Harper`s Illustrated Biochemistry

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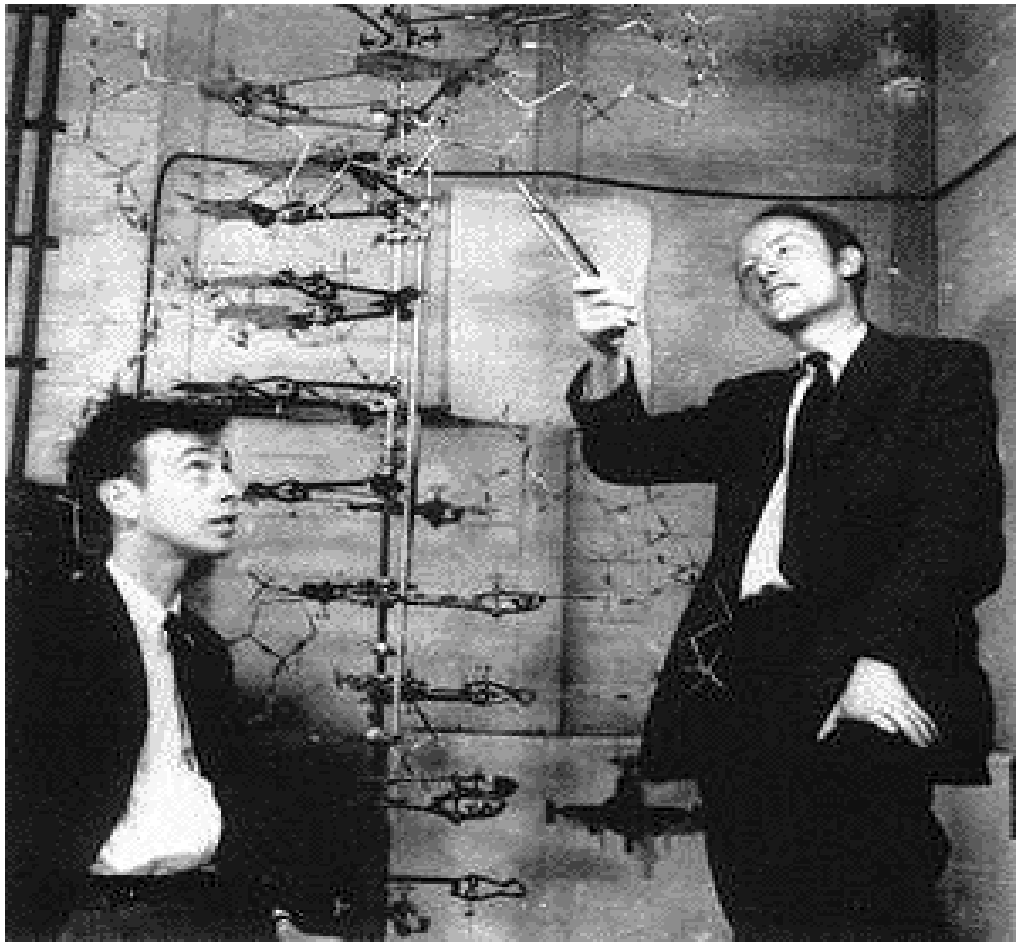
Biochemistry II
First Semester 2017 - 2018

- Section IV:
  Structure,Function,&Replication of Informational Macromolecules.
  Section V:
  Biochemistry of Extracellular&Intracellular Communication.
- Section VI:
  Selected Special Topics.

Structure,Function,&Replication of Informational Macromolecule

- How it all began



Biomedical Importance

- The main function:
  Building blocks of nucleic acids.
- Energy Metabolism:
  Example?
- Protein synthesis
  Example?
- Regulation of enzyme activity
  Example?
- Signal Transduction
  Example?

Biomedical importance

- Additional functions:
  -they form a part of many coEnzymes
  -Donors of phosphoryl groups(ATP-GTP)
  -Donors of Sugars (UDP-Glucose)
  -Donors ofLipids (CDP AcylGlycerol)
  -Regulatory nucleotides

Purines,Pyrimidines,Nucleosides& Nucleotides

- Purine

Pyrimidine

Purines and Pyrimidines

Deffinition:

Nitrogen containing heterocyclic compounds.

