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SYNTHESIS, STEREOCHEMISTRY AND ANTIMICROBIAL ACTIVITY OF COPPER(II) AND NICKEL(II) COMPLEXES OF 4-PHENYLSEMICARBAZONES

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ABSTRACT. 2-Acetylpyridine-(4-phenylsemicarbazone) and *o*-vanillin-(4-phenylsemicarbazone) have been prepared and characterized on the basis of elemental analyses, infrared, electronic, ^{1}H and ^{13}C NMR spectra. Several nickel(II) and copper(II) complexes have been obtained from these ligands. The IR spectra of the ligands as well as those of their complexes suggest that 2-acetylpyridine-(4-phenylsemicarbazone) is a neutral tridentate molecule while *o*-vanillin-(4-phenylsemicarbazone) is a monobasic tridentate molecule. On the basis of the analytical data, magnetic moments and spectral data, a square-planar geometry has been proposed for the nickel(II) and copper(II) complexes with these ligands. Some representative complexes of copper(II) and nickel(II) were found to have remarkable antifungal and antibacterial activity.

KEY WORDS: 4-Phenylsemicarbazone, Metal complexes, Stereochemistry, Antimicrobial activity

INTRODUCTION

Semicarbazones are among the most relevant nitrogen-oxygen donor ligands [1]. A good deal of work has been reported on the preparation and structural investigation of semicarbazones and their complexes [2, 3]. This is due partially to their capability of acting as multidentate, NO, NNO and ONNO donors with the formation of either mono- or bi- or polynuclear complexes [4, 5]. In addition thio- and semicarbazones possess a wide range of bioactivities, and their chemistry and pharmacological applications have been extensively investigated. The more significant bioactivities of a variety of semicarbazones (antiprotozoa, and anticonvulsant) and thiosemicarbazones (antibacterial, antifungal, antitumoral, antiviral) and their metal complexes have been reviewed together with the proposed mechanism of action and structure reactivity relationship [6, 7]. Given these appreciable biochemical applications, as well as the diverse stereochemistry of semicarbazone metal complexes [8-13], this group of ligands deserve further investigations. Furthermore, very little has been reported on 4-phenylsemicarbazone derivatives [14, 15]. In view of this, we describe herein the synthesis of *o*-vanillin-(4-phenylsemicarbazone) (**I**) (H*o*-VSe) and 2-acetylpyridine-(4-phenylsemicarbazone) (**II**) (HacPSe) (Figure 1) and of their nickel(II) and copper(II) complexes (**IIIa** and **IIIb**) (Figure 2). We also report spectral data, magnetic moment measurements and antibacterial and antifungal activities of these compounds.

EXPERIMENTAL

Materials

All chemical used were A.R. grade (USA). Solvents were doubly distilled.

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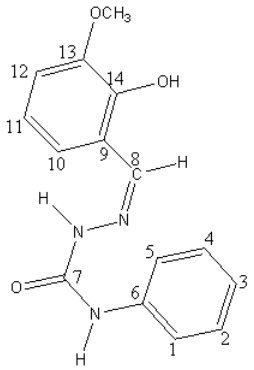
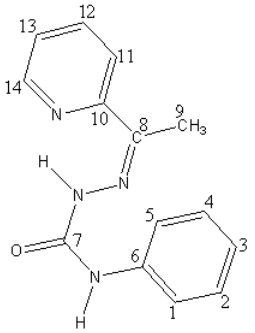


(**I**) H*o*-VSe



(**II**) HacPSe

Figure 1. Structural formulas of the ligands.

Preparation of ligands

2-Acetylpyridine-(4-phenylsemicarbazone) (HacPSe). 4-Phenylsemicarbazide (15.12 g, 0.1 mol) was dissolved in warm ethanol (150 mL) in the presence of glacial acetic acid (1.0 mL). To this solution, 2-acetylpyridine (12.16 g, 0.1 mol) was added while stirring and the resulting solution was boiled under reflux for 1 h. A white microcrystalline precipitate was obtained when the solution was cooled in the refrigerator. The product was crystallized in absolute ethanol and dried over P_2O_5 in a desiccator. The purity of the ligand was checked by a melting point determination and elemental analyses.

o-Vanillin-(4-phenylsemicarbazone)(Ho-VSe). 4-Phenylsemicarbazide (15.12 g, 0.1 mol) was dissolved in warm ethanol (150 mL) in the presence of glacial acetic acid (1.0 mL) and was treated with an ethanol solution of *o*-vanillin (15.22 g, 0.1 mol). The resulting clear solution gradually turned to pale yellow on refluxing for 1 h. The solution was cooled in the refrigerator to give light brown microcrystals which were recrystallized in absolute ethanol and dried over P_2O_5 in a dessicator. The purity of the ligand was checked by its melting point and elemental analyses.

