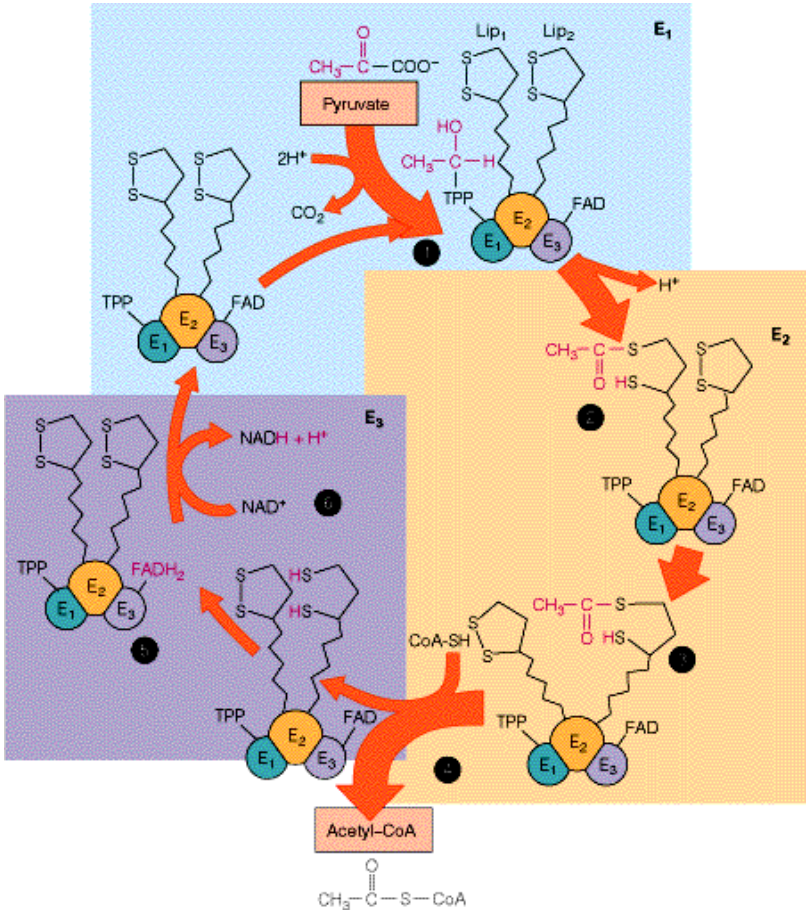
Tema 7: Algunos mecanismos de enzimas transportadoras de grupos.



Complejo de la Piruvato Deshidrogenasa (PDH)

Vitamina B1: tiamina

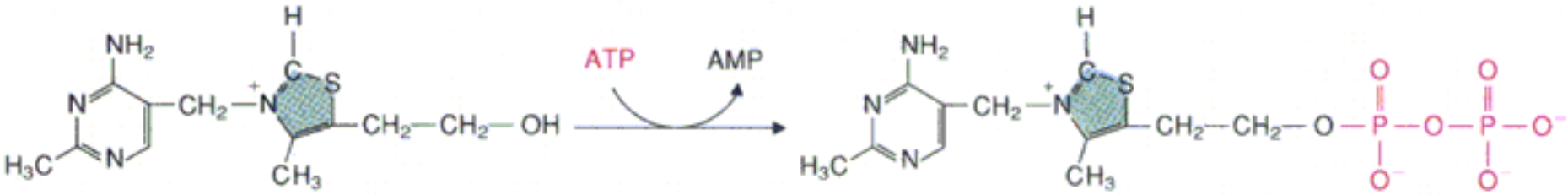
Coenzima: pirofosfato de Tiamina

Funciones: Descarboxilación de piruvato y reacción de transcetolasas a través de la formación de aldehídos activos

Fuentes: Vegetales, granos integrales, germen de trigo.

Requerimientos diarios: 1,4 mg

Síntomas de carencia: Polineuritis (beriberi)



Thiamine

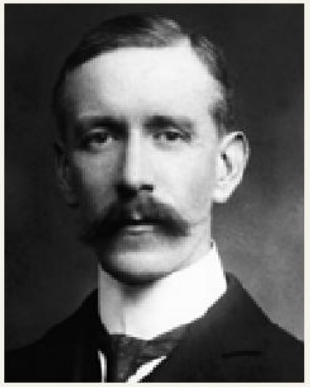
Thiamine pyrophosphate



Casimir Funk

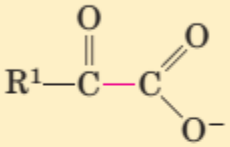
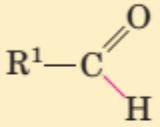
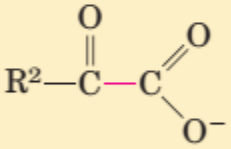
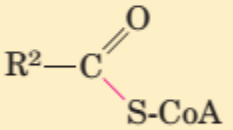
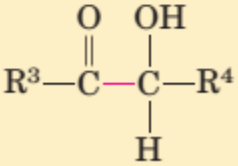
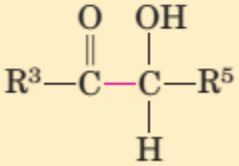


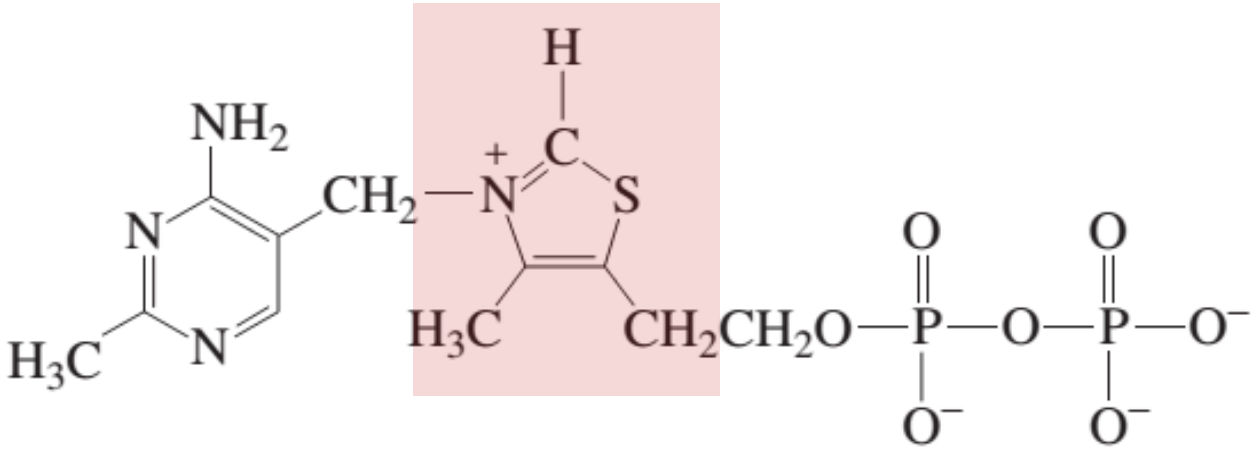
Christiaan Eijkman



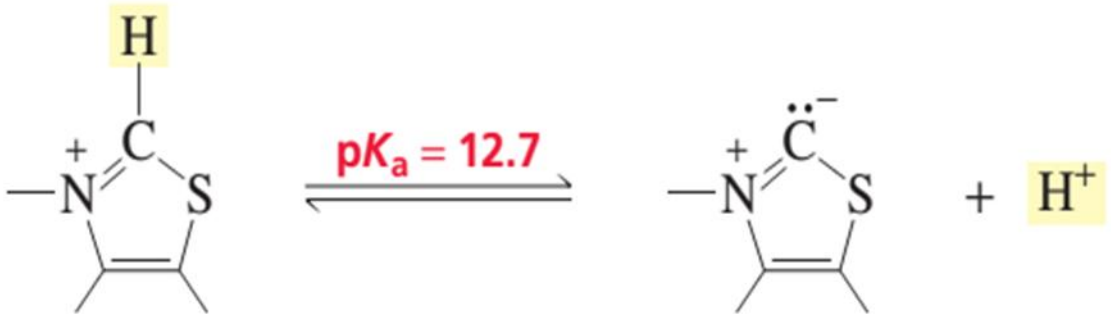
Sir Frederick Hopkins

Algunas reacciones dependientes de TPP

Enzyme	*Pathway(s)*	*Bond cleaved*	*Bond formed*
Pyruvate decarboxylase	Ethanol fermentation		
Pyruvate dehydrogenase α-Ketoglutarate dehydrogenase	Synthesis of acetyl-CoA Citric acid cycle		
Transketolase	Carbon-assimilation reactions Pentose phosphate pathway		



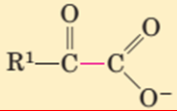
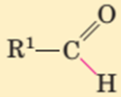
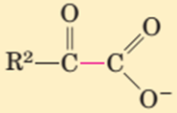
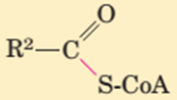
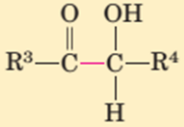
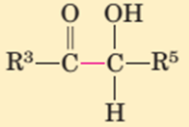
thiamine pyrophosphate
TPP



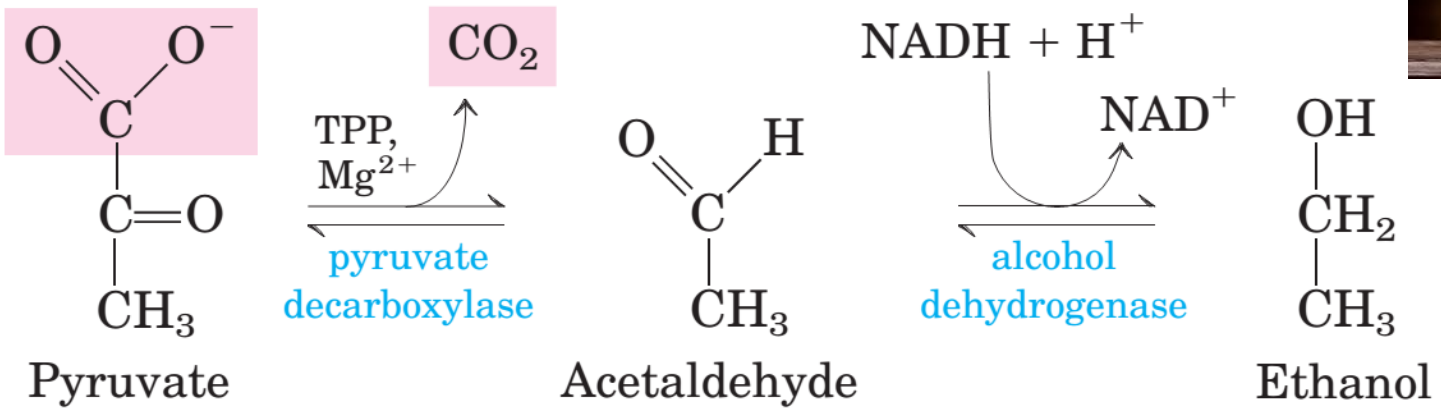
Anillo de tiazol

Carbanión iluro

TABLE 14–1 Some TPP-Dependent Reactions

Enzyme	*Pathway(s)*	*Bond cleaved*	*Bond formed*
Pyruvate decarboxylase	Ethanol fermentation		
Pyruvate dehydrogenase α-Ketoglutarate dehydrogenase	Synthesis of acetyl-CoA Citric acid cycle		
Transketolase	Carbon-assimilation reactions Pentose phosphate pathway		





