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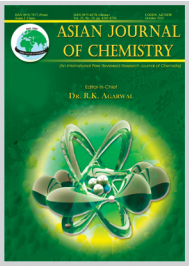


# Supramolecular Water Morphology and Methanol Solvate in a Functionalized Pymetrozine Host

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The crystals of functionalized pymetrozine hydrochloride salts in water (crystal **1**) and neutral pymetrozine in methanol (crystal **2**) have been obtained. The carbonyl group and the nitrogen atom of Schiff base group of pymetrozine interact with hydrophilic groups (-OH) of methanol or water molecule to form one five-member ring *via* functional hydrogen bonds. Present results provide new insight and an understanding of the three-dimensional structural aspects of hydrogen bonded liquids with important implications in the structure and behaviour of functional molecules in biological systems.

**Key Words: Crystal, Hydrogen bonded liquids, Pymetrozine.**

## INTRODUCTION

The chemistry, physics and biological aspects of hydrogen bonded liquids have attracted considerable theoretical and experimental interests[1-4]. Water and methanol constitute important prototypes of hydrogen bonded liquids and the investigations toward understanding hydrogen bonding patterns that exist within the individual liquids has been at the focus of attention for a number of decades[1-4]. Water plays an indispensable role in life-sustaining processes, investigations on its structure, properties and functions have received more scientific attention than any other substance[1-4]. Moreover, water chains are of great interest as many fundamental biological processes appear to depend on their unique properties[5,6].

Hydrogen bonding liquid methanol (MeOH) is the simplest amphiphile functionalized with hydrophobic (-$CH_3$) and hydrophilic groups (-OH). Understanding of the solvation properties of MeOH as it relates to the disposition of hydrophobic/hydrophilic groups in polar or nonpolar solvents is of fundamental importance in biological and chemical sciences because amphiphiles are essential constituents making up cell membranes and are also extensively used in chemical industries as micelles (*e.g.*, detergent action)[7-10].

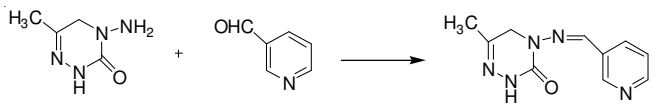
Organic compounds with functional moieties that are present in biological molecules can help stabilize various hydrogen bonded liquids topologies in environments resembling those in living systems[11]. Pymetrozine, 3,4,5-tetrahydro-3-oxo- [(pyridine-3-ylmethylene)amina]-6-methyl-1,2,4-triazine, an antifeedant that interacts with chordotonal sensillae throughout the insect muscular system, results in death by starvation, however the precise molecular mechanism for this is still unclear[12]. Taking this fact into consideration, we have examined the crystal structure of the supramolecular assembly of pymetrozine in methanol and its hydrochloride salts in water for better understanding the structure and behaviour of functional molecules in biological systems.

## EXPERIMENTAL

All chemicals or reagents were purchased from standard commercial suppliers and used without further purification.

**Preparation of 3,4,5-tetrahydro-3-oxo-[(pyridine-3-ylmethylene)amina]-6-methyl-1,2,4- triazine:** 4-Amino-6-methyl-2,3,4,5-tetrahydro-3-O-1,2,4-triazin was prepared according to a literature procedure[13,14]. Then, 3-pyridine-aldehyde (1 mmol) was added to a solution of compound 4-amino-6-methyl-2,3,4,5-tetrahydro-3-O-1,2,4-triazin (1 mmol) in 15 mL ethanol at 50 ºC. When the solid was found, the reaction mixture was heated to reflux. The reaction time was monitored by TLC (ethyl acetate/petroleum ether = 2:1). After the reaction finished, the mixture was cooled by ice-water and the pymetrozine was precipitated and recrystallized by methanol (**Scheme-I**). Yield: 92 %. m.p. 228.3-229.2 ºC. $^1$H NMR (DMSO-$d_6$, 500 MHz): 10.18 (s, 1H, NH), 8.60 (s, 1H, CH), 8.15 (d, 1H, $J$ = 4.04 Hz, CH), 8.19 (d, 1H, $J$ = 7.87 Hz, CH), 7.90 (s, 1H, CH), 7.55 (t, 1H, CH), 4.37 (s, 2H, $CH_2$), 1.94 (s, 3H, $CH_3$); IR (KBr, $cm^{-1}$): 3300, 3220, 3100, 2920, 1700, 1660, 1470, 1320, 1240, 1150, 730.

