Structural Analysis of Polymeric Copper(II)–Pyrazinamide Complexes Prepared from Two Different Copper(II) Salts

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Abstract. In crystal engineering, the presence of different types of anion may alter the structure of transition metal complexes. Thus, the anions may also govern the properties of the metal complexes. Hereby we reported a structural analysis of polymeric copper(II)-pyrazinamide (pza) complexes prepared from copper(II) sulphate and copper(II) chloride. The complexes were crystallised using a bench-top technique with copper(II):pza molar ratio of 1:2 in a layered H2O-CH3OH solvent at room temperature. Single crystal XRD, ATR-IR and melting point apparatus were used to analyse the structure and characterise the complexes. Single crystal XRD analyses reveals that both complexes, [Cu(μ-pza)(SO4)(H2O)2]n (A) and [Cu(pza)2(μ-Cl)2]n (B) forms a 1D polymeric structure with different metal-ligand connectivity around the octahedral copper centre. The copper centres are also linked by different ligand, namely pyrazinamide in A and chloride in B. Thus, the Cu⋯Cu distances in both complexes are different, 6.719 Å in A and 3.658 Å in B. Unlike in A, the crystal structure of B has two unique copper centres. In addition, crystal structures of A and B were also compared to closely related copper(II)-pza complexes from published literature. As also observed in many metal complexes, crystal structures of copper(II)-pza complexes were affected by the anion of the metal salts used in the reaction, in which the anion also involves in the crystal structures.

1. Introduction

In late 1960s, copper(II)-pyrazinamide complexes were reported by Sekizaki and Yamasaki [1]. Eckberg and Hatfield (in 1975) [2] and Allan et al (in 1988) [3] then continue to study this compound and proposed several copper(II)-pyrazinamide complexes formulas and structures based on their magnetic behaviour. Although pyrazinamide (C4N2H3-CONH2) or pyrazine-2-carboxamide has been extensively explored due to its antimicrobial ability, such as for cancer and tuberculosis treatment [4], their metal complexes also display interesting properties such as electroluminescence [5], magnetism [6], etc.

Pyrazinamide has both chelating and coordinating ability to a metal ion and may act as monodentate terminal ligand or polydentate bridging ligand. Coordination modes of pyrazinamide toward metal ions are illustrated in Figure 1 [7]. Different synthetic method and slight variation on the reaction conditions (e.g. anion, molar ratio, solvents, etc.) may lead to a different product [8]. This rule also apply in many copper(II) pyrazinamide complexes, in which in this paper, anion of the metal salts does matters. Sulphate and chloride salts of copper(II) were used in this work. The anions may act as ligand or counter ion, or as both. Previous copper(II) pyrazinamide complexes utilised anions such as
ClO$_4^-$, BF$_4^-$, PF$_6^-$ [9], SO$_3^{2-}$ [10], 2-nitrobenzoate [11], etc., resulting in a range of discrete and polymeric complexes. Meanwhile, a bench-top method with layered technique [12] was used in this work to crystallise the copper(II) pyrazinamide complex. This method promotes green chemistry concept. It is straightforward (one-pot reaction), only requires simple apparatus and less chemicals, works at room temperature, and the product is easy to isolate.

![Figure 1. Several pyrazinamide modes with metal ion (M)](image)

In this paper, we reported a structural analysis of polymeric copper(II)-pyrazinamide (pza) complexes prepared from copper(II) sulphate and copper(II) chloride. The complexes were crystallised using a bench-top technique with copper(II):pza molar ratio of 1:2 in a layered H$_2$O-CH$_3$CH$_2$OH solvent at room temperature. Infrared analysis and melting point of the complexes are also discussed.