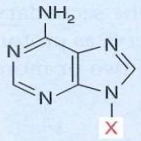
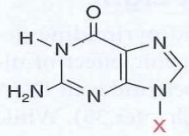
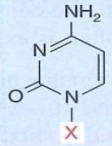
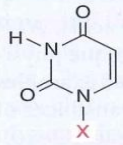
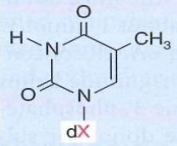
Charachteristics

-Weak bases

-Planar structure allow for close stacking (Why?)

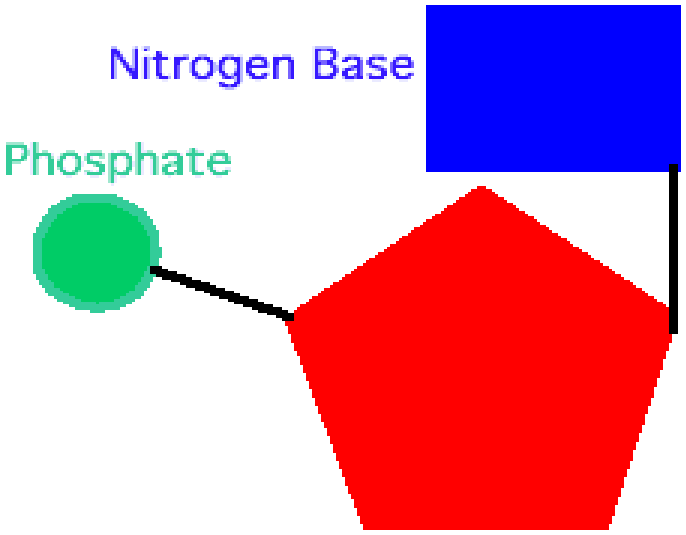
Structure of Purines and Pyrimidine

TABLE 32–1 Purine Bases, Ribonucleosides, and Ribonucleotides

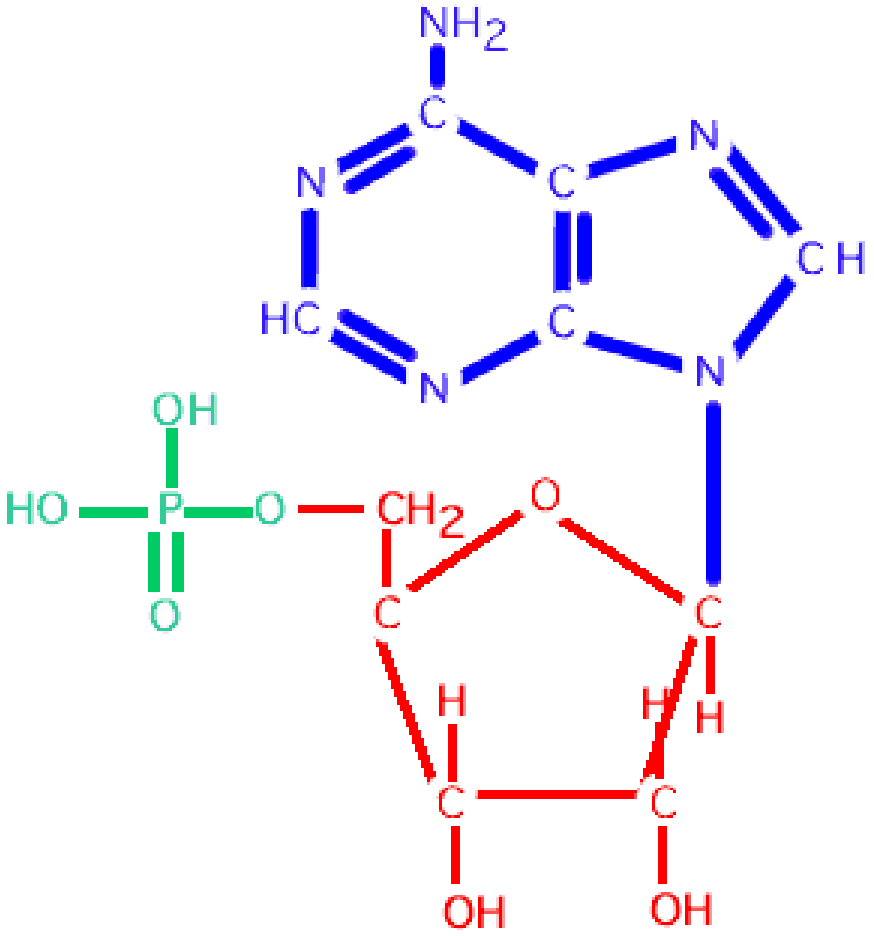
Purine or Pyrimidine	X = H	X = Ribose	X = Ribose Phosphate
	Adenine	Adenosine	Adenosine monophosphate (AMP)
	Guanine	Guanosine	Guanosine monophosphate (GMP)
	Cytosine	Cytidine	Cytidine monophosphate (CMP)
	Uracil	Uridine	Uridine monophosphate (UMP)
	Thymine	Thymidine	Thymidine monophosphate (TMP)

