Synthesis, Characterization and Chelating Properties of Novel Metal Chelates

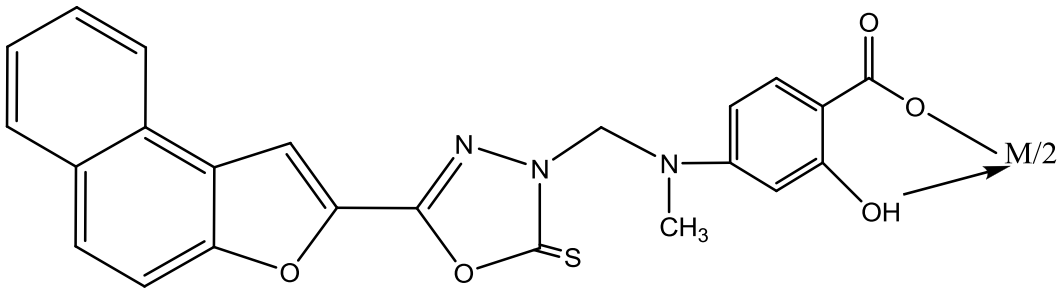
VARDE GOVINDKUMAR R., DR.G.D.ACHARYA, MILAN KUMAR, ARJUNBHAI SHARDA
R.R.Mehta College of Science & C.L.Parikh College of Commerce,
Opp.S.T.Workshop, Palanpur

Abstract:
The novel heterocyclic ligand says,2-hydroxy-4-(methyl((5-(naphtho[2,1-b]furan-2-yl)-2-thioxo-1,3,4-oxadiazol-3(2H)-yl)methyl) amino)benzoic acid (NFODNMSA) prepared by Mannich reaction between 5-(naphtho[2,1-b]furan-2-yl)-1,3,4-oxadiazole-2(3H)-thione and p-(N-methyl)amino salicylic acid. The prepared ligand was characterized by elemental analysis and spectral studies. The transition metal chelates viz. Cu^{2+}, Ni^{2+} , Co^{2+} , Mn^{2+} and Zn^{2+} of NFODNMSA were prepared and characterized by metal-ligand (M:L) ratio, IR and reflectance spectroscopies and magnetic properties. The antifungal activity of NFODNMSA and its metal chelates was examined against various fungi.

Keywords: *Naphtho[2,1-b]furan, 1,3,4-oxadiazole, p-(N-methyl)amino salicylic acid, Magnetic moment, Spectroscopies study and Antifungal properties.*

1. Introduction

Nowadays numbers of research are carried out in the field of metal complex because of their industrial as well as biological applications [1-5]. Salicylic acid and their derivatives is well known for their number of application like as complexing agent, as anti-tubercular agent and as antibiotic agent. [6-9] The metal complexes of p-(N-methyl)amino salicylic acid have been reported and investigated for tuberculolstatic effect [10]. They also show antibacterial as well as antifungal activity. [11] The metal complex with heterocyclic compounds shows the pharmaceutical as well as biological activity [12,13]. The metal complex of oxadiazole and their derivatives show diverse biological activities like antituberculostic, antiinflamatory, analgesic, antibacterial and antifungal activity [14,15]. The reaction of oxadiazole derivatives with Salicylic acid has not been reported so far. Hence, it was thought that oxadiazole and Salicylic acid into one molecule may afford good biological active compound. The present article discuss about synthesizes and characterization and of 2-hydroxy-4-(methyl((5-(naphtho[2,1-b]furan-2-yl)-2-thioxo-1,3,4-oxadiazol-3(2H)-yl)methyl)amino)benzoic acid(NFODNMSA) **(Scheme-1)**.



NFODNMSA matel complex

Where M= Cu2+, Ni2+ , Co2+ , Mn2+ and Zn2+

Experimental

All other chemicals used were of laboratory grade. 5-(naphtho[2,1-b]furan-2-yl)-1,3,4-oxadiazole-2(3H)-thione (NFOD) was prepared by reported method [16,17].

Synthesis of 2-hydroxy-4-(methyl((5-(naphtho[2,1-b]furan-2-yl)-2-thioxo-1,3,4-oxadiazol-3(2H)-yl)methyl)amino)benzoic acid (NFODNMSA)

The mixture of 5-(naphtho[2,1-b]furan-2-yl)-1,3,4-oxadiazole-2(3H)-thione (0.1mol) in ethyl alcohol (10ml), formaldehyde (0.1mole) and p-(N-methyl)amino salicylic acid (SA) in R-sprite (10ml) (0.12mol) and the reaction mixture was stirred for 15-17 hrs. The product that separated as solid was filtered and washed with R-sprite. Recrystallyzed using aqueous R-sprite. **Yield:** 67%, **M.P.** 219-221°C (decompose) uncorrected. **Elemental Analysis:** $C_{23}H_{17}N_3O_5S$ (447) **Calc.(%):** C, 61.74; H, 3.83; N, 9.39; S, 7.17 and **Found(%):** C, 61.72; H, 3.80; N, 9.38; S, 7.15. **IR Spectral (cm^{-1})** at 3020-2920 for Ar C-C, 1680 CO of COOH and 3200-3600 of OH group, **^{1}HNMR (δ ppm):** 6.33-8.67 (m,10H,Ar-H), 5.45 (s,1H,OH), 11.82 (s,1H,COOH), 4.53 (s,2H,CH_2), 3.12 (s,3H, CH_3).

