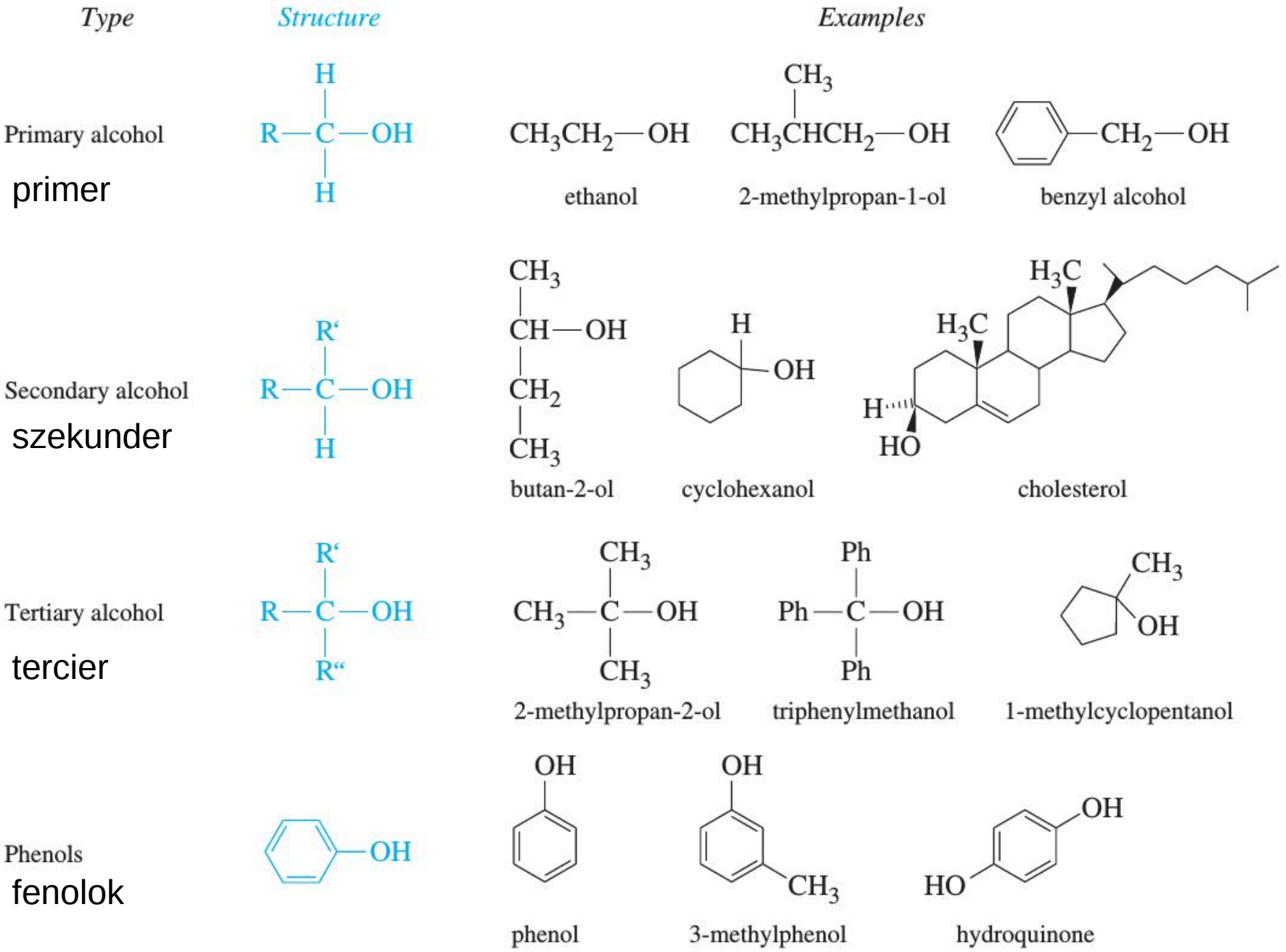
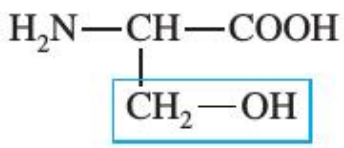
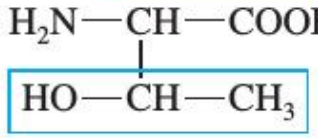
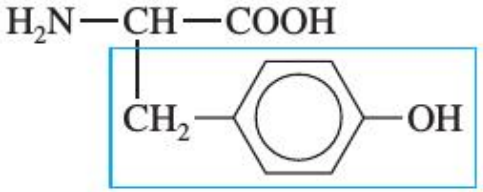
Oxo- és hidroxivegyületek

Alkoholok rendűsége, fenolok

Alkohol rendűsége = a hidroxilcsoportot hordozó szénatom rendűsége



Hidroxilcsoportot tartalmazó aminosavak

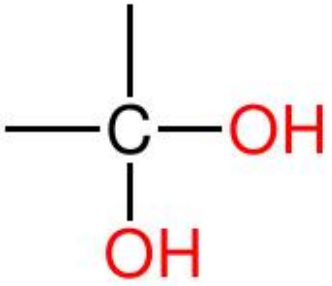
Name	Symbol	Abbreviation	Structure	Functional Group in Side Chain	Isoelectric Point
side chain contains an —OH					
serine szerin	S	Ser		hydroxyl group	5.7
*threonine treonin	T	Thr		hydroxyl group	5.6
tyrosine tirozin	Y	Tyr		phenolic—OH group	5.7

Jelentőségük többek között: foszforiláció lehetősége

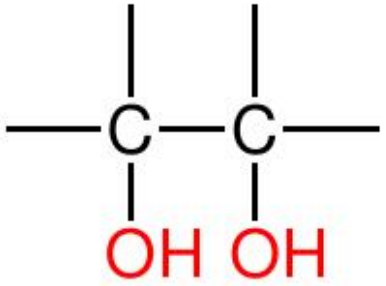
Figyeljük meg a hidroxilcsoportot tartalmazó szénatomok rendűségét, valamint az aminosavak sztereokémiáját!

Többértékű alkoholok

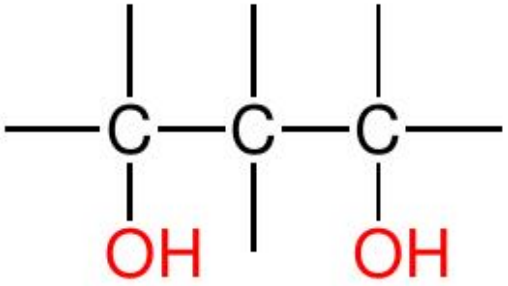
Alkohol értékűsége = a hidroxilcsoportok száma



geminális



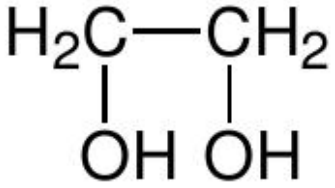
vicinális



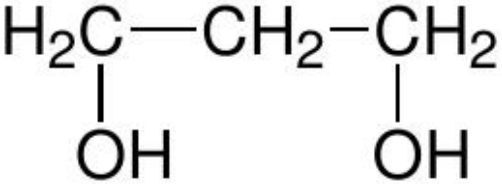
diszjunkt

Kétértékű alkoholok (diolok): változatok a hidroxilcsoportok kölcsönös helyzetére

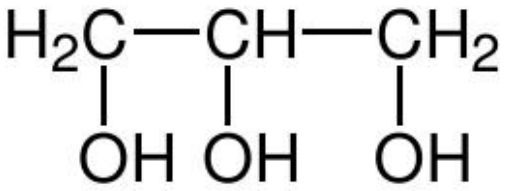
metándiol
(nem létképes)



etilénglikol



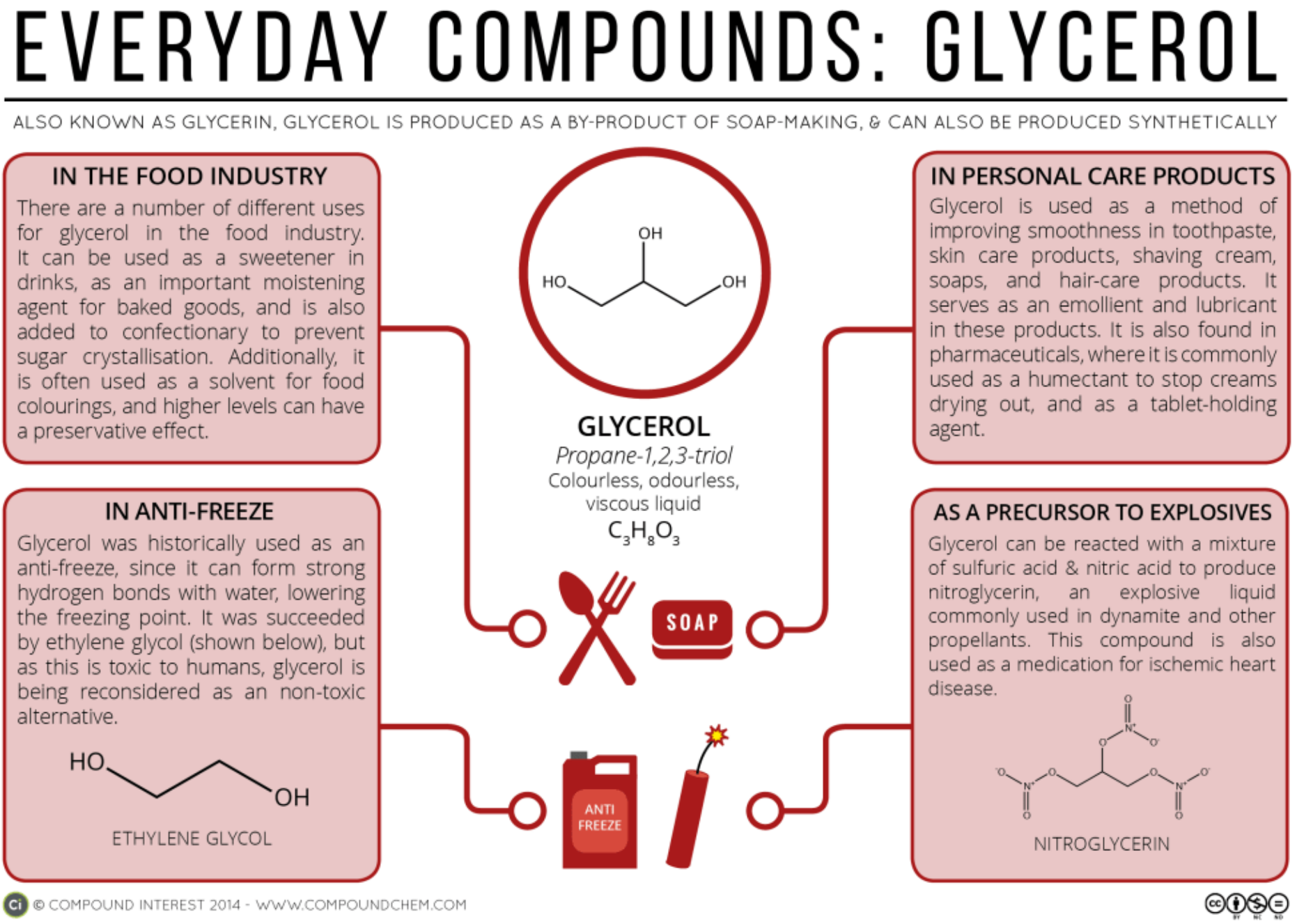
propán-1,3-diol



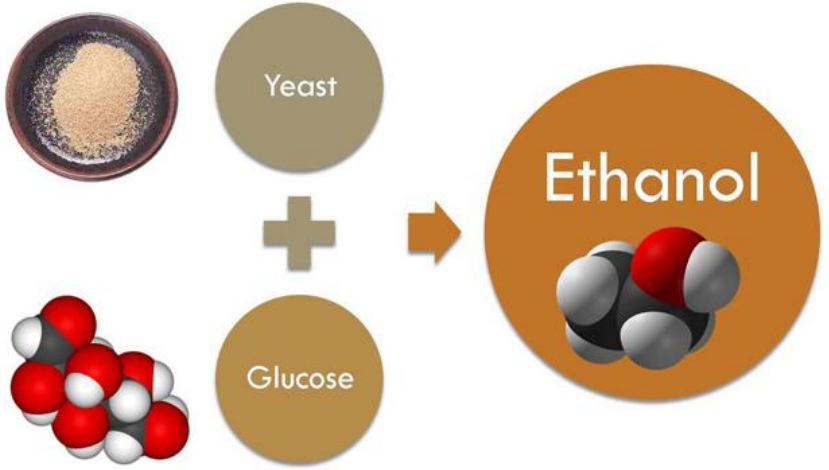
glicerin

Egy vicinális triol

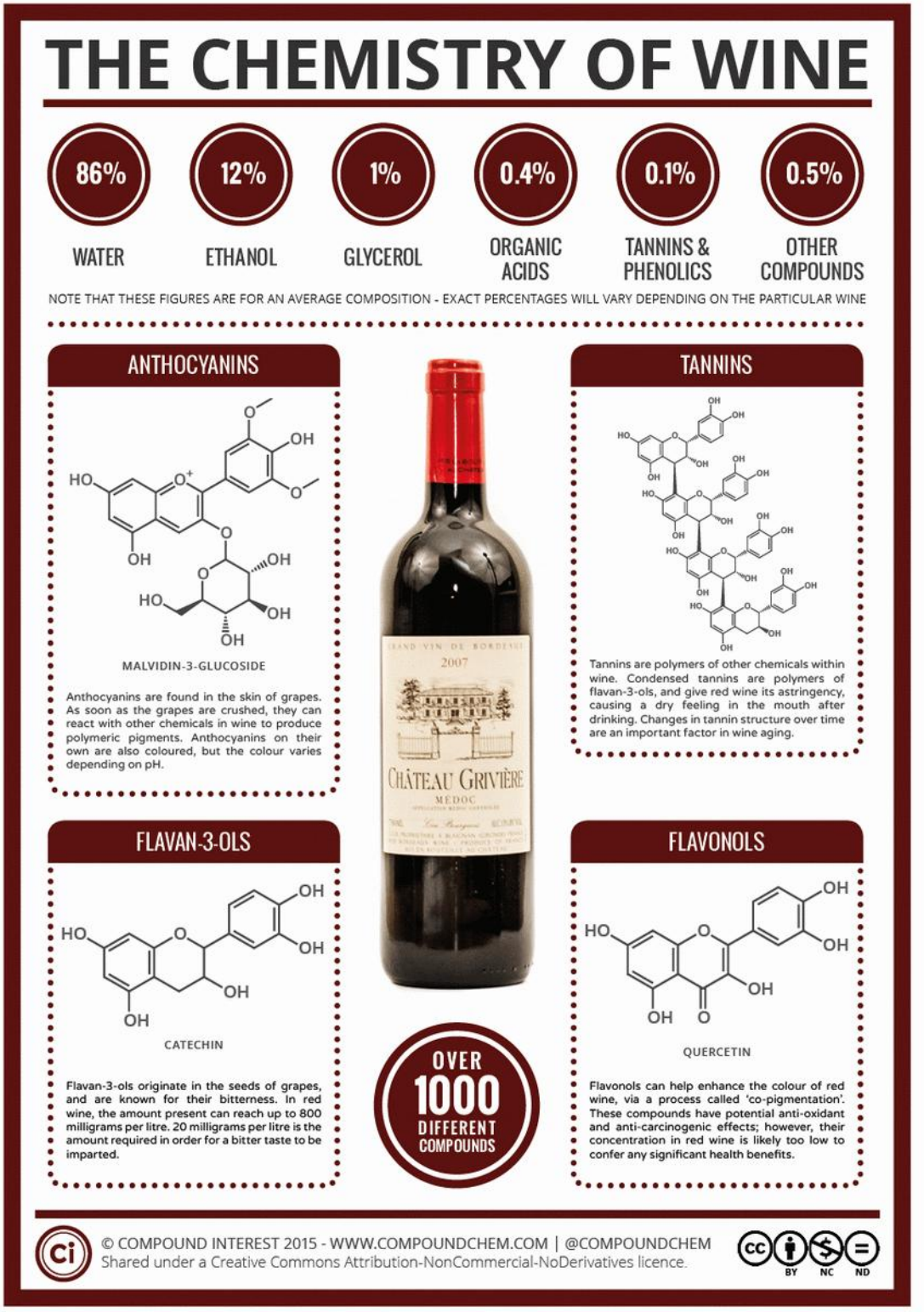
Kitekintés: mire jó a glicerin?



