World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-15, October 2022
ISSN: 2749-3644

SYNTHESIS AND STUDYING BIOLOGICAL ACTIVITY OF TRANSITION METAL COMPLEXES WITH NEW AZO-SCHIFF LIGAND

Safeer Kareem Mizher[1], Fawzi Yahya Waddday[2]
[1]Ministry of Education, The General Directorate of Educational in Najaf Al-Ashraf, Najaf, Iraq Corresponding author email: Kareemsafeer79@gmail.com
[2]Department of Chemistry, Faculty of Science, Kufa University, Al-Najaf-Iraq

Article history:
Received: August 1st 2022
Accepted: September 1st 2022
Published: October 4th 2022

Abstract:
New tetradentate ligand (BHAP)(5-bromopyridin-2-yl)imino)ethyl)-2-hydroxy -5-methyl phenyl)azo)-1-phenyl-2,4-dihydro-3N-pyrazol-3-one was prepard by the reaction of 3-amino-1-phenyl-2-pyrazolin -5-one and 2-hydroxy-5-methylaceto phenone to form azo compound,then this compound react s with 2-amino -5-bromopyridine to required (BHAP)ligand. Series of mononuclear complexes of (BHAP) ligand were prepared with Mn(II), Co(II), Zn(II), Cd(II), Ag(I), Pd(II) ions, which have a general formula $[M(BHAP)ClH_2O].\ nH_2O$ for Mn(II), Co(II), Zn(II), Cd(II), Pd(II), complexes (n=1,2,3...) while the complexes of other ions have ageneral formulas [Ag(BHAP)], and [Pd(BHAP)]Cl .The synthezid ligand and it`s complexes were charaterized by (mass, (^{1}H,^{13}C-NMR), Element analysis, FT-IR, UV-Vis, Molar condictivity, solubility, Magnetic susceptibility, melting point,and (TLC), form the results that obtained from previous measurments tetrahedral geometry of Ag(I) complex, square planer of Pd(II) complexe, and octahedral geometry for the complexes of other ions were proposed. Stability constants of the complexes were calculated at (25)^{0}C by using Mole Ratio method, their data agreed with Irving –Williams series as the following sequence for octahedral divalent metal ions of the first series:Mn(II) < Co(II) < Zn(II). Also the preperd complexes showed high stability with time, and good inhiption activity against two types of pathogenic bacteria (*Staphylococcus aureus*, and *Escherich ia coli*).

Keywords: Azo, Schiff base, Ligand, complexes, Anti-bacterial activity.

INTRODUCTION

Coordination chemistry has recently attracted a lot of attention in chemistry due to its quick advancement in the scientific method of creating and diagnosing coordination complexes. These complexes have a wide range of applications in the sectors of pollution control, industry, and medicine [1, 2]. The most significant organic ligands involved in the creation of many coordination complexes by providing electrons to metallic elements are azo compounds and Schiff bases [3,4]. Because the heterocyclic azo compounds contain electron-donating atoms like oxygen, sulfur, and nitrogen in addition to the azo bridge group (-N=N-), we discover that azo compounds have expanded extensively and obtained applications and uses in the industrial [5], biological, and pharmaceutical fields[6,7].

EXPERIMENTAL SECTION

Instruments, materials and approaches

All of the compounds utilized in the study are distinguished by their high purity and reliable provenance. The following tools were used to perform analytical and physical measurements on the prepared Ligand and its complexes: Using a PH-meter,720, WTW 82362, the acidity function of the prepared solutions was measured. With the use of a tool called a UV-Visible Spectrophotometer, the spectra of the ligand and its metal complexes were scanned to create calibration curves, and the absorption of the solutions was measured at wavelengths between (Shimadzu-UV-1700). The Testscan Shimadzu FTIR 8000 series instrument was used to measure the Ligand's infrared spectrum and the spectra of its complexes. An apparatus was used to determine the ligand's and its complexes' melting points. Stuart Melting point devices, , Using a WTW inolab cond 720 digital conductivity meter, measurements of electrical conductivity for complexes were made at (25oC) for a

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-15, October 2022
ISSN: 2749-3644

10-3 mol.L-1 solution of the materials in dimethyl sulfoxide (DMSO). Mass spectra in the Agilent mass spectrometer 5975 quadropole analyzer have gained on microelemental analysis (C.H.N.) on a Eure EA 3000 Elemental analyzer. A DRX (500-MHz) spectrometer has been used to analyze the 1H and 13C NMR spectra in DMSO and Bruner DRX (500-MHz) systems. Relative to internal Me4Si, chemical changes are expressed in ppm. The Euro Vectro-3000A has been used to implement elemental microanalyses of the ligand and their complexes. The materials and solutions used in the biochemical analysis are sterilized using the Gallen Kamp autoclave. Dishes containing the grown bacteria were incubated using a Memmert Incubator at 854 Schwach. Analytic Jena's (A.A350) atomic absorption spectrophotometer was used to use the atomic absorption technique to detect the metal content of complexes. Through the Gouy method and Johnson Mattey Catalytic system, magnetic susceptibility magnitudes have been lowered below room temperature. Thin Layer Chromatography (TLC): Iodine was used to identify the samples after the TLC was completed on Al coated plates with silica gel (Fluka).

