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# Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry

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# Synthesis and Structural and Biochemical Activity Studies of Dioxime Ligand and its Mononuclear Cu(II), Ni(II), and Co(II) Complexes

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# Synthesis and Structural and Biochemical Activity Studies of Dioxime Ligand and its Mononuclear Cu(II), Ni(II), and Co(II) Complexes

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**A new tetradentate ligand incorporating dioxime moities has been synthesized. Its copper(II), nickel(II), and cobalt(II) complexes have been prepared and characterized by spectral methods. Elemental analyses and spectroscopic data of the metal complexes are consistent with the formation of the mononuclear copper(II), nickel(II) and cobalt(II) complexes. The crystal structure of the (2*E*, 2′*E*)-butane-2,3-dione 2,2′-{$O^2$,$O^{2'}$-[1,2-phenylenebis(methylene)]oxime compound (3) was determined by single-crystal x-ray diffraction technique. The free ligand and copper(II), nickel(II), and cobalt(II) complexes (5–7) were tested against the morphology of series bacteria. The Cu(II), Ni(II), and Co(II) complexes exhibit higher activity than dioxime ligand under identical experimental conditions.**

**Keywords** antimicrobial activity, dione dioxime, metal complexes

Over the years, oximes have been widely used as very efficient complexing agents in analytical chemistry for isolation, separation, and extraction of different metal ions.[1–4] The incorporation of oxime functions in multidonor ligands may give rise to strong chelating agents.[2–4] Oximes and oxime ethers are important building blocks in organic synthesis. The addition of organometallic or radical species to oxime ethers is a synthetically valuable protocol for the construction of C–C bonds, and various useful reactions are built through this methodology.[5–8] Generally, oxime ethers were prepared from *O*-alkyl hydroxylamines and the corresponding aldehydes.[9] The direct preparation of oxime ethers from oximes has been commonly limited to the reaction of oximes with alkyl halides under basic conditions.[10,11] Recently, several new methods have been discovered by using oximes in transition metal-catalyzed allylic substitution[12,13] and Michael addition,[14] as well as Cu-catalyzed cross-coupling reaction.[15]

This article describes the syntheses and characterization of the new ligand (2*E*, 3*E*, 2′*E*, 3′*E*)-butane-2,3-dione 2,2′, 3,3′-{$O^2$, $O^{2'}$-[1,2-phenylenebis(methylene)]oxime}, ($H_2L$), and its new complexes with Cu(II), Ni(II), and Co(II). The properties of the complexes were investigated by magnetic, physical, and spectral methods. Furthermore, the crystal structure of the (2*E*, 2′*E*)-butane-2,3-dione 2,2′-{$O^2$,$O^{2'}$-[1,2-phenylenebis(methylene)]oxime, (**3**) was determined by single-crystal x-ray diffraction technique. The dioxime ligand ($H_2L$) and its Cu(II), Ni(II), and Co(II) complexes were evaluated for antimicrobial activity against one gram-positive bacterium (*Staphylococcus aureus*), a gram-negative bacterium (*Escherichia coli*), and the fungi *Aspergillus niger* and *Trichoderma*. The antimicrobial activities are presented in Table 1, showing that the dioxime ligand and Cu(II), Ni(II), and Co(II) complexes exhibit antibacterial activity against both strains.

## EXPERIMENTAL

$^1$H-Nuclear magnetic resonance (NMR) and $^{13}$C-NMR spectra were recorded on a Varian Gemini 200 spectrometer. $CDCl_3$ and dimethyl sulfoxide (DMSO)-$d_6$ were used as solvent. Chemical shifts ($\delta$) were reported in parts per million (ppm) relative to tetramethylsilane, using the solvent signal as the internal reference. Elemental analyses (C, H, and N contents) were performed on a Costech 4010 CHNS elemental analyzer, and metal contents were estimated spectrophotometrically. Infrared (IR) spectra were recorded on an ATI Unicam Matson 1000 model Fourier-transform IR (FTIR) spectrophotometer and ultraviolet–visible (UV-Vis) spectra on an ATI Unicam UV2 model UV/Vis spectrophotometer. Mass spectra (electrospray ionization, ESI) were recorded on a Micromass Quanto LC-MS/MS spectrophotometer. Room-temperature magnetic susceptibility

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TABLE 1
Antibacterial activity of compounds (diameter of inhibition zone in mm) and antifungal activity weight (mg) (% inhibition) of the ligand and complexes

| | Antibacterial activity (mg mL$^{-1}$) | | | | Antifungal activity (mg mL$^{-1}$) | | | |
|---|---|---|---|---|---|---|---|---|
| | *E. coli* | | *S. aureus* | | *A. niger* | | *Trichoderma* | |
| Compound | 0.5 | 1 | 0.5 | 1 | 0.5 | 1 | 0.5 | 1 |
| Ciprofloxin/control | 40 | 45 | 42 | 44 | 74 | 72 | 66 | 62 |
| $H_2L$ | 10 | 12 | 10 | 12 | 65 (12) | 60 (15) | 40 (30) | 25 (60) |
| **5** | 25 | 35 | 20 | 27 | 45 (44) | 12 (85) | 30 (60) | 20 (65) |
| **6** | 12 | 14 | 13 | 17 | 47 (40) | 15 (80) | 30 (50) | 25 (60) |
| **7** | 22 | 20 | 15 | 19 | 50 (29) | 20 (75) | 35 (55) | 24 (61) |

measurements were done on a PAR model 155 vibrating sample magnetometer. All chemicals were of the highest quality available, obtained from local suppliers, and used as received.

