

Lab 3:

Modeling Reaction Mechanisms and Kinetics

In this third computer exercise, you will learn how to identify and optimize the geometries of transition states. You will also construct a potential energy diagram and investigate the effect of solvation on an S_N2 reaction.

Methods:

In this exercise, the level of theory will be Density Functional Theory (DFT), using the B3LYP functional. Use the Def2-SVP basis set for all optimizations and subsequent frequency analyses. Use Grid4 for all calculations except for the scan, for which this keyword should be omitted. Other specifics will be provided below.

Optimization of Reactants, Products and Intermediates:

The focus of this lab is the S_N2 reaction between chloride and bromomethane:



This is a bimolecular reaction mechanism that involves free species, pre- and post-reaction complexes and one transition state structure.

First, build and optimize the molecules CH₃Br and CH₃Cl. Note the bond length between the halides and the carbon. Also compute the energies of the isolated Cl⁻ and Br⁻ anions.

Next, take the optimized CH₃Br molecule and place the chloride anion at a distance of ≈3.7 Å from the methyl carbon. Optimize the geometry of the pre-reaction complex. Remember to correctly input the charge of the complex. Do the same for the post-reaction complex.

Follow up all optimizations in this lab with a frequency analysis, and take note of the Final Gibbs free enthalpy, G, **and** the Gibbs free enthalpy minus the electronic energy, G-E(el). ORCA per default calculates the thermochemical properties at 298 K.

Importantly(!): The Gibbs energy calculation will fail for Cl⁻ and Br⁻, because the vibrational entropy correction term includes a divide by zero (there are no vibrational frequencies). Calculate the total Gibbs energy for Cl⁻ and Br⁻ as: $G = H - T S_{\text{trans}}$, where H is the total enthalpy and T*S_{trans} is the translational entropy, as written out by ORCA. You can then calculate the G-E(el) correction manually by subtracting the final single point energy, E(el).

Before moving on to the transition state search: which structure before the transition state has the lowest Gibbs energy? This structure will be your reference point, ΔG = 0.0, when drawing a reaction profile.

Searching for a Transition State:

To search for the approximate transition state structure, we begin with the optimized pre-reaction complex, and scan the Cl-C bond distance. This means optimizing the structure while keeping the Cl-C distance frozen at different values. Scan from 2.9 to 1.9Å with 0.2Å increments. Use the following commands in your input file:

```
! def2-SVP B3LYP Opt
%geom
    Scan B NC NCl = 2.9, 1.9, 6
end
end
```

where N_C and N_{Cl} are the atom numbers of the carbon and chlorine atoms in your structure. The indices correspond to the order in which the atoms are listed in the structure coordinates. You can visualize the numbering in Avogadro by going to *Display settings* and selecting *label*. Select the *Tools* icon and mark *Atom number*. **Importantly(!):** The numbering in the Scan block in ORCA starts from 0 while it starts at 1 in Avogadro, therefore subtract 1 from the indices given by Avogadro.

The energies of the constrained minimizations are listed at the end of the output file, together with the corresponding value of the scan parameter under the header ‘The Calculated Surface using the ‘Actual Energy’’. ORCA produces xyz files describing the molecular structure at each step along the scan. They are named corresponding to the step number, for example *name.001.xyz* would be the structure at the first step of the scan. Use the structure corresponding to the highest point in the energy profile as your guess input for a full transition state optimization followed by a frequency analysis. Use the following in your input for a TS optimization:

```
! def2-SVP Grid4 B3LYP OptTS Freq
%geom
    Calc_Hess true #Calculates the exact Hessian before optimization.
end
```

The transition state is a saddle point on the PES, and must be a minimum in all but the reaction coordinate. This means the transition state must be characterized by one, and only one, imaginary frequency. The frequencies of the optimized structure are listed under the last instance of the header “VIBRATIONAL FREQUENCIES”. Once one imaginary frequency has been confirmed in the output file, visualize the imaginary mode in Avogadro. To do this, generate a xyz trajectory file by writing the following in in command prompt:

```
orca_pltvib name.hess Iimag
```

where I_{imag} is the index of the transition state mode found in the output file. Take note of the imaginary frequency of the transition state, and the halide-carbon bond distances for all structures. If the structure you find does not have an imaginary frequency you can redo the initial scan with more steps than 6. Look at the Mulliken charges of the halides and the carbon atom at each structure. Draw the charges together with the different structures on top of the now-calculated potential energy diagram of the reaction.

Single Point Calculations

To get more accurate energies perform single point calculations at the B3LYP/Def2-TZVPD level of theory on all stationary points and the transition state. Single point = no geometry optimization.

Add the Gibbs energy corrections, G-E(el), calculated previously with the smaller basis set, to correct the new total energies for thermal and entropic effects. This so you *do not* have to do the frequency calculations with the large basis set, which is very time consuming:

$$G = E_{\text{Def2-TZVPD}} + G\text{-E}(\text{el})_{\text{Def2-SVP}}$$

Add the newly calculated relative Gibbs energies, ΔG , for each structure, to the reaction diagram to illustrate the effect of a larger basis set. Briefly discuss differences.

Solvent Effects:

Thus far you have only considered the reaction in the gas-phase. ***Before you do any calculation*** discuss with each other what you expect will happen when the reaction is instead taking place in a *polar* solvent. Will the barrier get larger or smaller? If your chemical intuition is failing (due to lacking training in organic chemistry), can the calculated Mulliken charges give you a guide?

To estimate the solvent effect set up three single point calculations with the Def2-TZVPD basis set. Calculate the pre- and postreaction complexes and the transition state using implicit consideration of dimethylformamide (DMF) solvation. To do this, add CPCM(DMF) to the input line.

