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DFT Study: Geometry Optimization and Electronic Properties of Steroid Derivative Compounds

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ABSTRACT

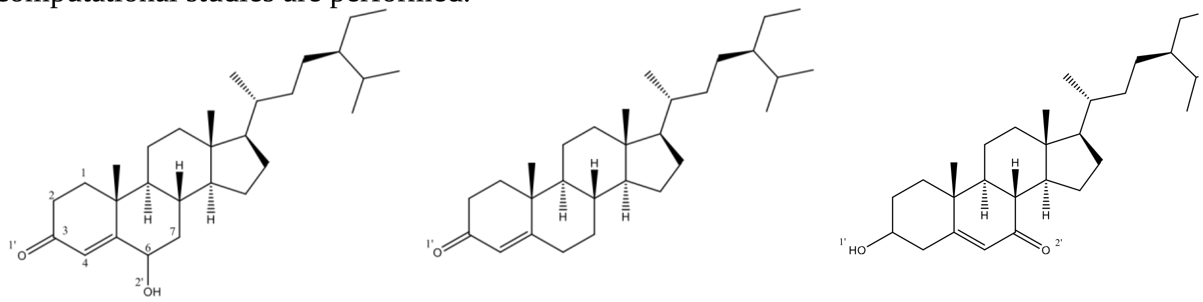
Stigmastane steroids are natural compounds that exhibit diverse biological activities and attract significant interest for further chemical and pharmacological investigations. This study aims to investigate the structural and electronic properties of 6-hydroxystigmast-4-en-3-one (1), stigmast-4-en-3-one (2), and 3-hydroxystigmast-5-en-7-one (3) using a theoretical approach. Density Functional Theory (DFT) calculations were performed at the B3LYP/6-31++G(d,p) level to obtain optimized geometrical structures and evaluate the electronic characteristics of the molecules. Frontier molecular orbital analysis, global reactivity descriptors, and molecular electrostatic potential (MEP) mapping were employed to examine the electronic distribution and reactive sites of the compounds. The results indicate that the hydroxyl and carbonyl functional groups play important roles in the electronic behavior of the molecules, acting as potential regions for electron donation and electrophilic interactions. In addition, several quantum chemical descriptors, including hardness (η), softness (σ), electronegativity (χ), chemical potential (μ), and electrophilicity index (ω), were calculated to describe the chemical reactivity of the studied compounds. These findings provide theoretical insights into the structural stability and reactivity of stigmastane derivatives and may serve as a basis for further studies related to their molecular interactions and biological activities.

Keywords: DFT, HOMO-LUMO, MEP

I. INTRODUCTION

Stigmastane steroids are secondary metabolites widely distributed in nature, particularly in higher plants. Steroids are lipid-derived compounds characterized by a core structure known as perhydrocyclopentanophenanthrene, which consists of three fused cyclohexane rings resembling a phenanthrene framework and an additional cyclopentane ring forming a tetracyclic skeleton (Borah & Banik, 2020). Due to their structural diversity, steroid derivatives have attracted considerable attention because of their broad range of biological activities, including antimicrobial, anti-inflammatory, anticancer, and antiplasmodial activities.

Three stigmastane derivatives have been isolated from the stem bark of *Dryobalanops oblongifolia*, namely 6-hydroxystigmast-4-en-3-one (1), stigmast-4-en-3-one (2), and 3-hydroxystigmast-5-en-7-one (3) (Indriani et al., 2020). These compounds have been evaluated for their antiplasmodial activity, indicating their potential as candidates for antimalarial drug development. However, understanding the molecular-level interactions of these molecules requires accurate structural information. Therefore, structural modeling and geometry optimization are essential to obtain stable molecular conformations before further computational studies are performed.



