Research Paper Medical Science

Novel Synthesis, Spectral and Antimicrobial Studyof Fourco - Ordinate Complex and Adducts of Ni (II)

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ABSTRACT

Heterocyclic base adducts of Ni (II) complex have been synthesized by reacting the metal (II) chlorides with 5-chloro 2-hydroxy acetophenone N(4) phenyl thiosemicarbazone and in presence of heterocyclic bases like pyridine (py), α-picoline (α-pico), β-picoline (β-pico) and γ-picoline (γ-pico). Thiosemicarbazones have been characterized by 13C, 1H NMR as well as IR, electronic spectra and ESI-MS. The synthesized complexes were characterized by elemental analysis, IR, electronic spectroscopy,ESI-MS as well as by TGA, DSC, magnetic and conductivity measurement. The magnetic and spectroscopic data indicated square planer geometry for the four coordinate complexes. Antimicrobial assay have also been carried out for synthesized compounds. The thiosemicarbazones and their metal complexes show growth inhibitory activity against Pseudomonas Pudia, Escherichia Coli, Aspergillus Niger and Candida Albicans. Antioxidant studies revealed the pro-oxidative nature of thiosemicarbazones and metal complexes.

KEYWORDS Thiosemicarbazone,N(4) phenyl thiosemicarbazone, Bioactive metal complexes, NiCl2.6H2O.

Introduction

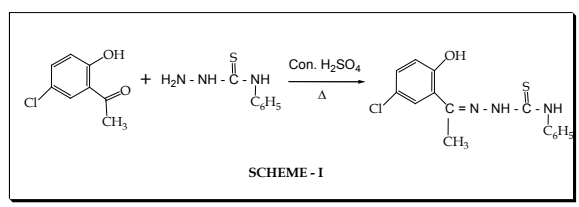
The coordination compounds have been widely used in catalysis and as potential drugs in biological fields [1,2]. Thiosemicarbazones are highly reactive compounds which form chelate complexes with metal ions. There are many complexes with sulphur and nitrogen as donor atoms [3]. Thiosemicarbazones possess beneficial biological activities. The biological activies of thiosemicarbazones are due to their ability to coordinate to metal centres in enzymes. Some pharmaceutically promising thiosemicarbazone derivatives have additional functional groups which are not coordinated to their "primary" metal ion. Thus biological activity is also dependent on the non-coordinating groups. Thiosemicarbazones have variable biological activities and prospective use as drugs [4]. Earlier research revealed that the biologically active thiosemicarbazone molecules were planar consisting of pyridine ring or a NNS tridentate system [5]. The biological activity of thiosemicarbazones is also depended on parent aldehyde or ketone [6,7]. The presence of a bulky group at the terminal nitrogen raises the activity [8]. The presence of bulky groups at the N(4) position of the thiosemicarbazone moiety together with an additional binding site was found to greatly effect biological activity [9-11]. Mossbaur spectral data have been obtained for Fe (II) and Fe (III) complexes of thiosemicarbazones of salicyladehyde and biacetyl monoxime at 80 and 300 °K. Square planar adducts of Ni (II) complex of salicylaldehyde thiosemicarbazone ($ONSH_2$) have been studied. They are red brown and diamagnetic with general composition [Ni(ONS)B] (B = H_2O, NH_3, pyridine, aniline). Here the ligand acts as a doubly charged tridentate by losing protons from phenolic and mercapto groups. Studies on several such adducts of Ni (II) complexes of substituted salicylaldehyde thiosemicarbazones have been reported. Nickel is divalent and exists as Ni (II) in most complexes. Ni (II) complexes exhibit usually four coordinate square planer or tetrahedral geometries. Six coordinate octahedral complexes of Ni (II) have also been reported [12,13]. Ni (II) complexes are generally diamagnetic and some paramagnetic complexes have also been reported [14]

In present work we report the synthesis, spectral characterisation and biological studies of four coordinate complex and adducts of Ni (II) with 5-chloro 2-hydroxy acetophenone N(4) phenyl thisemicarbazone.

