



CRYSTAL STRUCTURE OF 2-BROMO-4-HYDROXYPYRIDINE: HYDROGEN AND HALOGEN BONDING

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Keywords: crystal structure; hydrogen bonding; halogen bonding.

The crystal structure of 2-bromo-4-hydroxypyridine (**1**) at 120 K is reported. The compound crystallizes in the monoclinic space group $C2/c$ with $a = 15.6770(6)$ Å, $b = 3.86471(13)$ Å, $c = 18.0645(7)$ Å and $\beta = 90.916(3)^\circ$. The compound exhibits both the 4-hydroxypyridine and 4-pyridone tautomers as exhibited by the disordered proton which occupies the O-H and N-H positions equally. Hydrogen bonding links the molecules into chains parallel to the ac -face diagonal. Halogen bonds [Br ... O = 3.0809(15) Å] roughly parallel to the a -axis link the chains into layers roughly parallel to the bc -face diagonal. π -stacking interactions complete the stabilization of the structure.

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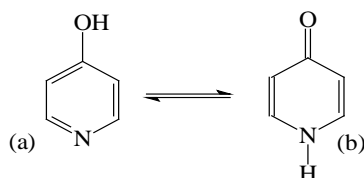
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pyridine. An investigation of the literature showed only two reported crystal structures involving such a potential ligand and both are esterified at the O-atom.⁹ Here we report the crystal structure of 2-bromo-4-hydroxypyridine.

Introduction

2- and 4-Hydroxypyridine molecules are known to be in equilibrium with their tautomeric pyridone forms as shown in Scheme 1.



Scheme 1. The tautomeric forms of (a) 4-hydroxypyridine and (b) 1(H)-4-pyridone.

The crystal structure of the parent compound shows it to be in the 1(H)-4-pyridone form in the solid state, with two polymorphs reported.¹ The tautomerizable hydrogen atom was located in the lattice and its position refined to clearly demonstrate the tautomer present. The molecules are linked into chains via strong hydrogen bonds ($d_{N-H...O} = 2.66$ Å). As a result of the possibility of different tautomers, multiple coordination modes are available to the ligand. Coordination in the pyridone form through the O-atom is clearly preferred and multiple compounds have been reported with the O-coordinated to both transition metal² and lanthanide ions.³ The O-atom is also known to bridge alkali earth metal,⁴ transition metal⁵ and lanthanide metal ions.⁶ Some coordination complexes are known with the molecule N-coordinated in the hydroxypyridine form, but most of these involve 2nd and 3rd row transition metal ions.⁷

We have become interested in the use of hydroxypyridine/pyridone molecules as ligands⁸ in particular because of the potential for hydrogen bonding and related intermolecular interactions assisting in the stabilization of extended lattices. One such system is 2-halo-4-hydroxy-

Experimental

2-Bromo-4-hydroxypyridine was purchased from Ark Pharmaceutical and recrystallized from methanol.

X-Ray structure analysis

Data for **1** were collected using an Agilent Technologies Gemini Eos CC X-ray diffractometer with Mo $K\alpha$ radiation ($\lambda = 0.71073$ Å). Data reduction and correction for Lp and decay were performed using CrysAlisPro.¹⁰ A Gaussian absorption correction was applied via ABSPACK.^{Hiba! A könyvjelző nem létezik.} The structure was solved using the SHELXS-97 program¹¹ and refined via least-squares analysis via SHELXL-2016.¹² Non-hydrogen atoms were refined using anisotropic thermal parameters. Hydrogen atoms bonded to nitrogen and oxygen atoms were located in the difference Fourier maps and their positions refined using fixed isotropic thermal parameters. Antibumping restraints were applied to both N11-H11 and O14-H14 to avoid unrealistically short bond lengths. The remaining hydrogen atoms were placed in geometrically calculated positions and refined using a riding model and fixed isotropic thermal parameters. Crystallographic information and details of the data collection can be found in Table 1.

Results

Compound **1** crystallizes in the monoclinic space group $C2/c$. The molecular unit is shown in Figure 1. The tautomerizable proton (H11/H14) is disordered over the two positions. The occupancy was allowed to refine freely and resulted in equal occupancies for the two sites [0.50(3)]. This suggests equal contributions to the structure from the 4-hydroxypyridine and 4-pyridone forms of the molecule.

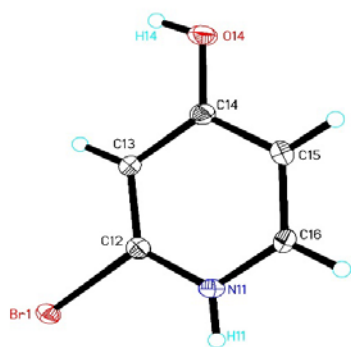


Figure 1. Thermal ellipsoid plot of the molecular unit of **1** showing 50% probability ellipsoids. Only the asymmetric unit and those H-atoms whose positions were refined are labelled.

