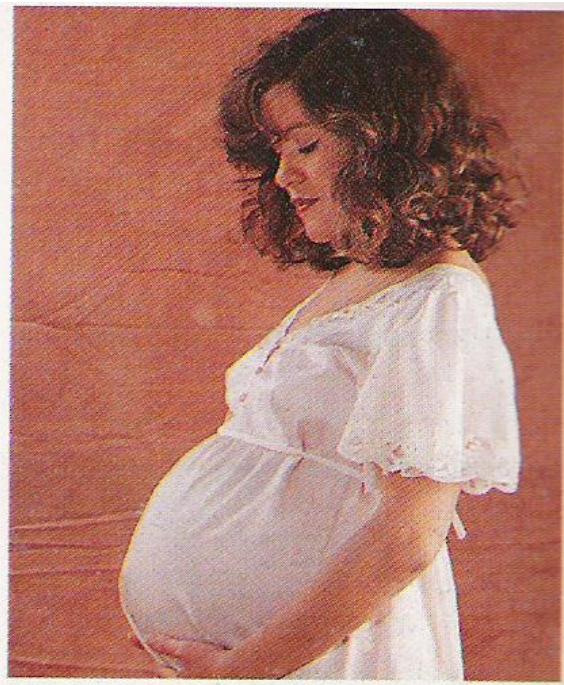
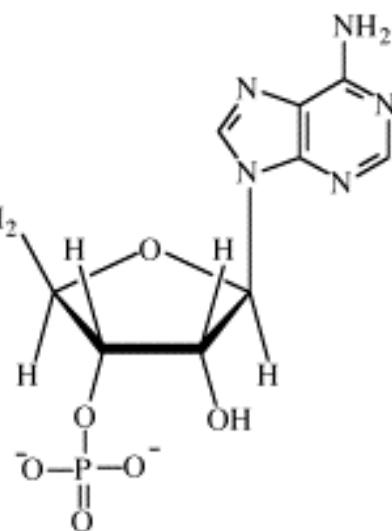
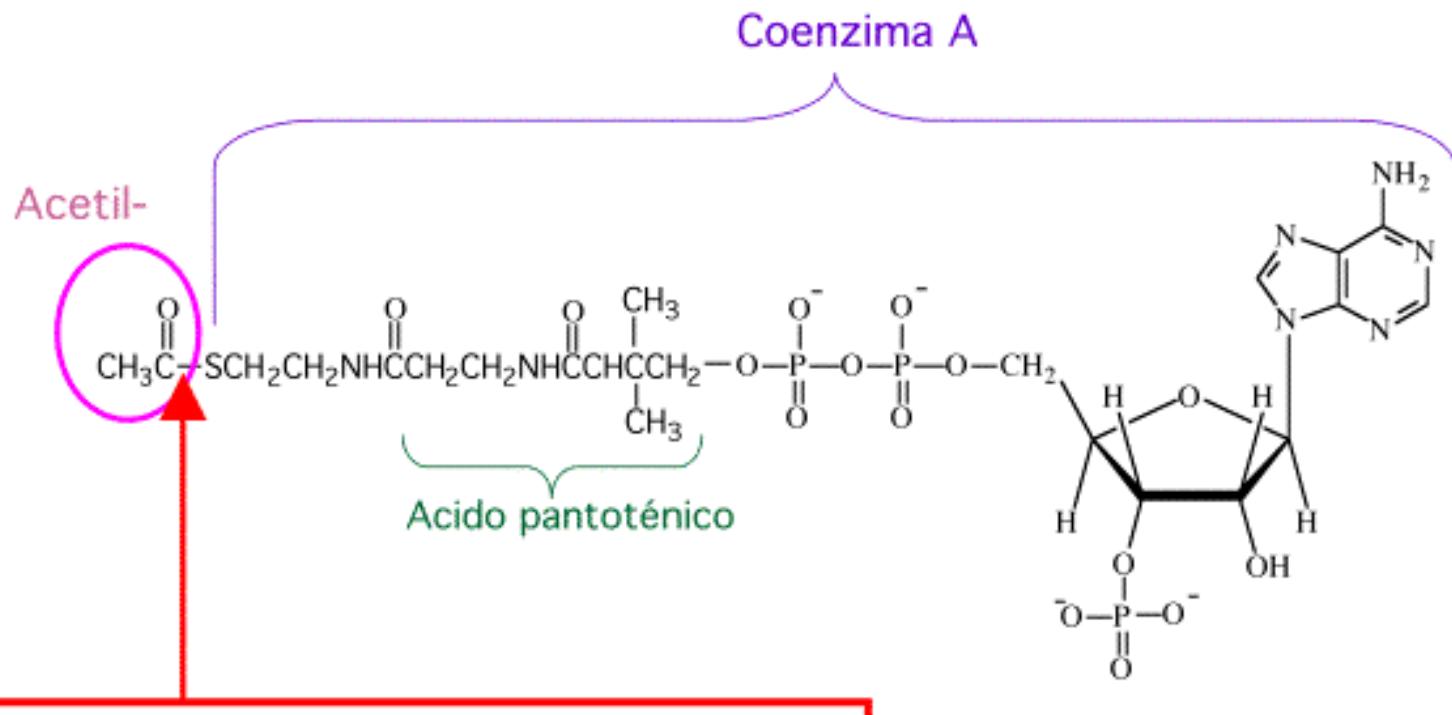


Tema 4: Esteroides. Estructuras análisis conformacional. Reacciones





Enlace tioéster de alta energía: su hidrólisis libera energía al transferirse el grupo acetilo

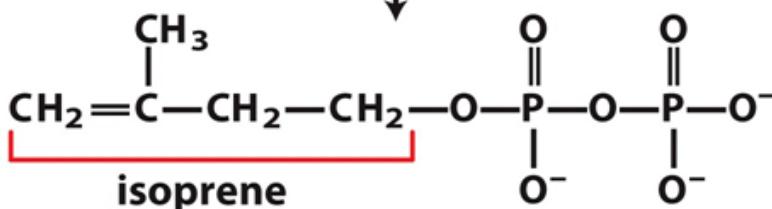
$3 \text{CH}_3-\text{COO}^-$ Acetate

1



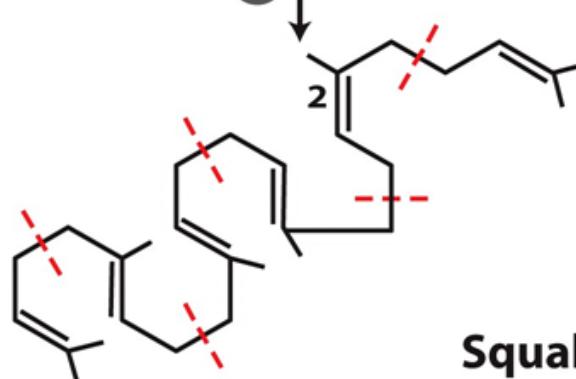
Mevalonate

2



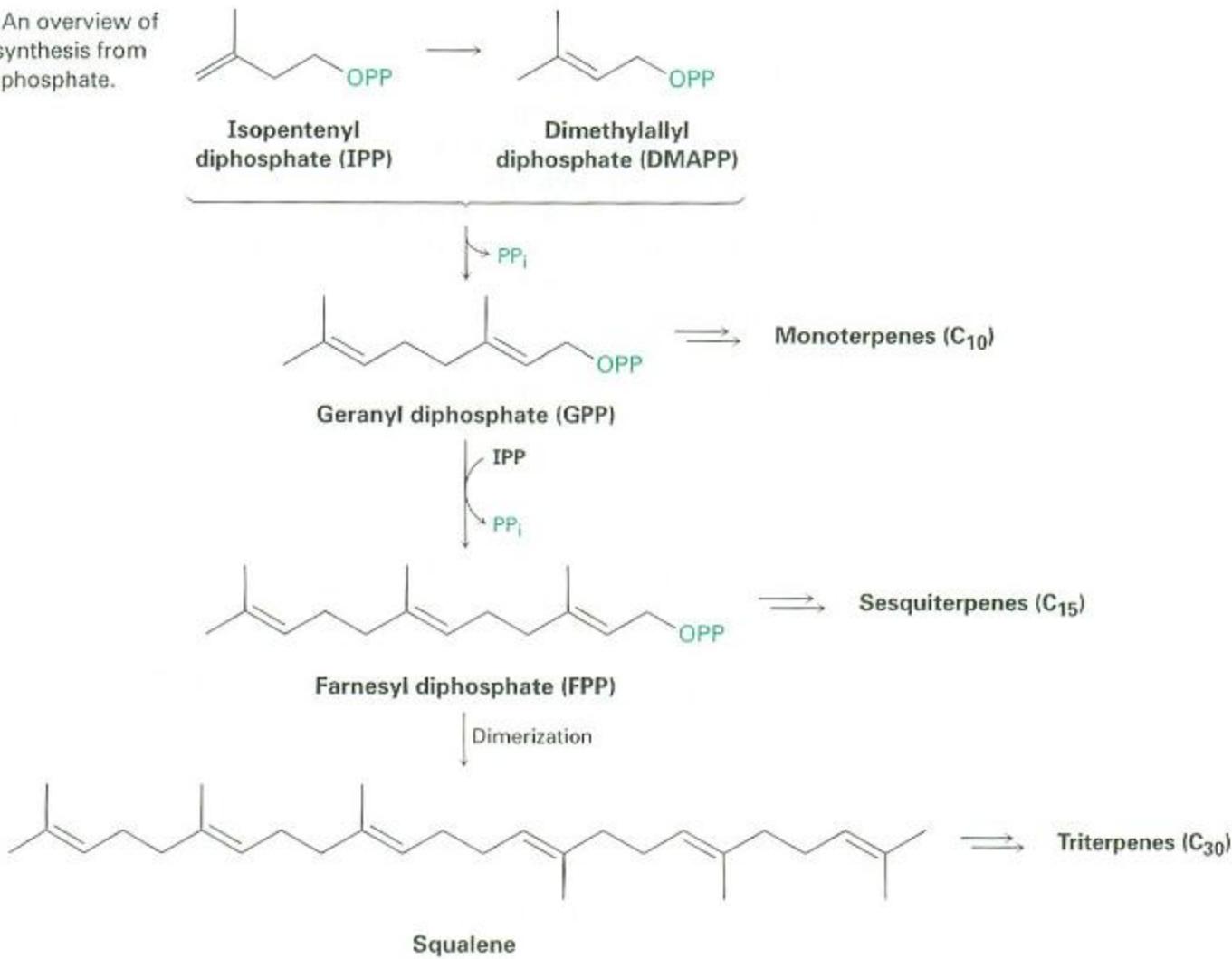
Activated isoprene

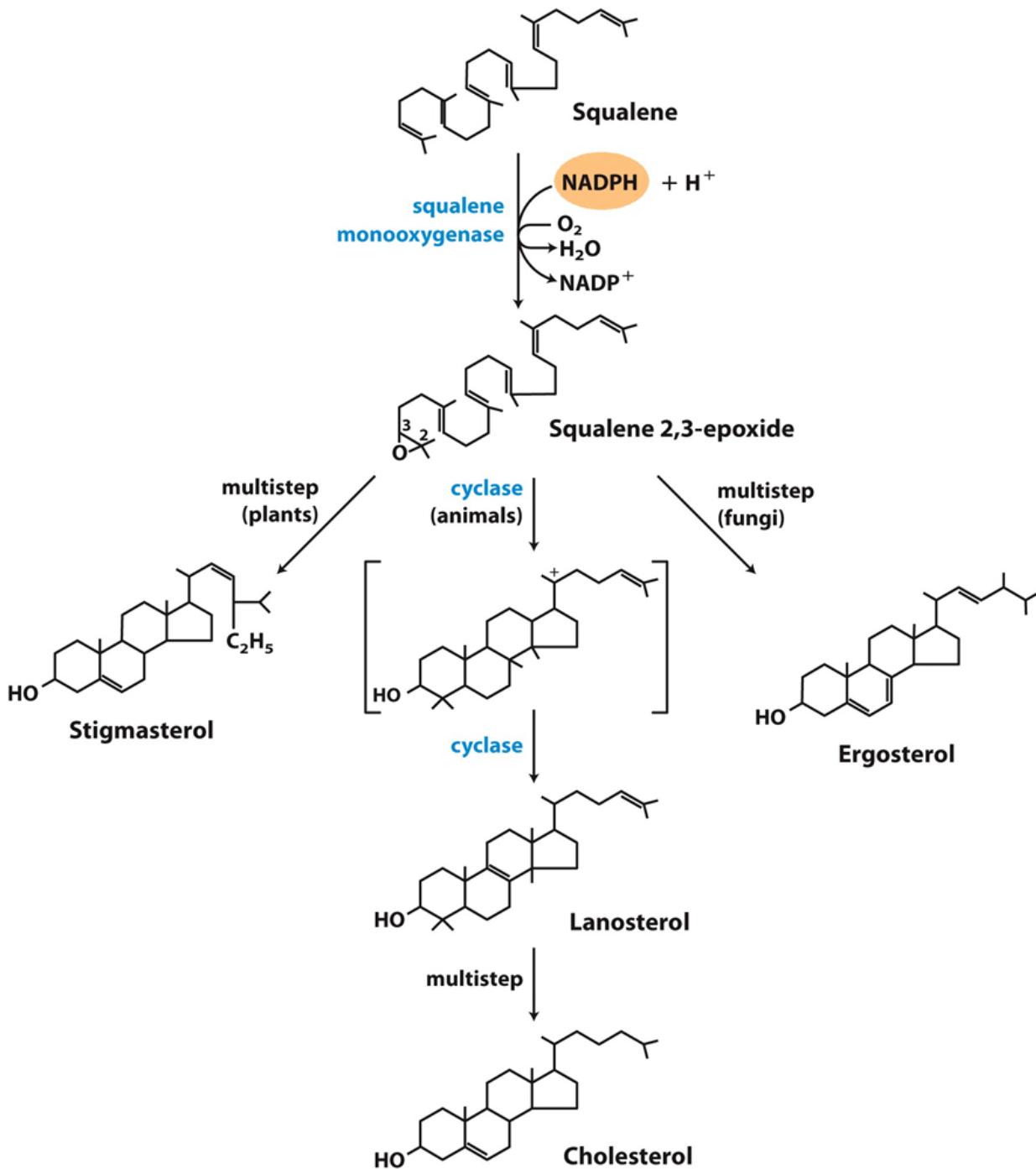
3

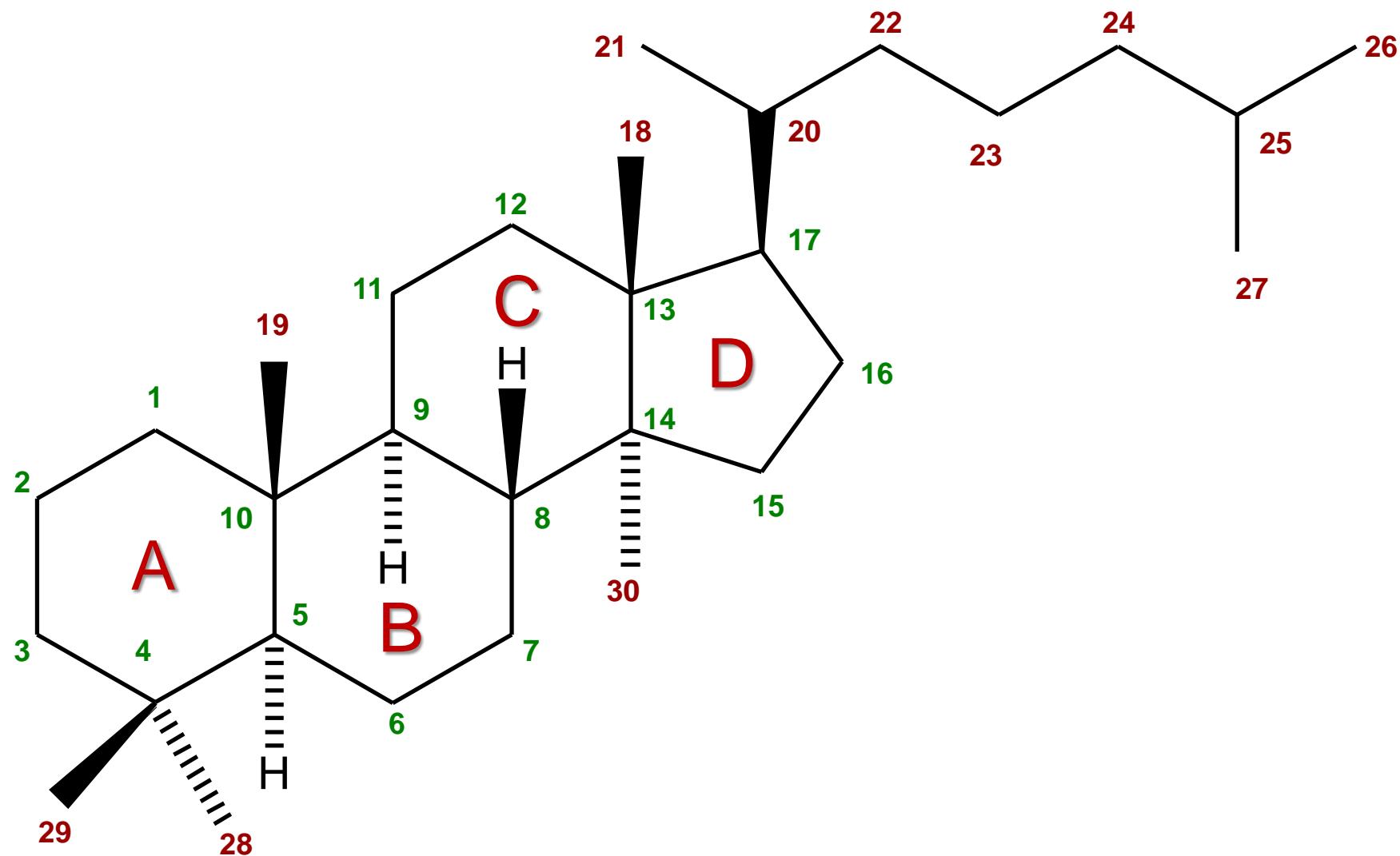


Squalene

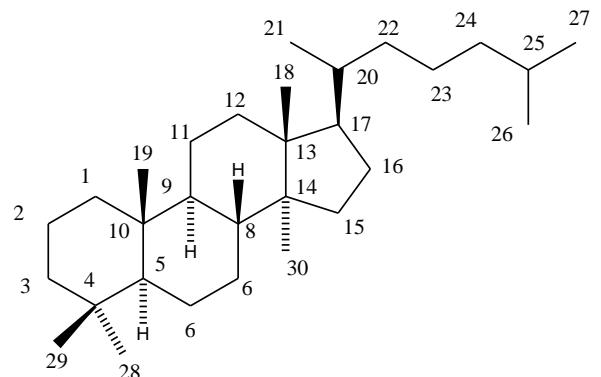
Figure 27.8 An overview of terpenoid biosynthesis from isopentenyl diphosphate.