Experimental

Materials and instrumentation

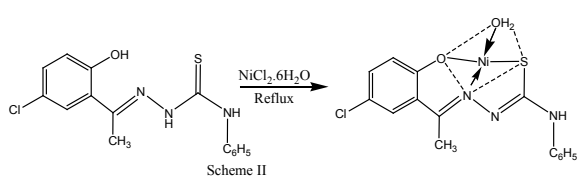
The N(4) thiosemicarbazone was synthesized by refluxing 5-chloro 2-hydroxy acetophenone and N(4) phenyl thiosemicarbazide in ethanol in the mole ratio 1:1 for 4 hours for two hours. The product obtained was filtered , washed with cold ethanol and then diethyl ether. It was recrystalised from acetic acid and dried over P_2O_5 in vacuum.



SCHEME - I

Synthesis of complex

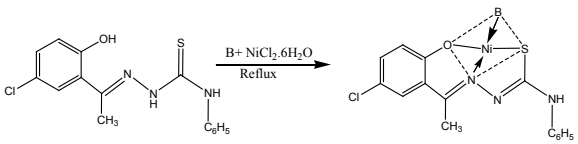
Ni (II) salt was dissolved in absolute ethanol.The ethanolic solution of thiosemicarbazone in slight excess over the metal: ligand ratio of 1:1 was added to it The aqueous solution of sodium cetate was added to the hot (~50^{0}C) reaction mixture dropwise and with constant stirring. The reddish brown product thus obtained was filtered and washed with a small portion of hot water,cold ethanol and then diethyl ether.The product was then dried over P_2O_5 in vacuum.



Scheme II

Synthesis of adducts

Ni (II) salt was dissolved in distilled water.The ethnolic ligand solution containing heterocyclic base (~10 ml pyridine, , α-picoline, β-β —picoline,γ-picoline) in slight excess over the metal: ligand ratio 1:1 was dded to it dropwiw with constant stirring.The mixture ws refluxed for 30 minute on a hot water-bath.The reddish brown product was filtered and washed with hot water,cold ethanol and then with diethyl ether.and dried over P_2O_5 in vacuum.



Scheme III

(B = pyridine,α/β/-γ-picoline)

hysical measurements

Magnetic measurements were carried out by Faraday method. High purity [$Co(SCN)_4$] was used as standard. Diamagnetic corrections were made by Pascal's constants. IR spectra were recorded in the range 4000-200 cm^{-1}. NMR spectra were recorded in the mixture of $CDCl_3$ and DMSO-d_6 (1:1 v/v) with a Bruker AC-300F 300MHz spectrometer. Conductivity measurements were carried out on Conductivity Bridge, Systonics conductivity meter-304. UV-Visible spectra were measured on Jasco UV-visible double beam spectrophotometer.Metal in the complex and adducts was estimated by E.D.T.A using muroxide as an indicator.

Table 1 Physical measurements

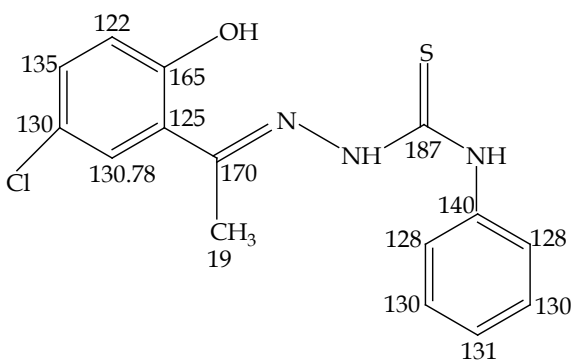
Compounds	Colour	Empirical Formula	Molar conductance $Ohm^{-1}cm^2mole^{-1}$	Magnetic Moment B.M.
L	Yellow	$C_{15}H_{14}N_3ClOS$	-	-
Ni-L.H_2O	Reddish Brown	$C_{15}H_{14}N_3O_2ClSNi$	48.8	Diamagnetic
Ni-L.Py	Reddish Brown	$C_{20}H_{17}N_4OClSNi$	90.5	Diamagnetic
Ni-L. α-Pico	Reddish Brown	$C_{21}H_{19}N_4OClSNi$	75.5	Diamagnetic
Ni-L. β-Pico	Reddish Brown	$C_{21}H_{19}N_4OClSNi$	65.7	Diamagnetic
Ni.L.γ-Pico	Reddish Brown	$C_{21}H_{19}N_4OClSNi$	47.7	Diamagnetic

