Chimie Biologique

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http://sondesfluorescentes.unice.fr/etudiants/L2SV/portail-l2sv.html

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La chimie des lipides

Les triacylglycérols

Les terpénoïdes

Les stéroïdes

Les triacylglycérols

– Les acides gras

- Présents dans les graisses animales et végétales, les huiles végétales ou les cires, sous forme d'esters, les triglycérides

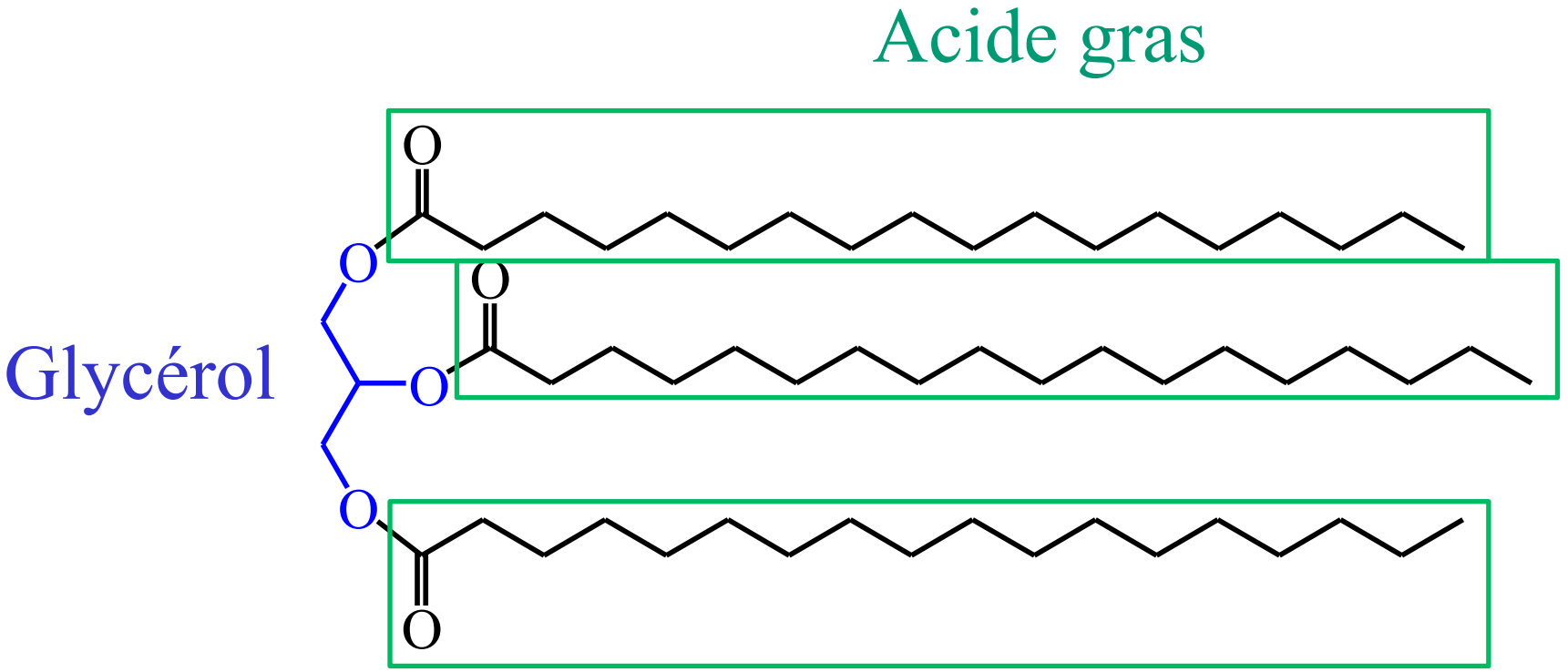
- Rôle structurel important à travers divers types de lipides, organisation en réseaux bidimensionnels structurant toutes les membranes biologiques

- Constituent une source importante d'énergie métabolique : les acides gras stockage 37 kJ d'énergie (9 kcal) par gramme de lipides

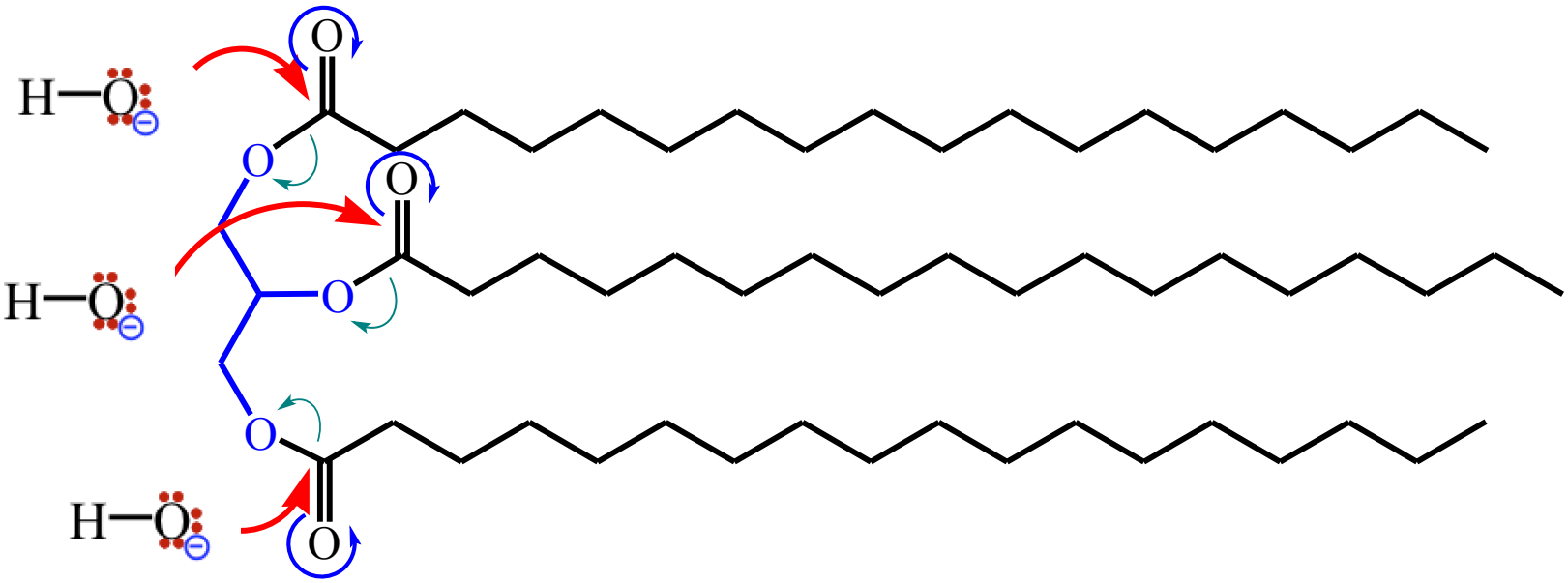
- Leur dégradation par la β-oxydation suivie du cycle de Krebs produit de grandes quantités d'ATP, molécule énergétique privilégiée des cellules

- Peuvent être synthétisés par l'organisme => processus métabolique (lipogenèse). Apportés en grandes quantités par l'alimentation

Les triacylglycérols (triglycérides) :

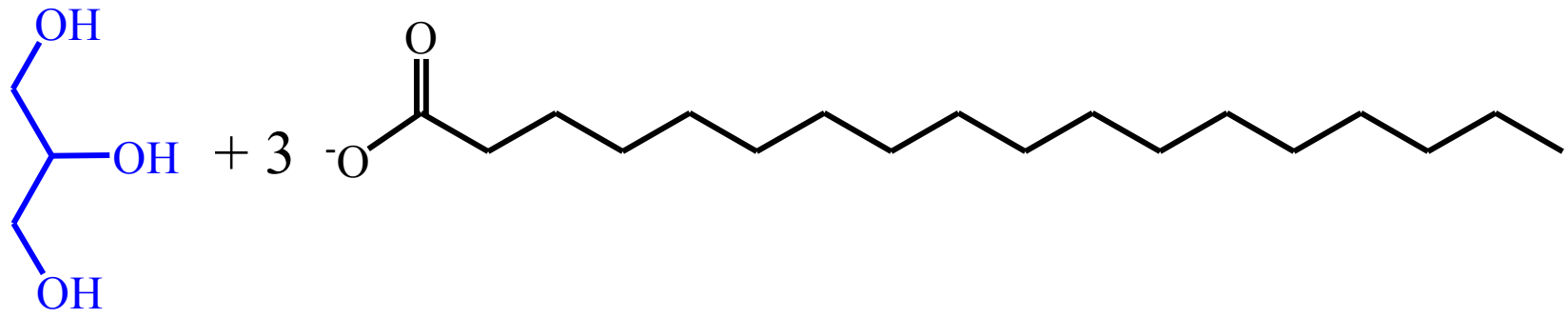


La saponification



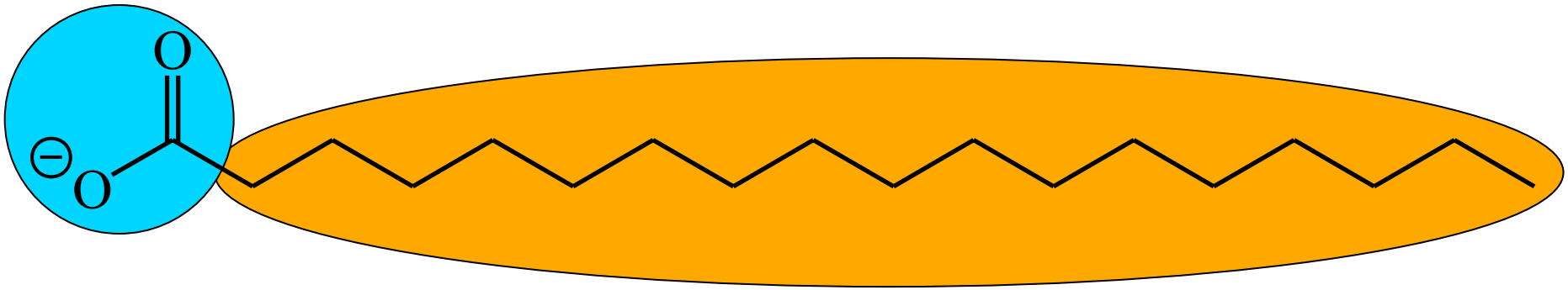
Hydrolyse basique d'un ester

Glycérol



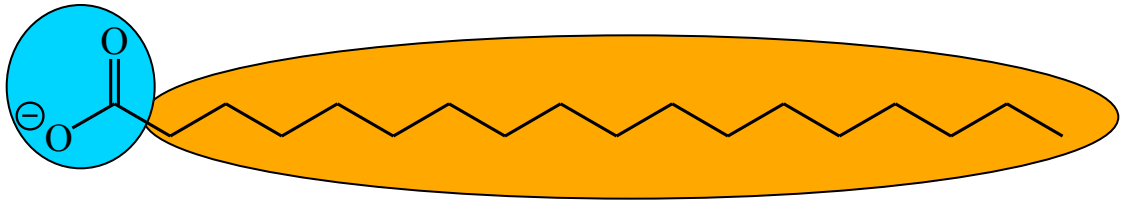
Les acides gras

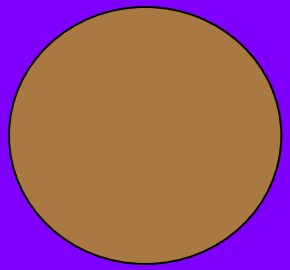
Tête
hydrophile



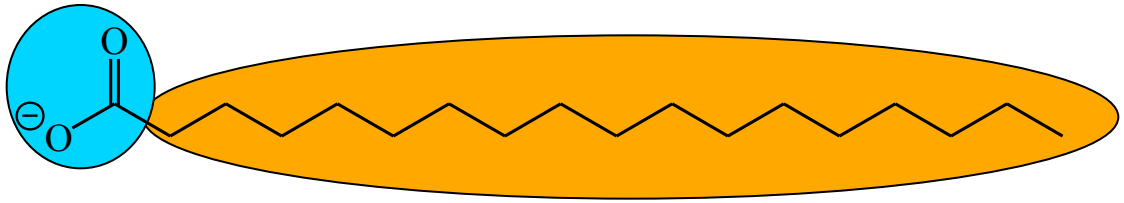
Queue hydrophobe

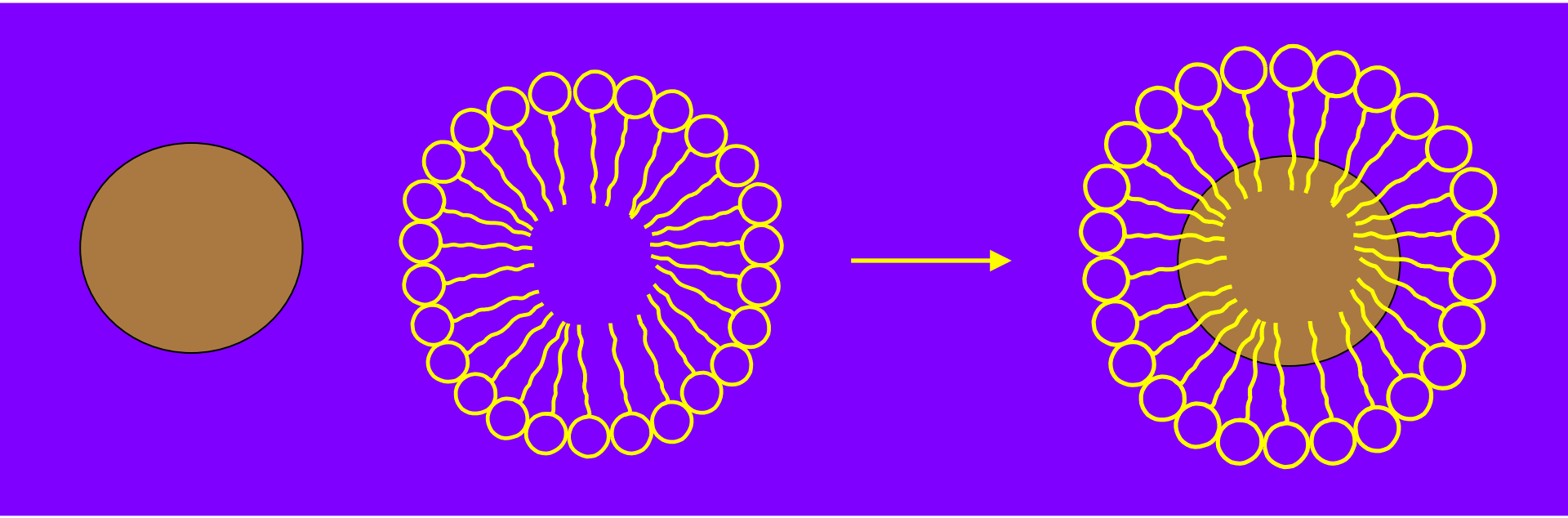
Les savons



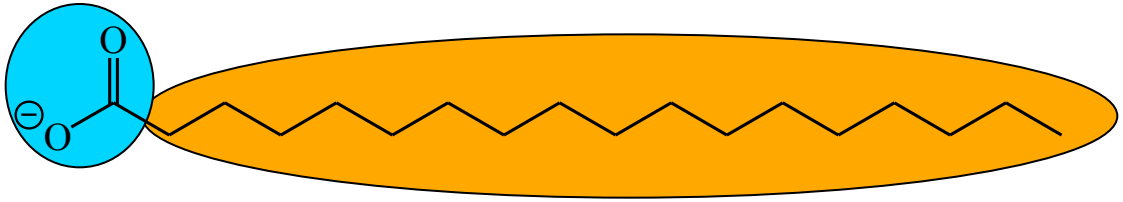


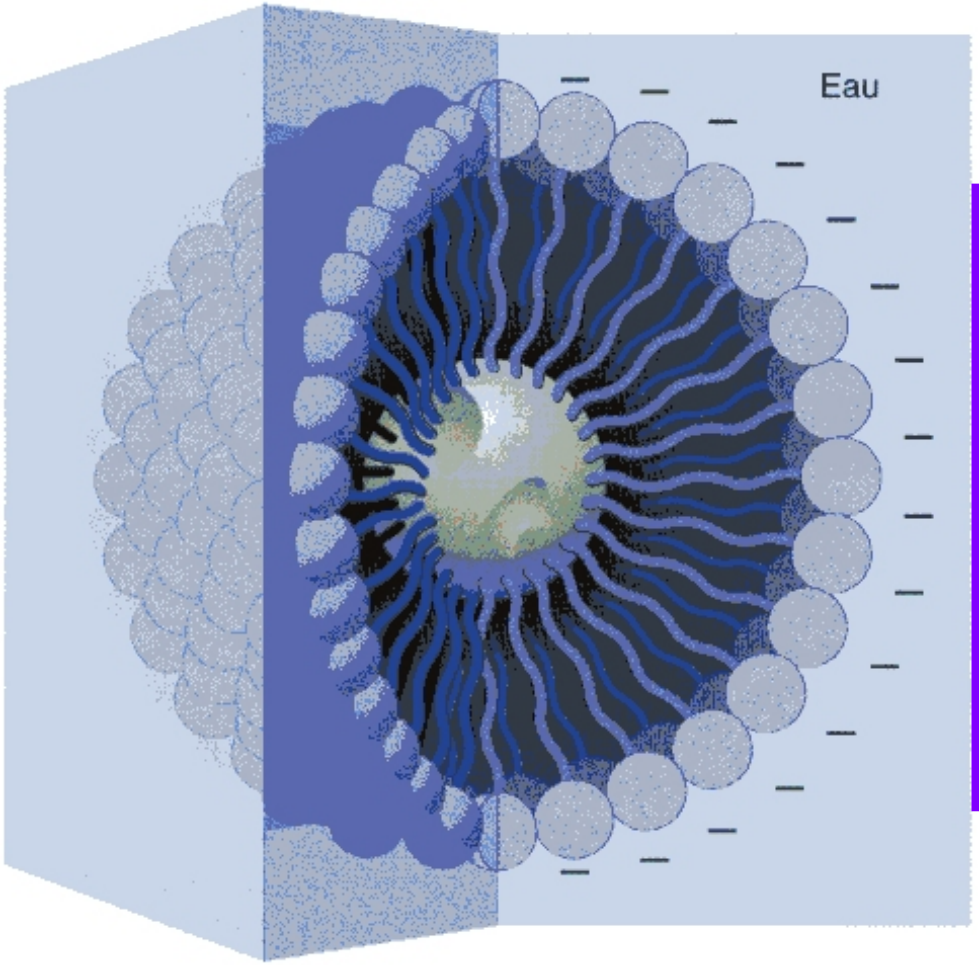
Les savons

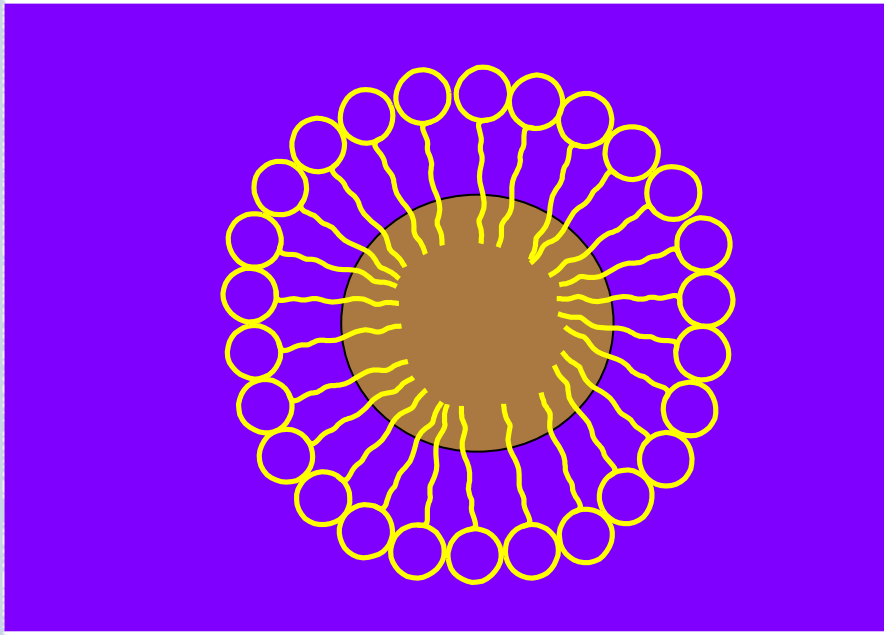




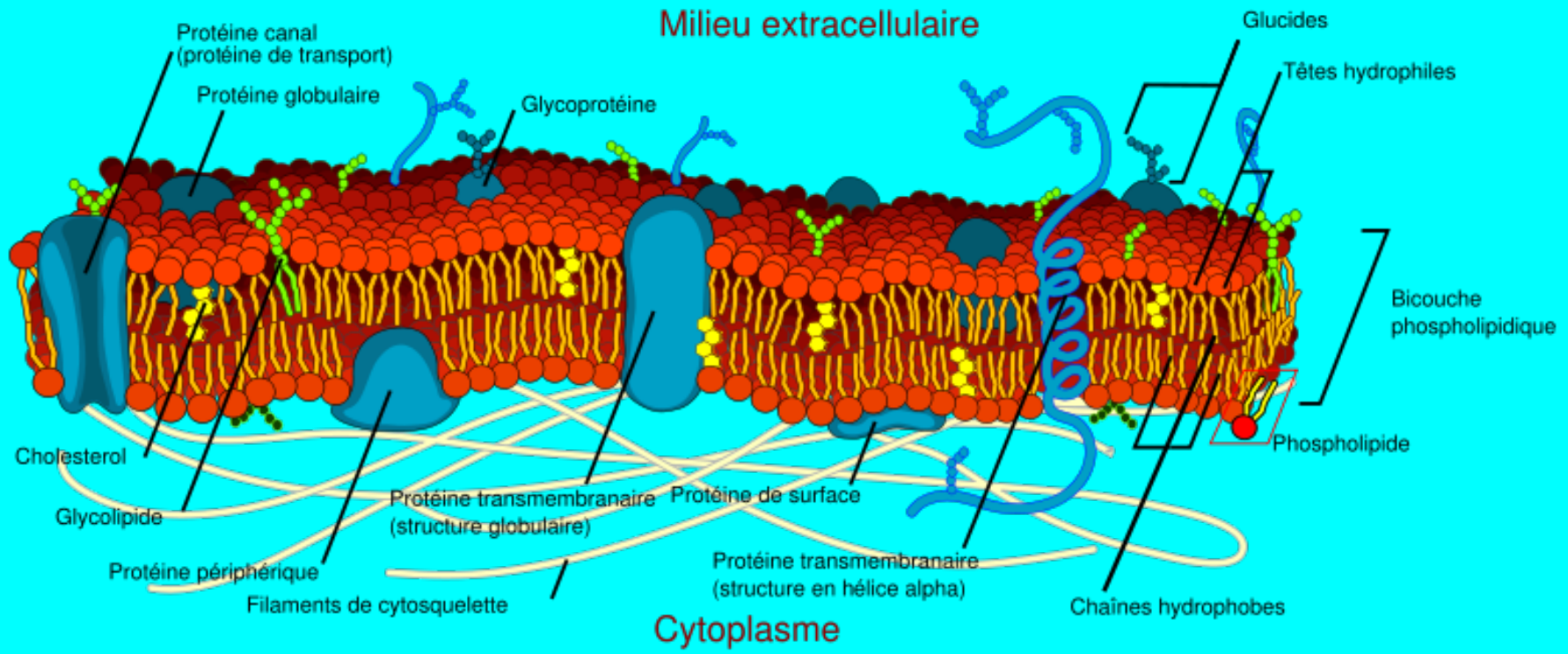
Les savons



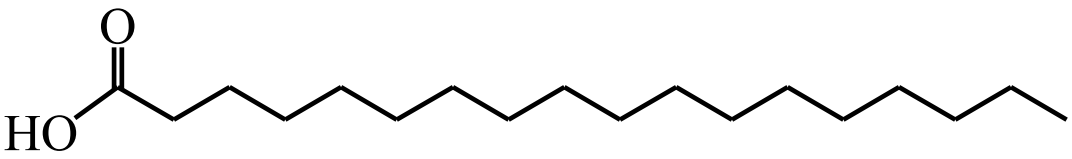




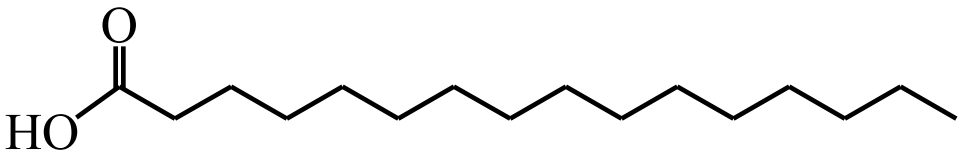
Les membranes



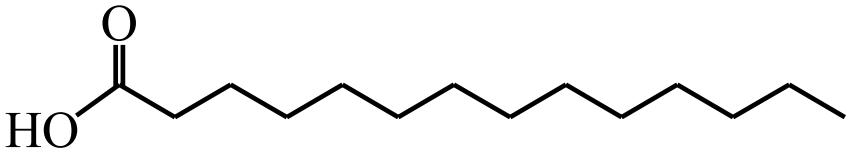
Les acides gras essentiels :



Acide stéarique (C18:0)

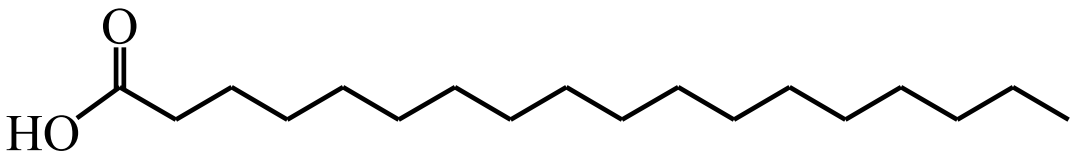


Acide palmitique (C16:0)

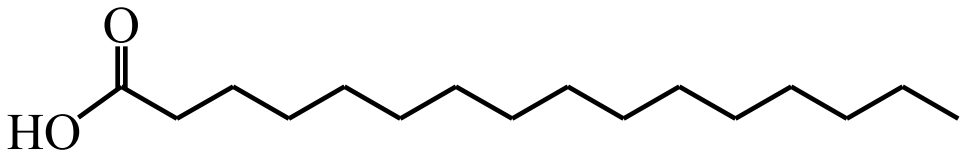


Acide myristique (C14:0)

Les acides gras essentiels :



Acide stéarique (C18:0)



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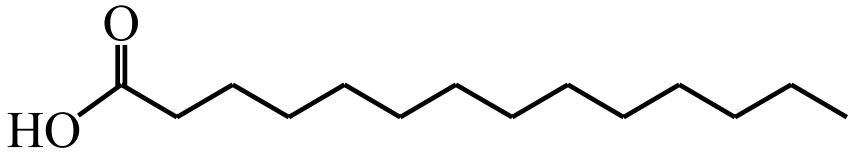

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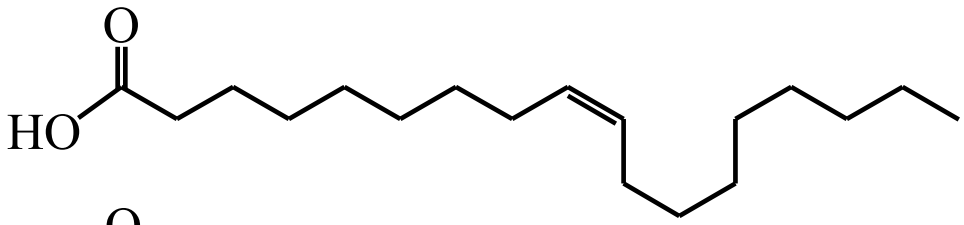
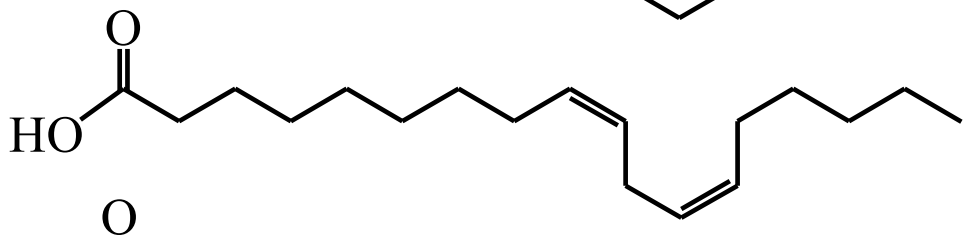
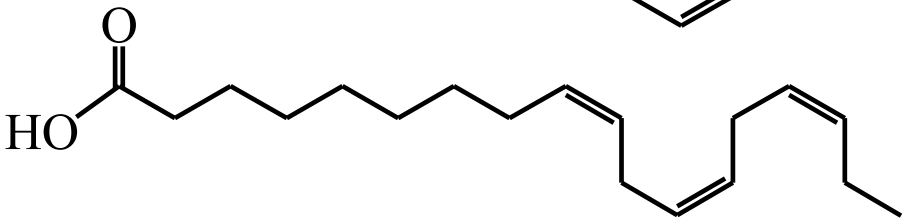


Acide oléique (C18:1 *cis*-9)



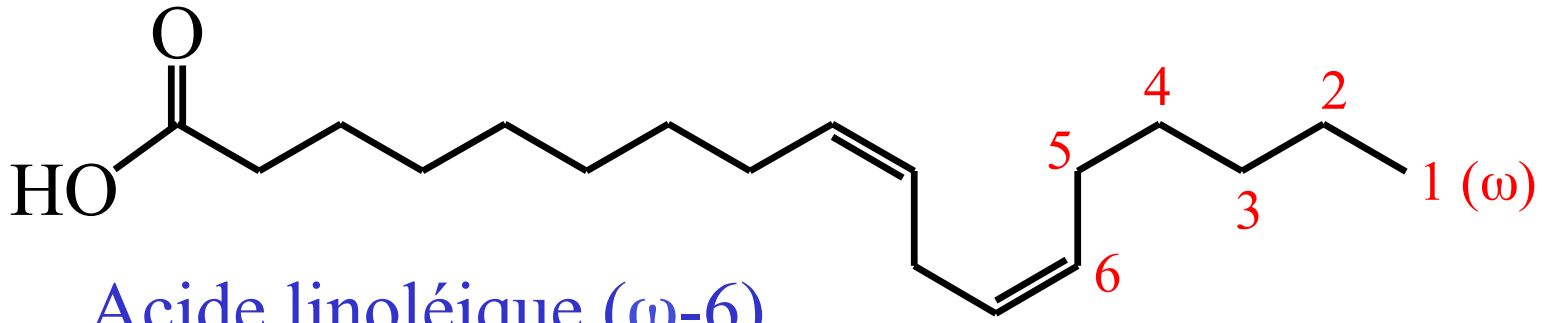
Acide linoléique
(C18:2 *cis*-9,12)



Acide linolénique
(C18:3 *cis*-9,12,15)

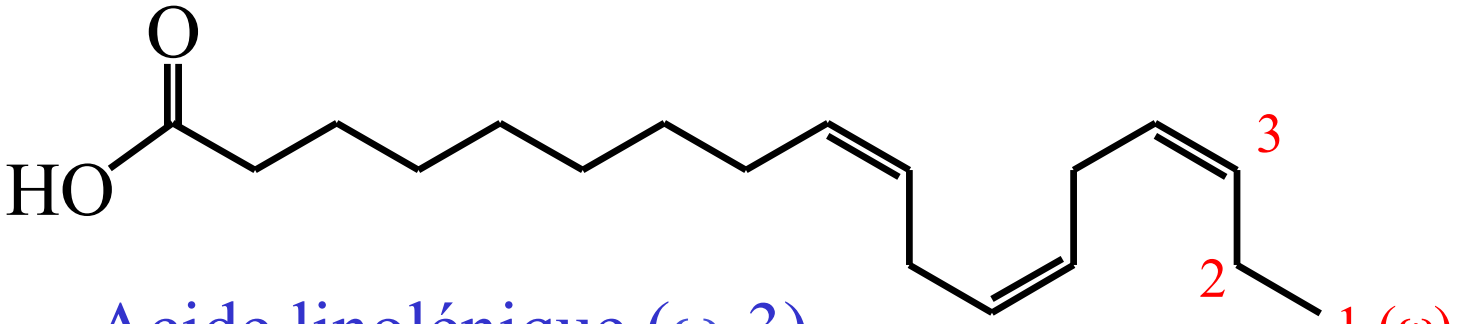
Les acides gras essentiels :

- Nomenclature Biochimie



Acide linoléique (ω-6)

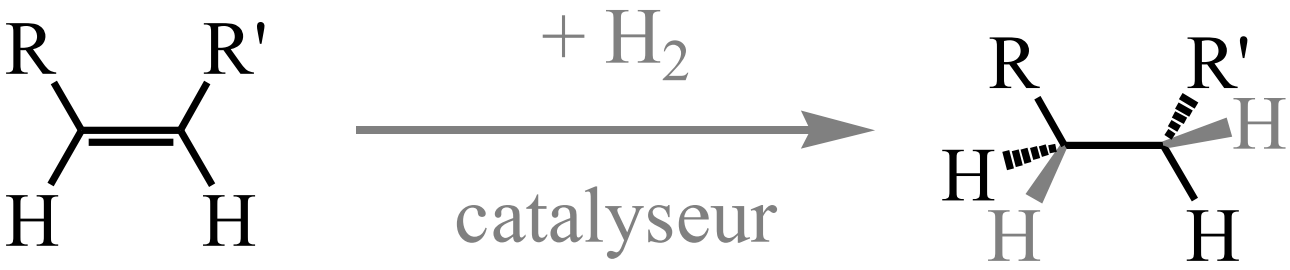
18:2(n-6)



Acide linolénique (ω-3)

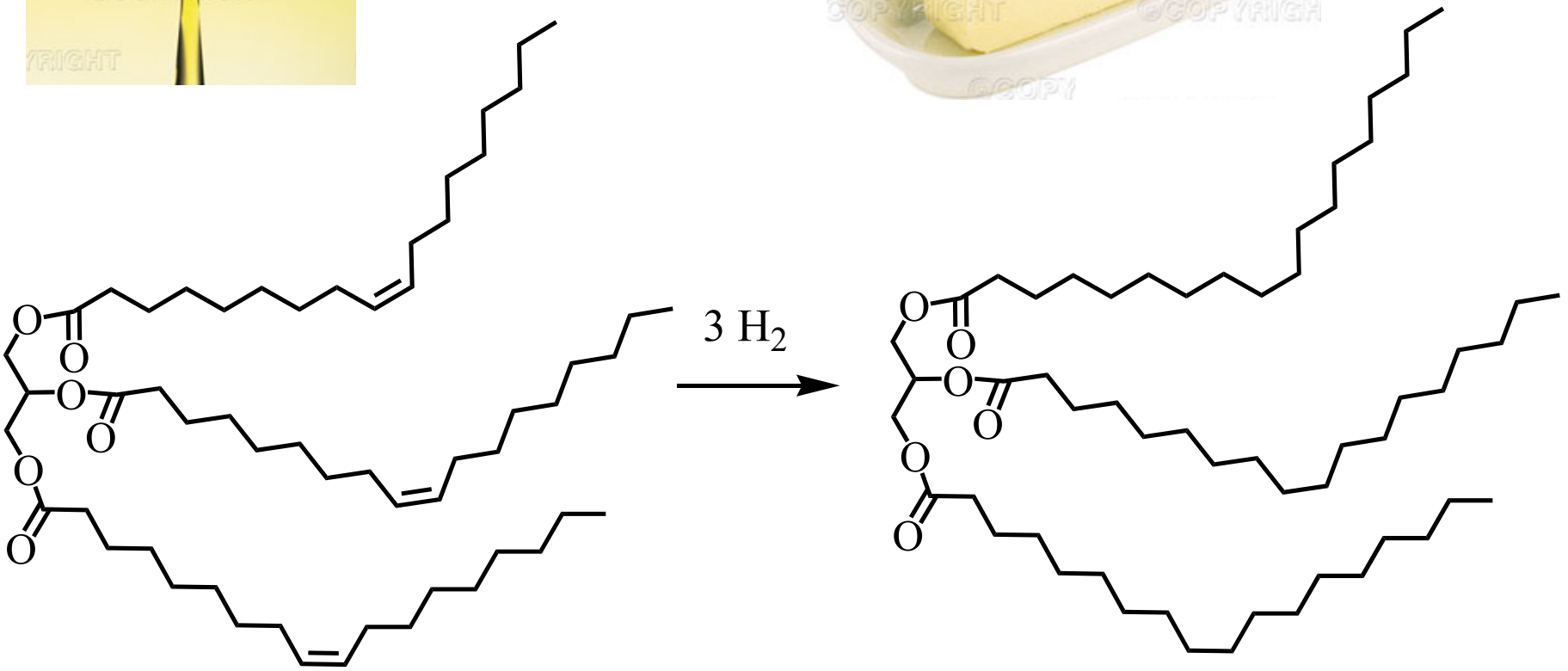
18:3(n-3)

L'hydrogénation catalytique :

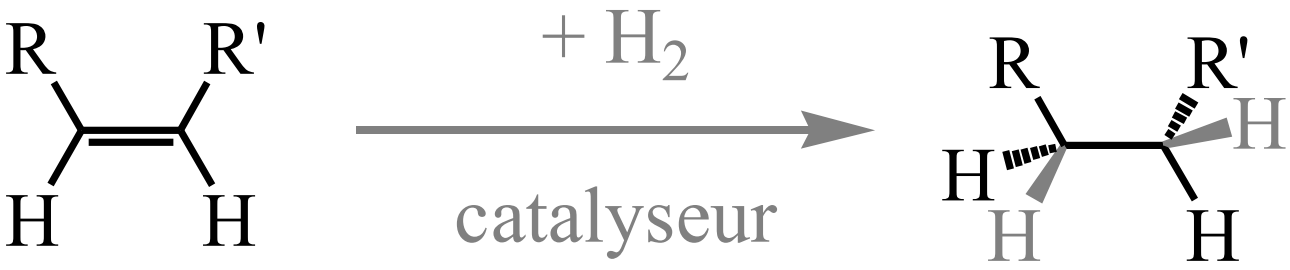


Catalyseur : Ni, Pt, Pd ou Rh

L'hydrogénation des huiles végétales :

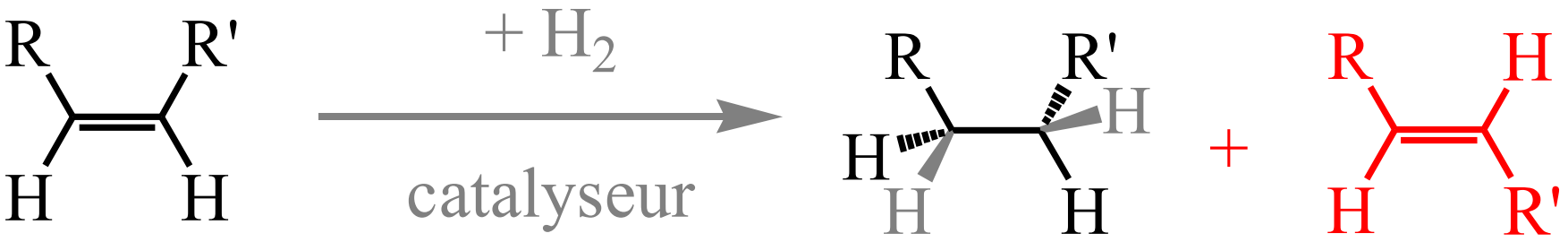


L'hydrogénation catalytique :



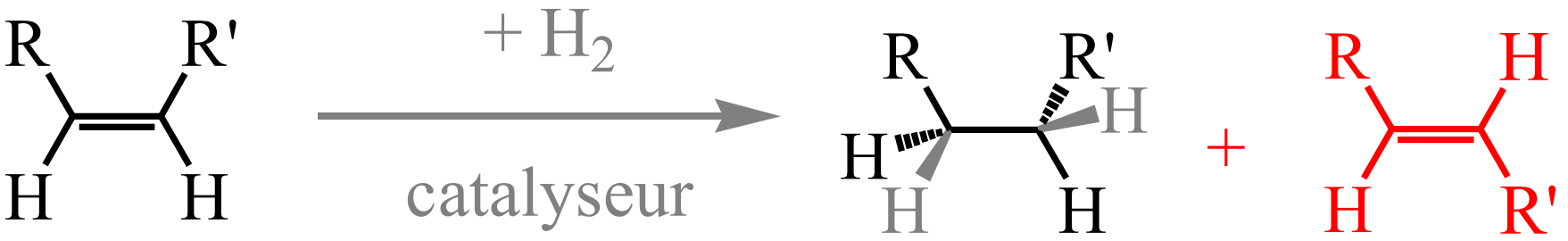
Catalyseur : Ni, Pt, Pd ou Rh

L'hydrogénation catalytique :



Catalyseur : Ni, Pt, Pd ou Rh

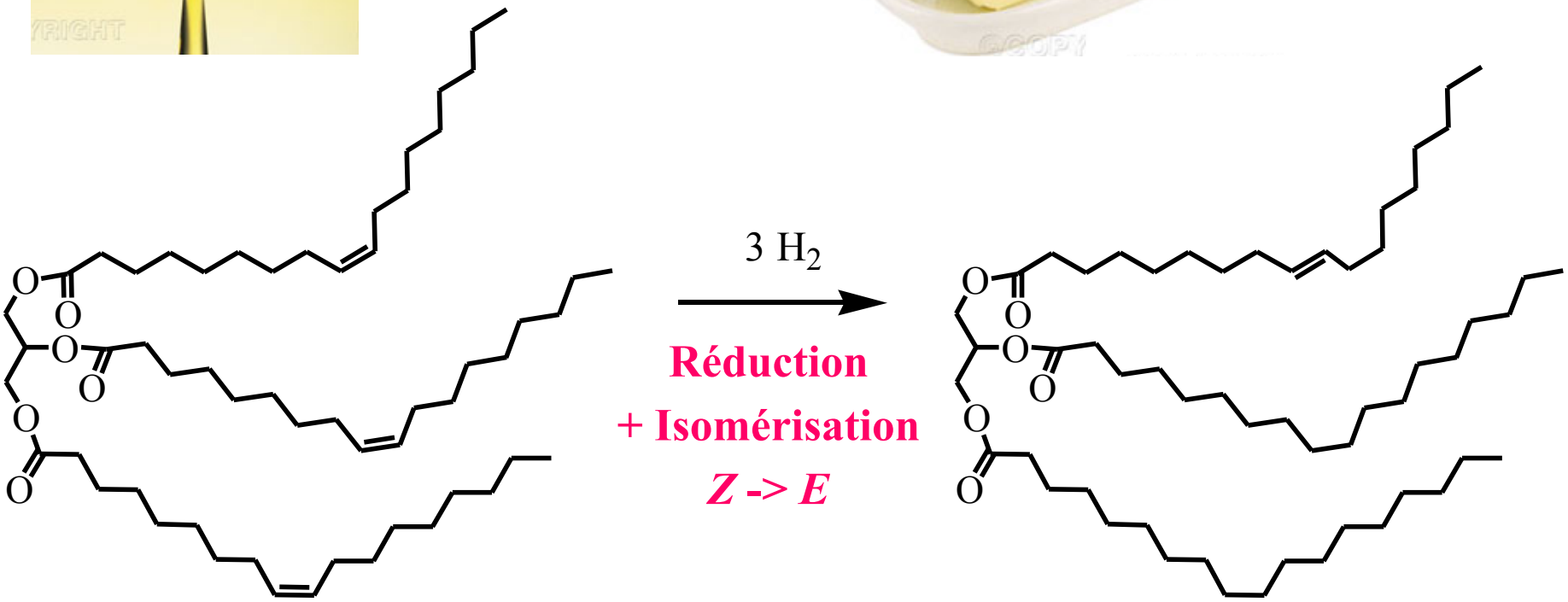
L'hydrogénation catalytique :



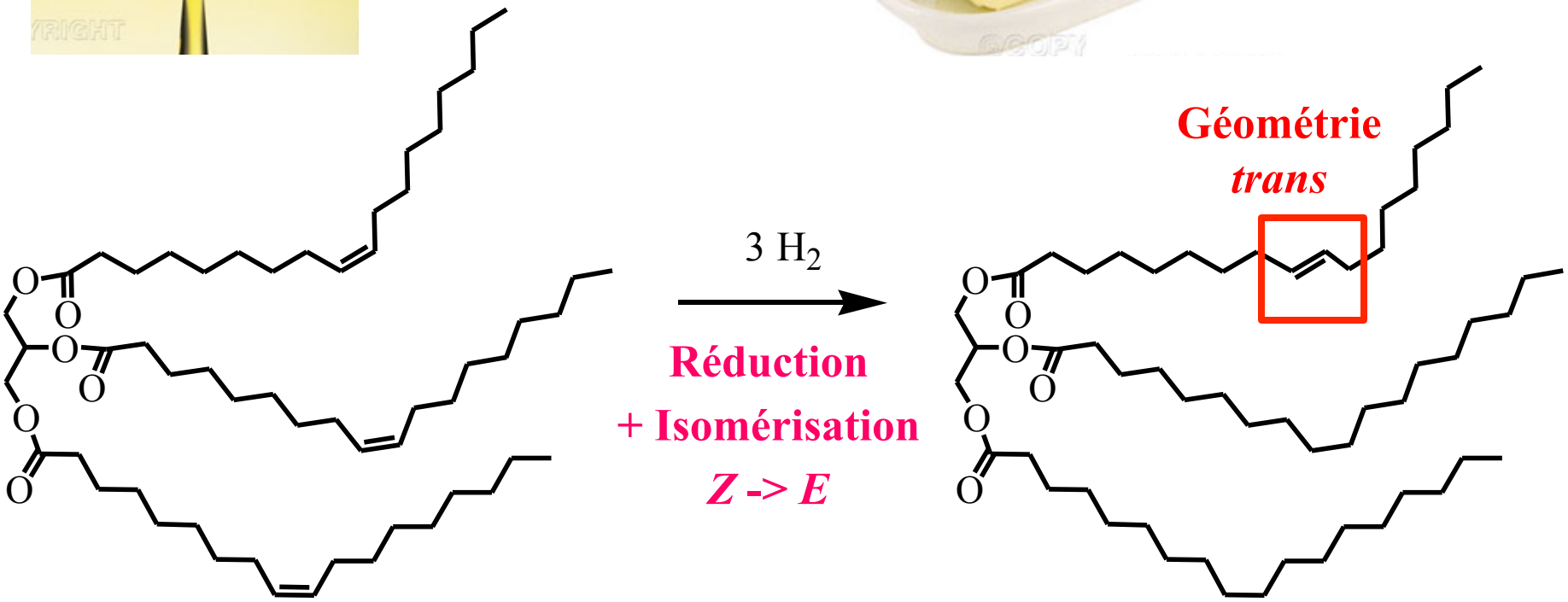
(*Z*) (*E*)

