

Exercise Ex9

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Please use this template to submit your answers.

If you had to modify code from the notebook, please include the modified code in your submission either as screenshot or in a

```
\begin{lstlisting}[language=Python]  
\end{lstlisting}
```

environment.

You only need to include the code cells that you modified.

Note, that references to other parts of the documents aren't resolved in this template and will show as ???. Check the text of the exercises on website for the reference

Exercise 1

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.

The reaction proceeds via a base-induced intramolecular S_N2 mechanism: deprotonation to an alkoxide, then backside attack on the C–Cl bond to give the epoxide and Cl⁻.

Because S_N2 causes inversion of configuration, the stereochemistry at the reacting carbon is not preserved.

In the chloropropanol, the chirality centre is the central carbon CH(CH₃)(CH₂OH)Cl.

In propylene oxide, the chirality centre is the ring carbon bearing the CH₃ group, bonded to CH₃, CH₂, O and H.

If the chlorohydrin is formed as a racemate, the epoxide is obtained as a racemic mixture of the two enantiomers.

Exercise 2

Suggest possible transition state structures.

When following the minimum energy path from the first reactant to the final product, we expect two first-order saddle points i.e. two transition states.

The first transition state corresponds to the moment where the proton is going from alcohol OH to the base $\text{^-\text{OH}}$ by its action. At this point the proton is between the two oxygens and this forms a three-centre $\text{O}-\text{H}-\text{O}$ arrangement. The bond $\text{O}-\text{H}$ of alcohol is breaking while the bond $\text{O}-\text{H}$ towards the base is forming. At the end of the process we are left with an alkoxide O^- and a water molecule H_2O

The second transition state corresponds to the moment when the negatively charged oxygen O^- is attacking the carbon bearing the chlorine to form the epoxide. At this point, the oxygen, carbon, and chlorine atoms are almost aligned ($\text{O}-\text{C}-\text{Cl}$): the $\text{C}-\text{O}$ bond is half formed while the $\text{C}-\text{Cl}$ bond is half broken, just before the epoxide ring closes and Cl^- leaves.

Each of these structures is a first-order saddle point on the PES, Hessian possesses exactly one negative eigenvalue associated with motion from reactants to products.

Exercise 3

Include a screenshot of the transition state in your report that you obtained and the corresponding Z-matrix for the transition state guess

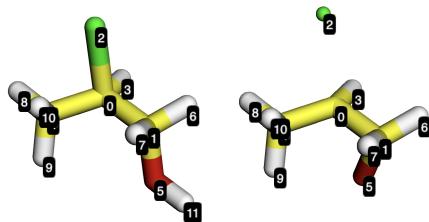


Figure 1: Reactant state and Transition state guess

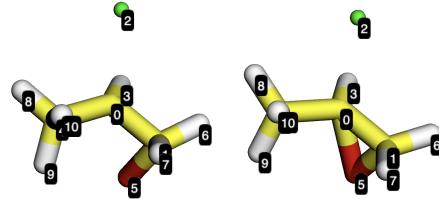


Figure 2: Transition State Guess and Constrained-Optimized Transition State

We changed the length of $C - Cl$ bond to 2.4, the oxygen angle to 80 degrees, removed the oxygen-hydrogen bond and change the charge to -1 as follows :

```

1 ts_guess = psi4.geometry("""
2 -1 1
3 symmetry c1
4
5 c      1 cc2
6 cl     1 clc3      2 clcc3
7 h      1 hc4       2 hcc4      3 dih4
8 c      1 cc5       2 ccc5      3 dih5
9 o      2 oc6       1 occ6      3 dih6
10 h     2 hc7       1 hcc7      6 dih7
11 h     2 hc8       1 hcc8      6 dih8
12 h     5 hc9       1 hcc9      2 dih9
13 h     5 hc10      1 hcc10     9 dih10
14 h     5 hc11      1 hcc11     9 dih11
15
16 cc2    =   1.500000
17 clc3   =   2.400000 # we changed this line
18 clcc3  =   109.471
19 hc4    =   1.089000
20 hcc4   =   109.471
21 dih4   =   100.000
22 cc5    =   1.500000
23 ccc5   =   109.471
24 dih5   =   -100.000
25 oc6    =   1.430000
26 occ6   =   80.0000 # we changed this line
27 dih6   =   180.000
28 hc7    =   1.070000
29 hcc7   =   109.471
30 dih7   =   120.000
31 hc8    =   1.070000
32 hcc8   =   109.471
33 dih8   =   240.000
34 hc9    =   1.070000
35 hcc9   =   109.471
36 dih9   =   180.000
37 hc10   =   1.070000
38 hcc10  =   109.471
39 dih10  =   120.000
40 hc11   =   1.070000

