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Synthesis, characterization and biological activities of metal(II) dipicolinate complexes derived from pyridine-2,6-dicarboxylic acid and 2-(piperazin-1-yl)ethanol

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ABSTRACT

The new water-soluble and air stable compounds $(H_2ppz)[Co(dipic)_2]\cdot 6H_2O$ (**1**), $(H_2ppz)[Ni(dipic)_2]\cdot 6H_2O$ (**2**) and $(H_2ppz)[Zn(dipic)_2]\cdot 6H_2O$ (**3**) were prepared by the reaction of corresponding metal(II) acetates and a proton transfer salt, (H_2ppz) $(Hdipic)_2$, (**4**) of pyridine-2,6-dicarboxylic acid (H_2dipic) and 2-(piperazin-1-yl)ethanol (ppz). The compounds **1**–**3** were characterized by elemental, IR, UV–vis. thermal analyses, magnetic measurement and single crystal X-ray diffraction studies. The molecular structures of the title compounds consist of one 1-(2-hydroxyethyl)piperazine-1,4-diium (H_2ppz^{+2}) cation, one bis(pyridine-2,6-dicarboxylate)metal(II) $[M(dipic)_2]^{2-}$ anion, and six uncoordinated water molecules. In compounds **1**–**3** the metal ions coordinate to two oxygen and one nitrogen atoms of two pyridine-2,6-dicarboxylate molecules forming an octahedral environment. Antimicrobial activities against Gram (−) wild type (*Escherichia coli* and *Pseudomonas aeruginosa*), Gram (+) wild type (*Staphylococcus aureus, Staphylococcus epidermidis, Bacillus cereus* and *Bacillus subtilis*) and clinical isolate (*Morganella morganii, Proteus vulgaris and Enterobacter aeruginosa*) were also studied. The results were reported, discussed and compared with the corresponding starting materials ((H_2ppz) $(Hdipic)_2$ (**4**), H_2dipic and ppz). MIC (Minimal Inhibition Concentration) values of the newly synthesized compounds were determined as 4000 μg/ml (except *B. subtilis* and clinical isolate *E. aeruginosa*, >4000 μg/ml).

1. Introduction

Pyridine-2,6-dicarboxylic acid (H_2dipic) is a fully acknowledged structural component in many metal-organic frameworks [1–8] in biochemistry and in the formation of water clusters [9–15]. For chemical systems, the degree of structuring of water cluster can be of importance for the design as well as the stabilization of new structures [16]. H_2dipic has a rigid 120° angle between the central pyridine ring and two carboxylate groups. Proton donating and accepting capabilities for hydrogen bonding via the oxygen atoms of its carboxylate groups [17] provide various coordination modes to form both discrete and polymeric metal complexes under an appropriate synthesis condition [2].

Metal complexes of H_2dipic and some of their derivatives have shown antimicrobial activities in recent years [18,19]. The enhancement of the antimicrobial activity of certain chemicals can be achieved by the addition of metals. The role of metals in antimicrobial activity is shown in many studies [20–24].

The metal complexes with mixed ligands of these compounds have shown better biological activities than the simple ones [25–29]. Continuing the path to synthesize proton transfer compounds, our group has focused on forming ion pairs between H_2dipic and various organic bases, such as 2-aminobenzothiazole [30], 2-amino-6-chlorobenzothiazole [29], 2-amino-6-methylbenzothiazole [31], 2-amino-6-methoxybenzothiazole [32], 2-amino-4-methylpyridine [26], 2-(piperazin-1-yl)ethanol (ppz) [18].

In this study, we report three new compounds (H_2ppz)

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[Co(dipic)$_2$].6H$_2$O (**1**), (H$_2$ppz)[Ni(dipic)$_2$].6H$_2$O (**2**) and (H$_2$ppz)[Zn(dipic)$_2$].6H$_2$O (**3**) of a proton transfer salt (H$_2$ppz) (Hdipic)$_2$ (**4**) (H$_2$ppz = 1-(2-hydroxyethyl)piperazine-1,4-diium). The characterization has been made by using elemental and thermal analysis, magnetic measurement, IR and UV–vis electronic spectra of the compounds (**1**–**3**). The molecular structures of **1**–**3** were elucidated by a single crystal X-ray diffraction studies.

2. Experimental

2.1. Materials

All chemicals used were of analytical grade purchased from Aldrich. ^{1}H NMR spectra were recorded by 500 MHz UltraShield NMR spectrometer (SiMe$_4$ as internal standard and 85% H$_3$PO$_4$ as an external standard). Elemental analyses for C, H and N were performed on a Leco CHNS-932 instrument. IR spectra were recorded on a Bruker Optics, vertex 70 FT-IR spectrometer using ATR techniques. Thermal analyses were performed on SII Exstar 6000 TG/DTA 6300 model using platinum crucible with 10 mg sample. TG/DTA measurements were taken in static air within a 30–700 °C temperature range. The UV–vis spectra were carried out with a SHIMADZU UV-2550 spectrometer in the range 900–200 nm. Magnetic susceptibility measurements at room temperature were taken using a Sherwood Scientific Magway MSB MK1 model magnetic balance by the Gouy method using Hg[Co(SCN)$_4$] as calibrant. Molar conductance of the compounds was determined in DMSO (10^{3-} M) at room temperature using a WTW Cond 315i/SET Model conductivity meter.

2.2. Synthesis of compounds (*1*–*3*)

The proton transfer salt (H$_2$ppz) (Hdipic)$_2$ (**4**) was prepared according to the method reported previously [18].

