Research Article

Zr(IV), La(III), and Ce(IV) Chelates with 2-[(4-[(Z)-1-(2-Hydroxyphenyl)ethylidene]aminobutyl)-ethanimidoyl]phenol: Synthesis, Spectroscopic Characterization, and Antimicrobial Studies

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La(III), Zr(IV), and Ce(IV) chelates of 2-[(4-[(Z)-1-(2-hydroxyphenyl)ethylidene]aminobutyl)-ethanimidoyl]phenol were synthesized and characterized by using several physical techniques. The Schiff base was obtained by refluxing of *o*-hydroxyacetophenone with 1,4-butanediamine in 2:1 molar ratio. The CHN elemental analysis results showed the formation of the Schiff base and the chelates has been found to be in 1:1 [M:L] ratio. The molar conductance measurements revealed that all the chelates are nonelectrolytes. Structural elucidations of the ligand and its chelates were based on compatible analytical and spectroscopic evidences. The infrared spectral data revealed that the Schiff base coordinates to the metal ions through active sites which are -OH and -C=N groups. According to the electronic spectral data, an octahedral geometry was proposed for the chelates. The synthesized ligand and its metal chelates were screened for their antimicrobial activity against two Gram negative (*Escherichia coli*, *Salmonella kentucky*) and two Gram positive (*Lactobacillus fermentum*, *Streptococcus faecalis*) bacterial strains, unicellular fungi (*Fusarium solani*), and filamentous fungi (*Aspergillus niger*). The activity data showed that the metal chelates have antibacterial and antifungal activity more than the parent Schiff base ligand against one or more bacterial or fungi species. The results also indicated that the metal chelates are higher sensitive antimicrobial agents as compared to the Schiff base ligand.

1. Introduction

Schiff bases are most widely used as chelating ligands in coordination chemistry and have been investigated extensively for the past several decades leading to new synthetic routes of structure, biological, and industrial applications [1]. They are also useful in catalyst chemistry and in medicine (pharmacology) as antibiotic, antiallergic, and antitumor agents [2]. The complexes of the type MLX_n, where M=VO(IV), Mn(II), Fe(III), Co(II), Ni(II), Zn(II) and Cd(II), X=H₂O/Cl⁻, and L is the Schiff base ligand derived from 2,4-dihydroxy-5-acetylacetophenone and 1,4-diaminobutane have been synthesized and isolated in solid state; they are stable in air. The

physicochemical data suggested a square pyramidal structure for VO(IV), pseudo octahedral structure for Cu(II), and an octahedral structure for Mn(II), Fe(III), Co(II), Ni(II), and Cd(II) complexes. The ligand field parameters have been calculated and related to the electronic environment. The Schiff base and its complexes were screened for their antimicrobial activities against various bacteria and fungi [3]. The lanthanide(III) complexes of the chloro, hydroxo substituted 14-membered tetraazamacrocyclic solid complexes of La(III), Ce(III), and Pr(III) have been synthesized and characterized. From the microanalytical data, the stoichiometry of the complexes has been found to be 1:1 (metal:ligand). The TGA-DSC data suggested that all lanthanide(III) complexes

have one ionic nitrate, two coordinated nitrate ions, two water molecules for Ce(III), and four water molecules for La(III) and Pr(III). The X-ray diffraction data suggested an orthorhombic crystal system for La(III) and monoclinic crystal system for Ce(III) and Pr(III) complexes [4].

In the present study we have reviewed the synthesis and characterization of Schiff base and its chelates with Zr(IV), La(III), and Ce(IV) ions. The antimicrobial activity of the Schiff base and its chelates also was screened against some pathogenic bacteria and fungi.

2. Experimental

2.1. Materials and Methods. The chemicals used in this investigation are of pure grade (Merck or Aldrich), including 2-hydroxyacetophenone, 1,4-diaminobutane, $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$, $\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$, and $\text{Ce}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$, $\text{C}_2\text{H}_5\text{OH}$, CHCl_3 , DMF, DMSO, and NH_4OH solution. The synthesized Schiff base and its chelates were subjected to CHN elemental analyses using Perkin-Elmer 2400 elemental analyzer, infrared spectra were obtained by KBr disc technique by using IFS-25DPUSR\IR spectrometer (Bruker) in the range of $4000\text{--}400\text{ cm}^{-1}$, and proton nuclear magnetic resonance spectrum of the Schiff base was recorded on Varian Gemini 200-200 MHz spectrometer using TMS as internal standard and D^6 DMSO as a solvent (Figure 11). The electronic spectra of the Schiff base and its Zr(IV), La(III), and Ce(IV) chelates were measured in DMSO solvent using a Perkin-Elmer-Lambda β -spectrophotometer. The mass spectra were carried out by using Shimadzu QP-2010 Plus. The molar conductivity of the chelates was measured in DMSO solvent using digital conductivity meter CMD 650, at Chemistry Department, Sebha University, Sebha, Libya. All the mentioned analyses were done at Micro Analytical Center, Cairo University, Giza, Egypt.

