

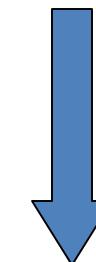
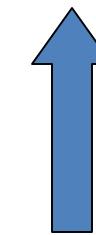
Synthesis and Degradation of Hormones

Chemistry of Hormones

- Steroids
- Small molecules - NO
- Amino acid derivates
 - Thyroid hormones

Receptor inside the cell

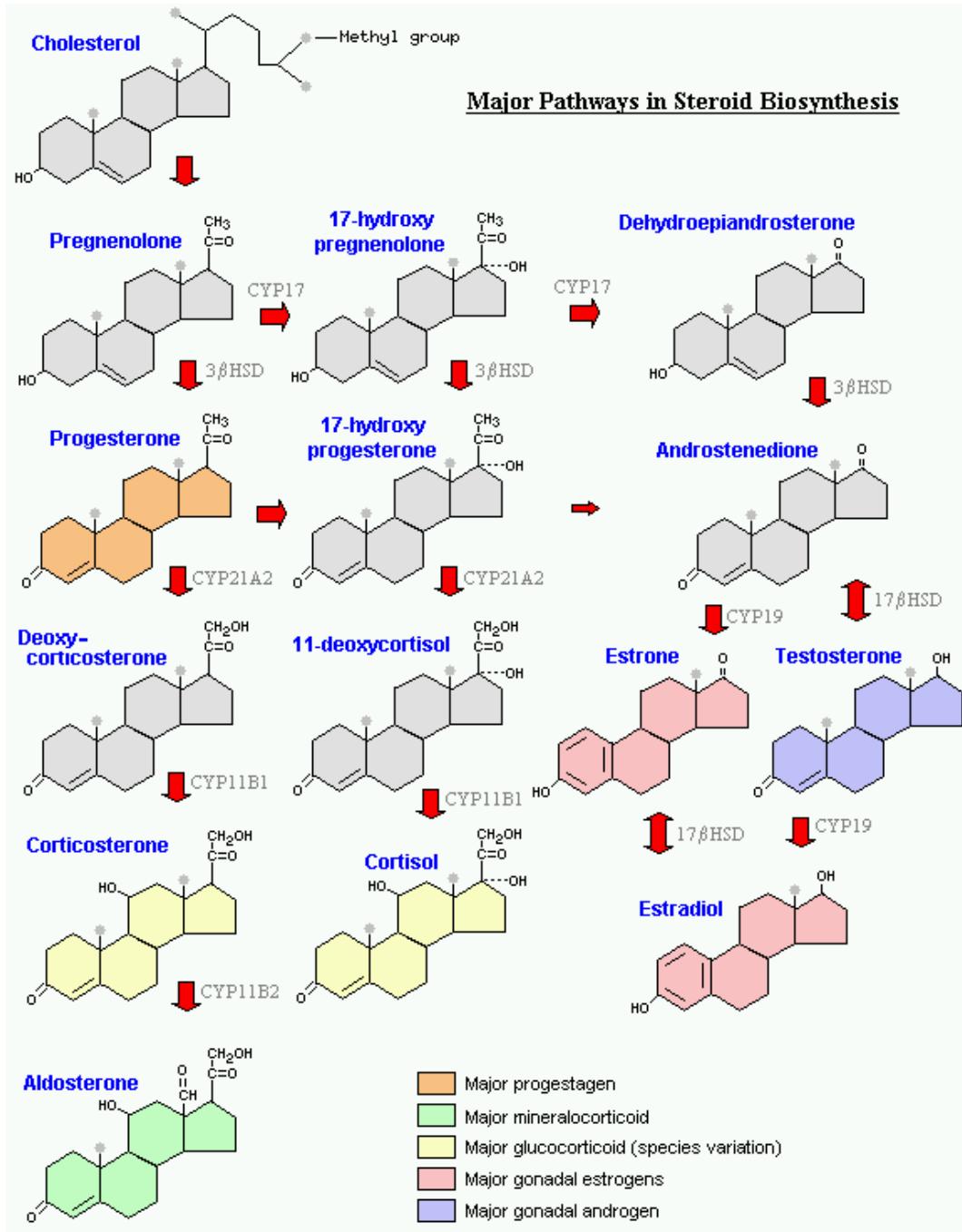
-
- Catecholamines
 - Proteins and peptides
 - FA derivates - eicosanoids



