Ab initio quantum chemical study of selenium dioxide mediated allylic hydroxylation of alkenes

A thesis submitted towards partial fulfillment of
5 year integrated BS-MS programme
by

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Certificate

This is to certify that this dissertation entitled "**Ab initio quantum chemical study of selenium dioxide mediated allylic hydroxylation of alkenes** " towards the partial fulfillment of the 5 year integrated BS-MS programme at the Indian Institute of Science Education and Research Pune, represents original research carried out by **Varun Kumar Rishi** at National Chemical Laboratory, Pune under the supervision of **Dr. Sudip Roy** during the academic year "2010-2011".

Varun Kumar Rishi
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Supervisor	Head
Date:	Date:
Place:	Place:

Acknowledgement

I would like to thank my guide. He encouraged me throughout and gave me all possible freedom. He listened to me when I needed to speak and was patient at difficult times.

Also I would like to thank my lab mates. I enjoyed my stay in the lab and was happy having different kind of discussions with them.

Abstract

The aim of the project was to study an organic reaction using ab-initio quantum chemical tools and apply the general ideas of physical chemistry to it. Selenium dioxide mediated allylic hydroxylation is a known reaction used to substitute hydroxyl group at allylic position of an alkene. The proposed mechanism of this reaction was verified for a simple substrate. This involved location of transition states on Potential Energy Surface (PES) and subsequently the energy profile of the reaction was constructed using the energies of the transition states. Furthermore an experimental study employing the same reaction showed a particular stereochemical preference amongst the isolated products. This particular observation was explained by applying the notion of thermodynamic and kinetic control to a constituent part of the reaction.

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1. Chemical reactions

As molecules are an essential part of this universe and of human life, we seek ways to synthesise them from various sources. Chemical reactions enable us create one molecule from another. Chemical reactions simply defined are "transformations at molecular level". This may imply breaking / forming of a bonds which may happen at a intermolecular or intramolecular level . Due to human curisoity and labour, thousands of chemical reactions have been discovered and subsequently used to artificially synthesise molecules of our interest. It is of utmost interest to us that as experiments in labs around the world continue to unveil these magic transformations rationally or serendipitously, there is also progress on understanding of these reactions at a more fundamental level and we gain “power of prediction” at certain level over them.

In this chapter we discuss about the general idea of a chemical reaction. Then we look at chemical reactions in terms of energy considerations and a simple picture of an energy profile is evoked. In the next section a particular organic reaction is discussed. The proposed mechanism for the reaction is explained. Finally we briefly reiterate the approach of the work.

1.1 Chemical reaction: transformations at molecular level

Chemical reactions involve breaking or forming of bond at atomic or molecular level .There is consideration of energetics in all chemical reactions as the processes of bonds breakage or formation or rearrangement of atomic positions either require or produce energy .

Considering a hypothetical chemical reaction,

$$A - B \longrightarrow A + B$$

In this case a bond is being broken in the substrate to give the products. A particular amount of energy is required to initiate this process of bond breaking which is generally defined as activation energy barrier. A typical energy plot showing the relative energies of the reactants, product and the activated complex (or the transition state) is shown in figure1.1.1.

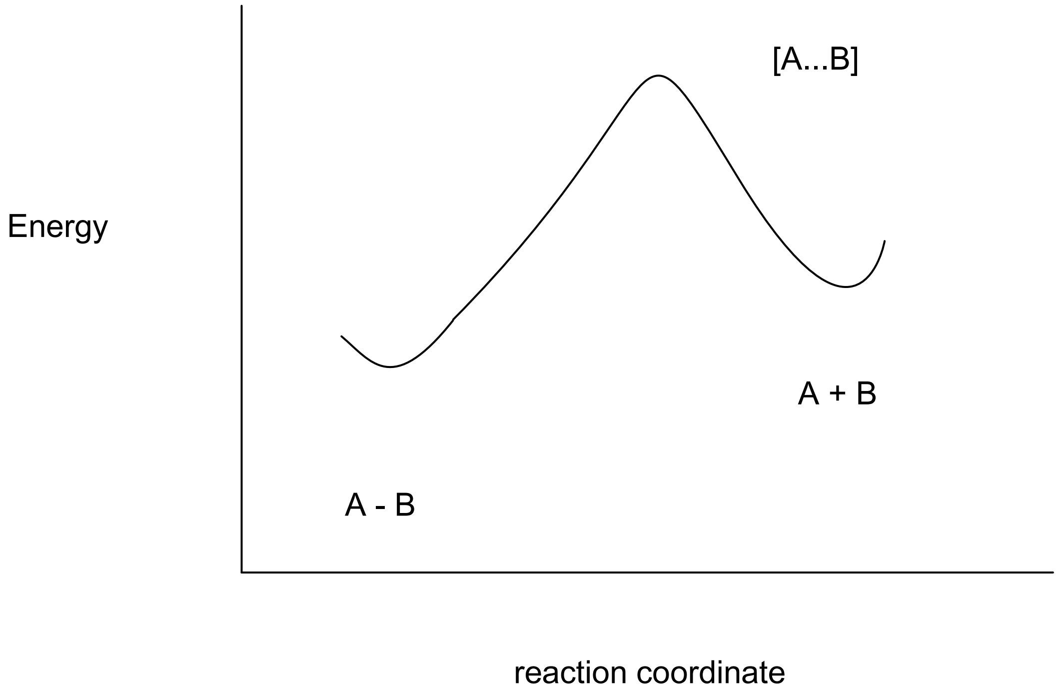


Figure 1.1.1 : Energy Profile for the above mentioned hypothetical reaction

This example introduces to us the concept of transition states and of activation energy barriers. Also one may stress at this point that the similar energetic considerations can be applied to study any chemical reaction.

1.2 The reaction of interest : Selenium dioxide mediated allylic hydroxylation

Selenium di oxide mediated oxidation of alkenes is known to be one of the most reliable methods of derivatization of allylic C-H bonds[1,2]. It basically helps substitute hydroxyl group at the allylic position .The mechanism of the reaction was not well resolved for a long period of time but a mechanistic proposal by Sharpless[3] in 1973 seemed to resolve the issue and is now well accepted. It was proposed that the reaction takes place via two consecutive pericyclic reactions of which the first one was an ene addition followed by sigmatropic rearrangement. Using propene as a substrate, the reaction with intermediate steps is shown below in figure 1.2.1.

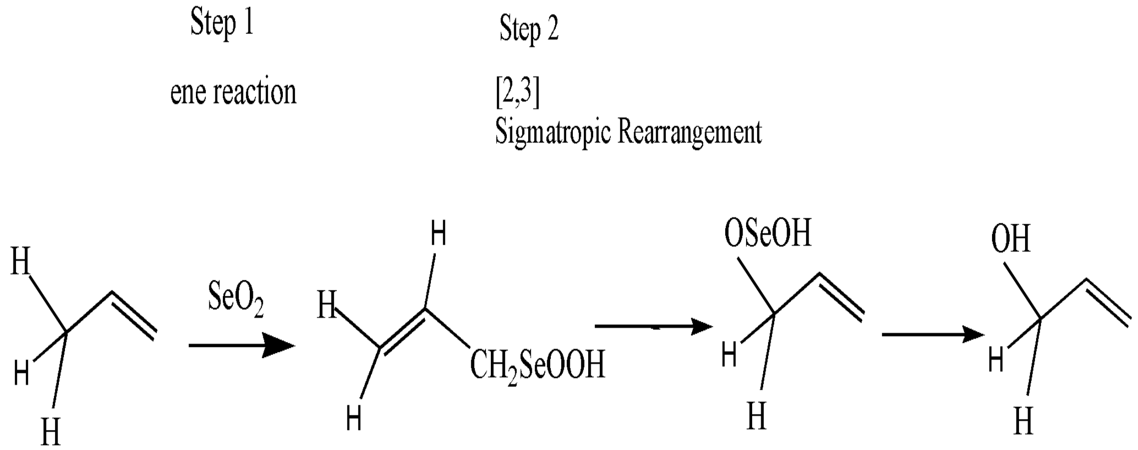


Figure 1.2.1: Selenium dioxide mediated allylic hydroxylation

An illustrative “curly arrow” mechanism for the two steps of the reaction is given below.

Step 1: (ene addition)

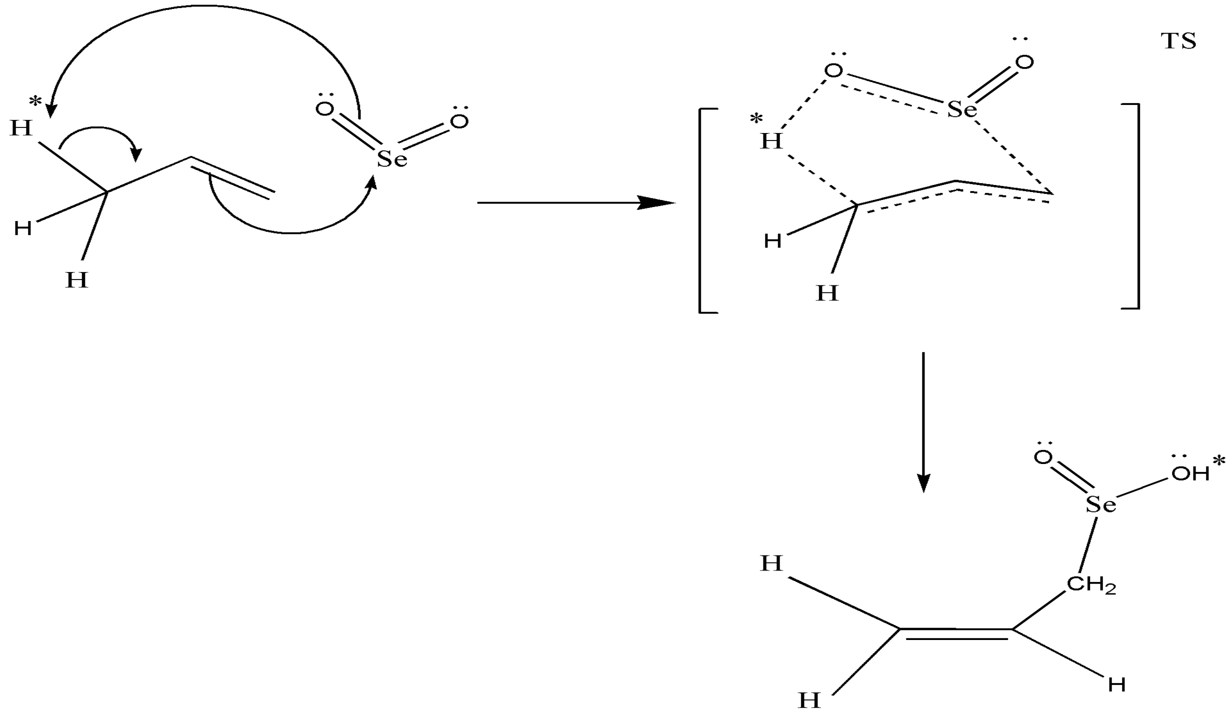


Figure 1. 2.2: Illustrative mechanism for ene addition

Step 2: [2, 3] Sigmatropic rearrangement

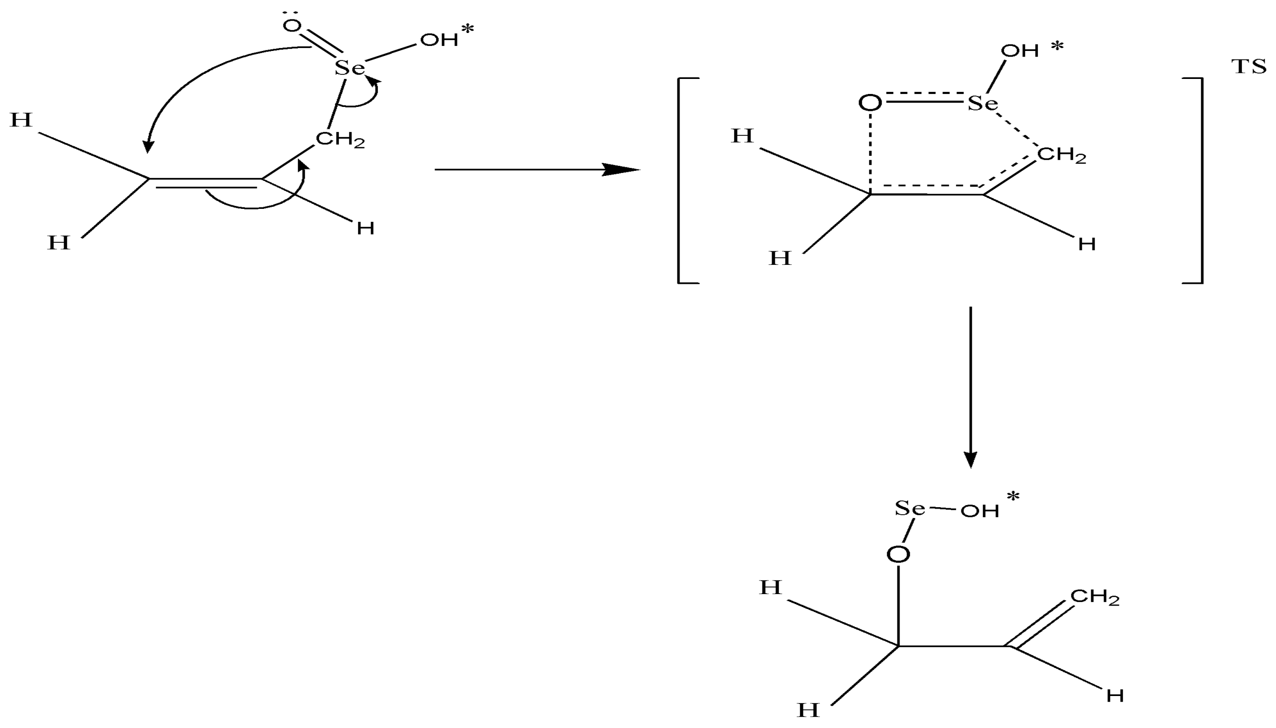


Figure 1.2.3 : Illustrative mechanism for Sigmatropic rearrangement

As one can notice that both of the intermediate reaction steps seem to have cyclic transition states. This is the defining property of a broad class of reactions named “pericyclic reactions”.