Preparation of complexes

A general method was used for the synthesis of the complexes. They were prepared by mixing an ethanolic solution (20 mL) 0.01 whole of the hydrated metal salt ($MCl_2.6H_2O$, $MBr_2.6H_2O$, $M(NO_3)_2.6H_2O$ or $M(OOCCH_3)_2.6H_2O$) and a warm ethanolic solution (20 mL) of the respective ligand (0.01 mol). The mixture was boiled under reflux for a period of 1-4 h, when the complexes separated out. They were filtered, washed several times with ethanol and dried over P_2O_5.

Physical measurements

Carbon, hydrogen and nitrogen were analyzed using a Perkin-Elmer 2400 elemental analyser (Japan). Magnetic susceptibility measurements were carried out on a Gouy balance using $Hg[Co(CNS)_4]$ as calibrating standard ($x_g = 16.44.10^{-6}$ cgs units at 20 ^oC). Infrared spectra were recorded on a Perkin-Elmer 598 spectrophotometer (Japan) and on a FT-IR Perkin-Elmer 2000 spectrometer (USA) as Nujol mulls between CsI plates. Electronic spectra of samples were

recorded in DMF using a Perkin-Elmer 575 spectrophotometer (USA). Nuclear magnetic resonance (NMR) spectra were obtained using a Joel 270 MHz spectrometer with TMS as internal standard (China). ESR spectra of the complexes were obtained on a Varian E4-EPR spectrometer at about 9.4 GHz and 100 KHz field modulation and phase sensitive direction.

The molar conductances of the complexes were measured by preparing a 10^{-3} M solution of the complex in DMSO employing a Systronic direct reading conductivity bridge supplied with a conventional dip-type black electrode. Melting points were recorded on a Thomas-Hoover capillary melting point apparatus. The halides were determined as their Ag salts. Copper was determined titrimetrically and nickel by a gravimetric method (as glyoximate) using standard procedures.

Antifungal activity

The antifungal activity of the ligands and their complexes in DMF solution was assayed against *Candida albicans*, *Aspergillus niger*, *Aspergillus fumigatus* and *Penicillium islandicum*. The agar plate technique employing 400, 200 and 100 mg/L concentrations of the compounds in DMF solution was used. The tests were done in triplicate for each sample and the results are presented as means and evaluated statistically using Student's t-test or the exact Fischer's test. The linear growth of the fungus was obtained by measuring the diameter of the colony on a Petri plate after 96 h and the percentage of inhibition was calculated from the following relationship:

$$\% \text{ inhibition} = [(C-T)/C] \times 100$$

where C = diameter (in mm)^2 of the fungus colony in the control plates after 96 h and T = diameter of the fungus colony in the treated plates. Nistatine was used as reference standard.

Antibacterial activity

The preliminary screening of the bacterial activity of the synthesized ligands and of their complexes in DMF solution was examined in vitro by the disk method. The disks (7.0 mm diameter) were soaked with different test samples (conc. 1000 ppm), drained and then placed on the nutrient agar plate using sterilized forceps. The plates were incubated at 37 ^{o}C for 24 h. At the end of the incubation period, the zones of inhibition around the disc were measured in mm.

On the basis of preliminary tests, the compounds effecting significant zones of inhibition (10 mm) were then selected and used for the minimum inhibitory concentration (MIC) determination. The MICs were determined by double serial dilution containing 500, 250, 125, 62.5, 31.25, 15.63, 7.81, 3.91 and 1.95 mg/L of the test compounds. Ampicillin was used as reference standard.

RESULTS AND DISCUSSION

The reaction of ethanol solutions of HacPSe and H*o*-VSe with metal salts gave complexes of the general formula [M(HacPSe)X]X where X = Cl^-, Br^-, NO^- and CH_3COO^- and of formula [M(*o*-VSe)X] where X = Cl^-, Br^-, NO_3^- and CH_3COO^-, respectively, as established on the basis of microanalyses and conductance values (Table 1). The general reaction can be expressed by the following equations:

$$MX_2.nH_2O + HacPSe \rightarrow [M(HacPSe)X]X$$

$$MX_2.nH_2O + Ho\text{-}VSe \rightarrow [M(o\text{-}VSe)X]nH_2O + HX$$

All the complexes are thermally and hydrolytically stable and could be stored for several months, and most of them have sharp melting points. They are poorly soluble in water, ethanol, and methanol and in other common organic solvents, but are soluble in DMF and DMSO. The

values of the molar conductance in DMSO for the complexes are in the range 8.00-10.50 $ohm^{-1}.mol^{-1}.cm^2$, suggesting their electrolytic nature.

Table 1. Physical characteristics and analytical data of the compounds.

