ISSN 1070-3632, Russian Journal of General Chemistry, 2020, Vol. 90, No. 6, pp. 1069–1073. © Pleiades Publishing, Ltd., 2020.

Synthesis, Characterization, and Antibacterial Activity of Complexes of Hg(II) with Mixtures of 3-Hydrazonoindolin-2-one and Diphosphine, or Diimine Ligands

A. A. Irzoqi[a],*, M. M. Salih[a], H. M. Jirjes[b], and M. K. Mensoor[c]

[a] *Department of Chemistry, College of Education for Pure Science, University of Tikrit, Tikrit, 34001 Iraq*
[b] *Department of Chemistry, College of Science, University of Tikrit, Tikrit, 34001 Iraq*
[c] *International Center for Training, Research and Development (ICTRD), Baghdad, 10011 Iraq*
**e-mail: ahmedirzoqi@tu.edu.iq*

Received April 5, 2020; revised May 27, 2020; accepted May 30, 2020

Abstract—In the current study, six new tetrahedral Hg(II) complexes of 3-hydrazonoindolin-2-one (HZI) with diphosphines (dppm, dppe, dppp, dppb) or diimines (bipy, phen) ligands have been prepared and characterized by molar conductivity, IR, ^{1}H, ^{13}C, and ^{31}P NMR spectra. Antibacterial activity of these complexes has been tested against three bacterial species: *Staphylococcus epidermidis* and *Staphylococcus aureus* (gram positive) and *Citrobacer freundii* (gram negative). All complexes are more active against *Staphylococcus aureus* than amikacin, while $[Hg_2(HZI)_2(dppm)_2]Cl_4$ (**1**), $[Hg(HZI)(dppe)]Cl_2$ (**2**), and $[Hg(HZI)(Phen)]Cl_2$ (**6**) complexes are more active against *Staphylococcus epidermidis* than amikacin. The complexes **2**, $[Hg(HZI)(dppp)]Cl_2$ (**3**), and **6** are active against *Citrobacter freundii*.

Keywords: isatin, shiff base, mercury complexes, diphosphines, antibacterial activity

DOI: 10.1134/S1070363220060213

INTRODUCTION

Isatin hydrazone derivatives can act as chelating ligands and demonstrate antibacterial, antifungal, anticonvulsant, and anti-HIV activities [1, 2]. High affinity to chelation of the Schiff bases towards transition metal ions is employed in preparing their complexes [3] that are characterized by a wide range of antibacterial [4, 5], antifungal [5, 6], antimicrobial [4, 7], and many other activities [8, 9].

The current study targeted synthesis of some Hg(II) complexes with 3-hydrazonoindolin-2-one (HZI) ligand in combination with phosphine or imine derivatives, and testing their biological activity against three bacterial species *Staphylococcus epidermidis* and *Staphylococcus aureus* (gram positive, and *Citrobacer freundii* (gram negative) using the antibiotic amikacin as a standard.

RESULTS AND DISCUSSION

The complexes under study (Schemes 1, 2) were characterized by the ratio of their components Hg(II): HZI ligand: diphosphine or diamine derivatives 1 : 1 : 1. They were determined to be stable in the air, partially soluble in common organic solvents and well soluble in DMF and DMSO.

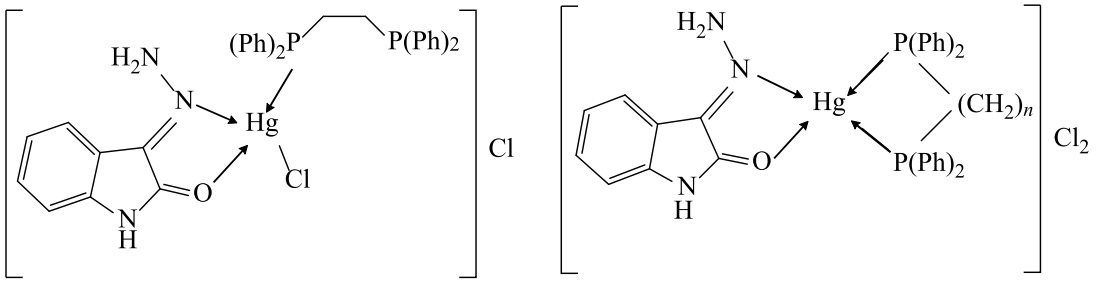
Electrical conductivity of the prepared complexes measured in DMSO solutions (10^{-3} M) was within the range of 70.86 to 84.67 Ω^{-1} cm^2 mol^{-1}, and indicated the complexes **2**–**6** as 1 : 2 electrolytes. While the complex $[Hg(HZI)_2(\mu\text{-}dppm)_2]Cl_4$ **1** conductivity value of 145.16 Ω^{-1} cm^2 mol^{-1} indicated it as 1 : 4 electrolyte [9, 10].

