Title: Sonochemical Synthesis, Crystal Structure, and Antimicrobial Property of One-dimensional Dinuclear Coordination Polymer

Authors: Sajjad Soltani, Kamran Akhbari,* Jonathan White,

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record.

To be cited as: 10.1002/zaac.202000268

Link to VoR: https://doi.org/10.1002/zaac.202000268
Sonochemical synthesis, Crystal Structure and Antimicrobial Property of One-dimensional Binuclear Coordination Polymer


[a] School of Chemistry, College of Science, University of Tehran, Tehran, Iran.
Tel.: +98 21 61113734; fax: +98 21 66495291.
E-mail address: akhbari.k@khayam.ut.ac.ir (K. Akhbari)

[b] School of Chemistry and Bio21 Institute, The University of Melbourne, VIC 3010, Australia

Abstract
Binuclear 1-D coordination polymer of [NaCu$_2$(pdc)$_2$(H$_2$O)$_4$(OH)$_n$]$_n$ (1) (H$_2$pdc = Pyridine-2,6-dicarboxylic acid) was synthesized by the solvothermal method, and its structure was investigated by single-crystal X-ray diffraction analysis. 1 has zigzag chains, which are converted to a 3-D network through hydrogen bond interactions. Also, 1 was synthesized by sonochemical method (1-Sono). The structures of 1 and 1-Sono were characterized by FT-IR, XRD, FE-SEM and thermogravimetric (TG) techniques. Antibacterial activity was evaluated by agar well diffusion method. Release of copper ions, chelation, and stability were the factors influencing antibacterial property. More effect of compounds against S. aureus strain was observed, and 1-Sono exhibited better antibacterial activity than 1.

Keywords: Coordination polymer; Heterometallic; Antibacterial; Sonochemical.

1. Introduction
Infectious agents are the cause of many chronic diseases and deaths in the world.[1] Over the past century, various drugs have been discovered and used to deal with pathogens, but the high use of them has led to drug resistance in pathogens.[2] This problem has reduced the effectiveness of drugs and imposed huge costs on the health system of
In addition to drugs, various materials have been used as antibacterial agents, including metal oxides, \cite{5} metal complexes, \cite{6-9} and organic-inorganic hybrid materials. \cite{10-11} Coordination polymers (CPs) are a kind of organic-inorganic hybrid materials, and there is considerable interest in the design and synthesis of them in the fields of supramolecular chemistry and crystal engineering. \cite{12-14} CPs are made from molecular self-assembly of bridging ligands and metal ions by non-covalent interactions, which among them, binuclear heterometallic structures have particular importance. \cite{15-17} These compounds have the potential of use in various applications due to their diversity in structure and properties. \cite{18-21} Advantages such as high efficiency, optimal chemical/thermal stability, and long-term release of antibacterial components make it possible to use these compounds as antibacterial materials. \cite{22-25} The properties of metal ions and ligands play an essential role in the design of coordination structures. Metal ions and ligands can have antibacterial properties. \cite{26-28} Copper is one of the most well-known metals with antibacterial property, and there are various reports on its use. \cite{29-31} Pyridine-2,6-dicarboxylic acid, commonly known as dipicolinic acid, has been considered very much due to the various coordination modes and the high tendency for hydrogen bonding. There are many reports of this ligand with a variety of metal ions in various applications. \cite{32-33} In this work, a binuclear metal-organic polymer of [NaCu$_2$(pdc)$_2$(H$_2$O)$_4$(OH)$_n$] (1) was synthesized by solvothermal and sonochemical methods and their antibacterial activities were evaluated by agar well diffusion method.

2. Experimental

2.1. Materials and Physical Techniques

Cu(NO$_3$)$_2$.3H$_2$O, NaOH and N,N-dimethylformamide (DMF) were purchased from Merck Company. Pyridine-2,6-dicarboxylic acid was bought from Sigma Aldrich Company. Powder X-ray diffraction (PXRD) patterns were recorded with Philips X’Pert Pro diffractometer (Cu Ka radiation, $\lambda=1.54184$ Å) in the 20 range 5–50°. IR spectra were achieved by Equinox 55 FT-IR spectrometer (Bruker, Bremen, Germany), in the range of 400-4000 cm$^{-1}$ with 16 scan’s numbers. The morphology was studied by scanning electron microscopy (FE-SEM) (MIRA3 TESCAN). TGA was performed using the PL-STA 1500 apparatus, in the range of 50–800 °C under argon atmosphere at
a heating rate of 10 °C/min. PARSONIC 15S ultrasonic generator was used with a frequency of 28 kHz.

