

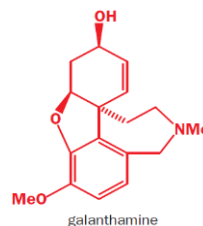
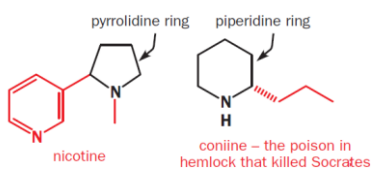
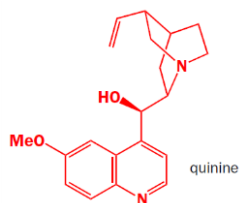
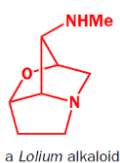
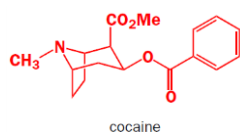
# Osnove kemije prirodnih organskih spojeva

## 7. Alkaloidi

Strukturne karakteristike. Dolaženje u prirodi. Izolacija i određivanje strukture. Biosinteza. Alkaloidi iz ornitina i lizina. Alkaloidi iz fenilalanina i tirozina. Alkaloidi iz triptofana. Sinteze alkaloida.

doc. dr. sc. Đani Škalamera

## Alkaloidi



Što je zajedničko svim ovim strukturama?

## Alkaloidi

- **Rane definicije:**

- 19. st. Maissner – prirodni spojevi bazičnih svojstvara, koji se mogu ekstrahirati iz lužnate vodene otopine

- 1982. Pelletier – sekundarni metaboliti, cikličke molekule koje sadrže barem jedan dušikov atom (ovdje ne spadaju jednostavni amini, nitro i nitrozo spojevi)

- **Najopćenitije:** svi sekundarni metaboliti koji sadrže dušik, a nisu peptidi ni nukleotidi

➤ većina alkaloida ima bazična svojstva zbog dušika kojeg posjeduju, makar postoje i neutralni alkaloidi, u kojima je dušik dio amidne veze

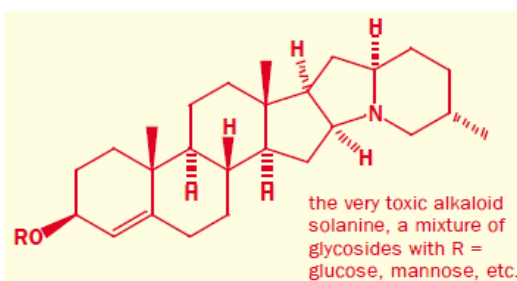
## Alkaloidi

- nekoliko klasifikacija (biogenetska, kemijska, farmakološka, taksonomska)
- kemijska klasifikacija – prema veličini prstena: piroolidinski, indolski, izokinolinski, ...)
- mogu sadržavati terpenske, steroidne ili peptidne fragmente
- pojavljuju se ponajviše u biljkama, ali i u manjim količinama i u mikroorganizmima i životinjama te u gljivama (npr. psilocibin)
- >27000 poznatih struktura, od čega 21000 iz biljaka
- biljkama i mikroorganizmima služe kao obrana
- obično su gorkog okusa
- izuzetno jaki biološki učinak – otrovi, analgetici, psihoaktivni spojevi

## Alkaloidi – biosinteza

- biosinteza iz aminokiselina: ornitina, lizina, nikotinske kiseline, tirozina, triptofana, antranilne kiseline, histidina
- u strukturama alkaloida često su prisutni dijelovi koji potječu iz acetatnog, šikimatnog, metileritritol-fosfatnog sintetskog puta. Nekad je samo dušik iz aminokiseline (transaminacija), a ostatak molekule može biti npr. steroidnog ili terpenoidnog tipa

