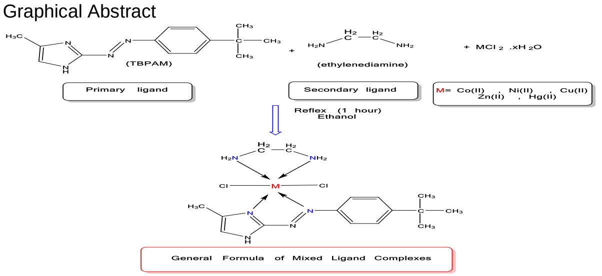
DOI: https://doi.org/10.53350/pjmhs22166579

ORIGINAL ARTICLE

Synthesis, Chemical Characterization, and Bacterial Inhibition Studying of New Mixed Ligand Complexes of 4-Methylimidazoleazo Ligand, and Ethylenediamine with Some Divalent Metal Ions

ISRAA N. WITWIT[1], HAWRAA M.FARHAN[2], HUSHAM M.MUBARK[3]
[1,2,3]University of Kufa, Factually of Science, Dept. of Chemistry, Najaf, Iraq
Corresponding author: Israa N. Witwit, Email: israa.witwit@uokufa.edu.iq

Graphical Abstract



ABSTRACT

New synthesized series of mixed ligand complex prepared for Co (II), Ni (II), Cu (II), Cd (II), and Hg (II) ions, with azo compound derived from 4-methylimidazole as a primary ligand (TBPAM) , and ethylene diamine as a secondary ligand. Mass , [1]HNMR, C.H.N, Uv-Vis, FT-IR, Atomic Absorption, Molar Conductivity, and Magnetic Susceptibility techniques were used to characterize the complexes, the results were indicated the octahedral geometry with a general formula [M(TBPAM)(en) Cl_2] for all complexes, where primary and secondary ligands behaved as a bidentate, finally a noticeable bacterial inhibition of the complexes and primary ligand at a concentration (100mg/ml) was appeared against complexes against Klebsiella, P.aeruginosa, and S. aureus bacteria

Keywords: Mixed ligand; Complexes, Biological investigation; imidazole; ethylenediamine.

INTRODUCTION

In the recent years, the researchers interesting focus on preparation and characterization of mix ligand complexes with different transition metal ions in different oxidation state which have more than one coordination position and have multiple types of ligands [1,2], which effects on the stability of the prepared compounds and exploiting their properties in various applications especially the antibacterial activity [3–6].

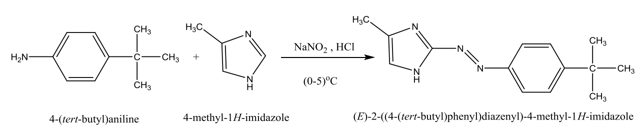
Azo imidazole compounds are a common type of ligands that exhibit multiple coordination behaviours depending on the location and type of substitution groups [7,8]. It is an efficient π - acid system, thus these organic compounds are employed as ligands to build stable complexes with low oxidation states of metal ions [9].

This study aimed to synthesis and characterize new mixed ligand complexes for a series of divalent transition ions using a primary azo imidazole ligand, and ethylene diamine as a secondary ligand, then investigation their bacterial inhibition against Klebsiella, P.aeruginosa , and S. aureus bacteria.

Chemicals and Instruments: All of the chemical compounds which used in this study were provided by Himedia, Thomas Baker, and Merck companies with high purity.

Mass spectrum recorded using mass analyzer model AB SCIEX (3200) , the electronic spectra carried out by Shimadzu Uv-1650 spectrophotometer, and FT-IR spectra performed by Shimadzu FT-IR8400s in the region between (400-4000) cm-1 , The element analysis was measured by Costech ECS Elemental 4010 , and the values of Molar conductivity measured by 720(WTW) , 1HNMR spectra in the DMSO-d6 solvent carried out by Bruker Avance-111 300 MHz NMR.

Preparation of Primary ligand (TBPAM): (TBPAM) Primary ligand was prepared by coupling reaction between diazonium salt (4-tetra-butyl aniline) and alcoholic solution of 4-methyl imidazole in the ice bath at a temperature between (0-5) ºC [10] the ligand was filtered and dried after neutralized the solution with diluted HCl and recrystallized from ethanol as shown in Scheme (1):



Scheme 1: Reaction path for preparation of (TBPAM) Primary ligand.

