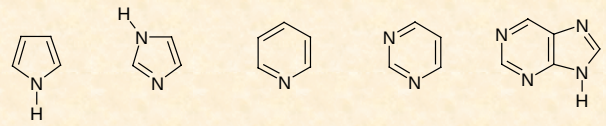
Chemistry of nucleic acids

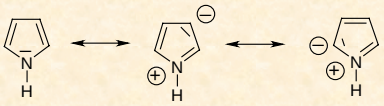
1. Basic properties of heterocycles

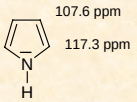


Pyrrole (Azole) | Imidazole (1,3-Diazole) | Pyridine (Azine) | Pyrimidine (1,3-Diazine) | Purine

Pyrrole

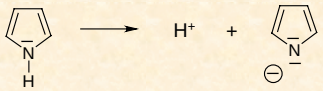
Pyrrole: Aromatic system (6 π-Electrons)



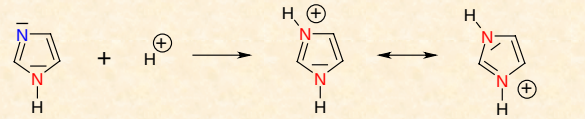


Resonance structures:
Electron rich system

N: lack of basicity

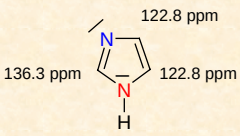


Imidazole

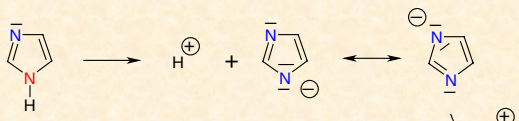


1. Basicity: resonance-stabilized cation

pK_B 7.0



Imidazole



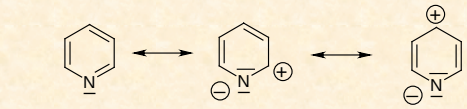
2. Acidity: resonance-stabilized anion

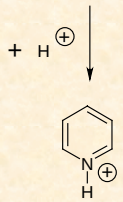
Dual role of N-atoms as general acid-base catalyst

Amino acid histidine present in the active site of many enzymes

Pyridine

Pyridine: 6 π-electrons

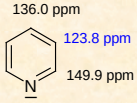




Resonance structures:
Electron-deficient aromatic system
(highest electron density at *m*-position)

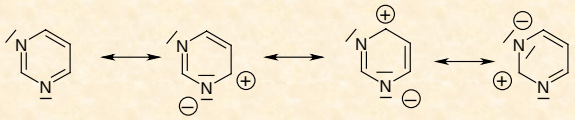
N: weak basicity

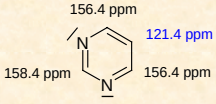
pK_B: 8.7



Pyrimidine

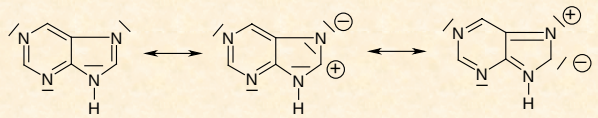
Pyrimidine: 6 π-electrons

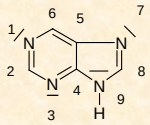




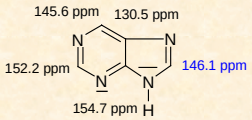
Reduced aromaticity
5-position relative high electron density

Purine



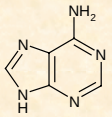


Reduced aromaticity
8-position relative high electron density

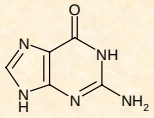


N-Bases of DNA and RNA

Purin bases

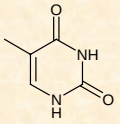


Adenine

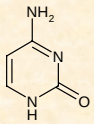


Guanine

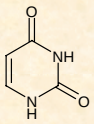
Pyrimidine bases



Thymine

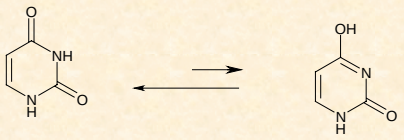


Cytosine



Uracil

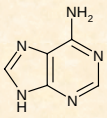
Lactame-Lactime Tautomers



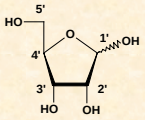
Uracil: Lactame form

Lactime form

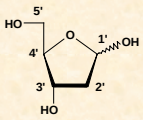
Nucleoside: *N*-Glycoside of N-bases



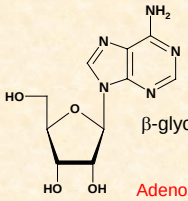
Adenine



Ribose
(Furanose)



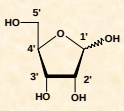
2'-Desoxyribose
(Furanose)



