

Preparation, Identification And Biological Activity Of Some Metals Complexes With A New Ligand (4-Nitro-N-((6-Oxo-6,9-Dihydro-1H-Purin-2-Yl)Carbamothioyl)Benzamid)

Abdullah Sh. Abdullah¹, Basima M. Sarhan²

¹Directorate of Institutional Development and Government Coordination

Iraqi Ministry of Education, Iraq

²Department of Chemistry, College of Education for Pure Sciences, Ibn Al –Haitham, University of Baghdad, Baghdad, Iraq.

KEYWORDS

Guanine, Nitro Benzoyl Chloride, Carbamothioyl, Coordination Complexes

ABSTRACT

This study aimed to synthesize and characterize a novel guanine derivative, namely (4-nitro-N-((6-oxo-6,9-dihydro-1H-purin-2-yl)carbamothioyl)benzamid) (abbreviated as NPBL4). This compound possesses an intriguing chemical structure, consisting of a guanine moiety (a bicyclic heterocyclic base) linked to a benzamide group through a carbamothioyl linker. The synthesis of this nitrogenous base derivative involved two steps. Firstly 4-nitro-N-thioformylbenzamide was synthesized by reacting 4-nitrobenzoyl chloride with ammonium thiocyanate in acetone. Subsequently, the obtained 4-nitro-N-thioformylbenzamide was reacted with guanine to yield the desired ligand. In addition to the ligand synthesis, the study focused on preparing complexes of various metal ions (Mn²⁺, Co²⁺, Ni²⁺, Cu²⁺, Zn²⁺, Cd²⁺, and Pd²⁺) with the prepared guanine derivative. The ligand and complexes were subjected to comprehensive characterization using techniques such as infrared spectra, ultraviolet-visible spectra, ¹H-NMR, ¹³C-NMR spectra, elemental analysis (C.H.N.S.), molar conductivity measurement, magnetic susceptibility, atomic absorption, melting point determination, and study the biological activity for the complexes. The results of these characterization studies led to the determination of the general formulas for the prepared complexes, which were found to be [MCl₂(NPB)₂], where M represents the respective metal ion (Mn²⁺, Co²⁺, Ni²⁺, Cu²⁺, Zn²⁺, Cd²⁺, and Pd²⁺). Notably, the geometric shape of all the prepared complexes was determined to be an octahedron. In summary, this study successfully synthesized and characterized a novel guanine derivative (NPB) and investigated its complexes with various metal ions. The findings provided valuable insights into the chemical properties and structural features of these compounds.

1. Introduction

Coordination chemistry finds applications in many areas, including catalysis, materials science, bioinorganic chemistry, and medicinal chemistry. It plays a crucial role in understanding the behavior of metal complexes in biological systems and developing metal-based drugs or catalysts with specific properties. Overall, coordination chemistry investigates the intricate relationships between metal ions and ligands, shedding light on their structures, properties, and reactivity, and offering a foundation for various practical applications. Bioinorganic chemistry is a specialized branch of chemistry dedicated to investigating the interactions between biological systems and inorganic molecules. It encompasses the examination of metal ions and their coordination chemistry within biological systems, as well as the roles played by inorganic elements and compounds in various biological processes [1,2]. An active research area within bioinorganic chemistry involves the synthesis of metallic coordination complexes with biological molecules, as these complexes possess diverse applications in biology. Notably, certain complexes have been explored for their potential as anticancer agents, antibacterial or antifungal agents, and catalysts for significant biological reactions [3–10]. The preparation of these complexes often necessitates modifications to the biological molecules, enabling them to act as ligands that can form stable complexes by coordinating with metal ions [3,10–14]. This process may involve utilizing techniques from synthetic organic chemistry to generate modified versions of naturally occurring biological molecules or creating entirely new ligands with properties similar to biological molecules [4,15–17]. In this study, our primary objective is to synthesize and evaluate the properties of a novel ligand NPB (4-nitro-N-((6-oxo-6,9-dihydro-

1H-purin-2-yl)carbamothioyl)benzamid), along with its complexes involving various metal ions.

2. Methodology

All reagents, chemicals, metal chloride salts and solvents were purchased from Merck,

Fluorochem, Fluka, Sigma- Aldrich, J.T.Baker, BDH, and Riedel-De haën Merck and Honeywell with high purity grade.

Instrumentation

The melting point and decomposition were determined for the ligands and their complexes that prepared by using KRÜSS Melting Point meter, The Infrared spectra were obtained with range (4000-200) cm^{-1} as CsI disk by using Shimadzu FT-IR 8400S spectrophotometer, The Uv-visible spectra for the solutions (10^{-3} molar in DMSO solvent) of the ligands and their complexes were recorded by using Shimadzu (UV-160A), with range (1100-200)nm, The (^{13}C , ^1H) NMR Spectra for ligands were recorded with few drops of DMSO by Ultra Shield 300 MHz, Bruker, Switzerland, Elemental analysis for the most exacting determination of CHNS for the ligands and their complexes were carried out with EuroVector S.p.A. - EuroEA3000 CHNS Analyzer, The Magnetic susceptibility for the prepared complexes were recorded at room temperature on the solids states applying a method using Balance Magnetic Susceptibility Model MSB-MKI, and The molar conductance of the complexes solutions in 10^{-3} mole. L^{-1} (DMSO) were measured by a Jenway Ltd. 4071 digital conductivity meter.

