Alkaloid as Natural Products

- **Largest class of secondary metabolites, >6500 compounds known**
- **Contains N, most compounds are basic (alkaline)**
- **Often highly toxic**
- **Found in certain higher plants**
- **Little is known regarding why alkaloids are produced**
- **Biosynthesis from amino acids**

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Many of these substances have marked physiological effects, a fact discovered by many ancient people long before organic chemistry developed.

Like, alkaloid quinine, a chief constituent of bark of Cinchona, has been used as effective antimalarial since 1639.

Alkaloids are produced by a large variety of organisms, including bacteria, fungi, plants and animals and are part of the group of natural products (also called secondary metabolites).

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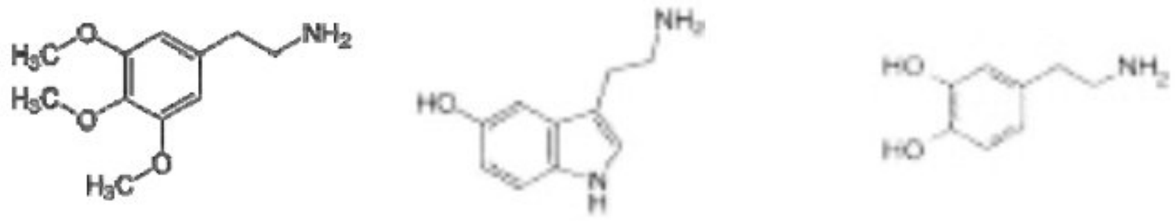
The boundary between alkaloids and other nitrogen-containing natural compounds is unclear.

Compounds like amino acid, peptides, proteins, nucleotides, nucleic acid, amines and antibiotics are usually not called alkaloids.

Natural compounds containing nitrogen in the exocyclic position (mescaline, serotonin, dopamine, etc.) are usually attributed to amines rather than alkaloids.



Some authors, however, consider alkaloids a special case of amines.

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Effects of alkaloids on humans

- High biological activity
- Produce varying degrees of physiological and psychological responses - largely by interfering with neurotransmitters
  - –others interfere with membrane transport, protein synthesis or other processes
- In large doses - highly toxic - fatal
- In small doses, many have therapeutic value
  - –muscle relaxants, tranquilizers, pain killers, mind altering drugs, chemotherapy

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Psychoactive alkaloids (affecting mental process)

- Although only a small percent are psychoactive, these get much focus
- Affect the central nervous system - often by influencing neurotransmitters
- Categories of psychoactive compounds
  - Stimulants
  - Hallucinogens
  - Depressants
- May also be narcotic (*addictive*)

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Psychoactive alkaloids

Stimulants	Hallucinogens	Depressants
Cocaine	Tropane alkaloids	Morphine
Ephedrine	Mescaline	Codeine
Caffeine	Psilocybin	Heroin
	Ergot alkaloids (LSD)	

