

Hydrolysis of protonated diazoalkanes: Tracing the mechanism of catalyzed and non-catalyzed reactions

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MASTER OF SCIENCE

By

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Declaration

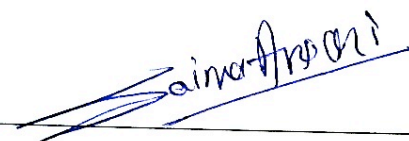
I hereby declare that the matter embodied in this report is the result of investigation carried out by me in the Department of Chemistry, Indian Institute of Technology Hyderabad under the supervision of Dr. Bhabani Shankar Mallik.

In keeping with general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

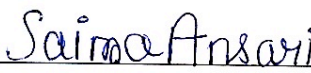


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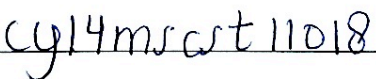
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Dedication

*This thesis is dedicated to
My family for their unconditional love.*

Acknowledgement

It is a genuine pleasure to express my deep sense of thanks and gratitude to my mentor Dr. Bhabani Shankar Mallik, IIT Hyderabad.

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I also express my gratitude to IIT Hyderabad for facilitating HPC workstation, which made my work much faster.

Lastly, I express love for my family and my friends who have supported me throughout.

Abstract

The reaction of protonated diazomethane with water and hydroxide spontaneously to give methanol and a nitrogen molecule is being studied computationally. Water attacks as the nucleophile following S_N2 mechanism and hydroxide attacks as a base as well as a nucleophile. The structures are optimized using software Gaussian 09. The method applied is DFT B3LYP having basis set 6-311G + (2d, p). The energies are compared relatively. The final product is found to be -34.7 kcal/mol stable than the reactant in case of the methane diazonium ion reacting with two water molecules. In case of hydroxide (nucleophile) the final product is found to be -233.2 kcal/mol stable. Reactions of the cation with hydroxide as a base, yields the product diazomethane and water and the energy of the isolated product is -184.3 kcal/mol. The driving force of the reaction is removal of nitrogen molecule as a byproduct (triple bonded, very stable).

The study has been taken further on $Ar^1Ar^2CHN_2^+$ cation where Ar^1 = phenyl and Ar^2 = tolyl. It is observed that the cation furnishes alcohol (Ar^1Ar^2CHOH) readily with hydroxide. On the other hand, in case of uncatalyzed hydrolysis, the cation leads to the formation of alcohol in presence of three or more water molecules.

Hydrolysis of Ruthenium catalyzed $Ar^1Ar^2CN_2$ is providing a diazene coordinated Ruthenium complex along with a ketone instead of an alcohol. The hapticity observed for diazene is one.

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Chapter 1

Introduction

1.1 Diazomethane

1.1.1 Structure: Diazomethane exists in ylide form. On protonation it gives methane diazonium ion (MDI) which can exist in two resonance forms (Figure 1). Ab initio molecular orbital calculations have shown that the C-protonated diazomethane is more stable than N (end) protonated diazomethane¹.

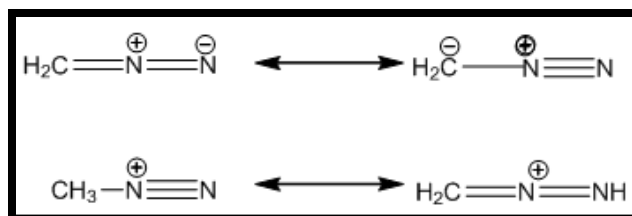


Figure 1 Resonance structures of Diazomethane and Protonated Diazomethane

Considering molecular orbital diagram for MDI, the primary interaction takes place between a lone pair orbital on N_2 and the lowest unoccupied orbital of CH_3^+ , which is the 2p orbital at C^+

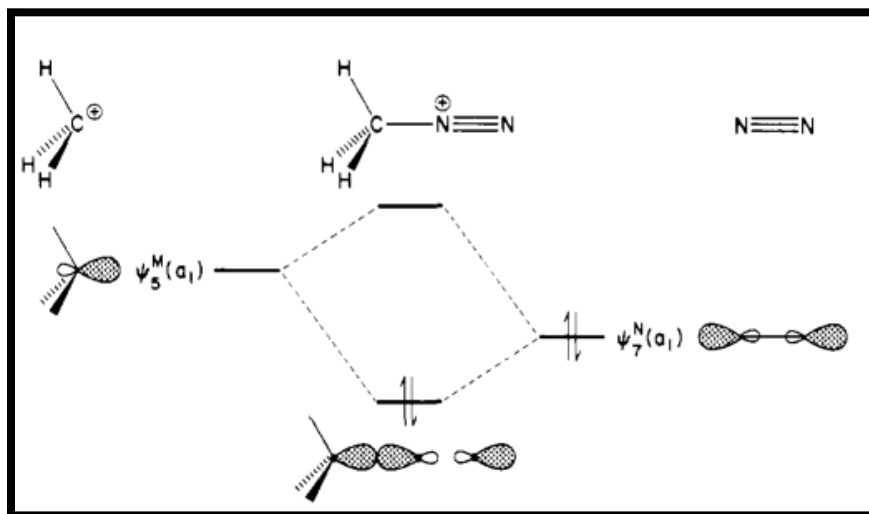
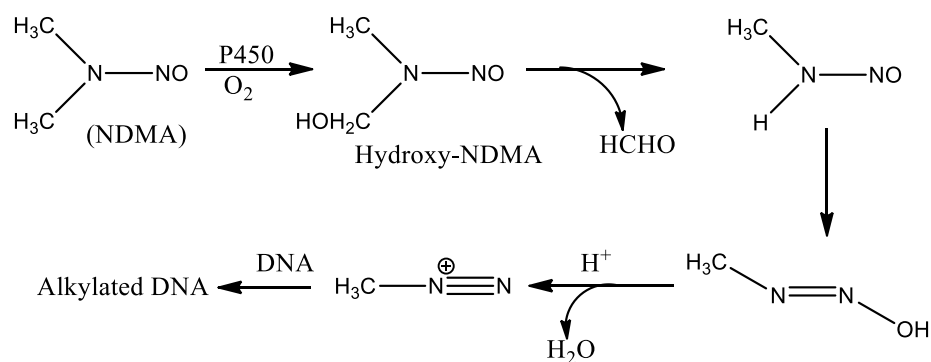


Figure 2 Orbital interaction diagram for MDI
Source: *J. Am. Chem. Soc.* 100, 3306–3312 (1978).

centre (Figure 2).

Vincent and Radom² concluded from their computational study that the favored structure of the methanediazonium ion (MDI) is an open structure with a C-N length slightly longer than normal C-N bonds and a N-N length very similar to that in molecular nitrogen. The N_2^+ as a substituent has been predicted to be a powerful σ electron acceptor, considerably more powerful, for instance, than NO_2^- and F^- . It can also behave as a strong π electron acceptor.

1.1.2 Properties: Diazomethane shows a broad, low-intensity absorption in the visible and near-ultraviolet, having an ill-defined maximum, somewhere between 350 and 400 nm. The maximum extinction coefficient is observed around ~ 6 . This band is attributed for giving it a yellow appearance³. It is very difficult to isolate the cation. Protonated diazomethane (positive charge on carbon end) can be observed in super acid media below -100°C ⁴. Diazomethane is highly toxic, carcinogenic and potentially explosive. Inside the body of animals, potential carcinogen N-nitroso dimethyl amine (NDMA) leads to the ultimate carcinogen i.e. protonated diazomethane which can alkylate DNA and hence causes cancer (Scheme 1)⁵.

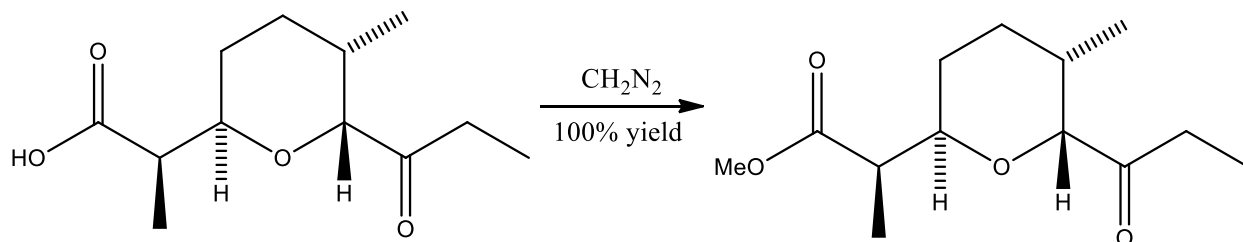


Scheme 1. Alkylation of DNA through Diazalkanes derived from NDMA

1.1.3 Reactivity: Under suitable conditions, diazomethane can behave as an acid or a base, as a nucleophile or an electrophile, as a carbene source or as a 1,3, dipole. Chemistry of Diazoalkanes comprises of cycloaddition, homologation, catalyzed alkylation and polymerization process⁶. The dissociation enthalpy MDI (CH_3N_2^+), has been measured in the gas phase and this process is surprisingly endothermic. Ab initio molecular orbital calculations also

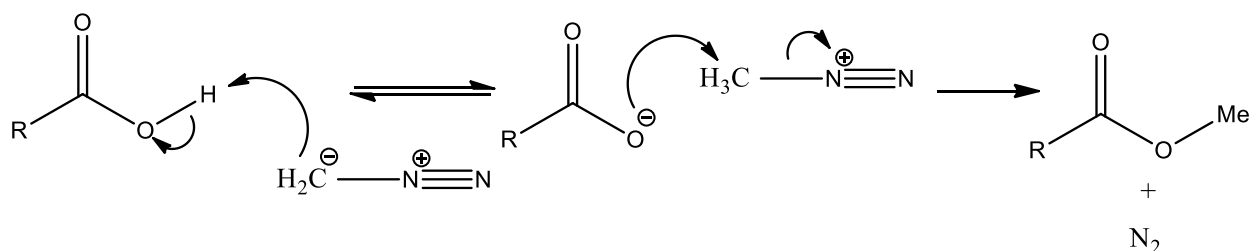
suggest that the gas-phase dissociation of MDI is endothermic, given as 36 kcal mol^{-1} as estimated by George P. Ford.⁷

Much study has been done in the past for diazomethane used as a methylating agent. For example diazomethane can be used to make methyl esters from carboxylic acids (Scheme 2)⁸.