In IR spectrum of 3-hydrazonoindolin-2-one ligand the azomethine group ν(C=N) was recorded by the band at 1589 cm^{-1}. Spectra of the complexes **1**–**6** demonstrated the carbonyl amide group bands within the range of 1681–1687 cm^{-1}, and their shifts indicated the carbonyl amide groups bonding with mercury.

The organomercury derivatives $[Hg(bipy)Cl_2]$ and $[Hg(phen)Cl_2]$ interacted readily with 3-hydrazonoindolin-2-one in the equimolar ratio giving the corresponding tetrahedral complexes **5** and **6** (Scheme 2).

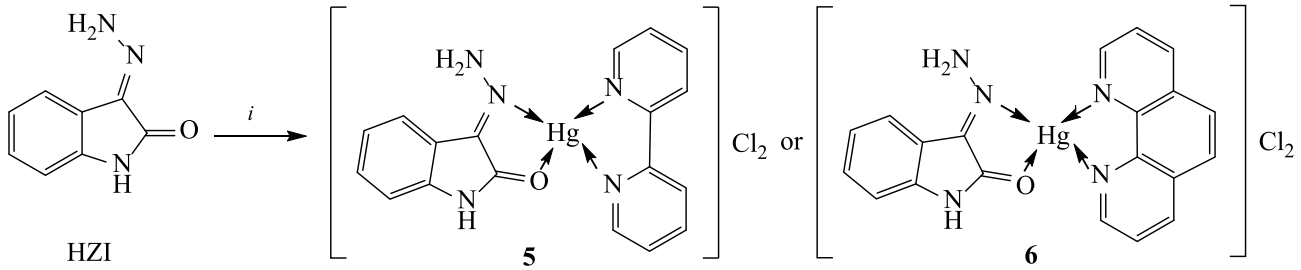
$^{31}P\{1H\}$ NMR spectrum of the complex **1** (Fig. 1) demonstrated a singlet at 23.54 ppm. $^{31}P\{1H\}$ NMR spectrum of the complex **2** indicated formation of two isomers with two equivalent atoms of phosphorus in **2a** and dppe acting as a bidentate ligand. In the spectrum of isomer **2b** two doublets at 30.44 ppm ($^{2}J_{PP}$ = 44.10 Hz) and –14.21ppm ($^{2}J_{PP}$ = 44.62 Hz) indicated

Scheme 1. Structures of complexes $[Hg_2(HZI)_2(\mu\text{-dppm})_2]Cl_4$ (**1**), $[Hg(HZI)(dppe)]Cl_2$ (**2a**), [Hg(HZI)(dppe)Cl]Cl (**2b**), $[Hg(HZI)(dppp)]Cl_2$ (**3**), $[Hg(HZI)(dppb)]Cl_2$ (**4**).



2b **2a**: n = 2, dppe; **3**: n = 3, dppp; **4**: n = 4, dppb.

Scheme 2. Preparation of complexes $[Hg(HZI)(bipy)]Cl_2$ (**5**) and $[Hg(HZI)(phen)]Cl_2$ (**6**).



i = $[Hg(bipy)Cl_2]$ (**5**), $[Hg(phen)Cl_2]$) (**6**).

two phosphorus atoms as nonequivalent with dppe acting as a monodentate ligand (Fig. 1). $^{31}P\{1H\}$ NMR spectra of complexes **3**, **4** demonstrated singlets at 26.74 and 31.12 ppm, receptively, pointing out equivalence of two phosphorus atoms and the bidentate character of dppp and dppb ligands [11, 12].