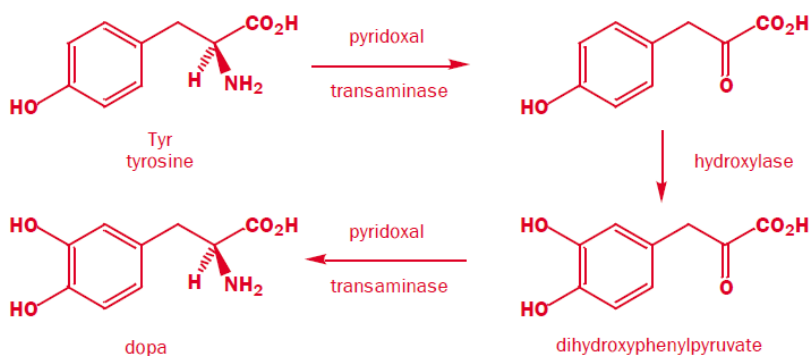
## Solanacea alkaloidi



- rajčica, krumpir, patlidan, beladona

## Amino-alkaloidi

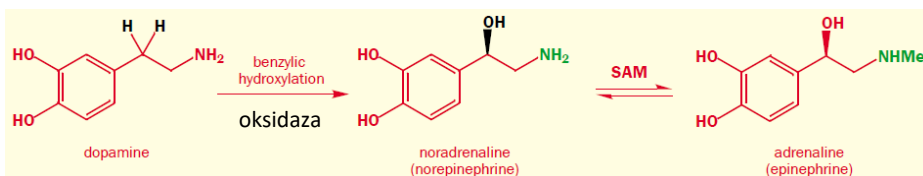
- biosinteza iz aminokiseline tirozina



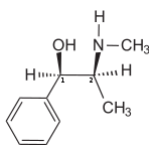
- L-dopa ili levodopa – kod čovjeka, nekih životinja i biljaka
- prekursor neurotransmitera dopamina, norepinefrina i epinefrina – zajedničkim se imenom zovu **kateholamini**

## Amino-alkaloidi

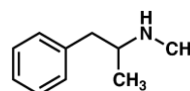
- dušik kao amin ili amid (nije dio heterocikličkog sustava)



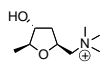
**efedrin** – snižuje krvni tlak, primjenjuje se kod astme, kod začepljenog nosa  
 iz *Ephedra sinica*



**metamfetamin** – vrlo jak stimulator CNS, droga



## Amino-alkaloidi

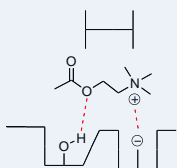


(+)-muskarin

•odtipovi kolinergičnih receptora

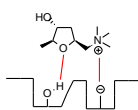
Vežanje acetilkolina  
na receptor

ca. 5Å

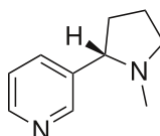
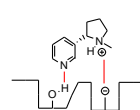


*Amanita muscaria*

muskarinski



nikotinski



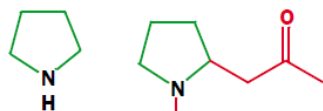
(-)-nikotin



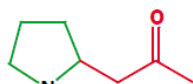
*Nicotiana glauca*  
Sokolovskaya  
Gerald D. Carr

## Pirolidinski alkaloidi

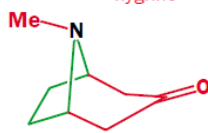
- u strukturi sadrže pirolidinski prsten
- biosinteza iz aminokiseline ornitina