Nucleosides-Nucleotides

Basic Nucleotide Structure



Example



Adenosine 5' phosphoric acid

Nucleosides

- Deffinition:
- They are derivatives of purines and pyrimidines that have a sugar linked to a ring nitrogen of the bases.
- The sugar is Ribose in Ribonucleosides or Deoxyribose in deoxyRibonucleosides.The sugar carbons are numbered with a prime (`) to diffrentiate the from base numbers.
- The linkage between sugar and base is β N Glycosidic bond.

Structure of Nucleosides

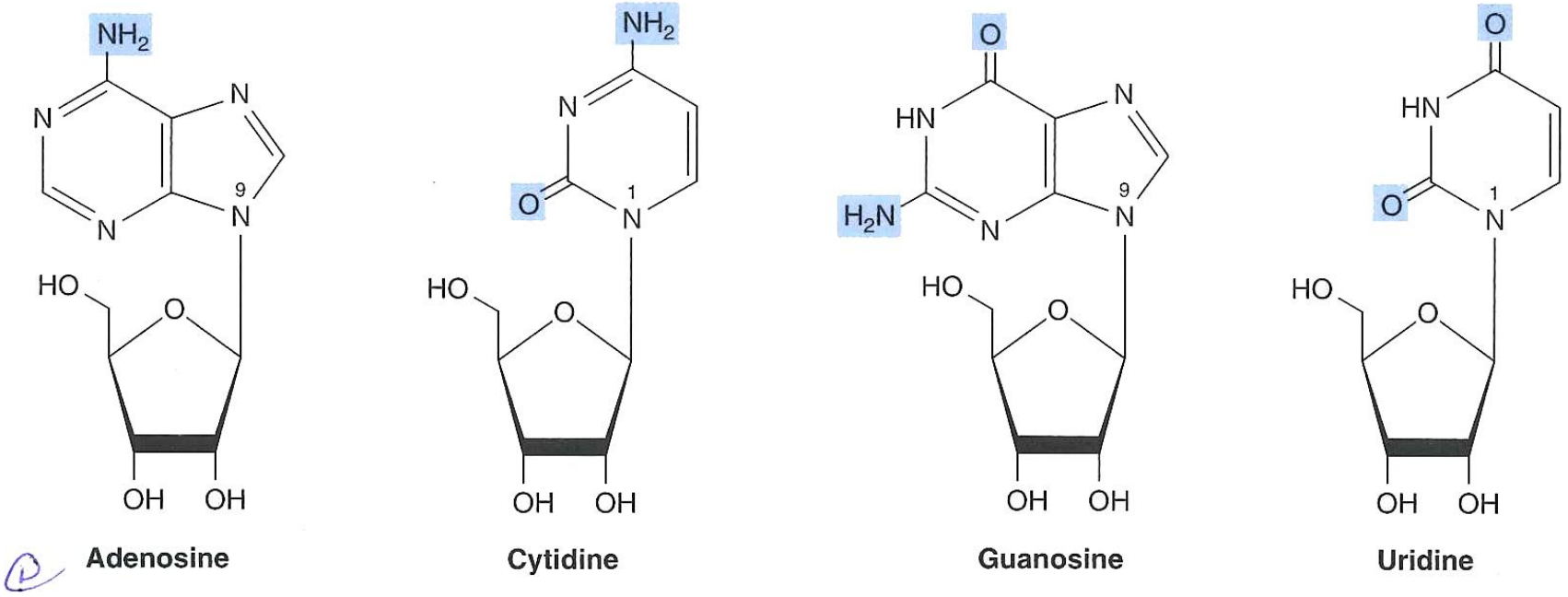


FIGURE 32–3 Ribonucleosides, drawn as the *syn* conformers.

