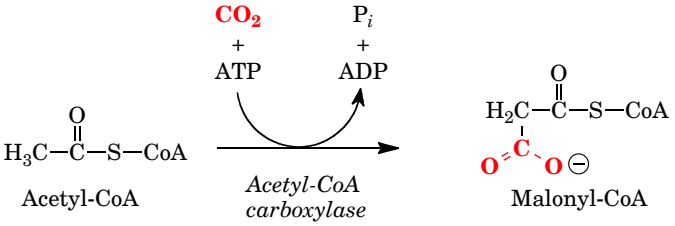
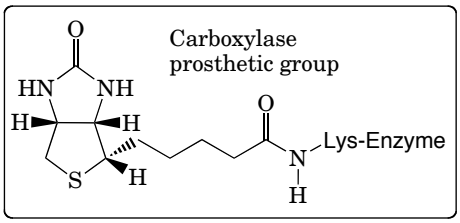
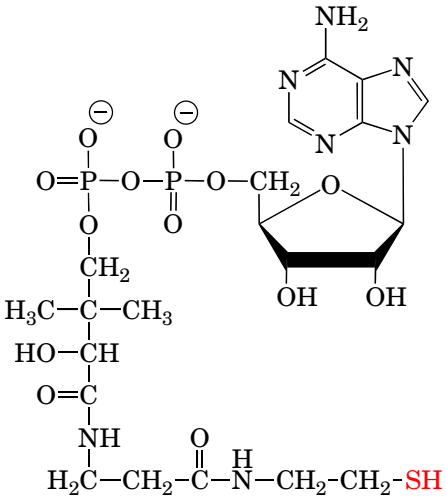
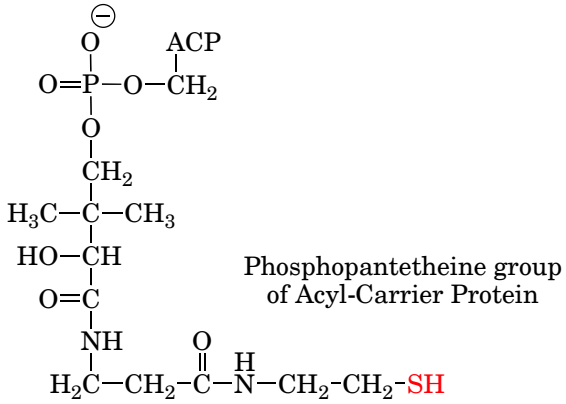
Fatty Acid Biosynthesis



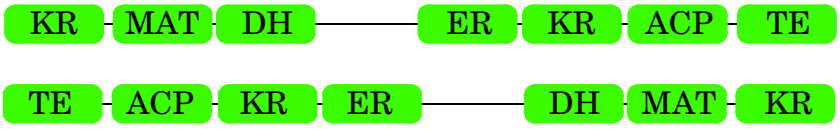


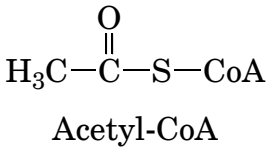


Coenzyme A (CoA-SH)

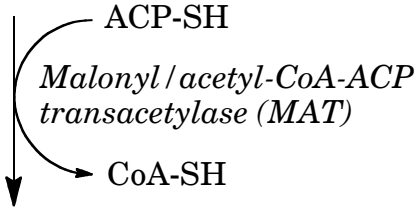


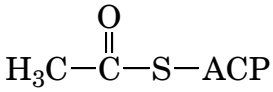
Phosphopantetheine group of Acyl-Carrier Protein