Compounds	Analysis (%) found (cald.)								
	M.p. (°C)	Yield (%)	C	H	N	M	X	μ_{eff} (BM)	Conductance Ω^{-1} cm^2 mol^{-1}
HacPSe $C_{14}H_{14}N_4O$	187.1	65	66.03 (66.13)	5.67 (5.65)	22.12 (22.03)	- -	- -	-	-
Cu(HacPSe)Cl $C_{14}H_{14}N_4OClCu$	246.6	57	43.74 (43.26)	3.79 (3.63)	14.58 (14.41)	16.11 (16.30)	18.13 (18.24)	1.89	10.20
Cu(HacPSe)Br $C_{14}H_{14}N_4OBrCu$	240.1	60	35.15 (35.20)	2.99 (2.95)	11.65 (11.73)	13.13 (13.29)	33.36 (33.46)	1.95	10.10
Cu(HacPSe)(NO_3) $C_{14}H_{14}N_6O_7Cu$	247.0	56	38.00 (38.05)	3.10 (3.19)	19.10 (19.02)	14.23 (14.36)	-	1.89	10.50
Cu(HacPSe)($OOCCH_3$) $C_{18}H_{20}N_4O_5Cu$	208.0	66	49.34 (49.59)	4.70 (4.62)	12.78 (12.85)	14.40 (14.58)	-	1.57	9.50
Ni(HacPSe)Cl $C_{14}H_{14}N_4OClNi$	350.0	60	44.02 (43.80)	3.82 (3.68)	14.67 (14.69)	15.07 (15.29)	18.25 (18.47)	dia.	10.20
Ni(HacPSe)Br $C_{14}H_{14}N_4OBrNi$	312.8	59	35.47 (35.56)	3.05 (2.98)	11.73 (11.85)	12.23 (12.41)	33.59 (33.88)	dia.	8.70
Ni(HacPSe)(NO_3) $C_{14}H_{14}N_6O_7Ni$	350.0	51	38.55 (38.48)	3.30 (3.23)	19.16 (19.24)	13.31 (13.43)	-	dia.	9.30
Ni(HacPSe)($OOCCH_3$) $C_{18}H_{20}N_4O_5Ni$	308.7	60	50.23 (50.15)	4.77 (4.68)	12.90 (13.00)	13.48 (13.61)	-	dia.	9.20
H*o*-VSe $C_{15}H_{15}N_3O_3$	208.7	71	63.10 (63.14)	5.34 (5.30)	14.66 (14.73)	-	-	-	-
Cu(*o*-VSe)Cl $C_{15}H_{15}N_3O_3ClCu$	196.6	63	46.70 (46.88)	3.82 (3.93)	14.66 (14.73)	16.45 (16.54)	9.15 (9.23)	1.91	10.50
Cu(*o*-VSe)Br $C_{15}H_{15}N_3O_3BrCu$	193.1	66	42.09 (42.02)	3.59 (3.53)	6.71 (9.80)	14.69 (14.82)	18.57 (18.64)	1.97	10.35
Cu(*o*-VSe)NO_3 $C_{15}H_{15}N_4O_6Cu$	200.4	51	43.93 (43.85)	3.69 (3.68)	13.64 (13.64)	15.33 (15.47)	-	1.90	10.40
Cu(*o*-VSe) ($OOCCH_3$) $C_{17}H_{18}N_3O_5Cu$	275.6	59	50.13 (50.06)	4.57 (4.45)	10.22 (10.30)	15.28 (15.56)	-	1.61	8.30
Ni(*o*-VSe)Cl $C_{15}H_{15}N_3O_3ClNi$	264.0	41	47.55 (47.48)	4.07 (3.98)	11.00 (11.08)	15.38 (15.47)	9.15 (9.34)	dia.	10.10
Ni(*o*-VSe)Br $C_{15}H_{15}N_3O_3BrNi$	263.2	50	42.43 (42.50)	3.48 (3.57)	9.87 (9.92)	13.75 (13.85)	19.95 (18.85)	dia.	10.15
Ni(*o*-VSe)NO_3 $C_{15}H_{15}N_4O_6Ni$	268.4	40	44.45 (44.37)	3.79 (3.72)	13.67 (13.80)	14.26 (14.46)	-	dia.	10.20
Ni(*o*-VSe) ($OOCCH_3$) $C_{17}H_{18}N_3O_5Ni$	350.0	51	50.58 (50.66)	4.61 (4.50)	10.38 (10.43)	14.41 (14.56)	-	dia.	10.05

NMR spectra

The structures as well as the bonding nature proposed for the two ligands in this investigation are supported by the ^1H and ^{13}C NMR spectra and chemical shift values (δ, ppm) obtained in DMSO-d_6 solution of the ligands and the nickel(II) complexes.