2.2. Synthesis of \([\text{NaCu}_2(\text{pdc})_2(\text{H}_2\text{O})_4(\text{OH})]_n\) (1) by solvothermal method
A solution from \(\text{Cu(NO}_3)_2\cdot 3\text{H}_2\text{O}\) (1 mmol, 0.2416 g), pyridine-2,6-dicarboxylic acid (1 mmol, 0.1664 g) and \(\text{NaOH}\) (1 mmol, 0.08 g) was prepared in a mixture of 5 mL distilled water and 15 mL DMF. After stirring for 1 h, the solution was sealed in a glass vial and heated at 50 °C for 24 h in the oven. Blue needle crystals were obtained and washed with DMF and distilled water several times. Yield: 80% based on copper.

2.3. Synthesis of \([\text{NaCu}_2(\text{pdc})_2(\text{H}_2\text{O})_4(\text{OH})]_n\) by sonochemical method (1-Sono)
\(\text{Cu(NO}_3)_2\cdot 3\text{H}_2\text{O}\) (1 mmol, 0.2416 g), pyridine-2,6-dicarboxylic acid (1 mmol, 0.1664 g) and \(\text{NaOH}\) (1 mmol, 0.08 g) were dissolved in a mixture of 5 mL distilled water and 15 mL DMF and subjected to ultrasonic bath for 1 h. The product was washed with DMF and distilled water several times and was collected by centrifugation at 7000 rpm and finally was dried.

2.4. Crystal structure determination
Single-crystal X-ray diffraction analysis of 1 was carried on four-circle diffractometer (XtaLAB Synergy, Dualflex, HyPix) using diffraction source of micro-focus sealed X-ray tube (PhotonJet (Cu) X-ray Source with Cu-K\(\alpha\) radiation (\(\lambda = 1.54184\) Å)), CCD plate detector (HyPix) and diffraction measurement method of 2theta/omega-scan. The molecular plots were drawn with the Mercury programs. The temperature during all data collections was maintained at 100.0 K. Multi-scan absorption corrections were applied. The structure was solved by direct method and refined on \(F^2\) by full-matrix least-squares. All the calculations were carried out with the SHELXL-2016/6 program packages. Non-hydrogen atoms were refined anisotropically.

2.5. Antibacterial test
\(Staphylococcus\ aureus\) (S. aureus) (ATCC 25923) and \(Escherichia\ coli\) (E. coli) (ATCC 25922) were chosen as Gram-positive and Gram-negative bacteria, respectively, and the effects of compounds against them were evaluated by agar well diffusion method. First,
bacteria were cultured 24 h at 37 °C. Then the plate containing sterile Mueller Hinton Agar was prepared. Inoculums of bacteria with a concentration of 0.5 McFarland were separately cultured on the plate, and then wells were created. Compounds of 1, 1-Sono and Pyridine-2,6-dicarboxylic acid were dispersed in 5% DMSO solvent to prepare a 10000 μg/mL solution. Finally, 50 μL from each sample was inoculated into wells and plates were incubated at 37 °C for 24 h.