Catalyseur : Ni, Pt, Pd ou Rh

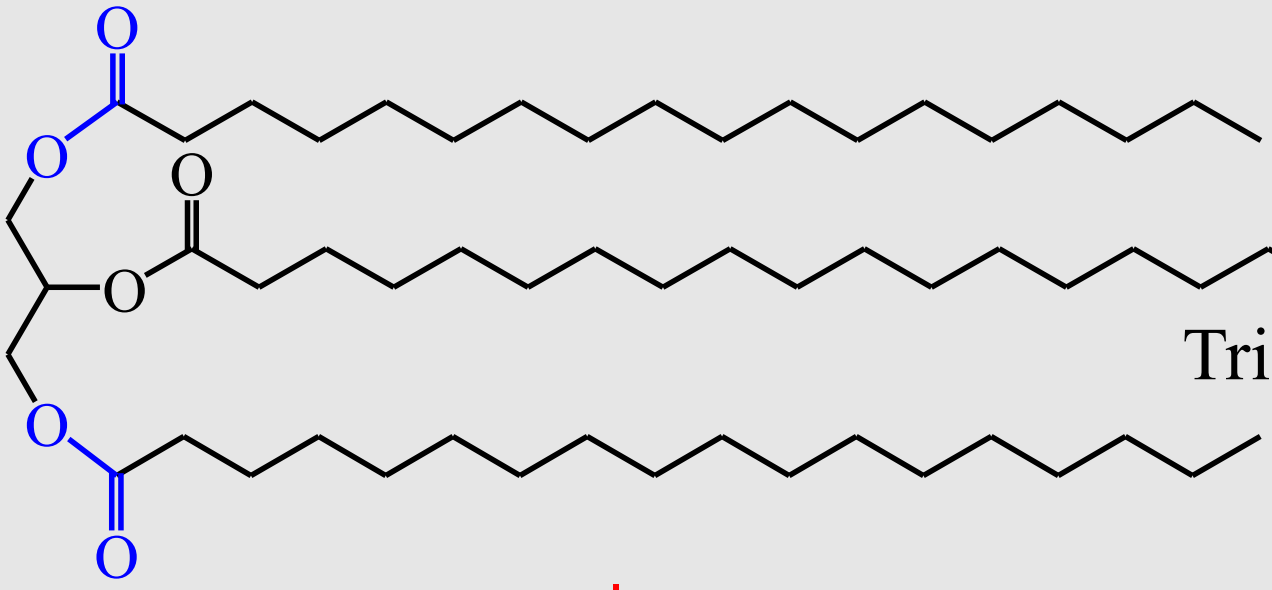
Formation des acides gras trans :



Formation des acides gras trans :

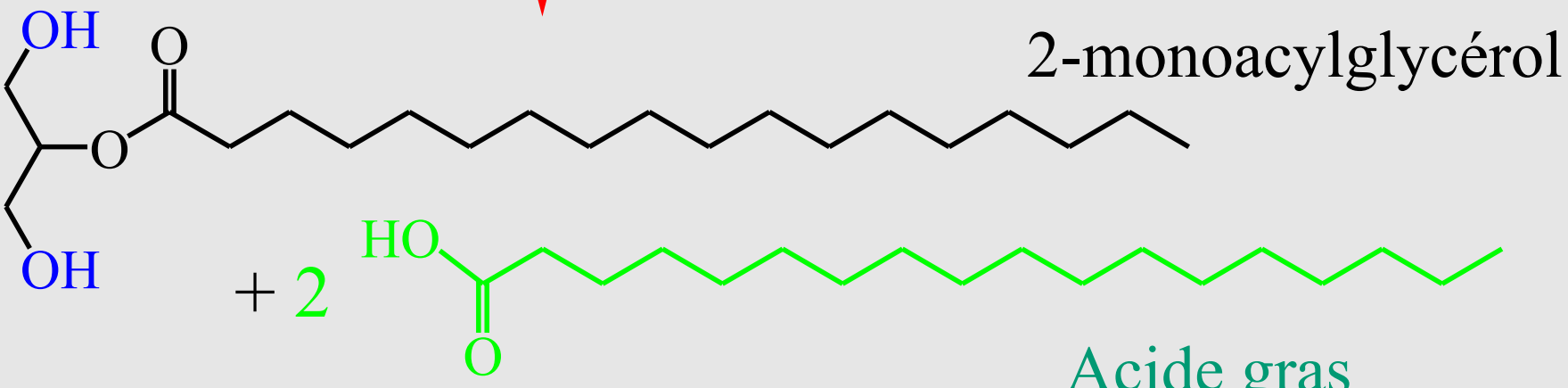


Le catabolisme des triglycérides : 1ère étape



Triacylglycérol

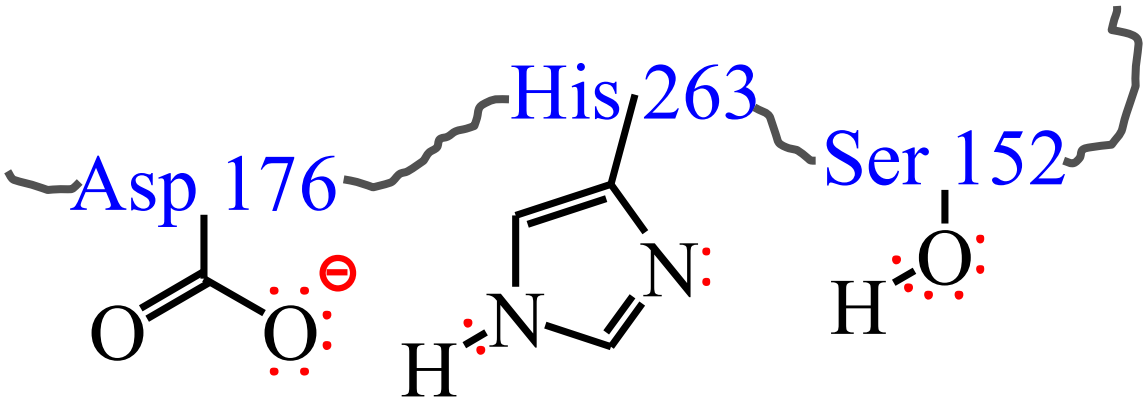
Lipase pancréatique



2-monoacylglycérol

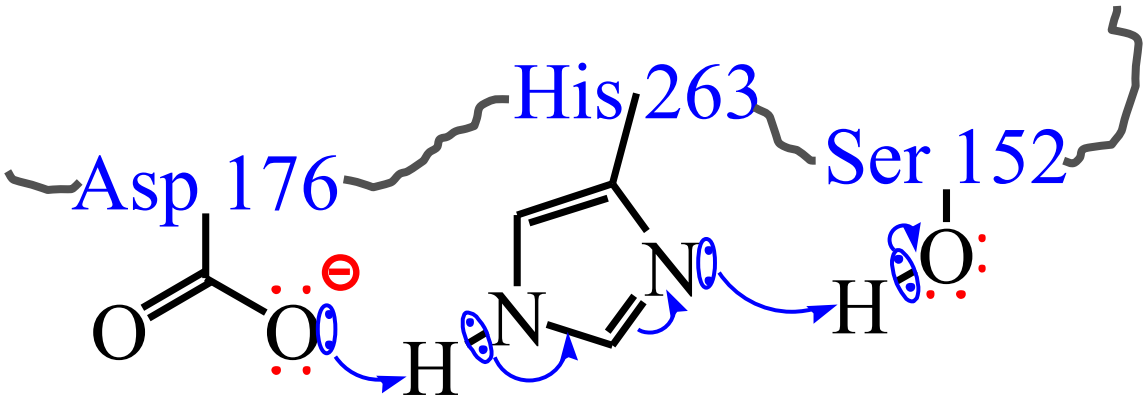
Acide gras

Hydrolyse des triacylglycérols :



pK_a (Asp) ~ 3.7
pK_a (His) ~ 6
pK_a (Ser) ~ 13

Hydrolyse des triacylglycérols :



pK_a (Asp) ~ 3.7
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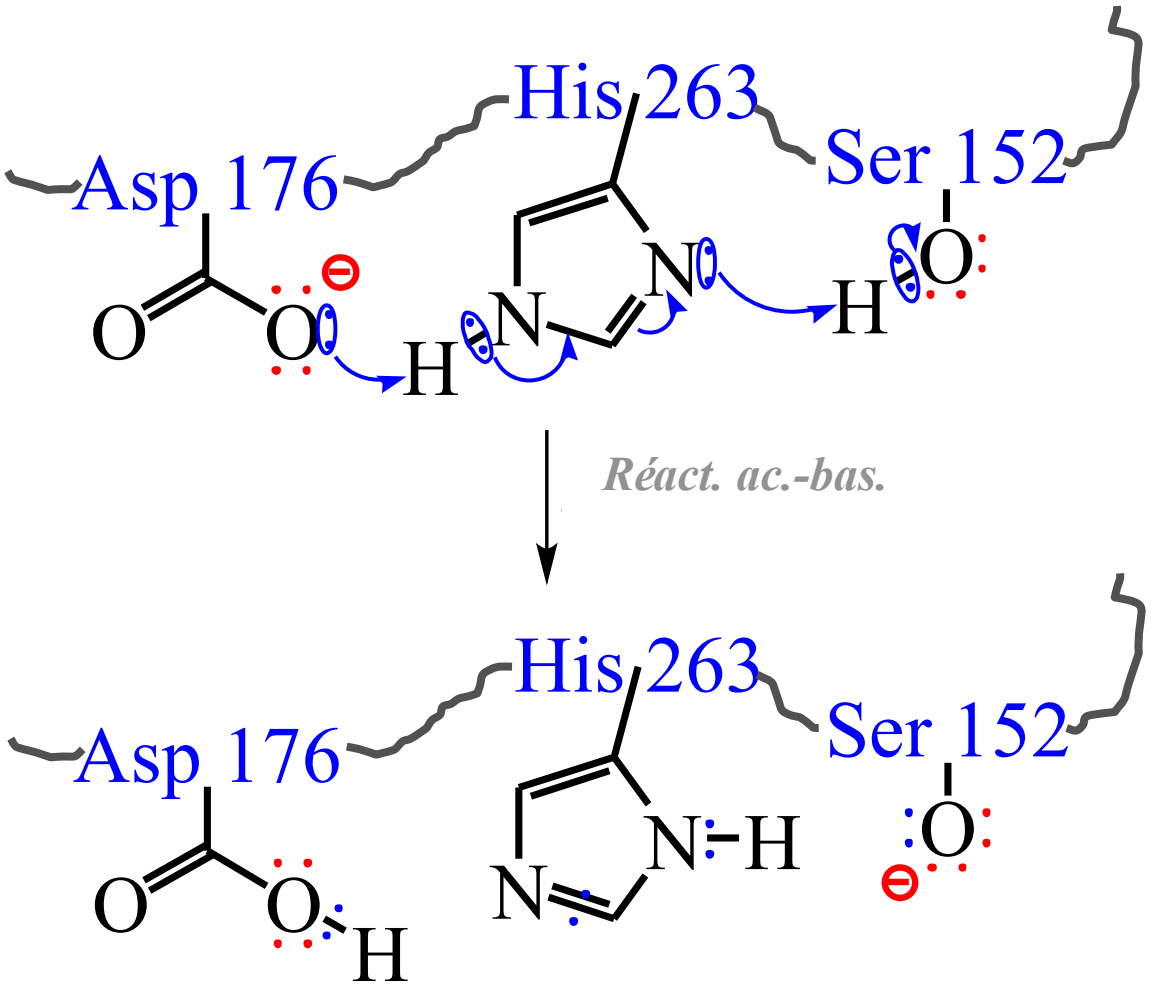
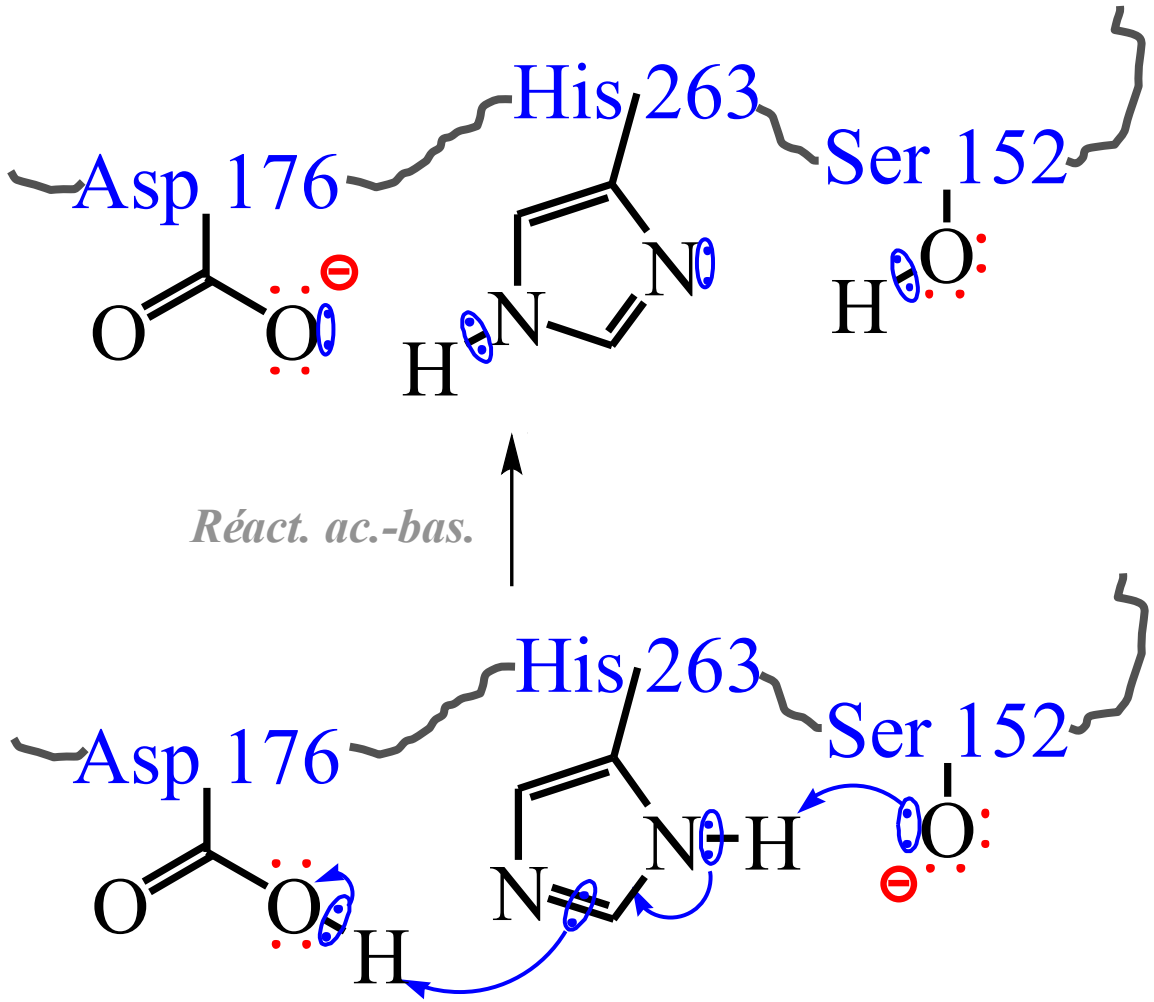
Hydrolyse des triacylglycérols :



pK_a *(Asp) ~ 3.7*
pK_a *(His) ~ 6*
pK_a *(Ser) ~ 13*

Hydrolyse des triacylglycérols :



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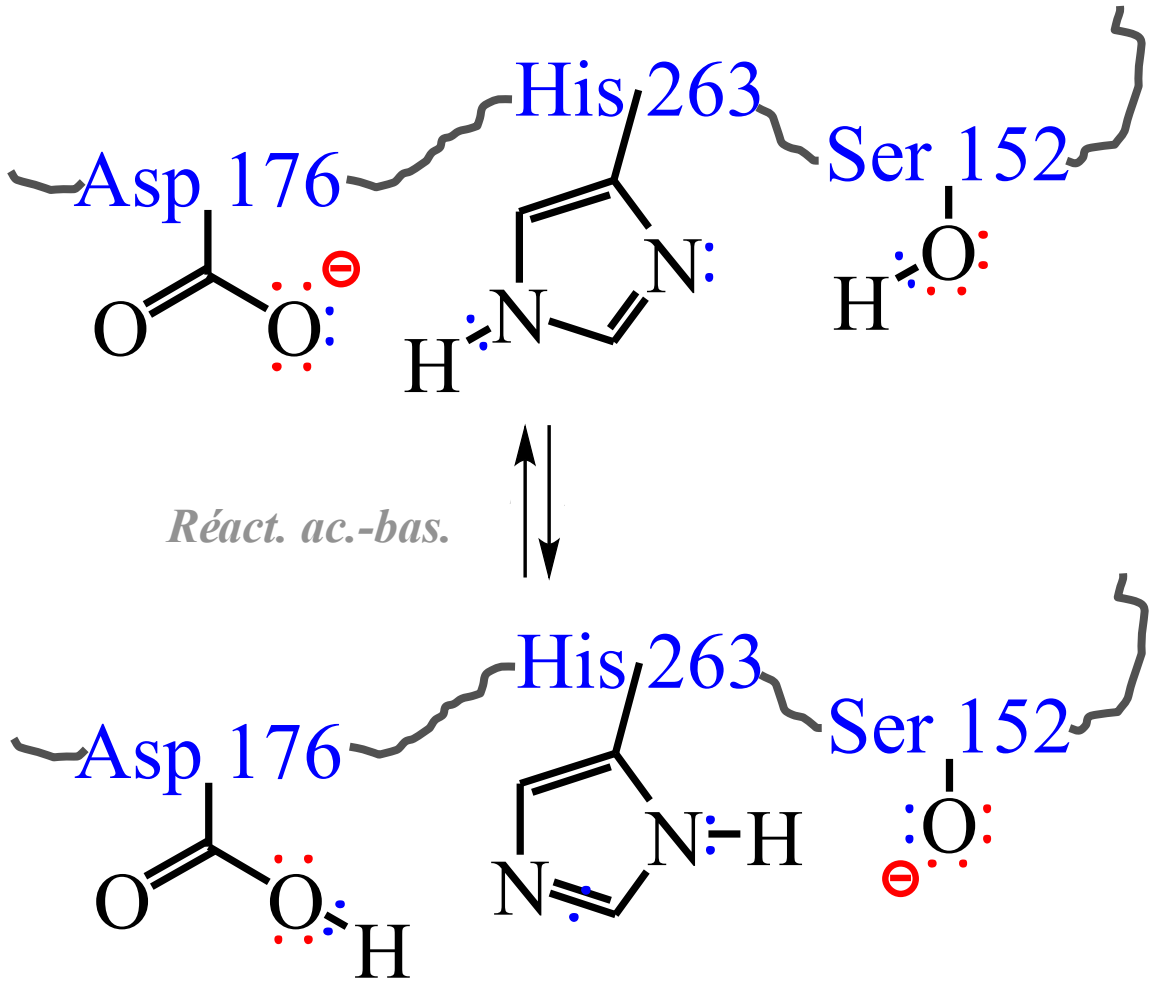
Hydrolyse des triacylglycérols :



pK_a *(Asp) ~ 3.7*

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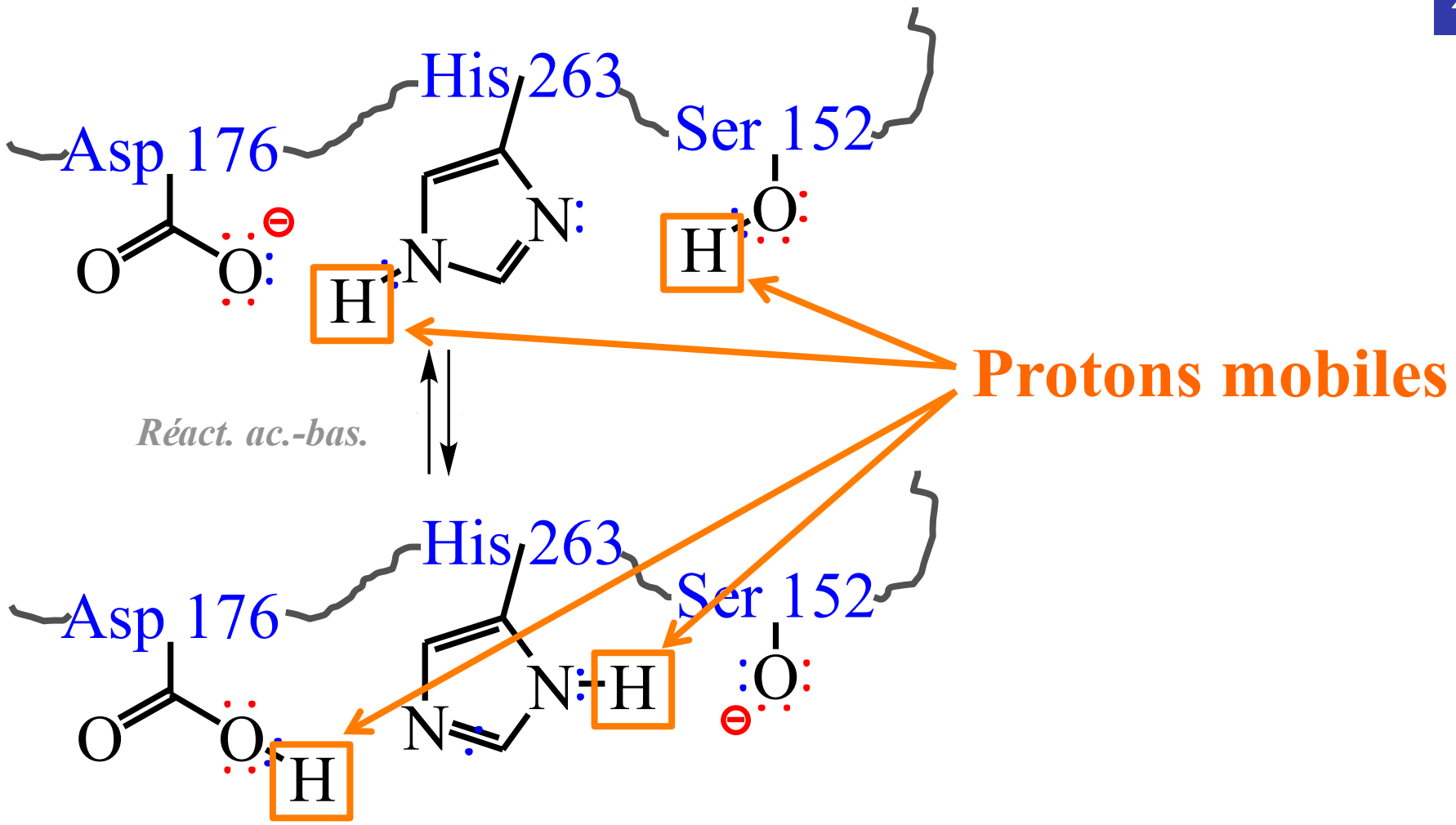
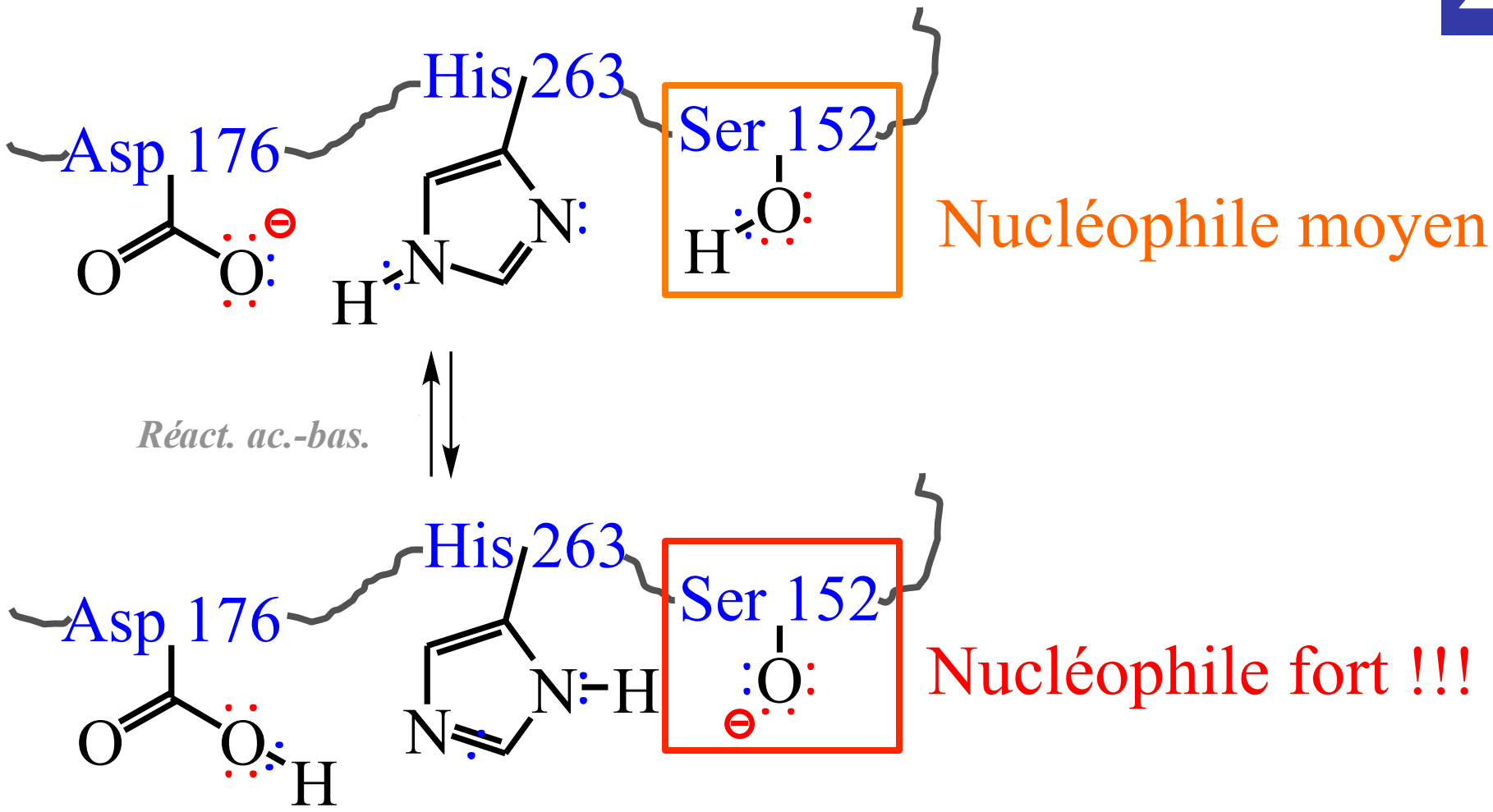
Hydrolyse des triacylglycérols :

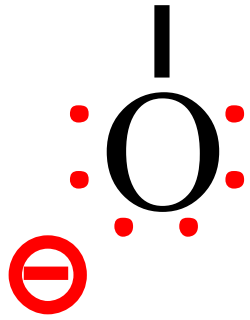
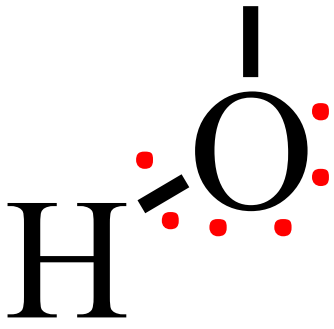


Hydrolyse des triacylglycérols :

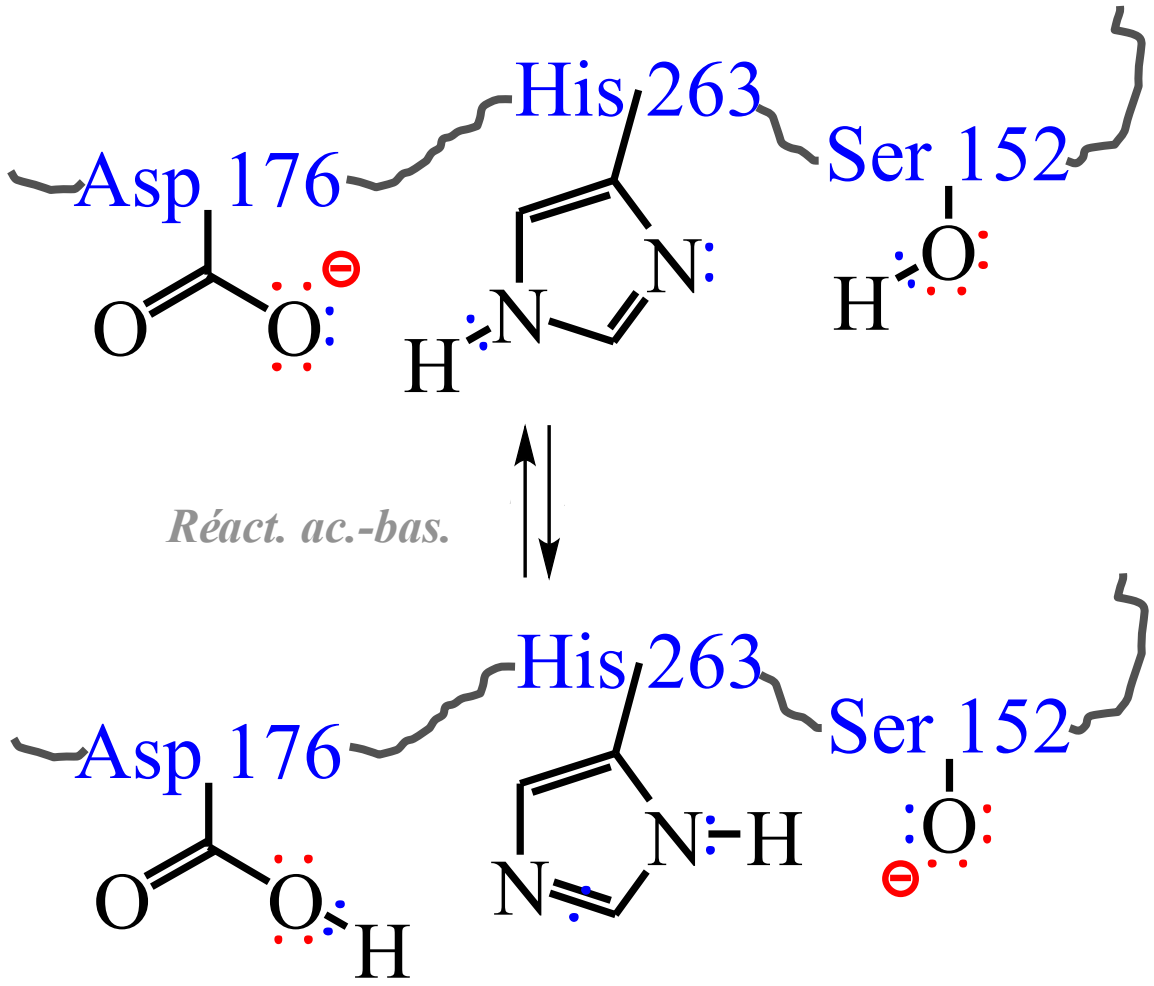


Nucléophile : Espèce/Site capable de **donner** une paire d'électrons (DL) pour créer une nouvelle liaison.

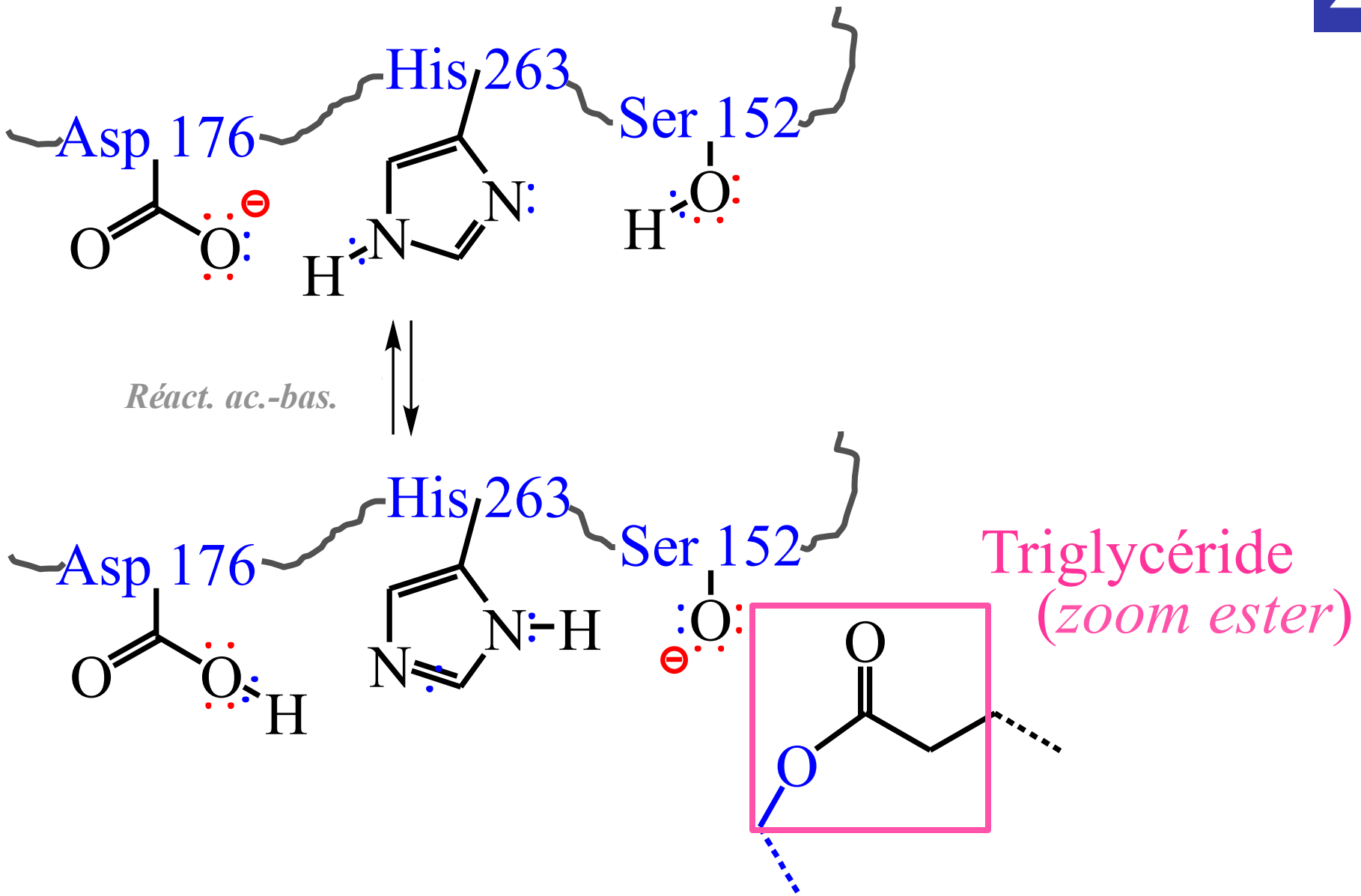
Nucléophilie :

Ser 152  > Ser 152 

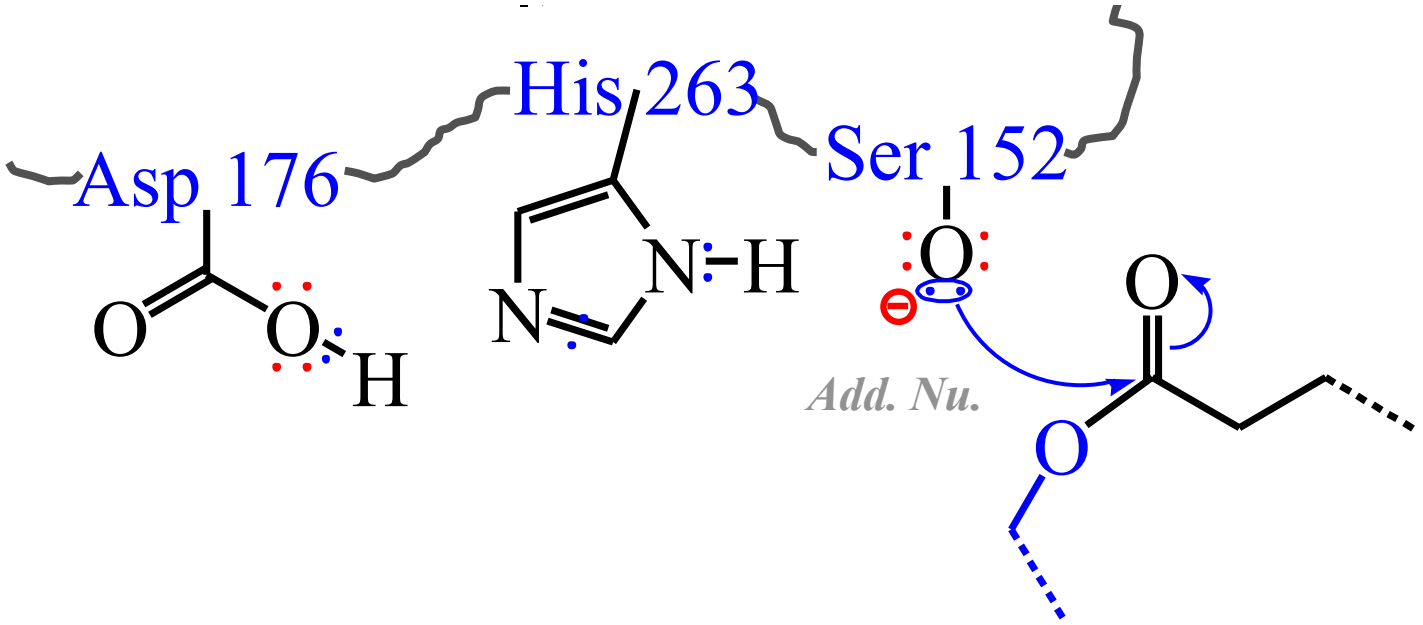
Hydrolyse des triacylglycérols :



Hydrolyse des triacylglycérols :



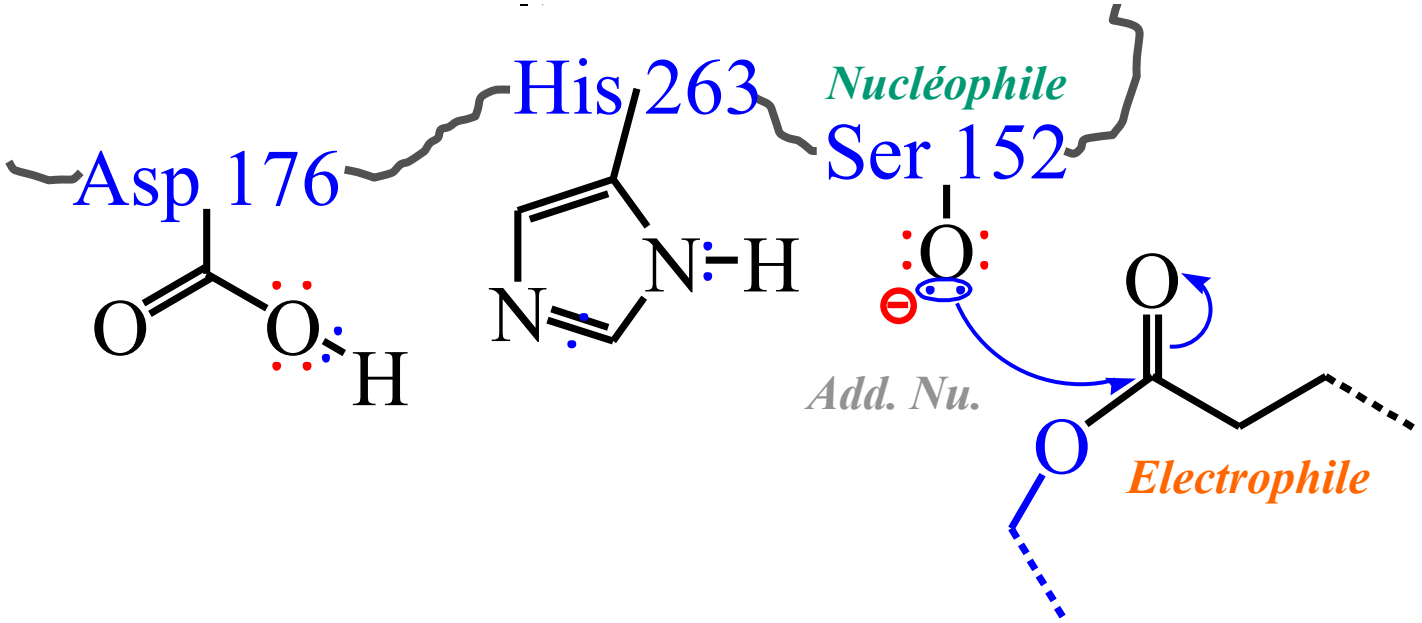
Hydrolyse des triacylglycérols :



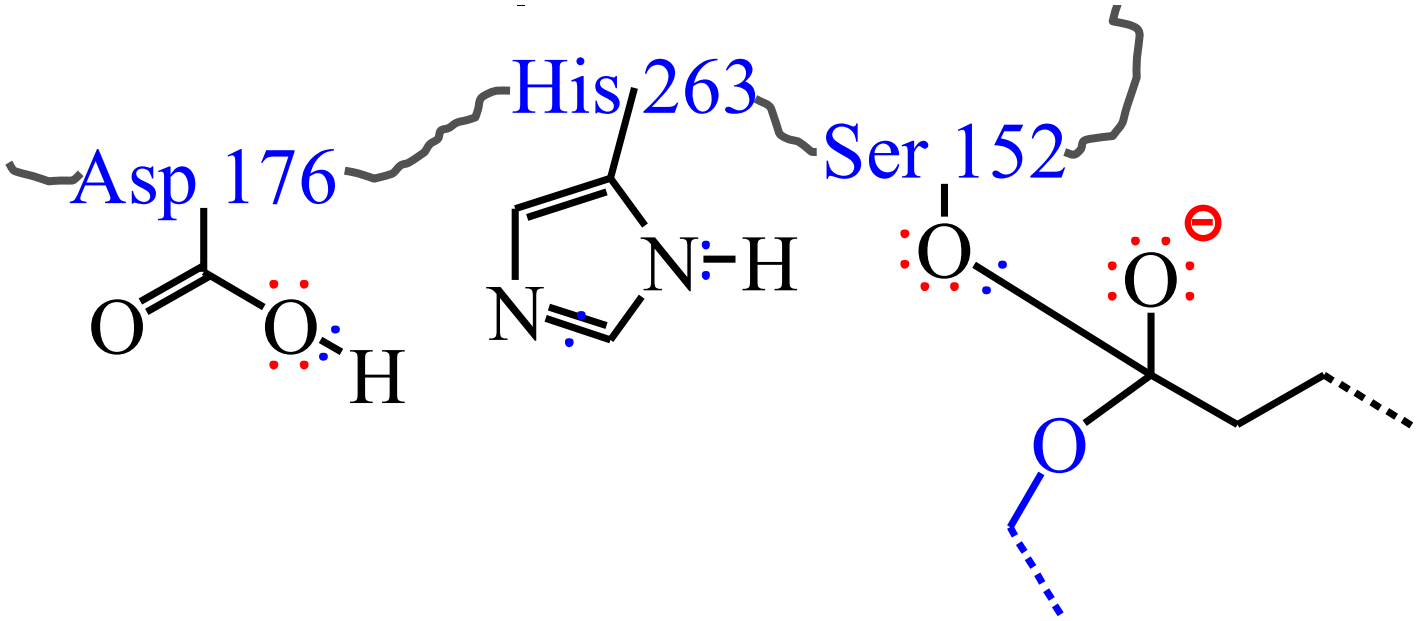
Hydrolyse des triacylglycérols :

Electrophile : Espèce/Site capable d'**accepter** une paire d'électrons (DL) pour créer une nouvelle liaison.

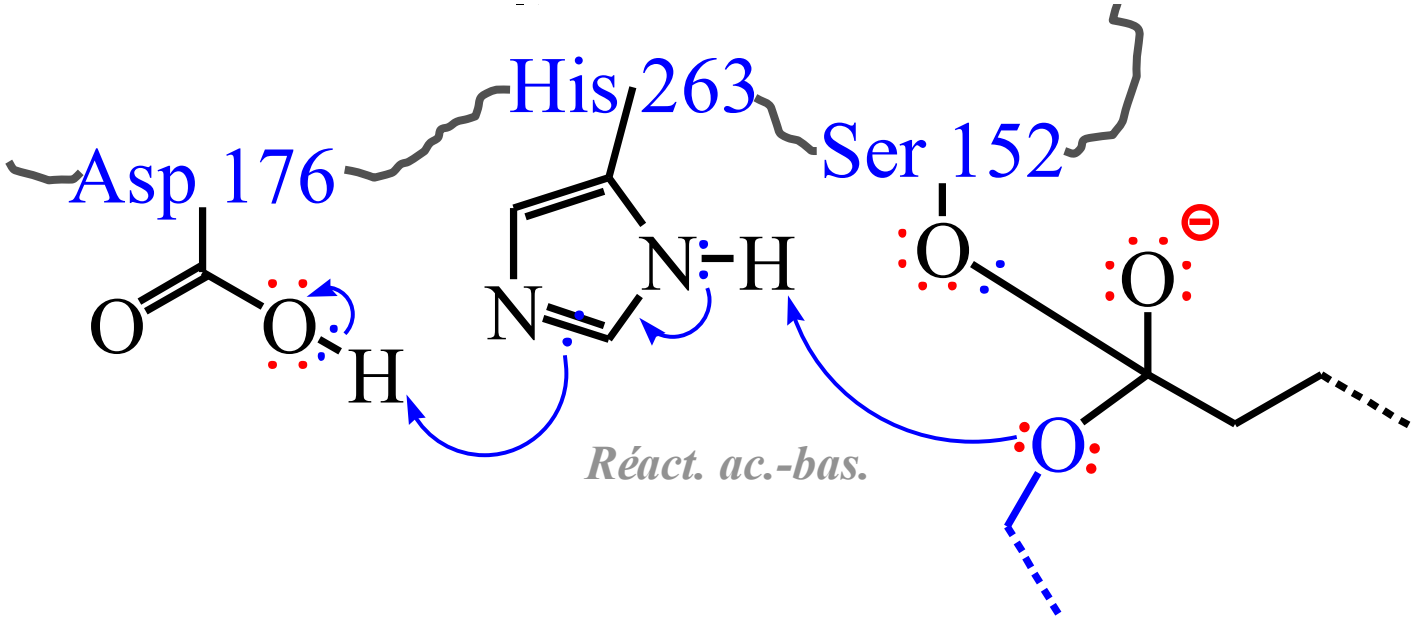
Nucléophile : Espèce/Site capable de **donner** une paire d'électrons (DL) pour créer une nouvelle liaison.



