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Research Article

A novel bonding of 6,7-dimethylquinoxalalitenine-2,3-dione, DMQX, to two molybdenum (0) metal centers: Synthesis, characterization, biological activity studies of $[(bpy)_2Mo(\mu_2\text{-}\kappa^2\text{:}\eta^6\text{-DMQX})Mo(CO)_3]$ complex.

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Abstract

In the present study a complex of the general formula $Mo_2(bpy)_2(DMQX)(CO)_3$, (where DMQX and bpy are 6,7-dimethylquinoxaline- 2,3-dione and 2,2`- bipyridine), was synthesized in two steps starting with the reaction of $Mo(CO)_6$ with bpy then followed by the addition of DMQX ligand. Initial characterization based on the elemental and mass analysis has suggested three possible structures (1–3)(scheme 1). In the three possible structures the DMQX ligand bonded to two Mo(0) metal centers; to one Mo metal through its C=O functional groups and the other through the aromatic ring forming η^6-arene type. In structure 1 the DMQX ligands bonded to $(bpy)_2Mo$ and $Mo(CO)_3$ moieties, whereas in the other structures the DMQX ligands bonded to Mo(bpy)(CO) and cis-$(bpy)(CO)_2Mo$ (2) or trans-$(bpy)(CO)_2Mo$ (3) moieties. The IR studies were useful in assigning the coordination modes of the ligands especially in the carbonyl region of the spectrum (Fig 3.2). ^1H NMR studies in DMSO-d_6 displayed typical patterns corresponding to cis-$(bpy)_2M$ moiety (Fig 3.3). The electronic absorption spectrum of the complex revealed two bands assignable to $Mo(d_\pi) \rightarrow$ arene(π^*) and Mo $(d_\pi) \rightarrow$ bpy(π^*) MLCT transitions (Fig 3.5). The thermogravimetric analysis gave more insight into the composition and the thermal stability of the complex(Table 3.1). Although, both DMQX ligand and the molybdenum complex showed antimicrobial activities, the complex inhibition to the studied microorganisms was higher.

Keywords: Quinoxaline, Molybdenum complex, Metal carbonyl, Bipyridine and Biological activity.

Introduction

Quinoxalines are important nitrogen containing heterocyclic compounds. Several quinoxaline derivatives are associated with a wide range of biological activities fungicides, herbicides as well as being important in human health behaving as anticancer, antiviral, and antibacterial, in addition to activity as kinas inhibitors Lindale, etal [1–4]. Although rarely described in nature, synthetic quinoxaline moiety is a part of number of antibiotics such as echinomycin, levomycin and actinomycin. Also quinoxaline ring is part of a number of synthetic antibiotics such as echinomycin, leromycin, and actinomycin, which are known to inhibit the growth of gram-positive bacteria and are also active against various transplantable tumors [5–7]. More than half a

century ago, Dwyer and coworkers [8–12] started to investigate the biological activities of simple coordination complexes such as ruthenium complexes with 2,2`-bipyridine (bpy) and 1,10 phenanthroline (phen) ligands. He discovered that some very hydrophobic complexes displayed bacteriostatic and bactericidal activities and were capable of inhibiting tumor growth [9,10]. Recently, Bregman.etal, Meggers and coworkers [13–15] have developed organoruthenium compounds as protein kinase inhibitors. Their work demonstrated how organometallic compounds of the type (arene)M(N–N)CO can make use of their unique structural opportunities to fill an enzyme active site and inhibit tumor growth. This study aimed at designing a synthetic, this rich area of research work has prompt us to design a complex containing quinoxaline, (bpy)M and (η^6-arene)M moieties. In the present work, we described the synthesis of a novel complex containing 6,7-dimethylquinoxaline-2,3-dione ligand that coordinates to $(bpy)_2Mo$ and $Mo(CO)_3$ moieties through its C=O and aromatic ring, respectively. Spectral, thermal and electronic studies were conducted as well to give more insight into the synthesized complex. Finally, the antimicrobial activities of the DMQX ligand and the $Mo_2(bpy)_2(DMQX)(CO)_3$ complex were studied to provide information about their inhibition activities against bacteria and fungi.