**X-ray crystallography:** Two single crystals of functionalized pymetrozine hydrochloride salts in water (**1**) and neutral pymetrozine in methanol (**2**) were obtained by slow evaporation



**Scheme-I:** Synthesis of pymetrozine

mounted on a glass fiber with epoxy cement. The crystal data were collected in air at room temperature. The colourless rectangular crystals were collected on a Rigaku AFC7R diffractometer at 293 K. The program package SHELX-97 was used for structure solution and full matrix least-squares refinement on $F^2$. Crytallographic data for the crystal structure have been deposited with the Cambridge Crystallographic Data (CCDC 689819 and CCDC 689820). This material can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: C44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

## RESULTS AND DISCUSSION

Pymetrozine hydrochloride salts crystallized in water (crystal **1**) and pymetrozine crystallized in methanol (crystal **2**) in the monoclinic system with space group P2(1)/c is presented. The monomeric supramolecular synthon generates a 3-D organic framework by a self-assembly process. The crystallographic data are summarized in Table-1. View of crystal structure and the hydrogen bonding network of these solids are shown in Fig. 1-3 and the overall metrical parameters of hydrogen bonding are presented in Table-2.

In the crystal structure of **1**, one pymetrozine cation interacts with three chloride anion and two water molecules,

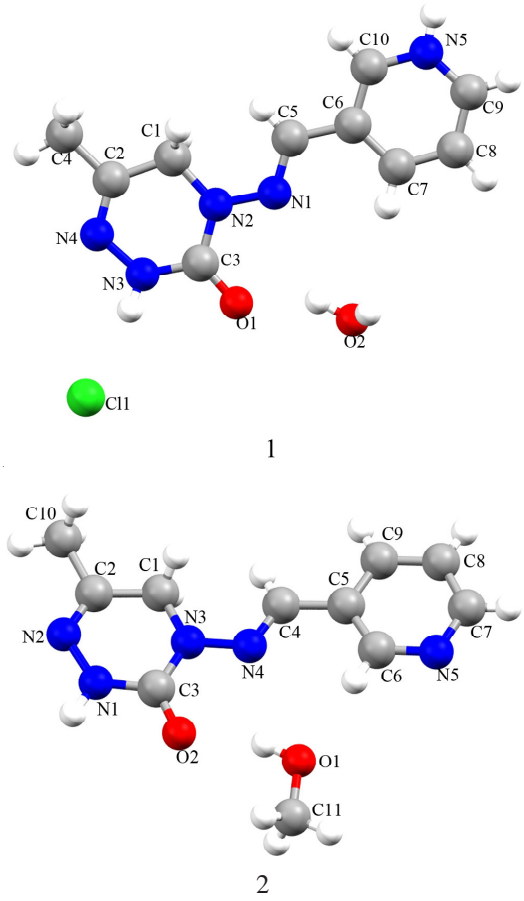



Fig. 1 View of the crystal structure **1** and **2**

TABLE-1
CRYSTALLOGRAPHIC DATA FOR THE CRYSTAL **1** AND **2**

| Compound | **1** (Pymetrozine hydrochloride salts·$H_2O$) | **2** (Pymetrozine·methanol) |
|---|---|---|
| Formula | $C_{10}H_{14}N_5O_2Cl$ | $C_{11}H_{15}N_5O_2$ |
| Formula weight | 271.71 | 249.28 |
| T | 293(2) K | 293(2) K |
| Wavelength (Å) | 0.71073 | 0.71073 |
| Crystal system, space group | Monoclinic, P2(1)/c | Monoclinic, P2(1)/c |
| a(Å) | 8.984(3) | 8.861(12) |
| b(Å) | 7.521(3) | 11.427(15) |
| c(Å) | 18.623(6) | 12.630(16) |
| Volume | 1234.1(7) Å | 1275.8(3) Å |
| Z, Calculated density | 4, 1.462 $Mg/m^3$ | 4, 1.298 $Mg/m^3$ |
| F(000) | 568 | 528 |
| Crystal size | 0.327 mm × 0.316 mm × 0.085 mm | 0.274 mm × 0.245 mm × 0.200 mm |
| Theta range for data collection | 2.23 to 26.00 deg | 2.30 to 27.00 deg |
| Reflections collected / unique | 6506 / 2413 [R(int) = 0.1033] | 7386 / 2787[R(int) = 0.0842] |
| R | 0.0760 | 0.0489 |
| Rw | 0.2027 | 0.0967 |

