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Synthesis, Structural Characterization and Antimicrobial Activity of a Novel Cobalt(II) Complex Based on 3-Methyl-1-Phenyl-4-(2-Thienoyl)-Pyrazol-5-One

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Abstract

New cobalt(II) complex, $[Co(O_2C_{15}H_{11}N_2S)_2(OH_2)_2]\cdot 2H_2O$ ($1\cdot 2H_2O$), has been synthesized upon reaction of cobalt chloride hexahydrate ($Co(Cl)_2\cdot 6H_2O$) with 3-methyl-1-Phenyl-4-(2-thienoyl)-pyrazol-5-one (referred as HL) in ethanol at room temperature. Single crystal X-ray diffraction (XRD), spectroscopic methods, and microelemental analyses were used to characterize $1\cdot 2H_2O$. Compound $1\cdot 2H_2O$ crystallizes in the orthorhombic crystal system with a Pbca space group and with the cobalt atom being pseudo-octahedral coordinated. The broth microdilution technique was used to screen the free ligand (HL) and the complex ($1\cdot 2H_2O$) for antimicrobial activities. HL has a low activity (MIC > 100 µg/mL) on all microorganisms, whereas compound $1\cdot 2H_2O$ displayed moderate activity (10 < MIC ≤ 100 µg/mL) on all *Salmonella* and, F1, and 018 yeasts. HL and $1\cdot 2H_2O$ exhibited bactericidal and fungicidal activity respectively on all the bacteria and yeasts tested. These findings reveal that the antimicrobial activity of HL was enhanced upon coordination to Co(II) ion against all microorganisms (bacteria and fungus).

Keywords

Cobalt, Acylpyrazolone, X-Ray Diffraction, Antimicrobial Activity, 3-Methyl-1-Phenyl-4-(2-Thienoyl)-Pyrazol-5-One

1. Introduction

The design and development of new compounds able to display unprecedented properties in catalysis and material sciences continue to be an exciting area of research in chemistry with increased interest from researchers [1] [2]. Metal complexes, in particular, play a crucial role in molecular material design and production [3]. Coordination complexes have been at the heart of a broad and intense research activity for many decades. Ligands are designed, synthesized and used in the complexation of transition metals with the resulting complexes finding applications in biological systems, polymer materials dyes and in the medical field [4]. Due to their intriguing physicochemical features, pyrazole-based compounds have proved to be pharmacologically active in several diseases and gained widespread attention in the pharmaceutical industries [5]. Many of the pyrazole's bio-activities have motivated chemists to look at the potential of pyrazole derivatives in order to explore further properties of this heterocyclic template. Therefore, pyrazole-containing compounds have been provided and successfully commercialized for example the blockbuster drugs Viagra (Sildenafil inhibits phosphodiesterase) [6], the Celebrex (Celecoxib demonstrates antiinflammation effect and inhibits COX-2) [7], and the Rimonabant (trade name Acomplia) functions as cannabinoid receptor and is utilized in obesity treatment.

Acylpyrazolones are a fascinating class of β-diketone chemicals that are commonly employed in metal ion solvent extractions, laser working materials, and NMR shift reagents [8] [9]. They can exist in numerous tautomeric forms (enol or keto), which allows them to produce various types of coordination compounds with distinct characteristics [10] [11]. The presence of several donor elements such as oxygen, sulfur, and nitrogen at different positions within the acylpyrazolones allows them to behave as multidentate ligands, resulting in the formation of metal complexes with a wide range of metal ions [12]. This β- diketone family has interesting properties such as a high metal extraction capacity that is ideal for practical applications in water treatment, limited solubility in certain solvents, and a vivid coloring of the complexes formed with these ligands [13]. Acylpyrazolones have also been demonstrated to have significant antihistaminic, analgesic, antifungal, anti-inflammatory, antibacterial, and anticancer effects [14]. As O,O'-bidentate ligands, 4-acyl pyrazolones are extremely valuable in coordination chemistry [15] [16]. Metal complexes of 4-acyl pyrazolones for d-block metals have been reported in the literature to have antimalarial, anticancer, antibacterial, antifungal, and catalytic properties [17] [18]. These chelating ligands have recently been shown to form complexes with specific metal ions

displaying unique structural properties [19]. Furthermore, their metal complexes have been shown to improve catalytic performance, biological activity, and luminescence [13]. Metal complexes with the oxygen-cobalt bond are used in oxidation processes [20]. Because it can adopt different modes of coordination depending on whether the ligand is N- or O-donor, Co(II) is an excellent option for the production of metal-organic compounds with magnetic or luminous characteristics [21] [22] [23]. Cobalt is a transition element that is essential for life. It has higher biological activity when it is incorporated into specific metal protein complexes where it participates in oxygen transport, electrical transfer processes, or ion storage [24]. Metal chelation has been proven to alter the antimicrobial/bioactive properties of organic ligands. As a result, attempts have been made to synthesize several transition metal complexes in this area [25]. To the best of our knowledge, the crystal structure of a cobalt(II) complex based on 1-phenyl-3-methyl-4-(2-thienoyl)-pyrazol-5-one complex has not yet been reported, as well as their antifungal and antibacterial characteristics. As a result, the primary goal of this study is to synthesize, structurally characterize, and conduct antimicrobial activity tests on this novel compound against Gram (+), Gram (−) bacteria species and fungi.