Kitekintés: a bor kémiája



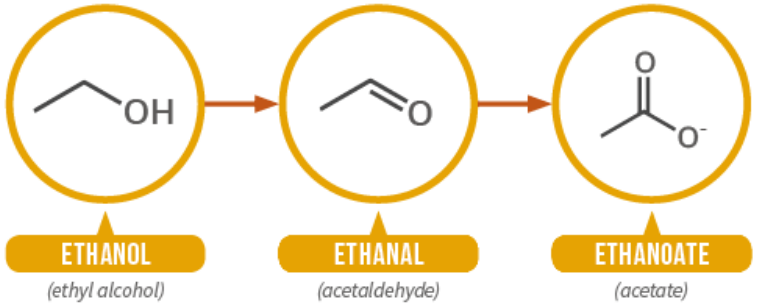
$$C_6H_{12}O_6 \rightarrow 2\ C_2H_5OH + 2\ CO_2$$



Kitekintés: a másnaposság

THE CHEMISTRY OF A HANGOVER

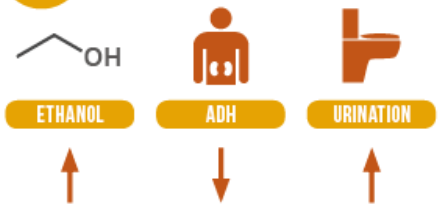
For most of us, a hangover is the price to pay for a night of drinking. However, we still don't know what exactly it is that causes them. In this graphic, we look at what happens to alcohol in your body, and some of the prime suspects for causing your hangover.



WHAT HAPPENS TO ALCOHOL IN YOUR BODY?

In the liver, ethanol is converted to acetaldehyde by the alcohol dehydrogenase enzyme, and then subsequently converted into acetate by the aldehyde dehydrogenase enzyme. Acetate can be broken down into carbon dioxide and water, then eliminated from the body. On average, the liver can break down alcohol at the rate of one unit (8 grams or 10 millilitres of pure alcohol) every hour.

1 DEHYDRATION

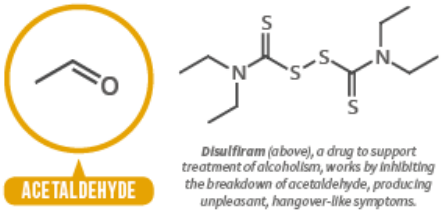


During alcohol intoxication, release of the anti-diuretic hormone (ADH) vasopressin is decreased, resulting in increased urination.

Alcohol has a diuretic effect on the body, increasing urine production. Alcohol-induced dehydration has been suggested as a cause for some hangover symptoms, but research suggests it isn't a major factor.

2 ACETALDEHYDE

Acetaldehyde is rapidly converted into acetate in the liver

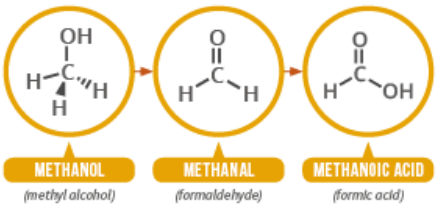


***Disulfiram** (above), a drug to support treatment of alcoholism, works by inhibiting the breakdown of acetaldehyde, producing unpleasant, hangover-like symptoms.*

Acetaldehyde, produced by the breakdown of alcohol, has toxic effects that could cause hangover symptoms. However, acetaldehyde concentration doesn't significantly correlate with hangover severity.

3 CONGENERS

Methanol is found in very small amounts in many alcoholic drinks



Congeners are compounds other than ethanol in drinks. These include alcohols such as methanol, which breaks down into toxic formaldehyde and formic acid. Congeners can increase hangover severity.

4 IMMUNE SYSTEM

Cytokines are small proteins released by cells which affect other cells. They play an important role in the immune system.

In particular, IL-12 & IFN-γ concentration changes show significant correlations with hangover severity

Alcohol causes changes in cytokine concentrations in the immune system. Studies have shown the effects caused by some cytokines are very similar to those of a hangover, strongly supporting their role.

Éterek

H—O—H
water

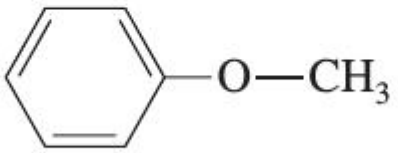
R—O—H
alcohol

R—O—R′
ether

Examples of ethers

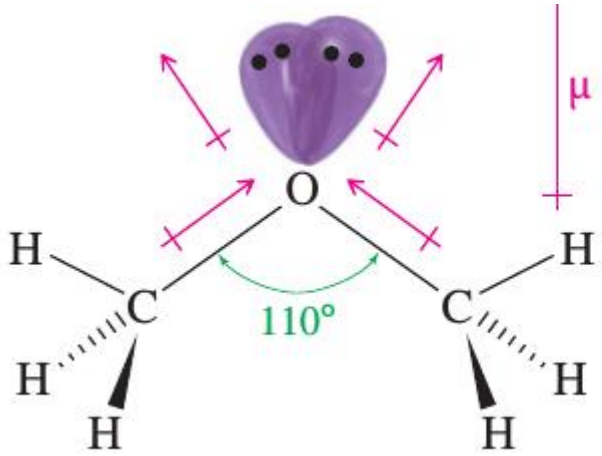
$CH_3CH_2—O—CH_2CH_3$

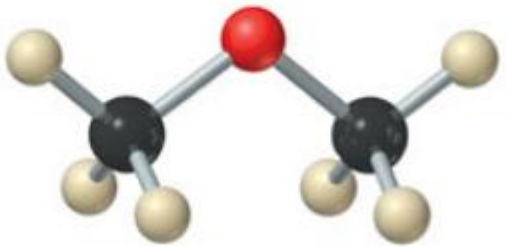
diethyl ether
(a symmetrical ether)

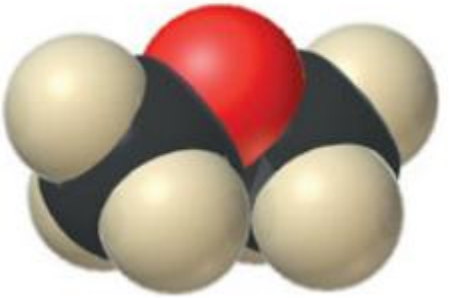


methyl phenyl ether
(an unsymmetrical ether)

tetrahydrofuran
(a symmetrical, cyclic ether)

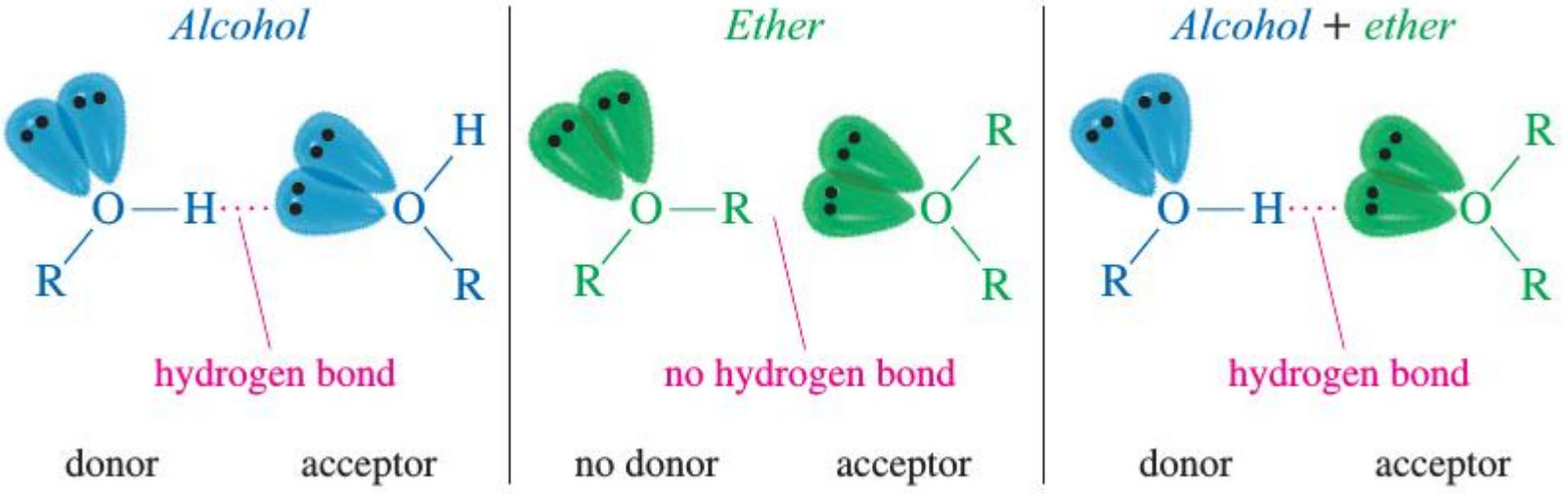




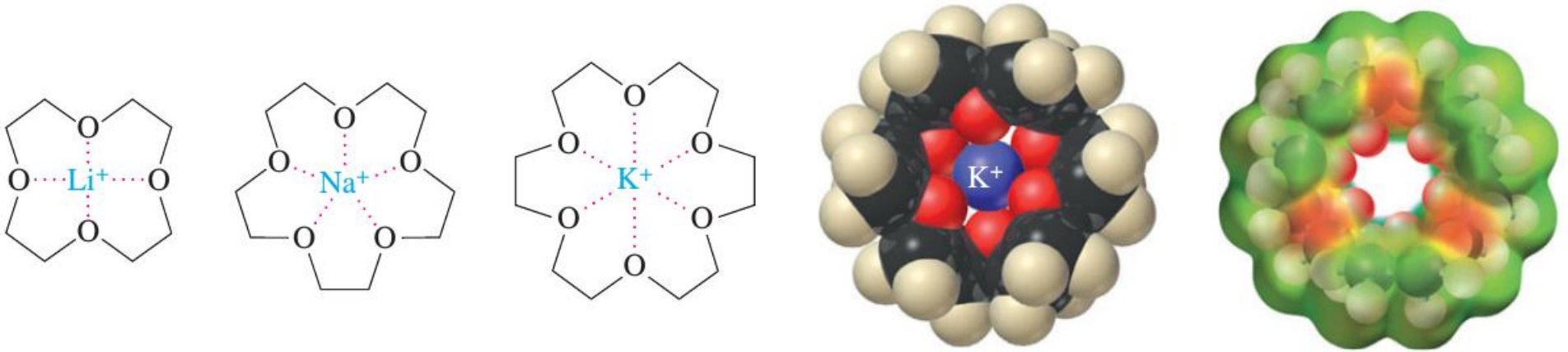


Éterek

Értelemszerűen hidrogénkötés-akceptorok lehetnek csak



Koronaéterek: ionok komplexálása (pl. radioaktív elemek eltávolításához is használhatóak)



12-crown-4 solvates Li^+

15-crown-5 solvates Na^+

18-crown-6 solvates K^+

18-crown-6 with K^+ solvated

EPM of 18-crown-6

Éterek előállítása

Bimolecular condensation

$$2\ R{-}OH \xrightleftharpoons{H^+} R{-}O{-}R + H_2O$$

Vízkilépés, savkatalizált reakció, pl.: ipari előállítás

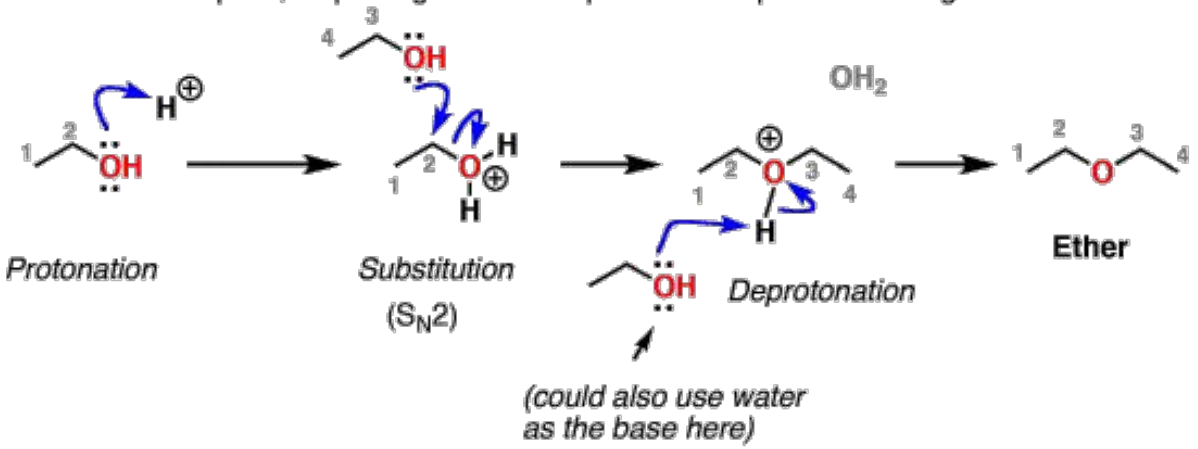
Examples

$$\underset{\text{methyl alcohol}}{2\ CH_3OH} \xrightarrow{H_2SO_4,\ 140\ ^\circ C} \underset{\text{dimethyl ether (100\%)}}{CH_3{-}O{-}CH_3} + H_2O$$