(1) (2) (3)

Figure 1. Molecule structures of 6-hydroxystigmast-4-en-3-one (1) , Stigmast-4-en-3-one (2) and 3-hydroxystigmast-5-en7-one (3)

Density Functional Theory (DFT) is a widely used quantum chemical approach for investigating the electronic structure of atoms, molecules, and solids. This method provides a good balance between computational cost and accuracy in predicting molecular properties (Nomura & Akashi, 2024). Through DFT calculations, important parameters such as optimized geometry, electronic distribution, frontier molecular orbitals, and chemical reactivity descriptors can be obtained (Tandon et al., 2019). These parameters are essential for understanding the physicochemical behavior of bioactive molecules. Therefore, this study aims to theoretically investigate the geometrical structure, electronic properties, and chemical reactivity of 6-hydroxystigmast-4-en-3-one (1), stigmast-4-en-3-one (2), and 3-hydroxystigmast-5-en-7-one (3) using Density Functional Theory calculations..

II. COMPUTATIONAL DETAIL

The DFT expressed in B3LYP/6-31++g (d,p) model was used to calculate the ground-state molecular structures. All of the calculations were performed with the Gaussian 09W program. The graphical interface Gauss View 6 was used to visualize the optimized geometry, HOMO-LUMO, and MEP.

III. RESULTS AND DISCUSSION

III.A Geometry optimization

The optimized molecular geometries of the studied compounds are presented in Figure 2. Geometry optimization was performed in the ground state using the B3LYP functional with the 6-31++G(d,p) basis set. This level of theory is commonly used in quantum chemical calculations because it provides a good balance between computational accuracy and efficiency for predicting molecular structures and electronic properties.

The optimized geometrical parameters, including selected bond lengths and bond angles, are summarized in Table 1. Geometry optimization aims to obtain the most stable molecular configuration by minimizing the total energy of the system. The resulting optimized structures represent the equilibrium geometry of the molecules in their ground state.

Based on the calculated structural parameters, several characteristic bond lengths can be observed in the studied molecules. For example, the C=O bond length (C3–O1') in compounds (1) and (2) is approximately 1.22 Å, which is consistent with typical carbonyl double-bond lengths reported for ketone functional groups. In contrast, compound (3) shows a longer C3–O1' bond length of 1.43 Å (Nomura & Akashi, 2024), indicating a single C–O bond that is consistent with the presence of a hydroxyl functional group in that position. Similarly, the C6–O2' bond length in compound (1) is about 1.43 Å, which is characteristic of a C–O single bond associated with a hydroxyl substituent.

Tabel 1. The calculated values of structure parameters, bond lengths and bond angles from the molecule structure (1), (2) and (3)

(1)		(2)		(3)	
Bonds/Angle	**B3LYP/ 6-31++g(d,p)**	**Bonds/Angle**	**B3LYP/ 6-31++g(d,p)**	**Bonds/Angle**	**B3LYP/ 6-31++g(d,p)**
C3-O1'	1.22	C3-O1'	1.22	C3-O1'	1.43
C6-O2'	1.43	C3-C2-O1'	119.68	C7-O2'	1.21
C2-C1-O1'	119.68	C4-C3-O1'	119.68	C_2-C3-$O_{1'}$	109.30
C4-C1-O1'	119.68			C_4-C3-$O_{1'}$	109.30
C5-C6-C2'	108.98			O_{31}-C_3-H	109.47
C7-C6-C2'	108.98			C6-C7-O2'	120.39
O31-C6-H40	109.46			C8-C7-O30	120.38

The calculated bond angles also reflect typical geometrical characteristics of the molecular framework. For instance, the bond angles around the carbonyl carbon, such as C2–C3–O1' and C4–C3–O1', are approximately 119.68°, indicating a trigonal planar geometry that is characteristic of sp^2-hybridized carbon atoms. Meanwhile, bond angles around saturated carbon atoms, such as C5–C6–C2' and C7–C6–C2', are close to 109°, which corresponds to the tetrahedral geometry typical of sp^3-hybridized carbon atoms.