Mecanismo de la piruvato descarboxilasa

Formación de hidroxietil-pirofosfato de tiamina

un aldehído activo

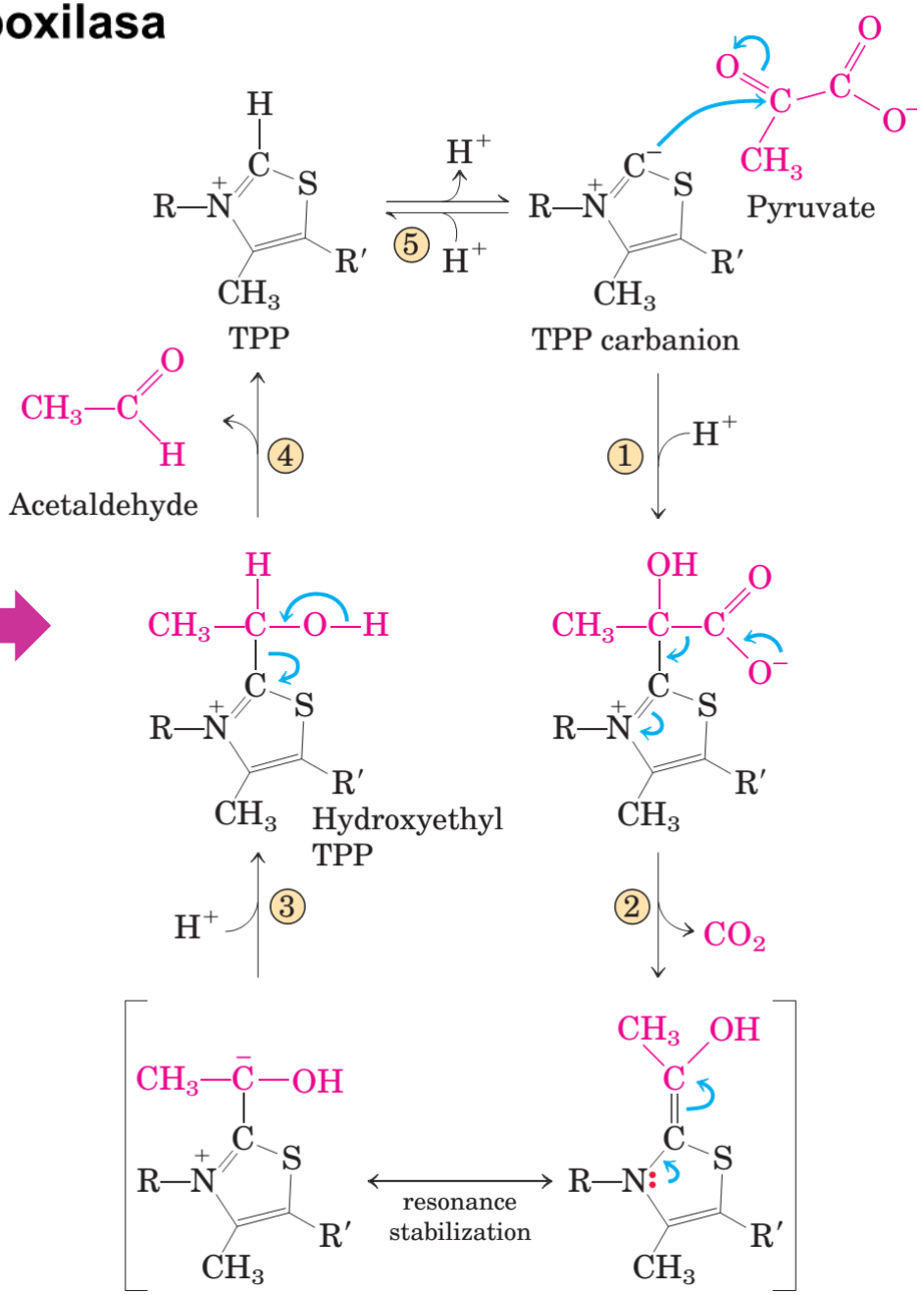
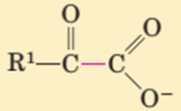
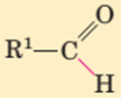
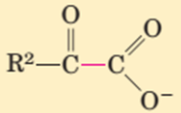
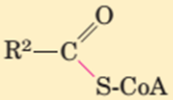
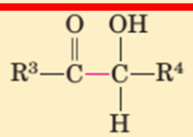
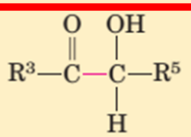
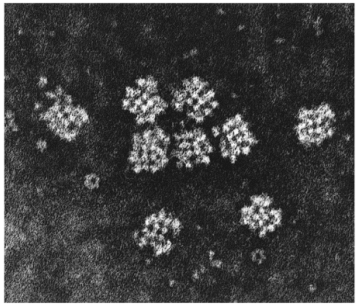


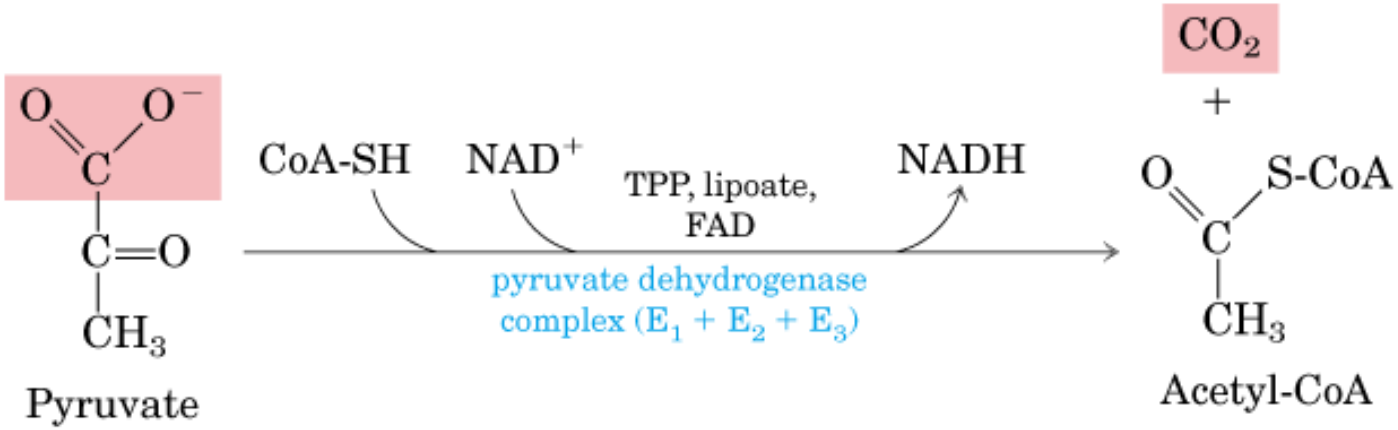
TABLE 14–1 Some TPP-Dependent Reactions

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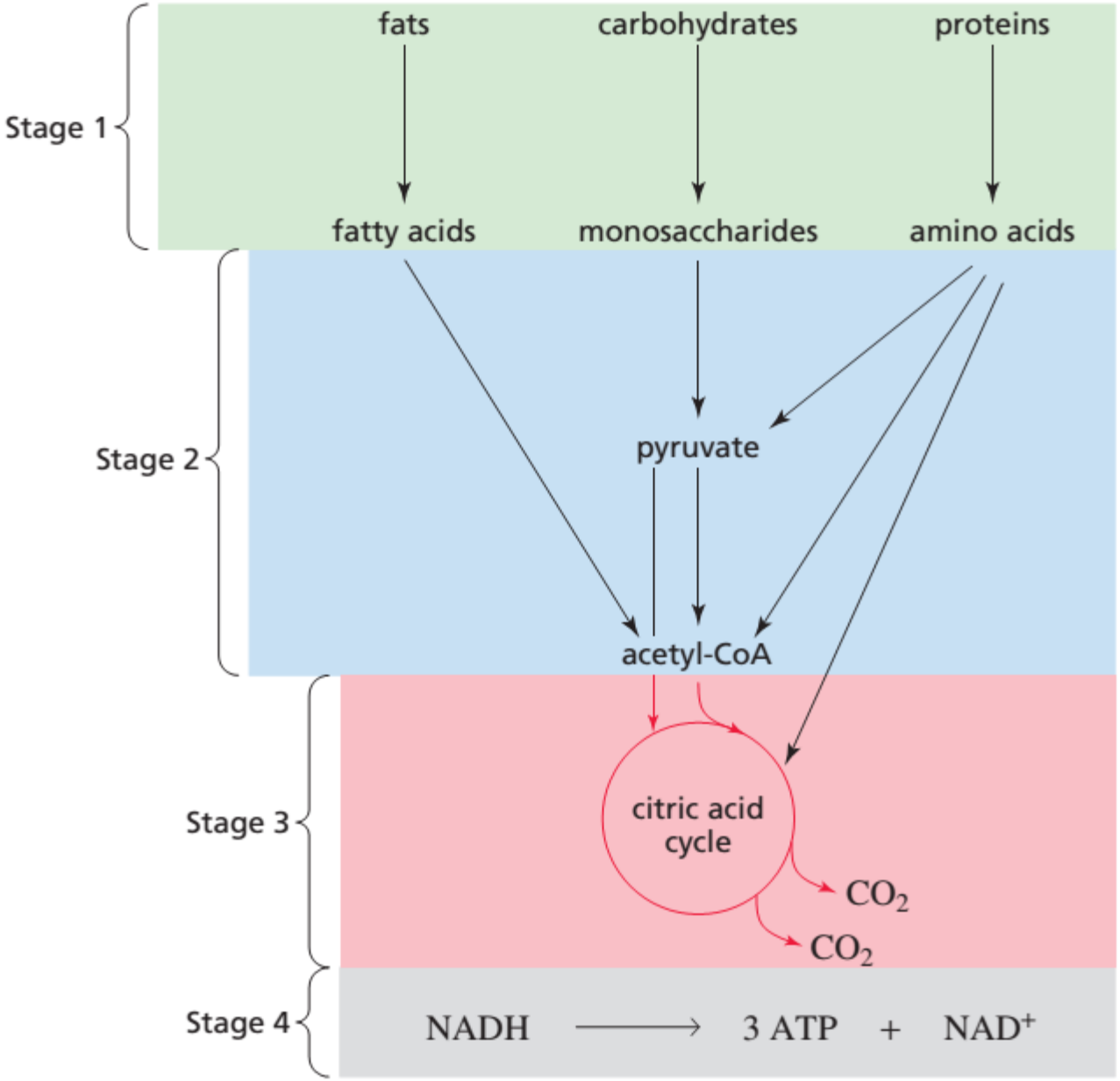


