Orthorhombic

\(Pbc a\)

\(a = 9.714 (2) \text{ Å}\)

\(b = 16.742 (2) \text{ Å}\)

\(c = 16.540 (2) \text{ Å}\)

\(V = 2689.9 (7) \text{ Å}^3\)

\(Z = 8\)

\(D_r = 1.673 \text{ Mg m}^{-3}\)

\(D_m\) not measured

Data collection

Enraf-Nonius CAD-4-MACHS

diffraclometer

\(\omega / 2\theta\) scans

Absorption correction:

Gaussian (Sheldrick, 1976)

\(T_n = 0.343, T_{max} = 0.876\)

3371 measured reflections

3010 independent reflections

2158 reflections with

\(I > 2\sigma(I)\)

Cell parameters from 25 reflections

\(\theta = 10.4 - 15.1^\circ\)

\(\mu = 2.195 \text{ mm}^{-1}\)

\(T = 293 (1) \text{ K}\)

Plate

\(0.70 \times 0.50 \times 0.06 \text{ mm}\)

Light brown

Refinement

Refinement on \(F^2\)

\(R[F^2 > 2\sigma(F^2)] = 0.027\)

\(wR(F^2) = 0.074\)

\(S = 1.031\)

2636 reflections

180 parameters

H atoms: see below

\(w = l/[aZ(Fo)^2 + (0.0408P)^2 + 1.7223P]\)

where \(P = (Fo^2 + 2Fc^2)/3\)

Selected geometric parameters (Å, °)

<table>
<thead>
<tr>
<th>Bond</th>
<th>Distance (Å)</th>
<th>Angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1-O1</td>
<td>1.201 (4)</td>
<td>1.146 (4)</td>
</tr>
<tr>
<td>C2-O2</td>
<td>1.222 (3)</td>
<td>1.148 (4)</td>
</tr>
<tr>
<td>C3-O3</td>
<td>1.230 (3)</td>
<td>1.137 (5)</td>
</tr>
<tr>
<td>C4-O4</td>
<td>1.341 (4)</td>
<td>1.139 (2)</td>
</tr>
<tr>
<td>C5-O5</td>
<td>1.290 (3)</td>
<td>1.173 (2)</td>
</tr>
<tr>
<td>C6-O6</td>
<td>1.216 (3)</td>
<td>1.191 (3)</td>
</tr>
<tr>
<td>C7-O7</td>
<td>1.213 (3)</td>
<td>1.178 (3)</td>
</tr>
<tr>
<td>C8-O8</td>
<td>1.219 (3)</td>
<td>1.183 (3)</td>
</tr>
<tr>
<td>C9-O9</td>
<td>1.224 (3)</td>
<td>1.179 (3)</td>
</tr>
<tr>
<td>C10-O10</td>
<td>1.224 (3)</td>
<td>1.179 (3)</td>
</tr>
<tr>
<td>C11-O11</td>
<td>1.216 (3)</td>
<td>1.191 (3)</td>
</tr>
<tr>
<td>C12-O12</td>
<td>1.201 (4)</td>
<td>1.146 (4)</td>
</tr>
</tbody>
</table>

The coordinates of the H atom attached to N were refined

\([N-H = 0.72 (3) \text{ Å}]\); other H atoms were treated as riding.

\(U_{iso}\) values of all H atoms were refined.

Table 1. Selected geometric parameters (Å, °)

<table>
<thead>
<tr>
<th>Bond</th>
<th>Distance (Å)</th>
<th>Angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Te—C14</td>
<td>2.120 (4)</td>
<td>1.146 (4)</td>
</tr>
<tr>
<td>Te—C1</td>
<td>2.122 (3)</td>
<td>1.148 (4)</td>
</tr>
<tr>
<td>O—C7</td>
<td>1.230 (3)</td>
<td>1.137 (5)</td>
</tr>
<tr>
<td>C14—Te—C1</td>
<td>96.66 (16)</td>
<td>1.201 (3)</td>
</tr>
<tr>
<td>C7—N—C8</td>
<td>129.0 (3)</td>
<td>1.173 (2)</td>
</tr>
<tr>
<td>C3—C2—C1</td>
<td>119.6 (3)</td>
<td>1.191 (3)</td>
</tr>
<tr>
<td>C5—C4—C3</td>
<td>121.3 (3)</td>
<td>1.178 (3)</td>
</tr>
<tr>
<td>C1—C2—C7</td>
<td>119.2 (3)</td>
<td>1.183 (3)</td>
</tr>
<tr>
<td>O—C7—N</td>
<td>122.4 (3)</td>
<td>1.179 (3)</td>
</tr>
<tr>
<td>C14—Te—C1—C6</td>
<td>19.2 (3)</td>
<td>3.20 (4)</td>
</tr>
<tr>
<td>C14—Te—C1—C2</td>
<td>162.1 (3)</td>
<td>3.34 (4)</td>
</tr>
<tr>
<td>C8—N—C7—O</td>
<td>5.8 (5)</td>
<td>1.177 (3)</td>
</tr>
<tr>
<td>C3—C2—C7</td>
<td>174.5 (3)</td>
<td>1.167 (3)</td>
</tr>
<tr>
<td>C2—C3—C7</td>
<td>145.9 (3)</td>
<td>1.154 (5)</td>
</tr>
</tbody>
</table>

