TÁMOP-4.1.1.F-14/1/KONV-2015-0006

SZTE TTIK, KTCS, 1a) Duális és moduláris képzésfejlesztés a mesterképzéshez

Telített heterociklusok

Pálinkó István, egyetemi tanár

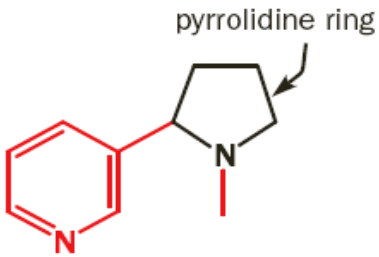
SZÉCHENYI 2020

Magyarország Kormánya

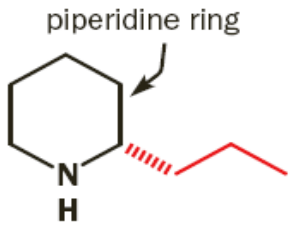
Európai Unió
Európai Szociális Alap

BEFEKTETÉS A JÖVŐBE

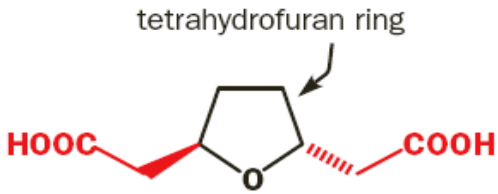
Fontos, gyakran a természetben is előforduló származékok



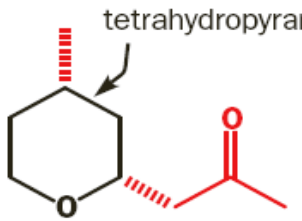
nicotine



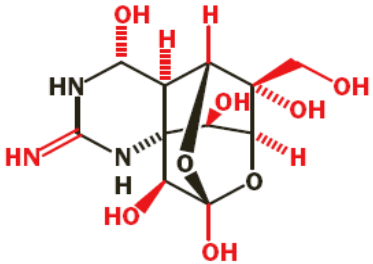
coniine – the poison in hemlock that killed Socrates



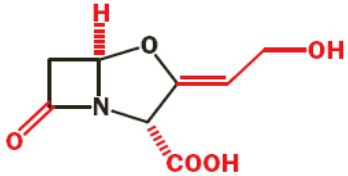
human waste product: 3–5 mg per day excreted in urine



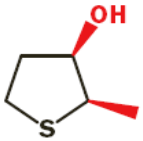
"rose oxide ketone" – isolated from geranium oil and used in the perfume industry



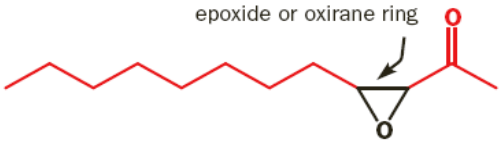
tetrodotoxin – lethal poison in wrongly prepared and cooked Japanese puffer fish



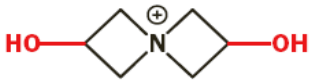
clavulanic acid – an antibiotic



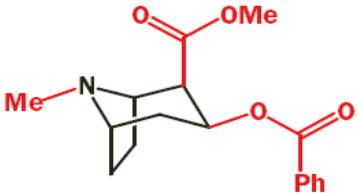
musty taste of "corked" wine



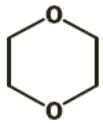
sex pheromone of the Grey Duiker antelope



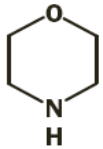
isolated from the green alga *Chara globularis*