COMPLEJO DE LA PIRUVATO DESHIDROGENASA

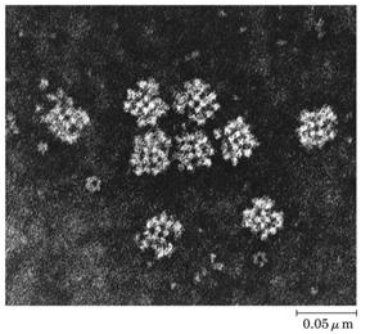
Reacción General

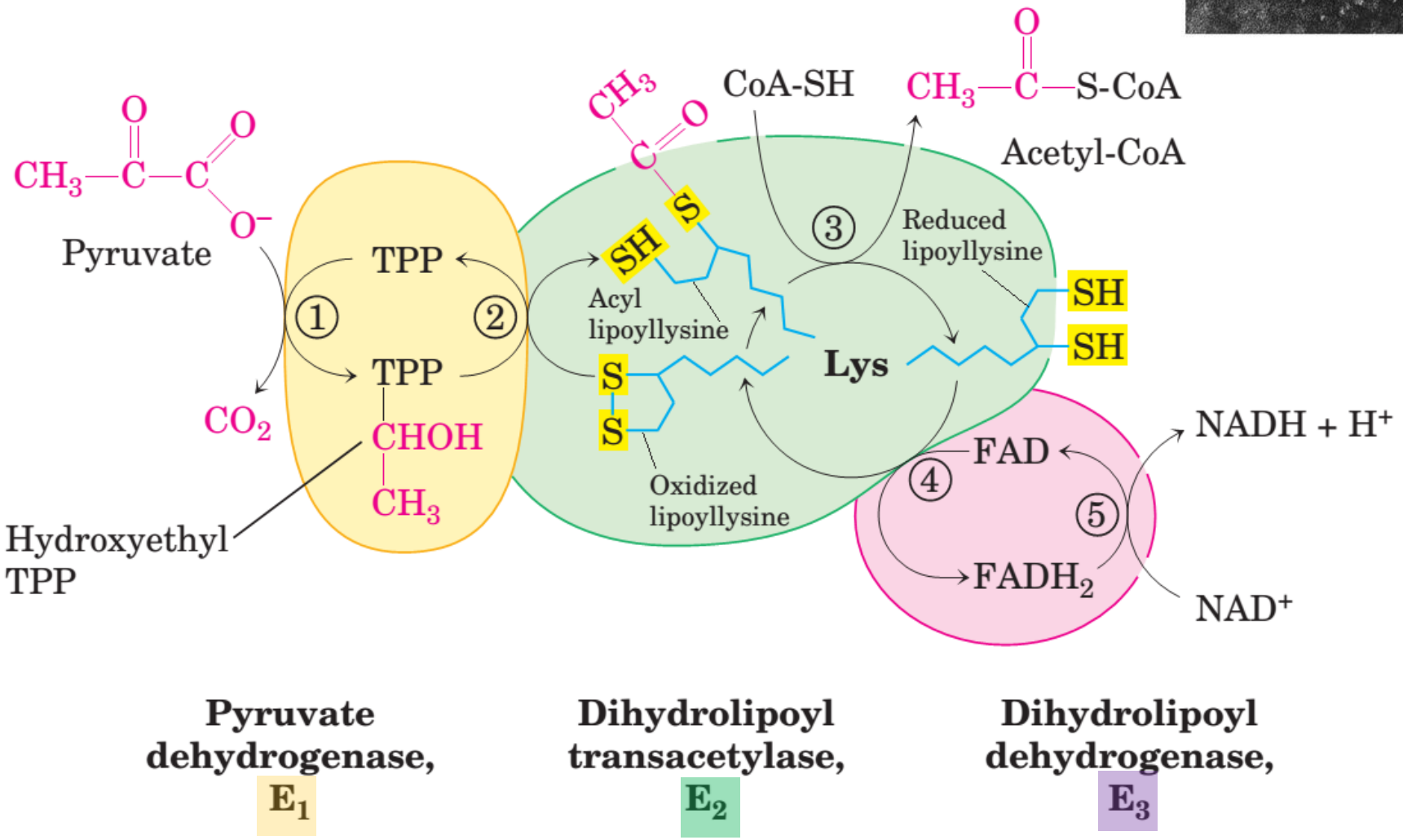


$\Delta G'^{\circ} = -33.4$ kJ/mol

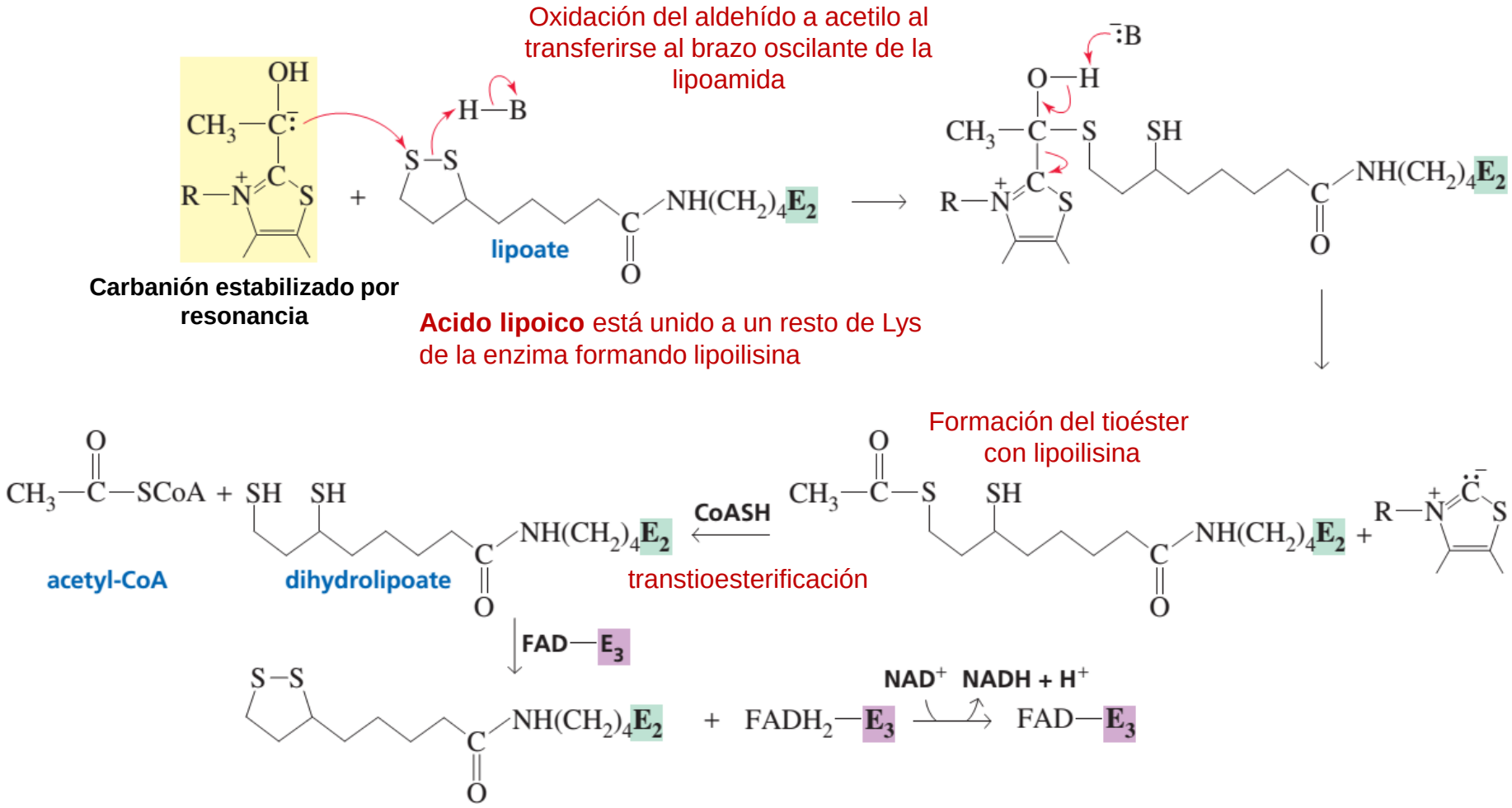

Stage 1
fats
carbohydrates
proteins
fatty acids
monosaccharides
amino acids
Stage 2
pyruvate
acetyl-CoA
Stage 3
citric acid cycle
CO_2
CO_2
Stage 4
NADH
3 ATP
+
NAD^+

COMPLEJO DE LA PIRUVATO DESHIDROGENASA

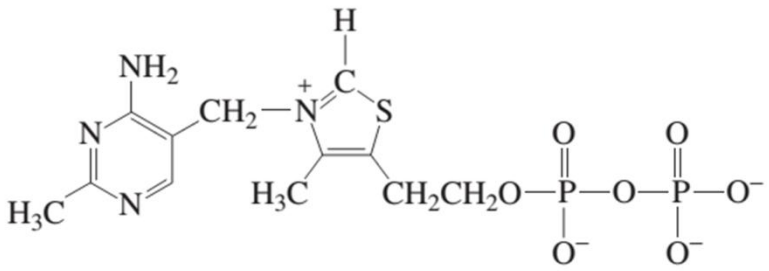




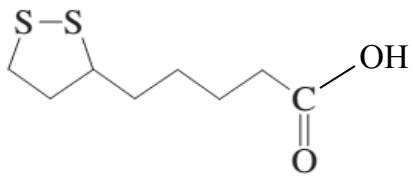
Mecanismo del Complejo de la Piruvato Deshidrogenasa