Scheme 2. Esters from carboxylic acid using diazomethane

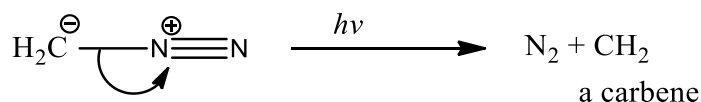
Mechanism (Scheme 3) involved for the above reaction is as follows.



Scheme 3. Mechanism involved for conversion of carboxylic acids to esters

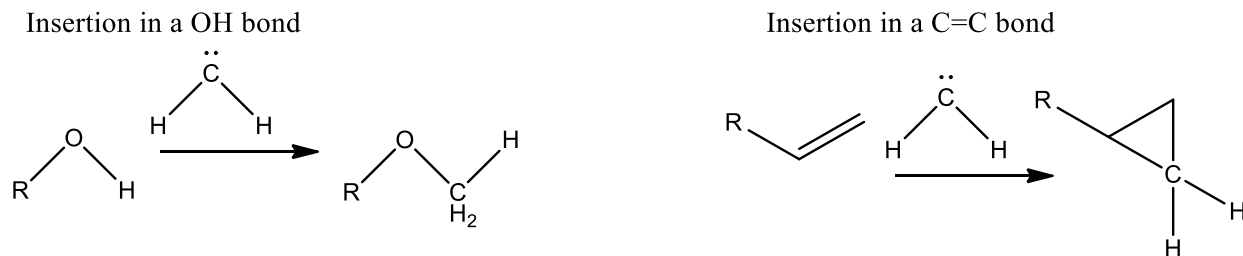
Similarly diazomethane can also methylate phenols because they are too acidic to protonate it.

Diazomethane is well known as a carbene source. Photolysis of diazomethane produces carbene (Scheme 4).



Scheme 4. Generation of a carbene

Now this carbene can insert itself into a σ bond or a π bond (Scheme 5). Typical carbene reactions are mentioned below.



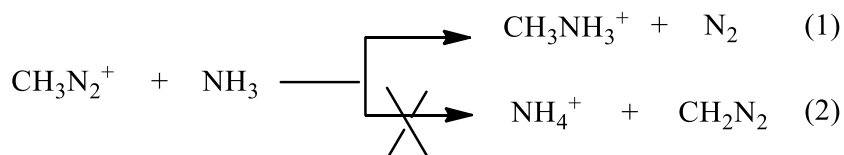
Scheme 5. Insertion of carbene

Of the simple alkanediazonium ions, the methyl analogue (MDI) has been predicted to be the most stable with respect to nitrogen loss⁷. The calculated thermodynamic quantities for diazomethane at 298 K are Heat of formation, $\Delta H_f(\text{CH}_2\text{N}_2) = 65.3$ kcal/mol, Proton affinity, $\text{PA}(\text{CH}_2\text{N}_2) = 211.9$ kcal/mol, and Methyl cation affinity, $\text{MCA}(\text{N}_2) = 43.2$ kcal/mol⁹ and Heat of formation, $\Delta H_f(\text{CH}_3\text{N}_2^+) = 223$ kcal/mol¹⁰.

Foster and Beauchamp put forth two criteria to describe the occurrence of gas phase nucleophilic displacement reactions¹⁰.

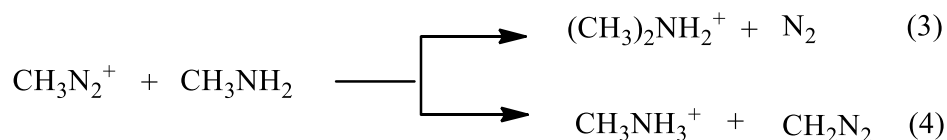
- i) The displacement process has to be exothermic.
- ii) Proton transfer from the substrate to the nucleophile has to be endothermic.

The expected behavior is observed in the case of ammonia (Scheme 6, reaction 1 and 2).



Scheme 6. Reaction of ammonia with MDI

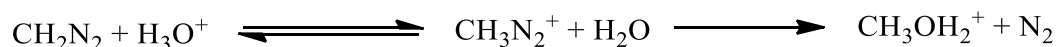
The above methyl transfer reaction is exothermic (-74 kcal/mol). However MDI contradicts this criteria in case of methylamine (Scheme 7). Competition between methyl cation transfer (reaction 3) and proton transfer (reaction 4) is observed. Reaction 3 is 80 kcal/mol exothermic.



Scheme 7 Reaction of methyl amine with MDI

1.1.4 History of Hydrolysis of Diazoalkanes:

John F. McGarrity and Timothy Smyth⁴ studied the reaction between diazomethane and the hydronium ion in a THF-water (60:40 v/v) mixture at 25°C. According to their study, the protonation rate of diazomethane was estimated as $4 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ as per kinetic and pH data. It was shown that the displacement of nitrogen was more rapid than deprotonation of methanediazonium ion in case of water whereas hydroxide acts more as a base than as a nucleophile (Scheme 8 and 9). The rates of nucleophilic attack of water and the hydroxide ion on methanediazonium ion were estimated as 1.8 s^{-1} and $1 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$, respectively, in THF-water (60:40 v/v). The pKa, of the methanediazonium ion in this medium was ten.

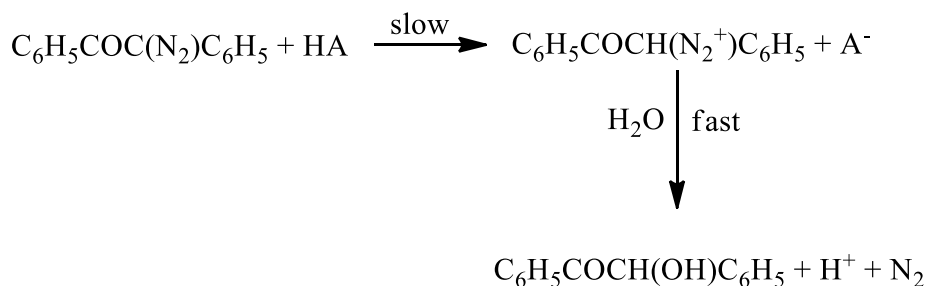


Scheme 8. Acidic hydrolysis of MDI



Scheme 9. Deprotonation of MDI

Engbersen et al¹¹ in 1974 have studied the acid catalyzed solvolysis of benzylphenyldiazomethane with butanol as solvent. Their data suggests that there exists a relationship between water acidity and solvent structural integrity in highly aqueous t-butanol-water solutions.



Scheme 10. Acid solvolysis of phenyl substituted diazoketone to produce benzoin

1.2. Coordinated Diazoalkanes

The chemistry of transition metal complexes containing diazoalkanes as ligands $[\text{M}]-\text{N}_2\text{CAr}^1\text{Ar}^2$ has long been under development. They are extensively studied because of their potential use in the synthesis of carbene complexes and mainly due to the different coordination modes and reactivities shown by the coordinate $\text{N}_2\text{CAr}^1\text{Ar}^2$ group.

1.2.1 Coordination modes of diazo ligands: Diazoalkane ligands, derived from either free diazoalkanes or other precursors such as coordinated dinitrogen, azines, and hydrazones.

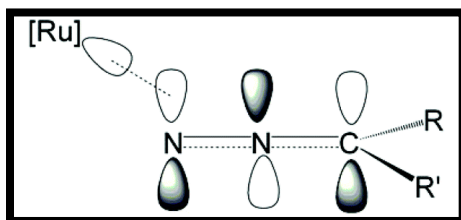


Figure 3 Bonding in Ruthenium and Diazo orbitals

They display number of coordination modes acting as π and/or σ -bound terminal, bridging, or chelating ligands. The reactivities of coordinated diazoalkanes are largely affected by their coordination modes. The variety of reactivities observed for these coordinated diazoalkanes is quite different from those of free diazoalkanes.