^{1}H-NMR

Signals at 11.6, 3.30 ppm are assigned to – OH, - CH_3 protons respectively.

L does not show any peak corresponds to S-H proton, indicating it exists in thioketo form. Absence of ^{2}NH proton signal suggests enolisation of ^{2}NH – C = S group to ^{2}N=C-SH. Little low field position of ^{4}NH (7.9 ppm) could be attributable to the deshielding caused by – N = C of the system N=CSH = NH. Aromatic protons show multiples at 6.9, 7.20 , 7.60,7.65,7.77,7.30,6.20,7.29 ppm range.

^{13}C-NMR (DMSO-D_6): δppm 122 (C=C), 135 (C=C), 130 (C=C-Cl), 130.78 (C=C), 125(C=C),165 (C=C-OH),170 (C=N),19 (=C-CH_3),187 (C=S),140 (NH-C=C),128 (C=C),130 (C=C),131 (C=C),130 (C=C),128 (C=C).



(Calcd) found ESI-MS m/z, ion M^+ : $C_9H_{10}ClN_3OS$ (319.77) 319.92, $C_{15}H_{14}N_3O_2ClSNi$ (394.48) 395.10, $C_{20}H_{17}N_4OClSNi$ (455.56) 455.01, $C_{21}H_{19}N_4OClSNi$ (469.96) 469.12, $C_{21}H_{19}N_4OClSNi$ (469.96) 469.19, $C_{21}H_{19}N_4OClSNi$ (469.96) 469.30.

Table.2 Analytical data

Compounds	Elemental Analysis Found (Calculated) %				
	Metal%	%C	%H	%N	%S
L	-	56.07 (56.34)	4.81 (4.41)	13.62 (13.14)	10.91 (10.03)
Ni-L.H_2O	14.12 (14.88)	46.12 (45.67)	3.07 (3.58)	11.10 (10.65)	8.87 (8.13)
Ni-L.Py	12.17 (12.88)	52.14 (52.73)	3.35 (3.76)	12.91 (12.30)	7.52 (7.04)
Ni-L. α-Pico	12.02 (12.49)	53.13 (53.67)	4.82 (4.07)	11.27 (11.92)	6.19 (6.82)
Ni-L. β-Pico	12.08 (12.49)	53.33 (53.67)	4.62 (4.07)	11.57 (11.92)	6.29 (6.82)
Ni.L.γ-Pico	12.10 (12.49)	53.03 (53.67)	4.82 (4.07)	11.33 (11.92)	6.32 (6.82)

Table 3 .Electronic spectral data (cm^{-1})

Compound	Mode	d-d	L→M	n→π*	π→π*
L	DMF	-	-	25971 28571	40865
Ni-L.H_2O	DMF	17,360	23,870	32,051	46,232
Ni-L.Py	DMF	17,099	26,250	33,548	42,023
Ni-L. α-Pico	DMF	17,547	23,820 27,780	32,030	44,014
Ni-L. β-Pico	DMF	17,510	23,645 25,860	32,052	42,232
Ni.L.γ-Pico	DMF	17,525	23,365	33,960	43,911

Infrared Spectroscopic data (cm^{-1})

IR-spectral data

1. L: ν (- OH) 3300; ν (C = N) 1640; ν (- C – S) 794 (s), 1360 (m); ν (N – N) 1055; ν (^{2}N-H) 3225; ν (C – O) 1290.

2 [Ni.L.(H_2O)]: ν (C = N) 1600; ν (C = N-N=C) 1555, ν (C-S) 725, 1295,ν (N-N) 1111, ν (M - N) 450, ν (M-O) 520, ν (M-S) 325, ν (C - O) 1233, ν(H_2O) 3555.