Experimental

Molybdenum hexacarbonyl ($Mo(CO)_6$, 2,2`-bipyridine (bpy), oxalic acid ($C_2H_2O_4.2H_2O$) and 4,5-dimethyl-1,2-phenylenediamine ($C_8H_{12}N_2$) were used as purchased from Sigma–Aldrich Chemical Co. Inc. 6,7-dimethylquinoxaline-2,3-dione (DMQX) ligand was synthesized following the reported procedure [16].

All Solvents used were dried according to standard procedures. Elemental analyses were performed using a Perkin–Elmer 2400 CHN elemental analyzer. Mass Spectra were obtained on a JEOL JMS-AX500 mass spectrometer. Thermogravimetric analysis (TGA) was carried out on a solid sample, under nitrogen atmosphere with a heating rate of 10˚C/min., using Shimadzu DT-50 thermal analyzer. ^{1}H NMR spectra were performed on a JEOL- 270 MHz NMR spectrometer in DMSO-d_6 solvent and TMS was used as an internal reference. Infrared spectra (4000–400 cm^{-1}) were recorded as KBr pellets on a Unicam Mattson 1000 FTIR spectrometer. The electronic absorption spectra were recorded by using Unicam UV2–300 UV–Vis spectrometer. Samples of $2.6x10^{-4}$ mol dm^{-3} concentrations in DMSO were measured against the solvent in the reference cell. Antimicrobial activity of the tested samples for the ligand and the complex was determined using a modified Kirby-Bauer disc diffusion method [17]. A 100 µL of the test bacteria or fungi were grown in 10 mL of fresh media until they reach a count of an approximately 108 cells/mL for bacteria and an approximately 105 cells/mL for fungi. A 100 µL of microbial suspension was spread onto agar plates corresponding to the broth in which they were maintained. Plates inoculated with Gram-positive bacteria (Staphylococcus aureus) and Gram-negative bacteria (Escherichia Coli) were incubated at 35–37 ˚C for 24–48 h. Whereas, filamentous fungus (Aspergillus flavus) and yeast fungus (Candida albicans) were incubated at 25 ˚C for 48 h and 30 ˚C for 24–48 h, respectively. Then the diameters of the inhibition zones were measured in millimeters. Standard discs of tetracycline (antibacterial agent) and Amphotericin (antifungal agent) served as positive control for antimicrobial activity, while filter discs impregnated with 10 µL of DMSO solvent were used as a negative control. Blank paper discs with a diameter of 8.0 mm were impregnated with 10 µL of the tested samples stock solution (0.02 g/mL) and inhibition zone diameters were measured.

Synthesis of $Mo_2(bpy)_2(DMQX)(CO)_3$ complex

The complex was synthesized using weights of 0.083, 0.150 and 0.054 g for bpy, $Mo(CO)_6$ and DMQX respectively. The reaction time was 22 hours and brown solid of the product was obtained. Crystallization of the product by a slow diffusion of a concentrated DMF solution into THF solvent has resulted in brown powder. The brown solids were deride under vacuum over night and gave 0.152 g of the product (74.1% yield). Anal. Calc. for

$C_{33}H_{26}Mo_2N_6O_5$ (Mr = 778.48): C, 50.91; H, 3.37; N, 10.80. Found: C, 48.76; H, 3.39; N, 11.03%.

Results and Discussion

Thermal reaction of $Mo(CO)_6$ with 2,2`-bipyridine followed by addition of DMQX ligand has resulted in a dinuclear molybdenum complex. Initial characterization of the complex based on the elemental analysis data has indicated the presence of a complex with the general formula; $Mo_2(bpy)_2(DMQX)(CO)_3$.