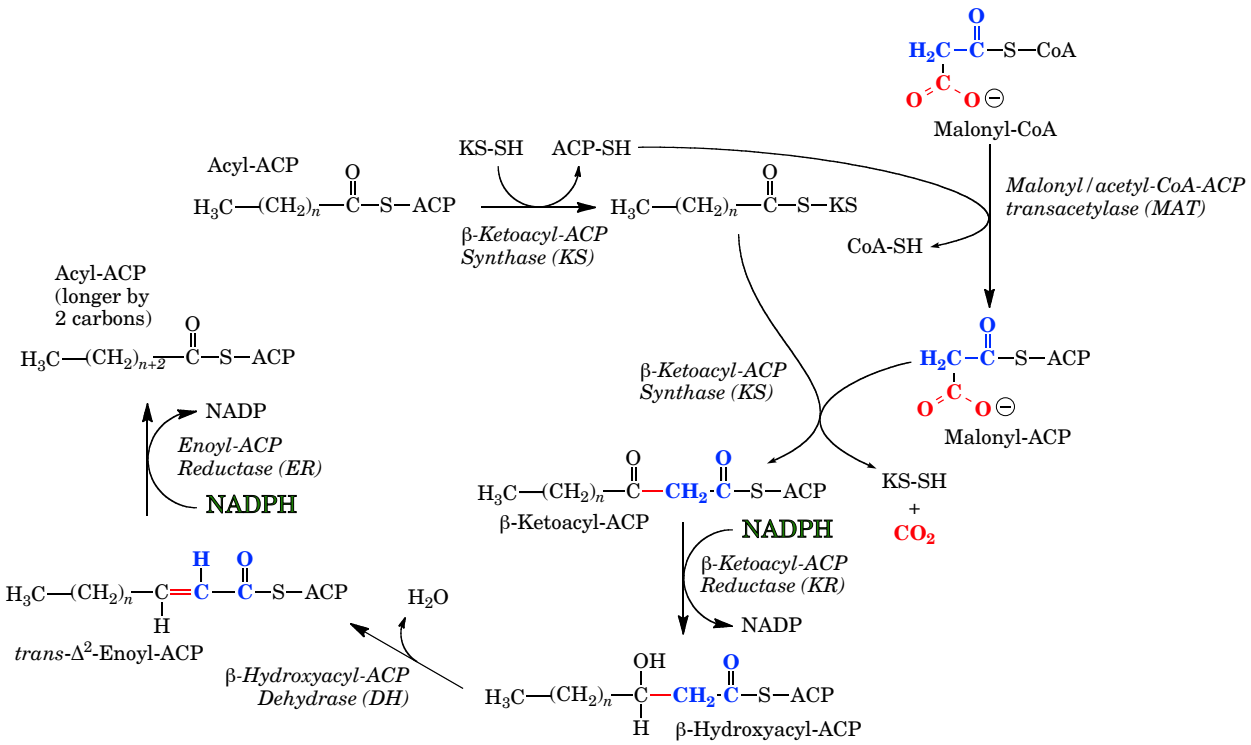


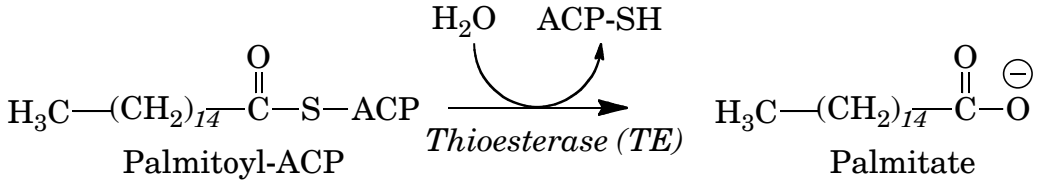


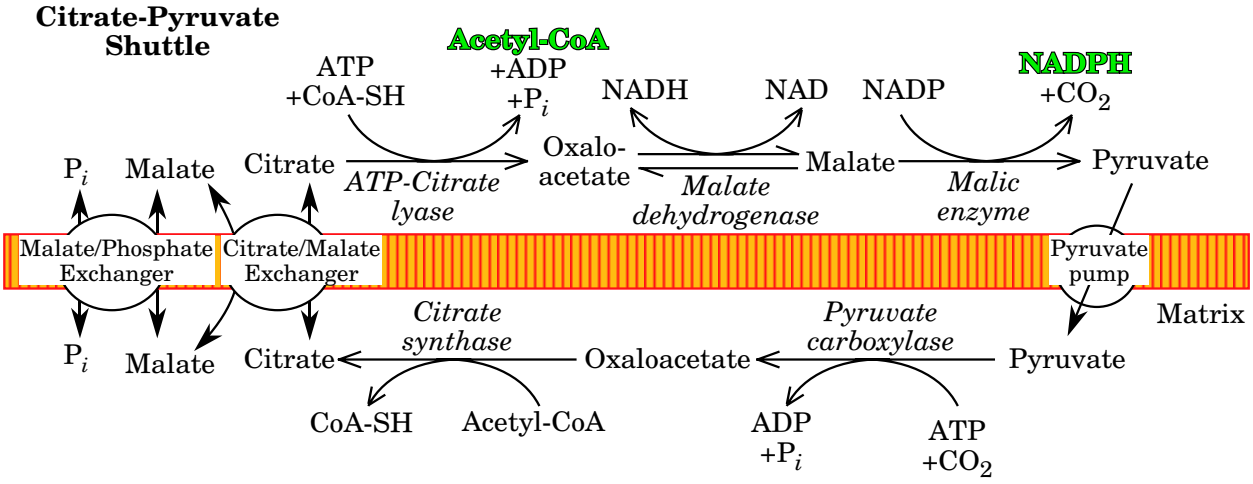
Acetyl-CoA



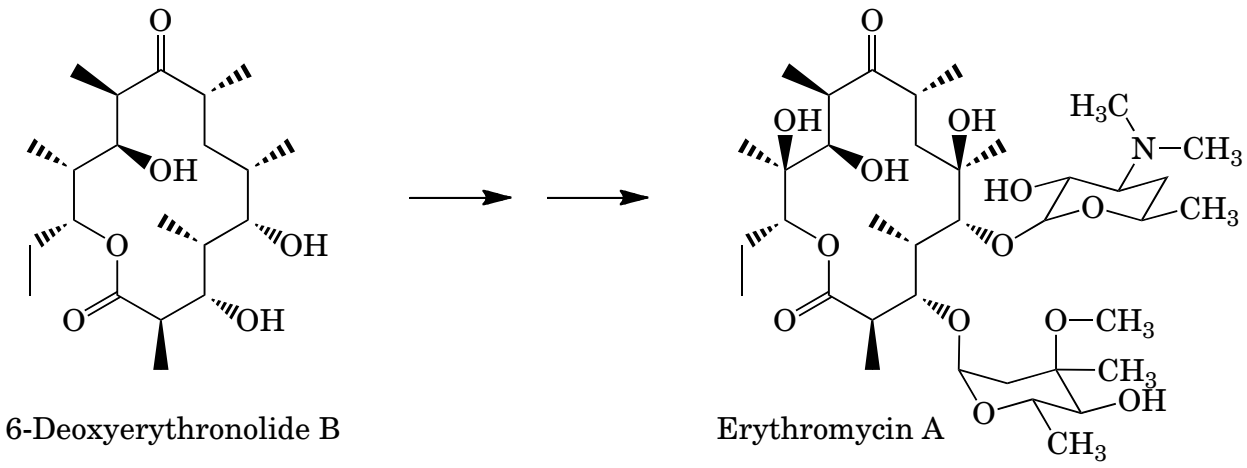



Malonyl-CoA
Acyl-ACP
KS-SH
ACP-SH
β-Ketoacyl-ACP Synthase (KS)
Malonyl / acetyl-CoA-ACP transacetylase (MAT)
CoA-SH
Acyl-ACP (longer by 2 carbons)
Malonyl-ACP
β-Ketoacyl-ACP Synthase (KS)
KS-SH
+
CO2
NADP
Enoyl-ACP Reductase (ER)
NADPH
β-Ketoacyl-ACP
NADPH
β-Ketoacyl-ACP Reductase (KR)
NADP
trans-Δ2-Enoyl-ACP
H2O
β-Hydroxyacyl-ACP Dehydrase (DH)
β-Hydroxyacyl-ACP

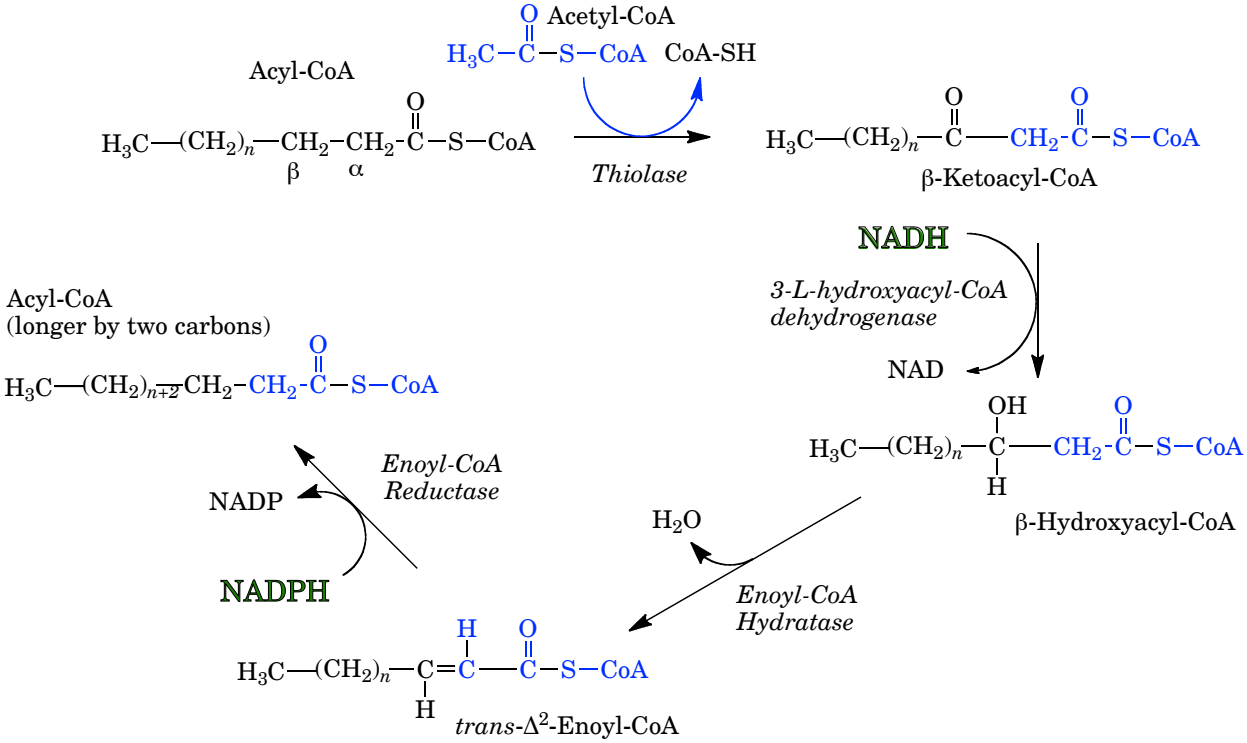

H2O
ACP-SH
Palmitoyl-ACP
Thioesterase (TE)
Palmitate


Citrate-Pyruvate Shuttle
Acetyl-CoA
ATP
+CoA-SH
+ADP
+Pi
NADH
NAD
NADP
NADPH
+CO2
Pi
Malate
Citrate
ATP-Citrate lyase
Oxalo-acetate
Malate dehydrogenase
Malate
Malic enzyme
Pyruvate
Malate/Phosphate Exchanger
Citrate/Malate Exchanger
Pyruvate pump
Matrix
Pi
Malate
Citrate
Citrate synthase
Oxaloacetate
Pyruvate carboxylase
Pyruvate
CoA-SH
Acetyl-CoA
ADP
+Pi
ATP
+CO2