2.2. Preparation of the Schiff Base (SB). A Schiff base (SB) of 2-[(4-[(Z)-1-(2-hydroxyphenyl)ethylidene]aminobutyl)-ethanimidoyl]phenol (**1**) was synthesized by mixing an ethanolic solution of *o*-hydroxyacetophenone (2.40 g, 0.02 mole) and 1,4-diaminobutane (0.88 g, 0.01 mole). The reaction mixture was left under refluxing for two hours. The formed solid product was separated by filtration, purified by crystallization from ethanol, and dried under vacuum over anhydrous calcium chloride [5]. The pale lemon-yellow product was produced in 85.61% yield and its melting point is in the range of $192\text{--}194^\circ\text{C}$.

2.3. Synthesis of Schiff Base Chelates. The Schiff base metal chelates were synthesized by dropwise addition of an ethanolic solution of the metal salts (0.01 mole; 3.22, 4.33 and 4.04 g) of $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$, $\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$, and $\text{Ce}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$ to the same ratio of an ethanolic solution of the Schiff base in a 1:1 [M:L] ratio. If the chelates were not isolated, a few drops of ammonia solution were added to adjust the pH = 7-8. The reaction mixtures were refluxed for four hours, then collected, and washed several times with hot ethanol until the filtrates become clear. The chelates were dried in desiccators

over anhydrous calcium chloride. The yields of the chelates were in the range of 63.76–86.42% and their melting points are above 300°C .

2.4. Antimicrobial Assays. The *in vitro* biological sensitivity of different compounds conjugated with Schiff base and its chelates was studied by Bauer et al. [6] paper disc diffusion method; they were tested against the bacterial species and fungal species.

2.5. Antibacterial Assay. The antibacterial activity of the Schiff base and its chelates was studied against two Gram positive bacteria (*Lactobacillus fermentum* and *Streptococcus faecalis*) and Gram negative bacteria (*Escherichia coli*, *Salmonella kentucky*) [7]. A stock solution of the metal chelate dissolved in DMSO solvent was prepared at a concentration of 1 mg/mL. Whatman filter papers number 1 were cut and sterilized in autoclave. These paper discs were soaked in 10 μL of different concentrations of the ligand/chelates (5, 50, and 500 $\mu\text{g/mL}$) solutions in DMSO solvent as negative control and were then placed aseptically in the Petri dishes containing Mueller Hinton Agar (MHA, Oxoid) inoculated with the above mentioned two bacteria separately. The Petri dishes were incubated at $37 \pm 1^\circ\text{C}$ and the inhibition zones were recorded after 20 h of incubation. The obtained results were compared with known antibiotic, ciprofloxacin. Three replicates were taken and average values are given in Tables 3 and 4.

2.6. Antifungal Assay. The compounds were screened for their antifungal activity against fungi, namely, *Aspergillus niger* and *Fusarium solani* [8]. These fungal species were isolated from the infected parts of the host plants, that is, Sabraud Dextrose Agar (SDA). The compounds were tested at the concentrations of the ligand/chelates (5, 50, and 500 $\mu\text{g/mL}$) in DMSO solvent prepared from a solution at a concentration of 1 mg/mL and compared with a known antibiotic as control. Miconazole was prepared for testing against spore germination of each fungus. The culture of fungi was purified by single spore isolation technique. Filter paper discs of 6 mm size, prepared by using Whatman filter paper number 1, were cut and sterilized in an autoclave. These paper discs were soaked with 10 μL of the compounds dissolved in DMSO solvent as negative control. The fungal culture plates were inoculated and incubated at $25 \pm 2^\circ\text{C}$ for 40 h are presented in Table 5. Since all the tested compounds and standard drugs were prepared in freshly distilled DMSO solvent, its zone of inhibition was found to be very negligible and taken as zero mm. Activity was determined by measuring the diameter of the zone showing complete inhibition (mm). Growth inhibition was compared with standard drugs. The plates were then observed and the diameters of the inhibition zones (in mm) were measured and tabulated and the activity index was also calculated by using the following equation (see [8, 9]):

$$\% \text{ Activity index} = \frac{C}{T} \times 100, \quad (1)$$

FIGURE 1: Synthetic scheme for construction of 2-[(4-[(Z)-1-(2-hydroxyphenyl)ethylidene]aminobutyl)-ethanimidoyl]phenol.

