

9. Előadás

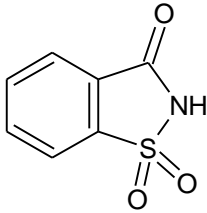
Szerves vegyületek kénatommal

SZERVES VEGYÜLETEK KÉNATOMMAL

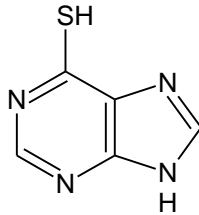
Példák:



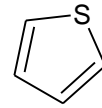
diallil-diszulfid (fokhagyma olaj)



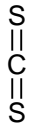
szacharin



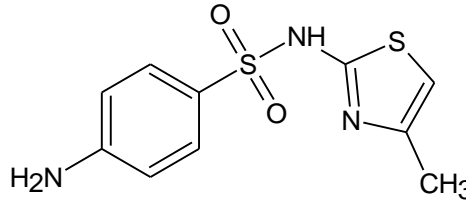
merkaptó-purin



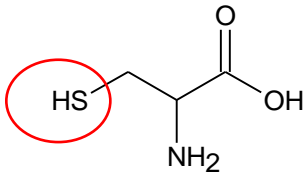
tiofén



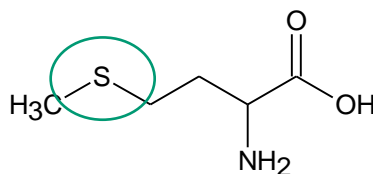
szén-diszulfid



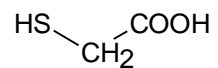
szulfonamid
(Ultraseptyl)



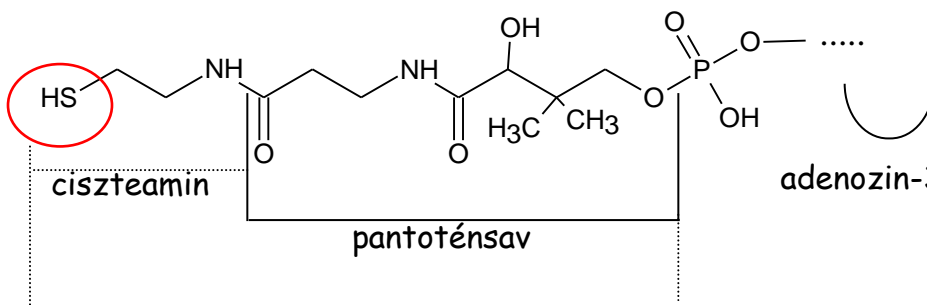
cisztein (Cys)



metionin (Met)



tio-glikolsav
(merkaptocetsav,
szulfhidril-ecetsav)



pantotein

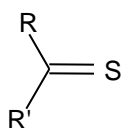
adenozin-3',5'-difoszfát

KOENZIM A

Áttekintés

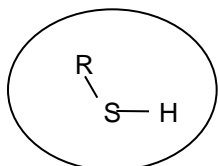
A kénatomhoz kapcsolódó ligandumok száma

[1]



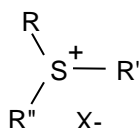
tiovegyület
(pl. tioketon)

[2]



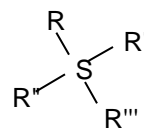
tiol

[3]

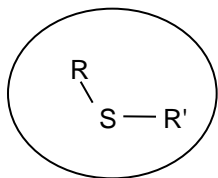


szulfóniumsó

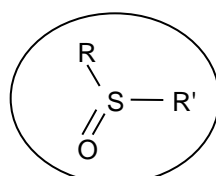
[4]



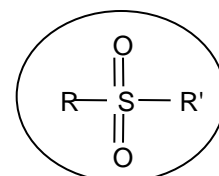
szulfurán



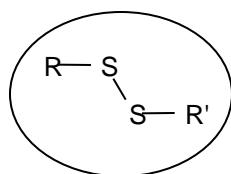
szulfid



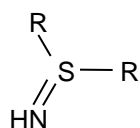
szulfoxid



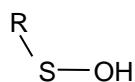
szulfon



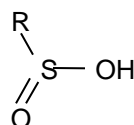
diszulfid



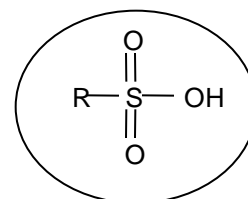
szulfilimin



szulfénsav

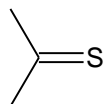


szulfinsav



szulfonsav

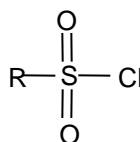
Csoportok:



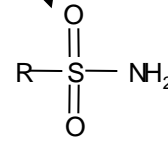
-SH

tiokarbonil

merkaptó-
(szulfhidril)

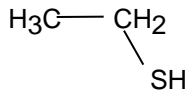


szulfonil-klorid

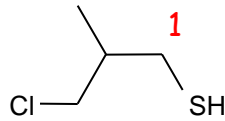


szulfon(sav)amid

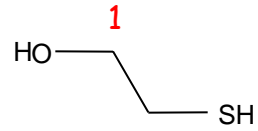
Nomenklatúra, példákkal



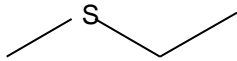
etán-tiol
(etil-hidrogénszulfid,
etil-merkaptán)



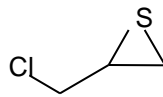
3-klór-2-metil-1-
propántiol



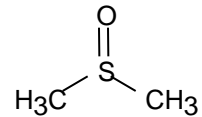
2-merkaptó-etanol



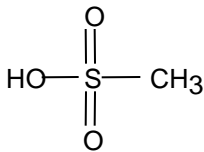
etil-metil-szulfid



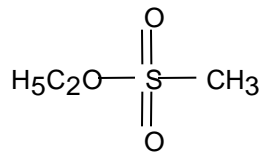
1-klór-2,3-epitio-
propán



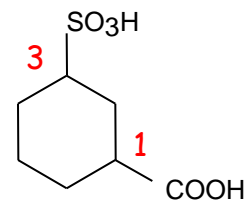
dimetil-szulfoxid



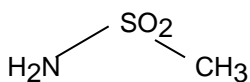
metánszulfonsav



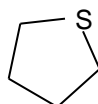
metánszulfonsav-
etilészter



3-szulfo-1-
ciklohexánkarbonsav



metánszulfonamid

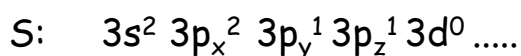


tetrametilén-szulfid

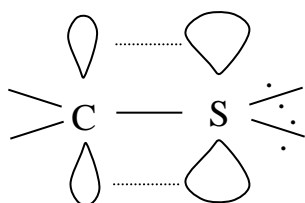
Szerkezet

Elektronok	I. sor	C	N	O	F	$S_{EN}(2,5) < O_{EN}(3,5)$
	II. sor	Si	P	S	Cl	

- Jellegzetességek
- A. analógia oxigénnel
 - B. nagyobb sugarú vegyértékhéj
kisebb EN
kisebb bázicitás
polározhatóság
 - C. különleges sztereokémia



1 ligandumos kénvegyületek (tiovegyületek)

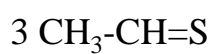


σ kötés: $C(2sp^2) - S(3sp^2)$

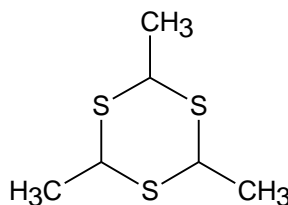
π kötés: $C(2p) - S(3p)$

nem stabil

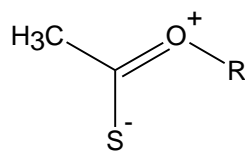
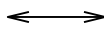
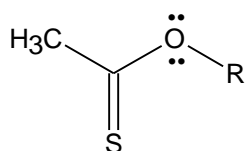
Példa:



tioaldehid



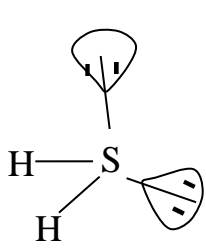
de:



stabil

tioészter: konjugált rendszer

2 ligandumos kénvegyületek (tiol, tioéter)