Synthesis of metal chelates of 2-hydroxy-4-(methyl((5-(naphtho[2,1-b]furan-2-yl)-2-thioxo-1,3,4-oxadiazol-3(2H)-yl)methyl)amino)benzoic acid (NFODNMSA)

The metal chelates of NFODNMSA with Cu^{2+}, Co^{2+}, Zn^{2+}, Mn^{2+}, and Ni^{2+} metal ions were prepared in two steps. All the metal chelates were prepared in an identical procedure.

(1) Preparation of NFODNMSA solution

NFODNMSA (0.05 mol) was taken in 500 ml beaker and formic acid (85% v/v) was added up to slurry formation. To this slurry water was added till the complete dissolution of NFODNMSA. It was diluted to 100 ml.

Table-1: Analysis Of Nfodnmsa Ligand and its Metal Chelates

Compounds	Elemental Analysis									
	C%		H%		N%		S%		M%	
	Cald	Found	Cald	Found	Cald	Found	Cald	Found	Cald	Found
NFODNMSA	61.74	61.72	3.83	3.80	9.39	9.38	7.15	7.17	-	-
$(NFODNMSA)_2Cu^{2+}$	57.53	57.51	3.75	3.73	8.75	8.73	6.67	6.65	6.62	6.60
$(NFODNMSA)_2Co^{2+}$	57.80	57.78	3.77	3.74	8.80	8.78	6.70	6.68	6.17	6.16
$(NFODNMSA)_2Ni^{2+}$	57.82	57.81	3.77	3.75	8.80	8.79	6.70	6.69	6.15	6.14
$(NFODNMSA)_2Mn^{2+}$	58.05	58.03	3.79	3.77	8.83	8.81	6.73	6.72	5.78	5.76
$(NFODNMSA)_2Zn^{2+}$	57.42	57.41	3.74	3.73	8.74	8.72	6.66	6.64	6.80	6.78

2. Synthesis of NFODNMSA-metal-chelates

To a solution of NFODNMSA (0.1 mole) in ethanol-acetone (1:1v/v) mixture (150 ml), 0.1N KOH solution was added drop wise with stirring. The pasty precipitates were obtained at neutral pH. These were dissolved by addition of water up to clear solution. It was diluted to 250 ml. by water and was known as stock solution. 25 ml of the stock solution (which contains 0.01 mole NFODNMSA) was added drop wise to the solution of metal salt (0.005 mole for divalent metal ions) in water at room temperature. Sodium acetate or ammonia was added up to complete precipitation. The precipitates were digested on water bath at 80° C for 2h. The digested precipitates of chelates were filtered washed with water and air dried. It was amorphous powder. Yield was almost quantitative. The detail is given in **Table-1**.

3. Measurements

The elemental contents were determined by Thermo Finigen Flash1101 EA (Itally) the metals were determined volumetrically by Vogel's method [18]. To a 100 mg chelate sample, each 1 ml of HCl, H_2SO_4 and $HClO_4$ were added and then 1 g of $NaClO_4$ was added. The mixture was evaporated to

dryness and the resulting salt was dissolved in double distilled water and diluted to the mark. From this solution the metal content was determined by titration with standard EDTA solution. Infrared spectra of the synthesized compounds were recorded on Nicolet 760 FT-IR spectrometer. NMR spectrum of NFODNMSA was recorded on 60 MHz NMR spectrophotometer. Magnetic susceptibility measurement of the synthesized complexes was carried out on Gouy Balance at room temperature. Mercury tetrathiocynatocobalate (II) $Hg[Co(NCS)_4]$ was used as a calibrant. The electronic spectra of complexes in solid were recorded on at room temperature. MgO was used as reference. Antifungal activity of all the samples was monitored against various fungi, following the method reported in literature [19].

4. Results and Discussion

The new ligand 2-hydroxy-4-(methyl((5-(naphtho[2,1-b]furan-2-yl)-2-thioxo-1,3,4-oxadiazol-3(2H)-yl)methyl)amino)benzoic acid (NFODNMSA) was synthesis performed by a simple Mannich reaction. The resulted NFODNMSA ligand was an amorphous pale yellow powder. The C,H,N contents of NFODNMSA **(Table-1)** are consistent with the structure predicted **(Scheme-1)**. The IR spectrum of NFODNMSA comprises the important bands due to Salicylic acid. The bands were observed at 1680 cm^{-1} for CO of COOH and 3240-3620 cm^{-1} for OH group.

