

The Crystal and Molecular Structure of DL-Tryptophan Ethyl Ester Hydrochloride*

BY B. K. VIJAYALAKSHMI AND R. SRINIVASAN

Centre of Advanced Study in Physics, University of Madras, Guindy Campus, Madras-600025, India

(Received 8 October 1974; accepted 21 November 1974)

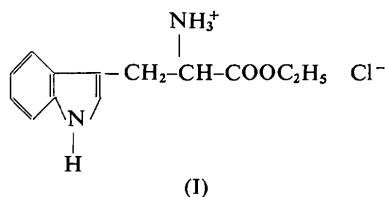
DL-Tryptophan ethyl ester hydrochloride, $C_{13}H_{16}N_2O_2 \cdot HCl$, is triclinic, space group $P\bar{1}$, with $a = 15.85$, $b = 8.73$, $c = 5.35$ Å, $\alpha = 82.73$, $\beta = 88.51$, $\gamma = 106.33^\circ$, $Z = 2$. The structure was solved by the heavy-atom method and refined by block-diagonal least-squares calculations to an R of 0.089 for 2012 observed reflexions. The indole ring plane forms an angle of 61.5° with the carboxylate plane. The D and L molecules are linked by $N-H \cdots Cl$ hydrogen bonds around the centre of symmetry. The hydrogen bonds sandwich the molecules into a double-layered system parallel to the bc plane.

Introduction

This investigation is part of a programme on the determination of the structures of organic compounds of biological importance.

Experimental

Single crystals of DL-tryptophan ethyl ester hydrochloride (I) were grown by evaporation of an aqueous solution. The crystals were colourless transparent parallelepipeds elongated along c and showed easy cleavage along the bc plane. Preliminary photographs showed that they were triclinic. Cell dimensions were determined from $h0l$ and $0kl$ precession photographs and the density by flotation.



Crystal data

$C_{13}H_{16}N_2O_2 \cdot HCl$, triclinic, $a = 15.85$ (2), $b = 8.73$ (1), $c = 5.35$ (1) Å, $\alpha = 82.73$ (0.2), $\beta = 88.51$ (0.2), $\gamma = 106.33$ (0.2)°; space group $P\bar{1}$; $Z = 2$, $M = 268.7$, $D_o = 1.25$, $D_c = 1.266$ g cm $^{-3}$, $\mu = 23.8$ cm $^{-1}$, λ (for Cu $K\alpha$ radiation) = 1.5418 Å.

A crystal ($0.05 \times 0.02 \times 0.02$ cm) was used to collect intensities by the multiple-film equi-inclination Weissenberg technique with Ni-filtered Cu $K\alpha$ radiation. The intensities of 2012 independent reflexions (hkl , $l =$

$0-4$, hkl , $k = 0-2$) were estimated visually and corrected for Lorentz and polarization factors. Corrections for spot shape were made with the equation $I_{true} = I_{e,c}(1 \pm K \cos \theta)$ (Dale, Hodgkin & Venkatesan, 1963), where e and c stand for extended and contracted spots respectively and θ is the Bragg angle. K was determined from reflexions measured on both sides of the central line. No absorption corrections were made ($\mu t \approx 0.45$). The data about the two axes were brought to a single scale (Rollett & Sparks, 1960).

The space group $P\bar{1}$ was assigned on the basis of the statistical averages of normalized structure factors and the distribution of the E values.

Structure determination and refinement

The structure was solved by the heavy-atom method. Refinement was by block-diagonal least-squares calculations with the program written by Shiono (1968), modified to suit the IBM-360 at Bangalore. Refinement with isotropic temperature factors and the weighting scheme $w = [4.0 + |F_o| + 0.036|F_o|^2]^{-1}$ (Cruickshank, Bujosa, Lovell & Truter, 1961) reduced R to 0.17. A difference map computed at this stage showed all the hydrogen atoms at the expected positions with peak heights ranging from 0.10 to 0.95 e Å $^{-3}$. These atoms were included during further refinement with isotropic temperature factors of the atoms to which they are bonded. Further refinement with anisotropic thermal parameters for all the non-hydrogen atoms reduced R to a final value of 0.089. The positions of the hydrogens were not refined. The maximum shifts in the positional parameters during the last cycle were less than one-fifteenth the estimated standard deviations.

Scattering factors for Cl^- , C, N, O and H are those listed in *International Tables for X-ray Crystallography* (1962).

The parameters of the non-hydrogen atoms are listed in Table 1. Table 2 gives the observed and calculated structure factors.

* Contribution No. 388 from the Centre of Advanced Study in Physics, University of Madras, Guindy Campus, Madras-600025, India.

1.39 Å. In all these cases, the carbon atoms of the ethyl ester group have abnormally high temperature factors, which may be due to disorder.

