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Intermolecular hydrogen bonding of the two independent molecules of *N*-3,5-dinitrobenzoyl-L-leucine

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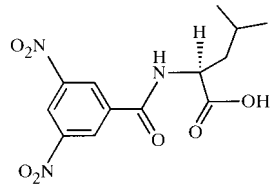
The title compound, $C_{13}H_{15}N_3O_7$, crystallizes as two independent molecules which differ in their conformation. Intermolecular hydrogen bonding between the amide and carboxylic acid groups as N—H···O=C interactions results in the formation of one-dimensional chains with N···O distances of 2.967 (6) and 3.019 (6) Å. Neighbouring chains are linked by C=O···H—O interactions to form a two-dimensional network, with O···O distances of 2.675 (6) and 2.778 (6) Å.

Comment

The study of biologically important molecules continues to be of primary importance in medicinal chemistry. Processes such as blood coagulation, hormone processing, viral replication and cancer-cell invasion are critically dependent on protease enzymes which are attractive target molecules in the design of specific and selective drugs. Important protease inhibitors are usually based on modified amino acids incorporating structural features which determine normal enzyme-substrate recognition processes. Structure-based drug design strategies to identify interactions between a potential inhibitor and target receptor require accurate inhibitor structures. We are currently studying structure–activity relationships and molecular-recognition processes in biologically important molecules such as the title compound *N*-3,5-dinitrobenzoyl-L-leucine, (I), for applications in drug design (Gallagher & Murphy, 1999; Gallagher *et al.*, 1999, 2000).



(I)

In (I), two independent molecules are present which differ in conformation in space group *P*1 (No. 1). The bond lengths are largely in accord with anticipated values (Orpen *et al.*, 1994). The molecules differ in conformation about the N1—C2 bond, with N1—C2—C4 angles of 115.9 (5) and 110.1 (5)°, and C1—N1—C2—C3 torsion angles of −56.1 (7) and 81.5 (7)° in *A* and *B*, respectively. The aromatic C1—C11—C12 and C1—C11—C16 angles are 123.1 (6)/116.7 (6)° in molecule *A* and 125.6 (5)/116.6 (5)° in molecule *B*. This results from the intramolecular contacts H16*A*···O5*A* 2.45 Å and H1*A*···H12*A* 2.08 Å in *A*, and H16*B*···O5*B* 2.42 Å and H1*B*···H12*B* 2.14 Å in *B* (O5*B*···H2*B* 2.48 Å). The aromatic ring planes are oriented at angles of 19.1 (4) (*A*) and 12.8 (6)° (*B*) to their respective amide groups (O5/C1/N1/C2) and the nitro groups are almost coplanar (<10° from the aromatic ring planes), with O4*A* deviating by 0.265 (11) Å from the C_6 ring plane. The carboxylate (C2/C3/O6/O7) groups are almost normal to the (C11/C1/O5/N1/C2) planes, with angles of 85.9 (2) and 79.1 (2)° in molecules *A* and *B*, respectively.

The molecules are aligned in one-dimensional chains as $[A\ldots]_n$ and $[B\ldots]_n$ with (amide)$_{[A/B]}$N—H···O=C$_{[A/B]}$(acid) hydrogen bonds and partial overlap due to π–π stacking of the 3,5-dinitrobenzoyl groups. The N···O distances are 2.967 (6) Å along $[A\ldots]_n$ and 3.019 (6) Å along $[B\ldots]_n$. Interactions between the neighbouring *A* and *B* chains arise as carboxylate (for $A \rightarrow B$) and 2.778 (6) Å (for $B \rightarrow A$) (where $\rightarrow$ indicates the direction of the hydrogen bonding). This association results in the formation of two 20-membered hydrogen-bonded ring systems each consisting of two *A* and two *B* molecules and differing by the direction of the hydrogen bonding, $[B\ldots]_n \rightarrow [A\ldots]_n$ and $[A\ldots]_n \rightarrow [B\ldots]_n$ (where $\rightarrow$ indicates the carboxylic acid to amide O=C hydrogen bonds). Both rings have graph-set $R_4^4(20)$ which repeats as a two-dimensional network in the lattice (rings *J* and *K* in the deposited figure). Examination of the structure with *PLATON* (Spek, 1998) showed that there were no solvent-accessible voids.

