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Research Article

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Studies in synthesis, characterization and microbicidal activity of metal chelates with novel amic acid derivative derived from 9,10,11,15-tetrahydro-9,10-[3,4]-furanoanthracene-12,14-dione

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ABSTRACT

The present work reports a new series of metal chelates of amic acid ligand derived from 9,10,11,15-tetrahydro-9,10-[3,4]-furanoanthracene-12,14-dioneand aromatic primary amine. The synthesized ligand was characterized by Elemental analysis, FT-IR, ^{1}H-NMR, TGA and non-aqueous conductometric titration while its metal complexes were characterized by Elemental analysis, FT-IR, Magnetic susceptibility and TGA. Further antibacterial and antifungal activities of this ligand and its metal chelates have been carried out.

Keywords: Amic acid derivatives, Metal chelates, Amic acid, Microbicidal activity

INTRODUCTION

The modern study of complex ions, coordination compounds or chelates, is the basis for some of the most exciting and active areas of chemical research today. New types of chelates and chelate forming agents are constantly under investigation, for possible analytical and industrial applications like gravimetric, titrimetric, colorimetric, physicochemical as well as biochemical measurements [1, 2]. Amic acid is an organic acid produced by simple condensation reaction between anhydride and aliphatic or aromatic amines. Literature survey reveals that there are reports about the amic acids based on maleic anhydride and aniline derivatives [3-10]. Most of the amic acids are used for metal complexes. A series of transition metal ions forms complexes with Schiff bases, hydroxamic acid, α-mercapto-2-aminophenyl acetohydroxamic acid [11]. The transition metal complexes of phthalamic acids are reported [6-15]. Ravindar V. and Lingaiah P. [5] reported that the fungicidal activity of ligands maleanilic acid (MA) against Drechslera rostrata, Curvularia lunata, Aspergillus niger depend on the type of metal ion and the type of ligand. Pd^{2+} complexes exhibited high fungistatic activity than did the free ligands. After proper literature survey it was noted that the reaction of 9,10,11,15-tetrahydro-9,10-[3,4]-furanoanthracene-12,14-dione with aromatic amine derivative like 4-methyl aniline has not been reported so far. Hence, so called N-substituted phenyl amic acid derivatives have been thought to prepare for metal chelation study.

Thus, the objective of the work is to synthesize, characterize and to study the chelating property as well as microbicidal activity of N-substituted phenyl amic acid derivative (Ligand L-1).

EXPERIMENTAL SECTION

All the chemicals used were of reagent grade and were purified by either distillation or recrystalization before use. Maleic anhydride and anthracene were purchased from local market. 4-Methyl aniline is used as aromatic amine.

Preparation method (schem-1) for the synthesis of amic acid derivative of 4-methyl aniline and its metal chelates is as under…