Nucleotides

- Deffinition :

  Nucleotides are phosphorylated Nucleosides.

The linkage is 3`or a 5` phosphoryl group (mostly the linkage is to a 5`hydroxyl group of the sugar)

According to the number of phosphate groups attached the nucleotide can be a mono or di or Tri nucleotide.

Structure of Nucleotides

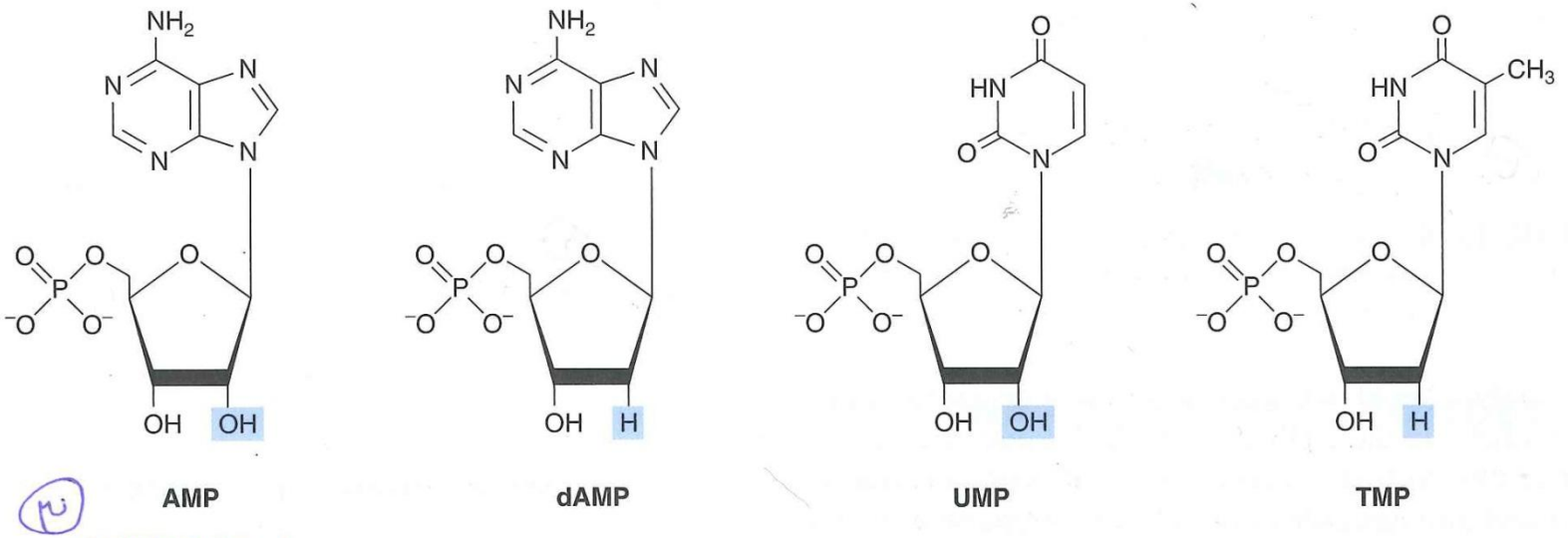
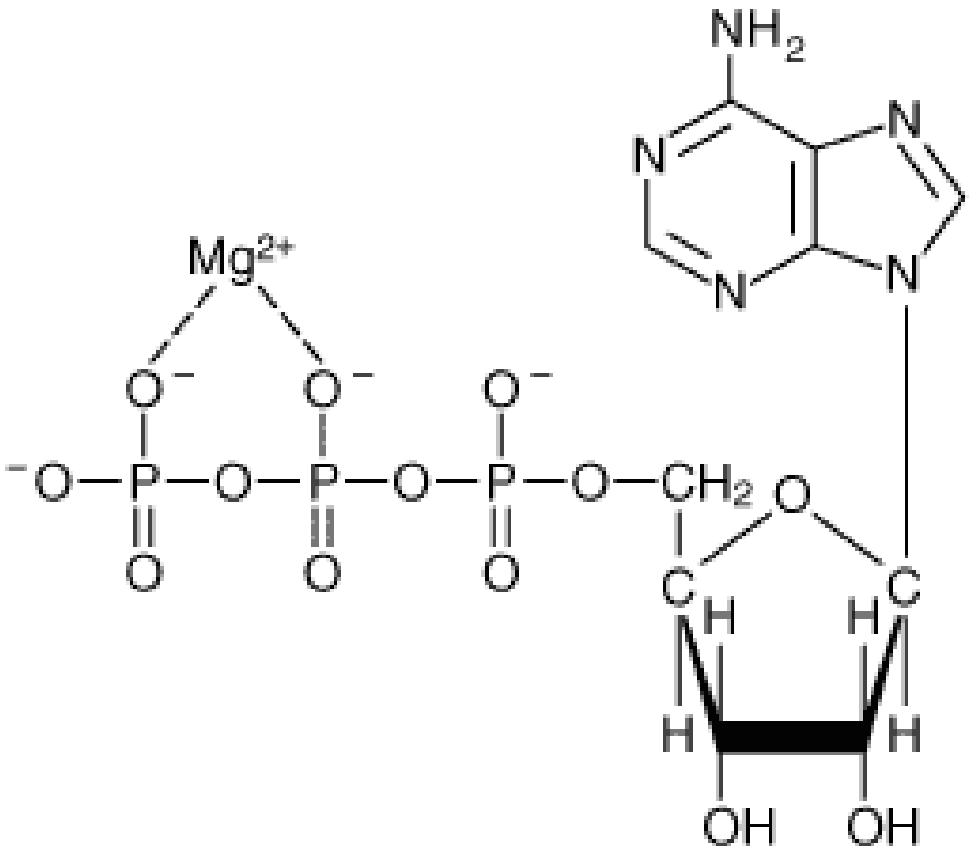
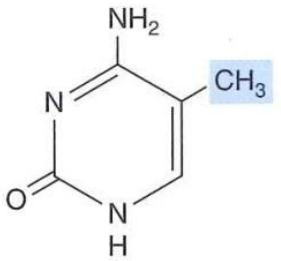


