



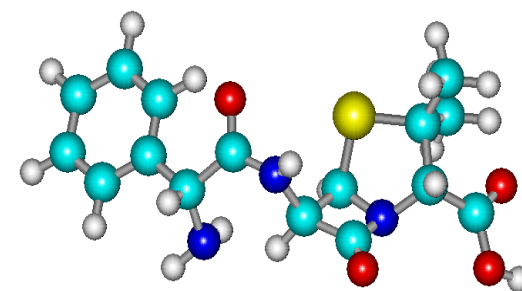
Financováno  
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Národní  
plán  
obnovy

MŠMT  
MINISTERSTVO ŠKOLSTVÍ,  
MLÁDEŽE A TĚLOVÝCHOVY

# *Chemie organických látek*



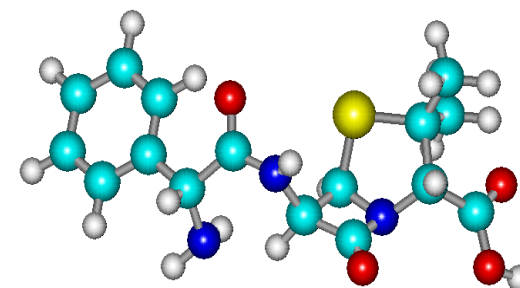
*doc. Ing. Pavel Bobál, CSc.*

MUNI  
PHARM

Ústav  
chemických  
léčiv

# Chemie organických látek

## 10. Chemie heterocyklů

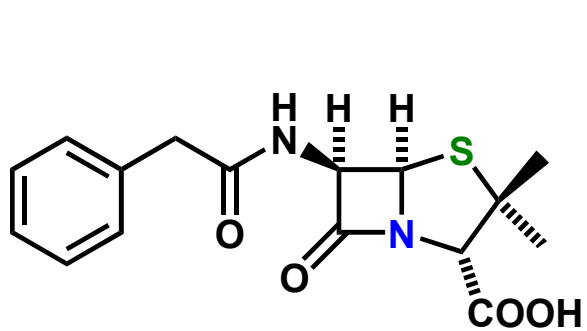


*doc. Ing. Pavel Bobál, CSc.*

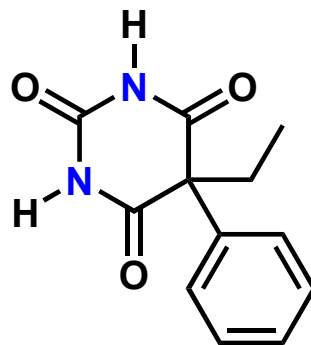
**MUNI**  
**PHARM**

Ústav  
chemických  
léčiv

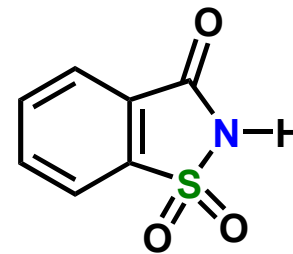
# Úvod



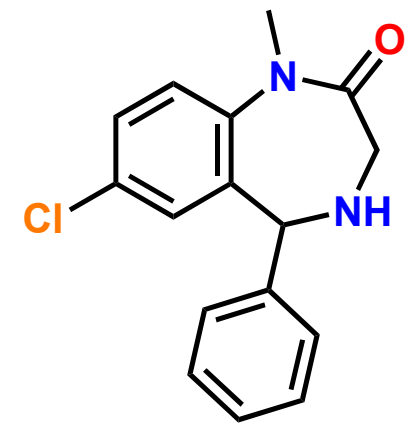
penicilin G



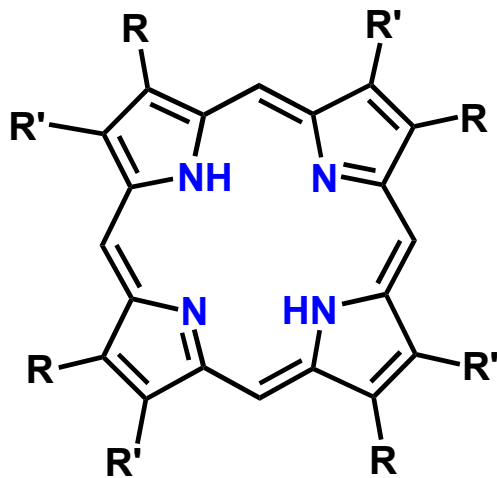
fenobarbital



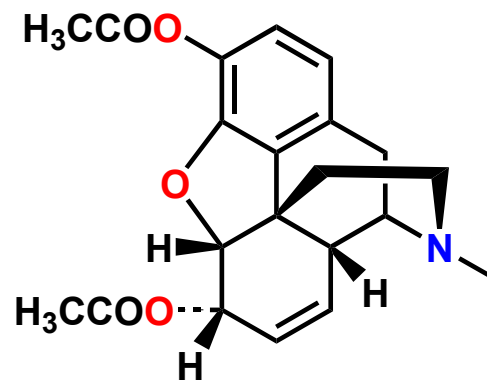
sacharin



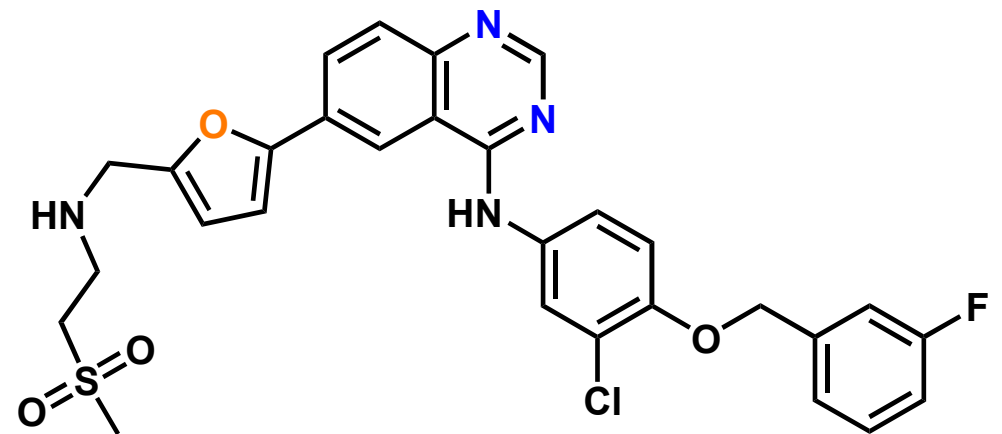
diazepam



porfyrin



heroin

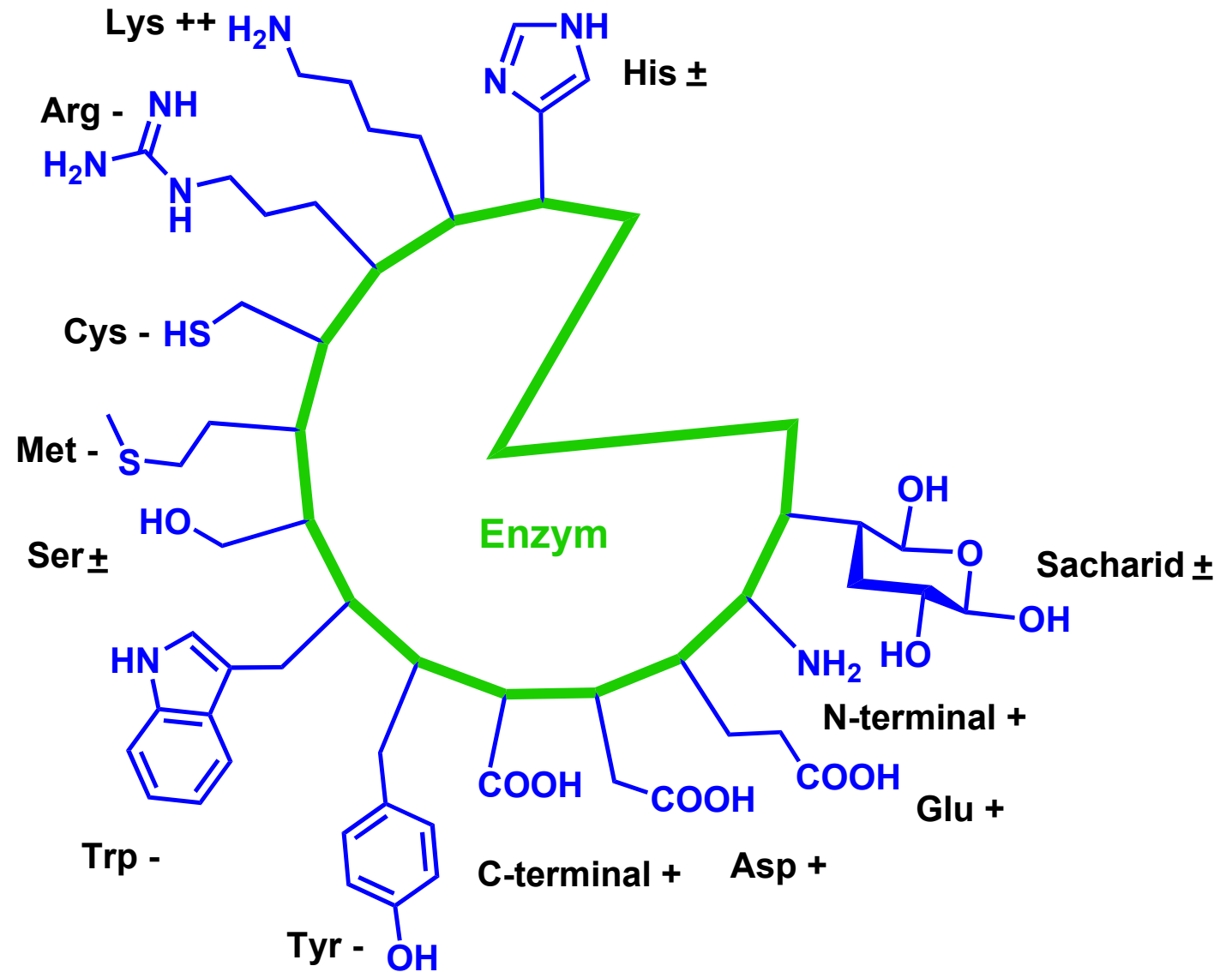


lapatinib



# Úvod

Enzymy (bílkoviny)



# Heterocykly: Názvosloví

## 1. Hantzschův-Widmanův systém

nejčastěji u heterocyklů se 3, 4 a 7-10 články a pro heterocykly obsahující větší počet heteroatomů

## 2. Záměnný princip názvosloví

užívá se pro cykly větší než 10 a pro menší cykly obsahující Si, používáme jej také u bicyklických a polycyklických systémů

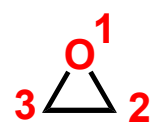
## 3. Triviální názvosloví monocyklických heterocyklů

u 5 a 6-ti člankových heterocyklů s jedním nebo dvěma heteroatomy

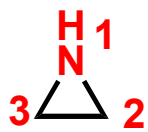
## 4. Systematické názvosloví *ortho*-kondenzovaných heterocyklů



