The Crystal Structure and the Conformational Analysis of Carbobenzoxy-L-leucyl-p-nitrophenyl Ester

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Carbobenzoxy-L-leucyl-p-nitrophenyl ester crystallizes in space group $P2_12_12_1$ with $a=8\cdot49_8$, $b=9\cdot40_1$ and $c=25\cdot21_7$ Å. 1398 independent reflexions were collected on a Philips automatic diffractometer. The structure was solved by direct methods, and refined isotropically by full-matrix least-squares calculations. The final R is 0·105. The molecule assumes a 'folded-back' conformation in the crystal, the folding occurring at the Leu residue. The two parts of the molecule departing from the Leu residue are in the extended conformation. The OC–NH group deviates significantly from planarity. The molecules are held together by hydrogen bonds and dipole–dipole and van der Waals interactions. The prediction of the conformational analysis, particularly for the fragment containing the Leu residue, is in accordance with the actual structure.
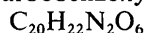
Introduction

The title compound, hereinafter referred to as ZLNP, has been studied for two main reasons. The first is related to a research programme concerning the prediction of the molecular conformation by potential energy calculations. The knowledge of the molecular geometry may be a considerable help in solving a crystal structure. The use of direct methods or potential energy calculations is simplified if an approximate molecular model is available. The interpretation of an E map is easier and the time required for a full search of the energy minima is considerably reduced if the degrees of freedom are decreased by fixing the intramolecular ones (Coiro, Giglio & Quagliata, 1972). Therefore we have carried out the conformational analysis of a molecule having many degrees of freedom, to verify the predictive reliability of potential energy calculations.

The other reason is connected with the study of the OC–NH group planarity which is important in the conformational analysis of cyclic and acyclic oligopeptides as well as polypeptides (Ramachandran, 1968; Coiro, Giacomello & Giglio, 1971; Ramachandran & Kolaskar, 1973). ZLNP is suitable for such investigation because of the presence of the bulky Leu residue which may cause a torsion around the ω angle of the peptide group.

Experimental

Single crystals of ZLNP were obtained as colourless prisms from a solution of ethyl acetate and n-hexane in the ratio 4:1.

Carbobenzoxy-L-leucyl-p-nitrophenyl ester:
$C_{20}H_{22}N_2O_6$
F.W. 386·4
λ(Mo $K\alpha$) = 0·7107 Å
Orthorhombic, $a= 8\cdot49_8(6)$ Å
$b= 9\cdot40_1(6)$
$c= 25\cdot21_7(18)$
$U=2014\cdot6$ Å³
$D_m=1\cdot26$, $D_c=1\cdot27$ g cm⁻³, $Z=4$
μ(Mo $K\alpha$) = 1·01 cm⁻¹
m.p. 96–98 °C.
Space group: $P2_12_12_1$ from systematic absences.

The density was measured in aqueous K_2CO_3 by flotation. A crystal of dimensions $0\cdot6 \times 0\cdot5 \times 0\cdot3$ mm was mounted on an automatic four-circle Philips PW 1100 single-crystal diffractometer, equipped with a scintillation counter, pulse-height analyser and graphite monochromator.

Intensities were collected with Mo $K\alpha$ radiation to the limit $2\theta = 50°$. Each reflexion was scanned once at a rate of $0\cdot1°$ s⁻¹ over a range of $1\cdot5°$. The moving-

crystal stationary-detector (ω scan) technique was used. The intensities of 1398 independent reflexions greater than $2\sigma(I)$ out of 2050 possible were collected. Three standard reflexions, measured every three hours, remained essentially constant, showing only deviations from the mean predicted by counting statistics. Background counts were taken for a time equal to that of the scan. The data were corrected first for counting losses (Arndt & Willis, 1966) with $t = 2.5 \times 10^{-6}$ s and $K = 1$ and then for background. Standard deviations were assigned according to $\sigma(I) = [P + B + (pI)^2]^{1/2}$ where P is the total integrated peak count obtained in the scan, B is the total background count, $I = P - B$ and p is the 'ignorance factor' (Corfield, Doedens & Ibers, 1967) fixed as 0.06. Lorentz and polarization factors were applied taking into account the monochromator crystal (Azároff, 1955).

Structure solution and refinement

The structure was solved by the multisolution technique of Main, Woolfson & Germain (1971). The reflexions listed in Table 1 were used to calculate the phases of the 196 reflexions with $[E] \geq 1.43$. From an E map, computed from the 'best' set of phases, all the non-hydrogen atoms except O(2), C(3), O(4), N(5), C(6), C(7) and O(8) were recognized. A structure-factor calculation was computed in order to phase a Fourier synthesis which unambiguously revealed the remaining atoms corresponding to the central part of the molecule. All these atoms with $z \sim \frac{1}{2}$ are located around the screw axis along a.