Synthesis of the ligand (BHAP):

The organic ligand was prepared **5-((3-(1-((5-bromopyridin-2yl)imino)ethyl)-2-hydroxyphenyl)diazenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-on**

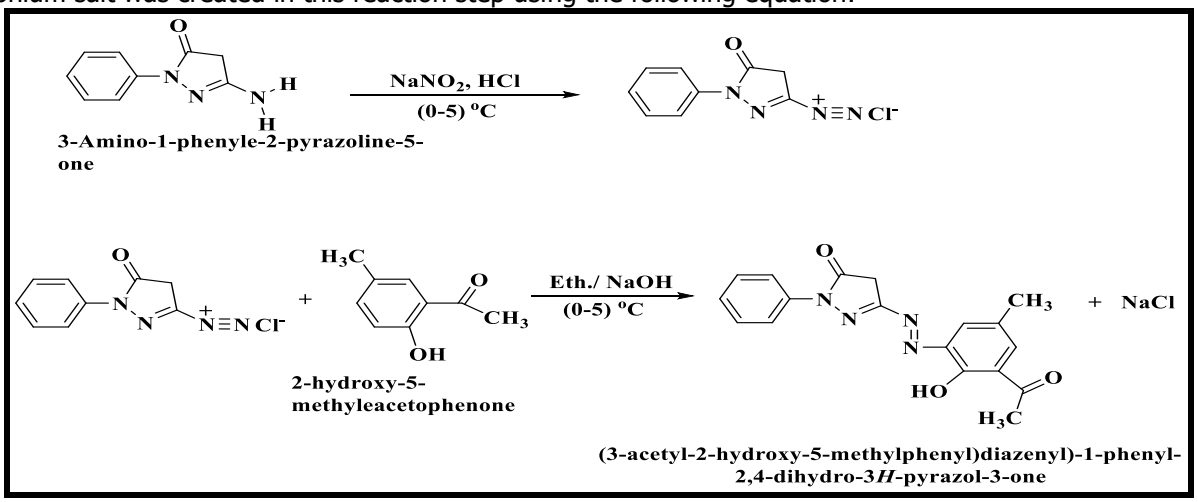
Chemical formula: $C_{22}H_{17}BrN_6O_2$

It is derived from the amine compound 3-Amino -1-phenyl-2-pyrazolin-5-One By a two-stage reaction.

Synthesis of (3-acetyl-2-hydroxy-5-methylphenyl)diazenyl)-1-phenyl-2,4-dihydro -3H-pyrazol-3-one (Azo compound)

According to the general[8] approach, the ligand was created by dissolving (1.751 g, 0.01 mol) 3-amino-1-phenyl-2-pyrazolin-5-one in a solution made up of (3 mL) concentrated hydrochloric acid, (ten) milliliters of ethanol, and ten milliliters of distilled water. To create the dizonium salt solution, the solution combination was cooled to a temperature of 5 °C, at which point 0.69 g of sodium nitrite in a solution of 10 mL of distilled water was dropped into the mixture while being stirred. After 20 minutes, the dizonium solution was gradually added to a basic ethanolic solution of 2-hydroxy-5-methylacetophenone (1.501 g, 0.005 mol) to produce the azo product. Dilute hydrochloric acid, sodium hydroxide, and a solid precipitation were used to neutralize the mixture's dark hue. The solid precipitation was then filtered out and repeatedly rinsed with distilled water. then recrystallized from hot absolute ethanol with a yield of 75% and a melting point of 158–160°C, according to scheme (2-1), which depicts the formation reaction of the azo compound.

The dysonium salt was created in this reaction step using the following equation:



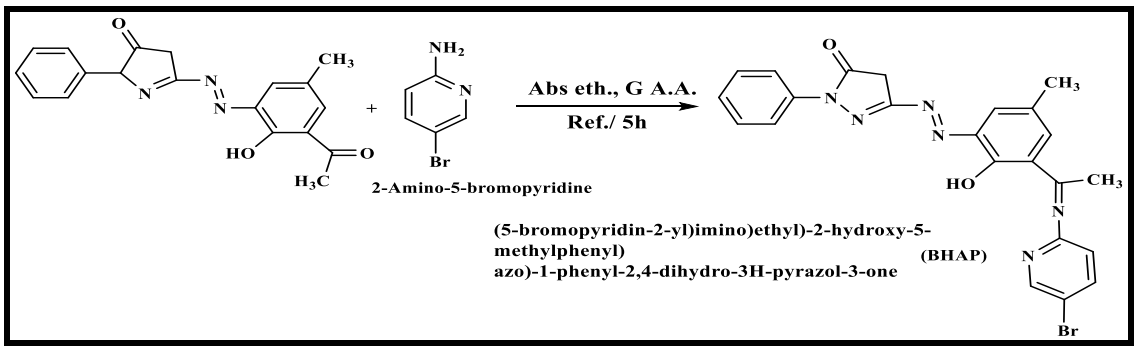
scheme (1) the formation reaction of the azo compound

