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Crystal structure of (*E*)-*N'*-(1-(2-hydroxy-4-methoxyphenyl)ethylidene)isonicotinohydrazide, C₁₅H₁₅N₃O₃

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.40 × 0.30 × 0.12 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.10 mm ⁻¹
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
$\theta_{\max}$, completeness:	47.0°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	114,957, 12,029, 0.020
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 10,312
$N(\text{param})_{\text{refined}}$:	235
Programs:	BRUKER [1], SHELX [2, 3], OLEX2 [4]

Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of material

To a solution of 103 mg (0.75 mmol) isonicotinic hydrazide in 5 mL 95% EtOH were added 125 mg (0.75 mmol) 2'-hydroxy-4'-methoxyacetophenone, and the reaction mixture was heated at 70 °C for 2 h. The resulting solution was brought to 4 °C and left for two days to deposit crystals as colorless blocks.

Experimental details

The hydrazide H1 atom was located in difference–Fourier maps while all other hydrogen atoms were initially placed in calculated positions. All hydrogen atom coordinates were allowed to refine freely, while displacement parameters were constrained ($U_{\text{iso}}(\text{methine H}) = 1.2U_{\text{eq}}$ and $U_{\text{iso}}(\text{methyl H}) = 1.5U_{\text{eq}}$).

Comment

The title compound, 2'-hydroxy-4'-methoxyacetophenone isonicotinoyl hydrazone (HMAIH), is a condensation product of two biologically active agents, an anti-inflammatory

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Abstract

C₁₅H₁₅N₃O₃, triclinic, $P\bar{1}$ (no. 2), $a = 9.0752(2)$ Å, $b = 9.1969(2)$ Å, $c = 9.9519(2)$ Å, $\alpha = 112.7059(8)^\circ$, $\beta = 92.4309(8)^\circ$, $\gamma = 115.2776(7)^\circ$, $V = 671.16(3)$ Å³, $Z = 2$, $R_{\text{gt}}(F) = 0.0347$, $wR_{\text{ref}}(F^2) = 0.1113$, $T = 100$ K.

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

Atom	x	y	z	U_{iso}^*/U_{eq}
C1	1.38839 (5)	1.54660 (5)	1.23512 (4)	0.01559 (5)
H1	1.4238 (11)	1.5677 (11)	1.3357 (9)	0.019*
C2	1.26066 (4)	1.37850 (5)	1.13136 (4)	0.01430 (5)
H2B	1.2052 (11)	1.2847 (11)	1.1577 (9)	0.017*
C3	1.22084 (4)	1.34826 (4)	0.98295 (4)	0.01247 (5)
C4	1.30377 (4)	1.48893 (5)	0.94615 (4)	0.01365 (5)
H4	1.2761 (10)	1.4733 (11)	0.8422 (9)	0.016*
C5	1.42654 (4)	1.65340 (5)	1.05875 (4)	0.01459 (5)
H5	1.4898 (10)	1.7537 (11)	1.0363 (9)	0.018*
C6	1.09154 (4)	1.16559 (5)	0.86686 (4)	0.01488 (5)
C7	1.07521 (4)	0.83347 (4)	0.52745 (4)	0.01247 (5)
C8	1.24427 (5)	0.90730 (6)	0.49466 (5)	0.02019 (7)
H8A	1.3179 (13)	0.8866 (13)	0.5385 (11)	0.030*
H8B	1.2969 (13)	1.0355 (13)	0.5292 (11)	0.030*
H8C	1.2340 (13)	0.8617 (13)	0.3902 (11)	0.030*
C9	0.94432 (4)	0.64664 (4)	0.43348 (3)	0.01144 (4)
C10	0.77924 (4)	0.58063 (4)	0.45476 (3)	0.01172 (4)
C11	0.65747 (4)	0.40107 (4)	0.36802 (4)	0.01260 (5)
H11	0.5439 (10)	0.3652 (11)	0.3897 (9)	0.015*
C12	0.69869 (4)	0.28329 (4)	0.26127 (4)	0.01195 (4)
C13	0.86150 (4)	0.34382 (4)	0.23877 (4)	0.01354 (5)
H13	0.8881 (10)	0.2575 (11)	0.1633 (9)	0.016*
C14	0.97989 (4)	0.52271 (5)	0.32373 (4)	0.01319 (5)
H14	1.0893 (10)	0.5636 (11)	0.3046 (9)	0.016*
C15	0.41500 (5)	0.05115 (5)	0.17986 (5)	0.01735 (6)
H15A	0.3526 (12)	-0.0773 (13)	0.1030 (10)	0.026*
H15B	0.3797 (12)	0.1246 (13)	0.1581 (10)	0.026*
H15C	0.4027 (12)	0.0560 (12)	0.2809 (10)	0.026*
N1	1.47189 (4)	1.68281 (4)	1.20065 (4)	0.01568 (5)
N2	1.14458 (4)	1.09676 (4)	0.74218 (3)	0.01441 (5)
H2A	1.2524 (12)	1.1488 (12)	0.7429 (10)	0.024*
N3	1.03301 (4)	0.92441 (4)	0.63899 (3)	0.01403 (4)
O1	0.95204 (4)	1.08579 (5)	0.88383 (4)	0.02588 (7)
O2	0.72951 (4)	0.68512 (4)	0.55778 (3)	0.01644 (5)
H2	0.8266 (13)	0.7914 (13)	0.6122 (11)	0.030*
O3	0.58672 (3)	0.10699 (4)	0.17321 (3)	0.01561 (5)