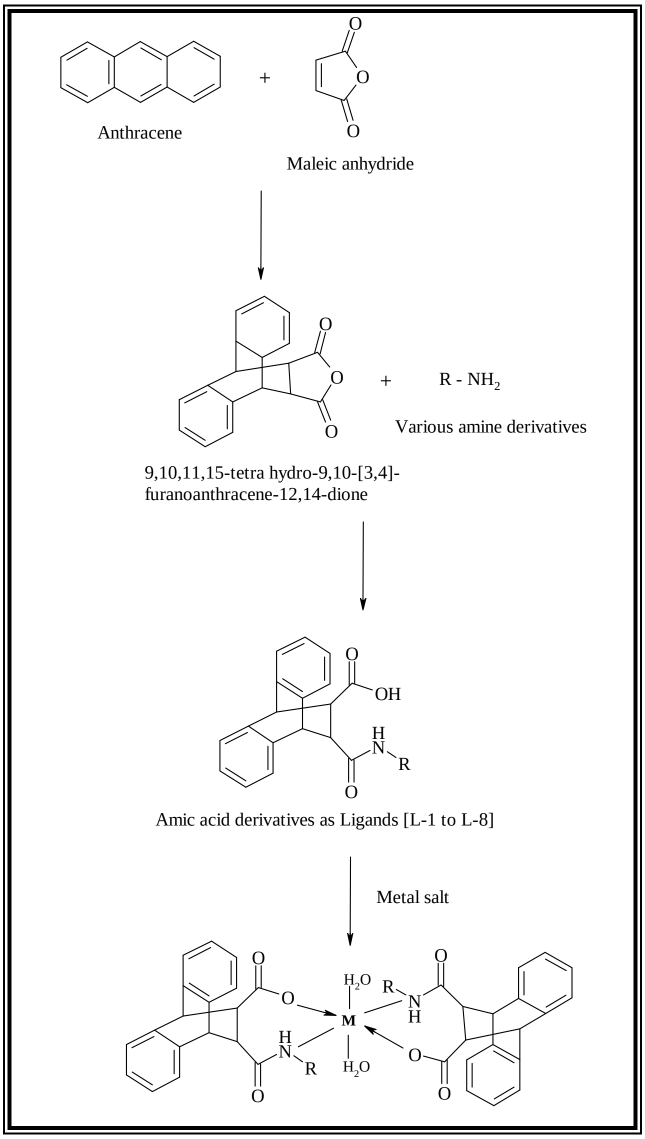

Figure - 1

Step-1: Synthesis of N-4-methyl phenyl amic acid derivative [L-1]:

The synthesis of ligand (L-1) comprises the two steps,

(A) Synthesis of of 9,10,11,15-tetrahydro-9,10-[3,4]-furanoanthracene-12,14-dione (adduct)

(B) Synthesis of 4-Methyl phenyl derivative of adduct (ligand L-1)

(A) Synthesis of of 9,10,11,15-tetrahydro-9,10-[3,4]-furanoanthracene-12,14-dione (adduct):

A mixture of anthracene (1.78gm, 0.01M) and maleic anhydride (0.980gm, 0.01M) in 50ml. of p-xylene was refluxed for about two hours in a round bottom flask on a sand bath. White crystalline product was obtained on cooling. Yield 2.45gm (89%), M.P: 262^{0}C., M.W. 276.29gm/mole.

(B) Synthesis of 4-Methyl phenyl derivative of adduct (Ligand L-1):

To a well stirred solution of (0.01mole,2.763g) 9,10,11,15-tetra hydro-9,10-[3,4]-furanoanthracene-12,14-dione (adduct) and 0.1 ml of pyridine in 100 ml acetone in round bottom flask, a solution of (0.01 mole, 1.07 g) 4-methyl aniline in 100 ml acetone was added portion wise with constant stirring within 20 minutes. The whole assembly was placed in ice- bath and maintained the temperature 0-5°C during the addition of 4-methyl aniline. The reaction mixture was kept aside with stirring for two hours. After completion of the reaction the crystalline precipitates were filtered off, washed with acetone and air-dried. The yield 3.26g.(85%), M.P: 153°C (uncorrected, DSC method), M.W. 383.45gm/mole., ($C_{25}H_{21}NO_3$), Calculated: C, 78.32; H, 5.48; N, 3.65%; Found: C, 78.30; H, 5.50; N, 3.60%. The chemical reaction is as follows.

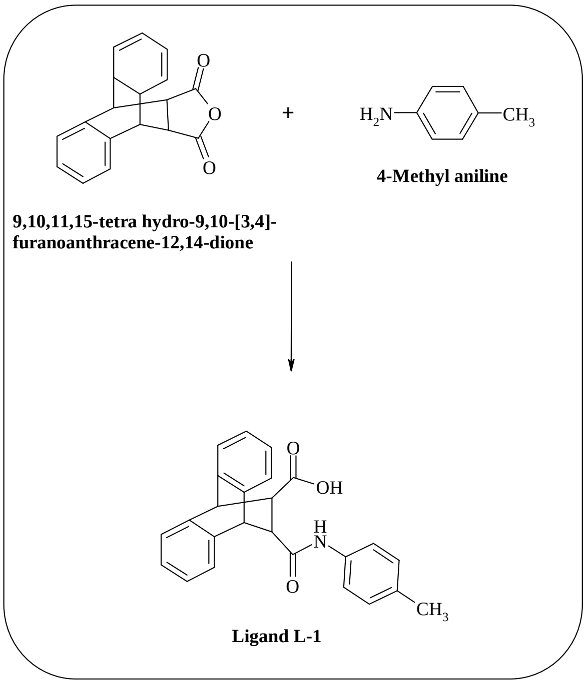

Figure - 2

Step-2 Synthesis of metal chelates of 4-Methyl phenyl amic acid derivative[L-1]:

A dried ligand sample (0.1 M) was stirred in 100 ml of 1:1 mixture of acetone and ethanol. Calculated amount of aqueous solution of 1 M NaOH was added drop wise to the ligand solution. During neutralization some pasty precipitates appeared. Minimum amount of water was added to dissolve the precipitates. The resulting solution was diluted to 250 ml by water and then designated as reagent solution. This solution was used for preparing all metal chelates.

Formation of Cu^{2+} chelates

The sodium salt solution (25ml containing 0.01M ligand) of each ligand was added drop wise to a solution of cupric nitrate hexahydrate (0.005 mole) in 100 ml of water with rapid stirring. The so called pH of the resultant solution was 4.5. A greenish blue solid precipitated out. It was allowed to settle. Then it was digested on water bath at 70ºC for about 2 hours. The blue- green solid mass was filtered, washed with 1:1 mixture of water–ethanol and finally with acetone, and air-dried. Yield 75%. The resulting chelate was powdered well and further dried at 70ºC over a period of 24 hrs.

The similar experimental procedure was followed to prepare metal chelates of other transition metals like Co, Ni, Zn and Mn.

Microbicidal Activity:

Antifungal and antibacterial activity study of all the compounds were carried out.

Table 1: Antifungal activity of ligand L-1 and its Metal Chelates

Sample	Zone of inhibition at 1000 ppm (%)				
	Penicillium Expansum	*Botrydepladia Thiobromine*	*Nigrospora Sp.*	*Trichothesium Sp.*	*A. Niger*
L-1	70	69	71	66	72
$(L\text{-}1)_2\ Cu^{+2}$	74	73	73	72	74
$(L\text{-}1)_2\ Mn^{+2}$	71	70	70	69	68
$(L\text{-}1)_2\ Co^{+2}$	68	67	71	72	66
$(L\text{-}1)_2\ Zn^{+2}$	72	73	71	74	73
$(L\text{-}1)_2\ Ni^{+2}$	73	71	66	68	68

Plant pathogenic organisms used were Penicillium expansum, Botrydepladia thiobromine, Nigrospora Sp., Trichothesium Sp. and Rhizopus nigricum.

Antifungal Activity:

The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro.

Antibacterial activity:

Table 2: Standard antibacterial activity

Sample	Zone of inhibition at 10 µg(in mm)			
	Gram + Ve		*Gram -Ve*	
	Bacillus megaterium	***Staphylococcus aureus***	***P. Aeruginosa***	***E-Coli***
CIPROFLOXACIN	12	11	11	10

Table 3: Antibacterial activity of ligand L-1 and its Metal Chelates

Sample	Zone of inhibition 150 µg(in mm)			
	Gram + Ve		*Gram -Ve*	
	Bacillus megaterium	***Staphylococcus aureus***	***P. Aeruginosa***	***E-Coli***
L-1	11	10	10	11
$(L\text{-}1)_2\ Cu^{+2}$	14	14	13	14
$(L\text{-}1)_2\ Mn^{+2}$	12	12	10	12
$(L\text{-}1)_2\ Co^{+2}$	12	13	13	12
$(L\text{-}1)_2\ Zn^{+2}$	14	13	13	14
$(L\text{-}1)_2\ Ni^{+2}$	13	11	12	12

RESULTS AND DISCUSSION

[A] Characterization of ligand:

The ligand derived from9,10,11,15-tetrahydro-9,10-[3,4]-furanoanthracene-12,14-dioneand aromatic primary amine was characterized as under…

ELEMENTAL ANALYSIS:

The C, H and N elements of all the samples were measured by Elemental analyzer Thermofinigan flash1101 EA.

