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Preparation and structure investigation of novel Schiff bases using spectroscopic, thermal analyses and molecular orbital calculations and studying their biological activities

By

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#### Abstract

Two novel Schiff's bases (EB1 and L1) as new macrocyclic compounds were prepared via condensation reactions between bisaldehyde (2, 2'-(ethane-1, 2- diylbis (oxy)) dibenzaldehyde): firstly with (hydrazine carbothioamide to give (EB1), secondly with (4, 6-diaminopyrimidine-2-thiol to give (L1). EB1 has a general formula  $C_{18}H_{20}N_6O_2S_2$  of mole mass = 416.520, and IUPAC name ((N,N'Z,N,N'E)-N,N'-(((ethane1,2diylbis(oxy))bis(2,1phenylene))bis(methanylylidene))bis(1hydrazinylmethan ethioamide). L1 has a general formula  $C_{20}H_{16}N_4O_2S$  of mole mass =376.10; and IUPAC name 1, 2-bis(2-vinylphenoxy)ethane4,6-diaminopyrimidine-2-thiol). The structures of the compounds obtained were characterized based on elemental analysis, IR and <sup>1</sup>HNMR mass, and thermogravimetric analysis (TG, DTG). The activation spectra, thermodynamic parameters, such as,  $\Delta E^*$ ,  $\Delta H^*$ ,  $\Delta S^*$  and  $\Delta G^*$  were calculated from the TG curves using Coats-Redfern method. It is important to investigate their structures to know the active groups and weak bond responsible for their biological activities. The obtained thermal (TA) and mass (MS) practical results are confirmed by semi-empirical MO-calculation using PM3 procedure, on the neutral and positively charged forms of these novel Schiff bases. Therefore, comparison between MS and TA helps in selection of the proper pathway representing the decomposition of these compounds to give indication about their structures and consequently their biological activities. Their biological activities have been tested in vitro against Escherichia coli, Proteus vulgaris, Bacillissubtilies and Staphylococcus aurous bacteria in order to assess their antimicrobial potential.

Keywords: Novel Schiff's bases; spectroscopic investigation; thermal analyses; molecular orbital calculation; biological activity.

#### Introduction

The preparation and characterization of new macrocyclic compounds with additional donor atoms appended to ring have attracted considerable interest because of their capacity to bind and transport metal ions from environmental media, and due to their biological activities [1]. Schiff bases are the most widely used organic compounds. They have been shown to exhibit a broad range of biological activities, including antifungal, antibacterial, antimalarial, anti-proliferative, anti-inflammatory, antiviral, and antipyretic properties. This review summarizes the synthesis and biological activities of Schiff bases and their complexes [2]. There is a continued interest in synthesizing macrocyclic ligands [3–7] because of their potential applications in fundamental and applied sciences [7–9] and importance in the area of coordination chemistry [10, 11]. The development of bio-organic chemistry field has been another important factor in spurring the growth in interest in macrocyclic compounds [12].

Schiff's bases were important class of compounds, due to their variety of applications including biological, clinical, analytical and industrial in addition to their important roles in catalysis and organic synthesis [13–17]. Schiff bases [18] were still regarded as one of the most potential group of organic compounds for facile preparations of metallo-organic hybrid materials. In the past two decades, the properties of Schiff base stimulated much interest for their noteworthy contributions to single molecule-based magnetism, material science [19], catalysis of many reactions like carbonization, oxidation, reduction [20], their industrial applications [21], complexing ability towards some toxic metals [22]. The interest in Schiff base compounds as analytical reagents is increasing since they enable simple and inexpensive determinations of different organic and inorganic substances [23]. The importance of the present work stems from

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preparation of two novel Schiff bases (EB1 and L1), its characterization and its hopeful applications in different industrial and life sides applications.

#### 2. Experimental

#### 2.1. Materials and reagents

All chemicals used in this study were of the analytical reagent grade and of highest purity available. Organic solvents used included absolute ethyl alcohol and dimethylformamide (DMF). These solvents were spectroscopic pure from British Drug House (BDH). Distilled water collected from all glass equipment was used in all studies in aqueous solutions. The other materials such as, (Salicylaldehyde, 1, 2-dibromoethane) (Sigma), (hydrazinecarbothioamide, 4, 6-diaminopyrimidine-2-thiol) (Aldrich) were also used as it is.

#### 2.2. Instruments

Elemental microanalyses of the prepared macrocyclic Schiff bases (EB1and L1) for C, H, N and S were performed in the micro-analytical center at Cairo University. The analyses were repeated twice to check the accuracy of the data. Infrared spectra were measured using a Perkin- Elmer FT-IR type 1650 spectrophotometer in the wavenumber region 4000– 400 cm<sup>-1</sup> as KBr disks. The <sup>1</sup>H-NMR spectra were recorded with a varian-300 MHz in DMSO-*d6* as solvent, where the chemical shifts were determined relative to the solvent peaks. The thermal analyses (TG and DTG) were carried out in dynamic nitrogen atmosphere (20 mL min<sup>-1</sup>) with a heating rate of 10°C min<sup>-1</sup>using Shimadzu TG-60H thermal analyzers. The mass spectrum was recorded by the EI technique at 70 eV using MS-5988 GS-MS Hewlett-Packard instrument.