Table 1: Some of physico-chemical properties of mixed ligand complexes of (TBPAM) and (en)

Compound Molecular Formula)	M.wt.	M.P.	Color	% pro.	Element analysis Calculated Found			
					C	H	N	M
[Co (TBPAM) (en) Cl_2] $C_{16}H_{26}Cl_2N_6$ Co	432.26	142-144	Brown	78	44.46 44.47	6.06 6.04	19.44 20.26	13.63 13.67
[Ni (TBPAM) (en) Cl_2] $C_{16}H_{26}Cl_2N_6$ Ni	432.02	138-140	Brown	75	44.48 44.50	6.07 6.09	19.45 19.42	13.59 13.60
[Cu (TBPAM) (en) Cl_2] $C_{16}H_{26}Cl_2N_6$ Cu	436.87	150-152	Brown	82	43.99 44.01	6.00 5.98	19.24 19.27	14.55 14.54
[Zn (TBPAM) (en) Cl_2] $C_{16}H_{26}Cl_2N_6$ Zn	438.71	147-150	Red	76	43.81 43.85	5.97 5.93	19.16 19.14	14.90 14.93
[Hg (TBPAM) (en) Cl_2] $C_{16}H_{26}Cl_2N_6$ Hg	573.92	163-165	Deep red	84	33.49 33.51	4.57 4.55	14.64 14.63	34.95 -----

Preparation of Solid mix ligand complexes: The solid complexes were prepared at mole ratio (1:1:1) [M: (TBPAM): (en)] by mixing (1mmole, 0.242 gm) of (TBPAM) ligand with (1 mmole, 0.0631 ml) of ethylene diamine, and (1 mmole) of each metal ion chloride salts. The mixture was dissolved in (20 ml) of ethanol, and reflexed for (60) min. with continuous following up of the reaction by (TLC), the precipitates were filtered after cooling, dried, and recrystallized from ethanol, and their physicochemical properties summarized in the table 1:

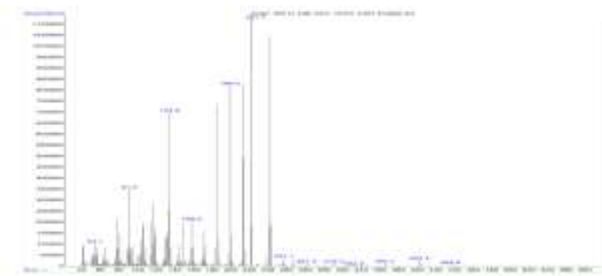
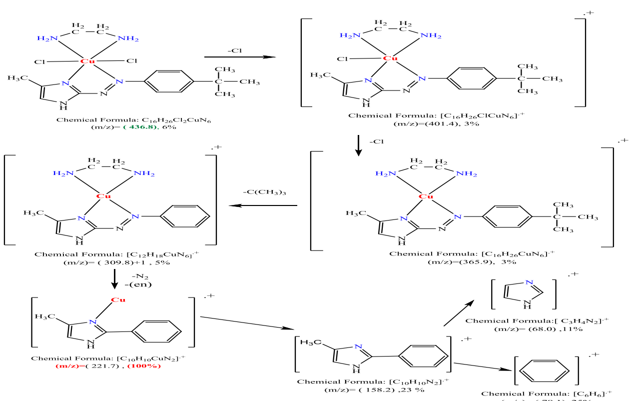


Figure 1: Mass Spectra of [Cu (TBPAM) (en) Cl2] complex



Scheme 2: Suggested Mass fragmentation path of [Cu (TBPAM) (en) Cl_2] complex

Mass spectrum of [Cu (TBPAM) (en) Cl_2] complex showed a fragment at (m/z) = (436.8) which was supported the molecular formula for this complex, The suggested fragmentation path was started by losing chloride ions at (m/z)= (401.4) , and (365.9) , the Base peak was appeared after losing (N_2) , and ethylene diamine molecules from $[C_{12}H_{18}CuN_6]^{+\cdot}$ fragment at (m/z) = 100%, as showed in the figure (1), and scheme (2).