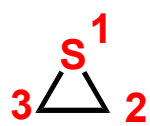
# Heterocykly - názvosloví: 3-, 4-, 7- a vícečlenné



oxiran



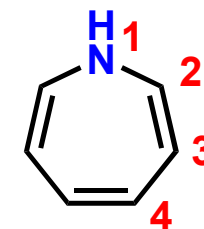
aziridin



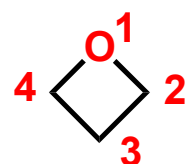
thiiran



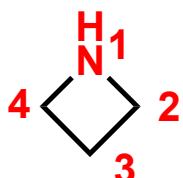
epichlorhydrin



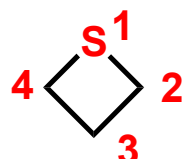
1H-azepin



oxetan

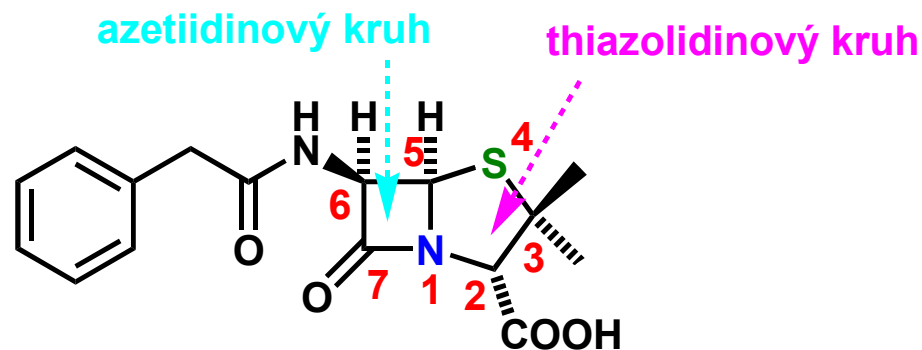


azetidin



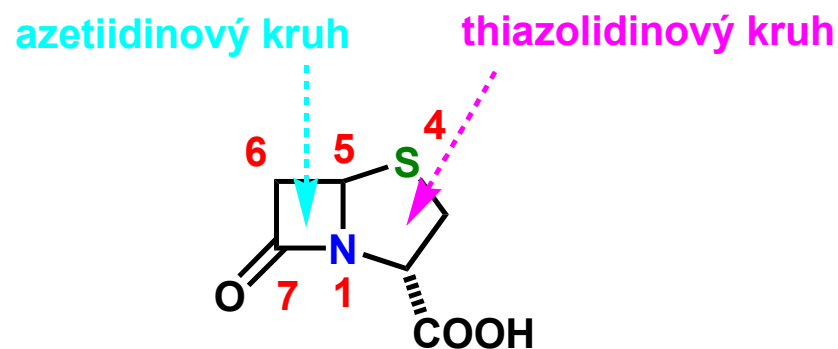
thietan

## Záměnný princip názvosloví



penicilin G

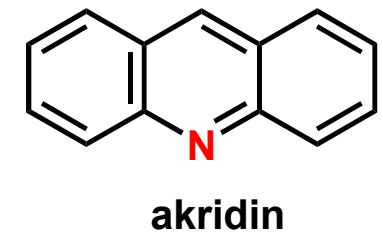
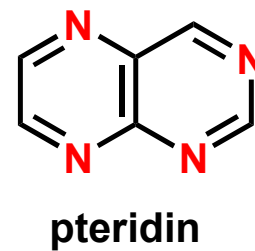
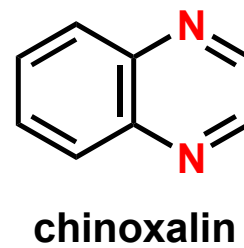
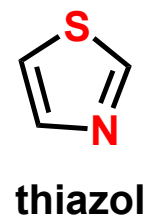
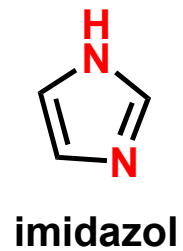
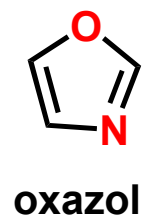
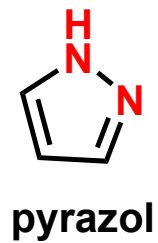
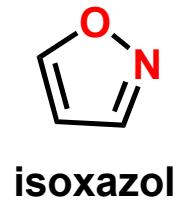
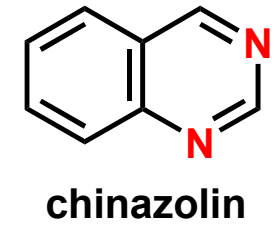
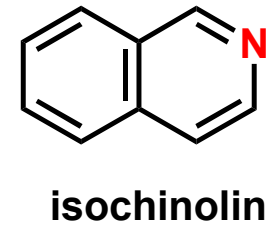
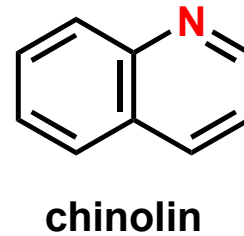
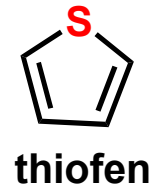
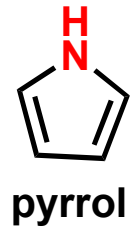
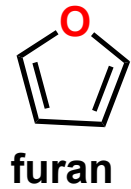
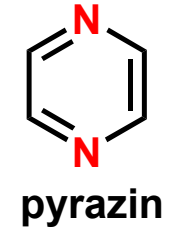
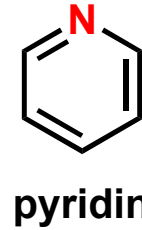
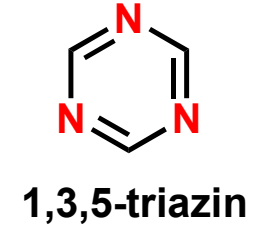
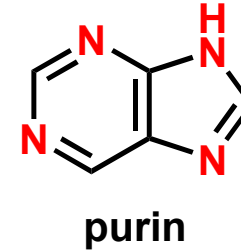
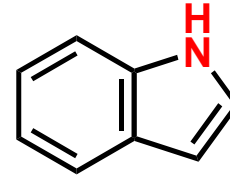
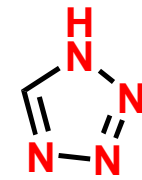
(2*S*,5*R*,6*R*)-6-(2-fenylacetamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyklo[3.2.0]heptan-2-karboxylová kyselina



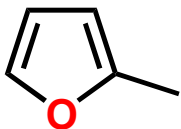
(2*S*)-7-oxo-4-thia-1-azabicyklo[3.2.0]heptan-2-karboxylová kyselina



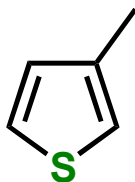
# Heterocykly: Názvosloví



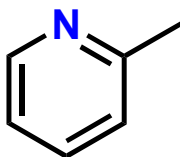
# Heterocykly: Názvosloví



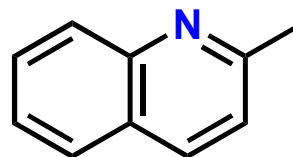
furan-2-yl-  
(2-furyl-)



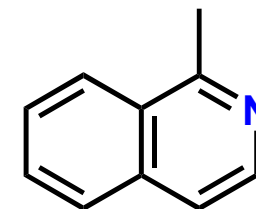
thiofen-2-yl-  
(3-thienyl-)



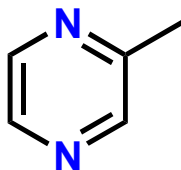
pyridin-2-yl-  
(2-pyridyl-)



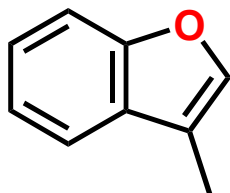
chinolin-2-yl  
(2-chinolyl-)



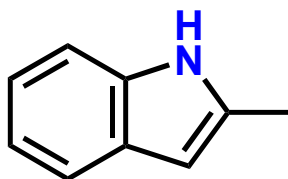
isochinolin-1-yl  
(1-isochinolyl-)



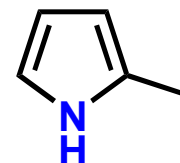
pyrazin-2-yl  
(pyrazinyl-)



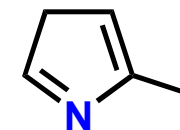
benzo[b]furan-3-yl  
(3-benzo[b]furanyl-)



1H-indol-2-yl  
(2-indolyl-)



1H-pyrrol-2-yl  
(2-pyrrolyl-)



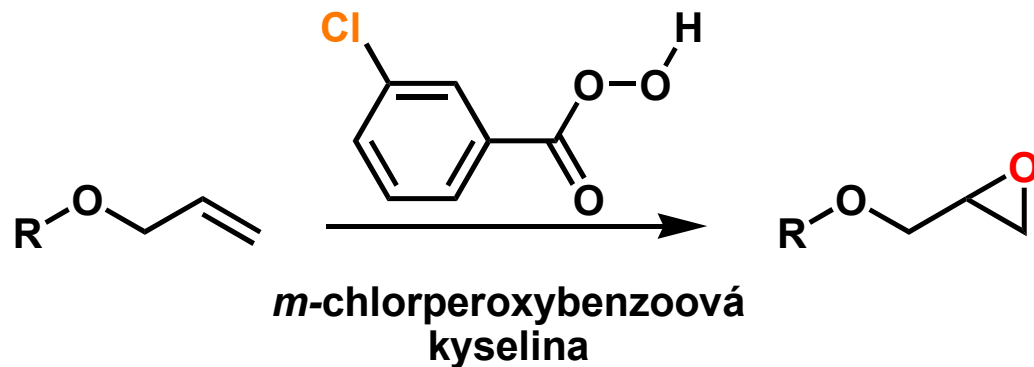
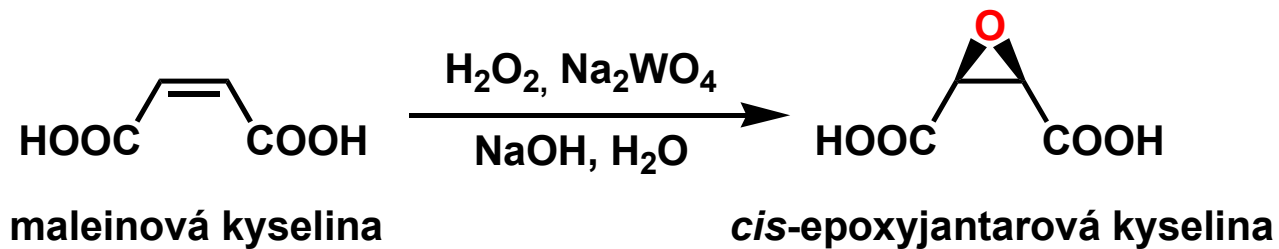
4H-pyrrol-2-yl