Procedure

Synthesis of the ligand (NPB)

A- Dissolved a (30mmol, 2.28g) of (ammonium thiocyanate) in (20ml) of acetone with stirring, then dissolved a (30mmol, 4.84g) of (4-nitro benzoyl chloride) in (20ml) of acetone, mixed the two solutions and stirred about 3 hours then filtered.

B- Dissolved a (30mmol, 4.53g) of (Guanine) in (20ml) of acetone then mixed with the former solution above, refluxed the mixture with water bath for (6 hours) and let it to dry, then recrystallized with ethanol. The product is yellowish white crystals, providing a yield of 76%. The melting point was measured as 93°C . The elemental analysis yielded the following results: Carbon (C) content found: 43.38% (calculated: 42.47%), Hydrogen (H) content found: 3.72% (calculated: 3.61%), Nitrogen (N) content found: 26.29% (calculated: 26.98%), and Sulfur (S) content found: 8.71% (calculated: 8.82%) [18,19] (see scheme-1).

Synthesis of metal complexes

A) A quantity of the guanine derivative (2 mmol, 0.718 g) was dissolved in 10 ml of ethanol.

B) Metal salts (1 mmol) including 0.197 g of $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, 0.237 g of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$, 0.237 g of $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$, 0.170 g of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 0.136 g of ZnCl_2 , 0.201 g of $\text{CdCl}_2 \cdot \text{H}_2\text{O}$, and 0.177 g of $\text{PdCl}_2 \cdot \text{H}_2\text{O}$ were dissolved in the minimum amount of ethanol. This solution was then added to the previously prepared guanine derivative solution. The resulting mixture was stirred for 4 hours, leading to the formation of a precipitate. The precipitate was separated by filtration, washed with ethanol, and left to dry. [19, 20]

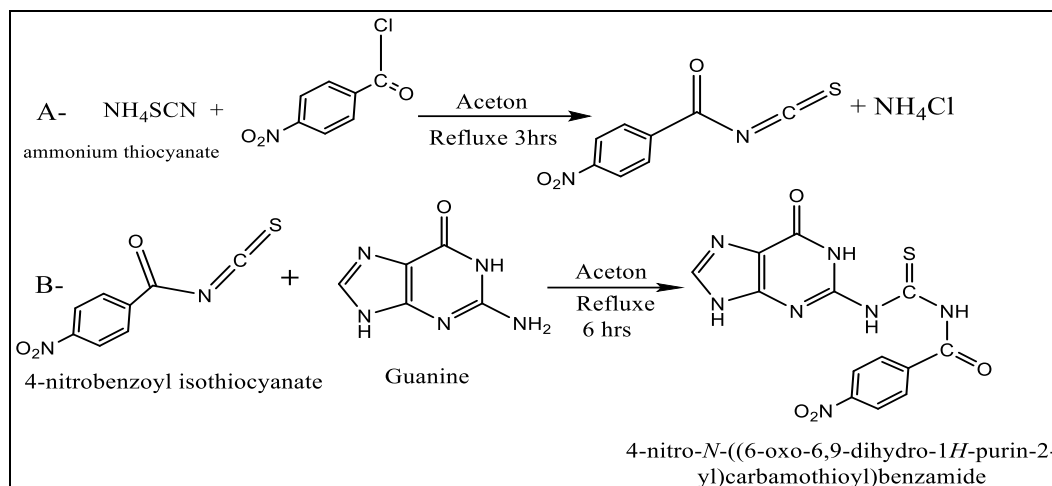


Figure 1. see scheme-1 Synthesis of the ligand (NPB)

3. Results and discussion

The solid complexes exhibited solubility in specific common solvents, such as dimethyl formamide and dimethyl sulphoxide, and demonstrated significant thermal stability. Upon dissolution in dimethyl sulphoxide (DMSO), all complexes displayed non-electrolytic behaviour, as confirmed by their molar conductivity. Table 1 presents the physical properties and metal percentages found in the complexes, along with the molar conductivity values of the ligand and its corresponding metallic complexes.

