Computational Study of Oxidation Potential Fluctuation of Ketone Molecule

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Abstract. *This study focus on investigating the oxidation potential fluctuation of organic molecule in the solution. The organic molecule that was investigated is 3-pentanone molecule that has oxidation potential 0.143 V experimentally. The oxidation potential was calculated using Born-Haber cycle approximation involving the calculation of gas phase Gibbs free energy and solvation energy of reduced and the oxidized state. The reduced state represents a neutral charge molecule and the oxidized state represents a radical cation molecule. The first, molecular dynamics (MD) simulation of both state was performed for 2 ns time. Then, 400 snapshot structures of both state molecule was captured. Gas phase Gibbs free energy and solvation energy were calculated using MP2 theory with cc-pvdz basis set and the solvation effect was approached using Polarizable Continuum Model (PCM). Normal Hydrogen Electrode (NHE), that has redox potential 4.44 V experimentally, was used as reference electrode. The result shows the different of gas phase Gibbs free energy average of both state was 756.97 ± 21.598 kJ/mol, and solvation energy average of reduced and oxidized state were -18.42 kJ/mol ± 1.482 kJ/mol, and -219.02 ± 1.094 kJ/mol respectively. Then, the oxidation potential was calculated by substituting gas phase Gibbs free energy and solvation energy into Born-Haber cycle approximation. The calculation result shows the average of oxidation potential value is 1.396 ± 0.225 V. The deviation of oxidation potential confirms the fluctuation of oxidation potential during the simulation.*

Keywords: oxidation potential, structural fluctuation, ketone, Gibbs free energy, solvation energy.

1 Introduction

The feasibility of atom or molecule in solution to donate electron is measured by oxidation potential. This property is fundamental in understanding chemical and biological electron transfer reactions [1][2]. It is also important to determine the chemical reactivity of chemical compound [2]. This property is used to estimate the toxicity of biological compound or drug efficacy [3]. By considering some importance of oxidation potential, it is necessary to improve the knowledge about this property. One of promising tools that can be facilitated in investigating oxidation potential is computational method. This method becomes powerful tool since its ability to cover some cases that difficult to perform experimentally, such as investigate the property of radical molecule.

One of the challenges in oxidation potential study is predicting redox potential of some organic molecules in solution. It will be helpful as preparation steps before performing the real experiment. So, this study will investigate the suitable method to calculate oxidation potential of organic molecule in the solution.

In this study, we use 3-pentanone molecule as investigated molecule which the structure is shown in Figure 1. This molecule is classified as ketone group molecule and has oxidation potential 0.143 V experimentally [4]. Ketone functional group molecule was chosen because some biological system
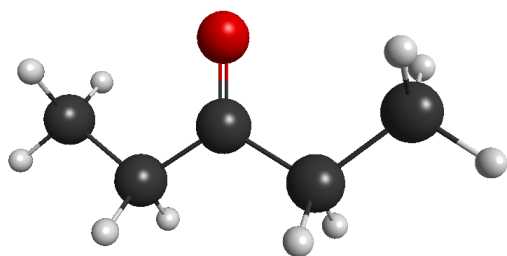
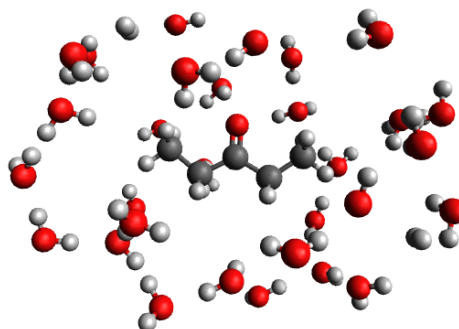Figure 1: Structure of 3-pentanone.

Figure 2: Ketone molecule surrounded by water molecule.

contains this functional group and it can be oxidized by reacting it with strong oxidizing agent, such as peroxide group, in certain condition [5].

Another thing that is considered in this study is the interaction between solute and solvent. Naturally, some of organic molecule exist in solution system, and one of favour solvent is water. So, in this study we considered the interaction between ketone molecule as solute and surrounded water molecule as solvent as illustrated in Figure 2. The interaction will impact to change of molecular conformation of solute molecule [6]. Oxidation potential can be fluctuated correspond to change of molecular conformation. The fluctuation can be explained using deviation value of oxidation potential.

