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MIXED-LIGAND COMPLEXES OF NICKEL (II) WITH 2-ACETYLPYRIDINE THIOSEMICARBAZONE AND SOME N/S MONODENTATE LIGANDS: SYNTHESIS, STRUCTURAL CHARACTERIZATION AND BIOLOGICAL ACTIVITY

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ABSTRACT

The preparation and spectral properties of five nickel (II) mixed-ligands complexes (Ni [2-Actsc.Y]Cl_2), derived from 2-acetylpyridinethiosermicarbazones and some nitrogen/sulphur monodentate ligands such as thiophene, ammonia, picoline, pyridine and aniline are described. The complexes have been characterized on the basis of 1H and 13C-NMR, IR and electronic spectra. These revealed the primary ligand to be a tridentate thiosemicarbazone that coordinate in a square planar conformation to nickel (II) *via* azomethine N, pyridyl N and thiolate S atoms and a monodentate donor molecuole. The antimicrobial activities of these mixed-ligands complexes were investigated. Nickel (II) mixed-ligands complexes derived from 2-acetylpyridinethiosemicarbazones and aniline or ammonia seem to be most efficient inhibitors among these tested compounds.

KEYWORDS: mixed-ligands complexes, square planar geometry, thiosemicarbazones, electronic spectra, biological activity.

INTRODUCTION

Thiosemicarbazones constitute an important class of nitrogen sulphur donor ligand because of their very interesting chemical, biological and medical properties (Offiong & Martelli 1995; Prabhakaran *et al* 2005; Kasuga *el al.* 2003; Nomiya *etal.*). They have been used for spectrophotometri analysis of metals, corrosion inhibition studies and as antimicrobial agent such as antibacterial, antifungal, antiamoebic, even anticonvulsant (Offiong *et al.* 1996; Taroua *et al.* 1996; Ekpe *et al.* 2001). Metal complexes of thiosemicarbazides and thiosemicarbazones have been investigated extensively. Their configurational flexibility creates the possiblitiy of variation in the coordination modes thus enhancing their chelating ability (Casas *et al* 1994; John *et al* 2004; West & Lewis 1988). Their azomethine (CNNCN) backbone kept planar by thione-thiol tautomerism formed the basis of the Lewis base behaviour (Philips *et al* 2004; Chandra *et al 1996).* Complexes of tridentate thiosemicarbazones have widely been reported to have relationship between the structure and antimicrobial activity (Philips *et al* 2004). However, few reports on structure and antimicrobial activity of nickel (II) mixed-ligands complexes have been documented (Taroua et al 1996). This paper describes the synthesis, spectral properties and the antimicrobial activities of nickel (II) mixed-ligands complexes of thiosemicarbazones derived from 2-acetylpyridine and some monodentate donor moleculres like thiophene, picoline pyridine, ammonia and aniline.

Experimental

Reagent grade of high purity materials were used as supplied. IR spectra were measured with a FT-IR Perkin-Elmer 1600 spectrophotometer. CHN analysis were performed using Perking-Elmer PE 240 automatic elemental analyzer. The ^{1}H and ^{13}C- NMR spectra of the ligands were recorded on a Joel 270 MHz spectrometer with TMS as internal reference This spectra were recorded in DMSO solution. The molar conductance measurements in DMF were carried out using a systronic direct reading conductivity bridge with a conventional dip-type black electrode.

Synthesis of the ligand

Thiosemicarbazones were prepared by the literature method (Offiong & Martelli 1995; West & Lewis 1988). In a typical synthesis, thiosemicarbazide (0.19g, 0.01mole) was dissolved in ethanol and glacial acetic acid added. The solution was warmed and treated with drop-wise addition of 2-acetylpyridine (1.21g, 0.01mole) under continuous stirring. The mixture was then heated under reflux for two hours and was then allowed to stand overnight. The precipitate formed was filtered, recrystallized from ethanol and dried over fused calcium chloride.