Synthesis of (5-bromopyridin-2-yl)imino)ethyl)-2-hydroxy-5-methylphenyl)azo)-1-phenyl-2,4-dihydro-3H-pyrazol-3-one (BHAP

In general, the reaction between the (3.361 g, 0.01 mol) from azo compound an above in paragraph (2.4.1) and (1.73 g, 0.01 mol) 2-amino-5-bromopyridine was used to create the Schiff base compound. The reaction mixture was then refluxed for five hours while the reaction was monitored using TLC with hexane-ethanol (3:7) (v/v) as the eluent. Following completion, the mass was recrystallized from ethanol, and the yield was 81%. The melting point of the resulting material was discovered to be 168–170

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-15, October 2022
ISSN: 2749-3644

oC. (0.59). The formation reaction of the ligans is depicted in the scheme (2-2)[13]



scheme (2) The formation reaction of the ligans

Prepare standard solutions of ions

By dissolving 0.001 mol of metal salt in ethyl alcohol, a volumetric flask with a 100 ml capacity was filled to the mark to create standard solutions with a concentration of (0.001M). From this solution, standard solutions of ions (Mn(II), Co(II), Zn(II) , Cd(II) , Ag(I) , Pd(II) were created, taking into consideration the molecular weight of each element, and from these solutions, further standard solutions were prepared by serial dilution in the same manner as before.

Preparation of Buffer Solutions:-

With a concentration of (0.0005) molar for each metal and ligand, solutions of the investigated metal ions were made with the ready ligand. By dissolving ammonium acetate in distilled water and measuring the absorbance for each complex, a wide range of acidic functions were chosen, ranging from (PH=3-10) to the previously created buffer solution. during longer wavelengths.

Calibration curve:

The calibration curve was established for solutions of metal ion complexes with the prepared ligand by examining a broad concentration range between (1*10-4 - 5.5*10-4 M). The following figures show the calibration curves for each complex, including the concentration range that applies with Beer's law and calculating the molar absorption coefficient and the correlation coefficient. From these values, we conclude that the spectroscopic method has good sensitivity.

The size of the ligand

The absorption of many metal-ligand solutions was measured at the ideal pH using the following mole Ratio technique in order to get the M:L ratio.

(BHAP)-Solid complexes' synthesis in order to create pure complexes, the ligand (BHAP) was heated under reflux in ethanol while the metal chloride salts (1:1) mole ratio, which included Mn(II), Co(II), Zn(II) , Cd(II) , Ag(I) , Pd(II), were added.

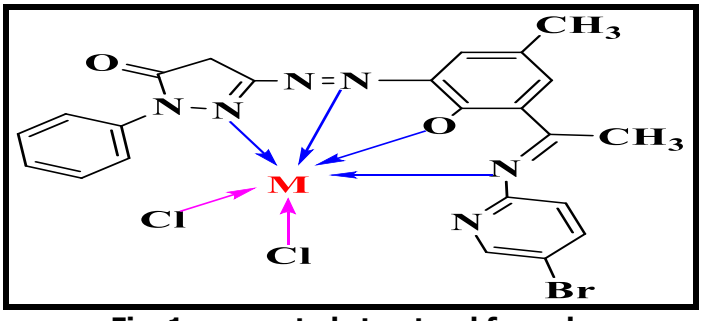


Fig. 1: suggested structural formula

Study of the solubility of complexes:

The solubility of these prepared complexes and the ligand in various polar and non-polar solvents, including water, ethanol, methanol, DMF, DMSO, di ethyl ether, petroleum ether, and aceton, was studied by placing very small amounts of each complex in a test tube, adding a small volume of the solvent, and then watching the complex dissolve in it**.**

Study of the biological activity of the ligand and its complexes:

Agar-well diffusion was used to assess the effectiveness of the ligand and its complexes against

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-15, October 2022
ISSN: 2749-3644

two strains of harmful bacteria, one strain of Gram Positive bacteria (Staphylococcus aureus) and one strain of Gram Negative bacteria (Escherichia coli)[5]. Petridishes and prepared agar were sterilized in an autoclave for 15 minutes at 120 oC. The various bacteria strains were dispersed across the dishes and on the Muller Hinton Agar surface. Using a cork-borer, the media was herded and then placed in holes in Petri dishes that were 6 mm in diameter. The studied microorganisms' broth culture was used to evenly inoculate the surface of the agar plates. Each hole in the solidified material was created to be 6mm in diameter, and 100 L of the produced compounds (1mg of the chemical dissolved in 1mL of DMSO solvent). These plates had a 37 oC incubation period (24 hrs.). Then, using a millimeter ruler, the inhibition zones induced by the different chemicals on the bacteria were measured.

