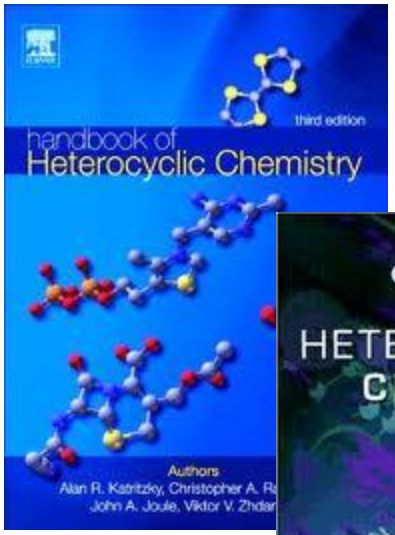
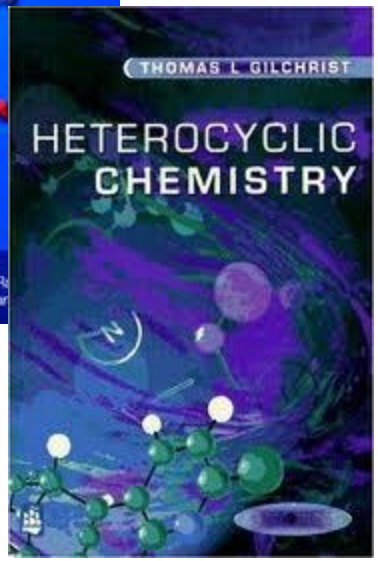
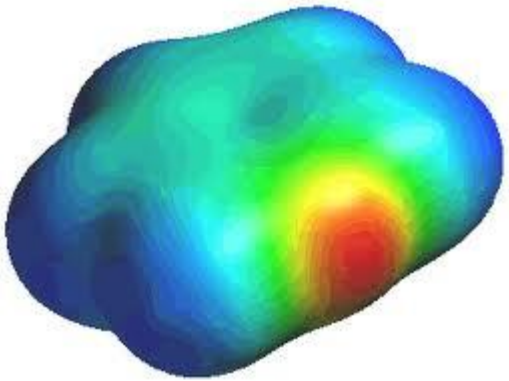
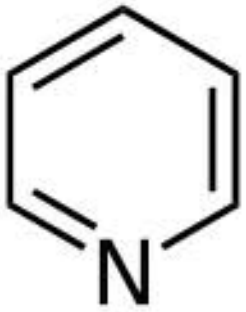
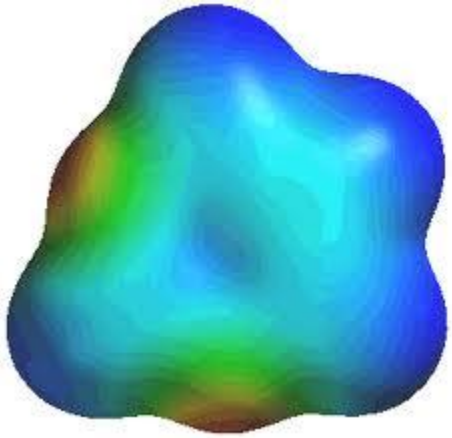
Heterocyklické sloučeniny

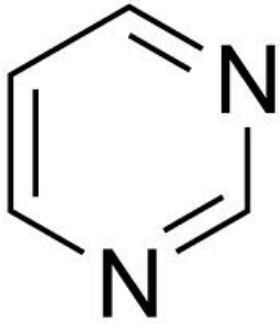






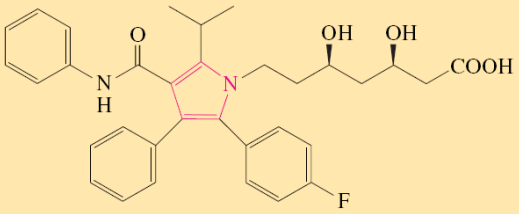






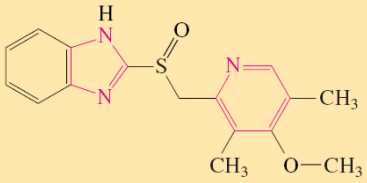
Většina klinicky používaných léčiv obsahuje alespoň jeden heterocyklický kruh

1. Atorvastatin (Lipitor)



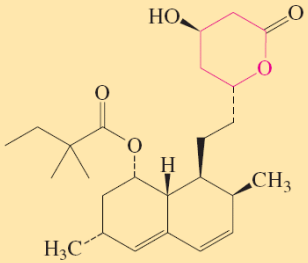
Cholesterol reducer

2. Omeprazole (Prilosec)



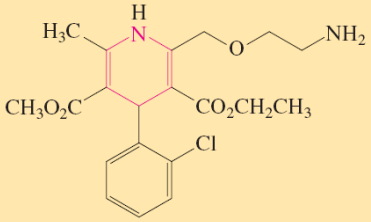
Antiulcerative

3. Simvastatin (Sivastin, Zocor)



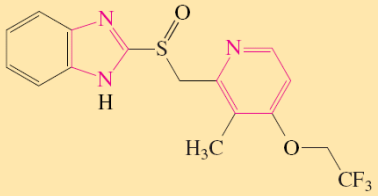
Antihypercholesterolemic

4. Amlodipine (Norvasc)



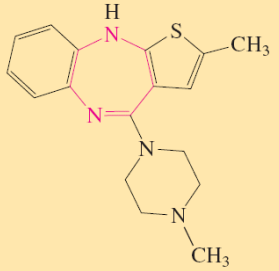
Antihypertensive

5. Lansoprazole (Prevacid)



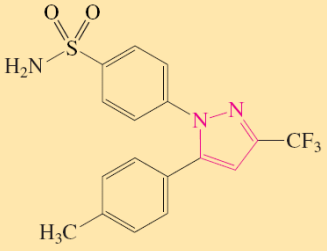
Antiulcerative

6. Olanzapine (Zyprexa)



Antischizophrenoid

7. Celecoxib (Celebrex)



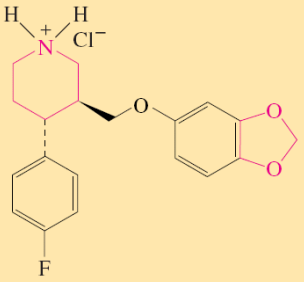
Antiarthritic

8. Erythropoietin (Procrit)

Ala-Pro-Pro-Arg-Leu-Ile-Cys-Asp-Ser-Arg-. . .
(165-Amino acid glycoprotein; see also Section 26-4)

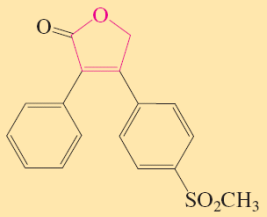
Antianemic

9. Paroxetine HCl (Paxil)



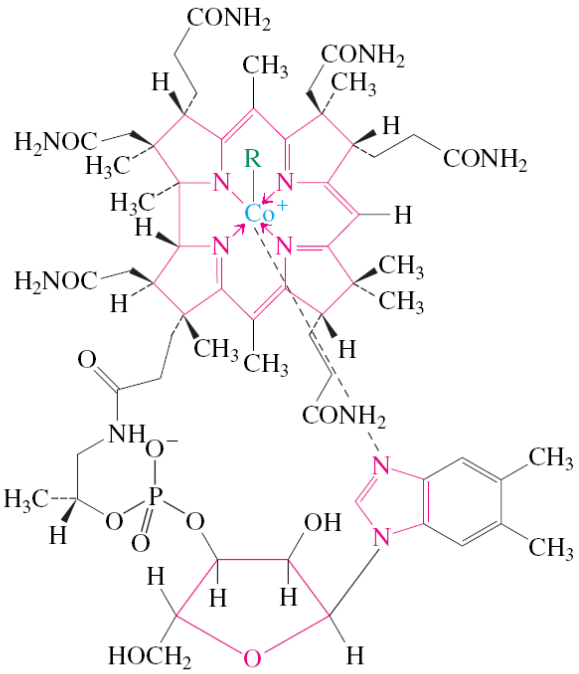
Antidepressant

10. Rofecoxib (Vioxx)



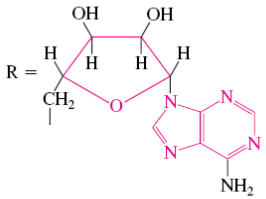
Antiarthritic
(Withdrawn in December 2004 because of safety concerns)

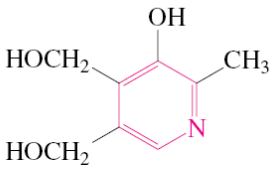
[a]Total U.S. sales of pharmaceuticals reached $224 billion in 2003, with lipitor leading at $6.3 billion.



Vitamin B_{12}
(Cobalamin)

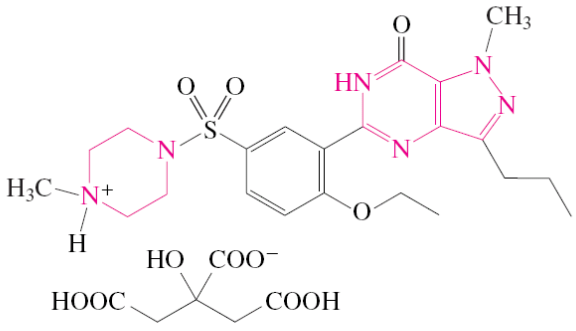
(Catalyzes biological rearrangements and methylations)





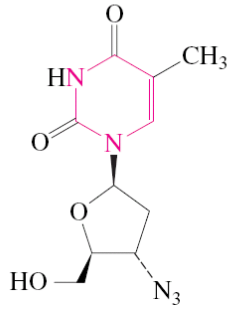
Pyridoxine, vitamin B_6

(Enzyme cofactor vitamin with multiple functions)



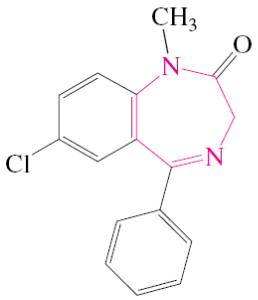
Viagra
(Sildenafil citrate)

(Treats erectile dysfunction; see also Chapter Integration Problem 25-25)



Zidovudine
(AZT)

(Antiviral AIDS drug, see Chemical Highlight 26-3)

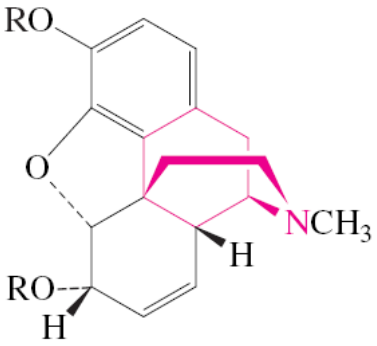


Diazepam
(Valium)

(Tranquilizer)

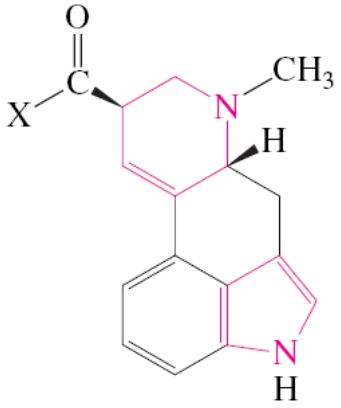
Alkaloidy

- rostlinné přírodní heterocyklické látky (biologické účinky: toxiny, halucinogeny, stimulanty atd.)



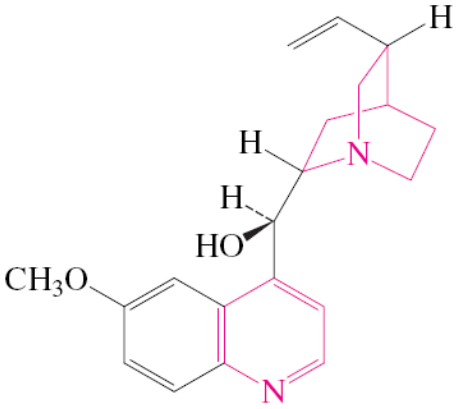
Morphine (R = H)

Heroin (R = $CH_3C(=O)$)

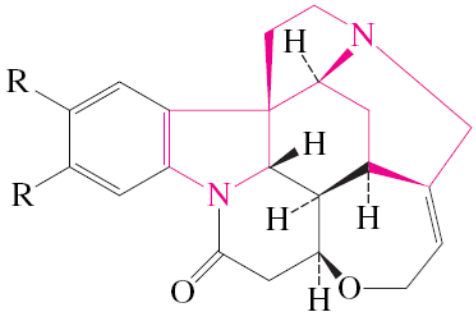


Lysergic acid (X = OH)

Lysergic acid diethylamide, LSD [X = $(CH_3CH_2)_2N$]

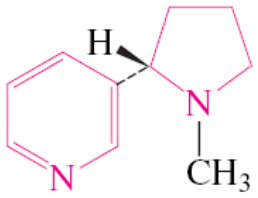


Quinine

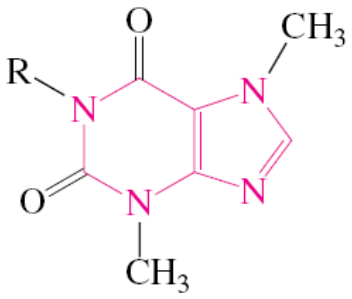


Strychnine (R=H)

Brucine (R=CH_3O)

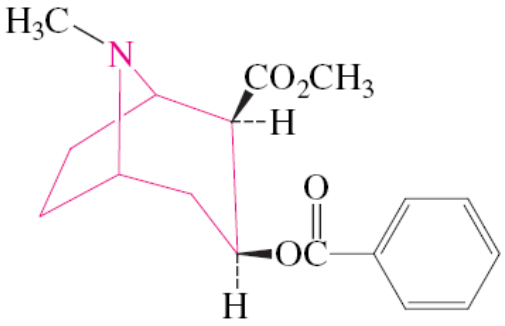


Nicotine



Caffeine (R = CH_3)

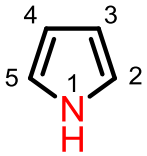
Theobromine (R = H)



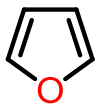
Cocaine

Názlosloví aromatických heterocyklů

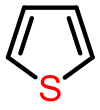
5-členné



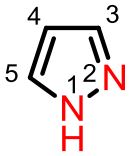
pyrrol



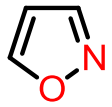
furan



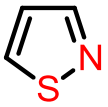
thiofen



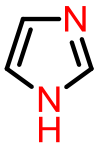
pyrazol



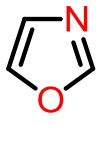
isoxazol



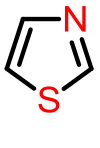
isothiazol



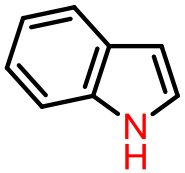
imidazol



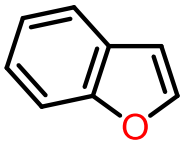
oxazol



thiazol

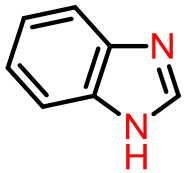


indol



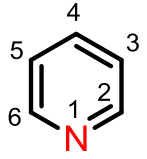
benzofuran

benzothiofen

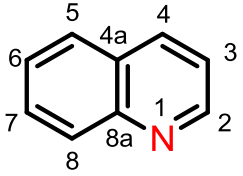


benzimidazol

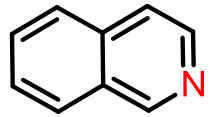
6-členné



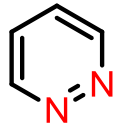
pyridin



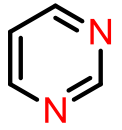
chinolin



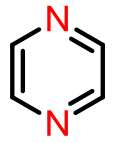
isochinolin



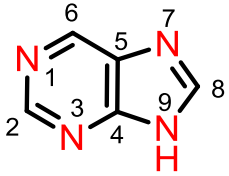
pyridazin



pyrimidin

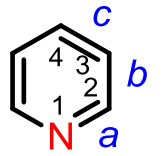


pyrazin

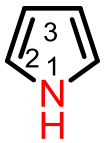


purin

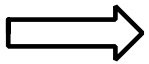
Princip tvorby názvů kondenzovaných heterocyklů

