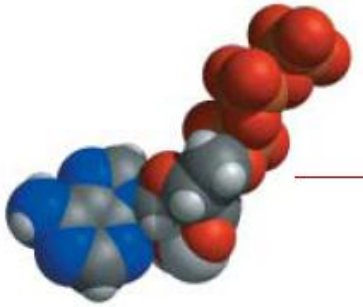
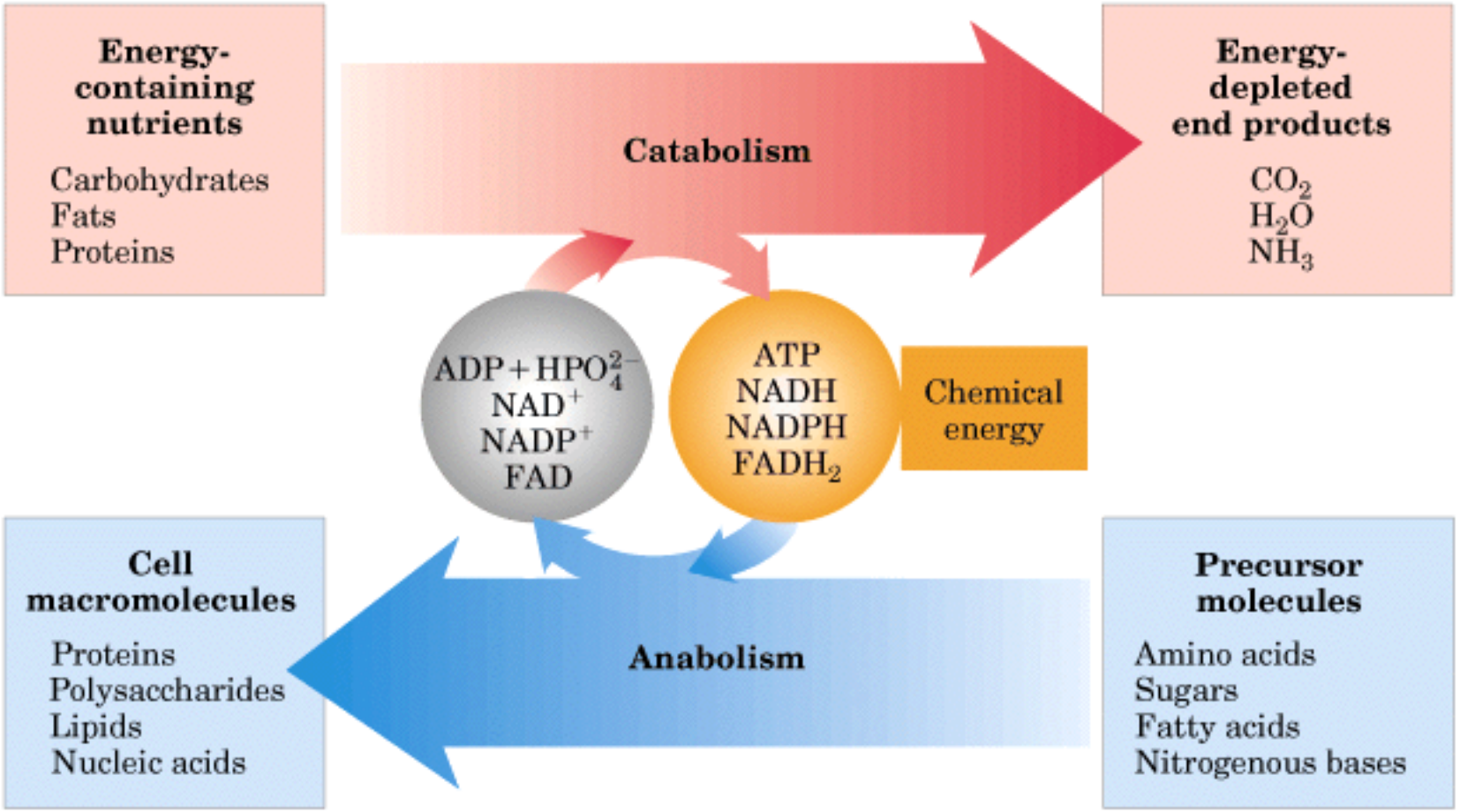
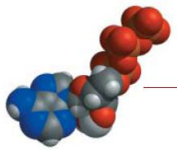
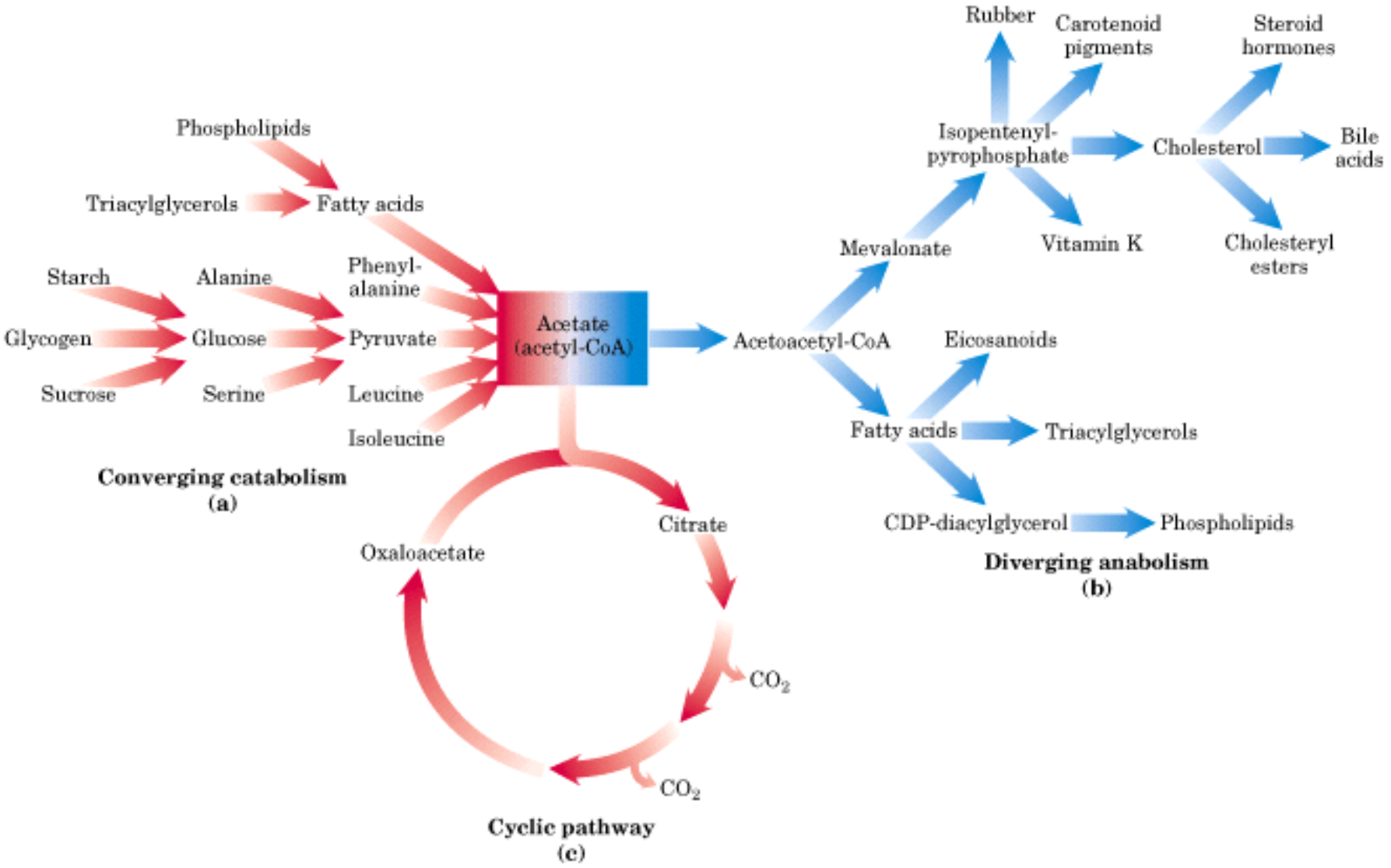
TEMA 6: NUCLEÓSIDOS FOSFATO BIOENERGÉTICA

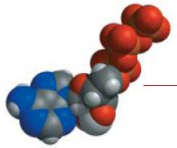


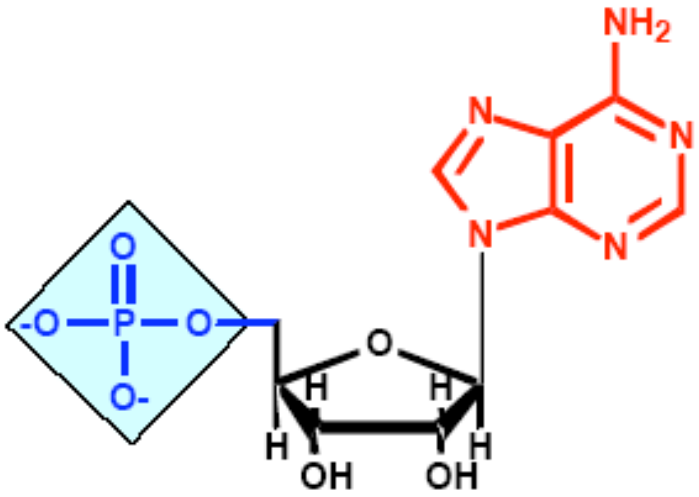




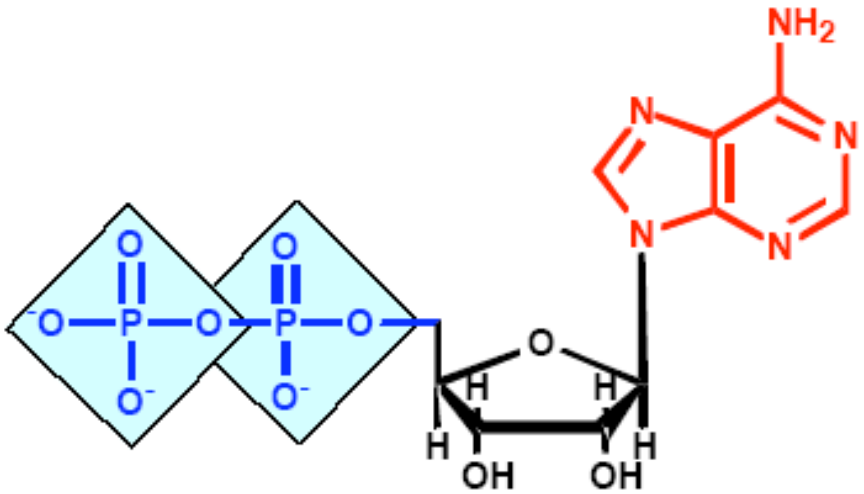

Phospholipids
Triacylglycerols
Fatty acids
Starch
Glycogen
Sucrose
Alanine
Glucose
Serine
Phenyl-alanine
Pyruvate
Leucine
Isoleucine
Acetate (acetyl-CoA)
Converging catabolism
(a)
Oxaloacetate
Citrate
CO_2
CO_2
Cyclic pathway
(c)
Acetoacetyl-CoA
Mevalonate
Isopentenyl-pyrophosphate
Rubber
Carotenoid pigments
Vitamin K
Cholesterol
Steroid hormones
Bile acids
Cholesteryl esters
Fatty acids
Eicosanoids
Triacylglycerols
CDP-diacylglycerol
Phospholipids
Diverging anabolism
(b)