In the ^1H NMR spectrum of H*o*-VSe, a signal due to methoxy protons appeared as a singlet at 3.85 ppm, whereas the multiplets between 6.80 and 7.70 ppm are all due to the aromatic protons of the phenyl rings. The azomethine (H-C=N-) proton gives a signal at 8.80 ppm. This signal undergoes deshielding to a magnitude of 0.2-0.3 ppm in the nickel(II) complexes, suggesting the involvement of the azomethine group in the bond formation. The signals at 8.85 and 9.40 ppm are attributed to ^4NH and ^2NH protons, respectively. These signals due to NH

protons are shifted downfield to the extent of ~0.2 ppm in the spectra of the nickel complexes. The broad band at δ 10.60 ppm in the ^{1}H NMR spectrum of H*o*-VSe assigned to the OH proton, disappears in the spectra of the nickel(II) complexes suggesting deprotonation of the OH group upon coordination to the metal ion.

The ^{13}C NMR spectrum of H*o*-Vse displayed well defined signals which have been assigned to carbon atoms, as labelled in Figure 1. C_1 and C_5 (128.7 ppm), C_2 and C_4 (119.9 ppm), C_3 (119.2 ppm), C_6 (122.6 ppm), C_7 (153.2 ppm), C_8 (148.1 ppm), C_9 (138.6 ppm), C_{10} (121.1 ppm), C_{11} (112.7 ppm), C_{12} (118.7 ppm), C_{13} (139.4 ppm), C_{14} (145.8 ppm) and C_{15} (56.1 ppm). Comparing the ^{13}C spectrum of *o*-VSeH with those of its nickel(II) complexes shows that the azomethine carbon (C_8) is significantly shifted downfield to 157.1 ppm. The signals assigned to the hydroxyl group carbon (C_{14}) shifted upfield from (145.8 to 37.4 ppm), also that of the (C=O) carbon (C_7) shifts from 153.2-45.3 ppm. These large chemical shifts support coordination via azomethine, hydroxyl and amide group. The shifts affecting other carbon signals were not quite as significant.

^{1}H NMR spectrum of HacPSe gives a single peak at 2.25 ppm which is assigned to the methyl group, while the multiple peaks between 7.00 and 8.66 ppm are due to the aromatic (pyridyl and phenyl) protons in the molecule. The signals at 9.00 and 9.50 ppm are assigned to ^{4}NH and ^{2}NH protons, respectively. These peaks are shifted slightly downfield in the spectra of the nickel(II) complexes to the extent of ~0.2 ppm. This may be due to the reduced electron density at the nitrogen atom.

The ^{13}C spectrum of HacPSe gives 14 intense signals indicating the chemically non-equivalent carbon atoms in the molecule [16]. They are assigned to the carbon atoms, as labelled in Figure 1, as follows: C_1 (122.9 ppm), C_2 (120.3 ppm), C_3 (113.4 ppm), C_4 (120.2 ppm), C_5 (120.8 ppm), C_6 (123.9 ppm), C_7 (155.2 ppm), C_8 (153.4 ppm), C_9 (12.2 ppm), C_{10} (148.7 ppm), C_{11} (139.1 ppm), C_{12} (136.7 ppm), C_{13} (128.8 ppm) and C_{14} (147.0 ppm).

These peak positions are shifted in the nickel(II) complexes. Although most of these shifts are not very significant but a few are large shifts, particularly those of C_8, C_7 and C_{10}. The signal for the C_8, C_7 and C_{10} carbons in the nickel(II) complexes of HacPSe are observed at 160.2-164.3 ppm, 147.3-149.0 ppm and 144.5-145.3 ppm, respectively. Thus, the NMR spectra support the coordination of the azomethine group, CO group and pyridyl nitrogen atom to the metal ions.

IR spectra

The bonding sites of the ligands involved in coordination with the metal ions have been examined by careful comparison of the IR spectra of the ligand and complexes (Table 2).

The band at *ca* 3335 cm^{-1} in the spectrum of H*o*-VSe, which is absent in the spectra of complexes, is ascribed to the free hydroxyl group. The ν(NH) stretching vibration appeared as a medium-intensity band in the region 3270-3370 cm^{-1} for both ligands. The decreasing ν(OH) and ν(NH) wave numbers in the ligand compared to the free ν(OH) group (3700-3500 cm^{-1}) and free ν(NH) group (3500-3300 cm^{-1}), seems to suggest the participation of these groups in intermolecular and intramolecular hydrogen bonding [12, 17, 18]. The strong band at 1660 cm^{-1}, observed in the spectra of the two ligands is assigned to the ν(CO) stretching vibration. This also indicates that the ligands remain in the keto form [19]. A shift to lower frequency, $\Delta\nu \approx 40\pm5$ cm^{-1}, of this band in the spectra of the complexes suggests the involvement of the CO group in bond formation. The ν(CN) stretching vibration has been assigned to the bands at 1510 and 1570 cm^{-1} in the spectra of HacPSe and H*o*-VSe, respectively. In the spectra of complexes of HacPSe the ν(CN) band is shifted to lower frequency by *ca.* ≈20±2cm^{-1}, whereas a shift to higher frequency by *ca.* ≈ 15±5 cm^{-1} was in the spectra of the metal complexes of H*o*-VSe. The bands at *ca*. 1470-1500 cm^{-1} are attributed to ν(C-N) + δ(N-H), known as amide II bands. The