Table 1: The physical properties of the ligand and its metallic complexes

Compound	Color	M.Wt (g/mol)	M.p.(Dec.) °C	M% Calculation (Found)	Molar condu. Ohm ⁻¹ cm ² mol ⁻¹
(NPB)	yellow	359.32	93 (128)	-- (--)	---
[MnCl ₂ (NPB) ₂]	yellow	844.47	117 (173)	6.51 (6.58)	15
[CoCl ₂ (NPB) ₂]	Blue	848.47	134 (168)	6.95 (6.82)	16
[NiCl ₂ (NPB) ₂]	green	848.23	138 (191)	6.92 (7.01)	13
[CuCl ₂ (NPB) ₂]	Blue	853.08	--- (172)	7.45 (7.57)	13
[ZnCl ₂ (NPB) ₂]	White	854.92	--- (167)	7.65 (7.82)	9
[CdCl ₂ (NPB) ₂]	White	901.95	--- (192)	12.46 (12.54)	6
[PdCl ₂ (NPB) ₂]	brown	895.96	--- (187)	11.88 (11.94)	1

In Figure 1, the FT-IR spectrum of the free ligand (NPB) revealed distinct bands: a medium band at 3160 cm⁻¹ corresponding to ν(NH), another medium band at 1604 cm⁻¹ for ν(C=O amidic), and additional bands at 1226 cm⁻¹ for ν(C=S) and a strong band at 1695 cm⁻¹ for ν(C=O) of the guanine ring [21]. Table 2 further provides relevant data associated with these observations.

Table2: FT-IR bands for guanine and free ligand NPB

Compound	ν(N-H+OH)	ν(N-H ₂ +OH)	ν(C=O) Amide	ν(C=S)	ν(C=O) in purin ring
Guanine	3321 _(m)	3116 _(m)	---	---	1693 _(s)
NPB	----	3160 _(m)	1604 _(s)	1226 _(s)	1695 _(s)

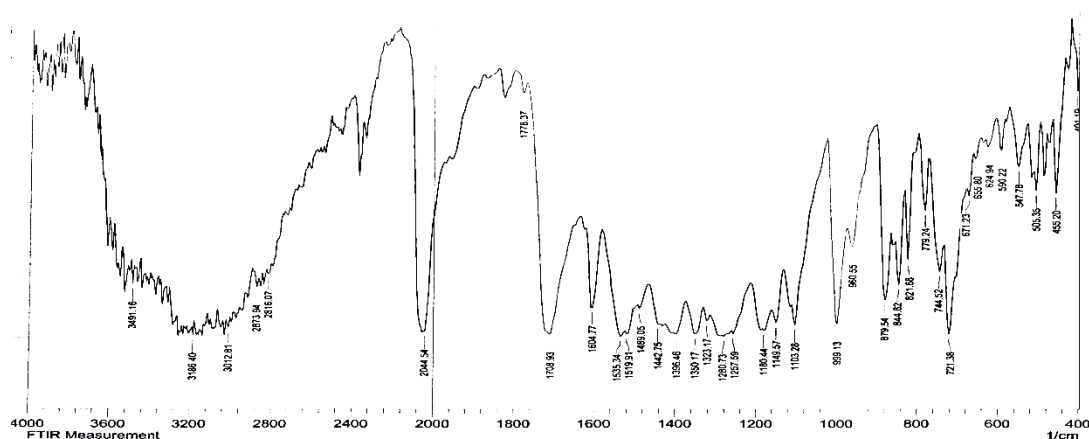


Figure 2: FT-IR spectrum of ligand (NPB)

In Figure 3, the ^1H -NMR spectrum of the ligand NPB in ($\text{DMSO}-d_6$) exhibited distinct signal as follows: a single signal at δ 7.109 ppm for one proton of NH of the imidazole ring; a single signal at δ 7.237 ppm for CH in the imidazole ring; a multiplet signal between δ 8.035-8.31 ppm of 4H four protons of aromatic ring; a single signal at δ 8.33 ppm for one proton of NH amine; a single signal at δ 8.34 ppm for one proton in NH amide. Additionally, there was a single signal at δ 12.325 ppm for one proton in NH guanidine [21]. Refer to Table 2 for further details related to these findings.