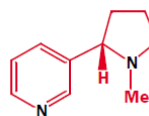
pyrrolidine



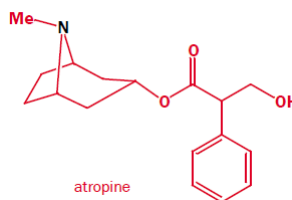
hygrine



tropinone

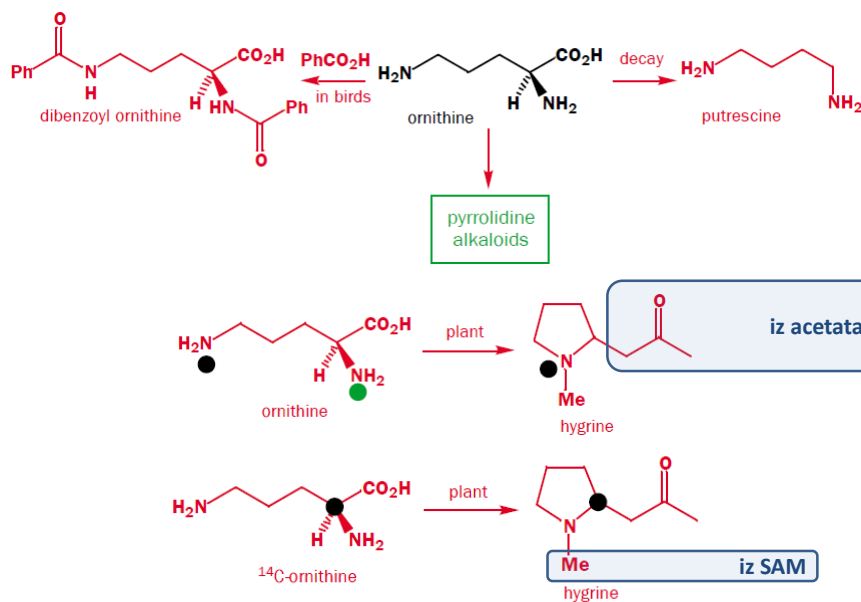


nicotine

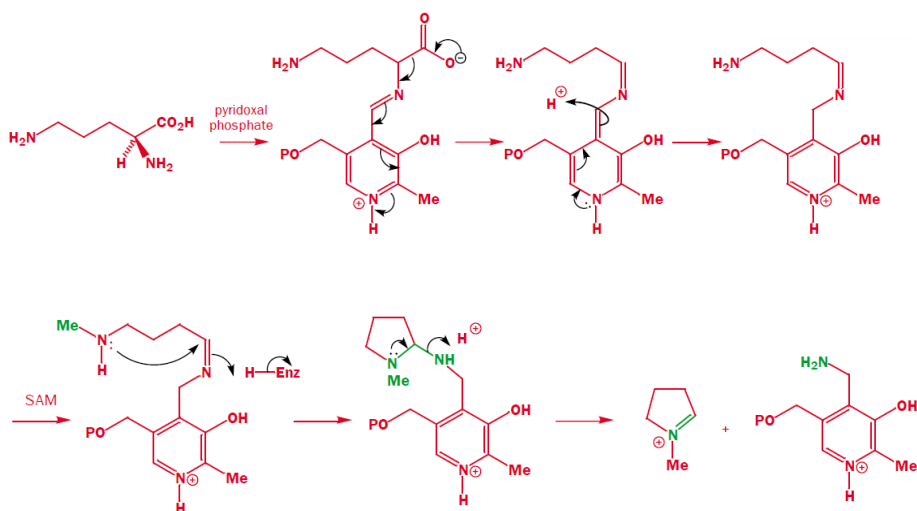


atropine

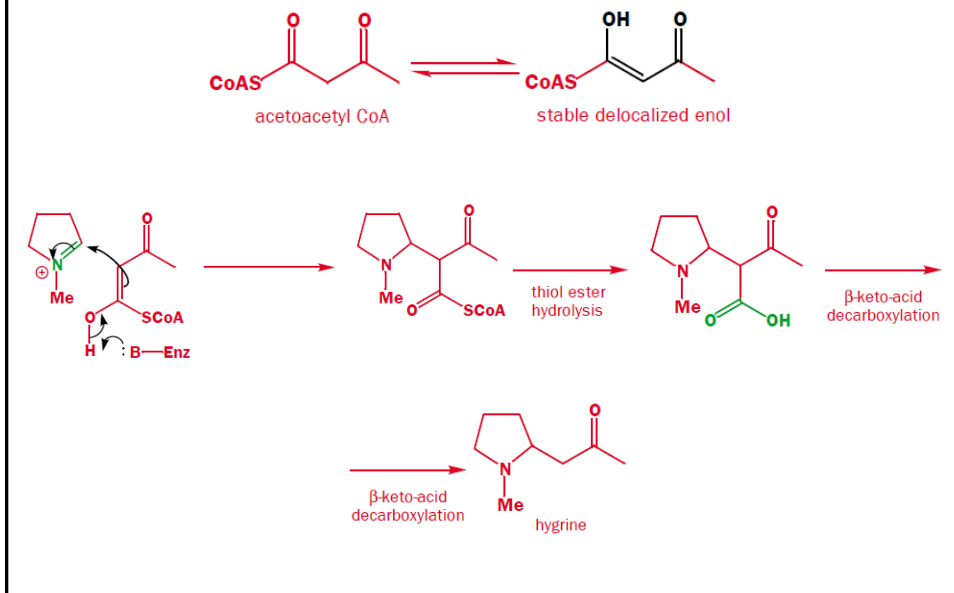
## Biosinteza pirolidinskih alkaloida iz ornitina



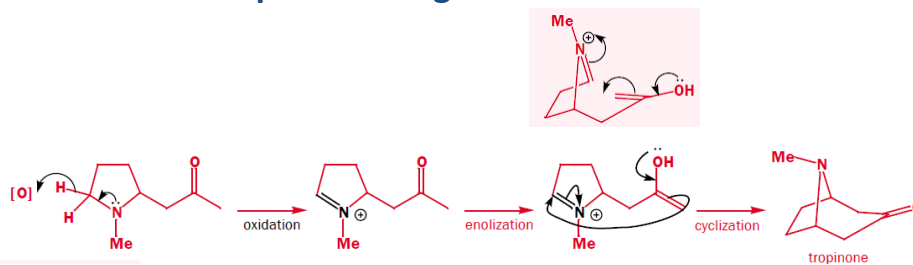
## Biosinteza pirolidinskih alkaloida iz ornitina



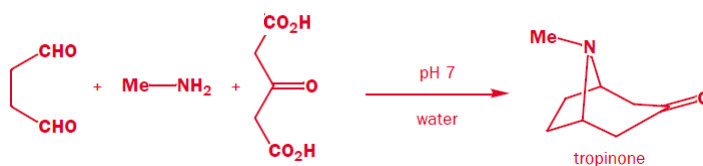
## Biosinteza pirolidinskih alkaloida iz ornitina



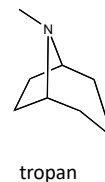
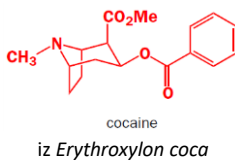
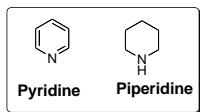
## Biosinteza tropinona iz higrina