cocaine



dioxane: a common solvent

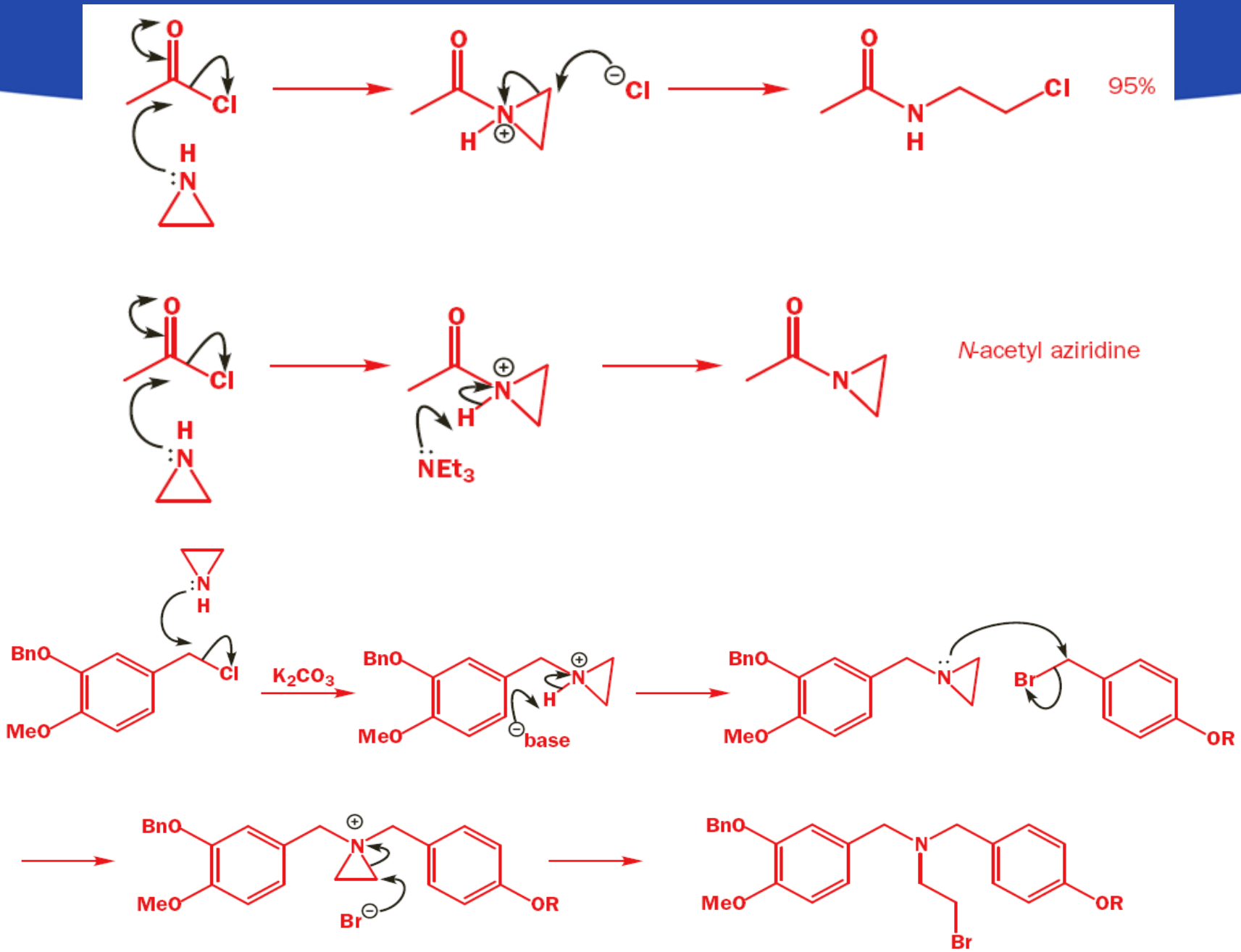


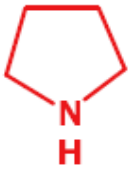
morpholine: an important base

Alapvegyületek és néhány reakciójuk

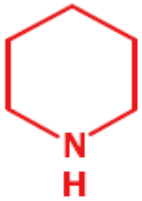
aziridine

azetidine

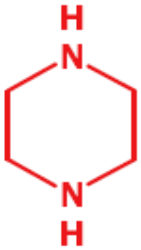

95%
N-acetyl aziridine
NEt3
K2CO3
base
BnO
MeO
OR
Br



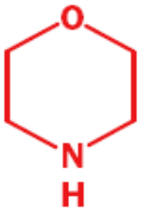
pyrrolidine



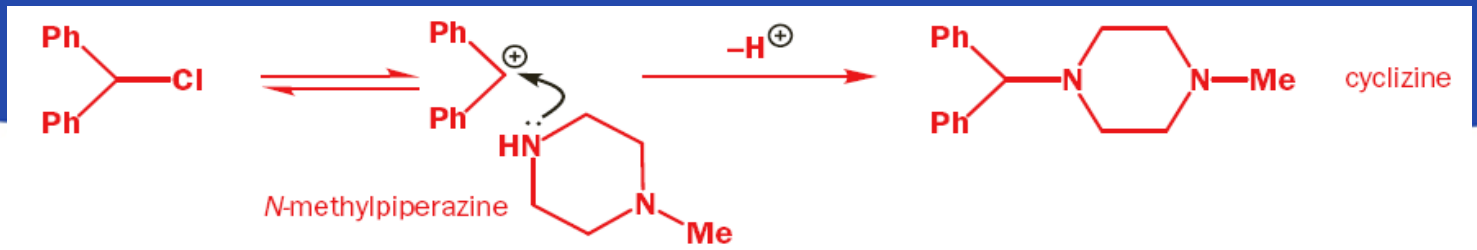
piperidine

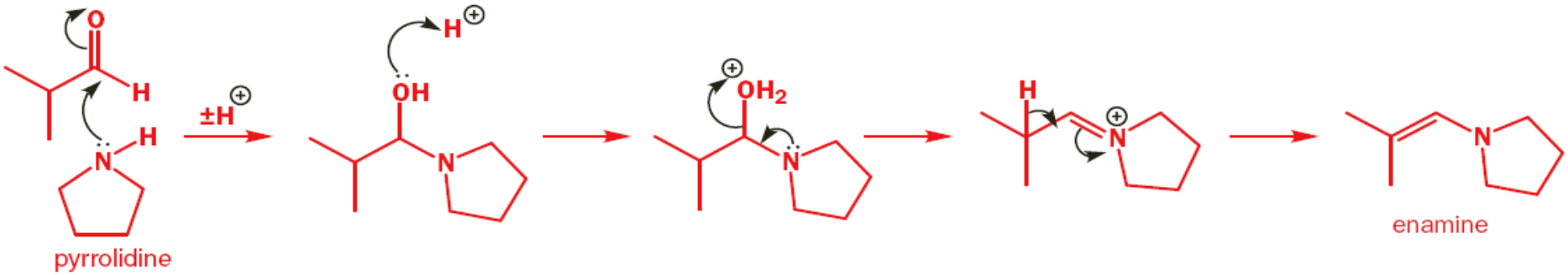


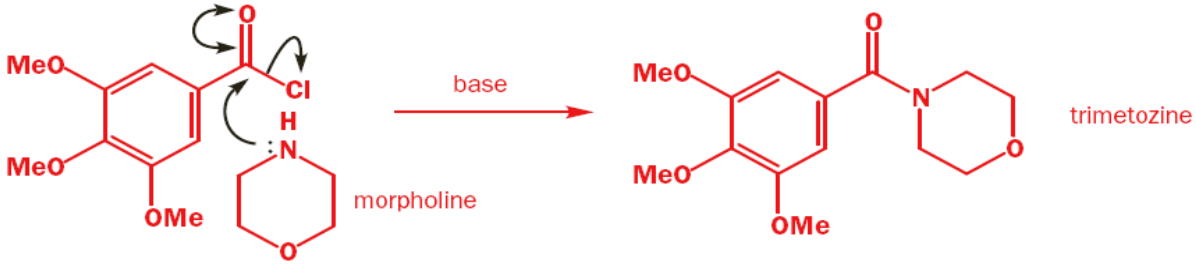
piperazine



morpholine


Ph
Cl
Ph
Ph
Ph
HN
N
Me
N-methylpiperazine
–H⊕
Ph
N
N
Me
Ph
cyclizine


O
H
H
N
pyrrolidine
±H⊕
H⊕
OH
N
OH2
N
H
N
N
enamine


O
MeO
MeO
OMe
Cl
H
N
O
morpholine
base
O
MeO
MeO
OMe
N
O
trimetozine

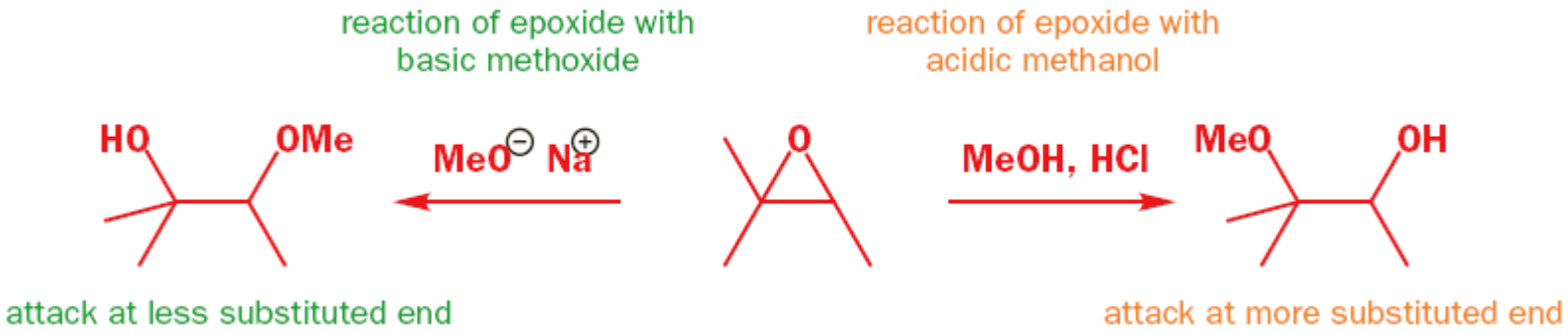
oxirane
(ethylene
oxide)

oxetane

tetrahydrofuran
(THF)

