BHARATHIDASAN UNIVERSITY

Program: M.Sc., Biomedical Science

Course Title : Neurobiology

Catecholamine Biochemistry

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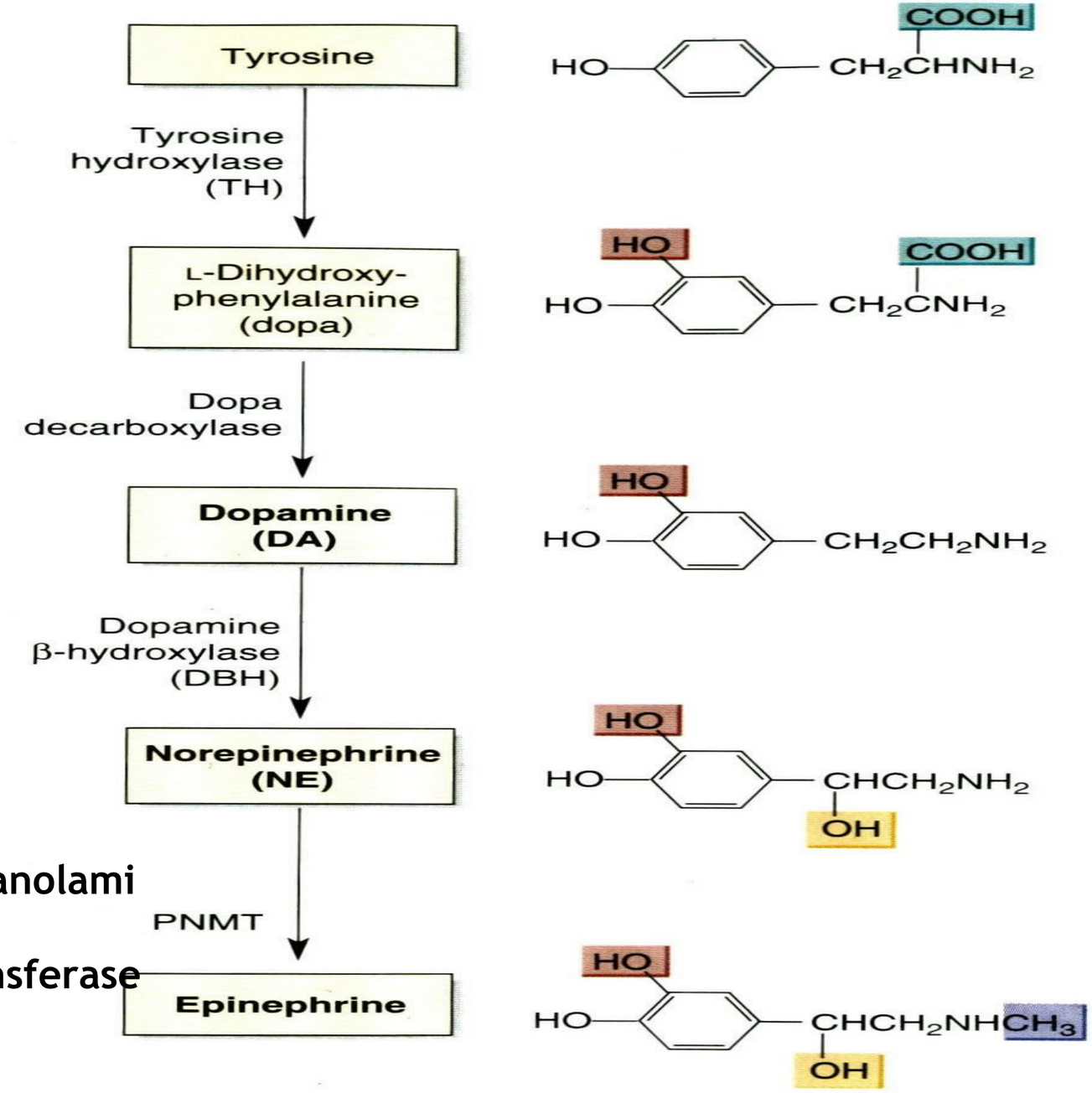
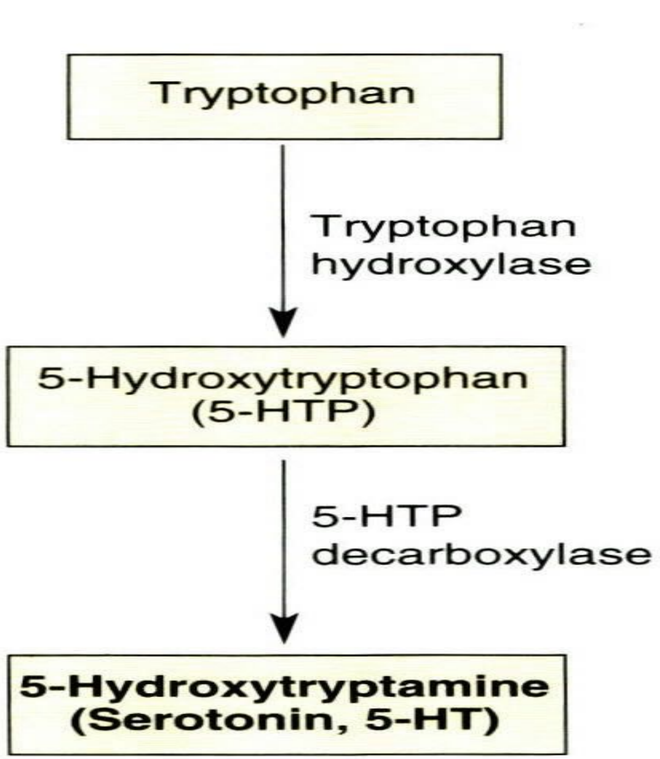
Dept. of Biomedical Science

