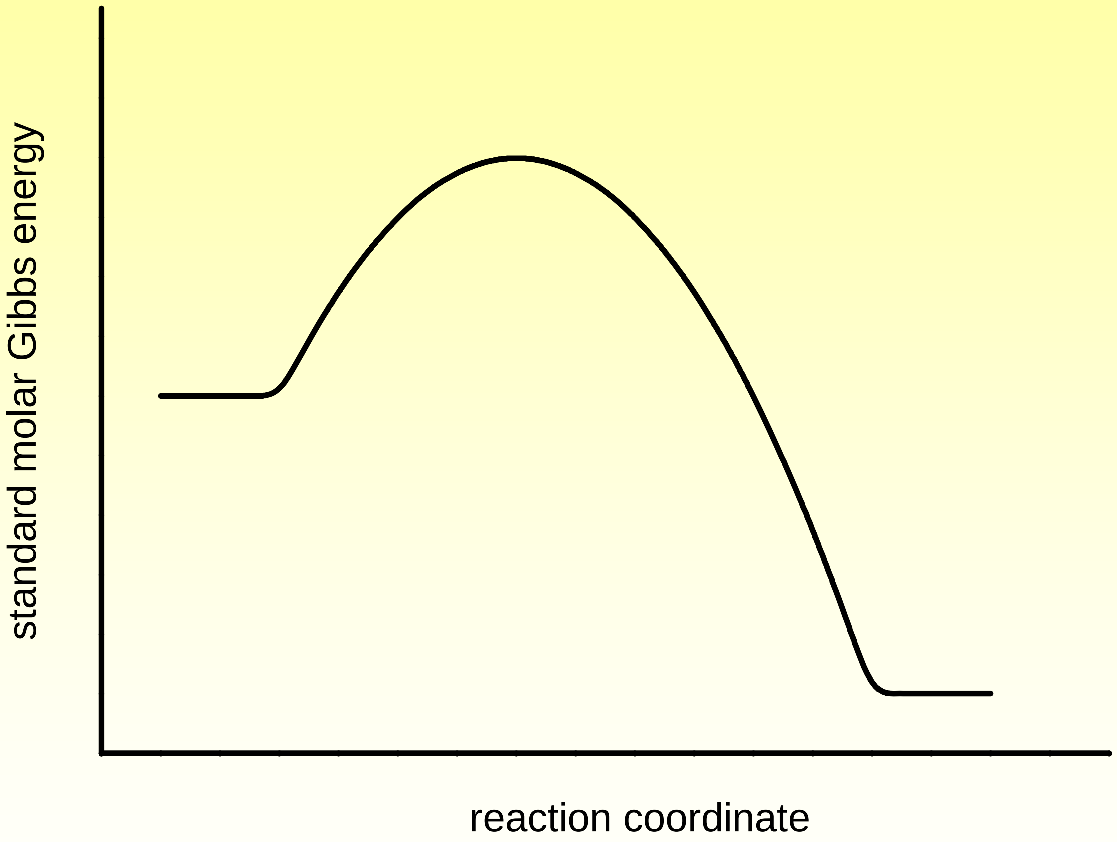
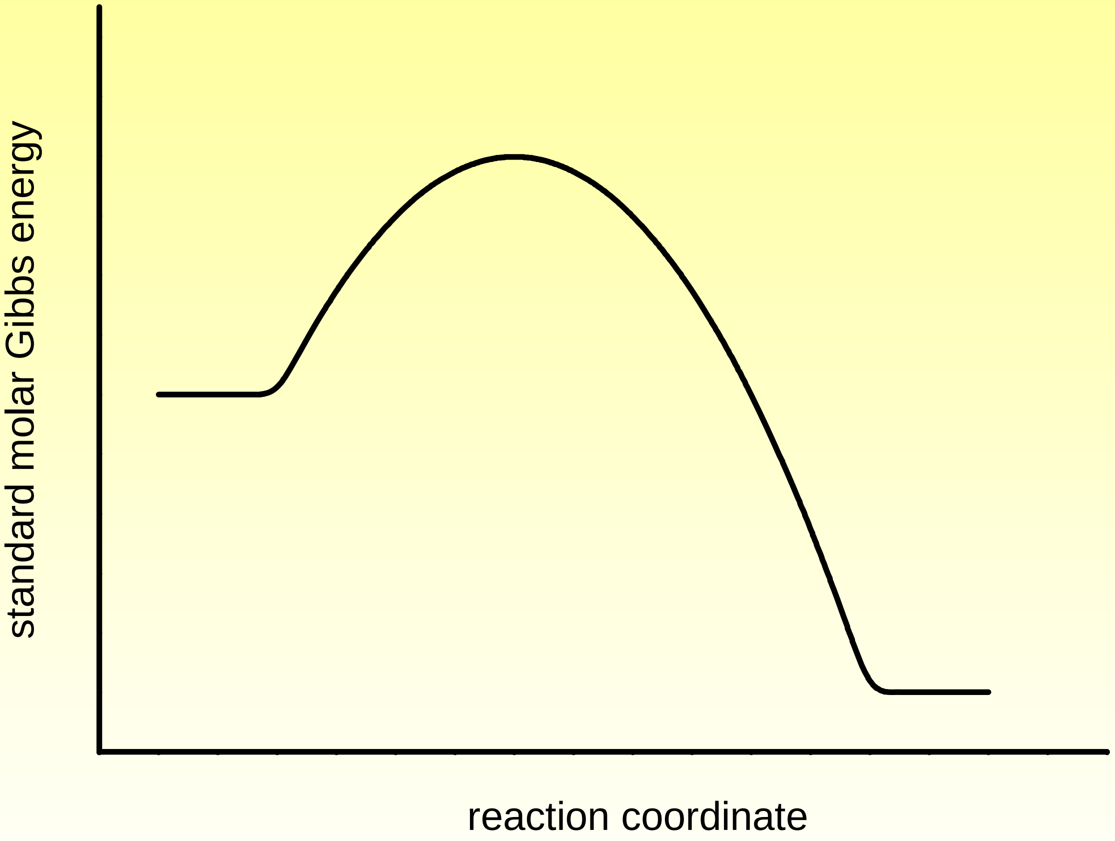
Introduction to Kinetics II

NJB

Transition State Theory


standard molar Gibbs energy
reaction coordinate

Transition State Theory



equilibrium constant

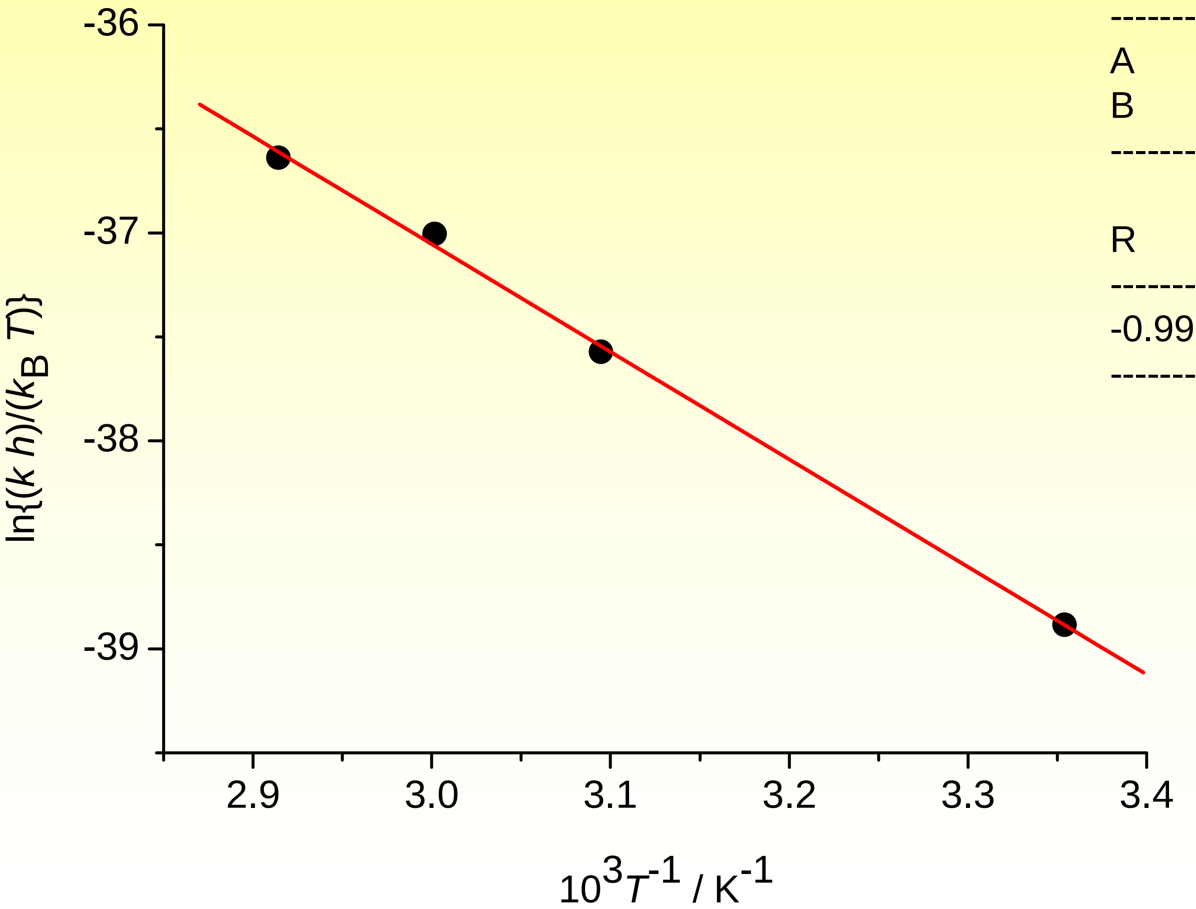
$$k = \frac{k_B T}{h} \cdot e^{-\frac{\Delta G^{\ominus\ddagger}}{RT}}$$

term related with crossing barrier

Eyring Plot

POC4SOC

$$\ln\left(\frac{k\cdot h}{k_B\cdot T\cdot\left(\mathrm{mol\,dm^{-3}}\right)^{1-n}}\right)=-\frac{\Delta H^{\ominus\neq}}{R\cdot T}+\frac{\Delta S^{\ominus\neq}}{R}$$



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Linear Regression for Data1_B:
Y = A + B * X

Parameter  Value       Error
------------------------------------------------------------