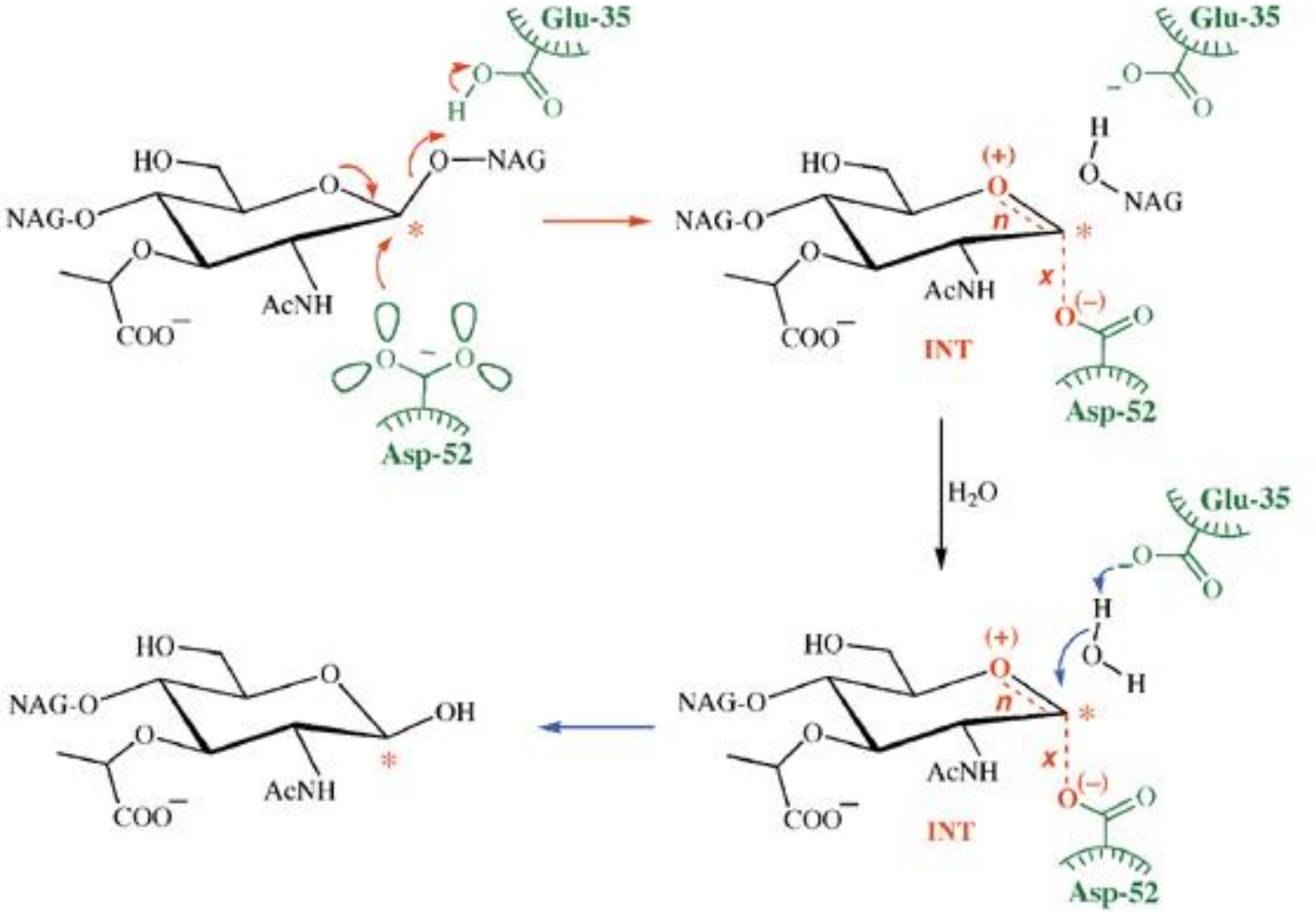
$$2\ \underset{\text{ethyl alcohol}}{CH_3CH_2OH} \xrightarrow{H_2SO_4,\ 140\ ^\circ C} \underset{\text{diethyl ether (88\%)}}{CH_3CH_2{-}O{-}CH_2CH_3} + H_2O$$

How It Works

Acid protonates the hydroxyl group, giving $R\text{-}OH_2^{\oplus}$. A second equivalent of alcohol then acts as nucleophile, displacing water. The product is deprotonated to give the final ether

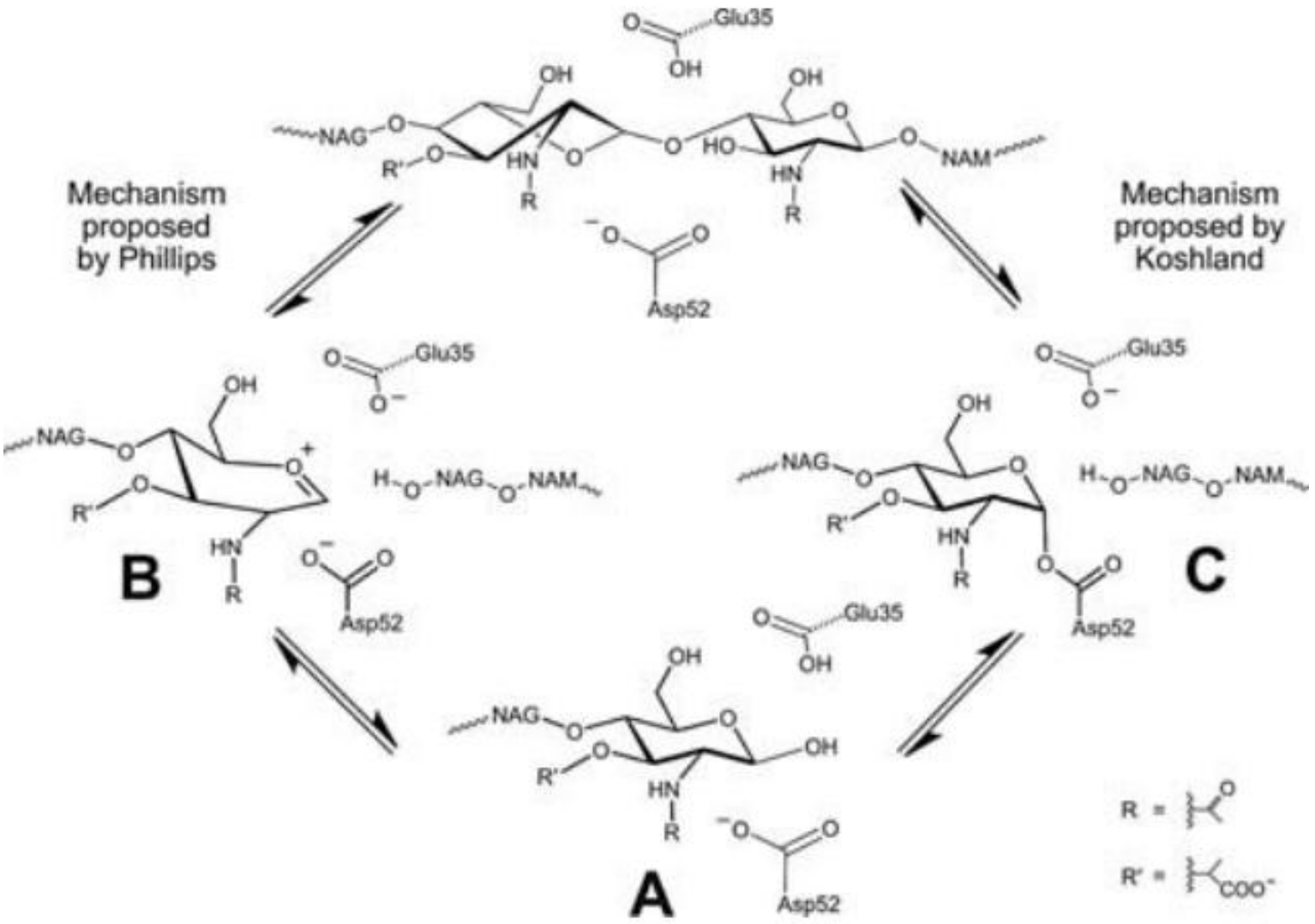


Kitekintés: a lizozim enzim mechanizmusa



A lizozim oligoszacharidok közötti glikozidos kötést (lásd később) bont. Ez éterkötés hidrolízisének felel meg. Figyeljük meg a sav-bázis katalízist (protonálási lépések), és hogy a reakciómechanizmus retenciót (=a konfiguráció megtartását) eredményez.

Kitekintés: a lizozim enzim mechanizmusa



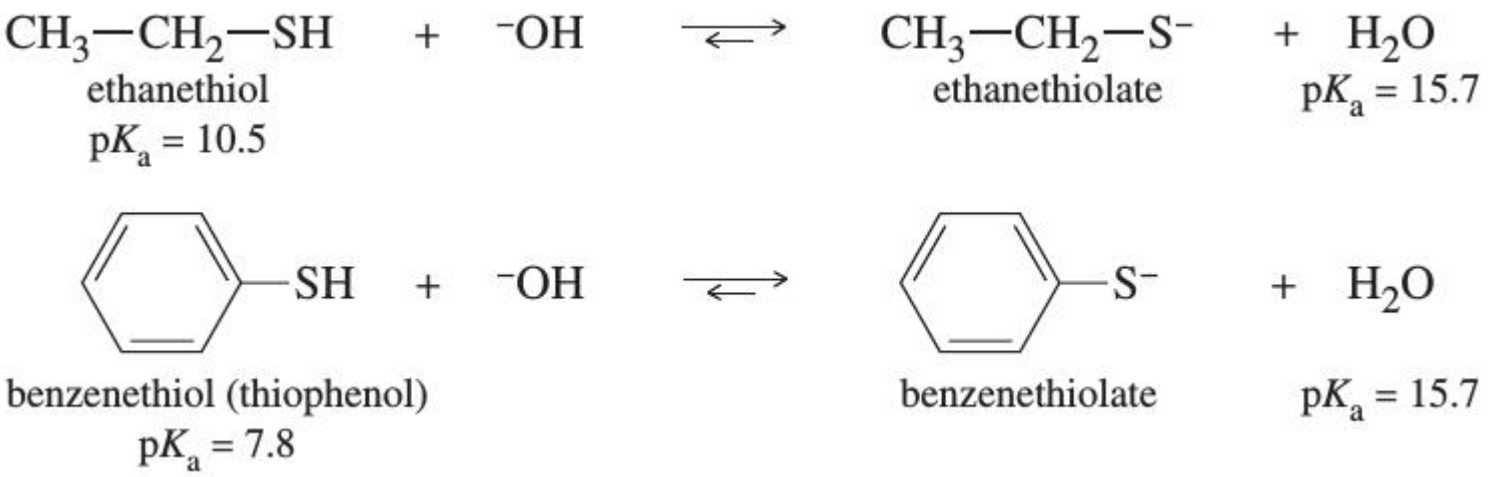
QM/MM számítások a Koshland-féle mechanizmust, a kovalens intermedier létrejöttét támasztják alá. A TS hasonlít az oxokarbénium ionra (a másik mechanizmusban javasolt intermedierre).

Tiolok

Alkoholok analógjai

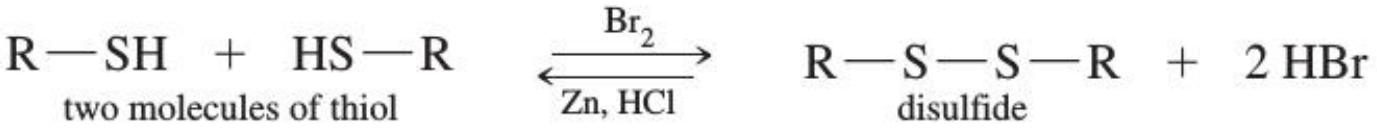
	$CH_3—SH$	$CH_3CH_2CH_2CH_2—SH$	$CH_3CH{=}CHCH_2—SH$	$HS—CH_2CH_2—OH$
IUPAC name:	methanethiol	butane-1-thiol	but-2-ene-1-thiol	2-mercaptoethanol
common name:	methyl mercaptan	*n*-butyl mercaptan		

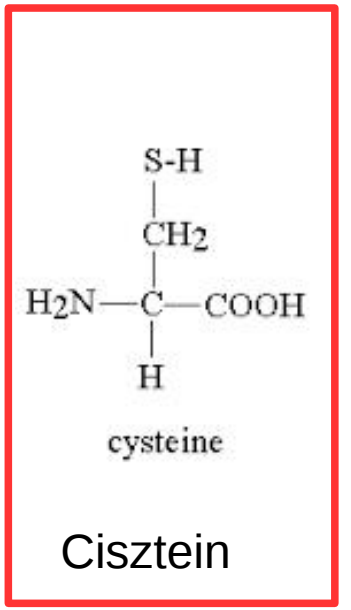
Bázikus közegben tiolátté alakulhatnak:



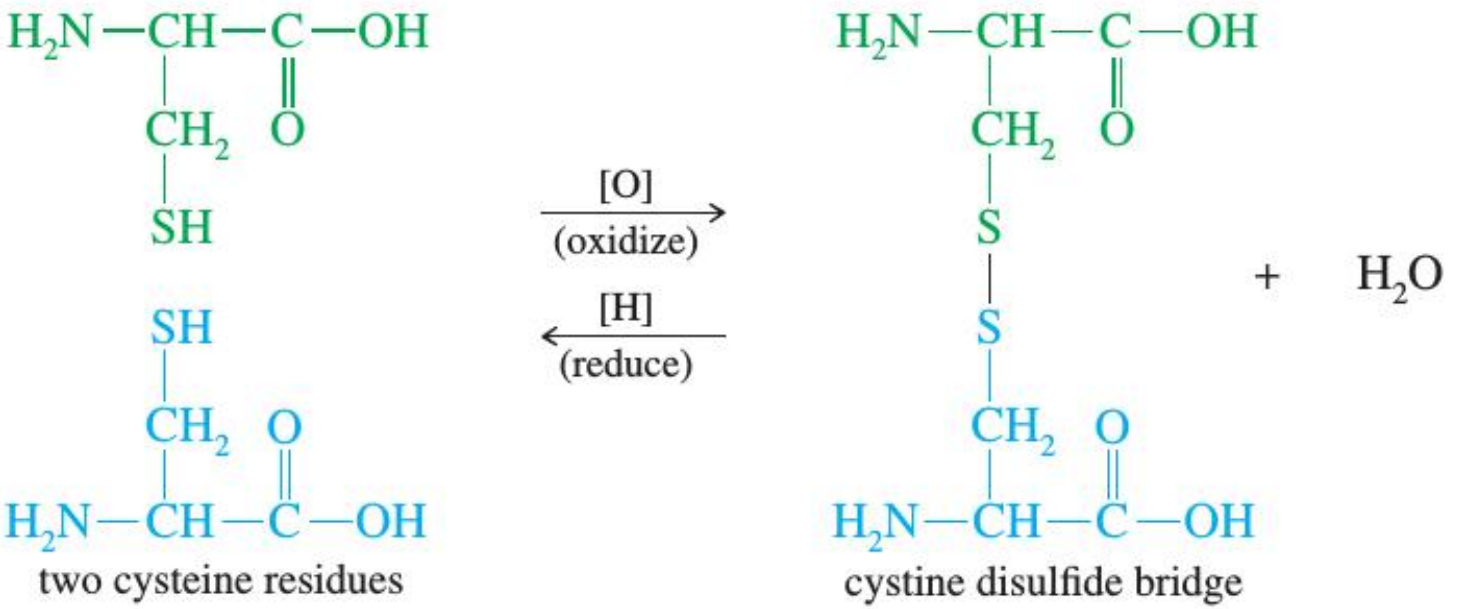
Előállítás: Na-hidrogén-szulfid és alkil-halid (alkil-halogenid), S_N2 reakció:

