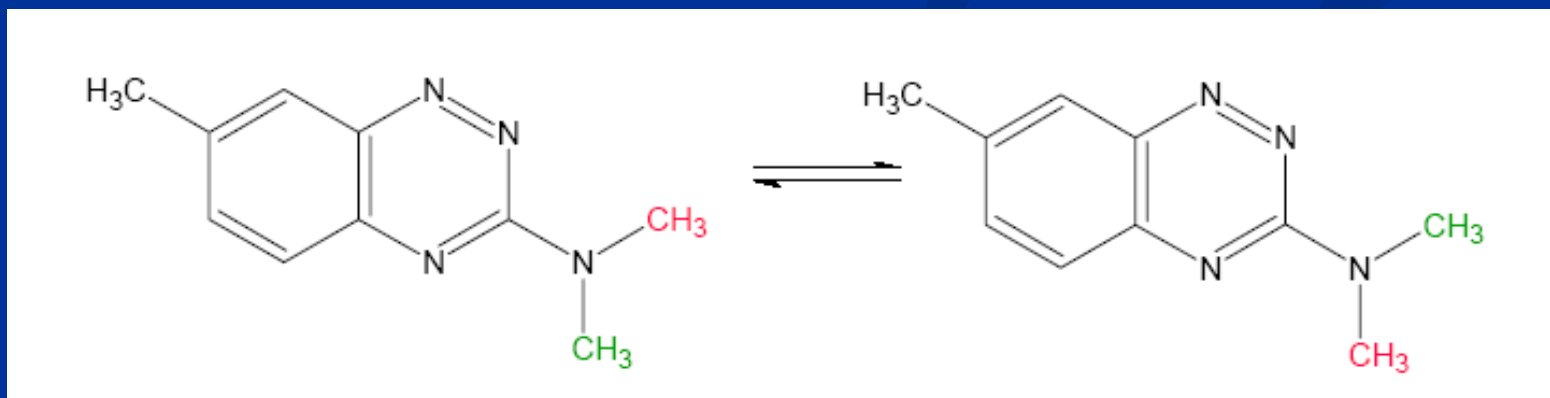


Spectroscopic Observation of Dynamical Processes

Spectroscopy of reversible reactions and processes

The lineshape of the resonances depends on the life-time of the molecular species that is on the rate of forward and backward reactions



Spectroscopic Observation of Dynamical Processes

A unique tool for investigating processes without
perturbing the system

NMR spectroscopy

UV-VIS spectroscopy

IR spectroscopy

(EPR spectroscopy)

Spectroscopic Observation of Dynamical Processes

Irreversible reactions:

For slow reactions (rate constants for the reactions are 10^{-6} to 10^{-3} s^{-1} typically): changes in concentration of products and/or reactants versus time are monitored. The variable temperature study allows determination of activation enthalpy and entropy.

For fast reactions: titration with the addition of the aliquots of one edduct to the another edduct. The increase in the products and decrease in edduct concentration could be seen from the spectra.

NMR spectroscopy, UV-VIS spectroscopy, IR spectroscopy

Timescale of Chemical Processes

Spectroscopy	Typical frequency difference	$\Delta\nu$ s ⁻¹	$k = 2.22\Delta\nu$ s ⁻¹	Processes occurring on this timescale
NMR	100 Hz	100	222	Intra- and intermolecular processes
IR	33 cm ⁻¹	1 10 ¹²	2.22 10 ¹²	Intramolecular processes (nuclei or electron movement)
UV-VIS	100 nm	3 10 ¹⁵	6.66 10 ¹⁵	Intramolecular electron movement

Chemical Exchange

NMR time scale: ms to μ s

$$k \gg \Delta\nu$$

Reversible processes

Activation energies 20 – 100 kJ mol⁻¹

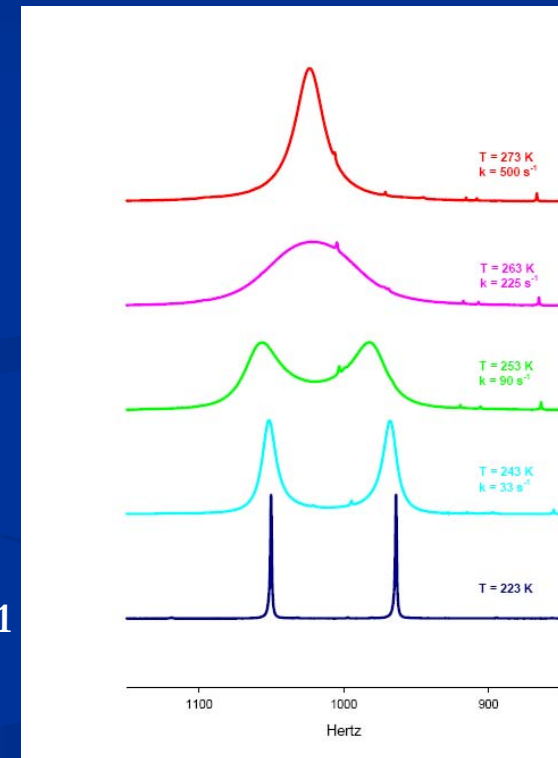
Stable isomers at room temperature

$\Delta G^\ddagger > 100$ kJ mol⁻¹

Methods:

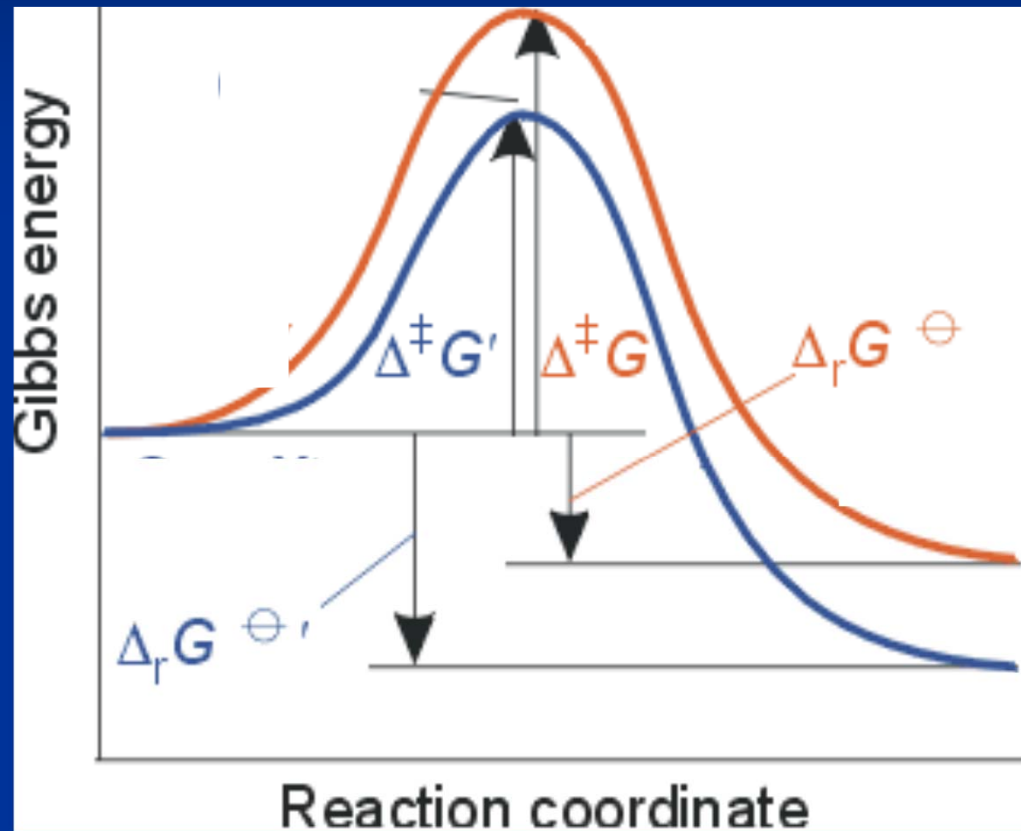
- Band shape analysis 20 – 80 kJ mol⁻¹
- Polarization transfer 80 – 100 kJ mol⁻¹

Temperatures –150 / +150 °C



$$k \ll \Delta\nu$$

Reaction Coordinate



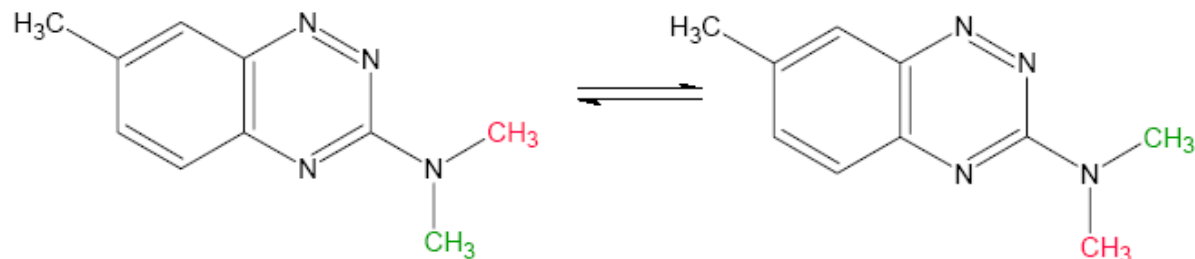
$$\Delta_r G^\ominus = -RT \ln K$$

$$\Delta_r G^\ominus = \Delta_r H^\ominus - T \Delta_r S^\ominus$$

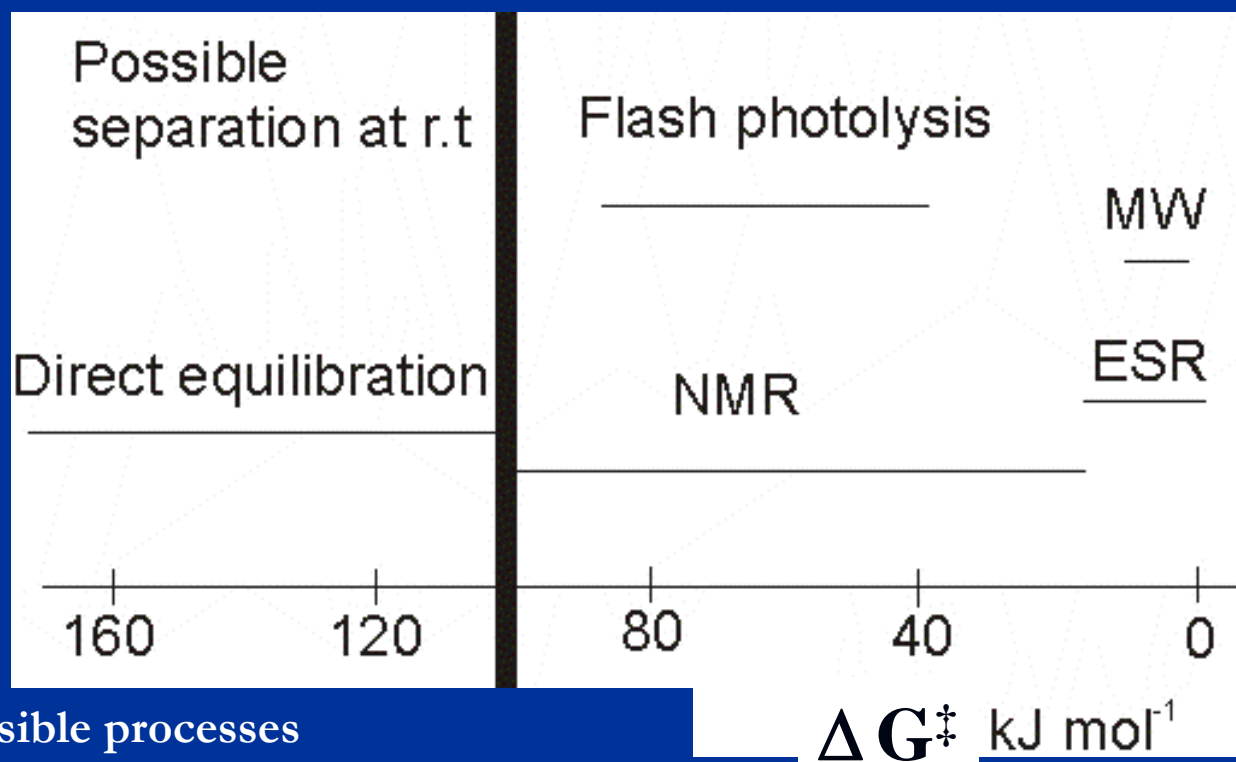
$$\Delta G^\ddagger = -RT \ln K^\ddagger$$