2. Experimental

2.1. Materials and Methods

All reagents and solvents were acquired commercially and used as supplied without further purification. The ligand 3-methyl-1-Phenyl-4-(2-thienoyl)-pyrazol-5-one acylpyrazol was synthesized according to the literature [26]. Weights were measured with a Sartorius 1409 electronic balance, and melting points were recorded and uncorrected with an SMP3 Stuart Scientific equipment running at 1.5˚C/ min. The samples for microelemental analyses were processed through a Fisson Instrument 1108 CHNS-O elemental analyzer after being dried in a vacuum to constant weight (20 uC, ca. 0.1 Torr). A Nicolet iD7 ATR spectrophotometer was used to record IR spectra ranging from 4000-500 cm^{-1}. A UV-vis spectrometer with the model number GENESYS 10S was used to scan the UV-visible absorptions between 200 and 800 nm. Single crystal of the material was put on a goniometer head, coated with dry perfluoropolyether, and placed at the end of a glass fiber in a stream of cold nitrogen at [T =173(2) K].

2.2. X-Ray Diffraction Analysis

The crystal was mounted on top of a human hair with per-fluorinated inert oil. Data were recorded on a Rigaku XtaLAB Synergy S Single Source diffractometer equipped with a PhotonJet Mo-microfocus source and a HyPix-6000HE detector. Data reduction was performed with CrysalisPro [27]. Absorption correction was based on multi-scans and additionally face indexation and integration on a Gaussian grid was applied. The structure was solved by intrinsic phasing with SHELXT-2018/2 [28] and refined on F2 using the program

SHELXL-2018/3 [29] in OLEX2 [30]. The hydrogen atoms of the water molecules have been refined freely. All other H atoms were placed in idealized positions and refined using a riding model. The corresponding crystallographic data were deposited with the Cambridge Crystallographic Data Centre (CCDC 2260191). The data can be obtained free of charge via https://www.ccdc.ac.uk/data.request/cif

2.3. Synthesis of Compound 1·2H_2O

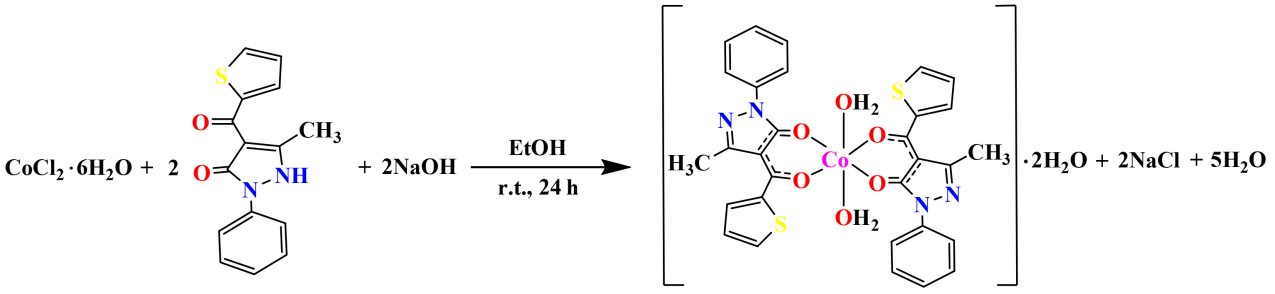
3-Methyl-1-phenyl-4-(2-thenoyl)-pyrazol-5-one [26] (140 mg, 0.50 mmol) was dissolved in a 100 mL round bottom flask with 50 mL of ethanol, after which a clear orange solution was obtained. Cobalt chloride hexahydrate salt (60 mg, 0.25 mmol) was added to this solution, which became brown-colored. A dark brown solution was obtained by treating this solution with sodium hydroxide (20 mg, 0.50 mmol), which slowly dissolved under stirring. The entire mixture was vigorously stirred for 24 h, whereby a yellow precipitate formed. The latter was filtered off, washed several times with ethanol and the residue was extracted with a lot of methanol and the solution filtered. The filtrate was concentrated and the resulting yellow powder was further recrystallized by slow solvent evaporation of a solution of the material in from N, N-dimethylformamide (DMF). Yellow crystalline solid (Scheme 1) was obtained over 30 days.

The compound is well soluble in DMF and DMSO and was found to have a melting point of 254˚C. Elemental analysis for $C_{30}H_{30}CoN_4O_8S_2$, calculated (%): C, 52.86; H, 4.44; N, 8.22; (Found) (%): C, 51.60; H, 4.30; N, 8.02, IR (cm^{-1}): 3600 cm^{-1} v(OH), 3100 cm^{-1} v(N-H), 1480, 1478 cm^{-1} v(C-O), v(C = O), 1593 cm^{-1}, 1568 vC = C, 1515 cm^{-1} v(C = N), 1020, ~CH 1090 cm^{-1}, 955 v(N-N), 926, 921 ~CH3, C-ph, UV-vis (DMF) λ_{max} (nm): 252; 288; 369.

