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Design,Spectral,Novel Synthesis, and Antimicrobial Study of Four Co¬-Ordinate Complex And Adducts of Ni (Ii)

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ABSTRACT

Ni (II) complex and adducts have been synthesized by reacting the Ni (II) chloride with 3,5-dichloro 2-hydroxy acetophenone N(4) methyl thiosemicarbazone and in presence of heterocyclic bases like pyridine (py),2-chloropyridine, 3-chloropyridine and 4-chloropyridine Thiosemicarbazone has been characterized by 13C, 1H NMR as well as IR, electronic spectra and EI-MS. The synthesized complex and adducts were characterized by elemental analysis, IR, electronic spectroscopy,EI-MS as well as by TGA, magnetic and conductivity measurement. The magnetic and spectroscopic data indicated square planer geometry for the four coordinate complex and adducts. Antimicrobial assay has also been carried out for synthesized compounds. The thiosemicarbazone and its metal complexes showed growth inhibitory activity against Staphylococcus aureu,Bacilus subtilis(Gram+ve), Escherichia Coli,Peudomonas aeruginosa (Gram-ve) bacterial species.

KEYWORDS : Thiosemicarbazone,N(4) methyl thiosemicarbazone, Minimum inhibitory concentration, $NiCl_2.6H_2O$.

Introduction

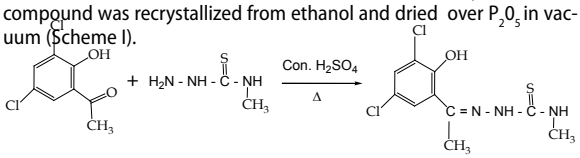
Thiosemicarbazones are the derivatives of thiourea and their study on chemical and structural properties is important attention due to the wide application in the chemotherapeutic field [1, 3]. Hence thiosemicarbazones is a subject of interest to researchers. Thioemicarbazones form complexes with many transition metals and these complexes have diverse chemical, physical and structural characteristics [1, 2]. The group N-C=S is chemotherapeutic interest and is responsible for the pharmacological activity. Thiosemicarbazones of or-(N)-heterocyclic aldehydes and ketones possess useful chemotherapeutic activities such as antimalarial, antibacterial, antiviral activities [4,5]. Thiosemicarbazones behave as monoanionic tridentate ligands coordinating to a metal centre through the deprotonated phenolic oxygen, thione sulfur and the azomethine nitrogen [6]. The study of the coordination chemistry of such ONS donors increased after the presence of ONS donor environment was detected at the active sites of some metalloenzymes [7-9]. In thiosemicarbazones and their metal complexes the important feature is the acid character of the 2NH;.This allows for either neutral or anionic ligands. The conjugation is extended to include the thiosemicarbazone moiety (ie C=N-N=C(S^-)-N) when coordinated as anionic ligands. Salicylaldehyde thiosemicarbazone Ni(II) complexes, are used as homogeneous catalysts. Complexes of metals with thiosemicarbazone ligands show wide range of biological properties, such as antibacterial, antimalarial, antiviral and antineoplastic activities [10]. Nickel(II) complexes containing sulfur donors showed a sulfur rich coordination environment in biological nickel centers such as at the active sites of certain ureases, methyl-S-coenzyme-M-methyl reductase, hydrogenases and may play a role in the supposed mutagenicity of nickel compounds. Biological nickel ions are unusual in the context of the known coordination chemistry of nickel [11]. Ni (II) complexes are generally diamagnetic and some paramagnetic complexes have also been reported [12]

The present work deals with the synthesis, structural and spectral characterization of Ni(II) complexes with N(4)-methyl Ithiosemicarbazone ligand.

Experimental

Synthesis of ligand:

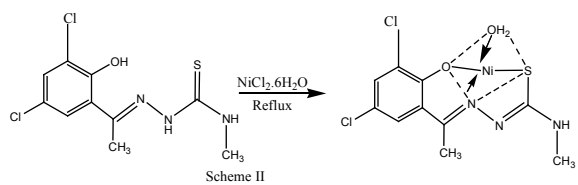
A 0.01 mole soution of 4- methyl-3-thiosemicarbazide in 20 ml ethanol was treated with 0.01 mole ethanolic soution of 3,5 dichloro 2-hydroxy acetophenone and refluxed for 3 hours. The reaction mixture was cooled and faint yellow compound separated out. The solution was filtered, washed well with ethanol and then diethyl ether. The compound was recrystallized from ethanol and dried over P_2O_5 in vacuum (Scheme I).



