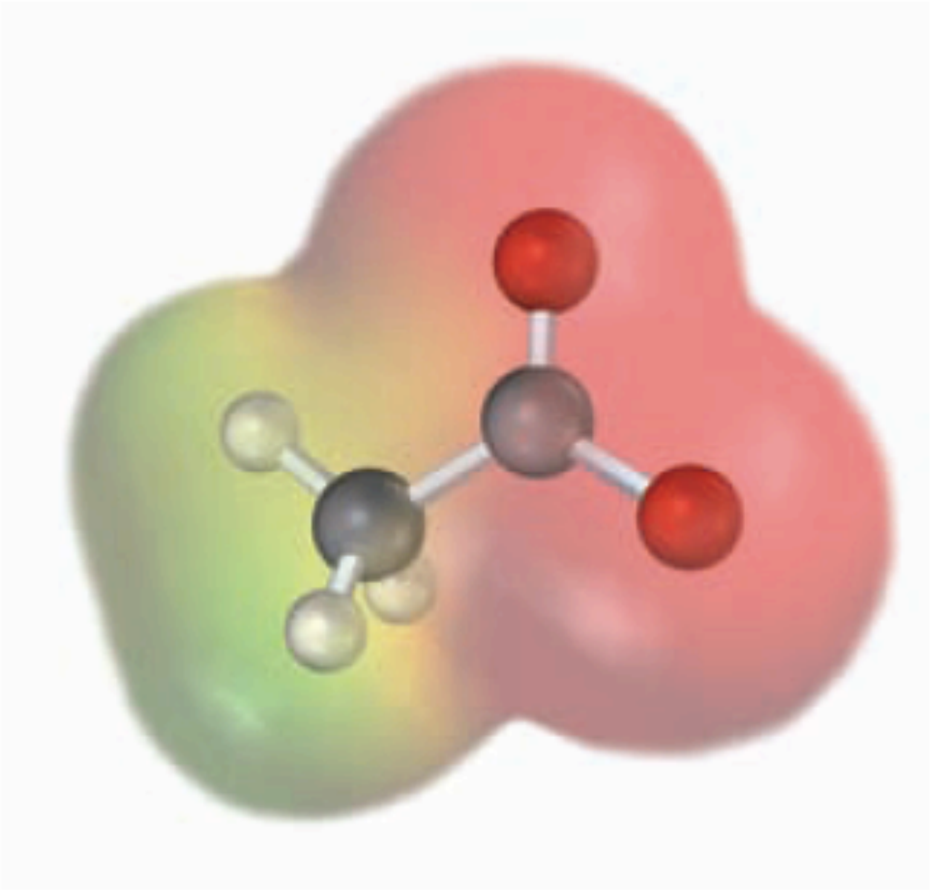
SNAc

Acidità
A. Costanti di ionizzazione acida

$$CH_3COOH + H_2O \rightleftharpoons CH_3COO^- + H_3O^+ \qquad K_a = \frac{[CH_3COO^-][H_3O^+]}{[CH_3COOH]} = 1.74 \times 10^{-5}$$

$$pK_a = 4.76$$





Acidità
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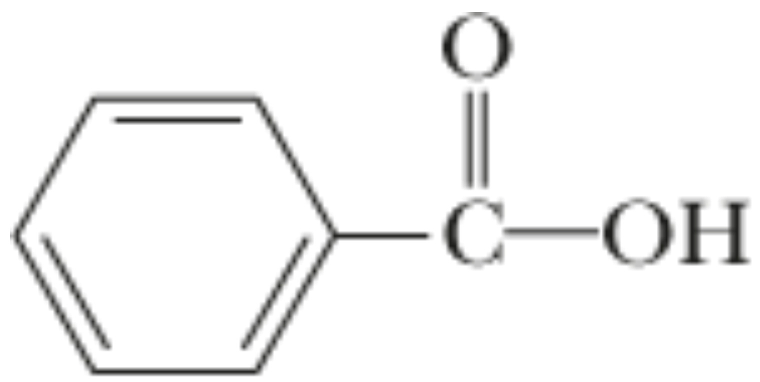
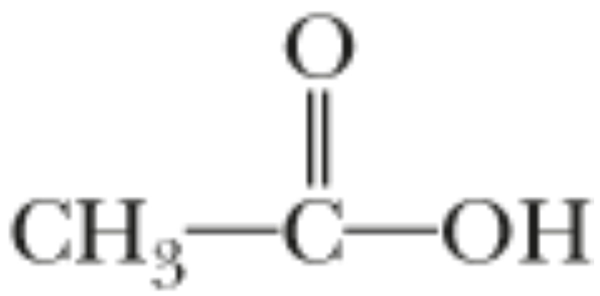


Acido benzoico
pK_a 4.19

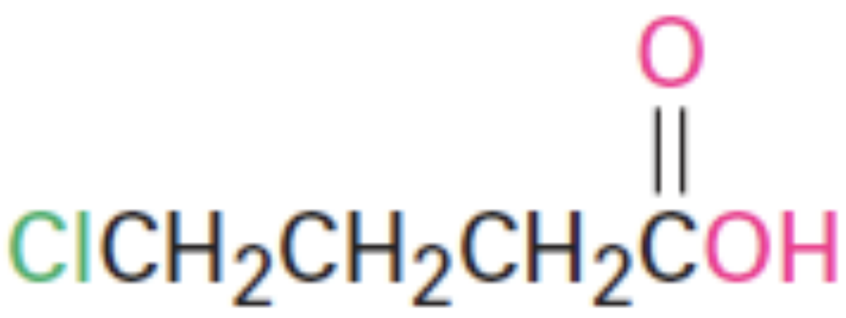


$CH_3-\overset{O}{\overset{\|}{C}}-OH$

Acido acetico
pK_a 4.76

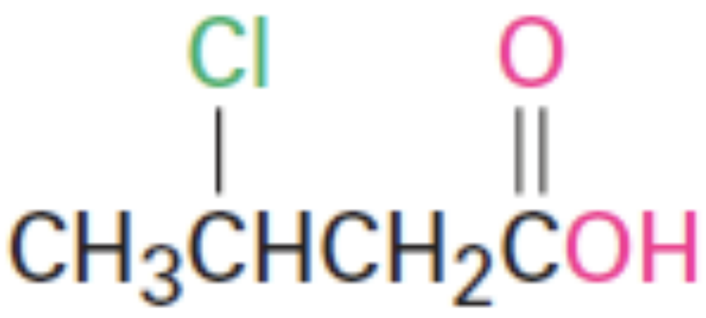
Formula	CH_3COOH	$ClCH_2COOH$	$Cl_2CHCOOH$	Cl_3CCOOH
Nome	**Acido acetico**	**Acido cloroacetico**	**Acido dicloroacetico**	**Acido tricloroacetico**
pK_a	4.76	2.86	1.48	0.70

Aumento della forza acida →



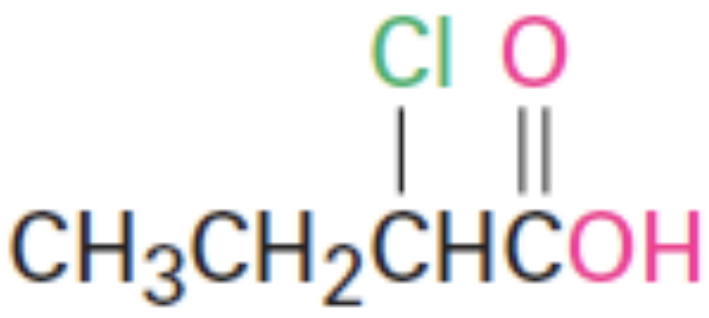
$ClCH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

$pK_a = 4.52$



$CH_3\overset{Cl}{\overset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}OH$

$pK_a = 4.05$

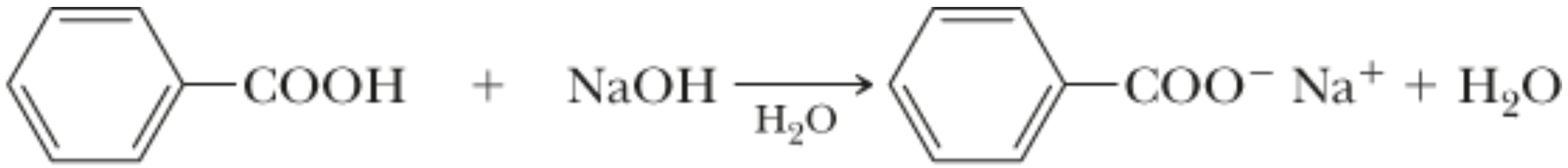


$CH_3CH_2\overset{Cl}{\overset{|}{C}}H\overset{O}{\overset{\|}{C}}OH$

$pK_a = 2.86$

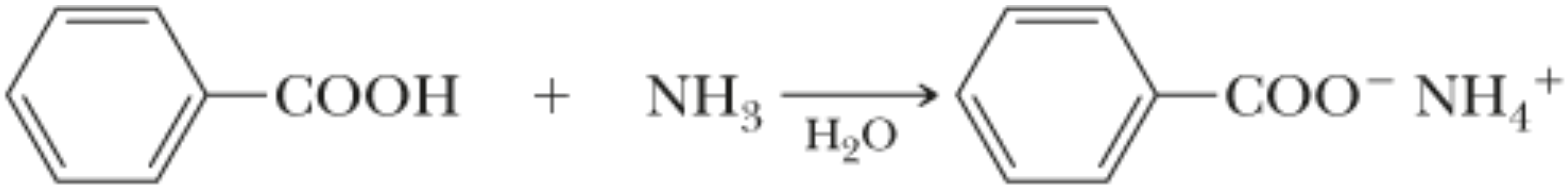
Acidity →

B. Reazioni con le basi



Acido benzoico
(poco solubile in acqua)

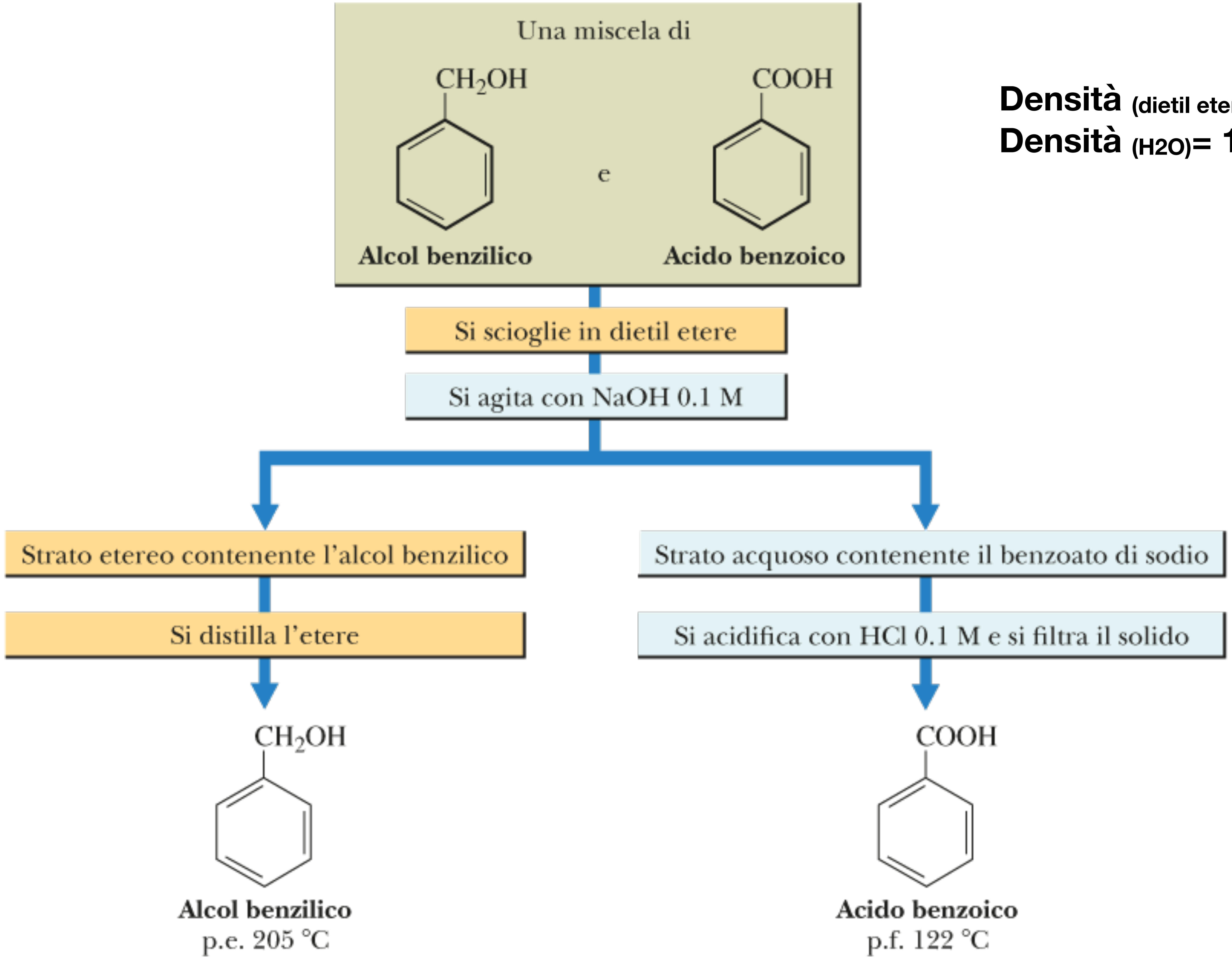
Benzoato di sodio
(60 g/100 mL di acqua)



Acido benzoico
(poco solubile in acqua)

Benzoato di ammonio
(20 g/100 mL di acqua)

Separazione dell'acido benzoico dall'alcol benzilico



Una miscela di

CH_2OH e $COOH$

Alcol benzilico **Acido benzoico**

Si scioglie in dietil etere

Si agita con NaOH 0.1 M

Strato etereo contenente l'alcol benzilico

Si distilla l'etere

CH_2OH

Alcol benzilico
p.e. 205 °C

Strato acquoso contenente il benzoato di sodio

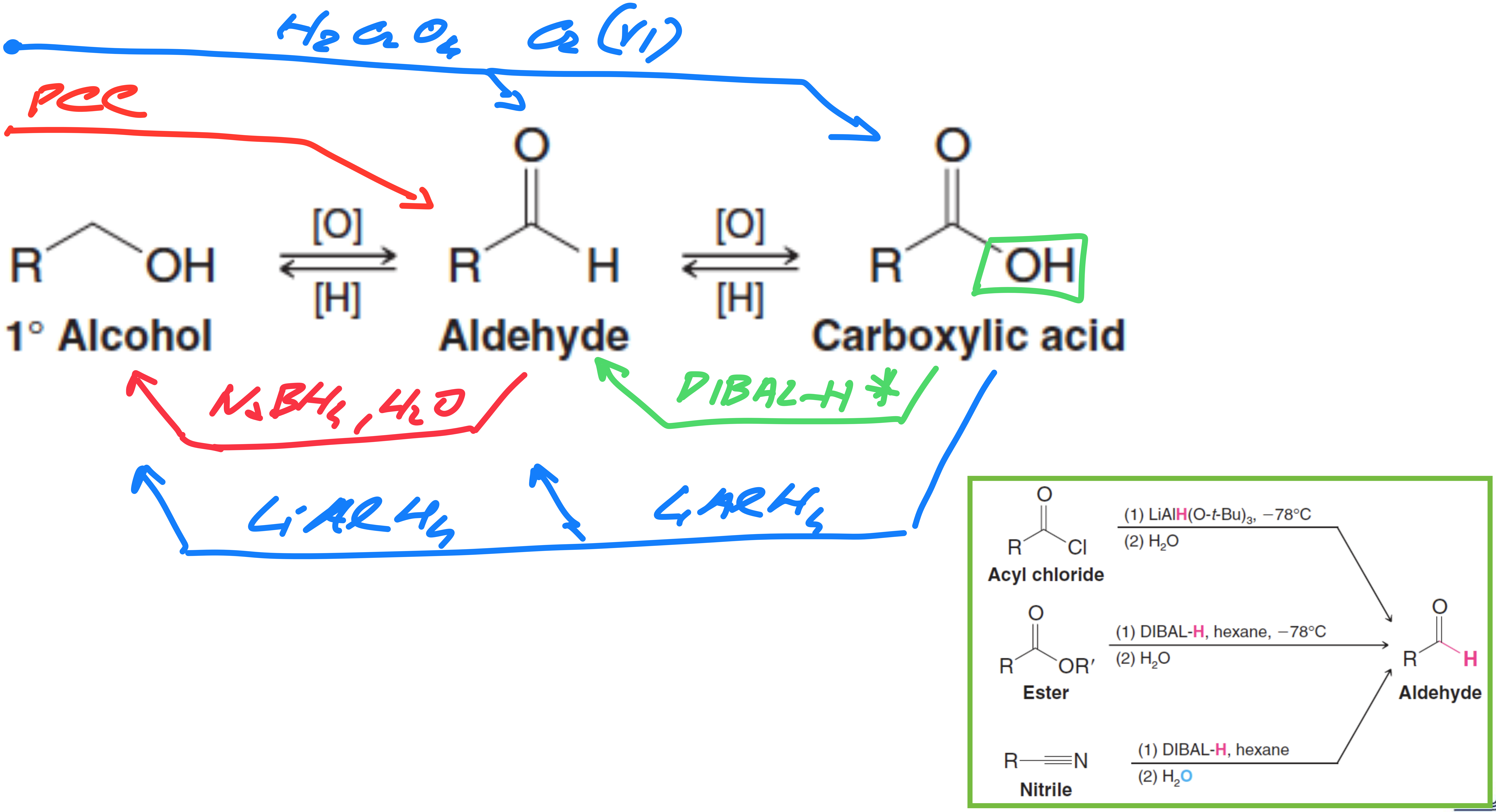
Si acidifica con HCl 0.1 M e si filtra il solido

$COOH$

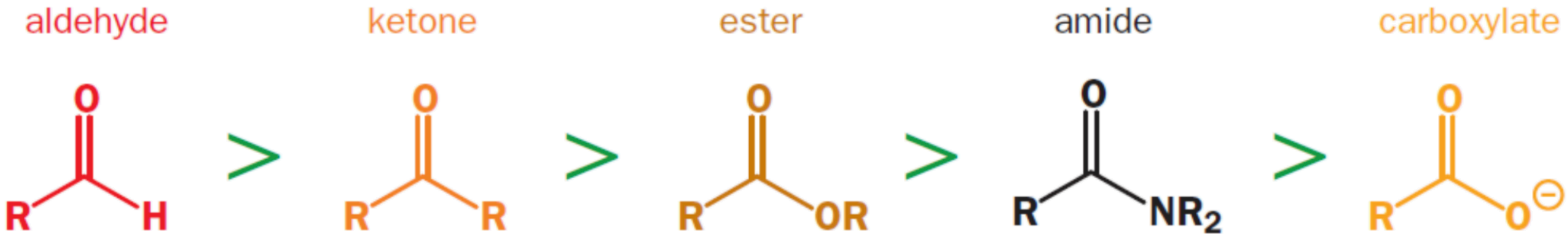
Acido benzoico
p.f. 122 °C

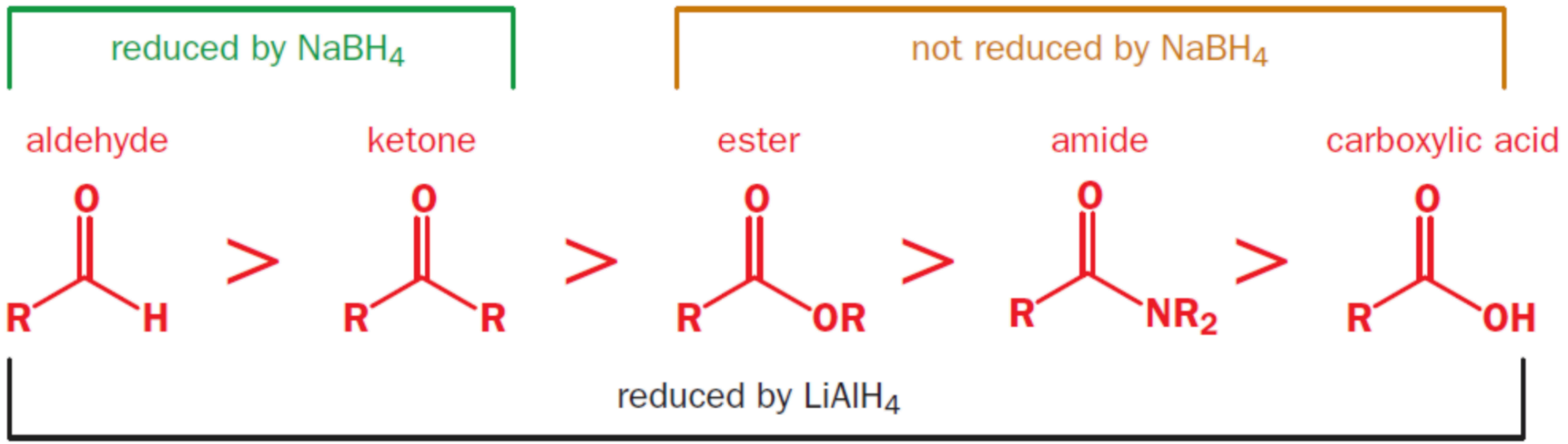
Densità $_{\text{(dietil etere)}}$= 0.71 g/cm^3
Densità $_{(H_2O)}$= 1.00 g/cm^3

Riduzioni degli acidi carbossilici



Reattività del gruppo carbonile verso i nucleofili

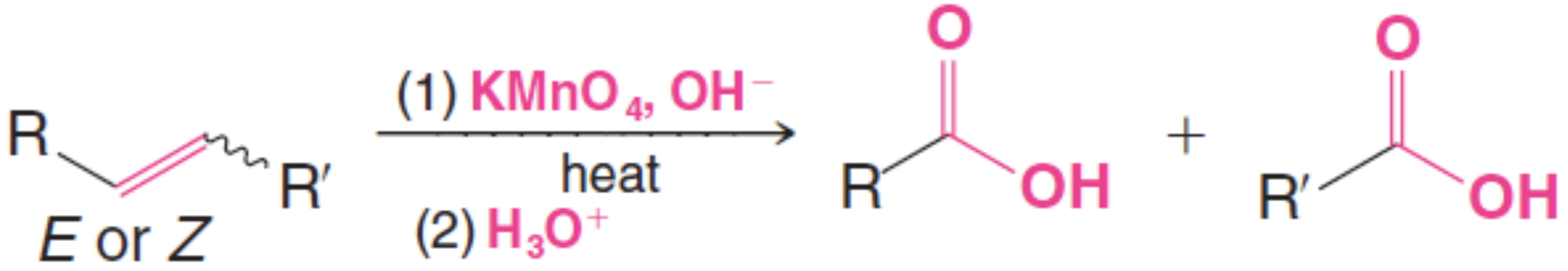




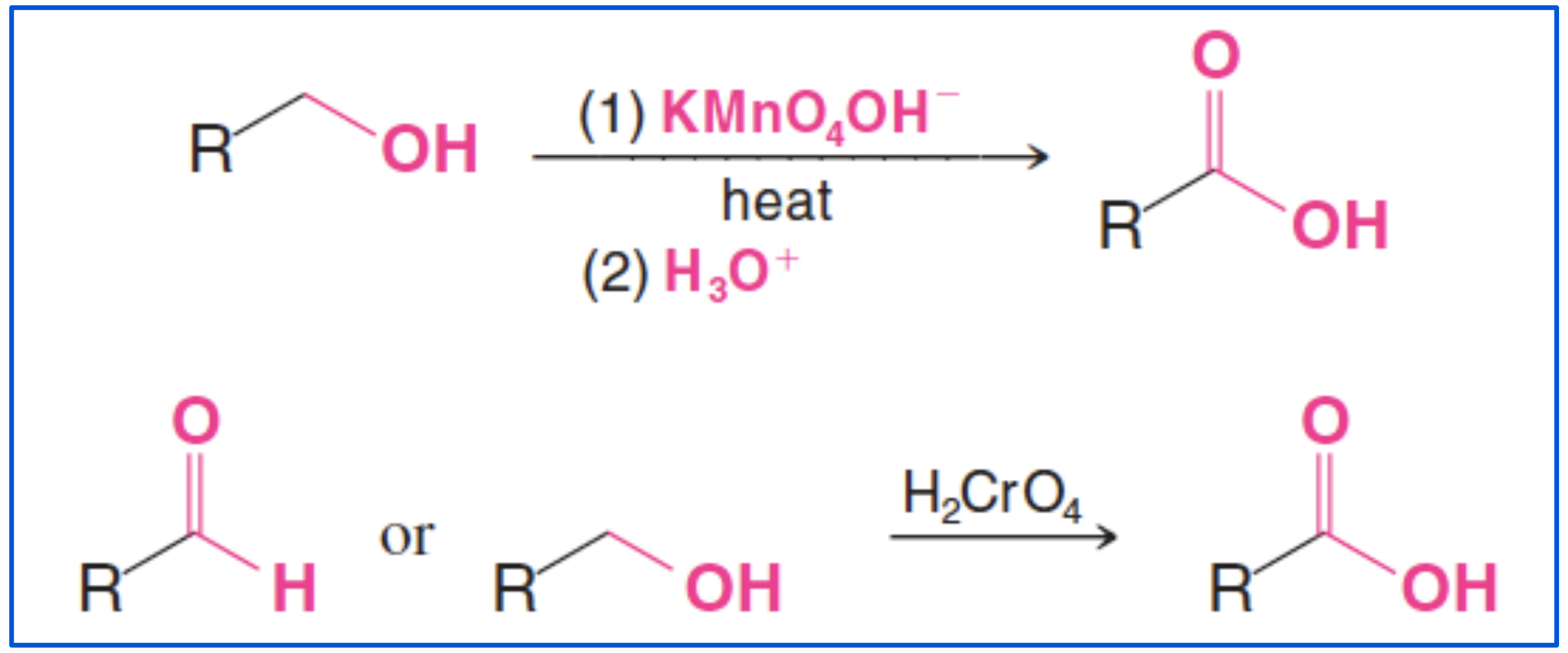
Formalmente, una riduzione con idruri assomiglia ad una sostituzione acilica in cui il nucleofilo è lo ione idruro. Il fato della reazione è controllato dalla presenza o meno di buoni gruppi uscenti.

Preparazione degli acidi carbossilici

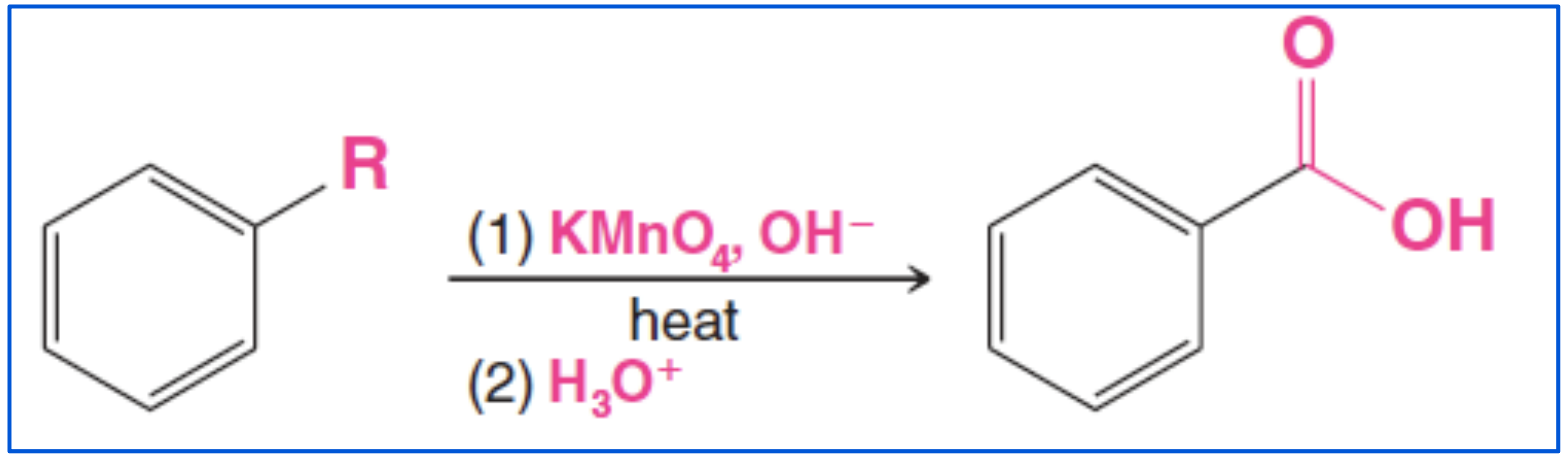
1. Ossidazione degli alcheni



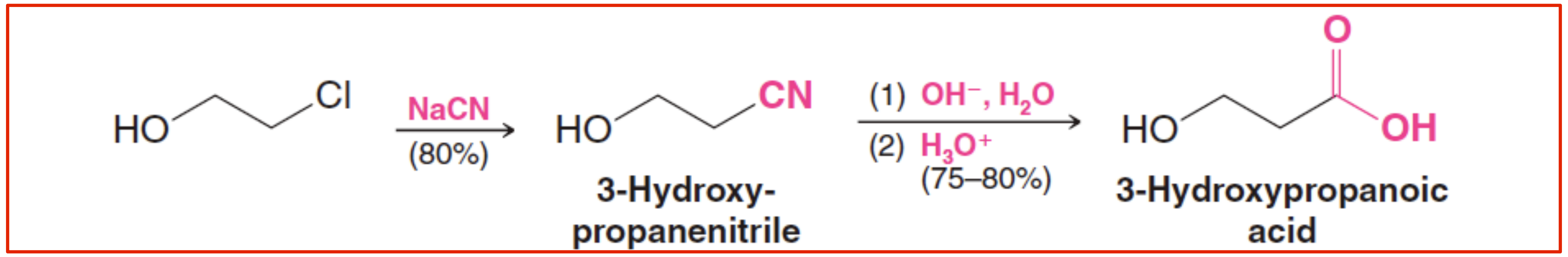
2. Ossidazione di aldeidi e alcoli primari



3. ossidazione degli alchilbenzeni



4. Idrolisi delle cianoidrine e di altri nitrili

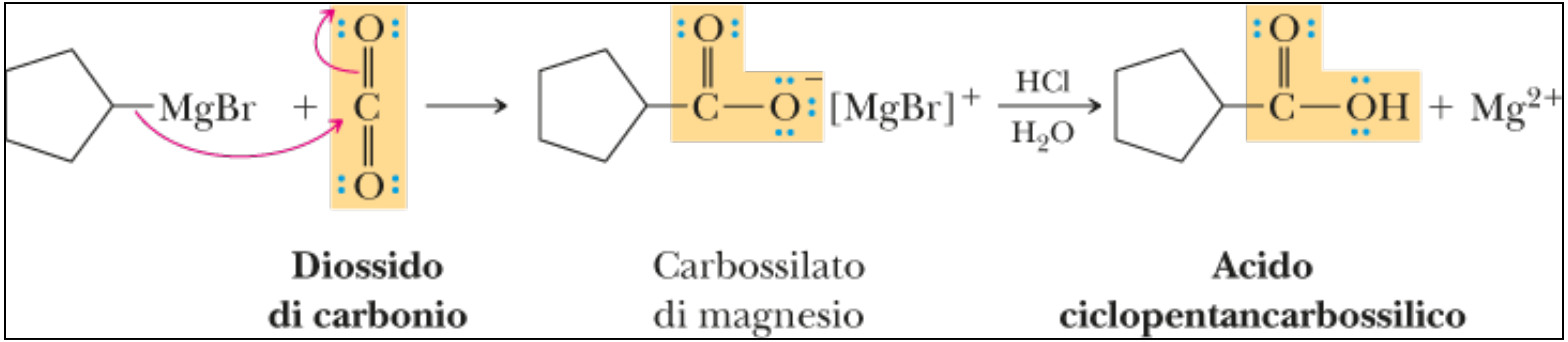


5.**carbonatazione con reagenti di Grignard. (Nuova sintesi)**

Carbonatazione con reagenti di Grignard. (Nuova sintesi)

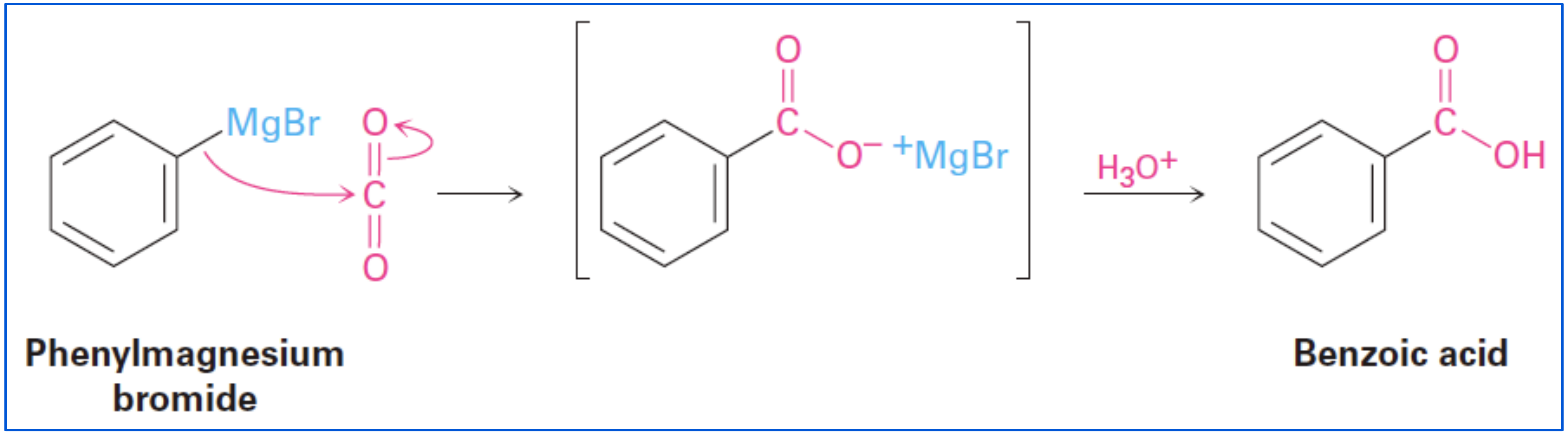
Preparazione degli acidi carbossilici

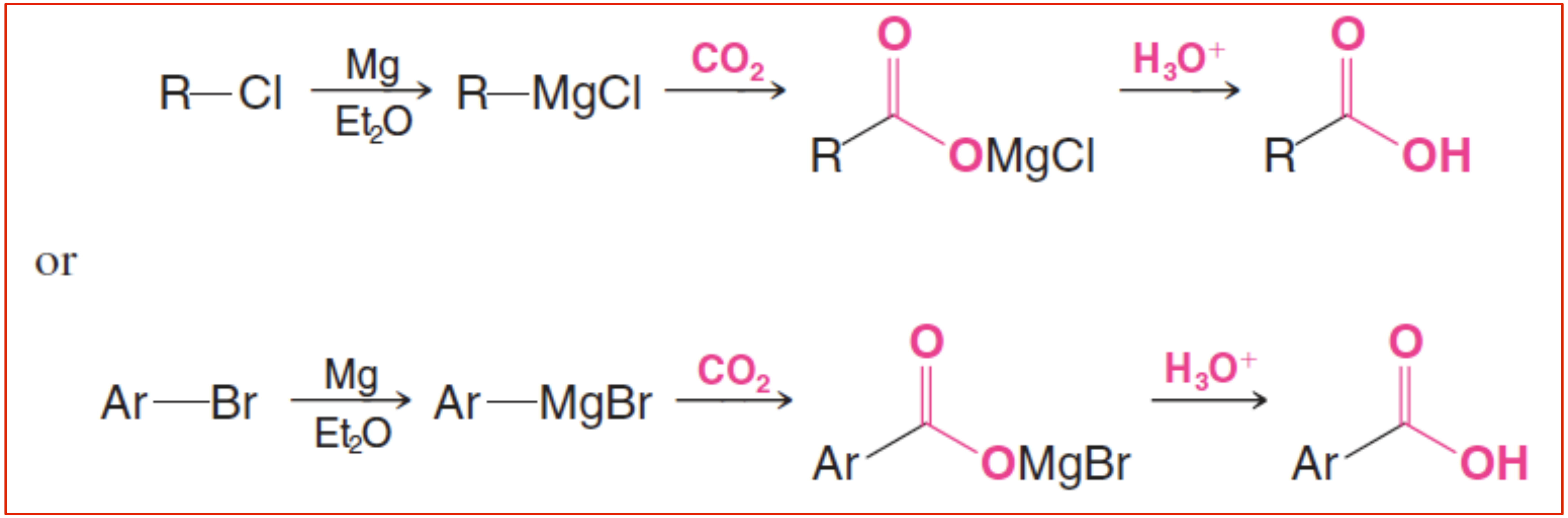
Per trattamento di un reattivo di Grignard con diossido di carbonio (CO_2) si ottiene il sale di magnesio di un acido carbossilico che, per protonazione con acido acquoso, dà l'acido carbossilico.



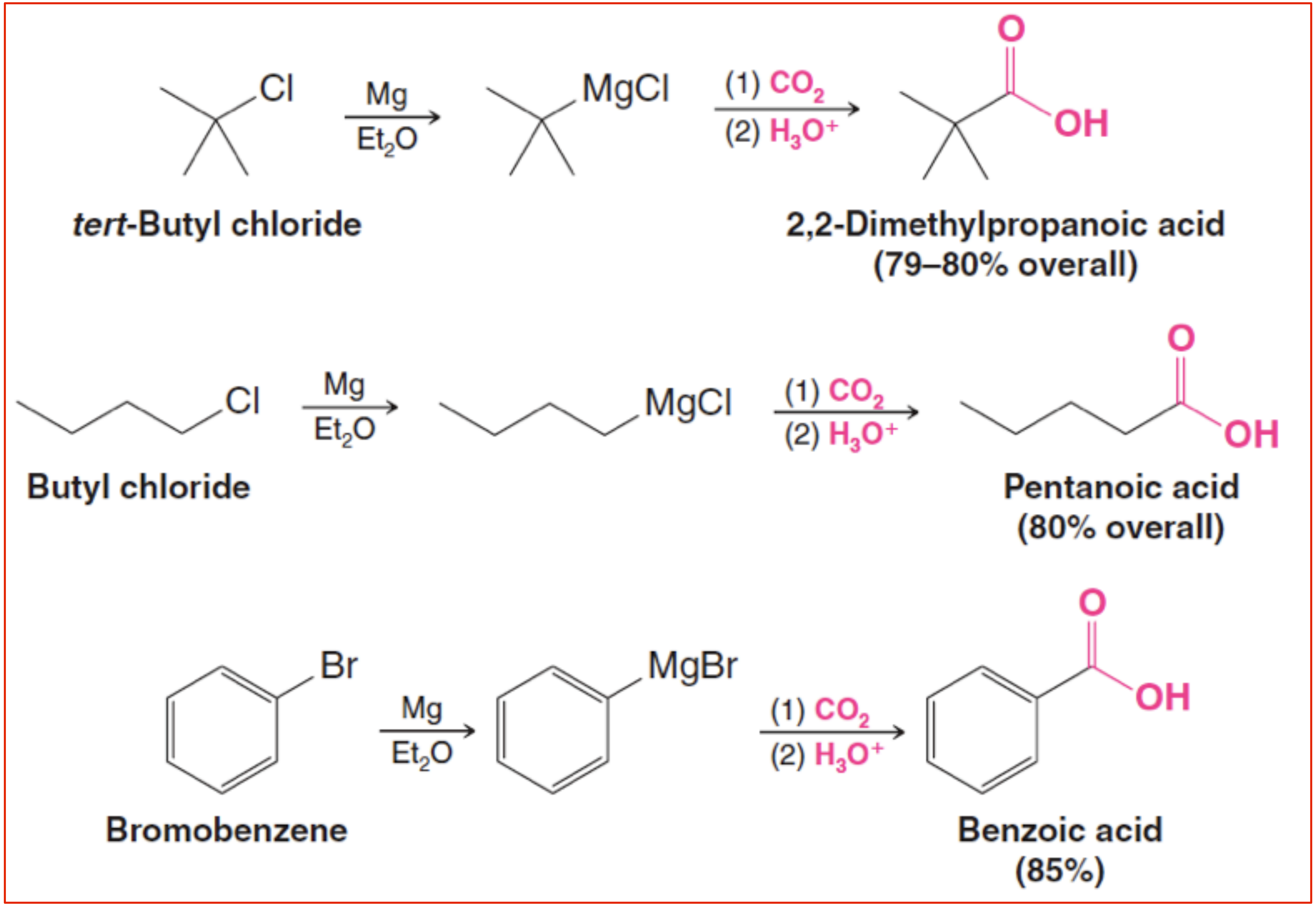
La carbonatazione di un reattivo di Grignard è dunque una via conveniente per convertire un alogenuro (alchilico o arilico) in un acido carbossilico.

Carbonatazione con reagenti di Grignard. (Nuova sintesi)





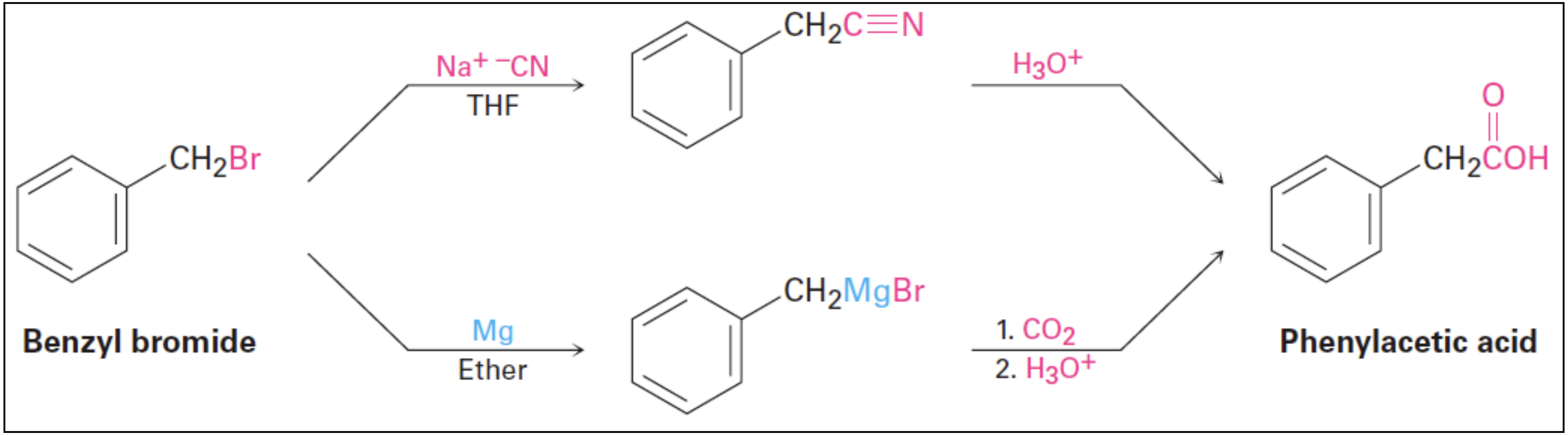
Carbonatazione con reagenti di Grignard. (Nuova sintesi)



Preparazione degli acidi carbossilici.

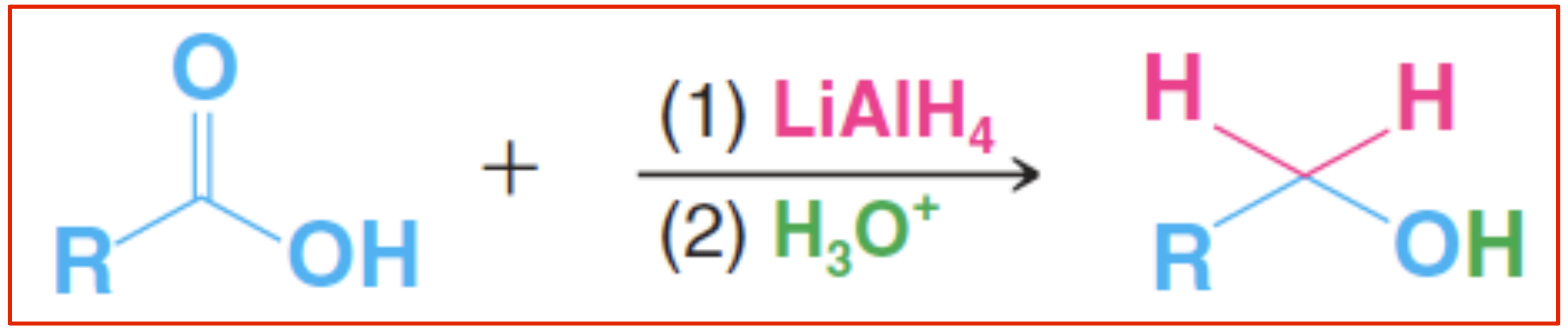
Problema:

Come preparereresti l'acido fenilacetico ($PhCH_2CO_2H$) dal bromuro di benzile ($PhCH_2Br$)?

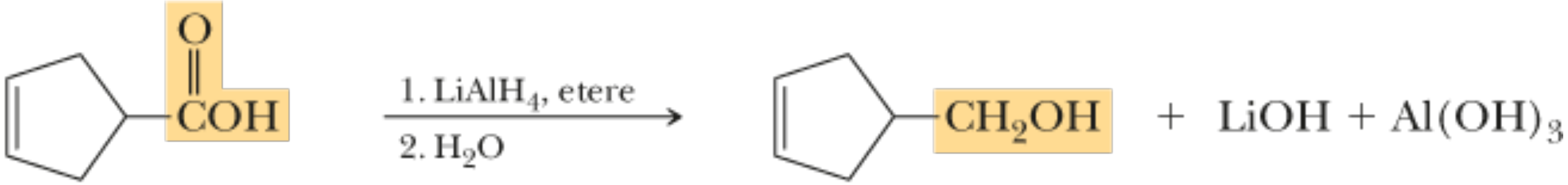


Riduzione

A. Litio alluminio idruro

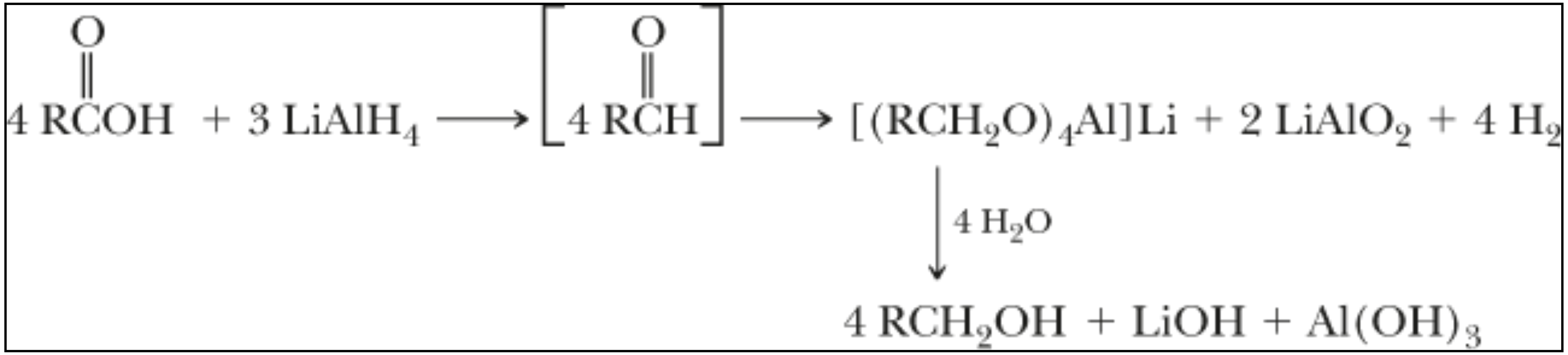


Il litio alluminio idruro, LiAlH₄ (LAH), riduce un acido carbossilico ad alcol primario con rese eccellenti, sebbene sia necessario il riscaldamento. Il LAH è generalmente sciolto in dietil etere o in tetraidrofurano (THF).



Acido 3-ciclopenten-carbossilico

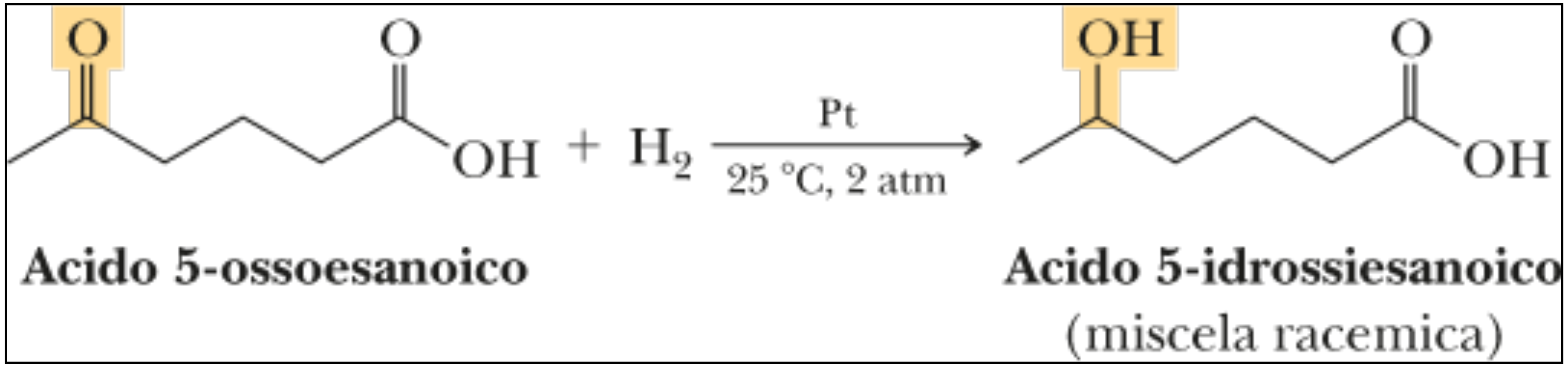
4-Idrossimetilciclopentene



$$4\,R\overset{O}{\overset{\|}{C}}OH + 3\,LiAlH_4 \longrightarrow \left[4\,R\overset{O}{\overset{\|}{C}}H\right] \longrightarrow [(RCH_2O)_4Al]Li + 2\,LiAlO_2 + 4\,H_2$$

$$\xrightarrow{4\,H_2O} 4\,RCH_2OH + LiOH + Al(OH)_3$$

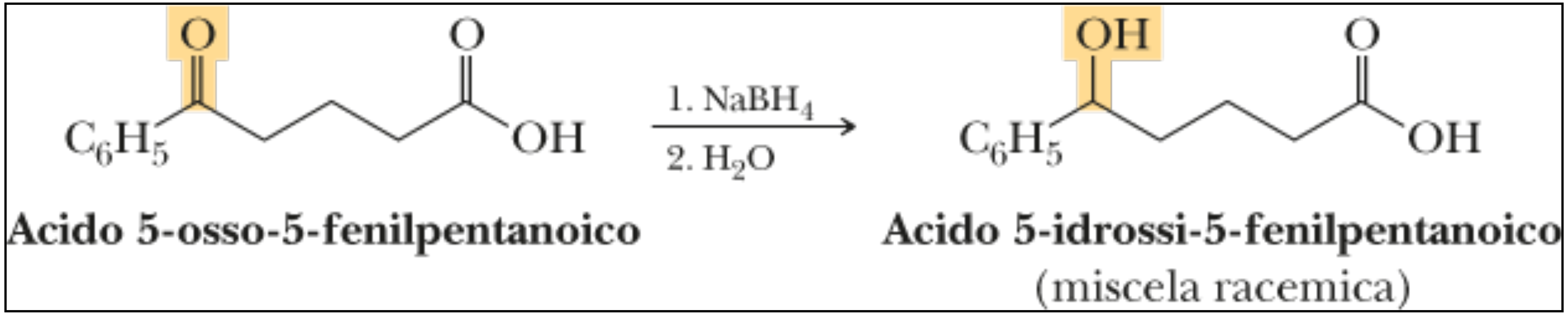
B. Riduzione selettiva di altri gruppi funzionali



Poiché i gruppi carbossilici sono stabili nelle condizioni di idrogenazione catalitica che normalmente riducono aldeidi, chetoni, alcheni e alchini, è possibile ridurre selettivamente questi gruppi funzionali ad alcoli o ad alcani in presenza di gruppi carbossilici.

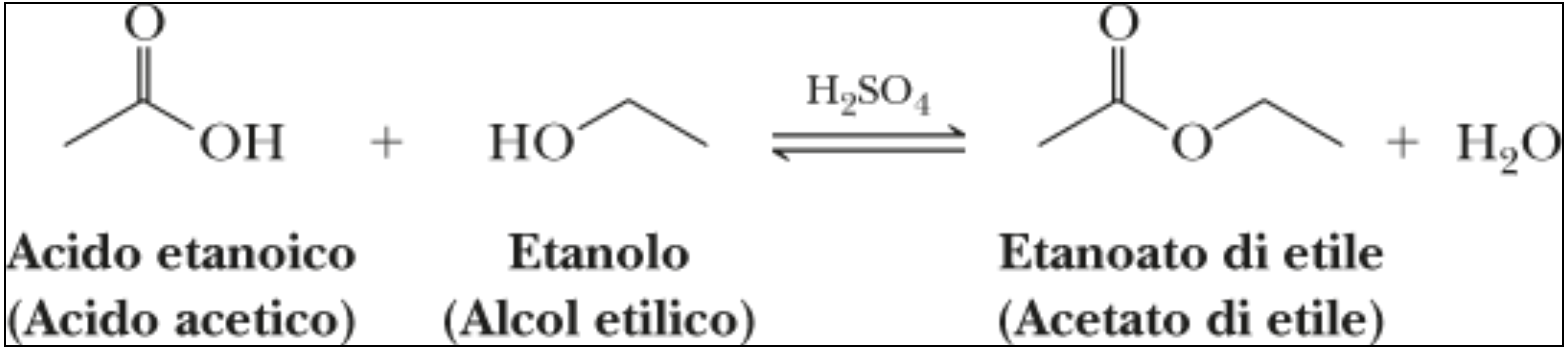
B. Riduzione selettiva di altri gruppi funzionali

Aldeidi e i chetoni sono ridotti ad alcoli sia da $LiAlH_4$ sia da $NaBH_4$.
Tuttavia, soltanto $LiAlH_4$ è capace di ridurre i gruppi carbossilici.
Pertanto, è possibile ridurre il gruppo carbonilico di un'aldeide o di un chetone in maniera selettiva in presenza di un gruppo carbossilico, facendo uso di $NaBH_4$ come riducente più blando.



Un esempio è la riduzione selettiva del seguente chetoacido a idrossiacido.

Esterificazione



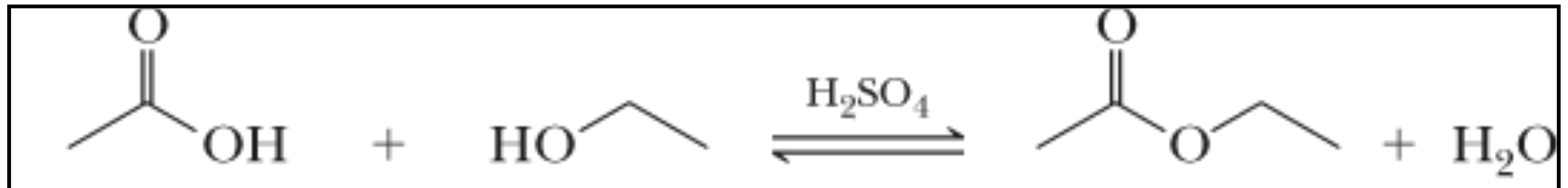
Acido etanoico
(Acido acetico)

Etanolo
(Alcol etilico)

Etanoato di etile
(Acetato di etile)

Il processo di formazione di un estere scaldando a riflusso un acido e un alcol in presenza di un catalizzatore acido, di solito H_2SO_4 o HCl.

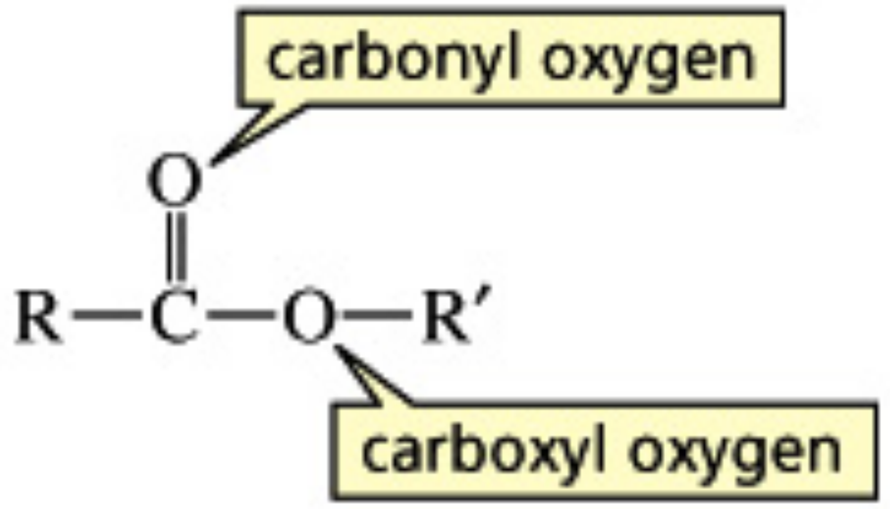
ESTERI



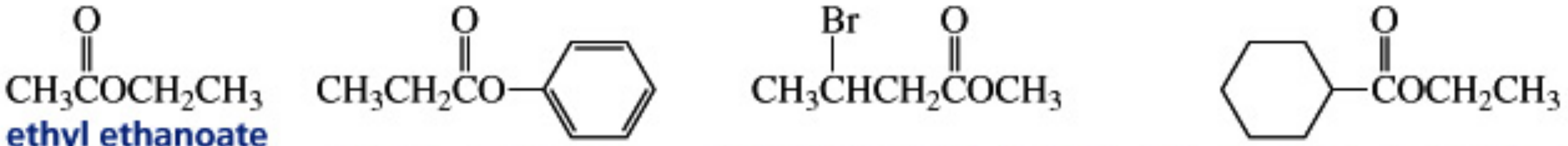
Acido etanoico
(Acido acetico)

Etanolo
(Alcol etilico)

Etanoato di etile
(Acetato di etile)

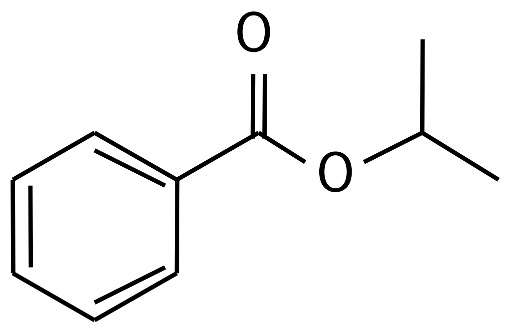


$$R-\overset{\overset{O}{\|}}{C}-O-R'$$

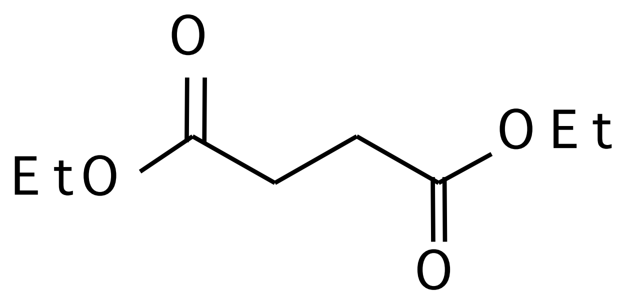


$$CH_3\overset{\overset{O}{\|}}{C}OCH_2CH_3 \qquad CH_3\overset{\overset{Br}{|}}{C}HCH_2\overset{\overset{O}{\|}}{C}OCH_3$$

systematic name:	**ethyl ethanoate**	**phenyl propanoate**	**methyl 3-bromobutanoate**	**ethyl cyclohexanecarboxylate**
common name:	**ethyl acetate**	**phenyl propionate**	**methyl *β*-bromobutyrate**	

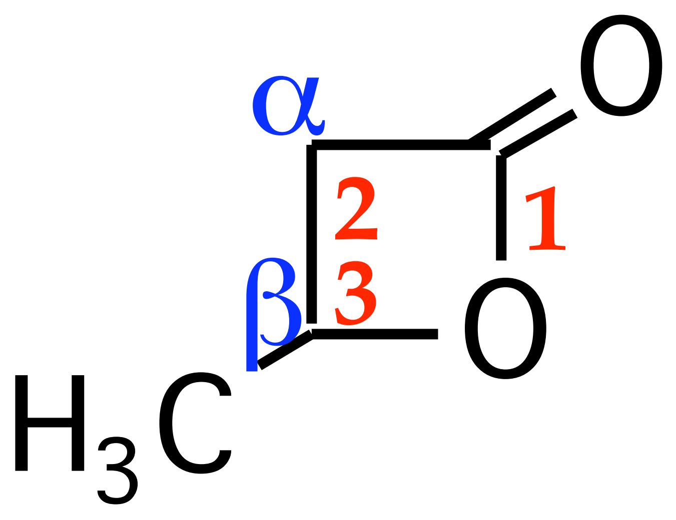


Isopropyl
benzoate

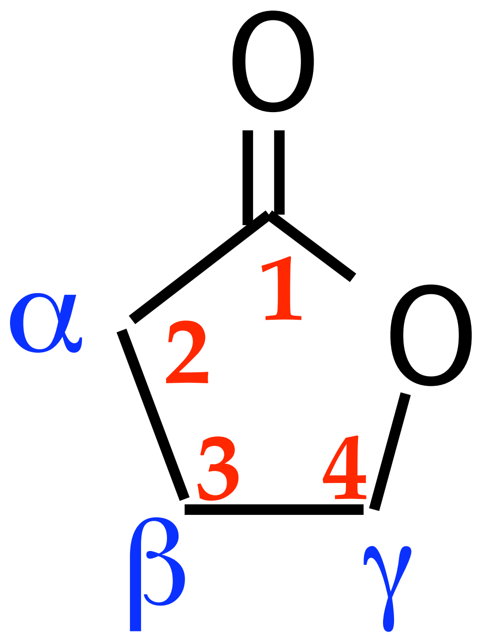


Diethyl butanedioate
(Diethyl succinate)

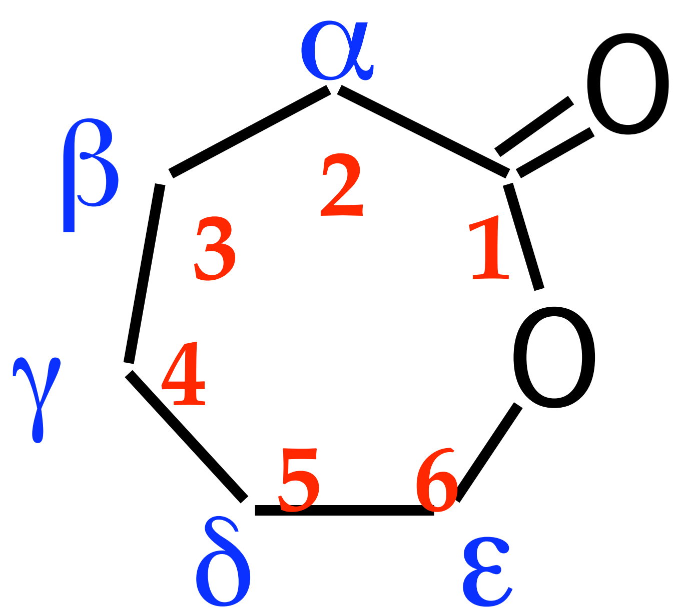
ESTERI CICLICI (LATTONI)



3-Butanolactone
(β-Butyrolactone)

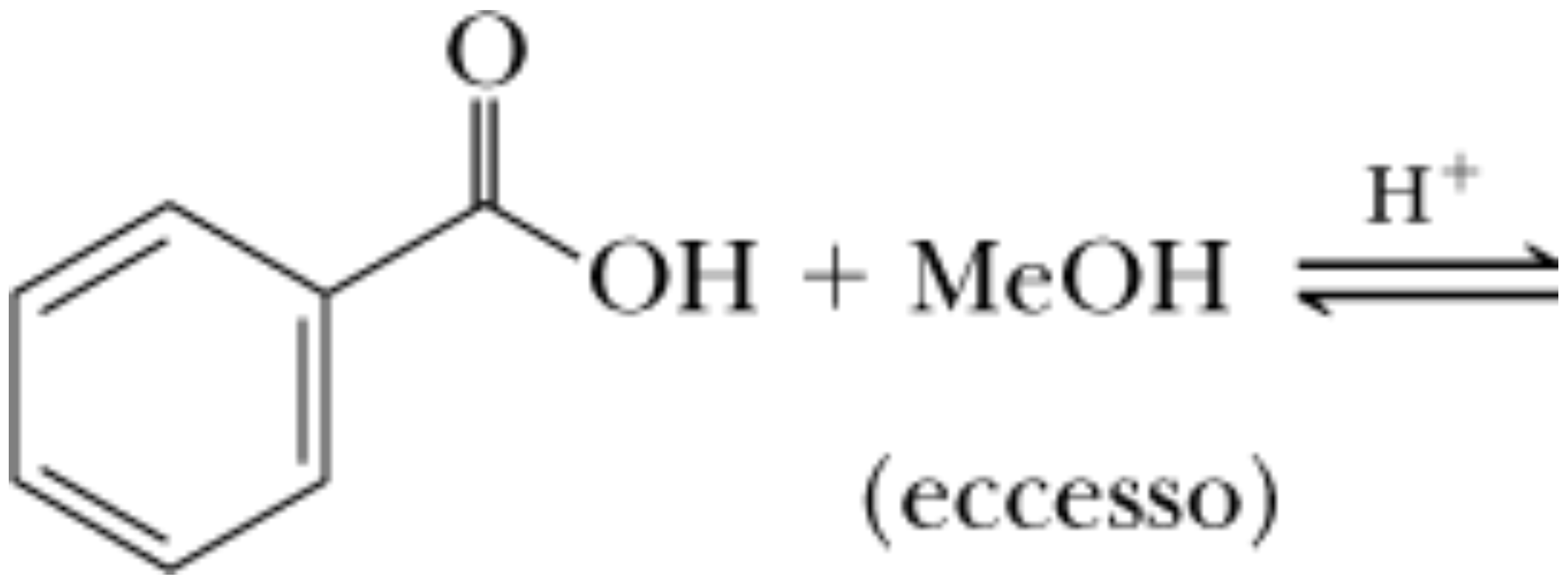


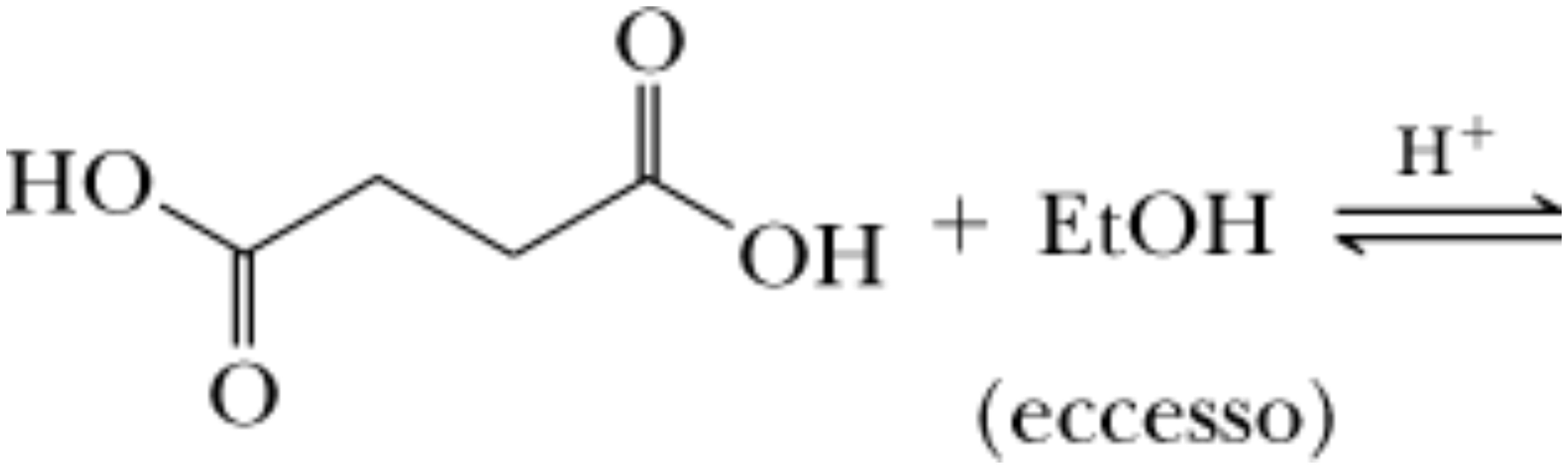
4-Butanolactone
(γ-Butyrolactone)