A          -21.53946   0.46944
B          -5.1717     0.15165
------------------------------------------------------------

R          SD          N          P
------------------------------------------------------------
-0.99914   0.04994     4          8.588E-4
------------------------------------------------------------
```

$\Delta H^{\ominus\neq}$ = 42 kJ $\mathrm{mol^{-1}}$

$\Delta S^{\ominus\neq}$ = -179 J $\mathrm{K^{-1}\,mol^{-1}}$

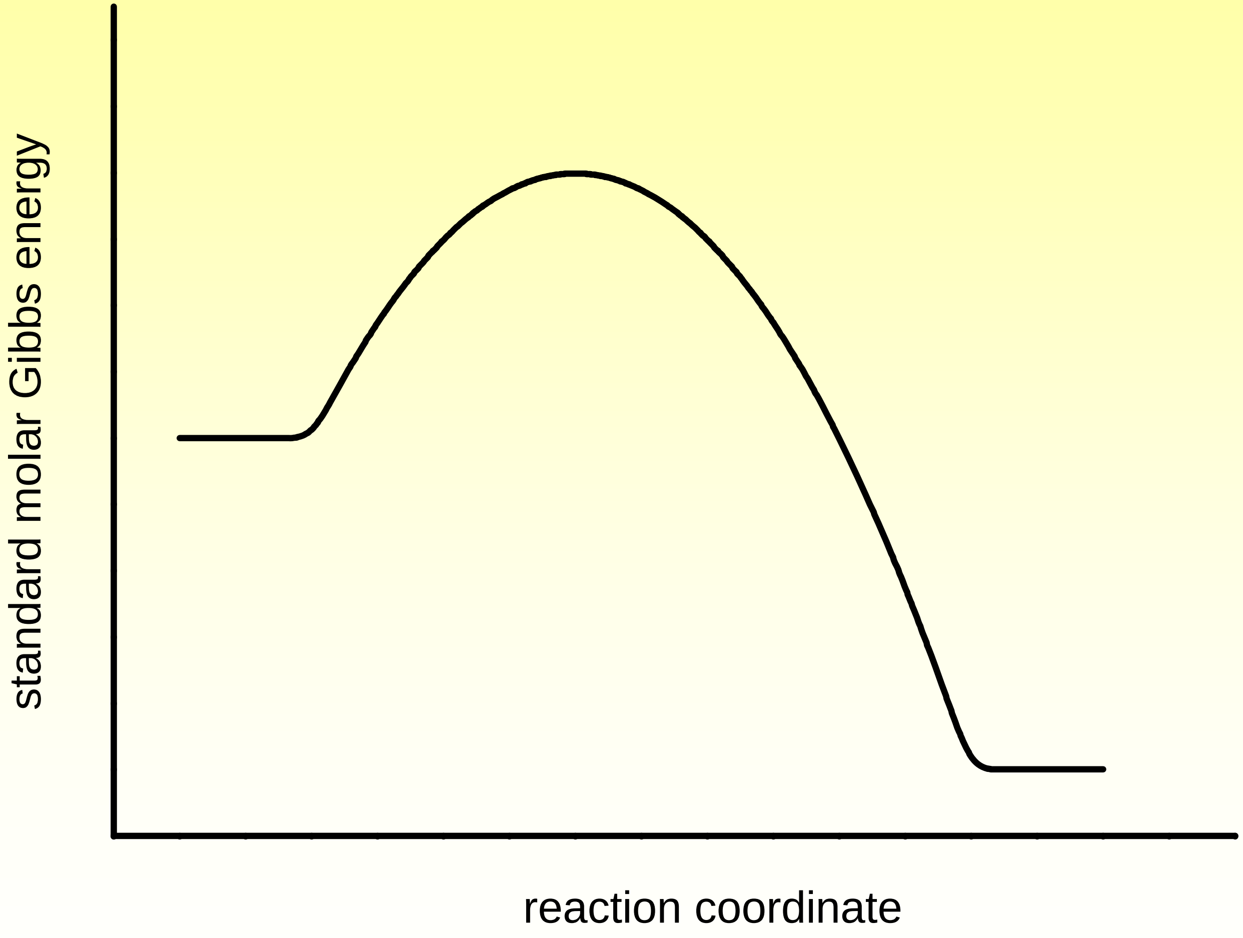
NJB

Activation parameters

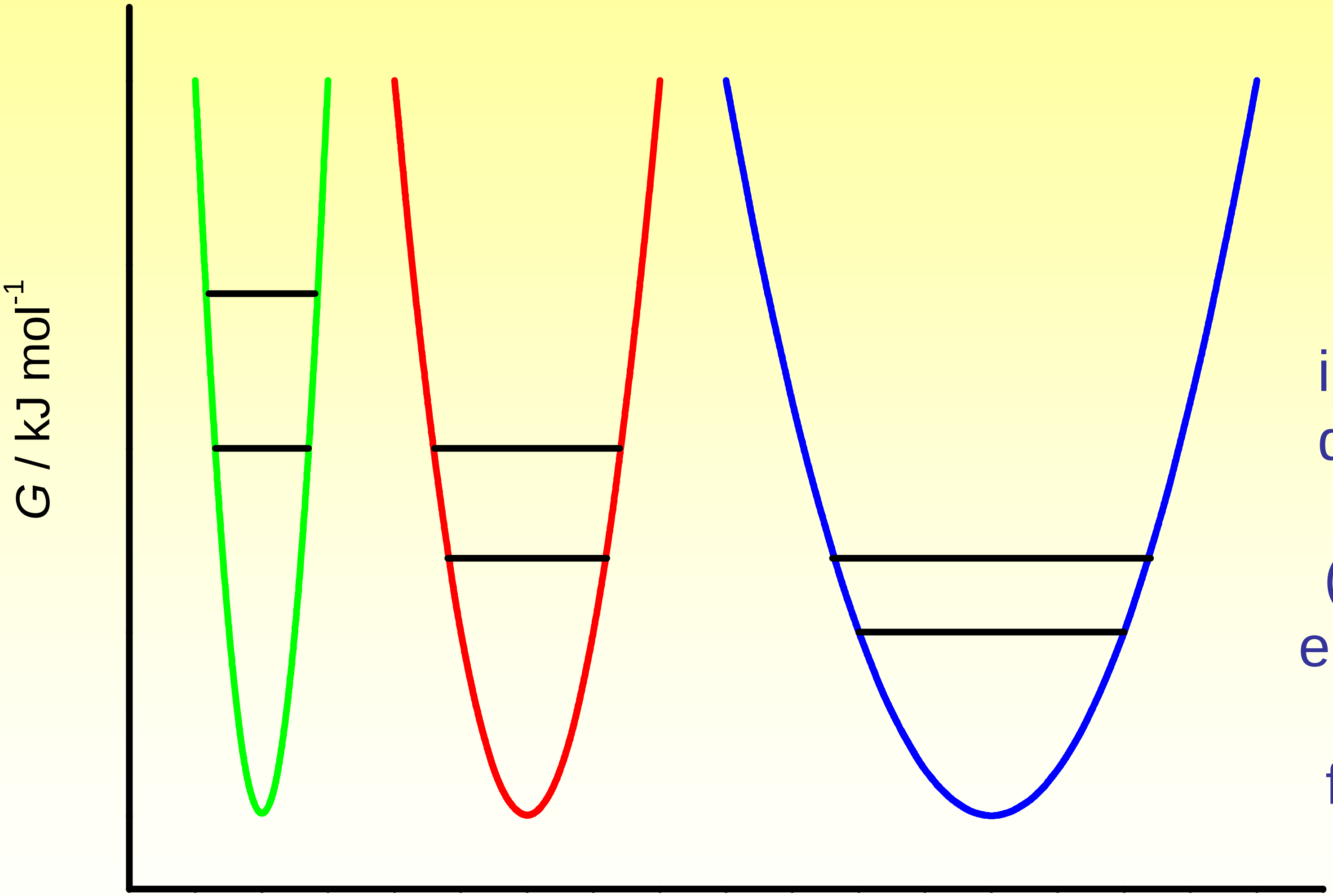
- Use as ‘reality checks’
  - – compare with theoretical estimates (at various levels of “theory”)

Kinetic isotope effects

what is the standard molar Gibbs energy and how can it depend on isotopes?

