Synthesis, Spectral Analysis and Biological Potency of
Hydrazoneoxime Ligands Incorporating Pyrazolone
Moieties and Their Metal Complexes

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http://dx.doi.org/10.13005/ojc/360626

(Received: October 09, 2020; Accepted: December 10, 2020)

ABSTRACT
A modest attempt has been made for the synthesis of hydrazoneoxime ligands bearing
pyrazolone group (1-4) and their successive metal complexes such as: 1(a-c), 2(a-c), 3(a-c) and
4(a-c). The precursor (1Z,2E)-2-(hydroxyimino) ethanehydroximohydrazide (GH2) was obtained
through coupling of (1Z,2E)-N-hydroxy-2-(hydroxyimino) ethanimidoyl chloride and hydrazinium
hydroxideto generate hydrazonoxime compounds bearing the pyrazolone group. The ligands (1-4)
were reacted with MX2.nH2O, where M = Co(II), Ni(II) and Cu(II) to obtain the successive metal
coordinated compounds into good yields. The ligands and their metal complexes were investigated
by using 1H NMR, 13C NMR, FT-IR, elemental analysis and magnetic susceptibility measurements.
Tautomerism in the ligands is investigated spectroscopically and biological activities are evaluated as
well. Finally, the findings of present study were found within good agreement with other workers.

Keywords: Pyrazolone, Hydrazoneoxime, Tautomerism, Metal complexes, Spectral studies,
Biological activities.

INTRODUCTION
Pyrazolone is considered as an important
component or structural unit which is present in
various active compounds. Owing to its convenient
synthesis as well as versatile biological applications
particularly its comprehensive antiseptics, antitumor,
antibacterial action14, pyrazolone and its complexes
have acquired a significant consideration in
coordination as well as in medicinal chemistry.

Pyrazolone derived product are paramount
kind of heterocyclic compounds that occurs in
various drugs as well as in synthetic products6,6.
These compounds show extraordinary analgesic7,
antitubercular8, antifungal, antibacterial10, anti-
inflammatory10, antioxidant and antitumor activities11.
Because of their facile synthesis and character
they are biologically active, pyrazolone arrangement
performs a significant function and reflects an effective
example for combinatorial and pharmaceutical chemistry. Furthermore, pyrazole derived products showed outstanding biological asset, for example, anti-microbial\(^{12}\), analgesic\(^{13}\), anti-inflammatory\(^{14}\) and anticancer activities\(^{15}\). This provided an enormous boost to explore for potentially active compounds having pyrazole substituents.

Here in, the derivatization of hydrazone oxime ligands bearing pyrazolone group (1-4) and their metal complexes\(^{1(a-c)}, 2(a-c), 3(a-c), 4(a-c)\) was reported. The ligands and its complexes were characterized by \(^1\)H NMR, \(^{13}\)C NMR, FT-IR spectroscopy, elemental analysis and magnetic susceptibility techniques. The proposed general structure of the ligand is given in scheme.\(^1\)

\[
[R_1; H= 1, p-CH_3=2, p-NO_3=3, p-OCH_3=4]
\]

**Scheme 1. The molecular formules of the ligands**

**EXPERIMENTAL**

**Instruments and reagents**

Reagents used in the experiment have been obtained from Sigma-Aldrich, Merck and Fluka and were handled as received. The melting point of the synthesised complexes and the ligands were verified and calculated by the Büchi SMP-20 apparatus using an open capillary method. For the calculation of FT-IR spectra, KBr discs on a Perkin Elmer Mattson 1000 spectrophotometer were used, \(^1\)H and \(^{13}\)C NMR spectra have been reported by Bruker-Spectrospin Avance DTX 400 Ultra-Shield in deuterated dimethyl sulphoxide (DMSO-\(d_6\)) and tetramethylsilane (TMS) used as an internal standard and chemical shifts considered in ppm. The Leco CHNS-932 analyzer used for the elemental analysis: and for the pH measurements, an Orion Expandable Ion Analyzer EA 940 was used. The melting point, colors, molecular weights, percentage of yield, molar conductance, magnetic susceptibilities (Sherwood Scientific) have been calculated and are given in the following sections.

**Preparation of the ligands and their nomenclature**

The precursor (1Z,2E)-2-(hydroxyimino)ethanethiohydrazide (GH\(_2\)) was prepared by the action of the (1Z,2E)-N-hydroxy-2-(hydroxyimino)ethanemidoyl chloride\(^{16}\) and hydrazinium hydroxide. Since the parent compound, GH\(_2\) is unstable at normal temperature, so it was utilized without further purification or as it was received. Hydrazone oxime ligands bearing pyrazolone group (1-4) have been prepared with the 5-pyrazolones as mentioned in the literature\(^{17}\) and characterized their structures by using spectral techniques.

