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 $N-H\cdots O=C$ interactions results in the formation of one-dimensional chains with $N\cdots O$ distances of 2.967 (6) and 3.019 (6) Å. Neighbouring chains are linked by $C=O\cdots H-O$ interactions to form a two-dimensional network, with $O\cdots O$ 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)
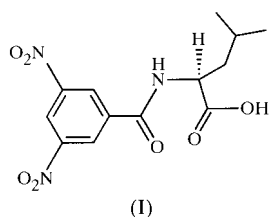
In (I), two independent molecules are present which differ in conformation in space group $P1$ (No. 1). The bond lengths are largely in accord with anticipated values (Orpen et al., 1994). The molecules differ in conformation about the N1—C2 bond, with N1—C2—C4 angles of 115.9 (5) and 110.1 (5)°, and 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 H16A···O5A 2.45 Å and H1A···H12A 2.08 Å in A, and H16B···O5B 2.42 Å and H1B···H12B 2.14 Å in B (O5B···H2B 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 O4A 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 → 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 → 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

$C_{13}H_{15}N_3O_7$
$M_r = 325.28$
Triclinic, $P1$
$a = 5.8046 (3)$ Å
$b = 10.6400 (17)$ Å
$c = 12.9556 (14)$ Å
$\alpha = 109.428 (11)°$
$\beta = 102.416 (7)°$
$\gamma = 90.250 (8)°$
$V = 734.44 (15)$ Å^3

$Z = 2$
$D_x = 1.471$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta = 9.3$–$22.0°$
$\mu = 0.121$ mm^{-1}
$T = 294 (1)$ K
Plate, colourless
$0.30 \times 0.20 \times 0.05$ mm

Data collection

Enraf–Nonius CAD-4 diffract-
ometer
ω–2θ scans
2621 measured reflections
2621 independent reflections
1326 reflections with $I > 2\sigma(I)$
$\theta_{max} = 25.0°$

$h = 0 \rightarrow 6$
$k = -12 \rightarrow 12$
$l = -15 \rightarrow 14$
3 standard reflections
  frequency: 60 min
  intensity decay: <1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.045$
$wR(F^2) = 0.079$
$S = 0.937$
2621 reflections
418 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0242P)^2]$
  where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.19$ e Å^{-3}
$\Delta\rho_{min} = -0.18$ e Å^{-3}
Extinction correction: SHELXL97
Extinction coefficient: 0.0111 (17)
Absolute structure: Flack (1983)
Flack parameter = -0.1 (16)

Table 1
Selected geometric parameters (Å, °).

O1A—N13A	1.226 (6)	O1B—N13B	1.220 (6)
O2A—N13A	1.232 (6)	O2B—N13B	1.230 (6)
O3A—N15A	1.237 (7)	O3B—N15B	1.218 (6)
O4A—N15A	1.218 (7)	O4B—N15B	1.224 (6)
O5A—C1A	1.235 (7)	O5B—C1B	1.235 (7)
O6A—C3A	1.321 (7)	O6B—C3B	1.345 (7)
O7A—C3A	1.198 (7)	O7B—C3B	1.201 (7)
N1A—C1A	1.343 (7)	N1B—C1B	1.337 (7)
N1A—C2A	1.478 (6)	N1B—C2B	1.458 (6)
N13A—C13A	1.468 (8)	N13B—C13B	1.474 (7)
N15A—C15A	1.477 (7)	N15B—C15B	1.487 (7)
C1A—C11A	1.505 (8)	C1B—C11B	1.486 (8)
C2A—C4A	1.523 (7)	C2B—C3B	1.509 (8)
C2A—C3A	1.524 (8)	C2B—C4B	1.528 (7)
C1A—N1A—C2A	123.3 (5)	C1B—N1B—C2B	121.9 (5)
O1A—N13A—O2A	123.9 (6)	O1B—N13B—O2B	123.8 (6)
O3A—N15A—O4A	124.2 (7)	O3B—N15B—O4B	125.3 (6)
O5A—C1A—N1A	122.9 (6)	O5B—C1B—N1B	122.5 (6)
O5A—C1A—C11A	120.0 (6)	O5B—C1B—C11B	118.7 (6)
N1A—C1A—C11A	116.9 (6)	N1B—C1B—C11B	118.8 (6)
N1A—C2A—C3A	108.3 (5)	N1B—C2B—C3B	111.6 (5)
N1A—C2A—C4A	115.9 (5)	N1B—C2B—C4B	110.1 (5)
C3A—C2A—C4A	112.1 (5)	C3B—C2B—C4B	113.0 (5)
O6A—C3A—O7A	123.5 (6)	O6B—C3B—O7B	122.7 (6)
O6A—C3A—C2A	111.2 (5)	O6B—C3B—C2B	112.3 (5)
O7A—C3A—C2A	125.2 (6)	O7B—C3B—C2B	124.9 (6)
C2A—C4A—C5A	115.7 (5)	C2B—C4B—C5B	111.5 (5)
C4A—C5A—C6A	113.3 (6)	C4B—C5B—C6B	112.0 (6)
C12A—C11A—C1A	123.1 (6)	C12B—C11B—C1B	125.6 (5)
C16A—C11A—C1A	116.7 (6)	C16B—C11B—C1B	116.6 (5)

C2A—N1A—C1A—O5A	−8.9 (9)	C2B—N1B—C1B—O5B	4.3 (9)
C1A—N1A—C2A—C4A	70.8 (7)	C1B—N1B—C2B—C3B	81.5 (7)
N1A—C2A—C3A—O7A	120.7 (6)	N1B—C2B—C3B—O7B	−124.8 (7)
N1A—C2A—C4A—C5A	55.1 (7)	N1B—C2B—C4B—C5B	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: SET4 and CELDIM (Enraf–Nonius, 1992); data reduction: DATRD2 in NRCVAX96 (Gabe et al., 1989); program(s) used to solve structure: SHELXS97 (Sheldrick, 1997); program(s) used to refine structure: NRCVAX96 and SHELXL97 (Sheldrick, 1997); software used to prepare material for publication: NRCVAX96, SHELXL97 and PREP8 (Ferguson, 1998).

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