

**FIRST OROTIC ACID AND ISONICOTINIC
ACID BASED Zn COMPLEX:
HYDROTHERMAL SYNTHESIS, CRYSTAL STRUCTURE,
AND THERMOGRAVIMETRIC ANALYSIS**

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New supramolecular synthon induced complex [Zn(Hor)(Hiso)·3H₂O]·H₂O (**1**) is obtained in a self-assembly reaction of zinc nitrate with orotic (H₃Or, 1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinecarboxylic acid) and isonicotinamide. The isonicotinamide molecule is hydrolyzed *in-situ* into isonicotinic (Hiso, pyridine-4-carboxylic) acid. A detailed structural analysis and the role of hydrogen bonding synthons in deciding the overall structural diversity is discussed. The {...H-N-C=O...}₂ and {...H-O-C=O...}₂ dimers play an important role in the metal-organic architecture of **1**. Complex **1** is insoluble in almost all organic solvents as well as in water. The complete decomposition of the compound is achieved above 445°C.

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INTRODUCTION

Crystal engineering is concerned with the rational and planned synthesis of an organic or metal-organic solid-state supramolecular structure from its molecular building blocks involving supramolecular synthons as potential connectors. Furthermore, synthons are kinetically defined structural units that convey the essential features of a crystal structure, and a critical assumption is that the synthon is a reasonable approximation to the whole crystal. The closer the structure of a small synthon is to the actual crystal, the more useful the entire concept. In such cases, the process of building up a crystal from molecules takes its place in a well-organized and regular way, and crystal engineering becomes viable [1-3].

In comparison with organic systems [1b, 2a], the intricacies of the crystal packing of coordination compounds are still not well understood due to the inherent complexities in predicting the final supramolecular architecture [4]. In the context of metal-organic complexes, if a ligand is likely to form a particular set of synthons (after complexation), then these structural patterns will recur that result in the metal-organic systems [5-7].

The final supramolecular structure is affected by different factors, such as metal and ligand geometries and denticities, counterions, and reaction conditions [7]. Orotic acid (H₃Or, vitamin B13) and its metal complexes continue to attract attention because of its multidentate functionality and great significance in living organisms as a precursor of

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pyrimidine nucleosides [8]. Nickel, magnesium, palladium, and platinum orotate complexes have been screened as therapeutic agents for cancer treatment [9]. In basic solutions (pH 9), both carboxylic group and heterocyclic N atom are deprotonated, enabling the orotate anion to act as a bidentate ligand. The existing studies of metal orotates demonstrate that it occurs as a dianion with in-built hydrogen bonding groups, often coordinating via the N atom and the carboxylic acid group, thus forming a five-membered chelate ring [10].

As a part of our ongoing research on supramolecular synthon induced metal-organic architectures [5, 6], we report here the crystal structures of a mixed ligand Zn complex $[\text{Zn}(\text{Hor})(\text{Hiso})\cdot 3\text{H}_2\text{O}]\cdot \text{H}_2\text{O}$ (**1**). In this complex, the in-built hydrogen bonding group in the second coordination sphere participates in elevation of a discrete metal-organic unit to the glorious status of a hydrogen bonded network involving $\text{N}-\text{H}\cdots\text{O}$ and $\text{O}-\text{H}\cdots\text{O}$ synthons as connectors.

EXPERIMENTAL

Materials and methods. All chemicals of reagent grade were commercially available and used without further purification. Isonicotinamide, orotic acid, $\text{Zn}(\text{NO}_3)_2\cdot 6\text{H}_2\text{O}$, and NaHCO_3 were purchased from Sigma Aldrich and used as such. Thermal analysis (TG-DTA) was carried out with a TGA Q500 V6.7 Build 203 instrument.

Crystallography. A single crystal of **1** (size $0.50\times 0.45\times 0.30$ mm) was mounted on a Bruker Apex DUO CCD area-detector, equipped with a graphite monochromator and a MoK_α radiation source ($\lambda = 0.71073$ Å). The unit cell dimensions and intensity data were measured at 100(2) K. The structure was solved by direct methods and refined by the full matrix least squares treatment based on F^2 with anisotropic thermal parameters for the non-hydrogen atoms using Bruker APEX (Bruker 2009) for data collection and SAINT (Bruker 2009) for cell refinement, Bruker SAINT (data reduction), SHELXS-97 (structure solution) [11], SHELXL-97 (structure refinement) [12], and Bruker SHELXTL (molecular graphics) programs [13]. A multi-scan absorption correction (SADABS) was applied. Hydrogen atoms were included in geometrically calculated positions using a riding model and refined isotropically. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre www.ccdc.cam.ac.uk/data_request/cif upon quoting CCDC code 1018095.