The IUPAC name of the ligands may be given as 2-[(1Z,2E)-N-hydrokis-2-(hydrokisimino)ethanimidoil]-5-metil-4-[(Z)-(4-nitrofenil)diazienil]-2,4-dihidro-3H-pirazol-3-on (1), 2-[(1Z,2E)-N-hydrokis-2-(hydrokisimino)ethanimidoil]-4-[(Z)-(4-metoksifenil)diazienil]-5-metil-2,4-dihidro-3H-pirazol-3-on (2), 2-[(1Z,2E)-N-hydrokis-2-(hydrokisimino)ethanimidoil]-4-[(Z)-(4-metilfenil)diazienil]-5-metil-2,4-dihidro-3H-pirazol-3-on (3) and 2-[(1Z,2E)-N-hydrokis-2-(hydrokisimino)ethanimidoil]-5-metil-4-[(Z)-(4-metilfenil)diazienil]-2,4-dihidro-3H-pirazol-3-on (4). The preparation procedures were followed as given in the literature\(^{18-20}\).

For the synthesis of (1-4) the common route follows as given in the Scheme 2.

**General procedure of synthesis**

**Synthesis of hydrazonexoxide ligands bearing pyrazolone group (1-4)**

Aniline derivatives 10 mmol (0.69 g, aniline; 1.38 g, 4-nitroaniline; 1.23 g, p-anisidine; or 1.04 g, p-toluidine respectively) were taken and dissolved in a mixture of 1:1 ratio of glacial acetic acid and concentrated hydrochloric acid (20 mL) and cooled the solution upto 0–5\(^{\circ}\)C. Sodium nitrite (0.69 g or 0.01 mol) was taken and dissolved in 10 mL water and then added dropwise to the above-prepared solution mixture with vigorous stirring for nearly one hour to maintain the solution temperature between 0-5\(^{\circ}\)C. The obtained product was separated by means of diluting with water (50 mL), filtered, washed several times with distilled water and finally dried.
2-[(1Z,2E)-N-hydrokis-2-(hydrokisimino) etanimidoil]-5-metil-4-[(2Z)-fenildiazenil]-2,4-
dihidro-3H-pirazol-3-on(1)

The analytical and physical properties of the ligand (1) and its metal complexes (1a-1c) are provided in Table 1. Appearance: yellow powder; Yield=87%, m.p. (decomp.) 165°C; The reaction scheme is given in Scheme 2. The compound is soluble in commonly used solvents like CH\(_2\)Cl\(_2\), CHCl\(_3\), DMF, EtOH and DMSO.

The infrared spectral of the ligand (1) is given in Table 2. FT -IR (KBr, \(\nu_{\text{max}}/\text{cm}^{-1}\)): 3271 (N-H), 3681(O-H), 2970 (C-H Arom.), 2844 (C-H Aliph.), 1598-1664 (C=N Oxim.), 1556 (C=N Hydr.), 1033(N-O), 1484 ve 1441 (N-N Azo.). The FT-IR spectrum of ligand (1) is given in Fig. 1.

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\(^{13}\)C NMR peaks of the compound: (CDCl\(_3\), TMS, (d) ppm):148.35(N-C=N-OH); 148.80(CH=N-OH); 156.99 (C=N-N),12.03 (CH\(_3\)); 158.17 (C=N-NH);159.76 (C=O); 129.96, 116.68, 126.05, 142.80 (Ar-C).

| Compound                      | Molecula Composition | M.W. (g/mol) | Appearance     | Melting Point (°C) | Yield (%) | Calculated (Found) % |
|-------------------------------|----------------------|--------------|----------------|-------------------|-----------|-----------------------|
| Ligand (1)                    | C\(_{12}\)H\(_{12}\)N\(_6\)O\(_3\) | 288.27       | Yellow         | 165               | 87        | 50.00 (50,60) 4,20 (4,40) 29,15 (29,21) |
| Complex(1a)                   | C\(_{24}\)H\(_{22}\)N\(_{12}\)Ni | 633.21       | Red-brown      | >370*             | 52        | 45,52 (45,60) 3,50 (3,43) 26,54 (26,47) |
| Complex(1b)                   | C\(_{24}\)H\(_{22}\)N\(_{12}\)Co | 633.45       | Dark-brown     | 230*              | 76        | 45,51 (45,58) 3,50 (3,43) 26,53 (26,44) |
| Complex(1c)                   | C\(_{24}\)H\(_{22}\)N\(_{12}\)O\(_6\)Cu | 638.06       | Dark-brown     | 193*              | 68        | 45,18 (45,59) 3,48 (3,55) 26,34 (25, 77) |

(d)*: decomposition
Table 2: Infrared data for the ligand (1) and its complexes

| Compound       | ν(O-H) | ν(N-H) | ν(C=O) | ν(C=N)oxim | ν(C=N)hydr | ν(CH)Arom. | ν(CH)Alip. | ν(N-N) | ν(N-O) | ν(OH-O) |
|----------------|--------|--------|--------|------------|------------|------------|------------|--------|--------|---------|
| Ligand (1)     | 3681w  | 3271w  | 1667s  | 1536-1556m | 2970m      | 3088m      | 1484-1441m | 1033m  | -      | -       |
| Complex (1a)   | 3271m  | 3271m  | 1667w  | 1536-1556m | 2970m      | 2844m      | 1449-1484m | 1033m  | 1738m  |
| Complex (1b)   | 3271m  | 3271m  | 1667w  | 1536-1556m | 2970m      | 2844m      | 1449-1484m | 1033m  | 1738m  |
| Complex (1c)   | 3168m  | 3168m  | 1655m  | 1536-1556m | 2970m      | 2864m      | 1449-1484m | 1033m  | 1738m  |

