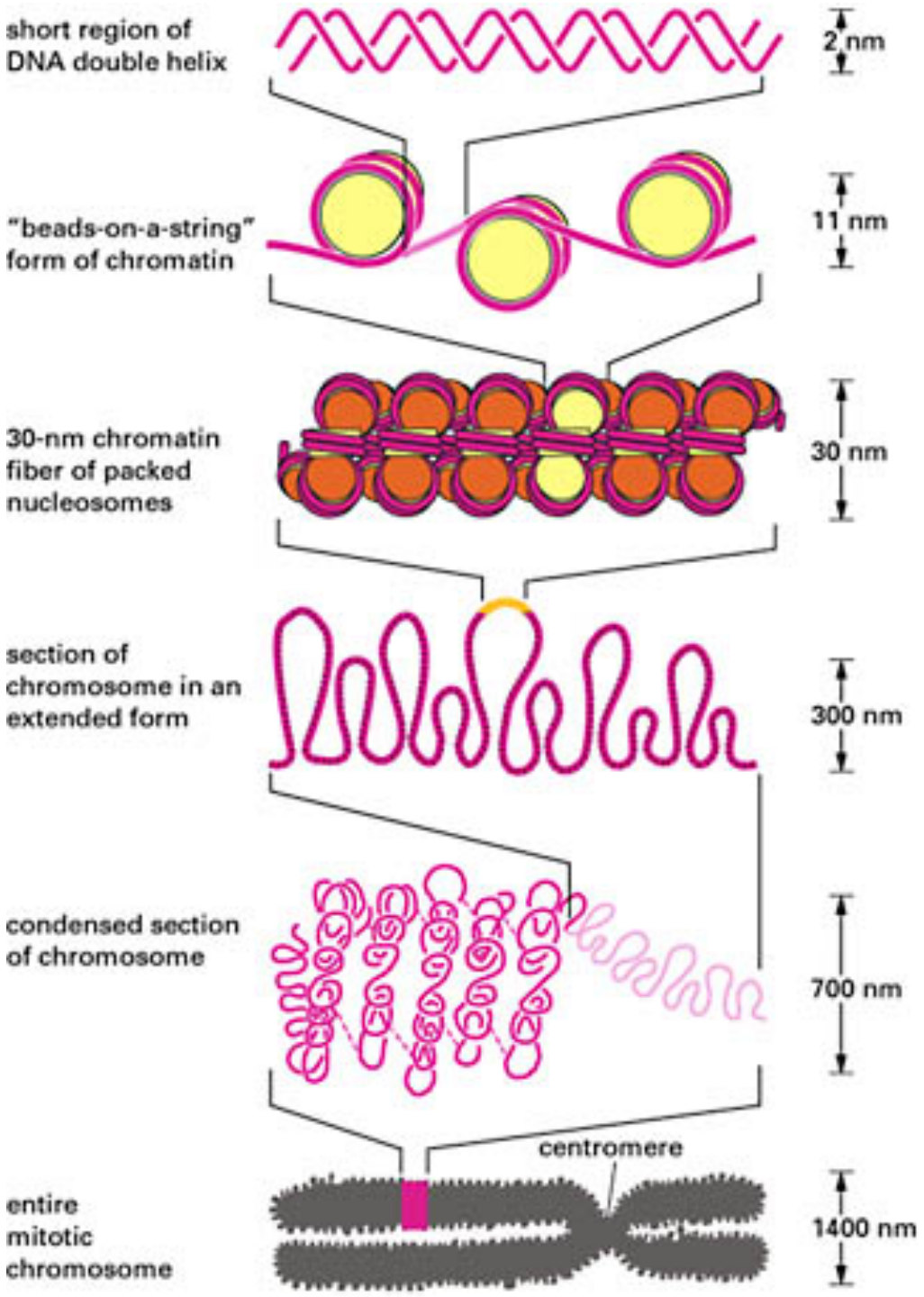
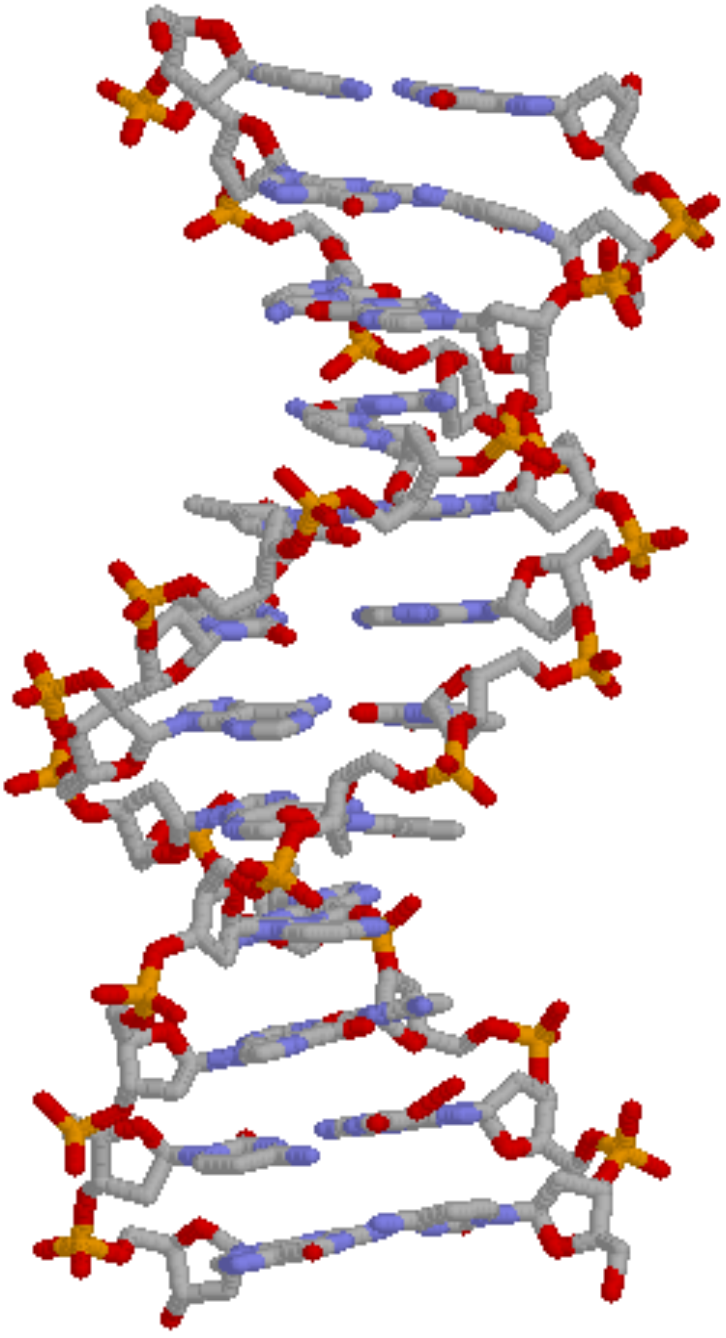
Structure and Properties of Nucleic Acid Components

Human DNA: 3 Billion Base Pairs

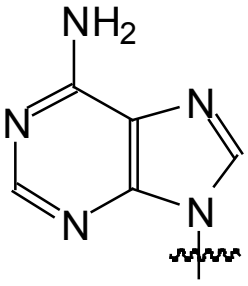


NET RESULT: EACH DNA MOLECULE HAS BEEN PACKAGED INTO A MITOTIC CHROMOSOME THAT IS 50,000x SHORTER THAN ITS EXTENDED LENGTH