TABLE 1: CHN elemental analysis data and some physical properties of Schiff base ligand and its chelates.

Schiff base/chelate	Mol.Wt	Colour	m.p. (°C)	Yield %	Elemental analysis%			Λ^*
					Cal	(Obs)		
					C%	H%	N%	
SB	324.43	Lemon-yellow	194	85.61	74.20 (74.00)	7.38 (7.46)	8.69 (8.64)	—
[Zr(L)(OH) ₂] ₂ ·4H ₂ O	537.84	Shinny white	>300	63.76	38.14 (38.24)	7.37 (7.45)	4.45 (4.55)	5.28
[La(L)(OH) ₂] ₂ ·5H ₂ O	587.55	Yellow canary	>300	73.91	47.99 (48.52)	7.51 (7.39)	3.66 (3.62)	4.31
[Ce(L)(OH) ₂] ₂ ·3H ₂ O	550.56	Canary	>300	67.70	34.43 (35.13)	7.08 (7.09)	4.01 (4.33)	2.49

$\Lambda^* = \Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$.

where AI% means activity index, C diameter of zone inhibition of microorganisms in check, and T diameter of the disc (the zone of inhibition was measured after 18–20 hrs). Ciprofloxacin ($5 \mu\text{g disc}^{-1}$) and miconazole ($25 \mu\text{g disc}^{-1}$) were used as positive standard.

3. Results and Discussion

Schiff base ligand (1) (Figure 1) was obtained by the reaction of *o*-hydroxyacetophenone and 1,4-diaminobutane in (2:1) ratio. Only one type of Schiff base compound (1) was formed.

3.1. CHN Elemental Analyses and Molar Conductivity. It is found that the found data are in good agreement with those theoretical ones (Table 1). The newly synthesized Schiff base chelates are very stable in air and generally soluble in DMF and DMSO solvents. The CHN elemental analytical data of the chelates reveal that the chelates are formed in 1:1 [M:L] ratio. The molar conductance values of the chelates were determined by using 10^{-3} M concentration in DMSO solvent, and their values (Table 1) suggest nonelectrolyte nature [10, 11].

3.2. Thermogravimetric Analysis of Ce(IV) Chelate. The thermogravimetric analysis was performed to assist in predicting the molecular structures of the chelates and the weight losses were measured from the ambient temperature up to 1000°C using a heating rate of 10°C/min [12]. The TG curve of Ce(IV) chelate of the formula $[\text{Ce}(\text{L})(\text{OH})_2] \cdot 3\text{H}_2\text{O}$ exhibits three steps of decomposition. The first step of decomposition involves the elimination of three hydrated water molecules

at weight loss of 10.00% (calcd. 9.81%) at temperature of $50\text{--}315^\circ\text{C}$. In the second step the decomposition occurs at temperature of $315\text{--}762^\circ\text{C}$ indicating the loss of the Schiff base as carbonate or oxalate ion [13], whereas, in the final step, stable state was observed above 762°C indicating the presence of thermally stable residual metal oxide. The weight percentage of residual metal oxide (CeO_2) was found to be 50.00% which is very close to the theoretical value 48.15% [14] (Figure 2). Thermal stability places the chelate in the following order:

3.3. Infrared Spectra. The IR spectra of the chelates were compared with those of the free ligand in order to determine the involvement of coordination sites in chelation. Characteristic peaks in the spectra of the ligand and chelates were considered and compared. The significant IR bands for the Schiff base ligand as well as for its metal chelates and their tentative assignments are compiled and represented in Table 2 and Figures 3–6. In the IR spectrum 2-[(4-[(Z)-1-(2-hydroxyphenyl)ethylidene]aminobutyl)-ethanimidoyl]phenol exhibits a band of the azomethine ($\text{C}=\text{N}$) at 1612 cm^{-1} .

TABLE 2: Infrared band assignments (cm^{-1}) and electronic spectral data (nm, cm^{-1}) of Schiff base (SB) and its chelates.