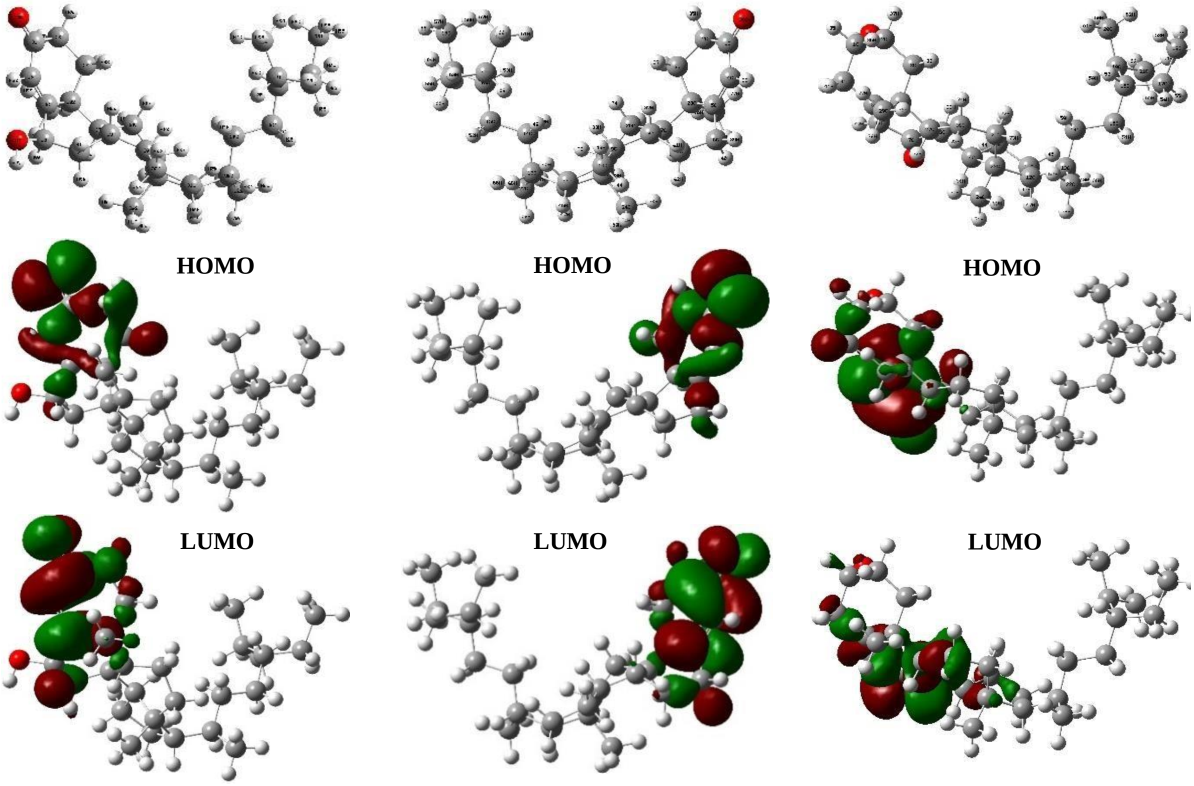
III.B HOMO-LUMO Analysis

The HOMO–LUMO analysis was carried out based on the frontier molecular orbital (FMO) theory to explain the interaction between the Highest Occupied Molecular Orbital (HOMO) and the Lowest Unoccupied Molecular Orbital (LUMO) (Deghady et al., 2021). In molecular orbital theory, HOMO represents the highest energy orbital containing electrons and is associated with the molecule's ability to donate electrons, whereas LUMO corresponds to the lowest energy orbital capable of accepting electrons. The interaction between these two orbitals plays an important role in determining molecular stability, chemical reactivity, and charge transfer processes.

One of the important parameters derived from this analysis is the energy gap (ΔE) between HOMO and LUMO orbitals. This energy gap represents the minimum energy required to excite an electron from the HOMO level to the LUMO level (Xu et al., 2021). In general, molecules with smaller energy gaps tend to exhibit higher chemical reactivity and lower kinetic stability, whereas molecules with larger energy gaps are considered more stable.

Figure 2 shows the spatial distribution of the frontier molecular orbitals of the studied compounds. The electron densities of both HOMO and LUMO orbitals are mainly localized around the hydroxyl and carbonyl functional groups, indicating that these regions play an important role in electronic transitions. These functional groups are therefore predicted to act as the most reactive sites and may participate in intermolecular interactions such as electron transfer or hydrogen bonding.