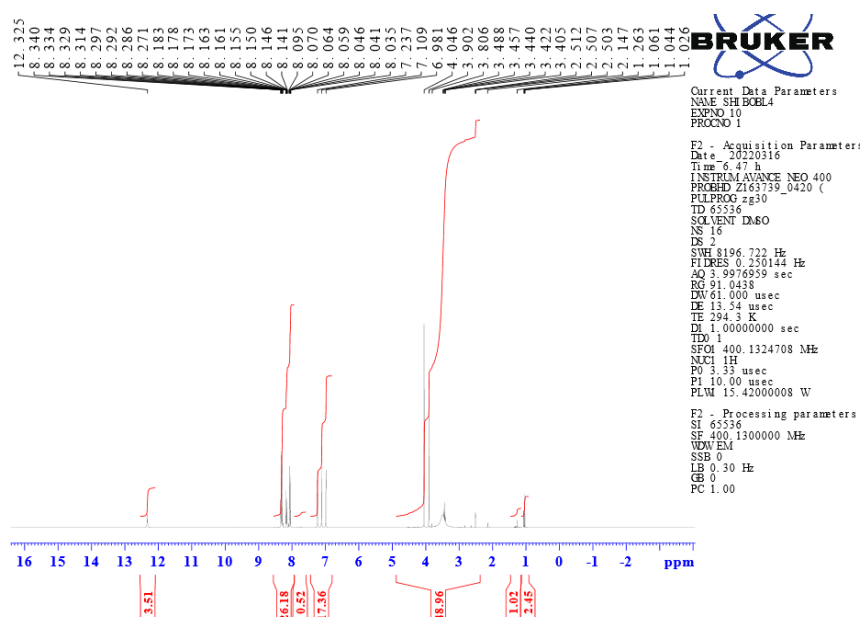


Figure 3: ^1H -NMR spectrum of ligand (NPB)

Table 3 :the ^1H NMR signals for ligand (NPB)

Symbol	Δppm	Signal	No.of point	Group
a	7.109	Singlet	1H	NH, imidazole ring
b	7.237	Singlet	1H	CH, imidazole ring
c	8.035-8.31	multiplet	4H	Aromatic ring
d	8.33	Singlet	1H	N-H ,amine
e	8.34	Singlet	1H	N-H ,amide
f	12.325	Singlet	1H	N-H ,guanidine

Current Data Parameters
NAME SH BOBL4
EXPNO 11
PROCNO 1

F2 - Acquisition Parameters
Date_ 20220316
Time 7.48 h
INSTRUM AVANCE NEO 400
PROBHD ZIG300 0420 (PULPROG zgpg30)
TD 65536
SOLVENT DMSO
NS 1024
DS 4
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 1.3762560 sec
RG 52.6101
DW 21.000 usec
DE 20.00 usec
TE 295.2 K
D1 2.00000000 sec
d11 0.03000000 sec
TD0 1
SFO1 100.6228298 MHz
NUC1 13C
P0 2.67 usec
P1 8.00 usec
PLW1 90.00000000 W
SFO2 400.1316005 MHz
NUC2 1H
PCPD2 90.00 usec
PLW2 15.42000008 W
PLW12 0.19036999 W
PLW13 0.09575700 W

F2 - Processing parameters
SI 32768
SF 100.6127685 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Table 4: the ^{13}C NMR signals for ligand (NPB)

Symbol	Δp_{ppm}	Group
a	123	C- imidazole ring
b	124-139.3	C ,Aromatic ring
c	140.40	CH in purine ring
d	149.49	C-NH in purine ring
e	150.64	C=O in purine ring
f	164.27	C-NH in purine ring
g	165.22	C=O, amid
h	190.41	C=S

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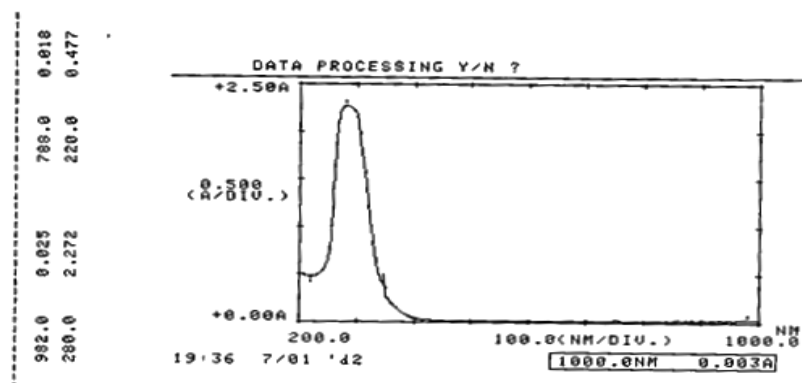


Figure 5: The UV-visible spectrum of ligand (NPB)

-[MnCl₂(NPB)₂] d⁵, displayed distinct spectral bands at (33444), (26666), and (11273) cm⁻¹ were due to (L.F.) transitions, (C.T.), and (⁶A_{1g} → ⁴T_{1g}) transitions respectively [18], [22].

-[CoCl₂(NPB)₂] d⁷ Figure6, exhibited clear spectral bands at (33670), (26315), (18867), and (11627) cm⁻¹, which were associated with (L.F.), (C.T.) that mixed with (⁴T_{1g} → ⁴T_{1g}) transitions, (⁴T_{1g} → ⁴A_{2g}) transition, and (⁴T_{1g} → ⁴T_{2g}) transition respectively [23], [24].