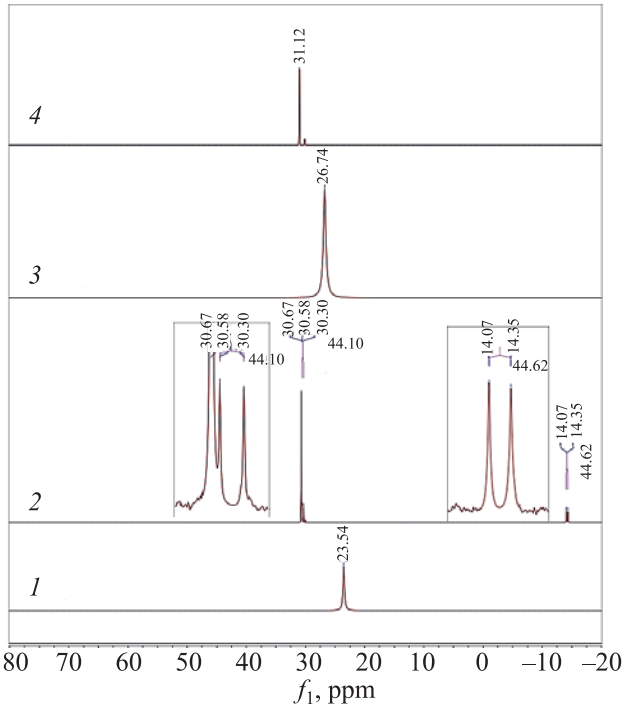


Fig. 1. $^{31}P\{H\}$ NMR spectra of complexes (*1*) **1**, (*2*) **2**, (*3*) **3**, and (*4*) **4**.

Biological activity of the prepared compounds. Biological activity of the complexes was tested (0.01, 0.001, 0.0001 mg/mL) against three bacterial species: *Staphylococcus epidermidis*, *Staphylococcus aureus* (gram positive), and *Citrobacer freundii* (gram negative) using the antibiotic amikacin as a standard. All complexes demonstrated activity (Fig. 2a) against *Staphylococcus aureus* higher than that of amikacin. Whereas the synthesized complexes **1**–**6** were selectively active against *Citrobacter freundii* and *Staphylococcus epidermidis* (Figs. 2b, 2c).

EXPERIMENTAL

All chemicals were used without purification. NMR spectra were measured on a Bruker 400 MHz spectrometer using DMSO-d_6 as a solvent. IR spectra (KBr) were recorded on a Shimadzu FT-IR 8400S spectrophotometer. Melting points were recorded on an Automatic SMP30 melting point apparatus. Molar conductivity of 10^{-3} M freshly prepared DMSO solutions of the complexes was measured on a Starter 3100c digital conductivity meter. CHN analysis was carried out on an Elementar vario El III CHN analyzer.