The C-H lengths vary from 0.89 to 1.25 Å and the

N-H lengths from 0.88 to 0.91 Å. The angles involving the hydrogens in the aromatic part range from 111.9 to 128.4° while in the linear part they range from 91.7 to 121.4°.

Table 2. Observed and calculated structure factors

h	k	l	F _o	F _c	h	k	l	F _o	F _c	h	k	l	F _o	F _c	h	k	l	F _o	F _c
0	0	0	100	100	0	0	0	100	100	0	0	0	100	100	0	0	0	100	100
0	0	1	100	100	0	0	1	100	100	0	0	1	100	100	0	0	1	100	100
0	0	2	100	100	0	0	2	100	100	0	0	2	100	100	0	0	2	100	100
0	0	3	100	100	0	0	3	100	100	0	0	3	100	100	0	0	3	100	100
0	0	4	100	100	0	0	4	100	100	0	0	4	100	100	0	0	4	100	100
0	0	5	100	100	0	0	5	100	100	0	0	5	100	100	0	0	5	100	100
0	0	6	100	100	0	0	6	100	100	0	0	6	100	100	0	0	6	100	100
0	0	7	100	100	0	0	7	100	100	0	0	7	100	100	0	0	7	100	100
0	0	8	100	100	0	0	8	100	100	0	0	8	100	100	0	0	8	100	100
0	0	9	100	100	0	0	9	100	100	0	0	9	100	100	0	0	9	100	100
0	0	10	100	100	0	0	10	100	100	0	0	10	100	100	0	0	10	100	100
0	0	11	100	100	0	0	11	100	100	0	0	11	100	100	0	0	11	100	100
0	0	12	100	100	0	0	12	100	100	0	0	12	100	100	0	0	12	100	100
0	0	13	100	100	0	0	13	100	100	0	0	13	100	100	0	0	13	100	100
0	0	14	100	100	0	0	14	100	100	0	0	14	100	100	0	0	14	100	100
0	0	15	100	100	0	0	15	100	100	0	0	15	100	100	0	0	15	100	100
0	0	16	100	100	0	0	16	100	100	0	0	16	100	100	0	0	16	100	100
0	0	17	100	100	0	0	17	100	100	0	0	17	100	100	0	0	17	100	100
0	0	18	100	100	0	0	18	100	100	0	0	18	100	100	0	0	18	100	100
0	0	19	100	100	0	0	19	100	100	0	0	19	100	100	0	0	19	100	100
0	0	20	100	100	0	0	20	100	100	0	0	20	100	100	0	0	20	100	100
0	0	21	100	100	0	0	21	100	100	0	0	21	100	100	0	0	21	100	100
0	0	22	100	100	0	0	22	100	100	0	0	22	100	100	0	0	22	100	100
0	0	23	100	100	0	0	23	100	100	0	0	23	100	100	0	0	23	100	100
0	0	24	100	100	0	0	24	100	100	0	0	24	100	100	0	0	24	100	100
0	0	25	100	100	0	0	25	100	100	0	0	25	100	100	0	0	25	100	100
0	0	26	100	100	0	0	26	100	100	0	0	26	100	100	0	0	26	100	100
0	0	27	100	100	0	0	27	100	100	0	0	27	100	100	0	0	27	100	100
0	0	28	100	100	0	0	28	100	100	0	0	28	100	100	0	0	28	100	100
0	0	29	100	100	0	0	29	100	100	0	0	29	100	100	0	0	29	100	100
0	0	30	100	100	0	0	30	100	100	0	0	30	100	100	0	0	30	100	100
0	0	31	100	100	0	0	31	100	100	0	0	31	100	100	0	0	31	100	100
0	0	32	100	100	0	0	32	100	100	0	0	32	100	100	0	0	32	100	100
0	0	33	100	100	0	0	33	100	100	0	0	33	100	100	0	0	33	100	100
0	0	34	100	100	0	0	34	100	100	0	0	34	100	100	0	0	34	100	100
0	0	35	100	100	0	0	35	100	100	0	0	35	100	100	0	0	35	100	100
0	0	36	100	100	0	0	36	100	100	0	0	36	100	100	0	0	36	100	100
0	0	37	100	100	0	0	37	100	100	0	0	37	100	100	0	0	37	100	100
0	0	38	100	100	0	0	38	100	100	0	0	38	100	100	0	0	38	100	100
0	0	39	100	100	0	0	39	100	100	0	0	39	100	100	0	0	39	100	100
0	0	40	100	100	0	0	40	100	100	0	0	40	100	100	0	0	40	100	100
0	0	41	100	100	0	0	41	100	100	0	0	41	100	100	0	0	41	100	100
0	0	42	100	100	0	0	42	100	100	0	0	42	100	100	0	0	42	100	100
0	0	43	100	100	0	0	43	100	100	0	0	43	100	100	0	0	43	100	100
0	0	44	100	100	0	0	44	100	100	0	0	44	100	100	0	0	44	100	100
0	0	45	100	100	0	0	45	100	100	0	0	45	100	100	0	0	45	100	100
0	0	46	100	100	0	0	46	100	100	0	0	46	100	100	0	0	46	100	100
0	0	47	100	100	0	0	47	100	100	0	0	47	100	100	0	0	47	100	100
0	0	48	100	100	0	0	48	100	100	0	0	48	100	100	0	0	48	100	100
0	0	49	100	100	0	0	49	100	100	0	0	49	100	100	0	0	49	100	100
0	0	50	100	100	0	0	50	100	100	0	0	50	100	100	0	0	50	100	100
0	0	51	100	100	0	0	51	100	100	0	0	51	100	100	0	0	51	100	100
0	0	52	100	100	0	0	52	100	100	0	0	52	100	100	0	0	52	100	100
0	0	53	100	100	0	0	53	100	100	0	0	53	100	100	0	0	53	100	100
0	0	54	100	100	0	0	54	100	100	0	0	54	100	100	0	0	54	100	100
0	0	55	100	100	0	0	55	100	100	0	0	55	100	100	0	0	55	100	100
0	0	56	100	100	0	0	56	100	100	0	0	56	100	100	0	0	56	100	100
0	0	57	100	100	0	0	57	100	100	0	0	57	100	100	0	0	57	100	100
0	0	58	100	100	0	0	58	100	100	0	0	58	100	100	0	0	58	100	100
0	0	59	100	100	0	0	59	100	100	0	0	59	100	100	0	0	59	100	100
0	0	60	100	100	0	0	60	100	100	0	0	60	100	100	0	0	60	100	100
0	0	61	100	100	0	0	61	100	100	0	0	61	100	100	0	0	61	100	100
0	0	62	100	100	0	0	62	100	100	0	0	62	100	100	0	0	62	100	100
0	0	63	100	100	0	0	63	100	100	0	0	63	100	100	0	0	63	100	100
0	0	64	100	100	0	0	64	100	100	0	0	64	100	100	0	0	64	100	100
0	0	65	100	100	0	0	65	100	100	0	0	65	100	100	0	0	65	100	100
0	0	66	100	100	0	0	66	100	100	0	0	66	100	100	0	0	66	100	100
0	0	67	100	100	0	0	67	100	100	0	0	67	100	100	0	0	67	100	100
0	0	68	100	100	0	0	68	100	100	0	0	68	100	100	0	0	68	100	100
0	0	69	100	100	0	0	69	100	100	0	0	69	100	100	0	0	69	100	100
0	0	70	100	100	0	0	70	100	100	0	0	70	100	100	0	0	70</		