#### 2.3. Synthesis of the Schiff bases

EB1 Schiff base was synthesis by reaction of 30 mL of ethanol hot solution (60°C) of bisaldehyde (2, 2'-(ethane-1,2-diylbis(oxy))dibenzaldehyde)(1g,  $3.7x10^{-3}$  mole) and 30 ml hot ethanol solution (60°C) of ( hydrazine carbothioamide)(0.674g,  $7.4x10^{-3}$  mole) in ratio (1:2). In preparation of L1 Schiff base 30 mL of ethanol hot solution (60°C) of bisaldehyde (2, 2'-(ethane-1,2-diylbis(oxy))dibenzaldehyde)(1g,  $3.7x10^{-3}$  mole) was mixed with 30 ml hot ethanol solution (60°C) (4,6-diaminopyrimidine-2-thiol)(0.525g,  $3.6x10^{-3}$  mole) in ratio (1:1). Then sulfuric acid was added to eliminate water through condensation, and then the reaction mixture was left under reflux for 2 h.

The formed solid Schiff's bases were separated by filtration and purified by crystallization from ethanol. This preparation can be summarized in the following scheme Acceleration 1:



Scheme 1: Preparation of EB1 and L1 Schiff's bases

#### 3. Results and Discussion

### 3.1. Characterization of the prepared Schiff's bases

The Schiff's bases under investigation were characterized by elemental, spectroscopic (FT-IR, <sup>1</sup>H-NMR, mass) and thermal analyses (TG and DTG). They are stable at room temperature and commonly soluble in DMF and DMSO. The elemental analyses, yields and melting points, of these compounds are presented in Table 1.

#### Table 1

Schiff's bases	Colour	M.P		% Found	l (Calcd.)	
	(% yield)	(°C)	С	Н	N	S
EB1	Pale	230	51.59	4.51	19.92	15.47
$C_{18}H_{20}N_6O_2S_2$	yellow		(51.90)	(4.84)	(20.18)	(15.40)
mole mass = $410.320$	( 09 )					
L1	White	250	64.07	4.43	14.28	9.14
$C_{20}H_{16}N_4O_2S$	(77)		(63.81)	(4.28)	(14.88)	(8.52)
mole mass $= 376.10$						

Elemental and physical data of Schiff's bases (EB1 and L1)

The proposed structural formulae of EB1 and L1 and their numbering systems are given by Figs. 1 and 2 respectively.



Fig 1: The numbering System of EB 1





Fig 2: Numbering System of L1

# 3.1.1. <sup>1</sup>H-NMR

The <sup>1</sup>H-NMR data of the prepared Schiff's bases are given in Fig 3.



#### Fig 3:<sup>1</sup>HNMR of Schiff's bases

The <sup>1</sup>H-NMR data of (2, 2'-(ethane-1,2-diylbis(oxy))dibenzaldehyde) bis aldehyde is featured by the appearing of a peak at chemical shift of 4.560 ppm which concerned to CH<sub>2</sub> group at aliphatic region and peaks from 6.980-8.521 ppm concerned to phenyl group at aromatic region and a peak of aldehydic group CHO at 10.302 ppm. These peaks are considered as finger print for bis aldehyde. The <sup>1</sup>H-NMR for hydrazine carbothioamide is characterized by chemical shift of NH group at 2.0 ppm and NH<sub>2</sub> group at 8.56 ppm. The <sup>1</sup>H-NMR for 4, 6-diaminopyrimidine-2-thiol is characterized by NH<sub>2</sub> group at 7.74 ppm and a peak of SH group appeared at 12.15 ppm. Through the preparation of EB1; the condensation reaction between (2, 2'-(ethane-1, 2-diylbis (oxy)) dibenzaldehyde) bis aldehyde and hydrazine carbothioamide lead to disappear of CHO group (10.302 ppm) and NH<sub>2</sub> peak for hydrazine carbothioamide. The remaining peaks of

CH<sub>2</sub> (at 4.560 ppm); phenyl groups at aromatic region, and the NH, NH<sub>2</sub> peaks at 3.8 and 12.2 ppm in H1-NMR of EB1 Schiff base confirm its formation via condensation of the given reactants. On formation of L1 Schiff base, the signals of CHO (10.302 ppm) and NH<sub>2</sub> (12.2 ppm) groups are disappeared during condensation process between reactants. The remaining signals of CH<sub>2</sub> (4.560 ppm) for bisaldehyde, and of SH group (5.2 ppm) for 4, 6-diaminopyrimidine-2-thiol through the condensation reaction; confirms the formation of L<sub>1</sub> [24, 25].

#### 3.1.2. FT-IR spectral studies

The FT-IR spectral data of (2, 2'-(ethane-1, 2-divlbis (oxy)) dibenzaldehyde) bis aldehyde is characterized by appearing of a peak at 3000 cm<sup>-1</sup> which characterized to CH<sub>2</sub> group. The peaks from 1700 - 1500 cm<sup>-1</sup> are assigned to phenyl groups and a peak of aldehydic group CHO at (1720 cm<sup>-1</sup>), these peaks are considered as underling featured for the bis aldehyde. The FT-IR spectral data for hydrazine carbothioamide are featured by NH and NH<sub>2</sub> groups at 3100-3500 cm<sup>-1</sup> and of C=S peak at 1180 cm<sup>-1</sup>. The FT-IR spectral data for 4,6-diaminopyrimidine-2-thiol are characterized by NH<sub>2</sub> group at 3200 cm<sup>-1</sup>, the azomethine stretching modes at 1597-1580 cm<sup>-1</sup> and a peak of SH group appeared at 3300 cm<sup>-1</sup> [26, 27]. Through the preparation of EB1; the condensation reaction between (2,2'-(ethane-1,2-diylbis(oxy))dibenzaldehyde)bisaldehyde and hydrazine carbothioamide lead to the disappear of CHO group (1720 cm<sup>-1</sup>) and NH<sub>2</sub> peak (3400 cm<sup>-1</sup>) for hydrazine carbothioamide. The remaining peaks of CH<sub>2</sub> at 3000 cm<sup>-1</sup>, of phenyl groups at 1600cm<sup>-1</sup>, the NH, NH<sub>2</sub> peaks at 3100, 3382 cm<sup>-1</sup>, the appearance of (N-N) group at 1238 cm<sup>-1</sup> and a band at 1520 cm<sup>-1</sup> characteristic of the azomethine stretching modes confirm the formation of EB1 Schiff base [28]. On formation of L1 Schiff base, the peaks of CHO (1720 cm<sup>-1</sup>) and NH<sub>2</sub> (3400 cm<sup>-1</sup>) groups are disappeared. The remaining of signals of CH<sub>2</sub> (3000 cm<sup>-1</sup>) for bis aldehyde and SH group (3128 cm<sup>-1</sup>) for 4, 6-diaminopyrimidine-2-thiol through the condensation reaction also confirms the formation of  $L_1$  [29].

