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

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ABSTRACT
  Schiff bases have been synthesized, identified by FTIR and ultra violet-visible (UV-Visible) spectroscopy. The theoretical calculations of Schiff base was studied through the optimized structures of the Schiff base ligand was obtained by density functional theory at B3LYP/6-31G level. Also total energy, heats of formation, dipole moment, point group, molecular orbital's energy of higher occupied molecular orbital (HOMO) and lower 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 functions theory (DFT), L1 possess higher stability state compared with other Schiff bases studied.

تحضير ودراسة نظرية لبعض ليكندات وقواعد شف لـ 2،4،6- ثلاثي هيدروكسي اسيتوفينون

تم تحضير وتشخيص قواعد شف بواسطة مطيافية الاشعة تحت الحمراء (FTIR) والاشعة الفوق البنفسجية المرئية (UV-Visible). درست الحسابات النظرية لقواعد شف من خلال التركيب الامثل لهذه القواعد والتي تم الحصول عليها بواسطة نظرية الكثافة الالكترونية للمستوى B3LYP/6-31G . كذلك تم قياس الطاقة الكلية ، حرارة التكوين ، عزم ثنائي القطب ، نقطة المجموعة ، طاقات الاوربتالات الجزيئية للـ HOMO و LUMO ، فجوات الطاقة و طاقة كبس، ومنها تم التكهن بافضل تركيب ممكن لقاعدة شف. حسب النتائج لدالة الكثافة الالكترونية (DFT)، فان الليكند L1 يملك اعلى حالات الاستقرارية مقارنة مع بقية قواعد شف التي تمت 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, thiosimicarbazide , p-aminoacetophenone , m-hydroxyphenol and p-hydroxyش) in ratio 1:1 mole, and the mixture were 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 estimate 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:

$$X = -½ (E_{HOMO} + E_{LUMO})$$

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. 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:

$$η = -½ (E_{HOMO} - E_{LUMO})$$

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:
$$S = 1/η = -2/(E_{HOMO} - E_{LUMO})$$
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:

$$ω = X^2/(2η)$$

According to the definition this index measures the affinity of a species to accept electrons. The higher 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_{LUMO} through the equation:

$$EA = -E_{LUMO}$$

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_{HOMO} through the equation:
$$IP = -E_{HOMO}$$

Results and Discussion
Experimental results

Her 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).
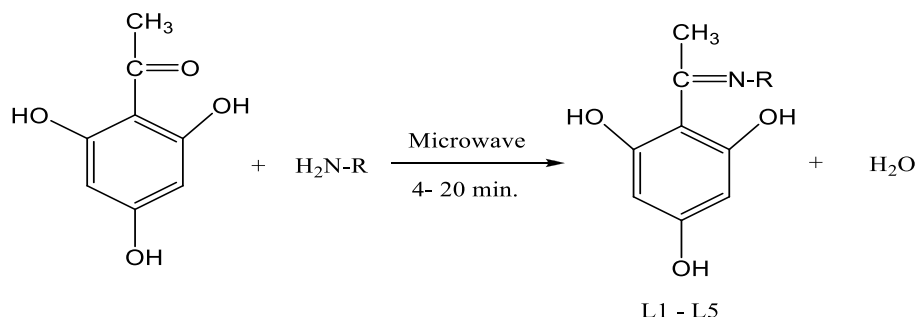
Scheme (1): General equation of the prepared ligands.

Where

H_2N-R mean (4-aminoantipyrine, thiosimicarbazide, and p-aminoaceto-phenone, m-hydroxyphenol and p-hydroxyphenol).

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

Compounds	-R	Colour	Yield %	Time Taken (min)	Molecular mass (amu)	Molecular Formula	M.P. °C
(L1) 1,5-Dimethyl-2-phenyl-4-[1-(2,4,6-trihydroxy phenyl) ethylenediamino]-1,2-dihydro-pyrazole	$-C_3N_2(CH_3)_2$ $(O)-C_6H_5$	Pale yellow	90	4	353	$C_{19}H_{19}N_3O_4$	106-108
(L2) 2-[1-(Thiourea imino)-ethyl] benzene-1,3,5-triol	$-NH-C(S)-NH_2$	Brown	69	13	241	$C_9H_{11}N_3O_3S$	156-158
(L3) 1-{4-[1-(2,4,6-Trihydroxy phenyl)-ethylideneamino]-phenyl} ethanone	$-C_6H_4-C(O)$ CH_3	Grey-black	84	6	285	$C_{16}H_{15}NO_4$	48-50
(L4) 2-[1-(3-hydroxy-phenylimino)-ethyl] benzene-1,3,5-triol	$-C_6H_4-OH$ Meta	Red	94	10	259	$C_{14}H_{13}NO_4$	70-72
(L5) 2-[1-(4-hydroxy-phenylimino)-ethyl] benzene-1,3,5-triol	$-C_6H_4-OH$ Para	Olive	88	20	259	$C_{14}H_{13}NO_4$	90-92

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 a in the range (4000 - 400) cm^{-1}. The OH group were appeared at (3280 - 3300 cm^{-1}), the absorption bands at (1626 - 1631 cm^{-1}) corresponding to (C=C) of 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.