2. Materials and Methods

2.1. Materials and Measurements

Sigma–Aldrich chemicals and solvent (pyrazinamide, CuSO$_4$·5H$_2$O, CuCl$_2$·2H$_2$O, and ethanol) were used as received. Agilent ATR spectroscope was used for infrared analyses at 4000-600 cm$^{-1}$ and Electrothermal Apparatus was used for melting point measurement in open capillaries. Bruker Apex II KAPPA CCD with Mo-Ka radiation (λ = 0.71073 Å) equipped with an Oxford Instruments nitrogen gas cryostream was used for low-temperature (123K) single-crystal X-ray diffraction analyses. The crystal structures were solved using SHELXS and refined using SHELXL-13 [13-14] with Olex2 as the graphical interface [15]. All hydrogen atoms were refined using a riding model, while all non-hydrogen atoms were refined using an anisotropic model.

2.2. Synthesis of the Complexes

2.2.1. [Cu(µ-pza)(SO$_4$)(H$_2$O)$_2$]$_n$ (A). A 4 mL ethanolic solution of pyrazinamide (50 mg, 0.406 mmol) was carefully layered on top of a 2 mL aqueous solution of CuSO$_4$·5H$_2$O (50.7 mg, 0.203 mmol), separated by 3 mL buffer layer of H$_2$O:CH$_3$CH$_2$OH (1:1). Two weeks later, blue block crystals start forming. The crystals then isolated a month later, washed with water and then air-dried for overnight (yield = 55 mg, 85%).

2.2.2. [Cu(pza)$_2$(µ-Cl)$_2$]$_n$ (B). A 4 mL ethanolic solution of pyrazinamide (50 mg, 0.406 mmol) was carefully layered on top of a 2 mL aqueous solution of CuCl$_2$·2H$_2$O (34.6 mg, 0.203 mmol), separated by 3 mL buffer layer of H$_2$O:CH$_3$CH$_2$OH (1:1). Two weeks later, light green needle crystals start forming. The crystals then isolated a month later, washed with water and then air-dried for overnight (yield = 60 mg, 78%).

3. Result and Discussion

3.1. Crystal Structure

Crystal structures of [Cu(µ-pza)(SO$_4$)(H$_2$O)$_2$]$_n$ (A) and [Cu(pza)$_2$(µ-Cl)$_2$]$_n$ (B) were solved in monoclinic $P2_1/c$ space group and triclinic $P$-1 space group, respectively. The data completeness for B was less than ideal (89.0% to $\theta = 50.5^\circ$), and thus the precise metrical data should be treated with some caution. Despite this, the overall connectivity in complex B is unambiguous. Each complex has
octahedral geometry around the copper centre with different metal-ligand connectivity. The asymmetric unit of A consist of two half copper(II) ions, two water ligands, one sulphate ligand, and one pyrazinamide ligand, whereas the asymmetric unit of B consist of half copper(II) ions, one chloride ligand, and one pyrazinamide ligand, thus both complexes are neutral complex with no solvents or ions in the lattice (Figure 2).

Figure 2. Asymmetric units of [Cu(µ-pza)(SO$_4$)(H$_2$O)$_2$]$_n$ (left) and [Cu(pza)$_2$(µ-Cl)$_2$]$_n$ (right) shown with thermal ellipsoids at 50% probability (note: C = grey, H = white).

In complex A, the Cu1 is surrounded by two monodentate sulphate ligands in a trans relationship and two chelated pyrazinamide ligands through carbonyl oxygen (O1) and pyrazine nitrogen (N1) atoms. Meanwhile, the Cu2 of complex A is coordinated by two pyrazinamide ligands in a trans relationship through another pyrazine nitrogen (N2) atom and four water ligands. The pyrazinamide ligand bridges two copper centre in complex A with a Cu1···Cu2 distance of 6.719 Å, thus complex A forms 1D polymeric structure.

In complex B, the copper centre is surrounded by two monodentate pyrazinamide ligands in a trans relationship and four chloride ions. The pyrazinamide ligands coordinate through one of the pyrazine nitrogen (N1) atom and leaving the carbonyl and the amide groups free. Two chloride ions bridges two neighbouring copper centre in complex B with a Cu1···Cu1 distance of 3.658 Å. Consequently, complex B forms 1D polymeric structure as also observed in complex A. Although both complexes display 1D polymeric structures, different bridge motif are displayed by both complexes, namely Cu–pza–Cu motif in complex A and Cu–(Cl)$_2$–Cu motif in complex B (Figure 3).