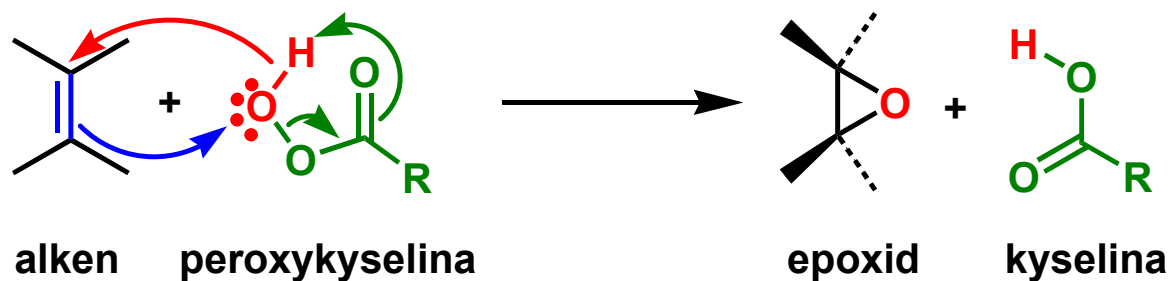


# Příprava oxiranů

- oxidací alkenů

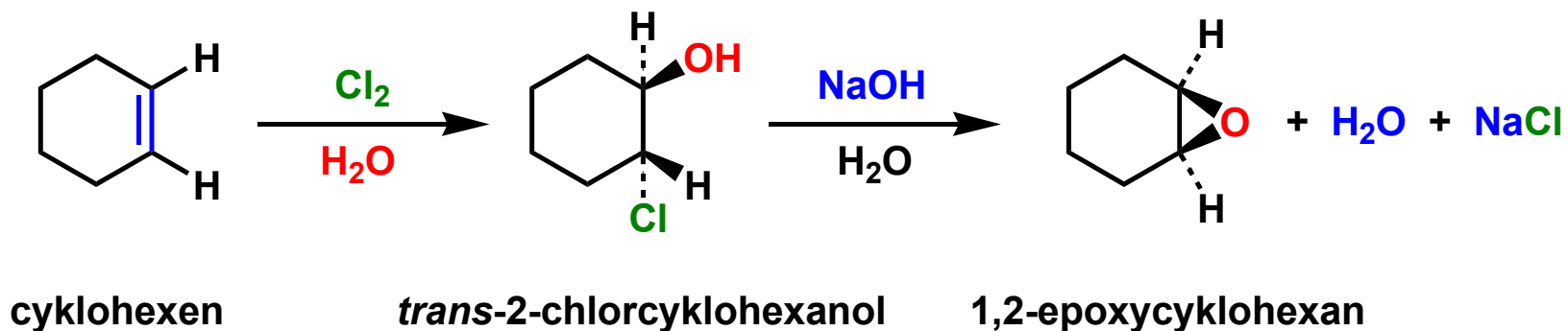


- mechanismus

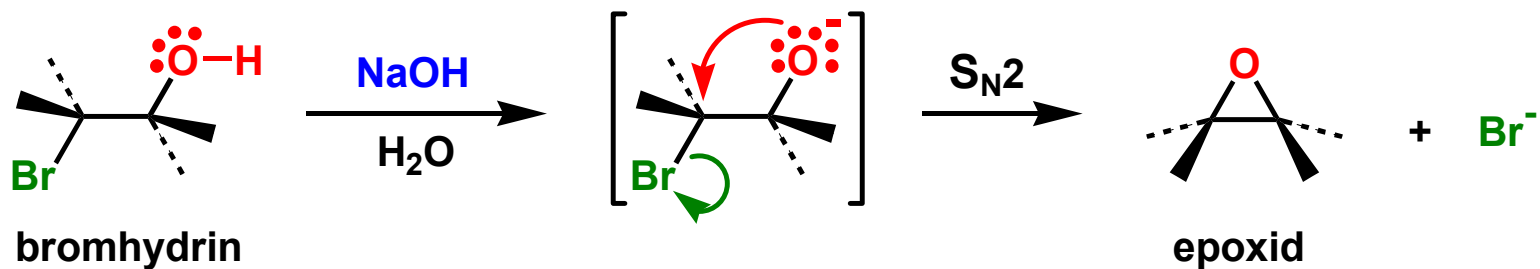


# Příprava oxiranů

- z halohydrinů působením bází

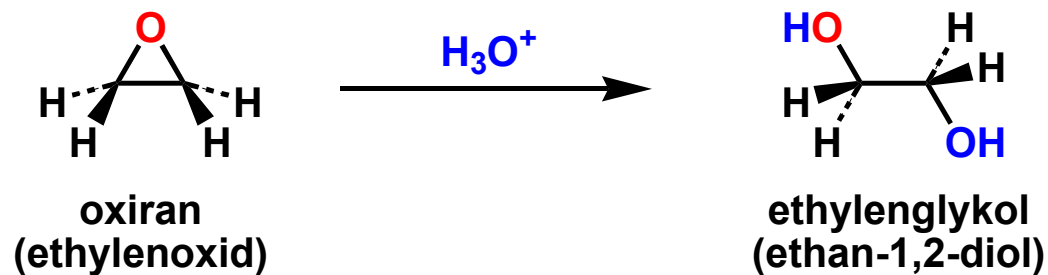


- mechanismus

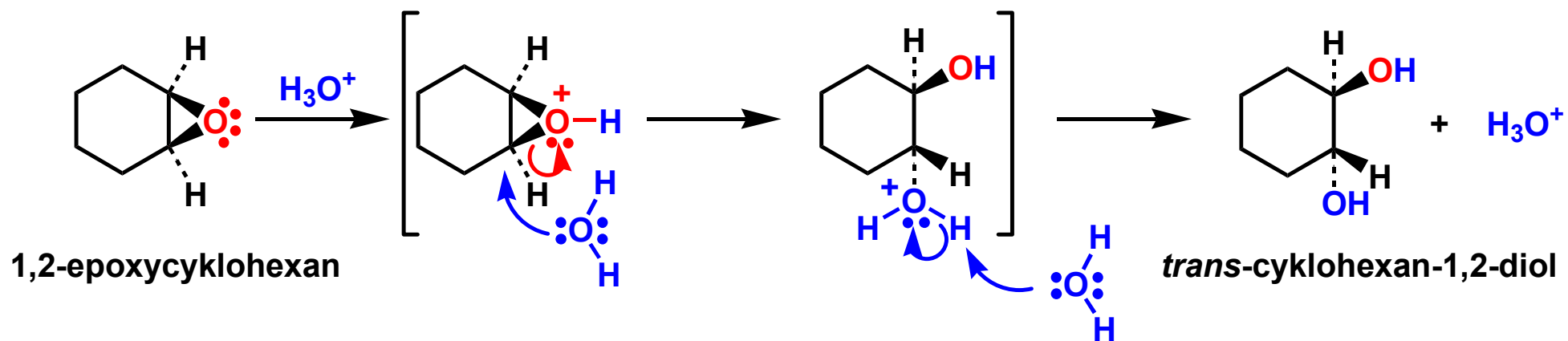


# Reaktivita oxiranů: Kysele katalyzované otevírání oxiranů

- příprava vicinálních glykolů – 1,2-diolů

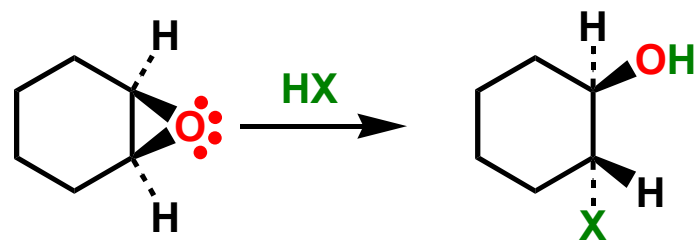


- mechanismus



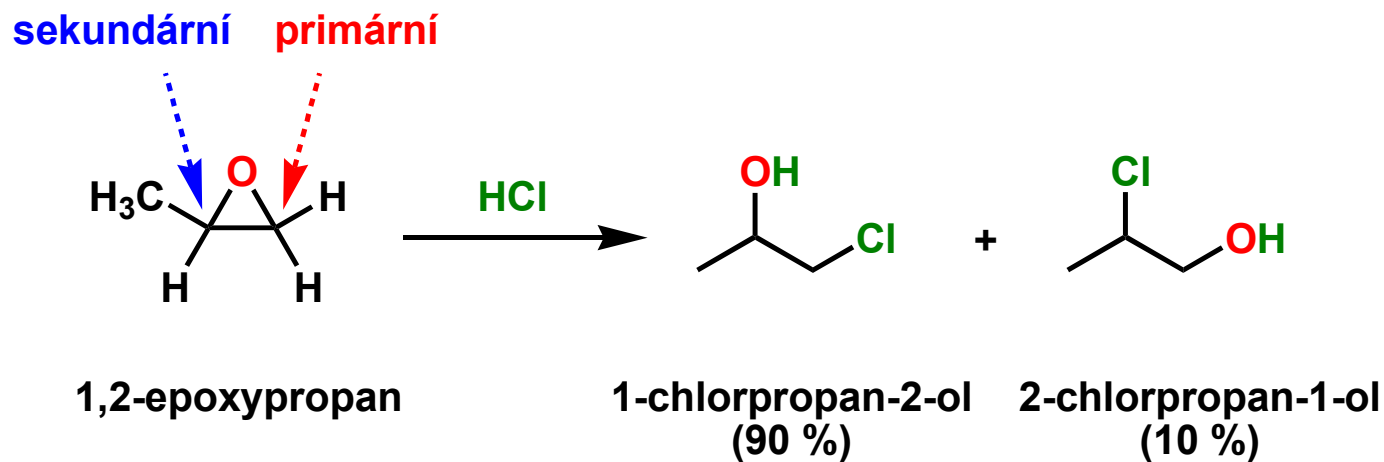
# Reaktivita oxiranů: Kysele katalyzované otevírání oxiranů

- otevírání - halogenovodík HX



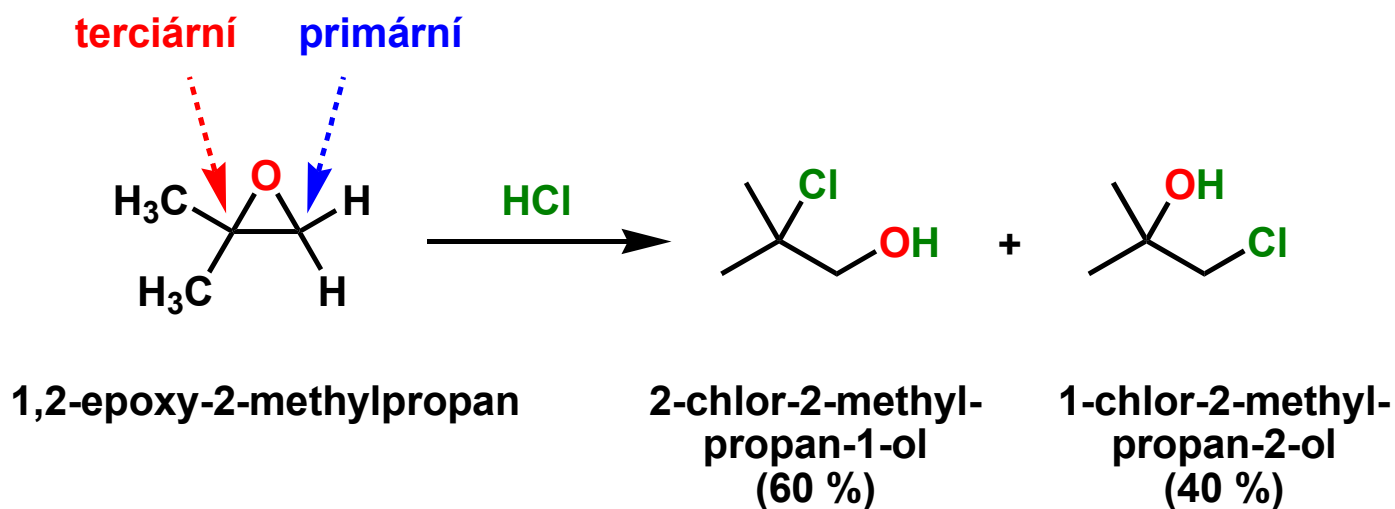
X = F, Br, Cl, I

- mechanism – primární a sekundární – nukleofil atakuje méně stericky bráněnou polohu