$$\Delta G^\ddagger = \Delta H^\ddagger - T \Delta S^\ddagger$$

Intramolecular Mobility

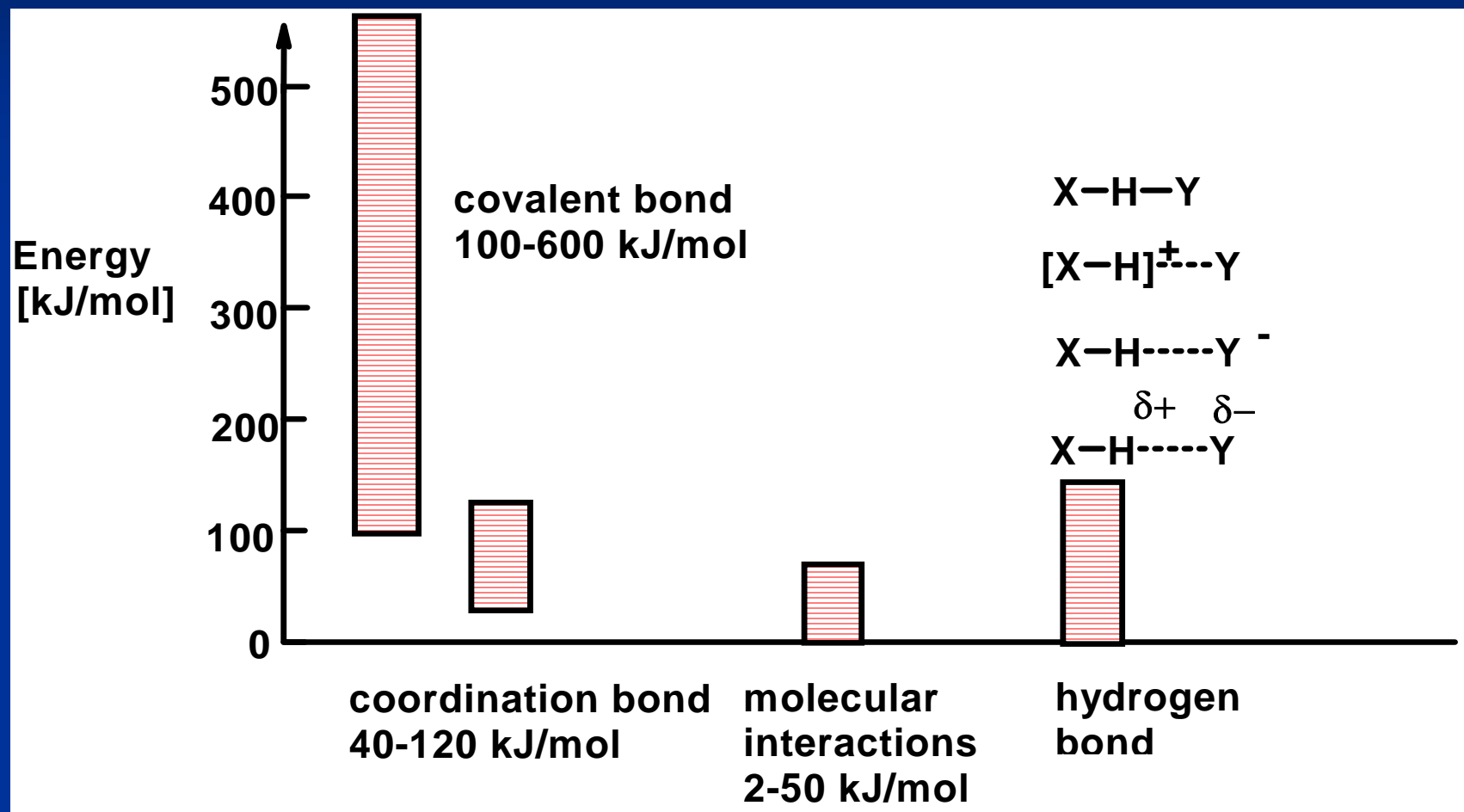


$$\Delta G^\ddagger = \Delta H^\ddagger - T \Delta S^\ddagger$$



Reversible processes
Activation energies 20 – 100 kJ mol⁻¹

Bond Energies



Reaction Rate

$$-\frac{d[A]}{dt} = k[A]$$

$$\ln \frac{[A]}{[A]_0} = -kt$$

$$[A] = [A]_0 \exp(-kt)$$

Arrhenius equation

$$k = Ae^{-E_a/RT}$$

Theory of Activated Complex



Equilibrium constant of activated complex

$$K^\ddagger = [\text{ActC}]^\ddagger / [\text{A}] [\text{B}]$$

$$\text{Rate} = k_3 [\text{ActC}]^\ddagger = k_3 K^\ddagger [\text{A}] [\text{B}]$$

$$k_3 = t f = t k_B T / h$$

t = transmission factor (= 1)

f = frequency of ActC decomp.

$$\text{Rate} = (t k_B T / h) K^\ddagger [\text{A}] [\text{B}]$$

$$k = (t k_B T / h) K^\ddagger$$

$$\Delta G^\ddagger = -RT \ln K^\ddagger$$

$$\Delta G^\ddagger = \Delta H^\ddagger - T \Delta S^\ddagger$$

Eyring Equation

$$\text{Rate} = (t k_B T / h) K^\ddagger [A] [B]$$

$$k = (t k_B T / h) K^\ddagger$$

use: $\Delta G^\ddagger = -RT \ln K^\ddagger$

t = transmission factor = 1

$$\Delta G^\ddagger = \Delta H^\ddagger - T \Delta S^\ddagger$$

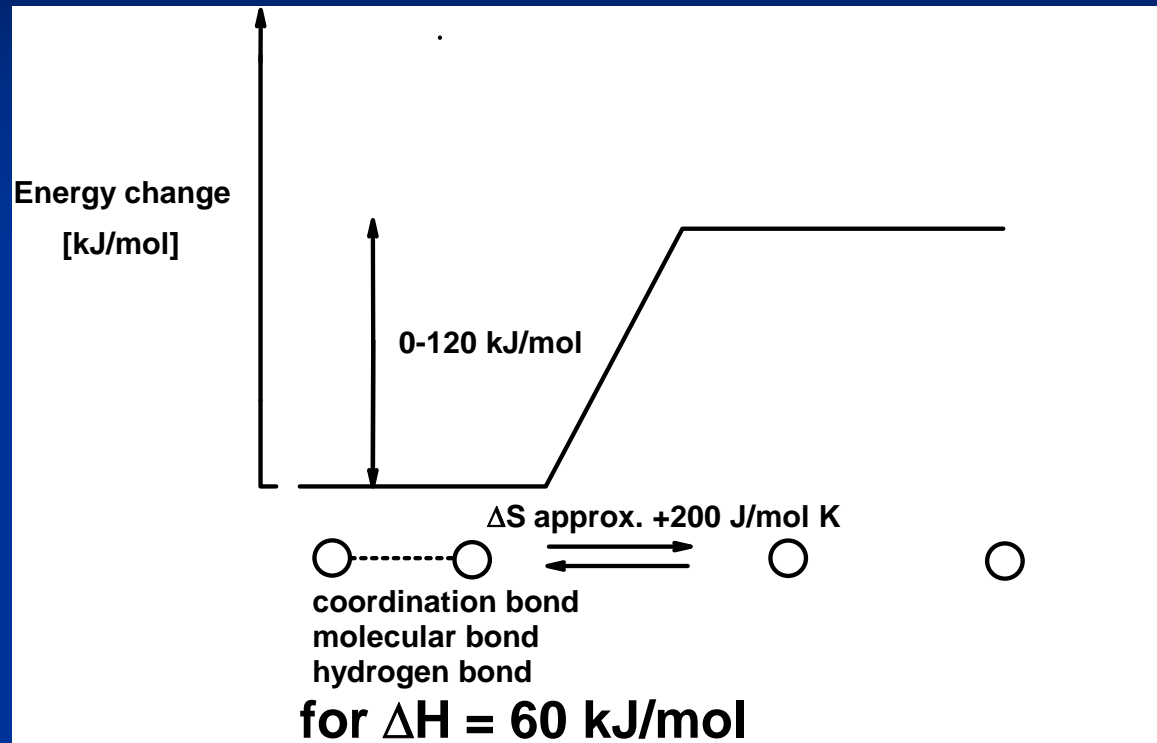
$$k = \frac{t k_B T}{h} K^\ddagger = \frac{t k_B T}{h} \exp\left(\frac{-\Delta G^\ddagger}{RT}\right) = \frac{t k_B T}{h} \exp\left(\frac{-\Delta H^\ddagger}{RT}\right) \exp\left(\frac{\Delta S^\ddagger}{R}\right)$$

$$\ln k = \ln \frac{t k_B T}{h} - \frac{\Delta H^\ddagger}{RT} + \frac{\Delta S^\ddagger}{R}$$

$$\ln \frac{k}{T} = \ln \frac{t k_B}{h} - \frac{\Delta H^\ddagger}{RT} + \frac{\Delta S^\ddagger}{R}$$

Activation Parameters

Thermodynamics



$$T = 300 \text{ K}, \Delta G = \Delta H - T\Delta S = 60 \text{ kJ/mol} - 300 \text{ K} \times 200 \text{ J/mol K} = 0 \text{ kJ/mol}$$

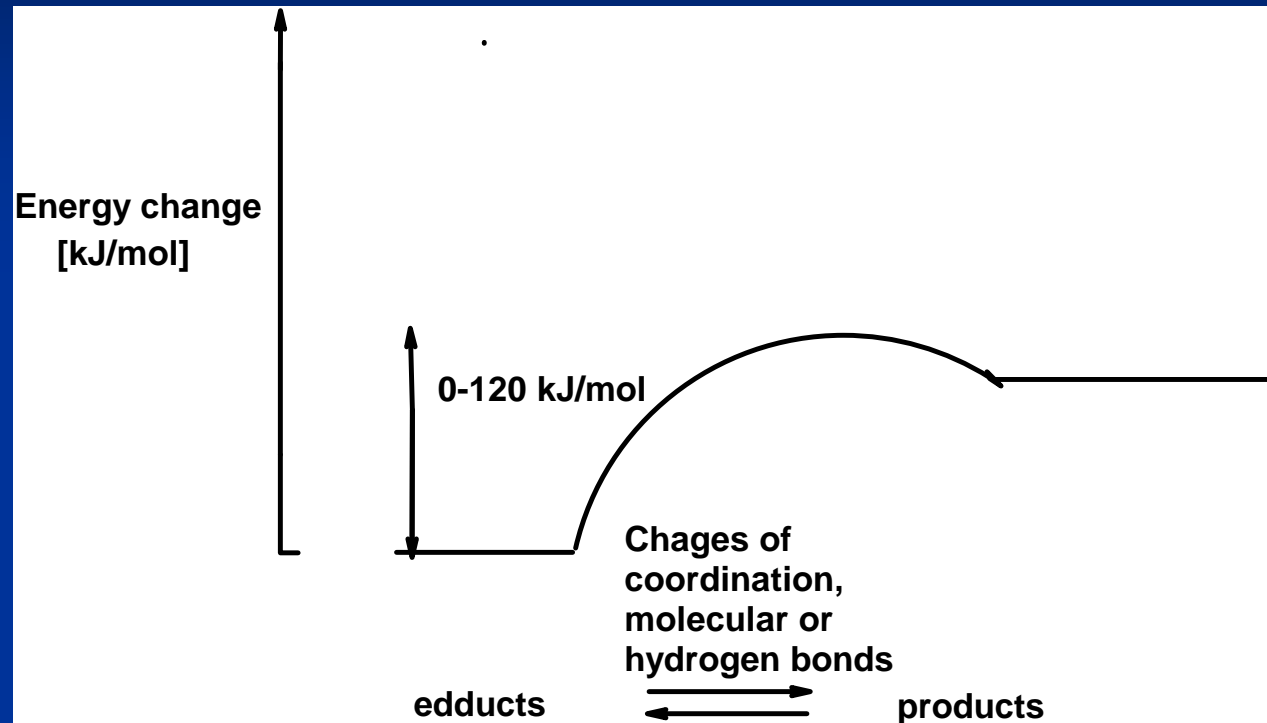
$$T = 200 \text{ K}, \Delta G = \Delta H - T\Delta S = 60 \text{ kJ/mol} - 200 \text{ K} \times 200 \text{ J/mol K} = 20 \text{ kJ/mol}$$

$$\Delta G = -RT \ln K$$

$$K = 1, \quad T = 300 \text{ K}$$

$$K = 6 \times 10^{-6}, \quad T = 200 \text{ K}$$

Kinetics



for $\Delta G^\ddagger = 60 \text{ kJ/mol}$

$$\Delta G^\ddagger = RT[23.76 - \ln(k/T)]$$

$$k = 600 \text{ s}^{-1} \quad T = 300 \text{ K}$$

$$k = 0.0009 \text{ s}^{-1} \quad T = 200 \text{ K}$$

Chemical Equivalence by Interconversion

Intramolecular exchange

- Tautomeric Interconversion (Keto-Enol)
- Restricted Rotation
- Ring Interconversion
- Ring whizzing
- Conformational equilibria

Intermolecular exchange

- Binding of small molecules to macromolecules
- Protonation/deprotonation equilibria
- Isotope exchange processes

Types of Chemical Exchange

Dynamical processes

change (equilibrium constant, rate constant) with temperature

Intermolecular processes

- Chemical reactions with formation of covalent bond: irreversible or reversible
- Formation of coordination bond: reversible
- Association of molecules, hydrogen bonding, solvation of ions and molecules: reversible

Intramolecular processes: reversible

- Fluxionality is the conversion between non-distinguishable species
 $\Delta G^\circ = 0$
- Isomerization is the conversion between different species (keto/enol tautomerism)
 $\Delta G^\circ \neq 0$