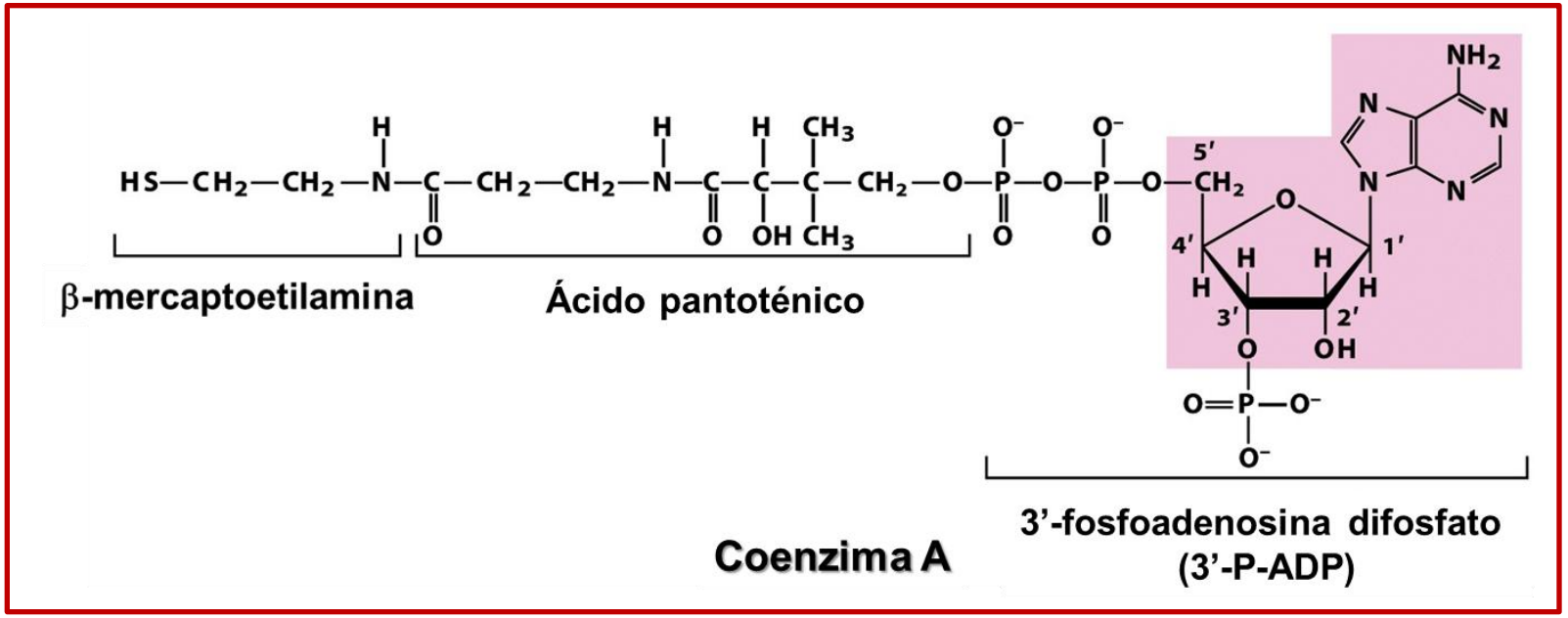
COENZIMAS TRANSPORTADORAS DE GRUPOS INVOLUCRADAS



Pirofosfato de tiamina (TPP)



Ácido lipoico



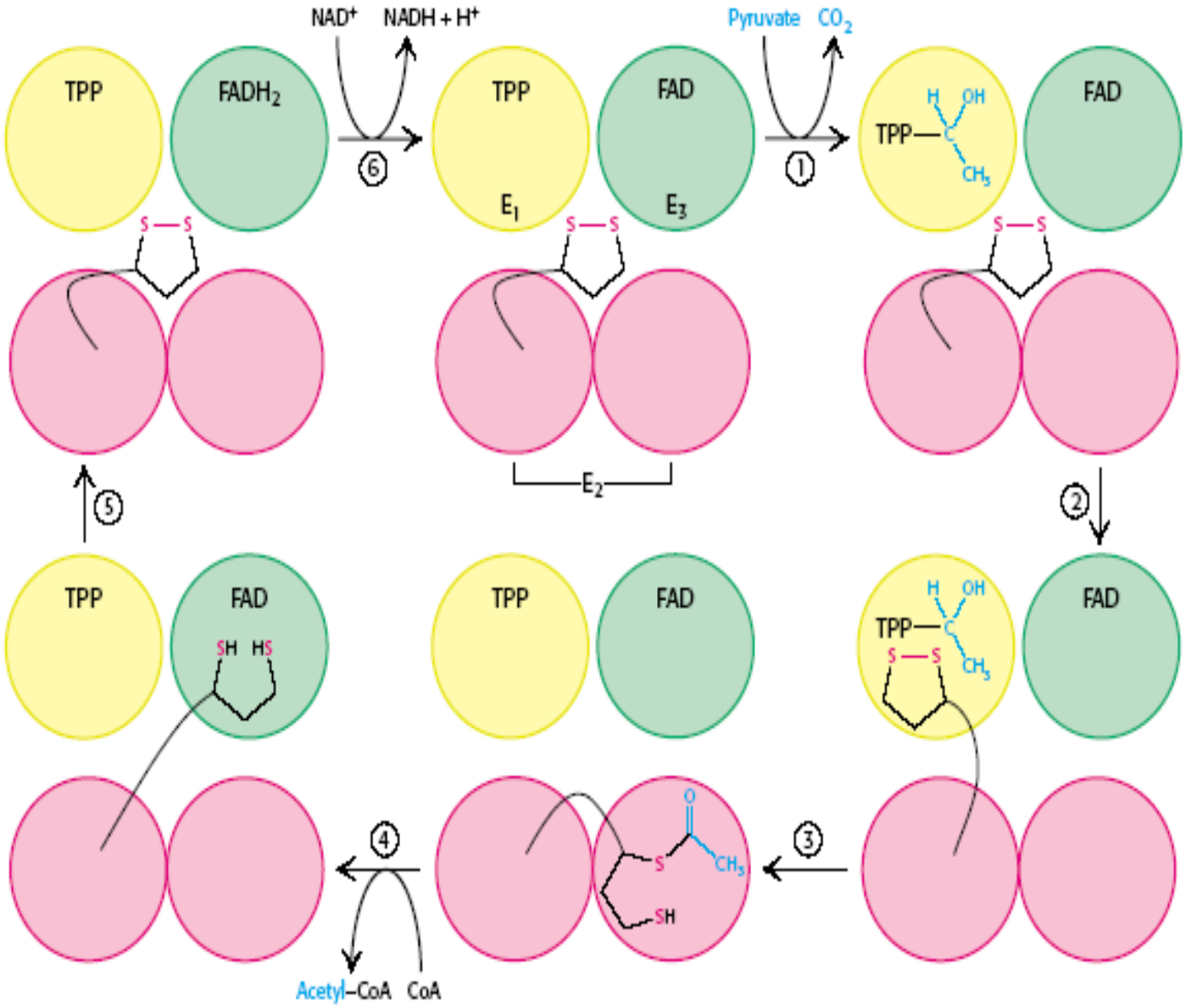
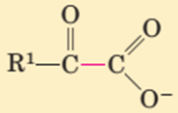
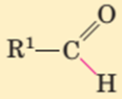
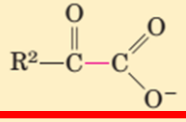
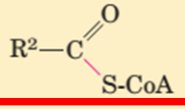
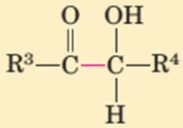
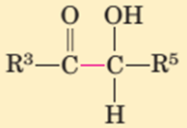
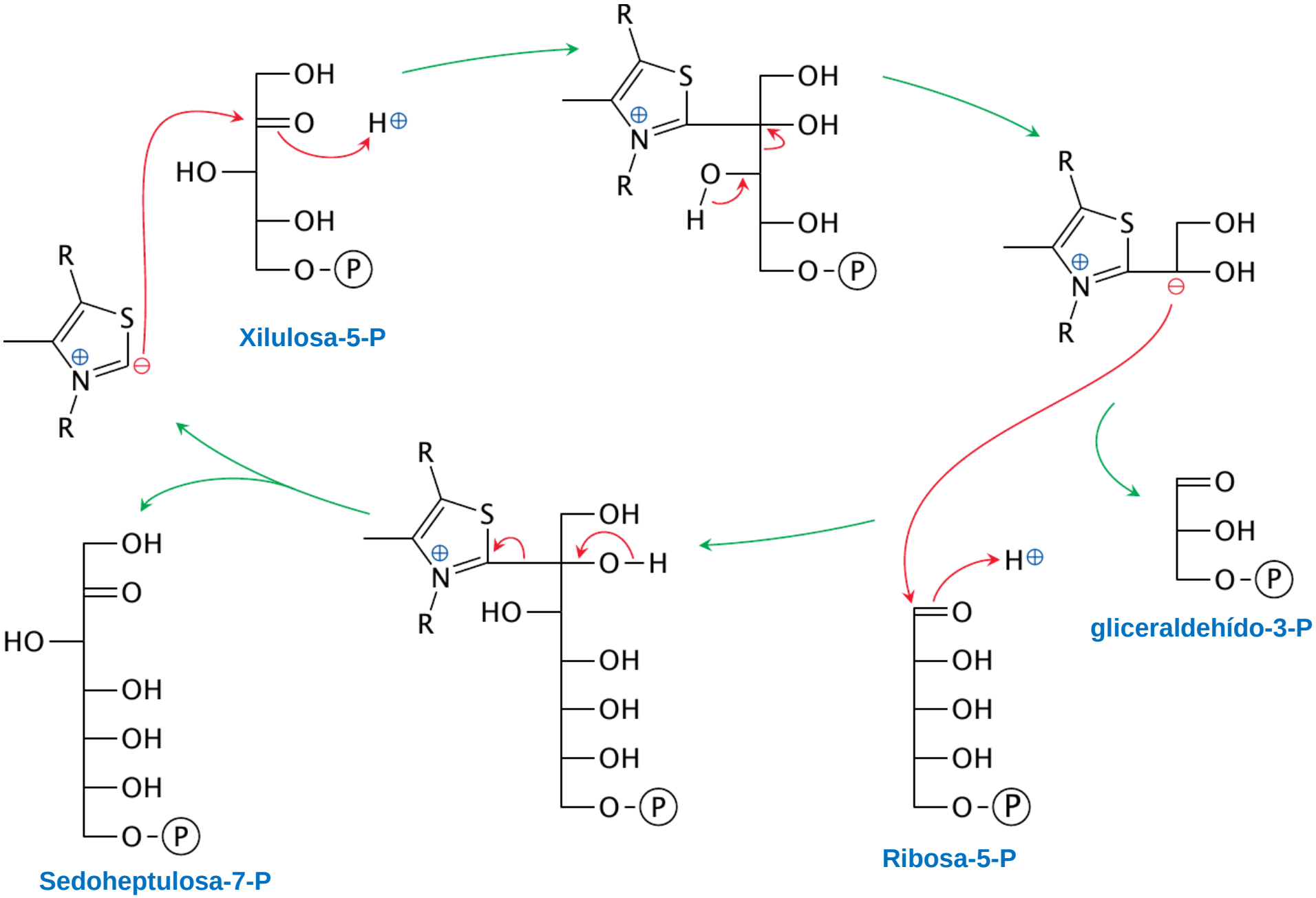

NAD+
NADH + H+
Pyruvate
CO2
TPP
FADH2
TPP
FAD
E1
E3
TPP
FAD
H
OH
CH3
S—S
E2
1
2
3
4
5
6
TPP
FAD
SH HS
TPP
FAD
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O
S
CH3
SH
Acetyl–CoA
CoA