3. Results and Discussion

3.1. Structural description

The reaction between pyridine-2,6-dicarboxylic acid, copper(II) nitrate trihydrate and sodium hydroxide resulted in the formation of the single-crystals of [NaCu_2(pdc)_2(H_2O)_4(OH)]_n (1) with the monoclinic crystal system and I2/a space group (Scheme 1). Experimental details of X-ray data collection for 1 are summarized in Table 1, and selected bond lengths and angles are listed in Tables S1 and S2 in the ESI, respectively. The Primary building unit comprises self-assembly of two Cu atoms, one Na atom, two pdc^2- ligands, four water molecules and one hydroxyl group (Fig. 1a). As shown in Fig. 1b, each Cu atom has a distorted square-pyramidal coordination environment, and is coordinated with the oxygen atom of one water molecule (O6) with Cu–O distance of 2.315 Å, oxygen of hydroxyl group (O5) with Cu–O distance of 1.874 Å and carboxylate oxygen atoms and the nitrogen atom of tridentate pdc^2- ligands with the average Cu–O bond lengths of 2.047 Å and Cu–N bond length of 1.903 Å, which are smaller than previous reports.^{34-35} Also, each Na atom sets a distorted octahedral coordination environment and is coordinated with oxygen atoms of four water molecules (two O6 and two O7) with the average Na–O bond lengths of 2.347 Å and two oxygen atoms (O3) of pdc^2- ligands from two adjacent units with the Na–O bond lengths of 2.601 Å. Two oxygen atoms are connected simultaneously to two metal atoms (O3 and O6) give rise to a force that brings the copper and sodium atoms to close together and creates a weak interaction between them. In the primary building unit, two asymmetric units are linked to each other through the oxygen atom of the hydroxyl group (O5) with an angle of 130.22(11)°. Fig. S1 shows that the primary building units are linked together by eight intermolecular hydrogen bonds that arose from the coordinated water molecules, carboxylate oxygen atoms, pyridine rings and hydroxyl
groups (Table S3 in the ESI). Also, the connection of adjacent unit made the zigzag metal-organic chains extending along the crystallographic a-axis (Fig. 2a) with the Cu(1)-Na(1)-Cu(1) angle of 180° and repeating intermolecular hydrogen bonds between the one-dimensional coordination chains constructed three-dimensional network in other axes (Fig. 2b).

3.2. FT-IR spectroscopy
Vibrational modes of the samples were investigated by FT-IR spectroscopy (Fig. 3). In the case of compound 1 strong band centered at 3398 cm\(^{-1}\) corresponds to asymmetric and symmetric O-H stretching vibrations modes of water molecules.\[^{36}\] The strong bands at 1625 and 1670 cm\(^{-1}\) are attributed to asymmetric (COO\(^{-}\)) stretching and the strong band at 1344 cm\(^{-1}\) is attributed to symmetric stretching of carboxylate groups.\[^{37-38}\] The absence of a strong absorption band for the stretching vibrations of the C=O bonds in the 1700-1730 cm\(^{-1}\) region represents the complete deprotonation of carboxylic acid groups of pdc\(^{2-}\) ligand. The band at 684 cm\(^{-1}\) is indicated Cu-O bond.\[^{39}\] Also, 1-Sono sample has the same spectrum with the single crystal of 1, which indicates that they are identical in structure.

3.3. Powder X-ray diffraction study
The powder X-ray diffraction (PXRD) analysis was performed to study the structure of the samples (Fig. 4). The absence of additional peaks in the diffraction pattern of 1 and 1-Sono compared to the simulated pattern indicate their phase purity. The observed reflections, especially characteristic reflections on 2θ of 8.4, 10.75, 13.9, 18.06 and 30.94 degrees in the pattern of 1-Sono are in a good match with a simulate pattern of compound 1, which indicate the successful synthesis of 1-Sono using the sonochemical method. The strong intensity of the peaks in 1-Sono indicates its good crystallinity. The average grain size of 1 and 1-Sono were calculated using Scherrer's equation,\[^{40}\] and the values of 55.5 nm and 36.5 nm were obtained, respectively. The broadening of diffraction patterns in 1-Sono compared to 1 is also due to this grain size reduction.\[^{41-42}\] There is a small shift to higher 2θ in the peak position of 1-Sono compared to 1 that is due to the formation of smaller structures using the sonochemical method rather than the solvothermal method.\[^{43}\]
3.4. SEM images

The morphology of 1-Sono was investigated by field emission scanning electron microscopy (FE-SEM). The bulk form sample does not have a definite shape and is composed of particles with several micrometers in size. (Fig. 5a). However, with a look at images with higher magnification (Fig. 5b), it becomes clear that microstructures of 1-Sono are composed of particles with nanometer-size.