The crystal structure refinement and unit cell parameters of complex **1** are given below: molecular formula $\text{C}_{11}\text{H}_{15}\text{N}_3\text{O}_{10}\text{Zn}$; crystal system triclinic; space group $P\bar{1}$; $a = 5.4668(6)$ Å, $b = 10.3861(12)$ Å, $c = 13.2743(15)$ Å; $\alpha = 87.5330(10)^\circ$, $\beta = 85.0790(10)^\circ$, $\gamma = 80.4640(10)^\circ$; cell volume 740.153 Å³; $Z = 2$, $Z' = 0$; R -factor = 3.24%, wavelength 0.71073 Å, temperature 100(2) K, d_{calc} 0.792 g/cm³, absorption coefficient 1.724 mm⁻¹, $F(0\ 0\ 0)$ 424; crystal size $0.50\times 0.45\times 0.30$ mm; θ range for data collection from 1.54° to 25.97° ; index ranges $-4 < h < 6$, $-12 < k < 12$, $-16 < l < 15$; reflections collected 2747; completeness to θ of 25.97° 99.3%; absorption correction Multi-Scan; maximum and minimum transmission 0.6258 and 0.4794; refinement method is full-matrix least-squares on F^2 ; data/restraints/parameters = 2837/13/290; goodness-of-fit (*GOOF*) on F^2 1.038; final R indices [$I > 2\sigma(I)$] $R_1 = 0.0333$, $wR_2 = 0.0879$; R indices (all data) $R_1 = 0.0324$, $wR_2 = 0.0873$; largest diff. peak, hole, e/Å³ 0.792, -0.610.

Synthesis of $[\text{Zn}(\text{Hor})(\text{Hiso})\cdot 3\text{H}_2\text{O}]\cdot \text{H}_2\text{O}$. 0.5 mmol of orotic acid, 0.5 mmol of $\text{Zn}(\text{NO}_3)_2\cdot 6\text{H}_2\text{O}$, 0.5 mmol of isonicotinamide, NaHCO_3 (0.5 mmol), and 5 ml of a 25% ammonia solution were mixed in a 7-ml Teflon reaction vessel. The reaction vessel was then placed in a stainless steel reactor and heated at 120°C in a high-precision programmed oven at a heating rate of $20^\circ\text{C}/\text{h}$ for a period of 20 h. After heating the reaction vessel was cooled at the same rate. The pale-yellow clear solution thus obtained was filtered and kept for crystallization at room temperature. After 13 days air-stable colorless block-shaped crystals of **1** suitable for X-ray diffraction were collected. The composition was established by the X-ray analysis. Complex **1** was found to be stable in air and insoluble in common organic solvents, such as acetone, chloroform, ethanol, acetonitrile, DMF, and water.

RESULTS AND DISCUSSION

The molecular structure of complex **1** (Fig. 1) reveals that isonicotinamide is hydrolyzed into isonicotinic (pyridine-4-carboxylic) acid (Scheme 1).

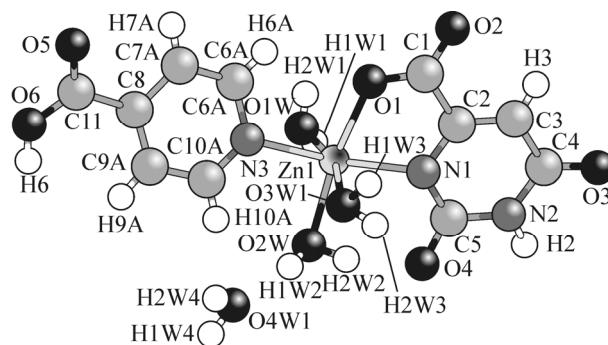
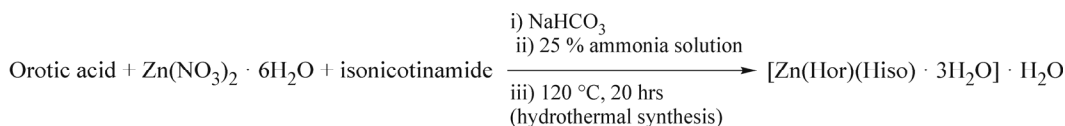


Fig. 1. Asymmetric unit showing Zn²⁺-orotate-isonicotinic acid complex (**1**). The central metal ion Zn²⁺ is coordinated with three aqua ligands, one isonicotinic acid (Hiso) molecule in a monodentate fashion, and orotate (Hor²⁻) in a chelating fashion. The crystal lattice has one water molecule.