3 [Ni.L.py]: ν (C = N) 1603; ν (C = N-N=C) 1560, ν (C-S) 725, 1303; ν (N-N) 1122, ν (M - N) Base 270, ν (M - N) 460, ν (M - O) 525, ν (M-S) 310, ν (C - O) 1235, Band due to HB 1470.

4 [Ni.L.α-pico]: ν (C = N) 1608; ν (C = N-N=C) 1570, ν (C-S) 735, 1310, ν (N-N) 1129, ν (M - N) Base 271, ν (M - N) 459, ν (M - O) 533, ν (M-S) 333, ν (C - O) 1247, Band due to HB 1450.

5 [Ni.L.β-pico]: ν (C = N) 1610; ν (C = N-N=C) 1540, ν (C-S) 702, 1245, ν (N-N) 1128, ν (M - N) Base 238, ν (M - N) 458, ν (M - O) 538, ν (M-S) 325, ν (C - O) 1250, Band due to HB 1490, ν(H_2O) 3572.

6. [Ni.L.γ-pico]: ν (C = N) 1615; ν (C = N-N=C) 1542, ν (C-S) 715, 1331,ν (N-N) 1130, ν (M - N) Base 231, ν (M - N) 444, ν (M - O) 540, ν (M-S) 337, ν (C - O) 1256, Bands due to HB 1442,

TGA analysis data:

The TGA curves of complexes were recorded between the temperatures 30 °C to 800 °C

1. Ni.L.H_2O: First step, 115 °C, Mass loss 4.58 % second step, 138.29 °C, Mass loss, 15.54 % Third Step 245.43 °C, Mass loss, 30.02 % Fourth Step, 365 °C, Mass loss .60.5 %, Residue 800 °C, % of NiO, 18.23 (18.93).

2. Ni.L.py.$(H_2O)_2$: First step, 200 °C, Mass loss 1.23 % second step,351 °C, Mass loss, 53.41 % , Residue, 778 °C, % of NiO, 16.03 (16.40).

3. Ni.L.α-pico. : First step, 200 °C, Mass loss 3.57 % second step 380 °C, Mass loss, 57.52 % , Residue 780 °C, % of NiO, 15.27 (15.89).

4. Ni.L.β-pico : First step, 214 °C, Mass loss 7.70 % second step, 318 °C, Mass loss, 40.70 % , Residue, 782 °C, % of NiO, 15.27 (15.89).

5. Ni.L. γ-pico: First step, 215 °C, Mass loss 7.70 % second step,311 °C, Mass loss, 46.32 % , Residue 780 °C, % of NiO, 15.35 (15.89).

Biological activity (Agar well diffusion method)
Table.4 % Activity index of L , Ni (II) complexes and standered

