



SYNTHESIS, CHARACTERIZATION, CHELATING PROPERTIES AND ANTIMICROBIAL ACTIVITY OF PYRIMIDINE -PHTHALIC ANHYDRIDE COMBINED MOLECULE

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ABSTRACT

The reaction between 4,6-Diphenyl-2-amino pyrimidine with phthalic anhydride form compound was designated as 2-(4,6-diphenylpyrimidin-2-ylcarbonyl)benzoic acid (PY-PA). The transition metal complexes of Cu^{2+} , Co^{2+} , Ni^{2+} , Mn^{2+} , Zn^{2+} and Fe^{3+} of PY-PA have been prepared and characterized by elemental analyses, spectral studies, magnetic moment determination, molar conductivity measurement and microbicidal activity.

Keywords: 4,6-Diphenyl-2-amino pyrimidine, phthalic anhydride, metal chelates, spectral studies, magnetic moment, antibacterial and antifungal activity.

INTRODUCTION

Pyrimidine belonging to the heterocyclic system prepared from α,β -unsaturated Carbonyl compound with Guanidine are associated with diverse pharmaceutical activities such as antibacterial¹, insecticidal, fungicidal, antimicrobial, asvitronectal receptes, antagonist, anthelmintic, anti-inflamatory, antiviral, antitumor and antimicrobial agents²⁻¹⁰ etc. Recently the Pyrimidine derivative has been reported with remarkable antimicrobial activity¹⁰. The reaction of Pyrimidine derivative with phthalic anhydrides has not been reported so far. Thus this may afford good chelating ligand. Hence it was thought interesting to prepare the ligand having pyrimidine-phthalic anhydride moieties. Thus the present communication comprises the studies on pyrimidine-phthalic anhydride combined molecule and its metal chelates. The research work is illustrated in Scheme-1.

EXPERIMENTAL

Materials

4,6-Diphenyl-2-amino pyrimidine was prepared by method reported in literature¹¹. phthalic anhydride was obtained from local dealer. All other chemicals used were of analytical grade.

Synthesis of 2-(4,6-diphenylpyrimidin-2-ylcarbonyl)benzoic acid

Formation PY-PA

The solution of 4,6-Diphenyl-2-amino pyrimidine (PY) (0.02 mole) in acetone is cooled to 10° C to this solution phthalic anhydride (PA) (0.02 mole) was added with stirring. The resultant solid product designated as PY-PA was isolated and dried in air. Yield was 76%. It's m.p. was 188-90° C (uncorrected).

Elemental Analysis:	C%	H%	N%
$\text{C}_{24}\text{H}_{17}\text{O}_3\text{N}_3$ (395)			
Calculated	72.91	4.30	10.63
Found	72.89	4.29	10.61
Acid Value:			

Theoretical	198.8 mg KOH/1g. Sample	
Found	196 KOH/1g Sample.	
IR Features:		
3030, 1500, 1600 cm ⁻¹	Aromatic	
1680 cm ⁻¹	CO of COOH	
3400 cm ⁻¹	Sec.NH	
NMR (DMSO) δ ppm		
7.2 – 7.6 (15H)	Multiplet	Aromatic
10.1 (1H)	Singlet	COOH
2.8 (1H)	Singlet	NH

Synthesis of metal chelates of PY-PA

The Cu²⁺, Co²⁺, Ni²⁺, Mn²⁺, Zn²⁺, and Fe³⁺ metal ion chelates of PY-PA have been prepared in a similar manner. The procedure is as follow.