Consequences and Discussion

Burnt orange serves as the ligand for Azo-Schiff (BHAP), which is soluble in certain solvents but not in water.

Table (1): Solubility of Ligand (BHAP) in different solvents

Solvent	L=(BHAP) ($C_{22}H_{19}BrN_6O_2$)
EtOH	**+**
MeOH	**+**
DMSO	**+**
H_2O	**-**
DMF	**+**
CCl_4	**÷**
Diethyl ether	**-**
Acetone	**÷**
Petrolium ether	**-**

(+) soluble , (-)insoluble , (÷) sparingly

Elemental microanalysis and some physical properties of ligand (BHAP)

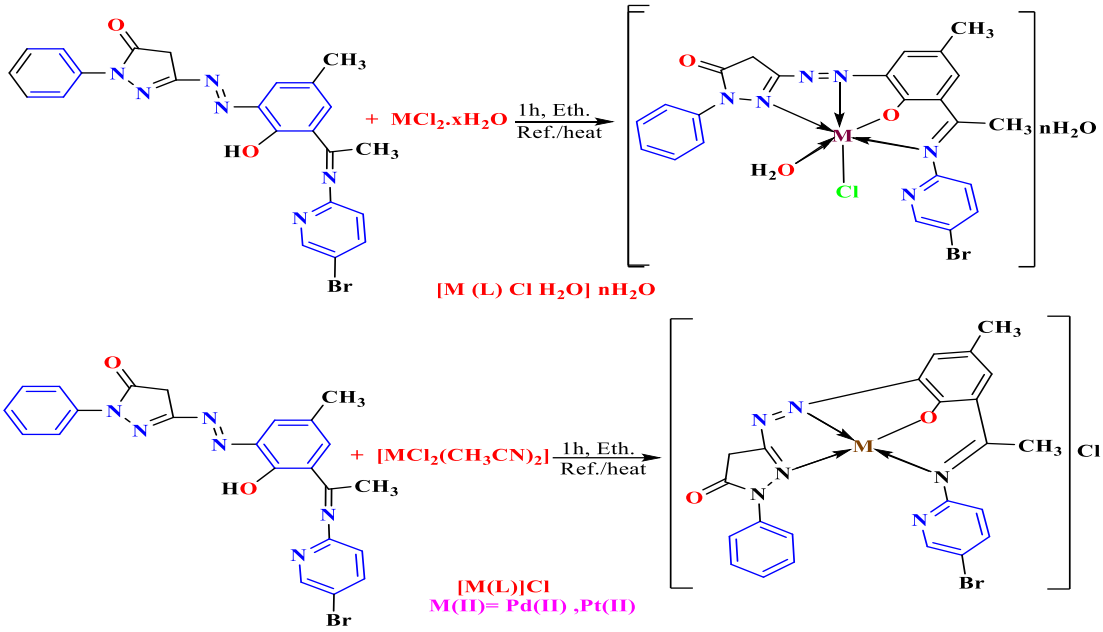
Table lists some of the physical characteristics and elemental microanalysis of the ligand (BHAP) (3-2). The findings of the elemental microanalysis and the suggested molecular formula agreed well.

Table (2): Some physical properties and elemental analysis of ligand (BHAP)

Empirical formula	M.wt $g.mol^{-1}$	Color	m.p°C	Element analysis found (calc.)%			
				C	H	N	O
L= ($C_{23}H_{19}BrN_6O_2$)	491.35	Burnt orange	168-170	th. 56.22 ex.(56.31)	3.90 (3.84)	17.10 (17.06)	6.51 (6.62)

Crystals of various colors are produced when this ligand interacts with the metal ions. Insoluble in water and stable in air, all complexes are soluble in most organic solvents including DMSO, DMF, acetone, etc. Analyses of physical characteristics and elements, After stabilizing the pH, molar ratio, and optimal concentration, the complexes produced by the interaction of the ligand with several metal ions (Mn(II), Co(II), Zn(II) , Cd(II) , Ag(I) , Pd(II)) are as follows:

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-15, October 2022
ISSN: 2749-3644



Scheme3: synthesis new complexes

Table provides an explanation of the physical characteristics, findings from C.H.N.O. tests, and metal content of the structured compounds (3).

