Transition State Theory

(Teorie aktivovaného komplexu)

- lecture 8 -

Eyring's derivation:
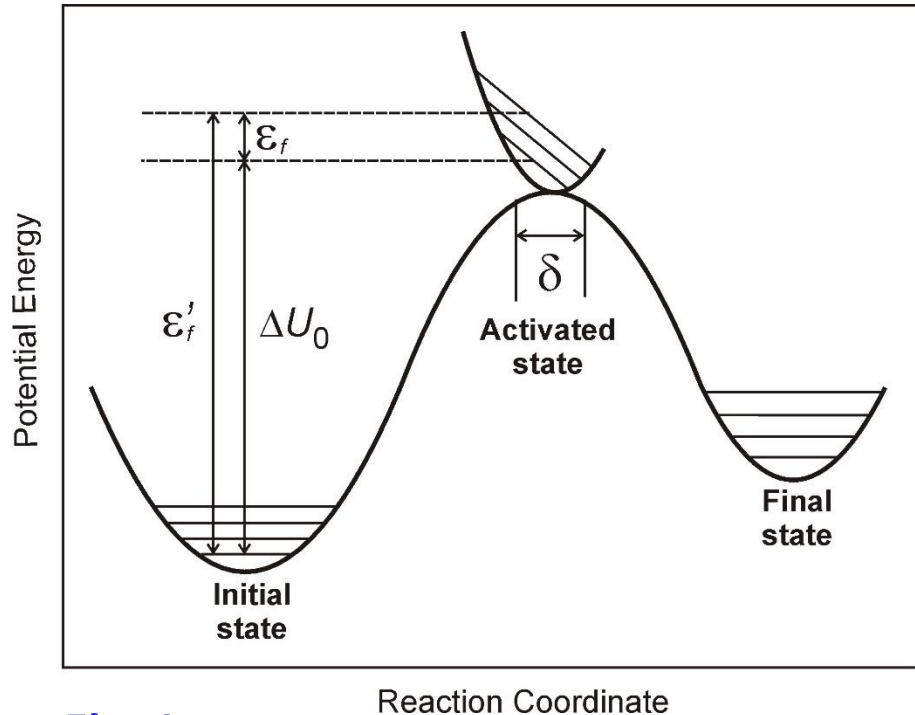

Fig. 1

δ – length representing the activated state at the top of the barrier

[TS] – is the number of activated complexes per unit volume lying in the length δ of reaction coordinate – concentration of "Transition State"

$v°$ – mean velocity of crossing towards products

$v° = (k_B T/2\pi m_{rc})^{1/2}$

(Maxwell-Boltzmann distribution used)

whit m_{rc} as the effective mass of the complex

in the coordinate of reaction

$\tau = \delta/v°$ – the average time of crossing the barrier

$v = 1/\tau = v°/\delta$ – the frequency at which activated complexes pass over the barrier

Concentrations of reactants

Rate of reaction = **k[A]…** = $v \times$ **[TS]** = $(k_B T/2\pi m_{rc})^{1/2}/\delta \times$ **[TS]**

➔ $$k = \frac{[TS]}{[A]…} (k_B T/2\pi m_{rc})^{1/2}/\delta$$ eq. 1

…and since $\boxed{K = \dfrac{[TS]}{[A]\ldots} = \dfrac{Q^{\circ}_{TS}}{Q^{\circ}_{A}\ldots}}$ eq. 2

where K is the equilibrium constant

and $Q^{\circ}_{(TS/A)}$ is the complete partition function (of the activated state/reactant) for unit volume:

$$\boxed{Q^{\circ}_f = \sum_f g_f\, e^{-\varepsilon'_f/k_B T} \;=\; e^{-\Delta U_0/k_B T} \sum_f g_f\, e^{-\varepsilon_f/k_B T} \;=\; Q_f\, e^{-\Delta U_0/k_B T}}$$ eq. 3

with ΔU_0, ε'_f and ε_f defined in **Fig. 1**

Combining eqs. 2 and 3:

$$K = \frac{Q_{TS}}{Q_A\ldots}\, e^{-\Delta U_0/k_B T}$$

eq. 4 ➜

Combining eqs. 2 and 4:

$$k = \frac{Q_{TS}}{Q_A\ldots}\, (k_B T/2\pi m_{rc})^{1/2}/\delta\;\; e^{-\Delta U_0/k_B T}$$ eq. 5

Instead of using Q_{TS}, it is convenient to use a new partition function, $Q^{\neq}_{TS}$, which does not include the contribution $q_{trans,TS}$ due to translational motion in the one degree of freedom along the reaction coordinate:

$$\boxed{Q_{TS} = q_{trans,TS} \times Q^{\neq}_{TS}}$$ eq. 6

with $q_{trans,TS} = (2\pi m_{rc} k_B T)^{1/2}/h \times \delta$

here, a length, δ, can be also considered as a volume in one dimension.

