TÁMOP-4.1.1.F-14/1/KONV-2015-0006
SZTE TTIK, KTCS, 1a) Duális és moduláris képzésfejlesztés a mesterképzéshez

(Fél)kvantitatív szerves kémia 2.

Izotópeffektusok – sav-bázis katalízis

Pálinkó István, egyetemi tanár

SZÉCHENYI 2020
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Európai Szociális Alap
BEFEKTETÉS A JÖVŐBE

Kinetikus deutérium izotópeffektus

E1 vagy E2 típusú az elimináció?

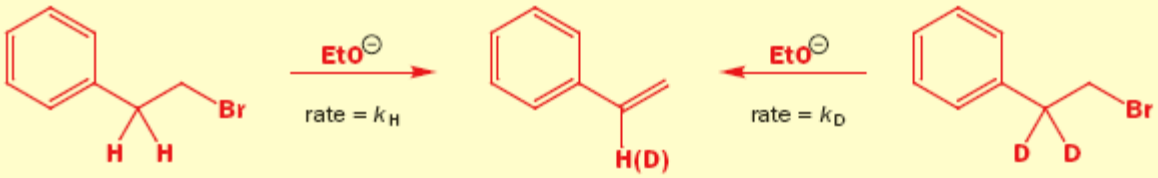
How to distinguish E1 from E2: kinetic isotope effects

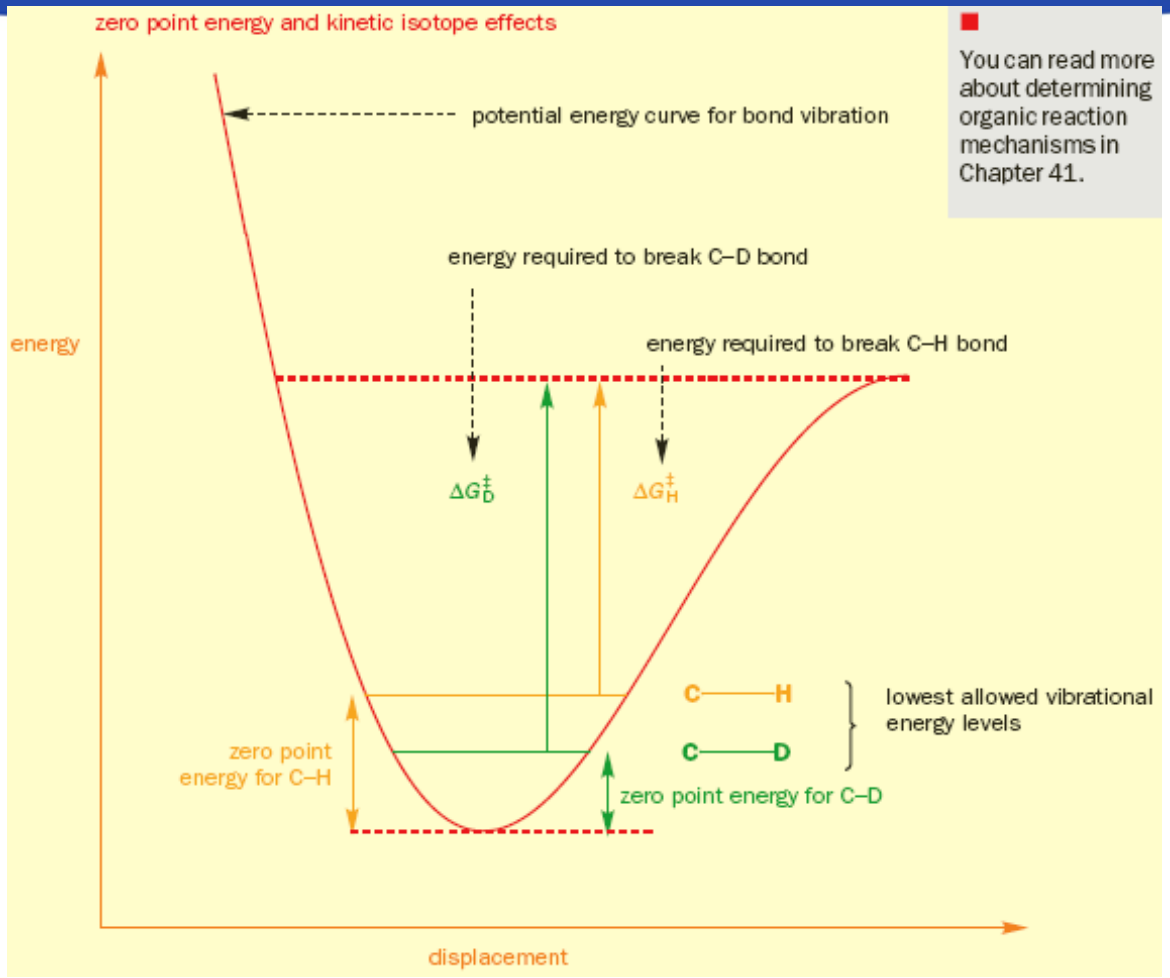
We have told you what sorts of starting materials and conditions favour E1 or E2 reactions, but we haven't told you how we know this. E1 and E2 differ in the order of their rate equations with respect to the base, so one way of finding out if a reaction is E1 or E2 is to plot a graph of the variation of rate with base concentration. But this can be difficult with E1 reactions because the base (which need be only very weak) is usually the solvent. More detailed evidence for the differences between reaction mechanisms comes from studying the rates of elimination in substrates that differ only in that one or more of the protons have been replaced by deuterium atoms. These differences are known as **kinetic isotope effects**.