```

```

41 hcc11 = 109.471
42 dih11 = 240.000
43 ho = 0.97
44 hoc2 = 109.471
45 dih12 = 180.0
46 """

```

Exercise 4

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

First, in the Constrained-Optimized state, we see that we are closer to the product system, indeed the ring epoxyde is formed in which the angle of the oxygen bended towards the chiral carbon. On the other hand, the Optimized Transition State structure unfolded the oxygen angle such that *O C* (chiral carbon) and *Cl* are almost aligned. This corresponds well to the transition state where the *C – O* bond is forming, the bond *C – Cl* is breaking, and *O C Cl* are almost aligned like in an *S_N2* reaction (which is supposed to happen here).

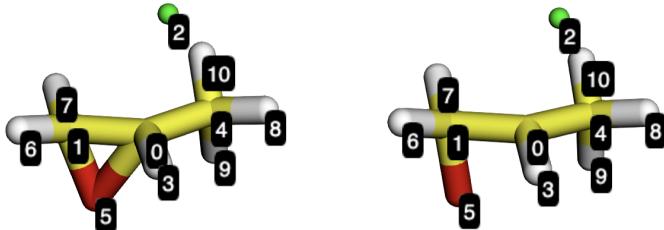


Figure 3: Constrained-Optimized Transition State and Optimized Transition State structure

Exercise 4

Report the value of the negative frequency that you obtain. What motion is this mode related to? What motions are associated with low and high vibrational frequencies? Choose two positive vibrational modes and describe their particular associated motion.

The negative frequency obtained is -384.8319238404 . This normal mode corresponds to the chiral carbon moving forward and backwards between the oxygen and the chlorine. This corresponds exactly to the mode we want to optimize since the *C – Cl* must break, while the bond *C – O* is forming to create

an epoxyde.

Small and positive vibrational frequencies corresponds to twist, global bend and soft movements of the molecule.

Intermediate frequencies, corresponds to the deformation of bonds that are more rigid such as $C - C - C$, $C - O$, etc.

High frequencies corresponds to elongating $C - H$ bonds which are the hardest.

We choose two frequencies among the listed in the output :

- Taking 1447.68248566, we observe that the chiral carbon is stretching its bond with one of the three carbons C by moving towards the last C . We also see that $C - H$ bonds do not elongate but H atoms move somewhat around their carbon. This corresponds well to the behaviour described above for intermediate frequencies.
- Taking 3278.4086170346, we observe that the bond $C - H$ of the chiral carbon is elongating/streching. other $C - H$ move only slightly since the latter bond is the hardest in the molecule. This again corresponds well to the behaviour described above for high vibrational frequencies.

Exercise 5

Is the transition state you predicted an early or a late transition state?
What about the guess?

The predicted transition state widens the oxygen angle, $C Cl O$ are mostly aligned. this is an early transition state. By its configuration, the system is closer to the reactant on the PES (early).

Concerning the guess, it had an angle of 80° which is closer to the reagent around 90° than the product (60°). By its configuration, the system is closer to the reactant on the PES (early).

If the Constrained-optimized is also needed, the epoxyde is formed carbon and the three atoms are not aligned anymore, it is a late transition state. By its configuration, the system is closer to the product on the PES (late).

Exercise 6

Having found a transition state, how would you now obtain the barrier height for your reaction? Are there ways of verifying whether you have found a meaningful transition state? **Bonus:** How would you define ‘meaningful’ in this context?