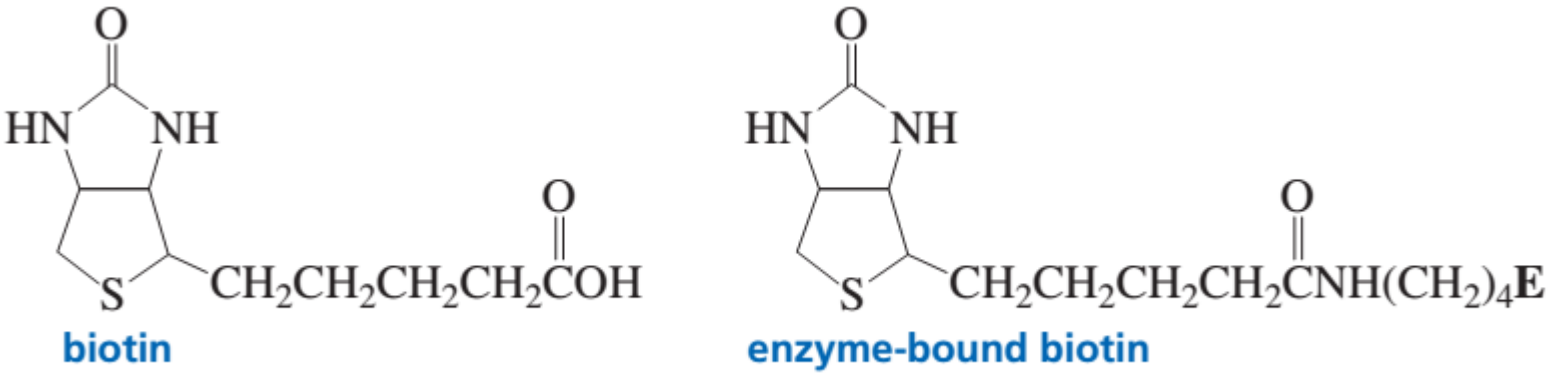
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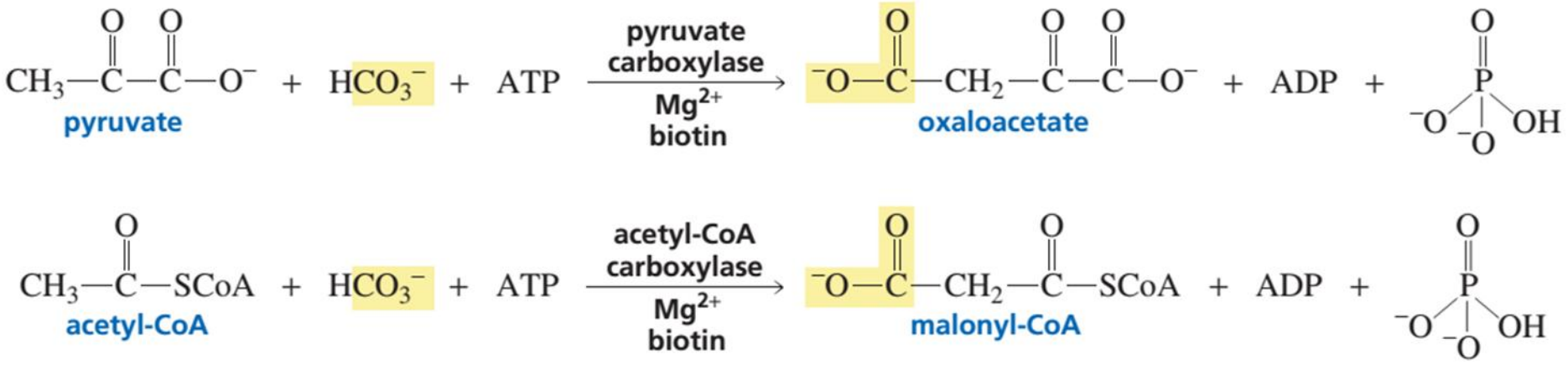
PPT en transcetolasas

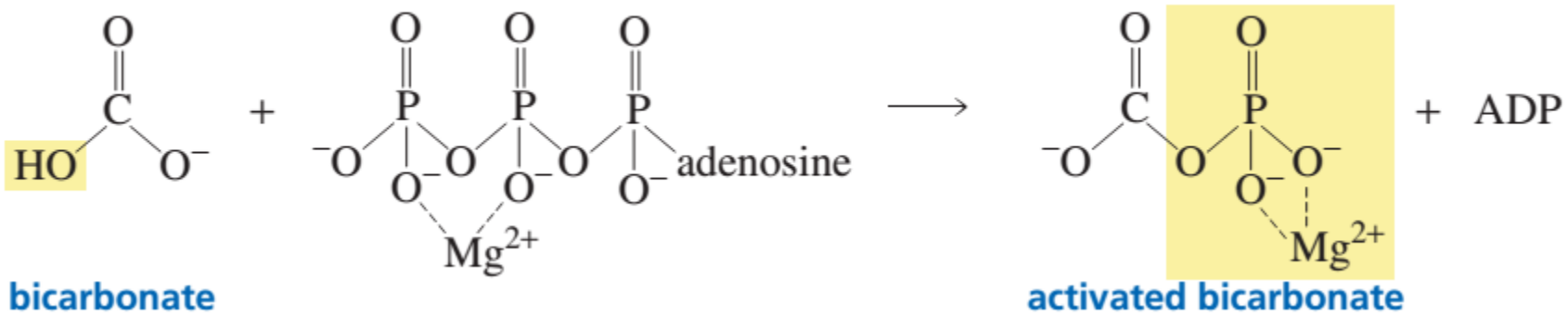


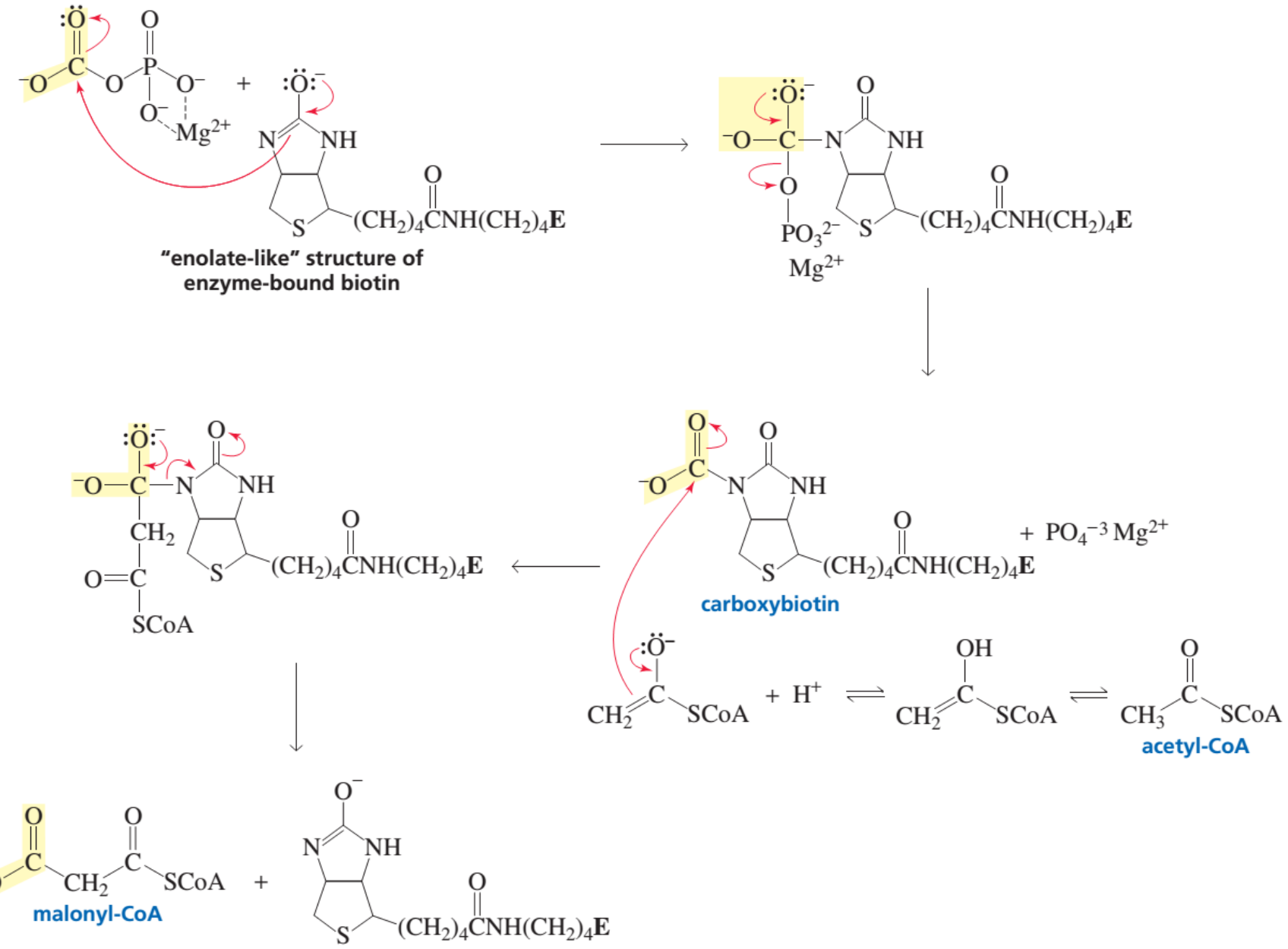
Vitamina H: Biotina



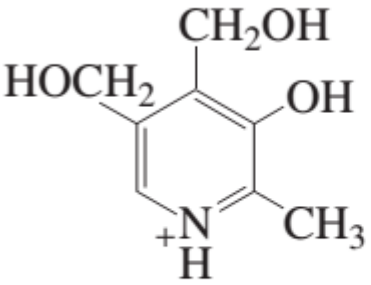
Fuente: sintetizada por bacterias de la microbiota intestinal
Funciones: *Carboxilación de enlaces adyacentes a grupos carbonilos*



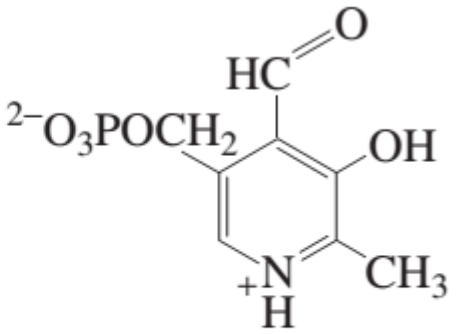

HO
adenosine
Mg^{2+}
+ ADP
bicarbonate
activated bicarbonate


"enolate-like" structure of enzyme-bound biotin
carboxybiotin
acetyl-CoA
malonyl-CoA

Vitamina B6: Piridoxina



pyridoxine
vitamin B_6



pyridoxal phosphate
PLP

Requerimientos diarios: 2,2 mg

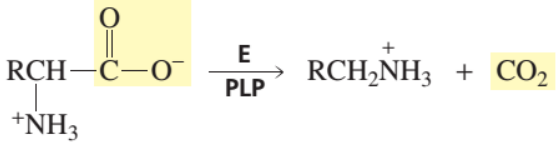
Fuentes: hígado

Síntomas de carencia: Dermatitis, trastornos psíquicos

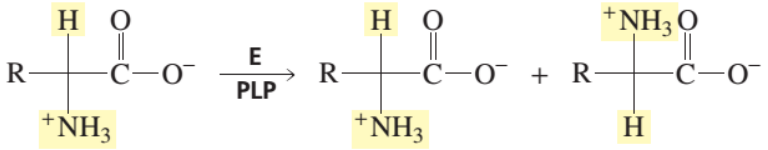
Coenzimas: fosfato de piridoxal, fosfato de piridoxamina

