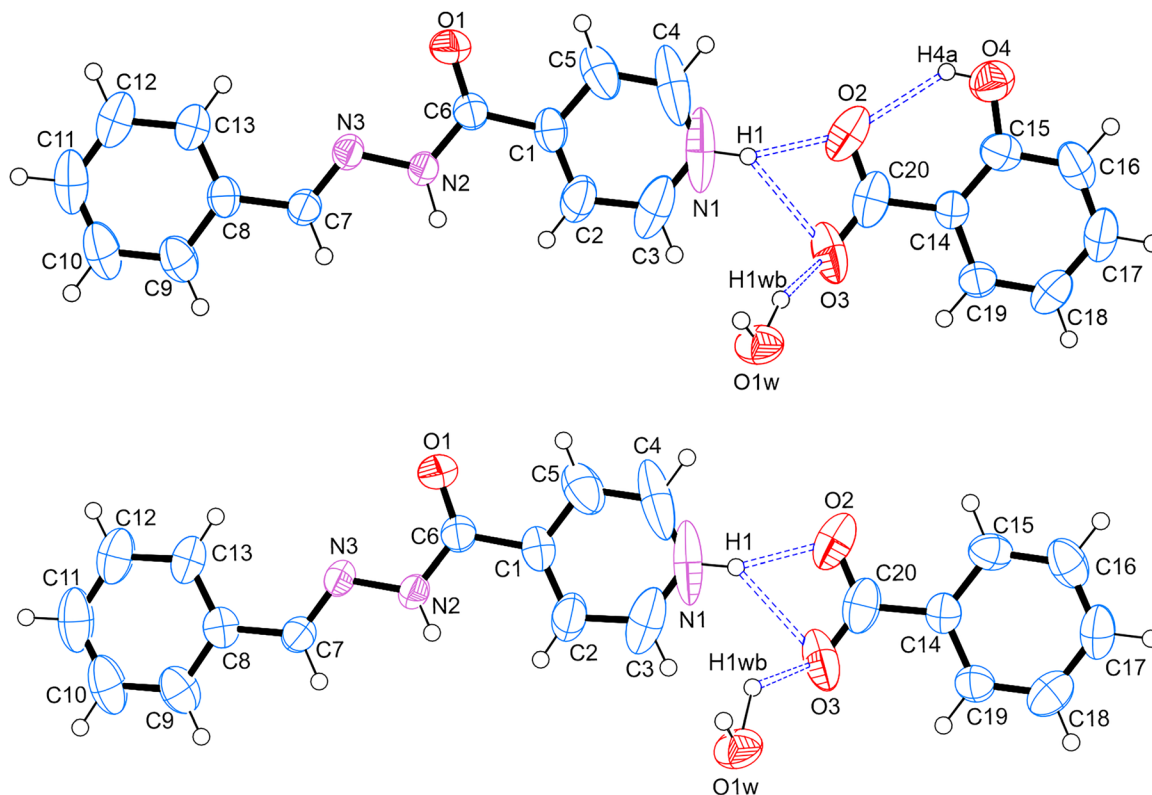


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The hydrated double salt structure of (E)-4-(2-benzylidenehydrazine-1-carbonyl)pyridin-1-ium cation with 2-hydroxybenzoate and benzoate anions



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Abstract

$2(\text{C}_{13}\text{H}_{12}\text{N}_3\text{O})^+, 2(\text{C}_7\text{H}_4.5\text{O}_2.5)^-, 2(\text{H}_2\text{O})$, orthorhombic, *Pbca* (no. 61), $a = 8.2775(5) \text{ \AA}$, $b = 12.6054(9) \text{ \AA}$, $c = 35.082(2) \text{ \AA}$, $V = 3,660.5(4) \text{ \AA}^3$, $Z = 4$, $R_{\text{gt}}(F) = 0.0663$, $wR_{\text{ref}}(F^2) = 0.1864$, $T = 173 \text{ K}$.

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1 Source of materials

To synthesize the title compound, 0.23 g (167 mmol) isonicotinic acid hydrazide and 0.23 g (166 mmol) salicylic acid were weight out in a Dram vial and dissolved in 3 mL benzaldehyde. The vial was closed tightly and reacted at 333 K, and stirred at 300 rpm for 24 h. The solution was

Table 1: Data collection and handling.