To get the barrier height, a possibility consists in optimising the reactant structure to its minimum on the PES and computing its energy. The activation

barrier is then given by the energy difference of the energy of the transition state with the energy of the reactant state:

$$\Delta E = E_{\text{TS}} - E_{\text{reactant}}$$

In order to verify if we found a meaningful state one can compute and diagonalise the Hessian matrix at this geometry. A proper transition state must have only one negative eigenvalue, (one imaginary vibrational frequency) all the other eigenvalues must be positive. The corresponding imaginary normal mode should be tested in order to confirm that it corresponds to the expected motion between reactant and product, in our case it was a bond breaking/forming along the reaction coordinate and alignment of atoms.

Bonus: A "meaningful" transition state is a first order saddle point that lies on the minimum-energy reaction path bridging the desired reactant and product states. Its imaginary mode corresponds to the expected chemical transformation.

Exercise 8

Is the stereochemistry at the carbon at which the reaction takes place retained?

The reaction takes place with a S_N2 mechanism at the chiral carbon. In this kind of reaction, the nucleophile attacks from the backside while the leaving group goes off, which leads to an inversion of configuration at the centre. This means that the stereochemistry at the chiral carbon is not retained: we start from one enantiomer and the reaction leaves us with the opposite enantiomer.

Exercise 7

Take a screenshot of the graph of the potential energy profile you recorded. Why is the barrier for the epoxide formation so low? Will this be the overall barrier for the reaction as depicted in the previous section?

From the IRC profile we see that the transition state lies only a few kcal mol⁻¹ above the reactant minimum (around 3 kcal mol⁻¹), whereas the product epoxide is more than 19 kcal mol⁻¹ lower in energy. The small barrier reflects the fact that we are modelling only the intramolecular S_N2 ring-closure of a pre-organised alkoxide. Indeed we didn't treat the first transition state and here the barrier is low since the oxygen is a very strong nucleophile and highly reactive, already positioned close to the reactive carbon. Moreover we could think that solvation and entropic penalties have been largely neglected in this gas-phase DFT model, which leads to a very easy ring-closure. This barrier therefore corresponds only to this single elementary step. This means that it will not be the overall barrier for the full synthetic sequence that we've seen, which also involves the proton-transfer steps; the true overall barrier is the largest of all these elementary barriers, and is expected to be higher than the one obtained here for epoxide formation.

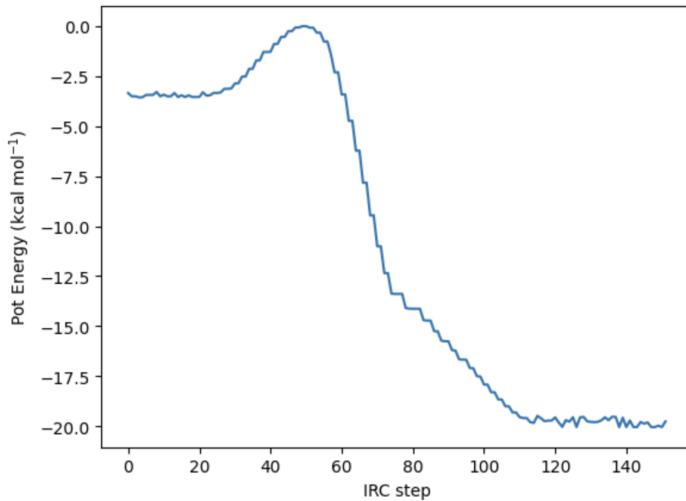


Figure 4: Potential profile recorded along IRC

Exercise 9

How do the C–Cl and the two relevant C–O bond lengths change during the trajectory? Does the C–C bond in the ring contract as the epoxide is formed? Show a graph depicting the evolution of these parameters as the reaction progresses.