Tiolok: diszulfidok

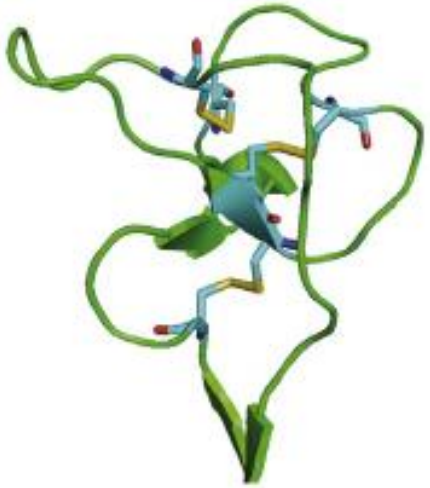




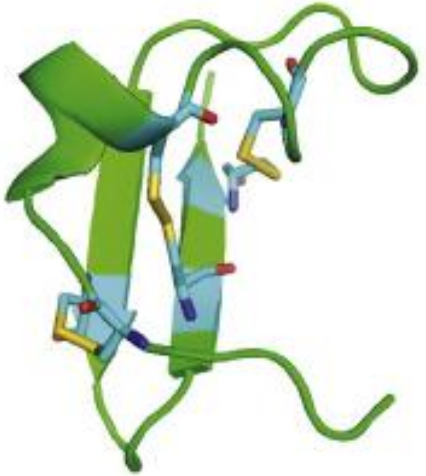
Example



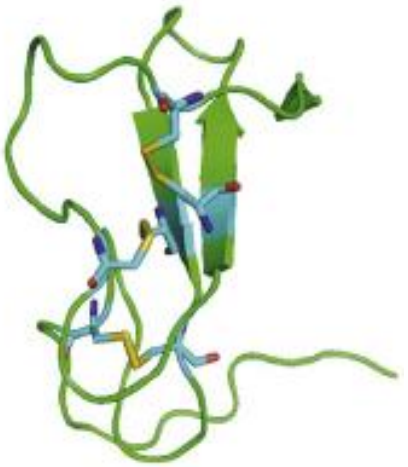
Kitekintés: diszulfid-gazdag peptidek és fehérjék



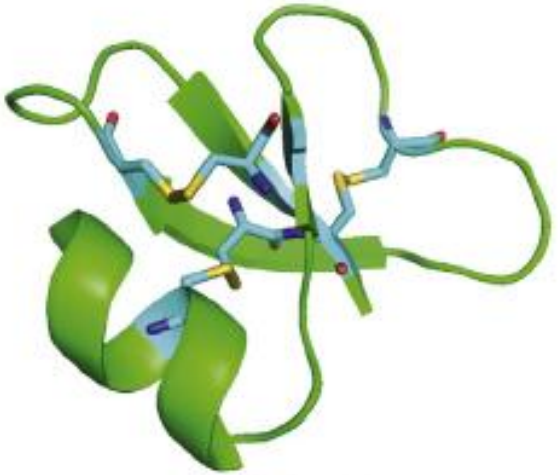
BLV1H12 knob



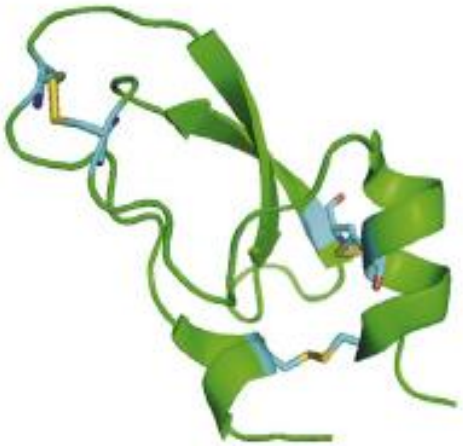
mokatoxin



EGF



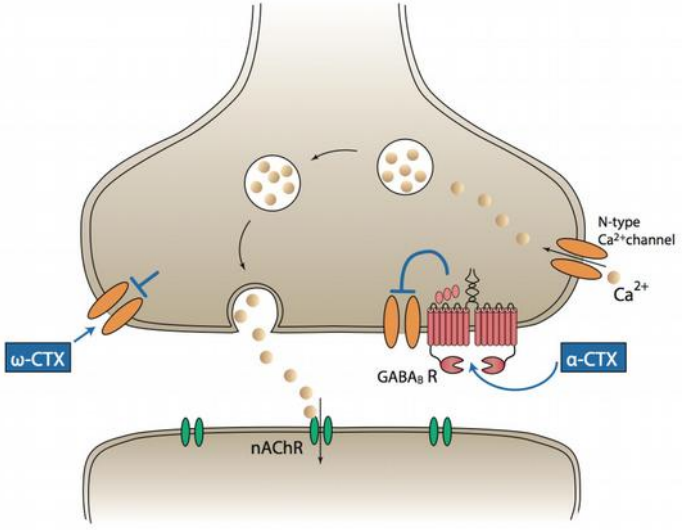
β-defensin

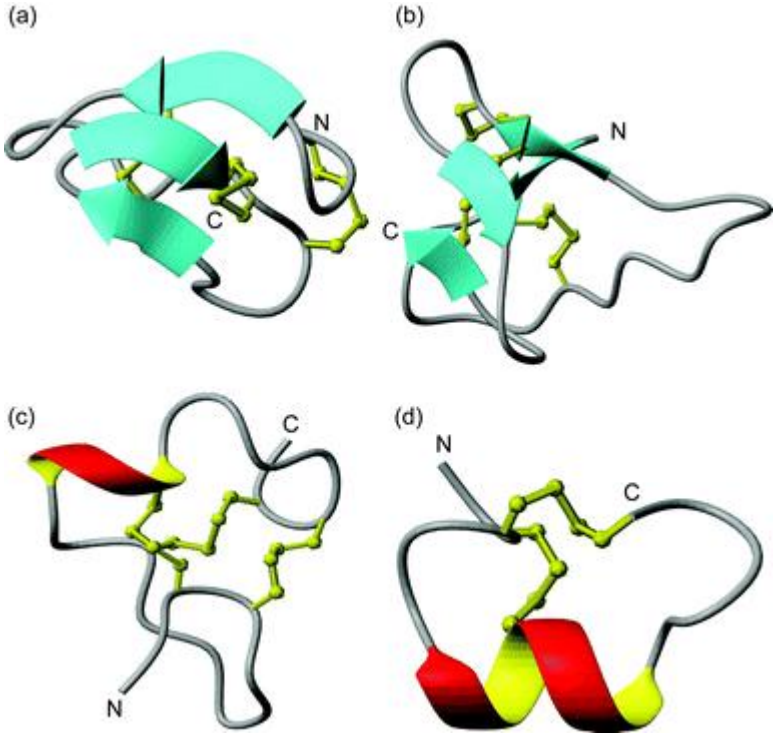


pancreatic trypsin inhibitor

Kitekintés: conotoxinok

Toxin	Sequence	Species
δ – Conotoxins		
TxVIA	WCKQSGEMCNLLDQNCCDGY-CIVLVCT	*C. textile*
PVIA	EACWAPGTFCGIKPGLCCSEF-CLPGVCFG*	*C. purpurascens*
ω – Conotoxins		
GVIA	CKSOGSSCSOTSYNCCR-SCNOYTKRCY*	*C. geographus*
MVIIA	CKGKGAKCSRLMYDCCTGSCRS--GKC*	*C. magus*
κ – Conotoxins		
PVIIA	CRIONQKCFQHLDDCCSRKCNRF-NKCV	*C. purpurascens*
Disulfide Bridges	C------C------CC---C------C	
μ – Conotoxins		
GIIIA	RDCCTOOKKCKDRQCKOQRCCA*	*C. geographus*
PIIIA	ZRLCCGFOKSCRSRQCKOHRCC*	*C. purpurascens*
Disulfide Bridges	CC-----C----C----CC	

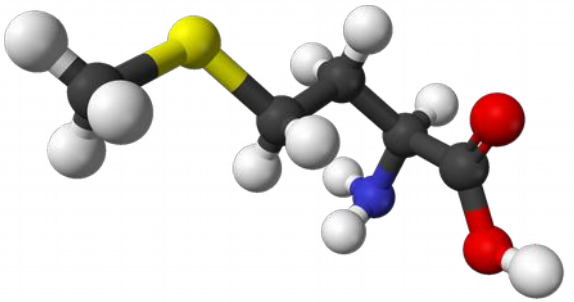


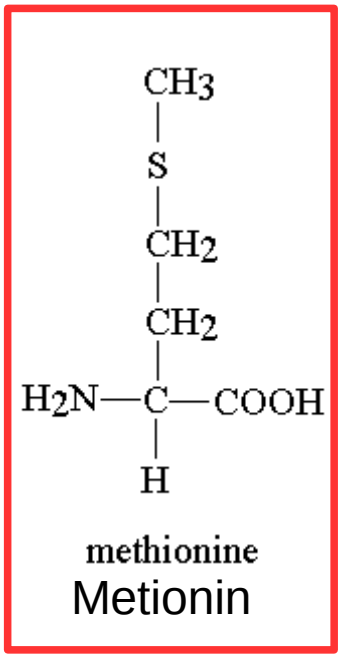


Kúpcsigák (*Conus spp.*) mérge, idegi jelátvitelt gátolják

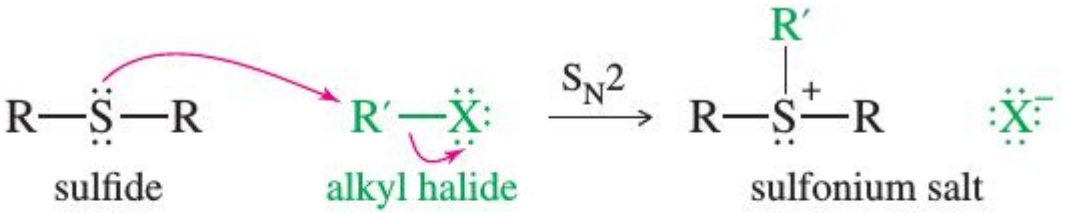
Tioéterek (szulfidok)

Éterek analógjai:

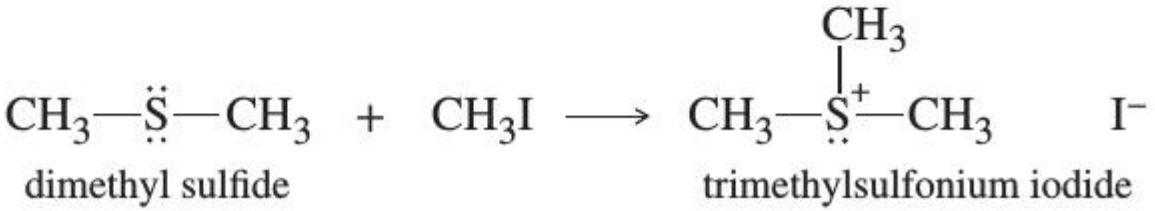




Alkil-halogenidekkel szulfóniumsót alkotnak:



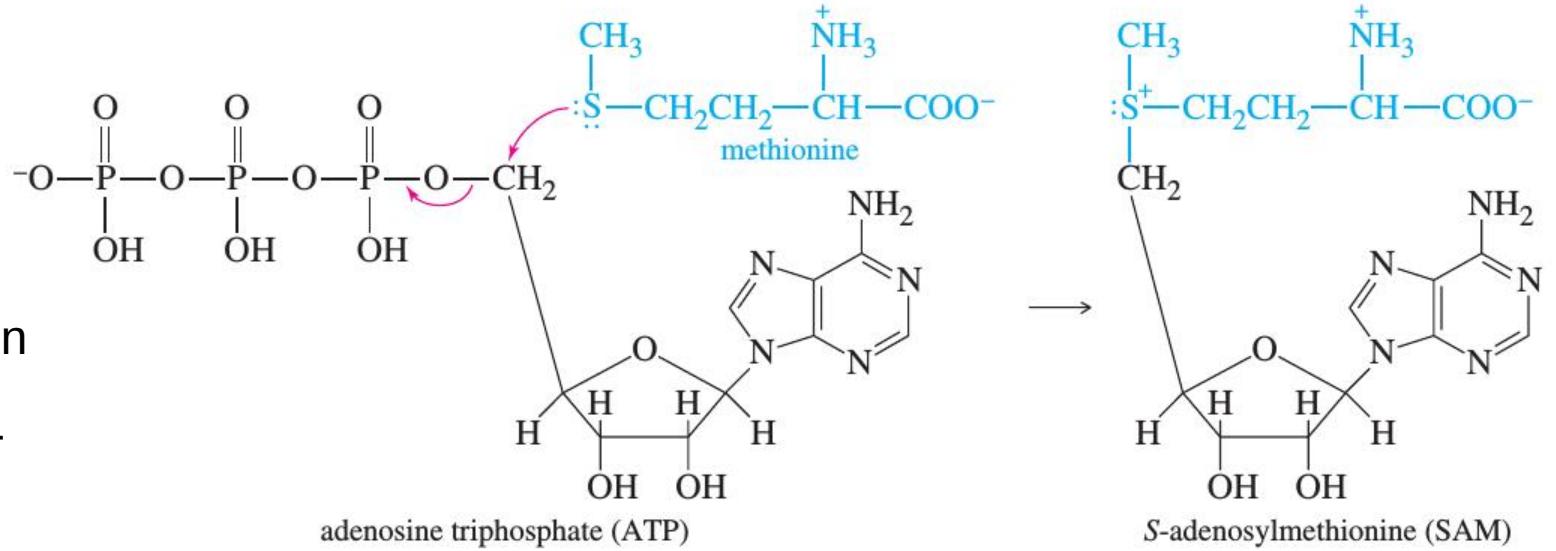
Example

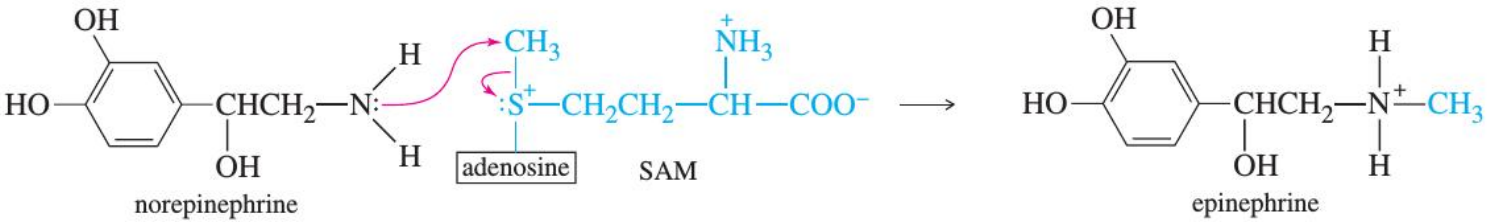


A szulfóniumsók hatékony alkilálószerek

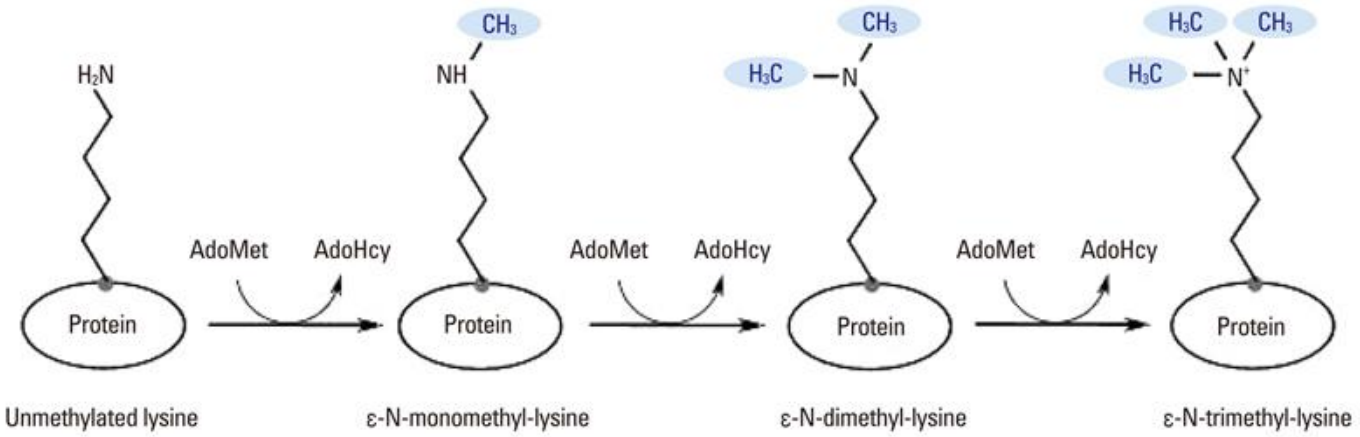
Kitekintés: (~~uncle~~) SAM (=AdoMet)

