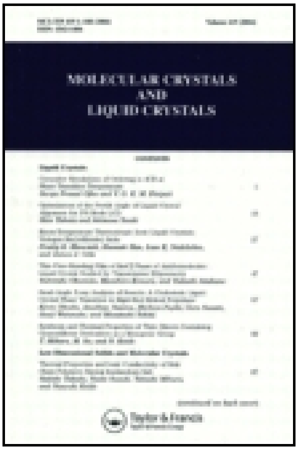

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Crystal Packing and Hydrogen-Bonding Studies: The Crystal and Molecular Structures of the Nonhydrate and Hydrate Forms of 2,6-Di(propanoylamino)pyridine

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The crystallization of 2,6-di(propanoylamino)pyridine ($[CH_3(CH_2)_{n\text{-}1}CONH]_2C_5H_3N$, $n = 2$, *[2Apy]) from hexane/ethyl acetate mixed solvent gives two types of crystals, 2APy and 2Apy* $\cdot$ $2H_2O$. *The crystal data, packing structures, and hydrogen bonding network of both crystals suggest that 2APy and 2APy* $\cdot$ $2H_2O$ *are not structurally similar. In the crystal structure analysis of 2APy, two crystallographically independent 2APy molecules were observed in its asymmetric unit, whereas the asymmetric unit of 2APy* $\cdot$ $2H_2O$ *consists of one crystallographically independent 2APy molecule and two crystallographically independent water molecules (Ow, Ow′). The water molecules (Ow, Ow′) are connected via Ow⋯Ow′ intermolecular hydrogen bonds to form two chains in a one-dimensional arrangement along the direction of c-axis, built up of two crystallographically independent water molecules. The driving force behind the molecular aggregation of 2APy is mainly N⋯O=C hydrogen bonding, whereas those of 2APy* $\cdot$ $2H_2O$ *are N⋯Ow, C=O⋯Ow, and Ow⋯Ow′ hydrogen bonding. The differences in the kind of hydrogen bonding networks in both crystals contribute to the differences in the packing modes observed in 2APy and 2APy* $\cdot$ $2H_2O$.

Keywords: crystallography; crystal structure; 2,6-di(propanoylamino)pyridine; hydrogen bonding; molecular assembly; molecular interactions

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INTRODUCTION

The concepts of crystal engineering and molecular recognition are exceedingly similar, and both fields are concerned with manipulation of intermolecular interactions in the architecture of supramolecular assemblies. The understanding of intermolecular interactions in the context of crystal packing and in the utilization of such understanding in the design of new solids with desired physical and chemical properties is called crystal engineering.

The exploitation of intermolecular forces in the self-assembly of molecules into molecular systems with novel functions is one of the most fascinating and rapidly emerging fields of supramolecular chemistry [1]. Currently, we are interested in exploiting the intermolecular forces as well as the packing modes in the self-assembly of 2,6-di(acylamino) pyridines (hereafter, nAPys; (Fig. 1a) molecules to design molecular systems of solid-state supramolecular complexes of nAPys. Liquid crystals studies [2] have shown that the supramolecular complexes (liquid crystalline complexes) of nAPys with alkoxybenzoic acids (Fig. 1b) have potential usefulness for generation of novel materials. The detailed information on the intermolecular forces and packing modes in these supramolecular complexes, through X-ray crystallographic methods, will enhance our knowledge in understanding the physical and chemical properties of the liquid crystalline complexes of the nAPys.

As part of our initial approach to studies on solid-state supramolecular complexes of nAPys, we have chosen to investigate the structural characteristics of nAPys and utilize the knowledge of its molecular organization by the intermolecular forces to obtain a solid-state molecular system of nAPys forming supramolecular complexes with alkoxybenzoic acids. Thus, with respect to the significance of structural studies of the nAPys, our present goal of research is to investigate the series of nAPys to know the molecular aggregation modes and the driving force(s) behind such assemblies. A series of nAPys with various lengths of hydrophobic alkyl chains (n = 1, 2, 3,. . .,18) were chosen to prepare single crystals of the nAPys.

Just recently, after several attempts to obtain such single crystals, we have obtained the first crystallized compound [2,6-di(propanoylamino)pyridine (hereafter, 2Apy)]. The 2APy crystallized into two forms, and the crystal structures of the two different forms of 2APy crystals were investigated by X-ray crystallographic methods. It is anticipated that they may behave as probable model systems for preparing supramolecular complexes (solid state complexes) of nAPys yet to be known. The first structural characterization of 2APy in respect to its crystal and molecular structures is reported in this article.