2.4. Antimicrobial Activities

2.4.1. Microorganisms and Conservation

Five (5) multi-resistant bacteria, including strains of [strain *Salmonella Typhi* ATCC6539 (STS); *Salmonella Typhi* (ST); *Salmonella Typhimurium*(STM), *Salmonella Paratyphi* B (STB) and *Salmonella Paratyphi* A (STA), obtained from the Medical Bacteriology Laboratory of "Centre Pasteur, Yaoundé", Cameroon,



Scheme 1. Synthesis of compound 1·2H_2O.

were tested, as well as four (4) multi-resistant fungi, including strains of *Candida Krusei* ATCC14243(F1), *Candida tropicalis* 018 (CPC-BACT-018), *Candida albicans* 7a (F2) and *Candida albicans* 18ca (F5) obtained at Bafoussam Regional Hospital. Microorganisms were kept at −18˚C, on Mueller Hinton Agar (MHA) (OXOID, Denmark) and Sabouraud Dextrose Agar (SDA) for bacteria and fungi respectively. Subcultures were used after being freshly prepared. In the various studies, Mueller Hinton Broth (MHB) (OXOID, Denmark) and Sabouraud Dextrose Broth (SDB) were employed as the basal enrichment medium for aerobic culture at 37˚C while stirring at 150 rpm.

2.4.2. Preparation of Bacterial Inocula

A fresh 18-hour bacterial colony was extracted from the MHA/SDA and suspended in a sterile 0.9% saline solution to achieve a concentration of 1.5×10^8 colony forming units/mL (CFU/mL), which corresponds to the 0.5 McFarland turbidity scale. The basal enrichment medium was then used to dilute these bacterial/fungal suspensions to a cell concentration of 1.5×10^6 CFU/mL.

2.4.3. Determination of the MIC, MFC and MBC

MICs were determined using the 2-(4-iodophenyl)-3-(4-nitrophenyl)-5-phenyltetrazolium chloride (INT) rapid colorimetric test [31] [32]. The ligand and $1{\cdot}2H_2O$ were first emulsified in 1% DMF/SDB (for fungi), 1% DMF/MHB (for bacteria). In a 96-well plate containing 100 µL of MHB or SDB culture medium corresponding to the type of microorganism, 100 µL of the solution to be tested was then added to the first row of each column and diluted in series by a factor of two. One hundred microliters (100 µL) of inoculum (1.6×10^6 CFU/mL) prepared in a corresponding nutrient medium was then added. Wells containing the nutrient medium (100 µL of inoculum and 1% DMF) served as the negative control. Nystatin (for fungi) and ciprofloxacin (for bacteria) were used as positive controls. Plates were then covered and incubated at 37˚C for 18 hrs for bacteria and 48 hrs for fungal after which 40 µL of INT 0.2% was introduced and plates were reincubated at 37˚C for 30 min. Viable microorganisms reduce the INT yellow dye to pink. The lowest concentration of the sample that completely inhibited microbial growth and therefore prevented this color change was considered the minimal inhibitory concentration (MIC). The MBC of bacteria and MFC of fungi were determined by adding 50 µL of the sample-treated cells, which did not show any visible color change during MIC determination, into 150 µL of freshly prepared nutrient medium. These mixtures were reincubated at 37˚C for 48 h. MBC and MFC were determined as the lowest concentrations of the ligand and complex that completely inhibit the growth of microorganisms after addition of INT. The Kuete scale [33] was used to compare the MICs obtained from the ligand and complex. According to this scale applicable to antibiotics and pure compounds, sample with MIC ≤ 10 µg/mL, 10 < MIC ≤ 100 µg/mL or MIC > 100 µg/mL is considered to have significant, moderate, or low activity respectively. Gatsing and Adoga [34] scale was also used to compare the

"cidal" and "static" potency of pure compounds. Thus, when the MFC/MIC or MFC/MIC ratio is ≤4 the pure compounds are bactericidal or fungicidal; and when the ratio is >4, the pure compounds are bacteriostatic/fungiostatic.

3. Results

3.1. Elemental Analysis

The results of elemental analysis (C, H, and N) along with molecular formula and melting points are presented in Table 1.

Compound (1·2H_2O) is yellow colored microcrystalline material and is air-stable. The complex is insoluble in ethanol, water, n-hexane, MeCN and dichloromethane, slightly soluble in methanol, and well soluble in DMSO and DMF from which suitable crystals were collected.

3.2. Infrared Spectroscopy Data

The comparative infrared spectra of the ligand and the complex 1·2H_2O are given in Figure 1.