phytochemical Paeonol and an anti-tubercular drug Isoniazid. HMAIH is a structural analogue of salicylaldehyde isonicotinoyl hydrazone (SIH), which possesses high affinity to intracellular iron. In that capacity, SIH and similar hydrazide-hydrazones have been actively studied as potential anti-inflammatory [5], anti-tumour [6], or cardioprotective [7] agents. We have explored the utility of chelators for inhibition of iron-dependent cytotoxic virulence factors from drug-resistant bacteria [8, 9] and, in the course of the study, have prepared a series of hydrazide-hydrazones, including the title compound.

HMAIH crystallizes in the triclinic $P\bar{1}$ space group, with two equivalent molecules per unit cell. The asymmetric

unit of the title structure thus contains one molecule of HMAIH, shown in the upper part of the Figure. The bond lengths and angles are in the expected ranges. The major portion of the molecule, excluding the pyridyl ring, is approximately flat: all atoms are located within 1.05 Å of the phenyl ring plane. The pyridyl ring plane is at 69.3° to the phenyl ring plane. The conventional hydrogen bonding in crystal structure of HMAIH is limited to one bifurcated intramolecular bond ($O2\cdots N3 = 2.5188(5)$ Å, $H2\cdots N3 = 1.681(12)$ Å, $O2-H2\cdots N3 = 150.4(11)^\circ$ and $O2\cdots O1 = 3.470(1)$ Å, $H2\cdots O1 = 2.719(10)$ Å, $O2-H2\cdots O1 = 139.9(9)^\circ$) and one intermolecular heteroatom contact ($N2\cdots N1 = 3.0763(6)$ Å, $H2A\cdots N1 = 2.208(11)$ Å, $N2-H2A\cdots N1 = 166.9(8)^\circ$) shown in the upper part of the Figure. In the crystal, the H-bonded molecules form dimers that are reinforced by the π - π stacking. In addition, a short intermolecular contact, the $C11-H11\cdots O2$, which satisfies to the distance and directionality conditions ($C11\cdots O2 = 3.4354(6)$ Å, $H11\cdots O2 = 2.441(10)$ Å, $C11-H11\cdots O2 = 172.2(8)^\circ$), may contribute to the stability of the molecular packing in the HMAIH crystal, as well [12]. The pyridyl rings are engaged into strong π - π stacking interactions, with the shortest contact between the rings $Cg1\cdots Cg1' = 3.4775(2)$ Å ($' = 3 - x, 3 - y, 2 - z$). A short $C4-H4\cdots Cg2''$ ($H4\cdots Cg2'' = 2.406(9)$ Å, $'' = 2 - x, 2 - y, 1 - z$) contact is a significant contributor to the non-polar interactions in the crystal structure, as well. To account for all interactions involved in the build-up of the crystal structure, we have performed DFT calculations, at the B3LYP/6-31G(d,p) theory level [10, 11], of the electrostatic, dispersion, polarization, and repulsion energies in the HMAIH crystal structure. According to the calculations, the interactions between hydrogen-bonded pairs of molecules provided the largest contribution, about 23%, to the lattice energy, with the dispersion energy contributing the most for the attractive forces between neighbouring molecules of HMAIH (i.e. $E_{elstat} = -34.7$ kJ/mol, $E_{disp} = -78.0$ kJ/mol for $2 - x, 2 - y, 1 - z$). The spatial distribution of the energetically most significant interactions is illustrated in the lower part of the Figure, showing the dispersion energy framework as green cylinders penetrating the crystal lattice of HMAIH. The cylinders connect centroids of the interacting molecules, and their diameters are proportional to the total energies of the interactions, with the 16 kJ/mol cut-off, for clarity. The most extensive intermolecular interactions occur in the directions parallel to (100). To estimate the lattice energy, all total energies of unique pairwise interactions between molecules were summed up, thus yielding $E_{lattice} = -329$ kJ/mol for the HMAIH crystal.

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