### (2E,2′E)-Butane-2,3-dione 2,2′-{$O^2$,$O^{2'}$-[1,2-Phenylenebis (methylene)]oxime} (3)

To a vigorously stirred solution of 2,3-butanedione monoxime (2.1 g, 20 mmol) and 1,2-bis(brommethyl)benzen (2.5 g, 10 mmol) in 1:1 MeOH/$H_2O$ (25 mL) was added a solution of KOH (1.12 g, 20 mmol) in MeOH (10 mL) at 0°C over ~30 min. After stirring for 24 h at room temperature, the reaction mixture was filltered and washed with MeOH. The crude product was recrystallized from EtOH as a white microcrystalline solid, melting point (m.p.) 60°C. Yield: 3.0 g (96%). MS (ESI): *m/z* = 327 $[M+Na]^+$. Elemental analysis (%): calculated: C, 63.14; H, 6.62; N, 9.20; found: C, 63.10; H, 6.50; N, 9.30.

### (2E,3E,2′E,3′E)-Butane-2,3-dione 2,2′,3,3′-{$O^2$,$O^{2'}$-[1,2-Phenylenebis(methylene)]-oxime}, ($H_2L$)

A solution of (2*E*,2′*E*)-butane-2,3-dione 2,2′-{$O^2$,$O^{2'}$-[1,2-phenylenebis(methylene)]oxime} (3.0 g, 10 mmol) and $HONH_2$.HCl (9.87 g, 142 mmol) in pyridine (50 mL) was stirred at room temperature for 24 h and the mixture was then poured into ice-cold $H_2O$ (200 mL). The resulting precipitate was collected, washed successively with ice-cold $H_2O$ and $Et_2O$, and dried in vacuo over $P_2O_5$. Recrystallization from 1:1 EtOH/DMSO (30 mL) gave ($H_2L$) as a colorless microcrystalline solid, m.p. 180–181°C. Yield: 3.1 g (92%). MS (ESI): *m/z* = 357 $[M+Na]^+$. Elemental analysis (%): calculated: C, 57.47; H, 6.63; N, 16.76; found: C, 57.40; H, 6.70; N, 16.65.

### Preparation of Metal Complexes

The $[Cu(HL)(H_2O)]ClO_4$ (**5**), $[Ni(HL)(H_2O)_2]ClO_4$ (**6**) and $[Co(HL)(H_2O)_2]ClO_4$ (**7**) complexes have been synthesized by the same method. A solution of $M(ClO_4)_2 \cdot 6H_2O$ (2 mmol) in $Me_2CO$ (25 mL) was added to the ligand (0.670 g, 2 mmol) solution in $Me_2CO$ (25 mL), and the mixture was boiled under reflux with stirring for 10 h. The products were filtered off, washed with $H_2O$, MeOH, and $Et_2O$, and dried over $P_2O_5$.

For $[Cu(HL)(H_2O)]ClO_4$, (**5**), elemental analysis (%): calculated: C, 37.36; H, 4.50; N, 10.89; Cu, 12.35; found: C, 37.50; H, 4.45; N, 10.90; Cu, 12.20. Yield: 0.75 g (73%). MS (ESI): *m/z* = 415.8 $[Cu(HL)(H_2O)+1]^+$. Yield, a green-brown solid: 0.670 g (65%). For $[Ni(HL)(H_2O)_2]ClO_4$ (**6**), elemental analysis (%): calculated: C, 36.36; H, 4.73; N, 10.60; Ni, 11.17; found: C, 36.30; H, 4.65; N, 10.67; Ni, 11.05. Yield, a pale-red solid: 0.60 g (57%). MS (ESI): *m/z* = 429.5 $[Ni(HL)(H_2O)_2+1]^+$. For $[Co(HL(H_2O)_2]ClO_4$ (**7**), elemental analysis (%): calculated: C, 36.35; H, 4.72; N, 10.60; Co, 11.18; found: C, 36.30; H, 4.65; N, 10.65; Co, 11.15. Yield, a deep-brown solid: 0.70 g (67%). MS (ESI): *m/z* = 430.49 $[Co(HL(H_2O)_2\ +1]^+$.