Up to now you have probably (and rightly) been told that isotopes of an element (that is, atoms that differ only in the number of neutrons their nuclei contain) are chemically identical. It may come as a surprise to find that this is not quite true: isotopes do differ chemically, but this difference is only significant for hydrogen—no other element has one isotope twice as massive as another! Kinetic isotope effects are the changes in rate observed when a (^{1}H) hydrogen atom is replaced by a (^{2}H) deuterium atom in the same reaction. For any reaction, the kinetic isotope effect is defined as

$$\text{KIE} = \frac{k_H \text{ (rate with substrate containing } ^1\text{H)}}{k_D \text{ (rate with substrate containing } ^2\text{H)}}$$

Changing H for D can affect the rate of the reaction only if that H (or D) is involved in the rate-determining step. The theoretical maximum is about 7 for reactions at room temperature in which a bond to H or D is being broken. For example, the rates of these two eliminations can be compared, and k_H/k_D turns out to be 7.1 at 25 °C.

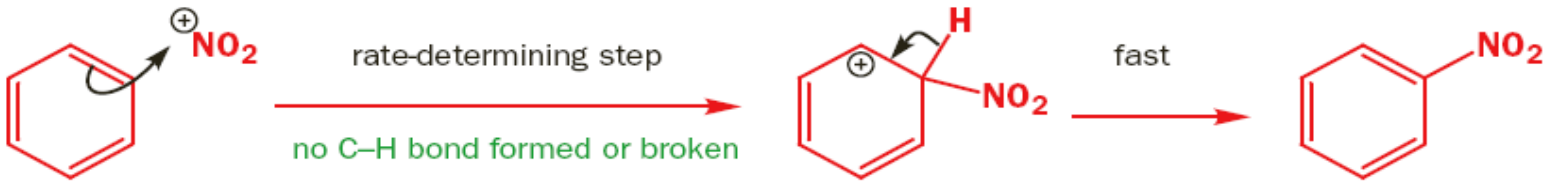




You can read more about determining organic reaction mechanisms in Chapter 41.

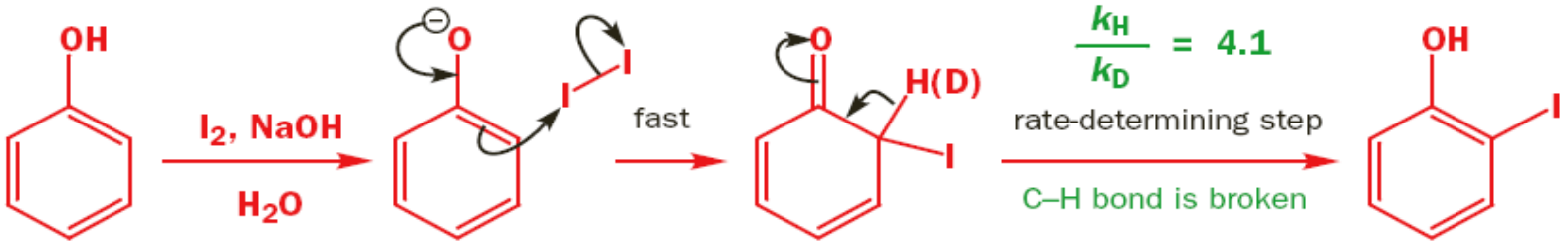
Benzol nitrálásakor melyik a sebességmeghatározó lépés?

