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Title: **Two polymorphs of *N*-phenylpyridin-4-amine**

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Abstract

The title compound, *N*-phenylpyridin-4-amine, forms two polymorphs I and II which were obtained from acetonitrile or tetrahydrofuran, respectively. The molecular structures in both polymorphs are similar one another. The pyridyl rings show better conjugation with the lone pairs of the nitrogen atom than phenyl rings. In both polymorphs, the molecules also form a similar sheet structure in which they make zigzag hydrogen bonds. Judged by powder XRD analysis, polymorph I was considered to be the most stable phase at room temperature.

Key words: polymorph; DFT calculation; pyridylamine; hydrogen bond; C-H... π interaction

1. Introduction

Crystal polymorphs play a crucial role especially on the pharmaceutical industry [1], and several factors, such as intermolecular interaction or condition for crystallization, have significant effects upon formation of polymorphs. It is also well known that molecular crystals having intermolecular hydrogen bonds tend to show crystal polymorphism owing to wide variation of their hydrogen-bonding patterns.

The title compound, $C_{11}H_{10}N_2$, is a 4-aminopyridine derivative, which was first prepared by Koenigs and Heinz [2], and has been an important raw material for agricultural chemicals. 4-aminopyridines and their protonated species have been mainly used as a ligand or a counter cation for metal-organic complexes. There are some polymorphs among these complexes [3-7], while only a few examples have been reported as their own crystals [8-10]. Here we wish to report two crystal polymorphs, (I) and (II), originating in weak $C-H\cdots\pi$ interactions, which is an unusual case in $N-H\cdots N$ hydrogen bonded crystals.

2. Results and Discussion

2-1 Crystal Structure of Polymorph I

Recrystallization from an acetonitrile solution of the title compound gave polymorph I as shown in Figure 1. It could be also obtained by recrystallization from ethanol or acetone. Crystal data and geometrical parameters for polymorph I are summarized at Table 1 and Table 2, respectively.

There are two independent molecules (IA, IB) in the asymmetric unit. In IA, the dihedral angles of the N1/C1/C7 plane with the C1-C6 phenyl and the N2/C7-C11 pyridyl rings are $41.05(3)^\circ$ and $5.48(3)^\circ$. In IB, the dihedral angles of the N3/C12/C18 plane with the C12-C17 phenyl and the N4/C18-C22 pyridyl rings are $41.31(3)^\circ$ and $6.35(3)^\circ$. In both molecules, the electron-deficient pyridyl rings make good conjugation with the lone pairs of the nitrogens. This tendency is usually recognized at diphenylamine derivatives [11-13].

In I, the molecules form a sheet structure parallel to the (1 0 -1) plane, where either IA or IB makes individual sheets (Figures 2 and 3). The molecules make one-dimensional zigzag hydrogen-bonding chains along the [1 0 1] direction. The

intermolecular distances of N-H...N are 2.006(16) Å and 1.997(15) Å as summarized in Table 3, indicating more than 25 % in shrinkage compared with the sum of van der Waals radii. There are weak van der Waals contacts, which expand 1-D chain structure into 2-D sheet structure. Some C-H... π interactions are observed between the sheets as shown in Figure 4 which make 3D arrangement of the molecules.

2-2 Crystal Structure of Polymorph II

The polymorph II was given by recrystallization from a tetrahydrofuran solution as shown in Figure 5. Crystal data and geometrical parameters for polymorph II are also summarized at Table 1 and Table 2, respectively. It could be also obtained by recrystallization from methanol, and consists of two independent molecules (IIA, IIB) in the asymmetric unit, whose structures are very similar to those of polymorph I. The dihedral angles of the N1/C1/C7 plane in IIA with the C1-C6 phenyl and the N2/C7-C11 pyridyl rings are 42.45(7)° and 6.59(7)°. In IIB, the dihedral angles of the N3/C12/C18 plane with the C12-C17 phenyl and the N4/C18-C22 pyridyl rings are 38.44(7)° and 4.72(7)°.