^{1}HNMR spectrum of [Hg (TBPAM) (en) Cl_2] complex in DMSO-d6 solvent showed a signal (s ,1H,-NH-) of imidazole ring at (12.68) ppm [11], while the doublet-doublet signals between (7.53-7.77) ppm refers to (m, Ar-H) of the aromatic ring [12,13], also the signals for the protons of a secondary ligand ethylene diamine (en) (m,4H ,-CH_2-) appeared at (2-49-2.89) ppm , as well the protons for the methyl groups of a primary ligand (TBPAM) (s,3H,-C(imidazole)-CH_3) , and (s,9H, -$C(CH_3)_3$) exhibited a signals at (2.26) , and (1.34) ppm respectively , the proton of imidazole ring (H-C=C-) appear at (2.09) ppm, finally the signal of terminal protons of ethylene diamine(s,2H,-NH_2) manifested at (7.05) ppm as shown in figures (2) and (3).

Figure 2: ^{1}HNMR spectrum of (TBPAM) primary ligand in DMSO-d6 solvent

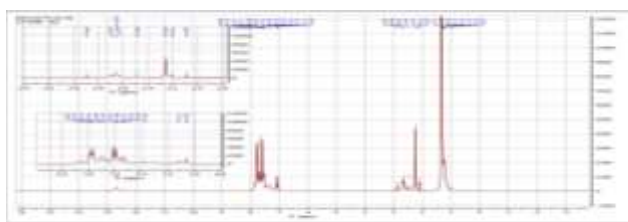


Figure 3: 1HNMR spectrum of [Hg (TBPAM) (en) Cl_2] complex in DMSO-d6 solvent

Uv-Vis. spectrum of primary (TBPAM) ligand exhibited two peaks at (214) and (268) nm due to (π–π*) of aromatic rings, There is no noticeable changes of their positions in the complexes spectra, but there is a red shift of (n-π*), and (ILCT) transitions at (368, 380) nm respectively in the complexes spectra due to the participation of this primary ligand in the coordination, as explained in table 2.

Table 2: Types of electronic transitions, values of (μ.eff.), Conductivity measurements, and type of the geometry of Primary (TBPAM) ligand and it's mixed ligand complexes.

Chemical Structure of the compound	Value of λ max (nm)	Type of transition	Values of Molar Conductivity S.Cm2.mole		μ.eff. (B.M.)	Proposed Geometry
			Ethanol	DMF		
(TBPAM)	214, 268 368 380	π–π* n-π* ILCT	-------	-------	------	-------
[Co (TBPAM) (en) Cl_2]	200, 277 375 462	π–π* ILCT MLCT	14.3	12.8	4.73	Octahedral
[Ni (TBPAM) (en) Cl_2]	202, 273 376 468	π–π* ILCT MLCT	14.0	12.3	2.81	Octahedral
[Cu (TBPAM) (en) Cl_2]	206, 278 384 503	π–π* ILCT MLCT	16.4	13.5	1.72	Distorted Octahedral
[Zn (TBPAM) (en) Cl_2]	208, 278 387 518	π–π* ILCT MLCT	15.7	12.6	Dia	Octahedral
[Hg (TBPAM) (en) Cl_2]	208, 278 392 524	π–π* ILCT MLCT	16.2	13.3	Dia	Octahedral

FT-IR spectra measurements of purified solid complexes revealed a small significant changes in position and intensity for v(N-H) of imidazole ring at (3420) cm^{-} in the primary (TBPAM) ligand , and v(N-H) of amine group in the secondary (en) ligand at (3441) ,and (3385) cm^{-} , while there was noticeable shifting to the higher frequencies of v(C=N) and v(C-N) which belongs to the imidazole ring in (TBPAM) ligand at (1577) cm^{-} and (1374) cm^{-} [14,15] due to the participation of (N3) atom in the coordination , while the frequencies of v(-N=N-) at (1428) cm^{-} [16,17] has shifted to the higher values as a result of coordination through one nitrogen atom of azo functional group, also there was observable shifting of v(C-N) of C-C-NH_2 and v(C-C-NH_2) for ethylenediamine at (1403) cm^{-}, and (1567) cm^{-} respectively [18] to the lower frequencies as a result of coordination of this secondary ligand through nitrogen atom of terminal (-NH_2) group, the complexes spectra also distinct new peaks between (420 – 437) cm^{-} due to v(M-N) [19–21] frequencies bond after the coordination between both of primary and secondary ligands , as shown in the table (3), and figures (4-6).