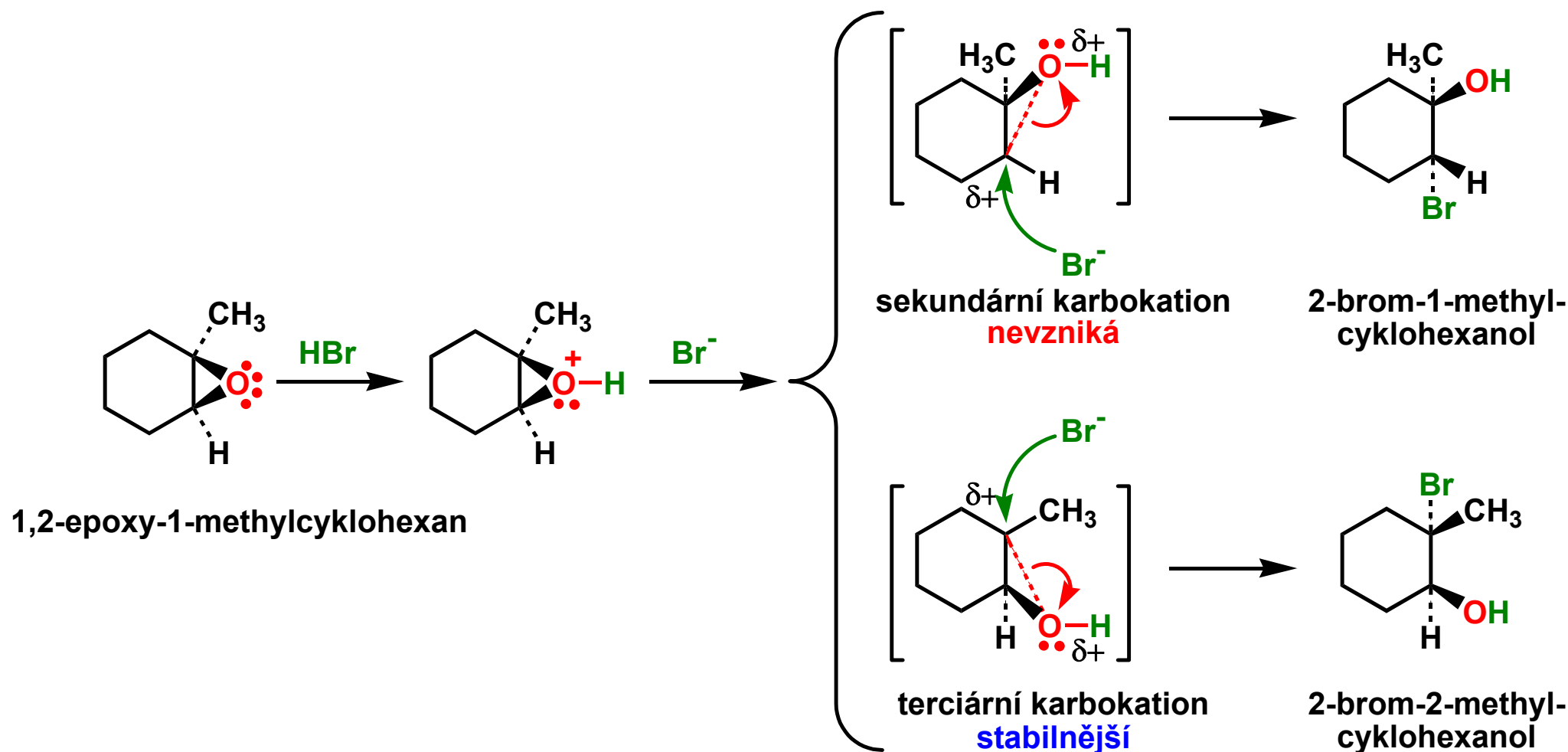
# Reaktivita oxiranů: Kysele katalyzované otevírání oxiranů

- terciární - mechanismus  $S_N1$

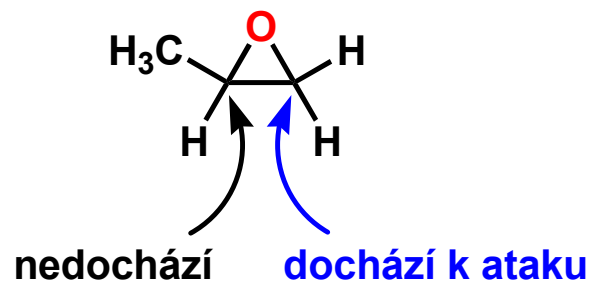
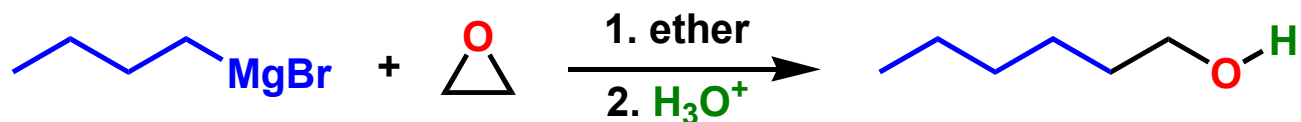
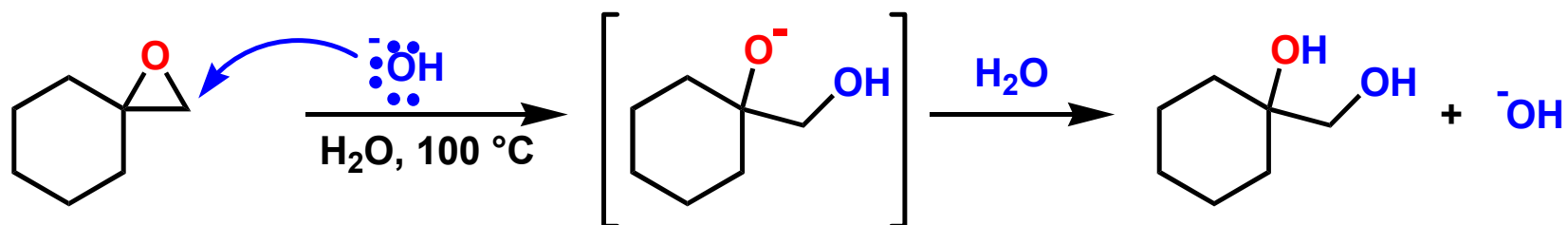


# Reaktivita oxiranů: Kysele katalyzované otevírání oxiranů

- složitější mechanismus – současně rysy mechanismu  $S_N1$  a  $S_N2$



# Reaktivita oxiranů: Bazicky katalyzované otevírání oxiranů

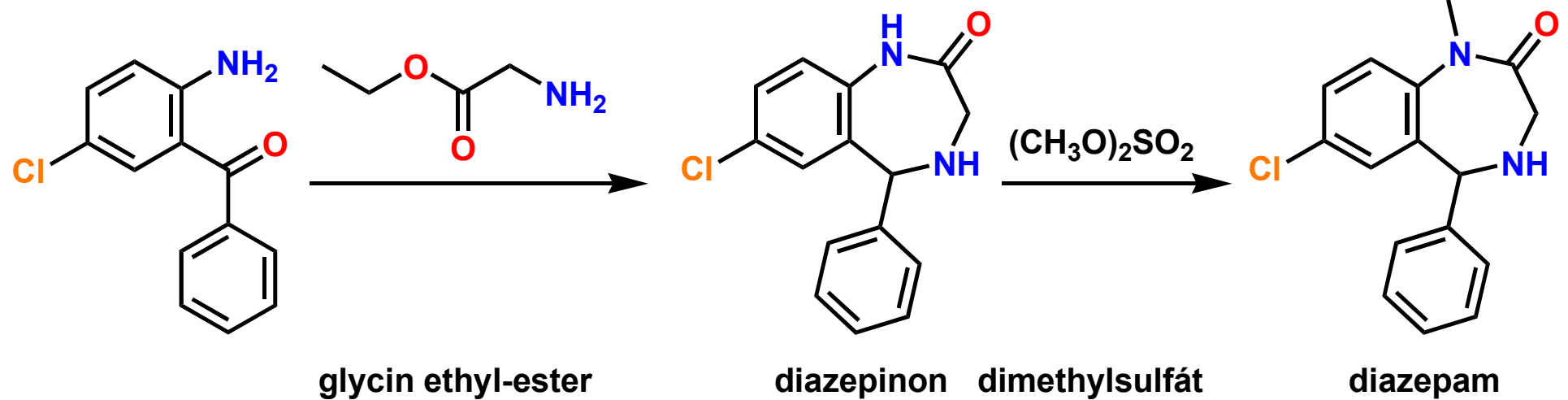


# Heterocykly: 3-, 4-, 7- a vícečlenné

Příprava aziridinů – obdobná

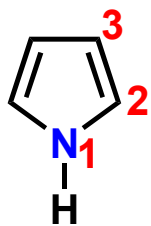
Příprava 4-členných kruhů

Příprava 7-členných kruhů

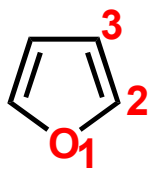




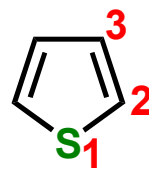
# Heterocykly: Názvosloví



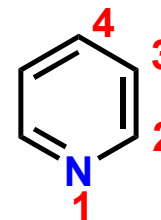
pyrrol



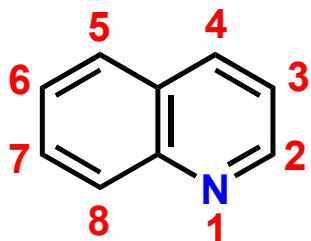
furan



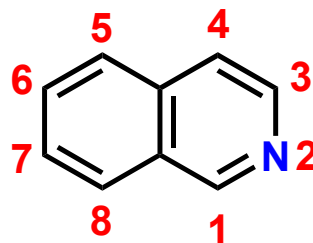
thiofen



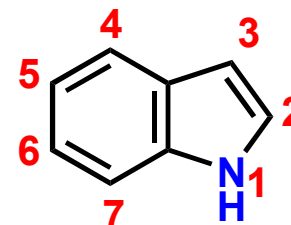
pyridin



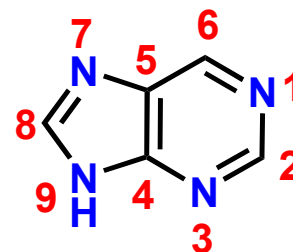
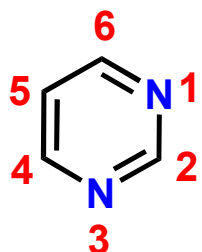
chinolin



