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Synthesis, Structure and Antibacterial Activities of Schiff Base Derived from PMBP with 2-Furfurylamine and Its Complexes

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4-Acyl-5-pyrazolone is a family of flexible β-diketonate, which are widely used and well known for their applications as analgesics, antipyretics, anti-inflammatory and insecticides [1,2]. Therefore, the studies of derivatives of 4-acyl-5-pyrazolone are the focus of many research groups working in the fields of coordination chemistry, biomedicine and pharmaceutical chemistry [3]. In order to extend our knowledge of 4-acyl-5-pyrazolone, several Schiff bases derived from TTA [4,4,4-trifluoro-1-(2-thienyl)-1,3-butanedione] were studied [4–6]. In this communication the synthesis, structure and antibacterial activities of the title compounds are reported.

20 mL (0.01 mol) of 2-furfurylamine ethanol solution was dropwise added into 22 mL (0.01 mol) of PMBP ethanol solution. Keeping the temperature at 70~80℃, the solution was stirred for about 3~4 h. The yellow crude product was isolated when the solvent had been evaporated out, and dried in air. After washing with cold anhydrous ethanol solution for several times, the ligand 4-[2-furfurylamine-5-methyl-2-phenyl-2H-pyrazol-3(4H) one ($C_{22}H_{19}N_3O_2$) was dried in a vacuum desiccator over $CaCl_2$. Yield: 84%, m.p.: 137~138℃. Bright yellow single crystal of the ligand suitable for X-ray analysis was obtained by slowly cooling from a warmed ethanol solution.

11 mL (0.01 mol) of $Cu(NO_3)_2 \cdot 6H_2O$, $Co(NO_3)_2 \cdot 6H_2O$, $Ni(NO_3)_2 \cdot 6H_2O$ and $Zn(NO_3)_2 \cdot 6H_2O$ ethanol solutions were added separately into 20 mL of 0.01 mol the ligand ethanol solutions, respectively. Adjusting the pH = 7~8 and stirring vigorously for 6~8h at 70~80℃, the products were precipitated, filtered and apart washed with benzene, anhydrous ethanol and water solution and dried in the vacuum desiccator over $CaCl_2$. Cu-complex (Y_1), $[C_{22}H_{18}N_3O_2]_2Cu \cdot 2H_2O$, brown, yield: 79%, m.p. > 320°C; Co-complex (Y_2), $[C_{22}H_{18}N_3O_2]_2Co \cdot 2H_2O$, green, yield: 81%, m.p. > 320℃; Ni-complex (Y_3), $[C_{22}H_{18}N_3O_2]_2Ni \cdot 2H_2O$, blue-green, yield: 78%, m.p. > 320℃; Zn-complex (Y_4), $[C_{22}H_{18}N_3O_2]_2Zn \cdot 2H_2O$, white, yield: 82%, m.p. > 320°C. The analyses confirm the compositions.

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IR spectra in the region of 400~4000 cm^{-1} were determined with KBr pellets using AVATAR 360 (U.S.A.) infrared spectrophotometer. Table 1 lists the IR data for the compounds. The ν_{N-H} appearance in the ligand and disappearance in the complexes and broad ν_{O-H} band at 3335~3391 cm^{-1} in the complexes indicate that the N–H and water molecules exist in the ligand and complexes, respectively. The $\nu_{C=N}$ (ring) observed at 1589 cm^{-1} in the ligand and change only slightly in the complexes ruling out the coordination through the nitrogen of the pyrazolinone ring. Absorption $\nu_{C=O}$, observed at 1637 cm^{-1} in PMBP, is shifted to 1634 cm^{-1} for the ligand, and to lower frequencies at 1558~1570 cm^{-1} in the complexes. New imine C=N absorption frequency is observed at 1524, 1506, 1489 and 1506 cm^{-1} in the Cu(II), Co(II), Ni(II) and Zn(II) complexes, respectively. It is in accordance with deprotonation of the ligand and involvement of carbonyls and imine nitrogen in bonding to metal in the complexes [7]. New δ_{O-H} absorption frequency, observed at 500~600 cm^{-1} in the complexes, indicate that water molecules had been coordinated to metal atom. New ν_{M-N} and ν_{M-O} absorption frequency observed at 570~620 and 450~530 cm^{-1} in the complexes confirm the participation of the atoms N and O in the coordination.