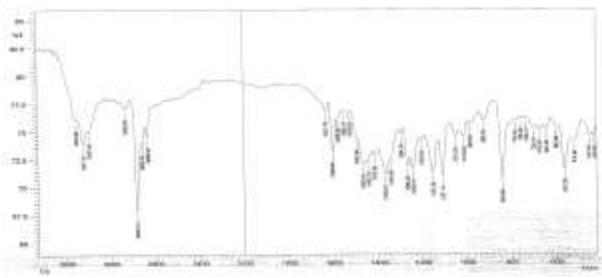


Figure 4: FT-IR spectrum of [Co (TBPAM) (en) Cl_2] complex

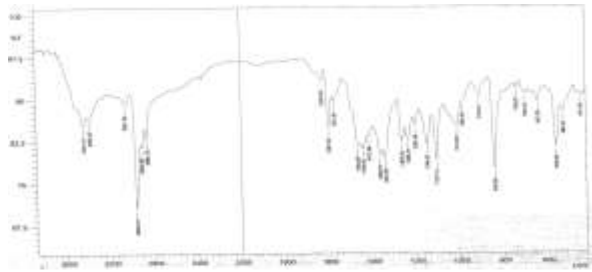


Figure 5: FT-IR spectrum of [Cu (TBPAM) (en) Cl_2] complex

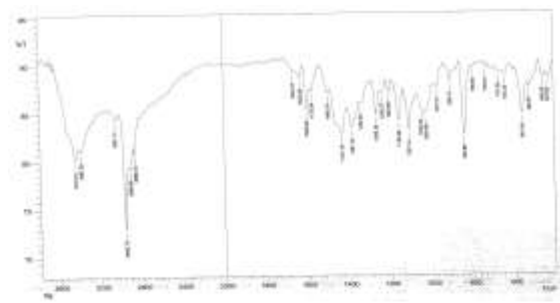


Figure 6: FT-IR spectrum of [Hg (TBPAM) (en) Cl_2] complex

Table 3: FT-IR frequency values (cm-1) for (TBPAM), and (en) ligands and their mixed ligand complexes

Frequencies	TBPAM	(en)	Co(II) Complex	Ni(II) Complex	Cu(II) Complex	Zn(II) Complex	Hg(II) Complex
v (C=N) of imidazole	1577 m	----	1598 m	1595 m	1597 m	1594 m	1590 m
v (C-C-N)	----	1567 m	1492 m	1465m	1463m	1493m	1469m
v (N=N)	1428 m	----	1442 m	1442m	1440 m	1438 m	1431m
v (C-N) of C-C-NH_2	----	1403 m	1363 m	1363 m	1360 m	1367 m	1381 m
v (M-N)	----	----	432 w	420 w	447 w	428w	437 w

m : medium , and w:weak

The calculated percentage values of (C.H.N) elements and metal ions in the complexes were found to be in good agreement with their measured values, confirming the chemical formulae of the synthesized compounds, and their purity as shown in table 1. The non-ionic character of all complexes has been clarified by the values of Molar Conductivity in both Ethanol and (DMF) solvents, as well as the absence of AgCl precipitate after adding $AgNO_3$ drops to the complexes solutions, indicating that chloride ions coordinated with each metal central ion inside the coordination sphere.

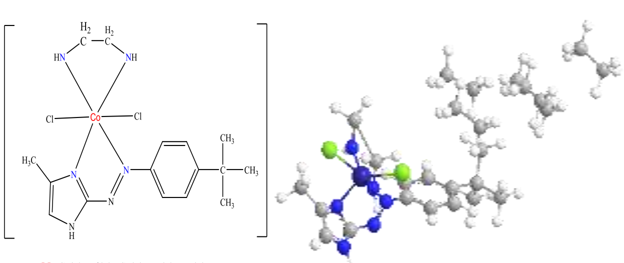

M= Co(II) , Ni(II) , Cu(II) , Zn(II) , Hg(II)

Figure 7: Proposed Structure of [M(TBPAM) (en)Cl_2] complexes

Bacterial inhibition of the primary ligand and it's prepared complexes were studied by using a concentration (100mg/ml) for each compound against three types of resistance isolated bacteria, Klebsiella and P. aeruginosa as gram negative, and S. aureus as Gram Positive. The results are confirmed that complexes have a good inhibition ability comparing the free ligand due to their affinity to break DNA bands of bacteria cells by electrostatic connections, on the other hand the activity towards gram negative bacteria is rather than the positive due to the type of central metal ion in the complexes, substituted groups, and their possibility to access through cell walls , the results were explained in figures (8-11) .


