Synthesis and Theoretical Study of Some 2,4,6 Trihydroxyacetophenone Schiff base Ligandes

Dr. Rashed Taleb Rashee.
Applied Sciences Department, University of Technology/Baghdad.
E-Mail: r_awsy@yahoo.com

Mahammed Shamil Ali
Applied Sciences Department, University of Technology/Baghdad.
E-Mail: msa_chemistry@yahoo.com

Hadeel Salah Mansoor.
Applied Sciences Department, University of Technology/Baghdad.

Dr. Hasan R. Obayes.
Applied Sciences Department, University of Technology/Baghdad.

Dr. Abdulnasser M. Al-Gebori.
Applied Sciences Department, University of Technology/Baghdad.

ABSTRACT
Schiff bases have been synthesized, identified by FTIR and ultraviolet-visible (UV-Visible) spectroscopy. The theoretical calculations of Schiff base were studied through the optimized structures of the Schiff base ligand was obtained by density functional theory at the B3LYP/6-31G level. Also total energy, heats of formation, dipole moment, point group, molecular orbital’s energy of highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO), energy gaps (Eg) and ΔG reaction were calculated. Here we suggest the optimized structure for the studied Schiff base. The theoretical study and based on the results of density function theory (DFT), L1 possess higher stability state compared with other Schiff bases studied.

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تحضير ودراسة نظرية لبعض ليكينت وقواعد شف 1-2،2،4،6- ثلاثي هيدروكسى

أسطوفينيون

تم تحضير وتشخيص قواعد شف بواسطة مطابقة نقطة الإشعة تحت الحمراء (FTIR) والأنشطة فوق البنفسجية (UV-Visible) المرنة. درست الحسابات النظرية لقواعد شف من خلال التركيب实事 لتحديد القواعد التي تم الحصول عليها بواسطة نظرية الكثافة الإلكترونية للمستوى B3LYP/6-31G. حزمة التركيب هما الحمل، نقطة المجموعة، قنوات الأيونات الجزئية للفوائد الطاقة وطاقة كبس، ومنها تم التكهن بالتركيب ممكن للقاعدة شف. حسب النتائج لذاكرة الكثافة الإلكترونية (DFT)، فإن الليكينت L1 يمكن اعتماد حالات الاستقرارية مقارنة مع بقية قواعد شف التي تحت دراستها.
INTRODUCTION

Compounds containing azomethine group (–C=N–) typically known as Schiff bases have been synthesized by the condensation of primary amines with active carbonyls. Schiff bases form a significant class of compounds in medicinal and pharmaceutical chemistry with several biological applications that include antibacterial [1-6], antifungal [3-6], and antitumor activity [7-8], also have uses as liquid crystals [4], and in analytical [5-7], medicinal [8], and polymer chemistry [9]. They have been studied extensively as a class of ligands [9-11], and are known to coordinate with metal ions through the azomethine nitrogen atom.

Conventionally Schiff bases have been prepared by refluxing mixtures of the amine and the carbonyl compound in an organic solvent, for example, ethanol or methanol [10]. In general, ketones react more slowly than aldehydes that require higher temperatures and longer reaction times [12].

In addition, the equilibrium must often be shifted, usually by removal of the water, either azeotropically by distillation or with suitable drying agents [13]. In recent years, environmentally benign synthetic methods have received considerable attention and some solvent-free protocols have been developed [14]. Grinding together solid anilines and solid benzaldehydes yielded various kinds of benzylideneanilines [15]. Imines can be synthesized by condensation of 2,4,6-trihydroxyacetophenone with amine derivatives under solvent free conditions [16]. Based on these facts, we decided to synthesize some Schiff bases derivative from 2,4,6-trihydroxyacetophenone primary amine derivative (thiosemicarbazide, m-hydroxyphenol, p-hydroxyphenol, 4-aminoantipyrine, and p-aminoacetophenone) under Microwave Irradiation.

Moreover, nowadays, computational chemistry methods offer a unique ability for the synthetic organic chemists to generate optimal geometry structures. The structural and electronic properties of reactants and products can make decisions as to which of the chemical transformations will occur in reactions [17]. The electrophilic substitution reactions with 2,4,6-trihydroxyacetophenone also were studied using computational chemistry methods.

