10.

seminář LC

HETEROCYKLICKÉ SLOUČENINY

- organické sloučeniny
- kruh — uhlíkové atomy
  jiné atomy („heteros") O, S, N a j.

obvykle: 3, 4, (5), (6) a (7) členné kruhy

Vzestup stability:

- s méně deformovanými vazebnými úhly (menší pnutí) 5 a 6 členné kruhy

- s maximem konjugovaných dvojných vazeb (aromatický charakter, delokalizované π-elektrony).

Malá stabilita:

- jednoduché laktony
- laktamy
- anhydridy dikarboxylových kyselin
- hemiacetaly (= cyklické formy monosacharidů)

chybí konjugované vazby !

O -ox-

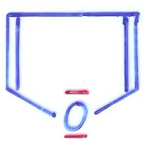
S -thi-

N -az-

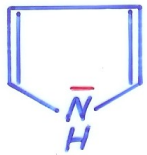
5 členný -ol

6 členný -in

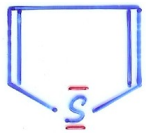
7 členný -epin



furan



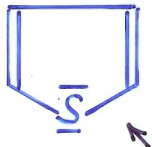
pyrrol/e



thiofen
thiophene

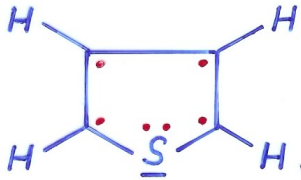
elektronegativita / electronegativity: C 2,5

O 3,5 N 3,0 S 2,5



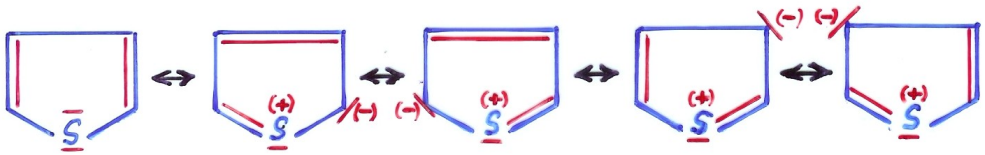
thiofen
thiophene

schematický vzorec
common formula



sextet
π-e⁻

elektronový vzorec
electron formula



mezomerie thiofenu
resonance in thiophene

aromatický charakter
→ „heteroarény"

aromatic character

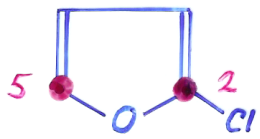
~~adiční reakce~~
↓ zásadité vlastnosti
~~addition reaction~~
↓ basic properties

Elektronová hustota

(vyšší v polohách 2 a 5
u 5členných heterocyklů)

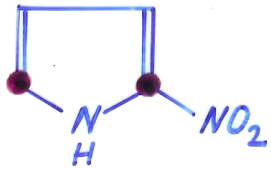
Electron density

(higher in the positions 2 and 5
in 5-membered heterocycles)



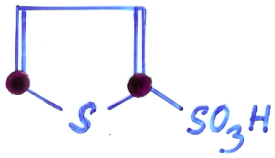
halogenace
halogenation

(2-chlor(o)furan)



nitrace
nitration

(2-nitro·pyrrol/e)



sulfonace
sulfonation

(2-thiofen-
sulfonová kys.
2-thiophene-
sulfonic acid)

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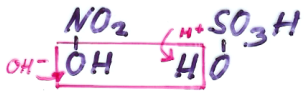
elektrofilní substituce
electrophilic substitution



$HNO_3 + H_2SO_4 \rightarrow NO_2^+ + HSO_4^- + H_2O$

nitronium

Elektronová hustota

(vyšší v polohách 3 a 5 u 6 členných heterocyklů)

Electron density

(higher in the positions 3 and 5 in 6-membered heterocycles)

Hückelovo pravidlo aromatičnosti :

monocyklické planární uhlovodíky,
které obsahují (4 n + 2) π elektrony (n = 0, 1, 2, 3, …)
mají velkou stabilizační (konjugační) energii
a nepodléhají reakcím typickým
pro sloučeniny s dvojnými vazbami
→ aromatický charakter → elektrofilní substituční reakce