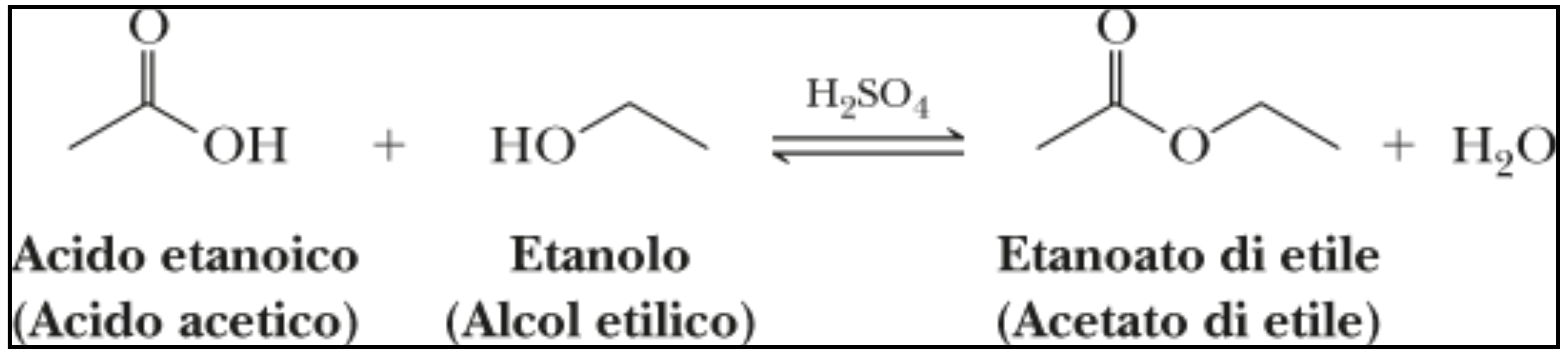
6-Hexanolactone
(ε-Caprolactone)

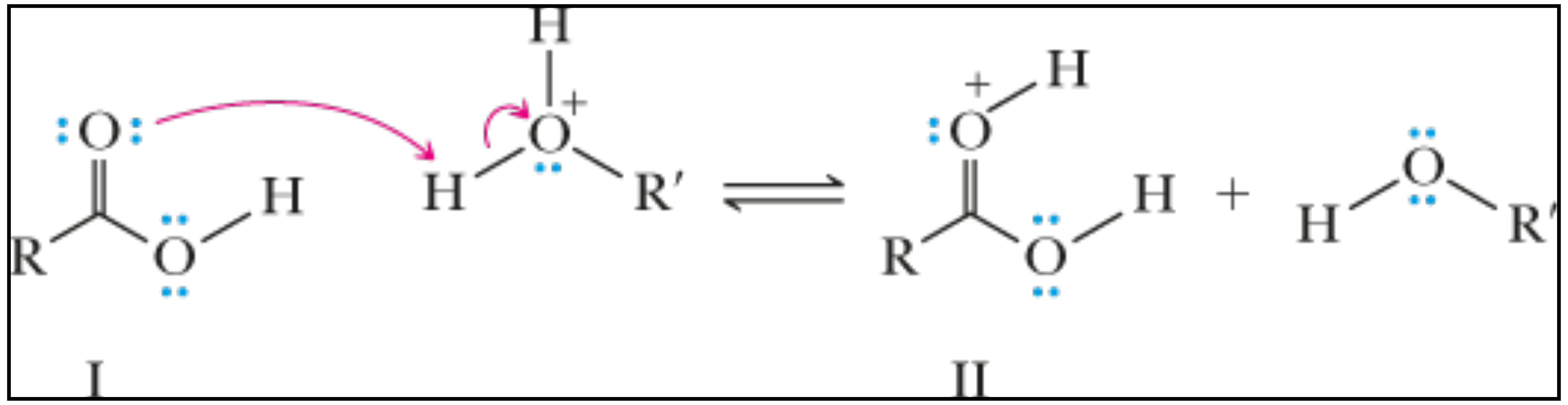
Completare le seguenti esterificazioni di Fischer



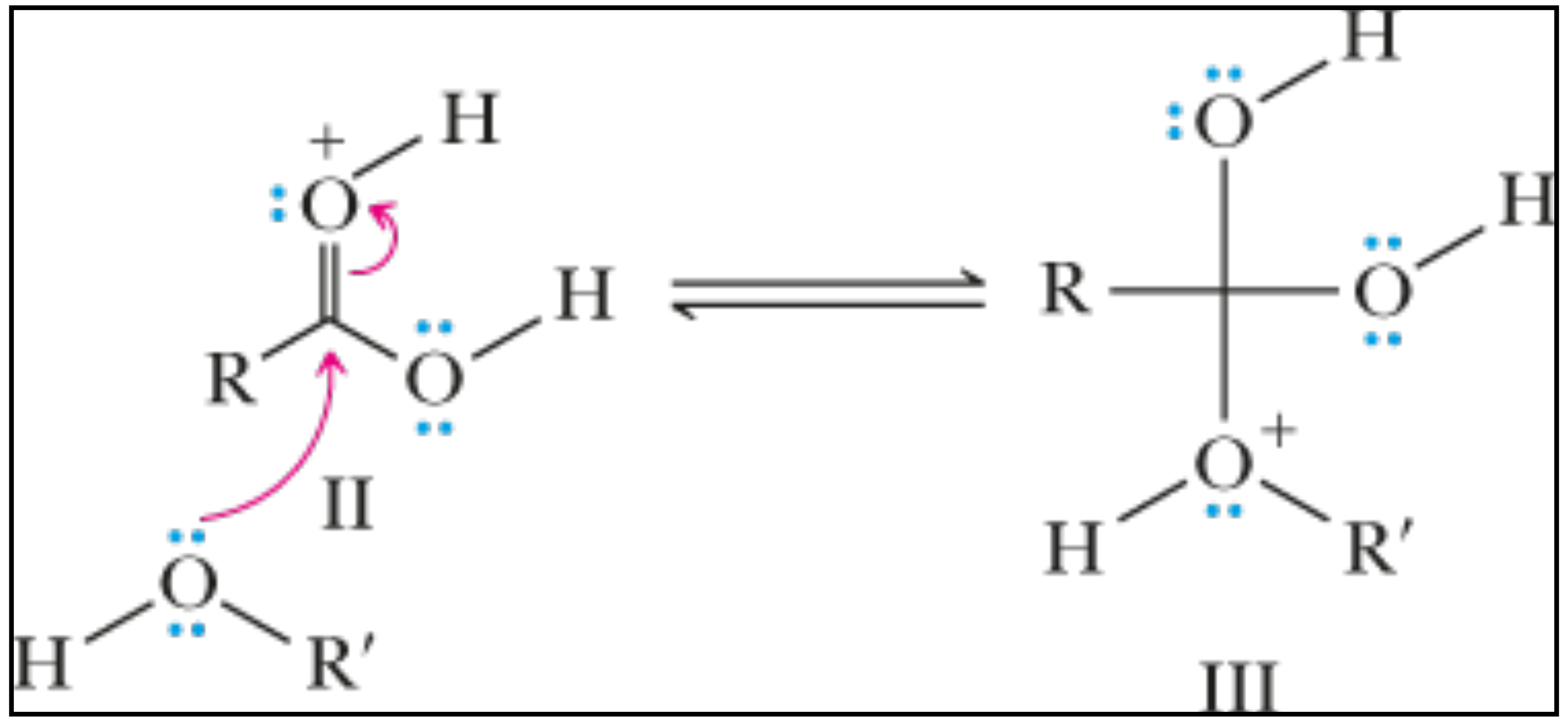


Meccanismo dell'esterificazione

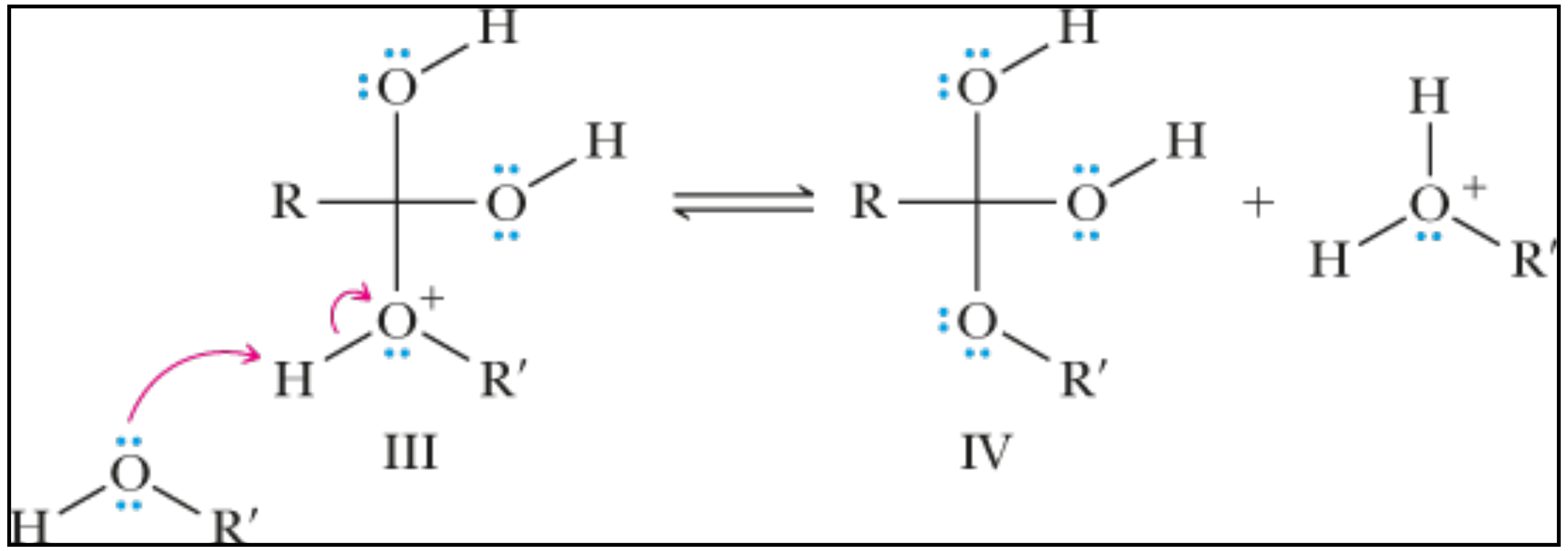




STADIO 1: Addizione di un protone

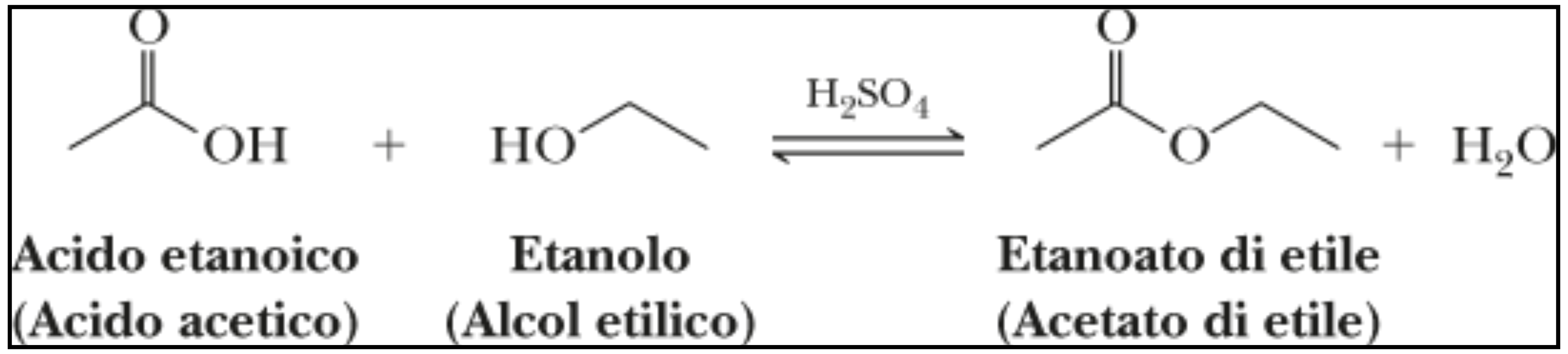


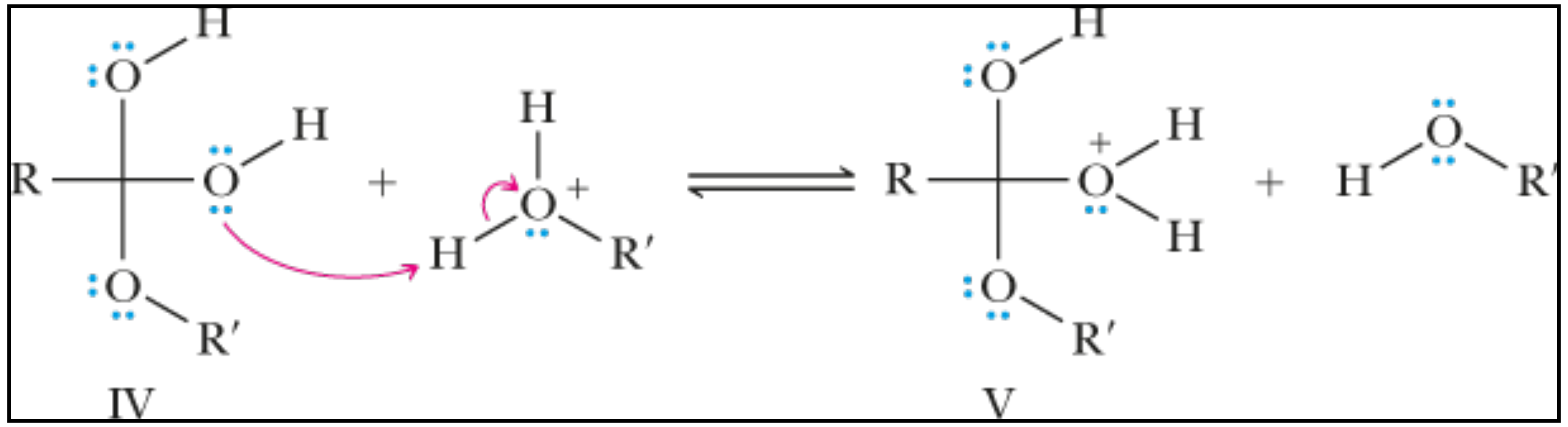
STADIO 2: formazione di un nuovo legame tra un nucleofilo e un elettrofilo



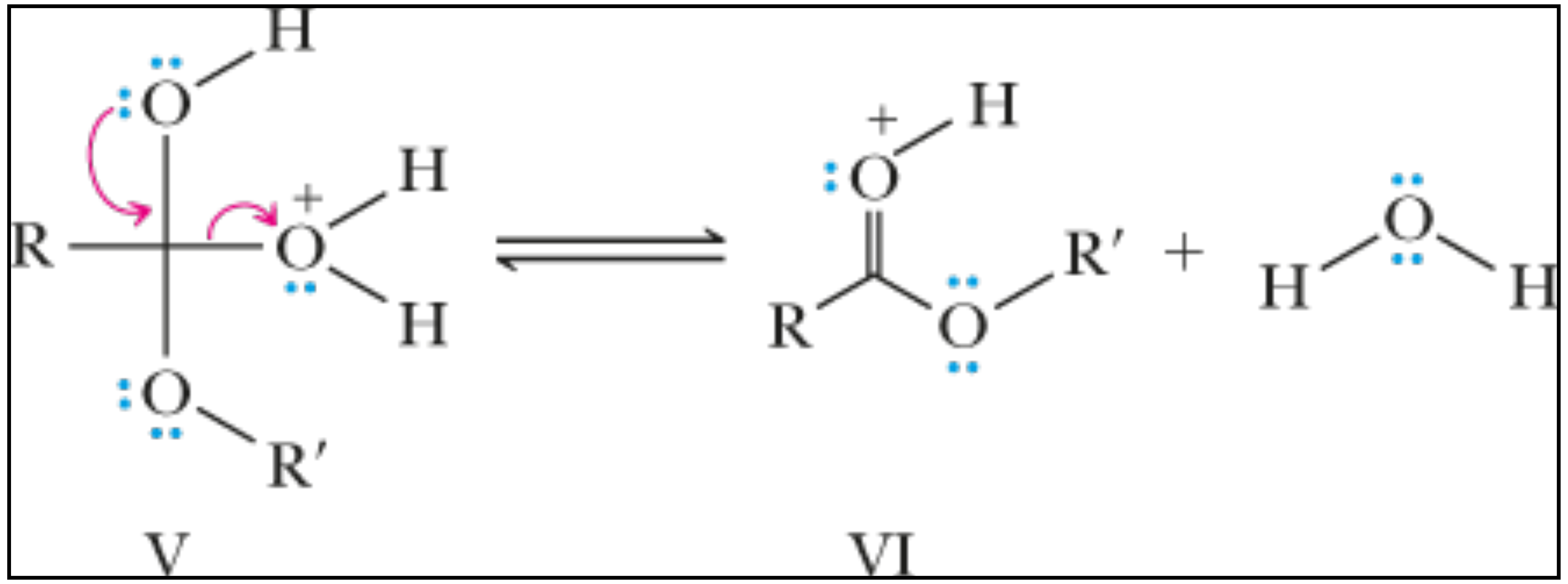
STADIOI 3: rimozione di un protone

Meccanismo dell'esterificazione

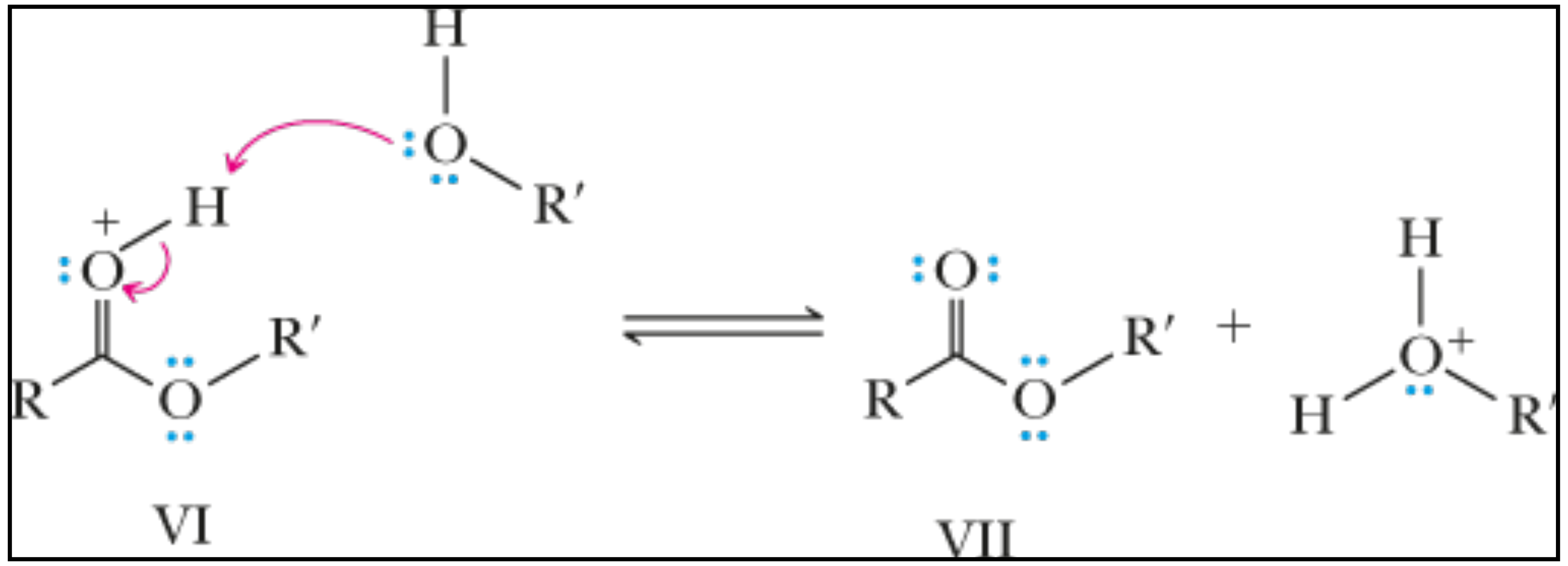




STADIO 4: Addizione di un protone



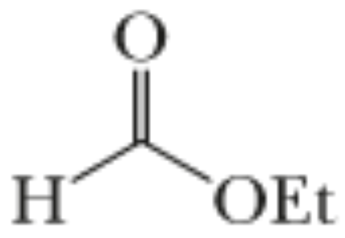
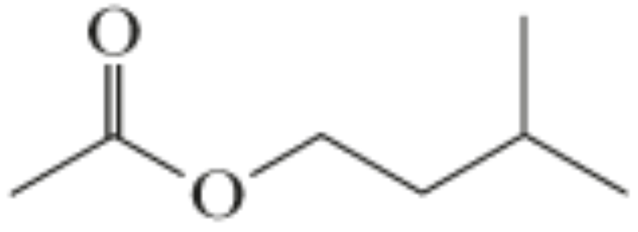
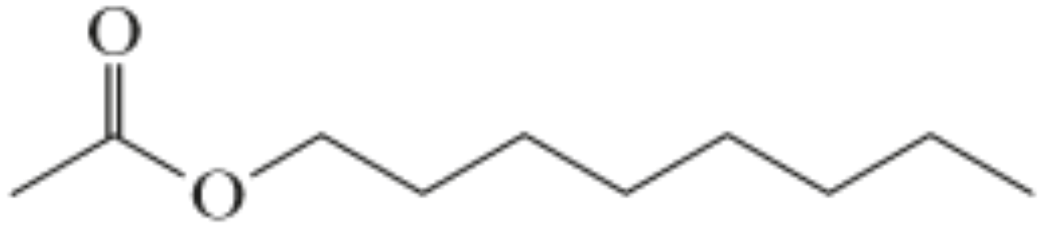
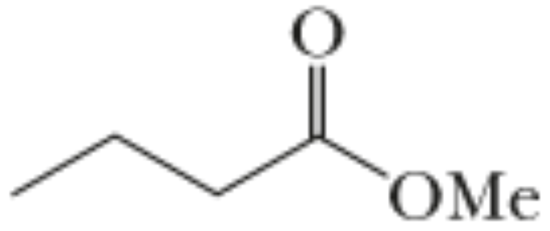
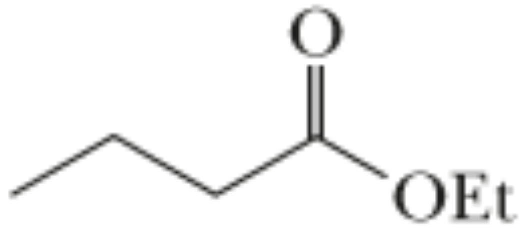
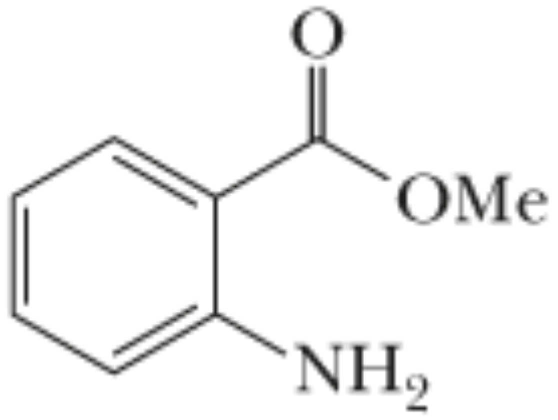
STADIO 5: rottura di un legame con formazione di molecole o ioni stabili.



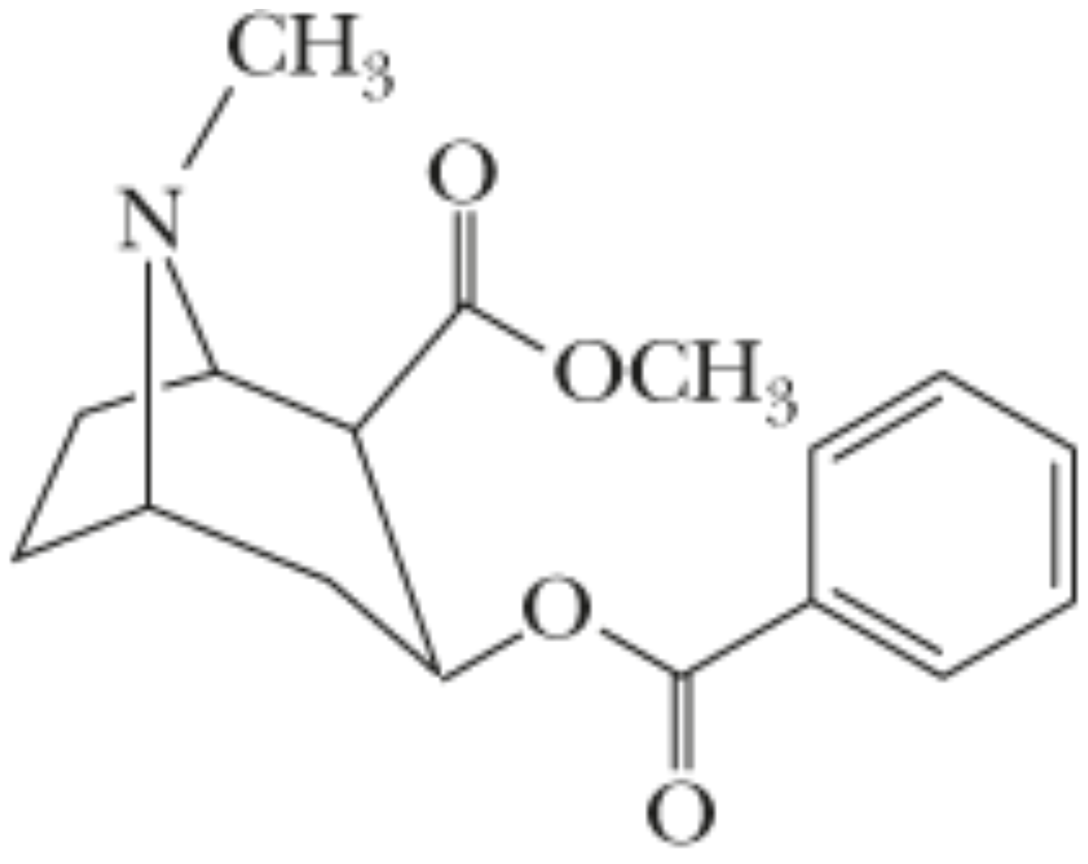
STADIOI 6: rimozione di un protone

Esteri come agenti aromatizzanti

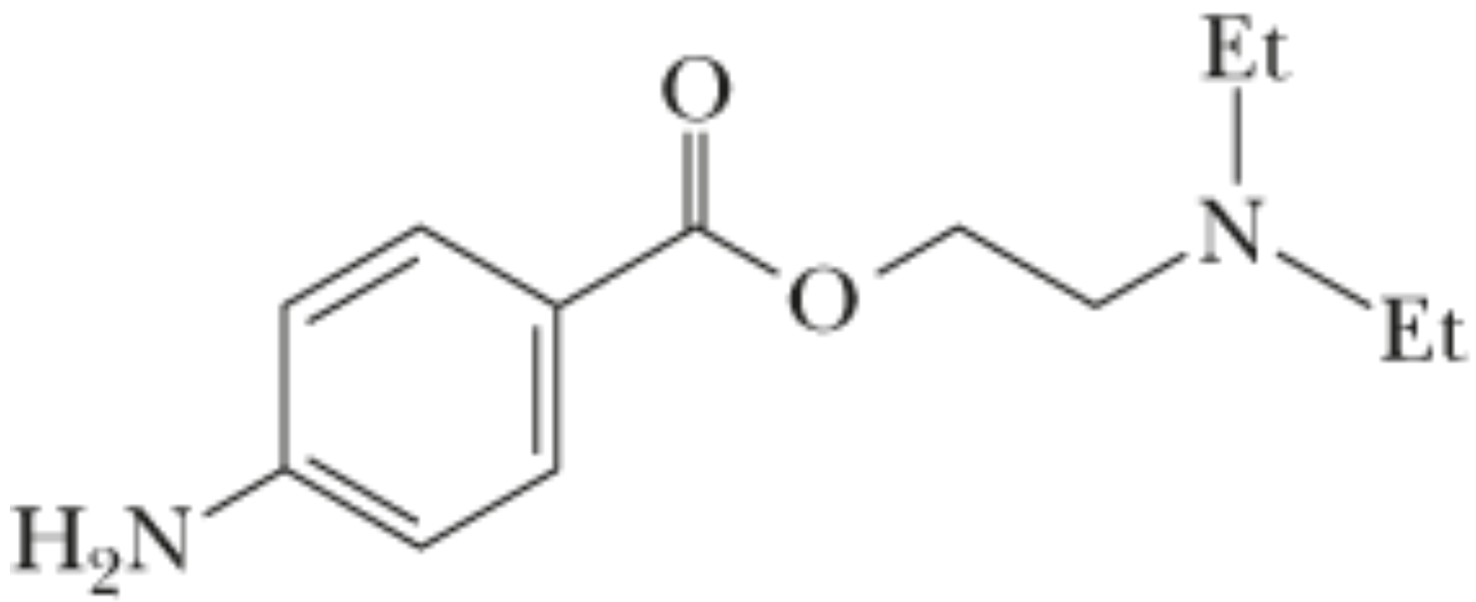
Gli aromi sono la classe più numerosa di additivi alimentari

Struttura	Nome	Aroma
	**Formiato di etile**	Rum
	**Acetato di (3-metil)butile (Acetato di isopentile)**	Banana
	**Acetato di ottile**	Arancia
	**Butanoato di metile**	Mela
	**Butanoato di etile**	Ananas
	**2-Amminobenzoato di metile (Antranilato di metile)**	Uva

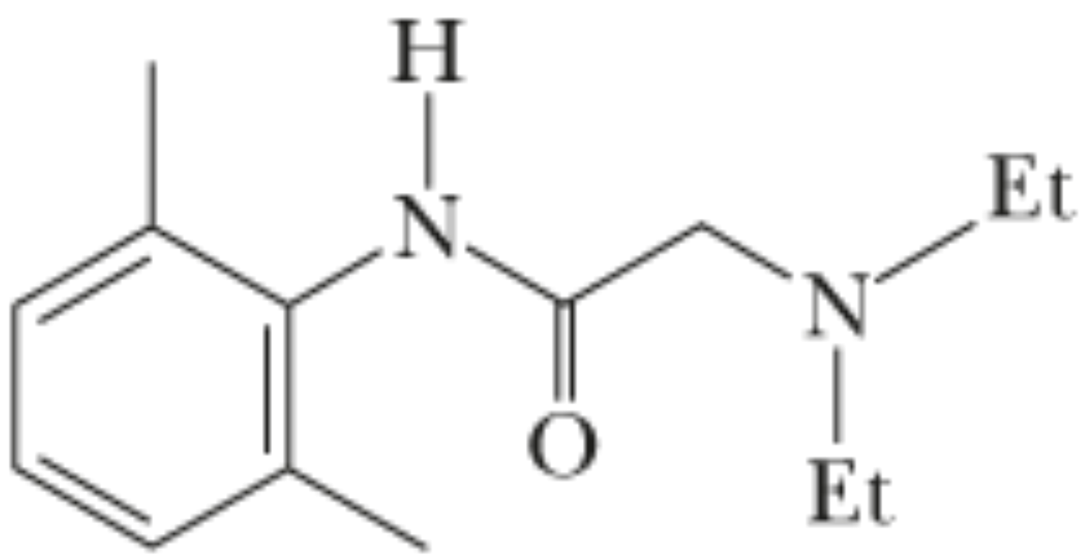
Esteri come anestetici locali



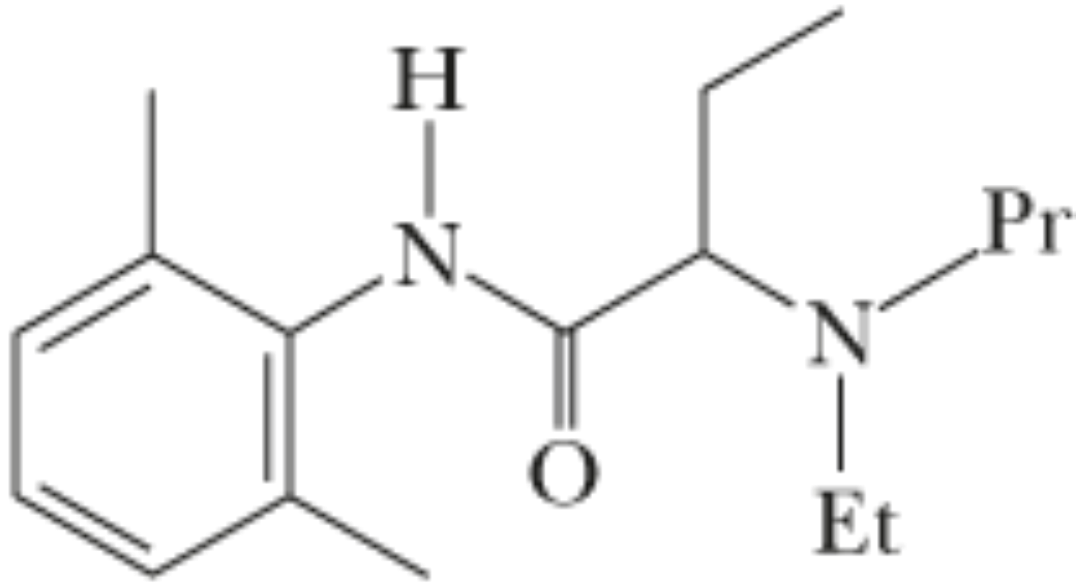
Cocaina



Procaina
(Novocaina)

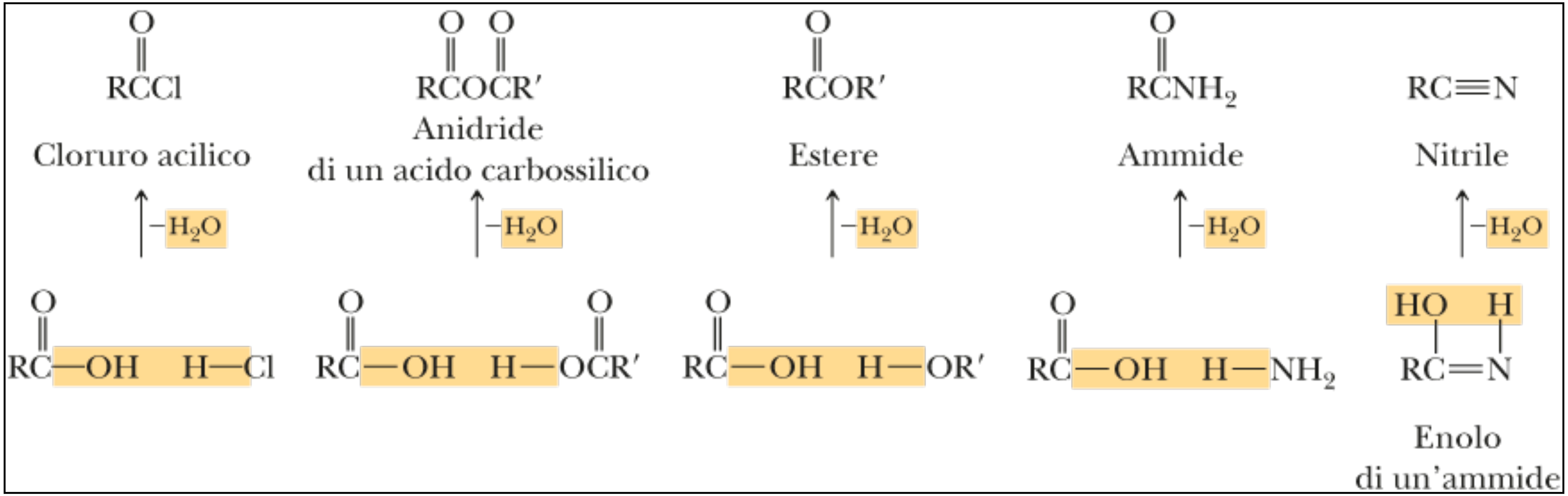


Lidocaina
(Xilocaina)

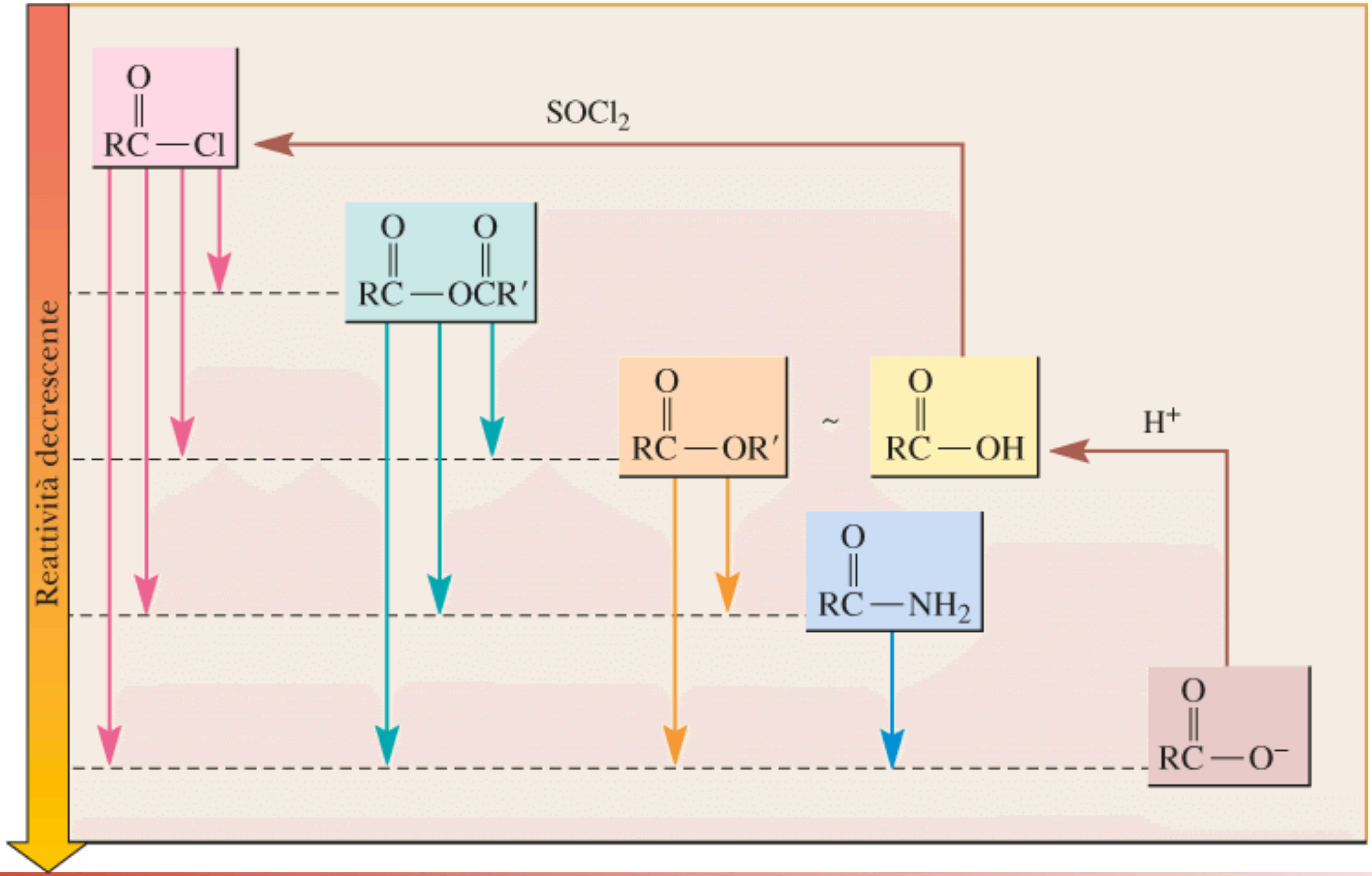


Etidocaina
(Duranest; racemo**)**

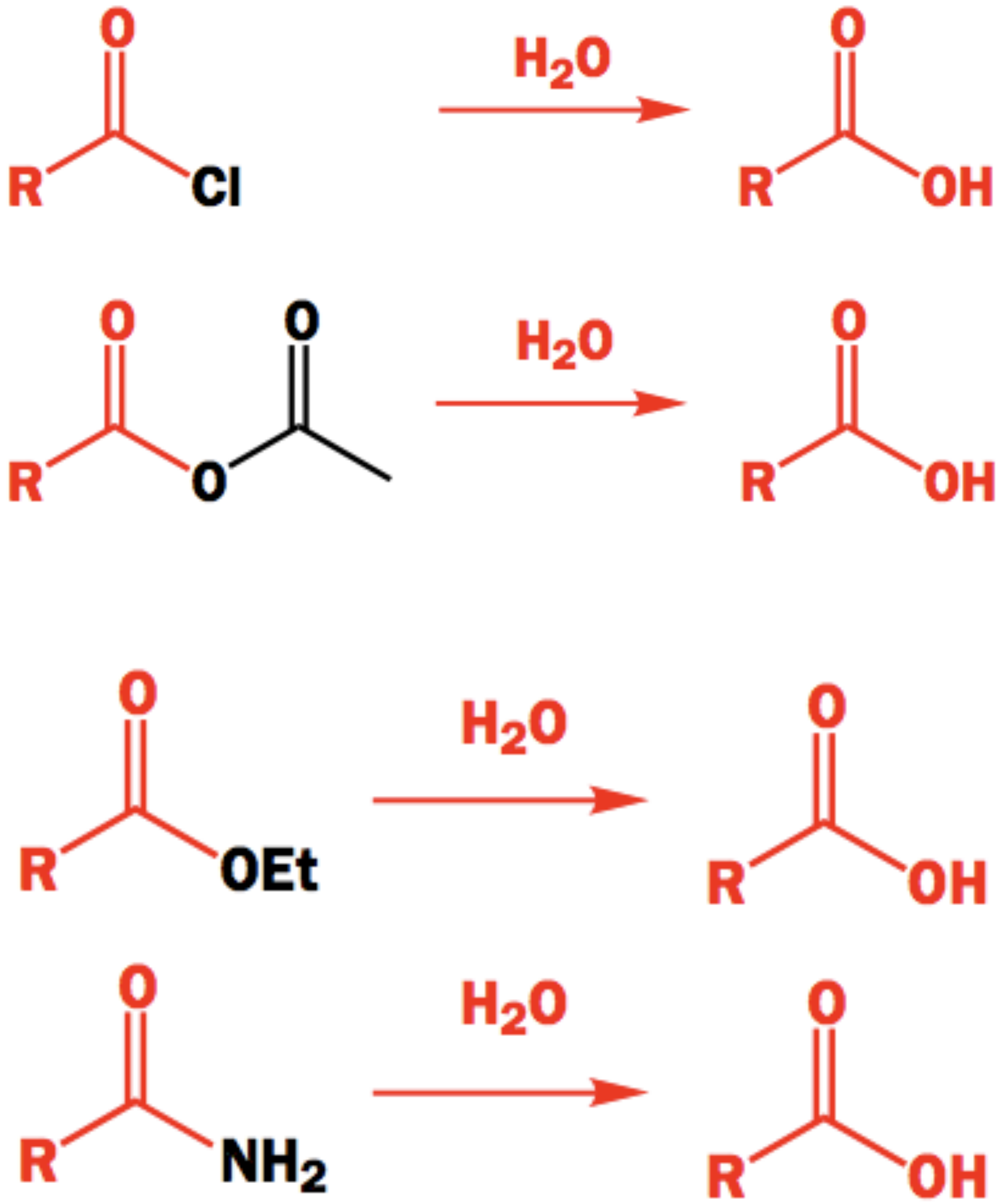
Derivati funzionali degli acidi carbossilici



Interconversione dei derivati funzionali



REATTIVITÀ del carbonio acilico



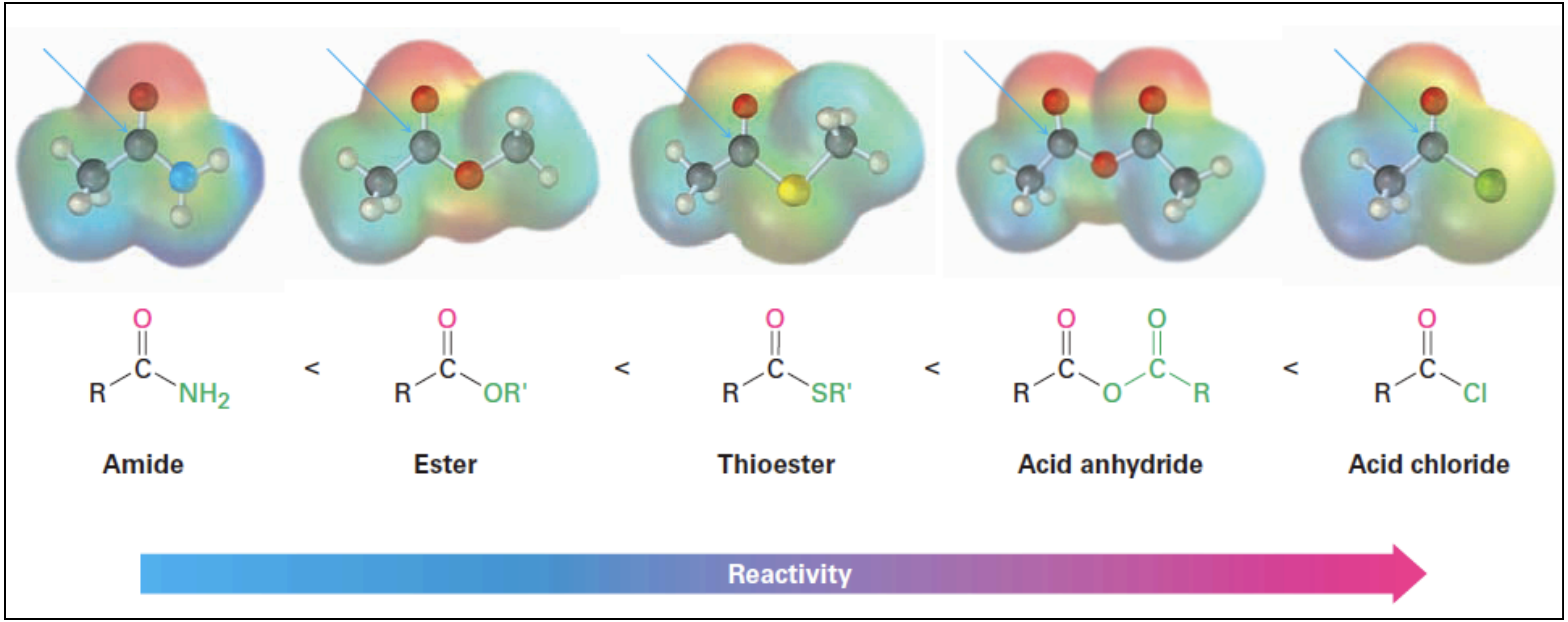
fast at 20 °C

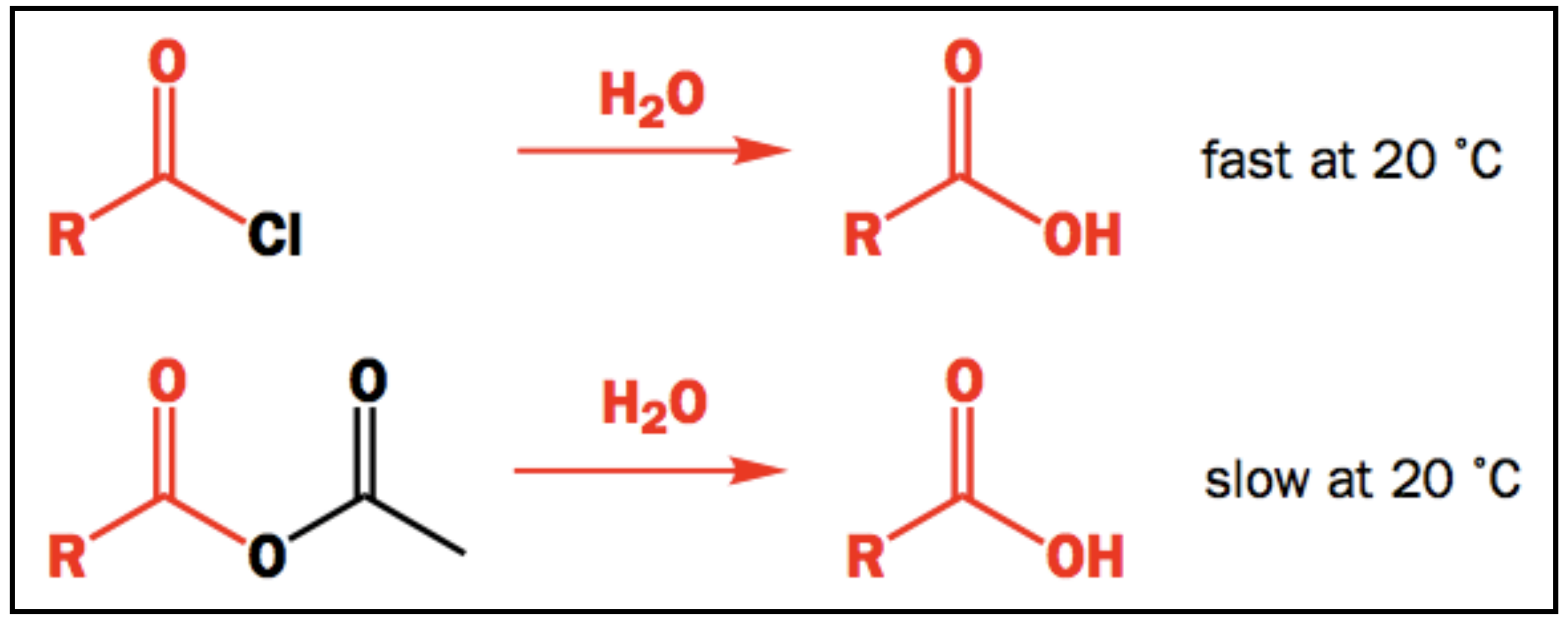
slow at 20 °C

only on heating with
acid or base catalyst

only on prolonged heating
with strong acid
or base catalyst

REATTIVITÀ del carbonio acilico

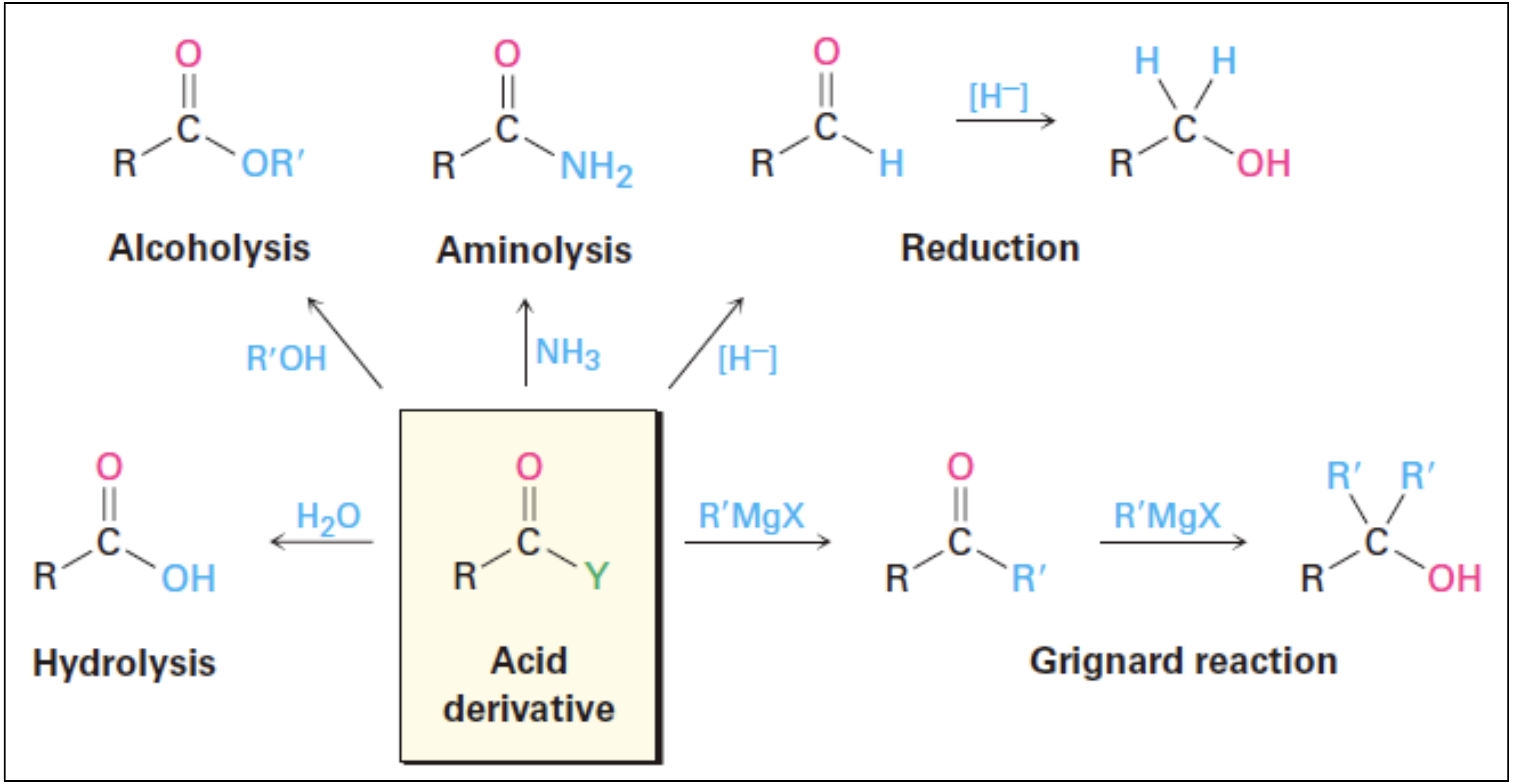




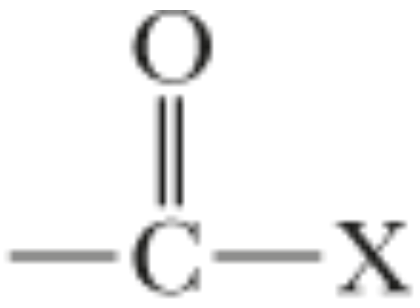
fast at 20 °C

slow at 20 °C

REATTIVITÀ del carbonio acilico

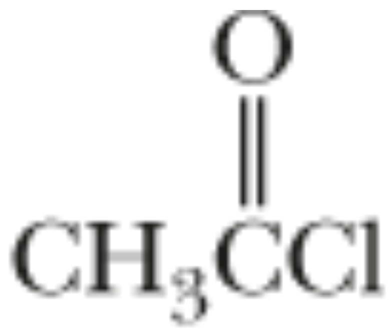


Conversione in cloruri acilici (Alogenuri acilici)



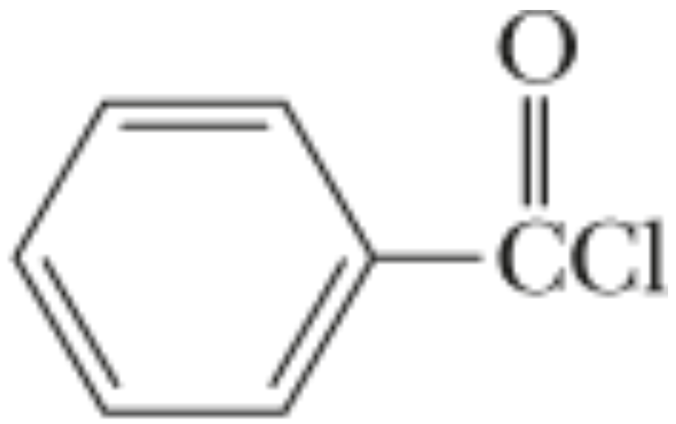
$-\overset{\overset{\displaystyle O}{\|}}{C}-X$

Gruppo funzionale
degli alogenuri acilici



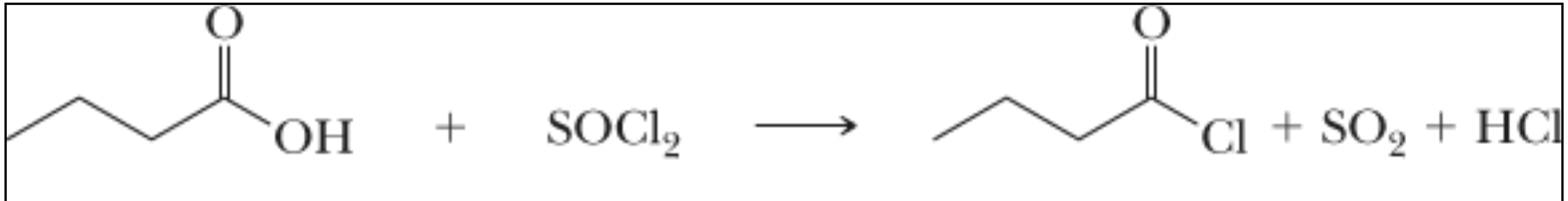
$CH_3\overset{\overset{\displaystyle O}{\|}}{C}Cl$

**Cloruro
di acetile**



**Cloruro
di benzoile**

Il gruppo funzionale di un alogenuro acilico è un gruppo carbonilico legato a un atomo di alogeno

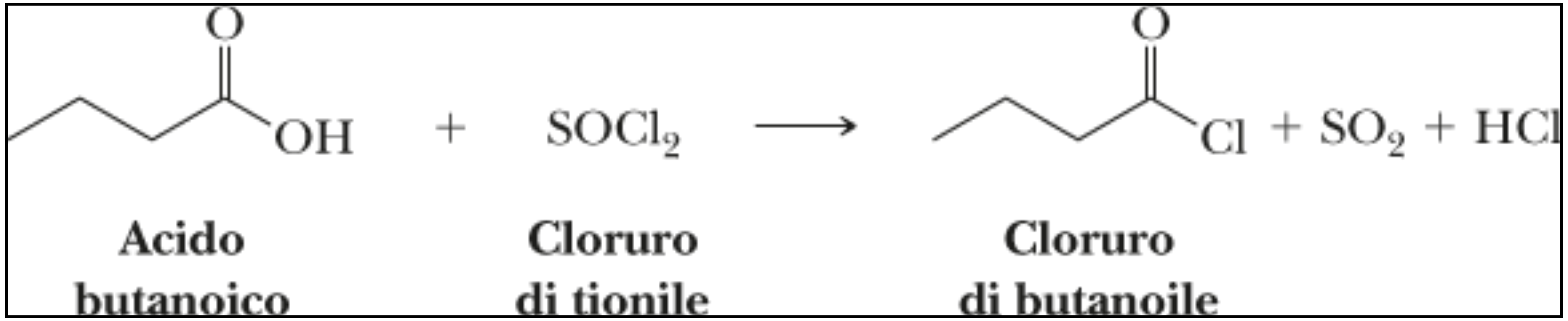


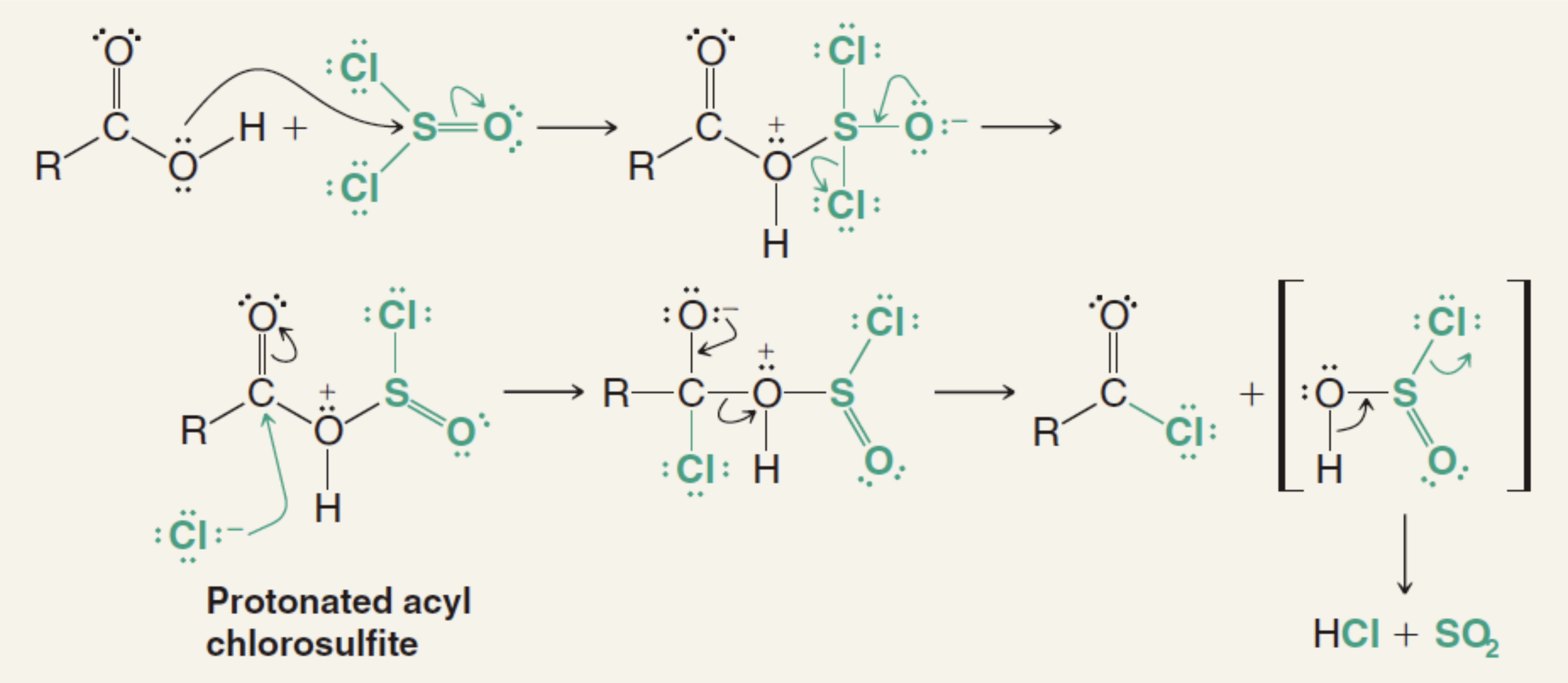
**Acido
butanoico**

**Cloruro
di tionile**

**Cloruro
di butanoile**

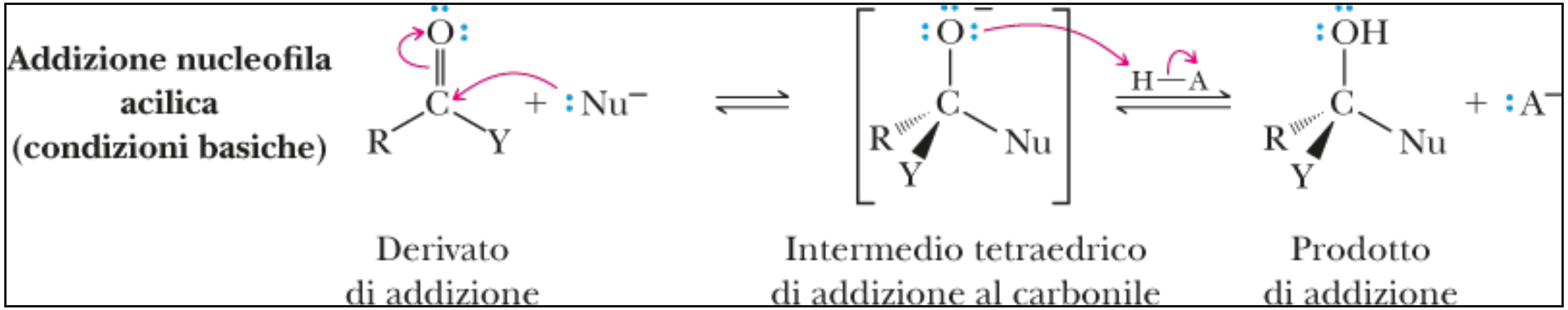
Conversione in cloruri acilici (Alogenuri acilici)

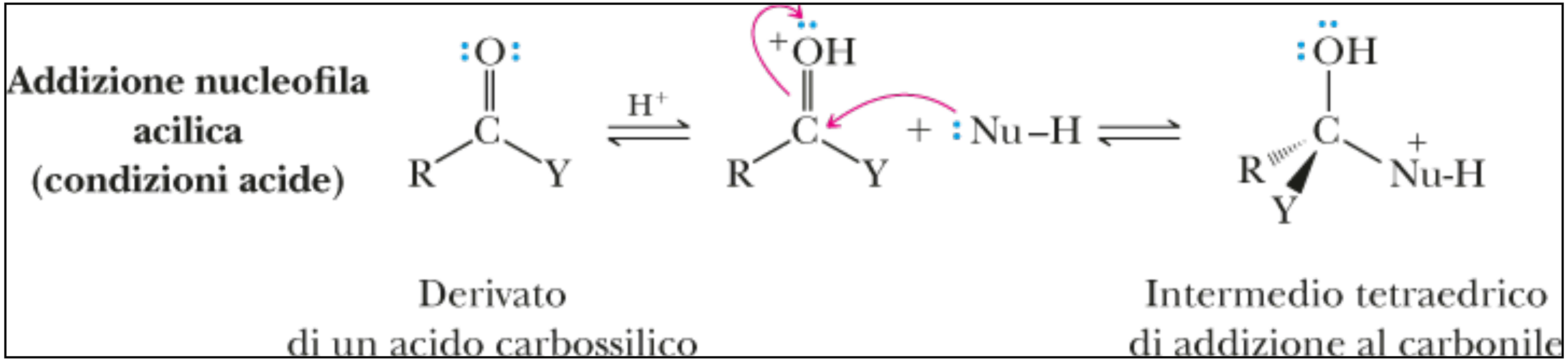




Reazioni di interconversione dei diversi derivati degli acidi carbossilici

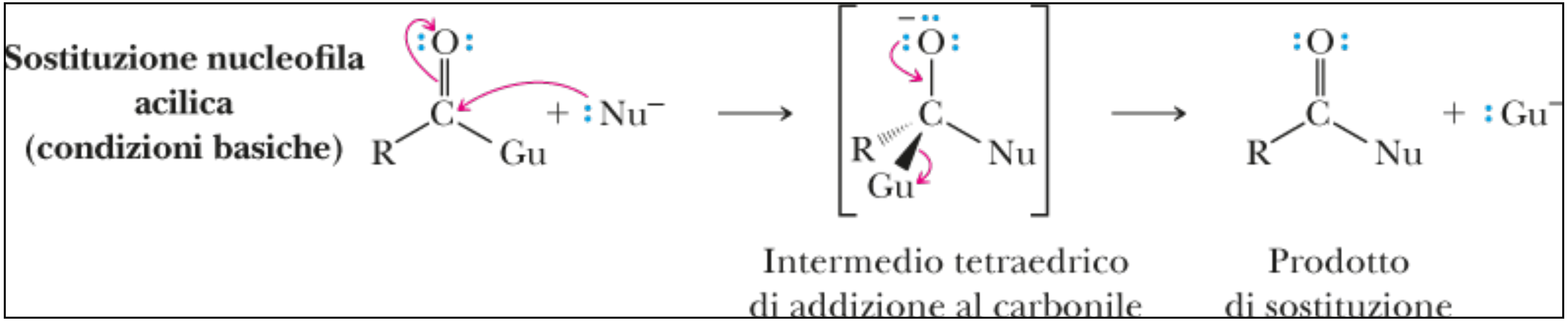
A. Addizione nucleofila acilica

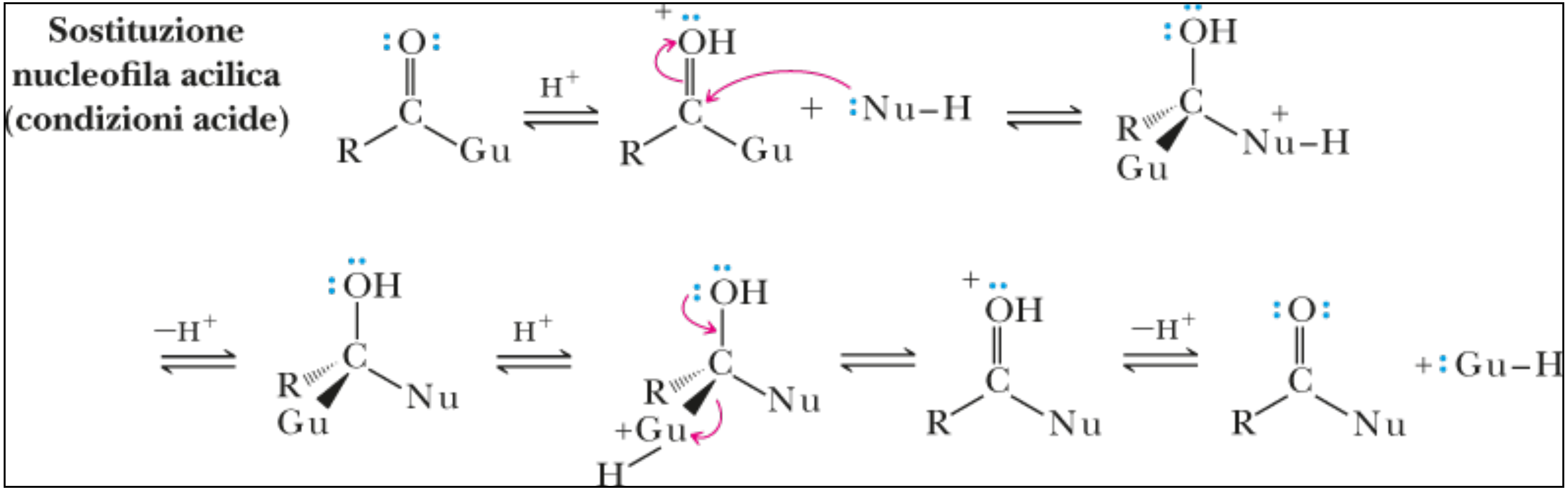




B. Sostituzione nucleofila acilica (S_NAc)

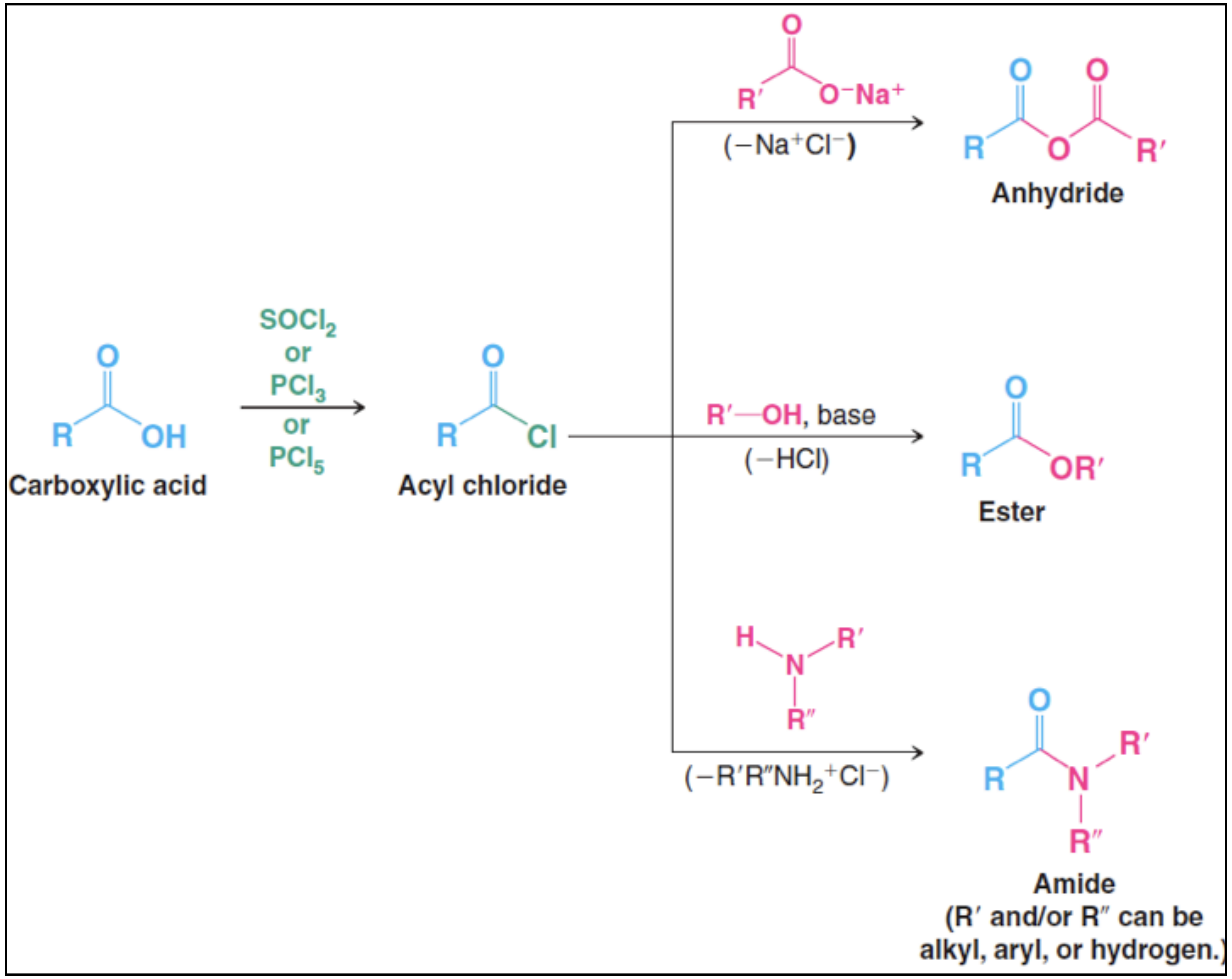
Una reazione in cui un nucleofilo legato al carbonio carbonilico acilico viene sostituito da un altro nucleofilo. Il risultato di questa sequenza di addizione-eliminazione è una sostituzione nucleofila acilica.