To a solution of PY-PA (31.3 g 0.1 mole) in ethanol-acetone (1:1v/v) mixture (150 ml), 0.1N KOH solution was added dropwise with stirring. The sticky precipitates were obtained at neutral pH. Then these were dissolved in water and diluted to 250 ml. by water and this was known as stock solution. 25 ml of the stock solution (which contains 0.01 mole PY-PA) was added drop wise to the solution of metal salt (0.005 mole for divalent metal ions and 0.0033 mole for Fe³⁺ ion) 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

Measurements

The elemental analysis for C, H and N were carried out on elemental analyzer TF-EA.1101 (Italy). IR spectra of PY-PA and its metal complexes were scanned on a Nicolet 760 FTIR spectrophotometer in KBr. The NMR spectrum of PY-PA was scanned on Bruker 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 ¹². Magnetic susceptibility measurement of all the metal complex was carried out at room temperature by the Gouy method. Mercury tetrathiocyanatocobalate (II) Hg [Co (NCS)₄] was used as a calibrant. The diffused reflectance spectra of solid metal complex were recorded on a Beckman DK Spectrophotometer with a solid 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.

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 ¹³. 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.

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

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

RESULTS AND DISCUSSION

The parent ligand PY-PA 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 PY-PA reveals that bands at 3030, 1500 and 1600 are characteristics of the phthalamic acid^{10,11}. The strong bands at 1680 for C=O and band at 3400 for sec. NH. The NMR data (shown in experimental part) also confirm the structure of PY-PA.

The Metal chelate of PY-PA with ions Cu²⁺, Co²⁺, Ni²⁺, Mn²⁺, Zn²⁺, Fe³⁺ vary in colours. On the basis of the proposed structure as shown in Scheme-1, the molecular formula of the PY-PA ligand is C₂₄H₁₇O₃N₃. Which upon complexation 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 [C₂₄H₁₇O₃N₃]₂M.2H₂O 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 PY-PA with that of its each metal chelates has revealed certain characteristics differences.

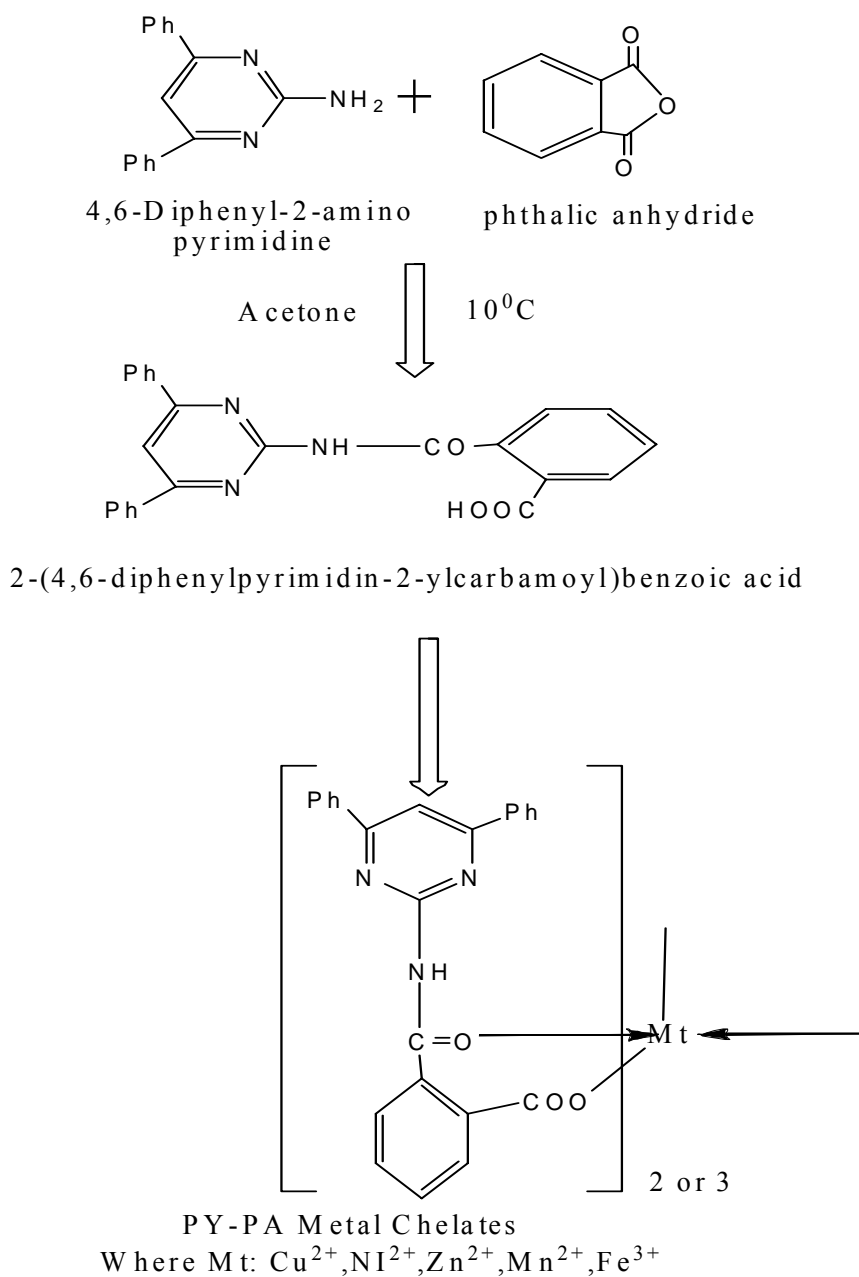
One of the significant differences to be expected between the IR spectrum of the parent ligand and its metal chelates is the presence of more broadened bands in the region of 1560-1670cm⁻¹ for the metal chelates as the oxygen of the Carbonyl group of the ligands forms a coordination bond with the metal ions¹³⁻¹⁵. 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 COO⁻ anion at 1600 cm⁻¹ in the IR spectrum of the each metal chelates. The band at 1400 cm⁻¹ in the IR Spectrum of HL assigned to inplane Carbonyl determination¹³⁻¹⁵ is shifted towards higher frequency in the spectra of confirmed by a weak bands at 1105 cm⁻¹ corresponding to C-O-M stretching¹³⁻¹⁵. 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 and 1:3 metal: ligand stoichiometry for Fe³⁺.