Funciones: *Transaminación*, *racemización* y *descarboxilación* de aminoácidos. Degradación de glucógeno (glucógeno fosforilasa)

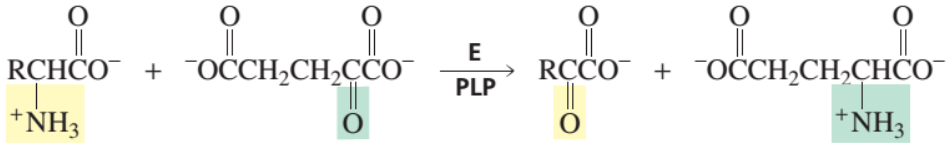
Descarboxilación



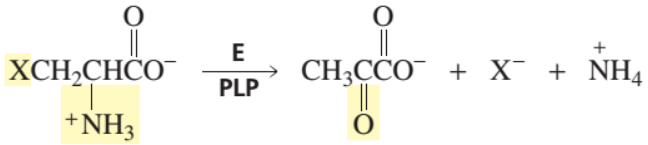
Racemización



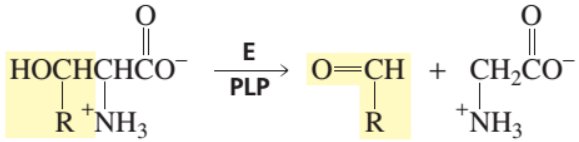
Transaminación



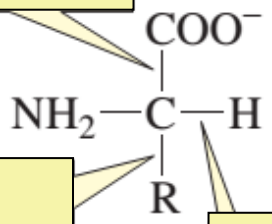
α,β-Eliminación



Ruptura de enlace Cα-Cβ



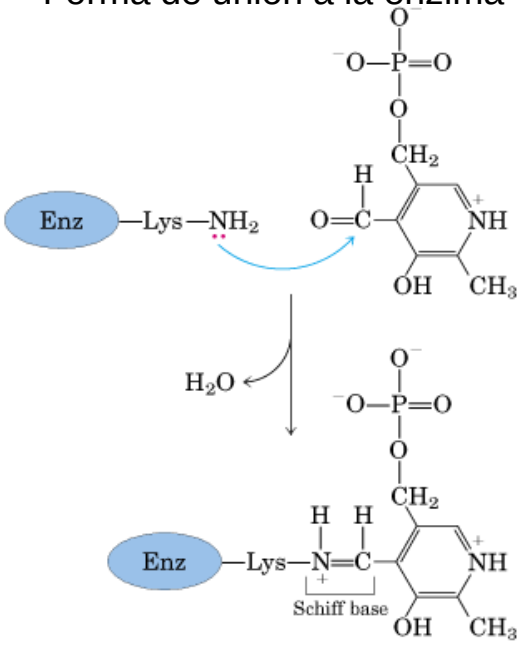
Enlace roto en la descarboxilación

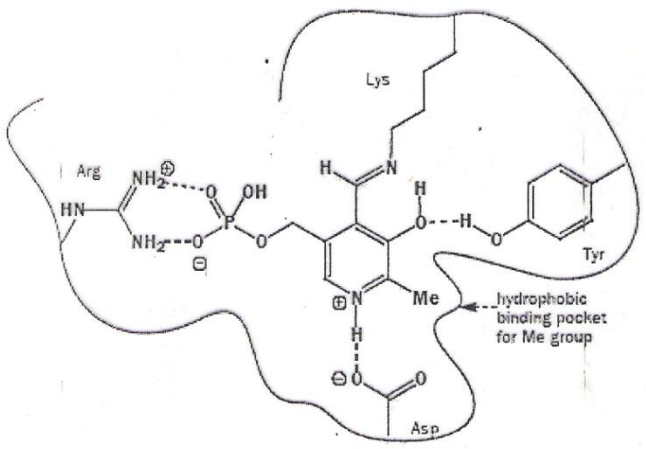


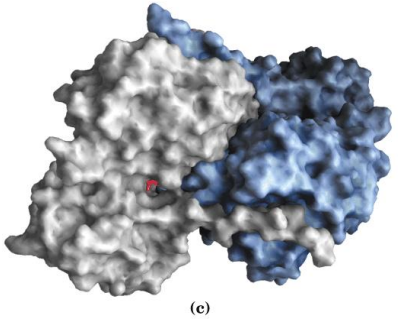
Enlace roto en el clivaje del enlace Cα-Cβ