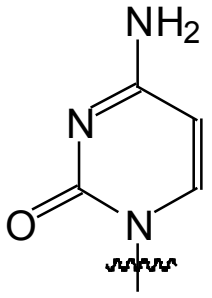
Double Helical B DNA



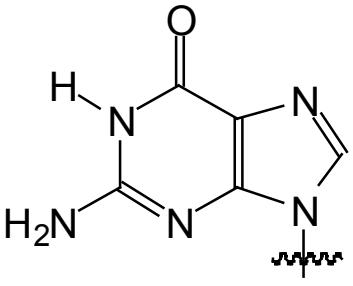
A



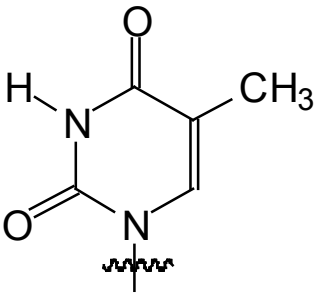
C



G



T



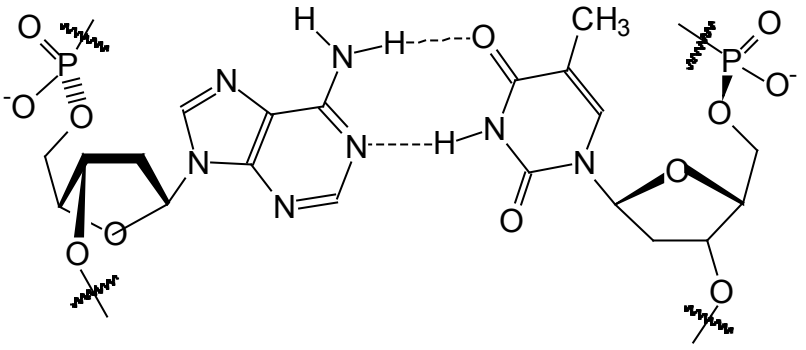
Bdl001.pdb

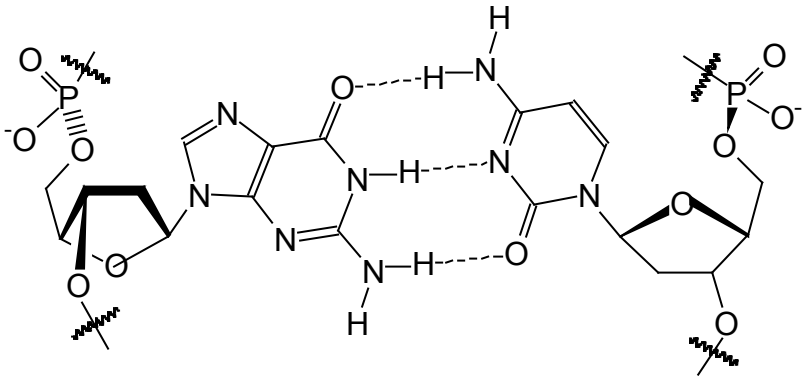
ACGT bases.cwg

THE FOUR LETTER CODE: A, C, G, T

COMPLEMENTARY WATSON CRICK BASE PAIRING BETWEEN TWO ANTIPARALLEL STRANDS

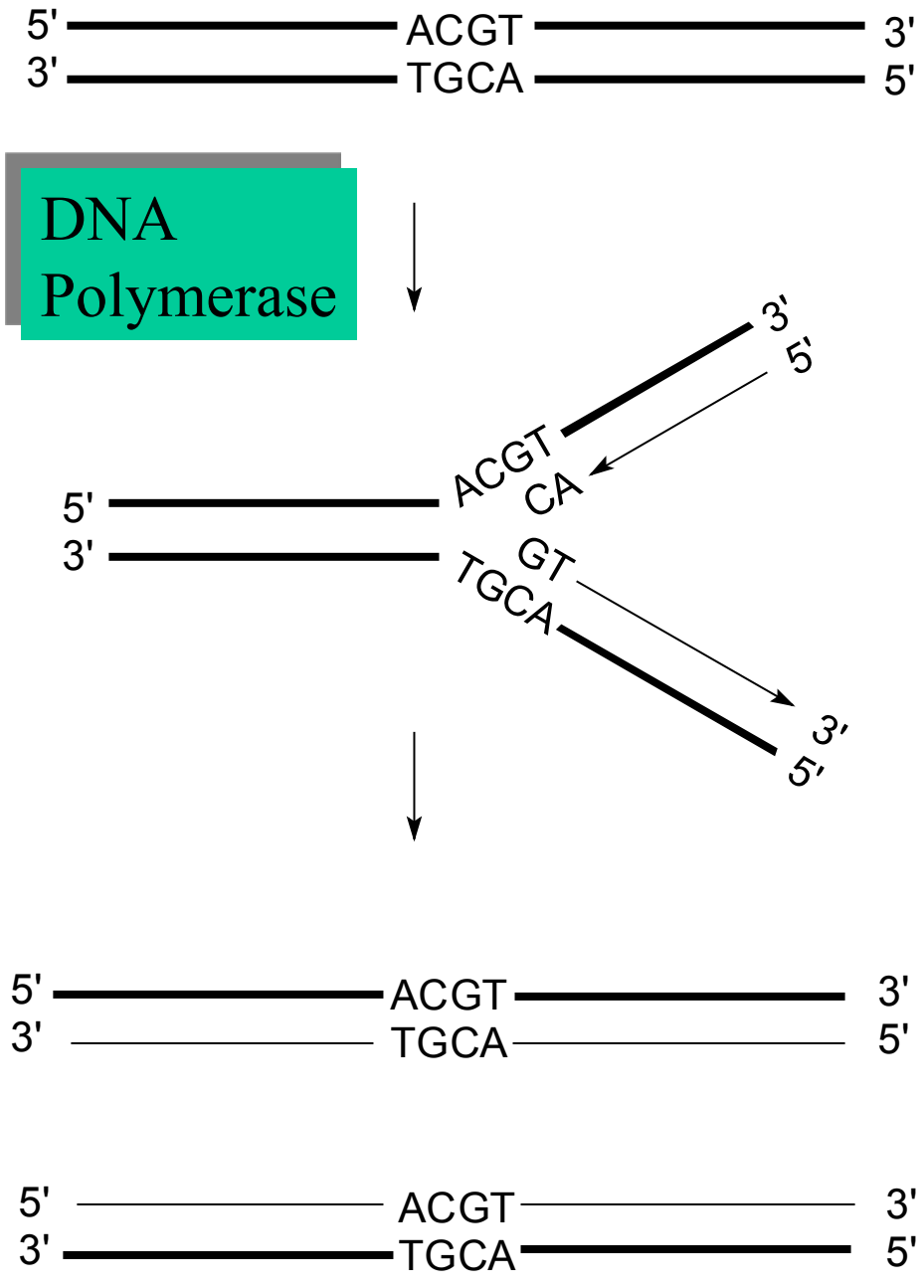
A base recognizes T, and G recognizes C



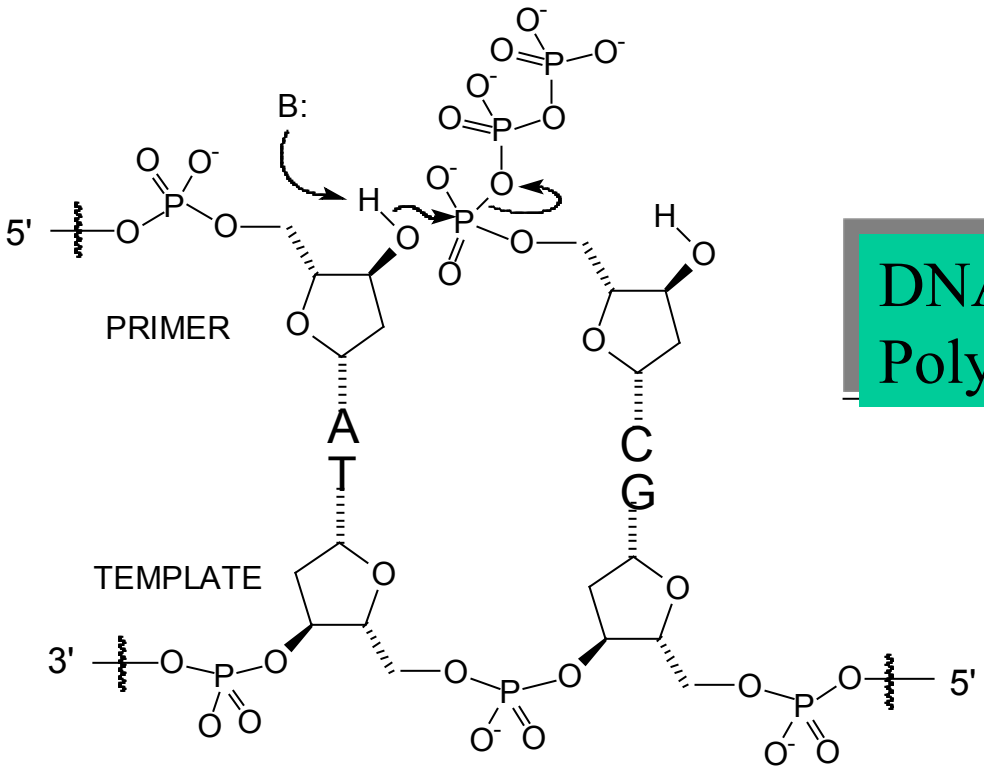


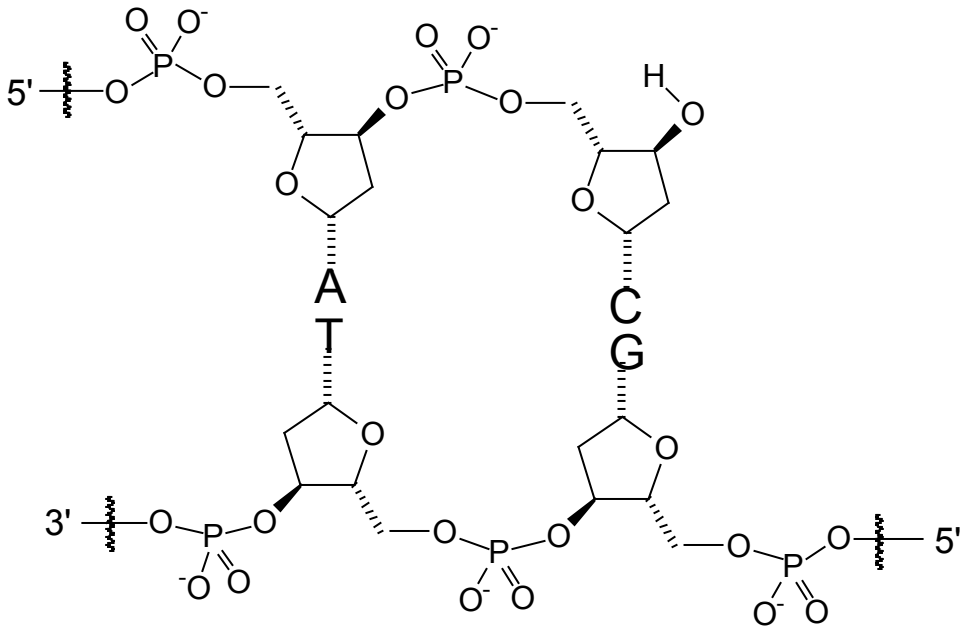
B DNA Structure

DNA Replication: 5' to 3', template directed via Watson Crick Base Pairing

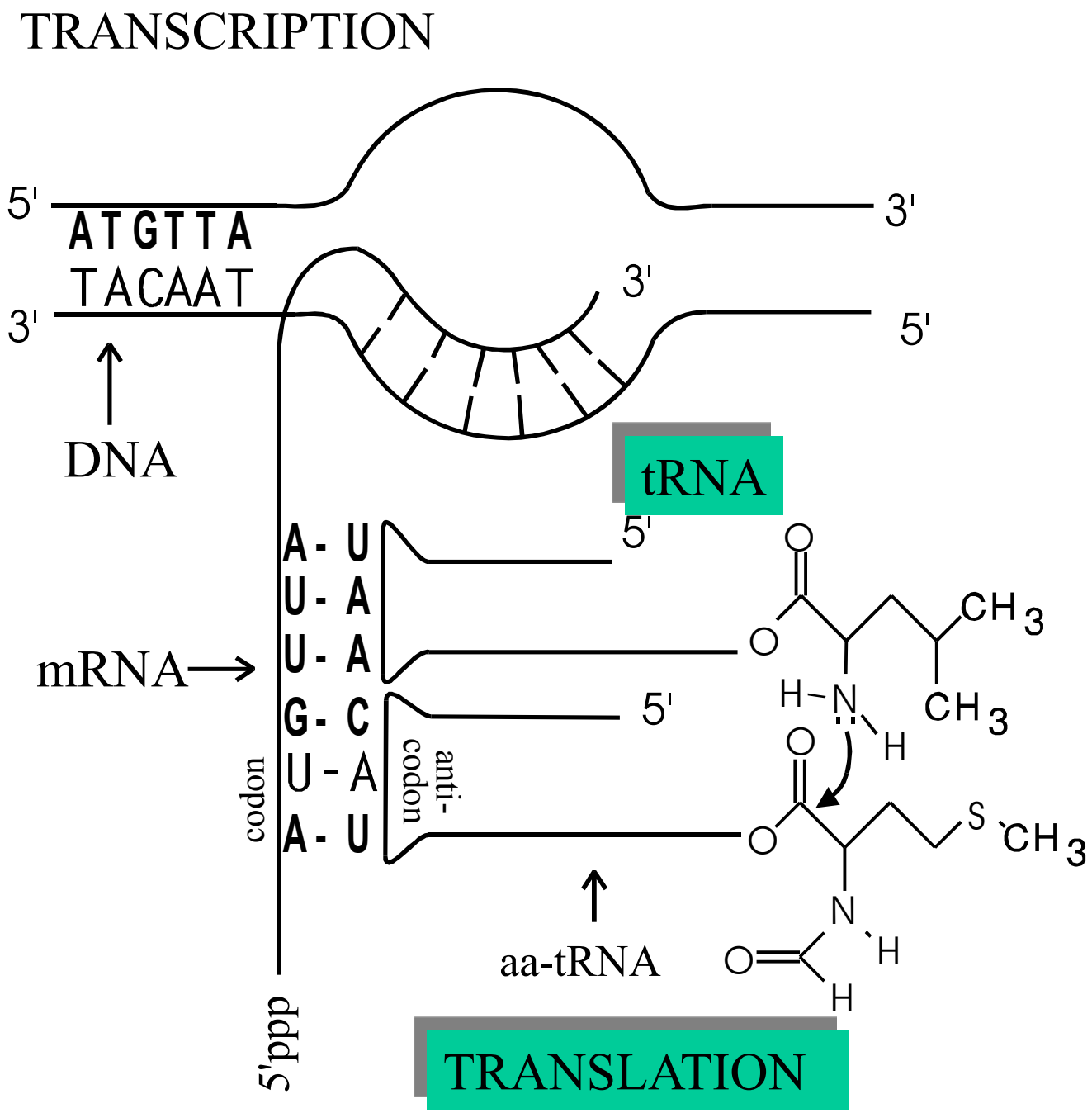


Replication of DNA

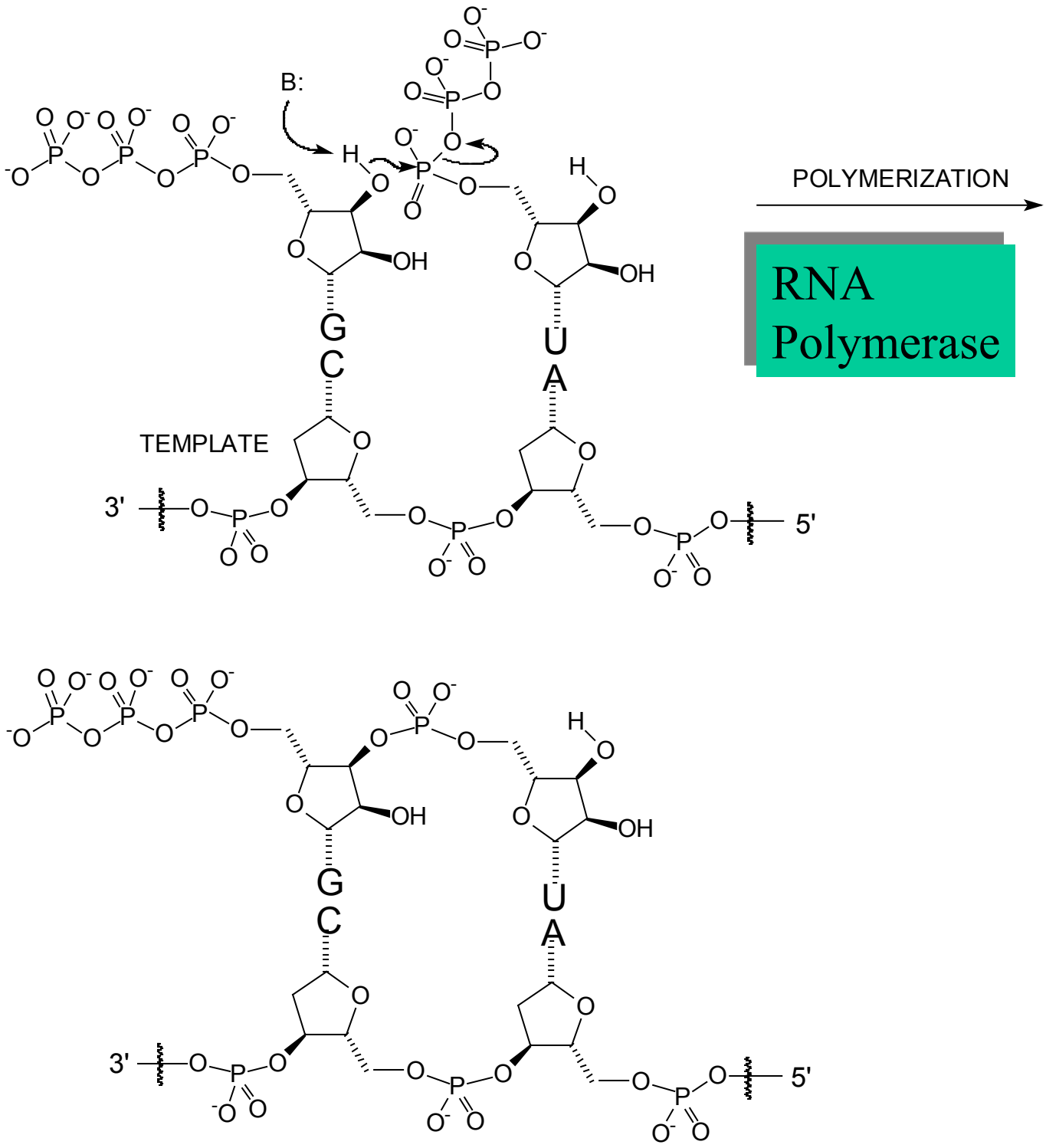




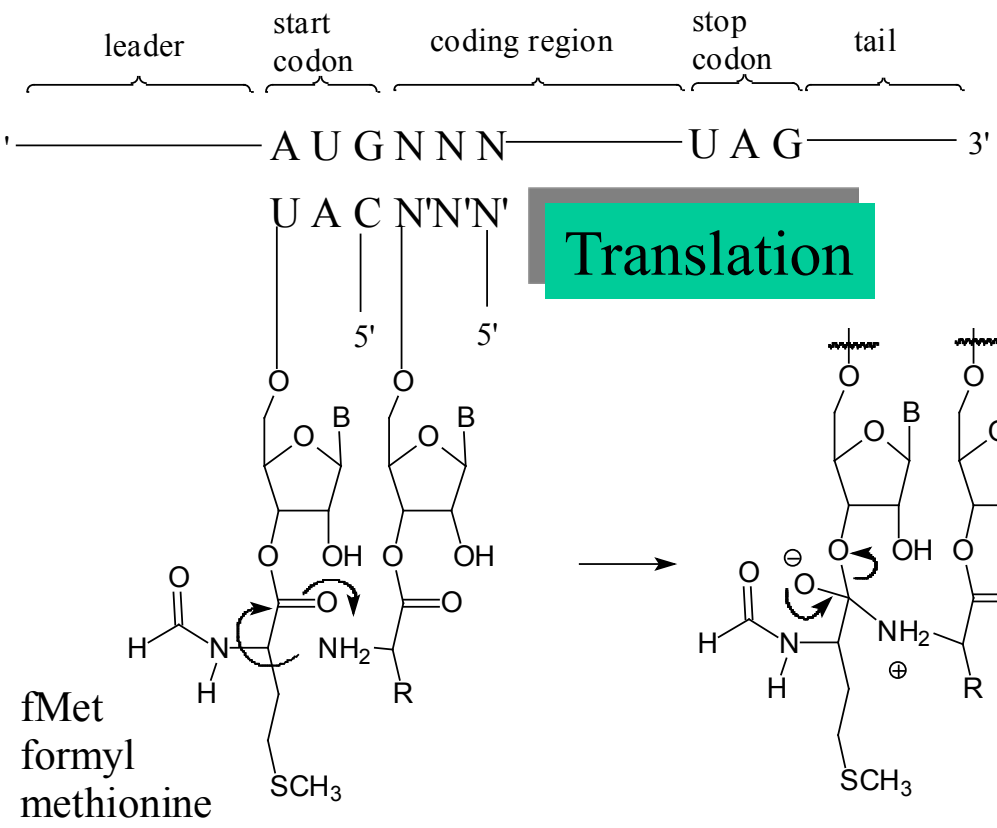
DNA to RNA to PROTEIN

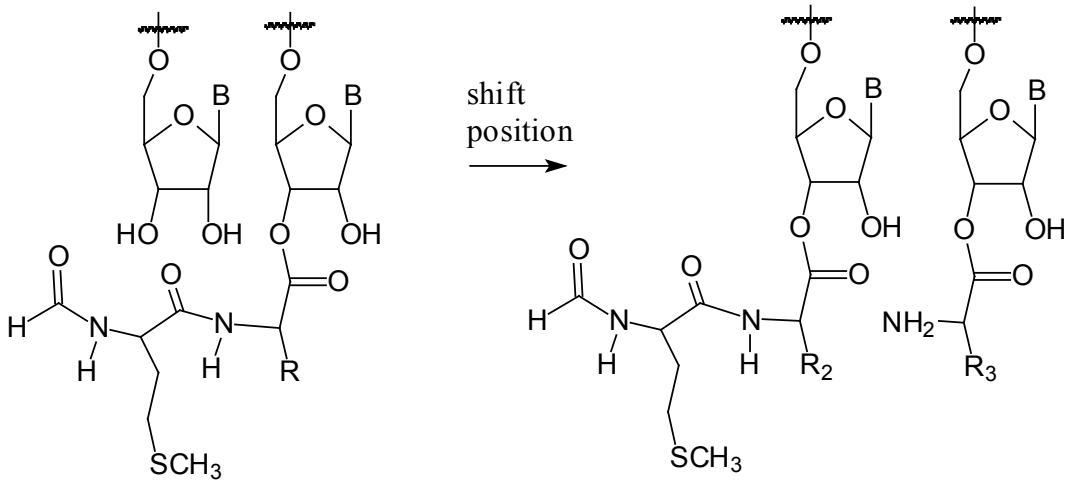


DNA to RNA: Transcription by RNA polymerase



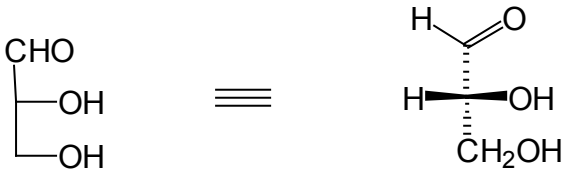
mRNA to Protein: Translation



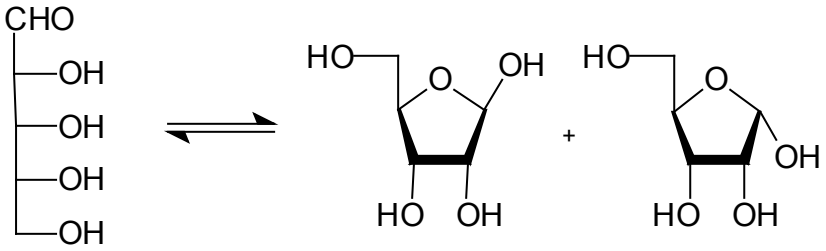


THE SUGAR SUBUNIT OF DNA AND RNA

FISHER PROJECTION



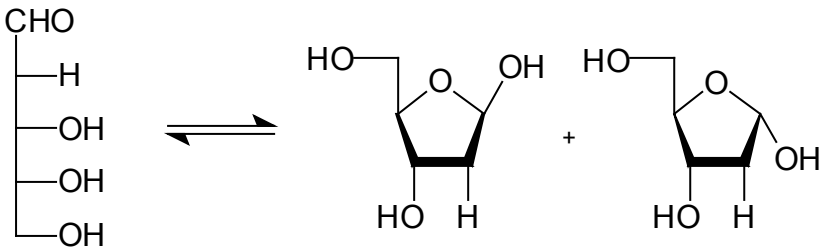
D-(+)-glyceraldehyde



D-(-)-ribose

beta-anomer alpha-anomer

D-ribofuranoside



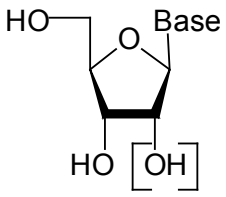
