

# Theoretical Study on the Reaction Mechanism of Acetalization of 3-Chlorobenzaldehyde Catalyzed by Halogen Acid

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**Abstract.** The reaction mechanism of the acetalization of 3-chlorobenzaldehyde have been studied by ab initio method. 3-Chlorobenzaldehyde is an organic compound that contains aromatic aldehyde group. The double bond and the carbon chain at the benzaldehyde compound can allow it to occur the acetalization reaction. This study focused to examine the acetalization of 3-chlorobenzaldehyde catalyzed by Lewis acid catalysts (HCl) through computational calculation with basis set 6-31 G\* within Hyperchem 8.0.3 program (Windows version). Based on the computational calculation showed that there are seven intermediate compounds and two resonance structure to produce acetal product. It is also known that the formation energy of the hemiacetal structure higher compared to all structure due to its lability. Whereas, the acetal product as the final product has the lower formation energy among the other structure due to its stability.

**Keywords:** ab initio method, acetalization, 3-Chlorobenzaldehyde, Lewis acid.

## 1 Introduction

Acetalization of 3-chlorobenzaldehyde is carried out between 3-chlorobenzaldehyde and an alcohol wherein acid is used as the catalyst as shown in Scheme 1. Currently, some acid catalysts have been successfully in the acetal formation include HCl, HBr, H<sub>4</sub>[SiW<sub>12</sub>O<sub>40</sub>]/SiO<sub>2</sub> [1], Mesoporous metal-organic framework MIL-100(Fe) [2], metal copper, iron, zeolite beta [3], and benzimidazoliumcation [4]. The utilization of acid catalysts such as benzimidazolium-organic frameworks (MOFs) based on the UiO-66(Zr) structure [5], aluminium and thiourea containing MOF [6][7], MOF MIL-101 bearing sulfonic acid groups [8], MCM-41 [9], indium triflate [10] and NCS/thiourea [11], cation catalyst, Cu<sub>3</sub>(BTC)<sub>2</sub>, and UIO 66 catalyst in the acetalization of benzaldehyde showed a good catalytic activity (>88%) [4][6][12]. Acetal is known to be useful as fragrances in cosmetics, food and beverage additives, pharmaceuticals, solvents, detergents, drug design, carbohydrate chemistry, intermediates or final products in petrochemicals, and in lacquer industries [13].

The acetals formation is the reversible reaction wherein the first step is the formation of a hemiacetal (hemi = half; hemiacetal = half acetal). Hemiacetal occurs through the protonation of benzaldehyde by an acid catalyst followed by nucleophilic attack of methanol. The last process was deprotonation to form a hemiacetal. The second step is the acetals formation from hemiacetals that only occur if catalyzed by acid followed by loss of water. The next steps were the nucleophilic attack of the second methanol. This step is analog with the S<sub>N</sub>1 reaction

mechanism that is carbocation formation and the nucleophilic attack. And the last process was deprotonation to form acetal product [14][15][16][17].

The reaction mechanism of acetal formation is interesting to learn because the formation energy of each step of the mechanism can be known. In addition, this study can also provide information about the steps of the SN1 reaction mechanism. The Mulliken charge of the atoms in each molecule is also calculated to determine the electronegativity of the atom.

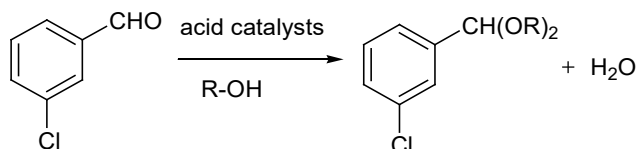


Fig. 1. Acetalization of 3-chlorobenzaldehyde using acid catalysts [14][15][16][17].

## 2 Experimental

Every model of the compound is created 2D structure with a software package Hyperchem version 8.0. The process continues with the geometry structure optimization to obtain stable structural conformation and also the minimization energy of the structure using the ab initio method. Convergence limit determined 0.1 kcal / (Å.mol) or about 32767 maximum cycles so that reaches gradient limit as close as possible.

The optimization method carried out based on the Polak-Ribiere method. The result of calculations includes energy data, electronic compounds structure, and Mulliken charge recorded on the log menu [18].