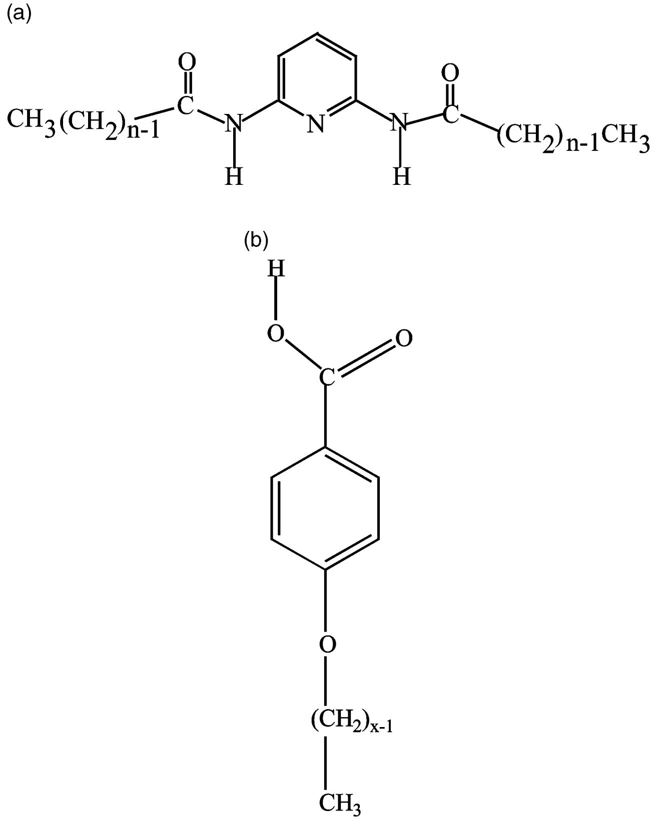


FIGURE 1 (a) Chemical structure of 2,6-di(propanoylamino)pyridine (nAPy: n = 2; 2APy) molecule; (b) chemical structure of an alkoxybenzoic acid.

EXPERIMENTAL METHODS AND CRYSTAL STRUCTURE DETERMINATION

Preparation of 2,6-Di(Propanoylamino)pyridine Single Crystals

The single crystals of the 2APy were obtained from hexane/ethyl acetate (1:4) mixed solvent by the slow evaporation method in an IUCHI PCI-300 incubator at about 293 K. The single crystals were obtained after 7–10 days. Analysis of the crystals obtained revealed that two forms of crystals were formed, viz. the nonhydrated (2APy) and hydrated ($2APy \cdot 2H_2O$). The inclusion of water molecules in 2APy is being investigated because neither the mixed solvent nor the 2APy used contained any trace of water. The 2APy crystals were colorless needle-shaped crystals, whereas those of 2APy · $2H_2O$ were colorless square-shaped crystals. These crystals were very stable in the open atmosphere. The crystals of each kind were collected and kept for X-ray diffraction studies.

Determination of Crystal Structures

The crystal structure studies of 2APy and 2APy · $2H_2O$ were performed using X-ray diffraction techniques. Data collection was performed on a MacScience DIP 2000 Image Plate using MoKα radiation ($\lambda = 0.7107$Å) operating at 6° intervals with exposure time of 600 s (10 min). Data collection and processing was carried with the DENZO software package [3], and the structure solution and refinement was performed using maXus program [4]. The crystal structure was solved by direct methods (SIR92) [5] and expanded using Fourier techniques (DIRDIF) [6]. All nonhydrogen atoms were refined anisotropically. The hydrogen atoms attached to the nitrogen atoms of the amide groups and those attached to Ow and Ow′ could not find their position in the difference Fourier map but were included by geometrical calculations and not refined. All the other hydrogen atoms were also introduced by geometrical calculations but not refined. The final cycles of full-matrix least-squares refinement were based on 2580 observed reflections, 289 variable parameters for 2APy, and 1565 reflections, 163 parameters for 2APy · $2H_2O$. The goodness of fit, final crystallographic R (calculated based on F) and Rw factors (calculated based on F^2) were 1.024, 0.079, 0.175 for 2APy and 0.95, 0.060, 0.186 for 2APy · $2H_2O$. The function minimized in all cases was $\sum w(|Fo| - |Fc|)^2$ where $w = 1/\sigma^2(Fo)$. The atomic coordinates, bond lengths, bond angles, torsional angles and thermal parameters can be obtained upon request from the director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

