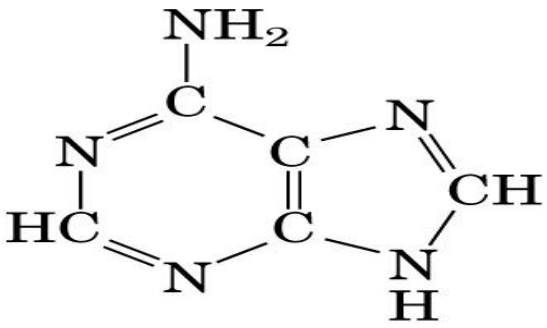
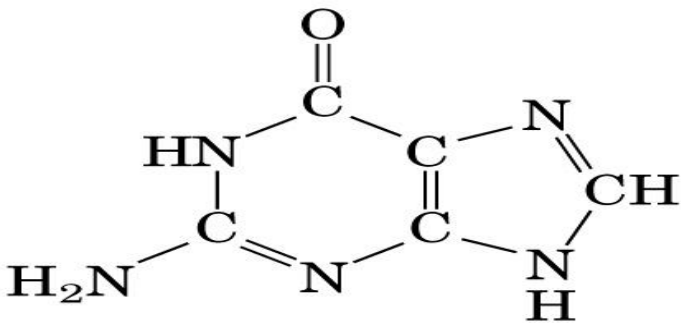
Purine Nucleotide Metabolism

Anabolism

Purines And Pyrimidines

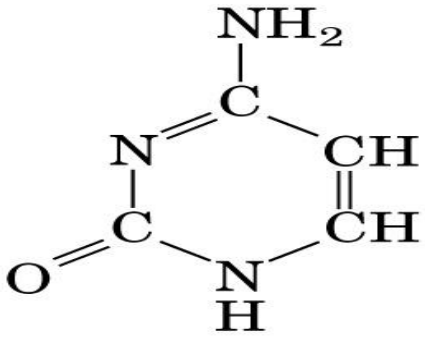


Adenine

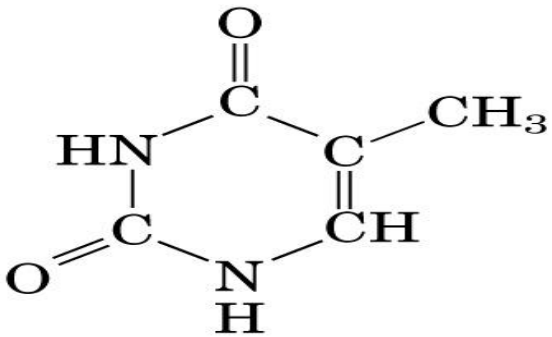


Guanine

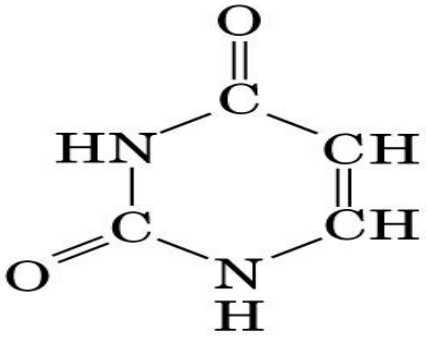
Purines



Cytosine



Thymine
(DNA)



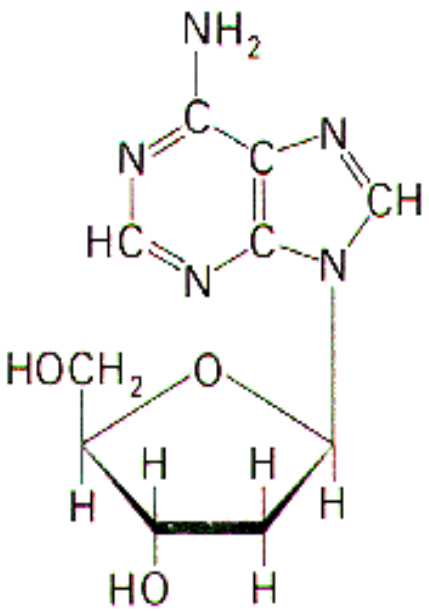
Uracil
(RNA)