Surface receptor

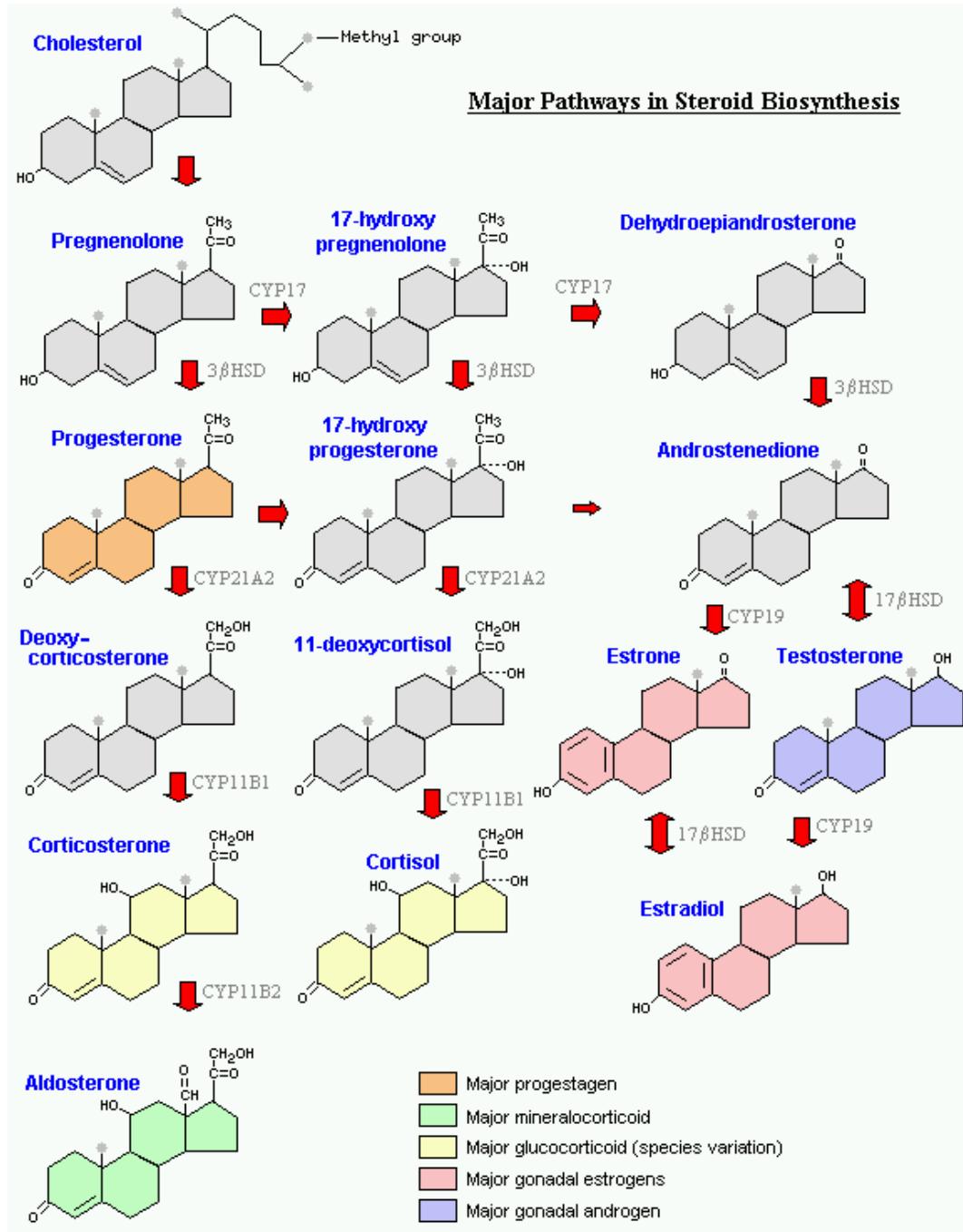
Steroid hormone synthesis

- C21:
 - Progesterone: directly from pregnenolone
 - Cortisol & Aldosterone: from progesterone



Steroid hormone synthesis

- C19
 - Testosterone
 - from progesterone or pregnenolone
 - 2c shortage
- C18 (estrogen):
 - Aromatase
 - Cleaves C18
 - Reduction