Enlace roto en la transaminación, racemización y eliminación α,β

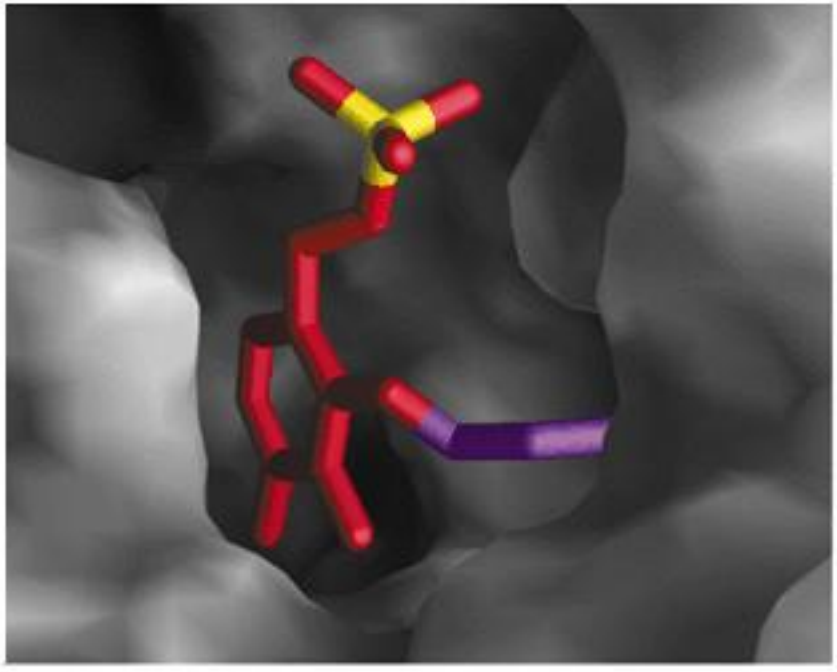
Forma de unión a la enzima

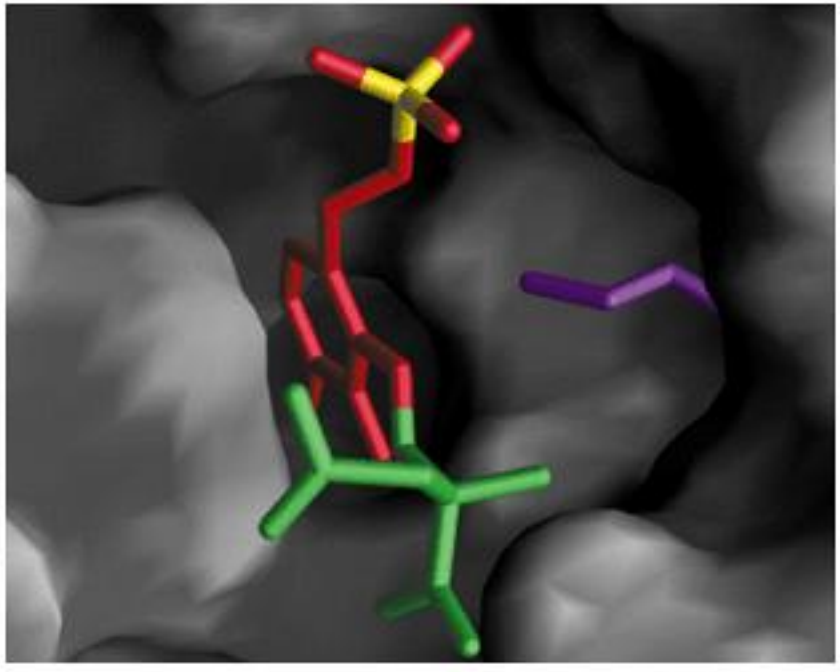






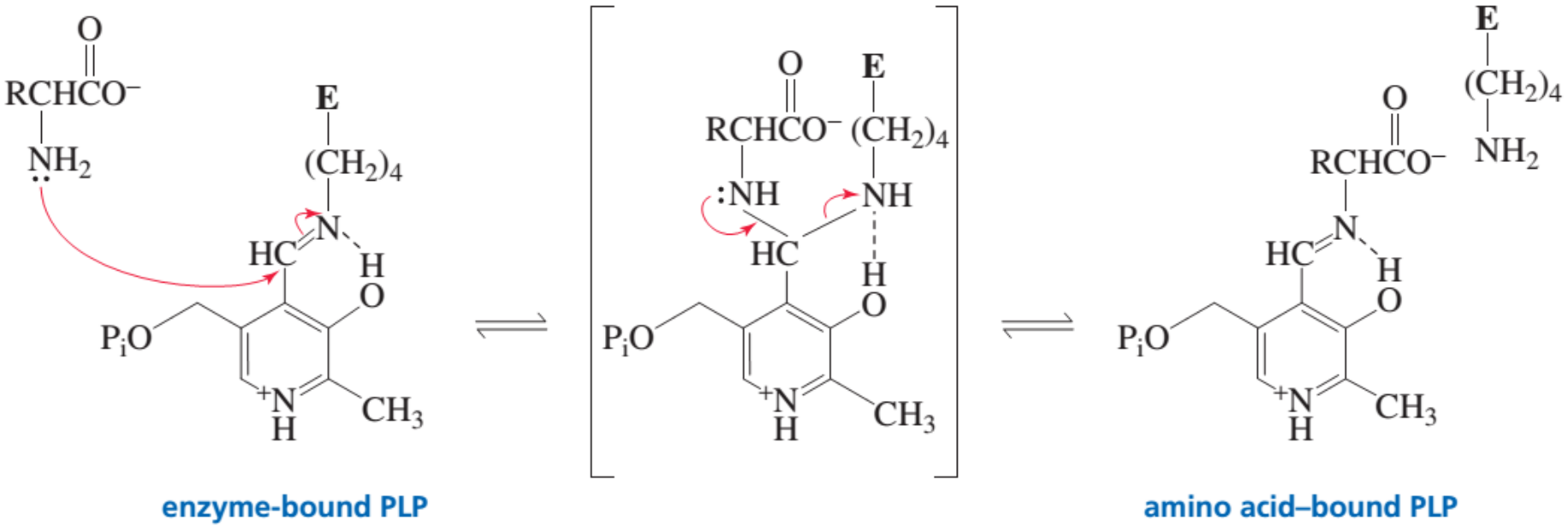
Entrada del aminoácido



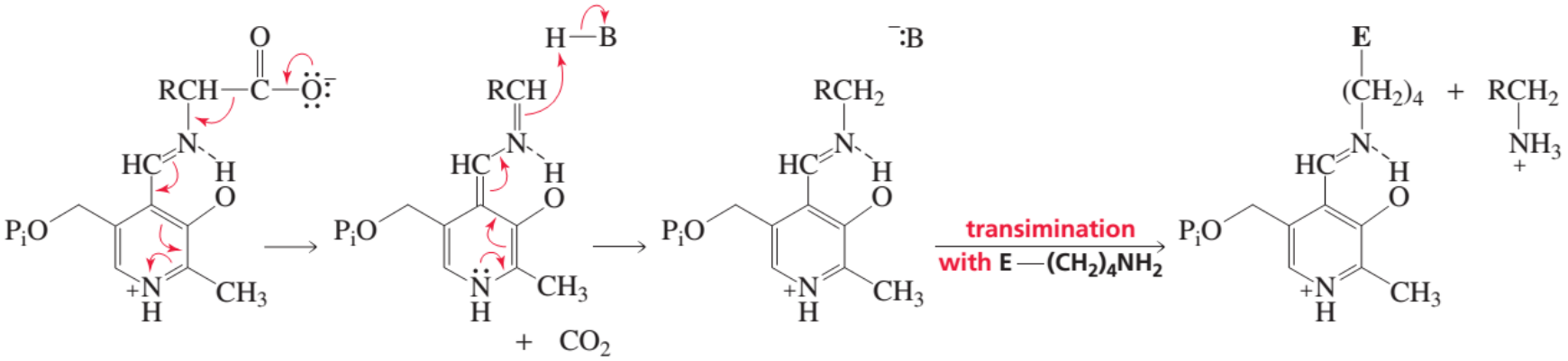


El primer paso en todas las enzimas que utilizan PLP es una *transiminación*

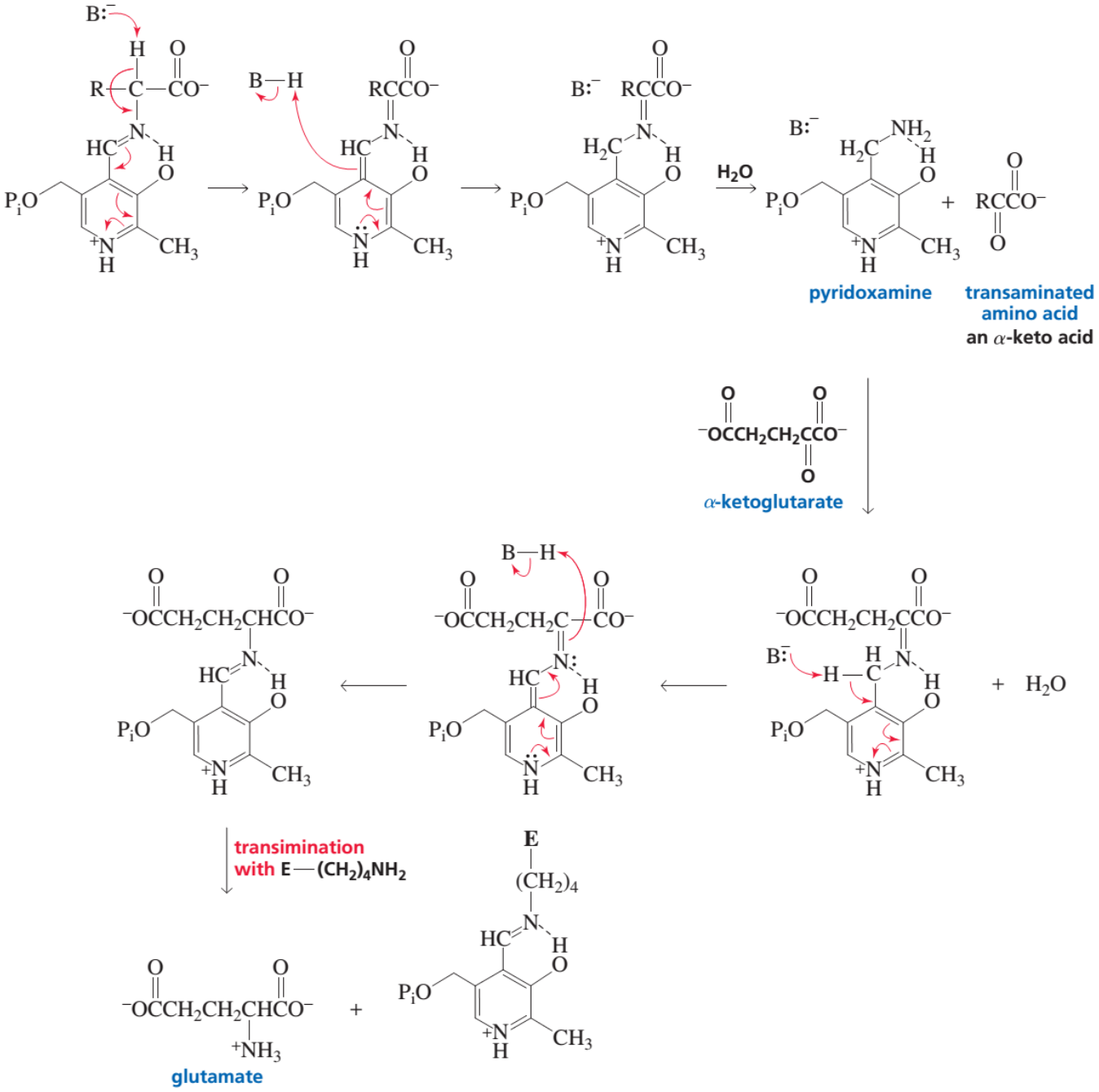
Transiminación



Mecanismo para la descarboxilación de un aminoácido catalizada por enzima-PLP



Mecanismo para la transaminación de un aminoácido catalizada por enzima-PLP



Aspartato aminotransferasa (AST) (EC 2.6.1.1) también llamada transaminasa glutámico oxalacético (GOT).
Reacción que cataliza:

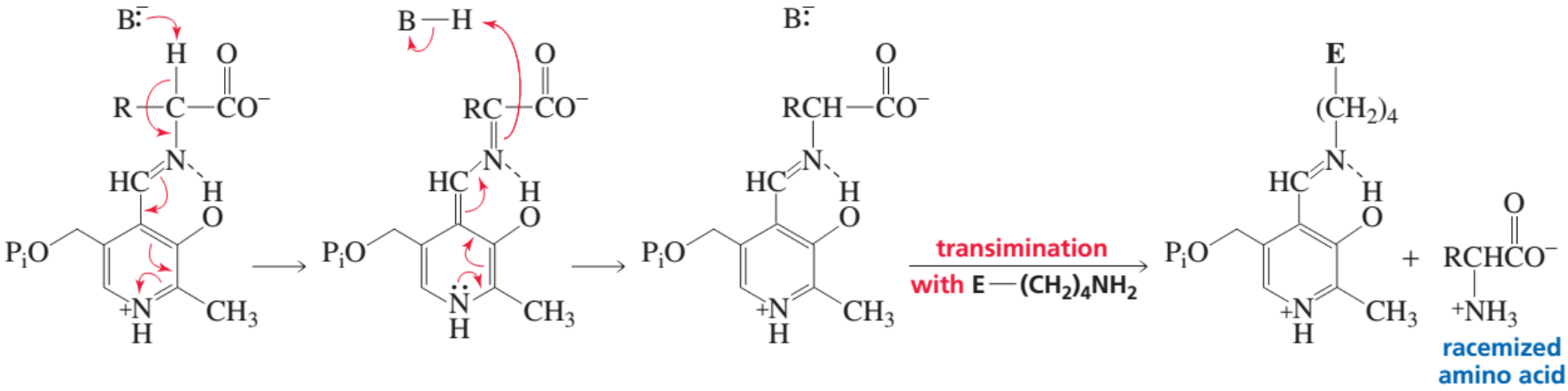
(GOT)
L-aspartato + 2-oxoglutarato ⇌ **o**xaloacetato + L-**g**lutamato

Alanino aminotransferasa (ALT), también llamada transaminasa glutámico pirúvica (GPT).
Reacción que cataliza:

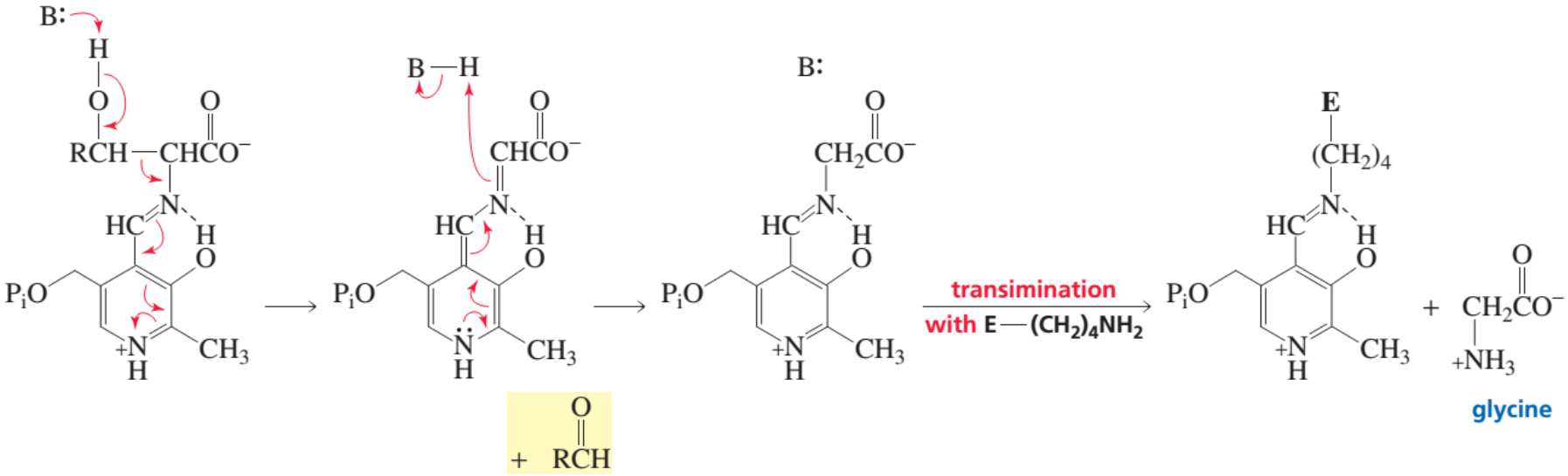
(GPT)
L-alanina + 2-oxoglutarato ⇌ **p**iruvato + L-**g**lutamato

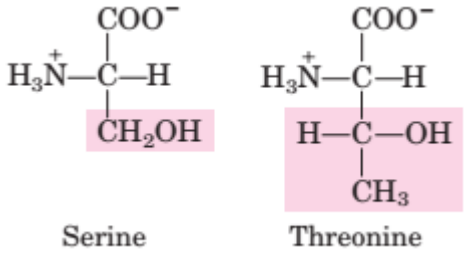
ácido α-cetoglutárico = 2-oxoglutarato

Mecanismo para la racemización de un L-aminoácido catalizada por enzima-PLP

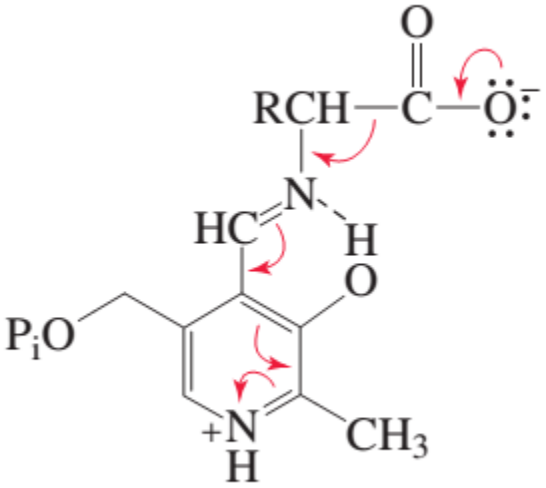


Mecanismo para la ruptura de enlace Cα-Cβ de un aminoácido catalizada por enzima-PLP