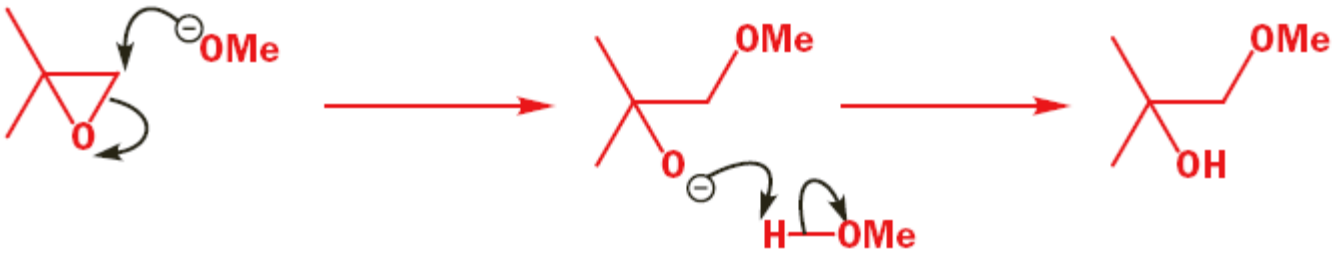
tetrahydropyran
(THP)

epoxidok gyűrűnyitási reakciói



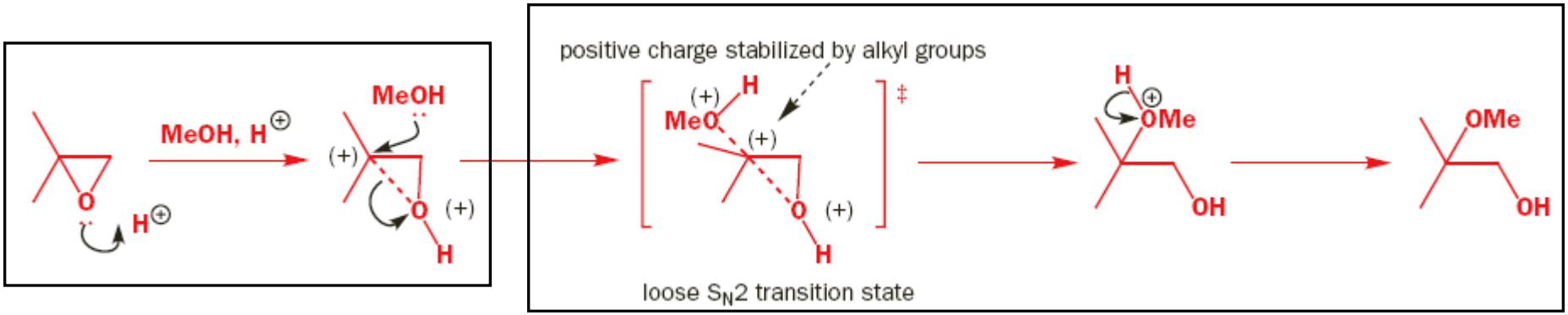
mechanizmusok

nukleofil támadás – protonálás nélkül az epoxid oxigén rossz távozó csoport: erős nukleofil kell és a sztérikus hatások lesznek a döntőek

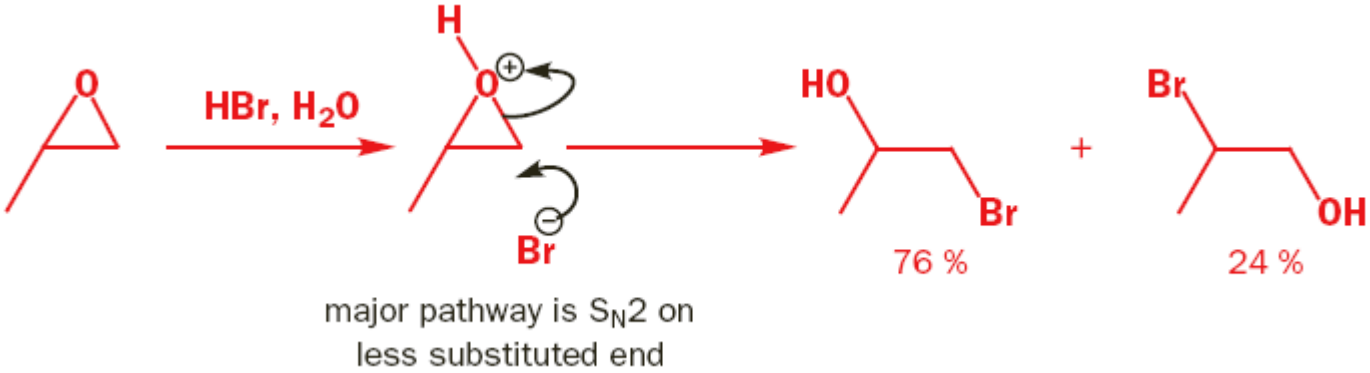


tiszta S_N2 reakció

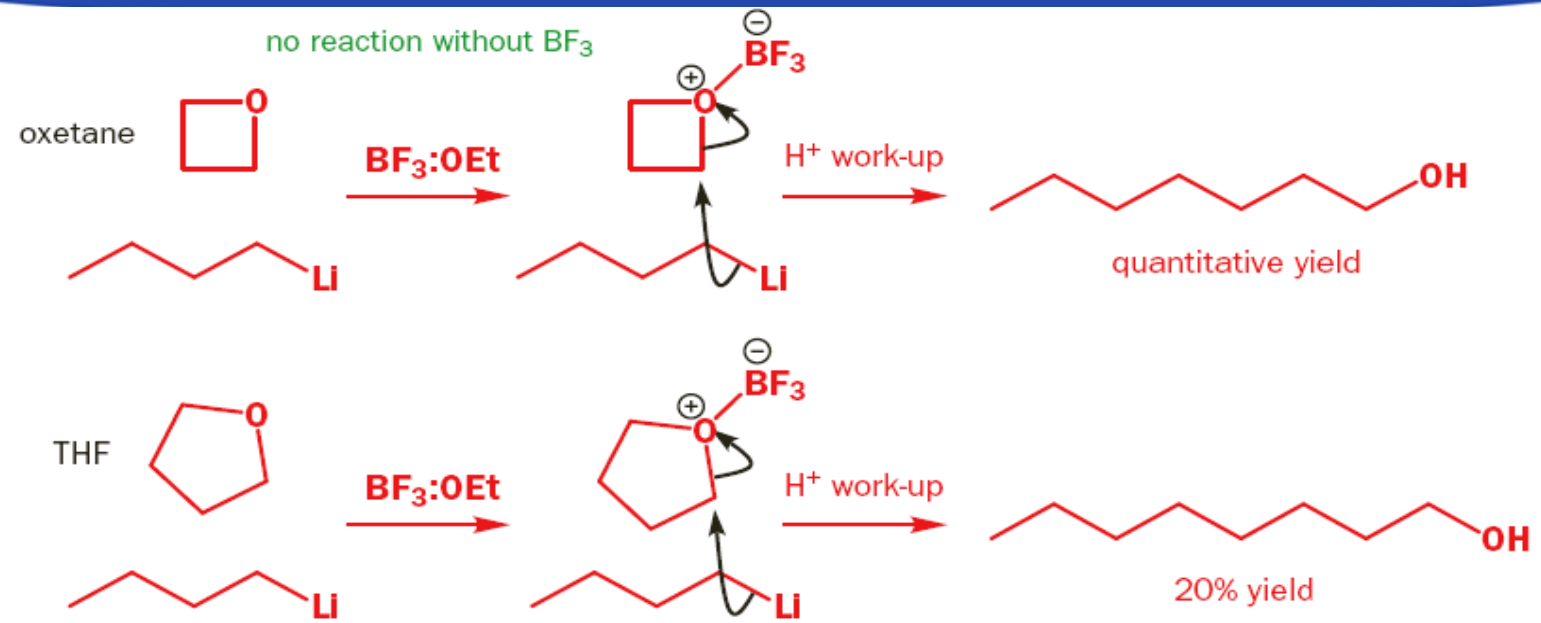
protonálódás először, majd nukleofil támadás