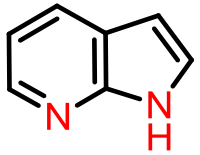


pyridin



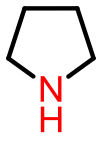
pyrrol



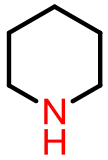


pyrrolo[2,3-*b*]pyridin

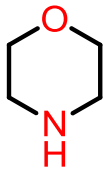
Názlosloví nearomatických (nasycených) heterocyklů



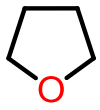
pyrrolidin



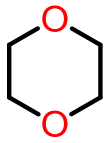
piperidin



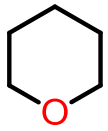
morfolin



tetrahydrofuran



1,4-dioxan



tetrahydropyran

oxiran

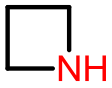
thiiran

aziridin

azirin

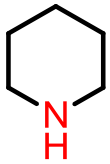
oxetan

thietan

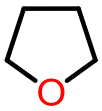


azetidin

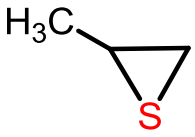
Alternativní názlosloví záměnným systémem



azacyklohexan

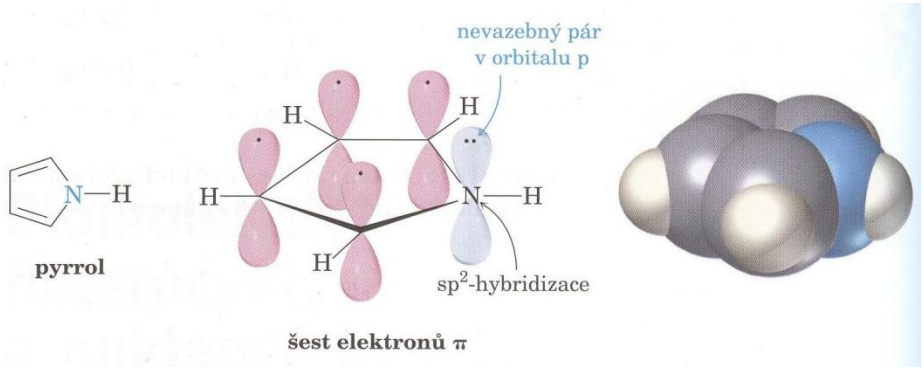


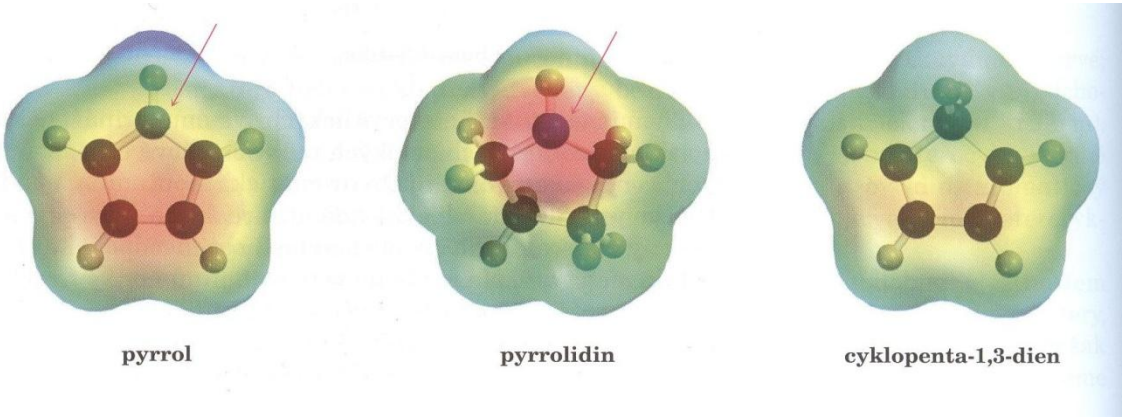
oxacyklopentan



2-methyl-thiacyklopropan

Pětičlenné heterocykly - pyrrol

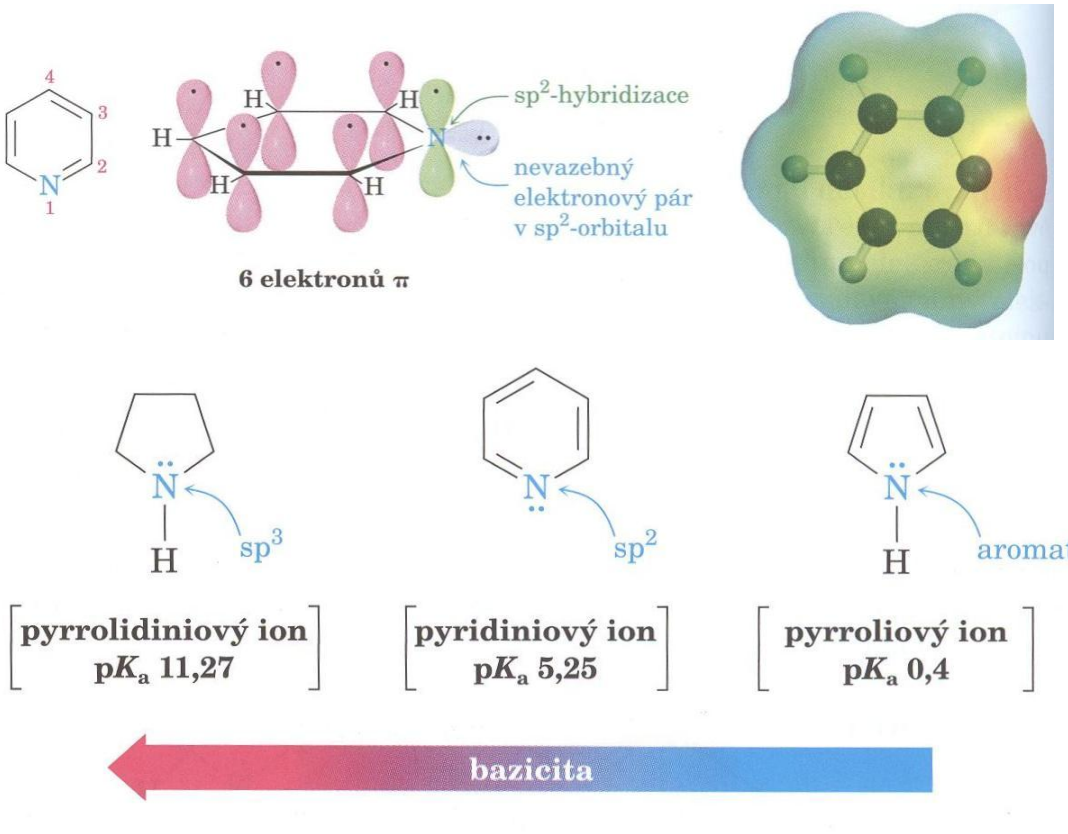




Pyrrol (a podobně i furan nebo thiofen) jsou **elektronově bohaté aromatické systémy**

- **snadná elektrofilní substituce**
- obtížná nukleofilní substituce

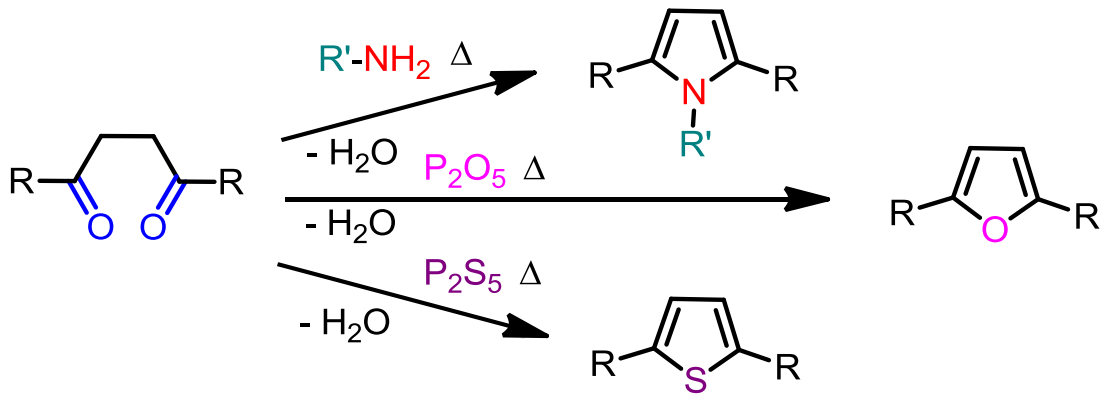
Šestičlenné heterocykly - pyridin



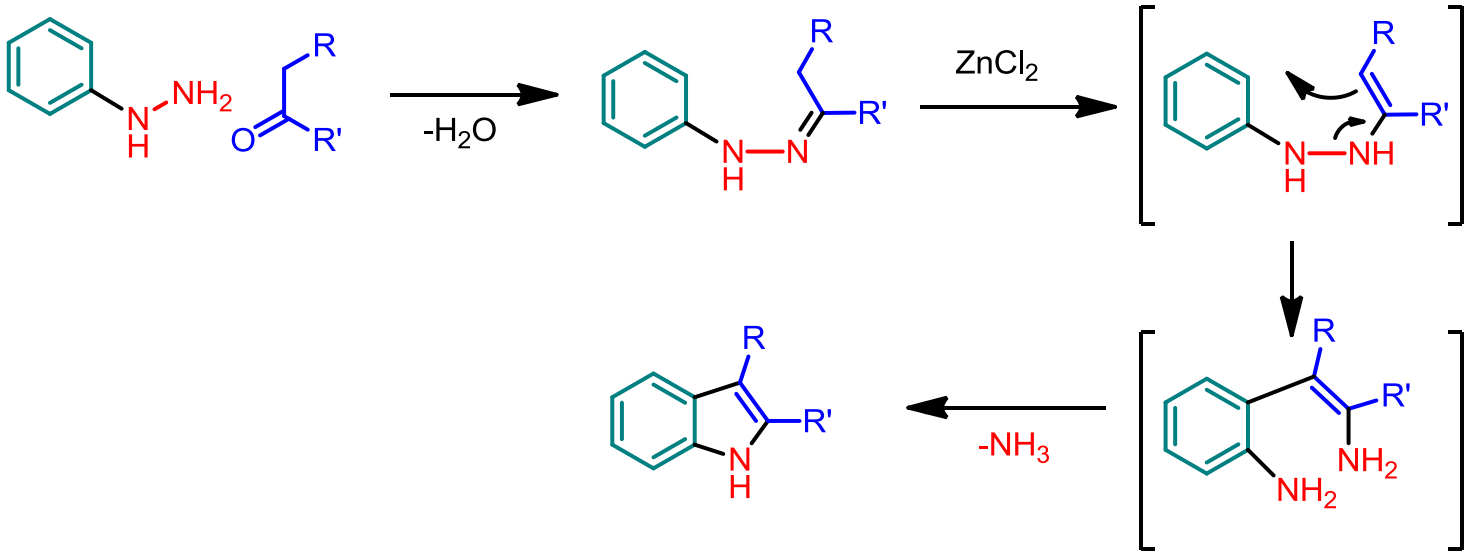
Pyridin (a podobně i pyrimidin) jsou **elektronově chudé aromatické systémy**

- obtížná elektrofilní substituce
- **snadná nukleofilní substituce**

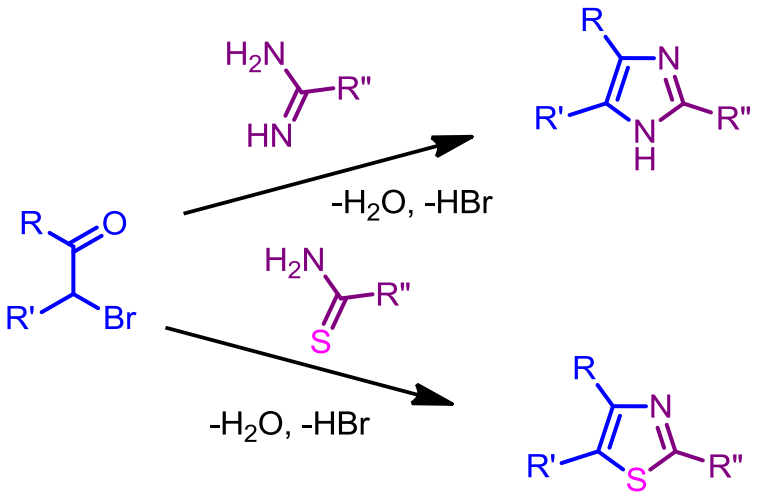
Paal-Knorrova syntéza 5-členných heterocyklů z 1,4-diketonů

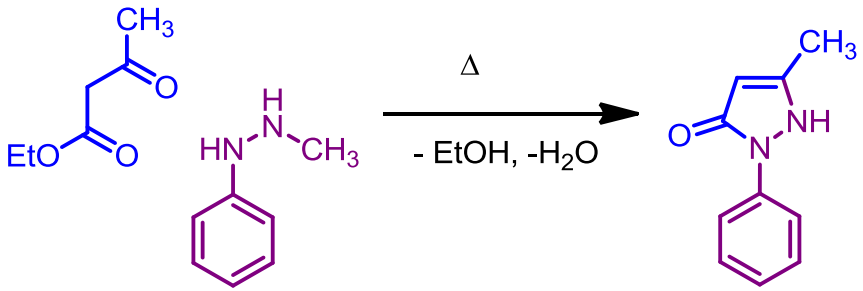


Fischerova syntéza indolů



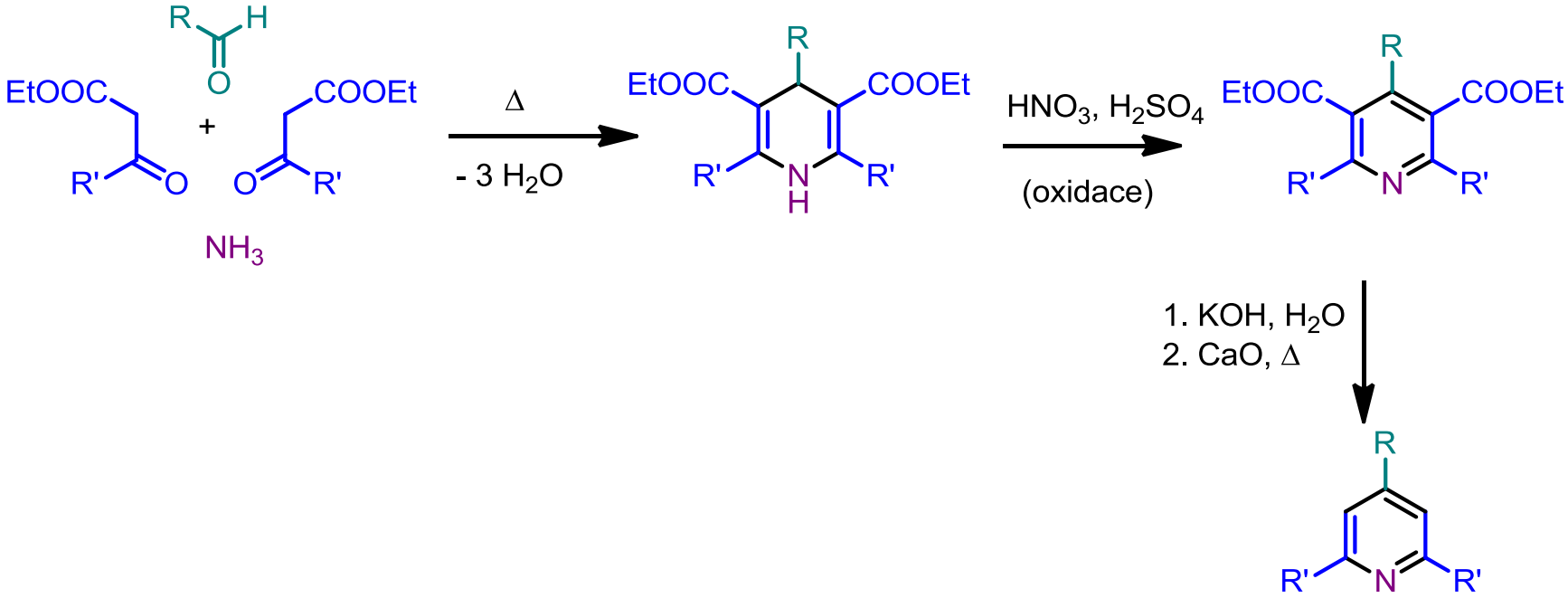
Syntézy azolů – heterocyklické kondenzace