2-[(1Z,2E)-N-hydrokis-2-(hydrokisimino)etanimido]-5-metil-4-[(Z)-(4-nitrofenil)diazenil]-2,4-dihidro-3H-pirazol-3-on (2)

Some important characteristics (analytical and physical) of the synthesized ligand (2) and its metal complexes (2a-2c) are given in Table 3. Appearance: Dark brown powder; Yield=75%; m.p.(decomposition) 250°C; For the synthesis of the compound (2), reaction arrangements are illustrated in Scheme 2. This compound is soluble in commonly used solvents like CH₂Cl₂, CHCl₃, DMF, EtOH and DMSO. Anal. Calcd. for C₁₂H₁₁N₇O₅ (333.27 g mol⁻¹): 43.25% C; 3.33% H; 29.42% N, Found: 43.83% C; 3.40% H; 29.35% N. The infrared spectral collected statistics of the ligand (2) are revealed in Table 4. FT-IR (KBr, νmax/cm⁻¹): 3271 (N-H), 3681(O-H), 2970 (C-H Arom.), 2864 (C-H Alip.), 1609-1677 (C=N Oxim), 1543 (C=N Hydr.), 1033(N-O), 1506 ve 1483 (N-N Azo), 1417 ve 1376 (-NO₂). The FT-IR spectrum of ligand (2) is given in Fig. 2.

1H NMR peaks (DMSO-d₆, (d) ppm): 2,20 (s, 3H, pyrazolone-CH₃); 7.68-7.78 (m,4H, Ar-H); 11.84; 12.22 (d, 2H (OH); 7.85 (s, 2H, CH=NOH); 13.03 (s, 2H -CH=N-NH).

13C NMR peaks of the compound: (CDCl₃, TMS, (d) ppm): 149.18 (N-C=N-OH); 147.47 (CH=N-OH); 157.40 (C=N-N); 12.07 (CH₃); 156.19 (C=N-NH); 158.05 (C=O); 116.89, 125.86, 129.41, 136.99 (Ar-C).

Table 3: Physical and analytical data of the hydrazoneoxime ligand (2) bearing pyrazolone group and its complexes

| Compound       | Molecula Composition (g/mol) | M.W. | Apperance         | Melting Point (d)* (°C) | Yield(%) | Calculated (Found)% |
|----------------|-------------------------------|------|-------------------|-------------------------|----------|---------------------|
| Ligand (2)     | C₁₂H₁₁N₇O₅                   | 333.26 | Light-brown       | 250                     | 75       | 43.25 (43.83)       |
| Complex(2a)    | C₂₄H₂₀N₁₄O₁₀Ni               | 723,21 | Red-brown         | 240*                    | 80       | 39,86 (39,93)       |
| Complex(2b)    | C₂₄H₂₀N₁₄O₁₀Co               | 723,45 | Dark-brown        | 200*                    | 76       | 39,85 (39,27)       |
| Complex(2c)    | C₂₄H₂₀N₁₄O₁₀Cu               | 728,06 | Dark-brown        | 195*                    | 65       | 39,59 (39,99)       |

(d)*: decomposition

Fig. 2. FT-IR spectrum of ligand (2)

Table 4: Infrared data for the ligand (2) and its complexes

| Compound       | ν(O-H) | ν(N-H) | ν(C=O) | ν(C=N)oxim | ν(C=N)hydr | ν(CH)Arom. | ν(CH)Alip. | ν(N-N) | ν(N-O) | ν(OH-O) |
|----------------|--------|--------|--------|------------|------------|------------|------------|--------|--------|---------|
| Ligand (2)     | 3681w  | 3271w  | 1667s  | 1536-1556m | 2970m      | 3088m      | 1484-1441m | 1033m  | -      | -       |
| Complex (2a)   | 3271m  | 3271m  | 1667w  | 1536-1556m | 2970m      | 2844m      | 1449-1484m | 1033m  | 1738m  |
| Complex (2b)   | 3271m  | 3271m  | 1667w  | 1536-1556m | 2970m      | 2844m      | 1449-1484m | 1033m  | 1738m  |
| Complex (2c)   | 3168m  | 3168m  | 1655m  | 1536-1556m | 2970m      | 2864m      | 1449-1484m | 1033m  | 1738m  |
2-[(1Z,2E)-N-hydrokis-2-(hydrokisimino) etanimidil]-4-[(Z)-(4-metoksifenil) diazenil] -5-metil-2,4-dihidro-3H-pirazol-3-on (3)