1.2.1 Pericyclic reactions

Pericyclic reactions are a class of reaction in which a concerted change of bonding relationship takes place and the transition states have a cyclic geometry. The term “concerted” refers to bond breakage and formation being simultaneous.

A large number of reaction fall under the broad category of Pericyclic reactions. They are briefly described under major categories as:

a .Electrocyclic reactions: There is creation of a new σ bond at the expense of π bonds or vice- versa (Cases of ring closure/opening).

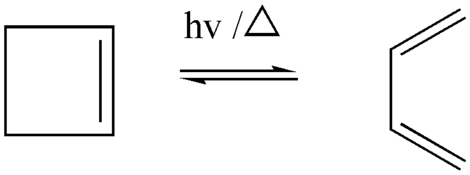


Figure 1. 2.4: Electrocyclic reaction (ring opening/ ring closing)

b. Cycloaddition: Two π systems react to form a cyclic ring creating σ bonds at the expense of π bonds.

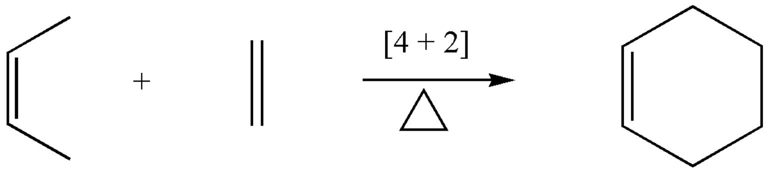


Figure 1.2.5: An example of cycloaddition reaction (Diels-Alder reaction)

c. Sigmatropic reaction: A rearrangement reaction in which a migration of a σ bond from one position in a conjugated system to another position in another conjugated system takes place while π bonds reorganize themselves. The nomenclature is [m, n] shift: where σ bond migrates across m atoms of one system and n atoms across another system.

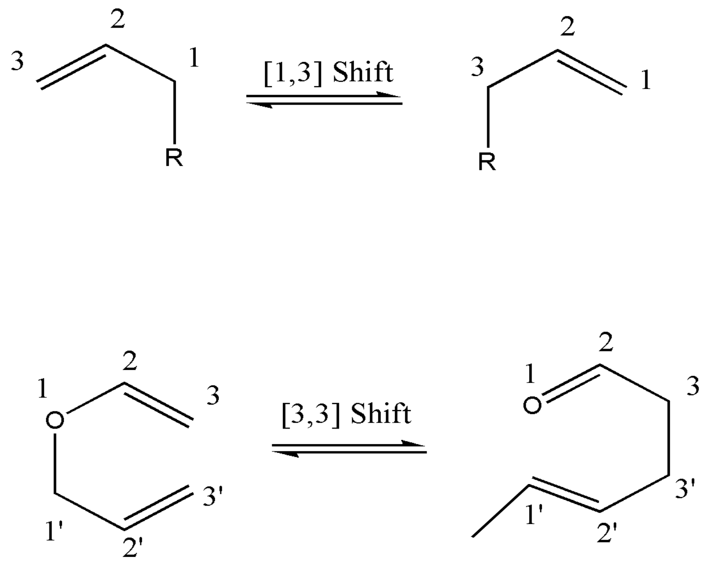


Figure 1.2.6: Examples of sigmatropic rearrangement reaction

1.3 Approach of this work

As will be described in Chapter 3, this work is a result of viewing the “Selenium dioxide mediated allylic hydroxylation reaction” on the basis of energy considerations. The basic idea of activation energy barriers is applied to explain experimental observations. But now we move on to the next chapter where the basic foundation for studying chemical systems purely on the basis of theory (ab initio approach) is laid.

2. Theory to study Chemical systems

In this chapter we try to see how the laws of physics can be used to study chemical reactions. Ab initio theoretical approach to chemical problems is based on quantum mechanics. We discuss the theory of quantum mechanics briefly. At first the fundamental equation governing chemical systems i.e. Schrödinger equation is introduced. Then we delve briefly into the theories that have flourished in the quest to solve this equation. A brief summary of Hartree-Fock (HF) theory and Density Functional theory (DFT) is given. Then we see the emergence of Potential Energy Surface (PES) as a natural consequence of Born-Oppenheimer hypothesis. We then discuss the important points lying on PES and how these points correlate with the imaginative picture of chemical reaction. We see how a transition state (TS) is a mathematically unique point on PES. We then briefly discuss important transition state search algorithms. Finally we connect the concept of PES to that of activation energy barriers.

2.1 Schrödinger Equation

All chemical systems are amenable to be studied under the laws of physics .The fundamental equation governing the molecules and their basic properties is Schrödinger equation[4].

$$\widehat{H}\ \psi = E\ \psi \qquad (2.\ 1)$$

Here Ψ is the wave function that fully describes the quantum mechanical system of interest as stated in one of the postulates of quantum mechanics[5].

Where $\widehat{H}$ refers to the hamiltonian operator which has a kinetic energy and a potential energy component.

$$\widehat{H} = \widehat{K} + \widehat{U} \qquad (2.\,2)$$

A general form of these operators in the case of chemical systems is

$$\widehat{K} = -\frac{\hbar^2}{2m}\frac{\partial^2()}{\partial r^2} \qquad (2.\,3)$$

m is the mass of particle of interest (electron/nuclei).

$$\widehat{U}= \frac{q_1 q_2}{r_{12}} \qquad (2.4)$$

Where q_1 and q_2 are the charges on the two particles and r_{12} is the distance between them.The solution of Schrödinger equation would give us the explicit form of Ψ as a function of electronic and nuclear positions and also the total energy of the system. The wave function Ψ can then be used to extract other properties of the system like total energy, ionization potential, electron affinity etc.

The total energy would be composed as
Total energy : E = K + U

K – Kinetic energy contribution from electrons and nuclei's

U – potential energy contribution
(electron- electron, nuclei – nuclei, electron -nuclei interaction)

Let us see the form of Hamiltonian operator for the case of Hydrogen atom which is a single electron system

$$\hat{H} = \hat{K} + \hat{U} \tag{2. 5}$$

$$\hat{H} = -\frac{\hbar^2}{2m_e}\frac{\partial^2()}{\partial r_e{}^2} - \frac{\hbar^2}{2m_N}\frac{\partial^2()}{\partial r_N{}^2} - \frac{e^2}{r_{eN}} \tag{2. 6}$$

The first component in the expression of Hamiltonian operator is kinetic energy contribution of the electron while the second component is kinetic energy contribution of the nucleus while the last component is the potential energy contribution due to coloumbic attraction between the electron and nuclei.

For any general atomic/molecular system with N electrons and M Nuclei's, Hamiltonian would be composed of the following parts

$$\hat{H} = \hat{K}_e + \hat{K}_N + \hat{U}_{ee} + \hat{U}_{eN} + \hat{U}_{NN} \tag{2. 7}$$

$$\hat{K}_e = -\sum_{i=1}^{N} \frac{\hbar^2}{2m_i}\frac{\partial^2()}{\partial r_i{}^2} \tag{2. 8}$$

$$\hat{K}_N = -\sum_{j=1}^{M} \frac{\hbar^2}{2M_j}\frac{\partial^2()}{\partial R_j{}^2} \tag{2. 9}$$

$$\hat{U}_{ee} = \sum_{i=1}^{N}\sum_{j>i}^{N} \frac{e^2}{r_{ij}} \tag{2 .10}$$

$$\hat{U}_{NN} = \sum_{i=1}^{M}\sum_{j>i}^{M} \frac{Z_i Z_j e^2}{R_{ij}} \tag{2. 11}$$

$$\hat{U}_{eN} = -\sum_{i=1}^{N}\sum_{j=1}^{M} \frac{Z_j e^2}{|r_i - R_j|} \qquad (2.\ 12)$$

Combining all parts together

$$\hat{H} = -\sum_{i=1}^{N} \frac{\hbar^2}{2m_i}\frac{\partial^2()}{\partial {r_i}^2} - \sum_{j=1}^{M} \frac{\hbar^2}{2M_j}\frac{\partial^2()}{\partial {R_j}^2}$$
$$+ \sum_{i=1}^{N}\sum_{j>i}^{N} \frac{e^2}{r_{ij}} + \sum_{i=1}^{M}\sum_{j>i}^{M} \frac{Z_i Z_j e^2}{R_{ij}} - \sum_{i=1}^{N}\sum_{j=1}^{M} \frac{Z_j e^2}{|r_i - R_j|} \qquad (2.13)$$

As we may note that the expression of $\hat{H}$ is quite complex and the problem would be very difficult to solve. In the next section we introduce an assumption which simplifies the expression of $\hat{H}$.

2.1.1 Born–Oppenheimer[6] approximation

It states that since a nucleus is quite heavier as compared to an electron ($\frac{m_e}{M_N} \ll 1$), it can be assumed that the electronic motion is quite fast as compared to the nuclear motion. Stated simply it says that nuclei's can be assumed to be stationary while we are bothered about electronic motion.

Therefore

$$\hat{K}_N \rightarrow 0 \qquad (2.14)$$

$$\hat{H} = \hat{K}_e + \hat{U}_{ee} + \hat{U}_{eN} + \hat{U}_{NN} \qquad (2.\ 14)$$

But Potential energy contribution due to nuclear interaction would be a constant if nuclei's are assumed to be at rest.

$$\widehat{U}_{NN} = \sum_{i=1}^{M} \sum_{j>i}^{M} \frac{Z_i Z_j e^2}{R_{ij}} = \text{constant} \qquad 2.\ 15$$

Thus we segregate the electronic part of Hamiltonian and write it as

$$\widehat{H}_{elec} = \widehat{K}_e + \widehat{U}_{ee} + \widehat{U}_{eN} \qquad 2.\ 16$$

Now the equation to solve would be

$$\widehat{H}_{elec}\,\psi = E_{elec}\,\psi \qquad 2.\ 17$$

This equation would be solved for various set of fixed nuclear positions.

And therefore $\Psi = \Psi(r_1, r_2, \dots\dots..r_N, R_1, R_2, \dots R_M)$ depends explicitly on electronic positions but parametrically on nuclear coordinates.

2.1.2 Potential energy Surfaces as a consequence of BO approximation

Here arises the concept of Potential Energy Surfaces (PES) which is basically a plot of electronic energy as a function of nuclear coordinates. PES and its relevance in studying chemical reactions would be discussed later in this chapter. Now we move on to see what approaches have been developed in the order to solve Schrodinger equation.

2.2 Theory to solve Schrödinger Equation

The Schrödinger equation is difficult to solve even for simple atoms. In reality, it has been exactly solved only for the case of hydrogen atom and H_2^+ molecule. Only approximate solutions have been possible for other systems.

Various theories have been proposed to solve schrödinger equation approximately.
Important among them are

a. Hartree-Fock (HF) Theory
b. Density Functional Theory (DFT)

2.2.1 Hartree-Fock[7] theory

In brief, HF theory proposes an approximation to the true wave function. This approximate wave function is a Slater determinant of spin orbitals. Then energy is expressed using this approximate wave function which is then minimised with respect to the constituent spin orbitals to get single electron equations (Hartree-Fock equations). These equations have to be solved iteratively until the solution converges (i.e. till wave function and field become consistent with each other).This theory therefore is also known as Self consistent Field theory.

Here we summarizes the important points of this theory

HF approximation

“Wave function is a Slater determinant of spin orbitals”

$$\Psi = SD\,\{\chi_1, \chi_2 \dots \dots . \chi_N\}$$

$$\Psi = \begin{vmatrix} \chi_1(1) & \chi_1(2)\cdots & \chi_1(N) \\ \chi_2(1) & & \chi_2(N) \\ \vdots & \cdots & \vdots \\ \chi_N(1) & \cdots & \chi_N(N) \end{vmatrix} \qquad (2.\ 18)$$

Energy expression (Expectation Value of energy)

$$E = \langle\ \Psi|\hat{H}|\Psi\ \rangle \qquad (2.\ 19)$$

$$E = \langle\ \Psi|\hat{K} +\ \hat{U}|\Psi\ \rangle$$

$$E = \langle\ \Psi|\hat{K}|\Psi\ \rangle + \langle\ \Psi|\hat{U}|\Psi\ \rangle \qquad (2.\ 20)$$

HF equations

$$f(1)\,\chi_i\ (1) = \epsilon_i \chi_i(1) \qquad (2.22)$$

f is known as fock operator and is given by

$$f(1) = h(1) + \sum_{j=1}^{N} J_j(1) - K_j(1) \qquad (2.\ 21)$$

Where h (1) is the single electron Hamiltonian given by

$$h(1) = -\frac{\hbar^2}{2m_1}\frac{\partial^2()}{\partial {r_1}^2} - \sum_{j=1}^{M} \frac{Z_j e^2}{|r_1 - R_j|} \qquad (2.22)$$

and J is the coulomb operator operator

$$J_j(1) = \int \chi_j * (2) \frac{1}{r_{12}} \chi_j(2)\, \mathrm{d}\tau_2 \qquad (2.\,25)$$

$$J_j(1)\, \chi_i\, (1) = [\int \chi_j * (2) \frac{1}{r_{12}} \chi_j(2)\, \mathrm{d}\tau_2]\, \chi_i\, (1) \qquad (2.\,23)$$

K is the exchange operator given by

$$K_j(1)\, \chi_i\, (1) = [\int \chi_j * (2) \frac{1}{r_{12}} \chi_i(2)\, \mathrm{d}\tau_2]\, \chi_j\, (1) \qquad (2.\,24)$$

SCF procedure

Initially one guesses a set of spin orbitals. These spin orbitals are then used to construct the fock operator. Then the single electron HF equation can be solved to give energy eigen values (orbital energies) and new spin orbitals. These new set of spin orbitals are again used in the same cycle as above. This process continues till our output set of spin orbitals are equivalent to the input set of spin orbitals. After convergence, the final set of spin orbitals could be used to construct the wave function. This cyclic process is known as Self consistent Field (SCF) method.