The calculated quantum chemical parameters are summarized in Table 2. The HOMO energies of compounds (1), (2), and (3) are −6.52224 eV, −6.56577 eV, and −6.58754 eV, respectively, while the LUMO energies are −1.47478 eV, −1.50199 eV, and −1.49927 eV. The resulting HOMO–LUMO energy gaps are approximately 5.04746 eV, 5.06378 eV, and 5.08827 eV for compounds (1), (2), and (3), respectively. These values indicate that the three molecules possess similar electronic characteristics, although compound (1) shows the smallest energy gap, suggesting slightly higher chemical reactivity compared to the other molecules.



(1) (2) (3)

Figure 2. The optimized structure of 1, 2 and 3 and their HOMO-LUMO

III.4 DFT Analysis

Global reactivity descriptors derived from density functional theory calculations provide useful information regarding the chemical behavior of molecules. Parameters such as electronegativity (χ), chemical potential (μ), hardness (η), and softness (σ) are commonly used to evaluate molecular reactivity and stability. These descriptors are obtained from the frontier molecular orbital energies and provide insight into the ability of a molecule to donate or accept electrons.

Tabel 2. The Calculated quantum parameters for the studied molecule

Molecular property	1	2	3
Total Energy, TE (a.u)	-1284.5288	-1209.3113	-1284.5394
E_{HOMO} (eV)	-6.52224	-6.56577	-6.58754
E_{LUMO} (eV)	-1.47478	-1.50199	-1.49927
Egab	-5.04746	-5.06378	-5.08827
Electronegativity, x	-2.52373	-2.53189	-2.54414
Chemical potential, μ	2.523728	2.531891	2.544135
Hardness, η	2.523728	2.531891	2.544135
Softness, σ	1.261864	1.265945	1.272068
Electrophilicity index, ω	8.037063	8.115303	8.233613

The calculated descriptor parameters for the studied compounds are presented in Table 2. The electronegativity values of compounds (1), (2), and (3) are −2.52373, −2.53189, and −2.54414, respectively, indicating similar tendencies of the molecules to attract electrons. The chemical potential values show only slight differences among the molecules, suggesting comparable charge transfer tendencies. The hardness values are also similar, indicating that the three compounds have comparable resistance to electron cloud deformation. In contrast, the softness values slightly increase from compound (1) to compound (3), suggesting that compound (3) may exhibit slightly greater polarizability during molecular interactions.

III. 5 Molecular Electrostatic Potential (MEP)

Molecular Electrostatic Potential (MEP) mapping is commonly used to analyze the charge distribution on the surface of a molecule and to predict potential sites for intermolecular interactions. This approach helps identify regions susceptible to electrophilic and nucleophilic attacks as well as possible protonation sites. Regions with negative electrostatic potential generally correspond to electron-rich areas that are favorable for electrophilic attack, whereas positive electrostatic potential regions are associated with electron-deficient areas that are susceptible to nucleophilic interactions (Drissi et al., 2015).