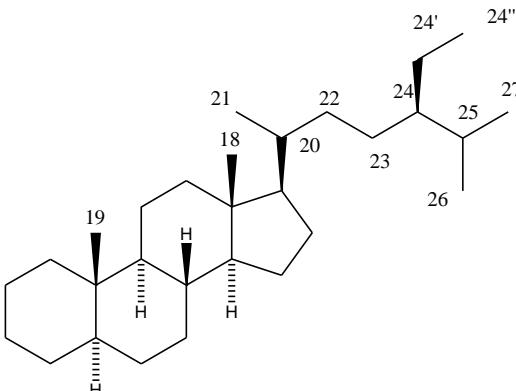




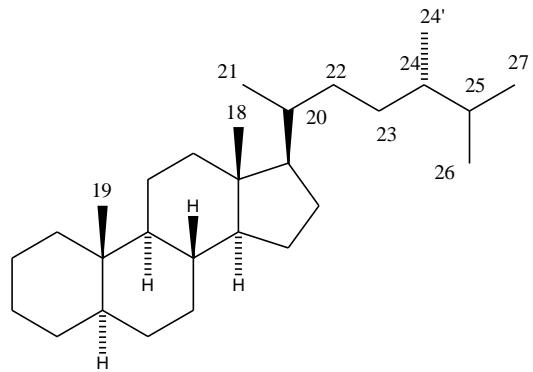
lanostano C30



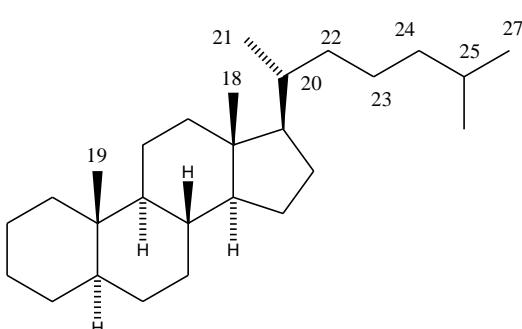
lanostano C30



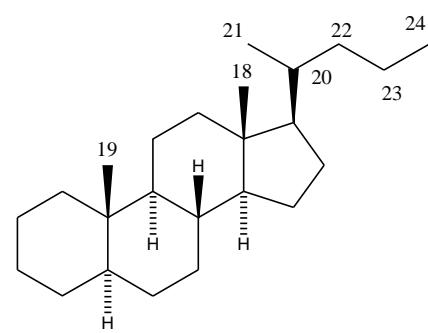
stigmastano C29



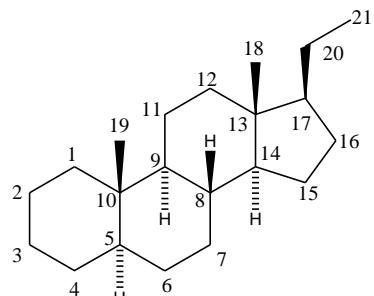
ergostano C28



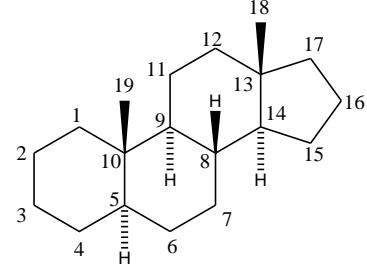
colestano C27



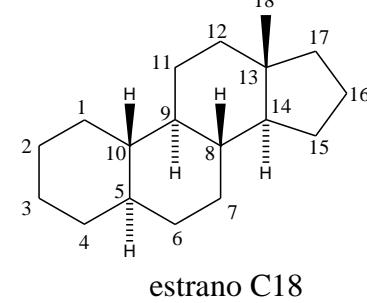
colano C24



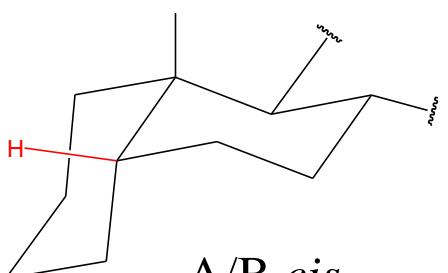
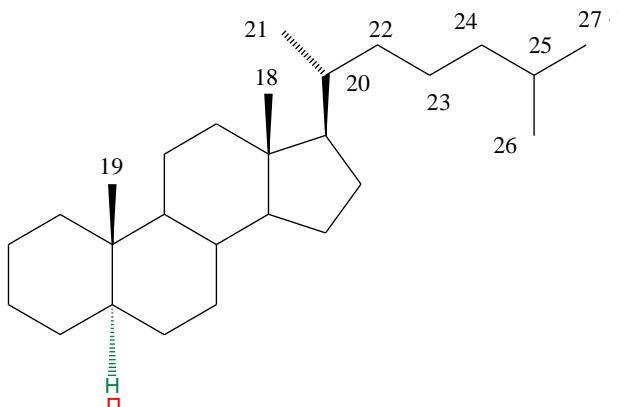
pregnano C21



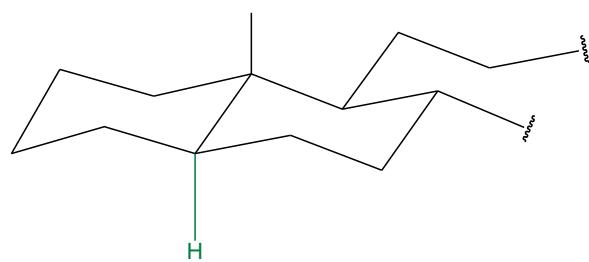
androstano C19



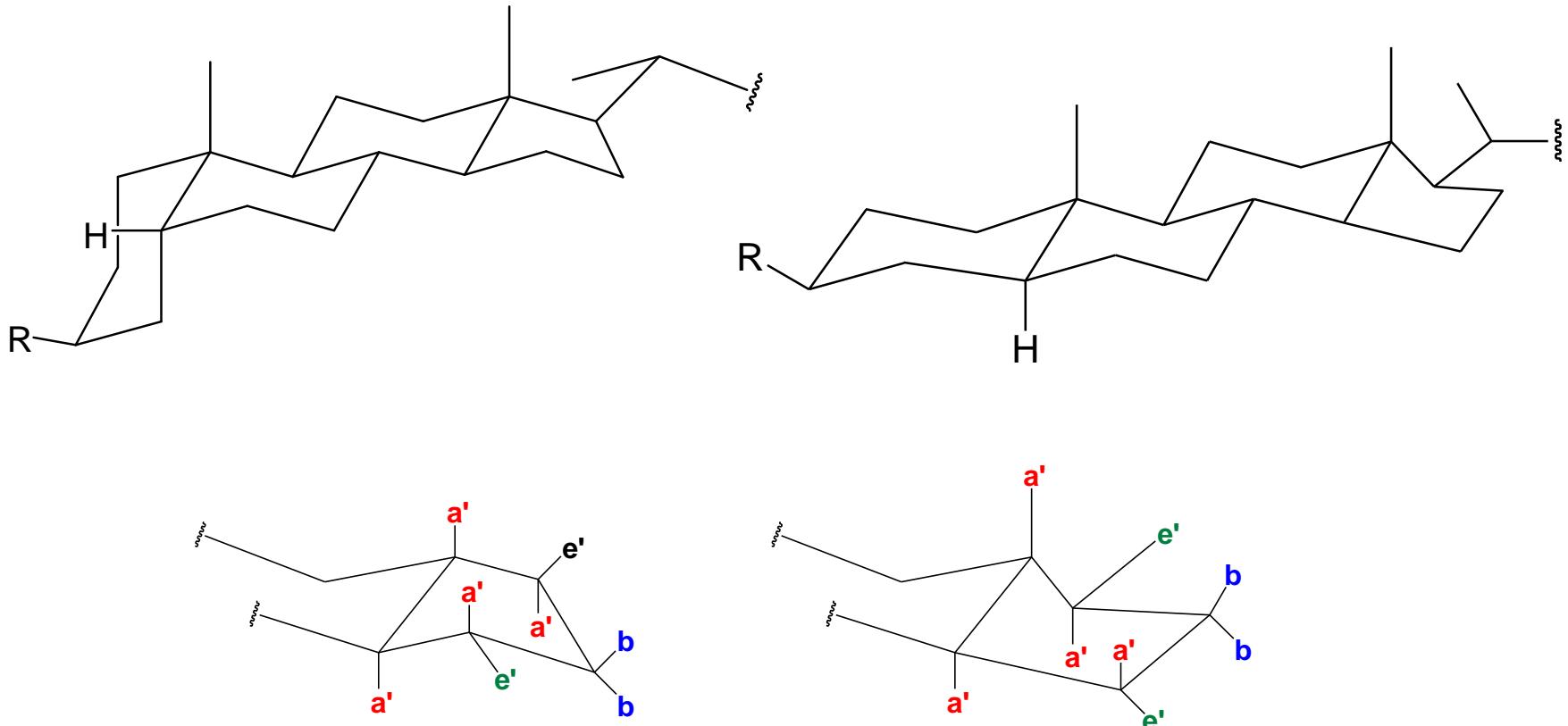
estrano C18



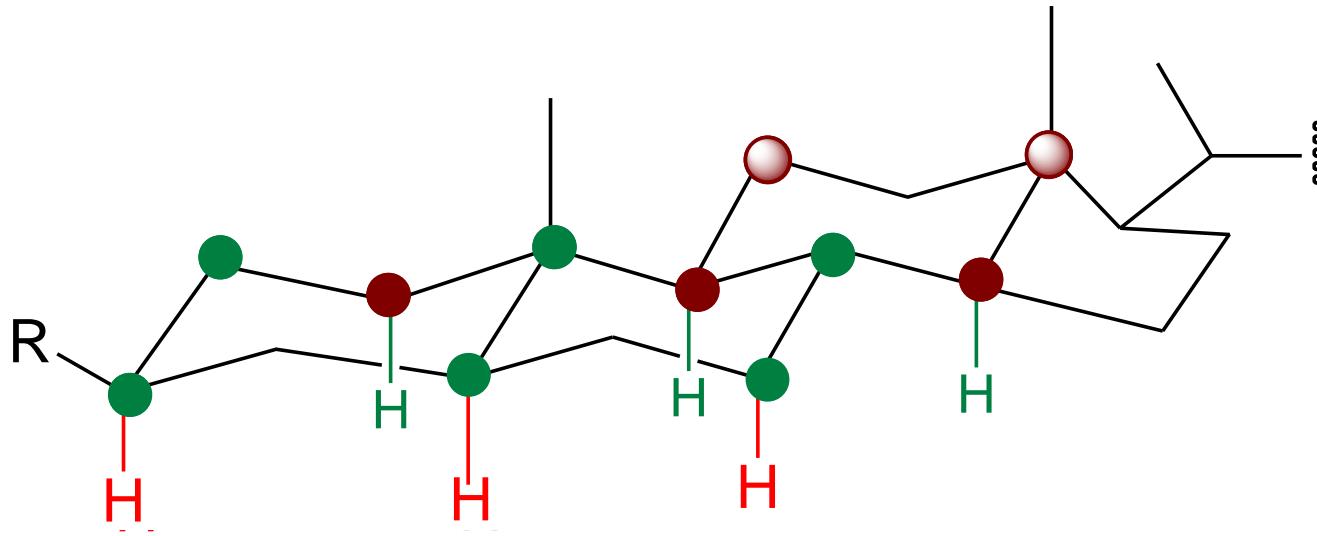
A/B *cis*
serie 5β
serie coprostanolo



A/B *trans*
serie 5α
serie colestanolo



a' = seudoaxial
 e' = seudoecuatorial
 b = biseccional



En un plano **H α de C-3, C-5 y C-7**

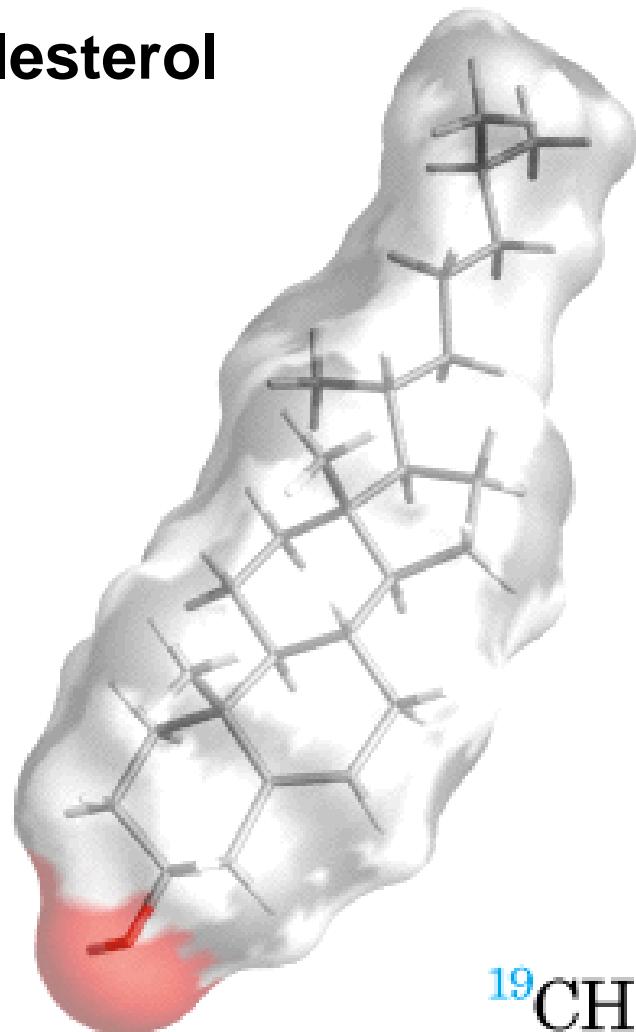
En un plano **H α de C-1, C-9 y C-14**

En un plano los pares de átomos **C2-C3, C10-C5, C8-C7**

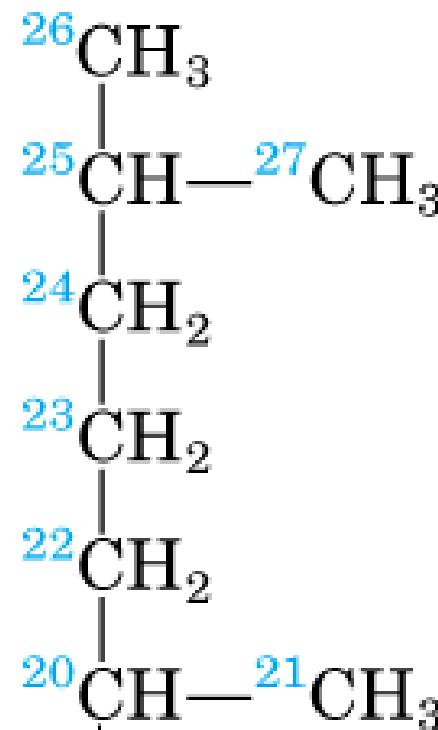
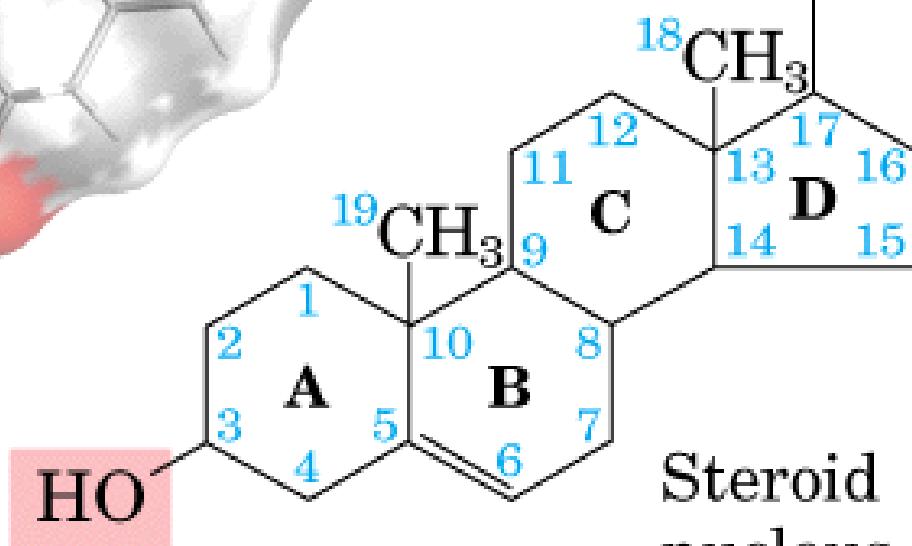
En un plano los de átomos **C-1, C-9 y C14**

