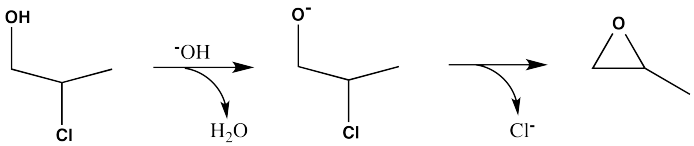
8 Finding Transition States and Barrier Heights: First Order Saddle Points

So far, you have already considered several systems that did not reside in a minimum of the potential energy surface. Both the bond breaking in the dissociation of H_2 as well as the internal rotation of butane were examples of off-equilibrium processes, where the system moves from one equilibrium conformer, *i.e.* from one minimum, to another. It is intuitively clear that the likelihood of two equilibrium conformers to be transformed into each other by moving along *some* random path is negligible, and different methods have been established to find reasonable paths for such transitions. A frequently used approach is *transition state theory*, which is concerned with finding a realistic path between potential energy minima. In this set of exercises, you will search for the transition state for a the cyclisation of a deprotonated chloropropanol to propylene oxide, and you will find the minimum energy path that connects reactants to products via this transition state.

8.1 Synthesis of Propylene Oxide

Corrosive propylene oxide (*cf.* figure 1) is the simplest chiral epoxide and of great industrial importance. The historically most important synthesis is based on hydrochlorination and ring closure of the resulting chloropropanols in a basic environment:



The resulting epoxide is most often directly used as a racemate.

a) What kind of reaction mechanism would you expect? Would you expect the stereochemistry at the chiral carbon to be preserved? Identify the chirality centre in the chloropropanoate and the product epoxide.

b) Suggest possible transition state structues.

Figure 1: Propylene oxide is a toxic, cancerogenic liquid that is produced on large industrial scale.

8.2 Transition State Theory

Any chemical reaction is nothing but a mere rearrangement of nuclei, and all the possible ways the nuclei could rearrange span a plethora of possible paths. Hence, there are usually many paths on the potential energy surface (PES) that connect reactants and products, and depending on the energy of the system, more or less of these paths will be accessible for the chemical transformation. Finding all of these paths is a daunting task, as all the involved degrees of freedom have to be mapped out of the full PES onto a reduced - but still multidimensional - PES. The study of these *rare events* using various mapping techniques is an involved subject; various elaborate techniques exist for elucidating possible paths. They are, however, often linked to computationally expensive molecular dynamics simulations (MD) and are more concerned with studying the free energy surface (FES; including entropic effects) rather than just the PES. For the study of the latter, simpler models exist, often yielding a qualitatively sufficient picture to explain many chemical transformations.

A Minimum (Potential) Energy Path

The fundamental concepts that greatly simplify the problem of finding reactive pathways on the PES were introduced as early as the nineteenth century, and in the 1930ies, their development culminated in a model called *Transition State Theory*. Assuming that the

