Synthesis, Characterization and Antimicrobial Activity of Metal Chelates of 5-[1(*H*)-Benzotriazole methylene]-8-quinolinol

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Abstract: 5-Chloromethyl-8-quinolinol was condensed stoichiometrically with benzotriazole in presence of potassium carbonate. The resulting 5-[1(*H*)-benzotriazole methylene]-8-quinolinol (BTMQ) was characterized by elemental analysis and spectral studies. The transition metal chelates *viz.* Cu²⁺, Ni²⁺, Co³⁺, Mn²⁺ and Zn²⁺ of BTMQ were prepared and characterized by metal-ligand (M:L) ratio, IR and reflectance spectral studies and magnetic properties. The antifungal activity of BTMQ and its metal chelates was screened against various fungi. The results show that all these samples are good antifungal agents.

Keywords: 1-(*H*)Benzotriazole, 8-Quinolinol, Magnetic moment, Metal Chelates and Antifungal properties.

Introduction

8-Hydroxyquinoline or 8-quinolinol is well known as an analytical reagent^{1,2}. Its various derivatives³ are also useful in pharmaceuticals. Several azo dyes based on 8-quinolinol are also reported for dyeing of textiles as well as their chelating properties^{4,5}. One of the derivatives, *viz.* 5-chloromethyl 8-quinolinol (CMQ) can be synthesized easily and studied extensively for number of derivatives⁶. Some of the ions exchanging resins are also reported with good potentiality⁷⁻¹⁶. The literature survey reveals that the reaction of CMQ with 4-substituted piperazine derivative has been reported recently¹⁷. One of the heterocyclic compounds such as 1-(*H*)-benzotriazole is found as an important heterocyclic compound. Its prime application is as corrosion inhibitors for copper or copper alloys^{18,19}. Ciba Geigy has introduced benzotriazole derivative under the trade name Trinvin-P²⁰. It is applied as an UV light absorber for stabilizing plastics and other organic materials against discoloration determination²⁰. It is also employed as photographic emulsion stabilizer²¹. In the peptide synthesis it acts in the form of an active ester²². If the 8-quinolinol introduced in the molecule of benzotriazole, the end molecule may play antimicrobial agent. Hence it was thought to study the benzotriazole and CMQ clubbed molecule. Thus the present paper comprises the synthesis, characterization, chelating properties and microbial activity of 5-[1(*H*)-benzotriazole methylene]-8-quinolinol (BTMQ) molecule. The reaction route is as shown in scheme.

Experimental

5-Chloromethyl-8-quinolinol (CMQ) hydrochloride was prepared according to method reported in literature⁶. Benzotriazole was prepared by reported method²³. All other chemicals used were of laboratory grade of purity.

Synthesis of 5-[1-(H)-benzotriazole methylene]-8-quinolinol.

Formation of BTMQ

In a round bottom flask, to a suspension of 5-chloromethyl-8-quinolinol (CMQ) hydrochloride (23 g, 0.1 mol) in dry acetone (100 mL), 1-(H)-Benzotriazole (0.1 mol) was added gradually at room temperature. Potassium carbonate (16.8 g) was added in the mixture and the mixture was refluxed on water bath for 8 h. The resulting solid mass was add in to water and the precipitation was filtered off, washed with boiling water and the air-dried. It was dark green amorphous powder. It was insoluble in common organic solvent but soluble only in formic acid and DMSO.

Analysis

Elemental analysis

$C_{16}H_{12}N_4O$ (276)

	C%	H%	N%
Calculated:	69.56	4.34	20.28
Found :	69.48	4.29	20.22

IR Features Cm^{-1} : 2980, 2850, 1470 (CH_2), 1630, 1575, 1500(8 H_Q)

NMR δ ppm : 5.85-8.3 (m 10H Ar-H), 3.8 (OH) 2.6(CH_2)

Synthesis of metal chelates of BTMQ

The metal chelates of BTMQ were prepared in two steps. All the metal chelates were prepared in an identical procedure. The details are given as follows.

