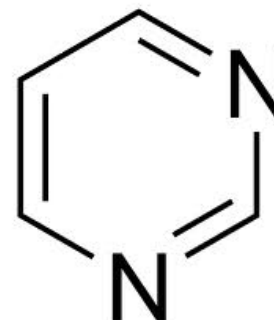
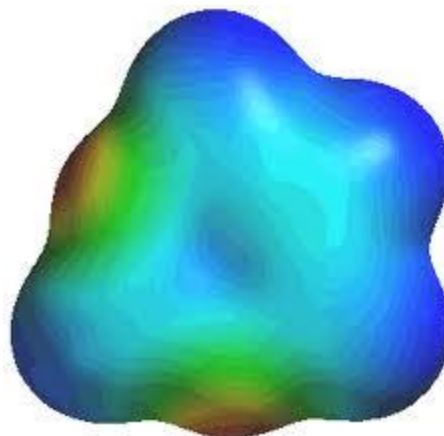
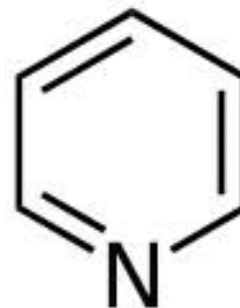
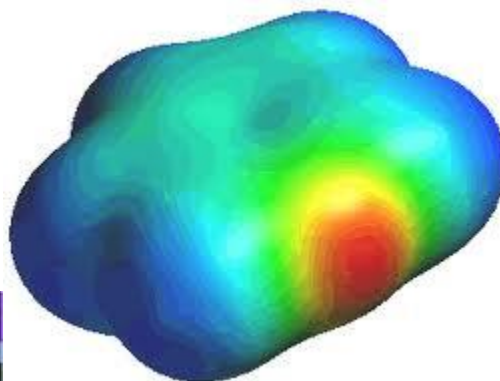
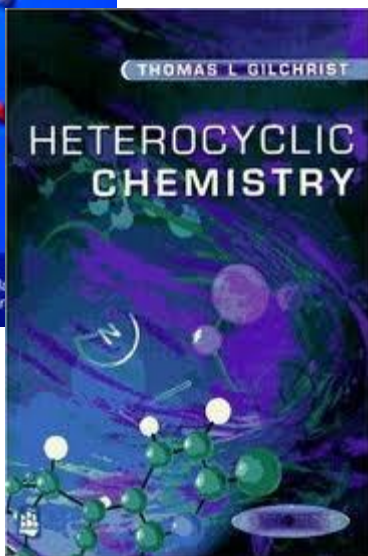
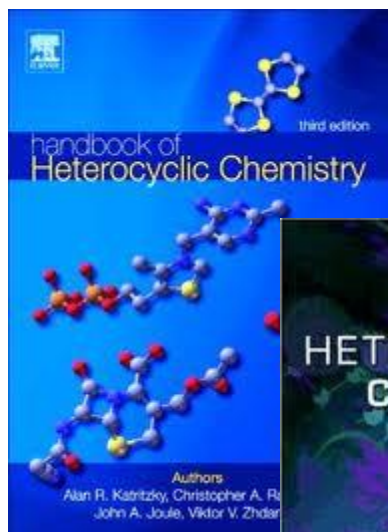
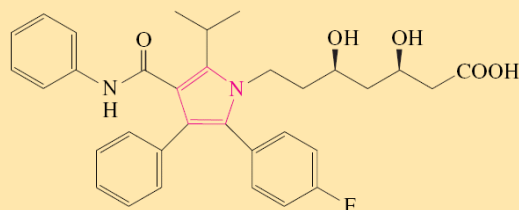


Heterocyklické sloučeniny



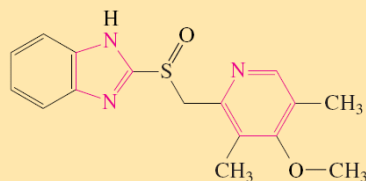
Většina klinicky
používaných léčiv
obsahuje alespoň jeden
heterocyklický kruh

1. Atorvastatin
(Lipitor)



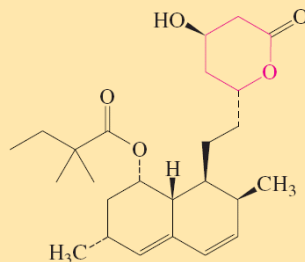
Cholesterol reducer

2. Omeprazole
(Prilosec)



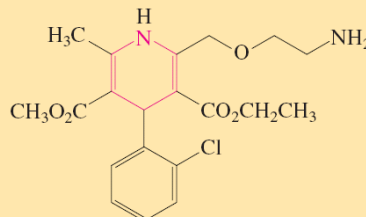
Antiulcerative

3. Simvastatin
(Sivastin,
Zocor)



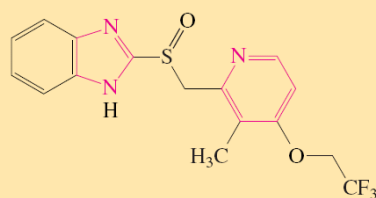
Antihypercholesterolemic

4. Amlodipine
(Norvasc)



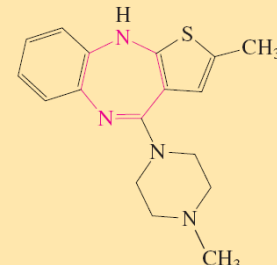
Antihypertensive

5. Lansoprazole
(Prevacid)



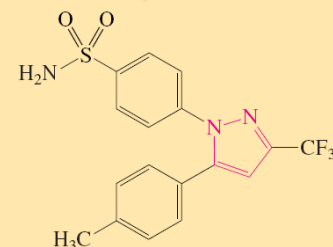
Antiulcerative

6. Olanzapine
(Zyprexa)



Antischizophrenoid

7. Celecoxib
(Celebrex)



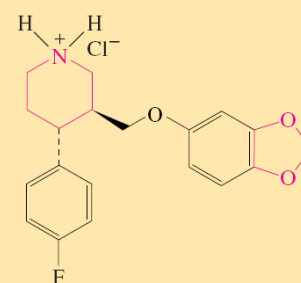
Antiarthritic

8. Erythropoietin
(Procrit)

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

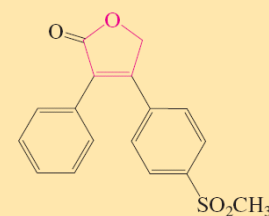
Antianemic

9. Paroxetine
HCl
(Paxil)



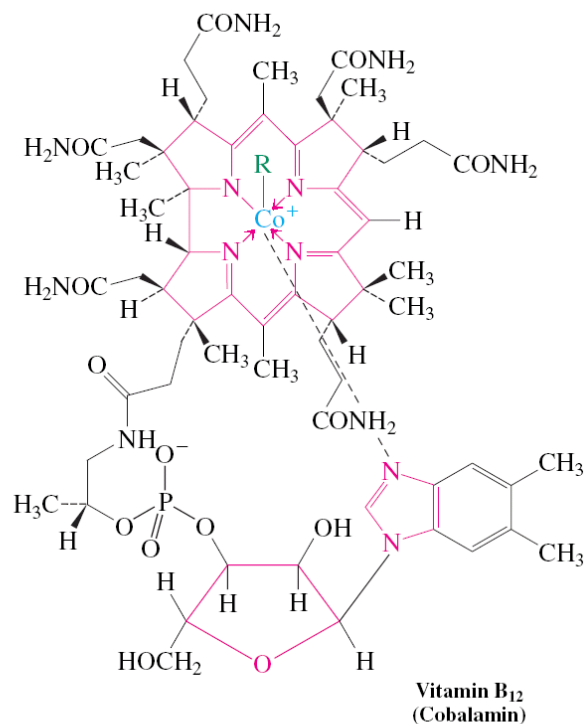
Antidepressant

10. Rofecoxib
(Vioxx)

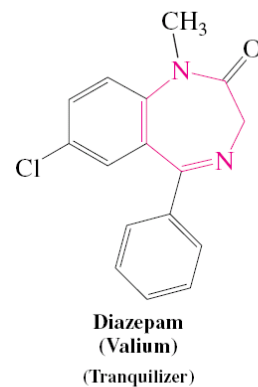
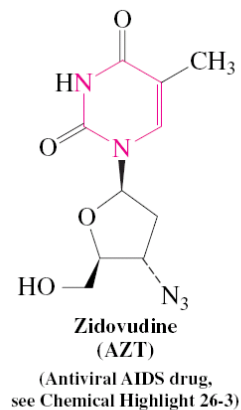
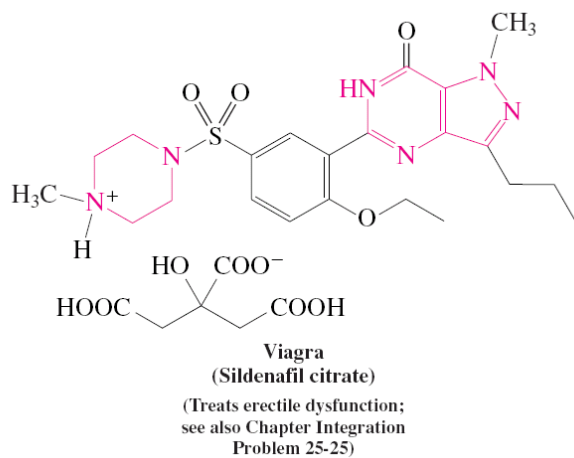
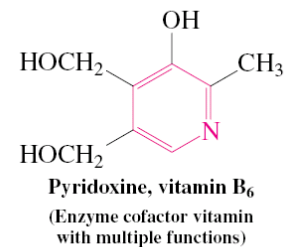
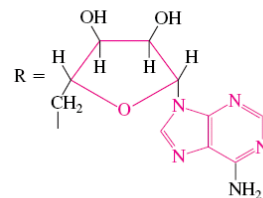


Antiarthritic
(Withdrawn in December 2004 because of
safety concerns)

^aTotal U.S. sales of pharmaceuticals reached \$224 billion in 2003, with lipitor leading at \$6.3 billion.

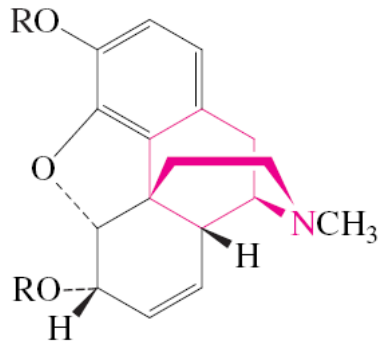


(Catalyzes biological rearrangements and methylations)



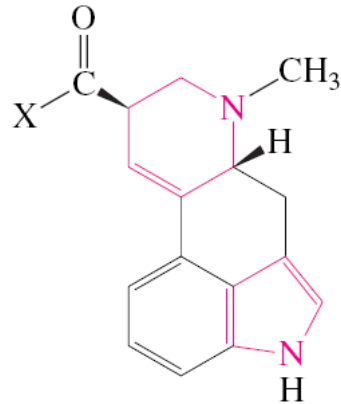
Alkaloidy

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

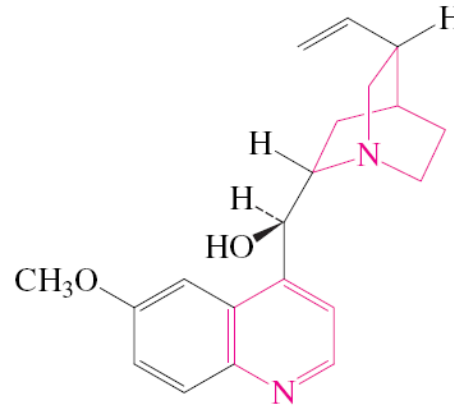


Morphine (R = H)

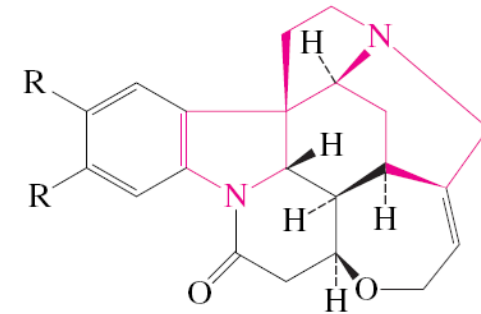
Heroin (R = CH₃C(=O))



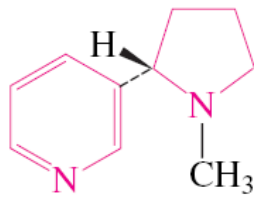
Lysergic acid (X = OH)
Lysergic acid diethylamide, LSD
[X = (CH₃CH₂)₂N]



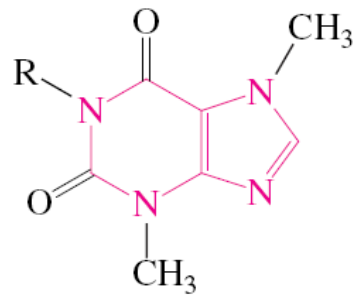
Quinine



Strychnine (R=H)
Brucine (R=CH₃O)

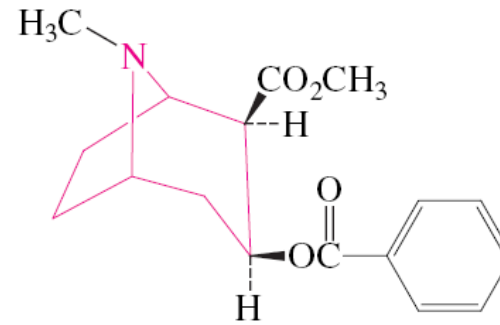


Nicotine



Caffeine (R = CH₃)

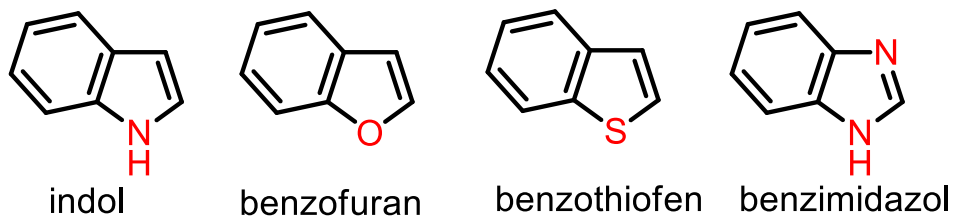
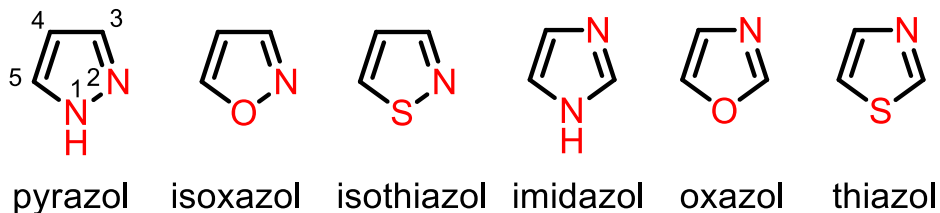
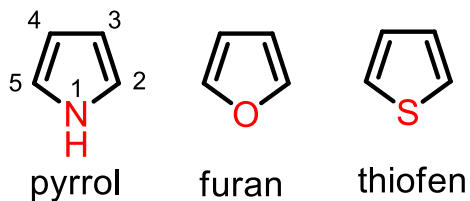
Theobromine (R = H)



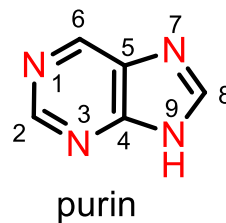
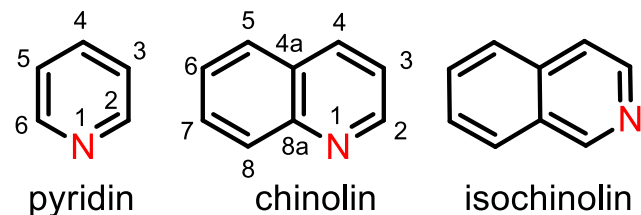
Cocaine

Názvosloví aromatických heterocyklů

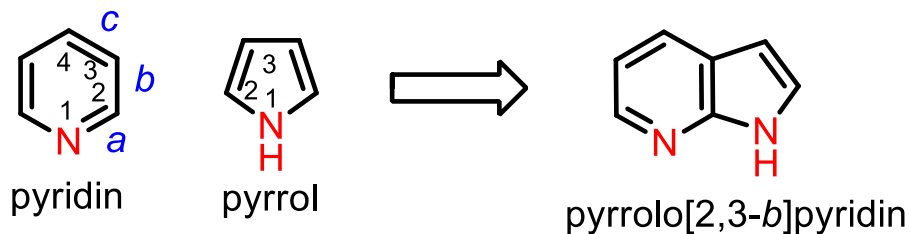
5-členné



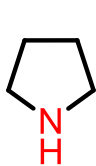
6-členné



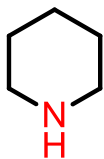
Princip tvorby názvů kondenzovaných heterocyklů



