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4-(2-Isonicotinoylhydrazino)-4-oxobutanoic acid

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Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.003 Å
R factor = 0.055
wR factor = 0.159
Data-to-parameter ratio = 11.4

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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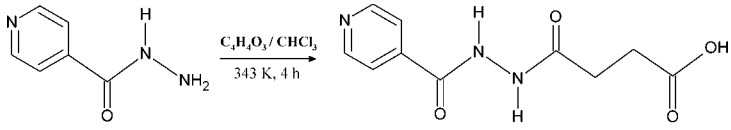
The title compound, $C_{10}H_{11}N_3O_4$, was synthesized by reacting isoniazid with succinic anhydride. The structure reveals an infinite two-dimensional network in the (011) plane, stabilized by intermolecular hydrogen bonds. Three of these hydrogen bonds are symmetrically independent.

Comment

In the last decade, tuberculosis (TB) has reemerged as one of the leading causes of death in the world, reaching nearly three million deaths annually (Bloom & Murray, 1992). Therefore, the search for new drugs for tuberculosis is of the utmost importance. Treatment regimens are based on long-term and combined chemotherapy. The most used first-choice drug is isoniazid, (I), a bactericidal drug that acts both intracellularly in the macrophages and extracellularly in the necrotic tissue (Loenhout-Rooyackers & Veen, 1998).



(I) (II)

The success of the drug depends significantly on patient compliance, since the interruption of the treatment is considered the main cause of bacterial resistance (World Health Organization, 1997). From this perspective, succinyl derivatives are good synthetic intermediates in design of prodrugs with prolonged action, which could improve the patient compliance by decreasing the doses to be taken. Once in the blood, the drug is expected to be slowly released from the prodrug (unpublished data).

Fig. 1 shows an *ORTEP*-3 (Farrugia, 1997) view of the title compound, (II). The main geometrical parameters are given in Table 1. As expected, the pyridine ring is planar and shows nearly equal C—C distances [mean distance 1.389 (5) Å]. The C—N bond lengths in the pyridine ring are slightly shorter than the C—C bond lengths [C2—N1 = 1.342 (2) Å and C3—N1 = 1.333 (2) Å]. The mean bond angle in the ring is 120 (3)°. The observed geometry of the ring agrees well with similar pyridine geometries (*e.g.* Bhat *et al.*, 1974). The group bound to the aromatic ring exhibits an extended conformation, in which the mean C—C and C—N bond lengths are 1.51 (1) and 1.344 (4) Å, respectively. The N—N bond length is 1.390 (2) Å. These distances are in good agreement with the expected values for formal C—C, C—N and N—N single bonds.

The crystal packing is governed by an infinite two-dimensional network in the (011) plane, stabilized by intermolecular hydrogen bonds (see Fig. 2). The compound exhibits three

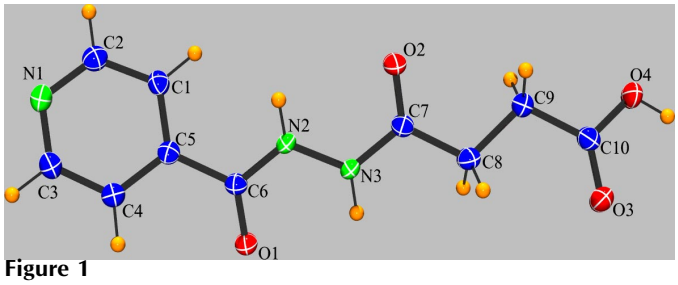


Figure 1
View of the title compound, with displacement ellipsoids shown at the 50% probability level.

