

The Crystal Structure of DL-N-Chloroacetylalanine*

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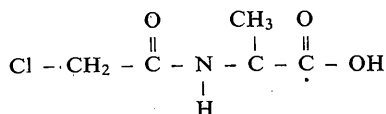
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DL-N-Chloroacetylalanine, $\text{ClCH}_2\text{CONHCH}(\text{COOH})(\text{CH}_3)$, crystallizes in the monoclinic space group $P2_1/c$ with unit-cell parameters $a=10.807 \pm 0.003$, $b=7.584 \pm 0.001$, $c=9.402 \pm 0.002$ Å and $\beta=108.97 \pm 0.12^\circ$ at $T=22^\circ\text{C}$. There are four molecules per unit cell. Intensity data complete to $\sin \theta/\lambda=0.61$ were collected by diffractometer methods using Cu $K\alpha$ radiation. The structure was deduced by direct methods and subsequently refined by block-diagonal least-squares methods to a weighted index of 0.055. The molecule exists in an extended configuration. The plane defined by the carboxyl group makes an angle of 20.1° with respect to the chain of the molecule. Hydrogen bonds link molecules together along the b axis.

Introduction

Electron spin resonance studies of several radiation-damaged α -amino acids and derivatives of these acids have been carried out by Horstfield, Morton & Whiffen (1961) and by Box & Wells (1966*a*). These studies have suggested that if a methyl group is present in the radical species, then this group either rotates or undergoes large thermal motion. Double resonance studies carried out on crystalline DL-N-chloroacetylalanine by Box & Wells (1966*b*) at 4°K have established that the principal radical species produced is



and that the methyl group of this species also exhibits the phenomenon described above.

Since little was known about crystalline DL-N-chloroacetylalanine, a detailed crystal structure analysis was undertaken to establish the exact geometry and environment of the molecule in the crystalline state, with the hope that the results obtained could be correlated with the electron spin resonance studies.

Experimental

Crystals suitable for X-ray studies were kindly provided by Mr J. Wells. The crystals were flat transparent plates elongated along the [010] direction and exhibited {100} and {001} faces. A crystal whose dimensions were approximately $0.2 \times 0.25 \times 0.25$ mm was selected for this investigation. Table 1 lists the space group, cell dimensions, and the observed and calculated densities. The cell dimensions and estimated standard deviations are the results of a least-squares treatment of 26 high order, general reflections.

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Table 1. Crystal data

Formula:	$\text{ClCH}_2\text{C}(\text{O})\text{NHCH}(\text{CH}_3)\text{COOH}$
M. W.	165.4 a.m.u.
Space group:	$P2_1/c$
ρ_{obs} :	1.49 g.cm^{-3}
ρ_{calc} :	1.50 g.cm^{-3}
	$a = 10.807 \pm 0.003$ Å
	$b = 7.584 \pm 0.001$
	$c = 9.402 \pm 0.002$
	$\beta = 108.97 \pm 0.02^\circ$
	$T = 22^\circ \pm 2^\circ\text{C}$
	$Z = 4$

The intensity measurements were made with a General Electric XRD6 diffractometer equipped with goniostat. The intensities were measured by the stationary-counter stationary-crystal method (Furnas & Harker, 1955) and monochromatization of the Cu $K\alpha$ radiation was effected by an almost perfectly balanced pair of Ross filters: Ni and Co. Data complete to $\sin \theta/\lambda=0.61$ amounting to 1362 reflections were collected. Approximately 88% of these reflections had observable intensities. The intensities were approximately corrected for absorption as a function of the angle φ , reduced to relative $|F_{\text{obs}}|^2$ values in the usual manner, and placed on an absolute scale (Wilson, 1942). Weights for each reflection were computed (Evans, 1961). The scaled $|F_{\text{obs}}|^2$ values were subsequently reduced to E 's whose statistical averages and distribution are listed in Table 2.