The structure of L-leucine has been reported previously (Harding & Howieson, 1976; Collect *et al.*, 1986; Görbitz & Dalhus, 1996) and contains two crystallographically independent zwitterions having similar conformations in the asymmetric unit, unlike (I) above, where the two molecules differ significantly in conformation.

Experimental

N-3,5-Dinitrobenzoyl-L-leucine was synthesized by the reaction of 3,5-dinitrobenzoyl chloride with the parent L-leucine. Recrystallization from ethanol/water afforded colourless plate-like crystals suitable for X-ray analysis [m.p. 451–453 K (uncorrected); literature 187° (Vogel, 1989)]. IR ν_{max}(KBr): 3400, 1725, 1650, 1550, 1350 cm^{-1}. ^{1}H NMR data (400 MHz, δ, DMSO): 0.87–0.94 [6H, *d*, *J* = 6.4 Hz, C(CH$_3$)$_2$], 1.59–1.82 (3H, *m*, CH$_2$CH), 4.47–4.53 (1H, *m*, NCHCO$_2$), 8.38 (1H, *d*, *J* = 7.9 Hz, NH), 8.96 (1H, *t*, *J* = 2 Hz, ArH-*para*), 9.10 (2H, *d*, *J* = 2 Hz, ArH-*ortho*).

Crystal data

$C_{13}H_{15}N_3O_7$	$Z = 2$
$M_r = 325.28$	$D_x = 1.471$ Mg m^{-3}
Triclinic, $P1$	Mo $K\alpha$ radiation
$a = 5.8046$ (3) Å	Cell parameters from 25 reflections
$b = 10.6400$ (17) Å	$\theta = 9.3$–$22.0°$
$c = 12.9556$ (14) Å	$\mu = 0.121$ mm^{-1}
$\alpha = 109.428$ (11)°	$T = 294$ (1) K
$\beta = 102.416$ (7)°	Plate, colourless
$\gamma = 90.250$ (8)°	0.30 × 0.20 × 0.05 mm
$V = 734.44$ (15) Å^3	

Data collection

Enraf–Nonius CAD-4 diffractometer	$h = 0 \rightarrow 6$
ω–2θ scans	$k = -12 \rightarrow 12$
2621 measured reflections	$l = -15 \rightarrow 14$
2621 independent reflections	3 standard reflections
1326 reflections with $I > 2\sigma(I)$	frequency: 60 min
$\theta_{max} = 25.0°$	intensity decay: <1%

Refinement

Refinement on F^2	$(\Delta/\sigma)_{max} = 0.001$
$R[F^2 > 2\sigma(F^2)] = 0.045$	$\Delta\rho_{max} = 0.19$ e Å^{-3}
$wR(F^2) = 0.079$	$\Delta\rho_{min} = -0.18$ e Å^{-3}
$S = 0.937$	Extinction correction: *SHELXL*97
2621 reflections	Extinction coefficient: 0.0111 (17)
418 parameters	Absolute structure: Flack (1983)
H-atom parameters constrained	Flack parameter = −0.1 (16)
$w = 1/[\sigma^2(F_o^2) + (0.0242P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$	

Table 1
Selected geometric parameters (Å, °).