3.2. Thermal analyses studies (TG and DTG) and Thermodynamic calculations in comparison with molecular orbital calculations (MOCs)

3.2a. TG and DTG

The TG and DTG results of thermal decomposition of the EB1 are recorded in Table (2).

Table 2

Thermal analyses results (TG and DTG) of Schiff's bases

Compound	TG range (°C)	DTG <sub>max</sub> (°C)	n <sup>*</sup>	Mass Loss Total mass Loss Calcd (Estim) %	Assignment
L1	45-448 448-863	300 640	1 2	36.8 (36.11) 63.15 (63) 99.95(99.11)	-Loss of $C_5H_5N_3S$ Mole mass = 139.18 -Loss of $C_{15}H_{15}NO_2$ mole mass = 241.29
EB1	220-282 282-380 400-600	231.4 323.2 579.43	1 2 3	23.36(24) 32.17 (33) 43.42(43) 98.95 (100)	-Loss of $C_2H_4N_3S$ Mole mass = 103 -Loss of $C_8H_8O_2$ mole mass = 138 - Loss of $C_8H_8N_3S$ Mole mass = 179

n<sup>\*</sup> = number of decomposition steps.

The thermogram of EB1 refers to the decomposition of this Schiff base in three steps of total estimated mass loss of 100.00 % (calcd. 98.95%). The first step occurs within the temperature range 220-282°C and exactly at 231.46 (DTG) of estimated mass loss of 24 % (calcd. 23.36%); which may be attributed to the decomposition of N-methylene-hydrazinecarbothioamide of chemical formula  $C_2H_4N_3S$  (mole mass =103.15). The second step occurs within the temperature range 282-380°C and exactly at 323.28°C (DTG). It refers to the estimated mass loss of 33 % (calcd. 32.17 %); which may be attributed to the decomposition of 2-phenoxyethanol of chemical formula  $C_8H_8O_2$  (mole mass = 138.16). Finally the third step occurs within the temperature range 400-600°C, and exactly at 579.43°C (DTG). It refers to the estimated to the decomposition of 2.3.42%); which may be attributed to the decomposition of (Z)-N-benzylidene-hydrazinecarbothioamide of chemical formula $C_8H_8N_3S$  (mole mass =179.24).

Thermal decomposition data of L1 are listed in Table (2) of total estimated mass loss of 99.95 % (calcd. 99.11%). It decomposes in two steps; the first step can be attributed to the loss of 4-(methyleneamino) pyrimidine-2-thiol of chemical formula  $C_5H_5N_3S$  (mole mass = 139.18) of an estimated mass loss 36.80% (calcd. 36.11%). It occurs within the temperature range 45-448°C and exactly at 300°C (DTG). The second step corresponds to the removal of (2-(2-phenoxyethoxy)phenyl) methanimine of chemical formula $C_{15}H_{15}NO_2$  (mole mass = 241.29 ) of an estimated mass loss 63.15% (calcd. 63%). It occurs within the temperature range 448-863°C and exactly at 640°C (DTG). The parent ion and the fragment ions obtained by cleavage of weak bonds in different positions in EB1 and L1 skeleton are shown in Scheme 2.





Scheme 2: Thermal decomposition pathways of Schiff's bases (EB1 and L1)

## 3.2b. Thermodynamic functions ( $\Delta H$ , $\Delta E$ , $\Delta G$ , $\Delta S$ )

The thermodynamic parameters obtained from TG data are given in Table 3.

Table 3

Thermodynamic data of the thermal decomposition steps of Schiff's bases

Schiff's	Decomp.	A	$\Delta E^*$ kJ mol <sup>-1</sup>	$\Delta S^*$	ΔH <sup>*</sup>	$\Delta G^*$
bases	Temp. °C	s <sup>-1</sup>		JK <sup>-1</sup> mol <sup>-1</sup>	kJmol <sup>-1</sup>	kJmol <sup>-1</sup>
L1	45-448	2.24 x10 <sup>8</sup>	28.26	-136.82	27.62	170.96
	448-863	3.79x10 <sup>5</sup>	31.42	-69.44	25.02	78.44

EB1 $150-375$ $375-530$ $1.02x10^6$ $70.20$ $-132.0$ $145$			$4.10 \times 10^{5}$	63.20	-37.00	60.80	90.00
	EB1	150-375 375-530 530-970	$1.02 \times 10^{6}$	70.20	-132.0	145.7	171.0
$530-970 \qquad 4.03 \times 10^8 \qquad 51.70 \qquad -187.0 \qquad 220$			$4.03 \times 10^8$	51.70	-187.0	220.3	247.0