TABLE-2
HYDROGEN BONDING DISTANCE (Å) AND ANGLES (deg) IN CRYSTAL **1** AND **2**

| Compd. | D–H···A | D(D-H) | D(H···A) | D(D···A) | A (D-H···A) |
|---|---|---|---|---|---|
| **1** | O(2)-H(2A)···O(1) | 0.899(19) | 1.860(3) | 2.670(5) | 149(4) |
| | O(2)-H(2A)···N(1) | 0.899(19) | 2.650(3) | 3.396(6) | 140(4) |
| | N(3)-H(3)···Cl(1) | 0.870(2) | 2.290(2) | 3.149(5) | 170(5) |
| | N(5)-H(5A)···O(2) | 0.869(19) | 1.780(2) | 2.648(6) | 175(4) |
| | O(2)-(2B)···Cl(1) | 0.900(2) | 2.190(2) | 3.086(4) | 172(8) |
| **2** | N(1)-H(1)···O(1W) | 0.930(2) | 1.990(2) | 2.915(2) | 179(2) |
| | O(2)-H(2)···O(1W) | 0.870(4) | 1.990(4) | 2.821(3) | 161(4) |
| | O(2)-H(2)···N(4) | 0.870(4) | 2.610(4) | 3.187(3) | 125(3) |

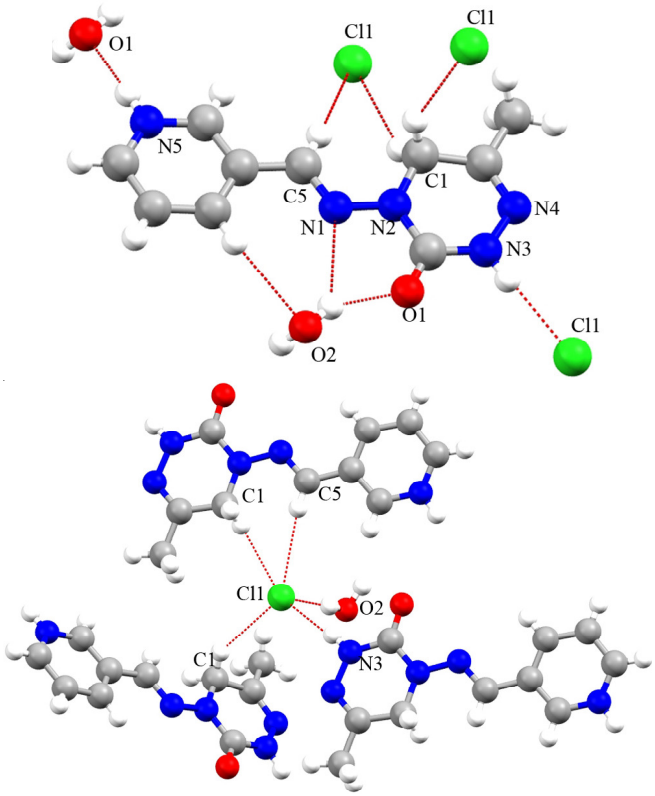



Fig. 2. Representation of the hydrogen bond, ionic hydrogen bond and short C-H···Cl⁻ contact for the crystal **1**