Aromatický charakter :

1/ nesnadnost adice

2/ odolnost vůči oxidačnímu štěpení

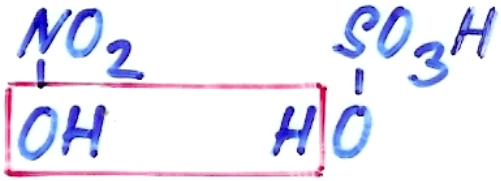
3/ substituce

4/ elektronegativní vliv na substituenty

5/ polarizace kruhu vlivem mesomerního efektu substituentů

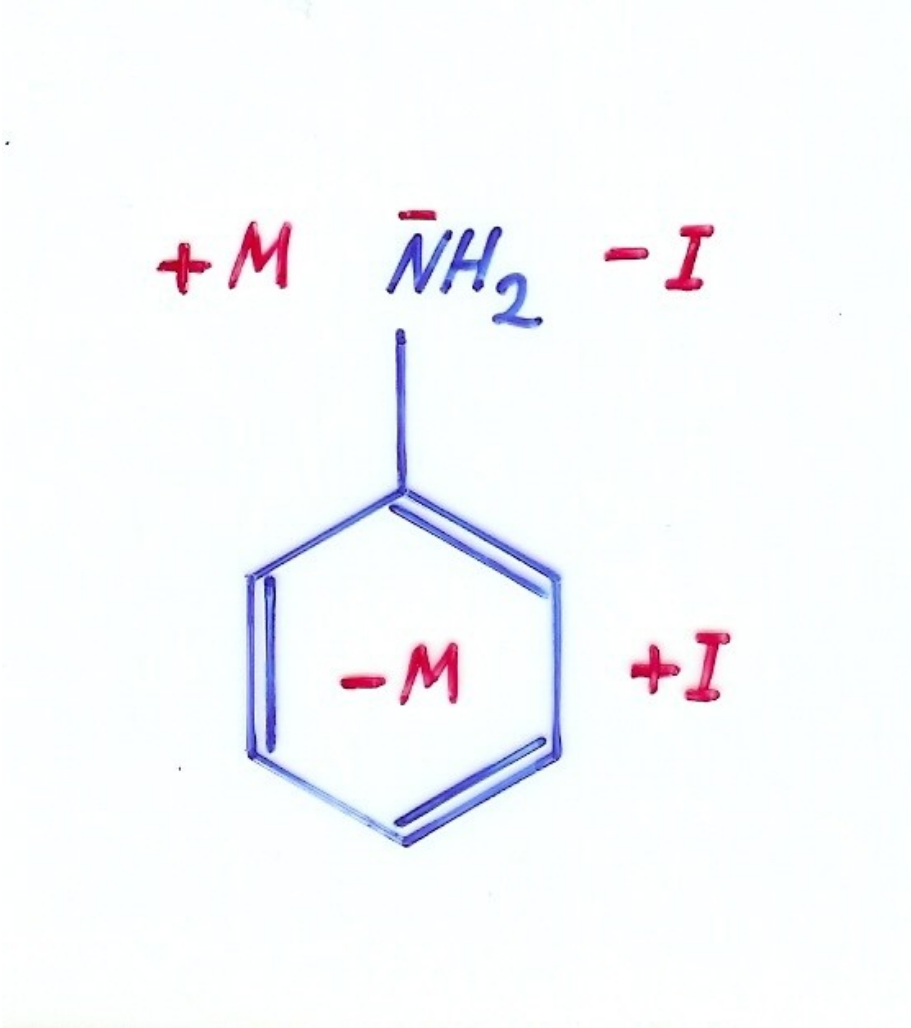
$HNO_3 + H_2SO_4 \longrightarrow NO_2^+ + HSO_4^- + H_2O$

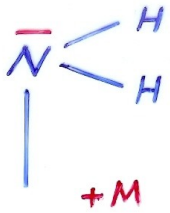
nitronium

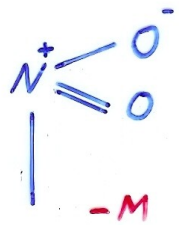


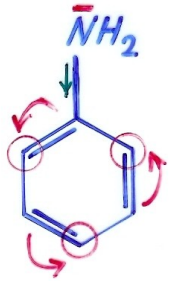
elektrofilní substituce

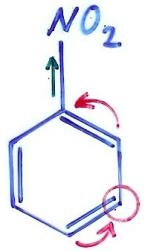
(nitrace, halogenace
sulfonace ...)