The broad band due to –OH group appeared at 3200-3600cm^{-1}. The 1HNMR spectrum of NFODNMSA in DMSO indicates that the singlet of 1 H at 5.45 δ ppm due to –OH group. The aromatic protons are appeared in multiplicity at 6.32-8.69 δ. Thus the structure of NFODNMSA is confirmed as shown in **Scheme-1**.

The metal and C,H,N contents of metal chelates of NFODNMSA **(Table-1)** are also consistent with the predicted structure. The results show that the metal: ligand (M:L) ratio for all divalent metal chelate is 1:2.

The infrared spectra of all the chelates are identical and suggest the formation of the entire metalocyclic compound by the absence of band characteristic of free –OH group of parent NFODNMSA. The other bands are almost at their respectable positions as appeared in the spectrum of parent-NFODNMSA ligand. However, the band due to (M-O) band could not be detected as it may appear below the range of instrument used. The important IR Spectral data are shown in **Table-2**.

Table-2 Spectral Featrues and Magnetic Moment of Nfodnmsa Metal Chelates

Metal Chelates	μ_{eff} (BM)	Electronic spectral data (cm^{-1})	Transition
NFODNMSA-Cu^{2+}	2.56	23425 13186	Charge transfer $^2B_{1g}\rightarrow{}^2A_{1g}$
NFODNMSA-Ni^{2+}	3.68	22576 15340	$^3A_{1g}\rightarrow{}^3T_{1g}(P)$ $^3A_{1g}\rightarrow{}^3T_{1g}(F)$
NFODNMSA-Co^{2+}	4.72	23713 19086 8907	$^4T_{1g}(F)\rightarrow{}^4T_{2g}(F)$ $^4T_{1g}(F)\rightarrow{}^4T_{2g}$ $^4T_{1g}(F)\rightarrow{}^4T_{2g}(P)$
NFODNMSA-Mn^{2+}	5.51	23212 19016 16825	$^6A_{1g}\rightarrow{}^6A_{2g}\ {}^4E_g$ $^6A_{1g}\rightarrow{}^4T_{2g}$ (4G) $^6A_{1g}\rightarrow{}^4T_{1g}$(PG)
NFODNMSA-Zn^{2+}	Diamag.		---------

Magnetic moments of metal chelates are given in **Table-2**. The diffuse electronic spectrum of Cu^{2+} chelates shows two broad bands around 13186 and 23425 cm^{-1}. The first band may be due to a $^2B_{1g}\rightarrow$

$^{1}A_{1g}$ transition. While the second band may be due to charge transfer. The first band shows structures suggesting a distorted octahedral structure for the Cu^{2+} metal chelates. The higher value of the magnetic moment of the Cu^{2+} chelate supports the same [4,5]. The Co^{2+} metal chelate gives rise to two absorption bands at 23713 and 19086 cm^{-1}, which can be assigned $^{4}T_{1g}\rightarrow {}^{2}T_{2g}$, $^{4}T_{1g}\rightarrow {}^{4}T_{1g}$(P)transitions, respectively. These absorption bands and the μeff value indicate an octahedral configuration of the Co^{2+} metal chelate [20]. The spectrum of Mn^{2+} polymeric chelate comprised two bands at 19016 cm^{-1} and 23212 cm^{-1}. The latter does not have a very long tail. These bands may be assigned to $^{6}A_{1g}\rightarrow {}^{4}T_{2g(G)}$ and $^{6}A_{1g}\rightarrow {}^{4}A_{2g(G)}$ transitions, respectively. The high intensity of the bands suggests that they may have some charge transfer character. The magnetic moment is found to be lower than normal range. In the absence of low temperature measuremet of magnetic moment it is difficult to attach any significance to this. The observed μeff values in the range 2.50-5.51 B.M are consistent with the above moiety [20].

Table-3: Antifungal Activity of Nfodnmsa Ligand and Its metal chelates

Sample	Zone of inhibition of fungus at 1000 ppm (%)			
	Nigrospora Sp.	***Botrydeplaia thiobromine***	***Asperginus niger***	***Rhisopus Nigricans***
NFODNMSA	59	54	38	45
NFODNMSA-Cu^{2+}	78	69	60	60
NFODNMSA-Co^{2+}	71	68	60	54
NFODNMSA-Ni^{2+}	66	65	58	57
NFODNMSA-Mn^{2+}	75	55	54	53
NFODNMSA-Zn^{2+}	79	68	49	63

The examination of antifungal activity of NFODNMSA ligand and its all chelates **(Table-3)** reveals that the ligand is moderately toxic against fungi, while all the chelates are more toxic than ligand. Among all the chelates the Cu^{2+} chelate is more toxic against fungi.

5. Conclusion

In present paper we reported about the synthesis and characterization of new ligand which contain heterocyclic azo dye moiety. The new synthesized all compound NFODNMSA and its metal chelates was examined for their antifungal activity against various fungi. They showed that ligand is moderately toxic against fungi, while all the chelates are more toxic than ligand. Among all the chelates the Cu^{2+} chelate is more toxic against fungi.

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