isochinolin

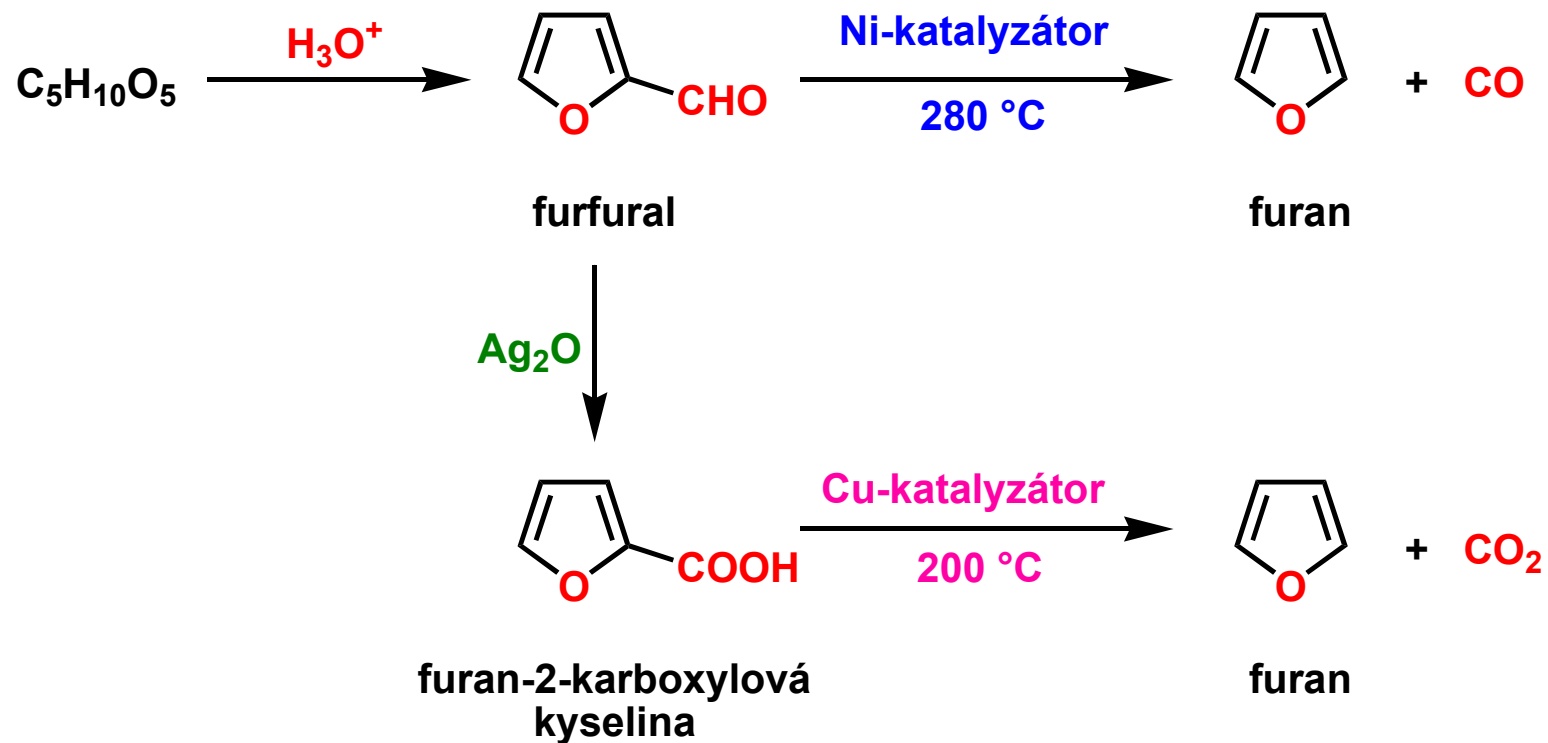


indol



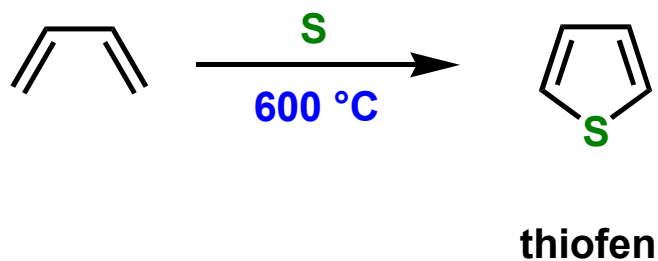
# Nenasycené pětičlenné heterocykly

**Furan** – dekarboxylací furfuralu (kysele katalyzovanou dehydratací pentos),  
– dekarboxylací furan-2-karboxylové kyseliny



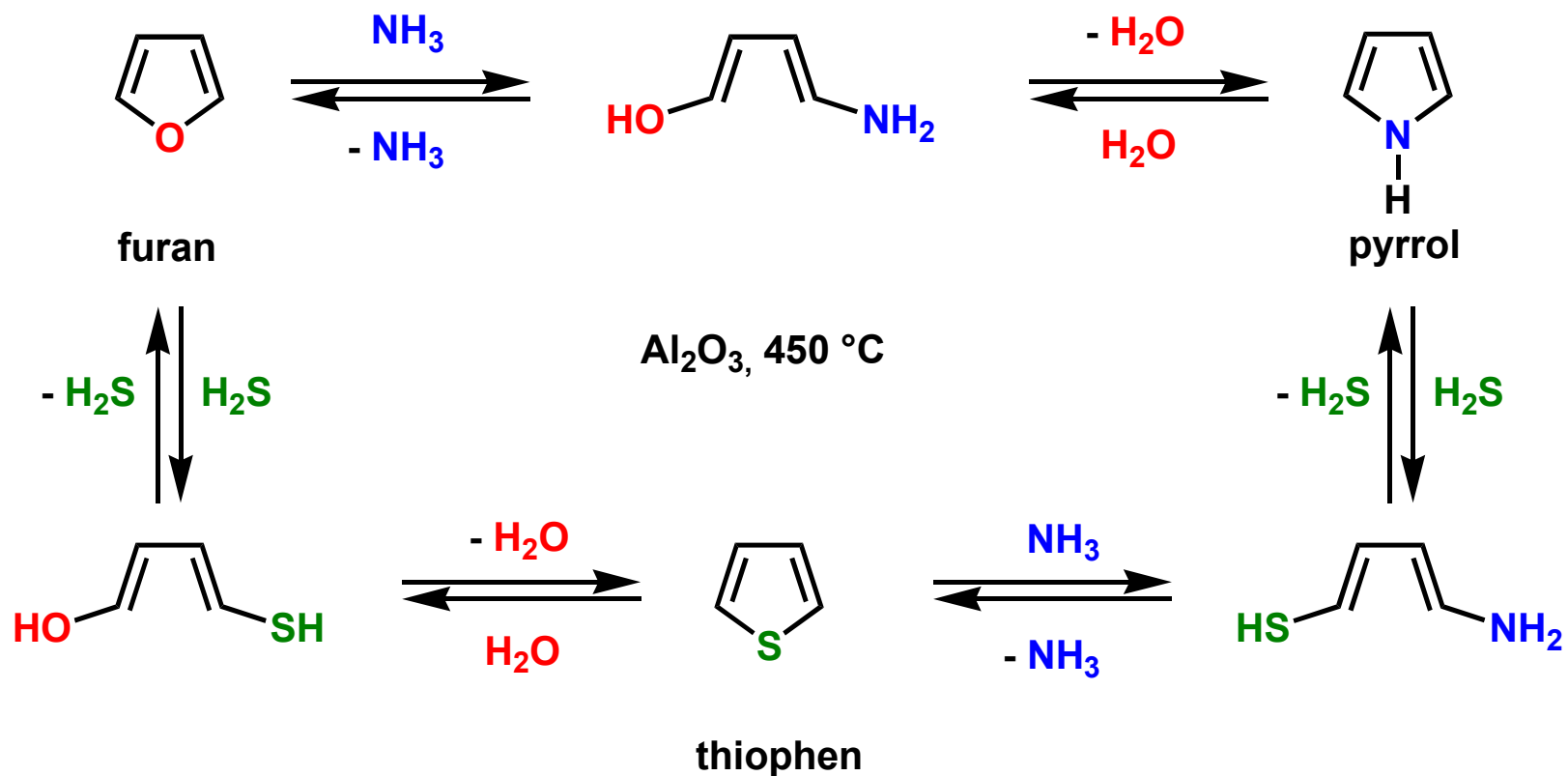
# Nenasycené pětičlenné heterocykly

**Thiofen** – cyklizací butadienu (butanu) se sírou

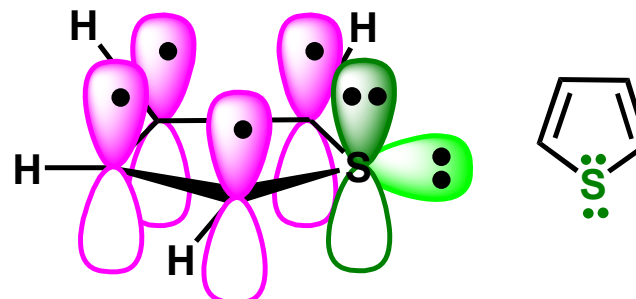
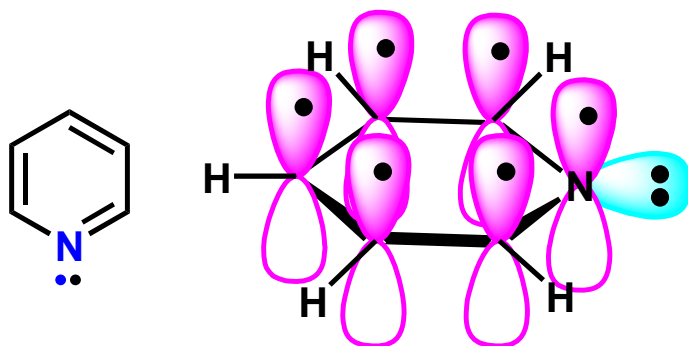
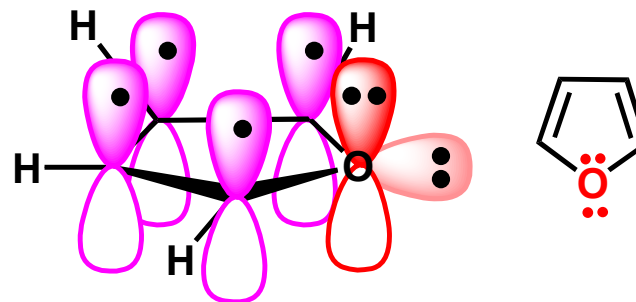
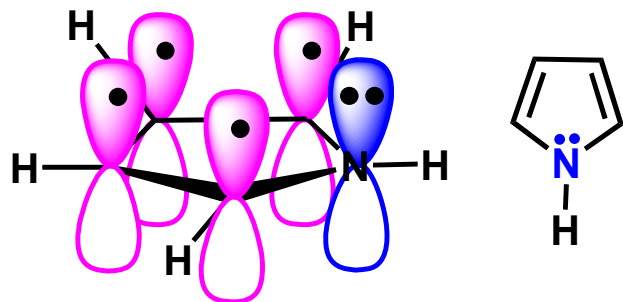


