Computational calculation of acetalization of 2-chlorobenzaldehyde reaction mechanism using hydrochloric acid catalyst with *ab initio* method

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Abstract

The aim of this research was to investigate the possible reaction mechanism steps in the formation of acetal from 2-chlorobenzaldehyde substrate. Asetal is a chemical compound that attracts the attention of the researchers because it has advantage in various fields of life. This study was conducted using Hyperchem software (OS Window's) with the ab initio method using a 6-31G* basis set. In this study, the 3-21G basis set was also used as a comparison. The calculations were performed for each steps of the reaction mechanism including the substrate, the formation of hemiacetal intermediate, and the formation of acetal products. Based on the results of computational calculations, the acetalization of 2-chlorobenzaldehyde reaction can occur in the presence of an HCl catalyst. The HCl catalyst serves as an acid catalyst where hydrogen ions will be protonated by the substrate and hemiacetal. Hemiacetal compounds based on calculations have the highest formation energy compared to the benzaldehyde substrate and acetal products. This is because hemiacetal has a low stability and is easily transformed into other compounds.

Keywords: Ab initio; 2-chlorobenzaldehyde; acetal

1. Introduction

The benzaldehyde dimethyl acetal compound is a compound that can be widely used in daily life. The compound has been used as a solvent in the pharmaceutical industry, detergents, varnishes, perfumes, cosmetics, food additives, and beverages (Parangi et al. 2013; Li et al. 2004). Besides that, acetal can also be used as motor oil, lubricant, hydraulic fluid and as an emulsion for petroleum drilling operations. The benzaldehyde dimethyl acetal compound is obtained through an acetalization reaction between an aldehyde compound with alcohol using an acid catalyst as

depicted in Fig 1. Its reaction is a of reversible reaction so that under certain conditions the product can turn into a reactant (Arrozi et al. 2014).

The acetalization reaction of benzaldehyde is a reaction which carried out by reacting benzaldehyde compounds with alcohol, diol or trioxane using acidic catalysts such as hydrochloric acid. In this study, methanol compounds function as solvents in neutral conditions. In addition, methanol is also more readily available than other solvents. Compared with ketones, acetalization is easier between aldehyde and alcohol. The catalysts commonly used in the acetalization reaction are protonic acids, organic metal frame work (MOF) containing thiourea (Luan et al. 2014), N-chlorosuccinimide/thiourea (May et al. 2009), amorphous cesium phosphate (Parangi et al. 2013), copper $[Cu_3(BTC)_2]$ (Dhakshinamoorthy et al. 2010; Jin et al. 2014), and UIO 66 (Arrozi et al. 2014).

The reaction mechanism of the acetalization involves several stages of reaction including the formation of a hemiasetal intermediate and acetal product. Hemiasetal is an unstable intermediate so it easily changes shape into other intermediate compounds such as acetal. The instability is caused by the hemiasetal compounds that have hydroxyl and ether groups on the same carbon atom. The study of hemiasetal formation shows that the three stages of hemiasetal formation are concerted, which are stimulatory reactions that are catalyzed by acids. The mechanism for the reaction of hemiasetal formation from benzaldehyde includes protonation by the catalyst, the addition of methanol and deprotonation. While the formation of acetal from hemiasetal also occurs through the same process including protonation by acid catalysts, the addition of methanol, and the deprotonation process (Yusuf et al. 2017; Yusuf et al. 2017a).

To make it easier for researchers to synthesize acetal, it is necessary to propose the stages of the acetalization reaction mechanism that is most likely by using a computational approach. Through a computational chemistry approach, the chemists can be helped in designing the initial process of synthesis of various types of reactions, determining the properties of a compound, proposing the most possible reaction mechanism, and conducting simulations for research in the field of chemistry. Meanwhile, computational chemistry is a branch of chemistry that uses mathematical calculations in the form of computer programs to determine the characterization of a compound, the energy of various reactions, and the properties of a chemical molecule (Priyanto, 2005).
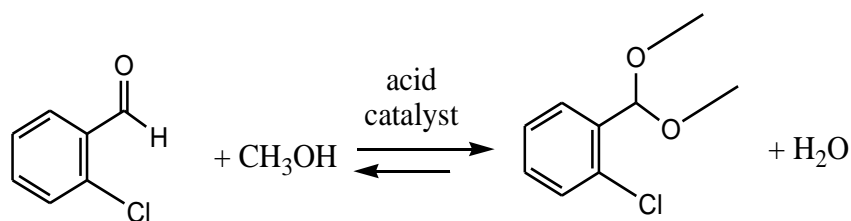

Fig 1. Acetalization reaction of 2-hydroxybenzaldehyde

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One of the chemical computing-based software that can be used to calculate chemical research is Hyperchem. This software can be used to calculate reaction mechanisms and molecular modeling using the Window's operating system. It's features are easier to operate than software using the Linux operating system. Hyperchem has several calculation methods including ab initio where the results are directly obtained from the calculation results without any experimental data. Other calculation methods that can be done are molecular mechanics, semiempiric, and density functional theory (Pranowo, 2000).