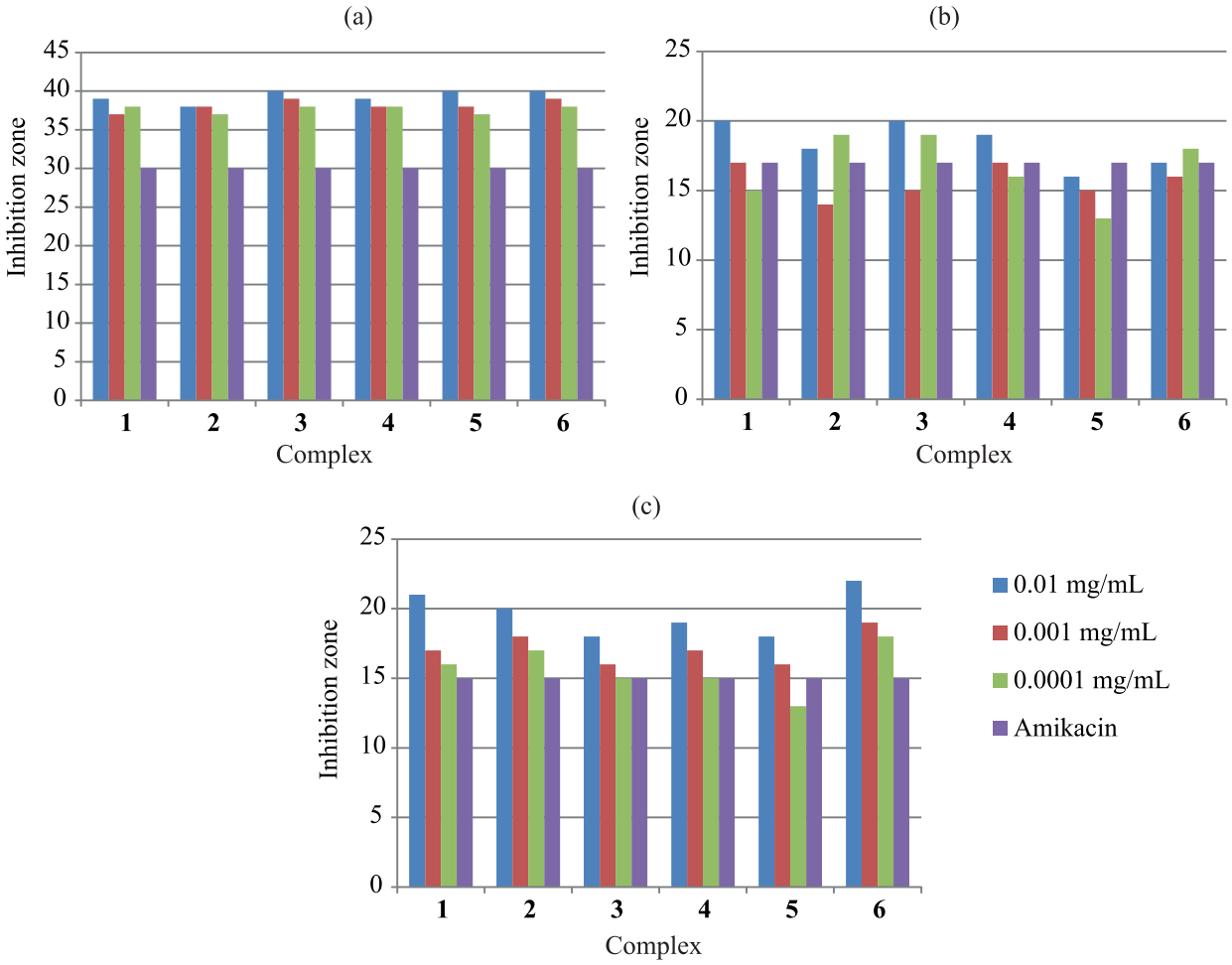


Fig. 2. Inhibitory activity of complexes **1**–**6** against the above bacteria: (a) *Staphylococcus aureus*, (b) *Citrobacter freundii*, and (c) *Staphylococcus epidermidis*.

Preparation of 3-hydrozonoindolin-2-one (HZI) ligand [8]. A solution of hydrazine (0.055 g, 1.1 mmol) in 10 mL of absolute ethanol was added to a solution of isatin (0.161 g, 1 mmol) in 10 mL of absolute ethanol, and a few drops from glacial acetic acid were added. The mixture was refluxed for 1 h then cooled down to room temperature, and a yellow solid was precipitated. It was filtered off and washed with cold ethanol, dried under vacuum and recrystallized from a mixture of EtOH–DMF to give yellow crystals. Yield 92%, mp 240–242°C. FTIR spectrum, ν, cm^{-1}: 3355 s, 3153 s, 3053 w, 1685 s, 1654 s, 1589 s, 1552 s, 1463 m, 1197 s, 977 m, 748 s. ^1H NMR spectrum, δ, ppm: 6.78 d (1H, J = 7.87 Hz), 6.98 t (1H, J = 7.70 Hz), 7.16 t (1H, J = 7.86 Hz), 7.36 d (1H, J = 8.03 Hz), 9.53 d (1H-NH_2, J = 13.92 Hz), 10.54 d (1H-NH_2, J = 13.95 Hz), 10.67 s (NH). ^{13}C NMR spectrum, δ, ppm: 111.35, 120.85, 121.9, 122.41, 129.54, 136.48, 140.48, 162.91. Found, %: C 59.88; H 4.52; N 26.31. $C_8H_7N_3O$. Calculated, %: C 59.61; H 4.39; N 26.07. Λ_o 3.24 Ω^{-1} cm^2 mol^{-1}.