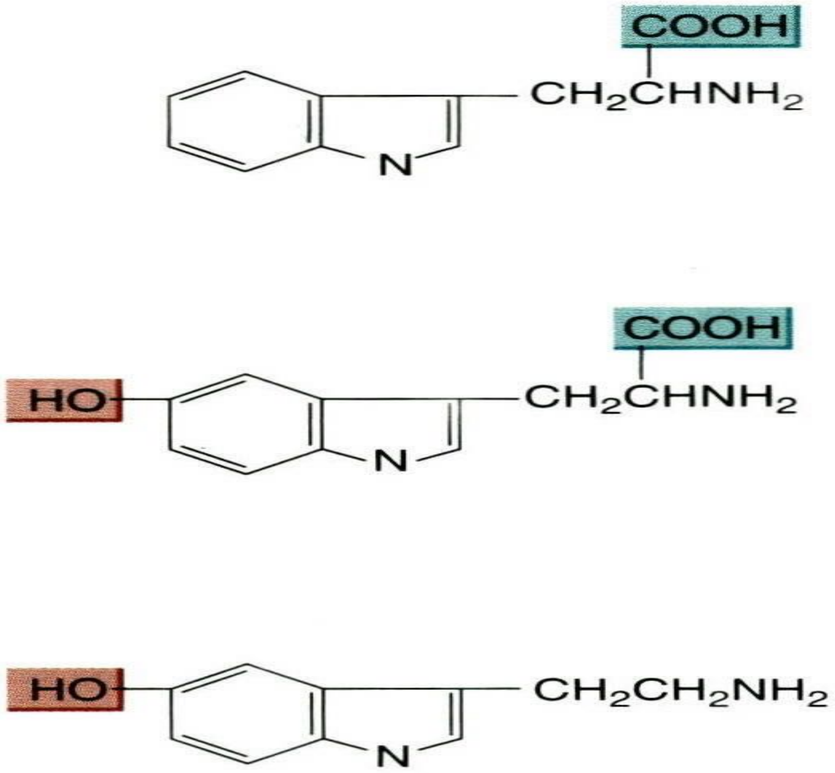
Catecholamine synthesis



phenylethanolamine N-methyltransferase

Serotonin synthesis





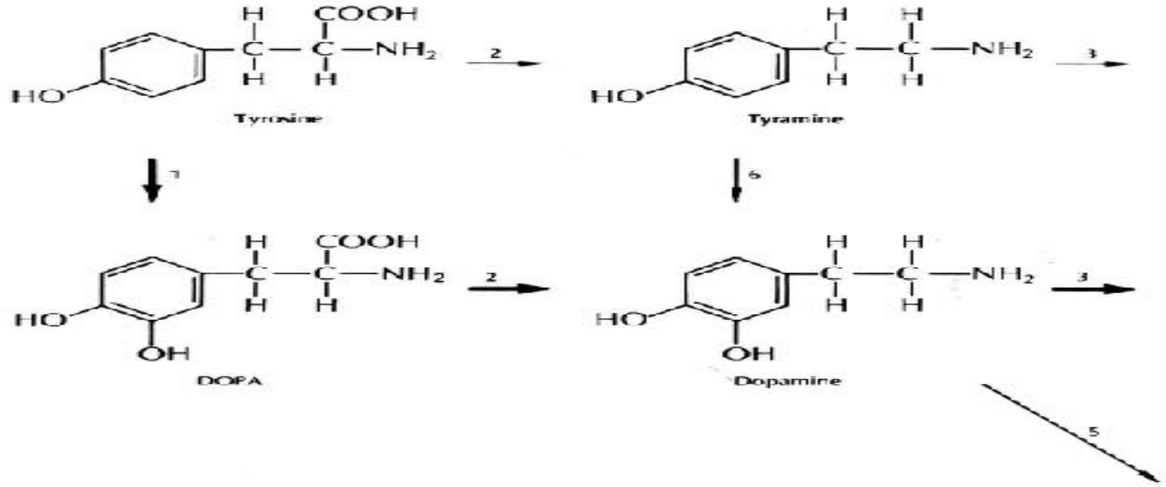


FIGURE 9-4. Primary and alternative pathways in the formation of catecholamine: (1) tyrosine hydroxylase; (2) aromatic amino-acid decarboxylase; (3) dopamine-β-hydroxylase; (4) phenylethanolamine-*N*-methyl transferase; (5) nonspecific *N*-methyl transferase in lung and folate-dependent *N*-methyl transferase in brain; (6) catechol-forming enzyme.

