IUCrData

ISSN 2414-3146

Acetylhydroxamic acid

Błażej Dziuk, Bartosz Zarychta,* Krzysztof Ejsmont and Zdzisław Daszkiewicz

Faculty of Chemistry, University of Opole, Oleska 48, 45-052 Opole, Poland. *Correspondence e-mail: bzarychta@uni.opole.pl

Received 23 September 2017
Accepted 26 September 2017

Edited by M. Bolte, Goethe-Universität Frankfurt, Germany

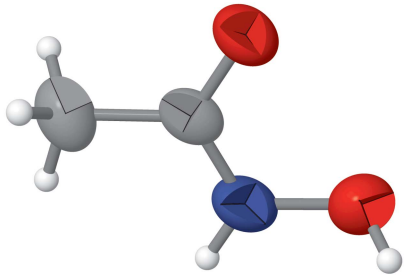
Keywords: crystal structure; acetylhydroxamic acid; hydrogen bonds.

CCDC reference: 1576592

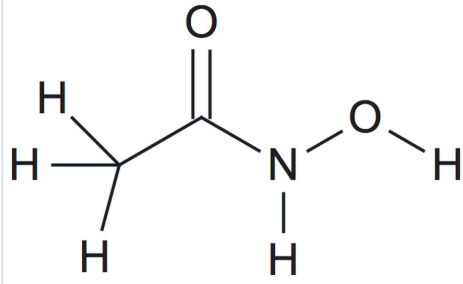
Structural data: full structural data are available from iucrdata.iucr.org

There is one independent molecule in the asymmetric unit of the title compound (alternatively named *N*-hydroxyacetamide), $C_2H_5NO_2$. It crystallizes in the noncentrosymmetric space group $P4_3$. The structure is an anhydrous form of acetylhydroxamic acid with typical geometry that corresponds well with the hydrated structure described by Bracher & Small [*Acta Cryst.* (1970), B**26**, 1705–1709]. In the crystal, N—H···O and O—H···O hydrogen bonds connect the molecules into chains in the *c*-axis direction.

3D view



Chemical scheme



Structure description

Hydroxamic acids were first described by Lossen (1869). Since then, intensive work has been focused on their reactions and structures. Acetylhydroxamic acid can exist in two tautomeric forms, *i.e.* amide and imide. In addition, each of these forms may be in the form of the *Z* or *E* isomer. Hydroxamic acids have the ability to coordinate metal ions and to form complexes, thereby *inter alia* participating in many biochemical processes. These acids belong to the siderophores and transport iron ions as bioligands in bacteria (Miller, 1989; Neilands, 1995). Hydroxamic acids are useful reagents with interesting biological and medical applications. This is also the result of their ability to form stable chelates with multiple metal ions (Kaczor & Proniewicz, 2004). Compounds containing hydroxamic groups are inhibitors of the activity of various metalloproteinases such as urease (Stemmler *et al.*, 1995), oxidase (Ikeda-Saito *et al.*, 1991) and zinc proteinases involved in neoplastic diseases (Groneberg *et al.*, 1999; Hajduk *et al.*, 1997). Enzyme activity is inhibited by urease inhibitors. These inhibitors do not allow the pH of the urine to rise and therefore do not allow the crystallization of calcium and magnesium. The first specific urease inhibitor was acetylhydroxamic acid. Acetylhydroxamic acid in the presence of urease-positive bacteria *in vitro* and *in vivo* reduces the pH of the urine and prevents the formation of urinary stones in rats. In higher doses *in vitro* studies

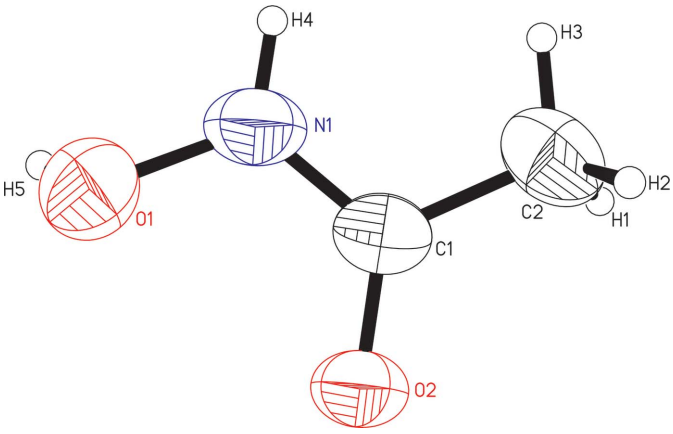


Figure 1
The molecular structure of the title compound, with displacement ellipsoids drawn at the 50% probability level.