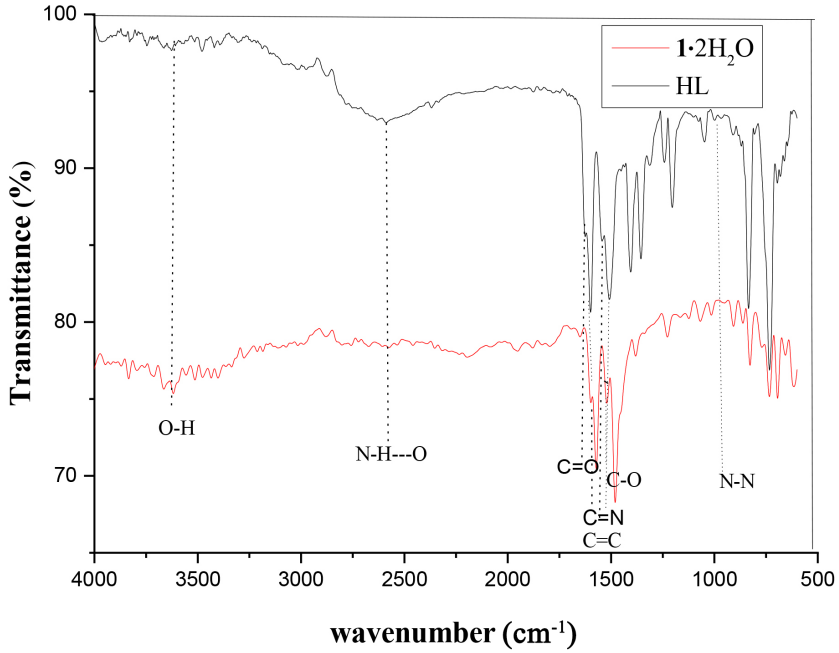


Figure 1. FT- IR comparative spectra of HL and 1·2H_2O.

Table 1. Analytical and physical data of (1·2H_2O).

Compounds	Compound formula/weight (g/mol)	Color	% Yield	M. P. (˚C)	Elemental analysis calc (found) %		
					C	H	N
1·2H_2O	$C_{30}H_{30}CoN_4O_8S_2$ (1·2H_2O) (697.63)	Yellow	59	254	(52.86) 51.60	(4.44) 4.300	(8.22) 8.02

The spectra present a number of important bands which can be easily assigned to different functional groups, OH vibration (at 3600 cm^{-1}), N-H (at 3100 cm^{-1}), the intermolecular N-H---O (at 2600 cm^{-1}), C = O, C = C, C = N and N-N (at 1624 - 1407 cm^{-1}) as reveal in previous works using 4-acetylbispyrazolone [3] [35] [36] or 1-phenyl-3-methylpyrazol-5-one [23] [37] [38] and their complexes.

A summary of the IR vibrational frequencies of the synthesized material (**1**·2H_2O) is presented in **Table 2**.

3.3. UV-Vis Studies

The following **Figure 2** shows the comparative UV-vis spectra of the ligand and complex (1·2H_2O) recorded in the wavelength region 200 and 800 nm in methanol

From this **Figure 2**, it appears that the ligand and 1·2H_2O have three absorption peaks, at 266, 242, 302 nm and 252, 288, 369 nm respectively. The peaks are assigned to intra-ligand π-π* transitions, n–π* transitions and Ligand to Metal Charge Transfer (LMCT) interactions. A similar values have been obtained with vanadium(IV) complexes based on 3-phenyl-4-methyl-acylpyrazol-5-one [39], with heterocyclic acylpyrazolone [40] or cobalt(II) complex based on nitroacyl-5-oxo-pyrazole [41]. **Table 3** shows the absorption values of the free ligand (HL) and its complex (1·2H_2O).

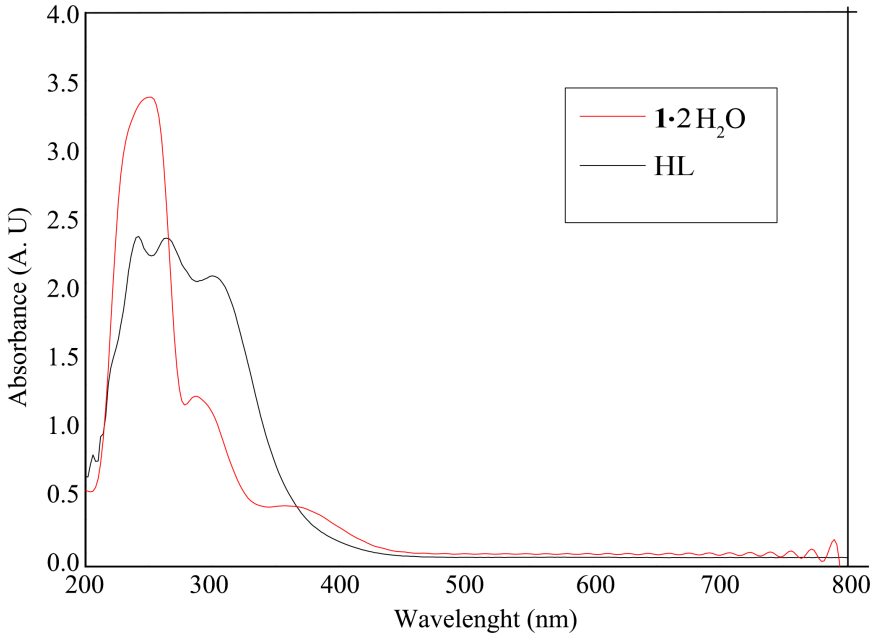


Figure 2. UV-vis spectra of HL and complex 1·2H_2O.

Table 2. Vibrational frequencies (cm^{-1}) of 1·2H_2O.

Vibration	-OH	$\upsilon_{C=O}$	$\upsilon_{C=N}$ & $\upsilon_{C=C}$	υ_{C-O}	υ_{N-N}
Complex (**1**·2H_2O)	3600	1593	1568 - 1515	1480 - 1478	955

Table 3. UV-vis analytical data of ligand HL and complex 1·2H_2O.