Table 1. *Results from MULTAN*

h	k	l	E	Code*	Possible phases	Starting phases that gave the solution
0	8	7	4.03	a	0	0
7	6	8	2.72	a	$\pm \pi/4$	$\pi/4$
1	11	3	2.39	b	$\pi/4$	$\pi/4$
1	2	10	2.00	c	$\pm \pi/4, \pm \frac{3}{4}\pi$	$-\frac{3}{4}\pi$
0	8	12	2.88	c	$0, \pi$	0
0	0	22	3.34	c	$0, \pi$	0

* a = origin definition, b = origin and enantiomorph definition, c = symbolic phases.

The positional and individual isotropic thermal parameters of all the non-hydrogen atoms were refined by full-matrix least-squares calculations, using all observed reflexions. Isotropic refinement was preferred since the number of available reflexions is too small for anisotropic refinement. The function minimized was $\sum w(|F_o| - |F_c|)^2$, w being equal to $1/(a + b|F_o| + c|F_o|^2)$ with $a = 9.0000$, $b = 1.0000$ and $c = 0.0125$.

The refinement was considered to be complete when the parameter shifts were less than 6% of the e.s.d.'s. The sum of the squares of the ratios between the parameter shifts and the e.s.d.'s was 0.02. The adequacy of the weighting scheme was checked by inspection of the mean of $\omega|\Delta F|^2$ as a function of $|F_o|$ and $(\sin \theta/\lambda)$ ranges: in both cases the function was nearly constant. The final positional and thermal parameters are reported in Table 2.

Table 2. *Final fractional coordinates and isotropic thermal factors with their standard deviations in parentheses*

	x	y	z	B (Å^2)
C(1)	-0.0373 (13)	1.0849 (12)	0.4454 (4)	4.8 (2)
O(2)	-0.1044 (7)	0.9582 (7)	0.4716 (2)	3.8 (1)
C(3)	-0.0042 (11)	0.8755 (9)	0.4982 (4)	3.4 (2)
O(4)	0.1339 (8)	0.9000 (8)	0.5023 (3)	4.3 (1)
N(5)	-0.0800 (9)	0.7672 (7)	0.5209 (3)	3.2 (1)
C(6)	0.0038 (11)	0.6481 (10)	0.5449 (4)	3.6 (2)
C(7)	0.0208 (11)	0.5302 (10)	0.5042 (3)	3.6 (2)
O(8)	-0.0101 (9)	0.4065 (8)	0.5112 (3)	4.9 (1)
O(9)	0.0757 (9)	0.5845 (8)	0.4587 (3)	4.8 (1)
C(10)	-0.0739 (12)	0.5980 (11)	0.5948 (4)	4.0 (2)
C(11)	-0.0975 (15)	0.7148 (14)	0.6360 (5)	6.0 (3)
C(12)	-0.1942 (24)	0.6536 (22)	0.6838 (7)	9.7 (5)
C(13)	0.0558 (22)	0.7804 (19)	0.6522 (7)	8.9 (4)
N(14)	0.1378 (15)	0.2629 (13)	0.2731 (4)	6.8 (3)
O(15)	0.2199 (16)	0.1640 (14)	0.2737 (5)	9.8 (3)
O(16)	0.0647 (13)	0.3031 (12)	0.2353 (4)	8.8 (3)
C(21)	-0.1519 (13)	1.1358 (12)	0.4053 (4)	4.6 (2)
C(22)	-0.1606 (16)	1.0768 (14)	0.3574 (5)	5.9 (3)
C(23)	-0.2605 (19)	1.1296 (18)	0.3174 (6)	7.7 (4)
C(24)	-0.3557 (21)	1.2421 (17)	0.3316 (6)	7.8 (4)
C(25)	-0.3506 (18)	1.3040 (17)	0.3804 (6)	7.2 (3)
C(26)	-0.2471 (13)	1.2503 (12)	0.4180 (4)	4.6 (2)
C(31)	0.0895 (12)	0.4984 (10)	0.4141 (4)	4.2 (2)
C(32)	0.0046 (14)	0.5371 (13)	0.3700 (4)	5.3 (2)
C(33)	0.0198 (14)	0.4607 (13)	0.3238 (4)	5.4 (2)
C(34)	0.1200 (13)	0.3475 (12)	0.3239 (4)	4.6 (2)
C(35)	0.2151 (13)	0.3092 (12)	0.3666 (4)	4.8 (2)
C(36)	0.1972 (13)	0.3853 (13)	0.4126 (4)	5.2 (2)

The hydrogen atoms were generated at the expected positions with C–H distances taken as 1.08 Å and N–H as 1.00 Å. They were included in the last structure-factor calculation with an overall isotropic temperature factor of 4 Å^2. The final R and weighted R are 0.105 and 0.149 respectively for all observed reflexions.* The scattering factors for carbon, nitrogen and oxygen were those given by Cromer & Mann (1968) and for H the values were taken from Hanson, Herman, Lea & Skillman (1964). The calculations were carried out on the UNIVAC 1108 computer of Rome University with a set of programs of Domenicano, Spagna & Vaciago (1969).