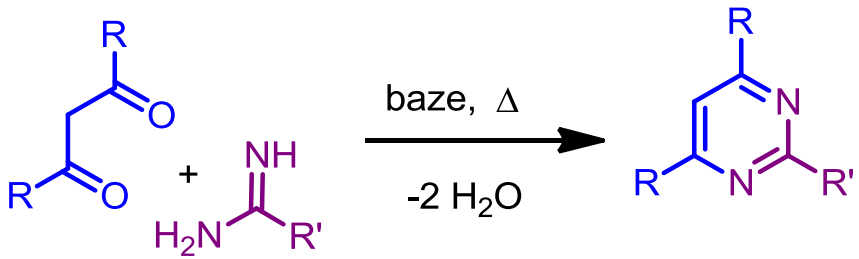


antipyrin

Hantschova syntéza pyridinů

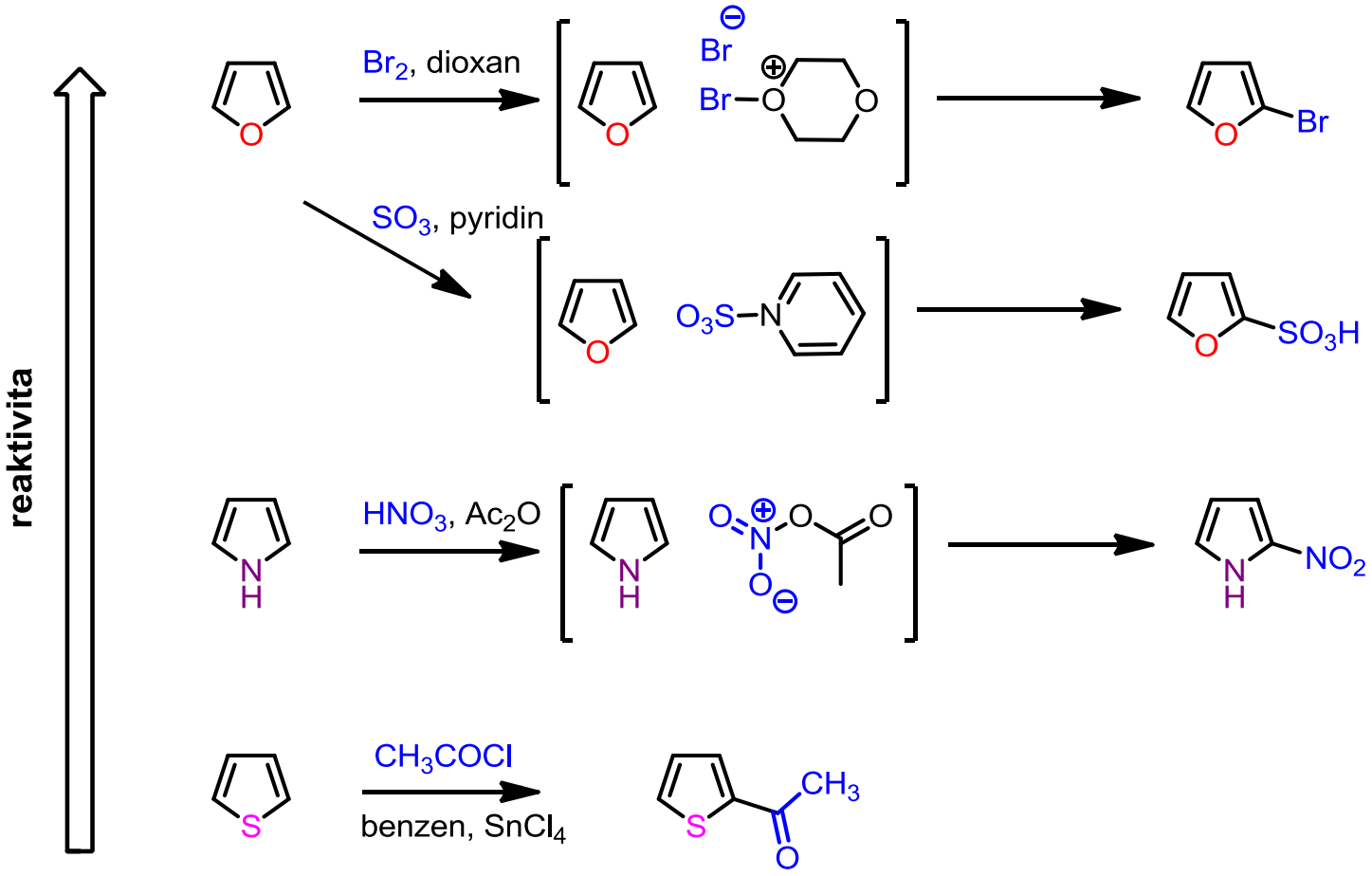


Příklad syntézy pyrimidinů



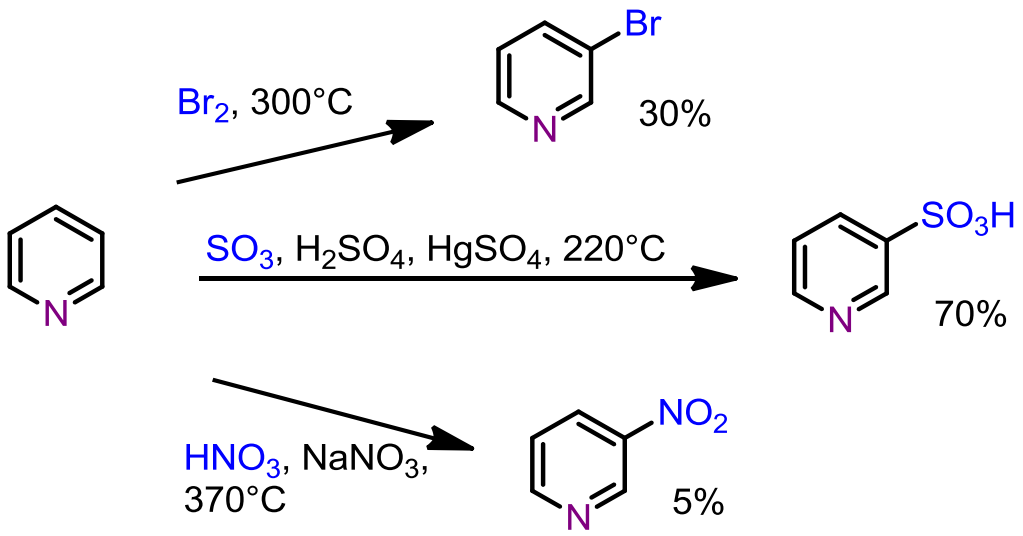
Elektrofilní substituce na 5-členných heterocyklech

- **probíhají extrémně snadno** a obvykle do polohy 2
- často nutno použít slabší činidla (jinak dochází k polymeracím)

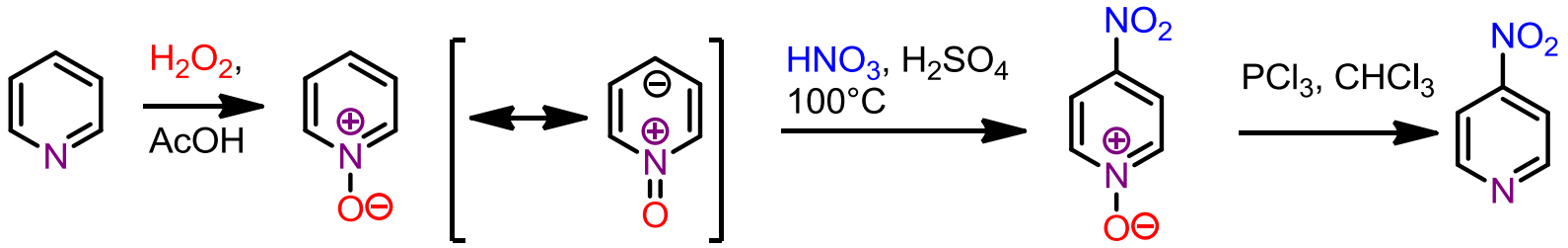


Elektrofilní substituce na 6-členných heterocyklech (např. pyridin)

- **probíhají extrémně obtížně** a do polohy 3
- nutno použít nejsilnější činidla a drastické podmínky (ale stejně nízké výtěžky)



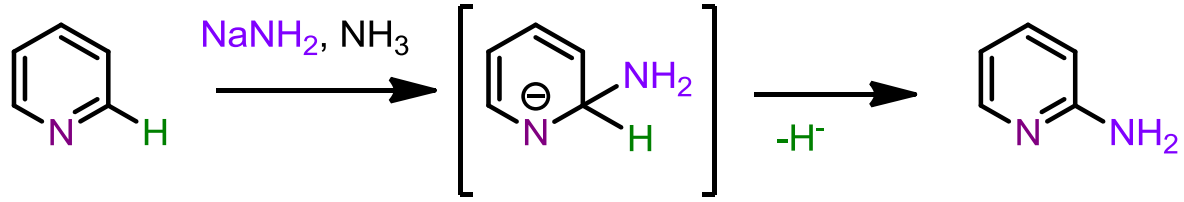
Převedením pyridinu na N-oxid se reaktivita vůči elektrofilní substituci zvyšuje



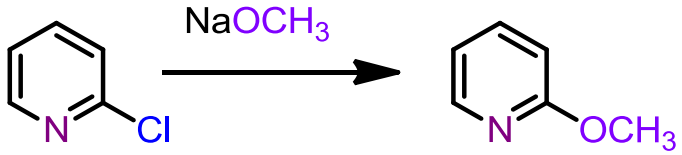
Nukleofilní substituce na pyridinu

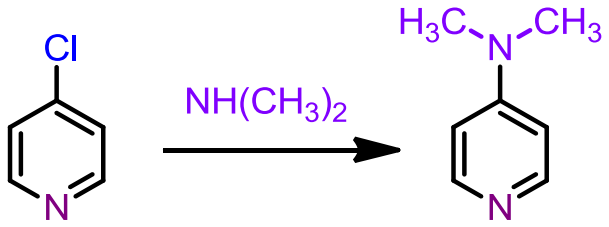
- **probíhají výrazně snadněji** než na benzenu