Pyrimidines

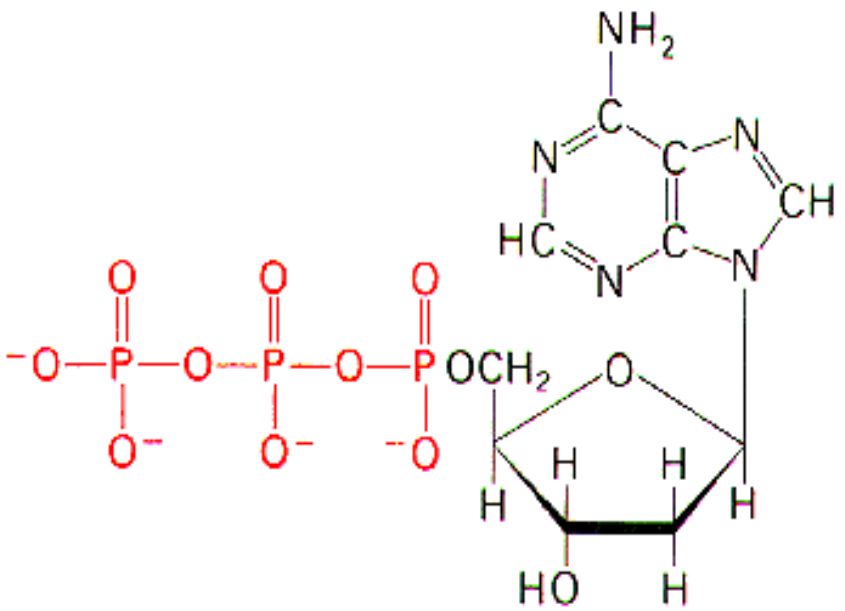
Nucleoside and Nucleotide

Nucleoside = Nitrogenous base — Ribose

Nucleotide = Nitrogenous base — Ribose — Phosphate



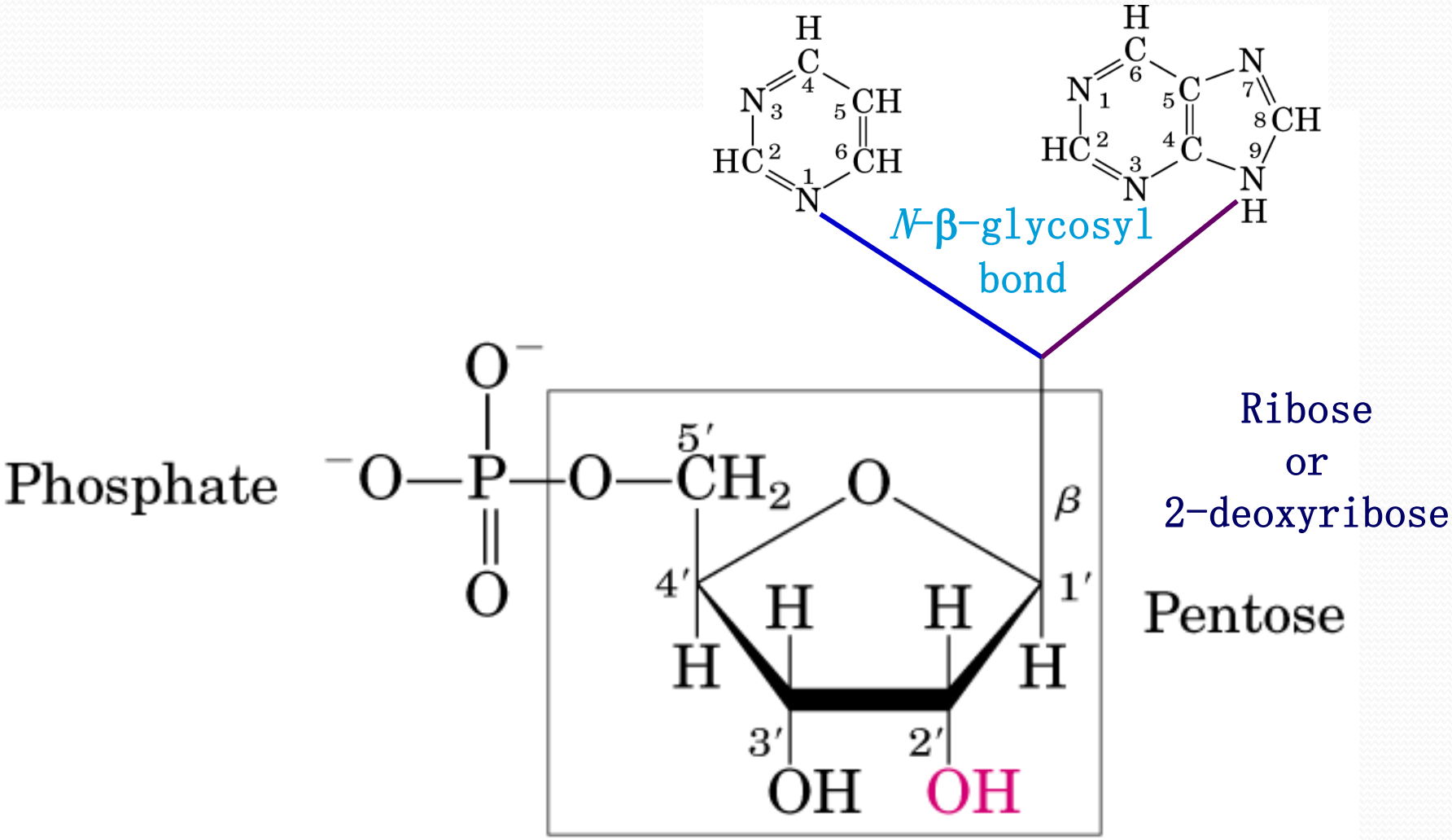
Deoxyadenosine
(A nucleoside)



Deoxyadenosine 5′-triphosphate
(dATP)
(A nucleotide)

Nucleotides
are
Building blocks
of
Nucleic acids

Structure of Nucleotides



There are two pathways leading to Biosynthesis of Nucleotides

- **De Novo Biosynthesis:**

- **This is a main synthetic pathway.**

  - **The biosynthesis of nucleotides begins /very new with the use of small metabolic precursors as a raw material:**

- **Amino acids, Ribose-5-phosphate, CO_2, and One-carbon units.**