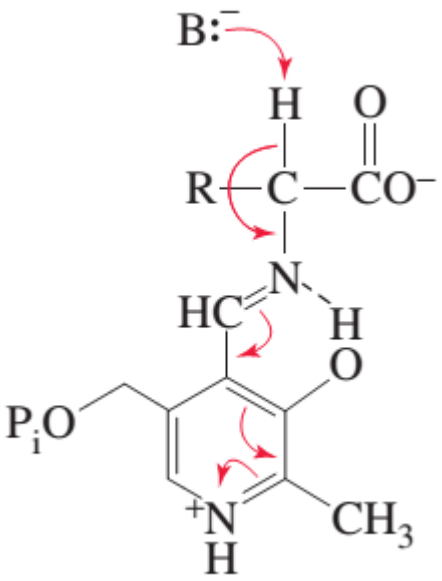




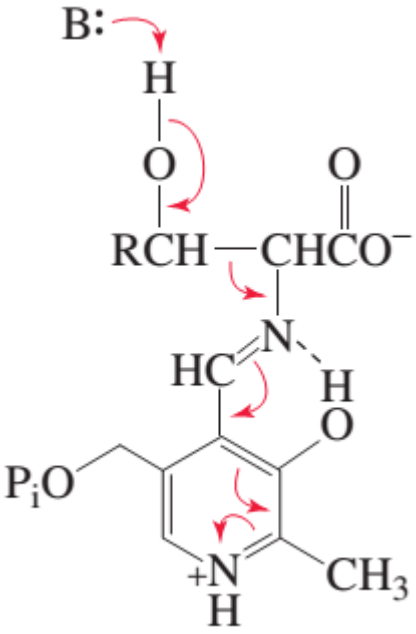
En todos los casos, el N cargado positivamente actúa como sumidero de electrones



Descarboxilación

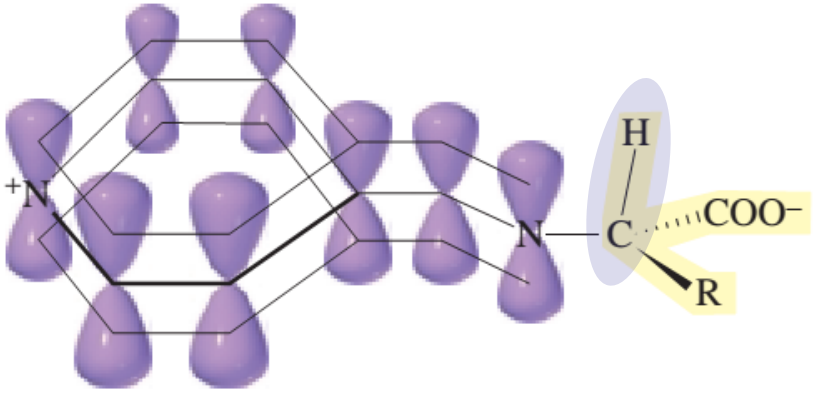


Transaminación
Racemización

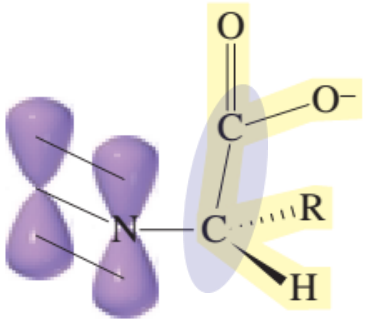


Ruptura enlace Cα-Cβ

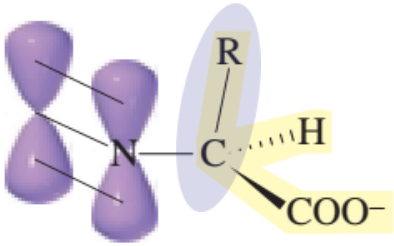
Las diferentes enzimas unen el correspondiente sustrato, de modo tal que el enlace que se va a romper quede ubicado en forma paralela a los orbitales p del sistema conjugado



Imina formada entre PLP y el aminoácido antes de romperse el enlace α C-H

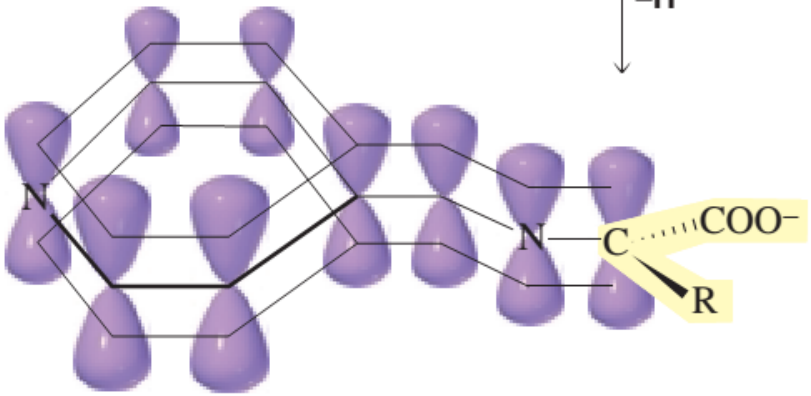


antes de romperse el enlace α C-CO_2



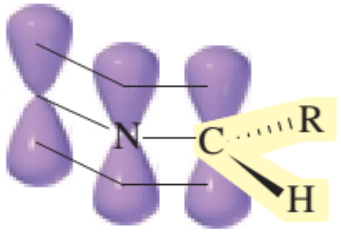
antes de romperse el enlace α C-R

–H



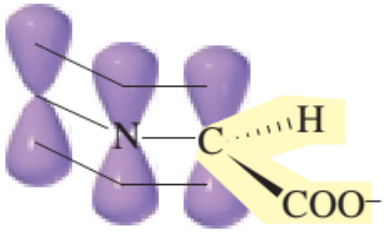
Después de la ruptura del enlace α C-H, los electrones en el orbital p pueden deslocalizarse en un sistema conjugado

$-CO_2$



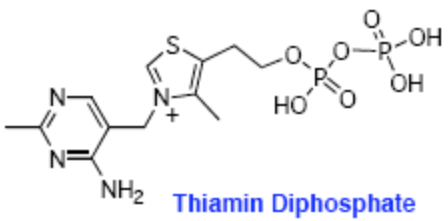
después de romperse el enlace α C-CO_2

–R

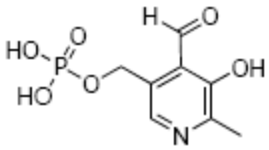


después de romperse el enlace α C-R

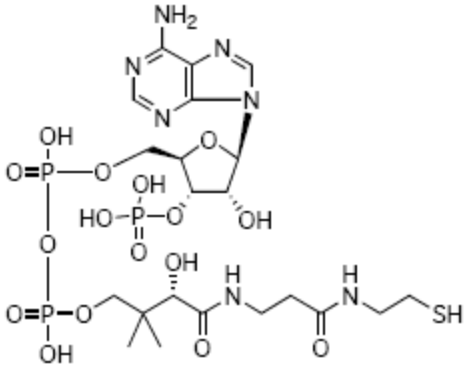
Algunos cofactores



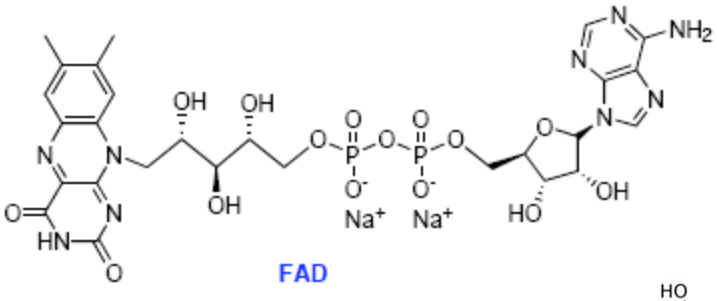
Thiamin Diphosphate



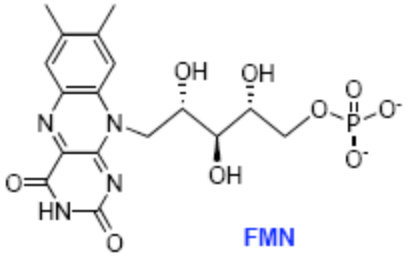
Pyridoxal Phophates



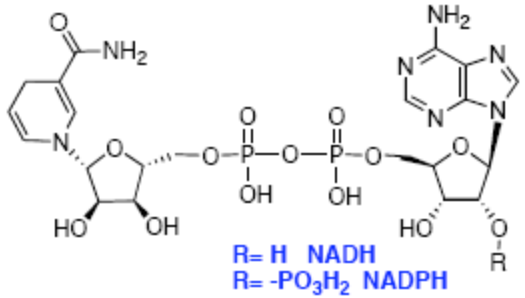
Coenzyme A (CoA)



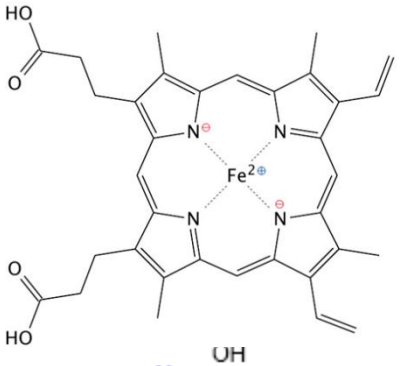
FAD



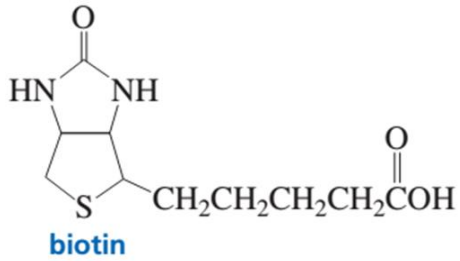
FMN



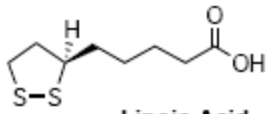
R= H NADH
R= -PO_3H_2 NADPH



Heme



biotin



Lipoic Acid

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-**PRINCIPIOS DE BIOQUIMICA**. Albert L. LEHNINGER. Ediciones Omega
-**BIOQUIMICA.** Mathews, C and Van Holde, K E. Ed. McGraw- Hill Interamericana. -**QUIMICA ORGANICA. ESTRUCTURA Y FUNCION**. Vollhardt, P and Schore, N. Ed. Omega. 3ra Edición, 2000.