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Department of Chemistry
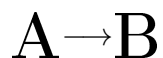## Computational Chemistry Workshop

Potential Energy Surfaces and Reaction Pathways

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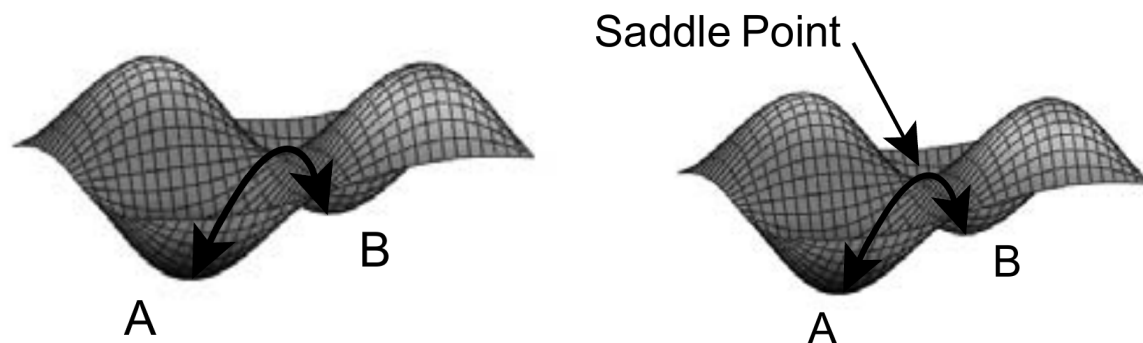angelo.rossi@uconn.edu

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Potential Energy Surface (PES), Transition State, and Saddle Point

A potential energy surface (PES) for the general reaction reaction

$$A \rightarrow B$$

may look like the following:

- The minima are represented by A and B which could be reactant and product, or two conformers.

- The **reaction path** is defined as the pathway between the two minima.

- The reactant passes through a maximum in energy the (**saddle point**) along the reaction pathway, connecting the two minima.

- There are minima in all other directions *perpendicular* to the saddle point on the reaction pathway.

- A transition state is a first order saddle point on a potential energy surface (PES) and has one imaginary frequency. potential energy (E) profile.

Reaction Pathway of a Chemical Reaction

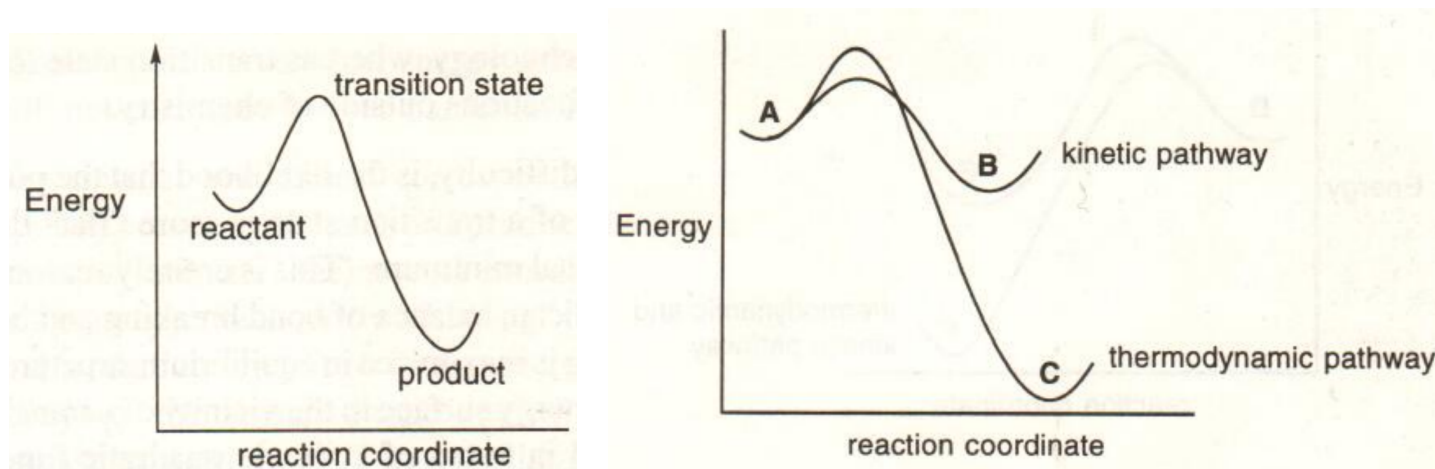For chemical reaction a reaction pathway (PES) might look as shown in Figure 1

Figure 1: Reaction Pathway Showing Reactant and Product Mininma and Transition State

- The minima are represented by **A** and **B**, which could be reactant and product, or two conformers.