Synthesis of [Hg(HZI)(diphos)]Cl_2 complexes 1–4, diphos = dppm, dppe, dppp, dppb. A solution of 1 M of HZI in absolute ethanol was added to 1 M suspension of [Hg(diphos.)Cl_2] in absolute ethanol, then the mixture was stirred for 1 h at room temperature. The white precipitate was separated by filtration, dried in an oven under vacuum, and recrystallized from ethanol to give the corresponding products **1**–**4**.

Complex 1. Pale yellow solid, yield 83%, mp 273–276°C. FTIR spectrum, ν, cm^{-1}: 3357 m, 3217 m, 3076 w, 1681 s, 1652 s, 1556 s, 1433 m, 1195 m, 1099 m, 744 s, 686 s. $^{13}P\{^1H\}$ NMR spectrum, δ, ppm: 23.54. ^1H NMR spectrum, δ, ppm: 2.87 t (2H, ^3J = 1.94 Hz, CH_2), 6.86 d (1H, ^3J = 7.56 Hz), 6.97 t (1H, ^3J = 7.52 Hz), 7.16 t (1H, ^3J = 7.64 Hz), 7.34 m, 7.47 m (21H, HZI, Ph), 9.64 d (2H,

^2J = 14.62 Hz, NH_2), 10.64 d (2H, ^2J = 14.08 Hz, NH_2), 10.76 s (NH). Found, %: C 48.01; H 3.42; N 5.23. Calculated, %: C 48.51; H 3.58; N 5.14. Λ_o 145.16 Ω^{-1} cm^2 mol^{-1}.

Complex 2. Pale yellow solid, yield 87%, mp 247–250°C. FTIR spectrum, ν, cm^{-1}: 3355 m, 3213 m, 3078 w, 1683 s, 1652 s, 1558 s, 1434 m, 1193 m, 1101 m, 746 m, 688 m. $^{13}P\{^1H\}$ NMR spectrum, δ, ppm: 30.67 (**2a**), 30.44 d (**2b**) ($^2J_{PP}$ = 44.10 Hz), –14.21 d ($^2J_{PP}$ = 44.62 Hz). ^1H NMR spectrum, δ, ppm: 2.04 t (4H, ^3J = 4.33 Hz, 2CH_2), 6.87 d (1H, ^3J = 7.23 Hz), 6.97 t. d (1H, ^3J = 7.50, ^4J = 1.15 Hz), 7.15 t. d (1H, ^3J = 7.62, ^4J = 1.39 Hz), 7.33 m (21H, HZI, Ph), 9.54 d (2H, ^2J = 14.42 Hz, NH_2), 10.55 d (2H, ^2J = 14.37 Hz, NH_2), 10.66 s (NH). Found, %: C 48.68; H 3.51; N 4.85. Calculated, %: C 49.14; H 3.76; N 5.06. Λ_o 84.67 Ω^{-1} cm^2 mol^{-1}.

Complex 3. Pale yellow solid, yield 92%, mp 232–235°C. FTIR spectrum, ν, cm^{-1}: 3361 m, 3205 m, 3041 w, 1687 s, 1656 s, 1581 s, 1433 s, 1101 m, 746 s, 690 s, 520 m. $^{13}P\{^1H\}$ NMR spectrum, δ, ppm: 26.74. ^1H NMR spectrum, δ, ppm: 1.86 s (2H, CH_2, 2.90 s (4H, CH_2, 6.84 d (1H, ^3J = 3.74 Hz), 6.98 t (1H, ^3J = 7.54 Hz), 7.15 t (1H, ^3J = 7.66 Hz), 7.35 d (1H, ^3J = 7.56 Hz), 7.56 m, 7.73 m (20H, Ph), 9.54 d (2H, ^2J = 14.92 Hz, NH_2), 10.53 d (2H, ^2J = 14.15 Hz, NH_2), 10.68 s (NH). Found, %: C 49.39; H 3.43; N 5.15. Calculated, %: C 49.74; H 3.94; N 4.97. Λ_o 80.27 Ω^{-1} cm^2 mol^{-1}.