2.2.2 Density functional Theory

This theory proposes that “ground electron density n(r) uniquely determines the ground state wave function”

i.e. $\Psi = \Psi(r_1, r_2, \ldots \ldots. r_N) = \Psi\left(n(r)\right)$ (2. 25)

Where n(r) is ground state electronic density defined as

$$\int n(r)\, dr = N \quad ; \textit{ where N is the total number of electrons.} \qquad (2.\ 26)$$

The above stated is known as Hohenberg-Kohn (HK[8]) theorm. This theory (DFT) is used to solve Schrödinger equation under a formalism developed by Kohn and Sham[9].

As a consequence of HK theorm, all the observables associated with our quantum mechanical system should also be a function of density n(r). So energy as a function of n(r) can be written as

$$E = \langle \Psi|\hat{H}|\Psi \rangle$$

$$E = \langle \Psi|\hat{K} + \hat{U}|\Psi \rangle$$

$$E = \langle \Psi|\hat{K}|\Psi \rangle + \langle \Psi|\hat{U}|\Psi \rangle$$

$$E(n) = K(n) + U(n) \qquad (2.\ 27)$$

Further the components that make up the kinetic energy can be written as

$$K\ (n) = K_s\ (n) + K_c\ (n) \tag{2. 28}$$

Where the first contribution is due to kinetic energy of a non-interacting N-electron system and second is kinetic energy contribution due to correlation effects.

Similarly the total potential energy can be broken down into

$$U\ (n) = U_H\ (n) + U_{exch}\ (n) + U_{cor}\ (n) \tag{2. 29}$$

$U_H\ (n)$ - Potential energy contribution assuming mean field of electrons (Hartree energy)

$U_{exch}\ (n)$ - Potential energy contribution due to exchange of electrons.

$U_{cor}\ (n)$ - Potential energy contribution due to electron correlation effects.

Combining all together, the the total energy is equal to

$$E(n) = K_s\ (n) + K_c\ (n) + U_H\ (n) + U_{exch}\ (n) + U_{cor}\ (n) \tag{2. 30}$$

Taking all the energy contributions due to exchange and correlation together

$$E(n) = K_s\ (n) + U_H\ (n) + E_{xc}(n) \tag{2.31}$$

Where exchange-correlation energy is defined as

$$E_{xc}(n) = K_c\ (n) + U_{exch}\ (n) + U_{cor}\ (n) \tag{2. 32}$$

The necessity in the DFT approach is explicit expression of all components of energy as a function of density i.e. explicit energy functionals. There have been several approximate expressions proposed in the past[10].

Amongst the earliest such approximations is Local density Approximation (LDA) proposed by Thomas and Fermi. It states that an inhomogeneous system may be assumed to be made up of homogeneous parts locally. It approximates the kinetic energy of a non – interacting system to be given by the following expression.

$$K_s\,(n) = \int \left(n(r)\right)^{5/3} d\tau \qquad (2.\,33)$$

It also gives an expression for the exchange energy contribution.

$$U_{exch}\,(n) = \mathrm{A} \int \left(n(r)\right)^{4/3} d\tau \qquad (2.\,34)$$

But there is no expression for correlation energy under LDA approach.

2.2.2.1 Introduction Of functionals

There have been several approaches towards getting a good functional to approximate E_{xc} .

$$E_{xc}(n) = K_c\,(n) + U_{exch}\,(n) + U_{cor}\,(n) \quad 2.\,35$$

Separate energy functional for exchange and correlation have been proposed. These are combined together to give the total exchange-correlation energy. One of such important combined functional is B3LYP. B3LYP functional combines Becke's[11] three parameter exchange functional and Lee-Yang-Parr's[12] correlation functional.

2.2.2.2 Introduction of basis sets

A general expression for a spin orbital is

$$\chi_i = \sum_j C_{ji}\phi_j \qquad (2.\ 39)$$

$\{\phi_j\}$ *are fictitious orbitals that form the basis set .*

Two types of orbitals are used as basis sets. Slater type Orbitals (STO) and Gaussian Type orbitals (GTO).

A general form of a GTO is given by

$$\phi(r) = A\, e^{-\alpha r^{2}} \qquad (2.40)$$

Futhermore contraction coefficients are used to form what are known as Contracted Gaussian type orbitals (CGTO).Using these CGTOs, one can construct the modernly used basis sets such as minimal basis sets (STO-3G), split valence basis sets (3-21G, 6-31G, 6-311G).Split valence basis sets are the basis sets in which the core orbitals are represented by a single set of functions (CGTO) while valence orbitals are represented by multiple sets of CGTO. Examples of split valence basis sets are given below.

3-21G: 1s is a combination of three CGTO, 2s and 2p each combination of two CGTO and 2s’ and 2p’ composed of one CGTO.
6-31G: 1s is a combination of six CGTO, 2s and 2p each combination of three CGTO and 2s’ and 2p’ composed of one CGTO.

2.3 Potential energy Surface

Theoretically chemical reactions can be imagined using the concept of potential energy surface (PES).As Potential energy surface is an imaginary surface constructed using the Born-Oppenheimer hypothesis, a chemical reaction may be said to be transformation that moves us ”from one well to another well on the PES ”.

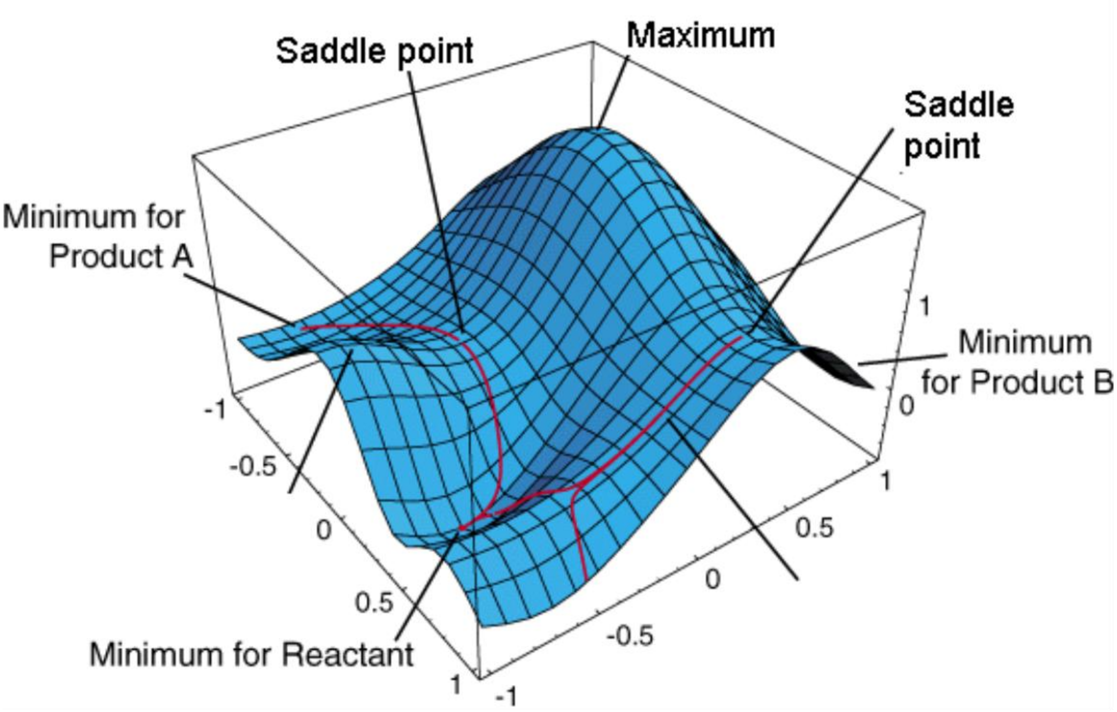


Figure 2.3.1: A representative image of PES

2.3.1 Distinction between Important points on PES

There are important points to be distinguished on the potential energy surface.There are points concerning the stable reactant and product molecules and also concerning the transition states . Mathematically these points are distinguished as shown below.

Let a point on PES be

$$(r_1, r_2, \dots r_i \dots\dots r_N) = \left((x_1, y_1, z_1), (x_2, y_2, z_2), \dots (x_i, y_i, z_i) \dots\dots (x_N, y_N, z_N)\right)$$

All the points of significance namely, maxima, minima and TS would have first derivative of energy with respect to nuclear axes as zero

$$\frac{\partial E}{\partial x_1} = \frac{\partial E}{\partial x_2} = \frac{\partial E}{\partial x_3} = \cdots = \frac{\partial E}{\partial x_N} = 0 \qquad \frac{\partial E}{\partial x_i} = 0 \quad (2.41)$$

$$\frac{\partial E}{\partial y_1} = \frac{\partial E}{\partial y_2} = \frac{\partial E}{\partial y_3} = \cdots = \frac{\partial E}{\partial y_N} = 0 \qquad \frac{\partial E}{\partial y_i} = 0 \quad (2.42)$$

$$\frac{\partial E}{\partial z_1} = \frac{\partial E}{\partial z_2} = \frac{\partial E}{\partial z_3} = \cdots = \frac{\partial E}{\partial z_N} = 0 \qquad \frac{\partial E}{\partial z_i} = 0 \quad (2.43)$$

The second derivatives uniquely define these points as follows

Maxima:

$$\frac{\partial^2 E}{\partial {x_i}^2} < 0 \ , \ \frac{\partial^2 E}{\partial {y_i}^2} < 0 \, , \frac{\partial^2 E}{\partial {z_i}^2} < 0 \quad (2.\ 44)$$

Minima:

$$\frac{\partial^2 E}{\partial {x_i}^2} > 0 \ , \ \frac{\partial^2 E}{\partial {y_i}^2} > 0 \, , \frac{\partial^2 E}{\partial {z_i}^2} > 0 \quad (2.\ 45)$$

TS (First order saddle point / Case of minimal maximum i.e. maximum along one direction, minimum along all other perpendicular directions)

$$\frac{\partial^2 E}{\partial {x_i}^2} < 0 \;, \quad \frac{\partial^2 E}{\partial {y_i}^2} < 0 \,, \frac{\partial^2 E}{\partial {z_i}^2} < 0$$

But for one of the 3N coordinates $\frac{\partial^2 E}{\partial {x_i}^2} > 0 \;\; or \;\; \frac{\partial^2 E}{\partial {y_i}^2} > 0 \;\; or \;\; \frac{\partial^2 E}{\partial {z_i}^2} > 0$ **(2.46)**

In matrix form, the first derivatives and second derivatives are put in Gradient and Hessian matrices respectively.

2.3.2 Ways of traversing Potential energy surfaces.

There have been many algorithms[13] proposed to walk on potential energy surface and locate important points such as maxima, minima and saddle points (transition state).
Two of such TS –searching algorithms that are relevant to this work are given below.

a. Quadratic Synchronous Transit[14]
b. Eigen vector Following

GAUSSIAN 03[15] implements these two algorithms in a combined form under the name of “QST3” which requires the optimised geometries of both the reactant and product and also a guess structure of the transition state.

While Quadratic Synchronous Transit method walks on a quadratic arc joining the reactant and product valley on PES and searches for the maximum along this arc. The Eigen vector following method involves computing the hessian at the starting point and subsequently diagonalising the matrix and thereafter moving along the eigenvector that has the most negative eigen value. Hessian and gradient are computed at each step and the process is repeated till the search for a first order saddle point (transition state) is complete.

2.3.3 Utility of ab-initio quantum calculations in constructing PES and calculating Activation energy barriers .

In the context of a chemical reaction, a 1D projection of PES[16] to gives us the simplistic picture of energy profile of the reaction. And thus arises the importance of location of transition state on PES and calculating its energy to construct energy profile of a reaction.