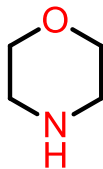
Názlosloví nearomatických (nasycených) heterocyklů



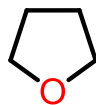
pyrrolidin



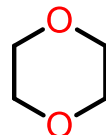
piperidin



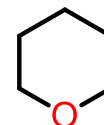
morfolin



tetrahydrofuran



1,4-dioxan



tetrahydropyran



oxiran



thiiran



aziridin



azirin



oxetan

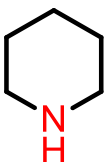


thietan

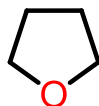


azetidin

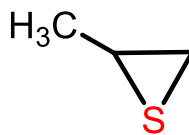
Alternativní názlosloví záměnným systémem



aza**cyklo**hexan

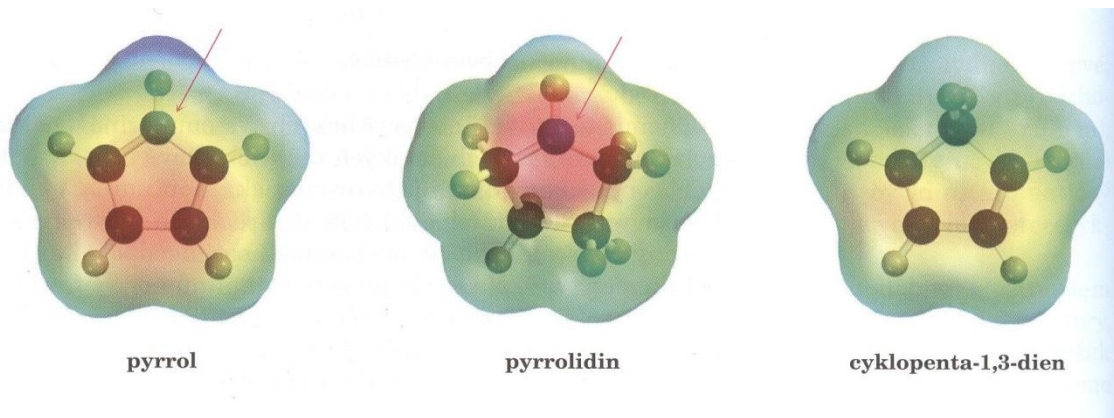
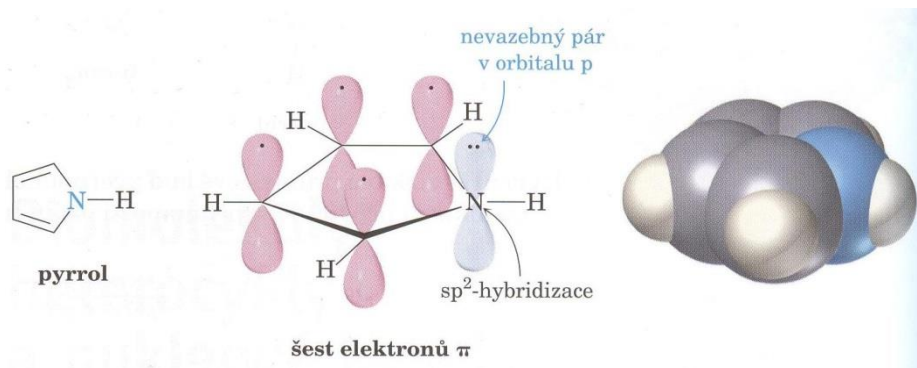


oxa**cyklo**pentan



2-methyl-thia**cyklo**propan

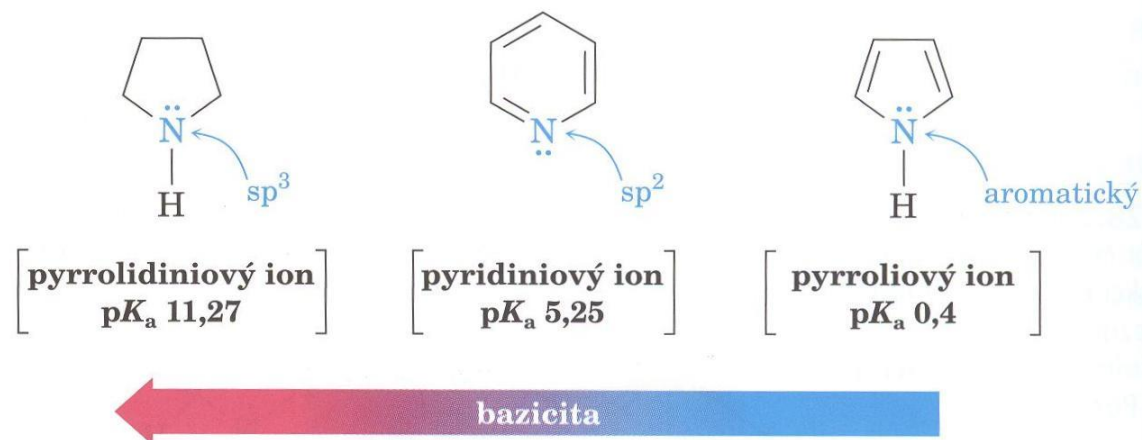
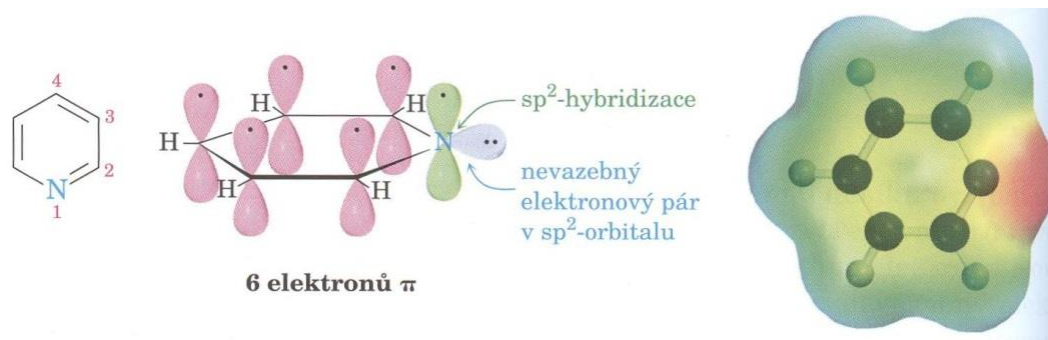
Pětičlenné heterocykly - pyrrol



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

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

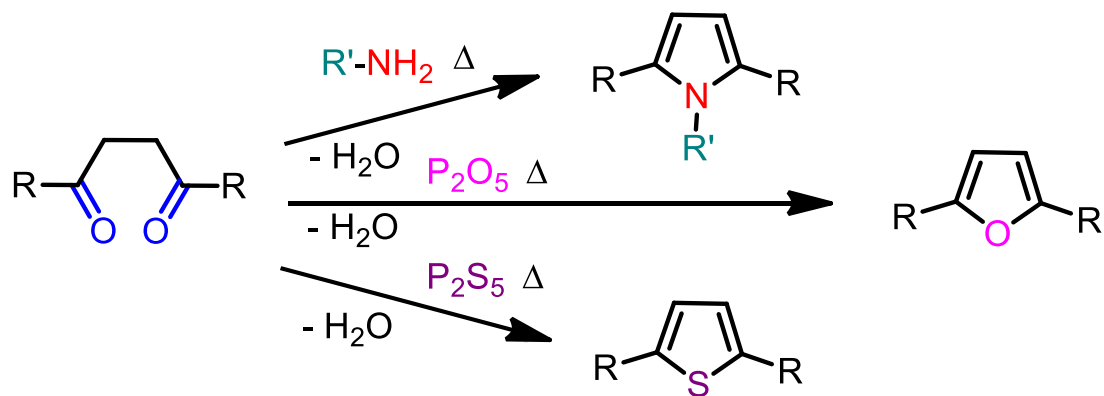
Šestičlenné heterocykly - pyridin



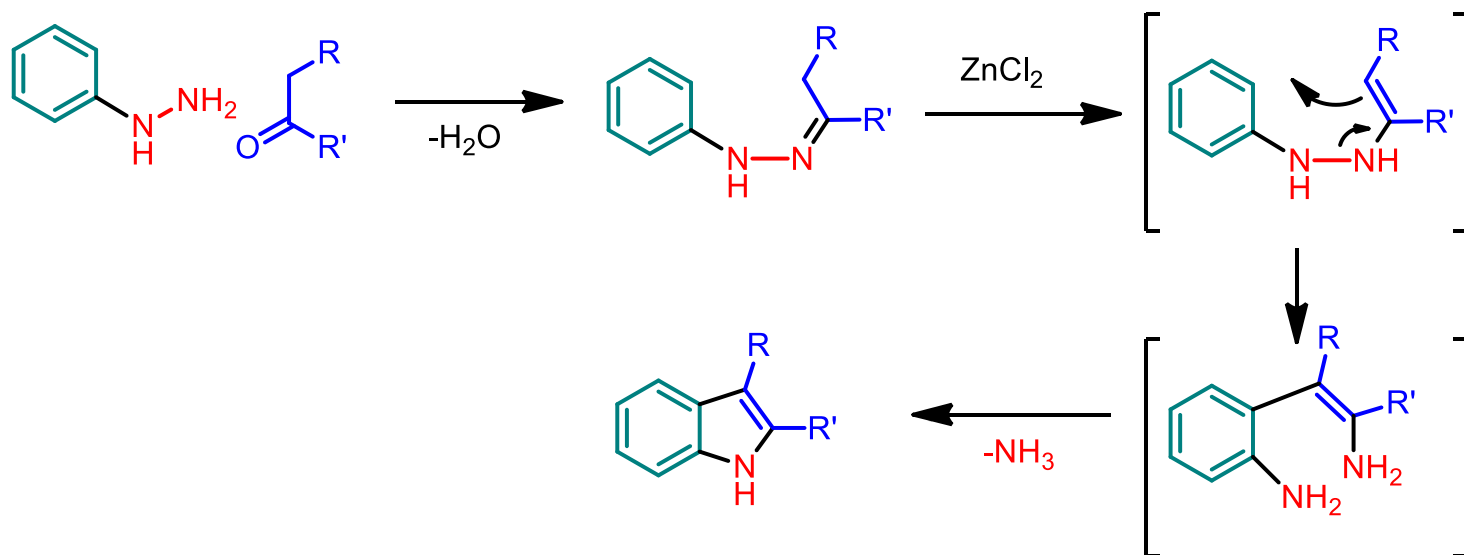
Pyridin (a podobně i pyrimidin) jsou **elektronově chudé aromatické systémy**

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

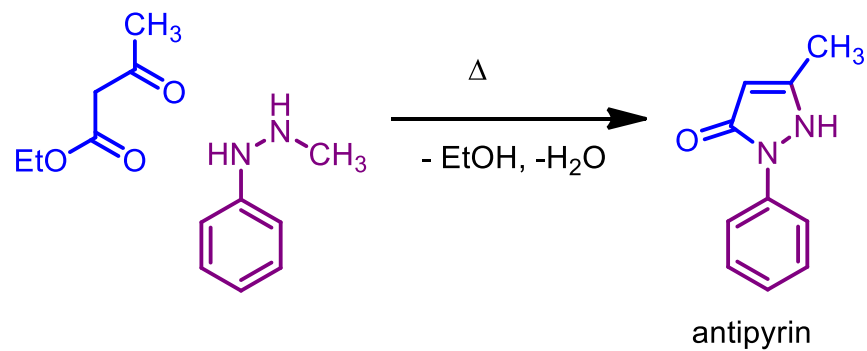
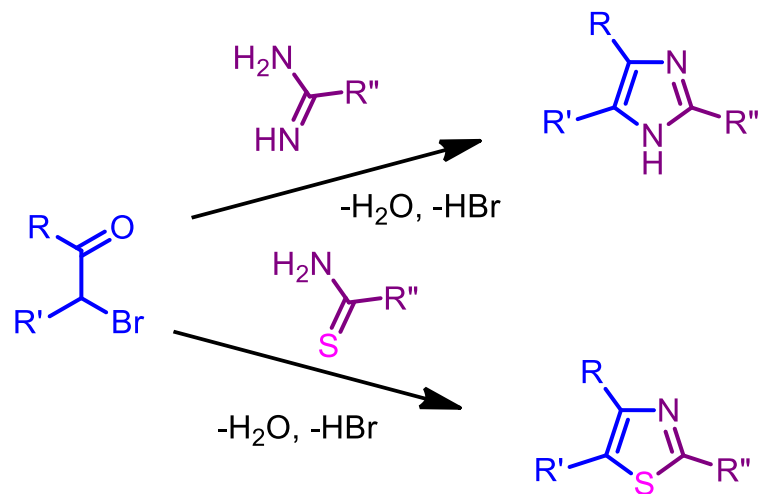
Paal-Knorrůva syntéza 5-členných heterocyklů z 1,4-diketonů



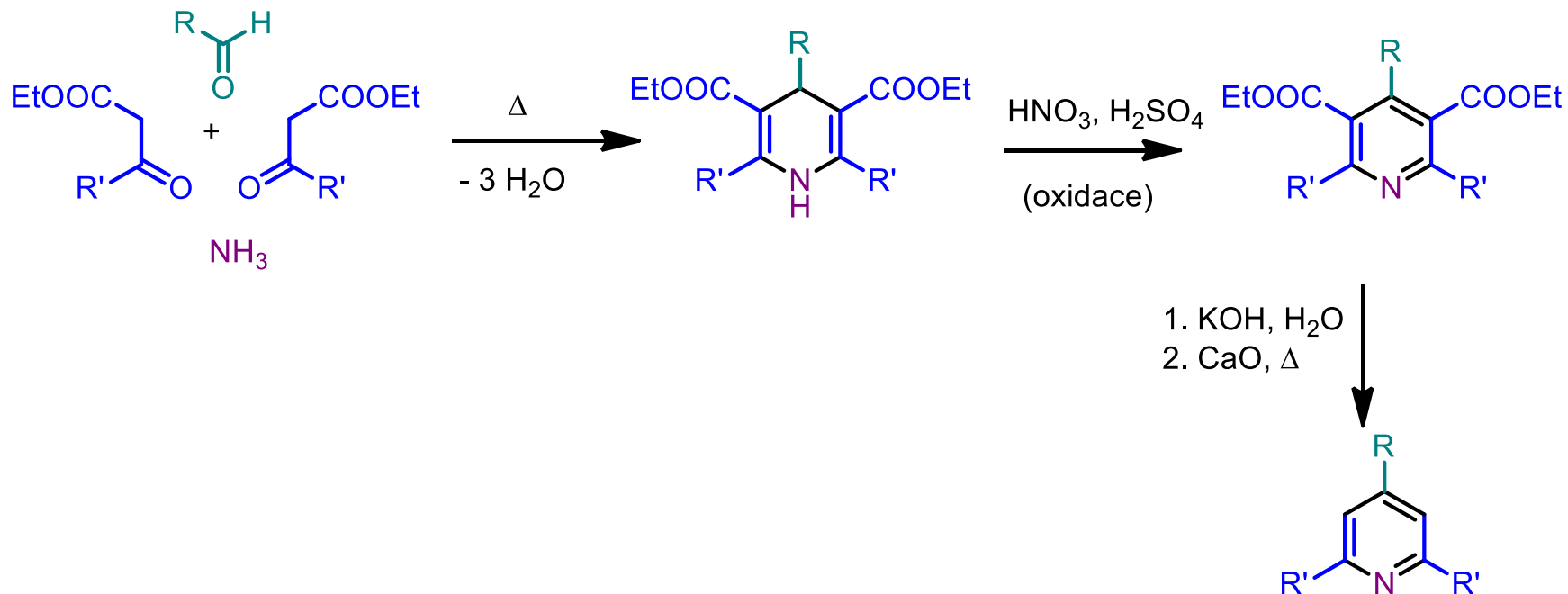
Fischerova syntéza indolů



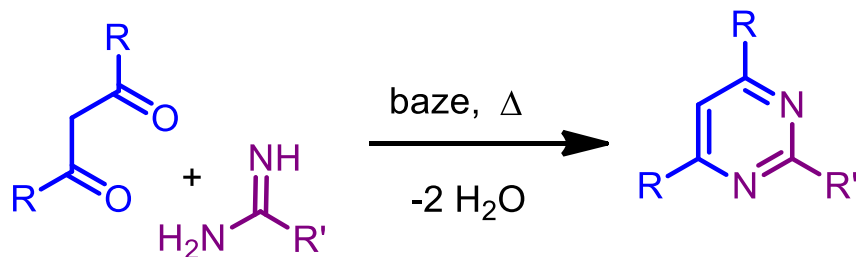
Syntézy azolů – heterocyklické kondenzace