Comp.	IR spectral data, cm^{-1}							Electronic spectral data, nm (cm^{-1})
	$\nu(\text{OH})$	$\nu(\text{C}=\text{N})$	$\nu(\text{CH}_3)$	$\nu(\text{CH})$	$\nu(\text{CH}_2)$	$\nu(\text{M}-\text{O})$	$\nu(\text{M}-\text{N})$	
SB	3416	1612	1308	755	2932	—	—	269 (37175), 329 (30395)
[Zr(L)(OH ₂) ₂].4H ₂ O	3413	1617	1330	863	2921	527	444	249 (40160), 322 (31055)
[La(L)(OH ₂) ₂].5H ₂ O	3545	1642	1339	819	2926	565	424	—
[Ce(L)(OH ₂) ₂].3H ₂ O	3402	1633	1428	748	3079	617	482	—

TABLE 3: Effect of used salts and Schiff base and its chelates on bacteria growth.

Diameter of inhibition zone (6 mm); concentration in $\mu\text{g/mL}$													
Gram negative organisms													
S.N	Comp.	<i>Escherichia coli</i>						<i>Salmonella kentucky</i>					
		% Activity index						% Activity index					
		5 $\mu\text{g/mL}$	50 $\mu\text{g/mL}$	500 $\mu\text{g/mL}$	5 $\mu\text{g/mL}$	50 $\mu\text{g/mL}$	500 $\mu\text{g/mL}$	5 $\mu\text{g/mL}$	50 $\mu\text{g/mL}$	500 $\mu\text{g/mL}$	5 $\mu\text{g/mL}$	50 $\mu\text{g/mL}$	500 $\mu\text{g/mL}$
1B	HAPH	0	0	0	0	0	0	5	8	10	13	20	25
2B	BD	0	10	14	0	25	35	7	11	19	28	35	45
3B	ZrOCl ₂ .8H ₂ O	0	0	0	0	0	0	0	0	16	0	0	40
4B	La(NO ₃) ₃ .6H ₂ O	8	13	18	20	33	45	8	11	16	23	31	46
5B	Ce(SO ₄) ₂ .4H ₂ O	0	0	8	0	0	20	8	10	13	23	29	37
1C	SB	0	0	0	0	0	0	0	0	0	0	0	0
2C	La(III) chelate	0	0	0	0	0	0	0	0	0	0	0	0
3C	Zr(IV) chelate	0	8	10	0	20	25	0	0	0	0	0	0
4C	Ce(IV) chelate	0	0	8	0	0	20	0	0	8	0	0	23
C	DMSO (Control)	0	0	0	0	0	0	0	0	0	0	0	0
CIP	Ciprofloxacin (Standard)	40	40	40	100	100	100	35	35	35	100	100	100

HAPH (*o*-hydroxyacetophenone), BD (1,4-butanediamine), *microgram per mL. $I\% = C - T/C \times 100$.

TABLE 4: Effect of used salts and Schiff base and its chelates on bacteria growth.

Diameter of inhibition zone (6 mm); concentration in $\mu\text{g/mL}$													
Gram positive organisms													
S.N	Comp.	<i>Lactobacillus fermentum</i>						<i>Streptococcus faecalis</i>					
		% Activity index						% Activity index					
		5 $\mu\text{g/mL}$	50 $\mu\text{g/mL}$	500 $\mu\text{g/mL}$	5 $\mu\text{g/mL}$	50 $\mu\text{g/mL}$	500 $\mu\text{g/mL}$	5 $\mu\text{g/mL}$	50 $\mu\text{g/mL}$	500 $\mu\text{g/mL}$	5 $\mu\text{g/mL}$	50 $\mu\text{g/mL}$	500 $\mu\text{g/mL}$
1B	HAPH	5	8	10	13	20	25	0	1	2	0	3	6
2B	BD	11	14	18	28	35	45	1	3	11	3	9	31
3B	ZrOCl ₂ .8H ₂ O	0	0	16	0	0	40	0	0	0	0	0	0
4B	La(NO ₃) ₃ .6H ₂ O	0	0	16	0	0	40	0	7	15	0	20	43
5B	Ce(SO ₄) ₂ .4H ₂ O	0	9	15	0	23	38	8	13	16	23	37	46
1C	SB	0	0	0	0	0	0	0	3	6	0	9	17
2C	La(III) chelate	0	0	0	0	0	0	0	2	16	0	6	46
3C	Zr(IV) chelate	0	0	0	0	0	0	0	0	9	0	0	26
4C	Ce(IV) chelate	0	0	0	0	0	0	0	0	0	0	0	0
C	DMSO (Control)	0	0	0	0	0	0	0	0	0	0	0	0
CIP	Ciprofloxacin (Standard)	40	40	40	100	100	100	35	35	35	100	100	100

HAPH (*o*-hydroxyacetophenone), BD (1,4-butanediamine), *microgram per mL. $I\% = C - T/C \times 100$.