As well as polymorph I, the molecules in II form a sheet structure (Figure 6), which

consists of both molecules and is parallel to the *ab* plane. The molecules make one-dimensional zigzag hydrogen-bonding chains along the *a* axis. The intermolecular distances of N-H...N are 2.06(2) Å and 2.06(3) Å as listed in Table 4. There are also weak van der Waals contacts between the molecules, which expand in 2-D sheet structure, and the sheets are connected by some C-H... π interactions as shown in Figure 7, making 3D arrangement of the molecules.

2-3 Comparison between the obtained structures

There are almost no significant differences in the molecular and structures between I and II. A difference is manner of sheet formation, namely individual sheets are formed in I, while shared sheets are constructed in II. Another difference exists in intersheet C-H... π interactions which are thought to connect the sheets in polymorph I slightly stronger than those in polymorph II.

Polymorph II has a slightly larger calculated density (1.292 g cm⁻³) than polymorph I (1.289 g cm⁻³), but polymorph I shows higher melting point (450 K) than that of polymorph II (448 K). A phase transition between two was not detected by DSC measurements. Powder XRD chart of the title compound formed by solidification from

a molten state of both polymorphs gave that of polymorph I. Therefore polymorph I was considered to be the most stable phase at room temperature.

To the best of our knowledge, similar six examples [14-21] were found on the CSD [22] where the compounds have polymorphs and strong secondary amino N-H...N(pyridine) hydrogen bonds. The difference in hydrogen-bonding pattern makes polymorphs in all examples. While the polymorphs of the title compound have similar hydrogen-bonding pattern, and it was thought to be an unusual case in hydrogen bonded crystals. This is presumably because the strong N-H...N hydrogen bonds mainly govern the local orientation of the molecules.

2-4 DFT calculation

DFT calculation of *N*-phenylpyridin-4-amine was performed by B3LYP 6-31G (*d*, *p*) level. The geometrical parameters were summarized at Table 2. The optimized structures are shown in Figure 8. The bond distances and angles of the optimized structure were almost consistent with those observed structures. However, the dihedral angles of the plane formed by the amino nitrogen and the adjacent two carbon atoms with the phenyl and the pyridyl rings are estimated to be ca. 30° and 14°, showing some

differences from the observed ones. The interchain and/or intersheet interactions are considered to make such differences.

3. Conclusion

We succeeded in crystallographical analyses of two polymorphs (I, II) of *N*-phenylpyridin-4-amine, depending on the recrystallization solvents. Judged by powder XRD analysis, it was found that either crystal could be obtained independently and that polymorph I was considered to be the most stable phase at room temperature.

The molecular structures in both polymorphs are similar one another and the pyridyl rings show better conjugation with the lone pairs of nitrogen than phenyl rings. The molecules also form a similar sheet structure in which they make zigzag hydrogen bonds. This is presumably because the strong N-H...N hydrogen bonds mainly govern the local orientation of the molecules. In contrast, weak interlayer C-H... π interactions were found to make these polymorphs.

The optimized structure reproduces the molecular structures well, but some differences were detected at the dihedral angles of the amino plane with the two aryl

rings because of the interchain and intersheet interactions.

4. Experimental Part

The title compound was purchased from Tokyo Chemical Industry Co., Ltd. The single crystals efficient quality for X-ray structural analyses were obtained from recrystallization from acetonitrile for (I) or tetrahydrofuran for (II).

X-ray crystallographic data were collected with a RIGAKU Saturn 724+ CCD device by using multi-layered mirror monochromatic Mo $K\alpha$ radiation at -180 °C. For II, Friedel pairs were merged because the molecule itself was achiral and because there were not any anomalous scattering effects. Both refinements were performed using all reflections except for one with very negative F^2 of each crystal. The weighted R -factor (wR) and goodness of fit (S) are based on F^2 . R -factor (gt) is based on F . The threshold expression of $F^2 > 2.0 \sigma(F^2)$ is used only for calculating R -factor (gt).