Complex 4. Pale yellow solid, yield 85%, mp 284–287°C. FTIR spectrum, ν, cm^{-1}: 3353 m, 3212 m, 3054 w, 1687 s, 1656 s, 1581 s, 1434 s, 1101 m, 746 s, 690 s, 520 m. $^{13}P\{^1H\}$ NMR spectrum, δ, ppm: 31.12. ^1H NMR spectrum, δ, ppm: 1.43 m (4H, CH_2), 2.23 t (4H, ^3J = 9.18 Hz, CH_2), 6.86 d (1H, ^3J = 7.58 Hz), 6.97 t. d (1H, ^3J = 7.58, ^4J = 1.05 Hz), 7.16 t. d (1H, ^3J = 7.65, ^4J = 1.30 Hz), 7.35 m (21H, HZI, Ph, 9.54 d (2H, ^2J = 14.67 Hz, NH_2), 10.54 d (2H, ^2J = 14.52 Hz, NH_2), 10.68 s (NH). Found, %: C 49.98; H 3.86; N 4.67. Calculated, %: C 50.33; H 4.11; N 4.89. Λ_o 78.87 Ω^{-1} cm^2 mol^{-1}.

Synthesis of complexes [Hg(HZI)(bipy)]Cl_2 (5) and [Hg(HZI)(phen)]Cl_2 (6). A solution of HZI (0.500 g, 3.103 mmol) in absolute ethanol (10 mL) was added to 1 M suspension of [Hg(bipy)Cl_2] (1.326 g, 3.103 mmol, or [Hg(phen)Cl_2] (1.401 g, 3.103 mmol) in absolute ethanol (10 mL). The mixture was refluxed for 2 h upon stirring, then it was separated as a pale yellow precipitate, filtered off, dried in the oven under vacuum, and recrystallized from ethanol.

Complex 5. Creamy solid, yield 81%, mp 212–215°C. FTIR spectrum, ν, cm^{-1}: 3384 m, 3220 m, 3015 w, 1685 s, 1658 s, 1589 m, 1548 m, 1463 m, 1193 m, 981 w, 748 w, 676 w. ^1H NMR spectrum, δ, ppm: 6.85 d (1H, ^3J = 7.66 Hz), 6.97 t (1H, ^3J = 7.48 Hz), 7.16 t. d (1H, ^3J = 7.65, ^4J = 1.29 Hz), 7.37 d (1H, ^3J = 7.52 Hz), 7.69 m (2H, bipy), 8.16 t. d (2H, ^3J = 7.88, ^4J = 1.81 Hz, bipy), 8.54 d (2H, ^3J = 8.04 Hz, bipy), 8.87 d. d (2H, ^3J = 5.25, ^4J = 1.71 Hz, bipy), 9.52 d (2H, ^2J = 14.92 Hz, NH_2), 10.53 d (2H, ^2J = 12.76 Hz, NH_2), 10.68 s (NH). ^{13}C NMR spectrum, δ, ppm: 110.44, 117.93, 121.83, 122.74, 126.76, 127.52, 129.15, 139.14, 140.05, 149.87, 163.26. Found, %: C 36.48; H 2.42; N 11.71. Calculated, %: C 36.71; H 2.57; N 11.89. Λ_o 71.42 Ω^{-1} cm^2 mol^{-1}.

