Applied
Organometallic
Chemistry

Received: 29 December 2009 Revised: 20 April 2010 Accepted: 25 April 2010

(wileyonlinelibrary.com) DOI 10.1002/aoc.1680

Synthesis, characterization and *in vitro* biological activity of cobalt(II), copper(II) and zinc(II) Schiff base complexes derived from salicylaldehyde and D,L-selenomethionine

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New cobalt(II), copper(II) and zinc(II) complexes of Schiff base derived from D,L-selenomethionine and salicylaldehyde were synthesized and characterized by elemental analysis, IR, electronic spectra, conductance measurements, magnetic measurements and biological activity. The analytical data showed that the Schiff base ligand acts as tridentate towards divalent metal ions (cobalt, copper, zinc) via the azomethine-N, carboxylate oxygen and phenolato oxygen by a stoichiometric reaction of M : L (1 : 1) to form metal complexes [ML(H_2O)], where L is the Schiff base ligand derived from D,L-selenomethionine and salicylaldehyde and M = Co(II), Cu(II) and Zn(II). ^1H NMR spectral data of the ligand and Zn(II) complex agree with proposed structures. The conductivity values between 12.87 and 15.63 S cm^2 mol^{-1} in DMF imply the presence of non-electrolyte species. Antibacterial and antifungal results indicate that the metal complexes are more active than the ligand.

Keywords: Schiff base; D,L-selenomethionine; complexes; antibacterial; antifungal

Introduction

Amino acid Schiff bases are an important class of ligands because such ligands and their metal complexes have a variety of applications including biological, clinical, analytical and industrial in addition to their important roles in catalysis and organic synthesis. In particular, transition metal complexes of salicylaldehyde-amino acid Schiff bases are non-enzymatic models for pyridoxal-amino acid systems, which are of considerable importance as key intermediates in many metabolic reactions of amino acids catalyzed by enzymes requiring pyridoxal as a cofactor. Considerable efforts have been devoted to the preparation and structural characterization of Schiff base metal complexes derived from salicylaldehyde and amino acids such as glycine, alanine, valine, threonine, serine, methionine, glutamic acid, phenylalanine, tryptophan and tyrosine.[1–8] Most of the model studies of such metal complexes have focused upon various binding modes of these ligands and the X-ray crystal structures of complexes reveal that the Schiff base ligands mainly act as tridentate moieties, coordinating through the phenolato oxygen, imine nitrogen and carboxylate oxygen. Moreover, a wide screening of biological activity has been carried out and radioprotective,[9] antibacterial, fungistatic,[10–12] DNA cleavable,[13] antipyretic and antidiabetic activities[14] have been discovered and interactions with different biomolecules described.[15–18]

Selenium is in the same column of the periodic table as sulfur and may substitute for sulfur in methionine to form selenomethionine. It is currently known as a predominant antioxidant.[19] Selenomethionine has also been found to be a very useful form for selenium supplementation.[20,21] Moreover, selenomethionine has been under intense study as a promising chemopreventive agent for different types of cancer. Recently, Meuillet *et al*. reviewed chemoprevention of prostate cancer with selenium to update current clinical trials and preclinical findings.[22] Significant progress has been achieved in understanding the chemistry and biological activity of selenomethionine in the past decades. However, there is comparatively little literature on the preparation of selenomethionine Schiff base and its metal complexes.

Recently, we reported a convenient synthesis of D,L-selenomethionine.[23] As part of extensive primary biological screening and interest in the nutritional and clinical role of selenomethionine and its transition metal complexes,[24] we have begun to investigate the synthesis, characterization and biological activity of novel tridentate Schiff base metal complexes [ML(H_2O)], where L is the Schiff base ligand derived from D,L-selenomethionine and salicylaldehyde, M = Co(II), Cu(II) and Zn(II). The Schiff base ligand and three metal complexes have been tested *in vitro* against a wide spectrum of bacteria and fungi. The results of biological activity show that the metal complexes are more antibacterial and antifungal as compared with their uncomplexed Schiff base and appear to be potentially useful as a novel pharmacological form for simultaneous metal and selenium supplementation.