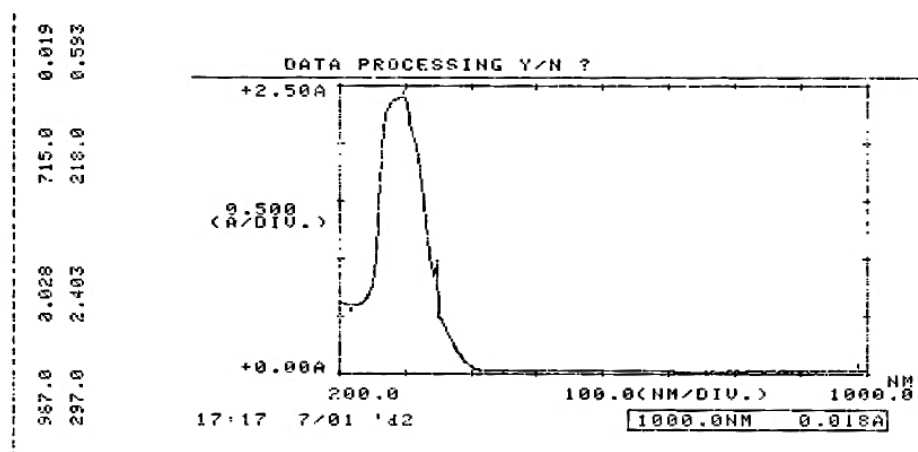


Figure6: The UV-visible spectrum of [CoCl₂(NPB)₂]

-[NiCl₂(NPB)₂] d⁸, The complex exhibited distinct spectral bands at (33898, 26525, 17857) and (11273) cm⁻¹, which were for (L.F.), (C.T.) that mixed with mix with (³A_{1g} → ³T_{1g}), (³A_{2g} → ³T_{1g}), and (³A_{2g} → ³T_{2g}) transition respectively [23], [24]

-[PdCl₂(NPB)₂] d⁸, The complex exhibited distinct spectral bands at (36363, 28735, 1124), and 12437) cm⁻¹, which were for (L.F.), (C.T.) that mixed with mix with (³A_{1g} → ³T_{1g}), (³A_{2g} → ³T_{1g}), and (³A_{2g} → ³T_{2g}) transition respectively [23], [24]

-[CuCl₂(NPB)₂] d⁹ Figure7, displayed distinct spectral bands at (35335, 26178, 10893) cm⁻¹ which were for (L.F.), (C.T.) and (²E_g → ²T_{2g}) transition respectively [22].

-The complexes of [ZnCl₂(NPB)₂] and [CdCl₂(NPB)₂], shows ligand field effects in range (33333-35335) cm⁻¹ and charge transfer of (M → L) in range (25773-27777) cm⁻¹ [23-].

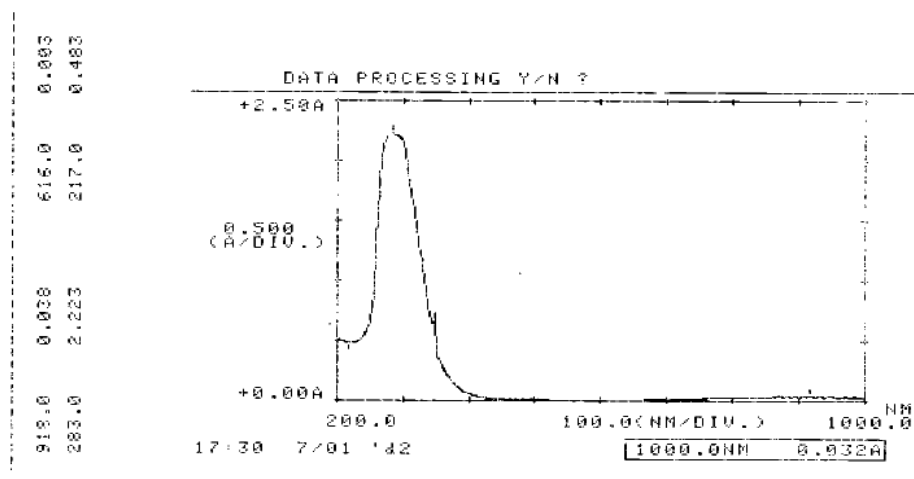


Figure7: The UV-visible spectrum of $[\text{CuCl}_2(\text{NPB})_2]$

Table 5: the UV-visible spectral data of the ligand NPB complexes and its complexes (10^{-3} M in DMSO)