Table 1. IR data of the ligand and its complexes (cm^{-1}).

No.	ν_{N-H}	ν_{O-H}	$\nu_{C=O}$	$\nu_{C=N}$ (ring)	$\nu_{C=N}$ (imine)	ν_{M-N}, ν_{M-O}
PMBP			1637	1589		
L	3422		1634	1589		
Y_1		3391	1570	1591	1524	621.0, 459.0
Y_2		3388	1558	1593	1506	609.5, 472.5
Y_3		3388	1558	1593	1489	611.4, 530.4
Y_4		3335	1558	1591	1506	576.7, 457.1

UV spectra were recorded using a Shimaduzu UV-2401 PC spectrophotometer. The bands for $\pi \rightarrow \pi$ transition observed at 206.0 and 254.5 nm for ligand were shifted to 206.5~207.5 nm and 242.0~245.5 nm for the complexes. The bands for $n \rightarrow \pi$ transition of C=N observed at 301.5 nm for the ligand were shifted to 281.5~290.0 nm for the complexes. New bands observed at 616, 602, 611 and 619 nm in the complexes confirm the six-coordinated octahedral configuration.

The following ^{1}H-NMR spectra data (δ, ppm) were recorded on a VARIAN 300 NMR instrument in $CDCl_3$ solvent: ligand: 1.21 (t, 3H, CH_3), 3.88 (s, 2H, CH_2), 7.34~7.48 (m, 5H, arom), 7.51~7.76 (m, 5H, N-arom), 7.78~7.89 (m, 3H, furan), 9.77 (s, 1H, NH); complexes: 0.91~1.12 (t, 6H, CH_3), 3.61~3.77 (s, 4H, CH_2), 7.04~7.31 (m, 10H, arom), 7.35~7.54 (m, 10H, N-arom), 7.61~7.74 (m, 6H, furan). The single signal due to –NH observed in the spectra of the ligand, disappeared in the spectra of complexes, thus suggesting that the donors coordinate the metal atom in the deprotonated form [8]. The resonance signals of methyl, phenyl and furan rings were shifted upfield upon coordination [9].

Results of IR, UV and ^{1}H-NMR characterizations indicate also that the keto-enamine and the imine Schiff base forms exist in the ligand and its complexes, respectively. This case is close to that reported in [10]. The structure of the ligand and tentative model of metal bonding in the complexes are presented in Figure 1.

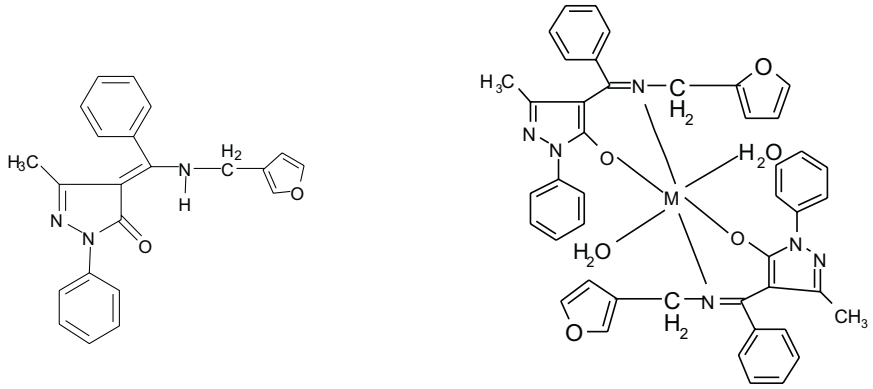

Figure 1. The structure of the ligand and tentative model of metal bonding in the complexes.

