

Calculating the Reaction Between Methyl Azide and Propyne, With and Without Homogeneous Catalysts

Can we get an insight on how the rate of the reaction between Methyl Azide and Propyne differs with and without a homogeneous catalyst?

IB Subject of Essay: Chemistry

Word Count: 3484

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Chapter 1

Introduction

1.1 General Introduction

The reaction between Methyl Azide(CH_3N_3) and Propyne($\text{CH}_3\text{C}\equiv\text{CH}$) is one of the most commonly used reactions within the field of Click Chemistry. It is the best click reaction to date, researchers were quickly able to find applications for it within chemistry, biology and materials science^[1] Fahmi Himo et al paper^[2] will be used to reference and compare to the results attained during the experiments of this paper.

Within the team's paper they investigated the activation energy required to start the reaction between Methyl Azide and Propyne with and without a catalyst as well as the geometry of both molecules. Their geometries and

¹"Copper(I)-Catalyzed Synthesis of Azoles. DFT Study Predicts Unprecedented Reactivity and Intermediates", Fahmi Himo et al, 2008

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energies were computed using the B3LYP density functional theory within the Gaussian 98 program, and using the triple- ζ plus polarization basis set 6-311G(d,p) they optimized the geometry.³

Reaction without Catalyst	
Reaction Step:	Energies(kcal/mol)
Transition State	25.7
Product	-60.8

1.2 Click Chemistry

Click chemistry is a field where chemists calculate, using different methods, the geometry of the product in a reaction, the transition state and the reaction enthalpy. With all that information, as well as the time each calculation took, chemists can assume the most efficient method that would consume the least amount of energy and time. "Click chemistry", a term that was first used by K. B. Sharpless in 2001 to describe reactions that are high yielding, wide in scope amongst other things.⁴ In click chemistry calculations are done using quantum mechanical methods and due to the number of calculations required as well as the time required, all the calculations are done a computer. Methods of calculating such as Hartree-Fock and DFT(density functional theory), on a computer, also require a basis set, which represents a series of

³"Copper(I)-Catalyzed Synthesis of Azoles. DFT Study Predicts Unprecedented Reactivity and Intermediates", Fahmi Himo et al, 2008

⁴Organic Chemistry Portal, <https://www.organic-chemistry.org/namedreactions/click-chemistry.shtml>, Accessed May 5, 2019

electronic wave function, in order to turn partial differential equations into algebraic equations due to them being more suitable for a computer.⁵

1.3 Quantum Mechanics Methods

In classical mechanics, Newton's three laws of motion are used to describe the motion of matter; however, the equations fail when describing light particles, such as electrons. Quantum mechanics is therefore used to solve these issues, and it does that by expressing the dynamic properties of the particles as a wavefunction rather than an object travelling through space.⁶ Solving for the wavefunction can be done by solving the Schrödinger equation (Equation 1.1). Austrian physicist Erwin Schrödinger in 1926 proposed the equation.⁷

$$H\Psi = E\Psi \quad (1.1)$$

Two different theories can be used to solve the Schrödinger equation.⁸ Both theories are discussed from subsections 1.3.1-1.3.4.

⁵Wikipedia, [https://en.wikipedia.org/wiki/Basis_set_\(chemistry\)](https://en.wikipedia.org/wiki/Basis_set_(chemistry)) Accessed May 5, 2019

⁶Potassium(I) in Water from Theoretical Calculations, Maria Rudbeck, 2006, Page 4

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1.3.1 Hartree-Fock (HF)

Hartree Fock (HF), describes the quantum state of many electron systems. Hartree Fock uses a wave function constructed as a single Slater determinant which involves single electron wave functions.⁹ Solving the HF equations (Equation 1.3) is done by minimizing the energy whilst still taking the spin of the orbitals into account.¹⁰

$$f_i \chi_i = \epsilon_i \chi_i \quad (1.2)$$

f_i in Equation 1.3 is the Fock operator which is an effective one-electron operator and to find this variable Equation 1.4 is used with ϵ_i as its eigenvalue.¹¹

$$f_i = -\frac{1}{2} \nabla_i^2 - \sum_{A=1}^M \frac{Z_A}{r_{iA}} + \sum_j (J_j - K_j) \quad (1.3)$$