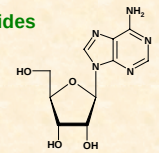
β-glycosidic bond (β-ribofuranoside)

Adenosine

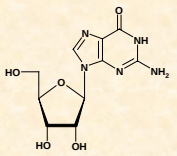
Purine nucleosides



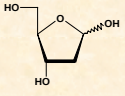
Ribose
(Furanose)



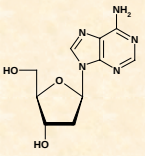
Adenosine



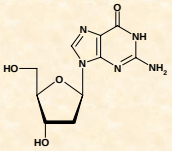
Guanosine



2'-Desoxyribose
(Furanose)

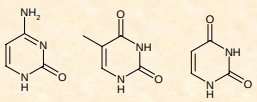


2'-desoxy-Adenosine
dA



2'-desoxy-Guanosine
dG

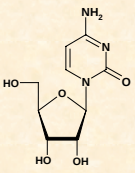
Pyrimidine nucleosides



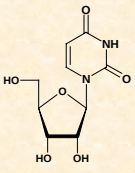
Cytosine

Thymine

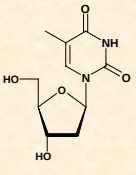
Uracil



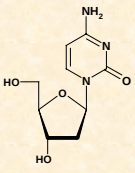
Cytidine
C



Uridine
U

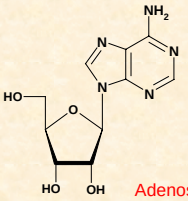


Thymidine
2'-Desoxyribosylthymine
dT

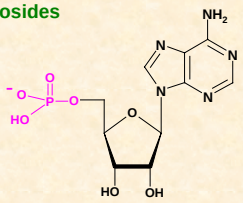


2'-desoxy-Cytidine
dC

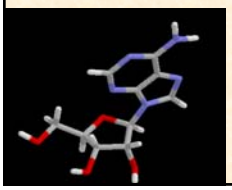
Nucleotides: phospho esters of nucleosides



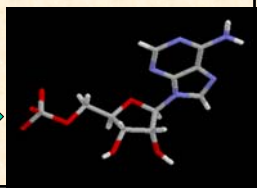
Adenosine



Adenosine 5'-monophosphate



Phosphomonoester



2. General properties

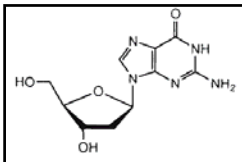
Solubility of pyrimidines and purines in water (1 g x g H_2O)

Heterocycle	x g H_2O	functional group
Pyrimidine	1	-
Uracil	280	2 OH
Thymine	250	2 OH, 1 Me
Purine.picrate	2	-
Adenine.picrate	1086	1 NH_2
Guanine.picrate	26000	1 OH, NH_2
2,8-Dihydroxyadenine	500000	1 OH, NH_2
Uric acid	39480	3 OH
Nucleosides, Nucleotides	soluble in hot, insolub. in cold water	

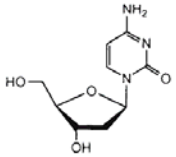
General properties

Dissociation equilibria in nucleotides

Functional group	Dissociation reaction	pK
1. Phosphate-OH	$RO\text{-}PO_3H_2 \Leftrightarrow RO\text{-}PO_3H^- + H^+$	0.7-1.6
-NH_2 of adenine	$R\text{-}NH_3^+ \Leftrightarrow R\text{-}NH_2 + H^+$	3.5-4.5
2. Phosphate-OH	$RO\text{-}PO_3H^- \Leftrightarrow RO\text{-}PO_3^{2-} + H^+$	5.8-6.6
Heterocycl. protons (U, T, G)	-NH-CO- $\Leftrightarrow$ -N=C(O^-)- + H^+	9.5
-OH of ribose	$R\text{-}OH \Leftrightarrow RO^- + H^+$	12.5

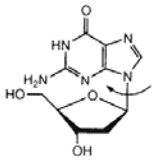


anti deoxyguanosine

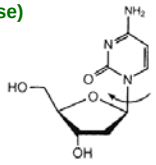


anti deoxycytidine

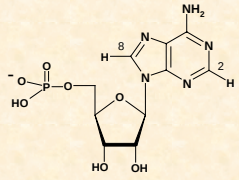
General properties conformations of nucleosides (Orientation of N-base)