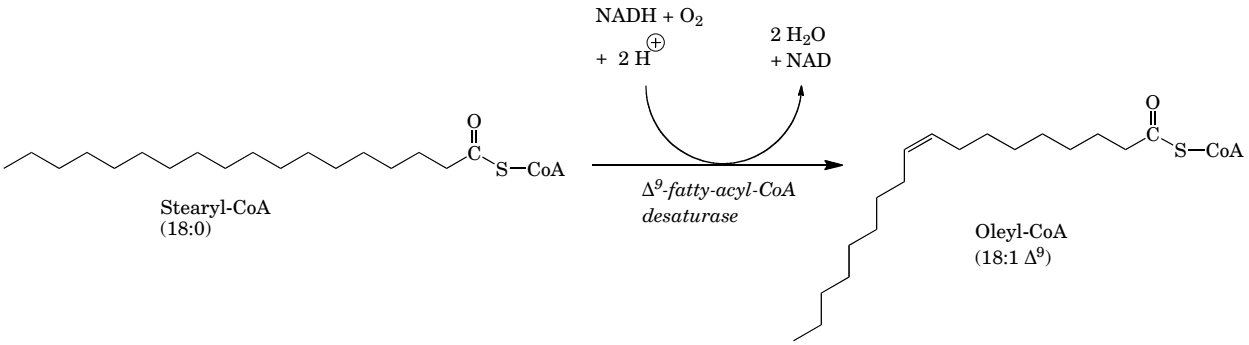
Polyketide Synthesis



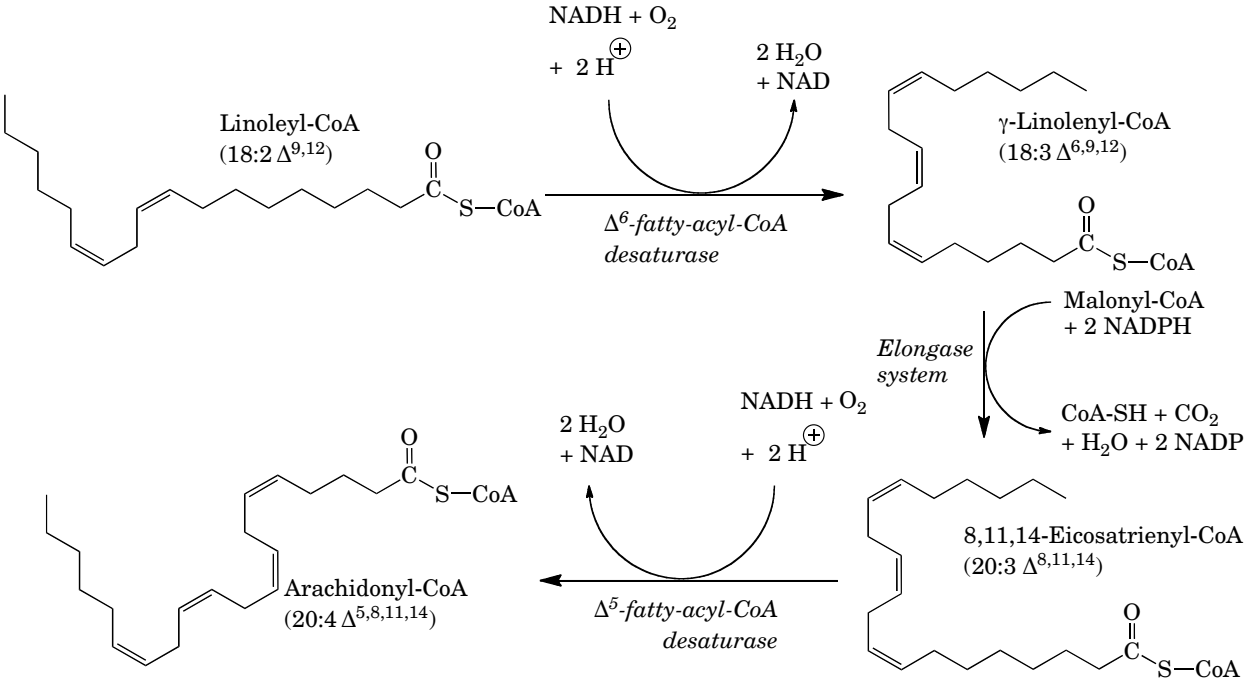
Elongation



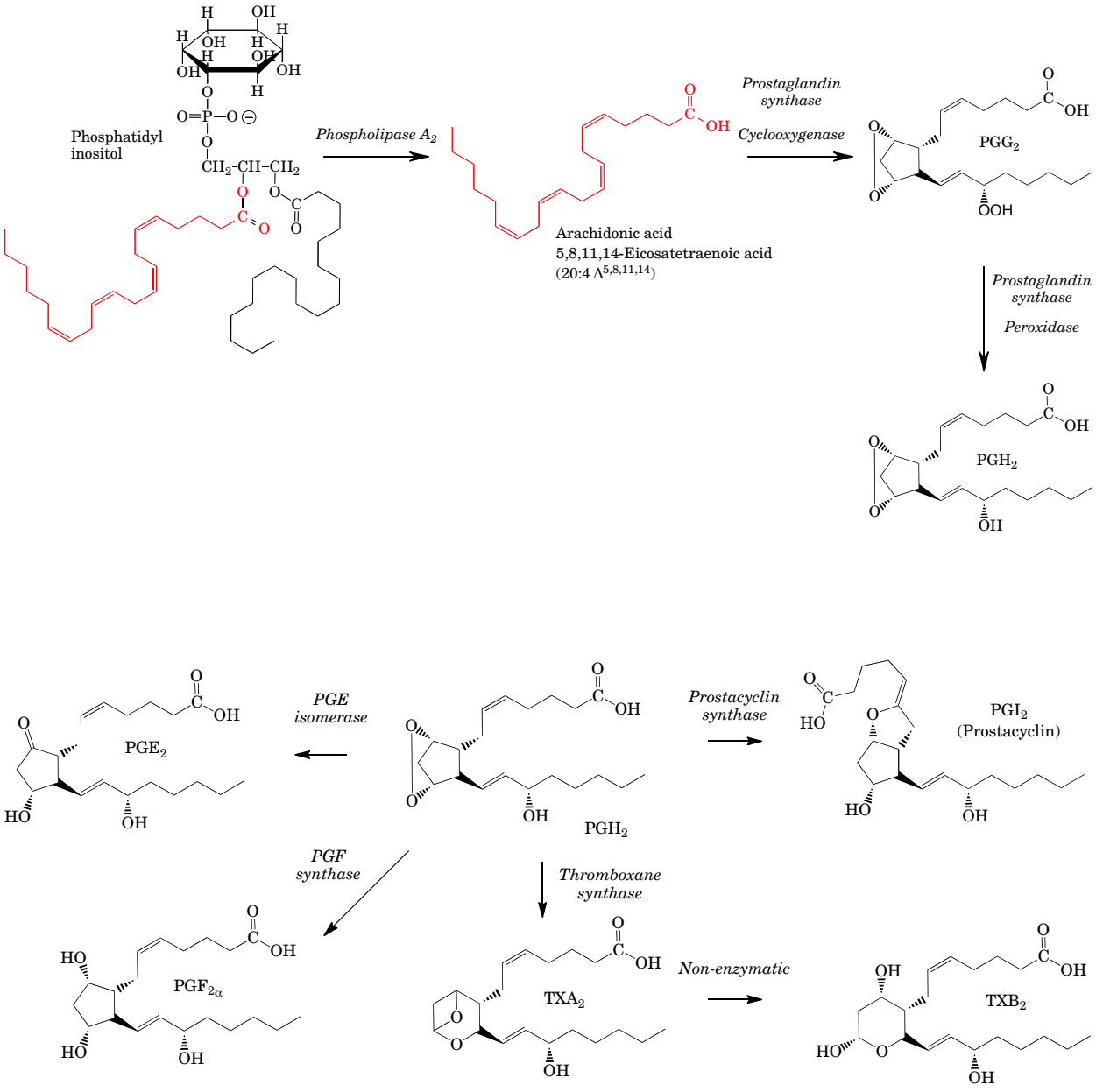
Desaturation



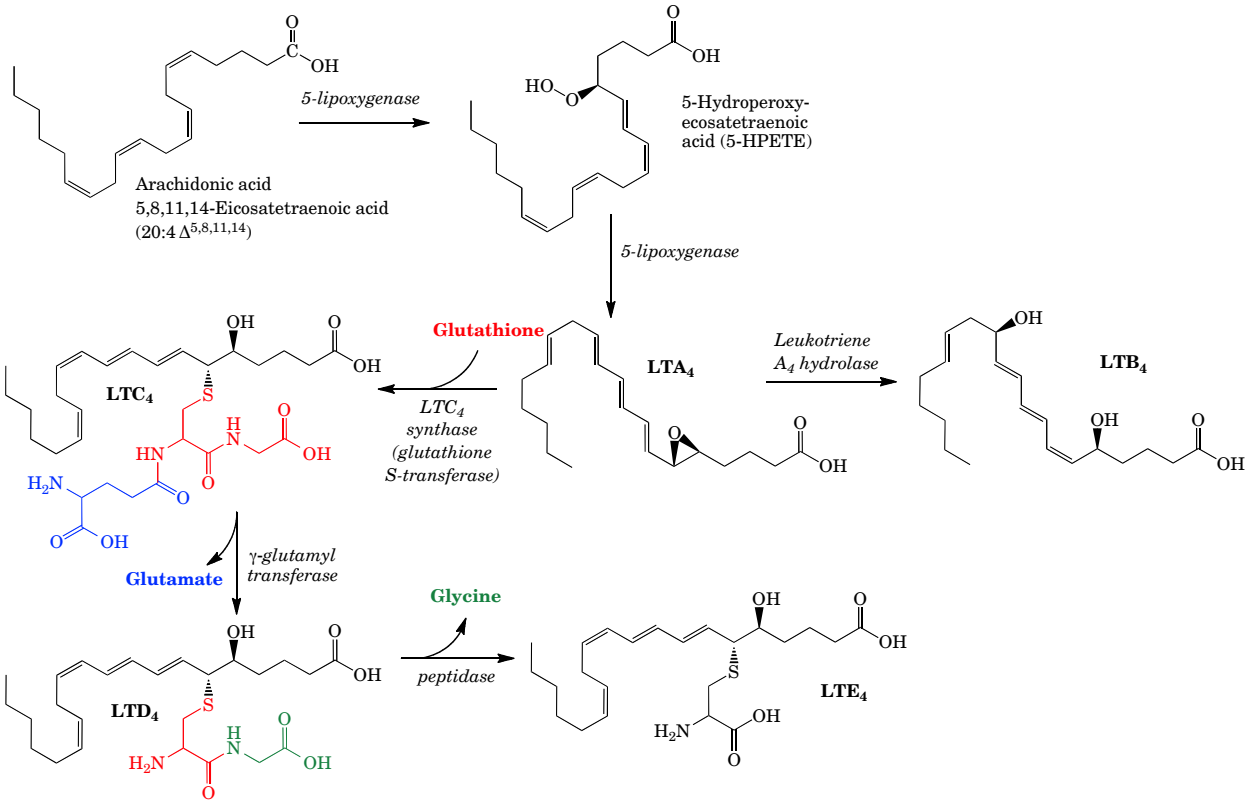
Arachidonic Acid Synthesis



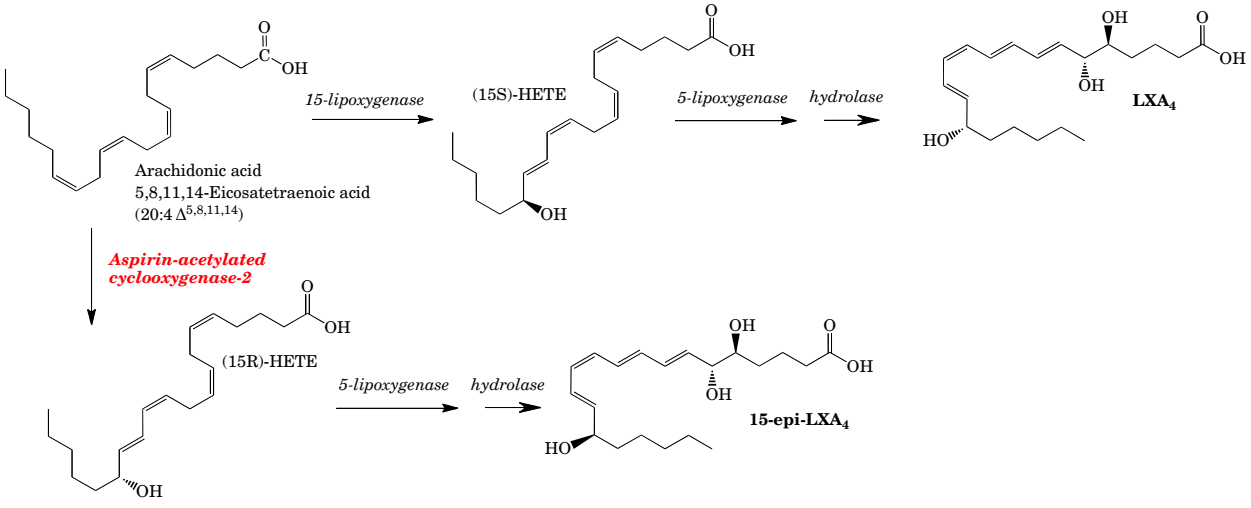
Prostaglandin Synthesis



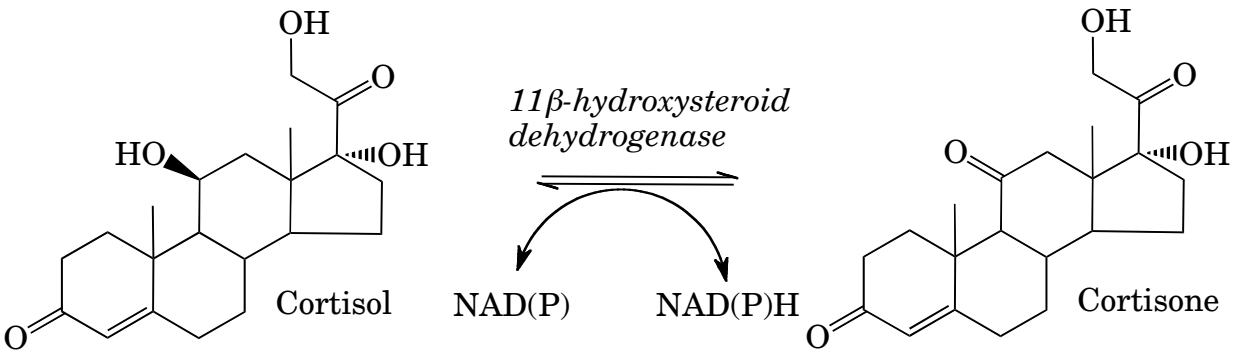
Leukotrienes

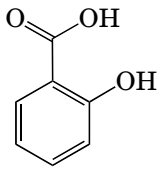


Lipoxins

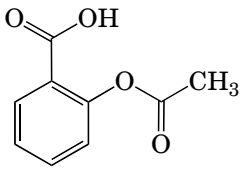


Anti-inflammatory Drugs

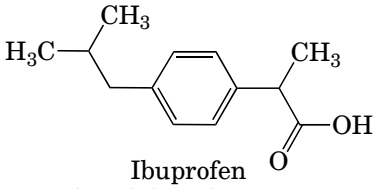




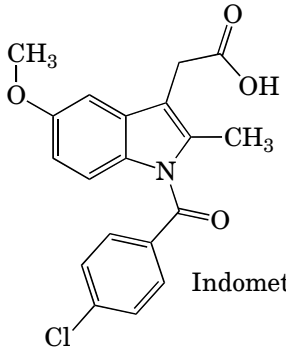