Scheme 1.

The asymmetric unit (Fig. 1) of **1** contains one crystallographically independent Zn²⁺ ion. The zinc sites exhibit a “[2+2]+2” distorted octahedral geometry with the basal plane defined by one carboxylate oxygen atom (O1), one aqua oxygen atom (O2w), one pyrimidyl nitrogen atom (N1), and isonicotinic nitrogen atom (N3); the axial site is occupied by two aqua oxygen atoms (Zn...O3w; Zn...O1w). The Zn–N distance for the pyrimidyl ring in coordinated orotate (Zn–N1 = 2.116 Å) is slightly shorter than that for coordinated isonicotinic acid (Zn–N3 = 2.141 Å). The Zn–O bonds are: Zn–O1 = 2.080 Å, Zn–O1w = 2.108 Å, and Zn...O2w = 2.121 Å, and Zn–O3w = 2.150 Å. Other selected bond lengths and bond angles are given in Table 1.

In **1** the regularly alternating hydrogen bonding connectivity between the imine hydrogen atom (N(2)–H(2)) and uncoordinated carbonyl oxygen atom (O4) of the orotate rings {...H–N–C=O...}₂ and {...H–O–C=O...}₂ (between the carboxylate groups of isonicotinic acid) results in the formation of a 1D tape (Fig. 2) running along the crystallographic *a* axis (N(2)–H(2)...O(4) = 176.83°; H(2)...O(4) = 1.974 Å, N(2)...O(4) = 2.853 Å, N(2)...H(2) = 0.880 Å).

The hydrogen bonding interaction of lattice water (O4w), coordinated water (O1w), and uncoordinated carbonyl oxygen atom (O3) of the orotate ring help to propagate further the connectivity with the formation of a 2D sheet (Fig. 3)

TABLE 1. Selected Bond Angles (deg) and Bond Lengths (Å) in **1**

Zn1–O3W2	1.986(12)	Zn1–O	12.0800(19)	Zn1–O1W	2.108(2)
Zn1–N1	2.116(2)	Zn1–O2W	2.121(3)	Zn1–N3	2.141(2)
Zn1–O3W1	2.150(3)				
O3W2–Zn1–O1	131.7(3)	O3W2–Zn1–O1W	131.7(3)	O1–Zn1–O1W	96.63(8)
O3W2–Zn1–N1	93.0(4)	O1–Zn1–N1	79.28(8)	O1W–Zn1–N1	97.16(8)
O3W2–Zn1–O2W	46.9(3)	O1–Zn1–O2W	171.74(9)	O1W–Zn1–O2W	85.49(10)
N1–Zn1–O2W	92.54(9)	O3W2–Zn1–N3	90.2(4)	O1–Zn1–N3	93.00(8)
O1W–Zn1–N3	86.21(8)	N1–Zn1–N3	171.86(8)	O2W–Zn1–N3	95.12(10)
O3W2–Zn1–O3W1	37.3(3)	O1–Zn1–O3W1	95.31(11)	O1W–Zn1–O3W1	164.37(11)
N1–Zn1–O3W1	94.95(10)	O2W–Zn1–O3W1	84.12(12)	N3–Zn1–O3W1	83.12(10)