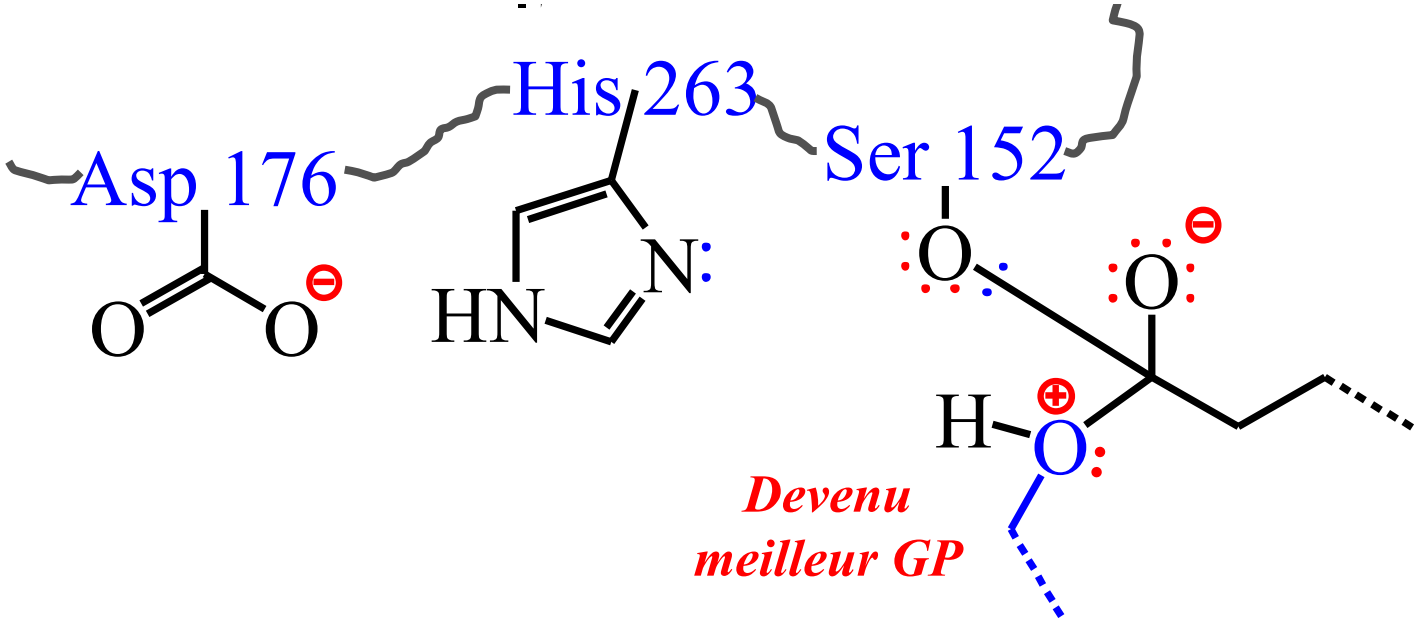
Hydrolyse des triacylglycérols :



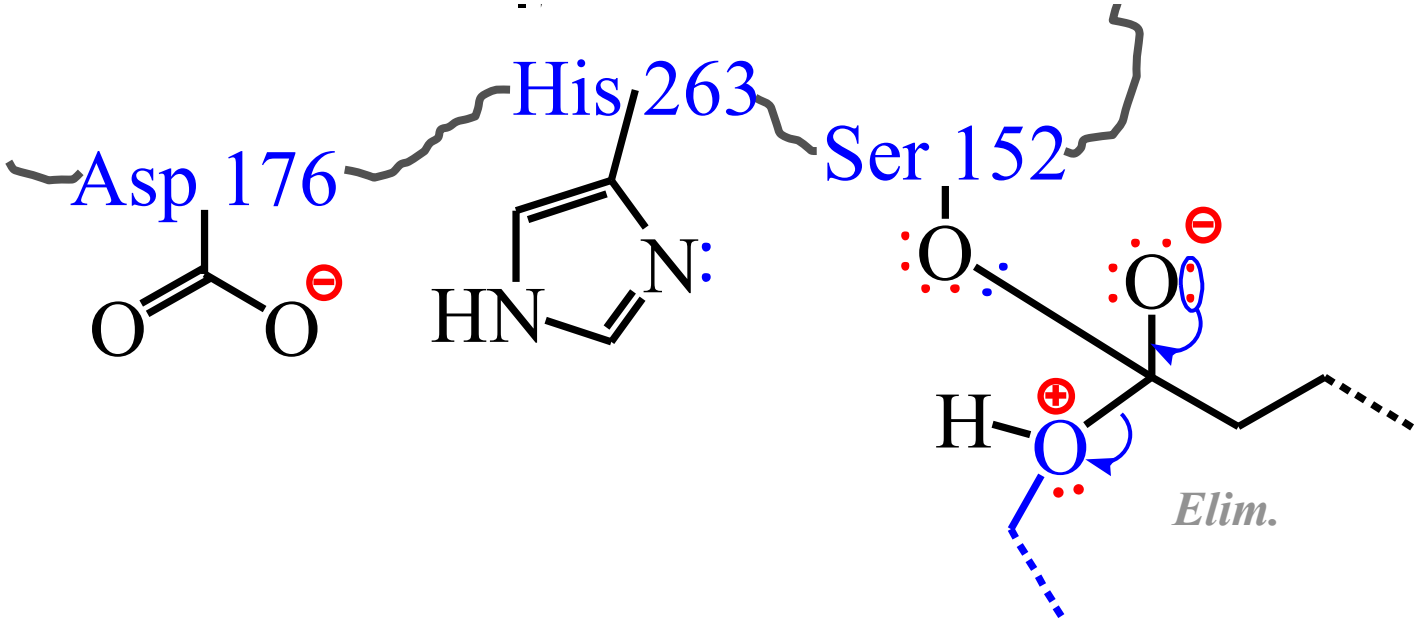
Hydrolyse des triacylglycérols :



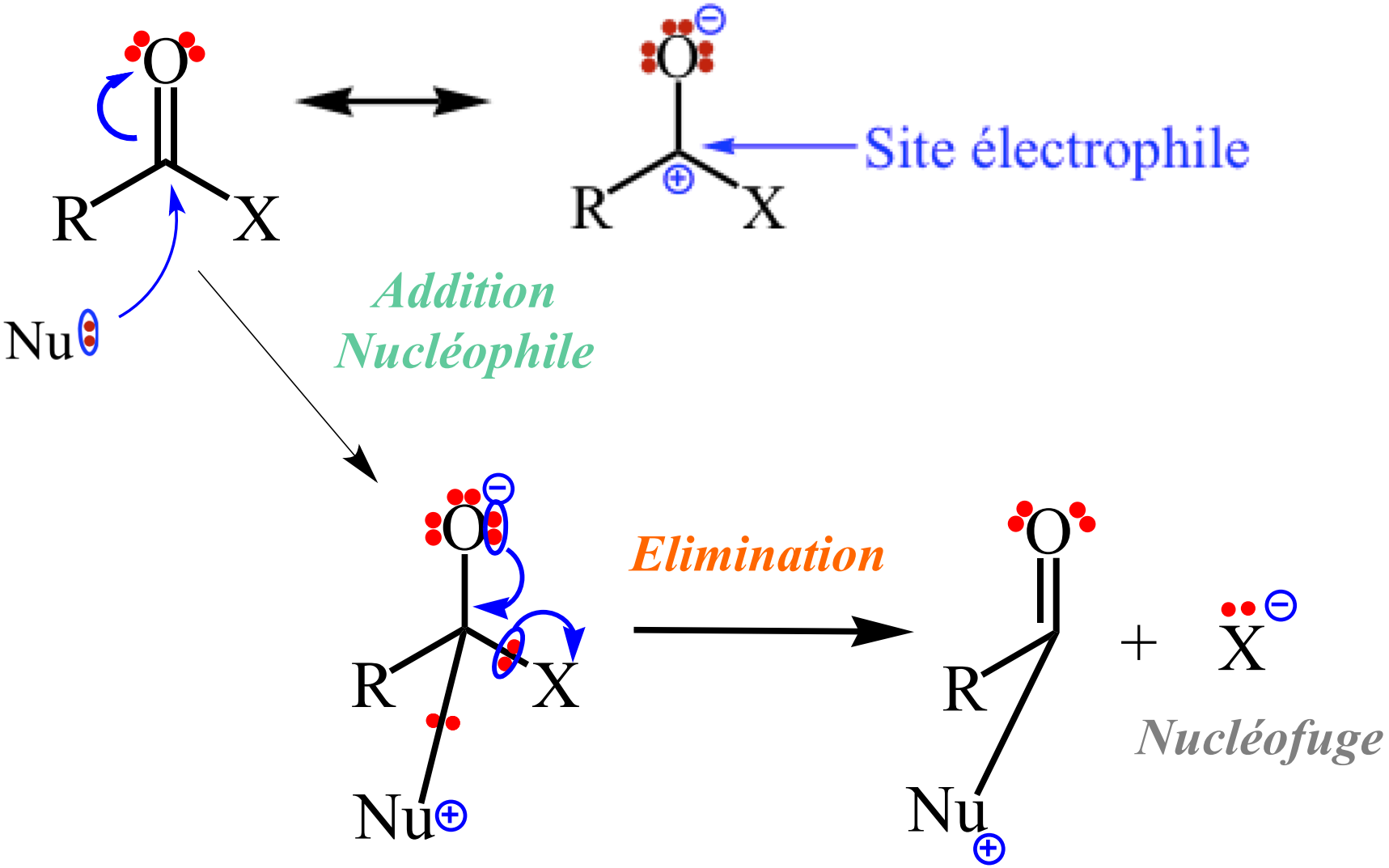
Hydrolyse des triacylglycérols :



Hydrolyse des triacylglycérols :



(Rappel : Addition-Elimination)



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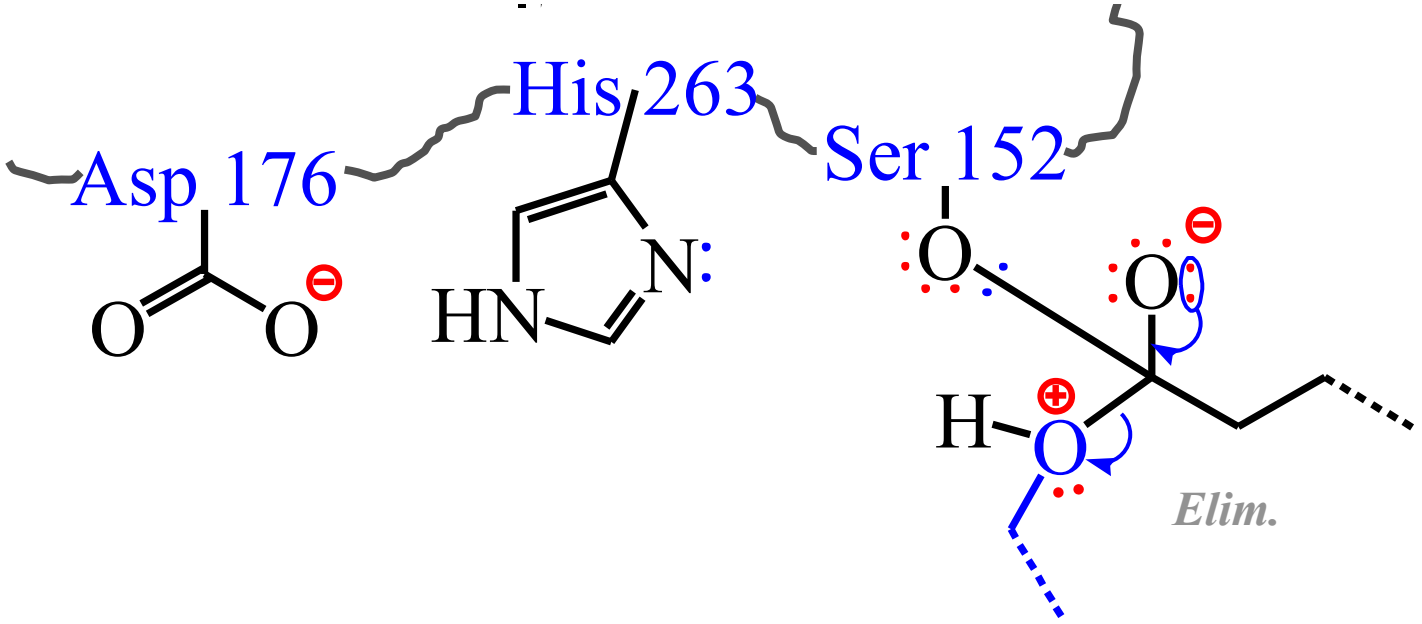
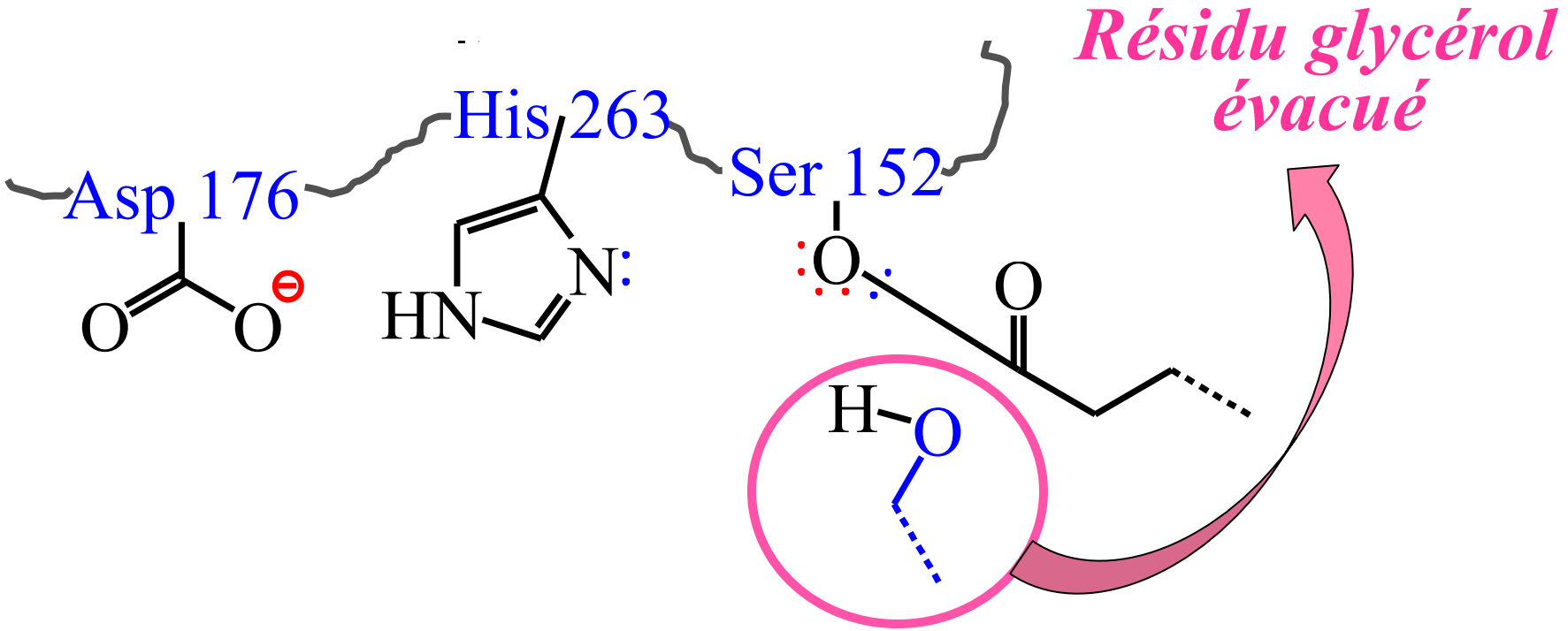
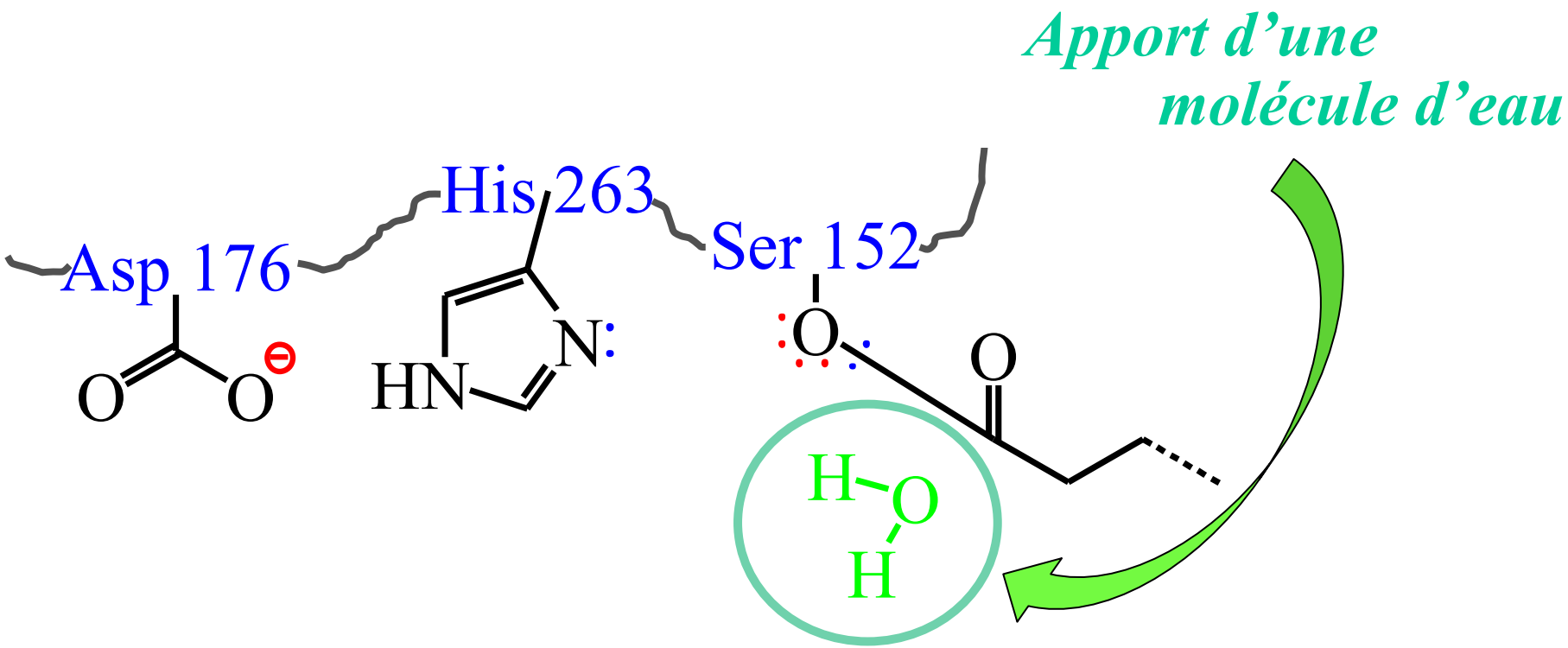


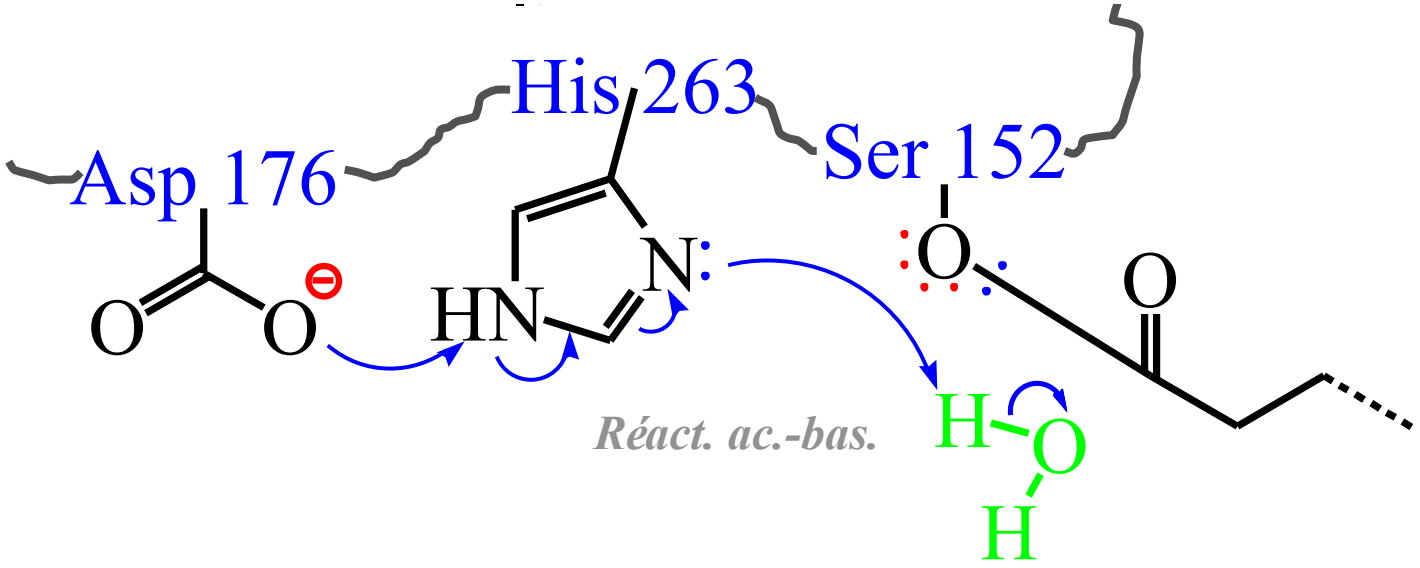
Hydrolyse des triacylglycérols :



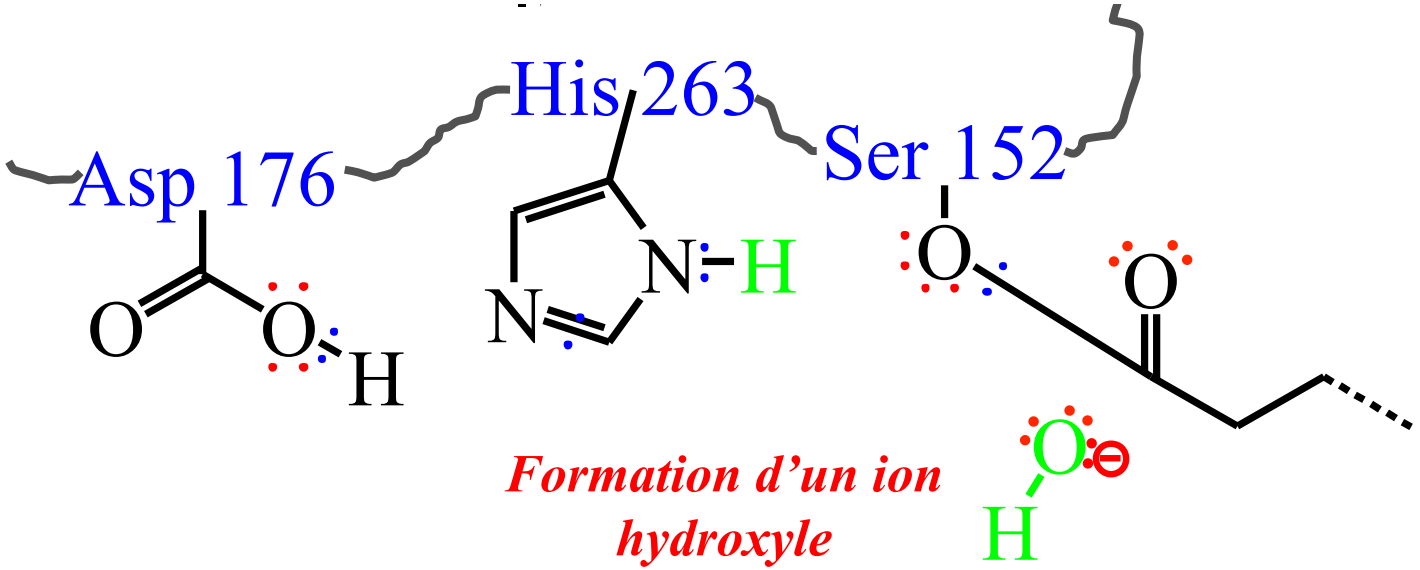
Hydrolyse des triacylglycérols :



Hydrolyse des triacylglycérols :

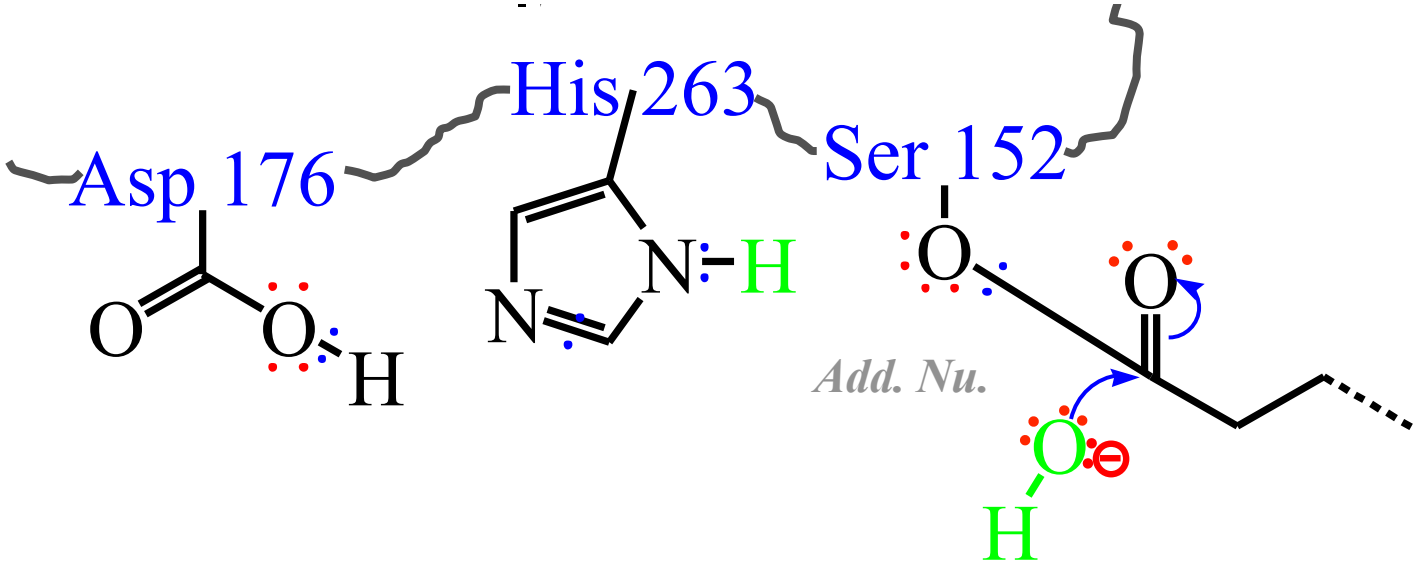


Hydrolyse des triacylglycérols :

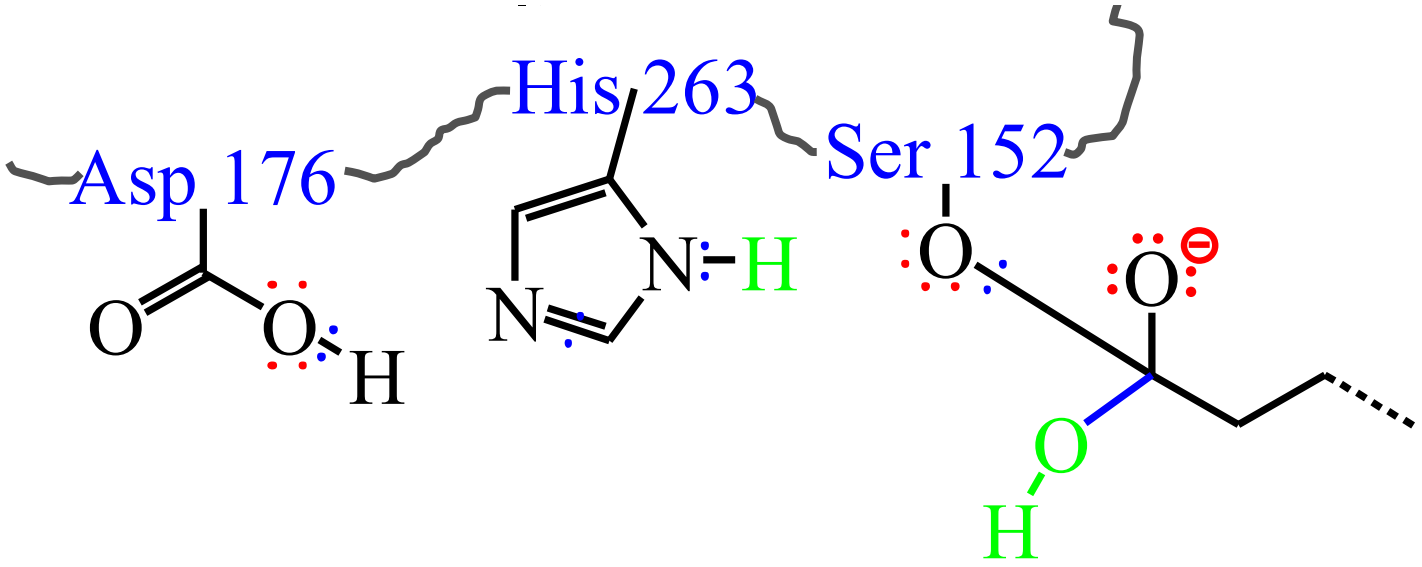


Formation d'un ion hydroxyle (basique & nucléophile)

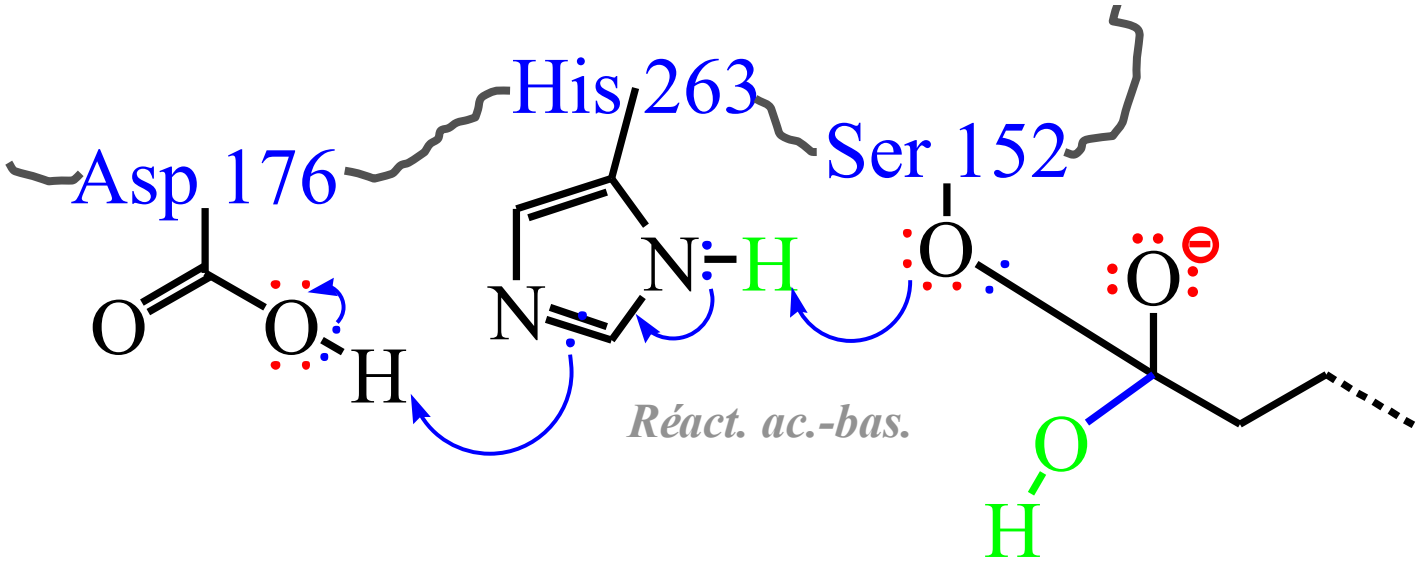
Hydrolyse des triacylglycérols :



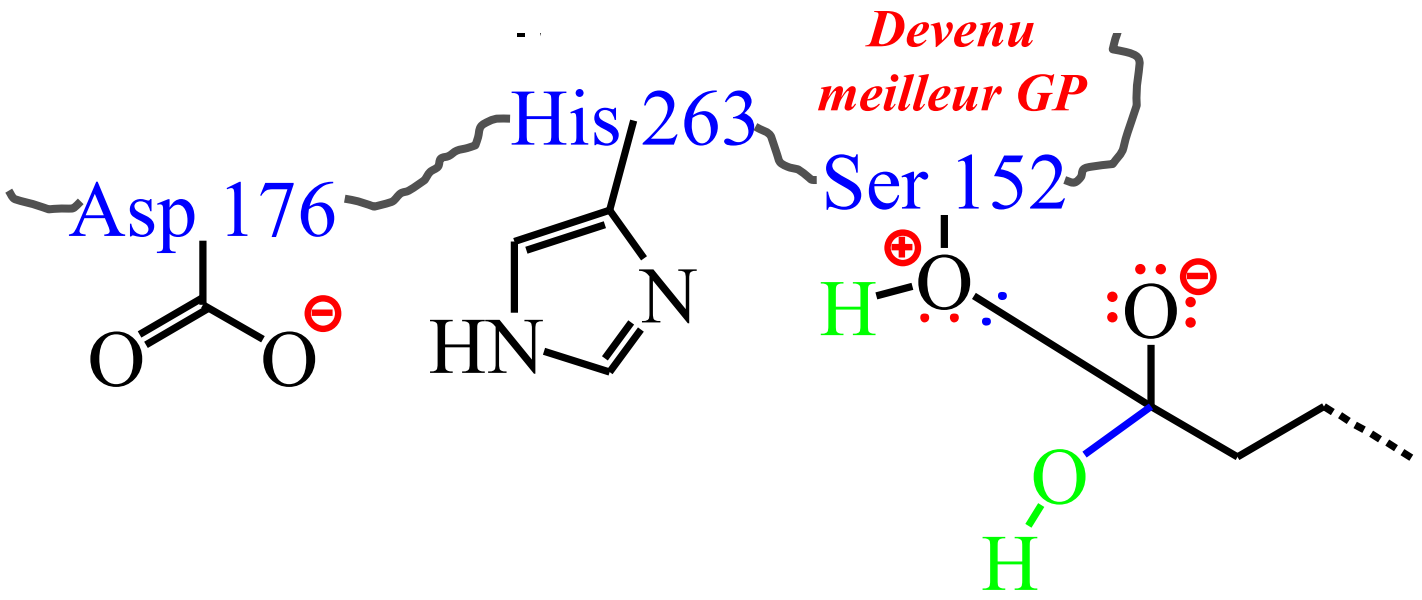
Hydrolyse des triacylglycérols :



Hydrolyse des triacylglycérols :



Hydrolyse des triacylglycérols :



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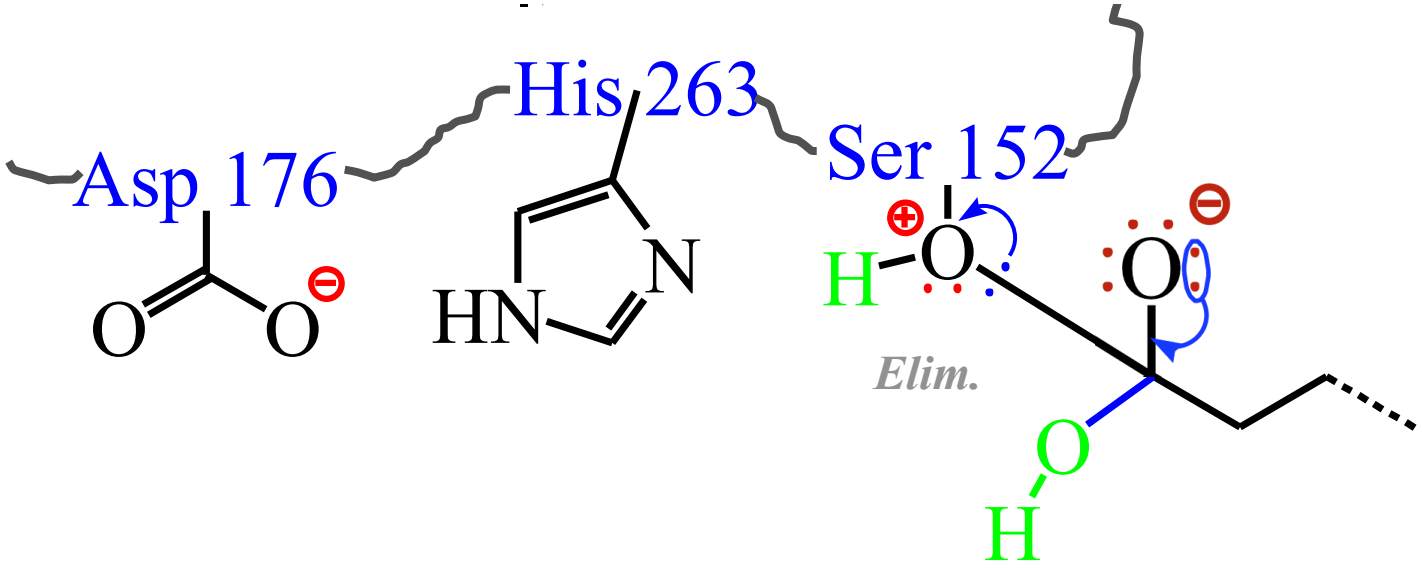
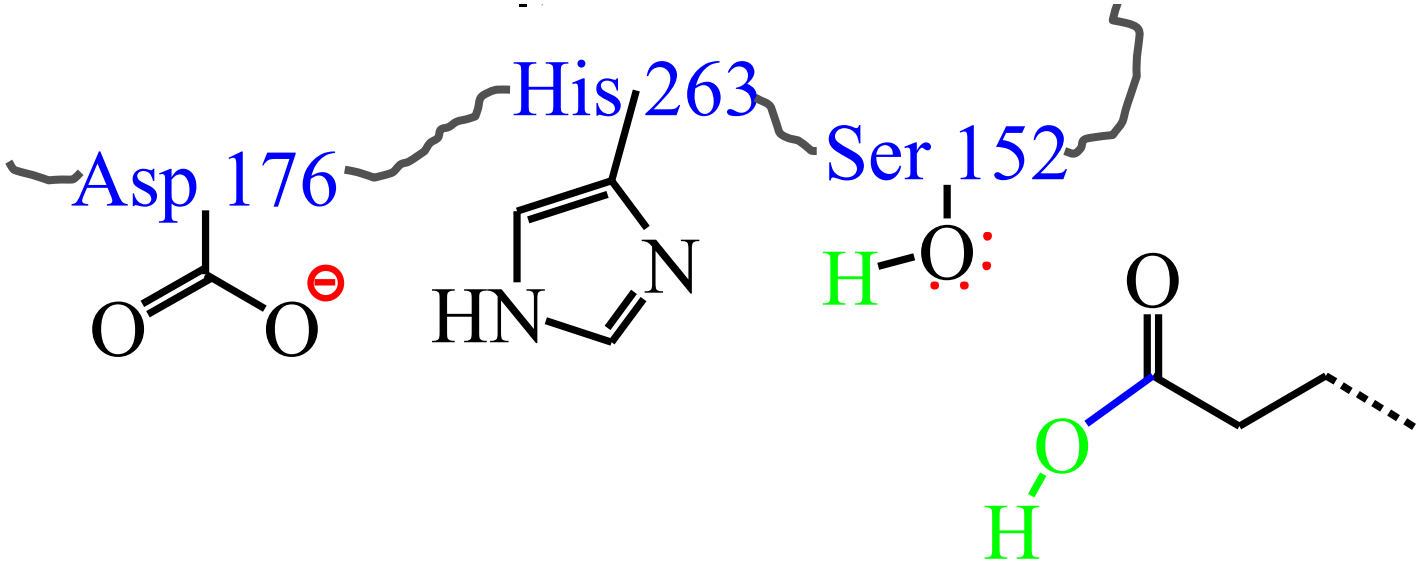
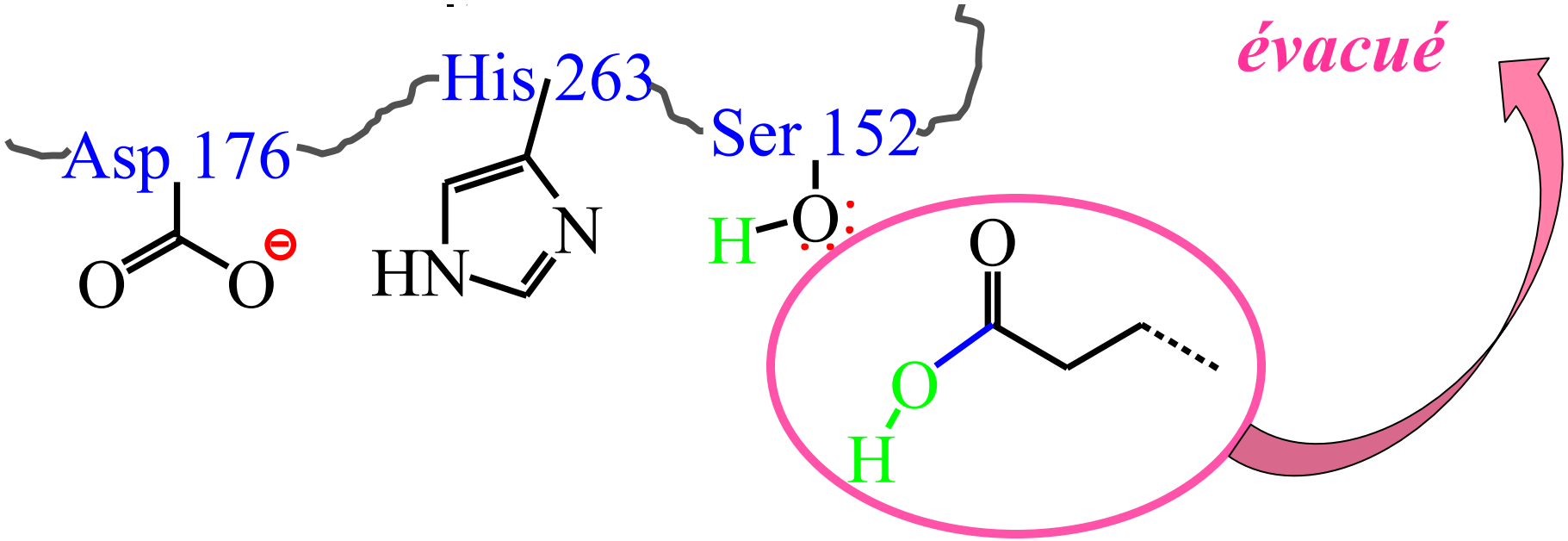


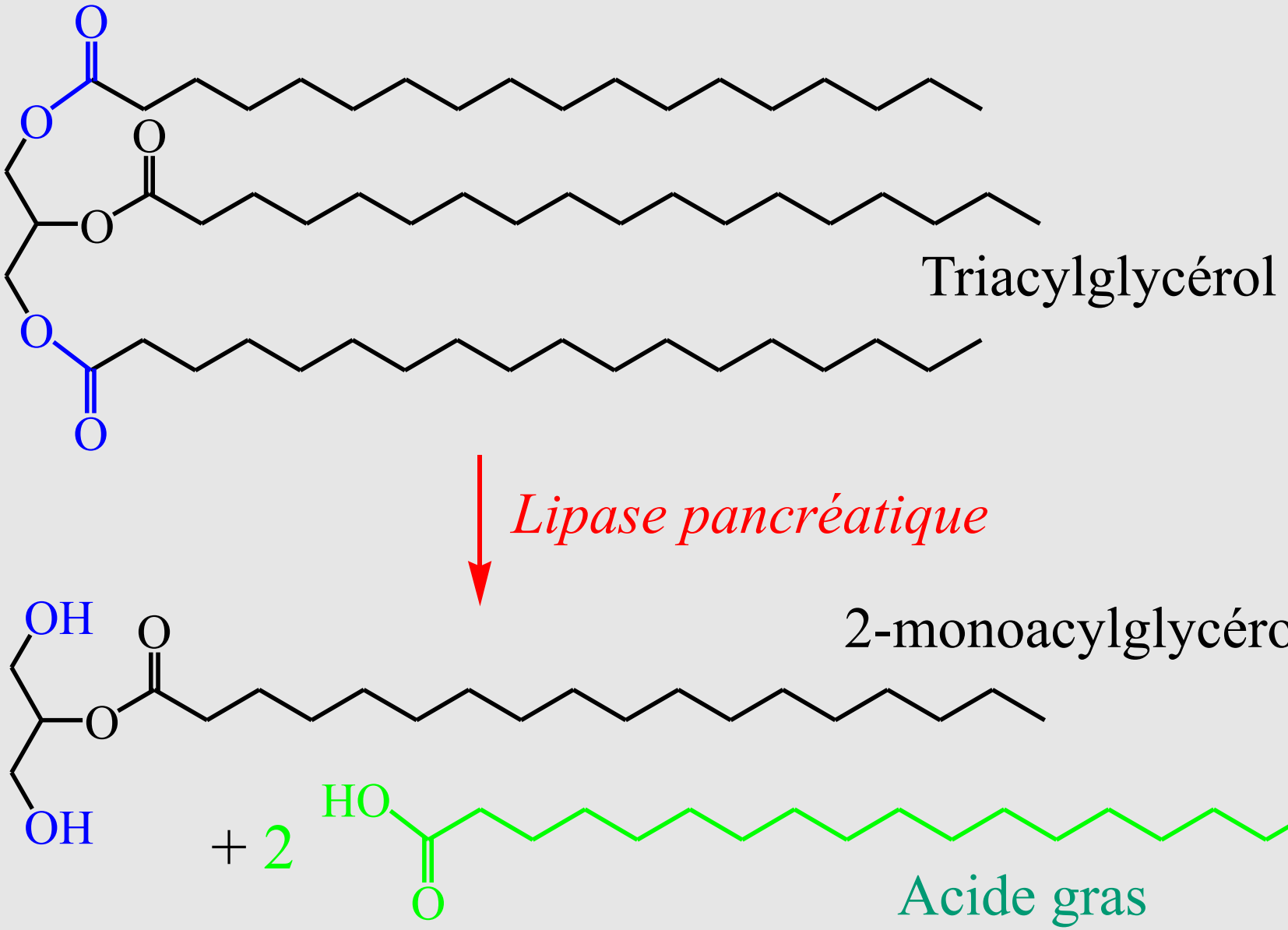
Hydrolyse des triacylglycérols :