Thus: The combination of eqs. 5 and 6 gives:

$$k = \frac{k_B T}{h}\, \frac{Q^{\neq}_{TS}}{Q_A\ldots}\; e^{-\Delta U_0/k_B T}$$ eq. 7

It is known from lecture 5 :

$$\Delta G_{(in\ solution)} = \Delta E_{elec} + \Delta ZPVE + (\Delta E_{solv}) - \Delta RT \ln Q$$

$$= \Delta U_{0,gp} + (\Delta E_{solv}) - \Delta RT \ln Q = \Delta U_0 - \Delta(RT \ln Q)$$
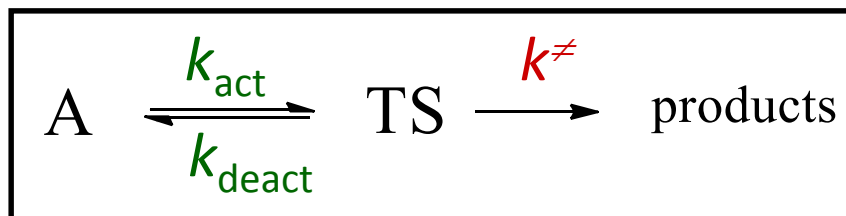
"internal energy of solute at 0K"

➔ $$e^{-\Delta G^{\neq}/RT} = e^{-\Delta U_0^{\neq}/RT}\ \frac{Q^{\neq}}{Q_A}$$ eq. 8

The combination of eqs. 7 and 8 gives:

! $$k = \frac{k_B T}{h} e^{-\Delta G^{\neq}/RT}$$ eq. 9

Alternative derivation I   **Consider the simple unimolecular reaction:**

$$A \underset{k_{\text{deact}}}{\overset{k_{\text{act}}}{\rightleftharpoons}} TS \overset{k^{\neq}}{\longrightarrow} \text{products}$$

$$v_{\text{react}} = k_{\text{react}}[A] = v^{\neq}[TS] \rightarrow \boxed{k_{\text{react}} = k^{\neq} K^{\neq}} \quad \text{eq. 1a}$$

where:

$$K^{\neq} = \frac{k_{\text{act}}}{k_{\text{deact}}} = \frac{[TS]}{[A]} = \boxed{e^{-(G_{TS}-G_A)/k_B T}} \quad \text{eq. 2a}$$

Since:

$$G = U_0 + PV - k_B T \ln Q \quad \text{eq. 3a} \ \left(\text{where } U_0 = E_{elec} + \frac{1}{2}\sum_i^{\text{modes}} h\nu_i\right)$$

Then, combination of eq. 2a and 3a gives:

$$K^{\neq} = \frac{Q_{TS}}{Q_A} e^{-(U_{TS,0}-U_{A,0})/k_B T} e^{-(PV_{TS}-PV_A)/k_B T} \approx \frac{Q_{TS}}{Q_A} e^{-(U_{TS,0}-U_{A,0})/k_B T} \quad \text{eq. 4a}$$

Insertion of eq. 4a into eq. 1a gives :

$$k_{\text{react}} = k^{\neq} \frac{Q_{TS}}{Q_A} e^{-(U_{TS,0}-U_{A,0})/k_B T} \quad \text{eq. 5a}$$

Reactant:

3N-6 vibrational degrees of freedom

Transition State:

3N-7 vibrational degrees of freedom => one 'lost' degree is **the reaction coordinate**

Partition function for the TS in the **3N-7** vibrational space ($Q^{\neq}$) can be obtained after a separation of the vibrational partition function for the reaction-coordinate degree of freedom (q_{rc}) from Q_{TS} (from eq. 5a):

$$Q_{TS} = q_{rc}Q^{\neq} = \frac{1}{1 - e^{-h\nu^{\neq}/k_B T}}Q^{\neq} \approx \frac{k_B T}{h\nu^{\neq}}Q^{\neq} \quad \text{eq. 6a}$$

Then, insertion of eq. 6a into eq. 5a gives:

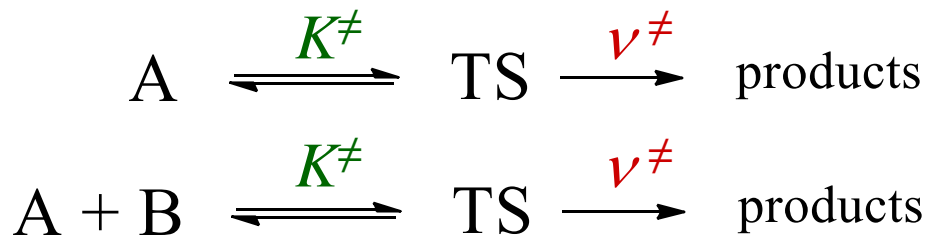$$k_{react} = \frac{k^{\neq}k_B T}{h\nu^{\neq}}\frac{Q^{\neq}}{Q_A}e^{-(U_{TS,0}-U_{A,0})/k_B T} \quad \text{eq. 7a}$$

and since $k^{\neq} = \nu^{\neq}$ (frequency of a reactive mode leading to the formation of products):

$$\boxed{k_{react} = \frac{k_B T}{h}\frac{Q^{\neq}}{Q_A}e^{-(U_{TS,0}-U_{A,0})/k_B T}} \quad \text{eq. 8a}$$

Eqs. 7 and 8a are identical, thus considering eq. 8, one ends up with Eyring equation again.