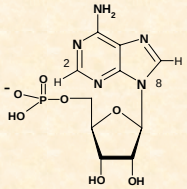
syn deoxyguanosine



Conformation of nucleotides



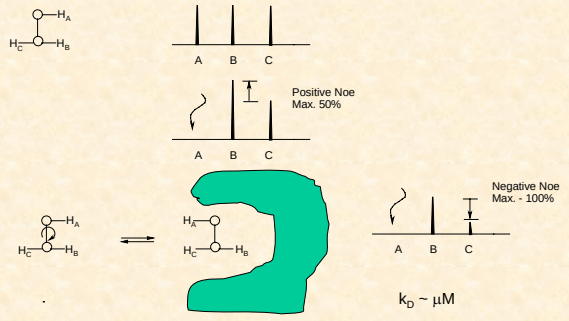
anti-conformation



syn-conformation

Orientation of the N-base relative to the pentose

Transfer-Noe: study of conformation of a ligand in the binding site

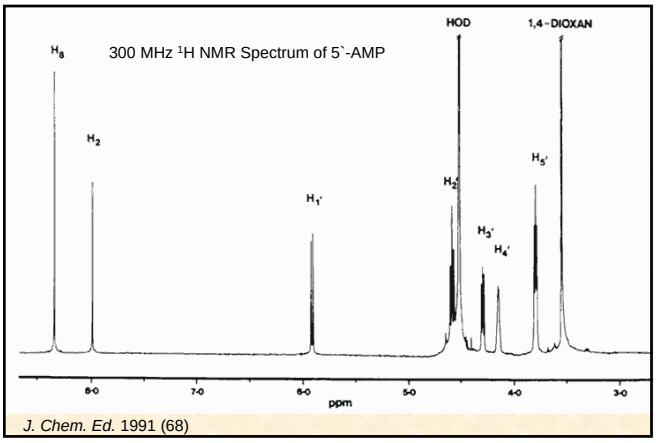


Free ligand

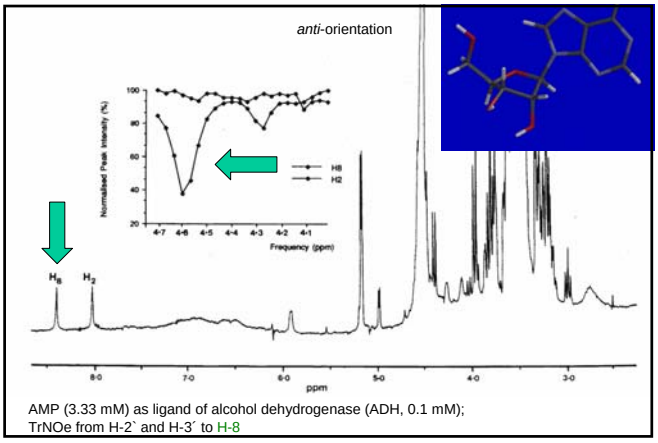
Bound ligand

k_D ~ µM

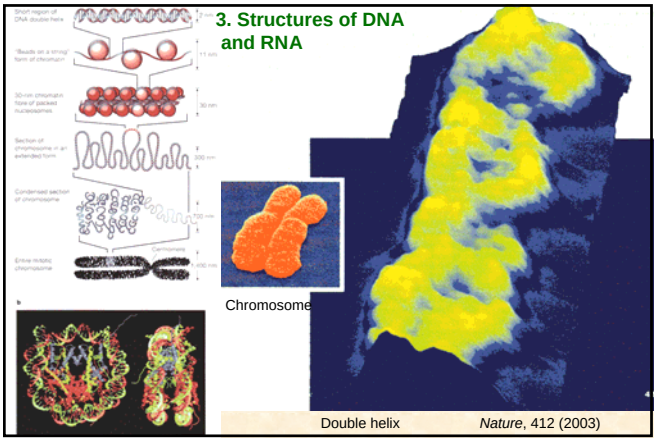
ligand : protein > 10 : 1



J. Chem. Ed. 1991 (68)



AMP (3.33 mM) as ligand of alcohol dehydrogenase (ADH, 0.1 mM);
TrNOe from H-2` and H-3´ to H-8