ν(N-N) band in HacPSe is assigned to the vibration at 1130 cm^{-1} and in H*o*-VSe to the vibration at 1040 cm^{-1}. The new bands in the spectra of the complexes in the regions 520-460, 420-390 and 350-280 cm^{-1} are most probably due to ν(M-O), ν(M-N) and ν(M-Cl) vibrations, respectively [20, 21].

Table 2. Characteristic IR bands (cm^{-1}) of the ligands and their complexes.

Compounds	ν(OH)	ν(NH)	ν(C=O)	ν(C=N)	ν(CN+δNH)	ν(N-N)	ν(M-O)	ν(M-N)	ν(M-X)
HacPSe	-	3370 m	1610 s	1510 s	1470 m	1130 w	-	-	-
Cu(HacPSe)Cl	-	3372 m	1621 s	1490 s	1463 m	1100 m	465 m	410 w	345 m
Cu(HacPSe)Br	-	3373 m	1618 s	1490 s	1462 m	1115 m	470 m	390 m	295 m
Cu(HacPSe)(NO_3)	-	3371 m	1620 s	1492 s	1463 m	1118 m	463 w	405 m	-
Cu(HacPSe)($OOCCH_3$)	-	3376 m	1634 s	1494 s	1464 m	1112 m	460 m	406 w	-
Ni(HacPSe)Cl	-	3372 m	1623 s	1490 s	1465 m	1114 w	468 m	411 m	340 m
Ni(HacPSe)Br	-	3369 m	1628 s	1489 s	1460 m	1120 m	471 w	395 m	300 m
Ni(HacPSe)(NO_3)	-	3372 w	1625 s	1491 s	1461 m	1120 m	469 m	405 m	-
Ni(HacPSe)($OOCCH_3$)	-	3370 w	1618 s	1493 s	1463 m	1123 m	468 m	400 w	-
H*o*-VSe	3335 m	3270 m	1660 s	1570 s	1500 m	1040 m	-	-	-
Cu(*o*-VSe)Cl	-	3271 m	1623 s	1587 s	1507 m	1055 m	511 m	419 m	335 m
Cu(*o*-VSe)Br	-	-	1620 m	1590 s	1510 m	1060 m	505 s	413 m	280 m
Cu(*o*-VSe)(NO_3)	-	3273 m	1621 s	1585 s	1508 m	1058 m	510 m	415 m	-
Cu(*o*-VSe) ($OOCCH_3$)	-	3271 w	1624 s	1583 s	1510 m	1050 w	508 m	414 m	-
Ni(*o*-VSe)Cl	-	3274 m	1619 m	1580 s	1508 m	1057 w	515 m	421 m	340 m
Ni(*o*-VSe)Br	-	3270 m	1615 s	1583 s	1509 m	1057 w	510 m	417 m	285 m
Ni(*o*-VSe)(NO_3)	-	3273 m	1620 s	1581 s	1516 m	1051 m	517 m	420 m	-
Ni(*o*-VSe) ($OOCCH_3$)	-	3270 m	1622 s	1582 s	1503 m	1054 m	510 m	415 m	-

Electronic spectra and stereochemistry

The electronic spectrum of H*o*-VSe showed a band at *ca.* 29,412 cm^{-1} assigned to the π-π* transition of the azomethine group and benzene ring [22]. Similarly, in HacPSe the electronic spectrum showed a band at *ca.* 31,250 cm^{-1} attributed to the π-π* transition of the azomethine and phenyl groups and another band at ca. 25,641 cm^{-1} which may be assigned to n-π* transition involving molecular orbital of the azomethine group chromophore [23, 24]. These bands have shifted to lower frequencies (Table 3) suggesting that the nitrogen atom of the azomethine group is coordinated to the metal ion [24].

The electronic spectra of the copper(II) complexes displayed a sharp band in the range 14,300-16,000 cm^{-1} and a well defined shoulder at 16,800-18,500 cm^{-1}.This main band and the shoulder may be assigned to the $^2B_{1g} \rightarrow {}^2E_g$ and $^2B_{1g} \rightarrow {}^2A_{1g}$ transitions, respectively, in a square-planar field.