Table 2. Statistical distribution of normalized structure factors

	Experimental	Theoretical	
		Centric	Acentric
$\langle E ^2 \rangle$	1.00	1.00	1.00
$\langle E \rangle$	0.773	0.798	0.886
$\langle E^2 - 1 \rangle$	0.948	0.986	0.736
% $E > 1.0$	31.1	32.0	36.8
% $E > 2.0$	4.8	5.0	1.8
% $E > 3.0$	0.36	0.3	0.1

Determination of structure

The structure was deduced using the symbolic addition procedure (Karle & Karle, 1953, 1966). The computer program SORTE (Bednowitz & Post, 1966) facilitated the phase determination process. In this investigation, the

origin of the unit cell was specified by assigning positive phases to three linearly independent reflections with large E values and participating in a large number of Σ2 interactions. Letter phases were assigned to two additional reflections in order to facilitate the application of the Σ2 relation. In all, a total of 135 phases for

Table 3. Observed and calculated structure factors (x 10)

Table with 40 columns (H, K, L, Fobs, Fcalc) and 40 rows of numerical data representing structure factors.

E 's greater than 1.5 were assigned. By employing the Harker-Kasper (1948) inequality, $|U_{hkl}|^2 < \frac{1}{2} + \frac{1}{2}(-1)^k U_{2h,0,2l}$, it was possible to reduce all symbolically assigned phases to 0 or π . A three-dimensional E map computed from the above phase assignment revealed all the non-hydrogen atoms.

Refinement of the structure

With the approximate positions of all the heavier atoms known, refinement was effected by means of a

series of least-squares analyses, minimizing the quantity $\sum w(|F_o| - |F_c|)^2$ where w is the weight applied to each reflection. The scattering factor tables used for the non-hydrogen atoms are those reported by Cromer & Waber (1965); the scattering factor table for hydrogen is the one reported by McWeeny (1951).

In the first stage of refinement, unit weights were assigned to all reflections. The refinement converged to $R=0.22$. A few low-order reflections having large intensities and showing large discrepancies (possibly extinction effects) were then omitted from any further

Table 4. Atomic parameters*

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Cl	0.0237 (0.9)	0.6078 (1)	0.7134 (1)	98 (1)	161 (1)	188 (1)	-35 (2)	146 (2)	-10 (3)
N	0.2378 (2)	0.4707 (3)	0.6134 (3)	93 (3)	81 (4)	147 (4)	2 (6)	121 (6)	13 (7)
C(1)	0.1212 (3)	0.7391 (4)	0.6343 (4)	107 (4)	111 (6)	185 (6)	5 (5)	168 (9)	14 (1)
C(2)	0.2201 (3)	0.6401 (3)	0.5828 (3)	73 (3)	82 (5)	122 (5)	-11 (4)	59 (7)	8 (8)
C(3)	0.3230 (3)	0.3609 (3)	0.5588 (3)	80 (2)	71 (5)	153 (5)	5 (7)	105 (7)	13 (8)
C(4)	0.4663 (3)	0.3778 (4)	0.6552 (4)	83 (4)	132 (7)	218 (7)	-12 (9)	89 (9)	15 (12)
C(5)	0.2776 (3)	0.1712 (4)	0.5624 (3)	86 (4)	89 (5)	146 (5)	10 (7)	104 (8)	10 (9)
O(1)	0.2804 (3)	0.7219 (3)	0.5124 (3)	101 (3)	85 (4)	176 (4)	14 (5)	152 (6)	23 (6)
O(2)	0.3267 (3)	0.0630 (3)	0.4874 (4)	123 (3)	93 (4)	175 (4)	-1 (6)	163 (6)	-19 (7)
O(3)	0.2080 (3)	0.1285 (3)	0.6329 (3)	200 (4)	100 (4)	309 (6)	-44 (7)	359 (9)	-26 (9)
H(1)	0.053 (3)	0.804 (4)	0.546 (3)	29					
H(2)	0.168 (3)	0.824 (4)	0.720 (3)	37					
H(3)	0.188 (3)	0.422 (4)	0.657 (3)	20					
H(4)	0.301 (3)	0.372 (4)	0.450 (3)	20					
H(5)	0.484 (3)	0.486 (4)	0.663 (3)	27					
H(6)	0.479 (3)	0.354 (4)	0.759 (4)	40					
H(7)	0.514 (3)	0.311 (4)	0.608 (3)	41					
H(8)	0.302 (3)	-0.059 (4)	0.507 (4)	68					