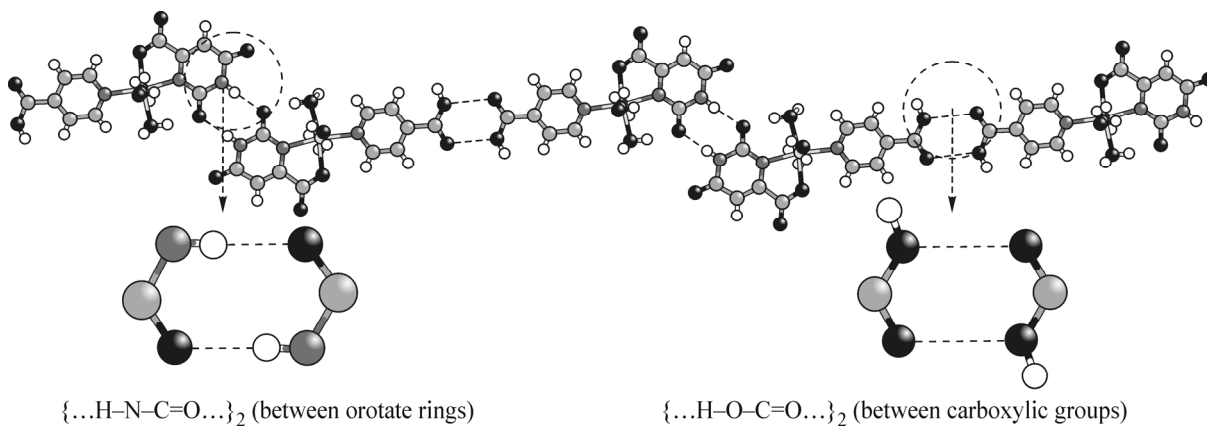


Fig. 2. 1D tape formed by the alternating acid...acid (right) and amide...amide dimers.