RESULTS AND DISCUSSION

Molecular Geometry, Packing Structure, and Intermolecular Interactions in 2APy and 2APy · $2H_2O$

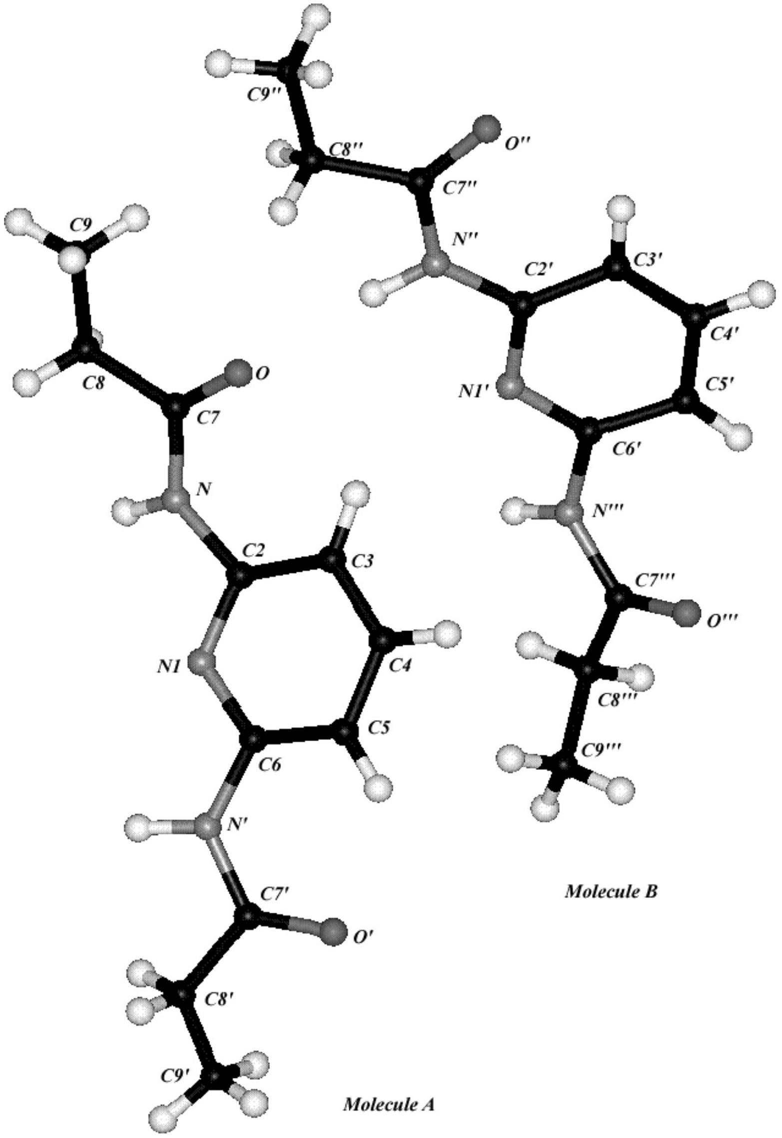
Table 1 summarizes the crystal data for the crystal structure determination of 2APy and 2APy · $2H_2O$. In the crystal structure analysis of 2APy (Fig. 2a), two crystallographically independent 2APy molecules (molecules A and B) are observed in an asymmetric unit, and the asymmetric unit of 2APy · $2H_2O$ (Fig. 2b) consists of one crystallographically independent 2APy molecule and two crystallographically independent