Mode of Binding: Well-defined monomeric complexes contain either the

- η^2 bound diazoalkane ligands through the N-N multiple bonds¹² (Figure 4)
- η^1 -diazoalkane ligands coordinated at the terminal nitrogen atom (Ru coordinated diazo groups)¹³

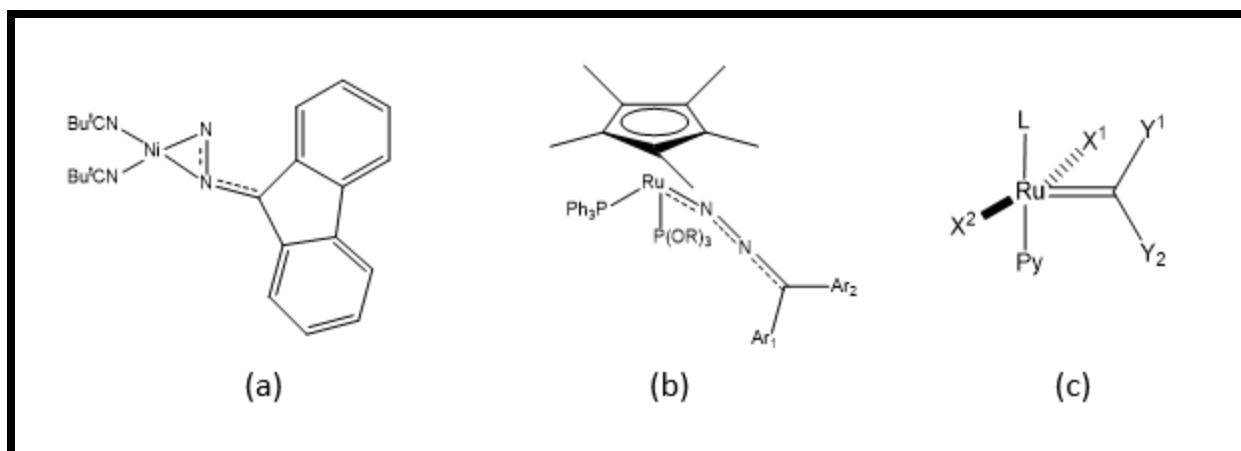
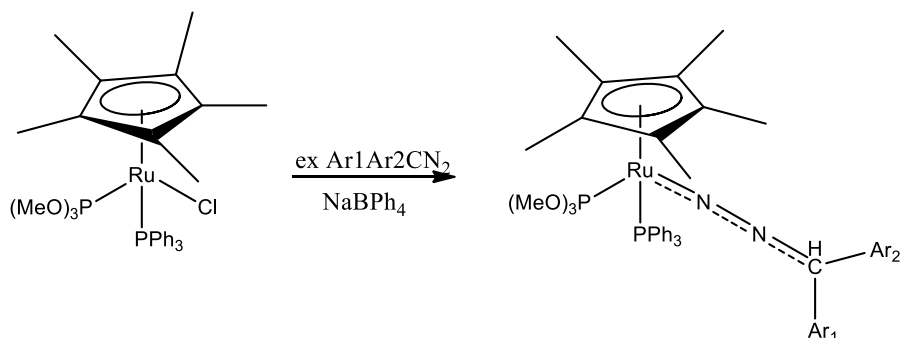


Figure 4 Mode of binding (a)Through N=N, Hapticity=2 (b) Through N , Hapticity=1 (c)As carbene, removal of nitrogen

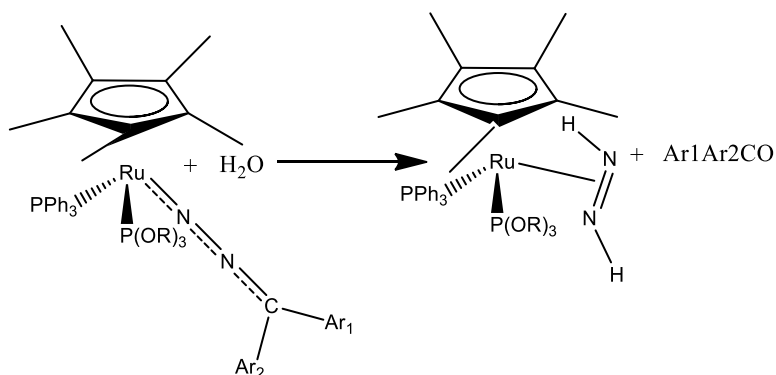
- As carbene which involves removal of nitrogen (eg. Rhodium catalysed carbene complexes)¹⁴

1.2.2 Hydrolysis of coordinated Diazoalkanes : A number of diazoalkane complexes of several metals have been reported and their reactivity studies have highlighted different pathways, depending on the mode of coordination and the nature of ancillary ligands. Thus, extrusion of dinitrogen with carbene formation is observed in η^2 -CN-coordinated species, whereas an η^1 -N-bound diazoalkane can yield dinitrogen $[M]-N_2$ complexes, convert carbene to imine, or cleave the N–N bond of the $N_2Car^1Ar^2$ group. Dipolar (3 + 2) cycloaddition of coordinated diazoalkane with alkene and alkyne, affording 3H-pyrazole derivatives, as well as hydrolysis, yielding η^2 -diazene derivatives has recently been reported¹¹.

Albertin et al performed the experimental study on the hydrolysis of Ruthenium coordinated diazoalkanes¹⁵. At room temperature, diazoalkane complex react with H_2O to furnish 1, 2-diazene derivatives $[Ru(\eta^5-C_5Me_5)(\eta^2-NH=NH)(PPh_3)\{P(OR)_3\}]BPh_4$, (Scheme 12) which was isolated in about quantitative yield and then characterized using X-ray, IR and NMR spectroscopy. The ketone Ar^1Ar^2CO was also separated from the reaction mixture in about quantitative yield.

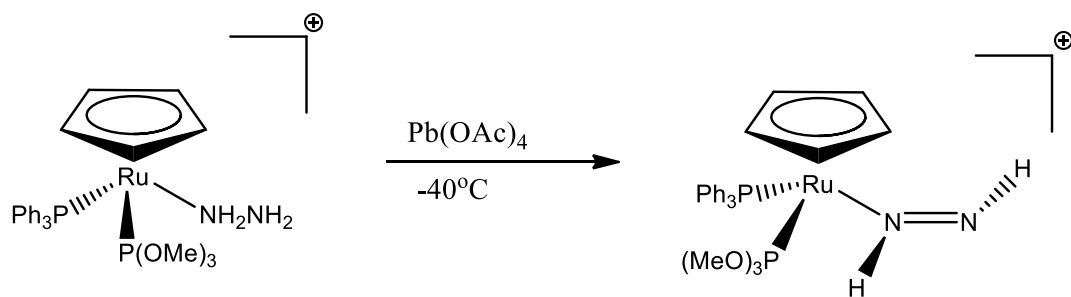


Scheme 11. Preparation of Ruthenium coordinated diazoalkanes

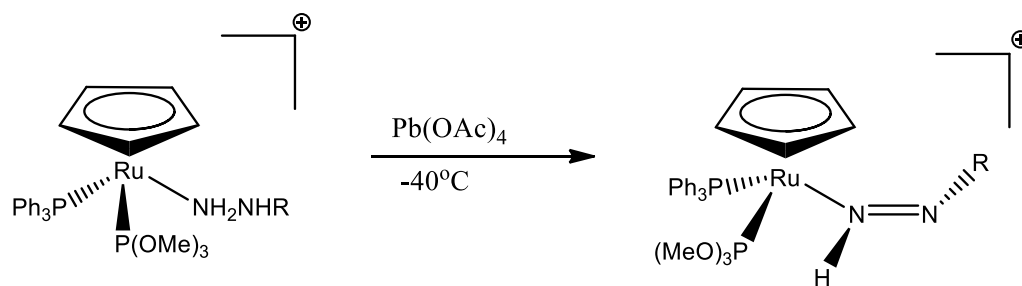


Scheme 12. Hydrolysis of the complex to yield diazene coordinated with Ru and side product as ketone

However, similar aryldiazine derivatives ($[\text{Ru}(\eta^5\text{-C}_5\text{H}_5)(\text{RN}=\text{NH})(\text{PPh}_3)\{\text{P}(\text{OMe})_3\}]\text{BPh}_4$, R=phenyl or p-tolyl) can be prepared by using Ruthenium complexes containing hydrazine as ligands but hapticity of diazene moiety is one (Scheme 13 and 14)¹⁶.



Scheme 13. Coordinated diazene from hydrazine



Scheme 14. Diazene derivatives from hydrazine

Objective

The aim of this project is to study the mechanism of hydrolysis of protonated diazoalkanes computationally. It is difficult to trace the mechanisms of protonated diazoalkanes since the reactions are very fast and the cation is very unstable. The systems under study are methane diazonium ion (MDI) with water and hydroxide as a base as well as a nucleophile. The interaction of MDI with water is studied upto four water molecules. The cation is further substituted with phenyl (Ar^1) and tolyl (Ar^2) group. The substituted diazocation ($\text{Ar}^1\text{Ar}^2\text{CHN}_2^+$) is again studied with water and hydroxide ion.

The project also comprises of hydrolysis of coordinated diazoalkanes. The objective here is to study the mechanism proposed by Albertin et. al. The feasibility of the reaction of Ru complex with water to give novel products (coordinated diazene and ketone) is to be studied computationally.

Chapter 2

Methodology

Theoretical chemistry is basically chemistry defined mathematically. Computational theoretical chemistry involves the computations or simulations using a computer program which is based on mathematical formulations of quantum chemistry. It all started in 1926 with Erwin Schrödinger¹⁷ who made an attempt to describe the so-called 'matter waves'. He implemented de Broglie's relations in order to describe hypothetical plane waves. This led to the most famous equation-time dependent Schrödinger equation.

$$i\hbar \frac{d}{dt} \psi(\vec{r}, t) = \hat{H} \psi(\vec{r}, t)$$

Where $\hbar = h/2\pi$

The necessity of computational chemistry arises because for many body problems the wave function depends on several parameters unlike diatomic system which depends on internuclear distance parameter¹⁸. The electronic wave function of a polyatomic molecules involves the bond distances, bond angles and dihedral angles parameters. Dihedral angles are significant since they specify the molecular conformation. To carry a complete theoretical treatment on a polyatomic molecule one needs to calculate the wave function for a range of these parameters. The calculations of equilibrium bond angles and bond distances are finalized when the molecule attains the minimum electronic energy including nuclear repulsion. The methods involved in computational chemistry consists of four main branches - Ab initio method, semi empirical methods, density functional method and molecular mechanics method.