2-deoxyribose

beta-anomer alpha-anomer

D-deoxyribofuranoside

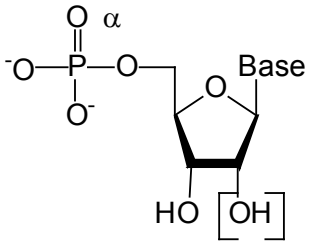
Nucleosides and Nucleotides

Nucleoside:



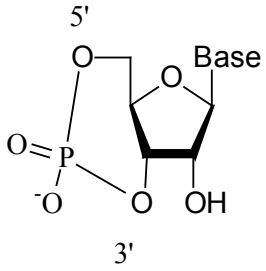
adenosine
cytidine
guanosine
uridine (RNA)
thymidine (DNA)

Nucleotide monophosphate:
NMP or dNMP

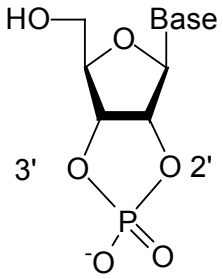


adenylic acid
cytidylic acid
guanylic acid
uradylic acid (RNA)

Cyclic Nucleotide

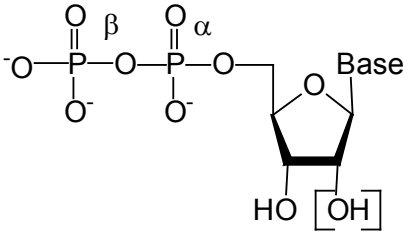


3',5'-cyclic AMP
(cAMP)



2',3'-cyclic AMP

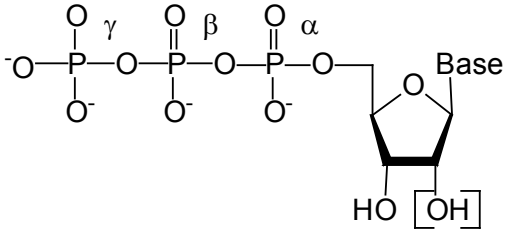
NDP or dNDP



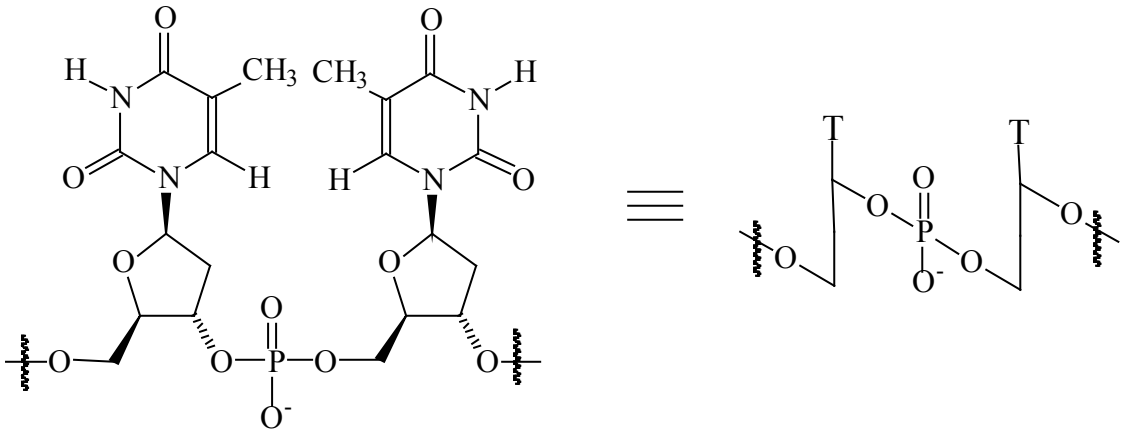
thymidylic acid (DNA)

NOTE: In DNA the OH in the brackets is absent

NTP or dNTP



Structure and Nomenclature for dinucleotides and polymers



dNpdNpdN = d(NpNpN) = d(NNN) for oligodeoxyribonucleotides

NpNpN = NNN for oligoribonucleotides

d(NNN)Nd(NNN) for mixed oligo ribo and deoxyribonucleotides
(embedded substrates, such as embedded RNA)

When strands associate the two sequences are given, both in the 5'-3'

d(ACGTATG)·d(CATACGT)

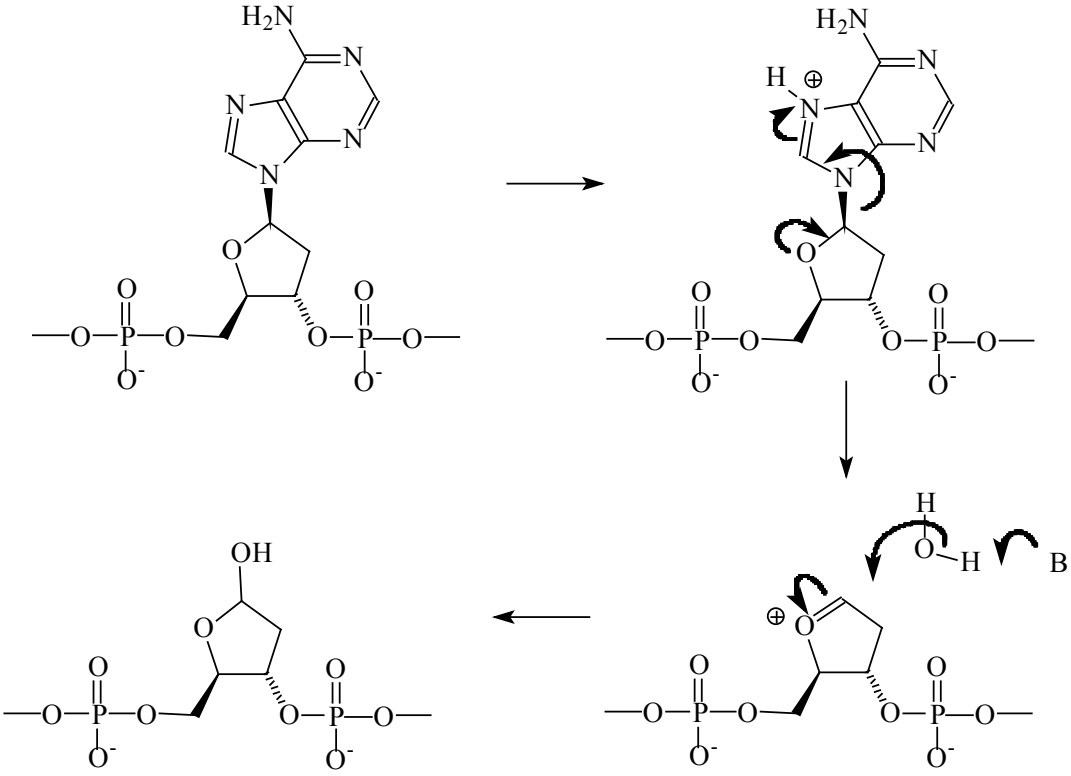
Polymers.

poly (dA) : homopolymer d(AAA)n = d(AAAAAAA...)
poly (dA-dT): heteropolymer d(AT)n = d(ATATATA...)
poly (dA,dT): random copolymer d(ATTAATTTTATATTA...)