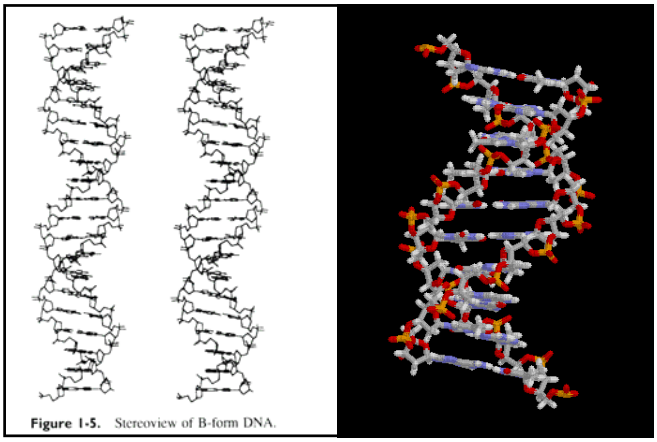
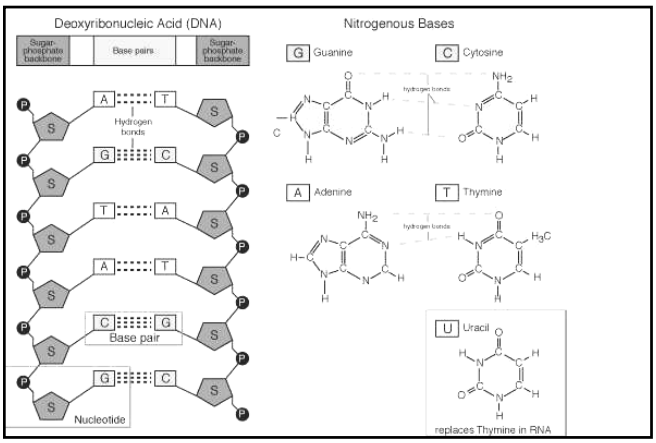
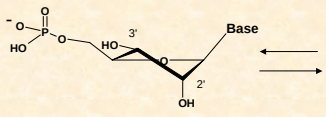


Figure 1·5. Stereoview of B-form DNA.

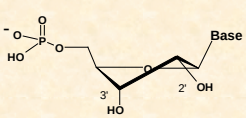


Conformations of nucleotides

Conformations of furanose rings: „Ring puckering", Example:
exo-, *endo*- Twistkonformation



$^{3}T_{2}$ 3'-*endo*-conformation



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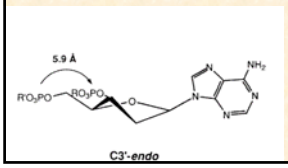

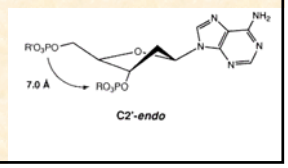

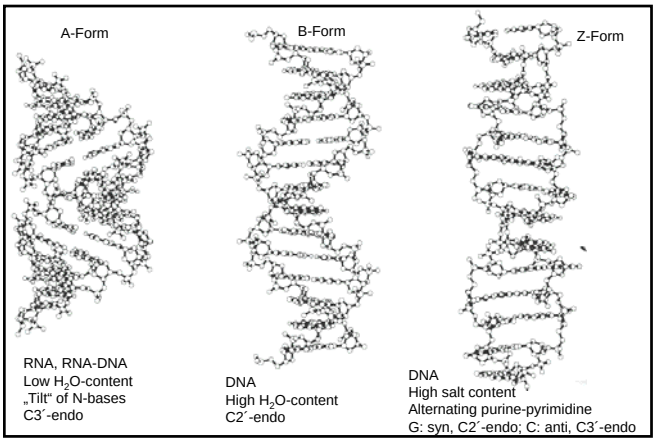

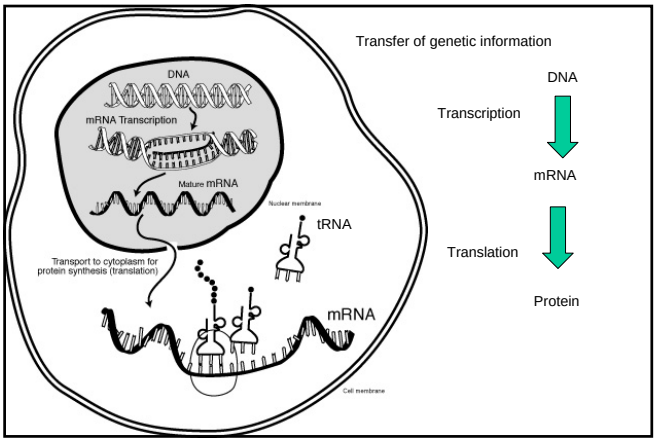

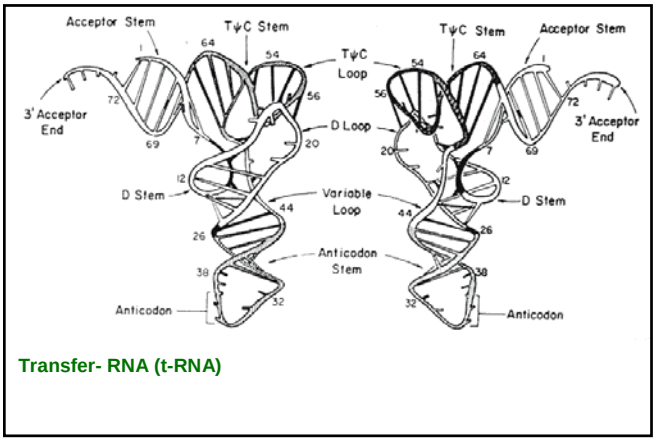

Transfer- RNA (t-RNA)