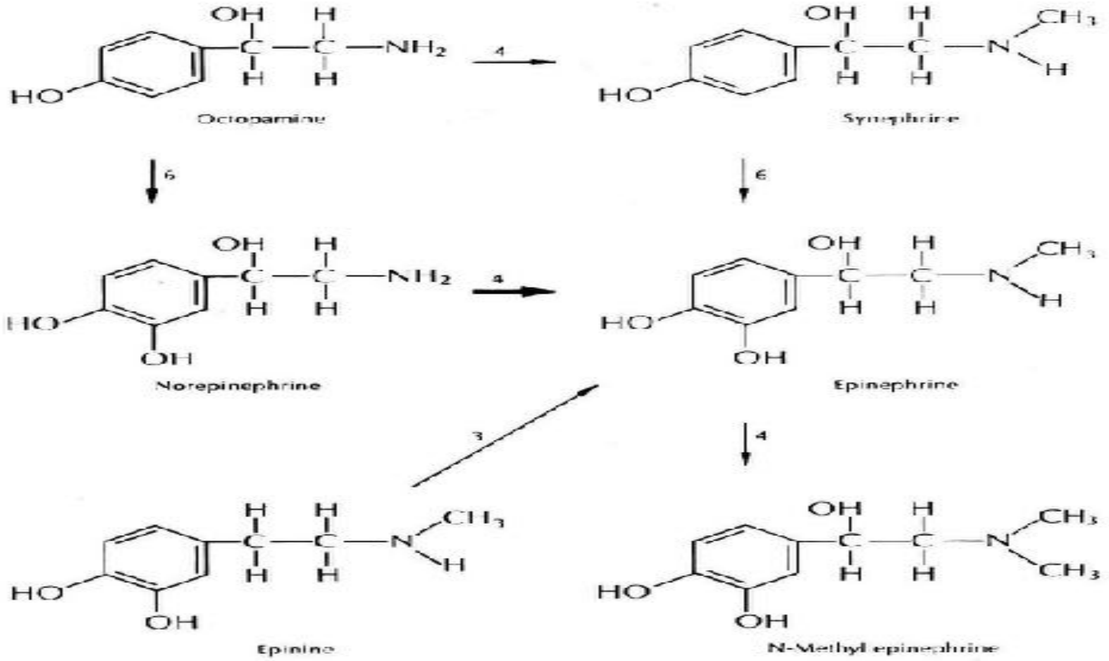


Figure 4.4 Catecholamines Share a Common Synthesis Pathway