Chemical Exchange in NMR

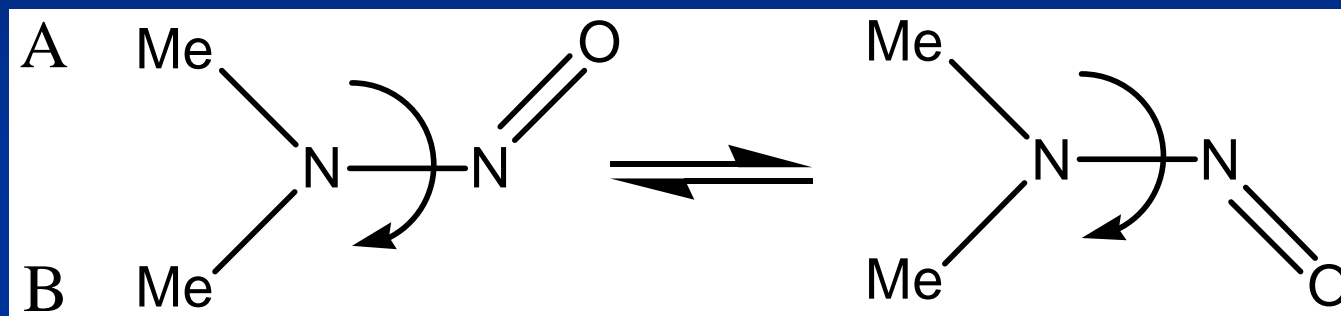
Magnetic site exchange

- Two-site
 - Multiple-site
-
- Bond breaking
 - Internal hindered rotation

Two classes of exchange processes:

- Mutual/degenerate exchange,
Fluxionality, topomerization, $\Delta G^\circ = 0$
- Non-mutual/nondegenerate exchange,
Isomerization, $\Delta G^\circ \neq 0$

Mutual/Degenerate Exchange



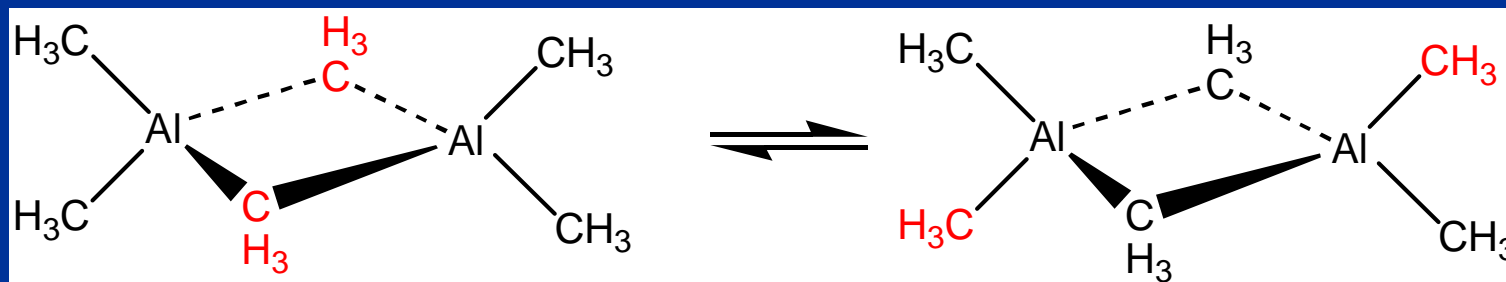
Only one distinguishable molecule (at a low temperature)

Fluxional molecules, topomerization

$$\Delta G^\circ = 0$$

Fluxional Molecules

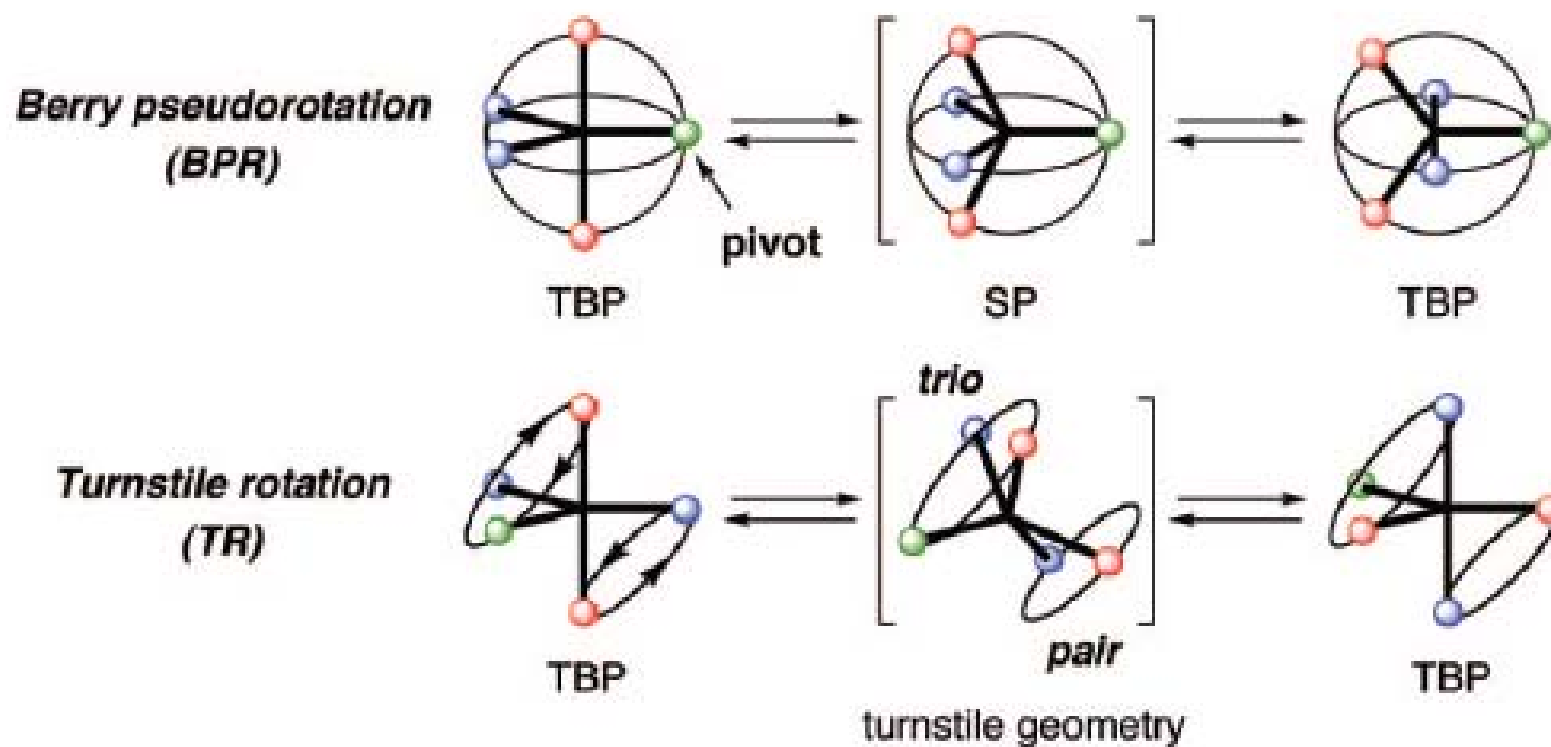
Bridging – terminal exchange



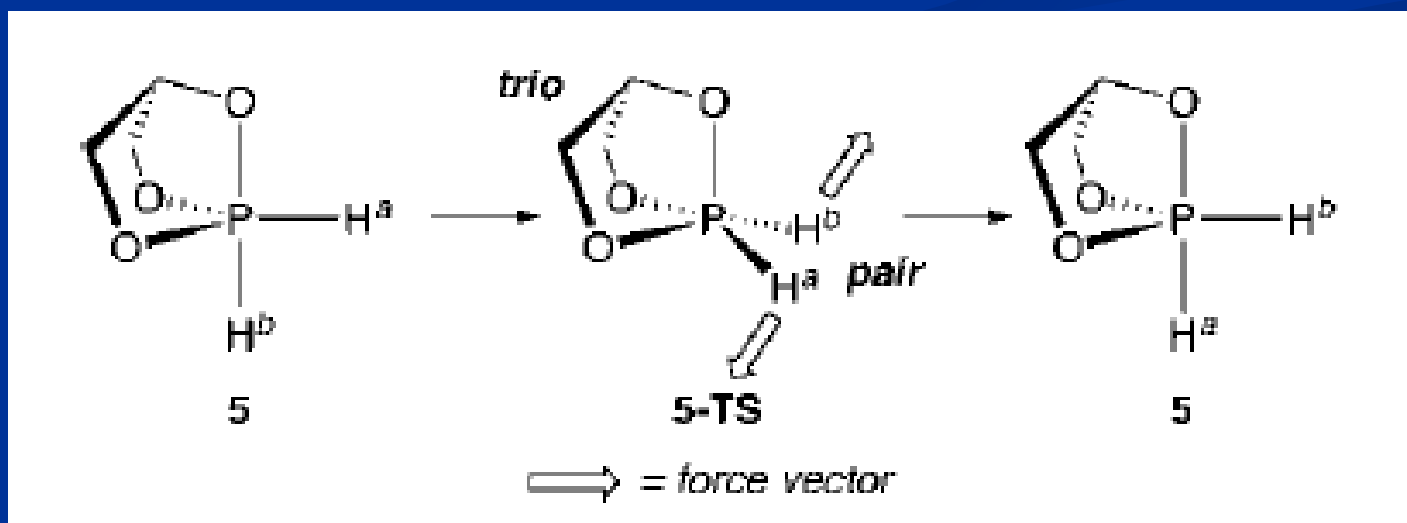
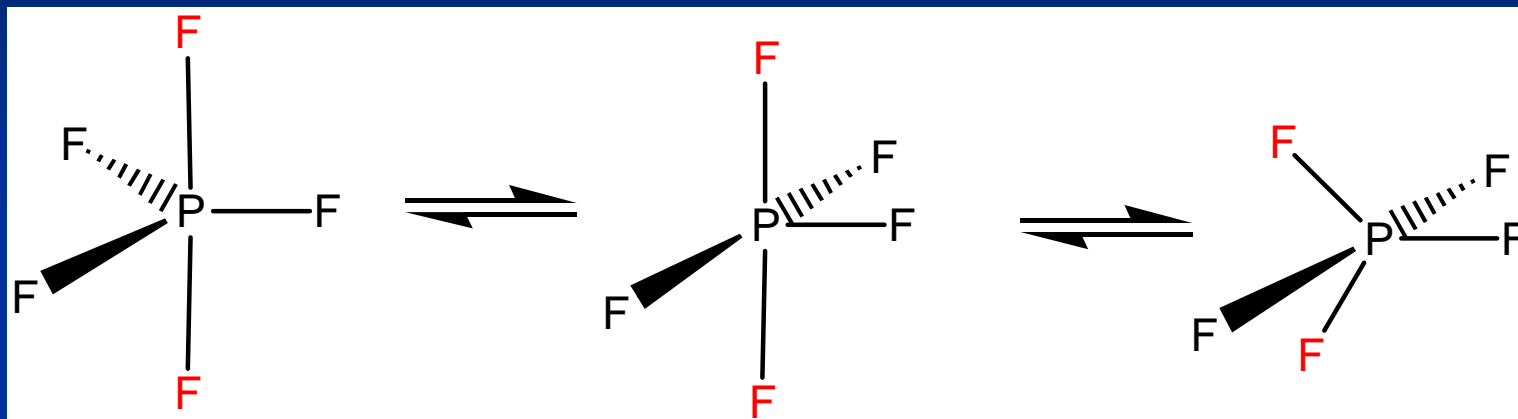
Fluxional Molecules

Polytopal rearrangements

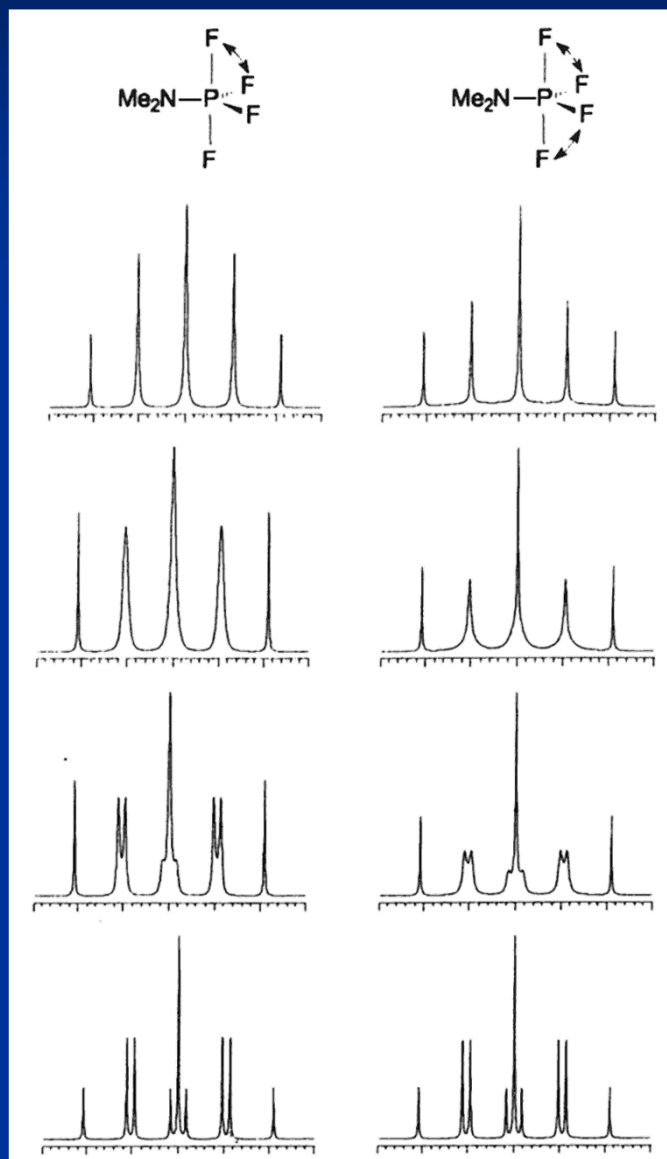
- Berry pseudorotation
- Turnstile rotation