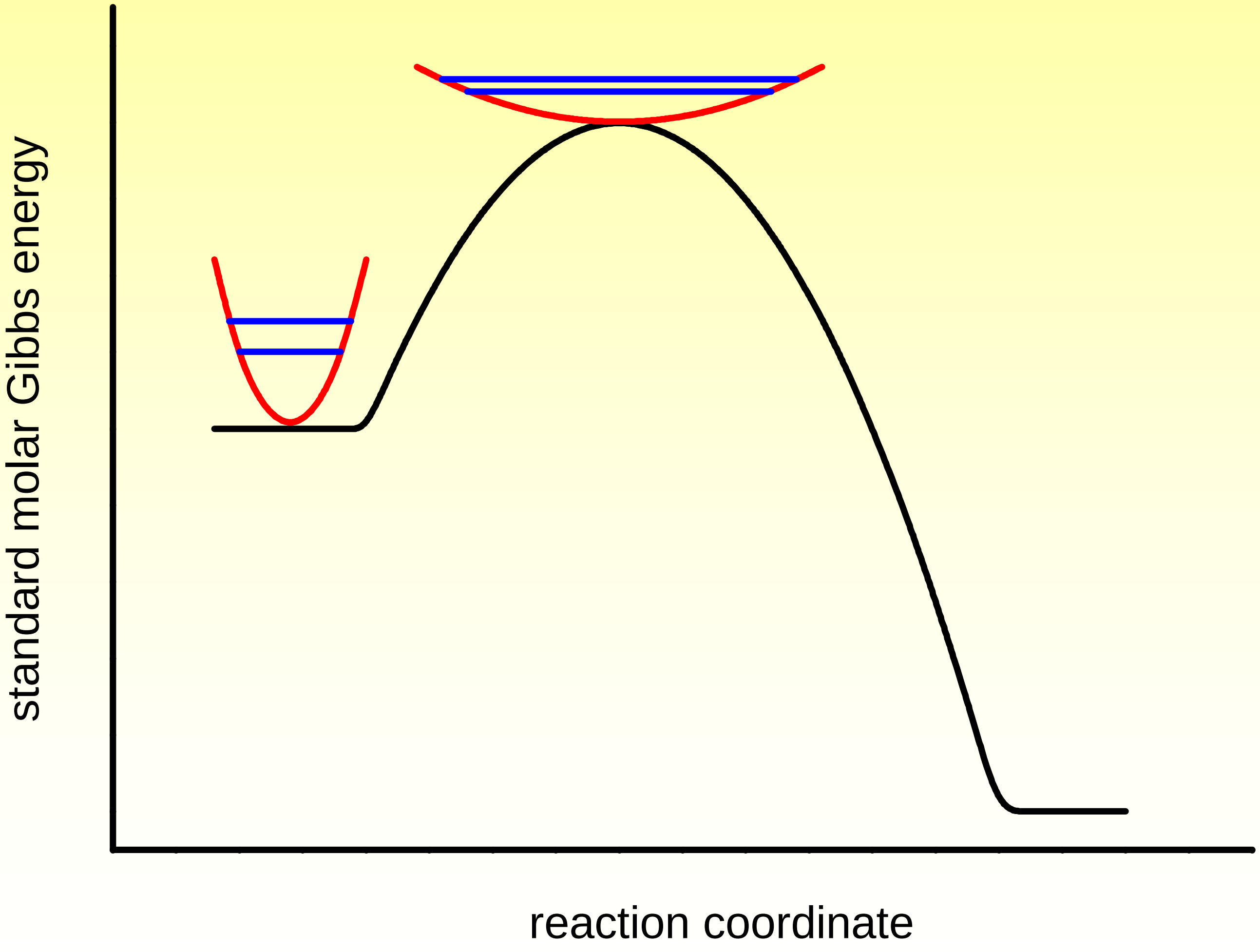


Zero point energy differences



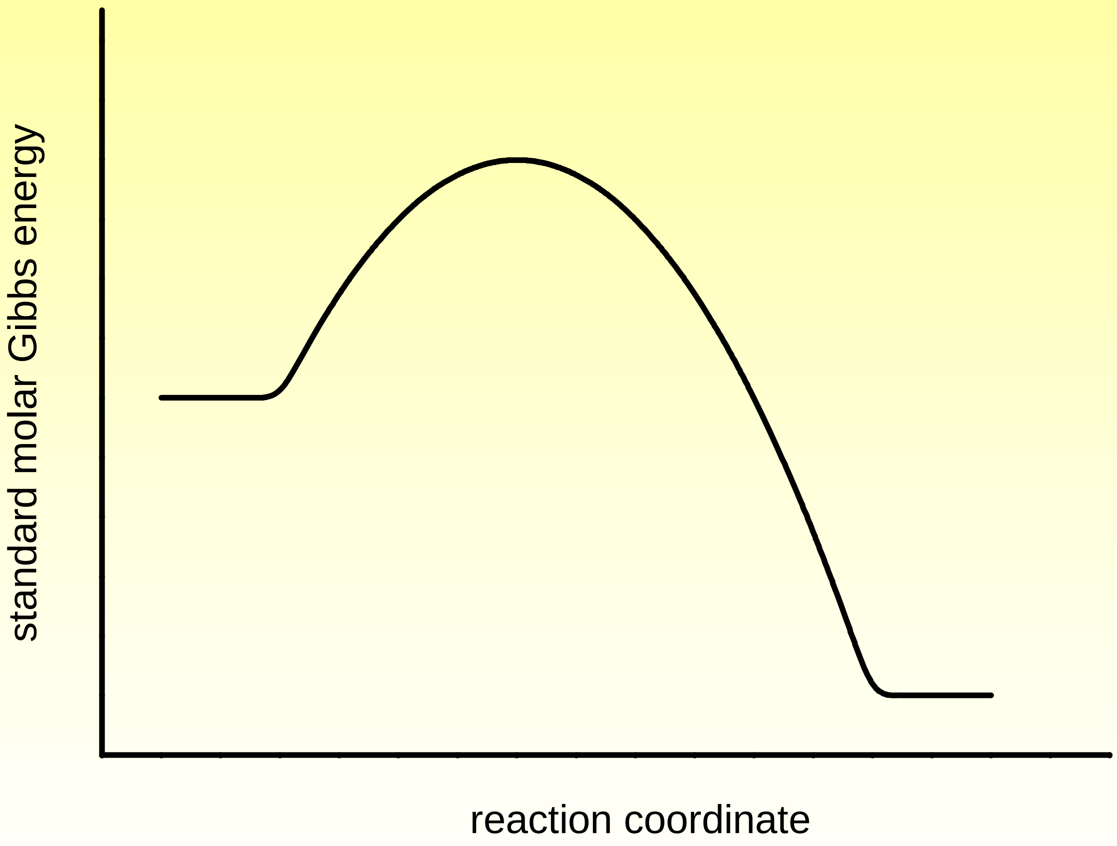
narrow potential wells increase the difference in zero point (vibrational) energy – note link with IR frequencies

Typical KIE


standard molar Gibbs energy
reaction coordinate

- This is fine for single-step reactions, but what if we are studying a multi-step reaction?