Table 3. *Least-squares planes*

Equation of the plane $AX+BY+CZ=D$ with respect to an orthogonal system, where X , Y , Z and D are in Å.

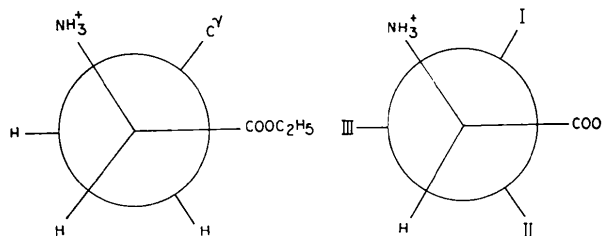
Plane I	Atom	Deviation (Å)	Equation of the plane	
Indole group	N(1)	-0.013	$-0.5515X + 0.6129Y + 0.5658Z = 4.6174$	
	C(2)	-0.007		
	C(3)	0.011		
	C(4)	-0.004		
	C(5)	-0.016		
	C(6)	0.010		
	C(7)	0.002		
	C(8)	0.008		
	C(9)	0.008		
	C(10)*	0.039		
Plane II	Carboxyl group	C(11)	0.000	$-0.5480X + 0.7066Y - 0.4475Z = 5.5940$
		C(12)	-0.001	
		O(1)	0.000	
		O(2)	0.000	
		C(10)*	-1.299	
		N(2)*	0.204	

* Atoms not included in the plane

(b) *Conformation of the molecule*

The equations to the two planes defined by the indole ring and the carboxylate group and the deviations of the atoms from them are given in Table 3. As found in related compounds, the indole part is planar, the maximum deviation being 0.019 Å. The carboxylate group, C(12), O(1), O(2), with C^α, is planar and the amino nitrogen N(2) is 0.204 Å out of this plane. The indole plane makes an angle of 61.5° with the carboxylate plane.