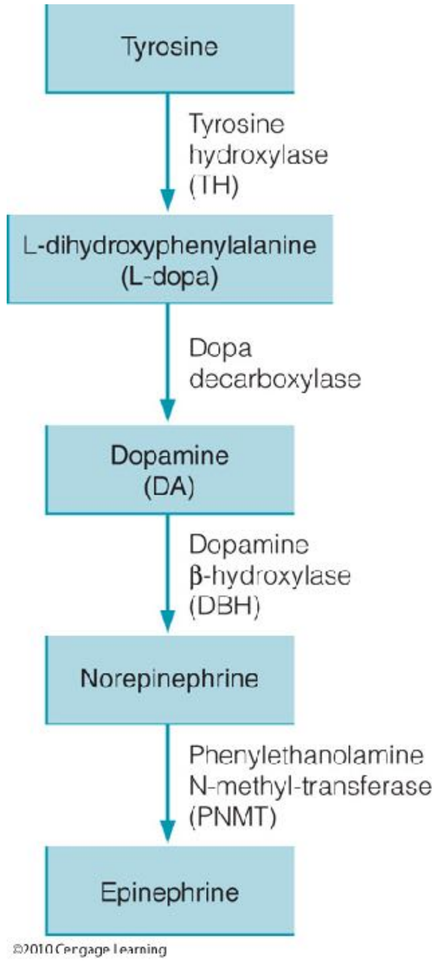


Figure 4.5 Dopaminergic Systems in the Brain

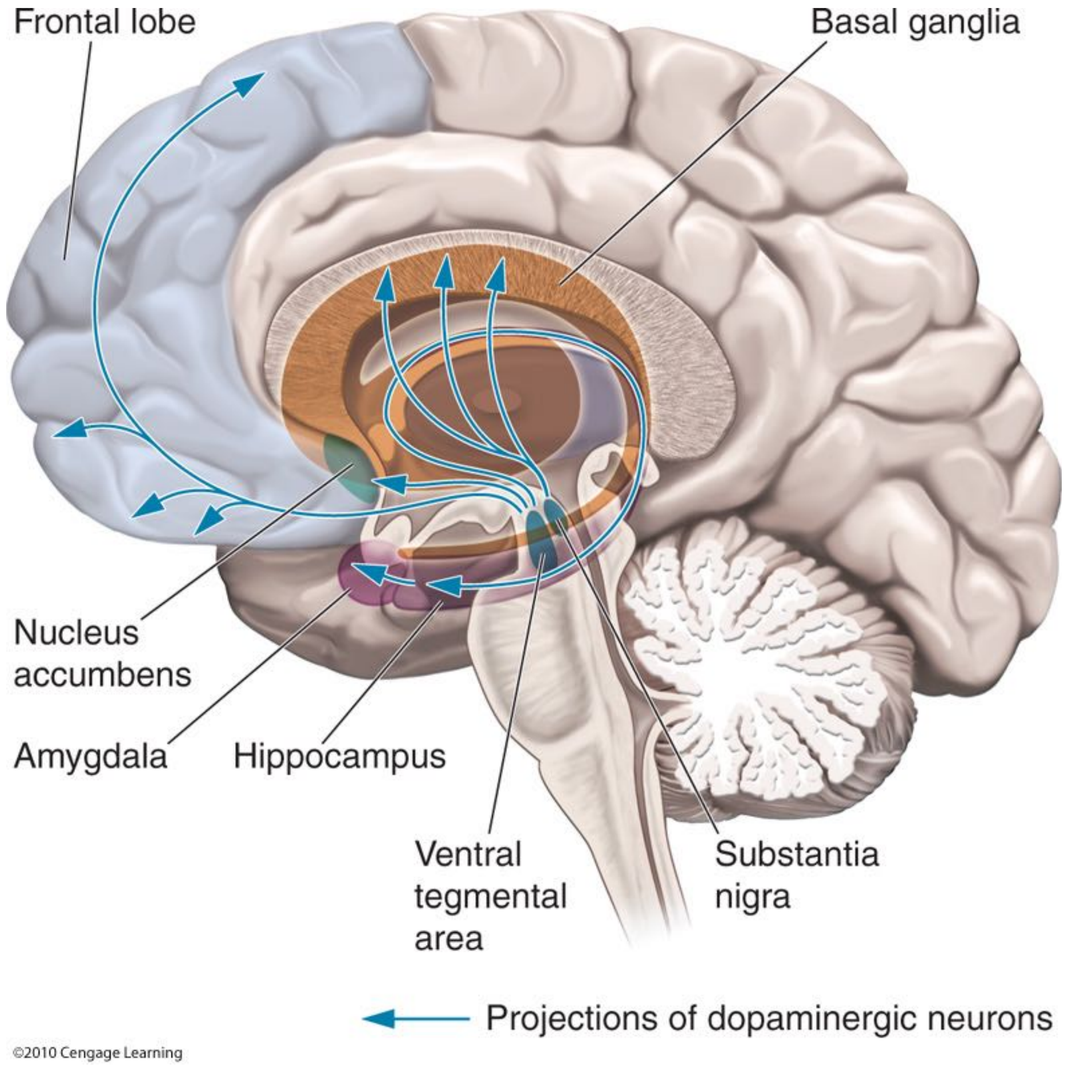