Compounds	λ (nm)	Assigment
HL	266, 242, 302	π-π*, π-π*, n-π*
Complex **1**·2H_2O	252, 288, 369	π-π*, n-π*, LMCT

3.4. X-Ray Diffraction Analysis

Complex material 1·2H_2O was subjected to single-crystal X-ray diffraction analysis. The crystallographic data collection and structure refinement details are summarized in **Table 4**, while selected bond distances and angles are presented in **Table 5**. **Figure 3** shows the structure of 1·2H_2O.

The X-Ray diffraction analysis results revealed that compound 1·2H_2O is a cobalt(II) complex of formula $[Co(O_2C_{15}H_{11}N_2S)_2(OH_2)_2]\cdot 2H_2O$, which crystallizes in an orthorhombic system with space group Pbca and lattice parameters a = 4.9828 (3) Å, b = 21.6367 (12) Å, c = 27.5969 (15) Å and $\alpha = \beta = \gamma = 90^\circ$. The asymmetric unit consists of one-half molecule with the cobalt atom on an inversion center.

The molecular structure of this compound shows that the cobalt atom lies in a pseudo-octahedral environment (**Figure 4**) where it is coordinated by four oxygen atoms O1 and O2 of the two acylpyrazolone ligands in bidentate mode (each ligand chelating through two O atoms) in an equatorial plane and the two-oxygen atom O3 of water molecules in the axial plane.

All trans angles (O(1)-Co(1)-$O(1)^{\#1}$, O(2)-Co(1)-$O(2)^{\#1}$ and O(3)-Co(1)-$O(3)^{\#1}$ are exactly 180˚ which results from the cobalt atom residing over an inversion center. All other bond angles at the cobalt atom are close to 90˚. Hence, we conclude that the geometry around the Co ion is slightly distorted octahedral [13] (**Figure 4**)

The bond lengths of O(1)-C(7) and O(2)-C(11) are 1.279(2) and 1.267(2) in each chelating ring of the complex, respectively, which are less than 1.43 Å for a C-O single bond and greater than 1.22 Å for a double C=O bonds in the enol-form of the ligand, indicating some delocalization around the chelate ring [42]. The C(12)-C(13) and C(14)-C(15) bond lengths are 1.375(2) Å and 1.371(3) Å, respectively, shorter than the C(12)-C(13) and C(14)-C(15) bond lengths in the free ligand. These changes indicate that during coordination delocalized pyrazolone-ring has averaged the bond length [23] [37] [40]. The C(1)-N(1) bond length is close to the C-N double bond length, confirming that the keto form of the ligand isomerizes to the enol form. The length of the N(1)-N(2) bond is 1.397(2)Å, in the complex, which is less than 1.401 Å for the length of the N(1)-N(2) bond in the free ligand. These changes indicate and confirm that there has been delocalization of electrons in the pyrazolone ring, which leads to averaging the bond length [37] [40]. These results were also observed by Li and co-workers [37], with the synthesis of a cobalt(II) complex based on an acylpyrazolone. This material presents differents types of inter and intramolecular interactions: weak intramolecular C(10)-H (10C)···N(2) (2.453 Å) interaction built up

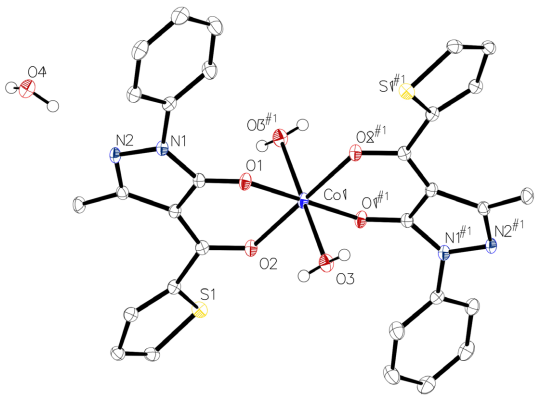


Figure 3. Structure of 1·2H_2O. H atoms, except those of the water molecules, were omitted for clarity. Symmetry transformation used to generate equivalent atoms: #1: $-x + 1$, $-y + 1$, $-z + 1$.

Table 4. Crystallographic data and structure refinement details of 1·2H_2O.

	1·2H_2O
Empirical formula	$C_{30}H_{30}CoN_4O_8S_2$
Formula weight	697.63
Temperature (K)	100 (2)
Wavelength (Å)	0.71073
Crystal system	Orthorhombic
Space group	Pbca
Unit cell dimensions	a = 4.9828 (3) Å, b = 21.6367 (12) Å, c = 27.5969 (15) Å, $\alpha = \beta = \gamma = 90^\circ$
Volume, Z	2975.3(3) Å3
Calculated density (Kg/m^3)	1.557
Crystal size (mm^3)	0.120 x 0.080 x 0.040
Goodness-of-fit on F2	1.055
Reflections collected	52135
Independent reflection	5308 [R(int) = 0.0718]
R indices (all data)	R1 = 0.0725, wR2 = 0.1006

Table 5. Selected bond lengths and angles in 1·2H_2O Symmetry transformation used to generate equivalent atoms: #1: −x + 1, −y + 1, −z + 1.