When polymer strands associate the stoichiometry is given:

poly (A) · 2 poly(U)

Mechanism for the acid hydrolysis of the glycosidic bond in DNA.

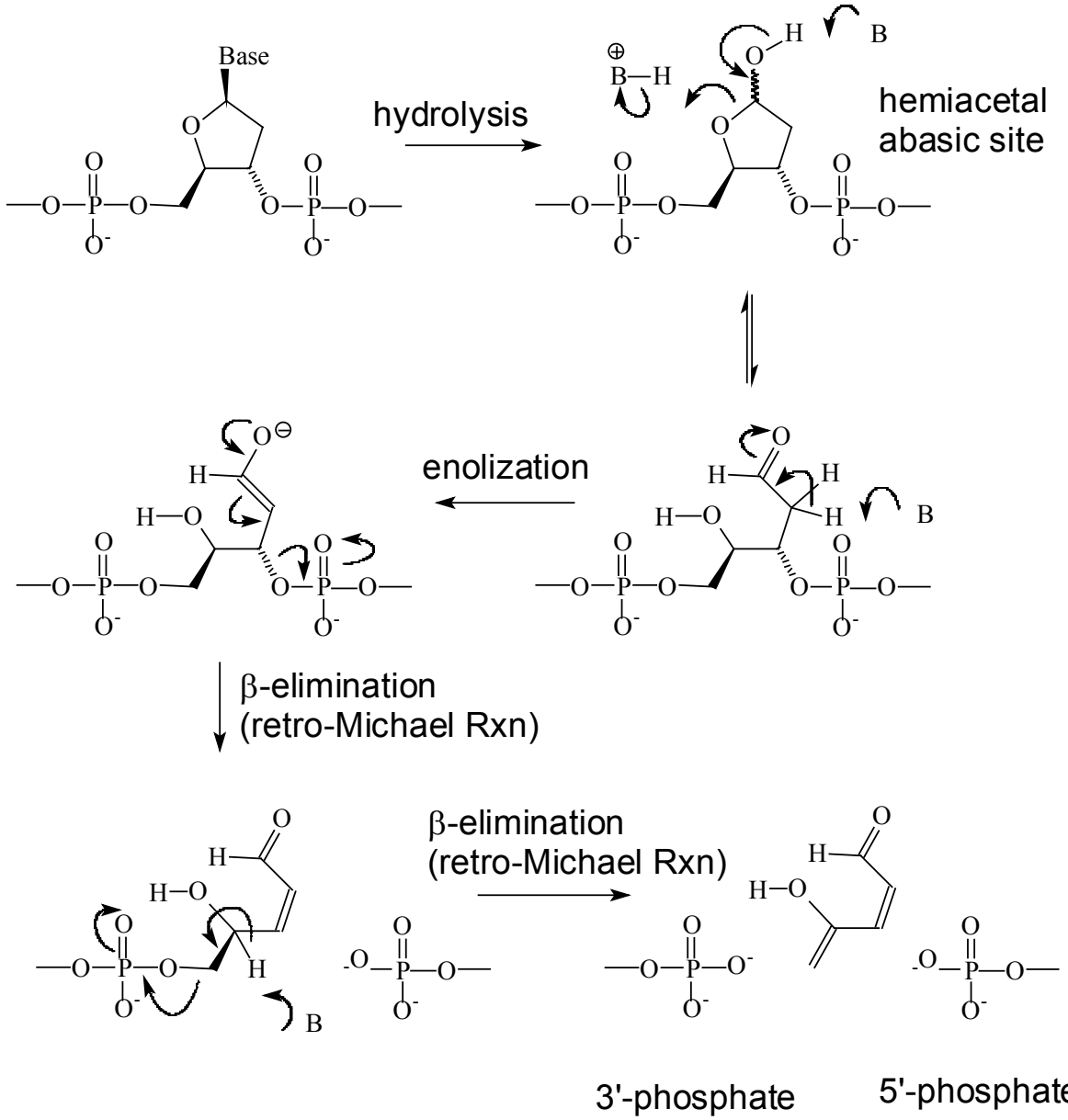


File: acidhyd.cwg

Table. Rate of hydrolysis of the bases at pH 1.
(Kochetkov and Budovskii 1972)

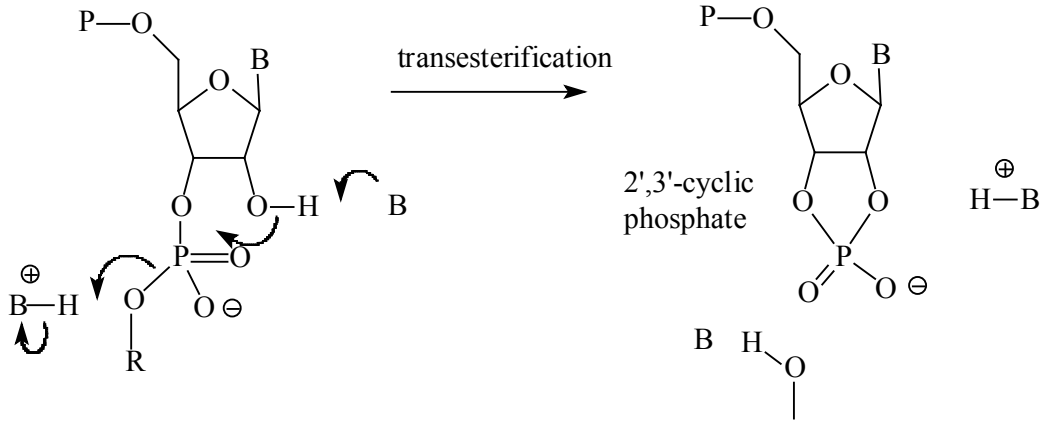
nucleoside	rate (´ 10^4 sec)
dA	4.3
dG	8.3
dC	.0011
dU	.001
A	.0036
G	.0093
C	.00001
U	.00001

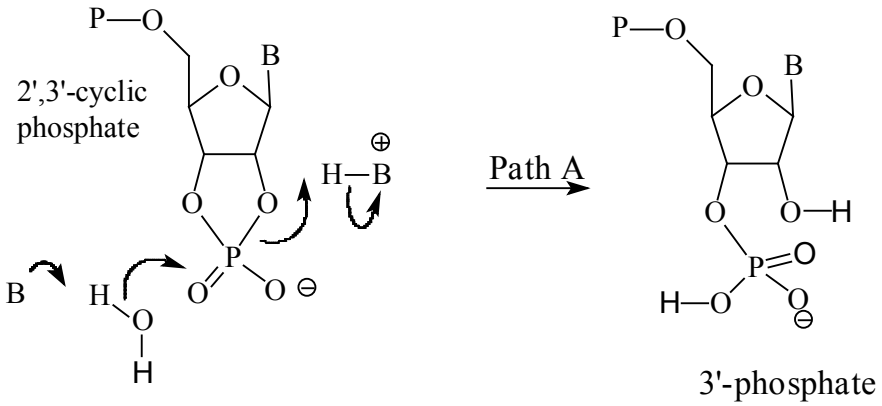
Mechanism of strand cleavage following glycosidic bond hydrolysis

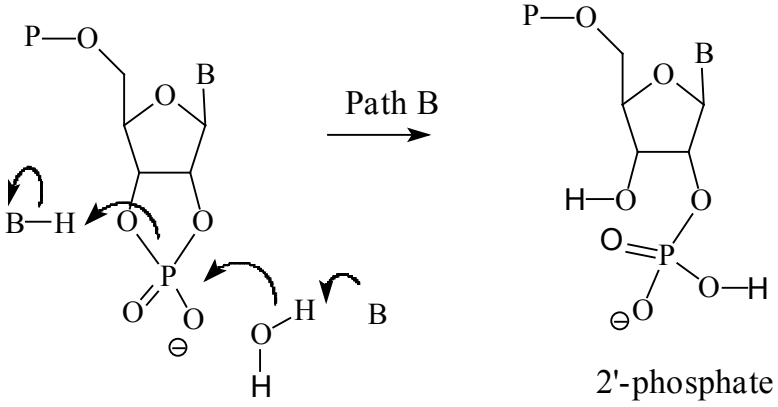


In the presence of piperidine, the b-elimination reactions may take place through the enamine.

RNA strand cleavage under basic condition







Rates of Hydrolysis of RNA under basic and acidic conditions

Table. Basic Hydrolysis of RNA.

Substrate	Conditions	Time	Temperature	Result
ApA	0.5 N NaOH	8 h	28ºC	47% hydrolysis
RNA	0.1 N NaOH	20 min	100ºC	mononucleotides
RNA	10% piperidine	90 min	100ºC	mononucleotides
RNA	1.0 N NaOH	0.7 min	27ºC	1% cleavage
RNA	pH 9	30 min	70ºC	1% cleavage

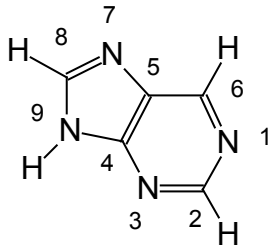
Table. Acidic Hydrolysis of RNA.

Substrate	Conditions	Time	Temperature	Result
ApA	0.3 N HCl	8 h	45ºC	69% hydrolysis
RNA	pH 1	100 min	20ºC	10% cleavage
RNA	pH 2	4 min	100 ºC	10% cleavage
RNA	pH 3	40 min	100 ºC	10% cleavage

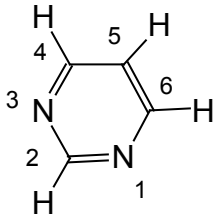
Basic Constituents of Nucleic Acids

THE BASES

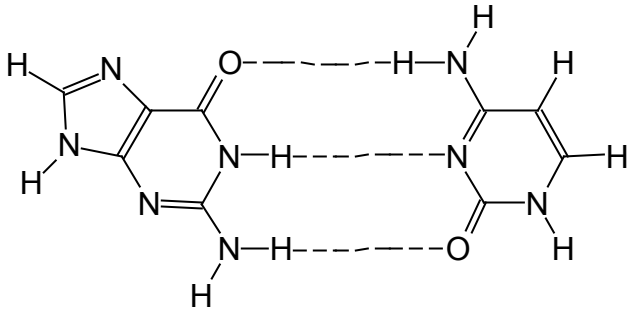
Purines



Pyrimidines

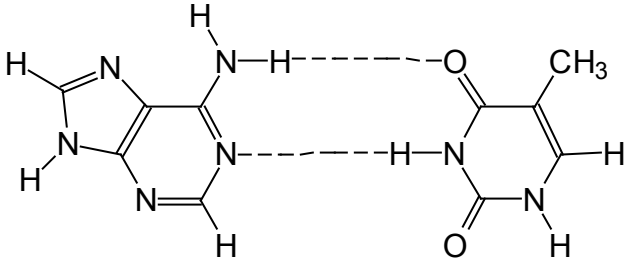


The Four Letter Code: A, C, G, T
where A recongizes T and C recognizes G



guanine
Gua

cytosine
Cyt

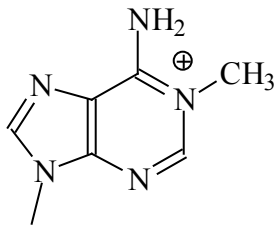


adenine
Ado

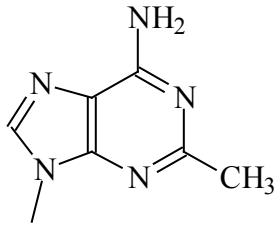
thymine
Thy

Bases are shown in their Watson Crick base-pairing arrangement

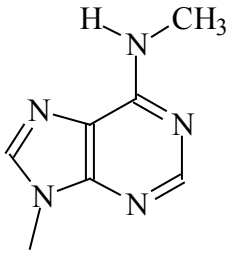
Minor RNA nucleosides, adenine derivatives



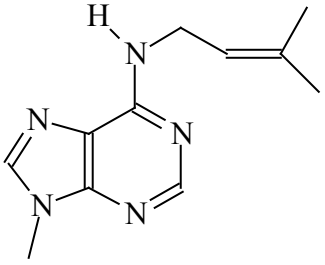
m^1A



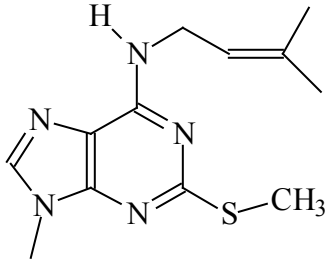
m^2A



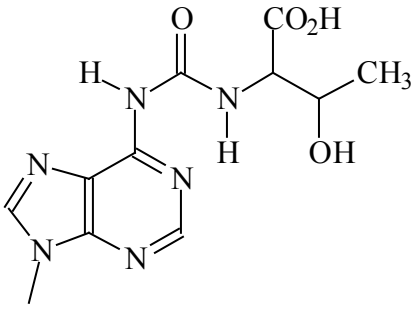
m^6A(dm^6A in DNA)