Hantschova syntéza pyridinů

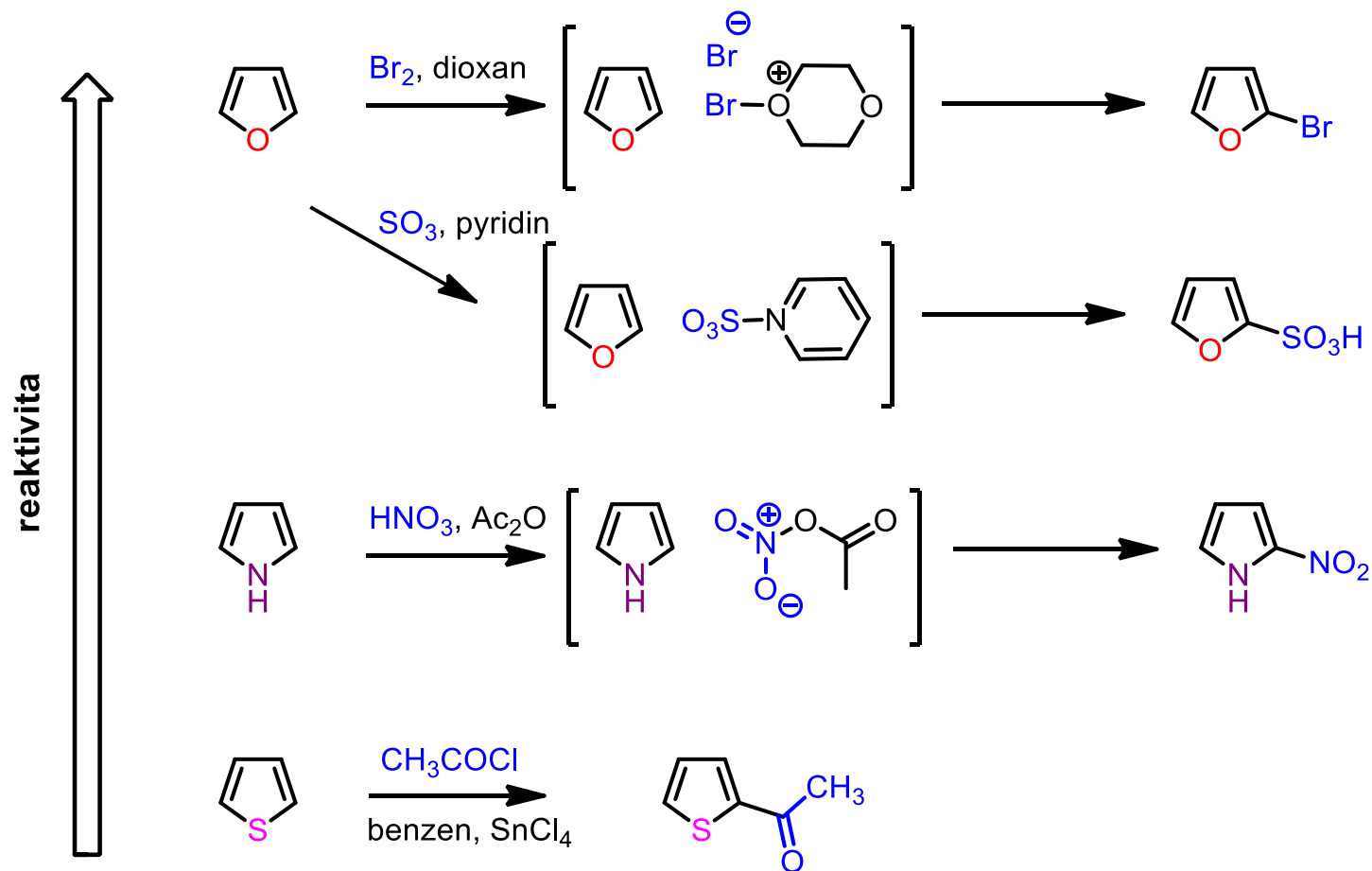


Příklad syntézy pyrimidinů



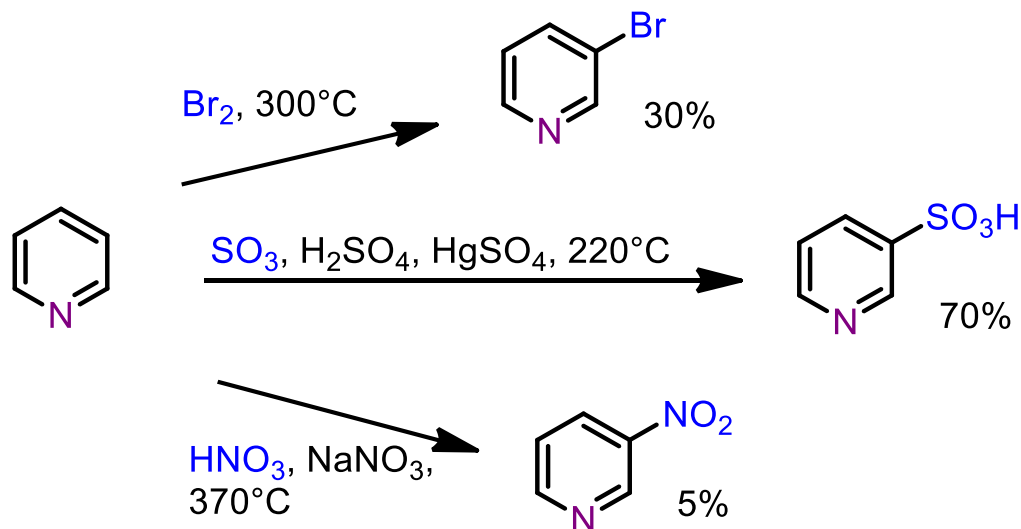
Elektrofilní substituce na 5-členných heterocyklech

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

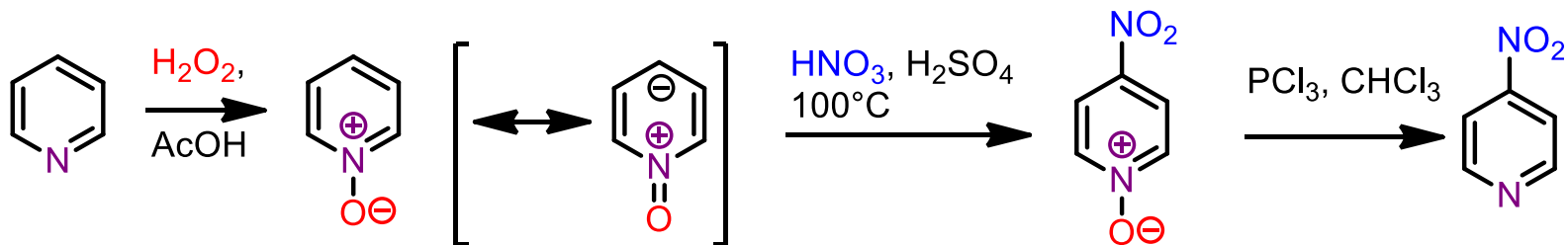


Elektrofilní substituce na 6-členných heterocyklech (např. pyridin)

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



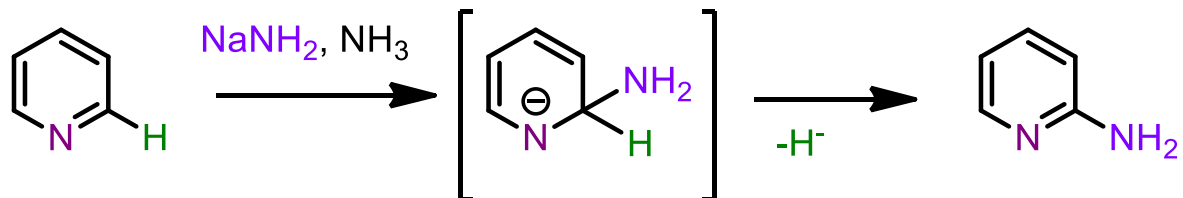
Převerněním pyridinu na N-oxid se reaktivita vůči elektrofilní substituci zvyšuje



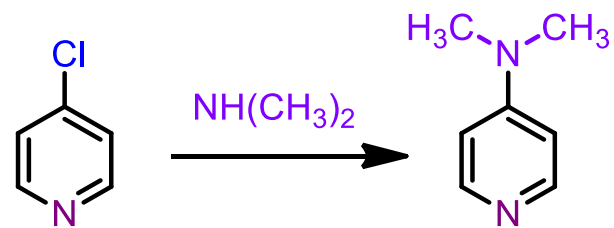
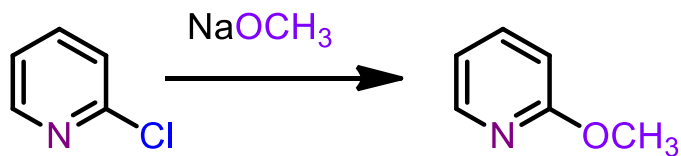
Nukleofilní substituce na pyridinu

- probíhají výrazně snadněji než na benzenu

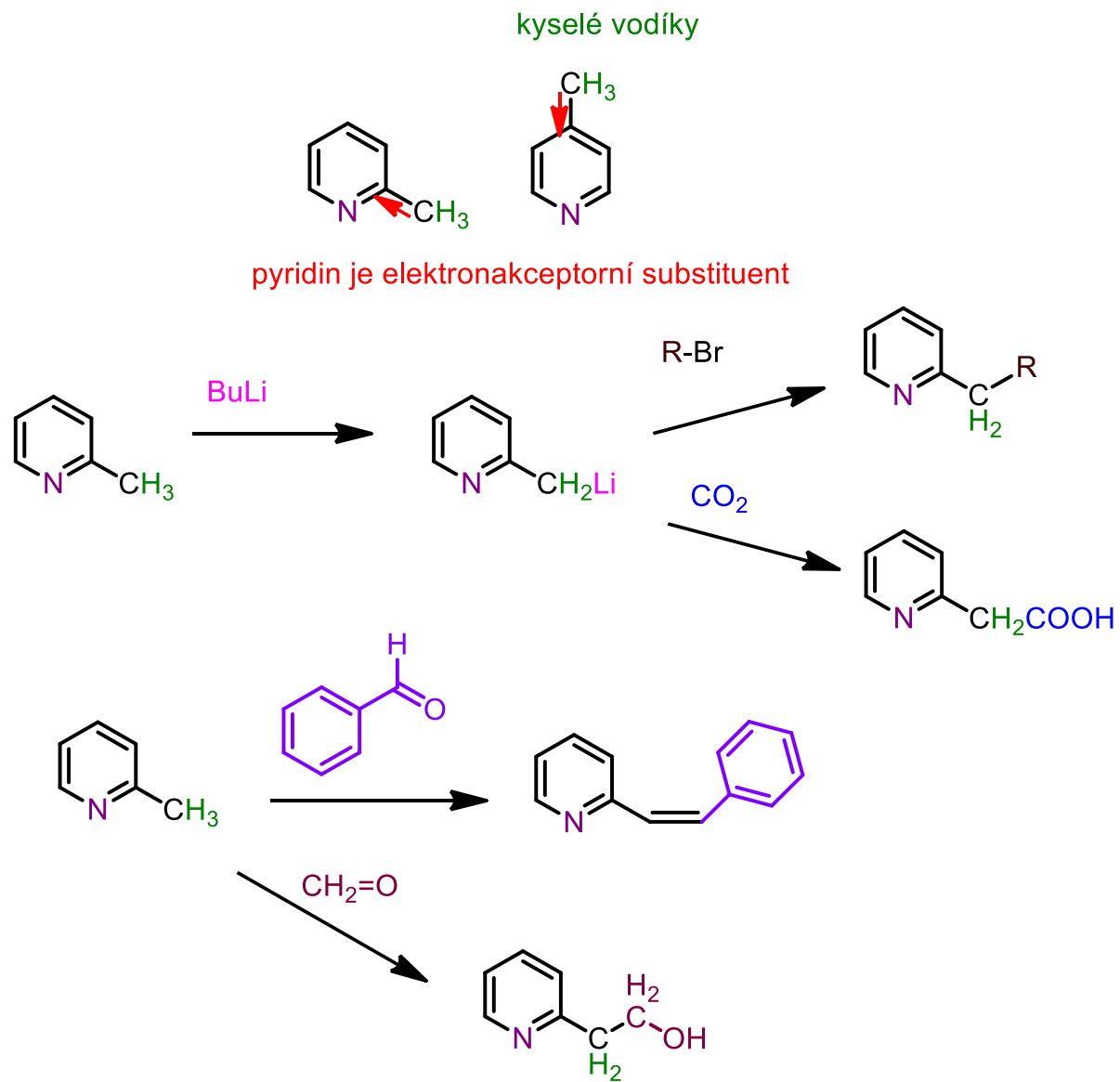
Čičibabinova reakce



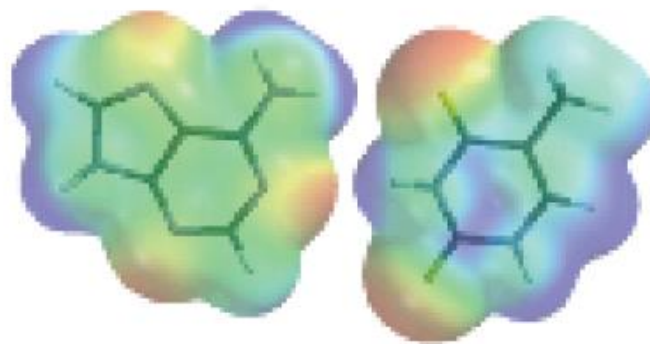
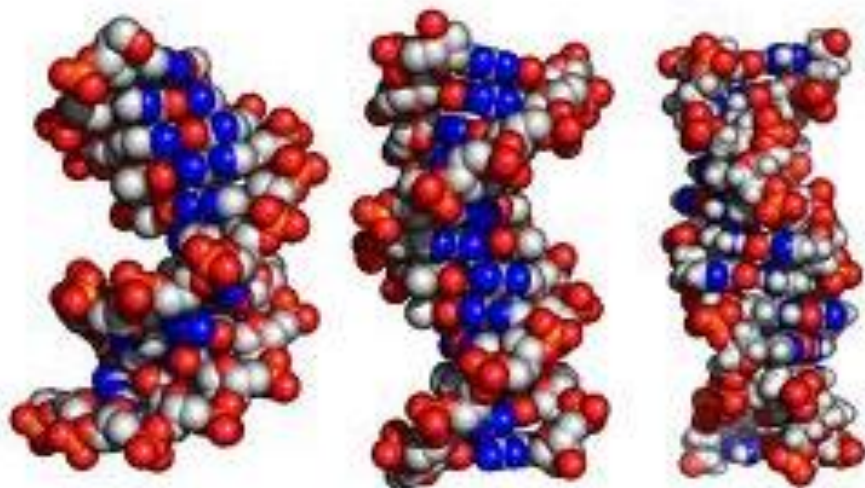
Nukleofilní substituce halogenpyridinů