Salicylic acid
[2-hydroxybenzoic acid]



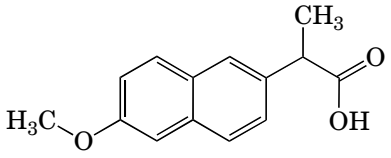
Aspirin
[acetyl salicylic acid]
[2-acetoxybenzoic acid]



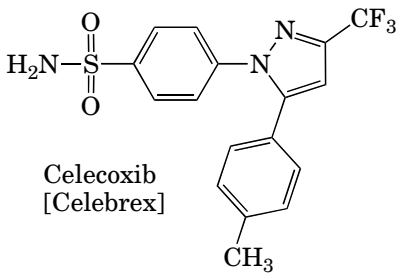
Ibuprofen
[2-(4-isobutylphenyl)propionic acid]



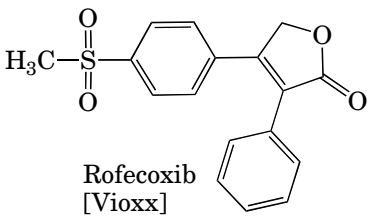
Indomethacin



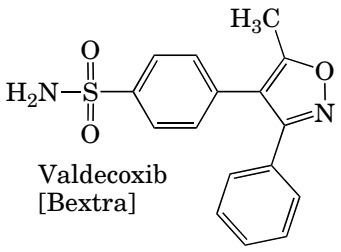
Naproxen
[2-(6-methoxynaphthyl)
propionic acid]



Celecoxib
[Celebrex]

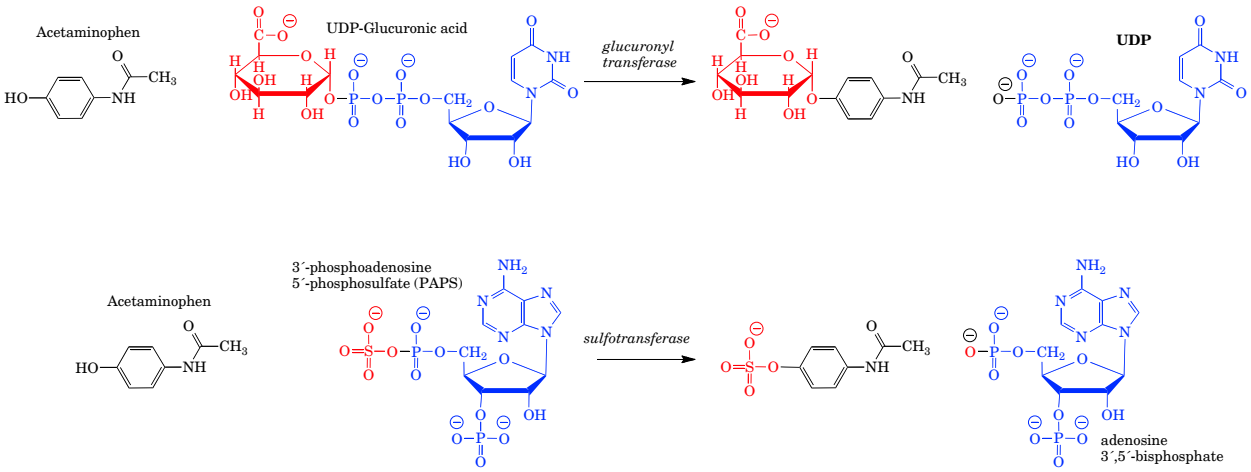


Rofecoxib
[Vioxx]

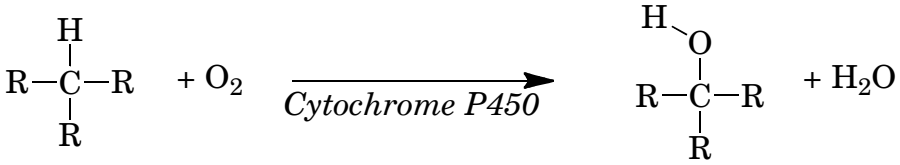


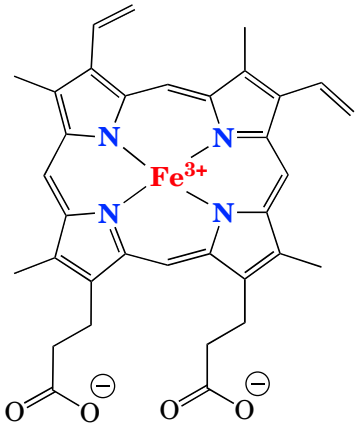
Valdecoxib
[Bextra]