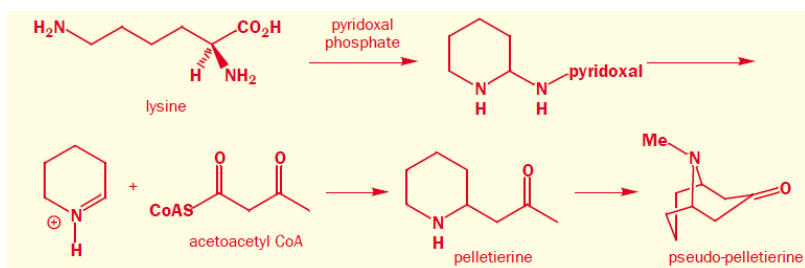
Robinson, 1917. – kemijska sinteza



## Piridinski i piperidinski alkaloidi

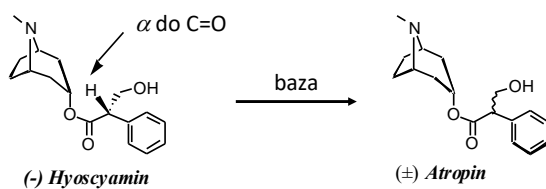
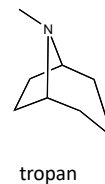
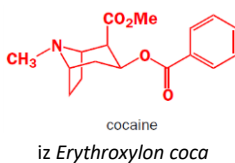
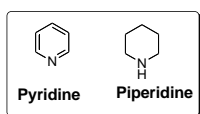


### Biosinteza



- pseudo-pelletierin je izoliran iz korjenja šipka (nara)
- aktivan je protiv ameba i crva

## Piridinski i piperidinski alkaloidi



- relaksira mišiće (npr. crijeva, oka)



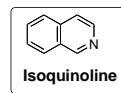
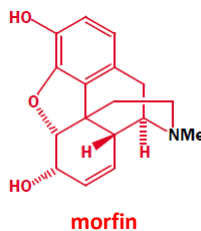
*Atropa belladonna*



## Izokinolinski alkaloidi

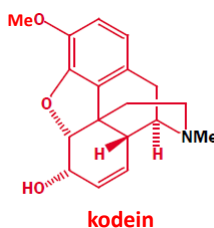
### Morfin

- 1803. morfin izoliran iz opijuma (Morpheus – grčki bog sna)
- vrlo jak utjecaj na centralni živčani sustav, smanjuje osjećaj boli
- nuspojave – smanjena potreba za disanjem, niski krvni tlak, stvara ovisnost

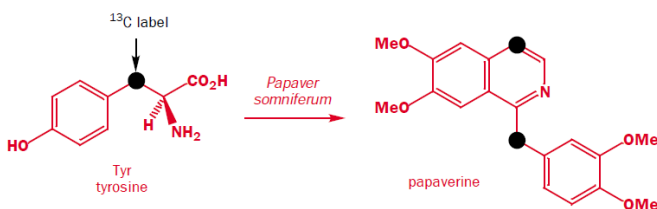
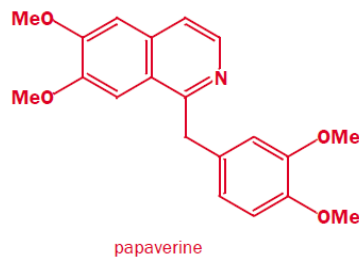
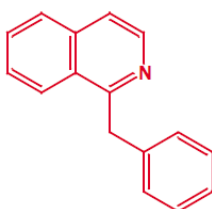
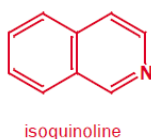


### Kodein

- manje količine u opijumskim glavama maka, lako se sintetizira iz morfina
- kod boli, kašlja ili dijareje
- nuspojave – smanjena potreba za disanjem, niski krvni tlak, stvara ovisnost