- The ***reaction path*** is defined as the pathway between the two minima.

- The reactant passes through a maximum in energy the (***saddle point***) along the reaction pathway, connecting the two minima.

- There are minima in all other directions *perpendicular* to the saddle point on the reaction pathway.

- A ***transition state*** is defined as the geometry at the peak of the free energy (ΔG) profile, while a ***transition structure*** defines the geometry at the peak of the potential energy (ΔE) profile.

Negative Activation Energies

There are several ways that a negative activation barrier might be reported from a computational method. These most often involve errors in treating the system or interpreting the data.

1. The barrier has been measured from reactants at infinite separation rather than from a pre-reaction complex that is lower in energy than the separated reactants.

   This happens most often there is a failure to confirm the TS via IRC and incorrectly assume the reference point.

2. The barrier is computed from free energies, and there is some significant error in the free energy corrections.

   This could be from large errors in entropy, not properly accounting for standard states in bimolecular reactions, etc., ...

3. The transition state and reactants are optimized at one level, followed by single-point energies calculated at a higher level, resulting in a computational artifact.

4. Some very low barriers in the energy surface, especially for hydrogen transfer type reactions, may have large zero point energy (ZPE) that can be above the transition state (TS).

   This gives a negative E_a when considering Gibbs Free Energies, Enthalpies or thermal corrections to E.

   While in some isothemmal reaction, the ZPE might really be above the TS, in significantly exothermal reactions it is most likely an artifact of using an harmonic potential to compute the vibrational frequencies.

5. Before reaching a conclusion, the activation energy must be clearly defined.

   In many computational calculations, it $\Delta E = E(TS) - E(reactants)$, in which case a negative E_a results from a poor computation.

   However, sometimes H or G (i.e. $\Delta H^{\ddagger}$ or $\Delta G^{\ddagger}$) are proposed, leading to confusion about ΔE_a.

   The "correct" activation energy is taken from the Arrhenius equation, $k = A \exp(-E_a/RT)$ as a derivative: $E_a = -R \cdot \frac{d(\ln k)}{(1/T)} = \Delta H^{\ddagger} + RT$ as obtained from Eyring's Transition State Theory (TST) leading to some ambiguity.

The Minima on a Potential Energy Surface

Following minimization, a molecule which is at a minimum on the PES is characterized by frequencies which are all **positive**, implying positive force constants. This means that the energy is a minimum in all directions. In order to verify if a stationary point is a minimum, a vibrational frequency calculation must be performed at the same computational level as for the geometry optimization to ensure that all vibrational frequencies are **positive**.

The Nature of Transition States

The vibrational spectrum of a transition state is characterized by one imaginary frequency, implying a negative force constant. This means that in one direction in nuclear-configuration space, the energy has a maximum, while in all other (orthogonal) directions, the energy is a minimum. In order to verify if a stationary point is a transition state, which connects reactants and products, a vibrational frequency calculation must be performed at the same computational level as for the geometry optimization. The normal mode corresponding to the imaginary frequency in the transition state usually reflects the change in geometry in going from reactants to products.

Locating transition states and estimating reaction barriers can be a rather difficult task. The first step is to obtain a reasonable guess for the structure of the transition state. In general, our intuition is not as well developed for transition states as it is for ground states. In addition, transition-state energies can be close to excited states, and this often implies that the usual MO-based computational methods may not be as accurate for transition states than they are for minima on a PES. A fairly high level of theory is often required to get a good quantitative estimate of a reaction barrier.

But, these exercises will be mainly focused on locating the transition state at lower levels of theory. Once a transition state is found at a lower level of theory, the calculation can be refined by re-optimizing the structure at a higher level of theory.