2   Method

2.1   Calculation Method

Most of recent computational works in oxidation potential calculation of organic molecule use Born-Haber cycle approximation [3][7][8]. The Born-Haber cycle of oxidation reaction is shown in Figure 3. The oxidation potential of molecule can be calculated using the relation of oxidation potential and Gibbs free energy as follows [11]

$$E_{\mathrm{ox}} = -\frac{\Delta G_{\mathrm{ox}}}{nF}$$

and the free energy difference of oxidation reaction ΔG_{ox} was calculated using Born-Haber cycle approximation.

According to Born-Haber cycle, free energy of oxidation reaction ΔG_{ox} can be expressed as

$$\Delta G_{\mathrm{ox}}(aq) = -\Delta G_{\mathrm{solv}}(\mathrm{red}) + \Delta G_{\mathrm{ox}}(g) + \Delta G_{\mathrm{solv}}(\mathrm{ox})$$

where $\Delta G_{\mathrm{ox}}(aq)$ and $\Delta G_{\mathrm{ox}}(g)$ are free energy difference of oxidation reaction in aqueous and gas phase respectively, $\Delta G_{\mathrm{solv}}(\mathrm{red})$ and $\Delta G_{\mathrm{solv}}(\mathrm{ox})$ are solvation free energy in reduced and oxidize state respectively. The reduced state represents the neutral charge molecule and oxidized state represents the radical cation molecule.
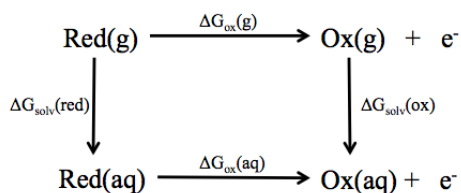
Figure 3: The Born-Haber cycle of oxidation reaction.

2.2 Computational Details

2.2.1 Molecular Dynamics Simulation

Molecular dynamics simulation was performed for both reduced and oxidized state. The basic different parameter of those state is shown in Table 1. Reduced state of molecule has neutral charge with multiplicity 1 and its parameter was easy to generate using Antechamber package[10]. Oxidized state of molecule has negative charge and multiplicity 2. Double multiplicity denoted this molecule is radical and can not be parametrized using Antechamber directly. Firstly, electrostatic potential of molecule should be calculated using Gaussian program [9]. Then, electrostatic potential was used in Antechamber package to generate the parameter.

The molecular dynamics simulation performed using sander package of Amber program [10]. The simulation was performed using NPT ensemble with constant temperature on 300 K and constant pressure on 1 bar which Langevin dynamics was used to control the temperature. The number of MD step is 1,000,000 steps with delta time 0.002 ps and totally the simulation was performed for 2,000 ps or 2 ns.

2.2.2 Oxidation Potential Calculation

After the MD simulation has been finished, 400 snapshot structures of each simulation was captured by running the simulation in VMD program [12]. Totally, there are 800 snapshot structures that should be calculated involving 400 snapshot structures of oxidized state and 400 snapshot structures of reduced state. The Born-Haber cycle approximation was used in calculating oxidation potential. The gas phase Gibbs free energy and solvation energy were calculated using Gaussian program [9]. The calculation was performed using Møller-Plesset second order correction (MP2) theory with cc-pvdz basis set.

The gas phase Gibbs free energy was calculated using frequency calculation in Gaussian program

Table 1: Parameter of Solute Molecule.

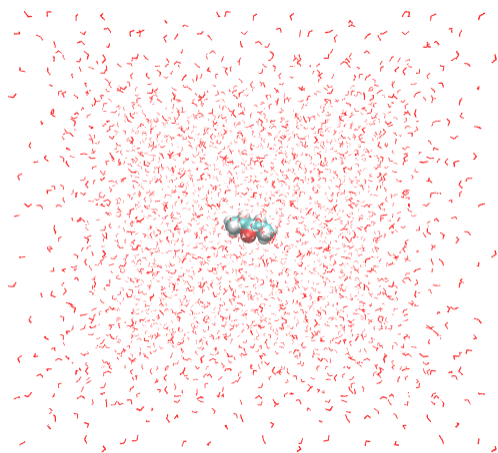| Reduced state	Oxidized state
Charge = 0	Charge = +1
Multiplicity = 1	Multiplicity = 2
Parameterized using antechamber package (Amber) [10]	Parameterized using Gaussian package [9] and antechamber package (Amber) [10]
Added ion = 0	Added ion = 1 Cl^-

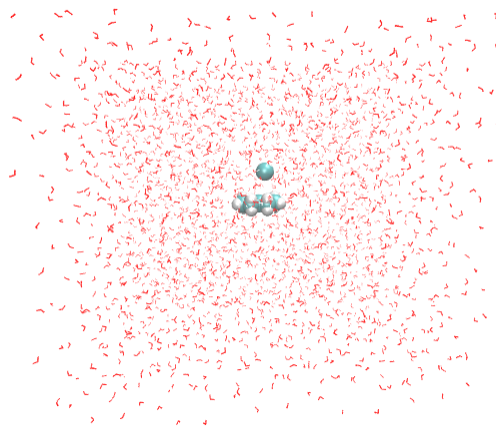Figure 4: The initial solution system of reduced state.

