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N-Chloroacetyl-β-alanine

Lourdes Urpí,[a] Katia Jiménez,[a] Xavier Solans,[b] Alfonso Rodríguez-Galán[a] and Jordi Puiggalí[a]*

[a]Departament d'Enginyeria Química, Universitat Politècnica de Catalunya, Av. Diagonal 647, E-08028 Barcelona, Spain, and [b]Departament de Cristal·lografia, Mineralogia i Dipòsits Minerals, Universitat de Barcelona, Martí i Franqués, E-08028 Barcelona, Spain
Correspondence e-mail: jordi.puiggali@upc.es

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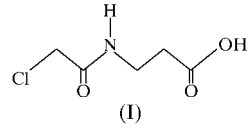
The β-alanine residue of the title compound, $C_5H_8ClNO_3$, has a *ggt* folded conformation, which is mainly stabilized through intermolecular N—H···O═C (amide–acid) and O—H···O═C (acid–amide) hydrogen bonds. In addition, a *cis* conformation is found for the Cl—CH_2—C(═O)—NH torsion angle, which is associated with the presence of an intramolecular hydrogen bond.

Comment

Polyesters constitute an important group of biodegradable polymers because of their potentially hydrolyzable ester bond. Furthermore, they have specialized applications in the field of medical technology, since both the polymers and their degradation products are usually non-toxic; an example is the use of polyglycolide, polylactide and poly(glycolide-*co*-lactide) as surgical sutures (Vert *et al.*, 1995). Nowadays, considerable efforts are being focused on improving the synthesis of polyesters and obtaining related polymers with enhanced properties. In this way, poly(ester amide)s derived from glycolic acid and amino acids, such as glycine or β-alanine, appear a viable alternative because of the properties afforded by the establishment of strong intermolecular hydrogen bonds. A further possibility is the solid-state polycondensation of halogenated carboxylates, which is an interesting method for the preparation of polyglycolide (Herzberg & Epple, 2001) and its derivatives; the resulting polymers display novel properties (porous micromorphology). A molecular solid-state reaction relies on a suitable arrangement of the reactants in the crystal and study of the relevant crystal structures is therefore fundamental. In general, this kind of halogen derivative yields microcrystals and, consequently, few structures have been solved by single-crystal diffraction (Epple & Kirschnick, 1997). The title compound, (I), has been chosen as the precursor of salts that could be polymerized in the solid state to obtain the sequential poly(ester amide) derived from glycolic acid and β-alanine.

The molecule of (I) is shown in Fig. 1, and selected torsion angles and hydrogen-bond geometry are reported in Tables 1 and 2. The amide and ester groups are planar within experimental error, with an r.m.s. deviation of the atoms from the best planes passing through them of 0.0022 and 0.0070 Å for the C4/C5/O2/O3 and C1/C2/O1/N1/H1/C3 planes, respectively. The packing is characterized by the establishment of a network of intermolecular hydrogen bonds involving amide–acid interactions between the H atoms of the NH and OH groups, and the CO group of the acid and amide groups, respectively. N—H···O═C interactions are established between molecules related by a binary axis, which consequently have an antiparallel arrangement, whereas O—H···O═C interactions link molecules related by the *c*-glide plane, which, therefore, have opposite signs for equivalent torsion angles. These hydrogen bonds combine to produce a ribbon structure, as depicted in Fig. 2, where a row of molecules linked by O—H···O═C interactions is aligned parallel to the *z* axis. In addition, weak C—H···O═C intermolecular hydrogen bonds were also detected (Table 2).