Synthesis of the mixed-ligands complexes

A solution made of 2-acetylpyridinethiosemicarbazone (0.97g, 0.05mole in ethanol) was added to another solution of nickel (II) chloride hexahydrate (1.19g.0.05moles in 10ml ethanol) and boiled under reflux for 20 minutes. 20mi of the ammonia was added and boiled under refluxed for another 2 hours. The precipitate formed were filtered, washed and recrystallized from ethanol and dried over fused calcium chloride. This procedure was repeated with thiophene, picoline, aniline, aniline and pyridine. Percentage yield of 25.95% for ammonia complex, 27.45% for thiophene complex, 20.50% for picoline complex, 26.02% for aniline complex and 29.55% for pyridine complex were obtained.

Antimicrobial Activity

The antimicrobial activity of nickel (II) mixed-ligands complexes derived from 2-acetylpyridinethiosemicarbazone and nitrogen/sulphur monodenate ligands (thiophene, pyridine, picoline, aniline and ammonia) was determined by the paper disc (7.0mm diameter) method and serial dilution method against *Staphylococcus aureus, Escheriachia coli, Bacillus anthracis Pseudornonanas aeruginosa. (bacteria) Candida albican, Aspergillus niger* and *penicillium marneffei* (fungi). These microbes were obtained from stock cultures and were maintained separately on solid medium containing agar (2% Difco 15/1), Bushnell and Hass salt mixture and glucose (1% W/V). All materials used were sterilized and the inocolum was prepared by treating the nutrient agar media with 3ml of suspension of the respective cell. The colony of each of the tested microbes were subculture and first incubated for about 5 – 8 hours before being poured into agar plates. The discs (7.0mm diameter) were soaked with different test samples (concentration 1000 µg/ml), drained and placed on the agar

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plates using sterilized forceps. The plates were incubated at 37°c for 48 hrs. At the end of the period, the zones of inhibition around the discs were measured.

The test samples effecting significant zones of inhibition (10mm and above) were then selected and used for the minimum inhibitory concentration (MIC) determination. The minimum inhibitory concentration were examine by double serial dilution containing 1000, 500, 250, 125, 62.5, 31.25, 15.63, 7.81, 3.91 and 1.95µg/ml of the test examples. Ampicillin was used as reference standard.

RESULTS AND DISCUSSION

Table 1 show a list of colours, partial elemental analyses and the molar conductance values for the mixed-ligand complexes. The IR and far-IR assignments most useful for the determination of the coordination modes are displayed in Table 2. Table 3 lists the spectral bands and their assignments and finally, Table 4 displays the data on antimicrobial activities of these mixed-ligands complexes.

Table 1: Elemental analysis, colours and molar conductance of Ni(II) mixed-ligands complexes.

Compound	Colour	Molar conductance in ohm^{-1} cm^{-2} mol^{-1} C	Found (calc.)% C	Foud (calc.)% H	Found (calc.)% N
Ni[2-Actsc. Th] Cl_2	Brown	172.2	42.78 (42.28)	4.15 (4.65)	16.58 (17.08)
Ni[2-Actsc. Py] Cl_2	Greenish Brown	165.3	47.06 (47.32)	4.48 (5.03)	21.08 (21.23)
Ni[2-Actsc. Pi] Cl_2	Brown	166.2	48.87 (49.20)	4.87 (4.37)	20.18 (19.78)
Ni[2-Actsc. An] Cl_2	Brown	174.1	48.68 (48.68)	4.57 (5.05)	20.26 (19.87)
Ni[2-Actsc. Am] Cl_2	Yellowish Brown	175.2	35.85 (33.89)	4.72 (5.32)	25.95 (24.42)