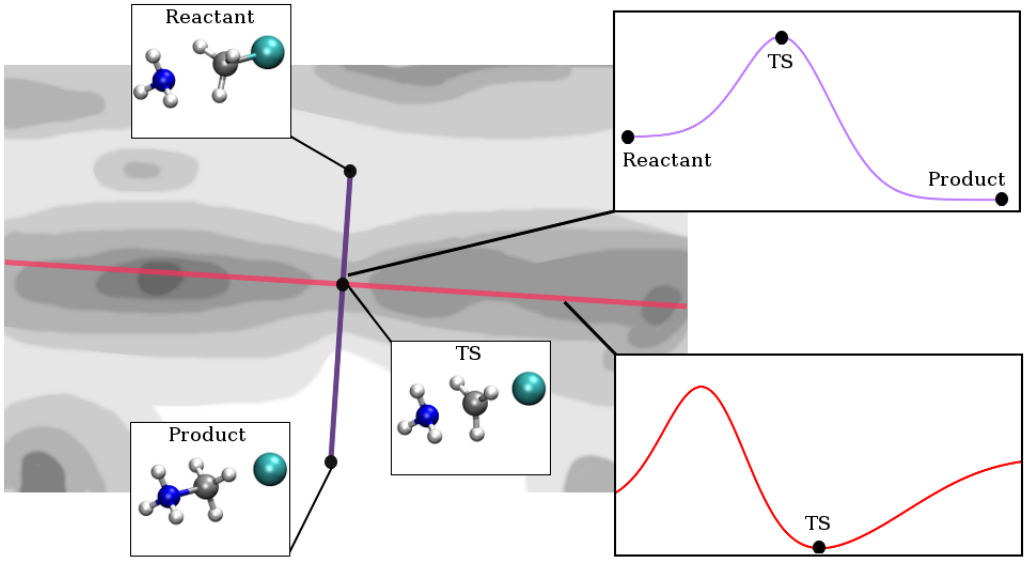


Figure 2: Visualisation of transition state theory in a ficticious 2D PES. Dark areas correspond to high-energy regions, whereas brightly coloured areas correspond to energetically lower lying states. Reactants and products are connected through a minimum energy path via a first-order saddle point, the transition state.

most likely path is also the unique path by which a reaction proceeds, one searches for the *minimum energy path* connecting reactants and products along the reaction coordinate. The energetically highest point along this path is a stationary point, the *transition state* (*cf.* figure 2). There is a striking analogy with lazy hikers that want to get from one valley to another: They will not choose the steepest path across a peak of 4000 m altitude, but they will rather choose a mountain pass (a *col*) to reach their destination with least effort. The villages in the valleys correspond to reactant and product states: In all directions, the path goes uphill.
It is straightforward to see from this analogy that the transition state is given by a *first order saddle point*. Along all possible coordinates except the reaction coordinate, the potential energy surface goes uphill; along the reaction coordinate, it goes downhill. This implies that the transition state is the highest energy point *along* the reaction coordinate, but the lowest energy point *perpendicular* to the reaction coordinate. This gives raise to the typical transition state diagrams that are frequently used to describe simple reactions in organic chemistry.

From Curvature to Vibrational Frequencies: The Hessian

(Local) Minima and saddle points of any order are all *stationary points*, stable points on the potential energy surface where the curvature is zero. This implies that the first derivative matrix of the nuclear coordinates vanishes at any stationary point. However, this information will not be sufficient to classify the nature of the stationary point. The matrix of second derivatives, the *Hessian*, has to be used instead. The Hessian matrix can be diagonalised, and the resulting eigenvalues contain the desired information on the stationary point: If all eigenvalues are negative, the corresponding geometry constitutes a local maximum; if they are all positive, the geometry corresponds to a local minimum. If positive and negative eigenvalues occur, one is dealing with an N^{th} order saddle point. The task of finding a transition state using the Hessian matrix of the system is therefore easy: One searches for the geometry that yields a Hessian with exactly one negative eigenvalue, *i.e.* a first-order saddle point - the transition state. (Similarly, the eigenvalue test can also be used to check whether a geometry optimisation has found a true minimum, or whether it is blocked in a flat region of the PES.)
The Hessian of the system contains further useful information. For instance, in the approximation of a *harmonic oscillator* in a quadratic potential, the vibrational eigenvalues are known:

$$E_\nu = \left(\nu + \frac{1}{2}\right)\hbar\omega \quad ; \quad \omega = \sqrt{\frac{k}{m}}, \tag{111}$$

where k is a force constant and m is the (reduced) mass of the oscillator. By locally approximating the PES to be harmonic, the (decoupled) vibrational frequencies for the corresponding geometries can be calculated from the Hessian matrix: It turns out that k is simply given by the eigenvalues of the Hessian evaluated in mass-weighted coordinates. For equilibrium geometries with positive Hessian eigenvalues, the molecular vibrational frequencies ω (as observed in IR spectroscopy) can easily be calculated, and

the corresponding vibrational modes can be visualised. The possiblity of visualising the frequencies opens up a valuable tool in the transition state search: As a first order saddle point will have one negative eigenvalue, the corresponding frequency will be imaginary. By visualising this imaginary frequency, one can immediately verify whether one has found a TS of interest, or just another, non-relevant first-order saddle point on the TS: If the imaginary vibrational node corresponds to a motion that transfers reactants to products, the search was successful.