The biologically active iron chelators

2-pyridyldcarboxaldehyde isonicotinoylhydrazone, 2-pyridyldcarboxaldehyde benzoylhydrazone monohydrate and 2-furaldehyde isonicotinoylhydrazone

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Abstract

In the crystal structures of the respective title compounds, \(\text{C}_2\text{H}_3\text{NO}_3\), \(\text{C}_2\text{H}_4\text{N}_3\text{O}_2\), and \(\text{C}_2\text{H}_5\text{N}_2\text{O}_2\), variations in the torsion angles of the aromatic pyridyl

Supplementary data for this paper are available from the IUCr electronic archives (Reference: JA1000). Services for accessing these data are described at the back of the journal.
and benzoyl groups are observed, and the disposition of the heterocyclic aldehyde is shown to be influenced by the ring size of this group.

**Comment**

Aroylhydrazone ligands continue to attract interest as potential chelators for the treatment of iron-overload disease and also as agents with considerable antitumour activity (Johnson *et al.*, 1982; Baker *et al.*, 1992; Richardson *et al.*, 1995; Richardson & Milnes, 1997). As part of our research programme examining the development of clinically useful iron chelators, we have synthesized and determined the crystal structures of three aroylhydrazones, namely 2-pyridylcarboxaldehyde isonicotinoylhydrazone, (1), 2-pyridylcarboxaldehyde benzoylhydrazone monohydrate, (2)-H$_2$O, and 2-furaldehyde (2-furfural) isonicotinoylhydrazone, (3). These chelators were designed to improve upon the aqueous solubility and iron-chelation efficacy of the pyridoxal isonicotinoylhydrazone analogues that were examined previously. Studies assessing the biological activity of compounds (1)–(3) have been completed and will be described elsewhere (Becker & Richardson, 1999). The title compounds have been known for some time [(1), Beyerman *et al.* (1954); (2), Grammaticakis (1956); (3), Fox & Gibas (1953)], but no crystal structures of this series have been published.

In the crystal structure of (1) (Fig. 1), the 2- and 4-pyridyl rings are each twisted slightly about their connecting C–C bonds, defined by the respective C$_3$--C$_2$--C$_1$--N$_1$ and C$_9$--C$_8$--C$_7$--N$_2$ torsion angles of 3.9 (9) and 9.7 (7)$^\circ$. The 2-pyridyl N atom (N$_3$) is *anti* with respect to the imine N atom (N$_1$), which avoids repulsion between the H atoms attached to C$_1$ and C$_3$. As a consequence, the molecule is unfavourably disposed to chelate a metal ion in a tridentate configuration. In order for this ligand to bind meridionally (through the donor atoms O$_1$, N$_1$ and N$_3$), the pyridyl group would have to rotate by ca 180$^\circ$ about C$_1$–C$_2$.

The crystal structure of the benzoyl analogue (2)-H$_2$O (Fig. 2) found the hydrazone and a water of crystallization each located on a general site. The bond lengths are similar to those found in (1). The phenyl ring is somewhat more twisted about the connecting C–C bond [N$_2$–C$_7$–C$_8$–C$_9$ torsion angle 22.6 (3)$^\circ$] than its 4-pyridyl analogue in (1). The disposition of the 2-pyridyl ring again finds N$_3$ *anti* to N$_1$. Hydrogen bonding with the water O atom (O$_2$) was also identified. The most significant contacts are O$_2$–H$_2$B..-N$_3$ i of 1.97 Å [O$_2$..-N$_3$' 2.875 (2) Å] and N$_2$–H$_2$N.–O$_2$ ii of 2.00 Å [N$_2$..-O$_2$ ii 2.852 (2) Å] [symmetry codes: (i) x+$\frac{1}{2}$, $-y+\frac{1}{2}$, $-z$; (ii) $-x+\frac{1}{2}$, $y+\frac{1}{2}$, $z$].