Compounds	$\lambda(\text{nm})$	$\nu(\text{cm}^{-1})$	ABC	ϵ_{max} molar- $^{-1}\text{cm}^{-1}$	Transitions
(NPB)	280	35714	2.272	2272	$\pi \rightarrow \pi^*$
	368	27173	0.455	455	$n \rightarrow \pi^*$
$[\text{MnCl}_2(\text{NPB})_2]$	300	33333	2.387	2387	(L.F.)
	737	13568	0.28	28	(C.T.)
	839	11918	0.027	27	$^6\text{A}_{1g} \rightarrow ^4\text{T}_{1g}$
$[\text{CoCl}_2(\text{NPB})_2]$	297	33670	2.403	2403	(L.F.)
	380	26315	0.650	650	(C.T.)mix $^4\text{T}_{1g} \rightarrow ^4\text{T}_{1g}$
	530	18867	0.030	30	$^4\text{T}_{1g} \rightarrow ^4\text{A}_{2g}$
	860	11627	0.025	25	$^4\text{T}_{1g} \rightarrow ^4\text{T}_{2g}$
$[\text{NiCl}_2(\text{NPB})_2]$	295	33828	2.402	2402	(L.F.)
	348	28735	0.710	710	(C.T.)mix $^3\text{A}_{1g} \rightarrow ^3\text{T}_{1g}$
	658	15197	0.032	32	$^3\text{A}_{2g} \rightarrow ^3\text{T}_{1g}$
	885	11299	0.025	25	$^3\text{A}_{2g} \rightarrow ^3\text{T}_{2g}$
$[\text{CuCl}_2(\text{NPB})_2]$	283	35335	2.223	2223	(L.F.)
	382	26178	0.675	675	(C.T.)
	918	10893	0.038	38	$^2\text{E}_g \rightarrow ^2\text{T}_{2g}$
$[\text{ZnCl}_2(\text{NPB})_2]$	300	33333	2.484	2484	(L.F.)
	388	25773	1.450	1450	(C.T.)
$[\text{CdCl}_2(\text{NPB})_2]$	283	35335	2.292	2292	(L.F.)
	360	29735	0.480	480	(C.T.)
$[\text{PdCl}_2(\text{NPB})_2]$	275	36363	2.007	2007	(L.F.)
	348	28735	1.145	1145	(C.T.)mix $^3\text{A}_{2g} \rightarrow ^3\text{T}_{1g}$
	708	14124	0.025	25	$^3\text{A}_{2g} \rightarrow ^3\text{T}_{2g}$
	804	12437	0.20	20	$^3\text{A}_{2g} \rightarrow ^3\text{T}_{2g}$

The FT-IR spectra of seven synthesized complexes were recorded in the range of 4000 to 200 cm^{-1} using CsI discs. These spectra exhibited notable disparities in the bands associated with the stretching vibration at 1207 cm^{-1} in the ligand spectrum, attributed to the $\nu(\text{C}=\text{S})$ range of 1207 to 1209 cm^{-1} . In the complex spectra, these bands exhibited a downward shift of 180-70 cm^{-1} , indicating the participation of the sulfur atom in the thione group in coordination [25] (refer to Table 6).

Furthermore, the band corresponding to $\nu(\text{C}=\text{O}$ amide) in the range of 1527 to 1519 cm^{-1} experienced a shift towards lower frequencies of 85-77 cm^{-1} . This suggests the potential coordination of the ligand via the oxygen atom at the carbonyl group [26]. For visual representation, consult Figures 8 and 9 depicting the metal complexes.

The coordination of M-O and M-S was confirmed by the emergence of stretching vibrations around 486 to 433 cm^{-1} , 360 to 325 cm^{-1} , and 285 to 262 cm^{-1} , corresponding to $\nu(\text{M-O})$, $\nu(\text{M-S})$, and $\nu(\text{M-Cl})$, respectively [27]. Refer to Table 6 for a comprehensive overview of the significant bands and their assignments for both the free ligand (NPB) and its prepared complexes.

