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Research Article

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Synthesis, characterization and chelating properties of furan ring containing organic ligands

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ABSTRACT

The treatment of 5-((diethylamino)methyl)furan-2-yl propionate with 4-amino salicylic acid afford a 4-(5-((diethylamino)methyl)furan-2-carboxamido)-2-hydroxybenzoic acid (DMFSA). The transition metal complexes of Cu^{2+},Co^{2+} ,Ni^{2+}, Mn^{2+} and Zn^{2+} of DMFSA have been prepared. DMFSA and all the metal complexes were characterized by elemental analyses, spectral studies, magnetic moment determination, molar conductivity measurement and antimicrobicidal activity.

Keywords: 5-((diethylamino)methyl)furan-2-yl propionate, 4-amino salicylic acid, Metal chelates, Spectral studies, Magnetic moment, Antibacterial and Antifungal activity.

INTRODUCTION

Literature survey indicates that compounds having furan nucleus possess broad range of their diverse biological activate and chemical applications [1] like such as antimicrobial [2], anthelmintic [3], anti-inflammatory [4], diuretic [5], analgesic [6]. The salicylic acid and its derivatives like 4-amino salicylic acid also act as good chelating agents [7,8], as well as potential pharmaceutical products [9,10]. The reaction between furan derivative with 4-amino salicylic acid (ASA) has not been reported so far. Though 4-amino salicylic acid is an excellent anti T.B agent and also acts as a chelating ligand with better microbicidal activity. Hence it was thought interesting to prepare the intermolecular ligands containing furan and salicylic acid moieties. Thus the present communication comprises the studies on furan-salicylic acid combined molecule and its metal chelates. The research work is illustrated in **Scheme-1**.

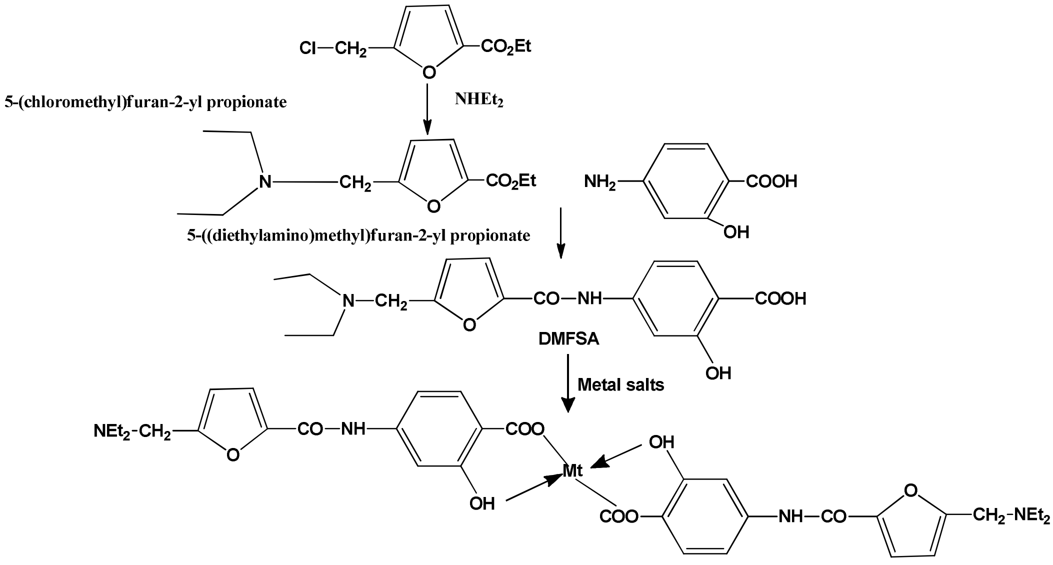
EXPERIMENTAL SECTION

Materials

Ethyl furan-2-carboxylate and p-Amino salicylic acid were obtained from local dealer. All other chemicals used were of analytical grade. 5-(chloromethyl)furan-2-yl propionate prepared according to literature [11].