Intrinsic Reaction Coordinate

Another feature that can be very useful when examining transition states is the Intrinsic Reaction Coordinate (IRC) which is related to the minimum energy path (MEP) and is defined as the steepest descent path starting from the transition state, initially going in the direction of negative curvature in the Hessian. The path can be followed backwards (to reactants) and forward (to products). Following this path can indicate, if the transition state that connects the two minima of interest, has really been found.

The IRC is defined in terms of mass-weighted Cartesian coordinates in the Gaussian program, and it has a well-defined step length. Computationally, once a transition state is found, it is possible to restart from the checkpoint file and perform and IRC.

Statistical Thermodynamics

Briefly, the total energy of a molecule consists, to a good approximation, of additive contributions from its electronic energy, nuclear repulsion, the translational energy, the rotational energy, and vibrational energy. The vibrational energy contribution may be divided into a component corresponding to the zero-point energy, E_{zpe}, which is the sum of the energies of all $\nu = 0$ vibrational levels and a thermal correction ($E_{\text{vib}*}$), derived from a Boltzmann-population for the higher vibrational levels of the system.

$$E_{\text{tot}} = E_{\text{elec}} + E_{\text{trans}} + E_{\text{rot}} + \underbrace{E_{\text{vib}*} + E_{\text{zpe}}}_{E_{\text{vib}}} \tag{1}$$

Contributions from translational, rotational and excited vibrational states are frequently negligible in comparison to the energies of different isomers, but the zero-point correction, where ν_k is the kth vibrational frequency of the molecule,

$$E_{\text{zpe}} = \sum_{k=1}^{3N-6} h\nu_k \tag{2}$$

may be important.

After determining several stationary points and their character on the potential energy surface which correspond to different conformers or electronic states, it may be of interest to determine the population of these states at a specified temperature. In this situation, Boltzmann statistics can be employed. In Boltzmann statistics the fractional population of the ith state is given by:

$$\frac{N_i}{N} = \frac{e^{-\frac{\epsilon_i}{k_B T}}}{\sum_j e^{-\frac{\epsilon_j}{k_B T}}} \tag{3}$$

where N_i is the number of molecules in the ith energy level, ϵ_i, N, the total number molecules, k_B is the Boltzmann constant, and T the temperature in Kelvin where the sum includes all energy states.

A word of caution: to find a transition state with quantum chemical programs is not an easy task. Since a calculation has no way to guess a transition state from a stable structure, it is important to guide the calculation to the desired transition state by providing structures that are close to the final TS. However, this means necessarily, that the outcome of the calculations depends on skill to guess a reasonable TS. There is no guarantee that the calculation, based on the initial guess, will lead to a TS with the lowest energy. If the calculation does not find a desired TS, it may be necessary to start over and provide a better starting structure. In calculating chemical reactions, chemical intuition, experience and luck are crucial for success.

Transition State Theory

From a microscopic point of view, one is interested in understanding the value of the kinetic reaction rate constant, k, from first principles. Phenomenologically, one already knows that k is temberature dependent and obeys the Arrhenius equation

$$k = Ae^{-\frac{E_a}{RT}} \tag{4}$$

where A is a pre-exponential factor, R the gas constant, T the temperature, and E_a is a key quantity, called the activation energy. The larger the value of E_a, the slower the reaction.

More detailed insight into reaction rates can be obtained from the *transition state theory* of Eyring. In this case, one assumes that two reactants, A and B, pass through a special geometrical arrangement, $(AB)^{\ddagger}$-*the transition state*, before decaying to the products C and D according to the equation

$$A + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (AB)^{\ddagger} \rightarrow C + D \tag{5}$$

The assumption of a pseudo-steady state concentration for $(AB)^{\ddagger}$, leads to the rate constant for bimolecular decay is given by:

$$k = K^* k^* \tag{6}$$

where K^* (equilbrium constant for transition state) $= \frac{k_1}{k_{-1}}$.