Table(3): Some Physical properties and elemental microanalysis of (BHAP) and its metal complexes

Empirical formula	M.wt g.mol^{-1}	Color	M.P °C	Element analysis found (calc.)%				
				C	H	N	O	M
(BHAP) = ($C_{23}H_{19}BrN_6O_2$)	491.349	Deep orange	168-170	**th.** 56.22 **ex.**(56.31)	3.90 (3.84)	17.10 (17.06)	6.51 (6.62)	-------
[Mn((BHAP)) H_2O Cl]H_2O	616.759	Dark Red	187-189	44.79 (44.72)	3.60 (3.52)	13.63 (13.60)	10.38 (10.41)	8.91 (9.68)
[Co (BHAP) H_2OCl]	602.739	Yellow	191-193	45.83 (45.95)	3.34 (3.31)	13.94 (13.97)	7.96 (7.88)	9.78 (9.54)
[Cd(BHAP) H_2OCl]	656.217	Light Orange	214-216	42.10 (42.08)	3.07 (2.92)	12.81 (12.73)	7.31 (7.37)	17.13 (17.02)
[Ag((BHAP)]	598.209	Orange	184-186	46.18 (46.23)	3.03 (2.06)	14.05 (14.16)	5.35 (5.19)	18.03 (17.91)
[Pd (BHAP)]Cl	632.211	Light Brown	223-225	43.70 (43.64)	2.87 (2.74)	13.29 (13.13)	5.06 (5.12)	16.83 (16.64)

Influence of pH

After fixing (max) for each complex and measuring the absorbance of the subsequent curve, the optimal pH of the metal ion complex solutions was confirmed.

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-15, October 2022
ISSN: 2749-3644