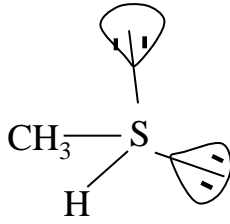
HSH \sphericalangle 92,5°

HOH 104,5°

σ : H(s) - S(p):

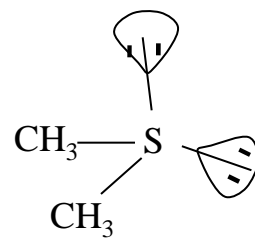
H - S: 335 kJ/mol

H - O: 452 kJ/mol



CSH \sphericalangle 96,5°

COH 105°



CSC \sphericalangle 98,5°

COC 112°

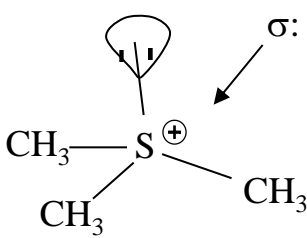
σ : C(2sp³) - S(3p)

C - S: 267 kJ/mol

C - O: 347 kJ/mol

nem
lineáris

3 ligandumos kénvegyületek (szulfoxid, szulfóniumsó)

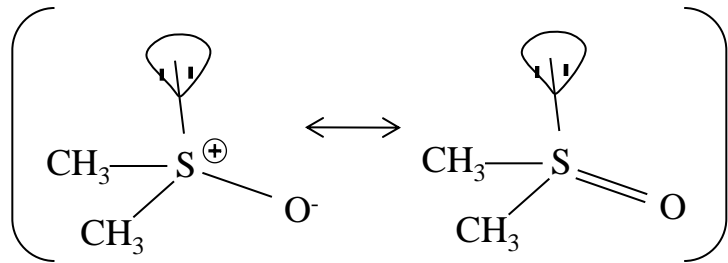


C - S: 1,83 Å

CSC kötésszög: 103°

piramisos, királis

σ : (3sp³) - (2sp³)



C - S: 1,81 Å

CSC kötésszög: 96,4°

piramisos, királis

C - O: 1,47 Å

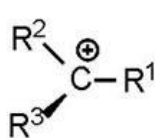
CSO: 106,7°

σ : C(2sp³) - S(3sp³)

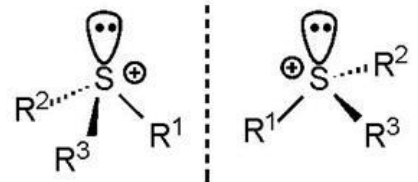
S(3sp³) - O(2sp²)

π : S(3d) - O(2p)

Összevetés

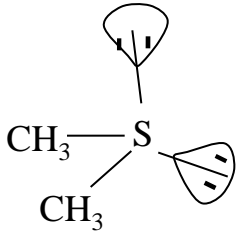


planáris, akirális

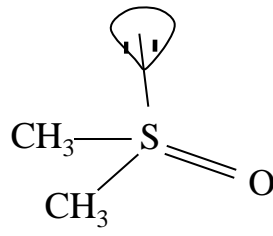


piramisos, királis

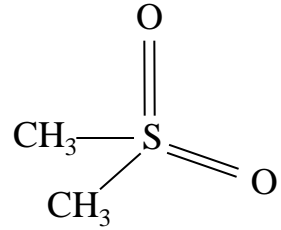
Összegzés



szulfid



szulfoxid



szulfon

Kötéshosszak:

C - S 1,82Å

C - S 1,81Å

C - S 1,78Å

S = O 1,47Å

S = O 1,44Å

Kötésszögek:

CSC 98,5°

CSC 96,4°

CSC 103°

CSO 106,7°

CSO 108,7°

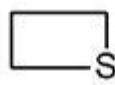
OSO 118°

DE:

C-S-C



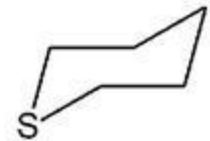
60°



78°



108°



100°

Fizikai tulajdonságok

A. Tiolok

1/10 millió

Forráspont (°C)	X=S	X=O
H_2X^*	- 62	100
CH_3XH^*	6	65
$CH_3CH_2XH^*$	35	78
CH_3XCH_3	37	- 24

nincs H-híd kötés*

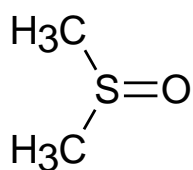
illékonyág: $CH_3CH_2CH_2SH$ hagyma

$CH_3(CH_2)_3SH$ görény

B. Szulfoxidok, szulfonok



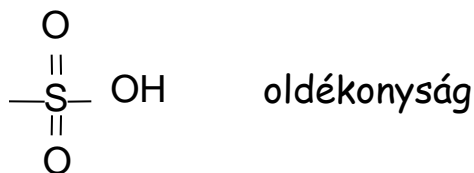
H-híd: akceptor



op: 18°C

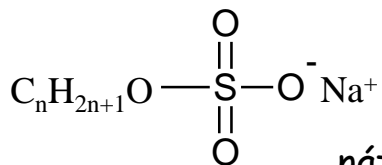
dipoláros, aprotikus oldószer

C. Szulfonsavak (O-H sav)



oldékonyág

detergensek:



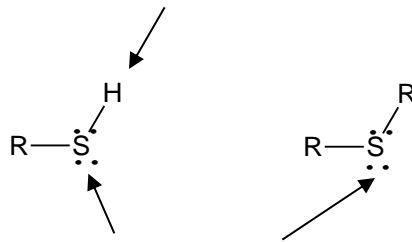
nátrium-alkilsulfát

Kémiai reakciók

1. Sav-bázis sajátság

Tiol, szulfid

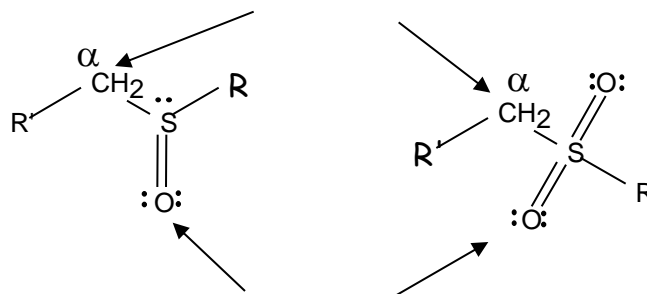
savas jelleg, $pK_a=11$ (vö. OH $pK_a=17$)



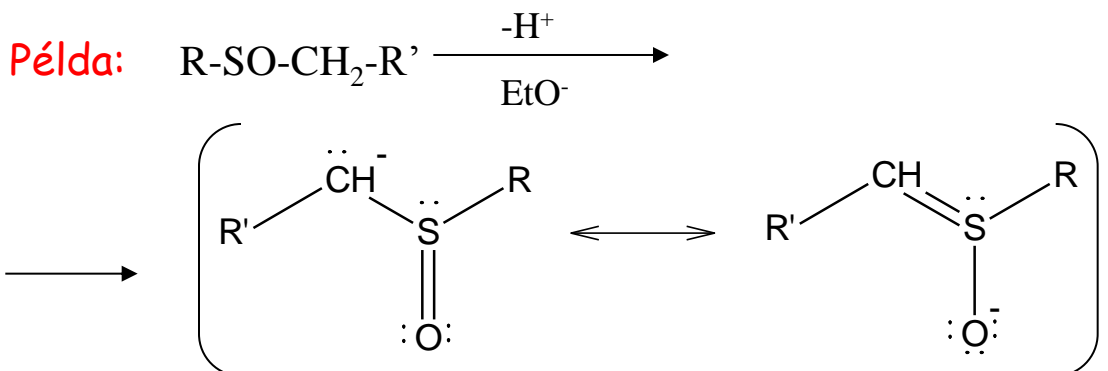
bázikus jelleg (gyengébb, mint $:O:$)

