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SYNTHESIS AND CHARACTERIZATION OF NOVEL HETEROCHELATE COMPOUNDS CONTAINING PYRIMIDINE AND 8-HQ

Ajay Solanki and Dr. S. V. Patel*

Chemistry Department, Sir P.T. Science College, Modasa-383315. Gujarat (India).

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***Corresponding Author**
Dr. S. V. Patel
Chemistry Department, Sir
P.T. Science College,
Modasa-383315. Gujarat
(India).

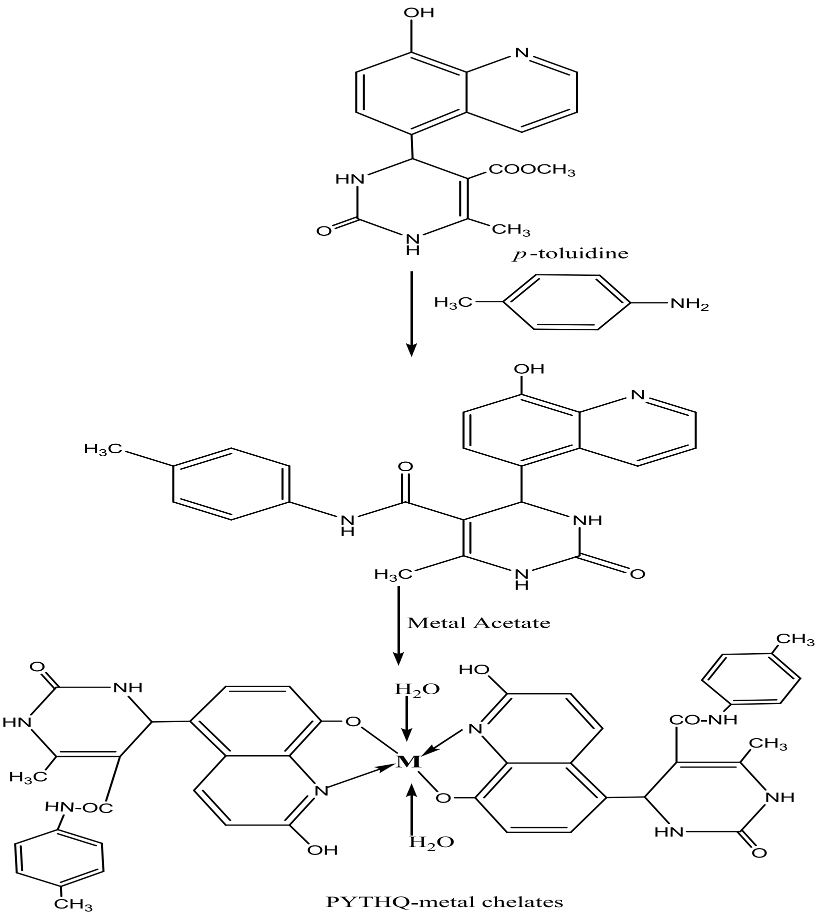
ABSTRACT

6-methyl-4-(8-hydroxyquinolin-5-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (PYHQ), react with p-toluidine yield 4-(8-hydroxyquinolin-5-yl)-6-methyl-2-oxo-N-p-tolyl-1,2,3,4-tetrahydropyrimidine-5-carboxamide (PYTHQ). The synthesized ligand characterized by elemental analysis and spectral studies. The transition metal chelates of Cu^{2+}, Ni^{2+} , Co^{2+} , Mn^{2+} and Zn^{2+} of PYTHQ were prepared and characterized by metal-ligand (M:L) ratio, IR and reflectance spectroscopies and magnetic properties. The PYTHQ and its metal chelates were screened for antifungal activity against various fungi.

KEYWORDS: 5-formyl-8-hyroxy quinolinol, Pyrimidine derivative, Magnetic moment and Antifungal properties.

INTRODUCTION

Numbers of research work are carried out in the world because heterocyclic compounds are important for human being. The most important heterocyclic compounds like, Pyrimidine has played a fundamental part in the manufacture of various biologically active drugs as antimicrobial, calcium channel blockers, antitubercular, antibacterial, anti-inflammatory.[1-4] The heterocyclic compound i.e. 8-Hydroxyquinoline is a well-known complexing agent and able to make chelates with a wide number of metal ions. 8-Hydroxyquinoline is well known as an analytical reagent.[5] Several 8-quinolinol derivatives are also reported for dyeing of textiles.[6] Recently, Some of the metal chelates containing 8-HQ are also reported with good biological potentiality.[7,8] The reaction of Pyrimidine derivatives with HQ has not been reported so far. Hence such type of heterocyclic ring and 8-HQ into one molecule may afford good biological active compound. The present paper discuss about synthesizes, characterization and antifungal properties of 4-(8-hydroxyquinolin-5-yl)-6-methyl-2-oxo-N-p-tolyl-1,2,3,4-tetrahydropyrimidine-5-carboxamide (PYTHQ) **(Scheme-1)**.



