

Studies on Chelating Properties of Transition Metal Chelates Derived From Benzofuran-1,3,4-Oxadiazole Combined Molecules

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ABSTRACT

The novel ligand 4-(ethyl((5-(naphtho[2,1-b]furan-2-yl)-2-thioxo-1,3,4-oxadiazol-3(2H)-yl)methyl)amino)-2-hydroxybenzoic acid (EENFODMSA) was synthesized by Mannich reaction between 5-(naphtho[2,1-b]furan-2-yl)-1,3,4-oxadiazole-2(3H)-thione (NFOD) and p-(ethylamino) salicylic acid (ESA). The synthesized ligand was characterized by elemental and spectral studies. Furthermore, transition metal chelates of EENFODMSA were evaluated for their chelating properties using by metal-ligand (M:L) ratio, IR, reflectance spectral study and magnetic properties. Also the all transition metal chelates and their parent ligand were examined for their antifungal activity against different fungal strains.

Keywords : P-(Ethylamino) Salicylic Acid, Benzofuran-1,3,4-Oxadiazole, Reflectance Spectral Study, Magnetic Moment, And Antifungal Activity

I. INTRODUCTION

Metal complexes synthesized from different ligands are found significant into different fields since its discovery [1,2]. Novel heterocyclic molecules are increasing interest as ligand for their possible coordination chemistry [3,4]. Salicylic acid derivatives established as a complexing agent over the years [5,6]. The numerous metal chelates containing salicylic acid nucleus has been reported for their noticeable biological activities like antibacterial, antifungal, antitubercular, anticancer, anti-HIV, anti-inflammatory, antianalgesic and antimalarial activities [7-11]. Also the water insoluble metal complexes of salicylic acid derivatives have been investigated for tuberculostatic effect [12]. The oxadiazole and their derivatives show diverse biological activities like antibacterial, antifungal, anti-inflammatory, antitumor and analgesic activity [13-16]. Moreover, coordination compounds containing 1,3,4 oxadiazole derivatives can be synthesized and studied recently for their numerous applications [17,18]. Hence, it was thought to prepare possible biologically active compound containing such an important biological molecule i.e. oxadiazole and salicylic acid. So, the present communication comprises synthesis and characterization, chelating properties and antifungal activity of metal chelates of ligand 4-

(ethyl((5-(naphtho[2,1-b]furan-2-yl)-2-thioxo-1,3,4-oxadiazol-3(2H)-yl)methyl)amino)-2-hydroxybenzoic acid (ENFODMSA) (**Scheme-1**).

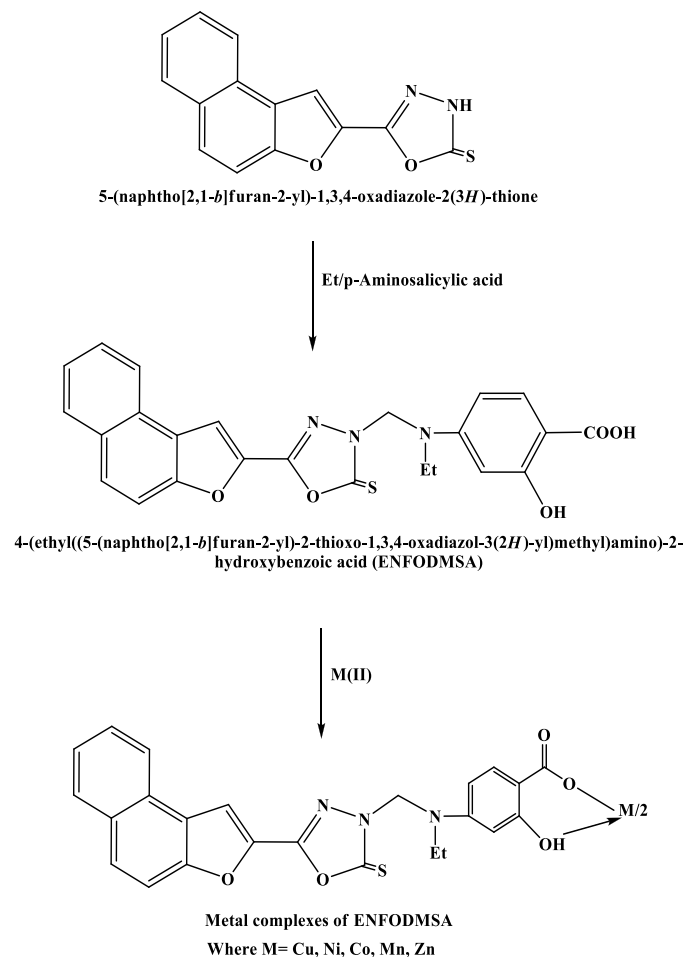
II. METHODS AND MATERIAL

5-(naphtho[2,1-b]furan-2-yl)-1,3,4-oxadiazole-2(3H)-thione (NFOD) was prepared by reported method [19]. All other chemicals and solvents used were of laboratory grade.