Correct also these energies for thermal effects by adding the G-E(el) energies calculated in the gas-phase. Add the new solvated ΔG values to the earlier reaction profile (in the same figure, if able), and discuss differences. The experimental barrier height in DMF solvent is 17.7 kcal/mol. (G. Caldwell et al., *J. Am. Chem. Soc.* **1984**, 106, 959). How close do you get?

Rate Estimation

Once you have calculated the relative Gibbs energy of the transition state, you can estimate the rate of reaction in DMF using Transition State Theory (TST) and the Eyring equation.

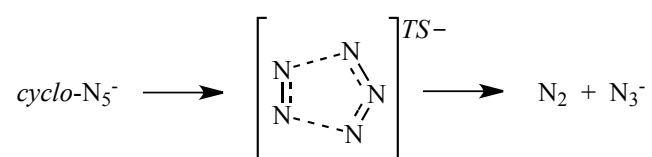
$$k = \kappa \left(\frac{k_B T}{h} \right) e^{-\Delta G^{TS}/RT}$$

(assume the transmission coefficient κ is unity)

Energetic Extra Assignment 3:
(to be included in individual lab report for higher grades)

Cyclopentadienide, *cyclo*-C₅H₅[−] is a known stable (and aromatic) anion and a common ligand in metallocenes. C₅H₅[−] is isoelectronic with the pentazole anion, *cyclo*-N₅[−]. Do you think it could be possible to prepare and handle *cyclo*-N₅[−] under ambient conditions? First, discuss what you expect, note arguments for and against. Then predict the stability using calculations!

Investigate the following decomposition mechanism:



Use the techniques learnt in the labs thus far to find the transition state and estimate a rate constant for the unimolecular decomposition of *cyclo*-N₅[−]. Before you start you now have a choice to make:

Either trust you can make a decent enough guess of the transition state structure from scratch (think half-broken bonds), and directly proceed to a transition state optimization. Or, alternatively, take the long way around, and begin by doing a scan of the reversed cycloaddition reaction. This type of scan is more involved since two bonds needs to be stretched simultaneously (instructions are found at the end).

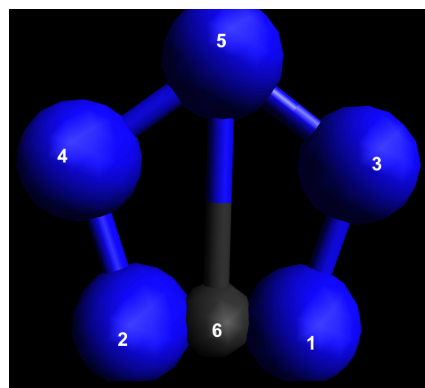
Confirm that the structure you identify is a true transition state by ensuring that it has one (and only one) imaginary vibrational mode that corresponds to the right reaction coordinate. When you have identified the right transition state structure, with or without using a scan, you need to figure out if the structure is high enough in energy relative to the ground state to allow for kinetic persistence of *cyclo*-N₅[−]. Assuming first-order rate kinetics, calculate the half-life of *cyclo*-N₅[−] in a water solution at room temperature. To include the solvent effects of water, include the keyword CPCM(water) in your single point calculations with the larger basis test. Based on your results, do you expect that *cyclo*-N₅[−] can be handled under ambient conditions?

Instructions on How to Scan with the Use of Dummy Atoms

(you can do this or manually construct a starting guess for the transition state search):

Begin with N_5^- and simultaneously scan two N-N bond distances to locate a good transition state guess.

There are a number of ways to go about scanning more than one bond. This exercise uses a "dummy atom" in the input file to help define the reaction coordinate along which we want to scan. A dummy atom has no nuclear charge, no electrons, and no basis functions. In the figure to the right you can see the setup of the system. We want to scan the distance from the middle of an N_2 fragment, defined by the dummy atom, to the center of a to-be N_3^- (azide) anion. This approach works particularly well for this system because the two opposite N-N bonds we want to break (2-4 and 3-1) will stretch with an equal amount over the scan.



- To define a point in the middle of the N_2 fragment, place an atom of your choice in-between the two nitrogen atoms, see figure.
- Then when you go to *Generate Orca Input*, change the atom type of the added atom to DA (dummy atom). That way ORCA will treat it as a non-interacting point in the structure.
- In your scan input block (example shown below) set up a scan of the distance between the dummy atom and the nitrogen atom in the center of to-be N_3^- part of the N_5^- structure (remember: dummy atom 6 in the Avogadro figure = atom 5 in ORCA).
- To make the nitrogen atoms of the N_2 fragment follow the dummy atom, freeze the distances between the dummy atom and nitrogen atoms 1 and 2. You can constrain bonds and angles in ORCA by creating a Constraints block inside the geometry block. An example geometry block describing a scan with additional bond constraints is:

```
%geom
      Scan B 5 4 = 2.0, 3.0, 5 end
      Constraints {B 5 0 C} {B 5 1 C} end
end
```

After identifying a guess structure from the scan, use the techniques learnt in the lab to find the transition state and estimate a rate constant for the unimolecular decomposition of *cyclo*- N_5^- . Finally, answer the questions asked in the previous section.

Reminder: Criteria for higher (4 or 5) grades on individual lab report:

You do not need to present background theory on DFT or DFT functionals. But you do need to include a correct method description. Think of it this way: you are writing to another quantum chemist, who should be able to understand and reproduce what you have done. A quantum chemist who ideally should appreciate what you have found out. It is therefore very important to reflect and discuss your results.

Grade 4: A minimum of two out of three (2/3) energetic extra assignments performed and presented very well.

Grade 5: All energetic extra assignments performed and presented excellently.