* The temperature factors for non-hydrogen atoms are of the form $\exp [-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + \beta_{12}hk + \beta_{13}hl + \beta_{23}kl)]$. The hydrogen atoms were given isotropic temperature factors. Listed above is $\beta_{ij} \times 10^4$ for non-hydrogen atoms. Thermal parameters for hydrogen atoms are $B \times 10$.

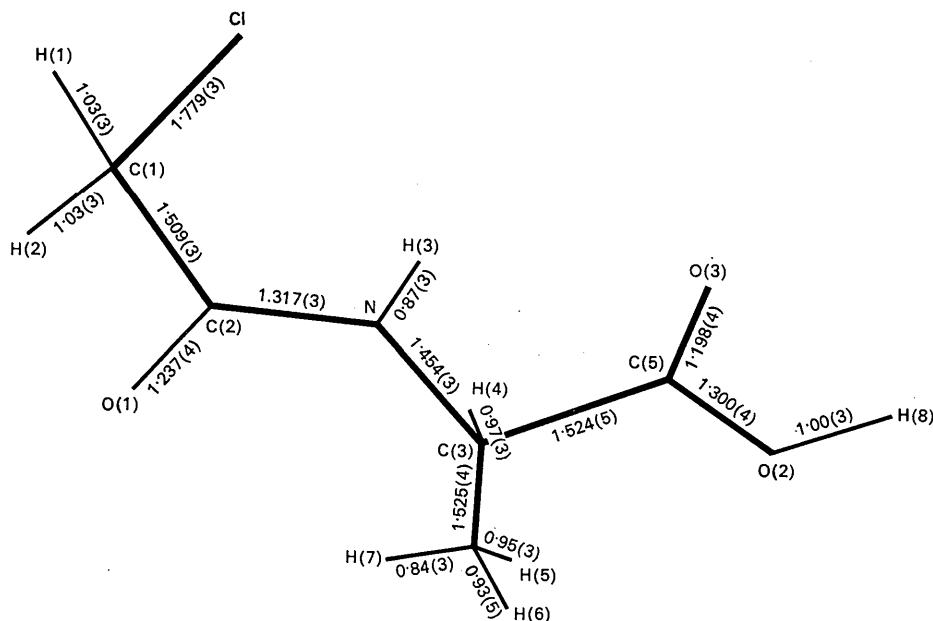


Fig. 1. Bond distances.

least-squares analyses. In the second stage individual weights for each reflection were applied. The scale factor, atomic coordinates and anisotropic temperature factors for the non-hydrogen atoms were then subjected to several cycles of least-squares which led to $R=0.082$.

An electron density difference Fourier synthesis computed at this stage revealed eight peaks whose maxima were between 0.32 and 0.42 e.Å⁻³. The coordinates of these peaks were introduced into the refinement as hydrogen atoms and were given isotropic temperature factors. The refinement then converged to $R=0.064$ for all reflections and 0.055 for those considered observable. The isotropic temperature factors for the hydrogen atoms ranged from 2.0 to 6.8. A second electron density difference map revealed no fluctuation greater than ± 0.16 e.Å⁻³, except in the region from which the chlorine had been subtracted.

Shifts in the atomic parameters at this stage were less than one-tenth the computed standard deviation. The refinement was terminated and the estimated standard deviations were computed from the sum of the residuals and the diagonal elements of the inverse matrix of the least-squares normal equations. The atomic parameters and estimated standard deviations are given in Table 3. The observed and calculated structure factors are listed in Table 4.

