





# Summer Fellowship Report On Computational Studies on finding the transition state of Chemical Reactions

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#### Chapter 1

### Computational Studies on finding the transition state of Chemical Reactions

#### 1. Introduction

The field of Computational Chemistry has developed a range of methods to discuss the theoretical possibilities of any chemical reactions. For a reaction to occur, the molecular trajectories of the reactions play an important role in determining how the reaction proceeds through the minimum energy path. Over a period of time, it is experimentally difficult to capture the transition state of chemical reactions due to its transient nature; however the quantum chemical methods using the derivatives of energy with the reaction coordinates have successfully predicted the transition state of chemical reactions. The theories of chemical kinetics helped explaining the concept of the rate law and rate expressions of chemical reactions. Some of the theories are discussed below.

#### **1.1 Theory of Chemical Reactions**

Let's discuss the collision theory of chemical reactions that predated the transition state theory. According to this theory the molecules are considered to be hard spheres and reaction is only going to occur when they collide with each other. The rate of reaction is governed by the collision frequency (Z) per  $m^3$  per sec given by the equation

n<sub>A</sub>- Number of molecules of A in unit volume

n<sub>B</sub> - Number of molecules of B in unit volume

 $\Box_{AB}$  - Collisional cross section given by  $\sigma_{AB} = \Pi (r_A + r_B)^2$  where  $r_A$  and  $r_B$  are radius of A and B in unit m

**k** - Boltzmann constant unit  $J \cdot K^{-1}$ 

 $\mu$  - reduced mass of the reactant A and B

T - temperature in Kelvin

The rate of the reaction is agreeing with the Arrhenius equation and is given by the following equation:

**Rate** =  $\rho \mathbf{Z}_{AB} \mathbf{e}^{-\mathbf{E}/\mathbf{RT}}$ 

- Z Collision frequency in units of  $m^{-3} \cdot s^{-1}$ .
- $\rho$  Steric factor
- E Activation energy in units of  $J \cdot mol^{-1}$ .
- **R** gas constant in units of  $J \mod^{-1} K^{-1}$ .
- T temperature in units of K.

But there were few limitations to this theory of chemical kinetics as there were very large discrepancies to the observed and calculated rate constants of various chemical reactions. It was hence taken into account that if the molecules undergo chemical reaction, they must not merely collide with sufficient mutual energy but they need to come in proper orientation so that the mutual bonds can be broken and made. The theory failed to explain the concept of energy barriers during the course of reaction and could be valid only for simple gaseous atoms. This theory was more advanced with Maxwell Boltzmann concept of energy distribution among the reactant molecules and later the principle of statistical mechanics was applied with the assumption that reaction is the motion of the particle in phase space.

The term 'dynamics' was later introduced in the chemical reaction which explained through the molecular trajectories the concept of col or saddle point on the potential energy surface. With this, came the discovery of transition state theory. Transition State Theory (TST) describes a hypothetical "transition state" that occurs in the space between the reactants and the products in a chemical reaction. The species that is formed during the transition state is known as the activated complex.

#### **1.2 Transition State Theory**

If the reactants have N atoms, that is, the number of atoms in reactant A plus the number in reactant B is N then the system AB may be described in terms of 3N coordinates and 3N conjugate momenta; the 6N-dimensional space of these variables is called phase space. A transition state is hypothetical system localized to a phase space hypersurface that divides the reactant region of phase space from the product region. Furthermore, a transition state hypersurface passes through a saddle point on the potential energy surface of the AB system. A saddle point on the potential energy surface yields an imaginary frequency mode which tells the position of the transition state on the surface. Consider the following reaction:

 $A + B \rightleftharpoons [AB]^* \rightleftharpoons C + D;$ 

[AB]\* is the activated complex or the transition state.

$$\mathbf{K}^{\#} = \frac{[AB]_{*}}{[A][B]} = e^{-\Delta G * RT} = e^{(-\Delta H * RT) + (\Delta S * R)};$$