Nuclear Magnetic Resonance Spectra

The ^{1}H-NMR spectrum of primary ligand shows signals at δ0.94, 3.03, 10.3 and within the range δ 1 – 8.4ppm; corresponding to NH(d), Methyl proton (b), NH(c) and pyridine ring protons respectively (a). The ^{13}C-NMR spectrum also shows signals at δ12.18ppm for methyl carbon atom (7), δ120.95ppm for carbon atom (3) δ148.5ppm for carbon atom (1) δ145.27ppm for carbon (4), the azomethine carbon atom is at δ154.7ppm while the thioketo carbon atom (8) is at δ179.1ppm. (figure 1)

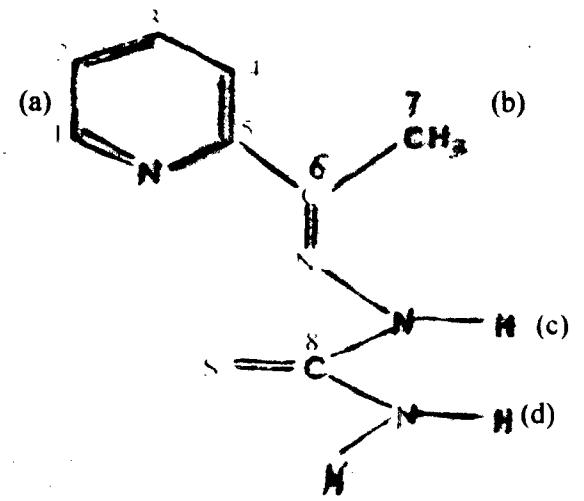

Fig. 1: ^{1}H and ^{13}C-nmr assignment on 2-acetylpyridine-thiosemicarbazone.

Infrared Spectra

The selected IR vibration bands shown on table 2 are the relevant bands for the determination of the coordination modes of the mixed-ligands complexes. The spectrum exhibits strong bands at 3373cm^{-1} and 3182cm^{-1} indicating $\nu_{as}(NH_2)$ and $\nu_s(NH)$ Vibrations.

The presence of ν(NH) in the spectra of the complexes provides good evidence for the ligand coordination around the Ni(II) ion through the thione sulphur atom, the azomethine nitrogen and the pyridyl nitrogen atom. The spectra of the complexes exhibit a systematic shift in the position of the bands in the region 1600 – 1350cm^{-1} due to ν(C = N) and ν(C = S) vibrational modes and their mixing patterns which are different from those present in the primary ligand spectrum. As a result of coordination, the bands corresponding to azomethine nitrogen ν(C = N) shift to higher wave numbers (Akinchan & Akinchan, 1994; Philips *et al*, 2004). The band 810cm-1 assigned to vC = S in free ligand shifted to lower wave numbers in the complexes suggesting changes in bands orders and strong electron-delocalization upon chelation. The appearance of new bands at 310, 269, 280, 240 and 342cm-1 are all attributed to coordination of Ni(II) ion to sulphur of thiophene and nitrogen of pyridine, picoline, aniline and ammonia moieties respectively.

Table 2: Selected IR and far IR vibration bands in cm-1 of nickel (II) mixed-ligands complexes with 2-acetypyridine thiosemicarbazone and N/S monodenate ligands.

Compound	$vaNH_2$	$vsNH_2$	vC=N	vC=S	vN-N	vM-S	vM-S	vM-S/N
Ni[2-Actsc. Th] Cl_2	3355	3170	1587	1205	1035	308	320	310 vm-s (thiophene)
Ni[2-Actsc. Py] Cl_2	3365	3155	1570	1430	1085	389	300	280 vM-N (Pyridine)
Ni[2-Actsc. Pi] Cl_2	3372	3155	1570	1205	1035	306	310	270 vM-N (picoline)
Ni[2-Actsc. An] Cl_2	3373	3183	1603	1250	1065	406	320	396 vM-N (aniline)
Ni[2-Actsc. Am] Cl_2	33653365	3180	1620	1230	1082	362	310	342 vM-N (ammonia)

Electronic Spectra

Solid state electronic spectra of 2-acetylpyridinethiosemicarba-zone and its mixed-ligands complexes of Nickel (II) ion (Table 3) were determined. The ligand has absorption maxima at 36550 and 35100cm^{-1} due to the $\pi \rightarrow \pi^*$ transition of the pyridyl ring and the imine function of the thiosemicarbazone moiety. These bands shift on complexation.