Discussion

The methyl group

Since all hydrogen atoms were unambiguously located, the assumption of hindered rotation of the methyl group in the undamaged molecule is not required. Furthermore, the thermal parameters (Table 4) of C(4), H(5), H(6) and H(7) are not excessively large and the root-mean-square components of C(4) (Table 8) do not suggest extreme anisotropic motion. In the radical species, the model which best describes the motion of the methyl group is that of a hindered rotor with a barrier of 0.19 kcal.mol⁻¹ opposing rotation at 2.4°K (Box & Wells, 1966*b*). However, the limited accuracy in determining the atomic coordinates and thermal parameters of the hydrogen atoms from X-ray diffraction measurements rules out any detailed description of the thermal motion of the methyl group in the undamaged molecule.

Intramolecular bond distances and angles

The intramolecular bond lengths and angles along with the corresponding estimated standard deviations are given in Fig. 1 and Table 5 respectively. The average estimated standard deviations in bond lengths are as follows: C-C, 0.004; C-N, 0.003; C-O, 0.004; C-H, 0.04 and O-H, 0.05 Å. Bond angles involving non-hydrogen atoms have a maximum estimated deviation of 0.3°; for those involving hydrogen atoms, the error is approximately 3°. These estimated errors, as usual, must be the lower limits of the actual errors.

Table 5. Bond angles

	Angle
C(2)-C(1)-Cl	115.7 (2)°
H(1)-C(1)-Cl	103.0 (2)
H(2)-C(1)-Cl	103.0 (2)
H(1)-C(1)-C(2)	111.0 (2)
H(2)-C(1)-C(2)	110.0 (2)
H(1)-C(1)-H(2)	111.0 (2)
O(1)-C(2)-C(1)	118.2 (2)
O(1)-C(2)-N	122.9 (3)
N-C(2)-C(1)	118.9 (3)
H(3)-N-C(2)	117.0 (2)
H(3)-N-C(3)	119.0 (2)
C(3)-N-C(2)	123.1 (2)
H(4)-C(3)-N	110.0 (2)
H(4)-C(3)-C(5)	118.0 (2)
H(4)-C(3)-C(4)	97.0 (2)
N-C(3)-C(4)	112.3 (2)
N-C(3)-C(5)	106.7 (2)
C(4)-C(3)-C(5)	109.8 (2)
H(5)-C(4)-H(6)	117.0 (3)
H(5)-C(4)-H(7)	89.0 (3)
H(5)-C(4)-C(3)	107.0 (2)
H(6)-C(4)-H(7)	117.0 (3)
H(6)-C(4)-C(3)	111.0 (2)
H(7)-C(4)-C(3)	106.0 (2)
O(3)-C(5)-O(2)	124.8 (2)
O(3)-C(5)-C(3)	122.1 (2)
O(2)-C(5)-C(3)	113.0 (2)
H(8)-O(2)-C(5)	107.0 (2)

Within the limits of error, the dimensions of the alanine group are in agreement with those found in glycyl-L-alanine hydrochloride (Tranter, 1956), DL-alanine (Donohue, 1950) and L-alanine (Simpson & Marsh, 1966). The N-C(3) distance is 1.454 ± 0.003 Å and is 0.03 Å shorter than the weighted average N-C distance of 1.487 (Marsh & Donohue, 1967) found in peptides. All other distances and angles are quite normal.

Least-squares planes

The molecule exists in an extended conformation in which the atoms Cl, C(1), C(2), O(1), N and C(3) are nearly coplanar. The least-squares plane defined by these atoms is $0.4244P + 0.1785Q + 0.8872R = 5.695$, where P , Q and R are Cartesian coordinates in Å units along \mathbf{a} , \mathbf{b} and \mathbf{c}^* .