Steroid hormone breakdown

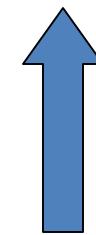
- Steran core cannot be cleaved
- In the liver: hydroxylation and conjugation with glucuronides or sulphates
- Urinary excretion:
 - Of metabolites
 - Of unchanged hormones

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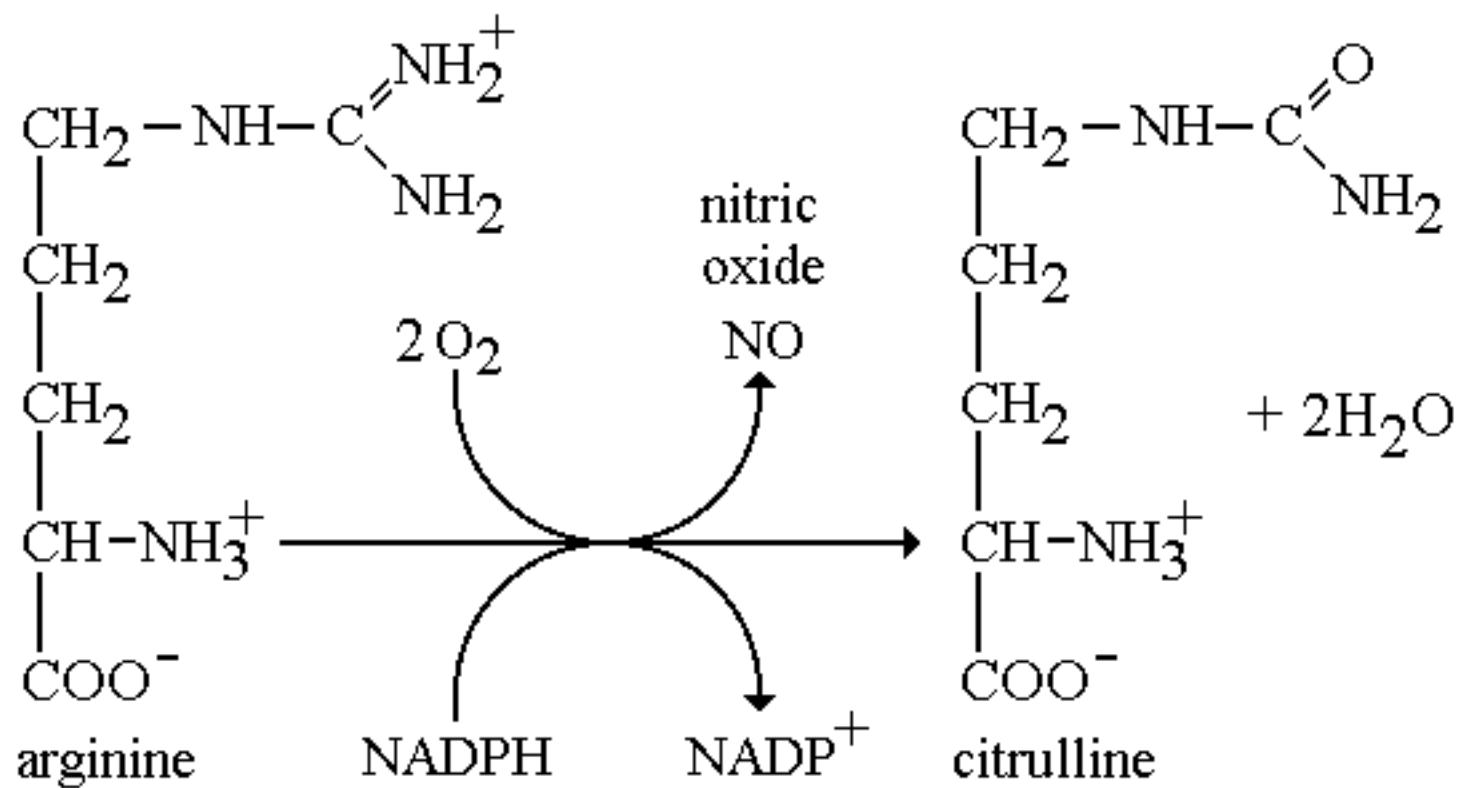
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Surface receptor