En un plano paralelo al anterior y separado a 0,77 A (la mitad de un enlace C-C) **los de átomos C-11y C13**

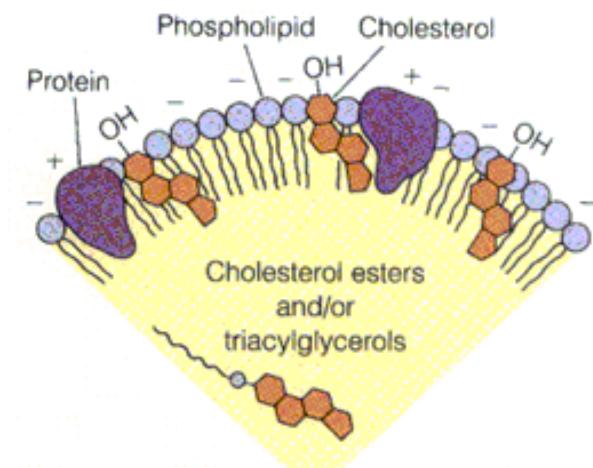
Colesterol



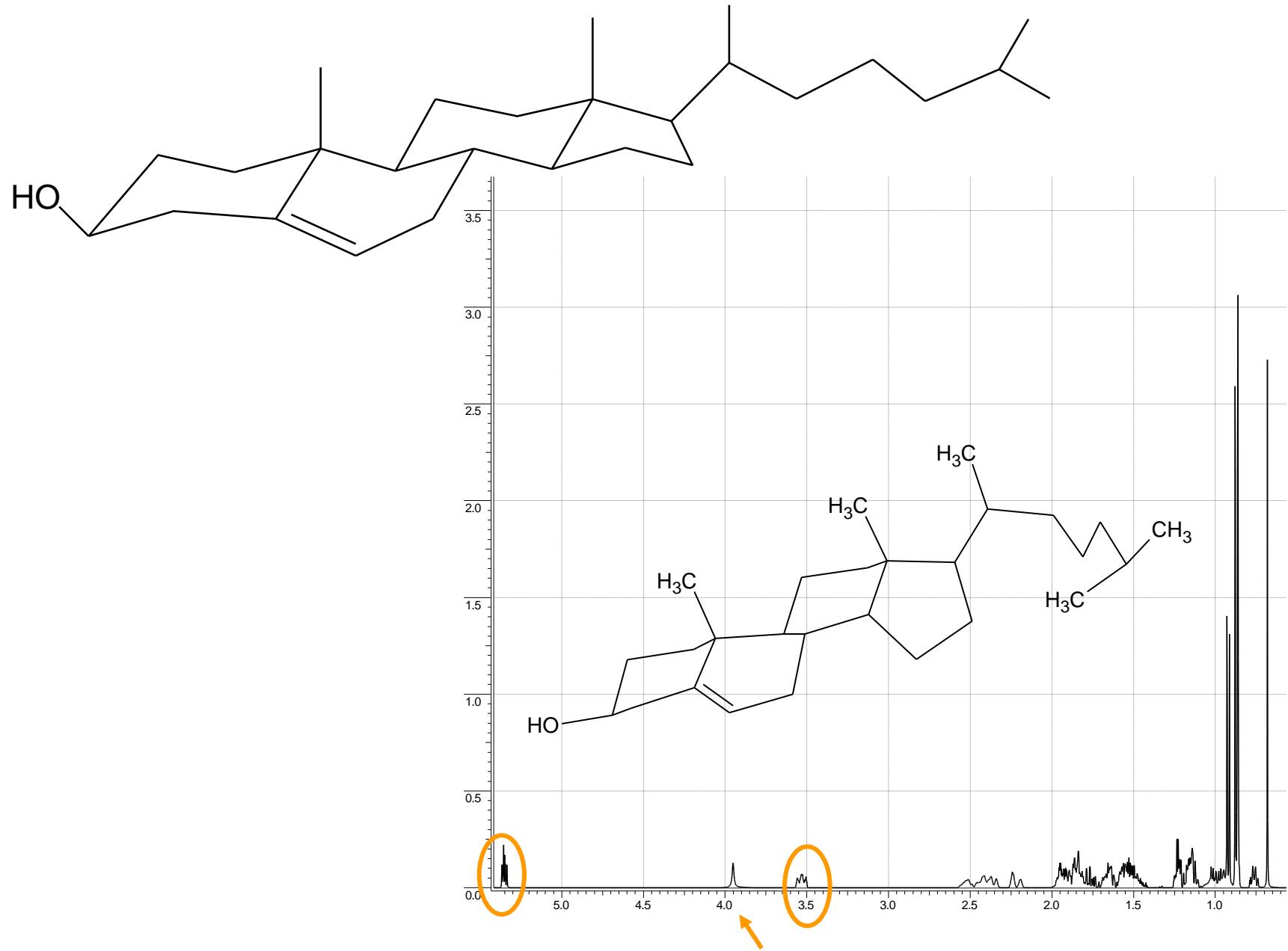
Polar head



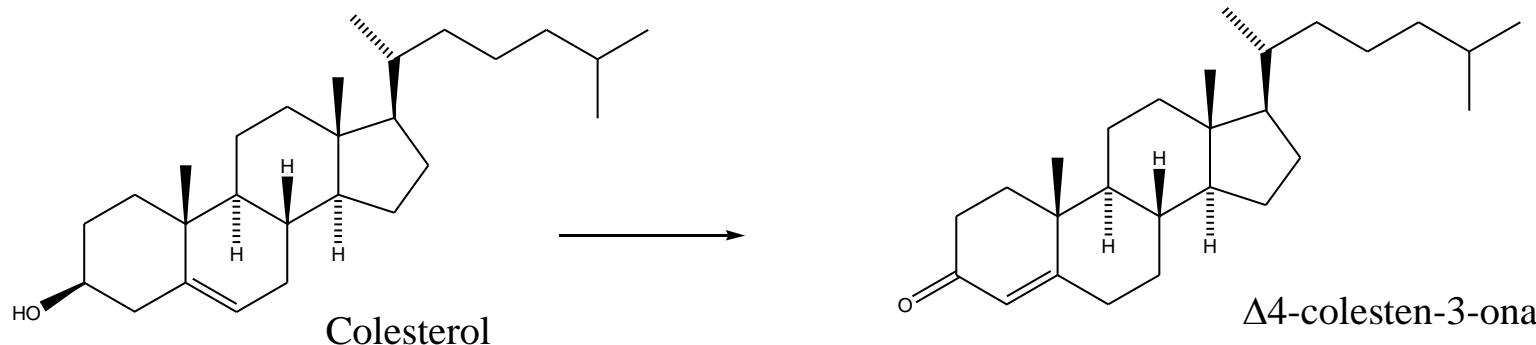
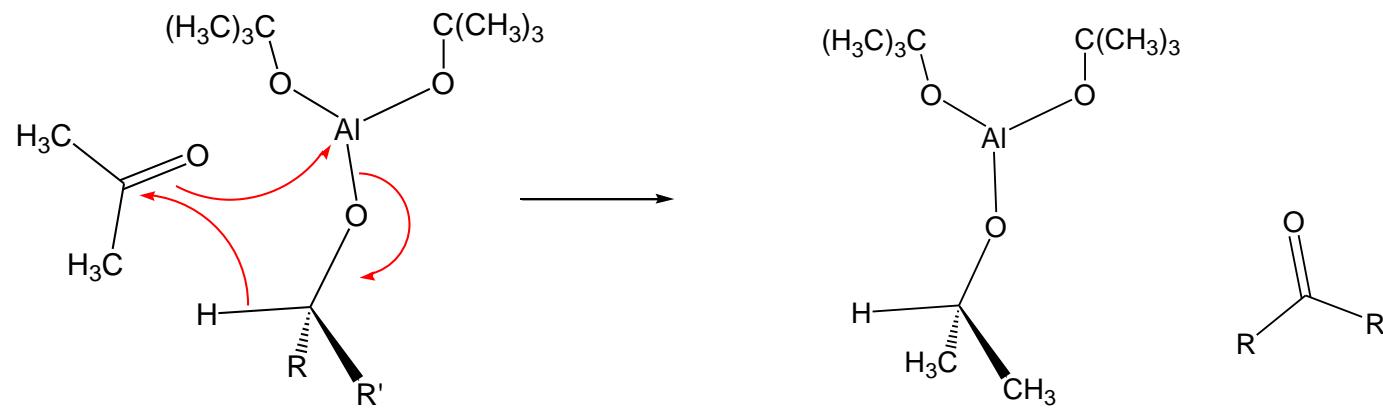
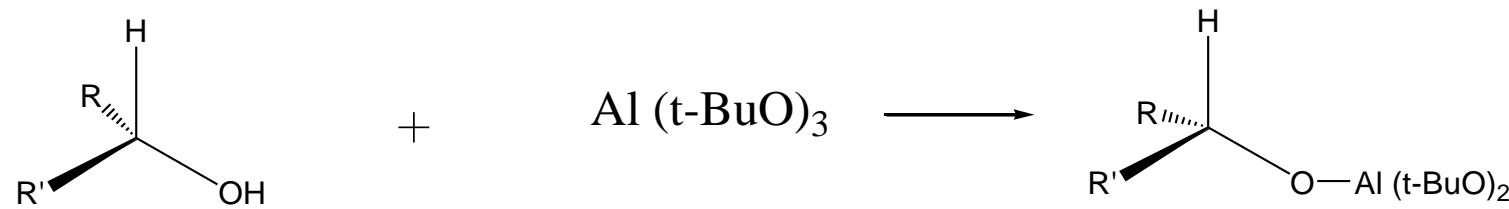
Alkyl side chain



Colesterol



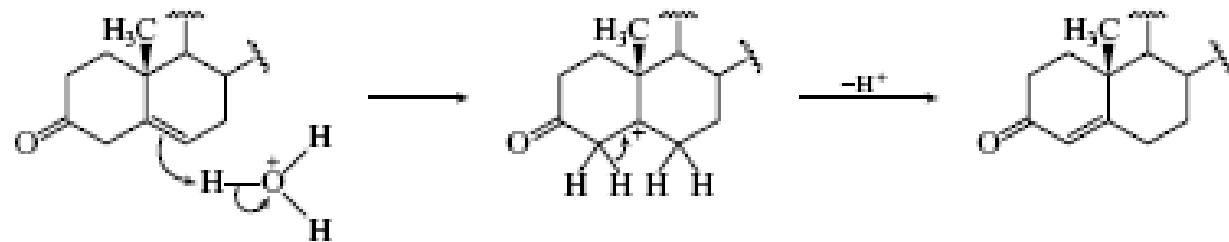
Oxidación de Oppenauer



Un par de mecanismos para interpretar la migración del doble enlace

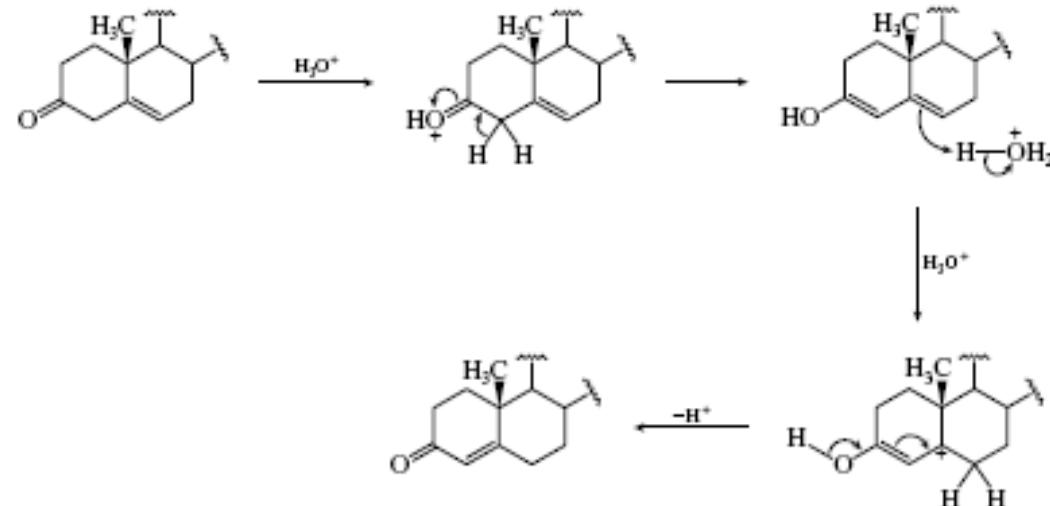
A

Por protonación
Directa del doble enlace

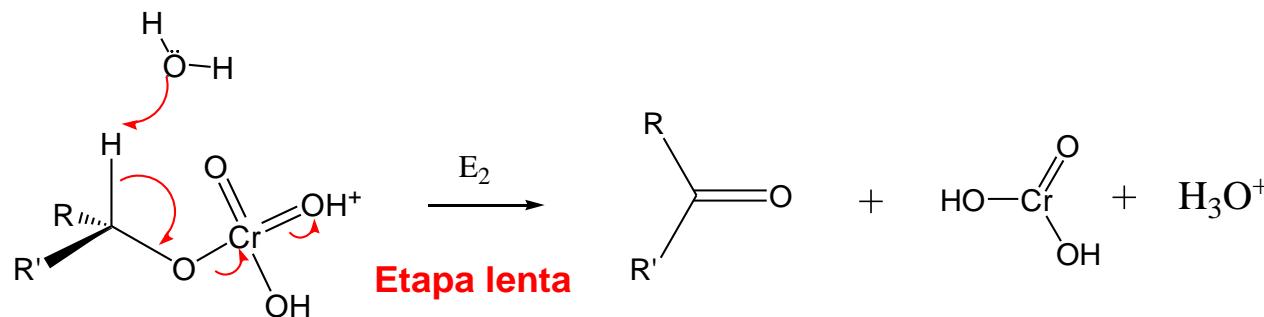
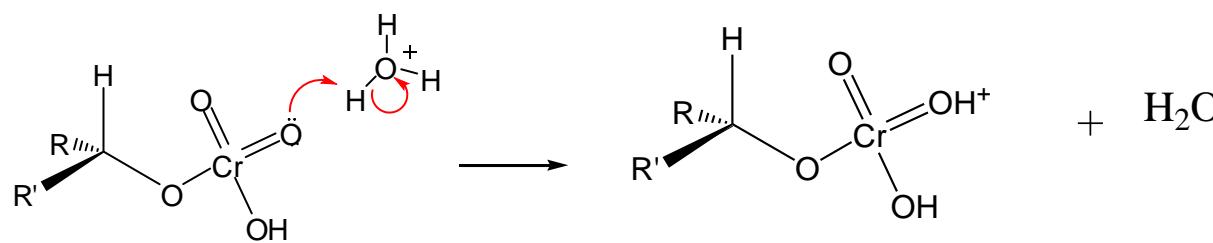
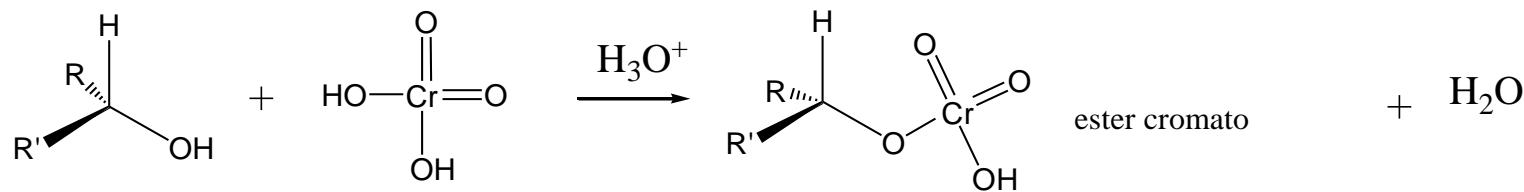