Crystal:	Colourless needles
Size:	$0.42 \times 0.27 \times 0.03$ mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.10 mm ⁻¹
Diffractometer, scan mode:	Bruker D8 Venture Photon, ω
$\theta_{\max}$, completeness:	25.7°, >99 %
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$:	28,159, 3,482, 0.083
R_{int} :	
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2\sigma(I_{\text{obs}})$, 2,434
$N(\text{param})_{\text{refined}}$:	267
Programs:	Bruker, ¹ SHELX, ^{2,3} WinGX/ORTEP, ^{4,5} PLATON ⁶

allowed to slowly evaporate at ambient temperatures between 298 and 300 K. Colourless needles were formed at the bottom of the vial after six weeks (Tables 1 and 2).

2 Experimental details

The C-bound hydrogen atoms were located in the difference map, then positioned geometrically. They were then allowed to ride on their respective parent atoms with thermal displacement parameters 1.2 times of the parent C atom. The coordinates and isotropic displacement parameters of the two N-bound and O-bound H atoms, namely H1 and H4A, were constrained to their parent atoms using the riding model approximation appropriate for their respective geometries. The other O and N-bound hydrogen atoms were allowed to refine freely. Diagrams and publication material were generated using ORTEP-3,⁴ WinGX⁵ and PLATON.⁶

3 Comment

Isonicotinic acid hydrazide (INH), commonly known as isoniazid is an anti-mycobacterial agent that is primarily used as a tuberculostatic drug and remains the first choice in the treatment of latent tuberculosis (TB).⁷ Isoniazid has a simple structure and contains two essential components, namely the hydrazide group and a pyridine ring, both which are required for anti-mycobacterial activity.⁸ This drug is commonly used to treat pulmonary and extra pulmonary TB infections and is also utilized as a chemoprophylaxis therapy to prevent or delay the appearance of microbial resistance.⁹ Many derivatives of the compound isoniazid have been synthesized over the years to counteract resistance of the mycobacterium species. These include the design of new compound derivatives such as isonicotinoylhydrazone with

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.6866 (3)	0.5026 (3)	0.53410 (7)	0.0470 (7)
C2	0.6477 (5)	0.3974 (3)	0.53390 (9)	0.0669 (10)
H2	0.684206	0.351752	0.514132	0.08*
C3	0.5527 (5)	0.3591 (4)	0.56373 (12)	0.0899 (15)
H3	0.522484	0.286376	0.5638	0.108*
C4	0.5434 (6)	0.5200 (6)	0.59176 (12)	0.113 (2)
H4	0.508254	0.563934	0.61215	0.135*
C5	0.6326 (5)	0.5640 (4)	0.56407 (9)	0.0748 (11)
H5	0.658724	0.63735	0.565084	0.09*
C6	0.7850 (3)	0.5570 (2)	0.50425 (7)	0.0433 (7)
C7	0.9367 (3)	0.4959 (2)	0.41461 (8)	0.0437 (7)
H7	0.895479	0.425757	0.412776	0.052*
C8	1.0349 (3)	0.5387 (2)	0.38367 (7)	0.0448 (7)
C9	1.0739 (4)	0.4727 (3)	0.35318 (8)	0.0598 (9)
H9	1.034625	0.401912	0.352506	0.072*
C10	1.1702 (4)	0.5104 (4)	0.32380 (10)	0.0762 (12)
H10	1.196917	0.465278	0.30305	0.091*
C11	1.2265 (4)	0.6119 (4)	0.32461 (10)	0.0784 (13)
H11	1.292833	0.637168	0.304462	0.094*
C12	1.1876 (4)	0.6785 (3)	0.35458 (10)	0.0699 (10)
H12	1.226805	0.749376	0.354901	0.084*
C13	1.0912 (4)	0.6418 (3)	0.38424 (8)	0.0531 (8)
H13	1.064151	0.687461	0.404813	0.064*
C14	0.1871 (3)	0.2487 (2)	0.68575 (7)	0.0424 (6)
C15	0.1297 (4)	0.3125 (3)	0.71500 (9)	0.0520 (7)
C16	0.0320 (4)	0.2677 (3)	0.74297 (9)	0.0638 (10)
H16	-0.008676	0.31095	0.762954	0.077*
C17	-0.0060 (4)	0.1629 (3)	0.74210 (9)	0.0691 (10)
H17	-0.074024	0.133686	0.76121	0.083*
C18	0.0541 (4)	0.0986 (3)	0.71351 (10)	0.0668 (9)
H18	0.029703	0.024977	0.713283	0.08*
C19	0.1492 (4)	0.1418 (2)	0.68541 (8)	0.0505 (7)
H19	0.189336	0.097864	0.665554	0.061*
C20	0.2852 (4)	0.2927 (3)	0.65401 (10)	0.0653 (10)
N1	0.5027 (4)	0.4214 (5)	0.59222 (10)	0.1094 (18)
H1	0.443286	0.395616	0.610853	0.131*
N2	0.8141 (3)	0.50176 (18)	0.47205 (6)	0.0404 (5)
N3	0.9055 (3)	0.55147 (18)	0.44407 (6)	0.0413 (5)
O1	0.8334 (3)	0.64760 (16)	0.50919 (6)	0.0609 (6)
O2	0.3379 (3)	0.3871 (2)	0.65791 (8)	0.0797 (8)
O1W	0.1945 (3)	0.20372 (18)	0.55182 (8)	0.0625 (7)
O3	0.3152 (3)	0.2389 (2)	0.62522 (7)	0.0840 (9)
O4 ^a	0.1610 (6)	0.4098 (4)	0.72475 (14)	0.0653 (12)
H4A ^a	0.220417	0.437932	0.70818	0.098*
H2A	0.775 (4)	0.432 (3)	0.4672 (8)	0.052 (8)*
H1WA	0.164 (7)	0.261 (4)	0.5405 (14)	0.119 (18)*
H1WB	0.234 (8)	0.237 (5)	0.577 (2)	0.19 (3)*