1.3.2 Deficiencies of Hartree-Fock

According to a paper written by Maria Rudbeck at Uppsala University, the Hartree-Fock method fails to describe the electron correlation and does not take the electrons opposite spin, which keeps them apart, into account.¹² The paper further states that the Hartree-Fock energies are too high due to the difference between the Hartree-Fock and the exact energy being defined as

⁹The Beauty of the Bitter Devils, Maria Rudbeck, 2011, Page 11

¹⁰IBID

¹¹IBID

¹²Potassium(I) in Water from Theoretical Calculations, Maria Rudbeck, 2006, page 7

the correlation energy.¹³

1.3.3 Density Function Theory (DFT)

The Density Functional Theory (DFT) is based on the fact that all properties of a system, including the ground-state energy, E (equation 1.1), are only obtained from the electron density, ρ (the square of the wavefunction).¹⁴ Hohenberg and Kohn were able to further develop the realization of Thomas, Fermi and Dirac, in which the energy of the system could be expressed as a functional of the electronic density without the need of dealing with the wave function.¹⁵

$$E[\rho(r)] = \int V_{ext}(r)\rho(r)dr + F[\rho(r)] \quad (1.4)$$

Equation 1.1, involves the first term describing the interaction between the electrons and an external potential V_{ext} , as well as the final term $F[\rho(r)]$ describing the sum of the of the electrons kinetic energy.¹⁶ Kohn and Sham also formulated an inter-electronic interaction.¹⁷

$$F[\rho(r)] = E_{KE}[\rho(r)] + E_H[\rho(r)] + E_{XC}[\rho(r)] \quad (1.5)$$

¹³IBID

¹⁴"The Beauty of the Bitter Devils", Maria Rudbeck, 2011, Page 12

¹⁵"Reaction Mechanisms of Metalloenzymes and Synthetic Model Complexes Activating Dioxygen", Valentin Georgiev, 2009, Page 27

¹⁶IBID

¹⁷IBID

In the equation 1.2, the density is developed in a set of one-electron orbitals which in other words are the Kohn-Sham orbitals.¹⁸ E_{KE} is the electrons kinetic energy, the E_H is the Coulomb energy between the electrons and the E_{XC} is the exchange correlation energy.¹⁹

1.3.4 Deficiencies of DFT

Throughout this paper all the calculations were calculated using DFT. According to a paper by Shilu Chen at the KTH university, recent development has made it an efficient tool in computational chemistry. However this wave-function method is not perfect yet and several deficiencies exist which involve self-interaction errors, and the lack of description of Van der Waals interaction.²⁰ In Hartree-Fock the electron and itself artificial repulsion is cancelled out by an exchange term.²¹ DFT Coulombic terms are described exactly.²² However, due to the exchange terms being described by an approximate functional the terms do not cancel out in DFT.²³ This causes the self-interaction error, and it artificially stabilizes delocalized transition states and decreases the activation energy.²⁴

¹⁸"The Beauty of the Bitter Devils", Maria Rudbeck, 2011, Page 13

¹⁹IBID

²⁰"Quantum Chemical Modeling of Binuclear Zinc Enzymes", Shilu Chen, 2008, Page 10

²¹IBID

²²IBID

²³IBID

²⁴IBID

The lack of description of the Van der Waals interactions leads to exaggerated repulsion when atoms are forced close each other.²⁵ This usually occurs in systems with large substituents or ligands.²⁶

1.4 Transition State Theory (TST)

The transition state is a point between the reaction and the product stage of a reaction. When the reaction has achieved its activation energy (amount of energy required to move from the reactants to the products) it is that state at which it is referred to 'the transition state'.