Eyring equation
Alternative derivation II

$$A \xrightleftharpoons{K^{\neq}} TS \xrightarrow{\nu^{\neq}} products$$

$$A + B \xrightleftharpoons{K^{\neq}} TS \xrightarrow{\nu^{\neq}} products$$

A, B – reactants
TS – transition state
$K^{\neq}$ – equilibrium between TS and reactant(s)
$\nu^{\neq}$ – frequency of a reactive mode leading to the formation of products

rate constant of elementary reaction:

$$k = \nu^{\neq} K^{\neq}$$

since $\Delta G^{\neq} = -RT\ln K^{\neq}$: $k = \nu^{\neq} e^{-\Delta G^{\neq}/RT}$

Postulated : *energy of a reactive mode equals to the averaged energy of one vibrational degree of freedom given by equipartition theorem:*

$$\tfrac{1}{2}h\,\nu^{\neq} = \tfrac{1}{2}k_B T$$

k_B – Boltzmann constant
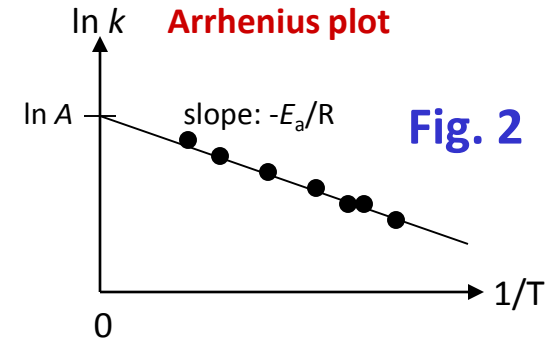
h – Planck constant

T – temperature

$$k = \frac{k_B T}{h} e^{-\Delta G^{\neq}/RT} \qquad \text{eq. 10}$$

$$= \frac{k_B T}{h} e^{-\Delta H^{\neq}/RT} e^{\Delta S^{\neq}/R}$$
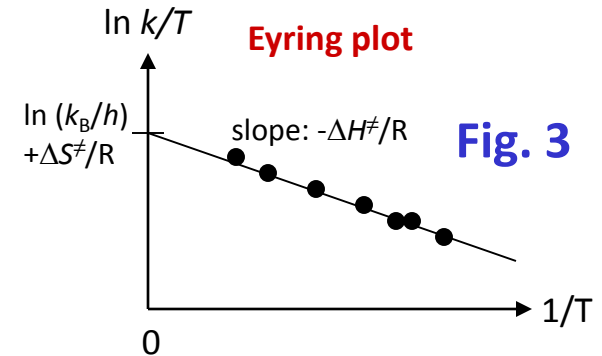
-Arrhenius *versus* Eyring equation-

Phenomenological **Arrhenius** equation:

$$k = A\, e^{-E_a/RT} \;\rightarrow\; \boxed{\ln k = -\frac{E_a}{R}\frac{1}{T} + \ln A}\;\; \text{eq. 11}$$

$\ln k$ **Arrhenius plot**

$\ln A$ slope: $-E_a/R$ **Fig. 2**

$1/T$

0

Standard **Eyring** equation:

$$k = \frac{k_B T}{h}\, e^{-\Delta H^{\neq}/RT}\, e^{\Delta S^{\neq}/R} \;\rightarrow$$

$$\boxed{\ln k/T = -\frac{\Delta H^{\neq}}{R}\frac{1}{T} + \frac{\Delta S^{\neq}}{R} + \ln(k_B/h)}\;\; \text{eq. 12}$$

$\ln k/T$ **Eyring plot**

$\ln(k_B/h)$
$+\Delta S^{\neq}/R$ slope: $-\Delta H^{\neq}/R$ **Fig. 3**

$1/T$

0

Relationship between **Arrhenius** and **Eyring** parameters

Arrhenius activation energy E_a is defined:
(**analogy to the van't Hoff equation**)

$$E_a = RT^2\,\frac{d(\ln k)}{dT}\;\; \text{eq. 13}$$

Insertion of eq. 10 into eq. 13 gives:

$$E_a = RT + RT^2\,\frac{d(\ln K^{\neq})}{dT} = \boxed{RT + \Delta H^{\neq} = E_a}\;\; \text{eq. 14}$$

Considering eq. 14 + comparing Arrhenius and Eyring equations gives:

$$\boxed{e^1 k_B T/h\, e^{\Delta S^{\neq}/R} = A}\;\; \text{eq. 15}$$

Limitations and assumptions of Eyring's transition state theory:

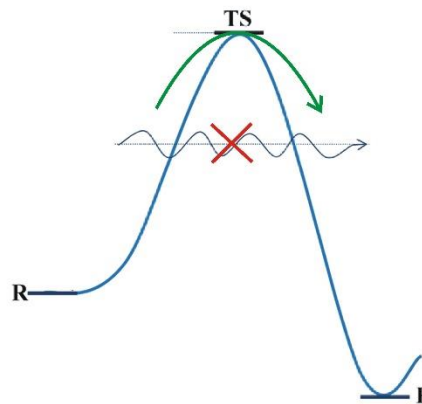1. **No recrossing** considered

→ **Recrossing dynamics:**
   some trajectories reaching the top of the barrier return back to the reactant state,
   thus $k_{\text{recrossing-corrected}} \leq k_{\text{Eyring}}$

→ **No-recrossing condition:**
   "one-dimensional" motion normal to the TS (reaction mode) is separable from the tangent to the TS (bath modes)

2. **No tunneling** through the barrier considered

3. Assumption that the reaction system will pass over
   the lowest first-order saddle point on the potential energy system

4. Assumption of long-lived intermediates along a reaction coordinate
   (Boltzmann distribution of energies before continuing to the next step)

Correction to the Eyring equation:

Tunneling through the barrier (τ_{tunnel})

$$k_{corrected} = \tau_{tunnel}\, k_{Eyring} = \tau_{tunnel}\, \frac{k_B T}{h}\, e^{-\Delta G^{\ddagger}/RT}$$ eq. 16

tunneling factor: $\tau_{tunnel} \geq 1$

'one-dimensional' approximations for the tunneling:

(i) Wigner tunneling factor: $\tau_{Wigner} = 1 + \frac{1}{24}\left(h\,|\nu^{\ddagger}|\,/k_B T\right)^2$ eq. 17

where $|\nu^{\ddagger}|$ is the magnitude of imaginary frequency of a reaction mode at TS

→ This correction for tunneling assumes a parabolic potential for the nuclear motion near the transition state

→ $|\nu^{\ddagger}|$ reflects a curvature of the potential (Hessian) at the top of the barrier and correlates with the thickness of the barrier. A larger $|\nu^{\ddagger}|$ reflects a larger curvature at TS and this implies steeper, narrower barrier, thus, higher probability for tunneling, i.e., a larger τ_{tunnel} factor.

…Crude approximation

(ii) Bell tunneling factor
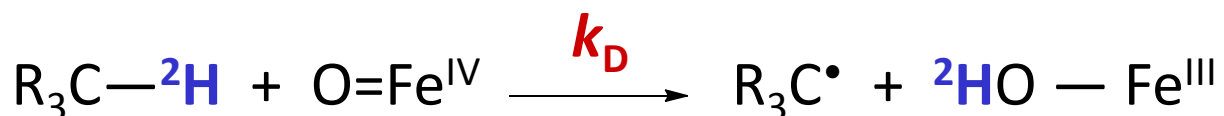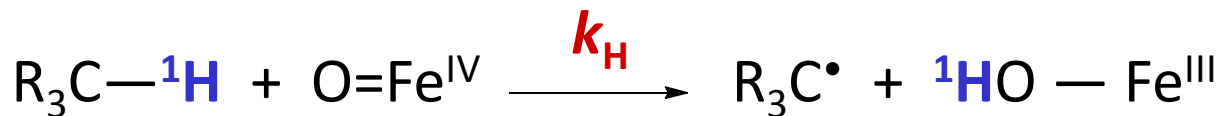
(iii) Eckart tunneling factor:

→ TheRate program

The Eckart method fits the Eckart barrier function to the computed barrier along the intrinsic reaction coordinate **(IRC)**, in mass weighted coordinates, using energies of the reactants, product and transition state. The transmission coefficient, τ, due to tunneling is calculated by integration of the barrier "penetration" probability as a function of the energy.

The effect of τ on the barrier is calculated: $\Delta\Delta E_{tun} = -RT \ln(\tau)$

IRC – mass-weighted steepest descent path on the potential energy surface (PES), starting from the transition structure (TS), that is, first-order saddle point.

Kinetic Isotope effects (KIE)

Example of primary KIE:

$$R_3C—{}^1H \ + \ O=Fe^{IV} \ \xrightarrow{\ \textit{k}_H\ } \ R_3C^\bullet \ + \ {}^1HO—Fe^{III}$$

$$R_3C—{}^2H \ + \ O=Fe^{IV} \ \xrightarrow{\ \textit{k}_D\ } \ R_3C^\bullet \ + \ {}^2HO—Fe^{III}$$

$$KIE = \frac{k_H}{k_D} = \frac{k_{Light\ Isotope}}{k_{Heavy\ Isotope}}$$

eq. 18

In terms of Eyring's TST, combining eqs. 18 and 10 :

$$KIE_{Eyring} = \frac{e^{-\Delta G^{\neq}_H/RT}}{e^{-\Delta G^{\neq}_D/RT}} = e^{(\Delta G^{\neq}_D - \Delta G^{\neq}_H)/RT} = \underbrace{e^{\Delta\Delta H^{\neq}_{D-H}/RT}}_{\approx\ e^{\Delta\Delta(ZPE)^{\neq}_{D-H}}} \underbrace{e^{-\Delta\Delta S^{\neq}_{D-H}/R}}_{\approx\ 0}$$

eq. 19

Tunneling-corrected KIE (derived from eq. 16) :

$$KIE = \frac{\tau_H}{\tau_D} \, e^{(\Delta G^{\neq}_D - \Delta G^{\neq}_H)/RT}$$

eq. 20

$KIE_{observed} > 5$ indicates a significant role of the tunneling effect, i.e., rate-determinig step (in a multistep reaction) involves a transfer of a light particle (e.g., H-atom abstraction)

