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Some new Cu(II) complexes containing an ON donor Schiff base: Synthesis, characterization and antibacterial activity

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2-Hydroxy-4-methoxy-benzaldehyde

ABSTRACT

Six new copper(II) complexes, $CuLCl{\cdot}H_2O$ (**1**), $CuL(NO_3){\cdot}2H_2O$ (**2**), $[Cu(L)_2]$ (**3**), $CuL(SCN){\cdot}2H_2O$ (**4**), $CuL(ClO_4){\cdot}2H_2O$ (**5**) and $(CuL)_2(SO_4){\cdot}4H_2O$ (**6**), where HL = 1-phenyl-2,3-dimethyl-4-(N-2-hydroxy-4-methoxy-benzaldehyde)-3-pyrazolin-5-one, have been synthesized. The characterization of the newly formed compounds was done by ^1H NMR, UV–Vis, IR, ESR spectroscopy, elemental analysis and molar electric conductivity. The crystal structure of 1-phenyl-2,3-dimethyl-4-(N-2-hydroxy-4-methoxy-benzaldehyde)-3-pyrazolin-5-one has been determined by X-ray diffraction studies, as well as the crystal structure of one of its copper(II) complexes, $[Cu(L)_2]$ (**3**). The copper atom is coordinated to two nitrogen and two oxygen atoms of the Schiff base ligand. The in vitro antibacterial activity against *Klebsiella pneumoniae ATCC 100131*, *Staphylococcus aureus var. Oxford 6538*, *Pseudomonas aeruginosa ATCC 9027* and *Escherichia coli ATCC 10536* strains was studied and compared with that of free ligand. The anti-microbial activity was dependent on the microbial species tested and the metal salt anion used.

1. Introduction

Pyrazolones constitute a group of organic compounds that have been extensively studied due to their properties and applications. On the other hand, pyrazolone-based Schiff base chemistry is less extensive. Some groups have reported the synthesis and characterization of pyrazolone-based Schiff base ligands and their Cu(II) complexes [1–4]. The Schiff base of 4-aminoantipyrine and its complexes have a variety of applications in biological, clinical, analytical and pharmacological areas [5–7]. Studies of a new kind of chemotherapeutic Schiff base are now attracting the attention of biochemists [8,9].

In a previous paper [10] we presented the synthesis of Cu(II) complexes derived from the new Schiff base ligands obtained by condensation of 4-amino-antipyrine with 2-hydroxybenzaldehyde, terephthalic aldehyde, 4-hydroxy-5-methoxy-isophthalaldehyde, 4,5-dihydroxy-isophthalaldehyde and 3-formyl-6-methyl-chromone. This paper is a continuation of our previous research and it presents the synthesis and characterization of new complexes of Cu(II) with a new Schiff base (Fig. 1) obtained by the condensation of 4-aminoantipyrine with 2-hydroxy-4-methoxy-benzaldehyde. The complexes and ligand were also tested for their in vitro antibacterial activity against *K. pneumoniae*, *S. aureus*, *P. aeruginosa* and *E. coli* strains using the paper disc diffusion method and the serial dilutions in liquid broth method [11,12].

2. Experimental

2.1. Materials

2-Hydroxy-4-methoxy-benzaldehyde (Aldrich) and 1-phenyl-2,3-dimethyl-4-amino-3-pyrazolin-5-one (Merck) were used as received. The metal salts $CuCl_2{\cdot}2H_2O$, $Cu(NO_3)_2{\cdot}3H_2O$, $CuSO_4{\cdot}5H_2O$, $Cu_2(OAc)_4{\cdot}(H_2O)_2$, $Cu(ClO_4)_2{\cdot}6H_2O$ and KSCN (Merck) were used as supplied. Solvents used for the reactions were purified and dried by conventional methods [13]. *Caution*! Perchlorate complexes of metals with organic ligands are potentially explosive and should be handled with care.