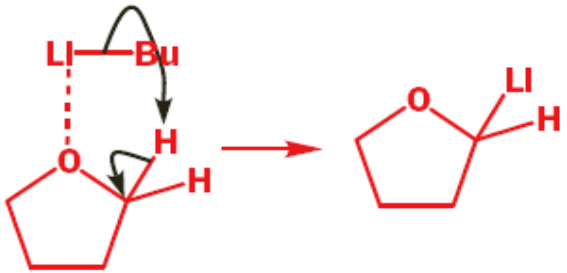
azért akadnak zavarok

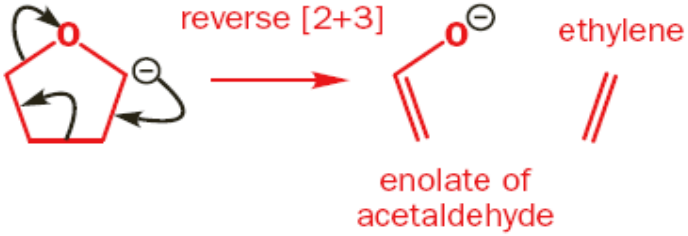


az oxetán és a tetrahidrofurán gyűrűnyitási reakciói

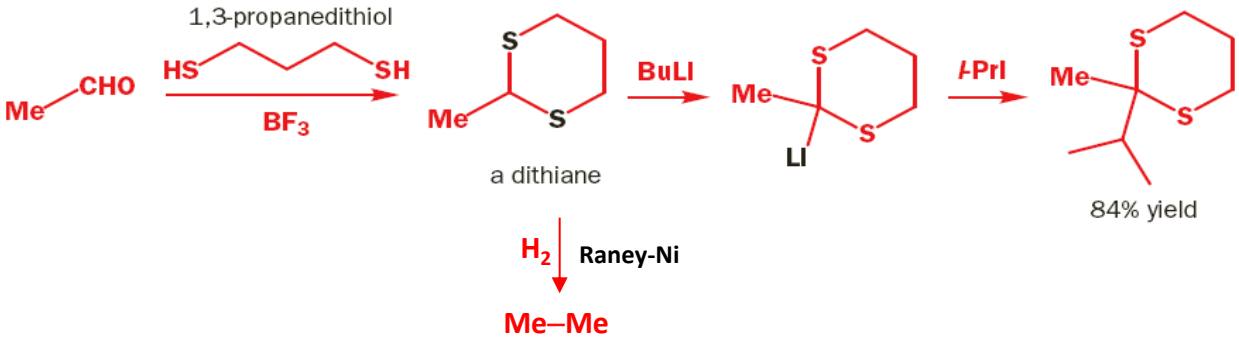


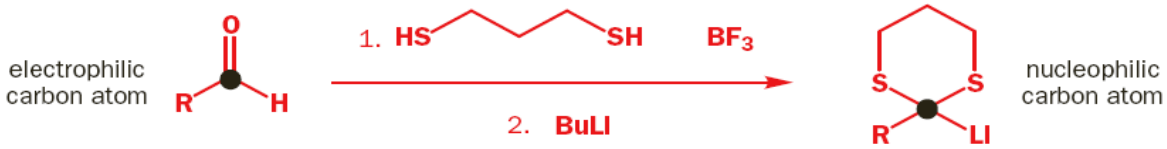
egyéb reakciók





dithiane





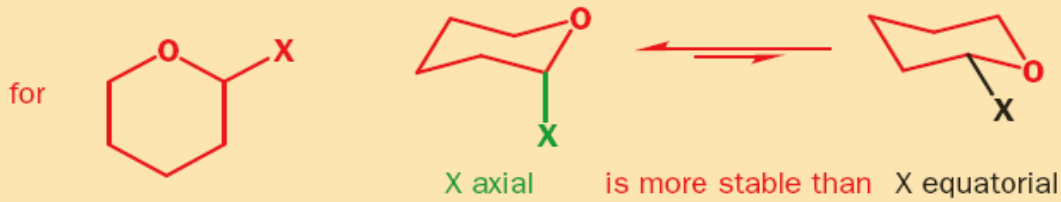
umpolung

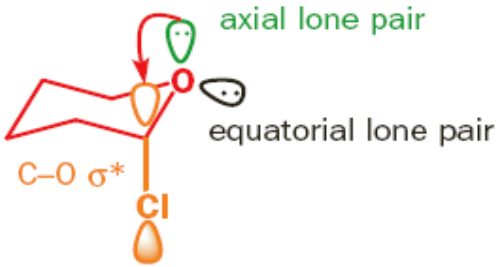
tudjuk, hogy a ciklohexán szubsztituensei ekvatoriális helyzetbe igyekeznek

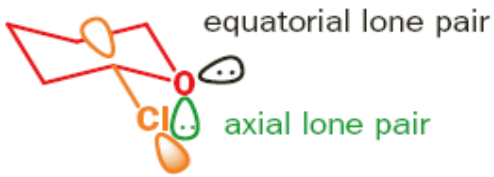
de

The anomeric effect

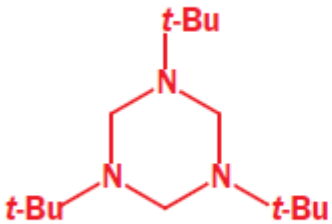
In general, any tetrahydropyran bearing an electronegative substituent in the 2-position will prefer that substituent to be axial. This is is known as the **anomeric effect.**