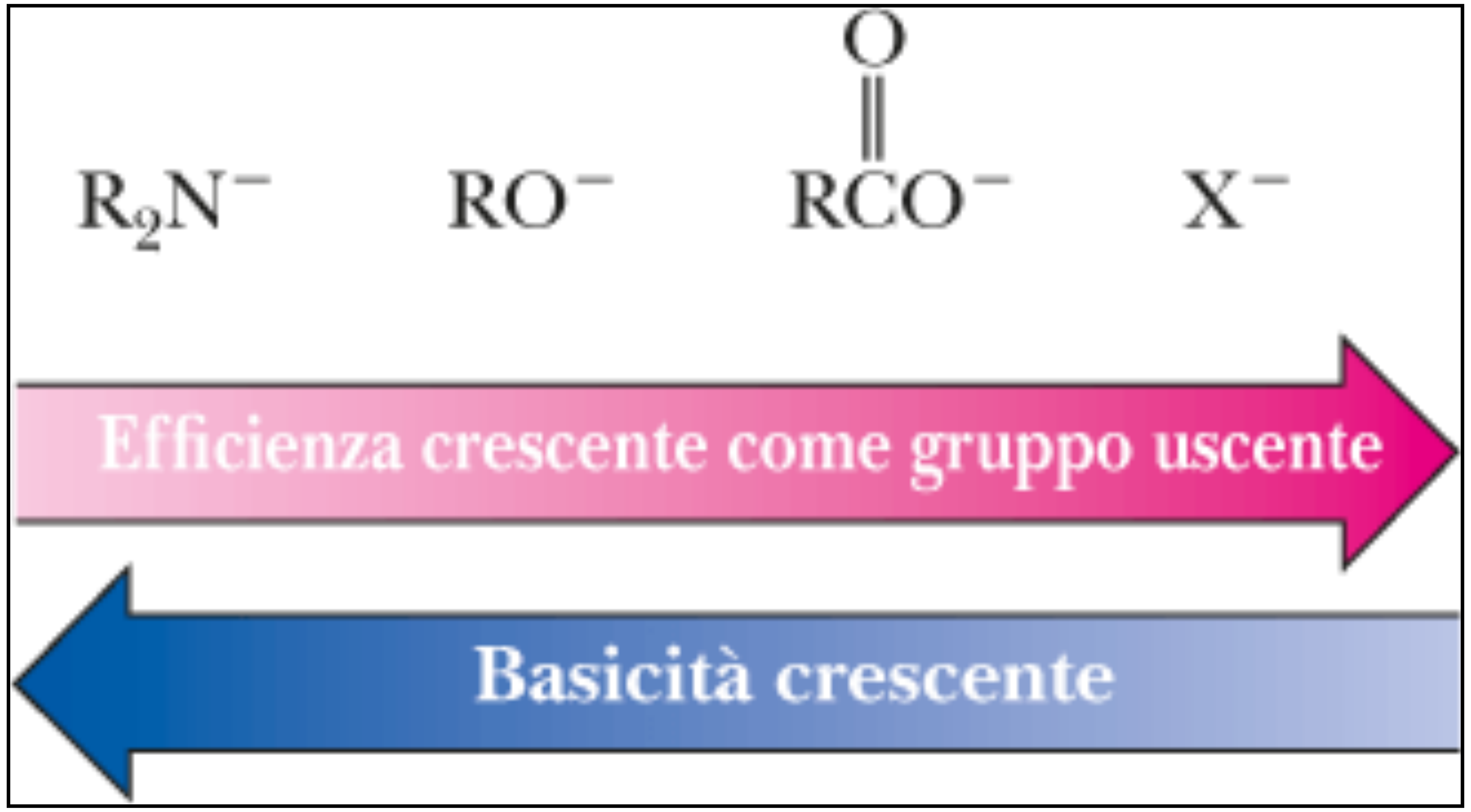
B. Sostituzione nucleofila acilica (S_NAc)

Una reazione in cui un nucleofilo legato al carbonio carbonilico acilico viene sostituito da un altro nucleofilo. Il risultato di questa sequenza di addizione-eliminazione è una sostituzione nucleofila acilica.

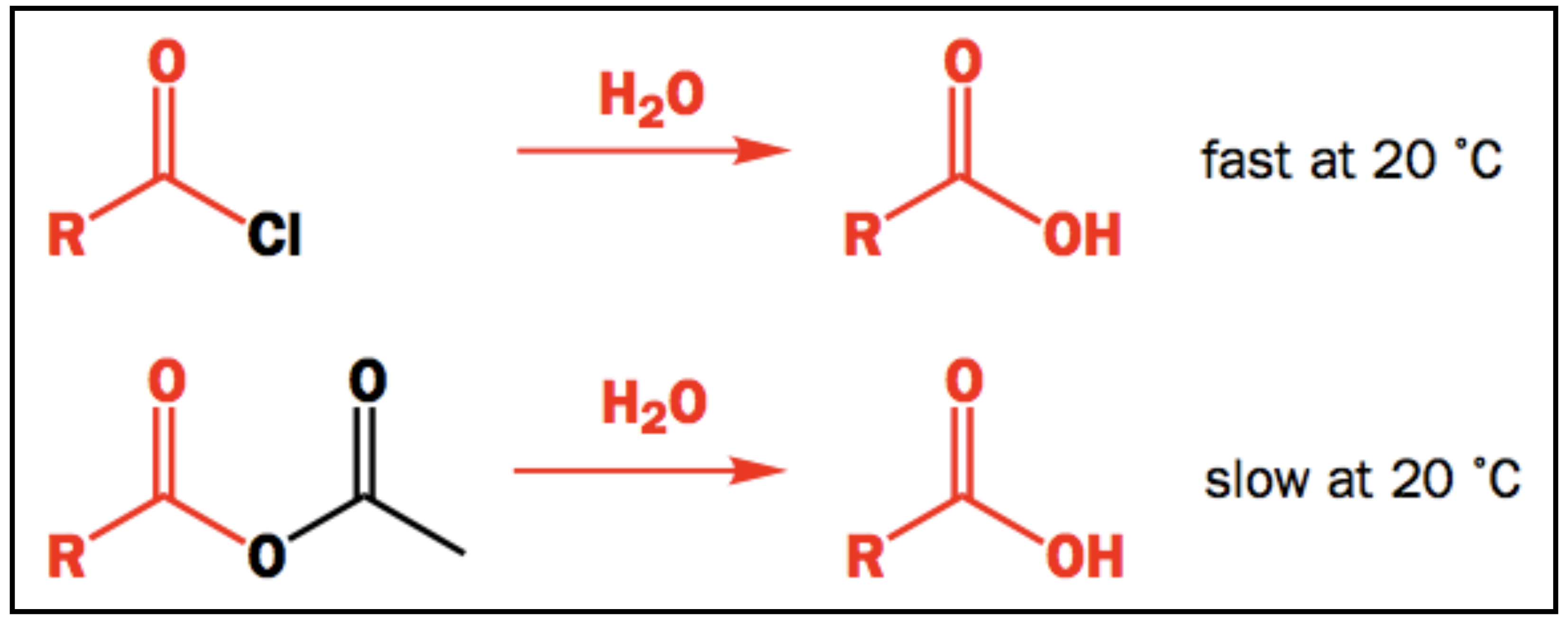


C. Reattività relativa

Questo andamento della reattività dipende da due effetti:
Il primo effetto è dato dalla capacità del gruppo uscente di agire come tale

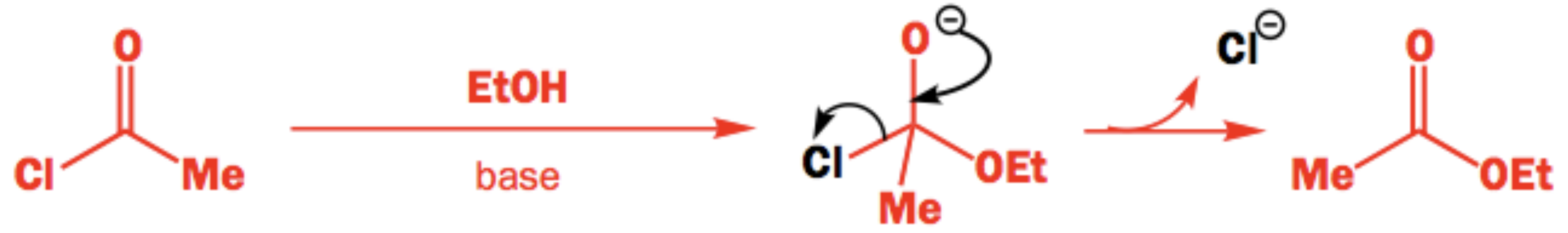


- Lo **ione alogenuro** è la base più debole e il migliore gruppo uscente; gli alogenuri acilici sono i composti **più reattivi** nella S_NAc
- Lo **ione ammide** (ammiduro) è la base più forte e il peggior gruppo uscente; le ammidi sono i composti **meno reattivi** nella S_NAc

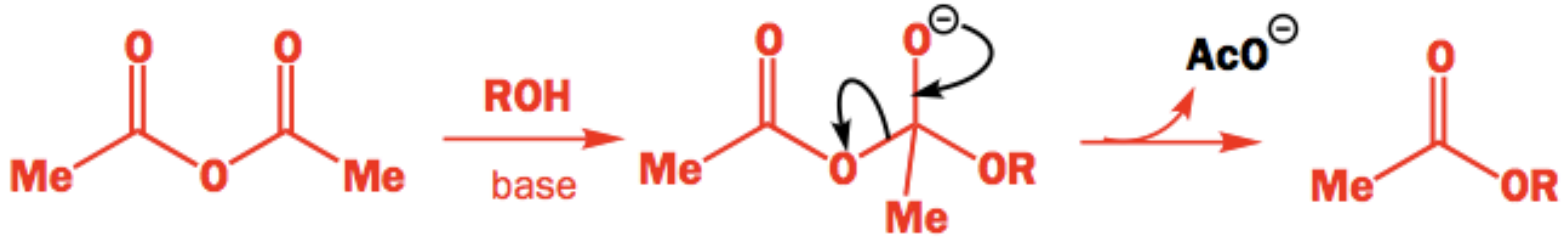


C. Reattività relativa: Il primo effetto è dato dalla capacità del gruppo uscente di agire come tale

Leaving group	**pK_{aH}**
Me^-	50
EtO^-	16
Cl^-	–7



Leaving group	**pK_{aH}**
Me^-	50
RO^-	16
$MeCO_2^-$	5



increasing pK_{aH}

Leaving group	**pK_{aH}**
R^-	50
NH_2^-	35
RO^-	16
RCO_2^-	5
Cl^-	–7

increasing leaving group ability

increasing pK_{aH}

Base	**pK_{aH}**
R^-	50
NH_2^-	35
RO^-	16
NH_3	9
RCO_2^-	5
ROH	–5
Cl^-	–7

increasing nucleophilicity

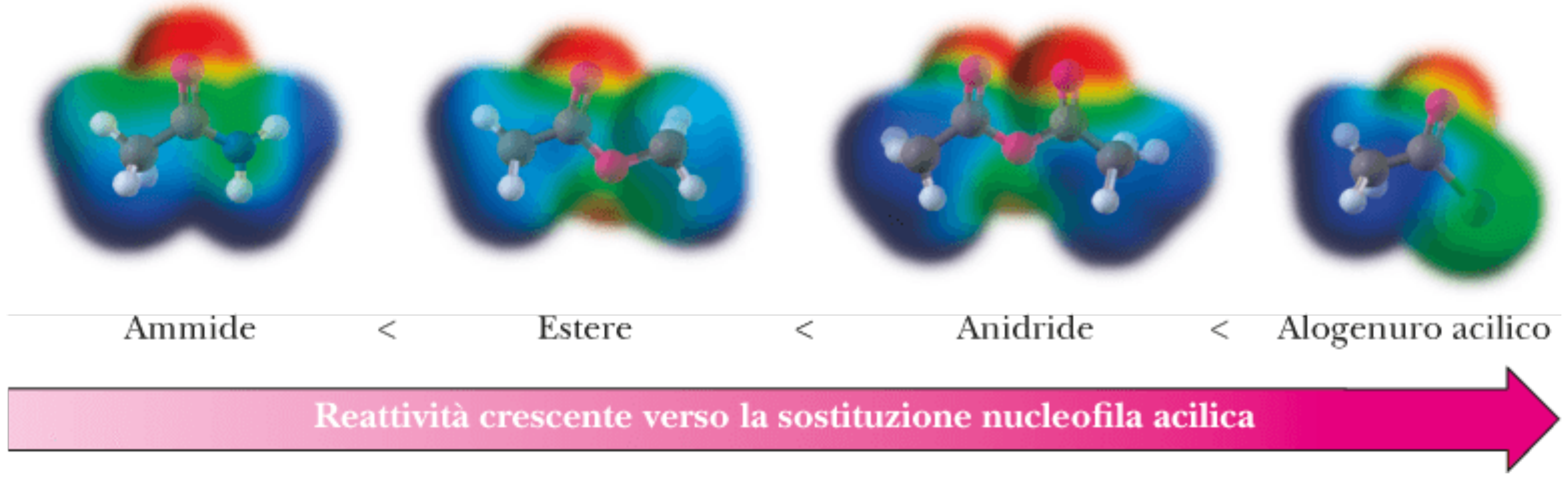
C. Reattività relativa

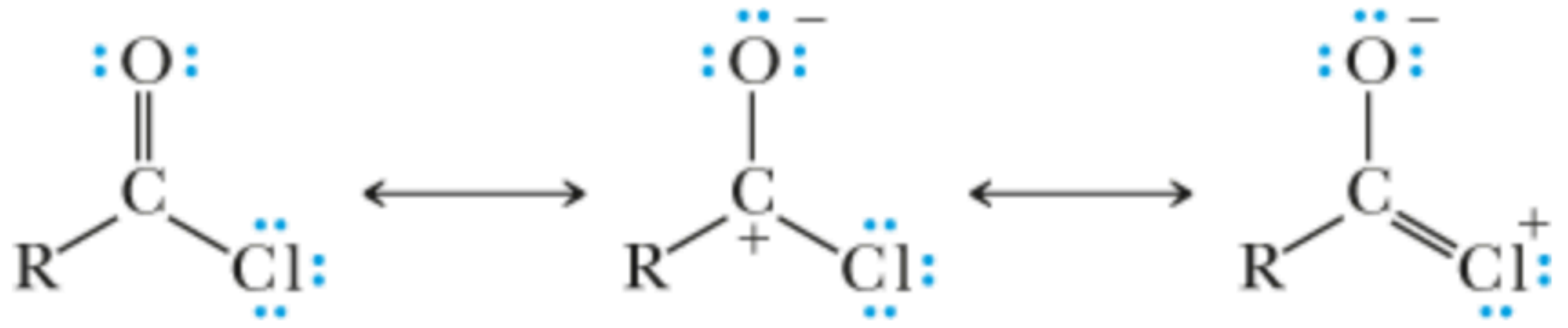
Il secondo effetto è dato dal grado relativo di stabilizzazione per risonanza dei derivati degli acidi carbossilici.

Ogni derivato può essere rappresentato come un ibrido di risonanza di diverse strutture limite, che contribuiscono alla stabilità della molecola.

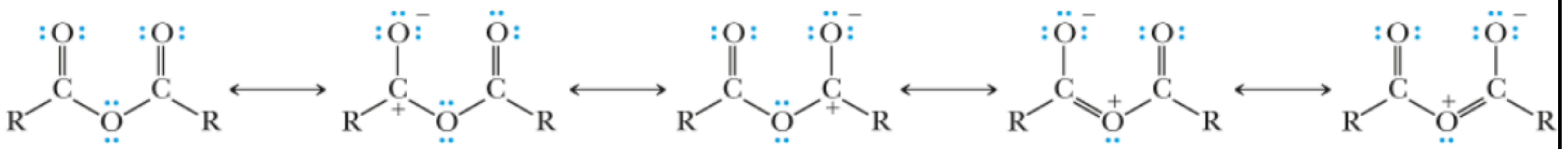
La seconda struttura di risonanza rappresentata per ciascun derivato ha una carica positiva sul carbonio carbonilico; questa struttura spiega il carattere elettrofilo del carbonio carbonilico.

Le altre strutture di risonanza, invece, spiegano il diverso grado di stabilità dei derivati degli acidi carbossilici.

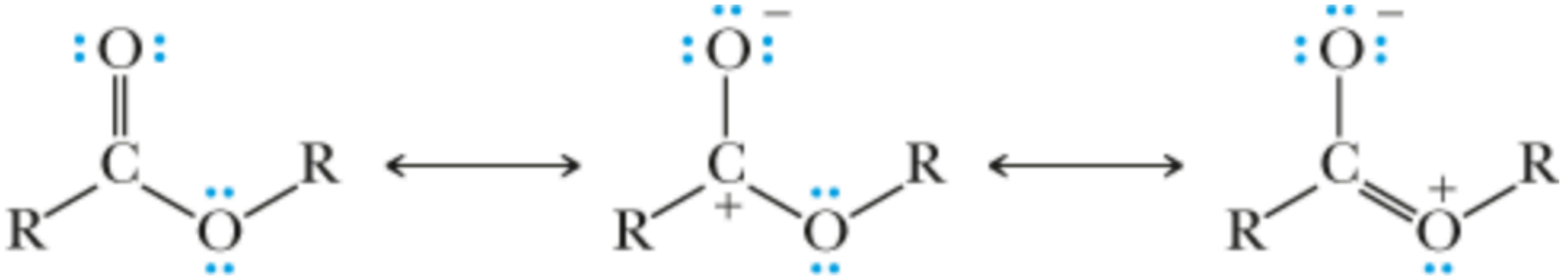




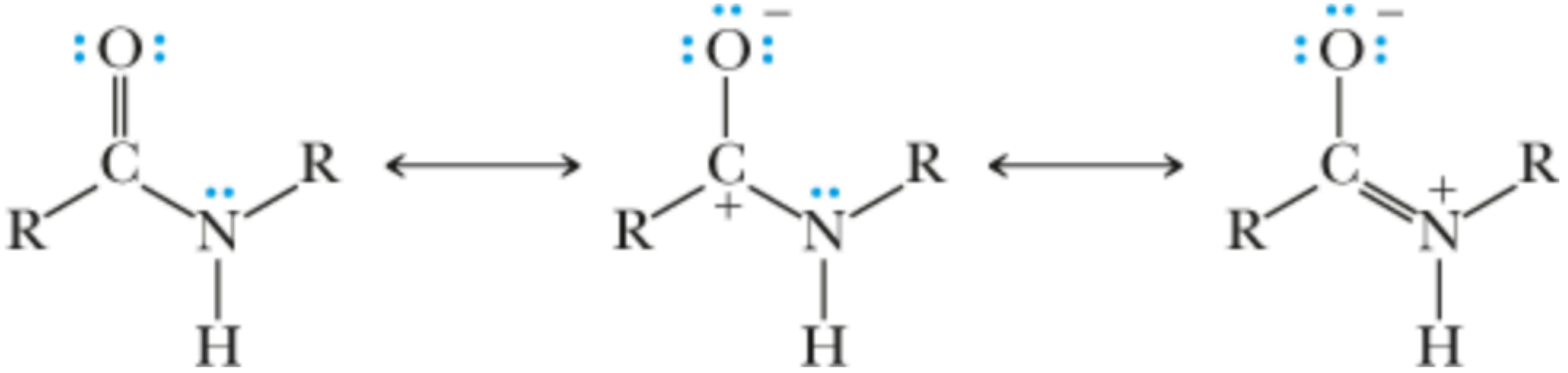
Strutture limite di risonanza di un'anidride



Strutture limite di risonanza di un estere

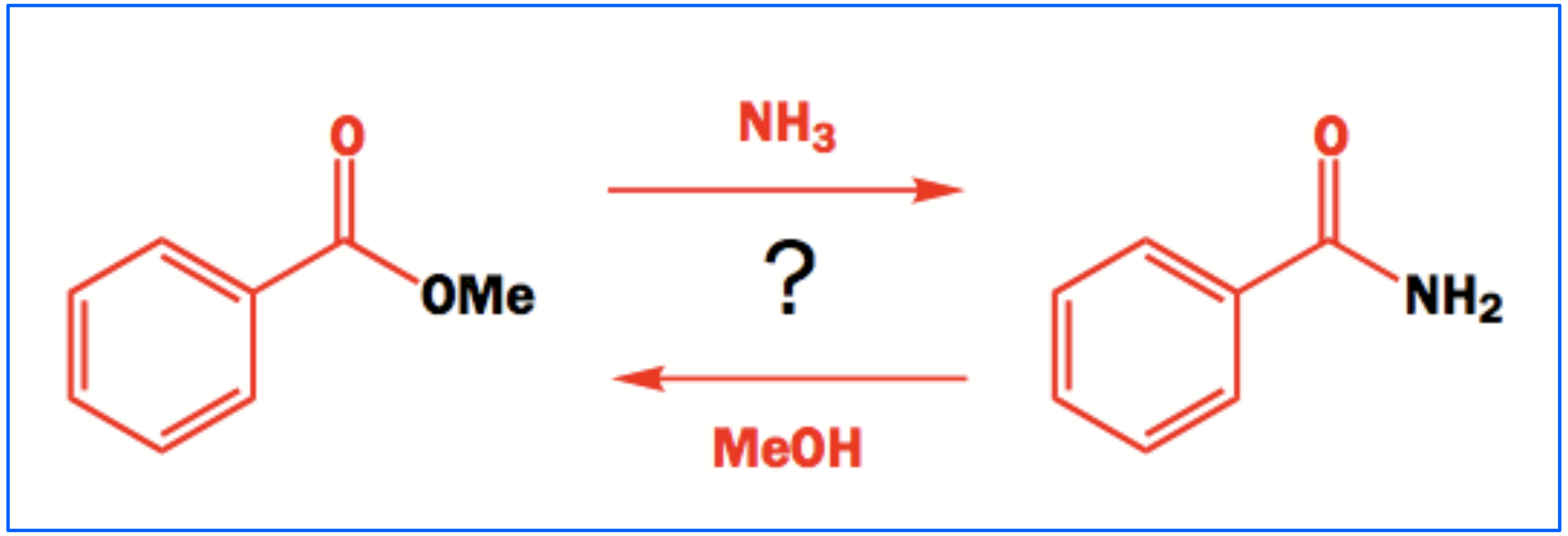


Strutture limite di risonanza di un'ammide

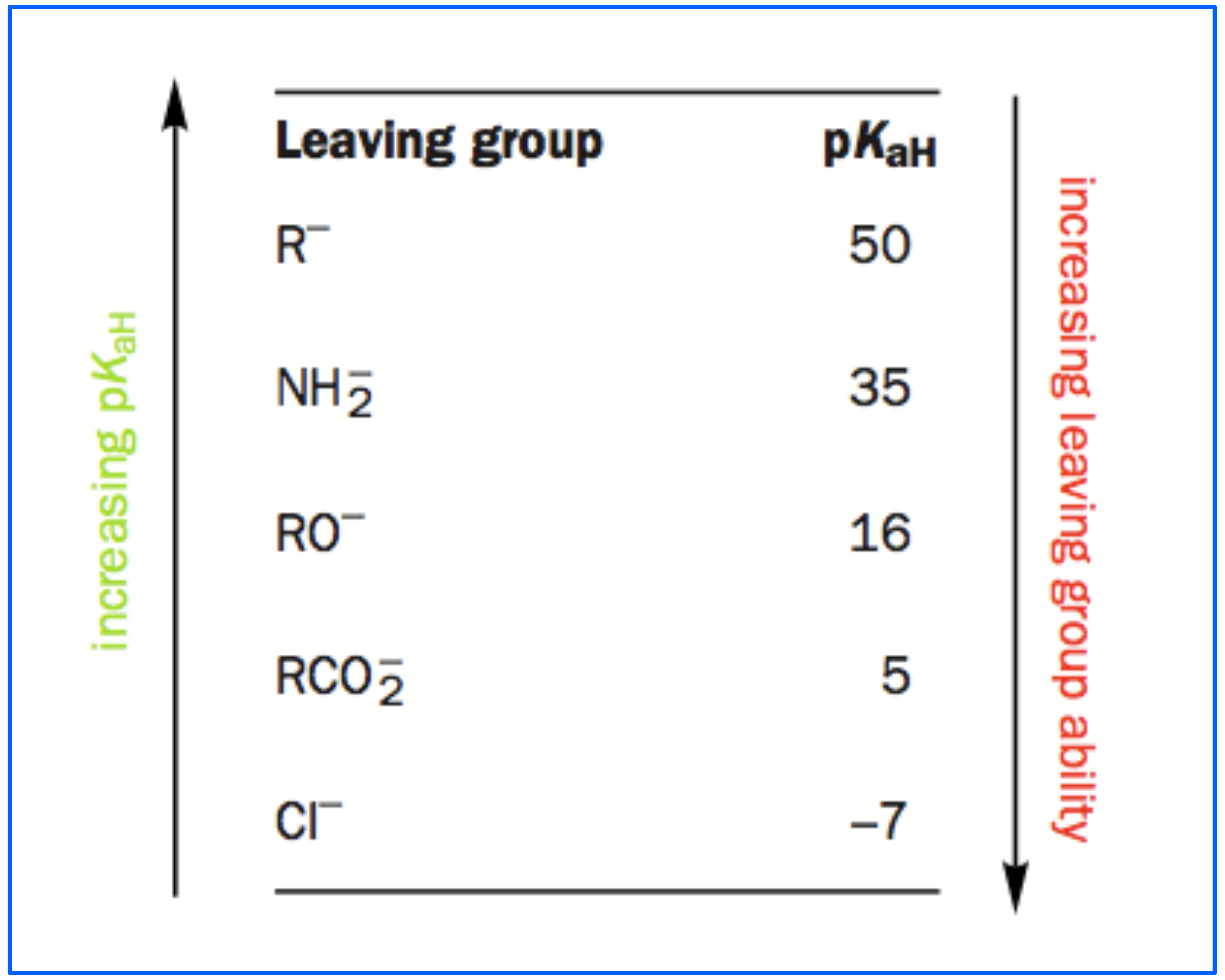


C. Reattività relativa: Il primo effetto è dato dalla capacità del gruppo uscente di agire come tale

Benzoato di Metila



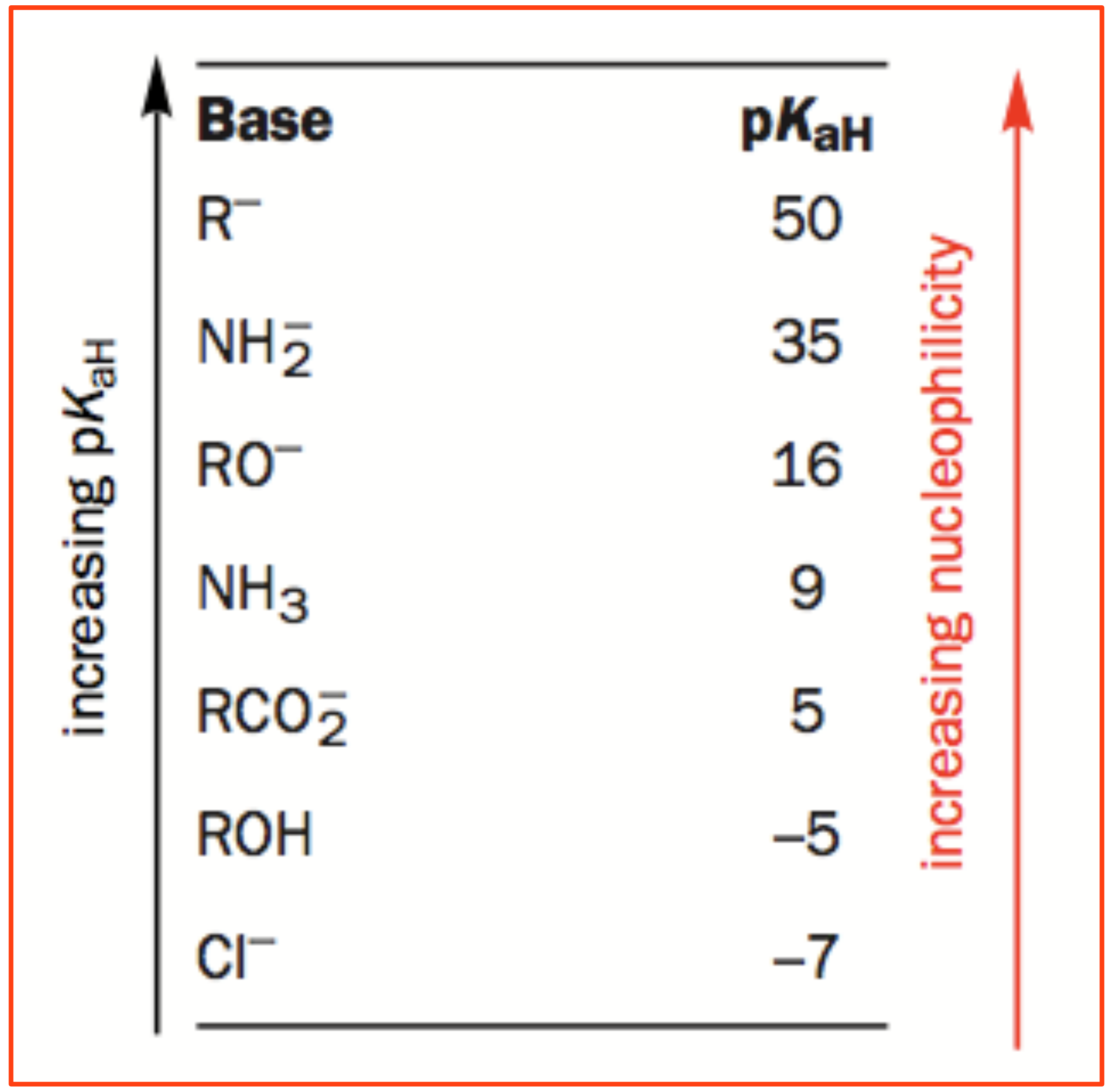
Benzamide



increasing pK_{aH}

Leaving group	pK_{aH}
R^-	50
NH_2^-	35
RO^-	16
RCO_2^-	5
Cl^-	–7

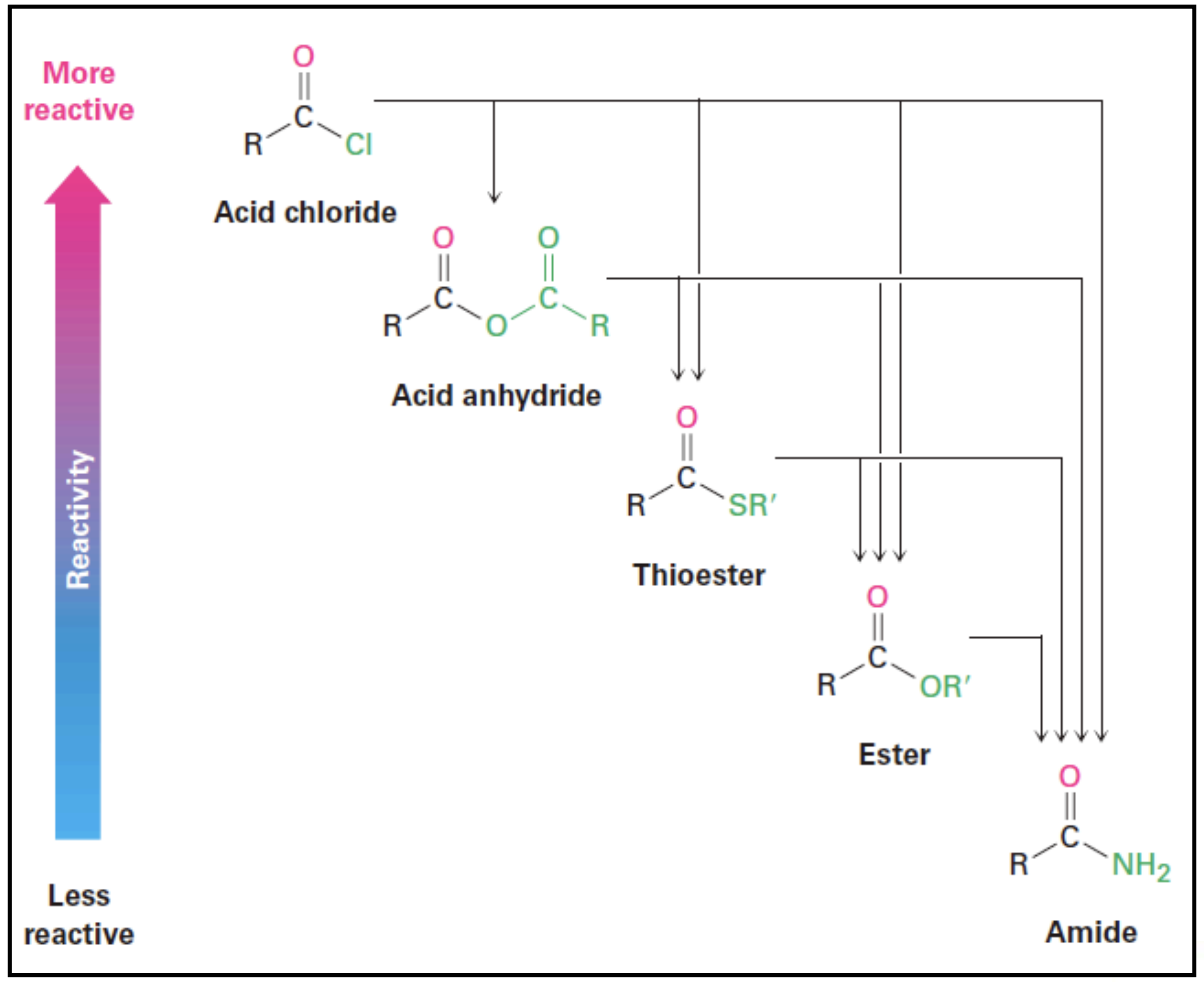
increasing leaving group ability



increasing pK_{aH}

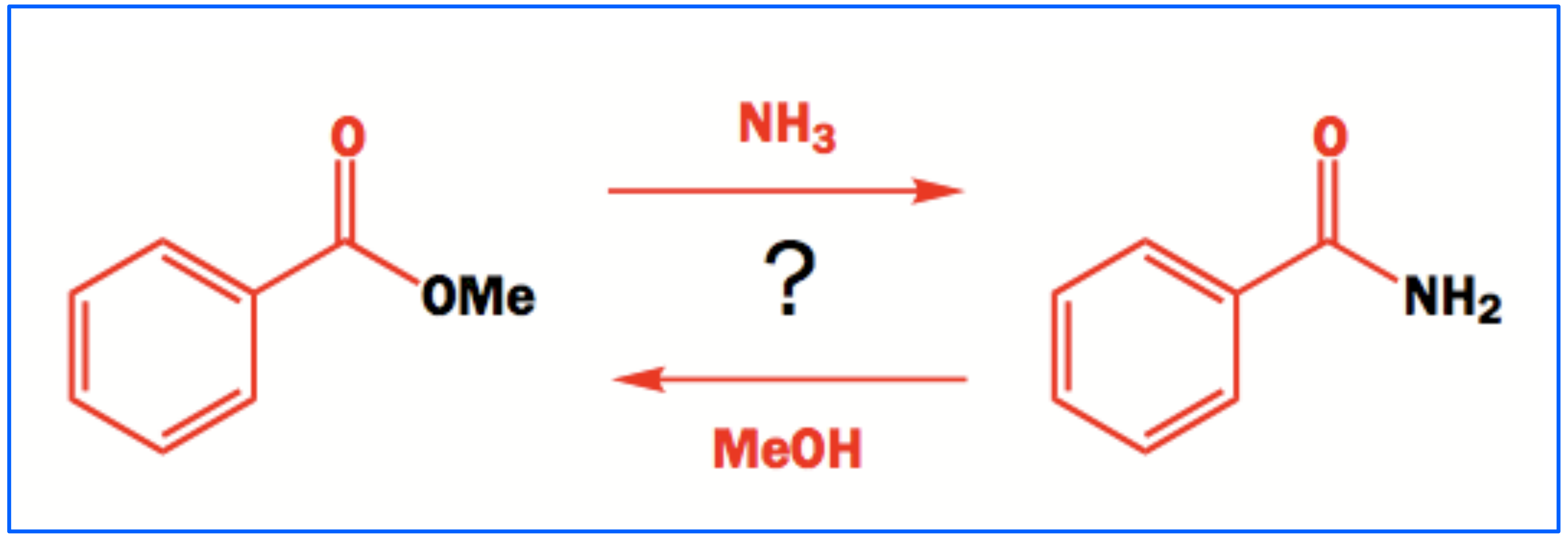
Base	pK_{aH}
R^-	50
NH_2^-	35
RO^-	16
NH_3	9
RCO_2^-	5
ROH	–5
Cl^-	–7

increasing nucleophilicity

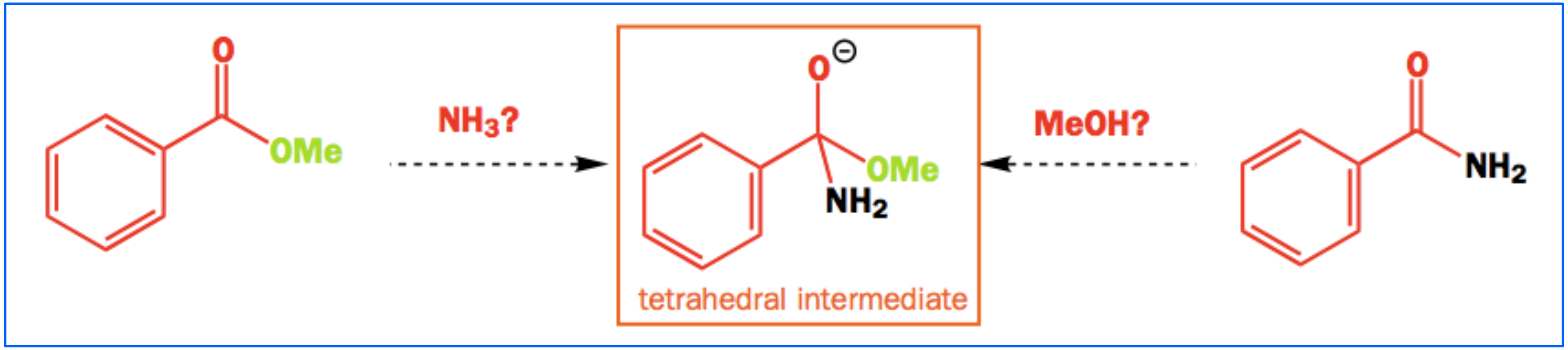


C. Reattività relativa: Il primo effetto è dato dalla capacità del gruppo uscente di agire come tale

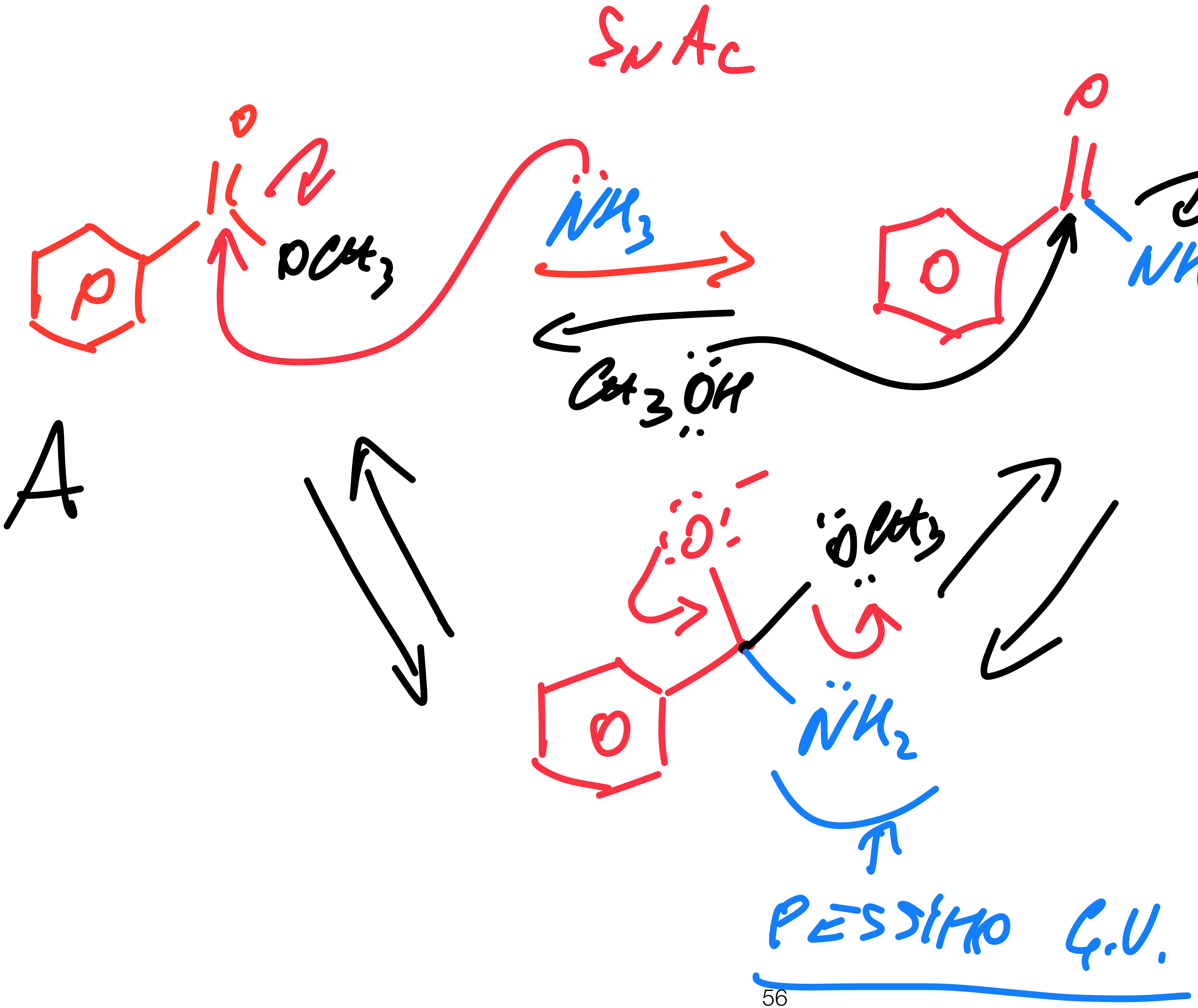
Benzoato di Metila



Benzamide



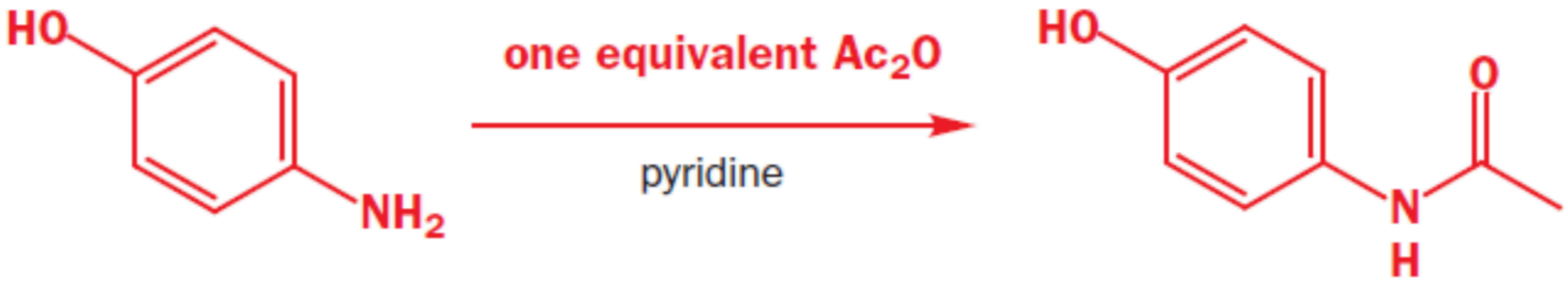
Possible leaving groups	pK_{aH}
Ph^-	45
NH_2^-	35
MeO^-	16



$pK_{aH} = 16-18$
CH_3OH

$pK_{aH} = 38$
NH_3

Selettività delle reazioni organiche

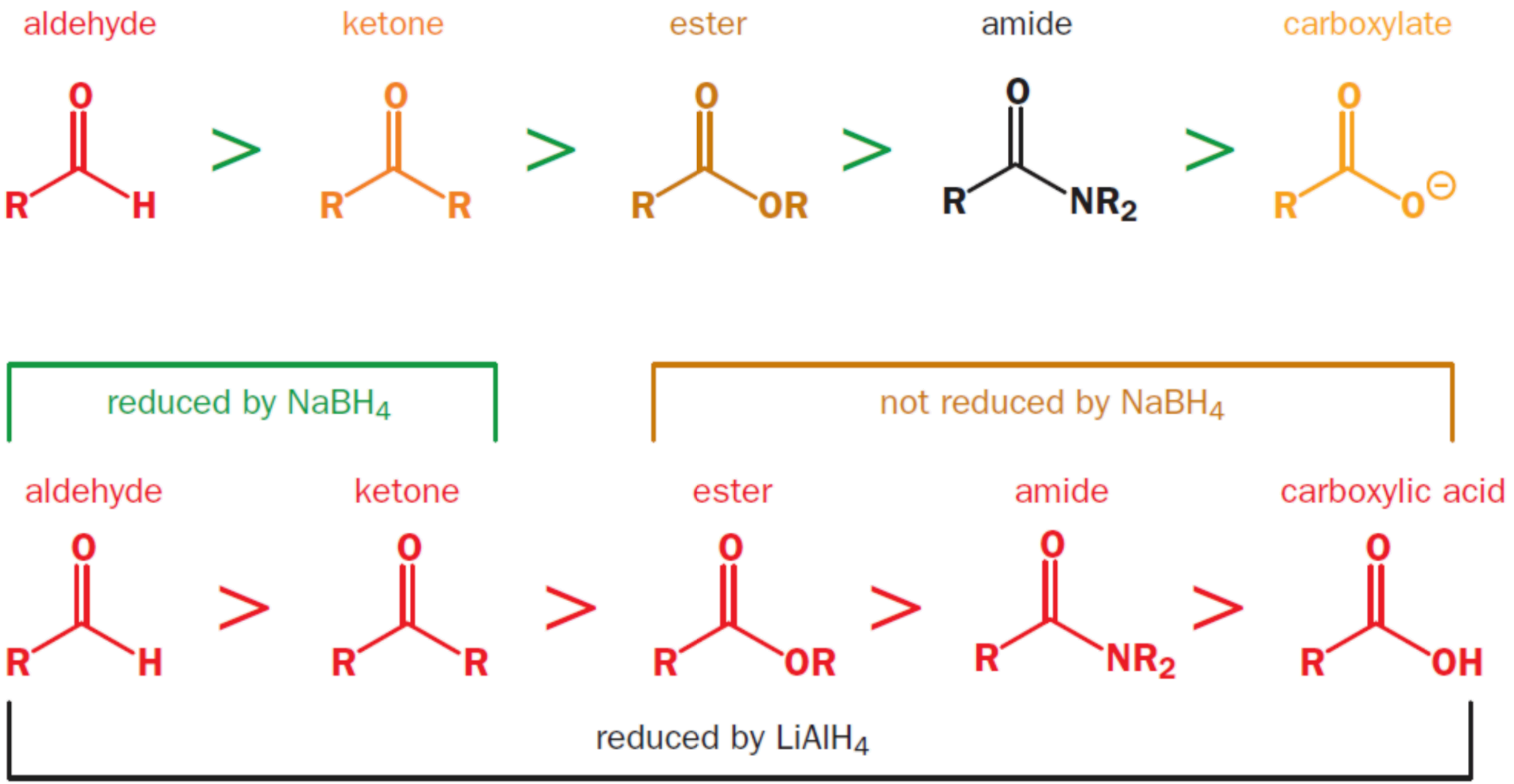


Chemoselettività: quale gruppo funzionale reagirà

Regioselettività: dove reagirà

Stereoselettività: come reagirà

Reattività del gruppo carbonile verso i nucleofili

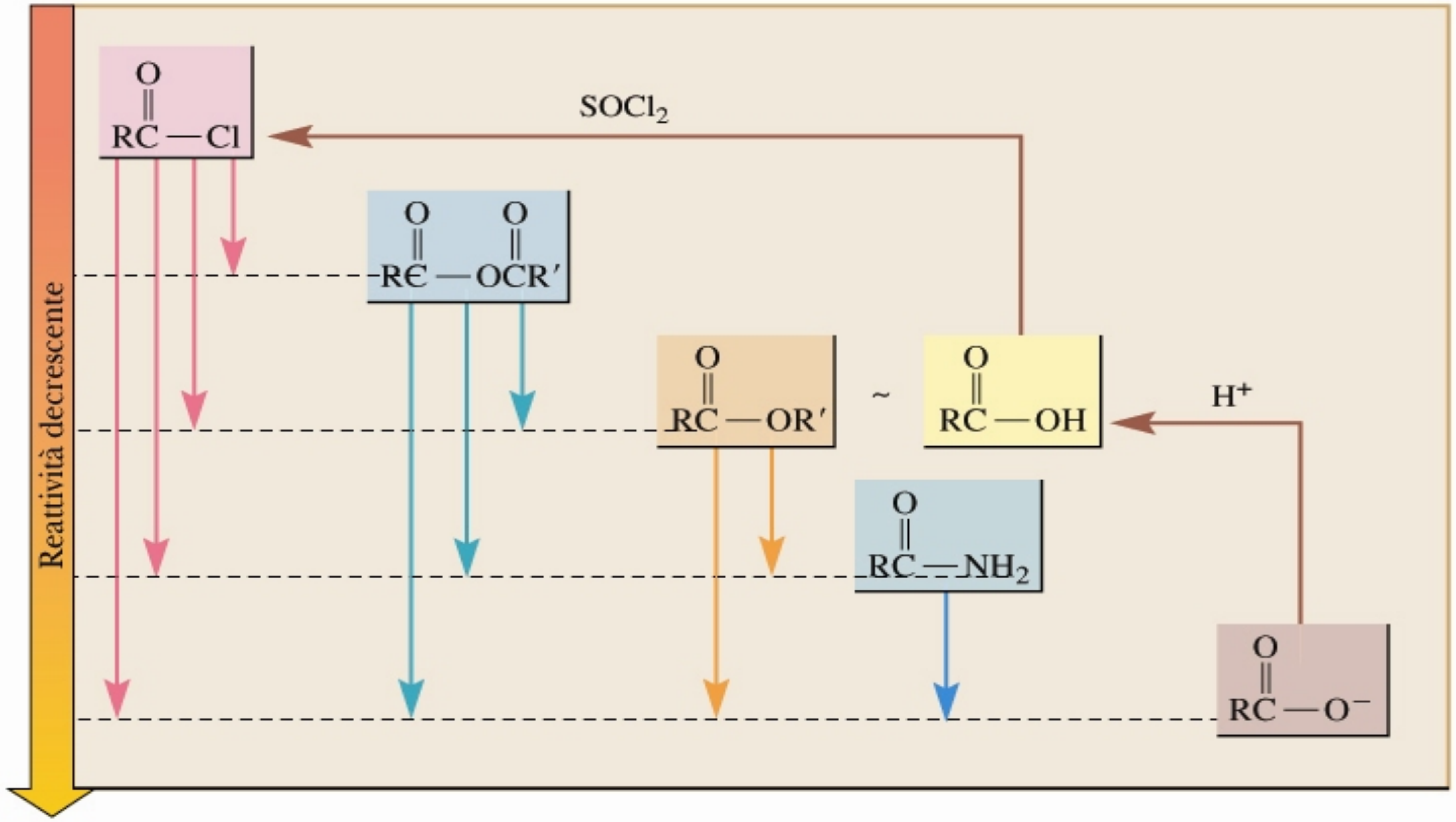


Formalmente, una riduzione con idruri assomiglia ad una sostituzione acilica in cui il nucleofilo è lo ione idruro. Il fato della reazione è controllato dalla presenza o meno di buoni gruppi uscenti.

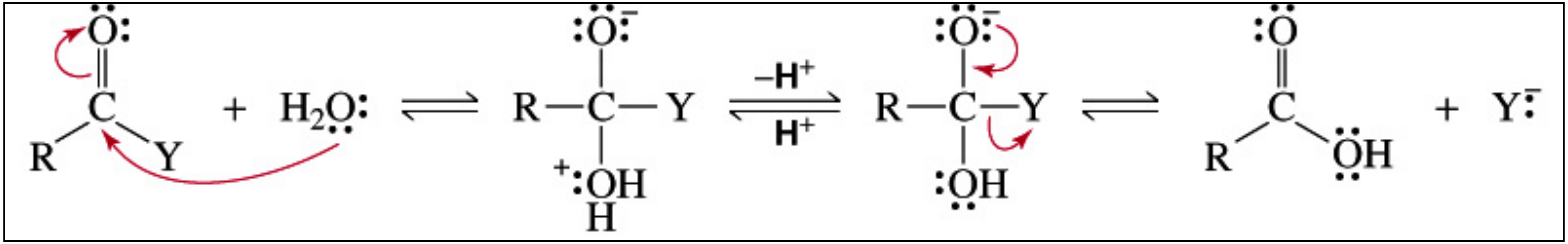
D. Catalisi

alogenuri acilici e le anidridi sono talmente reattivi che non si trovano in natura, mentre gli esteri e le ammidi sono composti ubiquitari.

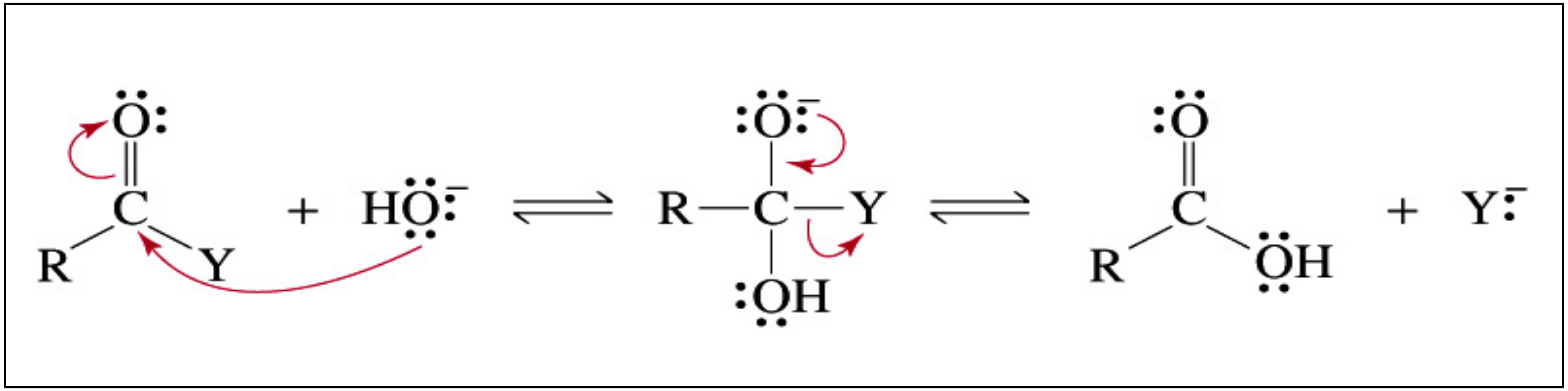
La reattività degli alogenuri acilici e delle anidridi è tale che i nucleofili comunemente utilizzati per interconvertire i derivati degli acidi carbossilici reagiscono direttamente con queste specie senza bisogno di catalizzatori. Al contrario, gli esteri e le ammidi sono così stabili che per farli reagire è richiesta una catalisi acida o basica. La catalisi acida viene utilizzata per aumentare il carattere elettrofilo del carbonio carbonilico e per facilitare la fuoriuscita del gruppo uscente.