SCHEME - I

Synthesis of complex:

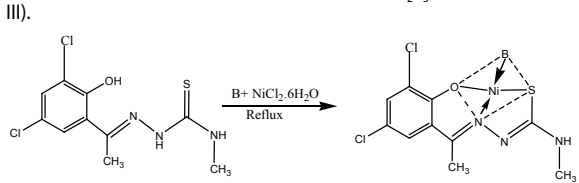
This complex was synthesized by refluxing an ethanolic solution of ligand (0.01 mole) with ethanolic solution of $NiCl_2.6H_20$ (0.01 mole) for 7 hours. The reddish brown complex formed was filtered, washed with hot water,cold ethanol and finally with ether and dried over P_20_5 in vacuo (Scheme II).



Scheme II

Synthesis of adducts

The adducts were synthesized by refluxing an ethanolic solution of ligand (0.01 mole) with ethanolic solution of $NiCl_2.6H_20$ (0.01 mole) and ethnolic ligand solution containing heterocyclic base (~10 ml pyridine, , 2-chloro pyridine,3-chloro pyridine, 4-chloro pyridine) in slight excess over the metal: ligand ratio 1:1 for 7 hours. The reddish brown compound formed was filtered, washed with hot water,cold ethanol and finally with ether and dried over P_20_5 in vacuo (Scheme III).



Scheme III

(B = pyridine, 2-chloro pyridine,3-chloro pyridine, 4-chloro pyridine)

Materials and methods

Elemental analysis wa recorded ona perkin elmer elemental analyzer. The infrared spectra of the olid sampexs were recorded in Jasco spectrometer in the range of 4000-200 cm^{-1} .Electronic pectra were recorded uing Jasco UV-visible double beam spectrophotometer using DMF olvent in the range of 200-800 nm.The molar conductivity measurements of the metal complexe werecarried out in ~10^{-3}M DMF solutions using digital conductivity meter.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. 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.Metal in the complex and adducts was estimated by E.D.T.A using muroxide as an indicator.

Table 1 Physical measurements

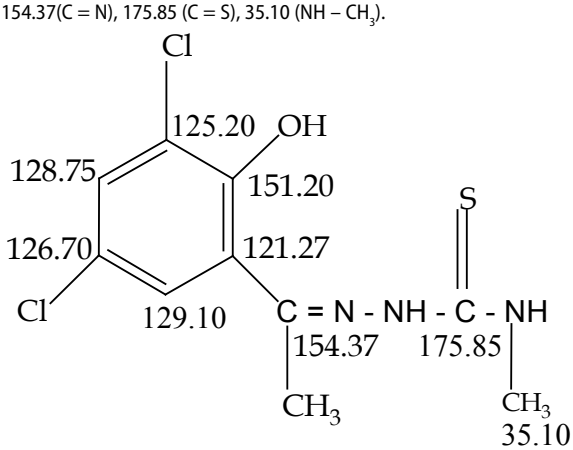
Compounds	Colour	Empirical Formula	Molar conductance $Ohm^{-1}cm^{-2}mole^{-1}$	Magnetic Moment B.M.
L	FaintYellow	$C_{10}H_{11}N_3OSCl_2$	-	-
Ni-L.H_2O	Reddish Brown	$C_{10}H_{11}N_3O_2SCl_2Ni$	55.8	Diamagnetic
Ni-L.Py	Reddish Brown	$C_{15}H_{14}N_4OSCl_2Ni$	88.5	Diamagnetic
Ni-L.2-Cl py	Reddish Brown	$C_{15}H_{13}N_4OSCl_3Ni$	78.5	Diamagnetic
Ni-L. 3-Cl py	Reddish Brown	$C_{15}H_{13}N_4OSCl_3Ni$	68.7	Diamagnetic
Ni.L.4-Cl py	Reddish Brown	$C_{15}H_{13}N_4OSCl_3Ni$	57.7	Diamagnetic

^{1}H-NMR

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

^{1}H-NMR signals at 12.00 and 2.4 ppm are assigned to – OH and – CH_3 protons respectively. The signals at 2.30, 3.01 correspond to ^{4}NH and H^{4}N-CH_3 respectively. Signal at 10.5 ppm corresponds to ^{2}NH. Aromatic protons show multiplets at 7.0, 7.20, 7.35, ppm.