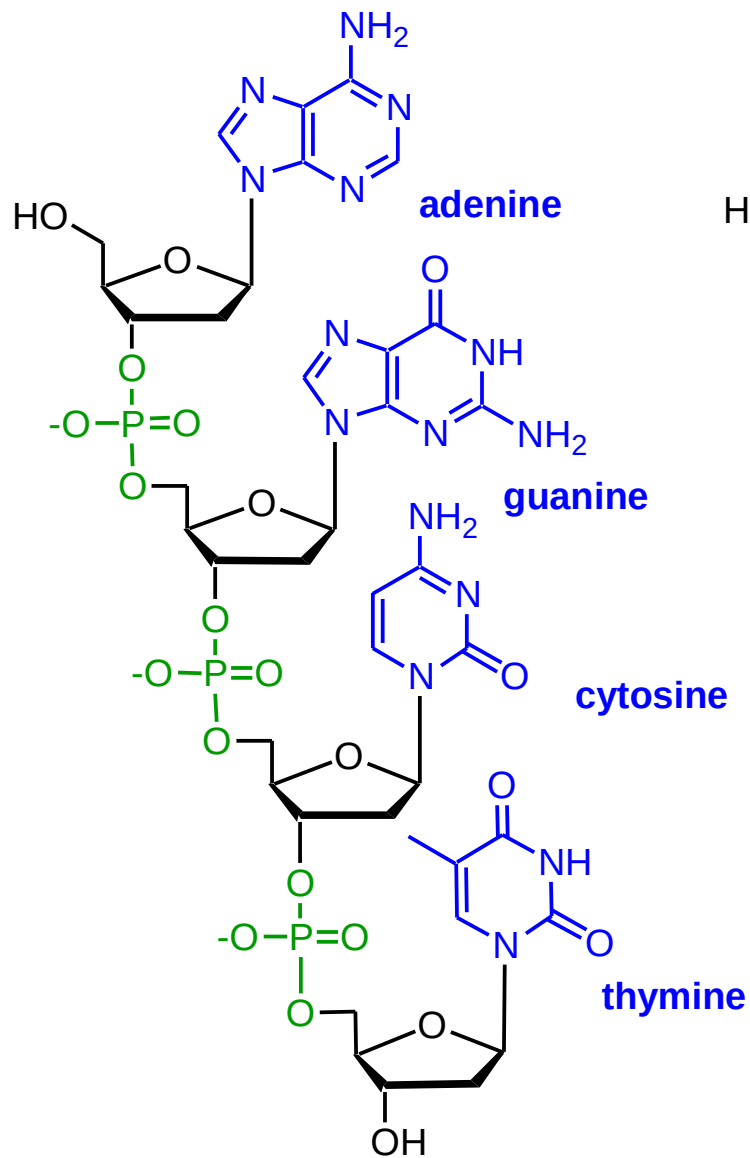


Reakce alkyldyridinů v α -poloze

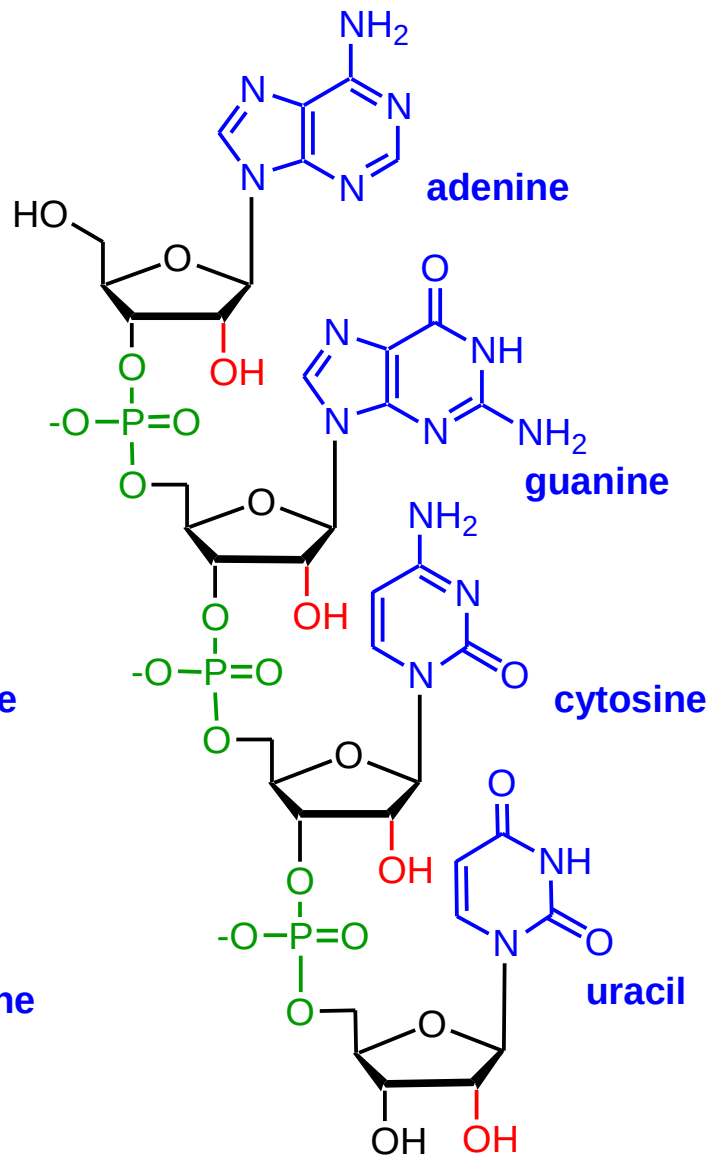


Nukleové kyseliny

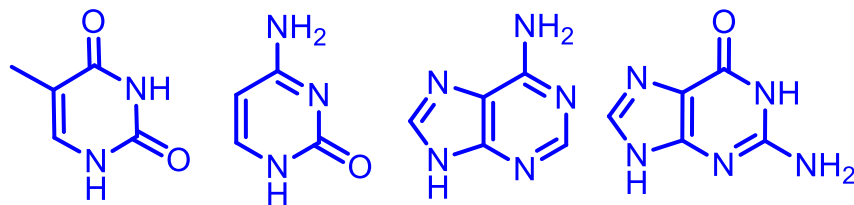




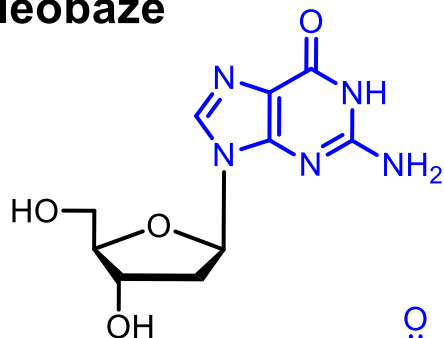
DNA



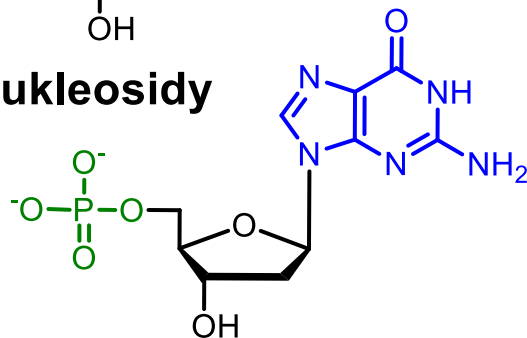
RNA



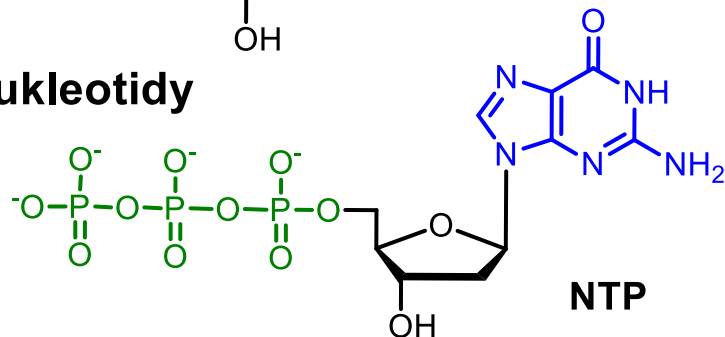
nukleobaze



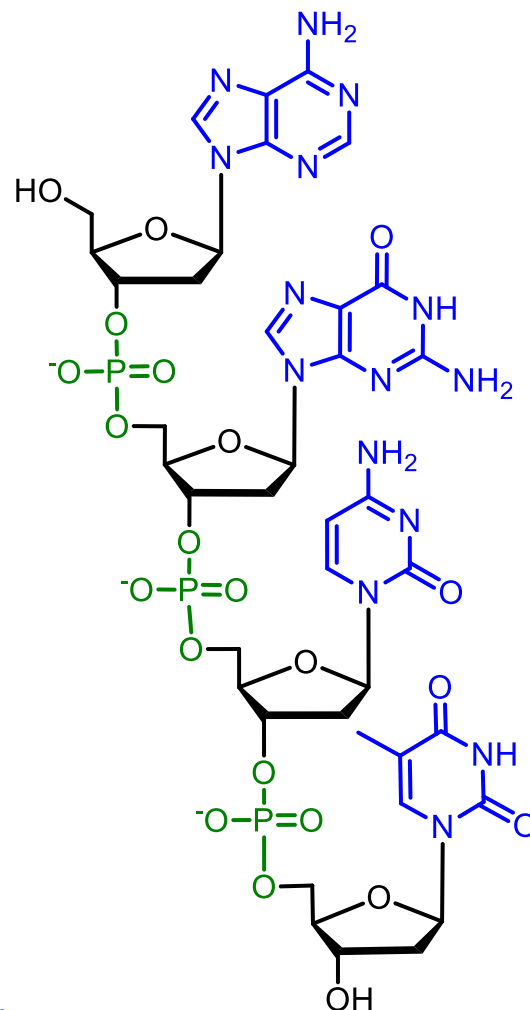
nukleosidy



nukleotidy



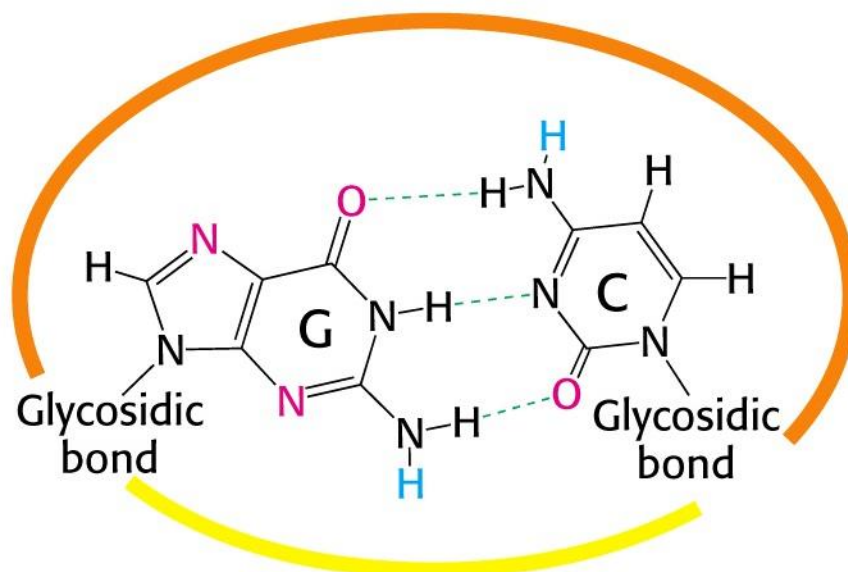
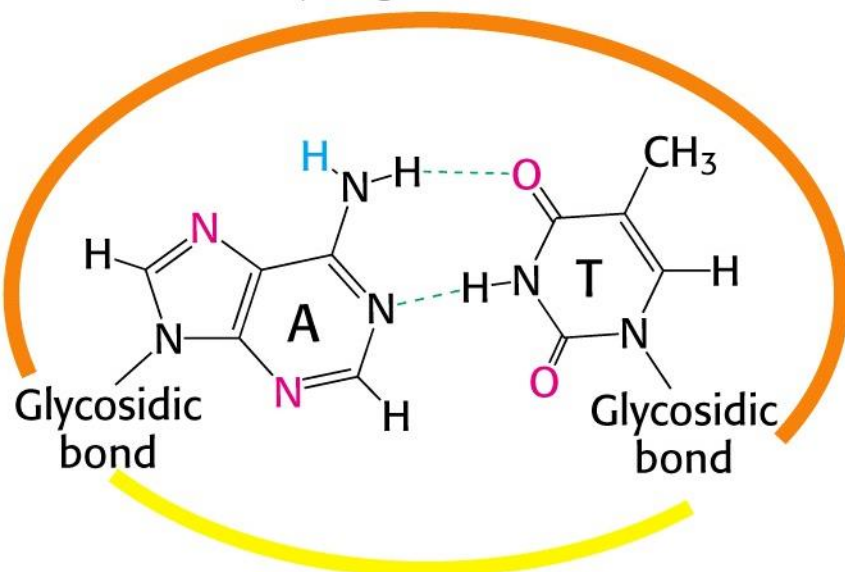
NTP



oligonukleotidy

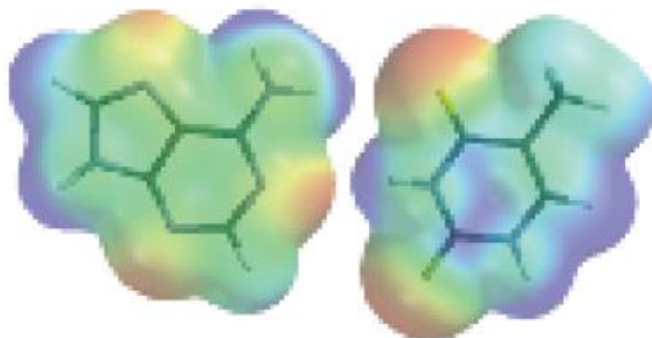
Watson-Crickovy páry bází

velký žlábek

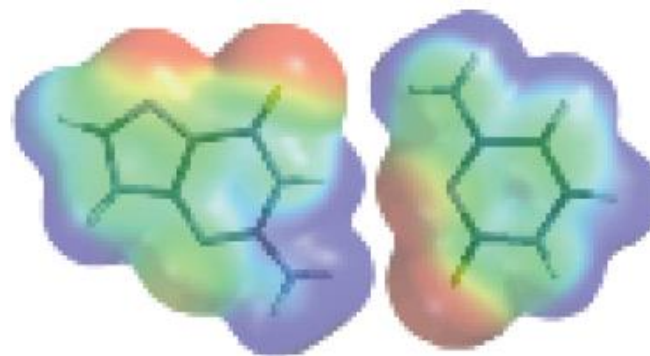


malý žlábek

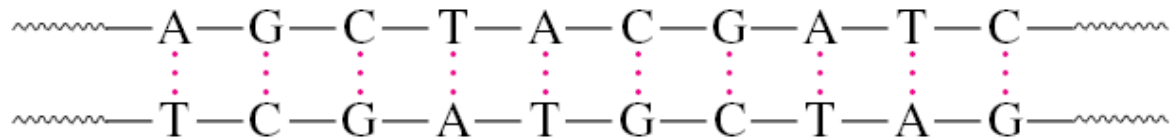
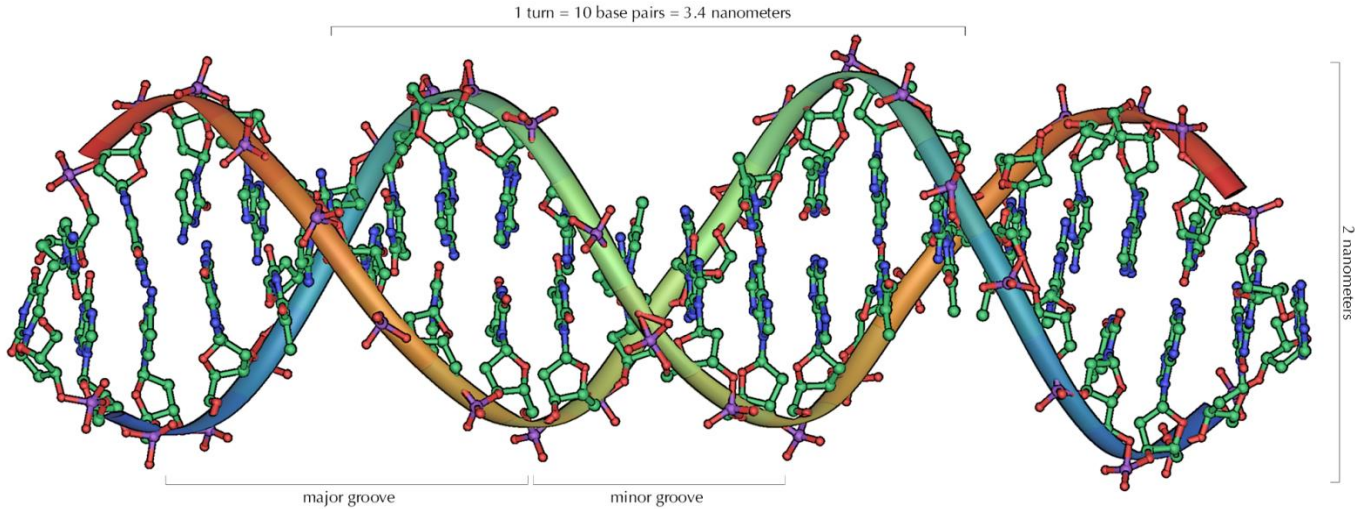
Adenin-Thymin



