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Synthesis, Characterization and Antibacterial Activity of some Hg(II) Complexes with Mixed Benzyl 2-(2-oxoindolin-3-ylidene) Hydrazinecarbodithioate and Phosphines or Amines Ligands

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ABSTRACT

Isatin-derived schiff bases with S-dithiocarbazate ester and their complexes are increasingly important for antibacterial activity, so new Hg complexes were prepared with benzyl 2-(2-oxoindolin-3-ylidene) hydrazinecarbodithioate (BHT) and diphosphines (dppm, dppe, dppp and dppb) or amines (bipy, phen). The phosphine complexes have the given formulas $[Hg_2(BHT)_2\mu(dppm)_2]Cl_4$, [Hg(BHT)(diphosphine)Cl]Cl (diphosphine; dppm, dppe), while the amine complexes have the formulas; $[Hg(BHT)(amines)]Cl_2$. The prepared complexes have been characterized by molar conductivity, elemental analysis, FTIR, ^{31}P-NMR and ^{1}H-NMR. Furthermore, this study concludes the evaluation of biological activity of prepared complexes against three bacterial species *Staphylococcus Epidermidis* and *Staphylococcus aureus* (gram positive) and *Citrobacer Freundii* (gram negative) by Agar well method where the antibiotic Amikacin used as a comparison material, prepared complex $[Hg(BHT)(bipy)]Cl_2$ showed activity against *Staphylococcus aureus* more than amikacin, while the $[Hg_2(BHT)_2\mu(dppe)_2]Cl_4$, $[Hg(BHT)(bipy)]Cl_2$ and $[Hg(BHT)(Phen)]Cl_2$ complexes showed activity against *Staphylococcus Epidermidis* more than amikacin, the $[Hg_2(BHT)_2\mu(dppe)_2]Cl_4$, $[Hg(BHT)(dppb)]Cl_2$, $[Hg(BHT)(bipy)]Cl_2$ and $[Hg(BHT)(Phen)]Cl_2$ complexes showed activity against *Citrobacter freundii* more than amikacin in the minimum concentration.

Keyword: Isatin, Dithiocarbazide, Mercury complexes, Diphosphines, Biological activity.

Introduction

Metal complexes of schiff bases containing S-dithiocarbazate ester have been the subject of considerable studies due to their hard N and soft S donor atoms which enable the Schiff bases to easily coordinate with metals.[1-3] Schiff bases derived from S-benzyldithiocarbazate with 5-haloisatins were found to be selectively active towards MCF-7 cancer cell,[4,5] S-dithiocarbazate compounds have a large range of applications like antimicrobial agent.[6,7] Isatin is a resourceful endogenous heterocyclic molecule identified in human being and rat tissues. In recent years, isatin and its derivatives have acquired conspicuous significance due to their wide spectrum biological activities.[8] Isatin schiff bases containing S-dithiocarbazate ester have shown coordination patterns with different metal ions because they contain donor nucleus at suitable positions. The coordination patterns can be bidentate through the N atom of the azomethin group and the S atom of the thion group.[9,10] The coordination also can be tridentate by incorporating the Oxygen of the carbonyl group in the Isatin.[11,12]
Isatin derived Schiff bases and their complexes are known to have antibacterial and antifungal activity.[13,14] Furthermore, the Schiff bases of isatin were also reported to possess cytotoxic and anticonvulsant activity.[15,16]
The anticancer evaluation of a substantial number of metal complexes containing isatin-based ligands has been described as antitumor compounds, especially Mg(II), Co(II), Ni(II), and Cu(II) complexes, with different coordination geometries and reactivities.[17]

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Materials and Methods

All the chemicals, reagents and solvents for the synthesis of compounds were supplied and used without more purification. The melting point of the prepared complexes was recorded on Automatic (SMP30) melting point apparatus. The molar conductivity of 10^{-3} M freshly DMSO solution of prepared complexes was measured using (Starter 3100c) digital conductivity meter at 25^{o}C. Microanalyses for carbon, hydrogen, nitrogen and sulfur were carried out using an Elementar vario El III CHN elemental analyzer. The IR spectra of the prepared complexes as KBr pellets were recorded using a Shimadzu FT-IR 8400S spectrophotometer (400-4000 cm^{-1}). NMR spectra were acquired on a Bruker 400 MHz spectrometer in DMSO-d6 as a solvent. The isolates of the pathological bacteria that were used in the research obtained from the laboratories of the Department of Life Sciences in the College of Education for Pure Sciences at the University of Tikrit.

Preparation of benzyl 2-(2-oxoindolin-3-ylidene)hydrazinecarbodithioate (BHT) ligand
The benzyl 2-(2-oxoindolin-3-ylidene)hydrazinecarbodithioate (BHT) Prepared by two steps:
First step: Preparation of S-Benzyldithiocarbazate (SBDTC). This compound was synthesized as previously reported,[18] the melting point was 124^{o}C where it was at 124–125^{o}C in the literature.[19]
Second step: To the hot solution of S-benzyldithiocarbazate, SBDTC (1.36g, 0.01 mol) in ethanol (35 mL), an equimolar amount of isatin

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(1.471g, 0.01mol) was added. The mixture was heated under stirring for 15 min and later allowed to stand for 20 min until a solid product was formed. Thereafter, the mixture was filtered, washed with ethanol and the required product was recrystallized from ethanol.[19]