# Nenasycené pětičlenné heterocykly

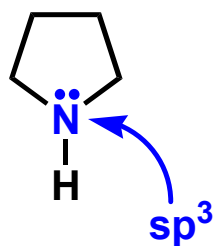
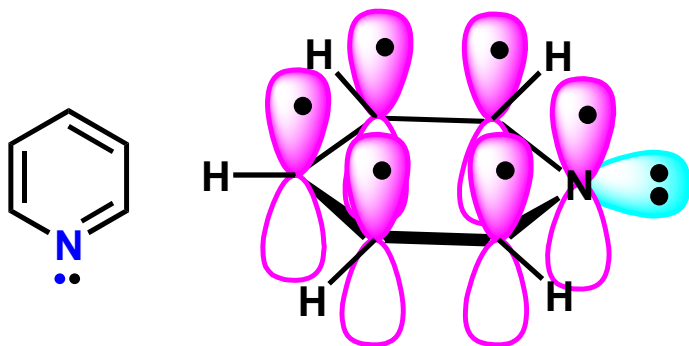
**Pyrrrol** – z černouhelného dehtu,  
– reakcí furanu s amoniakem v přítomnosti oxidu hlinitého  
**Jurjevovy reakce**



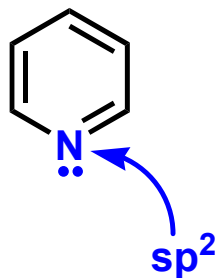
# Struktura pyrrolu, furanu a thiofenu



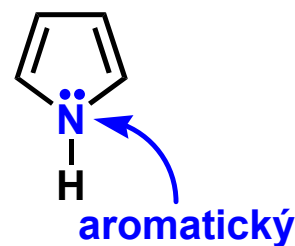
# Bazicita dusíkatých heterocyklů



pyrrolidiniový ion  
 $pK_a$  11,27  
25 % s charakter



pyridiniový ion  
 $pK_a$  5,25  
33 % s charakter



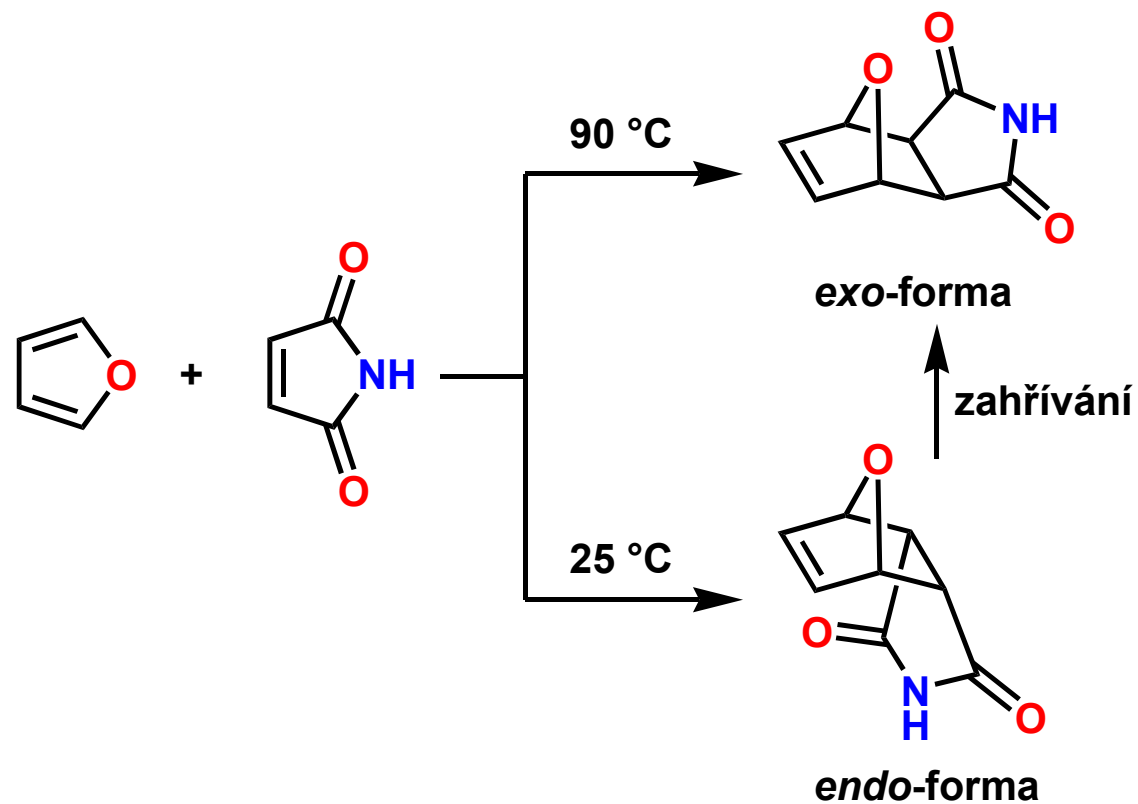
pyrroliový ion  
 $pK_a$  0,4





# Reaktivita furanu

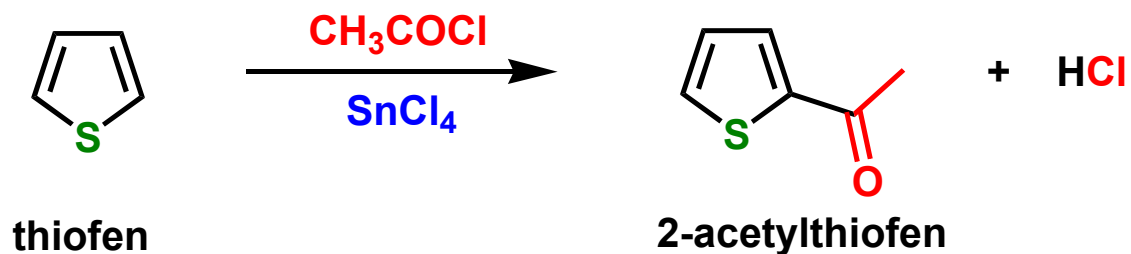
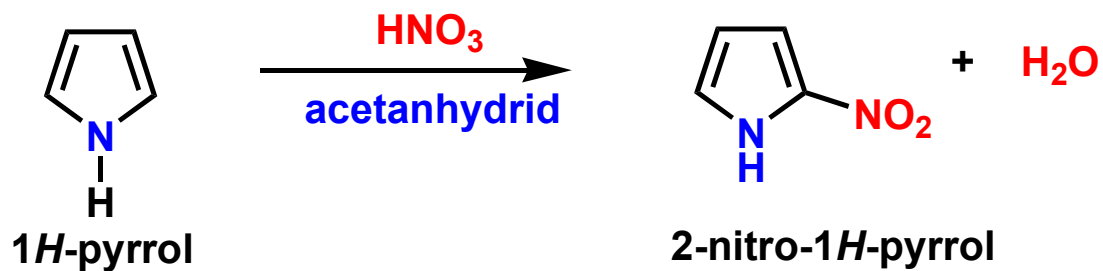
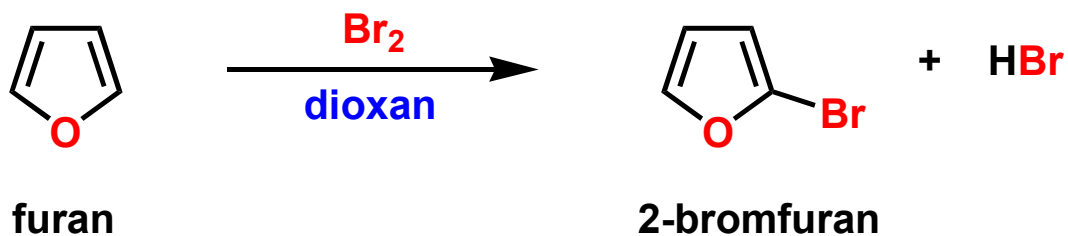
- aromatický charakter
- charakter dienu





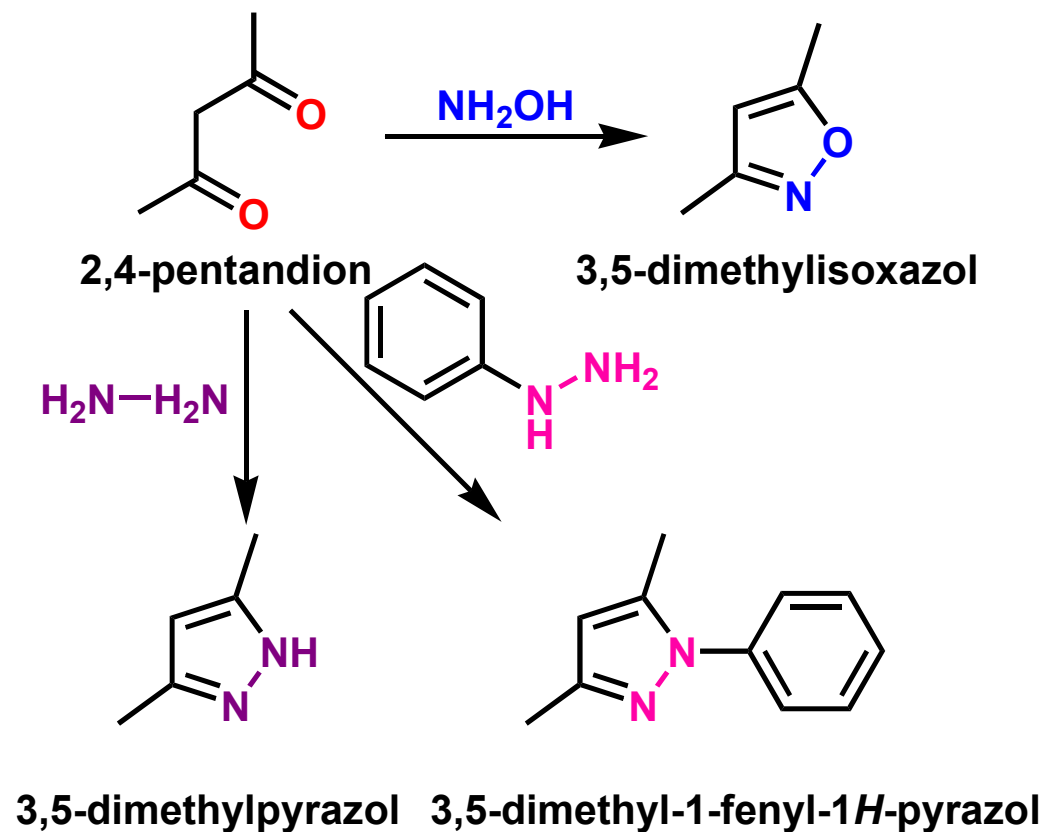
# Elektrofilní substituce pyrrolu, furanu a thiofenu