^aOccupancy: 0.5.

an intention to improve pharma-toxicological profiles of the drug towards the organism.¹⁰ However, in most cases they demonstrate low solubility. In such instances, it is more suitable to use a multicomponent form such as a co-crystal or

salt as these tend to be more soluble than the crystal form of an active pharmaceutical ingredient.¹¹ Co-crystallization or ionization of these derivatives is also likely to increase bioavailability of the drug.¹² The use of benzaldehyde as a solvent is commonly avoided as it is known to autoxidize at room temperatures to form benzoic acid.¹³ Although this reaction is known to be instigated by a catalyst, it can also occur spontaneously over a long period of time.¹⁴ However, in this case, benzaldehyde was used as very slow evaporation was desired.

The crystal structure of the title structure crystallised in the orthorhombic *Pbca* space group and the asymmetric unit contains one molecule of (*E*)-4-(2-benzylidenehydrazine-1-carbonyl)pyridin-1-ium, one molecule of water, and two anions, namely 2-hydroxybenzoate and benzoate with 50:50 occupancy (see the Figure). The benzoate anion is produced *in situ* via the autoxidation of the benzaldehyde solvent. In the asymmetric unit, the H1 atom of the carbohydrazide moiety is bonded via bifurcated hydrogen bonds to the two oxygen atoms of the carboxylate functional group of the 2-hydroxybenzoate or the benzoate anion, respectively. The O3 oxygen on the anion is also bifurcated and hydrogen bonded to both H1 as described above as well as to the H1wb atom on the water molecule. Each water molecule in the unit cell is connected to two carbohydrazide moieties. The first carbohydrazide moiety is hydrogen bonded to the water through the N2–H2...O1 hydrogen bond. The second carbohydrazide moiety has a bifurcated hydrogen bond between H1wa on the water molecule and O1 and N3 on the moiety. Furthermore, the second hydrogen atom on the water molecule, H1wb, is bonded to the O3 atom on the 2-hydroxybenzoate or benzoate molecule respectively. The salt is therefore stabilised by the water molecule in the crystal. The packing of the crystal contains an anticlockwise twofold screw rotation along the *b*-axis, resulting in a three-dimensional (3D) network in the crystal structure.

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