(BHT) Orange precipitate from ethanol, (2.485 g), yields 76%, mp: 232°C–235°C. FTIR(KBr): 3180m, 3064w, 2956w, 1695s, 1618m, 1583m, 1461s, 1230s, 1147s, 1064s, 977m, 784m. ^{1}H-NMR (DMSO-d6) δ(ppm): 13.97 (s, 1H, NH), 11.36 (s, 1H, NH, isatin), 7.53 (d, ^{3}J=7.55 Hz, 1H), 7.46 (d, ^{3}J=7.43Hz, 2H), 7.41 (t, ^{3}J=7.75Hz, 1H), 7.36 (t, ^{3}J=7.49Hz, 2H), 7.30 (t, ^{3}J=7.19Hz, 1H), 7.07 (t, ^{3}J=7.54 Hz, 1H), 6.95 (d, ^{3}J=7.83Hz, 1H), 4.56 (s, 2H, CH_2, BHT). ^{13}C-NMR (DMSO-d6): δ 39.02 (S-CH_2), 112.50-140.0 (aromatic), 129.46 (C=N), 164.89 (C=O), 193.78 (C=S) ppm. Elemental analysis calculated for $C_{16}H_{13}N_3OS_2$: C, 58.69; H, 4.00; N, 12.83; S, 19.59. Found: C, 58.35; H, 3.72; N, 12.43; S, 19.22. Λo (Ω^{-1}.cm^2.mol^{-1}):4.62.

Synthesis of [Hg(BHT)(diphos.)]Cl_2 complexes

diphos.= dppm, dppe, dppp, dppb

A solution of $HgCl_2$ (1.086 g, 0.00 4 mol) in absolute ethanol (20 ml) was added to the solution of one mole equivalent of diphosphine (dppm, dppe, dppp or dppb) in absolute ethanol (20 ml). The mixture was refluxed for two hours and a white suspension was formed. A solution of BHT (1.308 g, 0.004 mol) in absolute ethanol (20 ml) was added to the white suspension, and then the mixture stirred for three hours at 25^{o}C. Then the mixture was filtered, washed with hot ethanol and dried in desiccators over calcium chloride for 4 days, as shown as (Figure 1).

[Hg_2(BHT)$_2$μ(dppm)$_2$]Cl_4 and [Hg(BHT)(dppm)Cl]Cl **(1)** Orange from ethanol, (6.133g), yields 78%, mp: 290°C (decomposition). FTIR(KBr): 3411m, 3051m, 2960m, 1695s, 1622s, 1533s, 1433s, 1095m, 1026m, 744s, 694m, 646w. ^{13}P{^{1}H}NMR (DMSO-d6): [Hg_2(BHT)$_2$μ(dppm)$_2$]Cl_4 **(1a)** δ30.27ppm, [Hg(BHT)(dppm)Cl]Cl **(1b)** 30.21ppm (d, $^{2}J_{PP}$=47.01Hz), -14.32ppm (d, $^{2}J_{PP}$=47.35Hz), ^{1}H-NMR (DMSO-d6) δ(ppm): 13.90 (s, 1H, NH), 11.29 (s, 1H, NH, isatin), 7.91 (d, ^{3}J=7.19 Hz, 2H), 7.70 (t, ^{3}J=7.31Hz, 1H), 7.63 (t, ^{3}J=7.63Hz, 3H), 7.46, 7.34 (m, 21H, BHT, 4Ph), 7.15 (t, ^{3}J=7.48 Hz, 1H), 6.97 (d, ^{3}J=7.76Hz, 1H), 4.55 (s, 2H, CH_2, BHT), 2.97 (s, 2H, CH_2,dppm). Elemental analysis calculated for $C_{82}H_{70}Cl_4Hg_2N_6O_2P_4S_4$: C, 50.08; H, 3.59; N, 4.27; S, 6.52. Found: C, 49.73; H, 3.32; N, 4.13; S, 6.37. Λ$_o$ (Ω^{-1}.cm^2.mol^{-1}):137.74.

[Hg_2(BHT)$_2$μ(dppe)$_2$]Cl_4 **(2a)** and [Hg(BHT)(dppe)Cl]Cl **(2b)** Orange from ethanol, (3.269g), yields 82%, mp: 272-175°C. FTIR(KBr): 3417m, 3068m, 2926m, 1699s, 1618s, 1431m, 1097m, 1024m, 694m, 642w. ^{13}P{^{1}H}NMR (DMSO-d6): [Hg_2(BHT)$_2$μ(dppe)$_2$]Cl_4 **(2a)** δ28.34ppm, [Hg(BHT)(dppe)Cl]Cl **(2b)** 30.33ppm (d, $^{2}J_{PP}$=50.05Hz), -29.08ppm (d, $^{2}J_{PP}$=50.72Hz), ^{1}H-NMR (DMSO-d6) δ(ppm): 13.92 (s, 1H, NH), 11.30 (s, 1H, NH, isatin), 7.92 (d, ^{3}J=8.34 Hz, 2H), 7.71 (t, ^{3}J=7.26Hz, 1H), 7.64 (t, ^{3}J=7.35Hz, 3H), 7.42 (t, ^{3}J=7.76Hz, 3H), 7.52 (m, 20H, 4Ph), 7.14 (t, ^{3}J=7.57 Hz, 1H), 6.98 (d, ^{3}J=7.83Hz, 1H), 4.53 (s, 2H, CH_2, BHT), 2.04 (t, ^{3}J=4.36Hz, 2H, CH_2,dppe). Elemental analysis calculated for $C_{42}H_{37}Cl_2HgN_3OP_2S_2$: C, 50.58; H, 3.74; N, 4.21; S, 6.43. Found: C, 50.15; H, 3.38; N, 4.35; S, 5.97. Λ$_o$ (Ω^{-1}.cm^2.mol^{-1}):81.34.