### General Procedure for Single-Crystal X-Ray Structure Determination

The molecular data were collected on a STOE IPDS II (16) diffractometer using the $^{MoK_{\alpha}}$ radiation at room temperature. For the title compound, data collection: X-AREA; cell refinement: X-AREA; data reduction: X-RED32[16]; program used to solve structure: SHELXS97[17]; program used to refine structure: SHELXL97[18]; molecular figures: ORTEP III[18]; publication software: WinGX[19] and PARST.[20] The structure was solved by direct methods with SHELXS-97 and refined by full-matrix least-squares procedures on $F^2$, using the program SHELXL-97 computer program belonging to the WinGX software package. The refinement was carried out by full-matrix-least squares method on the positional and anisotropic temperature parameters of non-hydrogen atoms corresponding to 215 crystallographic parameters. Atoms H7A, H7B, H12A, and H12B were located in a difference Fourier map and refined isotropically, and the other H atoms were positioned geometrically and treated using a riding model, fixing the bond lengths at 0.93 and 0.96 Å for CH and $CH_3$, respectively. The displacement parameters of the H atoms were fixed at $U_{iso}(H) = 1.2U_{eq}$ ($1.5U_{eq}$ for methyl) of their parent atoms. The structure was refined to $R_{int} = 0.039$ with 2359 observed reflections by the condition of $I > 2\sigma(I)$ threshold. Details of the data collection conditions and the parameters of refinement process are given in Table 2.

TABLE 2
Crystallographic data for compound (**3**)

| | |
|---|---|
| CCDC deposition no. | 771226 |
| Color/shape | Colorless/prismatic plate |
| Chemical formula | $C_{16}H_{20}N_2O_4$ |
| Formula weight | 304.34 |
| Temperature (K) | 296 |
| Wavelength (Å) | 0.71073 Mo Ka |
| Crystal system | Triclinic |
| Space group | $P\bar{1}$ |
| Unit cell parameters | |
| a, b, c (Å) | 8.589(7), 10.015(6), 10.939(6) |
| $\alpha$, $\beta$, $\gamma$ (å) | 106.77(4), 96.68(5), 109.74(5) |
| Volume (Å$^3$) | 823.9(9) |
| Z | 2 |
| Calculated density (mg/m$^3$) | 1.227 |
| $\mu$ (mm$^{-1}$) | 0.09 |
| Absorption correction | Integration (X-RED32) |
| $T_{\min}$, $T_{\max}$ | 0.946, 0.975 |
| $F(000)$ | 324 |
| Crystal size (mm) | 0.73 × 0.57 × 0.37 |
| Diffractometer/measurement method | STOE IPDS II/rotation ($\omega$ scan) |
| Index ranges | $-10 \leq h \leq 10$, $-12 \leq k \leq 12$, $-13 \leq l \leq 13$ |
| Range for data collection (å) | $2.0 \leq \theta \leq 26.0$ |
| Measured reflections | 9093 |
| Independent/observed reflections | 3242/2359 |
| $R_{\text{int}}$ | 0.039 |
| Refinement method | Full-matrix least-squares on F$^2$ |
| Data/restraints/parameters | 3242/0/215 |
| Goodness-of-fit on F$^2$ | 1.07 |
| R indices [I > 2$\sigma$ (I)] | $R_1 = 0.049$, $wR_2 = 0.1337$ |
| R indices (all data) | $R_1 = 0.07$, $wR_2 = 0.144$ |
| Weighting scheme | $w = 1/[\sigma^2(F_o{}^2) + (0.0806P)^2 + 0.0448P]$ $P = (F_o{}^2 + 2F_c{}^2)/3$ |
| $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å$^{-3}$) | 0.18, –0.23 |

## Antimicrobial Activity

The antibacterial activity of dioxime ligand, its Cu(II), Ni(II), and Co(II) complexes, the metal salts, and the control (DMSO) was tested *in vitro* against gram-positive bacteria (*Staphylococcus aureus*) and gram-negative bacteria (*Escherichia coli*) by a paper disc method.[21] Sterile (10-mm diameter) Whatman number 42 paper discs were soaked in different concentrations of ligand/complexes (0.5 and 1 mg L$^{-1}$) in DMSO, dried, and then placed on nutrient agar plates. The plates were then incubated for 24 h at 37°C and the inhibition zone around each disc was measured. The results obtained were compared with those of ciprofloxin. Three replicates were taken and the average value is given in Table 1. The free ligand, its Cu(II), Ni(II), and Co(II) complexes, metal salts, and the control (DMSO) were screened for antifungal activity against the fungi *Aspergillus niger* and *Trichoderma* at 0.5 and 1 mg L$^{-1}$ by the mycelial dry weight (MDW) method.[22] The cultures of fungi were purified by single-spore isolation technique. The glucose nitrate (GN) medium was used for growth of fungi. The mycelial biomass was then dried along with filter paper in an oven at 65 ± 5°C to constant weight, cooled, and finally weighed. The MDW was obtained by subtracting the weight of mycelium-free filter paper from final dry weight.[23] Three replicates of each treatment were repeated in all experiments. The MDW was corrected each time by subtracting the dry weight obtained from the incubated flask under similar experimental conditions. The yields of MDW (mg) are presented in Table 1. The percentage error was found to be ±0.01. The percent decrease in MDW to the test compound in each case was calculated and tabulated in terms of average percentage inhibition. The results indicate that the ligand and its metal complexes arrested the growth of fungi.