This is further supported by the packing of the molecules in the lattice. Hydrogen bonding generates chains of molecules parallel to the *ac*-face diagonal in an alternating head-to-head/tail-to-tail fashion (Figure 2). The hydrogen bonding parameters are presented in Table 3.

Table 1. X-ray data of compound **1**.

Empirical formula	C₅H₄BrNO
Formula weight	174.00
Temperature	120.0(1) K
Wavelength	0.71073 Å
Space group	<i>C2/c</i>
<i>a</i>	15.6770(6) Å
<i>b</i>	3.86471(13) Å
<i>c</i>	18.0645(7) Å
α	90°
β	90.916(3) °
γ	90°
Volume	1094.34(7) Å ³
<i>Z</i>	8
Density (calculated)	2.112 Mg m ⁻³
Absorption coefficient	7.392 mm ⁻¹
<i>F</i> (000)	672
Crystal size	0.21 x 0.10 x 0.06 mm ³
θ range for data collection	5.179 to 26.35°
Index ranges	-19 ≤ <i>h</i> ≤ 19 -4 ≤ <i>k</i> ≤ 4 -22 ≤ <i>l</i> ≤ 22
Reflections collected	5856
Independent reflections	1112 [<i>R</i> (int) = 0.0300]
Absorption correction	Gaussian
Max. and min. transmission	0.960 and 0.887
Refinement method	Full-matrix least-squares on <i>F</i> ²
Data / restraints / parameters	1112 / 2 / 80
Goodness-of-fit on <i>F</i> ²	1.059
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	<i>R</i> ¹ = 0.0172, <i>wR</i> ₂ = 0.0396
<i>R</i> indices (all data)	<i>R</i> ¹ = 0.0191, <i>wR</i> ₂ = 0.0404
Largest diff. peak and hole	0.335 and -0.311 e Å ⁻¹

Adjacent molecules are related either by an inversion center (O14/O14B) or a two-fold axis (N11/N11A). The apparent double hydrogen bonds seen in Figure 2 are the result of the disorder of the hydrogen atom position.

Table 2. Selected bond lengths [Å] and angles [°] for **1**.

Bond	Distance (Å)
N11-H11	0.82(2)
O14-H14	0.81(2)
C14-O14	1.296(2)
Bond	Angle (°)
C12 N11 C16	117.67(17) 116.94(18)
C15 C14 C13	
O14 C14 C13	122.77(19)
O14 C14 C15	120.29(18)

In each case either H14 or H14B/H11 or H11A are present, but not both. Given the need to have one entire hydrogen atom present in each position to complete the hydrogen bonding, this suggests that in any given chain only one position is occupied, i.e. either H1A and H14, or H1 and H14B and that the chains are then unidirectional with respect to the orientation of the hydrogen atoms.

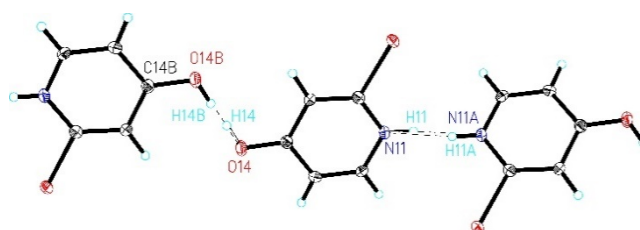


Figure 2. Chain formation via hydrogen bonding in **1**.

However, which chain is oriented in which direction must be random over the lattice, thus generating the disorder. In fact, the structure can be refined by locating the hydrogen atoms on their respective symmetry centers, but that results in unrealistically long O-H and N-H bonds.

Table 3. Hydrogen bonding parameters for **1**.

D-H...A	D-H (Å)	H...A(Å)	D...A(Å)	D-H...A(°)
N11-H11-N11A	0.82(2)	1.93(2)	2.756(3)	174(5)
O14-H14-O14B	0.81(2)	1.71(2)	2.521(3)	172(7)

Symm. op.: A, -*x*, *y*, ½ - *z*; B, -*x* - 1/2, ½ - *y*, 1 - *z*.

The molecule itself is nearly planar with a mean deviation of 0.0191 Å for the atoms within the ring. The oxygen and bromine atoms are displaced slightly to opposite sides of the plane of the ring (-0.0840 Å and 0.0237 Å respectively). The chains are linked into a complex system of interconnected pleated sheets via halogen bonds between the bromine atoms and adjacent oxygen atoms [*d*_{Br1...O14A} = 3.0809(15) Å, ∠_{C12-Br1...O14A} = 176.31(7)°, symm. op. A = ½ + *x*, *y* - ½, *z*]. The resulting layers are further connected into a three-dimensional motif via π -stacking interactions and short Br...Br contacts parallel to the *b*-axis as shown in Figure 4. The interplanar distance between rings is 3.43(1) Å and the slip angle (the angle between the intercentroid axis and the normal to the plane) is 27°. The ring centroids and Br atoms are related by a unit cell translation and are separated by 3.864 Å, corresponding to the *b*-axis length.