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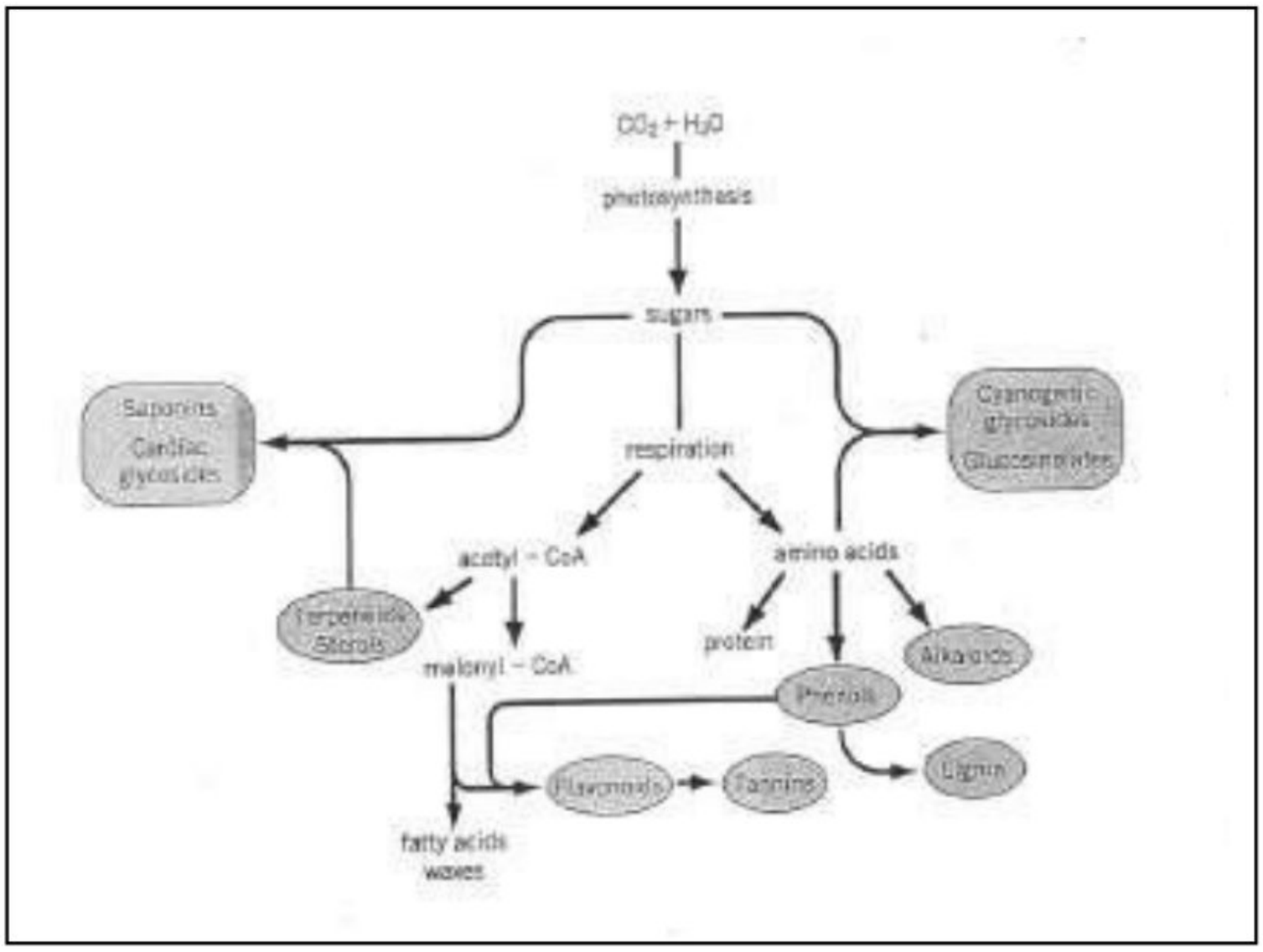

Tests for Alkaloids

- Most alkaloids are precipitated from neutral or slightly acidic solution by
- Mayer's reagent (potassiomercuric iodide solution) □ Cream coloured precipitate.
- Dragendorff's reagent (solution of potassium bismuth iodide)□ orange coloured precipitate.
- Wagner's reagent (iodine in potassium iodide) □ red-brown precipitate
- Hagers reagent (picric acid) □ yellow precipitate

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Physical & Chemical Properties of Alkaloids

MW: 100 – 900

Most bases which do not contain Oxygen are liquid at room temperature (nicotine), while those that do are solids.

In rare cases they are coloured.

Most solid bases rotate the plane of polarized light, have high melting points.

Normally are not soluble in water (occasionally slightly soluble).

Soluble in non polar or slightly polar organic solvents.

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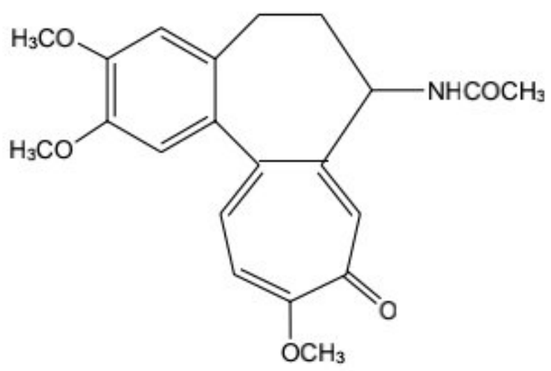
The basicity of alkaloids depends on the availability of the lone pair of electrons on the N atoms: Electron donating groups enhance basicity, while e-withdrawing groups decrease it.