Čičibabinova reakce

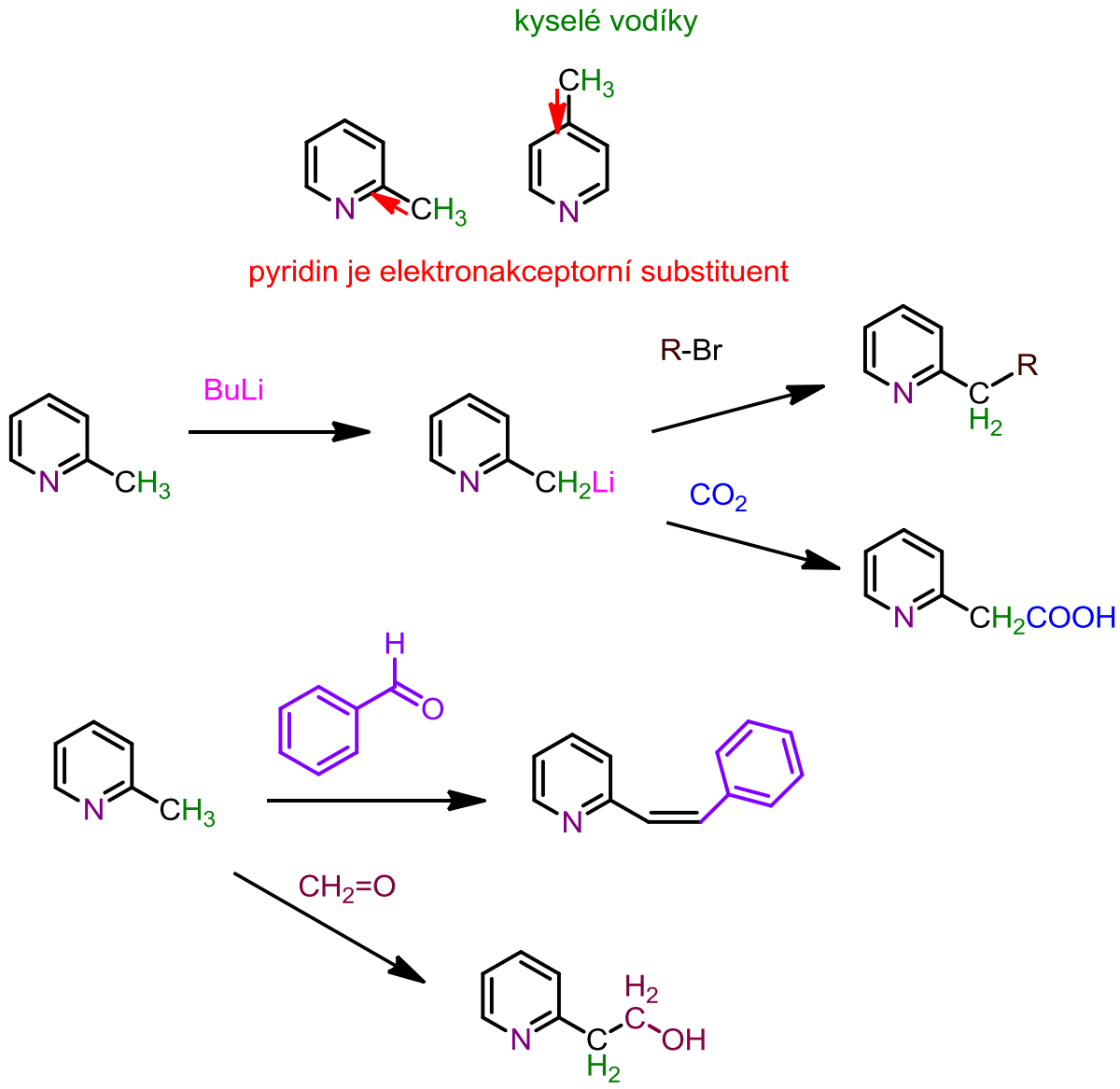


Nukleofilní substituce halogenpyridinů

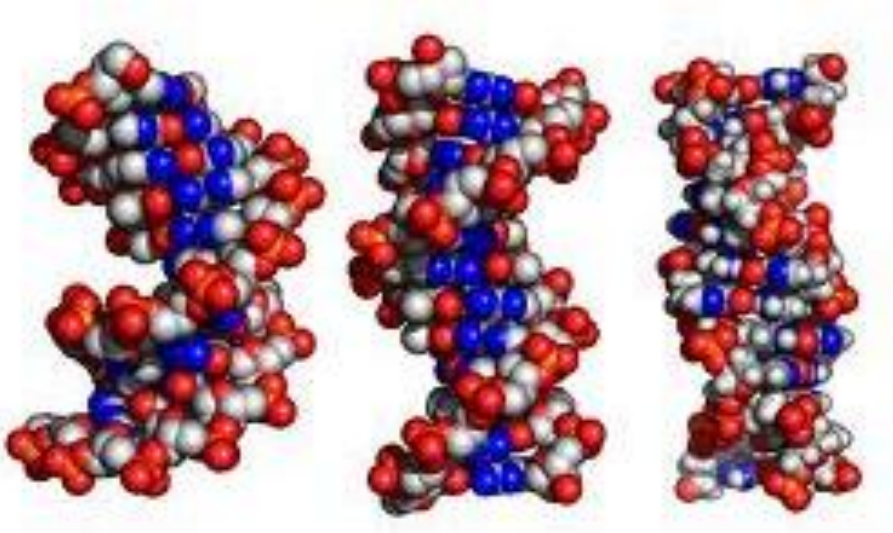


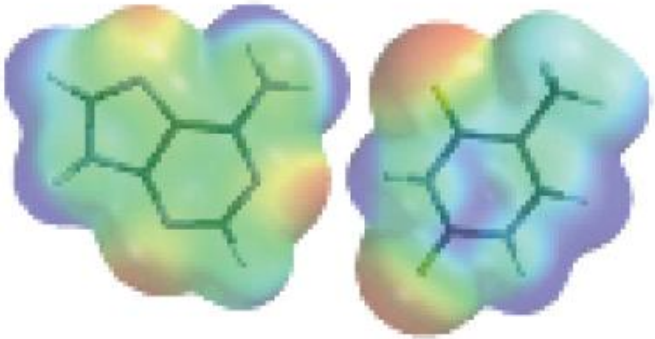


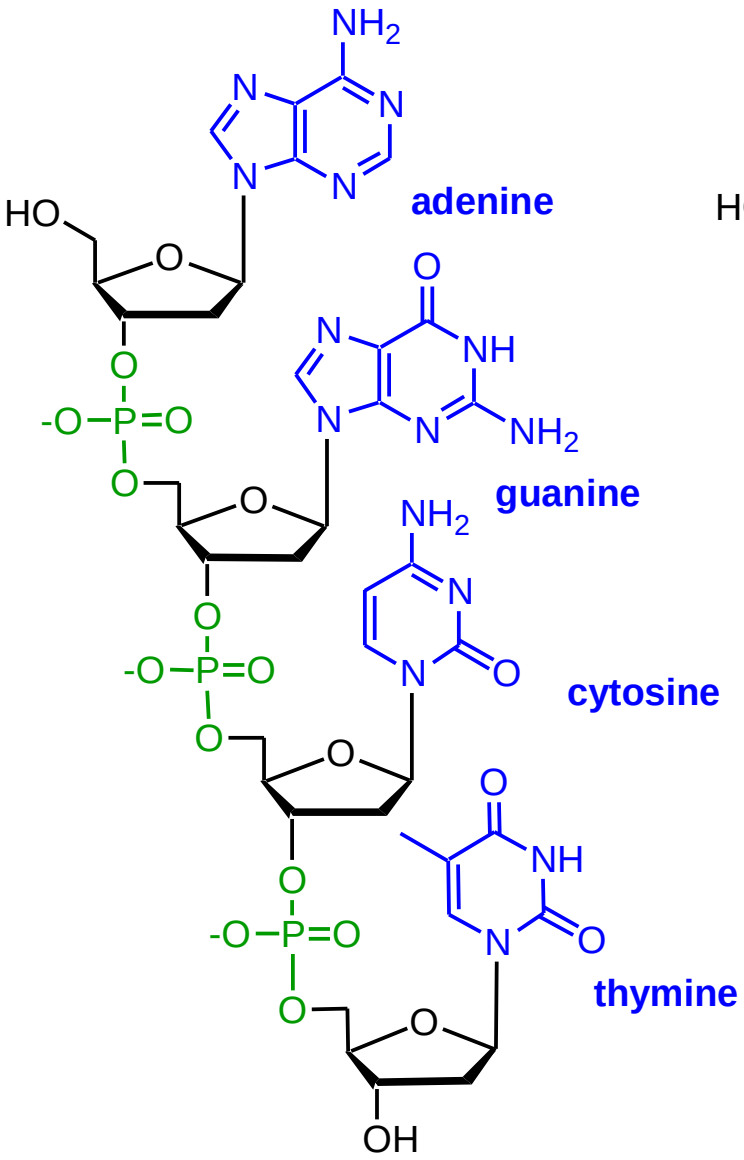
Reakce alkylpyridinů v α-poloze

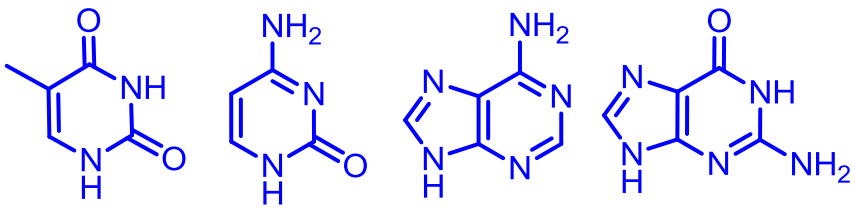


Nukleové kyseliny

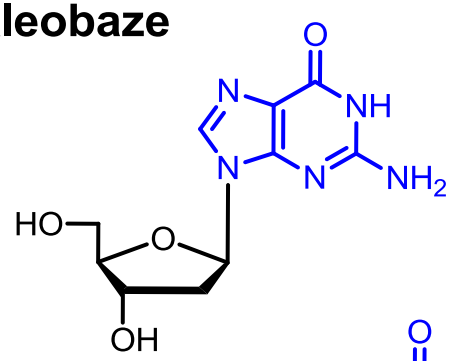




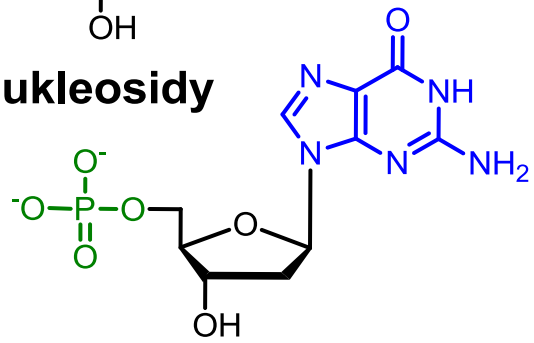

adenine
guanine
cytosine
thymine
DNA
adenine
guanine
cytosine
uracil
RNA



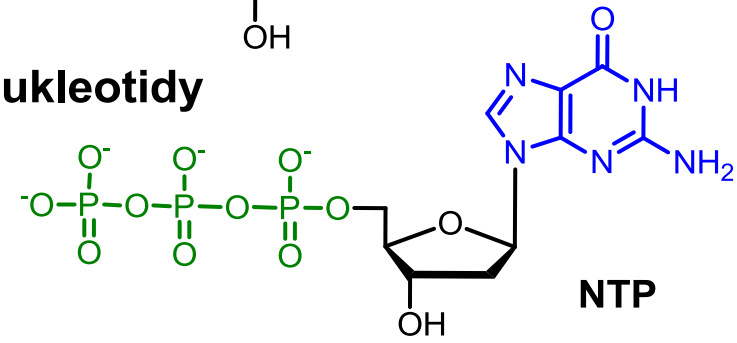
nukleobaze



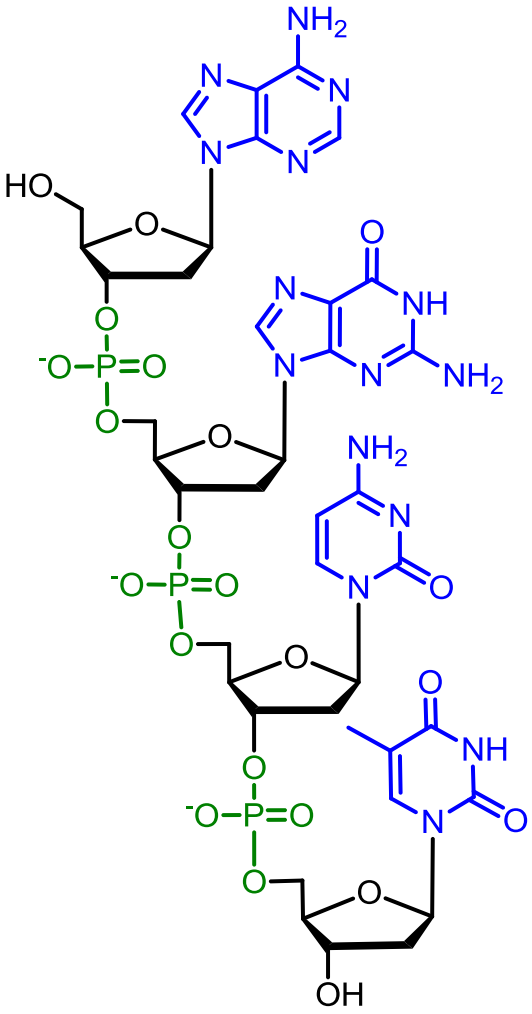
nukleosidy



nukleotidy



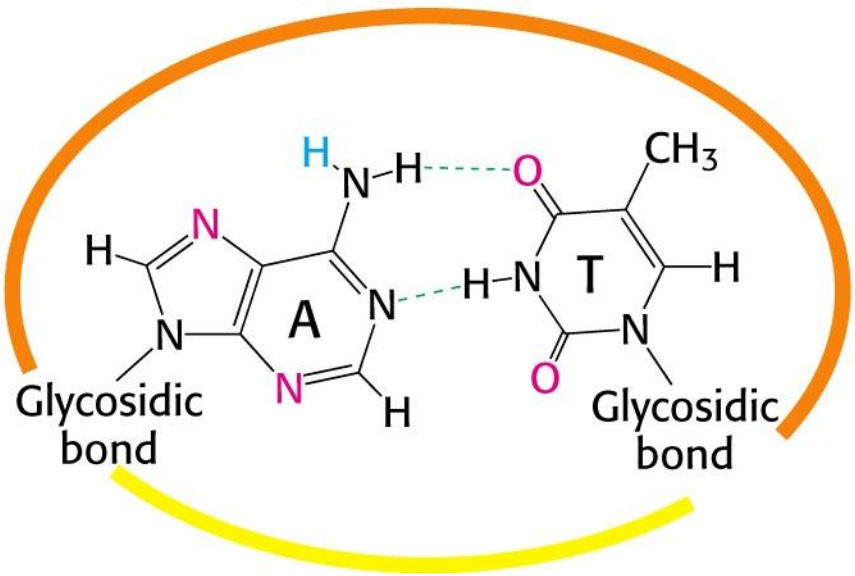
NTP

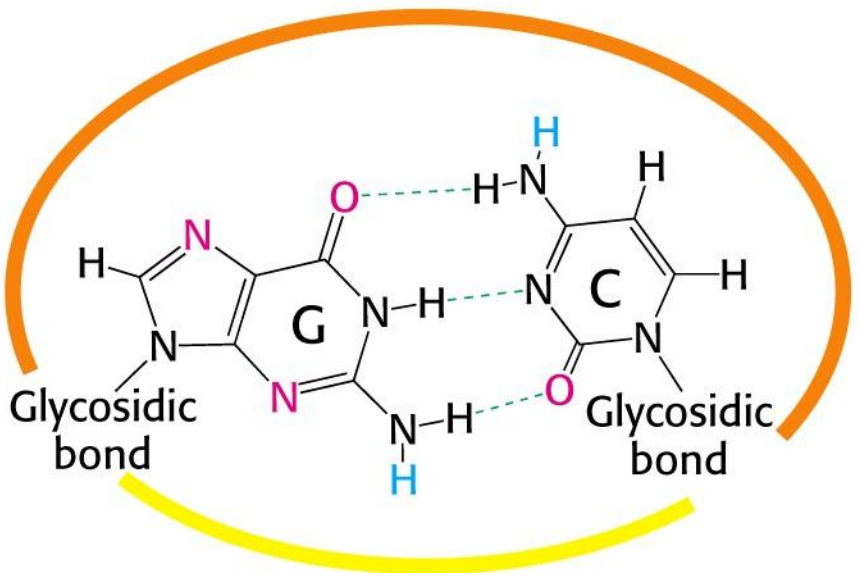


oligonukleotidy

Watson-Crickovy páry bází

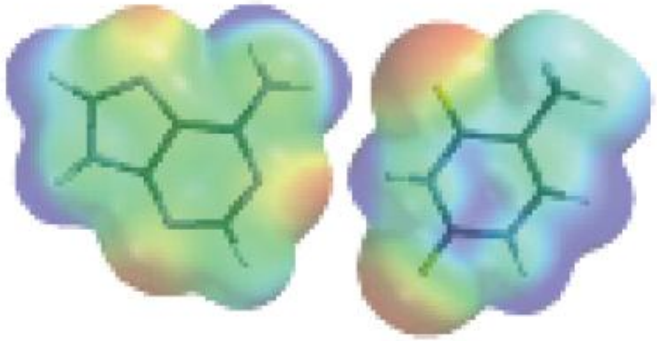
velký žlábek



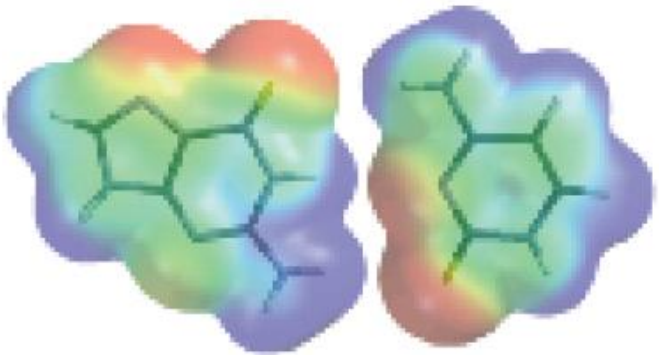


malý žlábek

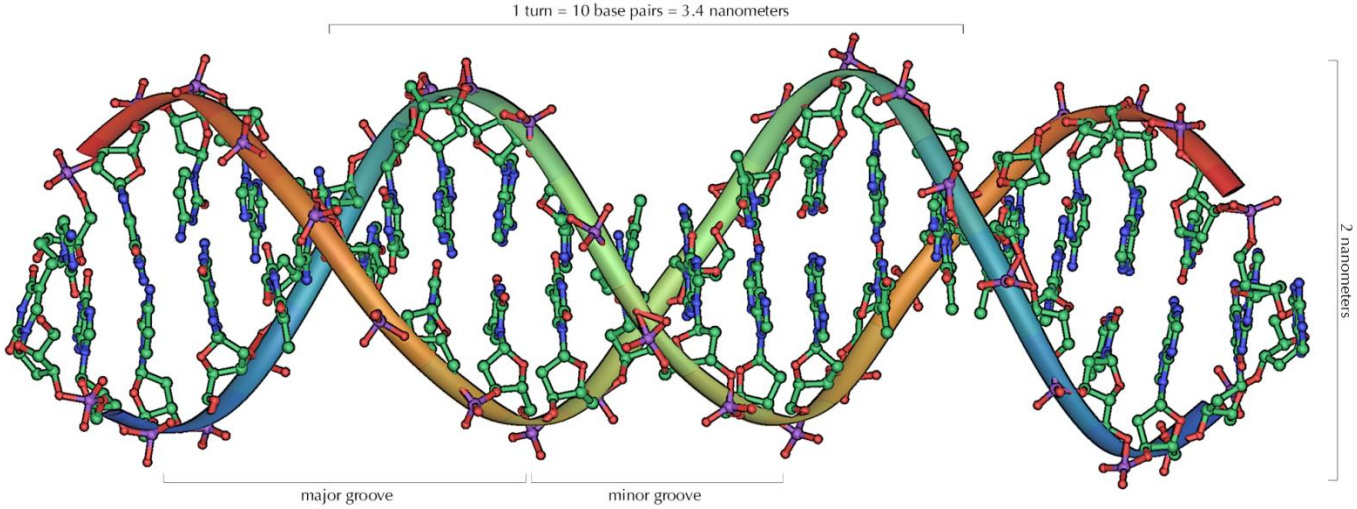
Adenin-Thymin

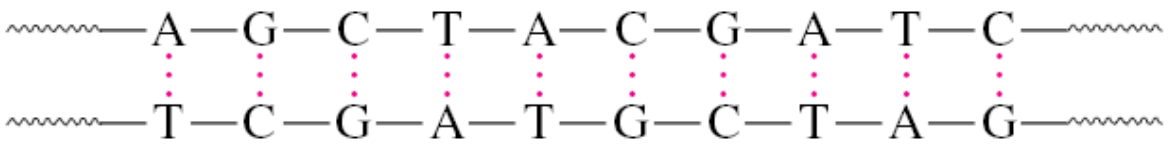


Guanin-Cytosin



Struktura DNA dvoušroubovice

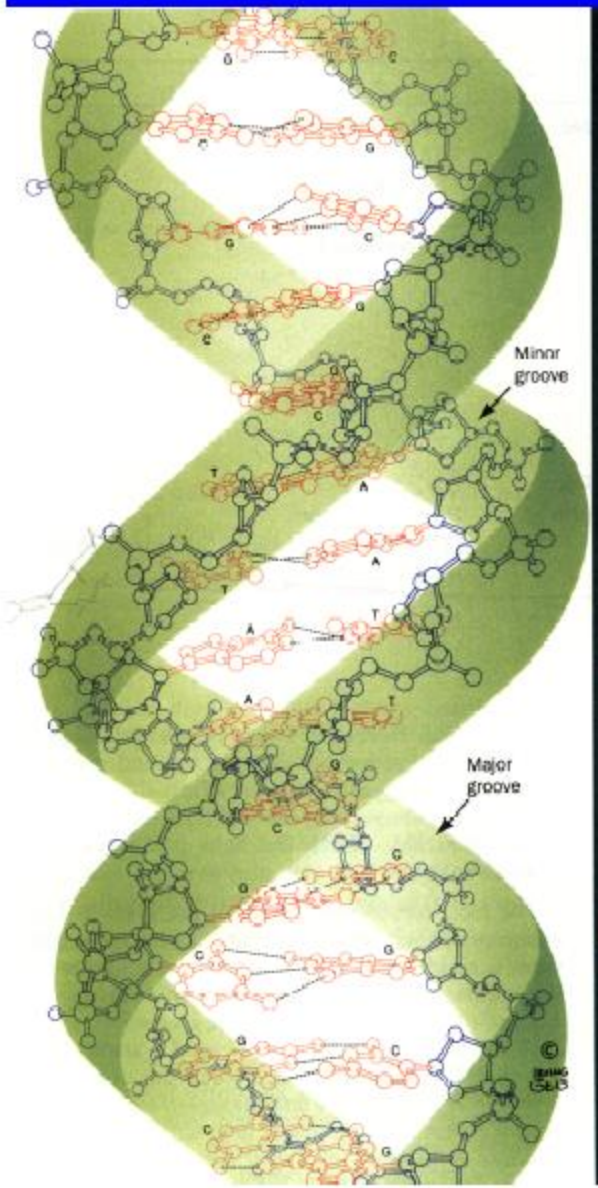


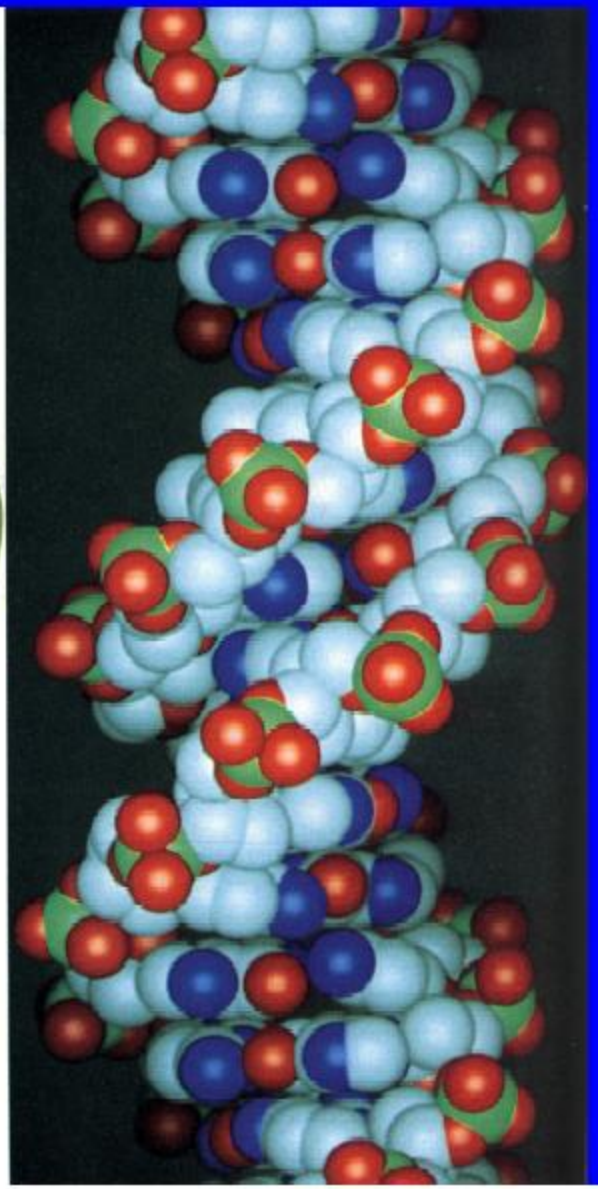


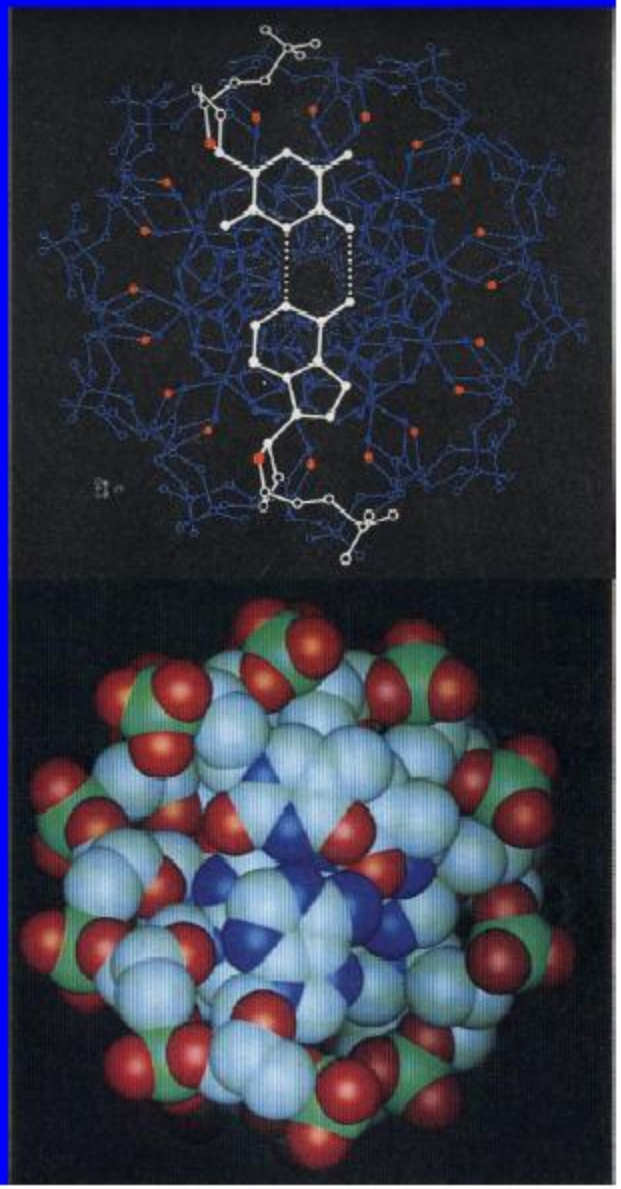
V sekvenci (pořadí) nukleotidů je zakódována genetická informace

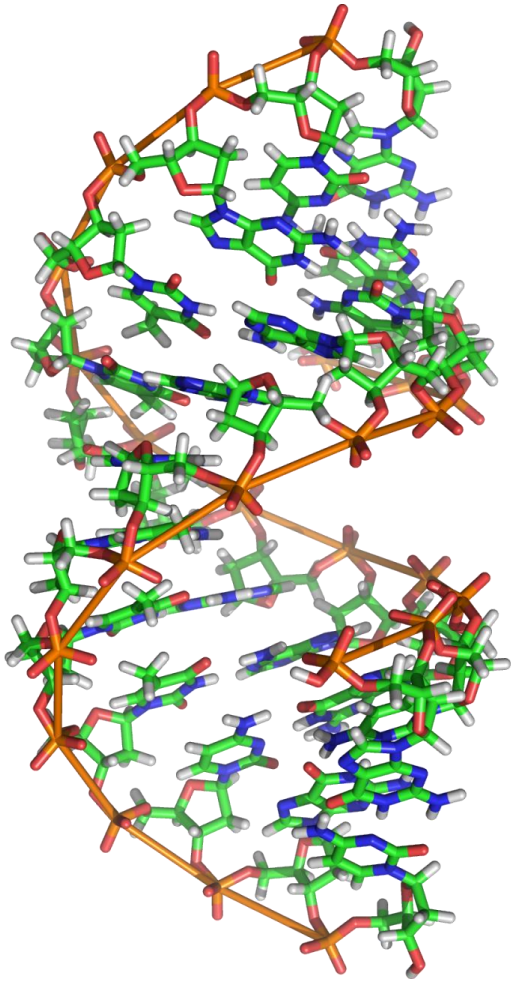
B-DNA

Structure type	Helix sense	Residues per turn	Twist per bp Ω°	Displacement bp D_a	Rise per bp/Å	Base tilt τ°	Sugar pucker	Groove width/Å Minor	Groove width/Å Major	Groove depth/Å Minor	Groove depth/Å Major
B–DNA	R	10	36	−0.2 to −1.8	3.3–3.4	−6	C2′–*endo*	5.7	11.7	7.5	8.8