 $\mathbf{K}^{\#}$  is rate constant for formation of activated complex

Rate = 
$$\left(\frac{KT}{h}\right)$$
[AB]\* =  $\left(\frac{KT}{h}\right)$ K<sup>#</sup>[A][B] = **k**[A][B]

**Rate constant** 
$$\mathbf{k} = \left(\frac{KT}{h}\right) \mathbf{K}^{\#} = \left(\frac{KT}{h}\right) e^{(-\Delta S * R)} \cdot e^{(-\Delta H * RT)}$$
 ......[2]

#### **1.3 Intrinsic Reaction Coordinate**

The Intrinsic Reaction Coordinate (IRC) is defined as the minimum energy path connecting the reactants to products via the transition state. In practice, the IRC is found by first locating the transition state for the reaction. The IRC is then found in halves, going forward and backwards from the saddle point, down the steepest descent path in mass weighted Cartesian coordinates. This is accomplished by numerical integration of the IRC equations, by a variety of methods. The intrinsic reaction coordinate (IRC) approach has been used extensively in quantum chemical analysis and prediction of the mechanism of chemical reactions. The IRC gives a unique connection from a given transition structure to local minima of the reactant and product sides. **[3]** 



Figure 1: Reaction Coordinate Diagram

Activation energy is the minimum amount of energy that is required to activate atoms or molecules to a condition in which they can undergo chemical transformation or physical transport. The higher activation energy of a reaction indicates that it is difficult for the reaction to take place while the lower activation energy indicates that the reaction occurs faster.

#### 2.0 Methodology

In order to perform the transition state geometry calculation the ORCA version and Avogadro version were used. The steps which were taken to obtain the results are explained below:

#### Step 1: Build the Reactant and the Product Molecules

The reactant and the product molecules were built using the Avogadro software. The structure was then optimized with the automatic optimization tool of Avogadro using the MMFF94 force field which is generally used for small organic molecules. Also generate the ORCA input files for the reactant and the product optimized geometry from the Extension menu bar in Avogadro.

#### Step 2: Geometry Optimization of the Reactant and the Product molecule using ORCA

The Optimized geometry of the molecules are needed before the transition state calculations, are performed. Here the following forcefield and formats are used inside the input files of the reactant and the product to generate the most optimized geometry

of the reactant and the product.

The geometry is optimized using the force field B3LYP and Note that the hashtag (#) marks a comment line that will not be considered as an input to the reaction. The exclamation mark (!) marks the main command for ORCA. The xyz coordinates are generated by Avogadro and the xyz 0 1 denotes that for this reaction, the initial charge is 0 and multiplicity is 1. You can anytime edit these lines by opening the files on the notepad.

After the files are ready open the command prompt terminal and direct the commands to the E drive. Then type the below mentioned command to run the Orca.

<b>B3LYP</b>	DEF2-SVP OPT		
xyz Ø	1		
С	-1.95083	2.58123	0.30684
С	-2.81345	1.69412	-0.20206
н	-2.18930	3.63985	0.31571
н	-0.99199	2.28365	0.71941
С	-2.58061	0.27301	-0.28875
Н	-3.74813	2.04846	-0.63252
С	-2.03635	-0.47378	0.67950
н	-2.92782	-0.20943	-1.20042
н	-1.70488	-0.04560	1.62018
н	-1.91627	-1.54437	0.54913
С	2.29025	1.91564	-0.27846
С	1.71541	0.71046	-0.31437
н	3.24286	2.06746	0.21894
н	1.81830	2.77330	-0.74757
н	2.18401	-0.14932	0.15349
н	0.76193	0.56042	-0.81217

# avogadro generated ORCA input file

# Basic Mode

<u>Step 3: Running the Nudged Elastic Band Method (NEB</u> <u>-TS ) method for calculating the Transition State</u> <u>Geometry.</u> Figure 2: Sample Input file

#### Nudged Elastic Band Method:

The nudged elastic band (NEB) method is a black box method that can find a guess for the transition state geometry based upon the geometries of the reactants and products. Instead of scanning along a bond or vector, for the NEB you input the starting and finishing coordinates, and ORCA will find the minimum energy pathway between the two geometries. The NEB is convenient for multi-step reactions, as it will combine multiple steps into one calculation and guess the TS based upon the multi-step reaction path. However, because it combines multiple steps it is also computationally expensive.