Nucleótidos

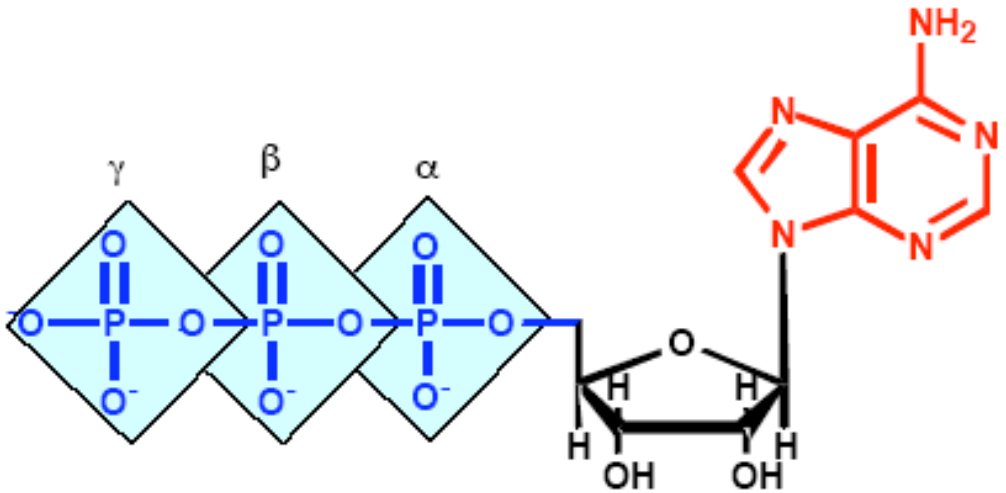




adenosina 5'-monofosfato
(AMP)

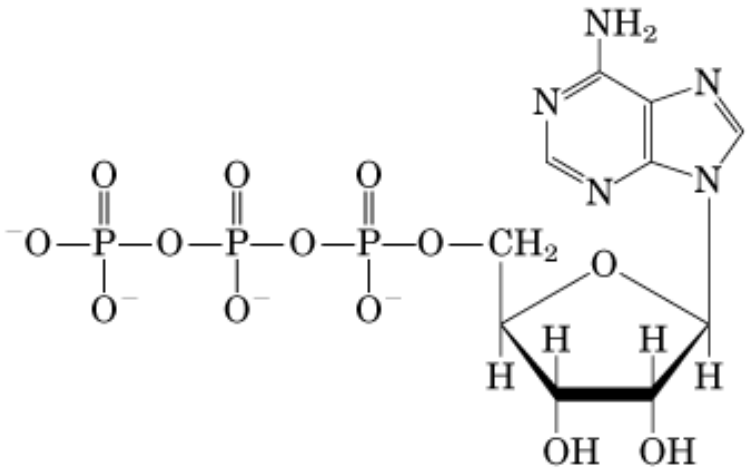


adenosina 5'-difosfato
(ADP)

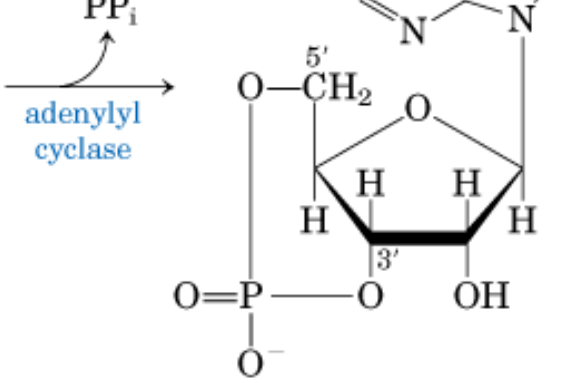


adenosina 5'-trifosfato
(ATP)

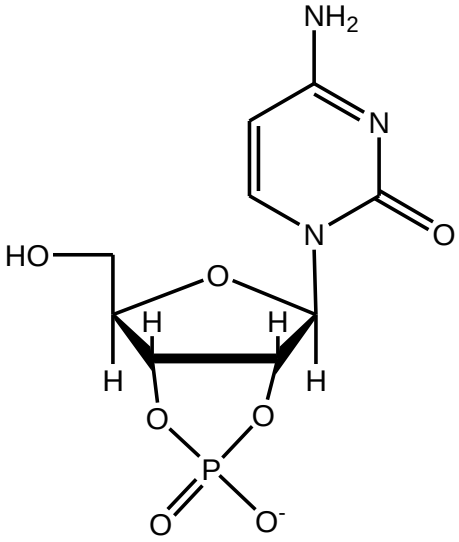
Nucleótidos cíclicos



ATP

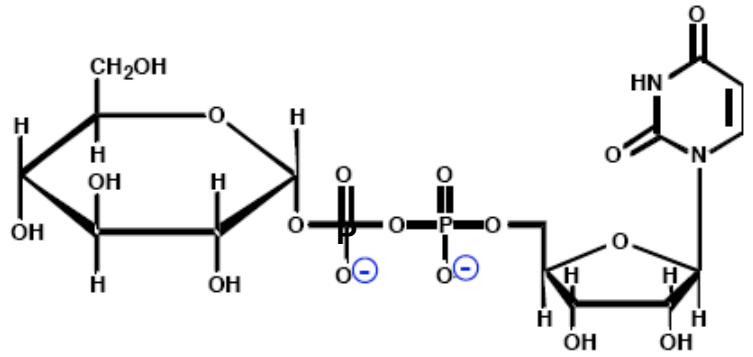


Adenosine 3′,5′-cyclic monophosphate (cAMP)

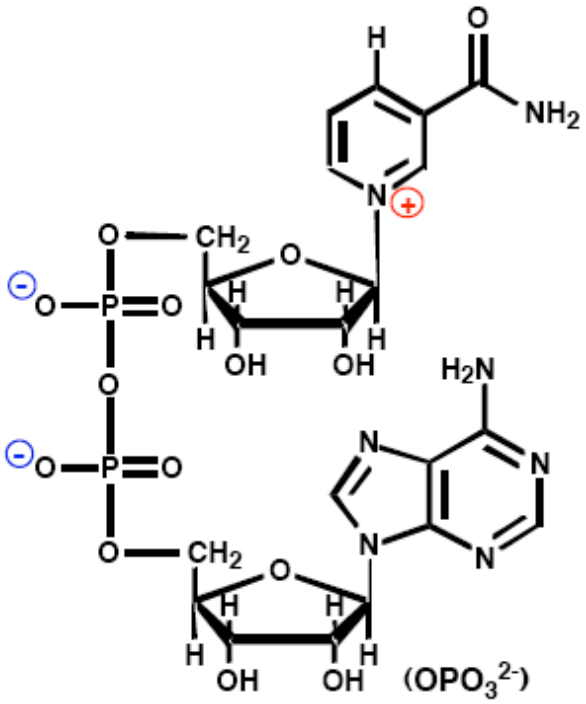


2',3'-Monofosfato de 1-β-ribofuranosilcitocina

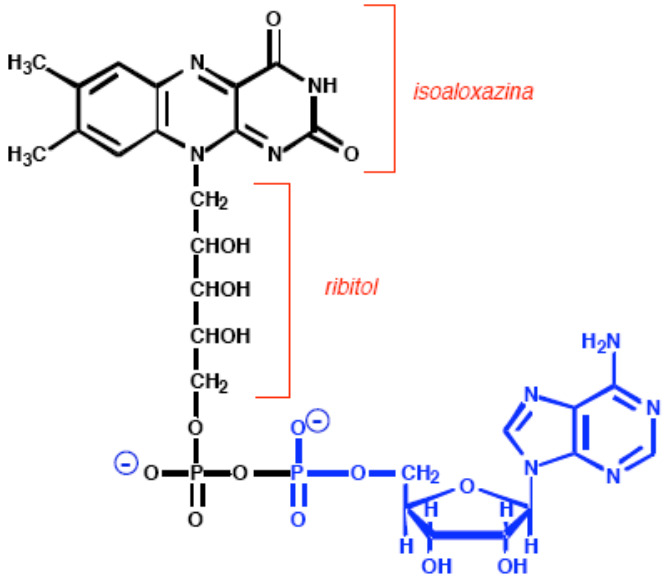
Otros nucleótidos de interés biológico



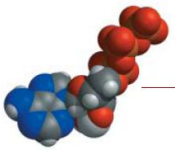
UDP-glucosa



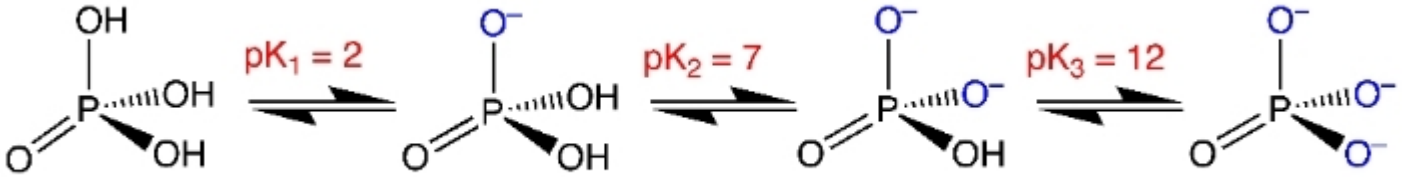
NAD+ (NADP+)