+M
$\bar{N}H_2$
-I
-M
+I







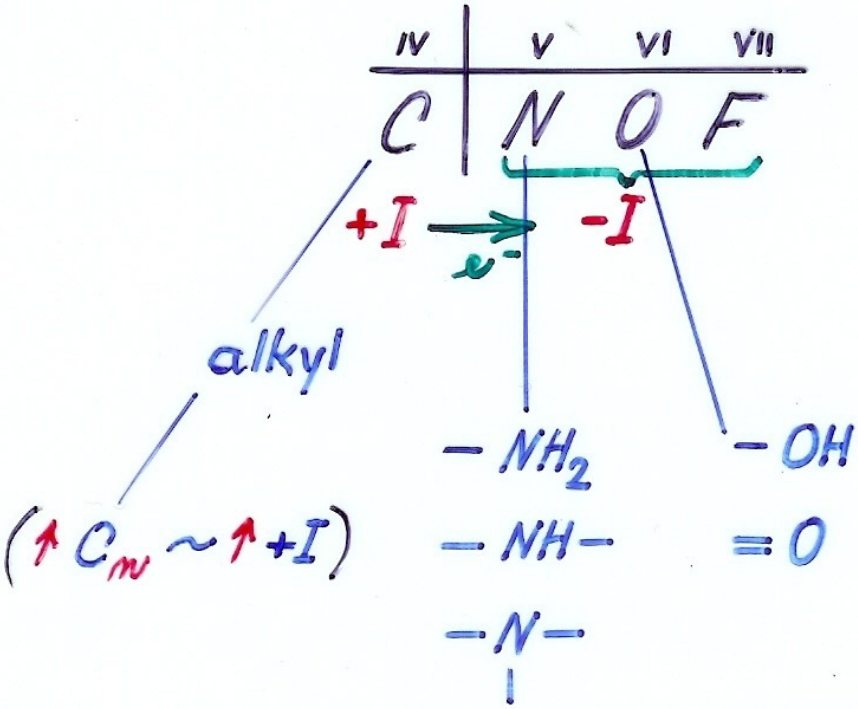


- Cl
- Br
- I

- O-H
- NH_2
- ....

- NO_2
- CHO
- COOH
- SO_3H
- ....

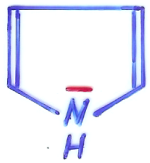
O ?
elektro-neg.



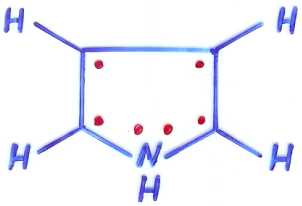
$R \longrightarrow \bar{N}H_2$

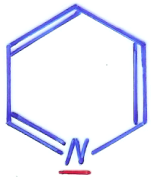
+I -I

- název: výsledný stav
- „součet" I

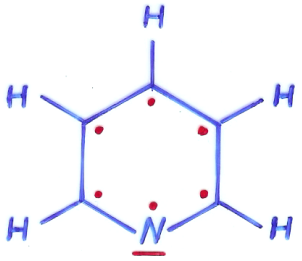


pyrrol/e





pyridin/e



V 5-členných heterocyklech heteroatom poskytuje 2 elektrony pro aromatický sextet π elektronů.

V 6- —— " ——

1 elektron —— " ——.