The copper(II) complexes gave magnetic moments in the range 1.60-1.97 B.M. corresponding to one unpaired spin [25]. Irrespective of the stereochemistry involved, copper(II) complexes contain one unpaired spin per copper atom, unless there is antiferromagnetic exchange interaction between copper pairs in which case lower magnetic moments or even diamagnetism may result. The stereochemistry of the copper(II) complexes is further revealed by the ESR spectra, discussed in the next section.

The complexes of Ni(II) are diamagnetic, suggesting a square-planar geometry. In addition, the electronic spectral bands in the range 16,800-18,500, 18,000-21,100 and 22,500-24,000 cm^{-1}, assigned to $^1A_{1g} \rightarrow {}^1A_{2g}$, $^1A_{1g} \rightarrow {}^1B_{1g}$ and $^2A_{1g} \rightarrow {}^2E_g$, respectively, are similar to those observed for other square-planar nickel(II) complexes [26, 27].

Table 3. Electronic spectral bands (cm^{-1}) and ESR data of the complexes.

Complex	$^2B_{1g}\rightarrow{}^2A_{1g}$	$^2B_{1g}\rightarrow{}^2E_g$	$^g\Pi$		^{g}ev	G
Cu(HacPSe)Cl	15,400(4550)	20,800(4500)	2.176	2.038	2.084	4.63
Cu(HacPSe)Br	14,300 (4890)	20,000(4890)	2.170	2.030	2.077	5.67
Cu(HacPSe)(NO_3)	16,000(4400)	20,500(4070)	2.155	2.027	2.070	5.74
Cu(HacPSe)($OOCCH_3$)	15,400(4290)	20,700(4010)	2.134	2.024	2.061	5.58
Cu(*o*-VSe)Cl	14,800(4700)	20,400(4700)	2.225	2.050	2.108	4.50
Cu(*o*-VSe)Br	14,300(4790)	20,000(4100)	2.221	2.040	2.100	5.53
Cu(*o*-VSe)NO_3	16,000(4350)	21,000(4350)	2.195	2.039	2.091	5.00
Cu(*o*-VSe) ($OOCCH_3$)	15,600(4450)	20,700(4030)	2.180	2.035	2.083	5.14
	$^{2A}{}_{1g}\rightarrow{}^{2A}{}_{2g}$	$^{1A}{}_{1g}\rightarrow{}^1B_{1g}$	$^{1A}{}_{1g}\rightarrow{}^1E_g$			
Ni(HacPSe)Cl	18,000(7010)	20,000(7010)	23,000(6550)			
Ni(HacPSe)Br	18,000(7950)	20,100(7900)	23,500(6790)			
Ni(HacPSe)(NO_3)	18,500(7000)	20,100(6950)	23,300(6400)			
Ni(HacPSe)($OOCCH_3$)	17,800(6800)	19,500(6800)	23,100(6050)			
Ni(*o*-VSe)Cl	17,100(7500)	19,000(7550)	23,600(6850)			
Ni(*o*-VSe)Br	17,000(7810)	18,700(7790)	23,800(6900)			
Ni(*o*-VSe)NO_3	17,000(7100)	18,900(7100)	24,000(6270)			
Ni(*o*-VSe) ($OOCCH_3$)	16,800(6920)	18,000(6910)	22,500(6000)			

^{g}ev = ($^g\Pi$ + $^{2g}\perp$)/3 (ϵ, $dm^3\ mol^{-1}cm^{-1}$) in parentheses.

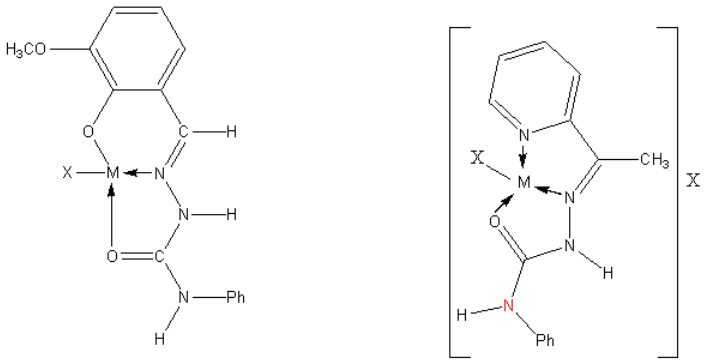
ESR spectra

The ESR spectra of copper(II) complexes were recorded as polycrystalline samples. All the complexes show anisotropic ESR spectra characteristic of tetragonal copper(II) complexes. The g-tensor values have been calculated by Kneubuhl's method [28] and are presented in Table 3. The $g_{\parallel}$ and $g\perp$ values obtained in this investigation are relatively lower than the g values reported for octahedral copper(II) complexes [29]. It follows also from a general observation that, for a D_{4h} molecule, when Δ_1 (d_x^2-$_y^2 \rightarrow d_{xy}$) and Δ_2 (d_x^2-$_y^2 \rightarrow d_{xz,}\ d_{yz}$) become very large, then the $g_{\parallel}$ and $g\perp$ values become smaller [23].