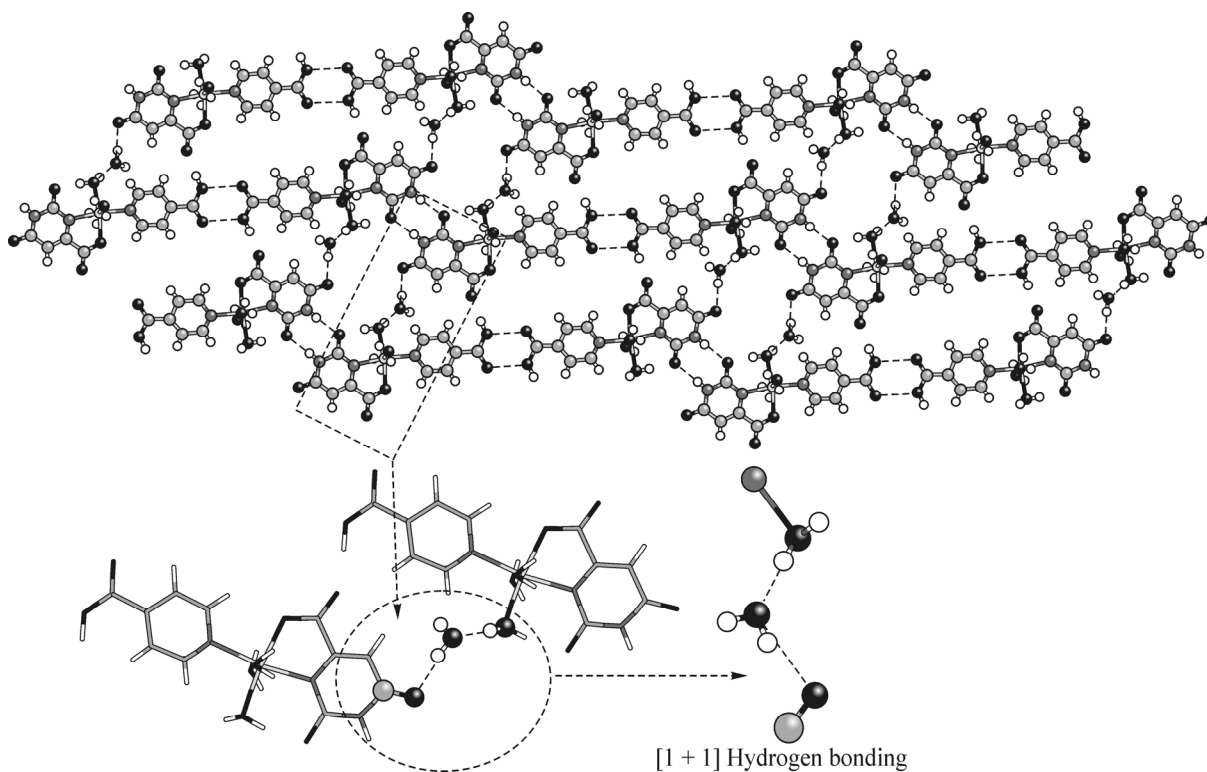


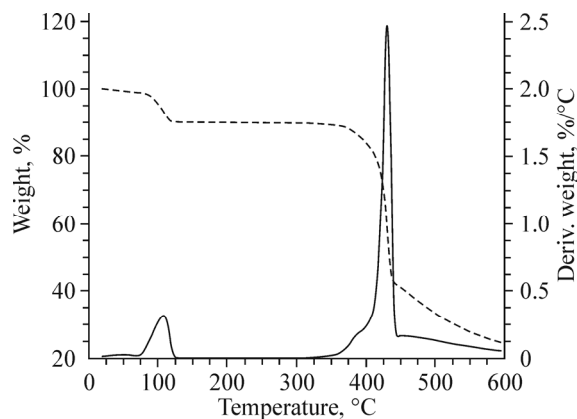
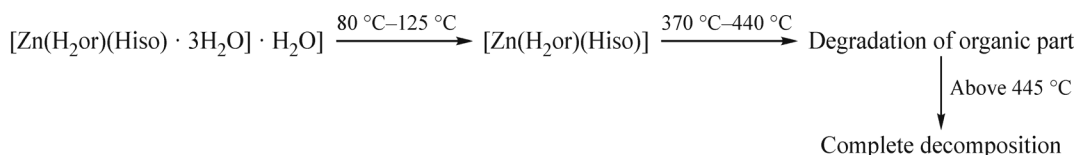
Fig. 3. View of the crystal lattice showing a 2D sheet formed by the hydrogen bonding interaction of lattice water (O4w), coordinated water (O1w), and an uncoordinated carbonyl oxygen atom (O3) of the orotate ring. Lattice water shows the [1+1] pattern of hydrogen bonding (inset).

(O(4)w–H1w4...O3 = 152.02°, H1w...O3 = 2.119 Å, O(4)w...O3 = 2.917 Å, O(4)w–H1w4 = 0.871 Å; O(2)w–H1w...O4w = 161.77°, H1w...O4w = 1.749 Å, O(2)w...O4w = 2.594 Å, O(2)w–H1w = 0.874 Å). Lattice water shows the (1+1) pattern of hydrogen bonding (Table 2).

Thermogravimetric analysis. The 2D structure is largely a consequence of hydrogen bonding interactions among coordinated water molecules and coordinated and free carboxylate oxygen atoms. This association is quite strong. Thermogravimetric analysis (Fig. 4) of **1** with a 6.4390 mg sample in N₂ shows that the compound begins to lose weight up to ~80°C. Water removal begins at 85°C and the loss of all the water molecules takes place at 123°C. The loss of coordinated orotate and Isonicotinate units occurs from 370°C to 440°C. The complete decomposition of the compound is achieved above 445°C. The DTA analysis of crystal showed two endothermic peaks at 115°C and 430°C, which is attributed to the release of lattice water, coordinated water, the orotate ion and the isonicotinate ion from the zinc ion respectively (Scheme 2).

TABLE 2. Conventional Hydrogen Bonding Parameter for **1** (Å and deg)

D–H···A	$d(\text{D–H})$	$d(\text{H···A})$	$d(\text{D···A})$	$\angle(\text{DHA})$
N2–H2...O4	0.880	1.974	2.853	176.83
O4w–H1w4...O3	0.871	2.119	2.917	152.02
O2w–H1w...O4w	0.874	1.749	2.594	161.77

**Fig. 4.** Weight loss curve of compound **1** on heating in N_2 .Scheme 2. Thermal behavior of **1**.

CONCLUSIONS

We have synthesized for the first time the supramolecular orotic- and isonicotinic acid-based Zn complex $[\text{Zn}(\text{Hor})(\text{Hiso}) \cdot 3\text{H}_2\text{O}] \cdot \text{H}_2\text{O}$ in which coordinated isonicotinic acid together with orotate and aqua ligands takes part in the hydrogen bonding after complexation. The acid...acid (between the isonicotinic acid molecules) and amide...amide (between the orotate ligands) dimer formation propagates with the formation of a 1D tape, which together with lattice water molecules further determine the overall 2D network.

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