The data of Schiff base (EB1) refer to the values of activation energy  $E^* = 63.20$ , 70.20 and 51.70 kJmol<sup>-1</sup> required for the three weight losses respectively. This means that the loss of aliphatic part of the Schiff base required 63.20 kJ mol<sup>-1</sup> and the second step required more energy = 70.20 kJ mol<sup>-1</sup> as a result of stability of the formed part in this step (scheme 1). The remainder part is easily decomposed at higher temperature as it required 51.70 kJmol<sup>-1</sup>  $\Delta$ H\* (60.80-220.30 k J mol<sup>-1</sup>) and  $\Delta$ G\* (247-290 kJmol<sup>-1</sup>) obtained as a result of three weight losses given in scheme 2. The variation of  $\Delta$ S\* negative values (-37.0 to - 187.0 J K<sup>-1</sup>mol<sup>-1</sup>) may refer to the variation of degree of disorder of the system during the various steps of weight losses. The high negative value of entropy of the third step may refer to the chemical rearrangement and/ or chemical recombination of the Schiff base fragments to give chemical formulae in scheme 1.

The thermodynamic parameters (Table 3) obtained from TG data of L1 of  $\Delta$ H\* (27.62 - 25.02 kJmol<sup>-1</sup>) and  $\Delta$ G\* (170.96-78.44 kJmol<sup>-1</sup>); confirm the mass losses in two steps (scheme 1). The obtained  $\Delta$ S\* negative values (-136.82 to -69.44 JK<sup>-1</sup>mol<sup>-1</sup>) refer to the variation of degree of disorder of the system during the various steps of weight losses. The less negative entropy values may refer to increase of disorder during the decomposition of this Schiff base, which may be attributed to the less stability of this Schiff base. The negative value of entropy may refer the chemical rearrangement and/ or chemical recombination of the L1 fragments to give chemical formulae in scheme 1.

3.2c. Comparison of TA data of EB1 and L1 and MOCs

The molecular orbital calculations (MOCs) were performed using PM3 procedure. These calculations depends on the numbering systems of EB1 (Fig 1) and L1 (Fig 2). The obtained data for both neutral and cationic forms of these Schiff's bases are represented in Table 4.

#### Table4

Comparison between computed bond length (in Å) and bond order using PM3 method for neutral and molecular cation of EB1 and L1

	Bond	Bond lengtl	n (Å ) (EB1)	Bond or	der(EB1)
	(EB1)	Neutral	Cation	Neutral	Cation
	C1-C17	1.465912	1.461237	0.997954	1.020780
	C2-O13	1.383317	1.382540	1.039134	1.027415
	C10-O16	1.380703	1.221653	1.016517	1.851539
	C11-C18	1.471868	1.405402	0.973985	1.300674
	O13-C14	1.415749	1.426426	0.968669	0.965761
	C17-N19	1.288453	1.293425	1.878477	1.834637
	N19-C21	1.416259	1.418929	1.083078	1.073761
	N20-C22	1.419334	1.378805	1.067639	1.232210
	C21-N23	1.402510	1.387189	1.235095	1.303649
	C22-N24	1.398227	1.388564	1.250409	1.256957
]	Bond(L1)	Bond l	ength (Å )	Bond or	der (L1)
		Neutral	Cation	Neutral	Cation
	C1-C17	1.463082	1.442052	0.997954	1.020780
	C2-O13	1.381855	1.367691	1.039134	1.027415
	C9-C10	1.398861	1.467544	1.378111	1.004718
	C11-C12	1.398157	1.381822	1.392363	0.997748
	C10-O16	1.393520	1.233220	1.016517	1.851539
	C11-C18	1.471065	1.467612	0.973985	1.300674
	O13-C14	1.421096	1.426807	0.968669	0.965761
	C14-C15	1.532990	1.466826	0.972974	1.025198
	C17-N19	1.296825	1.286409	1.878477	1.834637
	C18-N20	1.284715	1.261189	1.909550	1.403216
	N19-C22	1.410753	1.343037	1.083078	1.073761
				<sup> </sup>	

$\Delta H_{f}$ (kcal/n	$\Delta H_{f}$ (kcal/mol)(EB1)		)(EB1)	номо	LUMO(eV)(EB1)
Neutral	Cation	Neutral	Cation	(eV)(EB1)	
134.64	336.80	8.89	9.82	-8.89	-1.38
$\Delta \mathbf{H}_{\mathbf{f}} (\mathbf{kcal/mol}) (\mathbf{L1}) \qquad \mathbf{IE}(\mathbf{eV})(\mathbf{L1})$		номо	LUMO(eV)(L1)		