Kísérleti eredmény: $k_H/k_D=1.0$



És mi a helyzet, ha fenolt jódozunk lúgos körülmények között?

Kísérleti eredmény: k_H/k_D=4.1



Inverz kinetikus deutérium izotópeffektus

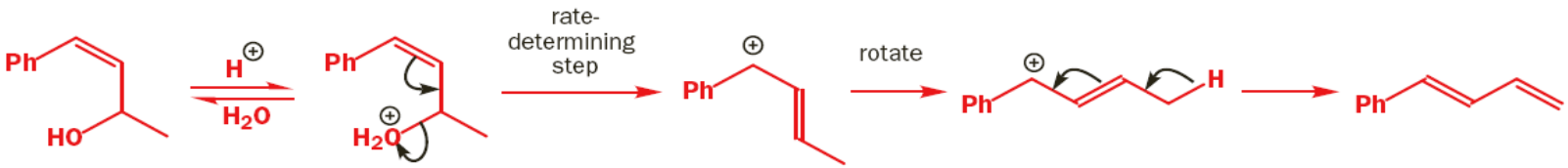
$$r = k[XH^+]$$

$$[XH^+] = K[H^+][X]$$

$$r = Kk[H^+][X]$$

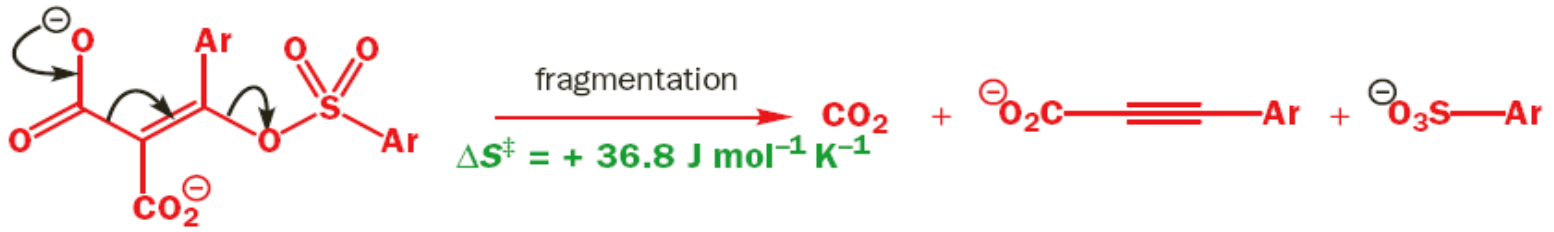
Kísérleti tapasztalat: a reakció gyorsabb D_2O-ban, mint H_2O-ban

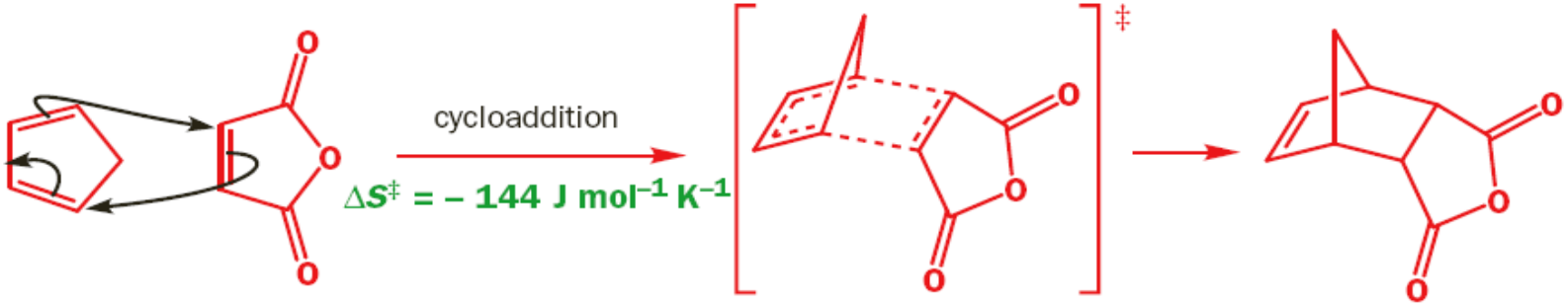
Magyarázat: D_3O^+ erősebb sav D_2O-ban, mint a H_3O^+ H_2O-ban