The mass spectrum of the dinuclear molybdenum complex, shown in **Figure 3.1**, is used to assign the composition of the complex. The spectrum showed parent peak due to molecular ions $[M-H]^+$ at 777.47. Other peaks corresponding to successive removal of the three CO ligands were found at 749.47, 721.46 and 693.46 m/z. Peaks corresponding to successive removal of the two bipyridine ligands were observed at 662.29 and 466.11. A peak corresponding to Mo(DMQX)Mo fragment was observed at 381.33 in the spectrum. In addition, the spectrum indicated the presence of three CO groups and two bpy ligands which were bonded to the Mo metal centers.

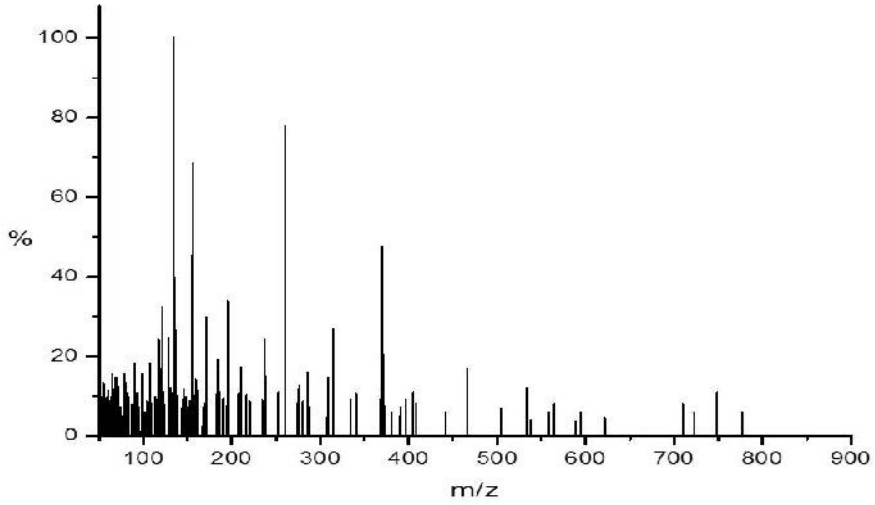
The IR spectrum of the $Mo_2(bpy)_2(DMQX)(CO)_3$ complex is shown in **Figure 3.2**. The spectrum pattern was similar to that of the corresponding dinuclear molybdenum complex of DMQX. The spectrum displayed vibrational bands characteristic of the coordinated bpy ligands at 1607 cm^{-1} (νC=N) and at 769 and 741 cm^{-1} due to the out-of-plane C-H stretches. The revealed two absorption bands in carbonyl region of the spectrum at 1874.2 and 1819.1 cm^{-1}. Vibrations characteristic of the C-H stretches of the phenyl ring and methyl groups were also observed. (**Fig. 3.2)**. Finally, the IR spectroscopy was useful in assigning the coordination modes of the DMQX ligand to Mo metal centers. In contrast, the stretching vibrations corresponding to the aromatic C–H group have shifted to higher frequencies at 3105 and 3081 cm^{-1}.