3.5. Thermogravimetric analysis

Thermal stability and decrease in the components' values in the 1 and 1-Sono by heating were evaluated with thermogravimetric analysis (TGA). There are two parts in the TGA curve of 1 (Fig. 6a). The first part, from 128 °C up to 210 °C is attributed to the loss of coordinated water molecules with a mass loss of about 12.5% (calculated 12.6%). The dehydrate compound is stable up to 260 °C. The second part from 260 °C is related to removing pdc$_2^-$ ligand from compound 1 that finally leads to the formation of copper and sodium oxides. A similar trend is observed for 1-Sono (Fig. 6b). The first part, from 110 °C up to 180 °C is attributed to the loss of coordinated water molecules with a mass loss of about 14%. The dehydrate compound is stable up to 257 °C and removes of pdc$_2^-$ ligands are beginning from this temperature and finally lead to the formation of copper and sodium oxides.

3.6. Antibacterial activity

Bacteria's susceptibility of compounds was evaluated by agar well diffusion method similar to our previous report.[44] The zone of inhibition as a clear zone shows a section in which bacteria have been inhibited from growth. According to Fig. 7 for S. aureus strain, 1 (a) and 1-Sono (b) have inhibitory effects of 11 mm and 13 mm, respectively, while H$_2$pd (c) does not show an inhibitory effect. On the E.coli strain plate, the inhibition zones are 10 mm and 11 mm, respectively, for 1-Sono and H$_2$pd, and 1 has no inhibition effect. In the case of S. aureus strain, comparison of the results of 1, 1-Sono and ligand with copper salt (Cu(NO$_3$)$_2$.3H$_2$O), with an inhibition diameter of 26 mm (Fig. S2), show that the dominant mechanism in antibacterial activity is dependent on copper ion, which is known to have antibacterial activity.[29] The lower activity of
the CPs is due to their lower solubility than metal salt. The presence of a coordination structure in the CPs causes the metal ions to be released at a slower rate than the metal salt, which leads to long-term activity in them with controlled antibacterial activity.\cite{45-47} This release depends on the chemical stability of the structure in the operating medium. Therefore, the difference in the stability of structures in the bacterial medium can cause the release of metal ions with variable values and velocities. In the metal salt, metal ions can easily move and come in contact with bacteria and prevent bacteria’s growth, but after participating in the structure, the number of contact decreases. According to another view, the lack of antibacterial activity in the ligand and its occurrence after the complex formation can be due to the increased lipophilic properties caused by the ligand and metal ions chelation. Due to the bacterial cell wall's lipid nature, materials with more lipophilic properties can more easily penetrate in their walls.\cite{48-50} In the case of E. coli bacteria, the suitable activity of metal salt with an inhibition diameter of 20 mm is observed (Fig. S2). The reduction of antibacterial activity in CPs compared to metal ions and ligands indicates higher E. coli resistance than S. aureus. Also, similar to previous reports, the activities of compounds against S. aureus strain were more than E.coli strain.\cite{51-53} These results are due to the different cell wall structures in the two bacteria, which leads to varying behaviors against antibacterial agents.\cite{54-55} About E.coli strain, the thinner layer of the peptidoglycan in the cell wall and the presence of an outer lipopolysaccharide layer on the cell wall could be the reason for its different behavior. This type of cell wall structure can affect its lipophilic properties.\cite{47} It can be concluded that after gradual degradation, the components of the CPs, unlike S. aureus, cannot penetrate the cell wall of E. coli and interfere with its physiological activity. Particle size can also be effective in antibacterial properties.\cite{56-57} As seen in the FE-SEM images, 1-Sono is made of smaller particles than 1 and its better antibacterial activity is derived from this factor. However, many other factors have been identified that could affect antibacterial activity\cite{58-61}, and each of them can contribute to our results.

4. Conclusion

In this work, binuclear 1-D coordination polymer of [NaCu$_2$(pdc)$_2$(H$_2$O)$_4$(OH)] (1) was synthesized by solvothermal and sonochemical methods. The crystal structure was
investigated by single-crystal X-ray diffraction analysis and the results show that the primary building unit of 1 is made of two tridentate pyridine-2,6-dicarboxylic acids, four water molecules, two Cu atoms, one Na atom and one hydroxyl group. Zigzag one-dimensional coordination polymer of 1 converted to a three-dimensional network through hydrogen bond intermolecular interaction. Antibacterial activities of 1 and 1-Sono were evaluated against Gram-negative and Gram-positive bacteria using agar well diffusion method. Due to the difference in the cell wall structure, two bacteria exhibited different behaviors against the compounds. S. aureus showed more susceptibility than E. coli, and the predominant mechanism of antibacterial activity was dependent on the presence of copper ions in the structure of the CPs. Chelation and stability in the antibacterial environment can also be other factors influencing the antibacterial results. The higher activity of 1-S originated from its smaller particle size than 1.

