Research Article

http://dx.doi.org/10.21060/cis.2015.332

Synthesis, crystal structure and biological activity of 1-(phthalazin-1(2H)-one)[(Pyridin-2-yl)ethylidene]hydrazone and its cobalt (III) complex

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Received: September 02, 2015; accepted: October 05, 2015

Abstract: A new mononuclear complex of cobalt (III) (2) with 1-(phthalazin-1(2H)-one)[(Pyridin-2-yl) ethylidene] hydrazone ligand (1) has been synthesized and characterized by elemental analysis, IR and mass spectroscopic techniques. The crystal structures of the free ligand (1) and its complex (2) have been determined by single crystal X-ray diffraction technique. In complex 2 the hydrazone ligand chelates to the cobalt (III) ion through nitrogen atoms in a tridentate manner, giving an octahedral geometry where the cobalt (II) was oxidized to cobalt (III). The antifungal activity of ligand 1 and its complex 2 was studied against *Aspergillus niger*, *Aspergillus flavus* and *Candida albicans*. The results revealed modest activity of complex 2 against the tested organism with inhibition zones of 14, 15 and 14 mm, compared to the free ligand 1 with the inhibition zones of 12, 11 and 12 mm for *A. niger*, *A. flavus*, *C. albicans* respectively.

Supporting information: X-Ray, IR, Uv-vis, HOMO-LUMO diagram.

Keywords: *Hydrazone ligand; Cobalt (III) complex; X-ray crystal structure; Antifungal activity.*

1. INTRODUCTION

1-hydrazinophthalazine (hydralazine) and its derivatives are being extensively studied for their biological and chemical properties. Their biological activities studies have revealed interesting pharmacological properties (antimicrobial, antimalarial and antitumor activity) [1-5]. They have also been reported to find wide applications in the treatment of tuberculosis, leprosy and mental disorder. Furthermore considerable interest of researchers to 1-hydrazinophthalazine (hydralazine) is due to the fact that its hydrochloride is an effective drug for emergency reduction of blood pressure in hypertensive crises [6, 7]. It has also been reported [8] that hydralazine and hydrochlorothiazide combination is used to treat high blood pressure, as they work by relaxing blood vessels and increasing the supply of blood oxygen to the heart while reducing its workload [9].

Their chemical properties are also interesting because the nature of hydrazone Schiff base they form are polydentate in nature and very versatile as well. These physiological and chemical importance of hydralazine derivatives have therefore led to great interest in their complexation tendency most especially with transition metal ions of biological importance. To date very few cobalt complexes of 1-phthalazinyl hydrazone have been reported in literature [9-11].

In continuation with our studies of metal complexes of hydralazine derivatives [12], the present work is devoted to the preparation of 2-acetylpyridine based hydralazine Schiff base and its Co(III) complex, which to the best of our knowledge, is the first example of an X-ray study of the ligand (1) and its mononuclear Co(III) complex (2). Furthermore, the antifungal activities of complex 2 and the free ligand 1 against various fungal strains have been evaluate.

2. EXPERIMENTAL

2.1 Material and physical measurements

The chemicals 2-acetylpyridine, 1-phthalazinohydrazine, $CoCl_2 \cdot 6H_2O$ and the solvents methanol and ethanol were used as purchased, without any further purification. The IR spectra were recorded on a Perkin-Elmer System 2000 FT-IR spectrometer scanning in the range of 4000-400 cm^{-1} using KBr pellets. The ESI mass spectra were recorded with an FT-ICR (APEX II) from Bruker Daltonics. Elemental analysis was performed on a VARIO EL (Heraeus).

2.2. Single crystal X-ray diffraction analysis and structure determination

The crystallographic data were collected on a Gemini diffractometer (Agilent Technologies) using Mo-Kα radiation (λ = 71.073 pm), ω-scan rotation. Data reduction was performed with the Crys Alis Pro [13] including the program SCALE3 ABSPACK [14] for empirical absorption correction. The structure was solved by direct methods (1= (SHELXS-97), 2 =SIR-92) and the refinement of all non- hydrogen atoms was performed with SHELXL-97 [15]. All non-hydrogen atoms were refined with anisotropic thermal parameters. For 1 a difference-density Fourier map was used to locate all hydrogen atoms whereas for 2 all hydrogen atoms are calculated. CCDC 1007670 and 1007671 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data request/cif (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ,UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.uk).The molecular graphics were done with ORTEP-3 [16] and Mercury (version 3) [17].