Acetaminophen Metabolism

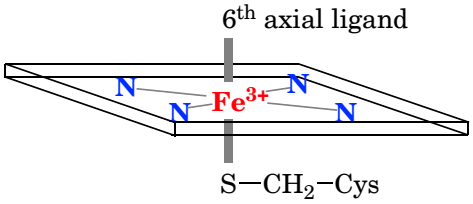


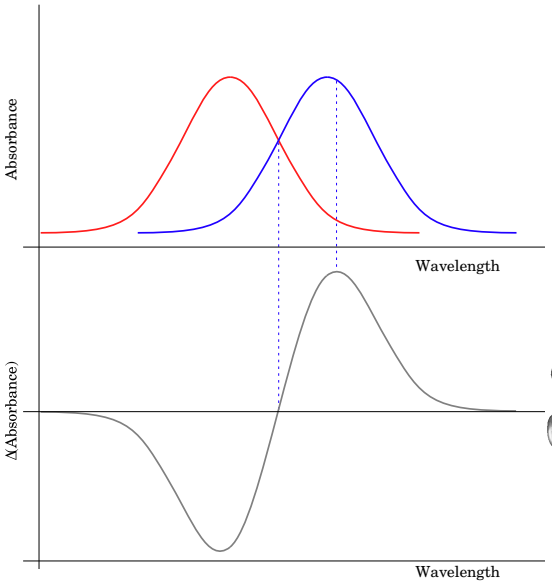
Cytochrome P450 Enzymes

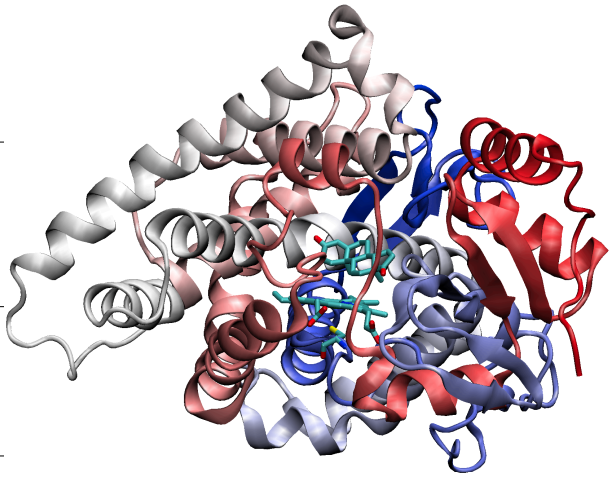




Iron-Protoporphyrin IX





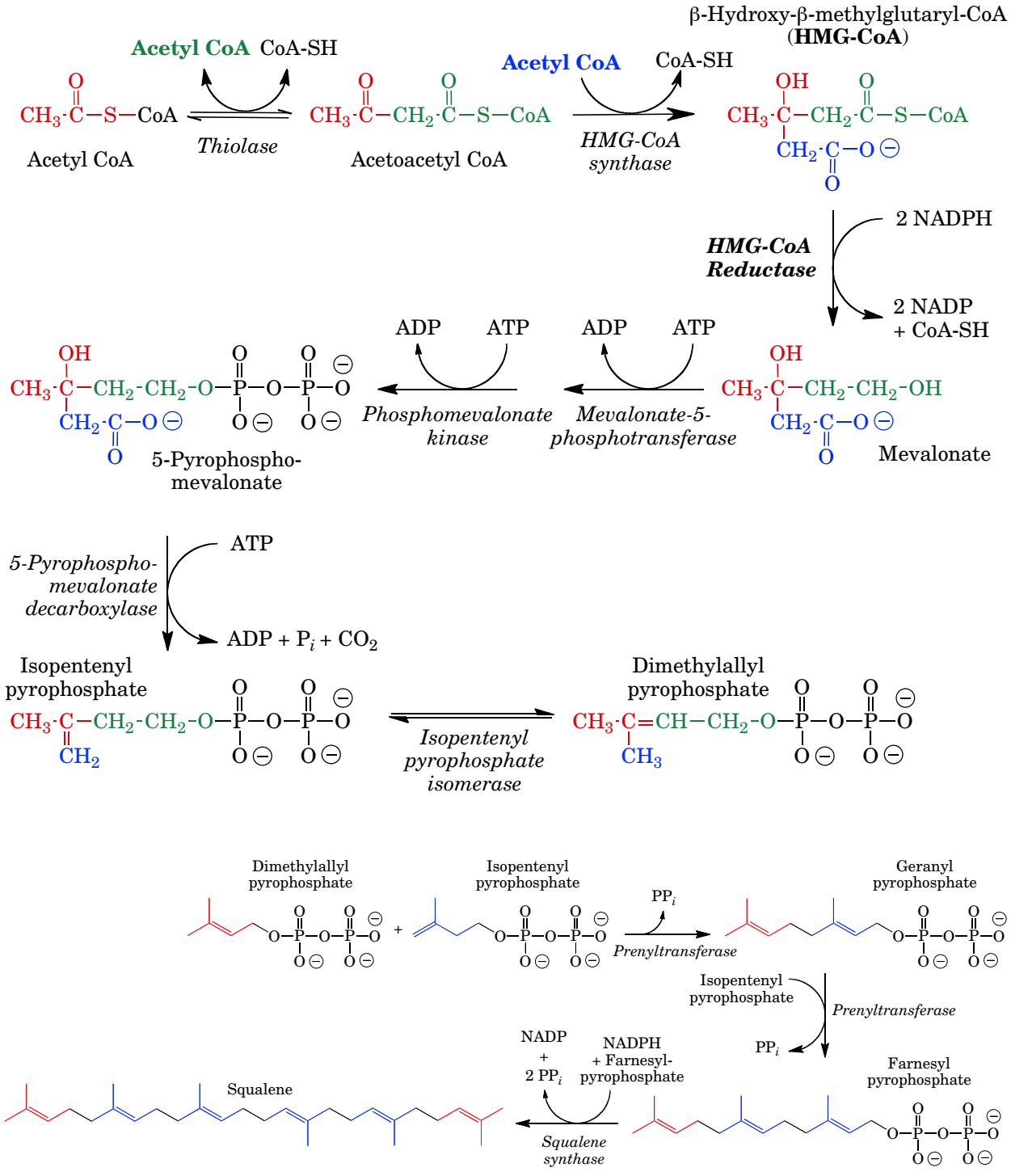


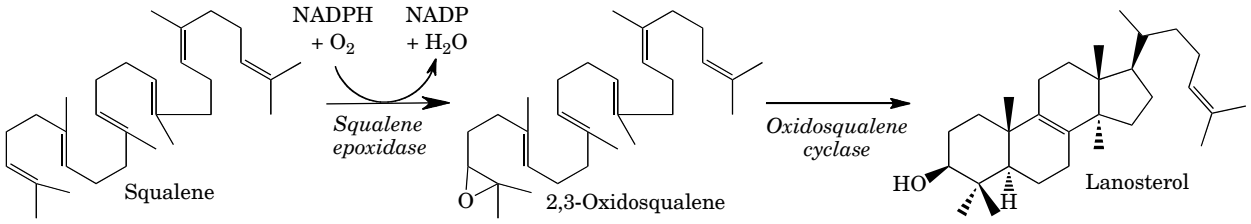
Classes of Cytochromes P450
Soluble
Mitochondrial
"Microsomal"