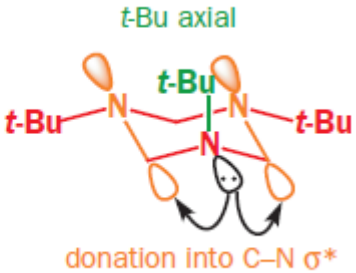




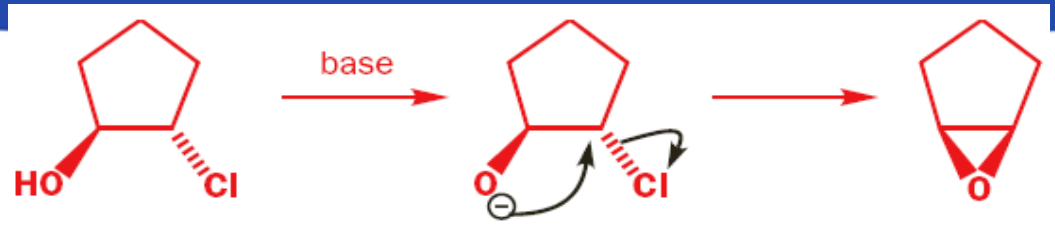


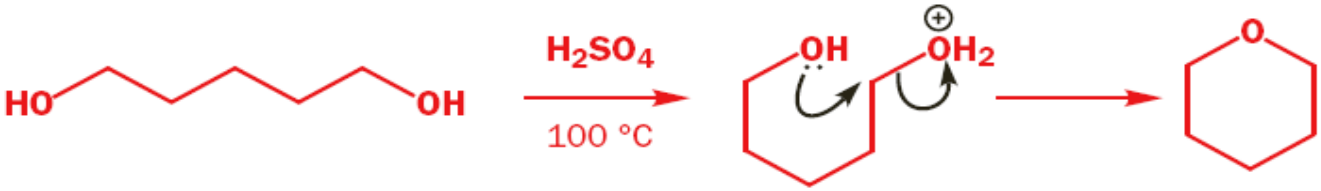
incorrectly aligned for overlap with either lone pair





Gyűrűszintézisek





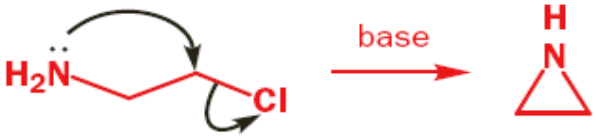
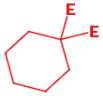
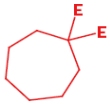
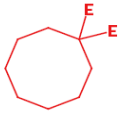


Table 42.2 Rates of ring-closing reactions

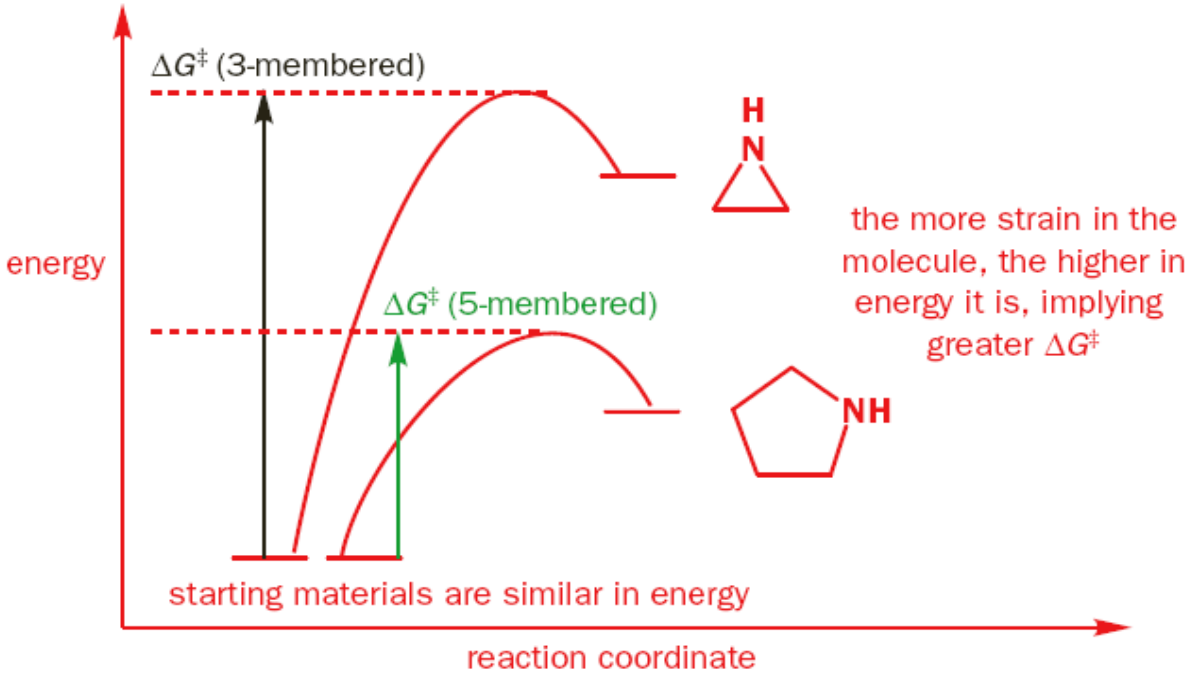
Ring size	Product	Relative rate[a]	Product[b]	Relative rate[a]	Assessment of rate
3		0.07			moderate
4		0.001		0.58	slow
5		100		833	very fast
6		1		1	fast
7		0.002		0.0087	slow
8				0.00015	very slow

[a] Relative to the six-membered ring formation (= 1).
[b] E = CO_2Et.

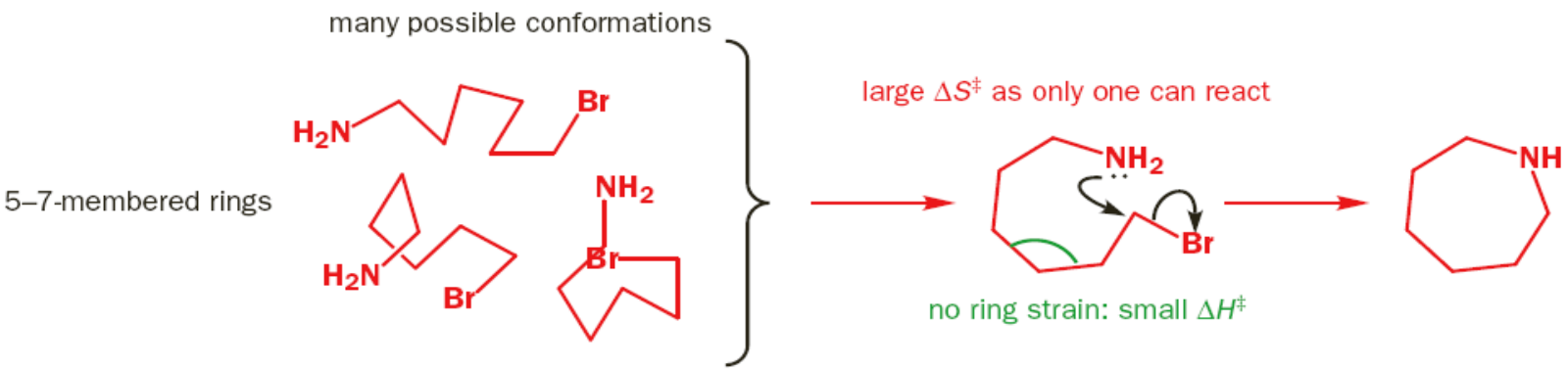
Rough guide to the rate of formation of saturated rings