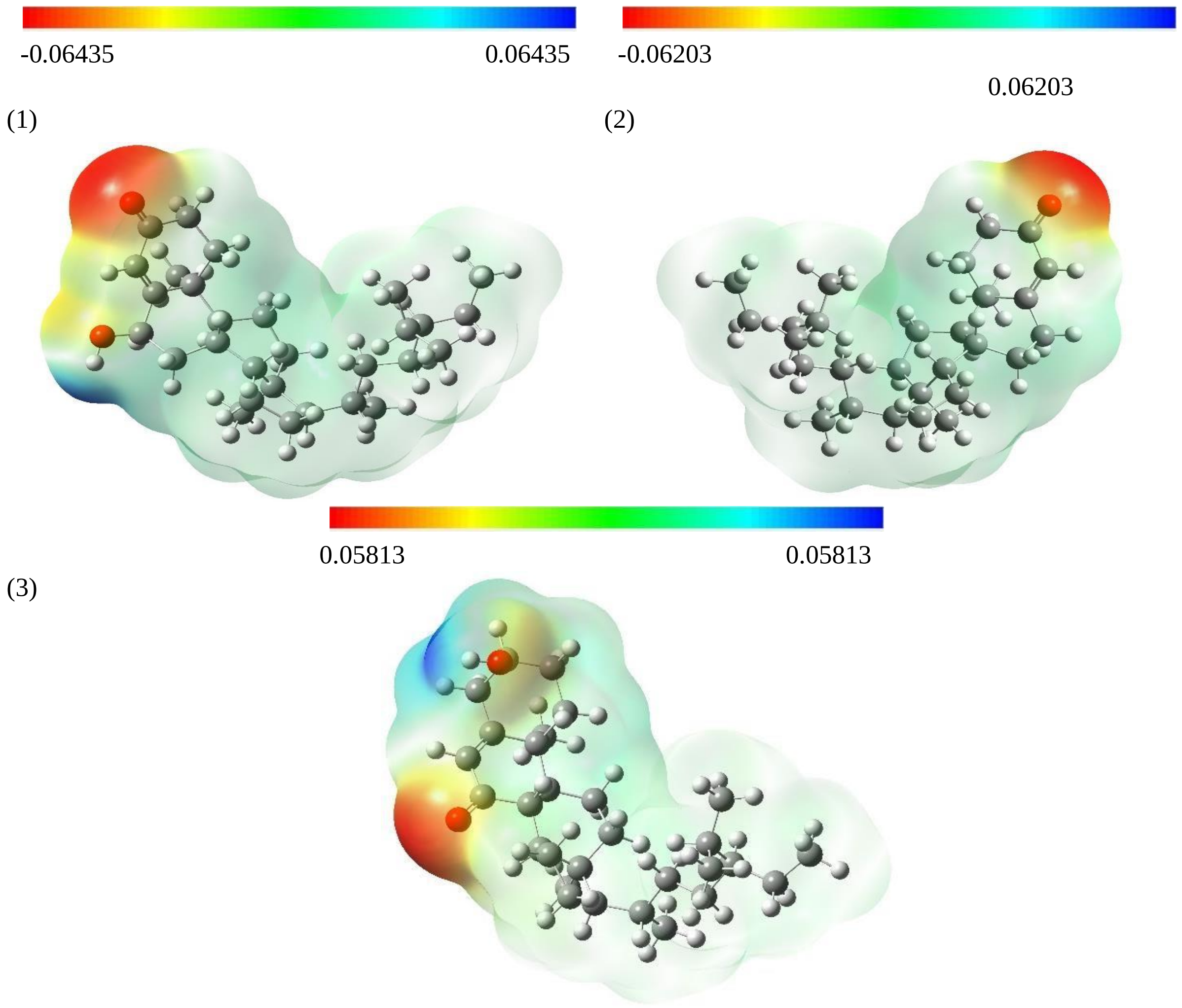


Figure 3. Molecular Electrostatic Potential surface of compound 1, 2 and 3

The MEP surfaces of the studied molecules are shown in Figure 3. In the MEP map, different colors represent variations in electrostatic potential on the molecular surface. The negative regions are typically indicated in red, while positive regions appear in blue, and areas with near-zero potential are shown in green. The electrostatic potential gradually increases following the color scale red → yellow → green → light blue → blue.

Based on the MEP distribution, the most negative regions are primarily localized around the carbonyl functional groups, indicating a high electron density in these areas. In contrast, positive electrostatic potential is observed around the hydroxyl groups, suggesting that these regions may participate in hydrogen bonding interactions. These observations indicate that the carbonyl groups may play an important role in intermolecular interactions, particularly in the formation of hydrogen bonds with biological targets(Deghady et al., 2021).

VI. CONCLUSION

In this study, Density Functional Theory (DFT) calculations at the B3LYP/6-31++G(d,p) level were performed to investigate the structural and electronic properties of 6-hydroxystigmast-4-en-3-one, stigmast-4-en-3-one, and 3-hydroxystigmast-5-en-7-one. Geometry optimization provided stable molecular structures with calculated bond lengths and bond angles that describe the equilibrium configuration of the molecules.

The frontier molecular orbital analysis and molecular electrostatic potential mapping revealed that the carbonyl groups are associated with electron-rich regions, indicating potential sites for electrophilic interactions, whereas the hydroxyl groups exhibit relatively positive electrostatic potential, suggesting possible sites for protonation and intermolecular interactions. These findings provide theoretical insights into the electronic characteristics and potential reactive sites of the studied stigmastane derivatives.

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