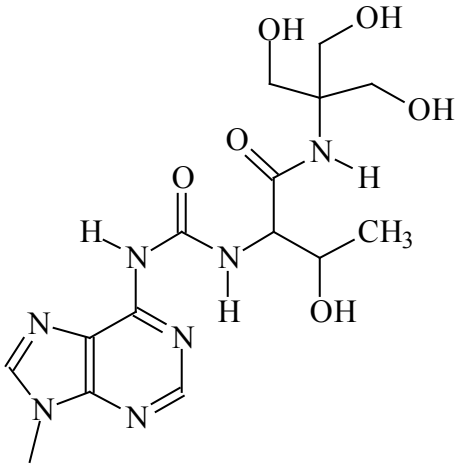
i^6A



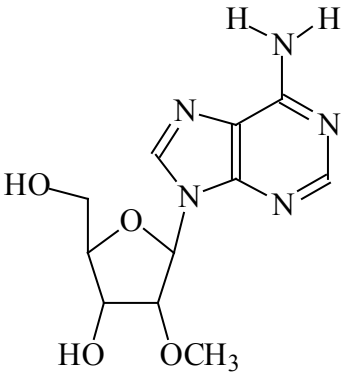
ms^2t^6A



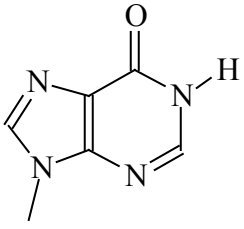
t^6A



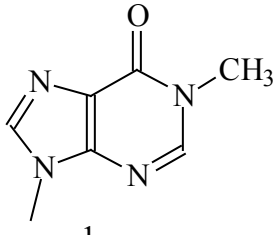
N^+



Am

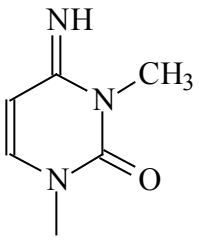


I

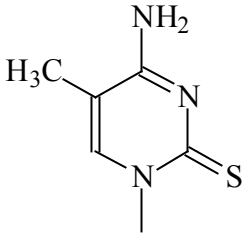


m^1I

Minor RNA nucleosides, cytosine derivatives

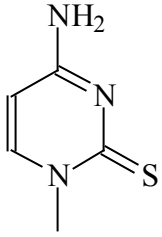


m^3C

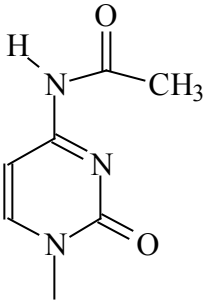


m^5C

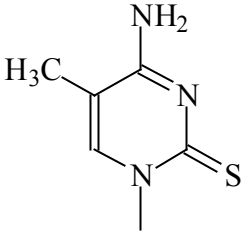
(dm^{5}C in DNA)



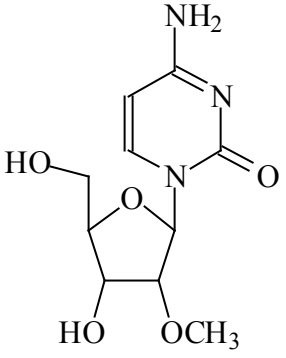
s^2C



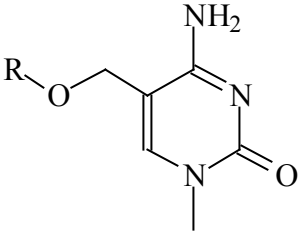
ac^4C



s^2m^5C

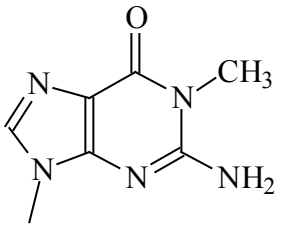


Cm

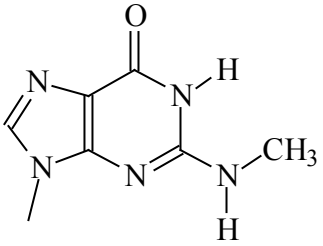


(DNA only, R=H or a sugar, found in T even bacteriophages)

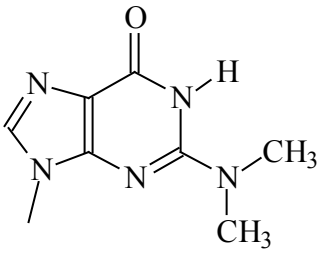
Minor RNA nucleosides, guanine derivatives



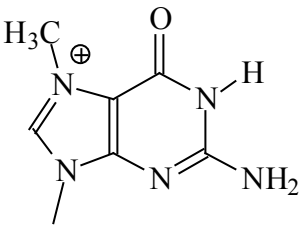
m^1G
(dm^1G in DNA)



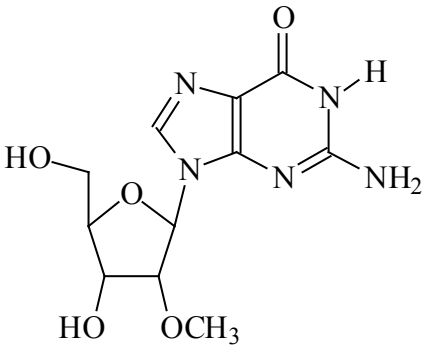
m^2G



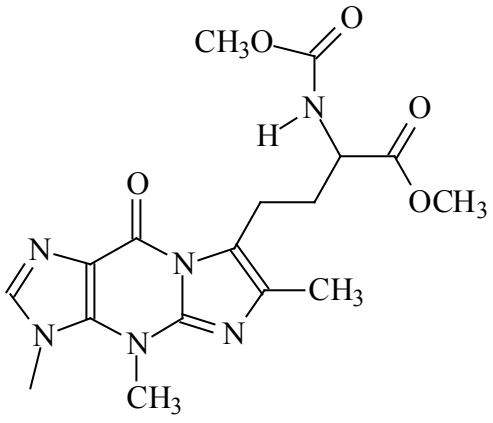
m_2^2G
(dm_2^2G in DNA)



m^7G
(dm^7G in DNA)

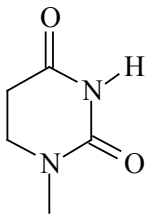


Gm

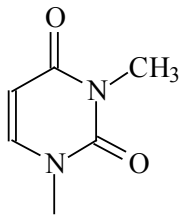


Y

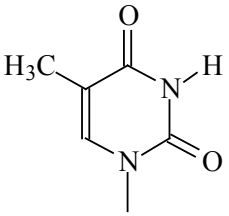
Minor RNA nucleosides, Uracil derivatives



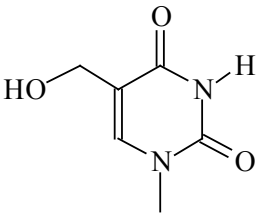
D or hU



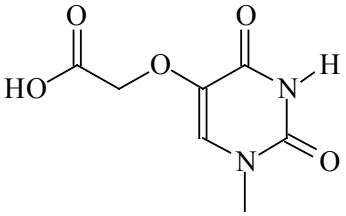
m^3U



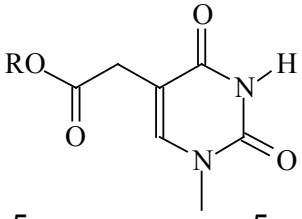
rT or T



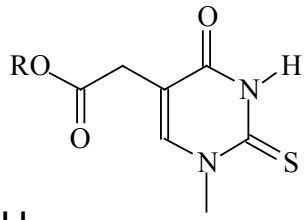
(found in DNA of SP 8 bacteriophage)



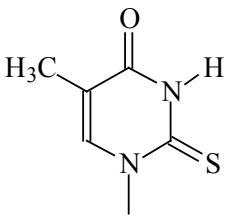
V



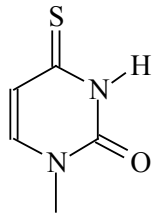
cm^5U R=H, cmm^5U, R=CH_3



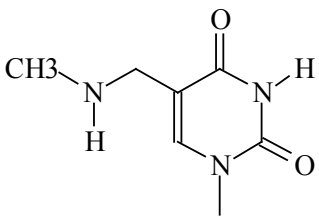
s^2cm^5U R=H, s^2am^5U, R=CH_3



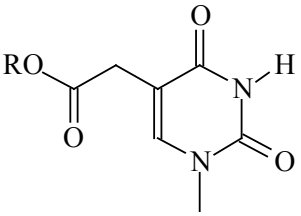
s^2m^5U

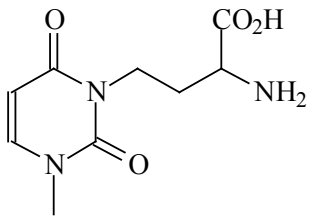


s^2U

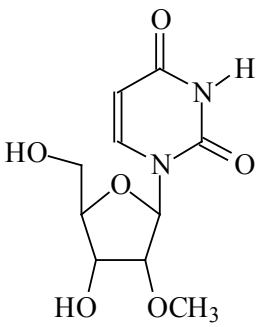


s^2mam^5U

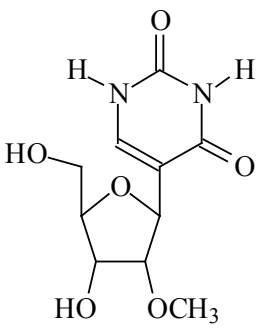




X



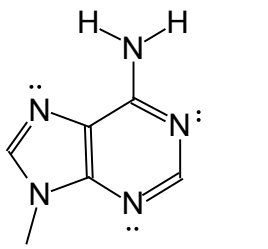
Um

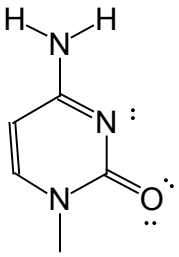


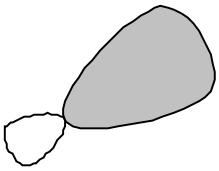
Y or YU

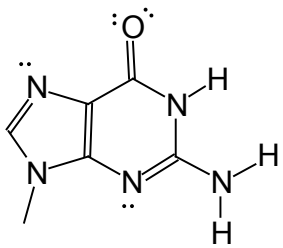
Localization of lone pairs in bases.

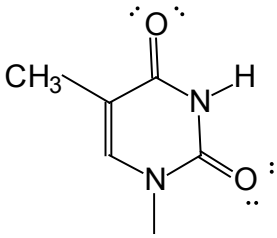
In plane lone pairs, σ type



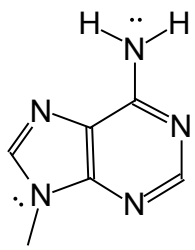


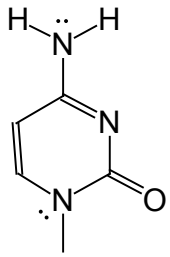


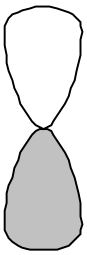


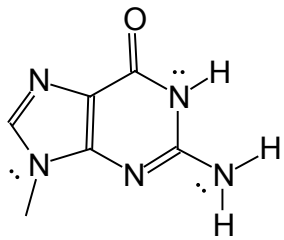


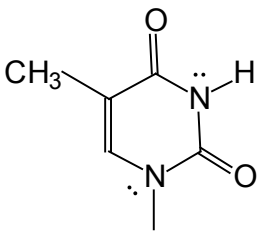
out of plane lone pairs, p type
conjugated to π system