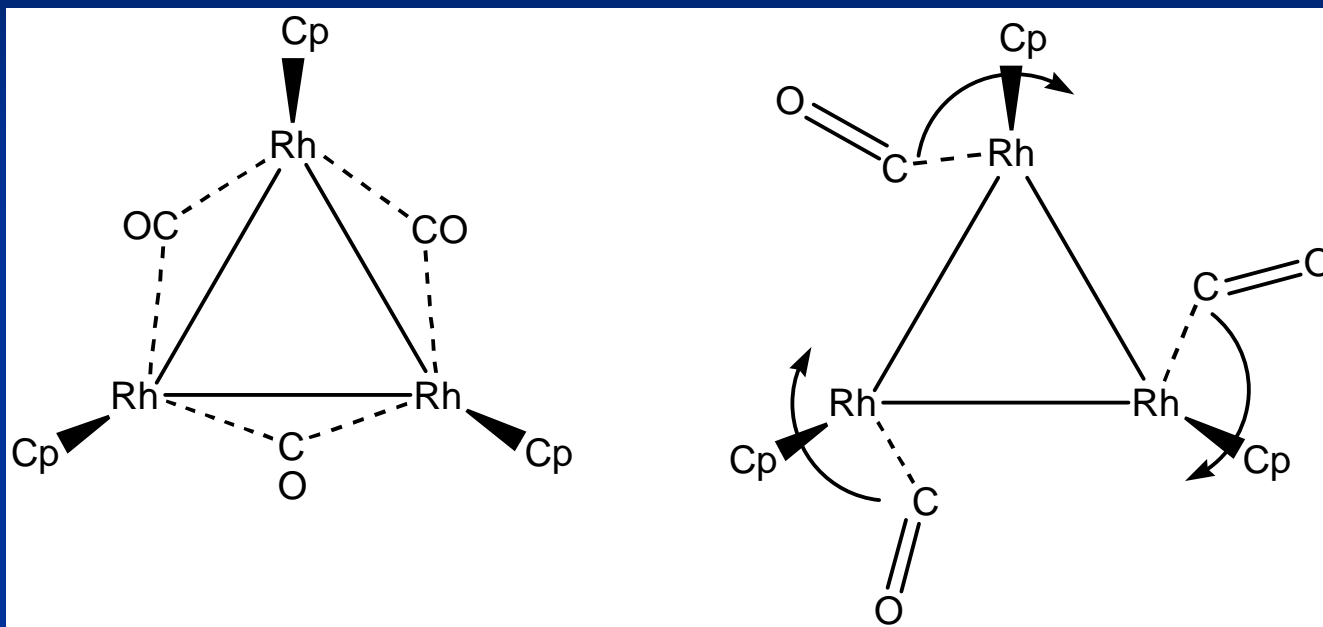
Fluxional Molecules



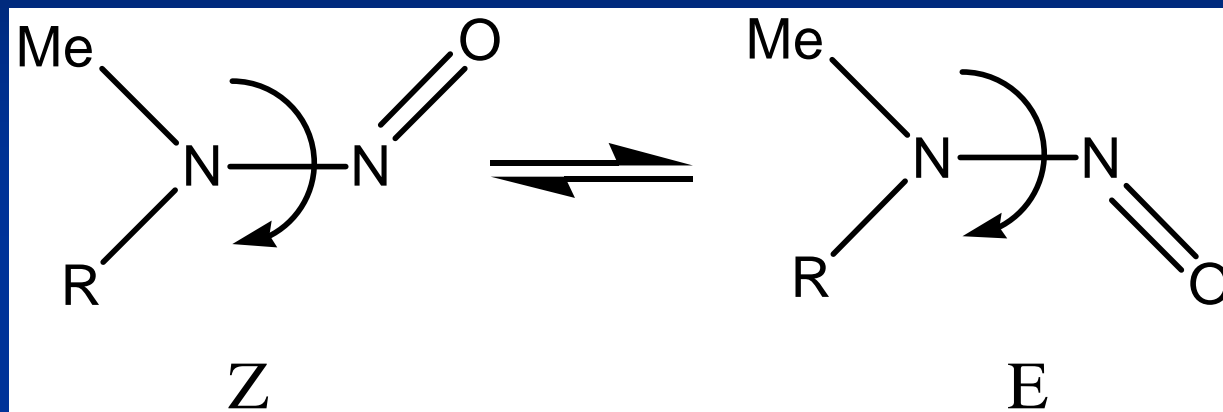
Fluxional Molecules



Fluxional Molecules



Non-mutual / Nondegenerate Exchange



Two or more distinguishable rotamers (at a low temperature)
Isomerization

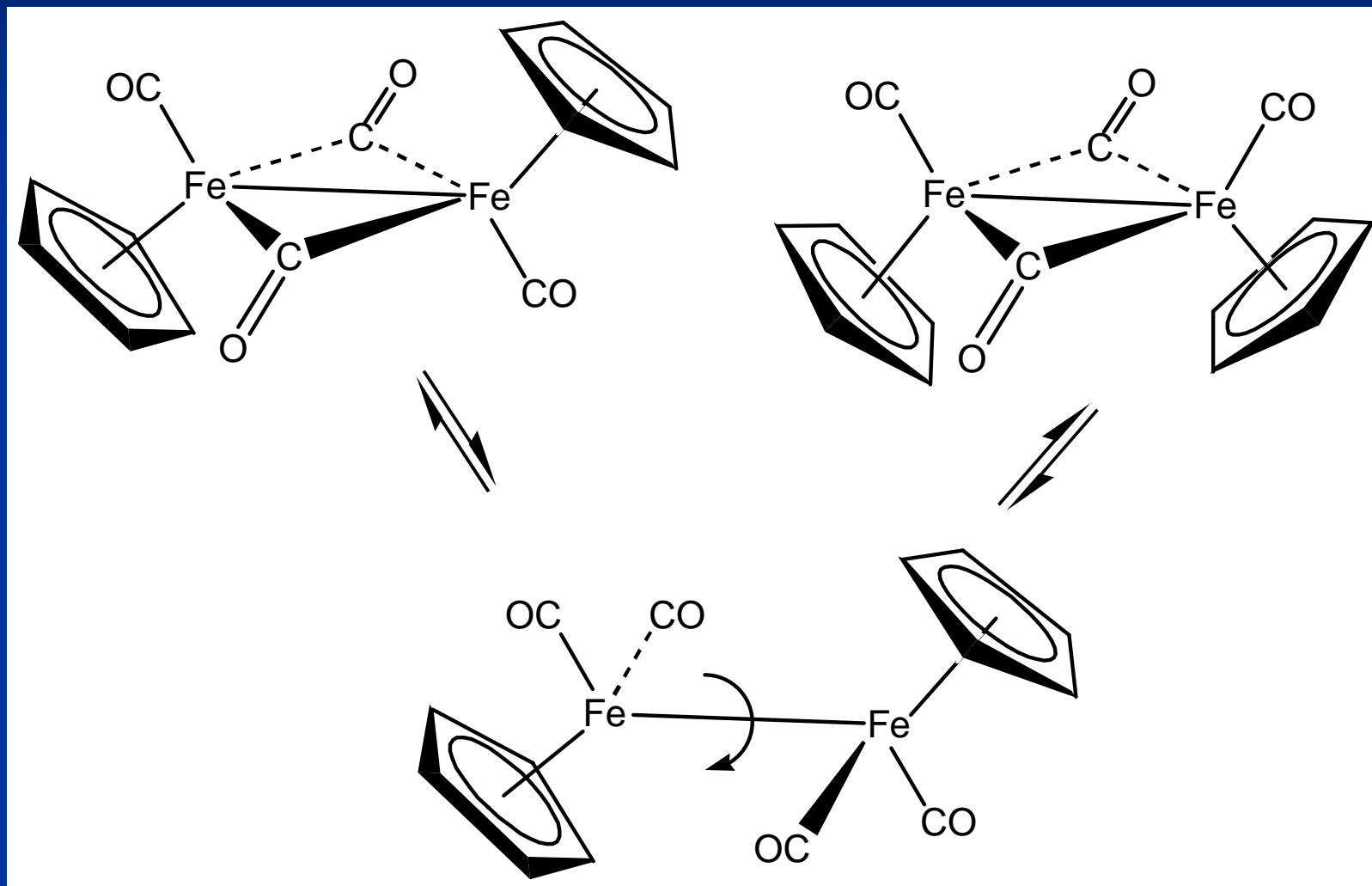
Stereochemically non-rigid molecules

$\Delta G^\circ \neq 0$

unequal populations (p)
equilibrium constant K

$$K = \frac{p}{1-p}$$

Stereochemically Non-rigid Molecules



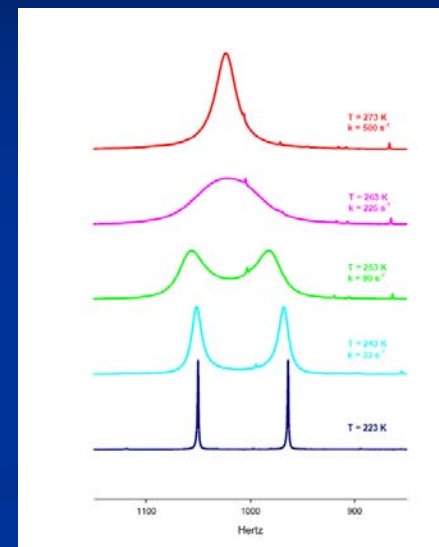
Study of Dynamic Processes in Solution by VT NMR

1. Indications of dynamic processes in solution:

- broad lines
- number of lines lower than expected
- dilution changes the spectrum
(indication of intermolecular processes)



- the change of the temperature changes the spectrum
- the addition of the molecules that participate in intermolecular processes changes the spectrum



Dynamic Processes by VT NMR

2. Recording of the spectra at different temperatures, if accessible in slow exchange, at coalescence and in fast exchange. Slow exchange limit (static conditions) is particularly important.

3. From slow exchange limit the species participating in dynamic processes are identified. Simulate the static spectrum. The chemical shifts, coupling constants, natural line-width and concentration is needed for the spectrum of each species.

Dynamic Processes by VT NMR

4. The possible dynamic processes are selected. Help with dilution of solution, addition of substance that could participate in processes, the free ligand or isotopically-labeled free ligand for example (intra- or intermolecular process).
5. Construct the exchange scheme = How the nuclei exchange their sites in the dynamic processes.
6. Simulate the spectra at the temperatures above the slow exchange limit by increasing the rate of the processes and/or changing the equilibrium concentrations. Compare the simulated and experimental spectra.

Dynamic Processes by VT NMR

7. The matching of experimental and simulated spectra means that the dynamic process is possible. Remember to consider other possibilities. You can never prove a mechanism, only disprove one. For example, perhaps there are *two* processes being observed, not just one.

8. The reaction rates from simulation of spectra are pseudo first order rate constants (reciprocal life-times of the nucleus at the site). The rates of the real dynamic processes are related to these first order rate constants.