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Experimental

Reactants

All chemicals were purchased from commercial sources (Sigma-Aldrich Co., Fluka Co.) and used as received without any further purification. All metal(II) were used as their acetate hydrate. D,L-Selenomethionine was synthesized according to a previous method.[23]

Analytical and Physical Measurements

The IR spectra were recorded using a Perkin Elmer FT-IR spectrometer Spectrum-one Model with KBr disks in the range 4000–400 cm^{-1}. Electronic spectra were recorded on a Perkin–Elmer Lambda-25 UV–vis spectrometer using MeOH as solvent. Element analyses of C, H, N were determined by the service Elementar Vario EL. The metal contents were determined by complexometric titrations with EDTA.[25] ^{1}H NMR spectra were obtained on a Bruker AV-400 and TMS was used as an internal standard. Thermogravimetric analysis measurements were carried out on a TGA 2050 thermogravimetric analyzer under nitrogen atmosphere with a heating rate of 10 °C/min in the 20–900 °C temperature range using a platinum crucible. The magnetic measurements were carried out on solid complexes using Gouy's method on a Sherwood Scientific Magnetic balance MSB-1 at room temperature. Diamagnetic corrections were estimated from Pascal's constants and magnetic data were corrected for diamagnetic contributions of the sample holder. Conductivity measurements were made on freshly prepared 10^{-3} mol/L solutions in N, N-dimethylformamide (DMF) at room temperature with a coronation digital conductivity meter.

Preparation of the Potassium *N*-salicylidene-selenomethioninate (KSal-SeMet)

The potassium salt of *N*-salicylidene-selenomethioninate was prepared by the following reaction: to a methanol solution of D,L-selenomethionine (0.196 g, 1 mmol) and potassium hydroxide (0.056 g, 1 mmol), the solution of salicylaldehyde (0.122 g, 1 mmol) in 10 ml of anhydrous methanol was added with stirring. When the reaction began, anhydrous Na_2SO_4 (0.142 g, 1 mmol) was added to remove resulting water. The resulting yellow system was stirred at 50 °C for 24 h. Then the mixture was filtered and the filtrate was reduced *in vacuo* using rotary evaporator. Anhydrous ether was added to deposit the yellowish precipitate and the crude product was re-crystallized from methanol. Yield: 73%, yellow solid. Anal. Found: C, 42.71; H, 4.32; N, 3.95%. Calcd for $C_{12}H_{14}NO_3KSe$: C, 42.60; H, 4.17; N, 4.14%. ^{1}H NMR (400 MHz; DMSO-d_6; δ, ppm; s, singlet; d, doublet; t, triplet; m, multiplet): 1.93(3H, s, -$SeCH_3$), 2.13–2.23 (2H, m, -CH_2-), 2.51 (2H, t, $J = 7.8$ Hz, -$SeCH_2$-), 3.80 (1H, t, $J = 6.8$ Hz, -CH-), 6.79 (1H, t, $J = 7.0$ Hz, -ph), 6.53 (1H, m, -ph), 7.20 (2H, m, -ph), 8.35 (1H, s, -CH=N). ^{13}C NMR (DMSO-d_6, δ, ppm): 3.47 (-$SeCH_3$), 20.10, (-$SeCH_2$), 31.98 (-CH_2), 55.12 (-CH-), 116.26, 117.51, 118.50, 130.25, 131.45, 165.77 (-ph), 162.45 (-C=N), 172.38 (-COO).

Preparation of Complexes: General Procedure

To a warm solution (60–70 °C) of the D,L-selenomethionine (5 mmol) in 10 ml of water, 5 mmol of salicylaldehyde in 10 ml of ethanol was added. The resulting solution was stirred until D,L-selenomethionine dissolved. A solution of metal(II) acetate monohydrate (5 mmol) dissolved in a minimum quantity of water was added dropwise. The mixture was stirred for 1 h and the colored precipitate obtained was filtered, washed with water, EtOH and Et_2O and dried in *vacuo*. The resulting solid was re-crystallized from either DMF or dimethyl sulfloxide (DMSO) (yield = 50–55%). Unfortunately only microcrystalline powders could be obtained, which could not be used for X-ray structural determinations. ZnL(H_2O): ^{1}H NMR (400 MHz; DMSO-d$_6$; δ, ppm): 1.93 (3H, s, -$SeCH_3$), 1.95–2.05 (2H, m, -CH_2-), 2.52 (2H, t, $J = 7.6$ Hz, -$SeCH_2$-), 3.69 (1H, t, $J = 6.7$ Hz, -CH-), 6.48 (1H, t, $J = 7.1$ Hz, -ph), 6.70 (1H, m, -ph), 7.17 (2H, m, -ph), 8.32 (1H, s, -CH=N). ^{13}C NMR (DMSO-d$_6$, δ, ppm): 3.39 ($SeCH_3$), 19.38 (-$SeCH_2$), 31.08 (-CH_2), 56.56 (-CH-), 117.30, 118.25, 119.21, 132.35, 133.52, 170.89 (-ph), 170.54 (-C=N), 174.13 (-COO).