[Hg(BHT)(dppp)]Cl_2 **(3)** Orange from ethanol, (3.477g), yields 86%, mp: 258–261°C. FTIR(KBr): 3417s, 3050w, 2921m, 1695m, 1629s, 1433m, 1099m, 1026w, 692m, 644w. ^{13}P{^{1}H}NMR (DMSO-d6): δ32.04ppm. ^{1}H-NMR (DMSO-d6) δ(ppm): 13.90 (s, 1H, NH), 11.23 (s, 1H, NH, isatin), 7.91 (d, ^{3}J=8.26 Hz, 2H), 7.70 (t, ^{3}J=7.69Hz, 1H), 7.63 (t, ^{3}J=7.35Hz, 3H), 7.53, 7.33 (m, 20H, 4Ph), 7.41 (t, ^{3}J=7.56Hz, 3H),7.12 (t, ^{3}J=7.54 Hz, 1H), 6.97 (d, ^{3}J=7.74Hz, 1H), 4.53 (s, 2H, CH_2, BHT), 2.22 (t, ^{3}J=7.49Hz, 4H, 2CH_2, dppp), 1.44 (m, 2H, CH_2, dppp). Elemental analysis calculated for $C_{43}H_{39}Cl_2HgN_3OP_2S_2$: C, 51.07; H, 3.89; N, 4.15; S, 6.34. Found: C, 50.76; H, 3.39; N, 4.37; S, 5.92. Λ$_o$ (Ω^{-1}.cm^2.mol^{-1}):79.51.

[Hg(BHT)(dppb)]Cl_2 **(4)** Pale orange from ethanol, (3.484g), yields 85%, mp: 274–277°C. FTIR(KBr): 3456s, 3058w, 2920w, 1693m, 1625m, 1433m, 1099m, 1024w, 694m, 645w. ^{13}P{^{1}H}NMR (DMSO-d6): δ30.20ppm. ^{1}H-NMR (DMSO-d6) δ(ppm): 13.91 (s, 1H, NH), 11.25 (s,1H, NH, isatin), 7.90 (d, ^{3}J=7.34 Hz, 2H), 7.70 (t, ^{3}J=6.18Hz, 1H), 7.63 (t, ^{3}J=7.13Hz, 3H), 7.51, 7.35 (m, 20H, 4Ph), 7.42 (t, ^{3}J=7.15Hz, 3H),7.13 (t, ^{3}J=7.88 Hz, 1H), 6.97 (d, ^{3}J=7.84Hz, 1H), 4.55 (s, 2H, CH_2, BHT), 2.22 (t, ^{3}J=6.88Hz, 4H, 2CH_2, dppb), 1.44 (m, 4H, 2CH_2, dppb). Elemental analysis calculated for $C_{44}H_{41}Cl_2HgN_3OP_2S_2$: C, 51.54; H, 4.03; N, 4.10; S, 6.25. Found: C, 51.12; H, 3.75; N, 4.29; S, 5.83. Λ$_o$ (Ω^{-1}.cm^2.mol^{-1}):81.64.

Synthesis of [Hg(BHT)(bipy)]Cl_2 (5) and [Hg(BHT)(phen)]Cl_2 (6) complexes

A solution of bipy (0.468 g, 0.003 mmol) or Phen (0.540 g, 0.003 mmol) in EtOH (10 ml) was added to the solution of $HgCl_2$ (0.814g, 0.003mmol) in absolute ethanol (20ml), the mixture was stirred for an hour at 25^{o}C, then BHT (0.981 g, 0.003mmol) was added to the above mixture. Thereafter, the final mixture was refluxed for two hours under stirring. The produced orange precipitate was initially filtered, washed several times with ethanol and then dried in desiccators over calcium chloride for 4 days, as shown as (Figure 2).

[Hg(BHT)(bipy)]Cl_2 **(5)** Orange precipitate from ethanol, (2.384g), yields 79%, mp: 156–159°C. FTIR(KBr) (cm^{-1}): 3413 (m), 3050 (m), 2900 (w), 1695 (s), 1620 (m), 1595 (m), 1095 (m), 1018 (m), 649 (m). ^{1}H-NMR (DMSO-*d*6) δ(ppm): 13.90 (s, 1H, NH), 11.26 (s, 1H, NH, isatin), 8.69 (d, 2H, ^{3}J = 3.82 Hz, bipy), 8.40 (d, ^{3}J = 7.85 Hz, 2H, bipy), 7.96 (td, ^{3}J = 7.69 Hz, ^{4}J = 1.80 Hz 2H, bipy), 7.91 (d, ^{3}J = 7.11 Hz, 2H), 7.69 (t, ^{3}J=7.07 Hz, 1H), 7.62 (t, ^{3}J = 7.82 Hz, 3H), 7.46 (m, 2H, bipy), 7.41 (t, ^{3}J = 8.27 Hz, 1H), 7.13 (t, ^{3}J = 7.55 Hz, 1H), 6.99 (d, ^{3}J = 7.70 Hz, 1H), 4.53 (s, 2H, CH_2). ^{13}C{^{1}H}NMR (DMSO-*d*6) δ(ppm): 193.97, 163.92, 153.84, 148.44, 139.31, 138.50, 137.81, 129.47, 128.66, 127.46, 124.61, 122.26, 121.89, 120.83, 112.08, 39.02. Elemental analysis calculated for $C_{26}H_{21}Cl_2HgN_5OS_2$: C, 41.36; H, 2.80; N, 9.27; S, 8.49. Found: C, 41.12; H, 2.31; N, 8.87; S,8.09. Λ$_o$ (Ω^{-1}.cm^2.mol^{-1}):73.85.