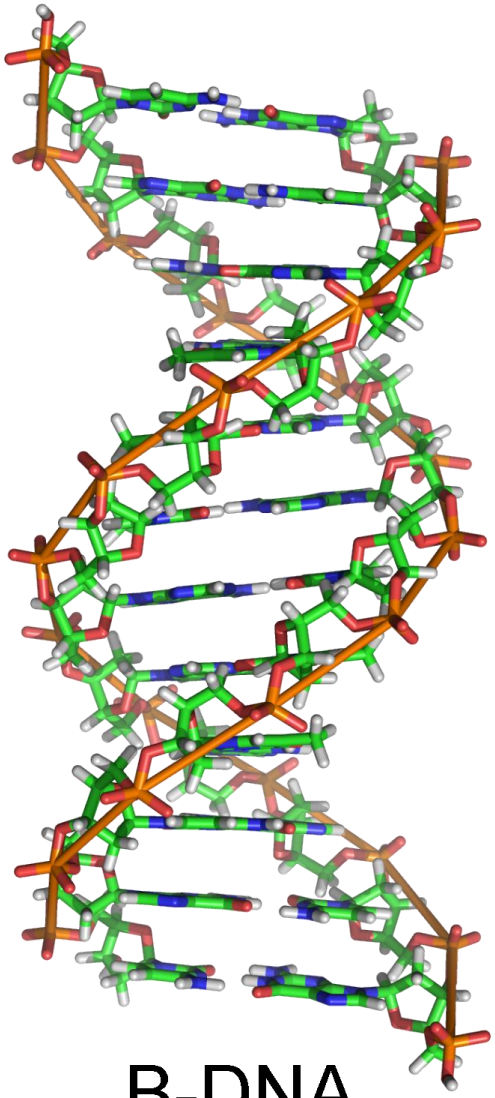




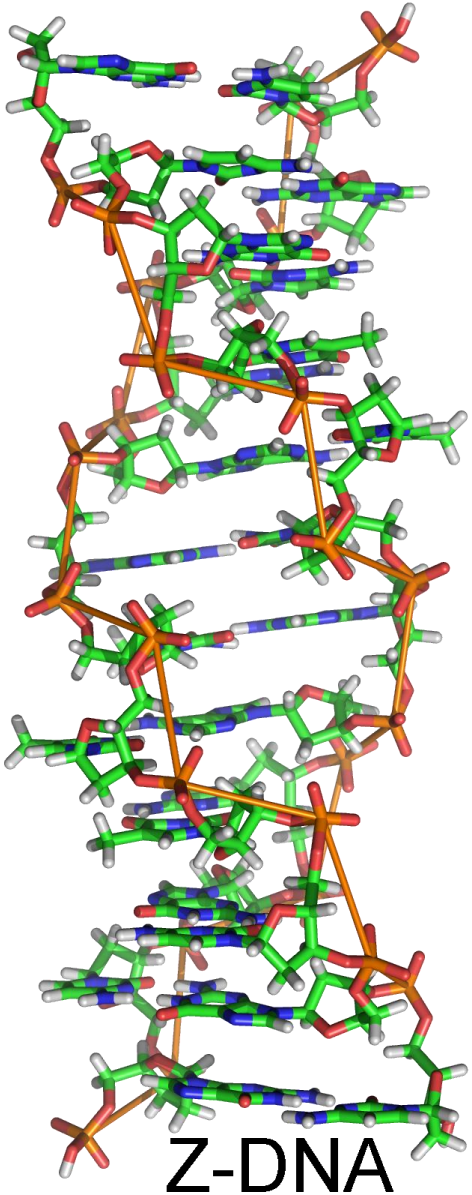




A-DNA

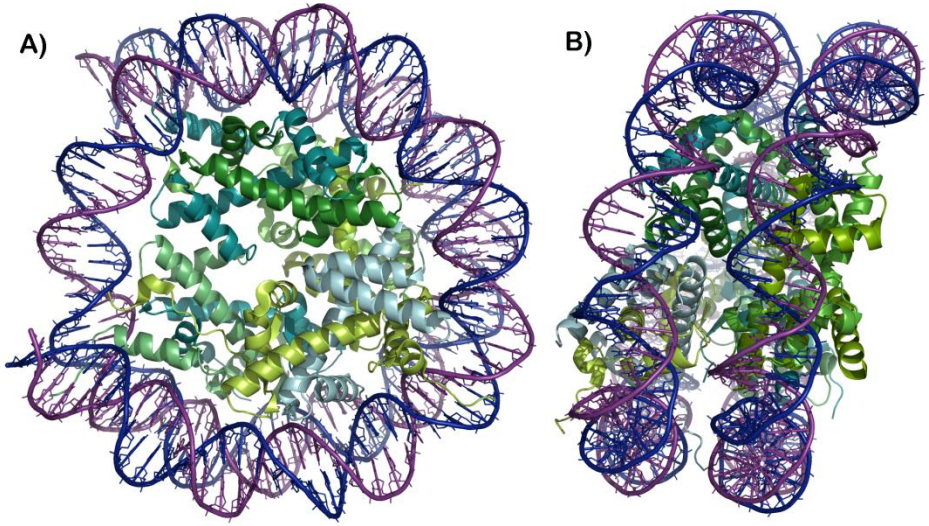


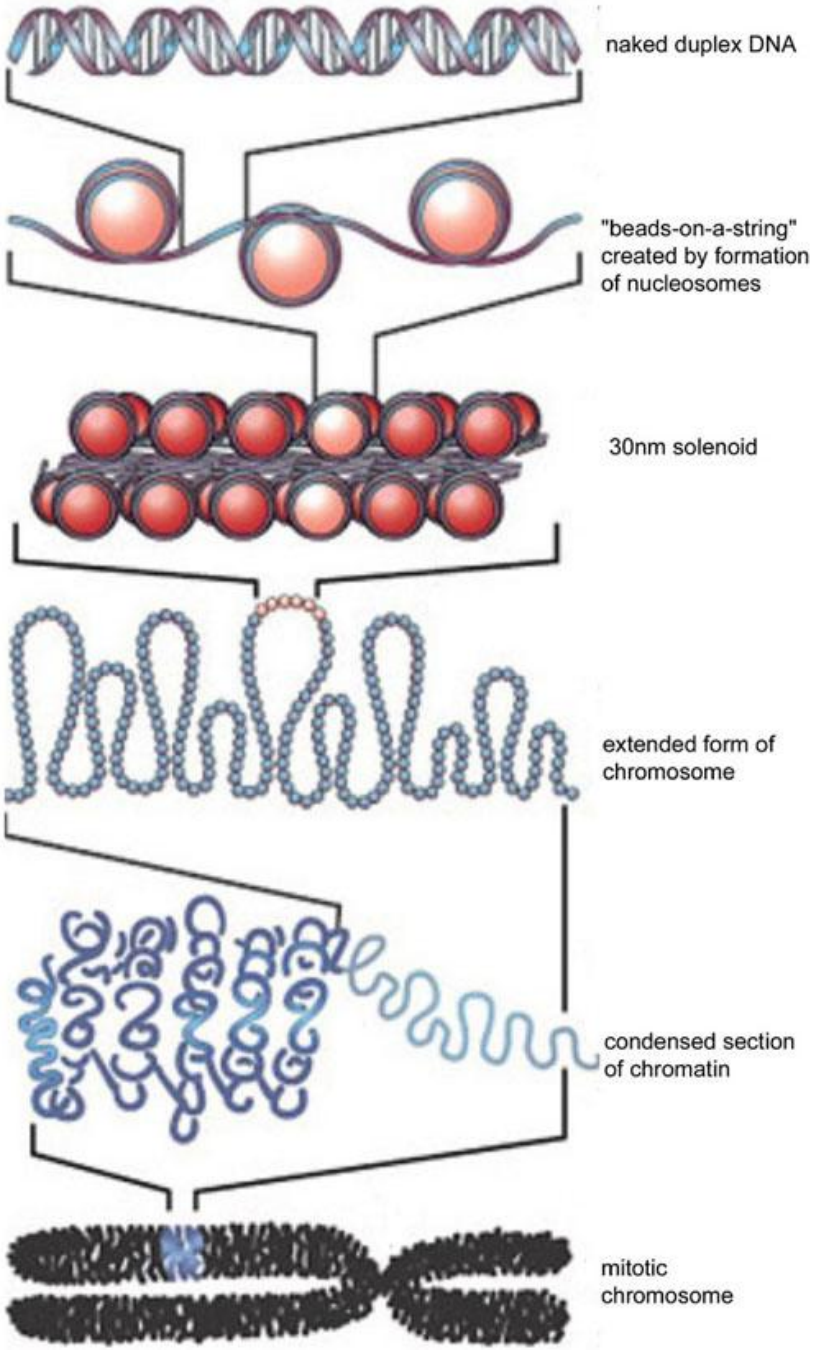
B-DNA



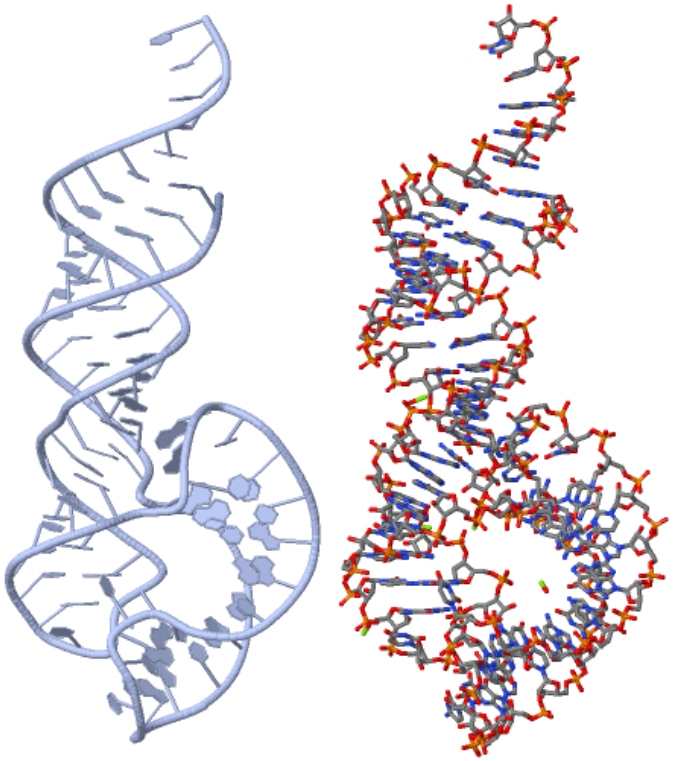
Z-DNA

Složení chromatinu a chromozomů

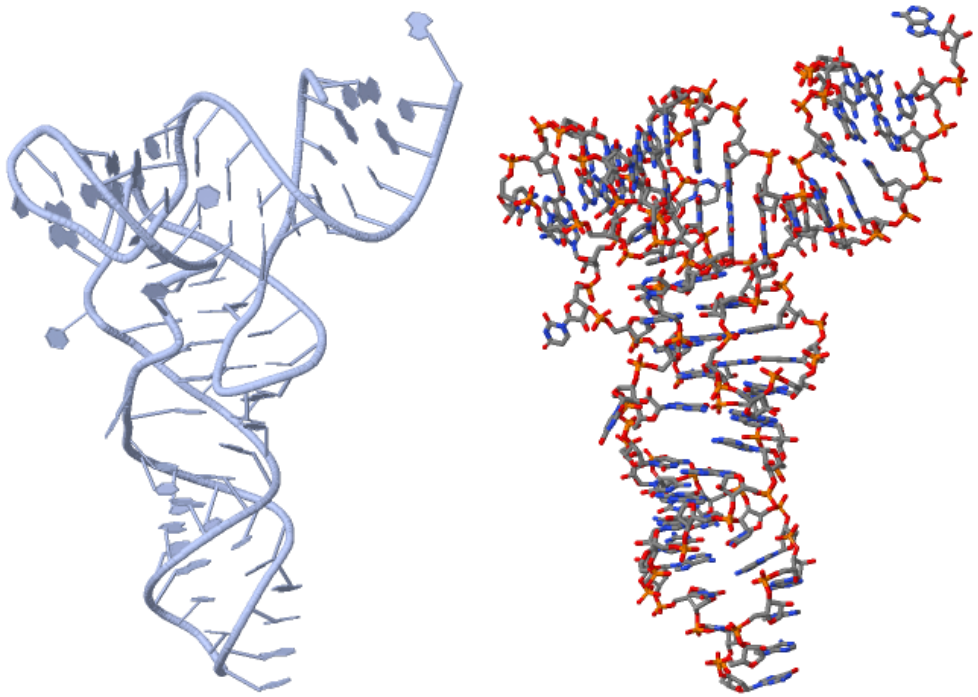




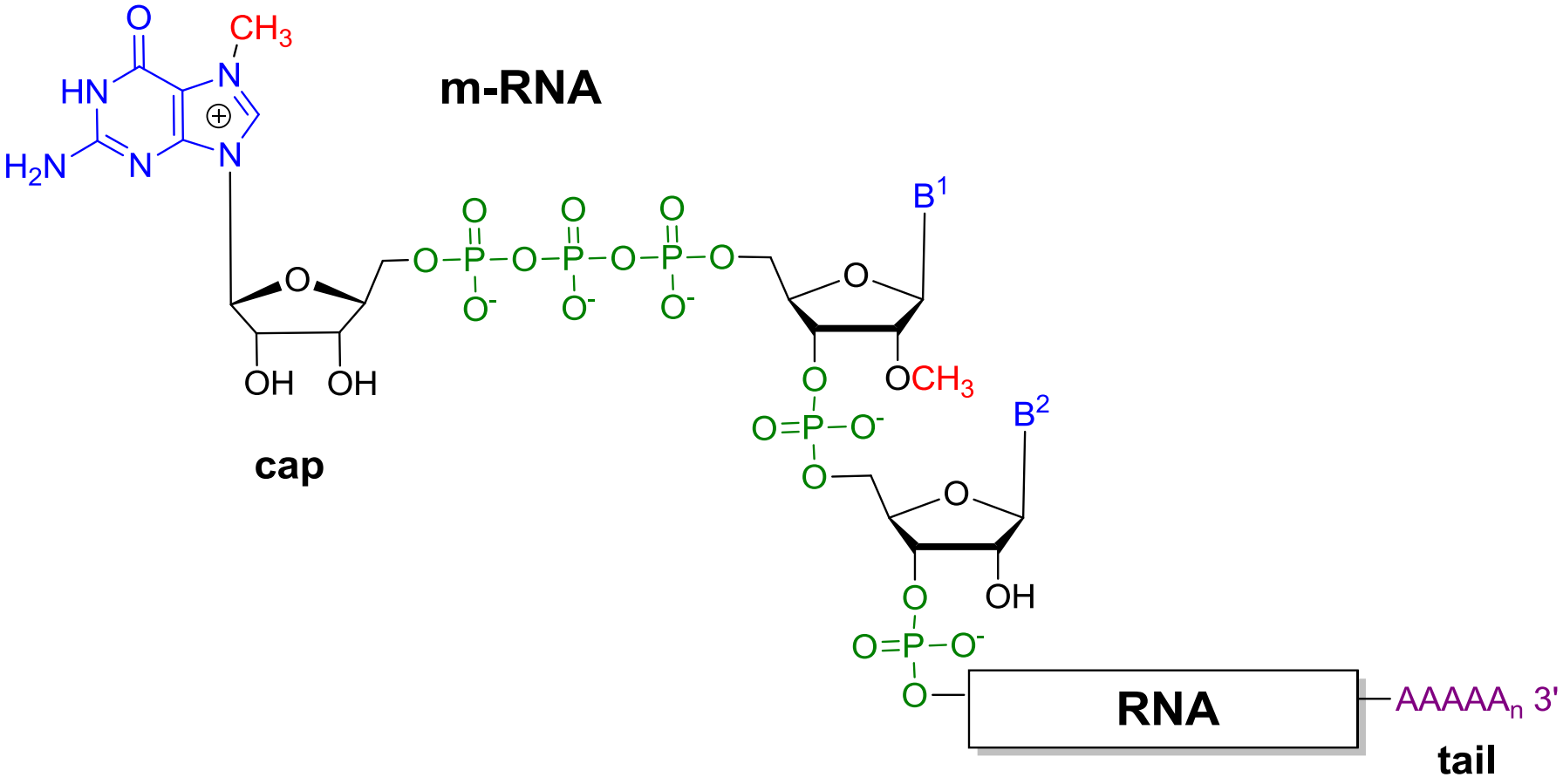
RNA



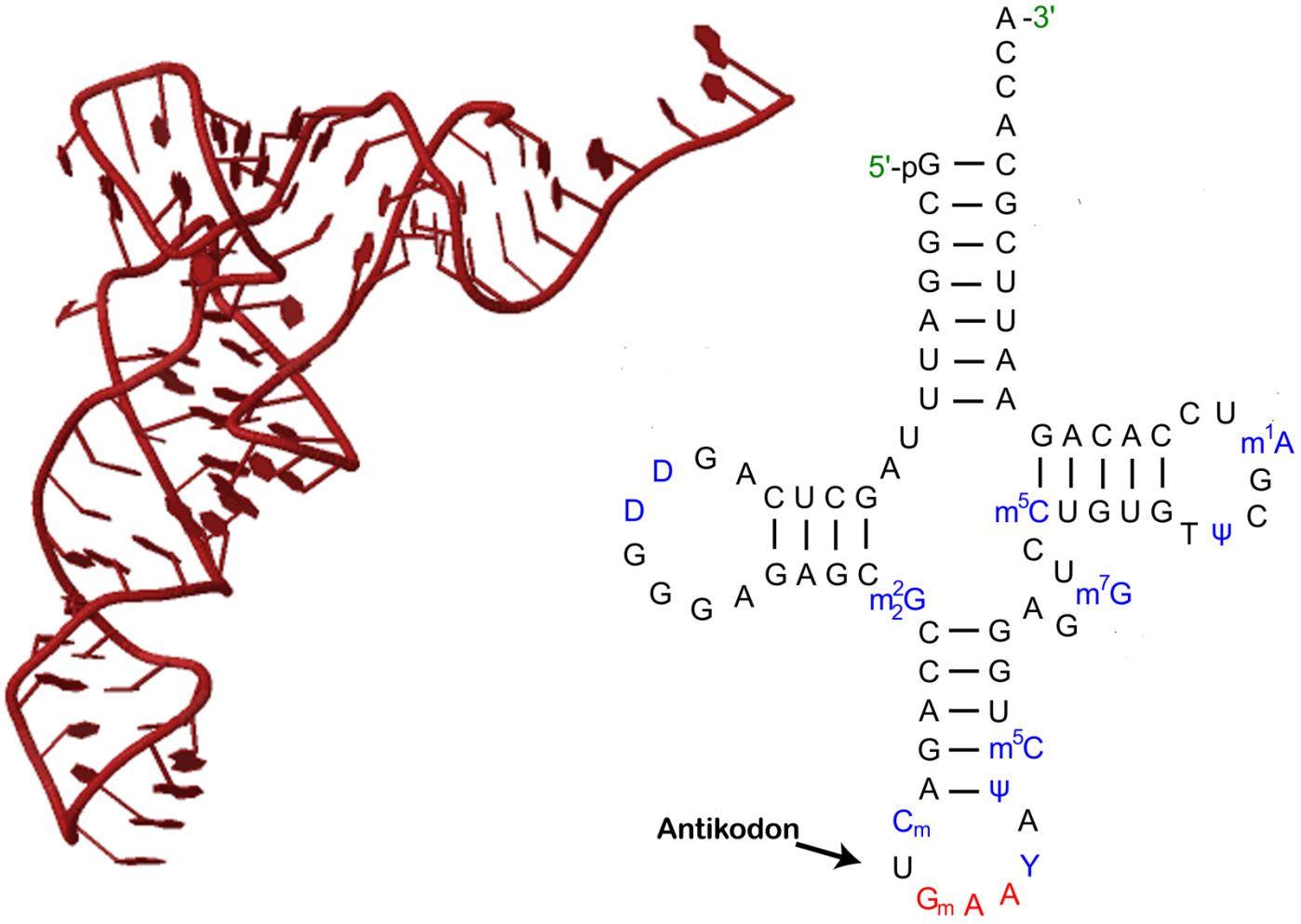
Hammerhead ribozyme



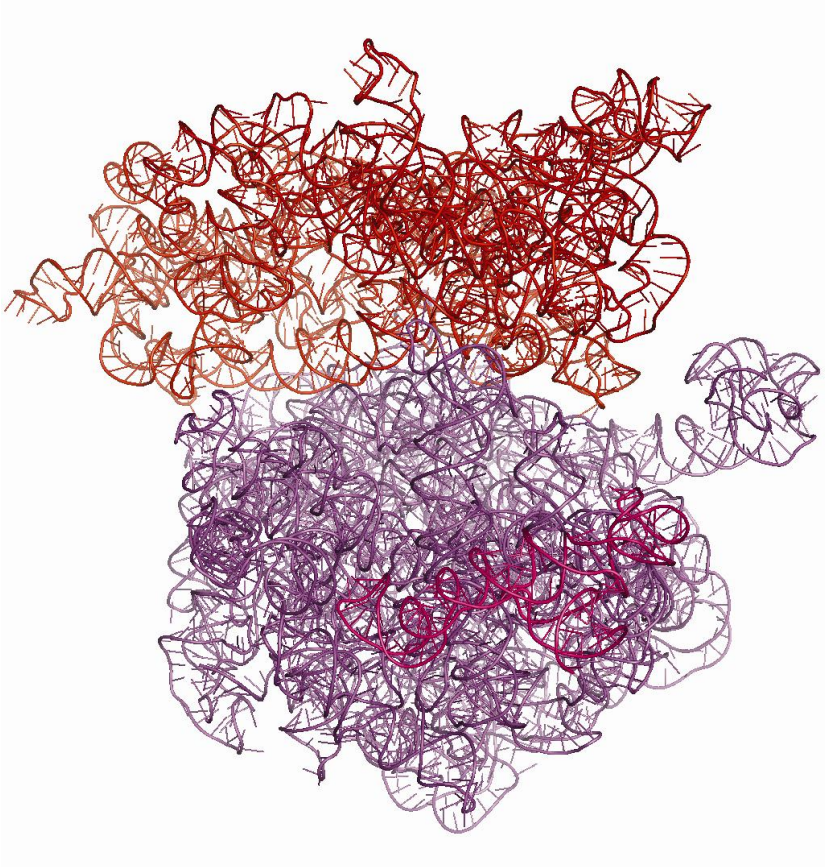
t-RNA(Phe)


m-RNA
cap
RNA
tail
AAAAA$_n$ 3'