Figure 3. 1D polymeric structures of [Cu(µ-pza)(SO$_4$)(H$_2$O)$_2$]$_n$ (top) and [Cu(pza)$_2$(µ-Cl)$_2$]$_n$ (bottom); CH hydrogen atoms in are omitted for clarity (note: C = grey, H = white).

Selected bond lengths and angles around the metal centres in the complex A and complex B are presented in Table 1. As frequently reported in many copper complexes, the John-Teller distortion is also occurred in both complexes. The bond lengths of Cu1–O4 (2.4284 (14) Å) and Cu2–O3 (2.3574
thiocyanate ligands bonding between neighbouring chains only.

Table 1. Selected bond lengths and angles around the metal centres in A and B

| Complexes | Bond Lengths (Å) | Angles (°) |
|-----------|-----------------|------------|
| A         |                 |            |
| Cu1–O1    | 1.9645(14)      | 180.0      | 180.0 |
| Cu1–O1a   | 1.9645(14)      | 98.32(5)   | 91.18(6) |
| Cu1–O4    | 2.4284(14)      | 81.65(8)   | 88.82(6) |
| Cu1–O4a   | 2.4284(14)      | 81.65(8)   | 88.82(6) |
| Cu1–N1    | 1.9799(16)      | 81.65(8)   | 88.82(6) |
| Cu1–N1a   | 1.9799(16)      | 82.66(6)   | 89.13(6) |
| Cu2–O3    | 2.3574(15)      | 97.34(6)   | 90.88(6) |
| Cu2–O3b   | 2.5374(15)      | 97.34(6)   | 90.88(6) |
| Cu2–O2    | 1.9718(15)      | 94.69(6)   | 89.76(6) |
| Cu2–O2b   | 1.9718(15)      | 94.69(6)   | 89.76(6) |
| Cu2–N2    | 2.0279(15)      | 94.69(6)   | 90.24(6) |
| Cu2–N2b   | 2.0280(15)      | 94.69(6)   | 90.24(6) |

Table 2. Hydrogen bond data of complex A and complex B (Å)

| Complex | D | H | A | D-H | H…A | D…A | DHA |
|---------|---|---|---|-----|-----|-----|-----|
| A       | O3| H3A| O7#f | 0.85 | 2.01 | 2.819(2) | 159.3 |
|         | O3| H3B| O5#g | 0.85 | 2.58 | 2.788(2) | 94.9 |
|         | O2| H2A| O5#h | 0.85 | 1.83 | 2.669(2) | 161.1 |
|         | O2| H2B| O7#g | 0.85 | 1.83 | 2.699(2) | 161.1 |
|         | N3| H3C| O6#i | 0.86 | 2.01 | 2.839(3) | 160.3 |
|         | N3| H3D| O4#g | 0.86 | 1.99 | 2.803(3) | 156.8 |
| B       | N3| H3A| O1#j | 0.86 | 1.97 | 2.824(15) | 173.6 |
|         | N3| H3B| N2#k | 0.86 | 2.50 | 3.169(15) | 134.9 |

Furthermore, six types of hydrogen bond (Table 2) are observed in complex A. This is due to there are sulphate and water ligands which extensively involve in intra- and intermolecular hydrogen bonding. In contrast, only two types of hydrogen bonds in complex B are formed and involving pyrazinamide ligands between neighbouring chains. Consequently, crystal packing of both complexes grew into 3D hydrogen-bonded networks (Figure 4). Particularly, the hydrogen bond types and the 3D hydrogen-bonded networks of complex B are identical to that of [Cd(pza)₂(μ-SCN)]₆ [7], in which the thiocyanate bridge in the cadmium complex is replaced with chloride bridge in complex B.
Figure 4. Crystal packings of [Cu(µ-pza)(SO₄)(H₂O)₄]ₙ (top) and [Cu(pza)₂(µ-Cl)₂]ₙ (bottom); hydrogen bonds are shown in blue and red dots and CH hydrogen atoms are omitted for clarity (note: Cu = yellow, S = green, Cl = purple, O = blue, N = red, C = grey, H = white).