Preparation of BTMQ solution

BTMQ (0.05 mol) was taken in 500 mL beaker. Formic acid was added up to slurry formation. To this slurry water was added till the complete dissolution of BTMQ. It was diluted to 100 mL.

Synthesis of BTMQ-metal-chelates

In a solution of metal acetate (0.005 mol) in acetone: water (50:50 v/v) mixture (40 mL), 20 mL of above mentioned BTMQ solution (*i.e.* containing 0.01 M BTMQ) 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.

Measurements

The elemental contents of C, H, N were determined by TF-Flash-1101 EA, The metals contents of metal chelates were determined volumetrically by Vogel's method²⁵. 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 spectrometers. NMR spectrum of BTMQ was recorded on 400 MHz NMR spectrophotometer. Magnetic susceptibility measurement

of the synthesized complexes was carried out on Gouy Balance at room temperature. 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 literature²⁶.

Results and Discussion

The synthesis of 5-[1-(*H*)-benzotriazole methylene]-8-quinolinol (BTMQ) was performed by a simple nucleophilic substitution reaction of 1-(*H*)-Benzotriazole and 5-chloromethyl-8-quinolinol hydrochloride (CMQ). The resultant BTMQ ligand was an amorphous green powder. The C, H, N contents of BTMQ (Table 1) are consistent with the structure predicted (Scheme 1). The IR spectrum of BTMQ comprises the important bands due to 8-quinolinol. The bands were observed at 1630, 1575, 1470, and 750 cm^{-1} .

The broad band due to $-\text{OH}$ group appeared at 3800-2700 cm^{-1} . In this band the inflections are observed at 2950, 2920 and 2850 cm^{-1} , while the latter two might be attributed to asymmetric and symmetric vibration of CH_2 of CMQ. The NMR spectrum of BTMQ in DMSO indicates that singlet. The NMR spectrum of BTMQ in DMSO indicates that the singlet of 2 H at 2.6 δ ppm of $\text{N}-\text{CH}_2-\text{Ar}$ group. While the singlet at 3.8 δ ppm due to $-\text{OH}$ group, the aromatic protons are appeared in multiplicity at 7.2 δ . The vigorous oxidation of BTMQ yield 8-hydroxy quinoline-5-carboxylic acid²⁷ m.p. 230 $^{\circ}\text{C}$. Thus the structure of BTMQ is confirmed as shown in Scheme 1.

Scheme 1.

The metal and C, H, N contents of metal chelates of BTMQ (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 1. Analysis of BTMQ ligand and its metal chelates

Empirical formula	Mol. Cal. g/mole	Yield, %	Elemental analysis, %							
			C		H		N		M	
			Cald	Found	Cald	Found	Cald	Found	Cald	Found
C ₁₆ H ₁₂ N ₄ O	276	85	69.56	69.4	4.38	4.2	20.28	20.1	----	----
C ₁₆ H ₁₂ N ₄ O Cu ²⁺ 2H ₂ O	375.54	70	51.12	51.1	4.26	4.2	14.91	14.8	16.92	16.8
C ₁₆ H ₁₂ N ₄ O Ni ²⁺ 2H ₂ O	370.96	65	51.75	51.7	4.31	4.2	15.09	15.0	15.82	15.8
C ₁₆ H ₁₂ N ₄ O Co ²⁺ 2H ₂ O	370.93	70	51.76	51.7	4.31	4.3	15.09	15.0	15.80	15.7
C ₁₆ H ₁₂ N ₄ O Mn ²⁺ 2H ₂ O	366.93	75	52.32	52.3	4.36	4.2	15.26	15.2	14.97	14.9
C ₁₆ H ₁₂ N ₄ O Zn ²⁺ 2H ₂ O	377.39	65	50.87	50.8	4.23	4.2	14.83	14.7	17.32	17.3
C ₁₆ H ₁₂ N ₄ O Cd ²⁺ 2H ₂ O	424.41	75	45.23	45.2	3.76	3.6	13.19	13.1	26.48	26.3