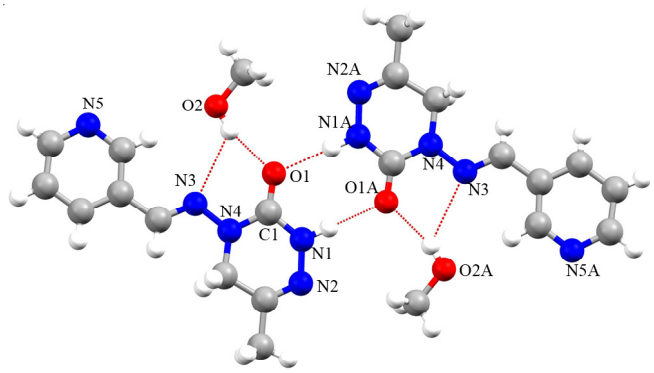



Fig. 3. Representation of the hydrogen bonding for the crystal **2**

respectively and each chloride anion is binding to three pymetrozine cations and one water molecule, respectively (Fig. 2). The distance (3.56 Å) and the core (74.4°) between the trizine ring and pyridine ring of another layer molecule suggest an evident slipped-parallel π/π interaction (Fig. 4) according to the criterion for the evaluation of intermolecular interaction between aromatic molecules (AIMI Model), which was proposed by Tsuzuki *et al.*[15]. The pyridine nitrogen atom of pymetrozine is protonated and forms functional N5-H5···O2 hydrogen bonds with the structural water molecule. Slight changes in N basicity and differences between conformations and close-packing modes of homologous bases could be used to prepare novel crystals[16]. The triazine NH groups of pymetrozine cation unit (N3-H) are engaged in a single N3-H3···Cl hydrogen bonding interaction with individual chloride ion. The carbonyl group and the nitrogen atom of Schiff base group form functional hydrogen bonds with another structural water

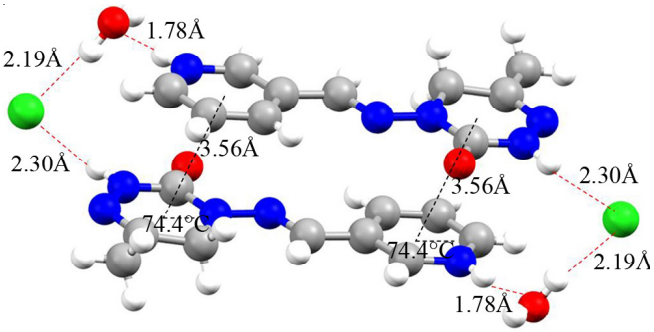



Fig. 4. Schematic representations of the intracolumnar π/π interaction networks observed in crystal **1**

molecule. The neutral and ionic hydrogen bonding in Schiff bases had already been studied[17]. Besides these bonds, the chloride anion could also form hydrogen bond with the water molecule in the structure which results in the formation of a three-dimensional extended structure. In the crystal structure of **2**, the asymmetric unit contains two pymetrozine molecules and two methanol molecules. Each pymetrozine molecule interacts with another pymetrozine molecule and one methanol molecule coplanarly. The carbonyl group and the nitrogen atom of Schiff base group of pymetrozine with another structural methanol molecule also form one five-member ring *via* functional O2-H2···O1 and O2-H2···N4 hydrogen bonds. Moreover, mutual actions are found between two pymetrozine molecules in the head-to-head mode *via* the functional N1-H1···O1 hydrogen bond (Fig. 3).