- How does one determine the rate-determining step?
- Is the rate-determining step always the rate-determining step?
- How do additional steps affect the observed kinetics?

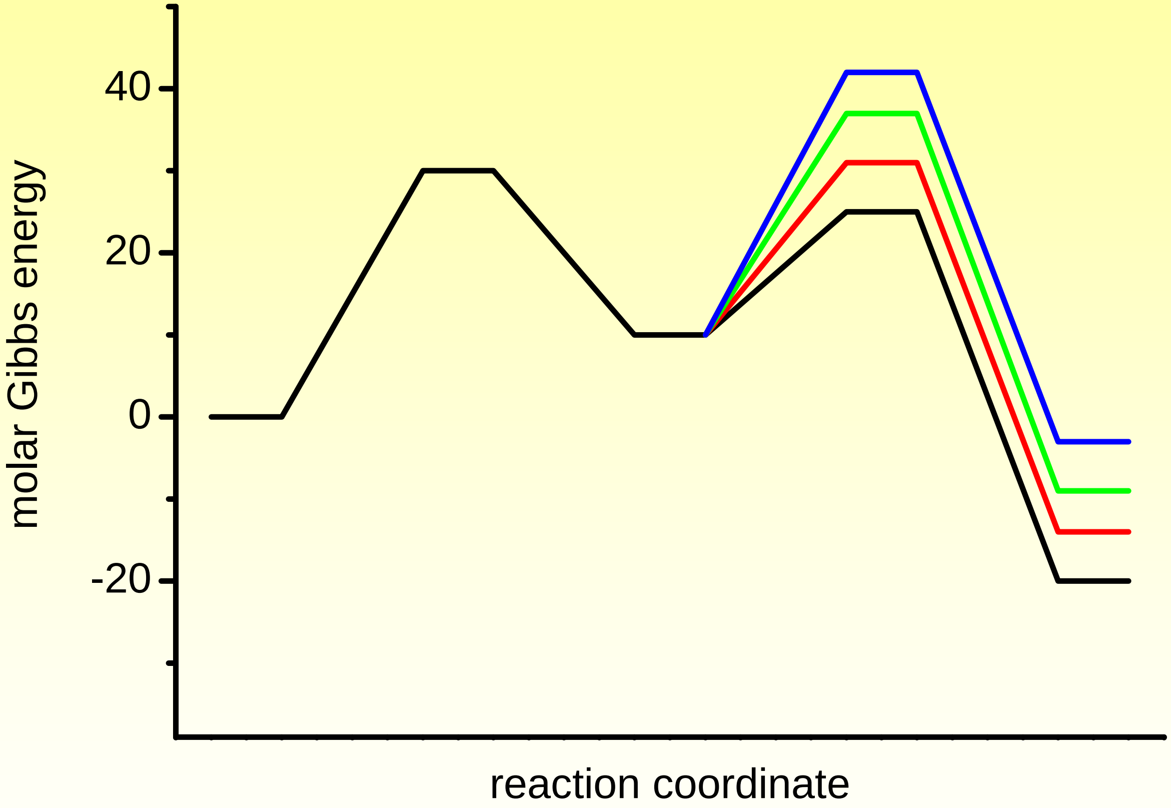
Transition State Theory


standard molar Gibbs energy
reaction coordinate

The standard molar Gibbs energy of activation $\Delta G^{ø\neq}$ is the change in the Gibbs energy of the system associated with the hypothetical formation of 1 mole of activated complex from reactant(s) at constant temperature with all species being in the standard state (normally 1 mol dm^{-3}).

A multistep reaction

A (+B)→TST (+B)→I + B→TST→P