TABLE 1 Crystal Data for 2APy and 2APy · $2H_2O$

Complex	2APy	2APy · $2H_2O$
Molecular formula	$C_{11}H_{15}N_3O_2$	$C_{11}H_{19}N_3O_4$
Formula weight	221.26	257.29
Color	Colorless	Colorless
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/a$ (#14)	$P2_1/c$ (#14)
a (Å)	8.1020 (6)	9.1140 (4)
b (Å)	34.825 (3)	15.7830 (4)
c (Å)	9.143 (7)	9.975 (12)
β (°)	112.860 (3)	110.610 (1)
Volume (Å^3)	2377.1 (2)	1343.0 (1)
Z	8	4
Dcalc (gcm^{-3})	1.240	1.270
F (000)	944	552
Crystal dimensions (mm)	0.1 × 0.2 × 0.2	0.2 × 0.2 × 0.3
R_{merge} (%)	10.8	8.5
Completeness (%)	95.8	98.2

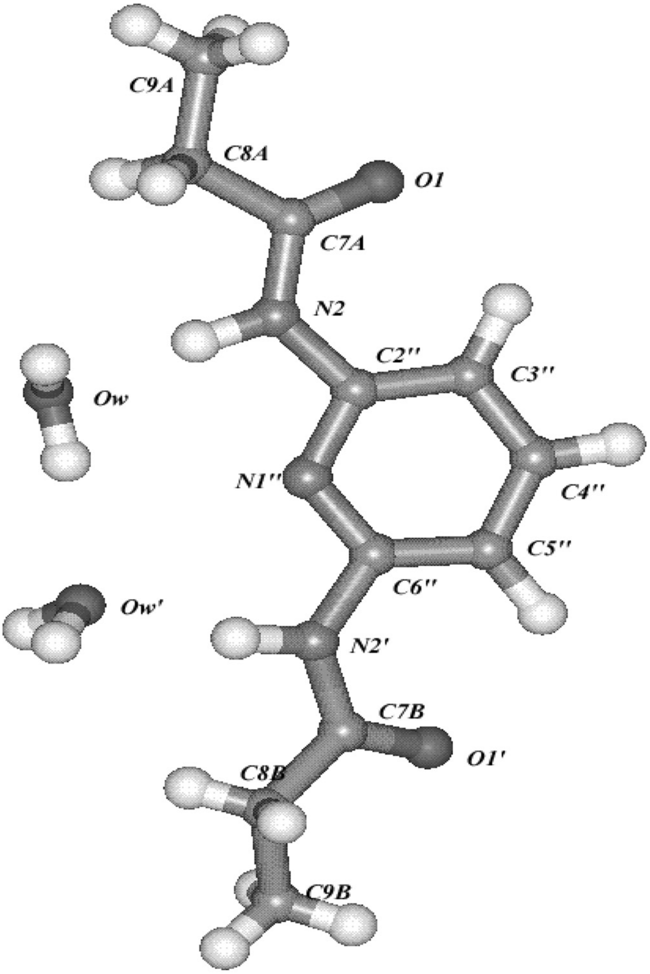
water molecules (Ow, Ow′). The space groups $P2_1/a$ (#14) for 2APy and $P2_1/c$ (#14) for 2APy · $2H_2O$ suggest that both crystals crystallize in monoclinic crystal system and their crystal structures include two-fold screw axis as the translational symmetry operation. The cell dimensions and volume (Table 1) of both 2APy and 2APy · $2H_2O$ suggest that the two compounds are not isostructural. Comparing the axial dimensions of each compound with the other, it is observed that there is no similarity or common cell dimensions between them, which suggests that the packing arrangement in each case differs from the other. The difference in the density of 2APy (1.24 g/cm^3) and 2APy · $2H_2O$ (1.27 g/cm^3) means that the molecular arrangement in the unit cells of 2APy and 2APy · $2H_2O$ is different. The crystal packing structures of 2APy and 2APy · $2H_2O$ viewed along *a*-axis are shown in Fig. 3.

In both compounds (Fig. 2a,b), the nitrogen atoms in the amide of an ethyl-amide chains are attached to the pyridine ring at C2 and C6. The pyridine ring atoms in 2APy and 2APy · $2H_2O$ molecules are planar. The torsional angles, bond angles, and bond lengths in the pyridine ring of both compounds have normal geometry. In the pyridine ring, the mean C–C distance in both 2APy (1.389 (1) Å) and 2APy · $2H_2O$ (1.383 (2) Å) can be compared with the mean value of 1.378 (2) Å in 6-chloro-2-hydroxypyridine [7] and 6-bromo-2-hydroxypyridine [7], and the mean value of 1.386 (2) Å in 2-amino-5-chloropyridine [8], 2-aminopyridine [9], and 3-aminopyridine [10]. In both 2APy and



(a)

FIGURE 2 (a) Molecular structure and atomic numbering of 2Apy; (b) molecular structure and atomic numbering of $2Apy \cdot 2H_2O$.