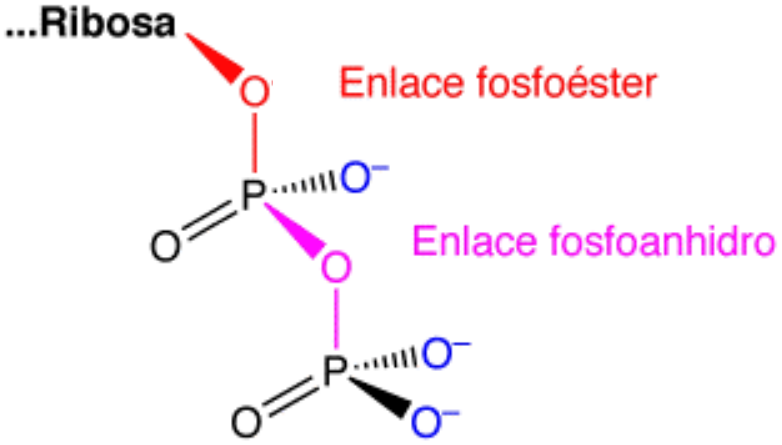
Flavin mononucleótido (FMN) y
Flavinadenin dinucleótido (FAD)



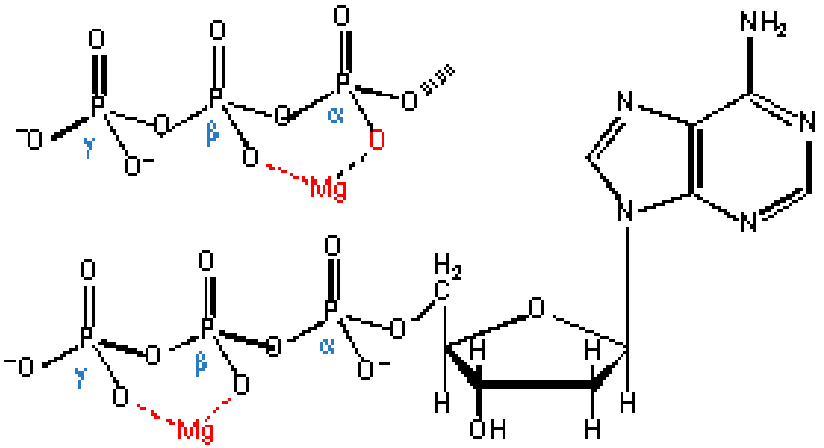
Ionización del grupo fosfato ATP

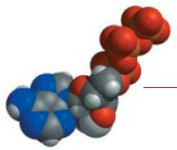


Tipos de enlaces fosfato en ADP



Estabilización de ATP con cationes divalentes





Reacciones en las que participa ATP u otros nucleósidos trifosforilados

a) Transferencia del grupo ortofosfato terminal (γ).

Ej. ATP + Glu→ADP + Glu-6-fosfato

b) Transferencia del grupo pirofosfato terminal (β y γ).

Ej. ATP + D-Ribosa-5-fosfato→AMP + 5-Fosforibosa-1-difosfato

c) Transferencia de AMP

Ej. ATP + nicotinamida mononucleótido → PPi+ NAD^+

d) Transferencia de adenosina

Ej. ATP + L-Met → Pi+ PPi+ S-adenosilmetionina

e) Utilización de la energía de hidrólisis de ATP por ligasas o sintetasas para unir otras moléculas

Ej. ATP + Acetato + CoA → Ppi + AMP + acetil-CoA

Some Physical Constants and Units Used in Thermodynamics

Boltzmann constant, $\mathbf{k} = 1.381 \times 10^{-23}$ J/K

Avogadro's number, $N = 6.022 \times 10^{23}$ mol^{-1}

Faraday constant, $\mathcal{F} = 96{,}480$ J/V · mol

Gas constant, $R = 8.315$ J/mol · K

$(= 1.987$ cal/mol · K)

Units of ΔG and ΔH are J/mol (or cal/mol)

Units of ΔS are J/mol · K (or cal/mol · K)

1 cal = 4.184 J

Units of absolute temperature, T, are Kelvin, K

25 °C = 298 K

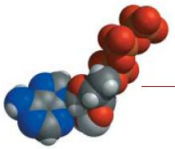
At 25 °C, $RT = 2.479$ kJ/mol

$(= 0.592$ kcal/mol)



"Now, in the *second* law of thermodynamics . . . "

Variación de energía libre de las reacciones químicas. Cálculo de ΔG°´



$$\Delta G'^\circ = -RT \ln K'_{eq}$$

$$\Delta G = \Delta G'^\circ + RT \ln \frac{[C][D]}{[A][B]}$$

Reacciones exergónicas y endergónicas.

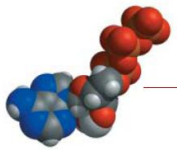
Relationships among K'_{eq}, $\Delta G'^\circ$, and the Direction of Chemical Reactions under Standard Conditions

When K'_{eq} is	$\Delta G'^\circ$ is	Starting with 1 M components the reaction
>1.0	Negative	Proceeds forward
1.0	Zero	Is at equilibrium
<1.0	Positive	Proceeds in reverse

Relationship between the Equilibrium Constants and Standard Free-Energy Changes of Chemical Reactions

	$\Delta G'^\circ$	
K'_{eq}	(kJ/mol)	(kcal/mol)*
10^3	−17.1	−4.1
10^2	−11.4	−2.7
10^1	−5.7	−1.4
1	0.0	0.0
10^{-1}	5.7	1.4
10^{-2}	11.4	2.7
10^{-3}	17.1	4.1
10^{-4}	22.8	5.5
10^{-5}	28.5	6.8
10^{-6}	34.2	8.2

*Although joules and kilojoules are the standard units of energy and are used throughout this text, biochemists sometimes express $\Delta G'^\circ$ values in kilocalories per mole. We have therefore included values in both kilojoules and kilocalories in this table and in Tables 14–4 and 14–6. To convert kilojoules to kilocalories, divide the number of kilojoules by 4.184.



Aditividad del ΔGº’

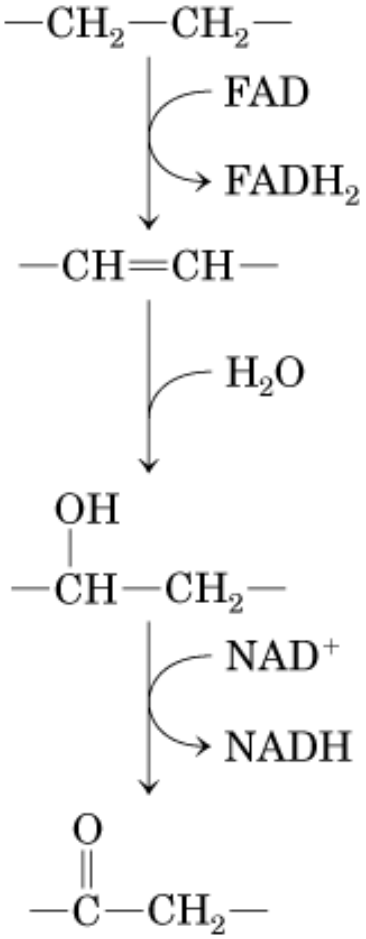
Cálculo de ΔG°´ Para la reacción $\mathbf{A \longrightarrow C}$

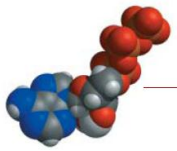
$$
\begin{array}{lllll}
(1) & \mathrm{A} \longrightarrow \mathrm{B} & \Delta G_1'^{\circ} & & \\
(2) & \mathrm{B} \longrightarrow \mathrm{C} & \Delta G_2'^{\circ} & & \\
\hline
\textit{Sum:} & \mathrm{A} \longrightarrow \mathrm{C} & \Delta G_1'^{\circ} & + & \Delta G_2'^{\circ}
\end{array}
$$

Energía de los enlaces químicos

most energy → least energy

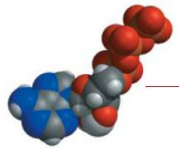
	Methane	Methanol	Formaldehyde	Formic acid	Carbon dioxide
$\Delta G^\circ_{oxidation}$ (kcal mol^{-1})	−196	−168	−125	−68	0
$\Delta G^\circ_{oxidation}$ (kJ mol^{-1})	−820	−703	−523	−285	0