Ab initio comes from Latin and it means 'from the beginning'. **Ab initio method** involves calculations based on fundamental principles. The method uses the exact Hamiltonian and does not involves experimental data other than fundamental physical constants. Notably, it is not necessary that the method always yields 100% correct results. The Hartree-Fock calculations come under ab initio methods. To deal with the complex and analytically not accessible many-body Schrödinger equation, Hartree and Fock introduced a set of self-consistent, wave-function

based equations. An iterative calculation of energies and other parameters is introduced¹⁹. Hartree Fock method is not effective for large systems investigation due to high cost of computation. The calculation of Hartree fock self consistent field (SCF) finds an antisymmetrized product ϕ of one electron function to minimise $\int \phi * \hat{H}\phi d\tau$, where \hat{H} is true Hamiltonian.

Semi empirical methods¹⁸ comprises of simpler Hamiltonian rather than the exact molecular Hamiltonian. The values of parameters are adjusted to coincide with experimental data or result from ab initio calculation. For example, in Huckel Molecular orbital treatment of conjugated hydrocarbons, the bond integrals are taken as adjustable parameters. They are not calculated theoretically.

In **density functional method**, instead of calculating molecular wave functions, a new parameter is calculated which is molecular electron probability density denoted by ρ . This is further used to calculate molecular electronic energy¹⁸. The method uses density functional theory introduced by Hohenberg and Kohn in 1964. They claimed that the electron density, a variable only depending on 3 spatial variables, can be used to extract all information about the ground state properties of a system²⁰. And due to the fact that the electron density is a much less complex quantity than the wave function, the computation time of DFT calculations are substantially lower. The significance of ‘functional’ can be explained as - a function takes a numerical input and generates a numerical output whereas a functional takes a function as input and generates a numerical output. A functional is a rule of associating a number with a function¹⁸. In 1998 Kohn got the Nobel prize in chemistry for his tremendous work²⁰.

Molecular mechanics method¹⁸ is quite different from quantum mechanical methods. It does not involve a Hamiltonian operator or a wave function. Instead, it considers the molecules as collection of atoms held together by bonds. Force constants for bending and stretching of bonds and other parameters are used to express the molecular energy.

The computational geometry optimization of the complexes are carried out using DFT B3LYP and basis set is 6-311G + (2d,p) set on the light atoms and the ECP-based LanL2DZ set on the ruthenium complexes.

Different conformations are studied for $n=2, 3$ and 4 water molecules for methanediazonium ion (MDI), in different arrangements. The binding energies of the different structural arrangements are then calculated by subtracting the optimized energies (i.e. local minima on the potential energy surface) of the molecule under study (diazoalkane ion) and the number of water molecules from the optimized energy of the respective micro-solvated arrangements. Similarly the reaction path for MDI system as well as $\text{Ar}^1\text{Ar}^2\text{CHN}_2^+$ system are studied with relative energy graph with respect to the reactant in a particular reaction.

The energies of the respective structural arrangements are corrected by performing the frequency calculation to extract the zero point energy (ZPE) correction as well as thermal energy correction. The energies are reported after including these corrections.

All the computational optimizations are performed using HPC workstation and the software used is Gaussian 09.

Note: All energies reported in this thesis are expressed in kcal mol^{-1} and all bond distances are reported in Å.

Chapter 3

Results and Discussions

3.1 Methane diazonium ion (MDI)

The ion was optimised using method DFT B3LYP(Figure 5). The structure obtained has bond

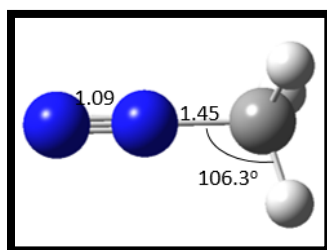


Figure 5 Optimised methane diazonium ion(MDI)

length of $\text{N}\equiv\text{N}$ as 1.09 Å and the C-N bond distance is found to be 1.45 Å. The angle between H-C-N is found slightly less than 109° . The bond angle is actually $\sim 106^\circ$.

The rather short NN bond lengths discussed by Vincent and Radom² in their earlier calculations on MDI is evident in the present work as well. Thus, with 6-311G +(2d,p) as basis set, the NN bond distances are calculated to be 0.02 Å shorter than in N_2 .

3.2 MDI : Monohydrate and Dihydrate

Solvating the cation gives a nucleophilic reaction in aqueous medium with water itself acting as

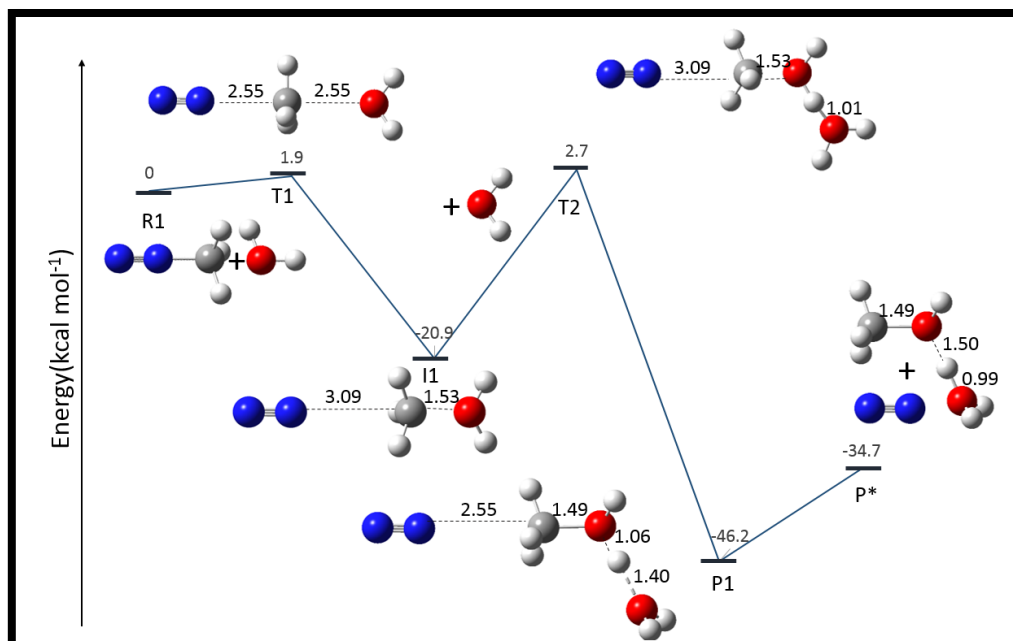


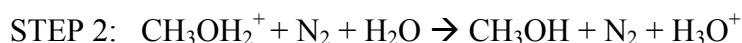
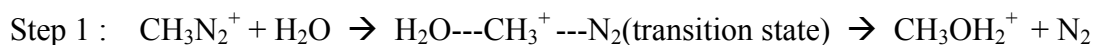
Figure 6 Reaction Coordinate for MDI with two water

a nucleophile. The attack takes place from the rear side of the molecule. The bond breaking (leaving nitrogen) and bond forming (methanol formation) takes place simultaneously. The reaction follows S_N2 mechanism. And the reaction is explained in two steps because bond formation between C of diazo and O of water (in case of two water molecules) takes place when the other water molecule comes in the vicinity to stabilize H^+ forming a hydronium ion, finally giving methanol as the product (Figure 6). The leaving group i.e. nitrogen being extremely stable having a triple bond with 940 kJ/mol as bond energy acts as the driving force of the reaction here.

Overall reaction is:



The reaction mechanism is –



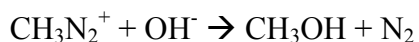
The reaction coordinate (Figure 6) is based upon the energies calculated from the frequency calculation of the optimized structures in DFT B3LYP (6-311G+(2d,p)). The energy of the reactant (R1) was kept at zero kcal/mol. Energy of P1 being negative with respect to R1 indicates the feasibility of reaction.

It is observed that R1 experiences a reaction barrier of 1.95 kcalmol⁻¹ to form the intermediate I1. Further, this I1 becomes a high energy system (T2) on introducing one more water molecule which finally leads us to the product (P1). T2 acts as the starting material for the next step. T1 corresponds to the transition state of S_N2 mechanism. The bond distance of C-N in diazomethane ion is 1.46Å but optimized structure with one water molecule gives the nitrogen 3.09Å away from -CH₃, depicting complete isolation of nitrogen molecule.

Addition of one more water to the monohydrate (I1) gives methanol. The reaction completion occurs with two water molecules. Methanol, nitrogen molecule and H₃O⁺ (P1) are obtained on carrying out the simulation of T2. The bond distance of C-O in methanol as a final product is found to be 1.49 Å whereas theoretical value is 1.427Å.

3.3 MDI with hydroxide as a nucleophile

The reaction strictly follows S_N2 mechanism to generate the expected product i.e. alcohol. The hydroxide ion reacts with diazomethane to give methanol and nitrogen gas. The relative energy graph shows the huge difference in energy of the product which is -233.2 kcal/mol (Figure 7).



