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5-Nitro-2-furaldehyde *N*-(hydroxymethyl)-semicarbazone

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Key indicators

Single-crystal X-ray study
T = 298 K
Mean *σ*(C–C) = 0.003 Å
Disorder in main residue
R factor = 0.039
wR factor = 0.111
Data-to-parameter ratio = 10.3

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

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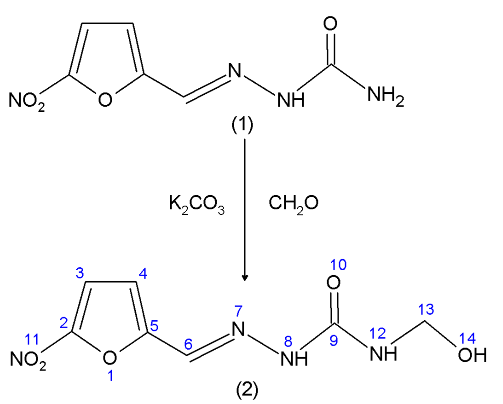
The title compound, $C_7H_8N_4O_5$, which is a potential anti-Chagas' derivative, was synthesized using a simple hydroxymethylation method in a basic medium with formaldehyde. The structure reveals two infinite two-dimensional networks in the $(\bar{1}02)$ and (001) planes, stabilized by intermolecular hydrogen bonds.

Comment

Chagas' disease has re-emerged as an important medico–social problem for people living in the Americas (Moncayo, 1992; World Health Organization, 2003). It is endemic in 21 countries, with approximately 16 to 18 million individuals infected with *Trypanosoma cruzi* and about 100 million people at risk of contracting the parasitosis. Among many compounds that are active against *T. cruzi*, aromatic nitroheterocyclic derivatives are, generally, very active (Cerecetto & Gonzalez, 2002; Maya *et al.*, 2003). Despite their toxicity, this class of compounds has been considered as important leads for molecular modification.



Nitrofurazone (1) is a 5-nitro-2-furfurylidenesemicarbazone and is primarily an antimicrobial agent active against Gram-positive microorganisms (Korolkovas, 2004). It has been used as a precursor to obtain potential anti-Chagas' derivatives (Chung & Ferreira, 1999). An intermediate compound in this synthesis is the title hydroxymethylnitrofurazone, (2), which has been shown to be active against the trypomastigote or amastigote forms of *T. cruzi*, as well as being about four times less mutagenic than nitrofurazone (Chung *et al.*, 2003).

Fig. 1 shows an *ORTEP-3* (Farrugia, 1997) view of (2). Relevant geometric parameters are given in Table 1. The molecule is essentially planar except for the hydroxyl group. Atom O5 deviates by 1.106 (7) Å from the least-squares plane through the furan ring. The C6—N4—C7—O5 torsion angle is

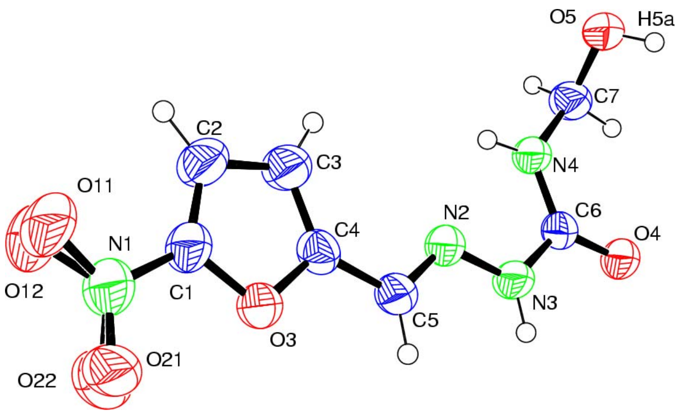


Figure 1
A view of (2), with displacement ellipsoids for shown at the 50% probability level. Both disorder components are shown.

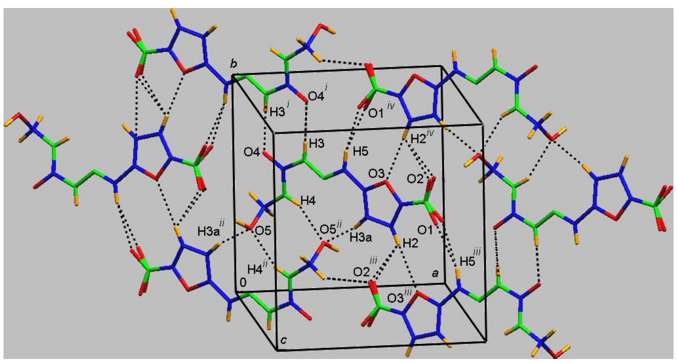


Figure 2
The packing of (2), showing the infinite two-dimensional network along the ($\bar{1}02$) plane. [Symmetry codes: (i) $\frac{1}{2} - x, \frac{3}{2} - y, -z$; (ii) $\frac{1}{2} - x, \frac{1}{2} - y, -z$; (iii) $\frac{3}{2} - x, y - \frac{1}{2}, \frac{1}{2} - z$; (iv) $\frac{3}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z$.] Both disorder components are shown.