(2–4 mg ml^{-1}) show that it inhibits urease activity and additionally has bacteriostatic effects (Cisowska, 2003).

The title compound crystallizes in the non-centrosymmetric space group $P4_3$ with one independent molecule in the asymmetric unit. The values of bond lengths and valance angles of the acetylhydroxamic acid are typical (Allen, 2002). The structure is the imidate of the *Z* isomer of acetylhydroxamic acid (Fig. 1).

In the crystal, there are intermolecular hydrogen bonds (Table 1), two N—H···O, one O—H···O and one C—H···O contact. The strongest hydrogen bond in the crystalline structure of acetylhydroxamic acid is the O1—H5···O2 hydrogen bond. This bond creates a twisted string along the *c* axis. It can be assumed that the next two hydrogen bonds of the type N—H···O have comparable strength. In the N1—H4···O2 hydrogen bond, the donor and the H atom are closer

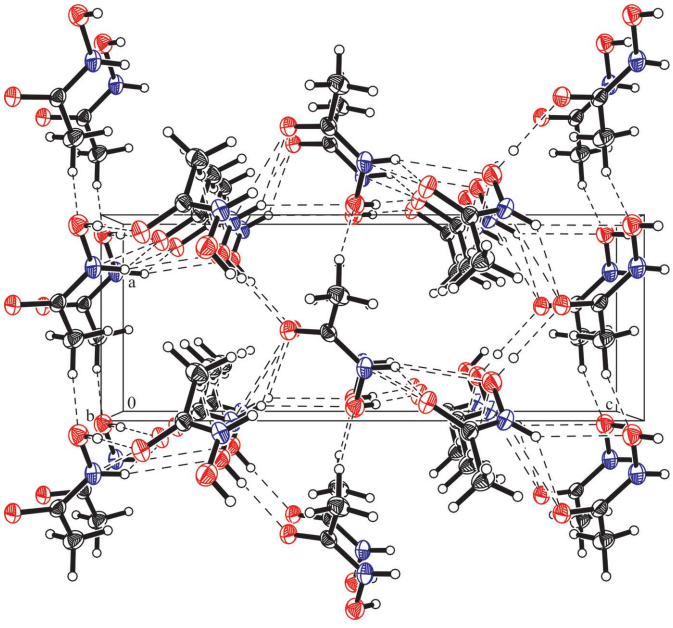


Figure 2
The crystal packing of the title compound, viewed along the *b* axis.

Table 1
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2···O1^{i}	0.96	2.45	3.300 (3)	147
N1—H4···O1^{ii}	0.86	2.48	3.246 (3)	149
N1—H4···O2^{ii}	0.86	2.26	2.917 (3)	133
O1—H5···O2^{iii}	0.82	1.81	2.624 (2)	176

Symmetry codes: (i) $x+1, y, z$; (ii) $-y, x, z+\frac{1}{4}$; (iii) $-y, x-1, z+\frac{1}{4}$.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_2H_5NO_2$
M_r	75.07
Crystal system, space group	Tetragonal, $P4_1$
Temperature (K)	293
a, *c* (Å)	5.2344 (6), 13.809 (2)
V (Å^3)	378.34 (10)
Z	4
Radiation type	Mo *Kα*
μ (mm^{-1})	0.12
Crystal size (mm)	0.05 × 0.04 × 0.03
Data collection	
Diffractometer	Xcalibur
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	2579, 751, 683
R_{int}	0.018
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.616
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.028, 0.086, 1.11
No. of reflections	751
No. of parameters	47
No. of restraints	1
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.10, −0.14
Absolute structure	Flack *x* determined using 307 quotients $[(I^+) - (I^-)]/[(I^+) + (I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter	0.0 (4)