PYTHQ-metal chelates
Where M: Cu^{2+}, Co^{2+}, Ni^{2+}, Mn^{2+}, Zn^{2+}
Scheme-1

EXPERIMENTAL

All other chemicals used were of laboratory grade. 5-formyl-8-hydroxy quinolinol and 4-(8-hydroxyquinolin-5-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carboxylate was prepared according to method reported in literature.[9,10]

Synthesis of 4-(8-hydroxyquinolin-5-yl)-6-methyl-2-oxo-N-p-tolyl-1,2,3,4-tetrahydro pyrimidine-5-carboxamide (PYTHQ)

Reflux the mixture of 4-(8-hydroxyquinolin-5-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carboxylate (0.1mole) and p-toluidine (0.1mole) for 6-7 hrs. Then distilled off solvent and the solid mass obtained was isolated and dried in air. Yield was 64%. It's m.p. was 171-173°C (uncorrected).

Analysis

		C%	H%	N%
Elemental Analysis	**Calculated:**	68.03	5.19	14.42
$C_{22}H_{20}N_4O_3$ (388)	**Found:**	68.01	5.18	14.40

IR Spectral Features (cm^{-1})

3650 (OH), 3352-3325 (NH), 1640 (C=O), 2980-2880 (CH_3, CH_2), 2850, 1630, 1575, 1500, 1470 (aromatic), 1640, 1575, 1475, and 755 (8-quinolinol).

^{1}H NMR (DMSO-d_6,300 MHz) δ (ppm): 2.28, 2.38 (s,6H,CH_3), 5.21 (s,1H, pyrimidine), 8.92-7.08 (m,9H,Ar-H), 10.32, 9.60, 9.70 (3H, NH, D_2O exchangeable), 5.27 (s, 1H,OH).

Synthesis of metal chelates of PYTHQ:

The metal chelates of PYTHQ with Cu^{2+}, Co^{2+}, Ni^{2+}, Mn^{2+} and Zn^{2+} metal ions were prepared in two steps. All the metal chelates were prepared as:

Preparation of PYTHQ solution

PYTHQ (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 PYTHQ. It was diluted to 100 ml.

Synthesis of PYTHQ -metal-chelates

In a solution of metal acetate (0.005 mol) in acetone: water (50:50 v/v) mixture (40 ml) the 20 ml of above mentioned PYTHQ solution (i.e. containing 0.01 M PYTHQ) was added with vigorous stirring at room temperature. The appropriate pH was adjusted by addition of sodium acetate for complete precipitation of metal chelate. The precipitates were digested on a boiling water bath. The precipitates of chelate were filtered off, washed by water and air-dried.

Table: 1 ANALYSIS OF PYTHQ LIGAND AND ITS METAL CHELATES

Empirical Formula	**Mol. Wt. gm/mole**	**Yield (%)**	**Elemental Analysis**							
			C%		**H%**		**N%**		**M%**	
			Cal.	**Found**	**Cal.**	**Found**	**Cal.**	**Found**	**Cal.**	**Found**
$C_{22}H_{20}N_4O_3$	388	64	68.03	68.0	5.19	5.1	14.42	14.4	-	-
$C_{44}H_{42}N_8O_8$ (Cu^{2+})	845.54	69	60.44	60.4	4.81	4.7	12.82	12.8	7.27	7.2
$C_{44}H_{42}N_8O_8$ (Co^{2+})	840.94	72	60.76	60.7	4.83	4.8	12.89	12.8	6.78	6.7

$C_{44}H_{42}N_8O_8$ (Ni^{2+})	840.71	76	60.78	60.7	4.83	4.8	12.89	12.8	6.76	6.7
$C_{44}H_{42}N_8O_8$ (Mn^{2+})	836.94	74	61.04	61.0	4.86	4.8	12.95	12.9	6.35	6.3
$C_{44}H_{42}N_8O_8$ (Zn^{2+})	847.38	68	60.32	60.3	4.80	4.7	12.79	12.77	7.47	7.45

MEASUREMENTS

The elemental contents were determined by Thermo Finigen Flash1101 EA (Itally) the metals were determined volumetrically by Vogel's method.[11] 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 PYTHQ was recorded on 60 MHz NMR spectrophotometer. Magnetic susceptibility measurement of the synthesized complexes was carried out on Gouy Balance at room temperature. Mercury tetrathio cynatocobalate (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.[12]

RESULTS AND DISCUSSION

The synthesis of 4-(8-hydroxyquinolin-5-yl)-6-methyl-2-oxo-N-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamide was performed by a simple reaction of p-toluidine with methyl 4-(8-hydroxy quinolin-5-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carboxylate (PYHQ). The resulted PYTHQ ligand was an amorphous pale white powder. The C, H, N contents of PYTHQ **(Table-1)** are consistent with the structure predicted **(Scheme-1)**. The IR spectrum of PYTHQ comprises the important bands due to 8-quinolinol. The bands were observed at 1640, 1575, 1475, and 755 cm^{-1}.