Nitric oxide (NO)

- NO: synthesized by NO-synthase



Nitric oxide synthase isozymes

- NO-synthase (NOS)
 - In neurons (NOS-I): neurotransmission
 - In macrophages (NOS-II): kills bacteria
 - Endothelial (NOS-III): smooth muscle → cGMP → vasodilation
- Clinical correlation:
 - Nitrates in the treatment of angina
 - Refractory hypotension during septic shock

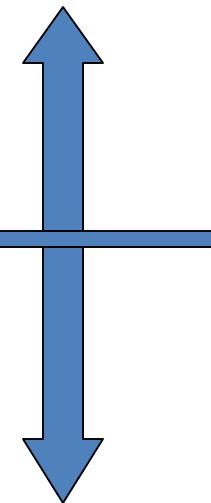
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– Thyroid hormones

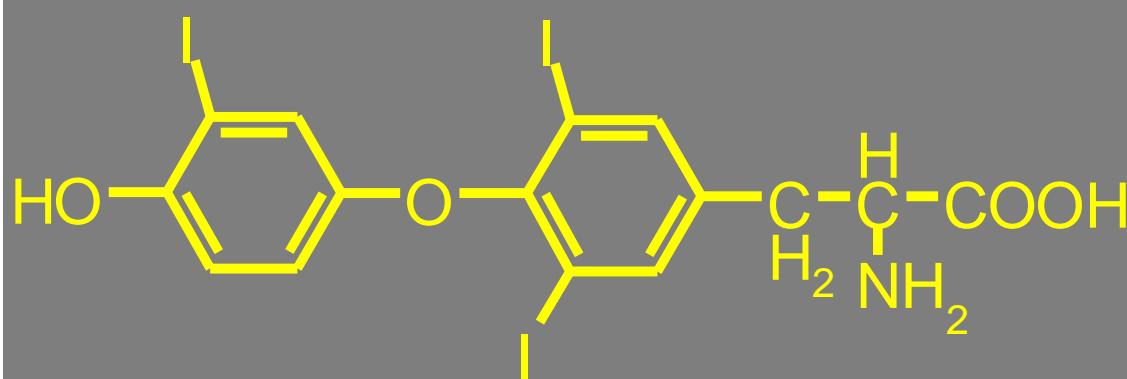
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Receptor inside the cell

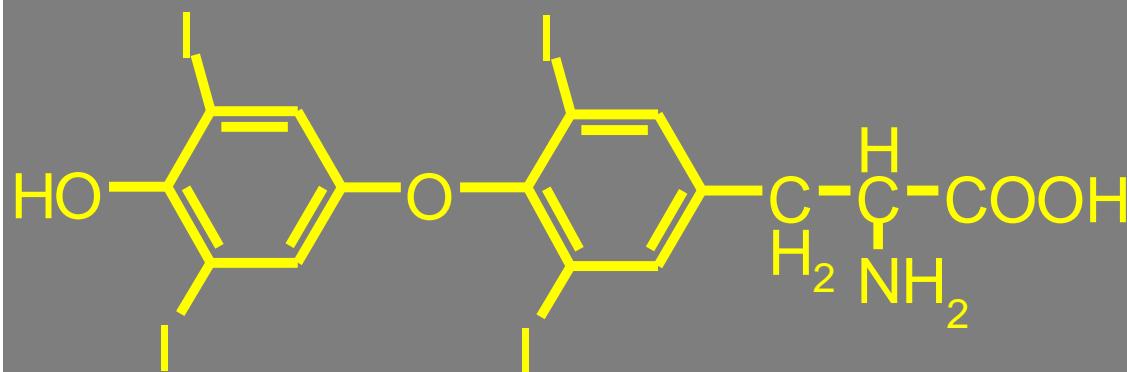


Surface receptor

Thyroid hormones



Triiodothyronine (T3)



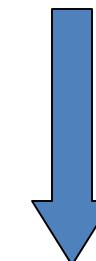
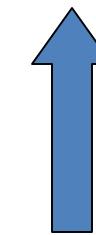
Thyroxine (T4)