-113.39 (18)°. Due to the disorder observed in the nitro group, the O atoms linked to atom N1 are also slightly displaced from the overall molecular plane. Atoms O11, O12, O21 and O22 deviate by 0.24 (1), -0.21 (1), 0.12 (1) and -0.30 (2) Å, respectively, from the best lequares plane through the furan ring.

The crystal packing of (2) is formed by two infinite two-dimensional networks. One of them, which is stabilized by several intermolecular hydrogen bonds (Fig. 2), is parallel to the ($\bar{1}02$) plane. The networks parallel to the ($\bar{1}02$) plane are themselves hydrogen-bonded *via* O5—H5*A*···O4 associations, forming another infinite two-dimensional network parallel to the (001) plane (Fig. 3). Details of all hydrogen-bond contacts involved in the networks are given in Table 2.

Experimental

5-Nitro-2-furfurylidenesemicarbazone, (1) (0.99 g, 5 mmol), was mixed with potassium carbonate (0.69 g, 5 mmol) and suspended in water (10 ml). Formaldehyde solution (37%, 18 ml) was added in two steps, half at the start of the reaction and the other half 2.5 h later. The reaction was stirred at room temperature for 5 h and then

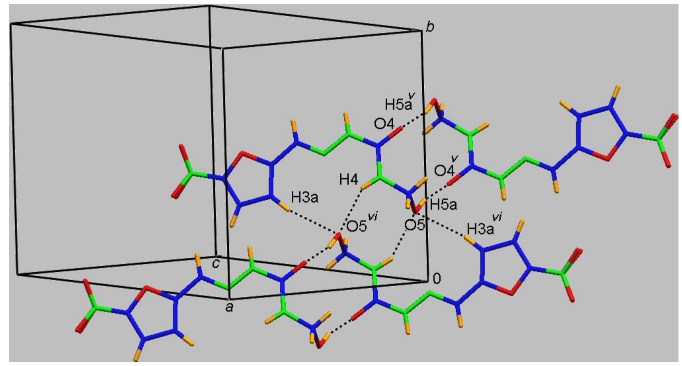


Figure 3
Part of the packing of (2), showing the infinite two-dimensional network parallel to the (001) plane. Both disorder components are shown. [Symmetry codes: (v) $-x, 1 - y, -z$; (vi) $\frac{1}{2} - x, \frac{1}{2} - y, -z$.]

filtered. The filtrate was evaporated under low pressure. The product, (2), was crystallized from methanol–water (6:0.1) and yellow crystals were obtained (yield 61.4%). The compound was identified as (2) by IR, ^{1}H and ^{13}C NMR and mass spectrometry. ^{1}H NMR spectroscopic data (300 MHz, DMSO-d_6, δ, p.p.m.): 11.02 (*s*, 1H, H_8), 7.81 (*d*, J = 3.9 Hz, 1H, H_4)*, 7.80 (*s*, 1H, H_6)*, 7.64 (*t*, J = 6.3 Hz, 1H, H_{12}), 7.25 (*d*, J = 3.9 Hz, 1H, H_3), 5.57 (*t*, J = 6.9 Hz, 1H, H_{14}), 4.61 (*t*, J = 6.6 Hz, 2H, H_{13}) (* denotes superimposed signals); ^{13}C NMR spectroscopic data (75 MHz, DMSO-d_6, δ, p.p.m.): 154.47 (C_9), 152.42 (C_5), 151.25 (C_2), 127.82 (C_6), 115.11 (C_4), 112.63 (C_3), 63.07 (C_{13}); IR data (KBr, ν, cm^{-1}): 3410 (ν_{O-H}), 3334 and 3162 (ν_{N-H}), 2980 and 2860 (ν_{C-H}), 1674 ($\nu_{C=O}$), 1522 and 1359 (ν_{NO2}). Mass spectrometry: m/z: 228 [M^+], 210, 198, 155.