Experimental detection of tunneling:

→ **Large KIE**

e.g.: **taurine dioxygenase (TauD)**

KIE = 35

Prolyl-4-hydroxylase (P4H)

KIE = 60
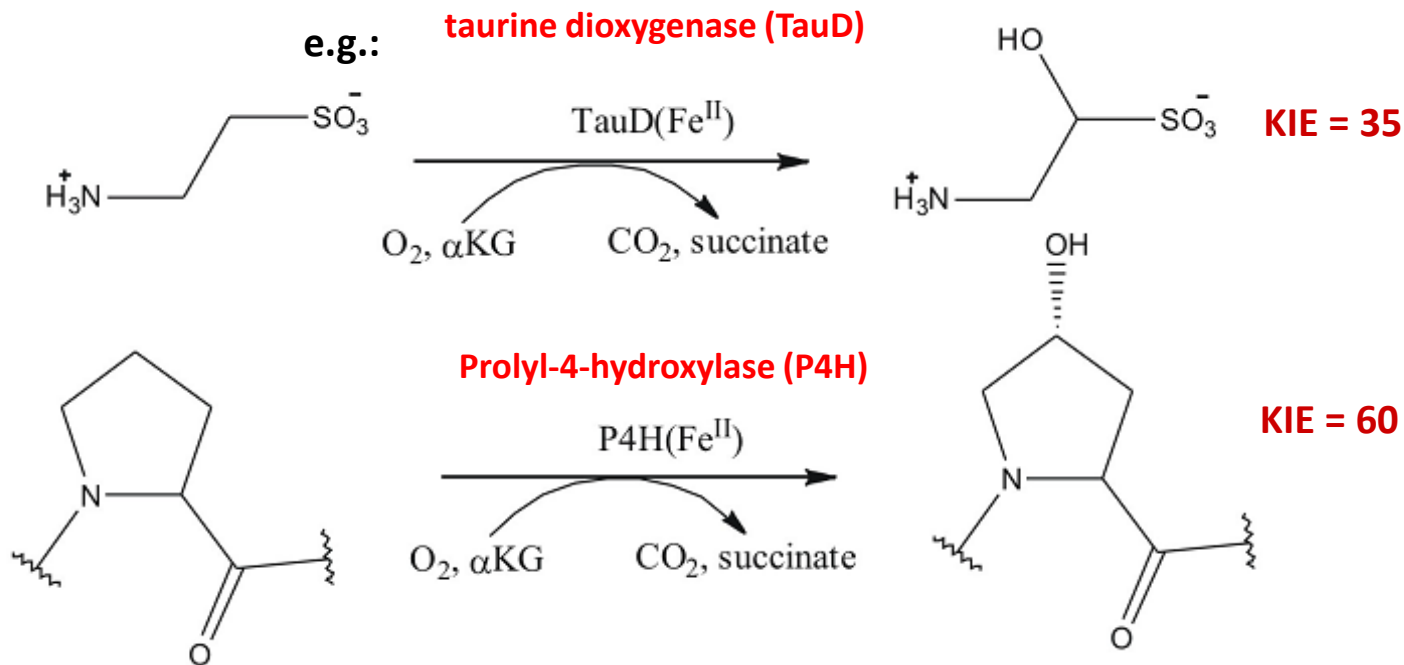
In both cases:
rate-determining step is the homolytic C-H bond cleavage alias H-atom abstraction