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 Zn²⁺, are Para magnetic while those of Zn²⁺ are diamagnetic. The diffuse electronic spectrum of the [Cu HL (H₂O)₂] metal complex shows broad bands at 15798 and 22705 cm⁻¹ due to the ²T→²T_{2g} transition and charge transfer, respectively suggesting a distorted octahedral structure¹⁶⁻¹⁸ for the [Cu HL (H₂O)₂] complex. Which is further confirmed by the higher value of μ_{eff} of the [Cu HL (H₂O)₂] complex. The [Ni HL (H₂O)₂] and [Cu HL (H₂O)₂] complex gave two absorption bands respectively at 14702, 22996 and 15798, 22701 cm⁻¹ corresponding to ⁴T_{1g}→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 an octahedral configuration for the [NiHL (H₂O)₂] and [Cu HL (H₂O)₂] complex. The spectra of [Mn HL (H₂O)₂] shows weak bands at 15410, 17656 and 22984 cm⁻¹ assigned to the transitions ⁶A_{1g}→⁴T_{1g} (4G), ⁶A_{1g}→⁴T_{2g} (4G) and ⁶A_{1g} (F) →⁴T_{1g}, respectively suggesting an octahedral structure for the [Mn HL (H₂O)₂] chelate. The spectrum of Fe³⁺ complex has not been adequately characterized. The spectrum comprised the band ground 19029cm⁻¹ and other weak band ground 23115cm⁻¹. The latter has not very long tail. These may have the transition ⁶A_{1g}→⁴T_{2g} (4G) and ⁶A₁→⁴T₁ (4G). 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 [Zn HL (H₂O)₂] polymer is not well resolved, it is not interpreted but its 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 electrolytic¹⁹ in nature of 1:2 type and molar conductivity values are in the range of 36.3-40.1 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 74%. Hence

produced metal chelates can be employed as garden fungicides. Further work in the direction is in progress.