B

Por enolización y
Posterior protonación

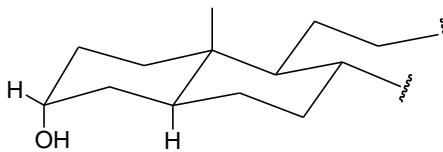


Oxidación de Jones



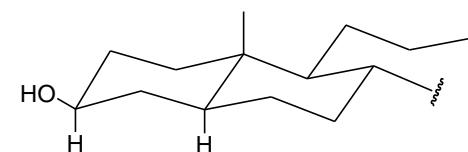
Velocidades relativas de oxidación

Alcoholes axiales



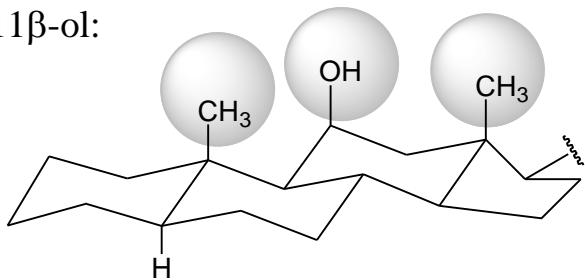
5α -colestan-3 α -ol	3
5α -colestan-1 α -ol	13
5α -colestan-2 β -ol	20
5α -colestan-4 β -ol	35
5α -colestan-6 β -ol	36
5α -colestan-7 α -ol	12.3
5α -colestan-11 β -ol	900

Alcoholes ecuatoriales

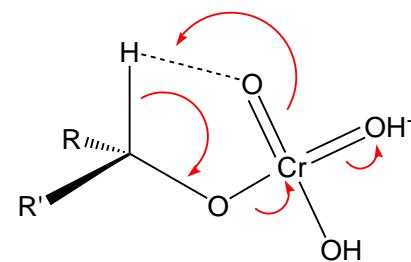


5α -colestan-3 β -ol	1
5α -colestan-1 β -ol	9.7
5α -colestan-2 α -ol	1.3
5α -colestan-4 α -ol	2
5α -colestan-6 α -ol	2
5α -colestan-7 β -ol	3.4
5α -colestan-11 α -ol	14

En 11 β -ol:



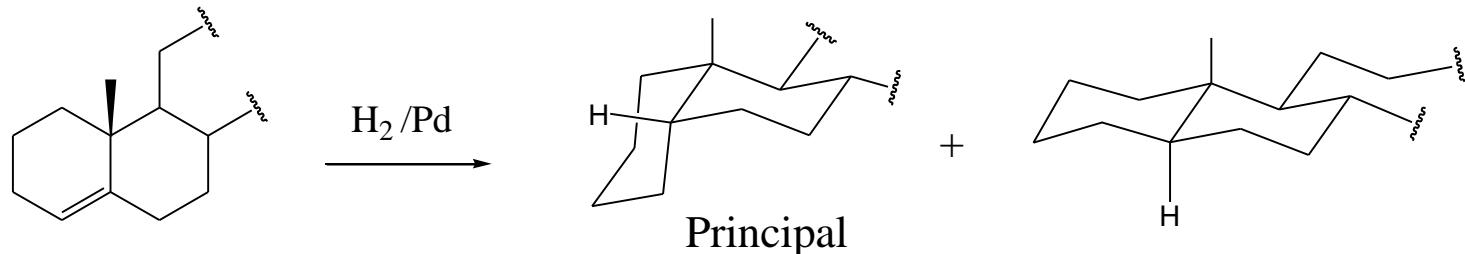
Gran alivio estérico al cambiar de conformación



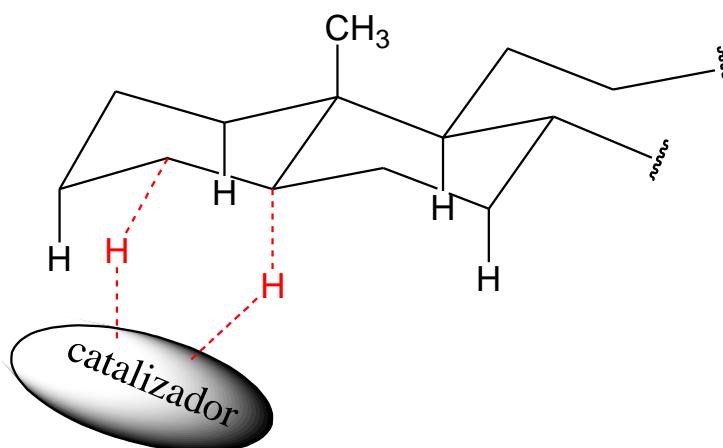
Estado de transición cíclico (sin necesidad de base externa)

Reducción catalítica de esteroides $\Delta 4$ y $\Delta 5$ con H_2/Pd

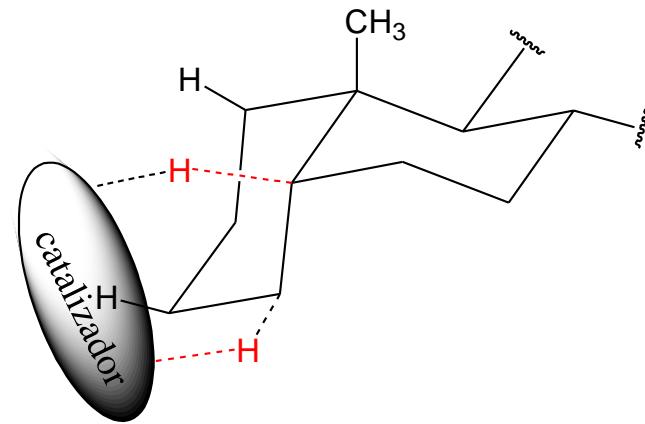
esteroides $\Delta 4$



El catalizador heterogéneo interacciona con H axiales

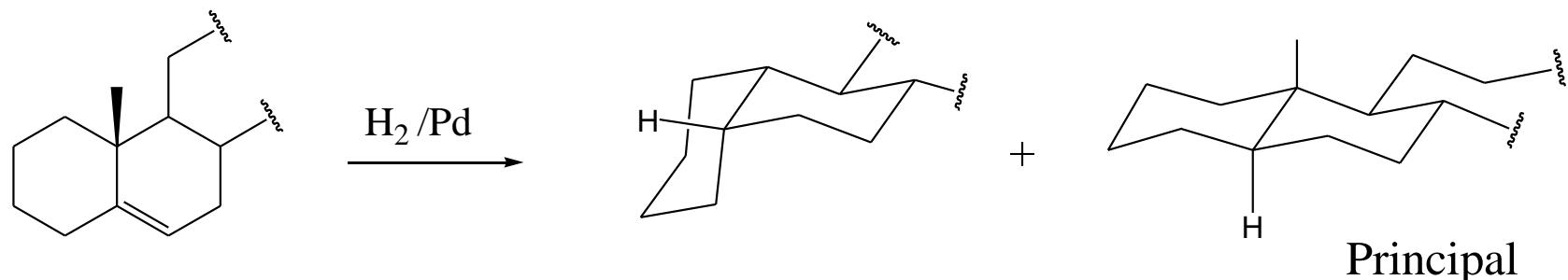


H axiales en posiciones 1, 3, 7 y 9

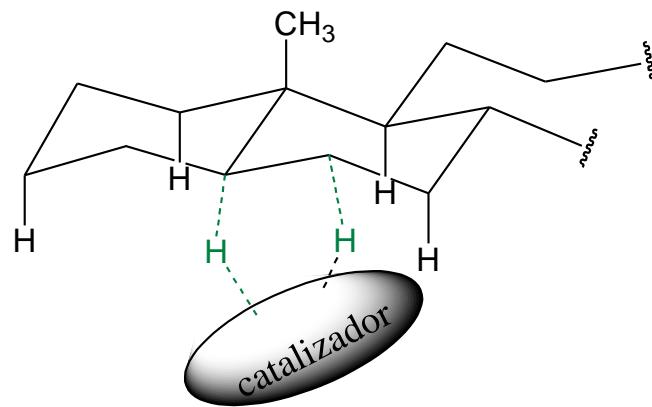


H axiales en posiciones 1 y 3

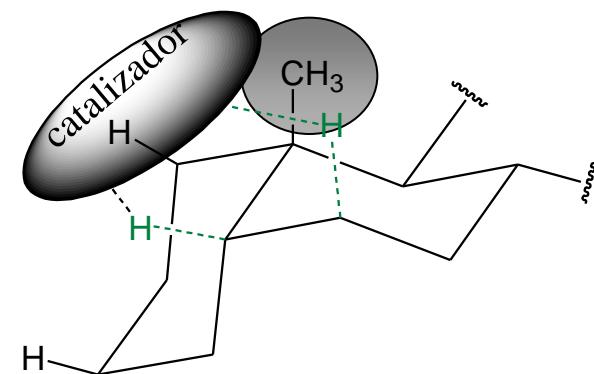
esteroides Δ5



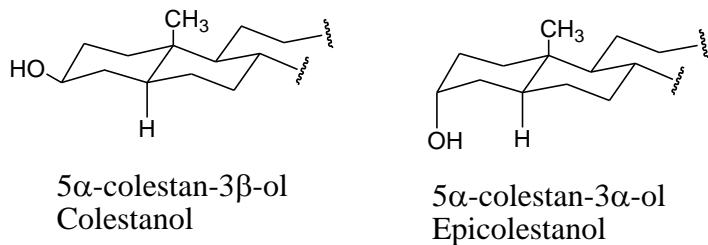
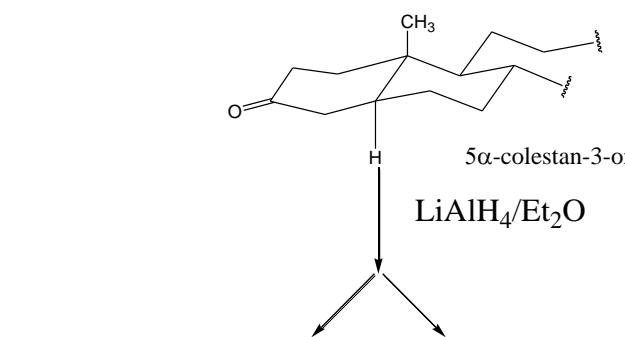
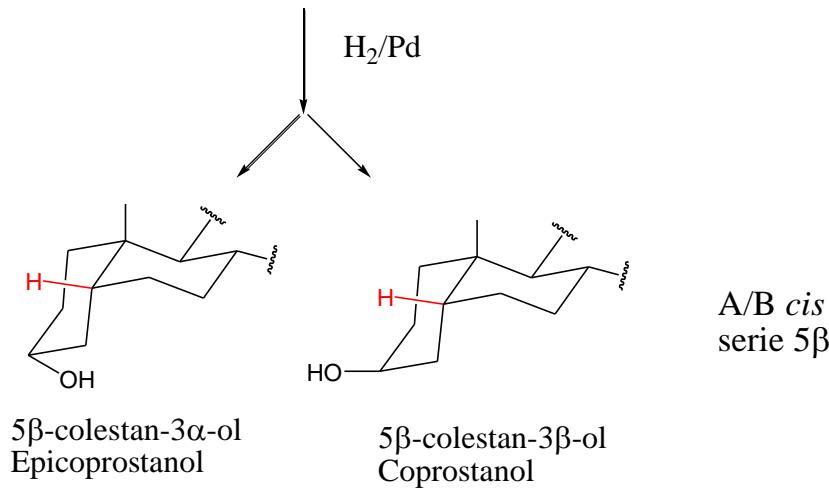
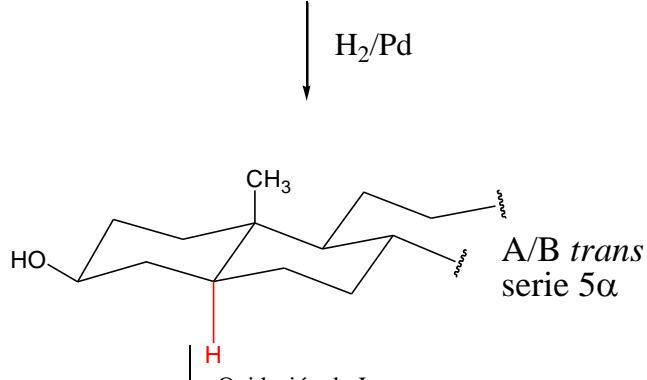
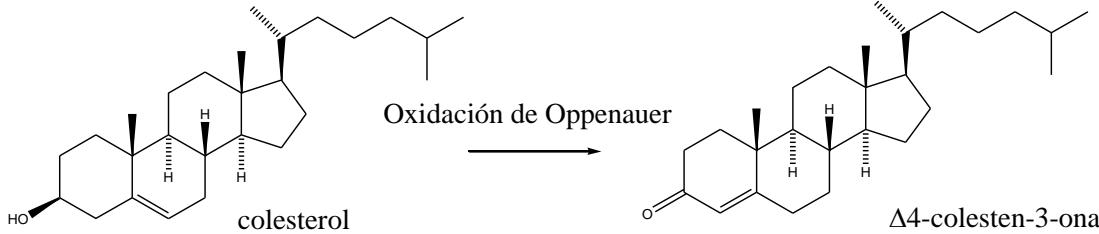
El catalizador heterogéneo interacciona con sustituyentes axiales



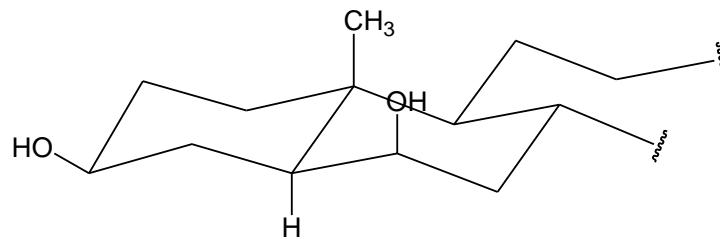
H axiales en posiciones 1, 3, 7 y 9



H axiales en posiciones 1 y 3
CH₃ axial en posición 10



Esterificación e hidrólisis

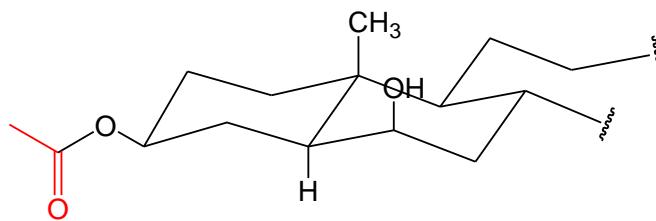


3 β ,6 β -diol

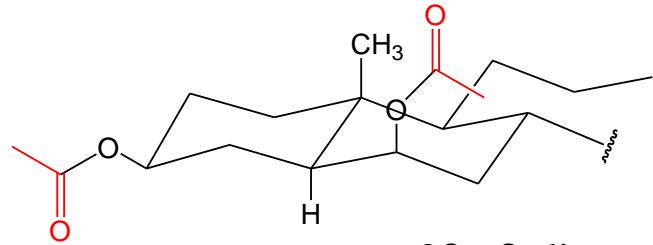
Condiciones controladas

Acetilación

Condiciones energicas

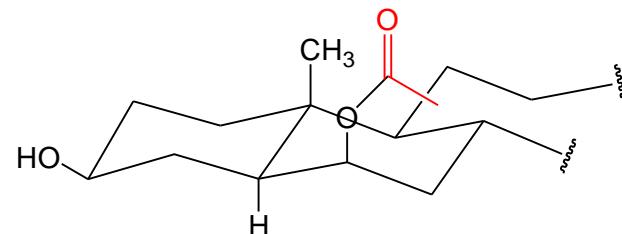


3 β -acetoxy,6 β -diol



3 β ,6 β -diacetoxi

Hidrólisis



6 β -acetoxi-3 β -ol

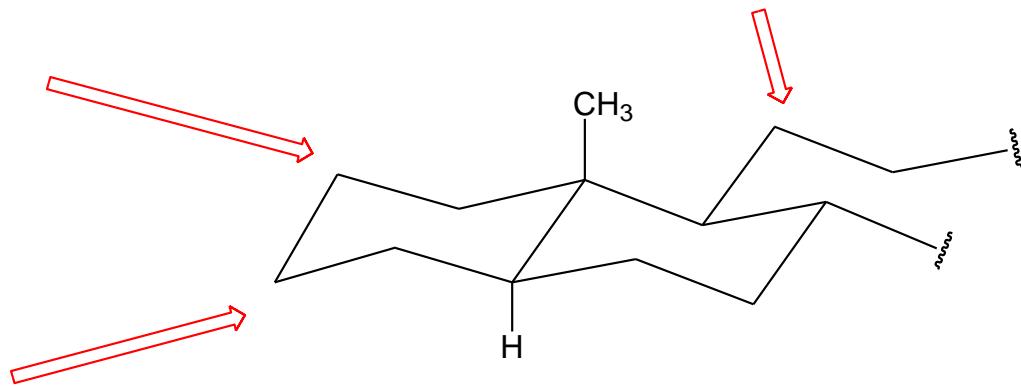
Hidrólisis

Condiciones: 5 α -colestanoles en KOH 0,01N a reflujo 30 min.