5 > 6 > 3 > 7 > 4 > 8–10

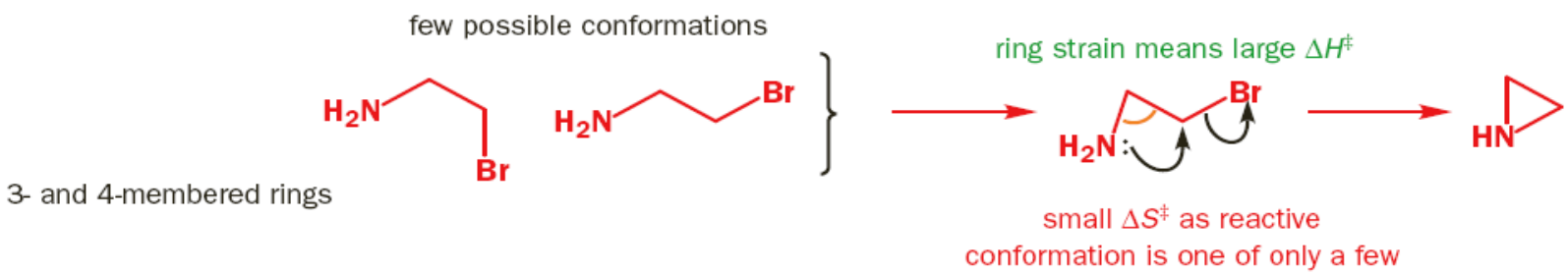
Miért?



alacsonyabb gyűrűtagszám esetén az energetikai viszonyok a meghatározók



magasabb gyűrűtagszám esetén az entrópiaviszonyok a meghatározók

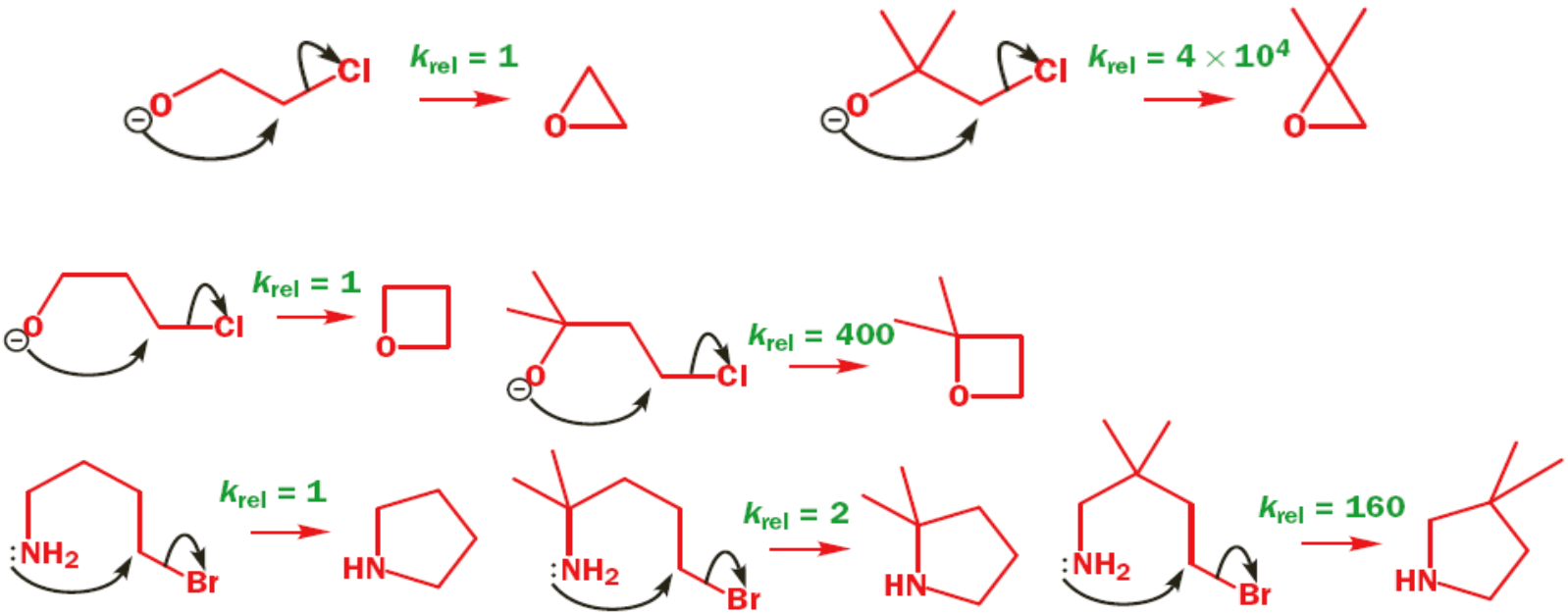


Ring formation

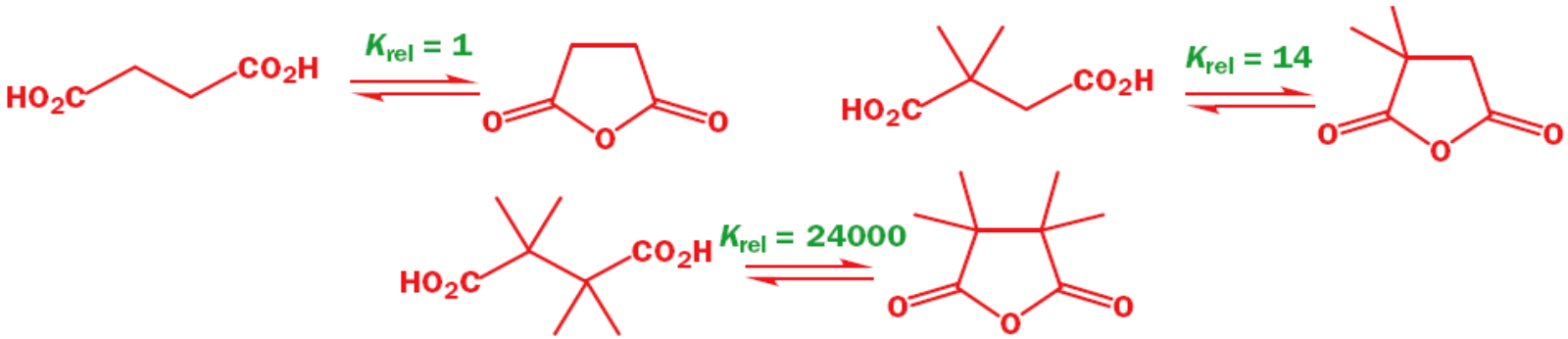
- Three-membered ring formation is fast—the product is strained so $\Delta H^{\ddagger}$ is large but this is offset by the reacting atoms being as close as they can get in a freely rotating chain
- Four-membered rings form slowly—the product is still significantly strained but the reacting atoms are now not right next to each other to offset this
- Five-membered ring formation is often fastest of all. Significantly less strain and the ends are still not too far apart
- Six-membered ring formation experiences no strain but neither does it have the advantage of the ends being close
- Seven-membered rings and beyond form more slowly as $\Delta S^{\ddagger}$ increases