Computer programs: *CrysAlis CCD* (Oxford Diffraction, 2008), *SHELXS2014* (Sheldrick, 2015*a*), *SHELXL2014* (Sheldrick, 2015*b*) and *SHELXTL* (Sheldrick, 2008).

to the acceptor but form a smaller angle than the N1—H4···O1 hydrogen bond. Those bonds form a chain of molecules along the *c* axis. The weakest hydrogen bond in the crystalline structure of acetylhydroxamic acid is C2—H1···O1. This hydrogen bond connects adjacent parallel molecules also along the *c* axis. The packing is shown in Fig. 2.

The geometry of the presented structure corresponds well with the structure described by Bracher & Small (1970).

Synthesis and crystallization

In this study, we prepared acetohydroxamic acid by heating equivalent proportions of acetamide and hydroxylamine hydrochloride. Dried ethyl acetate was used as a solvent for extracting and recrystallizing the product (yield 17.9 g; m.p. 354–355 K).

Refinement

All H atoms were found in a difference map but set to idealized positions and treated as riding, with methyl C—H = 0.96 Å and $U_{iso}(H) = 1.5U_{eq}(C)$, N—H = 0.86 Å and $U_{iso}(H) = 1.2U_{eq}(N)$, and O—H = 0.82 Å and $U_{iso}(H) = 1.5U_{eq}(O)$. Crystal data, data collection and structure refinement details are summarized in Table 2.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.

Bracher, B. H. & Small, R. W. H. (1970). *Acta Cryst.* B**26**, 1705–1709.

Cisowska, A. (2003). *Postępy Mikrobiol.* **42**, 3–23.

Groneberg, R. D., Burns, C. J., Morrissette, M. M., Ullrich, J. W., Morris, R. L., Darnbrough, S., Djuric, S. W., Condon, S. M., McGeehan, G. M., Labaudiniere, R., Neuenschwander, K., Scotese, A. C. & Kline, J. A. (1999). *J. Med. Chem.* **42**, 541–544.

Hajduk, P. J., Sheppard, G., Nettesheim, D. G., Olejniczak, E. T., Shuker, S. B., Meadows, R. P., Steinman, D. H., Carrera, G. M. Jr, Marcotte, P. A., Severin, J., Walter, K., Smith, H., Gubbins, E., Simmer, R., Holzman, T. F., Morgan, D. W., Davidsen, S. K., Summers, J. B. & Fesik, S. W. (1997). *J. Am. Chem. Soc.* **119**, 5818–5827.

Ikeda-Saito, M., Shelley, D. A., Lu, L., Booth, K. S., Caughey, W. S. & Kimura, S. (1991). *J. Biol. Chem.* **266**, 3611–3616.

Kaczor, A. & Proniewicz, L. M. (2004). *J. Mol. Struct.* **704**, 189–196.

Lossen, H. (1869). *Justus Liebigs Ann. Chem.* **150**, 314–316.

Miller, M. J. (1989). *Chem. Rev.* **89**, 1563–1579.

Neilands, J. B. (1995). *J. Biol. Chem.* **270**, 26723–26726.

Oxford Diffraction (2008). *CrysAlis CCD* and *CrysAlis RED*. Oxford Diffraction Ltd, Abingdon, Oxfordshire, England.

Parsons, S., Flack, H. D. & Wagner, T. (2013). *Acta Cryst.* B**69**, 249–259.

Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.

Sheldrick, G. M. (2015*a*). *Acta Cryst.* A**71**, 3–8.

Sheldrick, G. M. (2015*b*). *Acta Cryst.* C**71**, 3–8.