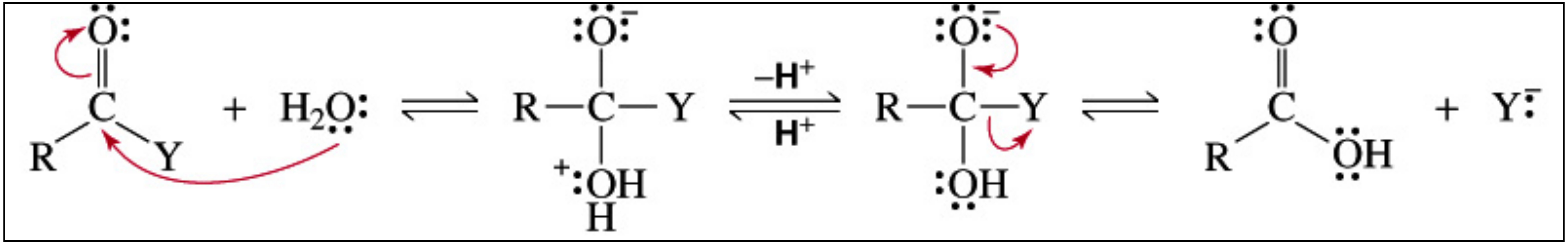


Meccanismo generale della S_NAc



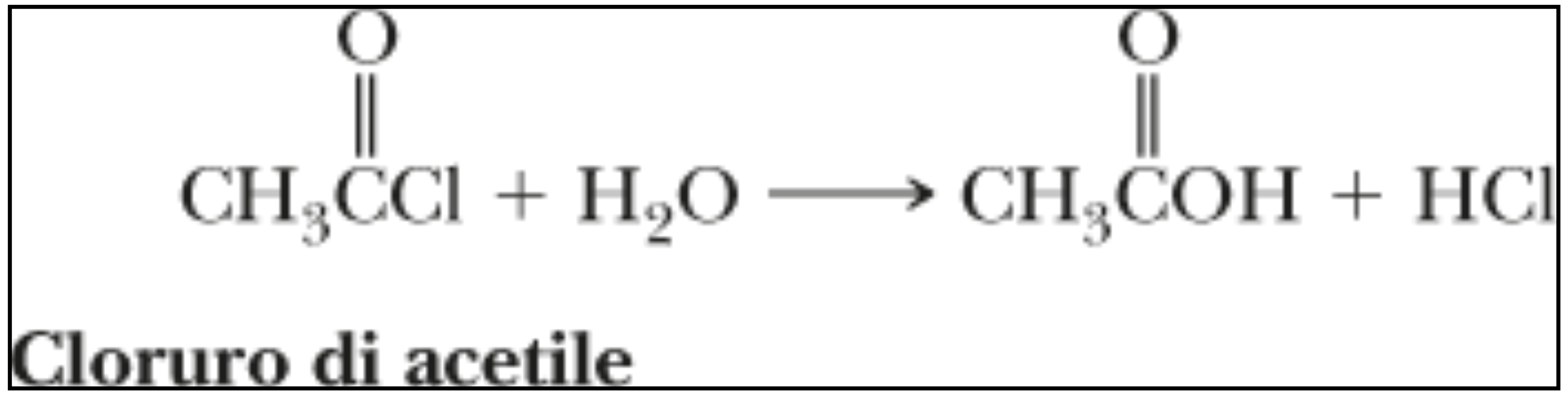
Meccanismo generale della S_NAc





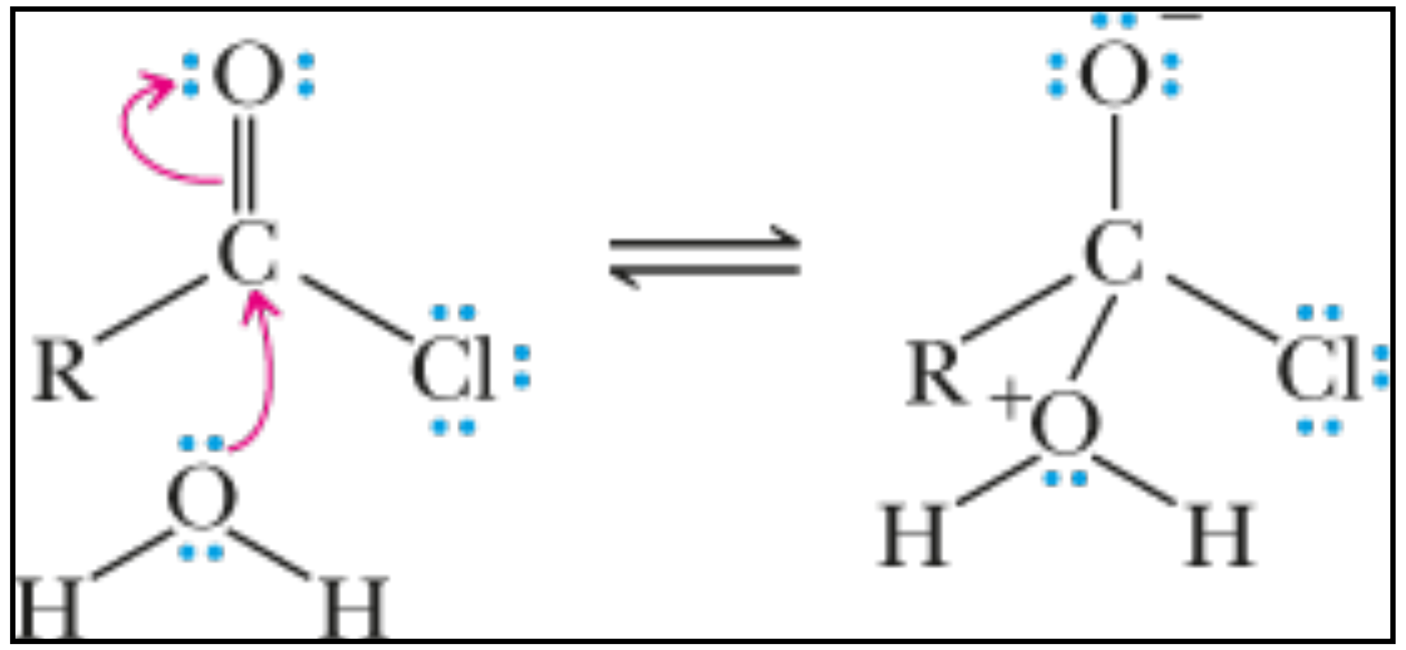
Reazione con l'acqua: idrolisi

A. Idrolisi di un Cloruro acilico

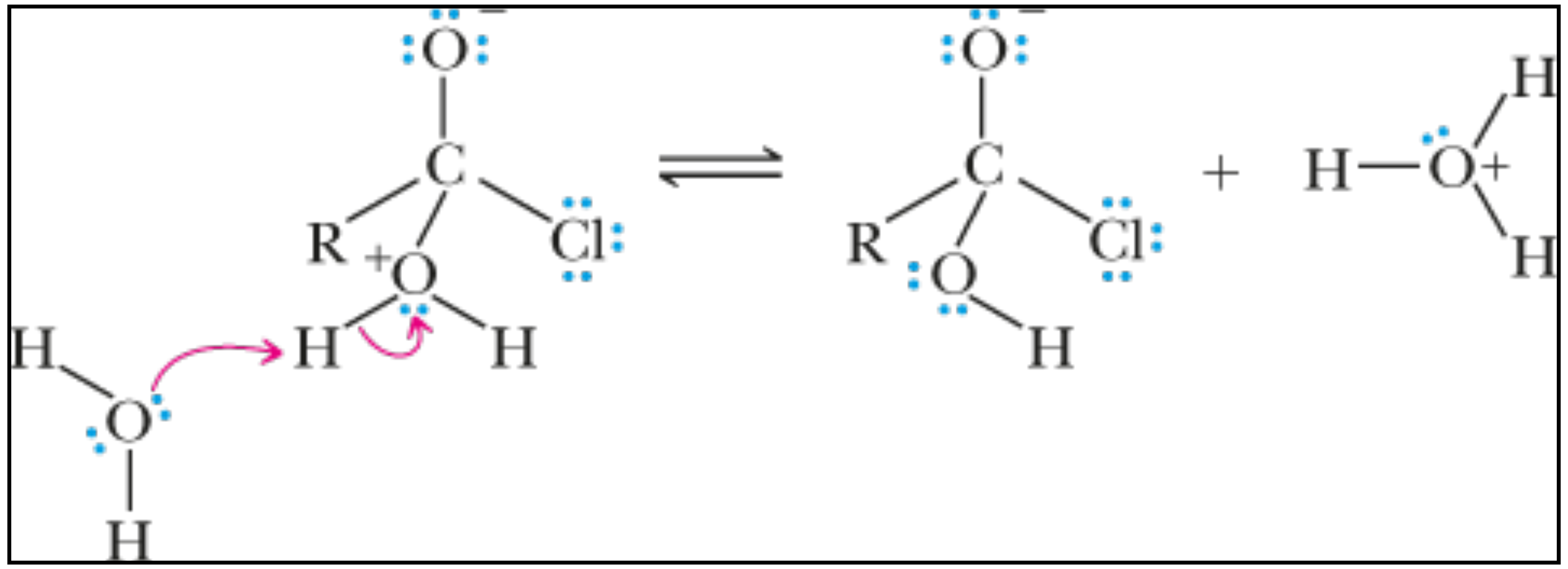


$$CH_3\overset{\overset{O}{\|}}{C}Cl + H_2O \longrightarrow CH_3\overset{\overset{O}{\|}}{C}OH + HCl$$

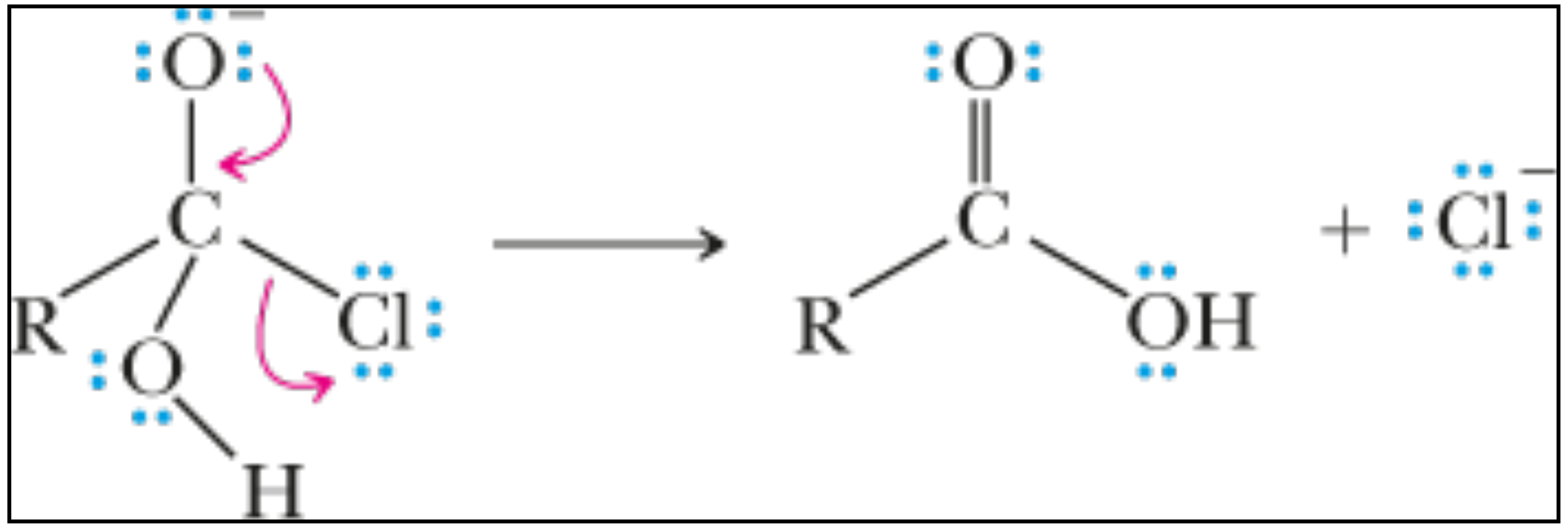
Cloruro di acetile



Stadio 1 Formazione di un nuovo legame tra un nucleofilo e un elettrofilo



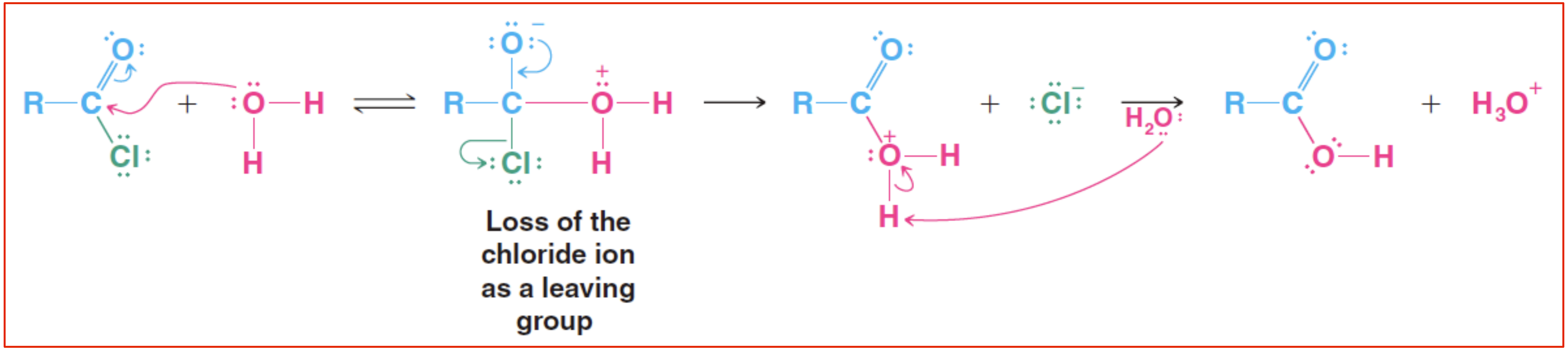
Stadio 2 Rimozione di un protone



Stadio 3 Rottura di un legame con formazione di molecole o ioni stabili.

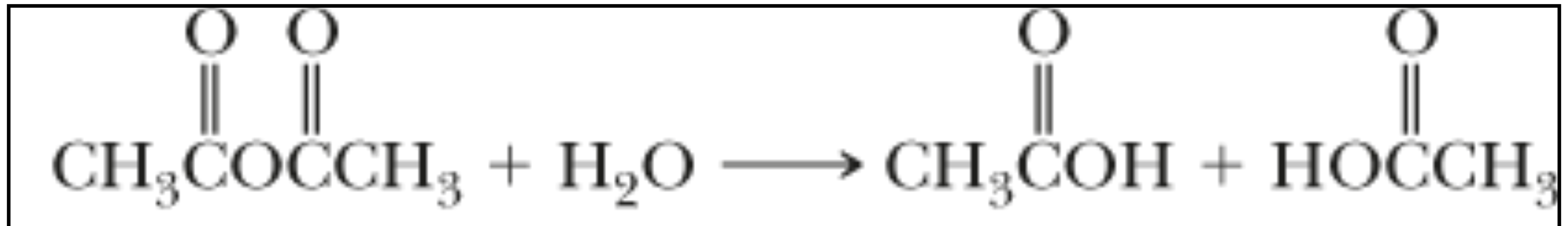
Questa reazione porta alla formazione dell'acido forte HCl (H3O+ e Cl2). I chimici spesso aggiungono una base debole, come la piridina, per neutralizzare l'acido che si è formato.

A. Idrolisi di un Cloruro acilico



Loss of the chloride ion as a leaving group

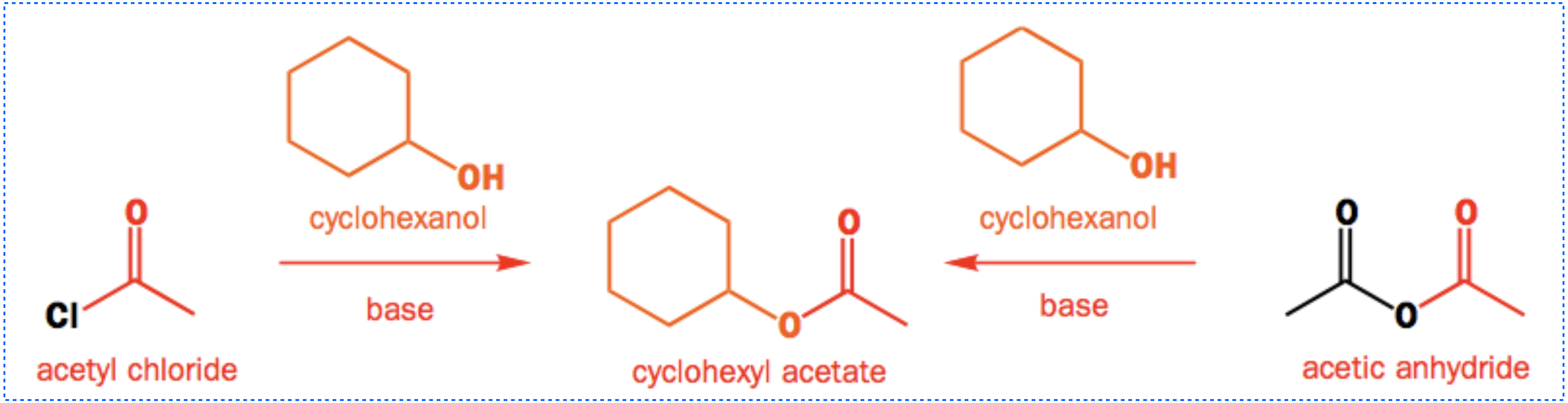
B. Idrolisi delle Anidridi degli acidi



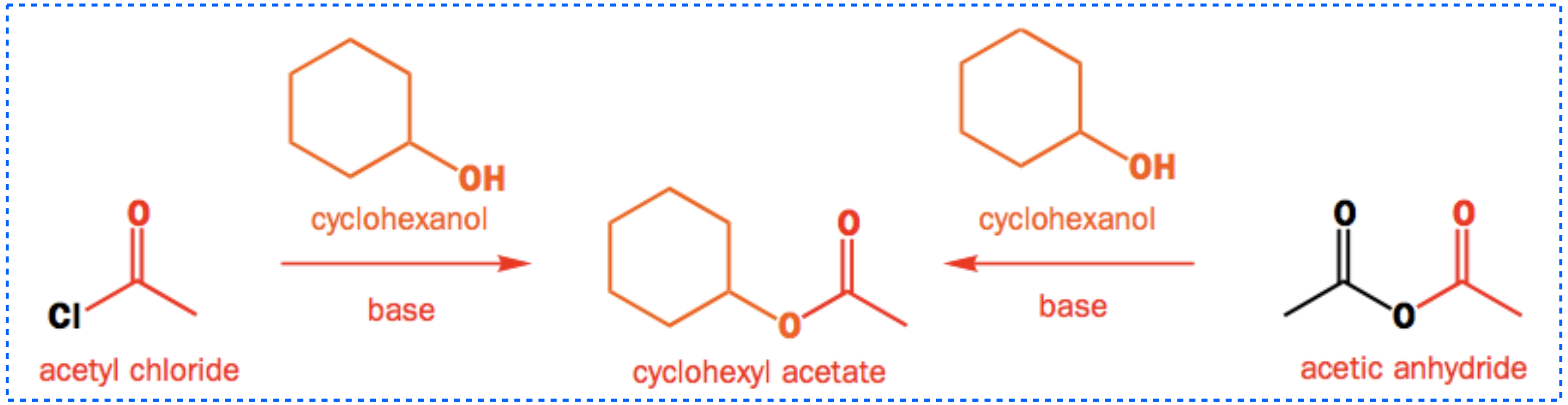
$$CH_3\overset{O}{\overset{\parallel}{C}}O\overset{O}{\overset{\parallel}{C}}CH_3 + H_2O \longrightarrow CH_3\overset{O}{\overset{\parallel}{C}}OH + HO\overset{O}{\overset{\parallel}{C}}CH_3$$

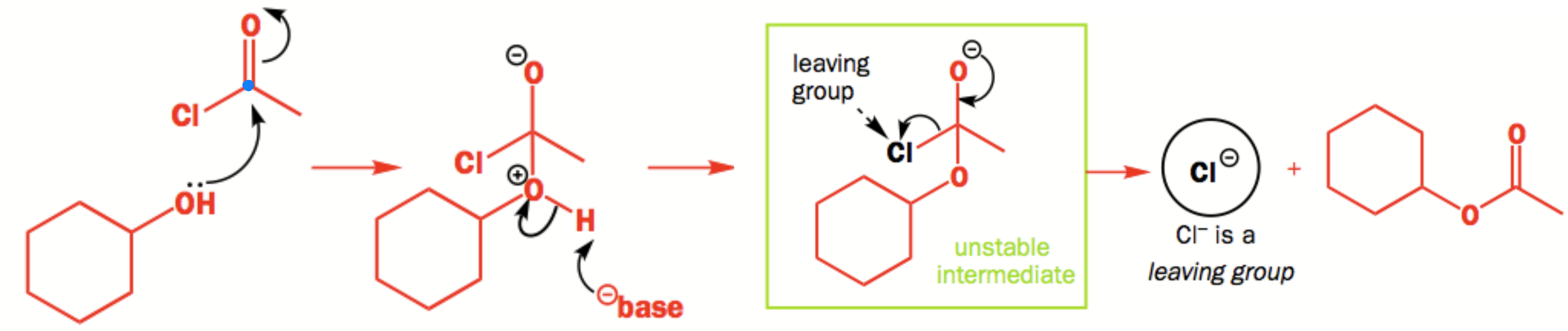
Anidride acetica

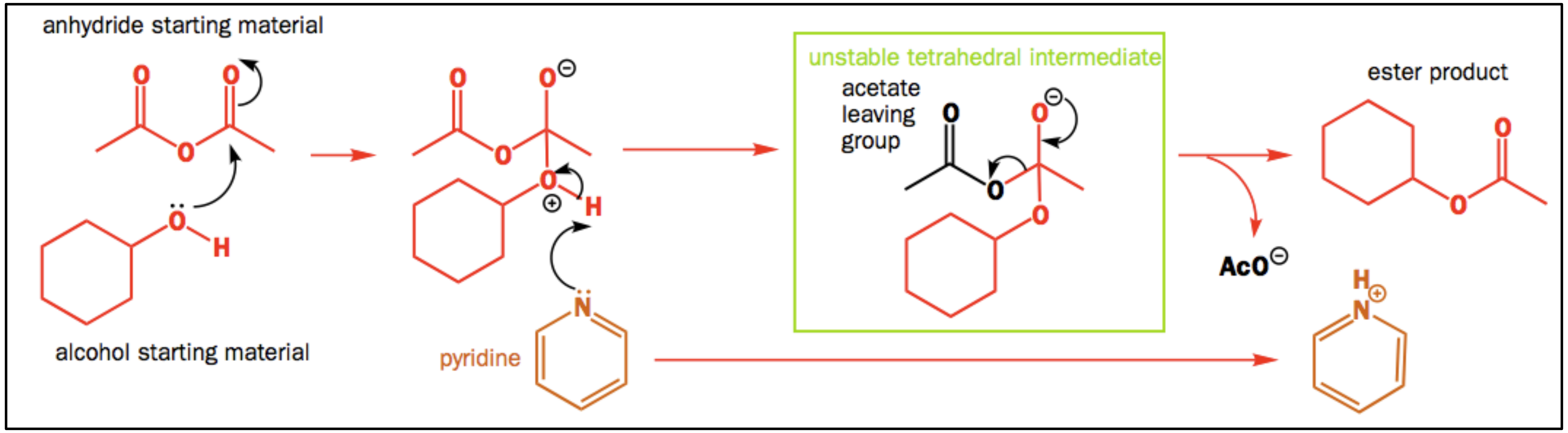
Meccanismo generale della S_NAc



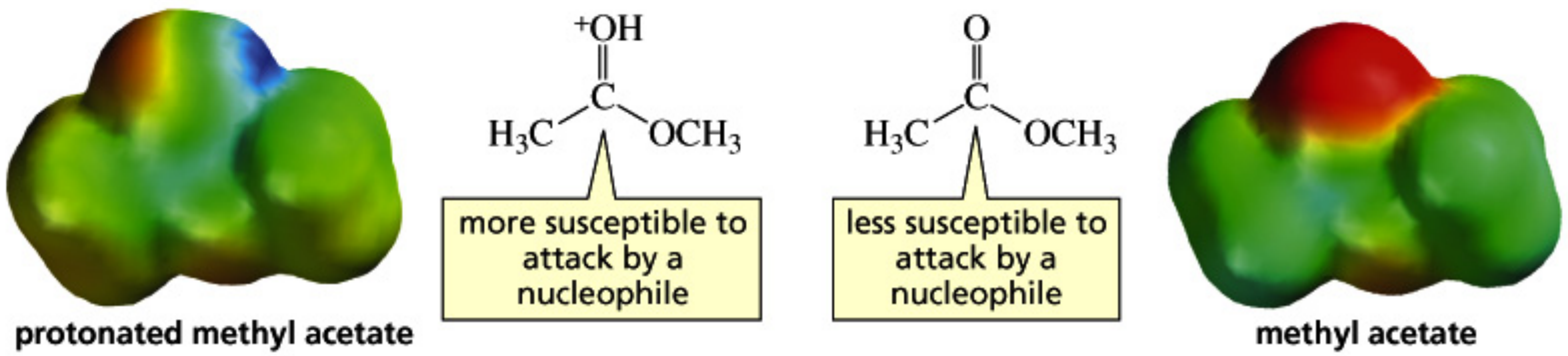
Meccanismo generale della S_NAc





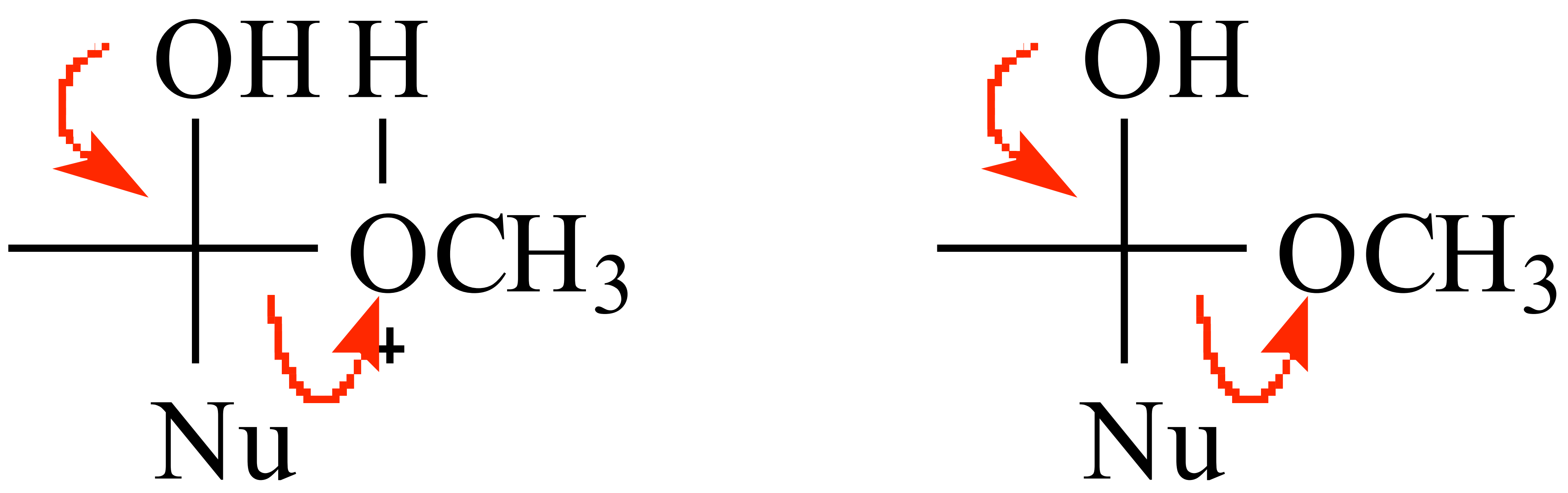


C. Idrolisi di un estere

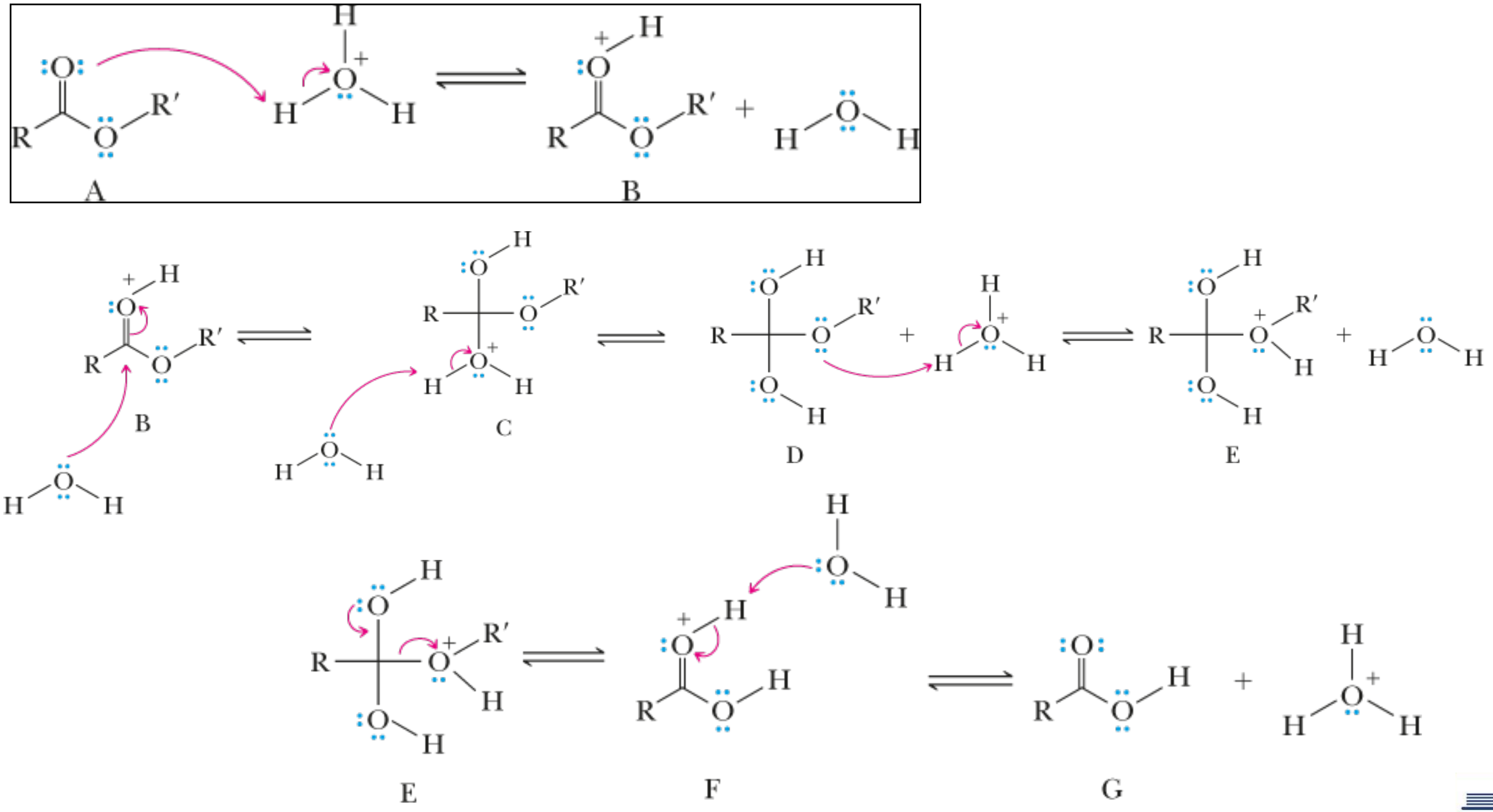

protonation of the carbonyl oxygen increases the susceptibility of the carbonyl carbon to nucleophilic attack

more susceptible to attack by a nucleophile

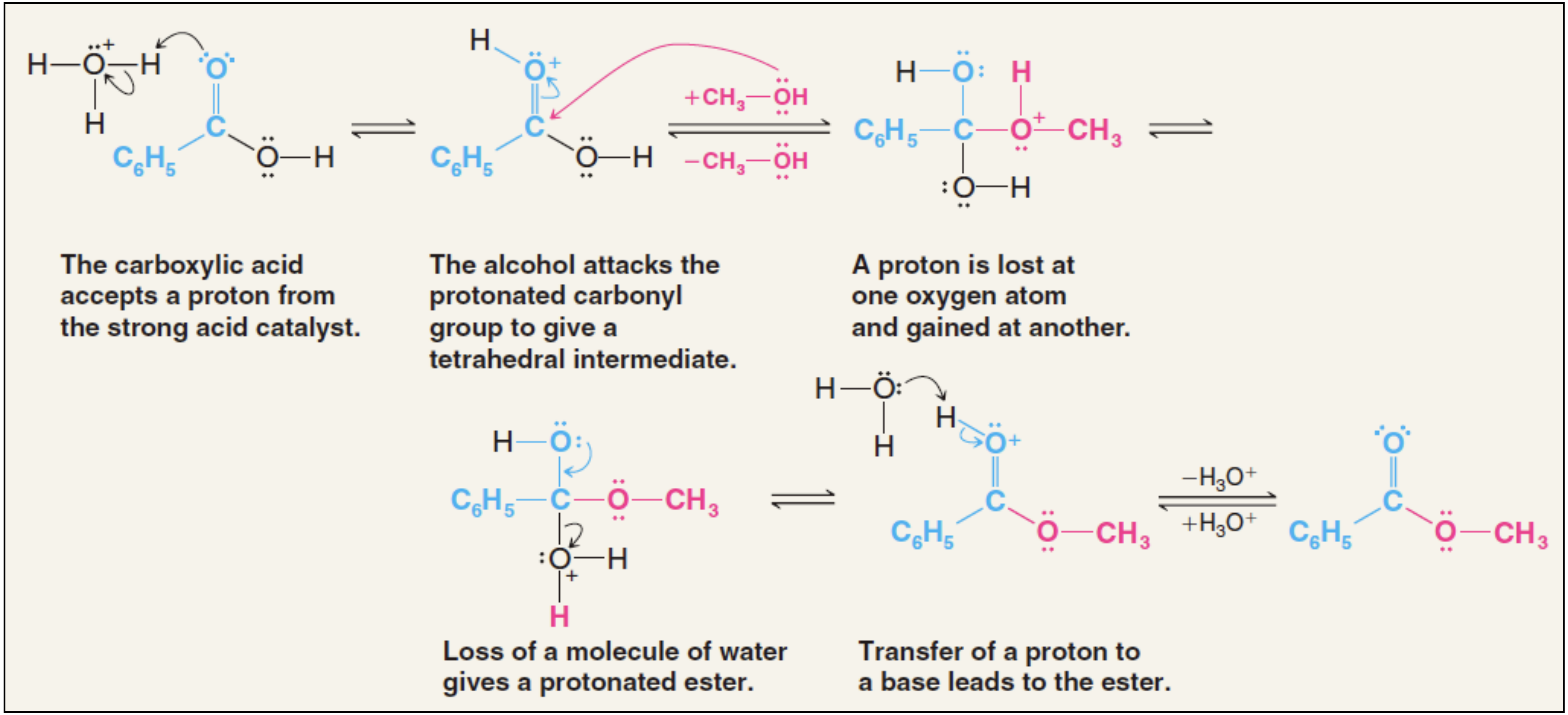
less susceptible to attack by a nucleophile



C. Idrolisi degli esteri catalizzata dagli acidi



C. Idrolisi degli esteri catalizzata dagli acidi



The carboxylic acid accepts a proton from the strong acid catalyst.

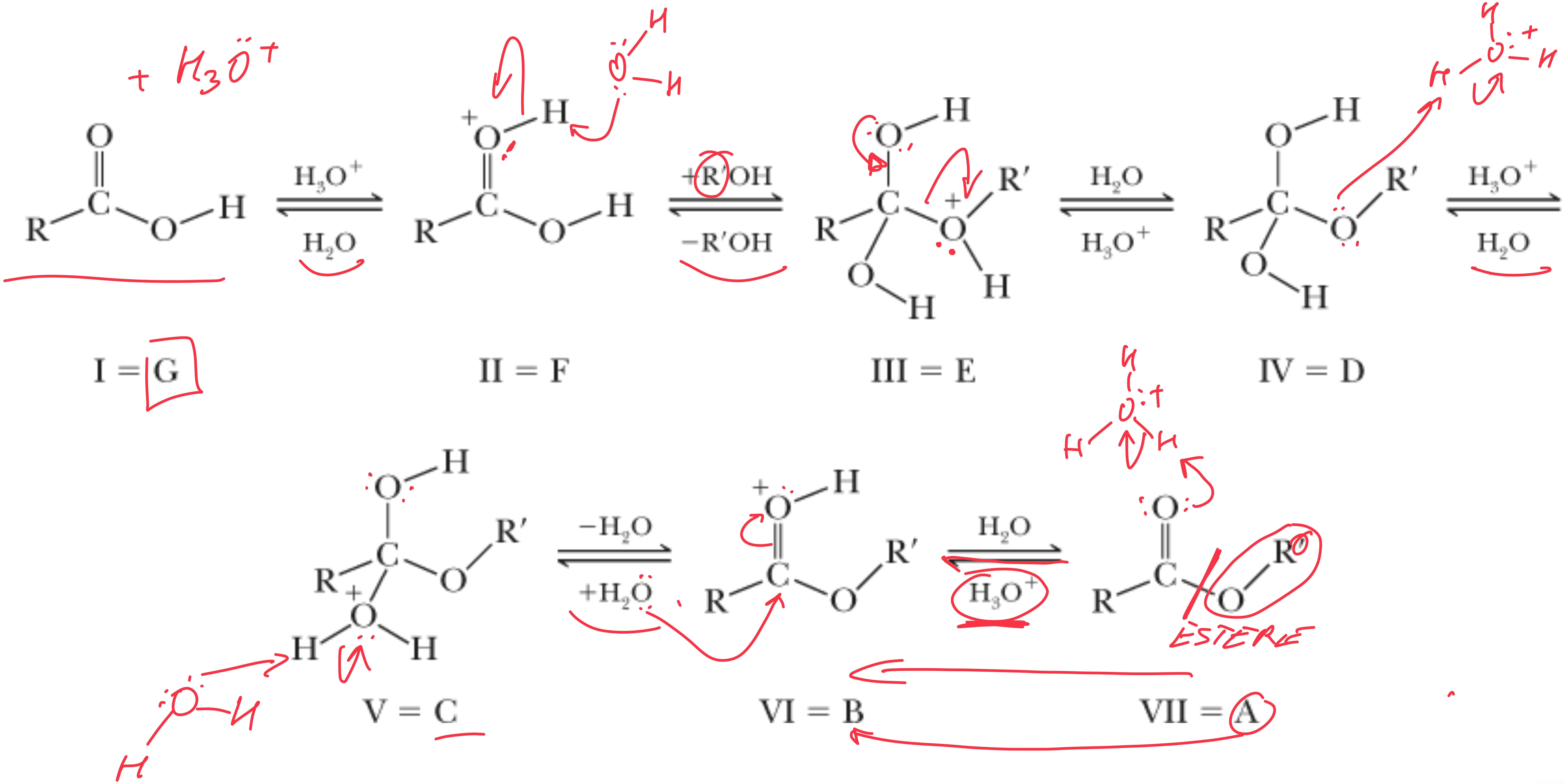
The alcohol attacks the protonated carbonyl group to give a tetrahedral intermediate.

A proton is lost at one oxygen atom and gained at another.

Loss of a molecule of water gives a protonated ester.

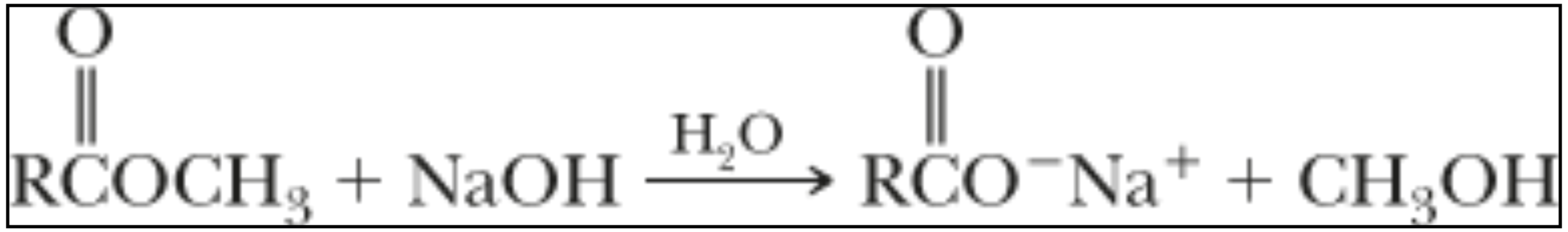
Transfer of a proton to a base leads to the ester.

A-G. Idrolisi degli esteri catalizzata dagli acidi
I - IV reazione di sterificazione in ambiente acido



Saponificazione

L’idrolisi degli esteri può anche essere condotta usando una base acquosa come NaOH a caldo.



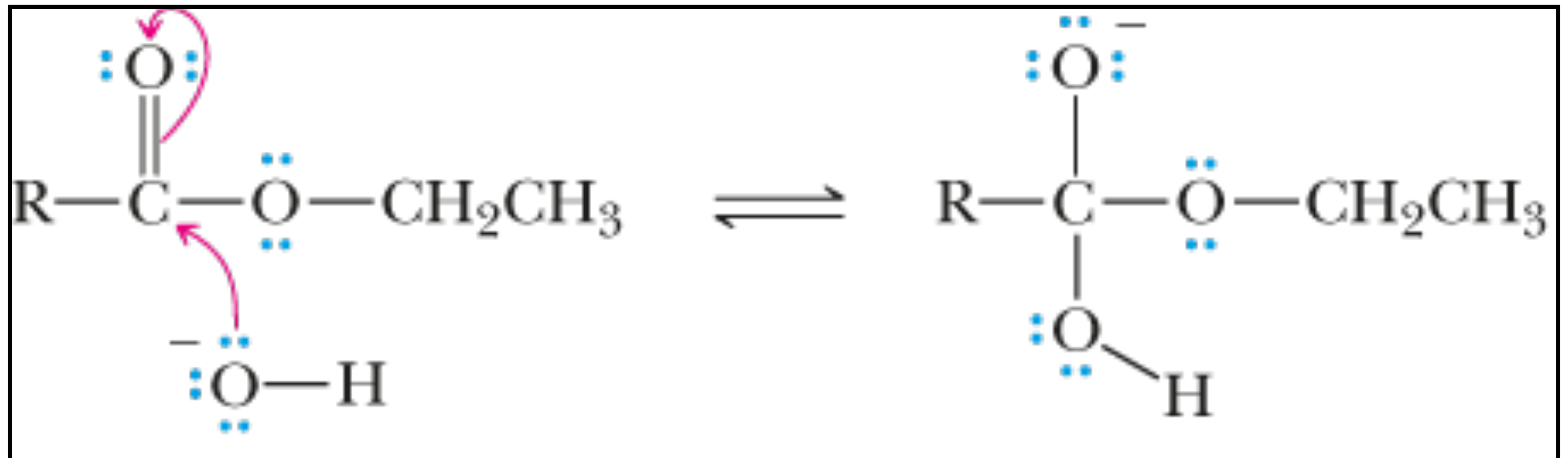
$$\mathrm{R\overset{\overset{O}{\|}}{C}OCH_3} + \mathrm{NaOH} \xrightarrow{H_2O} \mathrm{R\overset{\overset{O}{\|}}{C}O^-Na^+} + \mathrm{CH_3OH}$$

Vi sono due importanti differenze fra l’idrolisi degli esteri in presenza di un acido acquoso o di una base acquosa.

1. **Per l’idrolisi di un estere in acido acquoso sono sufficienti quantità catalitiche dell’acido,**

2. **mentre per l’idrolisi in ambiente basico la base è richiesta in quantità stechiometriche, dal momento che è un reagente, non un catalizzatore.**

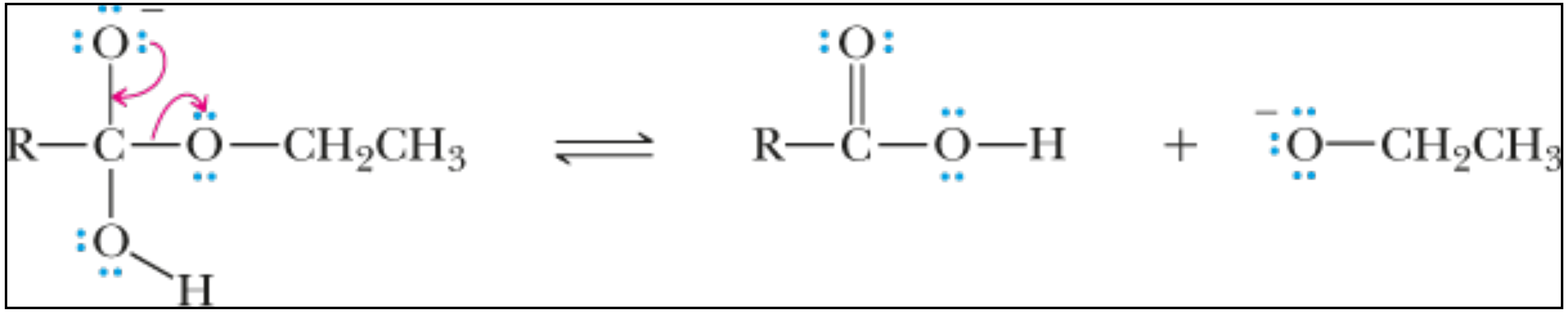
MECCANISMO: Idrolisi di un estere in una base acquosa (saponificazione)



$$R{-}C({=}O){-}O{-}CH_2CH_3 + {}^{-}OH \rightleftharpoons R{-}C(O^{-})(OH){-}O{-}CH_2CH_3$$

Intermedio tetraedrico di addizione

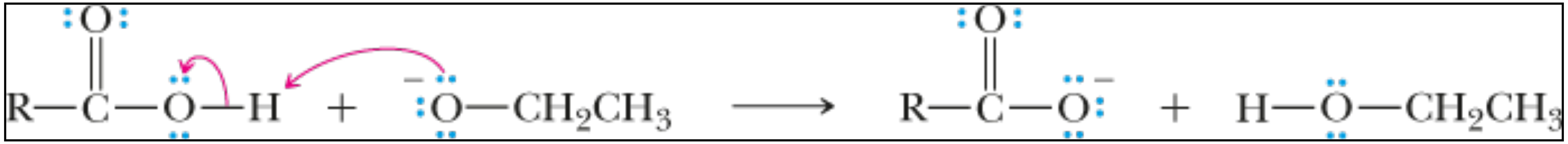
Stadio 1. Formazione di un nuovo legame tra un nucleofilo e un elettrofilo



$$R{-}C(O^{-})(OH){-}O{-}CH_2CH_3 \rightleftharpoons R{-}C({=}O){-}O{-}H + {}^{-}O{-}CH_2CH_3$$

Stadio 2. Rottura di un legame con formazione di molecole o ioni stabili.

Stadio 3. Rimozione di un protone.

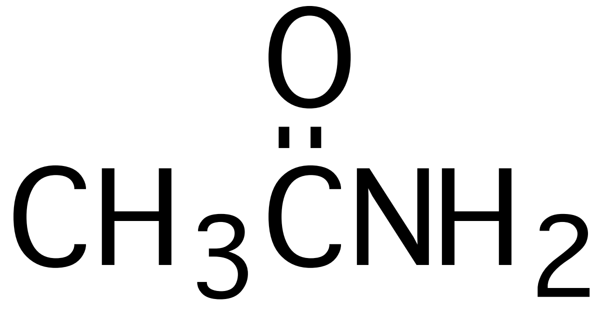


$$R{-}C({=}O){-}O{-}H + {}^{-}O{-}CH_2CH_3 \longrightarrow R{-}C({=}O){-}O^{-} + H{-}O{-}CH_2CH_3$$

AMMIDI

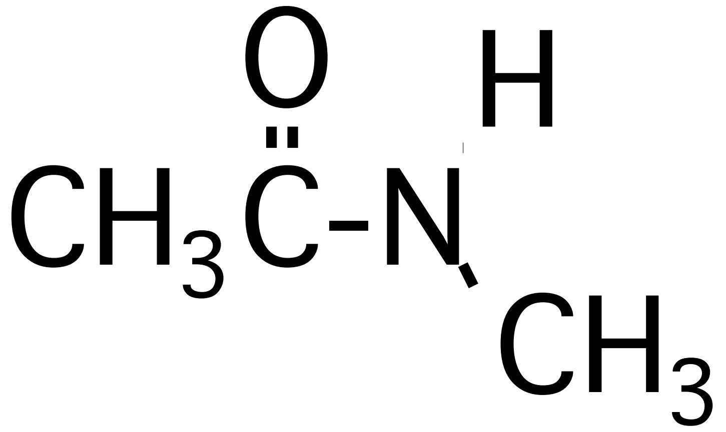
systematic name: ethanamide — 4-chlorobutanamide — benzenecarboxamide — *cis*-2-ethylcyclohexanecarboxamide

common name: acetamide — γ-chlorobutyramide — benzamide



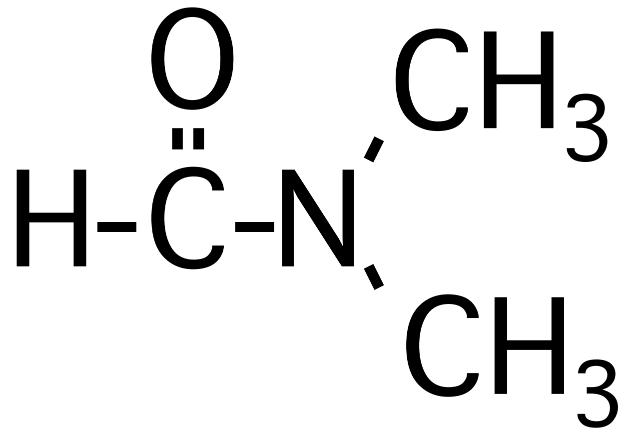
$CH_3\overset{O}{\overset{\|}{C}}NH_2$

Acetamide
(a 1° amide)



$CH_3\overset{O}{\overset{\|}{C}}-N(H)CH_3$

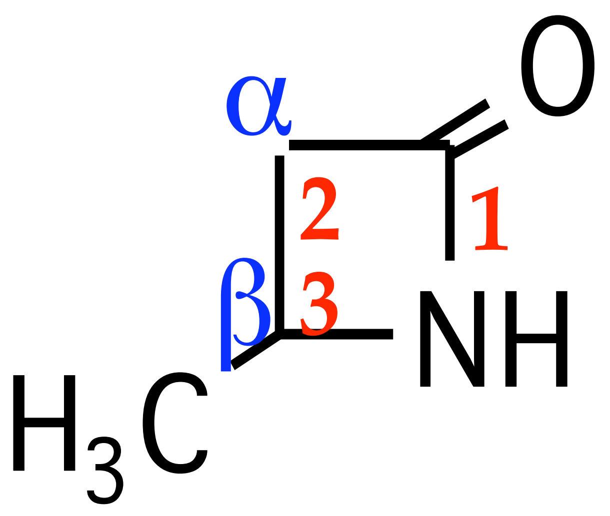
***N*-Methylacetamide**
(a 2° amide)



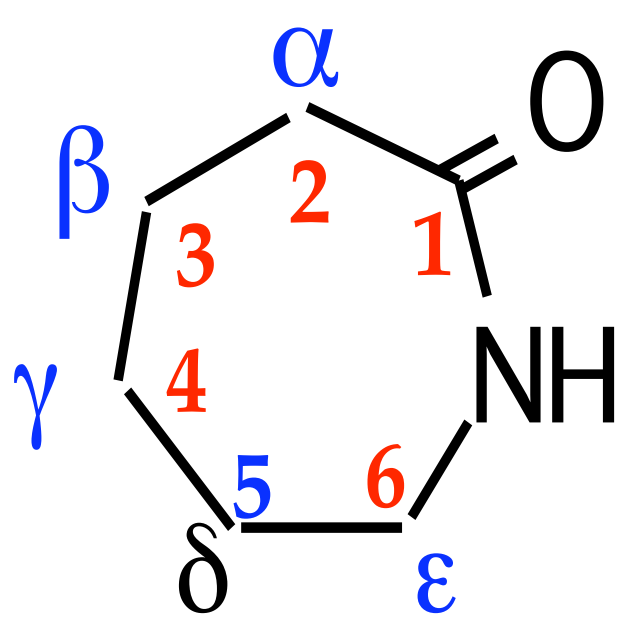
$H-\overset{O}{\overset{\|}{C}}-N(CH_3)_2$

***N,N*-Dimethyl-formamide (DMF)**
(a 3° amide)

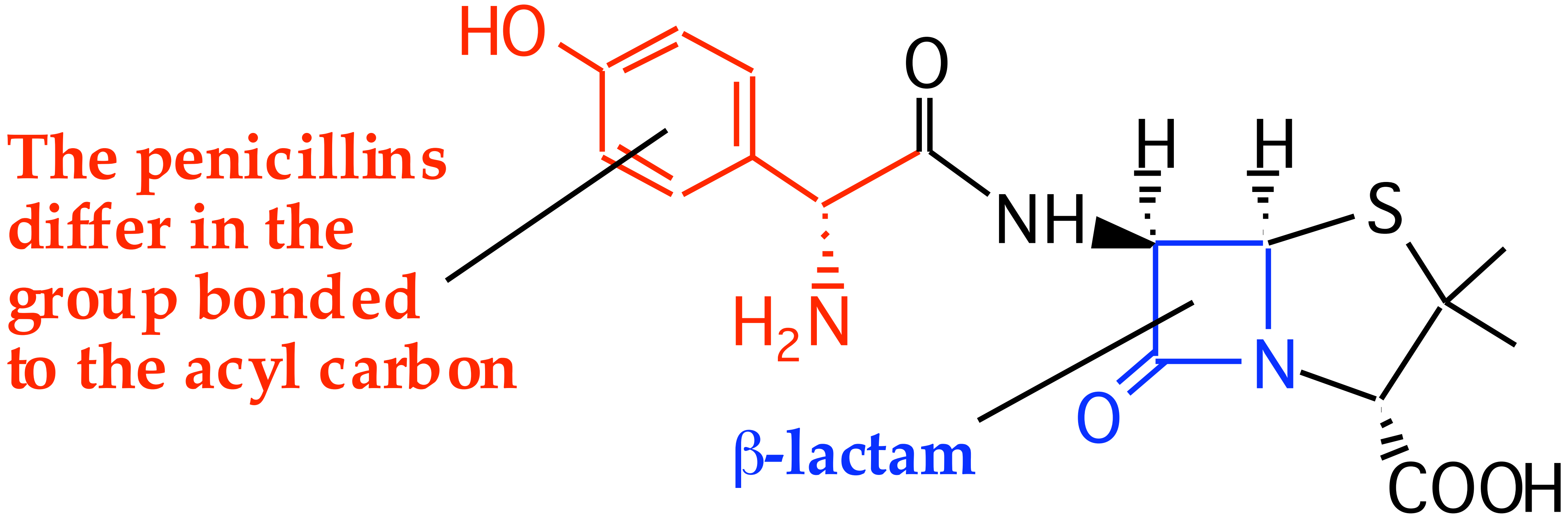
AMMIDI CICLICHE (LATTAMI)



3-Butanolactam
(β-Butyrolactam)

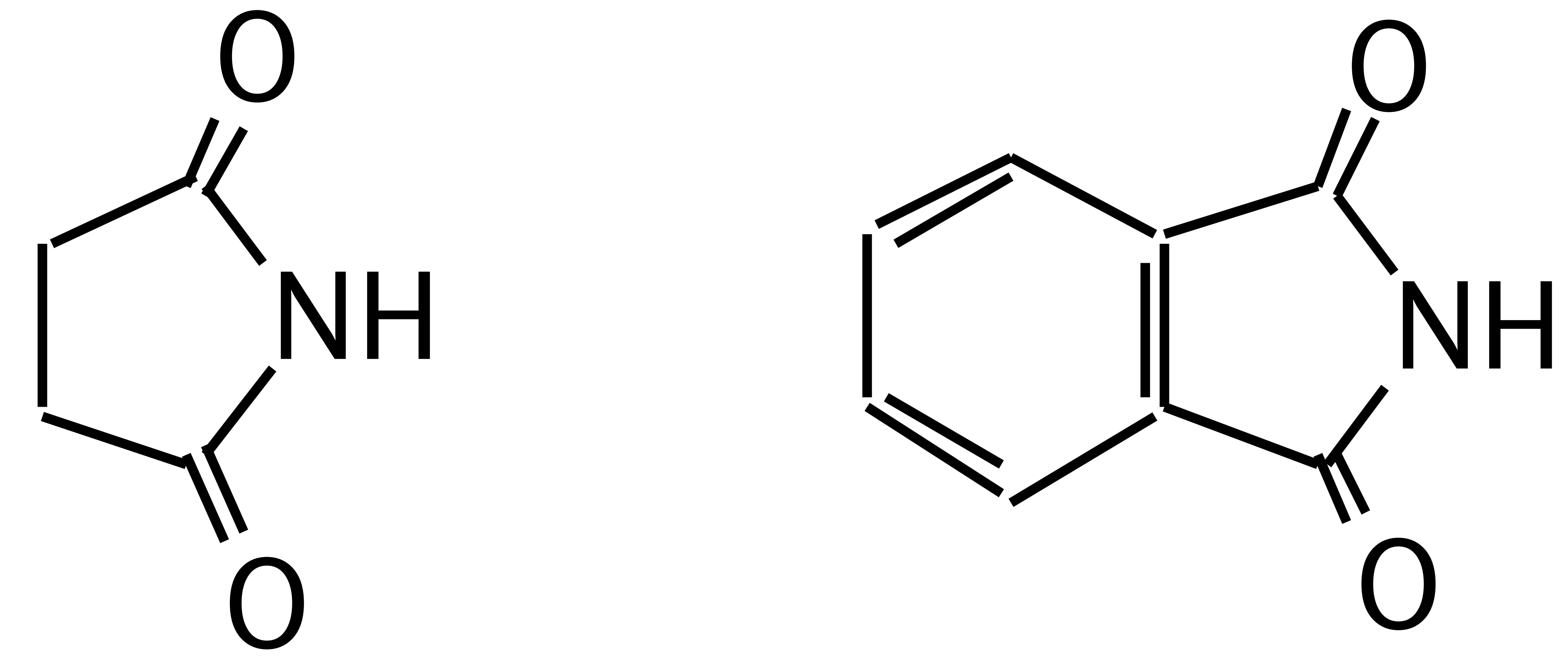


6-Hexanolactam
(ε-Caprolactam)

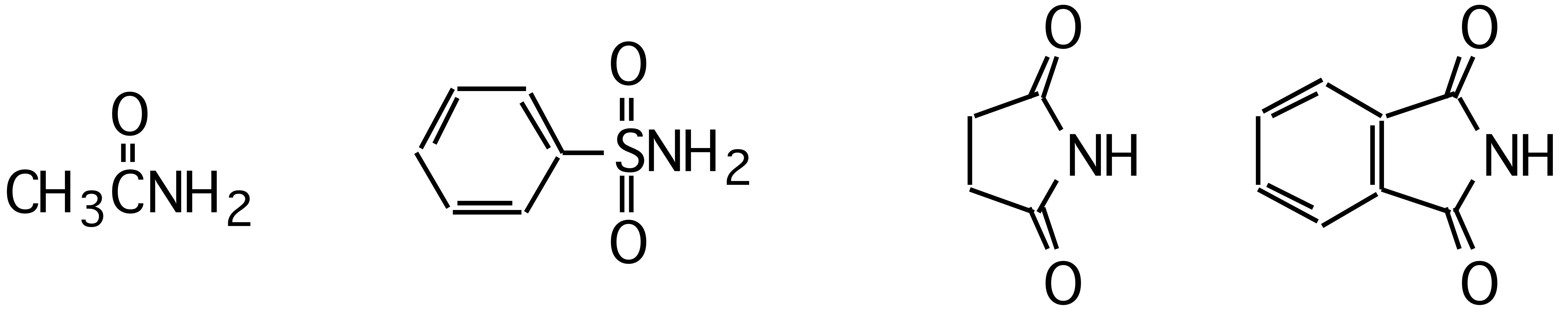


Amoxicillin
(a β-lactam antibiotic)

IMMIDI CICLICHE



Succinimide **Phthalimide**



$\mathrm{CH_3\overset{\overset{O}{\|}}{C}NH_2}$

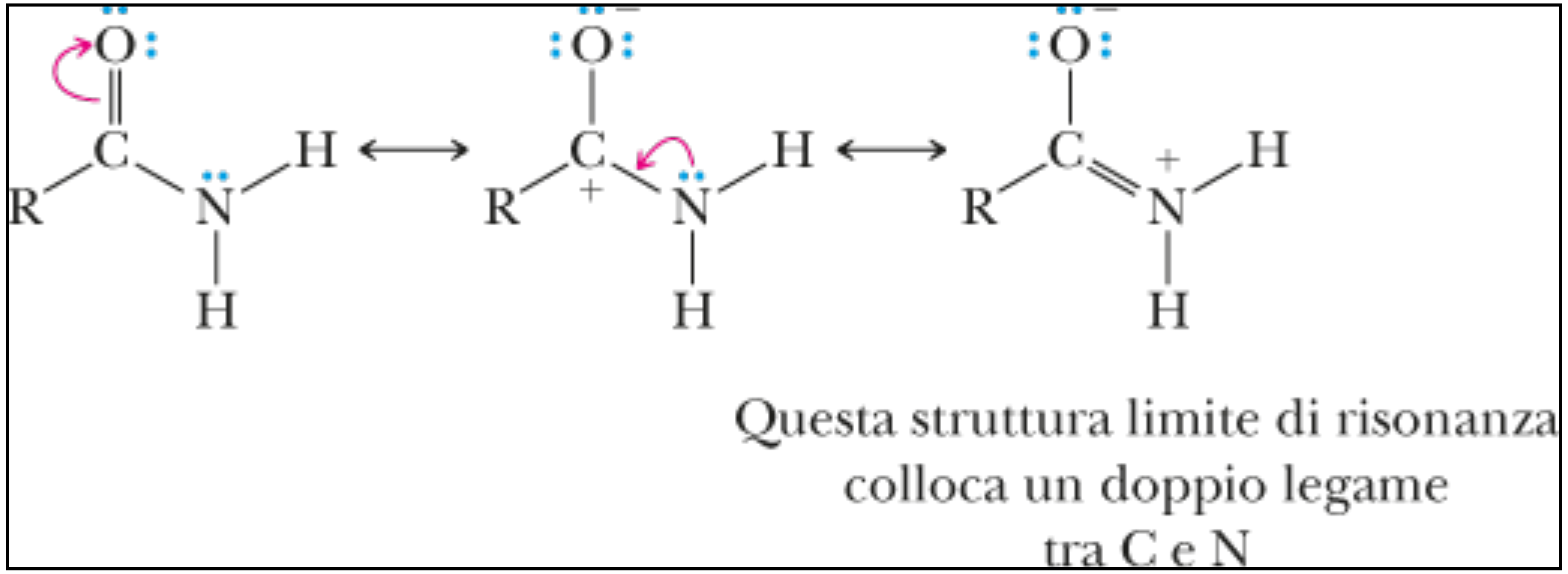
Acetamide
pK_a 15-17

Benzenesulfonamide
pK_a 10

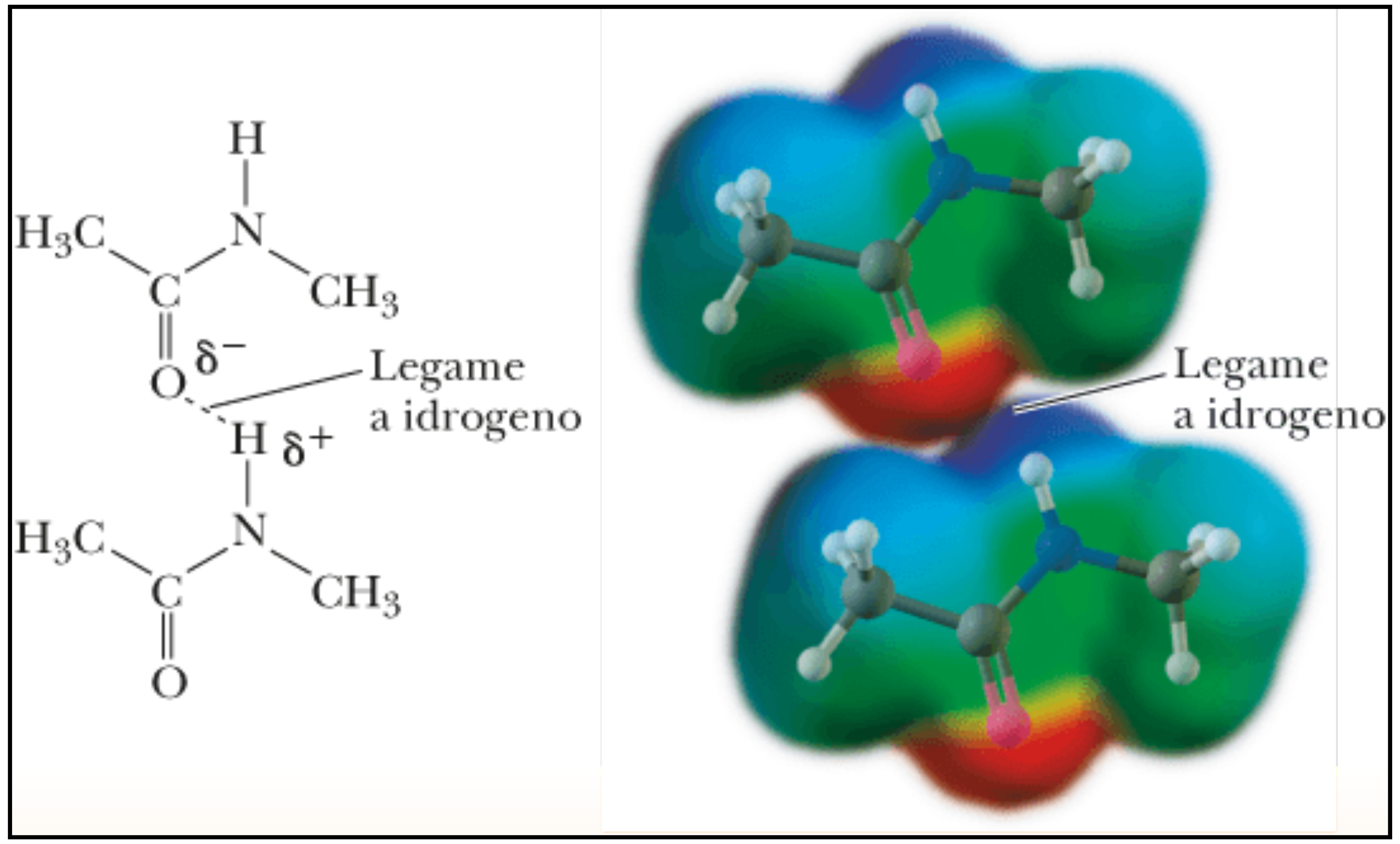
Succinimide
pK_a 9.7

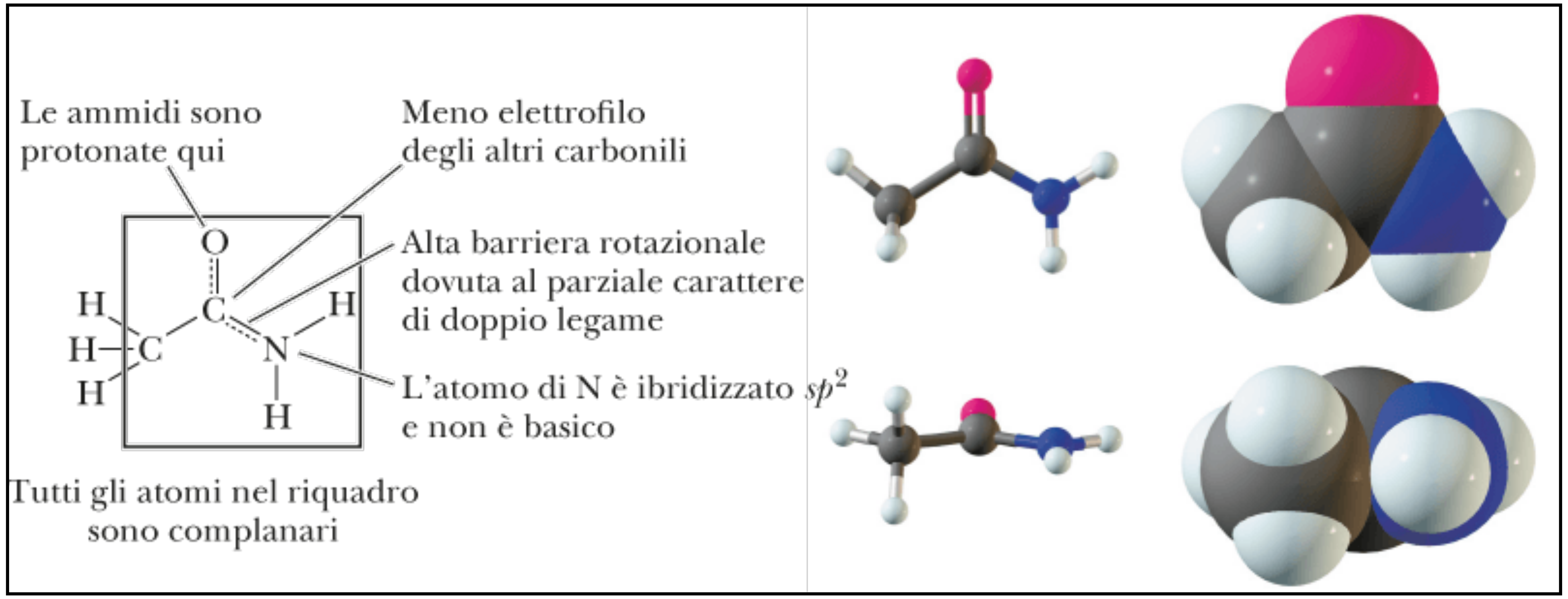
Phthalimide
pK_a 8.3

La particolare struttura dei legami ammidici



Questa struttura limite di risonanza colloca un doppio legame tra C e N





Le ammidi sono protonate qui

Meno elettrofilo degli altri carbonili

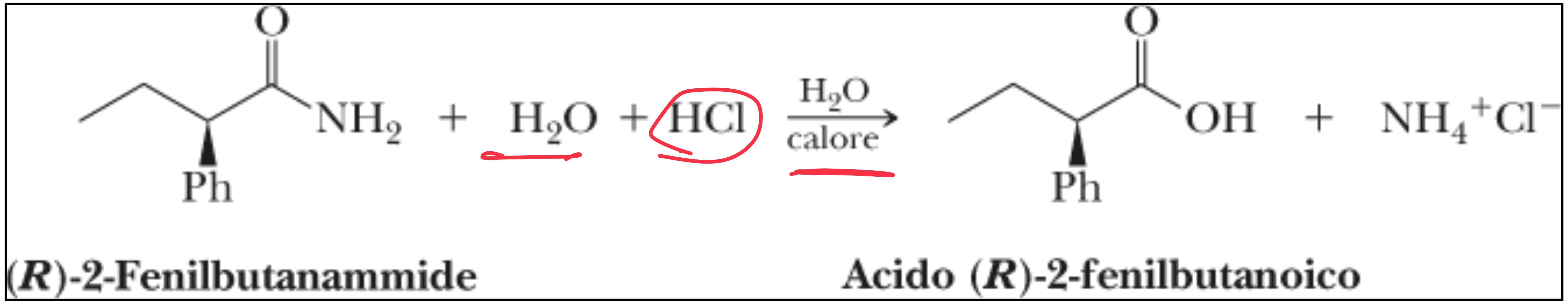
Alta barriera rotazionale dovuta al parziale carattere di doppio legame

L'atomo di N è ibridizzato *sp*^{2} e non è basico

Tutti gli atomi nel riquadro sono complanari

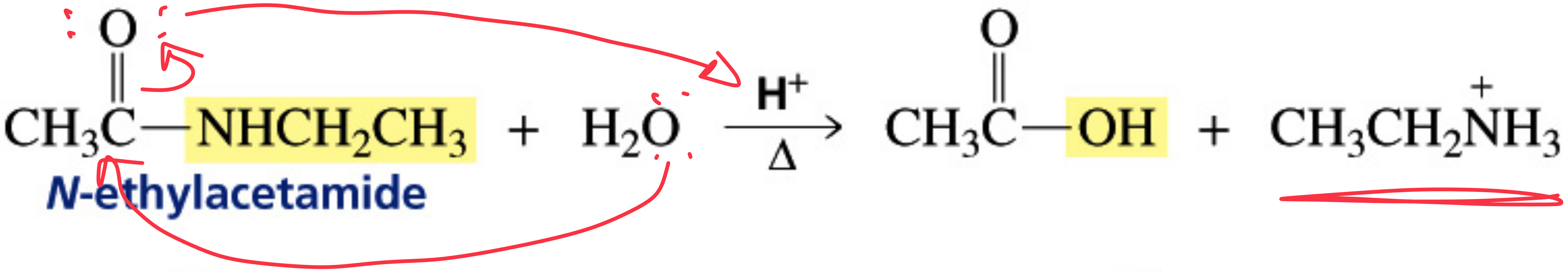
La presenza di un parziale doppio legame (legame π) nell'ibrido di risonanza indica che la rotazione attorno al legame C—N è impedita.