Measurements:

The elemental contents were determined by Thermo Finigan Flash1101 EA (Italy) the metals were determined volumetrically by Vogel's method [20]. To a 100 mg chelate sample, each 1 ml of HCl, H₂SO₄ and HClO₄ were added and then 1 g of NaClO₄ 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 EENFODMSA was recorded on 60 MHz

NMR spectrophotometer. Magnetic susceptibility measurement of the synthesized complexes was carried out on Gouy Balance at room temperature. Mercury tetrathiocyanatocobalate (II) $\text{Hg}[\text{Co}(\text{NCS})_4]$ 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 [21].



Synthesis of 4-(ethyl((5-(naphtho[2,1-b]furan-2-yl)-2-thioxo-1,3,4-oxadiazol-3(2H)-yl)methyl)amino)-2-hydroxybenzoic acid (ENFODMSA):

The equimolar mixture of 5-(naphtho[2,1-b]furan-2-yl)-1,3,4-oxadiazole-2(3H)-thione, ethanolate and p-amino salicylic acid in 20 ml ethyl alcohol was taken into round bottom flask and stirred for about 18 hrs. The solid product separated was filtered and wash with ethyl alcohol and further crystallized with ethyl alcohol. The solid products obtained was 4-(ethyl((5-(naphtho[2,1-b]furan-2-yl)-2-thioxo-1,3,4-oxadiazol-3(2H)-yl)methyl)amino)-2-Yield: 75%, M.P.242-244°C (decompose) uncorrected.

Elemental Analysis for $\text{C}_{24}\text{H}_{19}\text{N}_3\text{O}_5\text{S}$ (461) Calc. (found) (%): C, 62.46 (62.41) ; H, 4.15 (4.13); N, 9.11 (9.08); S,6.95 (6.92).

IR Spectral: 3450 cm^{-1} (-OH), 3047 cm^{-1} (C-H of Ar), 2950, 1369 cm^{-1} (-CH₃), 1687 (C=O, COOH), 1170 cm^{-1} (C=S), 776 cm^{-1} (C-O-C, furan ring). **¹HNMR(δ ppm):** 11.82 (s, 1H, COOH), 6.38-8.60 (m, 10H, Ar-H), 5.36 (s, 1H, OH), 4.50 (s, 2H, CH₂), 3.27 (q, 2H, CH₂), 1.20 (t, 3H, CH₃).

Synthesis of transition metal chelates of ligand (ENFODMSA):

The metal chelates of ENFODMSA 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 ENFODMSA solution:

ENFODMSA (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 ENFODMSA. It was diluted to 100 ml.

(2) Synthesis of ENFODMSA-metal-chelates:

To a solution of ENFODMSA (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 ENFODMSA) 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 details are given in **Table-1**.

III. RESULTS AND DISCUSSION

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IV. CONCLUSION

The proposed payment system combines the Iris recognition with the visual cryptography by which customer data privacy can be obtained and prevents

theft through phishing attack [8]. This method provides best for legitimate user identification. This method can

also be implemented in computers using external iris recognition devices.

Table-1 : Analysis of ENFODMSA ligand and its transition metal chelates

Molecular Formula	Yield (%)	Elemental Analysis									
		C%		H%		N%		S%		M%	
		Cald	Found	Cald	Found	Cald	Found	Cald	Found	Cald	Found
$C_{24}H_{19}N_3O_5S$	75	62.46	62.41	4.15	4.13	9.11	9.08	6.95	6.92	-	-
$C_{48}H_{36}CuN_6O_{10}S_2$	70	58.56	58.54	3.69	3.66	8.54	8.50	6.51	6.48	6.45	6.40
$C_{48}H_{36}NiN_6O_{10}S_2$	68	58.85	58.80	3.70	3.68	8.58	8.56	6.55	6.52	5.99	5.95
$C_{48}H_{36}CoN_6O_{10}S_2$	70	58.83	58.81	3.70	3.66	8.58	8.55	6.54	6.50	6.01	5.98
$C_{48}H_{36}MnN_6O_{10}S_2$	71	59.07	59.05	3.72	3.69	8.61	8.57	6.57	6.55	5.63	5.60
$C_{48}H_{36}N_6O_{10}S_2Zn$	66	58.45	58.42	3.68	3.64	8.52	8.49	6.50	6.46	6.63	6.61

4-(ethyl((5-(naphtho[2,1-b]furan-2-yl)-2-thioxo-1,3,4-oxadiazol-3(2H)-yl)methyl)amino)-2-hydroxybenzoic acid (ENFODMSA) was synthesized using Mannich reaction. The resultant ligand was an amorphous pale yellow powder. The C,H,N contents of ENFODMSA (Table-1) are well agreed with their predicted structure (Scheme-1). The IR spectrum of ENFODMSA confirms the presence of salicylic acid nucleus by two important bands found at 1687 cm^{-1} and 3450 cm^{-1} due to CO of COOH and OH group, respectively. The furan ring is supported by the band found at 776 cm^{-1} attributed to C-O-C ring. The other bands found at 1170 cm^{-1} (C=S), 3047 cm^{-1} (C-H of Ar), $2950, 1369\text{ cm}^{-1}$ ($-CH_3$) also support the structure of newly prepared ligand.