The broad band due to –OH group appeared at 3650 cm^{-1}. In this band the inflections are observed at 2970, 2930 and 2850cm^{-1}. The NMR spectrum of PYTHQ in DMSO indicates that the singlet of 3H at 2.28 for CH_3 and 5.21 CH of pyrimidine. While the singlet at 5.27 δ ppm due to –OH group. Thus the structure of PYTHQ is confirmed as shown in **Scheme-1**.

The metal and C,H,N contents of metal chelates of PYTHQ **(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.

TABLE: 2 SPECTRAL FEATRUES AND MAGNETIC MOMENT OF PYTHQMETAL CHELATES

Metal Chelates	**μ_{eff} (BM)**	**Electronic spectral data (cm^{-1})**	**Transition**
PODMHQ-Cu^{2+}	2.52	23450 13218	Charge transfer $^2B_{1g} \rightarrow ^2A_{1g}$
PODMHQ-Ni^{2+}	3.73	22595 15371	$^3A_{1g} \rightarrow ^3T_{1g}(P)$ $^3A_{1g} \rightarrow ^3T_{1g}(F)$
PODMHQ-Co^{2+}	4.75	23737 19103 8929	$^4T_{1g}(F) \rightarrow ^4T_{2g}(F)$ $^4T_{1g}(F) \rightarrow ^4T_{2g}$ $^4T_{1g}(F) \rightarrow ^4T_{2g}(P)$
PODMHQ-Mn^{2+}	5.56	23234 19038 16840	$^6A_{1g} \rightarrow ^6A_{2g}\ ^4E_g$ $^6A_{1g} \rightarrow ^4T_{2g}$ (4G) $^6A_{1g} \rightarrow ^4T_{1g}$(PG)
PODMHQ-Zn^{2+}	Diamag.		---------

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 PYTHQ. The other bands are almost at their respectable positions as appeared in the spectrum of parent-PYTHQ 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-3: ANTIFUNGAL ACTIVITY OF PYTHQ AND ITS METAL CHELATES

Sample	**Zone of inhibition of fungus at 1000 ppm (%)**			
	Asperginus niger	***Botrydeplaia thiobromine***	***Nigrospora Sp.***	***Rhisopus Nigricans***
PYTHQ	56	66	58	60
PYTHQ -Cu^{2+}	78	81	79	74
PYTHQ -Zn^{2+}	67	79	78	78
PYTHQ -Ni^{2+}	77	78	66	72
PYTHQ -Co^{2+}	78	80	71	69
PYTHQ-Mn^{2+}	72	77	75	68

Magnetic moments of metal chelates are given in **Table-2**. The diffuse electronic spectrum of Cu^{2+} chelates shows two broad bands around 13218 and 23450 cm^{-1}. The first band may be due to a $^2B_{1g} \rightarrow ^1A_{1g}$ 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.[13] The Co^{2+} metal chelate gives rise to two absorption bands at 23738 and 19103cm^{-1}, which can be assigned $^4T_{1g} \rightarrow {}^2T_{2g}$, $^4T_{1g} \rightarrow {}^4T_{1g}(P)$transitions, respectively. These absorption bands and the μeff value indicate an octahedral configuration of the Co^{2+} metal chelate. The spectrum of Mn^{2+} polymeric chelate comprised two bands at 19038cm^{-1} and 23234cm^{-1}. The latter does not have a very long tail. These bands may be assigned to $^6A_{1g} \rightarrow {}^4T_{2g(G)}$ and $^6A_{1g} \rightarrow {}^4A_{2g(G)}$ 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.[14] In the absence of low temperature measurement of magnetic moment it is difficult to attach any significance to this. As the spectrum of the metal chelate of Ni^{2+} show two distinct bands at 22595 and 15371 cm^{-1} are assigned as $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ transition, respectively suggested the octahedral environment for Ni^{2+} ion.[15] The observed μeff values in the range 2.52-5.56 B.M are consistent with the above moiety.[16]

The examination of antifungal activity of PYTHQ 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.

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