Because some alkaloids have a carbonyl group on the amide, they can also be neutral (colchicine & piperine).



Colchicine

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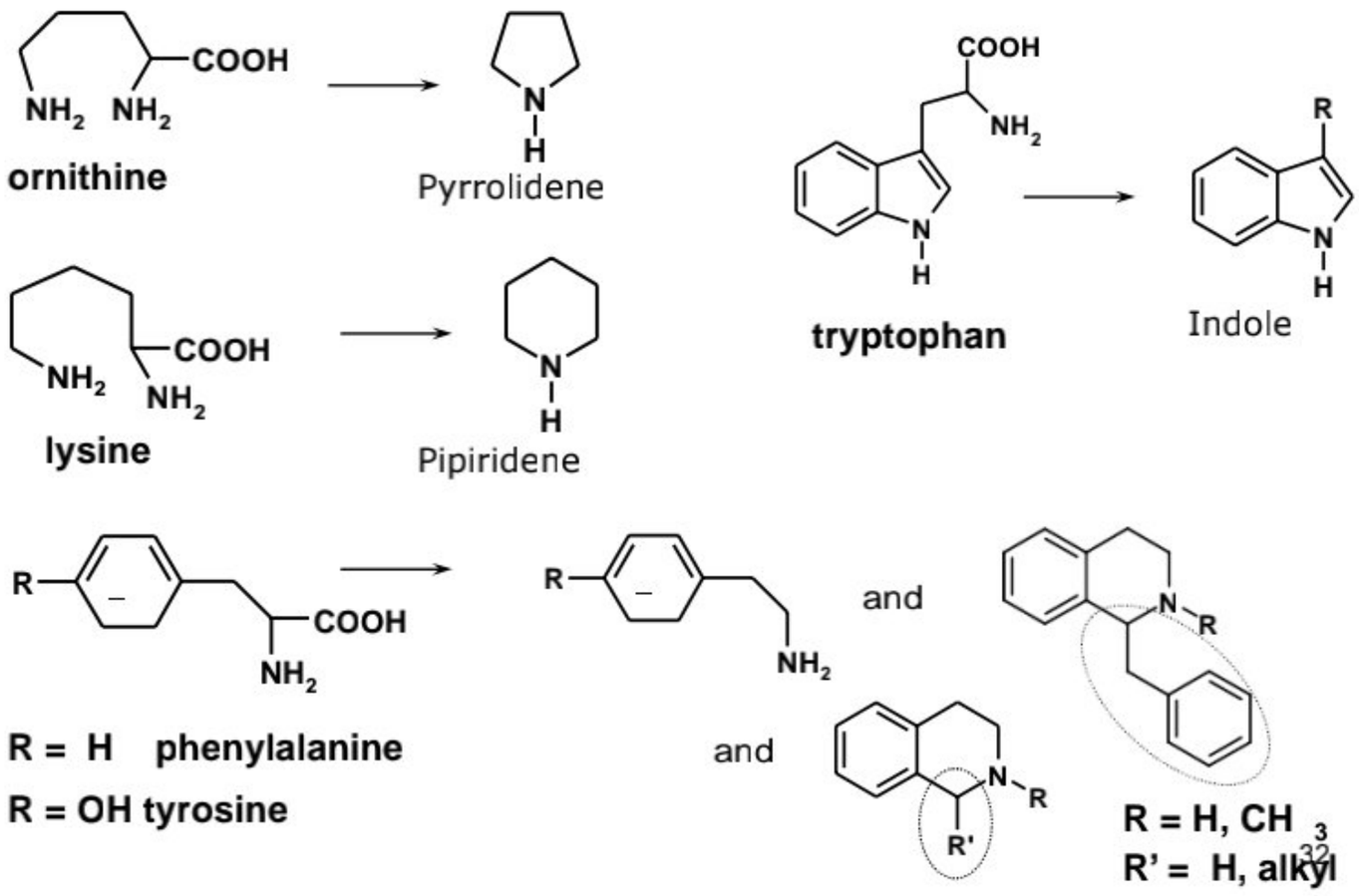
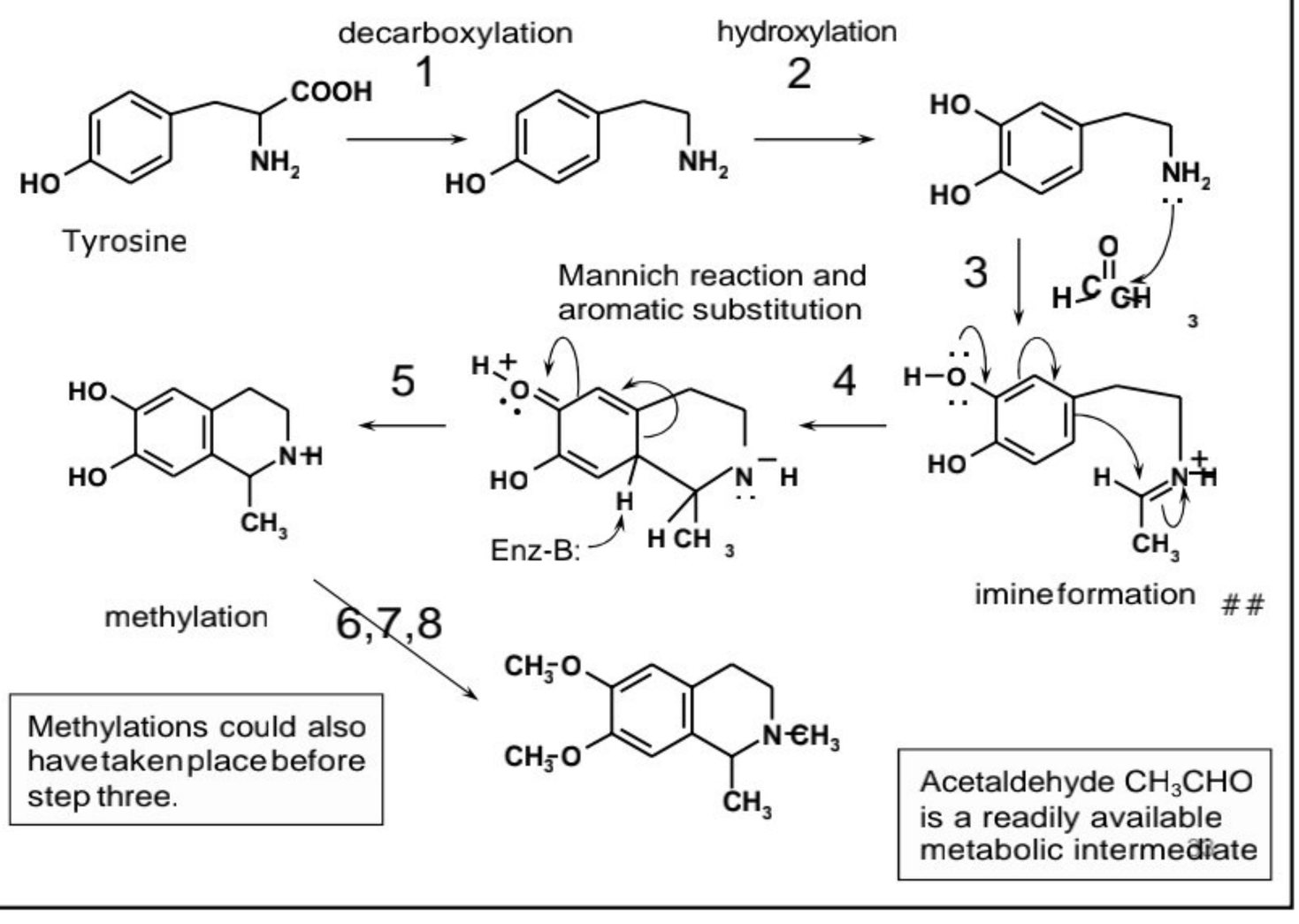
MOST ALKALOIDS ARE DERIVED FROM ?-AMINO ACIDS