2 α -acetoxi (e) 87%
2 β -acetoxi (a) 11%

3 β -acetoxi (e) 92%
3 α -acetoxi (a) 34%

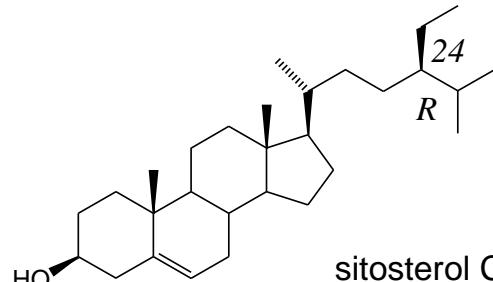
11 β -acetoxi (a) no hidroliza



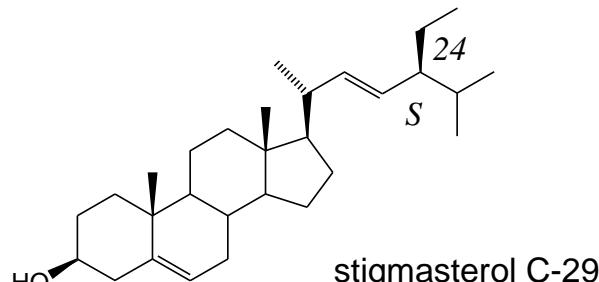
Compuestos esteroidales

Fitosteroles

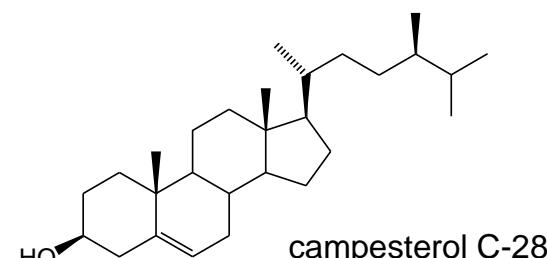
¿Por qué se invierte la configuración en C-24?



sitosterol C-29

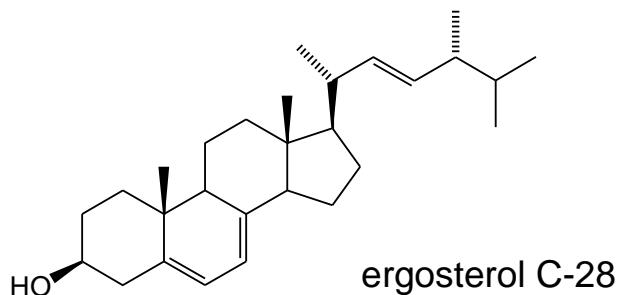


stigmasterol C-29



campesterol C-28

Esteroles fúngicos



ergosterol C-28

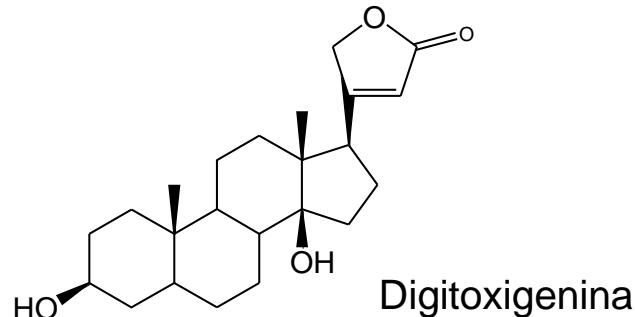
Compuestos esteroidales

Fitosteroles



Principios cardioactivos

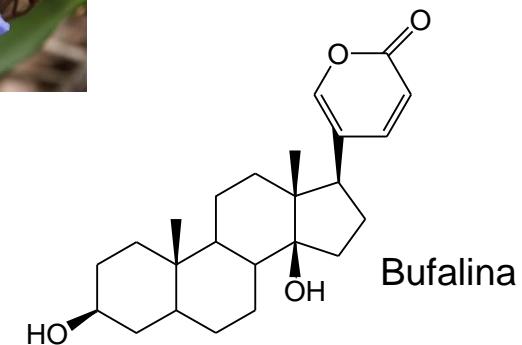
Cardenólidos C23



Digitoxigenina

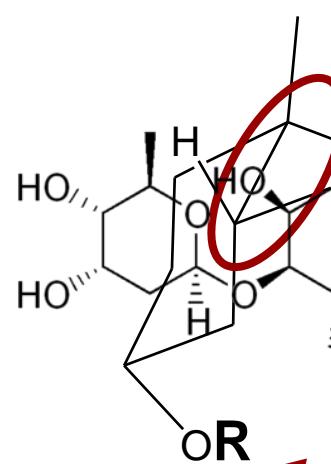


Bufadienólidos C24

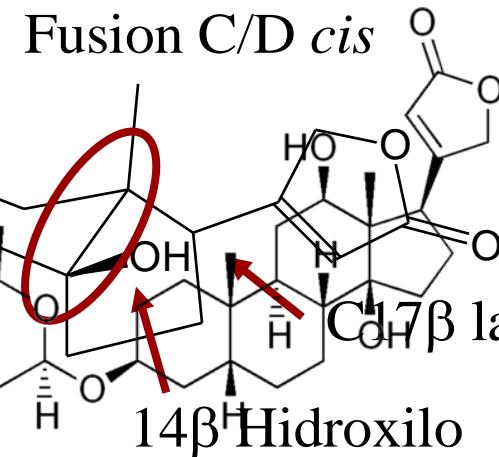


Bufalina

Fusion A/B *cis*



Fusion C/D *cis*



14 β Hidroxilo

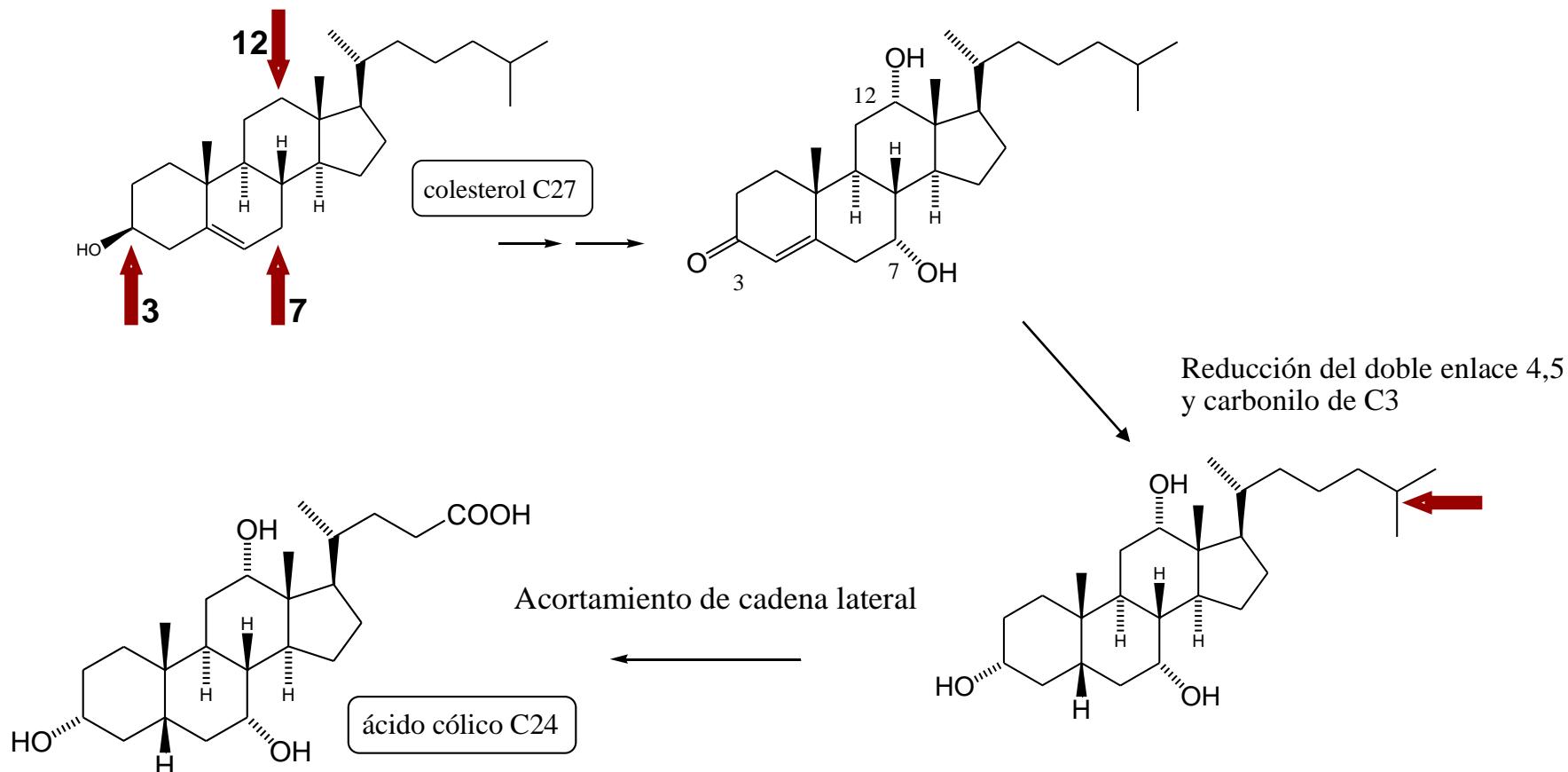
3 α Hidroxilo glicosidado



bufo bufo

Compuestos esteroideos

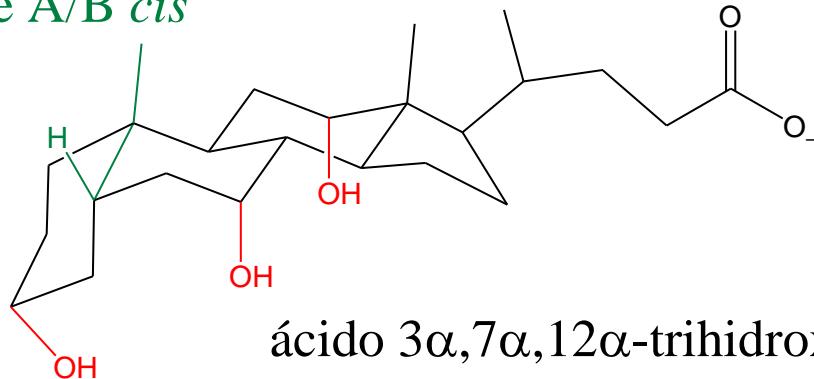
Acidos biliares C-24



Compuestos esteroidales

Acidos biliares

Cierre A/B *cis*



R = -OH
R = H

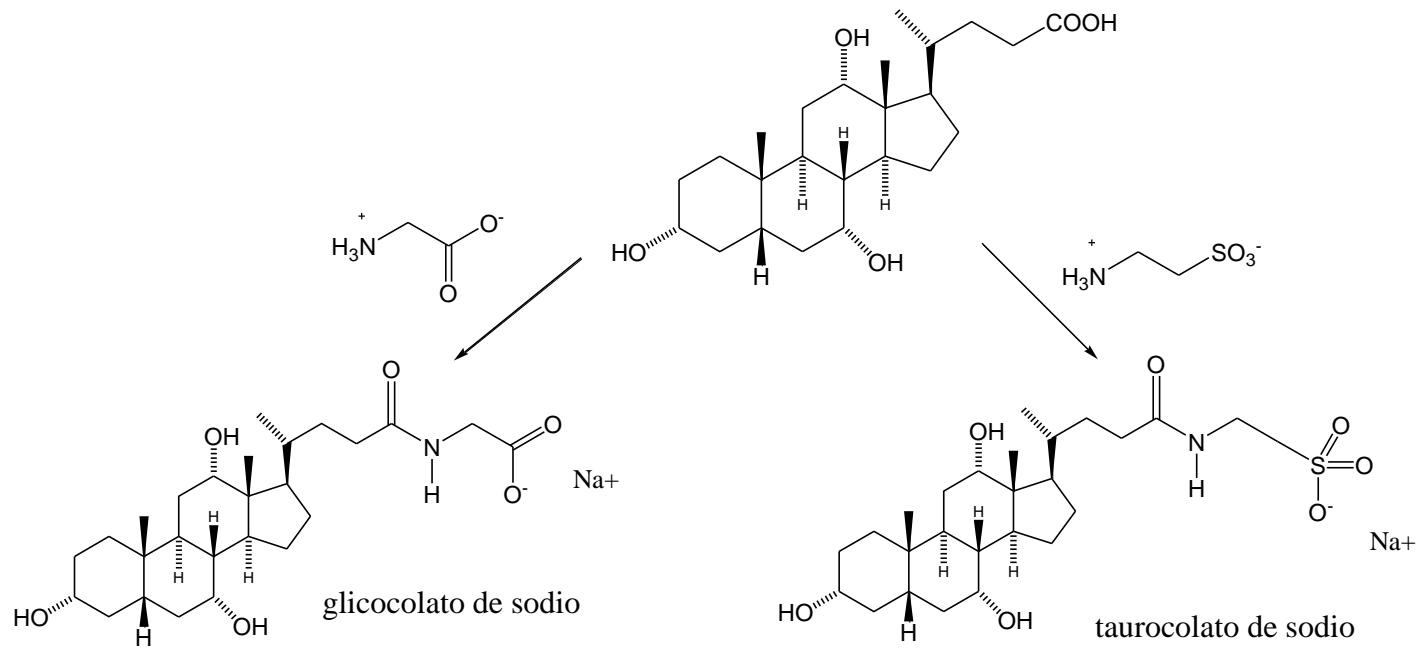
ácido cólico
ácido quenodesoxicólico

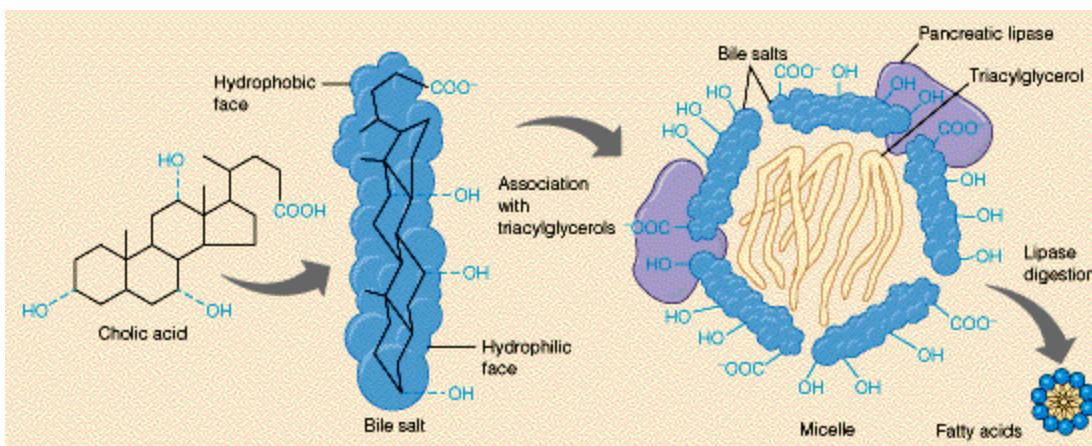
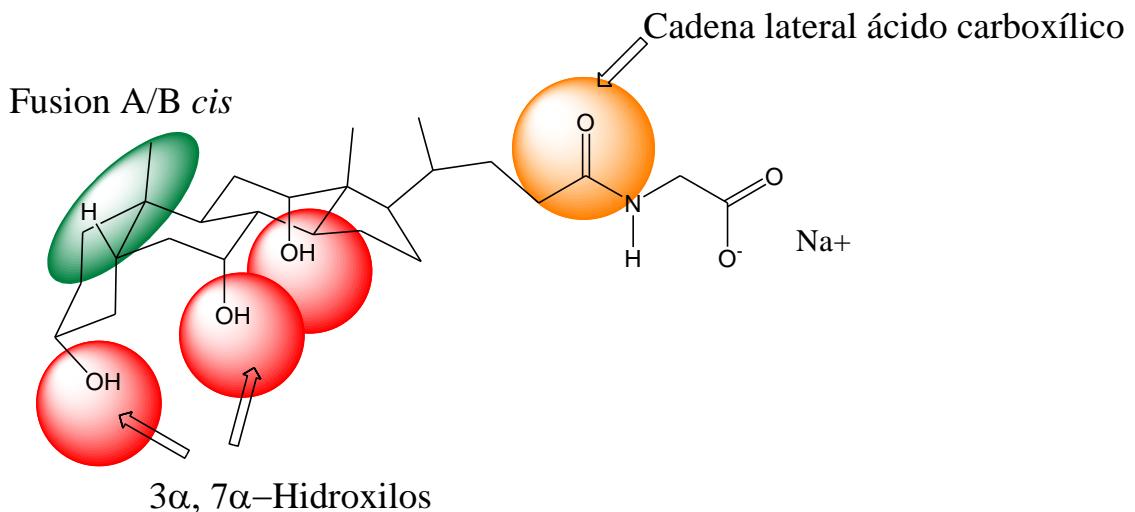
R = -OH
R = H