2.3. Antifungal studies

The antifungal activities of the compounds were evaluated by the well diffusion method [18] against the fungal strains *Aspergillus niger*, *Aspergillus flavus* and *Candida albicans* cultured on potato dextrose agar and compared using Amphotericin as standard drug at the same concentration. The stock solution (10^{-2} mol L^{-1}) was prepared by dissolving the compounds in ethanol and the solutions were serially diluted to find minimum inhibitory concentration values. The concentration of the compounds used in this study was 2000 ppm. In a typical procedure, a well was made on the agar medium inoculated with microorganisms. The well was filled with the test solution using micropipette and the plate was incubated 24 h for the fungi at 30°C. During this period, the test solution diffused and growth of the inoculated micro-organisms was affected. The inhibition zone was developed and the diameter measured in millimetres [19]. The experiment was done in triplicate for accuracy.

Table 1. Crystal data and structure refinement for ligand **1** and complex **2**

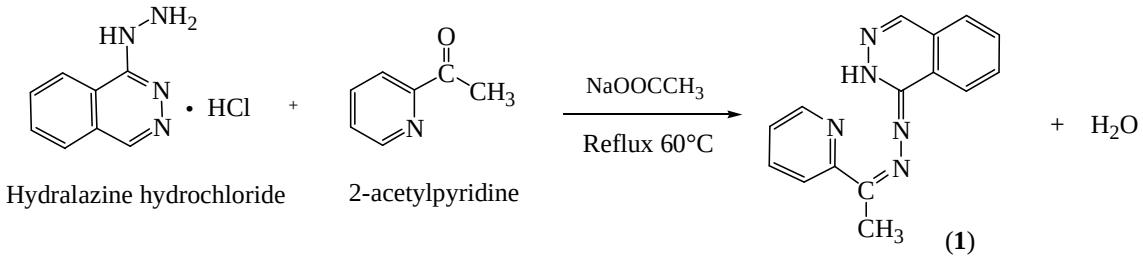
Compound	**1**	**2**
Empirical formula	$C_{15}H_{13}N_5$	$[C_{30}H_{24}N_{10}Co]Cl•3.5H_2O$
Formula weight	263.30	682.03
T(K)	130(2)	130(2)
Space group	P ī	P ī
Wavelength (Å)	0.71073	0.71073
Crystal system	Triclinic	Triclinic
Unit cell dimensions		
a (Å)	7.0992(2)	9.0287(2)
b (Å)	8.5903(3)	11.7378(3) .
c (Å)	10.8249(4)	16.6036(5)
α (°)	100.395(3).	105.001(2).
β (°)	96.799(3).	98.539(2)
γ (°).	103.962(3)	110.362(2)
Volume($Å^3$)	621.00(4)	1537.15(7)
Z	2	2
D_X (g cm^{-3})	1.408	1.474
μ(mm^{-1})	0.090	0.698
F(000)	276	706
Crystal size(mm^3)	0.35 x 0.35 x 0.3	0.4 x 0.3 x 0.15
ɵ range (°)	1.94 -33.13	3.11 - 30.50
Miller Index range	-9<=h<=10,-12<=k<=13,16<=l<=16	-12<=h<=12,-16<=k<=16,-23<=l<=23
Reflections collected	8036	32748
Independent reflections (R_{int})	4715 [(R_{int}) = 0.0191]	9381 [R(int) = 0.0249]
Completeness to $ɵ_{max}$(%)	100.0	99.9
Max. and min. transmission	1 and 0.99512	1 and 0.93806
Data / restraints / parameter	4715 / 6 / 233	9381 / 15 / 467
Goodness-of-fit (GOF) on F2	1.046	1.111
Final R indices [I>2σ(I)]	R1 = 0.0463, wR2 = 0.1235	R1 = 0.0437, wR2 = 0.1018
R indices (all data)	R1 = 0.0626, wR2 = 0.1353	R1 = 0.0512, wR2 = 0.1053
Largest diff. peak and hole (e.$Å^{-3}$)	0.407 and -0.252	0.529 and -0.653