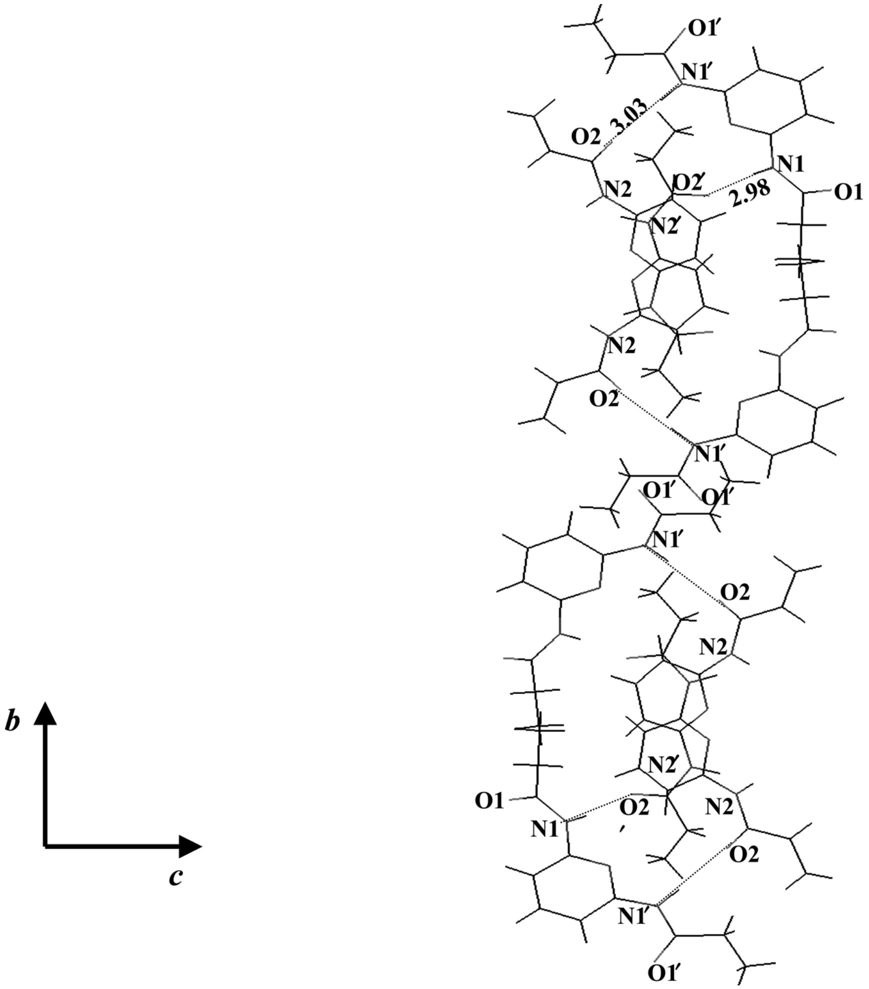


(b)

FIGURE 2 Continued.