Bright yellow single crystal of the ligand with the dimensions of 0.25×0.30×0.20 mm was mounted on a Bruker Smart-1000 CCD diffractometer at 293 K with a graphite monochromatic MoK$_\alpha$ radiation (λ = 0.071073 nm) by ω and ϕ scan. A total of 6225 reflections were measured (2.17° < θ < 23.28°), in which 2661 reflections with $I \geq 2.0\sigma(I)$ were used in the refinement (on F^2). The crystal data are as follows: monoclinic, C2/*c* *a* = 1.9169 (5), *b* = 1.1234 (3), *c* = 1.9247 (5) nm, β = 117.115 (5)°, V = 3.6893 (18) nm^3, Z = 4, Dc = 1.190 Mg · m^{-3}, μ = 0.073 cm^{-1}, F (000) = 1388, final R_1 = 0.0720, wR = 0.1467, S = 0.927. The structure was solved by direct method using SHELXS-97 program. The hydrogen atoms were located from the difference maps. During the final cycles of the refinements, anisotropic and isotropic thermal parameters were assigned to the non-hydrogen and hydrogen atoms in the structure, respectively. The maximum and minimum peaks in the final difference Fourier map are 402 and –457 e · nm^{-3}, respectively. An ORTEP view (50% probability displacement ellipsoids) of the ligand is shown in Figure 2. The selected bond distances and angles are listed in Table 2.

The bond lengths of O(1)–C(1), C(1)–C(2), C(2)–C(5) and C(5)–N(3) are 0.1250(6), 0.1432(7), 0.1394(7) and 0.1328(6) nm, respectively, between the classical single and double bond lengths. In the molecule, the O(1), C(1), C(2), C(5) and N(3) atoms form a basal plane roughly, the largest deviation from the basal plane is –0.00517(3) nm for C(5) atom. The dihedral angle between the basal plane and the pyrazolone ring is 5.25(3)°, which is very close to the value of 5.05(3)° reported in [11] due to a big conjugate system formed. The dihedral angle between the basal plane with phenyl of C(11)–C(16) is 20.30°, which indicates that there is a part of electron delocalization over this moiety. The dihedral angles between the basal plane with

phenyl of C(21)–C(26) and furan ring are 114.25 and 101.84°, respectively, due to steric hindrance effects.

A strong intra-molecular hydrogen bond [N(3)---O(1) 0.2717(5) nm and N(3)–H(3)---O(1) 142.7(4)°] is observed, resulting in a keto – enamine tautomerism. In the ligand, 0.1328(6) nm of C(3)–N(5) is longer than the 0.1285(2) nm of the imine bond length in the compound of picolinaldehyde thiosemicarbazone N-oxide Schiff base [12]. This case is close to the compound of 4-{[3,4-dihydro-5-methyl-3-oxo-2-phenyl-2H-pyrazol-4-yl-idene](phenyl)methylamino}-1,5- dimethyl-2-phenyl-1H-pyrazol-3(2H)-one [13].

The torsion angles of C(3)–C(2)–C(5)–C(21) and C(3)–C(2)–C(5)–N(3) are –9.5(4) and –12.3(8)°, respectively. The same small torsion angle has been observed in the 4-(antipyrin-4-ylimino-methyl) benzoic acid due to a big conjugate system [14]. The inter- hydrogen bond of C(15)–H(15)---O(1)^{i} (0.3372 nm, 141.9°; i: –x, –y, –z) indicates that the molecules stack in the crystal depend on the van der Waals and inter- and intra-hydrogen forces.

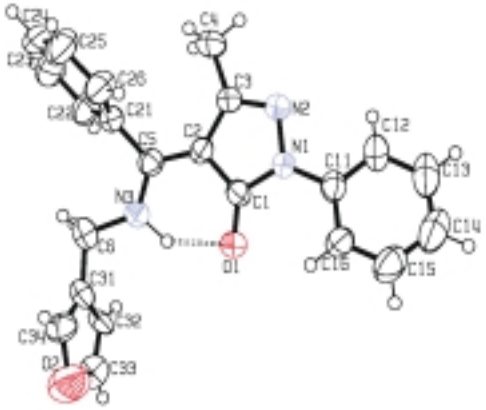

Figure 2. ORTEP view of the ligand.