TABLE 5: Effect of used salts and Schiff base and its chelates on fungi growth.

S.N	Comp.	Diameter of inhibition zone (6 mm); concentration in $\mu\text{g/mL}$											
		Fungi											
		<i>Aspergillus niger</i>						<i>Fusarium solani</i>					
		% Activity index						% Activity index					
		5	50	500	5	50	500	5	50	500	5	50	500
		$\mu\text{g/mL}$	$\mu\text{g/mL}$	$\mu\text{g/mL}$	$\mu\text{g/mL}$	$\mu\text{g/mL}$	$\mu\text{g/mL}$	$\mu\text{g/mL}$	$\mu\text{g/mL}$	$\mu\text{g/mL}$	$\mu\text{g/mL}$	$\mu\text{g/mL}$	$\mu\text{g/mL}$
1B	HAPH	0	0	19	0	0	90	0	0	0	0	0	0
2B	BD	11	17	23	52	81	109	0	0	0	0	0	0
3B	$\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$	0	0	4	0	0	19	0	0	0	0	0	0
4B	$\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$	0	0	3	0	0	14	0	0	0	0	0	0
5B	$\text{Ce}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$	0	1	8	0	5	38	0	0	0	0	0	0
1C	SB	0	0	0	0	0	0	0	0	0	0	0	0
2C	La(III) chelate	0	0	0	0	0	0	0	0	0	0	0	0
3C	Zr(IV) chelate	0	0	0	0	0	0	0	0	0	0	0	0
4C	Ce(IV) chelate	0	0	0	0	0	0	0	0	0	0	0	0
C	DMSO (Control)	0	0	0	0	0	0	0	0	0	0	0	0
CIP	Ciprofloxacin (Standard)	21	21	21	100	100	100	13	13	13	100	100	100

HAPH (*o*-hydroxyacetophenone), BD (1,4-butanediamine), * microgram per mL.
 $I\% = C - T/C \times 100$.

FIGURE 2: Thermogravimetric analysis of Ce(IV) chelate.

The shifting of this band during the chelate formation (Table 2) indicates its involvement in coordination with the metal ions through nitrogen atom of the azomethine group [15, 16]. The appearance of broad bands in the IR spectra of the Schiff base ligand and its chelates in the range of $3402\text{--}3545\text{ cm}^{-1}$ is due to the existence of water molecules [17]. The spectrum of Zr(IV) chelate shows a band at 1030 cm^{-1} which could be due to the presence of $\text{Zr}=\text{O}$ group [18]. New bands in the range of $527\text{--}617\text{ cm}^{-1}$ and $424\text{--}482\text{ cm}^{-1}$ which are not present in the free Schiff base are due to $\nu(\text{M}-\text{O})$ and $\nu(\text{M}-\text{N})$ vibration [19], and the appearance of these vibrations supports the involvement of nitrogen and oxygen atoms of the azomethine and C-OH groups in chelation with the metal ions.

3.4. Electronic Spectra and Magnetic Moments of the Chelates.
 The electronic spectral data of 2-[(4-[(Z)-1-(2-hydroxyphenyl)ethylidene]aminobutyl)-ethanimidoyl]phenol and its

FIGURE 3: Infrared spectrum of the 2-[(4-[(Z)-1-(2-hydroxyphenyl)ethylidene]aminobutyl)-ethanimidoyl]phenol.

Zr(IV), La(III), and Ce(IV) chelates were recorded in DMSO solvent and shown in Table 2 and Figures 7–10. In the spectrum of the Schiff base it exhibits two bands at 269 nm (37175 cm^{-1}) and 329 nm (30395 cm^{-1}) assigned to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions [20]. In the metal chelates, the octahedral chelates that contain a metal ion of d^0 electronic configuration are diamagnetic. The electronic spectrum of Zr(IV) chelate displays two absorption bands at 249 nm (40161 cm^{-1}) and 322 nm (31056 cm^{-1}) due to charge transfer transition [21]. The f-f transitions of the complexes are characteristic of the lanthanide and are not influenced by the ligand. Intensity of the peaks also varies according to the metal ion. The f-f bands are sharp and line-like. This is because of the effective shielding of the 4f orbital by the 5s, 5p octet and consequently minimum ligand field perturbation

FIGURE 4: Infrared spectrum of the Zr(IV) chelate.