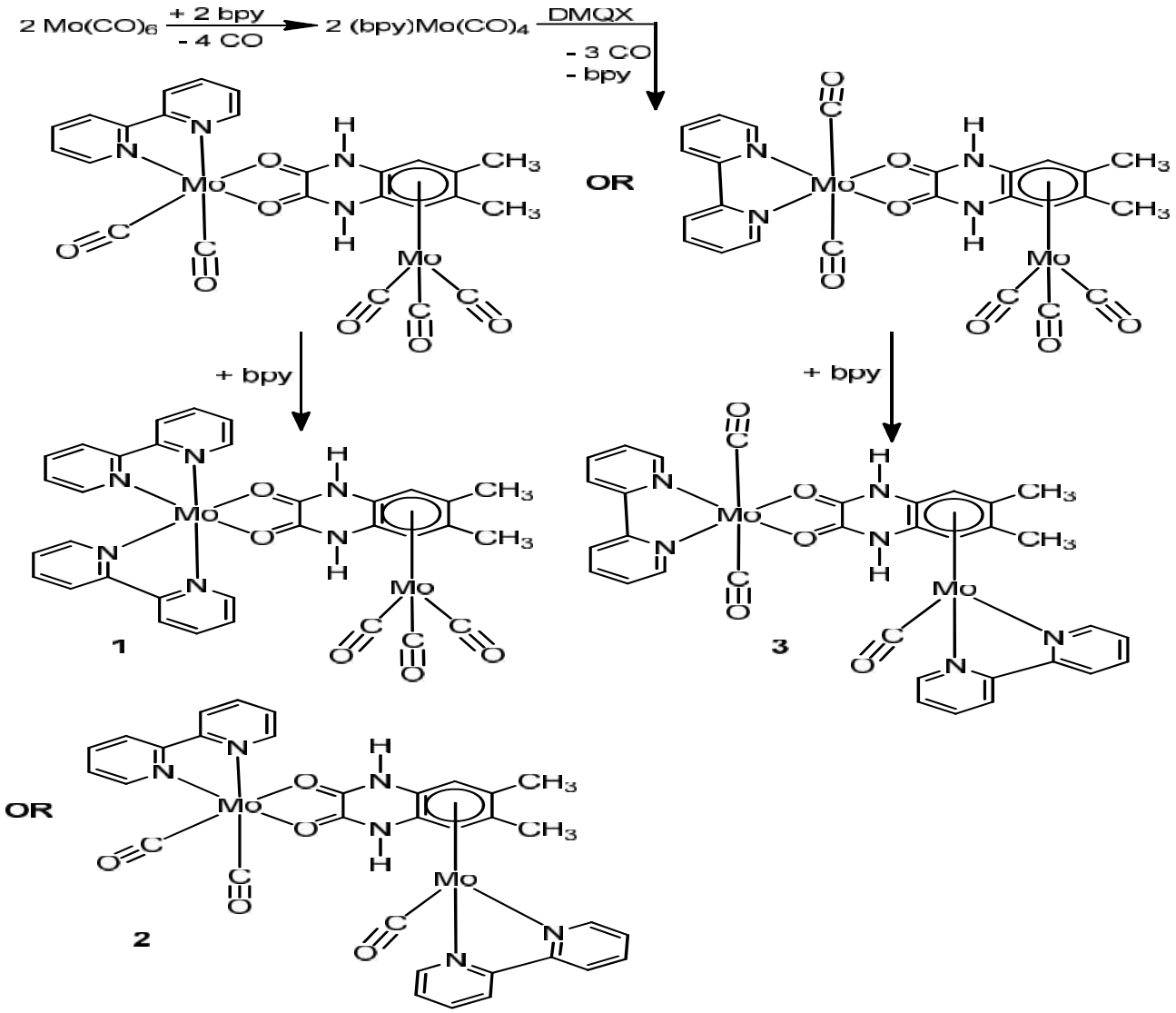
The ^{1}HNMR spectrum for the $Mo_2(bpy)_2(DMQX)(CO)_3$ complex shown in (**Fig.3.3**) was very useful in assigning the coordination environments of the bipyridine ligands. Only seven chemical shifts were observed and might be attributable to equivalence of the 3,3` protons in the bipyridine ligand [18, 19]. The chemical shifts for the bipyridine protons were observed at 7.47 (d, 2H), 7.65 (t, 2H), 7.95 (t, 2H), 8.19 (t, 2H), 8.40 (d, 2H), 8.63–8.70 (m, 4H), 8.99 (d, 2H) ppm. On the other hand, the signal observed at 6.60 ppm (s, 2H) which was assigned to arene protons has shifted by 0.05 ppm down field compared with the free ligand. In addition, the methyl protons were found in the 2.4-3.0 ppm region of the NMR spectrum.