Figure 4.6 Noradrenergic Systems in the Brain

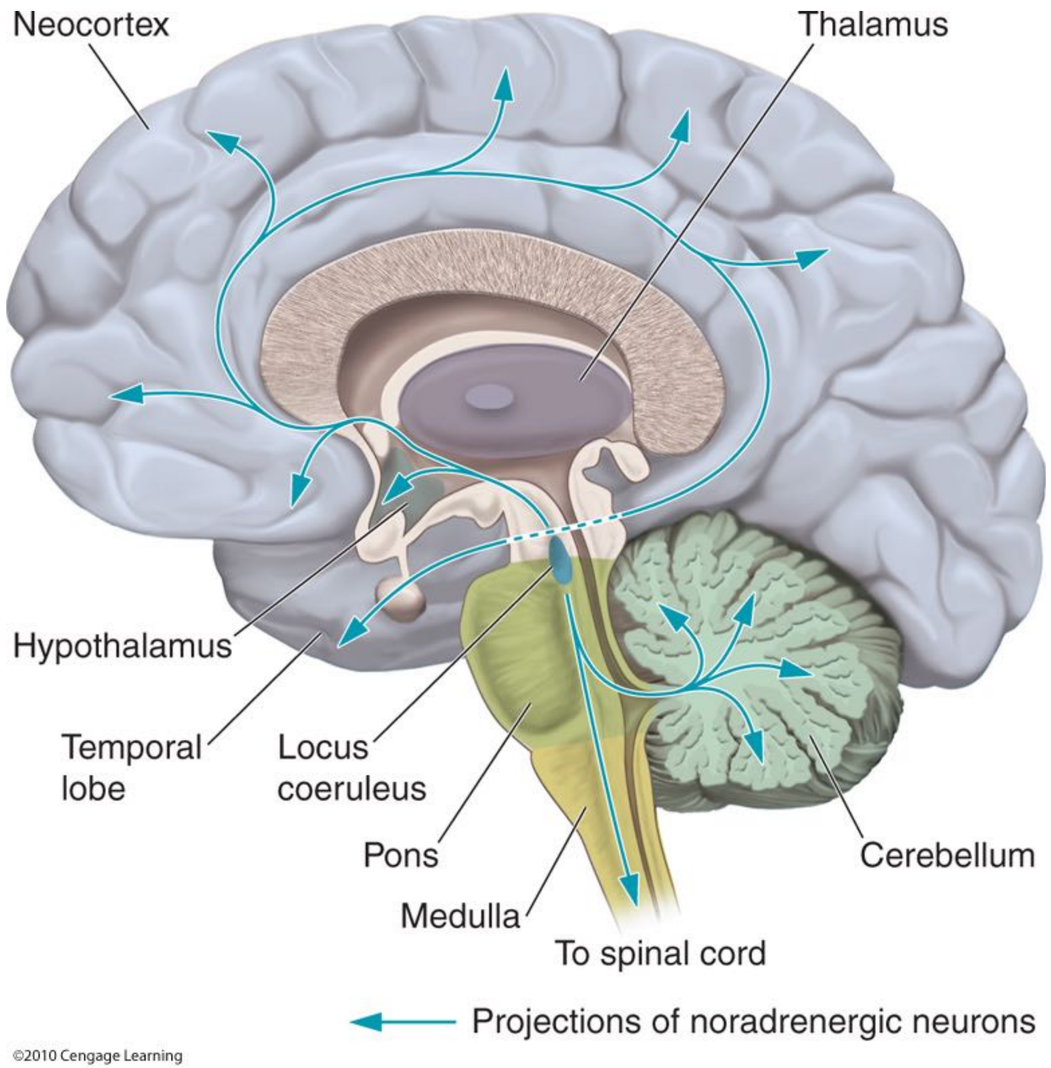
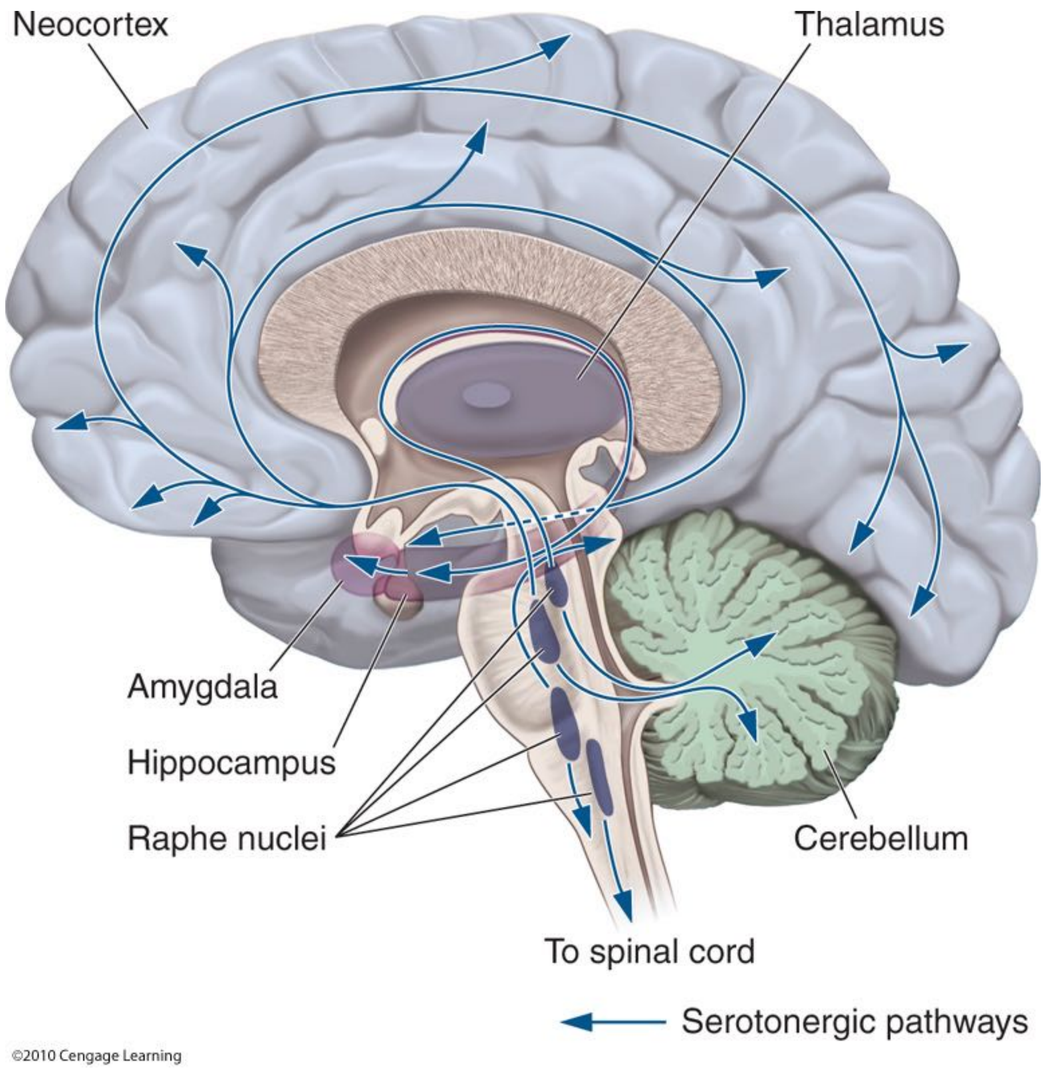