Crystal data

$C_7H_8N_4O_5$	D_x = 1.596 Mg m^{-3}
M_r = 228.17	Mo $K\alpha$ radiation
Monoclinic, $C2/c$	Cell parameters from 16323 reflections
a = 10.3757 (5) Å	θ = 2.9–27.5°
b = 10.8125 (5) Å	μ = 0.14 mm^{-1}
c = 16.9455 (8) Å	T = 298 (2) K
β = 92.095 (3)°	Block, yellow
V = 1899.8 (2) Å^3	0.2 × 0.1 × 0.1 mm
Z = 8	

Data collection

Nonius KappaCCD area-detector diffractometer	1367 reflections with $I > 2\sigma(I)$
φ scans, and ω scans with κ offsets	R_{int} = 0.036
Absorption correction: none	θ_{max} = 25.5°
13352 measured reflections	$h = -12 \rightarrow 12$
1755 independent reflections	$k = -13 \rightarrow 13$
	$l = -20 \rightarrow 20$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0609P)^2 + 0.6344P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.039	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2)$ = 0.111	$\Delta\rho_{max}$ = 0.18 e Å^{-3}
S = 1.07	$\Delta\rho_{min}$ = -0.17 e Å^{-3}
1755 reflections	Extinction correction: *SHELXL97* (Sheldrick, 1997)
170 parameters	Extinction coefficient: 0.013 (2)
H atoms treated by a mixture of independent and constrained refinement	

Table 1
Selected geometric parameters (Å, °).

N1—C1	1.415 (2)	N4—C7	1.436 (2)
N2—C5	1.274 (2)	O3—C1	1.355 (2)
N2—N3	1.354 (2)	O3—C4	1.373 (2)
N3—C6	1.369 (2)	O4—C6	1.240 (2)
N4—C6	1.335 (2)	O5—C7	1.400 (2)
C7—O5—H5*A*	109 (2)	O5—C7—N4	112.6 (1)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H3···O4^{i}	0.86	2.08	2.909 (2)	162
N4—H4···O5^{ii}	0.86	2.28	3.047 (2)	148
C2—H2···O21^{iii}	0.93	2.50	3.10 (2)	122
C2—H2···O22^{iii}	0.93	2.47	3.04 (2)	120
C3—H3*A*···O5^{ii}	0.93	2.55	3.446 (2)	162
C5—H5···O11^{iv}	0.93	2.48	3.37 (2)	162
C5—H5···O12^{iv}	0.93	2.51	3.42 (2)	167
O5—H5*A*···O4^{v}	0.90 (2)	1.92 (2)	2.799 (2)	166 (2)

Symmetry codes: (i) $-x+\frac{1}{2}, -y+\frac{3}{2}, -z$; (ii) $-x+\frac{1}{2}, -y+\frac{1}{2}, -z$; (iii) $-x+\frac{3}{2}, +y-\frac{1}{2}, -z+\frac{1}{2}$; (iv) $-x+\frac{3}{2}, +y+\frac{1}{2}, -z+\frac{1}{2}$; (v) $-x, -y+1, -z$.

The hydroxyl H atom, H5*A*, was located in a difference Fourier synthesis and refined isotropically. The H atoms of the amino and methyl groups were positioned geometrically and were refined using a riding model, with N—H = 0.86 Å and C—H = 0.93–0.97 Å, and with fixed individual displacement parameters of U_{iso}(H) = 1.2U_{eq}(C,N). Several least-squares refinements were performed in an attempt to model the disordered nitro group. The model splitting each O atom of the nitro group over two positions, O11 and O12, and O21 and O22, with 50% occupancy each, was found to be the best one.

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: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* for Windows (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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References

Cerecetto, H. & Gonzalez, M. (2002). *Curr. Top. Med. Chem.* **2**, 1187–1213.
Chung, M. C. & Ferreira, E. I. (1999). *Quim. Nova*, **22**, 75–84.
Chung, M. C., Guido, R. V. C., Martinelli, T. F., Goncalves, M. F., Polli, M. C., Botelho, K. C. A., Varanda, E. A., Colli, W., Miranda, M. T. M. & Ferreira, E. I. (2003). *Bioorg. Med. Chem.* **11**, 4779–4783.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
Korolkovas, A. (2004). *Dicionário Terapêutico 04/05*, pp. 18.6–18.7. Guanabara Koogan: Rio de Janeiro.
Maya, J. D., Bollo, S., Nunez-Vergara, L. J., Squella, J. A., Repetto, Y., Morello, A., Perie, J. & Chauviere, G. (2003). *Biochem. Pharmacol.* **54**, 999–1006.
Moncayo, A. (1992). *World Health Stat. Q.* **45**, 276–279.
Nonius (1998). *COLLECT*. Nonius BV, Delft, The Netherlands.
Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307-326. New York: Academic Press.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
World Health Organization (2003). *Chagas' Disease*, http://www.who.int/tdr/dw/chagas2003.htm.