An example of such an energy profile is as shown below …

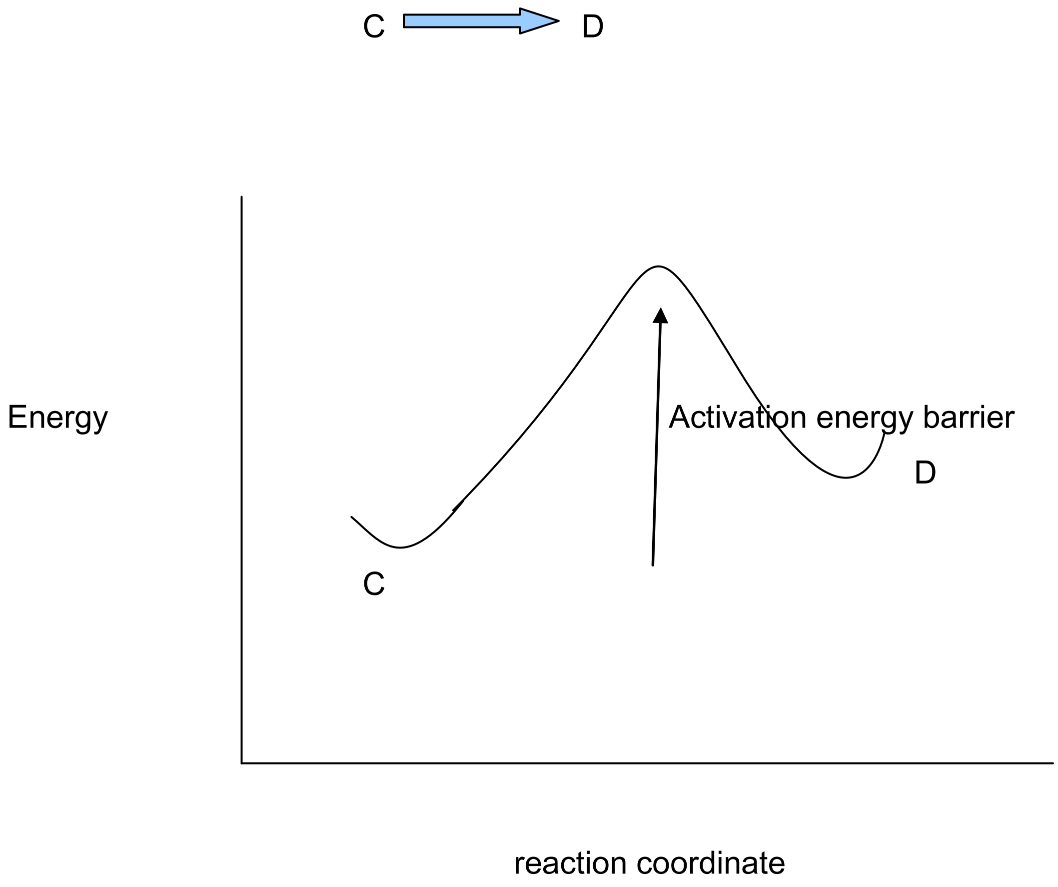


Figure 2.3.2: Energy profile of a hypothetical reaction.

3. Ab initio Quantum chemical investigations

Ab initio quantum chemical software packages have been developed to investigate chemical phenomenon of interest. These software packages are based on the basic quantum mechanical theory as outlined in the previous chapter. Using these quantum chemical tools we set out to do some chemical investigations. In the first experiment the organic reaction mentioned before was studied mechanistically for a particular substrate. The transition structures connecting reactants to intermediates and intermediates to products were found and a measure of energy barriers was estimated.Moving to the second experiment a particular stereochemical preference shown in a "wet lab study " employing the same reaction was approached theoretically and the notion of kinetic and thermodynamic control was applied to explain the observation. Previously theoretical studies[17,18] have been done on selenium dioxide mediated oxidation reaction and they served as an aid in terms of their approach and analysis of the reaction.

3.1 "Allylic hydroxylation of alkenes using selenium dioxide" – A mechanistic experiment

In order to justify for oneself the mechanism of the reaction, we set out to do a mechanistic study of the reaction. Our aim was to study the complete reaction and in process find out the relevant transition states for the intermediate steps in the reaction.We then constructed an energy profile for the whole reaction.

A simple substrate was chosen as shown below.The Schematic of the reaction is illustrated below.

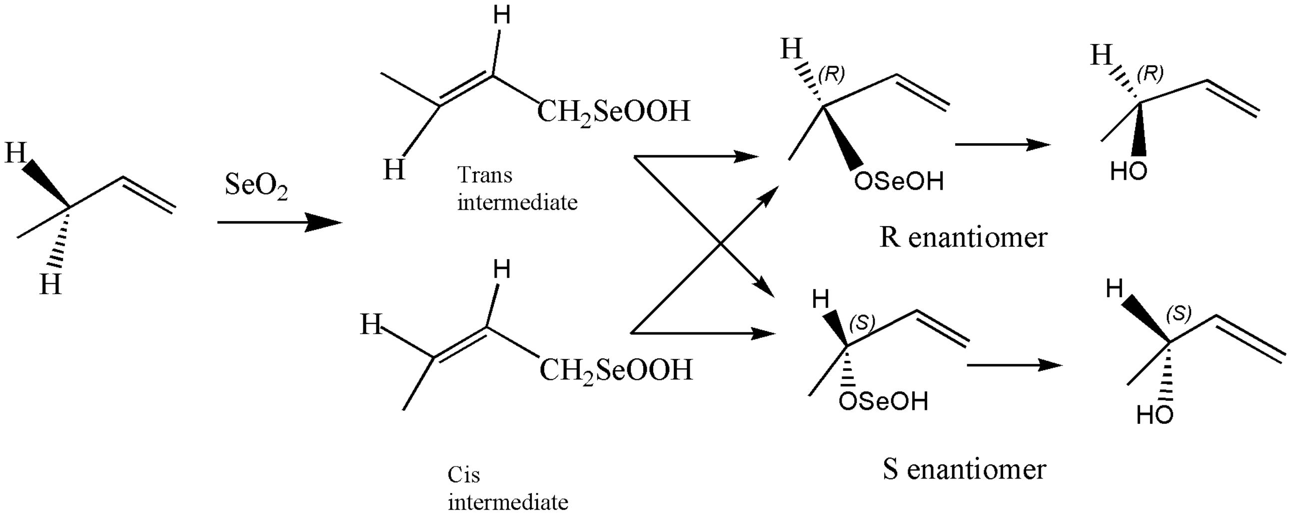


Figure 3.1.1: Allylic hydroxylation of butene

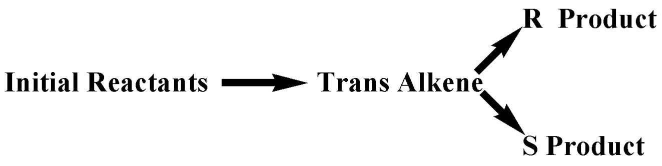
3.1.1 Approach & Methodology

Ab-initio Calculations were performed using Density Functional Theory (DFT).GAUSSIAN 03 software was used and calculations were done using B3LYPfunctional and 6-31 G basis set.

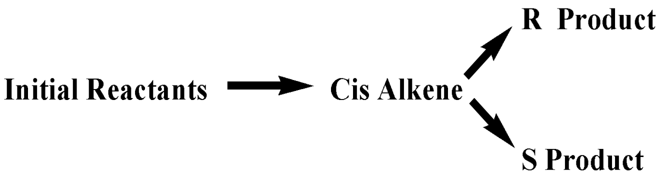
The Study generated the optimized structures of all the reactants,intermediates and products and their calculated energies.Initially the optimisation of reactant complex was carried out.Subsequently the relevant transition states for each of the two steps were found using QST3 method available in Gaussian03. The Transition structures were checked for presence of one and only one imaginary frequency and also verified for the geometrical validity as an intermediate geometry in a valid transformation from reactant to product.Compiling all the energy information gathered, we constructed the energy profile for the complete reaction.

The study of the whole reaction has been divided into two parts

1.



2.



3.1.2 Result and discussion

We seek to know the stability of the molecules relative to each other. In particular, we wished to know which one of the two intermediates was more stable and similarly which one of the products was more stable. Therefore taking the energies from optimization of these molecules, we plotted the energies of the intermediates and products relative to that of the initial complex which is shown below in Figure 3.1.2. It was found that Trans intermediate was more stable amongst the intermediates while S product was more stable amongst the products.

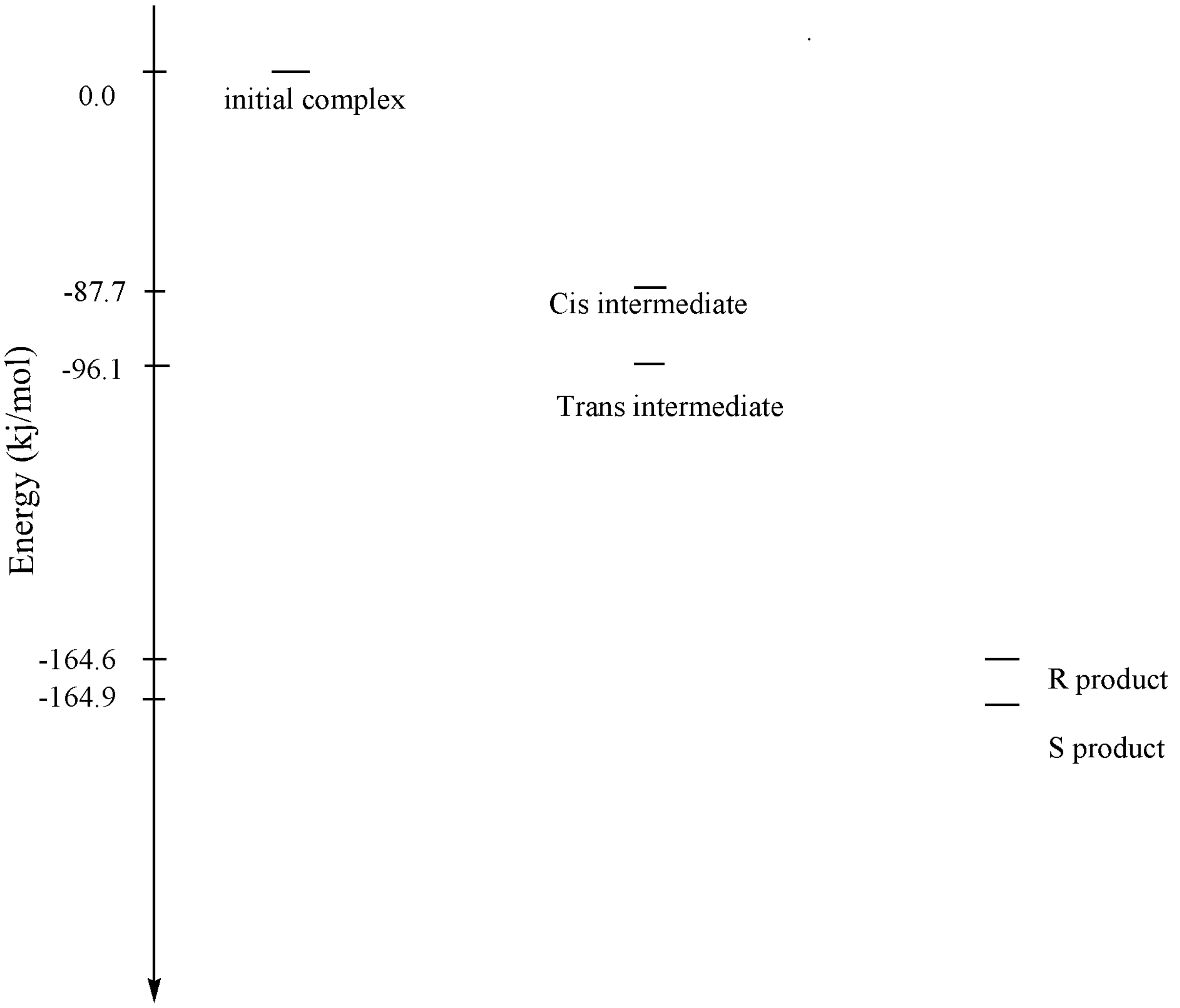


Figure 3. 1.2 : Plot of relative energies of reactant, intermediates and product

Now the transition states for the intermediate steps were found and their optimized geometries and energies were obtained. As the reaction was complex and gave rise to multiple intermediates, the study was divided into two parts as mentioned earlier.

Part 1

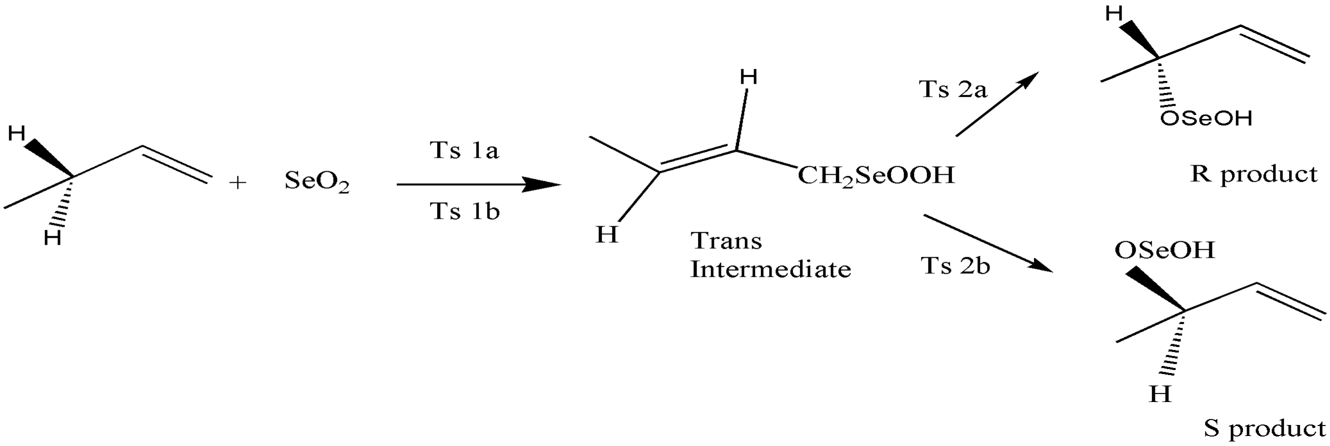


Figure 3.1.3: One part of the whole reaction through the trans intermediate.

