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N-(6-Amino-3,4-dihydro-3-methyl-5-nitroso-4-oxopyrimidin-2-yl)leucine: a three-dimensional hydrogen-bonded framework structure

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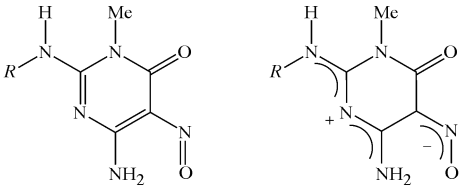
In the title compound, $C_{11}H_{17}N_5O_4$, the bond distances show evidence of a highly polarized molecular–electronic structure. The molecules are linked into a three-dimensional framework by a combination of O—H···O and N—H···O hydrogen bonds, including a very short O—H···O hydrogen bond [H···O = 1.67 Å, O···O = 2.494 (2) Å and O—H···O = 166°].

Comment

We report here the structure of the title compound, (I), which we briefly compare with the structures of its valine, methionine and threonine analogues, (II)–(IV), respectively (Low *et al.*, 1999, 2000), and those of the glycine, serine and isoleucine analogues, (V)–(VII), respectively, which all crystallize as hydrates (Low *et al.*, 1997, 2000, 2001). Compound (I) thus differs from its isomer (VII), which forms a 4:1 hydrate of overall composition $4C_{11}H_{17}N_5O_4{\cdot}H_2O$.



(I) R=CH(COOH)CH_2CHMe$_2$ (I*a*)
(II) R=CH(COOH)CHMe$_2$
(III) R=CH(COOH)CH_2CH_2SMe
(IV) R=CH(COOH)CH(OH)Me
(V) R=CH_2COOH
(VI) R=CH(COOH)CH_2OH
(VII) R=CH(COOH)CHMeCH_2Me

Within the molecule of (I) (Fig. 1), the bond distances (Table 1) in the heterocyclic ring and its immediate substituents are all very similar to the corresponding values in compounds (II)–(VII) and they provide evidence for extensive electronic polarization. In particular, the C5—N5 and N5—O5 distances in the C-nitroso group are very similar, the C4—C5 and C5—C6 bonds, which are formally single and double bonds, respectively, have distances identical within experimental uncertainly, and the C—N bonds involving atoms N1, N2 and N3, except for N2—C21, all have very similar distances, with the formally single C6—N6 bond shorter than the formally double N1═C2 bond. Taken together, these observations indicate a significant contribution to the overall molecular–electronic structure from the polarized form (I*a*). The C—O distances in the carboxyl group are consistent with the location of the acidic H atom deduced from the difference maps.

The combination of the high negative change on the nitroso O atom and the carboxylic acid functionality leads to a very short O—H···O hydrogen bond (Table 2), which is also a feature of the analogues (II)–(VI), although not of (VII), where the carboxyl group acts as hydrogen-bond donor to the

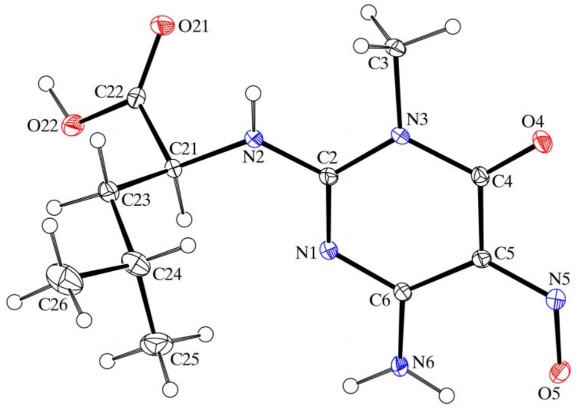


Figure 1
The molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

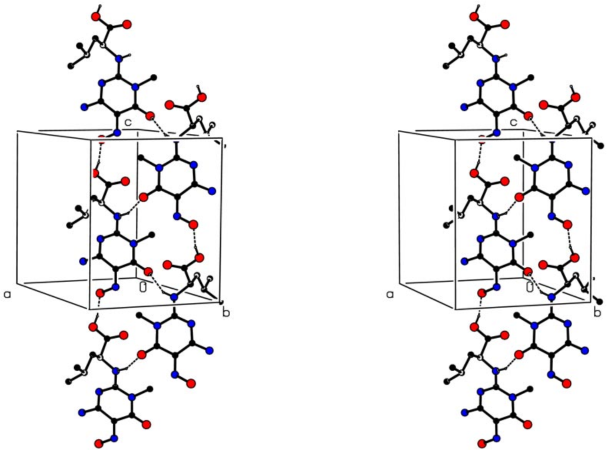


Figure 2
Stereoview of part of the crystal structure of (I), showing the formation of a chain of edge-fused $R_3^3(17)$ rings along [001]. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

water molecule rather than to the nitroso O atom. The effect of the O—H$\cdots$O hydrogen bond is to generate by translation a *C*(11) (Bernstein *et al.*, 1995) chain running parallel to the [001] direction (Fig. 2). *C*(11) chains generated by translation also occur in (II)–(IV), while there are similar *C*(11) chains generated by a glide plane in (V) and by a 2_1 screw axis in (VI).

