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RESEARCH ARTICLE

Synthesis and Antifungal Activity of Complexes of Cu(II), Co(II) and Fe(III) with Quaternary Ammonium Salts Derivatives of Diethylaminoethyl Methacrylate Containing Acetic Acid Group

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Abstract: In the present paper the synthesis and characterization of three new metal complexes of Cu(II), Fe(III) and Co(II), with quaternary ammonium salts used as ligand derived from 2-(diethylamino)ethylmethacylate (DEAEMA) have been successfully prepared in alcoholic medium. The ligand has got -COOH moiety which is capable of chelation. The ligand and its metal complexes were characterized by conductivity measurements, FTIR spectroscopy, electronic spectroscopy, ^{1}H and ^{13}C NMR spectroscopies and have been screened for their antifungal activities

Keywords: Quaternary ammonium salts, DEAEMA, Cu(II), Co(II), Fe(III) complexes, Antifungal activity

Introduction

Metal complexes offer a platform for the design of novel therapeutic compounds[1]. They are play essential role in pharmaceutical industry and in agriculture[2]. The coordination chemistry of oxygen donor ligands is an active area of research they have been widely studied for their biological activities as Antimicrobial[3,4], Antitubercular[5,6], Antiviral[7], Anticonvulsant[8,10], Antitumor[11,12], And anti-inflammatory activities[13,14].

Quaternary ammonium salts (QAS) are used successfully as extractants[15] are widely used as phase transfer catalysts in the field of organic synthesis[16], QAS have gained great importance because of their diverse biological properties, such as antibacterial[17,19] and antifungal[20,21]. The correlation of QAS with antifungal activity is related to fungal phospholipase inhibition[22]. Generally, the chelating ligand is a polyfunctional molecule which can encase the metal in an organic sphere[23]. A quaternary ammonium halides containing COOH group can be considered as bifunctional compounds[24]. Following all these observations, we report here the synthesis and structural studies on the complexes of Cu(II), Co(II) and Fe(III) with quaternary ammonium salts derivatives of diethylaminoethyl methacrylate containing acetic acid moiety.

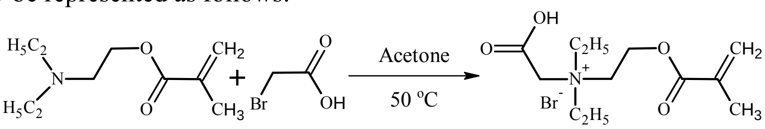
Experimental

All the solvents and reagents used in this study were obtained from Sigma Aldrich and BIOCHEM. Metal salts of Cu(II), Co(II) and Fe(III) were used as nitrates. The reaction progress was monitored by Thin layer chromatography (TLC) was performed throughout the reaction to optimized the reaction for purity and completion of reaction on Merck silica gel using $CHCl_3$ as the eluting solvent system, and spots were observed using iodine as visualizing agent. All the melting points were determined in open capillary tubes using BÜCHI 540 apparatus and are uncorrected .UV-Visible spectra were measured in DMSO solution at 10^{-3} molar concentration using Shimadzu UV-Visible recorder spectrophotometer with 1 cm matched quartz cells. The I.R spectra in the range of 4000-400 cm^{-1} were recorded as potassium bromid disc on Shimadzu FTIR-8300 Fourier transform infrared spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 300 MHz spectrometer, using TMS as internal standard and CD_3OD as a solvent, chemical shifts in ppm. Molar conductances of the solution of the metal complexes were determined with a conductivity meter type inoLab Level 1 Multiparameter. All measurements were carried out at room temperature with freshly prepared solution.