Figure 4.8 The Distribution of Serotonergic Pathways in the Brain



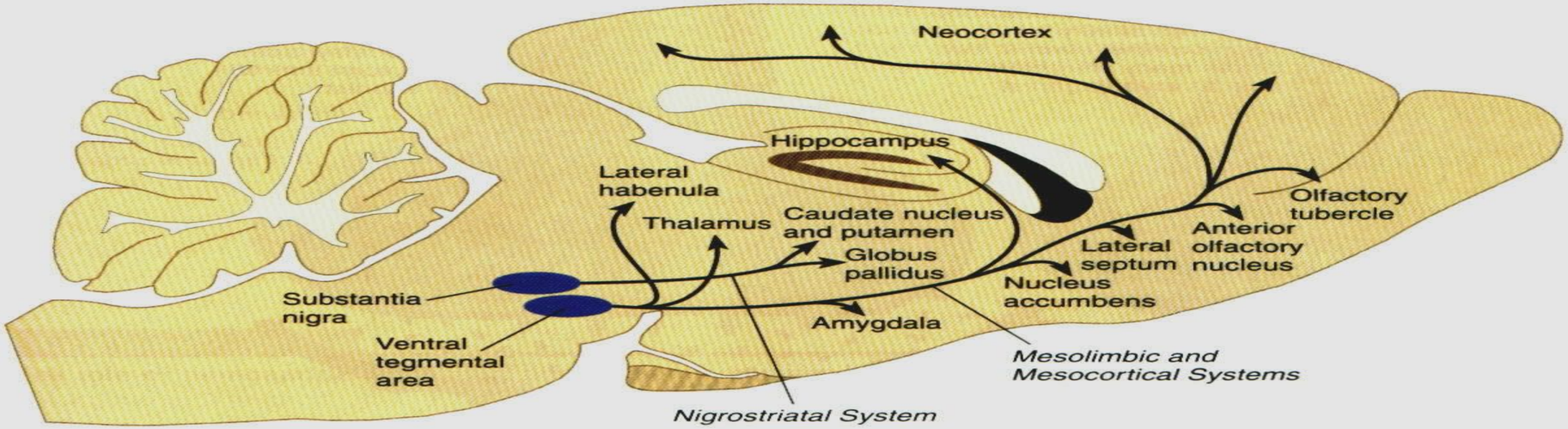


figure 4.13

A schematic midsagittal section of a rat brain, showing the locations of the most important groups of dopaminergic neurons and the distribution of their axons and terminal buttons.
(Adapted from Fuxe et al., 1985.)

Dopamine Systems

Catecholamine Synthesis (Dopamine, Norepinephrine and Epinephrine).

- **1) First Step: Hydroxylation:**
- In this step: the reaction involves the conversion of **tyrosine, oxygen and tetrahydrobiopterin to dopa & dihydrobiopterin. This reaction is** catalyzed by the enzyme **tyrosine hydroxylase**. It is irreversible reaction.
- **2) Second step: Decarboxylation:**
- In this step: the **dopa decaboxylase** will catalyze the **decaoxylation of dopa** to produce **dopamine. The deficiency of this enzyme can cause Parkinson's disease.** It is irreversible reaction. The cofactor in this reaction is the PLP (pyridoxal phosphate). In the nerve cells that secrete dopamine as neurotransmitter the pathway ends at this step.

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Catecholamine Synthesis (Dopamine, Norepinephrine and Epinephrine).

