Cadmium(II) and copper(II) complexes containing benzoate derivatives and 2-aminopyrimidine ligands: Synthesis, crystal structures and antibacterial activity

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Abstract. The new Cd(II) and Cu(II) complexes namely [Cd$_2$(2-OHbza)$_4$(apm)$_4$] (1), [Cu$_2$(2-OHbza)$_4$(apm)$_4$]$_2$(2-OHbza) (2) and [Cu$_2$(2-CH$_3$bza)$_4$(apm)$_4$]$_n$ (3) (2-OHbza = 2-hydroxybenzoate, 2-CH$_3$bza = 2-methylbenzoate and apm = 2-aminopyrimidine) were successfully prepared by using direct one pot synthesis method. All complexes were characterized by using CHN elemental analysis, FT-IR spectroscopy, powder X-ray diffraction and single crystal X-ray diffraction techniques. Compound 1 crystallized in monoclinic space group P21/c, while compound 2 and 3 crystallized in triclinic space group P-1. The dinuclear compound 1 consists of two seven-coordinated Cd(II) centers which are doubly bridged by 2-OHbza bridging ligands, while the rest two 2-OHbza and two apm are terminal ligand. The crystal structure of compound 1 is stabilized by the intermolecular hydrogen bonding and C-H•••π interactions and π•••π interactions. Compounds 2 and 3 present zigzag one-dimensional chainlike-structure which dimer Cu(II) units are linked by apm ligand. The crystal structure of these compounds is stabilized by π•••π and C-H•••π interactions. The photoluminescence properties of compound 1 has been studied comparing to those of 2-OHbza and apm ligands. The solid state PL emission spectrum of compound 1 shows similar intensity of free apm ligand and shape to free 2-OHbza ligand which present a single broad band centered at $\lambda_{em}$ 525 nm ($\lambda_{ex}$ 325 nm), but blue-shift. For solution PL experiment of compound 1 in various solvents, the results showed that compound 1 is selective PL quenching acetone. Electronic spectra for solid state and solution in different solvents of compounds 2 and 3 present the d-d absorption bands centered in the range of 701 – 794 nm. The highest red shifts of $\lambda_{max}$ are found for compounds 2 and 3 in DMSO. In addition, the antibacterial activity of all compounds are investigated for S.aureus and E.coil by agar diffusion method. The results show that compound 1 exhibits the activity against S.aureus better than E.coil.

Keywords: Cadmium(II) complex; Copper(II)complexes; 2-hydroxybenzoate; 2-aminopyrimidine;
1. Introduction
Transition metal complexes with Schiff base ligands have been extensively reported and applied in various fields because of the special molecular structure with specific properties such as antimicrobial agents [1,2], catalysts[3], light and optics[4], magnetism and molecular sensors[5]. The coordination chemistry of imidazole and its derivatives has attracted [6], imidazole heterocyclic ligands were used as anti-microbial agents, antioxidant and enzyme inhibitors[7–9]. Cadmium has long been regarded as a toxic metal element, but Cd(II) complexes have a benefit on photochemical and suitable for optoelectronic device applications[10,11]. While, the cadmium (II) ion has full d10 electronic configuration and provide a rich photoluminescence characteristic [12]. The metal benzoate derivatives complexes have been used as model compound in physical chemistry studies. They have been used as chelating ligands for lanthanides and transition metals and bidentate ligands with various metal cations [13]. The metal complexes can be designed and synthesized as a novel complex by working on the chemical identity of each polymorph which can be seen from properties such as colour, magnetic properties, and relative stability. The growth in synthesis of complexes is due to potential applications, molecular architectures, luminescence, bactericides, fungicides, and etc. Many metal complexes belong to this group of pharmacologically active compounds which have been shown to be more effective in treatment of diseases [14]. The wide variations of applications were influenced by chelate system ligands towards a large number of metal ions and many organic transformations. The further study on others applications of the transitional metallic complexes claimed they possess antibacterial activity and alcohol sensor [15,16]. Nevertheless, reports on X-ray crystal structures and theoretical studies of corresponding complexes derived from a benzoate derivatives and 2-aminopyrimidine ligands ligands were relatively scarce. In continuation of current research focus on the synthesis and characterization of new crystals of cadmium(II) and copper(II) heteroligand complexes, containing benzoate derivatives and 2-aminopyrimidine for the antibacterial activity.

