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# Computational study of the mechanism of the oxidation of ascorbic acid by iodine in the gas phase

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**ABSTRACT**

The reaction mechanisms of the oxidation of ascorbic acid by iodine have been examined using semi empirical pm3 method. The oxidation proceeded via two independent routes that can be separately monitored. One route involved a one step reaction mechanism while the other was a two steps reaction mechanism. The rsults were explained by analyses based on computational energetics of the optimised reactants, intermediates. Transition states and products of the reaction of iodine with ascorbic acid. The study showed that both proposed routes were possible by comparing the enthalpies of reactions of the two proposed pathways as well as the activation barriers of the respective rate determining steps.

**Keywords:** *Ascorbic acid, Vitamin C, Iodine, dehydroascorbic acid, computational, oxidation*

## 1. INTRODUCTION

Ascorbic acid is a water soluble sugar acid with antioxidant properties or with strong reducing action and it is an important co-enzyme for internal hydroxylation reaction [1]. The L-isomer of ascorbic acid is commonly known as vitamin C and is found naturally in fruits and vegetables [2-5]. Vitamin C (ascorbic acid) is an important component of our diet. Some of its functional roles include its use as: a nutrition food additive, antioxidant, reducing agent, stabilizer, modifier, color stabilizer [6]. Its absence in human leads to scurvy, a deficiency disease [7], where the protein, collagen, cannot form fibers properly and this results in skin lesions and blood vessel fragility [8-10]. Ascorbic acid is susceptible to oxidation in acidic, basic or neutral media. The oxidation of ascorbic acid is a very important redox reaction, as it has interesting biological properties and is also a powerful reductant. Ascorbic acid is a lactone with a 2,3-endiol group [11, 12] . It is very effective as a reducing agent and is quantitatively reversibly oxidized in aqueous solution by different oxidizing agents. The products of the oxidation depend largely on the pH of the reaction; however, its oxidation by various oxidizing agents in acid solution produces dehydroascorbic acid, a lactone whose ring can be easily hydrolyzed to give the free carboxylic group [11-13]. A number of papers have been devoted to the oxidation of ascorbic acid in acidic and basic media with various inorganic [14-19] and organic substrates [20, 21]. However, the reduction of Iodine with ascorbic acid though severally reported, were somewhat limited in kinetic and mechanistic details [22, 23]. Given the importance of the vitamin in human health and its widespread use as an antioxidant in processed foods, study of its degradation products is worthy of investigation [23].Iodine also is an essential component of the human diet and, in fact, appears to be the heaviest required element in a diet. Iodine compounds are useful in medicine and lack of iodine in the diet is a cause of goiter. Iodine is absolutely necessary

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for a healthy thyroid as well as ovaries, breasts and prostate. Iodine deficiency is in fact the largest preventable cause of mental retardation worldwide [24]. In severe cases, it can result in cretinism, a form of mental retardation. These are just a few of the reasons why the study of iodine is interesting.
The present paper desired to report the results of computational studies on the mechanism of the oxid ation of Ascorbicacid by iodine. The computational analyses of the structures using semi empirical ( PM3)are reported. Computational chemistry methods can be used to explore the theoretical chemistry behind reactive systems, to compare the relative chemical reactivity of different systems, and, by extension, to predict the reactivity of new systems. Transition states for reaction of Ascorbic acid with iodine were determined; equilibrium states of reactants, intermediates and products were se arched by computational means. The semi empirical models MNDO, AM1, and PM3 are often used in computational chemistry because they allow study of systems that are out of reach of more accura te methods[25-30].
Theoretical studies on compounds containing iodine, a $5^{th}$ period halogen atom, are less abundant compared to those containing F, Cl or Br which are $2^{nd}$, $3^{rd}$ and $4^{th}$ elements respectively. Heavy elements like iodine have a large number of core electrons which needs a large number of basis sets or functions to describe the corresponding orbitals. This makes computations with heavy elements like iodine very time consuming and expensive [31-33]. However, compounds containing iodine atom play very interesting and important roles in many chemical reactions, especially in the life sciences