^{13}C-NMR (DMSO-D_6): δppm 125.20 (C = C-Cl), 128.75 (C = C), 127.79 (C = C – Cl), 126.70 (C = C), 129.10 (C = C), 151.20 (C = C – OH), 154.37(C = N), 175.85 (C = S), 35.10 (NH – CH_3).



(Calcd) found ESI-MS m/z, ion M$^+$: $C_{10}H_{11}N_3OSCl_2$ (292.17) 292.89, $C_{10}H_{11}N_3O_2SCl_2Ni$ (366.86) 366.12, $C_{15}H_{14}N_4OSCl_2Ni$ (413.93) 413.33, $C_{15}H_{13}N_4OSCl_3Ni$ (448.37) 448.67, $C_{15}H_{13}N_4OSCl_3Ni$ (448.37) 448.69, $C_{15}H_{13}N_4OSCl_3Ni$ (448.37) 448.75.

Table.2 Analytical data

Compounds	Elemental Analysis Found (Calculated) %				
	Metal%	%C	%H	%N	%S
L	-	41.74 (41.11)	3.13 (3.79)	14.88 (14.38)	10.21 (10.97)
Ni-L.H_2O	16.25 (16.00)	32.34 (32.74)	3.74 (3.02)	11.84 (11.45)	8.14 (8.74)
Ni-L.Py	14.82 (14.18)	43.89 (43.52)	3.80 (3.41)	10.50 (10.15)	7.13 (7.75)
Ni-L.2-Cl py	13.77 (13.07)	40.57 (40.18)	2.10 (2.92)	9.81 (9.37)	7.88 (7.15)
Ni-L. 3-Cl py	13.88 (13.07)	40.53 (40.18)	2.62 (2.92)	9.78 (9.37)	7.62 (7.15)
Ni.L.4-Cl py	13.92 (13.07)	40.88 (40.18)	2.52 (2.92)	9.53 (9.37)	7.76 (7.15)

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

Compound	Mode	d-d	L –M	n –π*	π –π*
L	DMF	-	-	25,800 28,500	40,800
Ni-L.H_2O	DMF	17,550	23,500	33,100	46,267
Ni-L.Py	DMF	17,199	26,440	33,600	42,340
Ni-L.2-Cl py	DMF	17,400	23,750 27,900	32,250	44,023
Ni-L. 3-Cl py	DMF	17,850	23,200 25,870	32,280	42,363
Ni.L.4-Cl py	DMF	17,540	23,303	33,523	43,111

Infrared Spectroscopic data (cm^{-1})

IR-spectral data

1. **L**: ν (- OH) 3200; ν (C = N) 1642; ν (- C – S) 790 (s), 1365 (m); ν (N – N) 1060; ν (^{2}N-H) 3250; ν (C – O) 1295.
2. **[Ni.L.(H_2O)]:** ν (C = N) 1602; ν (C = N-N=C) 1551, ν (C-S) 719, 1296,ν (N-N) 1114, ν (M - N) 445, ν (M-O) 525, ν (M-S) 321, ν (C - O) 1230, ν(H_2O) 3550.
3. **[Ni.L.py]:** ν (C = N) 1605; ν (C = N-N=C) 1553, ν (C-S) 722, 1305; ν (N-N) 1117, ν (M - N) Base 272, ν (M - N) 450, ν (M - O) 528, ν (M-S) 325, ν (C - O) 1235, Band due to HB 1472.
4. **[Ni.L.2-Cl py]:** ν (C = N) 1605; ν (C = N-N=C) 1555, ν (C-S) 730, 1311, ν (N-N) 1120, ν (M - N) Base 273, ν (M - N) 460, ν (M - O) 530, ν (M-S) 330, ν (C - O) 1240, Band due to HB 1475.
5. **[[Ni.L.3-Cl py]:** ν (C = N) 1609; ν (C = N-N=C) 1558, ν (C-S) 732, 1315, ν (N-N) 1125, ν (M - N) Base 277, ν (M - N) 462, ν (M - O) 535, ν (M-S) 332, ν (C - O) 1245, Band due to HB 1480.
6. **[Ni.L.4-Cl py]:** ν (C = N) 1613; ν (C = N-N=C) 1560, ν (C-S) 715, 1320,ν (N-N) 1130, ν (M - N) Base 280, ν (M - N) 465, ν (M - O) 542, ν (M-S) 338, ν (C - O) 1250, Bands due to HB 1485,