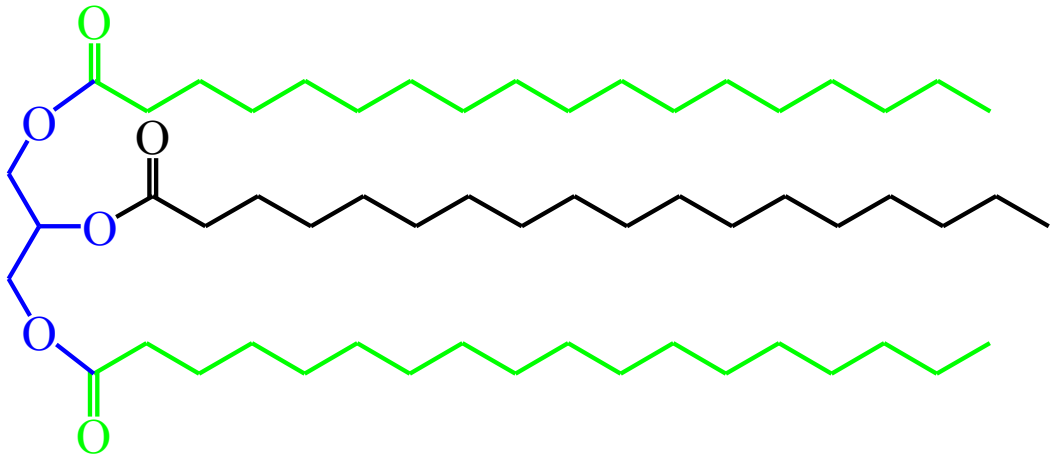


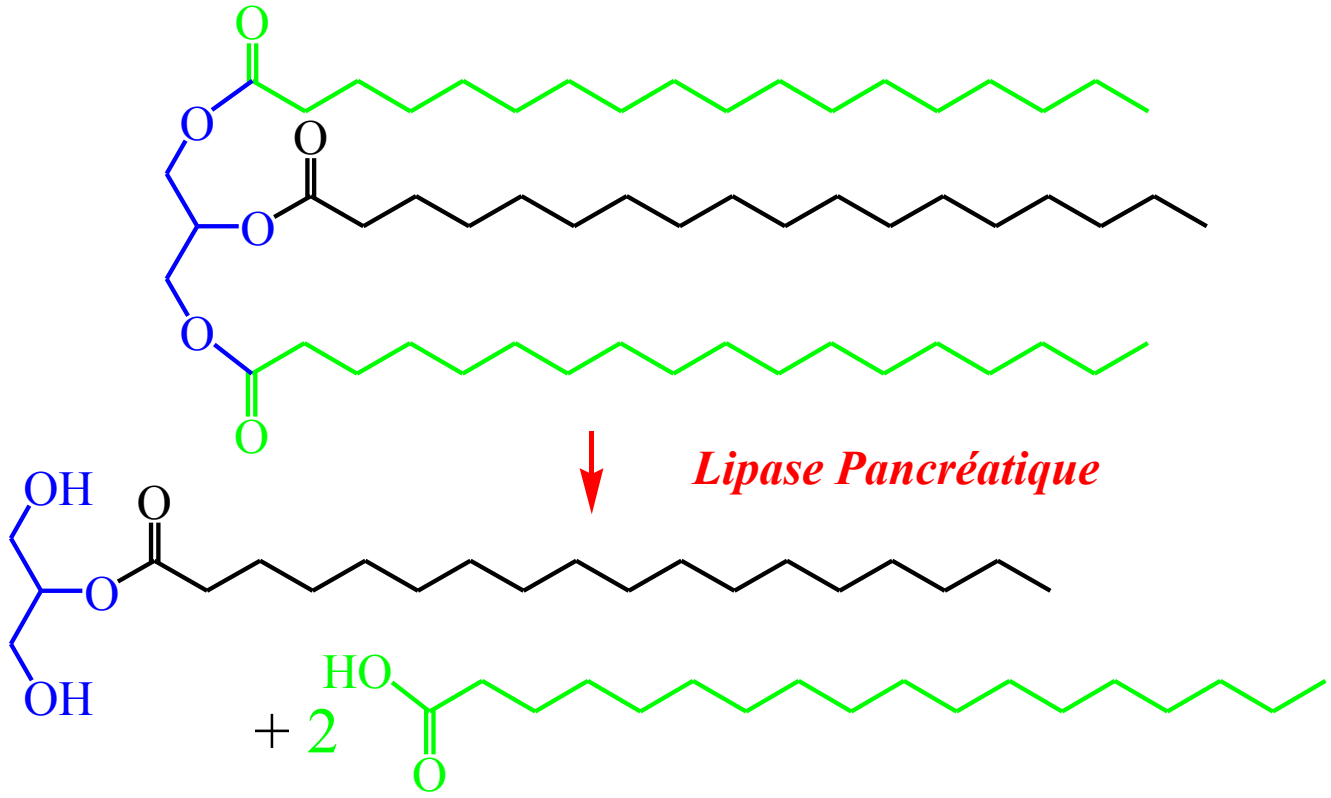
Hydrolyse des triacylglycérols :

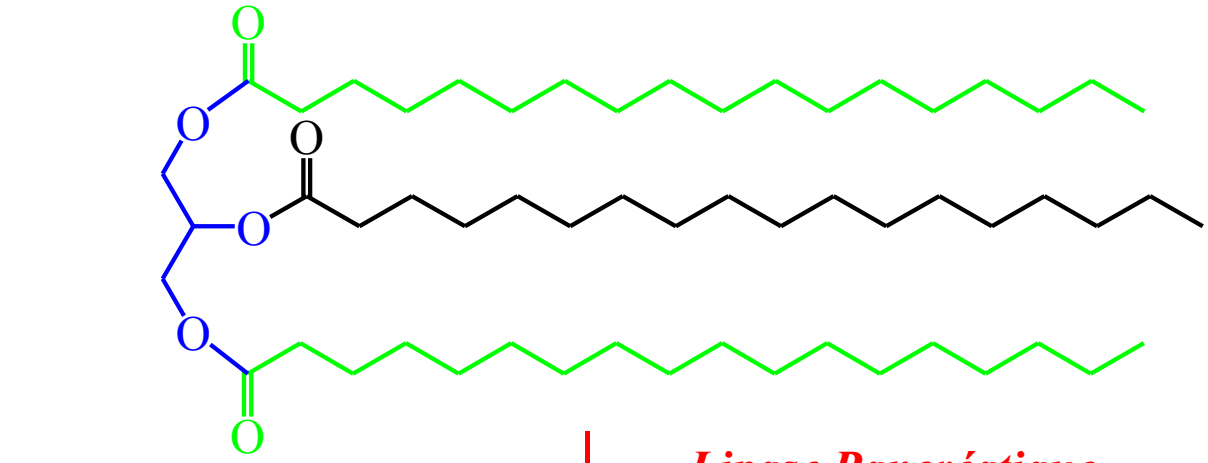


Bilan :

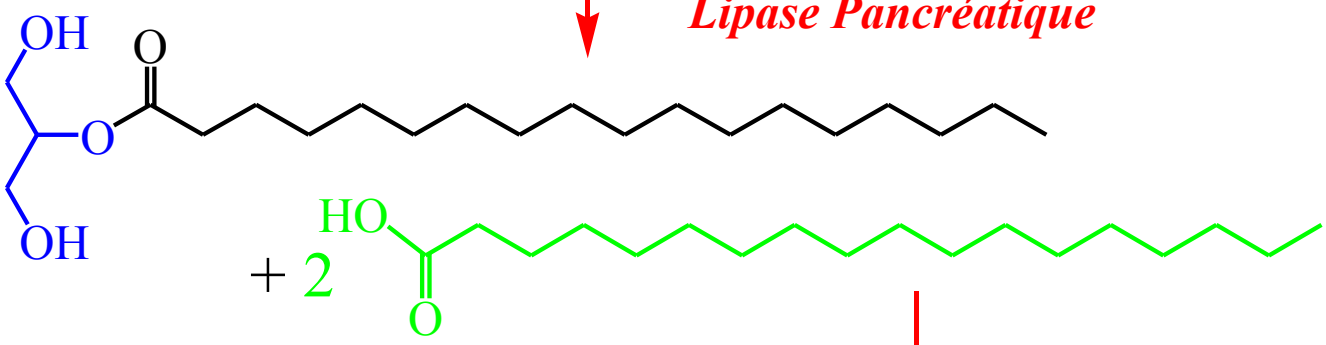

Triacylglycérol
Lipase pancréatique
2-monoacylglycérol
+ 2
Acide gras



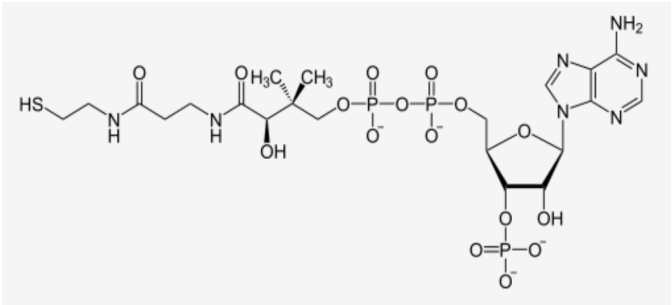

Lipase Pancréatique
OH
OH
HO
+ 2

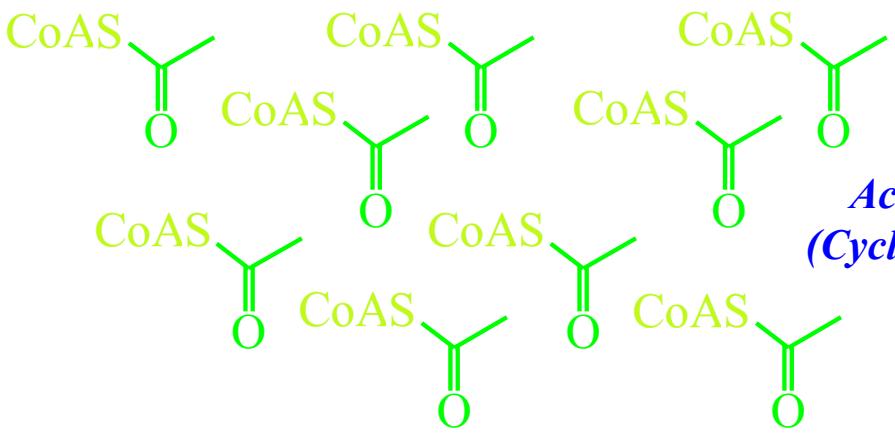


Lipase Pancréatique

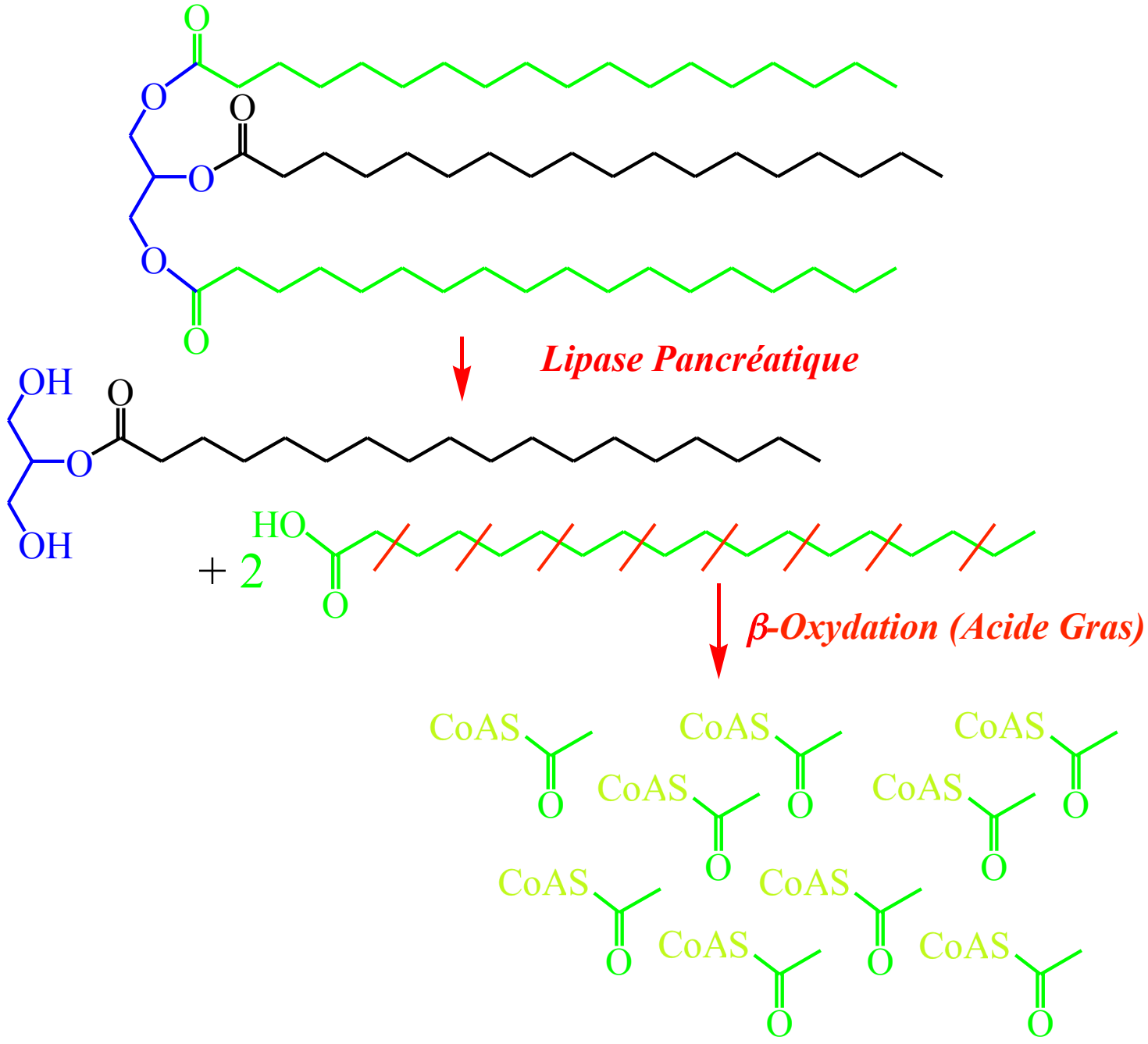


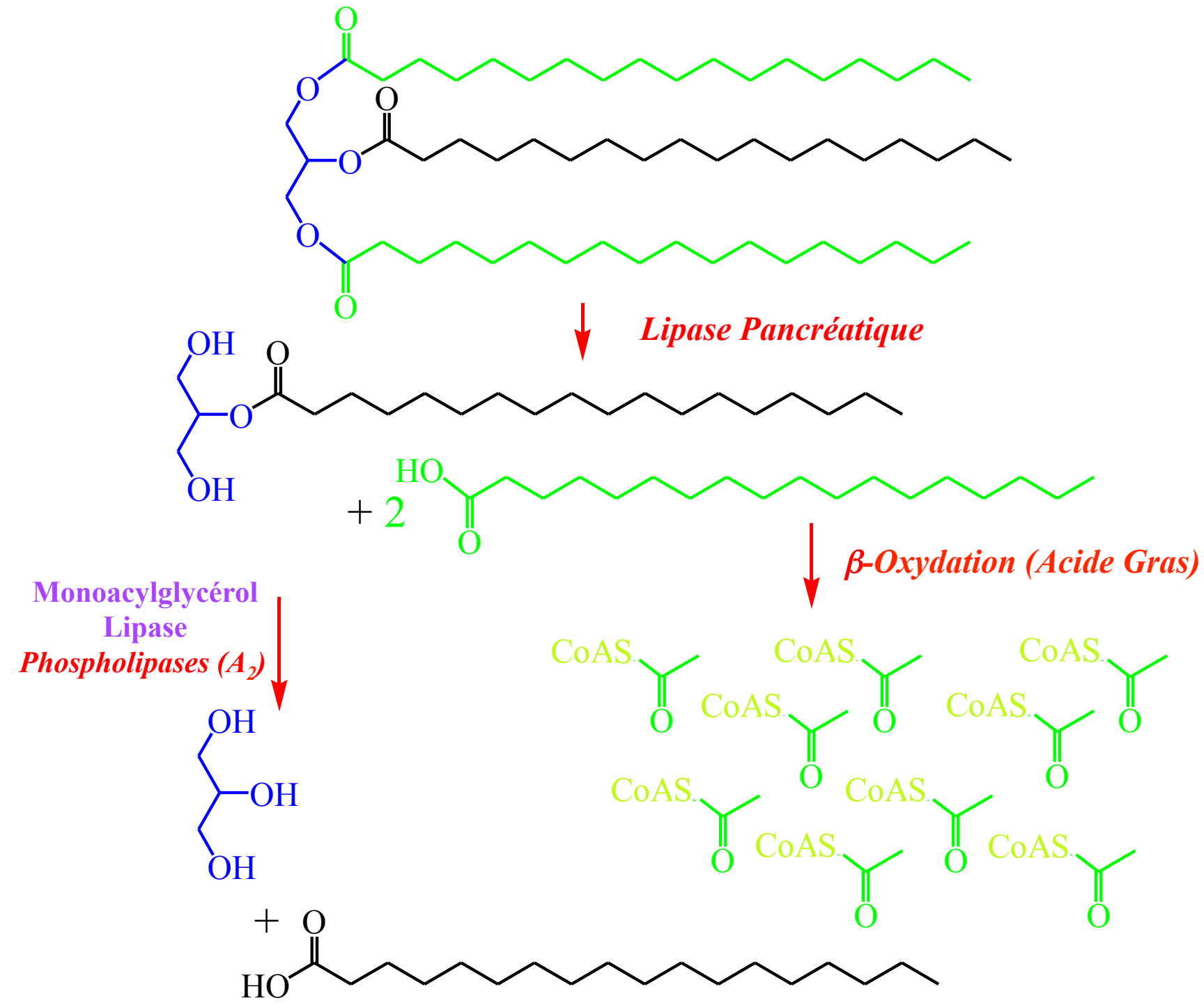
Coenzyme A (CoA)

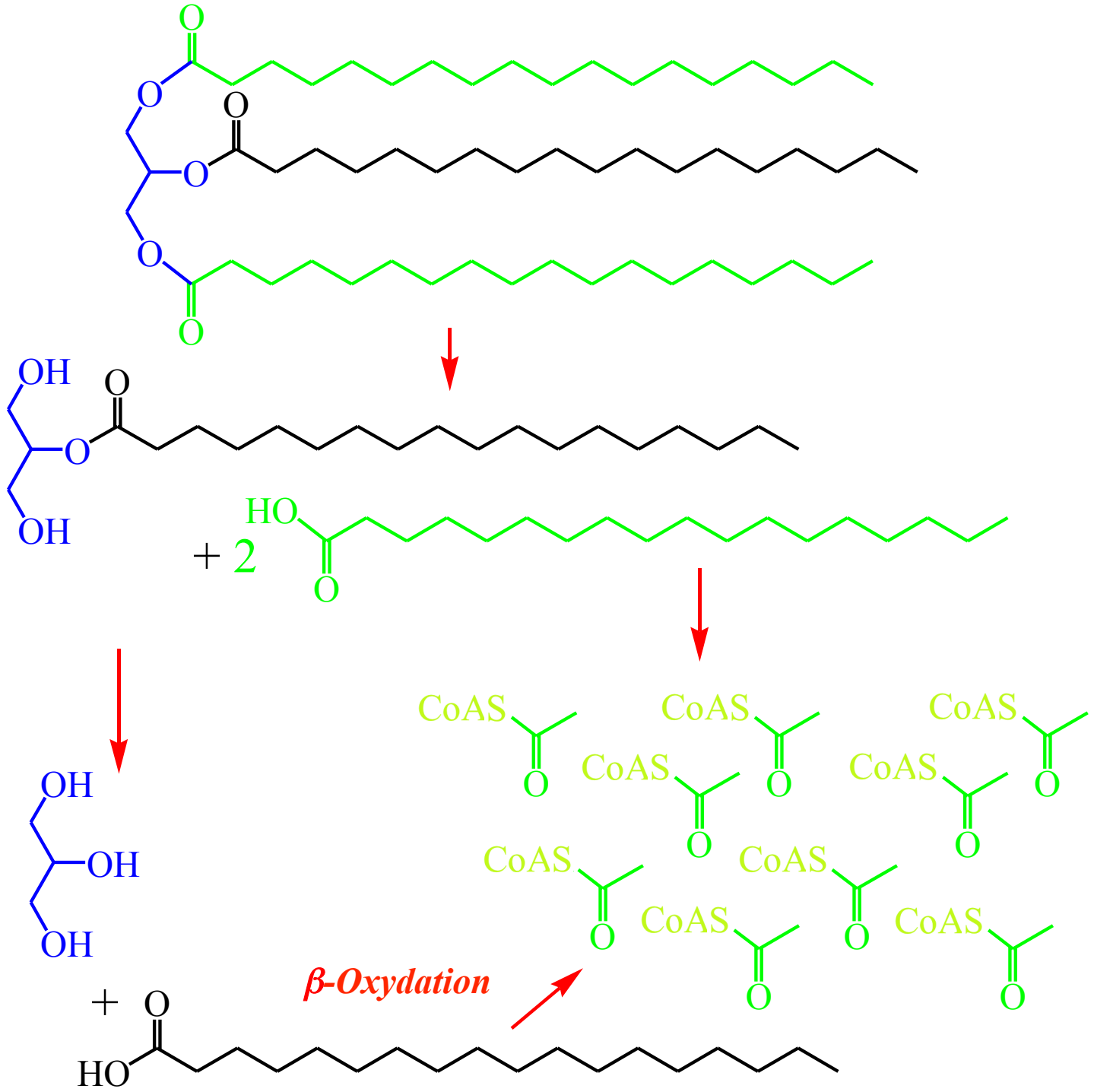




Acétyl-CoA (Cycle de Krebs)

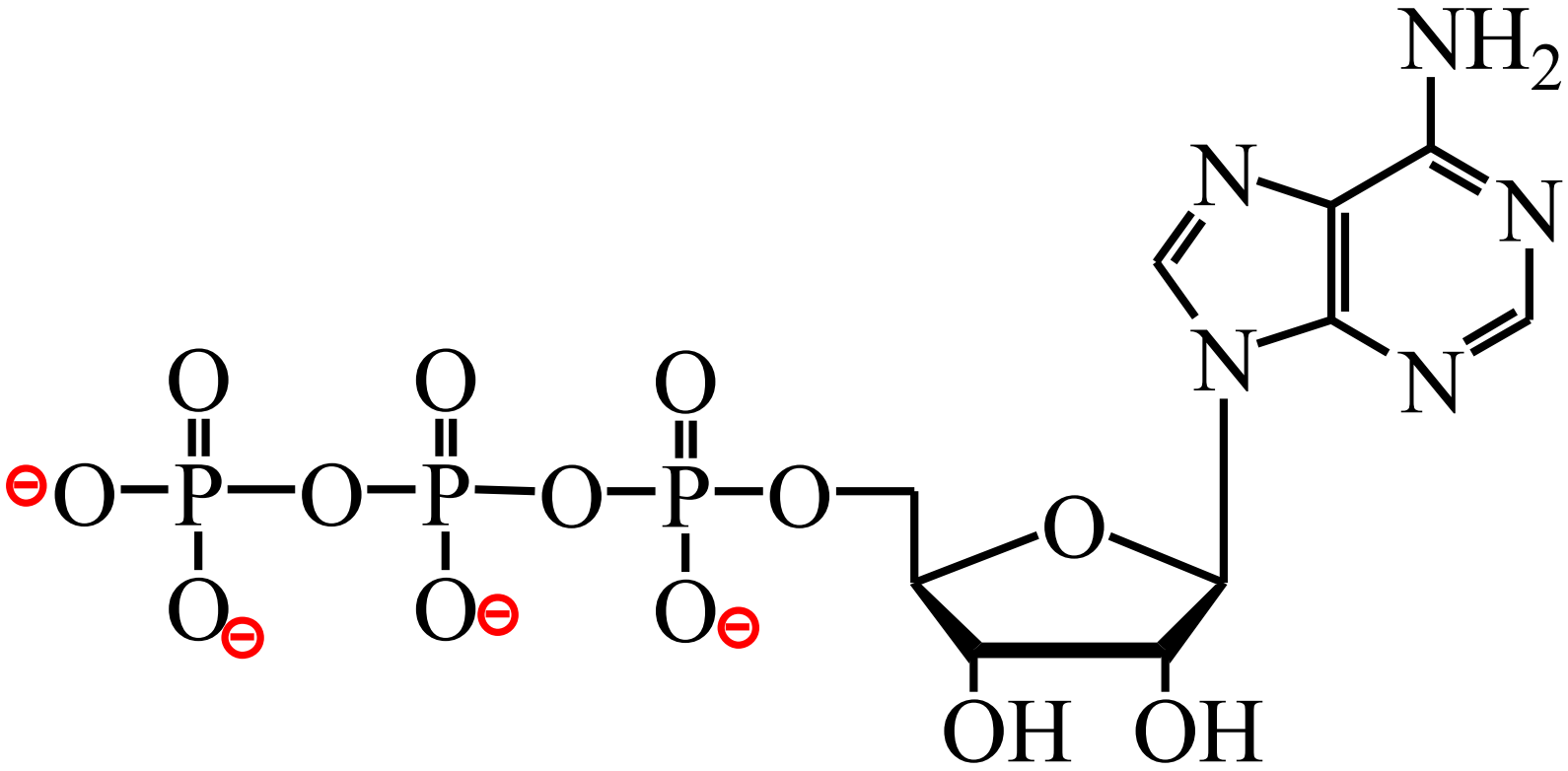

Lipase Pancréatique
β-Oxydation (Acide Gras)
+ 2


Lipase Pancréatique
+ 2
β-Oxydation (Acide Gras)
Monoacylglycérol
Lipase
Phospholipases (A2)
CoAS
+


O
O
O
O
O
O
OH
O
O
OH
+ 2
HO
O
CoAS
O
OH
OH
OH
+
O
HO
β-Oxydation

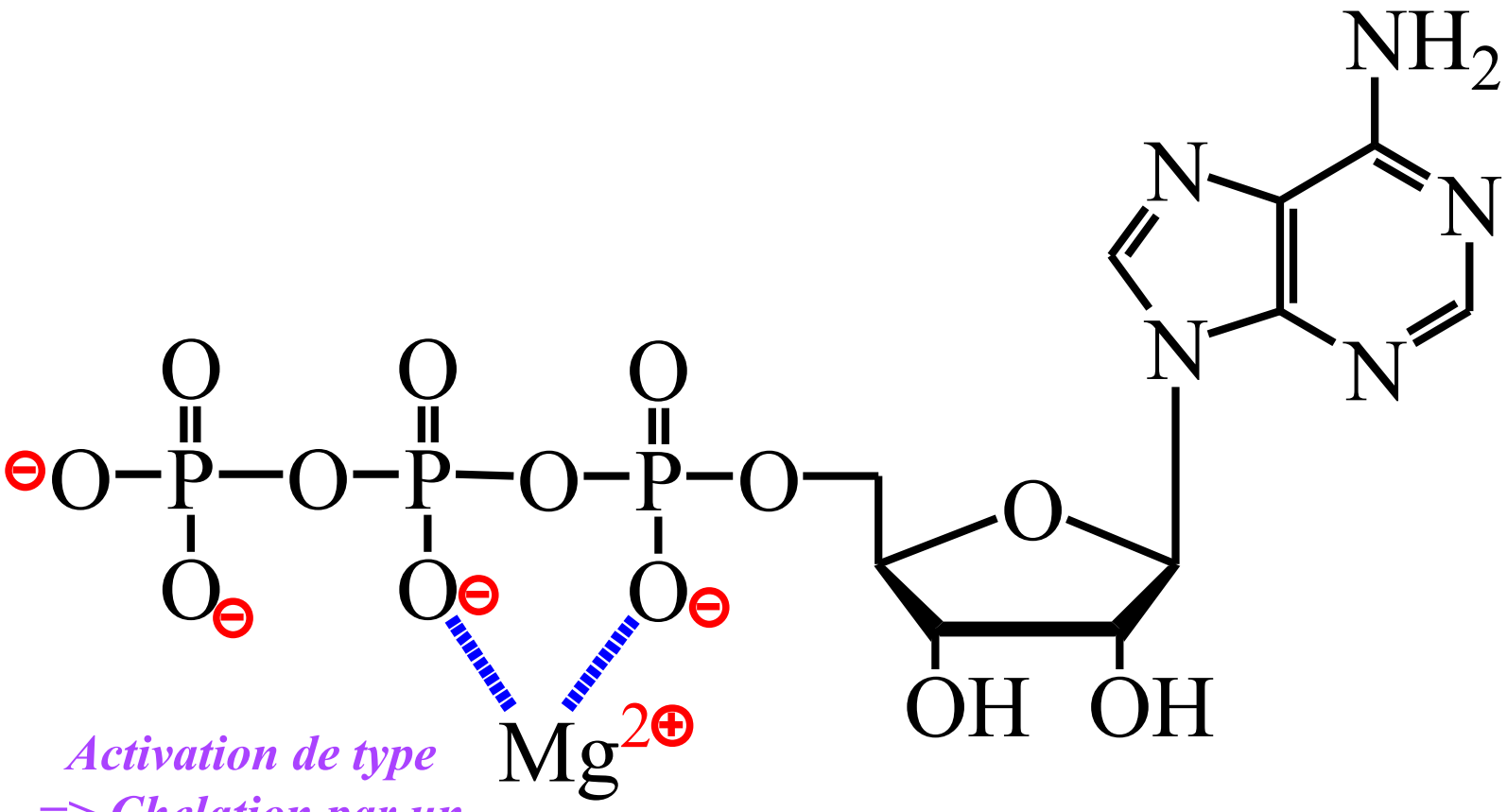
Catabolisme des acides gras (Activation)

Adénosine triphosphate (ATP) :



Catabolisme des acides gras (Activation)

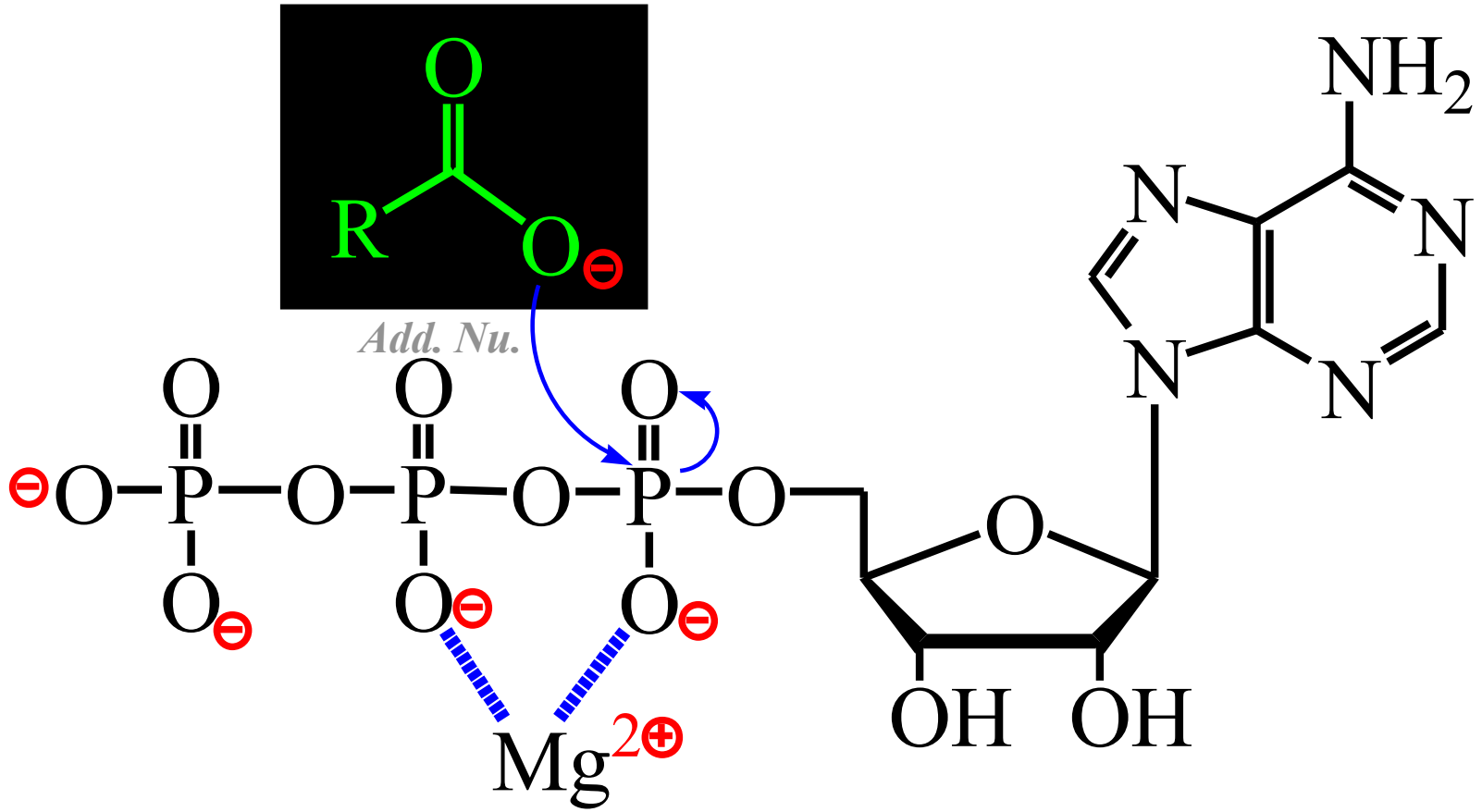
Adénosine triphosphate (ATP) :



Activation de type
=> Chelation par un
Acide de Lewis

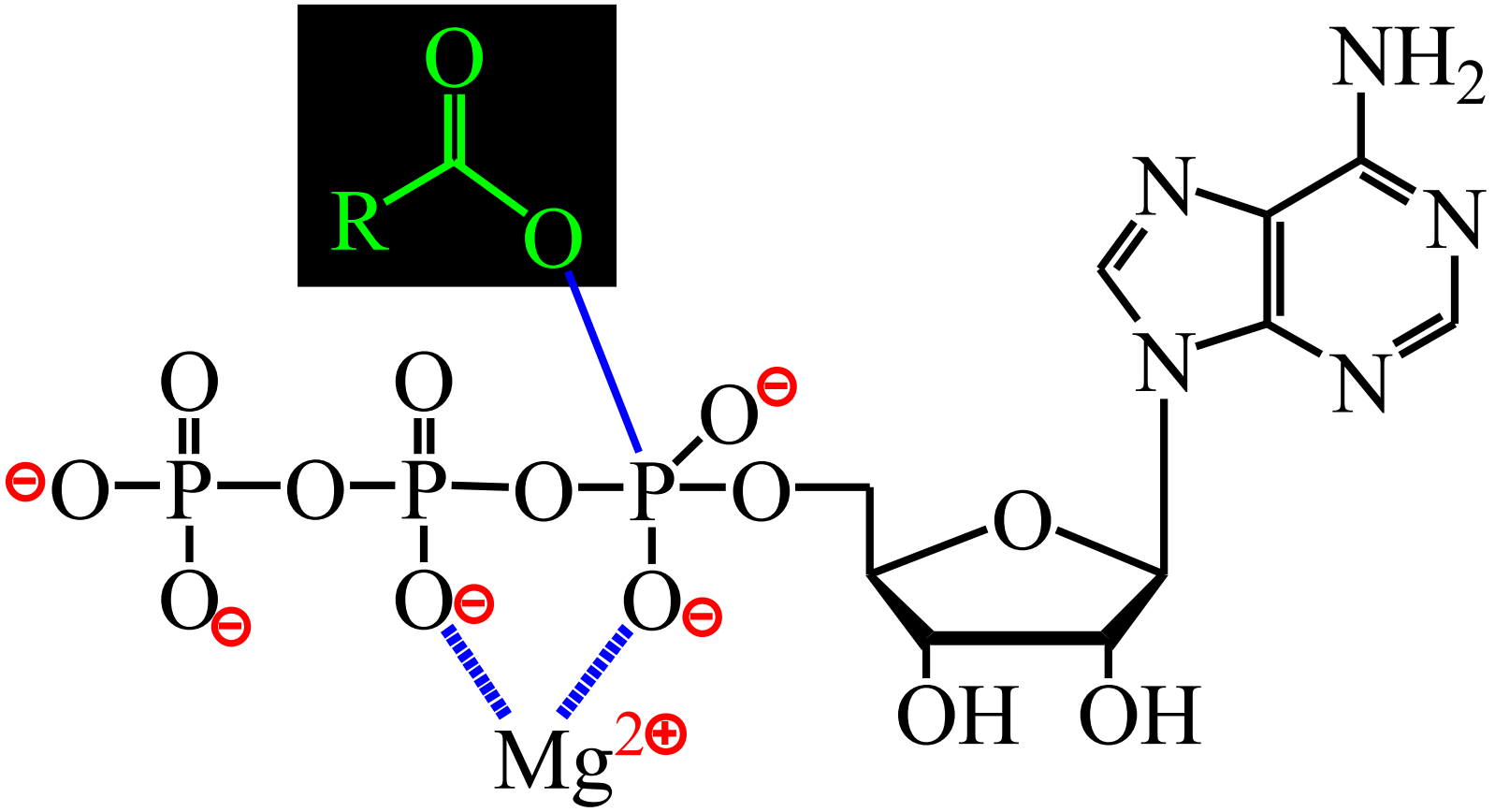
Catabolisme des acides gras (Activation)

Adénosine triphosphate (ATP) + carboxylate (Acide Gras) :



Catabolisme des acides gras (Activation)

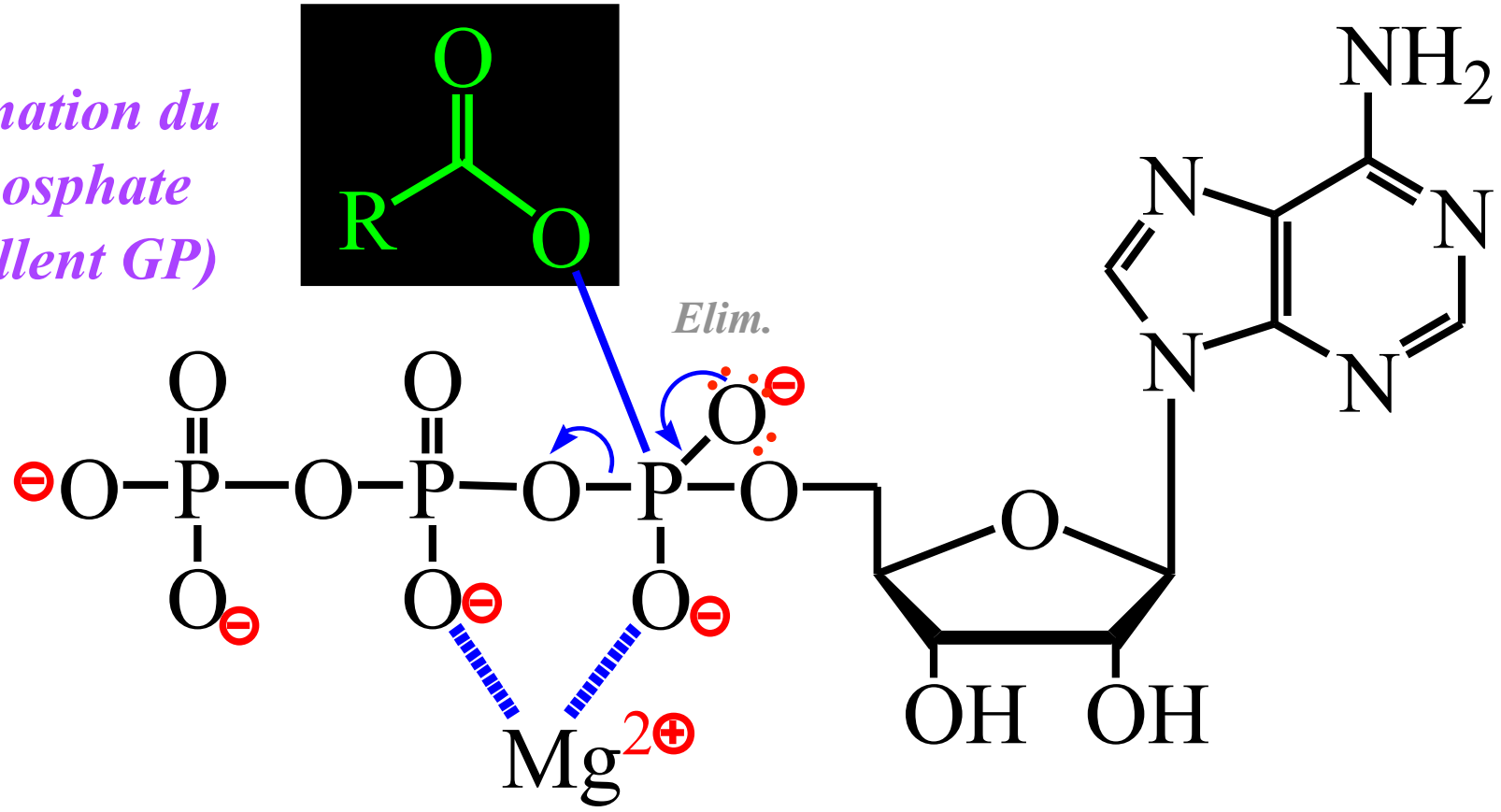
Adénosine triphosphate (ATP) + carboxylate (Acide Gras) :



Catabolisme des acides gras (Activation)

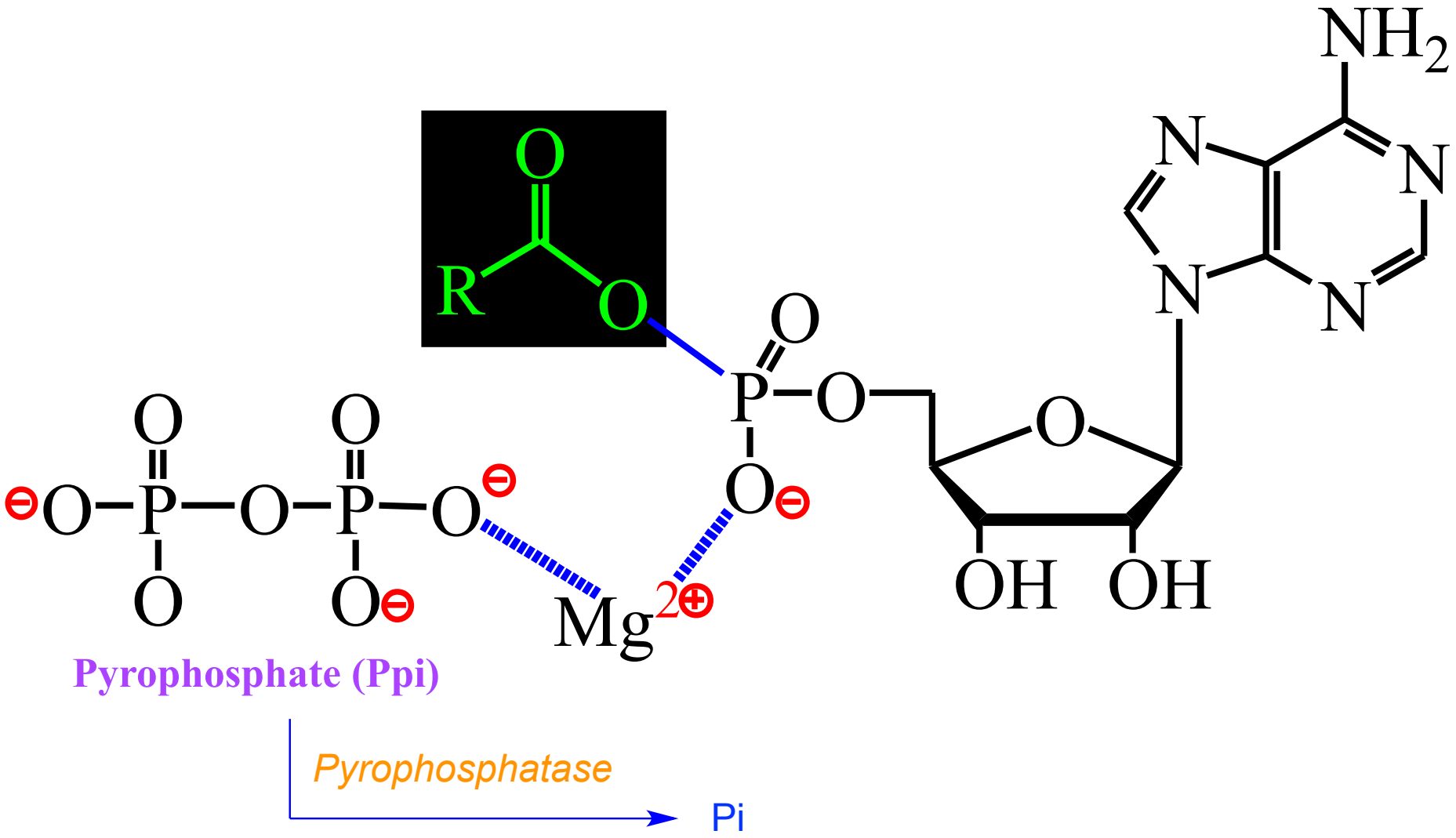
Adénosine triphosphate (ATP) + carboxylate (Acide Gras) :

Elimination du Diphosphate (excellent GP)



Catabolisme des acides gras (Activation)

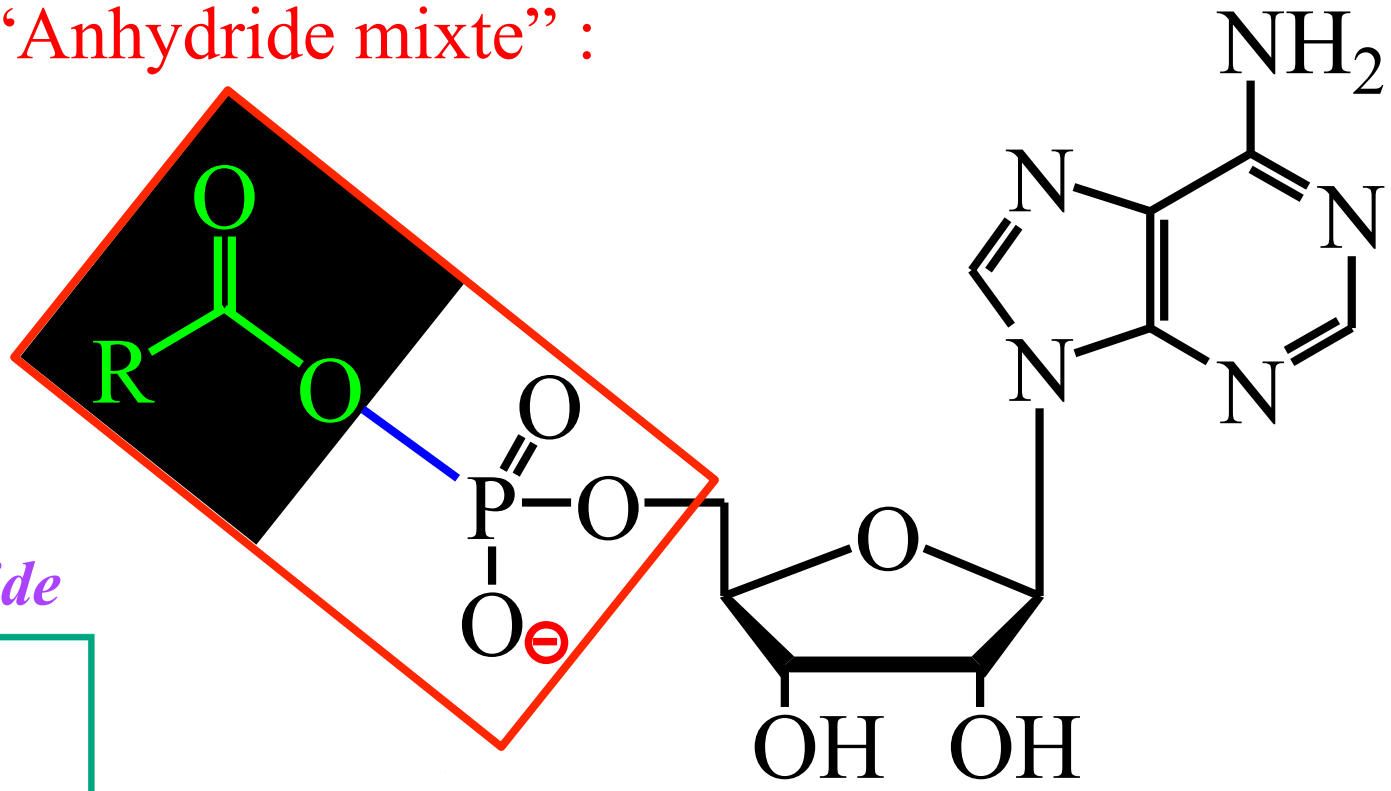
Adénosine triphosphate (ATP) + carboxylate (Acide Gras) :



Catabolisme des acides gras (Activation)

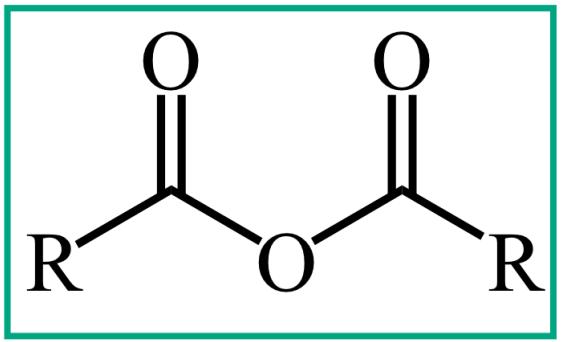
Adénosine triphosphate (ATP) + carboxylate (Acide Gras) :

Fonction “Anhydride mixte” :