In Vitro Biological Activity

Antibacterial bioassay

The synthesized ligand and corresponding metal(II) complexes were screened *in vitro* for their antibacterial activity against *E. coli*, *B. subtilis*, *P. vulgaris*, *S. aureus* and *E. aerogens* bacterial strains using the agar well diffusion method. Two hour-old bacterial inocula containing approximately 10^4–10^6 colony forming units (CFU) ml^{-1} were used in these assays. The wells were dug into the media with a sterile metallic borer with centers at least 24 mm part. The recommended concentration (100 µl) of the test sample (1 mg ml^{-1} in DMSO) was introduced into the respective wells. Other wells were supplemented with DMSO and reference antibacterial standard drug (imipenum). The plates were incubated at 37 °C for 20 h. Activity was determined by measuring the diameter of zones showing complete inhibition (mm). In order to clarify any participating roles of DMSO or metal(II) acetate monohydrate in the biological screening, separate studies were carried out with DMSO or solution of metal(II) acetate monohydrate alone, and they hardly showed activity against any bacterial and fungal strains. The tests were carried out in triplicate.

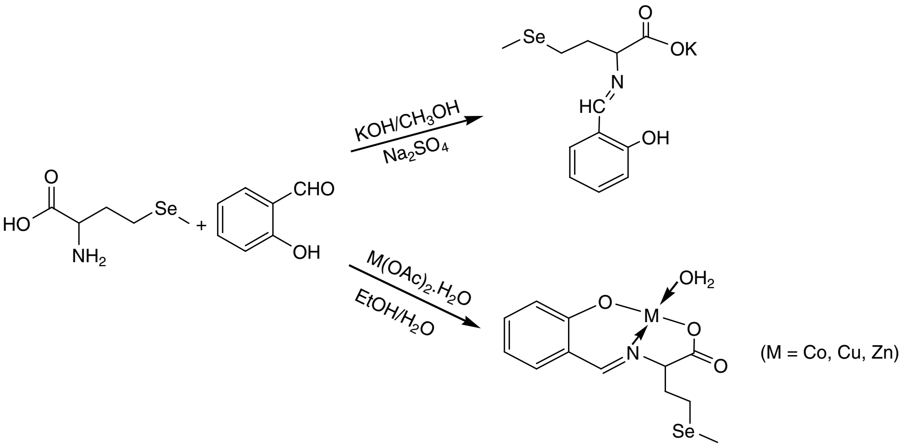
Antifungal activity

Antifungal activities of ligand and corresponding metal (II) complexes were studied against four fungal cultures, *A. flavus*, *A. niger*, *F. solani* and *Cladosporium*. Sabouraud dextrose agar (Guangzhou, China) was seeded with 10^5 CFU ml^{-1} fungal spore suspensions and transferred to Petri plates. Disks soaked in 20 ml (10 µg ml^{-1} in DMSO) of all compounds were placed at different positions on the agar surface. The plates were incubated at 37 °C for 3 days. The results were recorded as zones of inhibition in millimeters and compared with standard drug amphotericin B.

Results and Discussion

The problem of instability of the D,L-selenomethionine Schiff base was encountered, which was resolved by making an equimolar potassium salt of the Schiff base ligand. KSal-SeMet is a stable compound, and was successfully prepared by refluxing an appropriate amount of D,L-selenomethionine with salicylaldehyde in methanol, in 1 : 1 molar ratio in the presence of KOH and anhydrous Na_2SO_4. The synthesis of complexes proved to be straightforward in a simple one-pot reaction with moderate yields.

In this text, racemic D,L-selenomethionine was used as the starting amino acid. The potassium salt of Schiff base ligand (KSal-SeMet) derived from salicylaldehyde and D,L-selenomethionine as well as its metal complexes were also



Scheme 1. Synthetic route of Schiff base metal complexes [ML(H_2O)].