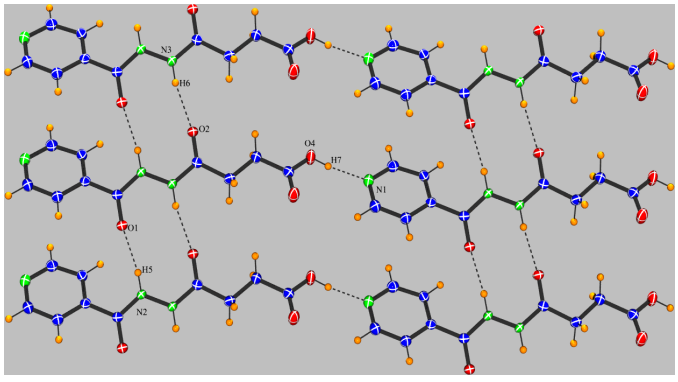


Figure 2
Packing of the title compound, showing the infinite two-dimensional network in the (011) plane. Hydrogen bonds are indicated by dashed lines.

independent intermolecular hydrogen bonds (Fig. 2 and Table 2). One of them is between the pyridine N atom and the terminal carboxylic acid group (O4—H7···N1^{iii}, symmetry code as in Table 2), and gives rise to an infinite chain along the [01$\bar{1}$] direction. The other two hydrogen bonds, which involve the carbonyl and amino groups (N2—H5···O1^{i} and N3—H6···O2^{ii}, symmetry codes as in Table 2), form another chain along the [100] direction.

Experimental

Succinyl isoniazid, (II), was obtained from the reaction of succinic anhydride with isoniazid, (I), in chloroform, at 343 K for 4 h. Pale yellow crystals were obtained by recrystallization from ethanol/H_2O (1:1).

Crystal data

$C_{10}H_{11}N_3O_4$
M_r = 237.22
Triclinic, $P\bar{1}$
a = 4.8140 (2) Å
b = 8.9168 (4) Å
c = 12.4943 (6) Å
α = 83.797 (2)°
β = 79.735 (2)°
γ = 81.035 (2)°
V = 519.51 (4) Å^3
Z = 2
D_x = 1.516 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1004 reflections
θ = 1–25°
μ = 0.12 mm^{-1}
T = 120 (2) K
Needle, pale yellow
0.40 × 0.06 × 0.06 mm

Data collection

Nonius KappaCCD diffractometer
φ and ω scans with κ offsets
6740 measured reflections
1753 independent reflections
1511 reflections with $I > 2\sigma(I)$
R_{int} = 0.104
θ_{max} = 25°
$h = -5 \rightarrow 4$
$k = -10 \rightarrow 10$
$l = -14 \rightarrow 14$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.055
$wR(F^2)$ = 0.159
S = 1.08
1753 reflections
154 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1004P)^2 + 0.0903P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < \rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.28 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

C2—N1	1.342 (2)	C7—N3	1.347 (2)
C3—N1	1.333 (2)	C10—O3	1.204 (2)
C6—O1	1.237 (2)	C10—O4	1.321 (2)
C6—N2	1.341 (2)	N2—N3	1.390 (2)
C7—O2	1.231 (2)		
N1—C2—C1	122.97 (16)	N3—C7—C8	114.49 (15)
N1—C3—C4	123.39 (16)	O3—C10—O4	123.07 (16)
O1—C6—N2	121.40 (16)	O3—C10—C9	124.51 (15)
O1—C6—C5	121.95 (15)	O4—C10—C9	112.42 (14)
N2—C6—C5	116.59 (15)	C3—N1—C2	117.80 (15)
O2—C7—N3	121.07 (16)	C6—N2—N3	118.20 (14)
O2—C7—C8	124.41 (15)	C7—N3—N2	119.21 (15)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N2—H5···O1^{i}	0.88	1.99	2.842 (2)	162
N3—H6···O2^{ii}	0.88	2.11	2.906 (2)	150
O4—H7···N1^{iii}	0.84	1.84	2.673 (2)	173

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

The H atoms were positioned stereochemically and were treated using the *SHELXL*97 default riding models. All H atoms were set isotropically, with displacement parameters 20% greater than the equivalent isotropic displacement parameters of the bonded atoms.

Data collection: *COLLECT* (Nonius, 1998); cell refinement: *HKL SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *HKL DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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