[Hg(BHT)(phen)]Cl_2 **(6)** Pale orange precipitate from ethanol, (2.523 g), yields 81%, mp: 247°C (decomposition). FTIR(KBr) (cm^{-1}): 3423 (m), 3049 (m), 2935 (w), 1695 (s), 1620 (m), 1585 (m), 1099 (m), 1027 (m), 642 (m). ^{1}H-NMR (DMSO-*d*6) δ(ppm): 13.91 (s, 1H, NH), 11.25 (s, 1H, NH, isatin), 9.19 (s, 2H, Phen), 8.80 (d, ^{3}J = 8.15 Hz, 2H, Phen), 8.20 (s, 2H, Phen), 8.07 (m, 2H, Phen), 7.90 (d, ^{3}J = 8.07 Hz, 2H), 7.70 (t, ^{3}J = 7.33 Hz, 1H), 7.62 (t, ^{3}J=7.89 Hz, 3H), 7.40 (t, ^{3}J=7.71 Hz, 1H), 7.13 (t, ^{3}J=7.55 Hz, 1H), 6.98 (d, ^{3}J=7.75 Hz, 1H), 4.54 (s, 2H, CH_2). ^{13}C{^{1}H}NMR (DMSO-*d*6) δ(ppm): 194.00, 163.91, 149.45, 144.60, 139.31, 138.50, 135.80, 134.18, 130.61, 129.42, 128.66, 127.50, 125.76, 122.94, 122.19, 120.87, 112.08, 39.02. Elemental analysis calculated for $C_{28}H_{21}Cl_2HgN_5OS_2$: C, 43.16; H, 2.72; N, 8.99; S, 8.23. Found: C, 42.75; H, 2.53; N, 7.91; S, 8.32. Λ$_o$ (Ω^{-1}.cm^2.mol^{-1}):75.16.

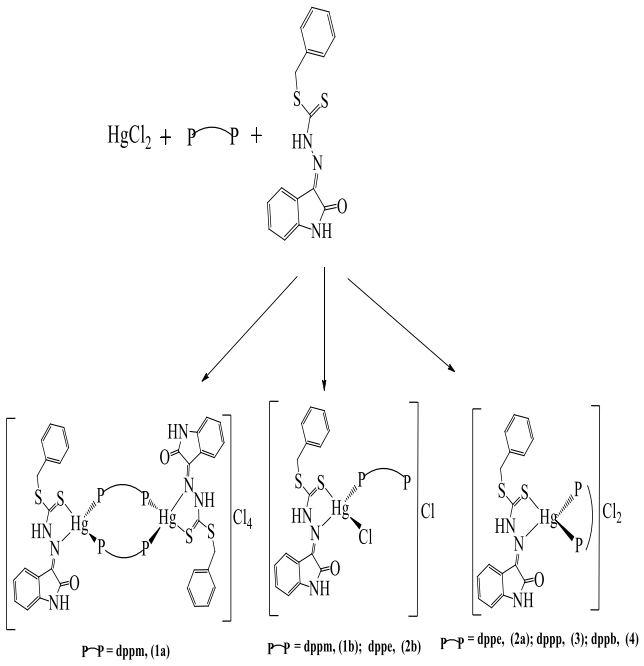

Figure 1: suggested structure of complexes [Hg_2(BHT)$_2$(μ-dppm)$_2$]Cl_4

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(1a), [Hg(BHT)(dppm)Cl]Cl **(1b)**, [Hg(BHT)(dppe)]Cl_2 **(2a)**, [Hg(BHT)(dppe)Cl]Cl **(2b)**, [Hg(BHT)(dppp)]Cl_2 **(3)**, [Hg(BHT)(dppb)]Cl_2 **(4).**

The biological evaluation method

The evaluation of biological activity of prepared complexes with three different concentrations (0.01, 0.001, 0.0001 mg/mL) against two bacterial types *Staphylococcus Epidermidis* and *Staphylococcus aureus* (Gram positive) and *Citrobacer Freundii* (Gram negative) by Agar well method.[30] The antibiotic Amikacin (0.001 mg/mL) was used as a positive control. The culture medium was prepared and then poured in Petri dishes and then left to be hardened. A quantity of activated bacteria was taken by a swab and placed on the culture medium Muller Hinton Agar by wiping it completely and was left for half an hour until it was absorbed, then the drilling was prepared using a sterile cork punch with a diameter of 5mm. Then four pits were made and 1 ml of the solutions of the compounds prepared was added in each pit with different concentrations .Then all the dishes were incubated for a period of (24 hours). Inhibition of the used bacteria was observed. Then the inhibition zone diameter of each complex was measured using a millimeter ruler and an average of three results was taken for each. Concentration with each bacterial species used, then compared with the average of the inhibition range of the antibiotic (amikacin).