				(eV)(L1)	
183.68	362.33	9.40	12.16	-9.40	-2.243

It seems important to compare between TA data and theoretical MOCs calculated parameters (Table 4) for neutral forms of the given Schiff's bases (EB1 and L1) in order to rationalize the thermal fragmentation pathways (Scheme 2) of these compounds depending upon strength ordering of compounds bonds (Table 4). The ordering of the compound bond depends on the values of bond length and bond orders. The weakest bond is that of longest bond length and of the lowest bond order values. The first step of thermal cleavage of EB1 starts by the weakest bond C11-C18 bond (1.471868, 0.973985); which gives  $C_2H_4N_3S$  (mole mass= 103.15) with percent mass loss = 24 %. This conclusion rationalized the first step of thermal fragmentation of EB1 Schiff base. It followed by the thermal cleavage of the second weak bond (C2-O13) of bond length and bond order (1.383317, 1.039134). This thermal cleavage in the second step gives two compounds  $C_8H_8N_3S$  (mole mass= 179.24 of 43%) and  $C_8H_8O_2$  (mole mass=138.16 of 33%); which confirms the proposed thermal scheme of EB1. The thermal fragmentation of L1 involved the thermal cleavage of the weakest bonds N20-C26 (3.539787, 1.067639) and C1-C17 (1.463082, 0.997954) consecutively according to MOCs data. This cleavage gives two paths ways. First one gives C<sub>5</sub>H<sub>5</sub>N<sub>3</sub>S (mole mass=139.18 of 36.8%) and second one gives  $C_{15}H_{15}NO_2$  (mole mass= 241.29 of 63.15%); which is reasonably assigned to the thermal fragmentation of L1 as given in scheme2. This discussion gives more clarification for thermal behavior of both EB1 and L1 Schiff's and confirm their proposed structural formulae. The positive values of the calculated thermodynamic parameters for the thermal decomposition three steps of EB1 ( $\Delta E^*$  = 63.20, 70.20 and 51.70 kJmol<sup>-1</sup>;  $\Delta H^* = 60.80-220.30$  k J mol<sup>-1</sup> and  $\Delta G^* = 247-290$ kJmol<sup>-1</sup>) and its positive heat of formation  $\Delta H_f = 134.64$  kcal mol<sup>-1</sup> and low ionization energy = 8.89 (eV) obtained from MOCs may refer to the less stability of EB1, which is main reason for its easily thermal fragmentation. Also the positive values of thermodynamic parameters (Table 3) obtained from TG data of L1 of  $\Delta H^* = 27.62$  -25.02 and  $\Delta G^* = 170.96-78.44 \text{ kJmol}^{-1}$ ,  $\Delta H_f = 183.68 \text{ kcal mol}^{-1}$ , and IE = 9.40 (eV)

obtained from MOCs; may rationalize the easily thermal decomposition of this Schiff's base in two steps as given in scheme 1.

#### 3.3. Mass spectra of EB1 and L1 Schiff's bases in comparison with MOCs

#### 3.3a. Mass spectra

The electron impact spectra (MS) of the newly prepared EB1 and L1 Schiff bases are recorded at 70 eV (Fig 4).



Fig 4: Mass spectra of Schiff's bases (EB1 and L1)

The mass spectra of EB1 show a peak of moderate intensity (RI% = 17.9%) at m/z = 416 ( $M^+$ ); which refers to the molecular ion of the Schiff base (mole mass =416). It also shows the fragment ions at m/z = 64, 91, 119, 103, 146 and 266. These peaks may be assigned to SO<sub>2</sub>

gas molecule, hydrazinecarbothioamide of chemical formula  $CH_5N_3S$ , 2-(iminomethyl) phenol ( $C_7H_7NO$ ), N-methylene-hydrazine carbothioamide of chemical formula  $C_2H_4N_3S$ , (2-ethoxyphenyl) methanimine ( $C_9H_{11}NO$ ) and ((ethane-1,2-diylbis(oxy))bis (2,1-henylene)) dimethanimine ( $C_{16}H_{16}N_2O_2$ ) fragments of mole masses 64, 91, 119, 103, 146 and 266 respectively. The parent and the fragment ions obtained by bond cleavage in different positions in EB1 molecule are shown in Scheme 3.





Scheme 3: Mass fragmentation pathways of Schiff's bases (EB1 and L1)

This scheme refers to the possible structural formulae of these fragments and their possible names using IUPAC system.

The mass spectra of L1 shows a molecular ion main peak at m/z= 377 (mole mass = 377). It also shows fragment ions of m/z = 63, 91, 119, 146, 181, 210, 238, and 264 respectively. These fragment ions may be assigned to the following molecules (Z)-penta-1,3-diene of chemical formula  $C_5H_8$ , toluene of chemical formula  $C_7H_8$ , ethoxybenzene of chemical formula  $C_8H_{10}O$ , 4,6-diaminopyrimidine-2-thiol of chemical formula  $C_4H_6N_4S$ , (2-(allyloxy)ethoxy)benzene of chemical formula C<sub>11</sub>H1<sub>4</sub>O<sub>2</sub>, 1,2-diphenoxyethane of chemical formula  $C_{14}H_{14}O_2$ , 1,2-bis(o-tolyloxy) ethane of chemical formula formula  $C_{16}H_{18}O_2$  and ((ethane-1,2-diylbis(oxy))bis(2,1-phenylene))dimethanimine of chemical formula  $C_{16}H_{16}N_2O_2$  of mole masses 63, 91, 119, 146, 181, 210, 238, and 264 respectively. It is obvious that, the molecular ion peaks of the prepared Schiff bases are is in good agreement with its suggested empirical formulae as indicated from elemental

analyses (Table1). The parent ion and the fragment ions obtained by cleavage of weak bonds in different positions in EB1 and L1 skeleton are shown in Scheme 2.

# 3.3. b. Correlation between mass spectral fragmentation and MO calculation for charged molecule.

The MOCs calculation of EB1 cationic form helps us to predict view of fragmentation process. The mass fragmentation of EB1 Schiff base followed the bond strength ordering due to the calculated values of bond length and bond order (Table 4) of its cationic form. This mass fragmentation starts with the cleavage of the weakest bond C15-O16 (5.301821, 0.000030) and N20-C22 (1.378805, 1.232210) which gives  $C_7H_7NO$  (mole mass=119) and agree well with mass fragmentation (m/z=119) (Table 4). It followed by C1-C17 bond cleavage of bond length and bond order values (1.461237, 1.020780) which gives  $C_2H_4N_3S$  (mole mass= 103.15) and this agrees well with mass fragmentation (m/z=103). The bond C17-N19 (1.293425, 1.834637) rupture gives  $CH_5N_3S$  (mole mass= 91.14) which agrees well with mass fragmentation (m/z = 91).  $SO_2$ gas (mole mass= 64) produced as a result of cleavage of bonds N20-C22 (1.378805, 1.232210) and C22-N24 (1.388564, 1.256957); which compatible with mass fragmentation (m/z=64). The rupture of bonds N20-C22 (1.378805, 1.232210) and N19-C21 (1.418929, 1.073761) gives  $C_{16}H_{16}N_2O_2$  (mole mass= 266); which of the same as mass fragment (m/z=266). The cleavage of bonds O13-C14 (1.426426, 0.965761) and N20-C22 (1.378805, 1.232210) gives  $C_9H_{11}NO$  (mole mass= 146); which agrees well with mass fragmentation (m/z=146).