Stemmler, A. J., Kampf, J. W., Kirk, M. L. & Pecoraro, V. L. (1995). *J. Am. Chem. Soc.* **117**, 6368–6369.

full crystallographic data

IUCrData (2017). **2**, x171390 [https://doi.org/10.1107/S2414314617013906]

Acetylhydroxamic acid

Błażej Dziuk, Bartosz Zarychta, Krzysztof Ejsmont and Zdzisław Daszkiewicz

N-Hydroxyacetamide

Crystal data

$C_2H_5NO_2$
M_r = 75.07
Tetragonal, $P4_1$
a = 5.2344 (6) Å
c = 13.809 (2) Å
V = 378.34 (10) Å^3
Z = 4
F(000) = 160
D_x = 1.318 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 2579 reflections
θ = 3.9–26.0°
μ = 0.12 mm^{-1}
T = 293 K
Plate, colourless
0.05 × 0.04 × 0.03 mm

Data collection

Xcalibur diffractometer
Radiation source: fine-focus sealed tube
Detector resolution: 1024 pixels mm^{-1}
ω–scan
2579 measured reflections
751 independent reflections
683 reflections with $I > 2\sigma(I)$
R_{int} = 0.018
θ_{max} = 26.0°, θ_{min} = 3.9°
h = −5→6
k = −6→5
l = −16→16

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.028
$wR(F^2)$ = 0.086
S = 1.11
751 reflections
47 parameters
1 restraint
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0584P)^2 + 0.0038P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.10 e Å^{-3}
$\Delta\rho_{min}$ = −0.14 e Å^{-3}
Extinction correction: SHELXL2014 (Sheldrick, 2015b), $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.24 (4)
Absolute structure: Flack x determined using 307 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons *et al.*, 2013)
Absolute structure parameter: 0.0 (4)

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.4274 (4)	0.0253 (4)	0.41879 (16)	0.0485 (5)
C2	0.6056 (5)	0.2400 (5)	0.4372 (2)	0.0672 (7)
H1	0.5655	0.3173	0.4984	0.101*
H2	0.7778	0.1769	0.4385	0.101*
H3	0.5888	0.3647	0.3867	0.101*
N1	0.2554 (4)	−0.0170 (4)	0.48604 (13)	0.0600 (6)
H4	0.2639	0.0612	0.5407	0.072*
O1	0.0601 (3)	−0.1893 (3)	0.46796 (13)	0.0663 (5)
H5	0.0673	−0.3064	0.5073	0.099*
O2	0.4385 (3)	−0.1073 (3)	0.34398 (11)	0.0584 (5)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0516 (12)	0.0508 (11)	0.0430 (10)	0.0120 (9)	−0.0098 (9)	−0.0019 (8)
C2	0.0614 (14)	0.0644 (15)	0.0759 (18)	−0.0010 (12)	−0.0132 (12)	−0.0134 (12)
N1	0.0744 (13)	0.0623 (10)	0.0433 (10)	−0.0005 (10)	0.0010 (9)	−0.0117 (8)
O1	0.0715 (11)	0.0685 (9)	0.0589 (10)	−0.0048 (9)	0.0023 (9)	0.0067 (8)
O2	0.0595 (10)	0.0706 (11)	0.0451 (9)	−0.0034 (7)	−0.0005 (6)	−0.0134 (7)

Geometric parameters (Å, º)

C1—O2	1.246 (3)	C2—H3	0.9600
C1—N1	1.312 (3)	N1—O1	1.386 (3)
C1—C2	1.482 (4)	N1—H4	0.8600
C2—H1	0.9600	O1—H5	0.8200
C2—H2	0.9600		
O2—C1—N1	121.6 (2)	H1—C2—H3	109.5
O2—C1—C2	122.4 (2)	H2—C2—H3	109.5
N1—C1—C2	116.0 (2)	C1—N1—O1	119.24 (17)
C1—C2—H1	109.5	C1—N1—H4	120.4
C1—C2—H2	109.5	O1—N1—H4	120.4
H1—C2—H2	109.5	N1—O1—H5	109.5
C1—C2—H3	109.5		
O2—C1—N1—O1	−9.0 (3)	C2—C1—N1—O1	170.80 (19)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2···O1^{i}	0.96	2.45	3.300 (3)	147
N1—H4···O1^{ii}	0.86	2.48	3.246 (3)	149

N1—H4···O2^{ii}	0.86	2.26	2.917 (3)	133
O1—H5···O2^{iii}	0.82	1.81	2.624 (2)	176

Symmetry codes: (i) $x+1, y, z$; (ii) $-y, x, z+1/4$; (iii) $-y, x-1, z+1/4$.