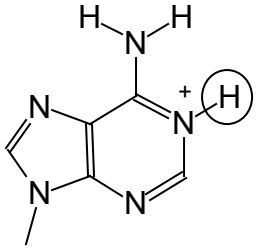






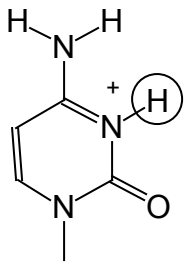


ACID-BASE PROPERTIES



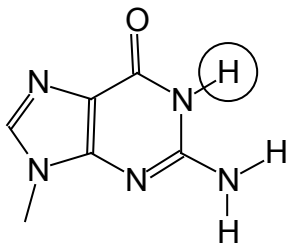
adenine

pKa=3.5



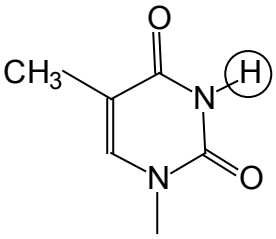
cytosine

pKa=4.2



guanine

pKa=9.4



thymine

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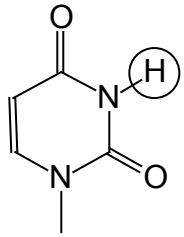
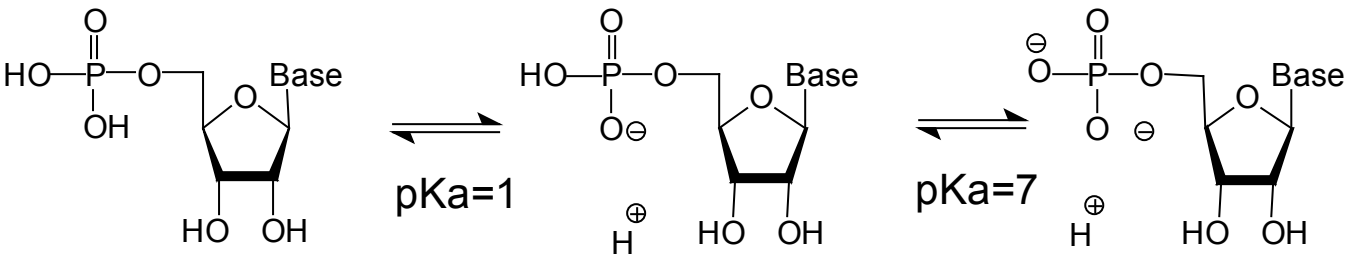
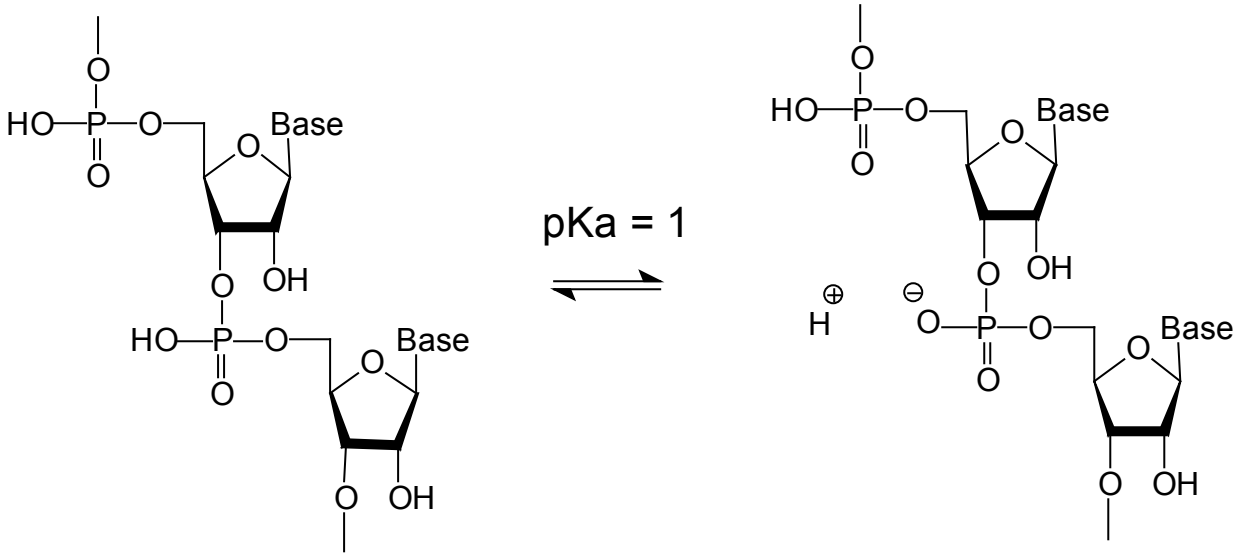


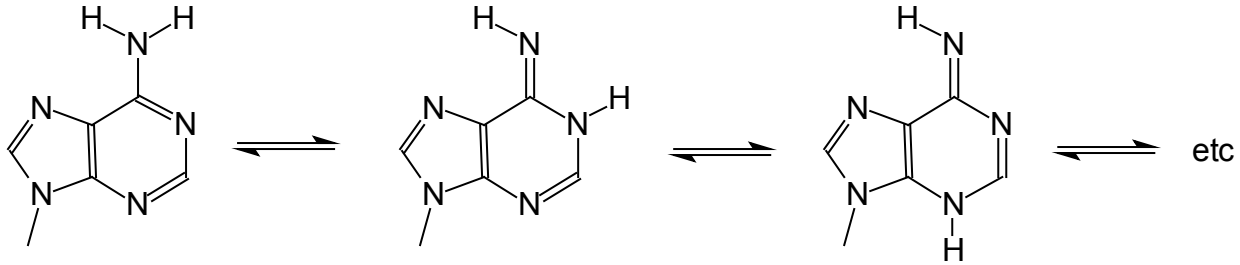
uracil

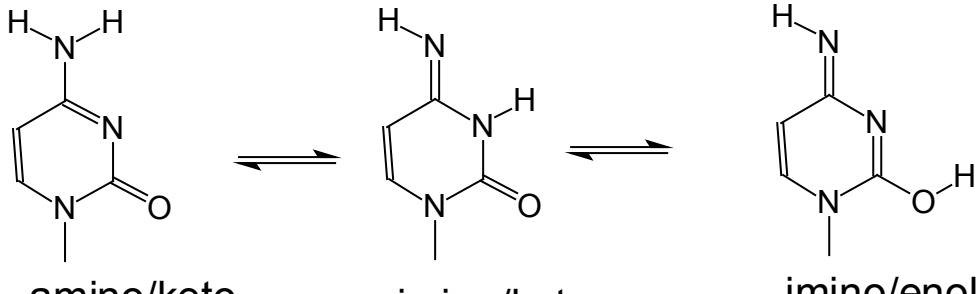
pKa=9.3

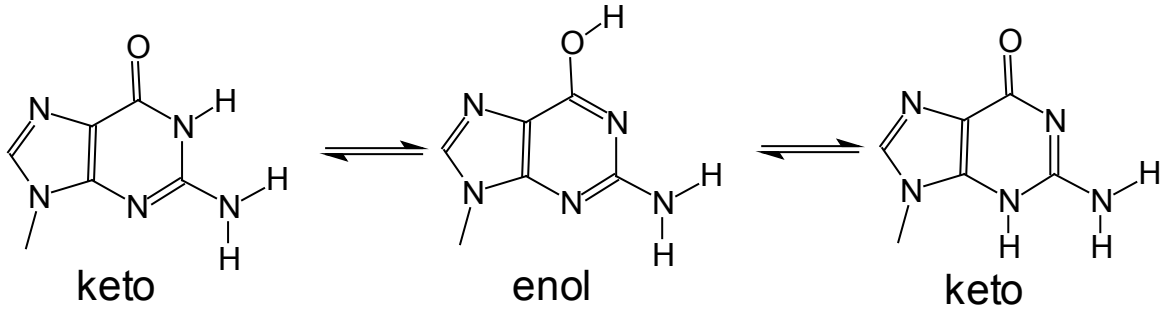


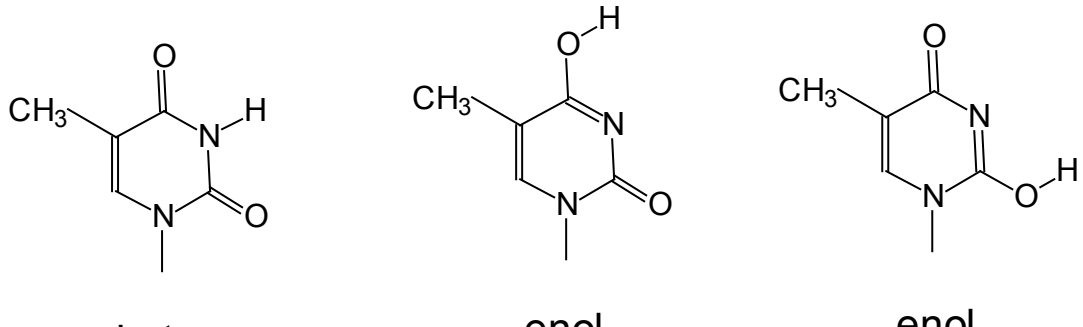


TAUTOMERS OF THE BASES







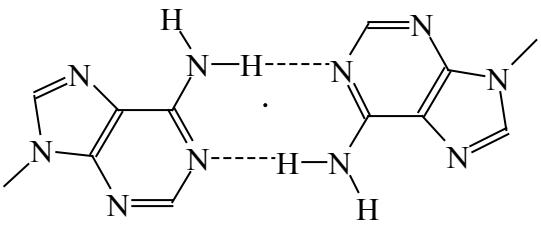


Base Pairing Combinations

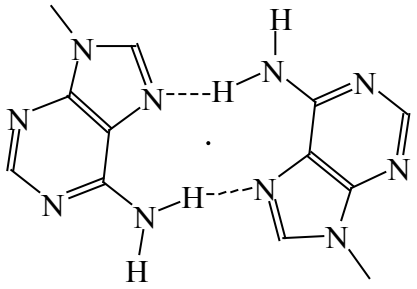
		No.	Figure
homo	purine	7	homops1.cw2
	pyrimdine	5	homopy1.cw2
hetero	purine	4	hetpu1.cw2
	pyrmidine	1	homopy1.cw2
purine-pyrimidine	AT	4	pupybp1.cw2
	GC	2	
Total		23	

Base pairing schemes for identical purines

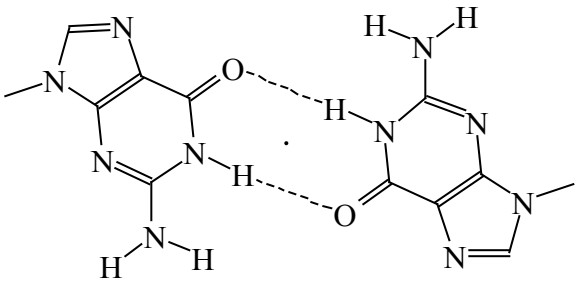
homo purine - symmetric



1



2



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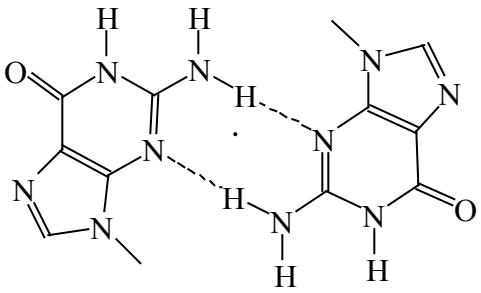
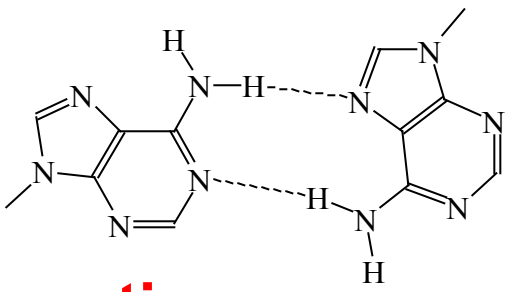