Salvage pathways:

- **The synthesis of nucleotide by recycle of the free Nitrogen bases or nucleosides released from nucleic acid breakdown.**
- This is important in **Brain and Bone marrow**

De Novo Biosynthesis Of Purine Nucleotides

Site Of Purine Nucleotide Biosynthesis:

- **Predominantly In cytosol of Liver,**
- **To some extent in small intestine and Thymus.**
- In humans, all **necessary enzymes for Purine Nucleotide** biosynthesis are **found in** the **cytoplasm** of the cell.
-

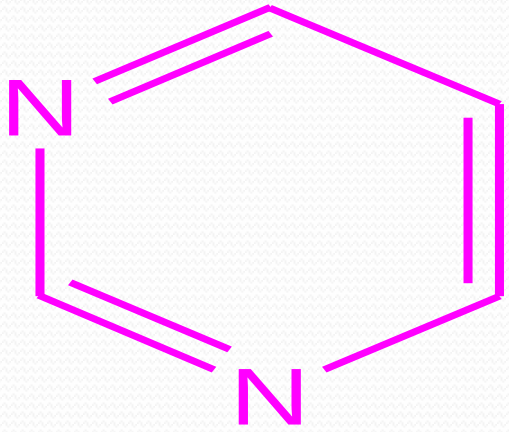
- Denovo biosynthesis occurs in **most of the cells**' cytosol
- **Except human Brain, Polymorphonuclear leukocytes and Erythrocytes.**