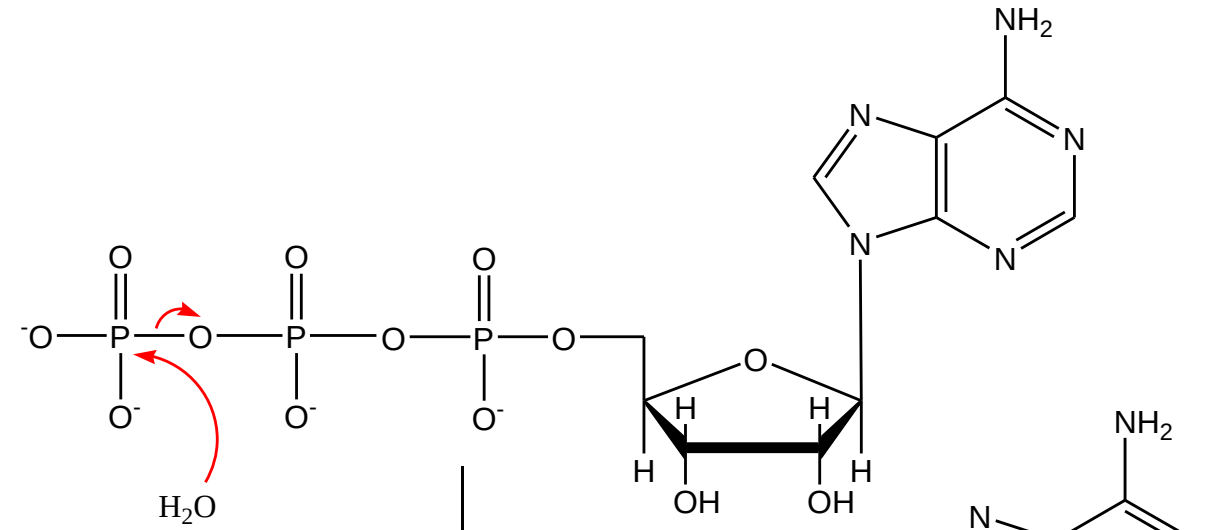


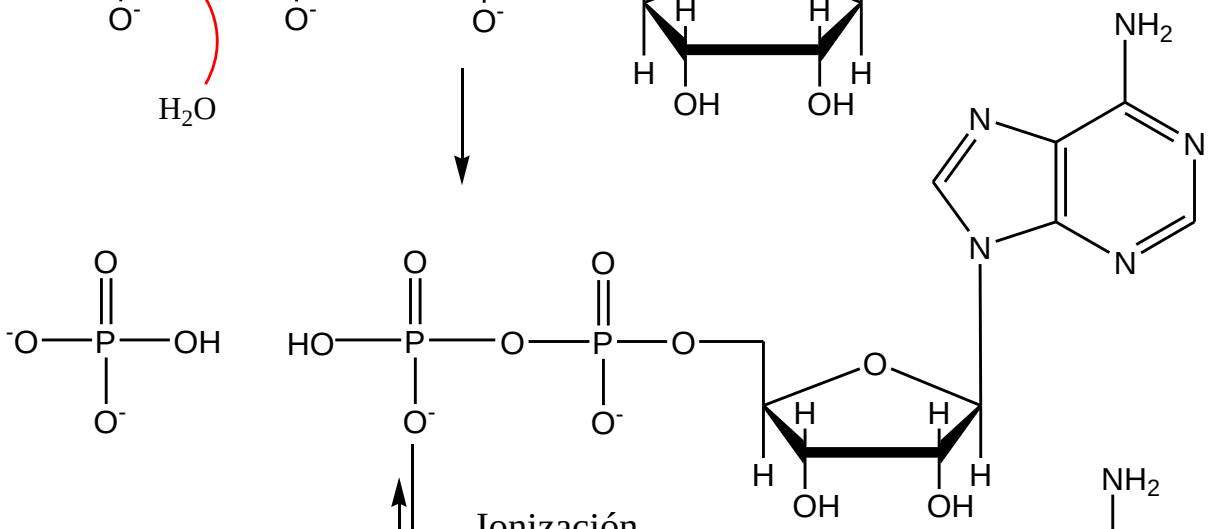


Standard Free-Energy Changes of Some Chemical Reactions at pH 7.0 and 25 °C (298 K)

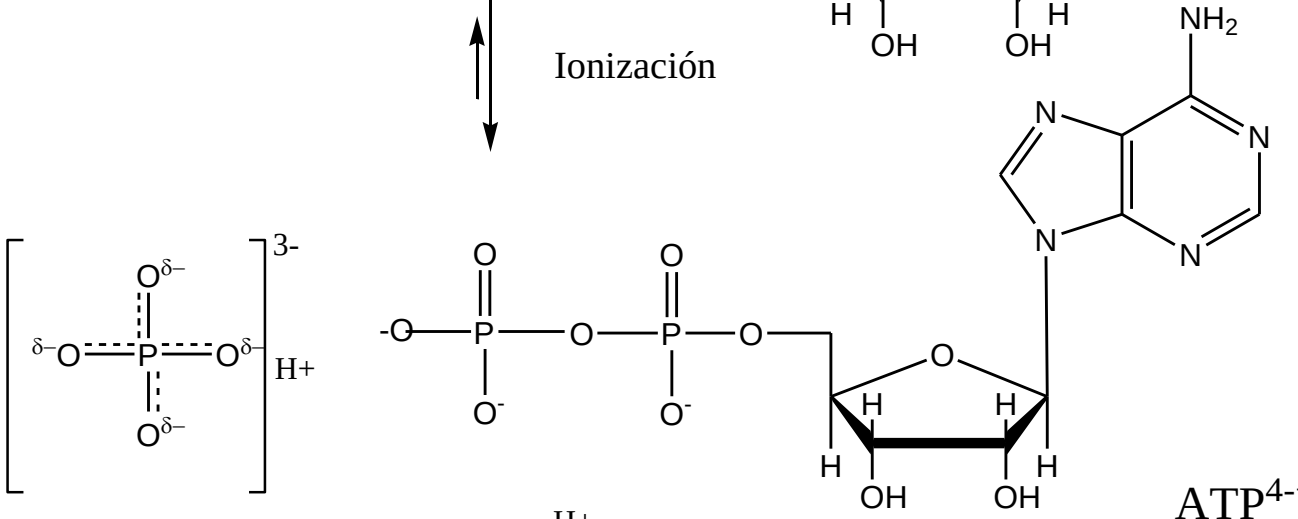
Reaction type	$\Delta G'°$ (kJ/mol)	$\Delta G'°$ (kcal/mol)
Hydrolysis reactions		
Acid anhydrides		
Acetic anhydride + $H_2O \longrightarrow$ 2 acetate	−91.1	−21.8
ATP + $H_2O \longrightarrow$ ADP + P_i	−30.5	−7.3
ATP + $H_2O \longrightarrow$ AMP + PP_i	−45.6	−10.9
PP_i + $H_2O \longrightarrow$ $2P_i$	−19.2	−4.6
UDP-glucose + $H_2O \longrightarrow$ UMP + glucose 1-phosphate	−43.0	−10.3
Esters		
Ethyl acetate + $H_2O \longrightarrow$ ethanol + acetate	−19.6	−4.7
Glucose 6-phosphate + $H_2O \longrightarrow$ glucose + P_i	−13.8	−3.3
Amides and peptides		
Glutamine + $H_2O \longrightarrow$ glutamate + NH_4^+	−14.2	−3.4
Glycylglycine + $H_2O \longrightarrow$ 2 glycine	−9.2	−2.2
Glycosides		
Maltose + $H_2O \longrightarrow$ 2 glucose	−15.5	−3.7
Lactose + $H_2O \longrightarrow$ glucose + galactose	−15.9	−3.8
Rearrangements		
Glucose 1-phosphate $\longrightarrow$ glucose 6-phosphate	−7.3	−1.7
Fructose 6-phosphate $\longrightarrow$ glucose 6-phosphate	−1.7	−0.4
Elimination of water		
Malate $\longrightarrow$ fumarate + H_2O	3.1	0.8
Oxidations with molecular oxygen		
Glucose + $6O_2 \longrightarrow 6CO_2 + 6H_2O$	−2,840	−686
Palmitate + $23O_2 \longrightarrow 16CO_2 + 16H_2O$	−9,770	−2,338







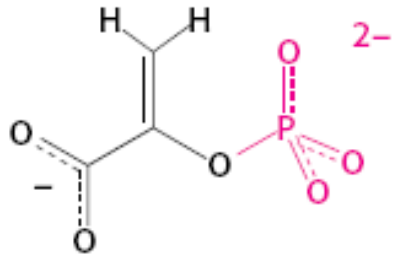
Ionización



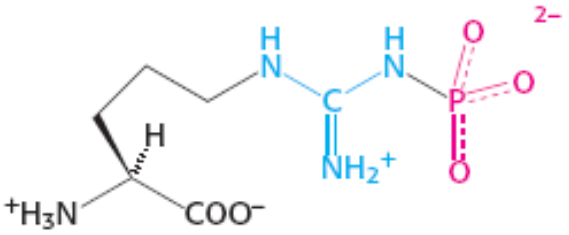
$\Delta G^{o'}$ = -30,5KJ/mol
= -7,3 Kcal/mol

$ATP^{4-} + H_2O \rightarrow ADP^{3-} + Pi^{2-} + H^+$

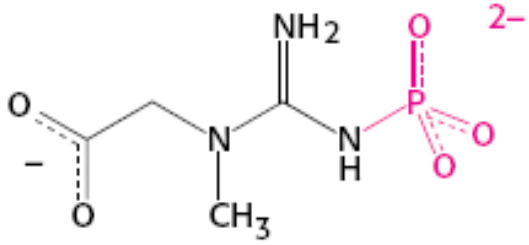
Otras moléculas fosforiladas



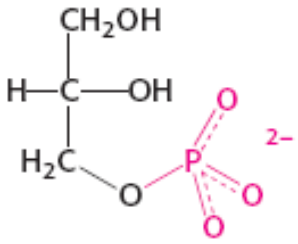
Phosphoenolpyruvate



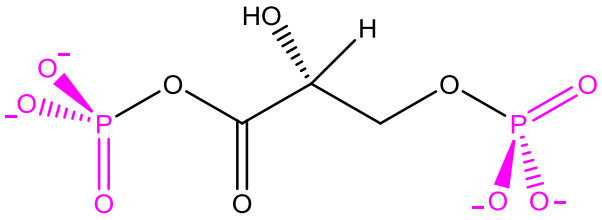
Arginine phosphate



Creatine phosphate



Glycerol 3-phosphate

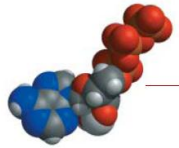


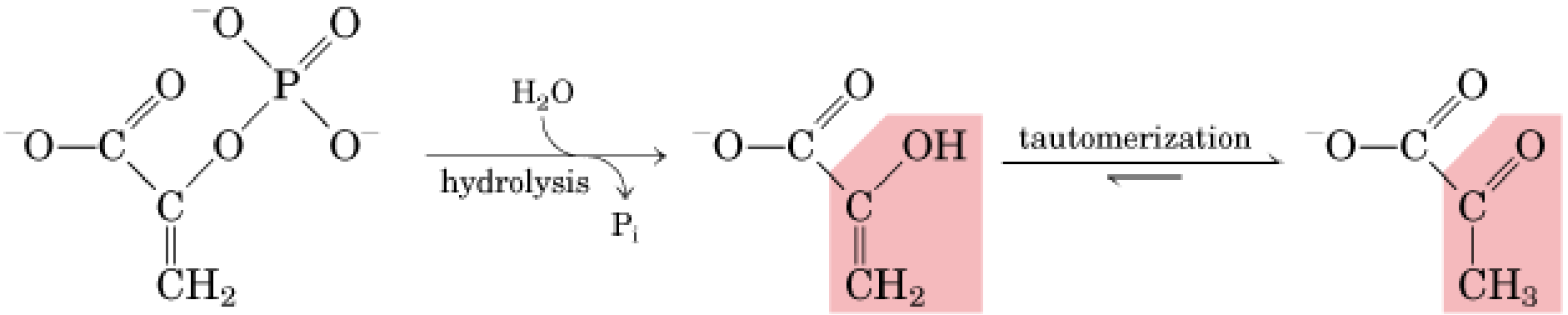
1,3-Bisphosphoglycerate

Standard Free Energies of Hydrolysis of Some Phosphorylated Compounds and Acetyl-CoA (a Thioester)

	$\Delta G'^{\circ}$	
	(kJ/mol)	(kcal/mol)
Phosphoenolpyruvate	−61.9	−14.8
1,3-bisphosphoglycerate (⟶ 3-phosphoglycerate + P_i)	−49.3	−11.8
Phosphocreatine	−43.0	−10.3
ADP (⟶ AMP + P_i)	−32.8	−7.8
ATP (⟶ ADP + P_i)	−30.5	−7.3
ATP (⟶ AMP + PP_i)	−45.6	−10.9
AMP (⟶ adenosine + P_i)	−14.2	−3.4
PP_i (⟶ $2P_i$)	−19	−4.0
Glucose 1-phosphate	−20.9	−5.0
Fructose 6-phosphate	−15.9	−3.8
Glucose 6-phosphate	−13.8	−3.3
Glycerol 1-phosphate	−9.2	−2.2
Acetyl-CoA	−31.4	−7.5

Source: Data mostly from Jencks, W.P. (1976) in *Handbook of Biochemistry and Molecular Biology*, 3rd edn (Fasman, G.D., ed.), *Physical and Chemical Data*, Vol. I, pp. 296–304, CRC Press, Boca Raton, FL.