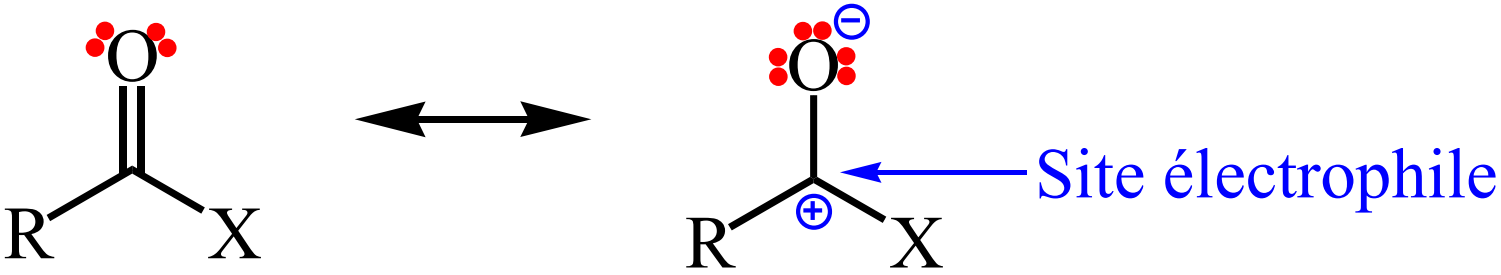


Rappel :

Anhydride d’acide



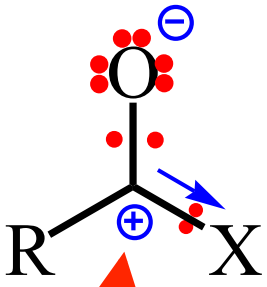
La fonction carbonyle dans RC(O)X



X : inductif attracteur

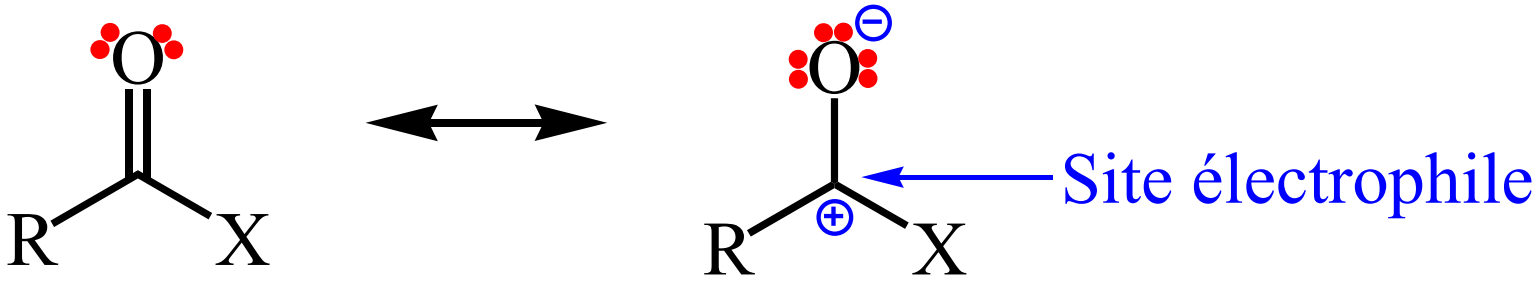
(Valable pour tout X plus électronégatif que C)

X* = *Halogène, N, O…



Electrophilie exaltée par effet inductif attracteur -I

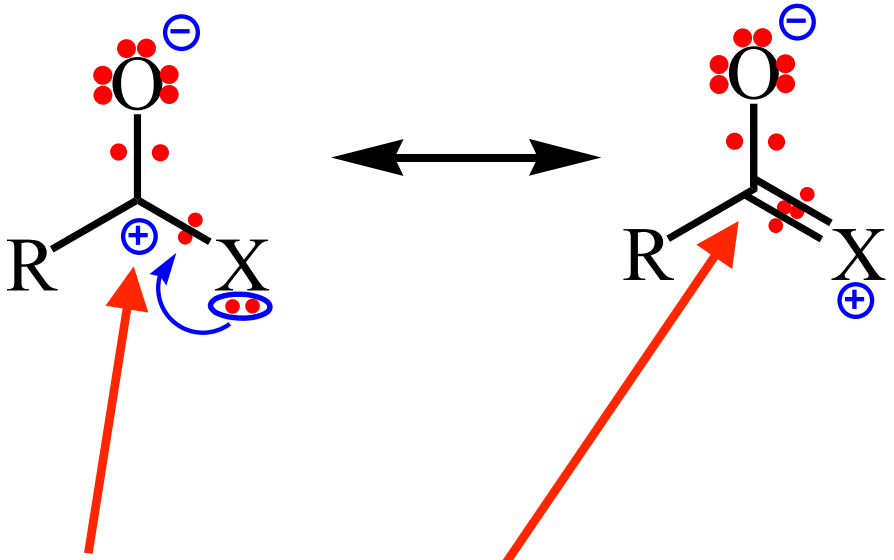
La fonction carbonyle dans RC(O)X



X : mésomère donneur

(Valable pour tout X porteur de doublet(s) libre(s))

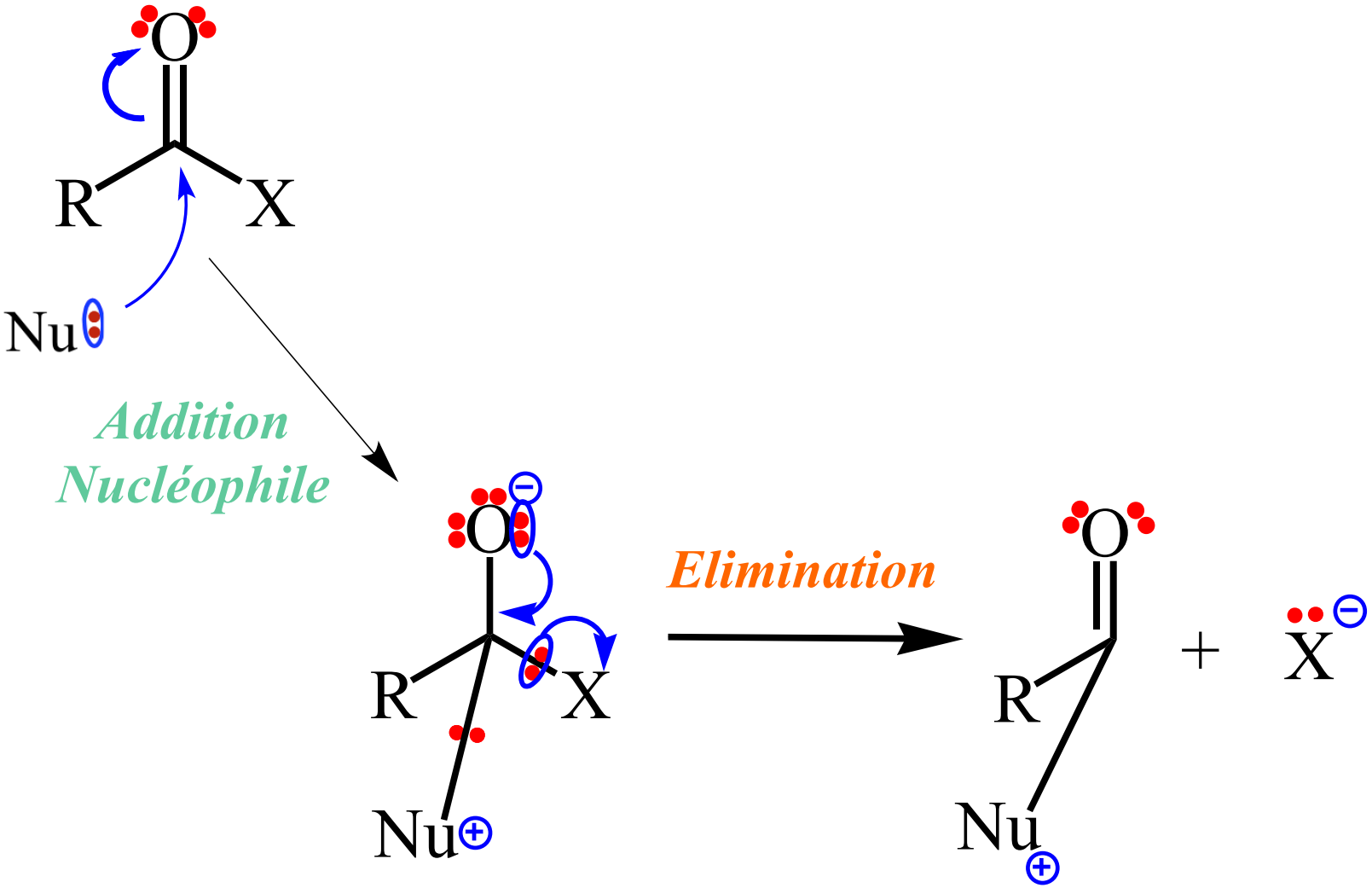
X* = *Halogène, N, O…



Electrophilie atténuée par effet mésomère donneur +M

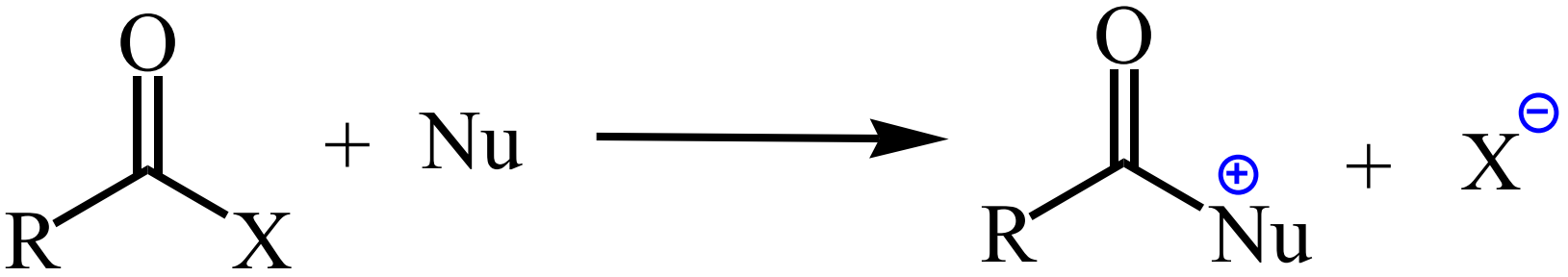
Réactivité de RC(O)X :

Addition-Elimination



Réactivité de RC(O)X :

Addition-Elimination :

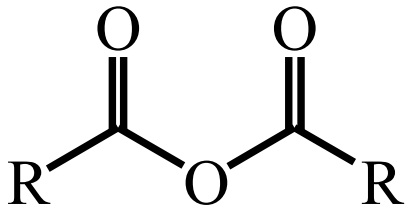


Substitution / C=O

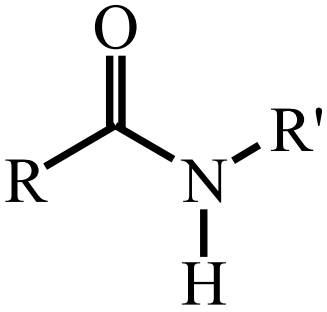
D'autant plus facilitée que :

1) Le carbonyle de RCOX est électrophile
2) X^- est un bon nucléofuge (*groupe partant*)

Réactivité de RCOX dans l'addition-élimination

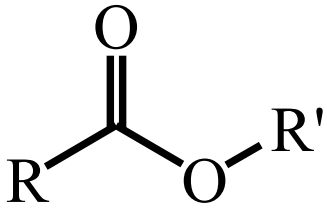


Anhydride



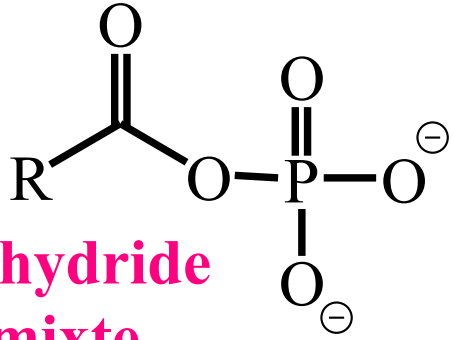
Amide

<

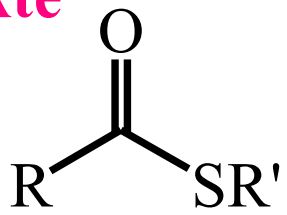


Ester

<

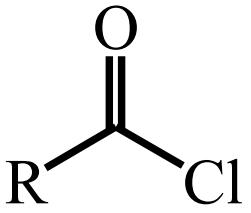


Anhydride mixte



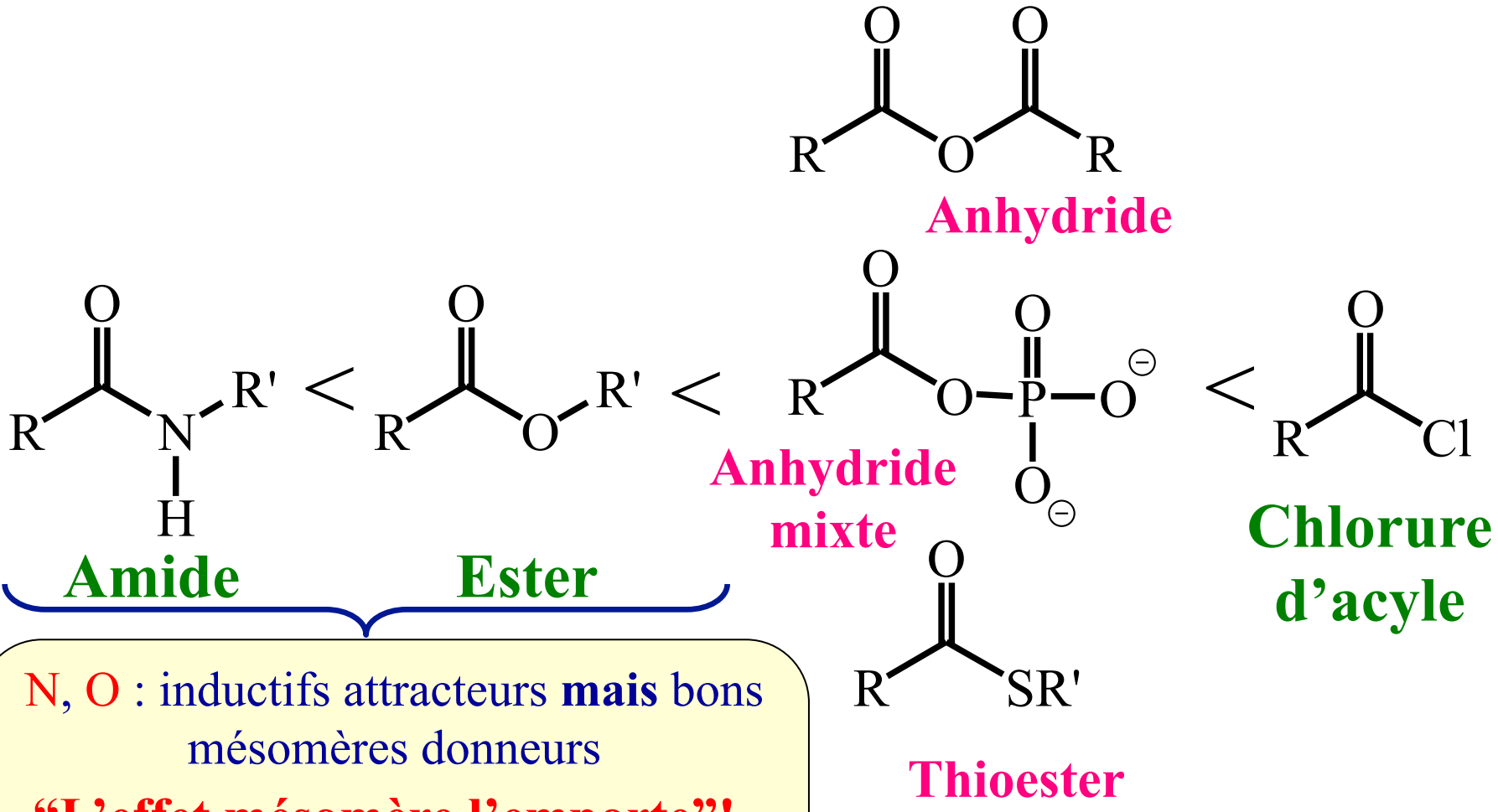
Thioester

<



Chlorure d'acyle

Réactivité de RCOX dans l'addition-élimination

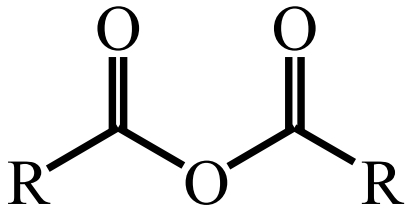


N, O : inductifs attracteurs **mais** bons mésomères donneurs

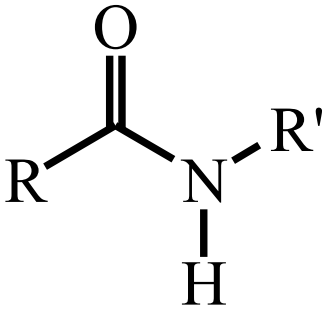
"L'effet mésomère l'emporte"!

R'NH^-, R'O^- : mauvais nucléofuges (*espèces très basiques*).

Réactivité de RCOX dans l'addition-élimination

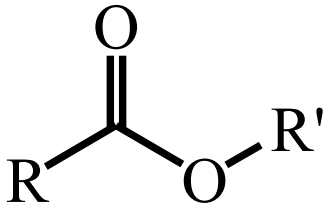


Anhydride



Amide

<



Ester

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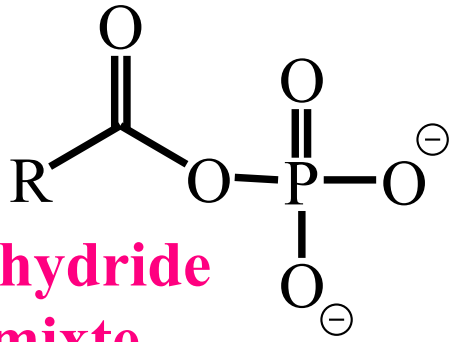
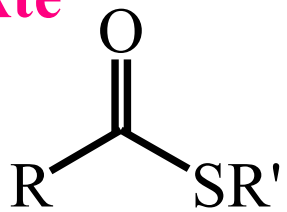
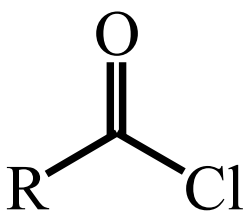


Anhydride mixte



Thioester

<

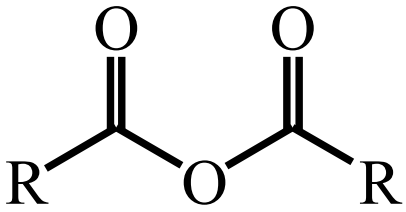


Chlorure d'acyle

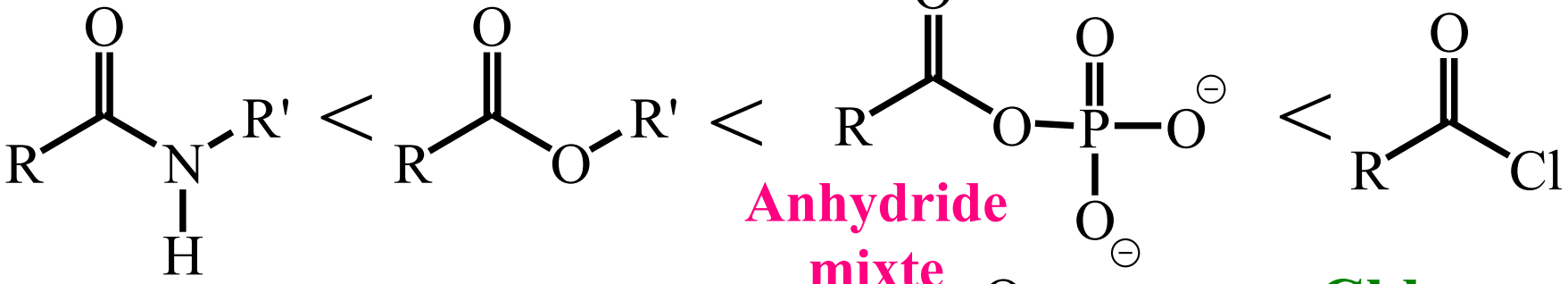
Cl : inductif attracteur fort, mauvais mésomère donneur

Cl^- : bon nucléofuge (*faiblement basique*)

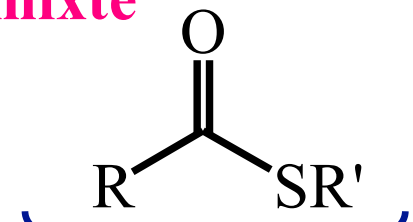
Réactivité de RCOX dans l'addition-élimination



Anhydride



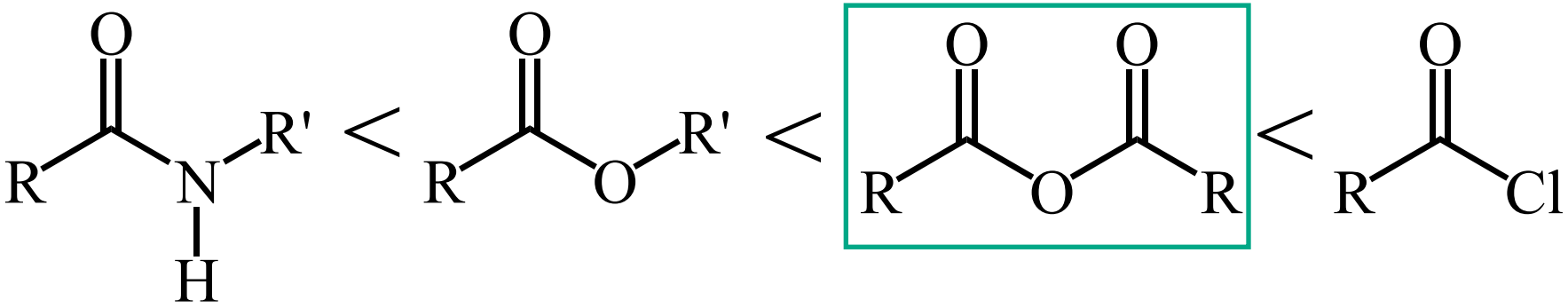
Amide **Ester** **Anhydride mixte** **Chlorure d'acyle**

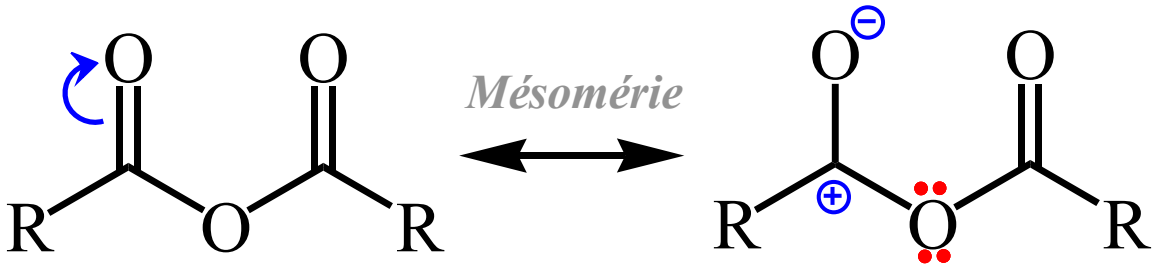


Thioester

S : inductif attracteur léger, mauvais mésomère donneur
RS^- : assez bon nucléofuge
(*moyennement basique*
pK_a = 10-11)

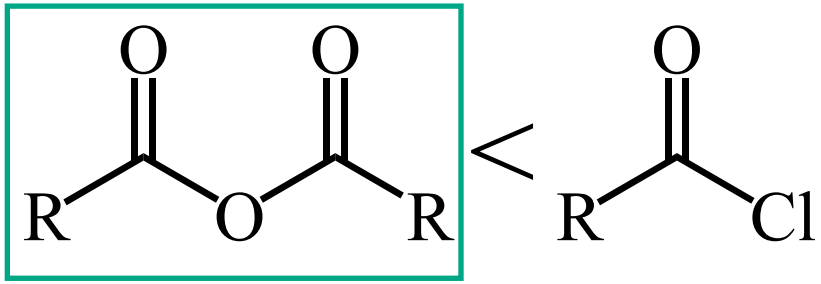
Le cas des anhydrides :

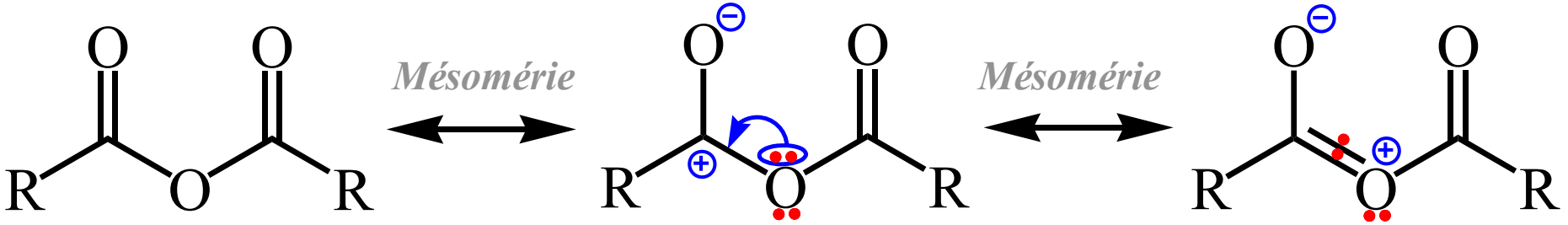




Le cas des anhydrides :

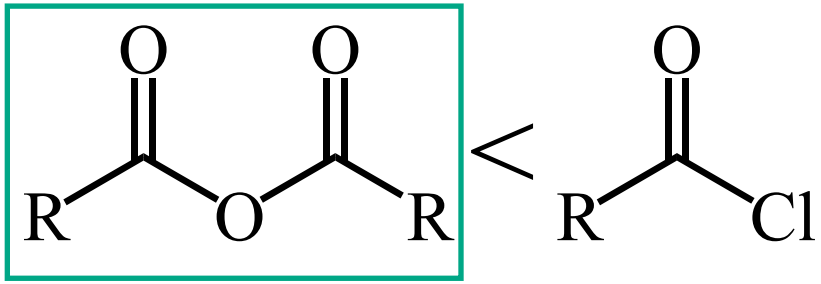
L'effet mésomère donneur + **M** du O central doit se partager entre 2 carbonyles : ***mauvaise atténuation de l'électrophilie***

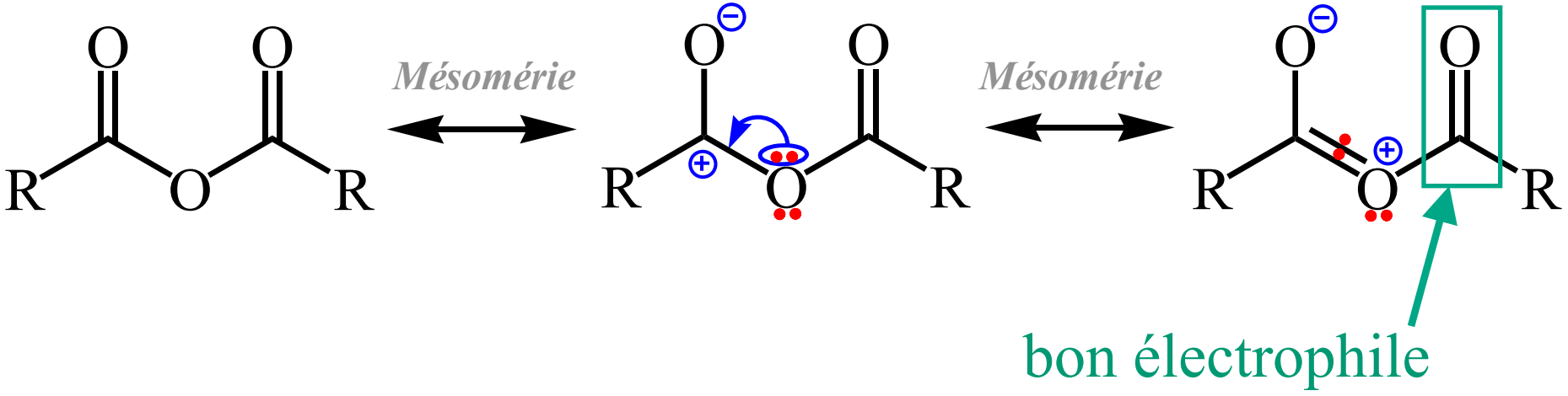




Le cas des anhydrides :

L'effet mésomère donneur + **M** du O central doit se partager entre 2 carbonyles : ***mauvaise atténuation de l'électrophilie***

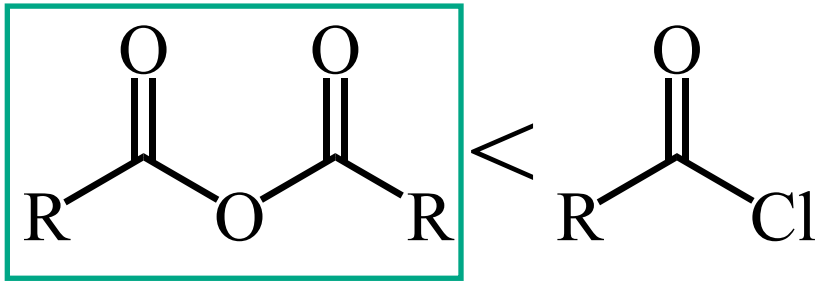


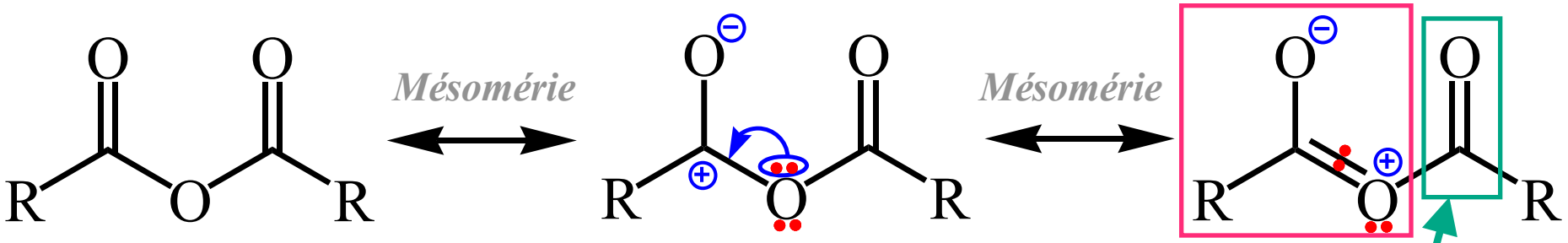


Le cas des anhydrides :

L'effet mésomère donneur + **M** du O central doit se partager entre 2 carbonyles : ***mauvaise atténuation de l'électrophilie***

Le nucléofuge est un anion carboxylate (*peu basique pKa = 4-5*)



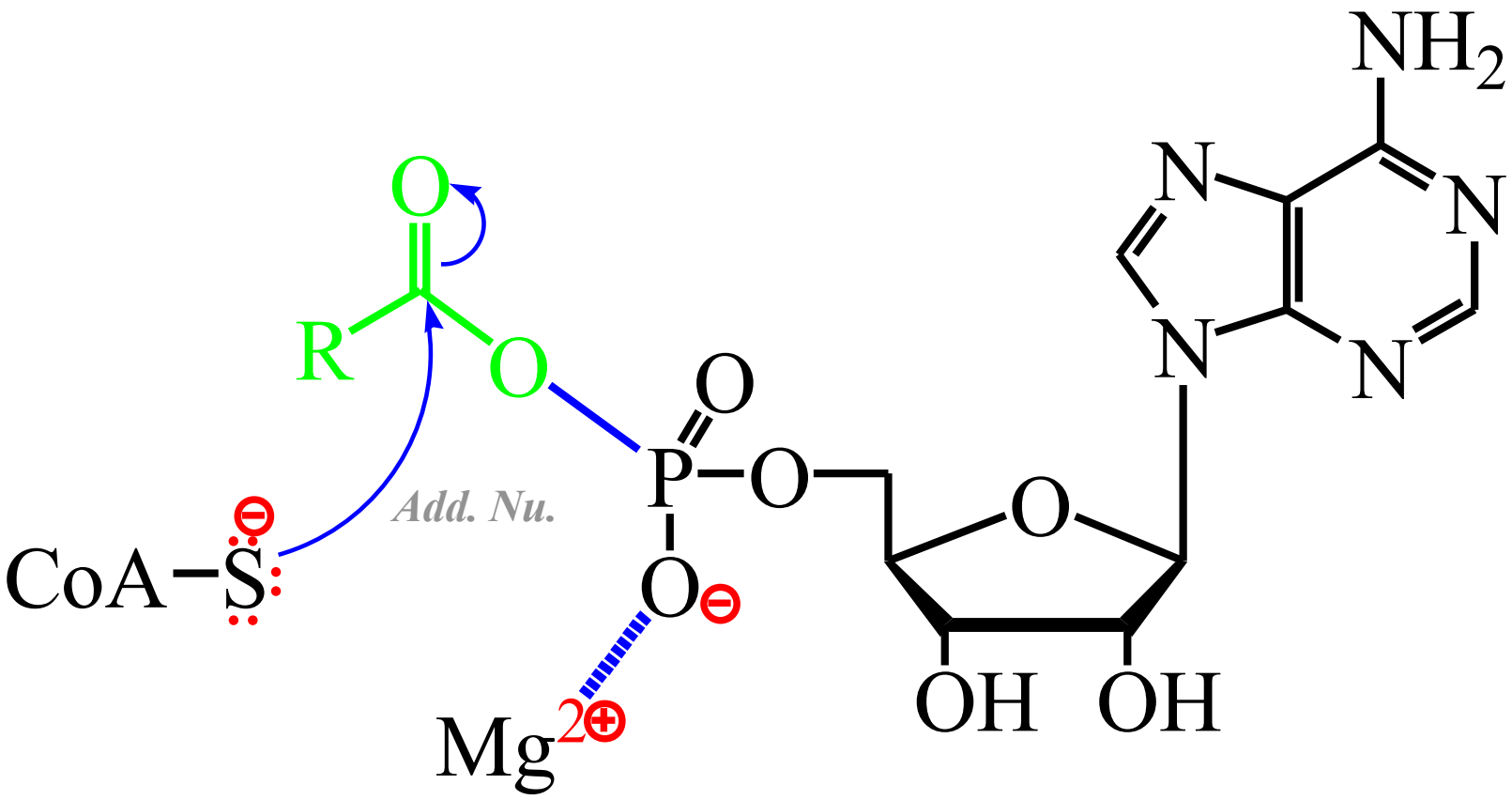


bon nucléofuge

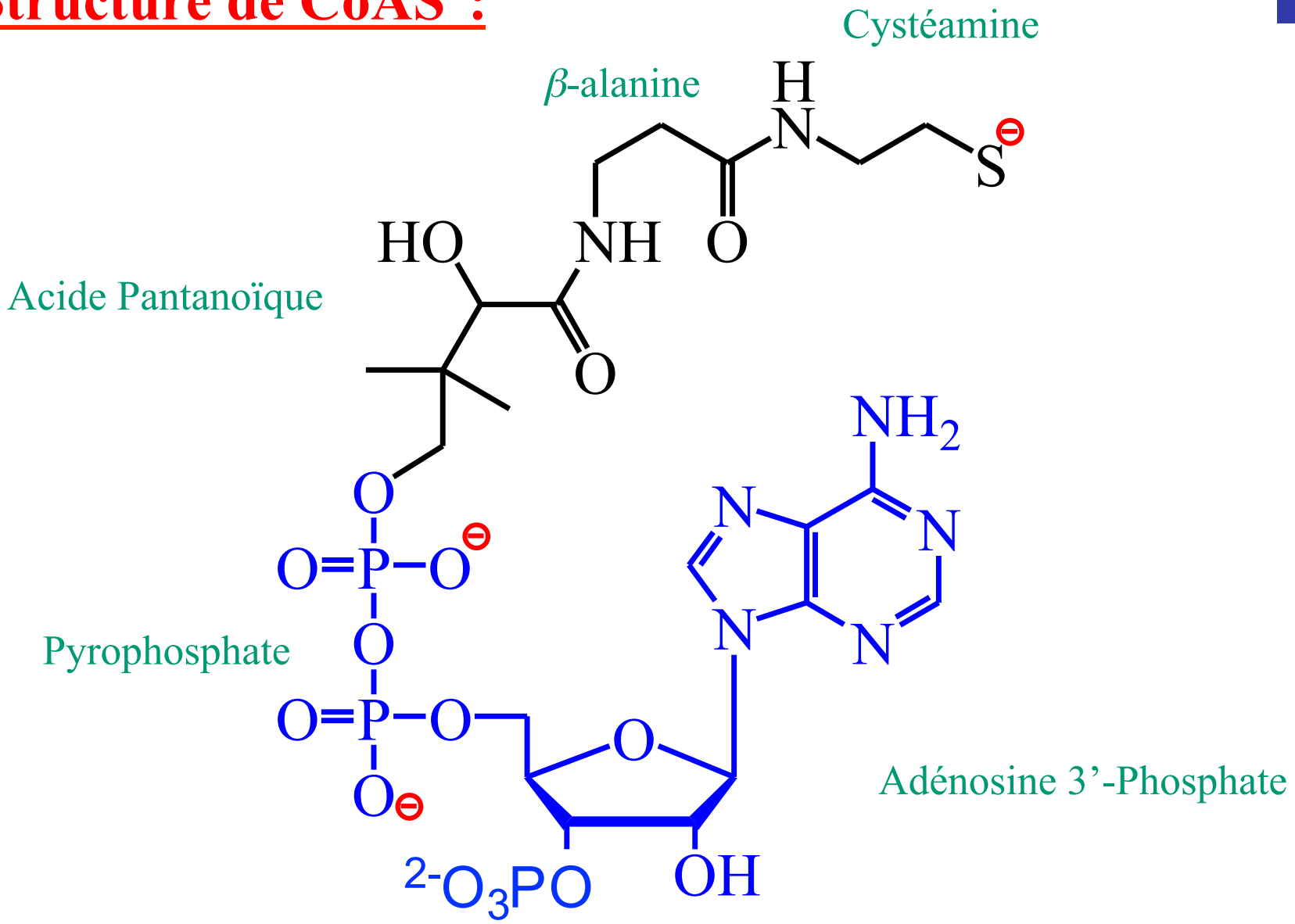
bon électrophile

Catabolisme des acides gras (Formation Acyl-CoA)

Adénosine triphosphate (ATP) + carboxylate + $CoAS^-$:

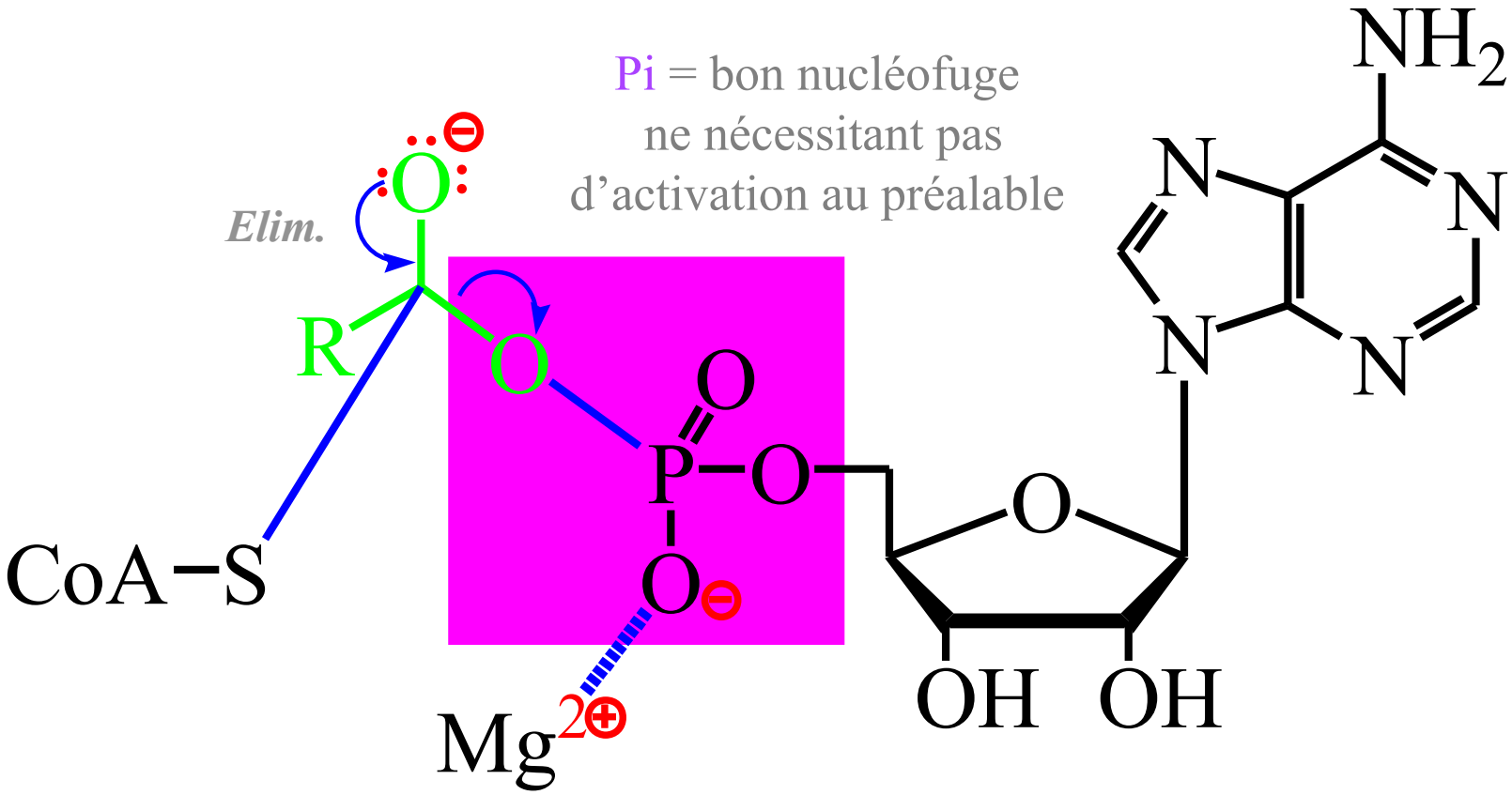


Structure de $CoAS^-$:



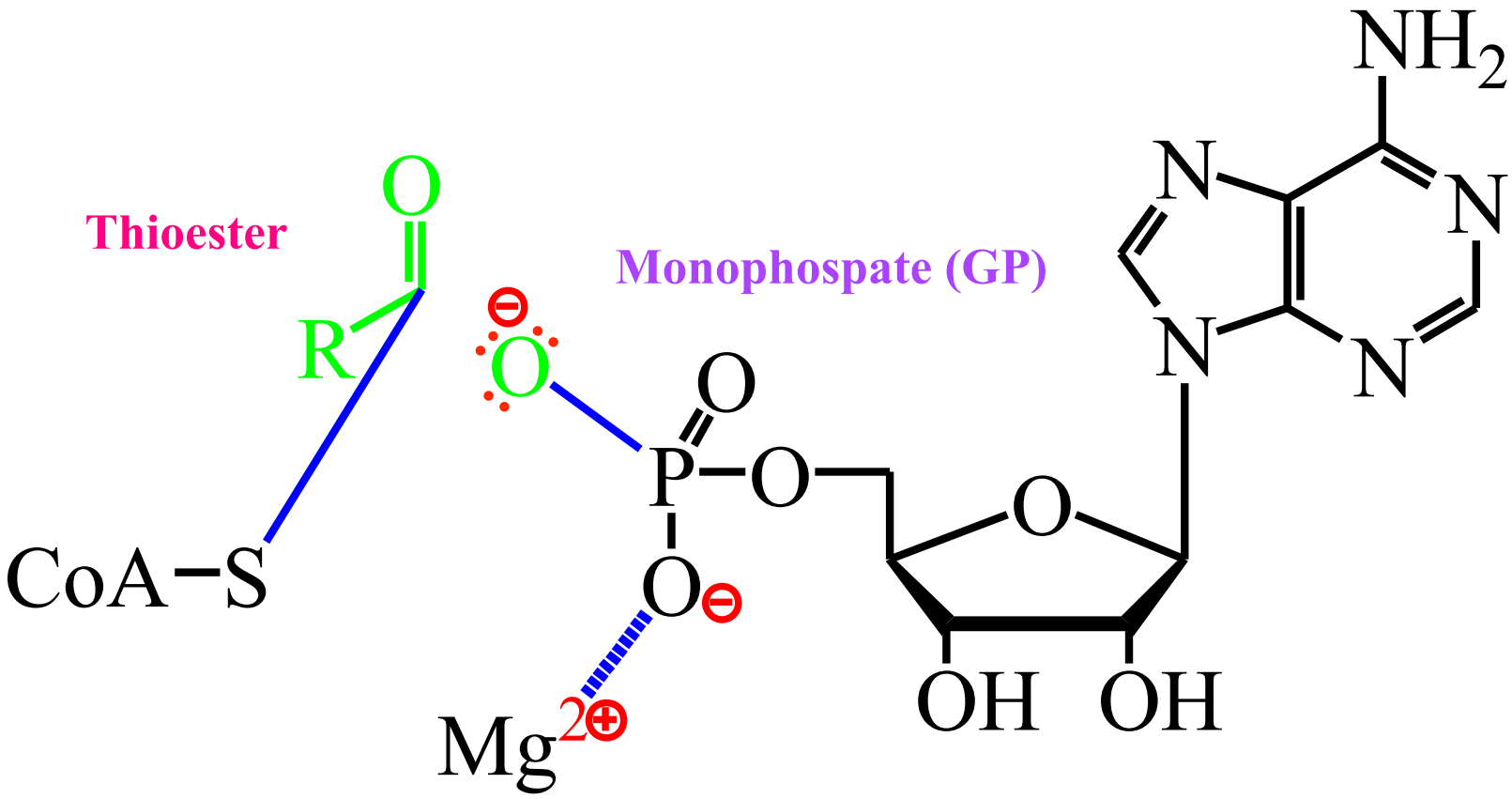
Catabolisme des acides gras (Formation Acyl-CoA)

Adénosine triphosphate (ATP) + carboxylate + $CoAS^-$:



Catabolisme des acides gras (Formation Acyl-CoA)

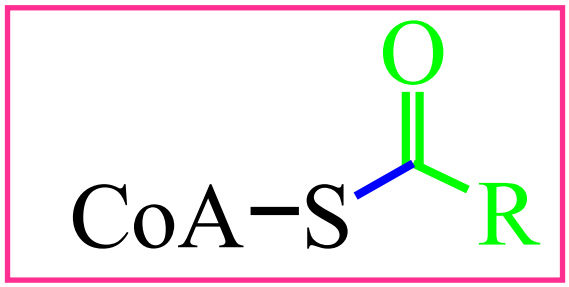
Adénosine triphosphate (ATP) + carboxylate + $CoAS^-$:



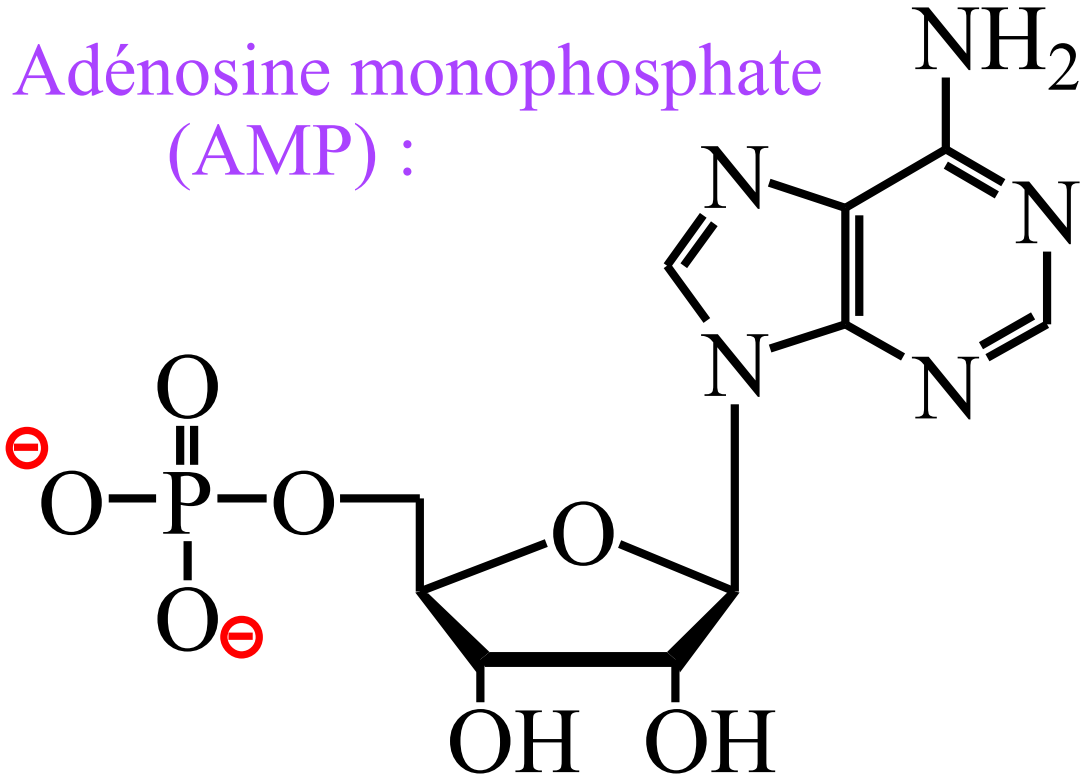
Catabolisme des acides gras (Formation Acyl-CoA)

Adénosine triphosphate (ATP) + carboxylate + $CoAS^-$:

Acyl-coenzyme A (*Acyl-CoA*) :



Adénosine monophosphate (AMP) :

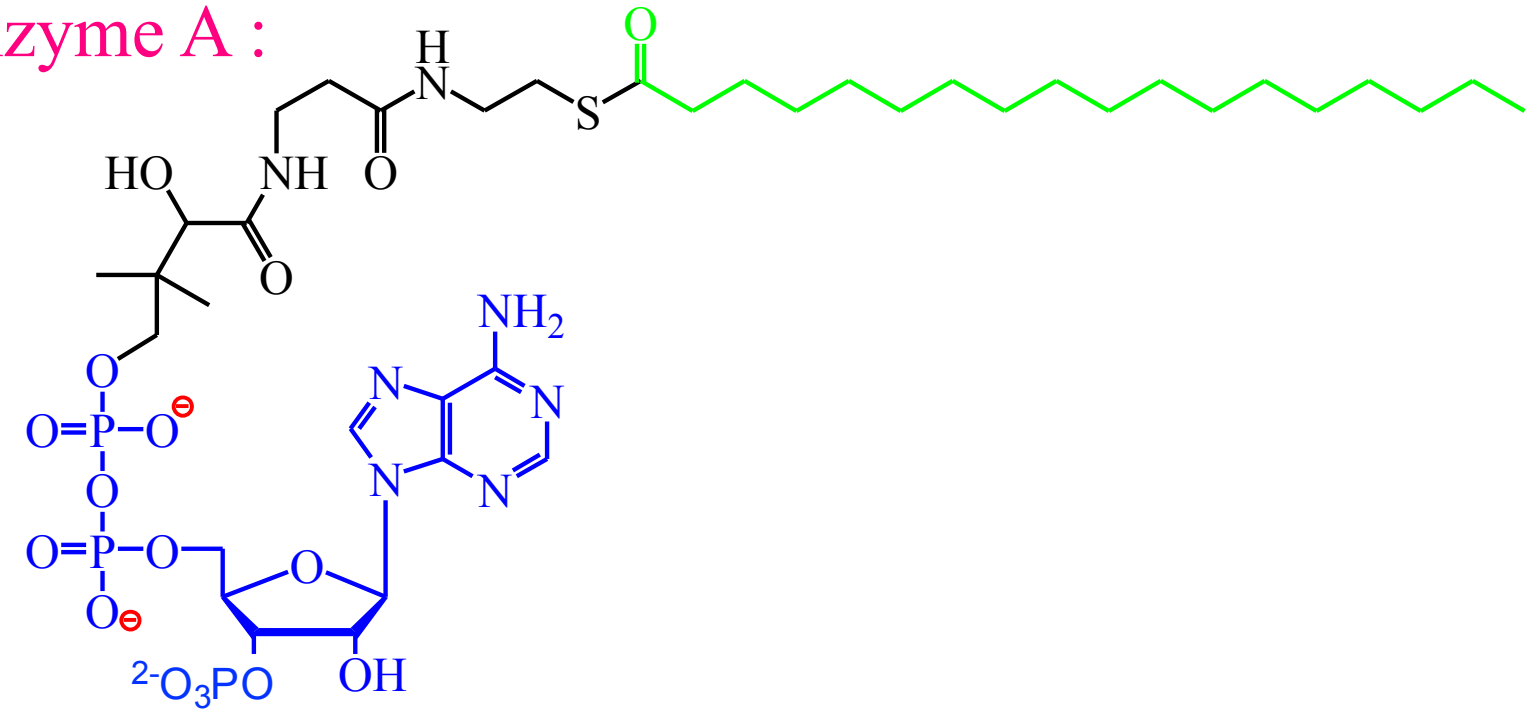


Catabolisme des acides gras (β-oxydation)

⇒ Dégradation de l'Acyl-CoA

1ère Etape : Formation Acyl-CoA insaturé

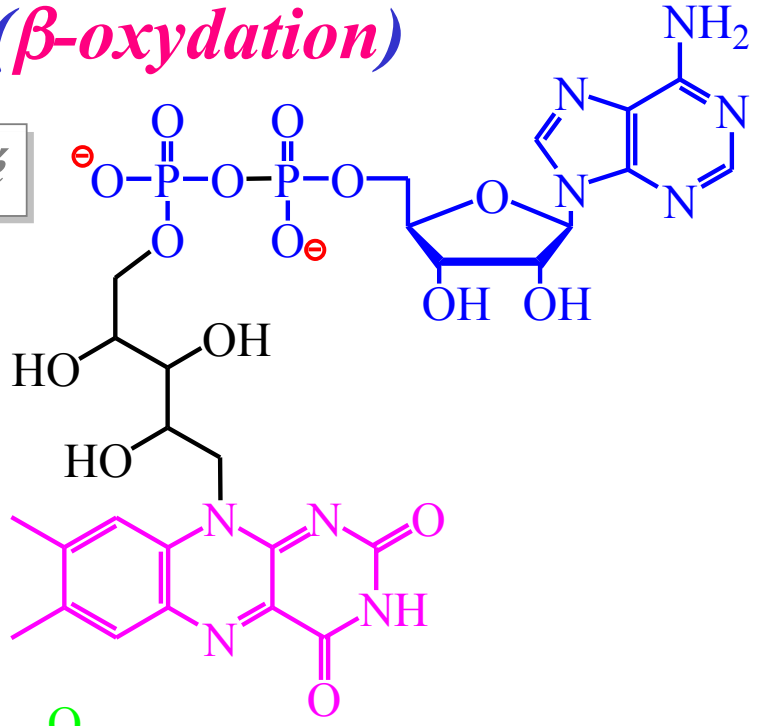
Acyl-coenzyme A :



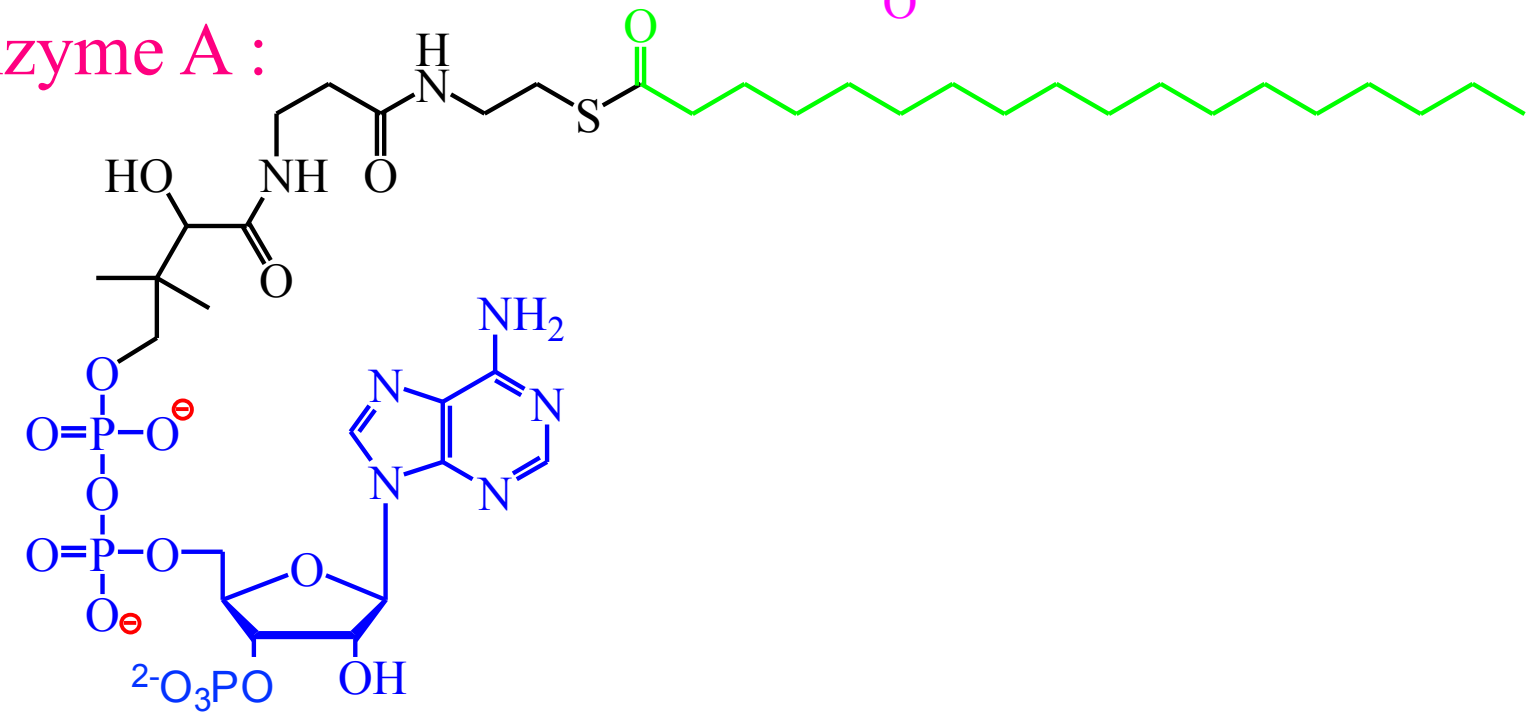
Catabolisme des acides gras (β-oxydation)

1ère Etape : Formation Acyl-CoA insaturé

Flavine Adénine Dinucléotide (FAD) :

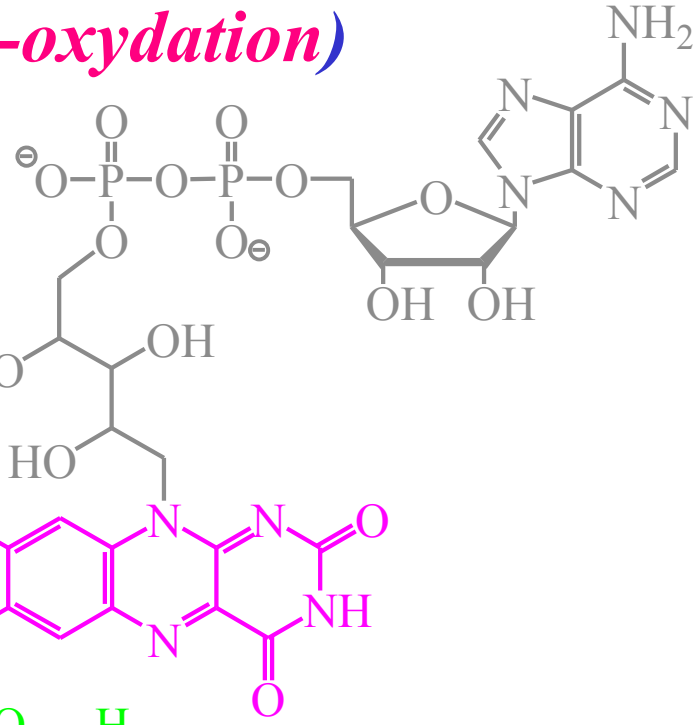


Acyl-coenzyme A :



Catabolisme des acides gras (β-oxydation)

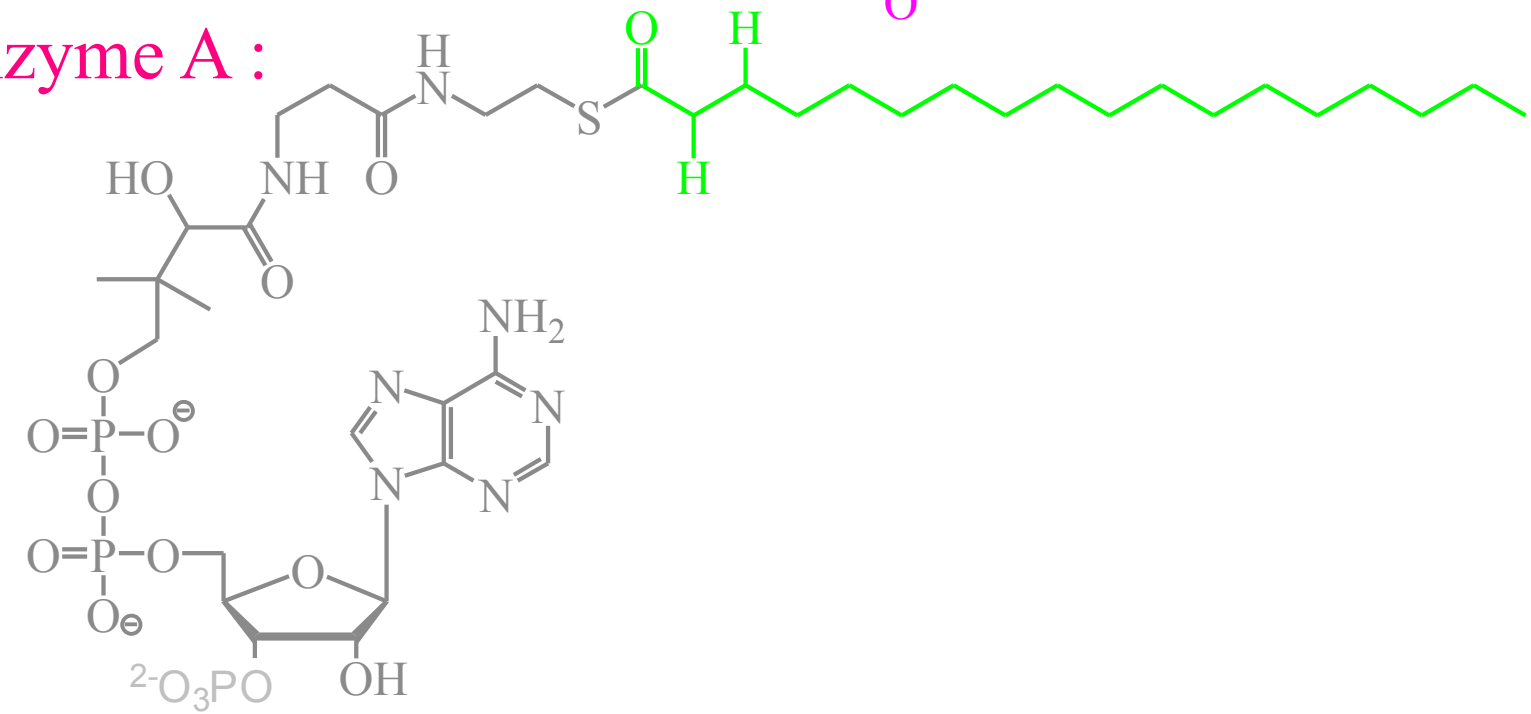
1ère Etape : Formation Acyl-CoA insaturé



Focus sur la partie Flavine

(~ *Accepteur de Michael*) :

Acyl-coenzyme A :

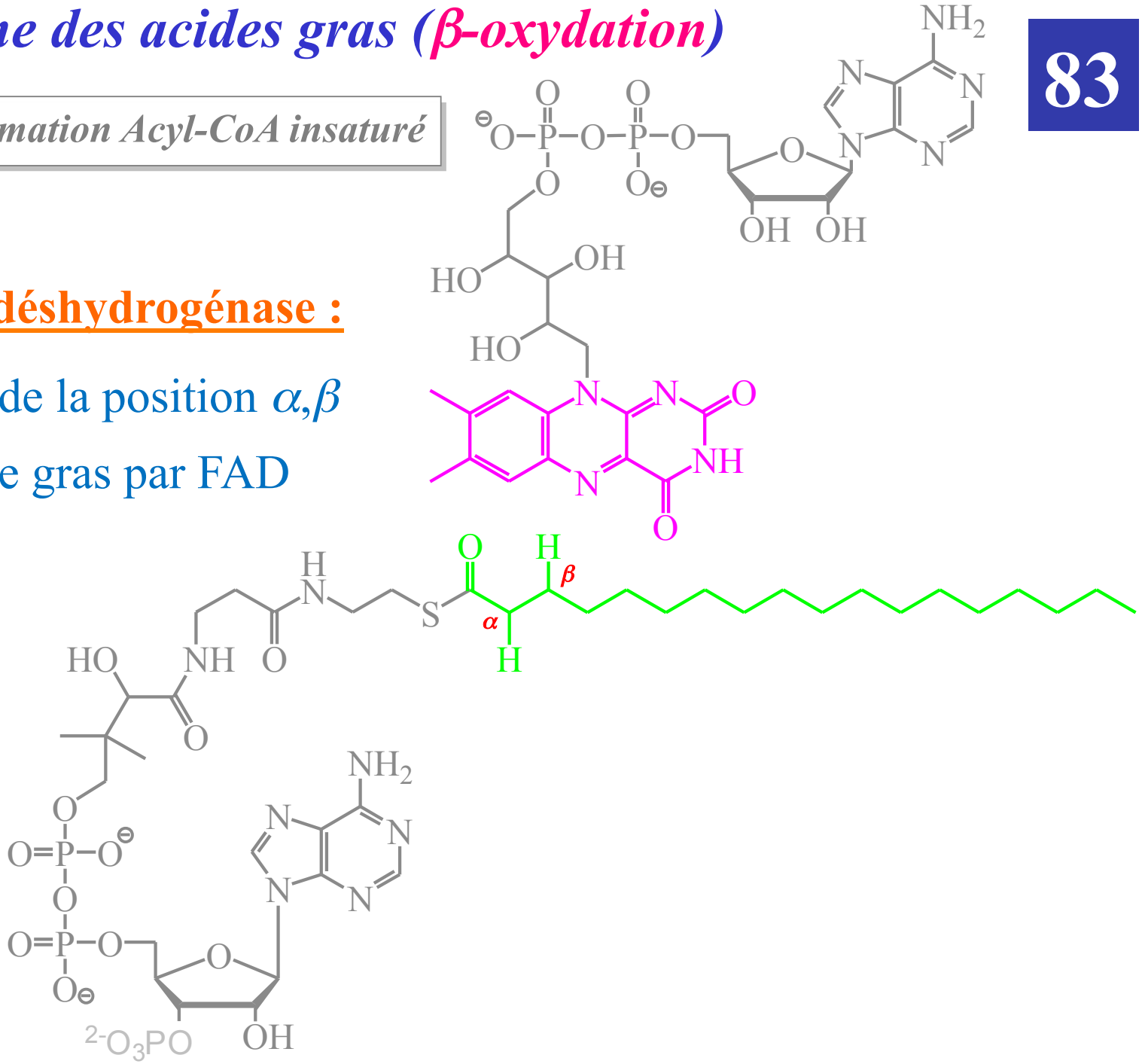


Catabolisme des acides gras (β-oxydation)

1ère Etape : Formation Acyl-CoA insaturé

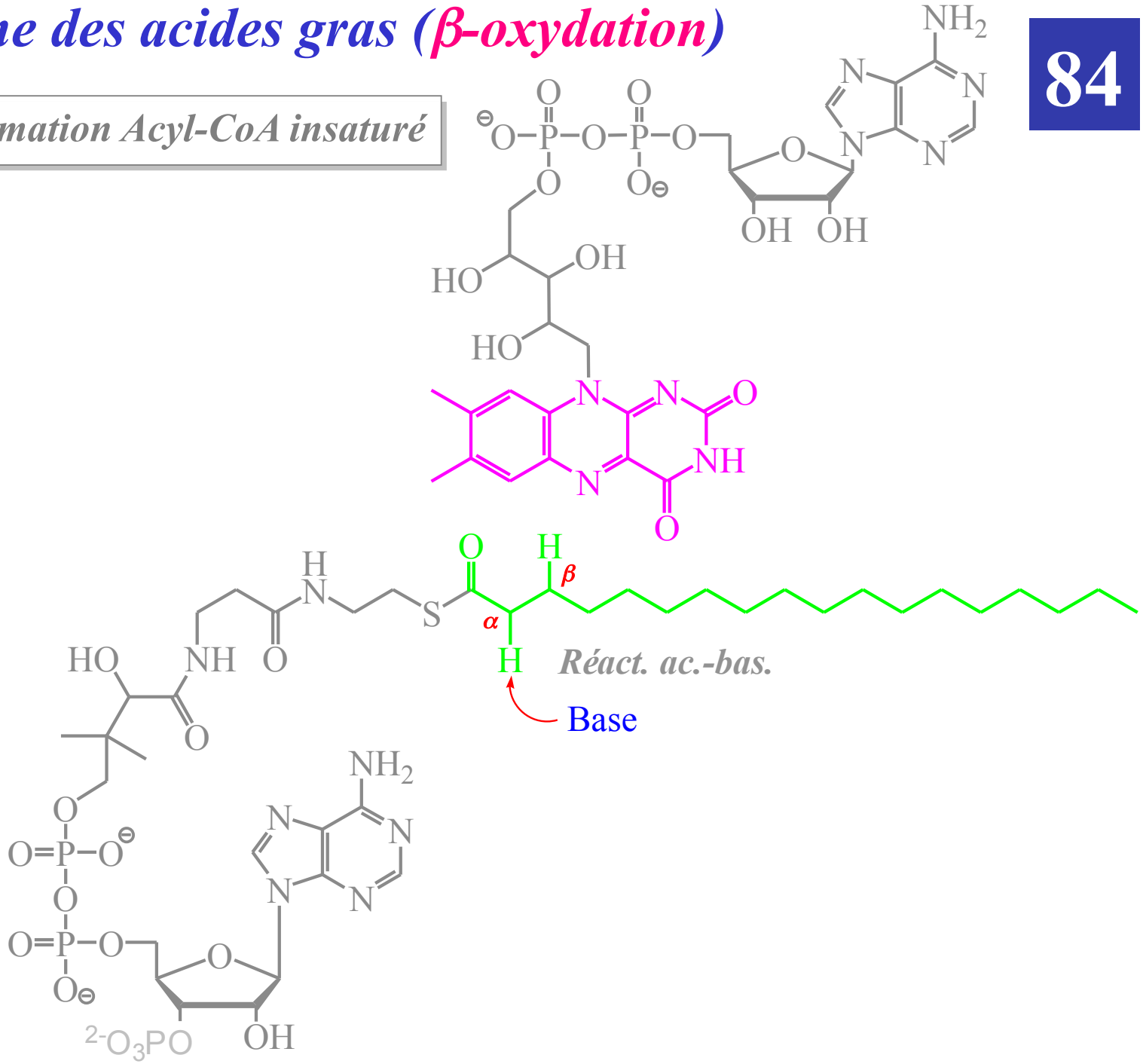
Acyl-CoA déshydrogénase :

Oxydation de la position α,β de l'acide gras par FAD



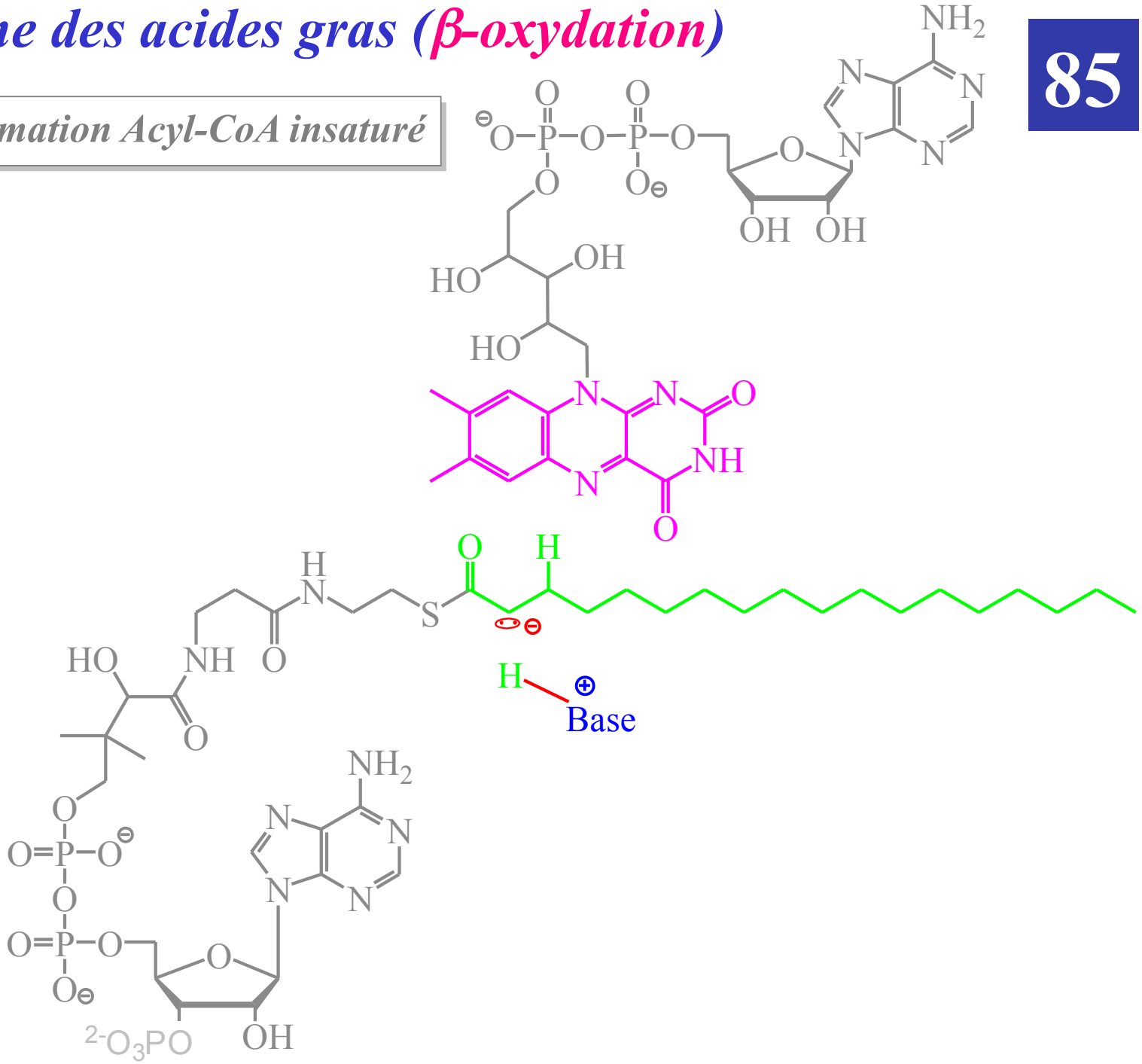
Catabolisme des acides gras (β-oxydation)

1ère Etape : Formation Acyl-CoA insaturé



Catabolisme des acides gras (β-oxydation)

1ère Etape : Formation Acyl-CoA insaturé



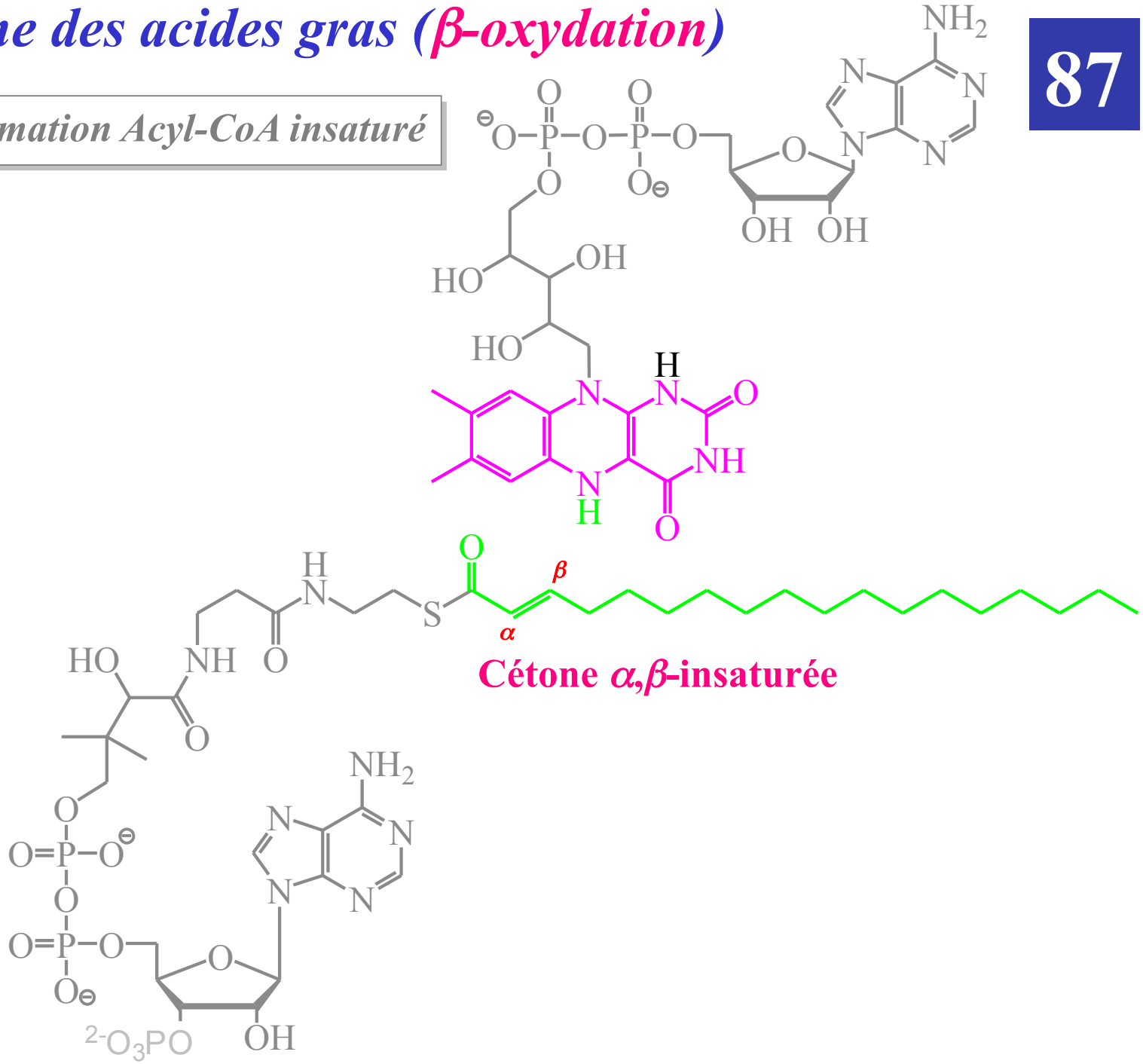
Catabolisme des acides gras (β-oxydation)

1ère Etape : Formation Acyl-CoA insaturé

Suite du mécanisme au tableau

Catabolisme des acides gras (β-oxydation)

1ère Etape : Formation Acyl-CoA insaturé

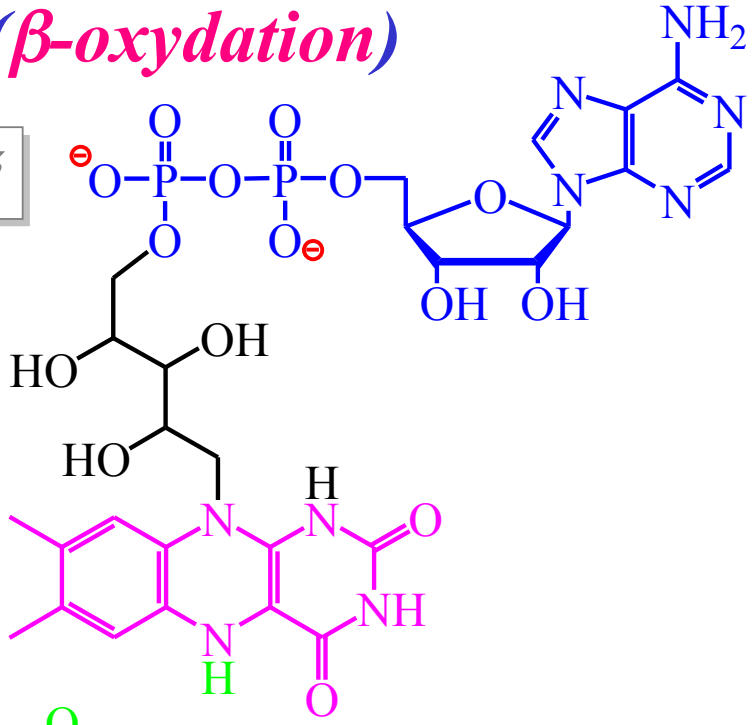


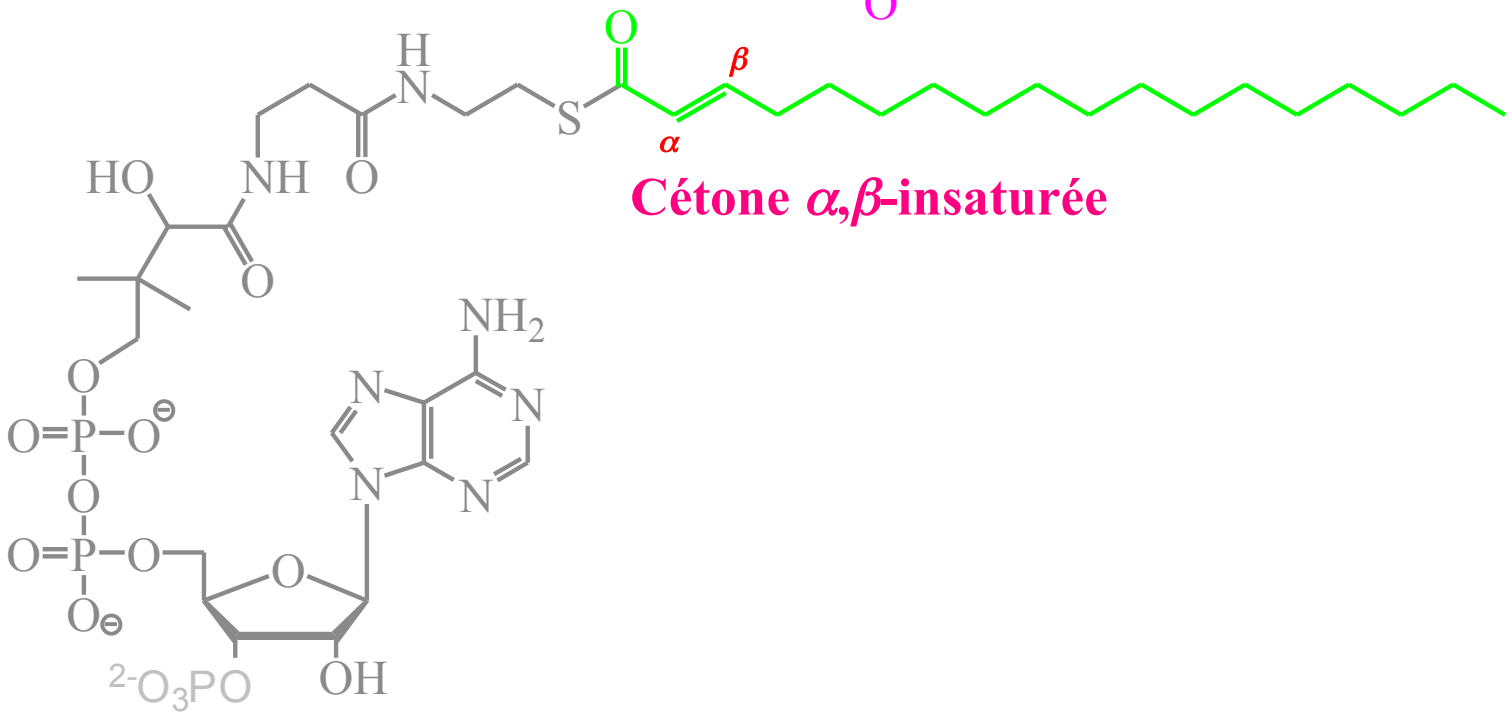
Cétone α,β-insaturée

Catabolisme des acides gras (β-oxydation)

1ère Etape : Formation Acyl-CoA insaturé

Flavine Adénine Dinucléotide **réduite** (FAD$\mathbf{H_2}$) :





Cétone α,β-insaturée

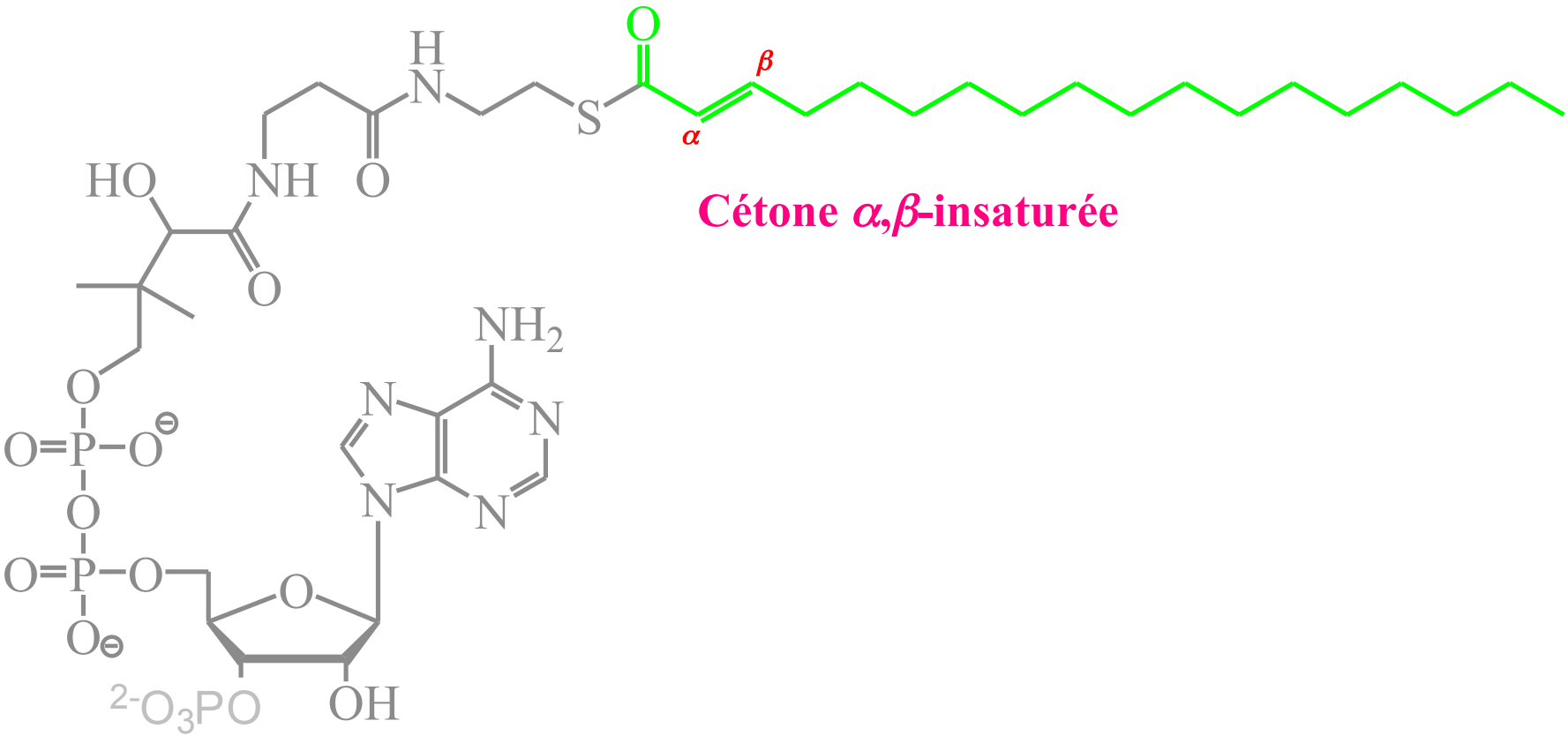
Catabolisme des acides gras (β-oxydation)

2ème Etape : Formation du β-Hydroxythioester

⇒ **Énoyl-coenzyme A hydratase**

Hydratation régiosélective (stéréosélective)

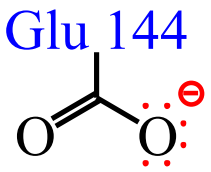
de l'oléfine en position α,β



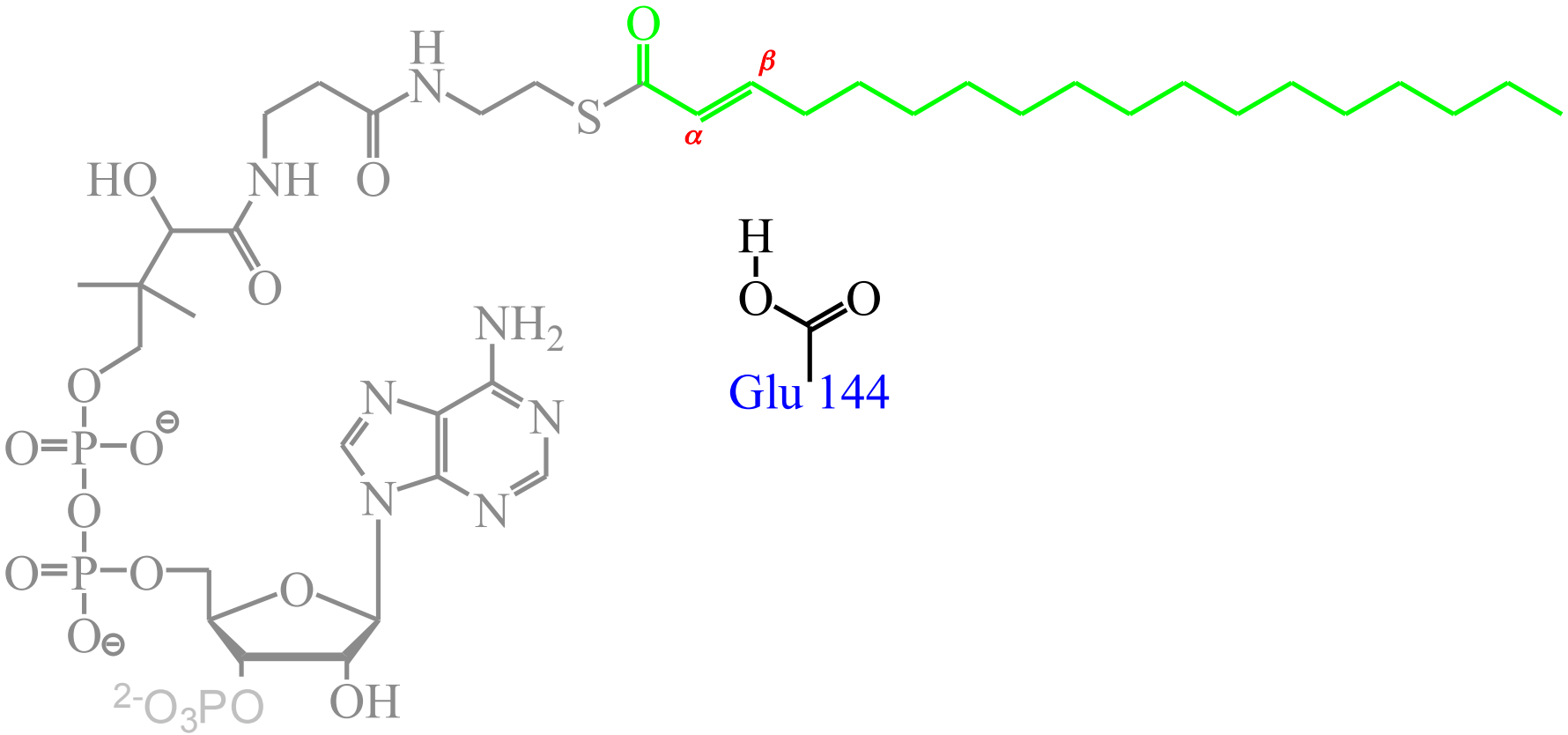
Cétone α,β-insaturée

Catabolisme des acides gras (β-oxydation)