The Nudged Elastic Band (NEB) method is used to find a minimum energy path (MEP) connecting two local energy minima on the potential energy surface (PES) and thereby an estimate of the activation energy for the transition. The two minima are referred to as the reactant and product in the following discussion. The path can have one or more maxima, each one corresponding to a first order saddle point on the energy surface. The NEB method offers an advantage over eigenvector-following methods in that it is guaranteed to find saddle points that connect the given reactant and product states. The minimum energy path is often used to represent the reaction coordinate of the transition between the two states. The NEB-TS keyword will use both the high convergence threshold for the minimum energy path and a medium convergence threshold for the climbing image. In addition, once a climbing image is found, the geometry of that step is fed into a transition state optimization calculation (OptTS) and an optimized geometry for the transition state will be a part of your output. **[4]** 

#### Vibrational frequency:

If with NEB-TS FREQ keyword is applied it also results in the vibrational frequency which if one of the vibrational frequency results in negative value, it indicates the saddle point as the imaginary node is formed at that point which is the indication of the transition state geometry.

These frequencies are obtained through calculating second derivatives of energy, which constitute the hessian matrix. Diagonalization of hessian matrix gives its eigenvalues and eigenvectors. Eigenvalues are squared harmonic frequencies of 3N-6 normal vibrations, while eigenvectors are 3N-6 normal coordinates. A negative eigenvalue means that one of its square roots (i.e. harmonic frequency) contains imaginary number as a factor, and hence the term imaginary frequency. Physically, a negative eigenvalue corresponds to negative curvature of corresponding normal coordinate. In other words, the geometry on which this second derivative is yielded is passing through an energy maximum (and geometry corresponds to a saddle point) along this particular normal coordinate. Hence an **imaginary vibrational frequency** corresponds to the saddle point which can be the transition state of that particular reaction. **[5]** 

Prepare the input file (let say reac\_prod.inp ) for NEB-TS calculation inside a new directory but in E drive. Make sure to direct the command prompt to the same directory where the input file is

present. Also take the most recent optimised .xyz files of reactant and the product to the same directory named as reactant.xyz and product.xyz

**NOTE** [ It is important to carefully prepare the reactant and product such that the position (or index) of the atoms is the same in the two configuration files, i.e., there should be one-to-one mapping between the reactant and product configurations.]

#### 3.0 Results and Discussions:

#### 3.1 Reaction 1: Diels Alder Reaction (Slower rate)



The trajectory of the following reaction

is shown and it shows how the reactant molecules combine to form the product.

The table below represents the corresponding activation energy of each of the images obtained in finding the transition state geometry of the following reaction.

Ima	nge E(Eh)	dE	max( Fp )	RMS(Fp)
0	-234.25277	0.00	0.01748	0.00586
1	-234.25552	-1.73	0.00062	0.00027
2	-234.24755	3.27	0.00210	0.00068
3	-234.23307	12.36	0.00460	0.00165
4	-234.19980	33.24	0.00314	0.00125

![](_page_8_Picture_10.jpeg)

Figure 4: Reaction 1 Trajectory Click here to view

5	-234.16565	54.67	0.00372	0.00138
6	-234.16188	57.04	0.00172	0.00063 <= CI
TS	-234.23101	13.65	0.00088	0.00028 <= TS
7	-234.16786	53.28	0.00228	0.00064
8	-234.19595	35.65	0.00113	0.00044
9	-234.33305	-50.38	0.01373	0.00479

Here the  $6^{th}$  image obtained is the climbing image representing the nearest geometry of the transition state. The Reaction coordinate diagram of the following reaction is shown below which represents the highest activation energy.