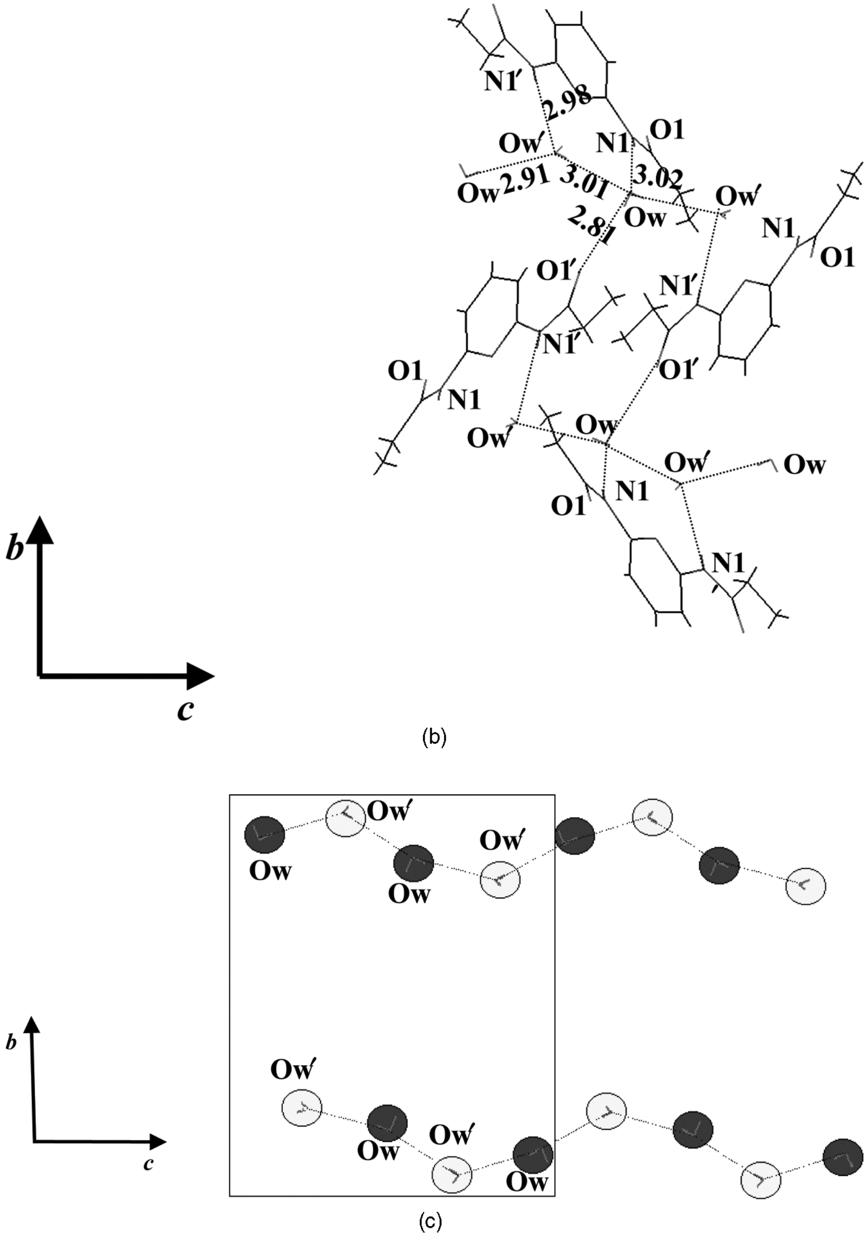
2APy · $2H_2O$ crystals, the longest C−C bond (1.390 (1) Å) is the one closest to the amide group. The C-N distances within the ring in both crystals are 1.329 (1), 1.348 (2) Å for molecule A, 1.330 (2), 1.340 (2) Å for molecule B of 2Apy; and 1.329 (1), 1.337 (3) Å for 2APy · $2H_2O$. These do not differ significantly from the C−N atoms encountered in those of 1.341 (2), 1.342 (2) Å in 2-amino-5-chloropyridine [8]; 1.331 (5), 1.336 (4) Å in 2-aminopyridine [9]; and 1.340 (2), 1.345 (2) Å in

3-aminopyridine [10]. There is a good agreement between corresponding mean values of C–C–C and C–C–N bond angles and C–N–C bond angles in molecules A and B of 2APy. The bond angles in 2APy are not unusual from those observed in $2APy \cdot 2H_2O$ and are also



(a)

FIGURE 3 (a) H-bond network in the crystal structure of 2APy viewed along *a*-axis. The broken lines depict H-bonds; (b) H-bond network in the crystal structure of $2APy \cdot 2H_2O$. Broken lines depict H-bonds; (c) View of the chains formed by the water molecules in $2APy \cdot 2H_2O$. The 2APy molecules are omitted for clarity. Broken lines depict H-bonds.