8.3 Locating Transition States: Constrained Optimisations

Unlike a geometry optimisation, a transition state search requires more than just *some* guess. Finding the transition state from a reactant or a product structure will be computationally unfeasible, as those structures are given by local minima on the PES. Hence, all possible paths originating from these minima will go uphill (recall the mathematical definition of a minimum with respect to its derivatives), and it cannot be clear in advance which paths will actually connect reactants and products, or which path(s) will proceed *via* the lowest lying transition state. Instead, one needs a guess that is reasonably close to the real transition state, such that the *curvature* of the potential energy surface close to the TS is known, making it possible to proceed uphill along the reaction coordinate until the transition state is reached. The general procedure for a transition state search includes the construction of a guess geometry that should be reasonably close to the expected TS, followed by a *constrained optimisation* (*cf.* figure 3).

In a constrained optimisation, all degrees of freedom which are not deemed relevant for the reaction are relaxed, whereas the relevant degree(s) of freedom is (are) kept fixed. After the optimisation, the curvature of the PES is evaluated at the chosen geometry (either analytically or numerically, *cf.* the following section). If the constrained degree(s) of freedom was (were) suitably chosen, the paths associated to the unconstrained N-1

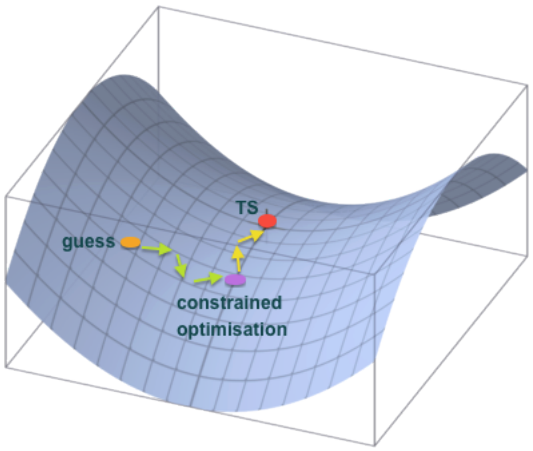


Figure 3: Finding a transition state from an initial guess by performing a constrained optimisation followed by a TS search.

degrees of freedom will go uphill in both directions, indicating that the corresponding structural parameters were properly relaxed. There should be one degree of freedom remaining that is associated to a path that goes downhill on one side and uphill on the other side: This will be the path that leads uphill to the transition state. As the associated degree of freedom is then known, the geometry can then be optimised to a transition state by selectively 'walking uphill' along this specific path.

Constructing a Guess

The easiest way of constraining certain parameters in a structure is using a suitably defined Z-matrix rather than xyz coordinates (recall the dihedral scan of butane). Launch Molden to construct a transition state guess for propylene oxide, starting from the *deprotonated* starting material. In the `ZMAT Editor`, create a `CH4` moiety and substitute the hydrogen that has no angle specification by a `-CH3` group. Substitute the hydrogen atom that is defined by only a bond length and angle by a chlorine atom (simply change the element specification in the editor). Then, find out which hydrogen atom of the methyl group that you added has a dihedral that is specified with respect to all the carbons and the chlorine atom. Replace it by an oxygen atom. Then, substitute one of the hydrogens that sits on the chlorine-substituted carbon by another methyl group. You now have a structural barebone for your transition state, but you still need to adapt the conformation to be reasonably close to the transition state. For the TS, one expects that the C-Cl bond will already be elongated, whereas the oxygen atom will start to form the epoxide ring. Change the bond angle of the oxygen atom to something smaller, such as 80°, and change the bond length to something typical for a C-O bond, 1.43 Å. Modify the bond length for the C-Cl bond to an elongated 2.40 Å. Finally, one would expect the substituents of the carbon at which the substitution takes place to be almost planar; whence, change the dihedral for the corresponding hydrogen and carbon to 100.0° and -100.0° respectively. Save the structure as a Z-matrix in Gaussian format.

a) Take a screenshot of the transition state you constructed.