## 2. EXPERIMENTAL SECTION

2.1. **Computational Methods.** The Spartan '14 v1.1.0 semi-empirical (PM3) method was used on Microsoft window XP professional version 2002 SP3 computer system, with Intel(R) Pentium(R) Dual CPU,E2200@2.20 GHz 219 GHz, 3.24GB of RAM. All the electronic structure calculations reported in this work were performed using the Spartan '14 v1.1.0 program packages. The geometries included in the reaction of Ascorbic acid with Iodine were fully optimized using the semi-empirical method [34, 35]. The semi empirical PM3 method was employed to optimize the geometries of the reactants, intermediates, transition states and products [34 - 37]. The starting geometries for all of the semi- empirical calculations were at first optimized in the Spartan '14 v1.1.0 Global calculations environment work space at the AM1 level, and then followed by the PM3 calculations. The optimized geometries of the reactants, intermediates, transition states and products were confirmed in terms of vibrational analysis [26]. The transition state for each step was located and confirmed by animating the vibration corresponding to the reaction coordinate by selecting the imaginary frequency at the top of the list of frequencies on the IR tab. No arbitrary assumptions were imposed on finding the most likely geometries for the transition state in each case.

## 3. RESULTS SECTION

**3.1. Published mechanism.** The outline of the published mechanism of the oxidation of Ascorbic acid with Iodine as given by several groups [22, 38, 39] is shown in scheme 1 below.

$$C_6H_8O_6 \rightarrow C_6H_6O_6 + 2H^+ + 2e^- \quad \ldots\ldots\ldots\ldots (1)$$

$$I_2 + 2e^- \rightarrow 2I^- \quad \ldots\ldots\ldots (2)$$

$$C_6H_8O_6 + I_2 \rightarrow C_6H_6O_6 + 2H^+ + 2I^- \quad \ldots\ldots\ldots (3)$$

**Scheme 1:** The reaction mechanism as proposed by several groups [22, 38, 39]

The various groups have shown that reaction between Ascorbic acid and Iodine would yield dehydroascorbic acid with $H^+$ and $I^-$ as byproducts. But both $H^+$ and $I^-$ are very reactive species and would not remain as ions in the reaction medium. It is the desire of this work to find out if we can account for the fate of these ions or, if we can even modify the mechanism presented in scheme 1.

**3.2. Geometry optimization of intermediates and transition states; and validity of the generally accepted mechanism.** Geometry optimization of the reactants, intermediates, transition states and products in the ascorbic acid reaction with Iodine was executed. The geometry optimizations of all these species were successfully completed and the heat of formation ($\Delta H^o$) at standard condition of 1 atmosphere and 298.15K were evaluated and presented together with other activation parameters in Table 1.

**Table 1:** Heat of formation at Standard Condition of 1 atmosphere and 298.15K of reacting species

| S/N | Reacting Specie | Heat of Formation and other activation parameters at 1 Atm. and 298.15K using PM3 method for Route 1 | | | Reacting Specie | Heat of Formation and other activation parameters at 1 Atm. and 298.15K using PM3 method for Route 2 | | |
|---|---|---|---|---|---|---|---|---|
| | | $\Delta H^o$ (kJ/mol) | $\Delta G^o$ (kJ/mol) | $\Delta S^o$ (kJ/mol.K) | | $\Delta H^o$ (kJ/mol) | $\Delta G^o$ (kJ/mol) | $\Delta S^o$ (kJ/mol.K) |
| 1 | $I_2$ | 99.61 | 22.70 | 257.97 | $I_2$ | 99.61 | 22.70 | 257.97 |
| 2 | AA | -973.83 | -705.13 | 451.41 | AA | -973.83 | -705.13 | 451.41 |
| 3 | $TS_1$ | -462.69 | -643.83 | 607.55 | $TS_{B1}$ | -351.56 | -590.46 | 801.27 |
| 4 | DAA | -924.50 | -694.55 | 440.80 | DAA | -924.50 | -694.55 | 440.80 |
| 5 | HI | 120.53 | 85.01 | 207.02 | HI | 120.53 | 85.01 | 207.02 |
| 6 | $R_1$ | -874.22 | | | $TS_{B2}$ | -632.22 | -1286.54 | 669.50 |
| 7 | $P_1$ | -683.44 | | | $I^-$ | 0.00 | | |
| 8 | | | | | $R_{B1}$ | -774.61 | | |
| 9 | | | | | $P_{B1}$ | -683.44 | | |
| 10 | | | | | $R_{B2}$ | -973.83 | | |
| 11 | | | | | $P_{B2}$ | -683.44 | | |

If we consider the heat of formation of the various optimized reaction species for route 1, the transition states TS1 with heat of formation of -462.29kJ/mol was observed to be a transition state because its position was a saddle point on the scaled energy diagram of the reaction. It was also confirmed by animating the vibration corresponding to the reaction coordinate by selecting the imaginary frequency at the top of the list of frequencies on the IR tab. The energy diagrams (Figures 1a) showed this vividly, where $R_1$ were the reactants in route 1, with TS as the possible transition states and $P_1$, the products of the same reaction.