Results and Discussion

Elemental analyses and conductivity measurements

The data prove the formation of the complexes with 1:1:1 (Hg ion: BHT ligand: diphos.) ratio. The methods used for the preparation of the mixed ligand complexes afforded high purity materials as supported by the analysis results. The complexes were stable in air. The prepared complexes were partially soluble in methanol, ethanol and acetone solvents and completely soluble in DMF or DMSO. The molar electrical conductivity of the prepared complexes was recorded as DMSO solutions at (25°C,10^{-3}M). The results showed that all the prepared complexes were within the range (73.85-81.64 $\Omega^{-1}.cm^2.mol^{-1}$), indicating the complexes **(2a)** and (3-6) were 1:2 electrolytes, while the complexes **(1b)** and **(2b)** were 1:1 electrolytes. Finally, the complex $[Hg_2(BHT)_2\mu(dppm)_2]Cl_4$ **(1a)** showed molar conductivity value (137.74 $\Omega^{-1}.cm^2.mol^{-1}$) indicating that this complex was 1:4 electrolytes.[20,21] This would probably lead to form a tetrahedral arrangement on the central Hg ion of the complexes and exclude the octahedral arrangement.

Infrared spectra

The spectrum of (BHT) ligand displayed the characteristic band of the azomethine group υ(C=N) at (1618 cm^{-1}) with the disappearance of the stretching band of υ(C=O) carbonyl ketone group in the free isatin which was at (1730 cm^{-1}). The υ(C=O) carbonyl of amide group appeared at (1695 cm^{-1}), while the υ(NH) group appeared at (3180cm^{-1}). Moreover, the spectrum showed the band of the υ(C=S) group at (1064cm^{-1}), [4] and the band of the υ(N-N) at (1149cm^{-1}).[2] IR spectra of the **(1-6)** complexes showed the υ(C=O) and υ(C=N) bands at the ranges (1693-1699cm^{-1}) and (1618-1629cm^{-1}), respectively. However, the bands of υ(C=N) was shifted to little higher frequency, indicates that the N atom bonded to the metal ion.[5] The IR spectra of the (BHT) ligand does not display υ(S–H) at (ca. 2570 cm^{-1}), indicates that the (BHT) ligand in solid-state remain in the thione form, where the υ(C=S) band was observed at (1095-1099 cm^{-1}), this bands shifted to higher frequency, indicates the S atom bonded to the metal ion. The υ(P-Ph) band of the **(1-4)** complexes were displayed within the range (1433-1431cm^{-1}), the two υ(P-C) bands were observed within the range (692-694 cm^{-1}).[22-24] The υ(C=N) bands of bipy and Phen in **(5, 6)** complexes were observed at (1595, 1585 cm^{-1}), respectively.[25]

NMR Spectra

^{1}H-NMR spectrum of (BHT) ligand displayed two singlets at (**δ**H=13.97ppm) and (**δ**H=11.36ppm) which are attributed to of the NH groups of hydrazone and isatin, respectively. Additionally, the spectrum displayed a doublet signal at (**δ**H=7.53ppm) due to H_a with a coupling constant of ($^3J_{Ha\text{-}Hb}$=7.55Hz). The spectrum also showed a doublet signal at (**δ**H=7.46ppm) due to H_e with a coupling constant of ($^3J_{He\text{-}Hf}$ = 7.45 Hz) whilethe protons of H_f and H_g appeared as two triplet signals at (δ_H = 7.41 ppm) and (δ_H = 7.36 ppm) with a coupling constant of ($^3J_{Hf\text{-}Hg}$ = 7.75 Hz) and ($^3J_{Hg\text{-}Hf}$ = 7.49 Hz), respectively. Moreover, the two triplets at (δ_H = 7.30ppm) and (δ_H = 7.07 ppm) with a coupling constant of ($^3J_{Hc\text{-}Hb}$ = 7.19 Hz) and ($^3J_{Hb\text{-}Hc}$ = 7.54 Hz) due to H_c, H_b, respectively. Finally, the spectrum showed a doublet signal at (δ_H = 6.95ppm) due to H_d with a coupling constant of ($^3J_{Hd\text{-}Hc}$ = 7.53 Hz) and the protons of CH_2 appeared as a singlet signal at (δ_H = 4.56 ppm).[5]

^{1}H-NMR spectra of the complexes **(1-4)** showed signals of CH_2 groups of phosphines as a singlet at (δ_H = 2.97 ppm, 2H) due to dppm, triplet at (δ_H = 2.04 ppm, 4H) due to dppe, triplet at (δ_H = 2.22 ppm, 2H) and quintet at (δ_H = 1.43 ppm, 4H) due to dppp, and two triplets at (δ_H = 2.22ppm, 4H), (δ_H = 1.45 ppm, 4H) due to dppb. The protons of phenyl groups of diphosphines showed multiplets within the (δH=7.33-7.53ppm) range. ^{1}H-NMR spectra of prepared complexes **(5,6)** appeared signals of protons of bipy ligand as a doublets at (δ_H = 8.69 ppm)(^3J = 3.82 Hz, 2H) due to H1, doublet at (δ_H = 8.40 ppm) (^3J = 7.85 Hz, 2H) due to H4, triplet of doublets at (δ_H = 7.96 ppm) (^3J = 7.69 Hz, ^4J = 1.80 Hz, 2H) due to H3, and a multiplet at (δ_H = 7.46 ppm) (2H) due to H2, the protons of Phen ligand as a, singlet at (δ_H = 9.19 ppm) (2H) due to H1, doublet at (δ_H = 8.80 ppm) (^3J = 8.15 Hz, 2H) due to H3, singlet at (δ_H = 8.20ppm) (2H) due to H4, doublet of doublets at (δ_H = 8.07 ppm) (^3J = 8.08 Hz, ^4J = 4.69 Hz, 2H) due to H2.