The ground state of copper(II) complexes can be derived from the g-tensor values [30, 31]. From the g-values obtained ($g_{\parallel} > g\perp$), it is evident that the unpaired electron lies predominantly in the d_x^2-$_y^2$ orbital with the possibility of some d_z^2 character being mixed with it because of the low symmetry [24]. The $g_{\parallel}$ values for the respective complexes studied follow the order $CH_3OO^- < NO_3^- < Br^- < Cl^-$ for the respective complexes, which may be taken as the order of the strength of the metal-anion bond in the complex. This agrees well with the position of the anions in the spectrochemical series [32].

The values of G have been calculated by using the expression $G = (g_{\parallel}-2)/(g-2)$. The value of G measures the exchange interaction between copper centers in the polycrystalline solid. According to Hathaway [33], if $G > 4$, the exchange interaction is negligible, whereas for $G < 4$, a considerable exchange interaction is indicated in the solid. The values of G calculated in the present investigation (Table 3) are greater than 4, indicating no significant interactions between the copper centers in the solid copper complexes.

On the basis of elemental analysis data, molar conductivity, magnetic moments, infrared, electronic and electron spin resonance spectra, the tentative general structures proposed for the complexes is presented in Figure 2.



(**IIIa**) H*o*-VSe complexes
M = Cu(II), Ni(II)
X = Cl^-, Br^-, NO_3^-, CH_3COO^-

(**IIIb**) HAcPSe complexes
M = Cu(II), Ni(II)
X = Cl^-, Br^-, NO_3^-, CH_3COO^-

Figure 2. Structures of the complexes.

Antimicrobial activity

The antifungal activity of HacPSe and H*o*-Vse as well as that of their metal complexes are presented in Table 4. The results show that *Candida albicans*, *Aspergillus niger* and *Penicillium islandicum* are relatively sensitive to the tested compounds. There is, generally, a marked improvement in the efficiency of the inhibition by the metal chelates in comparison to that obtained with their corresponding free ligands. HacPSe and its chelates appear to be the most active of the tested compounds with a relatively high percentage of inhibition.

Table 4. Antifungal activity of the ligands and their complexes.

Compound	Inhibition after 96 hours (conc. in µg/mL)											
	Candida albicans			*Aspergillus niger*			*Aspergillus fumigatus*			*Penicillium islandicum*		
	100	200	400	100	200	400	100	200	400	100	200	400
HacPSe	15.0	48.5	65.0	16.8	28.9	50.0	5.9	11.1	35.7	10.0	30.5	60.7
Cu(HacPSe)Cl	26.0	41.6	68.0	30.1	50.0	72.5	25.8	30.3	58.0	28.0	40.5	70.1
Cu(HacPSe)Br	25.1	43.5	67.0	28.0	42.7	58.3	24.0	30.0	56.7	25.6	40.0	69.1
Cu(HacPSe)(NO_3)	26.5	48.0	65.0	28.2	43.9	67.9	25.5	30.1	58.0	27.5	40.1	69.7
Cu(HacPSe)($OOCCH_3$)	25.3	40.5	65.0	28.6	45.5	57.9	23.8	28.7	55.1	27.0	45.2	69.8
Ni(HacPSe)Cl	17.0	36.5	59.0	27.0	40.1	50.0	23.1	27.3	54.7	27.5	41.5	65.8
Ni(HacPSe)Br	16.5	36.1	54.7	26.8	40.0	53.1	20.0	27.0	50.1	24.1	40.7	60.5
Ni(HacPSe)(NO_3)	16.3	37.2	55.3	27.1	48.0	56.0	22.9	28.0	53.7	25.1	41.5	61.1
Ni(HacPSe)($OOCCH_3$)	16.7	38.3	58.7	27.0	41.9	65.0	23.5	28.9	55.0	24.7	42.3	62.7
H*o*-VSe	-	8.1	25.7	-	-	6.5	-	7.5	36.0	6.3	30.1	50.2
Cu(*o*-VSe)Cl	16.7	28.9	40.7	10.0	23.5	36.5	11.7	28.2	46.2	16.3	50.7	68.9
Cu(*o*-VSe)Br	13.5	23.8	29.1	8.0	20.1	26.5	11.0	28.0	45.5	16.1	48.9	65.5
Cu(*o*-VSe)(NO_3)	15.5	28.0	40.0	9.1	23.5	35.0	11.0	27.9	46.4	16.3	49.0	67.1
Cu(*o*-VSe)($OOCCH_3$)	16.5	28.9	40.2	9.0	22.9	30.7	10.9	29.1	46.2	16.0	48.6	68.0
Ni(*o*-VSe)Cl	13.7	24.1	38.2	7.0	9.5	15.9	10.1	28.3	43.9	16.2	47.1	69.0
Ni(*o*-VSse)Br	-	20.0	26.8	-	8.0	11.7	10.3	28.7	45.0	15.4	45.1	65.3
Ni(*o*-VSe)(NO_3)	12.7	21.0	26.0	-	6.5	11.0	10.3	28.7	45.9	15.5	45.7	66.0
Ni(*o*-VSe)($OOCCH_3$)	13.0	22.3	39.0	6.0	8.9	19.0	10.5	29.0	49.3	15.8	45.2	66.8