The structural analysis of crystal **1** reveals that the pymetrozine molecules pack to a well-regulated slipped-parallel crystal. The adjacent pymetrozine cations are joined by pairs to form undulate ribbons (Fig. 5a) *via* a pair of C9-H···N4 bonds in the head-to-end mode and the ribbon is non-linear in that any two pymetrozine cations are non-coplanar. It is accordant to the critical evaluation of C-H···N hydrogen bonding in the crystalline state[18]. The identical fashion occurs in the extended structure of crystal **2** *via* the same path (Fig. 5b). Then, the adjacent pymetrozine ribbons are interconnected by water molecules in a shoulder-to-shoulder mode *via* hydrogen bonding networks N5-H···O2-H···O1 to form water morphology (Fig. 5a) in the crystal **1**. Water molecules act as a bridge chain between two pymetrozine molecules. Moreover, the distance of intermolecular H5 ···O2 hydrogen bond between pymetrozine molecule and water molecule in the crystal **1** is 1.780 Å and it is shorter than that of intermolecular H1···O1W hydrogen bond in the crystal **2**. So the hydrogen bonding interaction within pymetrozine and water molecule is significantly stronger than that between two pymetrozine molecules. It could be interpreted that the shoulder-to-shoulder stacking mode appears in the extended structure of crystal **1** instead of head-to-head mode. In the crystal **2**, the pyridine nitrogen atom of pymetrozine could not been protonated resulting in not forming functional hydrogen bonds with the structural methanol molecule. It means that methanol molecules could not participate in the extension of pymetrozine molecules in the 3D network. In the extended structure of crystal **2**, mutual actions among the pymetrozine molecules in the head-to-head mode *via* the functional N1-H1···O1 hydrogen bond have play the decisive roles (Fig. 5b).

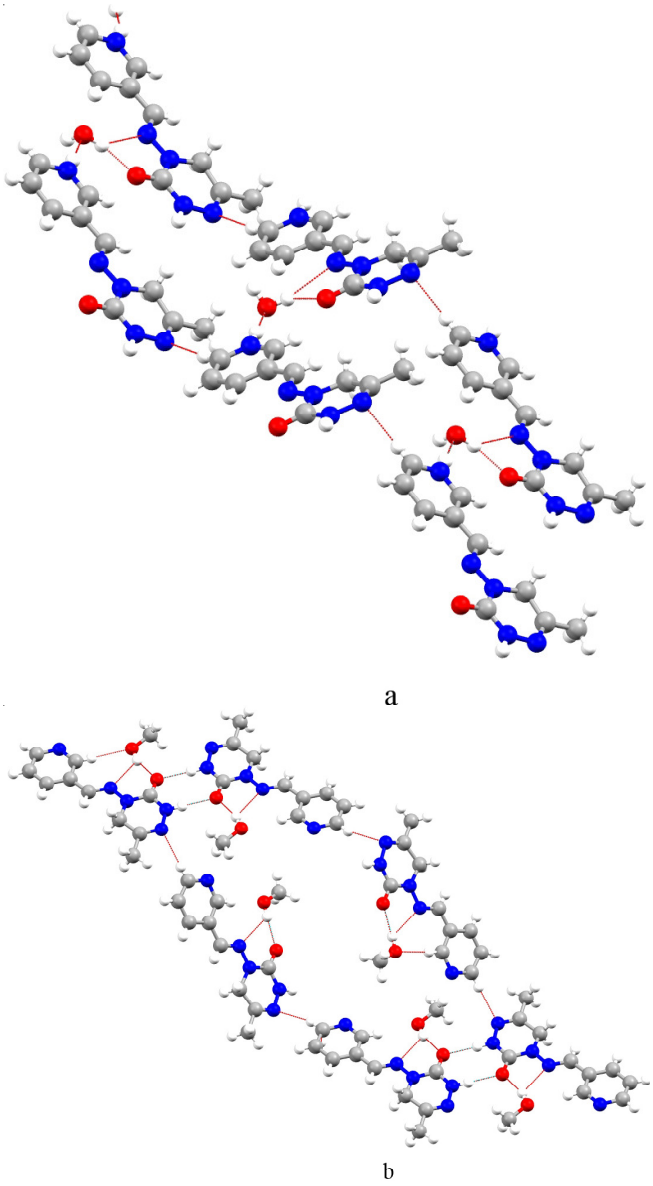



Fig. 5. (a) Water molecule-bridged chains of crystal **1** (b) Part of the unit cell of **2**, exhibiting the unique mutual interactions of crystal **2**

The extended structure of crystal **1** was stabilized by the cooperative effect of π/π interaction, the N3-H···Cl and O2-H···Cl ionic hydrogen bonds. The formation of strong, charge-assisted hydrogen bonding, $NH^+\cdots X^-$ and the π/π interactions dominate the extended structures. In addition, the relative weaker interactions among the N-substituents, the $X^-$ anions and CH bonds of the substituents play important roles in the structures of these materials (Fig. 6a). In the extended structure of crystal **2**, the formation of the three dimensional network is generated due to hydrogen bonds actions among the pymetrozine molecules. The three dimensional network of crystal **2** is shown in Fig. 6b.