2. Materials and methods

2.1 Synthesis of metal benzoate derivatives complexes

Metal benzoate delivertives complexes were prepared by using a modification of the previous published method [17,20].

2.2 Synthesis of [Cd(2-OHbza)₄(apm)₄][1]

Cd(NO₃)₂•4H₂O (1 mmol) was dissolved in water (2 mL) and kept stirring for 2 min to obtain a clear solution. 2-Hydroxybenzoic acid (2 mmol) in ethanol (2 mL) was added into the reaction solution and continued to stir for 5 min. After adjusting the pH to pH 7 by NaOH, 2-aminopyrimidine (1 mmol) was then added into the reaction solution and kept stirring for 5 min. After slow evaporation of reaction solution for 4 days, block light colourless crystals of complex were formed and collected by filtration, then washed with water and dried.

2.3 Synthesis of [{Cu₂(2-OHbza)₄(apm)}•2(2-OHbza)] n

CuSO₄•5H₂O (1 mmol) was dissolved in water (2 mL) and kept stirring for 2 min to obtain a clear solution. 2-Hydroxybenzoic acid (2 mmol) in ethanol (2 mL) was added into the reaction solution and continued to stir for 5 min. After adjusting the pH to pH 7 by NaOH, 2-aminopyrimidine (1 mmol) was then added into the reaction solution and kept stirring for 5 min. After slow evaporation of reaction solution for 3 days, block green crystals of complex were formed and collected by filtration, then washed with water and dried.
2.4 Synthesis of $[\text{Cu}_2(2-\text{CH}_3\text{bza})_4(\text{apm})]_n$

Cu(NO$_3$)$_2$.3H$_2$O (1 mmol) was dissolved in DMF (4 mL) and kept stirring for 2 min to obtain a clear solution. 2-methylbenzoic acid (2 mmol) in methanol (4 mL) was added into the reaction solution and continued to stir for 5 min. 2-aminopyrimidine (1 mmol) in methanol (4 mL) was then added into the reaction solution and kept stirring for 5 min. After slow evaporation of reaction solution for 3 days, block light green crystals of complex were formed and collected by filtration, then washed with water and dried.

2.5 Characterization

2.5.1 X-ray crystallography

Suitable crystals of 1–3 were mounted on MiTeGen micromounts using paratone oil (Hampton Research). X-ray diffraction data were collected using a Bruker D8 QUEST CMOS PHOTON II and operating at T = 296(2) K. Data were measured using $\omega$ and $\phi$ scans and using Mo–Kα radiation ($\lambda = 0.71073 \text{ Å}$). The total number of runs and images was based on the strategy calculation from the program APEX3 and unit cell indexing was refined using SAINT.$^{[21]}$ Data reduction was performed using SAINT and SADABS were used for absorption correction. The integrity of the symmetry was checked by using PLATON.$^{[22]}$ The structure was solved with the ShelXT structure solution program using combined Patterson and dual–space recycling methods.$^{[23]}$ The structure was refined by least squares using ShelXL.$^{[24]}$ In the final refinement cycles, all non−hydrogen atoms were refined anisotropically. All C–bound H atoms were placed in calculated positions and refined using a riding−model approximation with C–H = 0.93 Å and $U_{\text{iso}}$(H) = 1.2$U_{\text{eq}}$(C). While, all N− and O−bound H atoms were located in a difference−Fourier map and refined with N–H = 0.88 ± 0.01 Å and O–H = 0.84 ± 0.01 Å, respectively.