Szulfoxid, szulfon

savas jelleg



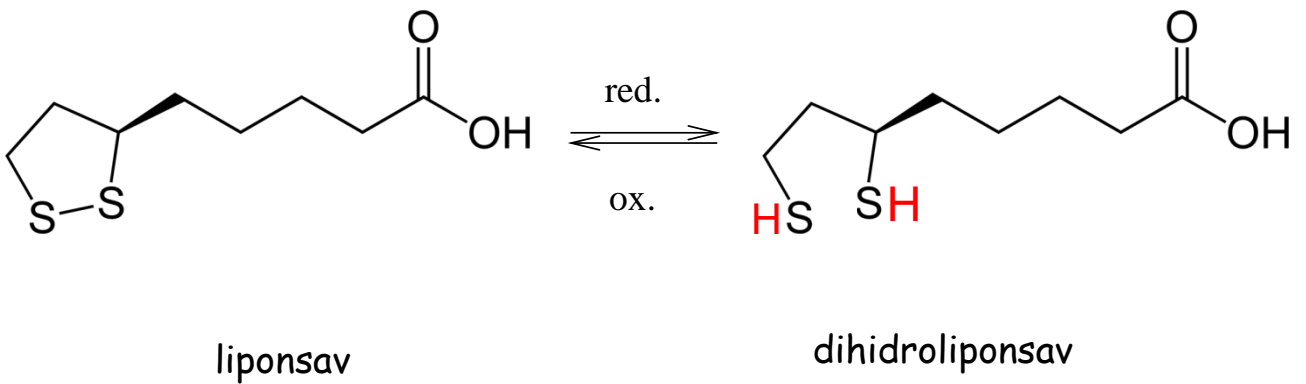
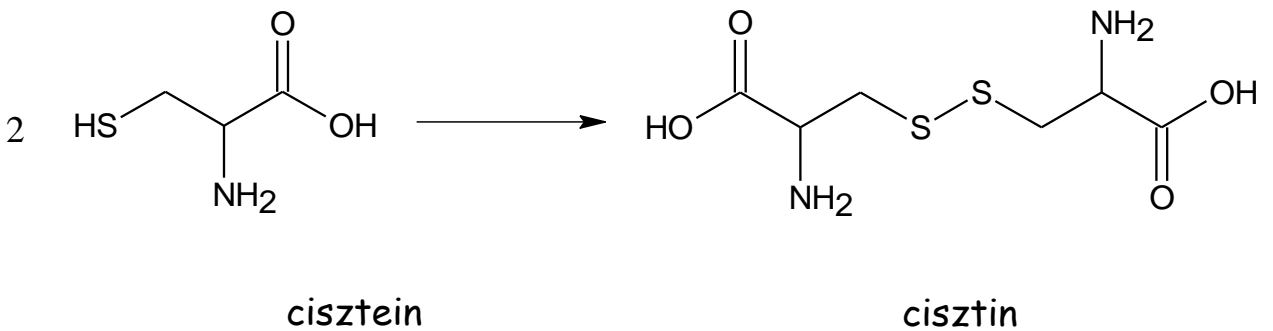
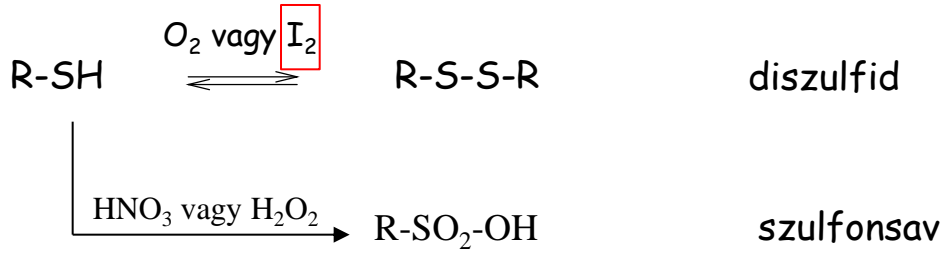
bázikus jelleg



konjugáció: delokalizált, nincs tautomerizáció!

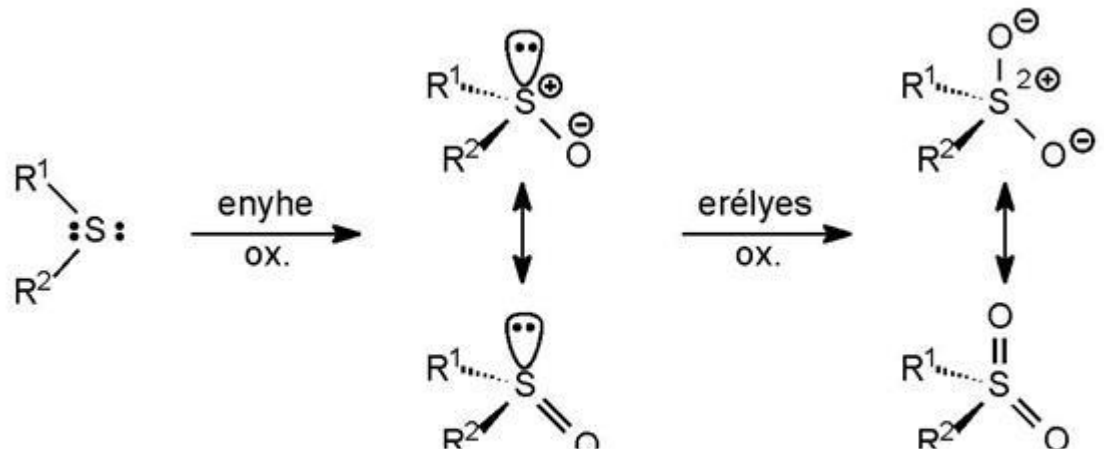
2. Oxidáció, redukció

Tiol



királis karbonsav,
kofaktor,
piruvát-dehidrogenáz komplex része,
antioxidáns

Szulfid

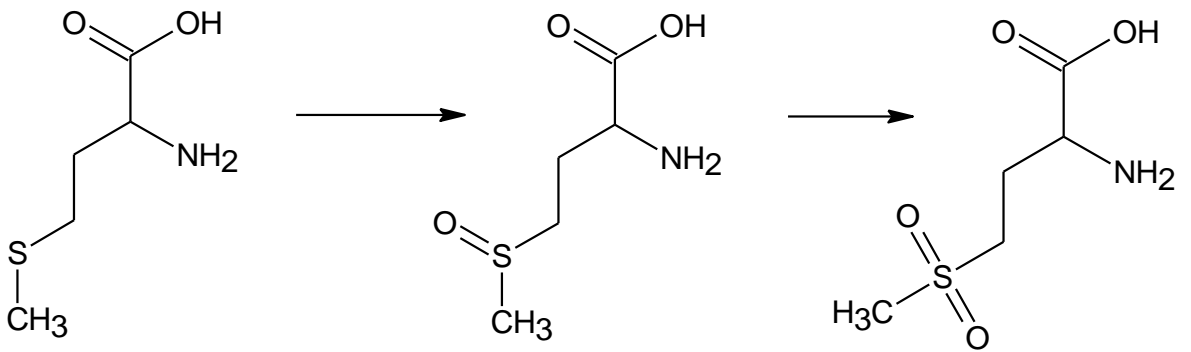


szulfid

szulfoxid

szulfon

Példa:



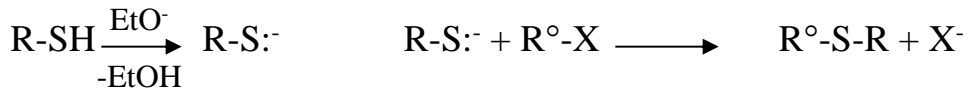
metionin

metionin
szulfoxid

metionin
szulfon

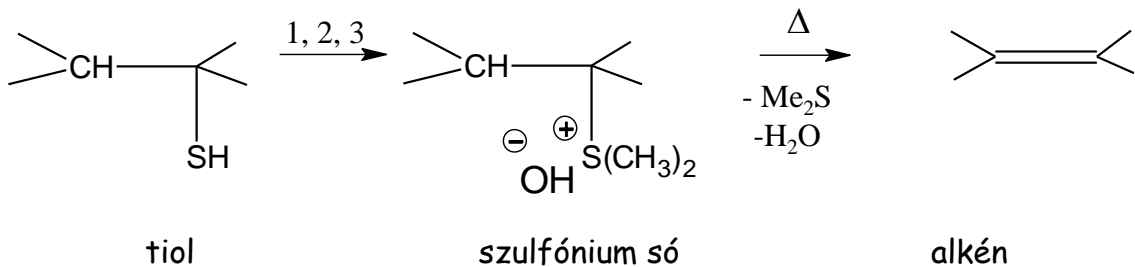
3. Nukleofil szubsztitúció

3.1. Alkilezés (tiol, tioéter)



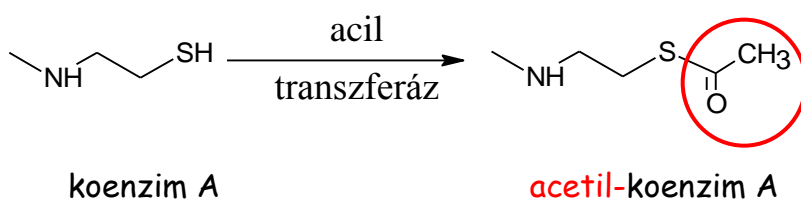
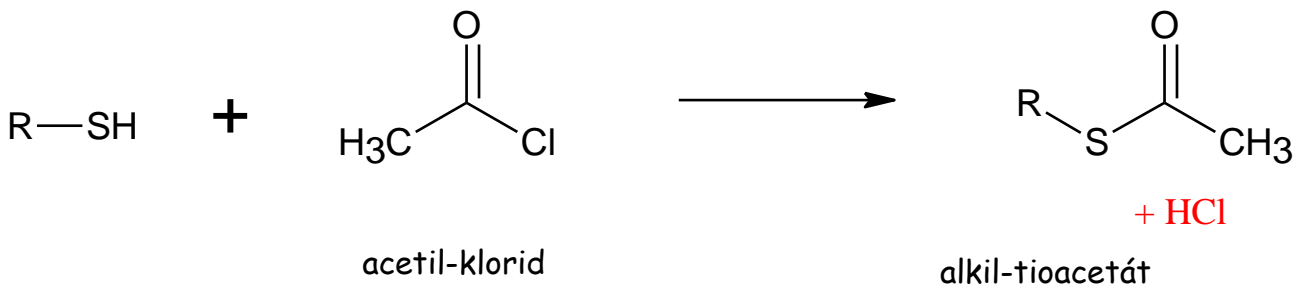
szulfóniumsó

Hofmann-analóg elimináció



1: EtO⁻, MeI; 2: MeI, éter; 3: Ag₂O, H₂O

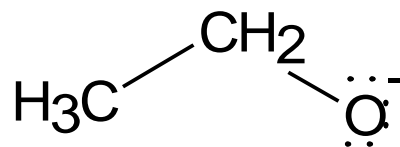
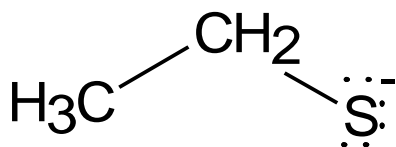
3.2. Acilezés



-SH vs -OH reaktivitása - összevetés

(tiol, merkaptán = „mercurium captans“)

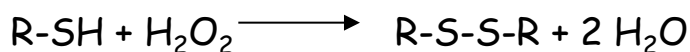
1. Nukleofil sajátság



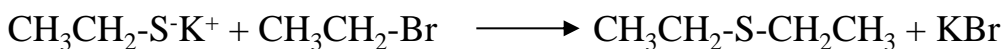
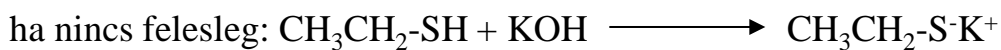
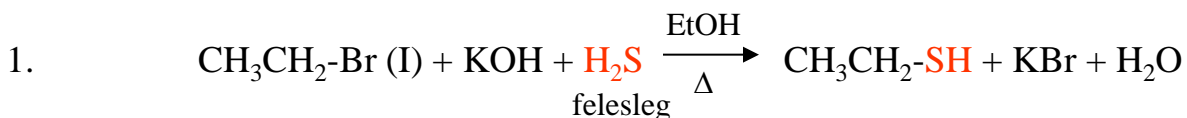
2. Savi jelleg



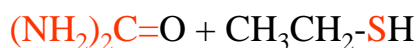
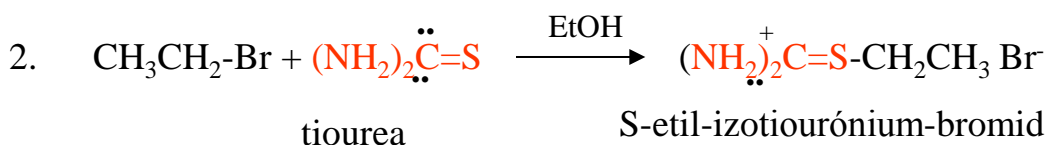
3. Oxidáció



Tiolok előállítása



tioéter



urea
(karbamid)

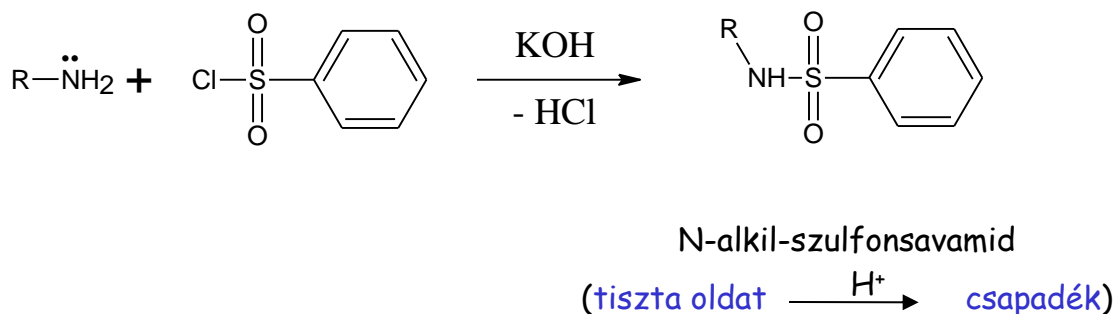
etántiol

1. OH/H₂O

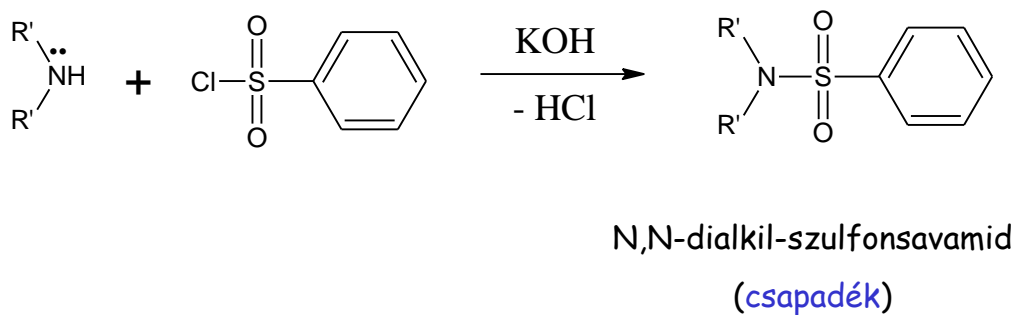
2. H⁺

Kimutatás: Aminok reakciója szulfonil-kloriddal (Hinsberg-reakció)

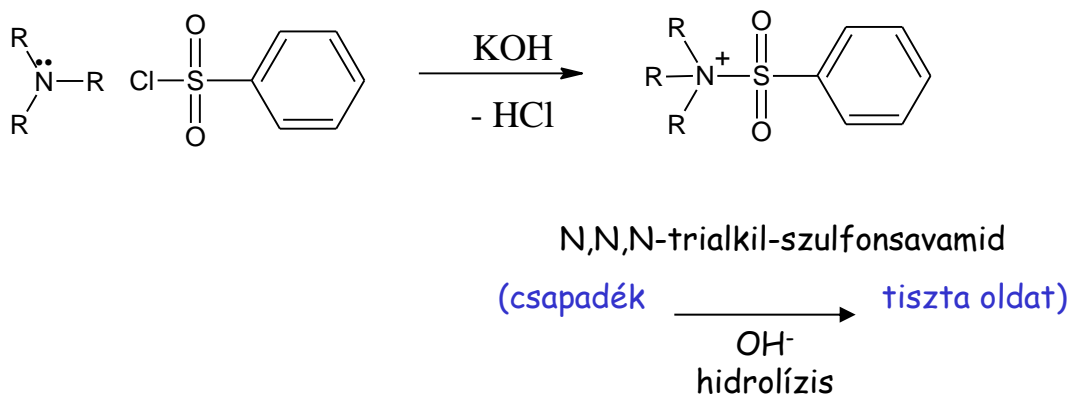
1. Primer amin



2. Szekunder-amin



3. Tercier-amin



Antibiotikumok

Definíció (klasszikus): **antibiotikum** olyan vegyület, amelyet mikroorganizmus (gomba) termel és képes más mikroorganizmus (gomba) elpusztítására (baktericid hatás) vagy a szaporodás gátlására (bakteriosztatikus hatás).