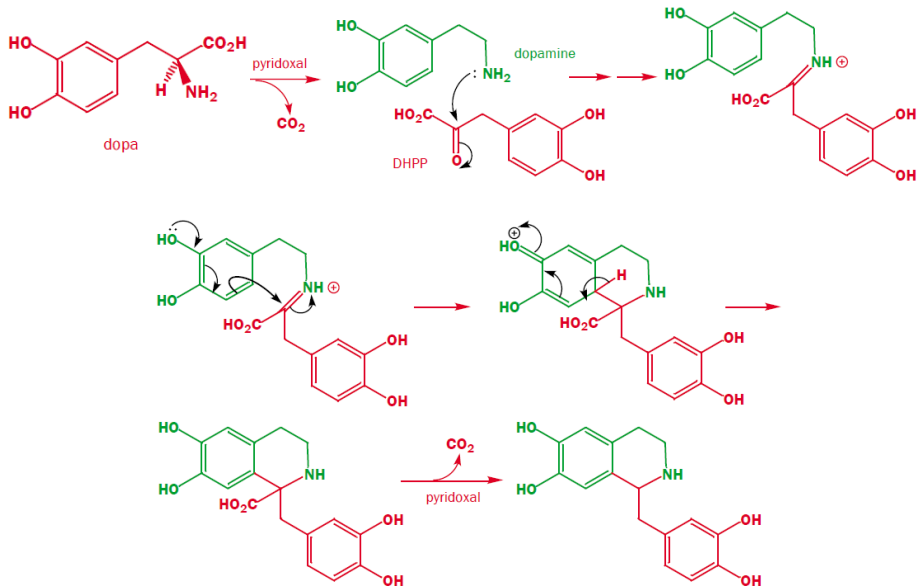
## Benzilizokinolinski alkaloidi iz tirozina



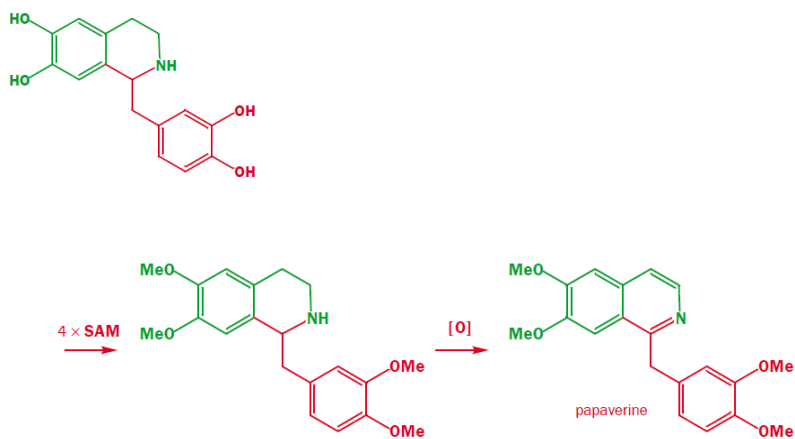
- jedna molekula tirozina gubi  $\text{NH}_3$ , druga  $\text{CO}_2$



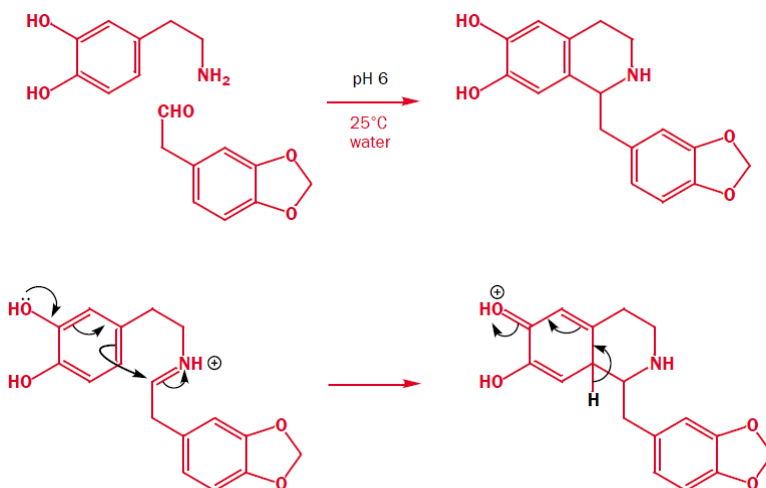
## Benzilizokinolinski alkaloidi iz tirozina - papaverin