Based on the description above, researchers conducted a study of the reaction mechanism of 2-chlorobenzaldehyde acetalization using a hydrochloric acid catalyst with the ab initio method. Previously, our research group had studied the mechanism of acetalization reaction on benzaldehyde, 2-hydroxybenzaldehyde, 2-methoxy benzaldehyde, benzaldehyde, and 3-chlorobenzaldehyde using a hydrochloric acid catalyst (Yusuf et al. 2019; Yusuf et al. 2019a). The results obtained illustrate how the interaction of substrate molecules, methanol and HCl catalysts and the energy changes that occur during the reaction. The difference between previous research and this research lies in the position of the chloride atom used adjacent to the aldehyde group as depicted in Fig 1.

2. Methods

The equipment used in this study is HyperChem version 8.0 with the Windows 7 professional 64-bit operating system. Base sets 3-21G and 6-31G * are used to count all atoms. The algorithm used is the Polak-Ribiere (Conjugate Gradient) with a maximum cycles of 32767 times. HyperChem software version 8.0 and ChemDraw version 8.0 are used to visualize the results of calculations. While the hardware used is a set of computers with Intel (R) core (TM) specifications i3-6100T, 3.20 GHz CPU, 4.00 GB Random Access Memory with System type 64-bit Operating System.

Geometry optimization calculations in this study were carried out through several stages in the Hyperchem and ChemDraw software, namely:
1. Molecular samples are modeled through the default element in the menubar build to bring up the periodic system of elements. Next select the atoms needed to form 2D molecules on the ChemDraw worksheet. Another method that can be used to model molecules is through the toolbar draw.
2. 2D molecular images are converted into 3D molecules and then the molecular energy is calculated using the Ab-Initio method. The basis sets used are small (3-21G) and medium (6-31G *).
3. Geometry optimization is done through the geometry optimization menu. Nominal 32767 is written in the maximum cycles dialog box. The calculation is complete after the status bar says converged = yes and the energy results are recorded in the form of kcal / mol. If it is not converged after all this time, it is necessary to improve the geometry of the molecules so that the space

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barriers become smaller. Geometry improvements are made by considering the distance of atoms, angles and dihedral angles.

4. The results of the geometry optimization calculations are then drawn with the reaction vs. energy coordinate graph (kJ/mol). The energy value used is the difference between the product energy and the substrate energy with the equation:
E.product-E.substrat.