Figure 8: Inhibition effect of (TBPAM) and it's mixed ligand complexes towards S. aureus bacteria

Figure 9: Inhibition effect of (TBPAM) and it's mixed ligand complexes towards Klebsiella Bacteria

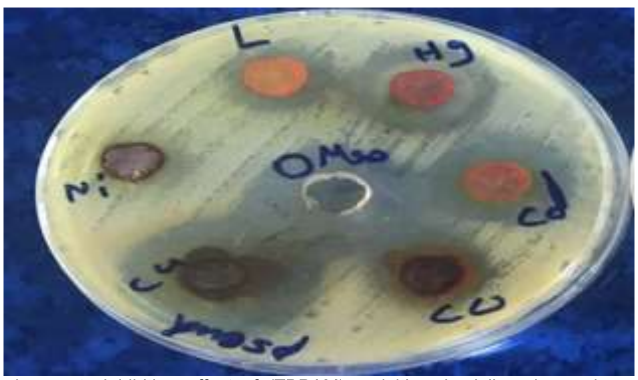


Figure 10: Inhibition effect of (TBPAM) and it's mixed ligand complexes towards P. aeruginosa bacteria

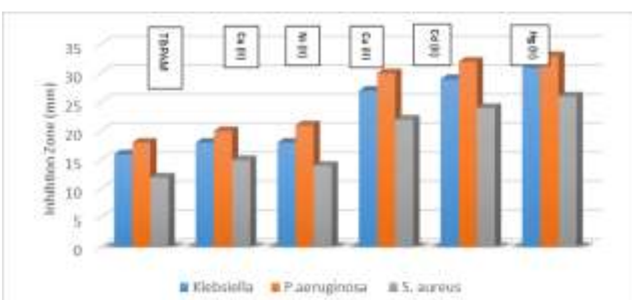


Figure 11: Inhibition zone (mm) of (TBPAM) and it's mixed ligand complexes towards Klebsiella , P.aeruginosa , and S. aureus

CONCLUSION

New mixed ligand complexes for (TBPAM) and (en) ligands were prepared with cobalt, nickel, copper, zinc, and mercury divalent ions. Both ligands behaved as bidentate through (N3) of the imidazole ring and one nitrogen atom of the azo group of the (TBPAM) ligand and through two nitrogen atoms of the terminal (-NH_2) groups of (en), formatting two five-member rings between these ligands and each metal ion.

REFERENCES

1 Singh N and Kumar A 2022 Mixed ligand complexes of nickel (ii): Synthesis and bio medicinal studies, Pharma Innovation 11 (3) 768-771

2 Obeten A U, Eno E A, Offiong O E and Akakuru O U 2022 Synthesis and characterization of copper (II) mixed ligand complexes with 3-proply-5-mercapto-1, 2, 4-triazole and 1, 10-phenanthroline World Sci News 166(1) 43–53

3 Yahya W I, Mgheed T H and Kadhium A J 2022 Preparation, Characterization of Some Metal Complexes of New Mixed Ligands Derived from 5-Methyl Imidazole and Study the Biological Activity of Palladium (II) Complex as Anticance NeuroQuantology 20(1) 71-83

4 Kudrat-E-Zahan M and Haque M M 2019 Synthesis, characterization and biological activity studies of mixed ligand complexes with schiff base and 2, 2'-Bipyridine Int J Appl 6(1) 1-7

5 Mahalakshmi R and Raman N 2016 A therapeutic journey of mixed ligand complexes containing 1, 10-phenanthroline derivatives: a review Chemistry (Easton) 16 1–6