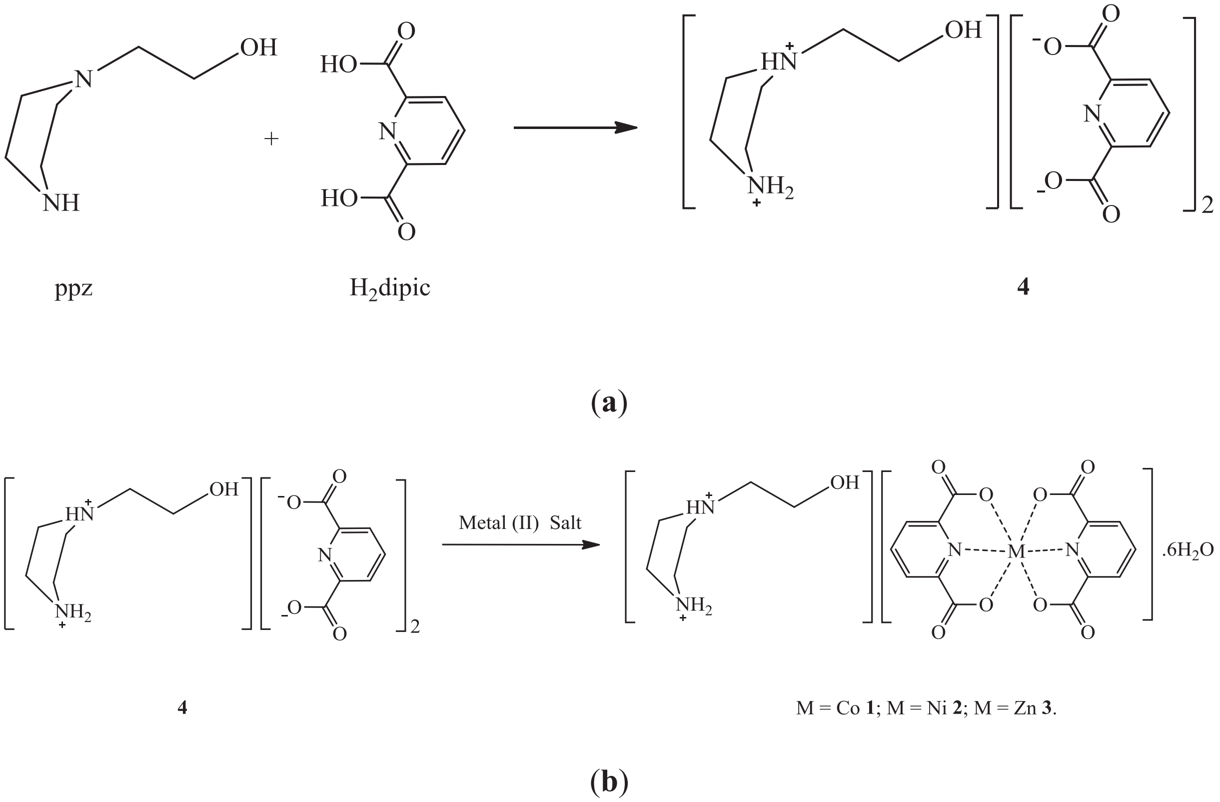
A solution of 1 mmol of a metal(II) salt [0.249 g Co(CH$_3$COO)$_2$.4H$_2$O or 0.248 g Ni(CH$_3$COO)$_2$.4H$_2$O or 0.220 g Zn(CH$_3$COO)$_2$.2H$_2$O] in water (10 mL) was added dropwise to the solution of **4** (0.462 g, 1 mmol) in water (10 mL) with stirring at room temperature for 2 h. The reaction mixture was kept at room temperature for two weeks to give purple crystalline solid for **1** (0.378 g, 60% yield), green crystalline solid for **2** (0.409 g, 65% yield), and colourless crystalline solid for **3** (0.445 g, 70% yield) (Scheme 1). The single crystals of all compounds suitable for X-ray diffraction were separated and washed with water.

Elemental analysis for the compounds **1**–**3** are as follows:

Anal. Calcd. for **1** ($C_{20}H_{34}N_4O_{15}Co$): C, 38.16%; H, 5.44%; N, 8.90%; Co, 9.36%, Found: (%): C, 37.97%; H, 5.28%; N, 8.80%; Co, 9.30%. Anal. Calcd. for **2** ($C_{20}H_{34}N_4O_{15}Ni$): C, 38.18%; H, 5.45%; N, 8.90%; Ni, 9.33% Found: C, 37.78%; H, 5.28%; N, 8.77%; Ni, 9.30%. Anal. Calcd. for **3** ($C_{20}H_{34}N_4O_{15}Zn$): C, 37.78%; H, 5.39%; N, 8.81%; Zn, 10.28%, Found: C, 37.31%; H, 5.22%; N, 8.63%; Zn, 10.30%.

2.3. X-ray crystal structure determination

The crystallographic data are given in Table 1; the selected bond lengths and angles are listed in Table 2; and the hydrogen-bond geometries are given in Tables S1–S4 for the compounds **1**–**3**. Intensity data were recorded on a Bruker Kappa APEXII CCD area-detector diffractometer using Mo K$_\alpha$ radiation (λ = 0.71073 Å) at T = 100(2) K. Absorption corrections by multi-scan [33] were applied. Structures were solved by direct methods and refined by full-matrix least squares against F^2 using all data [34]. All non-H atoms were refined anisotropically. In compounds **1**, **2** and **3**, atoms H10A, H10B, H11A, H11B, H12A, H12B, H13A, H13B, H14A, H14B, H15C, H15D (H$_2$O), H33A, H33B (NH$_2$) and H44 (NH) were located in difference Fourier maps and were freely refined. The



Scheme 1. Syntheses of compounds **1**–**4** (**a** for **4** and **b** for **1**–**3**).