Some important characteristics (analytical and physical) of the synthesized ligand (3) and its metal complexes (3a-3c) are given in Table 5. Appearance: Red powder; Yield=83%, m.p.(decomposition) 230°C; For the synthesis of the compound (3), reaction arrangements are illustrated in Scheme 2. This compound is soluble in commonly used solvents like CH\textsubscript{2}Cl\textsubscript{2}, CHCl\textsubscript{3}, DMF, EtOH and DMSO. Anal. Calcd. for C\textsubscript{13}H\textsubscript{14}N\textsubscript{6}O\textsubscript{4} (318.29 g mol\textsuperscript{-1}): 49.06% C; 4.43% H; 26.40% N, Found: 49.13% C; 4.37% H; 26.48% N. The infrared spectral collected statistics of the ligand (3) are revealed in Table 6. FT-IR (KBr, \nu\textsubscript{max}/cm\textsuperscript{-1}): 3235 (N-H), 3681 (O-H), 2970 (C-H\textsubscript{Arom.}), 2844 (C-H\textsubscript{Aliph.}), 1595-1648 (C=N\textsubscript{Diaz.}), 1533 (C=N\textsubscript{Hyd.}), 1033 (N-O), 1454 ve 1474 (N-N\textsubscript{Azo}), 1738 –C=O. The FT-IR spectrum of ligand (3) is can be seen in Fig. 3.

The infrared spectral collected statistics of the ligand (4) are revealed in Table 8. FT-IR (KBr, \nu\textsubscript{max}/cm\textsuperscript{-1}): 3168 (N-H), 3681 (O-H), 2970 (C-H\textsubscript{Arom.}), 2844 (C-H\textsubscript{Aliph.}), 1594-1669 (C=N\textsubscript{Diaz.}), 1536 (C=N\textsubscript{Hyd.}), 1492 ve 1449 (N-N\textsubscript{Azo}), 1738–C=O, 2970–CH\textsubscript{3}(phenil) ve CH\textsubscript{3}(methyl). The FT-IR spectrum of ligand (4) is given in Fig. 4. \textsuperscript{1}H NMR peaks (DMSO-d\textsubscript{6}, (d) ppm): 2.17 (s, 3H, pyazolone-CH\textsubscript{3}); 7.18-7.46 (m, 4H, Ar-H); 11.76; 12.18 (d, 2H (OH); 7.83 (s, 2H, CH=NOH); 13.05 (s, 2H -CH=N-NH); 2.27 (s, 3H –CH\textsubscript{3}(benzenil). The FT-IR spectrum of ligand (4) is given in Fig. 4. \textsuperscript{1}H NMR peaks (DMSO-d\textsubscript{6}, (d) ppm): 2.17 (s, 3H, pyazolone-CH\textsubscript{3}); 7.18-7.46 (m, 4H, Ar-H); 11.76; 12.18 (d, 2H (OH); 7.83 (s, 2H, CH=NOH); 13.05 (s, 2H -CH=N-NH); 2.27 (s, 3H –CH\textsubscript{3}(benzenil)

Table 5: Physical and analytical data of the hydrazoneoxime ligand(3) bearing pyrazolone group and its complexes

| Compound | Molecula Composition (g/mol) | M.W. | Apperance | Melting Point (d)* (°C) | Yield(%) | Calculated (Found)% |
|----------|-------------------------------|------|-----------|-------------------------|----------|---------------------|
| Ligand (3)| C\textsubscript{13}H\textsubscript{14}N\textsubscript{6}O\textsubscript{4} | 318.29 | Red | 230 | 83 | 49.06 (49.13) 4.43 (4.37) 26.40 (26.48) |
| Complex(3a)| C\textsubscript{26}H\textsubscript{26}N\textsubscript{12}O\textsubscript{8}Ni | 693.6 | Red-brown | >370* | 78 | 45.05 (45.13) 3.78 (3.72) 24.25 (24.32) |
| Complex(3b)| C\textsubscript{26}H\textsubscript{26}N\textsubscript{12}O\textsubscript{8}Co | 693.50 | Dark-brown | >350* | 65 | 45.03 (45.09) 3.78 (3.72) 24.24 (24.17) |
| Complex(3c)| C\textsubscript{26}H\textsubscript{26}N\textsubscript{12}O\textsubscript{8}Cu | 693.12 | Dark-brown | 196* | 68 | 44.73 (44.79) 3.75 (3.68) 24.08 (24.66) |

(d)*: decomposition
Table 6: Infrared data for the ligand(3) and its complexes

| Compound          | \(\nu(O-H)\) | \(\nu(N-H)\) | \(\nu(C=O)\) | \(\nu(C=N)_{oxim}\) | \(\nu(C=N)_{hyd}\) | \(\nu(CH)_{arom}\) | \(\nu(CH)_{alip}\) | \(\nu(N-N)\) | \(\nu(N-O)\) | \(\nu(OH-O)\) |
|-------------------|--------------|--------------|--------------|----------------------|----------------------|---------------------|---------------------|----------------|----------------|----------------|
| Ligand (3)        | 3681\(^w\)   | 3271\(^w\)   | 1667\(^s\)   | 1536-1556\(^m\)     | 2970\(^m\)           | 3088\(^m\)          | 1484-1441\(^m\)   | 1033\(^m\)      | -              |                |
| Complex(3a)       | 3271\(^m\)   | 3271\(^m\)   | 1667\(^w\)   | 1594-1677\(^m\)     | 2970\(^m\)           | 2844\(^m\)          | 1449-1484\(^m\)   | 1033\(^m\)      | 1738\(^m\)     |                |
| Complex(3b)       | 3271\(^m\)   | 3271\(^m\)   | 1667\(^w\)   | 1594-1677\(^m\)     | 2970\(^m\)           | 2844\(^m\)          | 1449-1484\(^m\)   | 1033\(^m\)      | 1738\(^m\)     |                |
| Complex(3c)       | 3168\(^m\)   | 3168\(^m\)   | 1655\(^m\)   | 1594-1677\(^m\)     | 2970\(^m\)           | 2864\(^m\)          | 1449-1484\(^m\)   | 1033\(^m\)      | 1738\(^m\)     |                |