ácido desoxicólico
ácido litocólico

Compuestos esteroidales

Acidos biliares





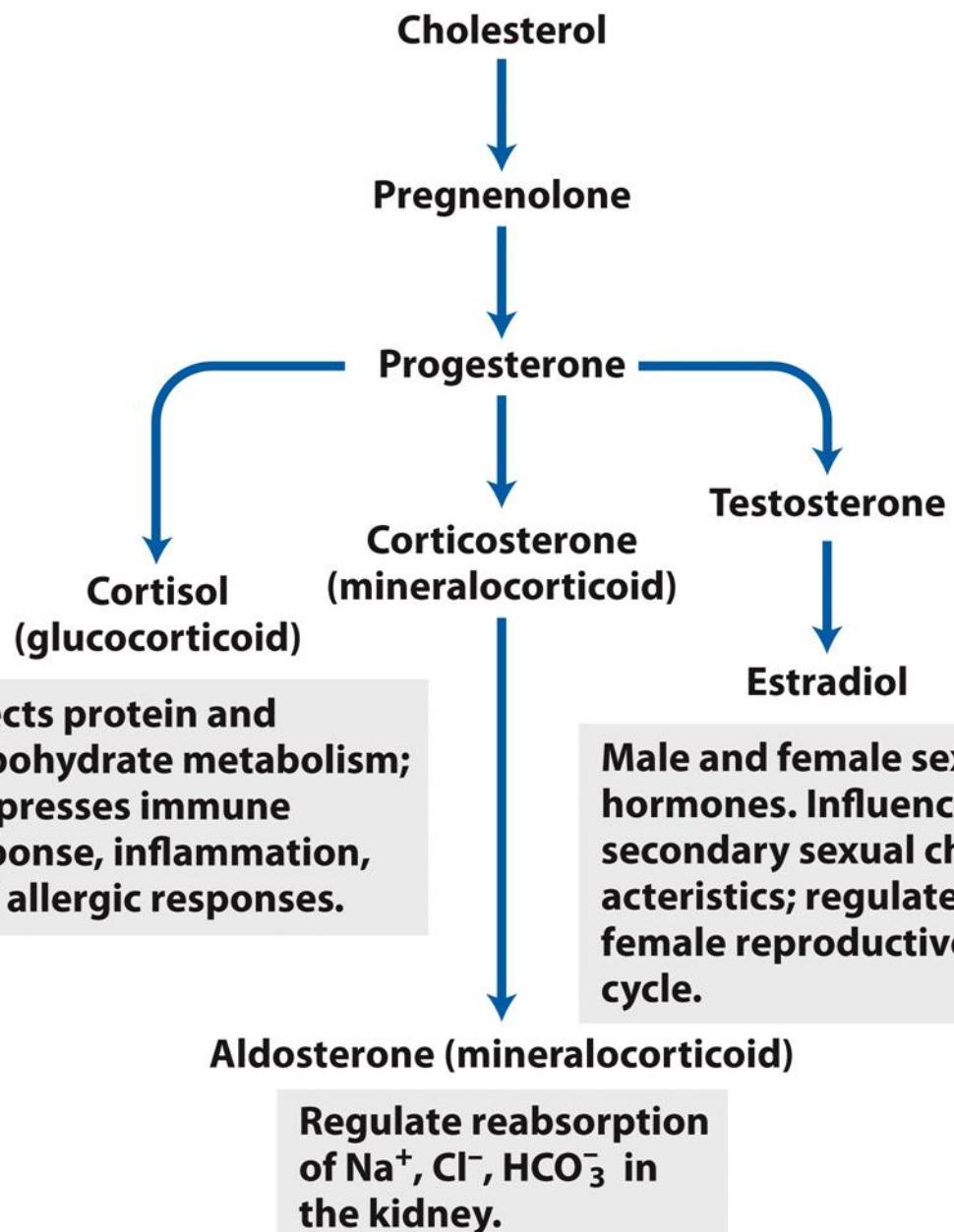
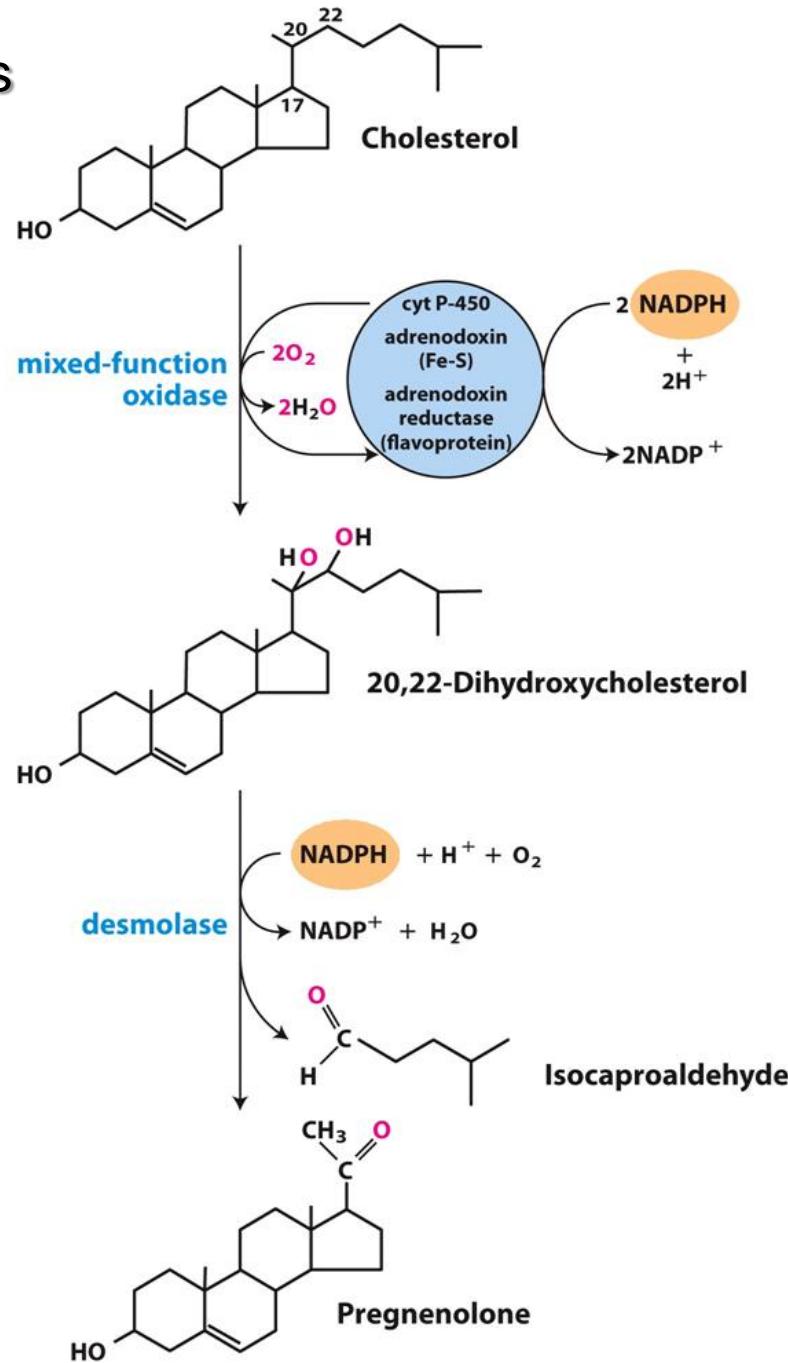


Figure 21-48

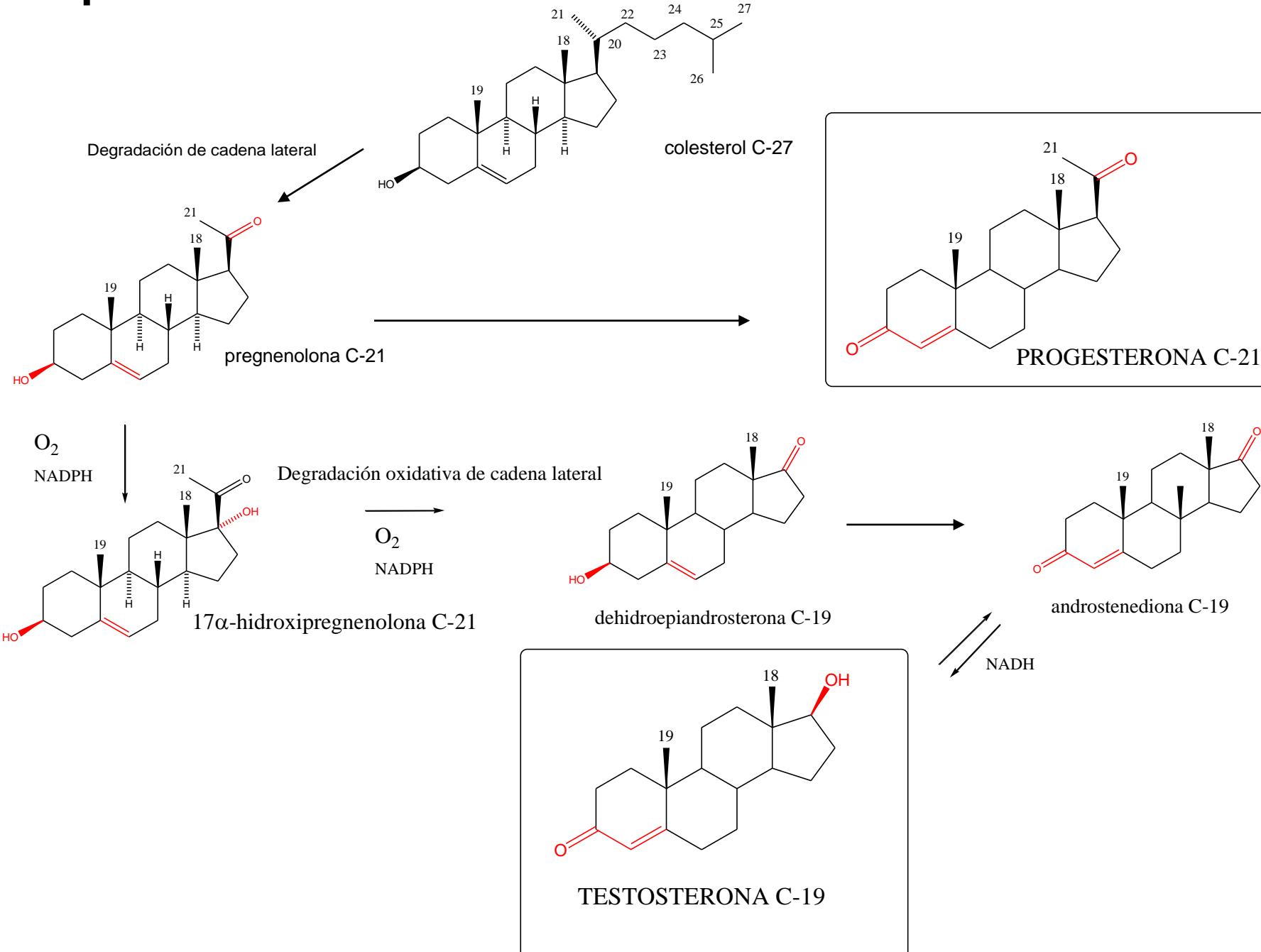
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

Síntesis de hormonas esteroideas



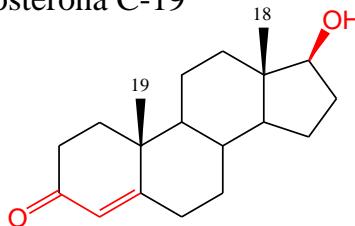
Compuestos esteroideos

Síntesis de hormonas sexuales

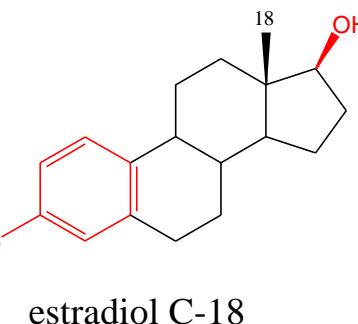


Compuestos esteroidales

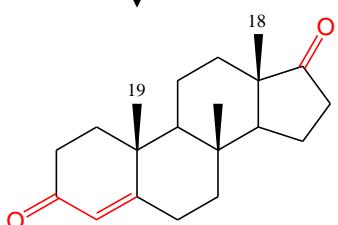
testosterona C-19



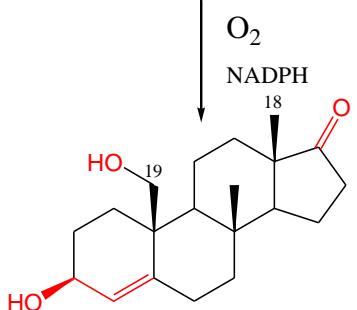
$\xrightarrow[\text{Aromatasa}]{\text{O}_2, \text{NADPH}}$



androstenediona C-19

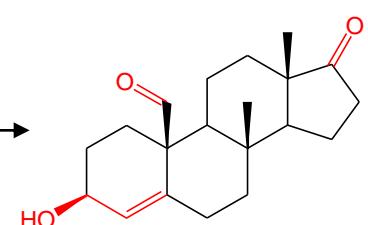


$\xrightarrow{\text{O}_2, \text{NADPH}}$

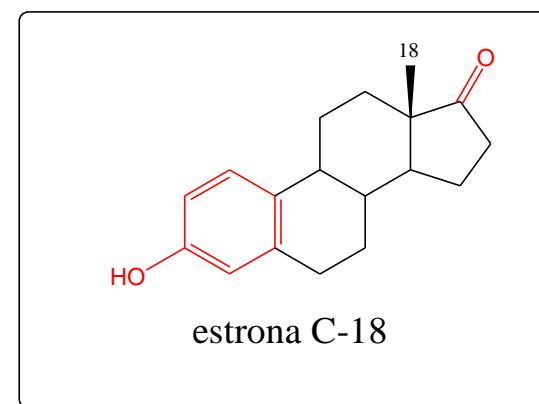


$\xrightarrow{\text{Aromatasa}}$

$\xrightarrow[\text{O}_2, \text{NADPH}]{}$



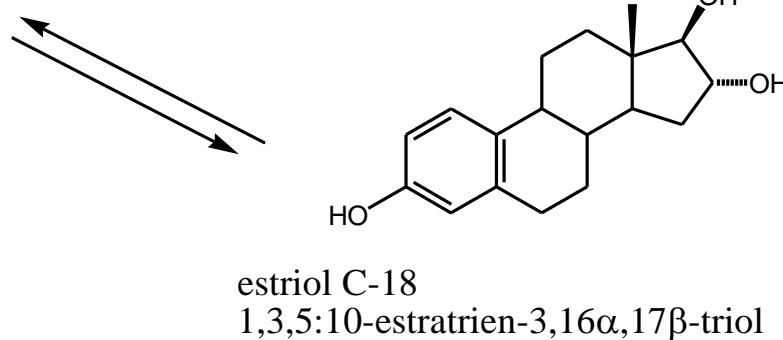
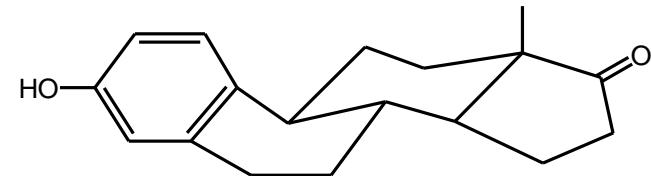
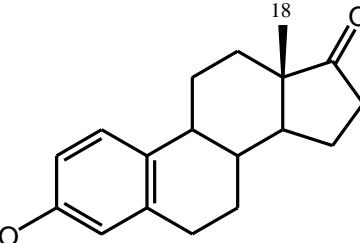
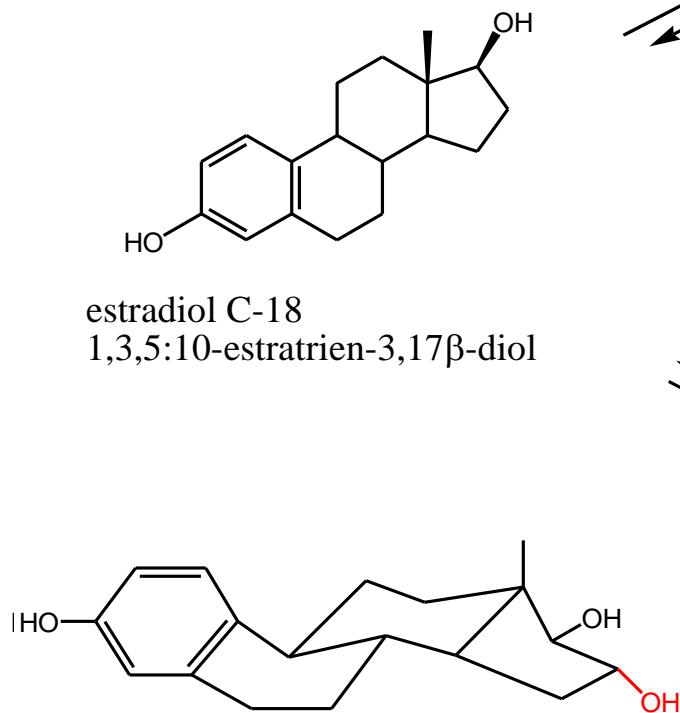
Eliminación oxidativa del grupo C-19 formilo