Guanin-Cytosin



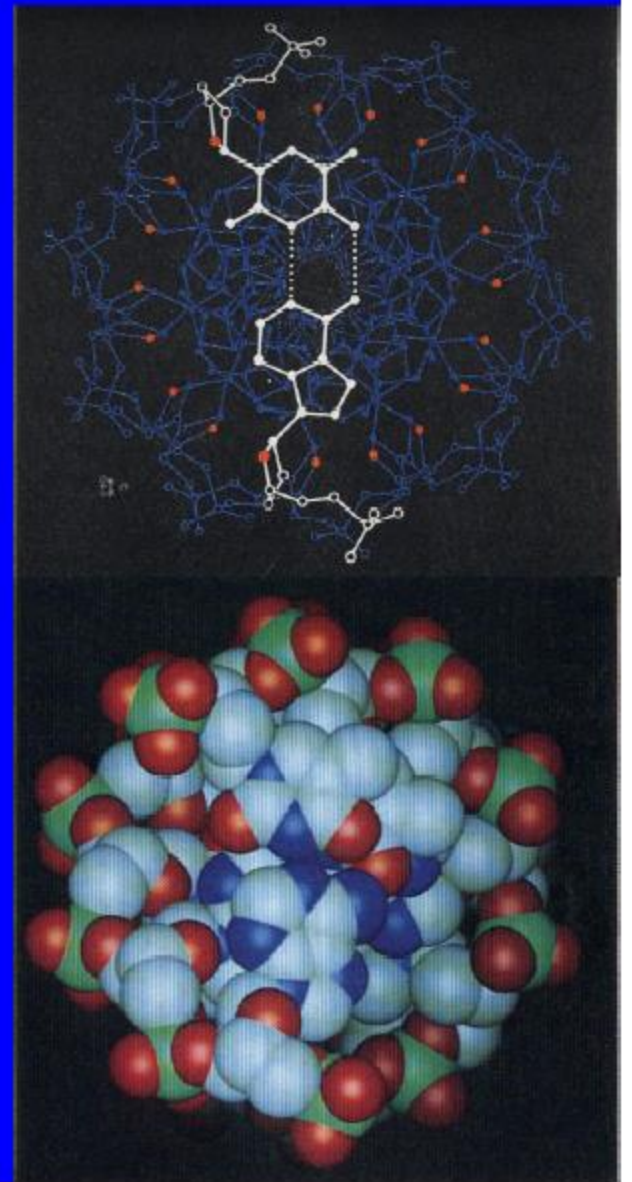
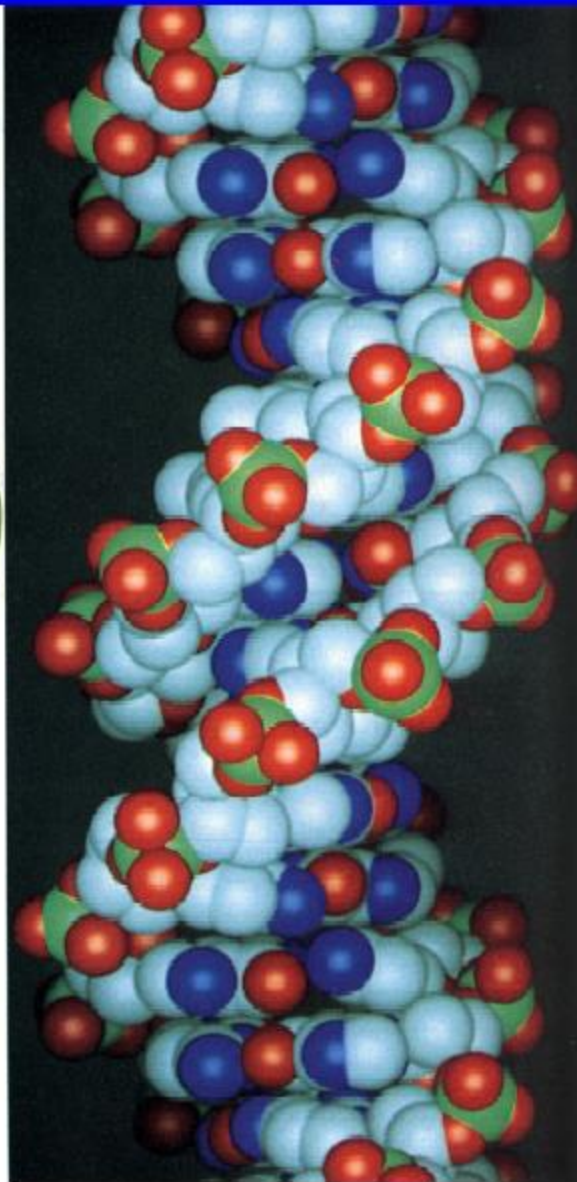
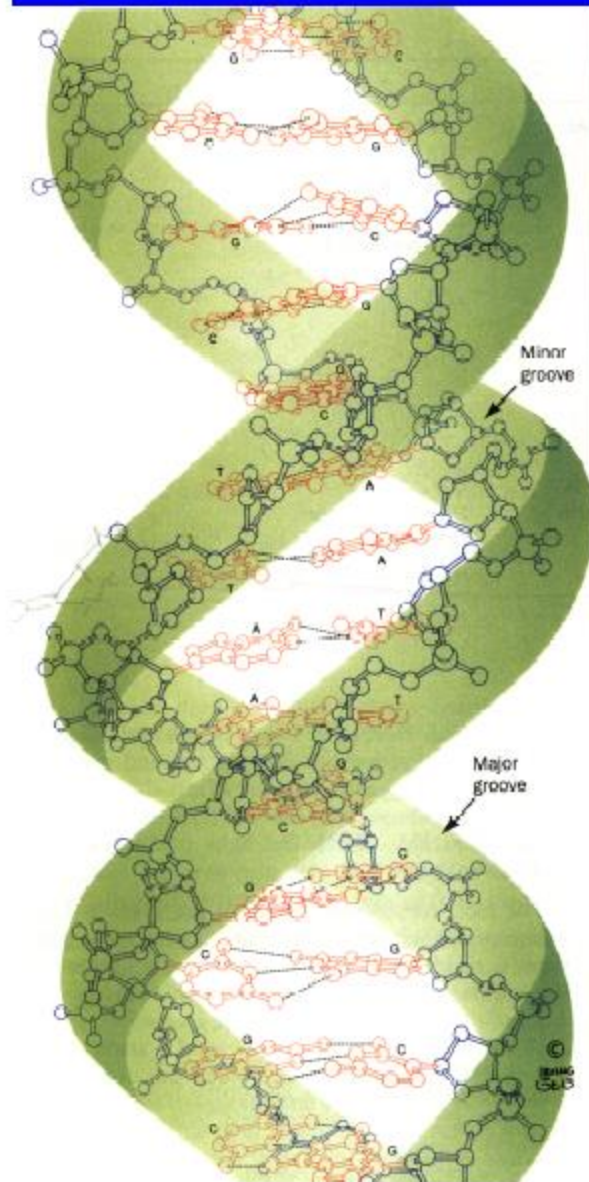
Struktura DNA dvoušroubovice

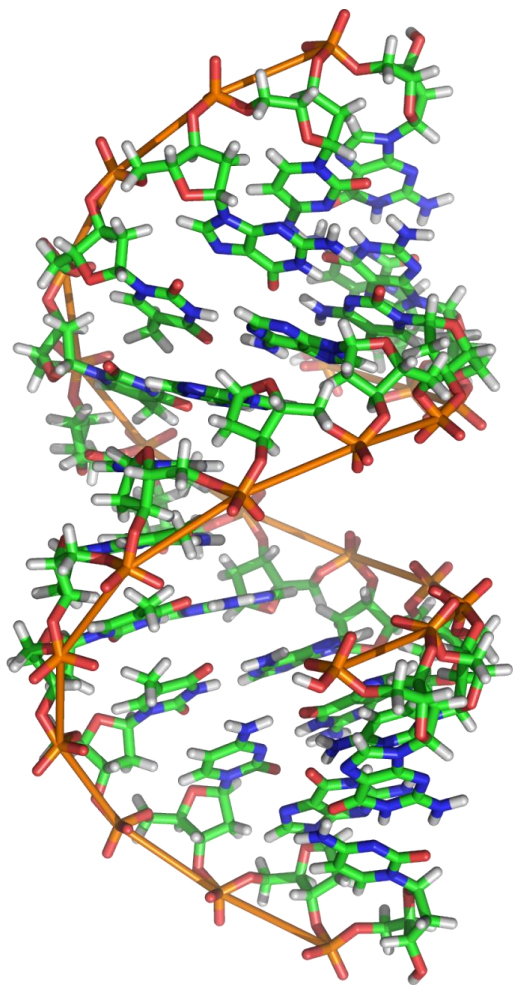


V sekvenci (pořadí) nukleotidů je zakódována genetická informace

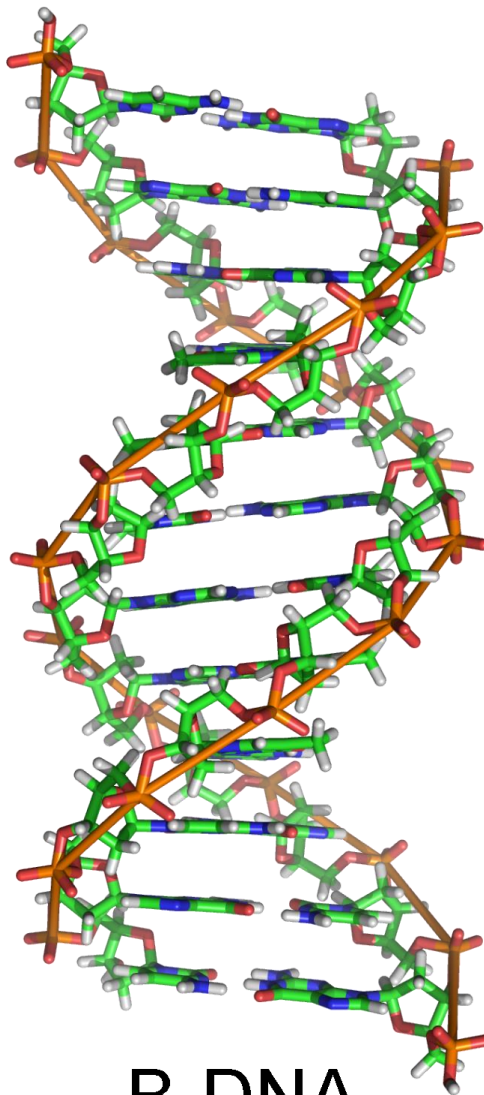
B-DNA

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

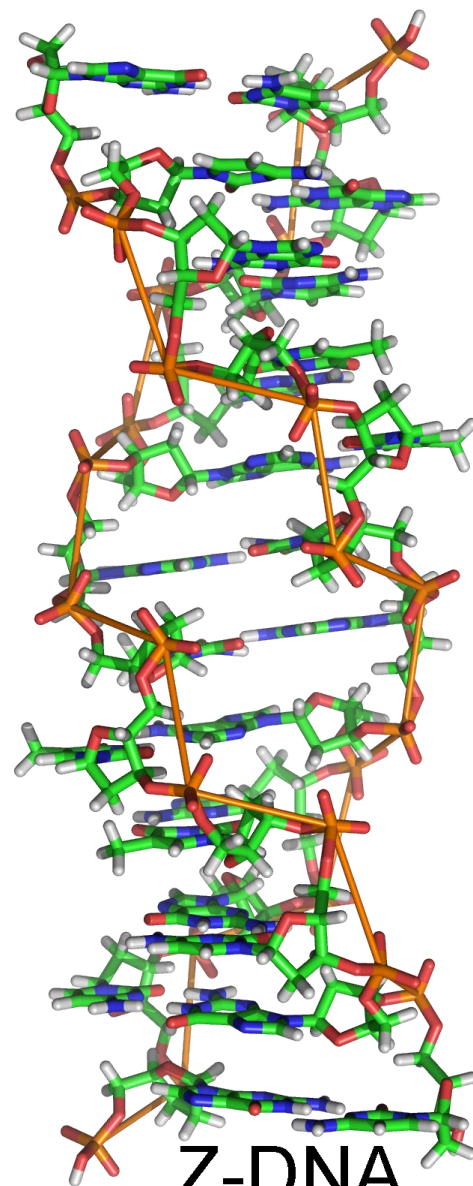




A-DNA

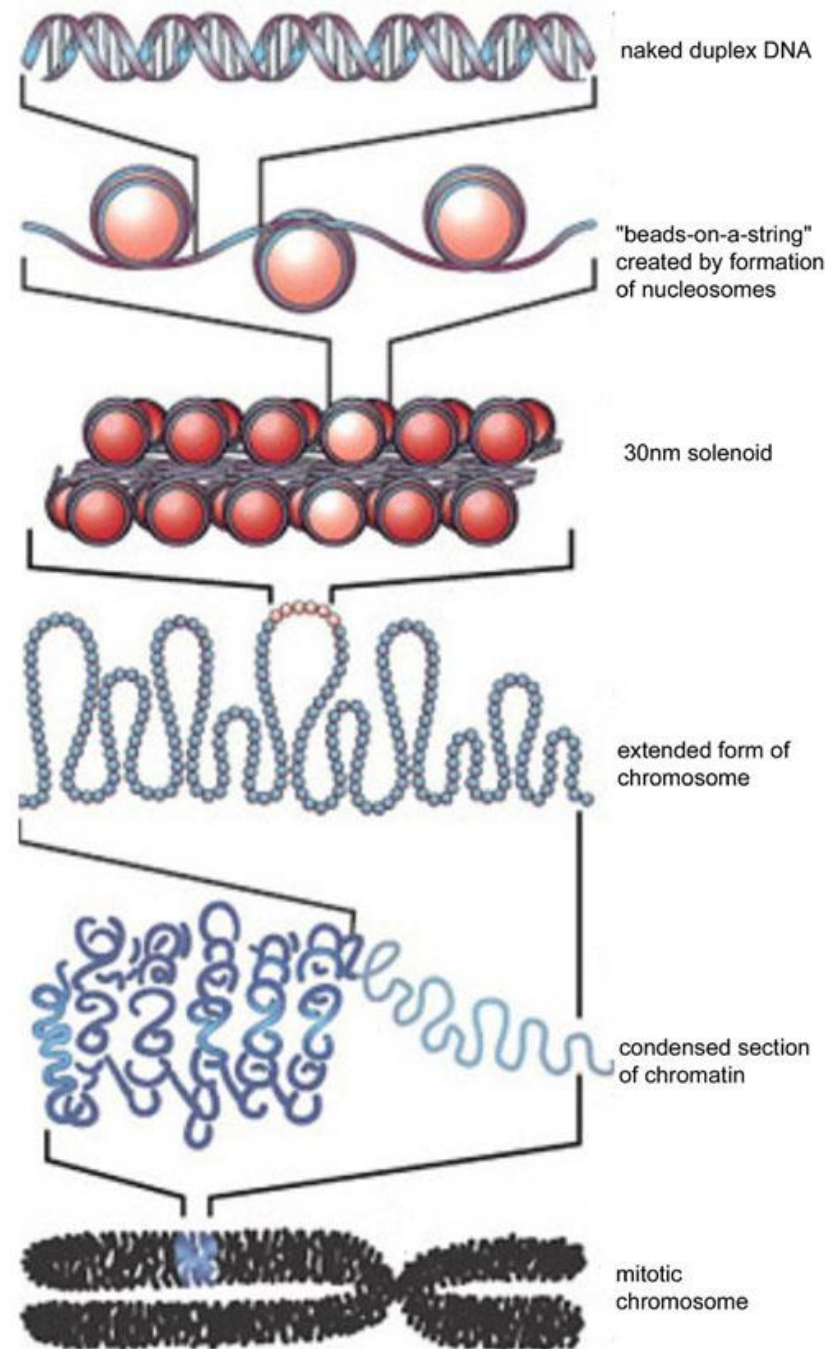
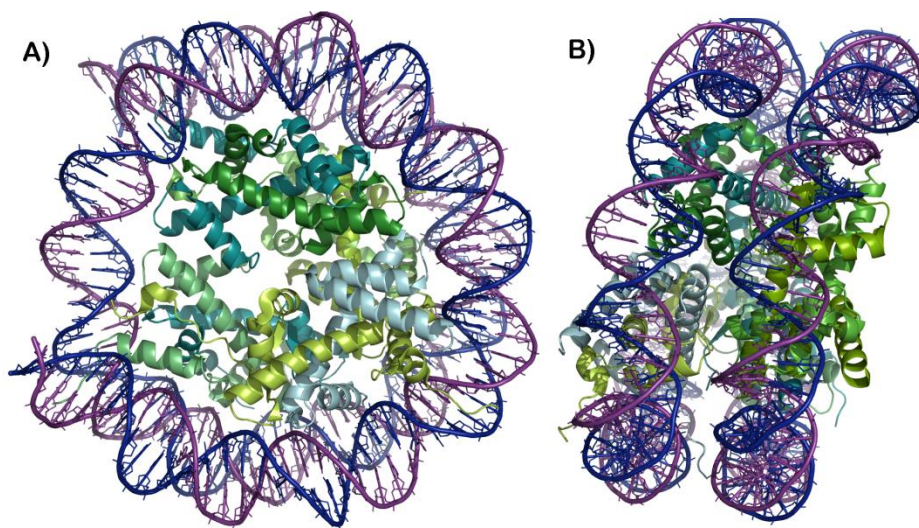