Table 1. Analytical and physical data of the Schiff base ligand and its complexes

Compound	Colour	Found (calculated) (%) C	H	N	M	Molar conductance (S cm^2 mol^{-1})	μ_{eff} (μ_B)
KSal-SeMet	Yellow	42.71	4.32	3.95	–	–	–
$C_{12}H_{14}NO_3SeK$		(42.60)	(4.17)	(4.14)	–		
[CoL(H_2O)]	Brown	38.64	4.24	3.59	15.52	15.63	4.05
$C_{12}H_{15}NO_4SeCo$		(38.42)	(4.03)	(3.73)	(15.71)		
[CuL(H_2O)]	Green	37.89	3.80	3.84	17.03	13.86	1.97
$C_{12}H_{15}NO_4SeCu$		(37.95)	(3.98)	(3.69)	(16.73)		
[ZnL(H_2O)]	White	37.47	4.32	3.74	17.04	12.87	Dia.
$C_{12}H_{15}NO_4SeZn$		(37.77)	(3.96)	(3.67)	(17.14)		

racemic mixtures. Similar behavior has been reported by Amendola *et al.* during the synthesis of the racemic form of Schiff base of ^{rac}5 (*trans-N,N′*-bis[1-(8-benzyloxyquinolin-2-yl)methylidene]cycloexane-1,2-diamine.[26] In that case, the racemic form of Schiff base was obtained from Schiff base condensation of the racemic *trans*-1,2-cyclohexanediamine with the pertinent aldehyde and was therefore a mixture of the two enantiomeric *R,R* and *S,S* forms. Masood *et al.* reported that the racemic mixture of the analogous ligand, obtained from Schiff base condensation of *trans*-1,2-cyclohexanediamine with the pertinent 2-pyridinealdehyde, reacts with copper(I) ions to give only a racemic mixture of the homochiral double helicate species.[27]

The complexes were soluble in DMF and DMSO, poorly soluble in MeOH and insoluble in some common organic solvents. Attempts to obtain single crystal suitable for X-ray determination were unsuccessful. The structures of the synthesized ligand and metal complexes (Scheme 1) were established with the help of elemental analyses data, IR and NMR spectra.

As shown in Table 1, the elemental analyses results obtained are in good agreement with those calculated for the suggested formulae of ligand and metal complexes. The analytical data show that the metal to ligand ratio is 1 : 1 in all the complexes. The molar conductance values in DMF (Table 1) for the complexes were found to be in the range 12.87–15.63 S cm^2 mol^{-1}. The relatively low values indicate the non-electrolytic nature of these complexes.[28] This can be accounted for by the satisfaction of the bivalency of metal by the carboxylate group and deprotonated phenolato oxygen.

IR Spectra

In the absence of a powerful technique such as X-ray crystallography, IR spectroscopy has proven to be suitable technique to elucidate the method of bonding of the ligand to the metal ion. The determination of the coordinating atoms is made on the basis of the comparison of the IR spectra of the ligand and the complexes, as shown in Fig. 1. The significant data are given in Table 2. The IR spectrum of the ligand shows the absence of bands at 3245 and 1745 cm^{-1} due to the ν(NH_2) group of D,L-selenomethionine and ν(HC=O) group of salicylaldehyde. Instead, a new strong band at 1645 cm^{-1} due to azomethine stretching vibration ν(C=N) appears in the ligand, indicating that condensation between aldehyde of salicylaldehyde and amino group of D,L-selenomethionine has taken place, resulting in the formation of the desired Schiff base ligand. On complexation, ν(C=N) shifts to lower frequency by 5–25 cm^{-1} and a new band in the 1620–1640 cm^{-1} range, indicating the coordination of the azomethine nitrogen atom to the central metal ion. Since no data is found in the literature for D,L-selenomethionine Schiff base metal complexes for the IR spectral region, it was found in this study that new bands at $\nu = 538$, 545, 567 cm^{-1} can be assigned to Co–N, Cu–N and Zn–N bonds, respectively. Similar assignments are reported in the literature for the Co–N, Cu–N and Zn–N bonds at $\nu = 537$, 584 and 580 cm^{-1} of Co(II), Cu(II) and Zn(II) complexes of the Schiff base derived from vanillin and D,L-α-aminobutyric acid.[29] Further confirmation is shown in the literature,[30,31] which shows stretching bands at