2.4. Synthesis of 1-(phthalazin-1(2H)-one)[(Pyridin-2-yl) ethylidene]hydrazone (1)

The ligand 1 was prepared by mixing equimolar amounts of 2-acetylpyridine (307 mg, 2.54 mmol), hydralazine hydrochloride (500 mg, 2.54 mmol) and sodium acetate (350 mg, 2.56 mmol) as a buffering agent in 50 ml ethanol. The mixture was then refluxed at 60 ^{o}C while stirring for 4 hr. The product was left overnight to cool, removed by vacuum filtration; washed several times with water and ethanol to give yellow powder. *Yield* 79 %. *Anal*. *Calcd*. for ($C_{15}H_{13}N_5$): C, 58.40; H, 5.60; N,22.70. *Found;* C, 58.40; H, 5.40; N, 22.43 %. IR (KBr, cm^{-1}): 3438.6, 3317.1, 3054, 2922.1, 1605.6, 1591.5, 1569.1, 1532.6, 1468.1, 1432.8, 1385.6, 1353.6, 1250.1, 1146.8, 1022.9, 990.4, 953.3 , 906.8, 780.5, 656.7; ESI [m/z (%)]: 286 (100 %) $[M+ Na]^+$, 264.2 (35 %) $[M]^+$.

2.5 Synthesis of $[CoL_2]$ Cl•3.5H_2O (2)

To a warm ethanolic solution (20 ml) of **1** (2 mmol, 526 mg), was added $CoCl_2$•6H_2O (1 mmol, 237 mg) dissolved in 20 ml ethanol and the mixture was heated under reflux at 60 °C with continuous stirring for 3 h. The precipitate formed was allowed to cool slowly at room temperature after which it was filtered and washed several times with ethanol. Yield: 69 %. *Anal*. *Calcd*. for ($[C_{30}H_{24}N_{10}Co]Cl$•3.5 H_2O): C, 47.20; H, 5.20; N, 18.20. *Found;* C, 47.70; H, 5.0; N, 18.20 %. IR (KBr, cm^{-1}): 3416.5, 3068.1, 2927.5, 1599.7, 1581.7, 1527.2, 1496.8, 1472.5, 1422.6, 1378.4, 1321.8, 1249.6, 1183.8, 1157.1, 1110.4, 1067.6, 1017.9, 912.2, 872.3, 783.9, 760.4, 652.7, 594.1; ESI [m/z (%)]: 584.2 (100 %) $[M–Cl]^+$.



Scheme 1. Synthesis of ligand **1**

3. RESULTS AND DISCUSSION

3.1 Infrared spectra

2-acetylpyridine reacted readily with one equivalent of 1-phthalazinehydrazine to form the new ligand 1-(phthalazin-1 (2H)-one) 2-[(Pyridin-2-yl) ethylidene]hydrazone (**1**) in good yield [Scheme 1]. The IR spectrum of the ligand **1** and the cobalt (III) complex (**2**) were recorded within the 4000-400 cm^{-1} region. The IR spectrum of the free hydrazone ligand revealed strong bands at 3438.6 and 3317.1 cm^{-1} attributed to υ(OH) from residual water molecules and υ(NH) [20] respectively. Strong bands appeared at 1606, 1591, 1569 and 1532 cm^{-1}. These bands are due to υ(C=N) and υ(C=N-N=C) of the hydrazone [9, 12, 20]. The pyridine ring-breathing modes of vibration was attributed to a band at 990 cm^{-1} [21-23].

In the spectrum of the metal complex **2**, the band at 3317.1 cm^{-1} is completely absent, indicating the deprotonation of the ligand up on coordination, while the υ(C=N) and υ(C=N-N=C) bands have shifted to lower frequencies of 1599, 1527, 1496, and 1422 cm^{-1} indicating coordination through the phthalazinyl, and the azomethine nitrogen atoms [12, 24]. The shift of the pyridine ring breathing modes of vibration in the ligand from 990 cm^{-1} to 1018 cm^{-1} in the metal complex confirms the coordination of the pyridine ring nitrogen atom to the metal ions. The pyridine ring-breathing modes of vibration are typically shifted to higher energy by 20-30 cm^{-1} on coordination [21-23, 25].

3.2 Molecular structure of 1 and 2

Pale yellow crystals of **1** were obtained from recrystallization in EtOH layered with DMF by slow evaporation at room temperature. Dark red crystals of **2** were obtained from slow evaporation of its ethanolic solution at room temperature. The crystal structure refinement data for compounds **1** and **2** are given in Table 1 and selected bond lengths and angles are listed in Table 2. Compound **1** (Fig. 1) and compound **2** (Fig. 2) crystallized as triclinic in the space group *P*ī with two molecules in the unit cell. In addition, Compound **2** crystallized with three and half non coordinated water molecules per formula unit.