The root-mean-square deviation of the five atoms from this plane is 0.05 Å. The nitrogen atom exhibits

Table 6. Deviation of atoms from the plane defined by chain of molecule

	Distance to plane
Cl	0.05 Å
N	0.07
C(1)	0.021
C(2)	0.02
C(3)	0.04
C(4)	1.27
C(5)	0.48
O(1)	0.05
O(2)	0.89
O(3)	0.39

the largest deviation (0.07 Å) of all atoms used in defining the plane. Table 6 lists the deviation of the non-hydrogen atoms from the above plane. This plane makes an angle of 20.1° with the plane defining the carboxyl grouping, described by the equation $0.5692P - 0.1303Q + 0.818R = 4.615$.

Intermolecular features

A view along [001] is illustrated in Fig. 2. The mol-

ecules are linked by hydrogen bonding between H(8) and O(1') where O(1') is related to O(1) by a unit translation along the *b* axis. The O---O distance, O-H-O angle, and C-O-H angle are 2.68 Å, 166° and 107° respectively. Other short intermolecular contacts are listed in Table 7; none of these indicate the presence of additional hydrogen bonding. The packing is such that methyl groups related by a twofold screw axis or center of inversion are in close contact. The carbon-

Table 7. Non-bonded contacts less than 3.5 Å*

Atom 1	Atom 2	Cell	<i>S</i> (<i>i</i>)	Distance
Cl	H(1)	010	4	3.11 Å
Cl	H(2)	0-11	3	3.18
Cl	O(3)	010	4	3.46
Cl	H(8)	101	3	3.36
Cl	H(3)	011	2	3.49
N	Cl	011	2	3.48
C(1)	O(3)	010	4	3.42
C(2)	H(2)	01-1	4	3.28
C(3)	H(8)	101	2	3.22
C(4)	H(5)	111	2	3.36
C(5)	O(3)	0-10	1	3.44
C(2)	H(2)	01-1	4	3.28
C(5)	H(5)	1-11	3	3.31
O(1)	C(1)	0-10	1	3.10
O(1)	H(1)	0-10	1	2.94
O(1)	H(2)	0-10	1	2.53
O(1)	H(8)	101	2	2.29
O(1)	H(2)	011	2	2.82
O(2)	H(5)	1-11	3	3.31
O(2)	H(6)	00-1	4	3.05
O(2)	H(3)	00-1	4	2.98
H(5)	H(6)	1-11	4	2.88

* 'Cell' refers to unit translations along the crystallographic axes. *S*(*i*) refers to the symmetry elements of the space group. *S*(1) = *x, y, z*; *S*(2) = *-x, -y, -z*; *S*(3) = *-x, ½+y, ½-z* and *S*(4) = *x, ½-y, ½+z*.