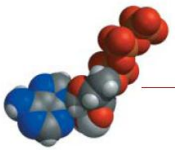
PEP

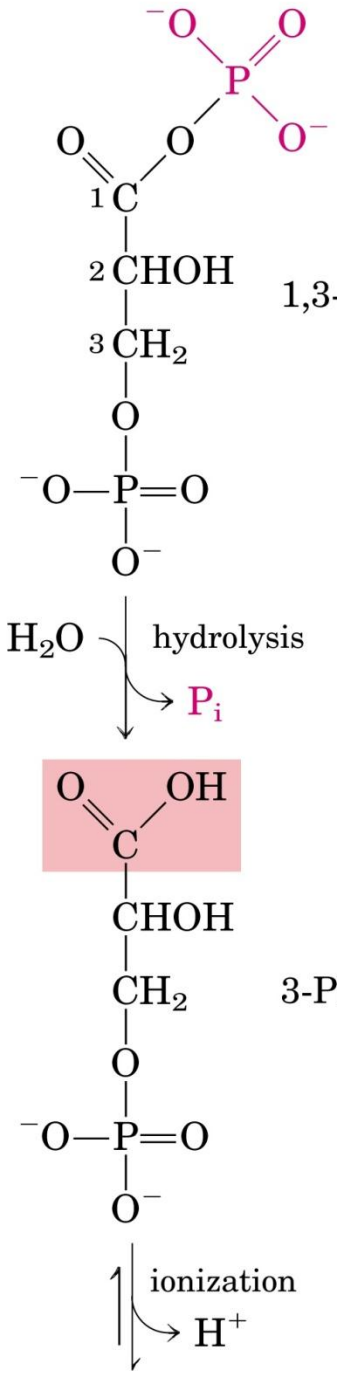
Pyruvate
(enol form)

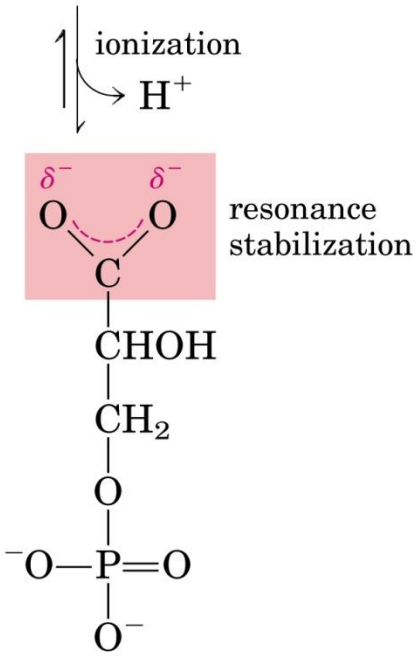
Pyruvate
(keto form)

$$PEP^{3-} + H_2O \longrightarrow pyruvate^- + P_i^{2-}$$

$$\Delta G'^\circ = -61.9 \text{ kJ/mol}$$

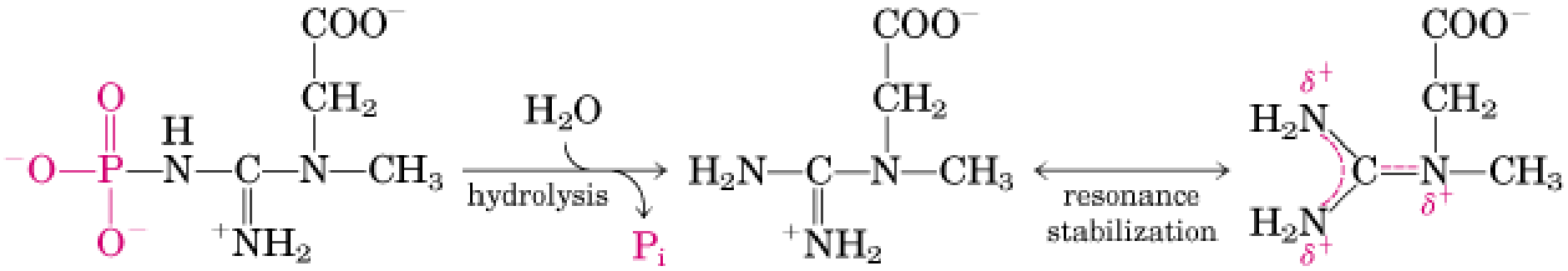






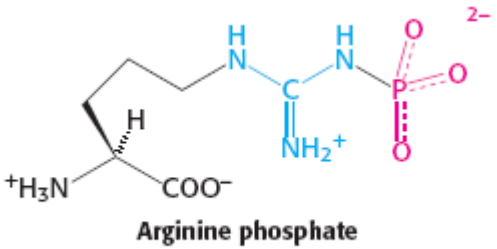
$$1,3\text{-Bisphosphoglycerate}^{4-} + H_2O \longrightarrow 3\text{-phosphoglycerate}^{3-} + P_i^{2-} + H^+$$

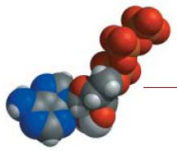
$$\Delta G'^\circ = -49.3 \text{ kJ/mol}$$

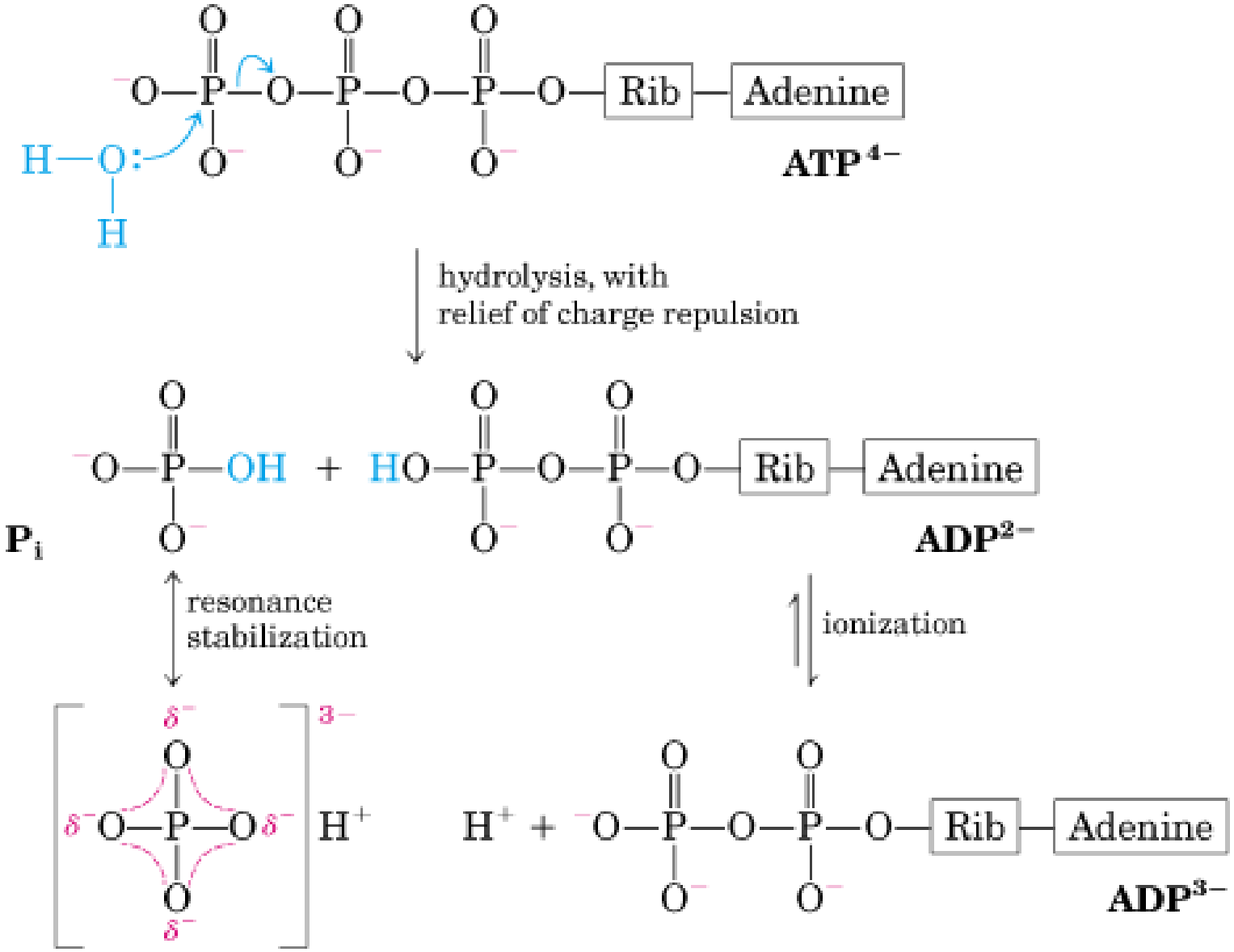


$$\text{Phosphocreatine}^{2-} + H_2O \longrightarrow \text{creatine} + P_i^{2-}$$
$$\Delta G'^{\circ} = -43.0 \text{ kJ/mol}$$