On the other hand  $L_1$  fragmentation according to MOCs starts with more long bonds length and less bond order (Table 4). It starts with the cleavage of the weakest bond C15-O16 (6.362245, 0.000030) to give C<sub>8</sub>H<sub>10</sub>O (mole mass=119) and this confirms the mass fragment ion (m/z=119). The bonds N20-C26 (3.955758, 1.232210) and N19-C22 (1.343037, 1.073761) rupture gives  $C_{16}H_{16}N_2O_2$  (mole mass= 264) and this confirms mass fragmentation (m/z=264). It followed by rupture of bonds C17-N19 (1.286409, 1.834637) and C18-N20 (1.261189, 1.403216) that gives a fragment  $C_{16}H_{18}O_2$ (mole mass=238); which harmonious with mass fragment ion (m/z=238). The rupture of bonds C11-C18 (1.467612, 1.300674) and C1-C17 (1.442052, 1.020780) gives  $C_{14}H_{14}O_2$ (mole mass= 210), this compatible with mass fragment ion (m/z=210). And follow- up

rupture of bond C11-C18 (1.467612, 1.300674) gives  $C_{11}H_{14}O_2$  (mole mass=181) and this is in agreement with mass fragment ion (m/z=181). The bonds C2-O13 (1.367691, 1.027415) and C17-N19 (1.286409, 1.834637) rupture gives  $C_7H_8$  (mole mass= 91) and this compatible with mass of fragment ion (m/z=91). The follow-up cleavage of bonds C9-C10 (1.467544, 1.004718) and C11-C12 (1.381822, 0.997748) gives  $C_5H_8$  (mole mass= 63); which compatible with mass fragmentation (m/z=63). The bonds cleavage C18-N20 (1.261189, 1.403216) and C17-N19 (1.286409, 1.834637) gives  $C_4H_6N_4S$ (mole mass=146; which agreement with mass fragmentation (m/z=146) (Table 4).

#### 3.4. Comparison between MOC, MS and TA

The MO calculation helps us to understand the correlation between thermal analysis and mass fragmentation. In case of EB1 the first bond cleavage C11-C18 in thermal analysis which give  $C_2H_4N_3S$  (mole mass = 103.15). This compound included hydrazinecarbothioamide compound of chemical formula  $CH_2N_3S$  (mole mass = 91.14); which is compatible with mass fragmentation (m/z=91). The second thermal fragment as a result of C2-O13 bond cleavage gives 2-phenoxyethanol compound of chemical formula:  $C_8H_8O_2$  (mole mass = 138.16); which included  $C_8H_6O$  (mole mass =119) that detected in mass fragmentation (m/z=119). Finally the last thermal fragment obtained as a result of C2-O13 bond cleavage gives  $C_8H_8N_3S$  (mole mass = 179.24); which included  $C_8H_4NS$  (mole mass = 146) that detected as mass fragment ion (m/z=146) (Table 4).

The thermal fragmentation of L1 refers to the cleavage of bonds (N20-C26, C1-C17); which gives two compounds. The first one is  $C_5H_5N_3S$  (mole mass=139.18). This compound included  $C_4H_5N_3$  (mole mass= 91.14); which is compatible with mass fragment ion (m/z=91). The second fragment is  $C_{15}H_{15}NO_2$  (mole mass= 241.29); which included the  $C_7H_7NO$  (mole mass = 119). This compound is also found in mass as fragment ion (m/z=119) (Table 4).

#### 3.5. Biological activity

Schiff bases are important class of compounds in medicinal and pharmaceutical fields. They show biological applications including antibacterial [30-33] and antitumor activities. Antibacterial activity of the Schiff bases (EB1 and L1) were tested by diffusion

agar method, Streptomycin was used as a reference compound for antibacterial activities. In testing the antibacterial activity of these compounds, more than one test organism was used to increase the chance of detecting antibiotic principles in tested materials. Two Gram-positive (*Bacillus subtilis* ATTC 6051 and *Streptococcus pneumonia* ATTC 12600) and two Gram-negative (*Escherichia coli* ATTC 11775 and Pseudomonas *aeruginosa* ATTC 13315) *bacteria* were used as test organisms. The antibacterial activity was evaluated by measuring the inhibition zone (mm) and MIC 50 Table (5). Also it is found that the Schiff-base L<sub>1</sub> has more sensitivity for gram positive (15.2 and 14.5 mm) in case of *B. subtilis* and *S. pneumonia* than gram negative *bacteria*. (10.2 and 11.6 mm) in case of P. aeruginosa and E. coli respectively, means The activity follows the order *B. subtilis* and *S. pneumonia* than gram positive (13.1 and 13.8 mm) in case of *B. subtilis* and *S. pneumonia* than gram negative *bacteria*. (12.9 and 12.7 mm) in case of *P. aeruginosa* and *E. coli* respectively, but recorded high MIC <sub>50</sub> (>100 mg mL<sup>-1</sup>) in both tested bacteria.