a szubsztituensek hatása a gyűrűzáródásra

kinetikai



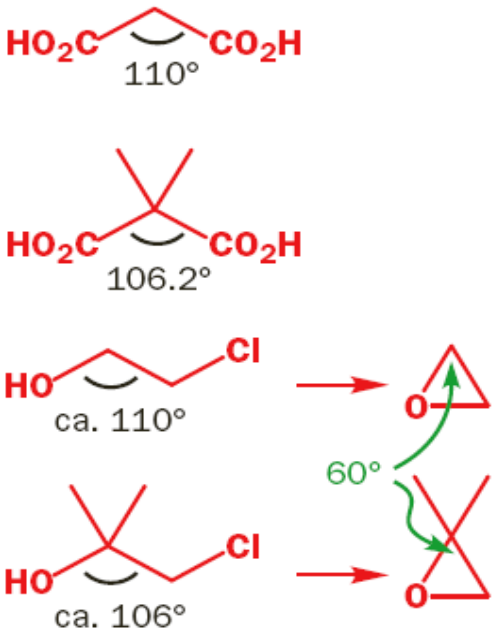
termodinamikai



The Thorpe–Ingold effect

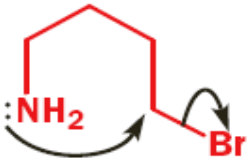
The Thorpe–Ingold effect is the way in which substituents on the ring increase the rate, or equilibrium constant, for ring-forming reactions.

kis gyűrűtagszám

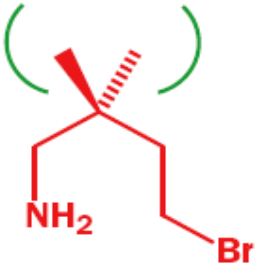


közepes és nagy gyűrűtagszám

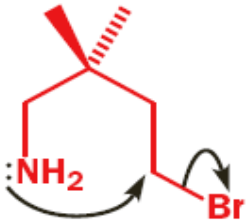
lowest energy conformation – many others possible: high ΔS^0



very negative $\Delta S^{\ddagger}$ to get to transition state



few conformations possible: lower ΔS^0



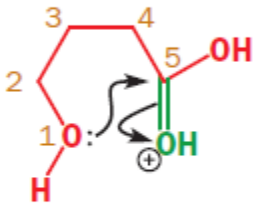
$\Delta S^{\ddagger}$ less negative

Baldwin-szabályok – gyűrűzáródási reakciók

a reakciók osztályozása

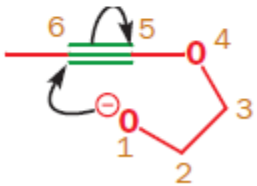
3-*exo-tet*

1. The ring being formed has three members; the breaking C–Br bond is outside the new ring (*exo*); the C carrying Br is a tetrahedral (sp^3) atom (*tet*)



5-*exo-trig*

2. The ring being formed has five members; the breaking C=O bond is outside the new ring (*exo*); the C being attacked is a trigonal (sp^2) atom (*trig*)

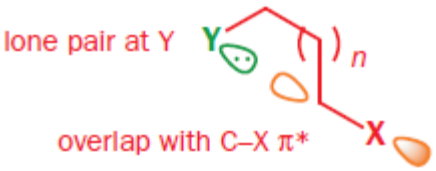


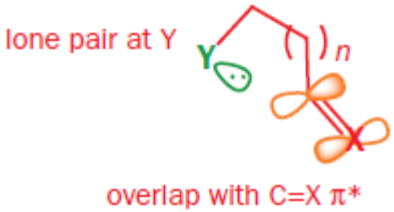
6-*endo-dig*

3. The ring being formed has six members; the breaking C≡C bond is inside the new ring (*endo*); the C being attacked is a digonal (sp) atom (*dig*)

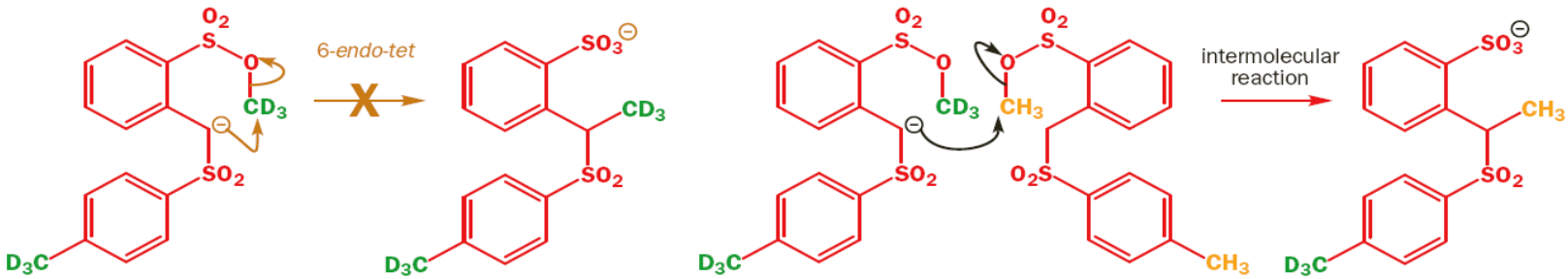
- All *exo-tet* cyclizations are favoured.

- All *exo-trig* cyclizations are favoured.

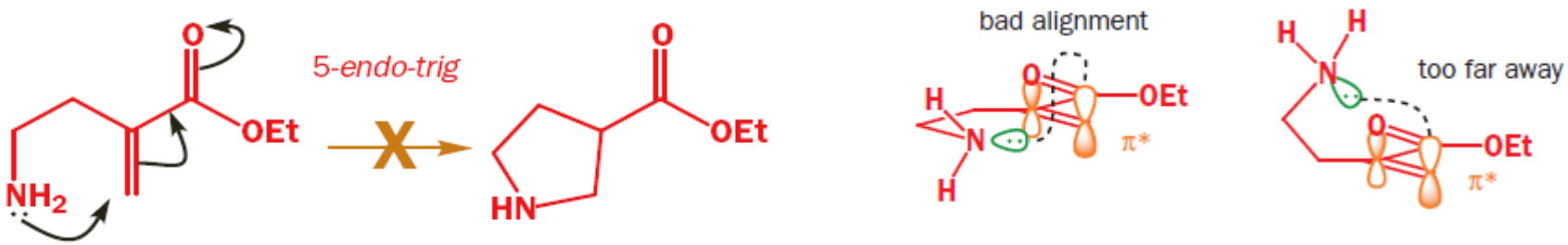




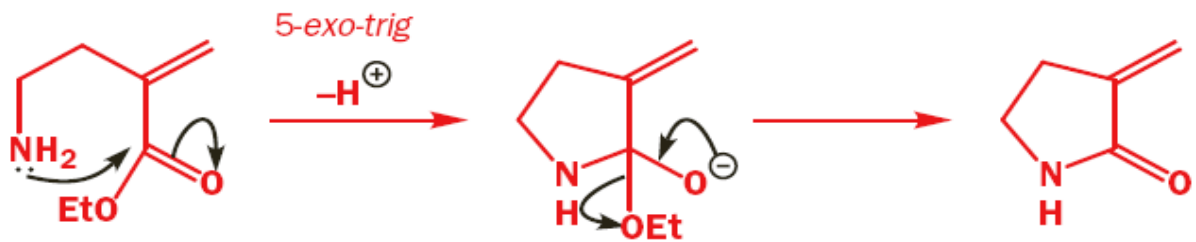
- 5- and 6-*endo-tet* are disfavoured.