Some experimental works demonstrate a large tunneling effect based on the **large A_H/A_D ratio** (A – Arrhenius prefactor is defined in terms of classical Eyring theory by **eq. 15**)
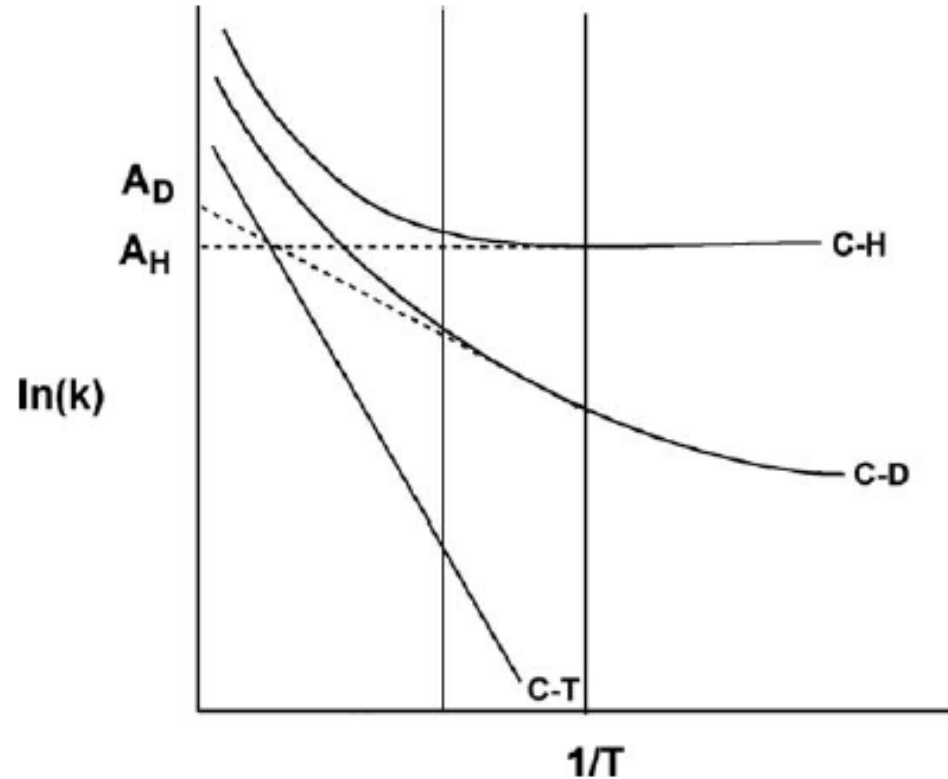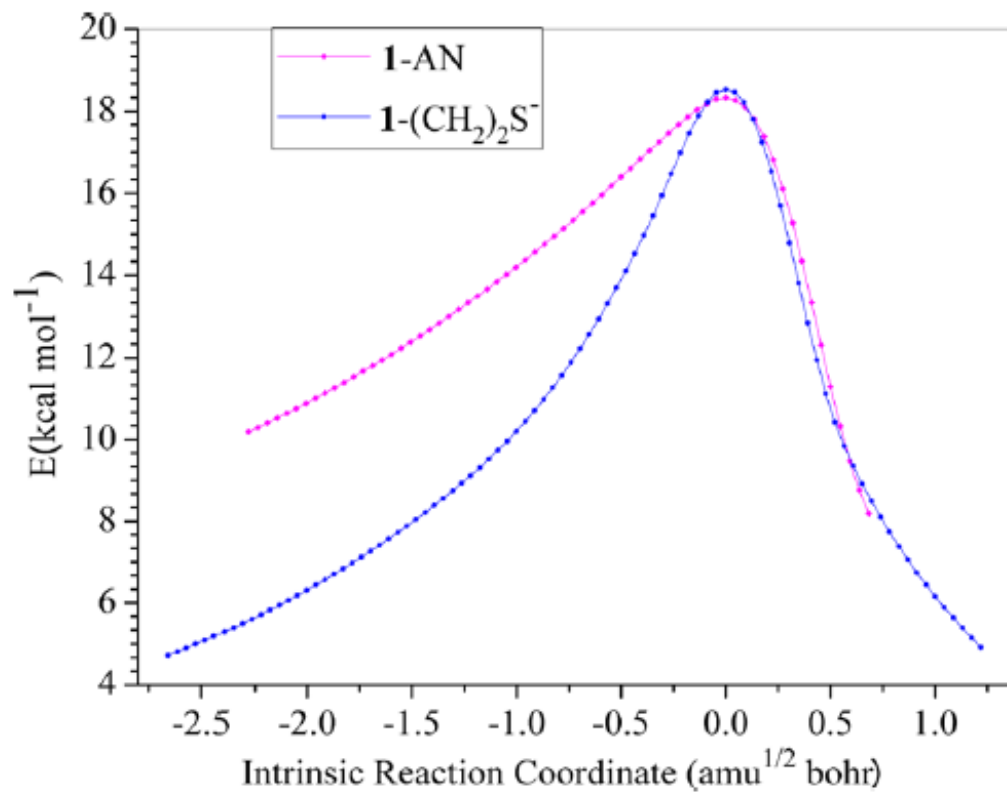

→ **Deviation from Arrhenius/Eyring plots at low temperatures**

C-H cleavage
by Fe^{IV}O:

$KIE_{Eckart}=12$
$KIE_{Eckart}=51$

Shaik, JACS
2015

Proton-Coupled Electron Transfer: Moving Together and Charging Forward

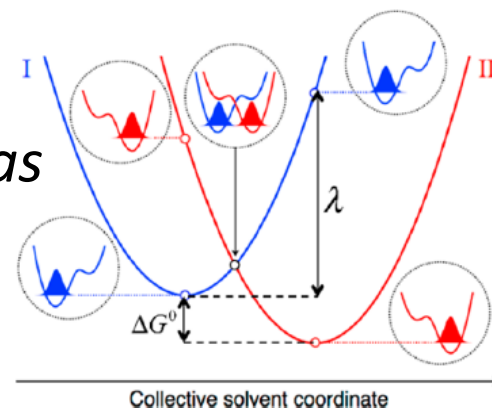*Larger proton donor-acceptor distance (larger width of the barrier) → Larger KIE*