Complex 6. Creamy solid, yield 83%, mp 217–220°C. FTIR spectrum, ν, cm^{-1}: 3357 m, 3161 m, 3058 w, 1685 s, 1656 s, 1585 s, 1550 s, 1463 m, 1197 s, 977 m, 842 s, 721 m. ^1H NMR spectrum, δ, ppm: 6.86 d (1H, ^3J = 7.53 Hz), 6.97 t. d (1H, ^3J = 7.48, ^4J = 1.04 Hz), 7.16 t. d (1H, ^3J = 7.60, ^4J = 1.29 Hz), 7.36 d (1H, ^3J = 7.39 Hz), 8.07 m (2H, phen, 8.20 s (2H, phen), 8.81 d. d (2H, ^3J = 8.17 Hz, ^3J = 1.70 Hz, phen), 9.20 s (2H, phen), 9.55 d (2H, ^2J = 14.65 Hz, NH_2), 10.55 d (2H, ^2J = 14.68 Hz, NH_2, 10.68 s (NH). ^{13}C NMR spectrum, δ, ppm: 110.44, 117.92, 121.83, 122.72, 125.66, 126.69, 127.51, 127.56, 129.22, 139.13, 139.71, 140.48, 150.29, 163.24. Found, %: C 38.78; H 2.41; N 11.40. Calculated, %: C 39.20; H 2.47; N 11.43. Λ_o 70.86 Ω^{-1} cm^2 mol^{-1}.

CONCLUSIONS

The tetrahedral complexes [Hg(HZI)(diphosphine)]Cl_2 and [Hg(HZI)(diimine)]Cl_2 have been prepared. The HZI ligand behaved as a bidentate via N atom of the azomethine group and O atom of the carbonyl group. Diphosphine and diimine ligands are acting as bidentate via P or N atoms, respectively. In complex **1** dppm behaves as a bridge ligand. For the complex **2** two isomers have been determined and distinguished by bidentate or monodentate character of the dppe ligand. The prepared complexes have demonstrated activity against *Staphylococcus aureus* higher than amikacin. Some complexes are active against *Staphylococcus epidermidis* and *Citrobacter freundii*.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

REFERENCES

1. Fadhil, G.F., Radhy, H.A., Perjéssy, A., Šamalíková, M., Kolehmainen, E., Fabian, W.M., Katri, L., and Šusteková, Z., *Molecules,* 2002, vol. 7, no. 11, p. 833. https://doi.org/10.3390/71100833
2. Mariar, C.R., Belicchi, F.M., Franco, B., Corrado, P., Giorgio, P., Silvana, P., and Monica, S., *J. Inorg. Biochem*, 2004, vol. 98, p. 313. https://doi.org/10.1016/j.jinorgbio.2003.10.006
3. Mohamed, G.G., Omar, M.M., and Hindy, A.M., *Turkish J. Chem.*, 2006, vol. 30, no. 3, p. 361.
4. Cerchiaro, G. and Ferreira, A.M.D.C., *J. Brazilian Chem. Soc.*, 2006, vol. 17, no. 8, p. 1473. https://doi.org/10.1590/S0103-50532006000800003
5. Sharma, V., Srivastava, S., and Srivastava, A., *Polish J. Chem.*, 2006, vol. 80, no. 3, p. 387.
6. Sharma, V.K., Srivastava, A., and Srivastava, S., *J. Serbian Chem. Soc.*, 2006, vol. 71, nos. 8–9, p. 917. https://doi.org/10.2298/JSC0609917S
7. Pandeya, S.N., Smitha, S., Jyoti, M., and Sridhar, S.K., *Acta Pharm.*, 2005, vol. 55, no. 1, p. 27.
8. Vatsa, G., Pandey, O.P., and Sengupta, S.K., *Bioinorg. Chem. Appl.*, 2005, vol. 3, nos. 3–4, p. 151. https://doi.org/10.1155/BCA.2005.151
9. Alam, M., Ahmad, M., Rasheed, A., Saleem, M., Javaid, M.K., and Ikram, S., *Indian J. Exp. Biol.*, 1990, vol. 28, no. 10, p. 940.
10. Ali, I., Wani, W.A., and Saleem, K., *Synth. React. Inorg., Metal-Org., and Nano-Metal Chem.*, 2013, vol. 43, no. 9, p. 1162. https://doi.org/10.1080/15533174.2012.756898
11. Hamon, P., Toupet, L., Roisnel, T., Hamon, J.R., and Lapinte, C., *Eur. J. Inorg. Chem.*, 2020, vol. 2020, no. 1, p. 84. https://doi.org/10.1002/ejic.201901086
12. Mannu, A., Ferro, M., Möller, S., and Heller, D., *J. Chem. Res.*, 2018, vol. 42, no. 8, p. 402. https://doi.org/10.3184/174751918X15333065984578