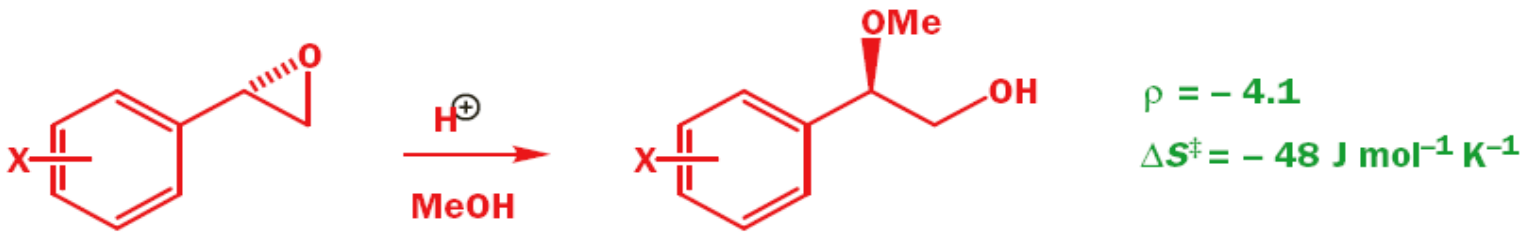
$$k(H_2O)/k(D_2O) = 1.0/2.5$$

Aktiválási entrópia


fragmentation
$\Delta S^{\ddagger}$ = + 36.8 J mol^{-1} K^{-1}
CO_2
Ar
O_2C
O_3S


cycloaddition
$\Delta S^{\ddagger}$ = – 144 J mol^{-1} K^{-1}
‡

az aktiválási entrópia és a Hammett-féle ρ paraméter kombinálható

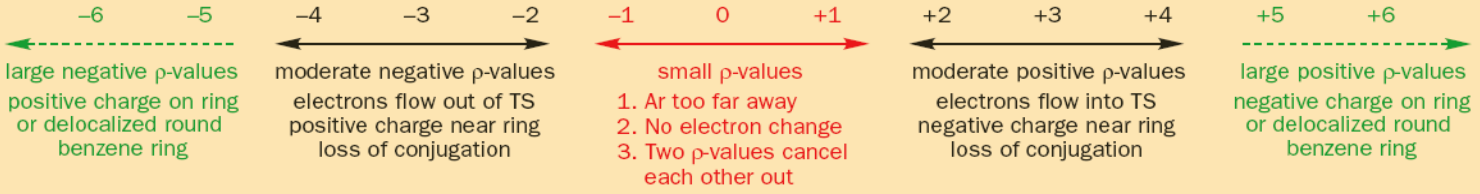


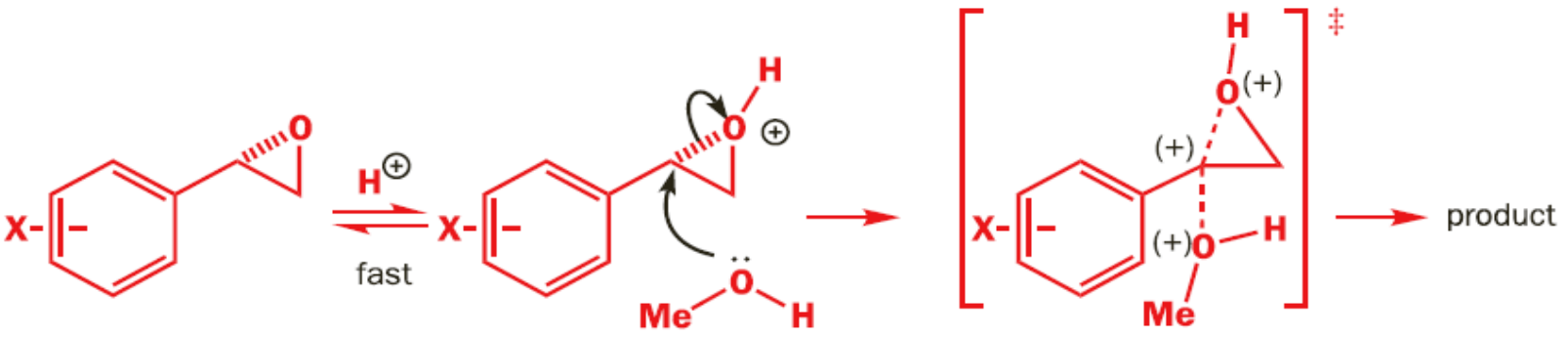
The Hammett reaction constant ρ measures the *sensitivity* of the reaction to electronic effects.