(I)

The molecular conformation of (I) shows interesting features concerning the chloroacetyl unit and the β-alanine residue, which is a constituent of some natural peptides (Bershon & Inhat, 1970; Bullough *et al.*, 1982). Accordingly, a number of small model peptides containing this residue have been investigated by X-ray crystallography (Banerjee & Balaram, 1997). Furthermore, conformational preferences of the dipeptide *N*-acetyl-β-alanineamide (Wu & Wang, 1998) have recently been studied using quantum mechanical gas-phase calculations. The results indicate that folded conformations, such as *ggt*, are energetically stabilized by an intramolecular six-membered hydrogen-bonded ring. This conformation is found in (I) and also in other compounds (Maji *et al.*, 2001) where intermolecular hydrogen bonds could be established in the solid state. However, the torsion angles of (I) deviate slightly from theoretical values [*e.g.* 80.5 (3)° *versus* 60° for the C(═O)—NH—CH_2—CH_2 angle] and, thus,

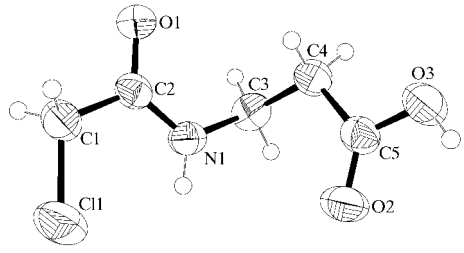


Figure 1
*ORTEP*II (Johnson, 1976) drawing of the title compound with the atom-numbering scheme for non-H atoms. Displacement ellipsoids are drawn at the 50% probability level and H atoms are drawn as circles of arbitrary radii.

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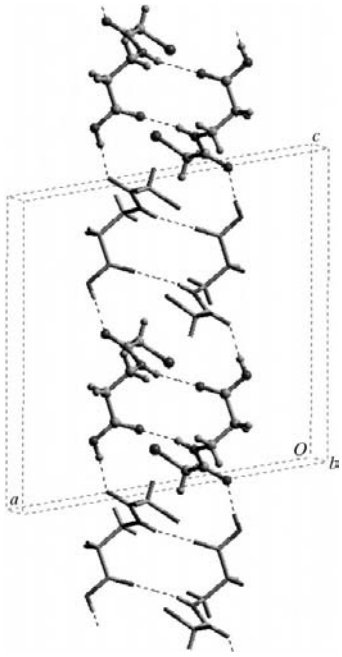

Figure 2
Crystal packing diagram of the title compound (*CERIUS*2; Accelrys Molecular Simulations), showing the network of hydrogen bonds (dashed lines) that give rise to a ribbon structure. Molecules with the same torsion-angle values are drawn in the same way (cylinders or balls and sticks). Only four molecules of the unit cell are drawn in order to simplify the representation. The unit cell is composed of four additional molecules that constitute a new ribbon shifted by *a*/2 and *b*/2 along the *a* and *b* axes, respectively.

the intramolecular hydrogen bond is weakened to such an extent that it effectively loses its identity [H1—O2 = 2.87 (3) Å, N1—O2 = 3.091 (3) Å and N1—H1—O2 = 98 (2)°]. This may be due to the competition of two hydrogen-bond acceptors (Cl1 and O2) for forming an intramolecular hydrogen bond with N1—H1; atom O2 is involved in an intermolecular hydrogen bond with N1—H1 (Table 2). A survey of the Cambridge Structural Database (Allen, 2002) shows 36 crystal structures containing a total of 55 *X*–C(═O)NHCH$_2$CH$_2$C(═O)–*X* units, which demonstrate the preferences for a folded conformation. Thus, the torsion angles φ [C(═O)—NH—CH$_2$—CH$_2$], ξ [NH—CH$_2$—CH$_2$—C(═O)] and ψ [CH$_2$—CH$_2$—C(═O)—O] preferentially adopt skew-*gauche* (45–34%), *gauche* (52%) and *trans* (43%) conformations, respectively.

Finally, it is noteworthy that the Cl—CH$_2$—C(═O)—NH torsion angle has a *cis* conformation, in agreement with the results obtained for other related structures, such as chloroacetylglycylglycine (Rao & Mallikarjunan, 1973) and 2-chloroacetamide (Kalyanaraman *et al.*, 1978). This conformation is clearly stabilized by an N—H···Cl intramolecular hydrogen bond (Table 2).