Molecular geometry

The intramolecular bond distances and angles are given in Figs. 1 and 2. The outermost atoms of ZLNP, C(12), C(13), O(15), O(16), C(23), C(24) and C(25) show the largest thermal parameters which may be caused by librational motions. The high temperature

factors of many atoms influence the standard deviations and give rise to not very accurate bond lengths and angles. The unusual C(21)–C(22) bond distance reflects this situation. The average value of the aromatic C–C distances is 1·38 Å for the two benzene rings.

The angular deformations found in the benzene ring of the nitrophenyl group are meaningful in the light of a recent paper by Domenicano, Vaciago & Coulson (1974) dealing with ring deformations induced in benzene derivatives by substitution. According to these authors, the angular deformations depend upon the
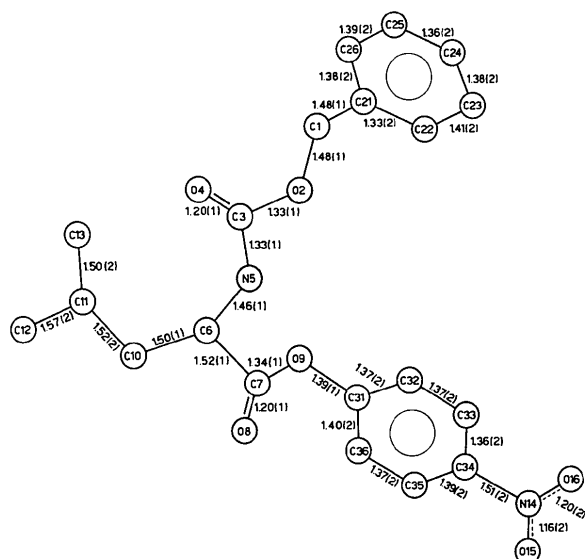

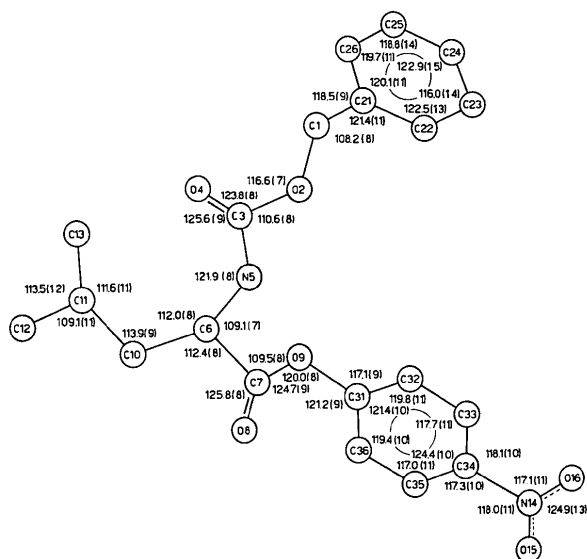Fig. 1. Bond distances (Å) of ZLNP with the estimated standard deviations in parentheses.

Fig. 2. Bond angles (°) of ZLNP with the estimated standard deviations in parentheses.

combined effects of the electronegativity and the σ-electron withdrawing or releasing properties of the substituent, the latter being influenced by the extent of conjugation with the ring. Moreover the deformations induced by substitution do not extend beyond the half of the ring nearest to the substituent. Therefore a second substituent *para* to the first is expected to have no appreciable effect on the geometry of the farthest half of the ring. Thus the electronegative and poorly conjugated nitro group should increase the endocyclic angle C(33)–C(34)–C(35) by a few degrees, while the two adjacent endocyclic angles C(32)–C(33)–C(34) and C(34)–C(35)–C(36) are expected to decrease. The other endocyclic angles of the nitrophenyl ring as well as the angles of the Z-ring do not significantly differ from 120°, since the electronegative and the conjugative effects of the substituents play an opposite role to each other. The angle C(6)–C(10)–C(11) in the Leu residue is larger than the regular tetrahedral value and this is a common feature found in other crystal structures (Ueki, Ashida, Kakudo, Sasada & Katsube, 1969). The widening of this angle may be due to repulsive interactions between C(13) and the hydrogen atom linked to C(6), as well as between N(5) and the hydrogen atom linked to C(11).

A list of the intramolecular torsion angles, according to Klyne & Prelog (1960), is given in Table 3. The resulting structure gives rise to a 'folded-back' conformation, rather than an extended one, the Leu residue being in the folded region.