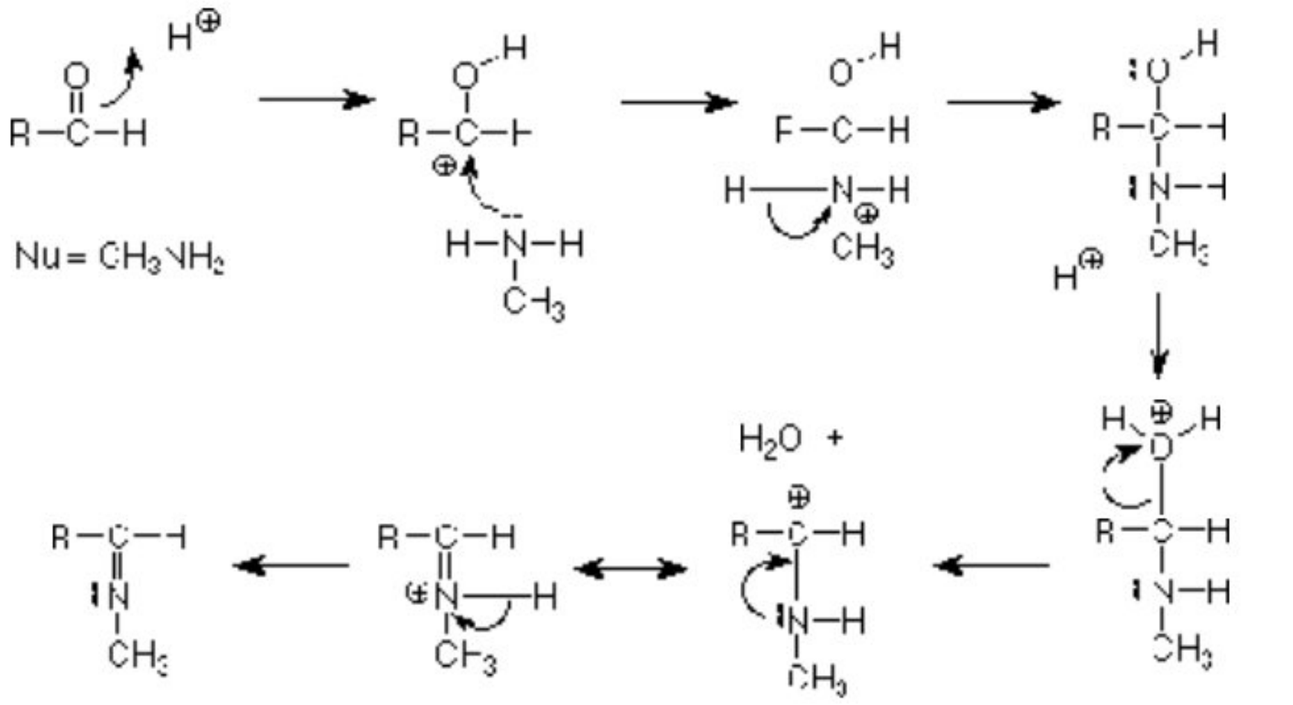
SOME OF THE MAJOR RELATIONSHIPS ARE SHOWN BELOW



Ex: FORMATION OF ISOQUINOLINE ALKALOIDS



Mechanism – Imine formation



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Biogenesis of Alkaloids

- Alkaloids are produced in plants by basic substances and reactions well-known in organic chemistry.
- Biosynthetic origin cannot be discussed in general terms for all alkaloids, instead it has to be covered separately for each of the major groups of alkaloids.
- True alkaloids are based on an amino acid (pre-cursor).
- Only a few amino acids form the pre-cursors for all alkaloids: ornithine, lysine, phenylalanine, tyrosine, tryptophan, histidine and anthranilic acid.

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- Alkaloid formation may require the involvement of only one molecule of amino acid, or 2 molecules of the same AA, or less commonly, 2 molecules of different AA or else several molecules of the same AA.
- The formation starts with the creation of a Schiff base or a Mannich reaction.
- When the alkaloid has additional C-atoms, these play important roles in other metabolic pathways.

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Alkaloids are often divided into the following major groups:

"**True alkaloids**", which contain Nitrogen in the heterocycle and originate from amino acids.

Their characteristic examples are atropine, nicotine and morphine.

This group also includes some alkaloids which beside nitrogen heterocycle contain terpene (e.g. evonine) or peptide fragments (e.g. ergotamine) as well as it also includes piperidine alkaloids coniine and coniceine although they do not originate from amino acids.

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