FIGURE 32–6 Structures of AMP, dAMP, UMP, and TMP.

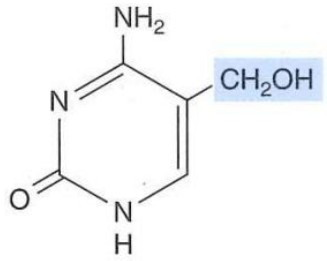
Structure of a nucleotidetriphosphate (ATP)



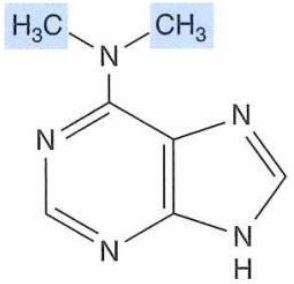
Modification of poly nucleotides can generate additional structures



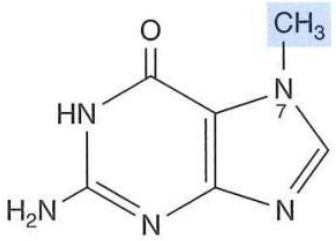
5-Methylcytosine



5-Hydroxymethylcytosine



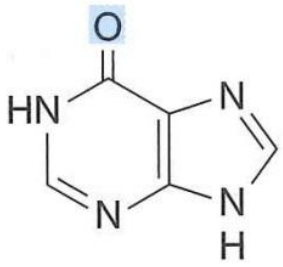
Dimethylaminoadenine



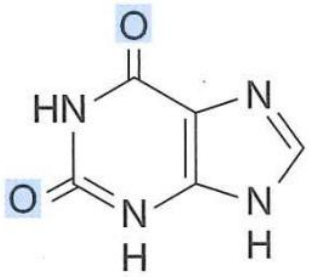
7-Methylguanine

FIGURE 32–7 Four uncommon but naturally occurring pyrimidines and purines.