D. Idrolisi di un'ammide in un acido acquoso



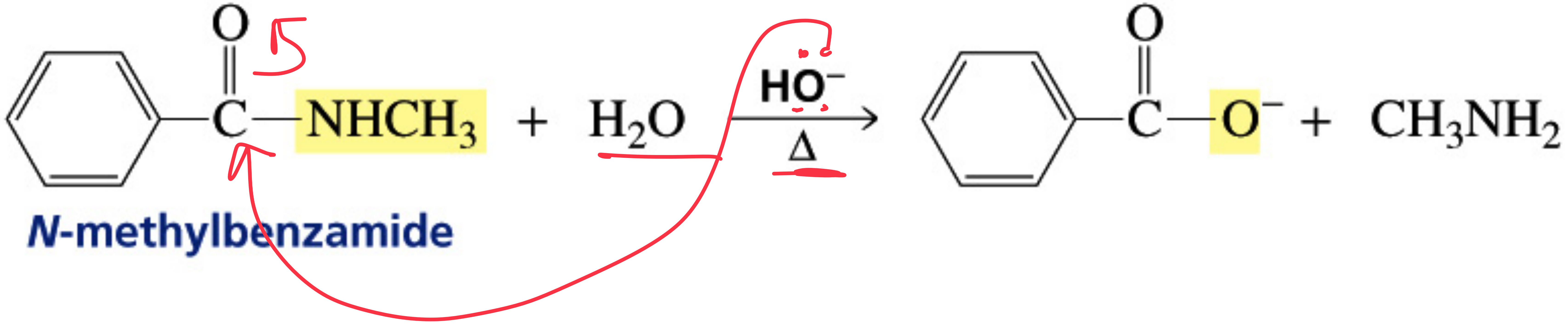
(*R*)-2-Fenilbutanammide

Acido (*R*)-2-fenilbutanoico



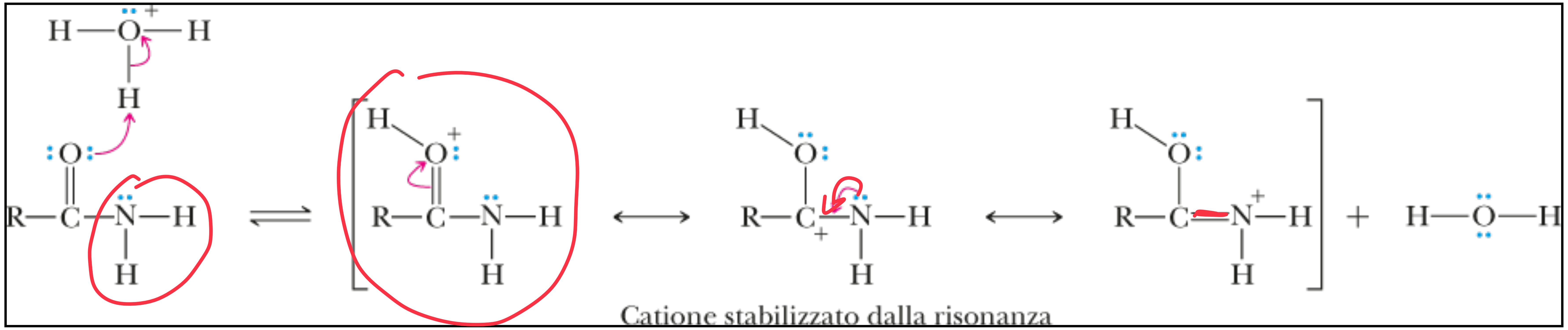
$$CH_3\overset{O}{\overset{\|}{C}}-NHCH_2CH_3 + H_2O \xrightarrow[\Delta]{H^+} CH_3\overset{O}{\overset{\|}{C}}-OH + CH_3CH_2\overset{+}{N}H_3$$

N-ethylacetamide

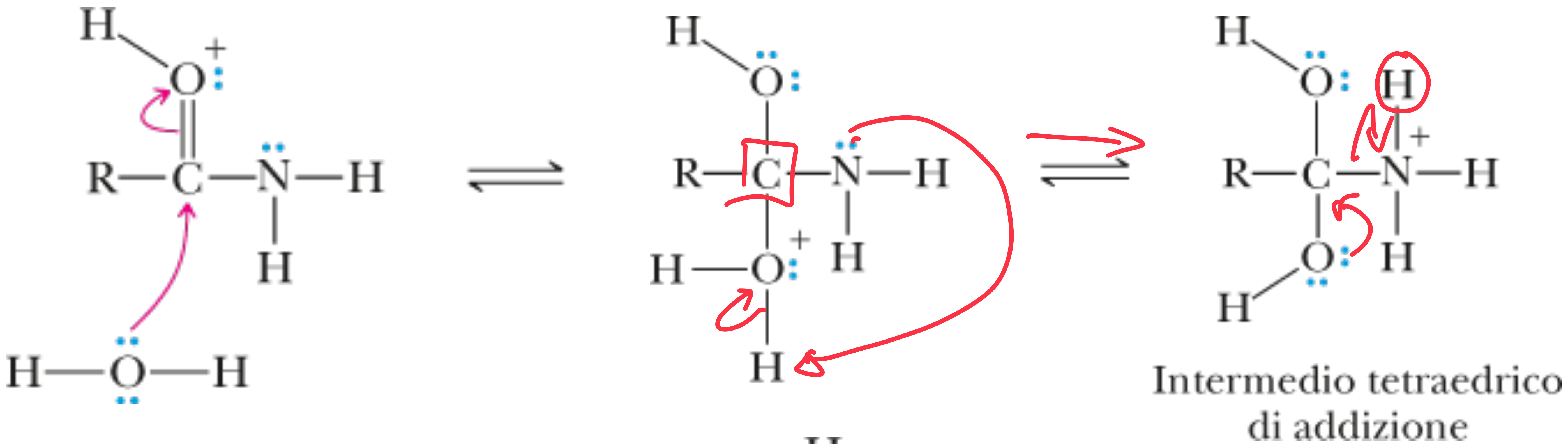


N-methylbenzamide

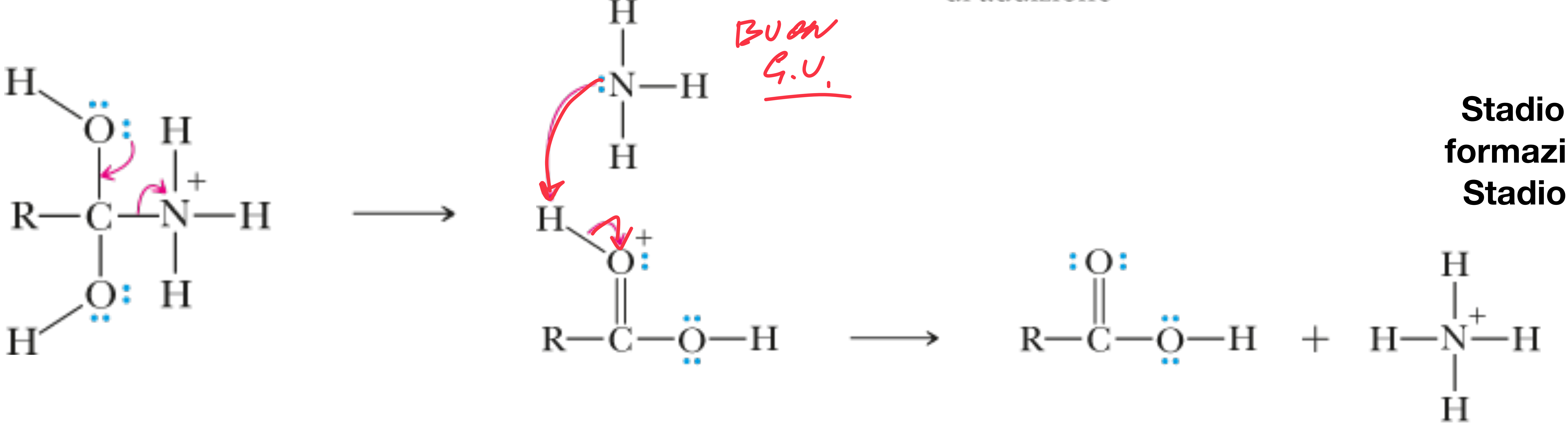
D. MECCANISMO: Idrolisi di un'ammide in un acido acquoso



Stadio 1 Addizione di un protone

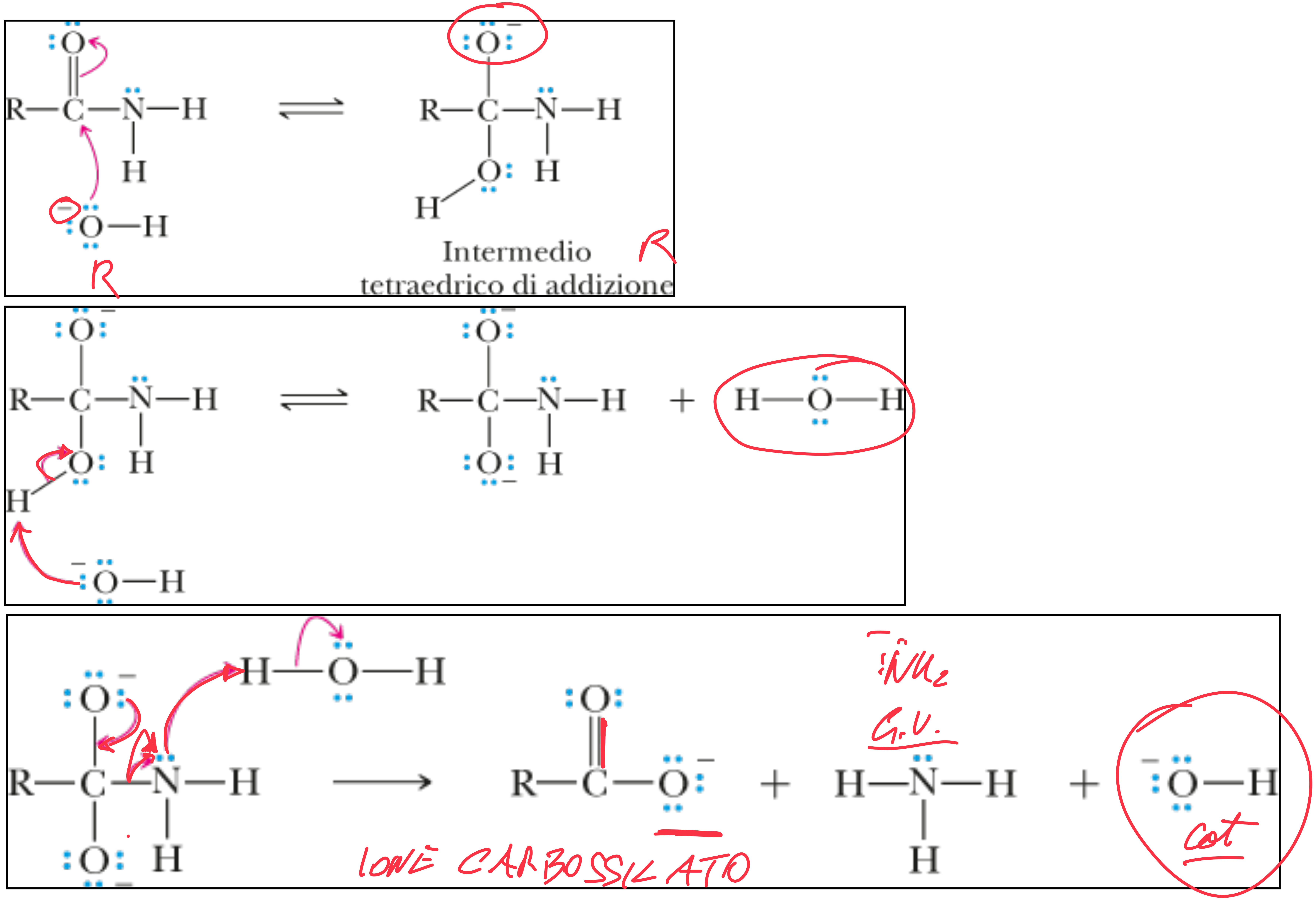


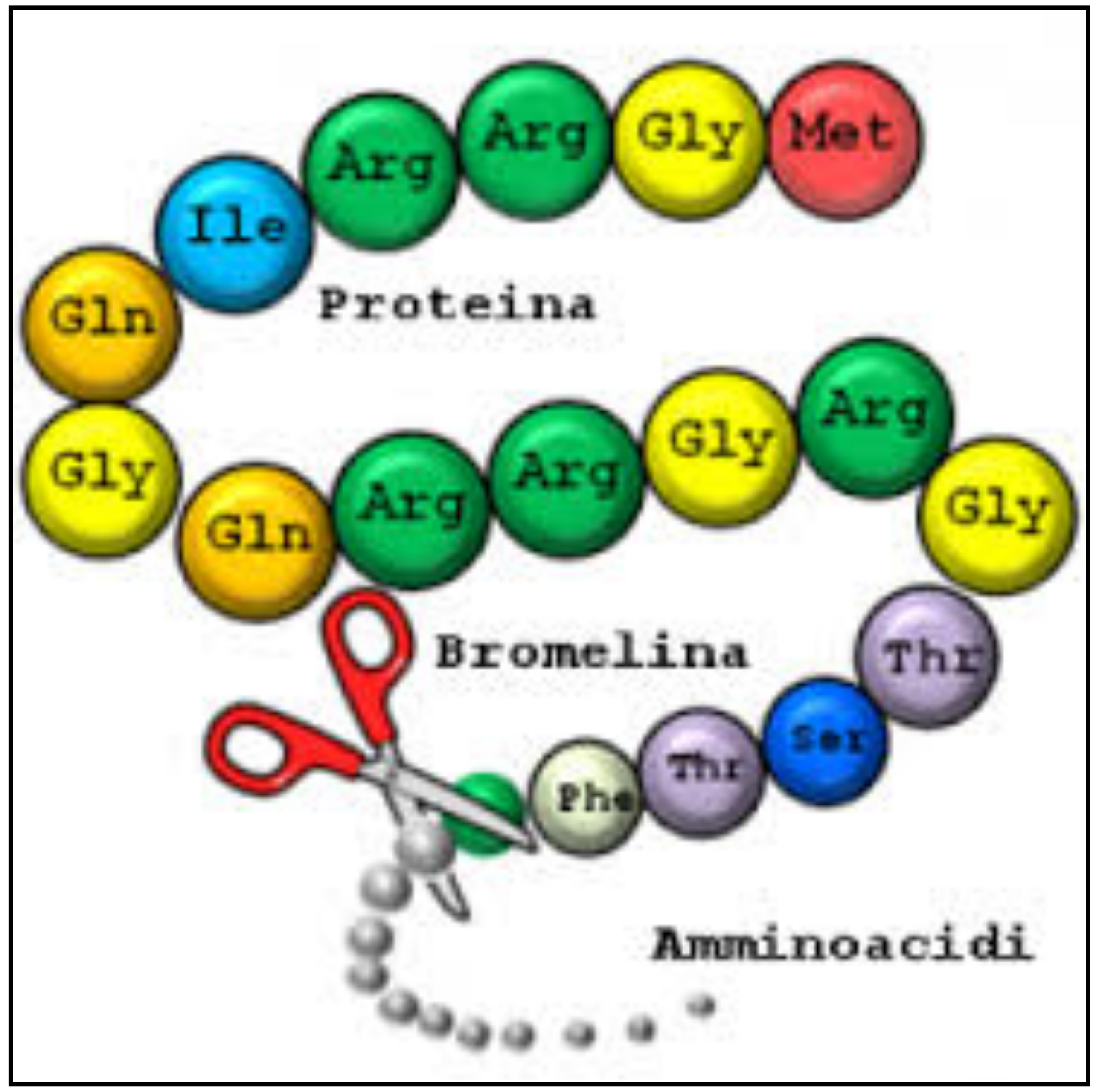
Stadio 2 Formazione di un nuovo legame tra un nucleofilo e un elettrofilo
Stadio 3 Rimozione di un protone/addizione di un protone.



Stadio 4 Rottura di un legame con formazione di molecole o ioni stabili
Stadio 5 Rimozione di un protone.

D. MECCANISMO: Idrolisi di un'ammide in una base acquosa





6 enzimas que ayudan a la digestión

PAPAÍNA - Papaya

Es excelente para descomponer proteínas. Se encuentra tanto en la papaya como en forma de suplementos.

LIPASA - Papaya y Aloe

Facilita la digestión.

GLUTATIÓN PEROXIDASA - Espárrago

Mejora la función hepática.

BROMELINA - Piña

Presente en el jugo de la piña, ayuda a la digestión de proteínas.

ALINASA - Ajo

Aunque es mejor conocida por sus propiedades antibióticas, es excelente para regular el colesterol.

ZINGIBAÍNA - Jengibre

Es excelente para prevenir la indigestión, especialmente después de consumir gran cantidad de proteína.

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Enzimi vegetali

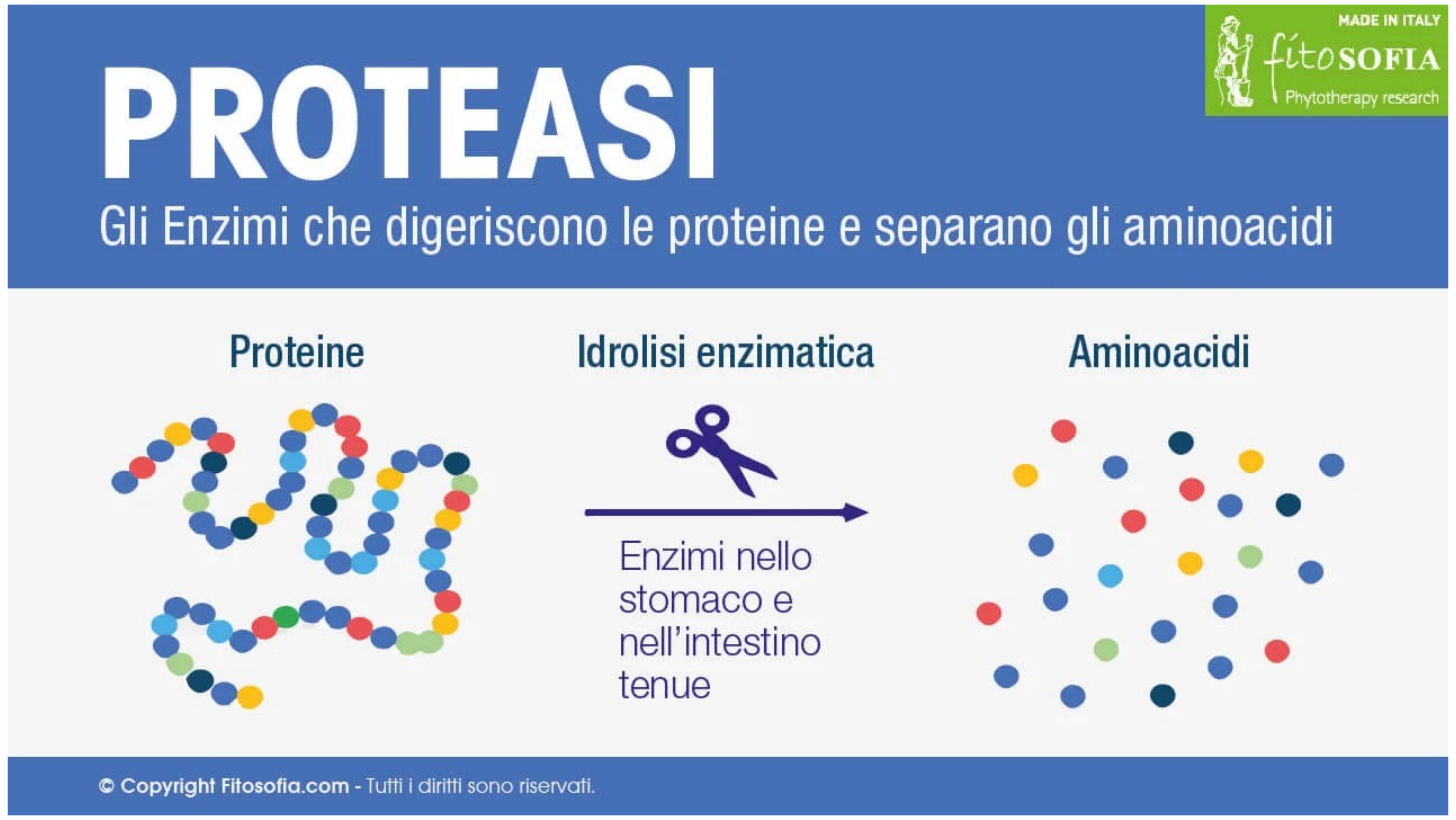
340 mg Bromelina, 170 mg Papaina ogni capsula.

Offerta: Acquista 3 contenitori, ottenere 4. uno gratuitamente

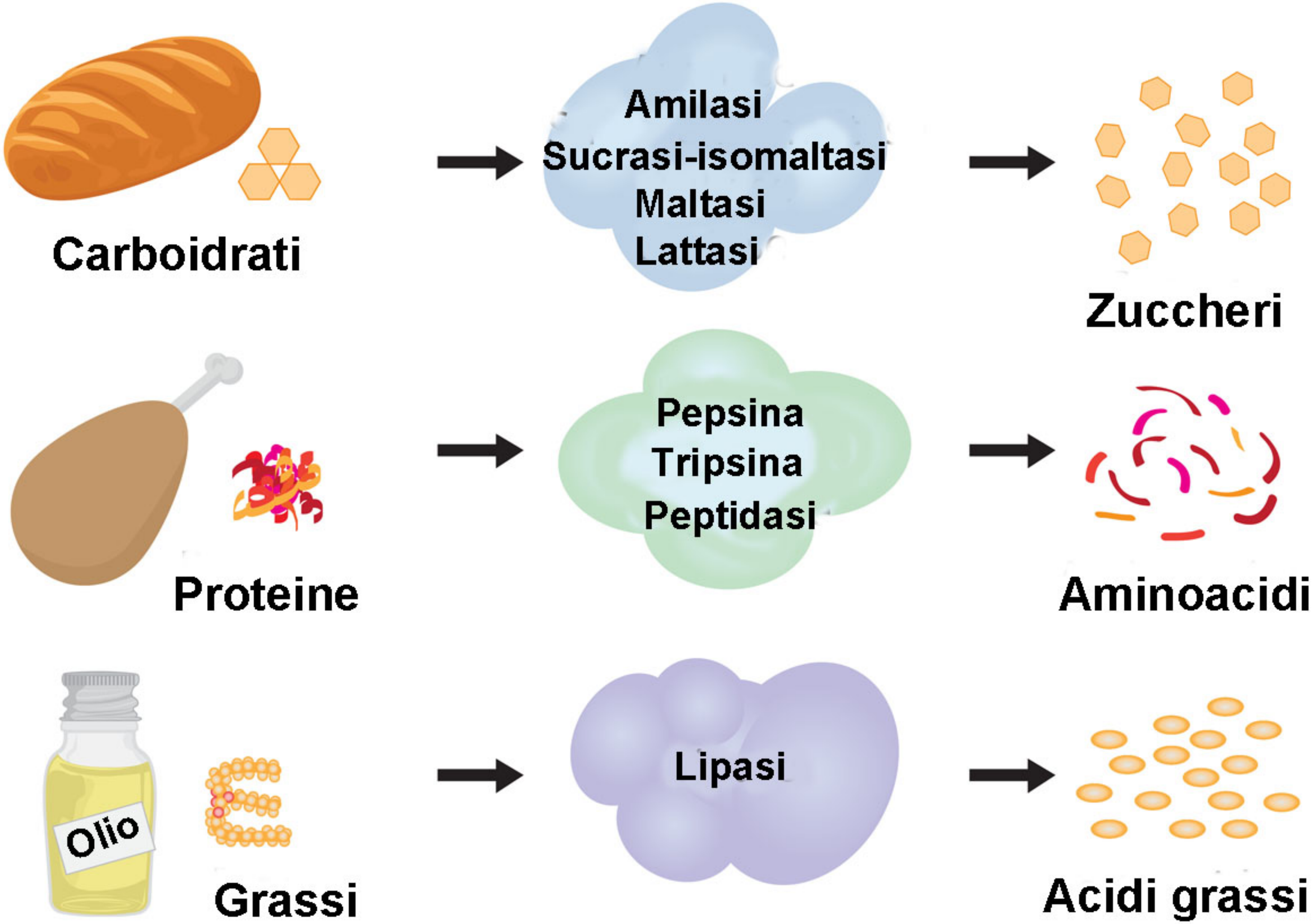
34,90 € 100 Capsule

(54,11 €/100g ; € 0,35 €/Capsula) IVA inclusa più Spese di spedizione

Termine di consegna 1-3 giorni



ENZIMI DIGESTIVI



Carboidrati → Amilasi, Sucrasi-isomaltasi, Maltasi, Lattasi → Zuccheri

Proteine → Pepsina, Tripsina, Peptidasi → Aminoacidi

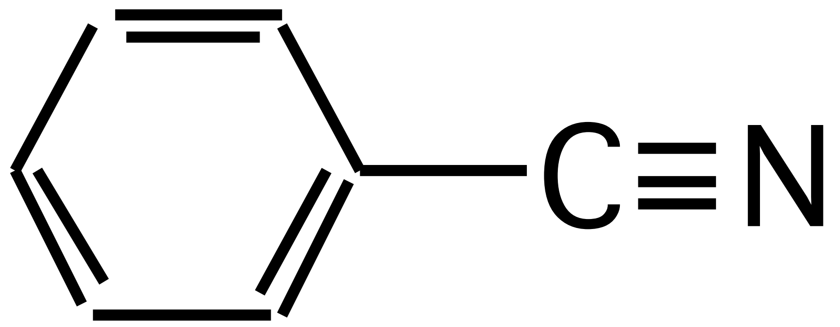
Grassi → Lipasi → Acidi grassi

NITRILI - ALCANONITRILE

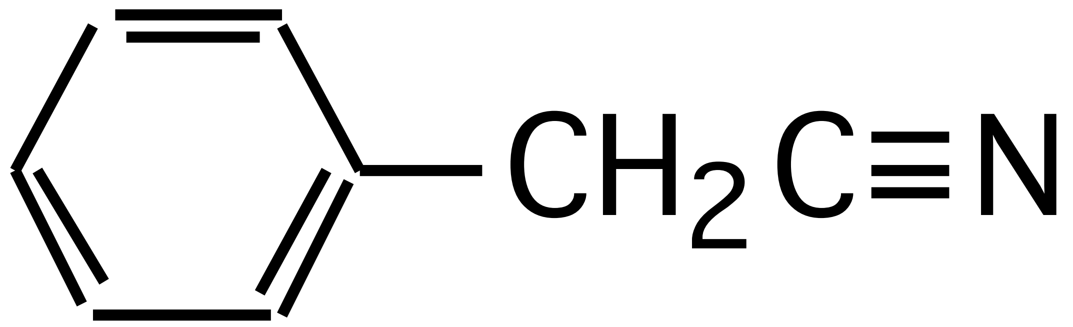
Gruppo funzionale: CIANO

$CH_3C\equiv N$

Ethanenitrile
(Acetonitrile)

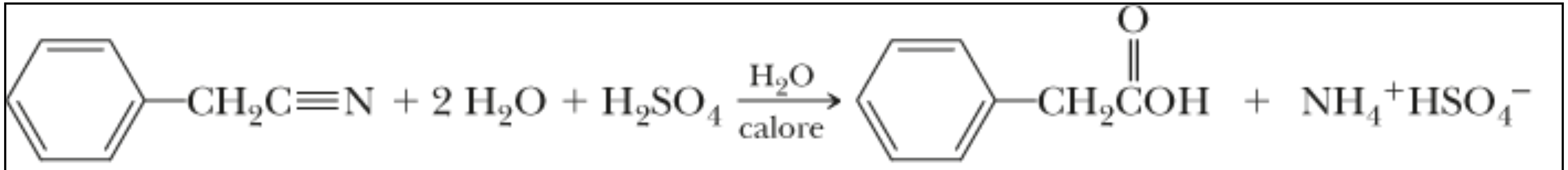


Benzonitrile

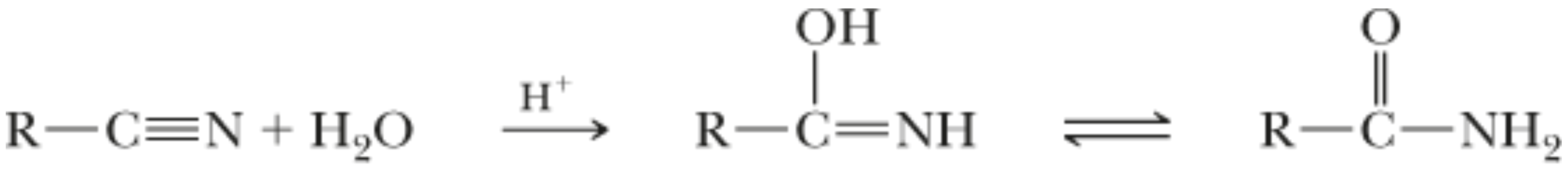


Phenylethanenitrile
(Phenylacetonitrile)

E. Idrolisi dei nitrili



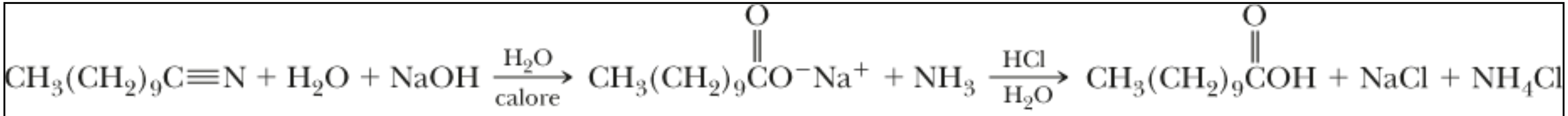
Fenilacetonitrile **Acido fenilacetico** **Idrogenosolfato di ammonio**



$$R-C\equiv N + H_2O \xrightarrow{H^+} R-\overset{OH}{\overset{|}{C}}=NH \rightleftharpoons R-\overset{O}{\overset{\|}{C}}-NH_2$$

Acido immidico
(enolo di un'ammide)

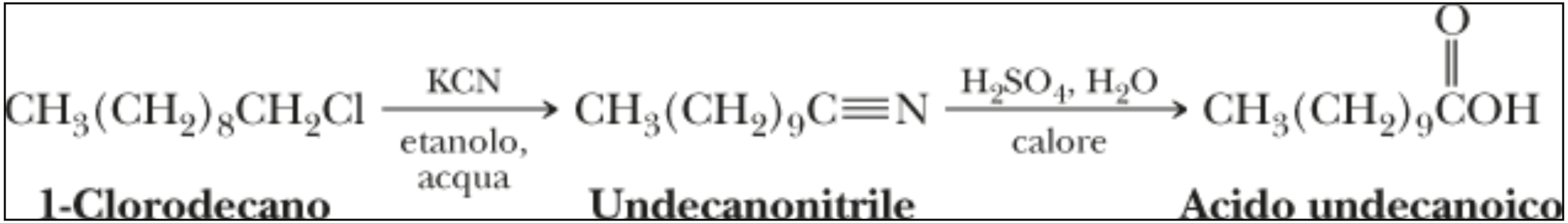
Ammide



$$CH_3(CH_2)_9C\equiv N + H_2O + NaOH \xrightarrow[\text{calore}]{H_2O} CH_3(CH_2)_9\overset{O}{\overset{\|}{C}}O^-Na^+ + NH_3 \xrightarrow[H_2O]{HCl} CH_3(CH_2)_9\overset{O}{\overset{\|}{C}}OH + NaCl + NH_4Cl$$

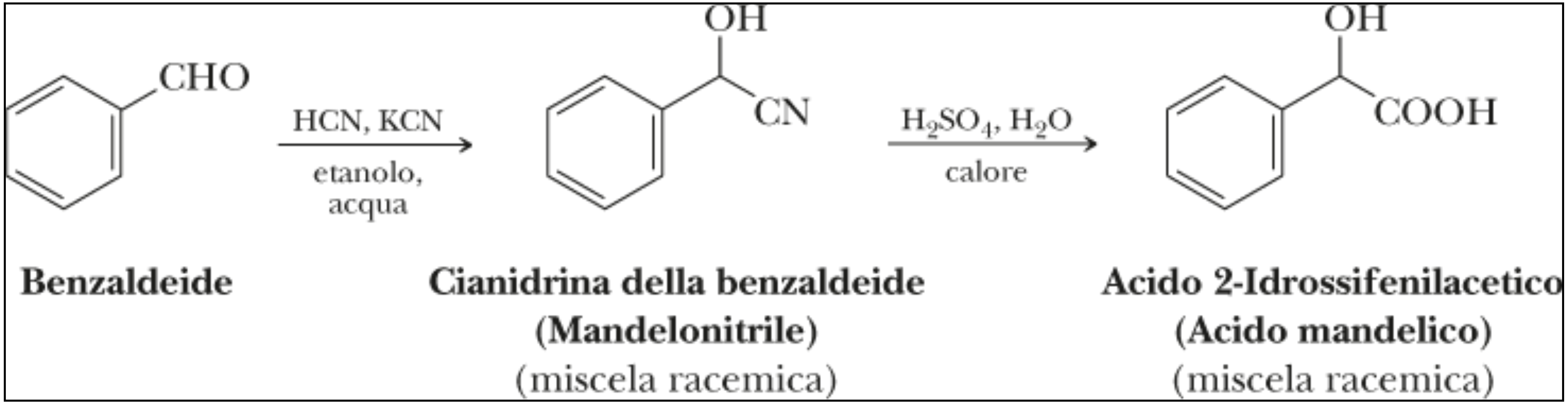
Undecanonitrile **Undecanoato di sodio** **Acido undecanoico**

E. Idrolisi dei nitrili



$$CH_3(CH_2)_8CH_2Cl \xrightarrow[\text{etanolo, acqua}]{KCN} CH_3(CH_2)_9C{\equiv}N \xrightarrow[\text{calore}]{H_2SO_4,\ H_2O} CH_3(CH_2)_9\overset{\overset{\displaystyle O}{\|}}{C}OH$$

1-Clorodecano **Undecanonitrile** **Acido undecanoico**

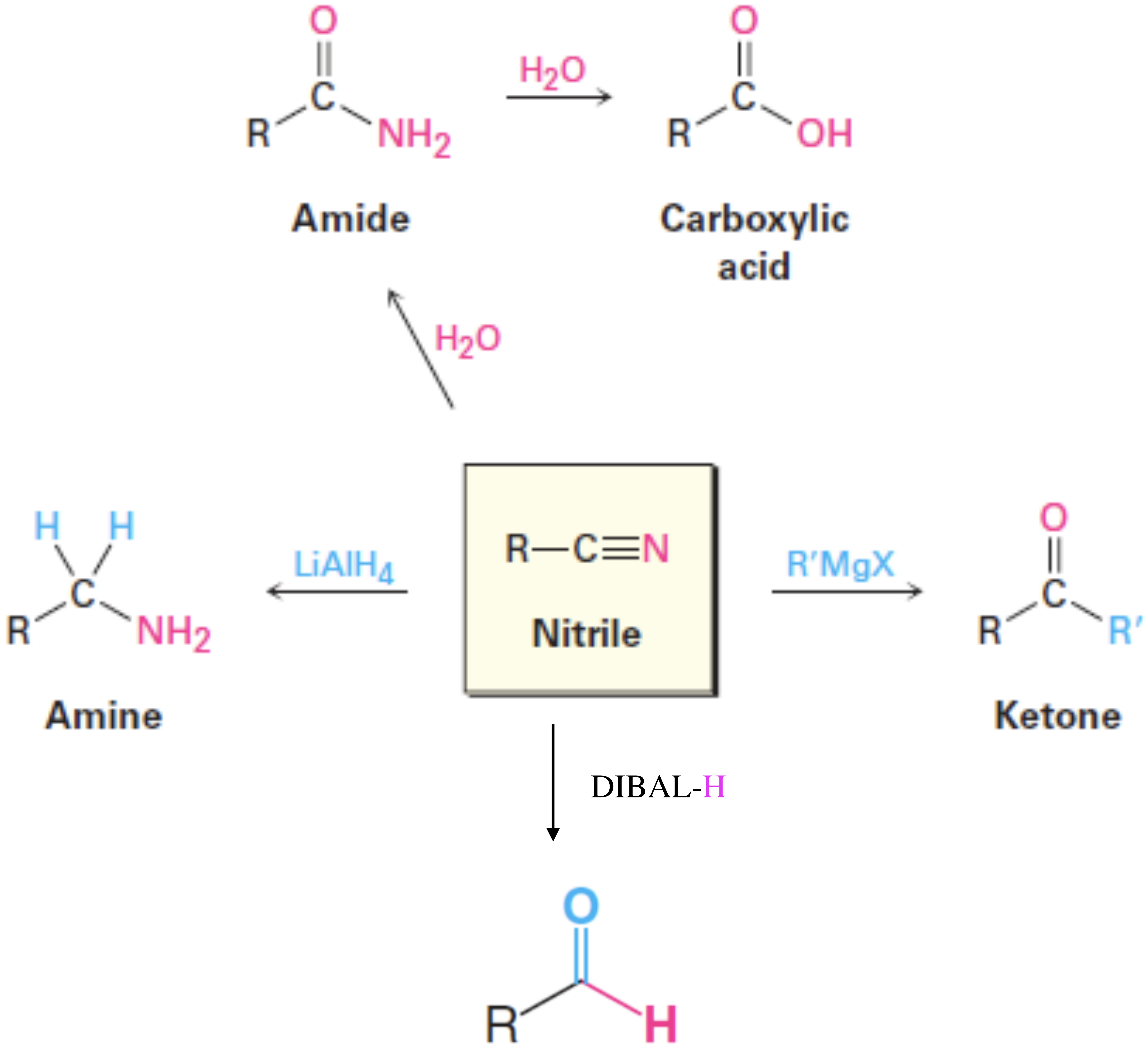


Benzaldeide

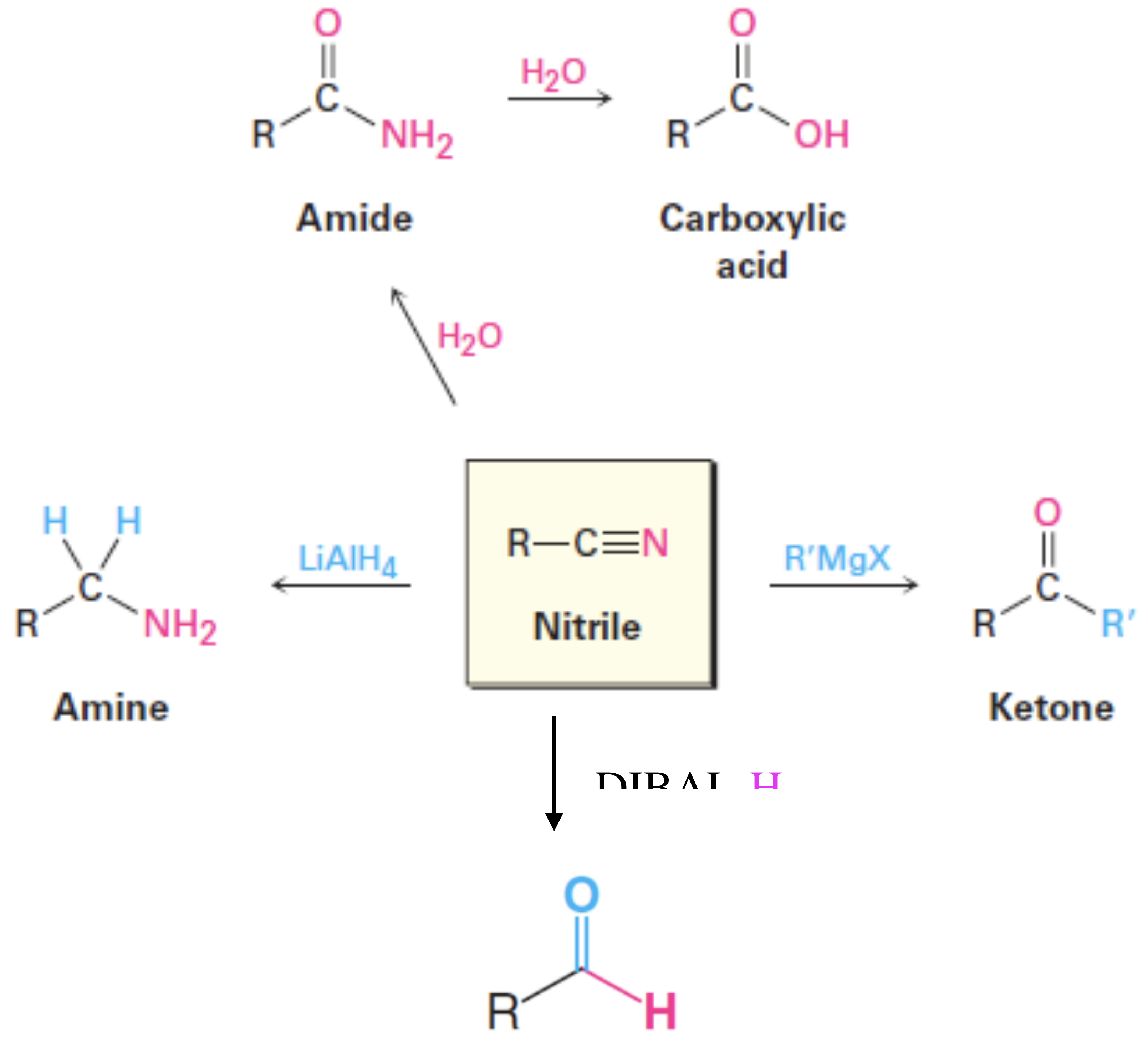
Cianidrina della benzaldeide
(Mandelonitrile)
(miscela racemica)

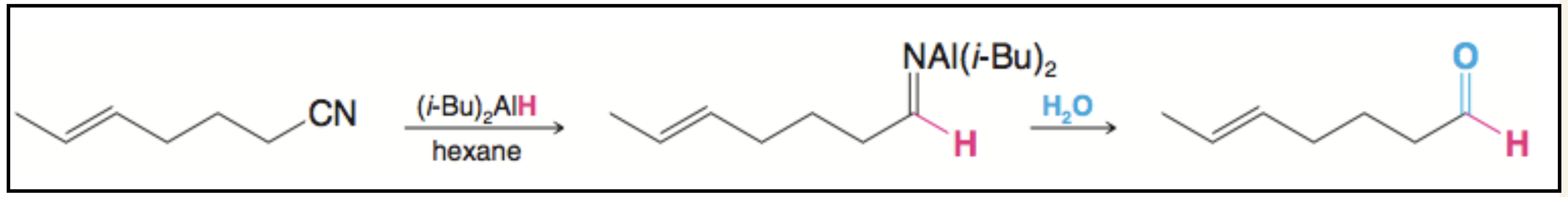
Acido 2-Idrossifenilacetico
(Acido mandelico)
(miscela racemica)

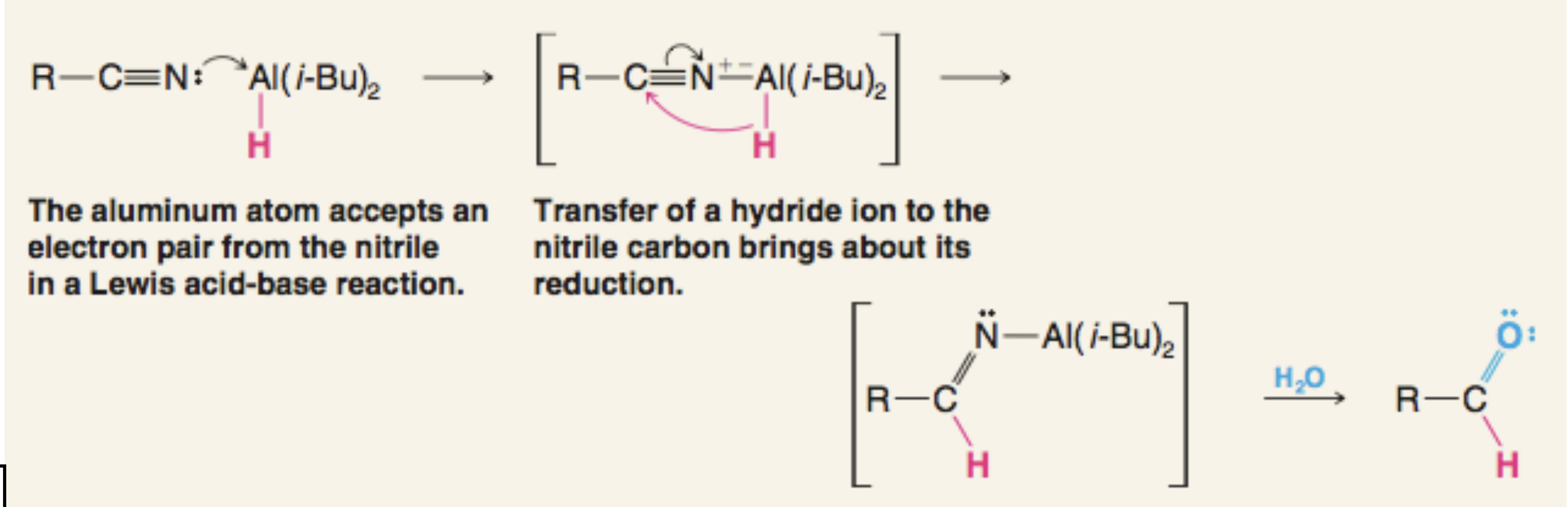
E. Reazioni dei nitrili



E. Reazioni dei nitrili







The aluminum atom accepts an electron pair from the nitrile in a Lewis acid-base reaction.

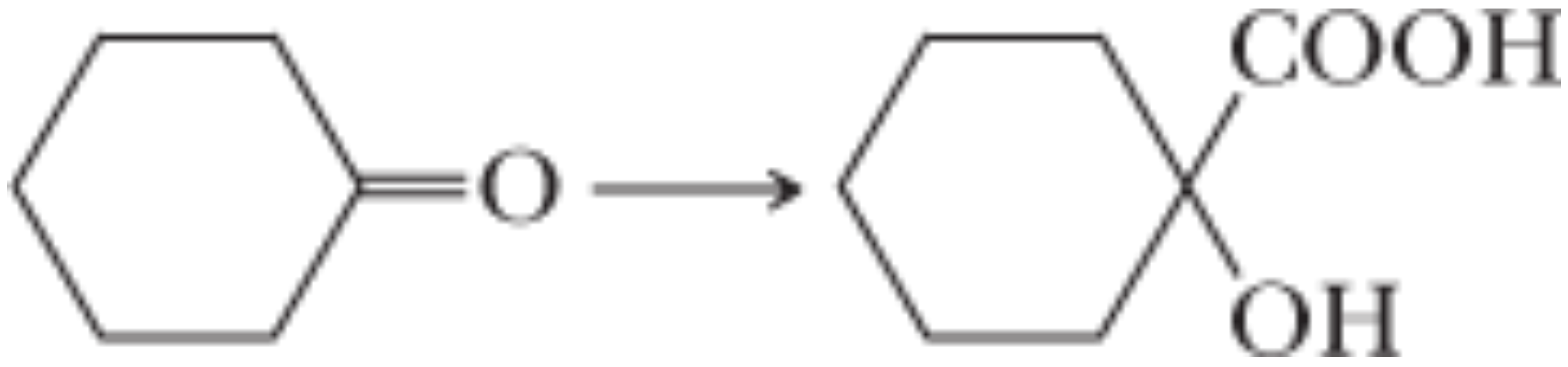
Transfer of a hydride ion to the nitrile carbon brings about its reduction.

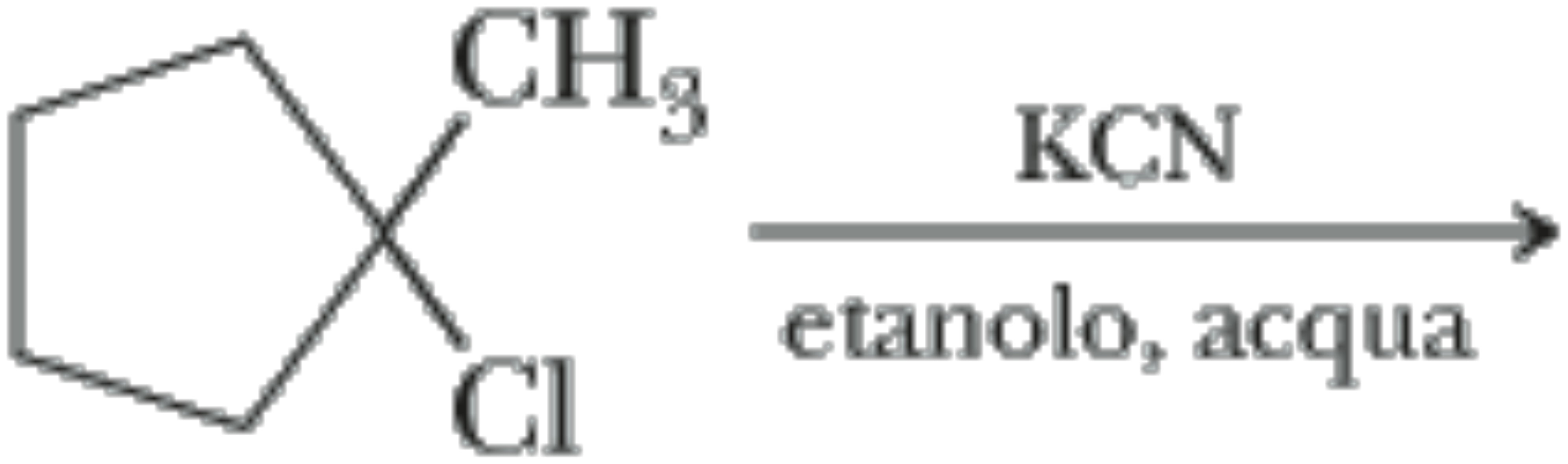
Addition of water at the end of the reaction hydrolyzes the aluminum complex and produces the aldehyde. (Several steps are involved. See Section 16.8 relating to imines.)

PROBLEMA: Mostrare come fare avvenire le seguenti trasformazioni sfruttando l'idrolisi di un gruppo ciano.

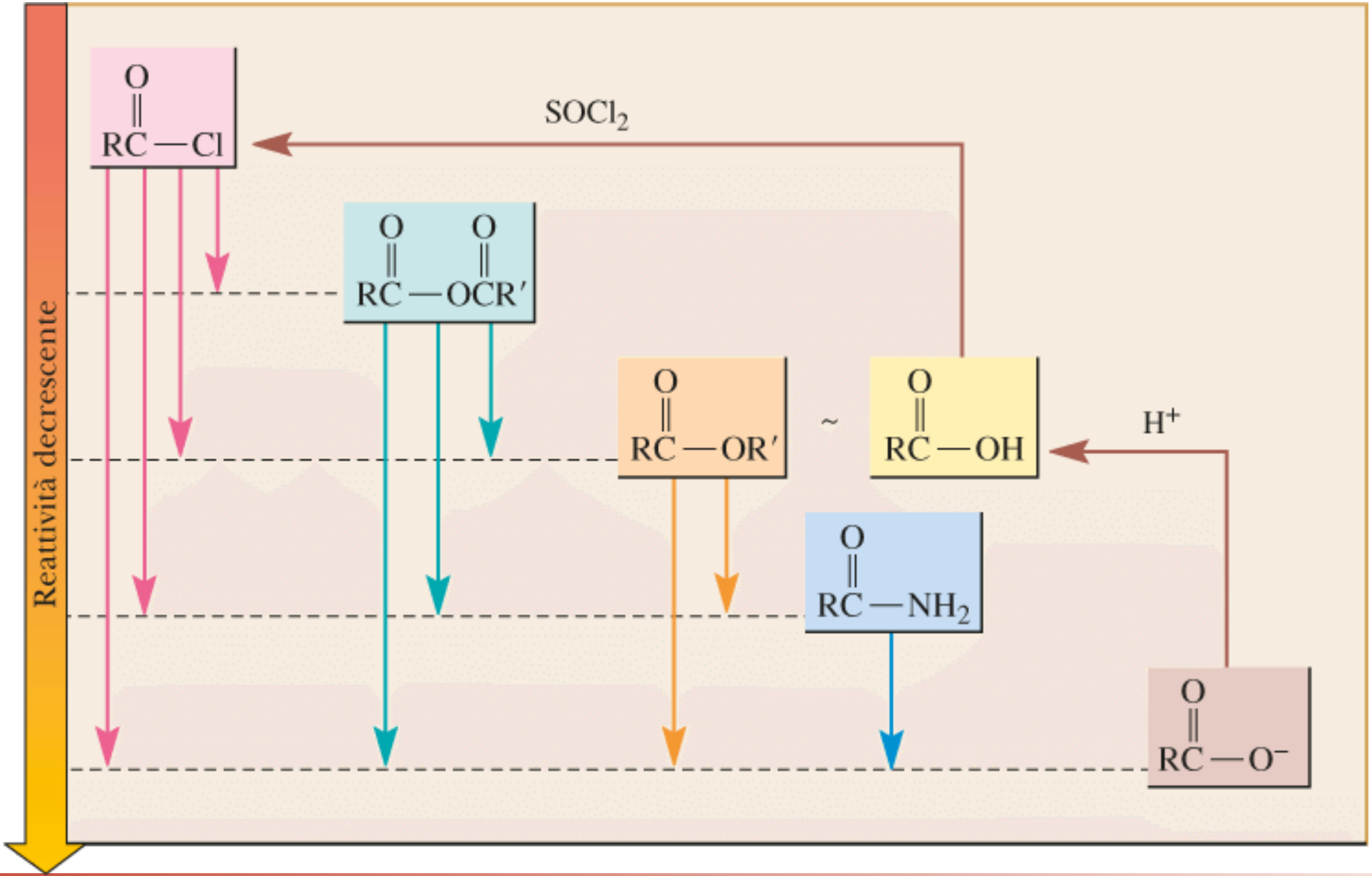
4-Cloroeptano

Acido 2-propilpentanoico
(Acido valproico)



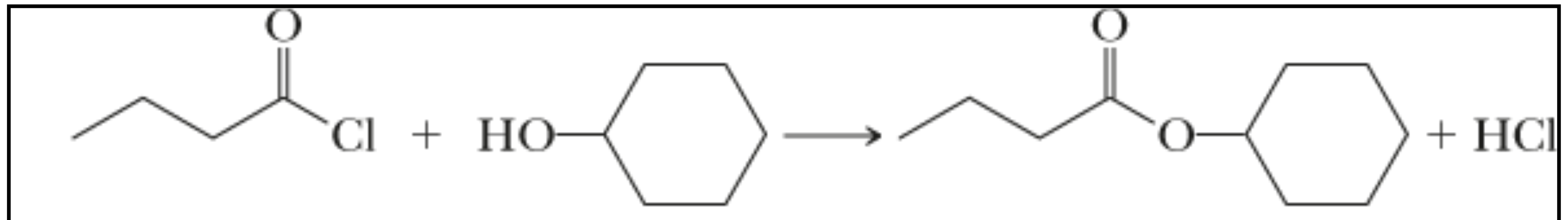


Interconversione dei derivati funzionali

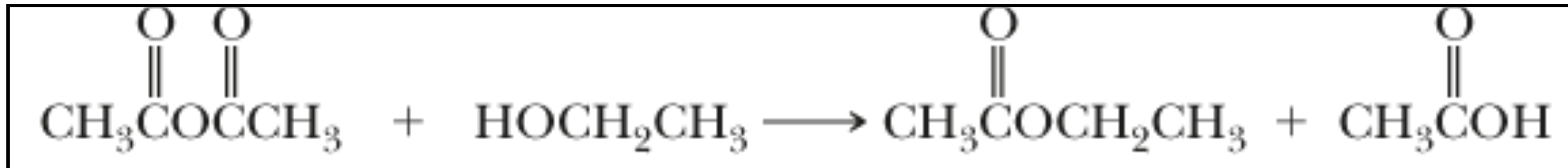


Reazione con gli alcoli

- **A.** **Alogenuri acilici**
- **B.** **Anidridi degli acidi**
- **C.** **Esteri**

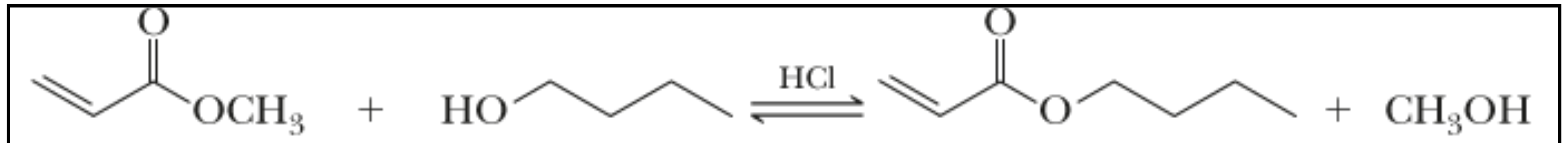


Cloruro di butanoile Cicloesanolo Cicloesil butanoato

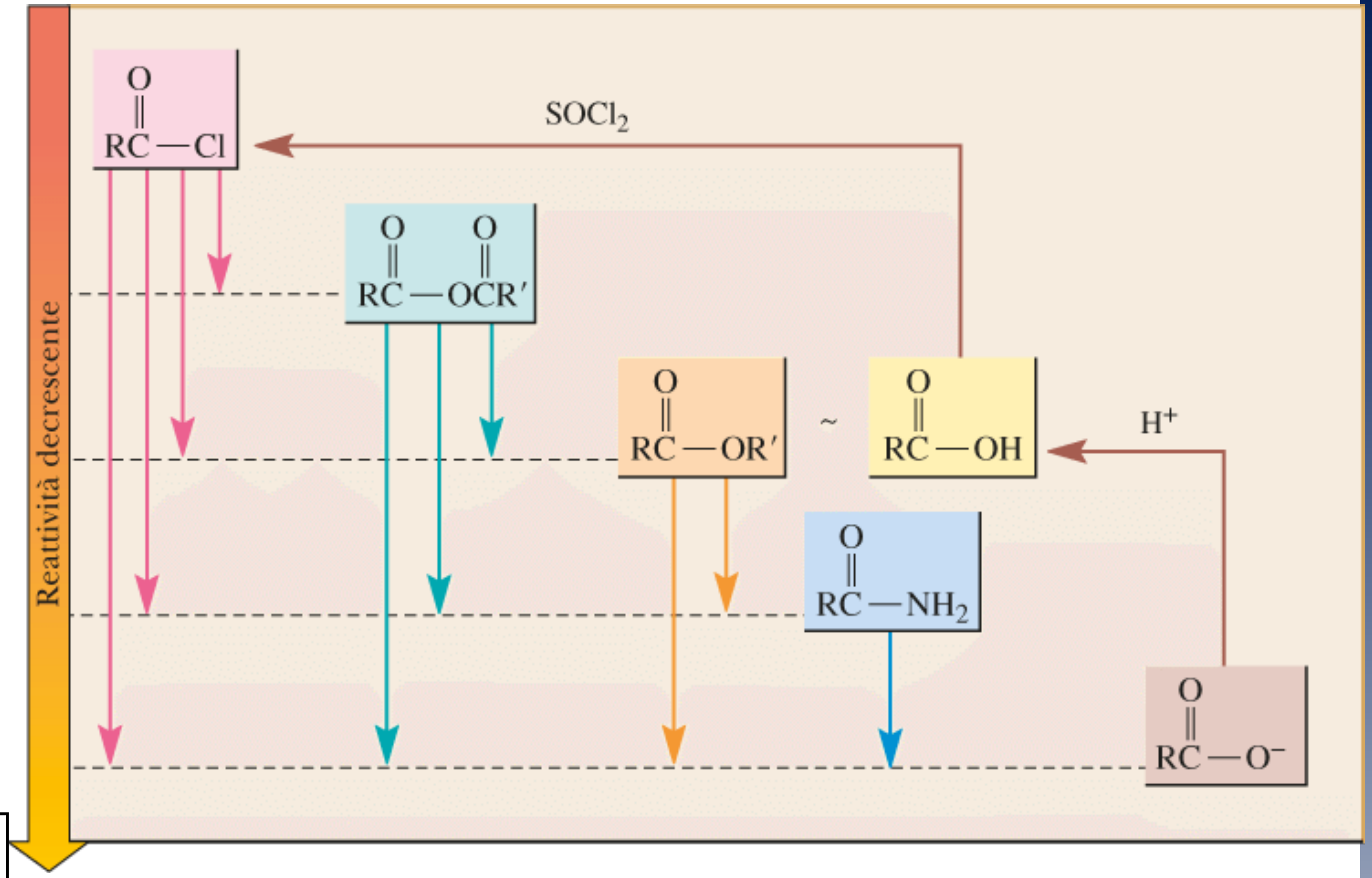


$$CH_3\overset{O}{\overset{\|}{C}}O\overset{O}{\overset{\|}{C}}CH_3 + HOCH_2CH_3 \longrightarrow CH_3\overset{O}{\overset{\|}{C}}OCH_2CH_3 + CH_3\overset{O}{\overset{\|}{C}}OH$$

Anidride acetica Etanolo Etil acetato Acido acetico



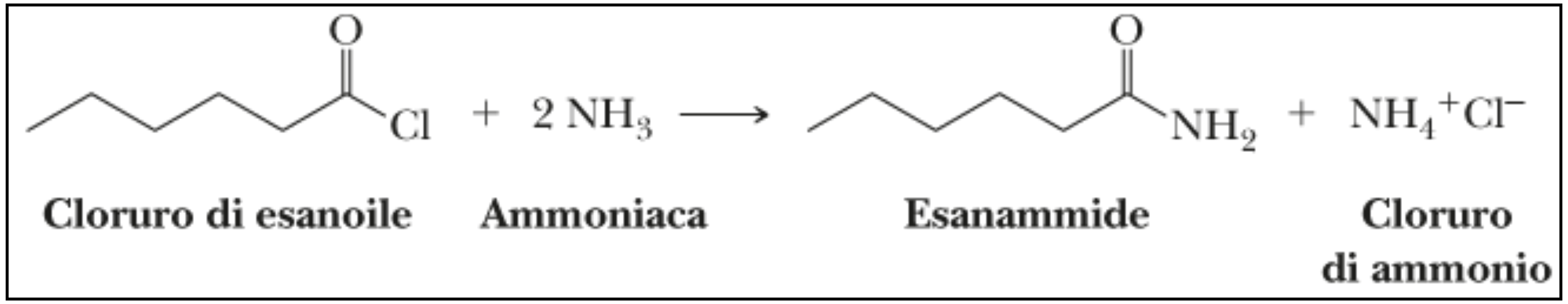
Metil propenoato (Metil acrilato) (p.e. 81 °C) 1-Butanolo (p.e. 117 °C) Butil propenoato (Butil acrilato) (p.e. 147 °C) Metanolo (p.e. 65 °C)

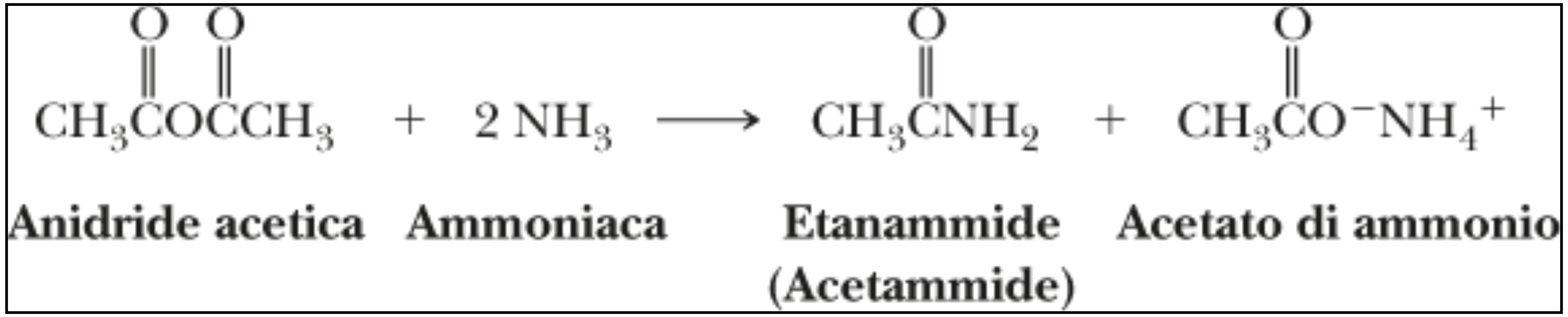


Le ammidi, i derivati funzionali degli acidi carbossilici meno reattivi, non reagiscono con gli alcoli. Quindi, la reazione di un'ammide con un alcol non può essere usata per preparare un estere.