Table 3. *Relevant intramolecular torsion angles* (°)

[C(26)–C(21)–C(1)—O(2)]	100·3 (1·1)
[C(21)–C(1)—O(2)—C(3)]	162·5 (0·8)
[C(1)—O(2)—C(3)—O(4)]	1·2 (1·3)
[C(1)—O(2)—C(3)—N(5)]	178·6 (0·7)
[O(2)—C(3)—N(5)—C(6)]	169·6 (0·7)
[O(4)—C(3)—N(5)—C(6)]	−13·0 (1·4)
[C(3)—N(5)—C(6)—C(7)]	−93·5 (0·9)
[C(3)—N(5)—C(6)—C(10)]	141·4 (0·8)
[N(5)—C(6)—C(7)—O(8)]	−131·1 (1·0)
[N(5)—C(6)—C(7)—O(9)]	48·8 (1·0)
[C(10)–C(6)—C(7)—O(8)]	−6·2 (1·4)
[C(10)–C(6)—C(7)—O(9)]	173·6 (0·8)
[C(6)—C(7)—O(9)—C(31)]	−175·0 (0·8)
[C(32)–C(31)–O(9)—C(7)]	119·7 (1·1)
[N(5)—C(6)—C(10)–C(11)]	−55·0 (1·1)
[C(7)—C(6)—C(10)–C(11)]	−178·3 (0·9)
[C(6)—C(10)–C(11)–C(12)]	174·4 (1·1)
[C(6)—C(10)–C(11)–C(13)]	−59·4 (1·3)

It would be interesting to establish whether the O(4)–C(3)–N(5)–H(5) group is planar. Since the hydrogen atoms cannot be located with sufficient accuracy by X-ray diffraction, this information may be obtained from the [O(4)–C(3)–N(5)–C(6)] and [O(2)–C(3)–N(5)–C(6)] torsion angles. As reported in Table 3 the corresponding values are −13·0° and 169·6°, which indicate a relatively large deviation from planarity, as has been found in other crystal structures (Ganis, Avitable, Benedetti, Pedone & Goodman, 1970; Coiro,

Giacomello & Giglio, 1971; Winkler & Dunitz, 1971; Ramachandran & Kolaskar, 1973, and references cited therein; Pattabhi, Venkatesan & Hall, 1973; Stenkamp & Jensen, 1973). All the experimental results suggest that the crystal field as well as the intramolecular interactions can easily distort the OC–NH group from planarity. Therefore this must be accounted for in the determination of the oligopeptide and polypeptide geometry by means of conformational analysis.

The conformation of the side chain of the Leu residue can be described by means of the torsion angles [C(7)–C(6)–C(10)–C(11)] ($\sim 180°$), [C(6)–C(10)–C(11)–C(12)] ($\sim 180°$) and [C(6)–C(10)–C(11)–C(13)] ($\sim -60°$).

These angles are in good agreement with those obtained for one of the two lowest minima in the conformational analysis of the central part of ZLNP (see below) and approximately agree with the values observed in leucylglycine.HBr (Thyagaraja Rao, 1969) and in leucylprolylglycine (Leung & Marsh, 1958).

The other minimum has been found in the crystal structures of *N*-methyl-DL-leucylglycine.HBr (Chandrasekaran & Subramanian, 1969), L-leucine.HBr (Subramanian, 1967) and glycyl-L-leucine (Pattabhi, Venkatesan & Hall, 1973). The part of ZLNP ending with the Z-group, as well as the one terminating with the nitrophenyl group, are extended. This can be deduced from the torsion angles [C(6)–N(5)–C(3)–O(2)], [N(5)–C(3)–O(2)–C(1)], [C(3)–O(2)–C(1)–C(21)] and [C(6)–C(7)–O(9)–C(31)] that are near to 180°. The Z-ring is almost perpendicular to the plane passing through O(2), C(1), C(21) and the ring of the nitrophenyl group is about 60° out of the plane defined by C(7), O(9), C(31). These twistings may be due mainly to steric hindrances between O(2) and the hydrogen atoms linked to C(22) and C(26) in one case, as well as between O(8) and the hydrogen atoms linked to C(32) and C(36) in the other. The nitro group is nearly coplanar with the benzene ring, the dihedral angle being 3·7°. The planarity of some groups of atoms can be inferred from inspection of Table 4, where the least-squares planes and the atomic deviations are reported.

The crystal packing

The molecules stack along the screw axis parallel to **a** by means of hydrogen bonds formed between the C(3)=O(4) group of the molecule at (x,y,z) and the N–H group of that at $(\frac{1}{2}+x, \frac{3}{2}-y, 1-z)$. The acceptor-donor distance O$\cdots$N is 2·95 Å corresponding to a rather weak hydrogen bond. If the hydrogen atom were located on the bisector of the angle C(3)–N(5)–C(6), with the N–H length of 1·00 Å, the distance between the proton and the carbonyl oxygen would be 2·21 Å, the angles C–O$\cdots$H and O$\cdots$H–N 118·2 and 129·7° respectively and the torsion angle [N(5)–H$\cdots$O(4)–C(3)] 179·9°. Thus the proton lies approximately on the symmetry axis of the oxygen lone pair, and the C–O and N–H bonds are nearly parallel.