In the 5-membered heterocycles, the heteroatom contributes 2 electrons to the aromatic 6π system,

whereas in 6- —— " ——

—— " — only 1 electron —— " ——.

pyrrol/e

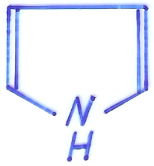
→ kyselý (bezvodé prostředí)

→ acidic / waterfree medium

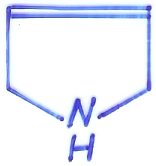
pyridin/e

→ zásaditý

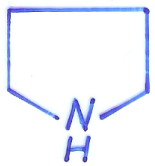
→ basic



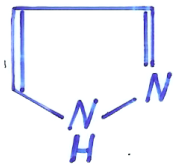
pyrrol/e
(azol/e)



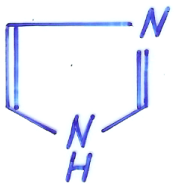
pyrrolin/e



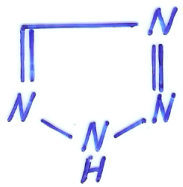
pyrrolidin/e



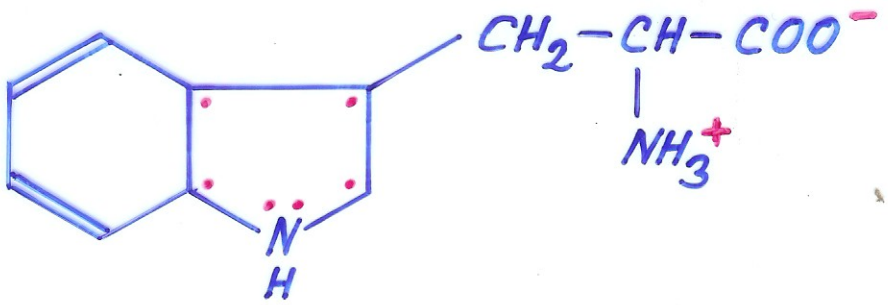
pyrazol/e
(1,2-diazol/e)



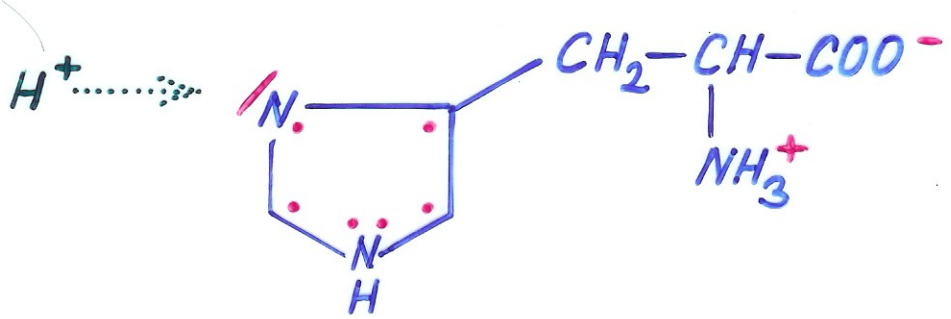
imidazol/e
(1,3-diazol/e)