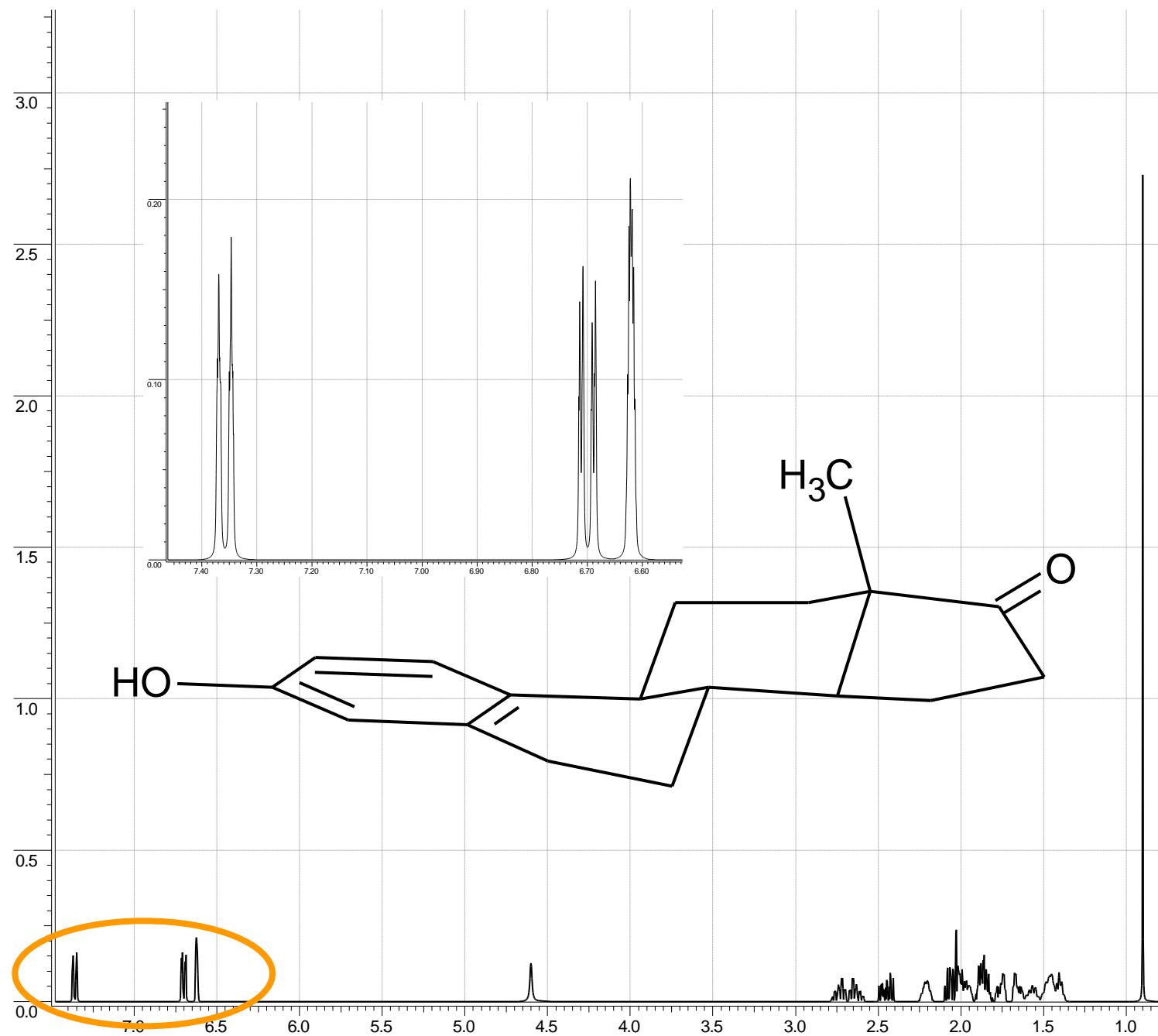
$\xleftarrow[\text{O}_2, \text{NADPH}]{}$

Compuestos esteroidales

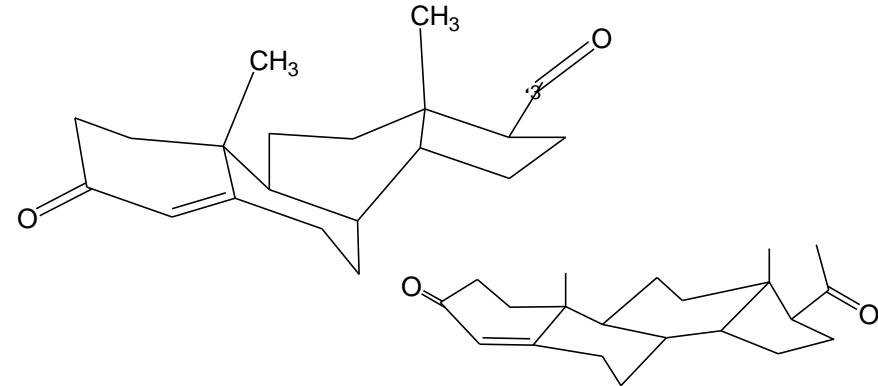
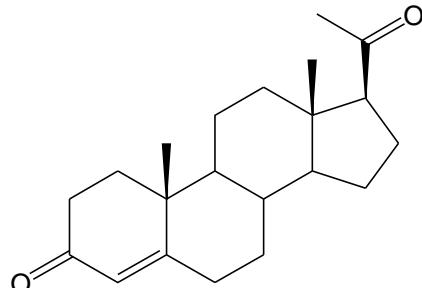
Estrógenos



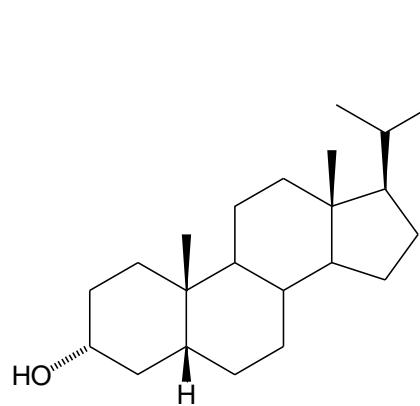
Estrona



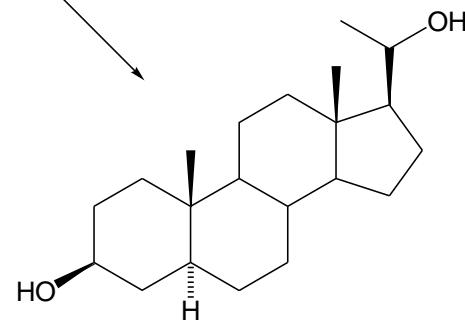
Progestágenos



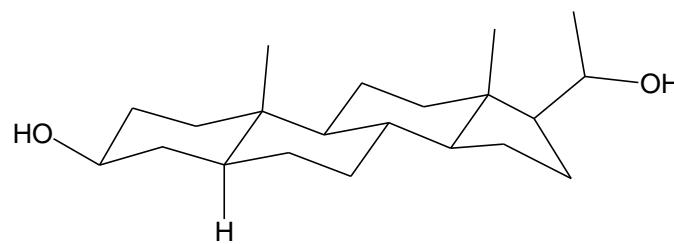
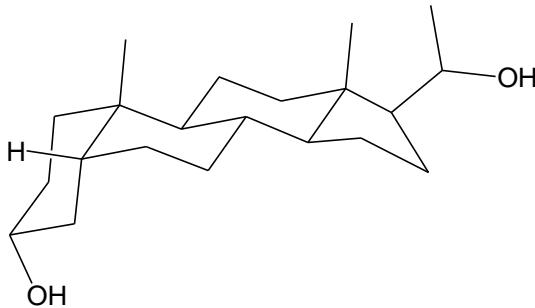
PROGESTERONA C-21



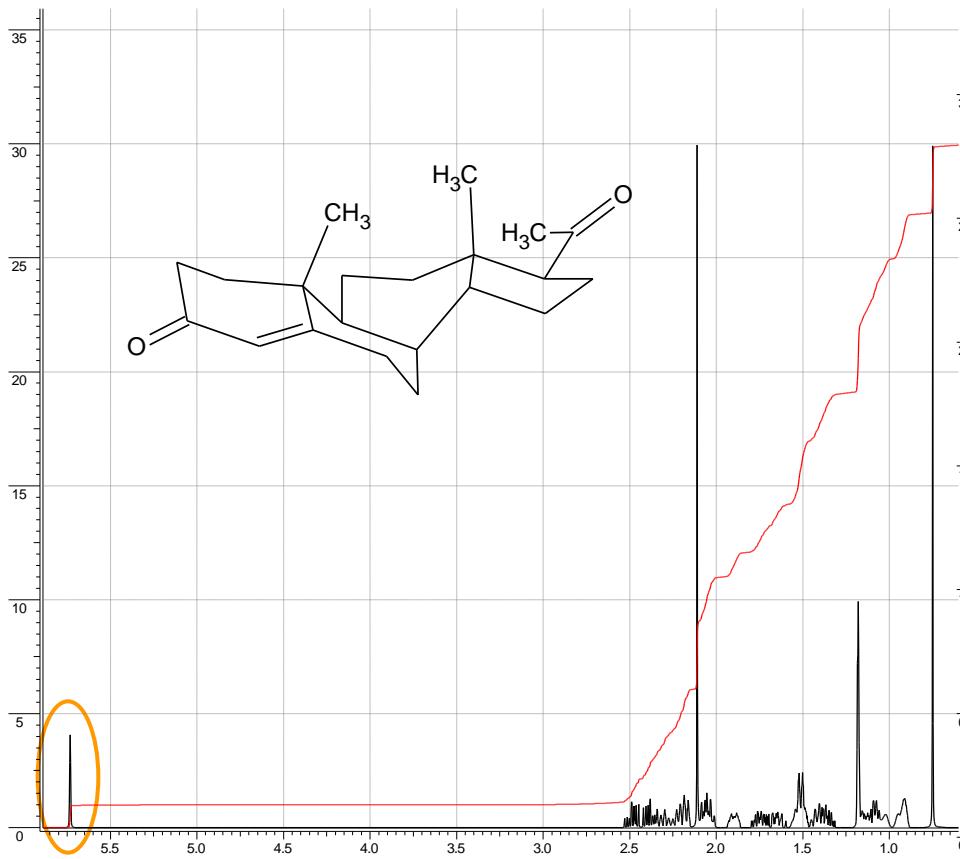
5 β -pregnan-3 α ,20(R)diol
Pregnandiol C21



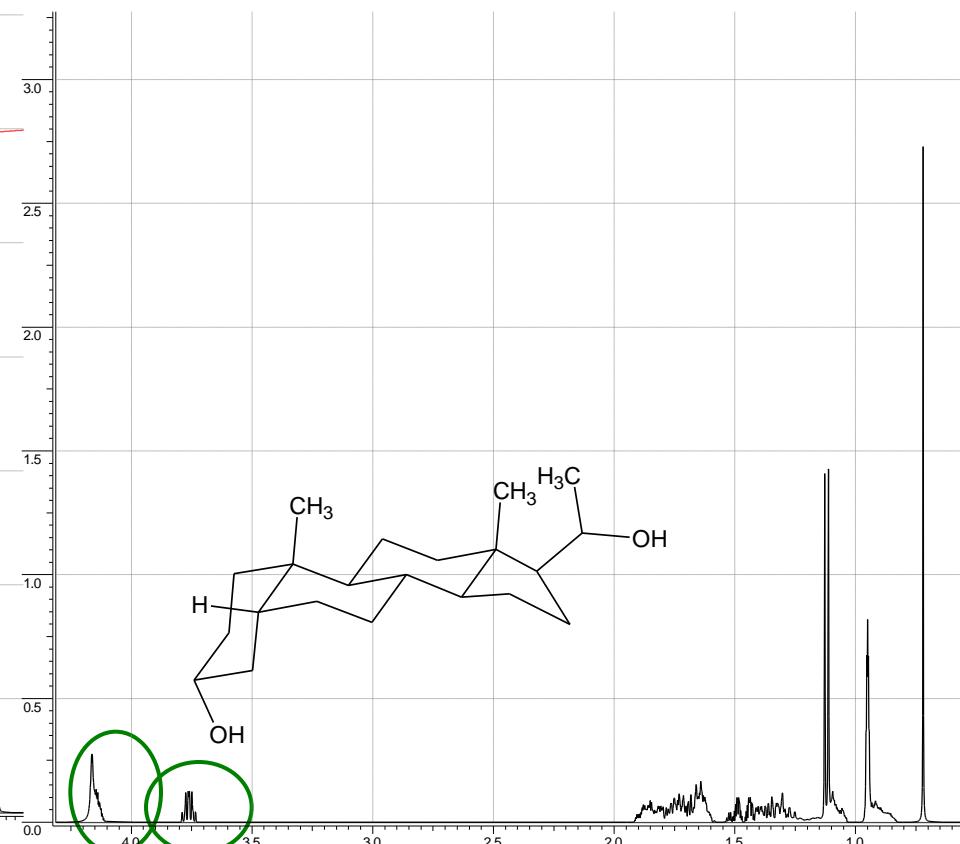
5 α -pregnan-3 β ,20(R)diol
allopregnandiol C21