Compounds	UV-Vis (nm)			FTIR (cm^{-1})		
	n-π*	π-π* C=N	π-π* C=C	O-H	C=C	C=N
L1	323	289	226	3280	1629	1599
L2	963	288	226	3292	1631	1600
L3	520	294	266	3300	1629	1593
L4	344	288	262	3290	1630	1597
L5	352	289	226	3298	1627	1593

Computational Results

Geometry optimizations for all compounds used in this research were fully optimized at the DFT/ B3LYP level of theory with a 6-311G method [18]. The calculated total energy, entropy (S), enthalpy (H), for prepared compounds are also reported in table (3). All compounds have C_1 symmetry.

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

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

B3LYP functional used in this study has a high efficiency to calculate the electronic properties for the studied organic molecules, such as the energy of the highest occupied molecular orbital (HOMO), as shown in Figure (1), 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 for 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 largest than that for other compounds.

The higher energy gap (Egap) and hardness index for ligand (L1) indicated its higher 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.
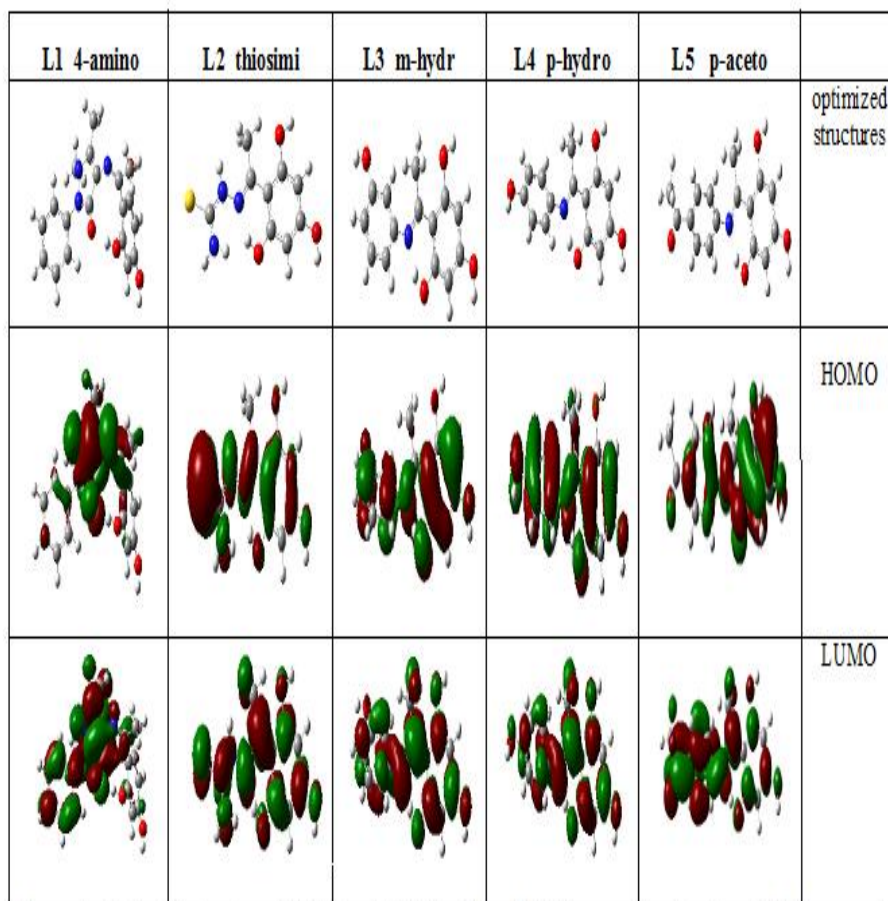

Figure 1. Optimized structures, HOMO and LUMO of the Schiff base species for the studied compounds (B3LYP/6-31G).

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

Sym.	E_{HOMO}	E_{LUMO}	E_{gap}	IP	EA	μ	X	η	S	ω
L1	-8.353	2.966	11.31	8.353	-2.966	6.470	2.693	5.659	0.176	0.641
L2	-5.551	-1.687	3.86	5.551	1.687	6.515	3.619	1.932	0.517	3.389
L3	-5.986	-1.850	4.13	5.986	1.850	5.593	3.918	2.068	0.483	3.712
L4	-5.741	-1.306	4.43	5.741	1.306	2.029	3.523	2.217	0.450	2.799
L5	-5.523	-1.278	4.24	5.523	1.278	1.760	3.401	2.122	0.471	2.725

E_{gap} is the energy difference between E_{HOMO} and E_{LUMO}; *IP* is the ionization potential; *EA* is the electron affinity in eV; μ is the dipole moment in Debye; *X* is the electronegativity; η is the hardness; *S* is the softness and ω is the electrophilicity index values.

On the other hand, the calculated values of global reactivity index (ω) show the nucleophility power of L1. We obtained lower (ω) value (0.641) eV for L1 that explain 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 (ω) value (3.712) eV, that explain better propensity of L3 to be involved in the reactions with nucleophility 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_{HOMO} and E $_{LUMO}$, 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 (ω), indicated that L1 compound has better propensity to be involved in the reactions with electrophiles compared to other prepared compound.

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