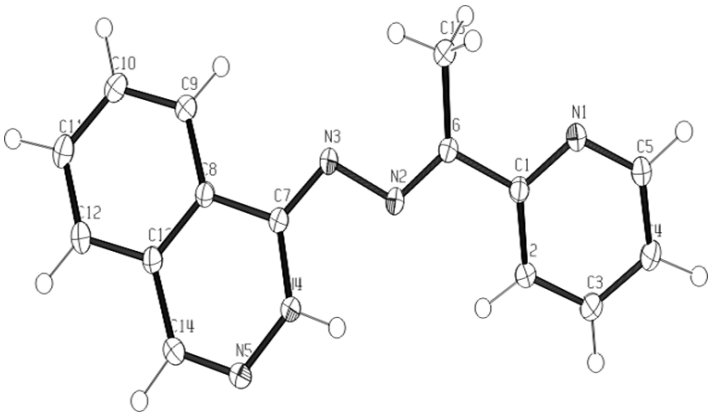


Figure 1. ORTEP plot of compound **1** (thermal ellipsoids are drawn at the 50% probability level).

Table 2. Selected Bond lengths (Å) and Bond angles (°) of ligand **1** and complex **2**

Bond lengths		Bond angles	
1			
N(5) - C(14)	1.294(1)	N(5) - N(4) - C(7)	126.76(8)
N(4) - N(5)	1.366(1)	N(3) - C(7) - N(4)	123.38(8)
N(2) - C(6)	1.289(1)	N(4) - C(7) - C(8)	116.06(8)
N(2) - N(3)	1.395(1)	N(3) - C(7) - C(8)	120.54(8)
N(4) - C(7)	1.367(1)	C(7) - N(3) - N(2)	111.22(8)
N(3) - C(7)	1.308(1)	C(6) - N(2) - N(3)	115.70(8)
N(4) - H	0.918(2)	N(2) - C(6) - C(1)	116.38(8)
		C(14) - N(5) - N(4)	116.85(8)
2			
N(4) - C(7)	1.360(2)	N(7) - Co(1) - N(2)	179.89(7)
N(7) - N(8)	1.363(2)	N(7) - Co(1) - N(9)	81.03(6)
N(9) - N(10)	1.355(2)	N(2) - Co(1) - N(9)	98.89(6)
N(7) - C(21)	1.307(2)	N(7) - Co(1) - N(4)	98.99(6)
N(8) - C(22)	1.344(2)	N(9) - Co(1) - N(4)	80.94(6)
N(2) - C(6)	1.307(2)	N(9) - Co(1) - N(4)	90.85(6)
N(9) - C(22)	1.358(2)	N(7) - Co(1) - N(6)	82.68(6)
N(2) - N(3)	1.358(2)	N(2) - Co(1) - N(1)	82.42(6)
N(3) - C(7)	1.340(2)	N(4) - Co(1) - N(1)	163.25(6)
N(4) - N(5)	1.361(2)	N(6) - Co(1) - N(1)	92.95(6)
Co(1) - N(1)	1.949(2)	N(7) - Co(1) - N(1)	97.64(6)
Co(1) - N(2)	1.873(1)	N(9) - Co(1) - N(1)	89.73(6)
Co(1) - N(4)	1.910(2)	N(2) - Co(1) - N(6)	97.41(6)
Co(1) - N(6)	1.942(1)	N(4) - Co(1) - N(6)	91.17(6)
Co(1) - N(7)	1.872(1)		
Co(1) - N(9)	1.896(1)		

In compound **1** the bond distance N(5)-C(14) of 1.294(1) Å indicates its double bond character. The bond lengths N(4)-N (5), N(4)- C(7), and N(3)-C(7) are equal to 1.366(1), 1.367(1) and 1.308(1) Å respectively. These data suggest a single bond between the endocyclic nitrogen atoms N(4) and N(5), while a double bond is assigned to N(3)-C(7). In the final stages of the refinement, a hydrogen atom was located 0.918(2) Å from N(4), confirming this assumption. The molecular structure of **1** correspond to the imino tautomer in which the hydrogen is located at the endocyclic nitrogen N(4). The position of the proton on the endocyclic nitrogen N(4) is similar to those reported in other hydrazinophthalazine derivatives [12, 27-29]. The bond distance N(2)-C(6) of 1.289(1) Å is closer to 1.285(2) Å [12] and 1.291 (5) Å [30] observed in similar Schiff bases.

In **1** the [N(4)-H(1N4) and N(5)] are involved in a strong intermolecular NH-N donor acceptor bonds, which allow the formation of a dimer (Fig. 3). This dimer is held together by weak intermolecular C-H-N hydrogen bonds through the pyridine-nitrogen, the phthalazine-hydrogen, the hydrazine-nitrogen and the methyl-hydrogen (Table 3) and the π-π interaction of the parallel-displaced configuration [31] of the pyridine rings through C1 and C3 atoms (Fig.4).