In addition, atom N2 in the molecule at (*x*, *y*, *z*) acts as a hydrogen-bond donor to atom O4 in the molecule at $(\frac{1}{2} - x, 1 - y, \frac{1}{2} + z)$, so forming a *C*(6) chain running parallel to the [001] direction and generated by the 2_1 screw axis along $(\frac{1}{4}, \frac{1}{2}, z)$ (Fig. 2). The combination of the *C*(6) and *C*(11) chains along [001] generates a chain of edge-fused $R_3^3(17)$ rings (Fig. 2).

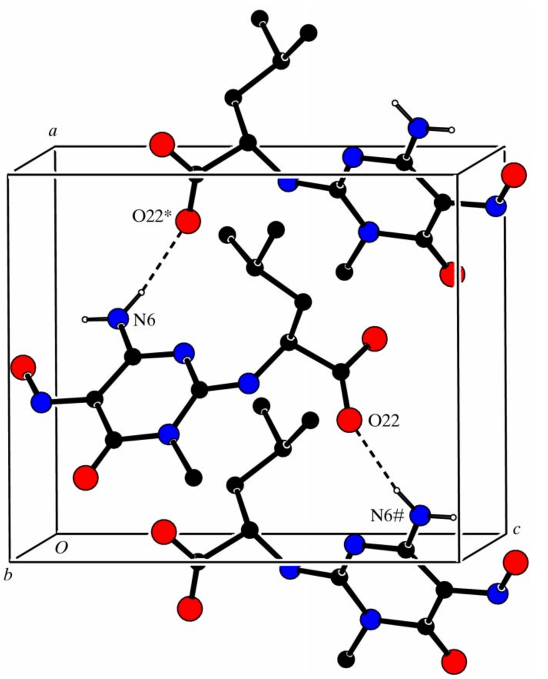


Figure 3
Part of the crystal structure of (I), showing the formation of a *C*(9) chain along [100]. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*) or a hash (#) are at the symmetry positions $(\frac{1}{2} + x, \frac{1}{2} - y, 1 - z)$ and $(x - \frac{1}{2}, \frac{1}{2} - y, 1 - z)$, respectively.

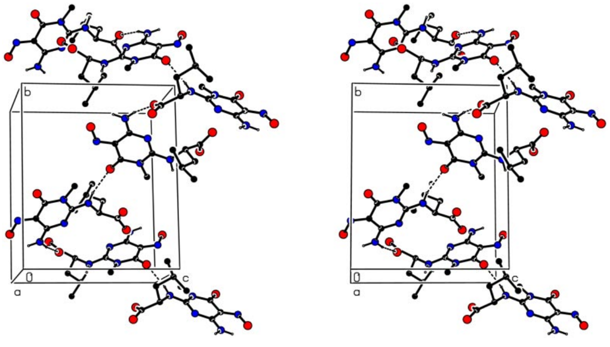


Figure 4
Stereoview of part of the crystal structure of (I), showing the formation of a $C_4^4(26)$ chain along [010]. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

Amino atom N6 acts as a double donor of hydrogen bonds. In addition to forming the intramolecular *S*(6) motif characteristic of nitropyrimidine of this type, atom N6 in the molecule at (*x*, *y*, *z*) acts as donor, *via* atom H6*B*, to carboxyl atom O22 in the molecule at $(\frac{1}{2} + x, \frac{1}{2} - y, 1 - z)$, so forming a *C*(9) chain running parallel to the [100] direction and generated by the 2_1 screw axis along $(x, \frac{1}{4}, \frac{1}{2})$ (Fig. 3). Thus, the intermolecular N—H$\cdots$O hydrogen bond with N2 as donor, acting alone, forms a chain along [001], while that with N6 as donor, again acting alone, forms a chain along [100]. However, the combination of the two intermolecular N—H$\cdots$O hydrogen bonds acting in concert forms a $C_4^4(26)$ chain running parallel to the [010] direction (Fig. 4). The combination of the [100], [010] and [001] chains then generates a continuous three-dimensional framework.

The anhydrous analogues (II)–(IV) all form three-dimensional hydrogen-bonded frameworks, but these differ in the details of their formation from the framework in (I) (Low *et al.*, 1999, 2000). Similarly, the hydrates (V)–(VII) all form three-dimensional frameworks, again all of different construction (Low *et al.*, 1997, 2000, 2001).

Experimental

The title compound was prepared by adding a suspension of 6-amino-3,4-dihydro-3-methyl-2-methoxy-5-nitroso-4-oxopyrimidine (5.00 g, 27.17 mmol) in acetonitrile (100 ml) to a suspension of L-leucine [(*S*)-2-amino-4-methylpentanoic acid; 3.90 g, 29.73 mmol] in aqueous KOH (60 ml of 0.5 *M* solution; 30.0 mmol). The mixture was stirred at 343 K for 1 h. The solution was then cooled to ambient temperature and the pH was adjusted to 3.0 by dropwise addition of aqueous HCl (0.1 *M*). After 8 h at room temperature, the orange crystalline solid which formed was collected by filtration and washed successively with water, ethanol and diethyl ether to yield the title compound (4.70 g, 16.60 mmol, 61%). Analysis found: C 45.9, H 5.6, N 25.1%; $C_{11}H_{17}N_5O_4$ requires: C 46.6, H, 6.0, N 24.7%.