Figure 5: The initial solution system of oxidized state.

[9]. Then, the different of Gibbs free energy of oxidation reaction ($\Delta G_{ox}(g)$) was calculated by subtracting the Gibbs free energy of oxidized state to reduced state; $\Delta G_{ox}(g) = G_{ox}(g) - G_{red}(g)$. The solvation energy was determined by the effect of solvent to the solute. The implicit solvent was used to accelerate the calculation which the solvent effect was approached using Polarizable Continuum Model (PCM). The solvation energy is different of the energy of solvated molecule and gas phase Gibbs free energy; $\Delta G_{solv} = G(aq) - G(g)$. Water was used as implicit solvent which has dielectric constant 1.

3   Results and Discussion

3.1   Molecular Dynamics Simulation

The initial solution system of reduced and oxidized state are shown in Figure 4 and 5 consecutively. Then, some properties are monitored to investigate that the simulation has been performed in desire condition. Those properties are energy, root mean square displacement (RMSD), temperature, and pressure.

3.1.1   Energy

Energy terms that are monitored consist of total energy, kinetic energy, and potential energy. The fluctuation of all energy terms that is shown by Figure 6 and 7 denotes that the trend of energy fluctuation of both system is similar. The first part of diagram shows the fluctuation that represent the equilibration process. The rest part of diagram is consistent and the fluctuation is not significant. This indicates that both of system has been reached equilibrium state according the energy aspect.
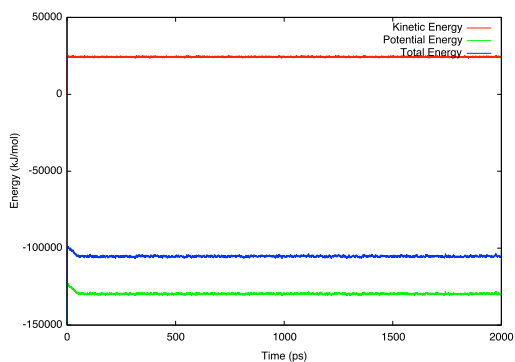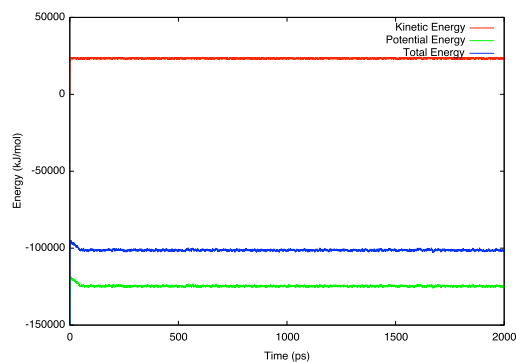
Figure 6: Energy profile of reduced state system.

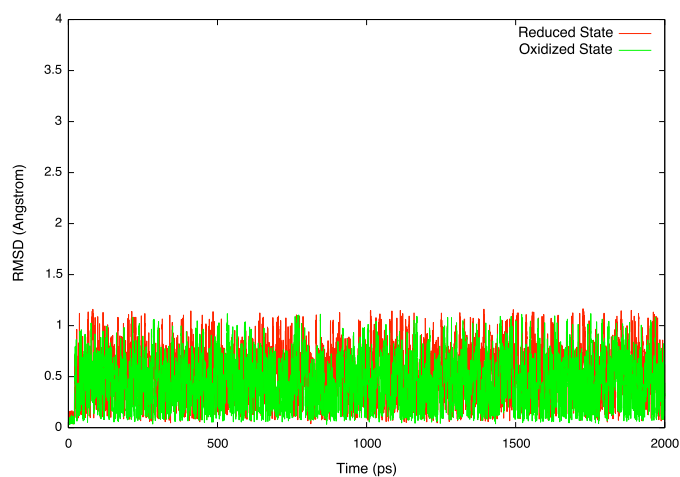

Figure 7: Energy profile of oxidized state system.

Figure 8: The plot of RMSD vs time

3.1.2   RMSD

The second investigated property is root mean square displacement (RMSD). This property is the average of atom fluctuation in solute molecule during the simulation. The RMSD of both systems that is shown in Figure 8 denotes that the RMSD profile of both systems is similar. The maximum RMSD is about 1 angstrom and constant until the simulation finished. The small RMSD change indicates that the conformation fluctuation is not significant and indicates that the molecule has been reached equilibrium.