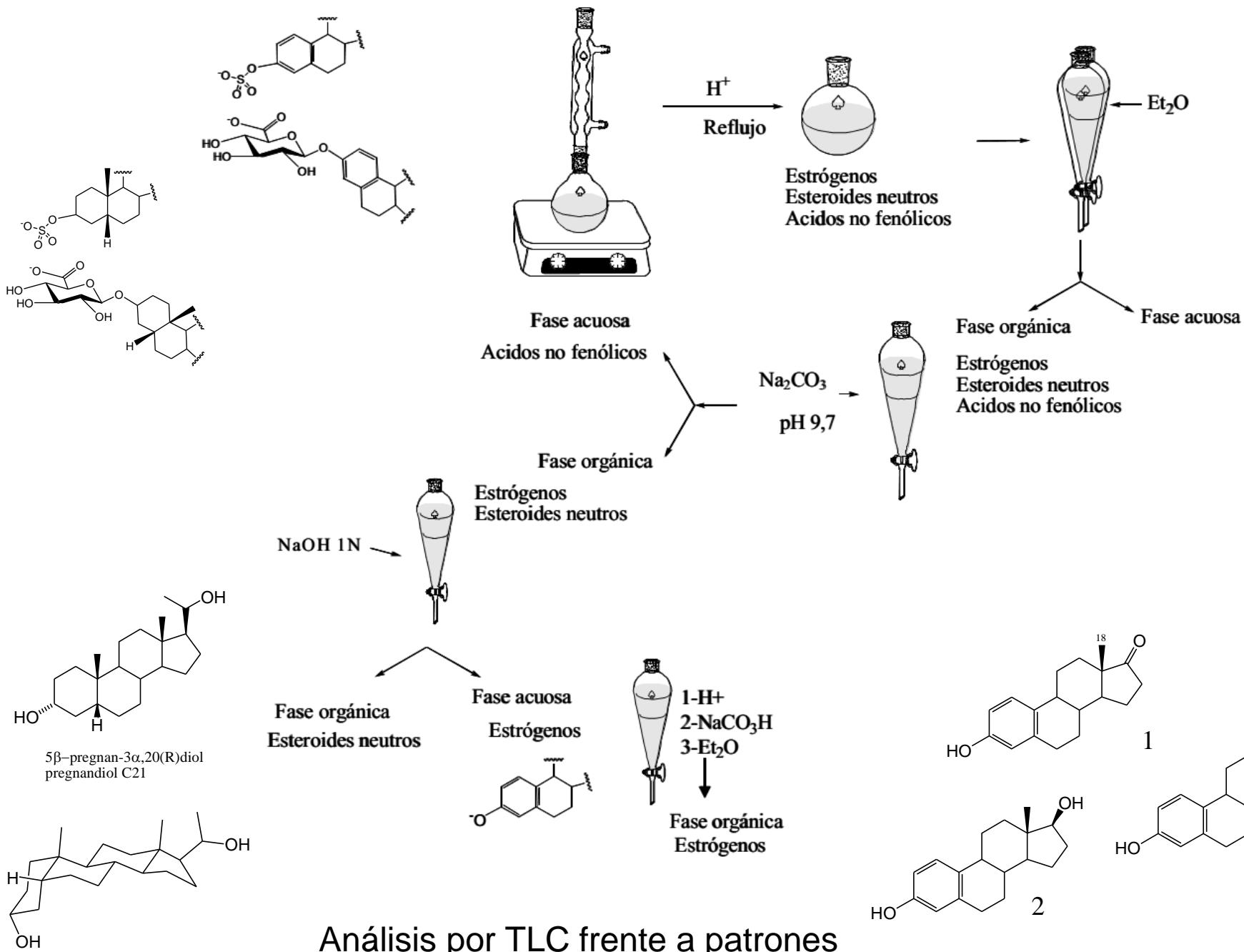


Progesterona

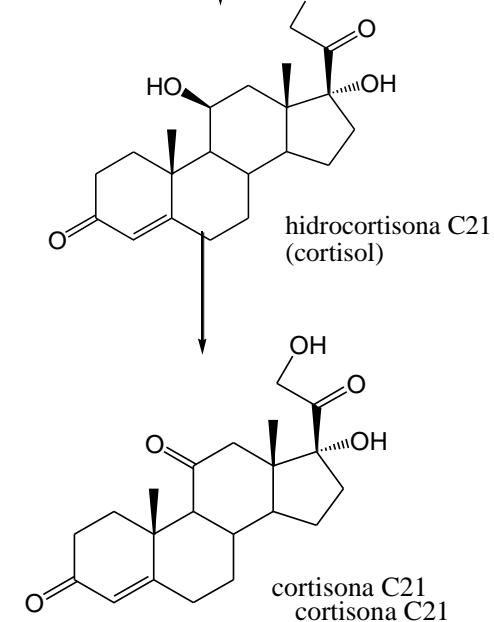
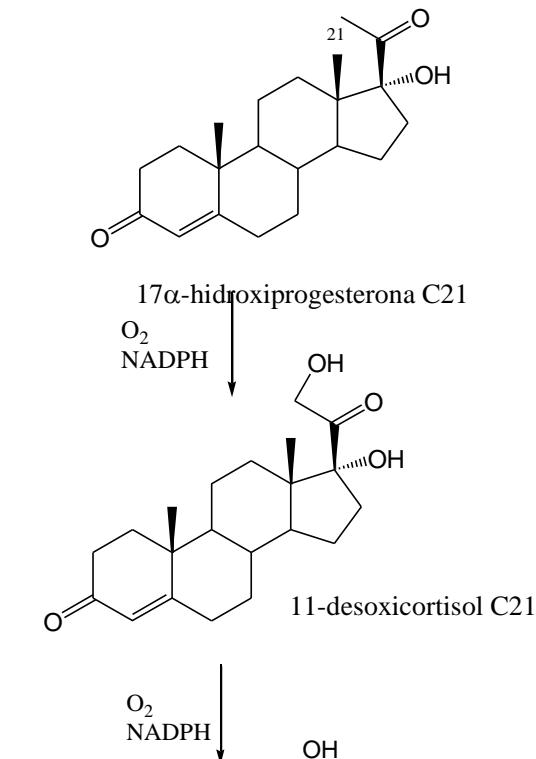
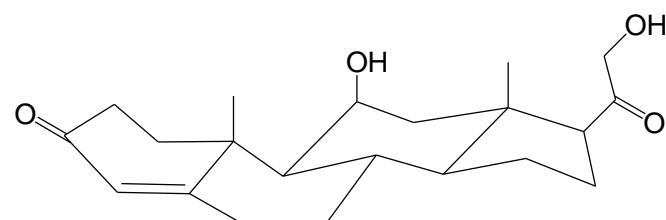
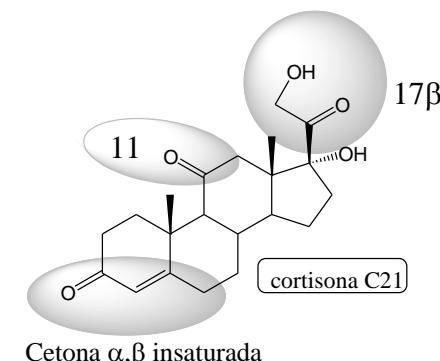
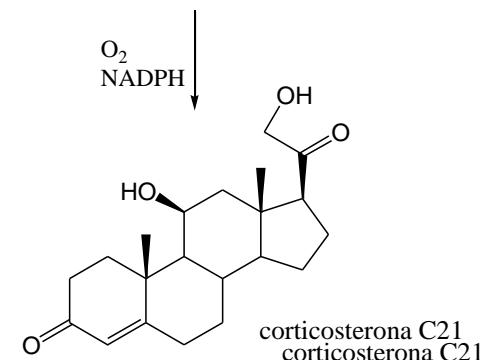
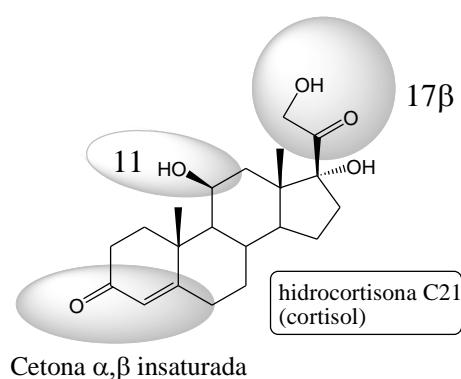
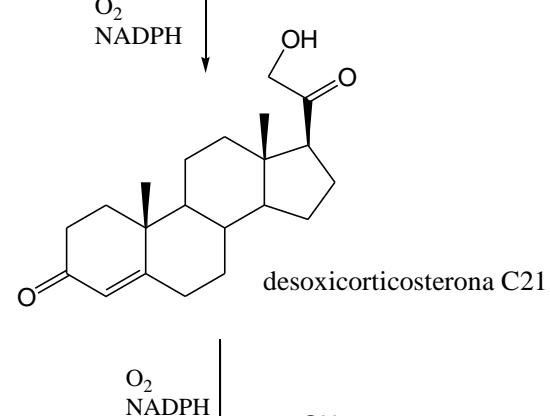
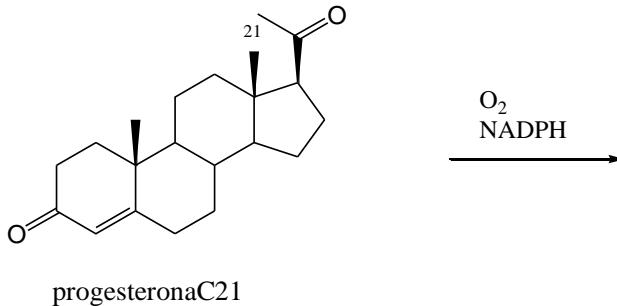
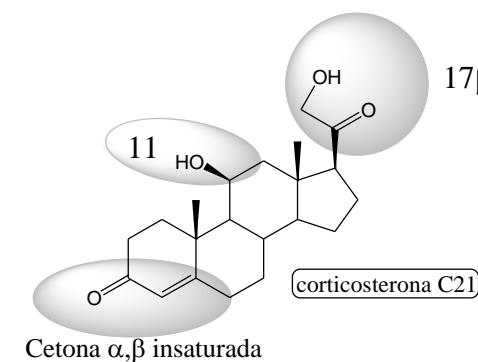


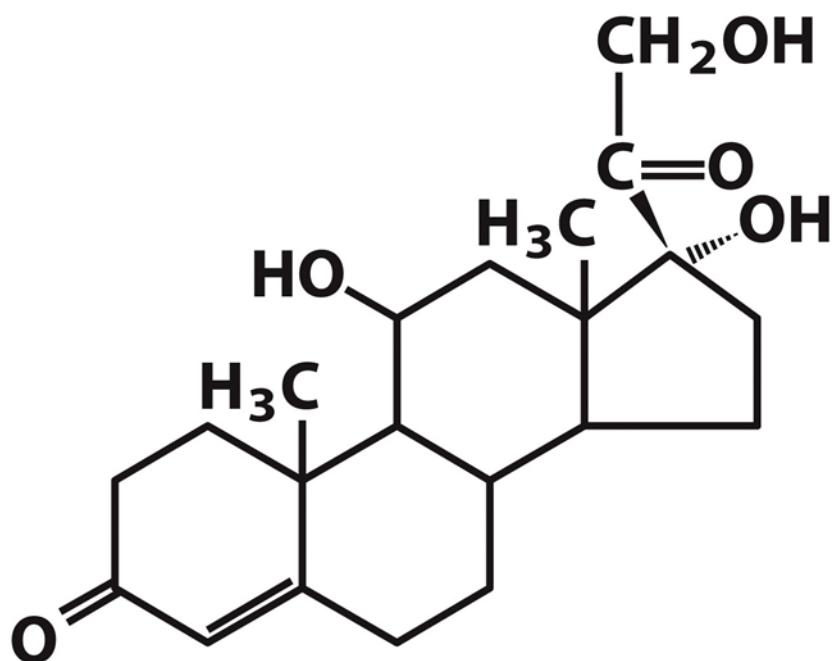
Pregnandiol



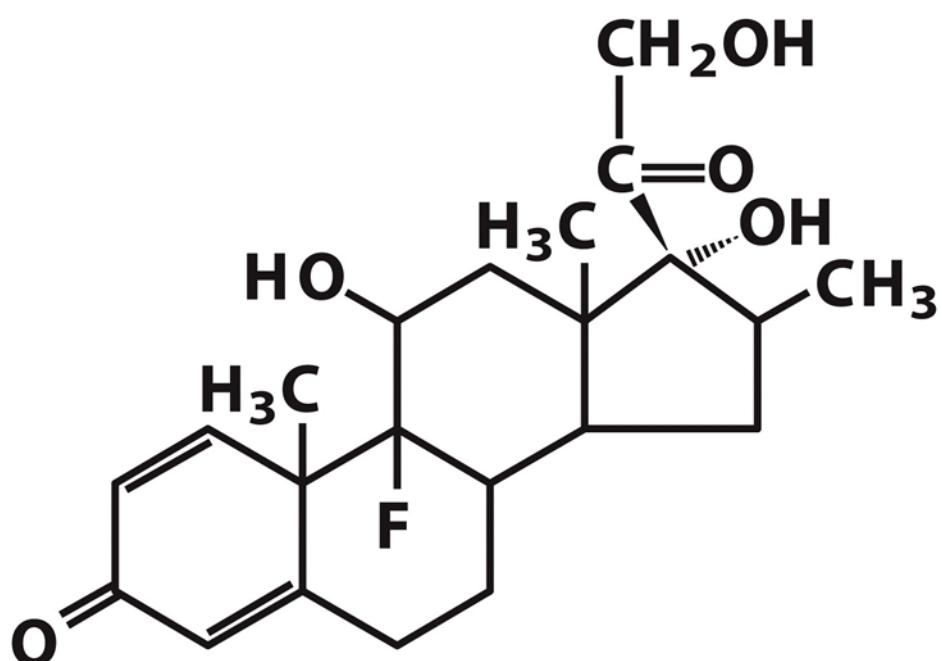


Glucocorticoides



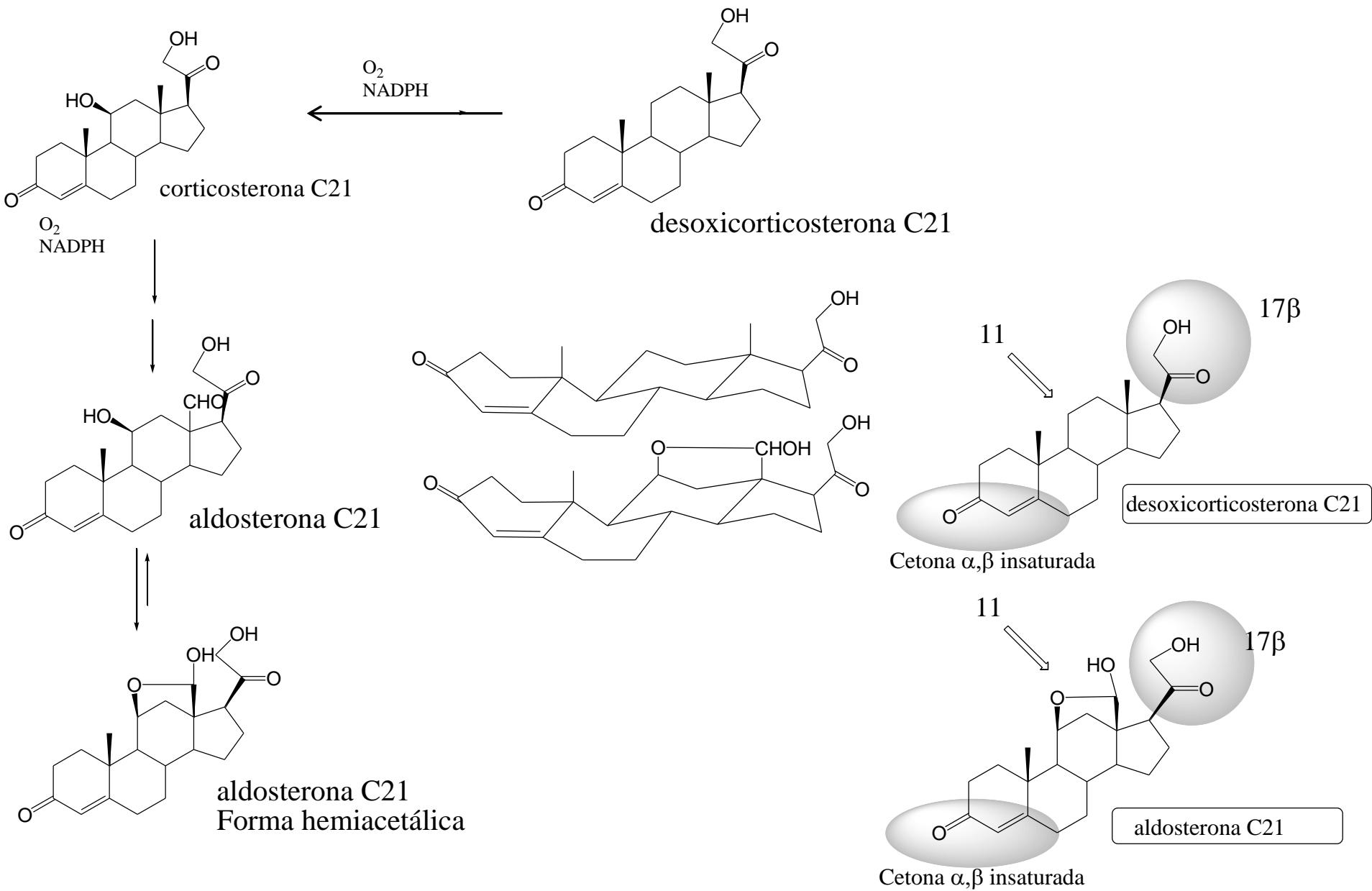


Cortisol



Dexamethasone

Mineralocorticoides



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