FIGURE 5: Infrared spectrum of the La(III) chelate.

FIGURE 6: Infrared spectrum of Ce(IV) chelate.

of the electronic energy levels in lanthanides. La(III) has no observable visible spectra and Ce(IV) has no transition in this region [22]. The observed f-f transitions in 500–700 nm region and the tentative assignments are given in Table 2.

3.5. ¹HNMR Spectra of the Zr(IV) Chelate. ¹HNMR spectra of Schiff base and its Zr(IV) chelate were recorded in d⁶-DMSO solvent. The ¹HNMR spectrum of the Schiff base 2-[(4-[(Z)-1-(2-hydroxyphenyl)ethylidene]aminobutyl)-ethanimidoyl]phenol in DMSO solvent shows signals of methyl protons at 2.368 ppm (s, 3H) and -CH at 6.712–7.323 (s, H). In addition, peak appeared at 2.25 ppm (s, 3H) which is assigned to methyl proton [23]. The spectrum shows sharp peak at

FIGURE 7: Ultraviolet spectrum of the 2-[(4-[(Z)-1-(2-hydroxyphenyl)ethylidene]aminobutyl)-ethanimidoyl]phenol.

FIGURE 8: Electronic spectrum of the Zr(IV) chelate.

16.625 (s, 1H) due to OH of 2-hydroxyacetophenone moiety indicating the formation of Schiff base ligand system, but in the case of Zr(IV) chelate, this group disappeared indicating the involvement of phenolic oxygen in the coordination via deprotonation. The appearance of a new singlet peak at δ 3.316 ppm is assigned to the presence of methyl group. The multiplet signals observed in the region at 6.987–7.556 ppm are assigned to the aromatic protons [24, 25].

3.6. Mass Spectra of Schiff Base and Schiff Base Chelates. The electron impact mass spectra of Schiff base ligand and chelates are recorded and investigated at 70 eV of electron energy. The mass spectra of the studied Schiff base and its chelates are shown in Schemes 1–4, and Figures 12–15. Fragment at $m/z = 325$ is due to the original molecular weight of the free Schiff base (SB). The fragment of Schiff base at $m/z = 191$ corresponds to $C_{12}H_{17}NO$ ion. Whereas the fragment at $m/z 136$ is analogous to $C_8H_{10}NO$ ion, the other molecular ion fragments that appeared in the mass spectrum are attributed to two fragmentations; first fragment at $m/z 121$ is corresponding to the loss of methyl group, and the second fragment at $m/z 112$ is analogous to the loss of C_2H_3N from the compound. The last fragment displays two fragments at m/z 80 and m/z 57 attributed to loss of different atoms which are shown in Scheme 1. The last fragment at m/z 55 is attributed to $C_4H_7^+$ ion. For $[Zr(L)(OH_2)_2] \cdot 4H_2O$ chelate, the spectrum exhibits a fragment at $m/z = 464$

FIGURE 9: Electronic spectrum of the La(III) chelate.

FIGURE 10: Electronic spectrum of the Ce(IV) chelate.

FIGURE 11: Proton magnetic resonance spectrum of the Zr(IV) chelate.

which is analogous to the loss of four water molecules and the fragments at $m/z = 239$ and 135 assigned to the loss of zirconium oxide. Meanwhile, the fragments have been observed at m/z values, 121, 108, and 81, suggesting different fragmentations (Scheme 2). Another important fragment appears at $m/z = 69$ which is due to the loss of C_5H_9 and the fragment at $m/z = 55$ is attributed to C_4H_7 . The mass spectrum of $[La(L)(OH)_2] \cdot 5H_2O$ chelate has been recorded. The spectrum of the La(III) chelate exhibited the molecular ion (M^+) peak at m/z 588 suggesting the monomeric nature of the chelate. The fragments at m/z values 496, 460, and 329 are analogous to the loss of $C_8H_{21}NO_8$ molecule from chemical formula of the chelate and fragments at m/z 232

FIGURE 12: Mass spectrum of the 2-[(4-[(Z)-1-(2-hydroxyphenyl) ethylidene]aminobutyl)-ethanimidoyl]phenol.