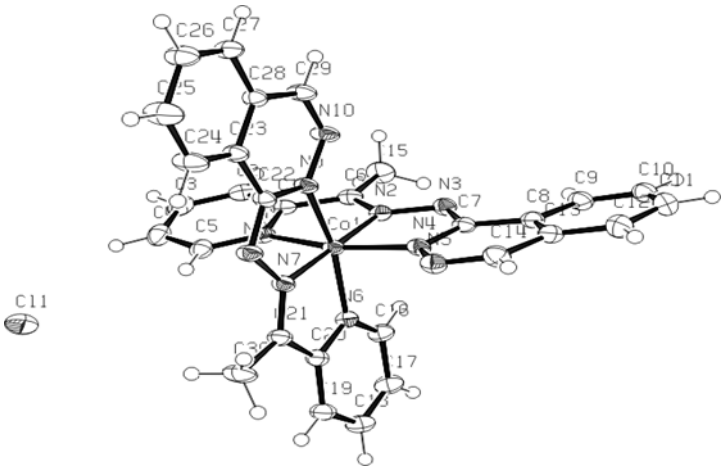


Figure 2. ORTEP plot of **2** (thermal ellipsoids are drawn at the 50 % probability level).

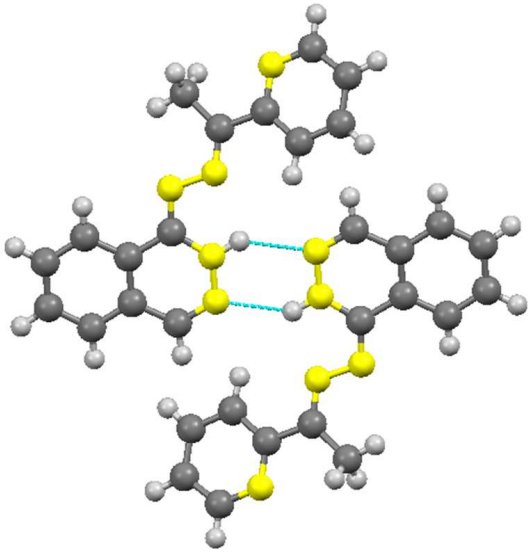


Figure 3. A dimeric specie of **1** showing intermolecular hydrogen bonding.

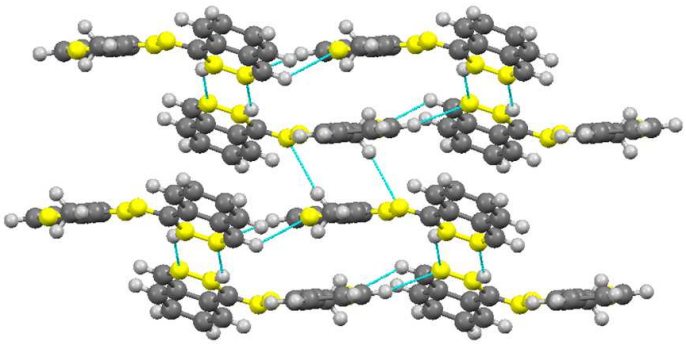


Figure 4. View of **1** showing C-H-N intermolecular interactions in dimers.

Table 3. Hydrogen bond distances (Å) and angles (°) for **1**

D-H...A	d(D-H) Å	d(H...A) Å	d(D...A) Å	D-H-A (°)
C(14) - H(14).....N(1) #1	0.979(2)	2.684(2)	3.398(1)	130.1(1)
C(15) - H(15C)...N(3) #2	0.971(1)	2.681(1)	3.614(1)	161.2(1)
N(4) - H(1N4).....N(5) #3	0.918(2)	230.5(2)	3.041(1)	136.9(1)

D, donor; H, hydrogen; A, acceptor
Symmetry transformations used to generate equivalent atoms.
#1 x, y, z –1 #2 –x + 1, –y + 2, –z + 1 #3 – x, –y +1, –z

In the molecular structure of 2, one chloride counter ion is found in the unit cell, pointing to the oxidation of Co^{II} to Co^{III}, and some disordered water molecules is also found in the lattice. The chloride anions and all water molecules are located in channels along the a-axis (Fig.5). These channels are running throughout the entire lattice and have the dimension of approximately 3.45 Å (Δx) and 4.25 Å (Δy).