2.5.2 Powder X-ray diffraction

Measure were done on a Bruker D8 Quest XRD diffractometer with using monochromatic using monochromatic Cu Kα radiation in the of 5–60° 2$\theta$ range, with a 0.020 step scan with 0.1 s per step. Inclusion compounds were studied at room temperature in an atmosphere of the corresponding guest, to prevent dissociation. Cold samples of the inclusion compound with methane were placed on a thermostated copper holder at liquid nitrogen temperature and were studied over a range of increasing temperatures.

2.5.3 Thermogravimetric analyses

Thermogravimetric analyses were carried out. Preparation sample sizes were 20 mg. The experiment were performed on samples consisting of numerous single crystals under a N$_2$ atmosphere 25.0 mL/min with a heating rate of 10 °C min$^{-1}$.

2.5.4 Electronic absorption

For the preparation of $[\{\text{Cu}_2(2-\text{OHbza})_4(\text{apm})\}]_n(1 \text{ mM solution})$, 0.0104 g and $[\text{Cu}_2(2-\text{CH}_3\text{bza})_4(\text{apm})]_n(1 \text{ mM solution})$, 0.0076 g of compounds were dissolved and made up to 10 mL by methanol (CH$_3$OH), ethanol (C$_2$H$_5$OH), acetone (C$_3$H$_6$O), chloroform (CHCl$_3$), dimethylformamide (DMF), and dimethyl sulfoxide (DMSO) in volumetric flask, depending on the solubility of each complexes. For the solid state of UV−Visible spectroscopy were collected, ranged from 200 to 1100 nm.

2.5.5 Biological activity

*Staphylococcus aureus* (ATCC 25923) and *Escherichia coli* (ATCC 25922) were used to test the antibacterial activity of all complexes. The antibacterial assay was evaluated by Agar-disk diffusion method. The test compounds were dissolved in dimethyl sulfoxide (DMSO) to
obtain a final concentration of 1 mg mL$^{-1}$ (1000 ppm). Sterilized Whatman no.1 filter paper (6 mm) was impregnated with 30 µL of each compound to get a concentration of 1000 ppm per disc. The DMSO was taken as a control solvent while the penicillin (1 mg mL$^{-1}$) was selected for positive control, both of then were separately load 30 µL in sterilized paper disc. The bacterial test pathogens were spread on fresh Agar plates and the filter paper disc impregnated with the test compound were place on the surface of plates seeded with test bacteria. The compounds were incubated at 37 ± 2°C for 24 hours. The inhibition zones around each disc were measured in millimeter (mm) units.

3. Results and Discussion

3.1 Synthesis and characterization of cadmium (II) and copper (II) benzoate derivatives complexes

The preparation of [Cd$_2$(2-OHbza)$_4$(apm)$_4$] (1), [{Cu$_2$(2-OHbza)$_4$(apm)}]$_2$(2-OHbza)$_n$ (2) and [Cu$_2$(2-CH$_3$)bza]$_2$(apm)$_n$ (3) complexes were successfully proceeded by using the modification of the published method [13, 14, 20, 23]. The reaction was stirring 2-OHbza ligand with metal(II) ion in ethanol, adjust the pH to neutral. The mixture was then added 2-aminopyrimidine and kept stirring for further 5 min. After slow evaporation of reaction solution for 4 days, block light clear crystals of complex 1 and block green crystals of complex 2 were formed and collected by filtration, then washed with water and dried. Complex 3 was prepared by dissolving metal (II) in DMF, obtained a clear solution. The 2-methylbenzoic acid in methanol was added into the reaction. The 2-aminopyrimidine in methanol was then added into the reaction solution. After slow evaporation of reaction solution for 3 days obtained block light green crystals of complex 3. All the synthesized complexes are stable in ambient condition. (Tables 1)