- inactive.

The antibacterial screening data of the ligands and of their complexes are presented in Table 5. The results show that the tested compounds are able to inhibit *S. aureus*, *E. coli*, *Pseudomonas*, *S. typhi*, *Klebsiella-Enterobacter* at low and high concentrations. The metal chelates are relatively more active than their corresponding ligands. Generally, the minimum inhibitory concentration (MIC) of the test compounds against *E. coli*, *Pseudomonas* and *Klebsiella-Enterobacter*, compared very favourable with that of the standard (Ampicillin).

Table 5. Antibacterial activity of the ligands and their complexes.

Compound	Minimum inhibitory concentration				
	S. aureus	*E. coli*	*Pseudomonas*	*S. typhi*	*Klebsiella-enterobacter*
HAcPSe	125.0	31.3	62.5	125.0	-
Cu(HacPSe)Cl	31.3	15.6	7.8	31.3	62.5
Cu(HacPSe)Br	62.5	62.5	15.6	62.5	-
Cu(HacPSe)(NO_3)	62.5	31.3	15.6	31.3	-
Cu(HacPSe)($OOCCH_3$)	15.6	15.6	7.8	31.3	125.0
Ni(HacPSe)Cl	62.5	31.3	7.8	31.3	125.0
Ni(HacPSe)Br	-	125.0	31.3	125.0	-
Ni(HacPSe)(NO_3)	125.0	125.0	31.3	62.5	-
Ni(HacPSe)($OOCCH_3$)	65.5	31.3	15.6	31.3	-
H*o*-VSe	31.3	62.5	125.0	125.0	125.0
Cu(*o*-VSe)Cl	15.6	31.3	31.3	62.5	62.5
Cu(*o*-VSe)Br	31.3	-	31.3	-	-
Cu(*o*-VSe)(NO_3)	31.3	31.3	62.5	62.5	125.0
Cu(*o*-VSe)($OOCCH_3$)	15.6	15.6	31.3	125.0	-
Ni(*o*-VSe)Cl	31.3	31.3	32.5	125.0	62.5
Ni(*o*-VSe)Br	-	62.5	-	-	125.0
Ni(*o*-VSe)(NO_3)	62.5	-	62.5	-	-
Ni(*o*-VSe)($OOCCH_3$)	15.6	31.3	62.5	62.5	-
Ampicillin	3.9	34.3	15.6	7.8	62.5

- inactive at conc. of 250 μg/mL and lower.

It has been observed in the present investigation that for the tested compounds, the cytotoxicity generally increases with increasing concentration. The enhanced toxicity of the metal chelates, compared to that of the free ligands, can be explained in terms of Tweedy's chelation theory, where chelation is considered to reduce the polarity of the metal ion because of partial sharing of its positive charge with the ligand. This increases the lipid solubility and, hence, favours its permeation into normal cell of the microbes [34].

It is however known, that chelation tends to make the ligands act as more powerful and potent bactericidal agents, thus killing more of the bacteria than the parent ligands, it is suspected that factors, such as solubility, conductivity, dipole moment and cell permeability mechanisms (influenced by the presence of metal ions) may be the possible reasons for increasing this biological activity [35].

CONCLUSIONS

We have synthesized and characterized two new ligands with its copper(II) and nickel(II) complexes. On the basis of the analytical data, the ligands have been found to tridentate in nature, coordinating through the pyridyl nitrogen, azomethine nitrogen and carbonyl oxygen in the case of HacPSe and through the hydroxyl oxygen, azomthine nitrogen and carbonyl oxygen in the case of H*o*-VSe ligand. Square planar geometries have been proposed for the metal complexes. The cytotoxicity of tested compounds generally increased with increase concentration and there were enhanced toxicity of metal chelates compared to that of the free ligands.

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