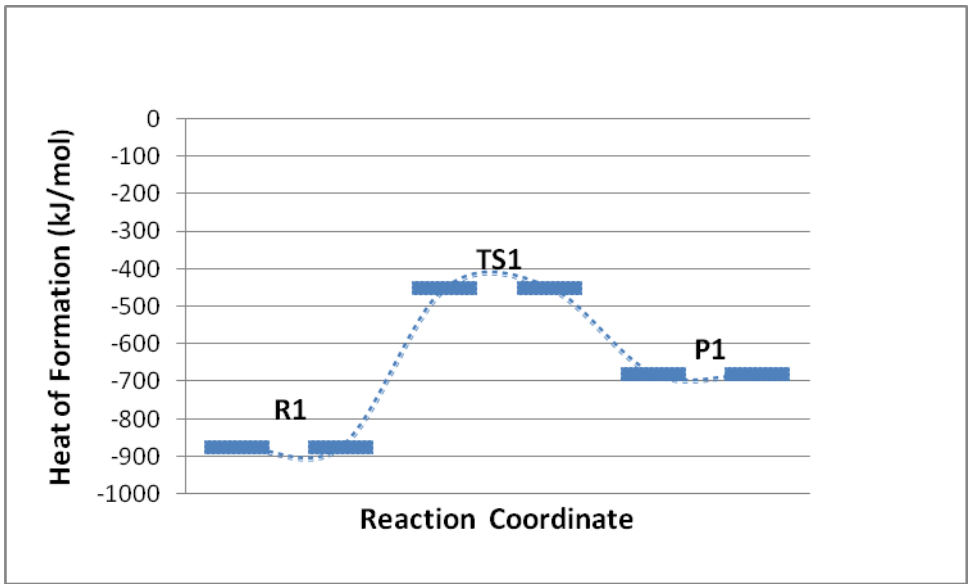



**Figure 1a:** Energy profile of the oxidation of Ascorbic acid by iodine according to the route 1 proposed mechanism

On the other hand $TS_{B1}$ and $TS_{B2}$ were also transition states with heats of formation of -351.56 kJ/mol and -632.22 respectively in the two steps mechanism as proposed in route 2. $TS_{B1}$ and TSB2 were real saddle points in the reaction. They were also confirmed by animating the vibration corresponding to the reaction coordinate by selecting the imaginary frequency at the top of the list of frequencies on the IR tab. The energy diagrams (Figures 2 ) showed this vividly also.