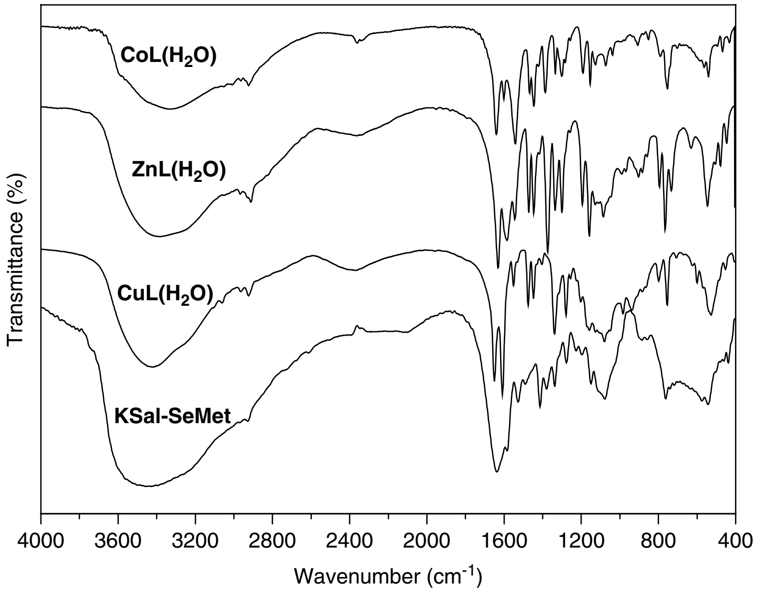


Figure 1. FT-IR spectra of KSal-SeMet and three complexes.

Table 2. Infrared spectral data of Schiff base ligand and its complexes (cm^{-1})

Compound	ν (C=N)	ν (O–H)	ν_{asym} (COO$^-$)	ν_{sym} (COO$^-$)	ν (M–N)	ν (M–O)
KSal-SeMet	1645	3459	1589	1331	–	–
[CoL(H$_2$O)]	1620	3408	1583	1348	538	464
[CuL(H$_2$O)]	1640	3448	1583	1339	545	457
[ZnL(H$_2$O)]	1628	3432	1575	1375	567	438

500–581 cm^{-1} in the spectra of the complexes corresponding to M–N vibration bands.

The participation of the phenolic group is deduced by clarifying the effect of chelation on the ν(C–O) stretching vibration. The shift in ν(C–O) of the phenolic group from 1336 cm^{-1} in the free ligand to 1282–1335 cm^{-1} in the complexes indicates the participation of the phenolic group in complex formation. In contrast to other vibrations, the positions of symmetric carboxyl stretching ν_s(COO$^-$) and asymmetric carboxyl stretching ν_{as}(COO$^-$) are distinct, and the difference between two values indicates the scale of electron delocalization of carboxyl group and thus the possible bridging function of the carboxyl group is evident. As compared with the values of ν_{as}(COO$^-$) and ν_s(COO$^-$) assigned to 1589 and 1331 cm^{-1} in the ligand, respectively, the ν_{as}(COO$^-$) is shifted to a lower frequency in the 1575–1583 cm^{-1} range and the ν_s(COO$^-$) is shifted to a higher frequency in the 1339–1375 cm^{-1} range, indicating the linkage between the metal ion and carboxylato oxygen atom.[32] The differences between ν_{as}(COO$^-$) and ν_s(COO$^-$) for the Co(II), Cu(II) and Zn(II) complexes in the present study are 235, 244 and 200 cm^{-1}, respectively. This value compares favorably with the values of 196–266 cm^{-1}, characteristic for the monodentate coordination of the carboxylato group.[33–35]

The spectra of the complexes show broad bands in the 3408–3448 cm^{-1} range, attributed to the stretching vibration of the O–H group of water molecules. The presence of water molecules in the complexes is also ascertained by the appearance of bending vibration modes of the water molecules; δ(H$_2$O), found in the range 992–960 cm^{-1}. The other bending vibration of the water molecules, δ(H$_2$O), is usually around 1600 cm^{-1}, which always interferes with the skeleton vibration of the benzene ring (C=C vibration). These observations indicate that a water molecule occupies the fourth position. Participation of the phenolic oxygen, carboxylato-oxygen atoms, and phenolic and water molecules is also confirmed by the appearance of new bands in the spectra of the complexes in the 438–464 cm^{-1} regions, which may be assigned to the ν(M–O) stretching vibration.[36]