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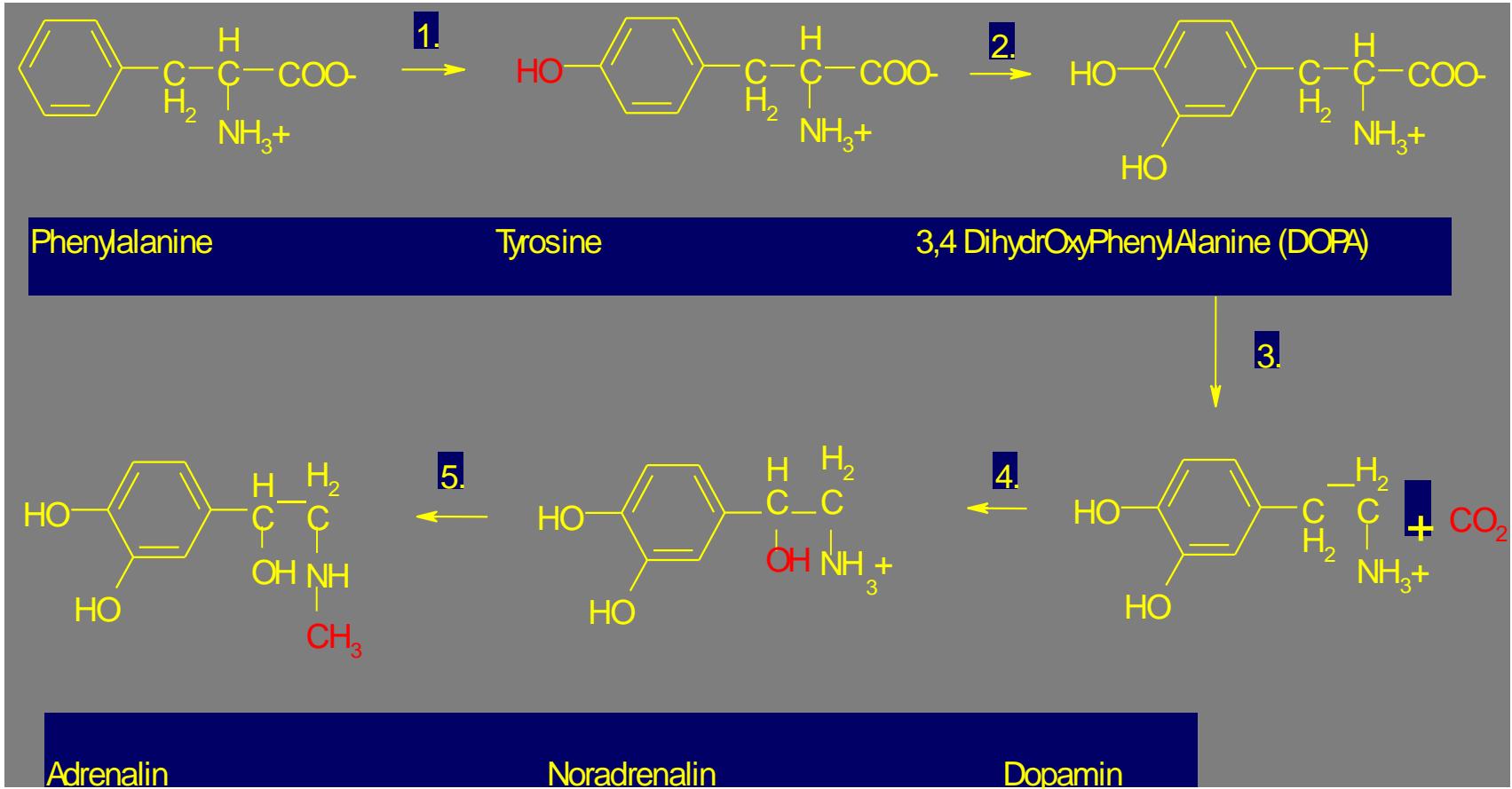