The data for thermal analysis (TGA), carried out on a solid sample of the $Mo_2(bpy)_2(DMQX)(CO)_3$ complex in the temperature range 20–1000 °C at heating rate of 10 °C/min. under nitrogen atmosphere, are compiled in (**Table 3.1)** and are characterized by five decomposition steps (**Fig.3.4**). The first step shows slow decomposition up to 164 °C with a net weight loss of 11.41% which is most probably due to loss of the three CO molecules and 2H atoms. This is followed by gradual decomposition of the two bipyridine ligands in three steps. One molecule of the bipyridine ligands was decomposed in the temperature range of 173-299 ^oC and half molecule in the 299-426 ^oC temperature range. In the range 426-625 ^oC, the residual of the bpy molecule decomposed and the DMQX ligand started to decompose. The thermal decomposition of the DMQX ligand was found to take place in two steps, in the temperature range 426-625 and 625-800 °C. The remaining residue was found 23.93% which is best ascribed to two Mo metals.

The electronic absorption spectrum of the $Mo_2(bpy)_2(DMQX)(CO)_3$ is expected to display with number of metal-to-ligand charge transfer transitions of the type $Mo(d\pi) \rightarrow$ arene(π^*) and $Mo(d\pi) \rightarrow bpy(\pi^*)$. These bands were observed respectively at 370 (5965) and 515 nm (3158 M^{-1} cm^{-1}) (**Fig. 3.5**). Although, the electronic absorption bands observed for the $Mo_2(bpy)_2(DMQX)(CO)_3$ complex. They showed hypthochromic shift of the band corresponding to the $Mo(d\pi) \rightarrow$ arene(π^*) transition by 17 nm. the band due to $Mo(d\pi) \rightarrow bpy(\pi^*)$ has shifted by 25 nm lower energy region. Interestingly, the electronic spectrum of the Mo2(bpy)2(DMQX)(CO)3 complex revealed a band at 311 nm (8509 $M^{-1}cm^{-1}$) which can be ascribed to the $Mo(d\pi) \rightarrow CO(\pi^*)$ MLCT transition . The free ligand

Fig.3.1. The mass spectrum of $Mo_2(bpy)_2(DMQX)(CO)_3$ complex





Scheme 1. Suggested structures for the $Mo_2(bpy)_2(DMQX)(CO)_3$ complex.