Table 3a: Electronic spectra bands/λ max in cm-1 for 2-acetylpyridinethio-Semicarbazone nickel (II) mixed ligands complexes

Compound	$^1A^{1g} \longrightarrow {}^1A_{2g}$	$^1A_{1g} \longrightarrow {}^2B_{1g}$	$^1A_{1g} \longrightarrow {}^1E_g$
Ni [2-Ac. tsc. Th] Cl_2	20630	22780	30400
Ni [2-Ac. tsc. Py] Cl_2	22530	26950	30490
Ni [2-Ac.tsc. Pi] Cl_2	20070	24850	27080
Ni [2-Ac. tsc. An] Cl_2	21820	23000	28920
Ni [2-Ac. tsc. Am] Cl_2	2250	24180	29860

Table 3b:

	v_2/v_1	v_3/v_1	$10D_q cm^{-1}$	Δ_1	Δ_2	Δ_3
Ni [2-Ac. tsc. Th] Cl_2	1.11	1.27	3590	35460	4980	4850
Ni [2-Ac. tsc. Py] Cl_2	1.16	1.27	5202	35202	6602	3530
Ni [2-Ac. tsc An] Cl_2	1.15	1.29	3420	25980	4820	3190
Ni [2-Ac. tsc. Am] Cl_2	1.16	1.30	5250	34450	6650	3970

The shift of $\pi \rightarrow \pi^*$ bands to the longer wave length region is the result of the C = S bond being weakened and the conjunction system being enhanced after the formation of the mixed –ligand complex. There is the absence of band below 10,000cm thereby confirming the square planar nature of the complexes. For these nickel (II) mixed-ligand complexes the d-d transition are assigned to $^1A_{1g} \rightarrow E_g$, $^1A_{1g} \rightarrow {}^1A_{2g}$ and $^1A_{1g} \rightarrow {}^1B_{1g}$ in order of decreasing energy. The d-d and ligand-metal charge transfer (LMCT) bands appear as weak shoulders centered around 24630cm^{-1} these is attributed to the presence of intense $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, still typical of square planar geometery (Saxena *et al*, 1986). The values of v_2/v_1 ratio range from 1.11 – 1.16 for the five nickel (II) mixed-ligands complexes and this is inconsistent with the values for octahedral geometry but rather these low values affirm the earlier suggested square planar geometry (Figure 2)