Both structures were solved by a direct method (ShelxD) [23], and were refined by full-matrix least squares method (Shelxl97) [24]. The positions of non-H atoms were obtained from a difference Fourier map and were refined anisotropically. The C-bound

H atoms were placed at ideal positions and were refined as riding on their parent C atoms. $U_{\text{iso}}(\text{H})$ values of the H atoms were set at $1.2U_{\text{eq}}(\text{parent atom})$. The N-bound H atoms were obtained from a difference Fourier map and were refined isotropically. In II, the restriction (the DFIX instruction of *SHELXL97*) of N-H range between 0.84 Å and 0.88 Å was applied.

Powder X-ray diffraction (PXRD) data were recorded on a RIGAKU MiniFlex II diffractometer with a monochromatic Cu K α radiation at ambient temperature. The solidified samples were prepared by annealing from a melt at a rate of -2.5 °C / min and holding at room temperature for a day.

Differential scanning calorimetry (DSC) measurements were carried out by a SHIMADZU DSC-50 calorimeter. DFT calculation of *N*-phenylpyridin-4-amine was performed on the Spartan 04 software [25] with B3LYP 6-31G (*d,p*) level.

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Figure 1. The asymmetric unit of polymorph I compound with atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres.

Figure 2. A view of the sheet structure formed by IA. [Symmetry codes: (i) $x-1/2, -y+3/2, z-1/2$ (ii) $x+1/2, -y+3/2, z+1/2$.] Red and blue dashed lines indicate intermolecular hydrogen bonds and interchain interactions, respectively.

Figure 3. A view of the sheet structure formed by IB. [Symmetry codes: (i) $x-1/2, -y+3/2, z-1/2$ (ii) $x+1/2, -y+3/2, z+1/2$.] Red and blue dashed lines indicate intermolecular hydrogen bonds and interchain interactions, respectively.

Figure 4. A view of intersheet interactions in polymorph I. [Symmetry codes: (i) $x, y, z-1$ (ii) $-x+1, -y+1, z+2$ (iii) $-x, -y+1, z+2$.] Blue dashed lines show intersheet C-H $\cdots \pi$ interactions.

Figure 5. The asymmetric unit of polymorph II with atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres.

Figure 6. A view of the sheet structure formed by IIA and IIB. [Symmetry codes: (i) $x-1/2, -y, z$ (ii) $x+1/2, -y+1, z$ (iii) $x+1/2, -y, z$ (iv) $x-1/2, -y+1, z$.] Red and blue dashed lines indicate intermolecular hydrogen bonds and interchain interactions, respectively.

Figure 7. A view of interlayer interactions in polymorph II. [Symmetry codes: (i) $-x+1/2, y, z+1/2$ (ii) $-x+3/2, y, z-1/2$.] Blue dashed lines show intersheet C-H $\cdots \pi$ interactions.

Figure 8. The optimized structure of the title compound.

Table 1. Crystal data and refinement details for polymorphs I and II.

Compounds	I	II
Empirical formula	$C_{11}H_{10}N_2$	
Formula weight	170.21	
Crystal system	<i>Monoclinic</i>	<i>Orthorhombic</i>
Crystal size	$0.20 \times 0.10 \times 0.10$	$0.16 \times 0.07 \times 0.06$
Crystal color	Colorless	
Space group	$P2_1/n$	$Pca2_1$
a (Å)	9.6547(19)	11.985(3)
b (Å)	19.330(4)	19.582(5)
c (Å)	9.681(2)	7.4569(17)
α (°)	90	90
β (°)	103.940(3)	90
γ (°)	90	90
V (Å ³)	1753.5(7)	1750.1(7)
Z	8	8
D_x (Mg/m ³)	1.289	1.292
μ (mm ⁻¹)	0.08	0.08
Theta range for data collection	2.1 – 31.3	2.0 – 31.2
Limiting indices	$-12 \leq h \leq 13, -26 \leq k \leq 25, -13 \leq l \leq 12$	$-16 \leq h \leq 13, -26 \leq k \leq 26, -10 \leq l \leq 9$
Reflections collected/unique	15862/4666 ($R_{int} = 0.028$)	15381/2505 ($R_{int} = 0.052$)
Reflections with $I > 2\sigma(I)$	3802	2318
Refined parameters/restraints	243/0	243/3
Goodness of Fit on F^2	1.09	1.08
R_1, wR_2	0.047, 0.127	0.052, 0.132
Data completeness	0.998	0.999
Data/restraints/parameters	4665/0/243	2318/3/243
Max. and min. transmission	0.992 and 0.988	0.995 and 0.986
Largest diff. peak and hole	0.34 and -0.22	0.29 and -0.23