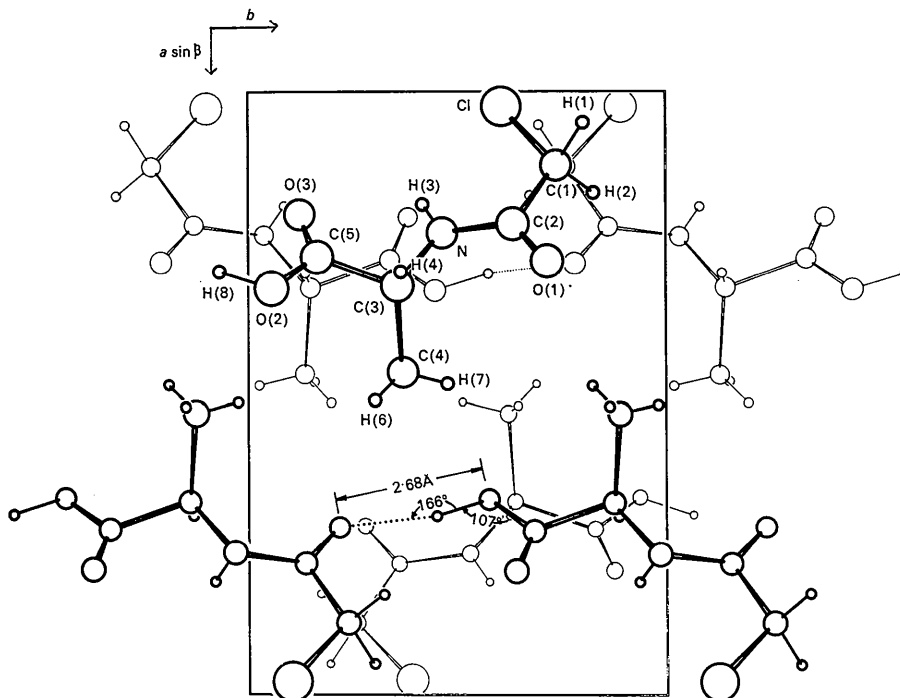


Fig. 2. View of the structure down [001].

Table 8. *Description of thermal ellipsoids*

	Axis (<i>i</i>)	<i>U</i> (<i>i</i>) Å	<i>C</i> (<i>ia</i>)	<i>C</i> (<i>ib</i>)	<i>C</i> (<i>ic</i> *)
C(1)	1	0.15	-0.0500	-0.9983	-0.0287
	2	0.19	0.9805	0.0436	-0.1913
	3	0.25	0.1897	0.0377	0.9811
C(2)	1	0.16	0.0911	-0.9937	0.0640
	2	0.20	-0.9600	-0.0706	0.2706
	3	0.24	-0.2644	-0.0861	-0.9605
C(3)	1	0.18	-0.0313	-0.9974	0.0642
	2	0.19	-0.9172	0.0542	0.3945
	3	0.28	-0.3970	-0.0465	-0.9166
C(4)	1	0.16	-0.1626	-0.9855	-0.0483
	2	0.19	-0.9755	0.1679	-0.1417
	3	0.22	0.1478	0.0240	-0.9887
C(5)	1	0.20	-0.4894	-0.8597	-0.1456
	2	0.21	-0.8500	0.5076	-0.1400
	3	0.30	0.1943	0.0552	0.9793
O(1)	1	0.17	-0.1528	0.9773	0.1465
	2	0.21	0.8602	0.2045	-0.4669
	3	0.28	0.4863	-0.0546	0.8720
O(2)	1	0.17	0.2373	0.9694	-0.0612
	2	0.21	0.8375	-0.2362	-0.4926
	3	0.38	-0.4920	0.0656	-0.8680
O(3)	1	0.16	-0.0354	0.9950	-0.0924
	2	0.19	0.9201	-0.0035	-0.3916
	3	0.27	0.3900	0.0989	0.9154
N	1	0.16	0.0004	-0.9986	0.0526
	2	0.19	-0.9425	0.1720	0.3337
	3	0.25	-0.3341	-0.0498	-0.9411
Cl	1	0.19	0.8808	0.4277	-0.2026
	2	0.23	-0.3812	0.8949	0.2317
	3	0.28	0.2805	-0.1269	0.9514

carbon distance across a center of inversion is 3.72 Å, while the carbon-carbon distance for methyl groups related by a twofold screw axis is 4.15 Å. The distance of 3.72 Å is considerably shorter than the accepted methyl-methyl van der Waals distance (Pauling, 1960). This distance, however, is misleading in that the shortest hydrogen-hydrogen contact between methyl groups is 2.88 Å and is approximately 0.5 Å longer than the sum of the van der Waals radii for two hydrogen atoms in non-bonded contact (Pauling, 1960).

Description of thermal motion

The magnitudes and direction cosines of the principal axes of thermal motion, as derived from the parameters of Table 4, are listed in Table 8. The range of the maximum r.m.s. components is from 0.22 for C(4) to 0.38 Å for O(2). The minimum components are from 0.15 Å for C(1) to 0.20 Å for C(5). The maximum r.m.s. displacements for all of the atoms listed are in the general direction of *c**; the minimum components are generally in the direction of *b*. Thus, a chain of molecules linked by hydrogen bonds along the *b* axis exhibits its maximum vibration essentially perpendicular to the chain and minimum vibration parallel to the chain.

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