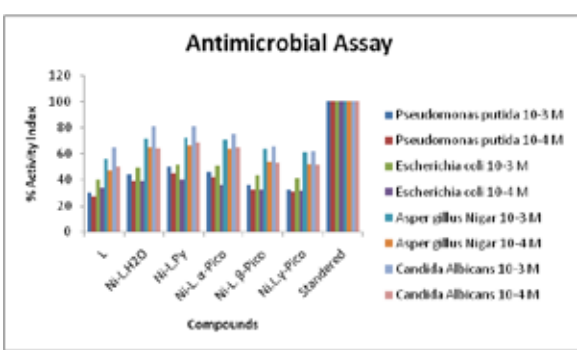
Compound % Activity Index	Pseudomonas putida		Escherichia coli		Asper gillus Nigar		Candida Albicans	
	10^{-3} M	10^{-4} M	10^{-3} M	10^{-4} M	10^{-3} M	10^{-4} M	10^{-3} M	10^{-4} M
L	30.41	27.00	40.32	33.30	55.60	47.36	64.71	50.00
Ni-L.H_2O	44.10	38.92	49.33	38.70	71.20	65.20	81.30	64.00
Ni-L.Py	50.05	44.50	51.00	39.72	72.21	66.17	81.35	68.10
Ni-L. α-Pico	46.08	41.68	50.51	36.39	70.80	63.90	75.10	65.12
Ni-L. β-Pico	36.26	32.32	43.16	32.40	63.60	53.90	65.45	53.01
Ni.L.γ-Pico	32.15	31.12	41.17	31.42	61.15	51.63	61.44	51.00
Standered	100	100	100	100	100	100	100	100

(Std-Bicip)

% activity index was calculated by the formula

$$\% \text{ Activity Index} = \frac{\text{Zone of inhibition of test compound}}{\text{Zone of inhibition of standard (diameter)}} \times 100$$

Fig.1 % Activity Index Bar Graph



Results and discussion

The colour, elemental analysis, stoichiometries of ligand and its complexes are presented in Table 1. Elemental analysis showed 1:1 ratio of metal ion, thiosemicarbazone for complex and 1:1:1 ratio for metal, thiosemicarbazone and heterocyclic base for all adducts. The complex and all adducts are insoluble in polar and non polar solvents. They are soluble in DMF in which conductivity measurements were made (30^0C), showing all complexes to be non electrolyte [15]. Mass spectral data confirmed the structure of the thiosemicarbazone and complexes as indicated by molecular ion peak (M + 1) corresponding to their molecular weights. The room temperature magnetic susceptibility of the complexes showed that complexes are diamagnetic (Table 1).

The planer complexes can be readily distinguished from octahedral and tetrahedral complexes by absence of transitions below 10,000 cm^{-1}. The electronic spectra showed band in 40,000-45,000 cm^{-1} range and 32,000 – 34,000 cm^{-1} range, these can be assigned to Π – Π* (aromatic ring) and n – Π* (thiosemicarbazone moiety) transitions respectively. The broad bands in 32,000 – 34,000 range are assigned for n – Π* transitions [16]. The shift of Π – Π* bands to the longer wavelength region is the result of the C = S bond being weakened and conjugation system being enhanced after the formation of the complex [17]. The spectra show shoulder bands at 17,000 – 18,000 cm^{-1} range. These d–d spectral transitions are assigned to $'A_1g \rightarrow 'Eg$ and $'A_1g \rightarrow 'A_2g$ [18]. The d–d bands appearing as weak shoulders centred around 17000 cm^{-1} region are typically of square planer Ni (II) complexes [19]. The bands at 23,000 – 28,000 cm^{-1} range correspond to L → M. It is associated with $'A_1g \rightarrow 'Eg$ transition. No band below 10000 cm^{-1} confirmed the planer structure of these complexes. This may be due to large crystal field splitting in square planer complex, the energy separation between $dx^2–y^2$ and lower orbital is greater than 10000 cm^{-1} [20].