Previous theories such as the Arrhenius equation are not very accurate in some areas and this is why in 1935, Henry Eyring helped develop a brand new theory 'The Transition State Theory' (Equation 1.5) which provided a greater understanding of the activation energy (E_a), as well as the thermodynamic properties of the transition state.²⁷ The transition state theory is more accurate than the aforementioned theory (Arrhenius equation).

$$v = \left(\frac{k_B T}{h}\right) \exp\left(\frac{-E}{RT}\right) \quad (1.6)$$

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²⁷Chemistry Libretexts, [https://chem.libretexts.org/Bookshelves/Physical_and_Theoretical_Chemistry_Textbook_Maps/Map%3A_Physical_Chemistry_for_the_Biosciences_\(Chang\)/09%3A_Chemical_Kinetics/9.07%3A_Theories_of_Reaction_Rates](https://chem.libretexts.org/Bookshelves/Physical_and_Theoretical_Chemistry_Textbook_Maps/Map%3A_Physical_Chemistry_for_the_Biosciences_(Chang)/09%3A_Chemical_Kinetics/9.07%3A_Theories_of_Reaction_Rates), Accessed 4 June, 2019

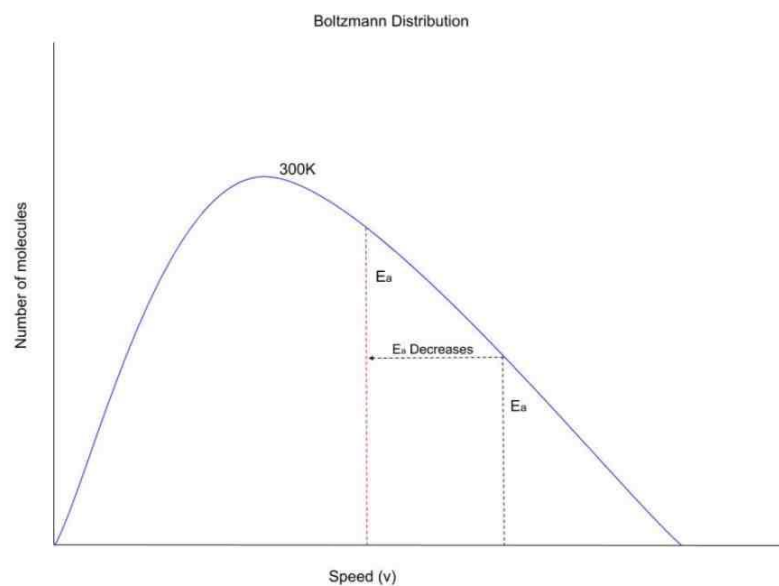
1.5 Research Question (RQ)

”Can we get an insight on how the rate of the reaction between Methyl Azide and Propyne differs with and without a homogeneous catalyst?”

The reaction between Methyl Azide(CH_3N_3) and Propyne($\text{CH}_3\text{C}\equiv\text{CH}$) is one of the most commonly used reaction in Click Chemistry. To answer the question “Can we get an insight on how the rate of the reaction between Methyl Azide and Propyne differs with and without a homogeneous catalyst?” A series of simulations will be conducted and calculated using a program called Gauss View to see how both reactants will react with each other when applying the calculating method B3LYP density functional theory (DFT). My main source will be a paper written in 2004 by professor Fahmi et al where they look into the reaction and try to assume the correct method of achieving the product. The method used to know how the rate of the reaction will differs with and without a catalyst is in the means of knowing that the energy required for a reaction to reach its activation energy is less with a catalyst and using the Boltzmann distribution could be shown to increase the rate constant as can be seen in the Arrhenius equation $k = Ae^{\frac{-E_a}{RT}}$ rewritten to $\ln(k) = \ln(A) + \frac{-E_a}{RT}$. The rate constant is important due to it being the multiple in the rate equation $rate = k[A]^m[B]^n$. The basis set that used for these calculations is 6-311G(dp) due to that being the basis set used in Fahmi et al’s paper. The results coming from this research would also be applicable

to other azides, nitrile oxides and alkalines.²⁸

The results expected is that the rate of reaction, for the reaction with a catalyst will increase as that is why catalysts are used (to increase the rate of a reaction). A more mathematical way of proving this would be by looking at the rate constant in the Arrhenius equation $k = Ae^{\frac{-E_a}{RT}}$ rewritten to $\ln(k) = \ln(A) + \frac{-E_a}{RT}$ which will increase, however it can also be further proven using the Maxwell-Boltzmann distribution.