5. The software used to draw graphics is ChemDraw.

3. Results and Discussion

Computational calculations are carried out to obtain optimized energy from each molecule. In this study, computational calculations of the 2-chlorobenzaldehyde acetalization reaction mechanism are proposed as shown in Fig 2. The purpose of the computational calculation is to obtain the most likely proposed reaction mechanism stages (Yusuf et al. 2017; Yusuf, 2017).
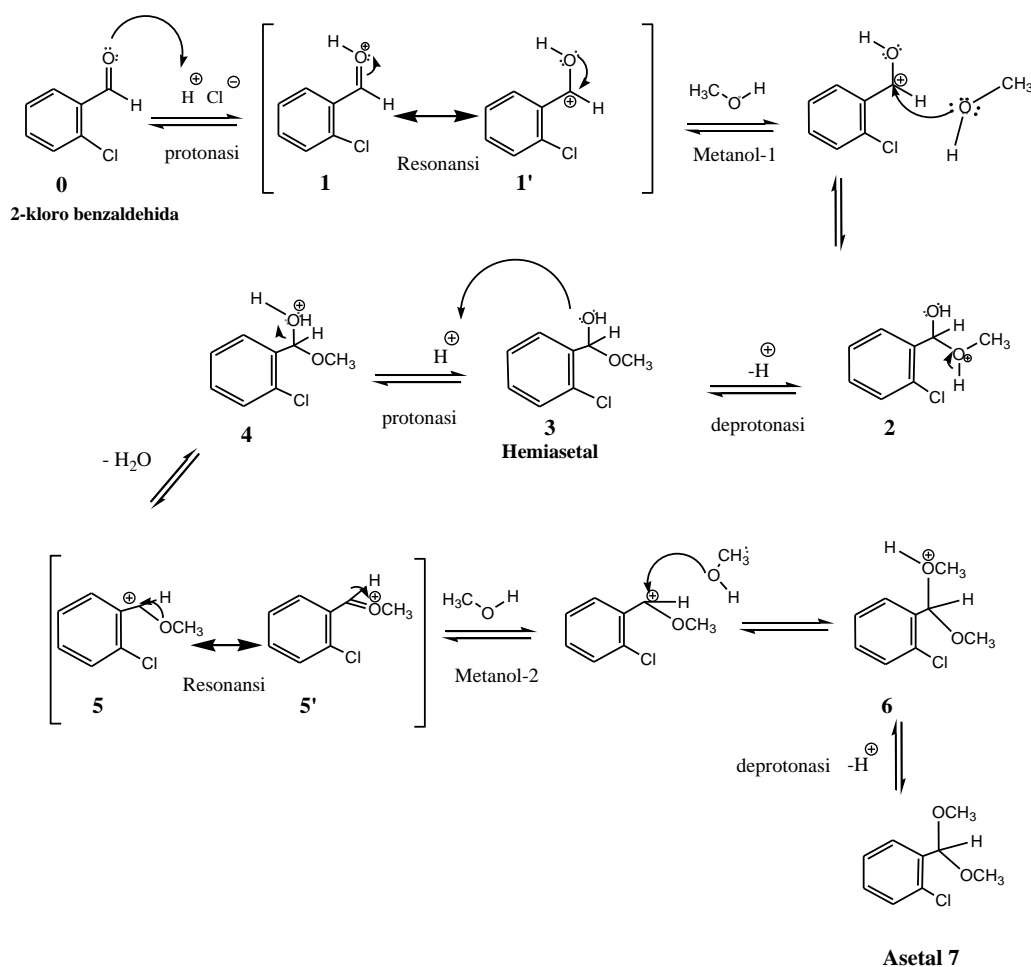

Fig 2. Mechanisms of the 2-chlorobenzaldehyde acetalization reaction to produce acetal

The computational calculation results of the reaction mechanism of the substrate, the intermediate state, and the product are presented in Fig 3. Each molecule has the same number of molecules so that the total energy can be compared. Based on this energy, energy levels are arranged for each stage of the acetalization reaction.
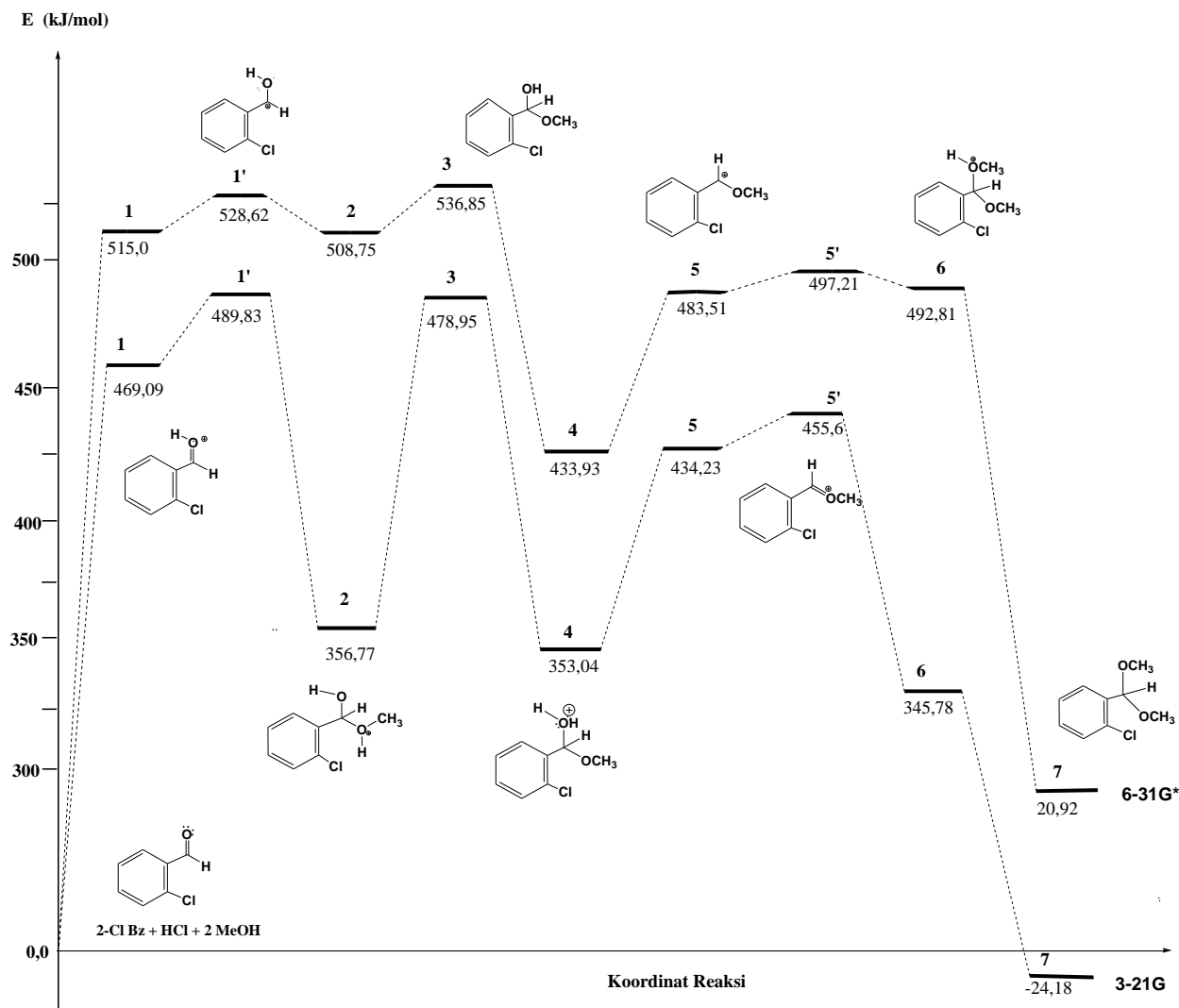