Synthesis of 5-((diethylamino)methyl)furan-2-yl propionate:

In a 250 ml RBF, 5-(chloromethyl)furan-2-yl propionate (0.01mole) and K_2CO_3 (0.02mole) were stirred at room temperature in DMF(20 ml) for 1.5hrs and pinch of KI was added. After that diethyl amine (0.01mole) was added to reaction mixture which was refluxed for 6 hrs. The reaction mixture was poured into water (20 ml) and the mixture was extracted with diethyl ether. The organic extracts were washed with water, dried over anhydrous sodium sulphate and concentrated to obtain crude product. The residue was recrystallized ethyl acetate from to give pure compound. Yield: 72%, m.p. 118-119°C,IR,cm^{-1}(KBr): 3335 (amine), 3070 (Ar.C-H), 2920 (aliphatic C-H), 1340 (-CN), 1715 (CO). ^1H NMR: δ 6.51-6.32 (2H,d,furan CH), 3.85 (2H,s,CH_2), 2.94-2.32 (6H,q,CH_2), 1.12-1.04 (9H,s,CH_3). Anal. Calcd for $C_{12}H_{19}NO_3$ (225): C,63.98; H, 8.50; N, 6.22; Found: 64.0; H, 8.4; N, 6.2.



Metal chelates of DMFSA

M=Cu^{+2},Co^{+2},Ni^{+2},Mn^{+2},Zn^{+2}

Scheme-1

Synthesis of 4-(5-((diethylamino)methyl)furan-2-carboxamido)-2-hydroxybenzoic acid (DMFSA)

A mixture of 5-((diethylamino)methyl)furan-2-yl propionate and (0.01 mole) and 4-amino salicylic acid (0.01 mole) in ethyl alcohol (60 ml) was heated under reflux for 5 hrs. Subsequently ethyl alcohol was distilled off and the solid mass obtained. The solid designated as DMFSA was isolated and dried in air. Yield was 78%. It's m.p. was 219-220°C (uncorrected).

Elemental Analysis: $C_{17}H_{20}O_5N_2$(332)

		C%	H%	N%
Calculated	:	61.44	6.07	8.43
Found	:	61.4	6.0	8.4

Acid Value **Theoretical:** 154mg KOH/1g. Sample.

Found: 157 KOH/1g Sample.

IR Features		
	3035, 1540, 1660 cm^{-1}	Aromatic
	1675 cm^{-1}	CO
	2900-3350 cm^{-1}	OH
	3420 cm^{-1}	Sec.NH
	2850, 2920 cm^{-1}	CH_2 , CH_3

NMR (DMSO)	δ ppm	
7.4 – 8.3 (3H)	Multiplet	Aromatic
6.6, 7.4(2H)	Doublet	Furan CH
3.8 (2H)	Singlet	CH_2
6.5 (1H)	Singlet	CO-NH
4.1 (1H)	Singlet	OH
2.9 (1H)	Singlet	NH
10.9(1H)	Singlet	COOH
1.2(6H)	Triplet	CH_3
3.1(2H)	Quartate	CH_2

Synthesis of metal chelates of DMFSA

The Cu^{2+},Co^{2+}, Ni^{2+}, $Mn^{2+}$and Zn^{2+} metal chelates of DMFSA have been prepared in a similar manner. The general procedure is as follow.

To a solution of DMFSA (33.2g, 0.1 mole) in ethanol-acetone (1:1v/v) mixture (150 ml), 0.1N KOH solution was added dropwise 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 DMFSA) 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 are given in **Table-1**.

Table-1. Analytical Data of the Metal Chelates of DMFSA

Empirical Formula	Yield (%)	Elemental Analysis							
		C%		H%		N%		M%	
		Cal.	Found	Cal.	Found	Cal.	Found	Cal.	Found
DMFSA	78	61.44	61.4	6.07	6.0	8.43	8.4	--	--
DMFSA Cu^{2+} $2H_2O$	71	53.58	53.5	5.52	5.5	7.35	7.3	8.34	8.3
DMFSA Co^{2+} $2H_2O$	67	53.90	53.8	5.55	5.5	7.40	7.3	7.79	7.7
DMFSA Mn^{2+} $2H_2O$	68	54.19	54.2	5.58	5.5	7.44	7.4	7.30	7.2
DMFSA Ni^{2+} $2H_2O$	65	53.92	53.9	5.55	5.5	7.40	7.3	7.76	7.7
DMFSA Zn^{2+} $2H_2O$	72	53.45	53.4	5.50	5.4	7.34	7.3	8.56	8.5