## RESULTS AND DISCUSSION

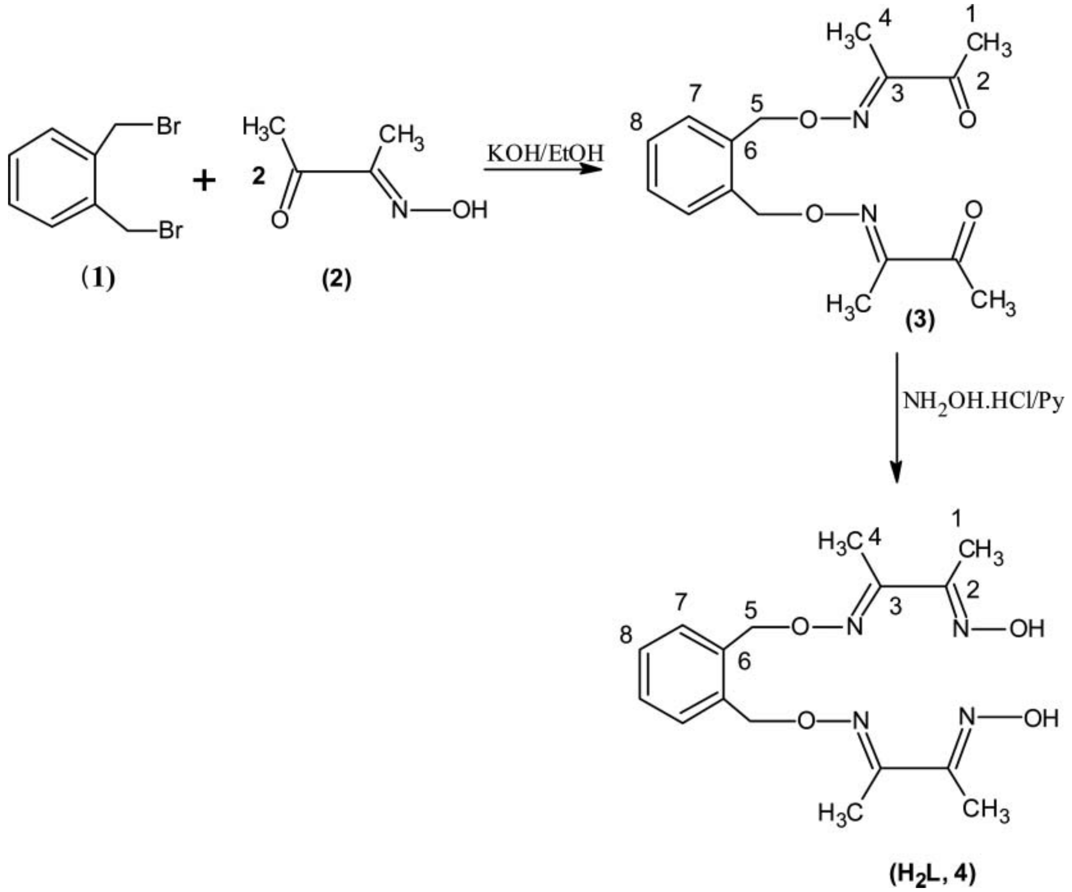
(2E,3E,2′E,3′E)-Butane-2,3-dione 2,2′,3,3′-{O2,O2′-[1,2-phenylenebis(methylene)]-oxime} ($H_2L$) was synthesized in EtOH by reacting (2*E*,2′*E*)-butane-2,3-dione 2,2′-{*O*$^2$,*O*$^{2\prime}$-[1,2-phenylene bis-(methylene)]oxime} (**3**) with hydroxylamine hydrochloride (Scheme 1). The dioxime ($H_2L$) and dione (**3**) were characterized by elemental analysis, $^1$H-NMR, $^{13}$C-NMR, IR, and mass spectral data. In addition, copper(II), nickel(II), and cobalt(II) complexes of dioxime have been prepared and characterized by elemental analyses and magnetic moment, UV-Vis, IR, and mass spectral data. In the proposed structure of ($H_2L$), $N_4$ units are available for the complexation of metal ions.

### NMR Spectra

The $^1$H-NMR spectra of dione (**3**) (in $CDCl_3$) and dioxime ligand ($H_2L$) (in DMSO-d$_6$) showed well-resolved signals as expected (Table 3). The proton NMR spectrum of compound **3** showed the following signals: $C_6H_4$ as multiplet at $\delta$ = 7.20–7.60, = C-CH$_3$ singlet at $\delta$ = 1.95 and 2.40, O-CH$_2$-singlet at $\delta$ = 5.40. The proton NMR spectrum dioxime ligand showed the following signals: $C_6H_4$ as multiplet at $\delta$ = 7.15–7.55, = C-CH$_3$ singlet at $\delta$ = 1.90 and 1.98, O-CH$_2$- singlet at $\delta$ = 5.25, = N-OH singlet at $\delta$ = 11.60. In the $^1$H-NMR spectra, integrated data are consistent with the formula. Eight resonance signals were observed in the $^{13}$C-NMR spectra of dione (**3**) and dioxime ligand ($H_2L$), which was also consistent with the formula for $H_2L$.