O1*A*—N13*A*	1.226 (6)	O1*B*—N13*B*	1.220 (6)
O2*A*—N13*A*	1.232 (6)	O2*B*—N13*B*	1.230 (6)
O3*A*—N15*A*	1.237 (7)	O3*B*—N15*B*	1.218 (6)
O4*A*—N15*A*	1.218 (7)	O4*B*—N15*B*	1.224 (6)
O5*A*—C1*A*	1.235 (7)	O5*B*—C1*B*	1.235 (7)
O6*A*—C3*A*	1.321 (7)	O6*B*—C3*B*	1.345 (7)
O7*A*—C3*A*	1.198 (7)	O7*B*—C3*B*	1.201 (7)
N1*A*—C1*A*	1.343 (7)	N1*B*—C1*B*	1.337 (7)
N1*A*—C2*A*	1.478 (6)	N1*B*—C2*B*	1.458 (6)
N13*A*—C13*A*	1.468 (8)	N13*B*—C13*B*	1.474 (7)
N15*A*—C15*A*	1.477 (7)	N15*B*—C15*B*	1.487 (7)
C1*A*—C11*A*	1.505 (8)	C1*B*—C11*B*	1.486 (8)
C2*A*—C4*A*	1.523 (7)	C2*B*—C3*B*	1.509 (8)
C2*A*—C3*A*	1.524 (8)	C2*B*—C4*B*	1.528 (7)
C1*A*—N1*A*—C2*A*	123.3 (5)	C1*B*—N1*B*—C2*B*	121.9 (5)
O1*A*—N13*A*—O2*A*	123.9 (6)	O1*B*—N13*B*—O2*B*	123.8 (6)
O3*A*—N15*A*—O4*A*	124.2 (7)	O3*B*—N15*B*—O4*B*	125.3 (6)
O5*A*—C1*A*—N1*A*	122.9 (6)	O5*B*—C1*B*—N1*B*	122.5 (6)
O5*A*—C1*A*—C11*A*	120.0 (6)	O5*B*—C1*B*—C11*B*	118.7 (6)
N1*A*—C1*A*—C11*A*	116.9 (6)	N1*B*—C1*B*—C11*B*	118.8 (6)
N1*A*—C2*A*—C3*A*	108.3 (5)	N1*B*—C2*B*—C3*B*	111.6 (5)
N1*A*—C2*A*—C4*A*	115.9 (5)	N1*B*—C2*B*—C4*B*	110.1 (5)
C3*A*—C2*A*—C4*A*	112.1 (5)	C3*B*—C2*B*—C4*B*	113.0 (5)
O6*A*—C3*A*—O7*A*	123.5 (6)	O6*B*—C3*B*—O7*B*	122.7 (6)
O6*A*—C3*A*—C2*A*	111.2 (5)	O6*B*—C3*B*—C2*B*	112.3 (5)
O7*A*—C3*A*—C2*A*	125.2 (6)	O7*B*—C3*B*—C2*B*	124.9 (6)
C2*A*—C4*A*—C5*A*	115.7 (5)	C2*B*—C4*B*—C5*B*	111.5 (5)
C4*A*—C5*A*—C6*A*	113.3 (6)	C4*B*—C5*B*—C6*B*	112.0 (6)
C12*A*—C11*A*—C1*A*	123.1 (6)	C12*B*—C11*B*—C1*B*	125.6 (5)
C16*A*—C11*A*—C1*A*	116.7 (6)	C16*B*—C11*B*—C1*B*	116.6 (5)
C2*A*—N1*A*—C1*A*—O5*A*	−8.9 (9)	C2*B*—N1*B*—C1*B*—O5*B*	4.3 (9)
C1*A*—N1*A*—C2*A*—C4*A*	70.8 (7)	C1*B*—N1*B*—C2*B*—C3*B*	81.5 (7)
N1*A*—C2*A*—C3*A*—O7*A*	120.7 (6)	N1*B*—C2*B*—C3*B*—O7*B*	−124.8 (7)
N1*A*—C2*A*—C4*A*—C5*A*	55.1 (7)	N1*B*—C2*B*—C4*B*—C5*B*	71.3 (7)

Molecule (I) crystallized in the triclinic system, space group $P1$ or $P\bar{1}$. The molecule is chiral and space group $P1$ was chosen and confirmed by the analysis. The absolute configuration is based on L-leucine. The crystal diffracted quite weakly but sufficient data (hemisphere) were collected to establish the structure and elucidate the hydrogen bonding interactions. The absolute structure is not reliably determined by this X-ray analysis, but is inferred from the known absolute configuration of the L-leucine used in the synthesis.

Data collection: *CAD*-4-*PC Software* (Enraf–Nonius, 1992); cell refinement: *SET*4 and *CELDIM* (Enraf–Nonius, 1992); data reduction: *DATRD*2 in *NRCVAX*96 (Gabe *et al.*, 1989); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *NRCVAX*96 and *SHELXL*97 (Sheldrick, 1997); software used to prepare material for publication: *NRCVAX*96, *SHELXL*97 and *PREP*8 (Ferguson, 1998).

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