Fig.3.3. The ^{1}HNMR spectrum of $Mo_2(bpy)_2(DMQX)(CO)_3$ complex d^6-DMSO

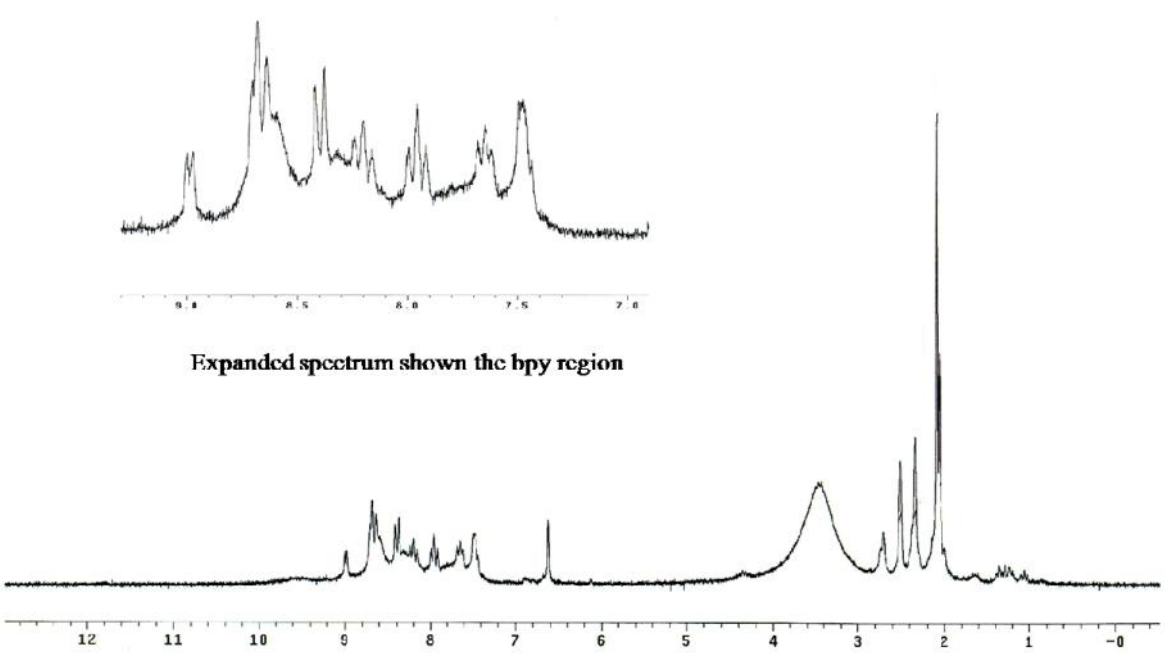


Table 3.1. Thermal analysis data for $Mo_2(bpy)_2(DMQX)(CO)_3$ complex

Decomposition Steps, °C	% weight loss	Molecular weight (found)	Molecular weight (Calced.)	Assigned species
52-173	11.017	85.764	86.046	3CO + H2
173-299	19.744	153.702	154.168	1bpy – H2
299-426	10.17	79.171	78.092	1/2 bpy
426-625	19.492	151.740	152.168	(1/2 bpy) + C6H2 (DMQX
625-973	15.644	121.785	116.124	C4H8N2O2 (remaining of DMQX)

Fig. I.4. The TGA thermogram of $Mo_2(bpy)_2(DMQX)(CO)_3$ complex

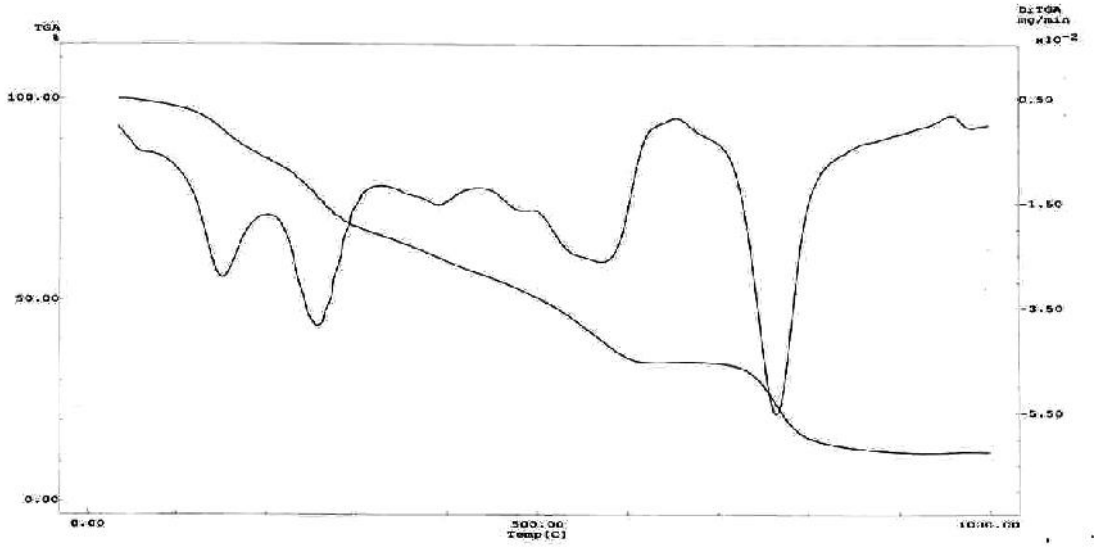


Fig. 3.5. The UV-vis spectrum of $Mo_2(bpy)_2(DMQX)(CO)_3$ complex in DMSO.