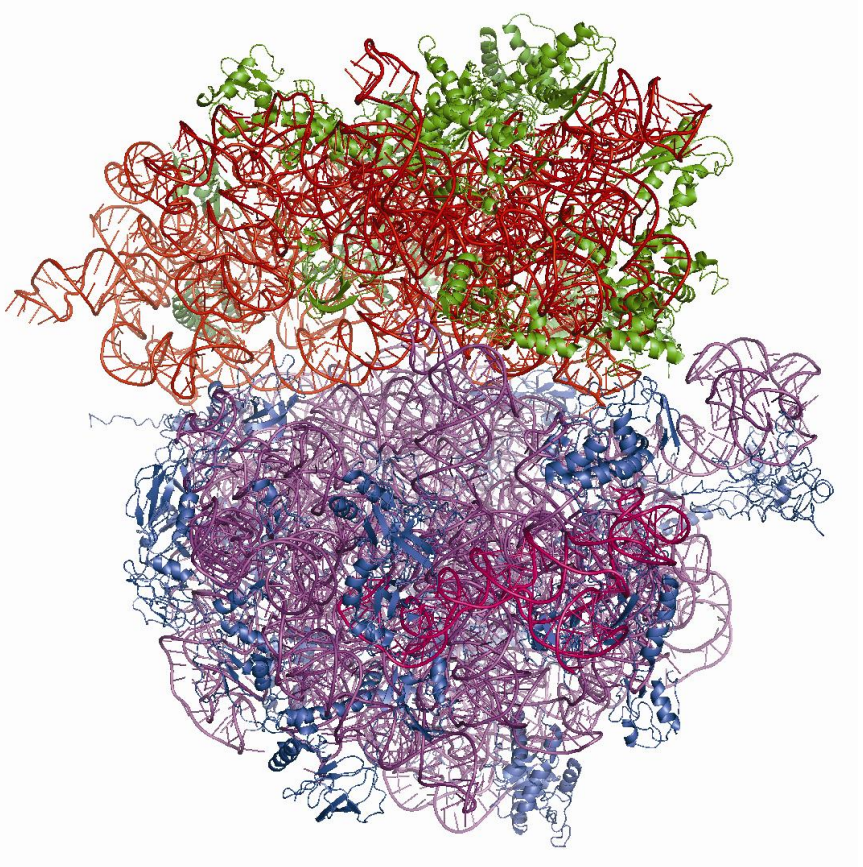
t-RNA


A -3'
C
C
A
5'-pG — C
C — G
G — C
G — U
A — U
U — A
U — A
U
G A C A C
C U
m1A
G
m5C U G U G
T ψ
C
C
U
m7G
A G
D
D
G
G G A
A
C U C G
G A G C
m22G
C — G
C — G
A — U
G — m5C
A — ψ
Cm
A
U
Y
Gm A A
Antikodon