#### 4. Conclusion

This manuscript involved preparation of two novel Schiff's bases (EB1 and L1) and their structures were characterized by elemental, spectroscopic (Ft-IR, <sup>1</sup>H-NMR, mass) and thermal techniques. Their structures were confirmed by comparatives studies between practical techniques (TA and MS) and theoretical molecular orbital calculations. Antibacterial activity of the Schiff bases (EB1 and L1) were tested by diffusion agar method, Streptomycin was used as a reference compound for antibacterial activities. They were found to be as biologically active macrocyclic compounds.

#### **Reference**:

- D. Sinha, A. K. Tiwari, S. Singh, G. Shukla, P. Mishra, H. Chandra, A. K. Mishra. Synthesis, characterization and biological activity of Schiff base analogues of indole-3-carboxaldehyde. Europ. J. Medic. Chem. 43 (1) (2008) 160–165.
- [2] W. Zoubi. Biological Activities of Schiff Bases and Their Complexes: A Review of Recent Works, Internat. J. Org. Chem. 3 (3A) (2013) 73-95.

- [3] J.L. Chen, X.Z. Tan, X.X. Chen, J.Y. Wang, X.F. Cao, L.H. He, J.Y. Hua, H.R. Wen, Luminescent mononuclear Pt(II) chloride complexes with C-linked 2,2'-bipyridyl tetrazole terdentate chelating ligands. Inorg. Chem. Commun. 30 (2013) 120–123.
- [4] O.A. El-Gammal, G. M. Abu El-Reash, M. M. El-Gamil, Structural, spectral, pHmetric and biological studies on mercury (II), cadmium (II) and binuclear zinc (II) complexes of NS donor thiosemicarbazide ligand. Spectrochim. Acta Part A: 123 (2014) 59–70.
- [5] G.M. Abu El-Reash, O.A. El-Gammal, M.M. El-Gamil, Structural, spectral, DFT, pH-metric and biological studies on Cr(III), Mn(II) and Fe(III) complexes of dithione heterocyclic thiosemicarbazide ligand. Spectrochim. Acta A 104 (2013) 383–393.
- [6] M. Kumru, T. Bardakc, S. Guner, Spectrochim, DFT calculations and experimental FT-IR, dispersive-Raman and EPR spectral studies of Copper (II) chloride complex with 3-amino-1-methylbenzene Spectrochim. Acta A 123 (2014) 187–193
- [7] M. Kumru, V. Kucuk, P. Akyurek, Vibrational spectra of quinoline-4-carbaldehyde: Combined experimental and theoretical studies. Spectrochim. Acta Part A 113 (2013) 72–79.
- [8] M. Labanowska, E. Bidzinska, A. Parab, M. Kurdziela, EPR investigation of Cu(II)complexes with nitrogen derivatives of dialdehyde starch. Carbohyd. Polym. 87 (2012) 2605-2613.
- [9] W. H. Mahmoud, G.G. Mohamed, M. M.I. El-Dessouky, Coordination modes of bidentate lornoxicam drug with some transition metal ions. Synthesis, characterization and in vitro antimicrobial and antibreastic cancer activity studies. Spectrochim. Acta Part A: 122 (2014) 598–608.
- [10] D.P. Singh', Ramesh Kumar, Jitender Singh, Synthesis and spectroscopic studies of biologically active compounds derived from oxalyldihydrazide and benzil, and their

Cr(III), Fe(III) and Mn(III) complexes. Europ. J. Med. Chem. 4 (44),(2009), 1731– 1736

- [11] R.M. Izatt, J.S. Brandshaw, S.A. Neilsen, J.D. Lamb, J.J. Christensen, D. Sen, Thermodynamic and kinetic data for cation-macrocycle interaction, Chem. Rev. 85 (1985) 271.
- [12] M. A. Subhan , J.H.Choi, X-ray structure and spectroscopy of novel *trans* [Ni(L)(NO<sub>3</sub>)<sub>2</sub>] and [Ni(L)](ClO<sub>4</sub>)<sub>2</sub>·2H<sub>2</sub>O complexes, Spectrochim. Acta Part A: 123 (2014) 410–415.
- [13] Hanan F. Abd El-halim M.M. Omar Gehad G. Mohamed, Synthesis, structural, thermal studies and biological activity of a tridentate Schiff base ligand and their transition metal complexes, Spectrochim. Acta Part A: 78 (1) (2011) 36-44.
- [14] H. F.Abd El-Halim, M. M. Omar, G. G. Mohamed, M.A. ElaSayed. Spectroscopic and biological activity studies on tridentate Schiff base ligands and their transition metal complexes. Europ. J. Chem. 2 (2), (2011), 178-188.
- [15] A. Datta, N.K. Karan, S. Mitra, G. Rosair, Synthesis and Structural Characterization of [Cu(NH<sub>2</sub>CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>N=CHC<sub>5</sub>H<sub>5</sub>N)Cl<sub>2</sub>]. Naturforsch. 57b (2002) 999-1002.
- [16] Suraj B Ade, Kolhatkar DG, Deshpande MN, Synthesis, Characterization, Spectroscopic Studies and Antimicrobial Activity of 2-(2-Hydroxy-3-methoxy benzylidene amino)-4-chlorobenzoic acid with chelates of Cd(II) and Hg(II) ions Internat. J. Res. Pharm. Biomed. Scien. 3 (1) 282-285.
- [17] H. Sharghi, M.A. Nasseri, Schiff-Base Metal(\_) Complexes as New Catalysts in the Efficient, Mild and Regioselective Conversion of 1,2-Epoxyethanes to 2-Hydroxyethyl Thiocyanates with Ammonium Thiocyanate, Bull. Chem. Soc. (Jpn.) 76 (2003) 1-37.