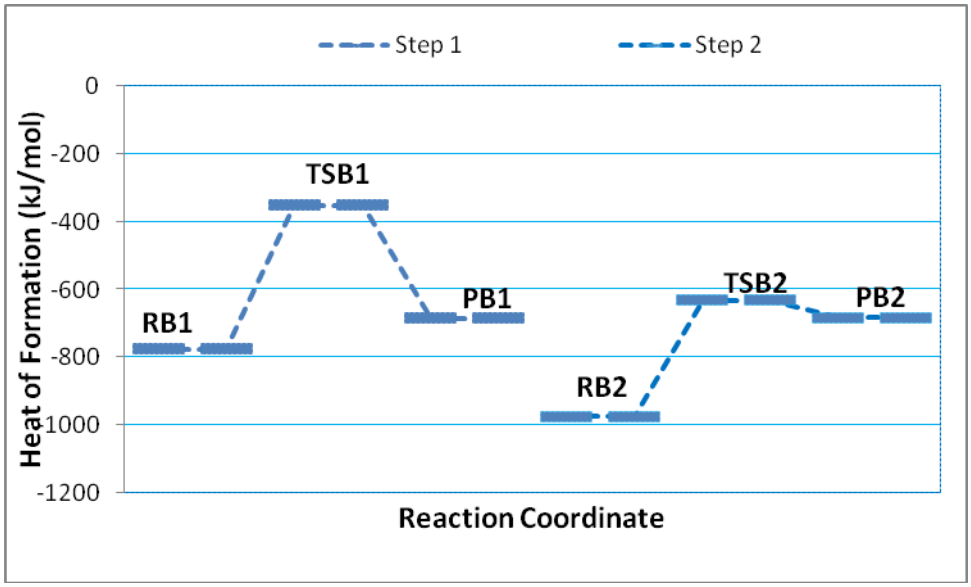
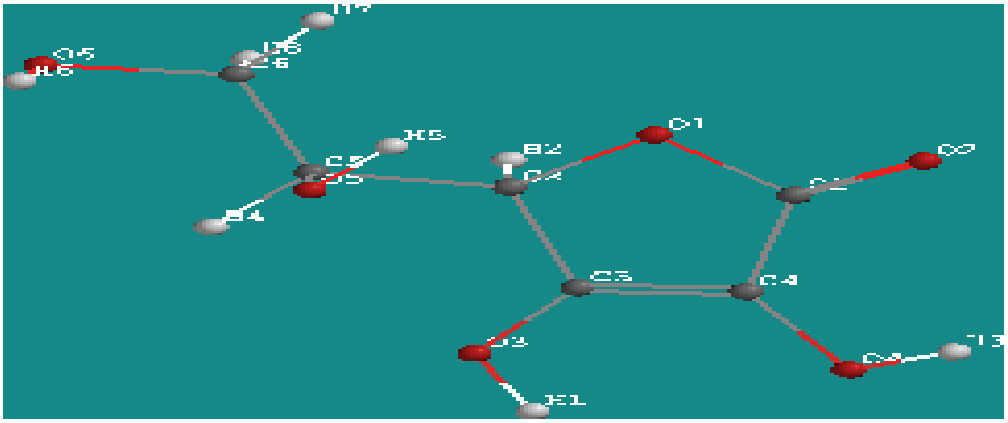



**Figure 1a:** Energy profile of the oxidation of ascorbic acid by iodine according to the route2 proposed mechanism

**3.3. Charge distribution.** The starting ascorbic acid molecule was optimized. The conformation with the lowest energy was optimized and calculated using the PM3 method. The oxidation of ascorbic acid by the various groups previously reported [22, 38, 39] showed that hydrogen ($H^+$) ions were abstracted from the ascorbic acid molecule. The identity numbers of all the atoms of the Ascorbic acid molecule labeled as in Scheme 2.




**Scheme 2:** Labeled structure of ascorbic acid

Molecular information such as how all the 8 hydrogen atoms were bonded (either as C-H or O-H), their bond lengths, the exposed surface of various hydrogen atoms available for reactions were obtained and presented in Table 2.

**Table 3:** Bond lengths of the reactive sites the transition states

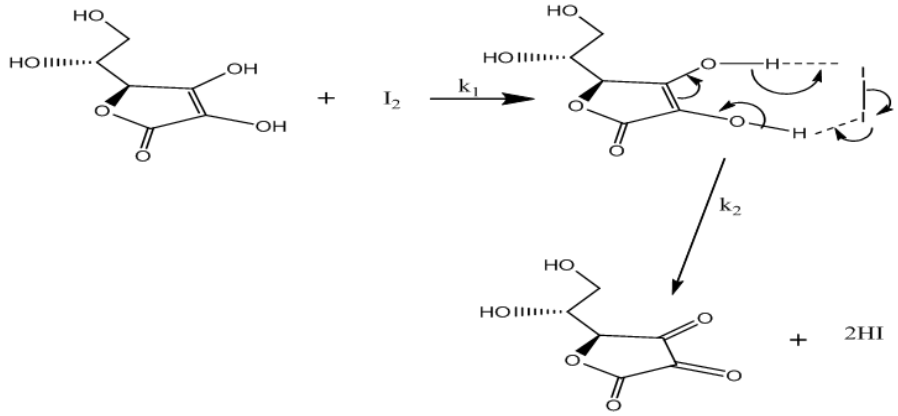
| Hydrogen Identity | Bond Type | Bond Length (Angstrom) | Exposed surface (Angstrom) |
|---|---|---|---|
| H1 | O-H | 0.951 | 8.05 |
| H2 | C-H | 1.115 | 5.59 |
| H3 | O-H | 0.950 | 8.06 |
| H4 | C-H | 1.117 | 5.68 |
| H5 | O-H | 0.948 | 7.59 |
| H6 | O-H | 0.949 | 7.95 |
| H7 | C-H | 1.104 | 4.93 |
| H8 | C-H | 1.108 | 5.58 |