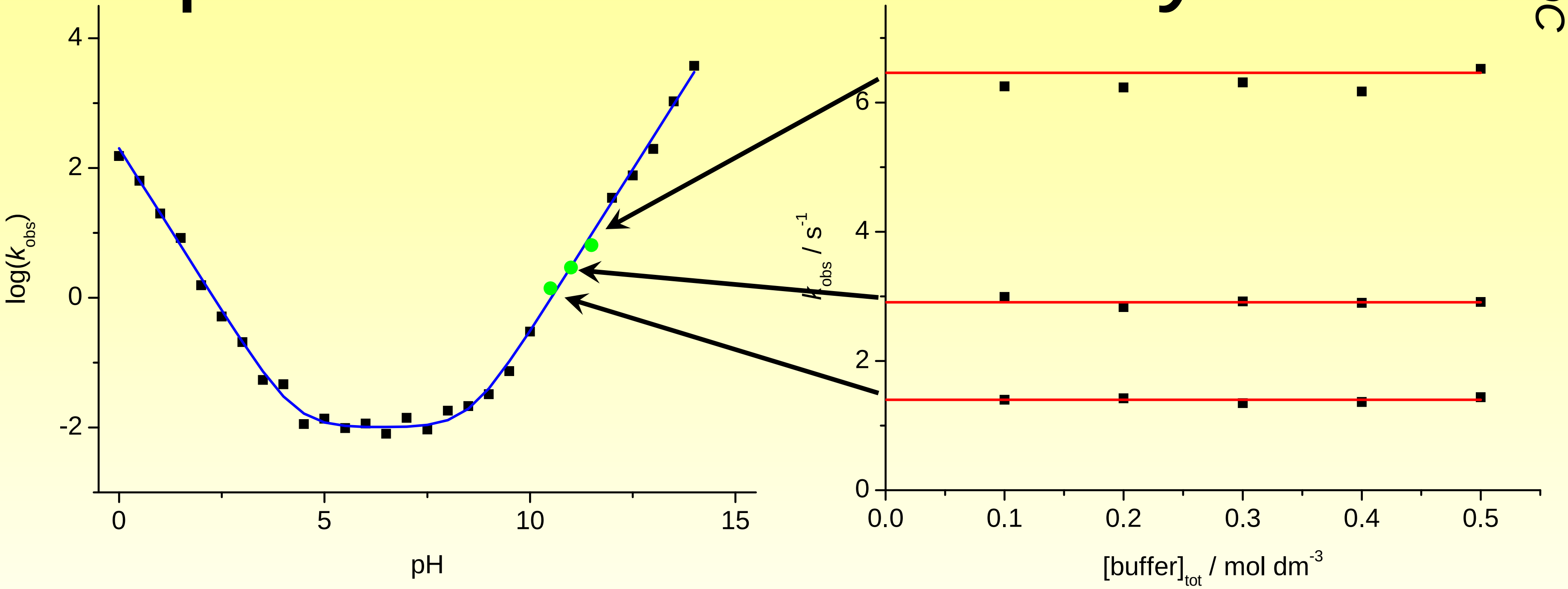


standard state
1 mol dm^{-3}

[B] = 1 mol dm^{-3}
[B] = 0.1 mol dm^{-3}
[B] = 0.01 mol dm^{-3}
[B] = 0.001 mol dm^{-3}

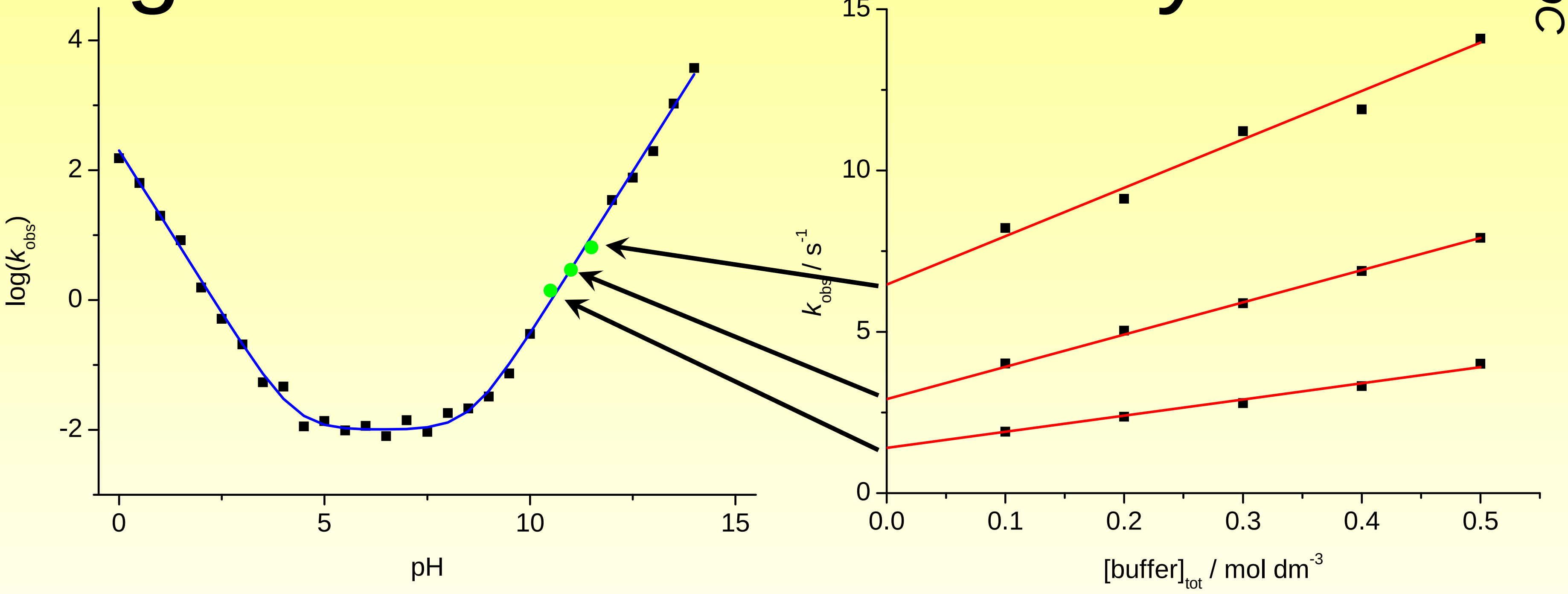
For 2 (or more) consecutive steps, the rds can depend on relative concentrations. At low [B], step 1 becomes an equilibrium

Determining a pH-rate profile – specific acid/base catalysis



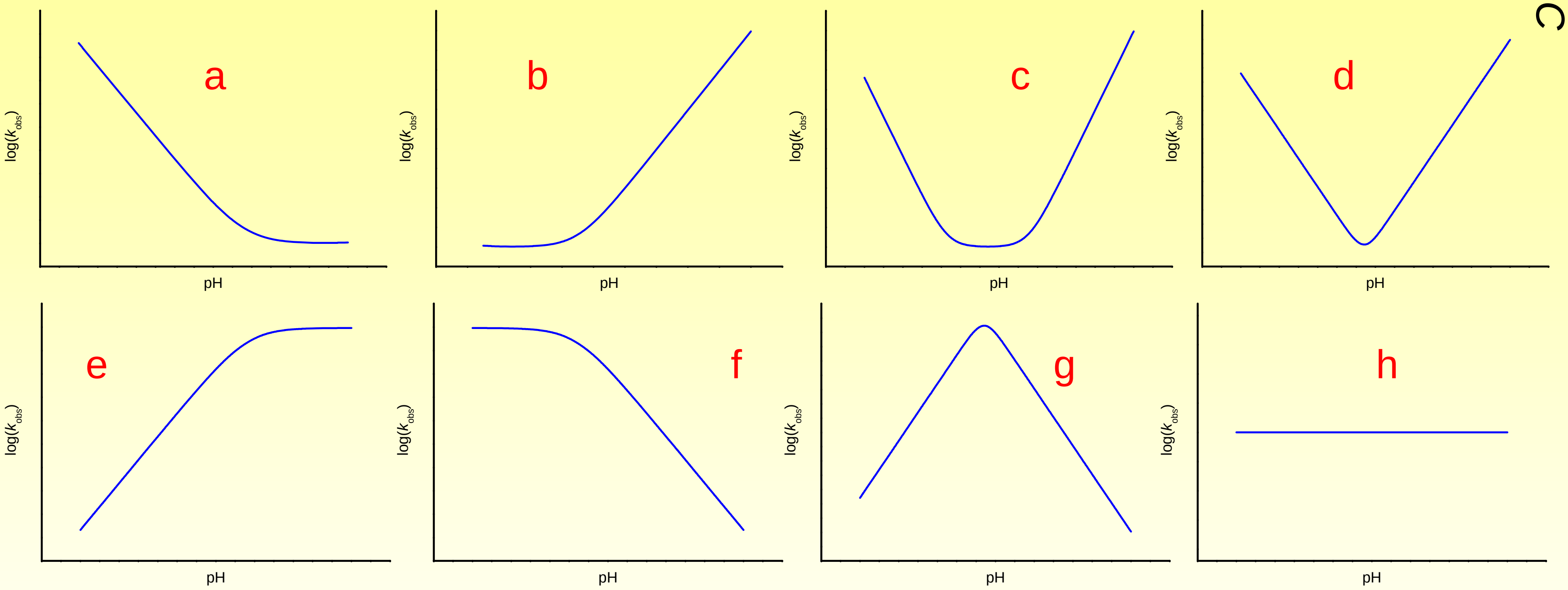
As an alternative to using buffer, effects at high and low pH, where OH^- and H_3O^+ are in large excess (pseudo first order conditions), can sometimes be determined directly using different $[OH^-]$ and $[H_3O^+]$.