rRNA

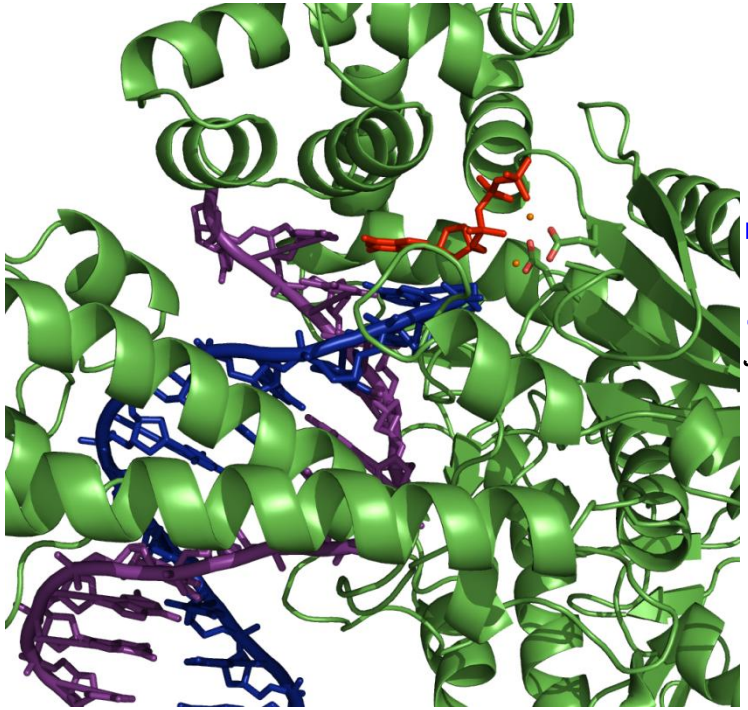


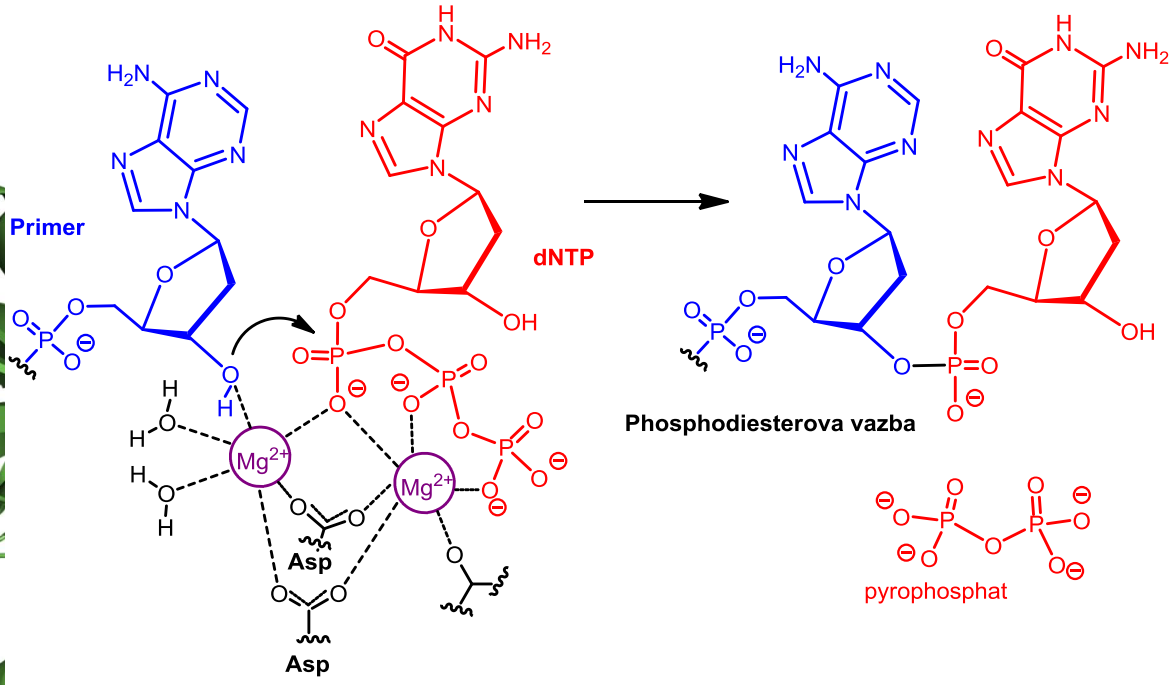
ribosomal RNA

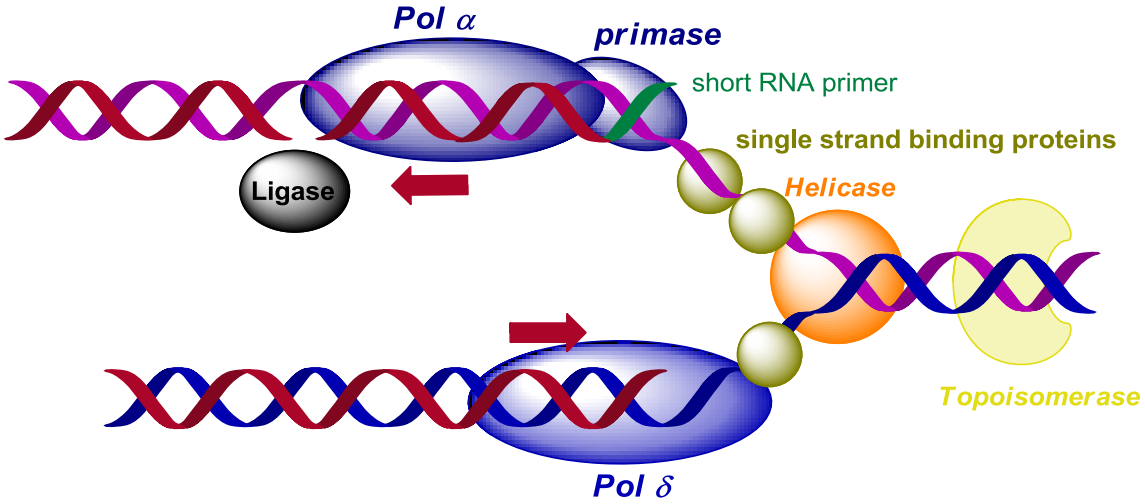


ribosomal RNA + proteins = ribosome

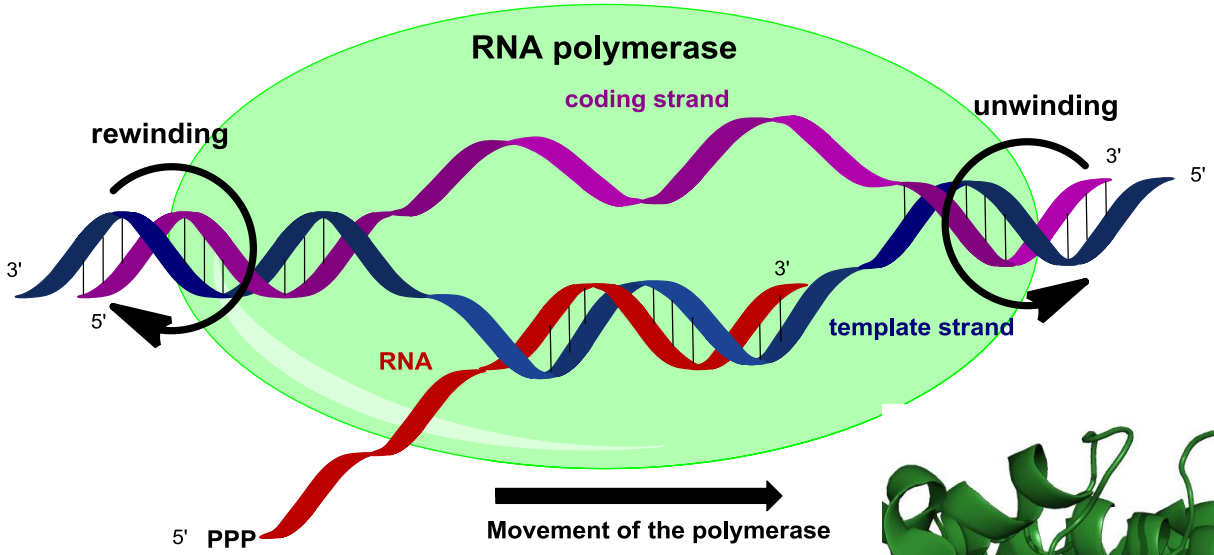
Biosyntéza DNA - DNA polymerasa

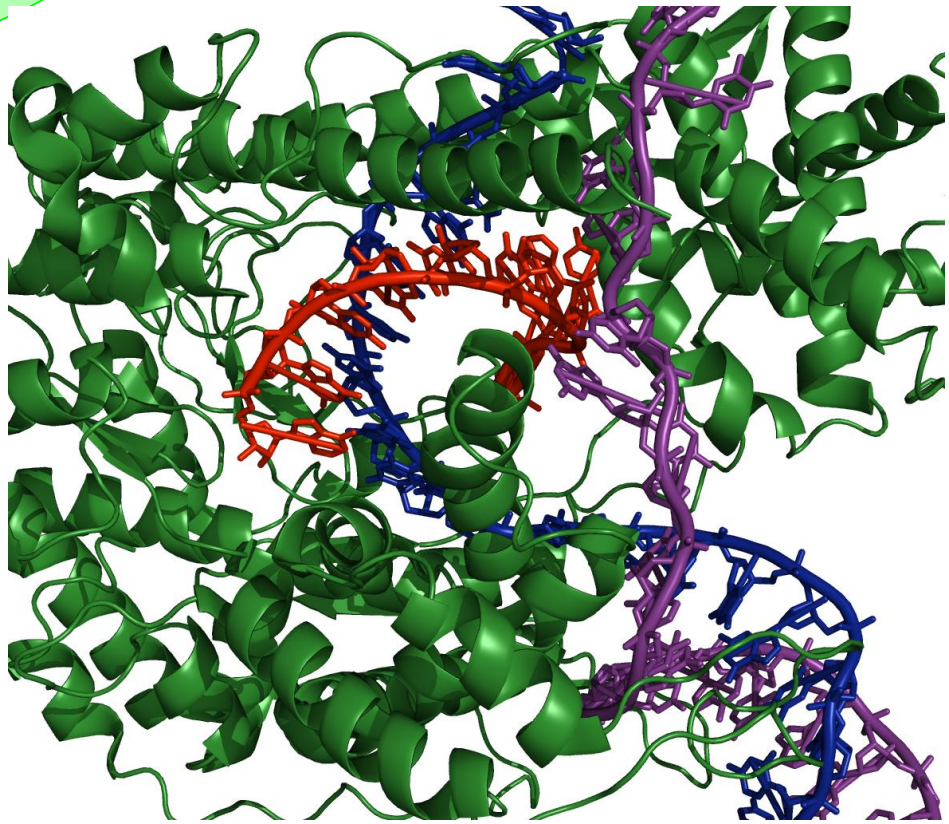




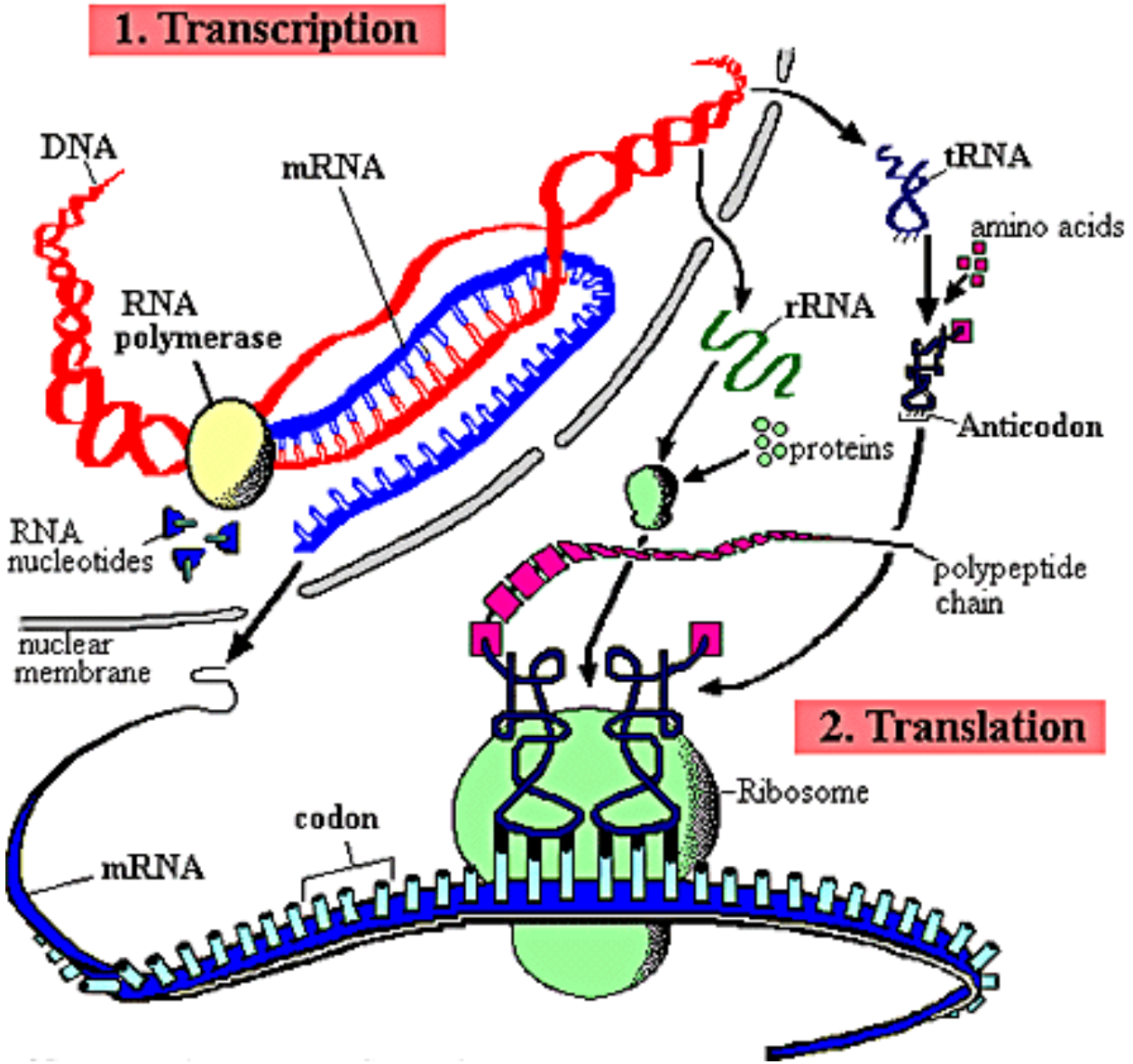


Biosyntéza RNA (transkripce) - RNA polymerasa

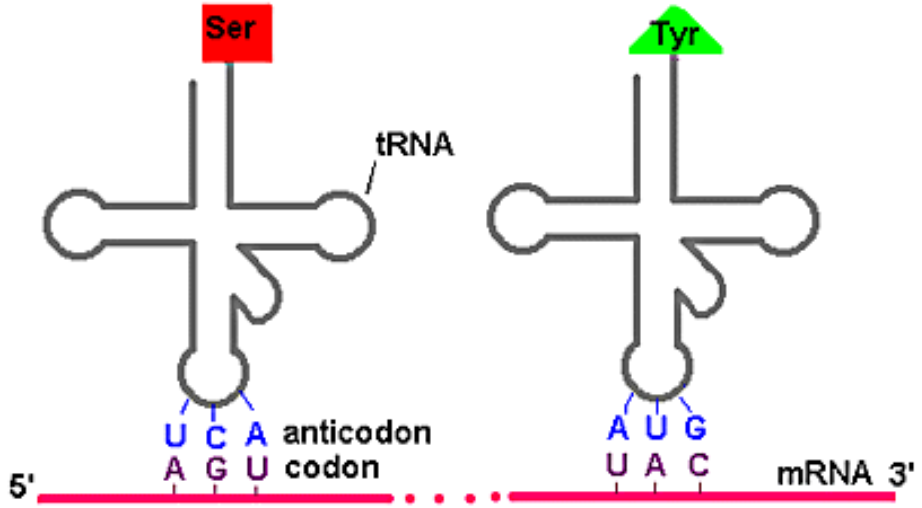




Centrální dogma molekulární biologie



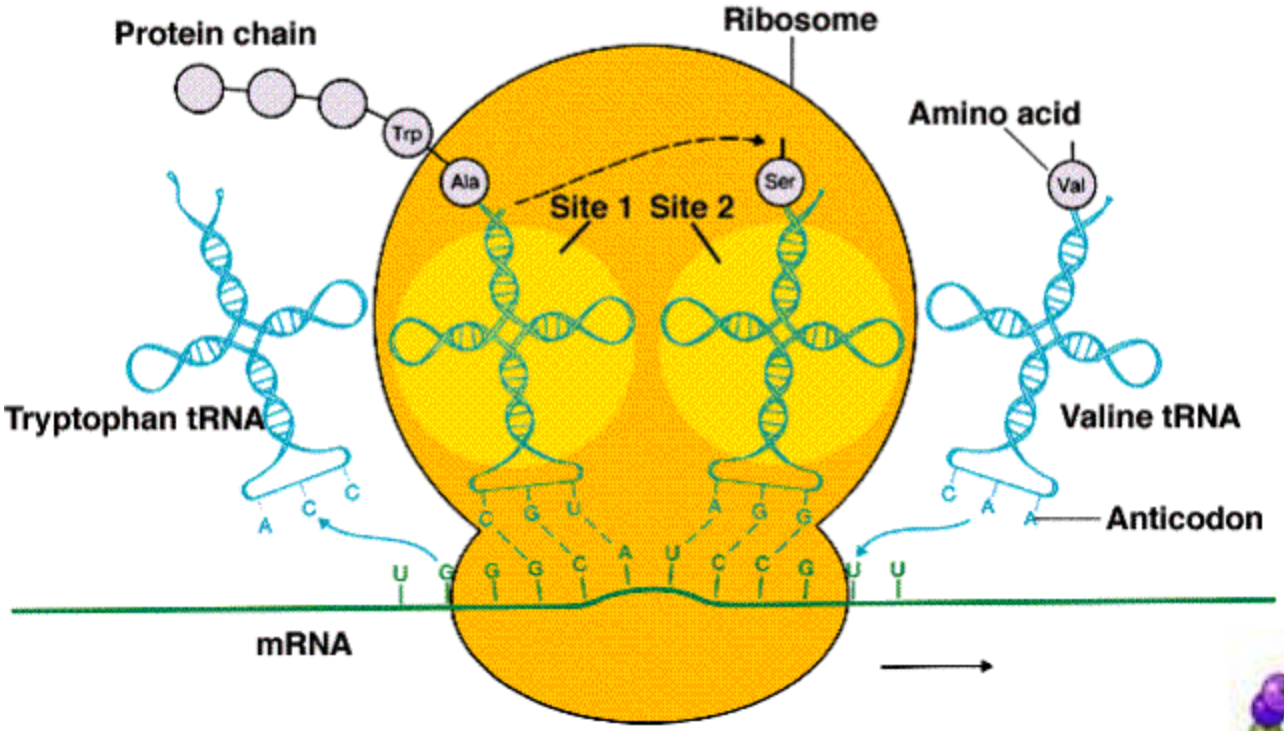