- A *positive* ρ value means *more* electrons in the transition state than in the starting material
- A *negative* ρ value means *fewer* electrons in the transition state than in the starting material

The meaning of Hammett ρ values

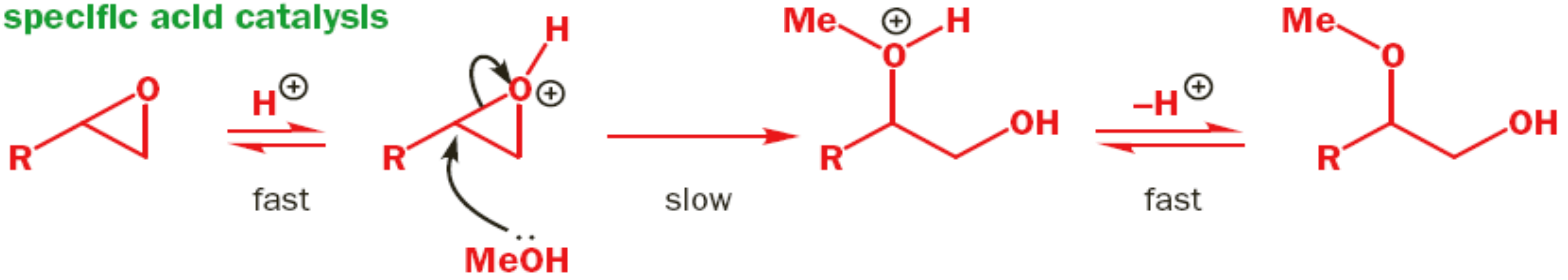
This then is the full picture. You should not, of course, learn these numbers but you need an idea of roughly what each group of values means. You should see now why it is unimportant whether the Hammett correlation gives a good straight line or not. We just want to know whether ρ is + or – and whether it is, say, 3 or 6. It is meaningless to debate the significance of a r value of 3.4 as distinct from one of 3.8.