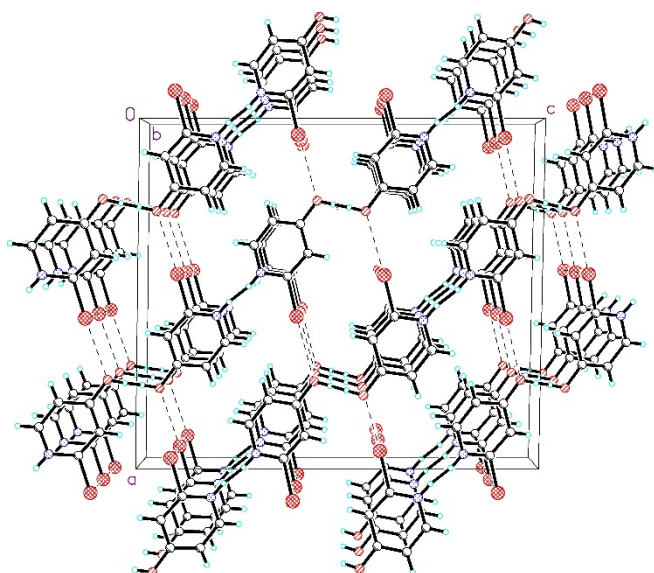


Figure 3. Packing of **1** viewed parallel to the *b*-axis showing the alternating layer structure.

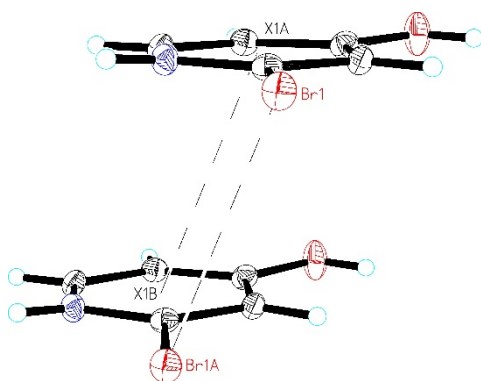


Figure 4. π -stacking between the pyridine rings of **1**. Dashed lines show connections between the ring centroids and short Br...Br contacts.

Discussion

The intermolecular interactions present in the 2-bromo-4-hydroxypyridine molecule make it a strong potential candidate for directing self-assembly of coordination complexes into three-dimensional lattices. The tautomeric forms provide the opportunity for coordination to the metal ions through either the N- or O-atoms. Hydrogen bonding between molecules is strong with D...A distances as short as 2.521(3) Å. The presence of the bromine atom makes distinct changes to the crystal structure. In the parent molecule, strong head-to-tail hydrogen bonding (D...A = 2.657 Å)^{Hiba! A könyvjelző nem létezik.} is observed in both polymorphs in contrast to the head-to-head/tail-to-tail form observed in **1**. Further, the halogen bonds (Br...O) in **1** form in linkages between the chains resulting in a sheet structure, while the parent molecule exhibits only chains. Halogen bonding is known to compete effectively with hydrogen bonding in several systems.¹³

However, coordination of the N-atom to a metal ion will eliminate that as a potential hydrogen bonding site. Further, the presence of additional hydrogen bonding partners may disrupt the hydrogen bonding between ligand molecules as seen in the structure of 4-hydroxypyridine hydrate.¹⁴ In this structure, there are several crystallographically independent molecules, most of which form the same head-to-tail hydrogen bonded dimers as seen in the parent molecule with additional hydrogen bonds to water molecules via the hydroxypyridine O-atom. In addition, there are 4-hydroxypyridine molecules in the lattice which exhibit only hydrogen bonding to water, generating a distinct chain structure of organic species alternating with pairs of water molecules.

Conclusions

It is clear that substitution of a bromine atom in the 2-position of 4-hydroxypyridine makes a distinct change in the structure of the material in the solid state. In addition to introducing halogen bonding, the conversion of the head-to-tail dimer structure normally seen in 4-hydroxypyridine to the head-to-head/tail-to-tail variety introduces new possibilities for the control of intermolecular forces in complexes of such ligands. Investigations of the corresponding 2-chloro compound are in progress.

Acknowledgements

MMT is grateful for the hospitality of the Chemistry Department at the University of Canterbury, Christchurch, New Zealand.

Supplementary data

CCDC 1921754 contains the supplementary crystallographic data for **1**. This data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/con-fts/retrieving.html>, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or email: deposit@ccdc.cam.ac.uk.

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Received: 10.06.2019

Accepted: 02.07.2019