### Crystal Data for (2E,2′E)-Butane-2,3-dione 2,2′-{O$^2$,O$^{2\prime}$-[1,2-Phenylenebis(methylene)]oxime} (3)

The crystal structure of the (2E,2′E)-butane-2,3-dione 2,2′-{O$^2$,O$^{2\prime}$-[1,2-phenylenebis(methylene)]-oxime (**3**),



SCH. 1. Preparation of ligands, $(H_2L)$.

$C_{16}H_{18}N_2O_4$, was determined by single-crystal x-ray diffraction technique. The compound **(3)** crystallized in the triclinic space group $P\bar{1}$ with the following unit-cell parameters: a = 8.589(7) Å, b = 10.015(6) Å, c = 10.939(6) Å, $\alpha$ = 106.77(4)å, $\beta$ = 96.68(6)å, $\gamma$ = 109.74(5)å, and V = 823.9(9) $Å^3$, with crystallographic data shown in Table 2. The molecular structure of (**3**), with the atom numbering scheme, is shown in Figure 1, and selected interatomic distances and angles are listed in Table 4. The compound **(3)** is not planar. The (C6/C7/O2/N2/C8/C11/C9) and (C1/C12/O1/N1/C13/C16/C14) moieties were oriented with respect to the phenyl ring A (C1–C6) at dihedral angles of 19.66(10)° and 82.70(11)°, respectively. The 2,3-butanedione monoxime fragment deviated from planarity because of a twist between the oxime and carbonyl C( = O)$CH_3$ groups about the C8–C9 and C13–C14 bonds; the N2-C8-C9-C10 and N1-C13-C14-C15 torsion angles were 12.5(3)° and 6.1(3)°, respectively. The C—N and N—O bond lengths in the oxime moities of (**3**) are in the normal ranges and compare well with the literature values for similar compounds.[24–26]

Molecular system exhibited weak intramolecular interactions, namely, C5–H5. . .O2, C11–H11A. . .O2, and C16–H16A. . .O1 and the details of them were shown in Table 4. These hydrogen bonds formed rings of graph-set motif S(5).[26] The $\pi$–$\pi$ contact between the phenyl rings, $Cg1$-$Cg1^{i}$ [symmetry code: (i) 1 – *x*, –*y*, –*z*, where $Cg1$ was centroid of the ring (C1/C2/C3/C4/C5/C6)], might further stabilize the structure, with centroid–centroid distance of 4.015(3) Å. To give an overall picture for just oxime, the Cambridge Structural

TABLE 3
$^1$H-NMR data of dione (**3**) and ligand $(H_2L)$

| Compound | $CH_3$–1 | $CH_3$–4 | −$CH_2$–5 | Ar-H | −OH |
|---|---|---|---|---|---|
| (**3**) | 2.40 (s, 6H) | 1.95 (s, 6H) | 5.40 (s, 4H) | 7.20–7.60 (m, 4H) | — |
| $H_2L$ (**4**) | 1.98 (s, 6H) | 1.90 (s, 6H) | 5.25 (s, 4H) | 7.15–7.55 (m, 4H) | 11.60 (s, 2H) |

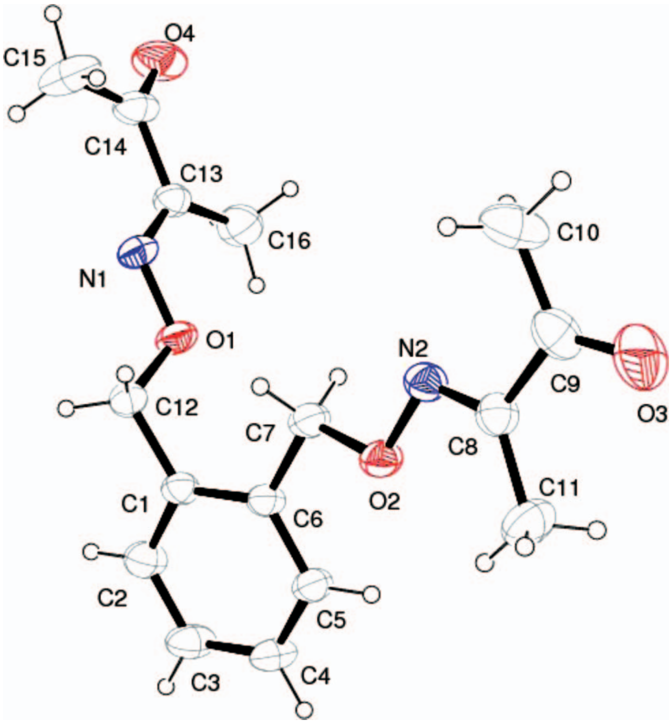


FIG. 1. Ortep III diagram of the title compound (**3**) (color figure available online).