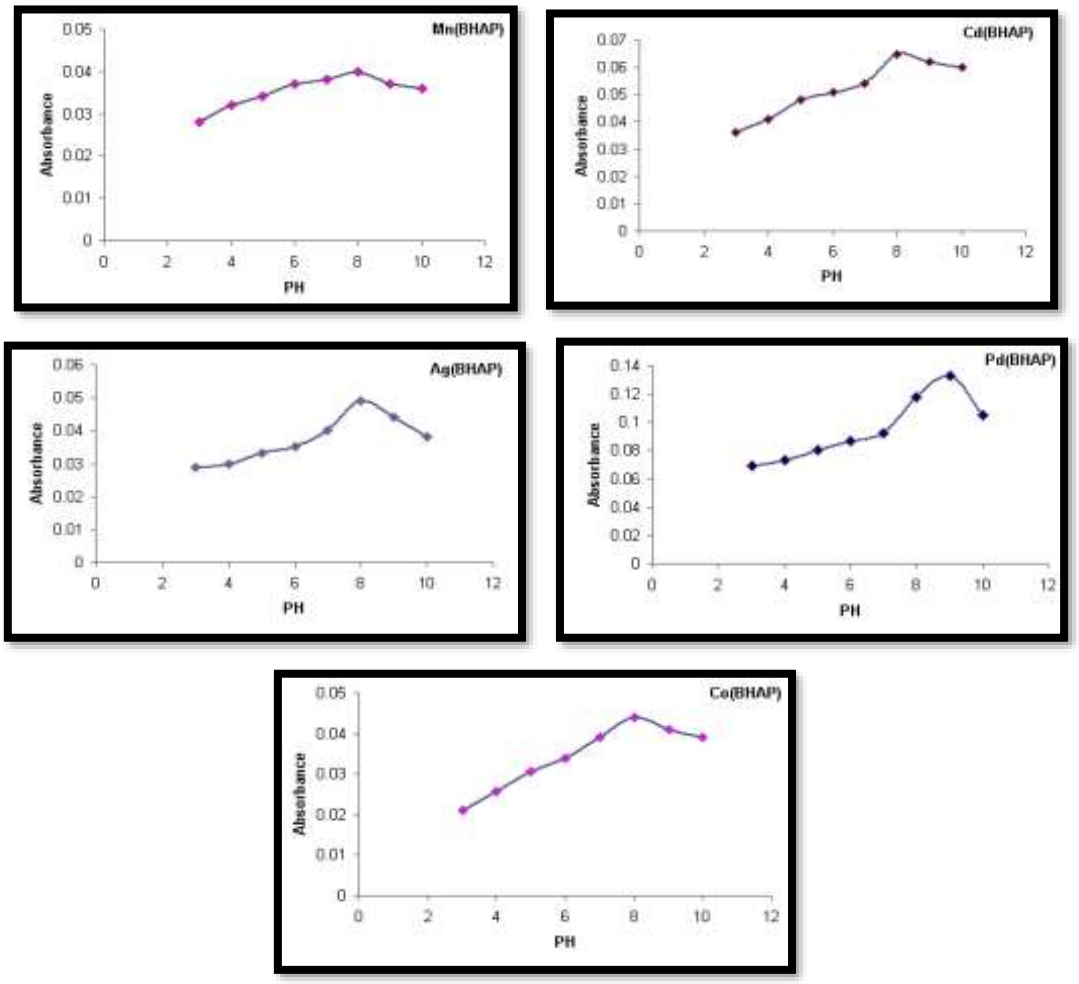


Fig. 2: Influence of pH

Mole Ratio [Metal: Ligand] Ratio

By selecting various volumes of the ligand against a given volume of the metal ion and measuring the absorbance after setting the maximum wavelength of the metal ion, the molar ratios approach was used to measure the size of the ligand against the metal ion. The calculations demonstrated that the ratio of the metal ligand is 1:1 through the graph between the absorbance and the chosen volumes. According to the diagrams below**:**

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-15, October 2022
ISSN: 2749-3644

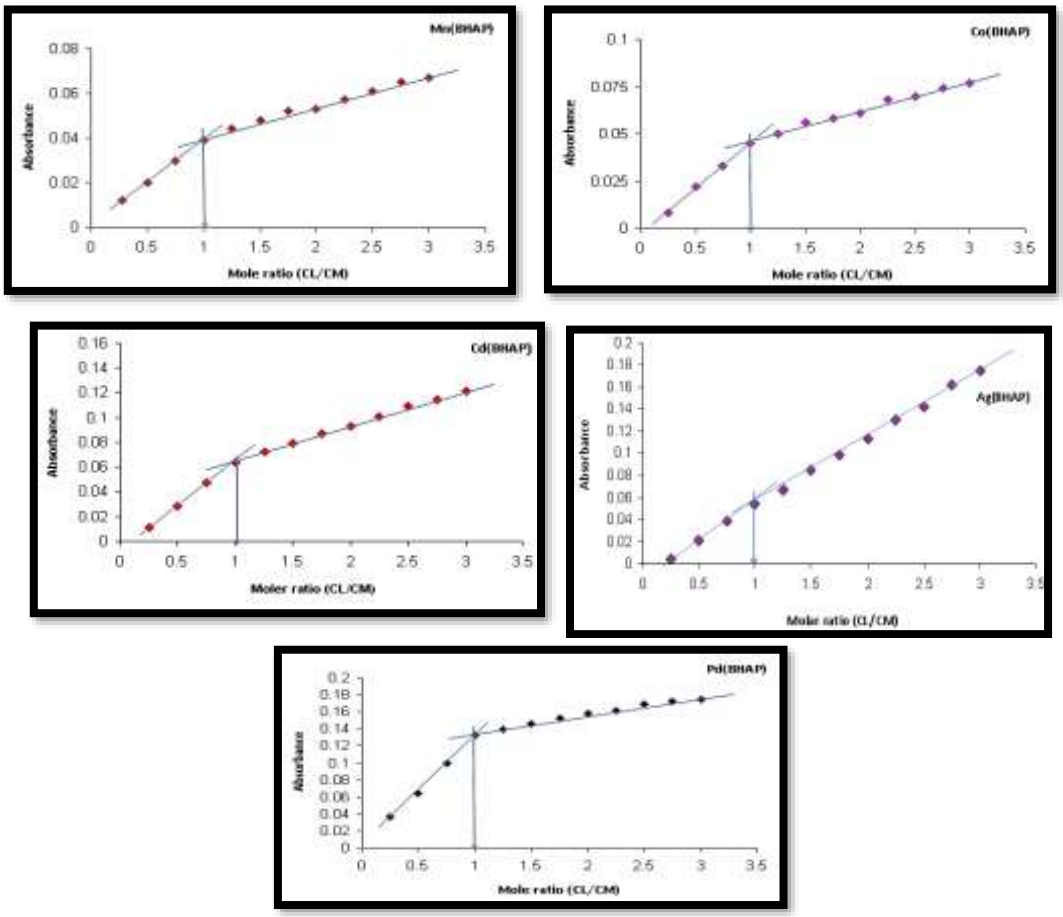


Fig.3: Mole Ratio [Metal: Ligand] Ratio

NMR Spectra for the Ligand(PABH)

One peak was visible in the ^{1}H-NMR spectra of the ligand (PABH) in DMSO-d6 Figure (4), which was attributed to the chemical shift of the OH proton in the 2-naphthol. (8.461 - 6.884) ppm) multiplet peak with occurred as a result of aromatic protons' chemical changes for 2-aromatic rings. phenyl and naphthol moiety. The doublet signal was seen at (3.561 - 3.514)ppm were given to the H-C-H protons on the ligand's pyrazolin ring moiety. spectra of ^{13}C-NMR A peak was shown in Figure 5 at (178.22) ppm, which is caused by pyrazolin carbonyl group, whereas the carbon signal from the C=N pyrazolin moiety is visible at δ (168.26) ppm. The cause of the multiplet peaks at (162.16 - 122.23) ppm is phenyl and 2-naphthol moieties. a maximum of 167.13 ppm. This is a signal at (121.81) duo to C=C-Br carbons in C=C-OH and two naphthol rings The peak at (163.74 ppm) results from 2-C=C-N site linking. Naphthol for the pyrazolin ring with an azo group. The signals are at ppm (47.34) given to the diaminobutane moiety's middle and final C-C carbon atoms.inside the ligand.