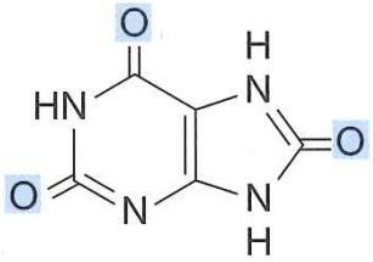
Intermediates on Catabolism of Nucleotides



Hypoxanthine
(6-oxopurine)



Xanthine
(2,6-dioxopurine)



Uric acid
(2,6,8-trioxypurine)

FIGURE 32–8 Structures of hypoxanthine, xanthine, and uric acid, drawn as the oxo tautomers.

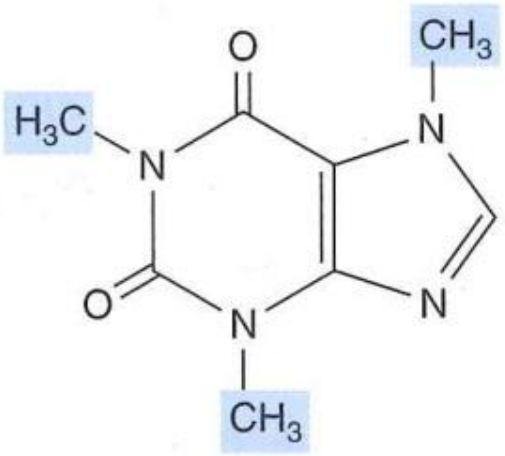


FIGURE 32–9 Caffeine, a trimethylxanthine. The dimethylxanthines theobromine and theophylline are similar but lack the methyl group at N-1 and at N-7, respectively.

Charachteristics and functions of Nucleotides

- Nucleotides are polyfunctional Acids
- Nucleotides Absorb ultraviolet light.
- Nucleotides serve diverse physiologic Functions.
- Nucleoside Triphosphates have high group transfer potential.
- Synthetic nucleotide analogs are used in Chemotherapy.
- NonHydrolyzable Nucleoside TriPhosphate Analogs serve as research tools.
- DNA & RNA are polunucleotides
- Polynucleotides are Directional Macromolecules.