From Quantum Mechanics,

$$k^* = \kappa \frac{k_B T}{h} \tag{7}$$

where $k_B = 1.38 \times 10^{-38} J/K$ is the Boltzmann constant, h Planck's constant, and κ is a transmission coefficient, which is usually close to unity. The equilibrium constant, K^*, is related to the free energy of the transition state relative to the reactant energies is by:

$$K^* = e^{-\frac{\Delta G^{\ddagger}}{RT}} \tag{8}$$

and

$$k = \frac{k_B T}{h} e^{-\frac{\Delta G^{\ddagger}}{RT}} = \frac{k_B T}{h} e^{-\frac{\Delta H^{\ddagger}}{RT}} e^{\frac{\Delta S^{\ddagger}}{R}} \tag{9}$$

Where $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are the enthalpy and entropy of the transition state. Thus, one identifies the parameters of the Arrhenius equation with:

$$A = \frac{k_B T}{h} e^{\frac{\Delta S^{\ddagger}}{R}}, \qquad E_a = \Delta H^{\ddagger} \tag{10}$$

$\Delta H^{\ddagger}$ can be calculated, but $\Delta S^{\ddagger}$ is slightly more difficult to obtain.

Exercises

Inversion of Ammonia, NH_3

A simple example of tracing a reaction path involves the inversion of ammonia, which proceeds from an initial pyramidal C_{3v} equilibrium geometry through a planar D_{3h} transition state, and back to an inverted pyramidal C_{3v} equilibrium geometry as shown in Figure 2:
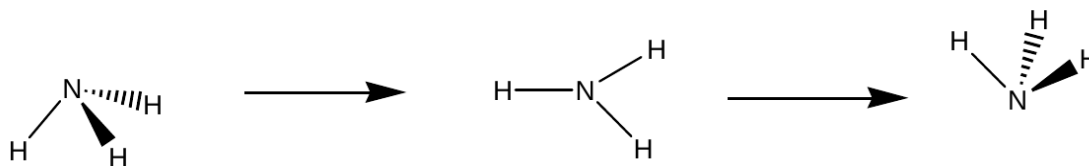

Figure 2: Inversion of Ammonia, NH_3

1. Optimize both the ground state and the transition state by imposing the proper symmetries.

2. Calculate vibrational frequencies for both the ground state and transition state.

   Label the frequencies according to the appropriate symmetry representations.

3. Locate the single imaginary frequency, and examine the corresponding normal mode. Verify that it corresponds to the inversion mode.

   What is the symmetry respresentation of the imaginary frequency. Does it make sense? Explain.

4. Perform an IRC calculation which shows the path connecting the two pyramidal structures.

   Use an appropriate step size, and sufficient steps to unambiguously establish the reaction path.

5. Locate the energies of reactants, products and transition state in their respective **.log** files.

   Calculate the activation energy, as well as the ΔG between reactant and product. The output from frequency calculations should provide information about ΔG energies.

   Using these results and those of the IRC calculation construct a reaction energy diagram, similar to the one in Figure 1, showing the reactant, transition state, and product for the inversion of ammonia, and be sure to include energies and label everything appropriately.

Isomerization of $H - C \equiv N$ to $C \equiv N - H$

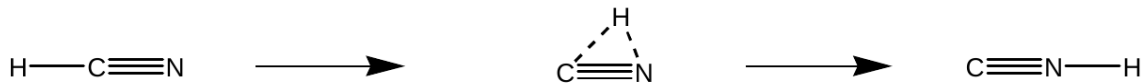As an example of a transition state search, consider the process of hydrogen migration shown in Figure 3:

Figure 3: Isomerization of $H - C \equiv N$ to $C \equiv N - H$

1. In this case, the minima of H−C≡N and C≡N−H can be obtained in the usual fashion, and verified as minima by calculating vibrational frequencies.

2. Next, construct a reasonable estimate of the transition state geometry by changing the $< \mathbf{H - C - N}$ angle from 180° to about 60°, but the H−C and N−H bond distances should be elongated as well.

   Then, perform a transition-state optimization using this initial geometry.

3. Optimizing to a transition state always requires the additional calculation of vibrational frequencies, because verification that there is precisely one imaginary frequency must be ascertained.

   After the calculation finishes in Step #2 finishes successfully, perform a frequency calculation, and view the vibrational frequencies using visualization software.