Experimental

Materials and Instrumentation

All chemicals and solvents used were analytical grade from Merck Company. Melting points were recorded by using Gallenkamp M.F.B- 600 F melting point apparatus. FTIR spectra were recorded as KBr discs using FTIR-8400S Shimadzu in the range of 4000-200 cm$^{-1}$. Electronic spectra were obtained using UV/VIS -1650 PC Shimadzu spectrophotometer, in the wavelength range (200-1100) nm at 25°C in 10$^{-3}$ M in ethanol. Microwave assisted procedures were carried out in a digital microwave oven Russell Hobbs model number RHM 2017 operating at 800 W.

General microwave procedure for the synthesis of Schiff bases.

2,4,6-Trihydroxyacetophenone was mixed with a (4-amino-antipyrine, thiosemicarbazide, p-aminoacetophenone, m-hydroxyphenol and p-hydroxyphenol) in ratio 1:1 mole, and the mixture was grinded in ceramic mortar. Then the contents were subjected to microwave irradiation at an interval of 1 min during 4-20 minutes.
Computational Details

Calculations were done using the Density Functional Theory (DFT) method with the B3LYP functional using the 6-31G. The addition of diffuse functions is meant to investigate their influence on the calculated molecular properties. DFT/B3LYP combination is known to produce good estimates of molecular properties related to molecular reactivity [18]. Among the molecular properties that are well reproduced by the DFT/B3LYP method include the energy of the highest occupied molecular orbital (HOMO), energy of the lowest unoccupied molecular orbital (LUMO), electronegativity, global hardness and softness, electron affinity, ionization potential, etc. According to Koopmans’ theorem [19], the electronegativity, global hardness and softness, electron affinity and ionization potential may be defined in terms of the energy of the HOMO and the LUMO. Electronegativity (X) is the measure of the power of an electron or group of atoms to attract electrons towards itself [20], it can be estimated by using the equation:

\[ X = \frac{1}{2} (E_{\text{HOMO}} + E_{\text{LUMO}}) \]

Chemical hardness (η) measures the resistance of an atom to a charge transfer [21]. There is also a relationship between hardness and stability. Parr and Pearson [22-25] reported the principle of maximum hardness: a rule that molecules arrange themselves to be as hard as possible. The DFT method provides definitions of important universal concepts of molecular structure and reactivity. It has been developed [24-25] as an operational approximation for absolute hardness η [17], estimated by using the equation:

\[ \eta = \frac{1}{2} (E_{\text{HOMO}} - E_{\text{LUMO}}) \]

Chemical softness (S) is the measure of the capacity of an atom or group of atoms to receive electrons [21], it is estimated by using the equation:

\[ S = \frac{1}{\eta} = -\frac{1}{2} (E_{\text{HOMO}} - E_{\text{LUMO}}) \]

Where S is the global hardness value. Global electrophilicity index (ω) is the measure of the electrophilic tendency of a molecule; it is estimated by using the electronegativity and chemical hardness parameters through the equation:

\[ \omega = \frac{X^2}{2\eta} \]

According to the definition this index measures the affinity of a species to accept electrons. The high reactivity of the nucleophile is characterized by a lower value of ω and in contrast, a good electrophile is characterized by a high value of (ω) [17].

Electron affinity (EA) is defined as the energy released when a proton is added to a system. It is related to \( E_{\text{LUMO}} \) through the equation:

\[ EA = -E_{\text{LUMO}} \]

Ionization potential (IP) is defined as the amount of energy required to remove an electron from a molecule [22]. It is related to the energy of the \( E_{\text{HOMO}} \) through the equation:

\[ IP = -E_{\text{HOMO}} \]
RESULTS and DISCUSSION

Experimental results

Here we describe the synthesis of Schiff base with a good yield; the ligand is stable at room temperature and is nonhygroscopic. In the given Scheme (1) the produced compounds (L1 - L5) were synthesized by the reaction between the substituted aromatic ketone (2,4,6-trihydroxyacetophenone) under microwave irradiation. The results of this study are summarized in Table (1).

![Scheme (1): General equation of the prepared ligands.]

Where

H$_2$N-R mean (4-aminoantipyrine, thiosimicarbazide, and p-aminoacetophenone, m-hydroxyphenol and p-hydroxyphenol).