Thermogravimetric analysis:

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

1. [**Ni.L.H_2O**]: First step, 110 °C, Mass loss 4.31 % second step, 138.29 °C, Mass loss, 20.54 % Third Step 245.43 °C, Mass loss, 50.02 % Fourth Step, 365 °C, Mass loss .61.5 %, Residue 800 °C, % of NiO, 20.91 (20.36).
2. [**Ni.L.py**]: First step, 202 °C, Mass loss 10.23 % second step,345 °C, Mass loss, 60.21 % , Residue, 780 °C, % of NiO, 18.64 (18.04).
3. **[Ni.L.2-Cl py]:.** : First step, 210 °C, Mass loss 13.57 % second step 350 °C, Mass loss, 60.52 % , Residue 780 °C, % of NiO, 16.04 (16.66).
4. **[Ni.L.3-Cl py]:**: First step, 212 °C, Mass loss 17.70 % second step, 318 °C, Mass loss, 50.70 % , Residue, 781 °C, % of NiO, 16.17 (16.66).
5. **[Ni.L.4-Cl py]:**: First step, 215 °C, Mass loss 17.70 % second step,315 °C, Mass loss, 55.30 % , Residue 780 °C, % of NiO, 16.20 (16.66).

Antimicrobial activity (Agar plate diffusion method)

Table.4 % Activity index of L , Ni (II) complexes,metal salt and standered

Compound % Activity Index	Staphylococcus aureu		Bacilus subtilis		Escherichia Coli		Pseudomonas aeruginosa	
	Gram positive				Gram negative			
	800 µg/ml	1000 µg/ml	800 µg/ml	1000 µg/ml	800 µg/ml	1000 µg/ml	800 µg/ml	1000 µg/ml
L	17.35	20.18	16.30	21.30	17.60	21.36	18.71	22.00
Ni-L.H_2O	28.17	32.92	29.33	33.70	27.20	33.20	26.30	32.00

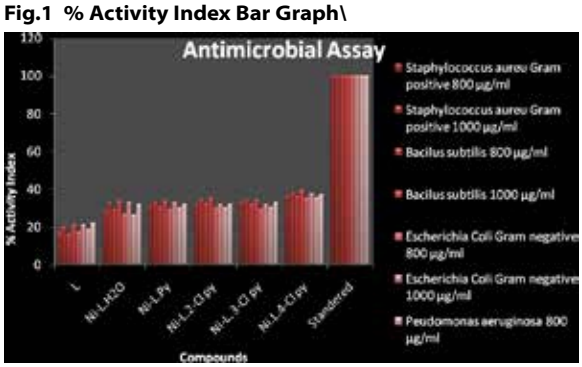
Ni-L.Py	31.05	33.50	31.00	33.72	29.21	33.17	30.35	32.10
Ni-L.2-Cl py	32.08	34.68	32.51	35.39	29.80	31.90	30.10	32.12
Ni-L. 3-Cl py	33.26	34.32	32.10	34.40	29.60	31.90	30.45	33.01
Ni.L.4-Cl py	36.15	38.12	36.17	39.42	35.15	37.63	35.44	37.00
Standered	100	100	100	100	100	100	100	100

(Std-Amphiciline)

% 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

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 soluble in DMF in which conductivity measurements were made (26^{0}C), showing all complexes are non electrolyte in nature [13]. Mass spectral data confirmed the structure of the ligand and complexes corresponding to their molecular weights.Magneticsusceptibility measurements at 296 K show that all the complexes and adducts are diamagnetic (Table 1). The diamagnetism of the Ni(II) complexes is strong evidence that coordination occurs through the thiolato sulfur atom, since thiols but not thioethers cause spin pairing in complexes of Ni(II). Its diamagnetism and the presence of d-d band in the range 565-570 nm in their electronic spectra suggest a square planar structure [14].