Felosztás:

Eredet

Szerkezet **β (Béta)-laktám antibiotikumok**

1. Monociklusos β -laktámok (Monobaktámok)
2. Penám vázas antibiotikumok
3. Kefémvázás antibiotikumok (kefalosporinok)

aminosav/peptid típusú

glikozid típusú

policiklusos

spirociklusos

Elnevezés: eredet, tulajdonság (pl. szín)

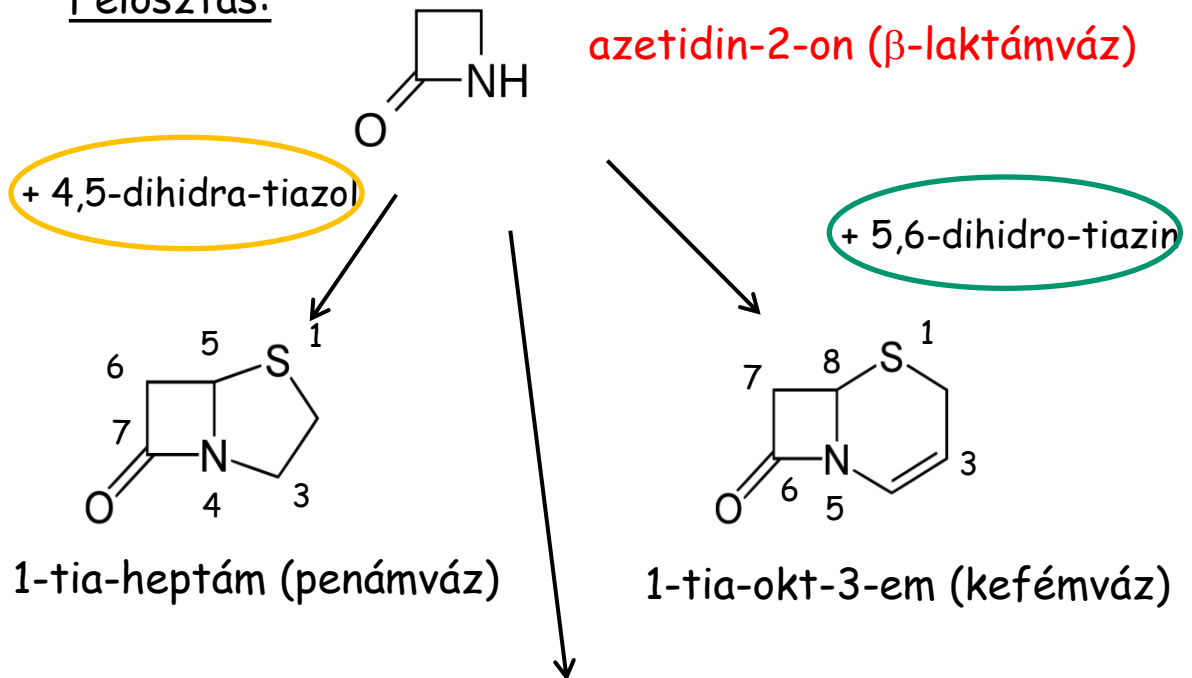
Előfordulás: mikroorganizmusok, gombák

Felhasználás: gyógyászat, agrárium

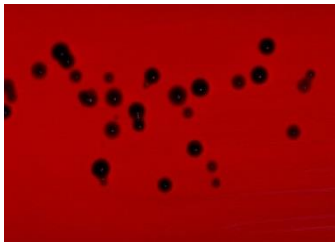
β (Béta)-laktám antibiotikumok

(közös elem: négytagú gyűrűs savamid)

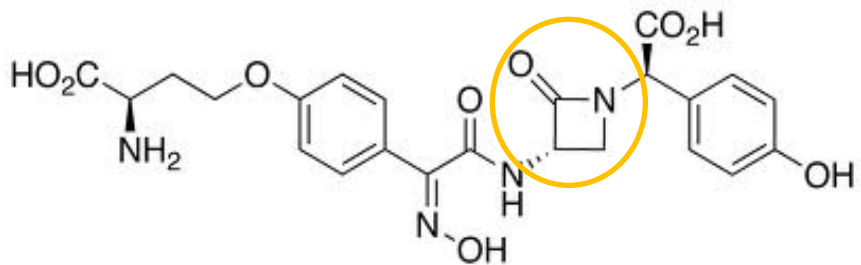
Felosztás:



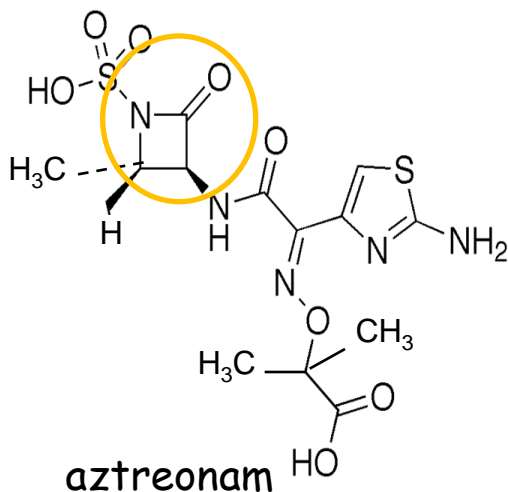
1. Monociklusos β -laktámok (Monobaktámok)



Chromobacterium violaceum



nocardicin A



aztreonam



Nocardia asteroides
(yellow colonies)

Izolálás:
A.H. Aoki. 1976

β(Béta)-laktám antibiotikumok

2. Penám vázas antibiotikumok



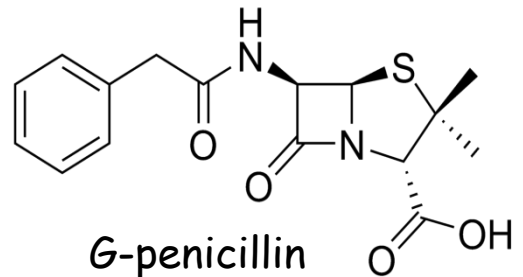
A. Fleming, E. B. Chain, H. W. Florey,
Nobel-díj, 1945

Penicillin (1928)

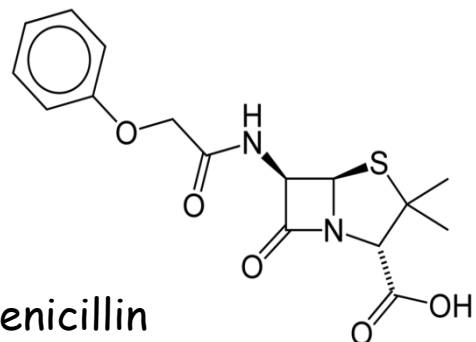
Felfedezés: Fleming
Izolálás: Chain, Florey,
1941



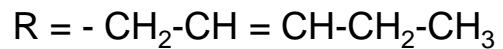
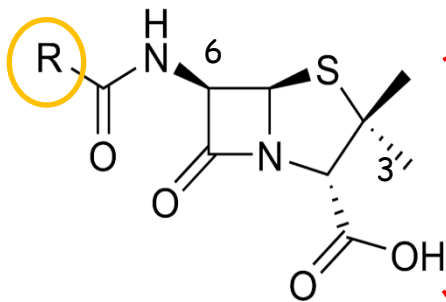
Penicillium notatum