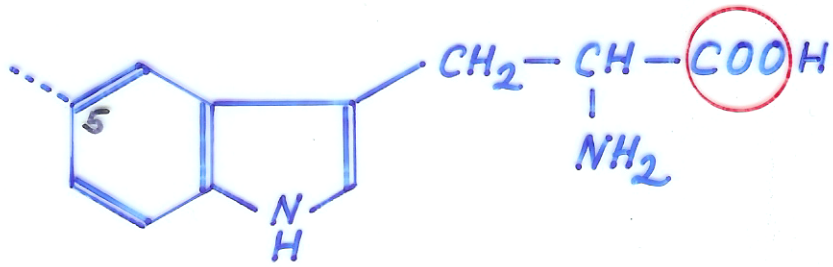
1,2,3,4-
tetrazol/e



Trp

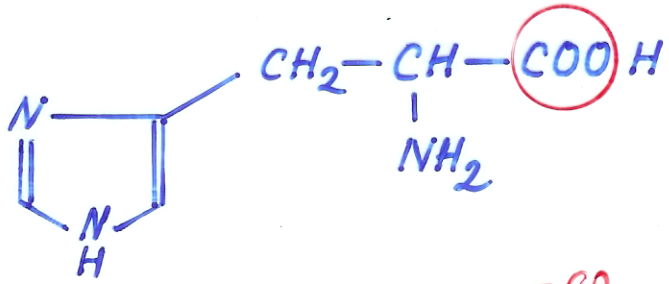


His

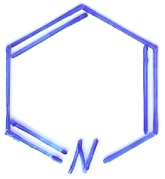


Trp $\xrightarrow{-CO_2}$ tryptamin/e

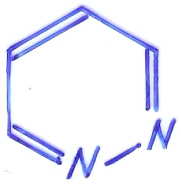
serotonin = 5-hydroxy-tryptamin/e



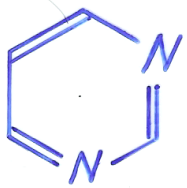
His $\xrightarrow{-CO_2}$ histamin/e



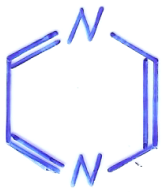
pyridin/e
(azin/e)



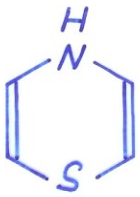
pyridazin/e
(1,2-diazin/e)



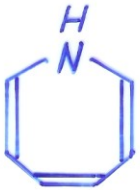
pyrimidin/e
(1,3-diazin/e)



pyrazin/e
(1,4-diazin/e)

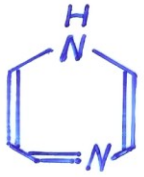


thiazin/e ‹θai'azi:n›



azepin/e ‹'azipən›

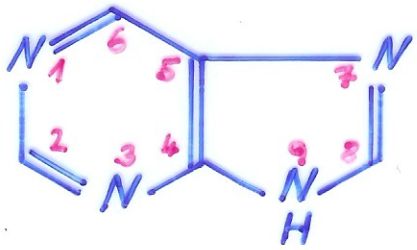
thiepin/e ‹θai'i:pin›



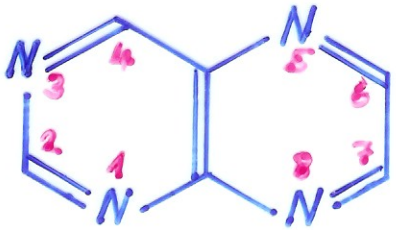
diazepin/e ‹dai'zi:pin›

di- thi- az- 6-in/e 7-epin/e

nenasycené
unsaturated
(Hantzsch + Widman)



purin/e

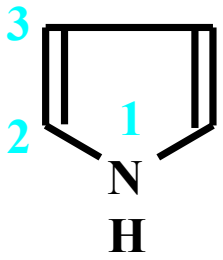


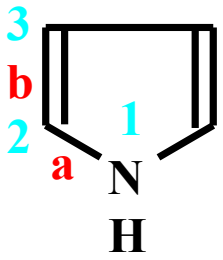
pteridin/e

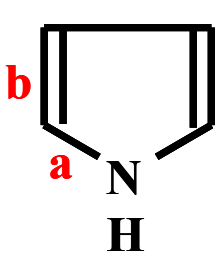
Označování vazeb pro připojení dalšího kruhu (1) :

1 – 2 – 3 – 4 – 5 – 6 – 7 – 8
a b c d e f g

Další kruh se napojuje na cyklus,
který měl své *původní* číslování
(a tedy i *původní* označení vazeb písmeny).
Uvažované místo kondenzace (zde „b“)
má nejnižší možná čísla atomů.







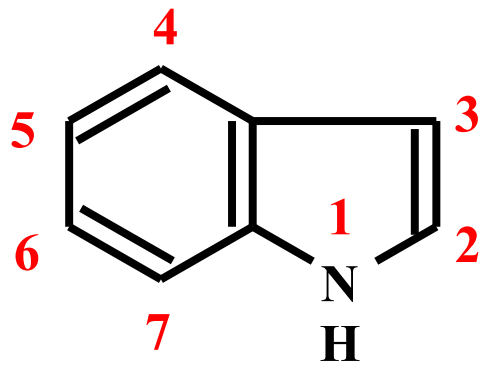
Označování vazeb pro připojení dalšího kruhu (2) :