Surface receptor

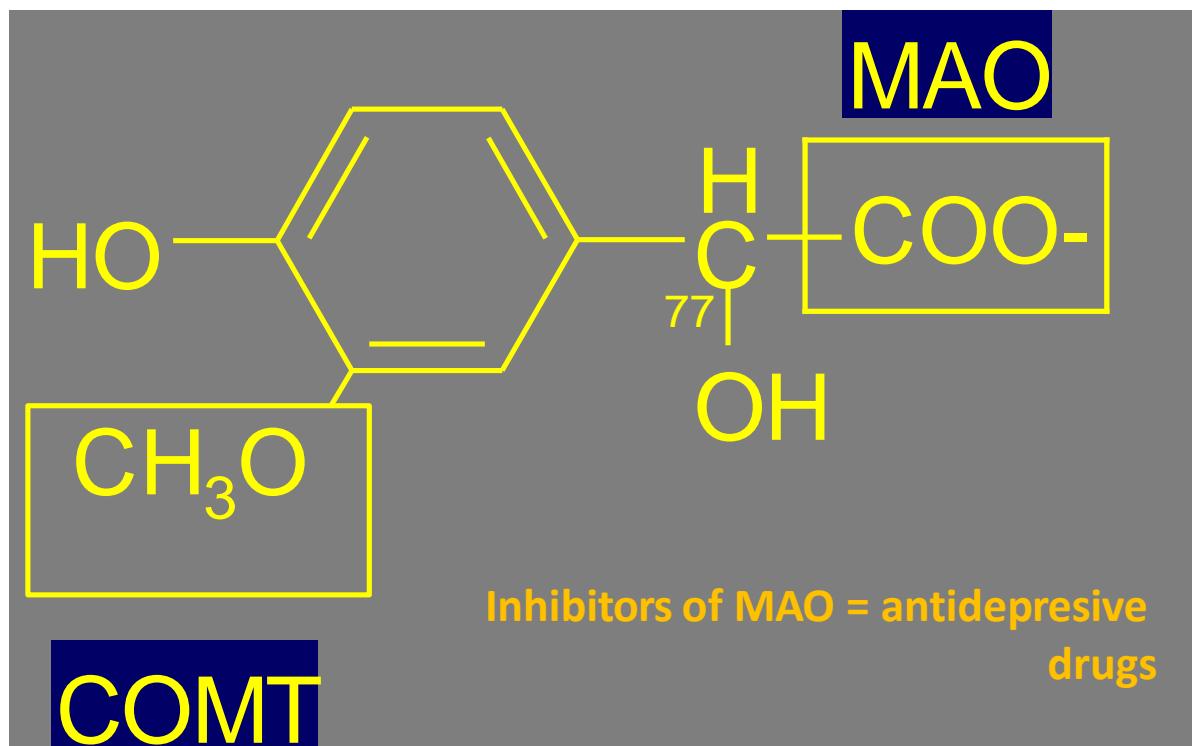
Catecholamine synthesis

- Substrate = Phe or Tyr
- Synthesis located in: adrenal medulla, nerve tissue
- Products:
 - Dopamine, adrenaline (hormones)
 - Noradrenaline (neurotransmitter)

Catecholamine synthesis



Catecholamine breakdown

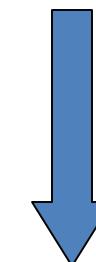
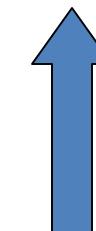


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Surface receptor

Protein and peptide hormones

- CNS mediators: neuropeptides, opioids
- Hypothalamic releasing hormones and pituitary peptides
- Insulin and glucagone
- Growth factors: IGF, CSF, EPO

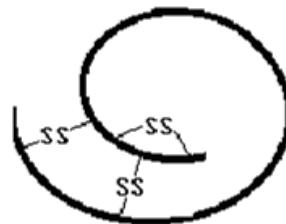
...and many others

General steps of peptide synthesis

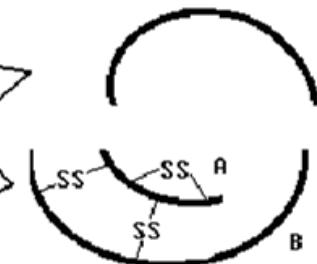
“Precursor Polypeptides”

- Expression of “pre-pro” protein

Proinsulin



C-peptide



- Transport to ER

- Splitting the signaling sequence

- Cleavage to definite peptide(s) and final modification in Golgi

- Proinsulin to insulin

- Proopiomelanocortine (POMC) to MSH and ACTH

Degradation of peptide hormones

- Lysosomal after endocytosis of complex hormone-receptor
- Chemical modification (liver): rearrangement of S-S bridges, cleavage
- Renal excretion of small peptides