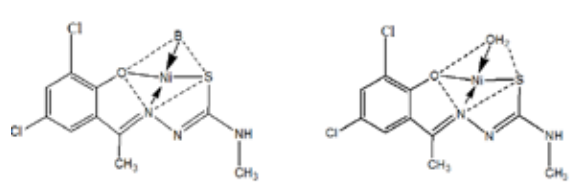
The electronic spectral data of the ligand and its complexes are presented in Table 3. Thiosemicarbazone shows a Π – Π* (aromatic ring) band in the range 40,000-41,000 cm^{-1} and n – Π* (thiosemicarbazone moiety) band in the range 25,000 – 29,000 cm^{-1} [15]. These bands are slightly shifted upon complexation. 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 [16, 17]. The n – Π* bands in the complexes are due to donation of lone pair of electrons to the metal and hence the coordination of azomethine with a reduction of intensity [16]. The planer complexes can be readily distinguished from octahedral and tetrahedral complexes by absence of transitions below 10,000 cm^{-1}. In complexes a broad d-d combination bands that appear as a shoulder on the intraligand and charge-transfer bands.These transitions can be assigned to $^1A1g \rightarrow {}^1Eg, {}^1A1g \rightarrow {}^1A;g$ and $^1Ag \rightarrow {}^1B_1g$ For a square planar complexes [18]. The absence of bands below 10000 cm'l confirms the square planar nature of the complexes.

The characteristic IR bands for the thiosemicarbazone is differ from those of its complexes and provide significant information regarding the bonding sites of the ligands. A band in the range 3200-3300 cm'1 in the free thioemicarbazone due to the ν(^{2}NH) vibration disappeared in the spectra of complexes indicate ligand coordination around the Ni(II) ion in its deprotonated form. The IR spectra of thiosemicarbazone exhibit \/(OH) vibration at 3200 which disappeared in the spectra of complexes [19]. The decrease in ν(CO) and an appearance of a band in the range 525-545 cm^{-1} is due to a \/(Ni-O) stretch in the spectra of complexes [20]. It indicates coordination via phenolic oxygen. On coordination of azomethine nitrogen, ν(C=Nazo) shifts to lower wavenumber from I642 cm^{-1} in the uncomplexed thiosemicarbazone to 1602 cm^{-1} in the spectra of complexes. The presence of new band in the range 445-465 cm^{-1}confirms the coordination of azomethine nitrogen in the complexes [21, 22]. The ν(N-N) of the thiosemicarbazone is found at the 1114 cm^{-1}. The increase in the frequency of this band in the spectra of the complexes, due to the increase in the bond strength, confirms the coordination via the azomethine nitrogen. The bands at the I365, 790 ccm^{-1} due to thioamide stretching and bending vibrations, respectively, of the thiosemicarbazone are shifted to lower values,providing evidence of coordination of the thiolate sulfur to the Ni(II) ion. This lowering in frequency can be due to a change of bond order and strong electron delocalization upon complexation [23,24]. The presence of new bands in the range 320-340 cm^{-1} confirm coordination via thiolato sulfur in the complexes [25, 26]. The coordination of heterocyclic nitrogen atom is confirmed by the presence of ν(Ni-N) band in the range 270-280 cm^{-1}.The IR spectra how characteristic bands of coordinated heterocyclic bases [27]. The band due to ν(H_2O) is observed in Ni.L.H_2O at 3550 cm^{-1}.

The coordinated water molecule in complex was removed in one step. In Ni.L.H_2O ,water molecule was removed at a temperature 110°C corresponding to mass loss 4.31 %. The TGA data of complex and adducts indicated that the decomposition proceeded in two steps in adducts. In between temperature 30-110 °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 ~780 °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 300-350°C. The second steps are in the range of 300-350 °C. The solid residue was of NiO [28]. Thus complexes prepared with different metals decompose in two steps. It is evauated that the coordination of metal ion to ligand makes the metal complexes stable [29].