- v poloze 2 ( $\alpha$ )



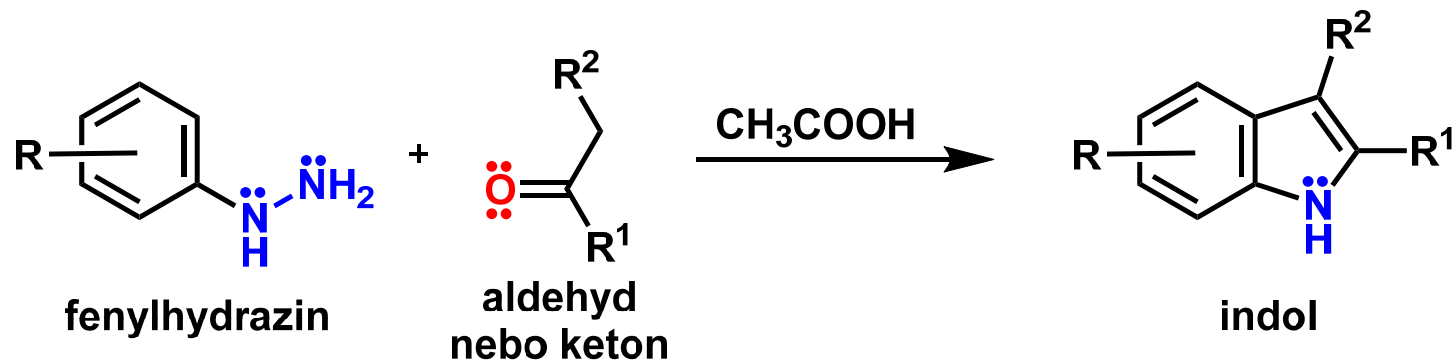
# Syntéza isoxazolů a pyrazolů

- například z 1,3-dikarboonylových sloučenin



# Fischerova syntéza indolů

- syntéza indolu

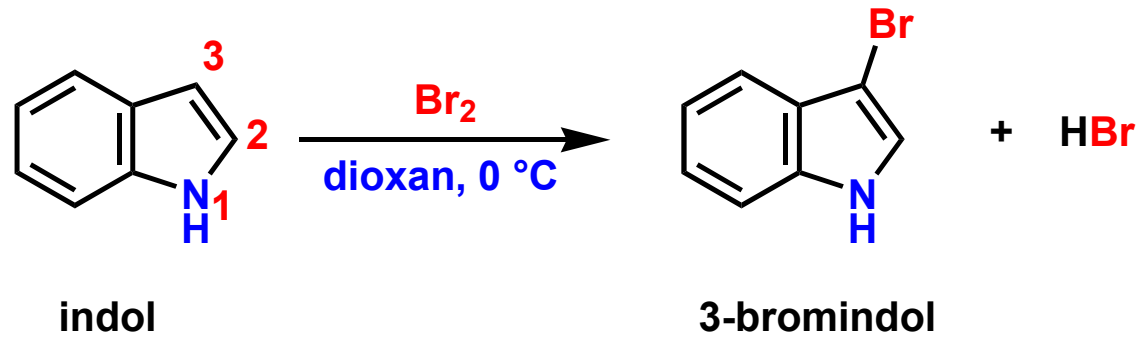


- katalýza – kyselinami (AcOH, H<sub>2</sub>SO<sub>4</sub>, ZnCl<sub>2</sub>, atd.)

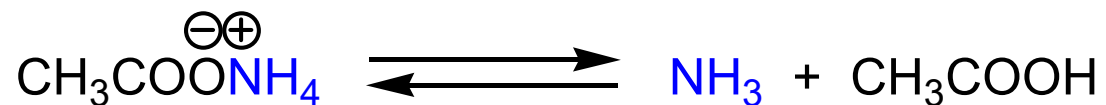
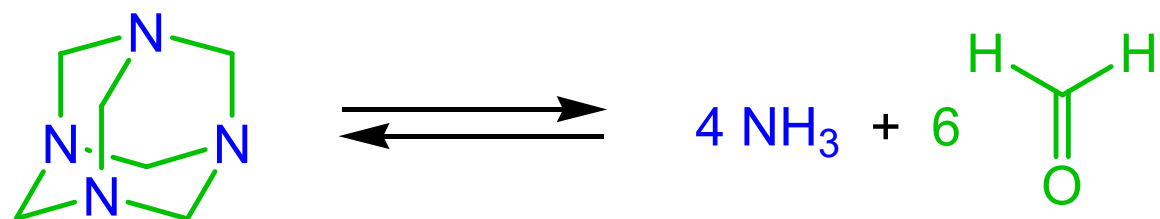
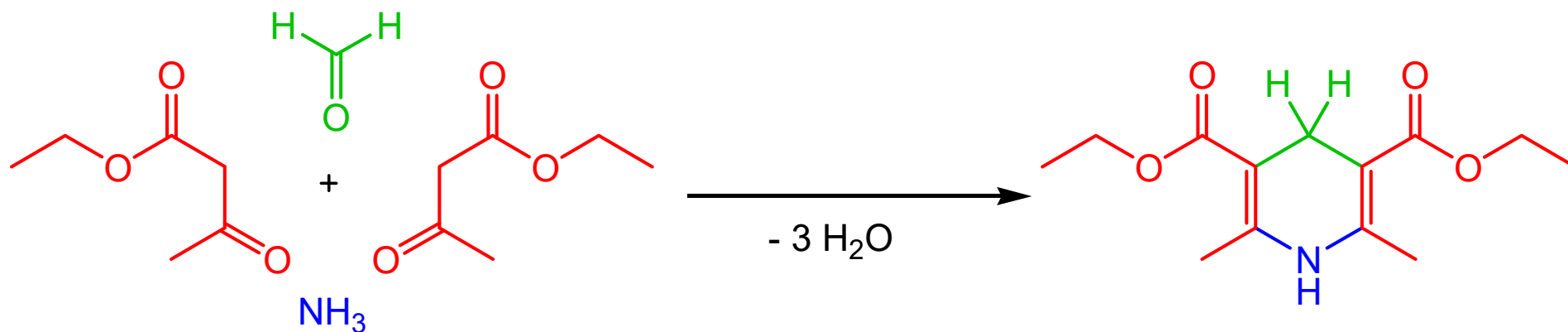


# Elektrofilní substituce indolu

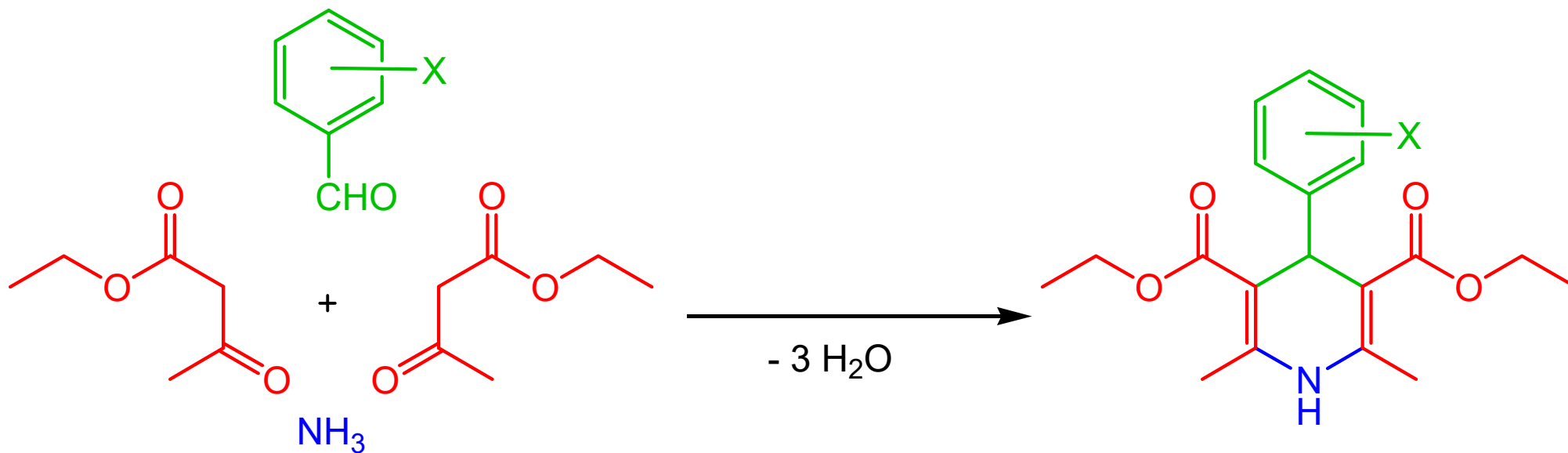
$S_E$  – v poloze 3 ( $\beta$ ) ?