Since Schiff base derived from D,L-selenomethionine and salicylaldehyde is a four-coordination point ligand, i.e. phenolic oxygen, azomethine nitrogen, carboxylato oxygen and methyl selenium groups, any possible participation of the methyl selenium group in the coordination of Schiff base ligand with Co^{2+}, Cu^{2+} and Zn^{2+} was also investigated. Only one weak band at 574 cm^{-1} assigned to a C–Se stretching vibration band was detected in the IR spectrum of the ligand. This is based on comparison with the IR spectral data of selenomethionine,[37] where 577 cm^{-1} is reported for stretching bands of the Se–Me group in the Raman spectrum of solid selenomethionine. The same band appears in the IR spectra of the Schiff base metal complexes in the 571–574 cm^{-1} range, which shows that no coordination with metal(II) occurred with methyl selenium group. The spectra of ligand and complexes appeared in the same region at 1268–1275 cm^{-1} corresponding to bending vibration of the -SeCH$_3$ group,[38] further suggesting that no coordination of -SeCH$_3$ with metal occurred.

From the IR results, it may be concluded that the ligand is tridentate (Scheme 1) and coordinates with the metal ion through the phenolic oxygen, azomethine nitrogen and carboxylato oxygen atoms.

^{1}H NMR Spectra

The ^{1}H NMR spectra of ligand and Zn(II) complex were recorded in DMSO-d_6. All the protons were found to be in their expected regions and numbers of protons calculated from the integration curves agreed with those obtained from the values of the C, H, N element analyses. In the spectra of diamagnetic Zn(II) complex,

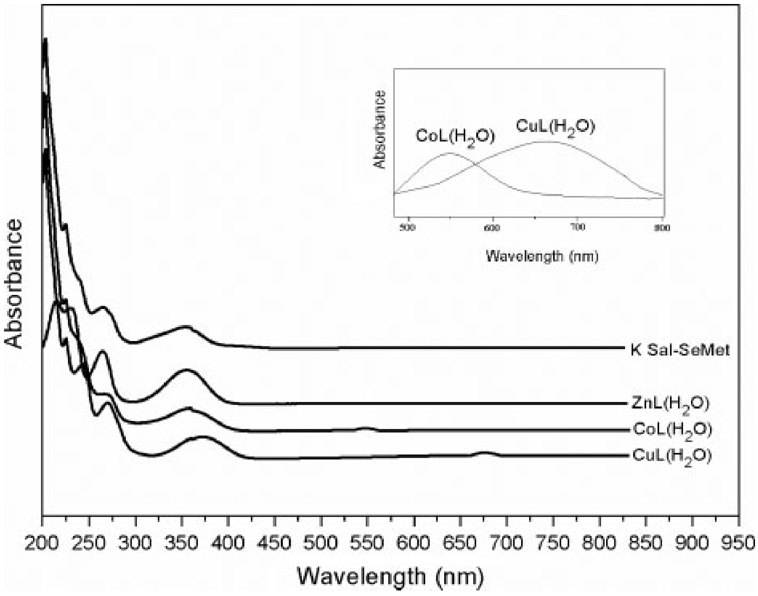


Figure 2. UV–vis spectra of KSal-SeMet and three complexes.

Table 3. Electronic spectral data (nm) of the ligand and its complexes

Compound	$\sigma \to \sigma^*$	$\pi \to \pi^*$	$n \to \pi^*$	d–d
KSal-SeMet	200, 220	264	357	–
[CoL(H$_2$O)]	201, 225	270	352	550
[CuL(H$_2$O)]	202, 224	271	356	675
[ZnL(H$_2$O)]	214, 231	267	352	–

signals shifted upfield, as compared with that the ligand. The -CH=N- proton of ligand resonated as a sharp singlet at 8.35 ppm. On complexation, this signal was shifted to 8.32 ppm. The phenyl protons (7.20, 6.79 and 6.53 ppm in the ligand) were recorded at 7.17, 6.70 and 6.48 ppm in the complex. The significant shift of the -CH- proton from 3.80 ppm in the free ligand to 3.69 ppm in the complex was observed. The shifts were caused by methylene protons from 2.13–2.23 ppm in the ligand to 1.95–2.05 ppm in the complex. Comparatively, methylene selenium at 2.51 ppm and methyl protons at 1.93 ppm were practically unaffected by complexation. The conclusions drawn from these studies lend further support to the mode of bonding discussed in IR spectra.