B-DNA

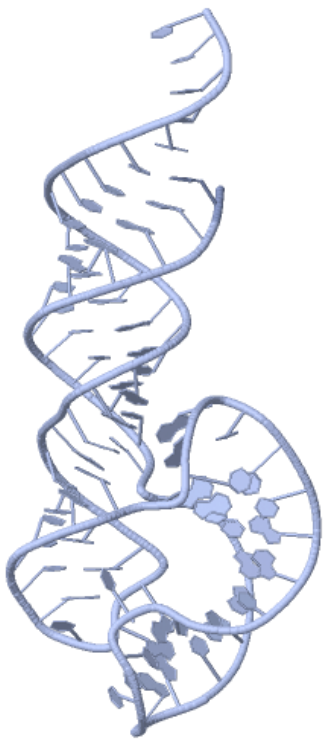


Z-DNA

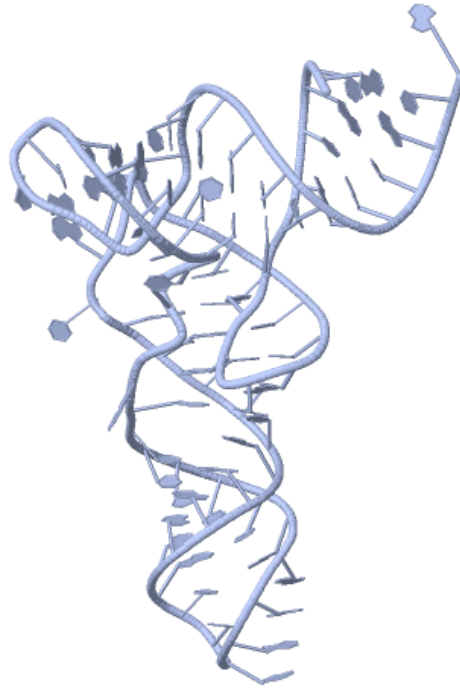
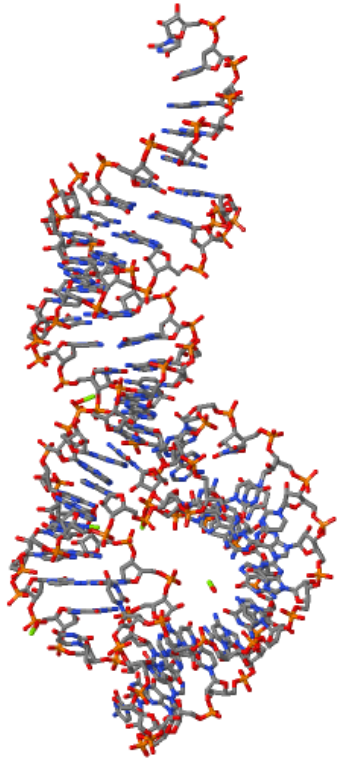
Složení chromatinu a chromozomů



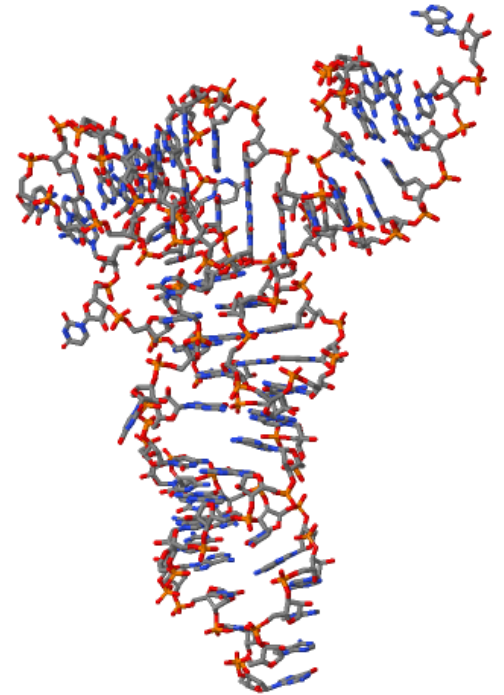
RNA

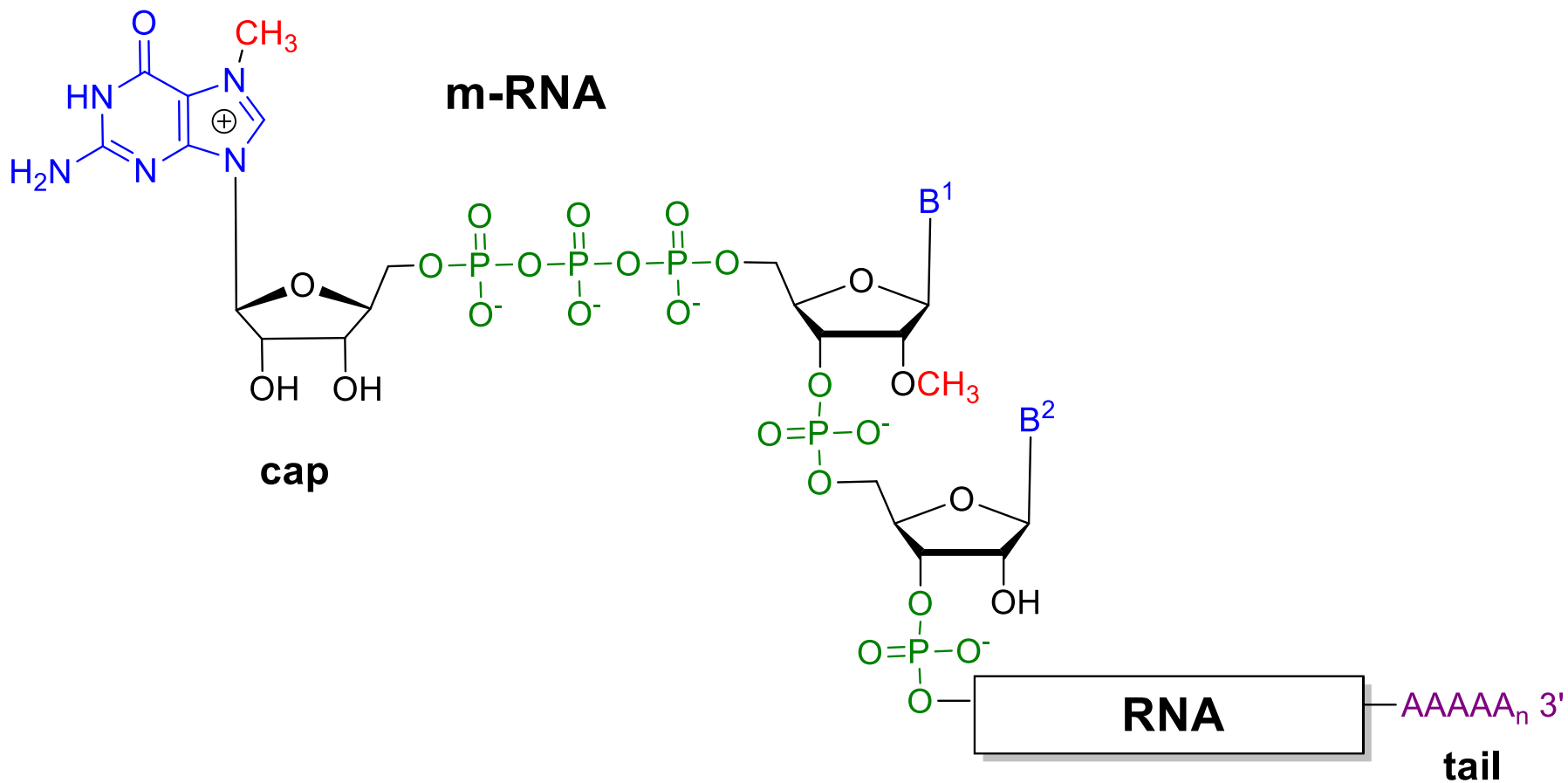


Hammerhead ribozyme

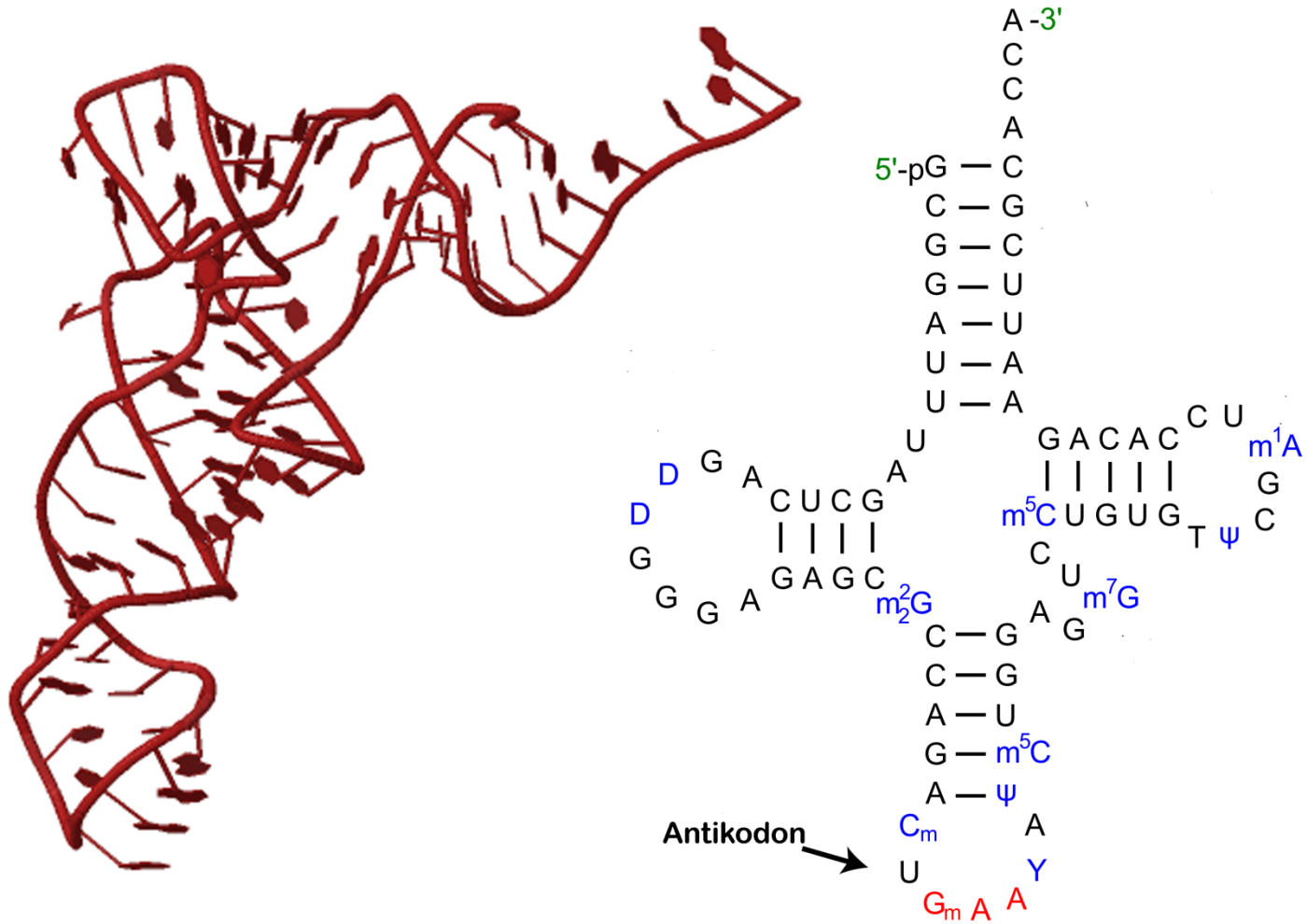


t-RNA(Phe)