The antimicrobial assay was carried out by the agar plate diffusion method. The activity was determined by measuring the diameter of the inhibition zone (in mm). Activity was measured in two different concentrations (800µg/ml, 1000µg/ml). The adducts showed maximum activity against bacterial species than free ligand. The results of antibacterial studies are given in Table 4. In these six compounds tested, adducts were found to be more active against four cultures. The thiosemicarbazone was found less active than its complex and adducts. The increase coordination number increases on complexation,this increases microbial activity. Thus it is evaluated that the coordination of metal ion to ligand enhances biological activity.More activity was observed at 1000µg/ml concentration.The minimum inhibitory concentration is 800µg/ml.Below this no activity was observed. Gram positive species showed better activity than gram negative pecies. It has been observed that the % activity index for free metal ion is higher than metal in binded form.

Expected structures



(B = pyridine, 2-chloro pyridine, 3-chloro pyridine, 4-chloro pyridine)

REFERENCES

1. M.J.M. Campbell, Coord. Chem. Rev. 15,1975, 279. 2. Padhye S, Kauffman G.B. Coord. Chem. Rev. 63, 1985, 127. 3. West D.X.,. Libena A.E, Padhye S.B., Chikate R.C., Sonawane P.B.,. Kumbhar A.S,. Yerande R.G, Coord. Chem. Rev. 123, 1993, 49. 4.. Klayman D.L,. Hoch J.M,. Scovill J.P, Lambross C.,. Dobeek A.S J. Pharm. Sci. 73 ,1984, 1763. 5.. Dodd R.H,. Quannes C,. Robert Gero M, Potier P. J. Med. Chem. 32 1989 ,1272. 6.. Purohit S,. Koley A.P,. Prasad L.S,. Manoharan P.T,. Ghosh S, Inorg. Chem. 28 ,1989 3735. 7. Kmger H.J.,. Peng G,. Holm R.H, Inorg. Chem. 30,1991,734. 8.. Holm R.H, Coord. Chem. Rev. 100 ,l990,l83. 9.. Meriwether L.S,. Marzluff W.F,. Hodgson W.G, Nature 212 ,1966, 465. 10.. Castineiras A,. Carballo R,. Perez T, Polyhedron 20 ,2001,441. 11. Naik A.D,. Annigeri S.M,. Gangadharmath U.B,. Revankar V.K,. Mahale V.B, J. Mol. Struct. 616 ,2002, 119. 12.Mathew M., Palenik G.J., Clark G.R., J. Inorg. Chem, 1973, 12, 346. 13.Geary W.J., Coord. Chem. Rev, 1971, 7, 81. 14. Gray H.B,. Ballhausen C.J, J. Am. Chem. Soc. 85, 1963, 260. 15. West D.X, Salberg M.M., Bain G.A., Liberta A.E, Trans. Met. Chem. 22 1997 180. 16.Philip V, Suni V. Kurup M .R.P., Polyhedron 25 ,2006, 1931. 17.. Li I-X,. Tang H.A, Yi-Zhi Li,. Wang M, Wang L.-F,. Xia C.-G J. Inorg. Biochem. 78,2000, 167. 18.Dave, P. Francis, Indian J. Chem. 22A, 1983, 422. 19.. Latheef L,. Manoj E, Kurup M.R.P.. Acta Crystallogr. C 62 ,2006, 16. 20.. Mikuriya M, Okawa H., Kida S. Bull. Chem. Soc. Japan 53 ,1980, 3717. 21.. Sousa P. Garcia-Vasquez J.A, Masaguer J.R, Trans. Met. Chem. 9 ,1984,318. 22.. West D.X,. Nassar A.A, E1-Saied RA,,. Ayad M.1, Trans. Met. Chem. 23,1998,423 23.. Bera P, Butcher R.J,,. Chaudhuri S ,. Saha N, Polyhedron 21 2005, 1. 24. Campbell M.J.M. Coord. Chem. Rev. 15 ,1975, 279. 25.. Nag S.K,. Joarder D.S, Can. J. Chem. 54 ,1976, 2827. 26.. Roy R,. Chaudhury M,. Mondal S.K, Nag K., J. Chem. Soc., Dalton Trans. ,1984, 1681. 27.. Sreeja P.B,. Kurup M.R.P, Spectrochim. Acta 61A ,2005, 331. 28.Sekerci M., Yakuphanoglu F., J. Therm. Anal. Cal, 2004, 75, 189. 29.Mohamed G.G., Nour-El Dien FA, El-Gamel E.A., J. Therm. Anal. Cal 2002, 67, 135