The ^1H NMR spectrum of ENFODMSA in DMSO indicates that the two singlet at $5.36\text{ }\delta$ ppm and $11.82\text{ }\delta$ ppm due to -OH and -COOH group. The aromatic

protons are appeared in multiplicity at $6.38\text{-}8.60\text{ }\delta$. While the singlet of two protons ($-CH_2$) found at 4.50 ppm. Also quartet of two protons and triplet of three protons at 3.27 and 1.20 , respectively suggest the substituted ethyl present in synthesized ligand. Thus the structure of ENFODMSA is confirmed as shown in

Scheme-1.

The metal and C,H,N contents of metal chelates of ENFODMSA (Table-1) are also consistent with the predicted structure while suggested metal: ligand (M:L) ratio for all divalent metal chelate is 1:2. The FTIR spectra of all the chelates are identical and support the formation of the entire metalocyclic compound by the absence of -OH band characteristic which present in their parent ligand. The other bands are almost at their respectable positions as appeared in the spectrum of parent-ENFODMSA ligand. Moreover, the chelation is confirmed by the band found due to M-L frequency for particular metal chelate.

Table-2 : Spectral features and Magnetic moment of ENFODMSA- M^{2+} chelates

Metal Chelates	μ_{eff} (BM)	Electronic spectral data (cm^{-1})	Transition
ENFODMSA- Cu^{2+}	2.54	23462 13217	Charge transfer $^2B_{1g} \rightarrow ^2A_{1g}$
ENFODMSA- Ni^{2+}	3.74	22525 15386	$^3A_{1g} \rightarrow ^3T_{1g}(P)$ $^3A_{1g} \rightarrow ^3T_{1g}(F)$

ENFODMSA-Co ²⁺	4.80	23754 19108 8923	⁴ T _{1g} (F) → ⁴ T _{2g} (F) ⁴ T _{1g} (F) → ⁴ T _{2g} ⁴ T _{1g} (F) → ⁴ T _{2g} (P)
ENFODMSA-Mn ²⁺	5.55	23250 19075 16836	⁶ A _{1g} → ⁶ A _{2g} ⁴ E _g ⁶ A _{1g} → ⁴ T _{2g} (4G) ⁶ A _{1g} → ⁴ T _{1g} (PG)
ENFODMSA-Zn ²⁺	Diamag.	---	---

Table-3 : Antifungal activity of ENFODMSA ligand and their transition metal chelates

Compound	Zone of inhibition of fungus at 1000 ppm (%)			
	<i>Nigrospora Sp.</i>	<i>Botrydeplai thiobromine</i>	<i>Asperginus niger</i>	<i>Rhisopus Nigricans</i>
ENFODMSA	59	55	48	50
ENFODMSA-Cu ²⁺	72	70	66	69
ENFODMSA-Co ²⁺	67	65	59	61
ENFODMSA-Ni ²⁺	64	62	57	58
ENFODMSA-Mn ²⁺	70	67	62	66
ENFODMSA-Zn ²⁺	65	59	53	57

The electronic spectra and magnetic moment are important feature to confirm the geometry of metal chelates. The electronic spectrum of Cu²⁺ chelates shows two important bands at 23462 and 13217 cm⁻¹ which attributed to charge transfer and ²B_{1g} → ¹A_{1g} transition, respectively. These bands suggest a distorted octahedral structure for the Cu²⁺ metal chelates further supported by the higher value of the magnetic moment found for Cu²⁺ chelate [22]. The Ni²⁺ metal chelate gives rise to two absorption bands at 22525 and 15386 cm⁻¹, which can be assigned to ³A_{1g} → ³T_{1g}(P) and ³A_{1g} → ³T_{1g}(F), respectively. The Co²⁺ metal chelate also shows two absorption bands attributed to ⁴T_{1g} → ²T_{2g}, ⁴T_{1g} → ⁴T_{1g}(P) transitions. These absorption bands and the μ_{eff} value suggest an octahedral configuration for both the metal chelates [22-24]. The spectrum of Mn²⁺ metal chelate comprised two bands at 19075 cm⁻¹ and 23250 cm⁻¹. The latter does not have a very long tail. These bands may be assigned to ⁶A_{1g} → ⁴T_{2g}(G) and ⁶A_{1g} → ⁴A_{2g}(G) transitions, respectively. The high intensity of the bands and magnetic moment value suggests that they may have some charge transfer character and confirms the octahedral geometry for Mn²⁺ metal chelate [24]. The Zn²⁺ found diamagnetic in nature as it do not show any characteristic d-d transitions.

The examination of antifungal activity of ENFODMSA ligand and its all chelates (Table-3) reveals that the ligand is moderately toxic against fungi, while all the

chelates are more toxic than its parent ligand. The Cu²⁺ chelate found more toxic to fungi compared to other metal chelates.

V. CONCLUSION

In present work, the Mannich base reaction was applied to prepared new ligand ENFODMSA. Further, the five transition metal chelates was synthesized and their chelating properties were evaluated. The results suggest octahedral geometry for all synthesized metal chelates. While evaluation of antifungal activity against various fungi suggest the superior activity of all metal chelates compared to its parent ligand.

VI. REFERENCES

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