Table 2. Selected bond lengths (nm) and angles (°) for the ligand.

Bond	Length (nm)	Bond	Length (nm)	Bond	Length (nm)
N(1)–C(1)	0.1377(6)	N(3)–C(6)	0.1471(6)	O(2)–C(33)	0.1371(9)
N(1)–N(2)	0.1404(5)	C(1)–C(2)	0.1432(7)	C(3)–C(4)	0.1494(6)
N(1)–C(11)	0.1410(6)	C(2)–C(3)	0.1424(7)	O(2)–C(34)	0.1312(7)
N(2)–C(3)	0.1309(6)	C(2)–C(5)	0.1394(7)	C(5)–C(21)	0.1480(6)
N(3)–C(5)	0.1328(6)	O(1)–C(1)	0.1250(6)	C(6)–C(31)	0.1486(6)

Table 2 (continuation)

Bond	Angle (°)	Bond	Angle (°)	Bond	Angle (°)
C(1)–N(1)–N(2)	111.4(4)	N(1)–C(1)–C(2)	105.0(4)	N(3)–C(5)–C(21)	119.1(4)
C(1)–N(1)–C(11)	129.4(4)	C(5)–C(2)–C(3)	132.3(4)	C(2)–C(5)–C(21)	122.1(4)
N(2)–N(1)–C(11)	119.1(3)	C(5)–C(2)–C(1)	122.4(4)	N(3)–C(6)–C(31)	111.0(4)
C(3)–N(2)–N(1)	106.0(3)	C(3)–C(2)–C(1)	105.3(4)	C(22)–C(21)–C(5)	121.0(4)
C(5)–N(3)–C(6)	125.6(4)	N(2)–C(3)–C(2)	111.9(4)	C(26)–C(21)–C(5)	120.1(4)
C(33)–O(2)–C(3)	102.2(5)	C(3)–C(2)–C(1)	105.3(4)	C(32)–C(31)–C(6)	116.4(5)
O(1)–C(1)–N(1)	125.8(4)	C(2)–C(3)–C(4)	128.5(4)	C(32)–C(33)–O(2)	112.6(5)
O(1)–C(1)–C(2)	129.2(4)	N(3)–C(5)–C(2)	118.7(4)	C(31)–C(34)–O(2)	105.5(5)

Using disc diffusion method [15] we tested the antibacterial activity of the compounds. The results (Table 3) showed that all compounds exhibit moderate activity against *Escherichia coli* and *Staphylococcus aureus* in which the ligand and its complexes have higher inhibition abilities than the PMBP. Among these compounds, the Co(II) complex exhibited better activity against *Escherichia coli* than the other complexes, according to Tweedy's chelating theory [16]. Chelating considerably reduces the polarity of the metal ion because of partial sharing of its positive charge with the donor groups and possible π-electron delocalization over the chelating ring. Such chelating could increase the lipophilic character of the central metal atom [17].

Table 3. The inhibition abilities (mm) for the compounds.

Compound	*Staphylococcus aureus*				*Escherichia coli*			
	1	2	3	average	1	2	3	average
PMBP	6.0	6.5	6.5	6.3	5.5	5.5	5.5	5.5
L	9.0	9.5	9.5	9.3	10.0	9.5	9.5	9.7
Y_1	7.0	7.0	7.0	7.0	9.5	9.5	10.0	9.8
Y_2	9.0	10.0	10.5	10.0	16.5	16.5	17.5	16.8
Y_3	9.0	9.0	9.0	9.0	9.0	9.0	12.0	10.0
Y_4	9.5	9.5	10.5	9.8	8.5	8.5	9.0	8.8

Supplementary material:
Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication No.CCDC – 212700. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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