Table 7: Physical and analytical data of the hydrazoneoxime ligand(4) bearing pyrazolone group and its complexes

| Compound          | Molecule Composition | M.W. (g/mol) | Appearance | Melting Point (\(^d\)\(^\circ\)C) | Yield(%) | Calculated | (Found) % |
|-------------------|-----------------------|--------------|------------|-----------------------------------|----------|------------|-----------|
| Ligand (4)        | \(C_{13}H_{14}N_{6}O_{3}\)  | 302.29       | Dark-yellow | 243                               | 76       | 51.65(51.70)| 4.67(4.71)| 27.80(27.74) |
| Complex(4a)       | \(C_{26}H_{26}N_{12}O_{6}\)Ni | 661.27       | Red-brown  | >370 *                            | 72       | 47.23(47.16)| 3.96(3.89)| 25.42(25.36) |
| Complex(4b)       | \(C_{26}H_{26}N_{12}O_{6}\)Co | 661.51       | Dark-brown | 230 *                             | 70       | 47.21(47.28)| 3.96(3.89)| 25.41(25.57) |
| Complex(4c)       | \(C_{26}H_{26}N_{12}O_{6}\)Cu | 666.12       | Dark-brown | 195 *                             | 64       | 46.88(46.81)| 3.93(3.88)| 25.23(27.17) |

(d)*: decomposition

Table 8: Infrared data for the ligand(4) and its complexes

| Compound          | \(\nu(O-H)\) | \(\nu(N-H)\) | \(\nu(C=O)\) | \(\nu(C=N)_{oxim}\) | \(\nu(C=N)_{hyd}\) | \(\nu(CH)_{arom}\) | \(\nu(CH)_{alip}\) | \(\nu(N-N)\) | \(\nu(N-O)\) | \(\nu(OH-O)\) |
|-------------------|--------------|--------------|--------------|----------------------|----------------------|---------------------|---------------------|----------------|----------------|----------------|
| Ligand (4)        | 3681\(^w\)   | 3271\(^w\)   | 1667\(^s\)   | 1536-1556\(^m\)     | 2970\(^m\)           | 3088\(^m\)          | 1484-1441\(^m\)   | 1033\(^m\)      | -              |                |
| Complex(4a)       | 3271\(^m\)   | 3271\(^m\)   | 1667\(^w\)   | 1594-1677\(^m\)     | 2970\(^m\)           | 2844\(^m\)          | 1449-1484\(^m\)   | 1033\(^m\)      | 1738\(^m\)     |                |
| Complex(4b)       | 3271\(^m\)   | 3271\(^m\)   | 1667\(^w\)   | 1594-1677\(^m\)     | 2970\(^m\)           | 2844\(^m\)          | 1449-1484\(^m\)   | 1033\(^m\)      | 1738\(^m\)     |                |
| Complex(4c)       | 3168\(^m\)   | 3168\(^m\)   | 1655\(^m\)   | 1594-1677\(^m\)     | 2970\(^m\)           | 2864\(^m\)          | 1449-1484\(^m\)   | 1033\(^m\)      | 1738\(^m\)     |                |

Compound’s Synthesis

For the synthesis of all three complexes, a general method was used.\(^{16}\) The 2 mmol of the above ligands (1-4), were dissolved in 10 mL absolute ethyl alcohol at refluxing temperature. A solution of NiCl\(_2\).6H\(_2\)O or CuCl\(_2\).2H\(_2\)O or CoCl\(_2\).6H\(_2\)O (1 mmol) with water (15 mL) is taken and then mixed dropwise over the ligand solution with vigorous stirring, a noticeable color change as well as a reduction in the pH value (~3.0–3.5) was observed. Sodium hydroxide (1%) in water (20 mL) has been mixed to adjust the pH ~5–5.5 and maintained the temperature of the reaction mixture nearly to room temperature. Mixtures have been stirred by the hour at 50\(^\circ\)C on a water bath so as to ensure complete precipitation of complexes. After one hour the precipitated solid has been filtered, washed by means of hot ethanol (3x5 mL) also dehydrated in vacuo, over anhydrous CaCl\(_2\). Proposed structures for the monomeric Co(II), Ni(II) Cu(II) as well as the ligands (1-4) are given in Scheme 3.

![Scheme 3. Structure of the metal complexes](image-url)
(1a) **Appearance:** Dark brown powder, Yield = 52%, m.p. (decomp.) > 370°C; This compound is soluble in commonly used solvents like CH₂Cl₂, CHCl₃, DMF, EtOH and DMSO. Anal. Calcd. for C₉H₅N₂O₄Ni (633.21 g mol⁻¹): 45.52% C; 3.50% H; 26.54% N; Found: 45.60% C; 3.43% H; 26.47% N.