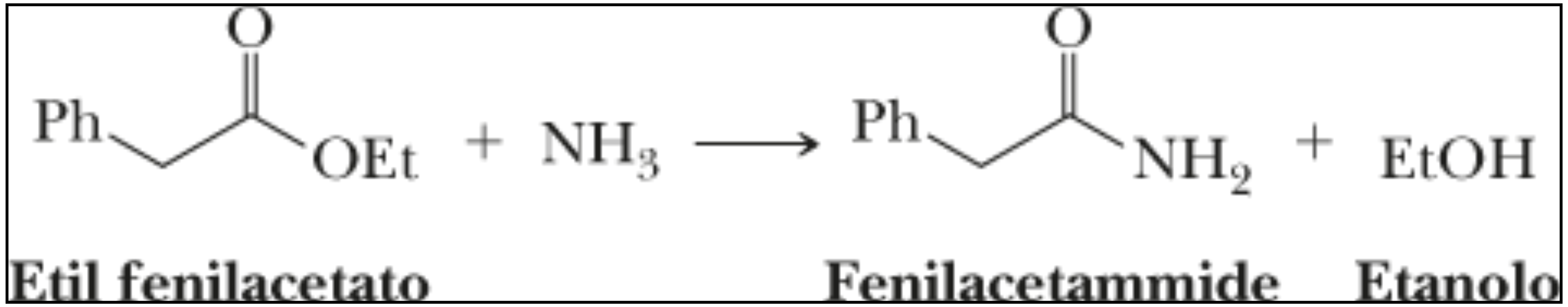
Reazioni con ammoniaca e ammine

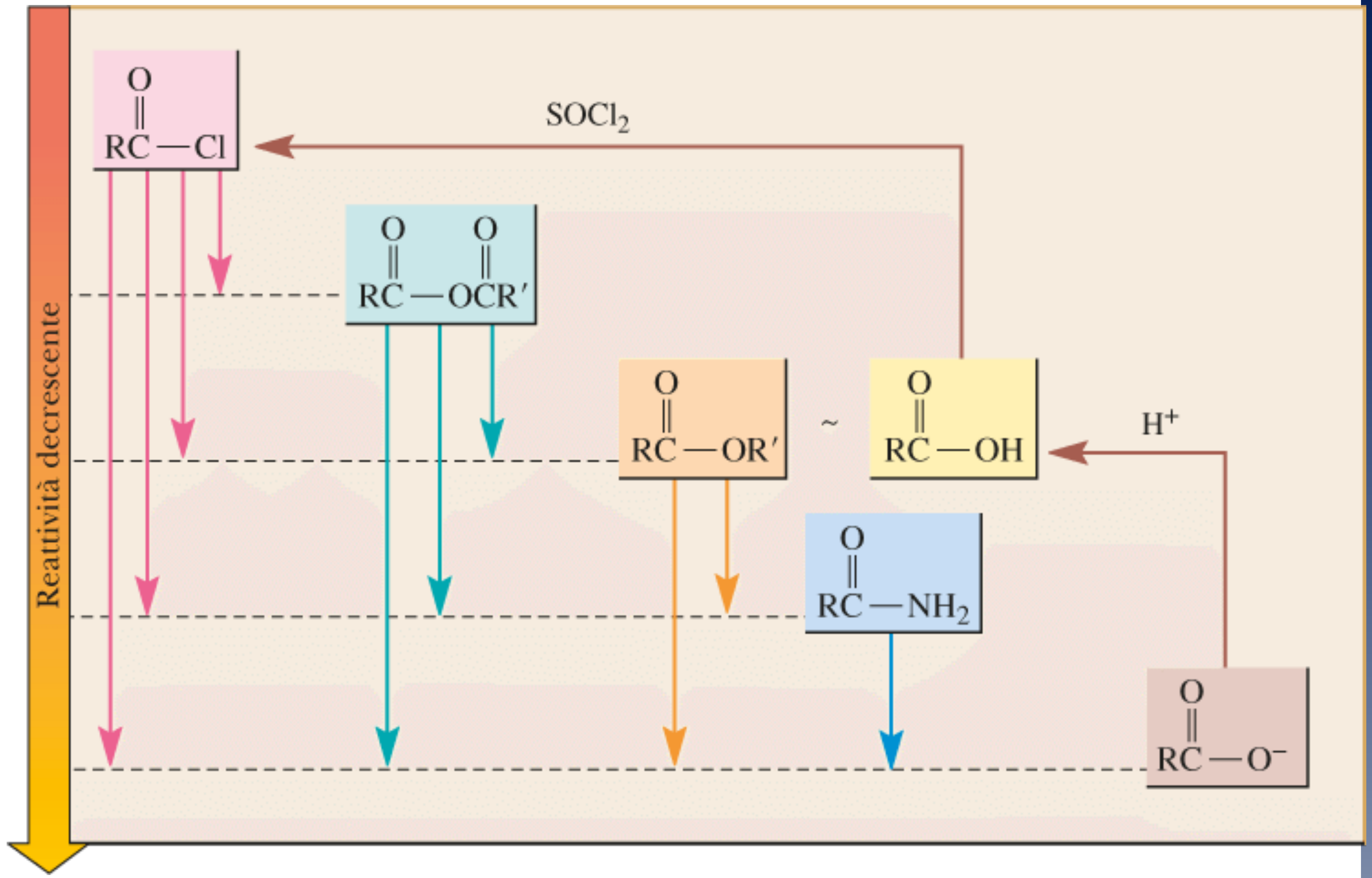
- **A.** Alogenuri acilici
- **B.** Anidridi degli acidi
- **C.** Esteri





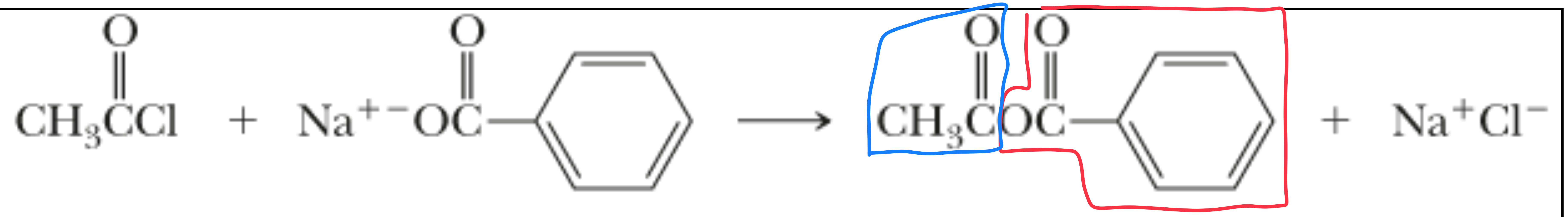
$$CH_3\overset{O}{\overset{\|}{C}}O\overset{O}{\overset{\|}{C}}CH_3 + 2\,NH_3 \longrightarrow CH_3\overset{O}{\overset{\|}{C}}NH_2 + CH_3\overset{O}{\overset{\|}{C}}O^-NH_4^+$$





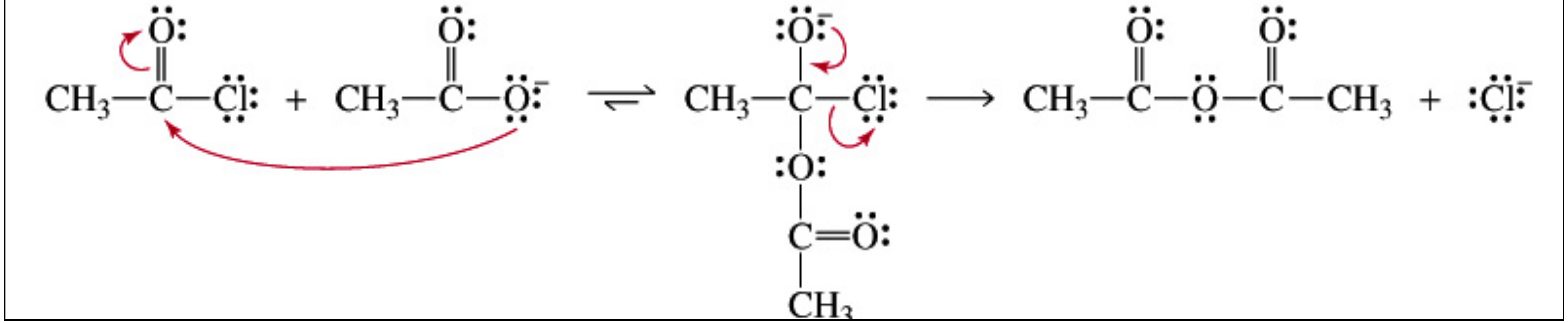
Le ammidi non reagiscono con l'ammoniaca né con le ammine primarie e secondarie.

Reazione dei cloruri acilici con i sali degli acidi carbossilici

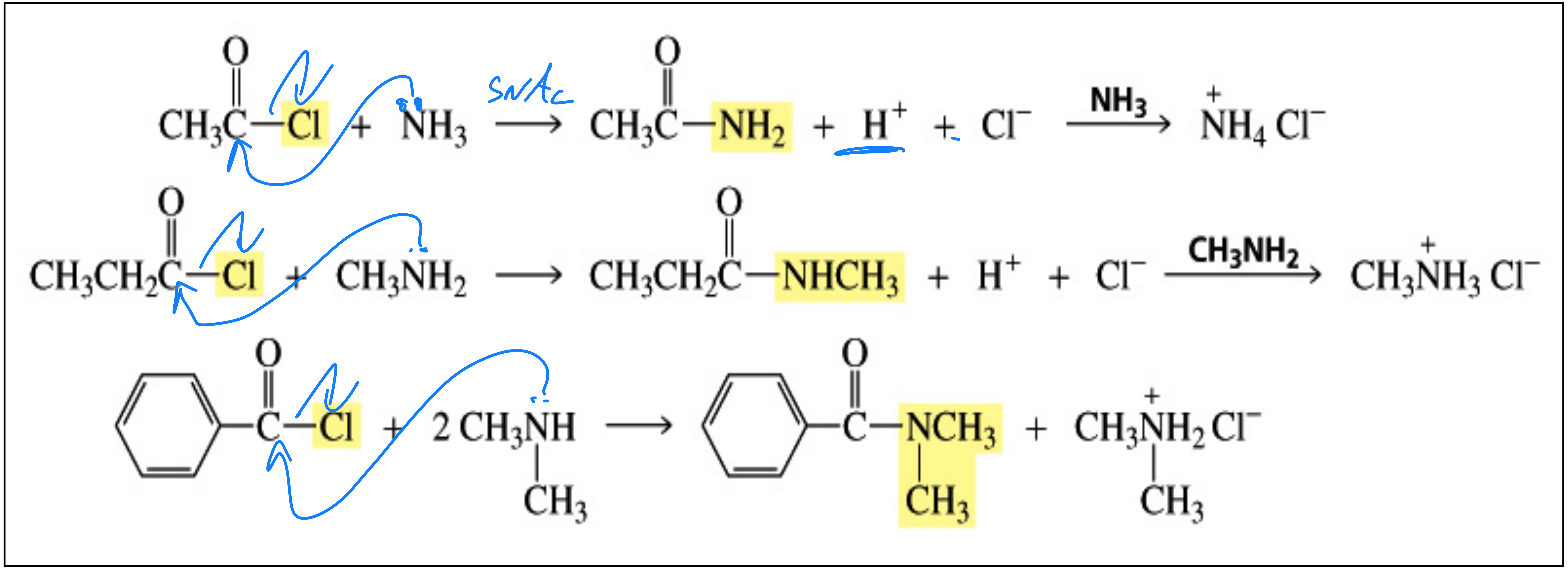


Cloruro di acetile Benzoato di sodio Anidride benzoica

mechanism for the conversion of an acyl chloride into an acid anhydride

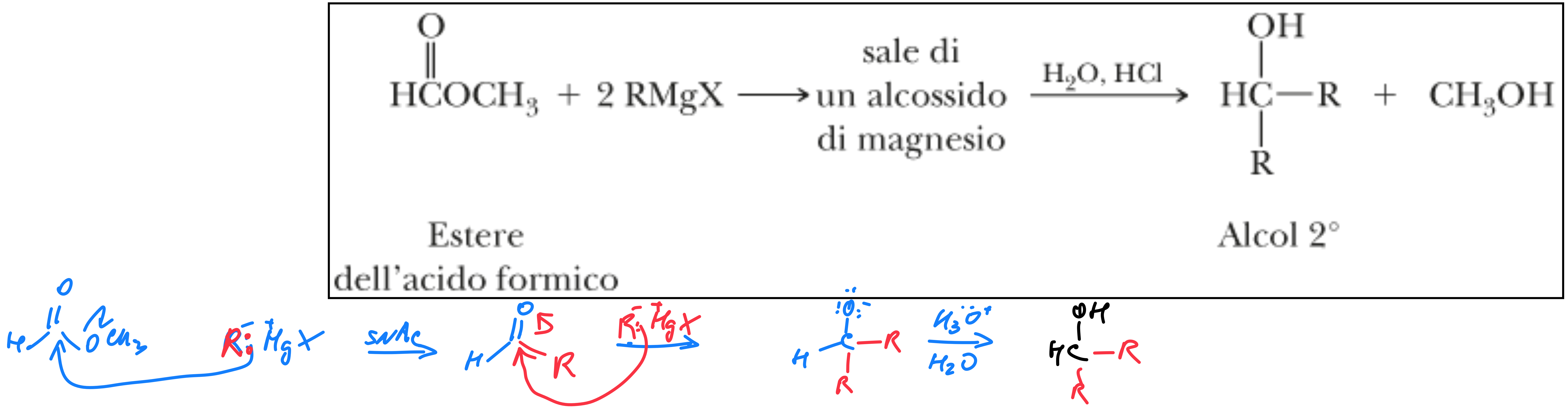


Reazione dei cloruri acilici con ammoniaca, ammine primarie e secondarie, ma non terziarie.



Reazioni con i composti organometallici

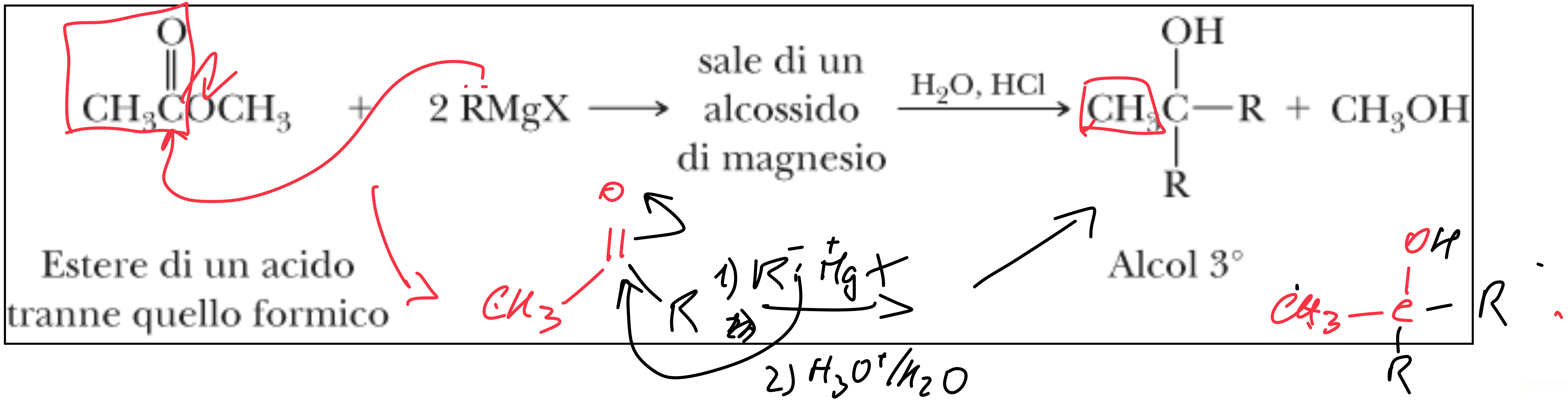
A. Reattivi di Grignard



$$HC(=O)OCH_3 + 2\,RMgX \longrightarrow \text{sale di un alcossido di magnesio} \xrightarrow{H_2O,\ HCl} HC(OH)(R)-R + CH_3OH$$

Estere dell'acido formico

Alcol 2°



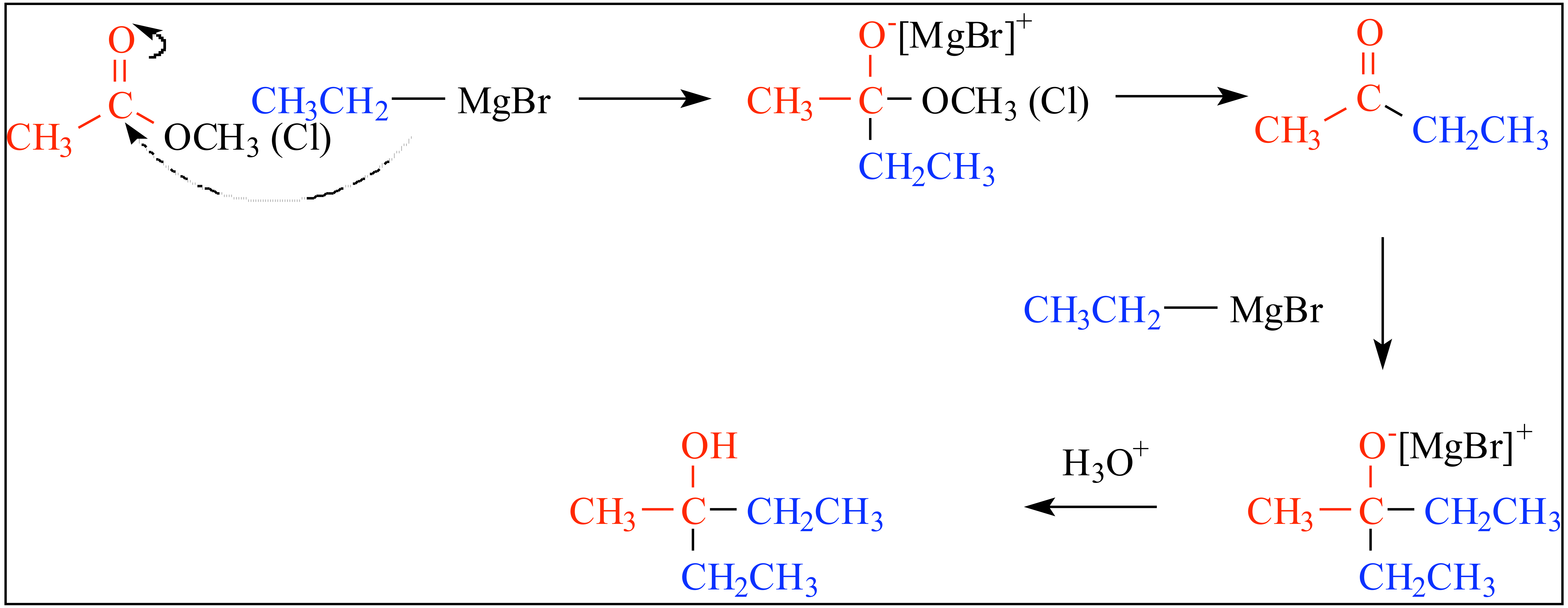
$$CH_3C(=O)OCH_3 + 2\,RMgX \longrightarrow \text{sale di un alcossido di magnesio} \xrightarrow{H_2O,\ HCl} CH_3C(OH)(R)-R + CH_3OH$$

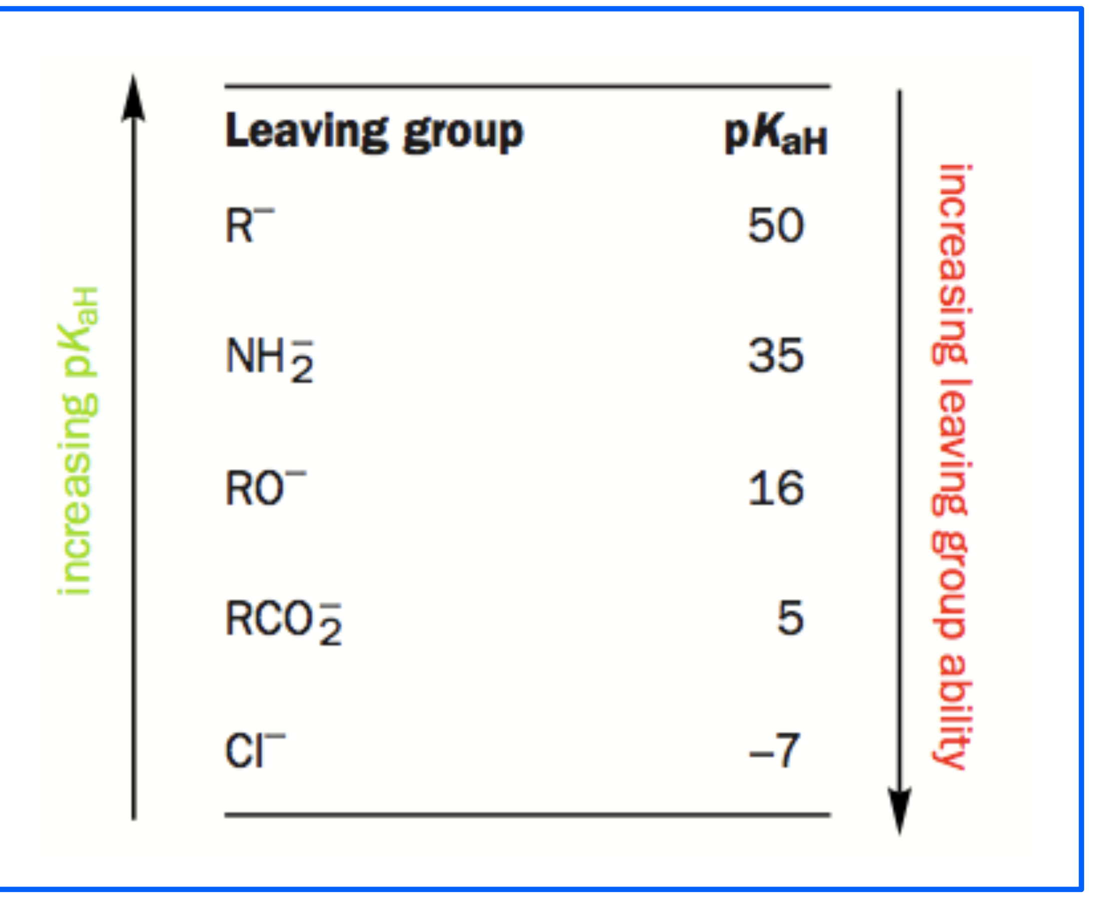
Estere di un acido tranne quello formico

Alcol 3°

Reazioni con i composti organometallici

A. Reattivi di Grignard

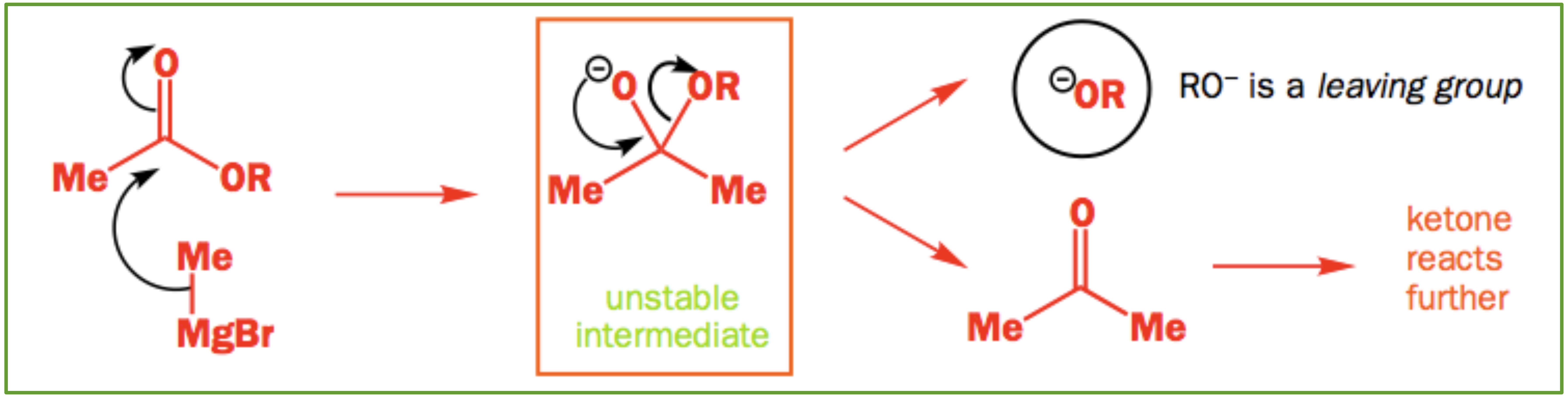




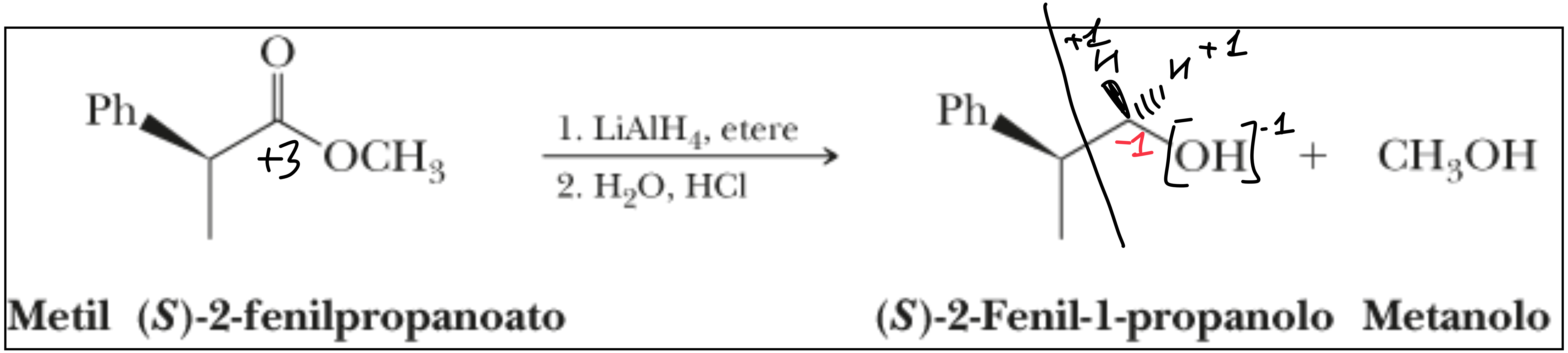
Leaving group	pK_{aH}
R^-	50
NH_2^-	35
RO^-	16
RCO_2^-	5
Cl^-	–7

increasing pK_{aH}

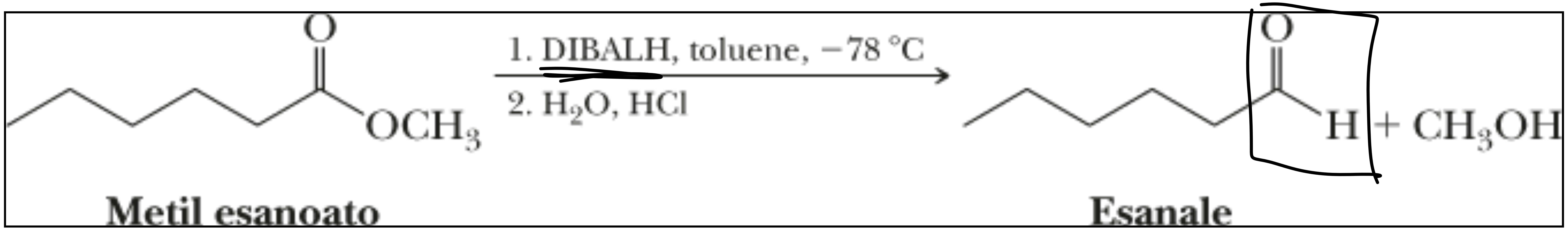
increasing leaving group ability



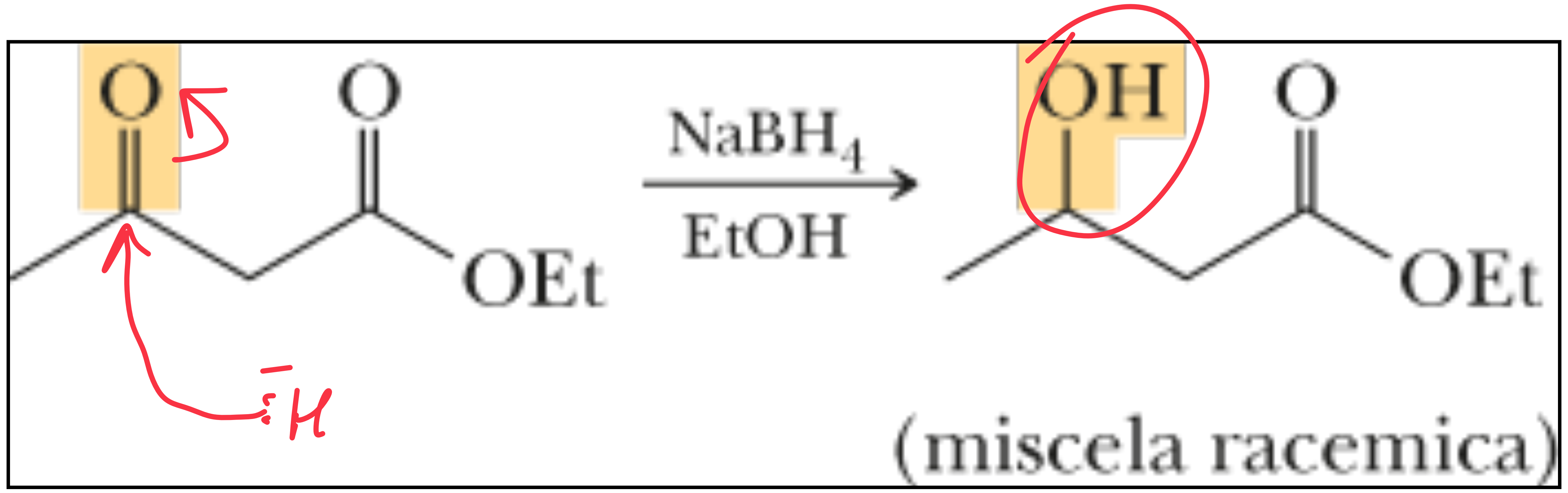
Riduzione degli esteri



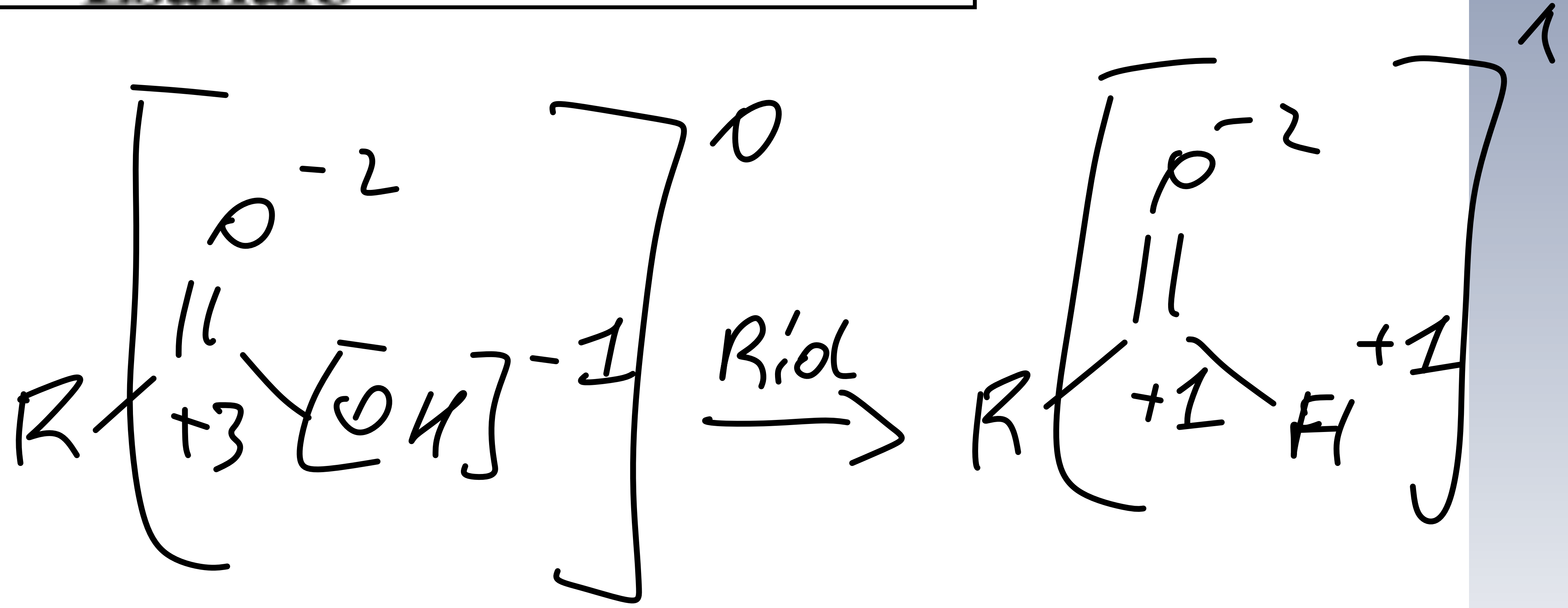
Metil (*S*)-2-fenilpropanoato (*S*)-2-Fenil-1-propanolo Metanolo



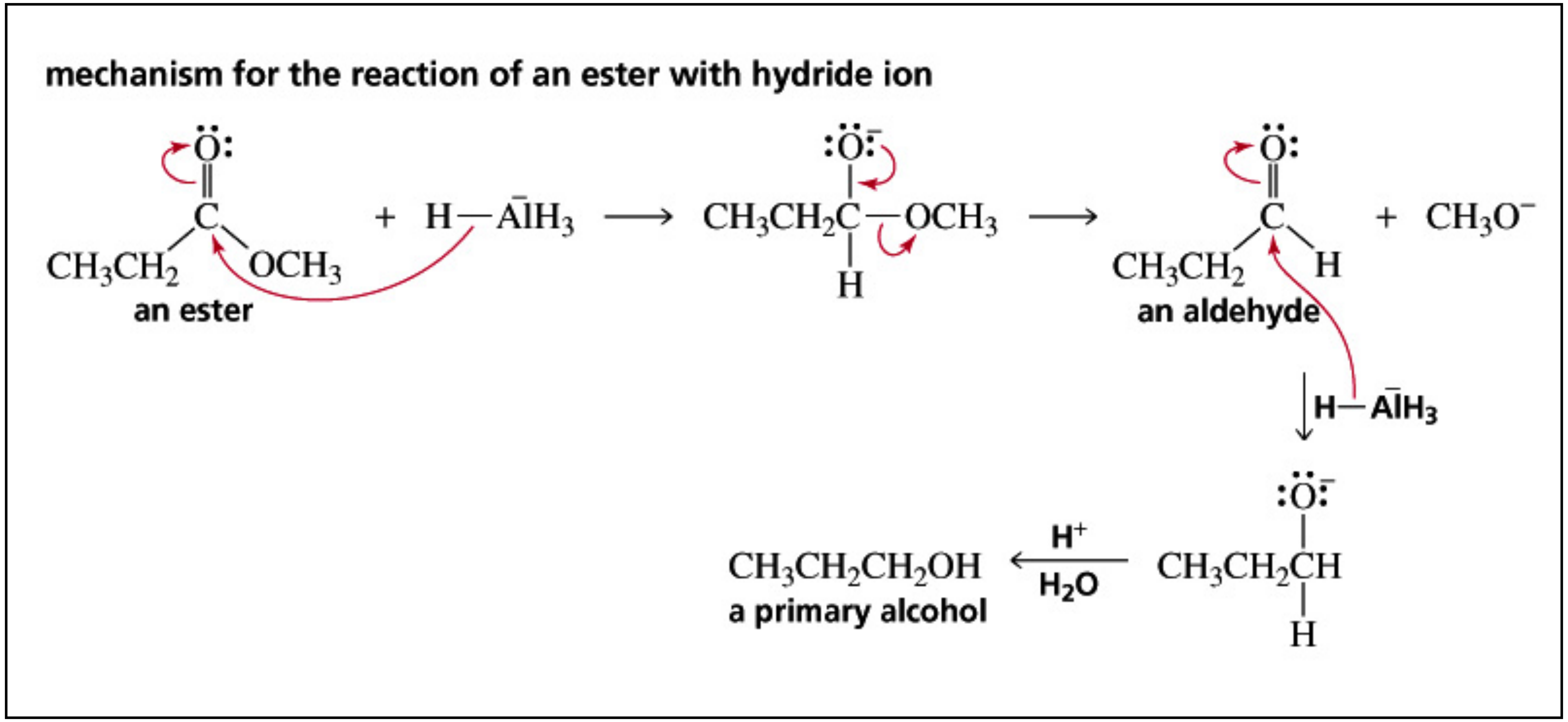
Metil esanoato Esanale

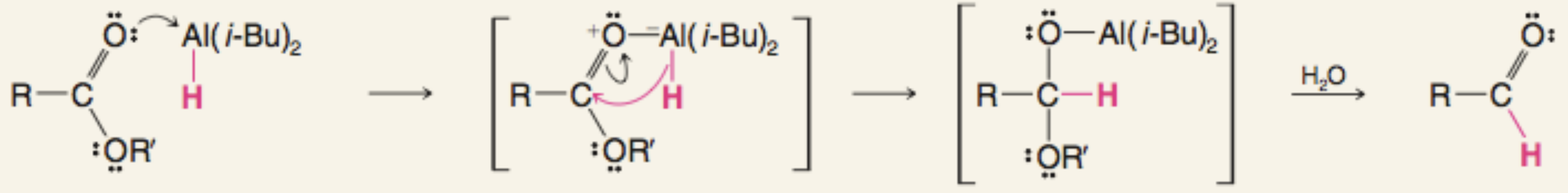


(miscela racemica)



MECCANISMO: Riduzione degli Esteri con $LiAlH_4$



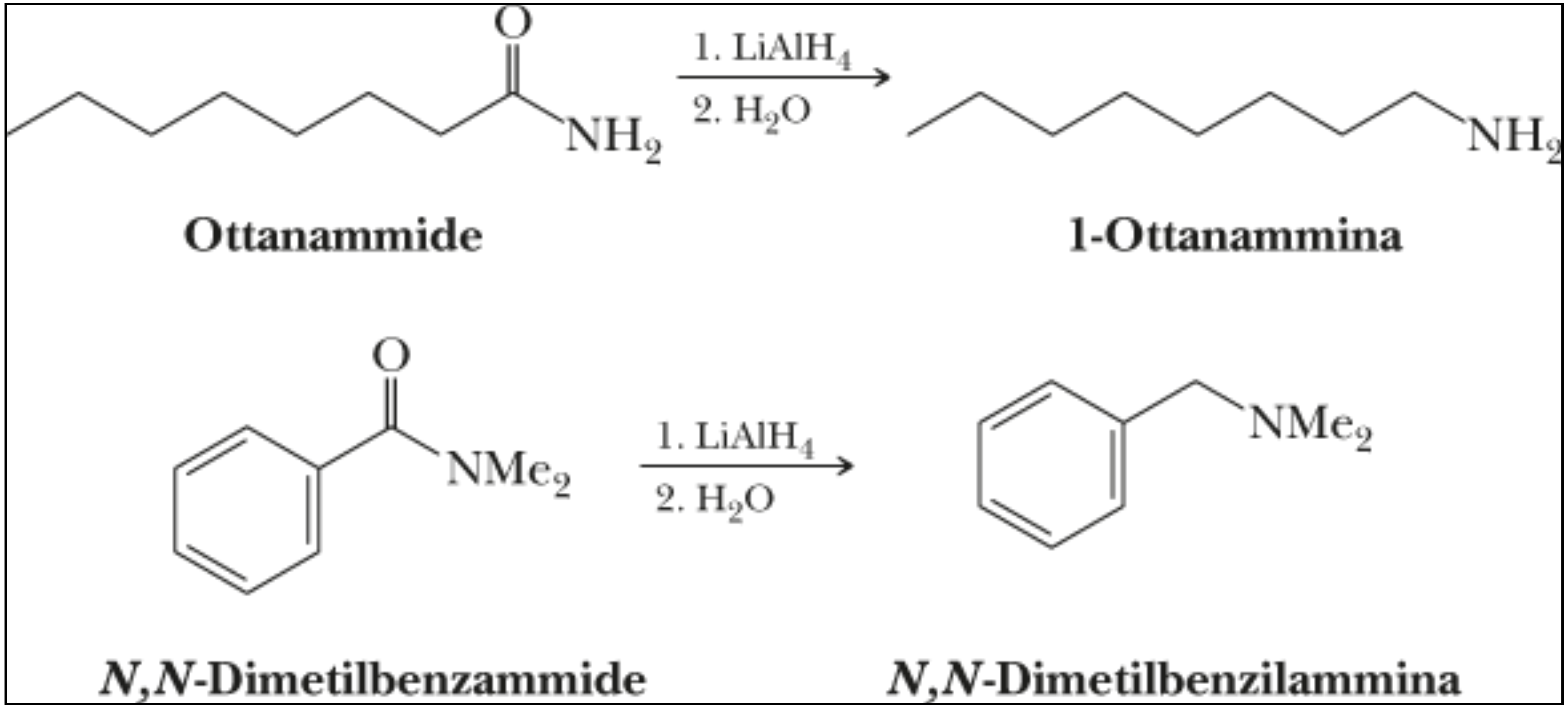


The aluminum atom accepts an electron pair from the carbonyl oxygen atom in a Lewis acid-base reaction.

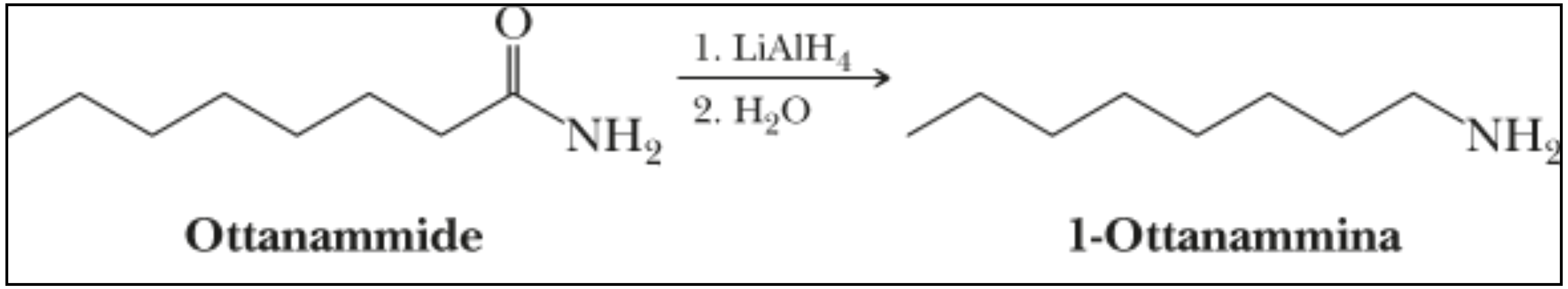
Transfer of a hydride ion to the carbonyl carbon brings about its reduction.

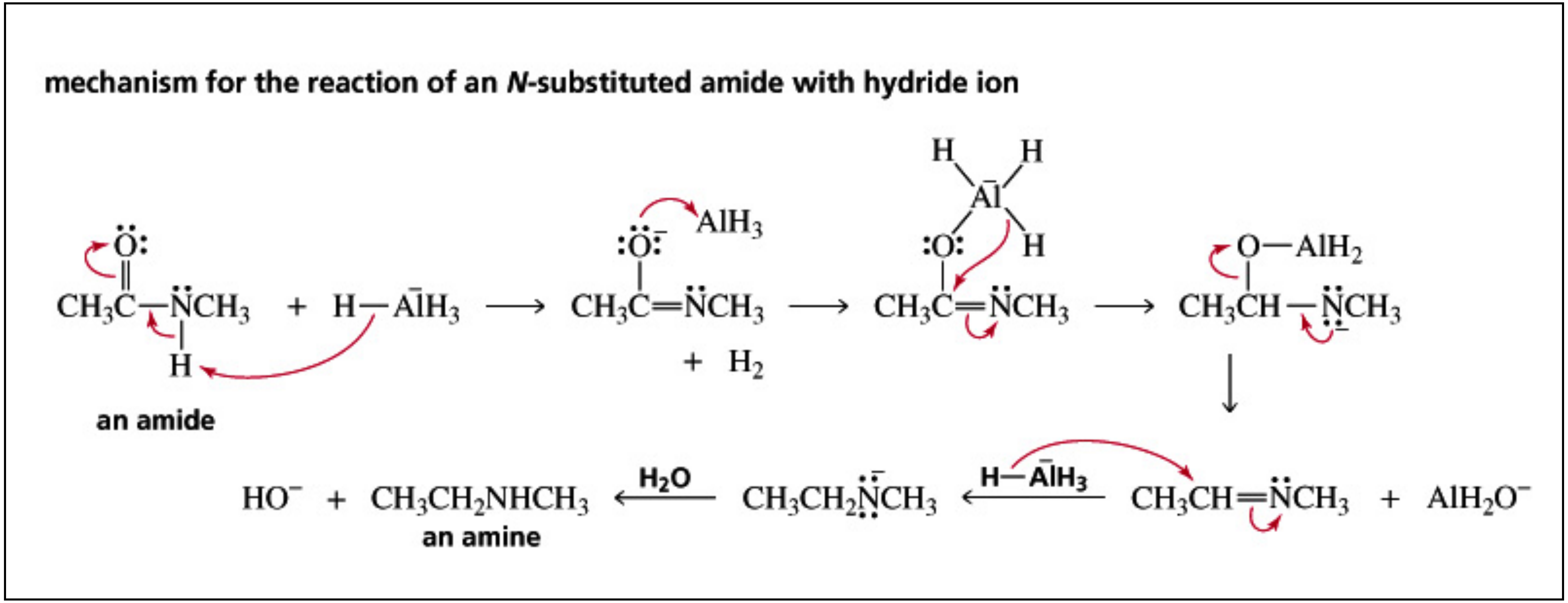
Addition of water at the end of the reaction hydrolyzes the aluminum complex and produces the aldehyde.

Riduzione delle ammidi

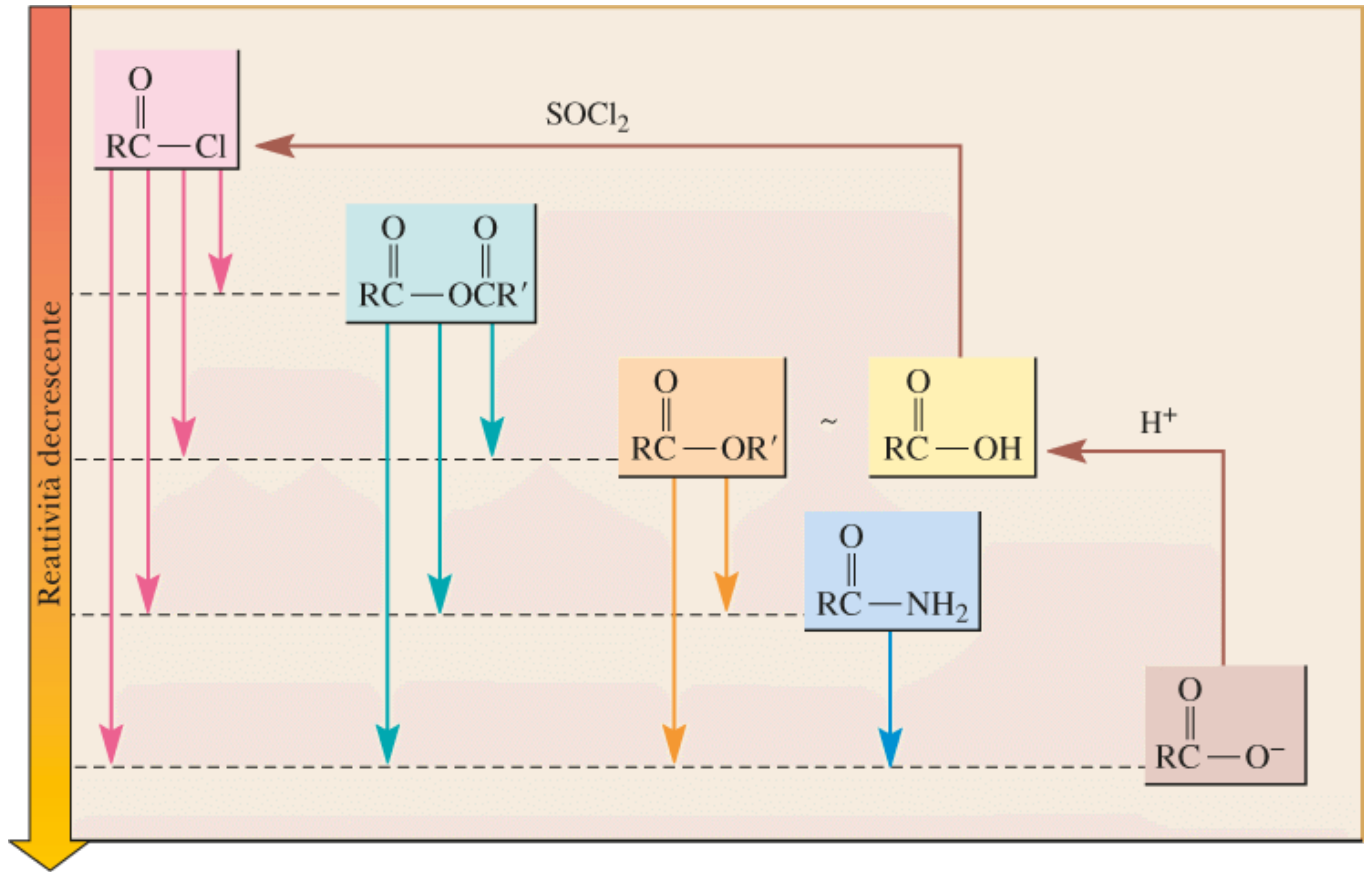


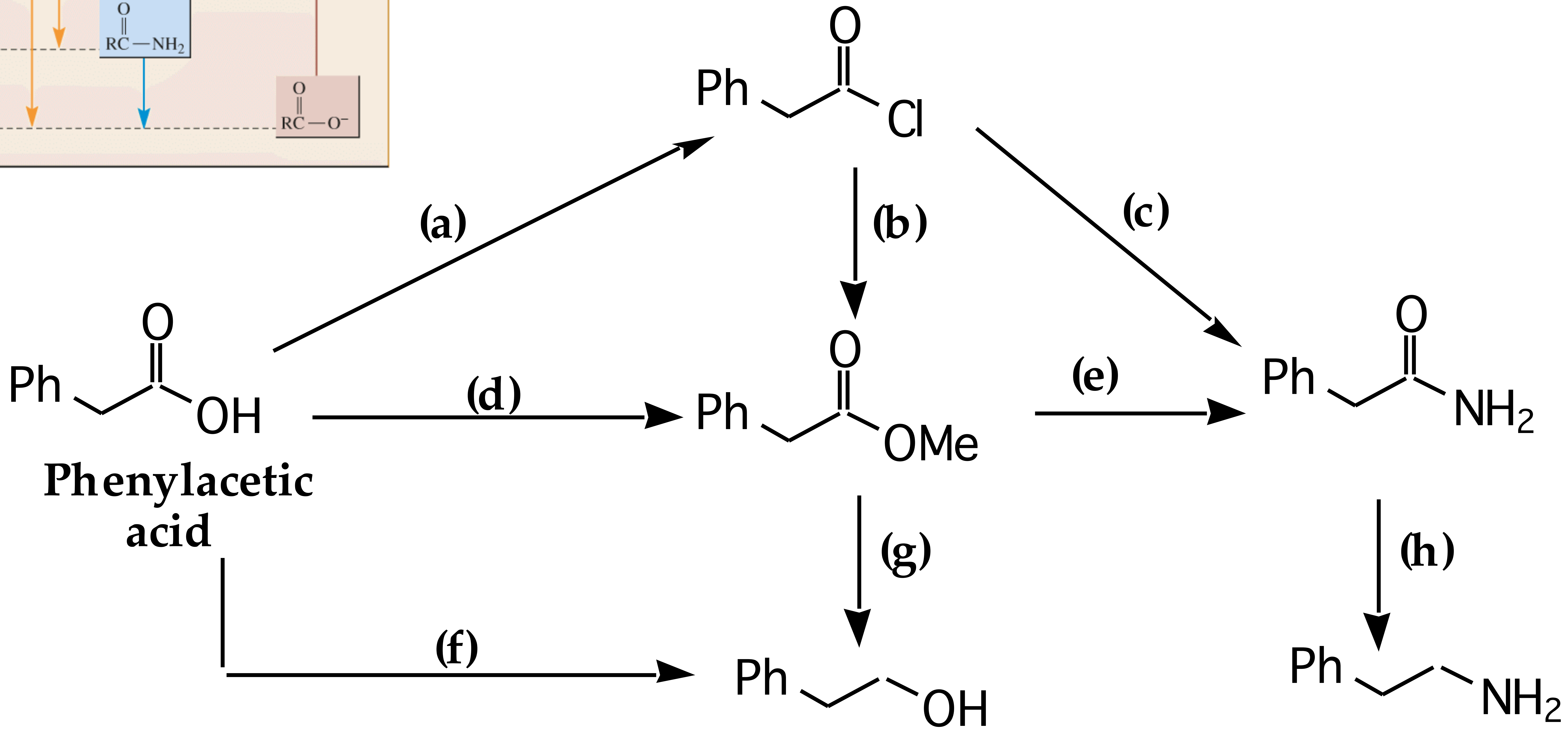
MECCANISMO: Riduzione delle ammidi




mechanism for the reaction of an *N*-substituted amide with hydride ion

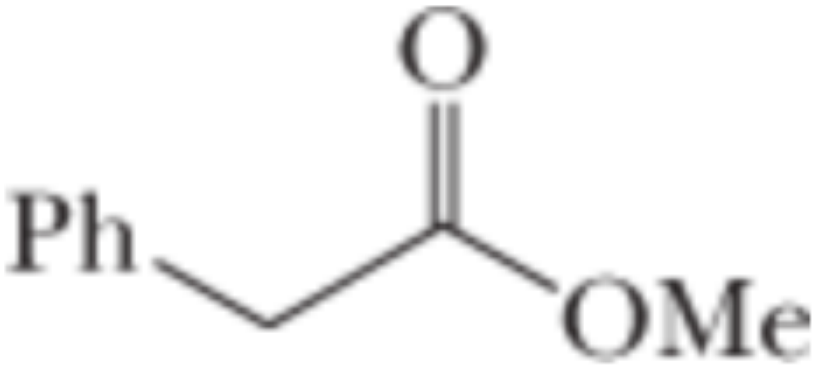
INTERCONVERSIONI



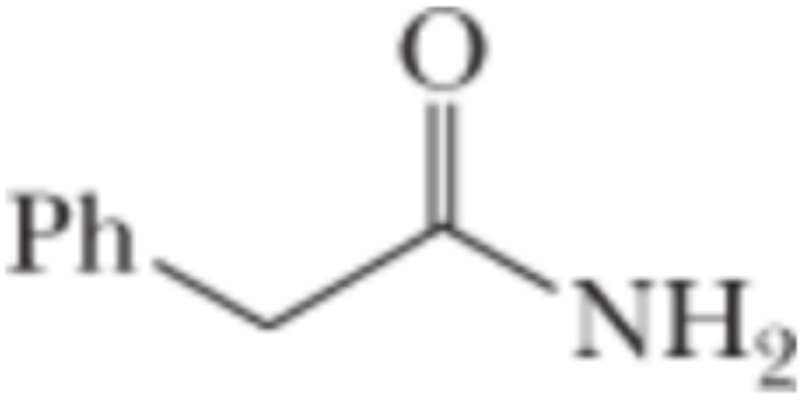


PROBLEMA: Suggerire come trasformare l'acido fenilacetico in ciascuno dei seguenti composti.

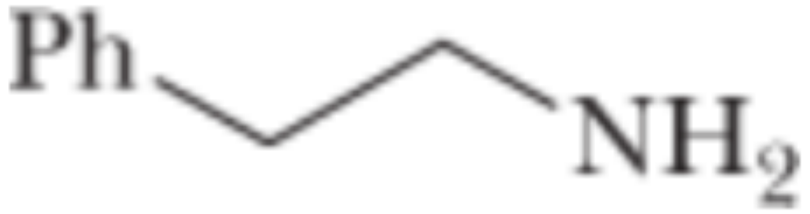
a.



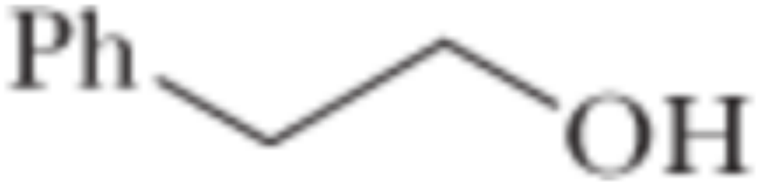
b.



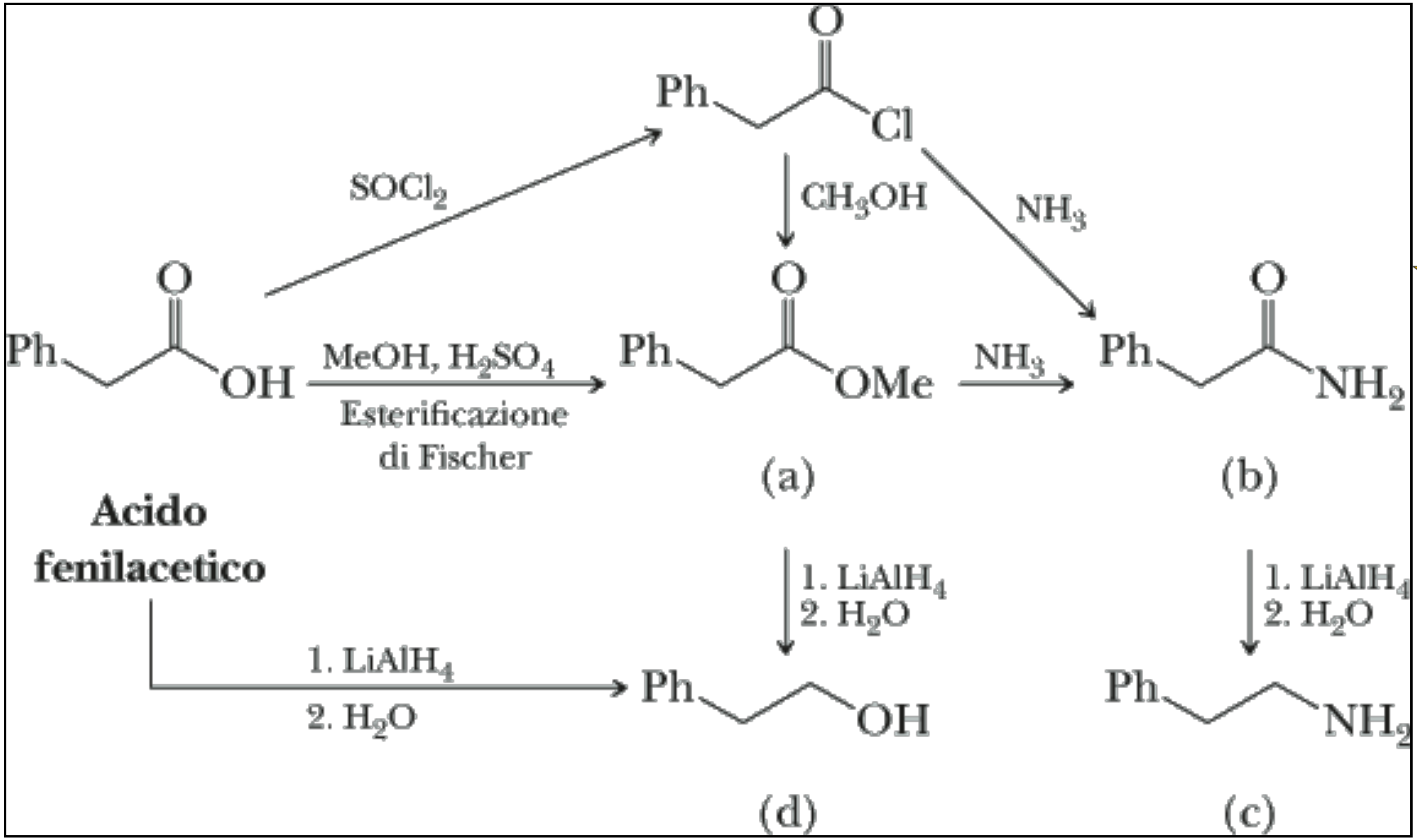
c.

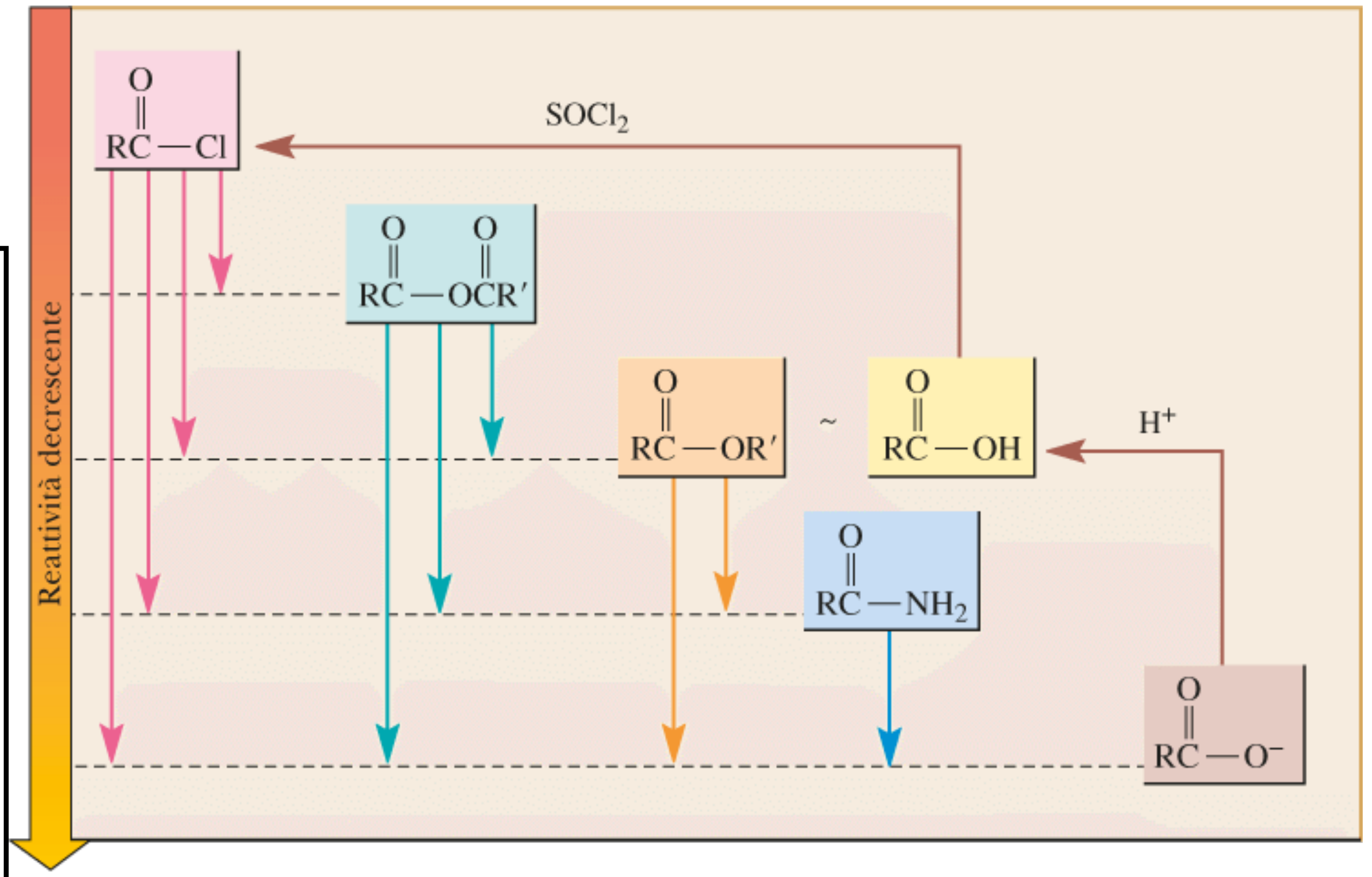


d.

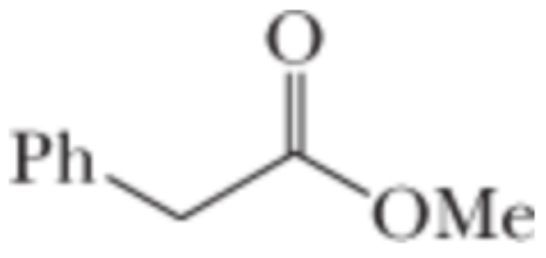


PROBLEMA: Suggerire come trasformare l'acido fenilacetico in ciascuno dei seguenti composti.

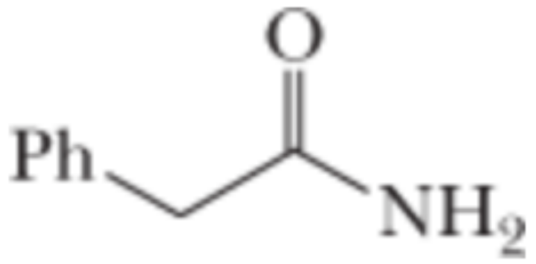




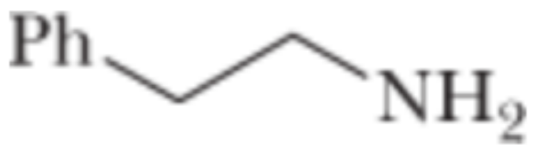
a.



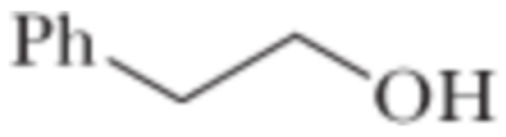
b.