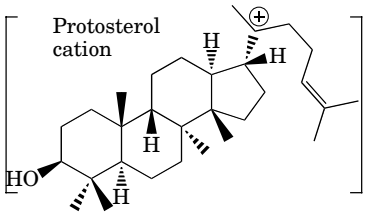
Ferredoxin Reductase
Ferredoxin

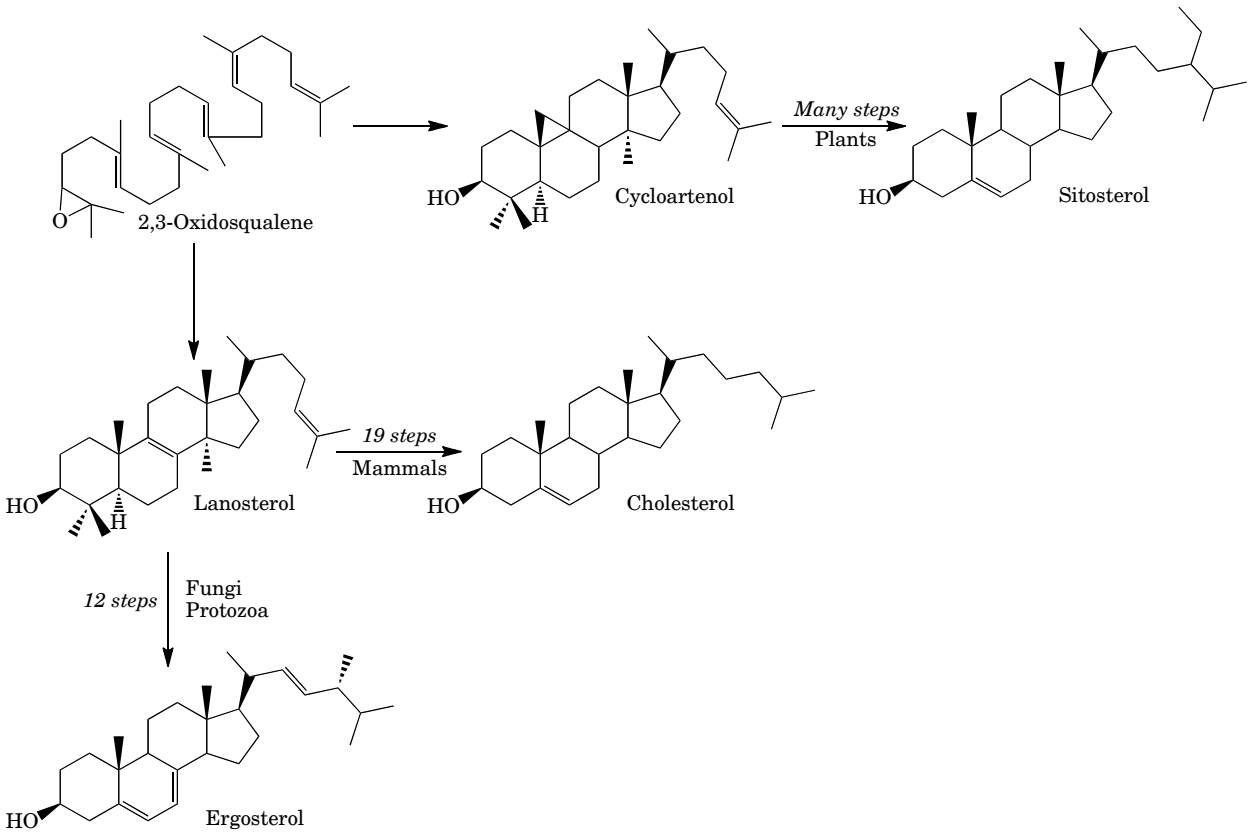
Cytochrome P450 Reductase

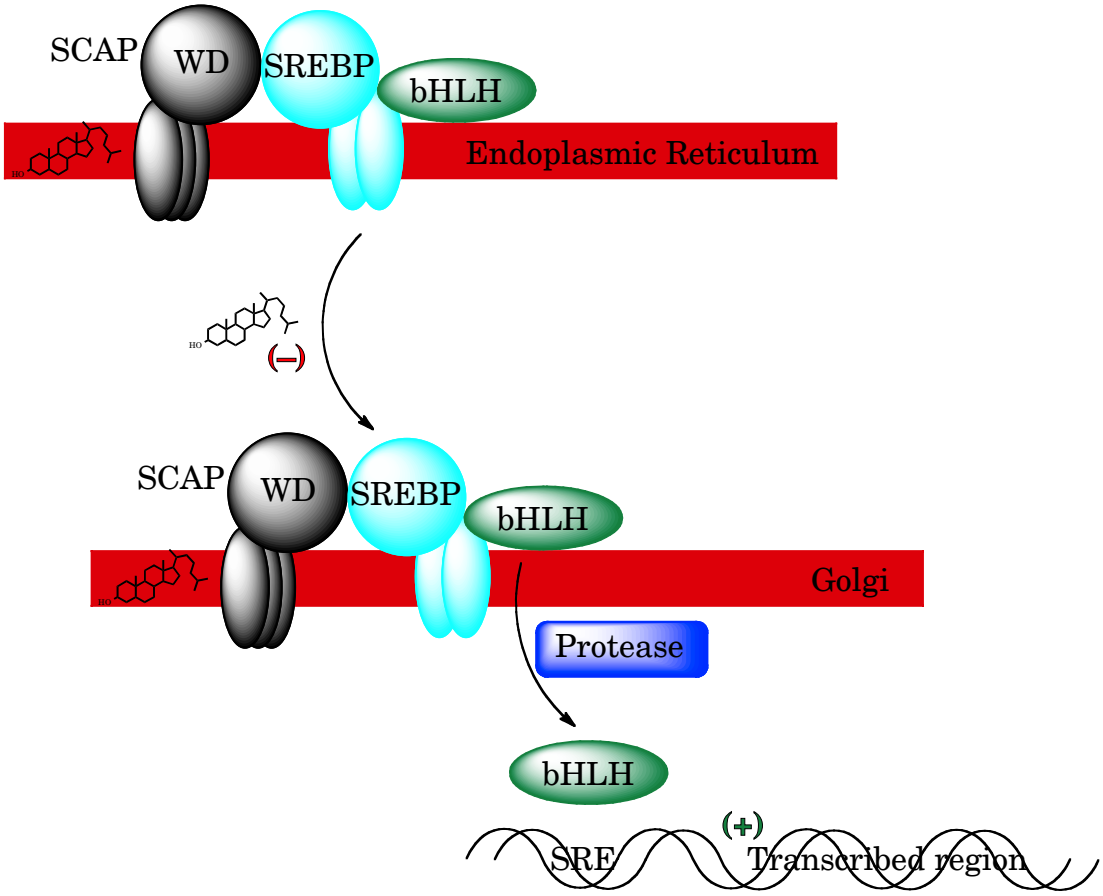
Cholesterol Biosynthesis

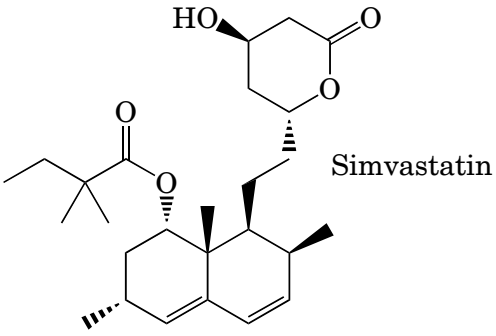



NADPH
+ O2
NADP
+ H2O
Squalene epoxidase
Squalene
2,3-Oxidosqualene
Oxidosqualene cyclase
HO
H
Lanosterol

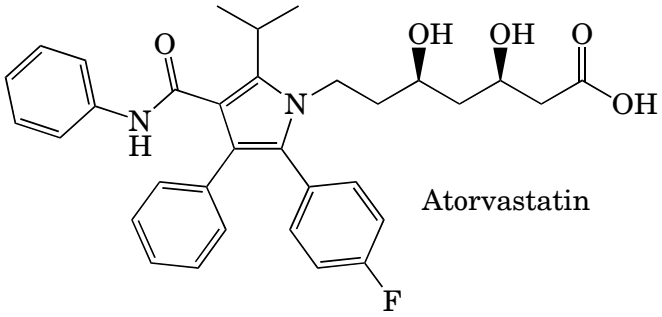

Protosterol cation
H
H
H
HO
H


O
2,3-Oxidosqualene
HO
H
Cycloartenol
Many steps
Plants
HO
Sitosterol
HO
H
Lanosterol
19 steps
Mammals
HO
Cholesterol
12 steps
Fungi
Protozoa
HO
Ergosterol