Requirements For De Novo Biosynthesis of Purine Nucleotides

- **Purines are synthesized using 5PhosphoRibose (R-5-P) as the starting mate**Requirements For De Novo Biosynthesis

- **PRPP (5-Phosphoribosyl-1-Pyrophosphate) is an active donor of R-5-P.**

Biosynthesis Of Pyrimidines Nucleotides



Pyrimidine Nucleotide Metabolism

- There are also two synthesis pathways of Pyrimidine nucleotides:
- Denovo Synthesis and Salvage pathway.

De Novo Synthesis Pathway

- In De novo pathway the Pyrimidine ring is assembled first and then linked to Ribose phosphate.

- The carbon and nitrogen atoms in the Pyrimidine ring are derived from:
  - **Bicarbonate**
  - **Aspartate**
  - **Glutamine**

Salvage Pathway

- **The significance of salvage pathway :**
  - **Save the fuel.**
  - **Some tissues and organs such as brain and bone marrow are only capable of synthesizing nucleotides by salvage pathway.**

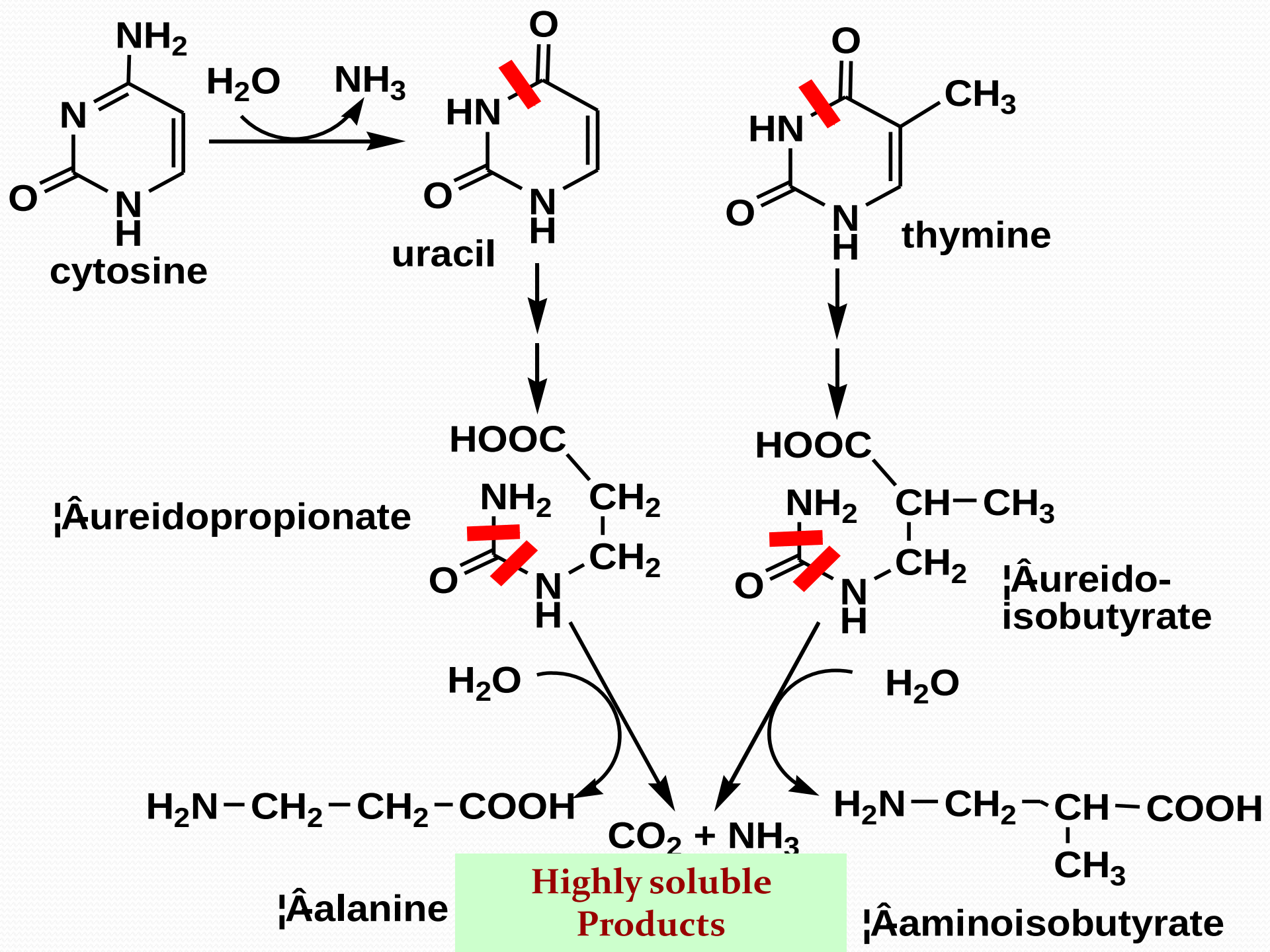
Catabolism Of Purine Nucleotides

- Uric acid is waste excreted end product of Purine catabolism.
- The rate of uric acid excretion by the normal adult human is about 0.6 g/24 h in urine.
- The normal concentration of uric acid in the serum of adults is in the range of 3-7 mg/dl.

Catabolism Of Pyrimidines

- Catabolism of Pyrimidine
- Nitrogen Bases **Cytosine** and **Uracil** yields :
  - β-Alanine,