Determining a pH-rate profile – general acid/base catalysis



The slopes of k_{obs} vs [buffer]$_{tot}$ give k_{gb} when buffer ratio is corrected for. Alternatively, k_{obs} is plotted as a function of [buffer]$_{basic}$ which should give parallel lines

pH rate profiles



a) acid catalysed and uncatalysed b) base catalysed and uncatalysed c) acid catalysed, uncatalysed and base catalysed d) acid catalysed, and base catalysed e) base catalysed with saturation f) acid catalysed with saturation g) base catalysed and acid catalysed with change in rds h) uncatalysed

catalysis by acids and bases

Specific acid catalysis

$$k_{\mathrm{obs}} = k_{\mathrm{o}} + k_{\mathrm{H_3O^+}} \cdot \left[\mathrm{H_3O^+}\right]$$

General acid (ga) catalysis

$$k_{\mathrm{obs}} = k_{\mathrm{o}} + k_{\mathrm{H_3O^+}} \cdot \left[\mathrm{H_3O^+}\right] + \sum_{\mathrm{i}} k_{\mathrm{ga,i}} \cdot \left[\mathrm{ga_i}\right]$$

Specific base catalysis

$$k_{\mathrm{obs}} = k_{\mathrm{o}} + k_{\mathrm{OH^-}} \cdot \left[\mathrm{OH^-}\right]$$

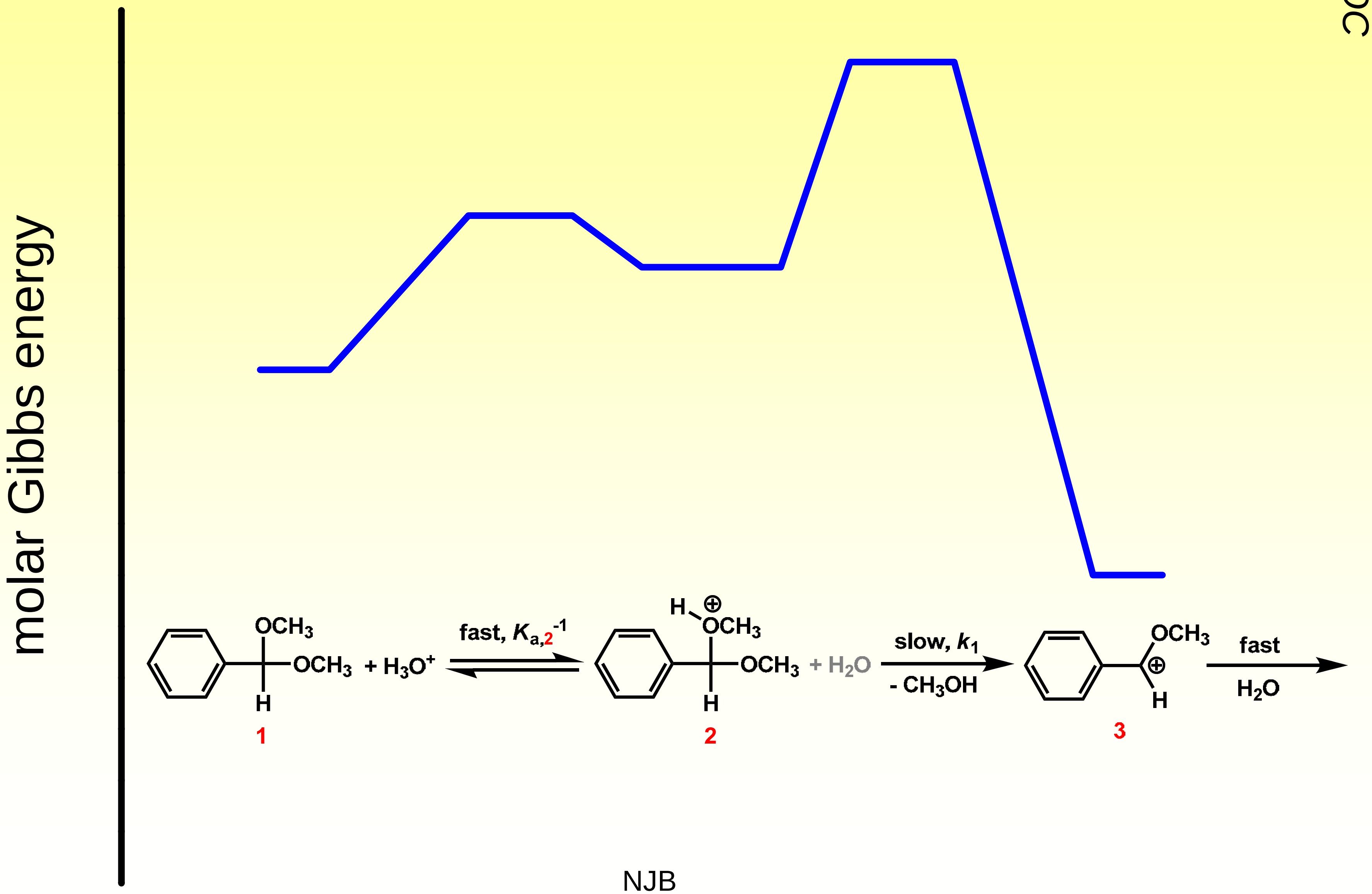
General base (gb) catalysis

$$k_{\mathrm{obs}} = k_{\mathrm{o}} + k_{\mathrm{OH^-}} \cdot \left[\mathrm{OH^-}\right] + \sum_{\mathrm{i}} k_{\mathrm{gb,i}} \cdot \left[\mathrm{gb_i}\right]$$

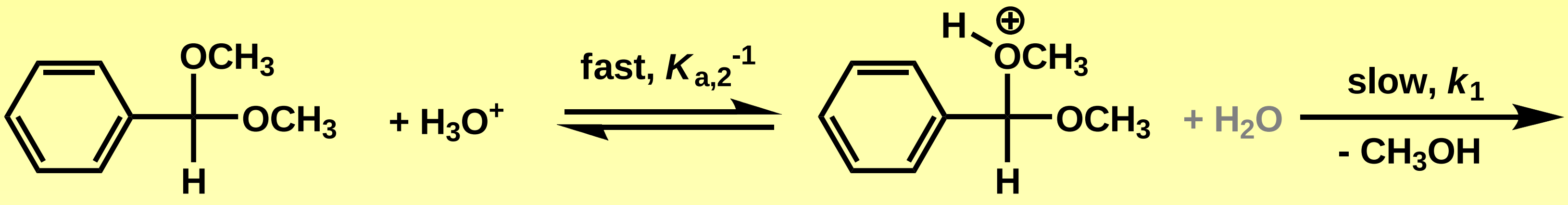
Specific acid catalysis rate law

- Rapid protonation resulting in a pre-equilibrium
- The pre-equilibrium is followed, at some stage, by the rate determining step
- The rate determining step does *not* involve proton transfer
- Deviations from linearity will be found for reactions where increasing extent of protonation (with increasing concentration of acid) leads to saturation, i.e. full protonation of the substrate.

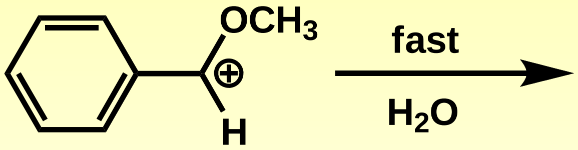
Specific acid catalysis


molar Gibbs energy
OCH_3
OCH_3
H
1
$+ H_3O^+$
fast, $K_{a,2}^{-1}$
H
⊕
OCH_3
OCH_3
H
2
$+ H_2O$
slow, k_1
$- CH_3OH$
OCH_3
⊕
H
3
fast
H_2O

Rapid pre-equilibrium protonation


OCH3
OCH3
H
+ H3O+
fast, Ka,2-1
H
OCH3
OCH3
H
+ H2O
slow, k1
- CH3OH

1 **2**


OCH3
H
fast
H2O

3

$$\frac{\mathrm{d}[\mathrm{P}]}{\mathrm{d}t} = k_1 \cdot [\mathbf{2}]$$

$$[\mathbf{2}] = K_{\mathrm{a},2}^{-1} \cdot [\mathbf{1}] \cdot \left[\mathrm{H_3O^+}\right]$$

These equations are true even for protonation reaching saturation. However, for such systems, the rate law is better expressed in terms of a total reactant concentration of [**1**]+[**2**].

$$\frac{\mathrm{d}[\mathrm{P}]}{\mathrm{d}t} = k_1 \cdot K_{\mathrm{a},2}^{-1} \cdot [\mathbf{1}] \cdot \left[\mathrm{H_3O^+}\right] = k_{\mathrm{obs}} \cdot [\mathbf{1}] \cdot \left[\mathrm{H_3O^+}\right]$$

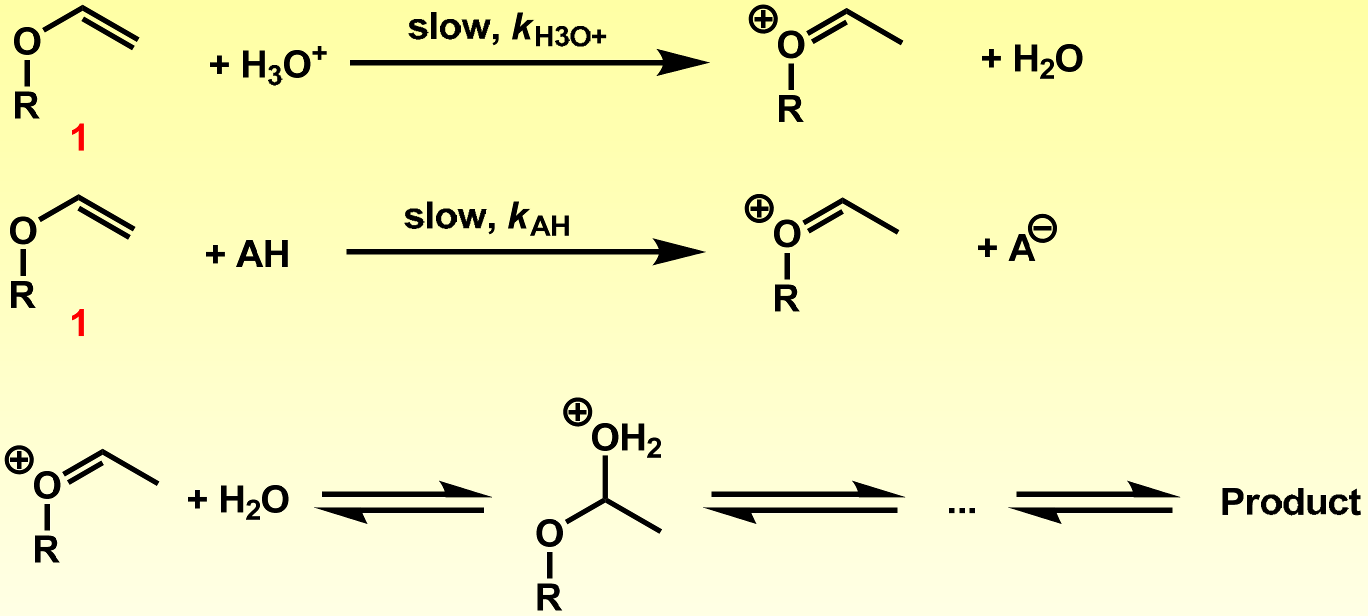
Rapid protonation vs catalysis

- Kinetic models analogous to specific acid catalysis are used for all reactions involving a rapid equilibrium preceding the rds
  - e.g. other catalytic species
- k_{obs} contains "contributions" of all steps up to and including the rds

General acid catalysis

- Mechanisms giving rise to general acid catalysis:
  - Rate determining proton transfer
  - Rapid protonation of the substrate in a pre-equilibrium followed by rate determining deprotonation at a different site by any base
  - Rate determining acid assisted nucleophilic attack

Rate determining proton transfer


O
R
1
+ H3O+
slow, kH3O+
⊕
O
R
+ H2O
O
R
1
+ AH
slow, kAH
⊕
O
R
+ A⊖
⊕
O
R
+ H2O
⊕
OH2
O
R
...