As can be seen from the Maxwell-Boltzmann distribution up above when the activation energy decreases there is a higher amount of molecules that can achieve the energy required to make the product. This shows that the

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rate of reaction increases, however, there is a more exact and mathematically theoretical method by using the Eyring equation also known as the Transition State Theory equation

$$v = \left(\frac{k_B T}{h}\right) \exp\left(\frac{-E}{RT}\right) \quad (1.7)$$

The equation involves the Boltzmann-constant (k_B), Planck's-constant (h), activation energy ($-E$), temperature (T) and the gas constant (R). Almost all the values are constants except for the activation energy “ $-E$ ” and the temperature. The temperature will be assumed to be around room temperature ($300K$). Using the Eyring equation it will be possible to insert the activation energies found within the research to uncover and compare the reaction rates of both reactions. For the sake of simplicity of calculating the rate, it will be assumed no entropy.

Chapter 2

Method

To be able to calculate the rate of reaction for both the catalyst and non-catalyst reactions the activation energy is required, and it can be found by making the reactants react to create the products. By doing this we can calculate the enthalpy change and therefore find the activation energy. All the reactant building, optimization and energy solving will be conducted on Gauss View 98.

The first step is to build the non-catalyst reactants and optimize the geometry of the reaction. The optimization of the geometry is to change the position of the reactants to their more natural geometry (section 2.2 for more information). Then the following step is to make Gauss View calculate the transition state. The calculations done by the program will be using DFT as the calculating method and B3LYP 6-311G(dp) as the basis set. After the

calculations the program will show the transition state of the reaction and give the amount of Hartree Energy the reaction needed. The energies will be useful when plotting the energies in the diagram to see whether the reaction is exothermic or endothermic.

The next step is to move the reactants closer to each other to force the reactants to bond and create the product further more then the results could be more similar to that of Fahmi et al's paper. It is at that point in which the transition state is optimized to get the more natural geometry before the reactants bond. With the new optimized geometry the program is to do another calculation using the same calculating method and basis as in the previous calculations. The calculation will then give the amount of energy in Hartree required to create the products from the transition state to the product as well further more the program will show the news bonds created. However the geometry could be incorrect therefore it is recommended to do another geometry optimization.

Using all the energies attained from the calculations it is now possible to calculate the activation energy for the reaction. However to begin with a diagram will be made from the energies attained to visualize the enthalpy change. When plotting the energies the reactants energy will begin at 0 and, the transition state and products will be measured as the difference however it is needed to convert the energies from hartree to kcal/mol to be able to plot the enthalpy change. The reason kcal/mol is used rather than J/mol is

due to kcal/mol being the used unit for measuring energy in click chemistry.

The mathematical way of writing the energy conversion method is so:

$$E_{H_2} - E_{H_1} = \Delta E_H$$

then

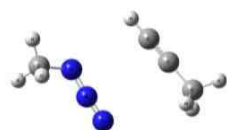
$$\Delta E_H \times A = E_E$$

E_H is the hartree energy, A is the Arrhenius constant (627.51), E_E is the enthalpy energy (kcal/mol).

When finding the energy for the product it will then be possible to calculate the enthalpy change. The enthalpy change throughout this paper will be written as ΔE . From the enthalpy change of the products and the reactants it will be visible whether the reaction is exothermic or endothermic. The enthalpy change between the transition state and the reactants will be the activation energy (E_a) and with the activation energy, the rate of the reaction can be calculated using the Eyring equation (equation 1.6).