The oxidation of Co^{II} to Co^{III} complex was also observed with other phthalazinohydrazone derivatives [31] in which oxygen was excluded as oxidizing agent, with the ligand more likely to provide the proton that oxidized the Co^{II} while reduced to H_2.

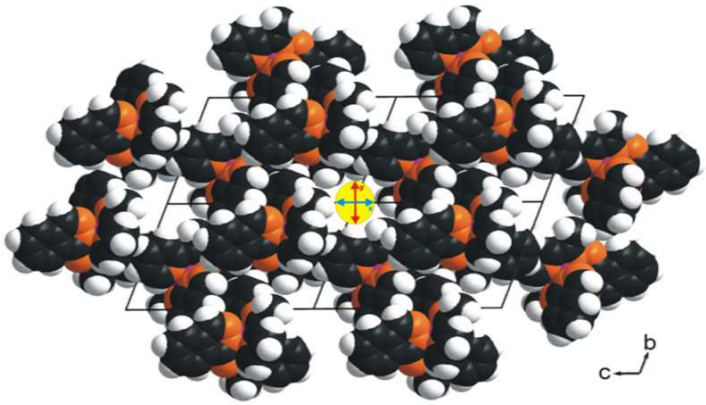


Figure 5. Channels viewed in **2** along a–axis

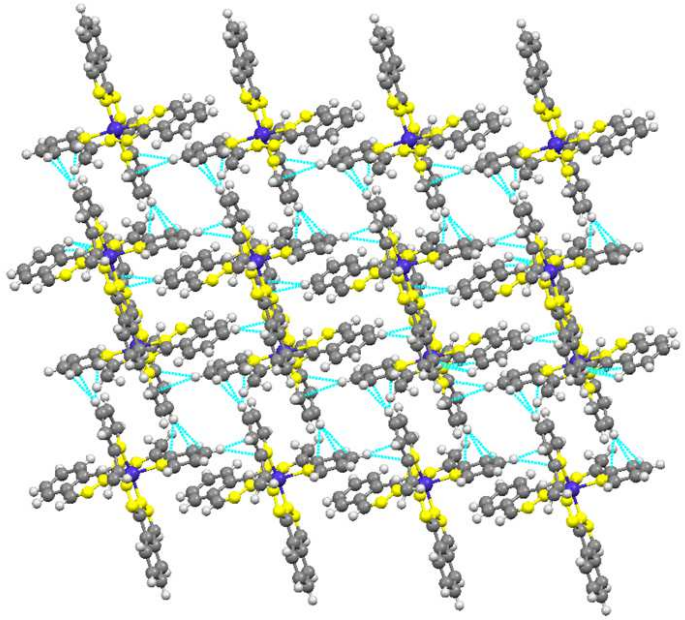


Figure 6. **π-π** interaction in the complex **2** along b-axis.

Furthermore, the reducing potential of Co^{III} to Co^{II} points toward a spontaneous oxidation of the metal in the presence of protons [31].

The molecular structure of **2** shows that the deprotonated ligand coordinates to the mononuclear central cobalt (III) ion in a tridentate mode; *via* the azomethine nitrogen, one of the phthalazine diazine nitrogen and the pyridine nitrogen, giving a distorted octahedral environment around the metal ion (Fig.2). The metal-nitrogen bond lengths of 1.872(1) to 1.949(2) Å is in agreement with reported values for Co^{III}-N in the range of 1.875 (8) to 1.948(7) Å [31]. The Co^{III}-N bond distances are shorter than Co^{II}-N bond distances [2.082(5) to 2.223(5) Å] [23] in a similar environment, due to increase electrophilicity of Co^{III} with respect to Co^{II}. Similar to the data reported in literature [31], the bonds were found to be shortest for the metal-imino nitrogen atoms N(7) and N(2) [1.872(1) and 1.873(1) Å] and longest for the metal- pyridine nitrogen atoms N(1) and N(6) [1.949(2) and 1.942(1) Å].

The C-N bond lengths [N(3)-C(7), N(8)-C(22)] and [N(2)-C(6), N(7)-C(21)] of 1.340(2), 1.344(2) Å and 1.307(2) Å became longer upon coordination compared to 1.308(1) and 1.289(1) Å in the free ligand. Furthermore, the N(2)-N(3) and N(7)-N(8) bond lengths of 1.358(2) and 1.363(2) Å became shorter upon coordination compared to 1.395(1) Å in the free ligand. All these variation in bond lengths suggest some electron delocalization due to the presence of the positively charge metal center.