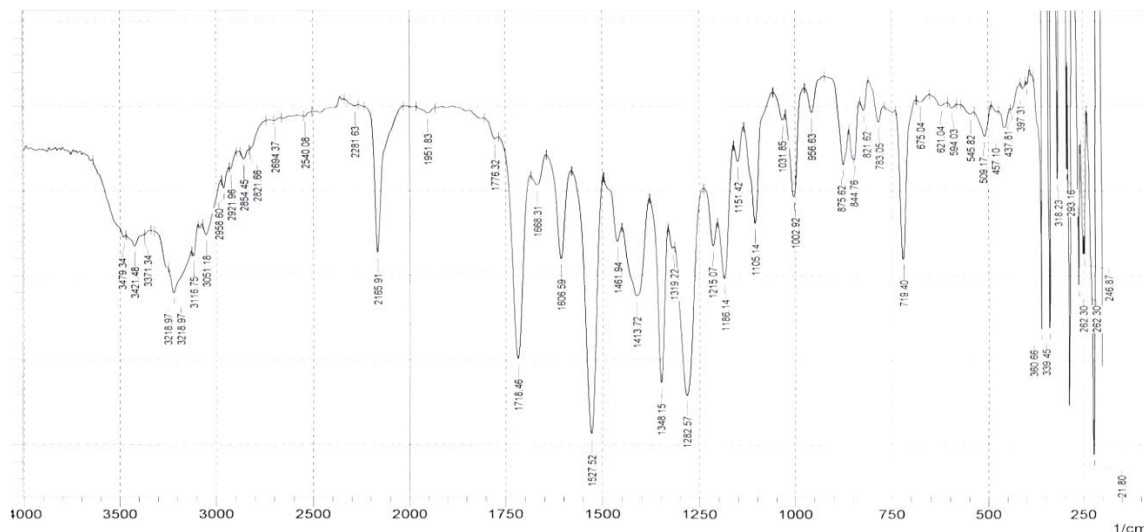


Figure 8: FT-IR spectrum of $[\text{NiCl}_2(\text{NPB})_2]$ complexes

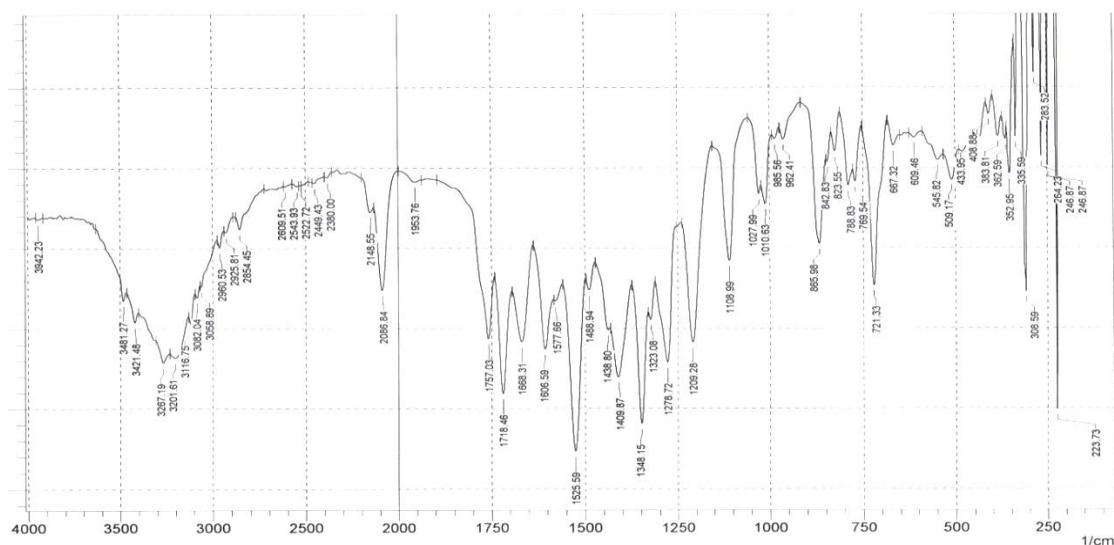


Figure 9: FT-IR spectrum of $[\text{ZnCl}_2(\text{NPB})_2]$ complexes

Table 6 : The important bands and assignment for (NPB) and its metal complexes.

Compound	$\nu(\text{N-H})$	$\nu(\text{C=O})$ Amide	$\nu(\text{C=S})$	$\nu(\text{M-O})$	$\nu(\text{M-S})$	$\nu(\text{M-Cl})$
Ligand (NPB)	3186 _(m)	1604 _(m)	1280 _(m)	-----	-----	-----
$[\text{MnCl}_2(\text{NPB})_2]$	3182 _(m)	1521 _(s)	1108 _(m)	482 _(w)	360 _(w)	285 _(w)
$[\text{CoCl}_2(\text{NPB})_2]$	3195 _(m)	1525 _(s)	1205 _(s)	457 _(w)	331 _(w)	264 _(w)
$[\text{NiCl}_2(\text{NPB})_2]$	3195 _(m)	1527 _(s)	1205 _(s)	457 _(w)	360 _(w)	262 _(w)
$[\text{CuCl}_2(\text{NPB})_2]$	3174 _(m)	1519 _(m)	1112 _(m)	460 _(w)	352 _(w)	264 _(w)
$[\text{ZnCl}_2(\text{NPB})_2]$	3201 _(m)	1525 _(s)	1209 _(s)	433 _(w)	352 _(w)	264 _(w)
$[\text{CdCl}_2(\text{NPB})_2]$	3193 _(m)	1523 _(s)	1195 _(s)	486 _(w)	325 _(w)	285 _(w)
$[\text{PdCl}_2(\text{NPB})_2]$	3172 _(m)	1523 _(s)	1107 _(s)	484 _(m)	325 _(w)	262 _(w)

The magnetic susceptibilities of these complexes were in good agreement with the anticipated values for high spin states[28]. You can find the specific magnetic susceptibility values for these complexes listed in Table 7.