Database gives the following summary of the N–O bond lengths in a group of a multi-compound: mean = 1.400 Å, median = 1.404 Å, standard deviation = 0.028 Å. Intramolecular hydrogen bonding is an important factor in crystalline oxime; Berthelot and co-workers found it to be present in each of the 57 compounds that they investigated.[27] They identified three types; the –NOH group can actually be involved in all three types of interaction, with three other molecules. Much more common, however, occuring in 35 of the 57 oximes, is for each –NOH to take part in two hydrogen bonds, forming dimers within the crystal. The N–O distances are typically 2.7–2.9 Å. Berthelot and co-workers observed a rough relationship, with the N–O bond tending to lengthen as the number of hydrogen bonds in which the –NOH group is participating increases. On occasion, a hydrogen bond may be to an acceptor other than an -NOH nitrogen or oxygen. This was observed by Berthelot and co-workers in which the donor –OH interacts with the nitrogen that is linked to the phenyl ring(which has a C-N-O angle of 120°). This result in the crystal containing chains of hydrogen bonded molecules. The two -C-N-O-H dihedral angles were found to be 120.7 and 120.8°.[28]

## Mass Spectra

The mass spectra of all compounds were recorded in pyridine solution. The mass spectra (ESI) exhibited the molecular ion at *m/z* = 327 $[M{+}Na]^+$ for dione (**3**) and *m/z* = 357 $[M + Na]^+$ for $H_2L$, which indicated formation of the dione and ligand. The molecular ion peaks appeared (*m/z*, ESI) at 415.8 $[M + 1]^+$, at 429.5 $[M + 1]^+$, and at 430.49 $[M + 1]^+$ for the $[Cu(HL)(H_2O)]$, $[Ni(HL)(H_2O)_2]$, and $[Co(HL(H_2O)_2]^+$, respectively. The mass spectra showed the formation of the ligand and its metal complexes.

## IR Spectra

Relevant IR bands were given in Table 5. In general, the complexes exhibited very comparable IR features, suggesting that they were of similar structure. The certain bands in the generally complicated IR spectra were used to establish the nature of the complexes. The strong band at 1640 $cm^{-1}$ might be assigned to $\nu(C = N)$ vibration.[29] In the IR spectrum of ligand ($H_2L^1$) was observed a weak band for $\nu$(O-H) at ~3450 $cm^{-1}$. The metal complexes show a triplet at ~1000, ~1100, ~1140, and a singlet at ~625 $cm^{-1}$. The presence of these bands shows that the perchlorate is uncoordinated in the complexes.[29,30] The (O–H-O) bridge was characterized by broad absorption for the bending vibration at ~1700 $cm^{-1}$ for the copper(II), nickel(II), and cobalt(II) complexes.[29] In the complexes, $\nu(C = N)$ and $\nu$(O-H) were shifted to lower or higher frequency, suggesting coordination of metal via nitrogen. Finally, the peaks appearing between 445 and 575 $cm^{-1}$ are attributed to $\nu$(M-N).[31] Bands at 520–530 $cm^{-1}$ were strong evidence for the participation of water molecule[32] in coordination. A strong band at 1640 $cm^{-1}$, which shifted by 40 $cm^{-1}$ toward lower frequency upon coordination, is assigned to $\nu(C = N)$. The significant shifts in $\nu(C = N)$ upon complexation support the concept of coordination of the ligand through the oxime nitrogen (Figure 2).

## Magnetic Properties and Electronic Absorption Spectra

Electronic spectra of the complexes were recorded in DMSO ($\varepsilon$ in L $mol^{-1}$ $cm^{-1}$). Electronic spectra of the Cu(II) complex show bands at 13,520 (737), 16,335 (615) and 25,650 (360) $cm^{-1}$ assignable to a $^2E_g \rightarrow {}^2T_{2g}$ transition and charge transfer. Electronic spectral data coupled with detected magnetic moment of 1.85 B.M. suggest octahedral geometry.[33] Ni(II) complex displays bands at 12,555 (1075), 17,450 (680), and 25,650 (375) $cm^{-1}$ assignable to $^3A_{2g} \rightarrow {}^3T_{2g}(F)$, $^3A_{2g} \rightarrow {}^3T_{1g}(F)$, and $^3A_{2g} \rightarrow {}^3T_{1g}(P)$, respectively. These electronic transitions along with magnetic moment 2.90 B.M. suggest octahedral geometry for Ni(II) complex.[34] The Co(II) complex shows three bands at 10,160 (986), 18,610 (545), and 25,585 (400) $cm^{-1}$ assignable to $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$, $^4T_{1g}(F) \rightarrow {}^4A_{2g}$, and $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ transitions, respectively. These transitions and observed magnetic moment of 4.72 B.M. indicate a high-spin octahedral complex.[35,36] The calculated values of ligand field splitting energy (10 Dq), Racah interelectronic repulsion parameter ($\beta$), covalent factor ($\beta$), ratio $\nu_2/\nu_1$, and ligand field stabilization energy (LFSE), given in Table 6, support the proposed geometry for all the complexes.