3.2   Oxidation Potential

The gas phase Gibbs free energy were was provided by showing the plot of internal structure of Gibbs free energy over time as shown in Figure 9. Generally the gas phase Gibbs free energy of reduced state is lower than oxidized state, this is related to the stability of the molecule. The reduced state molecule as neutral charge molecule is more stable then the oxidized state is radical which 1 unpaired electron. The average of gas phase Gibbs free energy different of both state is 756.971 ± 21.598 kJ/mol.

The solvation energy data were provided by showing the plot of internal structure of solvation energy over time as shown in Figure 10. The figure shows the fluctuation trend of both reduced and oxidation state is similar. Generally the solvation energy of oxidized state is lower than reduced state. This is caused by the positive charge of oxidized state that make good interaction with solvent and will solve easier. The result shows the solvation energy average of reduced state is -18.420 ± 1.482 kJ/mol and oxidation state is -219.015 ± 1.094 kJ/mol.

Substituting the calculation result of gas phase Gibbs free energy and solvation energy into Born-Haber cycle approximation results the oxidation potential value. The average of calculated oxidation potential is 1.396 ± 0.225 V. The deviation confirms the fluctuation of oxidation potential during the simulation. This fluctuation correspond to interaction solute-solvent in the solution that change molecular conformation of molecule. The conformation give the contribution to electron density of each atom and the propensity of molecule to release an electron.

To determine the calculation accuracy, we compare the calculation result to experimental data. The average of calculated oxidation potential is 1.396 ± 0.225 V and the experimental data is 0.143 V [4]. The comparison of both value indicates a problem of the calculation method. The problem can be investigated by trace the accuracy of each calculation. As the explanation above that the calculation of oxidation potential involving the calculation of gas phase Gibbs free energy and solvation energy. So, the analysis can be done by comparing both of data to the experimental data, unfortunately both of data is not available.

However, the most probable factor that caused this problem is the calculation of solvation energy of oxidized state. As known that the oxidized state has positive charge and radical molecule with 1 unpaired electron. This condition can change the kind of interaction between the solute and solvent. The usual interaction that can be happened between water as solvent and 3-pentanone as solute is van der Waals interaction between positive dipole and negative dipole. The strength
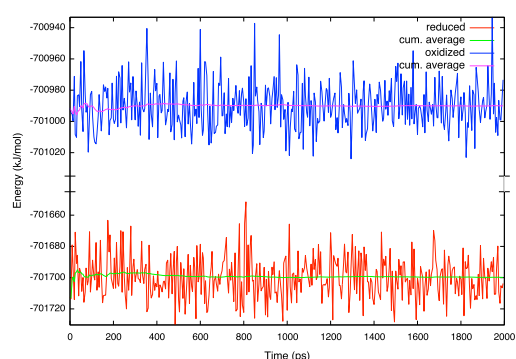

Figure 9: Plot of internal structure of Gas phase Gibbs free energy over time.
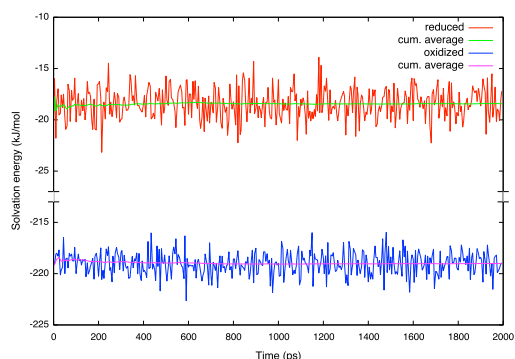
Figure 10: Plot of internal structure of solvation energy over time.

of the interaction involving radical molecule will weaker or stronger than usual. This condition should be treated properly to obtain good accuracy of calculation. This problem should be handle to get better sight about this oxidation potential calculation in the future.

One of the solution to handle this problem is considering another method that can calculate solvation energy more accurate, for example thermodynamic integration method. The calculation of oxidation potential is expected will be more accurate by correcting the accuracy of solvation energy calculation.

4   Conclusion

Oxidation potential of ketone molecule was fluctuated during the simulation that shows by deviation value of oxidation potential. The fluctuation is important because it confirms that molecular conformation give contribution to electron density of each atom and the propensity of molecule to release an electron. Another point related to used method in calculating the oxidation potential that is important to get good accuracy. The improvement of calculation method is necessary, especially in treating solvation energy of oxidized state.

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