Fig 3. Reaction mechanisms of the 2-chlorobenzaldehyde acetalization

The mechanism of the 2-chlorobenzaldehyde acetalization reaction takes place through several stages of the process as shown in Fig 2 and Fig 3. The calculations used in this study use a 6-31G * basis sets. Meanwhile, calculations using the basis sets 3-21G are only used as a comparison.

The first stage of the reaction mechanism is the protonation of the 2-chlorobenzaldehyde (0) compound by a hydrochloric acid catalyst (H + ion) to produce compound 1 which is positively charged 1. Oxygen atoms have a more electronegative charge than carbon so that compound 1 experiences structural resonance (1 '). The resonance structure 1 ' reacts with the first methanol to produce

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an intermediate state (2). In the intermediate 2, methanol compound bonded with 2-chlorobenzene. The intermediate 2 then undergoes deprotonation to form hemiasetal 3 which is unstable and has a high formation energy.
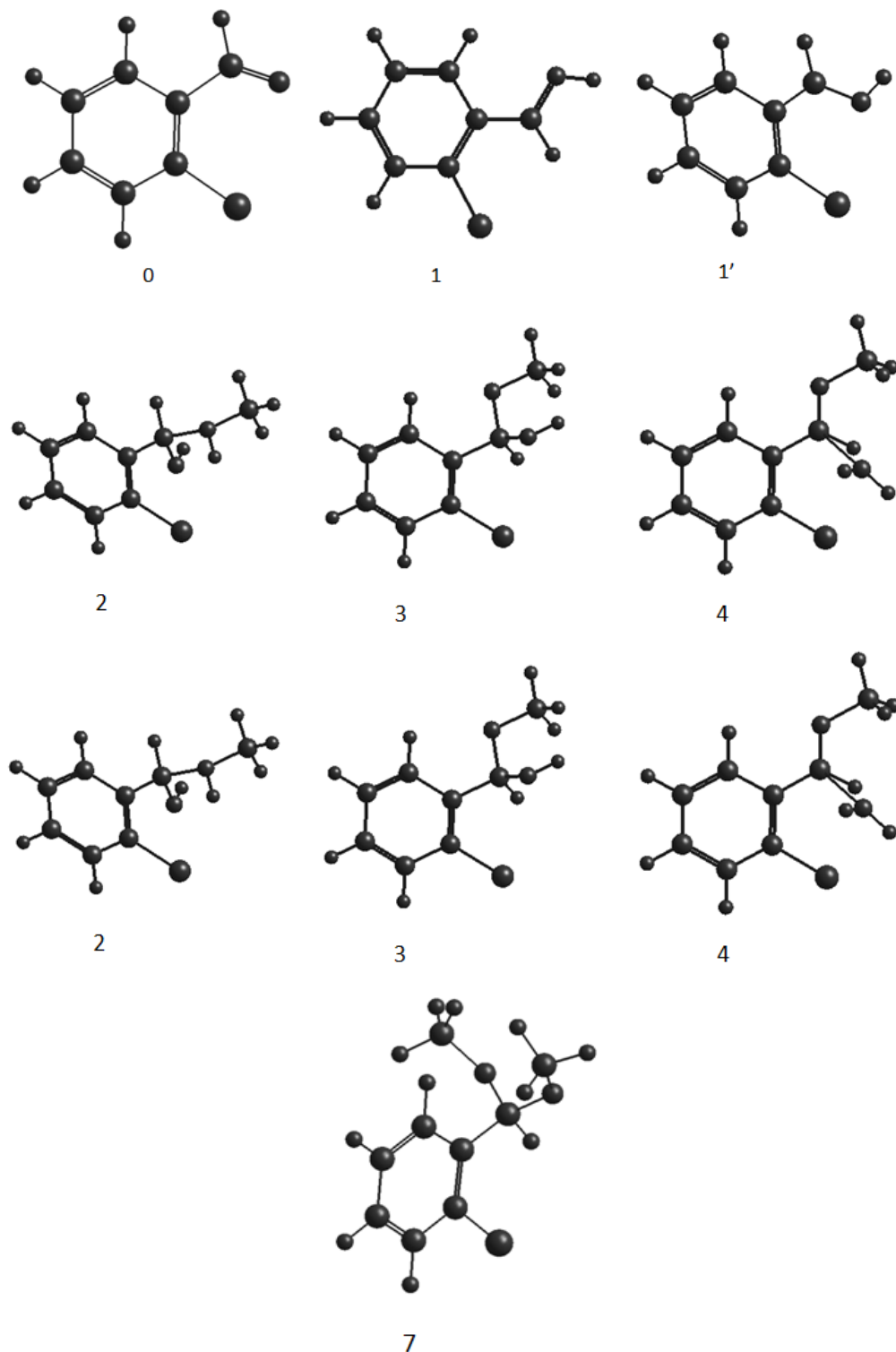