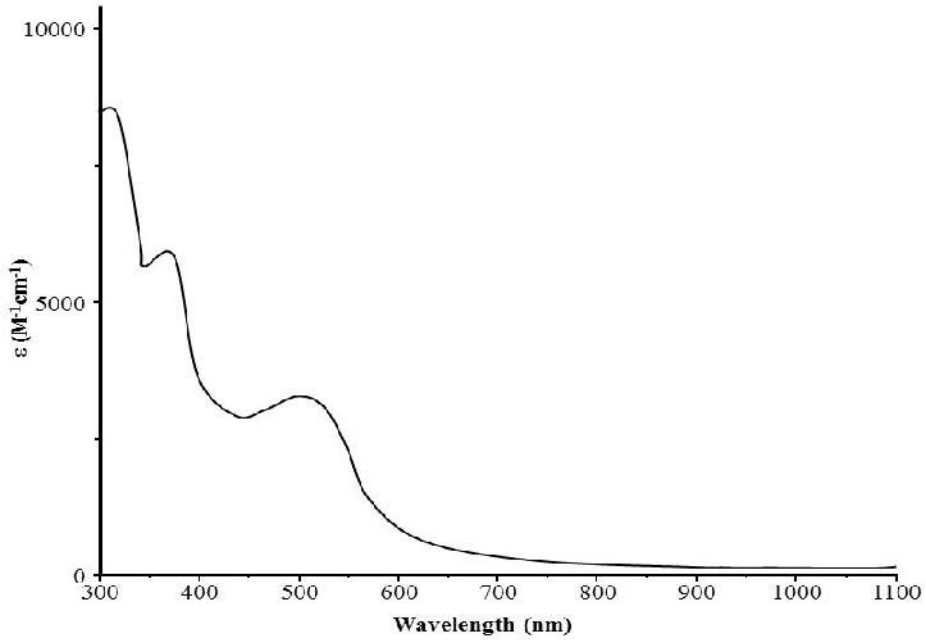


Table.3.2. Antimicorbial Activities of $Mo(bpy)_2(DMQX)(CO)_3$ complex

Sample	Inhibition zone diameter (mm/mg sample)			
	Escherichia Coli **(gram-negative)**	***Staphylococcus aureus*** **(gram-positive)**	***Aspergillus flavus***	***Candida albicans***
DMSO[a]	0.0	0.0	0.0	0.0
Tetracycline [b]	31	33	-	-
Amphotericin B[c]	-	-	17	21
DMQX	21	19	0.0	14
$Mo_2(bpy)_2(DMQX)(CO)_3$	17	15	15	15

[a] DMSO solvent was used as negative control.
[b] Standard antibacterial agent.
[c] Standard antifungal agent.

revealed two absorption at 350 and 445 nm attributable to the intraligand, π–π* and n-π* transitions, respectively.

Antimicorbial Activities of $Mo(bpy)_2(DMQX)(CO)_3$ complex

The antimicrobial activity IES of the DMQX ligand and their molybdenum complexes were tested by the disc diffusion method against two types of pathogenic bacteria, namely, S. aureus and E. coli by using DMSO as a solvent and tetracycline as a control. Also, the antifungal activity for the free ligands and the molybdenum complexes were tested against A. flavus and C. albicans fungi using Amphotericin as a control. The inhibition zone diameters for the antimicrobial activity were measured and the results are in line with findings of gamepads, et al [20]. Has synthesized some novel

condensed bridgehead nitrogen heterocyclic of quinoxalines. They demonstrated the antimicrobial activities of these compounds against the gram-positive bacteria Staphylococcus aureus and the gram-negative Escherichia coli they used DMSO as a solvent and Nalidixic acid as a control presented in **Table 3.2**. On the other hand, the biological activity studies of $Mo_2(bpy)_2(DMQX)(CO)_3$ complex showed comparable anti-bacterial activities to those of the DMQX ligand. In contrast, the complex showed higher antifungal inhibitory activities compared with those of the free DMQX ligand.

In conclusion, the data of the biological activity studies of both complexes indicated higher antimicrobial inhibitory activities (bacterial and fungual) for $Mo_2(bpy)_2(DMQX)(CO)_3$ complex showed only higher antifungal inhibitory activities compared with that of the free DMQX ligand.

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