The octahedral environment around the cobalt is slightly distorted by the four five-membered chelate rings generated by N(1), N(2), N(4) and N(6), N(7), N(9). The angles N(4)-Co-N(2) of 80.94°, N(2)-Co-N(1) of 82.42°, N(9)-Co-N(7) of 81.03°, and N (7)-Co-N(6) of 82.68° are far from the ideal angle of 90°, illustrating the equatorial compression, mainly due to the steric demand of the phthalazine rings.

In the molecular structure of **2**, the complex molecules are held together by the π-π interactions of the T-shaped configuration [30] of the pyridine rings through (C3 and C16, C20; C18 and C1, C2, C3) and the phthalazine rings through (C11 and C28, C29) resulting to the structure interaction depicted in Fig. 6.

3.3 Antifungal activity

The hydrazone ligand **1** and it cobalt complex **2** were tested for their inhibitory effect on the growth of *A. Flavius*, *A. niger* and *C. albicans* using Amphotericin as standard reference. The ligand **1** showed an inhibitory effect against all the tested organisms with diameter of inhibition zones of 9 millimeters each. The complex **2** was found to be more toxic than the parent hydrazone ligand with inhibition zones of 16, 16, 15 mm for *A. flavus*, *A. niger* and *C. albicans* respectively. All these values were comparable to amphotericin with values of 17 mm each against all the microorganisms. The increase in antifungal activity of the metal chelate may be due to effect of the metal ion on the normal cell process. A possible mode of toxicity increase may be considered in the light of Tweedy's chelation theory [26]. Chelation considerably reduces the polarity of the metal ion because of partial sharing of its positive charge with the donor group and possible pi-electron delocalization within the entire chelate ring system that is formed during coordination. Such chelation could enhance the lipophilic character of the central metal atom and hence increase the hydrophobic character and liposolubility of the complex favouring its permeation through the lipid layers of the cell membrane. Overall the results indicated enhanced activity against the tested fungal strains as compared with our previous results on another hydralazine derivative [12] and Amphotericin.

4. CONCLUSION

We have synthesized and characterized by X-ray diffraction, infrared, elemental analysis and mass spectrum a new mononuclear cobalt (III) complex of 1-phthalazinyl hydrazone of 2-acetylpyridine. The new ligand molecules chelate to the metal center in a tridentate manner through the azomethine, the phthalazinyl and the pyridine nitrogen atoms resulting in the formation of a distorted octahedral geometry cobalt (III) complex. The complex further showed an enhanced antifungal activity compared to the parent ligand.

Acknowledgements

ENN is thankful to DAAD for Research Fellowship and Prof. Dr. Rhett Kempe of the Inorganic Chemistry Institute, University of Bayreuth, Germany for hosting the fellowship while, FMM is thankful to Prof. Dr. Evamarie Hey-Hawkins of the Institute of Inorganic Chemistry, University of Leipzig, Germany for providing us X-ray analysis.

4. REFERENCES

[1] Jackson, S. H.; Shepher, A. M.; Ludden, T. M.; Janieson, M. J.; Woodworth, J.; Rogers, D.; Ludden, L.K.; Muir, K. T. *J. Cardiovasc. Pharmacol*. **1990**, 16 (4) 624.

[2] Zelenin, K. N.; Khorseeva, L. A. and Alekeseev, V.V. *Pharm. Chem. J*. **1992**, 26(5) 395.

[3] Kaminskas, L. M.; Pyke, S. M. and Burcham, P. C. *J. Pharm. Exper. Therap*. **2004**, 310 (3) 1003.

[4] Segura-Pacheco, B.; Trejo-Becerril, C.; Perez-Cardenas, E.;Taja-Chayeb, L.;Mariscal, I.; Chavez, A.; Acuna, C.;Salazar, M.; Lizano M. and Duenas-Gonzalez, A. *Clinical Cancer Research*, **2003**, 9 (5) 1596.

[5] Vincini, P.; Incerti, M.; Doytchinova, I. A.; La colla, P.; Busonera B.and Loddo, R. *Eur. J. Med. Chem.* **2006**, 48 (5) 624.

[6] Dray, J. and Tripod, I. *Antihypertensive Agent*. **1967**, 7, 223.

[7] Mashkovskii, M. D. Lekarstvennye sredstva (Remedies), Moscow: Medistsina, **1972 .**

[8] Mayo foundation for medical education, **7 January 2007.**

[9] Shoukry, A. A. and Shoukry M. M. *Spectrochim. Acta Part A.* **2008**, 70, 686.