We located the relevant transition states as depicted in the above scheme and the energy profile for this part of reaction was constructed based on the energy values of these transition states.

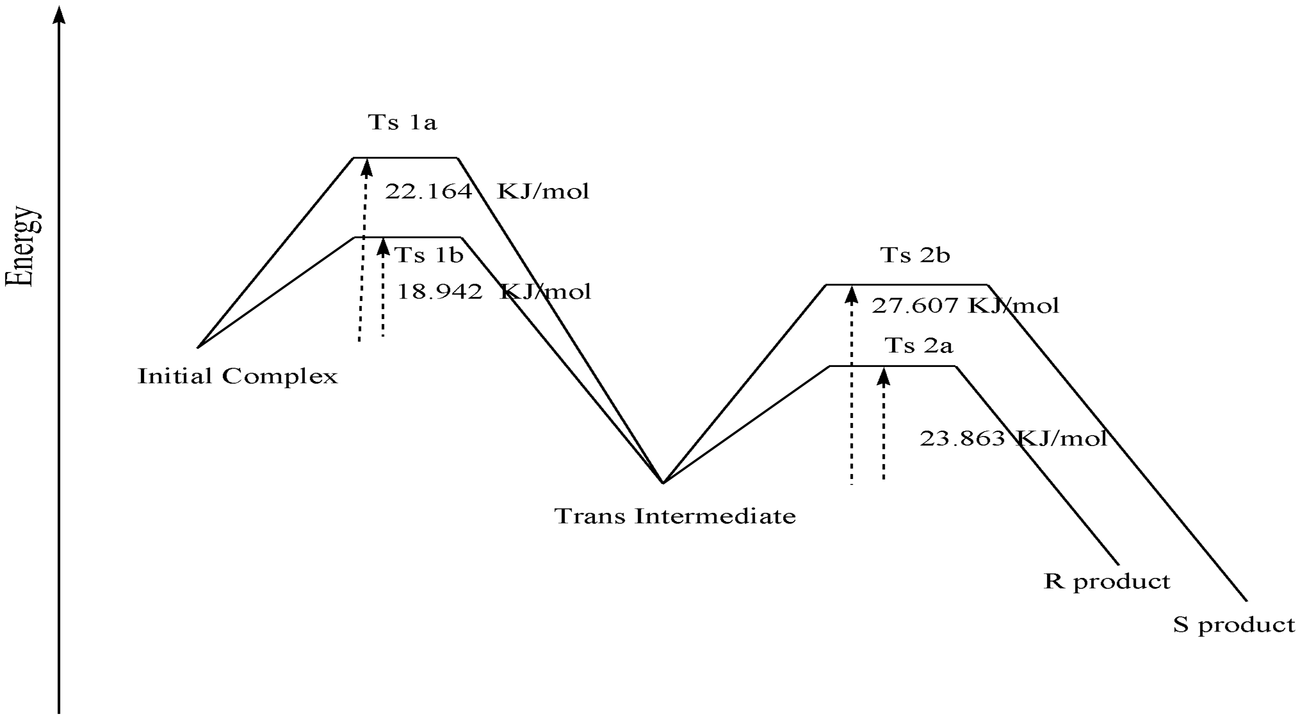


Figure 3.1.4 : Energy profile for the first part of the reaction.

Looking at transition state geometries and energies, one can note some particular characteristics. Amongst the two transition states (Ts 1a and Ts1b) joining the reactant complex and Trans intermediate, Ts 1b is lower in energy compared to Ts 1a by ~ 3 KJ/mol. This may arise due to greater degree of steric hindrance present in Ts 1a (Figure 3.1.5). Also the energy barrier for formation of R product from Trans intermediate is
~ 4 KJ/mol lower than that of S product.

The geometries of the transition states are depicted below in figure 3.1.5 – 3.1.6.

Ts 1a

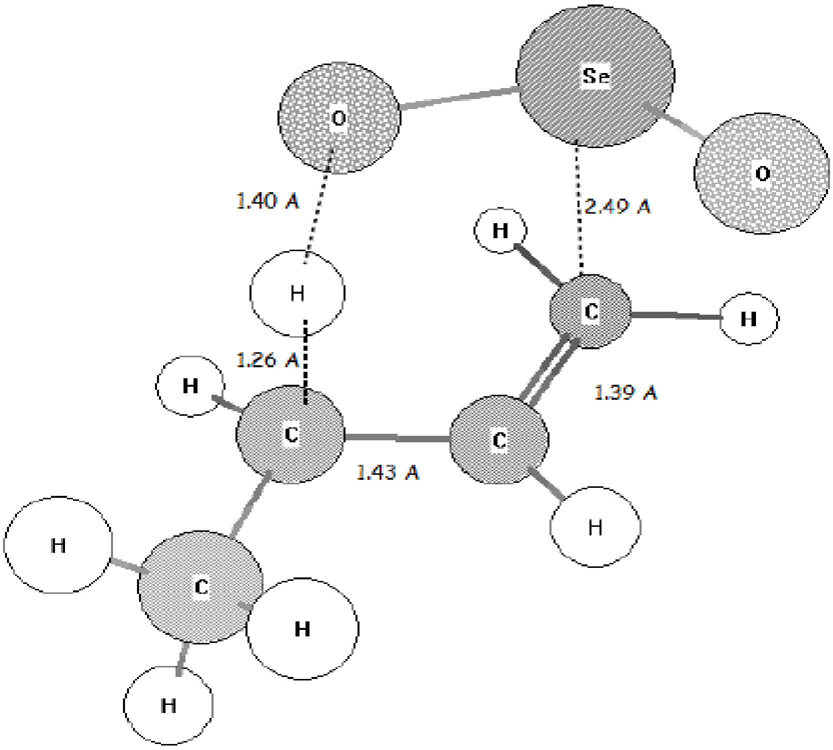


Figure 3.1.5: Optimized geometry of Ts 1a

Ts 1b

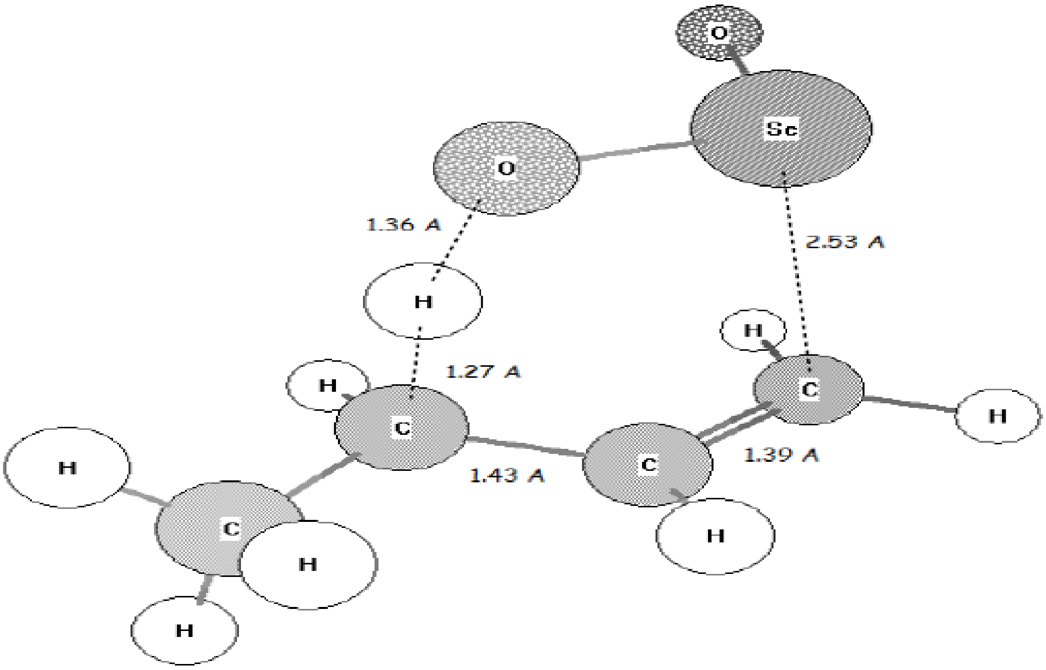


Figure 3.1.6: Optimized geometry of Ts 1b

Ts 2a

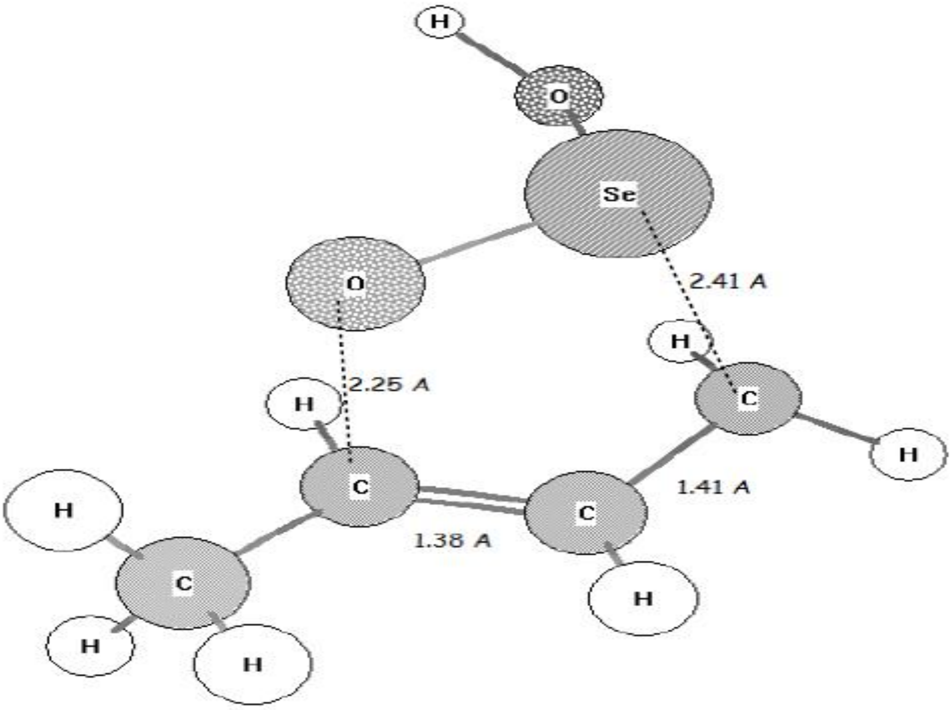


Figure 3.1.7: Optimized geometry of Ts 2a

Ts 2b

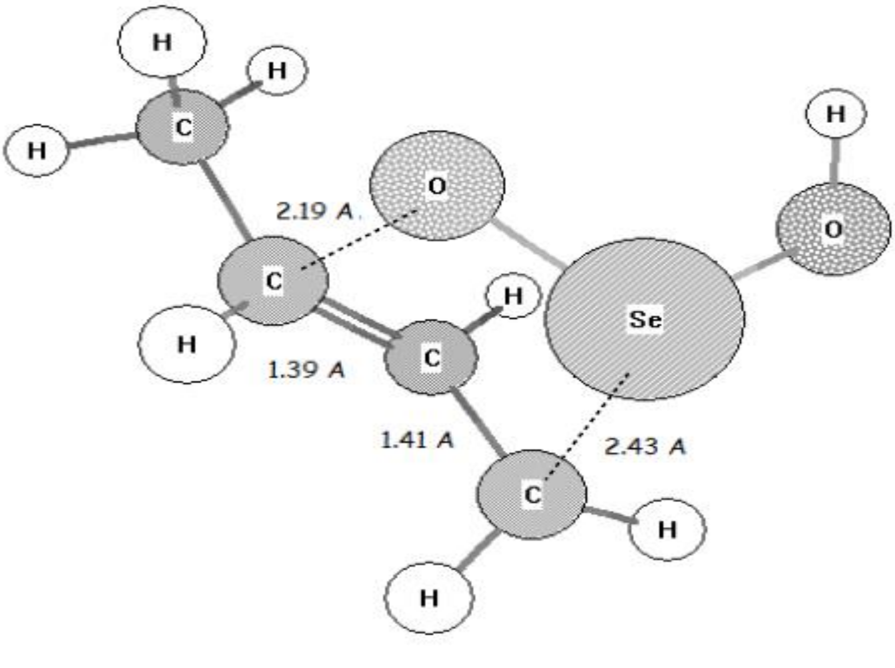


Figure 3.1.8: Optimized geometry of Ts 2b

Similar search for transition states was conducted for the next part of the reaction.