2ème Etape : Formation du β-Hydroxythioester

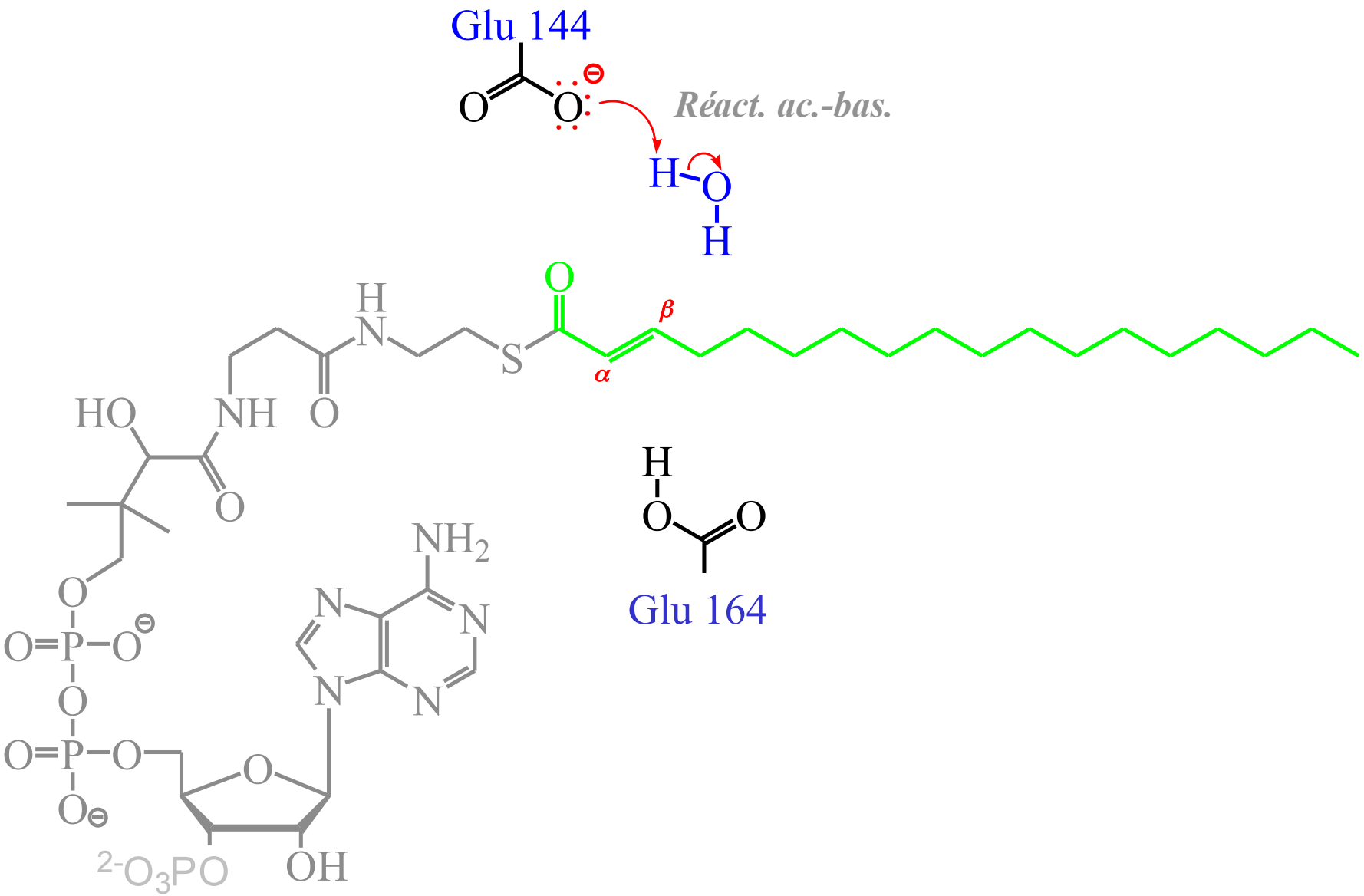


pK_a (Glu) ~ 4.2



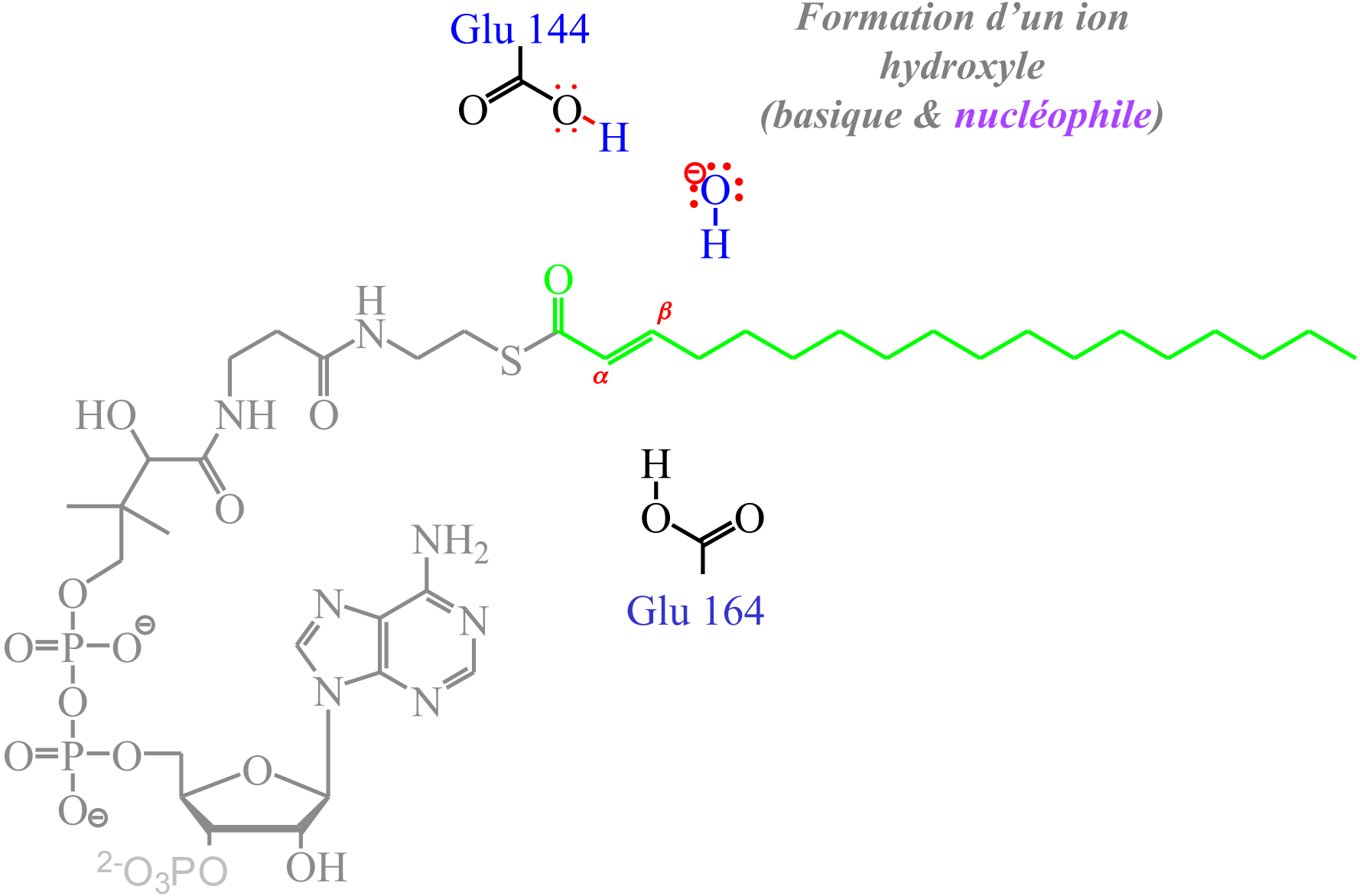
Catabolisme des acides gras (β-oxydation)

2ème Etape : Formation du β-Hydroxythioester

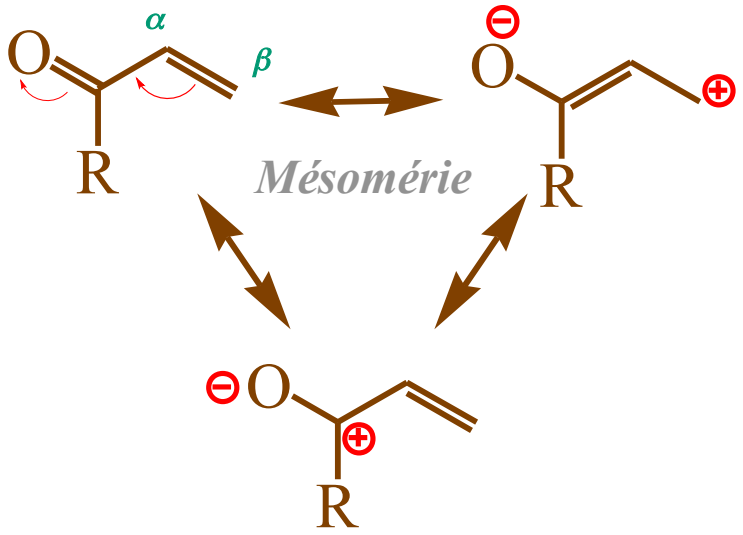


Catabolisme des acides gras (β-oxydation)

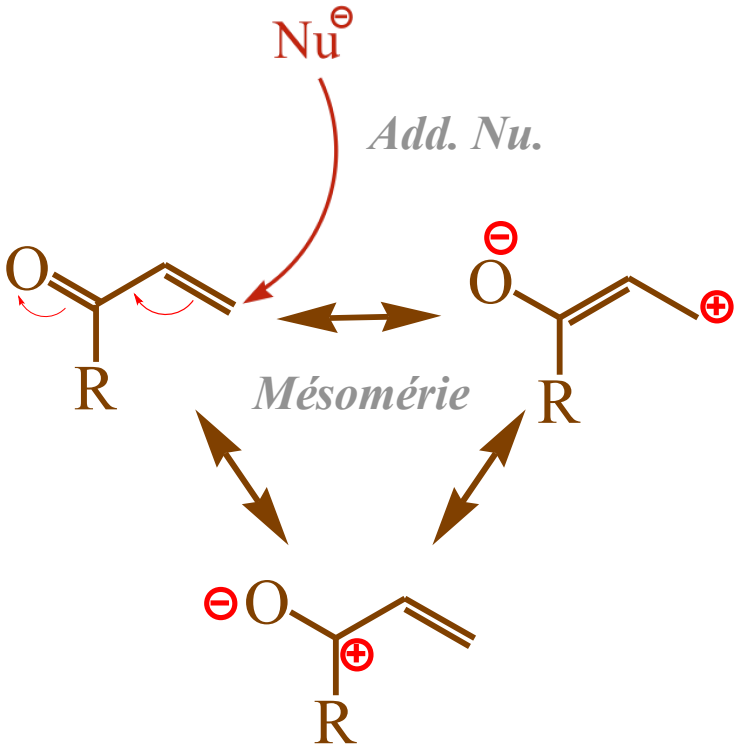
2ème Etape : Formation du β-Hydroxythioester



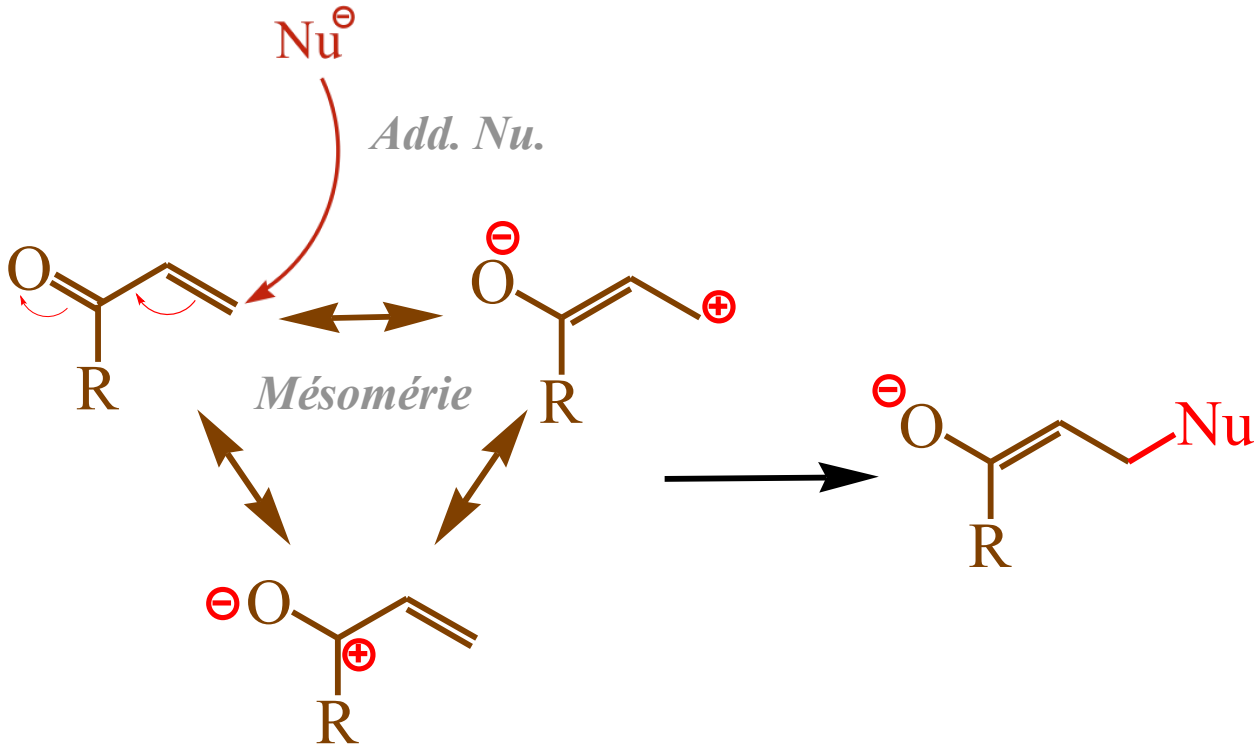
Addition de Michael



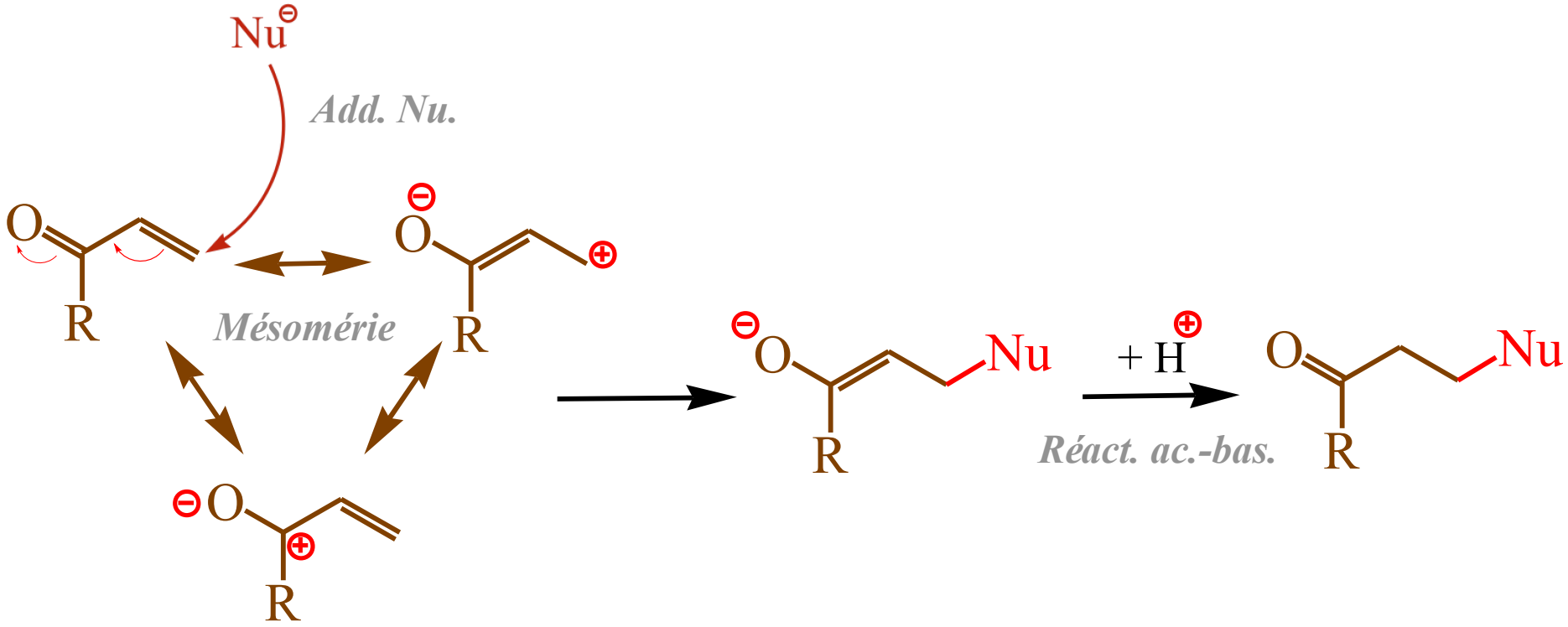
Addition de Michael



Addition de Michael

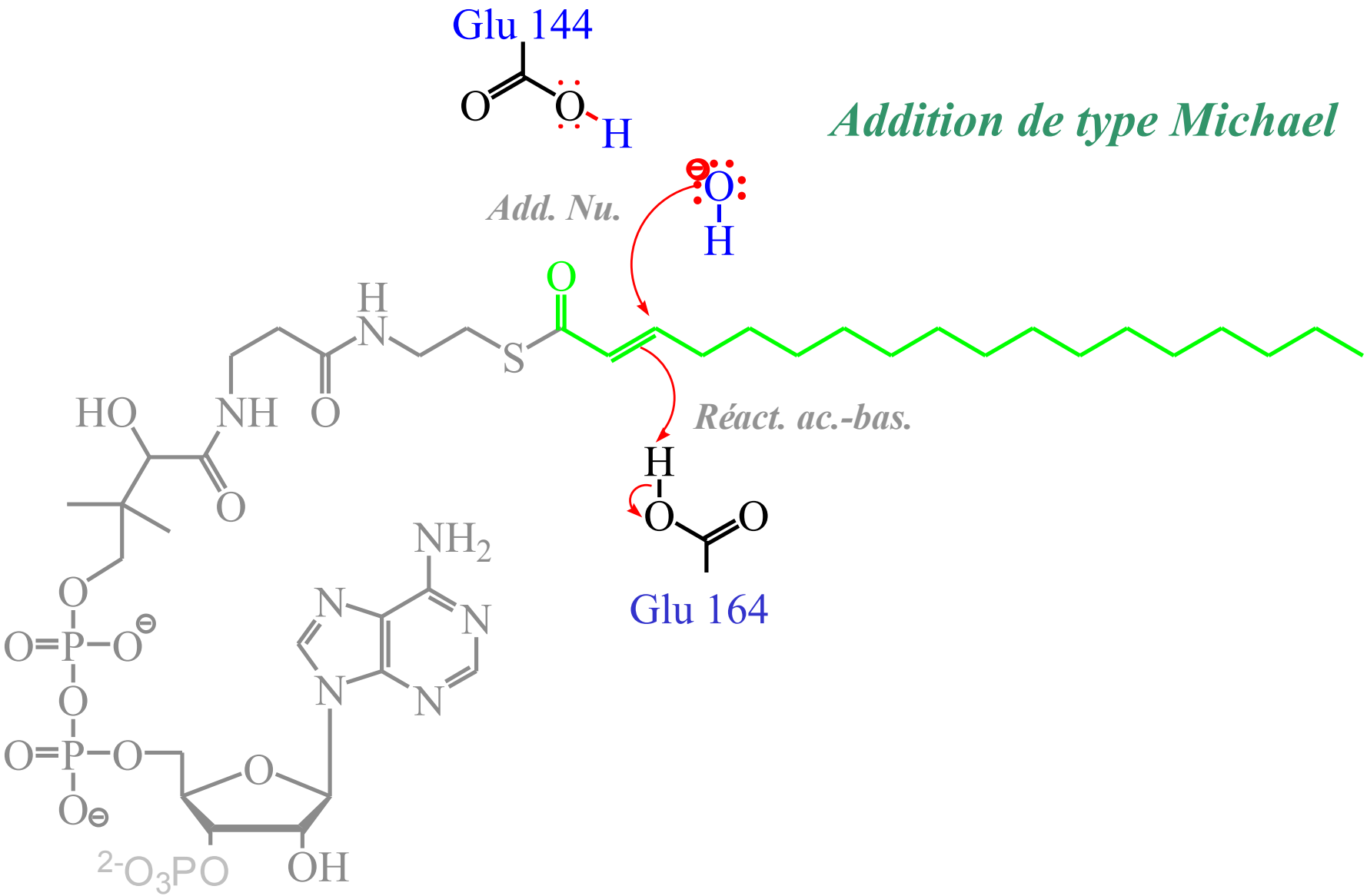


Addition de Michael



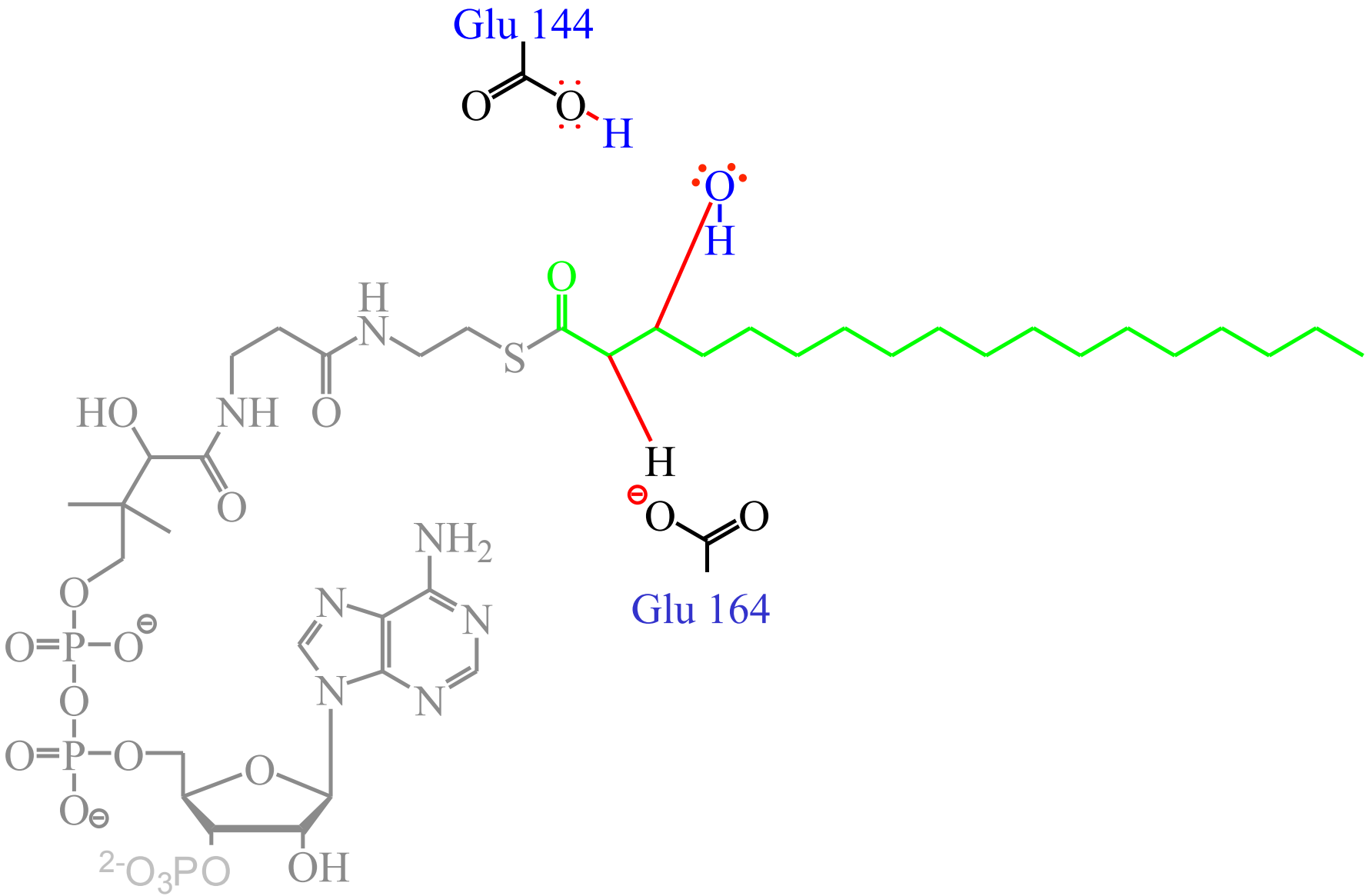
Catabolisme des acides gras (β-oxydation)

2ème Etape : Formation du β-Hydroxythioester



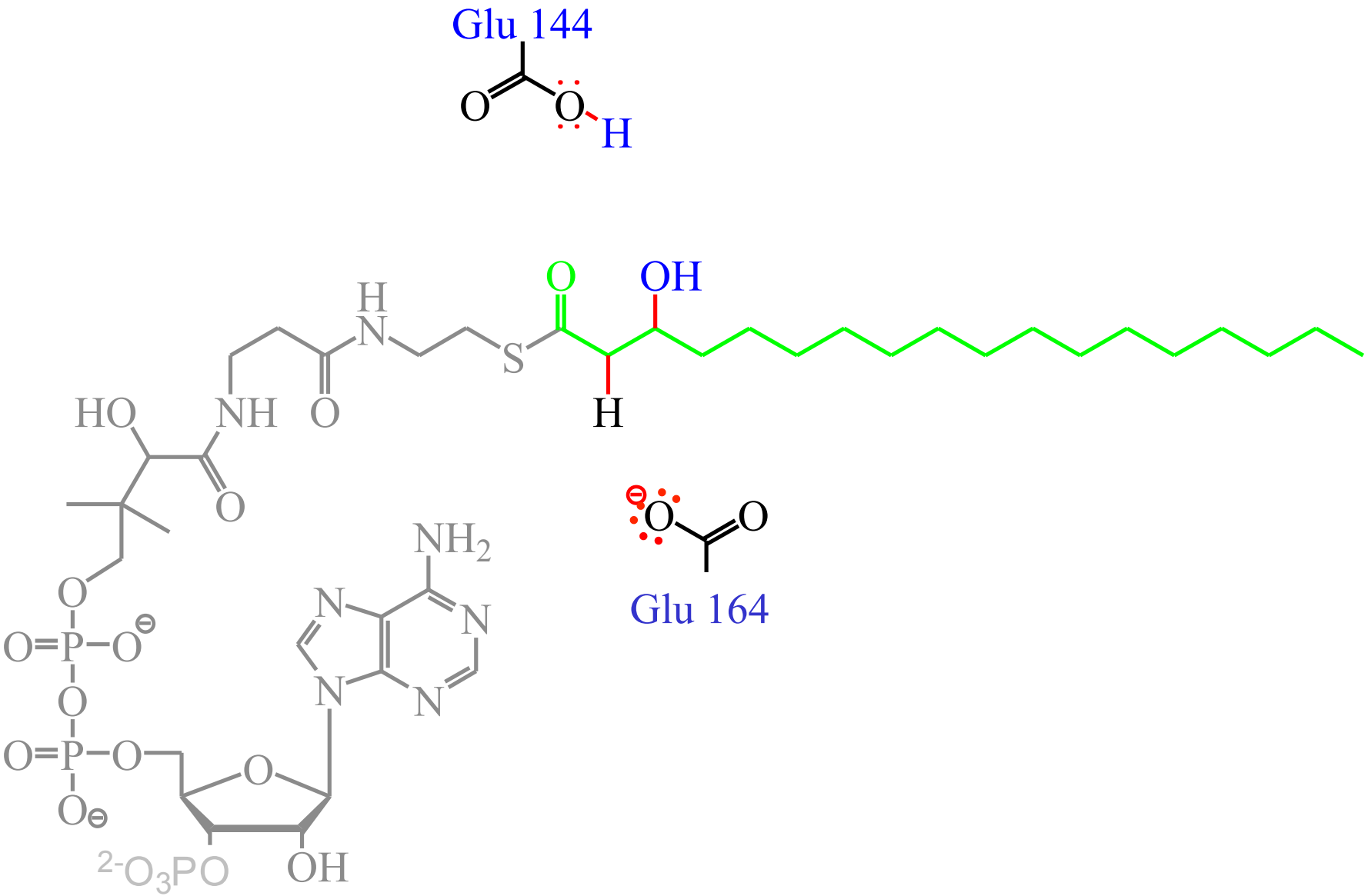
Catabolisme des acides gras (β-oxydation)

2ème Etape : Formation du β-Hydroxythioester



Catabolisme des acides gras (β-oxydation)

2ème Etape : Formation du β-Hydroxythioester



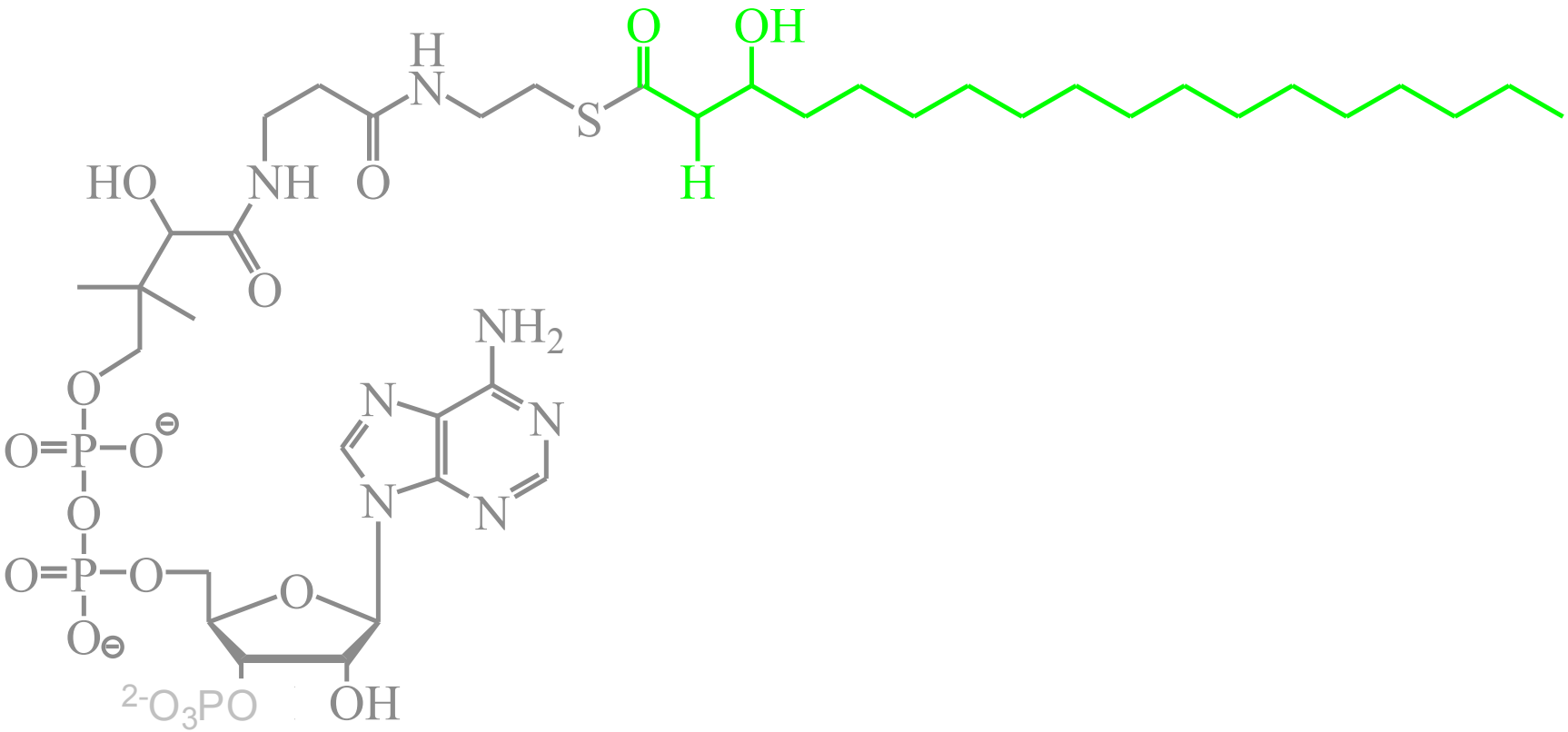
Catabolisme des acides gras (β-oxydation)

3ème Etape : Formation du 3-cétoacyl-CoA

⇒ **Hydroxyacyl-CoA déshydrogénase**

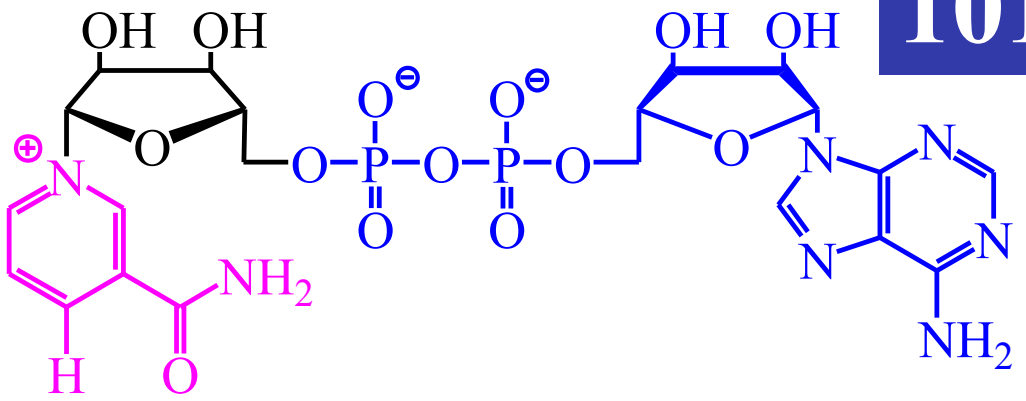
Oxydation de l'alcool secondaire

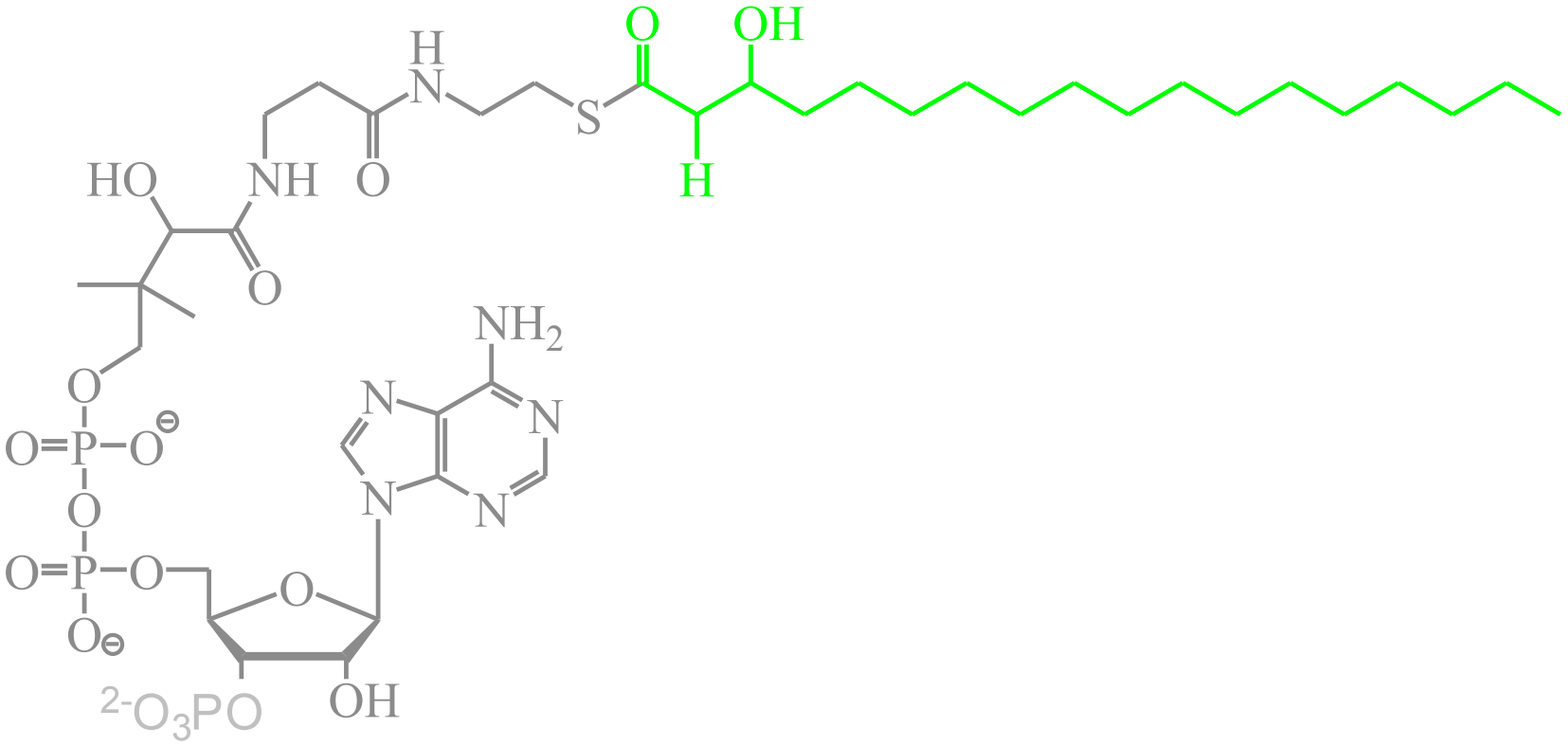
en cétone par NAD^+



3ème Etape : Formation du 3-cétoacyl-CoA

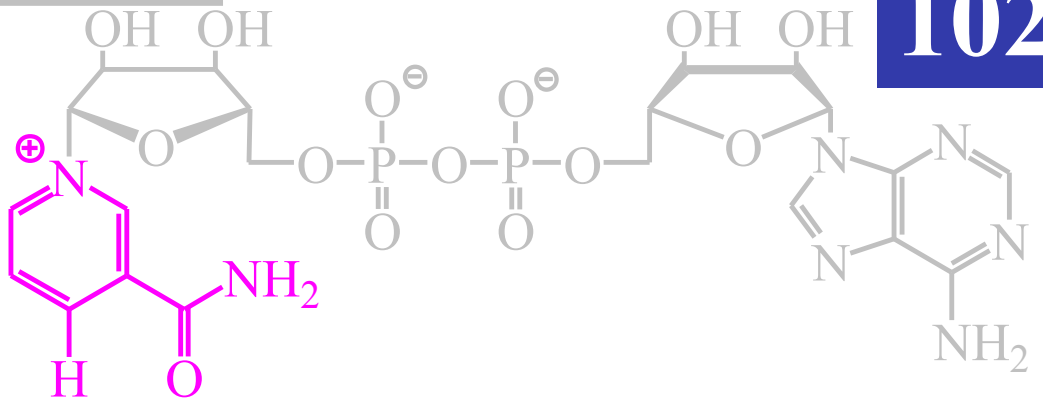
Nicotinamide Adénine Dinucléotide (NAD^+) :

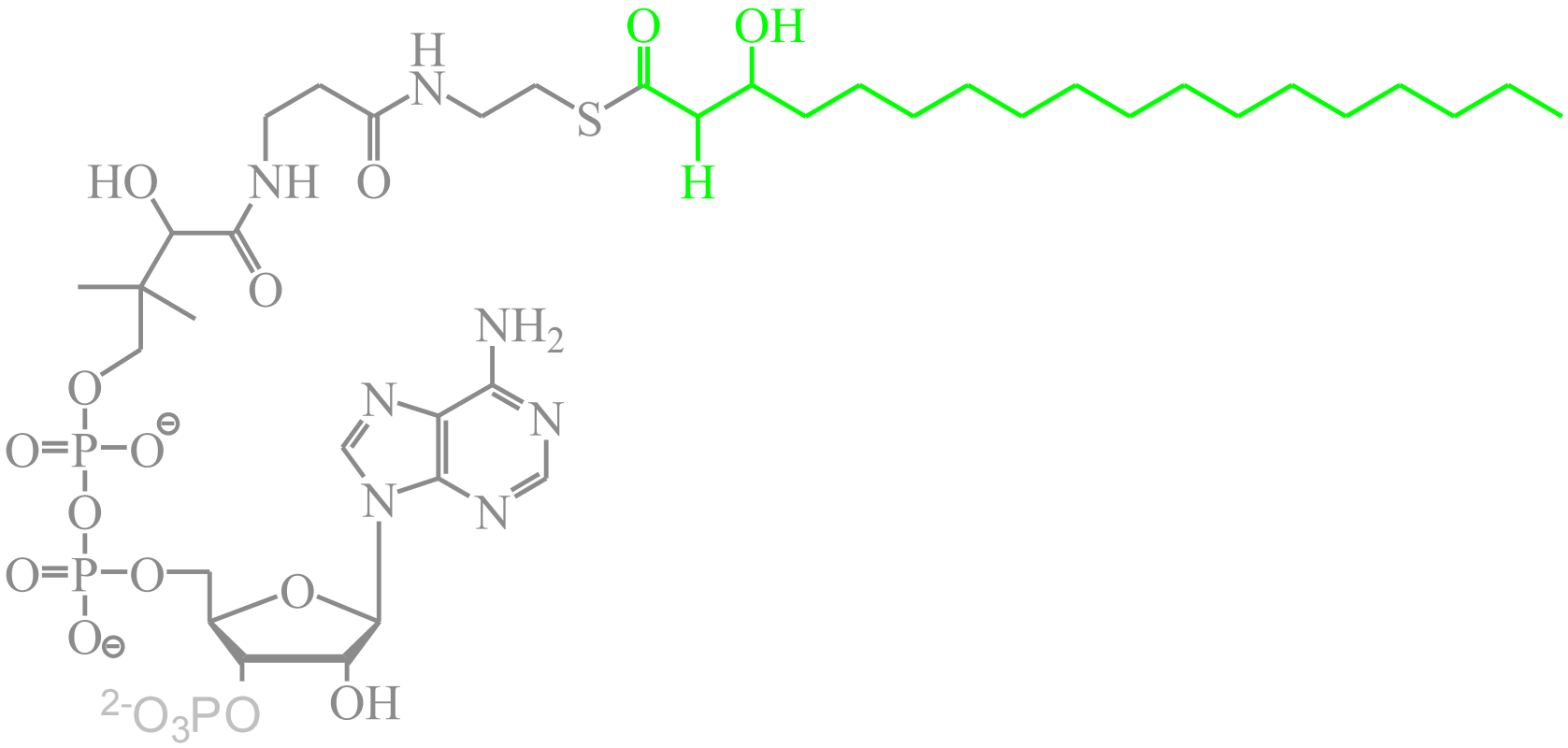




3ème Etape : Formation du 3-cétoacyl-CoA

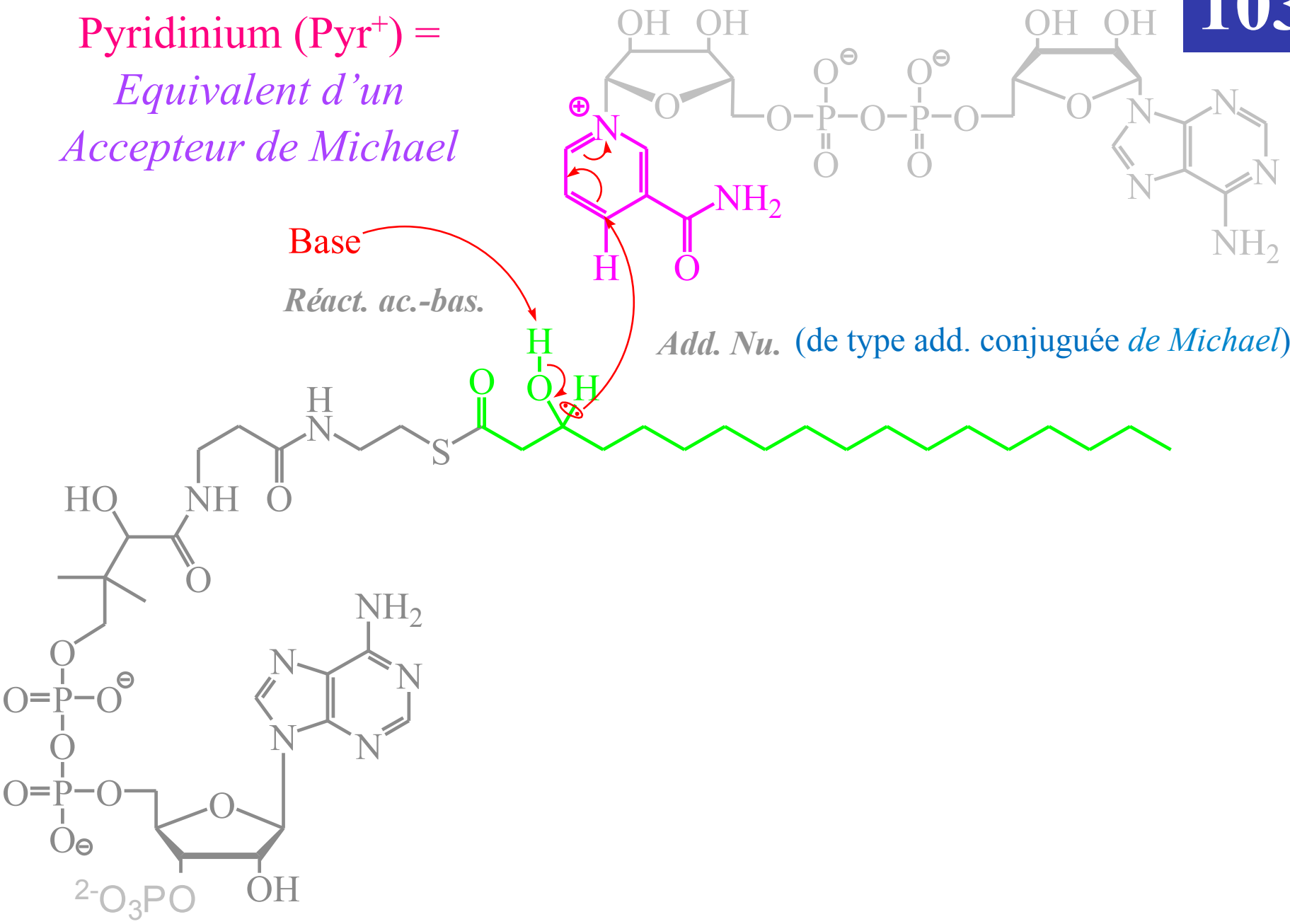
Focus sur la partie nicotinamide (~ *Pyridinium*) :





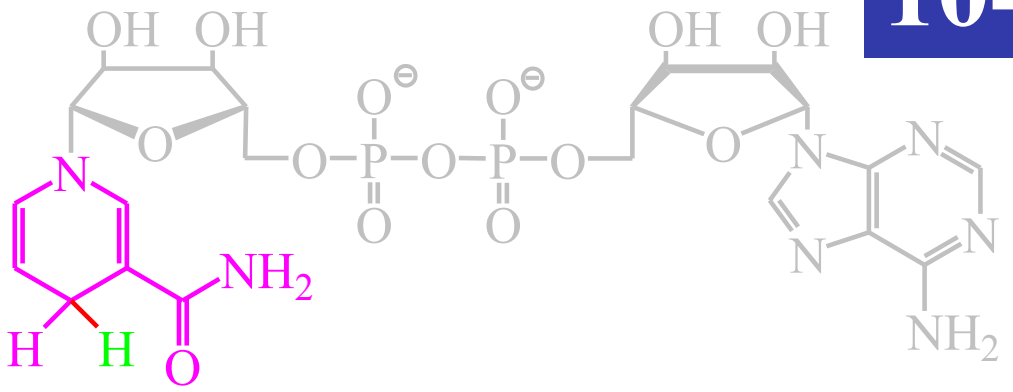
3ème Etape : Formation du 3-cétoacyl-CoA