Atoms	Bond lengths (Å)	Atoms	Angle (˚)
		O(2)-Co(1)-O(2)$^{\#1}$	180.00 (7)
Co(1)-O(1)	2.0246 (12)	O(1)$^{\#1}$-Co(1)-O(2)	91.18 (5)
Co(1)-O(2)	2.1156 (13)	O(1)-Co(1)-O(2)	88.82 (5)
		O(1)$^{\#1}$-Co(1)-O(3)	88.82 (5)
Co(1)-O(3)	2.1355 (14)	O(2)-Co(1)-O(3)	91.84 (5)
		O(2)$^{\#1}$-Co(1)-O(3)	88.16 (5)
		O(1)-Co(1)-O(3)$^{\#1}$	88.82 (5)

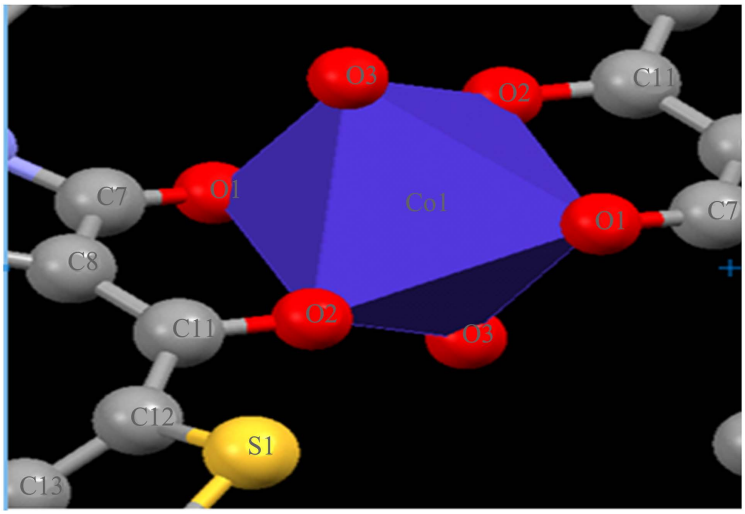


Figure 4. Distorted octahedral geometry around Co(II) in $1{\cdot}2H_2O$.

between C-H of the methyl group of the pyrazolone ring and the nitrogen N atom of pyrazolone ring, very weak intermolecular C(6)-H(6)···O(4) (3.039 Å) interaction, established between C-H of the phenyl ring and the oxygen atom of non-coordinated water, weak intermolecular O(4)-H(4B)···N(2) (2.084 Å) interaction, formed between C-H of thienyl ring and the carbon of the pyrazolone ring, very weak intramolecular O(3)-H(3A)···O(2) (3.026 Å) interaction, established between O-H of coordinated water molecule and the oxygen atom of CO group of the thienyl ring. These interactions give rise to 2D network sheet connected by intermolecular O-H···N, C-H···O H-bonding interactions (**Figure 5**) and, intramolecular C-H···N, O-H···O, H-bonding interactions observed (**Table 6**).

H-bonding interactions play an important role in forming the supramolecular structure by self-assembly and stabilizing [37] [43]. They also help to generate a network exhibiting some cavities shown in **Figure 6**.

3.5. Antimicrobial Studies

3.5.1. Antibacterial Activity

Table 7 gives in the minimal inhibitory concentrations (MIC) and bactericidal concentrations (MBC) of the ligand HL, $1{\cdot}2H_2O$ and the reference Ciproflxacine against certain resistant microorganisms.

Results from the table show that the antibacterial activity of the ligand and the complex vary from 32 to 256 μg/mL, on all microorganisms tested. The results also reveal that the activity of the complex (32 to 64 μg/mL) is considerably increased compared to that of the ligand (128 to 256 μg/mL). The best anti-salmonella activity of the complex (32 μg/mL) was obtained with *Salmonella Typhi* and *Salmonella Paratyphi* B. The complex presents a moderate activity ($10 < \text{MIC} \leq 100$ μg/mL) on all *Salmonella* while the ligand has a weak activity (MIC > 100 μg/mL) The ligand HL and the complex $1{\cdot}2H_2O$ are found to exhibit bactericidal activity on all the bacteria tested.