FIGURE 13: Mass spectrum of the Zr(IV) chelate.

may be due to $C_6H_{11}N$ ion. The same spectrum of chelate shows fragment at m/z 96 is corresponding to the loss of lanthanum(III) ion and the other important fragment at m/z 55 is assigned to the loss of C_4H_7 and C_4H_7 . For Ce(IV) chelate, the spectrum exhibits a fragment at m/z 550 due to the original molecular weight of the chelate. The mass spectrum of cerium chelate exhibits fragments at m/z values 461, 329, 260, 247, and 232 suggesting different fragmentations and the other fragment at m/z 93 is corresponding to the loss of cerium(IV) ion from chemical formula of the chelate. The final fragment at m/z 64 is analogous to the appearance of C_5H_4 ; these fragments are attributed to loss of different atoms (see Scheme 3). The above fragmentations illustrate the formation of the Schiff base and the formation of the chelates in 1:1 [M:L] ratio.

3.7. Biological Assay of the Schiff Base and Its Chelates. The *in vitro* biological activity of the synthesized Schiff base and its chelates were screened for their activity against *Escherichia coli* and *Salmonella kentucky* (Gram negative), *Lactobacillus fermentum* and *Streptococcus faecalis* (Gram positive), and antifungal activity against *Aspergillus niger* and *Fusarium solani* were carried out. The bactericidal and fungicidal investigation data of the compounds are summarized in the following results.

SCHEME 1: Mass spectral fragmentations of the 2-[(4-[(Z)-1-(2-hydroxyphenyl)ethylidene]aminobutyl)-ethanimidoyl]phenol.

FIGURE 14: Mass spectrum of the La(III) chelate.

SCHEME 2: Mass spectral fragmentations of the Zr(IV) chelate.

FIGURE 15: Mass spectrum of the Ce(IV) chelate.

SCHEME 3: Mass spectral fragmentations of the La(III) chelate.

3.7.1. Antibacterial Study. The results of antibacterial activity are presented in Tables 3 and 4 and Figures 16–19 and 22–25. The samples for the reagents to synthesize Schiff base and its corresponding chelates (1B, 2B, 3B, 4B, and 5B) showed good to moderate activity against the tested bacteria strains with a wide activity index range that varied between 0 and 46%. The sample (1B) for *o*-hydroxyacetophenone was ineffective against the proliferation of Gram negative bacteria *Escherichia coli* and Gram positive bacteria *Streptococcus faecalis* but slightly effective against *Salmonella kentucky* and *Lactobacillus fermentum* with activity index within 3–13%. The sample (2B) for 1,4-butanediamine was found to be active against all organisms at all tested concentrations with the activity index within 0–45%. The sample (3B) was found to be ineffective against *Escherichia coli* and *Streptococcus faecalis* at all the concentrations tested; however, it showed moderate activity against *Salmonella kentucky* and *Lactobacillus fermentum* at 500 µg/mL concentration with an activity index

of 40%. The samples (4B) and (5B) for La(NO₃)₃·6H₂O and Ce(SO₄)₂·4H₂O exhibited moderate activity against all the tested bacteria in the range of 0–46% activity index. Schiff base (1C) and La(III) chelate (2C) showed higher activity against *Streptococcus faecalis* with activity index of 17% and 46%, respectively, at 500 µg/mL concentration compared to the other bacterial strains. Zr(IV) chelate (3C) displayed antibacterial activity against *Escherichia coli* and *Streptococcus faecalis* with activity index of 25 and 26%, respectively, while it was ineffective against other bacteria. The sample 4C (Ce(IV) chelate) showed no growth inhibition against Gram positive bacteria and slight activity against Gram negative bacteria with activity index of 20–23%. To sum up, the best activity was recorded by Zr(IV) chelate and Ce(IV) chelate against both Gram negative bacteria tested. La(III) chelate showed the highest activity against Gram positive bacterium *Streptococcus faecalis*. However, all of the compounds were ineffective at growth inhibition of Gram negative bacterium

SCHEME 4: Mass spectral fragmentations of the Ce(IV) chelate.

FIGURE 16: Effect of *o*-hydroxyacetophenone and 1,4-butanediamine on *Escherichia coli*. FIGURE 17: Effect of *o*-hydroxyacetophenone and 1,4-butanediamine on *Salmonella Kentucky*.