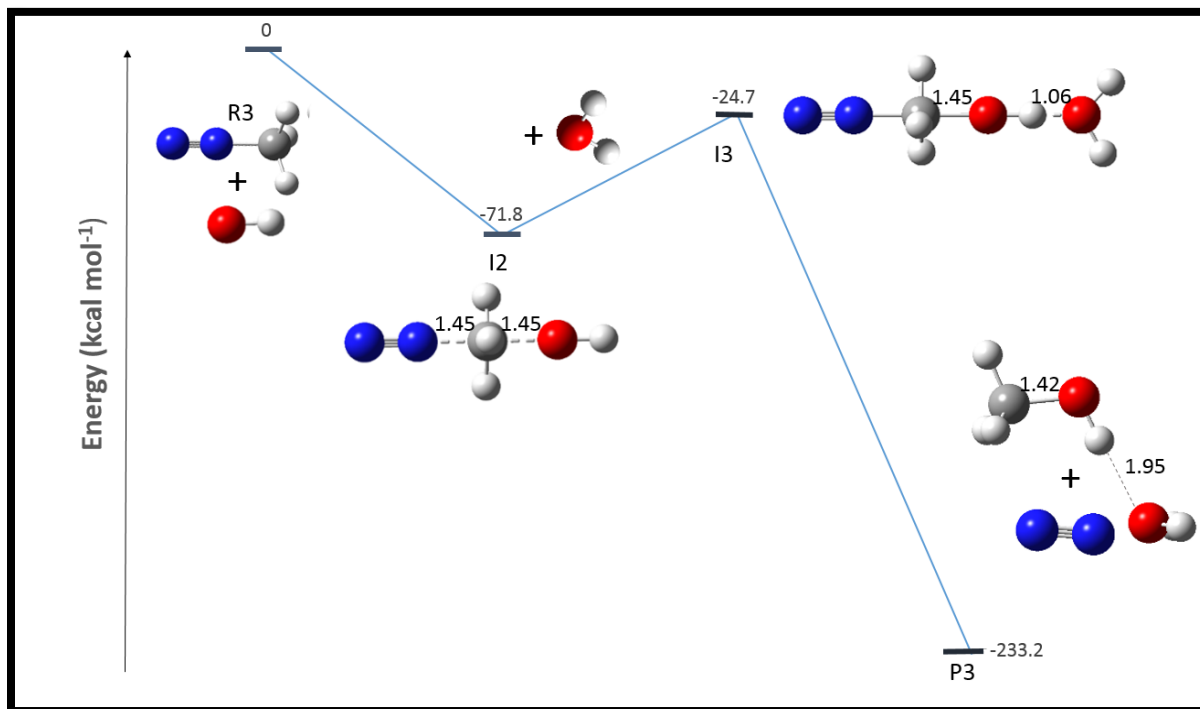


Figure 7 Reaction Coordinate for MDI with hydroxide as a nucleophile

McGarritty and Smyth⁴ concluded from their kinetic study that the rate of the reaction of OH⁻ with the cation is found 10⁴ times higher than the rate of water reacting as the nucleophile. This may be the reason of the intermediate (I2) is at much lower energy (-71.8 kcal/mol).

Introducing a water molecule in I2 (since reaction medium is aqueous) gives I3 which is -24.7 kcal/mol in energy w.r.to reactants. The rate in this case has to be faster. The reason can be attributed to the neutral products obtained from charged species. Also charged species are much more nucleophilic than uncharged. So hydroxide attacks easily on the cation forming the required products.

The bond length of C-O in alcohol is in good agreement with the theoretical value i.e. 1.42 Å.

3.4 MDI with hydroxide as a base

Hydroxide ion is a much stronger base than a nucleophile. Therefore another possible reaction path involves the deprotonation of methanediazonium ion facilitating the formation of diazomethane and a water molecule.

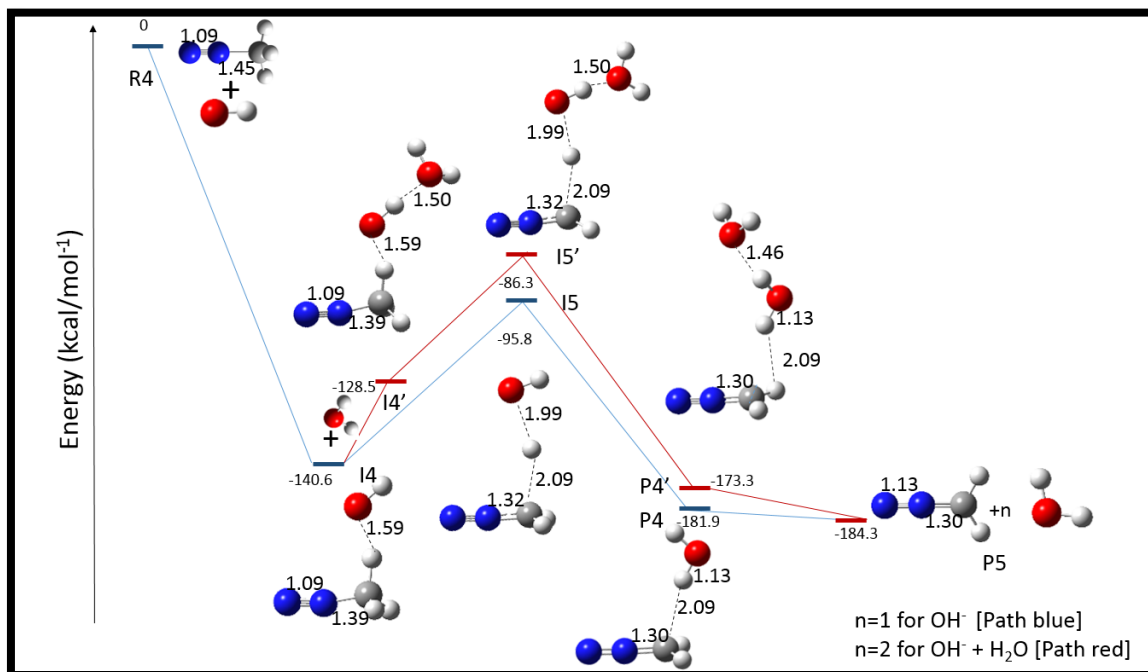
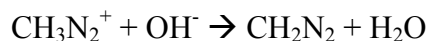


Figure 8 Reaction coordinate for MDI with Hydroxide as a base

On carrying out the simulations for the above reaction, it is found that the intermediate structures involved are much lower in energy as compared to the cation and OH⁻ system (R4).

The two systems (Figure 8) depicted here are concentrated base (red) and base in aqueous medium (blue). However, both the reactions are spontaneous but clearly the base when concentrated furnishes products (P4) more easily. This means water molecules in the vicinity are responsible for sterically hindering the attack of hydroxide on the cation. Nonetheless the reaction is still going forward leading to the neutral hence, stable products (P4).

The mechanism involves the shortening of C-N bond from 1.45 Å to 1.30 Å (single bond transforms into a double bond). Also there is elongation of NN bond in MDI from 1.09 Å to 1.13 Å.

P4 and P4' are having H-bonded water molecules and diazomethane. The energies are -181.9 and -173.3 kcal mol⁻¹. The final product (P5) is reported as -184.3 kcal mol⁻¹ in energy. Relative energy of P5 reported here is a sum of isolated diazomethane and water molecules. As compared with products obtained in section 3.3, the difference is ~49 kcal mol⁻¹. The products with substitution are lower in energy nonetheless here reaction mechanism involves intermediates much lower in energy to let us discern that the barrier might be lower in deprotonation than substitution.

3.5 MDI : Trihydrate

Solvation of the cation with three water molecules when kept in a certain arrangement gives the same result (nucleophilic substitution reaction) having the remaining water being hydrogen

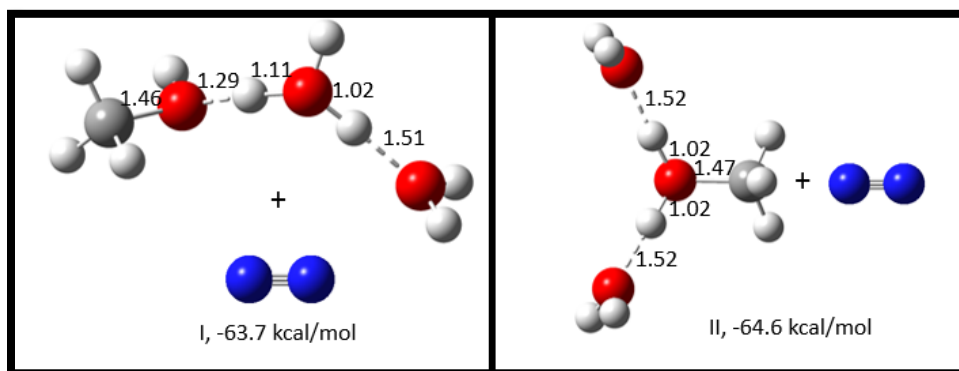


Figure 9 MDI with three water molecules(with reaction)

bonded to the methanol. Four arrangements are taken into account (Figure 9 and 10).

Initially, the water molecules are placed horizontally (I) with respect to the cation forming a chain in which first H₂O is facing the carbon side of the cation. In I, the foremost water's -OH part is taken for the methanol formation and the other hydrogen which was earlier 0.96 Å after optimization found at 1.29 Å. This hydrogen is found much closer to the next water 1.11 Å which is due to the hydronium ion formation. The 3rd water is strongly hydrogen bonded thereby found

at a distance of 1.51Å. In the other structure (II) water molecules are arranged in a T-shape configuration. The bond distance of C-O bond of methanol in I and II are 1.46Å and 1.47Å respectively. The values are in good agreement with the theoretical value (1.427Å). The structure with water arranged vertically is ~1 kcal/mol more stable than the other due to symmetry.