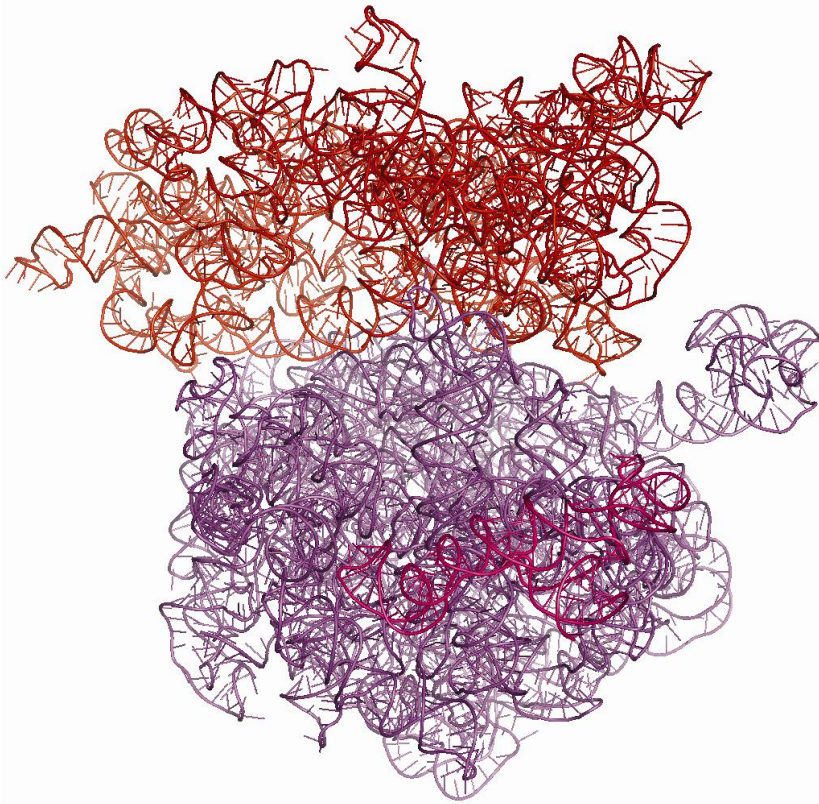




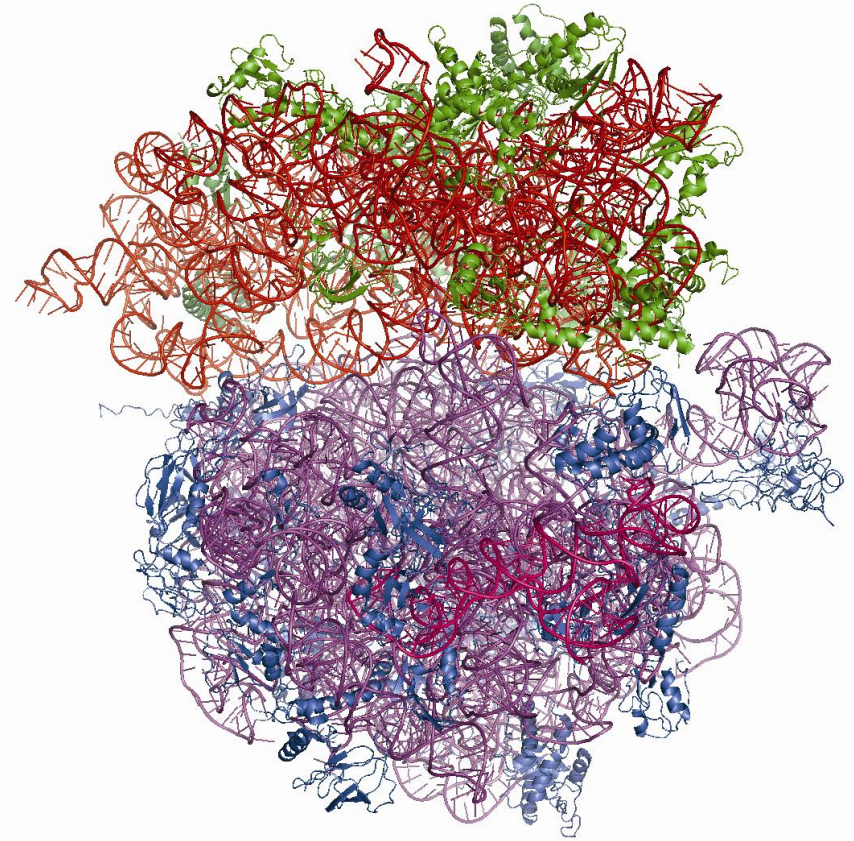
t-RNA



rRNA

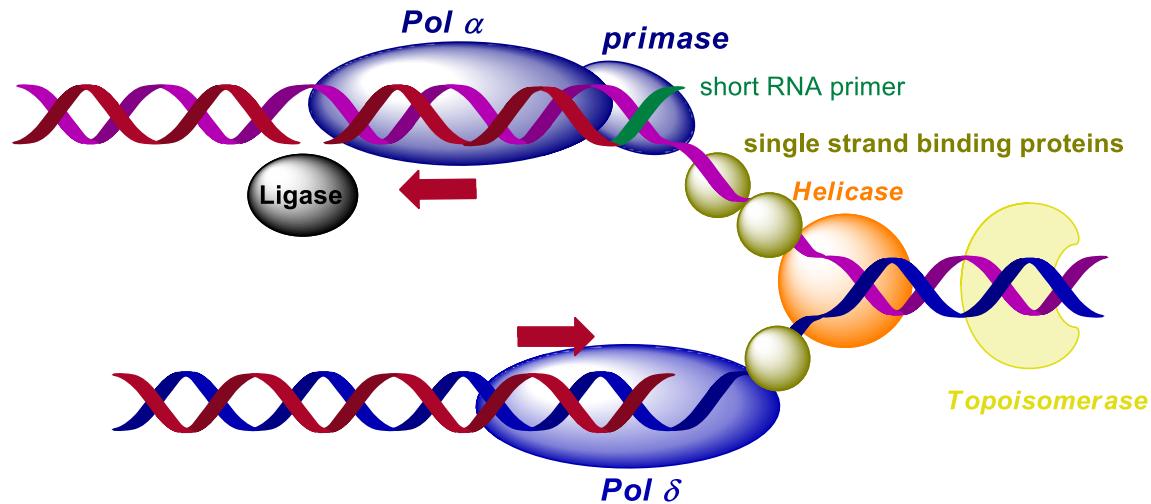
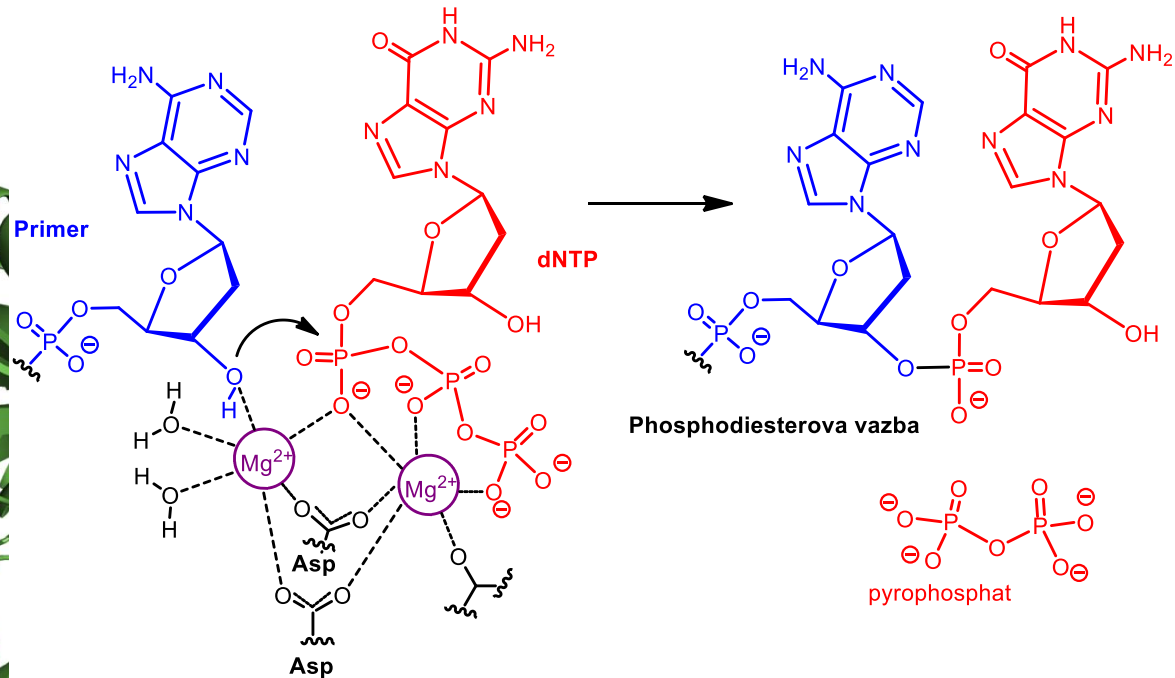
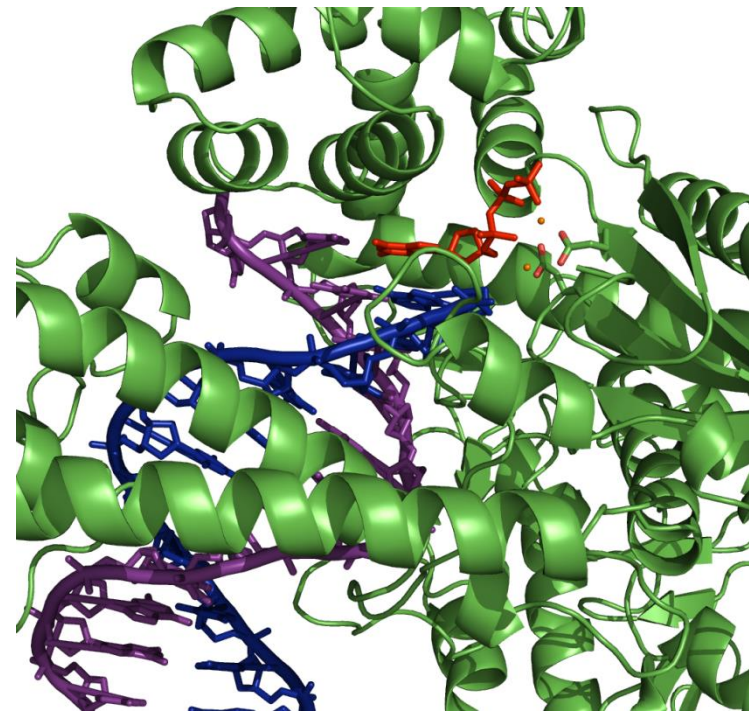


ribosomal RNA

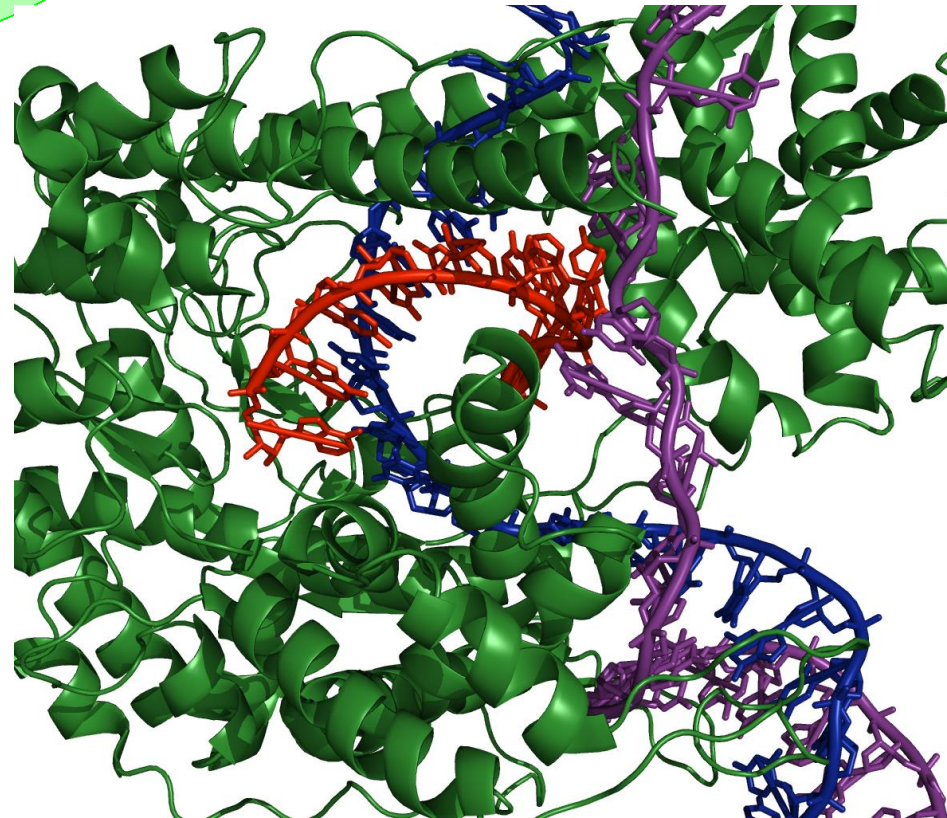
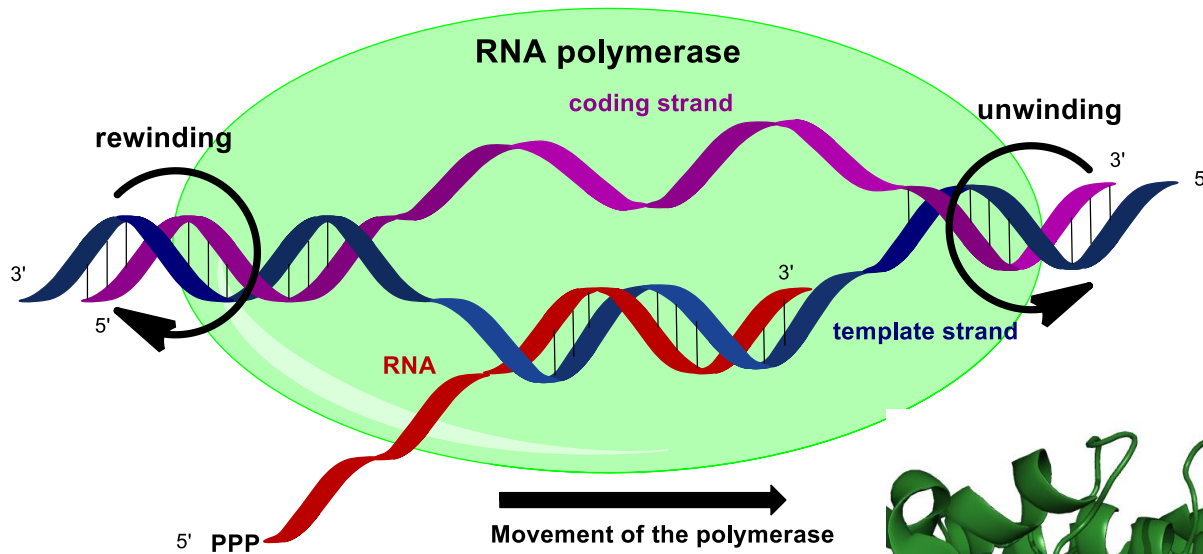