Crystal data

$C_{11}H_{17}N_5O_4$
$M_r = 283.30$
Orthorhombic, $P2_12_12_1$
$a = 9.4395$ (2) Å
$b = 13.1565$ (3) Å
$c = 10.9581$ (2) Å
$V = 1360.89$ (5) Å^3
$Z = 4$
$D_x = 1.383$ Mg m^{-3}

Mo *K*α radiation
Cell parameters from 1795 reflections
$\theta = 3.2$–$27.5°$
$\mu = 0.11$ mm^{-1}
$T = 120$ (2) K
Lath, orange
0.20 × 0.10 × 0.08 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{\min} = 0.982$, $T_{\max} = 0.992$
22570 measured reflections

1795 independent reflections
1644 reflections with $I > 2\sigma(I)$
$R_{\text{int}} = 0.024$
$\theta_{\max} = 27.5°$
$h = -12 \rightarrow 12$
$k = -17 \rightarrow 16$
$l = -14 \rightarrow 14$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.106$
$S = 1.06$
1795 reflections
185 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0702P)^2 + 0.2932P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.001$
$\Delta\rho_{\max} = 0.32$ e Å^{-3}
$\Delta\rho_{\min} = -0.30$ e Å^{-3}

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Table 1
Selected bond lengths (Å).

N1—C2	1.324 (3)	C2—N2	1.337 (3)
C2—N3	1.379 (2)	N3—C3	1.466 (3)
N3—C4	1.407 (2)	C4—O4	1.222 (2)
C4—C5	1.459 (3)	C5—N5	1.328 (3)
C5—C6	1.455 (3)	N5—O5	1.297 (2)
C6—N1	1.345 (2)	C6—N6	1.312 (3)
C22—O21	1.308 (3)	C22—O22	1.215 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O21—H21*A*···O5^{i}	0.84	1.67	2.494 (2)	166
N2—H2···O4^{ii}	0.88	2.15	2.958 (2)	153
N6—H6*A*···O22^{iii}	0.88	2.07	2.924 (2)	163
N6—H6*B*···O5	0.88	1.97	2.598 (2)	127

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

The space group $P2_12_12_1$ was uniquely assigned from the systematic absences. All H atoms were located from difference maps and were subsequently treated as riding atoms, with C—H distances of 0.98 (CH_3), 0.99 (CH_2) or 1.00 Å (CH), N—H distances of 0.88 Å and O—H distances of 0.84 Å, and with $U_{iso}(H) = 1.2U_{eq}(C,N)$, $1.5U_{eq}(C)$ for the methyl groups and $1.5U_{eq}(O)$. In the absence of significant anomalous scattering, the Flack (1983) parameter was indeterminate (Flack & Bernardinelli, 2000), and hence the Friedel-equivalent reflections were merged prior to the final refinements. The correct absolute configuration was set by reference to the known absolute configuration of the L-leucine employed in the synthesis.

Data collection: *COLLECT* (Hooft, 1999); cell refinement: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *OSCAIL* (McArdle, 2003) and *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *OSCAIL* and *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *PRPKAPPA* (Ferguson, 1999).

The X-ray data were collected at the EPSRC X-ray Crystallographic Service, University of Southampton, England.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1862). Services for accessing these data are described at the back of the journal.

References

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.

Ferguson, G. (1999). *PRPKAPPA*. University of Guelph, Canada.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Flack, H. D. & Bernardinelli, G. (2000). *J. Appl. Cryst.* **33**, 1143–1148.

Hooft, R. W. W. (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.

Low, J. N., Cannon, D., Quesada, A., Marchal, A., Melguizo, M., Nogueras, M., Sánchez, A. & Glidewell, C. (2001). *Acta Cryst.* C**57**, 604–607.

Low, J. N., Ferguson, G., López, R., Arranz, P., Cobo, J., Melguizo, M., Nogueras, M. & Sánchez, A. (1997). *Acta Cryst.* C**53**, 890–892.

Low, J. N., Godino, M. L., López, R., Pérez, A., Melguizo, M. & Cobo, J. (1999). *Acta Cryst.* C**55**, 1727–1730.

Low, J. N., López. M. D., Arranz Mascarós, P., Cobo Domingo, J., Godino, M. L., López Garzón, R., Gutiérrez, M. D., Melguizo, M., Ferguson, G. & Glidewell, C. (2000). *Acta Cryst.* B**56**, 882–892.

McArdle, P. (2003). *OSCAIL for Windows*. Version 10. Crystallography Centre, Chemistry Department, NUI Galway, Ireland.

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.

Sheldrick, G. M. (2003). *SADABS*. Version 2.10. University of Göttingen, Germany.

Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.

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