Pyridinium (Pyr^+) =
Equivalent d'un
Accepteur de Michael

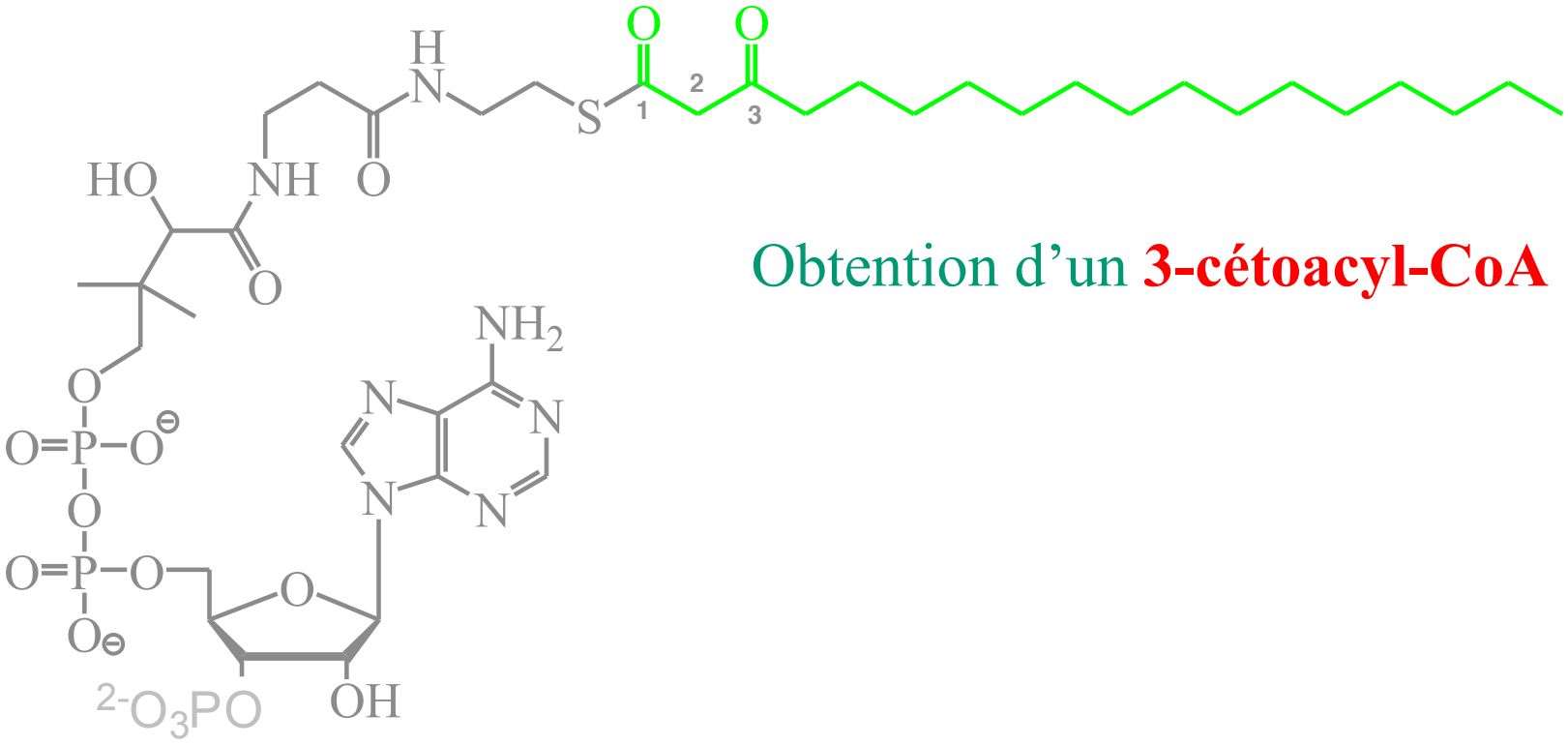


3ème Etape : Formation du 3-cétoacyl-CoA

Nicotinamide Adénine Dinucléotide **réduit** (NAD**H**) :



Base⊕–H



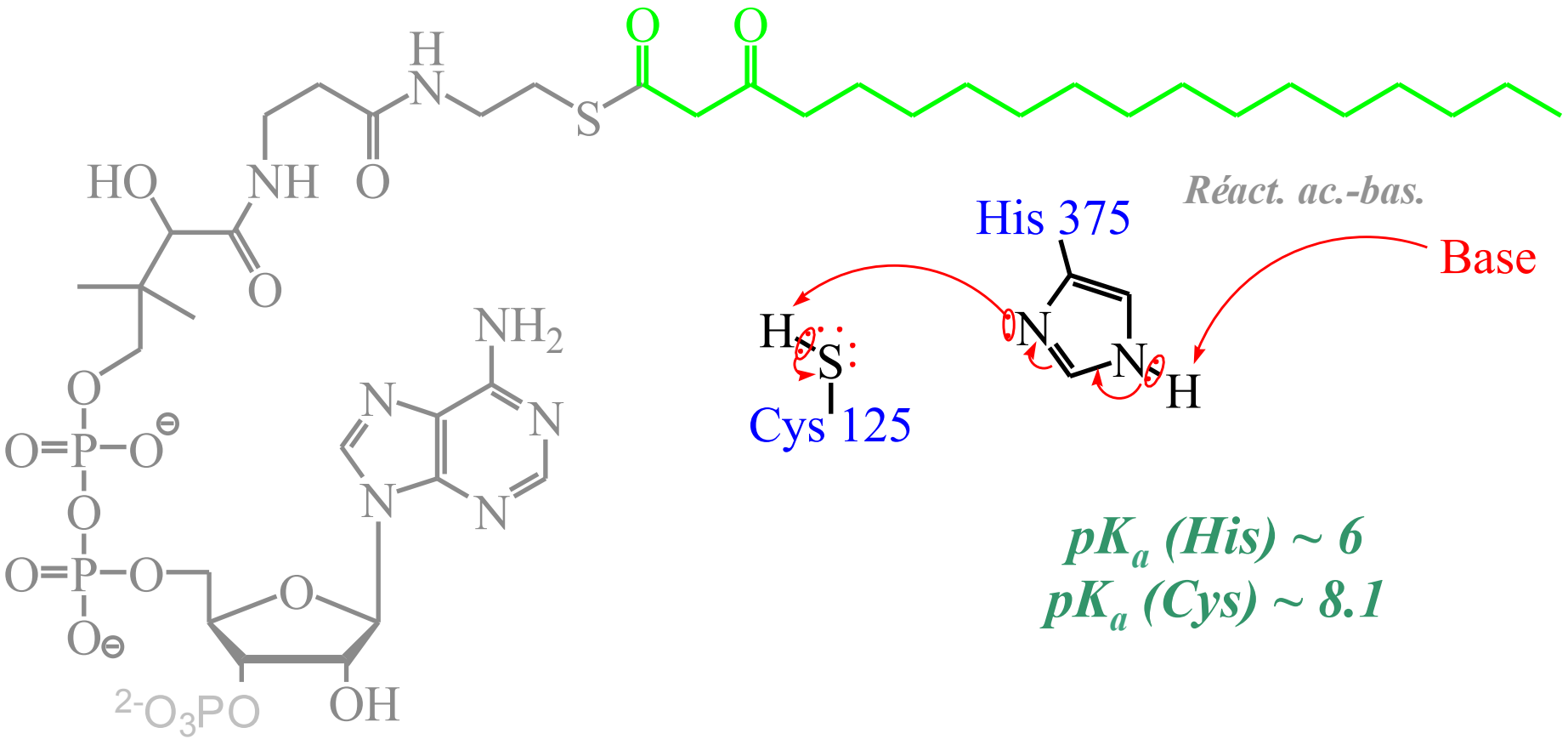
Obtention d'un **3-cétoacyl-CoA**

Catabolisme des acides gras (β-oxydation)

4ème Etape : Libération d'Acétyl-CoA

⇒ **Thiolyse catalysée par la β-cétoacyl-CoA thiolase (acétyl-CoA acyltransférase)**

Addition nucléophile d'un thiolate sur le carbonyle du 3-cétoacyl-CoA

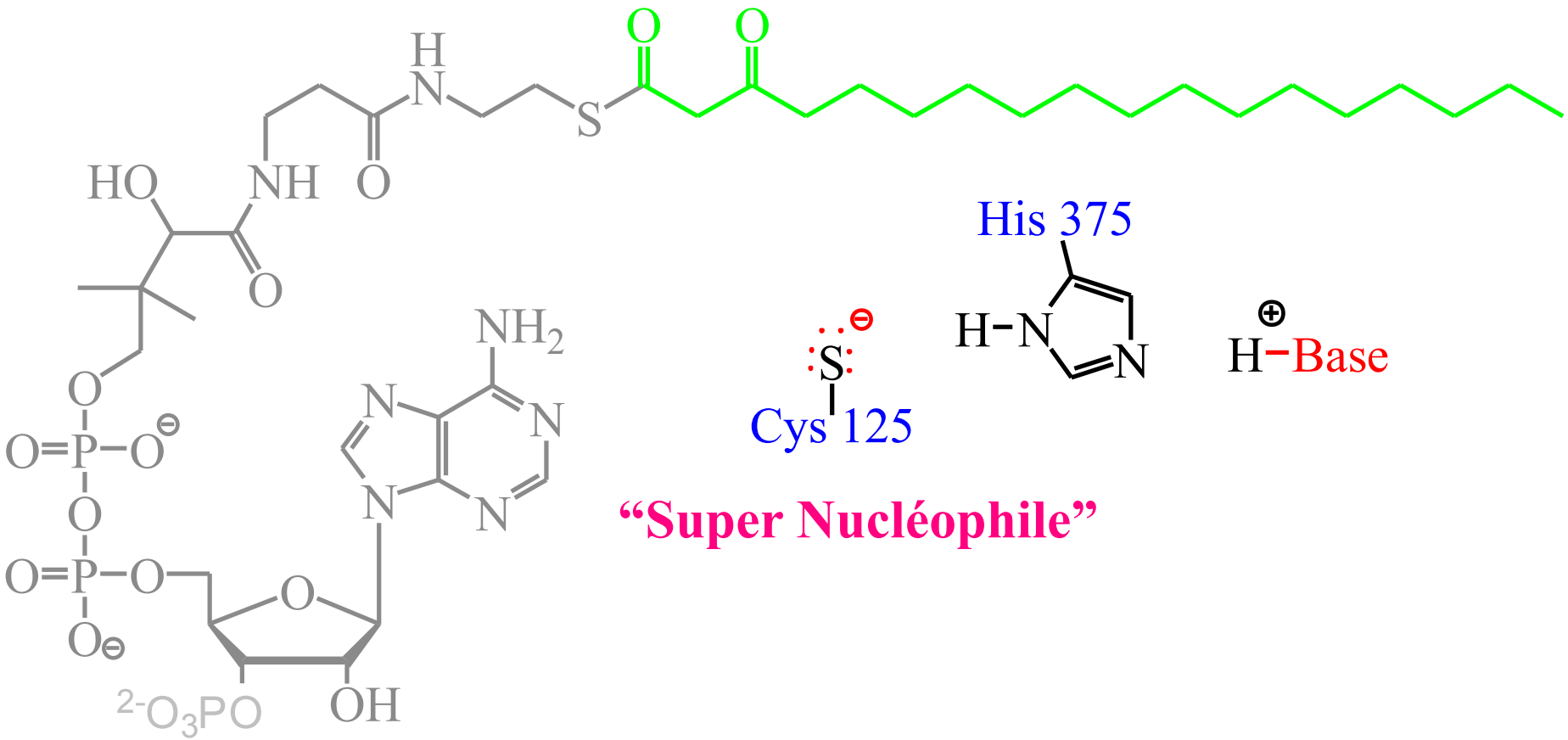


pK_a *(His) ~ 6*

pK_a *(Cys) ~ 8.1*

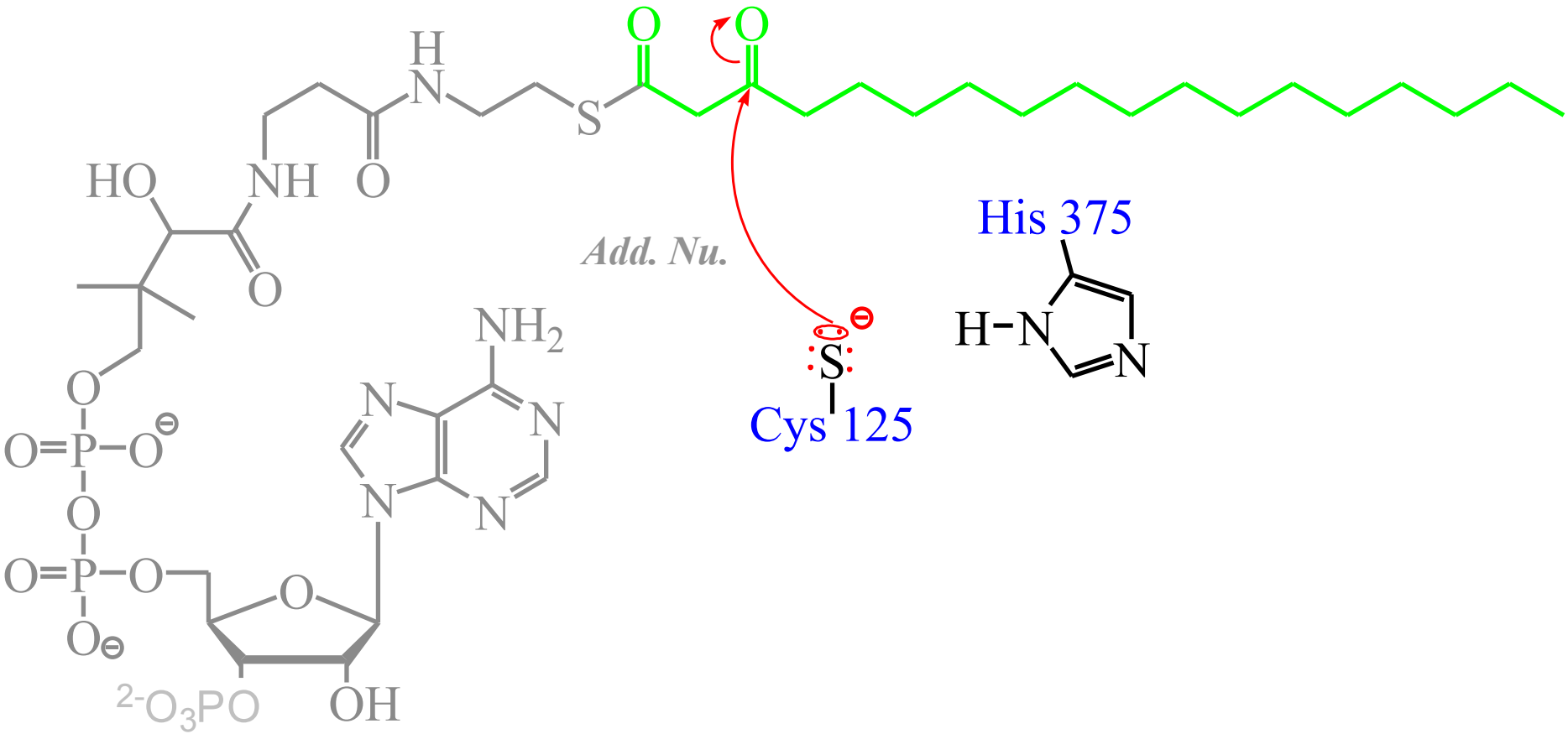
Catabolisme des acides gras (β-oxydation)

4ème Etape : Libération d'Acétyl-CoA



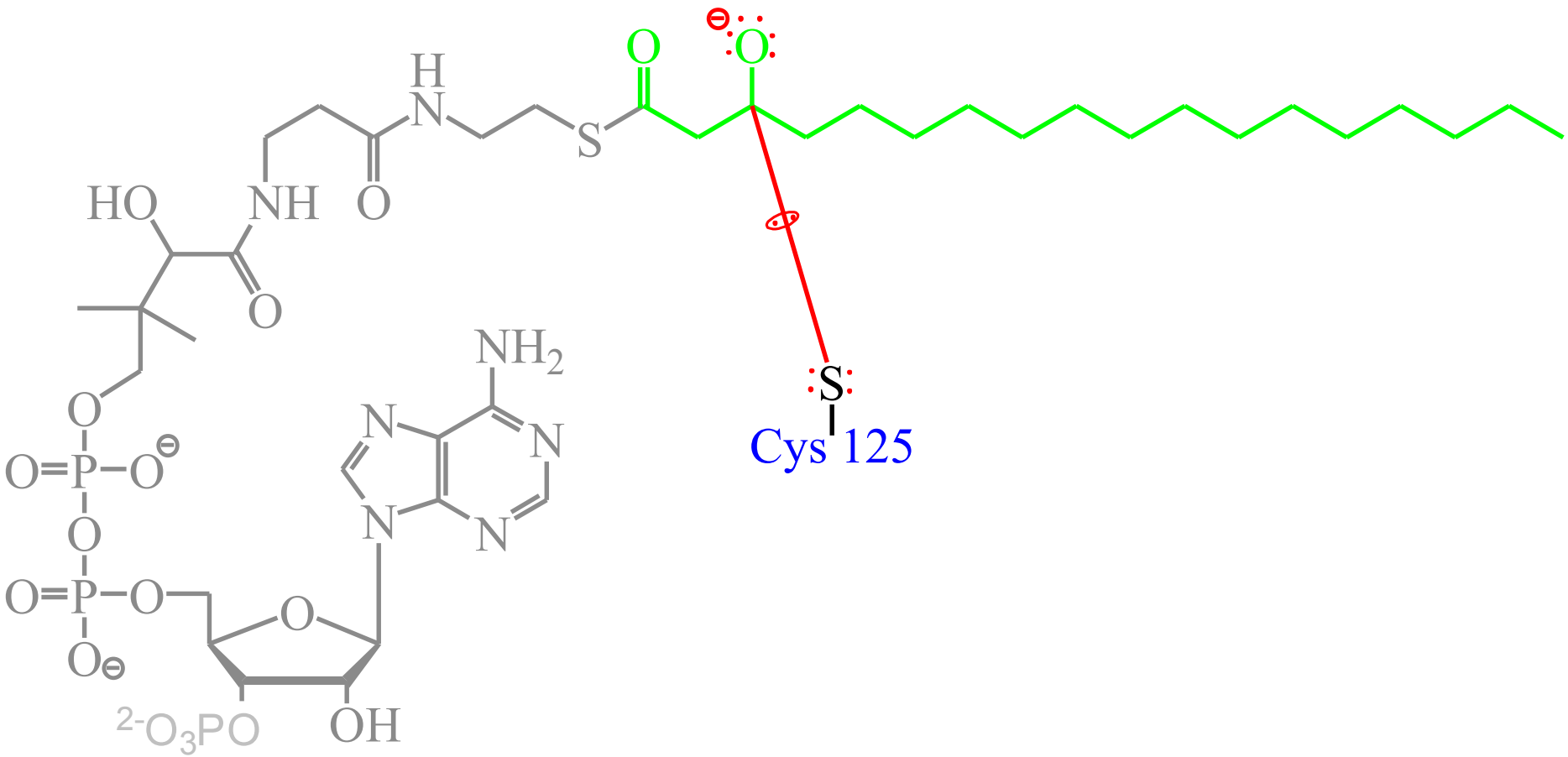
Catabolisme des acides gras (β-oxydation)

4ème Etape : Libération d'Acétyl-CoA



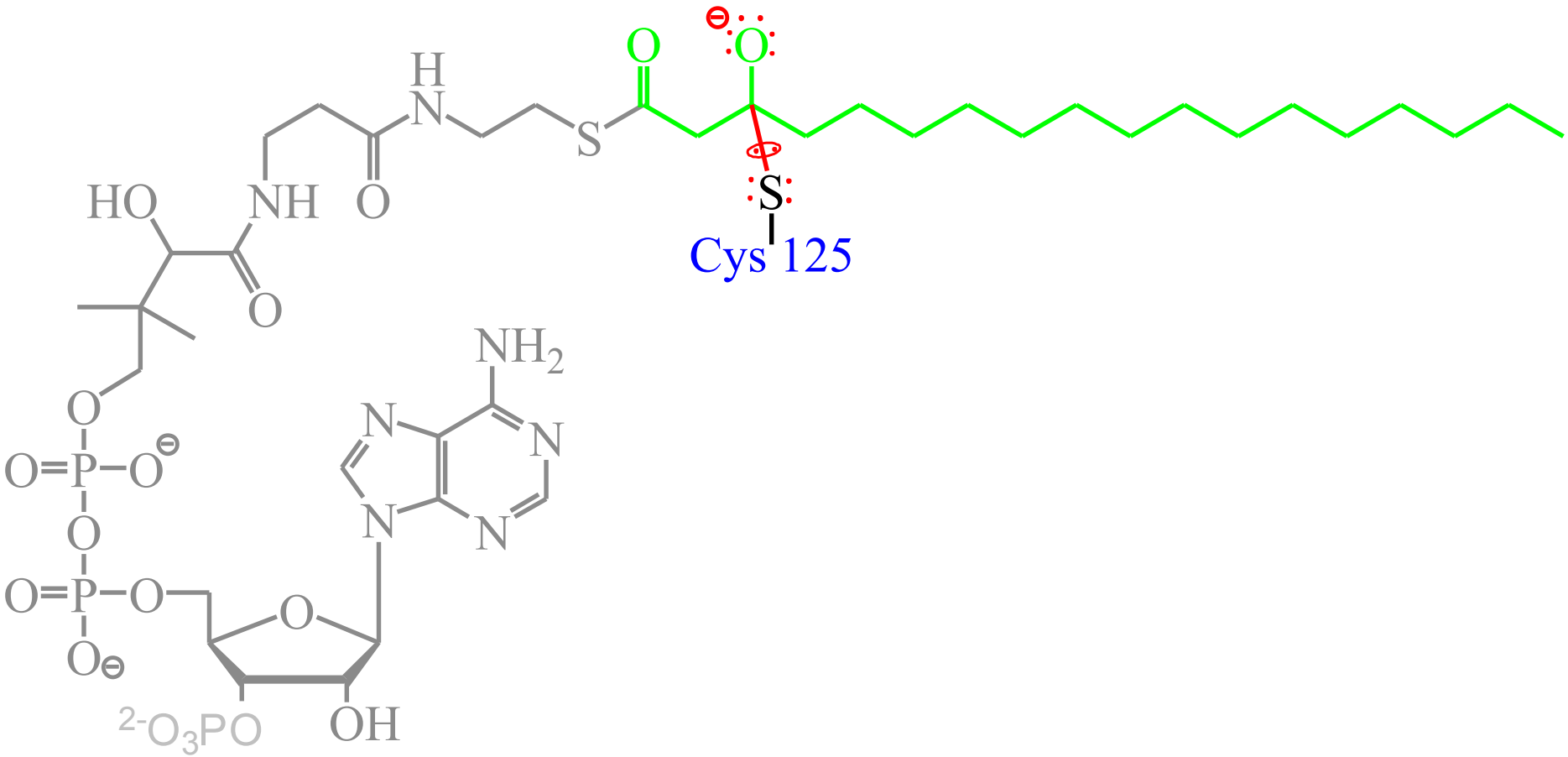
Catabolisme des acides gras (β-oxydation)

4ème Etape : Libération d'Acétyl-CoA



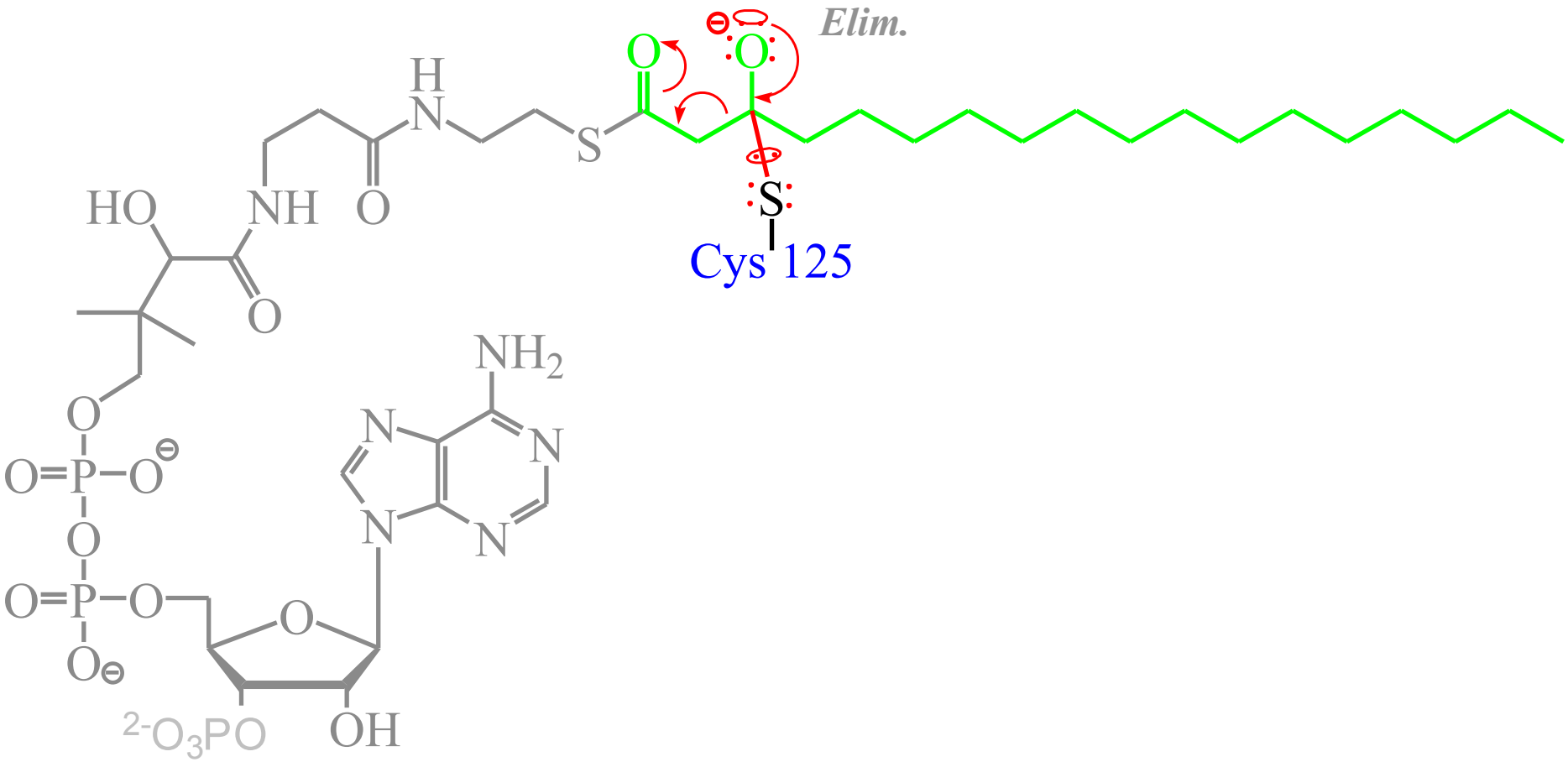
Catabolisme des acides gras (β-oxydation)

4ème Etape : Libération d'Acétyl-CoA



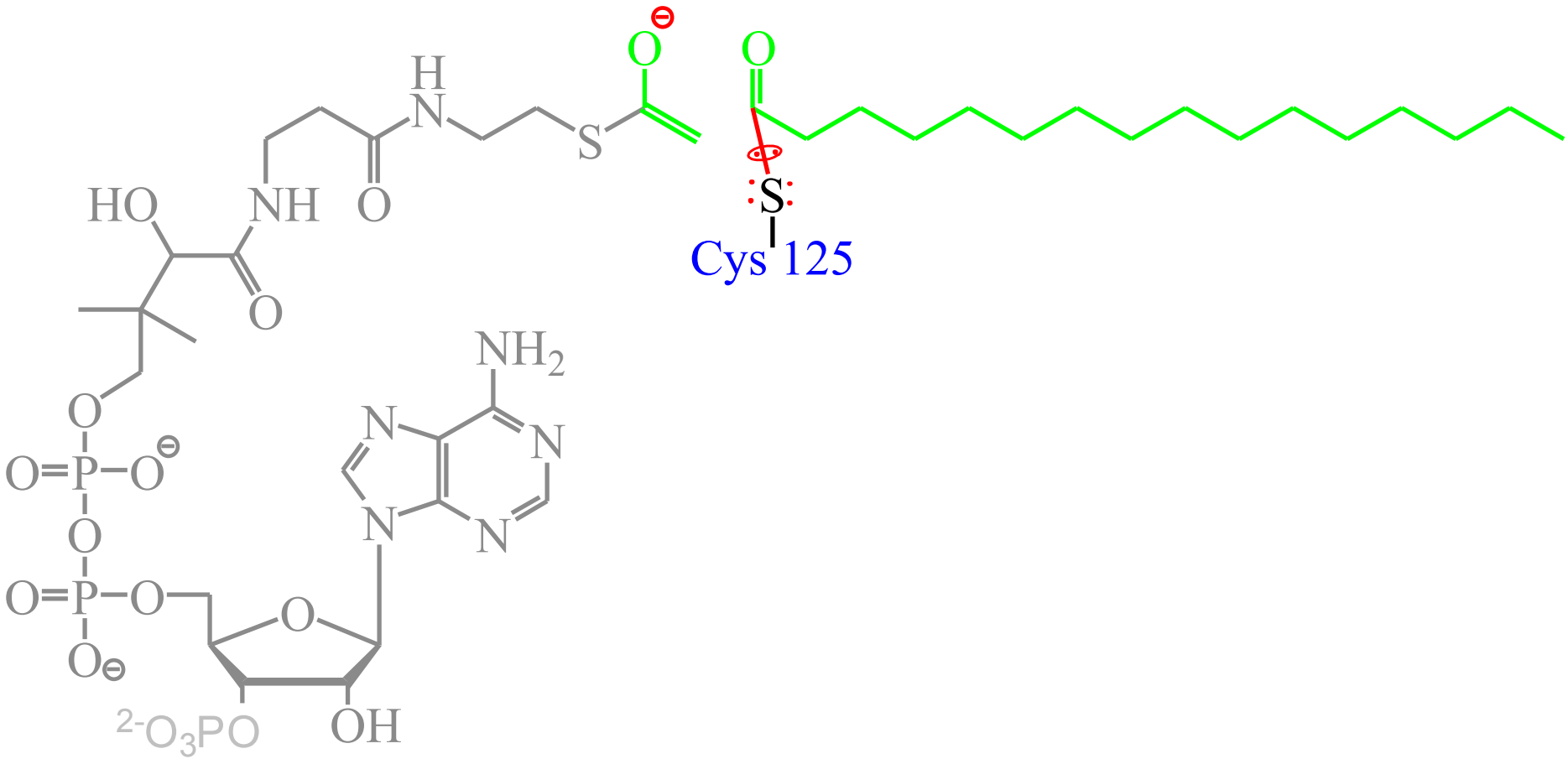
Catabolisme des acides gras (β-oxydation)

4ème Etape : Libération d'Acétyl-CoA



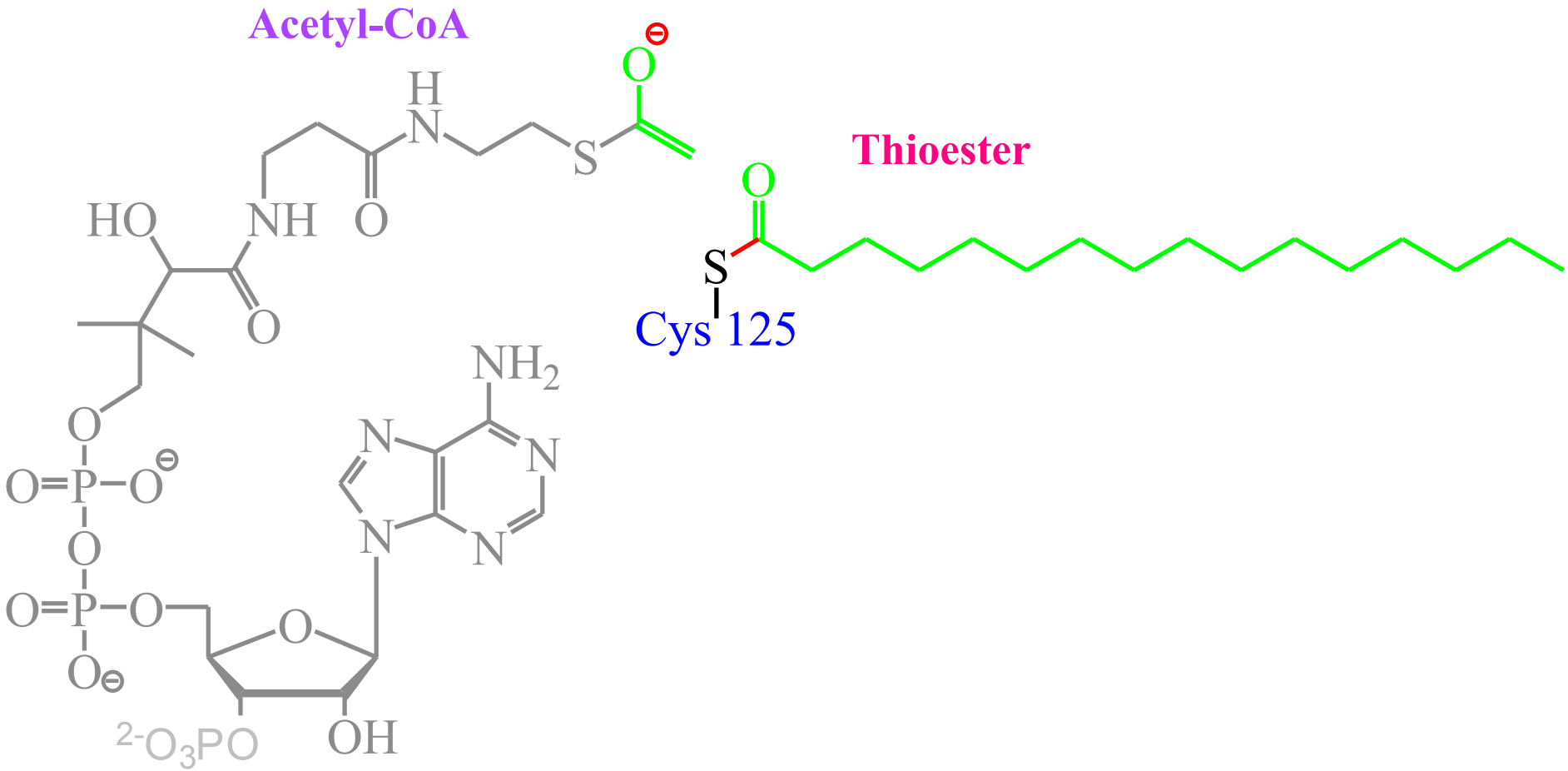
Catabolisme des acides gras (β-oxydation)

4ème Etape : Libération d'Acétyl-CoA



Catabolisme des acides gras (β-oxydation)

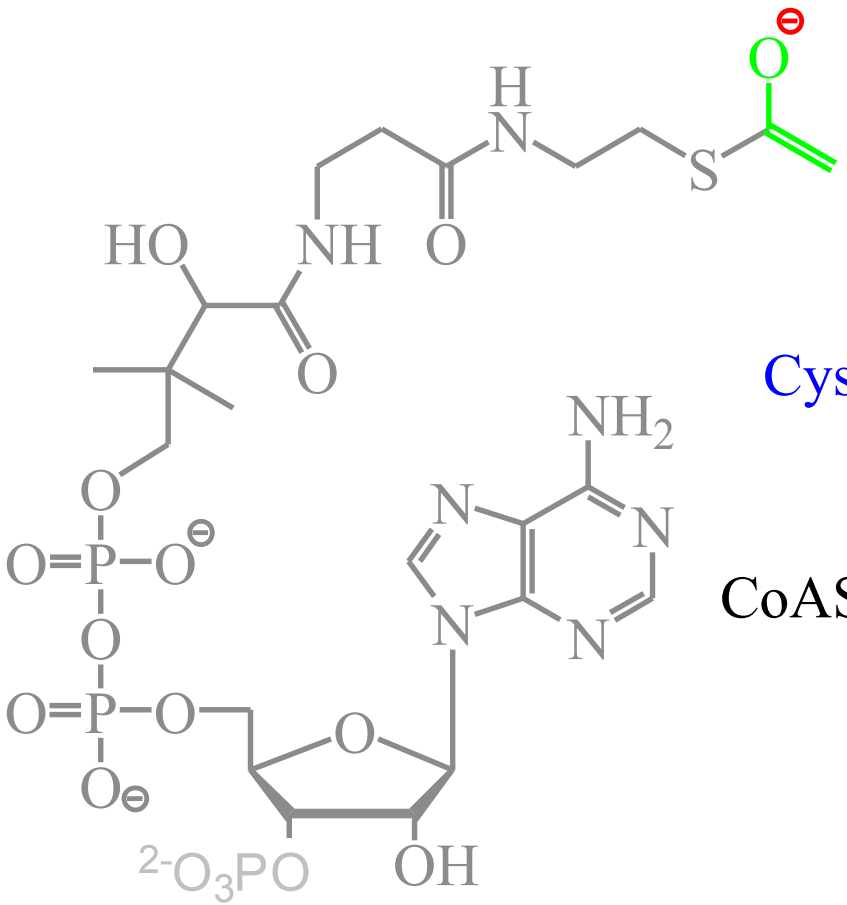
4ème Etape : Libération d'Acétyl-CoA

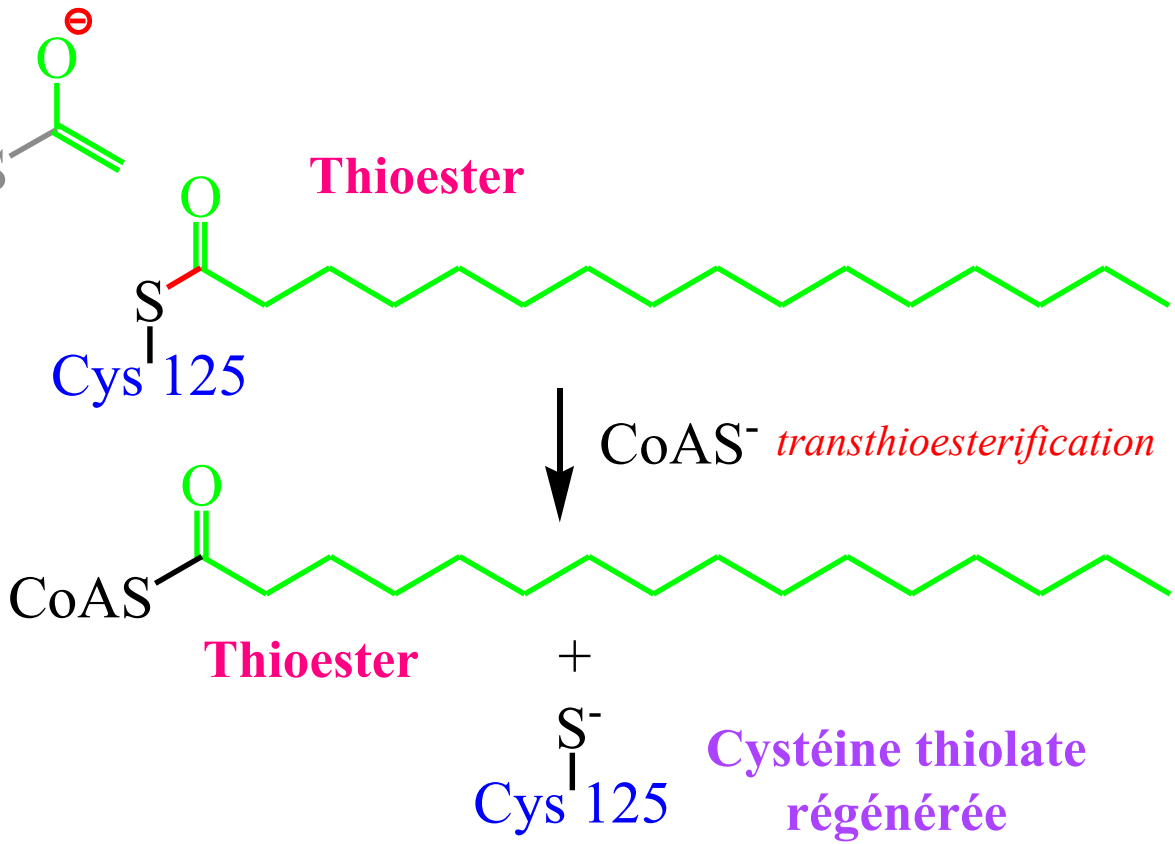


Catabolisme des acides gras (β-oxydation)

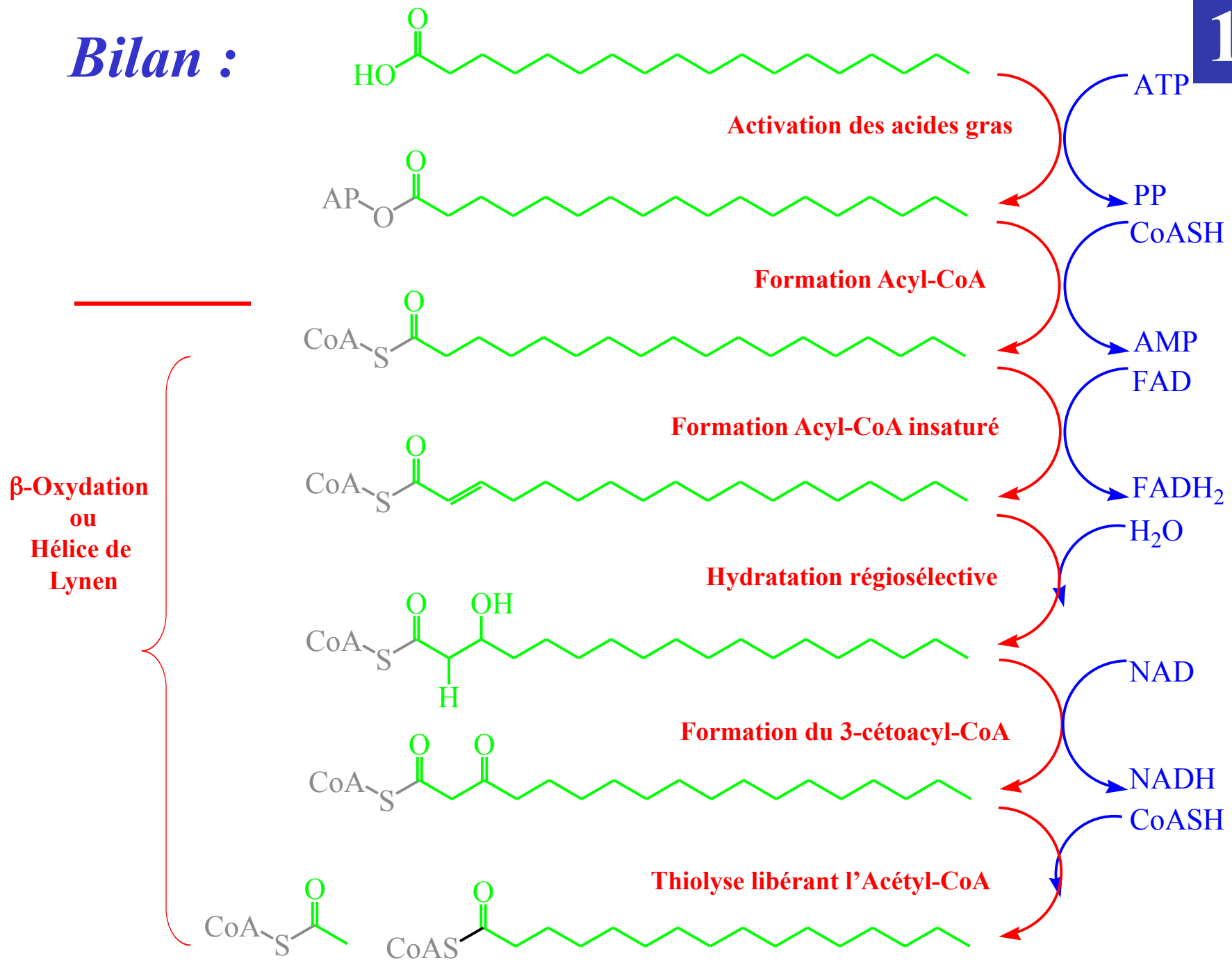
5ème Etape : Libération d'un Acyl-CoA à (n-2) carbones

mécanisme au tableau

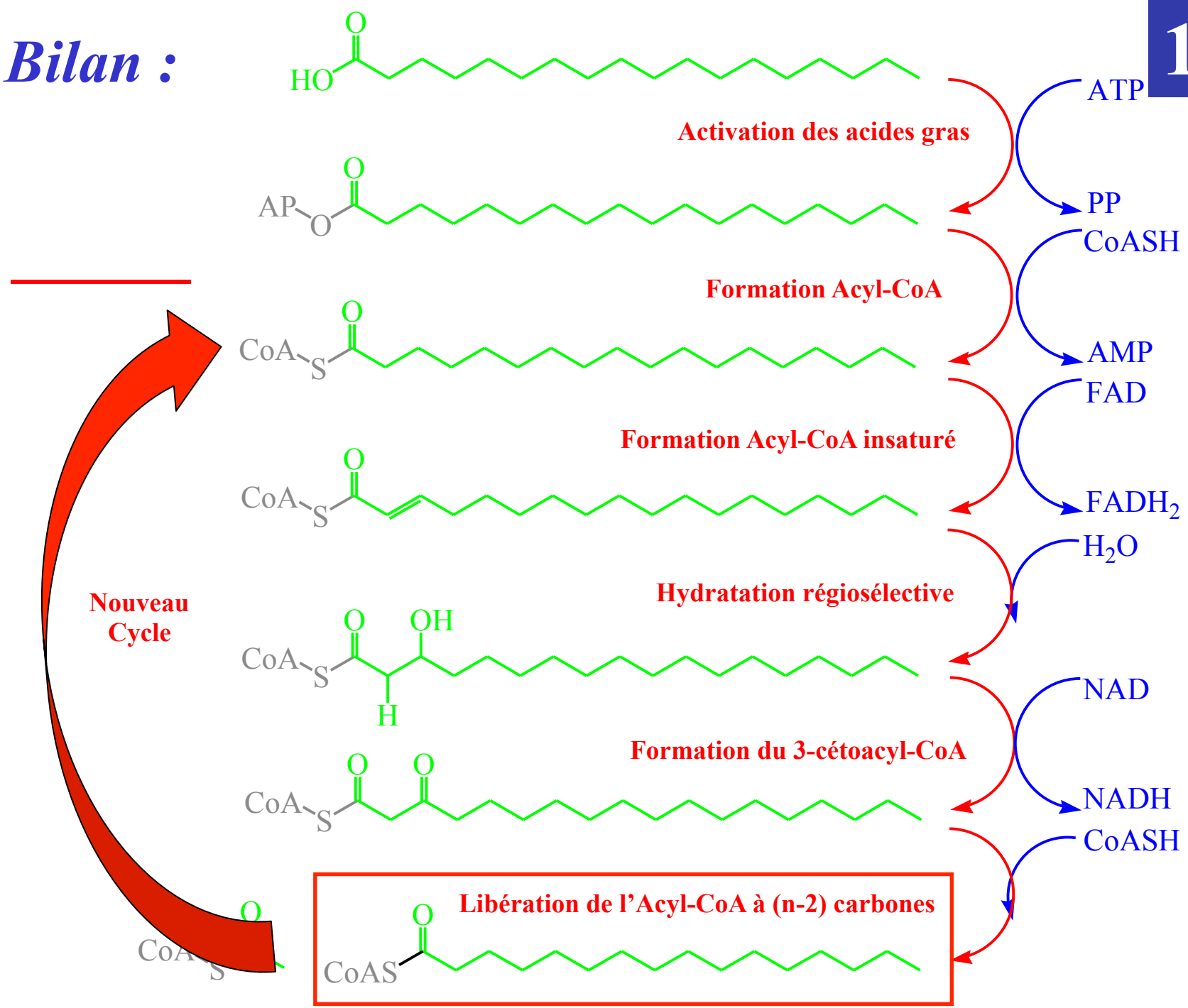




Bilan :


HO
O
Activation des acides gras
ATP
PP
AP
O
Formation Acyl-CoA
CoASH
AMP
CoA
S
Formation Acyl-CoA insaturé
FAD
FADH2
Hydratation régiosélective
H2O
OH
H
Formation du 3-cétoacyl-CoA
NAD
NADH
Thiolyse libérant l'Acétyl-CoA
CoASH
CoAS
β-Oxydation
ou
Hélice de
Lynen

Bilan :


HO
O
Activation des acides gras
ATP
PP
AP
O
Formation Acyl-CoA
CoASH
AMP
CoA
S
FAD
Formation Acyl-CoA insaturé
FADH2
H2O
Hydratation régiosélective
OH
H
NAD
Formation du 3-cétoacyl-CoA
NADH
CoASH
Libération de l'Acyl-CoA à (n-2) carbones
CoAS
Nouveau
Cycle