2.1 Reaction A

Reaction A is the reaction between Methyl Azide (CH_3N_3) and Propyne (C_3H_4) without the use of a Catalyst.



(a) Fig 2.1 Reactant Phase

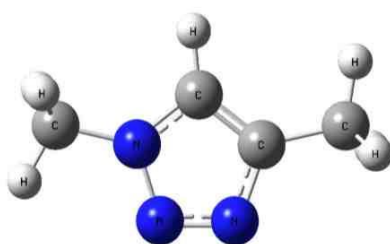


(b) Fig 2.1 Transition State

Figure 2.1 (a) above shows both reactants in the reactant phase after their geometry has been optimized.

Figure 2.1 (b) is the transition state of the reaction. No bonds will be breaking, however new bonds will be created between the carbon atoms in the Methyl Azide as well as the nitrogen atoms in the Propyne.

Figure 2.2: Product Phase



As can be seen in figure 2.3 both reactants bonded and two double bonds were created between the carbon and nitrogen atoms. With all the geometries found we can write down the calculated energy required for reaction phase in a table.

Table 2.1

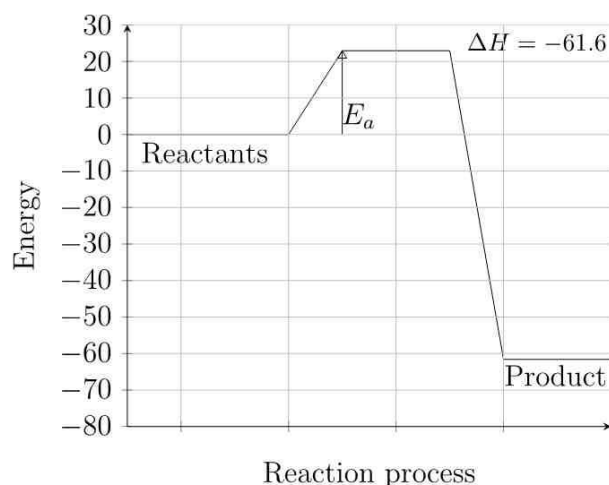
Reaction A Energies		
Reaction Step:	Energies: (Hartree)	$\Delta E \times A$: (kcal/mol)
Reactants	-320.84193997	0
Transition State	-320.80544173	22.9030105824
Product	-320.94010874	-61.6018848627

As can be seen in the table 2.1 showing the optimized energies of each reaction step as well as the energy in kcal/mol. From the table it is safe to assume that the reaction is exothermic due to the energy required for the product is less than that of the reactants. Inserting the data from the table into a potential energy profile will give more information for analysis.

Figure 2.3 shows the activation energy (E_a), the product below the reactants as well as the $\Delta H = -61.6$. ΔH being enthalpy and the change in energy between the final system's enthalpy(product) and the initial system's enthalpy(reactants), therefore the enthalpy can be found with the equation

$$H_f - H_i = \Delta H$$

Figure 2.3



The activation energy or that TS (Transition State) has a calculated energy barrier of 22.9 kcal/mol and the resulted product is 61.6 kcal/mol lower than the reactant.

2.1.1 Calculations and Results

With all the data acquired we can at this point in time calculate the rate of the reaction. Assuming the reaction happened in room temperature in kelvin (300K) and change the activation energy from kcal/mol to J/mol (Joule/mol) then the equation will look like the following:

$$v = \left(\frac{((1.381 \times 10^{-23}) \times 300)}{(6.626 \times 10^{-34})} \right) \exp\left(\frac{-95813.6}{(8.31 \times 300)} \right)$$

$$v = (6.252641111 \times 10^{12}) \times \exp\left(\frac{-95813.6}{(8.31 \times 300)}\right)$$

$$v = (6.252641111 \times 10^{12}) \times (2.03581053 \times 10^{-17})$$

$$v = 0.0001272919\text{s}^{-1}$$

What this number defines is the speed of the reaction per second. With the rate of reaction being 0.0001272919 it means that when adding both molecules together you will have to wait approximately 12000 seconds or 3.3 hours for the reaction to occur.