X-
O
H
fast
X-
O
H
Me
O
H
X-
H
O
(+)
(+)
(+)
O
H
Me
‡
product

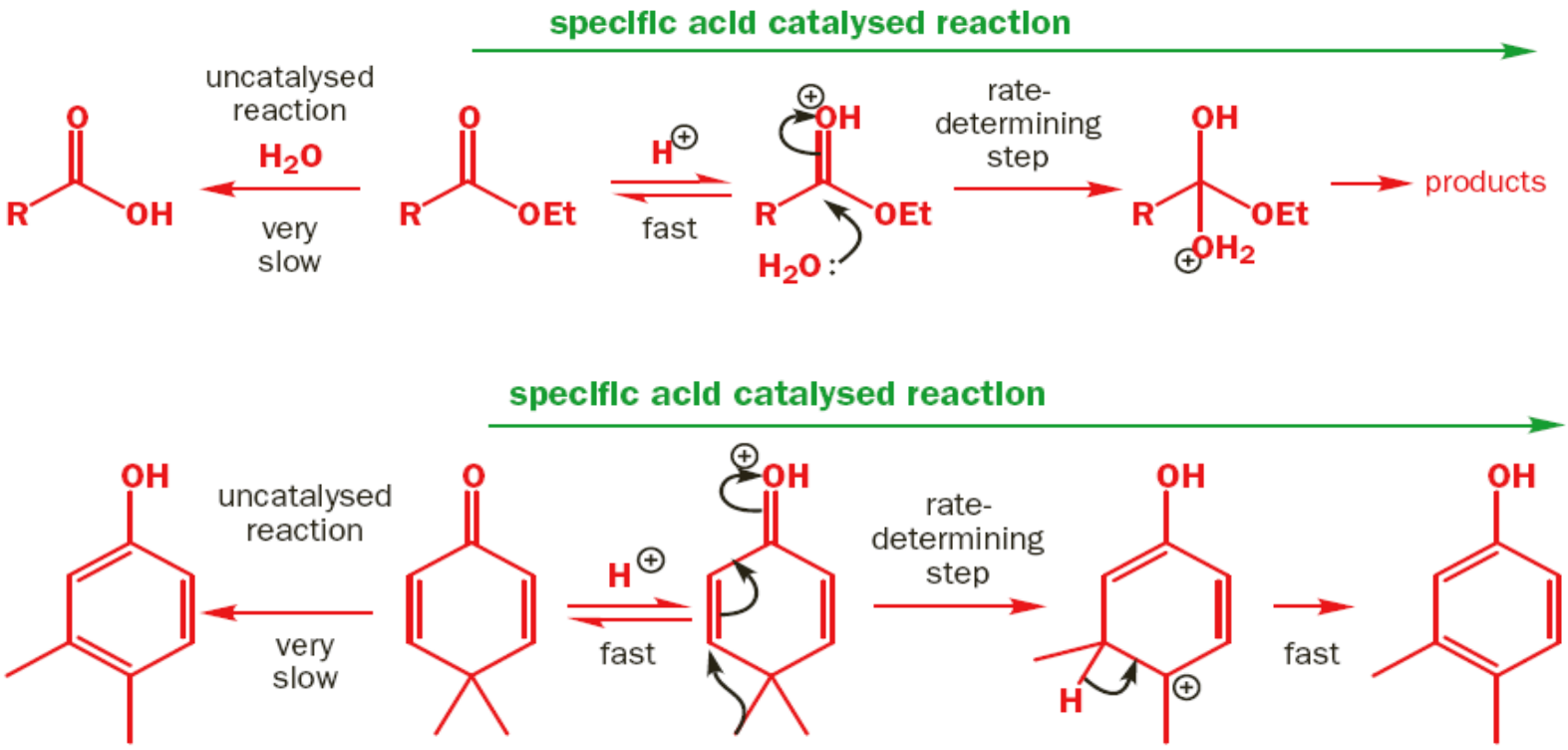
Sav-bázis katalízis

specific acid catalysis



specific base catalysis

Specifikus savkatalízis

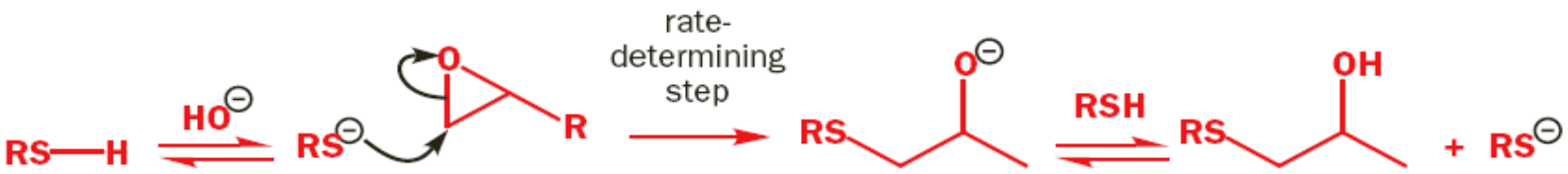


Kísérleti megfigyelések: (i) a reakciósebesség fordítva arányos a pH-val (a katalitikus hatás jelentős, ha a sav pK_a értéke kisebb, mint a szubsztráté), (ii) a reakció gyorsabban megy D_2O-ban, mint H_2O-ban (inverz deutérium izotópeffektus)

Summary of features of specific acid catalysis

1. Only H_3O^+ is an effective catalyst; pH alone matters
2. Usually means rate-determining reaction of protonated species
3. Effective only at pHs near or below the pK_{aH} of the substrate
4. Proton transfer is not involved in the rate-determining step
5. Only simple unimolecular and bimolecular steps—moderate + or $-\Delta S^{\ddagger}$
6. Inverse solvent isotope effect $k(H_2O) < k(D_2O)$

Specifikus báziskatalízis



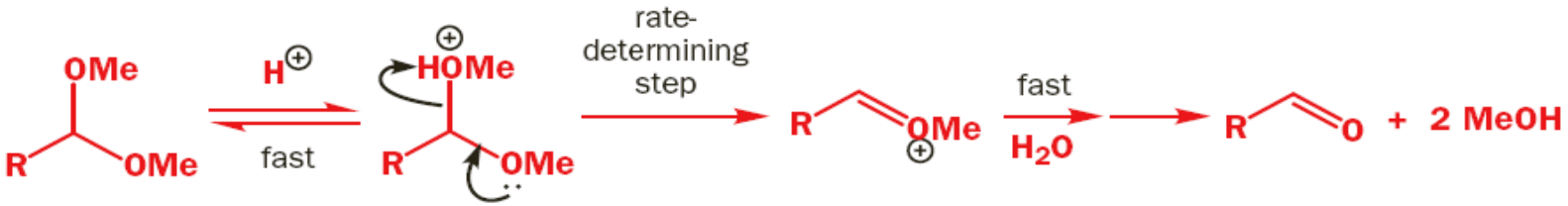
Kísérleti megfigyelések: (i) a reakciósebesség egyenesen arányos a pH-val (a katalitikus hatás jelentős, ha a szubsztrát pK_a értéke kisebb, mint a bázisé), (ii) a reakció gyorsabban megy D_2O-ban, mint H_2O-ban (inverz deutérium izotópeffektus)