**FT-IR (KBr, ν max/cm⁻¹):** 3271 (N-H), 3681 (O-H), 2970 (C-H Arom.), 1609-1677 (C=N), 2864 (C-H

(1b) **Appearance:** Red-brown powder, Yield = 76%, m.p. (decomp.) > 230°C; This compound is soluble in commonly used solvents like CH₂Cl₂, CHCl₃, DMF, EtOH and DMSO. Anal. Calcd. for C₉H₅N₂O₄Co (661.07 g mol⁻¹): 45.51% C; 3.50% H; 26.53% N; Found: 45.58% C; 3.43% H; 26.44% N.

**Yield:** 78%, m.p. (decomp.) > 240°C; This compound is soluble in commonly used solvents like CH₂Cl₂, CHCl₃, DMF, EtOH and DMSO. Anal. Calcd. for C₉H₅N₂O₄Ni (723.21 g mol⁻¹): 39.86% C; 2.79% H; 27.11% N; Found: 39.93% C; 2.85% H; 27.69% N.

(2a) **Appearance:** Dark-brown powder, Yield = 64%, m.p. (decomp.) > 195°C; This compound is soluble in commonly used solvents like CH₂Cl₂, CHCl₃, DMF, EtOH and DMSO. Anal. Calcd. for C₁₂H₁₀Ni₂O₄Co (661.51 g mol⁻¹): 47.21% C; 3.96% H; 25.42% N; Found: 47.28% C; 3.89% H; 25.57% N.

(3a) **Appearance:** Red-brown powder, Yield = 72%, m.p. (decomp.) > 230°C; This compound is soluble in commonly used solvents like CH₂Cl₂, CHCl₃, DMF, EtOH and DMSO. Anal. Calcd. for C₁₀H₈N₂O₄Ni (793.12 g mol⁻¹): 45.03% C; 3.78% H; 24.24% N; Found: 45.09% C; 3.72% H; 24.17% N.

(3b) **Appearance:** Dark-brown powder, Yield = 65%, m.p. (decomp.) > 350°C; This compound is soluble in commonly used solvents like CH₂Cl₂, CHCl₃, DMF, EtOH and DMSO. Anal. Calcd. for C₁₀H₈N₂O₄Co (793.50 g mol⁻¹): 45.03% C; 3.78% H; 24.24% N; Found: 45.09% C; 3.72% H; 24.17% N.

(3c) **Appearance:** Red-brown powder, Yield = 68%, m.p. (decomp.) > 196°C; This compound is soluble in commonly used solvents like CH₂Cl₂, CHCl₃, DMF, EtOH and DMSO. Anal. Calcd. for C₁₀H₈N₂O₄Cu (798.12 g mol⁻¹): 44.73% C; 3.68% H; 24.08% N; Found: 44.79% C; 3.68% H; 24.66% N.

(4a) **Appearance:** Red-brown powder, Yield = 70%, m.p. (decomp.) > 230°C; This compound is soluble in commonly used solvents like CH₂Cl₂, CHCl₃, DMF, EtOH and DMSO. Anal. Calcd. for C₁₂H₁₀Ni₂O₄Co (661.12 g mol⁻¹): 47.23% C; 3.96% H; 25.42% N; Found: 47.28% C; 3.89% H; 25.57% N.

(4b) **Appearance:** Dark-brown powder, Yield = 72%, m.p. (decomp.) > 370°C; This compound is soluble in commonly used solvents like CH₂Cl₂, CHCl₃, DMF, EtOH and DMSO. Anal. Calcd. for C₁₀H₈N₂O₄Co (661.12 g mol⁻¹): 47.23% C; 3.96% H; 25.42% N; Found: 47.28% C; 3.89% H; 25.57% N.

(4c) **Appearance:** Dark-brown powder, Yield = 64%, m.p. (decomp.) > 195°C; This compound is soluble in commonly used solvents like CH₂Cl₂, CHCl₃, DMF, EtOH and DMSO. Anal. Calcd. for C₁₀H₈N₂O₄Ni (798.12 g mol⁻¹): 44.73% C; 3.68% H; 24.08% N; Found: 44.79% C; 3.68% H; 24.66% N.

**In vitro antimicrobial activity**

The antimicrobial activity of the test compounds was evaluated by way of agar well diffusion method. 0.1 mL of the diluted inoculum (106 CFU/mL) of test organisms are taken and spread on NA/SDA (Nutrient agar/Sabouraud dextrose agar) plates. Wells of 6 mm diameter have been punctured into the agar medium and filled one by one with 150 mL of compound (150 µg/L) solvent blank and antibacterial (chloramphenicol, 100 µg/L) to which the test the sensitivity of bacteria. Fluconazole at the concentration of 10 µg/L has been applied for the monitor versus Candida albicans, Candida tropicalis and Candida glabrata. The plates were incubated for at 37°C 24 hours. Antimicrobial activity was has been assessed in order to the zone of inhibition versus the test organism.
RESULTS AND DISCUSSION

Spectral studies: structure of ligands and complexes

Synthesis of new hydrazoneoxime ligands bearing pyrazolone group (1-4) that were prepared by reaction of (1Z,2E)-N-hydroxy-2-(hydroxyimino) ethanimidoyl chloride with hydrazinium hydroxide and their metal complexes 1(a-c), 2(a-c), 3(a-c), 4(a-c) were reported (Scheme 2 and 3). The ligands used in this work were prepared using the literature mentioned elsewhere. The atomic arrangement of the synthesized ligands (1-4) including their metal complexes were established on the basis of their elemental analysis, FI-TIR, $^1$H NMR, $^{13}$C NMR, along with the calculation of their magnetic susceptibility as well. The analytical and physical properties of the prepared ligands including their metal complexes be summarised in Tables 1,3,5, along with 7.