Crystal structure of A is similar to that of reported by Shirvan in 2012 [10] although different solvent was used in this work. The small differences in unit cell parameters (Table 3) are due to different temperature during X-ray data collection, in which in a higher temperature, bigger unit cells are normally observed. To the best of our knowledge, crystal structure of B has never been reported based on single crystal XRD analyses. However, there are many papers have been proposed the structure of the same complexes based on magnetic and infrared studies [1-3]. In shorts, prediction
made by these papers on the structure of copper(II)-pyrazinamide-chloride complex was match with the XRD analyses reported here.

As observed in other related copper(II)-pyrazinamide complexes, such as [Cu(µ-pza)(SO₄)(H₂O)₂]ₖ (C), [Cu(pza)₂(2-nitrobenzoate)₂(H₂O)₃] (D), and [Cu(pza)₂(CF₃SO₄)₂]·H₂O (E), different anion resulting in different formula and crystal structure (ranged from discrete to polymeric structures), hence each complex has unique properties. Yoshida’s work also suggests the same result of copper(II) pyrazinamide complexes with anion such as ClO₄⁻, BF₄⁻, and PF₆⁻ [9]. Although both sulphate and chloride reported in this paper act as ligand and the complex forms 1D chains, their structures are completely different. Thus, the presence of different anion (in terms of ionic size, ionic charge) leads to different structure. Crystal structures of copper(II)-pyrazinamide complex were indeed affected by the anion of the metal salts used in the reaction. The anion involves in the crystal structures either as terminal or bridging ligand, and/or counter-ion. For comparison, selected crystallographic data of complexes A to E are presented in Table 3, whereas crystal structure of E is shown in Figure 5.

**Table 3.** Selected crystallographic data of complex A and complex B, and other close-related copper(II)-pyrazinamide complexes

| Complexes | A               | B               | C               | D               | E               |
|-----------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Formula   | C₂H₆CuN₃O₃S    | C₁₀H₆Cl₂CuN₃O₂  | C₁₂H₆CuN₃O₃S   | C₂₃H₂₄Cu₅N₄Cl₂ | C₁₂H₇CuF₃N₃O₆S₂ |
| FW (g/mol) | 318.75          | 380.68          | 318.75          | 678.03          | 625.94          |
| Crystal system | Monoclinic   | Triclinic      | Monoclinic      | Monoclinic  | Orthorhombic   |
| Space group | P2₁/c          | P-1            | P2₁/c          | P2₁/c        | Pbcn            |
| α / °    | 11.2758(4)      | 3.6580(7)       | 11.2699(12)     | 7.8974(3)      | 8.9014(7)       |
| b / Å    | 7.3110(3)       | 6.6120(13)      | 7.3799(7)       | 18.5360(8)    | 13.7809(11)     |
| c / Å    | 11.7878(5)      | 13.719(3)       | 11.8669(15)     | 10.9212(5)    | 18.8910(15)     |
| β / °    | 90              | 103.65(3)       | 90              | 90            | 90              |
| γ / °    | 95.0550(13)     | 90.01(3)        | 95.267(9)       | 119.549(3)    | 90              |
| Unit cell vol/Å³ | 967.98(7) | 321.36(12)      | 982.81(19)      | 1390.77(11)   | 2317.3(3)       |
| Temperature/K | 123(2)      | 123(2)         | 298             | 293           | 195             |
| Z        | 4               | 1               | 4               | 2             | 4               |

Note: A = [Cu(µ-pza)(SO₄)(H₂O)₂]ₖ; B = [Cu(pza)₂(µ-Cl)]ₖ; C = [Cu₂(µ-pza)(SO₄)₂(H₂O)₃]ₖ [10]; D = [Cu(pza)₂(2-nitrobenzoate)₂(H₂O)₃] [11]; E = [Cu(pza)₂(CF₃SO₄)₂]·H₂O [16].