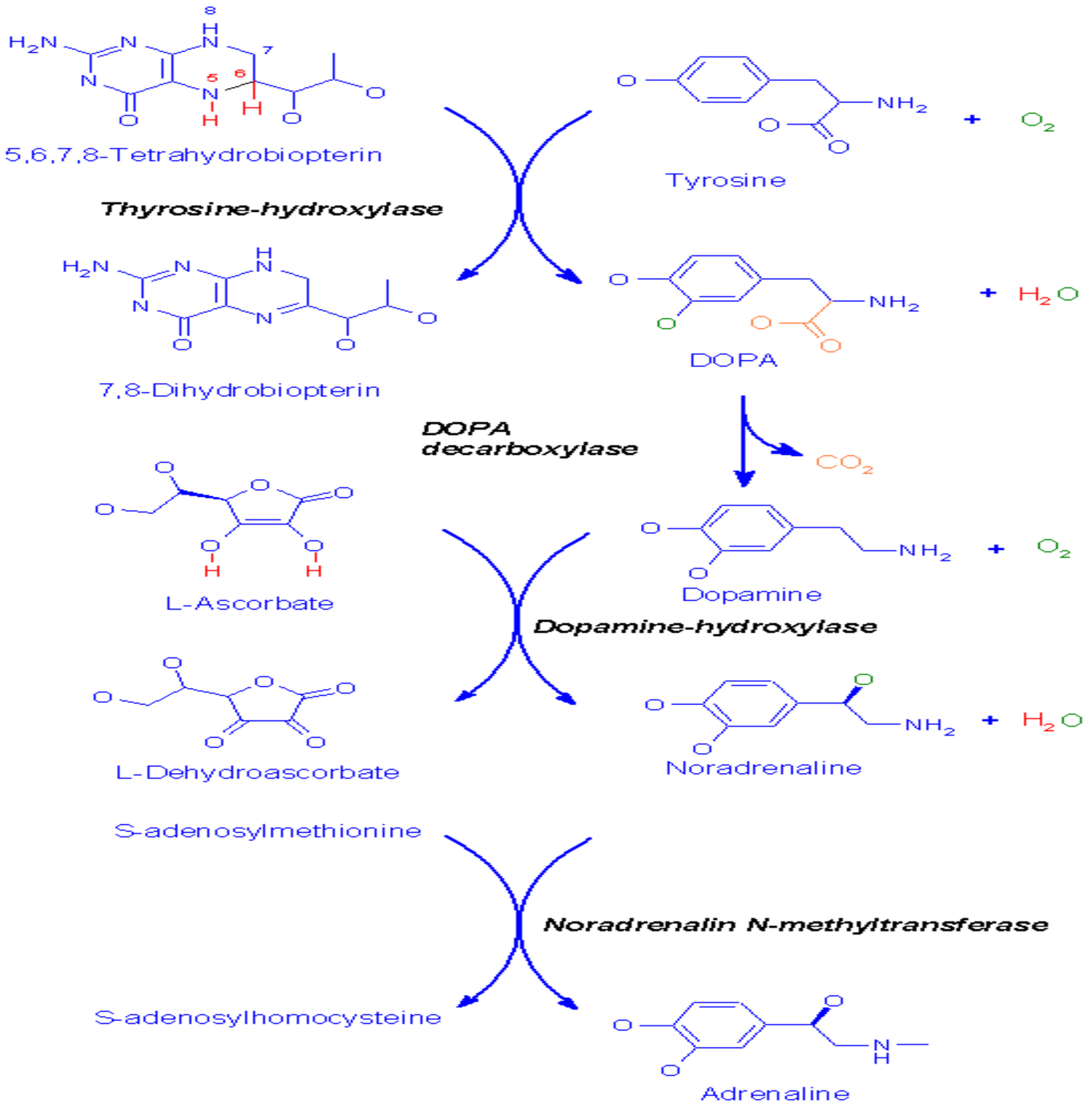
3) Third step: Hydroxylation:

This reaction is catalyzed by the enzyme dopamine β- hydroxylase. The reactants include dopamine, O_2 and ascorbate (vitamin C).

The products are norepinephrine, water and dehydroascorbate. It is an irreversible reaction). The end product in noradrenergic cells is norepinephrine and the pathway ends her.

4) Forth step: Methylation:

This reaction is catalyzed by phenylethanolamine N-methyltransferase. Norepinephrine and S-adenosylmethionin (ado-Met) form epinephrine and S-adenosyl homocysteine (ado-Hcy).


5,6,7,8-Tetrahydrobiopterin
Thyrosine-hydroxylase
Tyrosine
+ O2
7,8-Dihydrobiopterin
DOPA
+ H2O
DOPA decarboxylase
CO2
L-Ascorbate
Dopamine
+ O2
Dopamine-hydroxylase
L-Dehydroascorbate
Noradrenaline
+ H2O
S-adenosylmethionine
Noradrenalin N-methyltransferase
S-adenosylhomocysteine
Adrenaline

Serotonin synthesis:

•Serotonin is synthesized from the amino acid Tryptophan.