  - Ammonium ions
  - CO_2
- β-Alanine can be recycled into the synthesis of coenzyme A

- Catabolism of **Thymine** yields:
  - β-Aminoisobutyric acid
  - Ammonium ions
  - CO_2


NH2
N
O
N
H
cytosine
H2O
NH3
O
HN
O
N
H
uracil
O
CH3
HN
O
N
H
thymine
HOOC
NH2
CH2
CH2
O
N
H
¦Âureidopropionate
HOOC
NH2
CH
CH3
CH2
O
N
H
¦Âureido-
isobutyrate
H2O
H2O
H2N−CH2−CH2−COOH
CO2 + NH3
H2N−CH2−CH−COOH
CH3
¦Âalanine
Highly soluble
Products
¦Âaminoisobutyrate

Principal differences between metabolism of Purines and Pyrimidines

Character	Purines De Novo Synthesis	Pyrimidines De Novo Synthesis
Number Of Steps Involved	11 Steps	6 Steps
Precursors Of Ring	Amino acids :Asp Gly and Gln N10FormylTHF CO2	Amino acids :Asp and Gln CO2
Major Portion Of Ring provided by	Glycine	Aspartate

Character	Purines De Novo Synthesis	Pyrimidines De Novo Synthesis
Acquisition of Ribose-Phosphate	In Starting Steps	In End Steps
Formation of N-Glycosidic bond	In 1st step of their biosynthesis (PRPP is the 1st Substrate)	a heterocyclic ring is formed first, then it reacts with PRPP
products of degradation	**Uric acid** **(poor solubility in H_2O)** NH_3	CO_2, NH_3, β-Amino Isobutyrate and βAla (soluble in H_2O)

Character	Purines De Novo Synthesis	Pyrimidines De Novo Synthesis
Number Of ATPs Involved	6 ATPs	2ATPs
Nucleotide Produced in End	IMP	UMP
Ring Closure At	6 and 11 steps	3rd Step