   One frequency should be imaginary, and the corresponding normal mode represents the hydrogen migration. Also, examine the other normal modes in the transition state.

4. Perform IRC calculations, in both the forwared and reverse directions, which shows the path connecting the **H-CN** and **CN-H** structures.

   Use an appropriate step size, and sufficient steps to unambiguously establish the reaction path.

5. Locate the energies of reactants, products and transition state in their respective **.log** files.

   Calculate the activation energy, as well as the ΔG between reactant and product. The output from frequency calculations should provide information about ΔG energies.

   Using these results and those of the IRC calculation construct a reaction energy diagram, similar to the one in Figure 1, showing the reactant, transition state, and product for **HCN** isomerization reaction, and be sure to include energies and label everything appropriately.

Isomerization of $CH_3 - C \equiv N$ to $C \equiv N - CH_3$

Repeat the above steps for the isomerization of methyl isocyanide $(CH_3 - C \equiv N)$ to $C \equiv N - CH_3$.

What energetic changes would you expect when H is replaced with a CH_3 group?

Explain those differences on the basis of changes in electronic structure of the substituents.

SN2 Reactions

In an SN2 reaction a lone pair from a nucleophile attacks an electron deficient center and bonds to it, expelling a leaving group. For instance, the anion Cl^- can attack CH_3Cl. The reaction profile looks similar to the following figure:
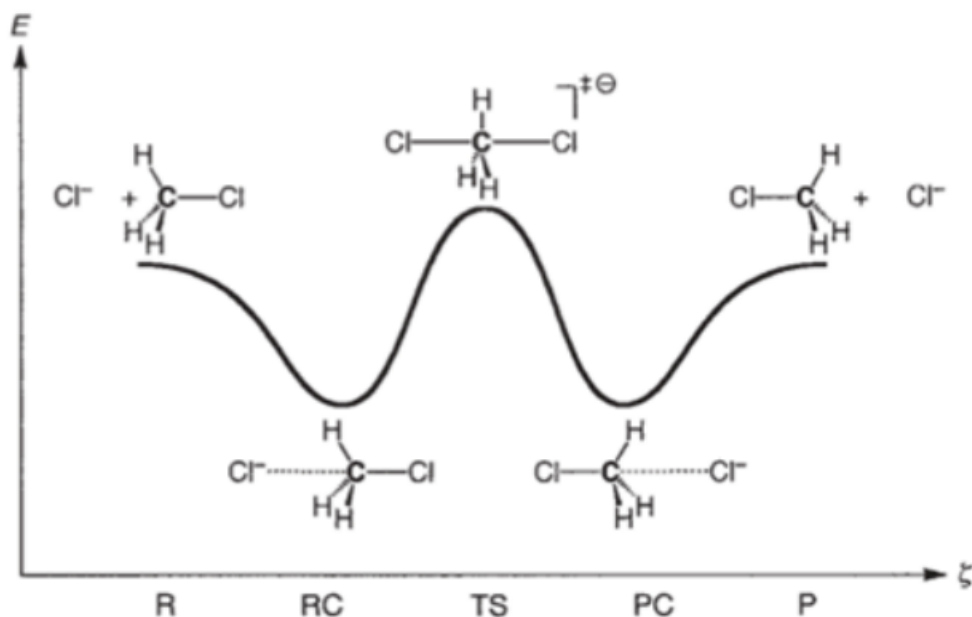

Figure 4: On the x-axis along the reaction coordinate, ζ, the stationary points are abbreviated R = Reactants, RC = Reactant Complex, TS = Transition State, PC = Product Complex and P = Products. The y-axis corresponds to energy.

In these exercises, a series of reaction barriers will be calculated, followed by a frequency analysis to validate which are minimum energy structures, or which are transition state structures.

How does one distinguish from a minimum energy structure (e.g. an RC or ion-dipole complex) and from a transition state structure (TS) based on a frequency analysis? Which conditions must be satisfied? What would would be defined as the reaction barrier? If a comparson of a series of reactions is performed, is it possible to predict which reaction most likely takes place and what factors should be taken into account?