# Příprava pyridinů – Hantzschova syntéza

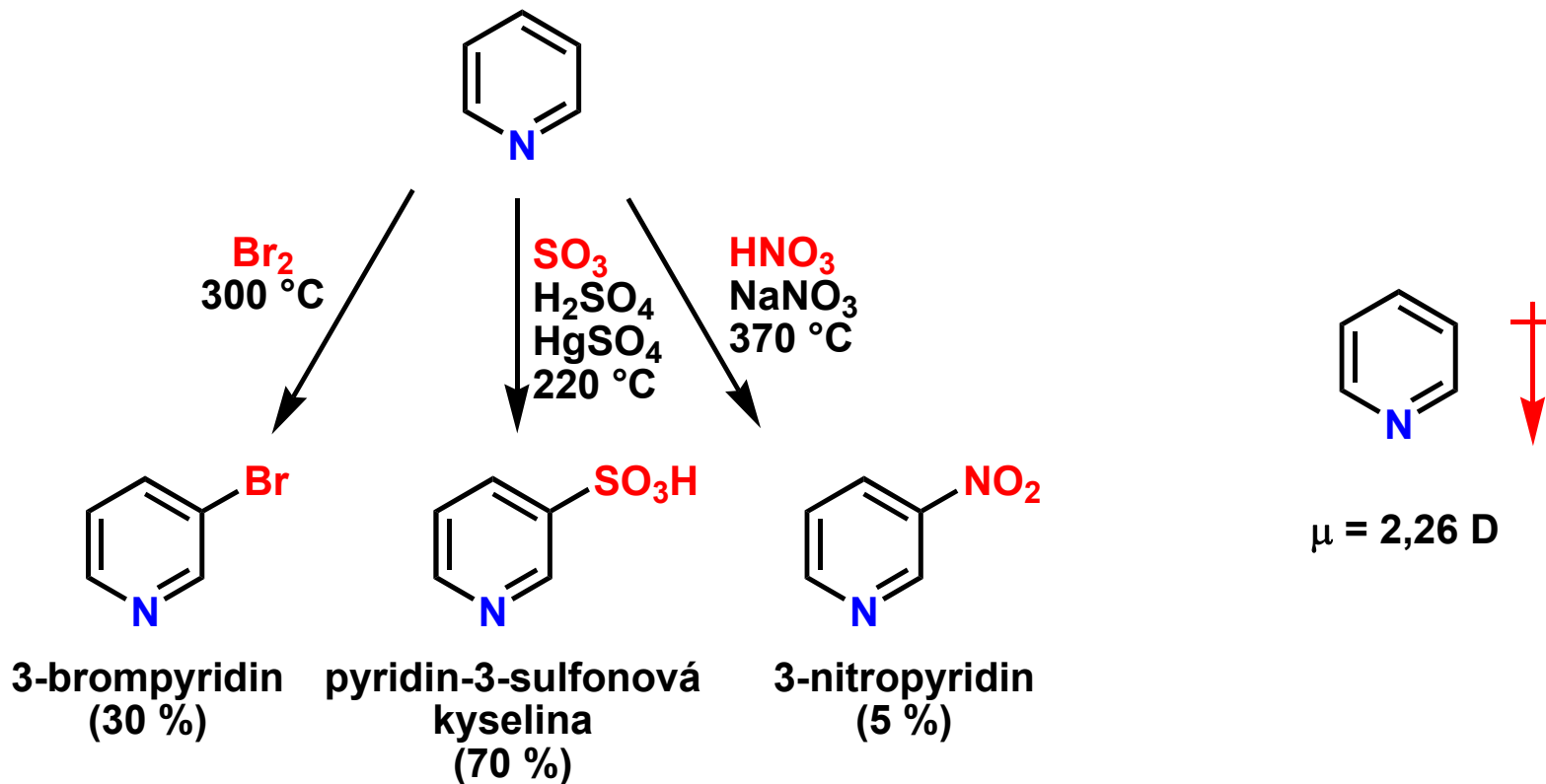


# Příprava pyridinů – Hantzschova syntéza



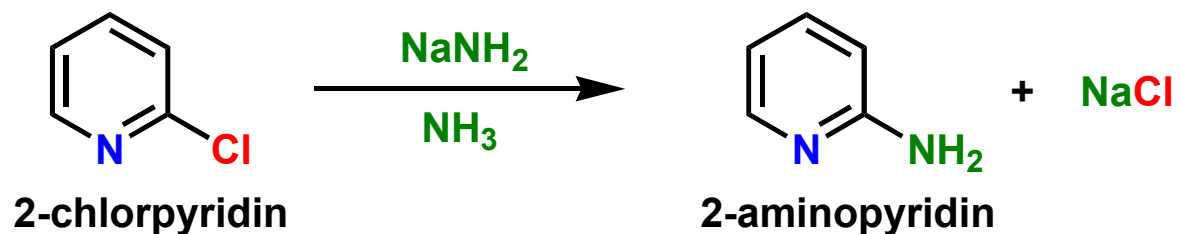
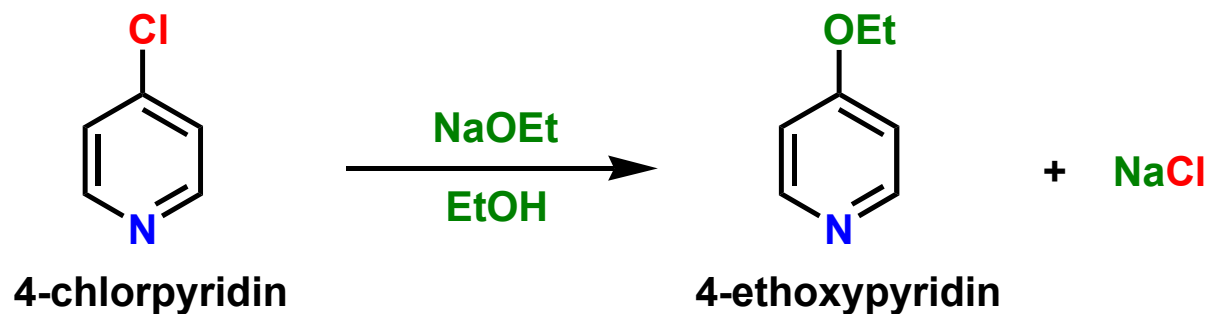
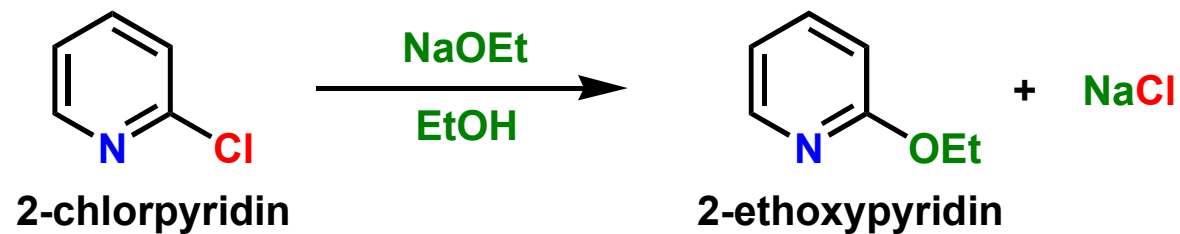
# Elektrofilní substituce pyridinu

- probíhá těžko – drastické podmínky – jenom do polohy 3 (?)



# Nukleofilní substituce pyridinu

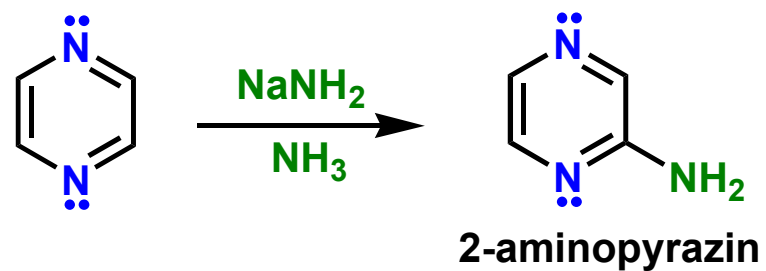
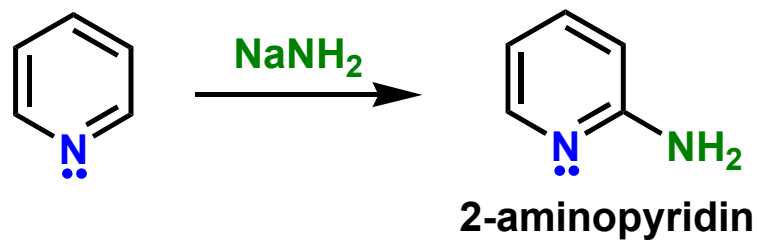
- pouze v polohách 2 a 4 (ne v poloze 3 !)





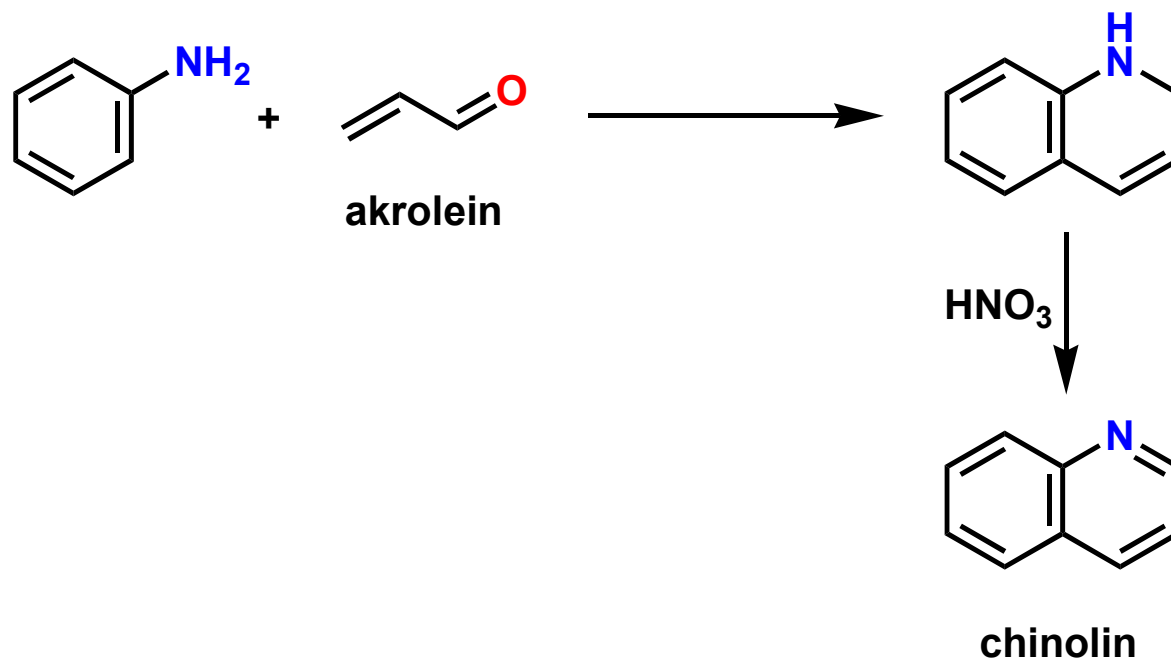
# Nukleofilní substituce pyridinu

- nukleofilní substituce vodíku v pyridinu – Čičibabinova reakce



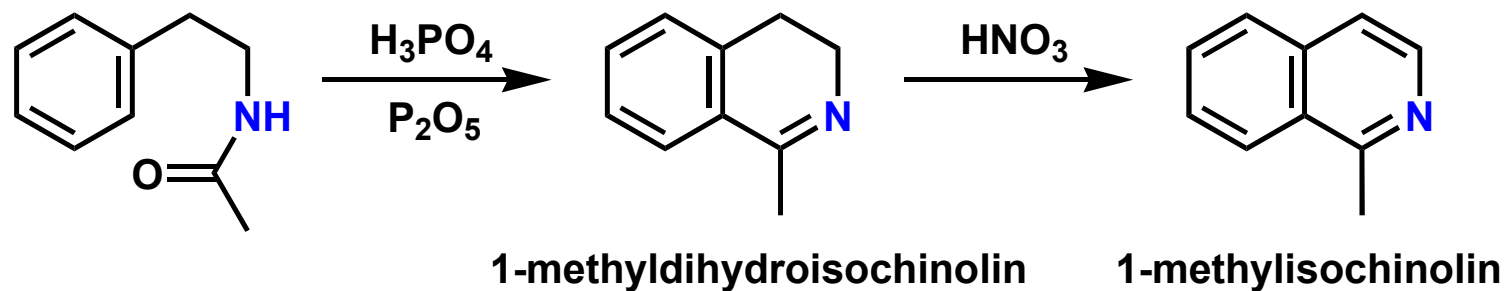
# Syntéza chinolinu a isochinolinu

- syntéza chinolinu – Skraupova syntéza



# Syntéza chinolinu a isochinolinu

- syntéza isochinolinu – **Bischlerova-Napieralského** cyklizace



# Elektrofilní substituce chinolinu a isochinolinu

$S_E$  reakce na aromatickém jádře přednostně