^{13}C{^{1}H}NMR spectrum of prepared complexes (5,6) showed a signal at (199.97, 199.50 ppm) respectively which is attributed to the carbon of (C=S) group, a signal at (163.92, 163.91 ppm), respectively which is attributed to the carbon of (C=O) group, a signal at (129.47, 129.42 ppm) respectively which is attributed to the carbon of (C=N) group, a signal at (39.02 ppm) which is attributed to the carbon of (S-CH_2) group. The remaining signals observed in the region of (112.08–153.84 ppm) may be assigned to carbons in the aromatic ring.

^{13}P{^{1}H}NMR spectrum of complex **(1)** displayed tow isomers, the mine isomer **(1a)** showed singlet at δ28.13ppm this indicated that the two phosphorus atoms were equivalent and the dppm ligand behaved as a bridge bidentate ligand,[26] as shown as (Figure 3), the other isomer **(1b)** showed two doublets at 33.35ppm ($^2J_{PA\text{-}PX}$ = 50.05 Hz), -29.28 ppm ($^2J_{PX\text{-}PA}$ = 50.69 Hz), this indicated that the two phosphorus atoms were nonequivalent and the dppm ligand behaved as a monodentate ligand through the P atom that positive chemical shift. The ^{13}P{^{1}H}NMR of complex **(2),** as shown as (Figure 4), displayed tow isomers, the first isomer **(2a)** showed singlet at δ31.43ppm, this indicated that the two phosphorus atoms were equivalent and the dppe ligand behaved as a bidentate ligand.[27] The second isomer **(2b)** showed two doublets at 31.36ppm ($^2J_{PA\text{-}PX}$=47.23Hz), -14.40ppm ($^2J_{PX\text{-}PA}$=44.63Hz), this indicated that the two phosphorus atoms were nonequivalent and the dppe ligand behaved as a monodentate ligand through the P atom that positive chemical shift. However, we were unable to separate the two isomers of complex **(1)** and complex **(2)** in solid state. The ^{13}P{^{1}H}NMR spectra of prepared complexes **(3,4)** showed singlet at δ27.83ppm, 30.02ppm respectively this clearly indicated that the two phosphorus atoms were equivalent and the dppp and dppb ligands behaved as bidentate ligands.[28,29]

Biological activity of the prepared complexes

The prepared complexes have shown antibacterial activity against the three bacterial species in this study in comparison with Amikacin. In addition, the effectiveness of complexes **(5,6)** was higher than that of complexes **(1-4)**. All complexes showed activity against *Staphylococcus aureus* but the complex **(5)** showed activity against *Staphylococcus aureus* more than the other complexes and amikacin at minimum concentration, while the **(2,5,6)** complexes showed activity against *Staphylococcus Epidermidis* mor than amikacin at minimum concentration, the complex **(5)** specialy and the complexes **(2, 4, 6)** showed activity against *Citrobacter freundii* more than amikacin in the minimum concentration, as shown in (Table 1).

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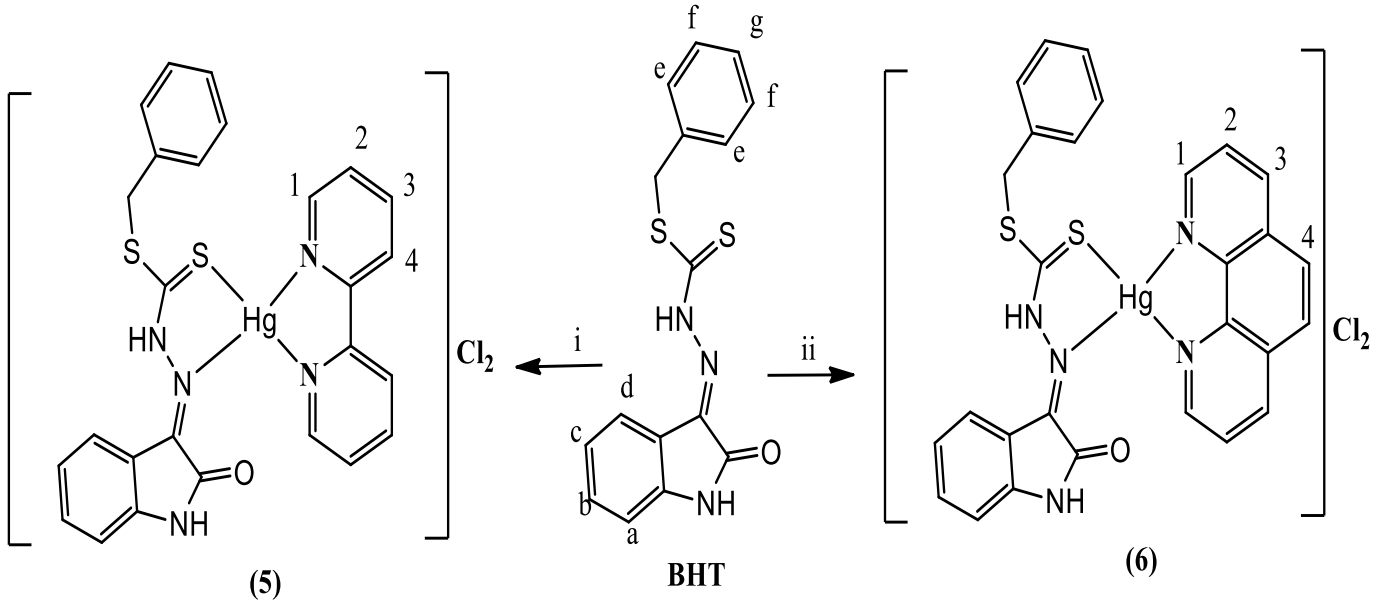