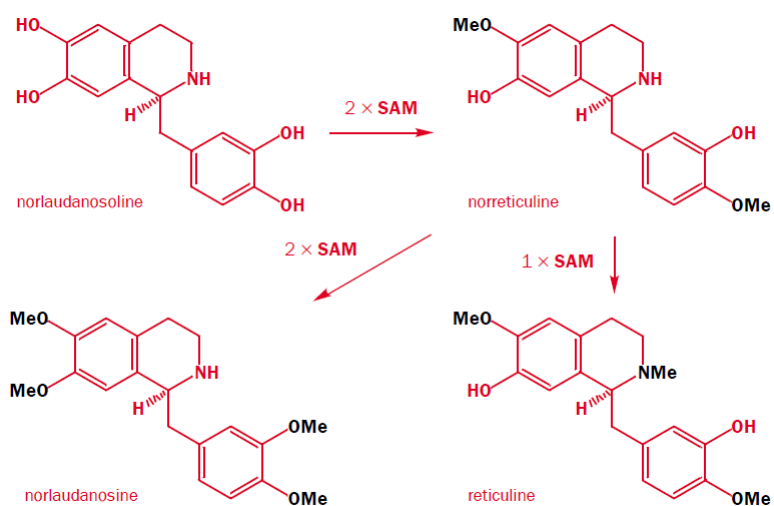
## Benzilizokinolinski alkaloidi iz tirozina - papaverin



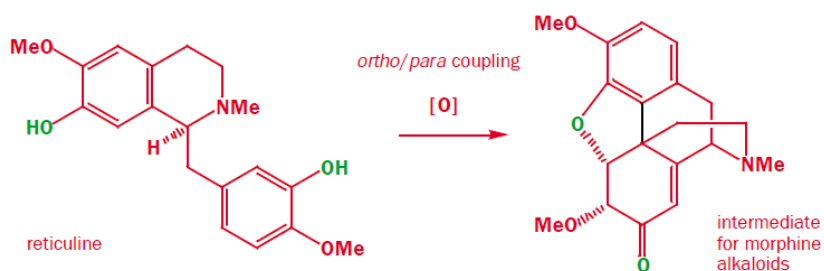
## Benzilizokinolinski alkaloidi – kemijska sinteza



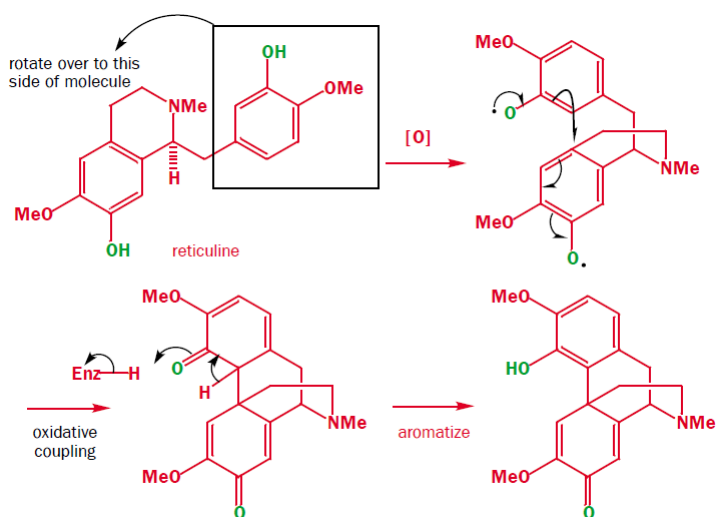
## Složeni benzilizokinolinski alkaloidi