**Supplementary material**

Complete bond lengths and angles, co-ordinates and displacement parameters have been deposited at Cambridge Crystallography Data Center. Supplementary data are available from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK on request, quoting the deposition number 1947036 for compound 1. Tables S1-S3 and Figures S1-S2 are presented in the Supporting information.

**Acknowledgements** The authors would like to acknowledge the financial support of the University of Tehran for this investigation under grant number 01/1/389845.

**References**


Table 1. Crystal data and structure refinement for [NaCu$_2$(pdc)$_2$(H$_2$O)$_4$(OH)]$_n$ (1).

<table>
<thead>
<tr>
<th>Compound</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C$<em>{14}$H$</em>{15}$Cu$_2$N$<em>2$NaO$</em>{13}$</td>
</tr>
<tr>
<td>Formula weight</td>
<td>569.35</td>
</tr>
<tr>
<td>Temperature</td>
<td>100.00(10) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>1.54184 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>I 2/a</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>$a = 16.4885(2)$ Å $b = 5.04280(10)$ Å $c = 21.6434(3)$ Å $\alpha = 90.00^\circ$ $\beta = 91.9980(10)^\circ$ $\gamma = 90.00^\circ$</td>
</tr>
<tr>
<td>Volume</td>
<td>1798.52(5) Å$^3$</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>2.103g.cm$^{-3}$</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>3.925 mm$^{-1}$</td>
</tr>
<tr>
<td>$F$(000)</td>
<td>1144</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>4.088 to 77.226°</td>
</tr>
<tr>
<td>Index ranges</td>
<td>$-19 \leq h \leq 20$ $-6 \leq k \leq 5$ $-27 \leq l \leq 24$</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>9788</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>1888[R(int) = 0.0300]</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>1888 / 3 / 165</td>
</tr>
<tr>
<td>Goodness-of-fit on $F^2$</td>
<td>1.102</td>
</tr>
<tr>
<td>Final $R$ indices [$I&gt;2\sigma(I)$]</td>
<td>$R_1= 0.0269$ $wR_2= 0.0743$</td>
</tr>
<tr>
<td>$R$ Indices (all data)</td>
<td>$R_1= 0.0273$ $wR_2= 0.747$</td>
</tr>
</tbody>
</table>
\[
\text{Cu(NO}_3\text{)}_2 \cdot 3\text{H}_2\text{O} + \text{NaOH} \xrightarrow{\text{H}_2\text{O/DMF}} [\text{NaCu}_2(\text{pdc})_2(\text{H}_2\text{O})_4(\text{OH})]_n \text{ (1)}
\]
Fig. 1. a) Primary building unit and, b) The coordinate geometry around copper and sodium atoms in 1 (H atoms were omitted).
Fig. 2. a) 1-D Coordination chains of 1 along the crystallographic $a$ axis (view from $b$ axis), b) the 3-D networks of 1 view from $a$ axis (left) and $c$ axis (right) (Cu=brown, Na=purple, N=blue, O=red, C=gray. H atoms were omitted for clarity).
Fig. 3. FT-IR spectra of 1 and 1-Sono.
Fig. 4. PXRD patterns of 1 and 1-Sono.
Fig. 5. FE-SEM images of 1-Sono. a) micro-scale, b) nano-scale.
**Fig. 6.** Thermogravimetric analysis of a) 1, b) 1-Sono.
Fig. 7. Zones of inhibition with agar well diffusion method for a) 1, b) 1-Sono and c) ligand.
Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:
Soltani, S; Akhbari, K; White, J

Title:
Sonochemical Synthesis, Crystal Structure and Antimicrobial Property of One-dimensional Dinuclear Coordination Polymer

Date:
2020-11-09

Citation:

Persistent Link:
http://hdl.handle.net/11343/276593