Table 1 Characteristic data for metal(II) complexes

| Compound | Empirical Formula | Color | Yield (%) | Elemental analysis (*) % | Formula weight |
|----------|------------------|-------|-----------|--------------------------|---------------|
| [Cd$_2$(2-OHbza)$_4$(apm)$_4$] (1) | C$_{44}$H$_{40}$Cd$_2$N$_{12}$O$_{12}$ | Yellow | 72.65 | 46.22 (45.81) | 3.42 (3.49) | 14.58 (14.57) | 1153.68 |
| [{Cu$_2$(2-OHbza)$_4$(apm)}]$_2$(2-OHbza)$_n$ (2) | C$_{46}$H$_{37}$Cu$_2$N$_3$O$_{18}$ | Green | 85.75 | 52.75 (52.76) | 3.78 (3.56) | 4.06 (4.01) | 1046.89 |
| [Cu$_2$(2-CH$_3$)bza]$_2$(apm)$_n$ (3) | C$_{36}$H$_{33}$Cu$_2$N$_3$O$_8$ | Green | 88.25 | 56.90 (56.69) | 4.20 (4.36) | 5.52 (5.51) | 762.76 |

*Theoretical Values are given in parentheses (n=1)

The important vibrational frequencies that were observed, including OH stretching, NH stretching, C-H stretching, C=O stretching, C=C stretching, C-O stretching, M-O stretching and M-N stretching modes. The infrared spectrum of compound 1 and 2 were shown as a representative. (Figure1)

![Figure 1. The IR spectrum of complexe 1 and 2.](image)
The solid state UV of complex 2 gave the lower absorption wavelength than complex 3, due to the hydroxyl-group substituent. (Figure 2a, b) The blue shift found when the complexes was dissolved in DMSO, suggesting the coordination between each complex with DMSO solvent. The complex 1 is a d^{10}-complex with a distorted octahedral geometry, thus no absorption found in UV-Vis spectroscopy.

![Figure 2](image1.png)

**Figure 2.** Solid state UV-Vis spectrum of complex 2 (a), 3 (b) and Emission spectra of 1 (c) in solid state at room temperature ($\lambda_{ex} = 325$ nm).

The emission spectra of $[\text{Cd}_2(2\text{-OHbza})(\text{apm})_4] \text{1}$ (Figure 2c) was examined. The solid state PL emission spectrum of compound 1 showed similar intensity of free apm ligand and 2-OHbza ligand which present a single broad band centered at $\lambda_{em}$ 525 nm ($\lambda_{ex} = 325$ nm) with a small blue-shift due to the d^{10} configuration of cadmium(II).

![Figure 3](image2.png)

**Figure 3.** Asymmetric unit of [Cd$_2$(2-OHbza)$_4$(apm)$_4$] 1(a), [Cu$_2$(2-OHbza)$_4$(apm)$_4$]·2(2-OHbza) 2(b) and [Cu$_2$(2-CH$_3$bza)$_4$(apm)$_4$] 3(c).

The complex 1 is crystallized in the monoclinic space group $P2_1/c$. The environment of cadmium center is a distorted capped octahedron. The dinuclear compound 1 consists of two seven-coordinated Cd(II) centers which are doubly bridged by 2-OHbza bridging ligands, while the rest two 2-OHbza and two apm are terminal ligand (Figure 4a). The crystal structure of compound 1 is stabilized by the intermolecular hydrogen bonding from apm ligand between asymmetric unit and C-H···π interaction from apm and 2-OHbza ligands between asymmetric unit and π···π interactions from 2-OHbza ligand between asymmetric unit. The complex 2 is crystallized in the triclinic space group $P1$. The environment of copper centre is a distorted square pyramidal with four oxygen atoms from 2-hydroxybenzoic acid ligands and one nitrogen atom from 2-aminopyrimidine ligands as shown in Figure 4b. Their inversion centers are located between the copper ions of dinuclear paddle-wheel. The Cu(II) atoms are linked to gather by 2-aminopyrimidine bridge resulting one dimensional zigzag chain structure. The molecular structure of this complex is stabilized by intramolecular π···π interaction from 2-OHbza ligand between chains, leading to three dimensional network. The complex 3 is crystallized in
the triclinic space group P-1. The environment of copper centre is a distorted square pyramidal with four oxygen atoms from 2-methylbenzoic acid ligands and one nitrogen atom from 2-aminopyrimidine ligands as shown in Figure 4c. Their inversion centers are located between the copper ions of dinuclear paddle-wheel. The Cu(II) atoms are linked to gather by 2-aminopyrimidine bridge resulting one dimensional zigzag chain structure. The molecular structure of this complex is stabilized by intramolecular C–H⋯π interactions from 2-CH₃bza ligand between chain lead to 2D supramolecular interaction in compound. The powder X-ray diffraction, an analytical technique used for phase identification of a crystalline material and can provide information on unit cell dimensions.