Among the 8 hydrogen atoms of the ascorbic acid molecule, H1, H3, H5 and H6 were bonded to oxygen atoms while the rest were bonded to Carbon atoms. The bond lengths of all the C-H bonds were longer than the O-H bonds. But of all the O-H bonds, H1 and H3 had the longest bond lengths of 0.951Å and 0.950Å respectively. These same hydrogen atoms had the largest exposed surfaces of 8.05Å and 8.06Å. The large exposed surfaces of these 2 hydrogen atoms showed that these atoms are active hydrogen atoms and can react easily [40]. In addition, the bonding contribution of LUMO (-64.77kJ/mol) for bond cleavage was smaller than that of HOMO (-962.93kJ/mol) for bond formation; thus it showed that there was bond formation between Ascorbic acid molecule and the electrophiles.

**3.4. Proposal of a more plausible mechanism for the reaction.** Considering the structure of the optimized Ascorbic acid molecule, there are two possible schemes of writing the reaction mechanism. These were presents as route 1 (scheme 2) and route 2 (scheme 3) respectively.

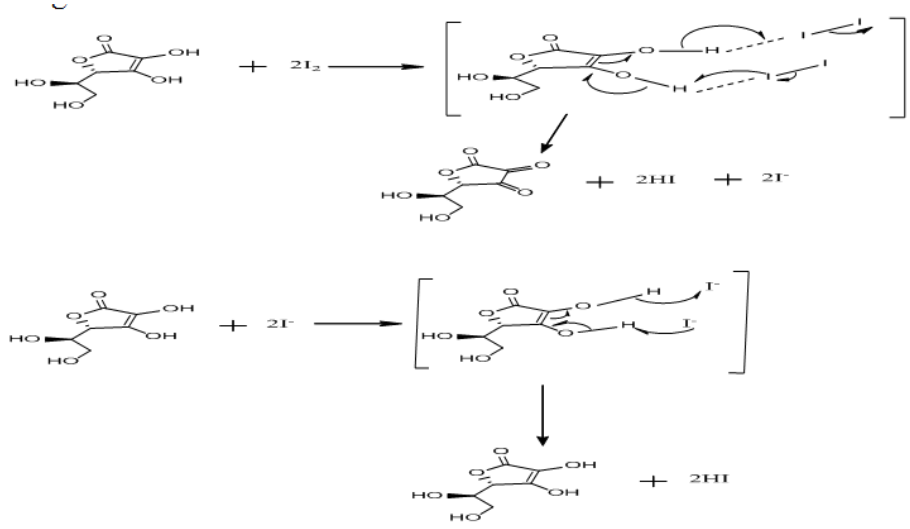
**3.4.1. Route 1.** In route1 the optimized ascorbic acid molecule reacted with an Iodine molecule to form a cyclic activated complex TS1 which, on disproportionation two hydrogen atoms were abstracted to give the products, a molecule of dehydroascorbic acid plus two molecules of hydrogen iodide. Even though the calculations have shown the reaction mechanism of route 1 is possible, it is doubted if the mechanism would be the most favored pathway. This is because H1 and H3 of the optimized ascorbic acid molecule were trans to each other therefore, the possibility of the same

molecule of iodine attacking the Hydrogen atoms at the same time is very limited. The route 1 mechanism is as given scheme 2.




**Scheme 2:** The one step reaction mechanism via the cyclic activated complex

**3.4.2. Route 2.** Route 2 described a two steps scheme in which the optimized ascorbic acid molecule reacted with two different Iodine molecules to yield dehydroascorbic acid plus two molecules of hydrogen iodide and two iodine radicals in the first step. In the second step another ascorbic acid molecule reacted with the two iodine radicals generated in the first step to yield another dehydroascorbic acid molecule plus two molecules of hydrogen iodide. The route 2 mechanisms seemed more feasible, especially as the two activated complexes $TS_{B1}$ and $TS_{B2}$ were true transition states. They both occupied saddle points along the energy profile of the reactions. The transition states were also confirmed by animating the vibration corresponding to the reaction coordinate by selecting the imaginary frequency at the top of the list of frequencies on the IR tab. The route 2 mechanism is also given scheme 3.