2.2 Reaction B

Reaction B is the reaction between Methyl Azide and Propyne with copper as a catalyst

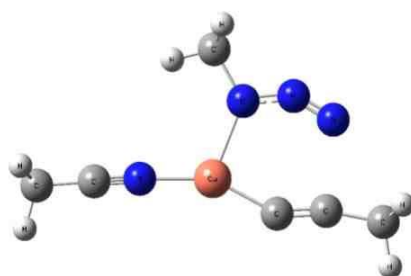


Figure 2.4: Reactant Phase

Reactants in figure 2.4 are bonded to a Copper catalyst along with C_2H_3N as a ligand.

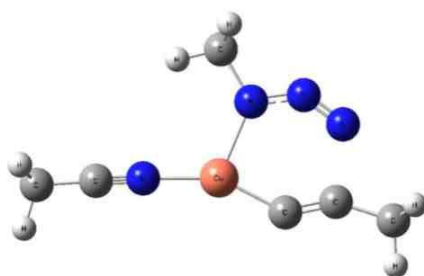


Figure 2.5: Transition State 1

Figure 2.5 shows the first transition state of the reaction. As can be seen a Nitrogen moved closer towards one of the Carbons to create a bond.

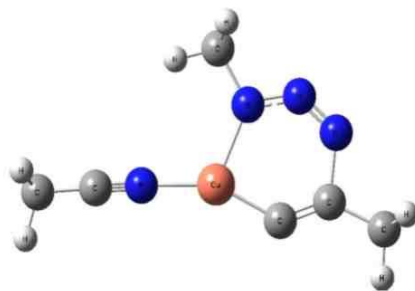


Figure 2.6: Intermediate

In the intermediate state the Nitrogen and Carbon atoms formed a bond. That first bond of the total of two that we are seeking in this reaction.

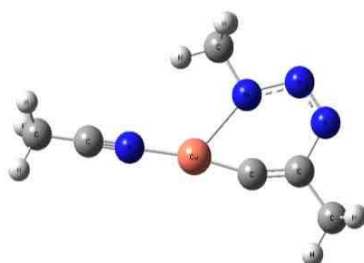


Figure 2.7: Transition State 2

In the second transition state one of the Nitrogen atoms moved in an unexpected direction however did get closer to another Carbon atom which seems to be the atom that the Nitrogen will bond to.

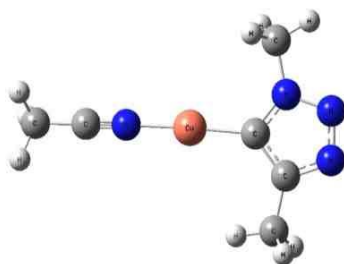


Figure 2.8: Product

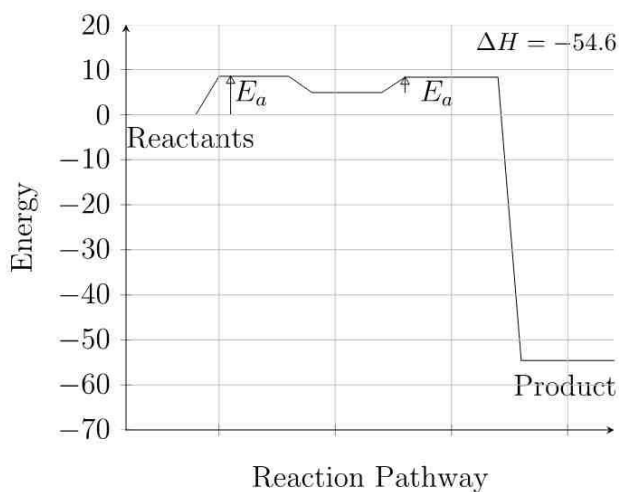
The product was successfully found in figure 2.8. All the atoms bonded with the correct type of bond. With these geometries found we can put all the calculated energies for each step into a table.