Fig 4. Structure of the results of molecular optimization during the stages of the acetalization reaction

The next step is the reaction of protonation by the hydrochloric acid catalyst in compound 3 so that the -OH group turns into a water group. The hydroxy group in compound 3 is a bad leaving group so it needs to attack the H+ ion from HCl to become an H_2O group (intermediate state 4). Water groups are good leaving groups due to instability of oxygen atoms which have 3 coordination with 2 hydrogen atoms and 1 carbon atom. The intermediate compound 4 produced is undergoes dehydrated to produce compound 5. The dehydration process is easy because the water molecule is a good leaving group. Compound 5 then undergoes structural resonance resulting in compound 5'. Resonance occurs because oxygen atoms are more electronegative than carbon. Furthermore, the reaction with the second methanol occurs with compound 5 'resulting in the compound 6. In the compound 6, the methanol bonded with 2-chlorobenzene so that compound 6 has two methoxy groups and one oxygen atom that has 3 unstable coordination. The hydrogen atom attached to the oxygen atom in compound 6 undergoes deprotonation as a result of the instability of the oxygen atom. This deprotonation process produces acetal products 7.

In overall, energy formation of hemiasetal (3) is higher than the substrate and product compounds that is 536.85 kJ/mol. Meanwhile, the substrate has a formation energy of 0 kJ/mol and a product of 20.92 kJ/mol. At the hemiasetal formation (3), it was found that the formation energy of compounds 1, 1 'and 2 was almost similar, in the range of 508.75 kj/mol to 528.62 kJ/mol. This is because these molecules have a similar molecular stability. While in the formation of acetal products (7) from hemiasetal (3), compounds 5, 5 ', and 6 also have almost the same energy in the range of 483.51 kj/mol to 497.21 kJ/mol. Whereas the intermediate compound 4 has a much lower formation energy compared to the other intermediate compounds due to its molecule having better stability which is equal to 433.93 kJ/mol. The structure of the results of molecular optimization during the stages of the acetalization reaction is shown in Fig 4.

4. Conclusion

Based on the results of computational calculations, it is obtained that, in general, the reaction mechanism of 2-chlorobenzaldehyde acetalization takes place through two stages, namely the formation of hemiasetal and product formation. Hemiasetal is formed from a substrate which is a replacement of a carbonyl group into a hydroxyl group and an ether on the same carbon atom. While the formation of acetal products from hemiasetal is the replacement of hydroxyl groups into ether groups on the same carbon atom. Based on the computational calculation, it is obtained that the hemiasetal compound is an unstable compound with an energy of 536.85 kJ / mol compared to the acetal product (20.92 kJ / mol) and 2-chlorobenzaldehyde substrate (0 kJ / mol).

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Acknowledgment

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