UV–vis Spectral Analysis

As shown in Fig. 2, UV–vis spectra of ligand and complexes measured in the range of 200–825 nm display two distinct regions. The lower wavelength in the range of 200–400 nm is specific for the electronic intra-ligand transitions. The higher wavelength region is specific for d–d transition. The observed absorption bands and their assignments are shown in Table 3.

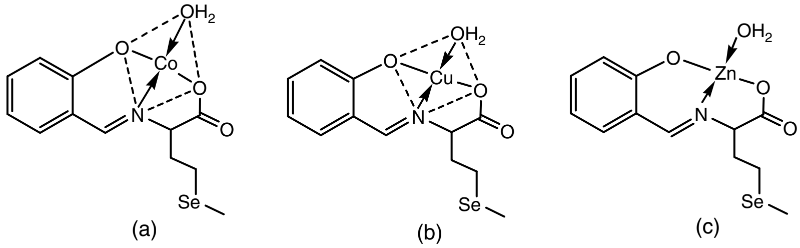
The spectra of complexes generally show the characteristic bands of the free ligand with some changes both in wavelengths (λ_{max}) and intensity together with appearances of new bands at longer wavelengths. The spectra of the KSal-SeMet and the complexes exhibit bands in the regions of 200–231, 264–271 and 352–357 nm, which may be due to the transition of $\sigma \to \sigma^*$, $\pi \to \pi^*$ or $n \to \pi^*$, respectively.[39] In addition, the Co(II) complex shows only one absorption band in the visible region at 550 nm, which is assigned to $^4A_2$ (F) $\to$ $^4T_1$(F) transition. This prefigures tetrahedral geometry for the Co(II) complex. The electronic spectrum of Cu(II) complex exhibits a broad band centered at 675 nm, indicating square planar geometry. In general, due to Jahn–Teller distortion, square planar Cu(II) complex displays a broad absorption band between 600 and 700 nm and the peak at 510 nm merges with the broad band, which is due to $^2B_{1g} \to {}^2E_g$ and $^2B_{1g} \to {}^2A_{1g}$ with the respective absorption bands.[40] However, the zinc complex only gives a high-intensity band at 352 nm due to absence of d–d transition, which is assigned to a ligand-metal charge transfer besides the characteristic ligand.[41] The proposed structures of metal(II) complexes are shown in Fig. 3.

Magnetic Susceptibility Measurements

The magnetic moments of the complexes determined at room temperature are given in Table 1. The Co(II) complex has a magnetic moment value of 4.05 μ_B, which compares favorably with that of 4.1–4.8 μ_B expected for the Co(II) complex with three unpaired electrons.[42,43] As a result, in agreement with the electronic spectral studies, Co(II) complex may have tetrahedral geometry. The magnetic moment of Cu(II) complex is 1.97 μ_B, indicating the presence of one unpaired electron.[44–46] This is consistent with the electronic spectral result that square planar geometry for the Cu(II) complex contains one unpaired electron and the μ_{eff} value would be in the range 1.8–2.1 μ_B. The zinc (II) complex is found to be diamagnetic,[47] as expected.

Thermal Analyses

The Thermogravimetry (TG) measurements of all the complexes were performed in nitrogen over the temperature range of 20–900 °C. In general, all complexes were stable up to 90 °C. Above this temperature, the sample weight decreased up to 164 °C, which is probably connected with the elimination of the coordinated water molecule, leading to the formation of intermediate ML. The intermediate was stable within the interval of 175–248 °C. The next decay proceeded in two steps without formation of thermally stable intermediates up 800 °C. Afterwards, a plateau could be



(a) (b) (c)

Figure 3. Proposed structures of (a) [CoL(H_2O)]; (b) [CuL(H_2O)]; (c) [ZnL(H_2O)].