TABLE 4
Selected distances (Å) and angles (°) for compound (**3**)

| | | | |
|---|---|---|---|
| Bond lengths | | | |
| O2–N2 | 1.391(2) | C14–O4 | 1.212(2) |
| O2–C7 | 1.426(2) | C14–C15 | 1.485(4) |
| N1–C13 | 1.277(2) | C14–C13 | 1.490(3) |
| N1–O1 | 1.397(2) | C13–C16 | 1.474(3) |
| N2–C8 | 1.279(2) | C8–C11 | 1.493(3) |
| O1–C12 | 1.444(2) | C8–C9 | 1.496(3) |
| C7–C6 | 1.502(3) | C9–O3 | 1.209(3) |
| C1–C12 | 1.501(3) | C9–C10 | 1.493(4) |
| Bond angles | | | |
| N2–O2–C7 | 109.17(14) | C15–C14–C13 | 119.51(19) |
| C13–N1–O1 | 111.51(15) | N1–C13–C16 | 125.92(17) |
| C8–N2–O2 | 110.48(15) | N1–C13–C14 | 115.05(17) |
| N1–O1–C12 | 109.01(13) | C16–C13–C14 | 119.03(18) |
| O2–C7–C6 | 108.44(15) | N2–C8–C11 | 125.86(17) |
| C2–C1–C12 | 119.30(17) | N2–C8–C9 | 114.98(18) |
| C6–C1–C12 | 121.63(15) | C11–C8–C9 | 119.15(18) |
| O1–C12–C1 | 106.89(14) | O3–C9–C10 | 122.8(2) |
| O4–C14–C15 | 121.6(2) | O3–C9–C8 | 118.1(2) |
| O4–C14–C13 | 118.9(2) | C10–C9–C8 | 119.1(2) |
| Torsion angles | | | |
| O1–N1–C13–C14 | −179.56(13) | O2–N2–C8–C9 | 178.35(15) |
| O4–C14–C13–N1 | −173.91(17) | N2–C8–C9–O3 | −167.6(2) |
| C15–C14–C13–C16 | −174.3(2) | C11–C8–C9–C10 | −168.9(2) |

Hydrogen bonds

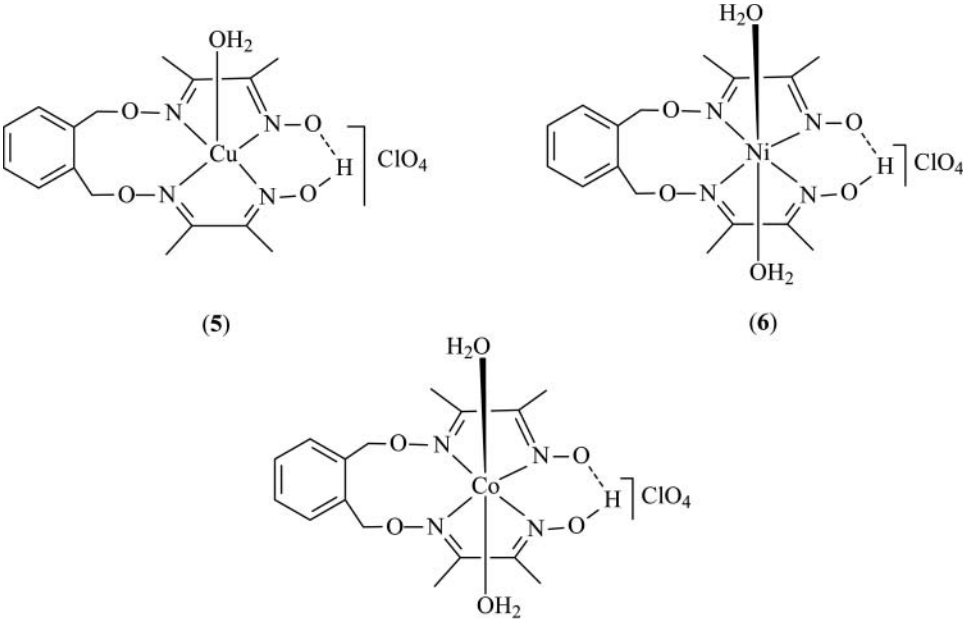
| D–H...A | D–H | H...A | D...A | D–H...A |
|---|---|---|---|---|
| C5–H5...O2 | 0.93 | 2.38 | 2.711(3) | 101 |
| C11–H11A...O2 | 0.96 | 2.21 | 2.642(4) | 106 |
| C16–H16A...O1 | 0.96 | 2.22 | 2.656(3) | 107 |

## Antimicrobial Activity

The dioxime ligand ($H_2L$) and its Cu(II), Ni(II), and Co(II) complexes were evaluated for antimicrobial activity against one gram-positive bacterium (*S. aureus*), a gram-negative bacterium (*E. coli*), and fungi *A. niger* and *Trichoderma*. The antimicrobial activities are presented in Table 1, showing that the dioxime ligand and Cu(II), Ni(II), and Co(II) complexes exhibit antibacterial activity against both strains. The Cu(II), Ni(II), and Co(II) complexes exhibit higher activity than dioxime ligand under identical experimental conditions. Antimicrobial inhibitions were compared with the activity of ciprofloxin as a standard, and dioxime ligand ($H_2L$) and its Cu(II), Ni(II), and Co(II) complexes showed less activity than the standard. The metal salts used for synthesis of complexes exhibit negligibly