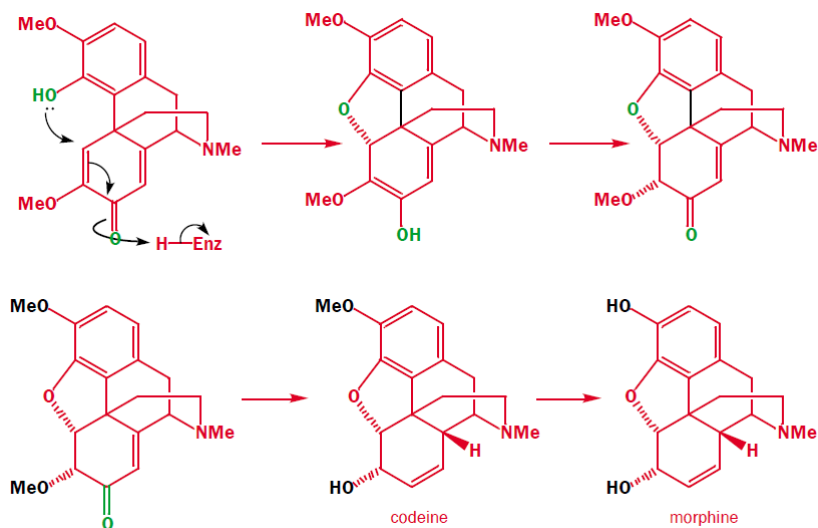
## Složeni benzilizokinolinski alkaloidi – biosinteza preko radikalskih reakcija



## Složeni benzilizokinolinski alkaloidi – biosinteza preko radikalskih reakcija



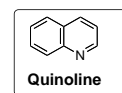
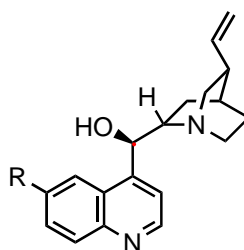
## Složeni benzilizokinolinski alkaloidi – biosinteza preko radikalnih reakcija



## Kinolinski alkaloidi

### Cinhona alkaloidi - kinin

- alkaloid iz kore kininovca
- antimalarik
- u nekim pićima (tonik, bitter lemon)

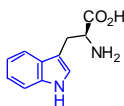
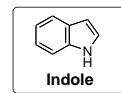


R = OMe – kinin  
R = H – kinidin

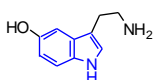


*Cinchona succiruba* - kininovac

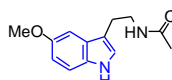
## Indolski alkaloidi



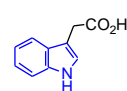
**triptofan**  
esencaijalna  
aminokiselina



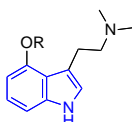
**serotonin**  
neurotransmiter



**melatonin**  
hormon



**auksin**  
hormon rasta  
kod biljaka



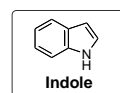
Halucinogeni iz gljiva *Psilocybe*

R = H: **psilocin**  
R = PO<sub>3</sub>H: **psilocibin**  $\xrightarrow{\text{in vivo}}$

- antagonisti serotonina
- ne razgrađuju se u organizmu
- jak, kontinuiran živčani impuls

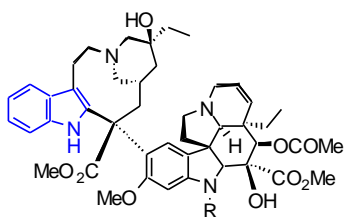


## Indolski alkaloidi



### Vinka alkaloidi

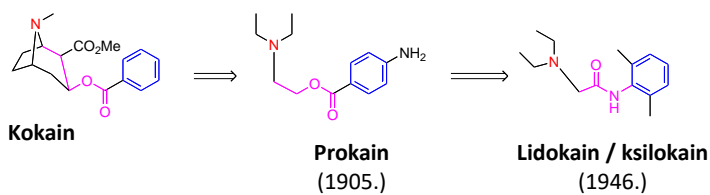
- iz *Vinca rosea*
- *antitumorska svojstva*



R=Me: **Vinblastin, Oncovin**®  
R=CHO: **Vinkristin, Velbe**®



## Kemijske modifikacije alkaloida



## ZADATAK

Svaki od sljedećih prirodnih spojeva svrstajte u odgovarajuću skupinu (metabolit aminokiselina, alkaloid, terpen, poliketid), a zatim i u specifičniju klasu (npr. tetraketid, seskviterpen).