**Figure 5.** Crystal structures [Cu(pza)₂(CF₃SO₄)₂]·H₂O (right) [16]
3.2. Infrared analyses

Infrared analyses were conducted to support the crystal structures obtained from XRD analyses. The spectra of both complexes are shown in Figure 6 and it was compared to non-coordinated pza spectra reported by Prananto (2017) [7]. The pza ligand in complex A is coordinated to copper centres in a tridentate chelating fashion, one copper centre is bonded via pyrazine nitrogen atom and the other copper centre is connected via chelation of pyrazine nitrogen atom and carbonyl oxygen atom. Therefore, it is expected that the infrared bands related to this coordination bonding should be shifted significantly than that of non-coordinated pza. Meanwhile, the pza ligand in complex B is only coordinated to copper centre in a monodentate fashion through one of the pyrazine nitrogen atom and the pza carbonyl group remains free. Thus, the C=O stretching band will not be shifted significantly. Moreover, the amide group in both complexes remains free and only involved in hydrogen bonds.

![Figure 6. Infrared spectra of [Cu(µ-pza)(SO₄)(H₂O)],n (top) and [Cu(pza)₂(µ-Cl)],n (bottom).](image-url)
The C=O stretching bands are observed at 1656 cm\(^{-1}\) for complex A and 1699 cm\(^{-1}\) for complex B. The C=O band in complex A is largely downshifted compared to that of non-coordinated pza (1706 cm\(^{-1}\)) due to coordinated to copper centre, whereas the C=O band in complex B only slightly downshifted because the C=O group forms hydrogen bonding with the amide group of adjacent chains.

The asymmetric and symmetric stretching mode of NH\(_2\) (which in non-coordinated pza occurred around 3450 and 3280 cm\(^{-1}\), respectively) was unobservable in complex A due to overlapping with a broad band of hydroxyl stretching mode from water ligands. But in complex B, because it has no water ligand or lattice water in the crystal packing, these bands were easily detected and shows up at 3433 and 3278 cm\(^{-1}\). The slight differences on the frequencies with that of non-coordinated pza are due to the amide in complex B also involved in hydrogen bonding with the carbonyl group of adjacent chains. Furthermore, the scissoring and bending mode of NH\(_2\) (which in non-coordinated pza occurred around 1606-s and 1590-m cm\(^{-1}\), respectively) are observed at 1581 and 1546 cm\(^{-1}\), respectively (complex A), and at 1589 and 1519 cm\(^{-1}\), respectively (complex B).

In addition, the monodentate sulphate ligands in complex A can be detected by infrared analyses and observed as sharp twin bands of v(SO) at 1159 and 1152 cm\(^{-1}\). Meanwhile for vibrational bands of Cu–O, Cu–N, and Cu–Cl were not observed in the infrared spectra because the measurement was only performed at 4000–600 cm\(^{-1}\). The three bands are predicted to occur around 400–200 cm\(^{-1}\) [17].

3.3. Melting point
Melting point of both complexes was measured for additional characterisation. Upon heating in open capillaries, both complexes did not undergo phase change from solid to liquid melt. Instead, the crystals were decomposed at 260°C (complex A) and 290° (complex B). The colour of complex A was changed from blue (RT) to dark blue and finally turn black at 260°C, whereas the colour of complex B was changed from light green (RT) to dark green and finally turn black at 290°C. Detail transformation of both complexes due to controlled heating from octahedral to tetrahedral as commonly observed in copper(II) complexes was unnoticeable.

4. Conclusion
Two polymeric complexes, [Cu(µ-pza)(SO\(_4\))(H\(_2\)O)\(_2\)]\(_n\) (A) and [Cu(pza)\(_2\)(µ-Cl)\(_2\)]\(_n\) (B), obtained from two different copper(II) salts (sulphate and chloride) were structurally analysed. Both A and B forms 1D polymeric structure with different metal-ligand connectivity around the octahedral copper centre. Unlike in A, the crystal structure of B has two unique copper centres. The copper centres are linked by different ligand, namely pyrazinamide in A and chloride in B. Infrared and melting point analyses suggest the structural differences between complex A and B as confirmed by XRD analyses. Different types of anion of the metal salt alters the structure and properties of copper(II)-pyrazinamide complexes.

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