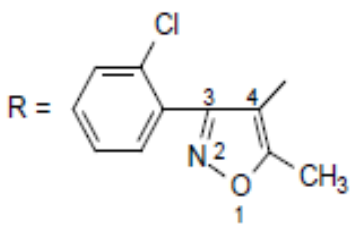
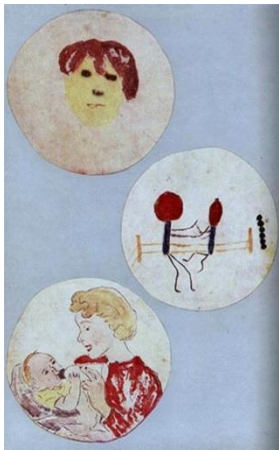
G-penicillin
(pl. agyhártya, szifilisz, tüdőgyulladás)



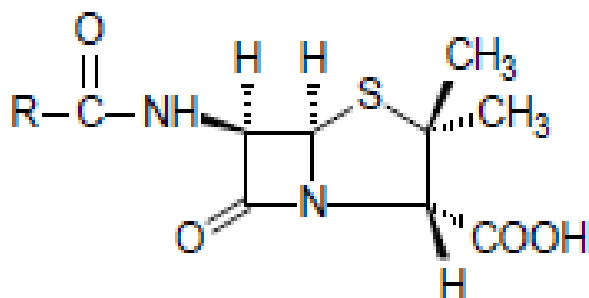
V-penicillin
(pl. torok, mandula gyulladás)



F-penicillin (pent-2-én-1-il-)

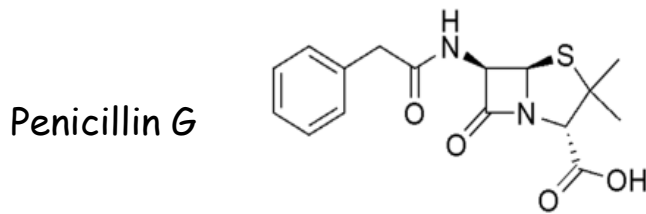
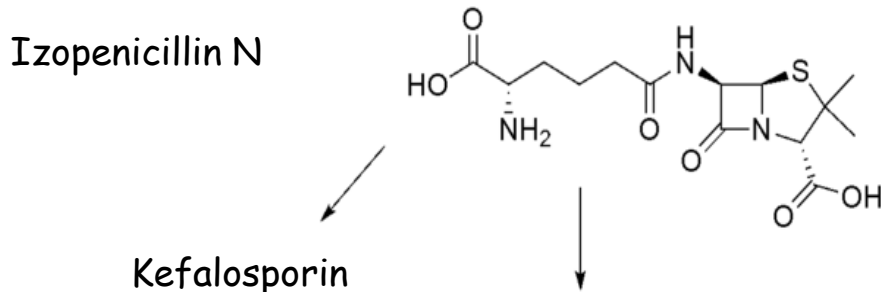
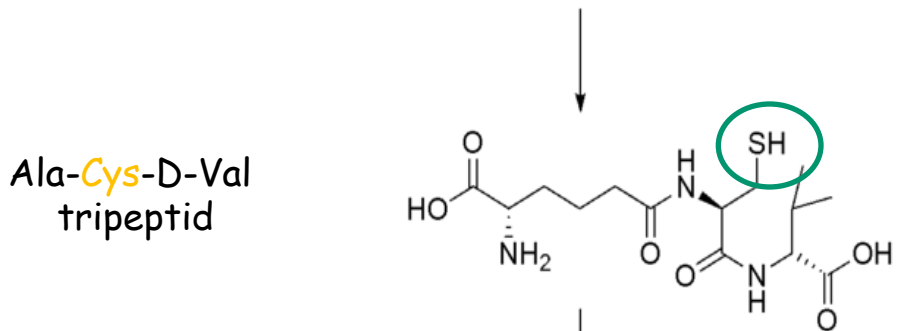
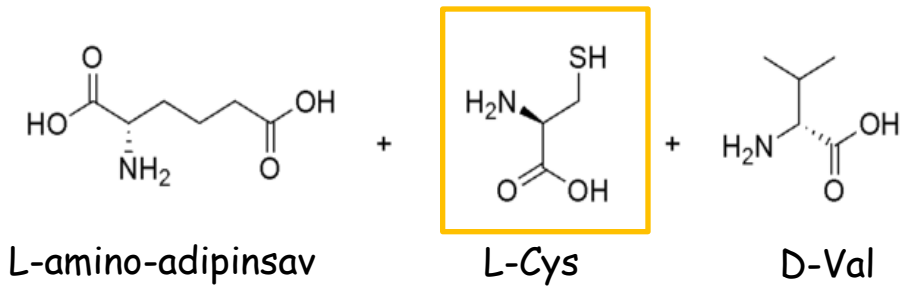


3-(2-klórfenil)-5-metiloxazolil



kloxacillin
(félszintetikus)

Bioszintézis



Bioszintézis (fermentáció):



Penicillium chrysogenum

+ fenilecetsav = penicillin G
+ fenoxiecetsav = penicillin V

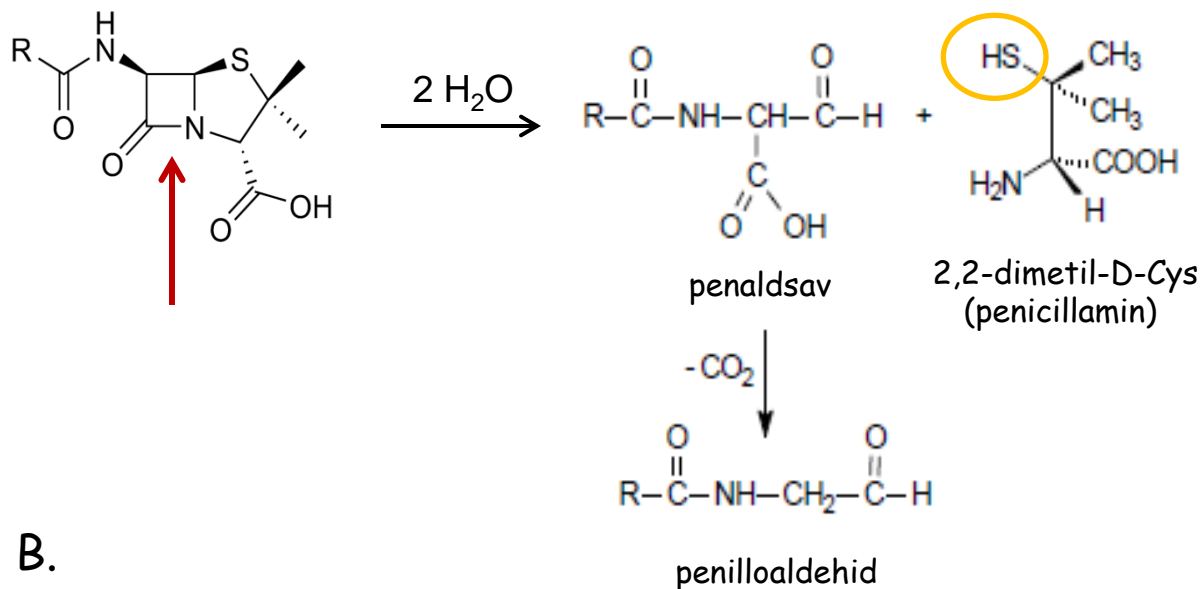
„One sometimes finds what one is not looking for.”