**Scheme 2:** The two steps reaction mechanism

**3.5. Enthalpy of Reaction and Rate constant calculations [41, 42].** The enthalpies of reaction were calculated by using the Spartan software package to calculate heats of formation at standard temperature of 298.15K and pressure of 1 atmosphere. The calculations were done by taking the appropriate sums and differences as given in equation (4).

$$\Delta_r H^o\left(298.15K\right) = \sum_{products} \Delta_f H^o_{prod}\left(298.15K\right) - \sum_{reactants} \Delta_f H^o_{react}\left(298.15K\right) \qquad (4)$$

The computed enthalpies of reaction at standard conditions were 190.78kJ/mol and 381.56kJ/mol for Scheme 2 and Scheme 3 respectively. Other activation parameters of the reaction at standard conditions, $\Delta G^o$ and $\Delta S^o$ were calculated by the Spartan software package by default and were as provided in table1. The activation barrier for the one step reaction (Scheme 2) was calculated as 411.53kJ/mol.; while that of the two steps mechanism (Scheme 3) was calculated as 423.05kJ/mol and 341.61kJ/mol for each of the respective steps. Evidently step 1 is the rate determining step for Scheme 3. In comparing activation barrier for the rate determining steps of Scheme 2 (411.53kJ/mol) and Scheme 3 (423.05kJ/mol), the difference is only 11.52kJ/mol. This shows that the reaction can follow either of the two routes proposed in this work. The proposed mechanisms also accounted for ions generated in the course of the reactions rather than leaving $H^+$ and $I^-$ in the reaction medium after the reactions were completed as seemed to have been suggested by the earlier workers in Scheme 1 [22, 38, 39]. The rate constant calculations were computed according to equation (5).

$$k(298.15K) = \frac{k_B T}{hc^o} e^{-\ddagger G^o/RT} \qquad (5)$$

Where k(298.15K) = reaction rate at temperature(298.15K); $k_B$ = Boltzmann constant (1.380662 X $10^{-23}$ J/K); T = temperature(298.15K); h = Planck's constant (6.626176 X $10^{-34}$ Js); $C^o$ = concentration (taken to be 1); $\Delta\ddagger G^o$ = Gibbs free energy of activation (kJ/mol); R = gas constant (8.31441 J/mol.K).

The rate constant, $k_1$ for route 1 was calculated to be 1.07 x$10^6$ $sec^{-1}$. For route 2, $K_1$ and $k_2$ were calculated as 4.80 x $10^{-4}$ $sec^{-1}$ and 2.51 x $10^{131}$ $^1dm^3mol^{-1}sec^{-1}$ respectively

## 4 . CONCLUSIONS

The mechanism of the reaction of ascorbic acid with Iodine was studied using computational semi empirical PM3 method. The results of this study were compared with previously published work on the reaction of ascorbic acid with Iodine. This work proposed two different pathways for the reaction. This work was also able to demonstrate that the reaction con follow either two routes proposed because the activation energies for the rate determining steps in both pathways were comparable. Compared to the previous studies carried out on the same reaction, this study also accounted all ions generated in the course of the reactions.

## 5. REFERENCES

[1] Rahman M. M., Rahman Khan M. M. and Hosain M. M., Analysis of Vitamin C (ascorbic acid) Contents in Various Fruits and Vegetables by UV-spectrophotometry, *Bangladesh Journal of Scientific and Industrial Research*, 42, 4, 417-424, **2007**.

[2] Kennedy J. F., White C. A., Warner F.P., Lloyd L.L and Rivera .Z.S., The identification and analysis of the oxidation products of L-ascorbic acid by HPLC, *Journal of Micronutrient Analysis*, 5, 91-109, **1989**.

[3] Rahman Khan M.M., Rahman M.M., Islam M.S., Begum S.A., A simple UV-spectrophotometric method for the determination of vitamin C content in various fruits and vegetables at Sylhet area in Bangladesh. *Journal of Biological Sciences*, 6, 388-392, **2006**.

[4] Dioha I. J., Olugbemi O., Onuegbu T. U. and Shahru Z. Determination of ascorbic acid content of some tropical fruits by iodometric titration. *International Journal of Biological and Chemical Sciences*, 5, 5, 2180-2184, **2011**.

[5] Okiei W, Ogunlesi M, Azeez L, Obakachi V, Osunsanmi M, Nkenchor G. The voltammetric and titrimetric determination of ascorbic acid levels in tropical fruit samples. *International Journal of Electrochemical Science*, 4, 276-287, **2008**.