Table 2.2

Reaction A Energies		
Reaction Step:	Energies:	$\Delta E \times A$: (kcal/mol)
Reactants	-2093.53935277	0
Transition State 1	-2093.52578654	8.5129449873
Intermediate	-2093.53145340	4.9569336687
Transition State 2	-2093.52602852	8.3611001175
Product	-2093.62641526	-54.6325830999

Table 2.2 shows similar things to the previous table 2.1 however one thing stands out and that is the energy required for the intermediate. Turning this table into a potential energy profile will ease visualizing it.

Figure 2.9



The energy profile (figure 2.10) shows the same reaction as in the previous energy profile, however this one is under the conditions of a homogeneous catalyst. There are 5 stages to this reaction unlike the previous reaction with only 3. During the reaction the reactants do not interact directly but through an intermediate. The activation energy required for this transition state is 8.51 kcal/mol. As mentioned prior the intermediate stands out. That is due to it being unstable. It is evident for the reason that its value is greater than that of the initial stage (reactants). The enthalpy will therefore be positive showing that this stage has an endothermic effect. The difference between the final stage and the initial stage is negative and therefore is an exothermic stage.

2.2.1 Calculations and Results

With all the data gathered about this reaction we can continue to calculate its rate. As done in the last calculation I will be assuming the temperature is around room temperature (300K) and will be changing the activation energy from kcal/mol to J/mol.

$$v = \left(\frac{((1.381 \times 10^{-23}) \times 300)}{(6.626 \times 10^{-34})} \right) \exp\left(\frac{-35605.84}{(8.31 \times 300)}\right)$$

$$v = (6.252641111 \times 10^{12}) \times \exp\left(\frac{-35605.84}{(8.31 \times 300)}\right)$$

$$v = (6.252641111 \times 10^{12}) \times (6.269954744 \times 10^{-7})$$

$$v = 3920377.68s^{-1}$$

This reaction occurs in 3.97 millionth of a second. That is a lot quicker than the previous 0.00012 times a second. This is due to the reaction with a catalyst having reactions that won't occur without a catalyst. Another reason to the massive increase is due to the reaction involving a much lower activation energy to reach its transition state. The previous reaction required 22.9 kcal/mol whilst this reaction only requires 8.51 kcal/mol which is 3 times less energy.

Chapter 3

Discussion

As could be seen when comparing both rates it can be seen that 'Reaction B' is much more efficient compared to 'Reaction A'. Not only does 'Reaction B' require 3 times less energy than 'Reaction A', its reaction occurs almost 33 billion times quicker than that of 'Reaction B'.

It is important to remember that these results are using a constant temperature of 300K. We can test out how the result differs due to it by the means of changing the temperature in 'Reaction A' to 3000K.

$$= \left(\frac{((1.381 \times 10^{-23}) \times 3000)}{(6.626 \times 10^{-34})} \right) \exp\left(\frac{-95813.6}{(8.31 \times 3000)}\right)$$

$$v = 1.339515335 \times 10^{12}$$

'Reaction A' with 3000K happens in 1.34×10^{12} th of a second and that is

unimaginably quick.

The answer my research question "Can we get an insight on how the rate of the reaction between Methyl Azide and Propyne differs with and without homogeneous catalysis" is yes. By using the Eyring equation it was possible to identify the reaction rate without the need of having concentrations for the molecules or even know the value of 'A' in the Arrhenius equation. However is it important to remember this paper is based on a theoretical reaction as well as theoretical mathematics and if conducted in a lab could give different results.

Chapter 4

Conclusion

In conclusion, the use of mathematical models can give us an insight into what is happening at the atomic level and why. The rate of reaction is one of the things mathematics can help us find and understand. Catalysts are seen in this paper to help accelerate reactions by giving an alternative way with lower activation energy. The use of the application Gauss View 98 made it possible to calculate the energies which would otherwise take months to calculate at high school mathematical level and the use of a basis set of 6-311G-(dp) gave more accurate geometries and energy values. The use of a different basis set such as 6-311G would give a different result and sometimes even the invalid result or at least results that were very different from that of Fahmi et al's paper¹. The only method, I am aware of, of deducing whether a basis set is incorrect would be to test it and see if you end up with a similar

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product.