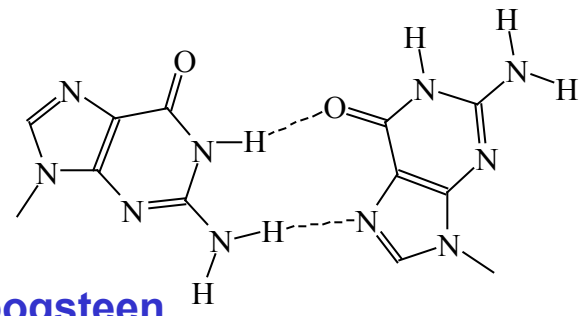
4

homo purine - asymmetric



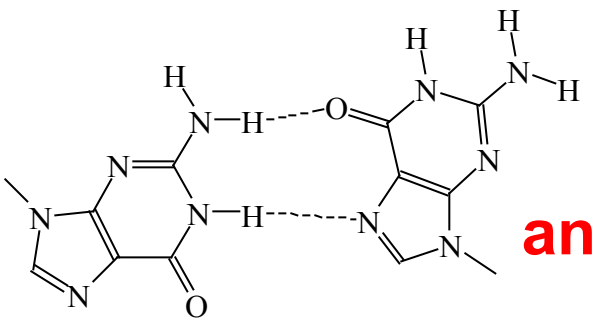
anti

5



Hoogsteen

6

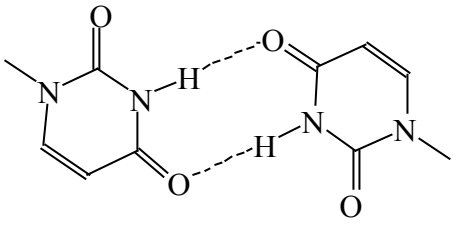


anti

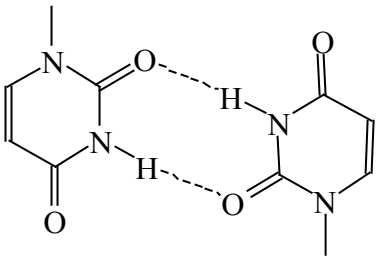
Reverse Hoogsteen

Base pairing schemes for pyrimidines

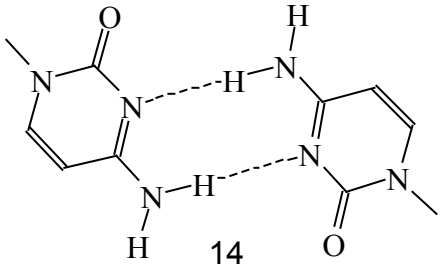
homo pyrimidine, symmetric



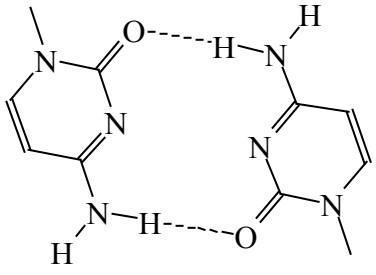
12



13

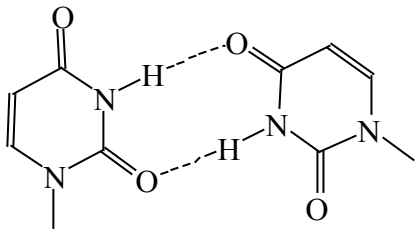


14



15

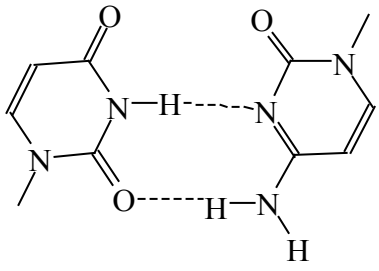
homo pyrimidine, asymmetric



16

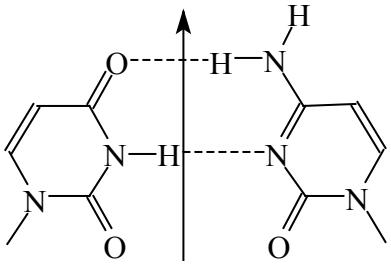
anti

hetero pyrimidine, symmetric



17

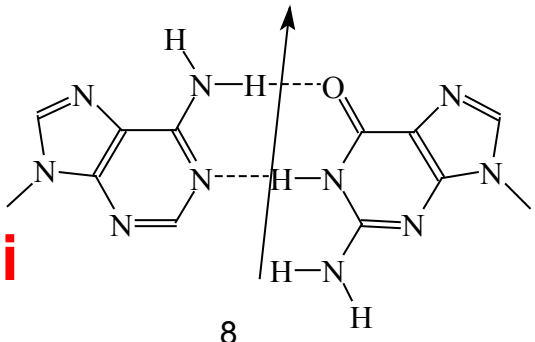
anti



18

Base Pairing Schemes for mixed purines

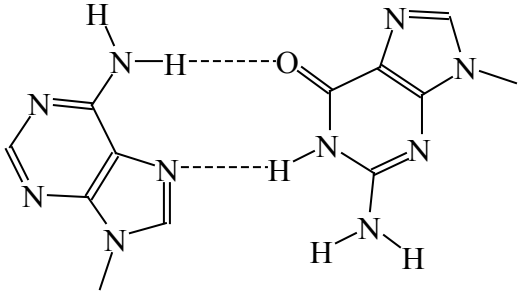
hetero purine symmetric



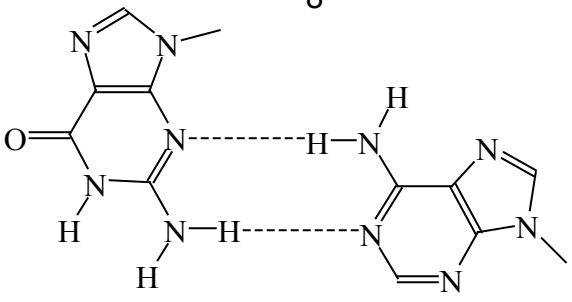
anti

8

heteropurine - asymmetric



9



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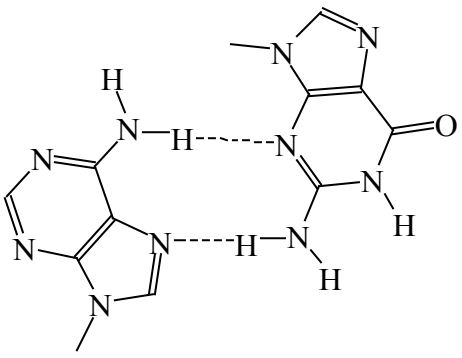


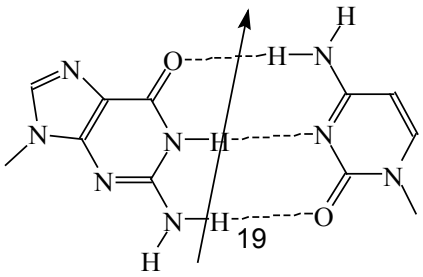
11

anti

Purine-Pyrimidine Base Pairs

Pseudosymmetric, Watson-Crick Base Pair

anti



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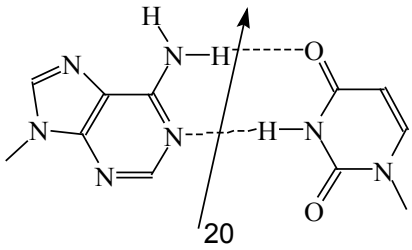
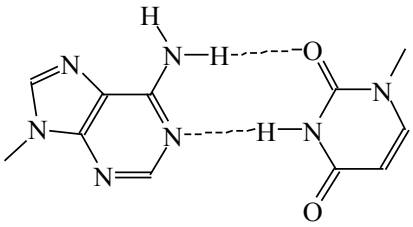


20

anti

Reversed Watson-Crick, assymetric



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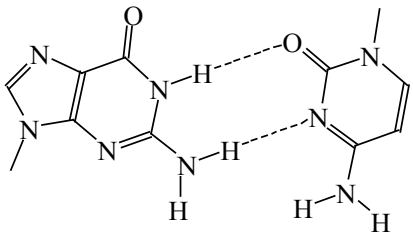

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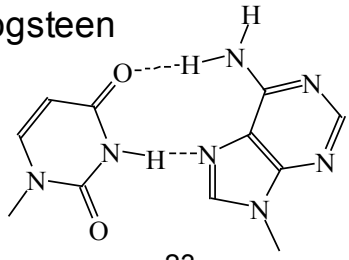
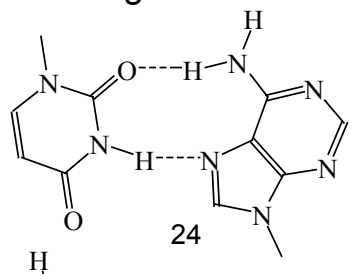
Hoogsteen



23

Reversed Hoogsteen

anti



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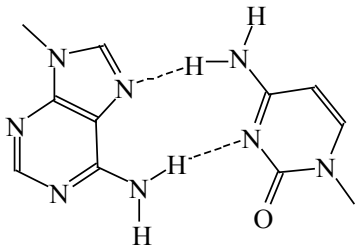
anti



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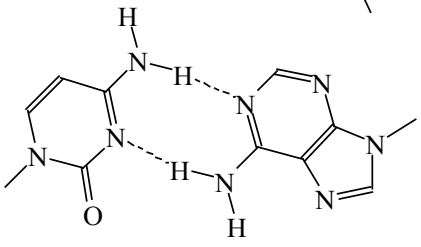

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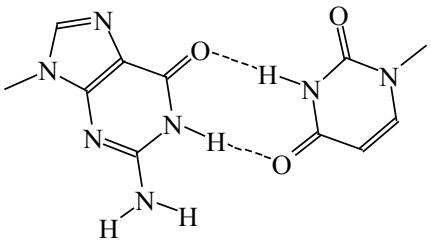

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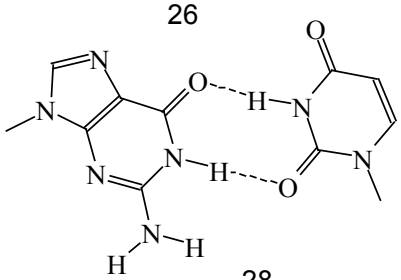
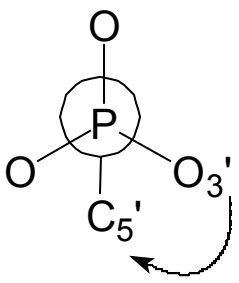


28

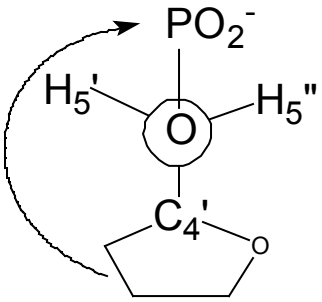
anti

Conformational Analysis of Nucleosides and Nucleotides

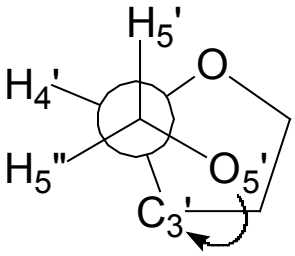
Definition of Angles in Nucleotides



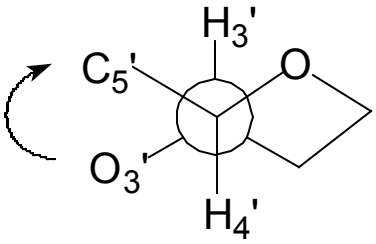
α



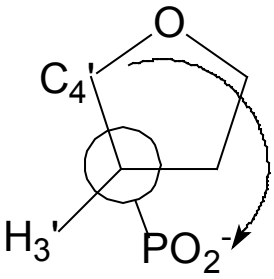
β

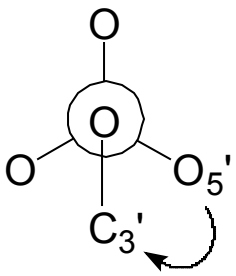


γ

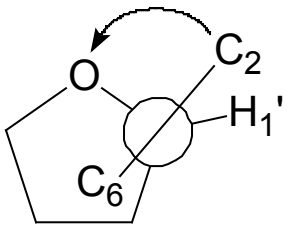


δ





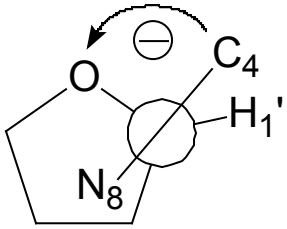
ε



pyrimidines

χ

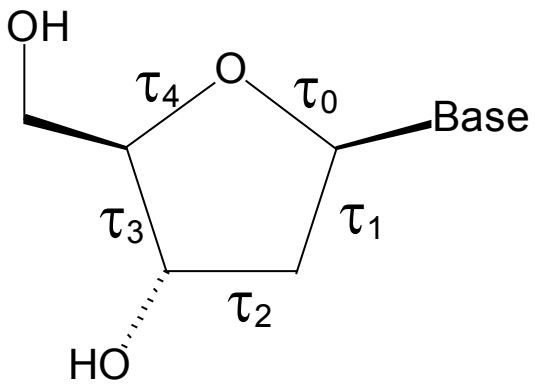
ζ



purines

χ

Definition of the bond angles in deoxyribose ring system and the pseudorotation equation



The torsion bonds are defined by the sugar ring atoms. Example, $\tau 1$ is defined by O4'-C1'-C2'-C3'

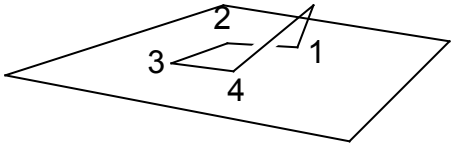
Pseudorotation equation:

$$\tau_i = \tau_{max} \cdot \cos(P + 144 \cdot (i+3))$$

where P is the phase angle

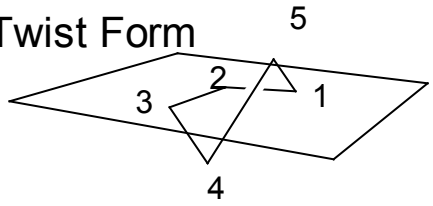
Definition of envelope and twist forms of deoxyribose ring system

Envelope form

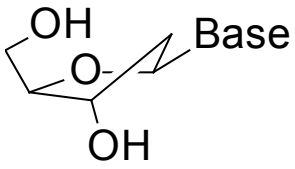


4 atoms in plane
1 atom out of plane (#5)

Twist Form

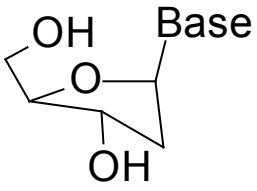


3 atoms in plane
1 atom below plane (#4)
1 atom above plane (#5)



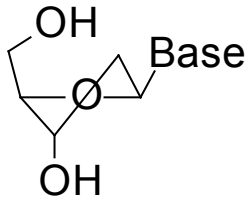
C_2'-endo

^2E



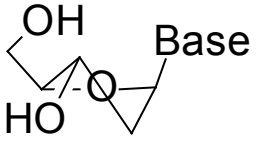
C_2'-exo

$_2E$



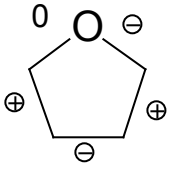
C_2'-endo, C_3'-exo

^2_3T



C_2'-exo, C_3'-endo

^3_2T



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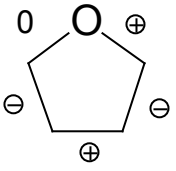

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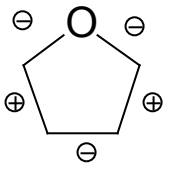