Table 4. *Relevant least-squares planes* and atomic displacements* (Å)

Plane (1): C(21)–C(26)
$$-0.7103X - 0.6283Y + 0.3174Z = -2.5434$$

C(21)	0·004	C(24)	−0·008
C(22)	−0·014	C(25)	−0·002
C(23)	0·015	C(26)	0·005

Plane (2): C(31)–C(36)
$$-0.7282X - 0.6169Y + 0.2985Z = -0.3467$$

C(31)	−0·018	C(34)	−0·026
C(32)	0·012	C(35)	0·019
C(33)	0·011	C(36)	0·003

Plane (3): O(2), C(3), O(4), N(5)
$$-0.1647X + 0.5483Y + 0.8199Z = 14.8324$$

O(2)	−0·004	O(4)	−0·005
C(3)	0·013	N(5)	−0·004

Plane (4): C(6), C(7), O(8), O(9)
$$0.9368X - 0.1643Y + 0.3088Z = 3.2721$$

C(6)	0·000	O(8)	0·000
C(7)	−0·001	O(9)	0·000

Plane (5): O(2), C(3), O(4), N(5), C(6)
$$-0.1607X + 0.4951Y + 0.8538Z = 14.8051$$

O(2)	0·048	N(5)	−0·091
C(3)	−0·002	C(6)	0·062
O(4)	−0·017		

* The equations are in the form $AX + BY + CZ = D$ where X, Y and Z are in Å.

The dihedral angle between the two benzene rings of ZLNP is only 1·6°. In addition the nitrophenyl group of the molecule at (x,y,z) faces the Z-benzene ring of that at $(1+x, y-1, z)$. Fig. 3 shows the projection of these two rings onto the least-squares plane of the nitrophenyl group. However no contact less than 3·5 Å has been found, so that the degree of overlap is rather small. The dipole–dipole interactions may play an essential role in stabilizing this system, which resembles a graphite-like structure. The two methyl groups of the Leu residue are engaged in very different interactions. One of them C(13) is more active in intramolecular contact, whereas the other, C(12), gives rise to approaches of 3·25 Å with O(15) of the molecule at $(-\frac{1}{2}+x, \frac{1}{2}-y, 1-z)$ and of 3·43 Å with O(16) of the molecule at $(-\frac{1}{2}-x, 1-y, \frac{1}{2}+z)$.

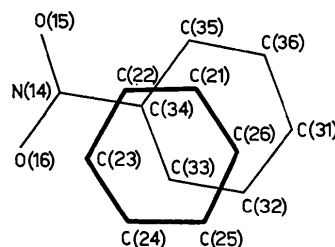In conclusion the molecular packing, shown in Fig. 4, seems to be mainly governed by hydrogen bonds

Fig. 3. Projection of the phenyl ring onto the least-squares plane of the nitrophenyl group.

along **a**, dipole–dipole forces along **b**, and methyl–oxygen interactions along **c**.

Conformational analysis

The conformation of a molecule may be established by intramolecular potential energy calculations as for *N,N'*-dicyclohexylurea (Coiro, Giacomello & Giglio, 1971) by fixing bond lengths and angles at standard values. ZLNP has 11 degrees of freedom if the methyl group is considered as one atom. Unfortunately the computing time required for the search of all the energy minima is too large and outside the present limits of a computer. Therefore we decreased the degrees of freedom to nine by fixing ω at 180° and the nitro group in the same plane of the benzene ring. Moreover the analysis was performed in three stages. In the first, only the central fragment of ZLNP, containing the atoms from O(2) to C(13) and the hydrogen atoms linked to them, was taken into account, the energy being computed as a function of four rotation angles $(\psi_1, \psi_2, \psi_3, \psi_4)$ as defined in Table 5. Subsequently the benzyl group was added to the initial fragment, and three more rotation angles (ψ_5, ψ_6, ψ_7) were allowed to vary, ψ_1, ψ_2, ψ_3, and ψ_4 being held fixed at values corresponding to the minima. Finally this procedure was repeated by including the nitrophenyl group and allowing two more rotation angles (ψ_8, ψ_9) to vary against the other previously fixed ψ's.

The van der Waals energy was computed by means of potentials previously verified in known and unknown crystal structures (Coiro, Giacomello & Giglio, 1971; Coiro, Giglio, Lucano & Puliti, 1973; Gavuzzo, Mazza & Giglio, 1974; and references cited therein). Their coefficients, which refer to the generalized form:

$$V(r) = \frac{a \exp(-br)}{r^d} - cr^{-6}$$

are listed in Table 6.