Write the header for a Gaussian input file:

```
%NProcShared=2
%Mem=1GB
#P B3PW91/6-31+G* Opt=(ModRedundant)

Propylene oxide

-1 1
```

where `Opt=(ModRedundant)` makes Gaussian read additional information on the Z-matrix such as constraints or modifications. As we lack the information of how quickly the ring is formed when the chlorine is dissociating, it is safest to only constrain the C-Cl bond to the slightly elongated length that you specified in the Z-matrix. (As a reminder, a C-Cl bond around equilibrium should be shorter than 2 Å.) Close and save the file. To

create the complete input file including all constraint information, append the Z-matrix to the Gaussian input header:

```
cat z_matrix >> gaussian_input
```

Open the Gaussian input file again and go to the bottom of the file. Add a blank line, followed by:

```
B 1 3 F
```

This forces Gaussian to constrain a bond (`B`) between atoms `1` and `3`, keeping the current bond length fixed (`F`). All the other variables of the Z-matrix will be allowed to relax during the optimisation. If you constructed the Z-matrix according to the above instructions, this will keep the C-Cl bond length from changing. Submit your job to Gaussian. If the job terminates normally, open the output in Molden and observe the changes in the structure during the constrained optimisation. Save the last, optimised structure as a new Z-matrix.

Frequency Analysis

Prepare a frequency calculation to verify that the Hessian yields only one negative eigenvalue:

```
%NProcShared=2
%Mem=1GB
%Chk=Freq
#P B3PW91/6-31+G* Freq

Freq

-1 1
```

`Freq` instructs Gaussian to perform a vibrational frequency analysis. Append the Z-matrix from the constrained optimisation to the input file:

```
cat new_zmatrix >> freq_input
```

Run the job and open the output file in Molden. In the Molden menu *Frequencies*, click on `Norm. Mode` and check the number of imaginary frequencies (which correspond to the longed for single negative eigenvalue of the Hessian). By clicking on the frequency, you can visualise the corresponding normal mode. You may also explore some other vibrations of the system, the intensity of which you may adjust by modifying the `Scale Factor`. If you find only one imaginary frequency, and if this frequency corresponds to a movement that links reactants and products, you have found a reasonable guess for the TS.

Finding the Transition State

You may now locate the first order saddle point that is associated to the imaginary frequency (negative Hessian eigenvalue). Create the following input file:

```
%NProcShared=2
%Mem=1GB
%OldChk=Freq
%Chk=TS
#P B3PW91/6-31+G* Opt=(RCFC,TS,noeigentest) Guess=Read Geom=Checkpoint

TS search

-1 1
```

In order to avoid explicitly writing the coordinates, we restart from the `Freq` geometry (`Geom=Checkpoint`) and wavefunction (`Guess=Read` using `%OldChk=`. `RCFC` specifies that the Hessian was pre-computed in the old Checkpoint file, which makes it possible to skip the calculation of the Hessian at the beginning of the TS run. `TS` indicates that a transition state rather than a minimum should be searched, and `noeigentest` is an (unethical) trick that we use to speed up the calculation for the exercises. Submit this job to Gaussian. Once it terminates, check in the output whether a `Stationary point` was found. Then, open the output file in Molden and follow the TS optimisation.

b) Take a screenshot of the optimised transition state structure. How did the structure change with respect to the constrained-optimised guess?

Finally, you may want to make sure that there was no error during the TS optimisation (which could happen with `noeigentest`), and that the imaginary frequency at the first-order saddle point still corresponds to the one you found after the constrained optimisation. Create another frequency job:

```
%NProcShared=2
%Mem=1GB
%OldChk=TS
%Chk=TSFreq
#P B3PW91/6-31+G* Freq  Geom=Checkpoint Guess=Read

TS Freq

-1 1
```

Open the output of this frequency job in Molden and analyse the vibrational modes. Save the optimised Z-matrix and the `TSFreq` Checkpoint file. Save these files somewhere where they will be accessible in the next exercise sesssion (you will need them).

c) Take a screenshot of the spectrum and note the imaginary vibrational mode. What motion is this mode related to? Do the same for two real vibrational modes of your choice.

d) Is the transition state you predicted an early or a late transition state?

e) Having found a transition state, how would you now obtain the barrier height for your reaction?

f) Are there ways of verifying whether you have found a meaningful transition state? **Bonus:** How would you define 'meaningful' in this context?