Chemical Synthesis

Synthesis of the ligand HL

According to the procedure adopted by Guiqian Lu *et al.*[25] a mixture of tertiary amines 2-(diethylamino)ethylmethacylate (3 g, 0.016 mol) and bromoacetic acid (2.36 g, 0.017 mol) dissolved in dry acetone (40 mL), in the presence of hydroquinone was gently refluxed for 40 hours on water bath. After cooling to room temperature, the solvent was evaporated and the residue were simply filtered and washed with cold diethyl ether. The synthesis of the ligand may be represented as follows:



Scheme 1. Synthesis of ligand

Synthesis of the metal complexes

To a methanolic solution (0.01 mol in 20 mL) of the required metal was added a methanolic solution (0.02 mol in 20 mL) of ligand HL in a 1:2 (metal: ligand) molar ratio for Cu(II), Co(II) metal , and 1:3 (metal : ligand) molar ratio for Fe(III) metal. Then the mixture was gently heated under reflux for 30 minutes and a crystalline colored precipitate was formed at room temperature. The precipitates were filtered out, washed with cold diethyl ether and dried in desiccators.

Results and Discussion

The formations of the ligand and its metal complexes were detected by thin layer chromatography (TLC) via their R_f which were different from starting materials. The complexes are of various colours varied from lawn green, dark green and brownish colour different from the colour of the ligand indicating that the colours formed depend on the metal ions. The melting points of the complexes are different (higher) than that of the ligand an evidence for complexation. The physical and analytical data of all the compounds studied has been summarized in Table 1.

Table 1. Physical properties and analytical data of the ligand and its complexes

Compound	Color	%Yield	Melting Point °C	Molar conductivity µS.cm^{-1}	R_f Value	Solvent system	Suggest formula
HL	White	76	104-105	34.5	0.42	$CHCl_3$	$C_{12}H_{22}BrNO_4$
Cu L_2(1)	lawn green	65	134-135	43	0.46	$CHCl_3$	$C_{24}H_{42}Br_2CuN_2O_8$
Co L_2(2)	dark green	68	182-183	27.7	0.61	$CHCl_3$	$C_{24}H_{42}Br_2CoN_2O_8$
FeL_3(3)	brown	54	154-155	36.8	0.38	$CHCl_3$	$C_{36}H_{63}Br_3FeN_3O_{12}$

UV spectral studies of the ligand and its metal complexes

The electronic spectra for the ligand and iis metal complex shows that the absorption bands in the UV region can be expressed as $\pi \rightarrow \pi^*$and $n \rightarrow \pi^*$ transition, the absorption data for the ligand and iis metal complex are given in Table 2. The electronic spectrum of the ligand HL shows two bands at 287.5 and 220.5 nm assigned to n→π*and π→π*respectively, the complex Cu(II) exhibited absorption bands at 217.50 nm which may be assigned to transition π→π*, And the Co(II) complex displayed an electronic spectrum with transitions at 214nm, these bands may be assigned to the transition π→π*.The electronic spectrum of the Fe(III) shows bands at 208 nm assigned to the π→π*transitions.

Table 2. Electronic spectral data of the ligand and its metal complexes 1 to 3 in DMSO

Compound	Absorption bands (nm)	ABS	Assigned transition
HL	220.5 - 287.5	3.4367	$\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$
CuL_2(1)	217.50	3.2439	$\pi \rightarrow \pi^*$
CoL_2(2)	214.00	3.1177	$\pi \rightarrow \pi^*$
FeL_3(3)	208.00	3.0683	$\pi \rightarrow \pi^*$

Infrared spectra studies of the ligand and its metal complexes

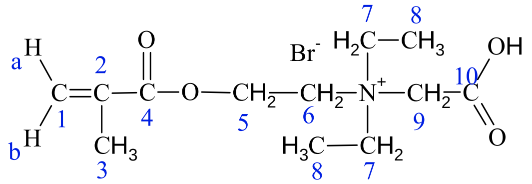
The IR spectra in the (4000–400 cm^{-1}) region provide information regarding the coordination mode in the complexes were analyzed by comparison with the data for the free ligand. The IR data of the ligand and complexes are shown in Table 3. The infrared spectrum of HL showed some characteristic stretching bands at 3431.1, 1745.5, 1635.5, 1164.9 cm^{-1} and assigned to υ(OH), υ(COO)as, υ(C=C)s, υ(C-O-C)s. The υ (O-H) band of the HL appeared at 3431.1 cm^{-1} was absent in the infrared spectra of complexes 1 to 3, indicating the deprotonation and coordination of the carboxylate anions to the metal atom moiety. And formation of M–O bond via deprotonation at 592–675.0 cm^{-1}.