S-adenozil metionin (SAM, AdoMet): metilcsoport-donor



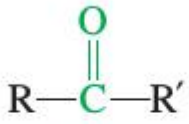
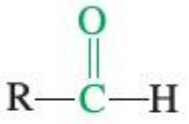
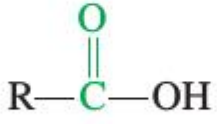
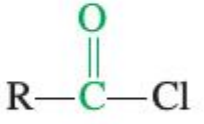
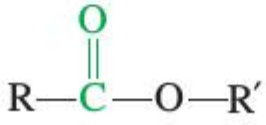
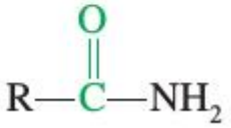


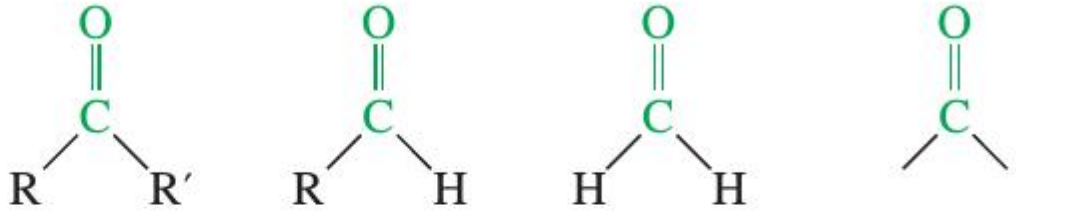
Példa #1: adrenalin (epinefrin) bioszintézis



Példa #2: hiszton metiláció (itt lizin aminosav oldalláncán)

Oxovegyületek fontosabb csoportjai

Class	General Formula	Class	General Formula
ketones		aldehydes	
carboxylic acids		acid chlorides	
esters		amides	

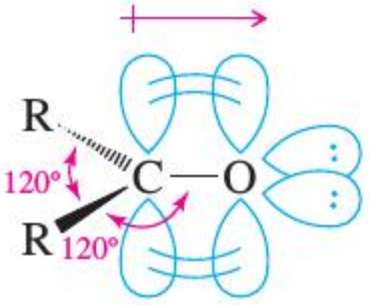


Ketone: Two alkyl groups bonded to a carbonyl group.

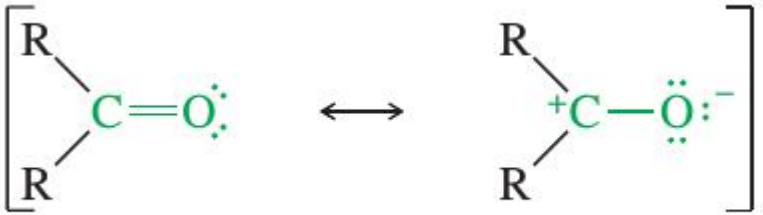
Aldehyde: One alkyl group and one hydrogen bonded to a carbonyl group.

Keton: két alkilcsoport kapcsolódik egy karbonilcsoporthoz
Aldehid: egy alkilcsoport és egy hidrogén kapcsolódik egy karbonilcsoporthoz

A C=O (karbonil) csoport szerkezete

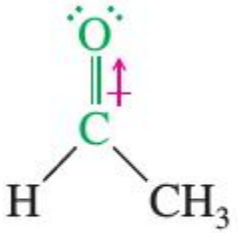


	length	*energy*
ketone C=O bond	1.23 Å	745 kJ/mol (178 kcal/mol)
alkene C=C bond	1.34 Å	611 kJ/mol (146 kcal/mol)

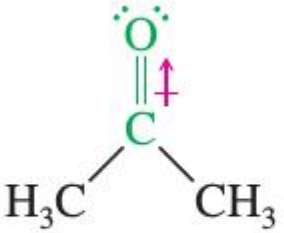


Rezonanciaszerkezetek

pozitív parciális töltés a szénatomon

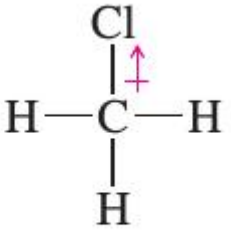


μ = 2.7 D
acetaldehyde

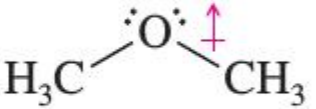


μ = 2.9 D
acetone

Compare with:



μ = 1.9 D
chloromethane



μ = 1.30 D
dimethyl ether

Viszonylag nagy dipólusmomentum

Kitekintés: az ázott kutya szaga

Aroma Chemistry

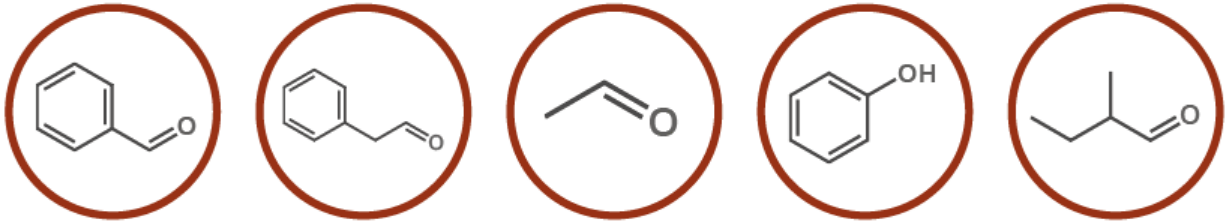
THE SMELL OF WET DOG

THE SOURCE OF DOG HAIR COMPOUNDS

Wet dog smell stems from microorganisms living in dog hair. They produce bad-smelling volatile organic compounds. Adding water helps these compounds break free from the hair as the water evaporates, increasing their concentration in the air.

COMPOUNDS WITH INCREASED CONCENTRATIONS IN WET DOG HAIR

The smell of dogs is complex: multiple chemical compounds contribute which individually do not have odours associated with dog smell, but produce it in combination. A pilot study found emitted concentrations of some compounds increased when dog hair was wet. Those shown on the top row below showed greater increases than those on the second row.



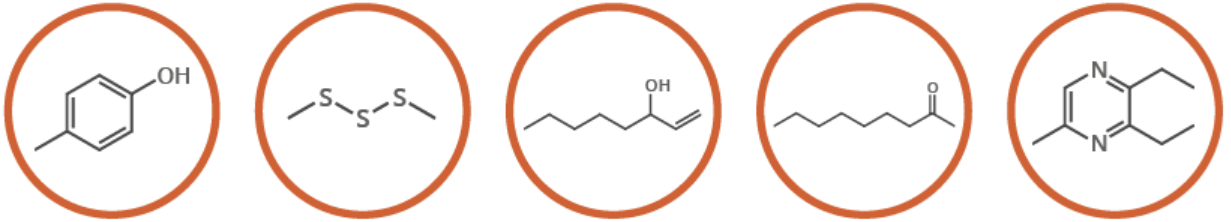
BENZALDEHYDE
almond-like

PHENYLACETALDEHYDE
honey/floral

ACETALDEHYDE
fruity/musty

PHENOL
medicinal

2-METHYLBUTANAL
musty/nutty



p-CRESOL
faecal

DIMETHYL TRISULFIDE
sulfurous

1-OCTEN-3-OL
mushroom-like

2-NONANONE
fruity

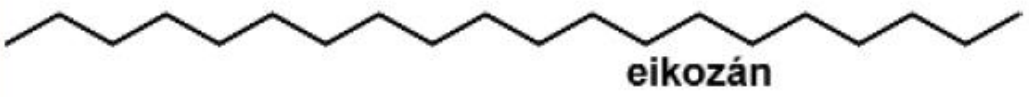
2,3-DIETHYL-5-METHYLPYRAZINE
earthy

Kitekintés: Parkinson-kór diagnosztika illékony vegyületek alapján

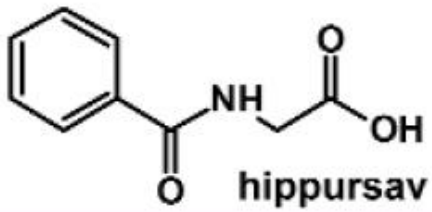
Parkinson-szag

A Parkinson-kór új biomarkereit sikerült azonosítani egy angol kísérletsorozatban, amelynek kiindulási pontja az a meglepő megfigyelés volt, hogy egy egészségügyi dolgozó saját bevallása szerint szaglással ismerte fel, hogy a házastársa ebben a betegségben szenved. A Manchesteri Egyetemen végzett gázkromatográfiás vizsgálatok megerősítették, hogy a Parkinson-kórban szenvedők bőrének felső rétege már a betegség legkorábbi, hagyományos diagnosztikai eszközökkel észrevehetetlen szakaszában is négy vegyület, az eikozán, az oktadekanal, a perillaledhid és a hippursav jellegzetes összetételű elegyét bocsátja ki, amelyet kivételesen érzékeny szaglású emberek már érzékelnek és azonosítanak. Ez a felfedezés új utakat nyithat a diagnosztikában, mert az illékony vegyületek kibocsátása már az első tünetek megerősítése előtt is lehetséges. *ACS Centr. Sci. 5*, 599. (2019)

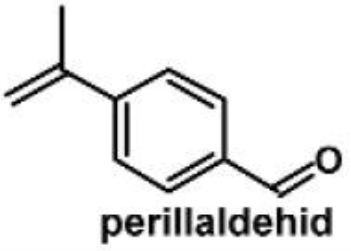
oktadekanal



eikozán

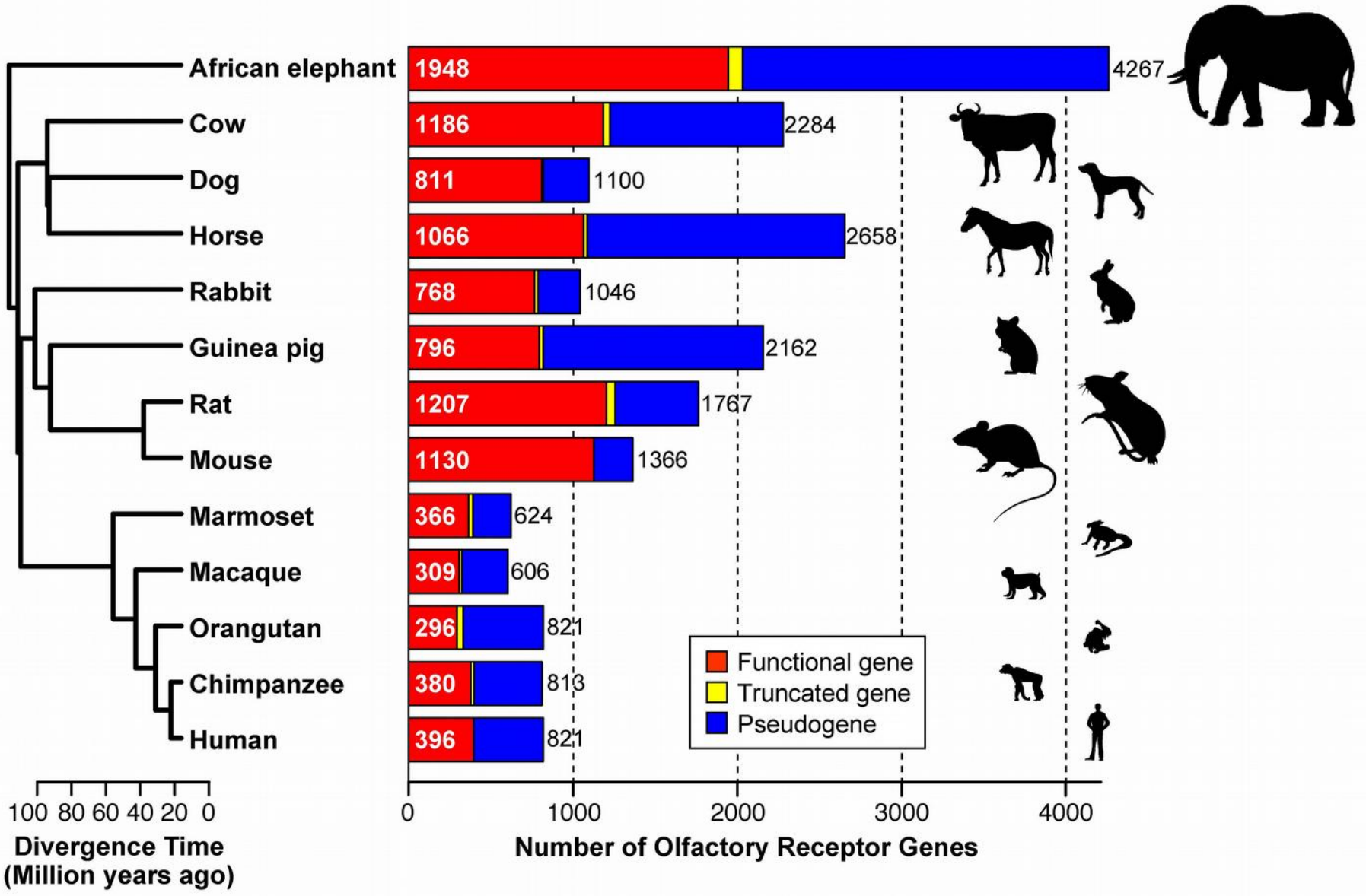


hippursav



perillaldehid

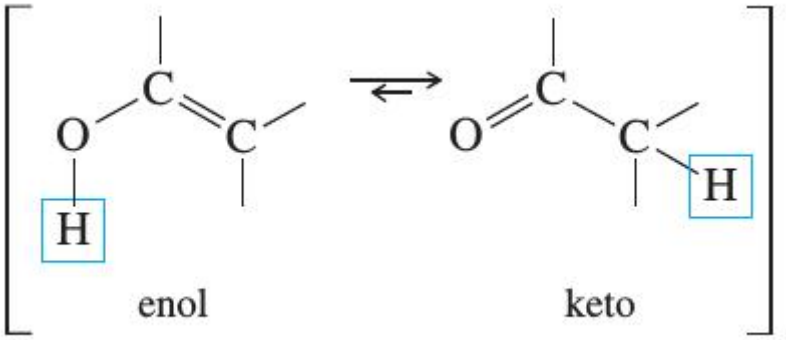
Kitekintés: szagérzékelő receptorok száma egyes emlősökben



Keto-enol tautoméria

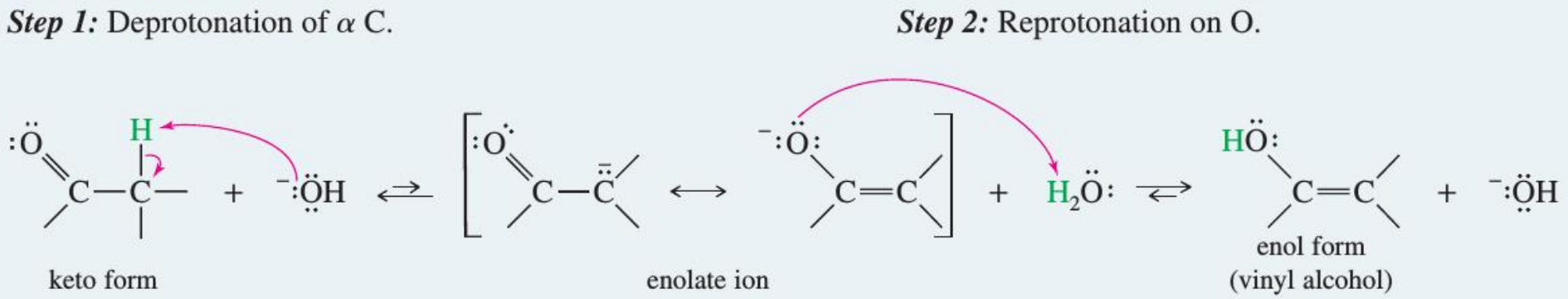
Tautoméria: az izoméria olyan formája, ahol egy kettős kötés és egy hidrogénatom helyzete változik meg (~ “helyet cserélnek”).