Dynamic Processes by VT NMR

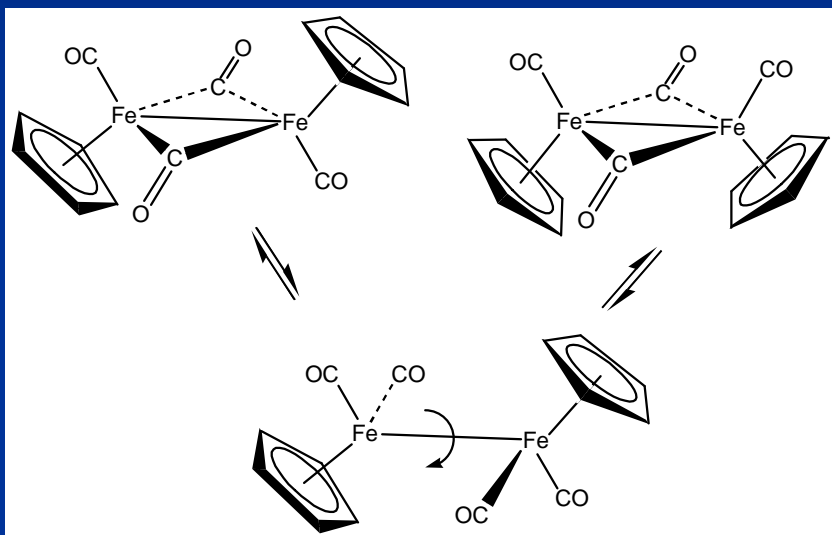
9. The Eyring plot of $\ln(k/T)$ versus $1/T$ results in activation enthalpy and activation entropy.

$$\ln \frac{k}{T} = -\frac{\Delta H^{act}}{RT} + \frac{\Delta S^{act}}{R} + 23.76$$

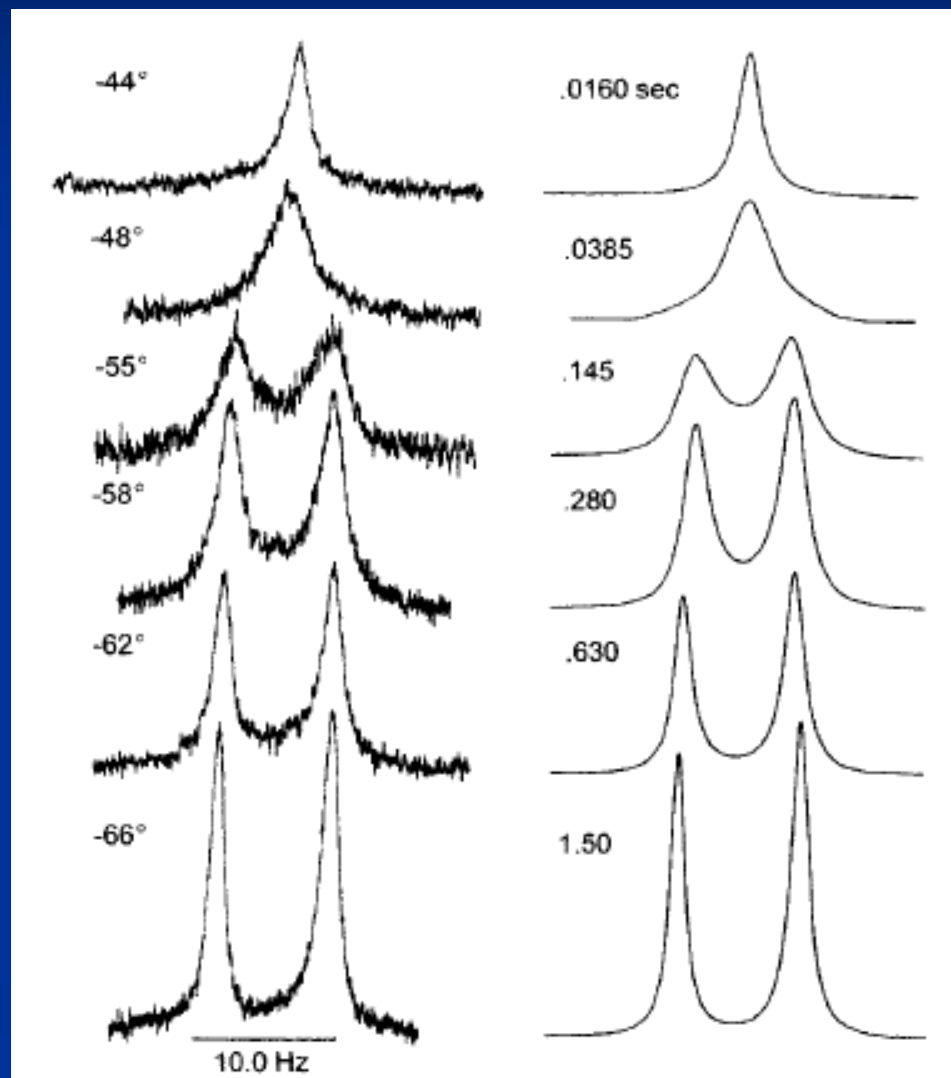
10. The van't Hoff plot of $\ln(K)$ versus $1/T$ results in reaction enthalpy and reaction entropy.

$$\ln K = -\frac{\Delta G^0}{RT} = -\frac{\Delta H^0}{RT} + \frac{\Delta S^0}{R}$$

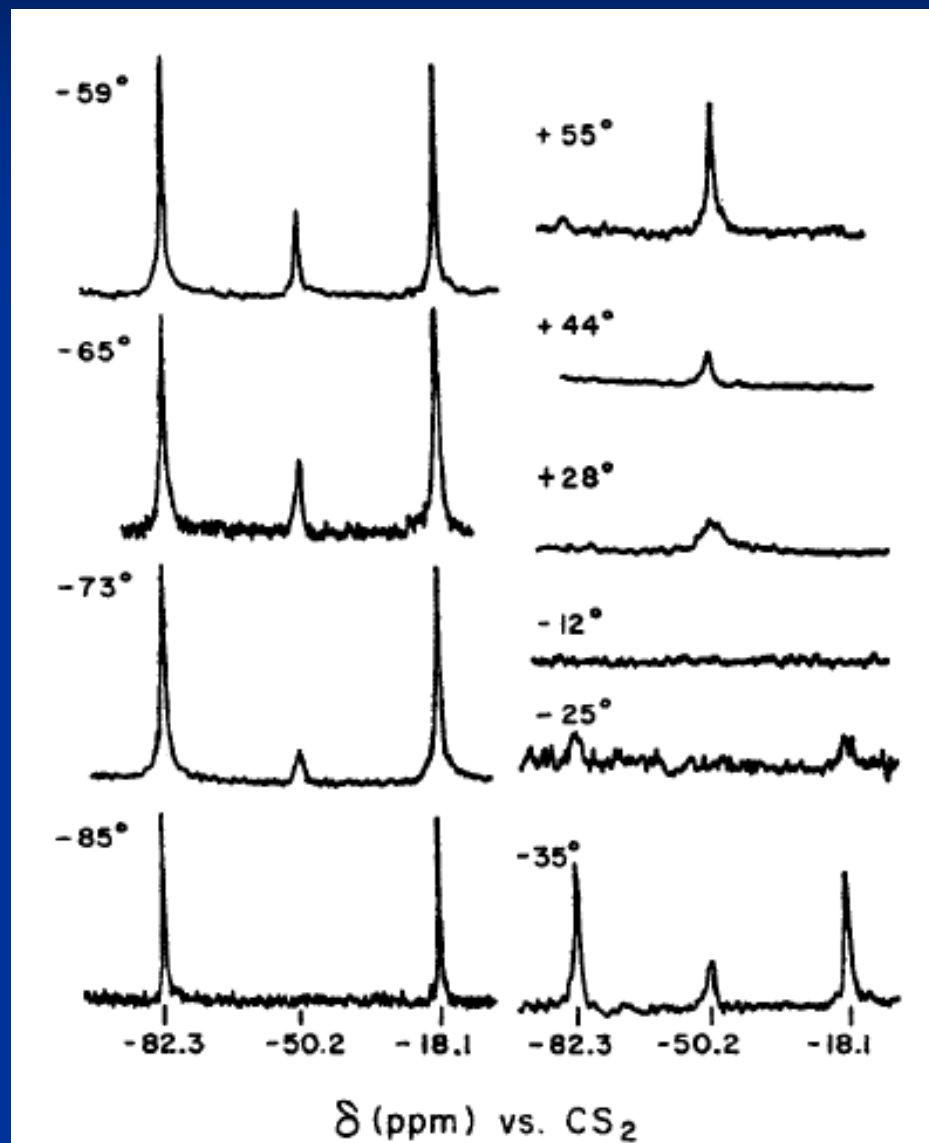
^1H NMR of $(\eta^5\text{-Cp})_2\text{Fe}_2(\text{CO})_4$



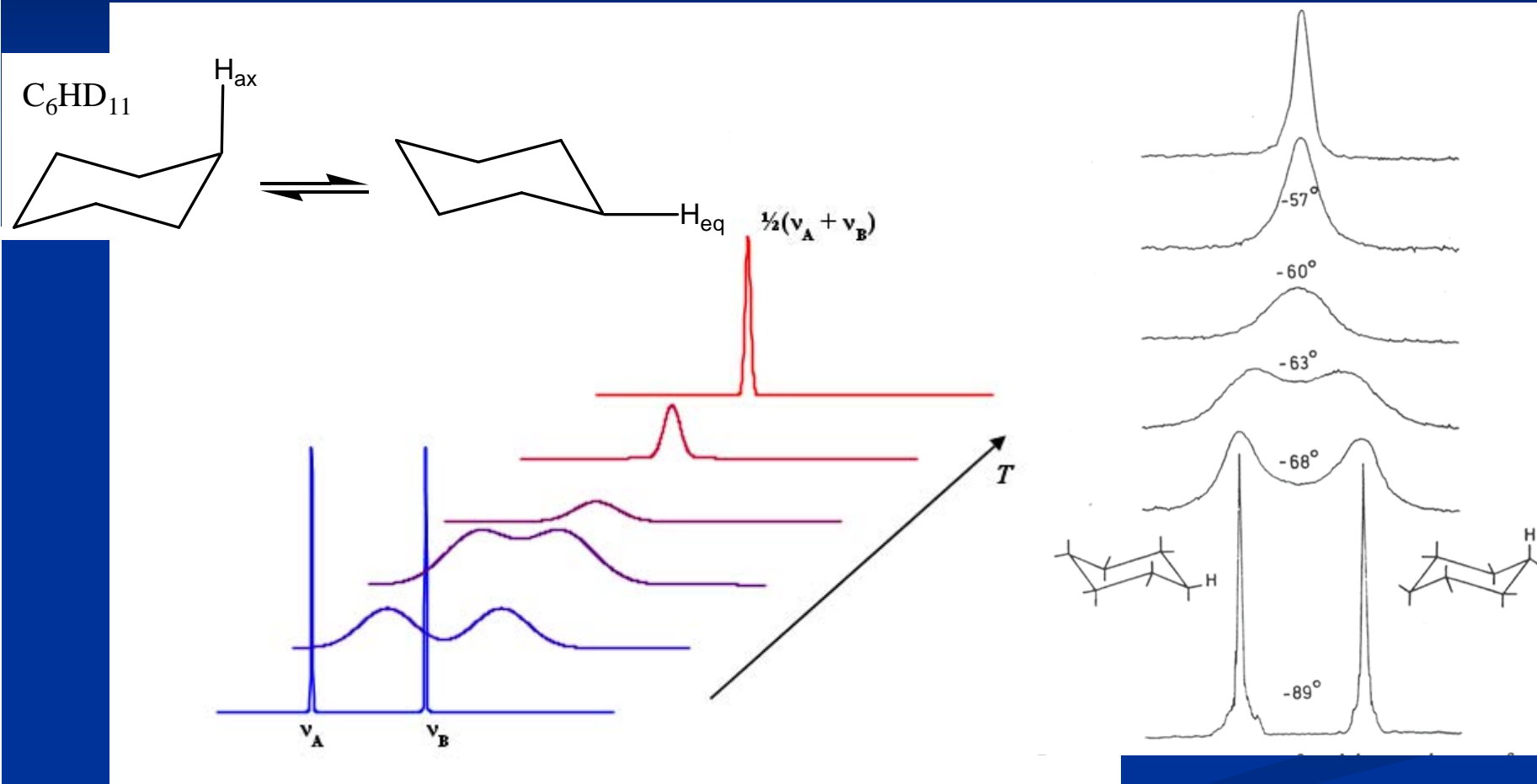
Cis – Trans isomer exchange



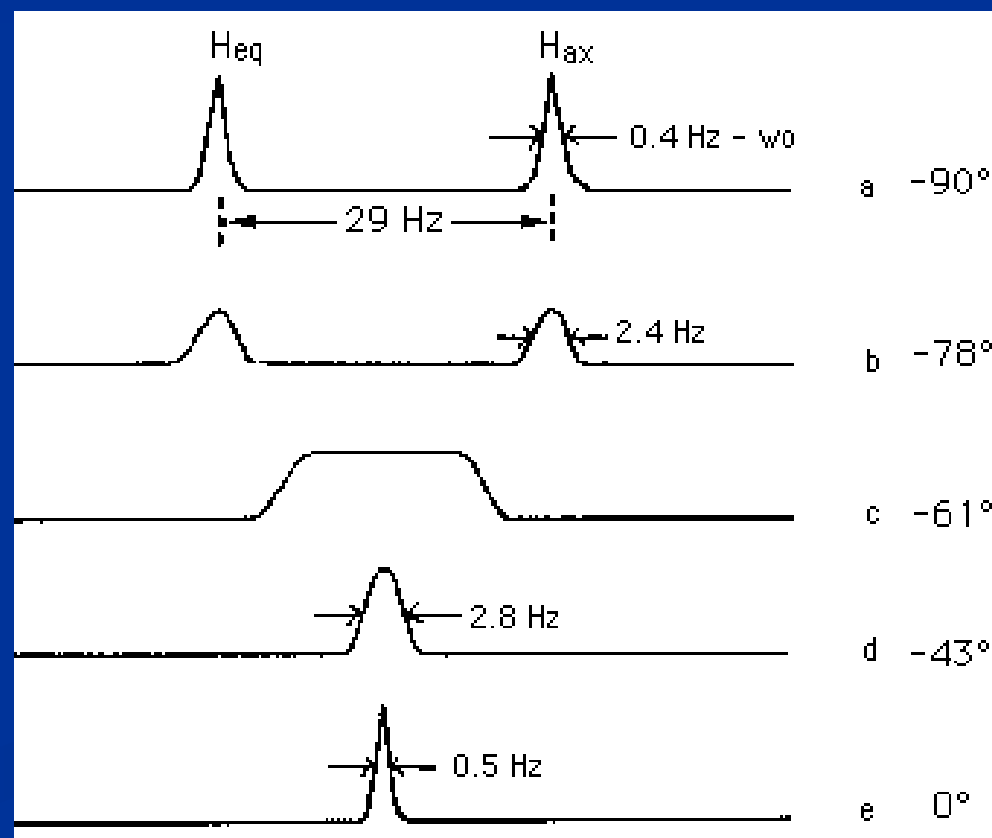
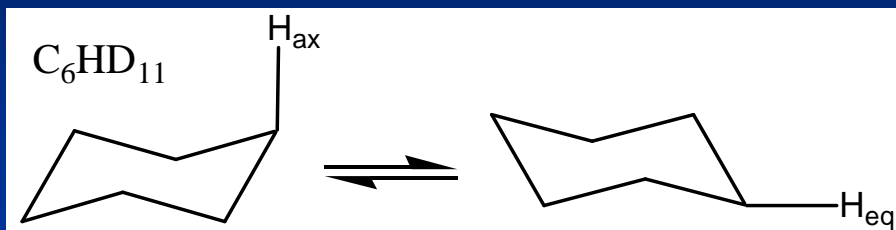
^{13}C NMR of $(\eta^5\text{-Cp})_2\text{Fe}_2(\text{CO})_4$