Product

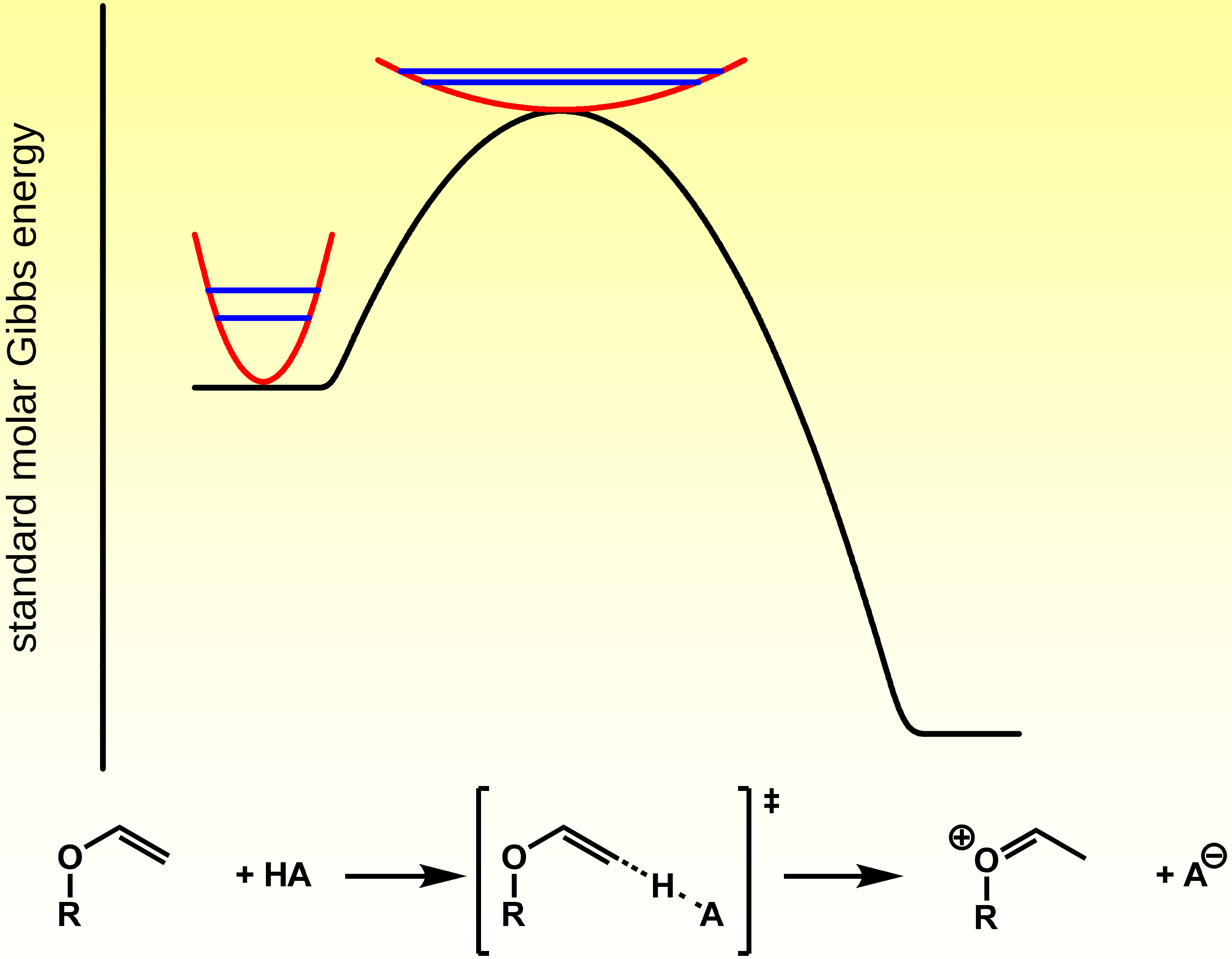
$$\frac{\mathrm{d}[\mathrm{P}]}{\mathrm{d}t} = k_{\mathrm{obs}} \cdot [\mathbf{1}] = \left\{ k_{\mathrm{H_3O^+}} \cdot \left[\mathrm{H_3O^+}\right] + k_{\mathrm{AH}} \cdot [\mathrm{AH}] \right\} \cdot [\mathbf{1}]$$

$$k_{\mathrm{obs}} = 2.08 \cdot \left[\mathrm{H_3O^+}\right] + 1.78 \cdot 10^{-3} \cdot [\mathrm{CH_3CO_2H}]$$

J. Chem. Soc. B, **1967**, 53-57

rate-determining H-transfer & KIE

POC4SOC


standard molar Gibbs energy
O
R
+ HA
O
R
H
A
‡
⊕
O
R
+ A⊖

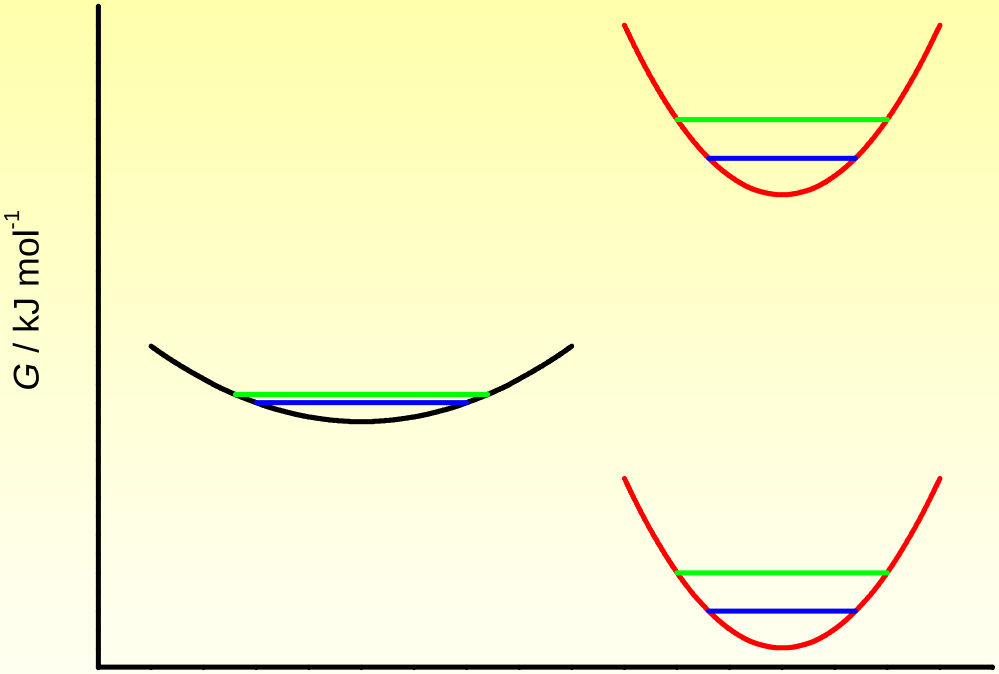
NJB

Solvent kinetic isotope effects

“D_3O^+ is a stronger acid than H_3O^+ because the O-H bond in H_3O^+ is the *floppiest* heavy-atom-to-proton bond in H_2O-solutions and the same is true for D_3O^+ in D_2O-solutions. This means that the isotope effect on all other heavy-atom-to-proton bonds is larger than that on the O-H and O-D bonds in H_3O^+ and D_3O^+, respectively. As a result, for protonation, equilibria in D_2O (for identical strong acid concentration, i.e. when pD=pH) lie further towards protonated substrate: $pK_a(D_2O) > pK_a(H_2O)$”

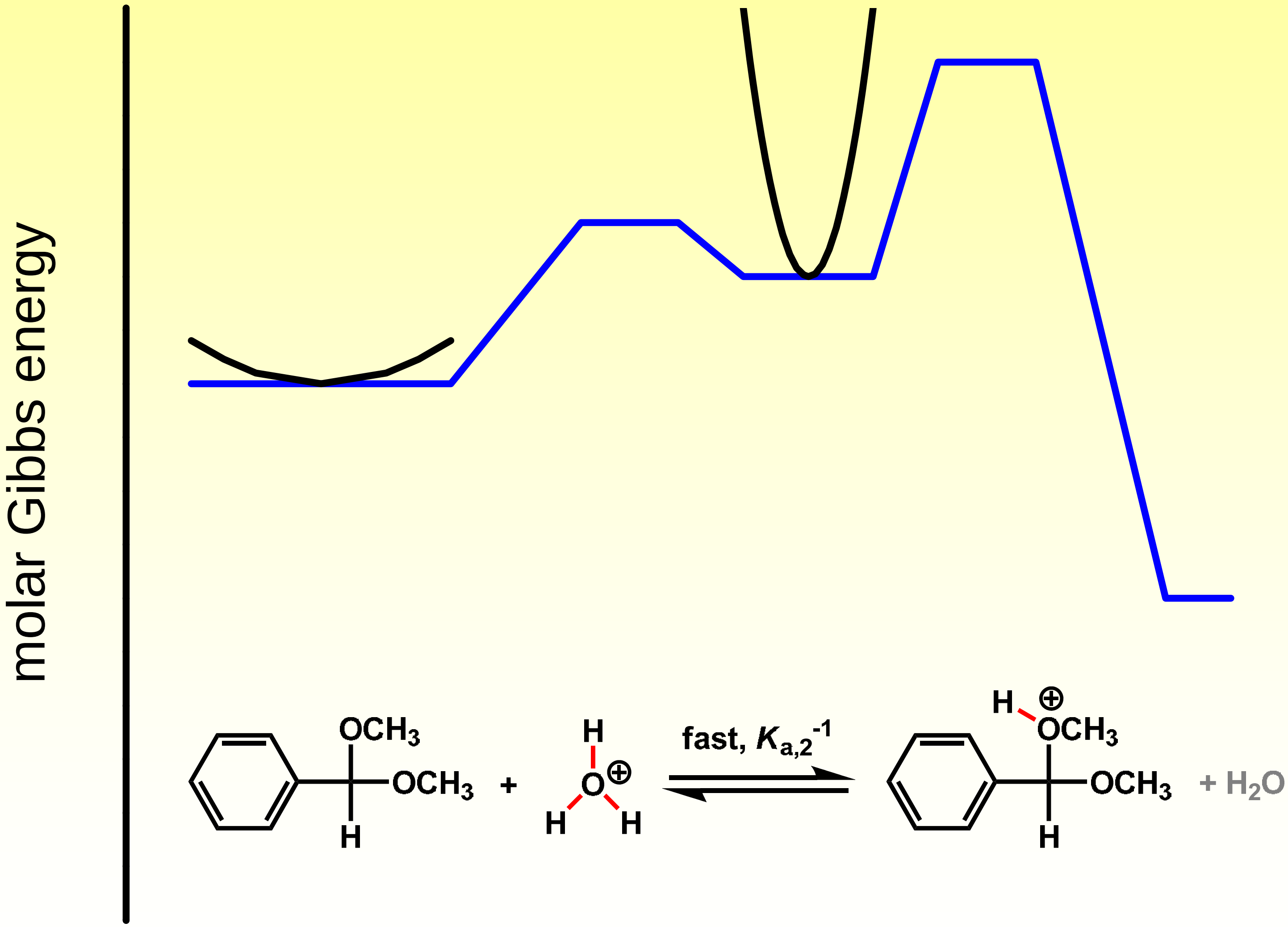
Solvent kinetic isotope effects

Empirically, potential wells for X-L bonds are *typically* narrower than the potential well for the O-L bond in L_3O^+



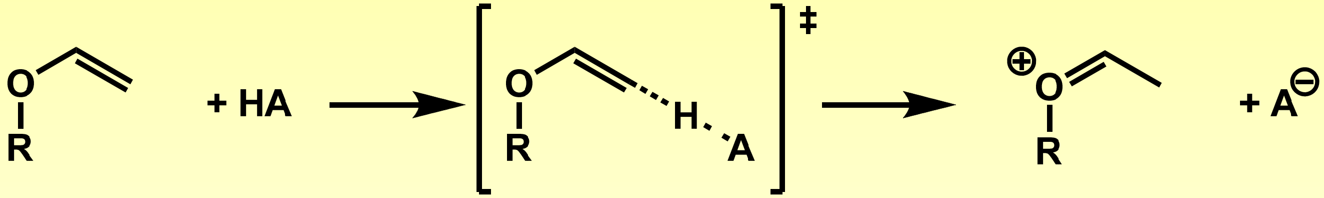