Scheme-1

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Table-1: Analytical Data of the Metal Chelates of HL₁ (i.e. PY-PA)

Compound	Empirical Formula	Mol. Cal. Gm/mol	Yield (%)	Elemental Analysis							
				C%		H%		N%		M%	
				Cald	Found	Cald	Found	Cald	Found	Cald	Found
HL (PY-PA)	C ₂₄ H ₁₇ N ₃ O ₃	395	76	72.91	72.89	4.30	4.29	10.63	10.61	--	--
(L) ₂ Cu ²⁺	C ₄₈ H ₃₀ N ₆ O ₆ Cu ²⁺ 2H ₂ O	885.54	58	65.04	65.02	3.83	3.81	9.48	9.46	7.17	7.15
(L) ₂ Co ²⁺	C ₄₈ H ₃₀ N ₆ O ₆ Co ²⁺ 2H ₂ O	880.94	60	65.38	65.37	3.85	3.82	9.53	9.50	6.69	6.68
(L) ₂ Mn ²⁺	C ₄₈ H ₃₀ N ₆ O ₆ Mn ²⁺ 2H ₂ O	880.71	64	65.40	65.38	3.86	3.84	9.53	9.52	6.66	6.65
(L) ₂ Ni ²⁺	C ₄₈ H ₃₀ N ₆ O ₆ Ni ²⁺ 2H ₂ O	876.94	54	65.68	65.64	3.87	3.85	9.57	9.55	6.26	6.24
(L) ₂ Zn ²⁺	C ₄₈ H ₃₀ N ₆ O ₆ Zn ²⁺ 2H ₂ O	887.38	63	64.91	64.90	3.83	3.80	9.46	9.44	7.36	7.34
(L) ₃ Fe ³⁺	C ₇₂ H ₄₅ N ₉ O ₉ Fe ³⁺ 3H ₂ O	877.85	58	67.03	67.01	3.95	3.94	9.77	9.76	4.33	4.32

Table -2: Magnetic Moment and Reflectance Spectral data of Metal Chelates of PY-PA ligand

Metal chelate	Magnetic Moment μ_{eff} (B.M.)	Molar Conductivity $\Omega \text{m} \text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$	Absorption band (cm ⁻¹)	Transitions
Cu-HL	1.98	39.3	22705 15798	C.T ² T→ ² T _{2g}
Ni-HL	3.89	37.0	14702 22996	3 A _{2g} → 3T _{1g} (p) 3 A _{1g} → 3T _{1g} (F)
Co-HL	4.55	36.3	15420 22735	4 T _{1g} (F)→ 4T _{2g} (F) 4 T _{1g} (F)→ 3A _{2g}
Mn-HL	5.16	38.6	15410 17656	6 A _{1g} → 4T _{1g} (4E _g) 6 A _{1g} → 4T _{2g} (4G)

			22984	6 A1g → 4T ₁ g(4G)
Fe-HL	5.88	40.1	19029	6 A1 → 4T ₂ g(4G)
			23115	6 A1g → 4T ₁ g(4G)

Zn²⁺ Diamagnetic in Nature.

Table-3: Antifungal Activity of Ligand HL₁ and its metal chelates.

Sample	Zone of inhibition of fungus at 1000ppm (%)						
	N	T	AN	BT	PE	RN	TL
HL1	63	65	62	63	66	66	61
(HL1)-Cu ²⁺	79	83	74	80	78	76	75
(HL1)-Co ²⁺	74	78	75	74	75	74	70
(HL1)-Mn ²⁺	72	72	70	75	66	71	72
(HL1)-Ni ²⁺	76	81	72	76	72	75	72
(HL1)-Zn ²⁺	72	78	73	74	70	73	70
(HL1)-Fe ³⁺	75	76	71	72	72	79	76
(HL1)-UO ²⁺	76	871	74	69	68	72	66

N=*Nigrospra sp.*; T=*Trichothesium sp.*;
AN=*Aspergillus niger.*; BT=*Botrydepladia thiobromine*;
PE=*Penicillium expansum*; RN=*Rhizopus ni8gricans*;
TL=*Trichoderna lignorum*

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