![](_page_9_Figure_3.jpeg)

Figure 5: Reaction Coordinate Diagram (1)

#### **Conclusion :**

- Very Slow reaction
- High Activation Energy
- Experimentally not possible

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#### 3.2 Reaction 2 : Diels Alder Reaction (Faster Rate)

![](_page_10_Picture_2.jpeg)

**Transition State** 

The trajectory of the following reaction is shown and it shows how the reactant molecules combine to form the product.

The table below represents the corresponding activation energy of each of the images obtained in finding the transition state geometry of the following reaction.

Ima	ige E(Eh)	dE	max( Fp )	RMS(Fp)
0	-326.38364	0.00	0.00060	0.00018
1	-326.38430	-0.42	0.00016	0.00006
2	-326.38496	-0.83	0.00042	0.00015
3	-326.38590	-1.42	0.00128	0.00052
4	-326.38626	-1.65	0.00236	0.00106
5	-326.37772	3.72	0.00360	0.00169
6	-326.36736	10.22	0.00376	0.00167
7	-326.36091	14.27	0.00199	0.00084 <= CI

![](_page_10_Picture_7.jpeg)

3-Cyclohexene-1-carbonitrile

![](_page_10_Picture_8.jpeg)

Figure 6: Reaction 2 Trajectory Click here to view

TS	-326.36683	10.55	0.00044	0.00010 <= TS
8	-326.38365	-0.01	0.00294	0.00126
9	-326.46209	-49.23	0.00067	0.00028

Here the 7<sup>th</sup> image obtained is the climbing image representing the nearest geometry of the transition state. The Reaction coordinate diagram of the following reaction is shown below which represents the highest activation energy.

![](_page_11_Figure_3.jpeg)

Figure 7: Reaction Coordinate Diagram (2)

#### **Conclusion:**

- > Reaction is faster as compared to the previously studied Diel's alder reaction
- > The Activation energy is comparatively less.
- > Reaction is faster due to presence of Electron Withdrawing group in dienophile.

#### 3.3 Reaction 3: Substitution Nucleophilic Bimolecular (SN2) in gas phase

The following SN2 reaction is taken into study In this reaction cyanide ion acts as a nucleophile and attack the alkyl halide to form the following product.

The reaction occurs as follows:

![](_page_12_Picture_4.jpeg)

In the transition state for the  $S_N 2$  mechanism, neither the nucleophile nor the leaving group is fully bonded to carbon. As the reaction proceeds through the transition state, a bond between carbon and the nucleophile forms and the bond between carbon and the leaving group breaks.

The trajectory of the following reaction is shown and it shows how the reactant molecules form the product on getting attached with the nucleophile.

The table below represents the corresponding activation energy of each of the images obtained in finding the transition state geometry of the following reaction.

Imag	ge E(Eh)	dE	max( Fp )	RMS(Fp)
0 -	-2745.58293	0.00	0.00203	0.00077
1 .	-2745.58113	1.13	0.00126	0.00050
2 -	-2745.57817	2.99	0.00153	0.00060
3 -	-2745.57454	5.26	0.00136	0.00050
4 -	-2745.57233	6.65	0.00148	0.00053 <= CI

CH3-CH2-Br ------ CH3-CH2-C≡N + \$Br

Bond formation and bond breaking (Concerted Mechanism)

![](_page_12_Picture_11.jpeg)

![](_page_12_Picture_12.jpeg)

![](_page_12_Picture_13.jpeg)

Figure 8: Reaction 3 Trajectory Click here to view

TS	-2745.57309	6.17	0.00012	0.00004 <= TS
5	-2745.57409	5.55	0.00178	0.00067
6	-2745.58033	1.63	0.00262	0.00083
7	-2745.61484	-20.02	0.01133	0.00349
8	-2745.65232	-43.54	0.00537	0.00158
9	-2745.65344	-44.25	0.00098	0.00025

Here the 4<sup>th</sup> image obtained is the climbing image representing the nearest geometry of the transition state. The Reaction coordinate diagram of the following reaction is shown below which represents the highest activation energy.

![](_page_13_Figure_3.jpeg)

Figure 9: Reaction Coordinate Diagram (3)

#### **Conclusion :**

- > Reaction is faster with lower activation energy in gas phase
- > The nucleophile attacks from position opposite to the leaving group favors SN2 reaction.