Table (1): Properties of Schiff bases synthesized by Microwave irradiation method.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>-R</th>
<th>Colour</th>
<th>Yield</th>
<th>Time Taken (min)</th>
<th>Molecular mass (amu)</th>
<th>Molecular Formula</th>
<th>M.P. °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>(L1)</td>
<td>C$_3$N$_2$(CH$_3$)$_2$</td>
<td>Pale yellow</td>
<td>90</td>
<td>4</td>
<td>353</td>
<td>C$<em>{19}$H$</em>{19}$N$_3$O$_4$</td>
<td>106-108</td>
</tr>
<tr>
<td>(L2)</td>
<td>-NH-C(S)-NH$_2$</td>
<td>Brown</td>
<td>69</td>
<td>13</td>
<td>241</td>
<td>C$<em>9$H$</em>{11}$N$_3$O$_3$S</td>
<td>156-158</td>
</tr>
<tr>
<td>(L3)</td>
<td>-C$_6$H$_4$C(O)CH$_3$</td>
<td>Grey-black</td>
<td>84</td>
<td>6</td>
<td>285</td>
<td>C$<em>{14}$H$</em>{13}$NO$_4$</td>
<td>48-50</td>
</tr>
<tr>
<td>(L4)</td>
<td>-C$_6$H$_4$OH</td>
<td>Red</td>
<td>94</td>
<td>10</td>
<td>259</td>
<td>C$<em>{14}$H$</em>{13}$NO$_4$</td>
<td>70-72</td>
</tr>
<tr>
<td>(L5)</td>
<td>-C$_6$H$_4$OH</td>
<td>Olive</td>
<td>88</td>
<td>20</td>
<td>259</td>
<td>C$<em>{14}$H$</em>{13}$NO$_4$</td>
<td>90-92</td>
</tr>
</tbody>
</table>
UV/Vis- spectra of Schiff base ligands exhibited three absorption bands at (266) nm suggesting (π-π*) transitions of (C=C) benzene ring, absorption bands at (288-294) nm may be assigned to the (π-π*) transitions of azomethine group (C=N) and absorption bands at (323-352) nm can be assigned the presence of (n-π*).

The Schiff base compounds were identified by FTIR spectroscopy in the range (4000 - 400) cm⁻¹. The OH group was appeared at (3280 - 3300 cm⁻¹), the absorption bands at (1626 - 1631 cm⁻¹) corresponding to (C=C) of the benzene ring, while absorption bands at (1593 - 15600 cm⁻¹) corresponding to (C=N). Table (2) shows some spectroscopic data of compounds.

Table (2): The spectroscopic data of prepared ligands.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>UV-Vis (nm)</th>
<th>FTIR (cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n-π*</td>
<td>π-π*</td>
</tr>
<tr>
<td>L1</td>
<td>323</td>
<td>289</td>
</tr>
<tr>
<td>L2</td>
<td>963</td>
<td>288</td>
</tr>
<tr>
<td>L3</td>
<td>520</td>
<td>294</td>
</tr>
<tr>
<td>L4</td>
<td>344</td>
<td>288</td>
</tr>
<tr>
<td>L5</td>
<td>352</td>
<td>289</td>
</tr>
</tbody>
</table>

Computational Results

Geometry optimizations for all compounds used in this research were fully optimized at the DFT/ B3LYP level of theory with a 6-31G method [18]. The calculated total energy, entropy (S), enthalpy (H), for prepared compounds are also reported in table (3). All compounds have C₁ symmetry.

Table (3): Total energy and some thermodynamic prosperities of studied compounds.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Total Energy a.u.</th>
<th>S Cal/Mol-Kelvin</th>
<th>H kCal/Mol</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1</td>
<td>-1192.817</td>
<td>158.833</td>
<td>254.828</td>
</tr>
<tr>
<td>L2</td>
<td>-1137.438</td>
<td>124.990</td>
<td>139.116</td>
</tr>
<tr>
<td>L3</td>
<td>-974.110</td>
<td>142.053</td>
<td>188.798</td>
</tr>
<tr>
<td>L4</td>
<td>-896.699</td>
<td>129.873</td>
<td>165.779</td>
</tr>
<tr>
<td>L5</td>
<td>-896.698</td>
<td>129.501</td>
<td>165.679</td>
</tr>
</tbody>
</table>

B3LYP functional used in this study has a high efficiency to calculate the electronic properties of the studied organic molecules, such as the energy of the highest occupied molecular orbital (HOMO), as shown in Figure (1), the energy of the lowest unoccupied molecular orbital (LUMO), ionization potentials (IP), electron affinities (EA), electronegativity (χ), absolute hardness (η), absolute softness (S) and electrophilic index (ω). The properties are displayed in table (4) lists the electronic properties of the molecules under study. It is clear from table (4) that the energy of the highest occupied molecular orbital (E_HOMO), ionization potential, electron affinity, energy gap (E_gap) and the hardness (η) for L1 molecule is larger than that for other compounds.