3.2 Biological activity

The complexes 1 2 and 3 were dissolved in DMSO with a concentration 1000 ppm, before added onto E. coli and S. aureus plate. The plate was incubated at 37 °C for 24 hr. The clear zone was analyzed with the subtraction of standard DMSO solvent. Moreover the reported data was compared with standard penicillin drug. The results revealed that 2-OHbza ligand exhibits the activity against E. coli and S. aureus better than 2-CH₃bza and apm ligands. Higher activity exhibited by complex 1 compared with complex 3. The complex 2 exhibits better activity against E. coli and S. aureus than complex 3. For the study on mentioned complex may lead to a new antibiotic drug in the future.

Table 2 Inhibition zone of antibacterial activity of complexes

| Compound | Diameter (mm) of Inhibition zone* |
|----------|----------------------------------|
|          | E. coli                          | S. aureus                        |
| [Cd₂(2-OHbza)₄(apm)₆] (1) | 6.50±0.408                       | 7.38±0.479                       |
| ([Cu₂(2-OHbza)(apm)·2(2-OHbza)]₀) (2) | 2.75±0.500                       | 5.50±0.408                       |
| [Cu₂(2-CH₃bza)(apm)₆] (3) | 3.38±0.479                       | 6.13±0.250                       |
| 2-OHbza ligand | 4.50±0.408                       | 5.25±0.289                       |
| 2-CH₃bza ligand | 3.25±0.289                       | 3.25±0.289                       |
| apm ligand       | 3.13±0.250                       | 3.25±0.289                       |
| DMSO             | 0                                | 0                                |
| Penicillin       | 0                                | 26.50±0.408                      |

*Inhibition diameter in mm, Concentration: 1000 ppm  *Data are already subtract DMSO Inhibition zone (solvent control)

4. Conclusion

The preparation of metal benzoate derivatives complexes containing 2-hydroxybenzoic acid (1 and 2), 2-hydroxybenzoic acid (3) and 2-aminopyrimidine ligands, were successfully. The complexes were characterized by CHN elemental analysis, FT-IR spectroscopy, powder x-ray diffraction and single crystal x-ray diffraction. The obtained products give a good yield. The complex 1, 2 and 3 yield 72.65 %, 85.75 % and 88.25%, respectively. Compound 1 crystallized in monoclinic space group P₂₁/c, while compound 2 and 3 were crystallized in triclinic space group P-1. The dinuclear compound 1 consists of two seven-coordinated Cd(II) centers which are doubly bridged by 2-OHbza bridging ligands, while the rest two 2-OHbza and two apm are terminal ligand. Compounds 2 and 3 present zigzag one-dimensional chainlike-structure which dimer Cu(II) units are linked by apm ligand. The photoluminescence properties of compound 1 has been studied comparing to those of 2-OHbza and apm ligands. The solid state PL emission spectrum of compound 1 is similar intensity of free apm ligand and shape to free 2-OHbza ligand which present a single broad band centre at λem 525 nm (λex = 325 nm), but blue-shift. For solution PL experiment of compound 1 in various solvents, the results showed that compound 1 is selective PL quenching acetone. For electronic spectra for solid state and solution in different solvents of compounds 2 and 3 present the d-d absorption bands centered in the range of 701 – 794 nm. The highest red shifts of λmax are found for compounds 2 and 3 in DMSO. In addition, the antibacterial activity of all compounds are investigated for S.aureus and E.coli by agar diffusion method. The results show that compound 1 exhibits the activity against S.aureus better than E.coli.
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