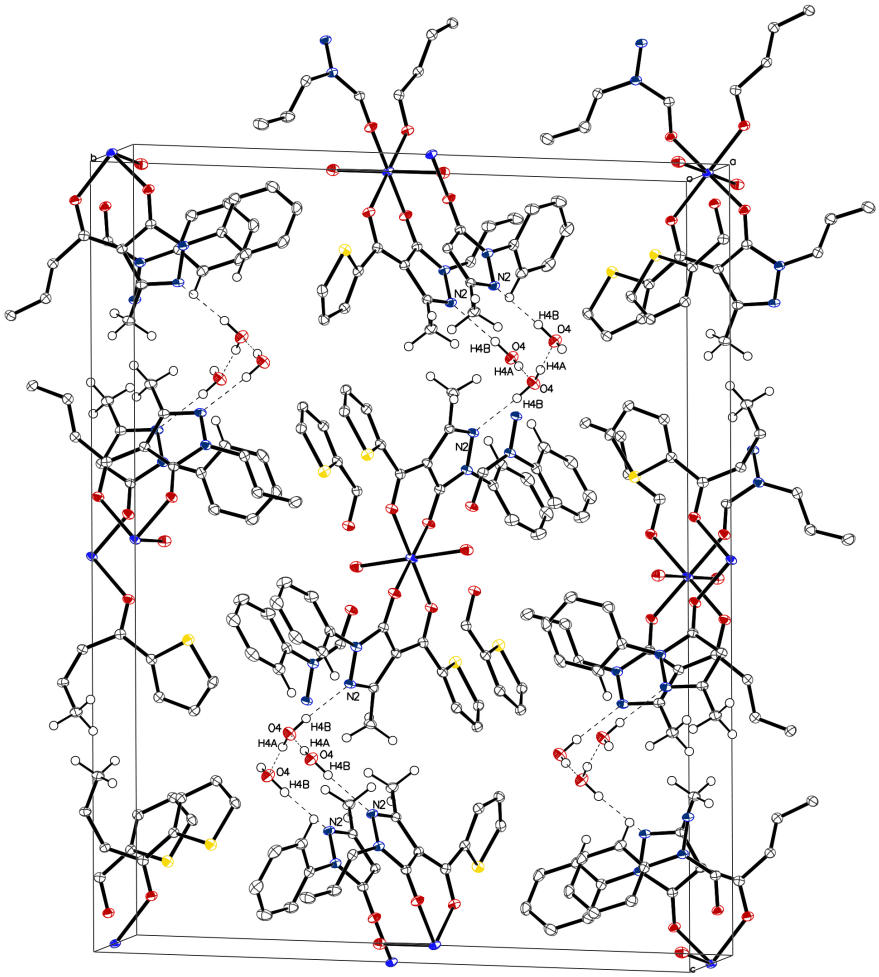


Figure 5. A view of the 2D network sheet of 1·2H_2O formed by H-bonding interactions (dashed lines). Hydrogen atoms other than those participating in hydrogen bonding are omitted for clarity. S (yellow), N (blue), O (red).

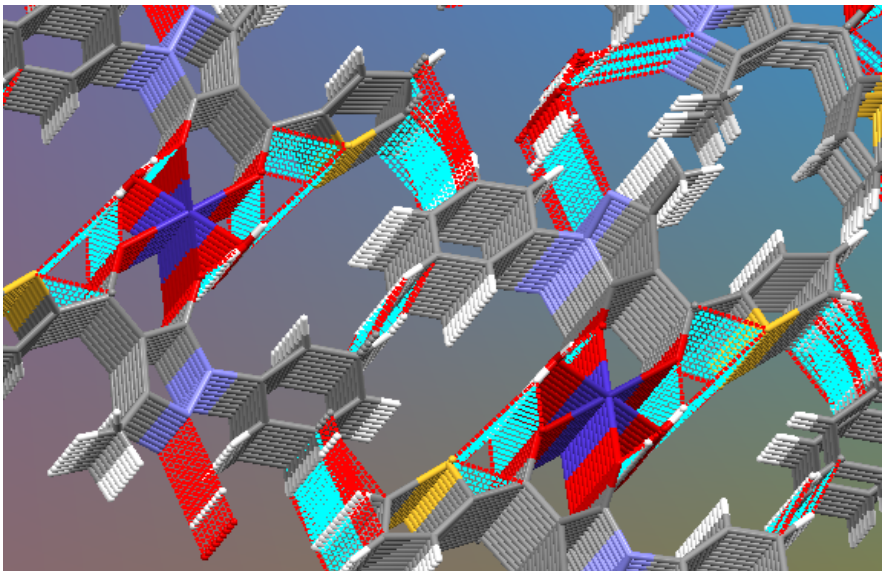


Figure 6. Some cavities are present in 1·2H_2O.

Table 6. Hydrogen bond lengths (Å) and angles (˚) in 1·2H_2O.

D-H…A	d (DH)	d (H…A)	d (D…A)	DHA
C(10)-H(10C)…N(2)	0.980	2.453	3.433	75.80
C(6)-H(6)…O(4)	0.950	3.039	3.989	103.40
O(4)-H(4B)…N(2)	0.820	2.084	2.904	175.52
O(3)-H(3A)…O(2)	0.732	3.026	3.758	85.27

Table 7. MIC and CMB of antibacterial activity of HL, 1·2H_2O and reference.

Compounds		Bacterial strain and isolates				
		STS	STM	ST	SPB	SPA
1·2H_2O	MIC	64	64	32	32	64
	MBC	128	128	128	64	128
	MBC/MIC	2	2	4	2	2
HL	MIC	128	256	128	128	256
	MBC	256	512	256	128	512
	MBC/MIC	4	2	2	1	2
Ciprofloxacine	MIC	<0.5	<0.5	<0.5	<0.5	<0.5
	MBC	<0.5	<0.5	<0.5	<0.5	<0.5
	MBC/MIC	1	1	1	1	1

MIC: Minimal Inhibitory Concentrations; MBC: Minimal Bactericidal Concentration; STS: *Salmonella Typhi* ATCC6539; ST: *Salmonella Typhi*; STM: *Salmonella Typhimurium*; STB: *Salmonella Paratyphi* Band STA: *Salmonella Paratyphi* A.