SN2 Exercises

The objective of this exercise involves finding stationary points of SN2 reactions, and making predictions about the reaction rate.

$Cl^- + CH_3Cl$ Reaction

- What is the nature of the reactants?

- Optimize the structure of all reacting species, and perform a frequency analysis on the stationary points along the reaction coordinate to determine the minima and transition state (TS).

  The TS is located at a saddle-point on the PES landscape obtained in potential energy scan.

- Perform an Intrinsic Reaction Coordinate calculation to obtain an approximate reaction path over the transition states between reactants and products.

  Does the result look like the energy profile depicted above?

- The transition states for this SN2 reaction is special cases because it is symmetric.

  Therefore, a much faster way of finding the transition state is the imposition of D_{3h} symmetry. Optimize the TS for a structure with D_{3h} symmetry and compare it to the previously calculated structure.

- How would the energy profile change if the reaction were performed in H_2O?

$Br^- + CH_3Cl$ Reaction

- Redo the above SN2 reaction, but now replace the reacting Cl^- ion with a Br^- ion.

- Calculate how many times the SN2 reaction with Cl^- is faster or slower compared to the SN2 reaction with Br^-.

  Hint: use the Arrhenius equation and assume that the prefactors A are identical for both reactions.

SN2 Background Information

- A. P. Bento, M. Sol, and F. M. Bickelhaupt, J. Comput. Chem. 26, 1497-1504 (2005)

- A. P. Bento, M. Sol, and F. M. Bickelhaupt, J. Chem. Theory Comput.4, 929-940 (2008), Erratum

- A. P. Bento and F. M. Bickelhaupt, Chem. Asian J. 3, 1783-1792 (2008)

Appendix: Important Reminders for Gaussian 16

- If geometric or basis set data is entered into a G16 input file, as opposed to reading it from the checkpoint file, end the input file with a blank line.

- In general, to find transition states, use **opt=(ts,calcfc)** keywords.

  If a transition state has a different symmetry from other points along the reaction path, then optimize the transition state in this unique symmetry, then do not use **opt=(ts,calcfc)**.

  If symmetry is preserved or there is no symmetry along the reaction path, then use **opt=(ts,calcfc)**.

  It may be necessary to eliminate a symmetry constraint entirely, and include the **nosymm** keyword when searching for a transition state.

  When looking for a TS, it is often helpful to use **opt=(ts,calcfc,noeigentest)**. The other keywords besides **ts** equest calculation of analytic force constants on the first step (**calcfc**), and that the job not stop, if other than exactly one negative force constant is found at some step (**noeigentest**).

- A great deal of CPU time can be saved by re-using information from previous calculations stored in the checkpoint file. Plan your calculations to try to save time. CPU time can also be saved by using symmetry when appropriate.

- The keywords **guess=read**, **geom=checkpoint**, and **guess=allcheck** read a previously calculated wave function, a previously calculated geometry, or both previously calculated geometry and wave function, respectively, from the last completed calculation.

  If an optimization calculation has been just performed, then a frequency calculation should certainly use these keywords.

  The old checkpoint file (**%OldCheck**) should be specified, when reading data from a previously completed calculation. For a combined optimization and frequency calculation, it is also possible to include both the **freq** and **opt** keywords in the same job.

  Frequencies must be calculated using the same level of theory and basis sets with which the geometry was optimized, in order to produce a consistent set of vibrational frequencies.

- An optimized geometry calculation at one level of theory, can be repeated at a different level by including the keyword **opt=(readfc)**, or **opt=(ts,readfc)** for a second pass at a transition-state optimization. This causes G16 to start with the force constants from the previous calculation and, may be efficient.

  It is usually a good idea to work your way up from a smaller basis set to a larger, more accurate basis set when performing a a geometry optimization so that computer time is not wasted because of a bad initial guess.

- An example of the G16 keyword for IRC is given by **irc=(forward,maxpoints=20,stepsize=10)** which involves taking 20 steps in the product (forward) direction from the TS.

- The **freqchk** utility of G16 may be used to rerun the thermochemical analysis, for a different temperatures, from the frequency data stored in a Gaussian checkpoint file. An additional frequency calculation is not needed for this.