Table 5. *Rotation angles considered in the conformational analysis of the central fragment of ZLNP*

$\psi_1 = 0°$	for	[H(11)–C(11)–C(10)–H''(10)]	*cis*
$\psi_2 = 0°$	for	[H'(10)–C(10)–C(6)–C(7)]	*trans*
$\psi_3 = 0°$	for	[H(5)–N(5)–C(6)–C(7)]	*cis*
$\psi_4 = 0°$	for	[N(5)–C(6)–C(7)–O(8)]	*cis*

Table 6. *The coefficients of the van der Waals potential functions*

The energy is in kcal per atom pair if the interatomic distance is in Å.

Interaction	$a (\times 10^{-3})$	b	c	d
H–H	6·6	4·080	49·2	0
H–C	44·8	2·040	125·0	6
H–N	52·1	2·040	132·0	6
H–O	42·0	2·040	132·7	6
H–CH₃	49·1	3·705	380·5	0
C–C	301·2	0·000	327·2	12
C–N	340·0	0·000	340·0	12
C–O	278·7	0·000	342·3	12
C–CH₃	291·1	1·665	981·1	6
N–N	387·0	0·000	354·0	12
N–O	316·2	0·000	356·0	12
N–CH₃	325·9	1·665	1020·5	6
O–O	259·0	0·000	358·0	12
O–CH₃	272·7	1·665	1026·3	6
CH₃–CH₃	273·9	3·329	2942·0	0

Angular increments of 20° were given in the first run, assuming a cut-off distance of 7 Å.

The regions of minima were subsequently explored by decreasing the angular increments to 10° and sometimes to 5°. By inspection of the models built up from the energy minima, it was soon clear that the lowest energy values corresponded to 'compact' molecular geometries, since better van der Waals contacts can be achieved. However, 'open' geometries may realize a good packing in the crystal, by means of intermolecular interactions among, for example, benzene rings. In this way, passing from a 'compact' to an 'open'
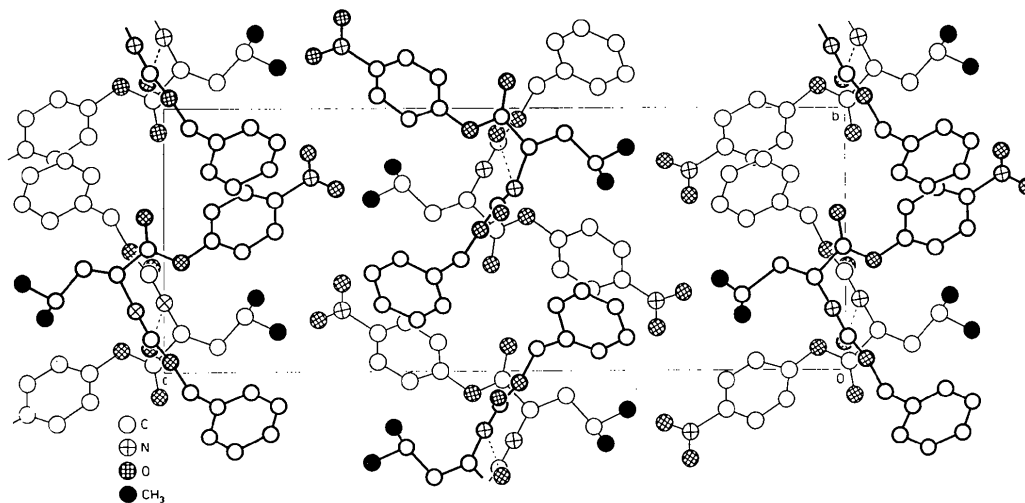

Fig. 4. Crystal packing viewed along the *a* axis. Dashed lines represent hydrogen bonds.

conformation, the loss of intramolecular energy is replaced by the gain of intermolecular energy. Therefore the actual structure can be derived by taking into account simultaneously both the intra- and intermolecular degrees of freedom. Since such analysis would require too large a computing time, we focused our attention on the conformation of the central fragment of ZLNP.

Table 7 lists the assumed bond lengths and angles. The starting position corresponding to $\psi_1 = \psi_2 = \psi_3 = \psi_4 = 0°$ has O(2), C(3), O(4), N(5), H(5), C(6), C(7), O(8) and O(9) in the same plane, C(10)–H'(10) and C(10)–H''(10) *trans* referred to C(6)–C(7) and C(6)–N(5) respectively, and C(11)–H(11) *cis* referred to C(10)–H''(10). A torsion angle *A–B–C–D* is taken as positive if the atom *D* is moved in a clockwise direction, looking along the *C–B* bond. The minima found in the energy search are grouped around $\psi_1 = 80°$, $\psi_2 = 140°$ and $\psi_1 = 160°$, $\psi_2 = 240°$, which represent the two lowest minima of the Leu residue. The region around $\psi_1 = 80°$, $\psi_2 = 140°$ corresponds to the actual structure and was therefore explored, whereas the other region corresponds approximately to the conformation found in the crystal structures of *N*-methyl-DL-leucylglycine.HBr (Chandrasekaran & Subramanian, 1969), L-leucine.HBr (Subramanian, 1967) and glycyl-L-leucine (Pattabhi, Venkatesan & Hall, 1973). A section at $\psi_1 = 70°$ and $\psi_2 = 125°$ is given in Fig. 5, showing that the energy is insensitive to ψ_4, while ψ_3 ranges from 240 to 300°. The black spot indicates the position of the experimental structure with respect to ψ_3 and ψ_4: the rotation angles ψ_1, ψ_2 and ψ_3 do not differ more than 10° from the observed values. A suitable model of the central part of ZLNP was thus derived from this analysis, although in our calculation ω was fixed at 180°.