Measurements

The elemental analysis for C, H and N were carried out on elemental analyzer TF-EA.1101 (Italy). IR spectra of DMFSA and its metal complexes were scanned on a Nicolet 760 FTIR spectrophotometer in KBr. The NMR spectrum of DMFSA was scanned on Brucker NMR spectrophotometer using DMSO solvent. The metal content of the metal chelate were performed by decomposing a weighed amount of each metal complexes followed by EDTA titration as reported in literature (Hong et al., 2008). Magnetic susceptibility measurement of all metal complexes were carried out at room temperature by the Gouy mehod. Mercury tetrathiocynatocobalate (II) Hg $[Co(NCS)_4]$ was used as a calibrant. The diffused reflectance spectra of solid metal complex were recorded on a Backman DK Spectrophotometer with a sodid reflectance attachment, MgO was employed as the reflectance compound. The electrical conductivity of all the complexes was measure in acetonitrile at 10^{-3} M concentration.

Table -2 Magnetic Moment and Reflectance Spectral data of Metal Chelates of DMFSA ligand

Metal chelate	Magnetic Moment μ_{eff} (B.M.)	Molar Conductivity Ωm ohm^{-1} cm^2 mol^{-1}	Absorption band (cm^{-1})	Transitions
Cu-DMFSA	1.94	32.3	22790 15967	C.T. $^2T \rightarrow {}^2T_2g$
Ni-DMFSA	3.86	35.9	14784 23082	3 A2g→ $3T_1g$(p) 3 A1g→ $3T_1g$(F)
Co-DMFSA	4.55	34.5	15479 22821	4 T1g(F)→ $4T_2g$(F) 4 T1g(F)→ 3A2g
Mn-DMFSA	5.14	36.7	15482 17752 23068	6 A1g→ $4T_1g$(4Eg) 6 A1g→ 4T2g(4G) 6 A1g→ $4T_1g$(4G)

Zn^{2+} Diamagnetic in Nature.

Antifungal activity

The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro plant pathogenic organisms listed in **Table-3**. The antifungal activities of all the samples were measured by cup plate method [12]. Each of the plant pathogenic strains on potato dextrose agar (PDA) medium. Such a PDA medium contained potato 200 gms, dextrose 20gms, agar 20gms and water 1 litre. 5 days old cultures were employed. The compounds to be tested were suspended (1000ppm) in a PDA medium and autoclaved at 120° C for 15 min. at 15 atm pressure. These medium were poured into sterile Petri plate and the organisms were inoculated after cooling the Petri plate. The percentage inhabitation for fungi was calculated after 5 days using the formula given below.

$$\textbf{Percentage of inhibition} = \frac{100\,(X-Y)}{X}$$

Where, X: Area of colony in control plate
Y: Area of colony in test plate

The fungicidal activity all compound are shown in **Table-3**.

Table 3. Antifungal Activity of Ligand DMFSA$_1$ and its metal chelates

Sample	**Zone of inhibition of fungus at 1000ppm (%)**			
	Botrydepladia thiobromine	***Nigrospra sp.***	***Rhizopus nigricans***	***Aspergillus niger.***
DMFSA	60	62	63	55
Cu-DMFSA	73	77	75	72
Ni-DMFSA	72	76	73	69
Co-DMFSA	65	70	71	69
Mn-DMFSA	71	75	78	71
Zn-DMFSA	62	62	57	58

RESULTS AND DISCUSSION

The parent ligand DMFSA was an amorphous brown powder, soluble in various solvents like dioxane, DMSO and DMF. The results of elemental analysis of the ligand are reported in experimental part. They are consistent with the predicted structure as shown in **Scheme-1**.

Examination of IR spectrum (not shown) of DMFSA reveals that broad band of phenolic hydroxyl stretching is observed at 2900-3350 cm^{-1} as well as additional absorption bands at 3035, 1540,1660 are characteristics of the salicylic acid [13]. The strong bands at 1675 for C=O and band at 3420 for sec. NH. The NMR data (shown in experimental part) also confirm the structure of DMFSA.