En invertebrados el rol lo cumple

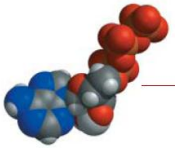




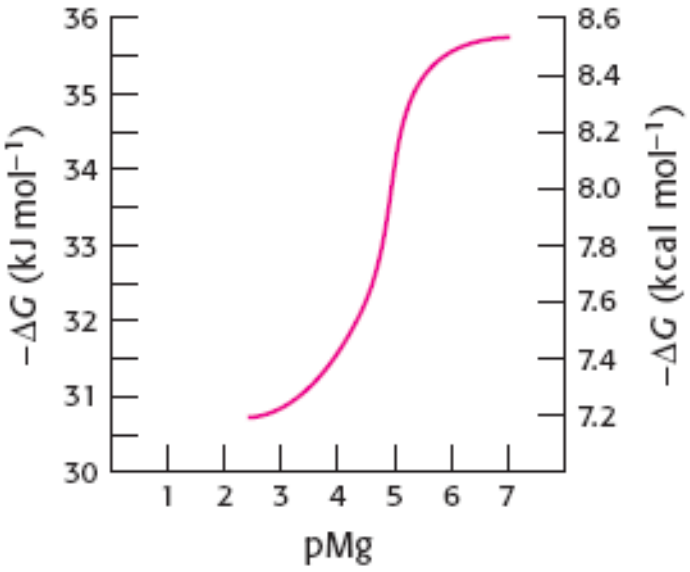


$$ATP^{4-} + H_2O \longrightarrow ADP^{3-} + P_i^{2-} + H^+$$

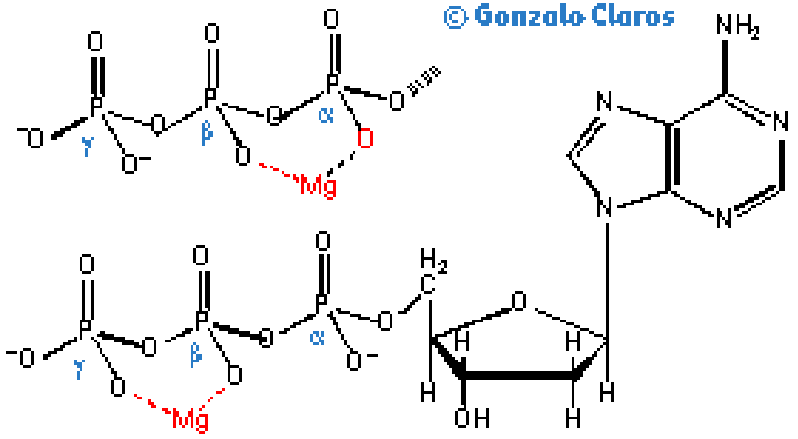
$$\Delta G'^{\circ} = -30.5 \text{ kJ/mol}$$



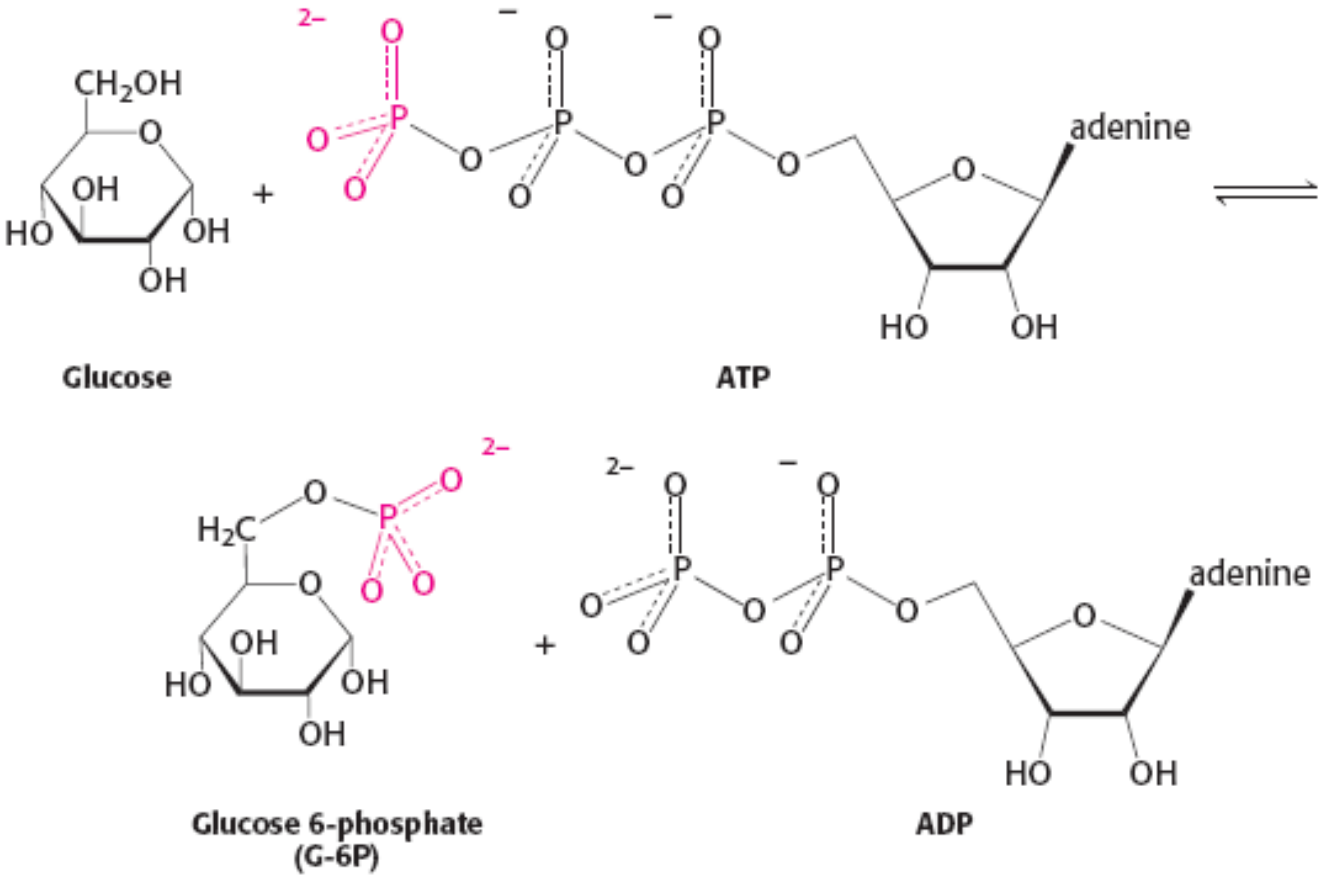
Cambios en el $\Delta G^{o'}$ de hidrólisis de ATP en función de la concentración de Mg^{++}



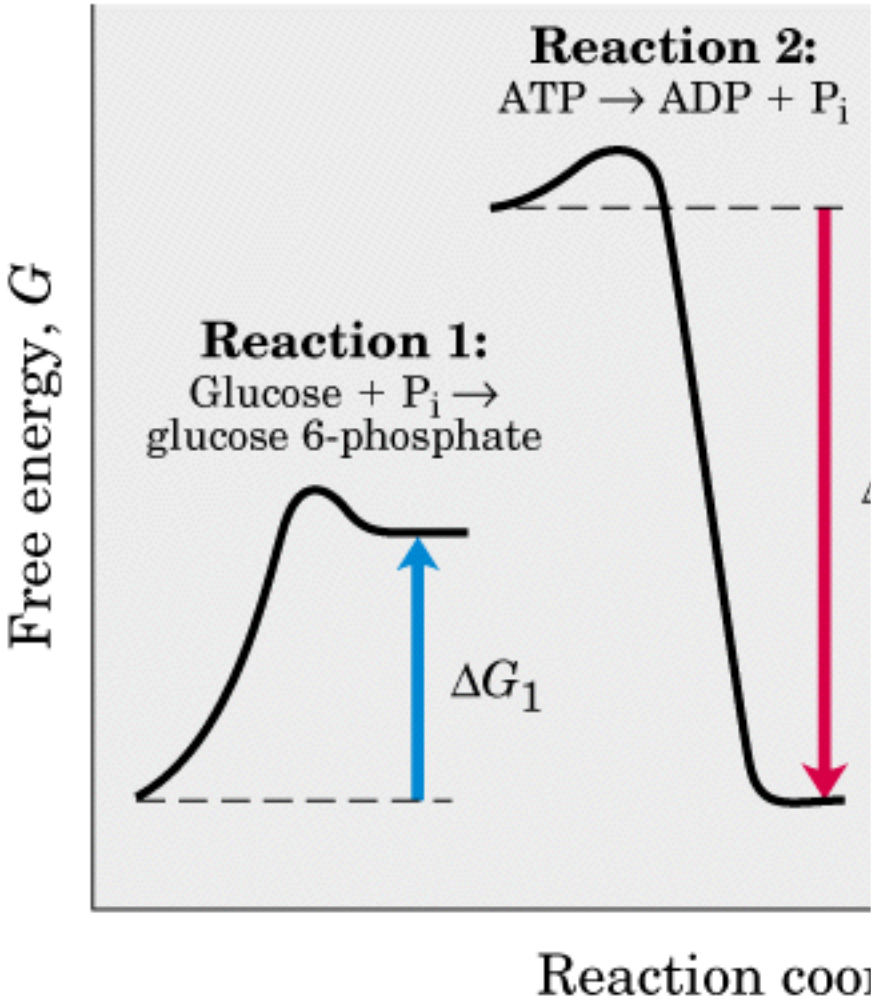
$(\mathrm{pMg} = \log 1/[\mathrm{Mg}^{2+}])$



Fosforilación de glucosa



$\Delta G^{o'}$= -5 Kcal/mol



$\Delta G_3^{o'}$= 3 Kcal/mol

$\Delta G_3^{o'}$= -7,3 Kcal/mol

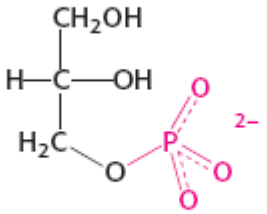
Fosforilación de glicerol

$$\text{ATP} + \text{H}_2\text{O} \rightleftharpoons \text{ADP} + \text{P}_\text{i} + \text{H}^+$$