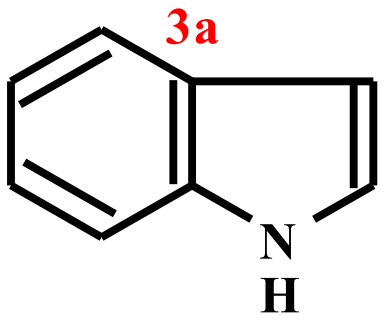
1 – 2 – 3 – 4 – 4a – 5 –
a b c d e f

Pokud se vyskytne samostatným číslem neoznačený atom (zde 4a), označují se i jeho vazby písmeny plynule dál.

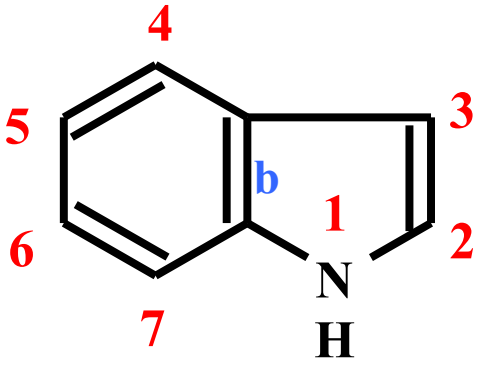
Samostatnými čísly se neoznačují atomy, které jsou všemi vazbami zapojeny do skeletu - jsou to místa, kde nemůže dojít k substituci (neexistujících H atomů).

Označování vazeb pro připojení dalšího kruhu (3) :



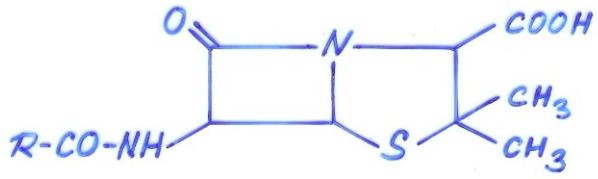


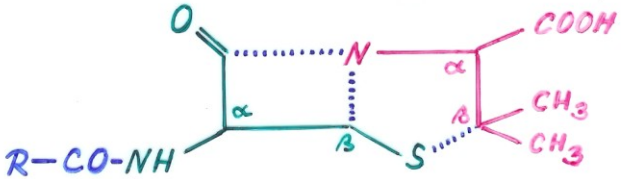
Kondenzovaná sloučenina (zde indol)
má odlišné od číslování (od původního pyrrolu) !!

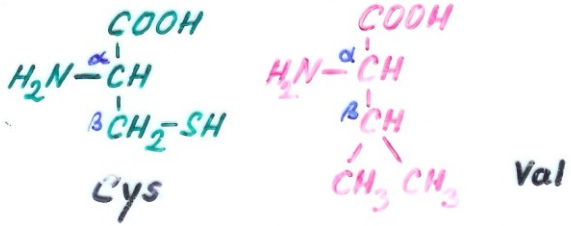


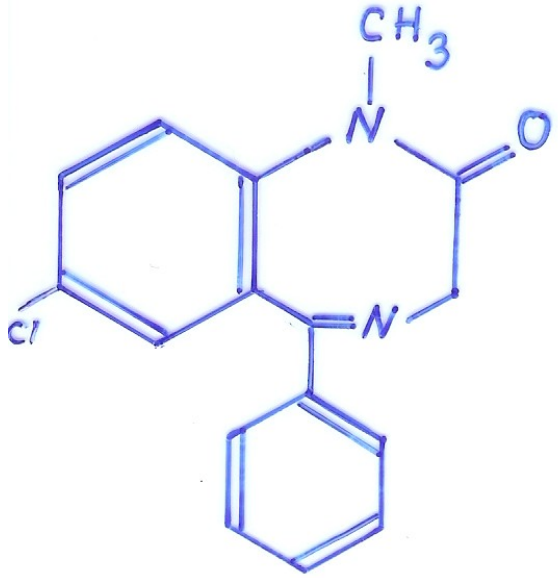
benzo[b]pyrrol
(indol)

penicilín
penicillin









Diazepam
Valium