This contradicts intuition which suggests that potential wells should be narrower for stronger (bond energy) bonds.

SKIE and specific acid catalysis


molar Gibbs energy
OCH3
OCH3
H
+
H
O⊕
H
H
fast, Ka,2-1
H
⊕
OCH3
OCH3
H
+ H2O

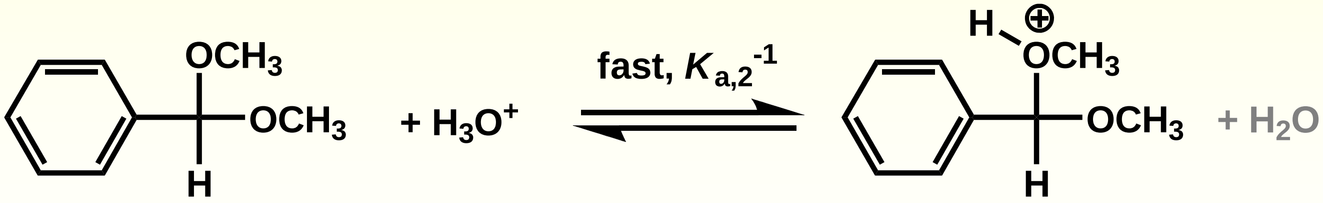
Solvent kinetic isotope effects

- In the case of general acid and general base catalysis, proton transfer in the rds is accompanied by a normal isotope effect: $k_{H2O}>k_{D2O}$.


O
R
+ HA
O
R
H
A
‡
⊕
O
R
+ A⊖

SKIE k_{H2O}/k_{D2O} = 2.95, H_3O^+ as general acid (*J.Chem.Soc.B*, **1967**,53-57)

- In specific acid and base catalysis, the proton transfer step is not the rds; one needs to know the effect of isotopic exchange on equilibrium constants.


OCH3
OCH3
H
+ H3O+
fast, Ka,2-1
H
⊕
OCH3
OCH3
H
+ H2O

1 **2**

SKIE k_{D2O}/k_{H2O} ~ 3 (*Chem.Rev*., **74**, 581-603)

Summary

- Eyring plot yields activation parameters; support (or not) proposed mechanisms
- Kinetic isotope effects provide information on rds and/or equilibrium protonation
- The rds of a reaction can depend on conditions

- Many of these aspects may seem difficult to take into account when designing experiment. In fact, one often gets things “wrong” the first (and second …) time around; this is why POC typically involves a series of experiments to check mechanistic predictions and often involves an “evolution” of a mechanistic description with increasing availability of data.