•The synthesis of serotonin involve two reactions:

1) 1) Hydroxylation:

Tryptophan ⟶ 5- Hydroxytryptophan

•The enzyme catalyzes this reaction is **Tryptophan Hydroxylase.**

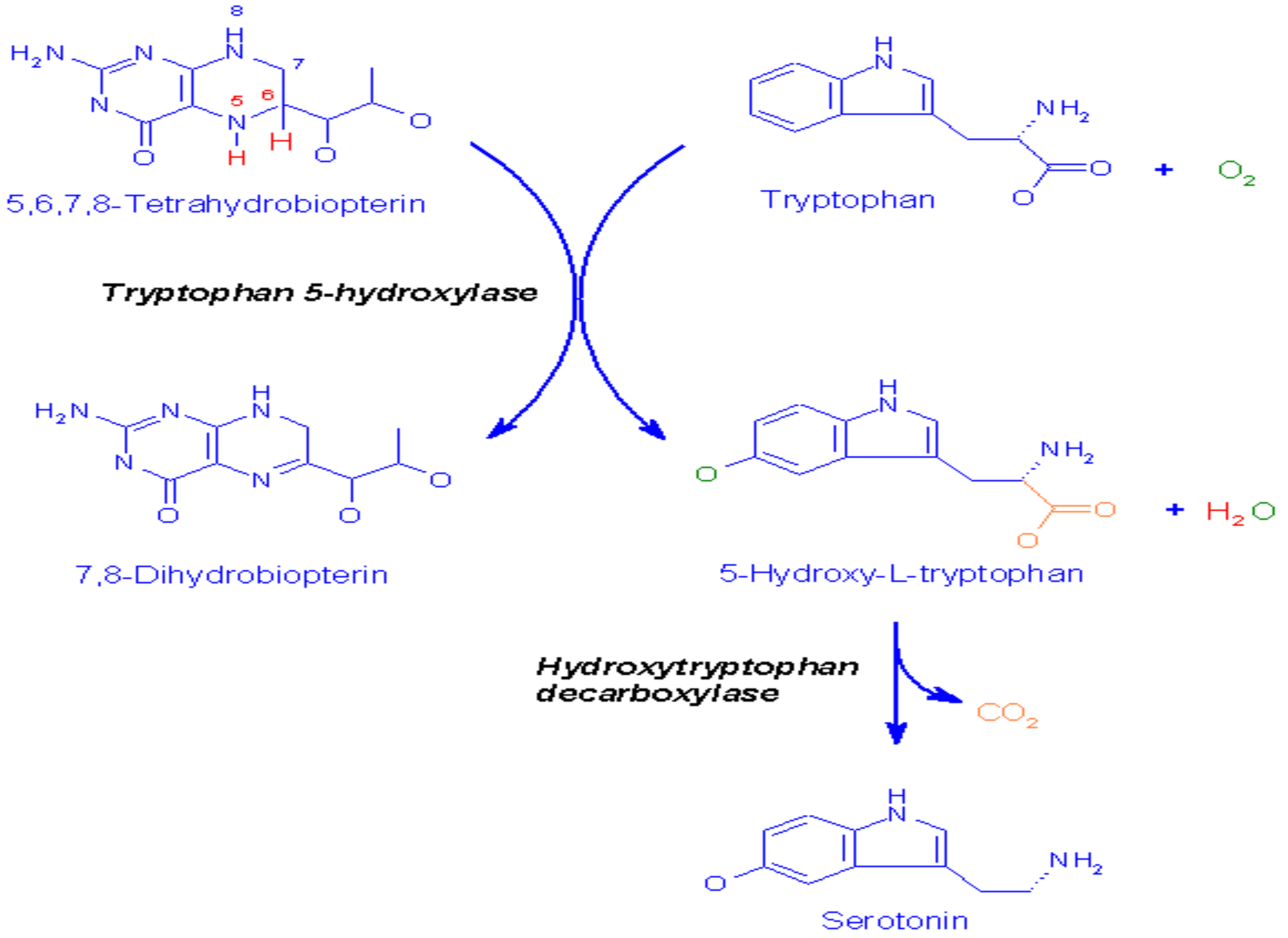
•The Co- factor is Tetrahydrobiopterin, which converted in this reaction to Dihydrobiopterin.

2) 2) Decarboxylation:

5- hydroxytryptophan ⟶ Serotonin

The enzyme is **hydroxytryptophan decarboxylase**.

•Serotonin is synthesized in CNS, & Chromaffin cells.


5,6,7,8-Tetrahydrobiopterin
Tryptophan
+ O_2
Tryptophan 5-hydroxylase
7,8-Dihydrobiopterin
5-Hydroxy-L-tryptophan
+ H_2O
Hydroxytryptophan decarboxylase
CO_2
Serotonin

Break down of serotonin:

- Serotonin is degraded in two recations

1) Oxidation:

5-hydroxytryptoamine + O2 + H2O —(**Monoamine oxidase**)→ 5- Hydroxyinodole-3-acetaldehyde

2) Dehydrogenation

5- Hydroxyinodole-3-acetaldehyde —(**Aldehyde dehydrogenase**)→ 5-hydroxindole-3-acetate

(Anion of 5-hydroxyindoleacetic acid)