The FT-IR spectrum related to the synthesized ligands (1-4) as well as metal complexes 1(a-c), 2(a-c), 3(a-c) and 4(a-c), 1-4 and 1(a-c), 2(a-c), 3(a-c) and 4(a-c) exhibited a carbonyl (keto) band at 1655-1667 cm$^{-1}$ and NH band (hydrazo) at 3168-3271 cm$^{-1}$ as shown in the IR spectral data of the representative ligand (1) (Fig. 1). The IR frequencies of the representative ligand and its complexes are shown in Table 1. The IR spectral collected statistics of the synthesized metal complexes has to be given into Tables 2,4,6 and 8. Such said values indicated that each complexes are exist in keto-hydrazo form (T$_2$) as well as in solid-state.

The $^1$H NMR spectra of all ligands (1-4) in DMSO-d$_6$ showed a single peak lying between 2.16-2.20 ppm corresponding to methyl protons (pyrazolone-CH$_3$) at. The $^1$H NMR spectral data of ligand (3) indicated a singlet for methoxy protons (Ph-OCH$_3$) at 3.74 ppm while another singlet for methyl protons (Ph-CH$_3$) at 2.27 ppm. The $^1$H NMR spectra of all the ligands (1-4) showed multiple peak at between 6.98-7.78 ppm for aromatic protons (Ar-H). The $^1$H NMR spectra of all ligands (1-4) also showed a single peaks for (CH=NOH) protons lying in the range of 7.83-7.85 ppm. They also exhibited a doublet for the characteristic oxime OH protons (OH) in the range 11.76-12.22 ppm. Such chemical shifts have to be distinctive values, favour hydrazones and oximes, that help in to ascertain the proposed structure.

The possible tautomeric forms of compounds (1-4) as indicated in Scheme 4. The compounds possibly be present in four likely tautomeric models i.e. keto-azo ($T_1$ and $T_4$), keto-hydrazo ($T_2$), as well as enol-azo ($T_3$). In accordance with the literature, better stabilize automeric model exist in the keto-hydrazo form ($T_2$). It may be due to the presence of the intramolecular O---H bond, can show the stability of compounds in corresponding tautomeric form. The result is consistent with the literature.
The coordination compounds of nickel(II), copper(II) and cobalt(II) have been synthesized as per general methodology\textsuperscript{1,16} as discussed previously (Scheme 3). The metal ion and ligands react in 1:2 molar ratios, where the ligands are attached to metal by using its two N atoms, like almost all of vic-dioximes act. All of this coordinated compounds are colored, amorphous solids, stable at room temperature as well. The discussed complexes are insoluble in commonly used organic solvents, but are soluble in DMF and DMSO. The recommended structures of the synthesized coordination compounds has been demonstrated in Scheme 3 that are supported by spectroscopic, FTIR spectral data and elemental analysis studies. As per the suggested structures, the complexes can have syn-or anti-conformation\textsuperscript{28}. The magnetic moment (\(\mu_{\text{eff}}\)) statistics further favoured the mononuclear structures of the coordinated complexes. The magnetic moment for the nickel(II) complexes are diamagnetic at room temperature, since it is expected due to the \(d^8\) and \(d^{10}\) electronic configurations\textsuperscript{30}. The magnetic moments (\(\mu_{\text{eff}}\)) of the copper(II) complexes are 1.63, 1.76, 1.77 and 1.77 BM, respectively, so they are paramagnetic in nature. The cobalt(II) complexes of ligands are paramagnetic and their magnetic moments (\(\mu_{\text{eff}}\)) are 2.05, 2.07, 2.08 and 2.09 BM, respectively. The lower figure possibly due to the anti ferromagnetic interaction between neighboring magnetic centers.

The another chemical environments will assign between two (O•••H–O) bridge protons in the \textit{cis}-form, at the same time one in the \textit{trans}-form. Experience of the H-bond (O•••H–O) in the IR and \(^1\)H NMR spectrum, appearing in single frequency in all cases, that indicates the nickel(II) complex is in the \textit{anti}-form media. On the basis of the above experimental findings, the geometry of the nickel(II) and copper(II) and cobalt(II) complexes are recommended as square-planar\textsuperscript{1,16}.

The possible tautomeric forms of new nickel(II) and copper(II) and cobalt(II) complexes \(1(a-c), 2(a-c), 3(a-c)\) and \(4(a-c)\) has to be explained in Scheme 5. The newly synthesized complexes possibly occurs into four probable tautomeric forms i.e. keto-azo (\(T_1\) and \(T_2\)), keto-hydrazone (\(T_3\)) as well as in enol-azo (\(T_4\)) form. As reported in the literature, utmost stabilized tautomeric form is a keto-hydrazone form (\(T_3\)) for azopyrazolone dyes. The complexes have an intramolecular hydrogen bonding N-H…O for keto-hydrazone (\(T_3\)) form and O-H…N for enol-azo (\(T_4\)) form. These results are consistent with the literature\textsuperscript{25,26-29,31}.