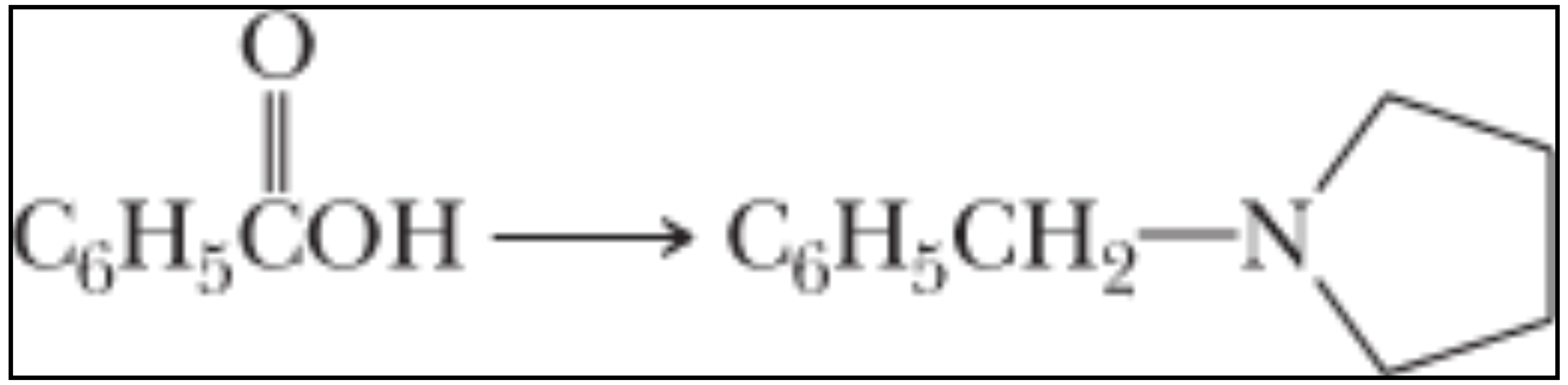
c.

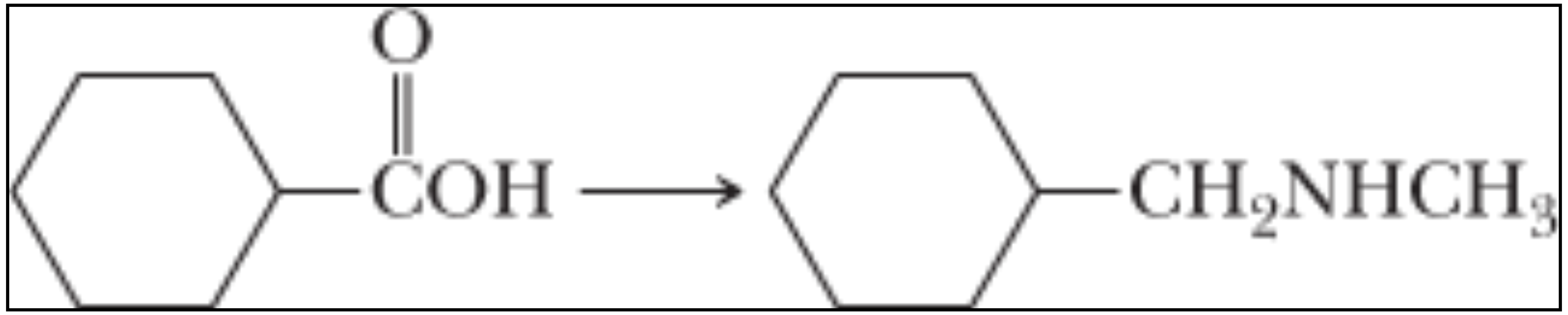


d.

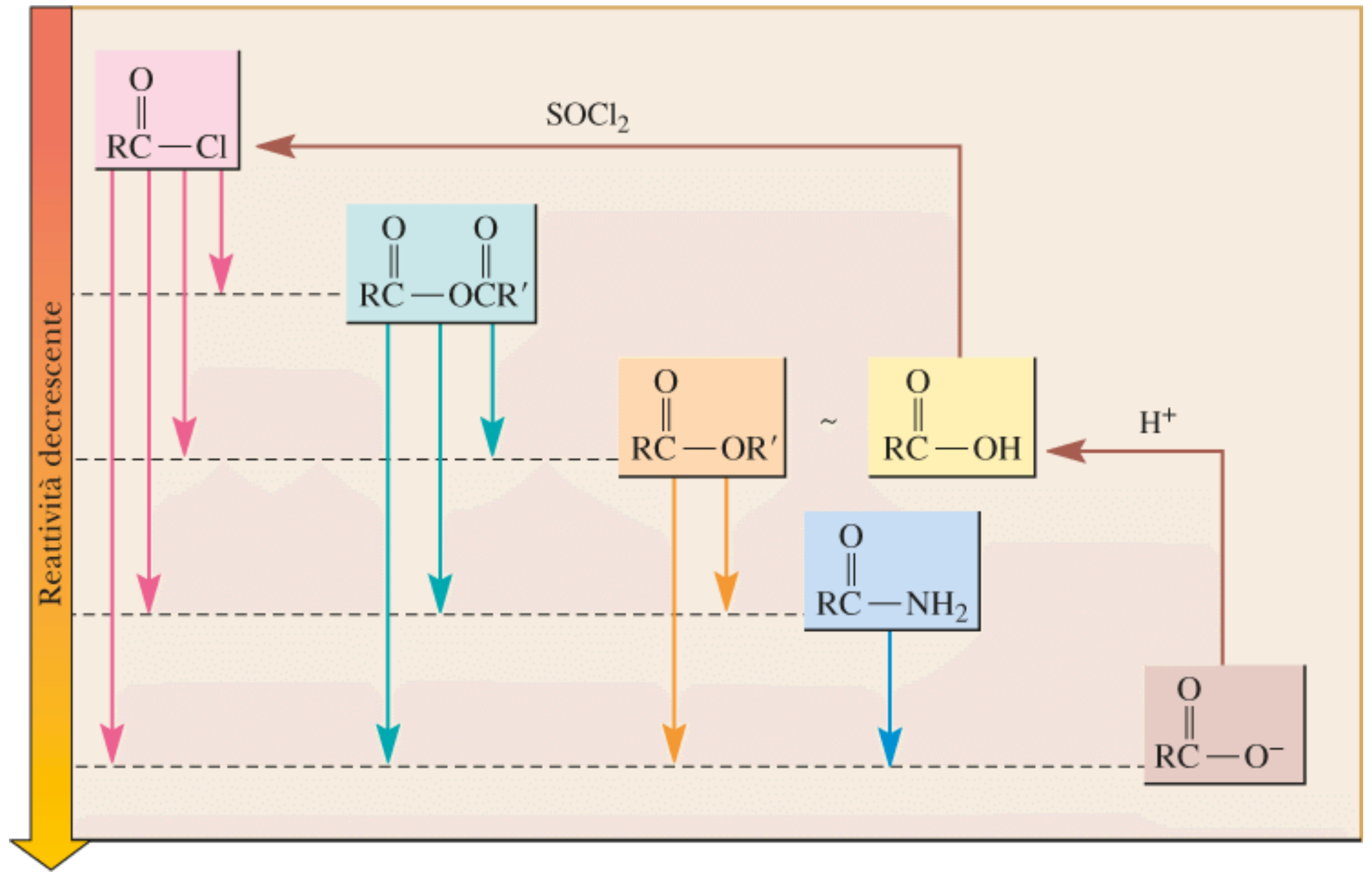


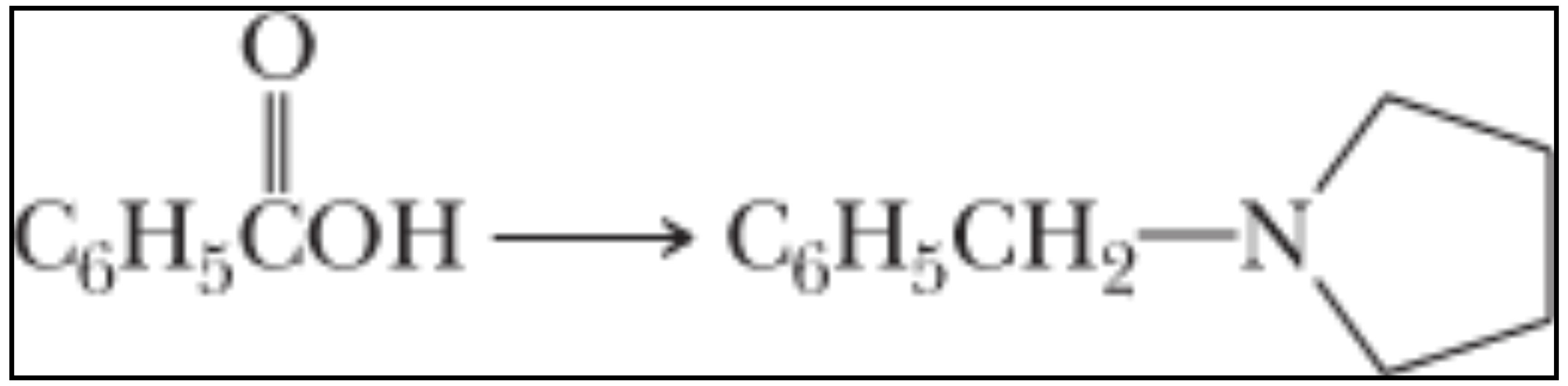
PROBLEMA: Suggerire come effettuare ciascuna delle seguenti trasformazioni.

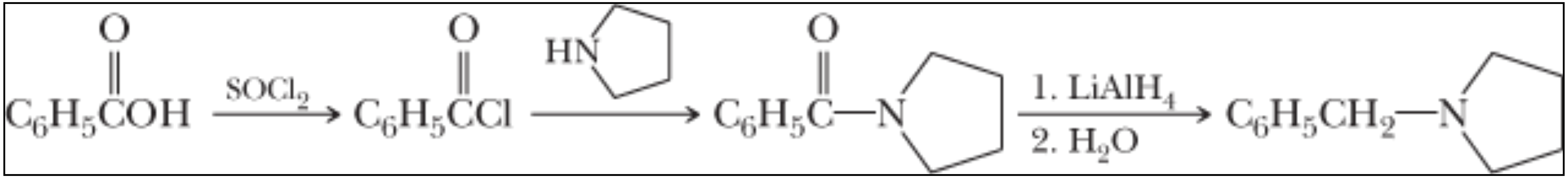




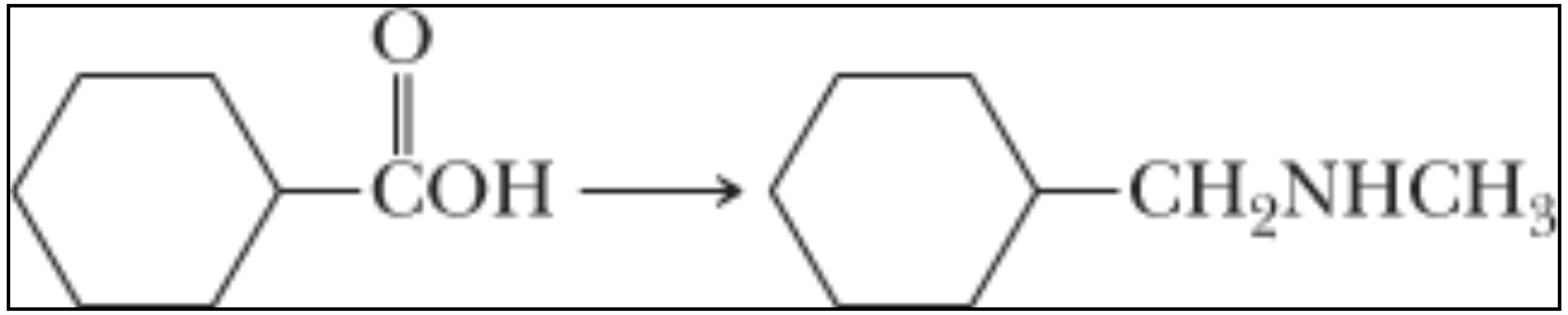
PROBLEMA: Suggerire come effettuare ciascuna delle seguenti trasformazioni.

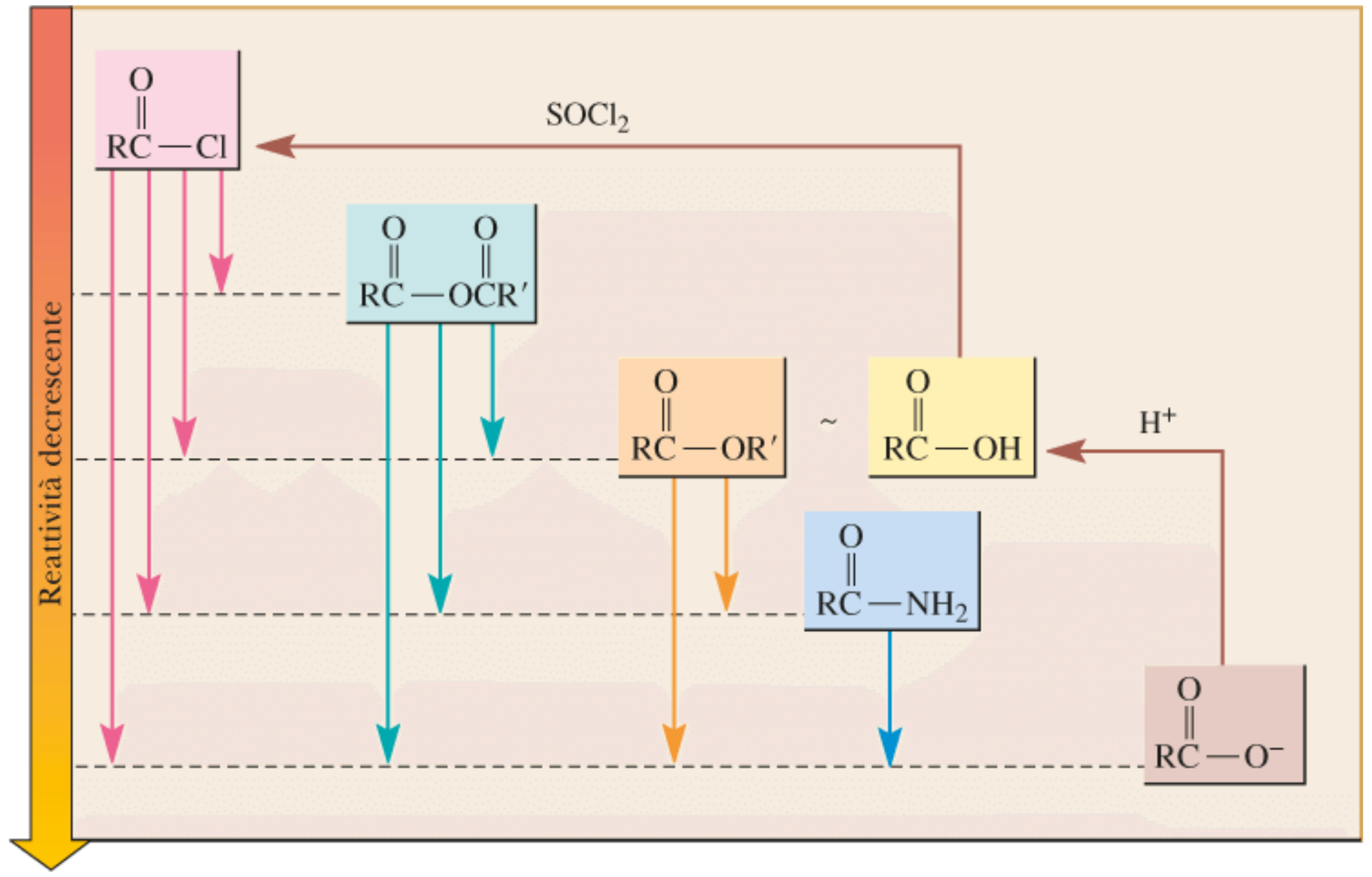


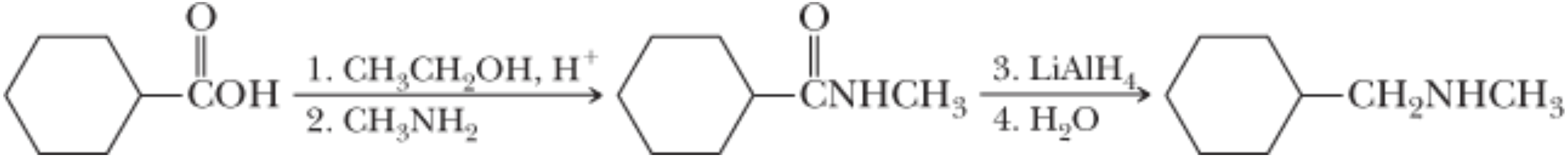




PROBLEMA: Suggerire come effettuare ciascuna delle seguenti trasformazioni.





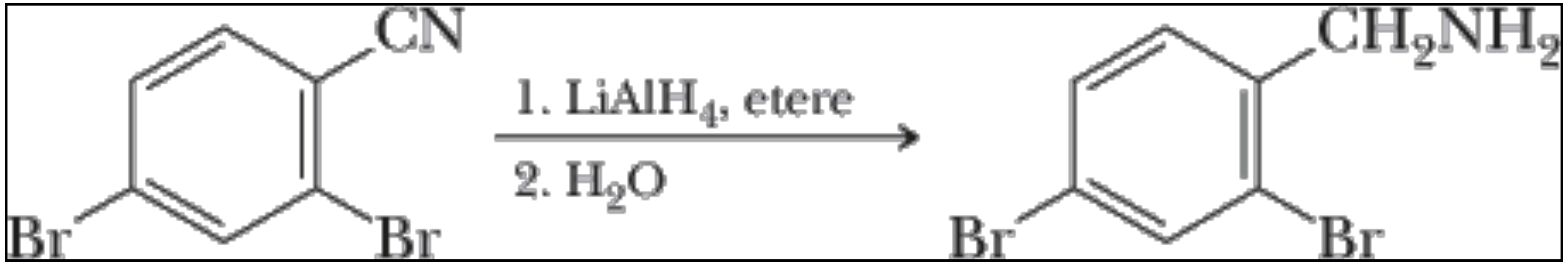


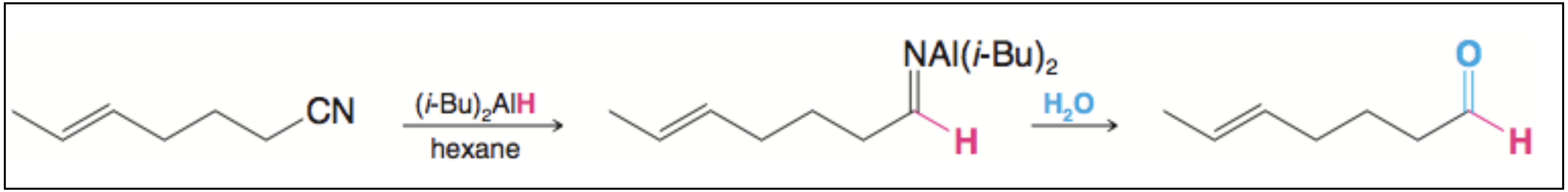
Riduzione dei nitrili

Il gruppo ciano viene ridotto dal litio alluminio idruro ad ammina primaria.

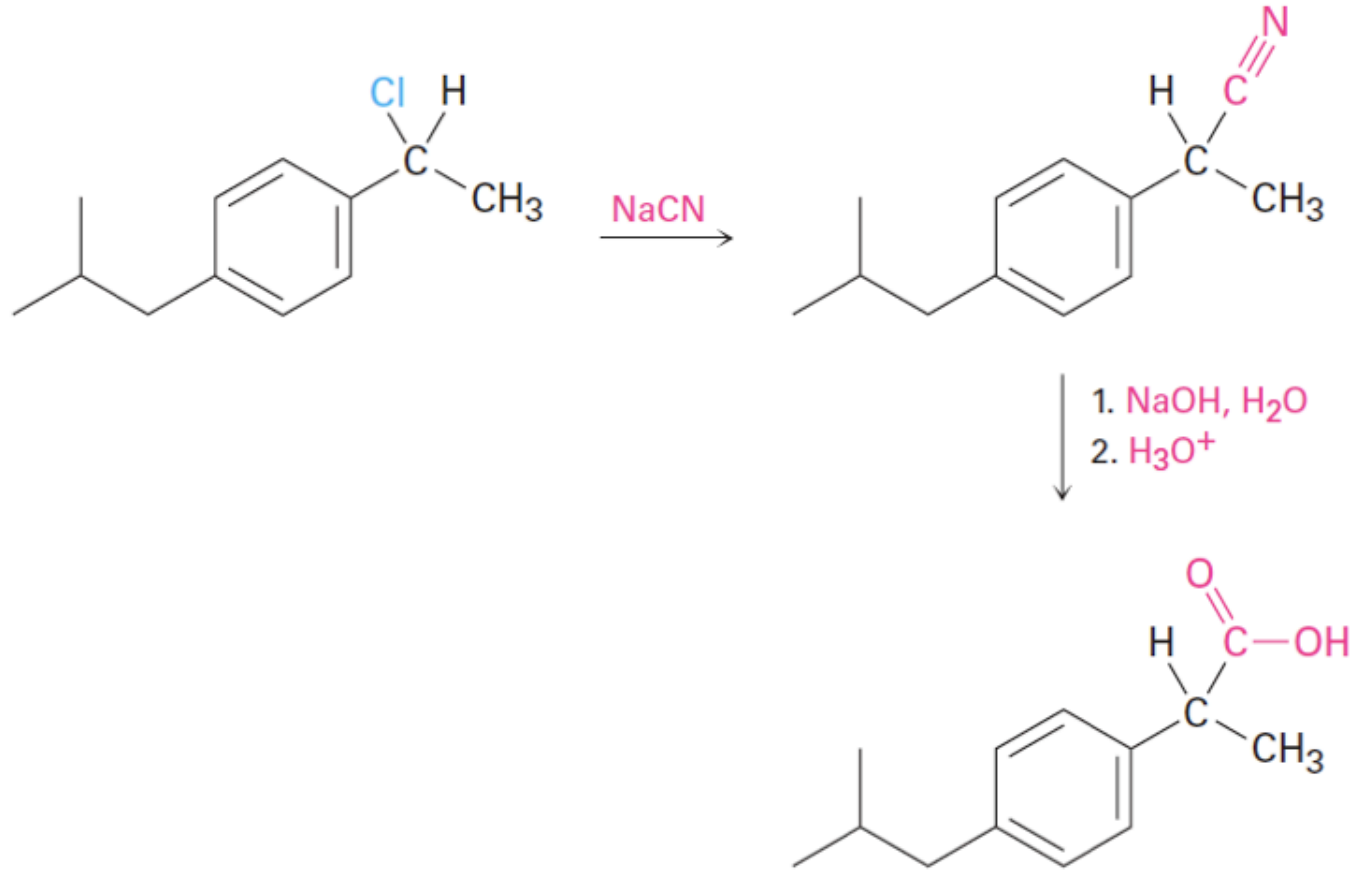
$$CH_3CH{=}CH(CH_2)_4C{\equiv}N \xrightarrow[2.\ H_2O]{1.\ LiAlH_4} CH_3CH{=}CH(CH_2)_4CH_2NH_2$$

6-Ottenonitrile **6-Otten-1-ammina**

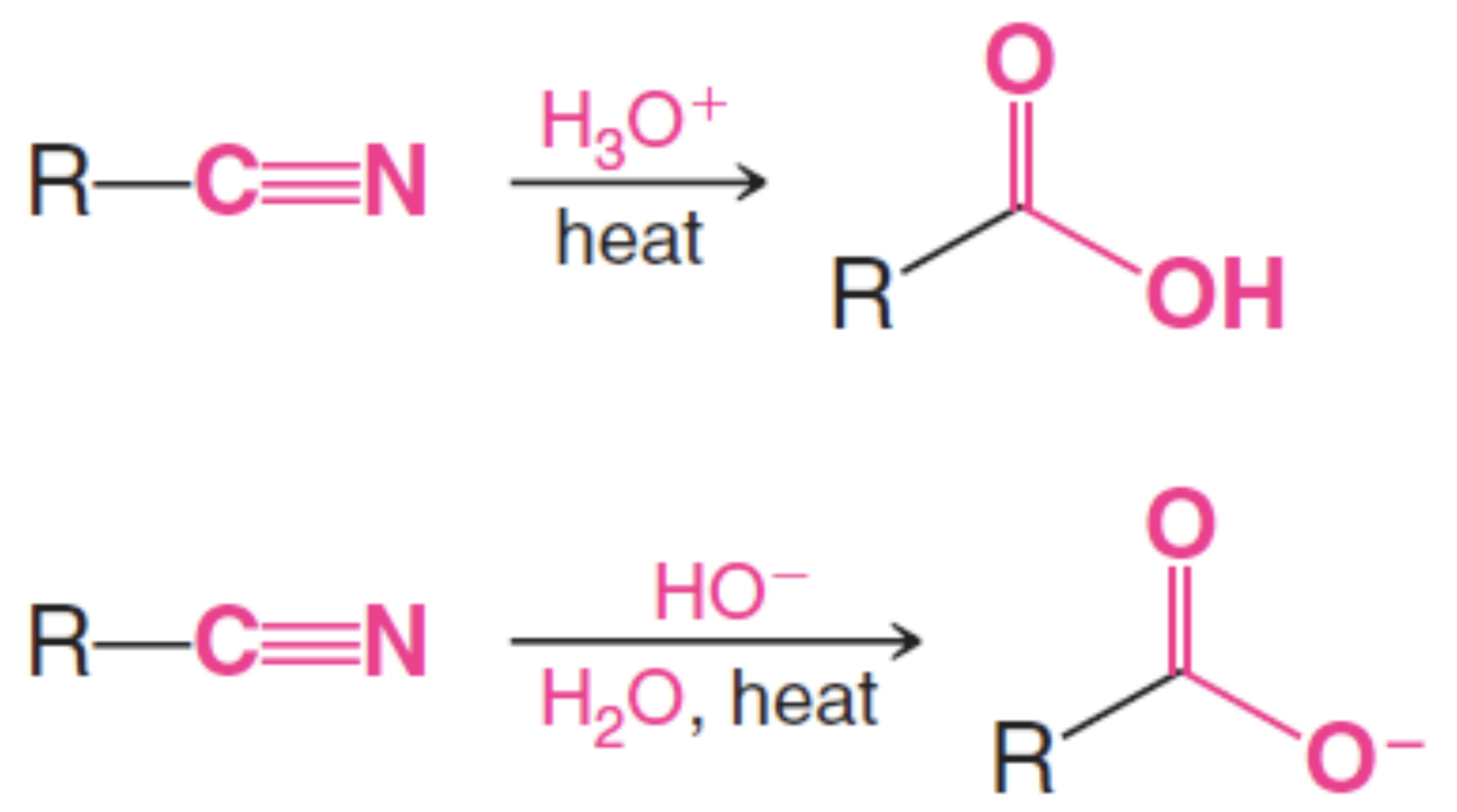




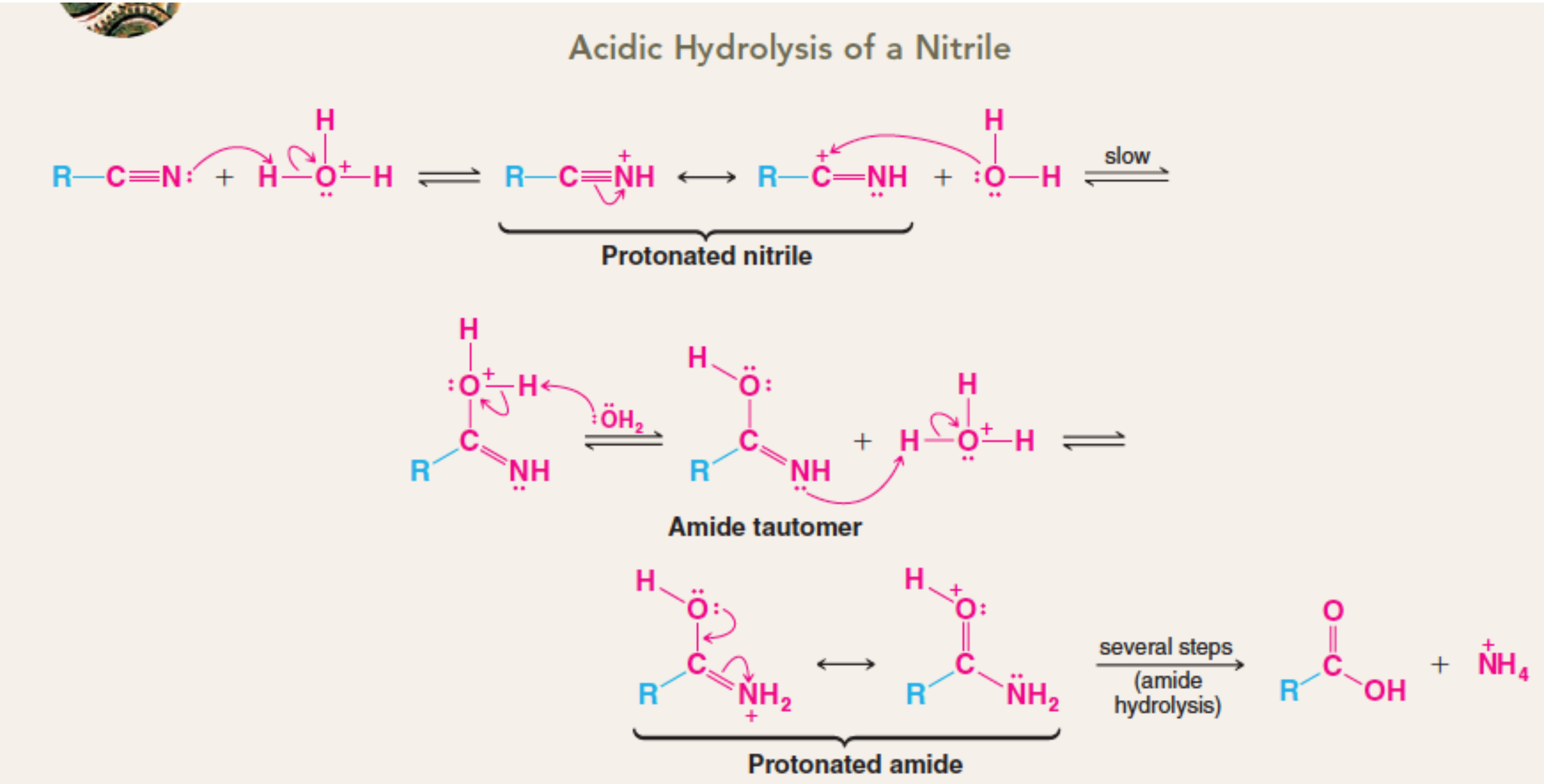
Idrolisi dei nitrili

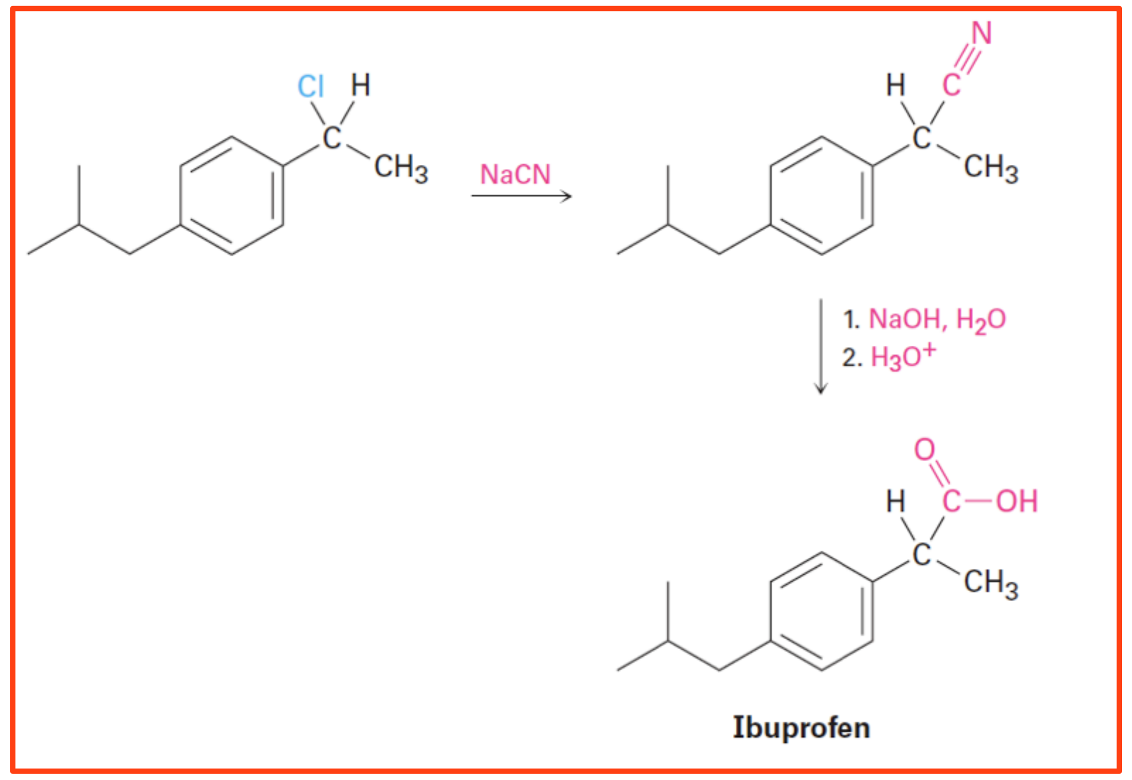


Ibuprofen

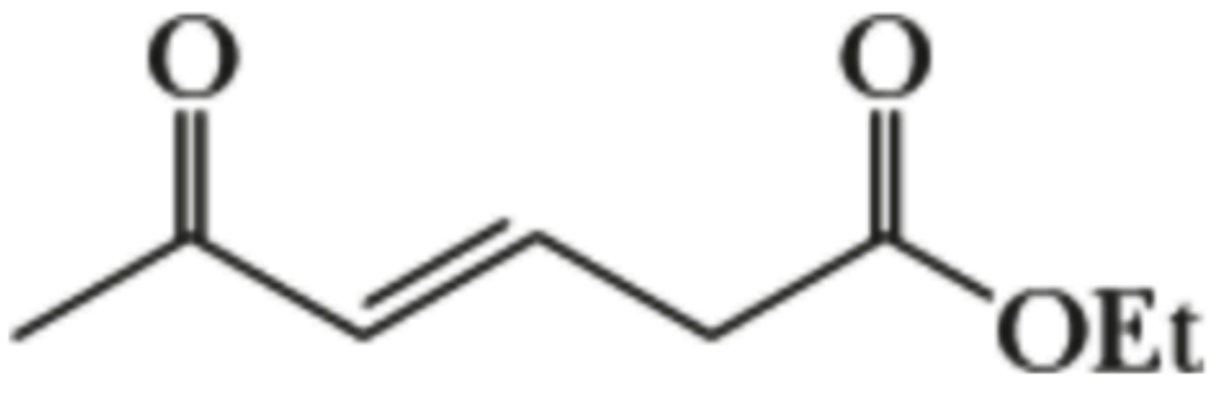


MEccanismo di Idrolisi dei nitrili





PROBLEMA: Mostrare il prodotto che si forma quando il seguente δ-chetoestere insaturo viene fatto reagire con ognuno dei seguenti reagenti.

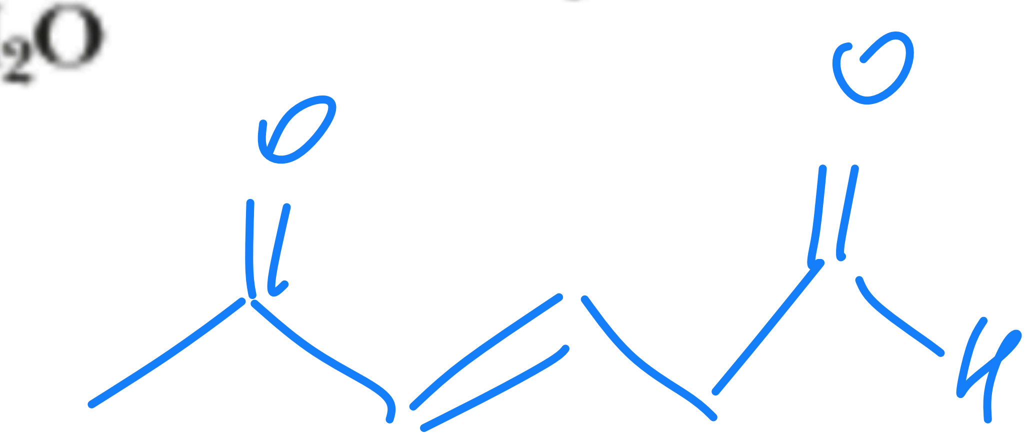


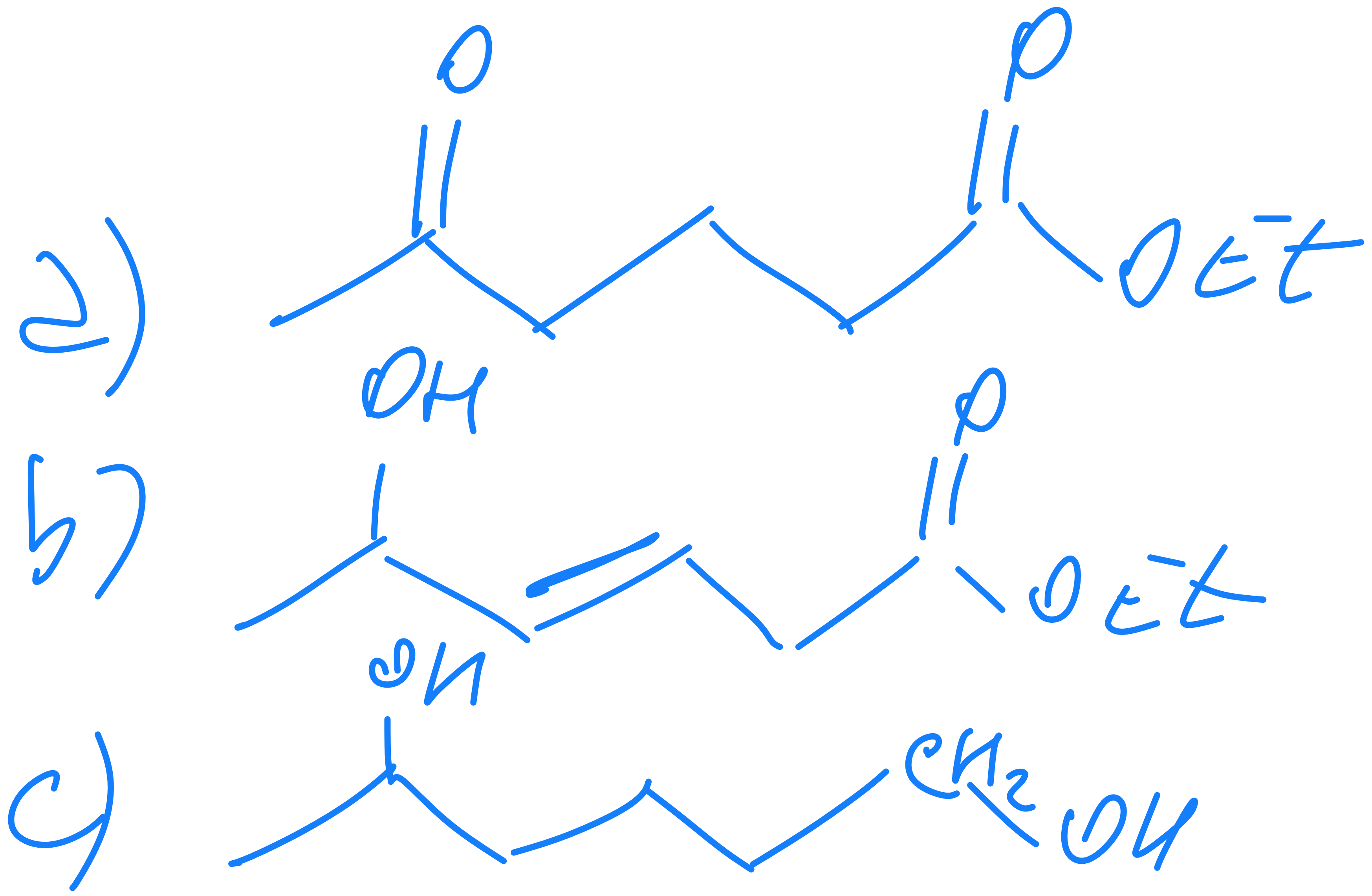
a. $\xrightarrow[\text{Pd, EtOH}]{H_2\text{ (1 mol)}}$

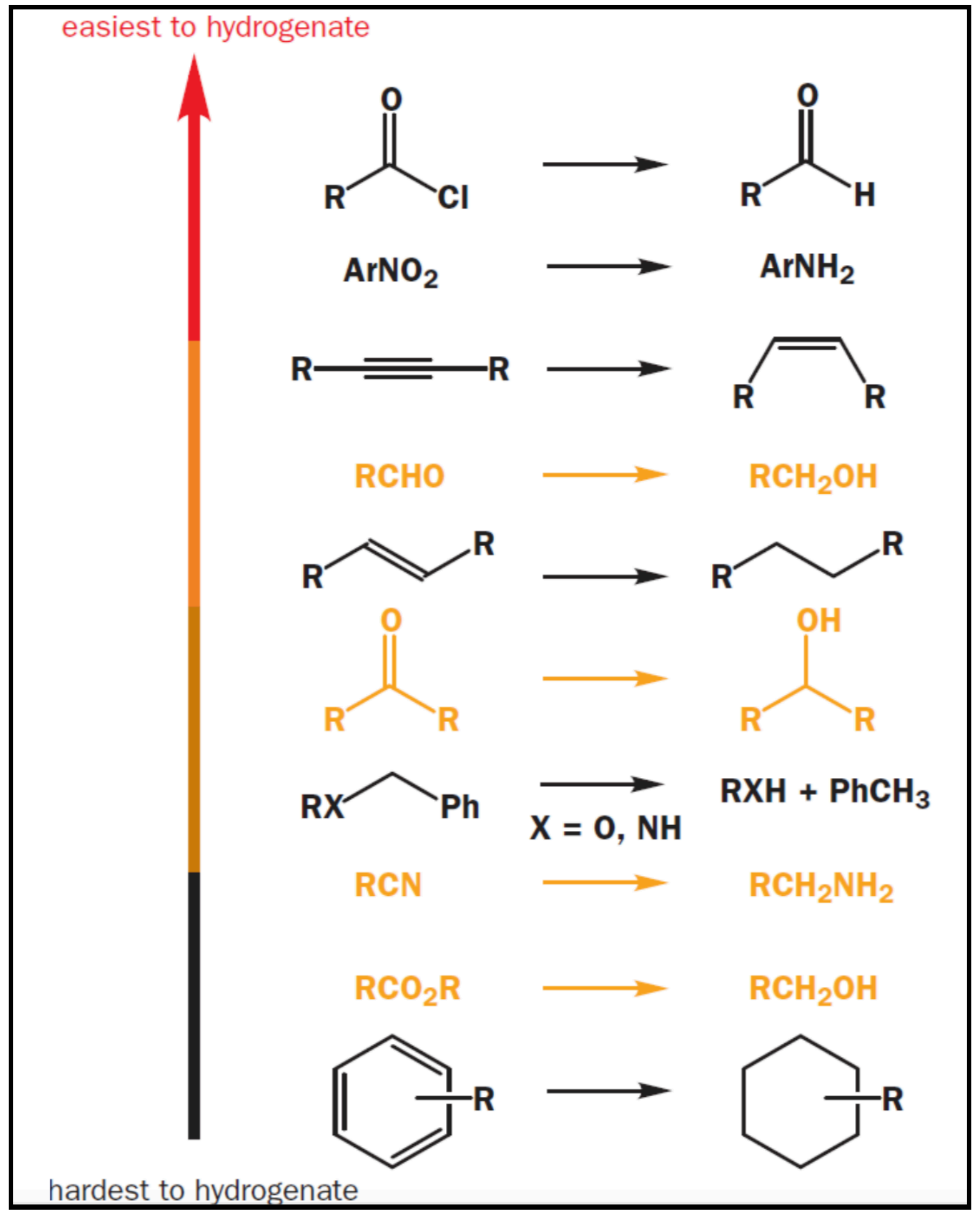
b. $\xrightarrow[CH_3OH]{NaBH_4}$

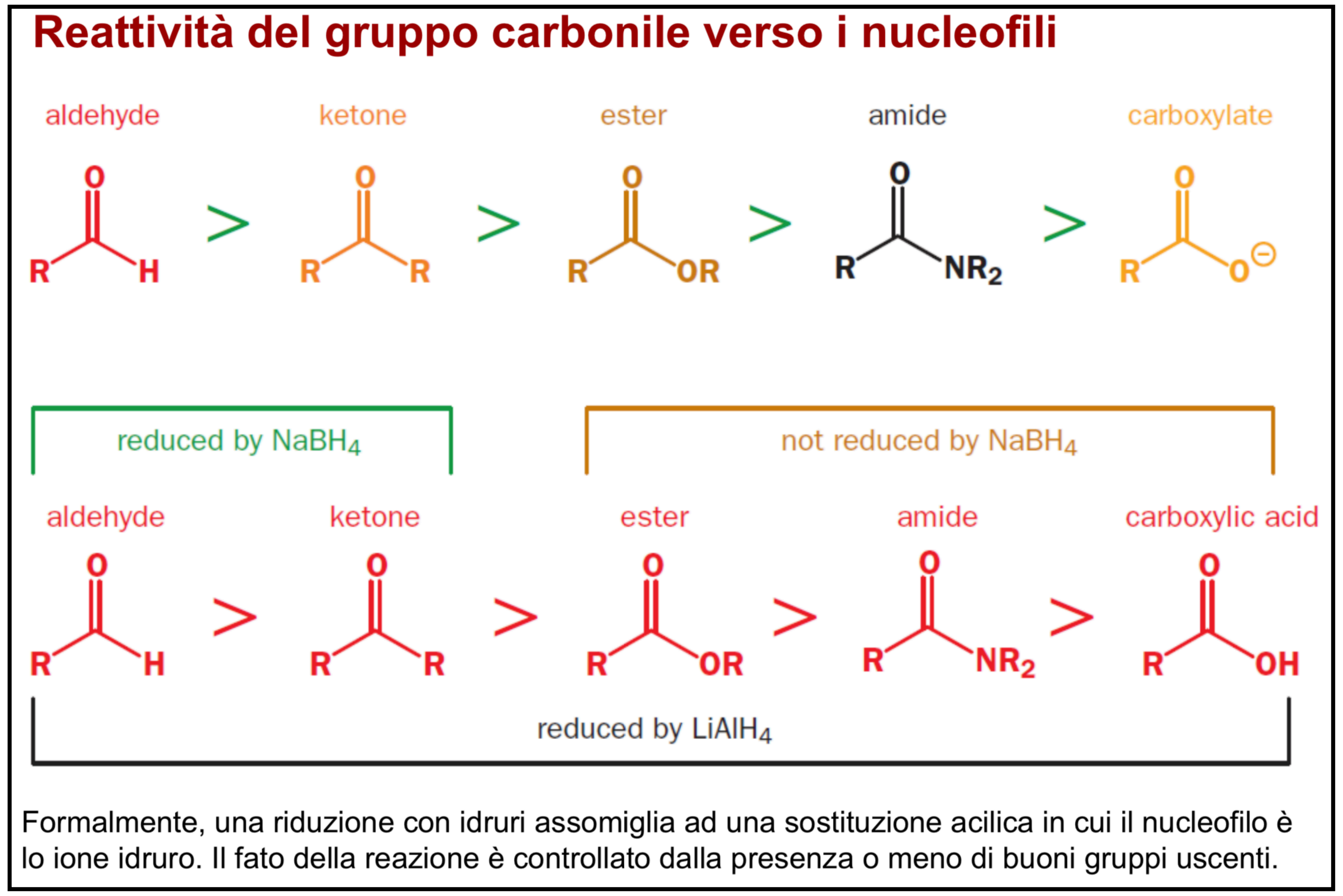
c. $\xrightarrow[\text{2. } H_2O]{\text{1. LiAlH}_4\text{, THF}}$

d. $\xrightarrow[\text{2. } H_2O]{\text{1. DIBALH, −78 °C}}$



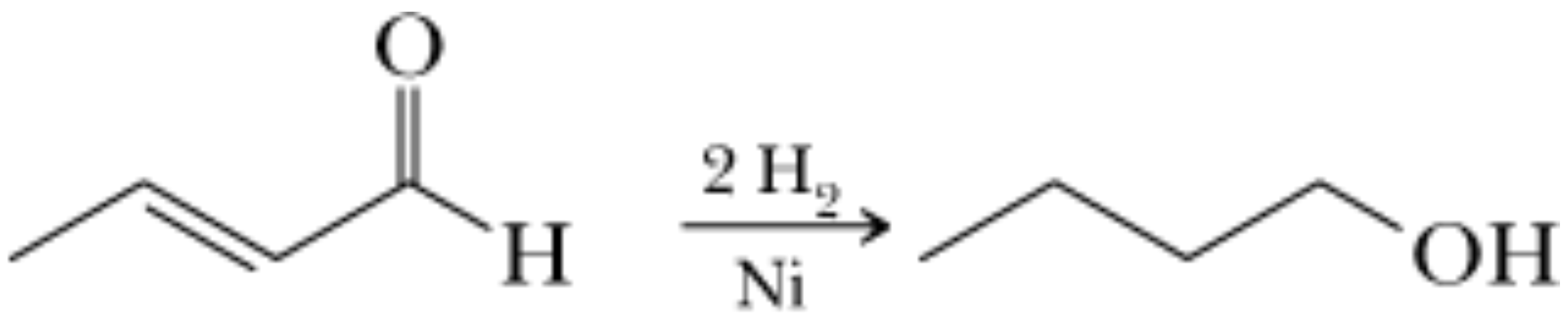






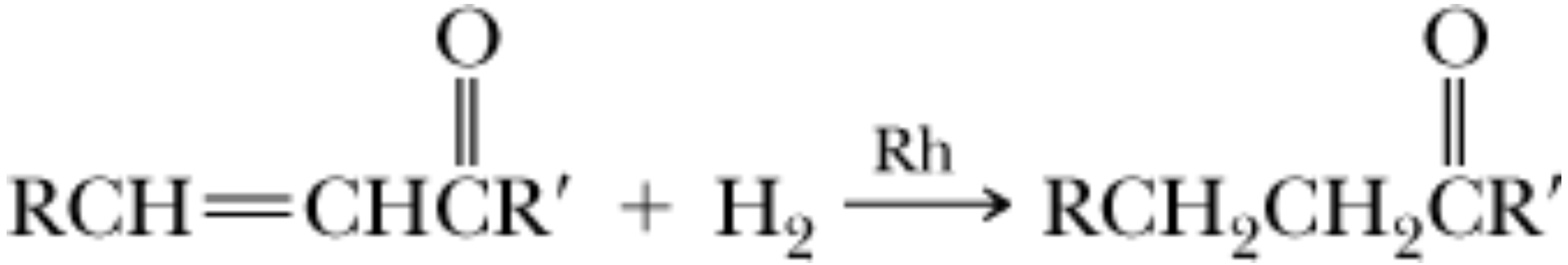
Reattività del gruppo carbonile verso i nucleofili

Formalmente, una riduzione con idruri assomiglia ad una sostituzione acilica in cui il nucleofilo è lo ione idruro. Il fato della reazione è controllato dalla presenza o meno di buoni gruppi uscenti.

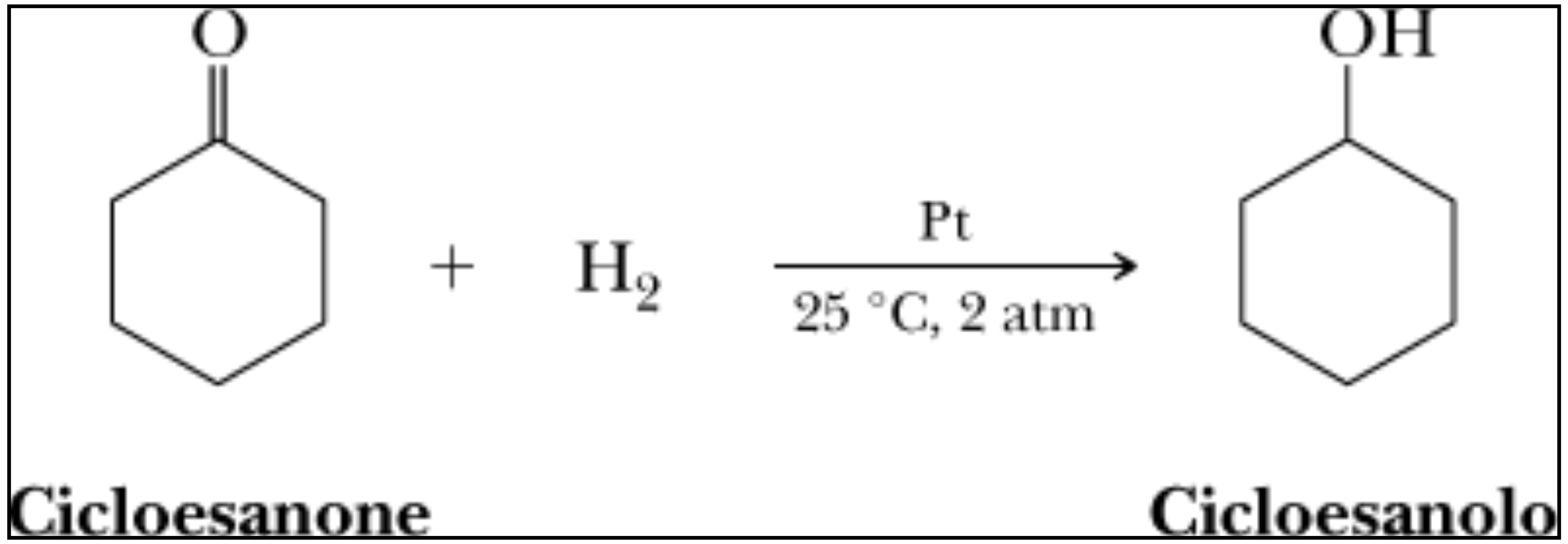


trans-**2-Butenale (Crotonaldeide)**

1-Butanolo

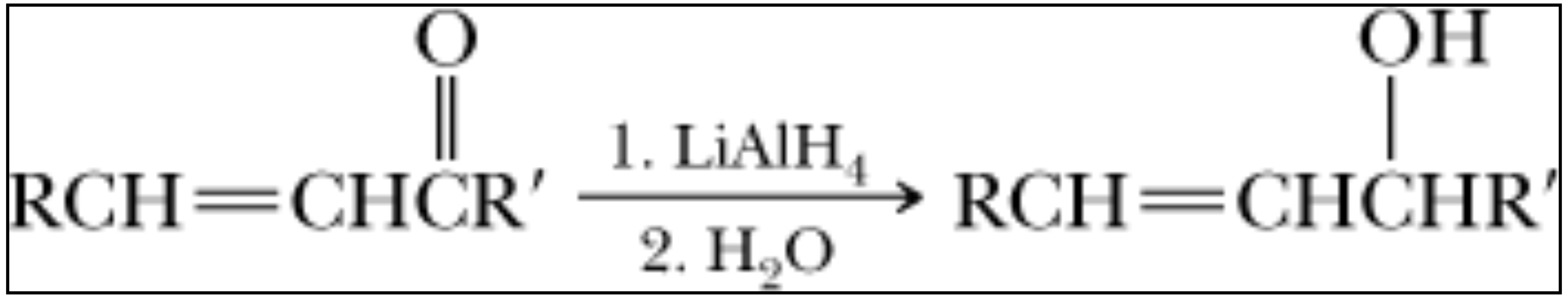


$$RCH{=}CH\overset{O}{\overset{\|}{C}}R' + H_2 \xrightarrow{Rh} RCH_2CH_2\overset{O}{\overset{\|}{C}}R'$$

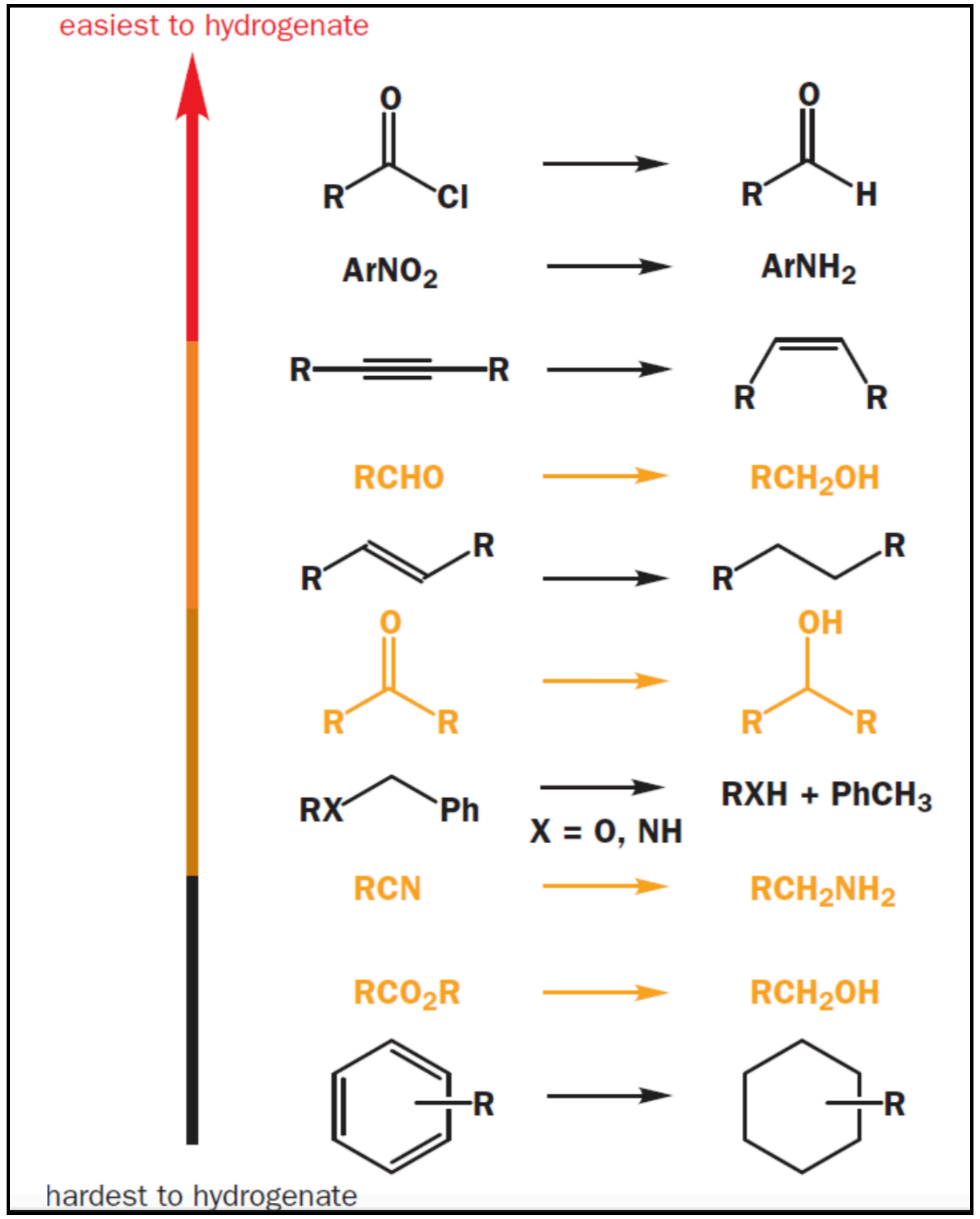


Cicloesanone

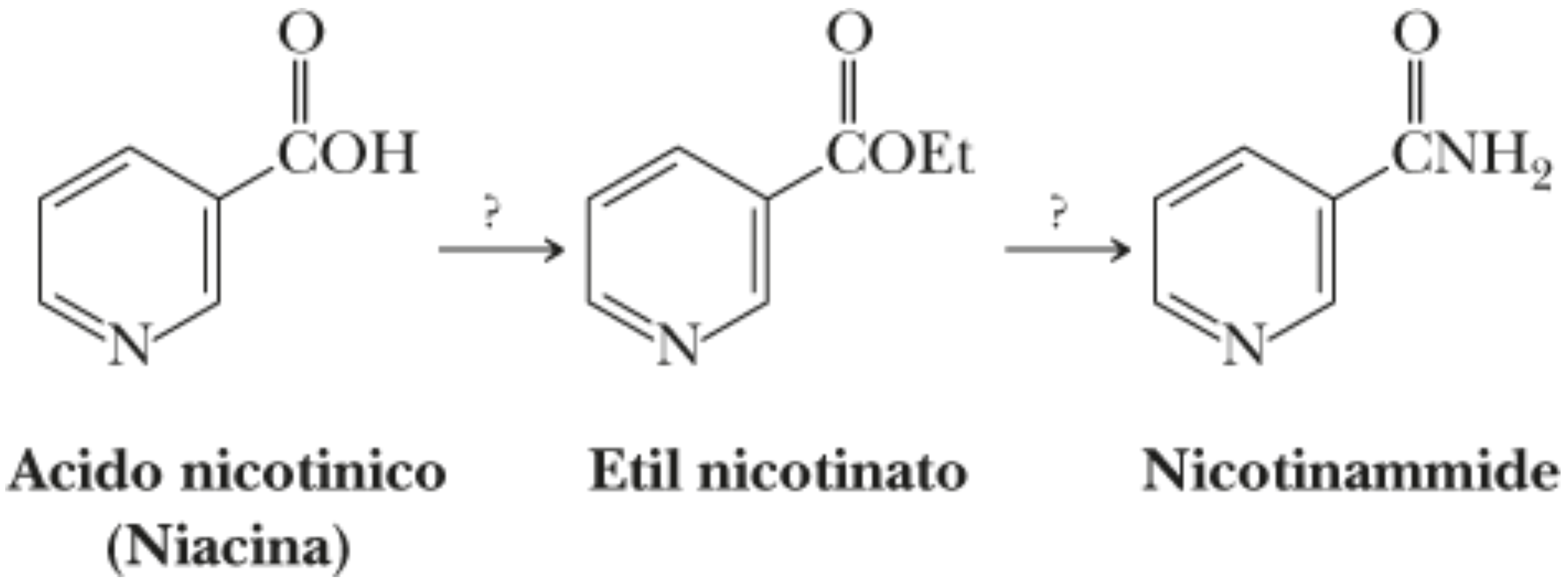
Cicloesanolo



$$RCH{=}CH\overset{O}{\overset{\|}{C}}R' \xrightarrow[2.\ H_2O]{1.\ LiAlH_4} RCH{=}CH\overset{OH}{\overset{|}{C}}HR'$$

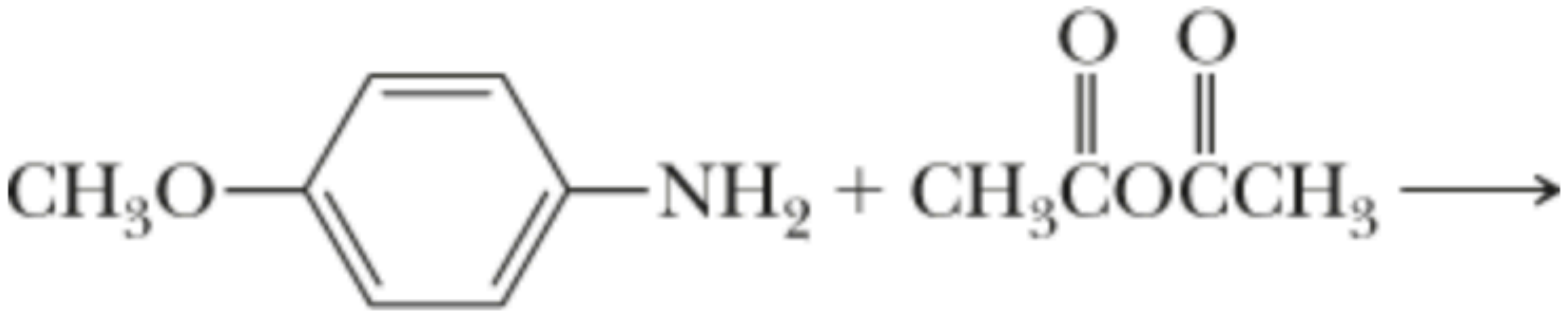


PROBLEMA: L'acido nicotinico, noto come niacina, fa parte del gruppo delle vitamine B. Mostrare come l'acido nicotinico possa essere trasformato (a) in nicotinato di etile e quindi (b) in nicotinammide.

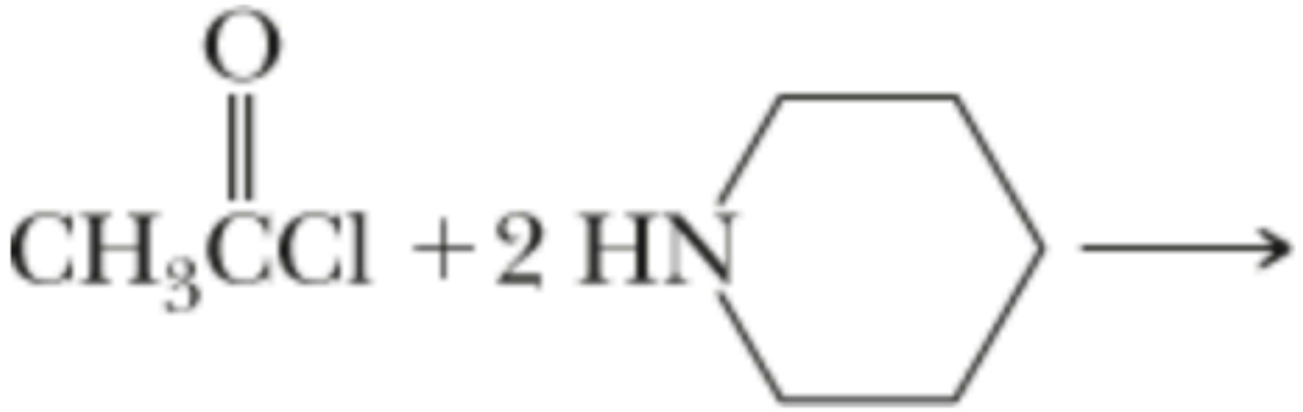


PROBLEMA: Completare le seguenti reazioni.

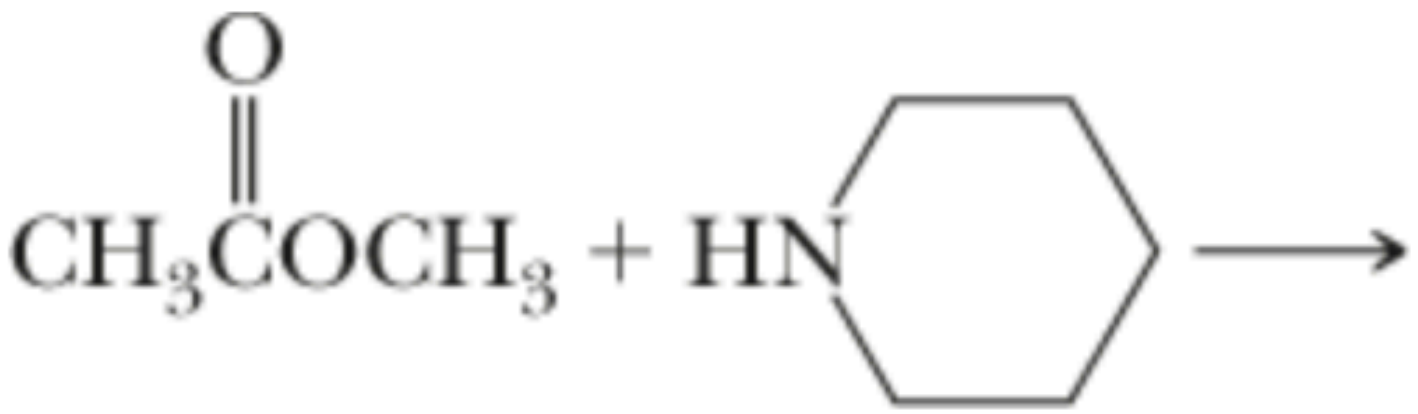
a.