^1H VT-NMR Spectrum of Cyclohexane- d_{11}

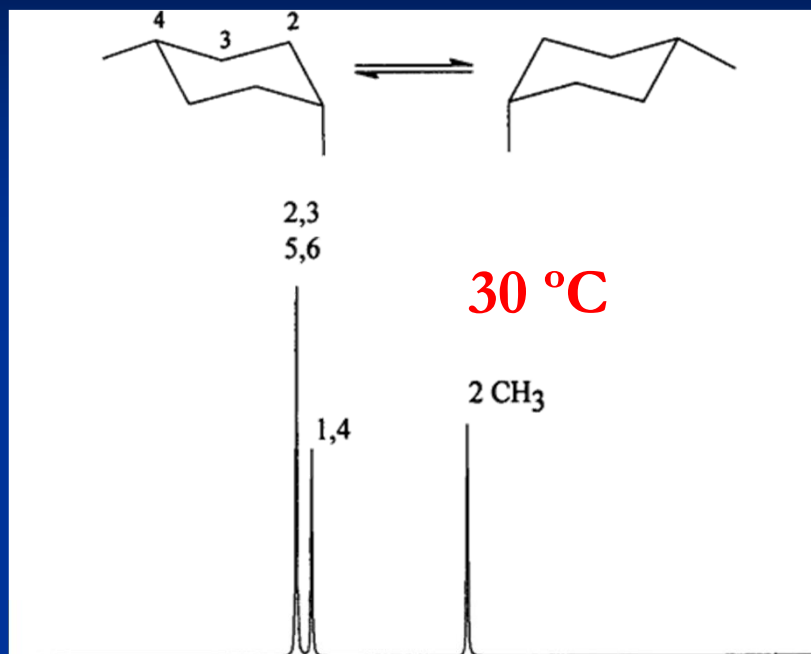


^1H VT-NMR Spectrum of Cyclohexane- d_{11}

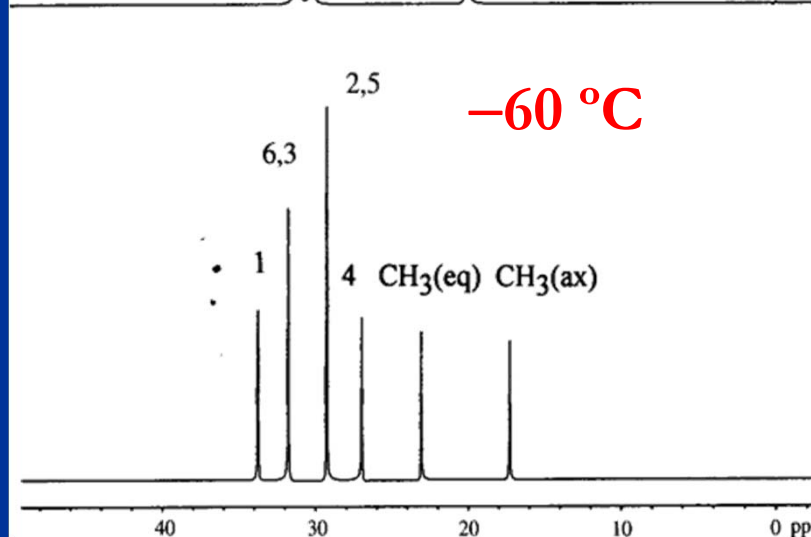


^{13}C NMR *Cis*-1,4-dimethylcyclohexane

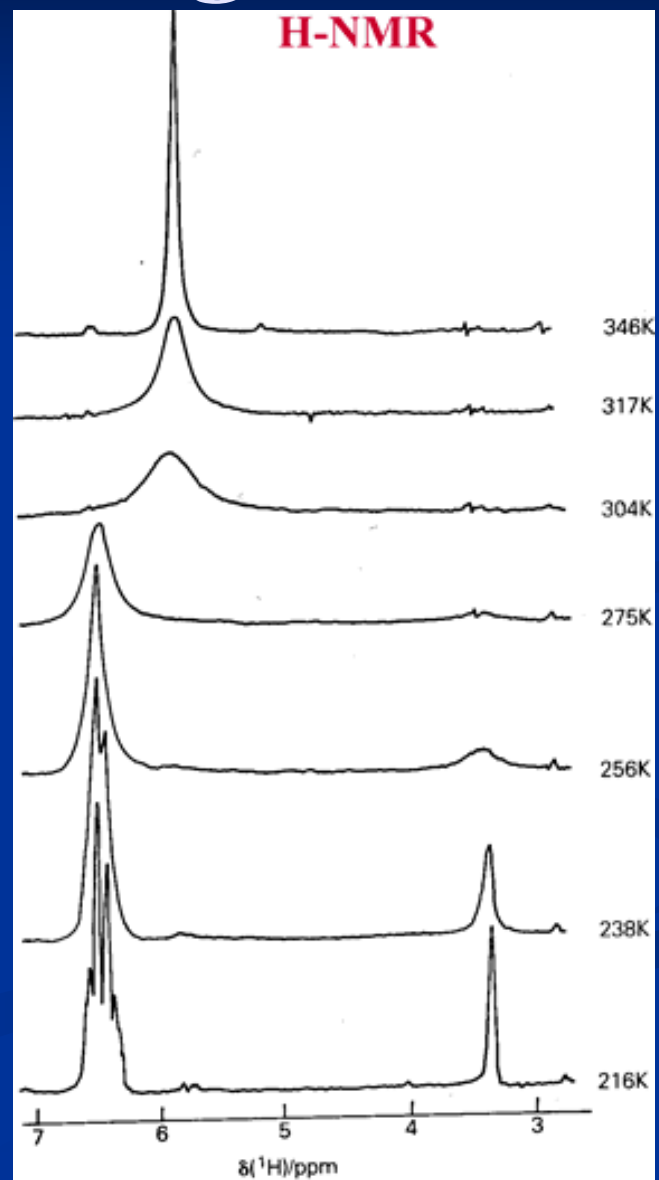
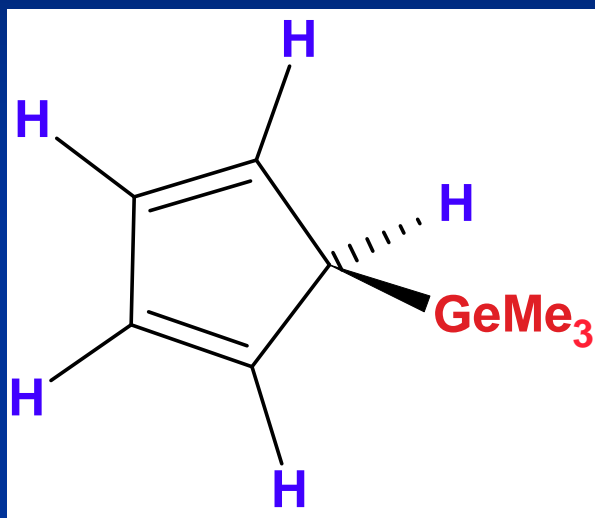
Fast exchange



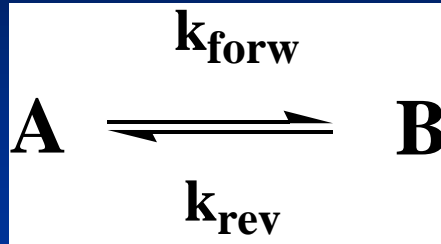
Slow exchange



Ring Whizzing



Two-State First Order Exchange



τ_A lifetime in site A [s]

τ_B lifetime in site B [s]

$$\tau_A = 1/k_{\text{forw}}$$

$$\tau_B = 1/k_{\text{rev}}$$

$$1/\tau = 1/\tau_A + 1/\tau_B \quad \text{single lifetime}$$

$$\frac{1}{\tau} = \frac{1}{\tau_A} + \frac{1}{\tau_B} = k_{\text{forw}} + k_{\text{rev}}$$

Heisenberg Uncertainty Principle

$$\Delta E \Delta t \geq h/2\pi \quad h = 6.626 \cdot 10^{-34} \text{ J s}$$

The broadening results from the finite lifetime of the spin states involved in the transition.

Energy levels are 'blurred' more for a shorter-lived state (because of the uncertainty relation).

As k increases at higher temperatures, the states involved in each transition have a shorter life-time and hence the uncertainty in each energy involved increases

$$\Delta \nu_{\frac{1}{2}} = \frac{1}{\pi\tau}$$

Heisenberg Uncertainty Principle

$$\Delta E \Delta t \geq h/2\pi \quad h = 6.626 \cdot 10^{-34} \text{ J s}$$

$$\Delta t = \tau_A \text{ lifetime in site A [s]} \quad \Delta t = \tau_B \text{ lifetime in site B [s]}$$

$$1/\tau = 1/\tau_A + 1/\tau_B \quad \tau_A = 1/k_{\text{forw}} \quad \tau_B = 1/k_{\text{rev}}$$

$$\Delta E = h/(2\pi \tau_A)$$

$$\Delta E = h \Delta \nu_{1/2} \quad \Delta \nu_{1/2} = \text{linewidth}$$

$$\Delta \nu_{1/2} \approx \frac{1}{\pi T_2}$$

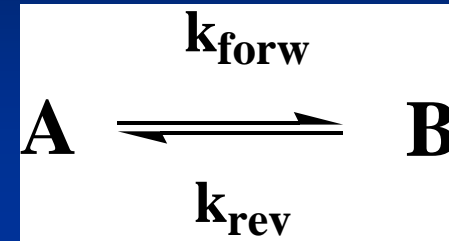
$$h/(2\pi \tau) = h \Delta \nu_{1/2}$$

$$\Delta \nu_{1/2} = (\pi \tau)^{-1}$$

$$\Delta \nu_{1/2} = \frac{1}{\pi \tau}$$

Line Shape Analysis

Two-State First Order Exchange



Line shape

$g(\nu)$ = intensity at the frequency ν

Variables ν_A , ν_B , τ - changed to fit experimental spectrum

$$g(\nu) = \frac{\text{const}(\nu_A - \nu_B)^2 \tau}{\left[\frac{1}{2}(\nu_A - \nu_B) - \nu \right]^2 + 4\pi^2 \tau^2 (\nu_A - \nu)^2 (\nu_B - \nu)^2}$$