2.2. Synthesis of the Schiff base 1-phenyl-2,3-dimethyl-4-(N-2-hydroxy-4-methoxy-benzaldehyde)-3-pyrazolin-5-one (HL)

A solution of 1-phenyl-2,3-dimethyl-4-amino-3-pyrazolin-5-one (0.203 g, 1 mmol) in ethanol (10 mL) was added to a solution

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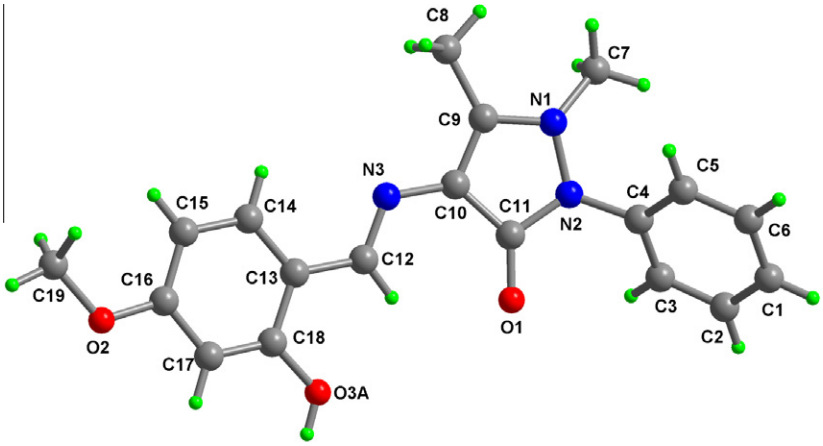

Fig. 1. Perspective view of the HL molecule, along with atom numbering scheme.

of 2-hydroxy-4-methoxy-benzaldehyde (0.152 g, 1 mmol) in ethanol (20 mL). The reaction mixture was stirred for 2 h at room temperature, then heated to reflux for 2 h and kept at 4 °C for three days. The characteristic yellow precipitate obtained was filtered and recrystallized by dissolving in methanol. Fine yellow crystals obtained upon slow evaporation at room temperature were characterized, including single crystal X-ray diffraction.

Yield 76%; M.p.: 192–193 °C; M.wt.: 337; *Anal.* Calc. for $C_{19}H_{19}N_3O_3$: C, 67.65; H, 5.63; N, 12.46. Found: C, 68.17; H, 5.22; N, 12.08%. The IR spectrum of the obtained ligand confirms the occurrence of an absorption band at 1629 cm^{-1} (st, intense), specific for the azomethinic group [14]. ^1H NMR ($CDCl_3$, δ, ppm, *J*, Hz): 2.35 (s, 3H, CH_3-8); 3.15 (s, 3H, N–CH_3-7); 3.76 (s, 3H, OCH_3); 6.42 (d, 8.5, 1H, H-17); 6.50 (d, 8.5, 1H, H-18); 7.32 (s 1H, H-15); 7.42–7.50 (m, 5H, 1, 2, 3, 5, 6); 9.57 (s, 1H, H-12, CH=N); ^{13}C NMR (DMSO-d_6, δ, ppm): 9.90 (C-8); 35.33 (C-7); 55.49 (OCH_3); 132.83 (CH-15); 134.39 (C-4); 149.68 (C-10); 157.97 (C-16); 159.43 (C-12); 162.58 (C-14).

2.3. General procedure for the preparation of the metal complexes (**1**–**6**)

Complexes **1**–**3**, **5** and **6** were prepared by the direct reaction between the ligand and the corresponding metal salts. Complex **4** was obtained by refluxing a mixture of $CuCl_2{\cdot}2H_2O$ and 1-phenyl-2,3-dimethyl-4-(N-2-hydroxy-4-methoxy-benzaldehyde)-3-pyrazolin-5-one with addition of KSCN [15].

2.3.1. Synthesis of the complex $CuLCl{\cdot}H_2O$ (**1**)

An ethanol solution of $CuCl_2{\cdot}2H_2O$ (2 mmol, 15 mL aqueous/ethanol 1:2 v/v) was added dropwise to a stirred ethanol solution of the Schiff base ligand HL (2 mmol, 15 mL). The resulting solution was stirring for 3 h at room temperature. The green–brown colored solid was filtered, washed with hot water, then ethanol followed by ether and dried in *vacuo*. Yield: 77%; M.p. >220 °C; M.wt.: 453; *Anal.* Calc. for $C_{19}H_{20}CuN_3O_4Cl$: C, 50.33; H, 4.41; N, 9.27; Cu, 14.01. Found: C, 50.72; H, 4.27; N, 8.98; Cu, 13.92%. Main IR peaks (KBr, cm^{-1}): υ(C=O) 1636; υ(C=N) 1607; υ(Ar–OH) 1120; υ(Ar–O–$C_{aliphatic}$) 1240, 1025, υ(OH^-) 3450. The complex is soluble in DMF and DMSO, and is partially soluble in chloroform and methanol.