(b)

(c)

FIGURE 3 Continued.

generally not significantly different from those observed in 2-amino-5-chloropyridine [8], 2-aminopyridine [9], and 3-aminopyridine [10]. In the pyridine ring of 2APy, the bond angles in molecules A and B are in the range from 116.7 (2) to 121.3 (3)° for C–C–C, from 122.1 (2) to 123.9 (2)° for C–C–N, and from 112.6 (2) to 114.2 (4)° for N–C–N. In $2APy \cdot 2H_2O$, they are from 116.6 (1) to 121.2 (3)° for C–C–C, from 123.8 (3) to 123.9 (6)° for C–C–N, and from 110.9 (1) to 111.4 (4) ° for N–C–N. The amide nitrogen-to-ring (C–N) bond length in 2APy has distances 1.391 (3), 1.410 (3) Å for molecule A, 1.390 (3), 1.410 (5) Å for molecule B, and 1.412 (1), 1.420 (2) Å for $2APy \cdot 2H_2O$ and are longer than the distance given for C–N bonds in 3-aminopyridine 1.350 (2) Å [10] and 4-aminopyridine 1.363 (2) Å [11] but comparable with 1.4302 (1) Å distance given for N–C single bonds [12]. The pyridine ring is planar in both molecules A and B of 2APy and $2APy \cdot 2H_2O$; the deviations of the carbon and nitrogen atoms from their least-squares plane are all less than or equal to 0.005 Å for 2APy and 0.004 Å for $2APy \cdot 2H_2O$. The amide N atoms in 2APy as well as those in $2APy \cdot 2H_2O$ all virtually lie in the ring plane. The O atoms of the amide group and C atoms of the ethyl groups in $2APy \cdot 2H_2O$ are nearly coplanar with the ring, but in 2APy the corresponding atoms deviate significantly (0.080 Å) from the ring plane.

In the ethyl-amide chain, the C–C and C–N bond lengths in molecules A and B of 2APy and $2APy \cdot 2H_2O$ have normal geometry. The mean C–C bond lengths are 1.490 (2) Å for molecule A and 1.470 (6) Å for molecule B and 1.500 (2) Å for $2APy \cdot 2H_2O$. The mean C–N bond length in both molecules A and B, and also in $2APy \cdot 2H_2O$, are consistent with each other (1.360 (2) Å). The dihedral angles in ethyl-to-amide chain are in the range of $180 \pm 30°$.

In Fig. 3a, the 2APy molecules arrange themselves in an intriguing fashion that enhances hydrogen bonding network between neighboring 2APy molecules. The pyridine moiety in the 2APy molecules are arranged in a wave-like fashion along the direction of *b*-axis. The packing structure of the alkyl chains are dependent on the packing fashion of the neighboring pyridine moiety of the 2APy molecules. In Fig. 3b, the presence of water molecules does not change the wave-like arrangement of the pyridine moiety in $2APy \cdot 2H_2O$ along the direction of *b*-axis. However, the arrangement of the alkyl chains are different from those observed in 2APy.

The substantial interactions between the molecules in 2APy and those in $2APy \cdot 2H_2O$ are driven by hydrogen bonding and are highly orientation dependent. Because the hydrogen atoms of 2APy and those of water molecules were not located in the Fourier difference map, the criterion for hydrogen bonding was based on the short contact distances between non-H atoms with values less than the sum of their van der Waals radii. Thus in 2APy (Fig. 3a), the hydrogen bonds formation exists between N1′···O2 3.03 (3) Å, N1···O2′ 2.98 (3) Å. These values are in the normally accepted range for a typical N···O=C bonding [13–18]. In 2APy · $2H_2O$ (Fig. 3b), the distances of the hydrogen bonds are N···Ow, (2.98 (1)–3.02 (1) Å), Ow···Ow′ (2.81 (1)–3.01 (1) Å), C=O···Ow (2.81 (4)). The C=O···Ow value is shorter than those of Ow···Ow′ (2.91 (2) Å). This can be attributed to the effect of stronger repulsive interactions in Ow···Ow′ than in O···Ow. The water molecules (Ow, Ow′) are connected via O···O hydrogen bonds to form two chains in a one-dimensional array along the direction of *c*-axis, built of two crystallographically independent water molecules (Fig. 3c). The differences in the kind of hydrogen bonding networks in both crystals contribute to the differences in the packing modes observed in 2APy and 2APy · $2H_2O$. The driving force behind the molecular aggregation of 2APy is mainly N···O = C hydrogen bonding, whereas those of 2APy · $2H_2O$ are N···Ow, C=O···Ow, and Ow···Ow′ hydrogen bonding. In both compounds, analysis of probable van der Waals contacts between carbon atoms of two pyridine moieties or those of alkyl chains which lie close to each other revealed that no short contacts of the nonbonded C···C atoms existed. It is worth mentioning that hydrophobic interactions between the alkyl chains in both compounds are not significantly pronounced.

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