Table 4: Characterization of Ligand L-1

Ligand No.	Molecular formula	Mol. Wt Gm/Mole	% yield	Elemental analysis					
				%C		%H		%N	
				Cal.	Found	Cal.	Found	Cal.	Found
L-1	$C_{25}H_{21}NO_3$	383	85%	78.32	78.30	5.48	5.50	3.65	3.60

IR (KBr) Cm^{-1}:

IR spectra of the ligand, exhibits absorption band at 3473.91 cm^{-1}, indicating N-H stretching in -NHCO-group. Absorption band at 3032.93cm^{-}1 indicates C-H stretching in aromatic rings. A band at 1704.53 cm^{-1}confirms the C=O stretching of –COOH group present in the ligand. In –NHCO group, C=O stretching was appeared at 1680 cm^{-1}.At 1601.49 and 1516.09 cm^{-1} absorption band appeared for C=C stretching in aromatic ring. Absorption band due to N-H bending of –NHCO- group was appeared at 1580 cm^{-1}.

^{1}H-NMR (DMSO):

PMR spectra were recorded on VNMRS 400 NMR spectro-photometer. PMR chemical shifts are recorded in δ - value using TMS as an internal standard.

Signals obtained in ^{1}H-NMR spectra confirm the formation of ligand. Signal obtained at 10.2 ppm (1H, m) shows the presence of –COOH group. Signal at 8.0 ppm. (1H, m) confirms the presence of sec. amide group. Total 12 protons of the three aromatic rings are appeared at 7.04– 7.52 ppm. and aromatic methyl group appeared at 2.35 ppm. (3H,s).

TGA ANALYSIS:

The thermo gravimetric analysis (TGA) of the sample has been carried out by using “PERKIN ELMER PYRIS 1 TGA” in a slow stream of air. The powdered sample (about 9 mg.) was placed in the boat.

The thermogram was analyzed to obtain information about percentage weight loss at different temperatures. Hence the TGA of ligands in air may cause decarboxylation as reported by Parekh [16].

- Examination of the TG curves of ligand sample reveals that ligand degrades in two steps.
- The first stage of degradation up to 150° to 250°C of the ligand indicates the weight loss in the range at 09 to 11% percentages depending on the molecular weight of sample.
- The IInd stage at degradation of the ligand beyond 200°C is rapid and loss about 90% at 300°C. depending on the nature of ligand.

- The ligand contains one –COOH group. The calculated value of CO_2 of ligand and % loss of 1st stage degradation of ligand is consistent with the calculated value. All these facts confirm the structure of ligand. Calculated: 11.49%, Found: 11.50%

NON-AQUEOUS CONDUCTOMETRIC TITRATION:

The ligand sample dried at 60°C was finely powdered and used for non-aqueous conductometric titration. A weighed amount of ligand sample (50 mg.) was dissolved in 40 ml of anhydrous pyridine. The base tetra n-butyl ammonium hydroxide (TBAH) (0.1 N), in pyridine was used as titrant.

The non-aqueous conductometric titration curve of the ligand has shown the presence of one break and the estimation of number of –COOH group from the break has shown the values 1.0, indicating the presence of one –COOH group. This is quite consistent with the proposed structure shown in scheme -1.1.

Table 5: Estimation of –COOH group

Ligand	Molecular weight	Millimoles of TBAH at break per 100 gm of sample.	Estimated No. of –COOH group.
L-1	383	261	1.00

[B] Characterization of Metal-chelate:

ELEMENTAL ANALYSIS:

The C, H and N elements of all the samples were measured by Elemental analyzer Thermofinigan flash1101 EA. The metal content of all the metal chelates was estimated by method reported [3]. Cu^{2+}, Ni^{2+}, Co^{2+}, Mn^{2+} and Zn^{2+} ions were estimated by EDTA titration. The metal composition suggested that metal: ligand (M : L) ratio is 1:2 for all divalent metal ions. These results are also supported by data of elemental analysis.