From the bond-length profile we see that the C(0)–Cl(2) distance starts at about 1.9 Å and then increases along the IRC, reaching more than 3.2 Å in the product region. This corresponds well with the expected behaviour where we have a cleavage of the C–Cl bond. On the other hand, the C(0)–O(5) distance is long (~ 2.35 Å) in the reactant region and decreases continuously to ~ 1.45 Å, showing the formation of the new C–O bond. The second C–O distance, C(1)–O(5), is initially ~ 1.33 Å and increases slightly to ~ 1.45 Å; in the product both C–O bonds converge to similar values, as expected for the two C–O bonds of the epoxide ring. Finally, the C(0)–C(1) bond contracts from about 1.56 Å to ~ 1.45 Å along the trajectory, indicating that the C–C bond in the ring indeed shortens as the epoxide is formed.

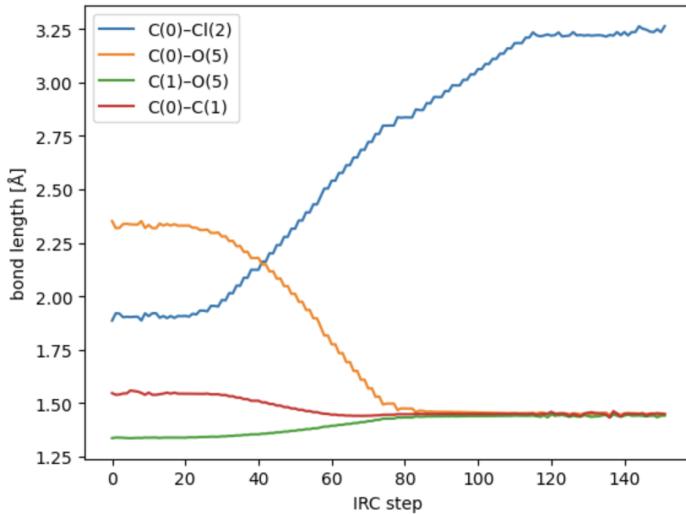


Figure 5: Bond lengths between recorded along IRC

Exercise 10

What is happening to the methyl group as the reaction proceeds? Find a suitable parameter (angle, dihedral) to describe and characterise possible changes you observe, change the code below. Explain in your report what atoms you considered and take and include the evolutions of the chosen parameters during the IRC procedure.

First, we included the $C - C - C$ angle in the analysis to better follow the bond reorganisation. The green curve, corresponding to the $4 - 0 - 1$ $C - C - C$ angle, stays almost constant along the IRC. This indicates that the framework around the central carbon does not bend significantly; instead, the whole methyl group mainly rotates while the $C - Cl$ bond breaks and the $C - O$ bond forms, allowing the system to keep a low-energy geometry.

From the graph we also see that the blue curve, which represents the intrinsic $H - C - H$ angle inside the methyl group, is essentially constant. This shows that the methyl group preserves its tetrahedral geometry throughout the reaction. In contrast, the dihedral angle (orange curve, $8 - 4 - 0 - 3$) changes significantly along the IRC. This variation reflects the rotation of the methyl group around the $C - C$ bond during the reaction.

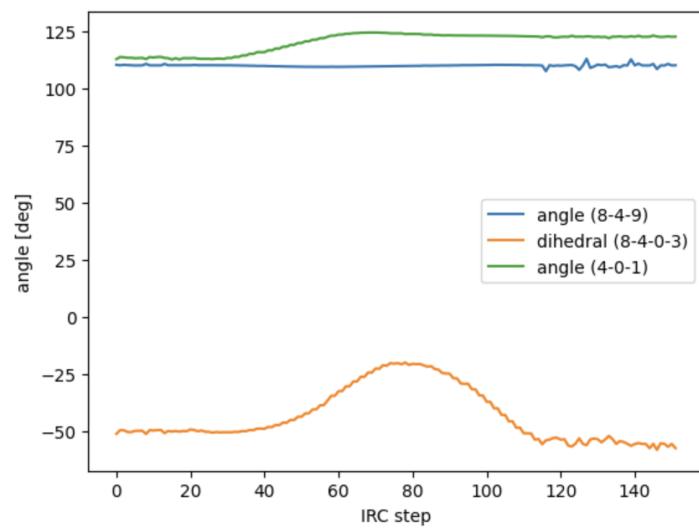


Figure 6: Angles and Dihedral angles along IRC