β (Béta)-laktám antibiotikumok

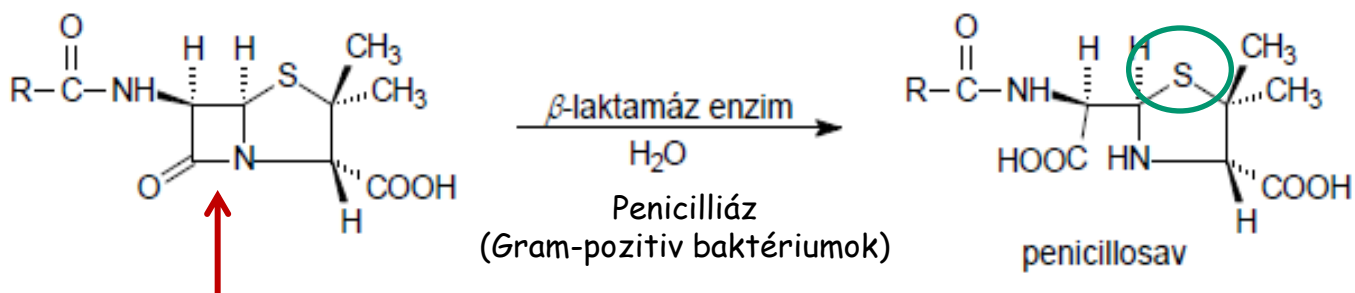
Penicillinek

Hidrolízis, stabilitás

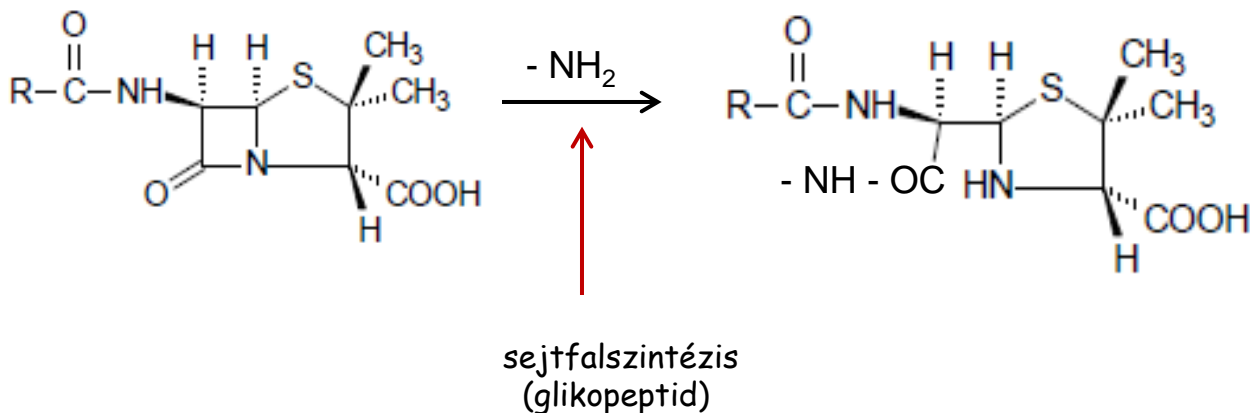
A.



B.

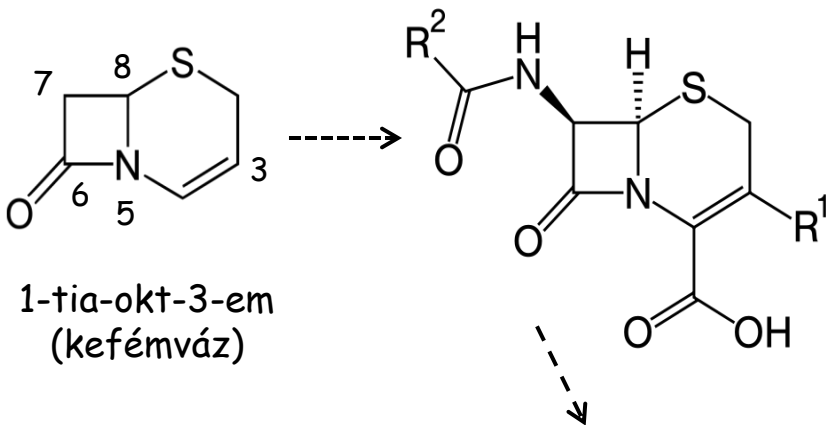


Acilezés (hatásmechanizmus)



β(Béta)-laktám antibiotikumok

3. Kefémvázak antibiotikumok (kefalosporinok)



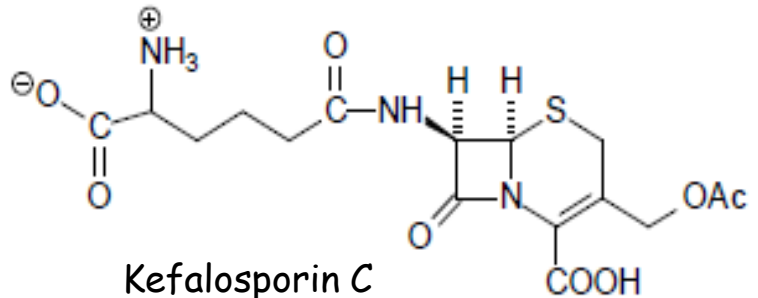
Acremonium falciforme
(*Cephalosporium*)

1-tia-8-oxa-3-azabicyclo[3.2.1]octán
(kefémváz)

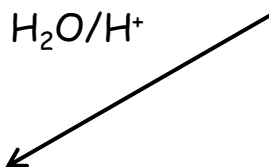
$R^1 = -CH_2O-COCH_3$

$R^2 = -(CH_2)_3-CH(NH_2)-COOH$

acil csoport: L-amino-adipinoil



Kefalosporin C

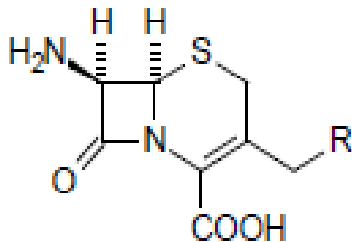


G. Brotzu, Szardínia, 1948

Szerkezet: E.P. Abraham, D. Hodgkin, 1961

Hatás: Gram pozitív és negatív

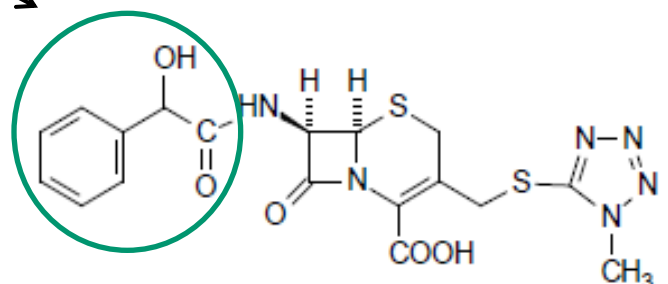
Ellenálló: penicillináz enzim



Félszintetikus kefalosporinok

acilezés

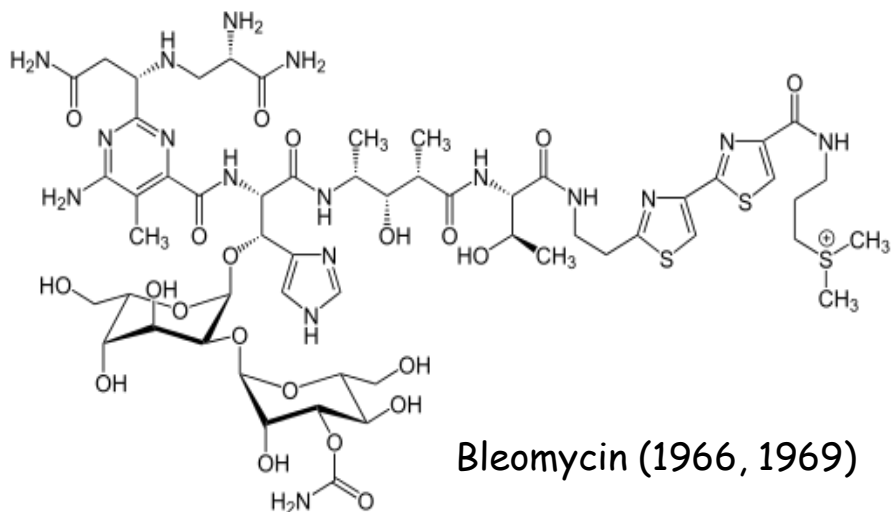
7-aminocephalosporinsav, $R = -O-COCH_3$
7-amino-3-dezacetoxisporánsav, $R = -H$



cefamandol

Tumorellenes hatású antibiotikumok

Peptid (glikozid) antibiotikum



Bleomycin (1966, 1969)