ribosomal RNA + proteins = ribosome

Biosyntéza DNA - DNA polymerasa

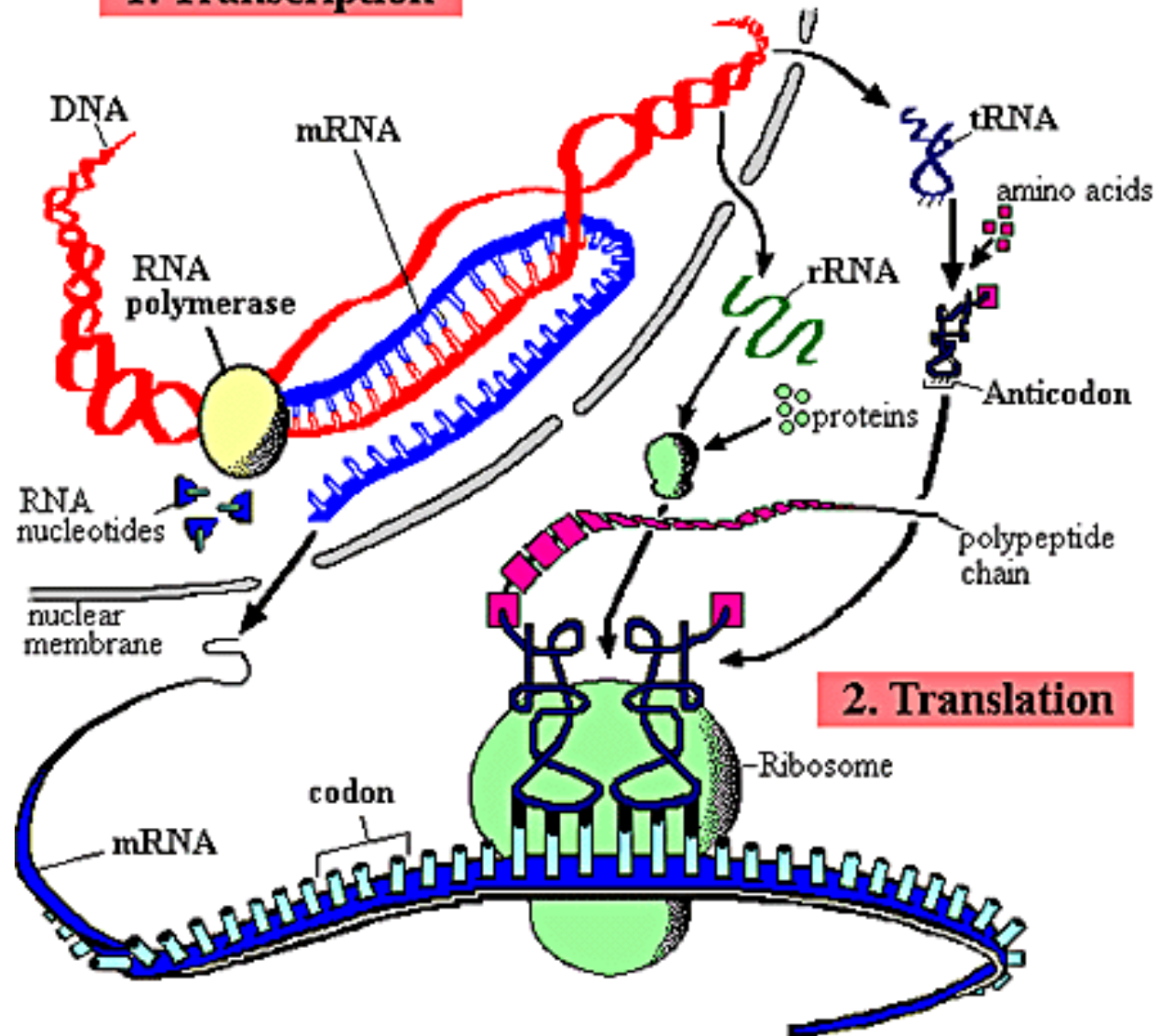


Biosyntéza RNA (transkripce) - RNA polymerasa

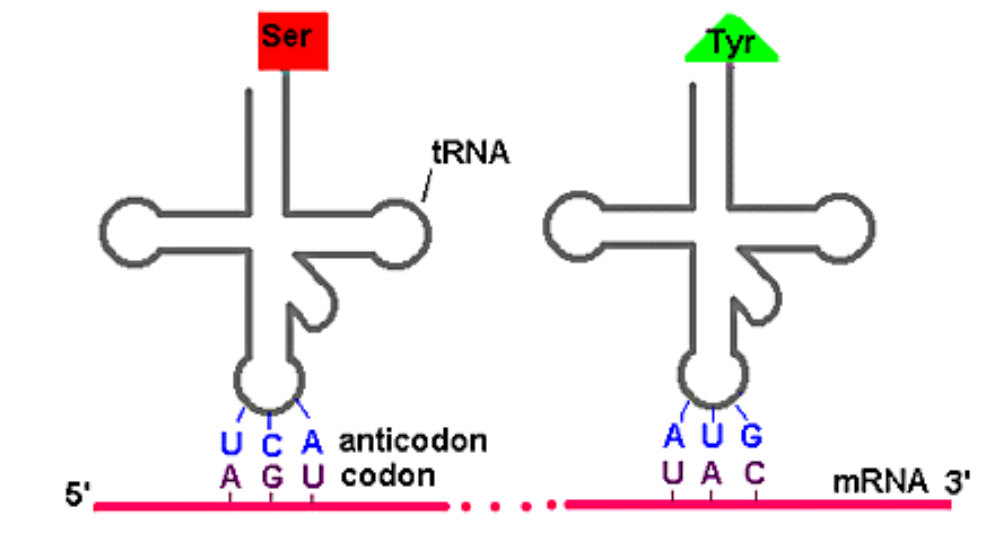


Centrální dogma molekulární biologie

1. Transcription

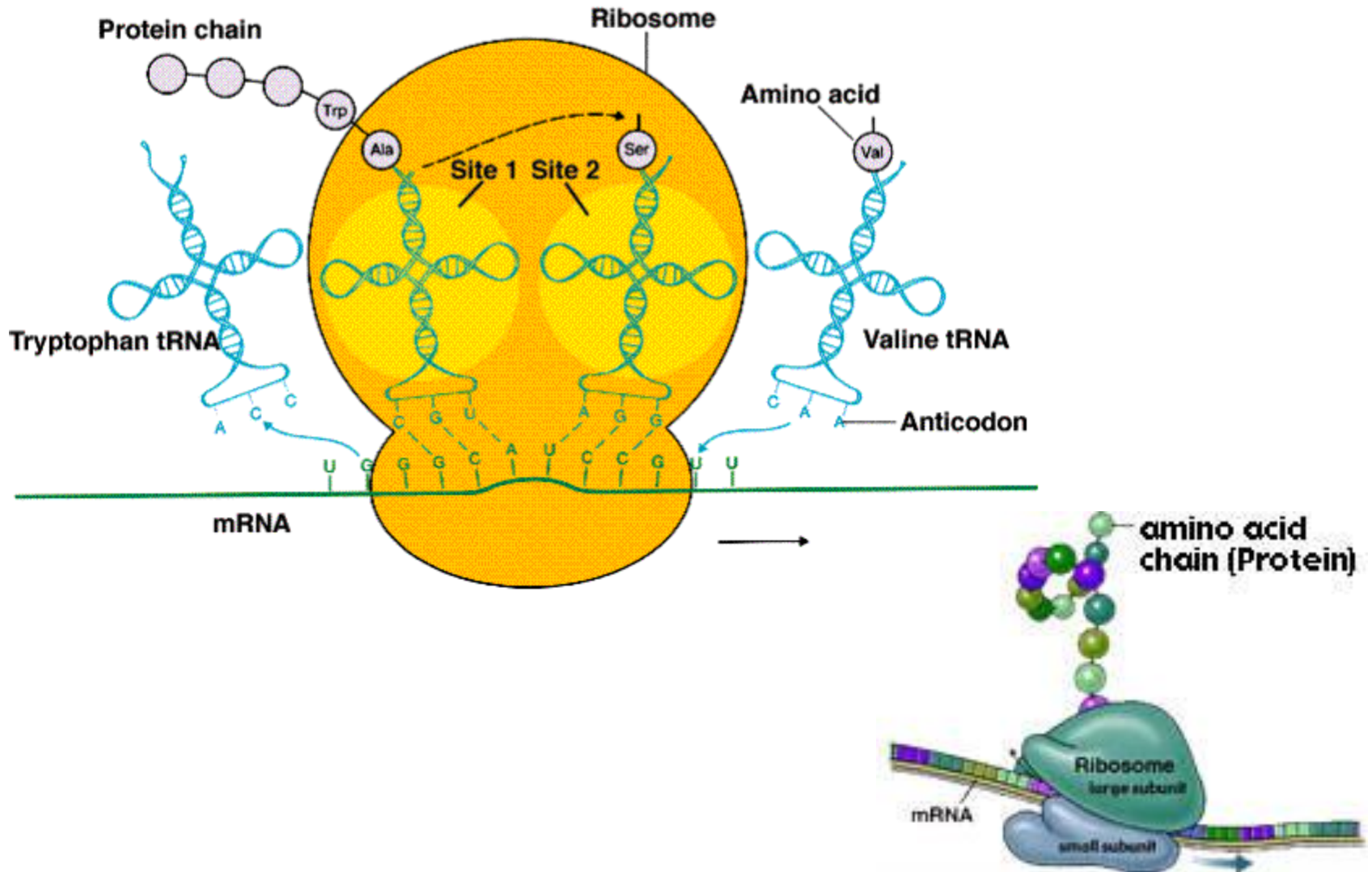


Genetický kód

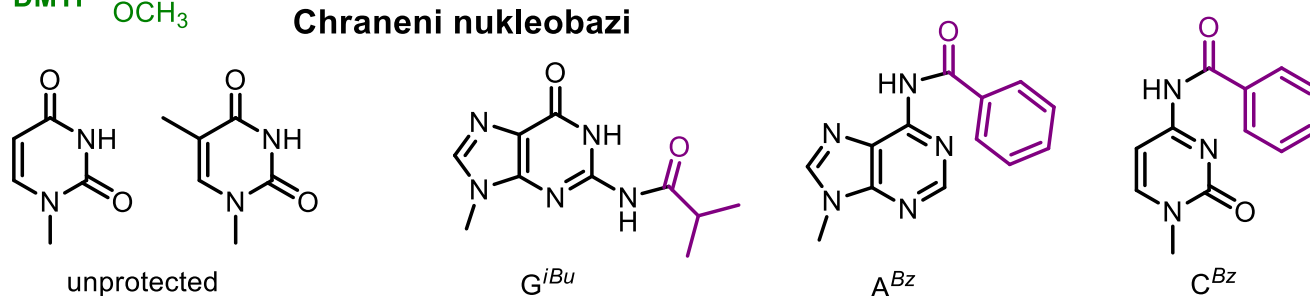
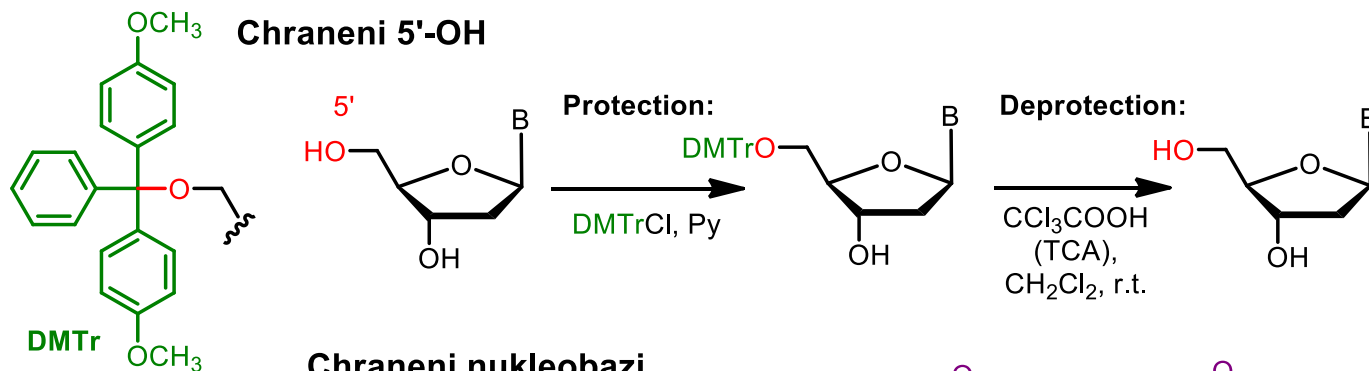


		2nd base in codon					
		U	C	A	G		
1st base in codon	U	Phe Phe Leu Leu	Ser Ser Ser Ser	Tyr Tyr STOP STOP	Cys Cys STOP Trp	U C A G	3rd base in codon
	C	Leu Leu Leu Leu	Pro Pro Pro Pro	His His Gln Gln	Arg Arg Arg Arg	U C A G	
	A	Ile Ile Ile Met	Thr Thr Thr Thr	Asn Asn Lys Lys	Ser Ser Arg Arg	U C A G	
	G	Val Val Val Val	Ala Ala Ala Ala	Asp Asp Glu Glu	Gly Gly Gly Gly	U C A G	

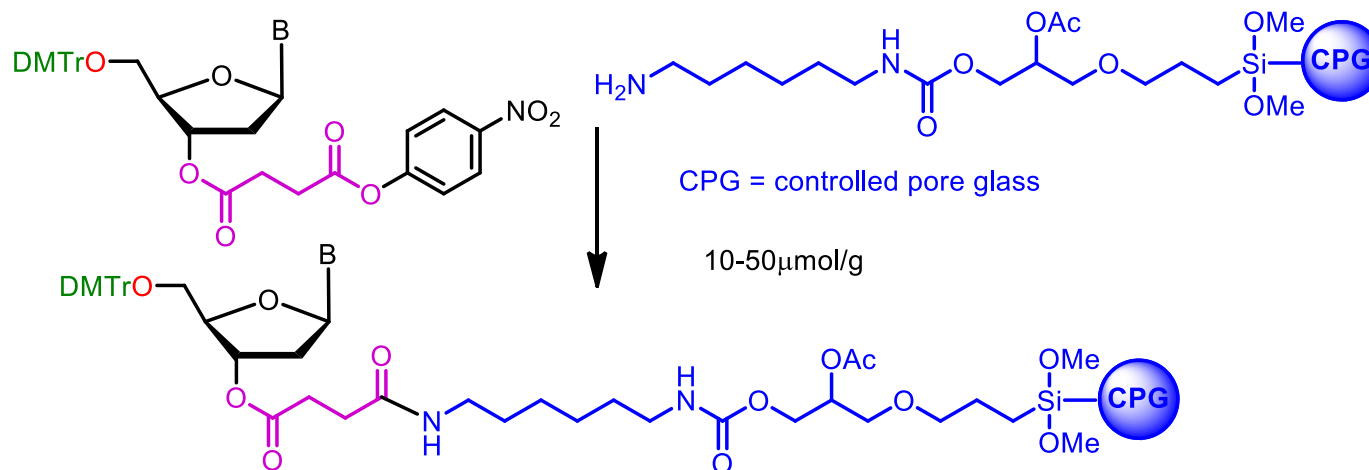
Syntéza proteinu na ribosomu (translace) – genová exprese



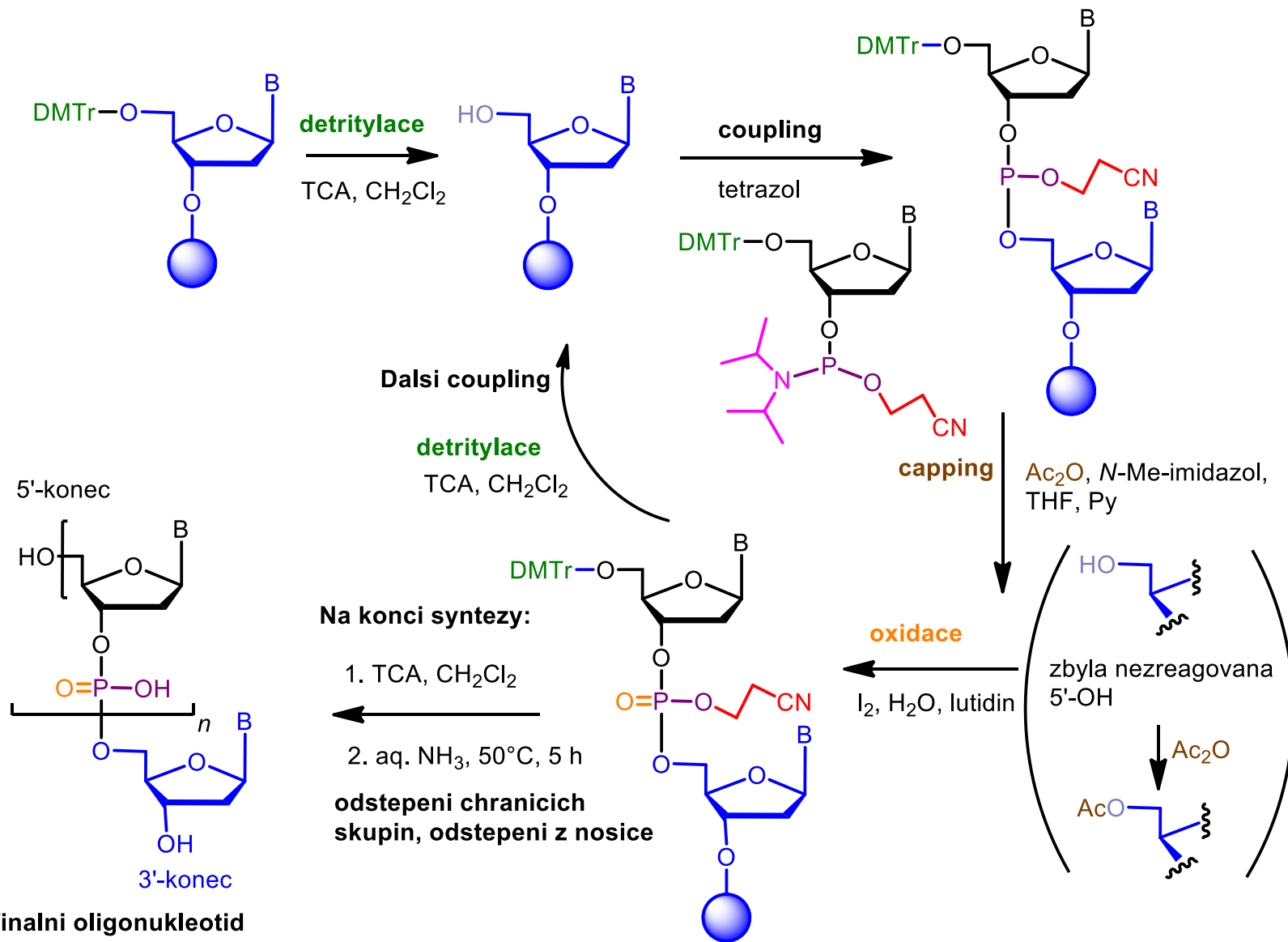
Syntéza oligonukleotidů

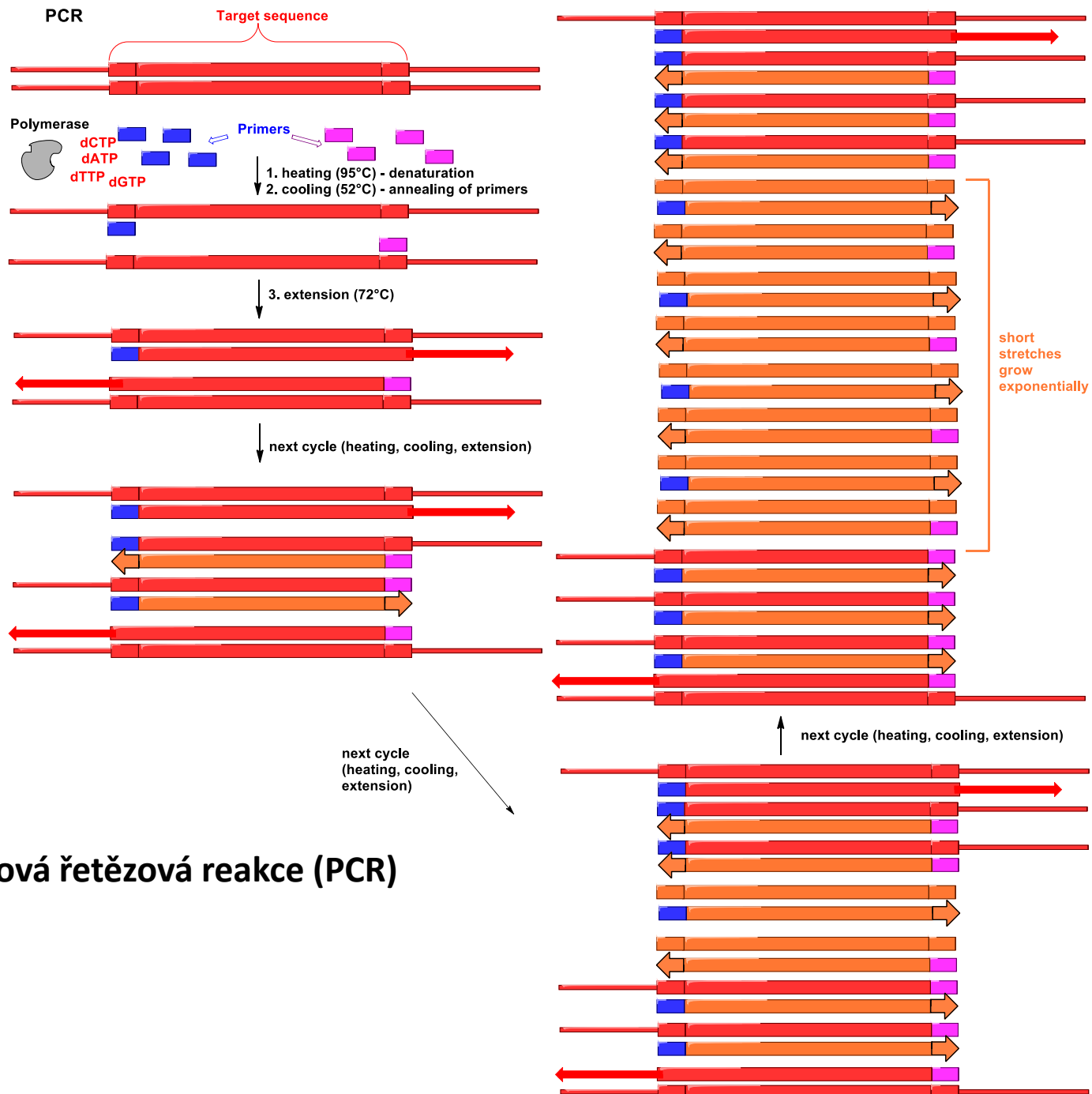


Pripojení k pevnému nosici



Syntéza oligonukleotidů





Polymerasová řetězová reakce (PCR)