Table 6: Characterization of Metal Chelates of Ligand L-1

Metal Chelates	Molecular formula	M.Wt gm/mole	Yield %	% Metal analysis		Elemental analysis					
						%C		%H		%N	
				Cald.	Found	Cald.	Found	Cald.	Found	Cald.	Found
$(L\text{-}1)_2\ Cu^{+2}$	$C_{50}H_{40}N_2O_6\ Cu^{+2}.2H_2O$	863.5	75	7.35	7.30	69.48	69.50	5.10	5.10	3.24	3.20
$(L\text{-}1)_2\ Ni^{+2}$	$C_{50}H_{40}N_2O_6\ Ni^{+2}.2H_2O$	859	72	6.86	6.80	69.85	69.80	5.12	5.10	3.26	3.20
$(L\text{-}1)_2Mn^{+2}$	$C_{50}H_{40}N_2O_6\ Mn^{+2}.2H_2O$	855	75	6.43	6.40	70.17	70.20	5.15	5.10	3.27	3.20
$(L\text{-}1)_2\ Co^{+2}$	$C_{50}H_{40}N_2O_6\ Co^{+2}.2H_2O$	859	68	6.86	6.80	69.85	69.80	5.12	5.10	3.26	3.20
$(L\text{-}1)_2\ Zn^{+2}$	$C_{50}H_{40}N_2O_6\ Zn^{+2}.2H_2O$	865	65	7.51	7.50	69.36	69.30	5.09	5.10	3.24	3.23

IR (KBr) Cm^{-1}:

All the IR spectra have identical bands at their respective positions. Most of the bands appeared in the spectra of corresponding ligand are observed at the similar position in the IR spectra of its metal complexes.

- The band due to C=O of -COOH group appeared in the spectra of ligand is almost vanished in the spectra of complexes. The new strong band around 1600 cm^{-1} is appeared and this might be responsible for $-COO^-$ anion. This is expected as the -COOH group of ligand is participating in metal chelate formation.
- Only a new band at 1095 cm^{-1} had appeared in the spectra of metal chelates. This may be assigned to $V_{c\text{-}o}$ of C-O-Metal bond formation.

MAGNETIC SUSCEPTIBILITY:

Magnetic susceptibility was determined by the Gouy method using mercury tetrathiocynatocobaltate (II) $Hg[Co(CNS)_4]$ as an all round calibrant.

Table 7: Experimental data of Magnetic moment of Metal Chelates of Ligand L-1

Metal Chelates	$\chi_g \times 10^{-6}$ (cgs)	$\chi_m \times 10^{-6}$ (cgs)	Observed Magnetic moment μ_{eff} (BM)	Calculated μ_{eff} = $\sqrt{n(n+2)}$ BM	μ_{eff} (BM) Expected
$(L\text{-}1)_2\ Mn^{+2}$	17.76	15187	5.97	5.91	5.2-6.0
$(L\text{-}1)_2\ Co^{+2}$	12.89	11083	5.10	3.87	4.4-5.2
$(L\text{-}1)_2\ Ni^{+2}$	5.40	4640	3.30	2.82	2.9-3.4
$(L\text{-}1)_2\ Cu^{+2}$	2.28	1969	2.15	1.73	1.7-2.2
$(L\text{-}1)_2\ Zn^{+2}$	-	-	-	-	D(*)

TGA ANALYSIS OFMATAL-CHELATES:

Thermogravimetric analysis of all the metal chelates of ligand (L-1) was carried out on PERKIN ELMER PYRIS 1 TGA.

- The degradation of all the chelates starts in the temperature range of 200 to 270^0C depending on the nature of chelates.
- The wt. loss amount in the first stage is between 4.0 to 5.0 %, this may be due to water molecules associated with the chelates. This is also supported by Nikolaev et al [17].
- Rapid loss of mass was observed due to "in situ" formation of metal oxide during degradation which accelerates the rapid degradation of chelate.
- The last stage of degradation causes a mass loss of about 85%. This is due to loss molecular fragments of ligand.

CONCLUSION

The metal chelates with novel Amic acid derivative derived from 9,10,11,15-tetrahydro-9,10-[3,4]-furanoanthracene-12,14-dione has been synthesized and characterized by various modern techniques. The synthesized Metal-ligand structures are in good agreement with the experimental results. Some of the metal chelates have shown good antibacterial and antifungal activities.

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