[10] Kogan, V. A.; Levchenkev, S. I.; Popov, L. D. and Shcherbakov, I. A. *Russian Journal of General Chemistry*. **2009**, 79 (12)2767.

[11] West, F.;Al-Assar, F.;Zelenin, K.N.; Lesiovskaya, E.E.;Bezant, I. P.; Chakchir. B. A. *Pharm. Chem.* **1992**, 36,598.

[12] Nfor, E. N.; Husian, A.; Majoumo–Mbe, F.; Njah, I. N.; Offiong O. E. and Bourne, S. A. *Polyhedron*. **2013**, 63, 207.

[13] CrysAlis Pro: Data collection and data reduction software package, Agilent Technologies.

[14] SCALE3 ABSPACK: Empirical absorption correction using spherical harmonics.

[15] SHELX includes SHELXS97, SHELXL97: Sheldrick, G. M. *Acta Cryst*. **2008**, A64, 112.

[16] Farrugia, L.J.; *J. Appl. Crystallogr*. **1997**, 30, 565.

[17] Macrae, C. F; Bruno, I.J.; Chisholm, J.A.; Edgington, P.R.; McCabe, P.; Pidcock, E.; Rodriguez-Monge, L.;Taylor, R.; van de Streek, J.; Wood, P. A.; *J. Appl. Crystallogr*. **2008**, 41, 466.

[18] Rahman, A.; Choudry, M.I.;Thomsen, W. J.; Bioassay Techniques for Drug Development, Harwood Academic Publishers, Netherlands, **2001.**

[19] Bauer, A. W.; Kirby, W. M.; Sherris, C.; Turck, M. *Am. J. Clin. Pathol*. **1966**, 45, 493.

[20] Popov, L. D.; Levchenkov, S. I.; Shcherbakov, I. N.; Kogan, V. A. and Tupolova Yu, P. *Russ. J. Gen. Chem.* **2010**, 80 (3) 493.

[21] Xu, Z.; Thompson, L. K.; Milway, V. A.; Zhao, L.; Kelly T. and Miller, D. O. *Inorg. Chem.* **2003**, 42, 2950.

[22] Paolucci, G.; Stelluto, S.; Sitran,S.; .Ajo', D.; Benetollo, F. and Polo, A. *Inorg. Chim. Acta*, **1992**,193, 57.

[23] Wen, T.; Thompson, L. K.; Lee, F. L. and Gabe, E. J. *Inorg. Chem*. **1988**, 27, (23) 4191.

[24] (a) Raphael, P. F.; Manoj, E.; Prathapachandra Kurup, M.R.; *Polyhedron* 2007, 26, 818; (b) Khandar, A. A.;Hosseini-Yazdi, S. A. *Polyhedron.* **2003**, 22, 1481; (c) Vicente, M.; Bastida, R.;Lodeiro, C.;Macias, A.; Parola, A. J.;Valencia, L.;Spey, S.E. *Inorg. Chem*. **2003**, 42, 6768; (d) Lodeiro, C.;Bastida, R.; Bertolo, E.; Macias, A.; Rodríguez, A.; *Polyhedron.* **2003**, 22, 1701.

[25] Thompson, L. K.; Chacko, V. T.; Elvidge, J. A.; Lever A. B. P.; Parish, R. V. *Can. J. Chem*., **1969**, 47, 4141.

[26] Popov, L. D.; Levchenkov, S. I.; Shcherbakov, I. N.; Starikova, Z. A.; Kaimakan, E. B.; Lukov, V. V. *Russ. J. Gen. Chem.* **2012**, 82, 465.

[27] Butcher, R. J.;Jasinski, J. P.;Yathirajan, H. S.; Vijesh, A. M.; Narayana, B. *Acta Crystallogr. Sect. E*. **2007**, E63. 03674.

[28] Ianelli, S. and CarcelliM. *Z. Kristallogr*. **2002**, NCS 217, 203.

[29] Georgi, G.; Ponticilli, F.; Chiasserini, F.; Pellerano, C. *Perkin Trans*. **2000**, 2, 2259.

[30] Sinnokrot, M. O.;Valeev, E. F. and Sherrill, C. D. *J. Am. Chem. Soc*. **2002,** 124, 10887.

[31] Grunwald, K. R.;Volpe, M.; Cias, P.; Gescheidt, G. and Mosch-Zanetti, N. C. *Inorg. Chem*. **2011**, 50, 7478.