Slow Exchange

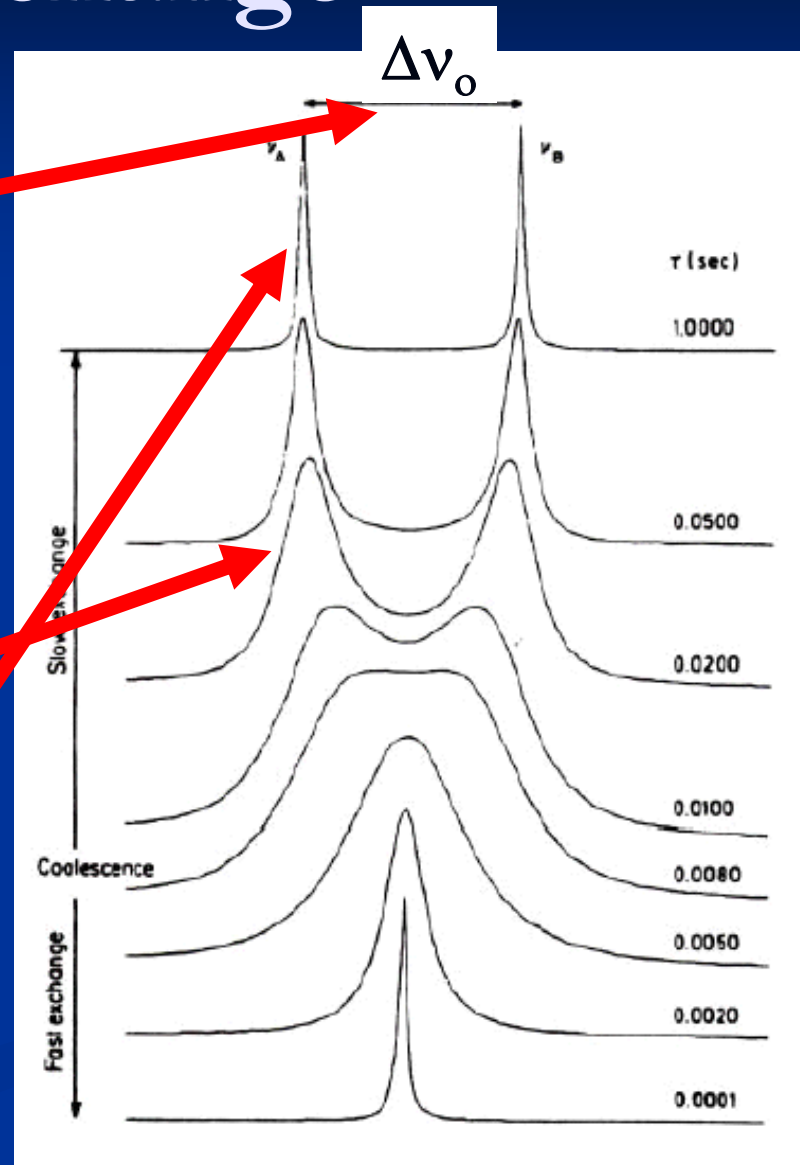
Slow Exchange $\Delta\nu_0 \gg k$
(less than ~20% overlap)

$\Delta\nu_0 = \nu_A - \nu_B$
the separation between
two peaks with no exchange

$$k = \pi(\omega - \omega_0)$$

ω = line width at the half
of the peak maxima at the given
temperature

ω_0 = line width at the half
of the peak maxima
at the slowest exchange (no exchange)



Intermediate Exchange

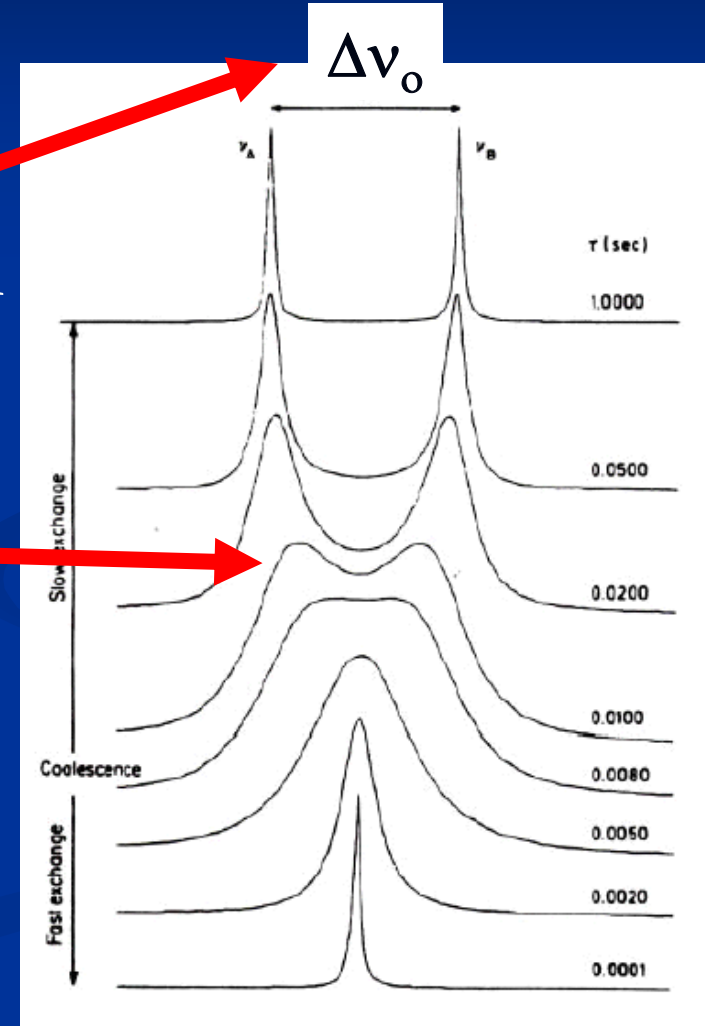
Intermediate Exchange
(more than ~20% overlap)

$\Delta\nu_0$ = the highest separation between two peaks at the slowest exchange

$\Delta\nu$ = separation between two peaks at a given temperature

$$k = \pi \sqrt{\frac{\Delta\nu_0^2 - \Delta\nu^2}{2}}$$

$\Delta\nu_0$ depends on B_0



Coalescence

Coalescence

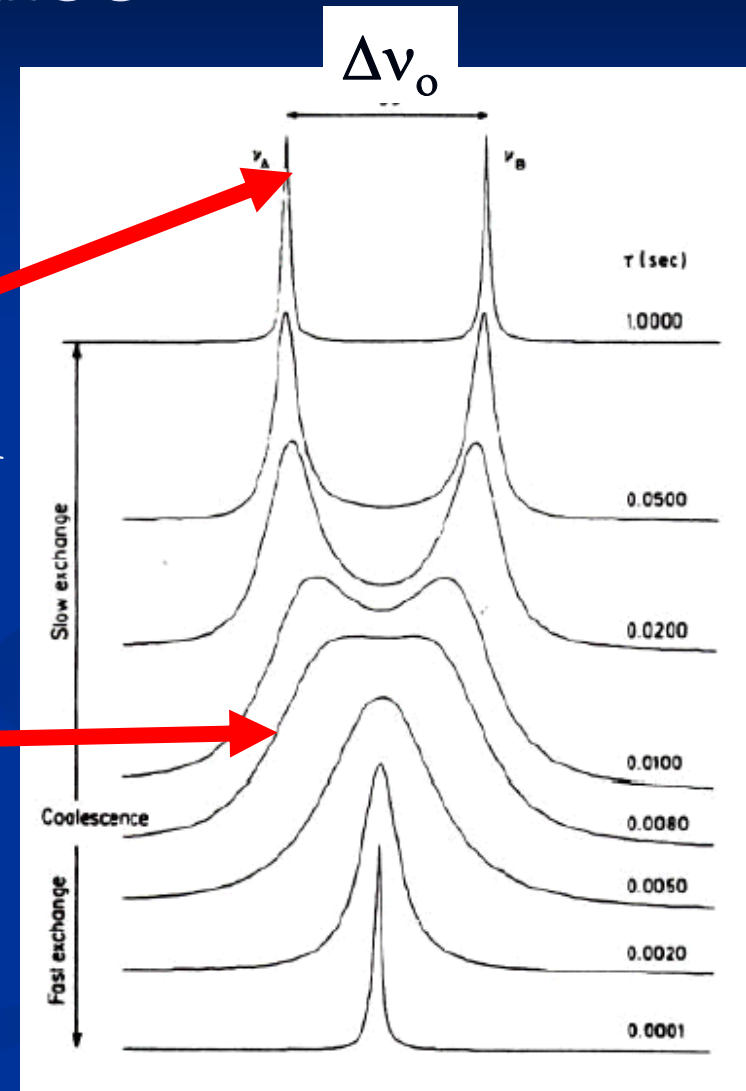
$$k_c = \pi \Delta\nu_0 / 2^{1/2}$$

Coalescence temperature T_c

$\Delta\nu_0$ = the highest separation between two peaks at the slowest exchange

$$k_c = \pi \frac{\Delta\nu_0}{\sqrt{2}}$$

- $T > T_c$, fast exchange
- $T < T_c$, slow exchange



Coalescence

Gutowsky–Holm equation

$$k_c = \pi \frac{\Delta v_0}{\sqrt{2}}$$

$$\Delta G_c^\ddagger = RT_c \left(23.76 - \ln \frac{k_c}{T_c} \right)$$


$$k = \kappa * k_B T / h * \exp(-\Delta G^\ddagger / RT)$$

$$k = \kappa * k_B T / h * \exp(\Delta S^\ddagger / R) * \exp(-\Delta H^\ddagger / RT)$$

Fast Exchange

Fast Exchange

(10 - 15 K above the coalescence point)

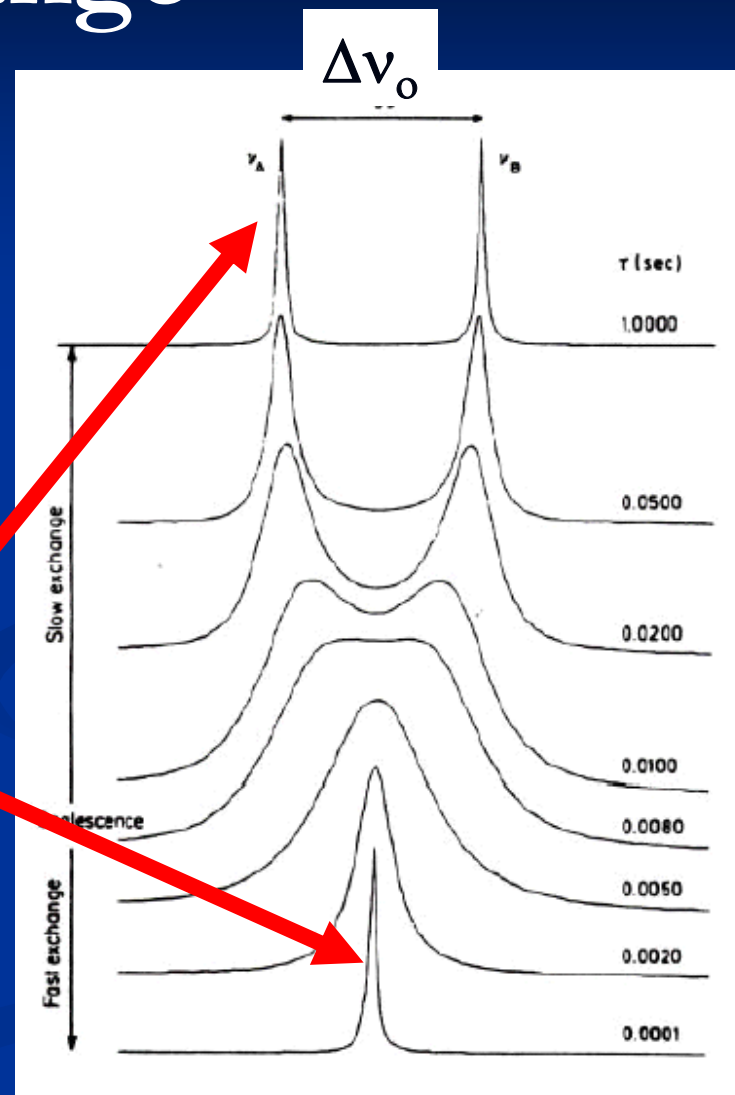
$$k = \pi \Delta\nu_0^2 / 2(\omega - \omega_0)$$

$\Delta\nu_0$ = the highest separation between two peaks at the slowest exchange

ω = line width at the half of the peak maxima at the given temperature

ω_0 = line width at the half of the peak maxima at the slowest exchange (no exchange)

$$k = \pi \frac{\Delta\nu_0^2}{2(\omega - \omega_0)}$$



Fast Exchange

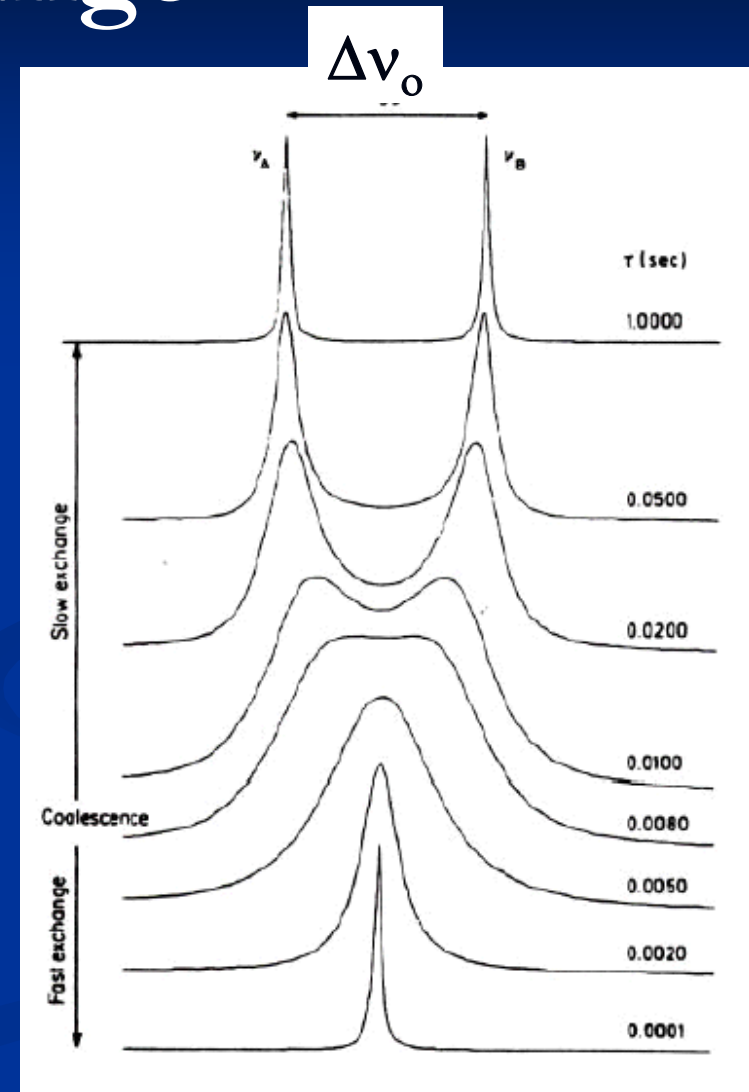
Fast Exchange

(10 - 15 K above the coalescence point)