The other two isomers (III and IV) are lacking the substitution reactions. III has a triangular shape with water molecules arranged at the vertices. MDI has the middle nitrogen with partial positive charge and therefore the oxygen of water molecules are oriented in such a manner that

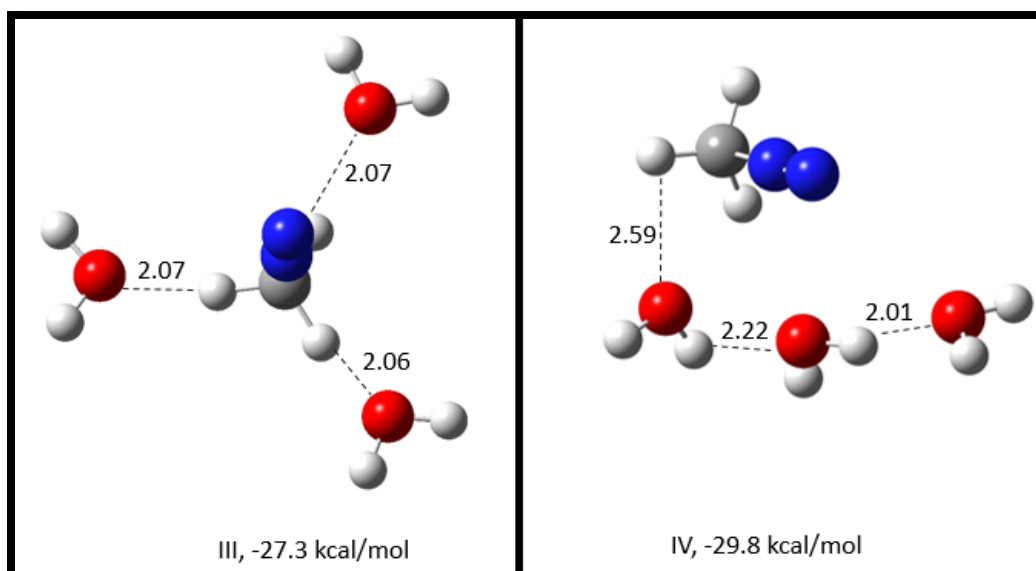


Figure 10 MDI with three water molecules(without reaction)

they stabilize the charge density of the cation. IV involves the water molecules arranged in a linear arrangement H-bonded to each other. Comparing the energies of the two systems-with reaction and without reaction (I, II, III & IV), the energies are almost double in first case than the latter.

3.6 MDI : Tetrahydrate

As the solvation increases, extensive hydrogen bonding comes into the picture. The same reaction was observed in this case containing water molecules hydrogen bonded with each other as well as methanol.

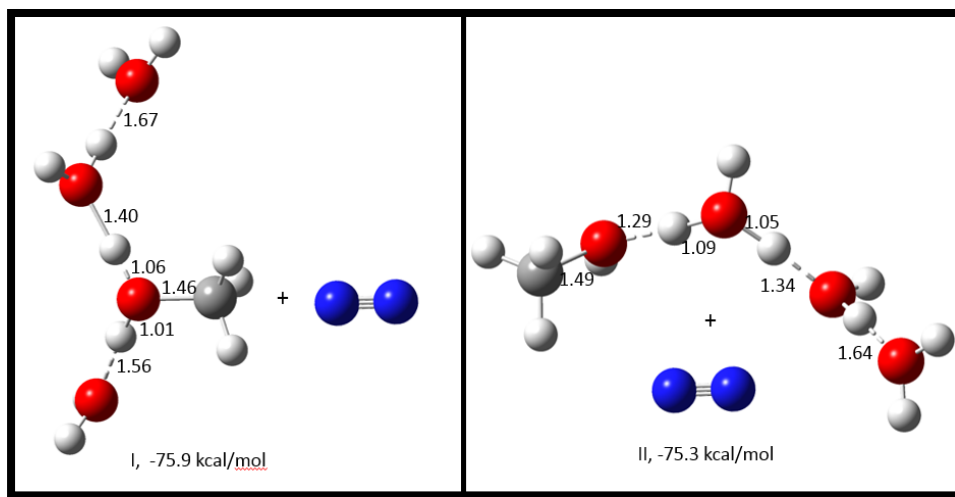


Figure 11 MDI with four water molecules (with reaction)

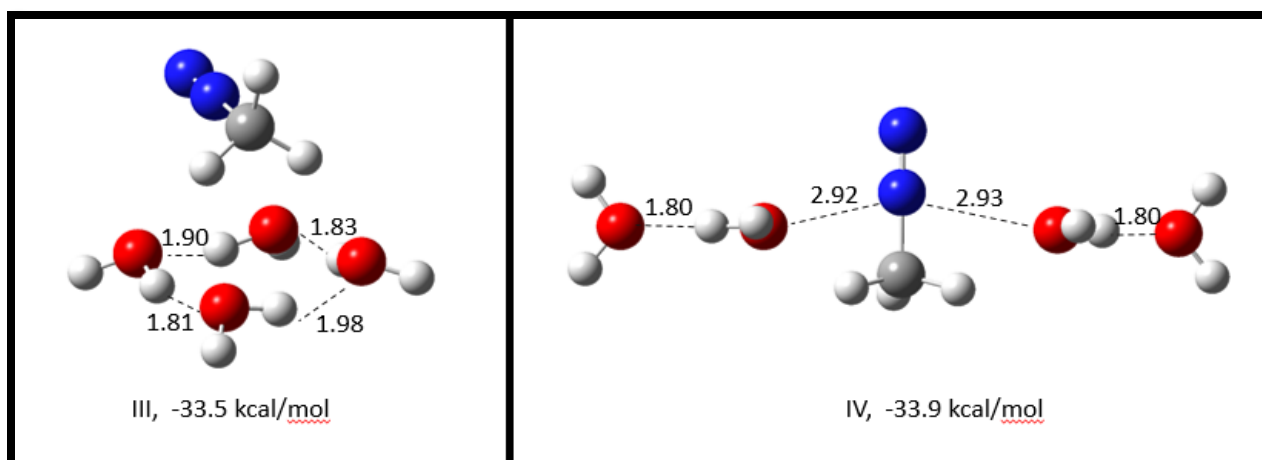


Figure 12 MDI with four water molecules (without reaction)

Four arrangements are taken into consideration. The first arrangement Figure 11 (I) resembles the second case of three water molecules, the one extra water molecule simply hydrogen bonded to it. The arrangement is an extended T-shape. Second one involves the chain structure (Figure 11 (II)). Interestingly, tetrahydrate follows the same trend as three water molecules giving the most stable arrangement which has the similar pattern as three (T-shape). The C-O bond distance were found to be 1.46 and 1.49 Å. Usual hydrogen bonding range is 1.50 Å to 2.5 Å but in II, the hydrogen which cleaves from the methanol's water is found at

much lower distance than the normal hydrogen bond distance (1.09Å) confirming the formation of hydronium ion.

In III and IV (Figure 12), there is no sign of substitution reaction but hydrogen bonding. III involves a cyclic system of hydrogen bonded water molecules whereas IV resembles a flying bird pattern. Both III and IV are having less negative energy as compared with I and II.

3.7 Protonated benzyl tolyl diazomethane with hydroxide

The reaction of substituted diazoalkane is further studied with hydroxide as a nucleophile. The intermediate structures of optimized product (using same basis set (6-311G+(2d,p))) depicted that the reaction follows S_N2 mechanism in spite of the stabilized carbocation involved. This is due to the fact that the hydroxide being a strong nucleophile reacts rapidly with the diazo compound.

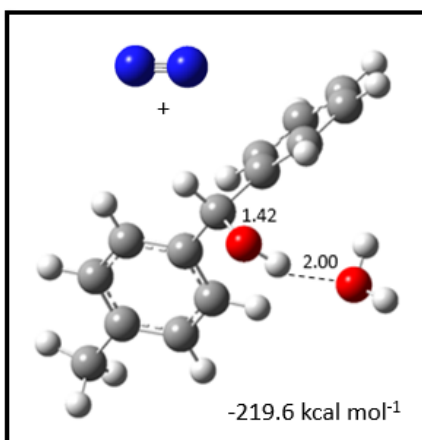
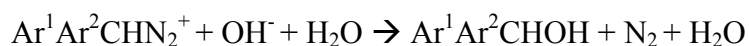


Figure 13 Benzyl tolyl diazomethane with hydroxide

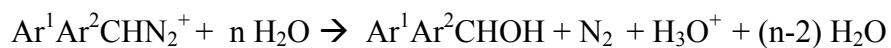
Hence the reaction follows concerted S_N2 mechanism rather than a two steps mechanism. The expected product i.e. alcohol derivative of the corresponding diazoalkane is obtained (Figure 13).



The bond length between the C-O in the alcohol is found to be 1.427Å which is the ideal bond distance (theoretical bond distance = 1.427Å).

3.8 Protonated benzyl tolyl diazomethane with water:

The reaction with water follows S_N1 mechanism since the water is not a strong nucleophile and the carbocation here is stabilized with the conjugated benzyl and tolyl groups.



With two water molecules: The activation barrier may be high enough that the formation of alcohol is not significant. This is evident from the distance between C and O which is 1.64 Å (Figure 18). Also the hydronium ion formation isn't significant enough nevertheless the bond distance of O-H increases from 0.96 Å to 1.02 Å (Figure 14).