Tipikusan legalább az egyik érintett atom viszonylag nagy elektronegativitású (O, N)

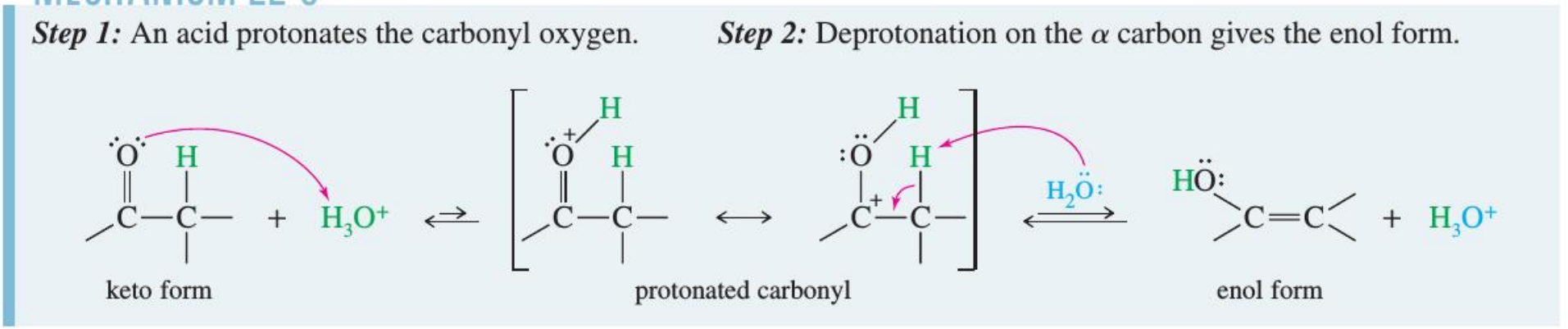


keto–enol tautomerism

MECHANISM 22-4 Báziskatalizált keto-enol tautomerizáció



MECHANISM 22-5 Savkatalizált keto-enol tautomerizáció



Nukleofil addíció karbonil csoportra

KEY MECHANISM 18-1 Bázikus körülmények között

Basic Conditions (strong nucleophile)

Step 1: A strong nucleophile adds to the carbonyl group to form an alkoxide.

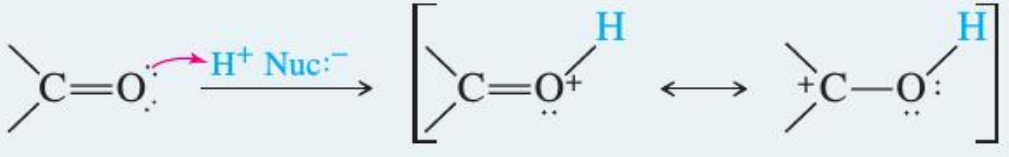
Emlékezzünk a karbonilcsoport rezonancia-szerkezeteire (pozitív szén-, negatív oxigénatom)!

Step 2: A weak acid protonates the alkoxide to give the addition product.

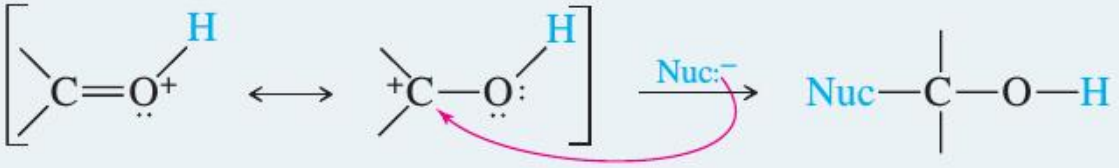
Savas körülmények között

Acidic Conditions (weak nucleophile, activated carbonyl)

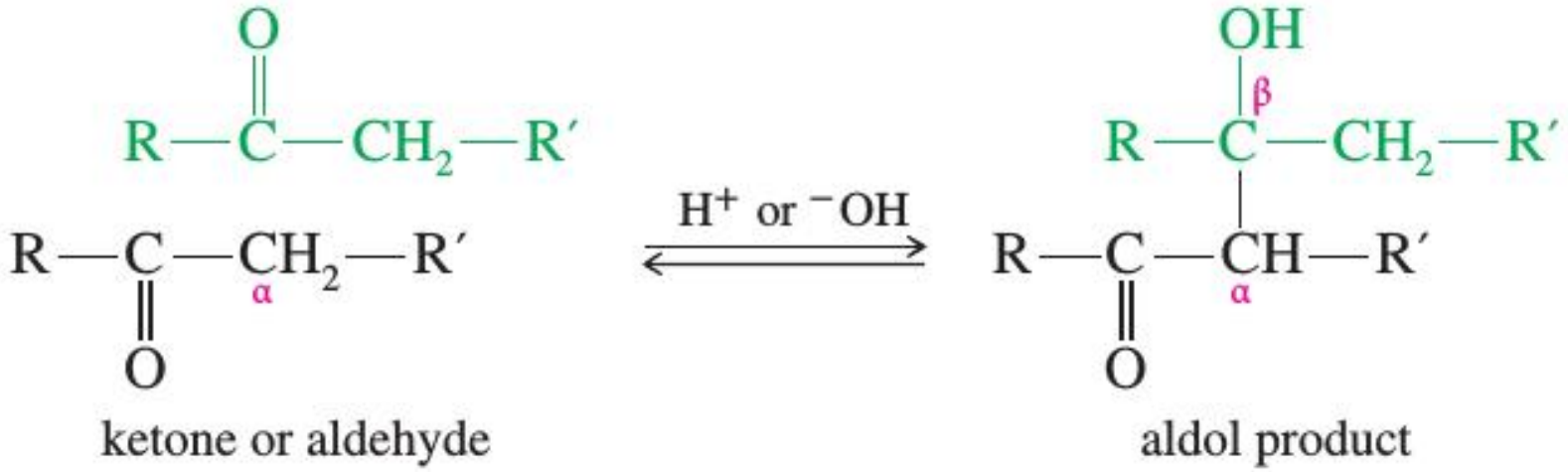
Step 1: Protonation activates the carbonyl group toward nucleophilic attack.



Step 2: A weak nucleophile adds to the activated (protonated) carbonyl group.



Aldol addíció oxovegyületek között



Két, oxocsoprtot tartalmazó vegyület addíciójával egy oxo- és hidroxilcsoportot tartalmazó termék (aldol) keletkezik

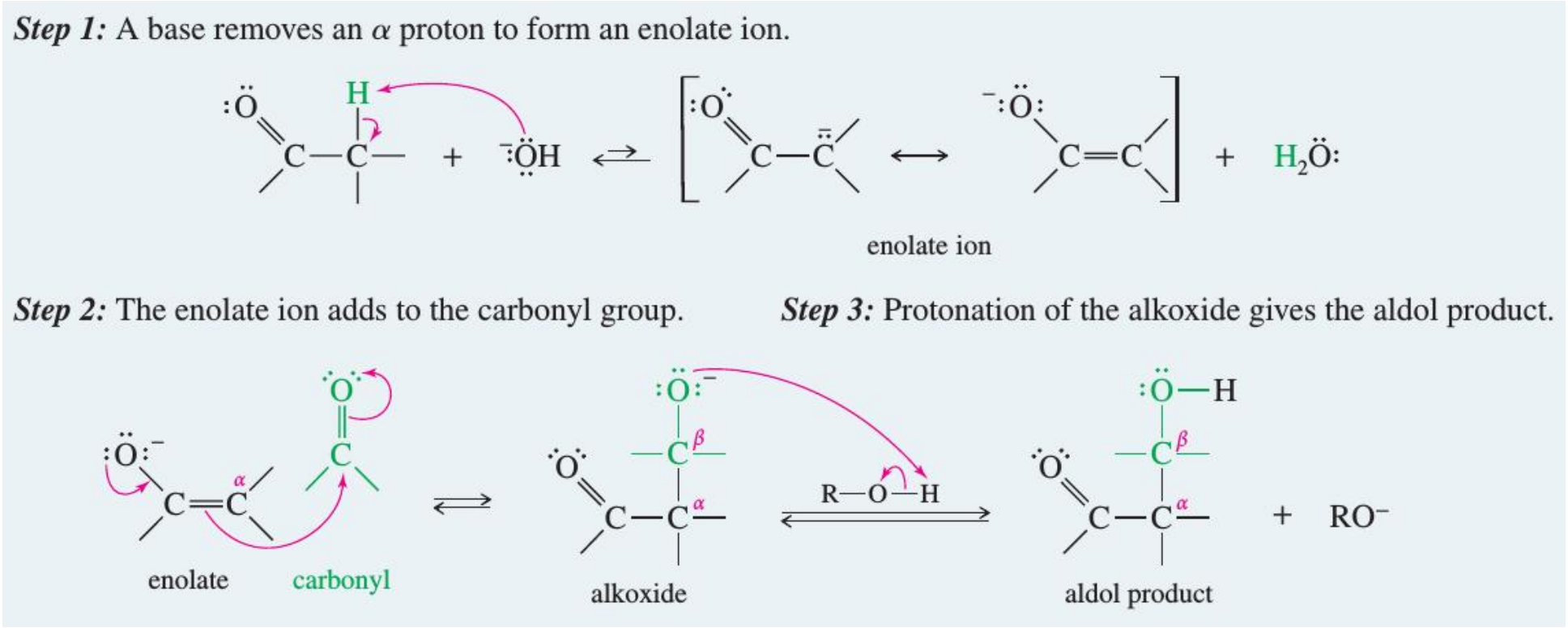
Szén-szén kötés keletkezik az egyik karbonil szén és a másik vegyület karbonilcsoporttal szomszédos szénatomja között

Sav- és báziskatalizát módon is megy

Nukleofil addíció az egyik molekula **karbonil szén**atomjára

Báziskatalizált aldol addíció

Enol forma, enolát ion: nukleofil ágens! (elektrongazdag szénatom a π-kötés miatt)
Az enolát mint nukleofil a karbonil szénatomot támadja.

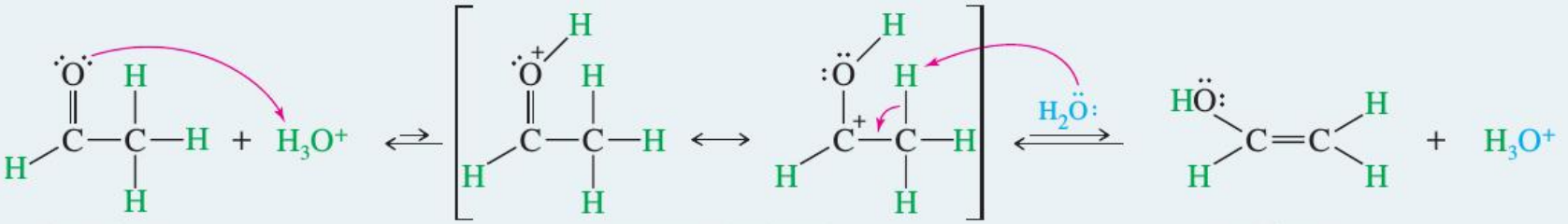


Ez az egyszerűbben érthető reakcióút:

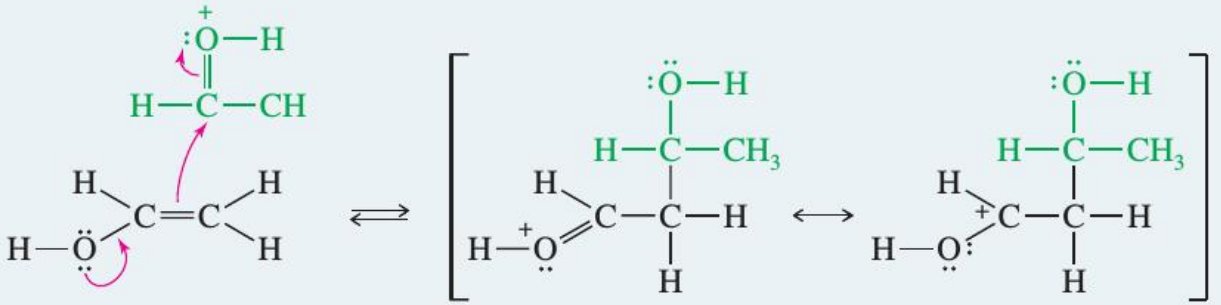
- a bázis elvon egy hidrogént a karbonilcsoporttal szomszédos szénről
- a kialakuló enolát ion elektrongazdag részlete nukleofil támadást intéz a másik molekula karbonil szene ellen
- az így keletkező addukt a felnyíló karbonilcsoport oxigénjén protonálódva stabilizálódik

Kitekintés: savkatalizált aldol addíció

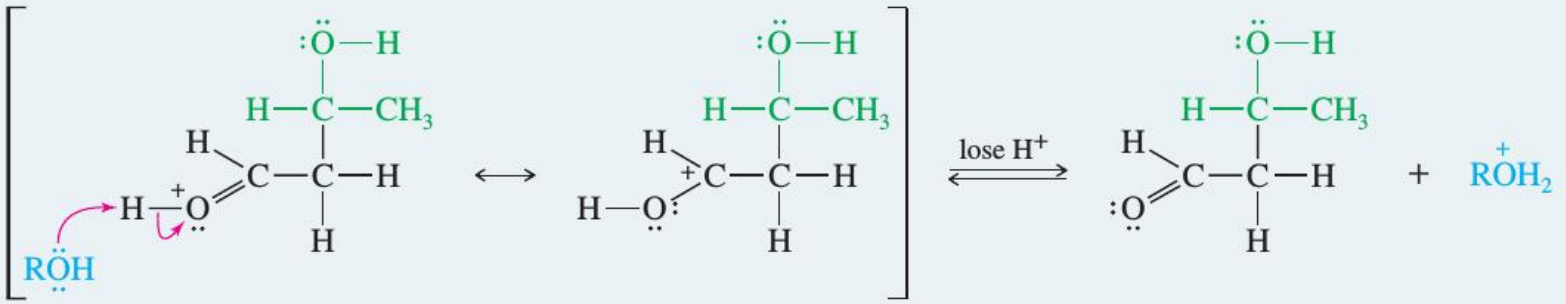
Step 1: Formation of the enol, by protonation on O followed by deprotonation on C.