Figure 2: Preparation of complexes [Hg(BHT)(bipy)]Cl_2 **(5)** (i = [Hg(bipy)Cl_2], EtOH, reflux 2h) and [Hg(BHT)(phen)]Cl_2 **(6)** (ii = [Hg(phen)Cl_2], EtOH, reflux 2h)

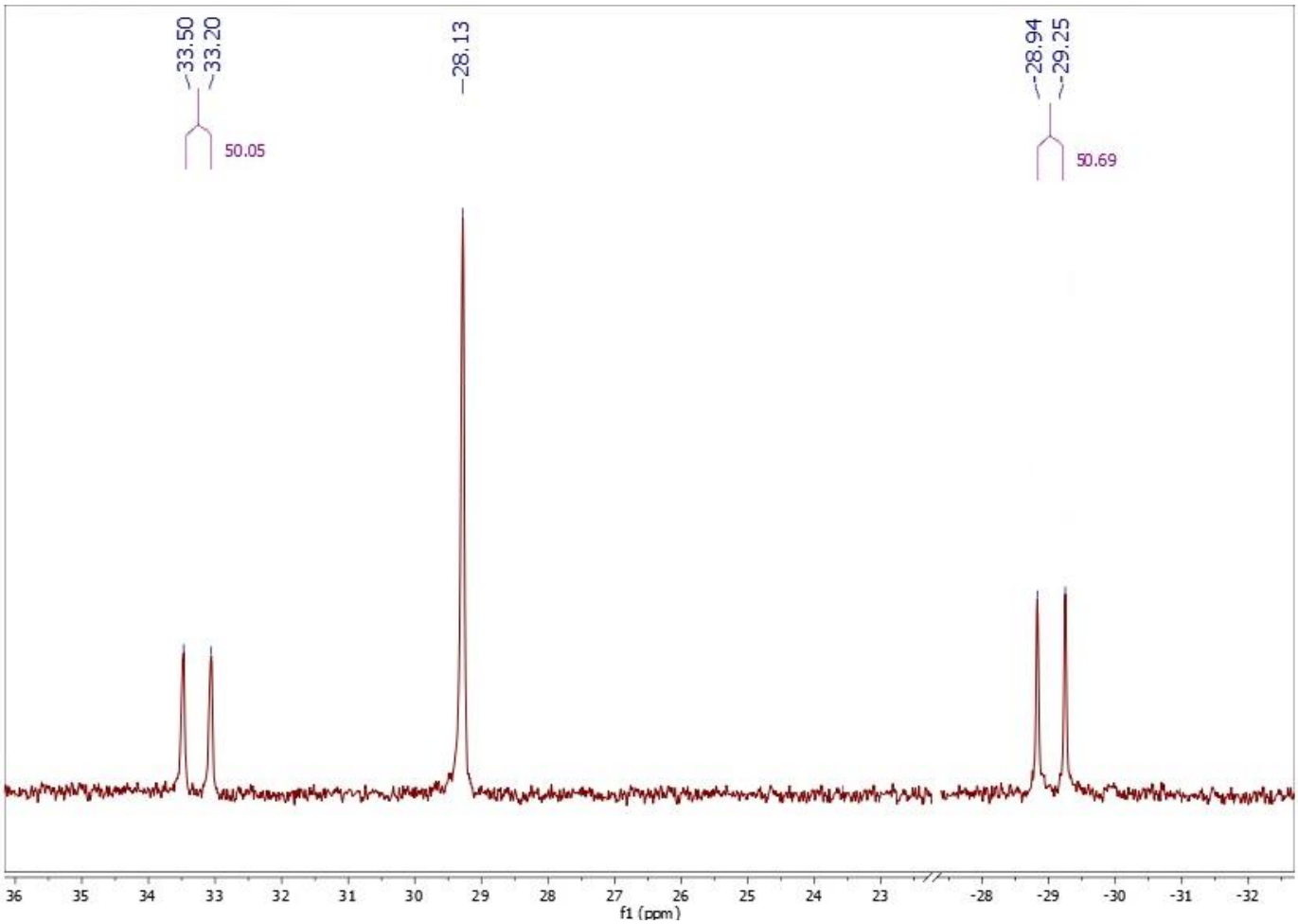

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Figure 3: ^{31}P-{^{1}H} NMR Spectrum of isomers $[Hg_2(BHT)_2\mu(dppm)_2]Cl_4$ **(1a)** and Hg(BHT)(dppm)Cl]Cl **(1b)**