Regulatory compounds

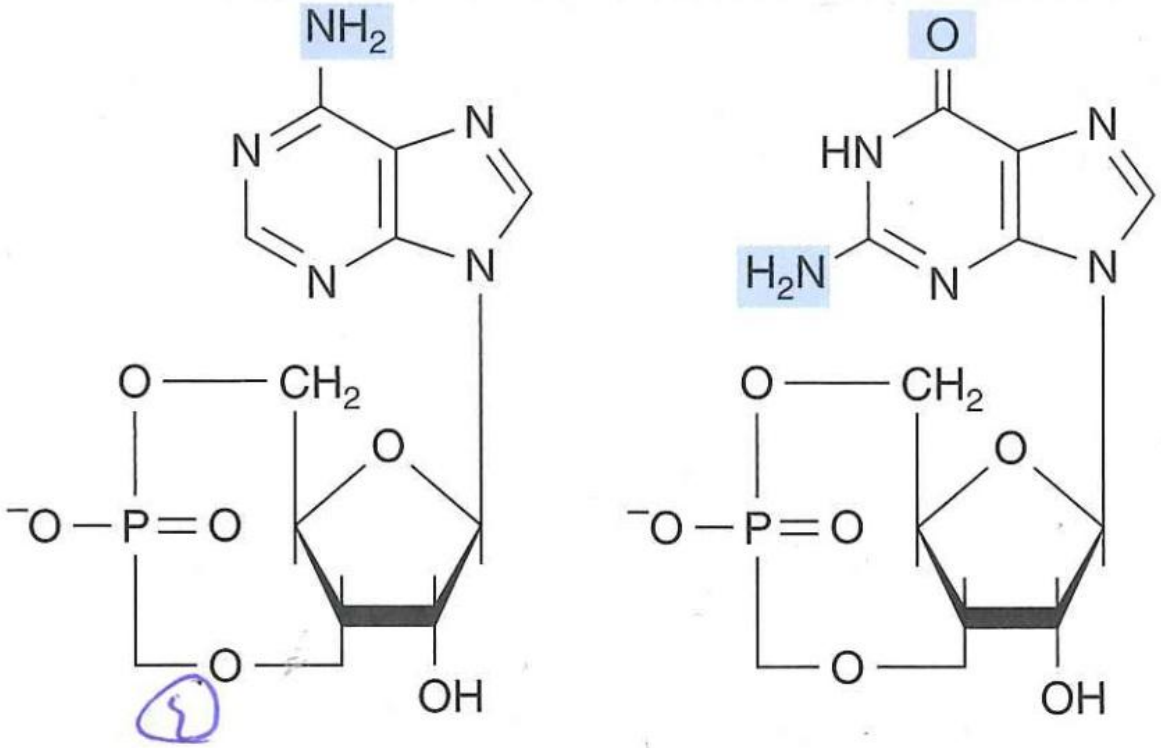
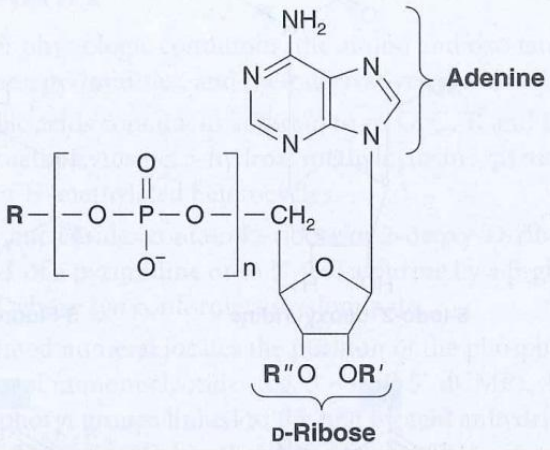


FIGURE 32–10 cAMP, 3′,5′-cyclic AMP, and cGMP, 3', 5'-cyclic GMP.

Components of Enzymes

TABLE 32–2 Many Coenzymes and Related Compounds Are Derivatives of Adenosine Monophosphate



Coenzyme	R	R′	R″	n
Active methionine	Methionine[a]	H	H	0
Amino acid adenylates	Amino acid	H	H	1
Active sulfate	SO_3^{2-}	H	PO_3^{2-}	1
3′,5′-Cyclic AMP		H	PO_3^{2-}	1
NAD[b]	Nicotinamide	H	H	2
NADP[b]	Nicotinamide	PO_3^{2-}	H	2
FAD	Riboflavin	H	H	2
Coenzyme A	Pantothenate	H	PO_3^{2-}	2

[a]Replaces phosphoryl group.
[b]R is a B vitamin derivative.