The furfural hydrazone (3) (Fig. 3) crystallizes with two independent molecules (n = A and B) in the asymmetric unit, but the structural differences between these molecules are negligible. The furyl O atom (O$_{1n}$) is *syn* with respect to the imine N atom (N$_{1n}$), in contrast to the structures of (1) and (2) where the heteroatoms were *anti*. In this case, the ca 10$^\circ$ more obtuse C$_{1n}$–C$_{2n}$–C$_{3n}$ angle enforced by the planar five-membered furyl ring (ca 130$^\circ$) relieves the C$_{1n}$–H..-H–C$_{3n}$ repulsion which led to the corresponding *anti* conformers (1) and (2). In (3), the 4-pyridyl ring is twisted significantly about its connecting C–C bond (C$_{8n}$–C$_{7n}$–C$_{6n}$–N$_{2n}$ ca 33$^\circ$), whereas the furyl ring torsion is relatively small (ca 4$^\circ$).
Fig. 3. View of (3) (one independent molecule) showing 30% probability ellipsoids.

We are currently exploring the coordination chemistry and biological activity of these three potential ligands and their analogues.

Experimental

The title compounds were prepared in good yield by Schiff base condensation between the corresponding aldehyde [2-pyridylcarboxaldehyde for (1) and (2), and 2-furfural for (3)] and acid hydrazide [isonicotinic acid hydrazide for (1) and (3), and benzoic acid hydrazide for (2)] in refluxing ethanol. The $^1$H NMR and microanalytical results are consistent with their formulation. Crystals of each compound were grown from saturated ethanolic solutions.

Compound (1)

Crystal data

C$_{12}$H$_{10}$N$_4$O

Mo Kα radiation

$\lambda = 0.71073$ Å

Orthorhombic

Cell parameters from 25 reflections

$\theta = 9.3 - 14.1^\circ$

$\mu = 0.097$ mm$^{-1}$

$T = 296$ (2) K

Prism

$0.50 \times 0.13 \times 0.10$ mm

Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer

$\omega-2\theta$ scans

Absorption correction: none

2163 measured reflections

1060 independent reflections

$I > 2\sigma(I)$

Refinement

Refinement on $F^2$

$R[F^2 > 2\sigma(F^2)] = 0.050$

$wR(F^2) = 0.122$

$S = 1.034$

(D/σ)max < 0.001

$\Delta F_{\text{max}} = 0.19$ e Å$^{-3}$

$\Delta F_{\text{min}} = -0.20$ e Å$^{-3}$

Extinction correction: none

Compound (2)

Crystal data

C$_{13}$H$_{11}$N$_3$O$\cdot$H$_2$O

Mo Kα radiation

$\lambda = 0.71073$ Å

Orthorhombic

Pbca

Cell parameters from 25 reflections

$\theta = 11.3 - 13.4^\circ$

$\mu = 0.089$ mm$^{-1}$

$T = 296$ (2) K

Prism

0.60 × 0.60 × 0.50 mm

Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer

$\omega-2\theta$ scans

Absorption correction: none

2250 measured reflections

2220 independent reflections

1548 reflections with $I > 2\sigma(I)$

Refinement

Refinement on $F^2$

$R[F^2 > 2\sigma(F^2)] = 0.034$

$wR(F^2) = 0.127$

$S = 1.059$

2220 reflections

158 parameters

H atoms constrained

$w = 1/[(\sigma(F^2) + (0.0743P)^2 + 0.2126P)]$

where $P = (F^2 + 2F^2)/3$

Compound (3)

Crystal data

C$_{11}$H$_9$N$_3$O$_2$

Mo Kα radiation

$\lambda = 0.71073$ Å

Monoclinic

$P2_1/c$

Cell parameters from 25 reflections

$\theta = 11.6 - 16.0^\circ$

$\mu = 0.101$ mm$^{-1}$

$T = 296$ (2) K

Plate

0.30 × 0.20 × 0.07 mm

Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer

$\theta_{\text{max}} = 24.96^\circ$

R$_{\text{int}} = 0.032$

1060 reflections

154 parameters

H atoms constrained

$w = 1/[(\sigma(F^2) + (0.0532P)^2)]$

where $P = (F^2 + 2F^2)/3$
For (1), the direction of the polar axis could not be determined reliably as the heaviest atom in the structure was oxygen. For structure (3), the presence of a pseudo-\(b\)-glide plane (perpendicular to \(a\)) was noted, but no alternative cell could be identified.

For all compounds, data collection: CAD-4 Software (Enraf-Nonius, 1989); cell refinement: SET4 in CAD-4 Software; data reduction: XtaL3.2 (Hall et al., 1992); program(s) used to solve structures: SHELXS86 (Sheldrick, 1990); program(s) used to refine structures: SHELXL97 (Sheldrick, 1997); molecular graphics: PLATON (Spek, 1990); software used to prepare material for publication: SHELXL97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: TA1264). Services for accessing these data are described at the back of the journal.

References