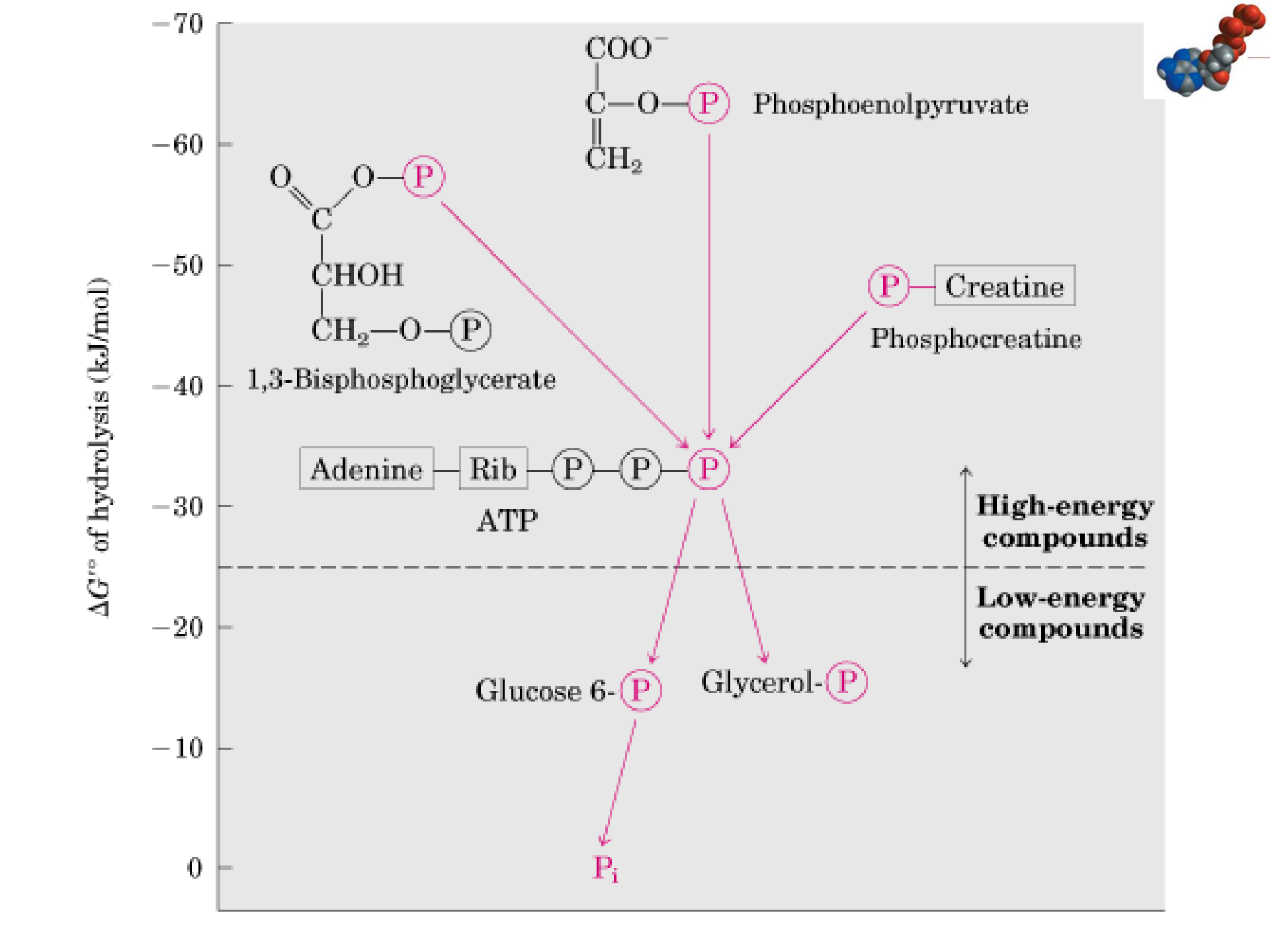
$$\Delta G^{\circ\prime} = -7.3\ \text{kcal mol}^{-1}\ (-30.5\ \text{kJ mol}^{-1})$$

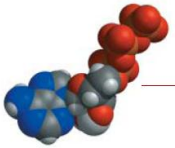
$$\text{Glycerol 3-phosphate} + \text{H}_2\text{O} \rightleftharpoons \text{glycerol} + \text{P}_\text{i}$$

$$\Delta G^{\circ\prime} = -2.2\ \text{kcal mol}^{-1}\ (-9.2\ \text{kJ mol}^{-1})$$



Glycerol 3-phosphate


−70
−60
−50
−40
−30
−20
−10
0
ΔG'° of hydrolysis (kJ/mol)
COO⁻
C—O—P
CH₂
Phosphoenolpyruvate
O
O—P
C
CHOH
CH₂—O—P
1,3-Bisphosphoglycerate
P—Creatine
Phosphocreatine
Adenine
Rib
P
P
P
ATP
High-energy compounds
Low-energy compounds
Glucose 6-P
Glycerol-P
Pi

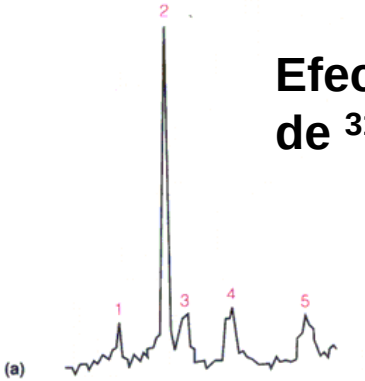


$$\text{Creatine phosphate} + \text{ADP} + \text{H}^+ \underset{}{\overset{\text{Creatine kinase}}{\rightleftharpoons}} \text{ATP} + \text{creatine}$$

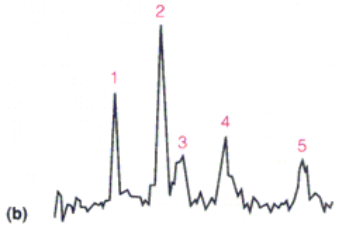
Adenine Nucleotide, Inorganic Phosphate, and Phosphocreatine Concentrations in Some Cells*

	Concentration (mM)				
	ATP	**ADP†**	**AMP**	**P_i**	**PCr**
Rat hepatocyte	3.38	1.32	0.29	4.8	0
Rat myocyte	8.05	0.93	0.04	8.05	28
Rat neuron	2.59	0.73	0.06	2.72	4.7
Human erythrocyte	2.25	0.25	0.02	1.65	0
E. coli cell	7.90	1.04	0.82	7.9	0

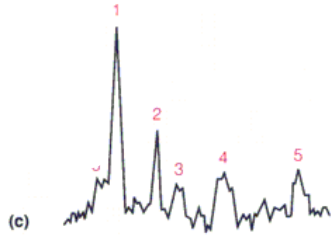
Efecto del ejercicio anaerobio sobre los espectros de RMN de ^{31}P del músculo de antebrazo humano