### Table 9: Antimicrobial activity of the synthesized compounds by well diffusion assay

| S. No | Compounds tested | Effective concentration (µg/well) | Antimicrobial activity of metal complexes [inhibition zone mm] |
|-------|------------------|-----------------------------------|---------------------------------------------------------------|
|       |                  |                                   | A    | B    | C    | D    | E    | F    | G    |
| 1     | 1a               | 150                               | 9    | 9    | 10   | 14   | 14   | 14   | 14   |
| 2     | 1b               | 150                               | 10   | 9    | 15   | 14   | 15   | 15   | 15   |
| 3     | 1c               | 150                               | 8    | 8    | 13   | 14   | 14   | 14   | 14   |
| 4     | 2a               | 150                               | 11   | 10   | 14   | 14   | 14   | 14   | 14   |
| 5     | 2b               | 150                               | 12   | 11   | 15   | 15   | 14   | 14   | 14   |
| 6     | 2c               | 150                               | 8    | 9    | 12   | 13   | 12   | 12   | 12   |
| 7     | 3a               | 150                               | 11   | 10   | 17   | 17   | 18   | 18   | 16   |
| 8     | 3b               | 150                               | 15   | 14   | 14   | 20   | 19   | 19   | 18   |
| 9     | 3c               | 150                               | 8    | 8    | 15   | 14   | 14   | 14   | 14   |
| 10    | 4a               | 150                               | 9    | 8    | 13   | 15   | 15   | 15   | 14   |
| 11    | 4b               | 150                               | 11   | 10   | 16   | 15   | 15   | 15   | 14   |
| 12    | 4c               | 150                               | 8    | 8    | 14   | 14   | 14   | 14   | 14   |
| Chloramphenicol | 100               | --                                | --   | --   | 30   | 30   | 30   | 30   | 30   |
| Fluconazole     | 100               | 28                                | 25   | 25   | --   | --   | --   | --   | --   |

### Biological activity
The synthesized compounds have been examined for their antimicrobial (antibacterial and anti-fungal) activity.

#### Antimicrobial activity
The \textit{In vitro} antimicrobial (\textit{S. aureus}, \textit{B. subtilis}, \textit{E. coli}, \textit{P. aeruginosa} and anti fungal (\textit{C. albicans}, \textit{C. tropicalis} and \textit{C. glabrata} laboratory isolate) activities of the compounds \textit{1a-4c} were evaluated by agar well diffusion method\textsuperscript{22}. The results for the antimicrobial study of the tested compounds against the test organisms are illustrated as in Table 9.
**A-Candida albicans, B-Candida tropicalis, C-Candida glabrata, D-Staphylococcus aureus, E-Bacillus subtilis, F-Escherichia coli, G-Pseudomonas aeruginosa**

Results of the synthesized compounds 1a, 1b, 1c, 2a, 2b, 2c, 3a, 3b, 3c, 4a, 4b and 4c are outlined for antimicrobial activity with respect to four bacteria *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa* and three fungal as *Candida albicans, Candida tropicalis* and *Candida glabrata* are illustrated in Table 9.

Antimicrobial activity against "*Gram-positive*", "*Gram-negative*" bacteria and against fungus have been seen across all the synthesized compounds. Newly synthesized compounds 3b showed significant gross broad-spectrum antimicrobial activity, i.e., against "*Gram-positive*", "*Gram-negative" bacteria as well as anti fungal. The effective concentration of these active compounds was 150 µg/well.

**CONCLUSION**

Investigations into the synthesis of new hydrazone oxime ligands having pyrazolone group and their metal complexes have been carried out in this study. The synthesized pyrazolone derivatives of Co(II), Ni(II) and Cu(II) complexes were isolated and their structures were characterized using physicochemical techniques. Also, tautomerism in the ligands was investigated by spectroscopic. Chemical properties of the complex compounds depend upon tautomerism and also physical properties like colour fastness depend on it. The attachment of ligands to the metal ion in a neutral bidentate form with the azomethine nitrogen (CN) and the carbonyl oxygen (C=O). The calculated magnetic moments of the coordinated complex compounds as 2.92 B.M for the nickel(II) and 1.65 B.M for the copper(II) are approximate the spin values only and propose a square planar geometry for the complexes. The compounds 3b exhibited broad-spectrum antimicrobial activity. Expeditions to explore their potentialities in the future for other biological assays are needed to investigate further. Furthermore, some Co(II) complexes act as potent anti-cancer agents due to their anti-proliferative effects; in this regard, the synthesized compounds should be investigated in the future as well. These complexes can be further explored in the dye/color industry due to the presence of chromophores.

**ACKNOWLEDGMENT**

We acknowledge to Aydın Adnan Menderes University Scientific Research Foundation for their financial support (Project No: FEF-18022).

**Conflict of Interest**

The authors declare that they have no conflict of interest.

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