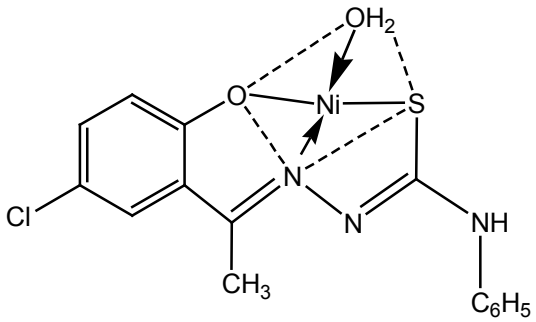
The position of bands in IR are helpful to detect the bonding sites of all ligand molecules interacted with metal. The coordination of azomethine nitrogen shifted ν(C = N) to lower wavenumbers. The band in spectra of uncomplxed thiosemicarbazones at 1640 cm^{-1} shifted to lower wavenumbers in spectra of complex. The coordination of azomethine nitrogen is confirmed by shifting ν(N-N) to higher wavenumber in spectra of complexes than that of thiosemicarbazones [21]. The new band at 440 – 460 $cm^{-1}$is assignable to ν(Ni – N) in the complexes,confirmed the coordination of azomethine nitrogen. There is a loss of – ^{2}NH proton on coordination via thiolate sulphur [22]. Decrease in ν(C = S) bands found at 794, 1360 in L and the presence of new band in the 310–340 cm^{-1} range assignable to ν(NiS), confirmed the coordination through sulphur. The phenolic oxygen occupies the third coordination on the loss of OH proton. This causes shifting of ν(CO) to lower wavenumbers. The band at 520–540 cm^{-1} is assignable to ν(Ni-O). The coordination of heterocyclic nitrogen atom is confirmed by the presence of ν(Ni-N) band in the range 230–272 cm^{-1}. The characteristic bands of coordinated heterocyclic bases observed in IR spectra of all the adducts. The band due to ν(H_2O) is observed in Ni.L.H_2O at 3555 cm^{-1}.

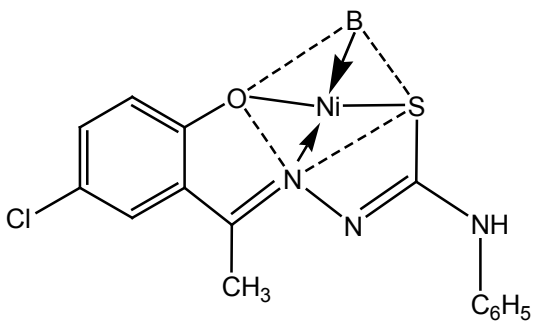
The coordinated water molecules in complex was removed in one step. In Ni.L.H_2O ,water molecule was removed at a temperature 115°C corresponding to mass loss 4.58 %. The TGA data of complex and adducts indicated that the decomposition proceeded in two steps in adducts. In between temperature 30-120 °C, hydration of water molecules were lost. There is no change up to~200 °C after that there is break in the curves due to evaporation of part of molecule of organic ligand, the remaining ligand is removed from the coordination sphere at ~ 600 °C. Finally the metal oxides were formed above 600 °C. The decomposition was completed at ~800 °C. It has been found that Ni (II) complex was stable up to 200 °C and decomposition started above this temperature was completed in the temperature range 300-380°C. The second steps are in the range of 310-380 °C. The solid residue was of NiO [23]. Thus complexes prepared with different metals decompose in two steps. It is evauated that the coordination of metal ion to ligand is responsible for the thermal stabilities of metal complexes [24].

The antimicrobial assay was carried out by the agar well diffusion method. The activity was determined by measuring the diameter of the inhibition zone (in mm). Biological activity was measured in two different molar concentrations (10^{-3}M, 10^{-4} M). The chelate Cu.L.bipy showed maximum activity against bacterial and fungal species than free ligand. The results of antibacterial and antifungal studies are given in Table 4. In these six compounds tested, Ni.L.py was found to be more active against four cultures. The thiosemicarbazone was found less active than its complex and adducts. Thus increase in coordination number in complexes increases microbial ac-

tivity. Thus it is evaluated that the coordination of metal ion to ligand is responsible for high biological activity.It has been observed that the % activity index decreases on dilution ie it is more in concentrated solution.

Expected structures





(B = pyridine, α-picoline, β-picoline,γ-picoline)

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