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 BTMQ. The other bands are almost at their respectable positions as appeared in the spectrum of parent-BTMQ 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 2. Spectral features and magnetic moment of BTMQ metal chelates

Metal Chelates	μ_{eff} (BM)	Electronic spectral data, cm ⁻¹	Transition	IR spectral features common for all, cm ⁻¹	
BTMQ-Cu ²⁺	2.12	23268	Charge transfer $^2B_{1g} \rightarrow ^2A_{1g}$	1630	Quinoline moiety
		15869		1575	
				1500	
BTMQ -Ni ²⁺	3.29	22575	$^3A_{1g} \rightarrow ^3T_{1g}(P)$ $^3A_{1g} \rightarrow ^3T_{1g}(F)$	2980	CH ₂
		15387		2850	
				1470	
BTMQ -Co ²⁺	4.65	22733	$^4T_{1g}(F) \rightarrow ^4T_{2g}(F)$ $^4T_{1g}(F) \rightarrow ^4T_{2g}(P)$ $^4T_{1g}(F) \rightarrow ^4T_{2g}(P)$	1100	C-O-M & O-M bands
		15255		500	
		8921			
BTMQ -Mn ²⁺	5.40	23870	$^6A_{1g} \rightarrow ^6A_{2g}$ $^6A_{1g} \rightarrow ^4T_{2g}(4G)$ $^6A_{1g} \rightarrow ^4T_{1g}(PG)$	710	Ar-Cl
		18337		750	
		16821			
BTMQ -Zn ²⁺	Diamag.		-----	-----	-----
BTMQ -Cd ²⁺	Diamag.		-----	-----	-----

Magnetic moments of metal chelates are given in Table 2. The diffuse electronic spectrum of Cu²⁺ chelates shows two broad bands around 13000 and 23000 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 Cu²⁺ metal chelates²⁸⁻²⁹. The higher value of the magnetic moment of the Cu²⁺ chelate supports the same. The Co²⁺ metal chelate gives rise to two absorption bands at 23800 and 19040 cm⁻¹, which can be assigned⁴. $T_{1g} \rightarrow ^2T_{2g}$, $^4T_{1g} \rightarrow ^4T_{1g}(P)$ transitions, respectively. These absorption bands and the μ_{eff} value indicate an octahedral configuration of the Co²⁺ metal chelate³⁰⁻³¹. The spectrum of Mn²⁺ polymeric chelate comprised two bands at 19010 cm⁻¹

and 23300 cm^{-1} . The latter does not have a very long tail. These bands may be assigned to ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g(\text{G})}$ and ${}^6\text{A}_{1g} \rightarrow {}^4\text{A}_{2g(\text{G})}$ 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. 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 sistint bands at $11960\text{--}11450$ and $17700\text{--}17400\text{ cm}^{-1}$ are assigned as ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})$ and ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})$ transition, respectively suggested the octahedral environment for Ni^{2+} ion. The observed μ_{eff} values in the range $3.01\text{--}3.2\text{ B.M}$ are consistent with the above moiety³²⁻³³.

The examination of antifungal activity of BTMQ 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.

Table 3. Antifungal activity of BTMQ ligand and its metal chelates

Sample	Zone of inhibition of fungus at 1000 ppm, %						
	BT	N	RN	AN	AF	AA	AK
BTMQ	55	54	53	63	63	67	70
BTMQ - Cu^{2+}	83	78	77	83	81	81	85
BTMQ - Zn^{2+}	75	64	63	77	83	83	84
BTMQ - Ni^{2+}	80	77	75	75	73	81	80
BTMQ - Co^{2+}	65	75	75	73	78	79	85
BTMQ - Mn^{2+}	79	74	73	75	80	77	83
BTMQ - Cd^{2+}	80	85	89	80	85	75	85

BT = *Botrydeplaia thiobromine* N = *Nigrospora Sp.* RN = *Rhisopus Nigricans* AN= *Asperginus niger* AF = *Aeprogines funigalus* AA = *anida Albicans* AK = *Andida krusegios candida grabrata*HO5

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