Analogs in Chemotherapy

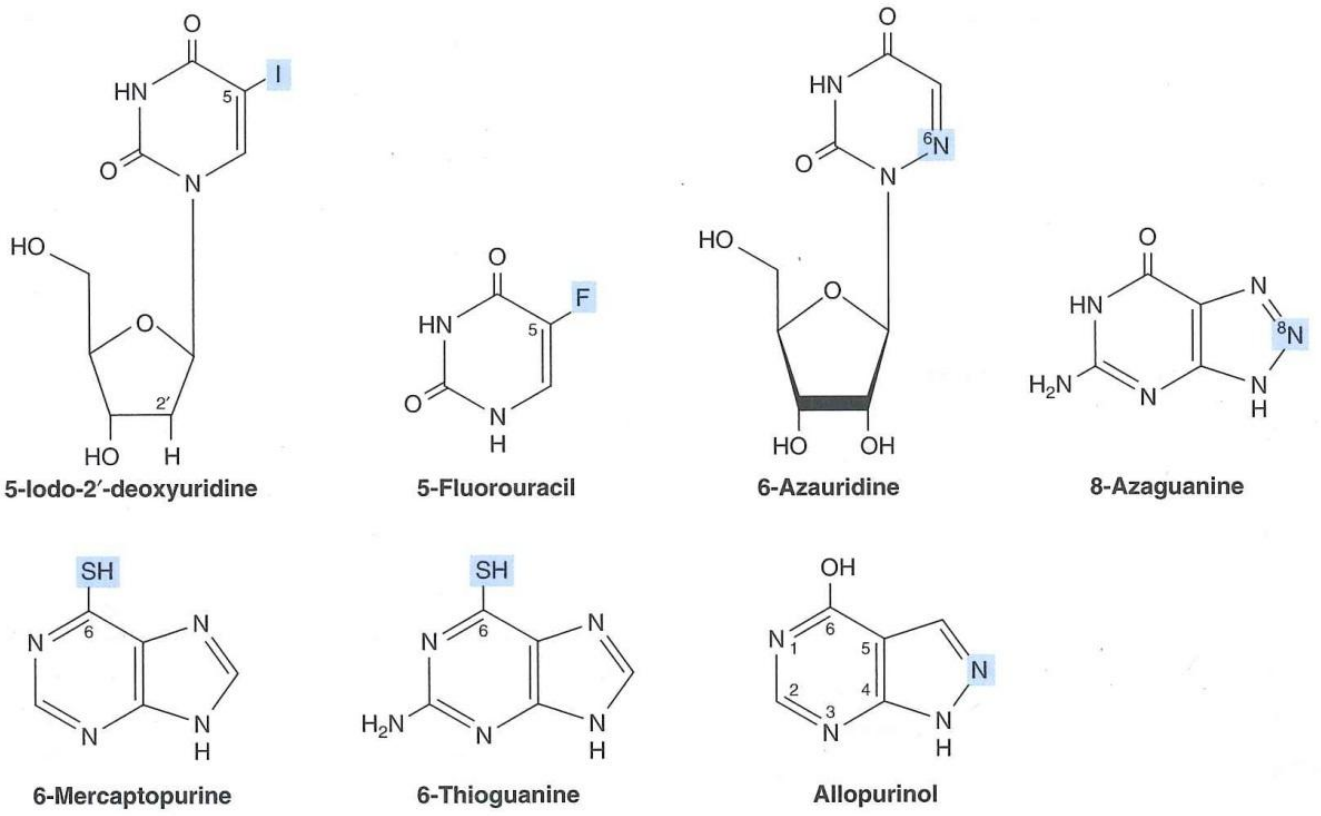
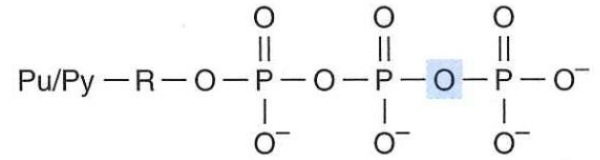
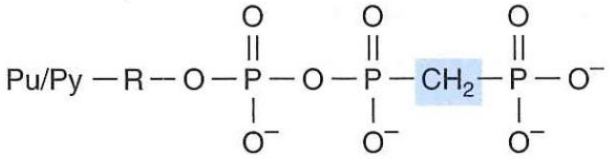


FIGURE 32–13 Selected synthetic pyrimidine and purine analogs.

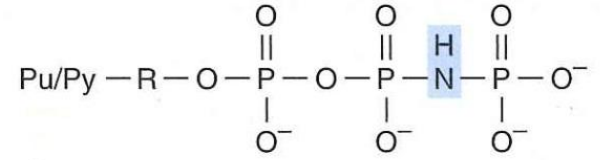
Synthetic Derivatives as research tools



Parent nucleoside triphosphate



β,γ-Methylene derivative



β,γ-Imino derivative

FIGURE 32–15 Synthetic derivatives of nucleoside triphosphates incapable of undergoing hydrolytic release of the terminal phosphoryl group. (Pu/Py, a purine or pyrimidine base; R, ribose or deoxyribose.) Shown are the parent (hydrolyzable) nucleoside triphosphate *(**top**)* and the unhydrolyzable β-methylene *(**center**)* and γ-imino derivatives *(**bottom**)*.