## 3 Result And Discussion

Based on the computational calculation, we have suggested seven intermediate structure and two resonance structure to produce acetal product. The energy level diagram as presented in Figure 1 is a different molecule, however, it has the same number of molecules so that can be compared. The most stable structure is stated with the lowest energy. To determine the most stable molecule structure is characterized by the lowest energy level.

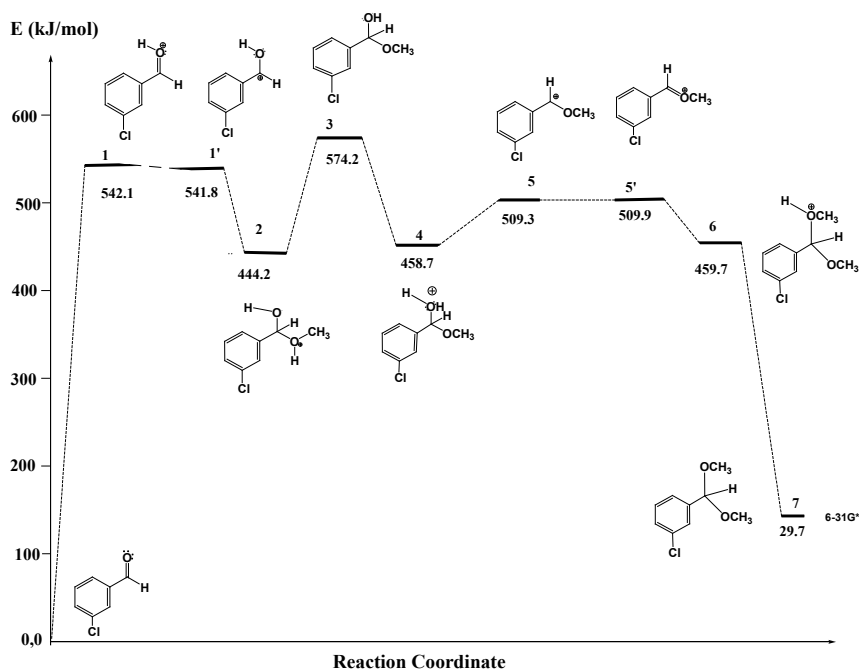


Fig. 1. Plausible reaction mechanism of acetalization of 3-chlorobenzaldehyde.

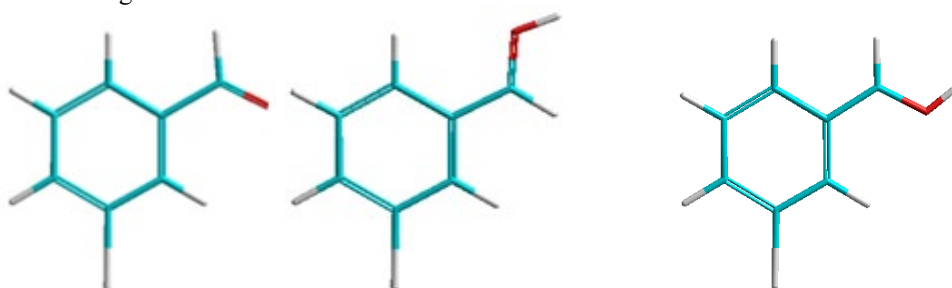
The formation of hemiacetal and acetal are the two main steps to produce 3-chlorobenzaldehyde dimethyl acetal. The first step to produce hemiacetal as shown in Figure 1 begins with carbonyl protonation on the benzaldehyde compounds by Brønsted acid site ( $H^+$  ion from acid catalyst) due to the presence of weak nucleophiles in the group (1). Because of the electronegativity of the oxygen atom, compound 1 also has another resonance structure (1'). The difference in bond energy and length is clearly seen in this protonation step where the substrate energy is 0 kJ/mol while the energy of the compounds (1) and (1') is almost similar (542.1 kJ/mol and 541.8 kJ/mol).