Experimental

The title compound was synthesized by dropwise addition of a diethyl ether solution of chloroacetyl chloride (0.88 mol in 180 ml) to an equimolar aqueous solution of β-alanine (0.8 mol in 200 ml) and sodium hydroxide. The reaction mixture was maintained at a temperature of 268 K and a pH close to 11–12 by gradual addition of a concentrated NaOH solution to neutralize the hydrochloric acid produced during the condensation. After 16 h of stirring at room temperature, the solution was evaporated under reduced pressure. The solid product was extracted with hot acetone, and the resulting solution was evaporated again. Finally, a white solid was obtained and recrystallized from 2-propanol to give colourless prismatic crystals (yield 55%, m.p. 365 K). ^{1}H NMR (CDCl$_3$/TFA, TMS, internal reference): δ 7.6 (*s*, 1H, COOH), 7.3 (*m*, 1H, NH), 4.2 (*s*, 2H, ClCH$_2$-CO), 3.7 (*m*, 2H, NHCH$_2$), 2.8 (*t*, 2H, CH$_2$COO).

Crystal data

$C_5H_8ClNO_3$	D_x = 1.450 Mg m^{-3}
M_r = 165.57	Mo $K\alpha$ radiation
Monoclinic, *C*2/*c*	Cell parameters from 25 reflections
a = 14.41 (2) Å	θ = 12–21°
b = 7.282 (6) Å	μ = 0.45 mm^{-1}
c = 14.672 (2) Å	*T* = 293 (2) K
β = 99.96 (6)°	Prism, colourless
V = 1516 (2) Å^3	0.2 × 0.1 × 0.1 mm
Z = 8	

Data collection

Enraf–Nonius CAD-4 diffractometer	θ_{max} = 26.4°
$\omega/2\theta$ scans	$h = -18 \rightarrow 17$
1632 measured reflections	$k = 0 \rightarrow 9$
1550 independent reflections	$l = 0 \rightarrow 18$
951 reflections with $I > 2\sigma(I)$	1 standard reflection
R_{int} = 0.020	frequency: 120 min
	intensity decay: none

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0647P)^2 + 1.1856P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.052	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2)$ = 0.145	$\Delta\rho_{max}$ = 0.32 e Å^{-3}
S = 1.03	$\Delta\rho_{min}$ = −0.24 e Å^{-3}
1550 reflections	
99 parameters	
H atoms treated by a mixture of independent and constrained refinement	

Table 1
Selected torsion angles (°).

C3—N1—C2—C1	−179.4 (3)	C5—C4—C3—N1	73.1 (3)
O3—C5—C4—C3	174.2 (3)	N1—C2—C1—Cl1	4.4 (4)
C2—N1—C3—C4	80.5 (3)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3—H3···O1^{i}	0.84 (4)	1.81 (4)	2.638 (3)	165 (4)
N1—H1···O2^{ii}	0.83 (3)	2.27 (3)	2.951 (5)	139 (3)
N1—H1···Cl1	0.83 (3)	2.56 (3)	2.982 (4)	112 (3)
C1—H1*A*···O2^{iii}	0.97	2.61	3.438 (4)	143
C1—H1*B*···O1^{iv}	0.97	2.57	3.414 (6)	146
C4—H4*A*···O1^{v}	0.97	2.67	3.448 (4)	137

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

Atoms H1 and H3, which are involved in hydrogen bonds, were located in difference Fourier maps and were refined isotropically. The remaining H atoms were placed in calculated positions and refined riding on their attached C atoms, with C—H distances of 0.97 Å and U_{iso} values equal to 1.2 times the U_{eq} values of the parent atoms.

Data collection: *CAD*-4 *Software* (Kiers, 1994); cell refinement: *CAD*-4 *Software*; data reduction: local program; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976) and *CERIUS*2 (Accelrys Molecular Simulations, 2002).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: JZ1532). Services for accessing these data are described at the back of the journal.

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