The Metal chelate of DMFSA with ions Cu^{2+},Co^{2+}, Ni^{2+}, Mn^{2+} and Zn^{2+} vary in colours. On the basis of the proposed structure as shown in **Scheme-1**, the molecular formula of the DMFSA ligand is $C_{17}H_{20}O_5N_2$. Which upon complexion coordinates with one central metal atom at four coordination sites and with two water molecules. Therefore the general molecular formula of the resulting metal chelate is $[C_{17}H_{19}O_5N_2]_2$ M.2H_2O for divalent metal ions. This has been confirmed by results of elemental analysis reported in **Table-1**. The data are in agreement with the calculated values.

Inspection of the IR Spectra (not shown) of metal chelates reveals that all the spectra are identical in all respects. The comparison of IR spectrum of the parent ligand DMFSA with that of its each metal chelates has revealed certain characteristics differences.

One of the significant differences to be expected between the IR spectrum of the parent ligand and its metal chelates is the presence of more broadened bands in the region of 3200-3600 cm^{-1} [14,15] for the metal chelates as the oxygen of the O-H group of the ligands forms a coordination bond with the metal ions [16,17]. This is explained by the fact that water molecule might have strongly absorbed to the metal chelates samples during their formation. Another noticeable difference is that the bands due to the CO at 1730 cm^{-1} in the IR spectrum of the each metal chelates. The band at 1400 cm^{-1} in the IR Spectrum of DMFSA ligand assigned to inplane OH determination [14-17] is shifted towards higher frequency in the spectra of confirmed by a week bands at 1095 cm^{-1} corresponding to C-O-M starching [14-17]. Thus all of these characteristics features of the IR studies suggested the structure of the metal chelates as shown in

Scheme

Examination of data of the metal content in each compound revealed a 1:2 metal: ligand (M: L) stoichiometry in all of the chelate of divalent metal ions.Magnetic moment (μ_{eff}) of each of the metal chelates is given in **Table-2**. Examination of these data reveals that all chelates other than that of Zn^{2+}, are Para magnetic while those of Zn^{2+} are diamagnetic.

The diffuse electronic spectrum of the [CuDMFSA(H_2O)$_2$] metal complex shows broad bands at 15967 and 22790 cm^{-1} due to the $^2T\rightarrow{}^2T_2g$ transition [18] and charge transfer, respectively suggesting a distorted octahedral structure [19-21] for the [CuDMFSA(H_2O)$_2$] complex. Which is further confirmed by the higher value of μ_{eff} of the [CuDMFSA(H_2O)$_2$] complex. The [NiDMFSA(H_2O)$_2$] and [CuDMFSA(H_2O)$_2$] complex gave two absorption bands respectively at 14784, 23082 and 15967, 22790cm^{-1} corresponding to $^4T_{14}g\rightarrow{}^2T_1g$ and ^4T_1g (p) transitions. Thus absorption bands at the diffuse, reflectance spectra and the value of the magnetic moments μ_{eff} indicate and octahedral configuration for the [NiDMFSA(H_2O)$_2$] and [CuDMFSA(H_2O)$_2$] complex [22]. The spectra of [MnDMFSA(H_2O) $_2$] shows weak bands at 15482, 17752 and 23068 cm^{-1} assigned to the transitions $^6A_{1g}\rightarrow{}^4T_{1g}$ (4G), $^6A_{1g}\rightarrow{}^4T_{2g}$ (4G) and $^6A_{1g}$ (F) $\rightarrow{}^4T_1g$, respectively suggesting an octahedral structure for the [MnDMFSA(H_2O)$_2$] chelate. The high intensities of the bands suggests that they might be charge transfer in origin μ_{eff} is found to be lower than normal range. In the absence of low temperature moments it is difficult to give any significance. As the spectrum of the [ZnDMFSA(H_2O)$_2$] polymer is not well resolved, it is not interpreted but it is μ_{eff} value shows that it is diamagnetic as expected.

Conductivities of all the complexes were measured in acetonitrile solvent and all the complexes were found to be electrolytic [15] in nature of 1:2 type and molar conductivity values are in the range of 32.3-36.7 Ohm^{-1} Cm^{-1}.

The antifungal activity of all the compounds measured for various plant pathogens. Inspection of the result shown in **Table-3** indicates that all compounds are good toxic for fungi. Out of all the compounds copper chelates is more toxic than other. These compounds almost inhibit the fungi about 72%. Hence produced metal chelates can be employed as garden fungicides. Further work in the direction is in progress.

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