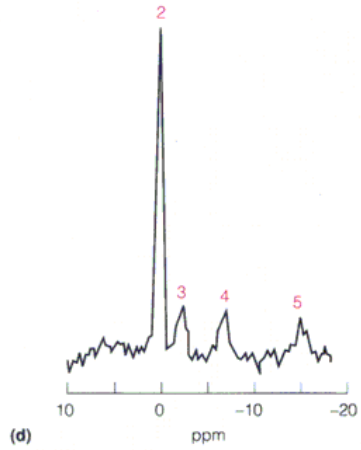
a) Antes del ejercicio



b) Primer minuto de un período de ejercicio de 19 minutos



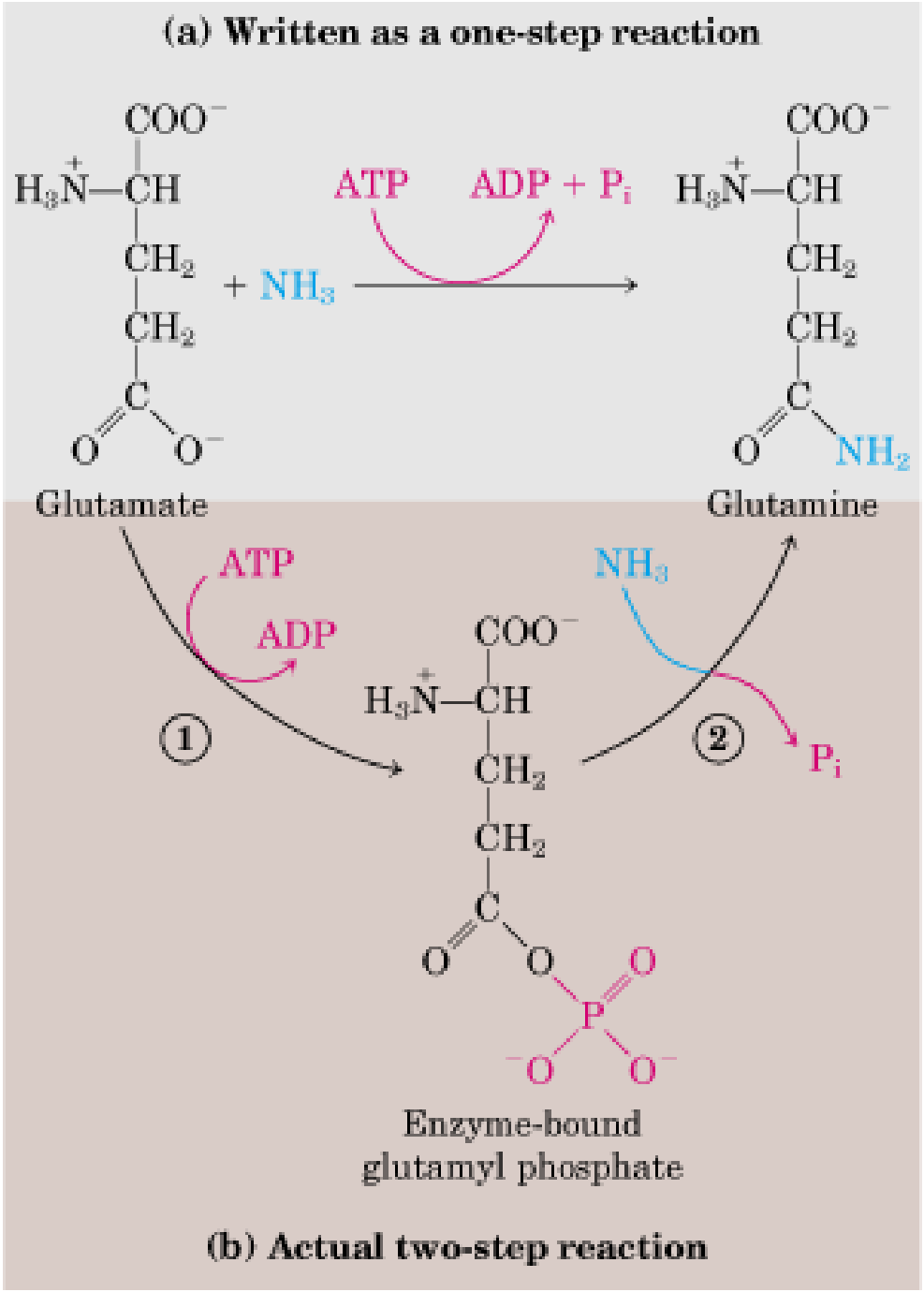
c) Minuto 19

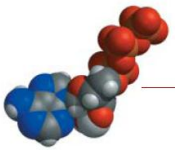


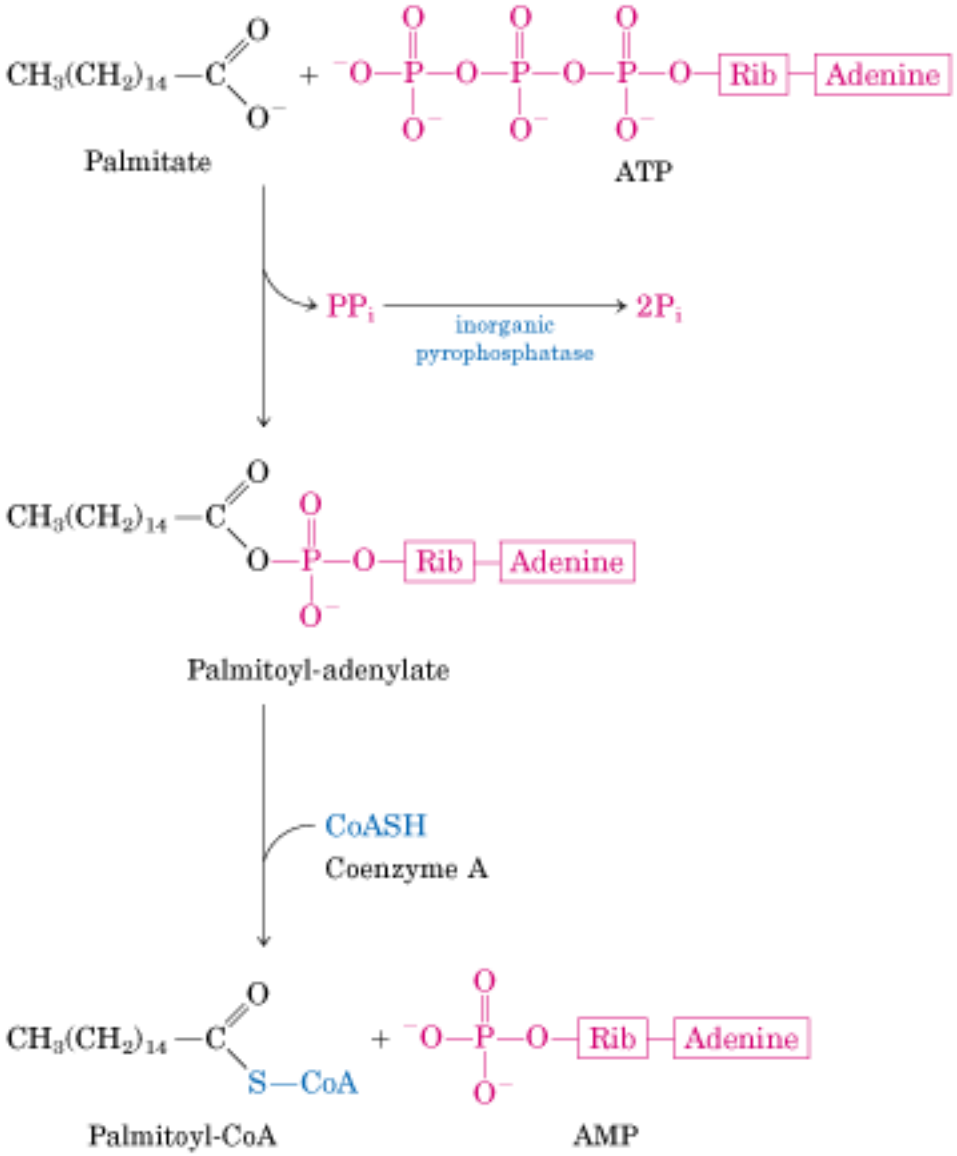
d) Reposo de 10 minutos después del ejercicio

1 Pi
2 Fosfocreatina
3 ATP γ-fosfato
4 ATP α-fosfato
5 ATP β-fosfato

Rol de ATP en biosíntesis de Gln







Overall reaction:

Palmitate + ATP + CoASH ⟶ palmitoyl-CoA + AMP + $2P_i$

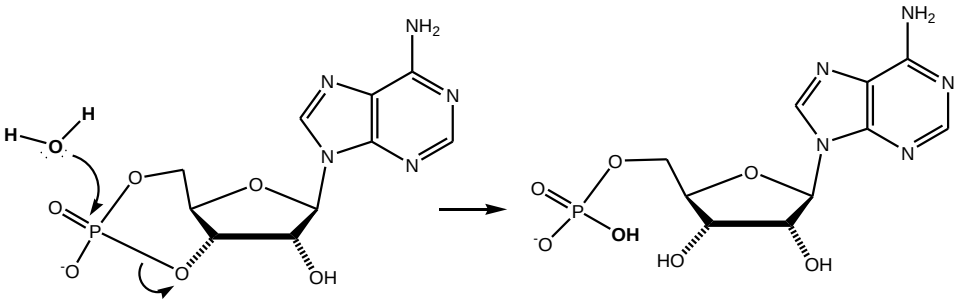
$\Delta G'^{\circ} = -32.5$ kJ/mol

Mononucleótidos 5’,3’-cíclicos

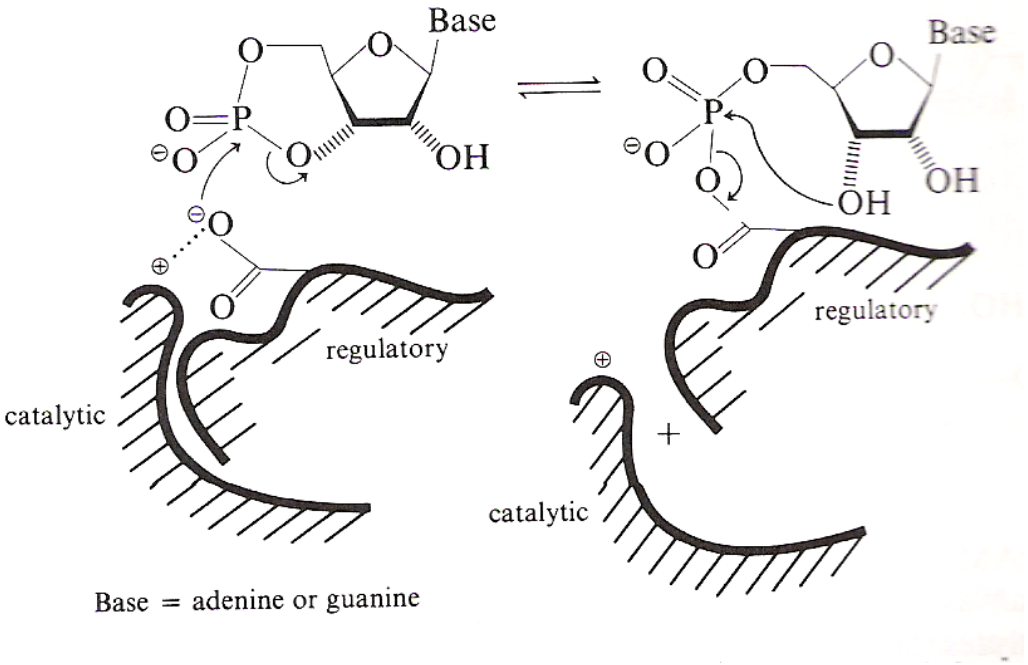
AMPc y GMPc son estructuras de alta energía

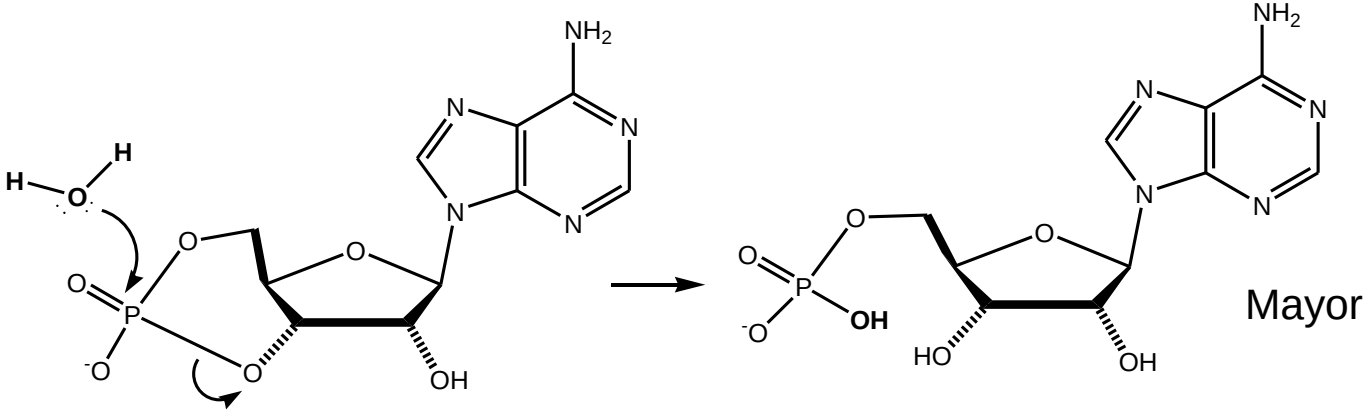
$\Delta G^{o'}_{hydr}$ (pH 7,3) -12,5 KJ/mol o – 3 Kcal/mol

$\Delta H^{o'}_{hydr}$ AMPc es -59,2 KJ/mol (-14.1 Kcal/mol)



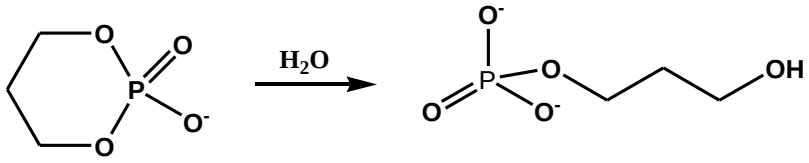
Su unión a las subunidades regulatorias de algunas enzimas (Ej. Protein quinasas)





Mayor energía de hidrólisis

ΔH°'= - 59,2 KJ/mol (-14,1Kcal/mol)

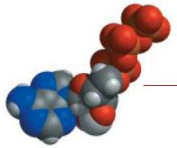


Menor energía de hidrólisis

ΔH°'= -12,6 KJ/mol (-3 Kcal/mol)

Para justificar la alta energía por la simple hidrólisis del anillo de seis miembros deberían coincidir los valores de ΔH

Se atribuye la mayor energía de hidrólisis del AMPc a que el éter cíclico de seis miembros esta sobre un anillo transfusionado



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