Table 3. The characteristic infrared absorptions of the ligand and its metal complexes

Compound	υ(OH)	υ(COO)as	υ C=C	υ(COO)s	υ (C–O–C)	υ (M-O)
HL	3431.1	1745.5	1635.5	1305.7	1164.9	–
Cu L_2 (1)	–	1741.6	1624.0	1384.8	1168.8	596.0
Co L_2 (2)	–	1745.4	1620.1	1380.9	1168.8	592.0
FeL_3 (3)	–	1743.5	1654.8	1379.0	1163.0	675.0

NMR Analysis studies of the ligand and its metal complexes

The ^1H and ^{13}C NMR chemical shifts of free ligand in CD_3OD at room temperature show the following signals.



^1H NMR (300MHz), δ (ppm):7.568 (1H, OH), 6.104(1Hb, C1), 5.785 (1Ha, C1), 4.635 (2H, C5), 4.184 (2H, C9), 3.346 (2H, C6), 2.982 (2H, C7), 1.805 (3H, C3), 1.564 (3H, C8). ^{13}C NMR chemical shifts are given in the following signals ^{13}C-NMR (300MHz), δ (ppm): 165.032 (C4), 164.591(C10), 134.062(C2), 124.707 (C1), 59.241(C6), 57.632(C5), 48.838 (C9), 46.972(C7), 15.239(C3), 6.492(C8).

In ^{13}C NMR spectra of free ligand C9, C10 of the carboxymethyl moieties were observed in 48.838 and 164.591 ppm respectively, indicated the formation of the ligand. The ^1H NMR spectra of complexes 1 to 3 gave an additional support for the formation of the complexation. The spectra of ligand, HL showed a sharp peaks, δ(OH) at 7.568 ppm which was absent in the spectra of the complexes 1 to 3 and indicated the deprotonation and complexation of carboxylate anions to metal ions. On the basis of the preceding discussion, the structure of the ligand and its metal complexes may be suggested as follows, the proposed structures are presented in Figures 1- 4.

Antifungal activities tests

The antifungal activities of the synthesized ligand HL and his metal complexes were studied in different concentrations (50, 100, 250 and 500 ppm) against three phytopathogenic fungal strains namely *Fusarium oxysporum, Fusarium commune* and *Fusarium rodelens.* The antifungal activity was determined by the radial growth method[26]. In this technique, sterilized hot PDA nutrient medium (composition: potato (200 g), dextrose (20 g), agar (15 g) and distilled water 1000 mL) and 4 mm diameter hole punch were used, on the PDA. After solidification of media, respective fungal spore suspensions were transferred to petri plates. Each test compound was dissolved in water and then diluted at the desired concentration. The fungal cultures were incubated at 37 °C for 4 days. Finally the zones of inhibition were carefully measured. The antifungal activity data are listed in Table 4.