The higher energy gap (E_gap) and hardness index for ligand (L1) indicated its high stability as compared to other ligands. The principle of maximum hardness
represents that the system would be more stable if the global hardness, related to energy gap, is a maximum.

Table (4): The molecular properties for the investigated compounds.

<table>
<thead>
<tr>
<th>Sym.</th>
<th>(E_{\text{HOMO}})</th>
<th>(E_{\text{LUMO}})</th>
<th>(E_{\text{gap}})</th>
<th>(IP)</th>
<th>(EA)</th>
<th>(\mu)</th>
<th>(X)</th>
<th>(\eta)</th>
<th>(S)</th>
<th>(\omega)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1</td>
<td>8.353</td>
<td>2.966</td>
<td>11.31</td>
<td>8.353</td>
<td>2.966</td>
<td>6.470</td>
<td>2.693</td>
<td>5.659</td>
<td>0.176</td>
<td>0.641</td>
</tr>
<tr>
<td>L2</td>
<td>5.551</td>
<td>1.687</td>
<td>3.86</td>
<td>5.551</td>
<td>1.687</td>
<td>6.515</td>
<td>3.619</td>
<td>1.932</td>
<td>0.517</td>
<td>3.389</td>
</tr>
<tr>
<td>L3</td>
<td>5.986</td>
<td>1.850</td>
<td>4.13</td>
<td>5.986</td>
<td>1.850</td>
<td>5.593</td>
<td>3.918</td>
<td>2.068</td>
<td>0.483</td>
<td>3.712</td>
</tr>
<tr>
<td>L4</td>
<td>5.741</td>
<td>1.306</td>
<td>4.43</td>
<td>5.741</td>
<td>1.306</td>
<td>5.239</td>
<td>3.523</td>
<td>2.217</td>
<td>0.450</td>
<td>2.799</td>
</tr>
<tr>
<td>L5</td>
<td>5.523</td>
<td>1.278</td>
<td>4.24</td>
<td>5.523</td>
<td>1.278</td>
<td>1.760</td>
<td>3.401</td>
<td>2.122</td>
<td>0.471</td>
<td>2.725</td>
</tr>
</tbody>
</table>

\(E_{\text{gap}}\) is the energy difference between \(E_{\text{HOMO}}\) and \(E_{\text{LUMO}}\); \(IP\) is the ionization potential; \(EA\) is the electron affinity in eV; \(\mu\) is the dipole moment in Debye; \(X\) is the electronegativity; \(\eta\) is the hardness; \(S\) is the softness and \(\omega\) is the electrophilicity index values.

On the other hand, the calculated values of the global reactivity index (\(\omega\)) show the nucleophilicity power of L1. We obtained lower (\(\omega\)) value (0.641) eV for L1 that explain the better propensity of L1 to be involved in the reactions with electrophiles as compared to L3. While L3 molecule has the highest of global reactivity index (\(\omega\)) value (3.712) eV, that explain the better propensity of L3 to be involved in the reactions with nucleophilicity reactions.
CONCLUSION

Five novel Schiff base compounds (L1- L5) have been prepared under microwave irradiation conditions and investigated by theoretical techniques and quantum chemical approaches. These parameters were calculated by the DFT/B3LY method. The Egap increases with increasing the hole of $E_{\text{HOMO}}$ and $E_{\text{LUMO}}$, and the stability increase, with increasing hardness. Therefore, the quantum chemical results have provided information that the L1 compound has energy gap and hardness with the highest (more stability) as compared to those of other prepared compounds, and the lower value of the electrophilicity index ($\omega$), indicated that L1 compound has a better propensity to be involved in the reactions with electrophiles compared to other prepared compound.

REFERENCES