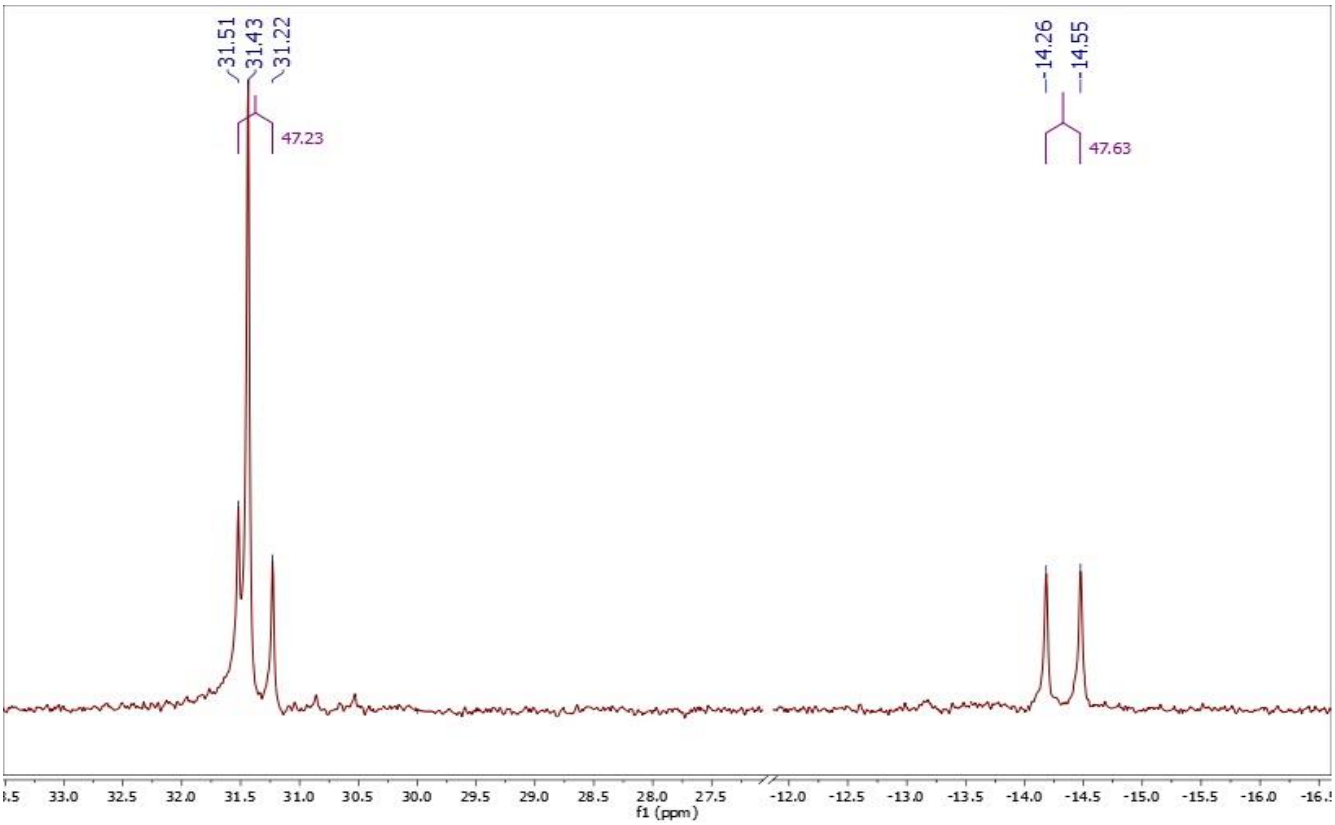

Figure 4: ^{31}P-{^{1}H} NMR Spectrum of isomers $[Hg(BHT)\mu(dppe)]Cl_2$ **(2a)** and [Hg(BHT)(dppe)Cl]Cl **(2b)**

Table 1: The Zone Inhibition in (mm) of Antibacterial of Prepared Complexes

			Staphylococcus aureus				
Concentration	**complex 1**	**complex 2**	**complex 3**	**complex 4**	**complex 5**	**complex 6**	**Amikacin**
0.01 mg/ml	36	36	33	33	39	37	-
0.001 mg/ml	34	35	32	32	37	35	30
0.0001 mg/ml	31	32	30	30	34	33	-
			Staphylococcus epidermidis				
Concentration	**complex 1**	**complex 2**	**complex 3**	**complex 4**	**complex 5**	**complex 6**	**Amikacin**
0.01 mg/ml	21	22	17	22	24	25	-
0.001 mg/ml	18	19	16	18	21	23	15
0.0001 mg/ml	14	17	14	15	19	20	-
			Citrobacter freundii				
Concentration	**complex 1**	**complex 2**	**complex 3**	**complex 4**	**complex 5**	**complex 6**	**Amikacin**
0.01 mg/ml	17	23	19	24	23	25	-
0.001 mg/ml	16	22	17	22	21	22	17
0.0001 mg/ml	14	20	16	19	22	20	-

Conclusion

The prepared complexes **(1-6)** has been tetrahedral complexes, the (BHT) ligand behaves as a bidentate through the N atom and S atom and diphosphines or amines ligands behaves as a bidentate through the P atoms or N atoms respectively. The evaluation of biological activity of prepared complexes against bacterial types *Staphylococcus Epidermidis* and *Staphylococcus aureus* (gram positive) and *Citrobacer Freundii* (gram negative), the prepared complex

$[Hg(BHT)(bipy)]Cl_2$ **(5)** showed activity against *Staphylococcus aureus* more than amikacin, while the $[Hg_2(BHT)_2\mu(dppe)_2]Cl_4$ **(2)**, $[Hg(BHT)(bipy)]Cl_2$ **(5)** and $[Hg(BHT)(Phen)]Cl_2$ **(6)** complexes showed activity against *Staphylococcus Epidermidis* more than amikacin, the $[Hg_2(BHT)_2\mu(dppe)_2]Cl_4$ **(2)**, $[Hg(BHT)(dppb)]Cl_2$ **(4)**, $[Hg(BHT)(bipy)]Cl_2$ **(5)** and $[Hg(BHT)(Phen)]Cl_2$ **(6)** complexes showed activity against *Citrobacter freundii* more than amikacin in the minimum concentration.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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