2.3.2. $CuL(NO_3){\cdot}2H_2O$ (**2**)

Dark-green solid. Yield: 89%; M.p. 220 °C; M.wt.: 497.5; *Anal.* Calc. for $C_{19}H_{22}CuN_4O_8$: C, 45.83; H, 4.42; N, 11.25; Cu, 12.76. Found: C, 46.14; H, 4.16; N, 11.02; Cu, 12.59%. Main IR peaks (KBr, cm^{-1}): υ(C=O) 1636; υ(C=N) 1602; υ(Ar–OH) 1117; υ(Ar–O–$C_{aliphatic}$) 1242, 1022; υ(OH^-) 3434; υ_5(NO_3^-) 1494; υ_1(NO_3^-) 1297; υ_2(NO_3^-) 925. The complex is soluble in DMF and DMSO, and is partially soluble in methanol.

2.3.3. $[CuL_2]$ (**3**)

Brown solid, X-ray quality single crystals were obtained. Yield: 83%; M.p. >220 °C; M.wt.: 735.5; *Anal.* Calc. for $C_{38}H_{36}CuN_6O_6$: C, 61.99; H, 4.89; N, 11.42; Cu, 8.63. Found: C, 62.28; H, 4.33; N, 11.16; Cu, 8.48%. Main IR peaks (KBr, cm^{-1}): υ(C=O) 1648; υ(C=N) 1609; υ(Ar–OH) 1121; υ(Ar–O–$C_{aliphatic}$) 1243, 1024. The complex is soluble in chloroform, DMF and DMSO, and is partially soluble in methanol.

2.3.4. $CuL(SCN){\cdot}2H_2O$ (**4**)

Green solid. Yield: 78%; M.p. >220 °C; M.wt.: 493.5; *Anal.* Calc. for $C_{20}H_{22}CuN_4O_5S$: C, 48.63; H, 4.45; N, 11.34; Cu, 12.86. Found: C, 49.08; H, 4,22; N, 11.07; Cu, 12.60%. Main IR peaks (KBr, cm^{-1}): υ(C=O) 1632; υ(C=N) 1610; υ(Ar–OH) 1120; υ(Ar–O–$C_{aliphatic}$) 1241, 1029; υ(OH^-) 3437. The complex is soluble in DMF, DMSO and chloroform, and is partially soluble in methanol.

2.3.5. $CuL(ClO_4){\cdot}2H_2O$ (**5**)

Green solid. Yield: 72%; M.p. >220 °C; M.wt.: 535; *Anal.* Calc. for $C_{19}H_{22}CuN_3O_9Cl$: C, 42.61; H, 4.11; N, 7.85; Cu, 11.86. Found: C, 43.14; H, 3.88; N, 7.55; Cu, 11.47%. Main IR peaks (KBr, cm^{-1}): υ(C=O) 1637; υ(C=N) 1605; υ(Ar–OH) 1120; υ(Ar–O–$C_{aliphatic}$) 1240, 1027; υ(OH^-) 3440. The complex is soluble in DMF, DMSO and chloroform, and is partially soluble in methanol.

2.3.6. $(CuL)_2(SO_4){\cdot}4H_2O$ (**6**)

Dark-green solid. Yield: 83%; M.p. >220 °C; M.wt.: 967; *Anal.* Calc. for $C_{38}H_{44}Cu_2N_6O_{14}S$: C, 47.15; H, 4.55; N, 8.68; Cu, 13.13. Found: C, 47.63; H, 4.31; N, 8.36; Cu, 12.76%. Main IR peaks (KBr, cm^{-1}): υ(C=O) 1636; υ(C=N) 1606; υ(Ar–OH) 1119; υ(Ar–O–$C_{aliphatic}$) 1243, 1024; υ(OH) 3436, υ_3(SO_4^{-2}) 1113; υ_4(SO_4^{-2}) 616. The complex is soluble in chloroform, DMF and DMSO, and is partially soluble in ethanol and methanol.

2.4. Physical measurements

C, H and N analyses were performed with a Carlo-Erba LA-118 microdosimeter whereas an AAS-1 N Carl-Zeiss-Jena spectrometer was used for the determination of Cu(II). Physico-chemical analyses were performed after drying the complexes at 105 °C. Infrared spectra (4000–400 cm^{-1}) were recorded on a BioRad FTS 135