Summary of features of specific base catalysis

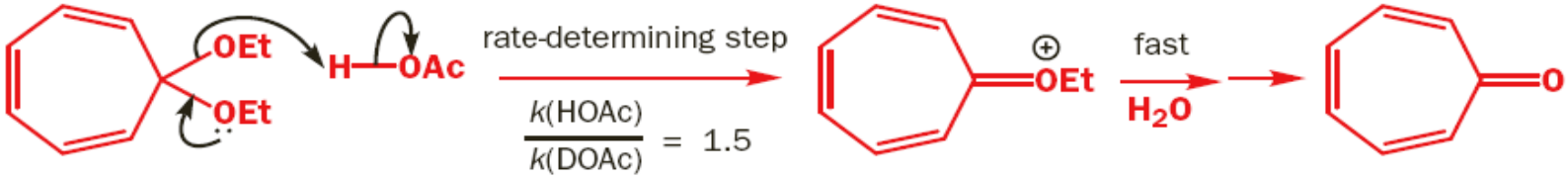
1. Only HO^- is an effective catalyst; pH alone matters
2. Usually means rate-determining reaction of deprotonated species
3. Effective only at pHs near or above the pK_a of the substrate
4. Proton transfer is not involved in the rate-determining step, unless C–H bonds are involved
5. Only simple unimolecular and bimolecular steps—moderate + or $-\Delta S^{\ddagger}$
6. Inverse solvent isotope effect $k(H_2O) < k(D_2O)$