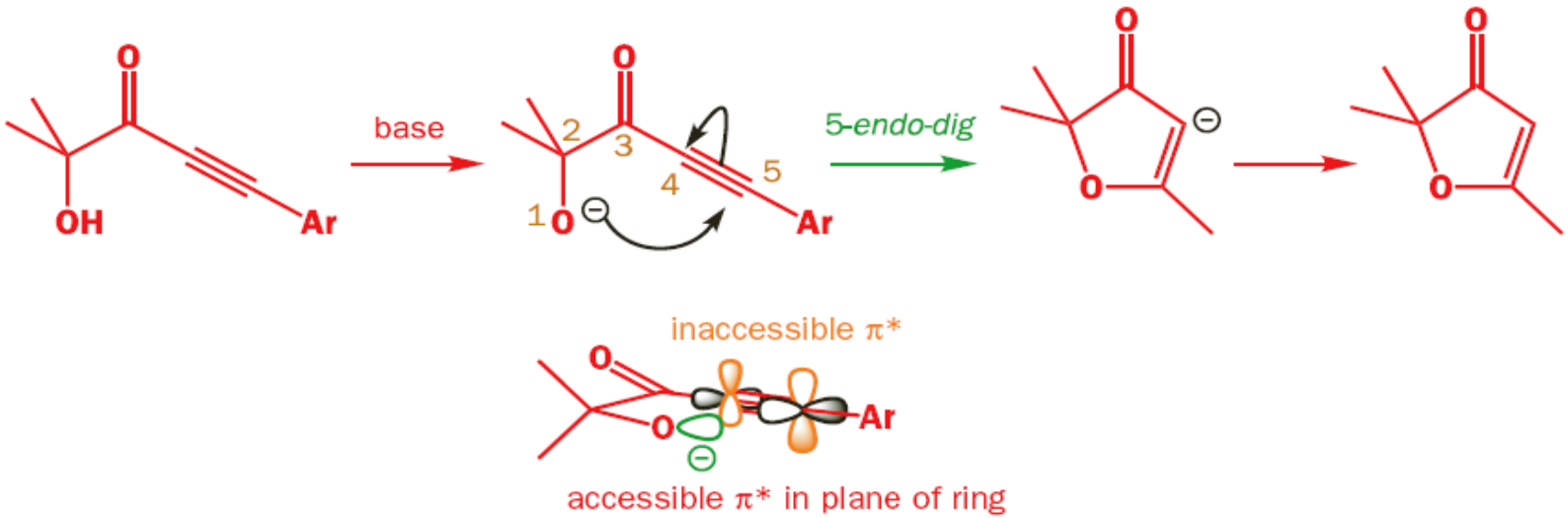
- 3-, 4-, and 5-*endo-trig* are disfavoured; 6- and 7-*endo-trig* are favoured.



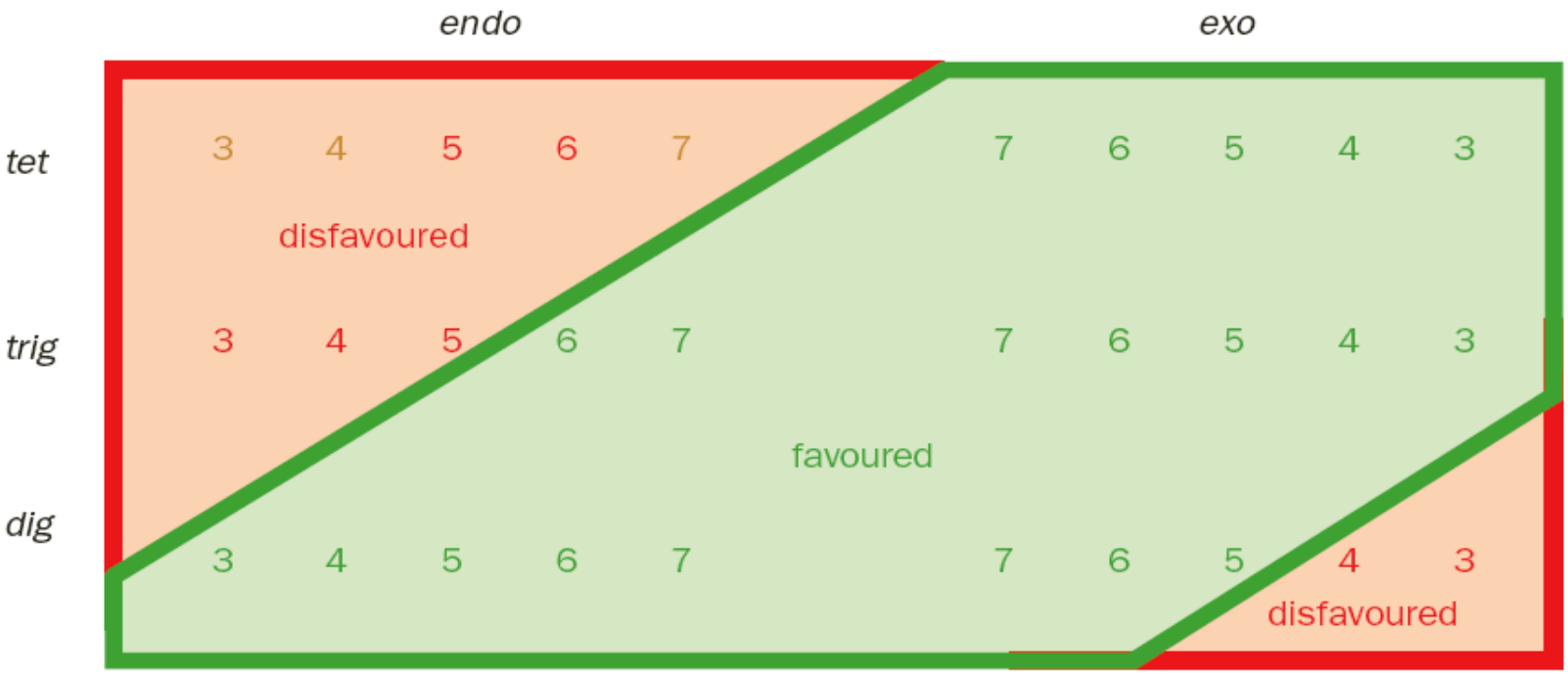
de



- All *endo-dig* cyclizations are favoured.



- 3- and 4-*exo-dig* are disfavoured; 5- to 7-*exo-dig* are favoured.


endo
exo
tet
3 4 5 6 7
7 6 5 4 3
disfavoured
trig
3 4 5 6 7
7 6 5 4 3
favoured
dig
3 4 5 6 7
7 6 5 4 3
disfavoured

KÖSZÖNÖM A FIGYELMET!

SZÉCHENYI 2020

MAGYARORSZÁG KORMÁNYA

Európai Unió
Európai Szociális Alap

BEFEKTETÉS A JÖVŐBE