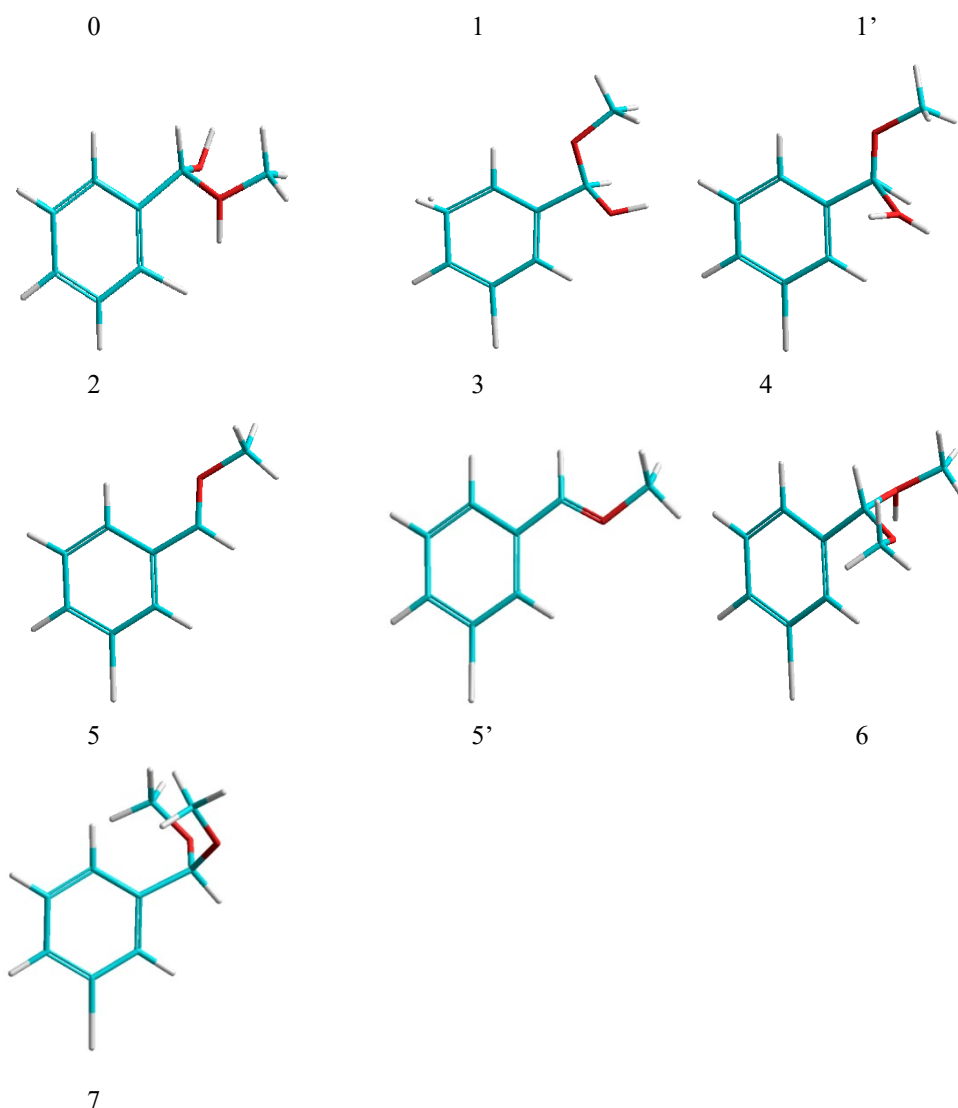
The formation of the second intermediates structure (2) occurs through the reaction of the resonance structure(1 or 1') with a first methanol. The formation energy decreased from 541 kJ/mol to 444.2 kJ/mol. It's mean compound 2 more stable than compound 1 and also compound 1'. The next step is the formation of the hemiacetal (3) through the process of losing protons from compound 2 (oxonium ion). The formation energy increased from 444.2 kJ/mol to 574.2 kJ/mol. Hemiacetal intermediate structure is the most unstable molecule during the reaction occur from the substrate until hemiacetal based on the formation energy (574.2 kJ/mol). Hemiacetal not only unstable molecule but also has a short lifetime so that tend to reverts back as a substrate or tend to produce acetal. Besides that, the yield of hemiacetal also cannot be isolated.

The next step is produce acetal product as shown in Figure 1. The process that occurs in the formation of acetal products is almost similar to hemiacetal formation. The first step to produce acetal product started from the formation intermediate structure (4). In this step, carbonyl protonation by Brønsted acid site (HCl) occurs again and produce a compound which has a good leaving group (OH<sub>2</sub><sup>+</sup>). The formation energy decreased from 574.2 kJ/mol to 458.7 kJ/mol. The next step is the formation of compound 5 by removing the leaving group from compound 4 (OH<sub>2</sub><sup>+</sup>). The resonance structure not only compound 2 but also compound 5. The formation energy increased from 458.7 kJ/mol to 509 kJ/mol. Both compound 5 and 5' has a similar formation energy due to both of that is a resonance structure(509 kJ/mol).