(concepts and theory from Marcus theory for electron transfer and analogous theories for proton transfer) : More specifically the expression derived in the vibronically nonadiabatic limit using the Fermi golden rule formalism in conjunction with a dynamical treatment based on the time Integral of the probability flux time correlation function…

$$k = \sum_{\mu} P_{\mu} \sum_{v} \frac{\left| V^{el} S^{(0)}_{\mu v} \right|^2}{\hbar} \exp\left[\frac{2k_B T \alpha^2_{\mu v}}{M\Omega^2} \right] \sqrt{\frac{\pi}{\lambda_s k_B T}} \exp\left[-\frac{\left(\Delta G_{\mu v} + \lambda_s \right)^2}{4\lambda_s k_B T} \right]$$

$$KIE \approx \frac{\left| S_H \right|^2}{\left| S_D \right|^2} \exp\left(\frac{2k_B T}{M\Omega^2}[\alpha_H - \alpha_D] \right)$$

Vibronic parabolas

Collective solvent coordinate

*Overlap of hydrogen and deuterium wavefunctions, respectively*

The overlaps decrease for both hydrogen and deuterium as the proton donor-acceptor distance increases, but the deuterium falls off faster because of its larger mass.

Soybean Lipoxygenase

KIE$_{expt}$ = 80

→   *reproduced by above mentioned PCET theory
and shown that KIE large due to small overlap
between the reactant and product vibrational wavefunctions*
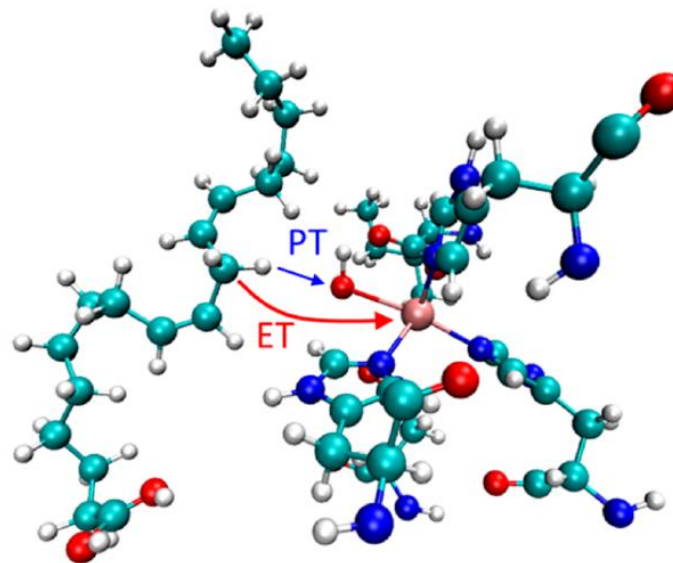
Mutant and Crystallographic studies:

KIE$_{expt}$ = 500-700

→   *expt/calc… larger proton donor-acceptor distance (about 0.1-0.2 Ang)*

An extension of the TST – variational TST

Within Eyring's TST, it is not garanteed that the free energy associated with the TS structure is the highest free energy of any point along the minimum-energy path (MEP) – it is only garanteed that it is the highest point of potential energy along the MEP.

e.g.:
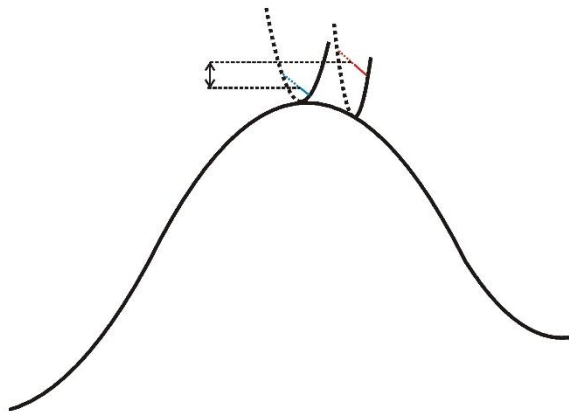
→ **Variational Transition State Theory (VTST) - modification of eq. 8a:**

$$k_{\text{react}}(T,s) = \min_s \frac{k_B T}{h} \frac{Q^{\neq}(T,s)}{Q_A} e^{-(U_{TS,0}-U_{A,0})/k_B T}$$