Classic examples to control the assembly of specialty chemicals were regularly demonstrated through the conversion of a pharmacologically active molecule into its chloride or nitrate salt[19]. However in these crystals, hydrogen bonding liquid molecule was seldom considered. Recently, significant progresses have been made on the structural characterization of one-dimensional aggregates such as water chains and

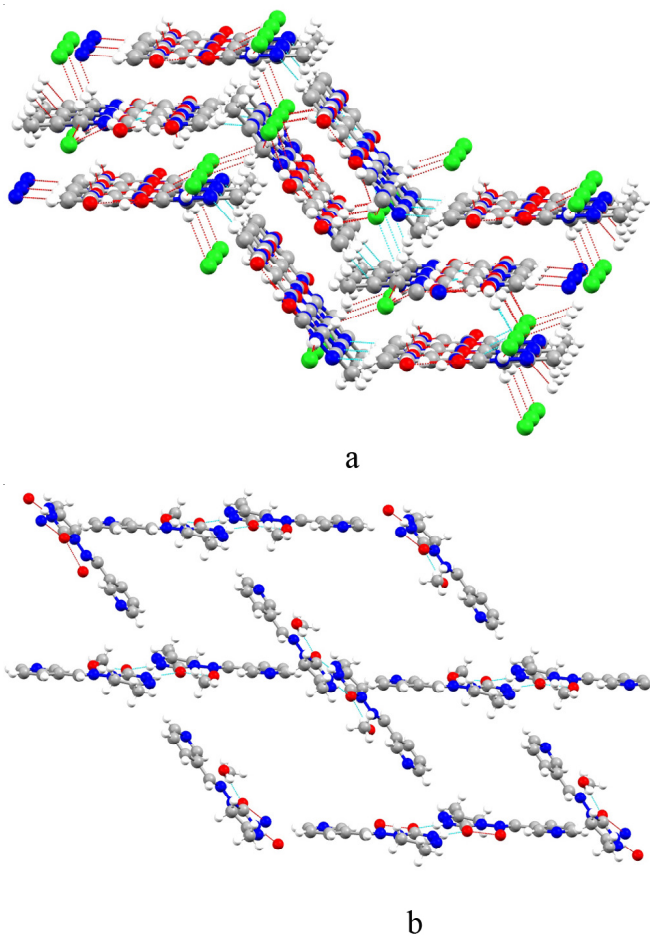



Fig. 6. (a) The 3D network model of the crystal **1** (b) The 3D network model of the crystal **2**

tapes[20,21]. In contrast, there are very few examples of two- or three-dimensional hydrogen bonding liquid polymers[22,23]. In our example, the cooperative effects of intermolecular hydrogen bonding, π/π interactions and ionic interactions represent essential forces for the self-organization of individual charged units into robust slipped-parallel supramolecules in the crystal **1**. Water molecules play apparent bridge roles for the extended crystal structure. While in the crystal **2**, methanol molecules were not observed such analogous bridge actions. The mutual actions between pymetrozine molecules in the head-to-head mode *via* the functional N1-H1···O1 hydrogen bond and in the head-to-end mode *via* the weak bonds appear to dominate the extended structures.

## Conclusion

New crystals of functionalized pymetrozine host with hydrogen bonded liquids have been obtained. Present results provide new insight and an improved understanding of the three-dimensional structural aspects of hydrogen bonded liquids with important implications in the structure and behaviour of functional molecules in biological systems. The carbonyl group and the nitrogen atom of Schiff base group of pymetrozine with hydrophilic groups (-OH) of hydrogen bonded liquids form one five-member ring *via* functional hydrogen bonds. This arrangement of hydrogen bonded liquids facilitates a complementary relationship resulting in inter and intramolecular hydrogen bonds within and between the amino

acid interfaces and provides a new macroscopic model for pymetrozine-amino acid interactions in terms of packing efficiency and maximization of macromolecular interactions.

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