Similar with the formation of compound 2, the formation of the intermediates structure 6 also occurs through the reaction of the compound 5 or compound 5' with methanol. The formation energy decreased from 509 kJ/mol to 459.7 kJ/mol. It's also mean compound 6 more stabil than compound 5 and also compound 5'. The final step is the formation of acetal products (7) which occur by deprotonation of compound 6. Acetal structure is the stable molecule (29.7 kJ/mol) during the reaction occur from compound 1 until acetal based on the formation energy (29.7 kJ/mol). But when compared to substrates, acetals are more unstable than substrates.

On the hemiacetal formation, the hemiacetal structure is the most unstable compared to other molecules (2, 1, 1', 0). On the hemiacetal formation, the hemiacetal structure is the most unstable compared to other molecules (2, 1, 1', 0). While on the formation of acetal from hemiacetal, resonance structure (5 and 5') showed higher energy compared to the other molecule (compound 4,6,7). On the hemiacetal formation, the hemiacetal structure is the most unstable compared to other molecules (2,1,1', 0). While on the formation of acetal from hemiacetal, resonance structure (5 and 5') showed higher energy compared to the other molecule (compound 4,6,7). Based on the reaction mechanism, there are 7 steps acetalization of 3-chlorobenzaldehyde that is protonation, 1,2-addition, deprotonation to form hemiacetal, protonation, removal of water, 1,2-addition, and a final was deprotonation to form acetal. The electronic compounds structure of all compounds in acetalization of 3-chlorobenzaldehyde shown in Figure 2.





**Fig. 3.** Optimized geometries of substrate, hemiacetal intermediate, and acetal product.

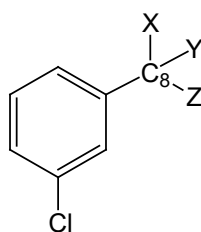
### 3.1 Mulliken Charge

Hyperchem is the software that can analyze the Mulliken charge of an atom in a molecule. Mulliken charge analysis is the most widely used method in various software because this method is easy to understand. The results of the Mulliken charge calculation showed that the order of Mulliken charge of C8 atom in the compound was  $3 > 7 > 6 > 4 > 5', 5 > 0 > 2 > 1, 1'$ . Hemiacetal compound (3) has the highest Mulliken charge on C8 atoms as shown in Table 1 compared to other compounds due to the presence of electron withdrawing group that is methoxy and hydroxy groups on that compound. Acetals also have a

high Mulliken charge on C8 atom also due to the presence of electron withdrawing group that is methoxy groups on that compound. Whereas compound 1 has a low Mulliken charge on C8 atom due without electron withdrawing groups. In addition, neighbor oxygen atoms also have the positive charge, thus weakening the Mulliken charge of a C8 atom. The molecule model of the compound represented in Figure 3.

**Table 1.** Mulliken charge of C<sub>8</sub> atom in compound 0 -7.

| Compound | Mulliken Charge of C <sub>8</sub> |
|----------|-----------------------------------|
| 0        | 0.337                             |
| 1        | 0.333                             |
| 1'       | 0.332                             |
| 2        | 0.335                             |
| 3        | 0.564                             |
| 4        | 0.425                             |
| 5        | 0.365                             |
| 5'       | 0.370                             |
| 6        | 0.469                             |
| 7        | 0.483                             |



**Fig. 4.** The molecule model of 3-chlorobenzaldehyde, intermediate, and acetal.

## 4 Conclusion

Theoretical study on the acetal formation has been done. Based on the reaction mechanism, the hemiacetal structure is the most unstable compound compared to other molecules according to the formation energy. The Mulliken charge of the C8 atom on the hemiacetal compound also higher compared to other molecules due to the presence of an electron withdrawing group that is methoxy and hydroxy groups. Whereas, the formation of acetal carried out by reaction of two equivalents of an methanol and elimination of water using acid catalysts (HCl). On the formation of acetal, SN1 reaction mechanism also studied especially in the compound 4, 5, 5', and 6.

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