A single resonance is observed, whose chemical shift is the weight average of the chemical shifts of the two individual states

$$\delta_{obs} = f_1\delta_A + f_2\delta_B$$

$$f_1 + f_2 = 1$$



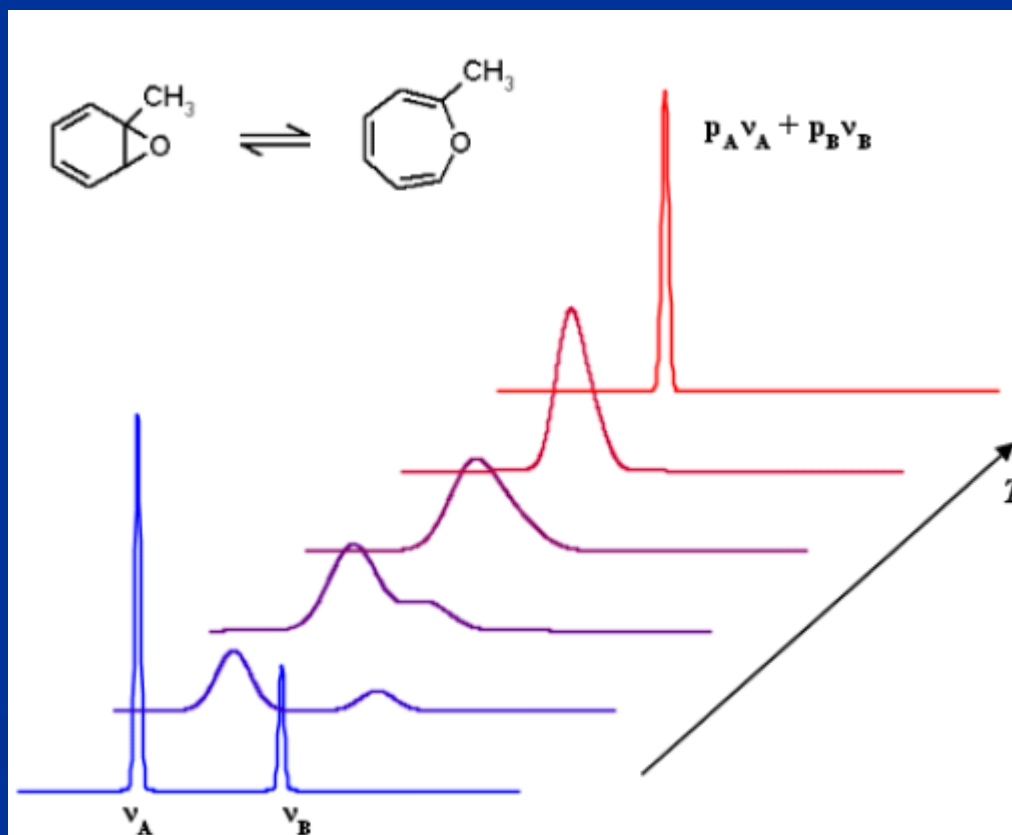
Fast Exchange

Fast Exchange

A single CH_3 resonance is observed, whose chemical shift is the weight average of the chemical shifts of the two individual states

$$\delta_{obs} = p_1\delta_A + p_2\delta_B$$

$$p_1 + p_2 = 1$$

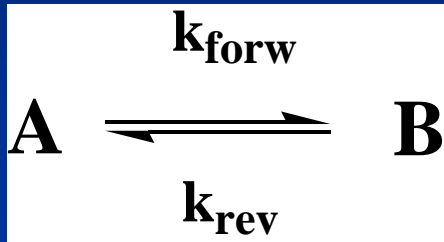


Equilibria

Fast processes (ms) = averaged singlet spectrum on NMR timescale (s)

- equilibria are temperature dependent
- exchanging species have different chemical shifts
- difference in enthalpy similar to the entropy difference times an accessible temperature
- the averaged chemical shift vary with temperature
- the chemical shift measured at many temperatures
- the values of the chemical shifts of each state
- enthalpy difference and entropy difference can be determined by a fitting function

Equilibria



$$K = \frac{[B]}{[A]} = \frac{k_{\text{rev}}}{k_{\text{forw}}} = \frac{p}{1-p}$$

$$\delta = (1-p)\delta_A + p\delta_B$$

Equilibria

$$\delta = (1 - p)\delta_A + p\delta_B$$

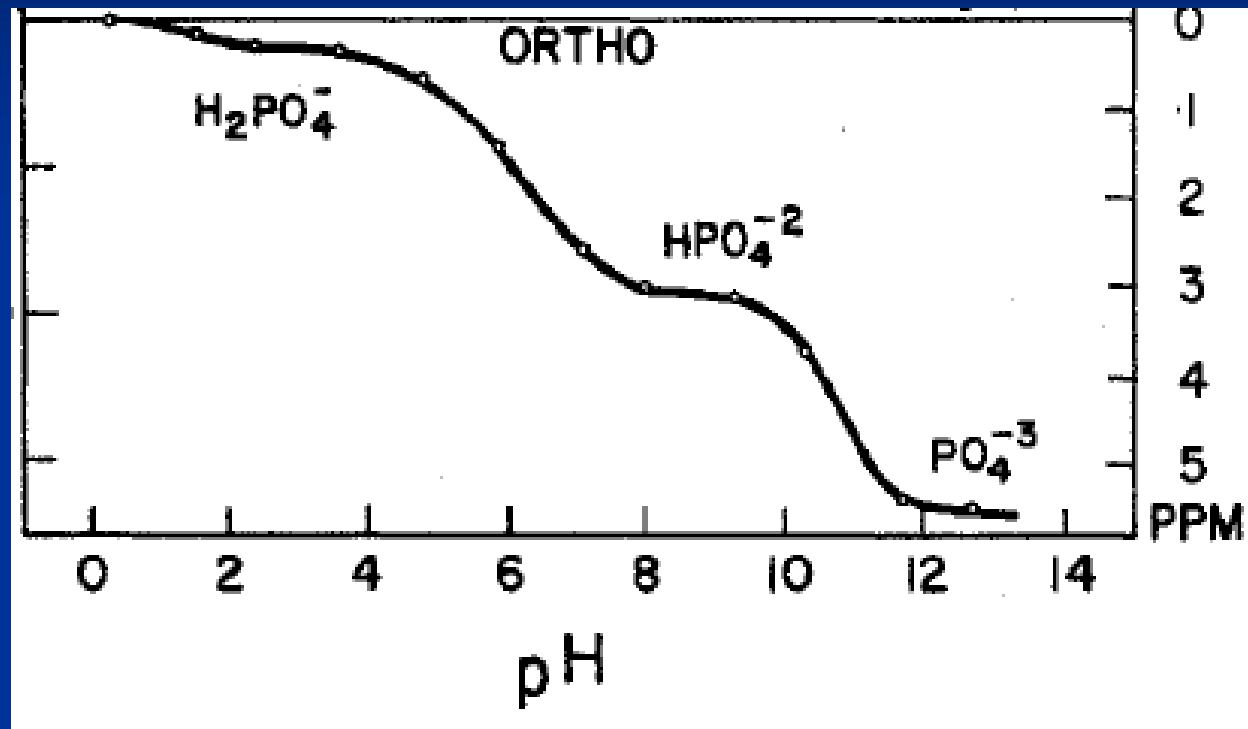
$$K = \frac{[B]}{[A]} = \frac{p}{1 - p}$$

$$p = \frac{(\delta - \delta_A)}{(\delta_B - \delta_A)}$$

$$K = \frac{(\delta - \delta_A)}{(\delta_B - \delta)}$$

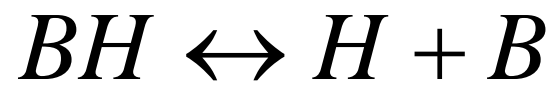
$$\ln K = -\frac{\Delta G^0}{RT} = -\frac{\Delta H^0}{RT} + \frac{\Delta S^0}{R}$$

^{31}P NMR of Orthophosphate



δ (^{31}P)


Acid-Base Equilibria



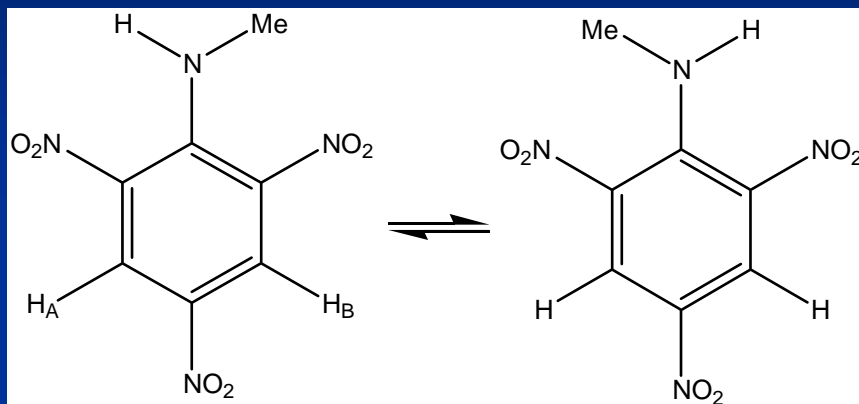
$$K_a = \frac{[H][B]}{[HB]}$$

$$\delta_{obs} = \frac{\delta_B [B] + \delta_{BH} [BH]}{[B] + [BH]}$$

δ_B δ_{BH} measured independently


$$pH = f(\delta_{obs}, \delta_B, \delta_{BH}, pK_a)$$

Exchange in Coupled Systems



$$k_c = \frac{\pi}{\sqrt{2}} \sqrt{(\Delta\nu)^2 + 6J_{AB}^2} = \frac{k_B T}{h} \exp\left(-\frac{\Delta G^\ddagger}{RT_c}\right)$$

Solvents for DNMR at Low Temperatures

Solvent	B.p. °C (1 atm)	M.p. °C (1 atm)
CDCl_3	61.2	-63.5
SO_2	-10	-72.7
Toluene- d_8	110	-95
$(\text{CD}_3)_2\text{CO}$	56	-95
CD_2Cl_2	40	-97
m-Fluorotoluene	116	-111
CS_2	45	-111.5
SO_2ClF	7.1	-124.7
CHCl_2F	8.9	-135
SO_2F_2	-55.4	-136.7
$(\text{CD}_3)_2\text{O}$	-24.8	-141.5
CCl_2F_2	-29.8	-158
Vinyl chloride	-13.9	-159.9
CHClF_2	-40.9	-160
CBrF_3	-57.8	-168
CClF_3	-81.4	-181
Propene	-47.7	-185.2

Solvents for DNMR at High Temperatures

Solvent	B.p. °C (1 atm)
$\text{Cl}_2\text{CDCDCl}_2$	146
CHBr_3	149.5
o-Dichlorobenzene	179
Benzonitrile	190.7
Hexachloro-1,4-butadiene	215
$\text{Br}_2\text{CDCDBr}_2$	240
Diphenyl ether	258

Transition State Parameters

Medium fast (s) exchanges = line broadening.

At the fast regime - a broadened singlet spectrum

Slow exchange - the spectrum splits into two
narrowing to two sharp spectra at slow exchange

Varying the temperature changes the exchange rate
the determination of thermodynamic constants of the
transition state
the transition state parameters for the exchange between
two states at the same energy.

Transition State Parameters

$$k = \pi \delta\nu^2 / 2(w - w_0)$$

$$k = K_B T \exp(-\Delta G^\ddagger / RT) / 2h$$

$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$$

k = rate constant, $\delta\nu$ = peak separation, w = observed line width, w_0 is natural line width, k_B = Boltzmann constant (1.38062×10^{-23} J/molK), R = gas constant (8.3143 J/Kmol), T = temperature, ΔG^\ddagger = free energy, ΔS^\ddagger = entropy, ΔH^\ddagger = enthalpy, h = Plank's constant (6.62620×10^{-34} Js).