Table7: Magnetic susceptibilities data of(NPB) complexes

complexes	Gram susce. $X_g \times 10^{-6}$	Molar susce. $X_M \times 10^{-6}$	Atomic susce. $X_A \times 10^{-6}$	μ_{eff} (B.M)	No. of unpaired electrons	Proposed structure
[Mn(NPB) ₂]	17.35	14651.5545	14810.4545	5.94	5	Oh
[Co(NPB) ₂]	11.15	94604405	9619.3405	4.78	3	Oh
[Ni(NPB) ₂]	4.95	41987.7385	4337.6385	3.22	2	Oh
[Cu(NPB) ₂]	1.30	1109.004	1267.904	1.74	1	Oh
[Zn(NPB) ₂]	0	0	0	0	0	Oh
[Cd(NPB) ₂]	0	0	0	0	0	Oh
[Pd(NPB) ₂]	3.80	3404.648	3563.548	2.91	2	Oh

$$D = -158.9 \times 10^{-6}$$

Biological Activity

In this study, we evaluated the antimicrobial efficacy of compounds (NPB) and their complexes against two types of bacterial species, namely *Staphylococcus aureus* (Gram Positive) and *E. coli* (Gram Negative), and a *candida albicans* fungus using the agar diffusion technique [29], while DMSO served as the solvent and control. To assess the potential activities of these compounds, they were dissolved in this solvent at concentration 10 mg/ml. This method entails exposing the zone of inhibition to the diffusion of microorganisms on agar plates. The plates were then incubated for 24 hours at 37°C [30]. The diameters of the inhibition zones around each well were measured in millimetres. Observing the results, we find all complexes that are clear effectiveness against fungi, as zinc complexes were found to have the greatest effectiveness, while antibacterial activity, it was observed that complexes containing manganese, copper, cadmium, and palladium demonstrated significant effectiveness against the bacteria *E. coli* exclusively, see table 7.

Table 7: show the biological activity of (NPB) and its complexes

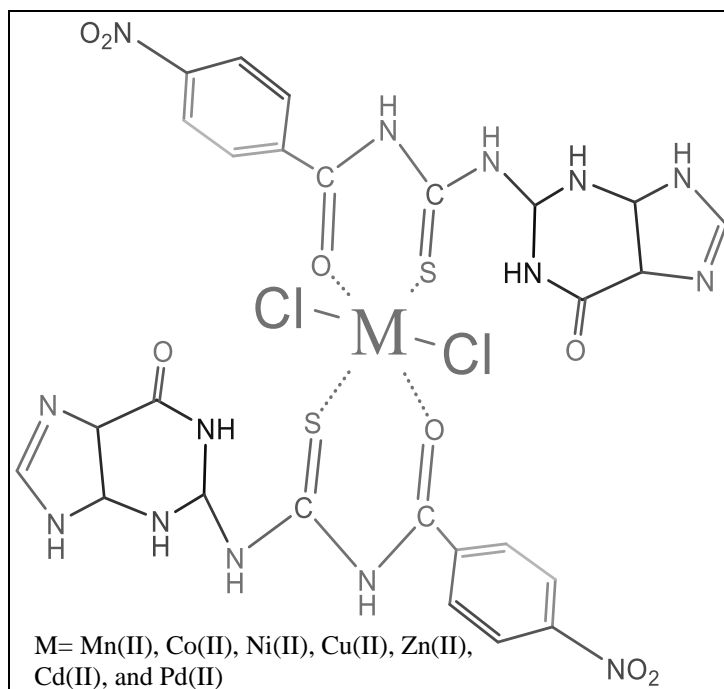
No.	compound	<i>E. coli</i>	<i>Staphylococcus aureus</i>	<i>candida albicans</i>
1	Ligand (NPB)	8	8	12
2	[MnCl ₂ (NPB) ₂]	8	-ev	16
3	[CoCl ₂ (NPB) ₂]	-ev	-ev	17
4	[NiCl ₂ (NPB) ₂]	-ev	-ev	15
5	[CuCl ₂ (NPB) ₂]	8	-ev	18
6	[ZnCl ₂ (NPB) ₂]	-ev	-ev	19
7	[CdCl ₂ (NPB) ₂]	8	-ev	35
8	[PdCl ₂ (NPB) ₂]	8	-ev	12

4. Conclusion and future scope

Utilizing molar conductivity, magnetic moment, and various spectroscopic analyses (including FT-IR, UV-Vis, ¹H-¹³C NMR, and atomic absorption), we have ascertained that the ligand NPB exhibits bidentate ligand behavior when binding with Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), and Pd(II) ions. Specifically, the oxygen atom of the amido group (C=O) and the sulfur atom of the thioamide group (C=S) are the primary sites of coordination with the metal ion. This observation supports the notion of an octahedral geometry around the metal ion for all the synthesized complexes in Scheme 2.

Furthermore, our FT-IR studies on the NPB ligand indicate its coordination through the aforementioned functional groups. This coordination leads to noticeable shifts in the chemical shifts

of the ligand peaks in the FT-IR spectra, implying the formation of stable complexes. In summary, our investigation provides valuable insights into the coordination behavior of the NPB ligand with diverse metal ions and offers a comprehensive understanding of the structures of the prepared complexes through a range of analytical techniques.



Scheme2: octahedral geometry of complexes

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