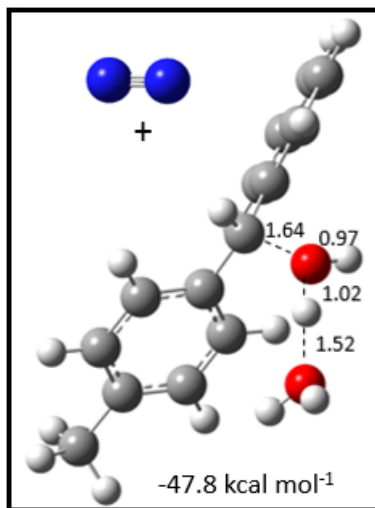


Figure 14 $\text{Ar}^1\text{Ar}^2\text{CHN}_2^+$ with two water molecules

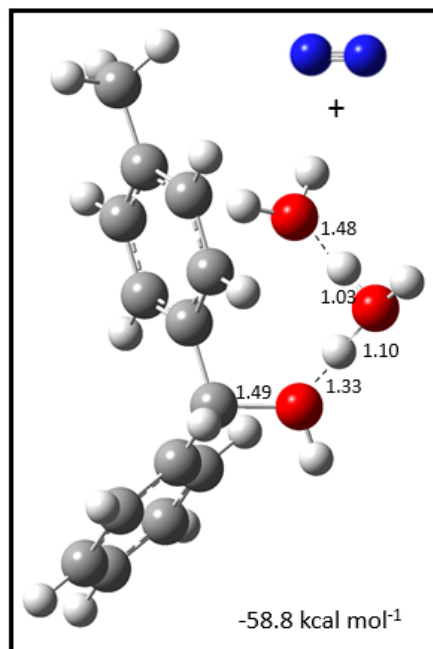


Figure 15 Benzyl tolyl diazomethane with three water molecules

With three water molecules: The system containing two water molecules depicted the weak nucleophilicity of water. In order to increase the bond polarity we introduce one more water molecule in the system (Figure 15). The basicity of second water molecule is increased due to the presence of third water molecule (cooperative effect) hence now it is easier to abstract the proton from the first water molecule so as to form hydronium ion. Hence the hydroxide ion can react with the cation easily. Therefore the formation of alcohol is significant and the bond distance is now 1.49 Å, which is comparable with the theoretical value (1.42 Å).

3.9 Hydrolysis of Coordinated Diazoalkanes (Ruthenium catalyzed):

Hydrolysis of coordinated diazoalkane was done using DFT B3LYP with the Lanl2DZ basis set.

3.9.1 The Reactant: The starting material was optimized (Figure 16) and it was found that there are certain deviations in the bond distance from the original values. The ancillary ligands, being so bulky, are responsible for the elongation of bond length. Ru-Cl bond should be around 2.38 Å but it was found to be 2.55 Å. Similarly in case of Ru-PPh₃ and Ru-P(OMe)₃, Ru-P bond length is found at 2.48 Å and 2.34 Å instead of 2.37 Å and 2.29 Å respectively. However the average bond distance for C₅Me₅ (2.29 Å) group was somewhat in agreement with the theoretical value (2.26 Å)²¹.

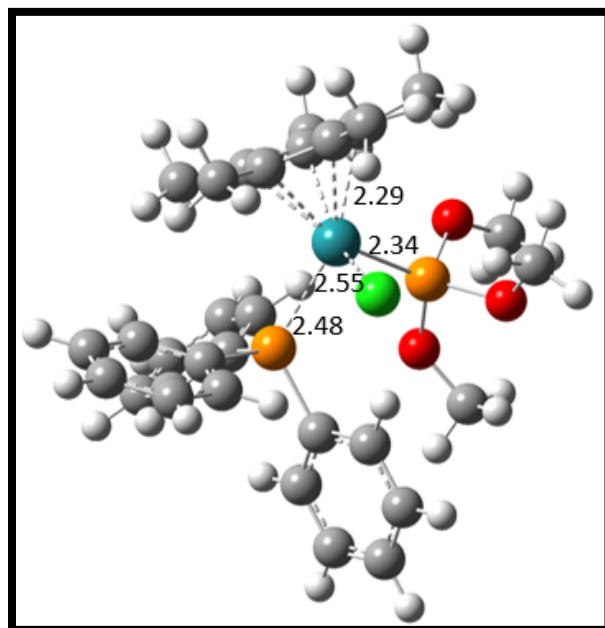


Figure 16 The reactant $\text{RuCl}(\eta^5\text{-C}_5\text{Me}_5)(\text{PPh}_3)\{\text{P}(\text{OR})_3\}$

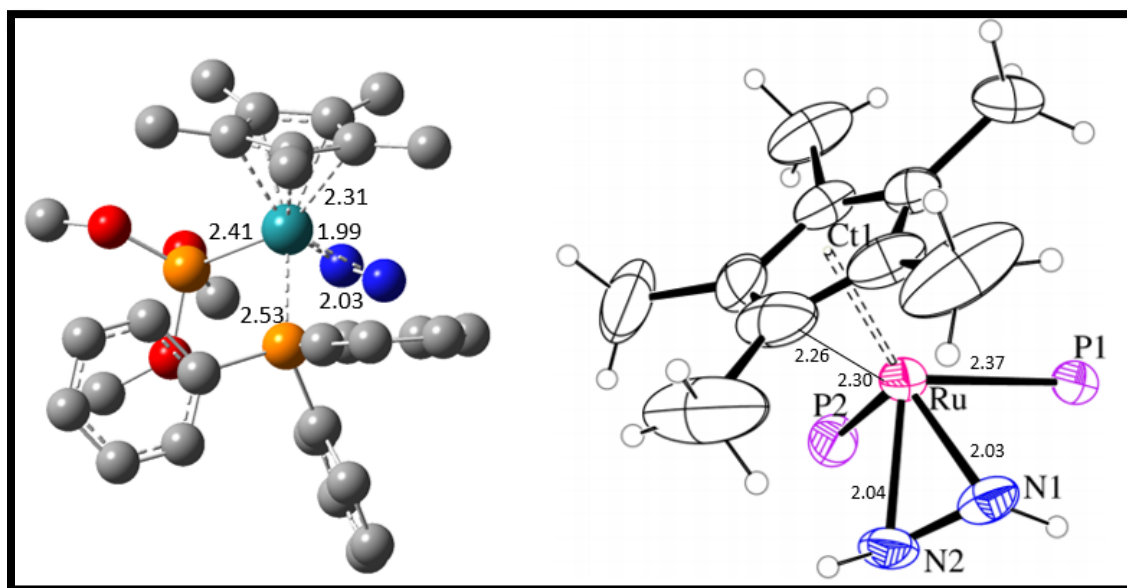


Figure 17 The product compared with ORTEP diagram (Source : Albertin et al , 2015)

3.9.2 The Product: Similarly the final product (Figure 17) was optimized and compared with the ORTEP diagram obtained by Albertin et al¹⁵.

The structure obtained has the bond distances different from x-ray crystallized ORTEP diagram. The Ru-P in P(OMe)_3 and PPh_3 are 2.41 Å and 2.53 Å respectively in contrast with ORTEP which

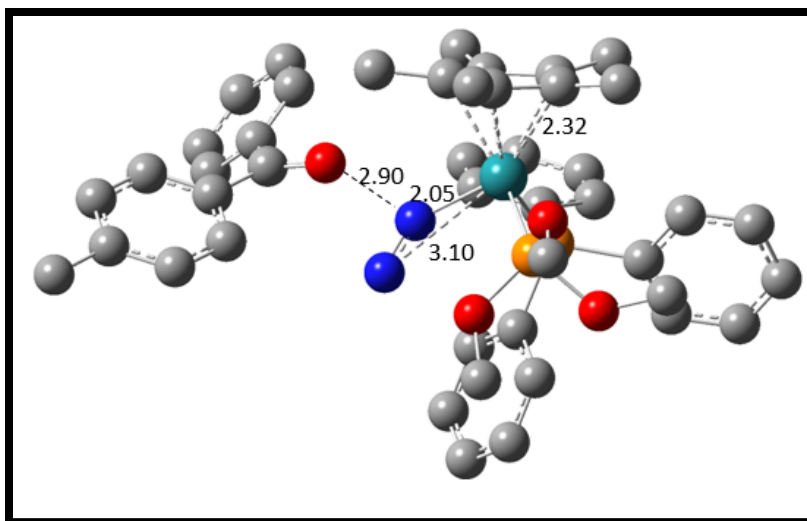
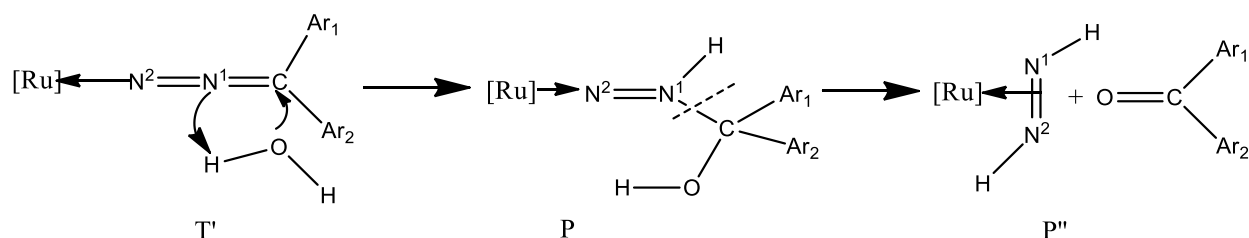


Figure 18 The final product obtained after optimisation

gives 2.30 Å and 2.37 Å for the same. The average bond distance in case of pentamethyl cyclopentadienyl is 2.31 Å which is greater than 2.26 Å. The product obtained by carrying out the ab initio simulation is as follows which involves the η^1 $\text{NH}=\text{NH}$ diazene coordinated with the Ru centre. N1 is at 2.05 Å from Ru whereas N2 is 3.10 Å far from the Ru atom (Figure 18).

3.9.3 Reaction profile for the hydrolysis of the coordinated diazoalkanes:

The formation of diazene complexes is rather surprising but is explained by Albertin et.al. as due to the nucleophilic attack of H_2O on the carbon atom of the coordinated diazoalkane, according to the reaction path shown in the following Scheme 15.



Scheme 15 Mechanism proposed by Albertin et. al.