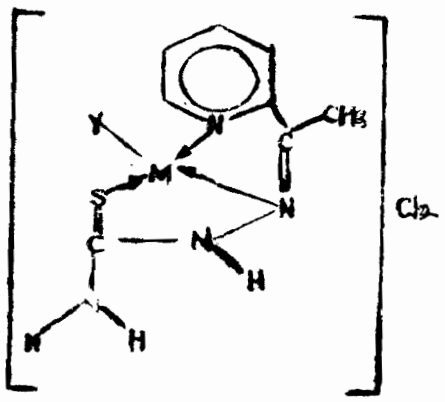

Fig. 2: Nickel (II) mixed ligand complex

Antimicrobial activity

All the synthesized compounds were evaluated for antimicrobial activity against *S aureus, B anthracis, E coli, P. aeruginosa, C. albican, A.niger and P. marneffei* at a concentration of 1000 $\mu g/ml^{-1}$. The active compounds effecting a minimum of 10mm zone of inhibition were used for minimum inhibitory concentration (MIC) determination. The results (Table 4) show that these compounds are able to inhibit these microbes at low and high concentrations. Among the test samples the most active nickel (II) mixed-ligands complex is that derived from 2-acetylpyridine thiosemicarbazone and aniline. This show an inhibition zone of 28 mm at minimum inhibitory concentration of 31.25μg/ml against *S. aureus*, a gram position bacteria, a zone of 25mm at a MIC of $1000\mu g/ml^{-1}$ against *P.aeruginosa* another gram positive bacteria and a zone of 15mm at a MIC of 125μg/ml against a yeast-*Candida albican*. The mixed-ligands complexes containing ammonia is also noted to effect a reasonable level of inhibition on the growth of fungi particularly Candida albican showing a zone of 20mm at a MIC of $62.5\mu g/ml^{-1}$ but less effectives for bacteria with exception of *staphylococcus aureus* (showing a zone of 11mm at a $62.5\mu g/ml^{-1}$). Nickel (ii) mixed-ligands complexes with thiophene and pyridine were the least effective inhibitors on the growth of the microbes.

Table 4: Antimicrobial Activities

Compound	Zone of inhibition at 1000μg/ml in mm	Minimum Inhibitory Concentration (MIC)μg/ml	Microbes
Ni [2-Ac. tsc. Th] Cl_2	11.00	500	*P. aeruginosa*
Ni [2-Ac. tsc. P_y] Cl_2	15.00	1250	*S. aureus*
Ni [2-Ac. tsc. An] Cl_2	10.00	500	*E. coli*
Ni [2-Ac. tsc. Am] Cl_2	25.00	1000	*P. aeruginosa*
Ni [2-Ac. tsc. An] Cl_2	12.00	1000	*P. aeruginosa*
Ni [2-Ac. tsc. Am] Cl_2	28.00	31.25	*S. aureus*
Ni [2-Ac. tsc. An] Cl_2	11.00	62.5	*S. aureus*
Ni [2-Ac. tsc. An] Cl_2	14	1000	*B. anthracis*
Ni [2-Ac. tsc. Th] Cl_2	4.00	1000	*B. anthracis*
Ni [2-Ac. tsc. P_y] Cl_2	7.00	500	*A. niger*
Ni [2-Ac. tsc. An] Cl_2	7.00	500	*A. niger*
Ni [2-Ac. tsc. Am] Cl_2	10.00	250	*A. niger*
Ni [2-Ac. tsc. Th] Cl_2	10.00	125	*C. albican*
Ni [2-Actsc. P_y] Cl_2	9.00	250	*C. albican*
Ni [2-Ac.tsc. Pi] Cl_2	13.00	250	*C. albican*
Ni [2-Ac. tsc. An] Cl_2	15.00	125	*C. albican*
Ni [2-Ac. tsc. Am] Cl_2	20.00	62 5	*C. albican*
Ni [2-Ac. tsc. Am] Cl_2	9.00	1000	*P. marneffei*

The structure-activity relationship in the nickel (II) complexes with thiosemicarbazone is a common report in literature (Kasuga et al, 2003; Das, 1989). Nickel (II) is a bordline acceptor, containing symbiotically induced soft chromophore and readily reacts with these types of Lewis bases to form diamagnetic complexes (Thrumaran and Ramalingam, 2000). The nickel (II) complexes show effective antimicrobial activities against two gram positive bacteria (*S.aureus* and *P.aeruginosa*). Only when they take a labile 4-coordiante structure consisting of a tridentate ligand (2-acetyl pyridinethiosemicarbazone) and one replaceable mondentate ligand such as aniline or ammonia molecule.

CONCLUSION

Five mixed-ligands complexes of nickel (II) 2-acetylpyridine thiosemicarbazone with thiophene, pyridine, picoline, aniline and ammonia were synthesized and characterized. 4-Coordinate configurations were revealed, each nickel (II) ion is coordinated to a neutral tridentate primary ligand (2-Actsc) and a monodentate molecule thereby giving a square planar geometrical structures.

The antimicrobial activity shows that all the test complexes are able to inhibit the microbes at low and high concentrations (II).

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