 $\overset{\delta_{+}}{\longrightarrow} \overset{0}{\longrightarrow} \overset{0}{\longrightarrow}$ СН3—СН2—Вг \$Br ---**:**C≡N Cyanide

#### 3.4 Reaction 4: Substitution Nucleophilic Bimolecular (SN2) in Solvent phase The following SN2 reaction is taken into study. In this reaction cyanide ion acts as a nucleophile and attack the alkyl halide to form the following product.

All the steps performed here are similar to what happened in reaction 3 but here the transition state geometry of the reaction is obtained at higher activation energy which decreases the rate of the reaction.

The decrease in the rate of the reaction is due to the solvation effect which stabilize the nucleophiles and hinders their reactivity.

The table below represents the corresponding activation energy of each of the images obtained in finding the transition state geometry of the following reaction.

Ima	ige E(Eh)	dE	max( Fp )	RMS(Fp)
0	-2745.67975	0.00	0.00385	0.00174
1	-2745.67947	0.18	0.00136	0.00052
2	-2745.67785	1.19	0.00218	0.00069
3	-2745.67551	2.66	0.00308	0.00091
4	-2745.67148	5.19	0.00270	0.00102
5	-2745.66564	8.85	0.00207	0.00087
6	-2745.66098	11.78	0.00140	0.00072
7	-2745.65921	12.88	0.00147	0.00066 <= CI
TS	-2745.65994	12.43	0.00021	0.00005 <= TS
8	-2745.66027	12.22	0.00166	0.00075
9	-2745.66283	10.62	0.00237	0.00092

-2745.66764	7.59	0.00189	0.00096
-2745.67797	1.11	0.00382	0.00154
-2745.70325	-14.75	0.00846	0.00333
-2745.74644	-41.85	0.00384	0.00157
-2745.74870	-43.27	0.00345	0.00138
-2745.74989	-44.02	0.00409	0.00186
-2745.75057	-44.45	0.00516	0.00206
-2745.74940	-43.71	0.00364	0.00152
	-2745.66764 -2745.70325 -2745.74644 -2745.74870 -2745.74989 -2745.75057 -2745.74940	-2745.667647.59-2745.677971.11-2745.70325-14.75-2745.74644-41.85-2745.74870-43.27-2745.74989-44.02-2745.75057-44.45-2745.74940-43.71	-2745.667647.590.00189-2745.677971.110.00382-2745.70325-14.750.00846-2745.74644-41.850.00384-2745.74870-43.270.00345-2745.74989-44.020.00409-2745.75057-44.450.00516-2745.74940-43.710.00364

Here the 7<sup>th</sup> image obtained is the climbing image representing the nearest geometry of the transition state. The Reaction coordinate diagram of the following reaction is shown below which represents the highest activation energy.

![](_page_15_Figure_3.jpeg)

*Figure 10: Reaction Coordinate Diagram (4)* 

#### **Conclusion :**

- Continuum Solvation Model is used to generate the result.
- > Polar protic solvent decreases the rate of SN2 reaction.
- > Increase in the activation energy of the reaction due to presence of polar protic solvent.

# Conclusion

Concerted reactions are those reactions which takes place in single step without the formation of the intermediate. In this project we included two types of concerted reaction namely Diels Alder Reaction and secondly, Substitution Nucleophilic Bimolecular Reaction (SN2).

These reactions were performed computationally to generate the computational results and the results obtained were verified with the experimental results. The reaction was performed in various environment like gas phase or solvent phase and the difference in their results was compared to generate useful information. The DFT level theory B3LYP was used to perform the calculations using basis set def2-SVP. The open-source software Orca and Avogadro was used to generate the desired output.

The reaction coordinate diagrams obtained tells the value of activation energy and Gibbs energy of the reaction. The trajectory of each of the reaction is attached along with the reaction which explains the orientation in which the reactant molecules combine to form the transition state and finally the products in just one step reaction mechanism.

The conclusion drawn for each of the reaction is pasted below the desired reactions.

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