6 Idoko O, Abubakar S, Emmanuel S A and Thomas S A 2013 Synthesis, Characterisation and Antimicrobial Activity of Mixed Ligand Complexes of Ni (II) and Co (II) with Furfuralurea as the Primary Ligand World Journal of Applied Chemistry 1(1) 22-25

7 Slassi S, El-Ghayoury A, Aarjane M, Yamni K and Amine A 2020 New copper (II) and zinc (II) complexes based on azo Schiff base ligand: Synthesis, crystal structure, photoisomerization study and antibacterial activity Appl Organomet Chem 34 e5503 1-10

8 Chhetri A, Chettri S, Rai P, Sinha B and Brahman D 2021 Exploration of inhibitory action of Azo imidazole derivatives against COVID-19 main protease (Mpro): A computational study J Mol Struct 1224 (129178) 1-9

9 Ghali A A and Mashkour D Z 2016 Combined-Cloud Point Extraction and Spectrophotometric Detection of Copper (II) by Using a New Synthesized Ligand J Chem Pharm Res 8(6) 279–87

10 Mubark H M H, Witwit I N and Ali A A M 2020 Synthesis of new azo imidazole ligand and fabricating it's chelate complexes with some metallic ions Journal of Physics: Conference Series (IOP Publishing) 1660(1) 12031

11 Witwit I N and Al-Waili M K 2021 New Azo Ligand Synthesis, Characterization, and Bacterial Inhibition Investigation as a Derivative of 4, 5-diphenylimidazole with Some Transition Metal Ions International Journal of Drug Delivery Technology 11(4) 1251-1257

12 Waheeb A S, Kyhoiesh H A K, Salman A W, Al-Adilee K J and Kadhim M M 2022 Metal complexes of a new azo ligand 2-[2′-(5-nitrothiazolyl) azo]-4-methoxyphenol (NTAMP): Synthesis, spectral characterization, and theoretical calculation Inorganic Chemistry Communications 138(1) 109267

13 Mahmoud W A, Ali A A M and Kareem T A 2015 Preparation and spectral characterization of new azo imidazole ligand 2-[(2-cyano phenyl) Azo]-4, 5-Diphenyl imidazole and its complexes with Co (II), Ni (II), Cu (II), Zn (II), Cd (II) and Hg (II) ions Baghdad Science Journal 12(1) 96-109

14 Babamale H F, Khor B-K, Chear N J-Y, Haque R A and Yam W 2022 The First tetrafluorinated azobenzene-imidazolium ionic conjugates as potential thermotropic liquid crystalline drugs: Self-assembly properties and cytotoxic effects Journal of Molecular Structure 1255(52) 1-9

15 Abdulraheem F S, Al-Khafaji Z S, Hashim K S, Muradov M, Kot P and Shubbar A A 2020 Natural filtration unit for removal of heavy metals from water IOP Conference Series: Materials Science and Engineering vol 888 (IOP Publishing) p 12034

16 Ahmed F, Dewani R, Pervez M K, Mahboob S J and Soomro S A 2016 Non-destructive FT-IR analysis of mono azo dyes Bulgarian Chemical Communications 48(1) 71–7

17 Jawad S A A and Kareem I K 2022 Synthesis, Characterization of New Azo-Schiff Ligand Type N2O2 and Metal Complexes with Di Valance Nickel, Palladium and Tetra Valance Platinum NeuroQuantology 20(1) 62-70

18 Bennett A M A, Foulds G A, Thornton D A and Watkins G M 1990 The infrared spectra of ethylenediamine complexes—II. Tris-, bis-and mono (ethylenediamine) complexes of metal (II) halides Spectrochimica Acta Part A: Molecular Spectroscopy 46(1) 13–22

19 Hameed G F, Wadday F, Farhan M A A and Hussain S A 2021 Synthesis, Spectroscopic characterization and bactericidal valuation of some metal (II) complexes with new Tridentate Heterocyclic Azo Ligand Type (NNO) Donor Egyptian Journal of Chemistry 64(3) 1333–1345

20 Jarad A J 2012 Synthesis and characterization of new azo dye complexes with selected metal ions Al-Nahrain J Sci 15 74–81

21 Cheng L, Deng L, Guo R, Leng Y and Wu J 2022 Synthesis and Characterization of Heteroleptic Bis-Cyclometalated Iridium (III) Complexes Journal of Organometallic Chemistry 972 122375