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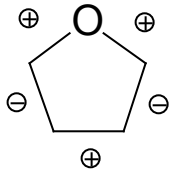
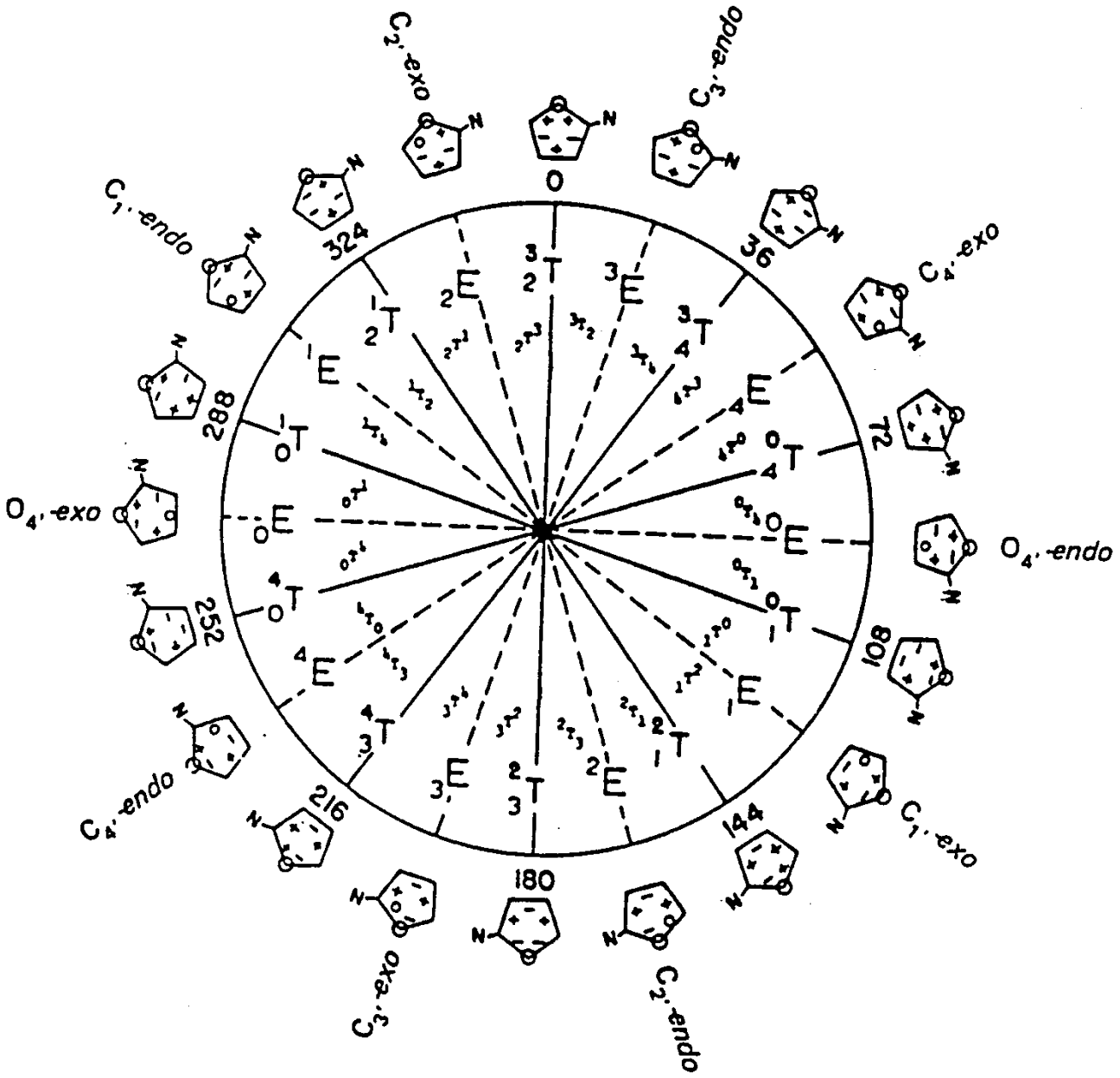
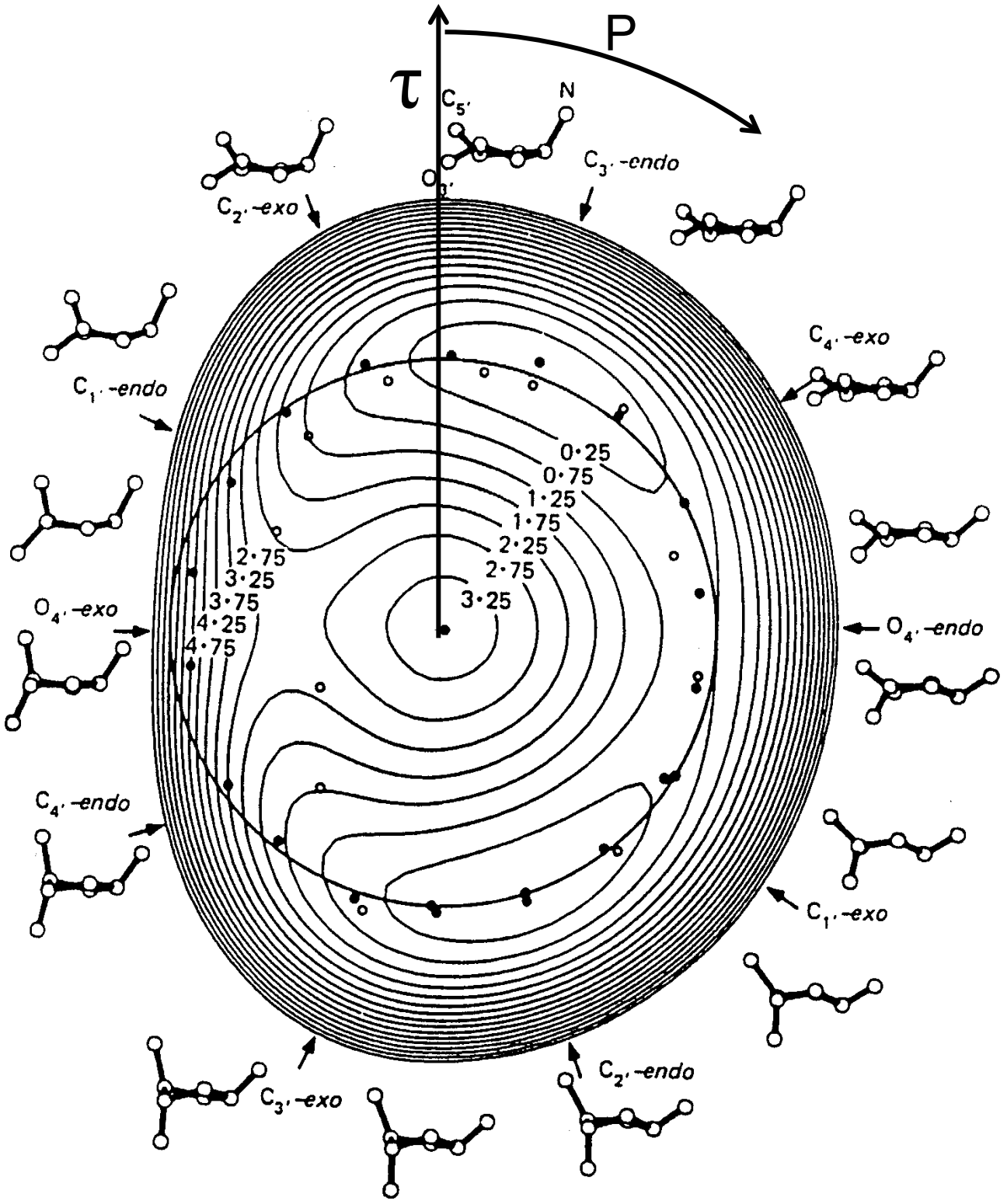


P=0

Pseudorotation Cycle for Ribose Ring

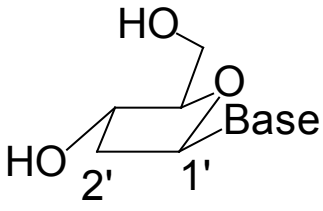


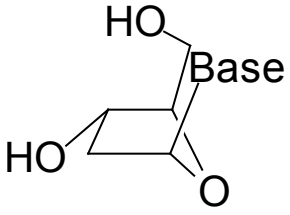
Potential Energy Surface for the Deoxyribose Ring System as a function of τ and P.

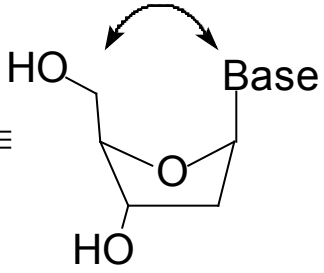


E = kcal, perpendicular to plane of paper

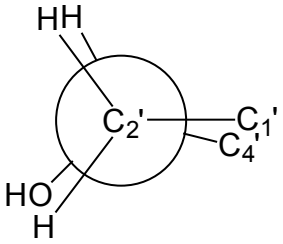
Origin of the high energy of the O4'-exo conformation of deoxyribonucleosides







Bad VDW interaction due to eclipsed bond



Bad VDW interaction

Glycosyl Bond Angle Terms

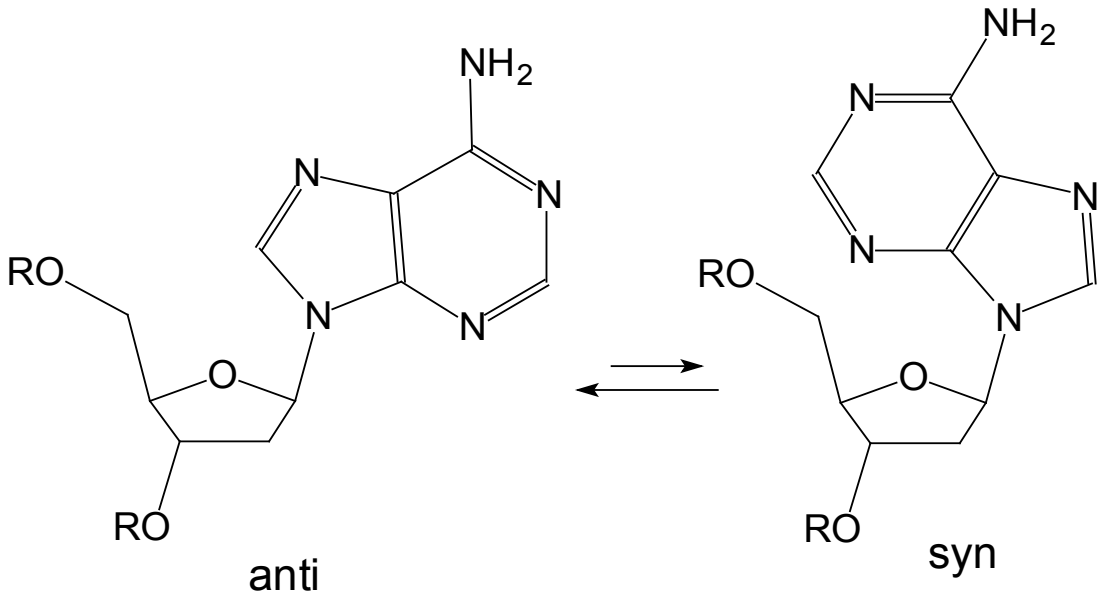
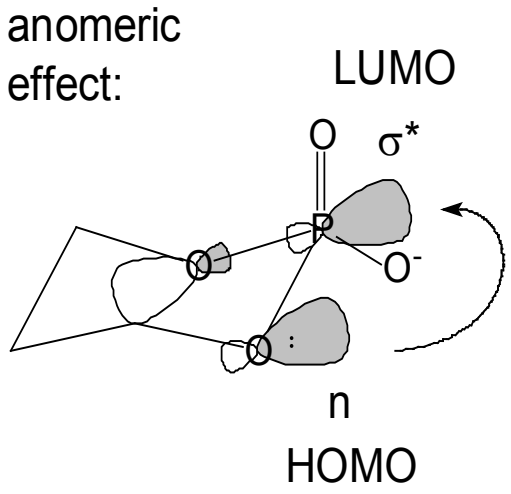


Figure: synant1.cw2

Anomeric effect in phosphodiesters explains preference for gauche conformations

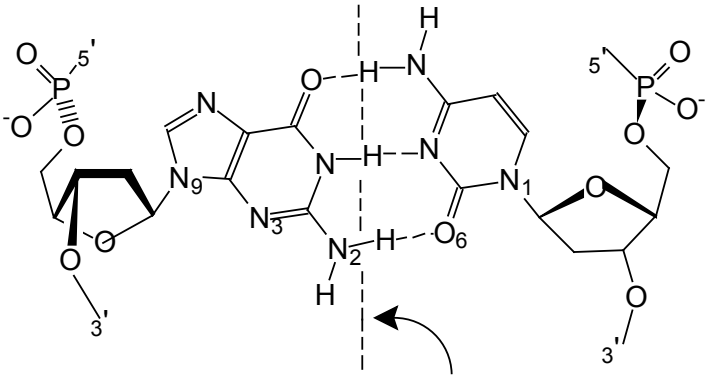


A & B duplex DNA

DIFFERENT PERSPECTIVES ON THE WATSON CRICK BASE PAIR (BP)

TOP VIEW

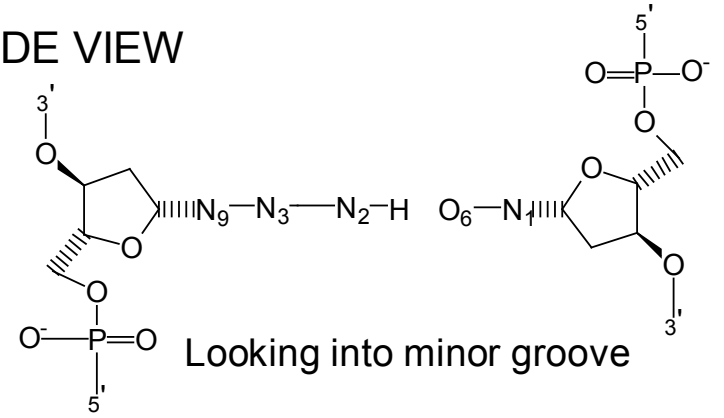
MAJOR GROOVE SIDE



C_2 pseudo axis of symmetry

minor groove side

SIDE VIEW



Looking into minor groove

SCHEMATIC VIEW