- [18] T. Sixt e W. Kaim, Copper(I) complexes with N,O-donor Schiff base ligands related to intermediate forms of the TPQ cofactor in amine oxidases. Inorg. Chim. 300 (2000) 762-768
- [19] M. Ulusoy, O. Birel, O. Sahin, O. Buyukgungor, B. Cetinkya, Structural, spectral, electrochemical and catalytic reactivity studies of a series of N<sub>2</sub>O<sub>2</sub> chelated palladium(II) complexes Polyhedron 38 (2012) 141-148.
- [20] D. Bose, J. Banerjee, S.K.H. Rahaman, G. Mostafa, H.K. Fun, W.R.D. Bailey, M.J.Zaworotko, B.K. Ghosh, Polymeric end-to-end bibridged cadmium(II)thiocyanates containing monodentate and bidentate N-donor organic blockers: supramolecular and/or  $C-H\cdots\pi$ synthons based on  $\pi - \pi$ interactionsPolyhedron 23 (2004) 2045-2053.
- [21] H.A. El-Boraey, Structural and thermal studies of some arolyhydrazone Schiff's ... complexes. J. Therm. Anal. Calorim.81 (2005) 339-346.
- [22] A.S.M. Al-Shirif, H.M. Abdel-Fattah, Thermogravimetric and spectroscopic characterization of trivalent lanthanide chelates with some schiff bases, J. Therm. Anal. Calorim.71 (2003) 643-649.
- [23] J. Estrela dos Santos, E.R. Dockal, E.T.G. Cavalheiro, J. Therm. Anal.Calorim. 79 (2003) 243.
- [24] Khalil, M. M. H., Mohamed, G. G., Ismail, E. H., Zayed, M. E., and Kamel, and B. A, Transition Metal Complexes Derived from Natural Schiff Bases for Determination of Fe (III) Spectrophotometrically in Natural Water, Chinese Journal of Inorganic Chemistry 28 (7) (2012) 1495-1505.
- [25] W. M. I. Hassan , E. M. Zayed , A. K. Elkholy, H. Moustafa , G. G. Mohamed, Spectroscopic and density functional theory investigation of novel Schiff base complexes, Spectrochimica Acta Part A 103 (2013) 378-387.
- [26] B. Schrader and W. Meier, Raman/IR Atlas of Organic Compounds

VerlagChemie, Weinheim, (1974), F1-16.

- [27] N. Raman, S. Sobha, A.Thamaraichelvan, A novel bioactive tyramine derived Schiff base and its transition metal complexes as selective DNA binding agentsSpectrochim.Acta, A. 78 (2011) 888-898.
- [28] S. Ilhan, H. Temel, I. Yilmaz, M.Sekerci, Synthesis, structural characterization and electrochemical studies of new macrocyclic Schiff base containing pyridine head and its metal complexes J. Organometall. Chem. 692 (2007) 3855-3865.
- [29] C.N.R. Rao,R. Venkataraghavan, The C=S stretching frequency and the "-N-C=S bands" Infrared Spectroscopy, 18, 1962, 541–547
- [30] M.S. Karthikeyan, D.J. Parsad, B. Poojary, K.S. Bhat, B.S. Holla, N.S. Kumari, Synthesis and biological activity of Schiff and Mannich bases bearing 2,4dichloro-5-fluorophenyl moiety Bioorg. Med. Chem. 14 (2006)7482–7489.
- [31] R Nirmal, CR Prakash, K Meenakshi, P Shanmugapandiyan, Synthesis and Pharmacological Evaluation of Novel Schiff Base Analogues of 3-(4-amino) Phenylimino) 5-fluoroindolin-2-one, J Young Pharm. 2(2) (2010) 162–168.
- [32] P. Panneerselvam, R.R. Nair, G. Vijayalakshmi, E.H. Subramanian, S.K. Sridhar. Synthesis of Schiff bases of 4-(4-aminophenyl)-morpholine as potential antimicrobial agents. European Journal of Medicinal Chemistry, 40 (2005)225–9.
- [33] K. Singh, M.S. Barwa, and P. Tyagi, Synthesis, characterization and biological studies of Co(II), Ni(II), Cu(II) and Zn(II) complexes with bidentate Schiff bases derived by heterocyclic ketone, European Journal of Medicinal Chemistry 41 (2006)147–53.

#### Table 5. Biological activity of Schiff's bases

Sample	Inhibition zone (mm/mg sample)/ MIC <sub>50</sub> (mg mL <sup>-1</sup> )							
	Gram negative		Gram	positive				
	Escherichia coli Pseudomonas		Bacillus	Streptococcus				
		aeruginosa	subtilis	pneumonia				
EB1	12.7	12.9	13.1	13.8				
	> 100	> 100	> 100	> 100				
L1	11.6	10.2	15.2	14.5				
	> 100	> 100	> 100	> 100				

#### **Graphical Abstract**

Two novel Schiff's bases as new macrocyclic compounds were prepared via condensation reactions between bisaldehyde (2, 2'-(ethane-1, 2- diylbis (oxy)) dibenzaldehyde): firstly with (hydrazine carbothioamide to give (EB1), secondly with (4, 6-diaminopyrimidine-2-thiol to give (L1). The structures of the compounds obtained were characterized based on elemental analysis, FT-IR and <sup>1</sup>HNMR spectra, mass (MS), and thermal analyses (TA).



## **High Lights**

- Preparation and characterization of two new macrocyclic Schiff bases (EB1 and L1).
- > They have great interest due to their environmental and biological activities.
- The thermal (TA) and mass (MS) results are confirmed by PM3 MOCs on compound forms.