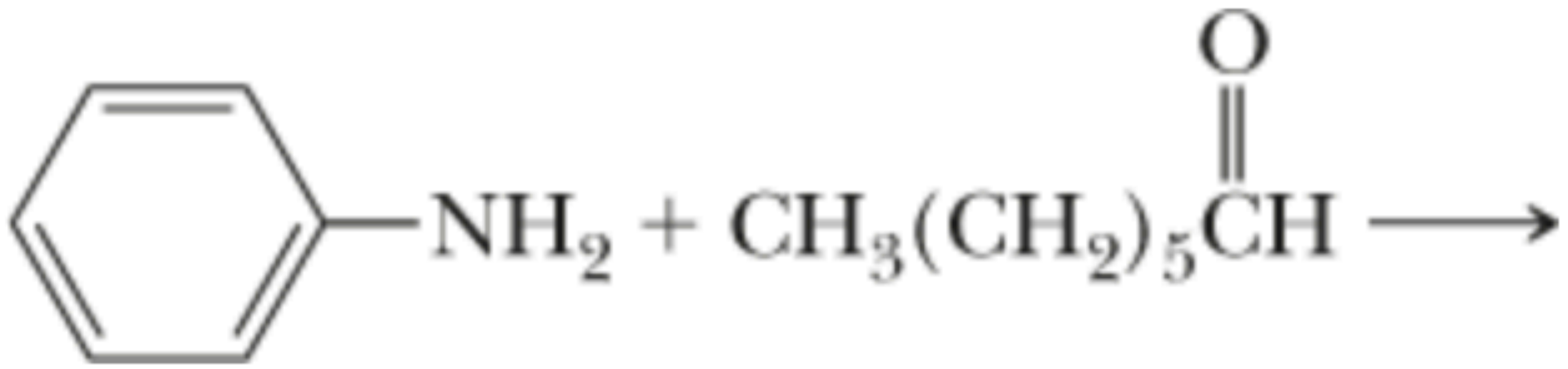
b.



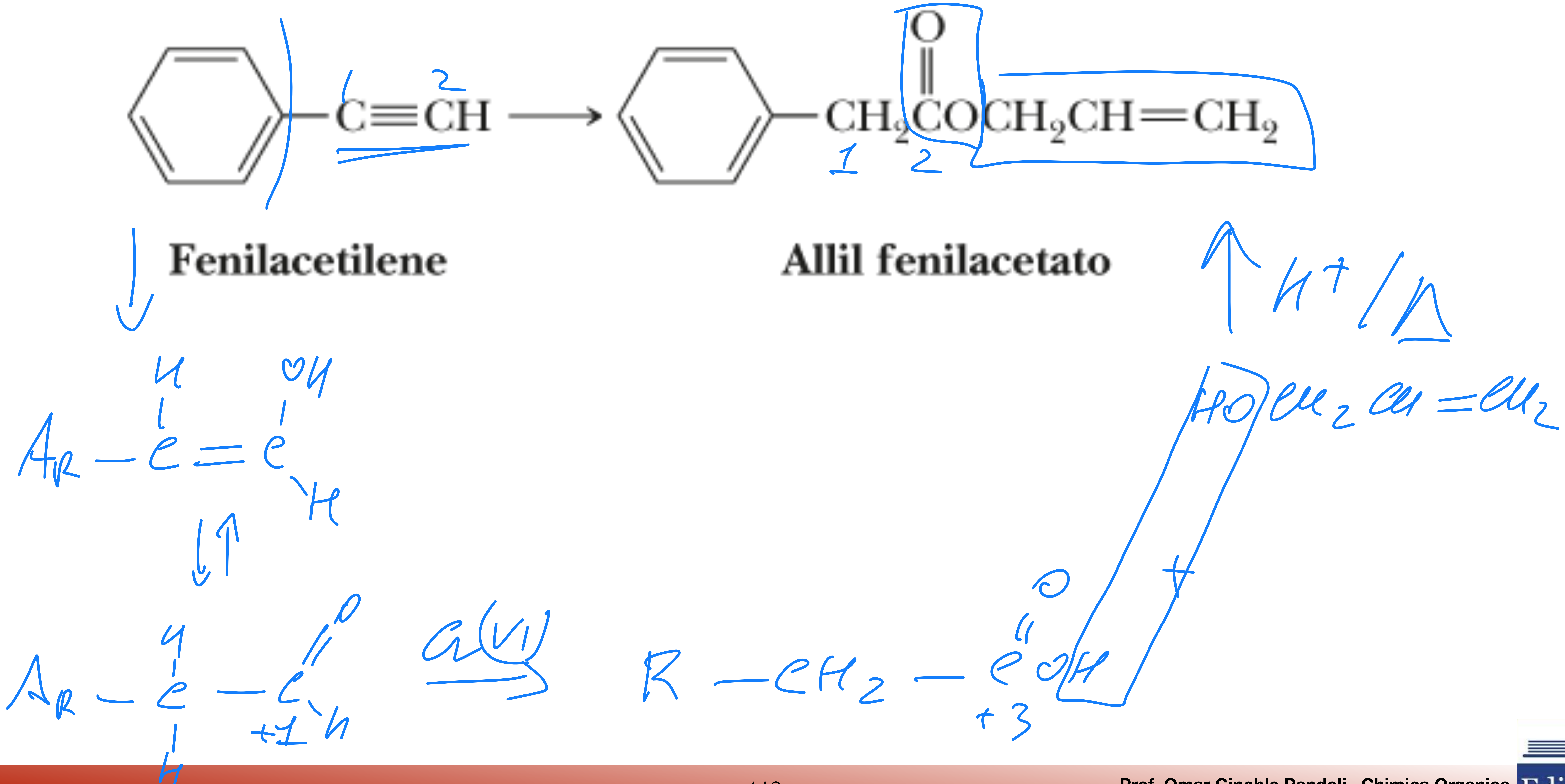
c.



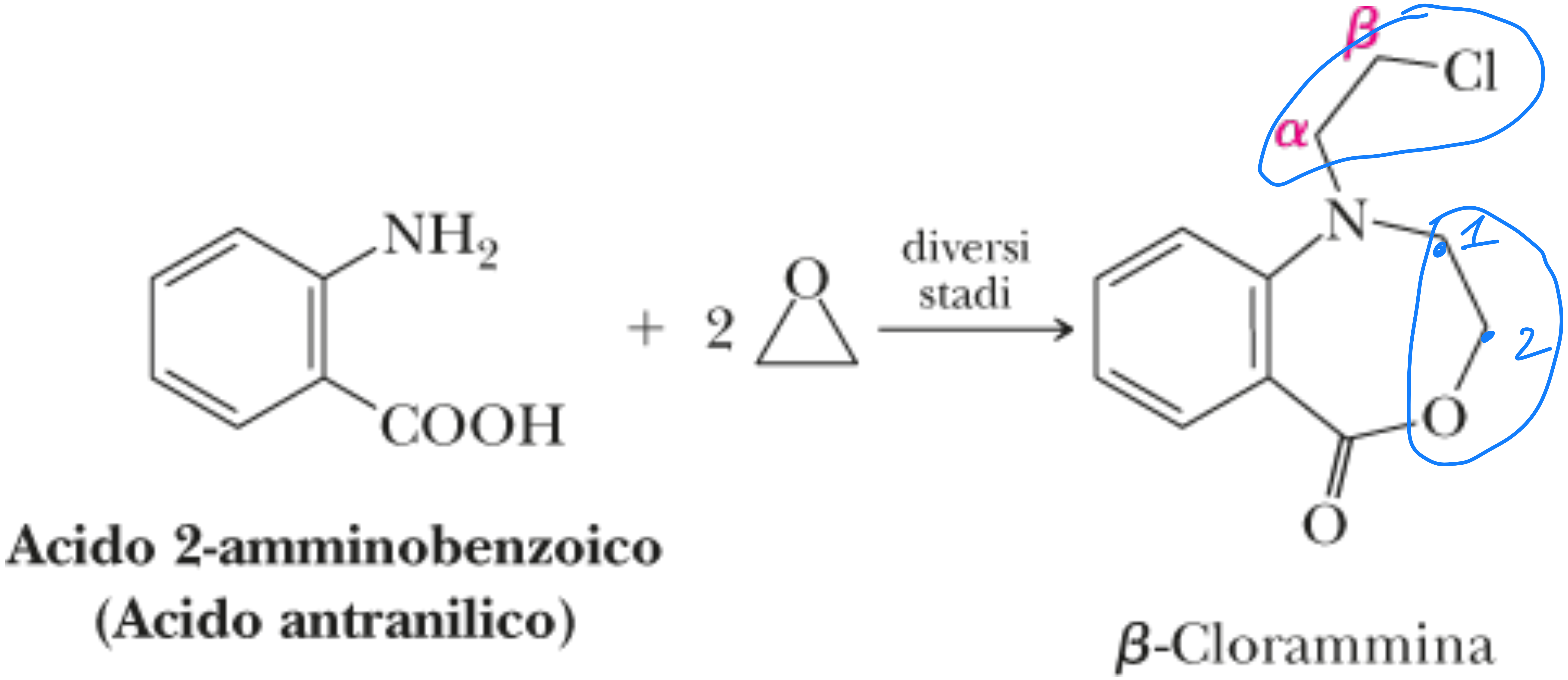
d.



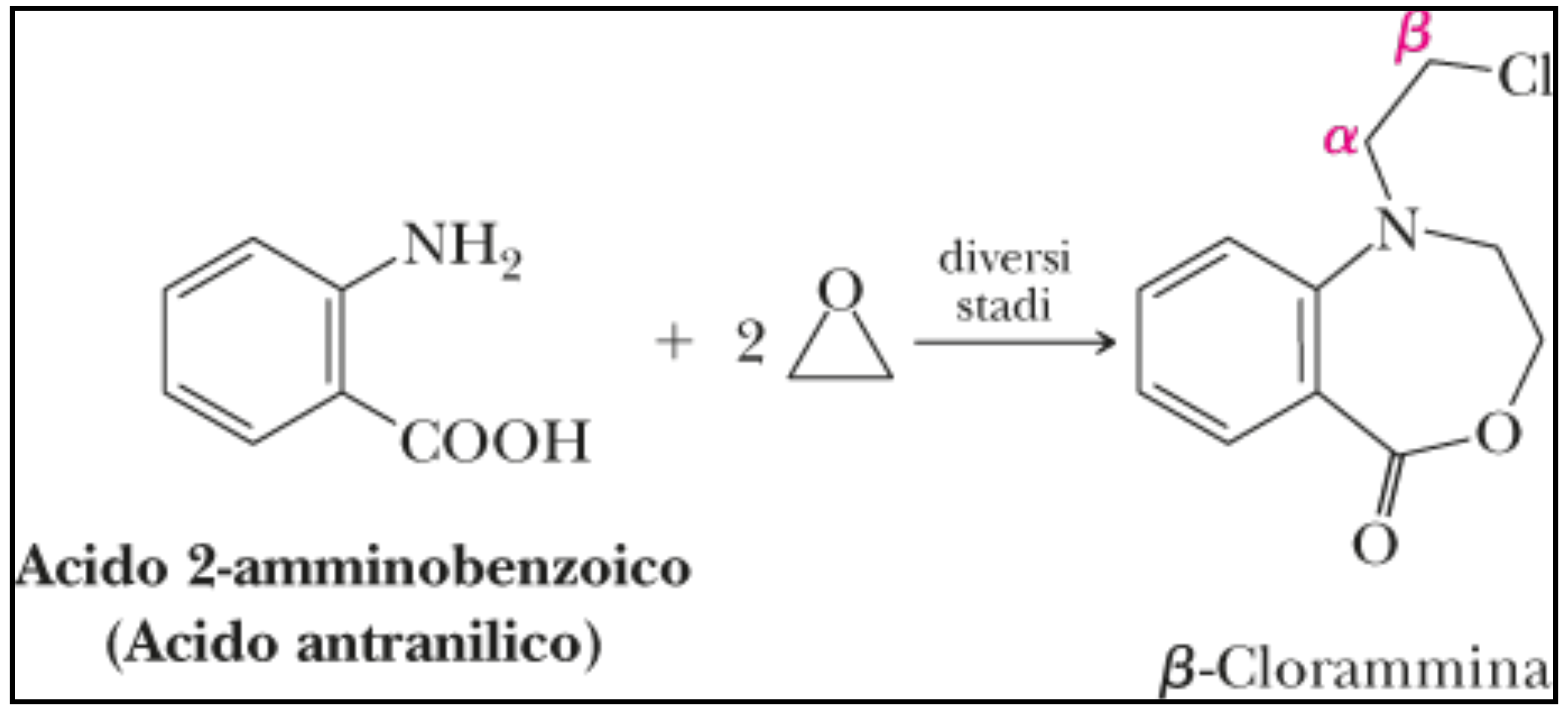
PROBLEMA: Suggerire come trasformare il fenilacetilene in fenilacetato di allile..



PROBLEMA: Il seguente composto appartiene alla famiglia delle β-clorammine, molte delle quali hanno attività antitumorale. Descrivere una sintesi di questo composto da acido antra-nilico e ossido di etilene.

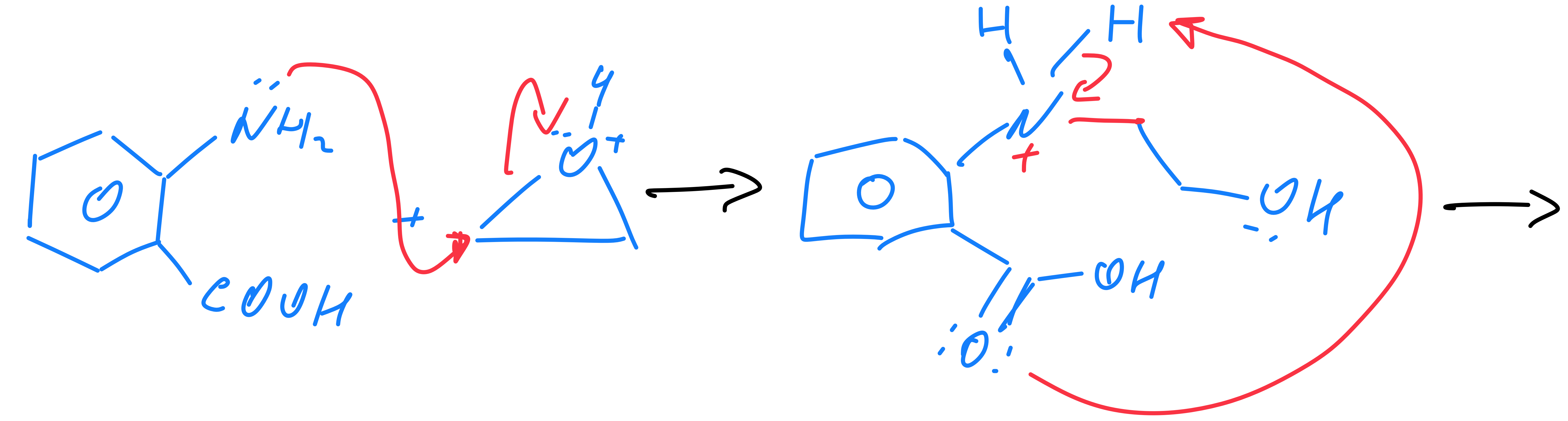


PROBLEMA: Il seguente composto appartiene alla famiglia delle β-clorammine, molte delle quali hanno attività antitumorale. Descrivere una sintesi di questo composto da acido antra-nilico e ossido di etilene.

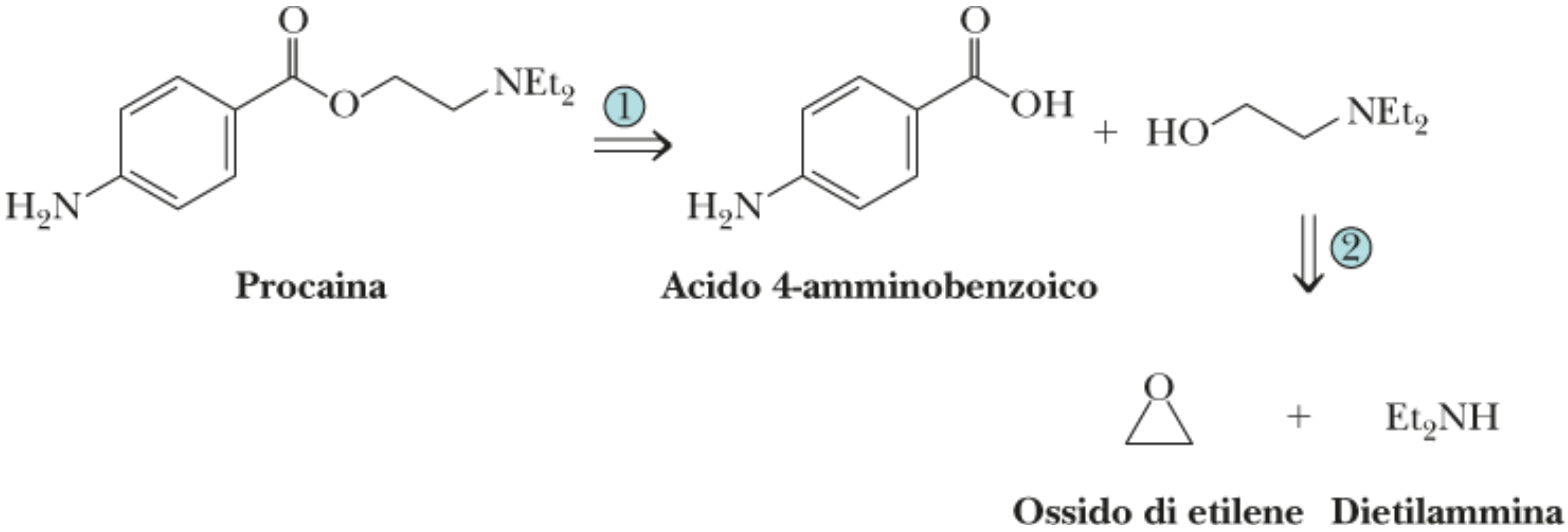


Acido 2-amminobenzoico
(Acido antranilico)

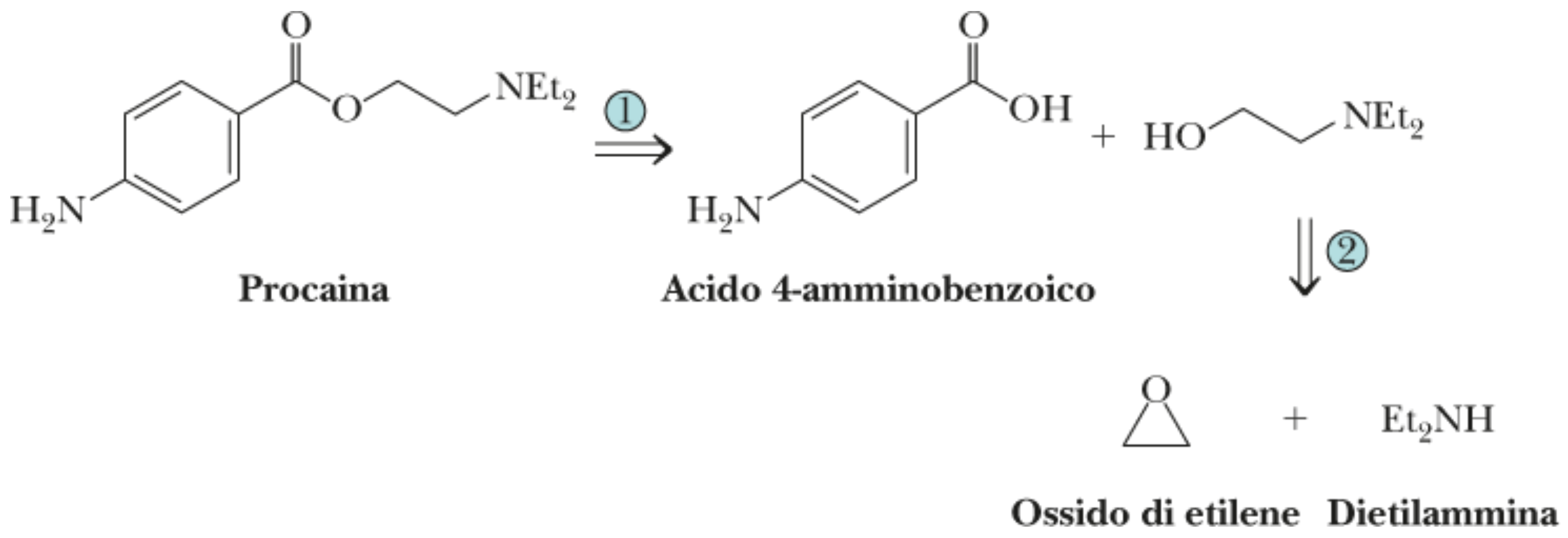
β-Clorammina



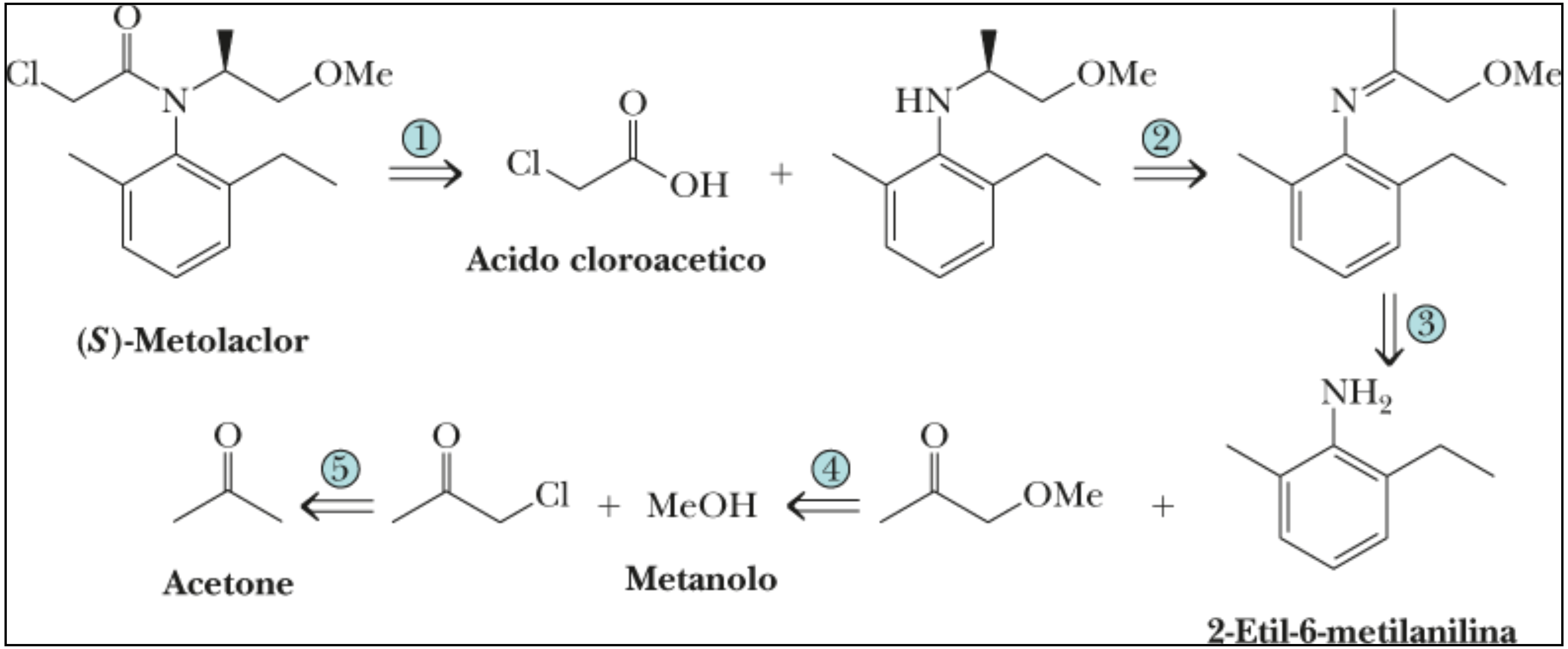
PROBLEMA: La procaina (il suo cloridrato è in commercio con il nome Novocaina) è stata uno dei primi anestetici per infiltrazione e nell'anestesia locale (vedi "Connessioni chimiche. Dalla cocaina alla procaina e oltre"). Secondo il seguente schema retrosintetico la procaina può essere preparata da acido 4-amminobenzoico, ossido di etilene e dietilam-mina come fonti di atomi di carbonio. Indicare i reagenti e le condizioni sperimentali per sintetizzare la procaina da questi tre composti.



PROBLEMA: La procaina (il suo cloridrato è in commercio con il nome Novocaina) è stata uno dei primi anestetici per infiltrazione e nell'anestesia locale (vedi "Connessioni chimiche. Dalla cocaina alla procaina e oltre"). Secondo il seguente schema retrosintetico la procaina può essere preparata da acido 4-amminobenzoico, ossido di etilene e dietilam-mina come fonti di atomi di carbonio. Indicare i reagenti e le condizioni sperimentali per sintetizzare la procaina da questi tre composti.



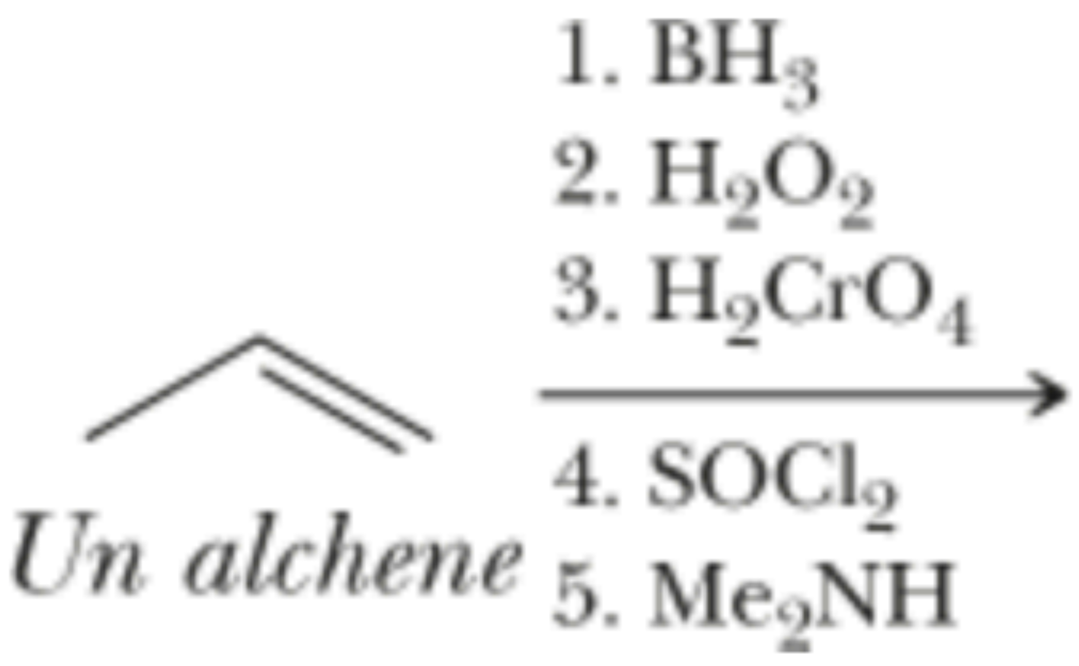
PROBLEMA: Quella che segue è l'analisi retrosintetica della sintesi dell'erbicida (S)-Metolaclor partendo da 2-etil-6-metilanilina, acido cloroacetico, acetone e metanolo.



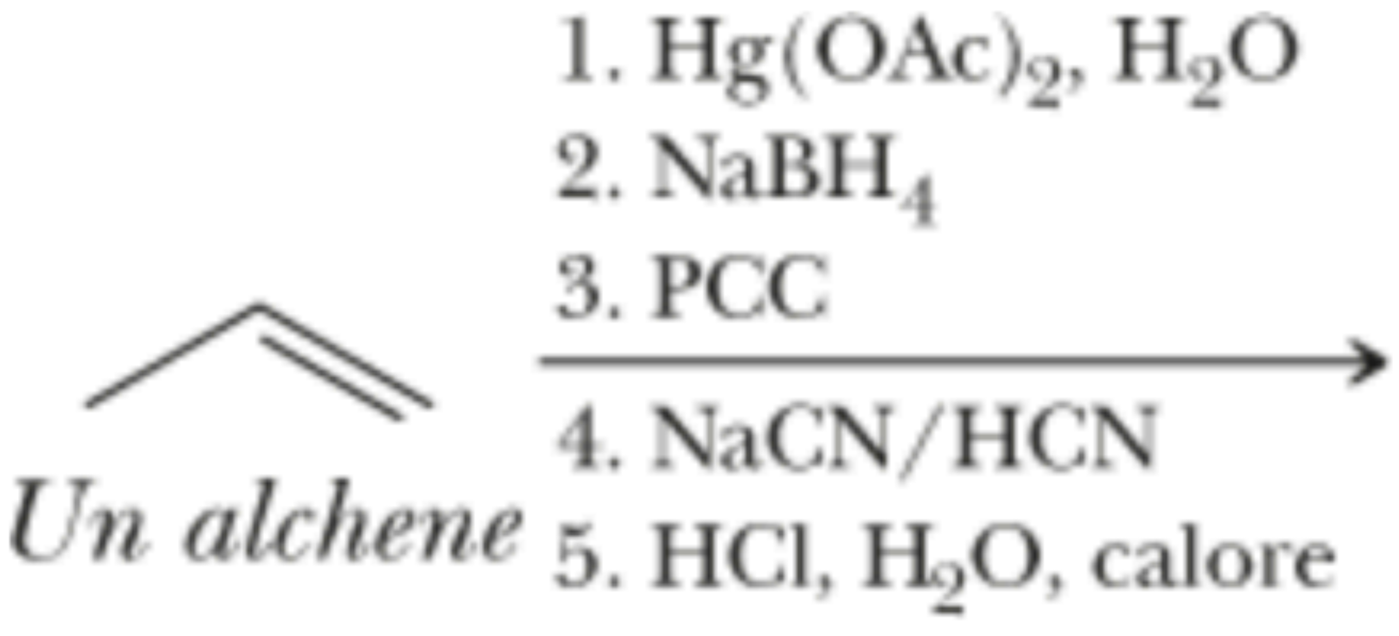
Indicare i reagenti e le condizioni sperimentali per la sintesi del Metolaclor a partire da questi quattro composti organici. La sintesi porterà verosimilmente a una miscela race-mica. Il catalizzatore chirale usato dalla Novartis per la riduzione del passaggio 2 porta a un arricchimento dell'80% nell'enantiomero S.

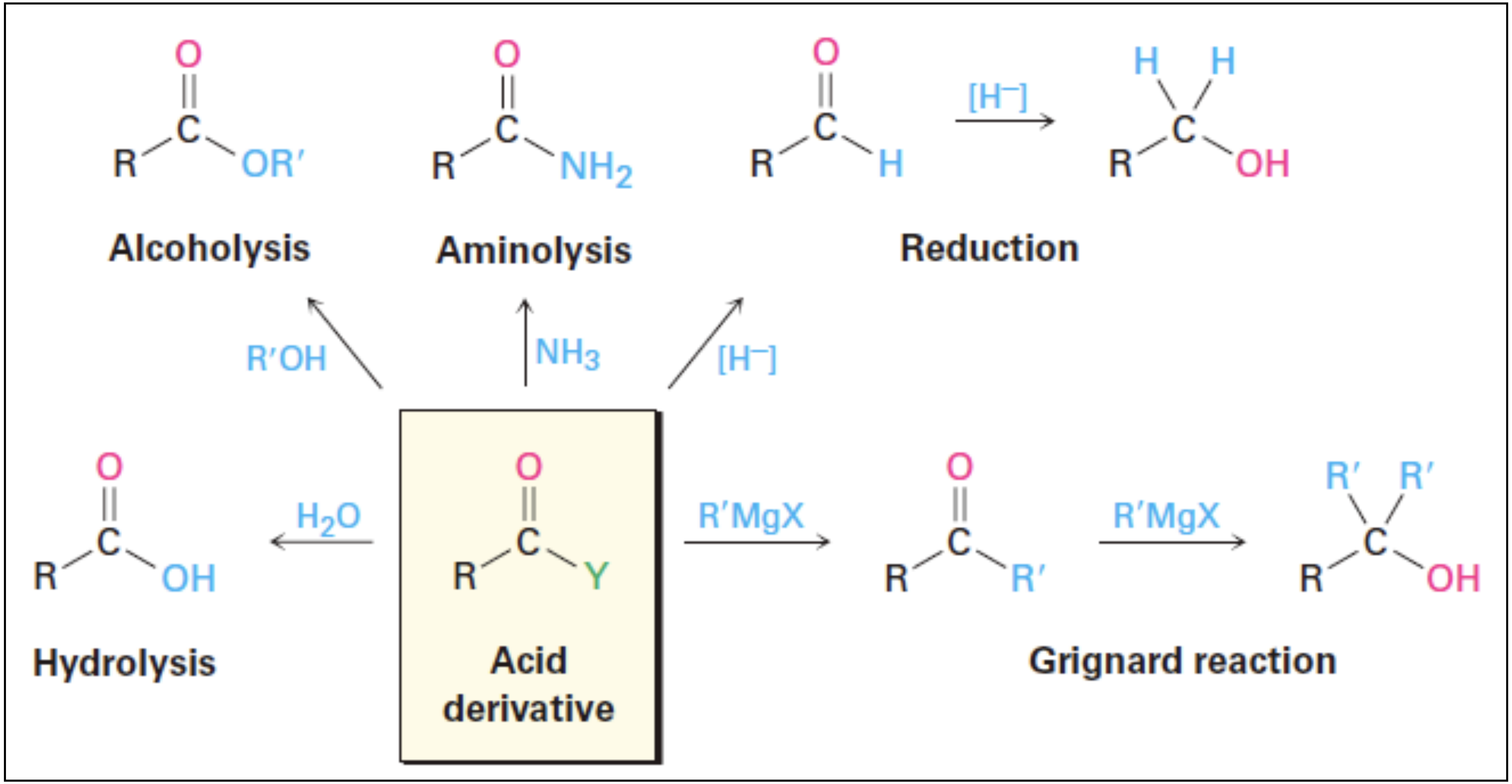
PROBLEMA: Indicare i prodotti delle seguenti reazioni. Fare riferimento alla propria mappa per verificare come, combinando le reazioni, si possa “navigare” tra i vari gruppi funzionali.

a.



b.

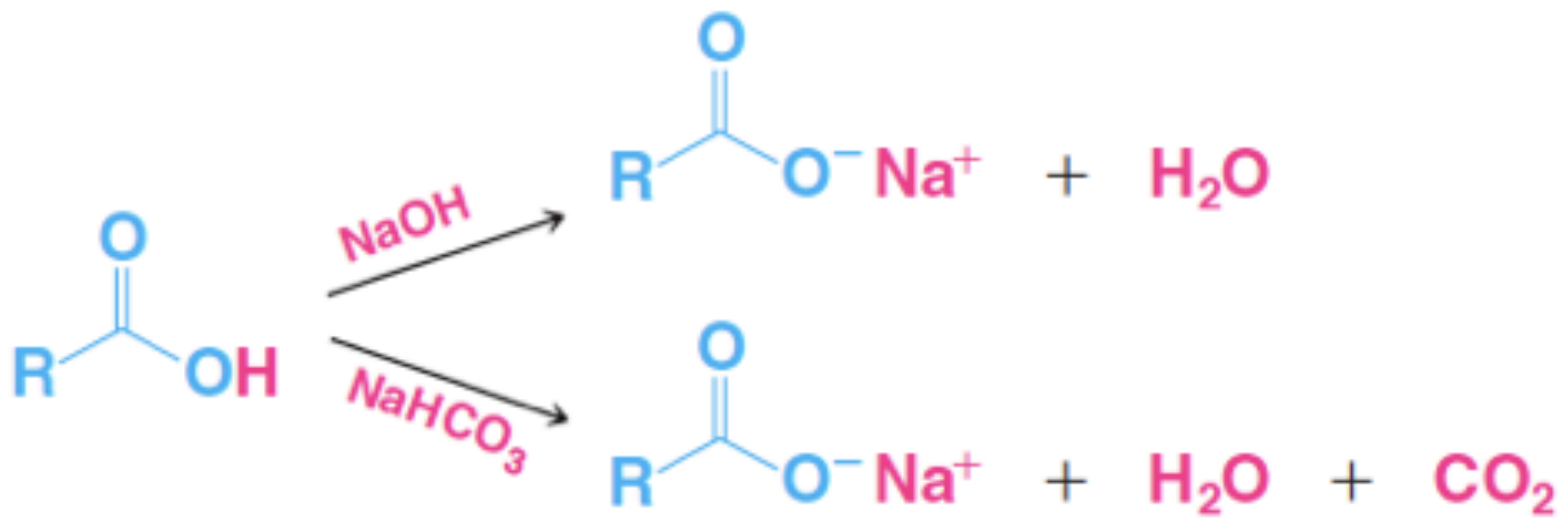



Alcoholysis
Aminolysis
Reduction
R′OH
NH_3
[H⁻]
[H⁻]
H_2O
R′MgX
R′MgX
Hydrolysis
Acid derivative
Grignard reaction
R, C, O, OR′
R, C, O, NH_2
R, C, O, H
R, C, H, H, OH
R, C, O, OH
R, C, O, Y
R, C, O, R′
R, C, R′, R′, OH

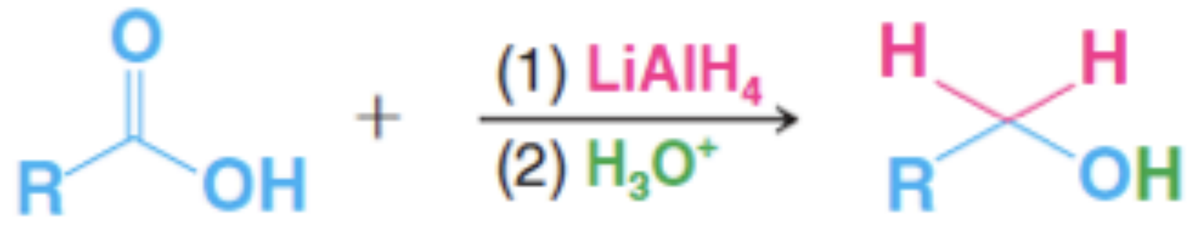
Riepilogo delle reazioni

Di acidi carbossilici

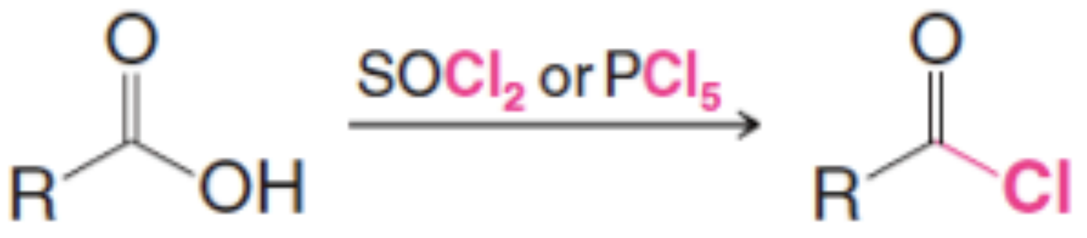
1. As acids (discussed in Sections 3.11 and 17.2C):



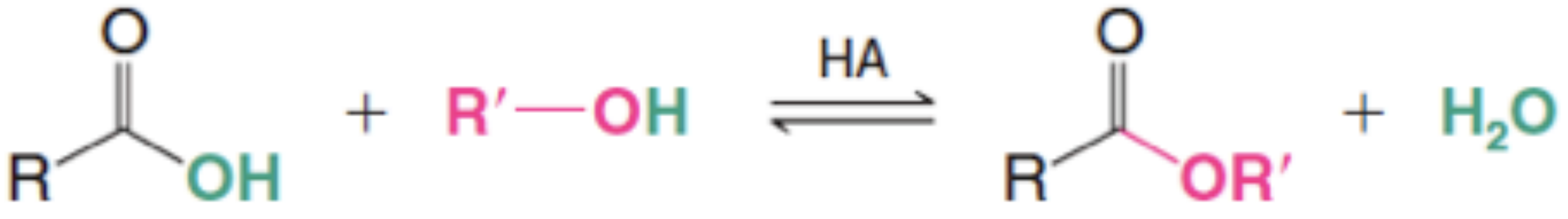
2. Reduction (discussed in Section 12.3):



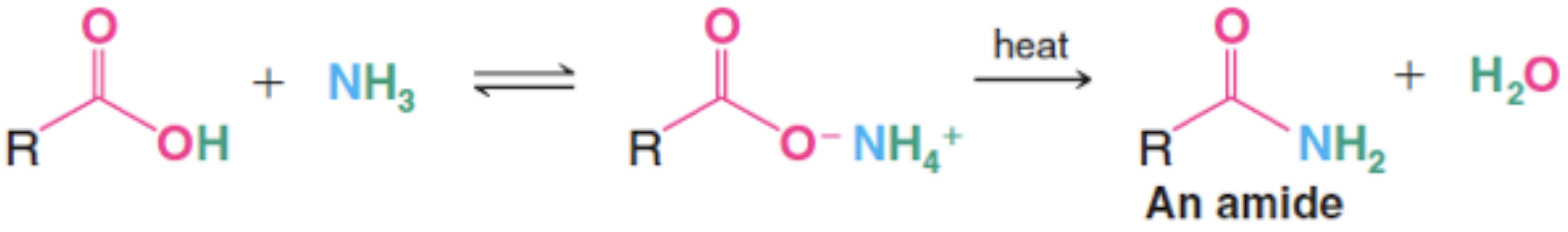
3. Conversion to acyl chlorides (discussed in Section 17.5):



4. Conversion to esters (Fischer esterification) or lactones (discussed in Section 17.7A):

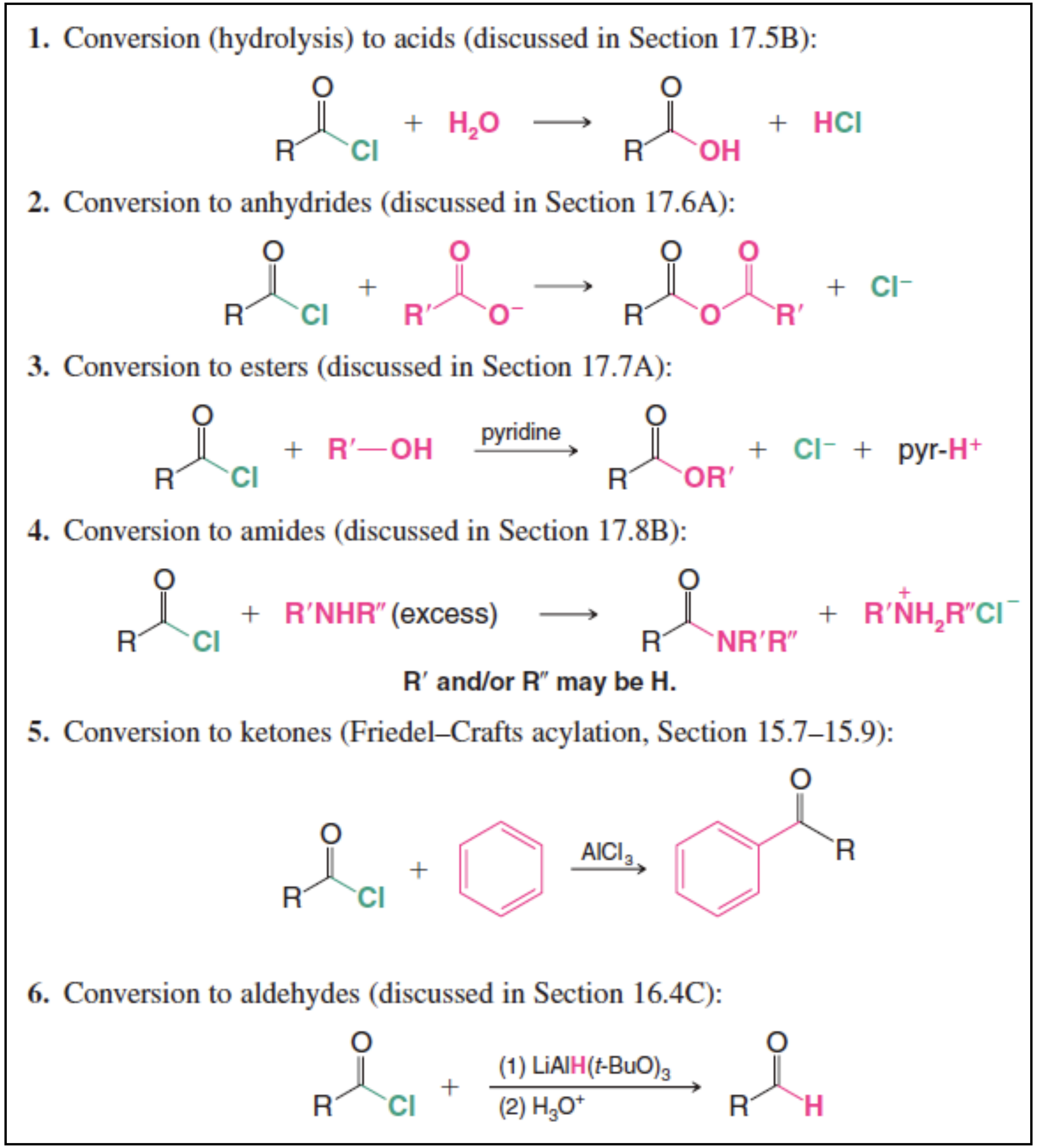


5. Conversion to amides (discussed in Section 17.8E):



Riepilogo delle reazioni

Dei cloruri acilici



1. Conversion (hydrolysis) to acids (discussed in Section 17.5B):

2. Conversion to anhydrides (discussed in Section 17.6A):

3. Conversion to esters (discussed in Section 17.7A):

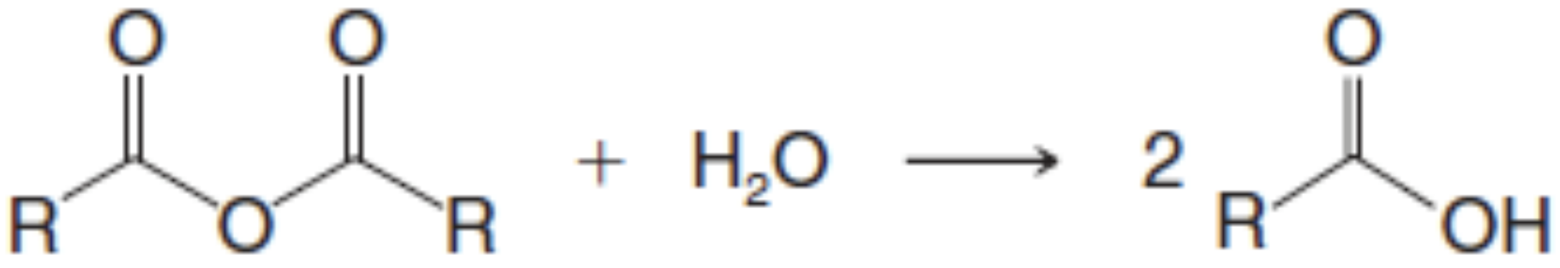
4. Conversion to amides (discussed in Section 17.8B):

R′ and/or R″ may be H.

5. Conversion to ketones (Friedel–Crafts acylation, Section 15.7–15.9):

6. Conversion to aldehydes (discussed in Section 16.4C):

1. Conversion (hydrolysis) to acids (discussed in Section 17.6B):

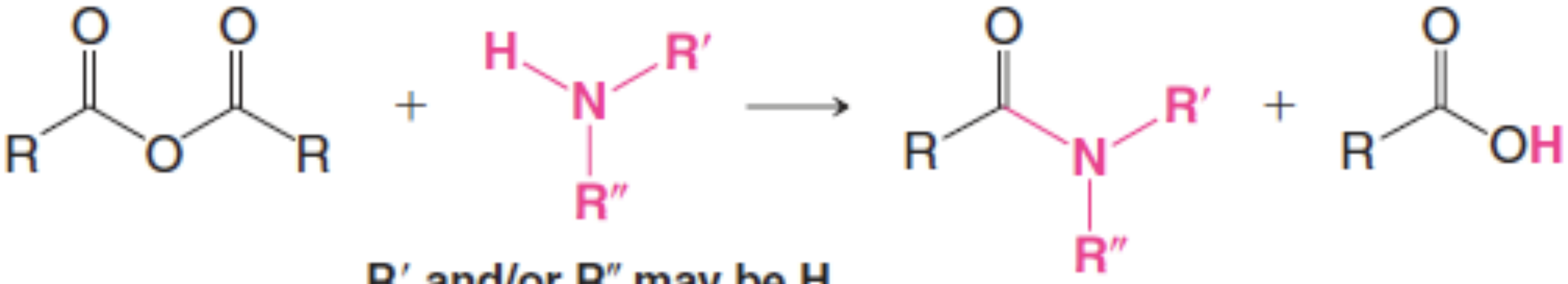


2. Conversion to esters (discussed in Sections 17.6B and 17.7A):

Riepilogo delle reazioni

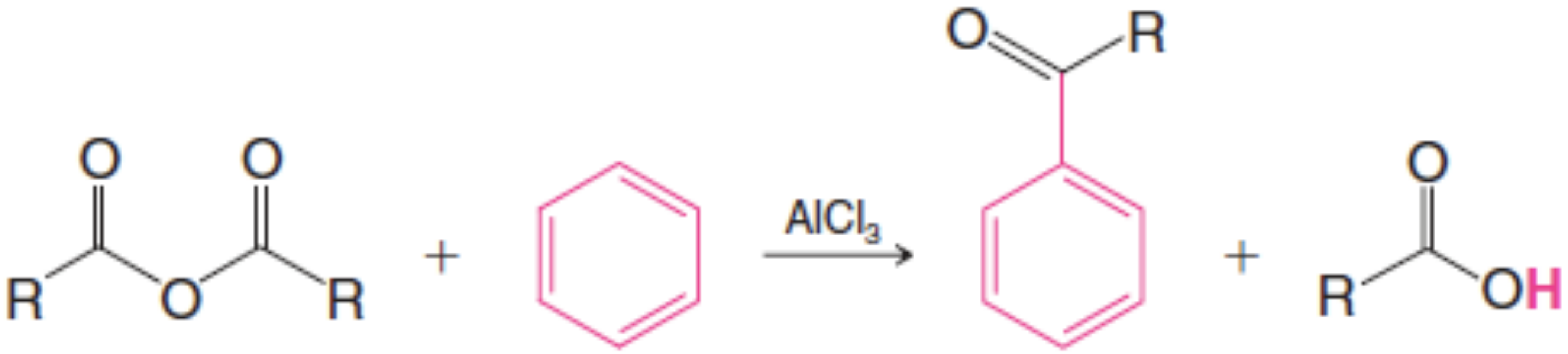
Delle anidridi

3. Conversion to amides (discussed in Section 17.8C):



R′ and/or R″ may be H.

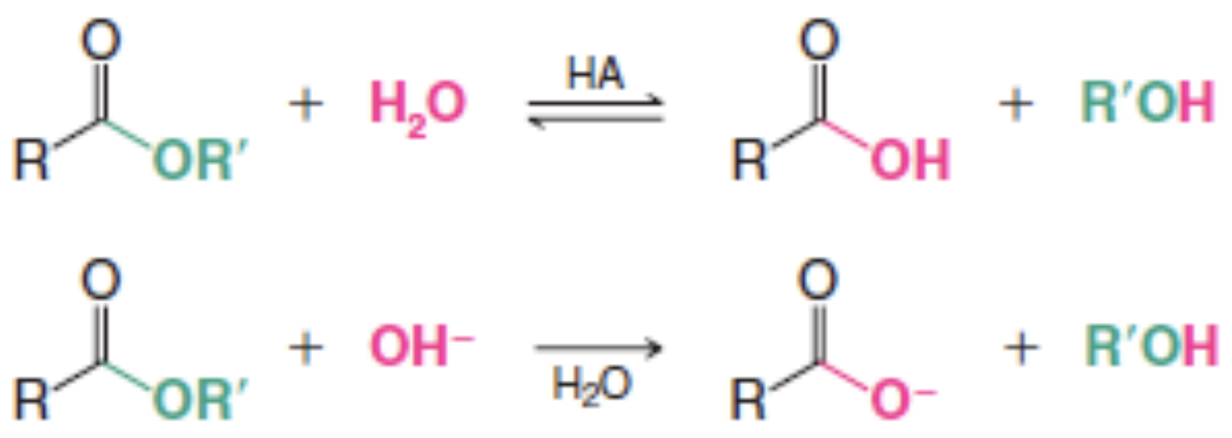
4. Conversion to aryl ketones (Friedel–Crafts acylation, Sections 15.7–15.9):



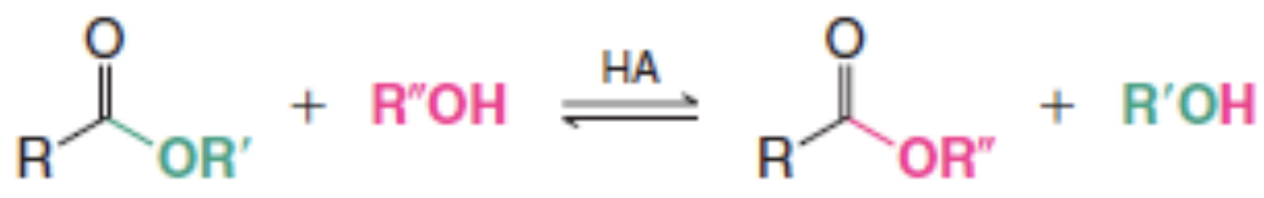
Riepilogo delle reazioni

Degli esteri

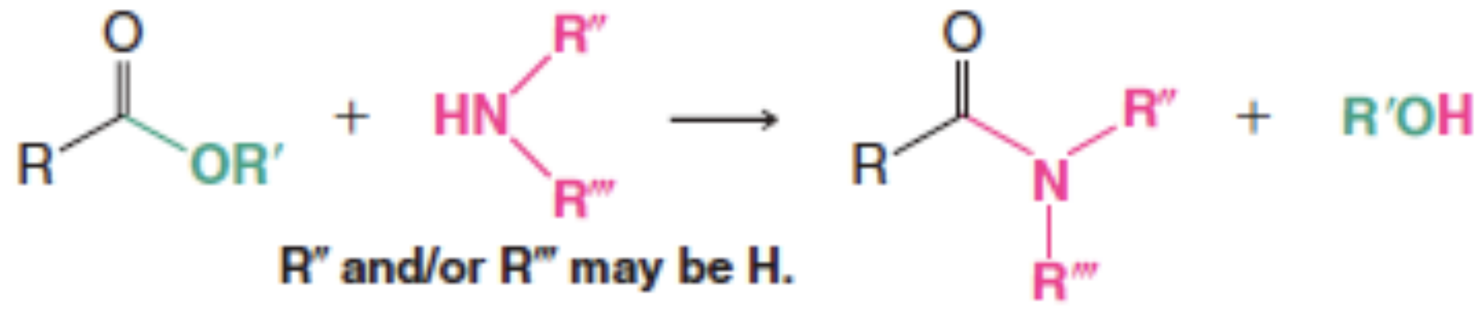
1. Hydrolysis (discussed in Section 17.7B):



2. Conversion to other esters: transesterification (discussed in Review Problem 17.10):



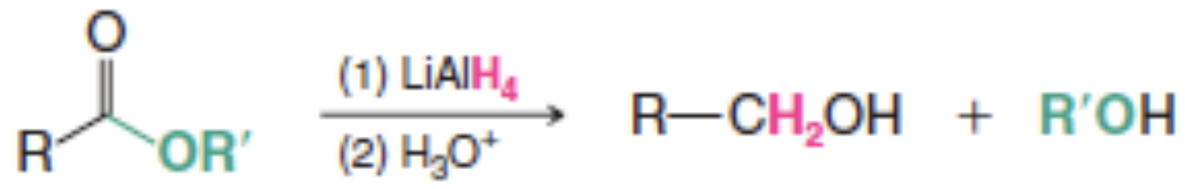
3. Conversion to amides (discussed in Section 17.8D):



R″ and/or R‴ may be H.

4. Reaction with Grignard reagents (discussed in Section 12.8):

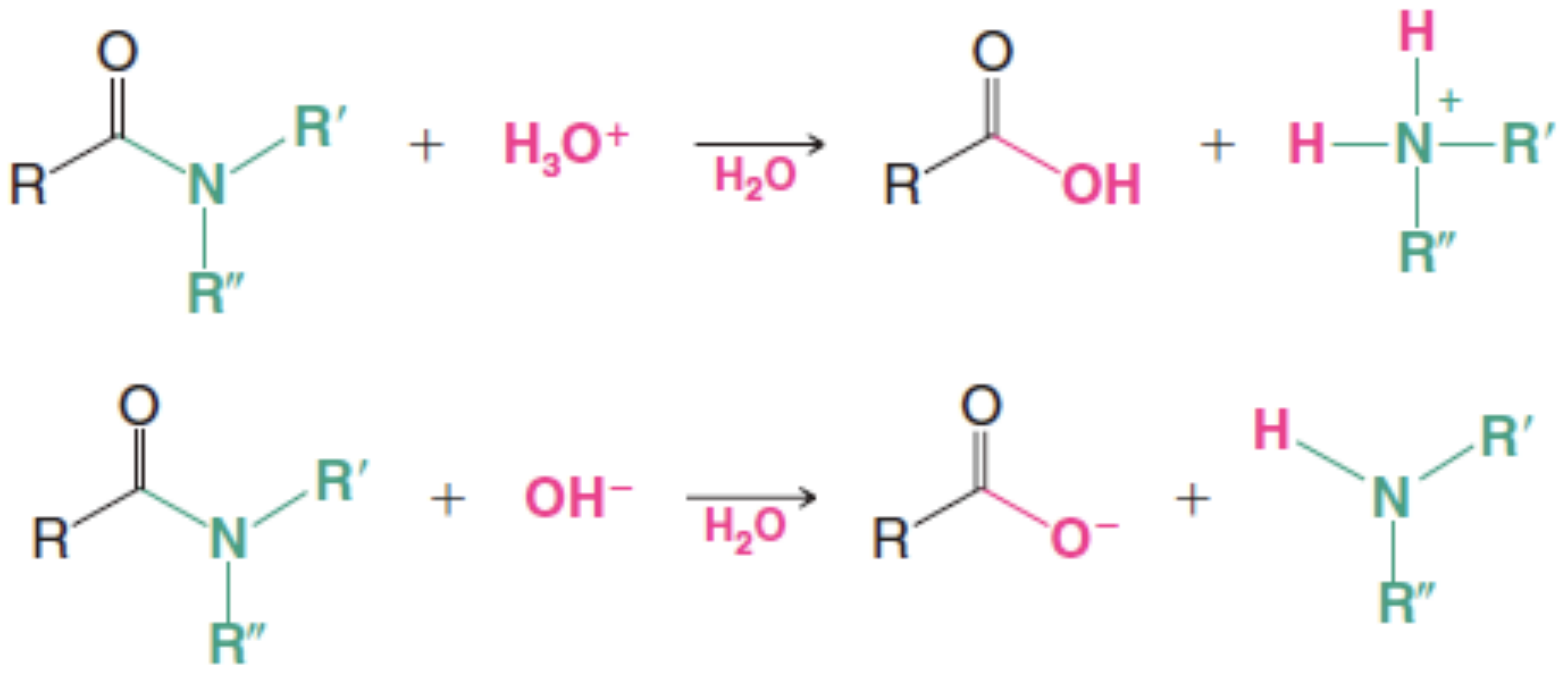
5. Reduction (discussed in Section 12.3):



Riepilogo delle reazioni

Delle ammidi

1. Hydrolysis (discussed in Section 17.8F):

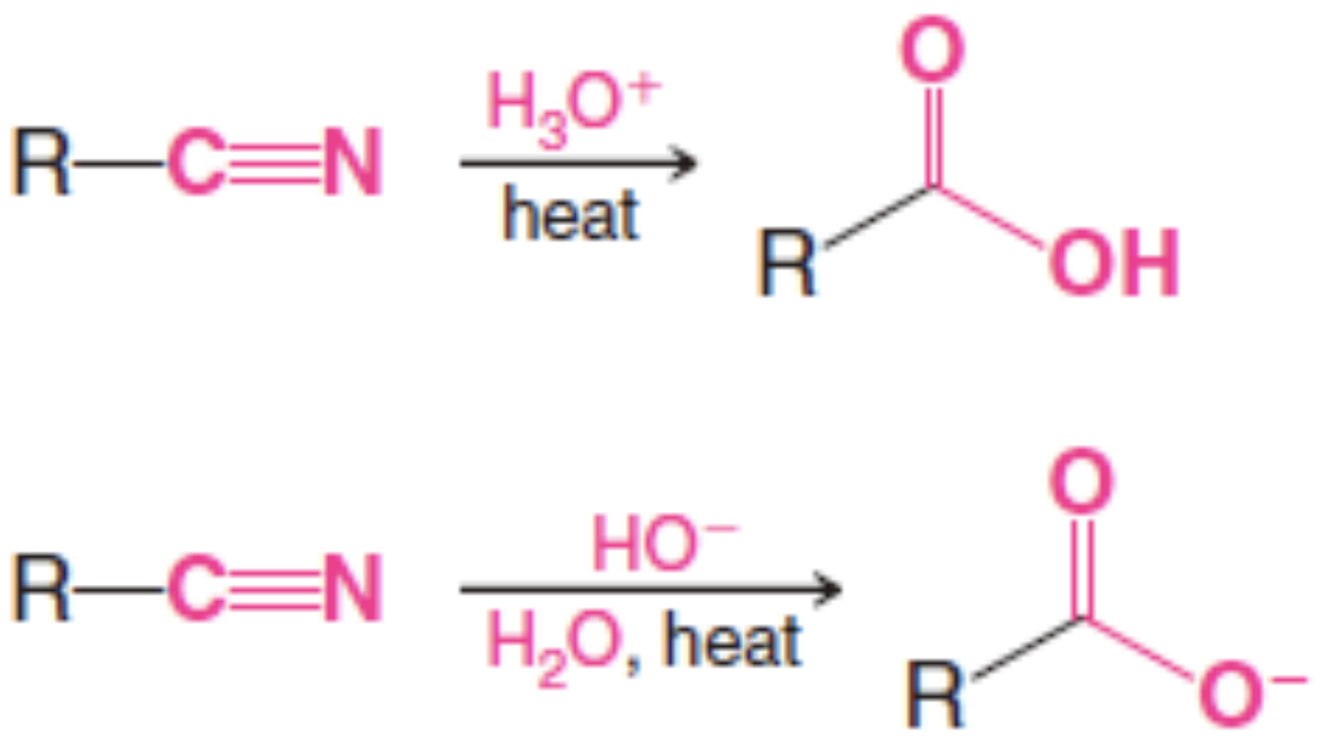


R, R′, and/or R″ may be H.

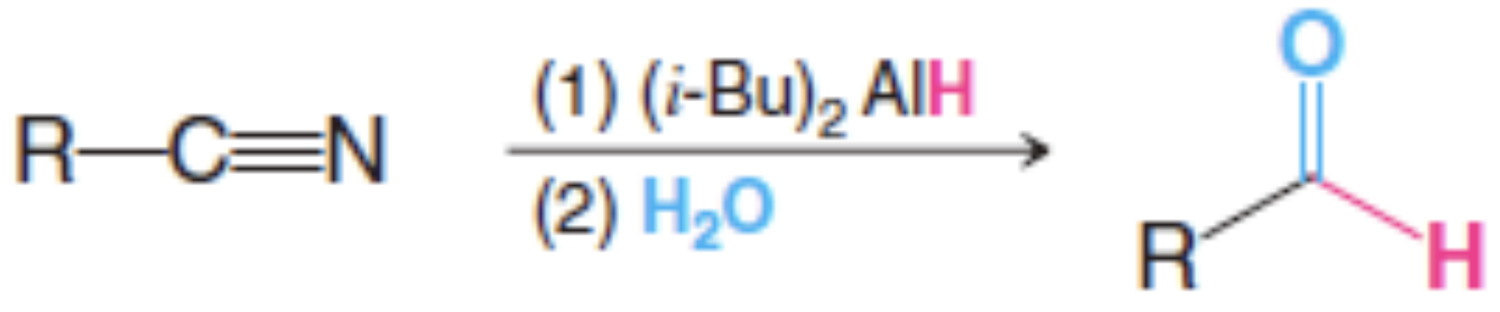
Riepilogo delle reazioni

Dei nitrili

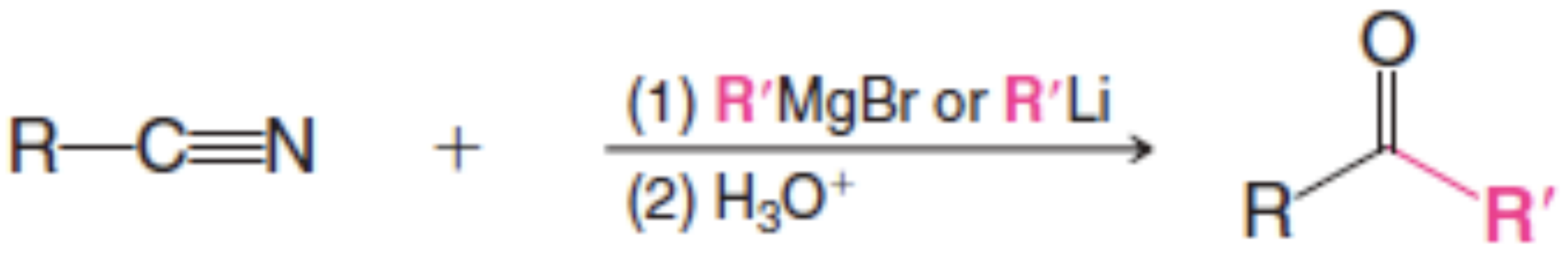
1. Hydrolysis to a carboxylic acid or carboxylate anion (Section 17.8H):



2. Reduction to an aldehyde with $(i\text{-Bu})_2AlH$ (DIBAL-H, Section 16.4C):



3. Conversion to a ketone by a Grignard or organolithium reagent (Section 16.5B):



11. Reazioni degli acidi carbossilici e dei derivati degli acidi carbossilici

(1) Struttura, proprietà fisiche degli acidi carbossilici;

(2) Struttura e reattività dei derivati degli acidi carbossilici (cloruro acilico, anidride, estere e ammide).

(3) Problemi