Table 4. Thermal analytical data for the complexes

Molecular formula	Molecular weight	Decomposition temperature (°C)	Mass loss found (%, calcd)	Eliminated species	Solid residue Mass found (%, calcd)
[CoL(H_2O)]	375.1	80–172	4.98 (4.81)	H_2O	CoSe
$C_{12}H_{15}NO_4SeCo$		248–615	58.18 (58.44)	$C_{12}H_{13}NO_3$	36.84 (36.76)
[CuL(H_2O)]	379.8	78–175	4.71 (4.74)	H_2O	CuSe
$C_{12}H_{15}NO_4SeCu$		250–650	58.05 (57.74)	$C_{12}H_{13}NO_3$	37.24 (37.52)
[ZnL(H_2O)]	381.6	80–174	5.01 (4.72)	H_2O	ZnSe
$C_{12}H_{15}NO_4SeZn$		250–625	57.75 (57.45)	$C_{12}H_{13}NO_3$	36.24 (37.83)

seen above 800 °C and the weight of the residue in the range of 36.24–37.24% was found to be in consistent with the formation of MSe as a final thermal decomposition product. The detailed data are shown in Table 4.

Antibacterial and Antifungal Bioassay

The ligand and its metal complexes were screened for their antibacterial and antifungal activities according to the respective literature protocol[48] and the results obtained are presented in Tables 5 and 6. The results were compared with those of the standard drug. All the metal complexes were more potent bactericides and fungicides than the ligand. Co(II) and Zn(II) complexes were much less microbially active than the Cu(II) complex. From Table 5, it can be seen that the highest inhibition of growth occurred on Cu(II) complex against the bacterium *B. subtilis* (23 mm). On the other hand, Cu(II) complex showd the best activity towards fungi against *A. niger* (26 mm) and the lowest against *Cladosporium* (15 mm), as shown in Table 6. There was a marked increase in the bacterial and fungi activities of the Cu(II) complex as compared with the free ligand and other complexes under test, which is in agreement with the antifungal and antibacterial properties of a range of Cu(II) complexes evaluated against several pathogenic fungi and bacteria.[49] For many years it was believed that a trace of Cu(II) destroys the microbe; however, a more recent mechanism is that activated oxygen in the surface of metal Cu kills the microbe because Cu(II) activity is weak.

This enhancement of metal complexes in the activity can be explained on the basis of chelation theory.[50] 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. Such a chelation also enhances the lipophililic character of the central metal atom, which subsequently favors its permeation through the lipid layers of cell membrane and the blocking of the metal binding sites on enzymes of microorganism. The variation in the effectiveness of different compound against different organisms depends either on the impermeability of the cell of the microbes or differences in the ribosomes of microbial cells.

Table 5. Results of antibacterial bioassay (concentration used in 1 mg ml^{-1} of DMSO)

Bacteria	Compound (zone of inhibition in mm)				
	K Sal-SeMet	[CoL(H_2O)]	[CuL(H_2O)]	[ZnL(H_2O)]	SD
E. coli	8	17	21	14	26
B. subtillis	7	19	23	15	25
S. aureus	9	18	22	17	24
P. vulgaris	12	18	21	14	25
E. aerogens	15	16	20	18	22

SD = imipenum. Ligand: >15 mm = significant activity; 7–14 mm = moderate activity; <7 mm = weak activity.

Table 6. Results of antifungal bioassay (concentration used 200 µg ml^{-1})

Organism	Compound (zone of inhibition in mm)				
	K Sal-SeMet	[CoL(H_2O)]	[CuL(H_2O)]	[ZnL(H_2O)]	SD
A. flavus	7	18	24	17	29
A. niger	12	15	26	19	28
F. Solani	11	17	25	17	27
Cladosporium	13	14	15	16	29

SD = amphotericin B. Ligand: >15 mm = significant activity; 7–14 mm = moderate activity; <7 mm = weak activity.

Conclusion

Three complexes, Co(II), Cu(II) and Zn(II), with a tridentate O,N,O-donor Schiff base derived from salicylaldehyde and D,L-selenomethionine were synthesized and characterized, and their biological activity was evaluated by antibacterial and antifungal bioassay. The results demonstrate that Co(II) complex probably have tetrahedral geometry, while the Cu(II) complex probably has square planar geometry. The non-electrolytic nature of the complexes is shown by the low values of the molar conductance of the complexes. The elemental analysis suggests that all metal complexes possess a coordinated water molecule, which is further evidenced by IR spectra and thermal analysis. The results of antimicrobial and antifungal activities show that the metal complexes are more active than the ligand; furthermore, Cu(II) complex is more active than Zn(II) and Co(II) complexes.

Acknowledgments

The support by National Natural Science Foundation of China (20904010) and the Fundamental Research Funds for the Central Universities (2009ZM0170) is gratefully acknowledged.

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