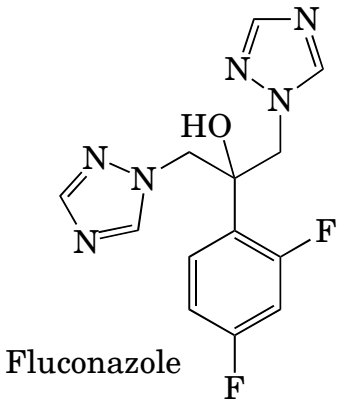




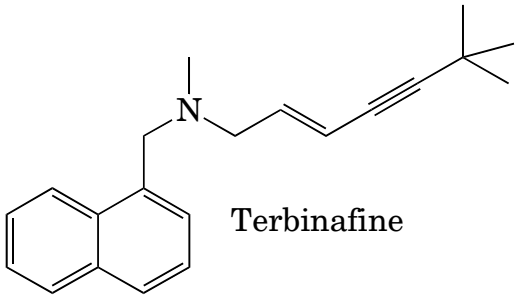
Simvastatin



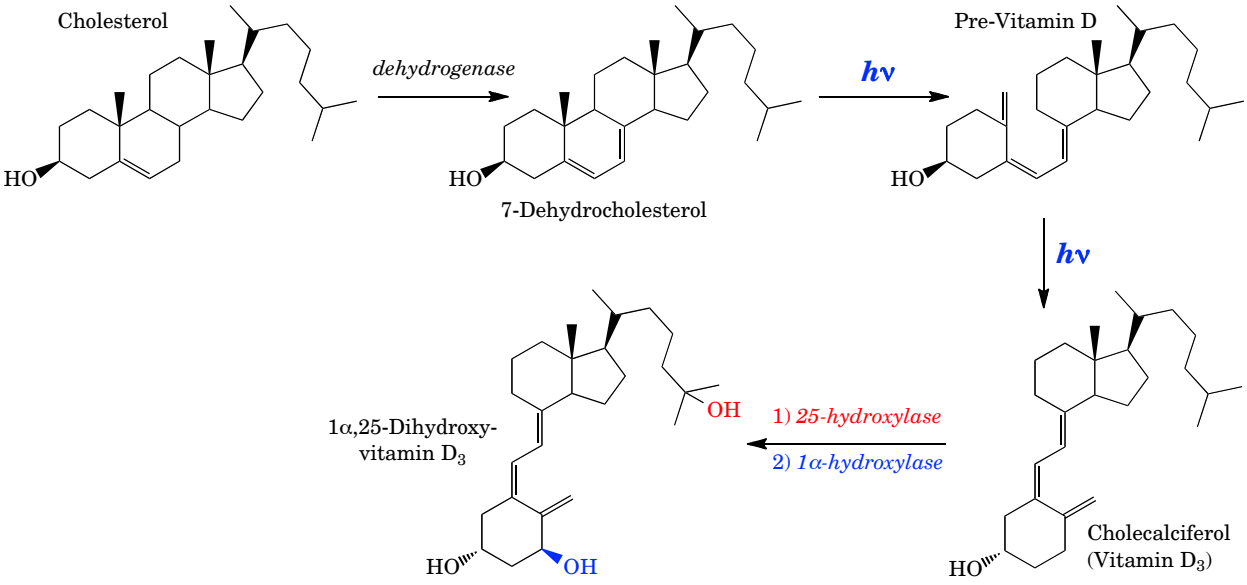
Atorvastatin



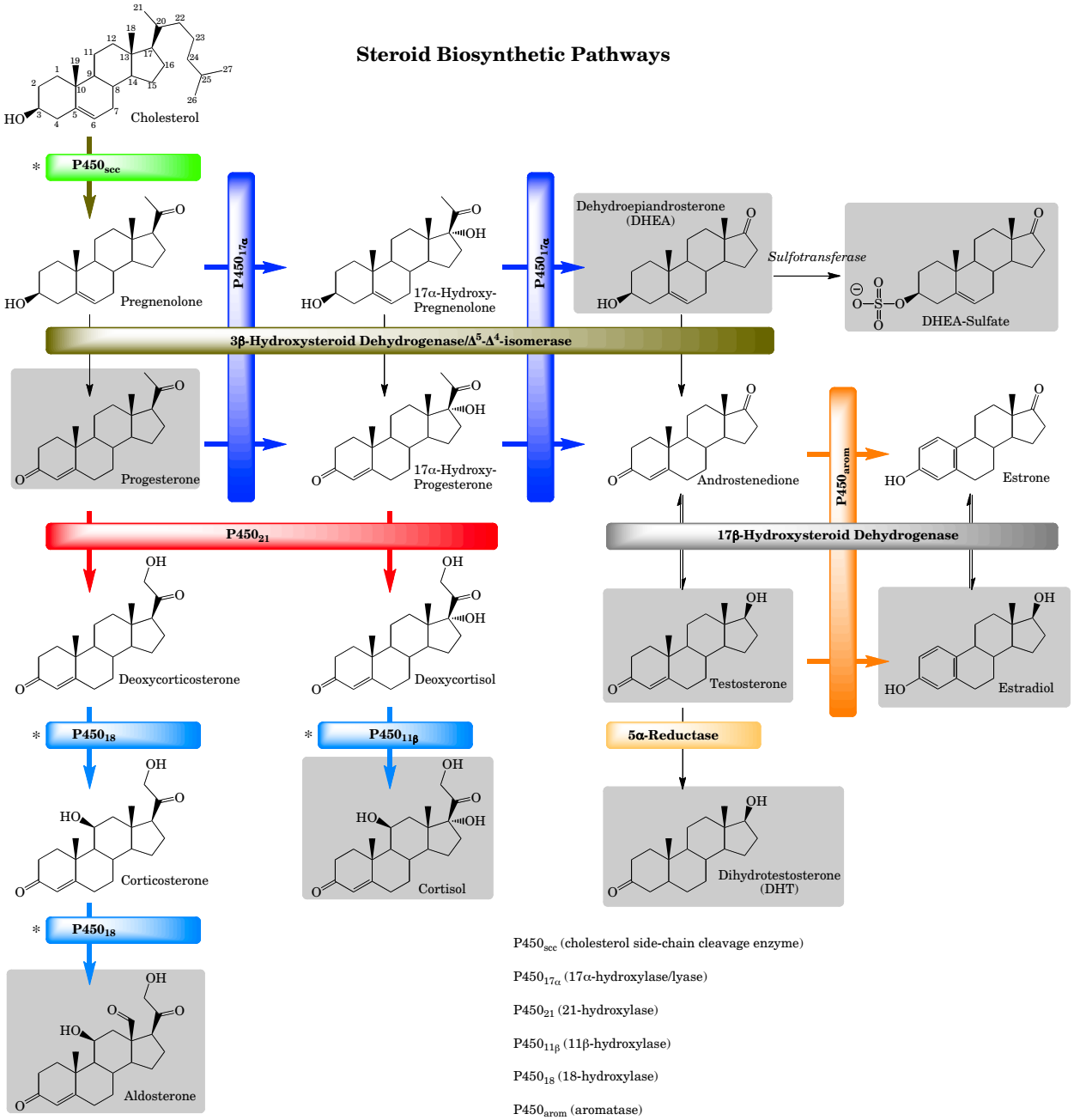
Fluconazole



Terbinafine



Steroid Biosynthetic Pathways



$P450_{scc}$ (cholesterol side-chain cleavage enzyme)

$P450_{17\alpha}$ (17α-hydroxylase/lyase)

$P450_{21}$ (21-hydroxylase)

$P450_{11\beta}$ (11β-hydroxylase)

$P450_{18}$ (18-hydroxylase)

$P450_{arom}$ (aromatase)

Glucocorticoid effects
Liver
↑Gluconeogenesis and glucose release
↑Glycogen synthesis
↑Amino acid uptake

↑Phosphoenolpyruvate carboxykinase
↑Fructose-bisphosphatase
↑Glucose-6-phosphatase
↑Glycogen synthase

Skeletal muscle
↓Glucose uptake
↓Amino acid uptake
↓Protein synthesis

↑Protein breakdown

Adipose Tissue
↓Glucose uptake
↑Hormone sensitive lipase expression
↑Lipid mobilization and redistribution

Immune System
↓Number and activity of lymphocytes
↓Capillary permeability
↓Inflammation

↑Susceptibility to infection

General Permissive effects
↑Maintenance of blood pressure
↑Kidney function
↑Survival of stress

Other effects
↓Insulin release
↓Insulin action

↓Short-term memory formation

↑Phenylethanolamine-N-methyltransferase (Adrenal medulla)

↑Lung surfactant formation

↓Wound healing

Mineralocorticoid Effects
↓Sodium excretion
↑Potassium excretion
↑Blood pressure

Estrogen effects
↑Maturation of internal sex organs in female
↑Breast development
↑Uterine lining growth

↑Skin structure
↑Blood vessel structure
↑Coagulation
↑Lipid profiles
↓Bone resorption

↑Progesterone receptor

Effects in brain

Progestin effects
↑Breast development
↑Uterine lining differentiation

↓Insulin levels

Effects in brain

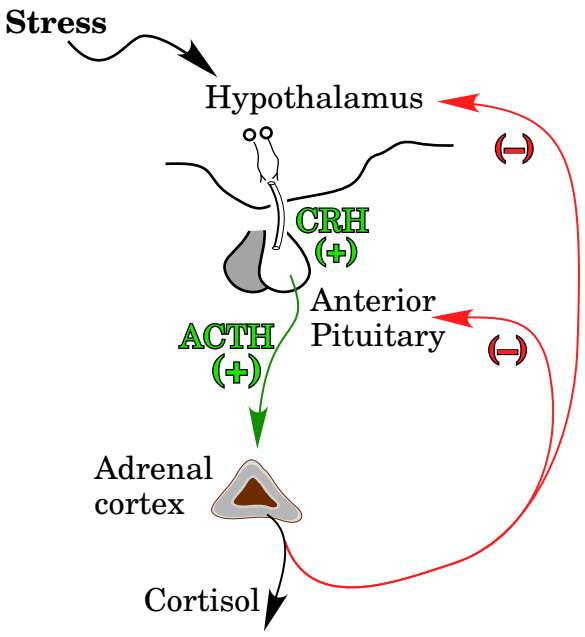
Androgen effects
↑Internal male sex organs
↑External male sex organs
↑Sperm production

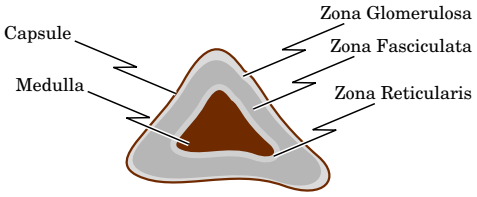
↑Skeletal muscle

↑Bone formation

↑Libido

Psychological effects



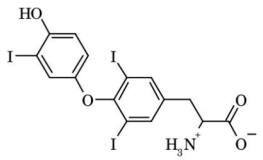
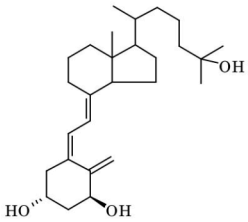
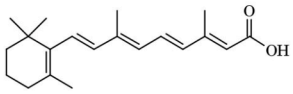
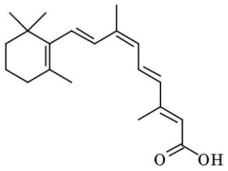
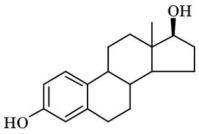
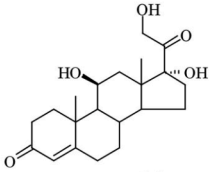
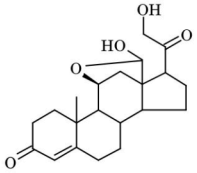
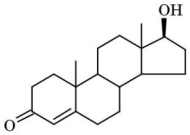
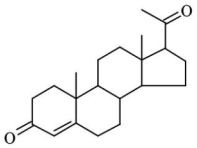


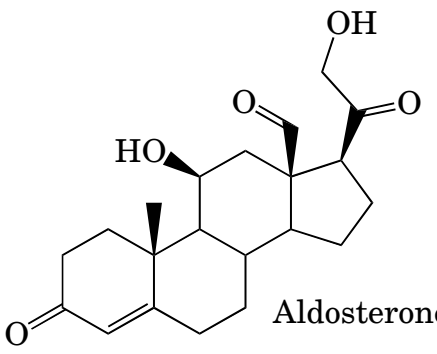
Structure	Products
Capsule	–
Zona Glomerulosa	Aldosterone
Zona Fasciculata	Cortisol, DHEA, DHEAS
Zona Reticularis	Cortisol, DHEA, DHEAS
Medulla	Epinephrine, other hormones