References

ARNDT, U. W. & WILLIS, B. T. M. (1966). *Single Crystal Diffractometry*, p. 144. Cambridge Univ. Press.

AZÁROFF, L. V. (1955). *Acta Cryst.* 8, 701–704.

CHANDRASEKARAN, R. & SUBRAMANIAN, E. (1969). *Acta Cryst.* B25, 2599–2606.

COIRO, V. M., GIACOMELLO, P. & GIGLIO, E. (1971). *Acta Cryst.* B27, 2112–2119.

COIRO, V. M., GIGLIO, E., LUCANO, A. & PULITI, R. (1973). *Acta Cryst.* B29, 1404–1409.

COIRO, V. M., GIGLIO, E. & QUAGLIATA, C. (1972). *Acta Cryst.* B28, 3601–3605.

CORFIELD, P. W. R., DOEDENS, R. J. & IBERS, J. A. (1967). *Inorg. Chem.* 6, 197–204.

CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A24, 321–324.

DOMENICANO, A., SPAGNA, R. & VACIAGO, A. (1969). *Atti Accad. Nazl. Lincei Rend. Classe Sci. Fis. Mat. Nat.* 47, 331–336.

DOMENICANO, A., VACIAGO, A. & COULSON, C. A. (1974). *Acta Cryst.* In the press.

GANIS, P., AVITABILE, G., BENEDETTI, E., PEDONE, C. & GOODMAN, M. (1970). *Proc. Natl. Acad. Sci. U.S.* 67, 426–433.

GAVUZZO, E., MAZZA, F. & GIGLIO, E. (1974). *Acta Cryst.* B30, 1351–1357.

HANSON, H. P., HERMAN, F., LEA, J. D. & SKILLMAN, S. (1964). *Acta Cryst.* 17, 1040–1044.

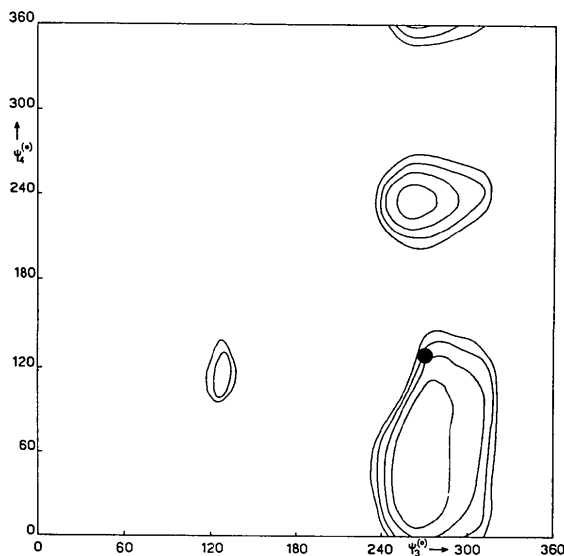Table 7. *Bond distances (Å) and angles (°) used in the conformational analysis of the central fragment of ZLNP*

The hydrogen atoms have the same numbers of the atoms to which they are covalently linked.

N–H	1·00	C—O	1·36
C–H	1·08	C(3)–N(5)	1·33
C–C	1·53	C(6)–N(5)	1·45
C=O	1·22		

O(2)–C(3)–O(4)	125	N(5)—C(6)—C(7)	110
O(2)–C(3)–N(5)	110	H'(10)–C(10)–H''(10)	105
O(4)–C(3)–N(5)	125	C(6)—C(10)–C(11)	112
C(3)–N(5)–H(5)	120	H'(10)–C(10)–C(6)	110
C(3)–N(5)–C(6)	120	C(6)—C(10)–H''(10)	110
H(5)–N(5)–C(6)	120	H'(10)–C(10)–C(11)	110
C(6)–C(7)–O(8)	125	H''(10)–C(10)–C(11)	110
C(6)–C(7)–O(9)	110	C(13)—C(11)–C(10)	110
O(8)–C(7)–O(9)	125	C(10)—C(11)–C(12)	110
N(5)–C(6)–H(6)	110	C(13)—C(11)–H(11)	110
H(6)–C(6)–C(7)	110	C(12)—C(11)–H(11)	110
N(5)–C(6)–C(10)	110	C(12)—C(11)–C(13)	112
C(7)–C(6)–C(10)	110	C(10)—C(11)–H(11)	105
H(6)–C(6)–C(10)	107		

Fig. 5. Section at $\psi_1 = 70°$ and $\psi_2 = 125°$ of the van der Waals energy map for the central fragment of ZLNP. The black spot corresponds to the experimental values found in the structure.