3.5.2. Antifungal Activity

Table 8 presents the activities in terms of minimal inhibitory concentrations (MIC) and minimal fungicidal concentrations (MFC) of the ligand HL, 1·2H_2O and the reference Nystatine against certain resistant microorganisms.

Analysis of these data shows that ligand HL and 1·2H_2O have fungistatic and fungicidal activities ranging from 64 to 1024 µg/mL on all the yeasts tested. These results also revealed that the activity, 64 to 128 µg/mL of 1·2H_2O is considerably increased as compared to the activity, 256 to 512 µg/mL of the ligand HL alone. The best antifungal activity of the complex was obtained on *Candida Krusei* ATCC14243 (F1) and *Candida tropicalis* 018 (018) with MICs of 64 µg/mL. The complex 1·2H_2O showed moderate activity (10 < MIC ≤ 100 µg/mL) on F1 and 018 yeasts compared to the ligand HL which has low activity (MIC > 100 µg/mL) on all yeasts. The ligand HL and the complex (1·2H_2O) exhibited fungicidal activity on all yeast tested.

3.5.3. Discussion

The ligand, HL and the Co(II) complex, 1·2H_2O have a broad spectrum of activity (antifungal and antibacterial). The ligand being a virtual β-diketo compound,

Table 8. MIC and MFC of antifungal activity of ligand HL, $1{\cdot}2H_2O$ and reference.

Compounds		Fungal strain and isolates			
		F1	F5	F2	018
$1{\cdot}2H_2O$	MIC	64	128	128	64
	MFC	256	512	1024	128
	MFC/MIC	4	2	2	2
HL	MIC	512	512	256	512
	MFC	1024	1024	512	1024
	MFC/MIC	2	2	2	2
Nystatine	MIC	<0.5	<0.5	<0.5	<0.5
	MFC	<0.5	<0.5	<0.5	<0.5
	MFC/MIC	1	1	1	1

MIC: Minimal Inhibitory Concentrations; MFC: Minimal Fungicidal Concentration; F1: *Candida Krusei* ATCC14243; 018: *Candida tropicalis* 018; F2: *Candida albicans* 7a; F5: *Candida albicans* 18ca.

it is found to exist in both the ketonic and enolic tautomeric forms. Hence, it is a suitable candidate for complexation with metals and can therefore improve the biological activity of complexes [44]. In addition, the structural components possessing additional (C = N) bonds with oxygen and/or nitrogen donor systems inhibit enzyme activity due to their deactivation by metal coordination [45] [46].

According to Kuete and co-workers [33], the complex showed moderate activity ($10 < MIC \leq 100$ µg/mL) on all *Salmonella* bacteria and on F1 and 018 yeasts compared to the ligand which has low activity (MIC > 100 µg/mL) on all microorganisms. Gatsing and Adoga [34] showed that the ligand and the complex exhibited bactericidal and fungicidal activity respectively on all the bacteria and yeasts tested. These results show that the complex has better antimicrobial activity on all microorganisms (bacteria and fungi) compared to the ligand. This could be explained by Tweedy's Chelation Theory [47]. Indeed, chelation reduces the polarity of the metal ion by partial positive charge exchange of the metal with the donor atoms of the ligand [48] [49] [50]. This leads to an increase in the delocalization of π-electrons throughout the chelating cycle, with a consequent increase in the lipophilic character of the complex. This lipophilic nature promotes greater penetration of the complex through the lipid layer of the cell membranes of microorganisms. Thus, this blocks the metal binding sites in the enzymes of bacteria and fungi [48] [49] [50]. The blocking of enzymes would therefore be at the origin of the antimicrobial activities of this complex. Generally, the complex exhibits good antimicrobial performance, such as low minimum inhibitory concentration ($MIC \leq 100$ µg/mL), bactericidal and fungal effect and broad spectrum of activity, which makes it a suitable candidate for the manufacture of drugs. Similar results were obtained by Taheri and co-workers

[51].

4. Conclusion

A new cobalt(II) complex, $[Co(O_2C_{15}H_{11}N_2S)_2(OH_2)_2]\cdot 2H_2O$ ($1\cdot 2H_2O$), has been synthesized upon reacting cobalt chloride hexahydrate, $Co(Cl)_2\cdot 6H_2O$, with 1-phenyl-3-methyl-4-(2-thienoyl)-pyrazol-5-one, $N_2C_{15}H_{12}O_2S$, in ethanol at room temperature. Single crystal x-ray diffraction (XRD), spectroscopic methods, and elemental studies were used to characterize $1\cdot 2H_2O$. Complex has a two-dimensional (2D) network structure that is formed by intra O-H···O, C-H···N, H-bonding interactions and inter C-H···H, O-H···N, C-H···O H- bonding interactions. Biological activities showed that the complex exhibits good antimicrobial performance, such as low minimum inhibitory concentration (MIC ≤ 100 μg/mL), bactericidal and fungicidal effect and broad spectrum of activity, which makes it a suitable candidate for the manufacture of drugs. Thus, there is hope that this complex could reasonably be used in designing more potent antibacterial and antifungal agents for the treatment of some common diseases caused by *Salmonella* and *Candida* species.

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Data Availability

Data is available upon request.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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