Part 2

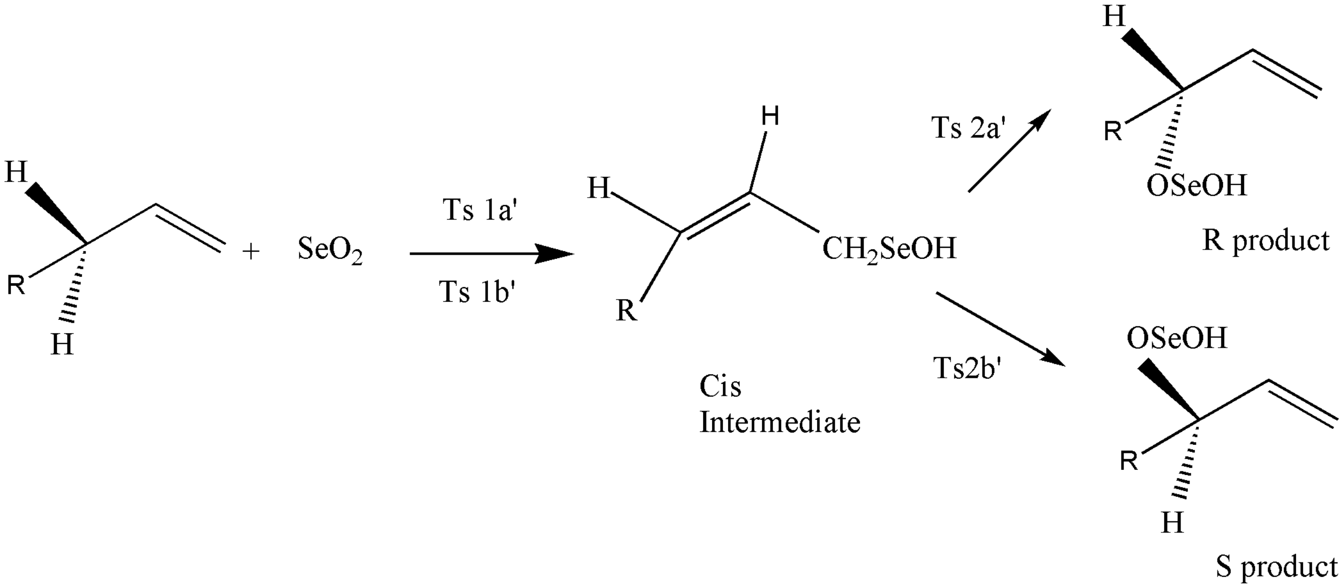


Figure 3.1.9: Second part of the reaction through cis intermediate.

The relevant transition states were located and energy profile for this part was constructed. (refer to figure 3.1.10)

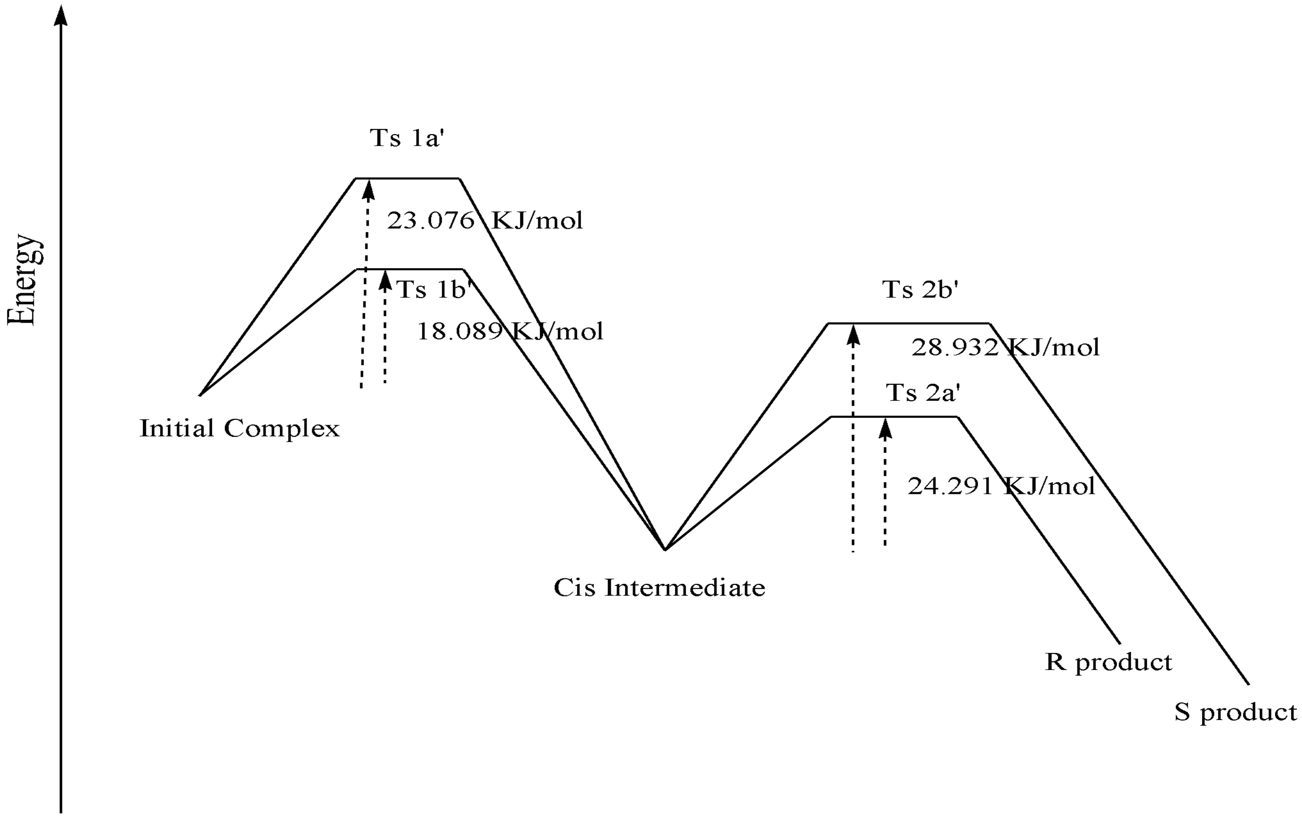


Figure 3.1.10: Energy profile for the second part of the reaction

Ts 1b’ is lower in energy as compared to Ts 1a’. Also the energy barrier for formation of R product from cis intermediate is lower by ~ 5 KJ/mol as compared to that for S product.

Ts 1a and Ts 1a’ are analogous to each other in terms of approach of selenium dioxide with respect to double bond plane as are Ts 1b and Ts 1b’ to each other. In the second step of the reaction i.e. sigmatropic rearrangement, above the plane or below the plane attack decides the stereochemistry of the resulting product.

Ts 1a’

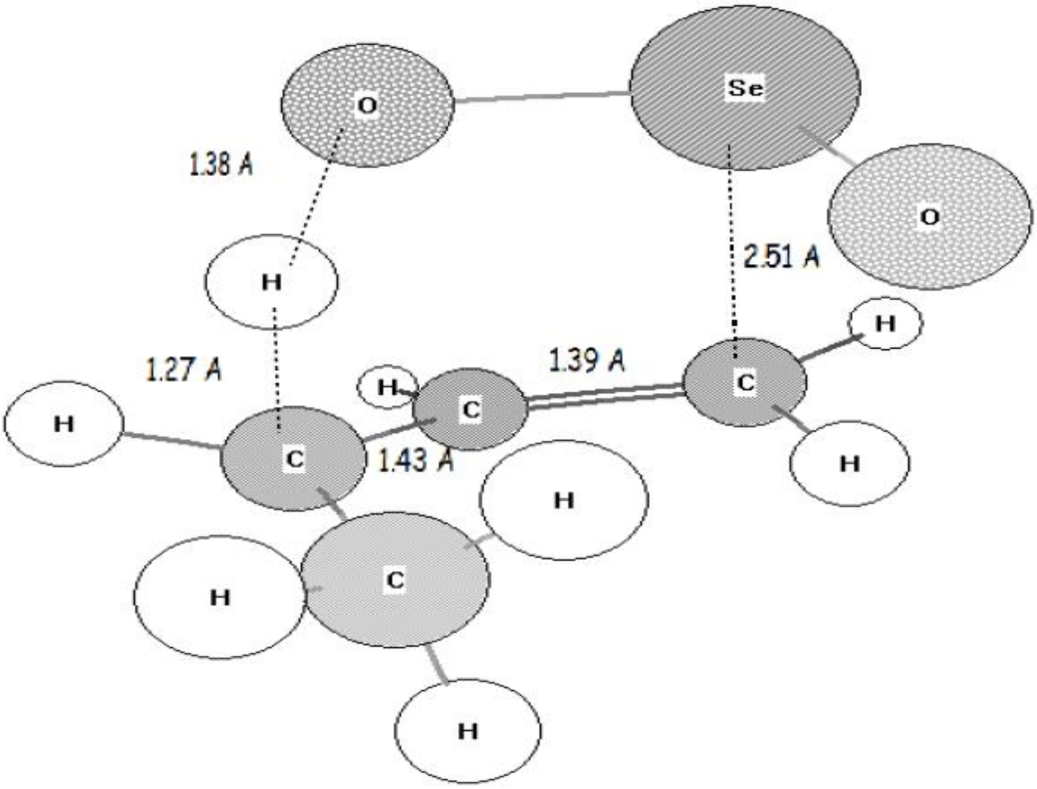


Figure 3.1.11: Optimized geometry of Ts 1a’

Ts 1b’

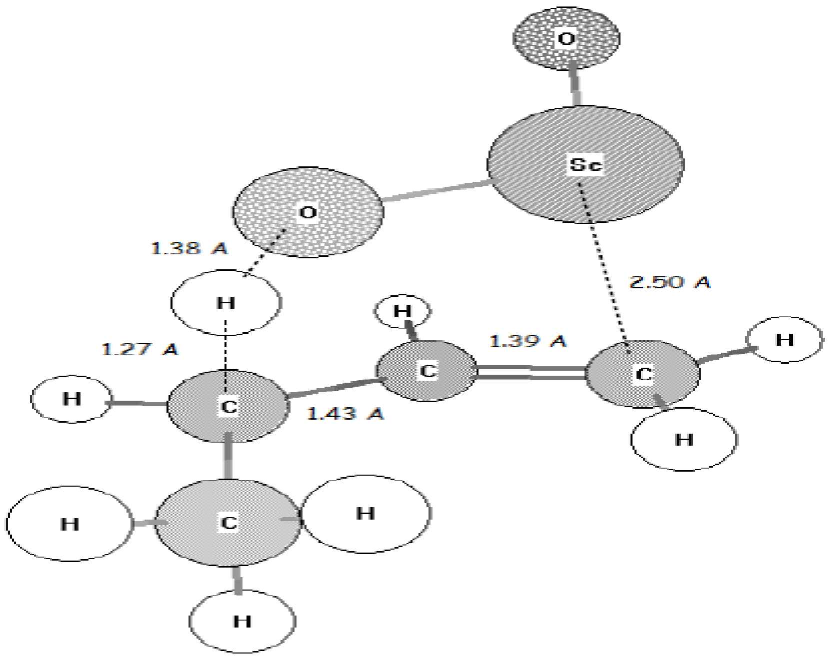


Figure 3.1.12: Optimized geometry of Ts 1b’

Ts 2a’

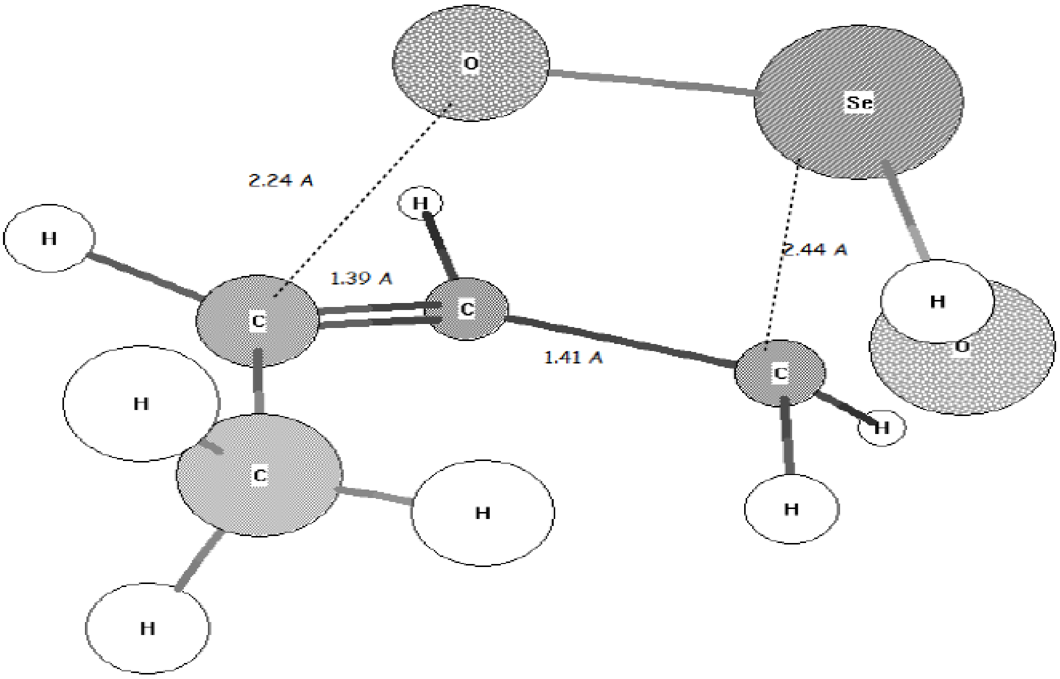


Figure 3.1.13: Optimized geometry of Ts 2a’

Ts 2b’