[6] Kapur A., Hasković A., Čopra-Janićijević A., Klepo L, Topčagić A., Tahirović I., Sofić E. Spectrophotometric analysis of total ascorbic acid content in various fruits and vegetables, *Bulletin of the Chemists and Technologists of Bosnia and Herzegovina*, 38, 39-42, **2012**.

[7] Eitenmiller R. R., Ye L., Landen W. O. *Vitamin analysis for the health and food sciences*, CRC Press, Taylor & Francis Group, UK., **2008**.
[8] Kuninori T. and Nishiyama J., Recent advances in dough improvement with ascorbic acid and its derivatives, *Cereal Foods World*. 38, 554, **1993**.
[9] Ryley J. and Kajda P. Vitamins in thermal processing, *Food Chemistry*, 49, 2, 119-129, **1994**.
[10] Cheema S.K and Pant M. R., Estimation Of Vitamin C In Seven Cultivated Varieties Of Capsicum Annuum L, *International Journal of Pharmaceutical Sciences* , 3, 2, 1397-1401, **2011**.
[11] Khan M. N,, Sarwar A., The Influence of Transition Metal Ions on the Kinetics of Ascorbic Acid Oxidation by Methylene Blue in Strongly Acidic Media, Turkish Journal of Chemistry, 25, 433 - 440, **2001**.
[12] Matei N., Birghila S., Popescu V., Dobrinas S., Soceanu A., Oprea C., Magearu, V., Kinetic Study Of Vitamin C Degradation From Pharmaceutical Products, Rom. Journ. Phys., 53, 1– 2, 343–351, **2008**.
[13] Linda Lloyd Agilent Technologies, Inc. www.agilent.com/chem © Agilent Technologies, **2011**.
[14] Rajanna K. C., Reddy K. N., Umesh Kumar U., Sai Prakash P. K., A kinetic study of electron transfer from L-Ascorbic acid to sodium perborate and potassium peroxy disulphate in aqueous acid and micellar media, International Journal of Chemical Kinetics. 28, 153-164 **1996**.
[15] Pal T., Jana N. R., Das P. K ., Kinetics Of Reduction of Silver(I) Gelatin Complex in Aqueous Alkaline Solution, Indian journal of chemistry. Sect. A: Inorganic, physical, theoretical & analytical, 33, 8, 760-762, **1994**.
[16] Per olav K. and Pedersen B., Oxidation of L-Ascorbic Acid with Hydrogen Peroxide inAqueous Solution, *Acta Chemica Scandinavica*. 48, 646-51, **1994**.
[17] Kagayama N., Sekiguchi M., Inada Y., Takagi H D., Fanahashi S., Mechanistic Study of the Reaction of L-Ascorbic Acid with Hexacyanometalate(III) Ions of Iron(III), Ruthenium(III), and Osmium(III) in Aqueous Acidic Solution at Elevated Pressures, *Inorganic Chemistry*, 33, 9, 1881–1885, **1994**.
[18] José M. Leal, Pedro L. Domingo, Begoña Garcia and Saturnino Ibeas . Alkali-metal ion catalysis of the oxidation of L-ascorbic acid by hexacyanoferrate(III) in strongly acidic media, *Journal of the Chemical Society, Faraday Transactions***,** 89, 3571-3577, **1993**.
[19] Martinez P., Zuluaga J. Noheda P. and Van Eldik. R., Kinetics of the oxidation of L-ascorbic acid by diaquatetraamminecobalt(III) in acidic aqueous solution. Application of the Fuoss model and the Marcus Sutin cross-relationship for electron-transfer processes, *Inorganica Chimica Acta* , 195, 2, 249–253, **1992**.
[20] Verma, K. K., Jain, A., Sahasrabuddhey, B., Gupta, K., Mishra, S. Solid-phase extraction clean-up for determining ascorbic acid and dehydroascorbic acid by titration with 2,6-dichlorophenolindophenol. *Journal of AOAC International*, 79, 1236, **1996**.
[21] Rao T. S., Kale N. R., Dalvi S. P., React. Kinetics and mechanism of the oxidation of L-ascorbic acid by 2,6-dichlorophenol-indophenol in aqueous solution, *Reaction Kinetics, Mechanisms and Catalysis*. 34, 1, 179-84, **1987**.
[22] Sitti Rahmawati and Bunbun Bundjali, Prosiding Seminar Kimia Bersama UKM-ITB VIII 9-11 Jun **2009.**
[23] Khan M. N And Sarwar A., The Influence of Transition Metal Ions on the Kinetics of Ascorbic Acid Oxidation by Methylene Blue inStrongly Acidic Media Turkish Journal of Chemistry, 25, 433-440, **2001**.
[24] Cao Xue Y. I,, Jiang Kareem A., Dou Z.H., Rakeman M.A, Zhan M.L and Dulong. G.R Iodination of irrigation waters as a method of supplying iodine to a severely Iodine deficient population in Xinjing, China, *The Lancet*. 344, 107-109, **1994**.
[25] Young, D. C., *Semi empirical Methods in Computational Chemistry: A Practical Guide for Applying Techniques to Real World Problems*, John Wiley & Sons, Inc., New York, USA, **2002**.
[26] Kahn K. and Bruice T. C., Transition state and ground state structures and their interaction with the active site residues in catechol O–methyltransferase, *Journal of the American Chemical Society*, 12, 1, 46 – 51, **2000**.
[27] Kahn K. and Tipton P. A., Kinetics and mechanism of allantoin racemization, *Bioorganic Chemistry*, 28, 2, 62 – 72, **2000**.
[28] Kahn K., Theoretical study of intermediates in the urate oxidase reaction. *Bioorganic Chemistry*, 27, 5, 351 – 362, **1999**.
[29 Stewart J. J. P., Optimization of parameters for semi empirical methods. V. Modification of NDDO approximations and application to 70 elements, *Journal of Molecular Modeling***,** 13, 1173-213, **2007**.
[30] Shaffer A. A. and Wierschke S. G., Comparison of computational methods applied to oxazole, thiazole, and other heterocyclic compounds, *Journal of Computational Chemistry*, 14, 1, 75-88, **1993**.
[31] Ayub K. and Mahmood T., DFT Studies of Halogen Bonding Abilities of Nitrobenzene with Halogens and Chlorofluorocarbons", *Journal of Chemical Society of Pakistan*, 35, 3, 617- 821, **2013**.