TABLE 5
Characteristic IR bands of the ligand and its metal complexes (in cm$^{-1}$)

| Compound | $\upsilon$(O−H) | $\upsilon$(C = O) | $\upsilon$(C = N) | $\upsilon$(C−O) | $\delta$(O-H) | $\upsilon$(M−N) | $\upsilon$ ($ClO_4$) | O-H...O |
|---|---|---|---|---|---|---|---|---|
| 3 | — | 1694 | 1630 | 1233 | — | — | — | |
| $H_2L$ | 3235 | — | 1640 | 1217 | 1365 | — | — | |
| $[Cu(HL)(H_2O)]ClO_4$ | 3258 (br) | — | 1600 | 1190 | — | 450 | 1004, 1142, 625 | 1690 |
| $[Ni(HL)(H_2O)_2]ClO_4$ | 3254 (br) | — | 1603 | 1189 | — | 445 | 1003, 1120, 1142–623 | 1696 |
| $[Co(H_2L)(H_2O)_2]ClO_4$ | 3255 (br) | — | 1602 | 1188 | 1350 | 473 | 1006, 1115, 1140, 624 | 1695 |



(5) (6) (7)

FIG. 2. Proposed structures for the metal complexes.

small antimicrobial activities.[37–39] Enhancement of activity of dioxime ligand after chelation can be explained on the basis of Overtones and Tweedy's concepts.[40] Inhibition was found to increase with increasing concentration of Cu(II), Ni(II), and Co(II) complex. The results showed that the Cu(II) complex exhibits higher activity against each class of organism. The activity is related to the nature and structure of the complexes.[41, 42] The higher activity of the Cu(II) complex may be attributed to its higher stability constants. All the dioxime ligand ($H_2L$) and its Cu(II), Ni(II), and Co(II) complexes show more activity against gram-negative *E. coli* than against gram-positive *S. aureus*. Antibacterial activity can be ordered as $[Cu(HL)(H_2O)]ClO_4 > [Co(H_2L)(H_2O)_2]ClO_4 > [Ni(HL)(H_2O)_2]ClO_4$, similar to earlier observations.[42] The Cu(II), Ni(II), and Co(II) complexes do not show strong concentration dependence of antimicrobial activity as compared to the antifungal activities of the same complexes. The relation between chelation and toxicity is very complex, expected to be a function of steric, electronic, and pharmakinetic factors along with mechanistic pathways.[43] Stability constants, solubility, particle size, size of metal ion, and magnetic moments may also be responsible for the antimicrobial activity of the complexes.[44, 45] Attempts to show a relationship between stability constants and antimicrobial activity of the complexes proved futile. Investigation of antifungal activity of the ligand and its metal complexes revealed that all the metal chelates are more toxic than the ligand (Table 1). The antifungal activity is enhanced several times on being coordinated with metal. Antifungal activity of the Cu(II), Ni(II), and Co(II) complexes increases as the stability of the complex increases. The activities of these complexes follow the order $[Cu(HL)(H_2O)]ClO_4 > [Co(H_2L)(H_2O)_2]ClO_4 > [Ni(HL)(H_2O)_2]ClO_4$, which is exactly same as the order of stability constants of these complexes. Comparison of activities shows that the copper complex is more active than the dioxime ligand against *A. niger*. Activity of dioxime ligand against *Trichoderma* increases after chelation; however, the extent of increase is less than that of *A. niger*.

TABLE 6
Ligand field parameter of the complexes

| Complex | Ligand field splitting energy (Dq $cm^{-1}$) | Racah interelectronic repulsion parameter (B $cm^{-1}$) | Covalent factor ($\beta$) | $\beta$ (%) | $\nu_2/\nu_1$ | LFSE (kcal $mol^{-1}$) |
|---|---|---|---|---|---|---|
| $[Cu(HL)(H_2O)]ClO_4$ | 1352.5 | 95.10 | — | — | — | 38.64 |
| $[Ni(HL)(H_2O)_2]ClO_4$ | 940.3 | 845.6 | 0.8115 | 23.45 | 1.59 | 26.87 |
| $[Co(H_2L)(H_2O)_2]ClO_4$ | 1025.3 | 915.5 | 0.9425 | 6.25 | 1.85 | 29.30 |

## CONCLUSIONS

In the present study, we have demonstrated the preparation of dioxime ligand providing $N_4$ donor array moiety, and their copper(II), nickel(II), and cobalt(II) complexes. The nickel(II) complex (**6**) and the copper(II) and cobalt(II) complexes (**5**, **7**) were paramagnetic. The metal ion was complexed with nitrogen atoms of ligands ($H_2L$) in an octahedral geometry for metal ions. All of the data obtained from spectral data supported the structural properties of ligands and its Cu(II), Ni(II), and Co(II) metal complexes. The dioxime ligand ($H_2L$) and its Cu(II), Ni(II), and Co(II) complexes were evaluated for antimicrobial activity against one gram-positive bacterium (*S. aureus*), a gram-negative bacterium (*E. coli*), and fungi *A. niger* and *Trichoderma*. The antimicrobial activities are presented in Table 1, showing that the dioxime ligand and Cu(II), Ni(II), and Co(II) complexes exhibit antibacterial activity against both strains. Antimicrobial inhibitions were compared with the activity of ciprofloxin as a standard, and dioxime ligand ($H_2L$) and its Cu(II), Ni(II), and Co(II) complexes showed less activity than the standard.

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