Streptomyces verticillus

Antibiotikumok: szulfonamidok

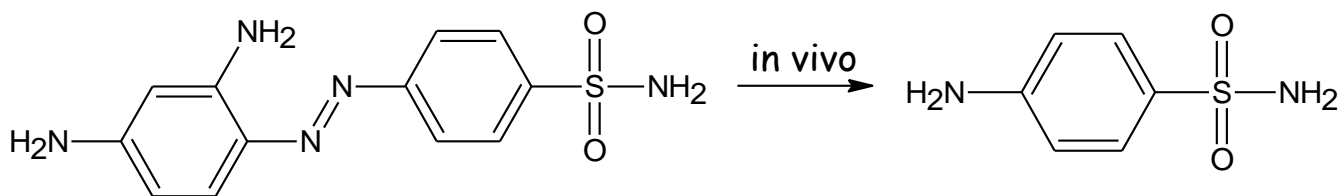


(1895 - 1964)

Gerhard Domagk (1932),
patológus, bakteriológus

Münsteri Egyetem, I.G. Farben

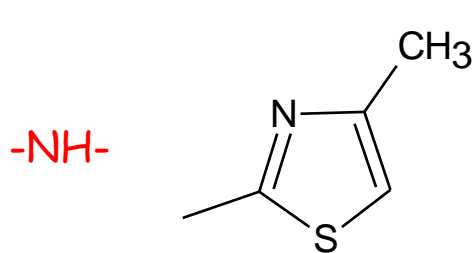
Nd. 1939→1947, az első kereskedelmi
forgalomba is kerülő antibiotikumok,
a szulfonamidok felfedezéséért



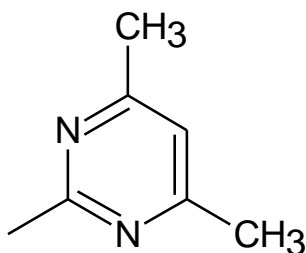
Prontosil (narancsvörös)

in vitro : „üvegben”
in vivo: „életben”

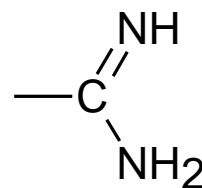
para-amino-benzol-
szulfonamid
(PABS, fehér)
(folsavsintézishez)



Ultraseptyl

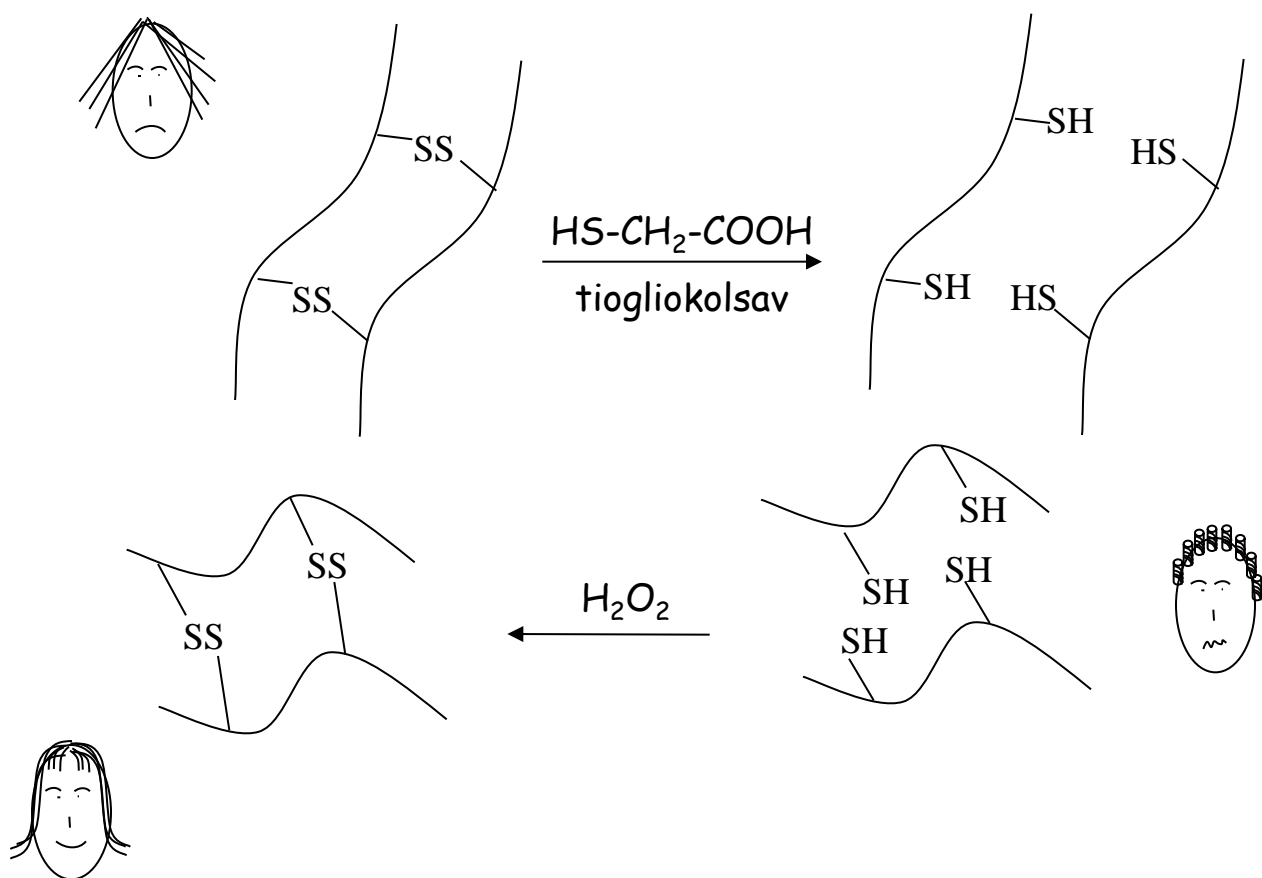


Superseptyl



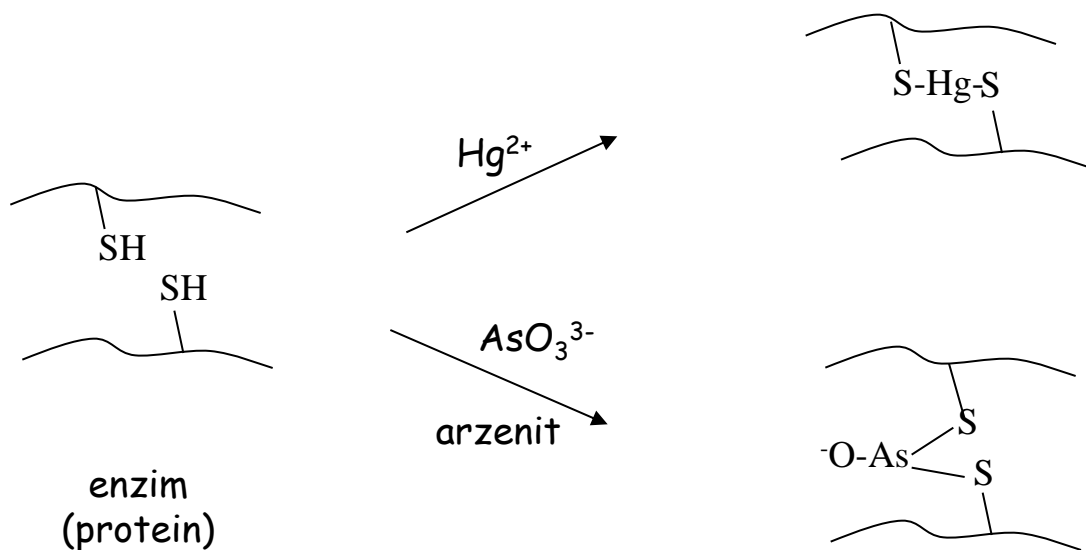
Sulfaguanidin

A fodrásznál



Mérgezés

(tiol, **merkaptán*** jelentése = „mercurium captans”, capturing mercury)



*1832, **William Christopher Zeise** , dán szerves kémikus, fémorganikus vegyületek