Causes of Congenital Adrenal Hyperplasia

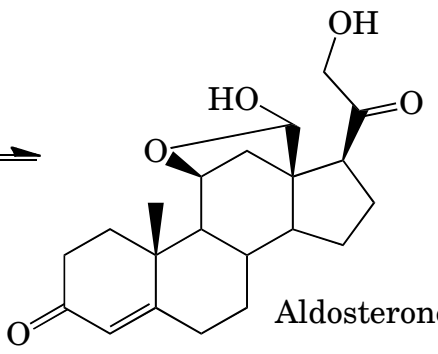
Disorder	21-Hydroxylase deficiency	11β-Hydroxylase deficiency	Aldosterone synthase deficiency	17α-Hydroxylase deficiency	3β-Hydroxysteroid dehydrogenase/Δ^5-Δ^4 isomerase deficiency	Lipoid hyperplasia
Defective gene	*CYP21*	*CYP11B1*	*CYP11B2*	*CYP17*	*HSD3B2*	*STAR*
Ambiguous genitalia	♀	♀		♂	♂	♂
Addison's	Yes	rare	loss of Na^+	No	Yes	Yes
Incidence	Classical 1:10,000 Non-classical 1:100	1:100,000				
Glucocorticoids	↓	↓	Normal	Corticosterone	↓	↓
Aldosterone	↓	↑	↓	↑	↓	↓
Androgens	↑	↑	Normal	↓	♂↓ ♀↑	↓
Blood pressure	↓	↑	↓	↑	↓	↓
Na^+ levels	↓	↑	↓	↑	↓	↓
K^+ levels	↑	↓	↑	↓	↑	↑

Members of the Steroid Hormone Receptor Superfamily

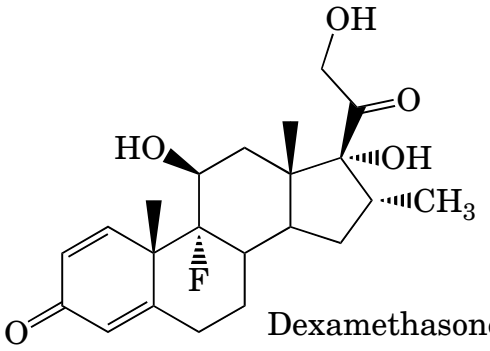
Receptor	Ligand	Length (amino acids)	Chromosome
Thyroid Hormone-α Thyroid Hormone-β (triiodothyronine)		490 456	17 3
Vitamin D ($1,25[OH]_2$-D_3)		427	12
Retinoic Acid-α Retinoic Acid-β Retinoic Acid-γ (all *trans*-retinoic acid)		462 448 454	17 3 12
Retinoid X-α Retinoid X-β Retinoid X-γ (9-*cis*-retinoic acid)		462 533 454	9 6 1
Estrogen-α Estrogen-β (estradiol)		595 477	6 14
Glucocorticoid (GR Type II) (cortisol)		777	5
Mineralocorticoid (GR Type I) (aldosterone)		984	4
Androgen (testosterone)		919	X
Progestin (progesterone)		934	11



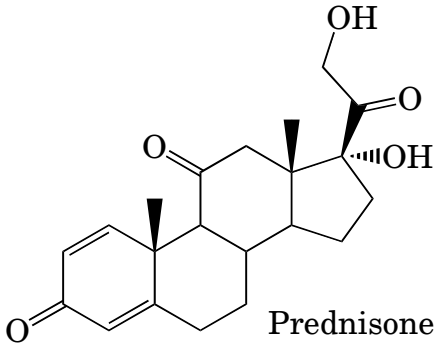
Aldosterone



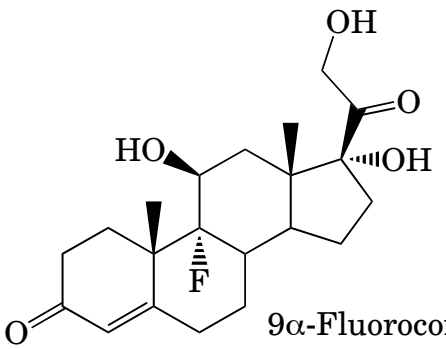
Aldosterone



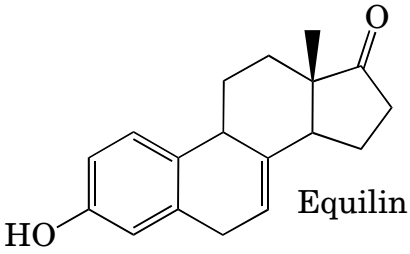
Dexamethasone



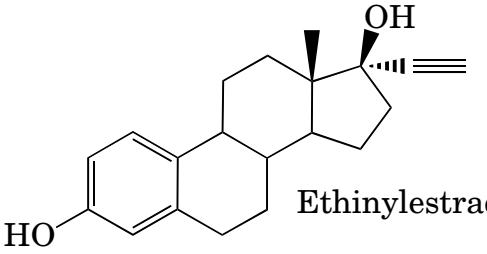
Prednisone



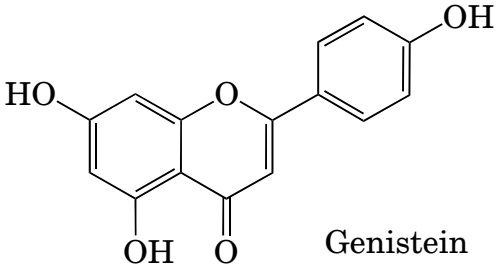
9α-Fluorocortisol



Equilin

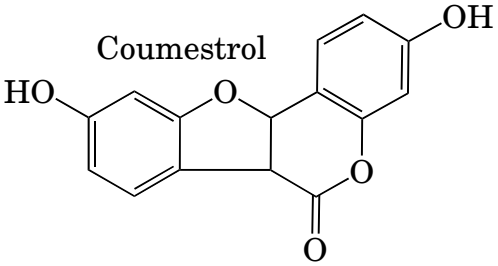


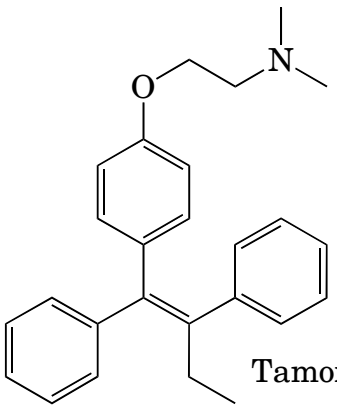
Ethinylestradiol



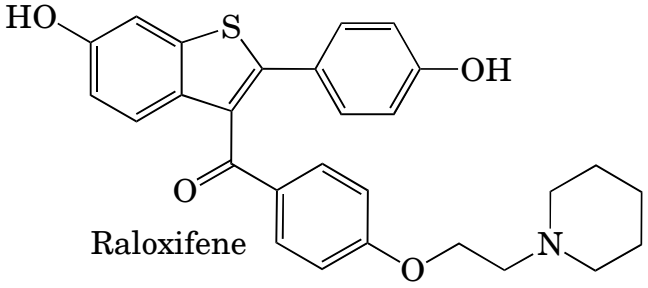
Genistein

Coumestrol

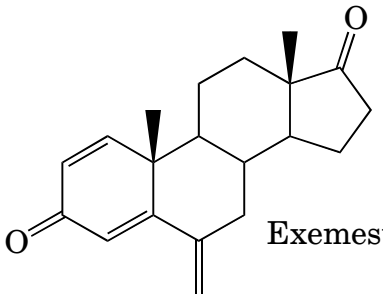




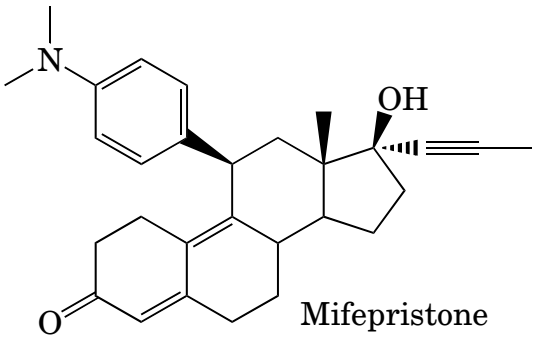
Tamoxifen



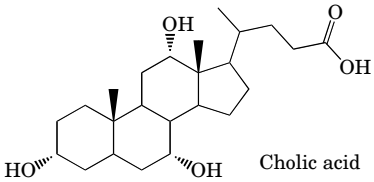
Raloxifene



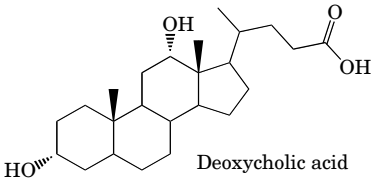
Exemestane



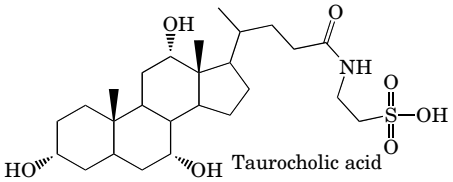
Mifepristone



Cholic acid



Deoxycholic acid



Taurocholic acid