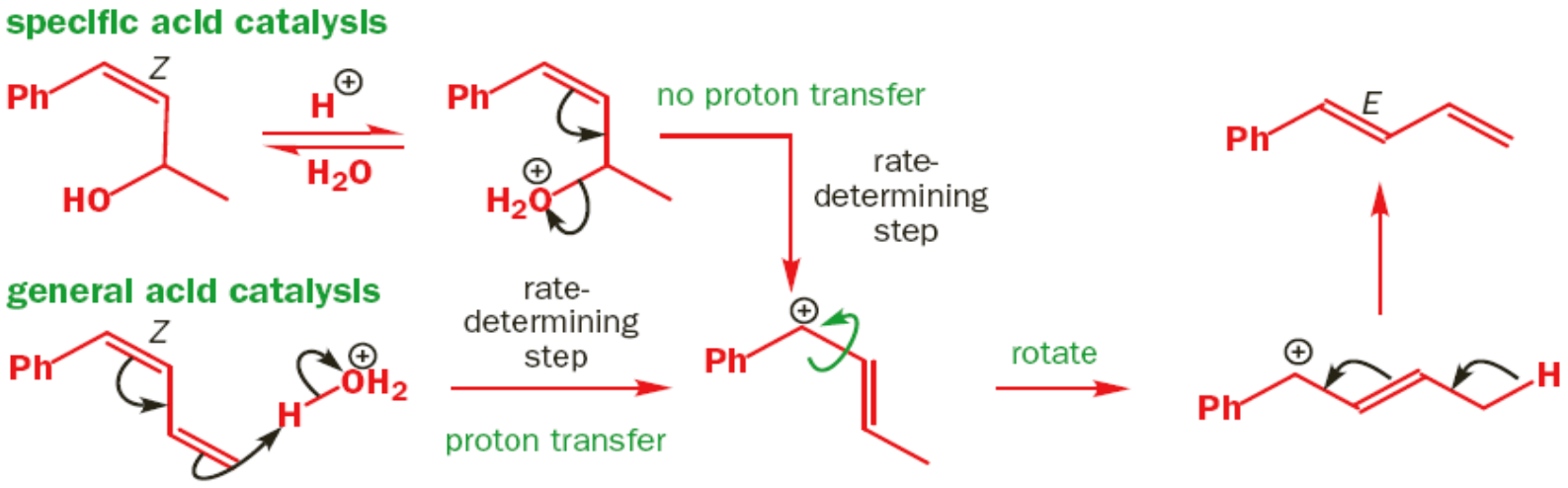
Általános savkatalízis

specific acid-catalysed acetal hydrolysis



general acid-catalysed acetal hydrolysis

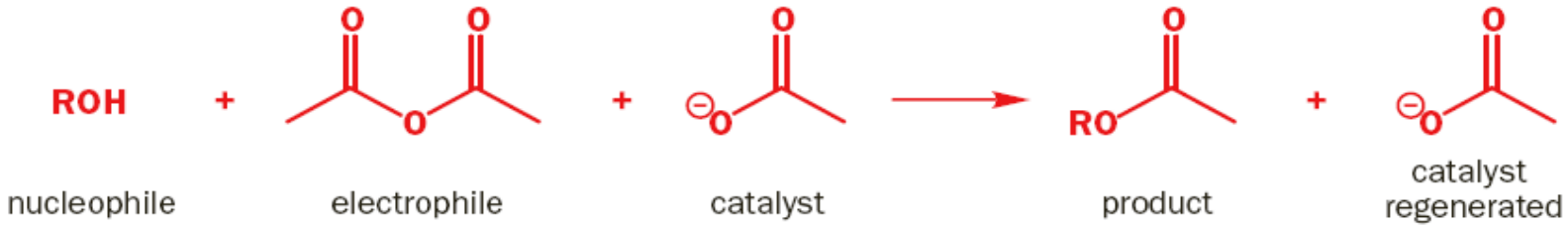



specific acid catalysis
Z
Ph
HO
H
H2O
Ph
H2O
no proton transfer
rate-
determining
step
general acid catalysis
Z
Ph
H
OH2
rate-
determining
step
proton transfer
Ph
rotate
E
Ph
Ph
H

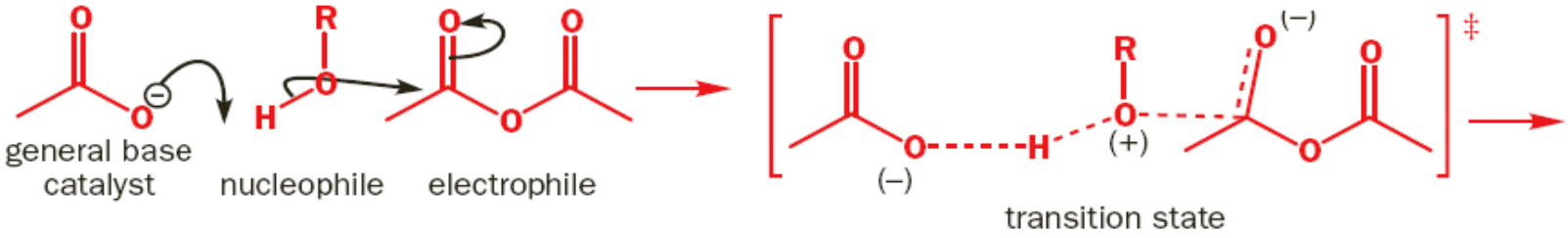
Summary of features of general acid catalysis

1. Any acid is an effective catalyst; pH also matters
2. Proton transfer is involved in the rate-determining step
3. Effective at neutral pHs even if above the pK_{aH} of the substrate
4. Catalyst often much too weak an acid to protonate reagent
5. Catalyst adds proton to a site that is becoming more basic in the rate-determining step
6. Some other bond-making or bond-breaking also involved unless proton is on carbon
7. Often termolecular rate-determining step: large $-\Delta S^{\ddagger}$
8. Normal kinetic isotope effect $k(\mathrm{H}) > k(\mathrm{D})$

Általános báziskatalízis



Kísérleti megfigyelések: (i) jobban megy a reakció, ha nő a pH, de leggyorsabb semleges pH-nál, (ii) a reakció gyorsabban megy ROH-val, mint ROD-vel ([normál] deutérium izotópeffektus), (iii) hatalmas entrópiacsökkenés



Summary of features of general base catalysis

1. Any base is an effective catalyst; pH also matters
2. Proton transfer is involved in the rate-determining step
3. Effective at neutral pHs even if below the pK_a of the substrate
4. Catalyst often much too weak a base to deprotonate reagent
5. Catalyst removes proton, which is becoming more acidic in the rate-determining step
6. Some other bond-making or bond-breaking also involved unless proton is on carbon
7. Often termolecular rate-determining step: large $-\Delta S^{\ddagger}$
8. Normal kinetic isotope effect $k(\mathrm{H}) > k(\mathrm{D})$

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