KLYNE, W. & PRELOG, V. (1960). *Experientia*, **16**, 521–523.

LEUNG, Y. C. & MARSH, R. E. (1958). *Acta Cryst.* **11**, 17–31.

MAIN, P., WOOLFSON, M. M. & GERMAIN, G. (1971). *MULTAN. A Computer Program for the Automatic Solution of Crystal Structures.* Univ. of York Printing Unit, York, England.

PATTABHI, Y., VENKATESAN, K. & HALL, S. R. (1973). *Cryst. Struct. Commun.* **2**, 223–227.

RAMACHANDRAN, G. N. (1968). *Biopolymers*, **6**, 1494–1496.

RAMACHANDRAN, G. N. & KOLASKAR, A. S. (1973). *Biochim. Biophys. Acta*, **303**, 385–388.

STENKAMP, R. E. & JENSEN, L. H. (1973). *Acta Cryst.* B**29**, 2872–2878.

SUBRAMANIAN, E. (1967). *Acta Cryst.* **22**, 910–917.

THYAGARAJA RAO, S. (1969). *Z. Kristallogr.* **129**, 50–64.

UEKI, T., ASHIDA, T., KAKUDO, M., SASADA, Y. & KATSUBE, Y. (1969). *Acta Cryst.* B**25**, 1840–1849.

WINKLER, F. K. & DUNITZ, J. D. (1971). *J. Mol. Biol.* **59**, 169–182.

A Neutron-Diffraction Study of Holmium Ethylsulfate Enneahydrate by the White-Radiation Method

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The structure of holmium ethylsulfate enneahydrate has been studied by the white-radiation neutron-diffraction method. Of 703 intensities collected in two days at the Ames Laboratory 5 MW reactor, 300 had $I > 3\sigma_I$. Linear programming proved to be an improved technique compared with least-squares procedures for unfolding the observed Laue intensities. The phased Fourier map, calculated using the unfolded structure factors, clearly revealed all hydrogen-atom positions, and the resulting peak heights were proportional to the neutron scattering lengths. A subsequent comparison of the Fourier and least-squares hydrogen atomic positions revealed that the average and maximum deviations were 0·17 and 0·28 Å. The structure was refined with isotropic thermal parameters to a final $RI_\omega = 0·139$ and $RI_\bar{\omega}^{3\sigma} = 0·111$. Several improvements of the white-radiation method are suggested based on this study and previous results. The space group was confirmed to be $P6_3/m$. The holmium ion is at the center of a slightly distorted tricapped trigonal prism of water molecules. Each water oxygen is hydrogen bonded to two ethylsulfate ions. The hydrogen bonding and oxygen lone pair–lone pair interactions reduce the D_{3h} rare-earth ion site symmetry to C_{3h}. The orientation of the two types of water molecules relative to the holmium is somewhat different as are associated O–H distances (0·92 *vs.* 1·04 Å).

Introduction

Using two and three-dimensional X-ray diffraction techniques Fitzwater & Rundle (1959) investigated a number of hydrated rare-earth ethylsulfates, including the yttrium, erbium and praseodymium salts. These salts were all isomorphous, and in each the rare-earth ion was located at the center of a trigonal prism of water molecules, with additional water molecules capping each rectangular face. From a consideration of the oxygen–oxygen distances and appropriate angles, they hypothesized numerous hydrogen bonds; no hydrogen-atom positions were determined however.

Because of the continuing interest in the rare-earth metals and their compounds in the Ames Laboratory, and to accurately elucidate the hydrogen bonding in these salts and the interplay with the coordination

forces, we decided to carry out a neutron investigation of a member of this series, $Ho(C_2H_5SO_4)_3 \cdot 9H_2O$.

The second major goal of this research was to gain further experience with the recently developed white-radiation method (Hubbard, Quicksall & Jacobson, 1971; Hubbard, Quicksall & Jacobson, 1972, hereinafter HQJ). These previous studies indicated that structure determination was not only possible using the white-radiation method, but also yielded comparable precision to that of conventional monochromatic-beam techniques while permitting use of smaller crystals and rapid data collection.

Experimental

$Ho(C_2H_5SO_3)_3 \cdot 9H_2O$, kindly supplied by Dr F. Spedding, was dissolved in distilled water and crystallized by slow evaporation. Initial studies indicated that a crystal of 9 mm³ volume (maximum dimension 3 mm) was sufficient to give reasonable scattering. After being mounted on a thin vanadium rod, the hygroscopic crystal was encapsulated within a quartz

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