To answer the research question “Can we get an insight on how the rate of reaction between Methyl Azide and Propyne differs with and without a catalyst” yes, it is possible to get an insight into how the rate of reaction differs, using mathematics. With the use of the Eyring equation, using both the quantum mechanical theories DFT and Hartree-Fock, as well as the use of the basis sets, it is possible to see how the reaction occurs at the atomic level. The results attained from both reactions turned out as hypothesized, with the reaction with a catalyst being significantly faster than the reaction without a catalyst. The results gathered in this paper are also similar to those of which Fahmi et al got in their research. The differences in enthalpy from this paper and Fahmi et al’s paper could be explained as a due to a certain bond being longer for the transition state or product, something within the calculation could have been different. However, the similarities shows the results of this paper can be, to some extent, trusted as theoretical proof to the research question. The Boltzmann distribution shows that a reaction with a catalyst will accelerate the reaction, and with this knowledge it can be assumed that the results in this research have some validity

The limitations of this research are the quantum mechanical methods. Due to Hartree-Fock and DFT’s deficiencies, as discussed in sub-chapters 1.3.2 and 1.3.4, they could to some extent give false results which will result in incorrect final results. Another limitation is the theoretical aspect. Since the

reactions are hypothetical and are done using a program, the program itself could cause some sort of incorrect result, such as an incorrect geometry which would, after calculating, give the wrong Hartree energy and also in-turn cause an incorrect final result. Furthermore, the reaction being theoretical does not give final results, an experiment in a lab would give more exact results.

The results of this research are not to be taken as fact due to more research needed in this topic as well as the quantum-mechanics

The results from this paper should not be taken as facts as more research is needed, however the results could be used for comparison if researching something similar.

Bibliography

- [1] "Copper(I)-Catalyzed Synthesis of Azoles. DFT Study Predicts Unprecedented Reactivity and Intermediates", Himo et al, JACS 2005, 127, 210
- [2] Organic Chemistry Portal, <https://www.organic-chemistry.org/namedreactions/click-chemistry.shtm>, Accessed May 5, 2019
- [3] Wikipedia, [https://en.wikipedia.org/wiki/Basis_set_\(chemistry\)](https://en.wikipedia.org/wiki/Basis_set_(chemistry)), Accessed May 5, 2019
- [4] "Potassium(I) in Water from Theoretical Calculations, Maria Rudbeck", 2006, <https://www.diva-portal.org/smash/get/diva2:304749/FULLTEXT01.pdf>
- [5] "The Beauty of the Bitter Devils", Maria Rudbeck", 2011, <https://www.diva-portal.org/smash/get/diva2:460894/FULLTEXT01.pdf>
- [6] "Reaction Mechanisms of Metalloenzymes and Synthetic Model Complexes Activating Dioxygen", Valentin Georgiev, 2009, <https://www.diva-portal.org/smash/get/diva2:273747/FULLTEXT08.pdf>

- [7] "Quantum Chemical Modeling of Binuclear Zinc Enzymes", Shilu Chen, 2008, <https://www.diva-portal.org/smash/get/diva2:127039/FULLTEXT01.pdf>
- [8] Chemistry Libretexts, [https://chem.libretexts.org/Bookshelves/Physical_and_Theoretical_Chemistry_Textbook_Maps/Map%3A_Physical_Chemistry_for_the_Biosciences_\(Chang\)/09%3A_Chemical_Kinetics/9.07%3A_Theories_of_Reaction_Rates](https://chem.libretexts.org/Bookshelves/Physical_and_Theoretical_Chemistry_Textbook_Maps/Map%3A_Physical_Chemistry_for_the_Biosciences_(Chang)/09%3A_Chemical_Kinetics/9.07%3A_Theories_of_Reaction_Rates), Accessed 4 June, 2019