eq. 21

Within VTST, the reference position is moved (**s**) along the MEP that is employed for the computation of the activated complex free energy, either backward or forward from the TS structure, until the rate constant is minimized. By convention, $s = 0$ is the saddle point on the MEP. In practice, minimization of the rate constant with respect to **s** is accomplished by standard search techniques for situations where analytic gradients of the function to be minimized are not available. **The variational TS can move with changes in temperature T.**
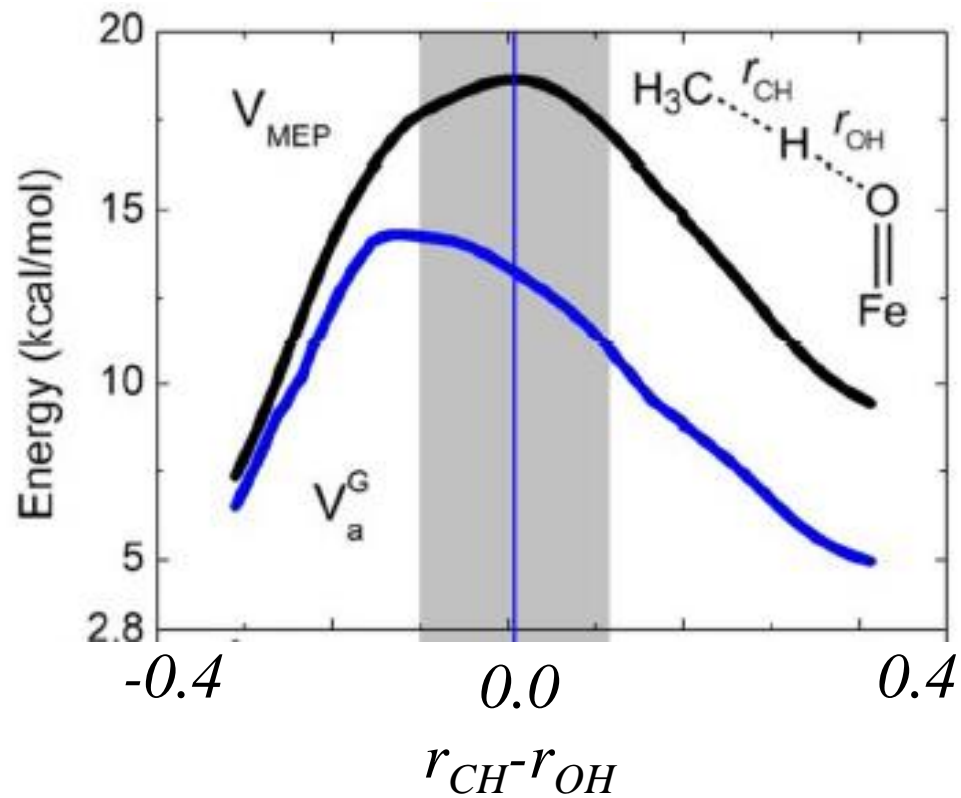
V_{MEP} – Potential energy profile

V_a^G – vibrationally adiabatic energy profile

Alternative theories to the TST

→ **Rice-Ramsperger-Kassel-Marcus (RRKM) theory**

Transition state theory formulated for a system of constant energy,
as opposed to constant temperature – i.e. microcanonical TST (μTST) ;

for the unimolecular case μTST = **RRKM.**

=> more appropriate for gas-phase reactivity

Assumption of RRKM theory:

1. Collisional activation, followed by intramolecular vibrational relaxation leading to the transition state.

2. Energized molecules pass through the transition state just once (as in TST)

3. Internal degrees of freedom of the energized molecules are designated as either *adiabatic* (quantum state does not change during reaction) or *active* (energy exchanged between active modes during reactions). Note, most internal modes would be active. Slow energy flow would reflect weak anharmonic coupling of modes.

→ Kramers theory

Using a model for Brownian motion over the barrier, where the reacting particle experiences friction due to the surrouding solvent molecules, Kramers was able to derive an expression for the rate contant:

$$k_{Kramers} = \frac{m\nu_B}{\zeta} \, k_{Eyring}$$

m – mass of the reactive particle

ν_B – barrier frequency

ζ – friction constant

This equation holds **in the limit of high friction**.

The Kramers rate is always lower than the rate calculated with TST. The reason is that now it is not sufficient for the particle to reach the top of the barrier, it has to have sufficient velocity to go over it, or it will be sent back to the reactant well.

Historical retrospective

"Pelzer and Wigner in their 1932 paper estimated the rate of conversion of para-hydrogen into normal hydrogen. In this very early paper one may find all the elements of much more sophisticated work which abounded in the second half of the 20th century…. To compute the reaction rate, they use a thermal equilibrium distribution in the vicinity of the saddle point of the potential energy surface and estimate the unidirectional classical flux in the direction from reactants to products. Already here, they note that they ignore the possibility of recrossings of the saddle point, pointing out that their probability at room temperature would be rather small. To get the rate they use the flux over population method after harmonically expanding the potential energy surface about the saddle point. The Pelzer and Wigner paper is the very first use of transition state theory to estimate reaction rates. It is however written in a rather specific form, as applied to the hydrogen exchange reaction. Eyring's later paper of 1935 provides general formulas which were then applied to many different activated reactions."

Pollak E., Talkner, P CHAOS 15, 026116 (2005)