[32] Zhang J. and Hase W. L., Electronic Structure Theory Study of the $F^-+CH_3I \rightarrow FCH_3 + I$ Potential Energy Surface, Journal of Physical Chemistry. Section A, 114, 9635–9643, **2010**.
[33] Jensen F., Introduction to Computational Chemistry, J. Wiley & Sons, Chichester, p.171,**1999**.
[34] Stewart J. J. P., Optimization of Parameters for Semi-Empirical Methods I-Method, *Journal of Computational Chemistry*, I0, 2, 209-220, **1989**.
[35] Stewart J. J. P., Optimization of Parameters for Semi-Empirical Methods II-Applications" *Journal of Computational Chemistry*, I0, 2, 221- 264. **1989**.
[36] Schlegel H.B., Potential energy curves using unrestricted Møller–Plesset perturbation theory with spin annihilation, *Journal of Chemical Physics*, 84, 4530–4534, **1986**.
[37] Kalkanis G. H. and Shields G.C., AMI and PM3 Calculations of the Potential Energy Surfaces for $CH_20H$ Reactions with NO and $NO_2$, *The Journal of Physical Chemistry*, 95, 13, 5085-5089, **1991**.
[38] University of Canterbury, Determination of Vitamin C Concentration by Titration, www.outreach.canterbury.ac.nz, **2014.**
[39] Morelli B., A kinetic experiment using a spring powered, stopped-flow apparatus, *Journal of Chemical Education*, 53(2), 119-122, **1976**.
[40] Ya-Yin Fang, Rong-Xin Shen, Hong-Wei Sun, Man-Xue Yuan, Jie Liu, Zheng-Ming Li, ChengMing Lai,Mechanism analysis of catalytic hydrogenation of 3-anilinomethylidene-6-alkyl-5,6-2H dihydropyran-2,4-diones, *Journal of Molecular Structure (Theochemmistry),* 578, 71-78, **2002**.
[41] Ochterski J. W., *Thermochemistry in Gaussian, Technical Support Information*, gaussian.com, 1-19, **2000**.
[42] Thomas Engel and Philip Reid, *Physical Chemistry*, Pearson Prentice Hall, Upper saddle River, NJ, 924, **2006**.