Genetický kód

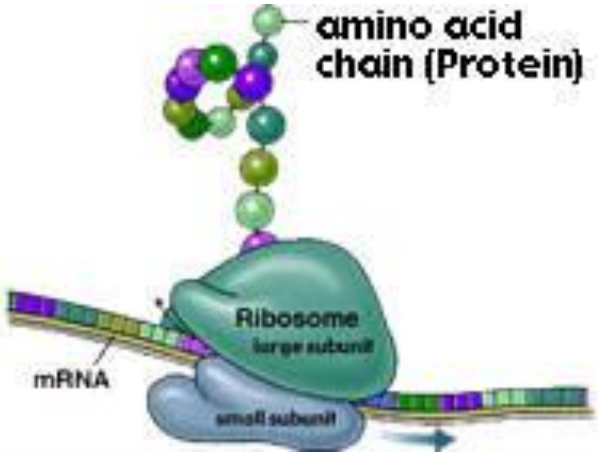


2nd base in codon

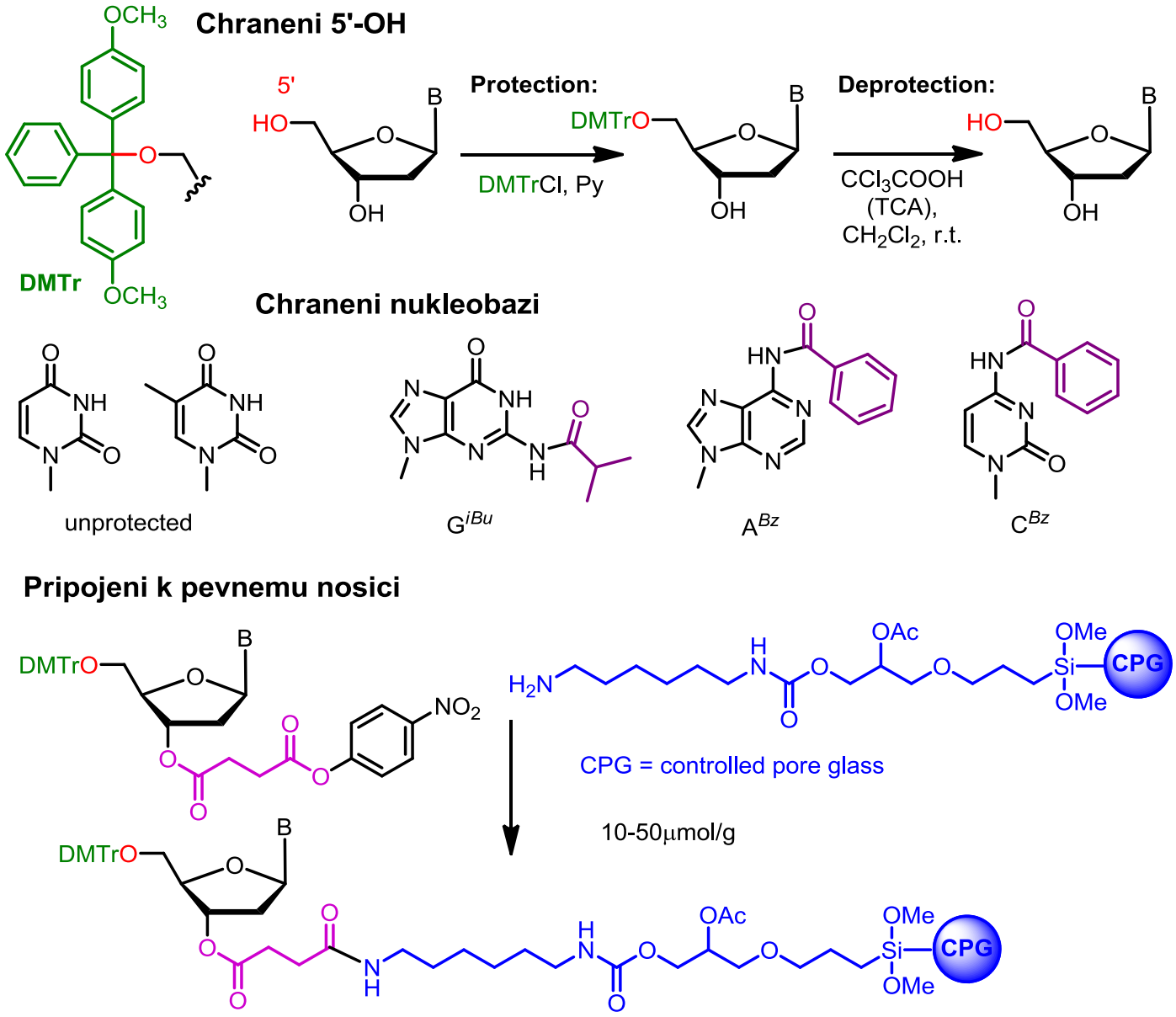
1st base in codon	U	C	A	G	3rd base in codon
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	STOP	STOP	A
	Leu	Ser	STOP	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

Syntéza proteinu na ribosomu (translace) – genová exprese

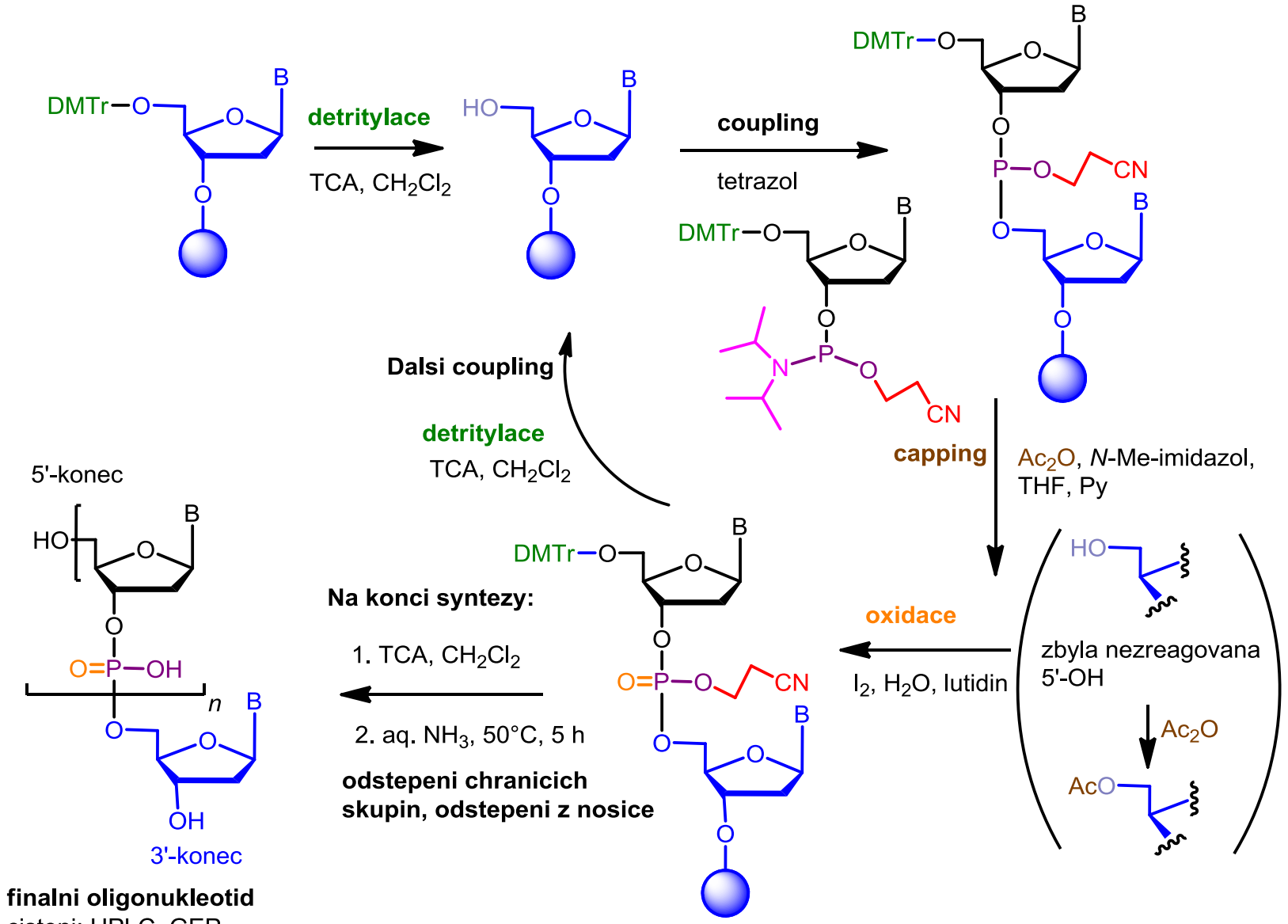


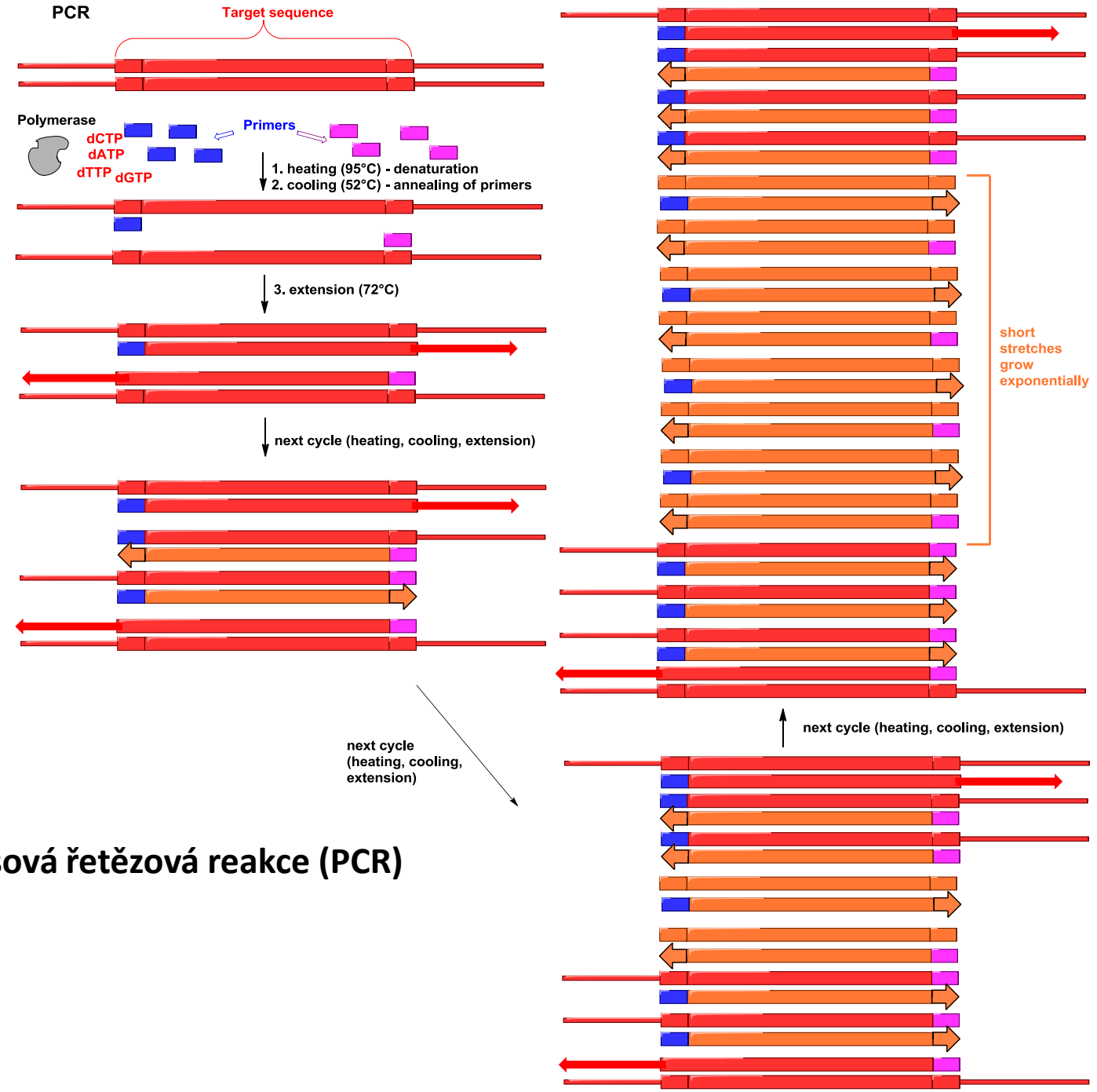


Syntéza oligonukleotidů



Syntéza oligonukleotidů





Polymerasová řetězová reakce (PCR)