Lactobacillus fermentum. In general, judging from the results it seems that chelation improved the antibacterial activity compared to the Schiff base.

3.7.2. Antifungal Study. The antifungal activity results are listed in Table 5 and Figures 20, 21, 26, and 27. The sample 2B was most effective against *Aspergillus niger* at 19 and 90% at concentration of 500 µg/mL and ineffective against *Fusarium*

FIGURE 18: Effect of *o*-hydroxyacetophenone and 1,4-Butanediamine on *Streptococcus faecalis*.

FIGURE 19: Effect of *o*-hydroxyacetophenone and 1,4-butanediamine on *Lactobacillus fermentum*.

FIGURE 20: Effect of ketone and 1,4-butanediamine on *Aspergillus niger*.

FIGURE 21: Effect of ketone and 1,4-butanediamine on *Fusarium solani*.

FIGURE 22: Effect of SB1 and Zr(IV), La(III), and Ce(IV) chelates on *Escherichia coli*.

FIGURE 23: Effect of SB1 and Zr(IV), La(III), and Ce(IV) chelates on *Salmonella kentucky*.

solani. Meanwhile, the CIP exhibited higher activity against fungus in the range of 13–100% activity index. The samples 1B, 3B, 4B, and 5B exhibited slight to moderate activity with the activity index of 0–38%, when compared to the standard drug miconazole with growth inhibition against *Aspergillus niger* expect *Fusarium solani* which showed ineffective. Therefore,

FIGURE 24: Effect of SB and Zr(IV), La(III), and Ce(IV) chelates on *Lactobacillus fermentum*.

FIGURE 25: Effect of SB and Zr(IV), La(III), and Ce(IV) chelates on *Streptococcus faecalis*.

Schiff base (1C), La(III) chelate (2C), Zr(IV) chelate (3C), and Ce(IV) chelate (4C) were found to be ineffective against the tested fungus represented by *Aspergillus niger* and *Fusarium solani*. The Schiff base and its chelates could enhance the antimicrobial effect on both strains probably by the azomethine nitrogen groups. The activities of all the tested chelates may be explained on the basis of chelation theory; chelation reduces the polarity of the metal atom mainly because of partial sharing of its positive charge with the donor groups and possible π -electron delocalization within the whole chelate ring. Also, chelation increases the lipophilic nature of the central atom which subsequently favors its permeation through the lipid layer of the cell membrane [26–29].

4. Conclusion

In this paper, a Schiff base ligand 2-[(4-[(Z)-1-(2-hydroxyphenyl)ethylidene]aminobutyl)-ethanimidoyl]phenol is derived from the condensation of 2-hydroxyacetophene and 1,4-diaminobutane. The synthesized ligand is used in making some chelates with Zr(IV), La(III), and Ce(IV) ions. Based on the data of the elemental analysis, molar conductivity,

FIGURE 26: Effect of SB and Zr(IV), La(III), and Ce(IV) chelates on *Aspergillus niger*.

FIGURE 27: Effect of SB and Zr(IV), La(III), and Ce(IV) chelates on *Fusarium solani*.

thermogravimetric analysis, IR, ^1H NMR, and electronic and mass spectra, an octahedral structure was suggested for all the chelates as shown in Figure 28.

The biological activity results showed that all chelates have been found to be moderately potent compared to their ligand because the process of chelation dominantly affects the overall biological behavior of the chelates. Some of the chelates have higher antibacterial and antifungal activities than the ligand. However, biological activities are less than standards. All these observations put together lead us to propose six coordinated octahedral structures to Zr(IV), La(III), and Ce(IV) chelates. These observations showed that the majority of the salts are more active than their respective Schiff bases. In some cases, Schiff base and its chelates have similar activity against bacteria and resistive fungi. Chelation may enhance or suppress the biochemical potential of bioactive organic species. The higher activity of the chelates may be owing to the effect of metal ions on the normal cell membrane. Metal chelates bear polar properties together; this makes them suitable for permeation to the cells and tissues. Changing hydrophilicity and lipophilicity probably leads to bringing down the solubility and permeability barriers of cell, which in turn enhances the bioavailability of chemotherapeutics on one hand and potentiality on another [30]. The biological activities of the Schiff base ligand under investigation and its chelates against bacterial and fungal organisms are promising which need further and deep studies on animals and humans.

FIGURE 28

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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