Step 2: Addition of the enol to the protonated carbonyl.

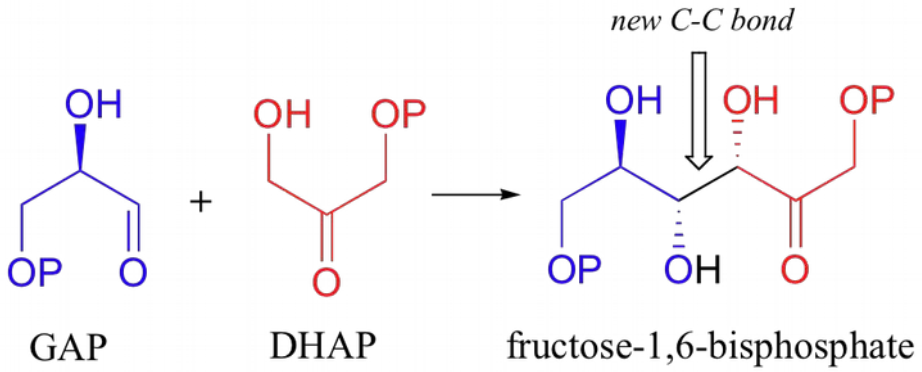


Step 3: Deprotonation to give the aldol product.



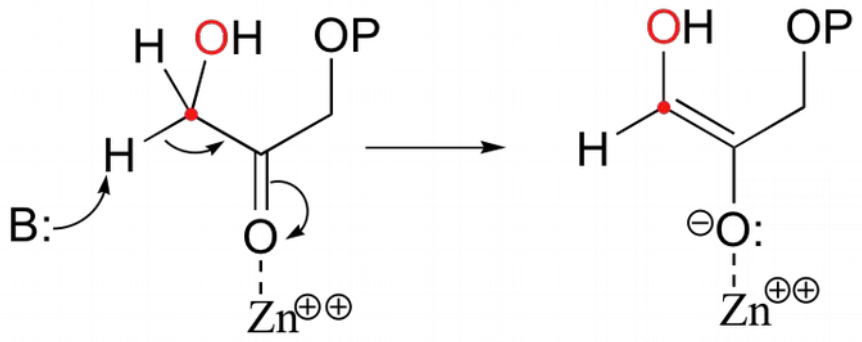
Kitekintés: aldol addíció a biokémiában

Aldoláz enzim:
fruktóz-1,6,-biszfoszfát ↔ glicerinaldehid-3-foszfát (GAP) + dihidroxiaceton-foszfát (DHAP)

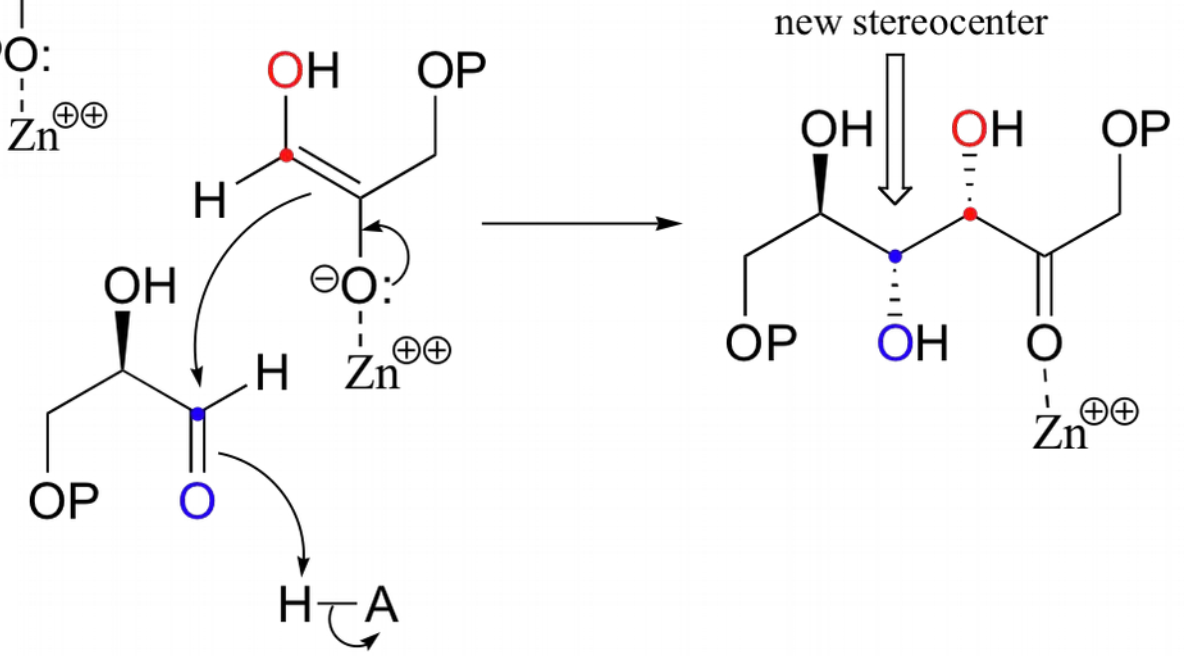


A glikolízisben és a glükoneogenezisben is szerepet játszó enzim

Természetesen mindkét irányú reakciót katalizálja, itt most az addíciós irányt nézzük (“glükoneogenezis irány”)



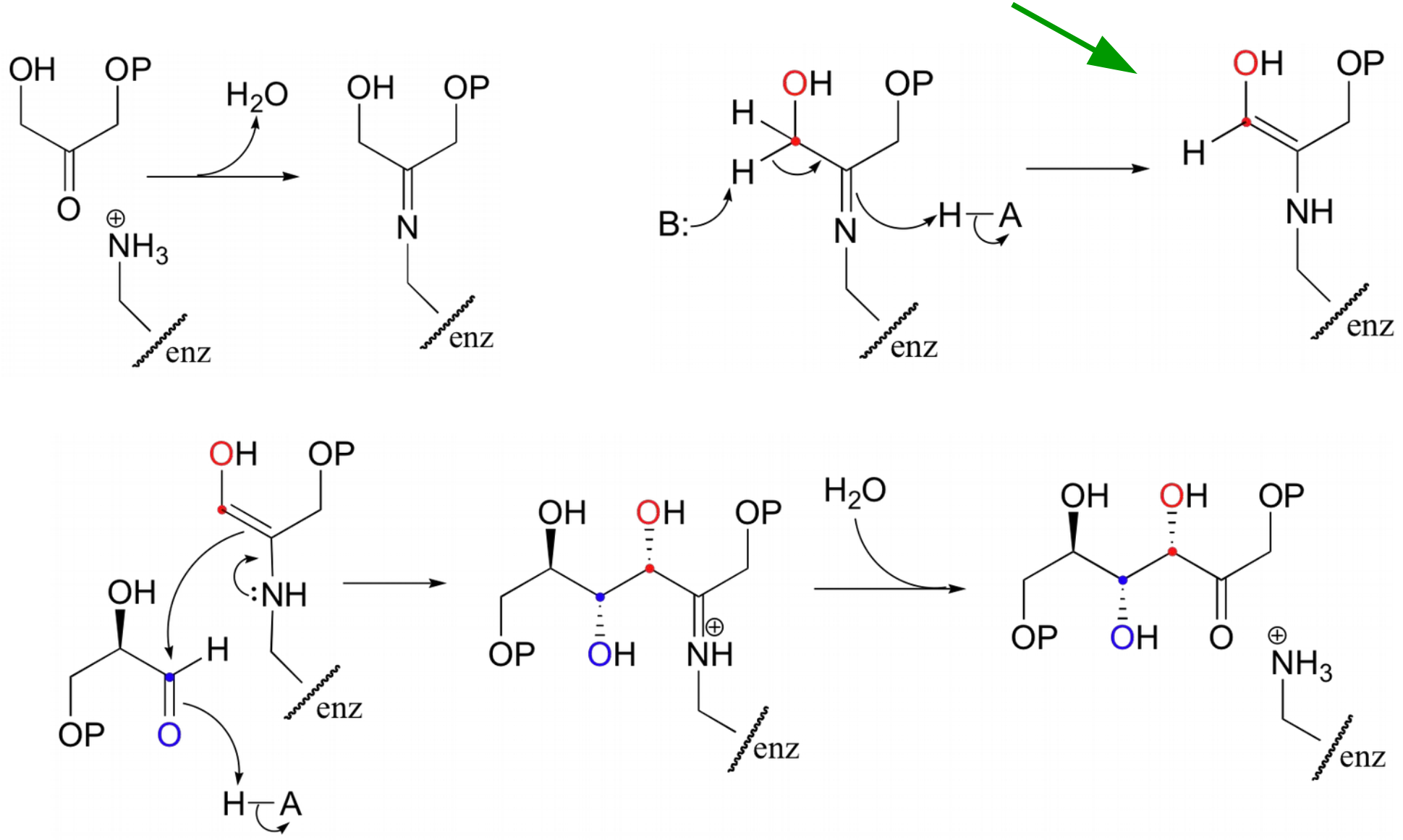
Class II aldoláz enzim (baktériumok):
enolát stabilizálás Zn^{2+} ion segítségével



Kitekintés: aldol addíció a biokémiában

Aldoláz enzim:
fruktóz-1,6,-biszfoszfát ↔ glicerinaldejhd-3-foszfát (GAP) + dihidrociaceton-foszfát (DHAP)

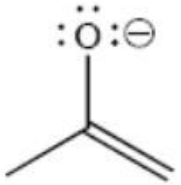
Class I aldoláz enzim (eukarióták): enamin mint nukelofil

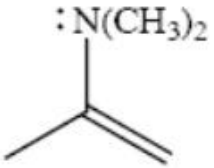


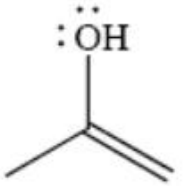
Kitekintés: enolát, enamin és enol nukleofilitása

Order of Decreasing Nucleophilic reactivity

ENOLATE > ENAMINE > ENOL







*electron-rich pi bond is a source of nucleophilic character in all three

Enolate is nucleophilic due to…

- ☑ Oxygen's small atomic radius
- ☑ Formal negative charge

Detractors to nucleophilicity:

- ☑ Oxygen is more electronegative than N

Enamine is moderately nucleophilic due to…

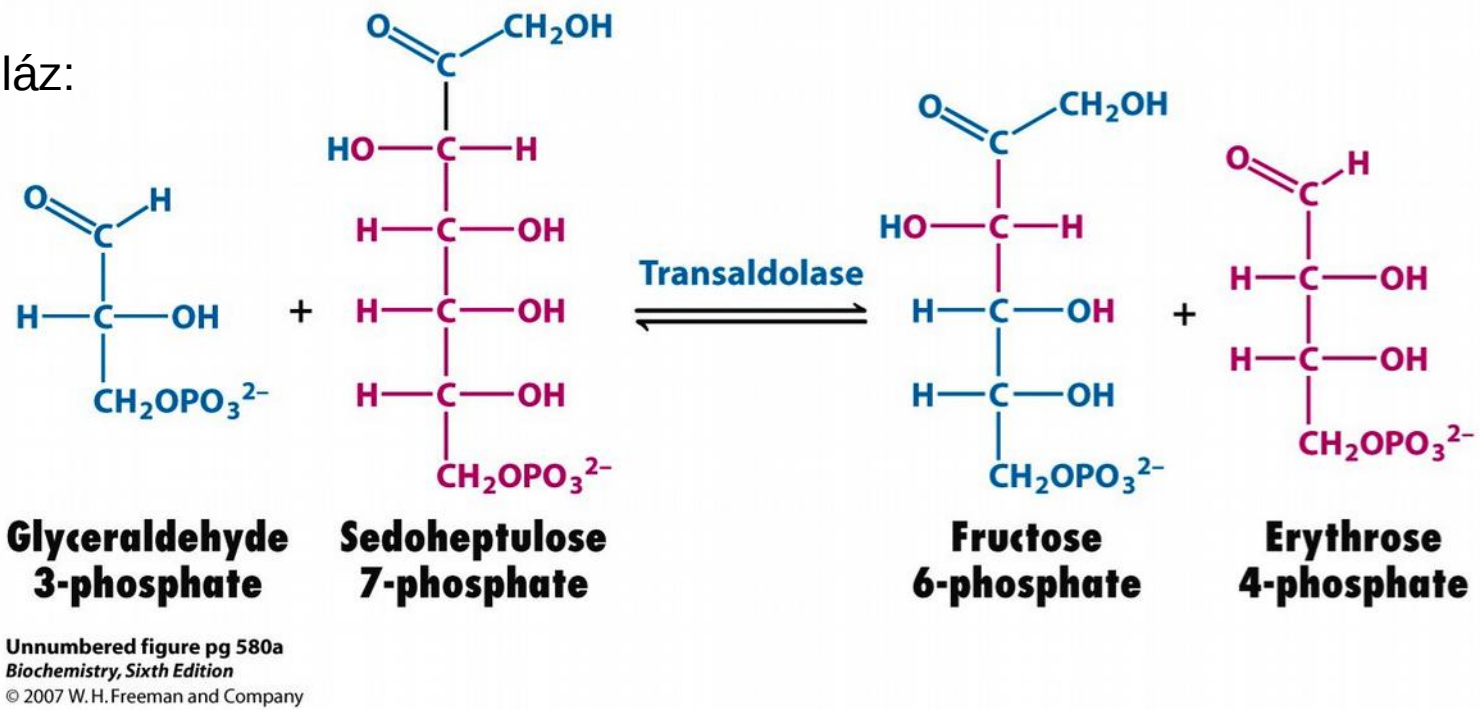
- ☑ N (EN=3) is less electronegative than oxygen (EN =3.5)

Enol is moderate nucleophile due to…

- ☑ Additional electron density from oxygen of hydroxyl group

Kitekintés: további hasonló biokémiai reakciók

Transzketoláz, transzaldoláz: szénhidrát anyagcserében különböző szénatomszámú monoszachararidok átalakítása