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-15, October 2022
ISSN: 2749-3644

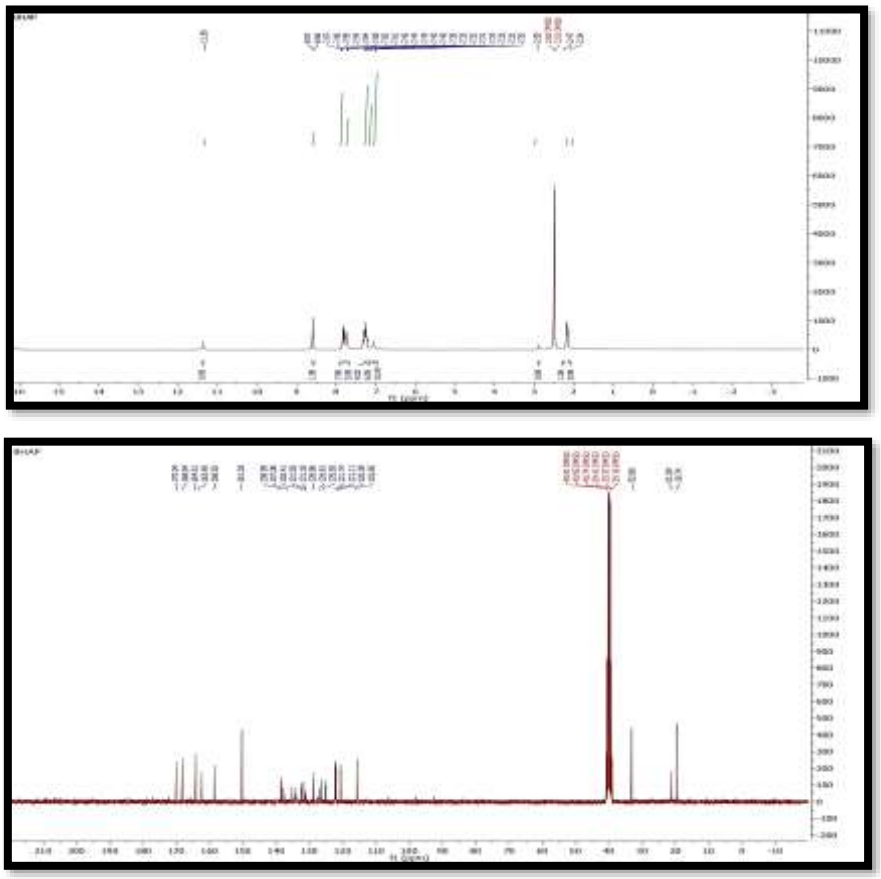


Fig. 4: NMR spectrum of ligand

UV-Vis Spectral Studies

The conductivity values and electronic absorption bands are summarized in Table (5). There were two absorptions at (270–420 nm) in the UV-visible spectra of the azo-schiff ligand Figure in ethanol (5x10–4 M) (270 and 340)nm (37037.03 and 29411.76) cm-1, which is due to $\pi-\pi^*$ transition and a broad low intensity band at (420) nm (23809) cm-1,which was attributed to n → п* 10526 transition of (C.T) intermolecular charge-transfer taken place through the azo (-N=N-) group.

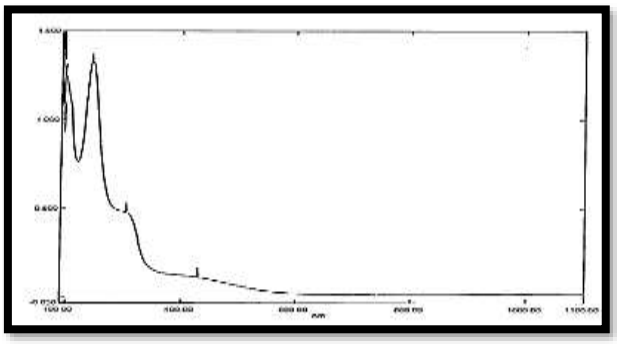


Fig. 5: UV-Vis Spectral of ligand

Bathochromic transferals of the ligand band could be seen in the spectra of the metal ions complexes within (5x10-4 M) at the ideal pH. For the Co(II), Ni(II), and Cu(II) complexes, the ascribed bands to intraligand п→п* were seen at (37811, 31523), (38500, 32172), and (37535, 31014) cm-1, in that order. The a large shift in the (max) and a change in the hue of free ligand solutions provide a worthy indication of intricate coordination.