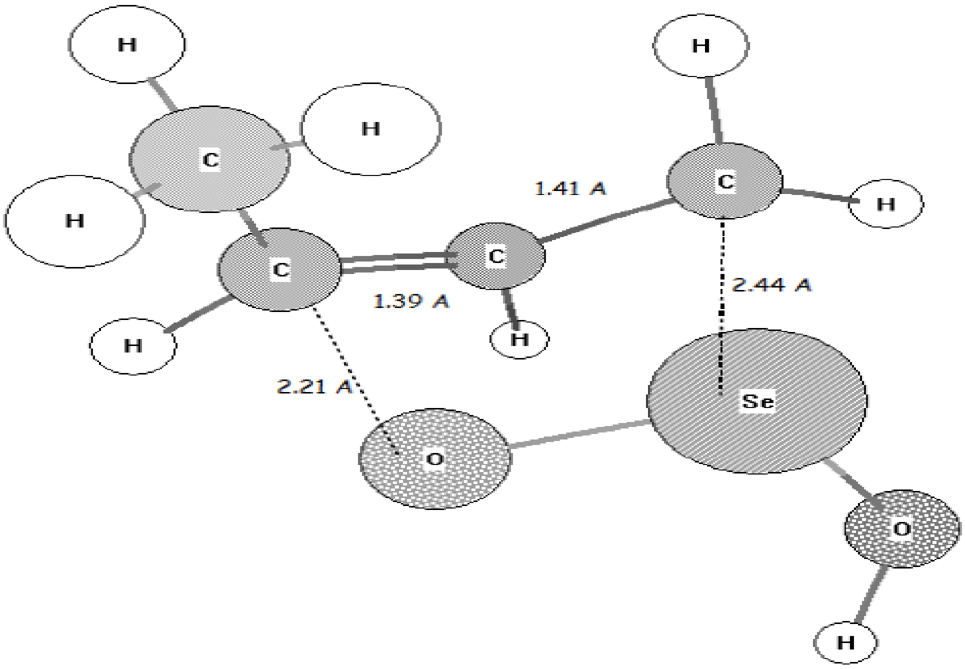
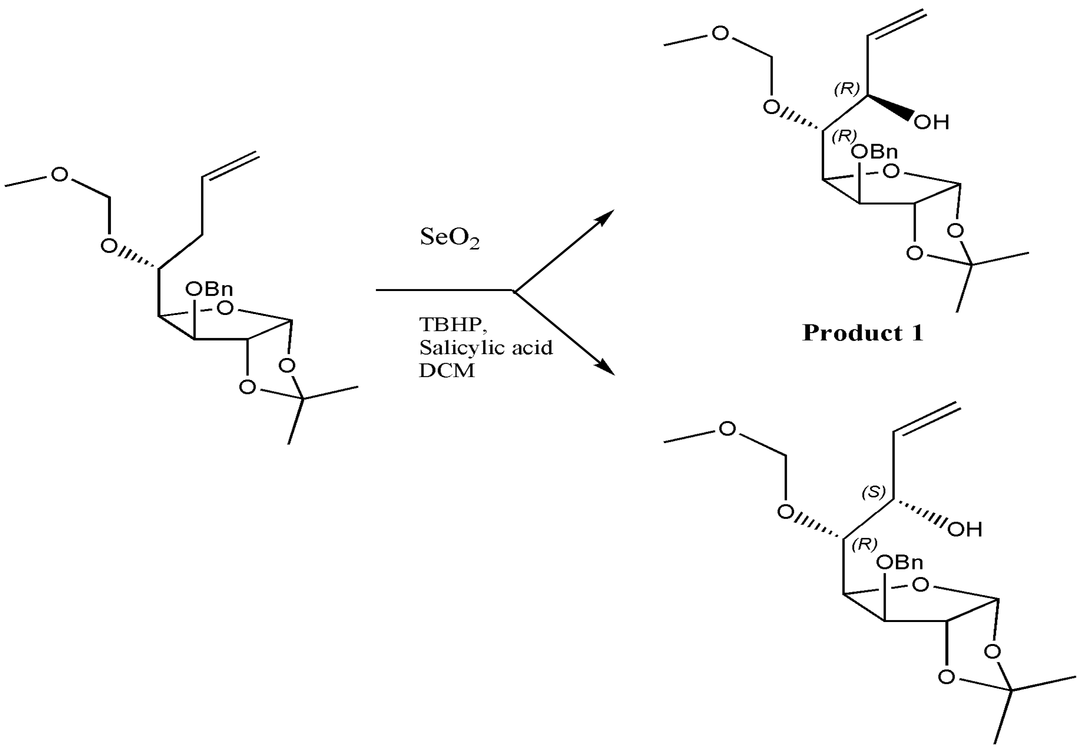


Figure 3.1.14: Optimized geometry of Ts 2b’

In summary, relevant transition states connecting the wells (reactant complex, intermediates, products) on PES were located. This helped us construct the energy profile of the reaction. We got a measure of the geometrical arrangement of attack in the ene addition step. We also could visualise the possibilty of above the plane / below the plane way of sigmatropic reaarangement of either of intermediates to give one or the other enantiomer.

3.2 In partnership with experiment : explaining stereochemical preference

A yet unpublished experimental study by Rale et al. employing the selenium dioxide mediated allylic hydroxylation reaction on D-glucose derived olefin was done.Two products with different chirality at the allylic position were isolated as expected. The reaction is shown below in figure 3.2.1.



Product 1

Product 2

Figure 3.2.1: Experimentally carried out selenium mediated allylic hydroxylation reaction with the isolated products.

Further characterisation (using X-ray crystallography) established that product 1 was the major product obtained.As one can see that the two products (1 and 2) differ only in terms of the chirality at the allylic position. It was an interesting challenge therefore to explain the stereochemical preference noticed.

To understand this, the mechanism of the reaction was investigated for the given substrate by ab-initio quantum chemical calculations.

As per the proposed mechanism by Sharpless explained earlier, the reaction proceeds via consecutive pericyclic reactions i.e ene reaction followed by [2,3]- sigmatropic rearrangement. When one applies this mechanism to the given substrate, one can have the possibilities of intermediates and products as shown in Figure 3.2.2.

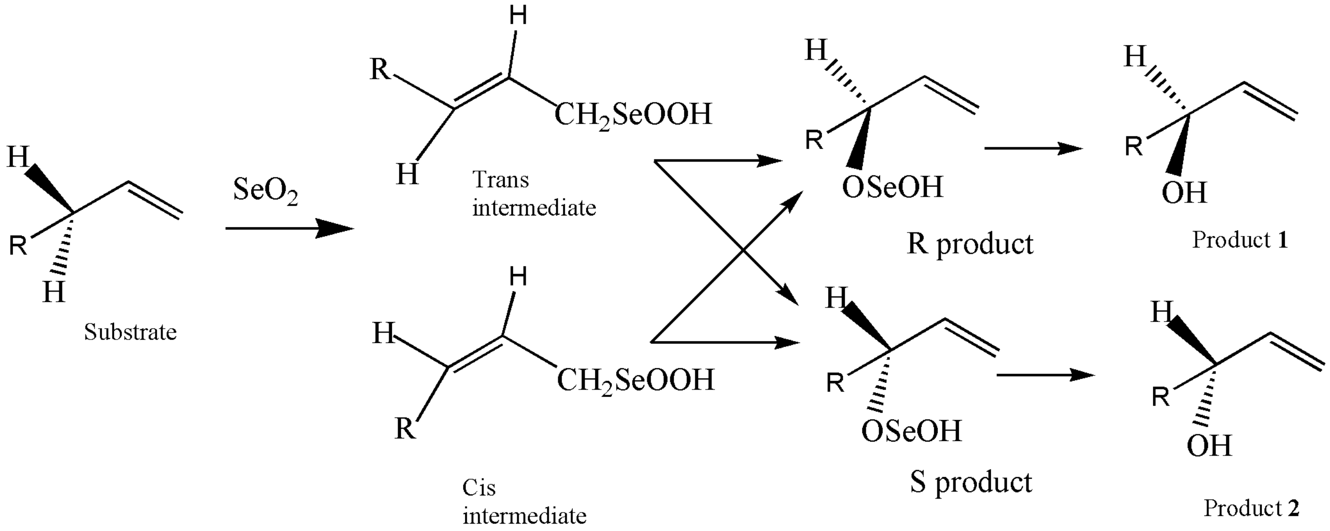
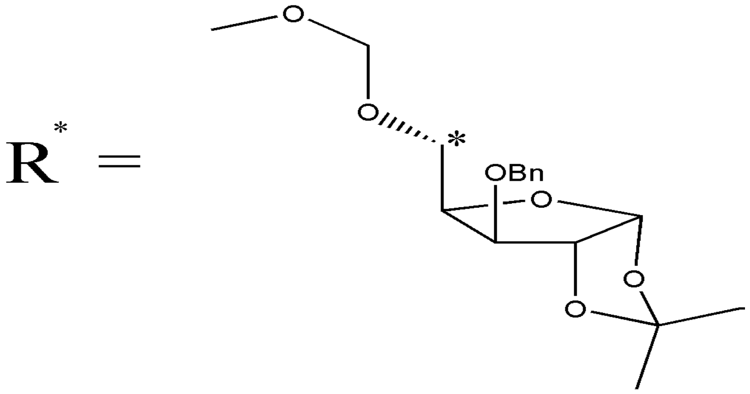


Figure 3. 2.2: Detailed representation of the reactants, intermediates and products for the given substrate .

where



3.2.1 Approach and methodology

The second step of the reaction i.e the sigmatropic rearrangement (refer to figure 3.2.2 and figure 3.2.3) is the key to explaining the stereochemical preference as a new chiral center is being created. The way the rearrangement occur i.e. top face attack or bottom face attack results in the formation of either of the two diastereoisomer (product **1** and **2**).

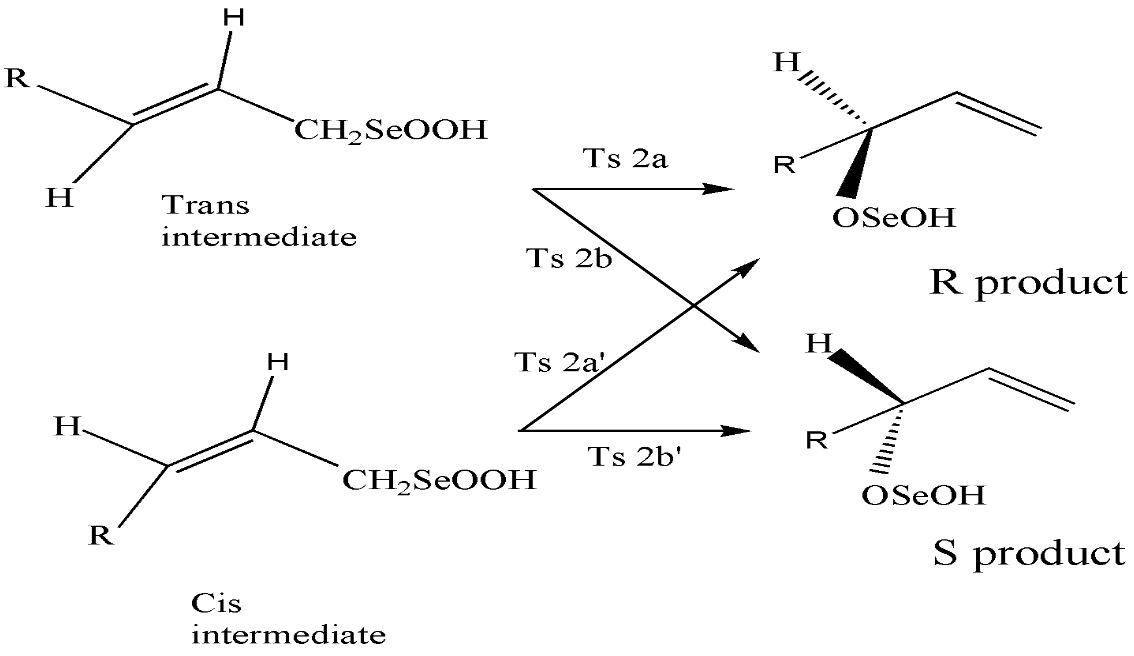


Figure 3.2.3: Sigmatropic rearrangement step with relevant transition states.

The energy optimizations of the reactants, intermediates, transition states and products were done by Gaussian03 code* under the framework of density function theory (DFT) with B3LYP functional and 6-31g basis set. The relevant transition states were found for the sigmatropic rearrangement step (Figure 3.2.3). The transition states were located using QST3 method in the Gaussian 03 software. Frequency calculations were further done for each of the transition state structures (TS) and an imaginary frequency was found in each case confirming that the structure found was indeed a transition state.

3.2.2 Results and discussion

In Figure 3.2.4, we have plotted the energies of the intermediates and products with respect to that of the initial reactant complex.