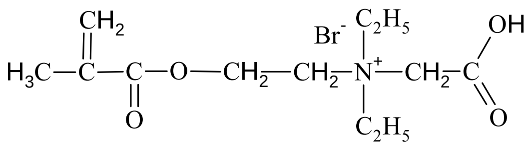


Figure 1. Structure of the ligands

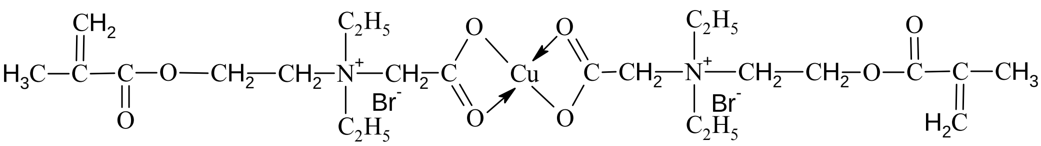


Figure 2. Proposed structure metal complexes of CuL_2

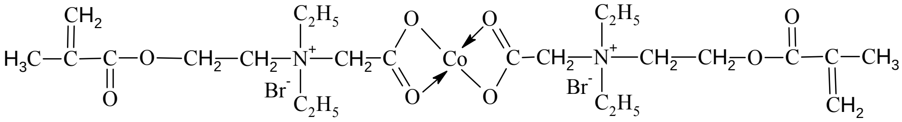


Figure 3. Proposed structure metal complexes of CoL_2

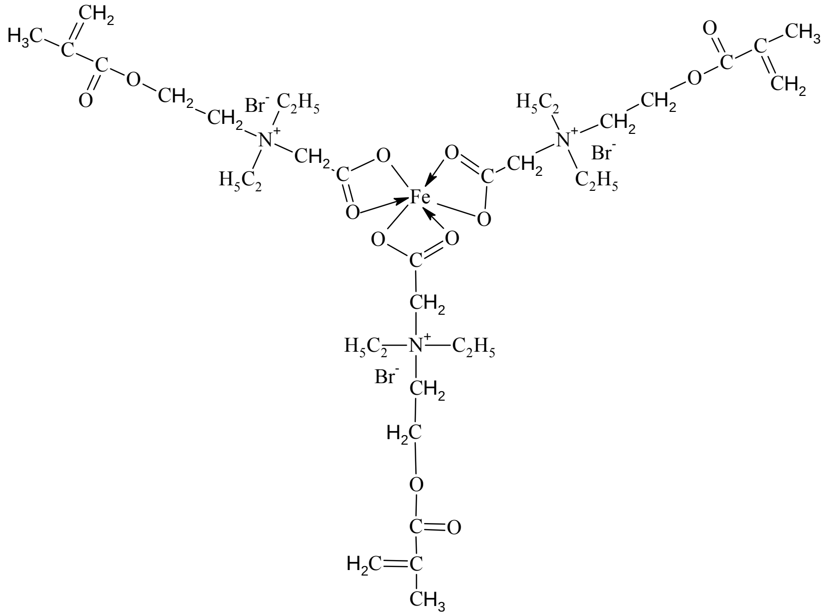


Figure 4. Proposed structure metal complexes of FeL_3

Table 4. Preliminary *in vitro* antifungal activity of the ligand and its metal complexes

	Inhibition Zone %											
Compounds	*Fusarium oxysporum*				*Fusarium commune*				*Fusarium rodelens*			
concentration in ppm	50	100	250	500	50	100	250	500	50	100	250	500
HL	9.52	19.42	22.47	46.6	0	0	0	7.64	0	0	2.70	3.18
Co L_2	0.54	22.54	24	26.36	0	0	0	7.05	0	0	0	0
Cu L_2	16.36	19.45	22.36	32.72	0	3.88	10.47	23.52	0	0	0	9.64
Fe L_3	39.41	44.58	65.29	71.05	0	8	21.05	38.11	0	0	14.58	22.35

As indicated in Table 4, at the concentration of 500 ppm, all of the tested compounds exhibited good inhibitory effects against *Fusarium oxysporum.* The Cu(II) and Co(II) complex showed moderate inhibition with *Fusarium commune* at the concentration of 500 ppm, the ligand and Cu(II), Co(II) complex showed a weak inhibition against *Fusarium rodelens.* The Fe(III) complex showed higher activities against all the tested strains.

Conclusion

In summary, we have described the synthesis of the ligand HL and his metal complexes, IR, UV-Visible, NMR spectral techniques were used to confirm their formation. The synthesized compounds showed promising antifungal potential against the phytopathogenic test fungi at high concentrations.

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