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-15, October 2022
ISSN: 2749-3644

Antimicrobial Activity

In the biological area, the ligand(BHAP)derivatives and their complexes play a significant role in inhibiting biological activity. Hybrid atoms like oxygen, nitrogen, and sulfur are suitable for forming bonds with various elements. We made the decision to research the novel (BHAP) ligand's biological activity and its For two types of pathogenic bacteria, synthetic complexes with some metal ions have been developed. (Gram-positive Staphylococcus aureus and Gram-negative Escherichia coli), It grows at a temperature of 37 °C on Muller Hinton Agar. Inhibitory zones created by the ligand (BHAP) and its complexes were against Staphylococcus aureus, their antibacterial activity was measured in millimeters. as well as E. coli. Tests revealed that the produced compounds provided different results. Inhibition outcomes for these microorganisms , and the reason is because of the various groups adhere to the substance. The following Table displays them. Table (4): Information on the ligand's antibacterial activity (zone of inhibition) in millimeters (BHAP) and its buildings are at (0.001M).

Table (4): Biological activity of (BHAP) and its metal complexes

Compound	Pathogenic bacteria	
	Sta. aureus-Gram(+)	E.coli - Gram(-)
Control (S) DMSO	6	6
Ligand	15	14
L-Mn	19	16
L-Co	17	15
L-Cd	19	18
L-Ag	19	20
L-Pd	19	16

CONCLUSION

The Azo-Schiff base complexes of were created and characterized using preliminary methods (Mn(II), Co(II), Cd(II) , Ag(I) , Pd(II)). Investigations using FTIR and NMR spectroscopy showed that the compounds were effectively produced. The antibiotic evaluation of the activity of all created (Mn(II), Co(II), Cd(II) , Ag(I) , Pd(II)) complexes gram-positive Gram-negative bacteria and S. aureus strains of the bacterium E. coli and the It was discovered that complexes were bacteriostatically stable. with growing concentration, complexes of (Mn(II), Co(II), Cd(II) , Ag(I) , Pd(II)) demonstrated a positive scavenging tendency.

REFERENCES

1. Pervaiz Muhammad , Sahar Sadiq , Amber Sadiq , Umer Younas , Adnan Ashaf b , Zohaib Saeed a , Muhammad Zuber b , Ahmad Adnan : Azo-Schiff base derivatives of transition metal complexes as antimicrobial agents , Department of Chemistry, Government College University, Lahore, Pakistan -2021 , Coordination Chemistry Reviews
2. Hussein Ali Kadhim Kyhoiesh , Khalid J. Al-Adilee : Synthesis, spectral characterization, antimicrobial evaluation studies and cytotoxic activity of some transition metal complexes with tridentate (N,N, O) donor azo dye ligand , a Ministry of Education, Directorate of Education Al-Muthanna, AL-Muthanna, Iraq , 2021 , Results in Chemistry .
3. El-Hawash S.; Badawey E. S. and El-Ashmawey I., Nonsteroidal antiinflammatory agents-part 2 antiinflammatory, analgesic and antipyretic activity of some substituted 3-pyrazolin-5-ones and 1,2,4,5,6,7-3Hhexahydroindazol-3-ones, Eur. J
4. Al-Aaraji. Z.A ; Ph.D. Thesis, Babylon University. " KOKALJ, Anton, et al. Simplistic correlations between molecular electronic properties and inhibition efficiencies: Do they really exist Corrosion Science, 179: 108856 ,(2021)
5. Berk B. , Ertas M. and Biltekin SN, (2017), "synthesis , Antimicrobial Activity studies and Molecular property predictions of Schiff bases Derived from Ortho-vanillin", Acta pharmaceutical Sciencia , vol, 55,No.1.pp 83-96
6. Aly, S. A., &Fathalla, S. K. (2020). Preparation, characterization of some transition metal complexes of hydrazone derivatives and their antibacterial and antioxidant activities. Arabian Journal of Chemistry, 13(2), 3735-3750.
7. Saeid Menati ,Reza A, bakht , Hadi ,A, Rudbari, Giuseppe Bruno Synthesis and

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-15, October 2022
ISSN: 2749-3644

characterization of four new azo-Schiff base and their nickel(II) complexes , Polyhedron 205 (2021) 115296 – 1
8. S. Manjula , S. Khana and A. Ahmed,Science Asia 33, 455-460 (2007).
9. Shibata, M. Furukawa and R. Nakashima, Syntheses of azo dyes containing 4,5-diphenylimidazole and their evaluation as analytical reagents, Anal. Chim. Acta, 81, (1976) 131-141.