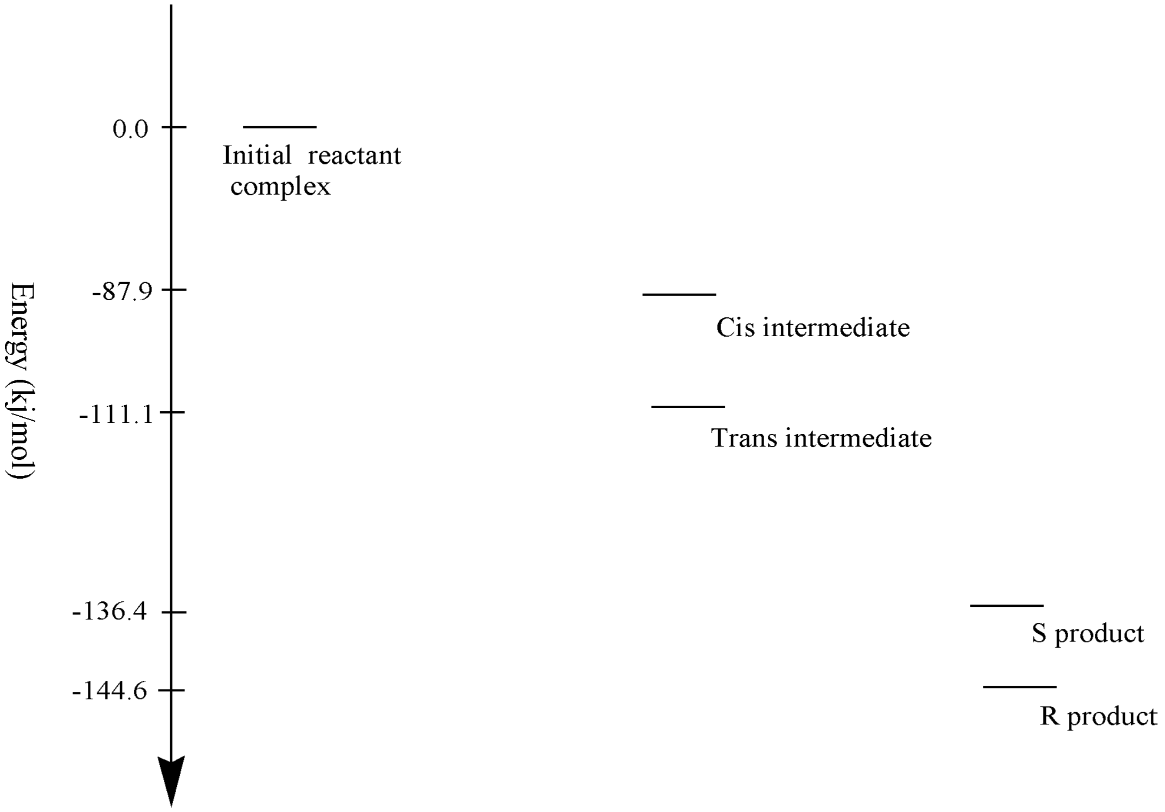


Figure 3.2.4: Relative energies of the optimized structures of the reactant complex, intermediates and products.

The calculations revealed that the R product was energetically more stable than S product by ~ 8 KJ/mol as shown in Figure 3.2.4. This means that R product would be formed in major proportion if the reaction was under thermodynamic control.

Using the energies of the TS's, the energy profile was constructed. (Refer to Figure 3.2.5)

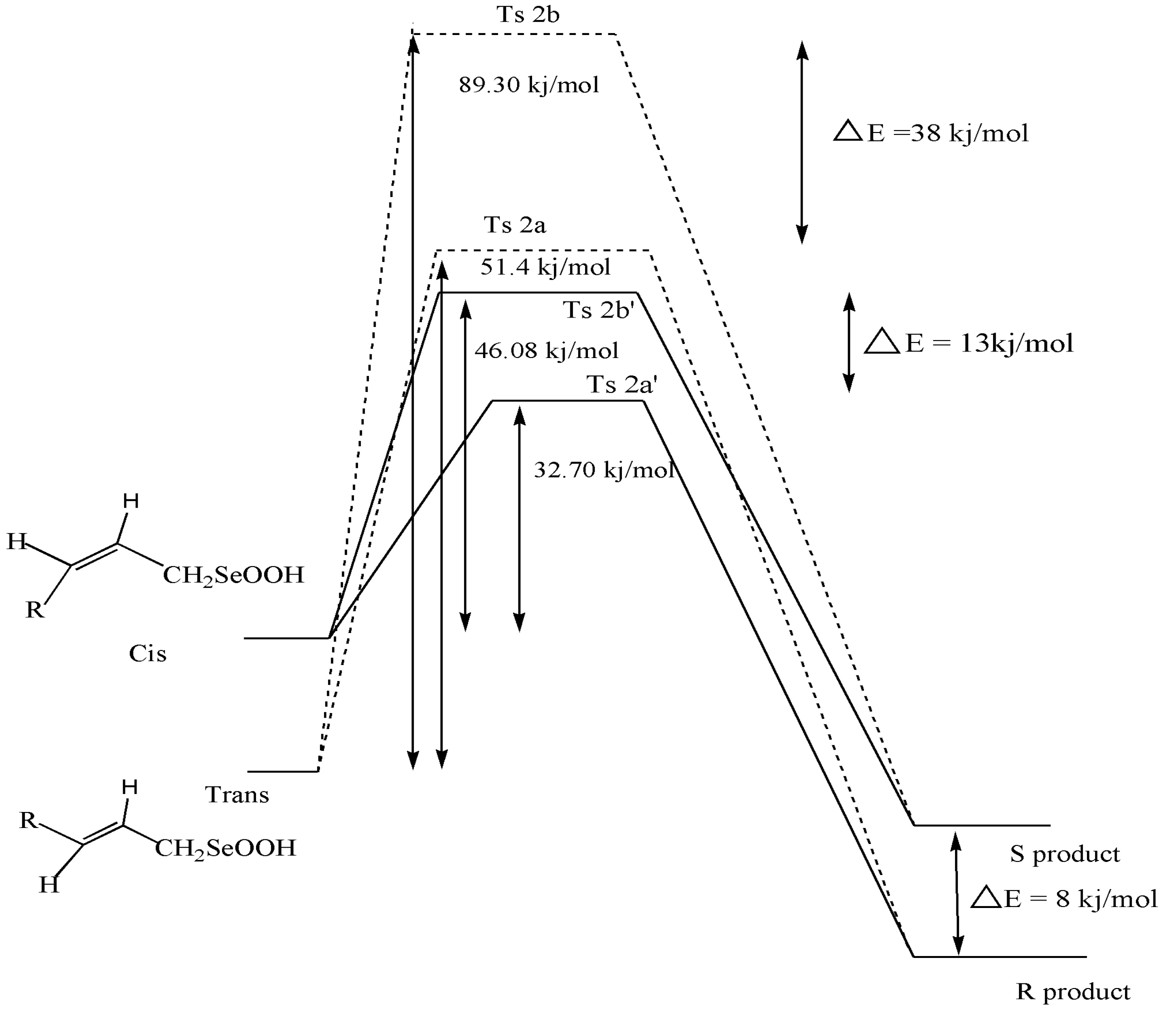


Figure 3.2.5 : Energy barriers for the Sigmatropic rearrangement step .

Further looking at the energy barriers for the sigmatropic rearrangement step, we note that the activation energy barrier for transformation from Trans intermediate to the R product is ~ 38 KJ/mol lower as compared to that to the S product. Similarly the energy barrier from Cis intermediate to R product is ~ 13 KJ/mol lower than that to the S product. It is evident from the above facts that the formation of R product is favoured kinetically from either of the two intermediates.

So, one can conclude that the formation of R product is favoured both kinetically and thermodynamically.

Below the optimized geometries of the transition states are given. One can draw similarities between the geometrical approach and atomic distances between the previous (Section 3.1) and this study.

Ts 2a

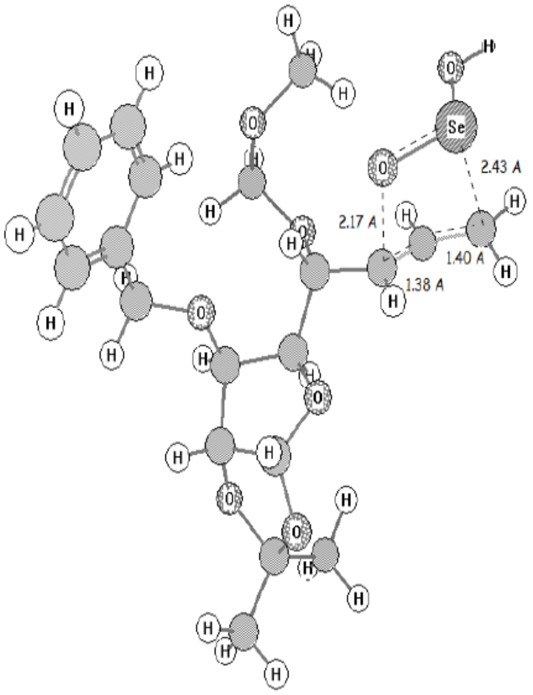


Figure 3.2.6: Ts 2a

Ts 2b

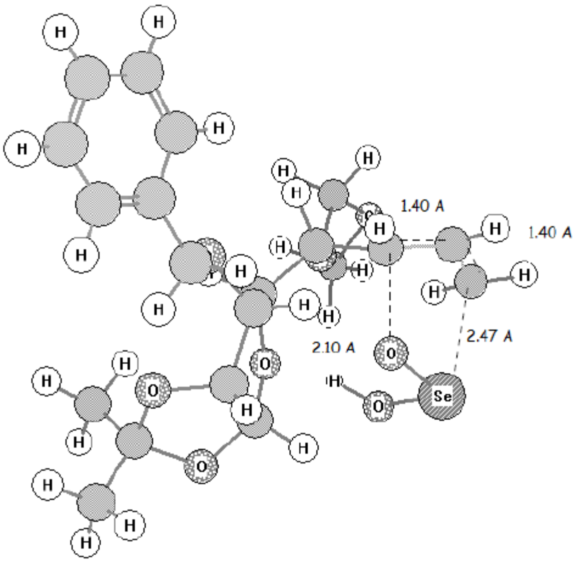


Figure 3.2.7: Ts 2b

Ts 2a'

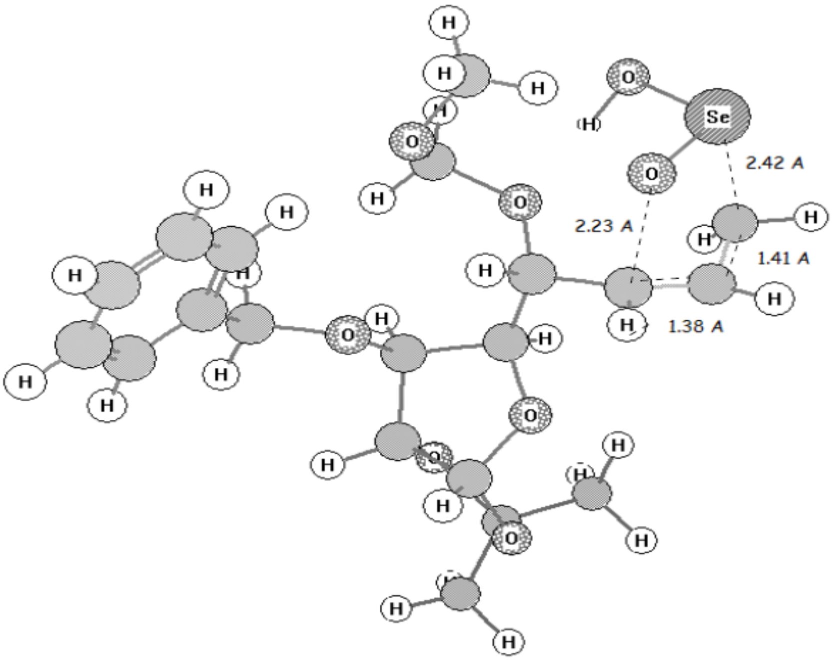


Figure 3.2.8: Ts 2a'

Ts 2b'

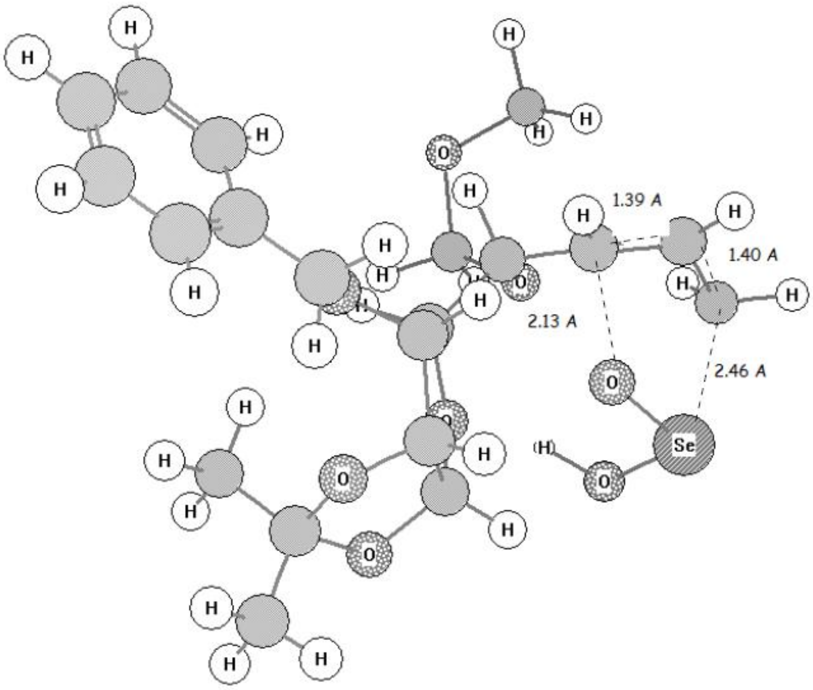


Figure 3.2.6: Ts 2b'

3.3 Discussion

As described in the sections 3.1 and 3.2, selenium dioxide mediated allylic oxidation reaction was studied using tools of ab initio quantum chemistry. The two step mechanism proposed by Sharpless et al. was verified. Transition states for the intermediate reaction steps of ene addition and sigmatropic rearrangement were found for the allylic hydroxylation of butene. The energy profile with the activation energy barriers hinted towards the viability of the reaction proceeding through these paths. Furthermore this study gave us a sense of geometrical approach in each of the intermediate steps. All of this acted as an aid while approaching the next problem which was to explain an experimental observation of stereochemical preference amongst the isolated products. Activation energy barriers were calculated at the level of Density Functional Theory (DFT) with B3LYP functional. Finally the idea of kinetic and thermodynamic control was applied and stereochemical preference shown in the reaction was explained.

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