Table 2. Selected experimental and calculated geometric parameters ($\text{\AA}$, $^\circ$) of *N*-phenylpyridin-4-amine.

	IA	IB	IIA	IIB	Cal. ^a
N1-C1, N3-C12	1.4076(16)	1.4093(16)	1.410(3)	1.412(3)	1.406
N1-C7, N3-C18	1.3700(14)	1.3727(14)	1.371(3)	1.378(3)	1.386
N2-C9, N4-C20	1.3429(16)	1.3422(16)	1.338(4)	1.345(4)	1.399
N2-C10, N4-C21	1.3478(15)	1.3491(15)	1.352(4)	1.354(3)	1.341
C1-C2, C12-C13	1.3985(17)	1.4004(17)	1.398(4)	1.400(4)	1.404
C1-C6, C12-C17	1.3957(16)	1.4004(16)	1.399(4)	1.397(4)	1.404
C2-C3, C13-C14	1.3889(17)	1.3879(17)	1.397(4)	1.386(4)	1.392
C3-C4, C14-C15	1.3898(17)	1.3921(17)	1.385(4)	1.383(4)	1.396
C4-C5, C15-C16	1.3885(17)	1.3925(17)	1.392(4)	1.390(4)	1.395
C5-C6, C16-C17	1.3885(17)	1.3865(17)	1.390(4)	1.385(4)	1.394
C7-C8, C18-C19	1.4053(15)	1.4065(15)	1.405(4)	1.402(4)	1.406
C7-C11, C18-C22	1.4062(17)	1.4073(17)	1.404(3)	1.398(4)	1.408
C8-C9, C19-C20	1.3814(16)	1.3822(16)	1.384(4)	1.388(4)	1.392
C10-C11, C21-C22	1.3821(16)	1.3751(16)	1.367(4)	1.380(4)	1.388
C1-N1-C7, C12-N3-C18	126.76(10)	126.48(9)	126.44(19)	127.3(2)	129.65
C9-N2-C10, C20-N4-C21	115.08(10)	115.02(10)	115.1(2)	114.7(2)	115.66
C1-N1-C7-C11	176.65(11)	-	175.5(2)	-	166.66
C12-N3-C18-C22	-	-175.66(10)	-	-177.6(3)	-

^a *B3LYP 6-31G(d,p) level.*

Table 3. Hydrogen-bonding geometry (Å, °) for polymorph I.

D–H...A	d(D–H)	d(H...A)	d(D...A)	∠ DHA
N1–H1...N2 ⁱ	0.925(16)	2.006(16)	2.9305(14)	177.5(18)
N3–H7...N4 ⁱⁱ	0.946(15)	1.997(15)	2.9417(14)	176.8(16)

Symmetry codes: (i) $x-1/2, -y+3/2, z-1/2$ (ii) $x+1/2, -y+3/2, z+1/2$.

Table 4. Hydrogen-bonding geometry (Å, °) for polymorph II.

D–H...A	d(D–H)	d(H...A)	d(D...A)	∠ DHA
N1–H1...N2 ⁱ	0.87(2)	2.06(2)	2.927(3)	177(3)
N3–H7...N4 ⁱⁱ	0.90(3)	2.06(3)	2.955(3)	177(3)

Symmetry codes: (i) $x-1/2, -y, z$ (ii) $x+1/2, -y+1, z$.