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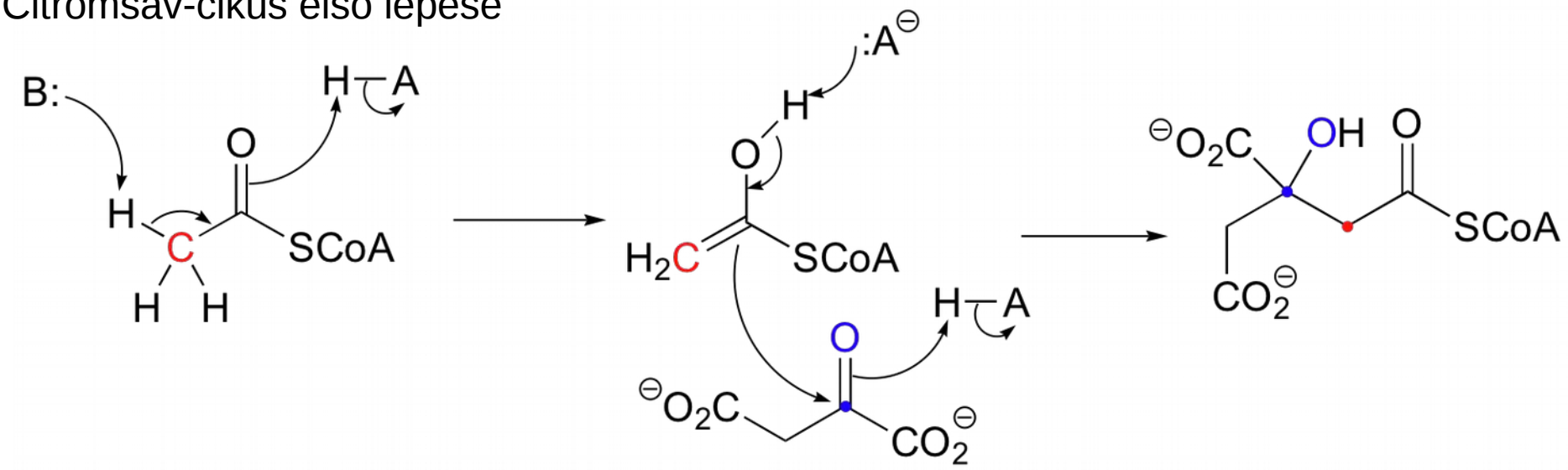
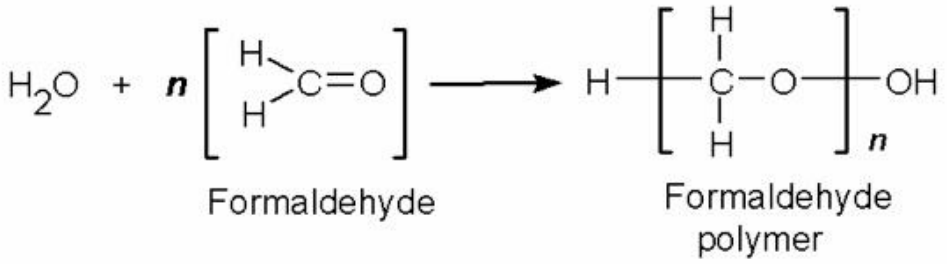
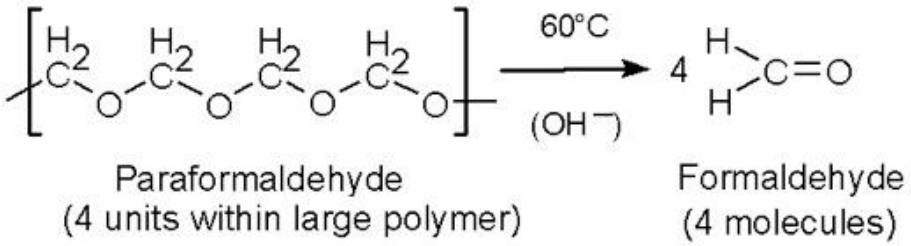
Biochemistry, Sixth Edition

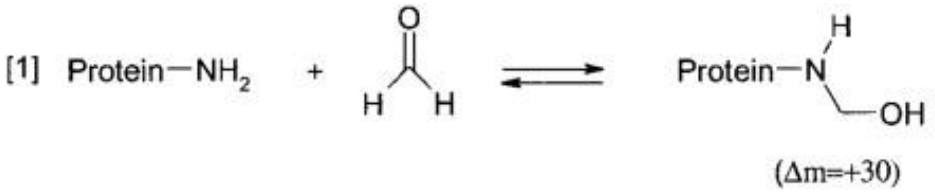
Citromsav-cikus első lépése

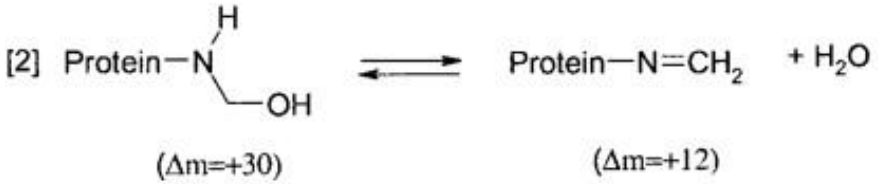


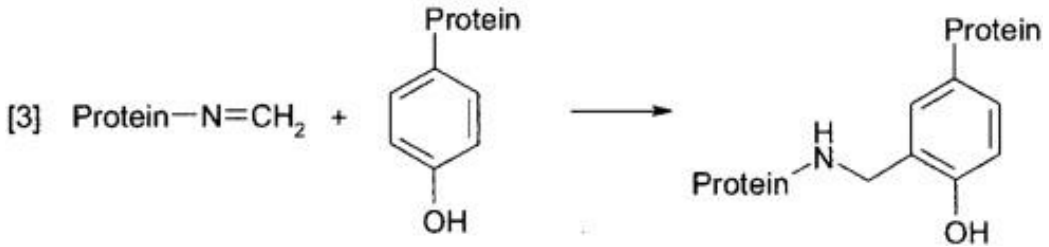
Kitekintés: a formaldehid mint fixálószer



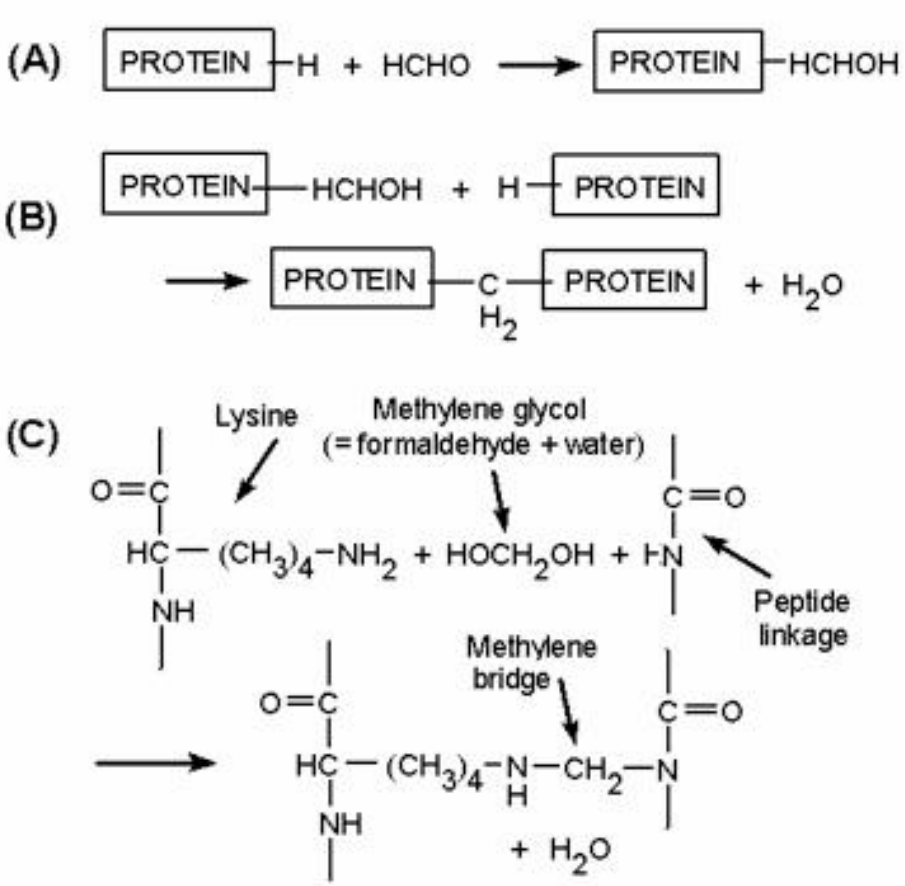




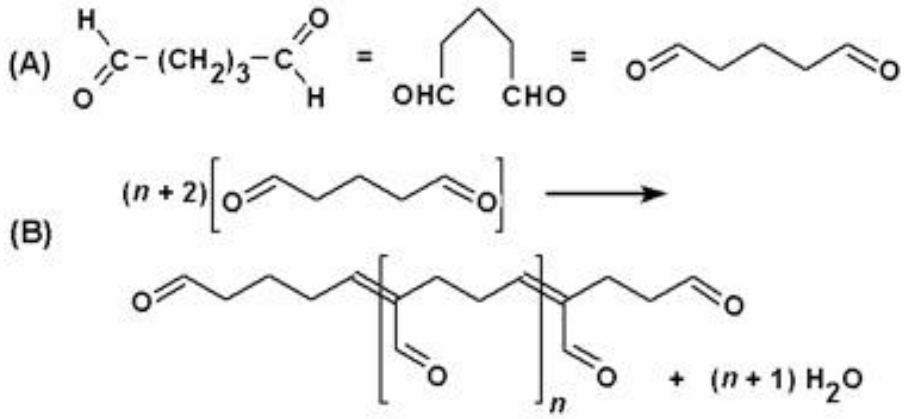


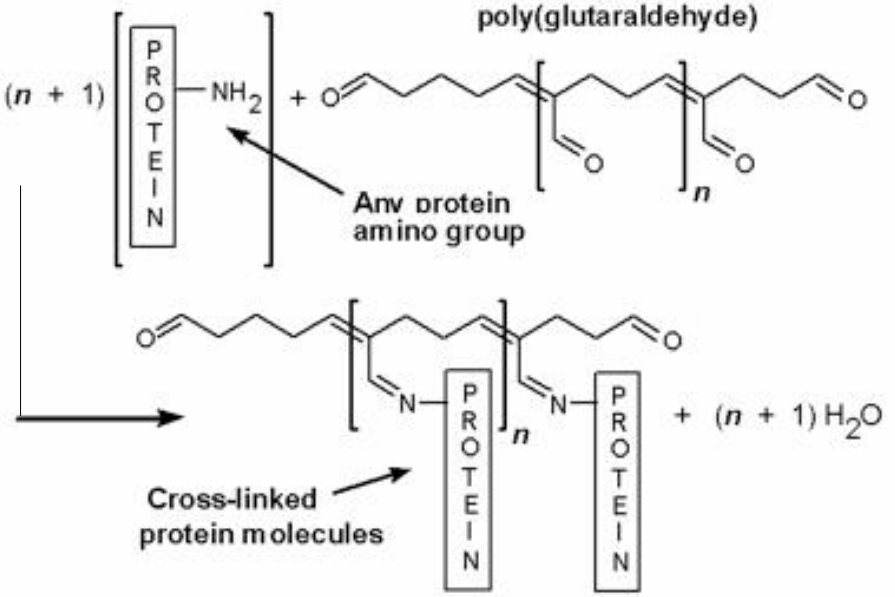


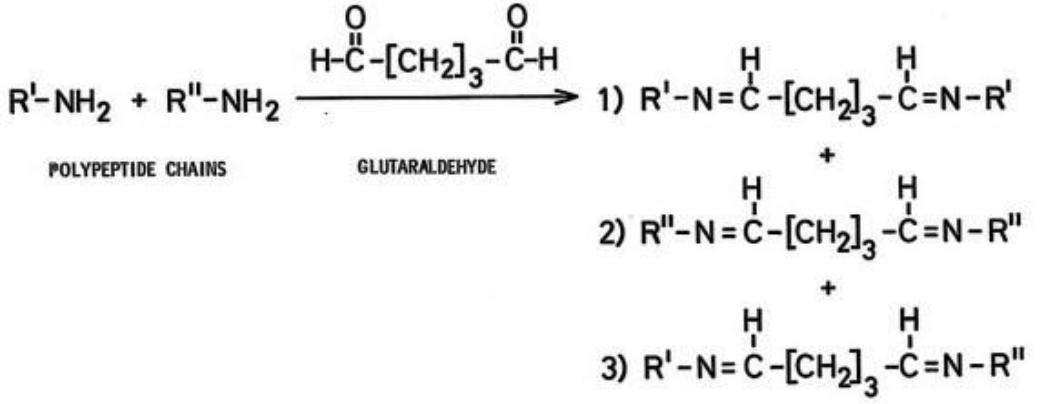
Fixation is a crucial step in processing of biopsy tissue specimen for the examination and archival preservation. Fixation helps to preserve cellular architecture and composition of cells in the tissue to allow them to withstand subsequent processing. Fixation also preserves the proteins, carbohydrate and other bio-active moieties in their spatial relationship to the cell, so that they can be studied



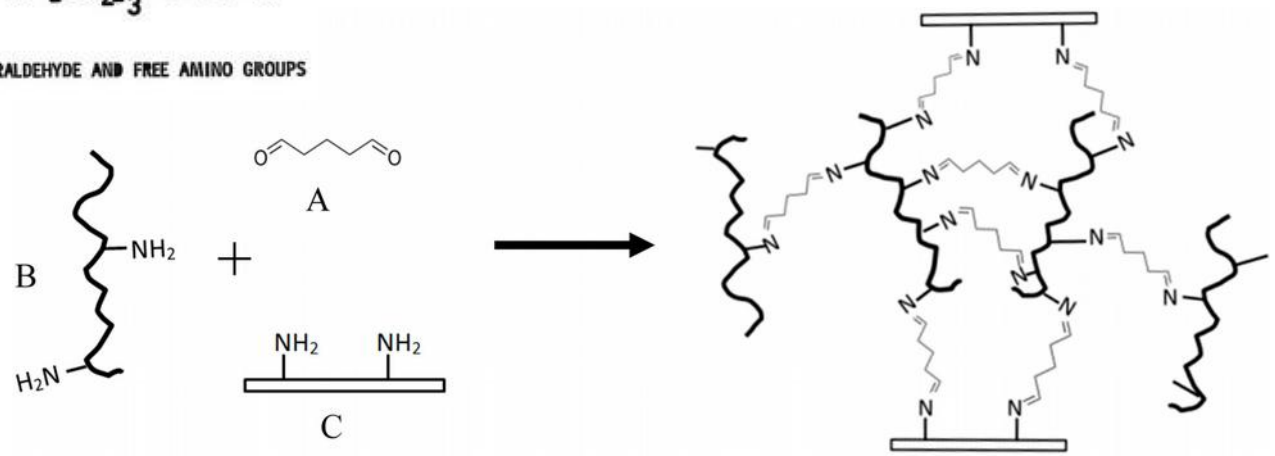
Kitekintés: a glutáraldehid mint fixálószer







SCHIFF's BASE FORMATION WITH GLUTARALDEHYDE AND FREE AMINO GROUPS



Mit kell tudni?

- Hidroxilcsoport, alkoholok rendűsége és értékűsége
- Éterek és származtatásuk,
- Tiolok, tioéterek, diszulfidok funkciós csoportja
- Karbonilcsoport, különbség aldehidek és ketonok között
- Keto-enol tautoméria, az aldol addíció mechanisztikus alapjai