According to the reaction mechanism given by Albertin et. al. , the simulations are carried out to get the reaction coordinate for the given mechanism where $[\text{Ru}] = [\text{Ru}(\eta^5\text{-C}_5\text{Me}_5)(\text{PPh}_3)\{\text{P}(\text{OR})_3\}]^+$. The plot obtained is as shown in Figure 19.

The Product obtained from the optimization of transition state T' is P. However, experimental study carried out by Albertin et. al. confirms the formation of P'' which has a diazene derivative involving both the nitrogen (N¹ and N²) coordinated with Ruthenium. But on carrying out the simulation for the transition state T'', it was found that only one nitrogen atom (N¹) was coordinated with Ru atom. The Hydrogen attached to N¹ was H-bonded to the carbonyl oxygen of the ketone obtained. Also it was observed that product P' is found comparatively more stabilized than P'' by a magnitude of 26.9 kcal mol⁻¹.

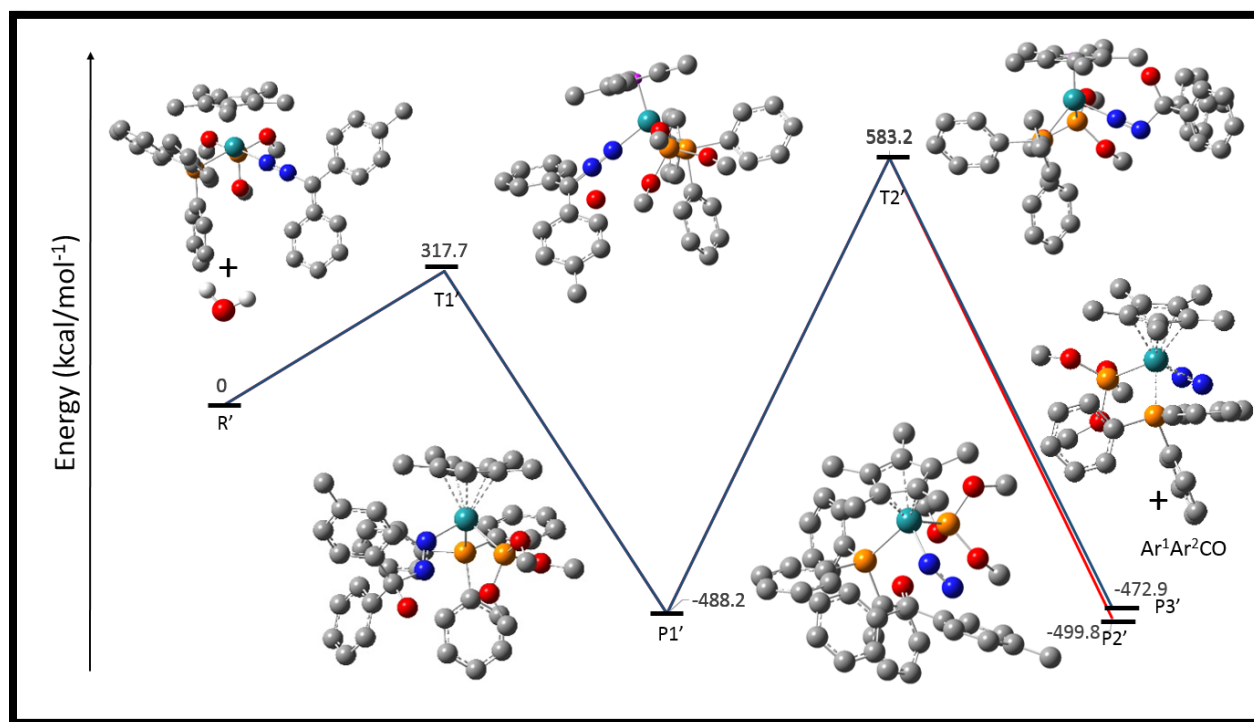
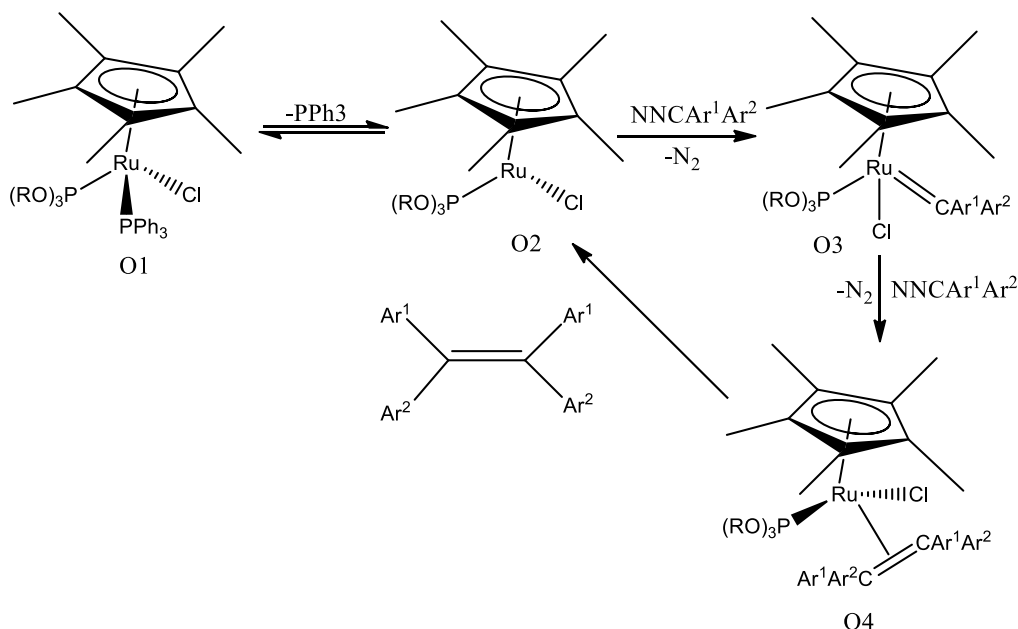


Figure 19 Reaction Coordinate for Hydrolysis of Ruthenium Coordinated Diazoalkane

3.9.4 Possibility of other product: Why alkene can not form?

It is also possible that the N_2 from diazo alkane can leave the complex and what we can expect to get is the dimer of alkane part of diazo group so as to produce an alkene from the given substrates (refer mechanism given below).

The reason here is the presence of Pentamethylcyclopentadienyl ($\eta^5\text{-C}_5\text{Me}_5$) ring as an ancillary ligand which is creating much steric hindrance that the two diazo substituents couldn't accommodate around Ru centre with η^2 carbons. Hence alkene doesn't form here.



Scheme 16 proposed for alkene formation from the given Ru complex

On studying the given mechanism computationally, it was observed that reaction goes on till O3 and afterwards formation of O4 is not observed (Figure 20).

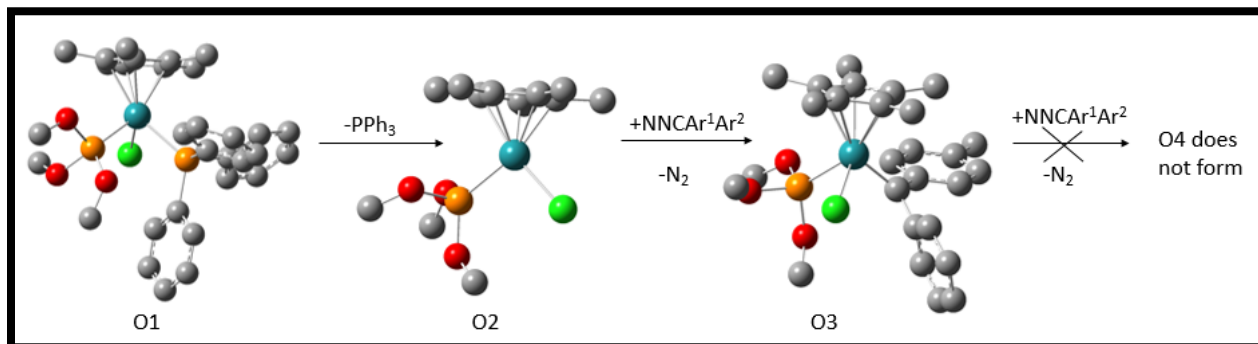


Figure 20 Failure of alkene formation

Chapter 4

Summary and Conclusions

This thesis is focused on the chemistry of diazoalkanes. In particular, DFT study on the hydrolysis of protonated diazoalkanes in unanalyzed as well as catalyzed (coordinated with Ru complex) is investigated here. It is well stated that the diazoalkanes follow S_N2 mechanism for nucleophilic substitution reactions. This trend is observed in case of hydrolysis carried out on aliphatic diazonium ions. On the other hand hydrolysis of aromatic diazoalkanes show S_N2 mechanism exclusively for hydroxide ion but with water the mechanism observed through DFT study is somewhat more inclined towards S_N1 mechanism. The expulsion of nitrogen takes place beforehand and then water as a nucleophile attacks the carbocation.

Water is a weak nucleophile here. Since a system containing two water molecules with the given aromatic diazocation could not facilitate the alcohol. The bond distance observed for C-O implies this. To increase the nucleophilicity of water, we introduce one more water molecule. Cooperative effect of hydrogen bonding comes into the picture and the nucleophilicity is increased such that the system renders alcohol as a product. The C-O bond distance coincides with the theoretical value and hence the complete reaction is observed.

The study of coordinated diazoalkanes with Ru atom is interesting. Since it leads to novel products- a ketone with a diazene derivative coordinated with Ru. Albertin et. al. generated a complex which has η^2 NH=NH ligand attached with Ru centre. What we observe is η^1 NH=NH ligand.

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