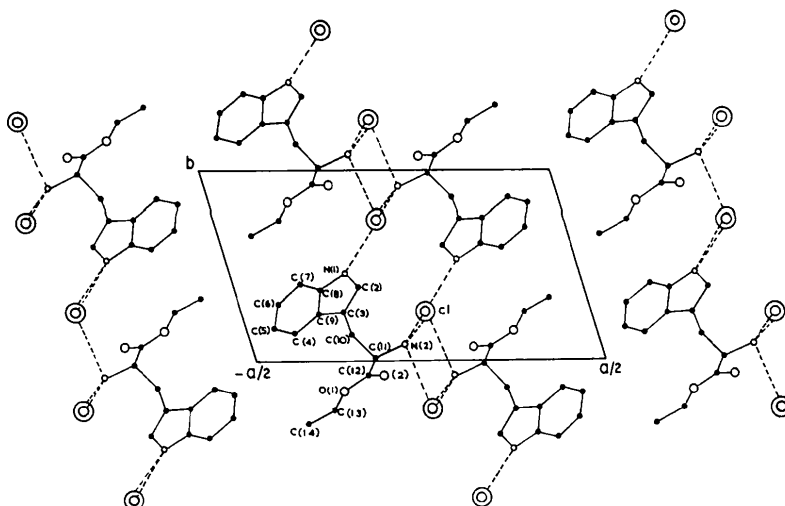
Regarding the conformation about the C^α-C^β [C(11)-C(10)] bond, the C^β-C^γ [C(10)-C(3)] lies

Fig. 2. Newman projections about the C^α-C^β bond.Table 4. *Hydrogen-bond lengths (Å) and angles (°)*

Donor	Acceptor	$D \cdots A$	$H \cdots A$	$D-H \cdots A$	$C-D \cdots A$	$H-D \cdots A$
C(8)					122.3	
>N(1)-H(1)	Cl ⁱ	3.275	2.404	173.2		5.0
C(2)					123.6	
C(11)-N(2)-H(15)	Cl ⁱⁱ	3.228	2.364	158.0	122.3	15.9
C(11)-N(2)-H(16)	Cl ⁱⁱⁱ	3.213	2.458	144.0	89.8	26.8
C(11)-N(2)-H(17)	Cl ^{iv}	3.179	2.320	165.7	112.8	10.4

Symmetry code

i	x	y	$z-1$
ii	$2-x$	$1-y$	$1-z$
iii	x	$y-1$	z
iv	$2-x$	$1-y$	$2-z$

Fig. 3. Packing of the molecules viewed down the c axis.

gauche with respect to both C^α -COOC₂H₅ and C^α -NH₃⁺. A similar conformation has been observed in L-tryptophan hydrochloride (Takigawa *et al.*, 1966). On the other hand, a different conformation has been observed in glycyl-L-tryptophan dihydrate (Pasternak, 1956), DL-tryptophan formate (Bye, Mostad & Rømming, 1973) and 5-hydroxy-DL-tryptophan (Wakahara, Kido, Fujiwara & Tomita, 1973). In all these cases, C^β - C^γ lies *trans* to C^γ -COO⁻ and *gauche* to C^α -NH₃⁺. In tryptophan, Ramachandran & Lakshminarayanan (1966) have pointed out that C^γ takes either position I or III (Fig. 2). The torsion angles C(2)-C(3)-C(10)-C(11) and C(9)-C(3)-C(10)-C(11) are 276.5 (or -93.5) and 96.2° respectively. From conformational studies and normal stereochemical rules, Chothia & Pauling (1969) have proposed two possible values for the former torsion angle, 0 and ±90°. While the observed values in most of the indole derivatives are close to these values, in 5-methoxy-(*N,N*)-dimethyltryptamine hydrochloride (Falkenberg & Carlström, 1971) and the serotonin-creatinine sulphate complex (Karle, Dragonette & Brenner, 1965), the observed angle (17.2°) differs from the predicted value.

(c) *Crystal packing and hydrogen bonding*

The packing of the molecules viewed along *c* is shown in Fig. 3. The D and L molecules are linked by N-H...Cl hydrogen bonds around the centre of symmetry. The chlorines bridge the molecules into an infinite three-dimensional network.

The four available protons all take part in intermolecular hydrogen bonding. The relevant lengths and angles are given in Table 4. The Cl⁻ ion acts as the acceptor for all four hydrogen bonds, three with the amino nitrogen and one with N(1). The hydrogen bonds sandwich the molecules into a double-layered system parallel to the *bc* plane. The double layers are held together only by van der Waals forces, which explains the easy cleavage along the *bc* plane.

One of us (B.K.V.) thanks the University Grants Commission, India, for a Junior Research Fellowship.

References

- BYE, E., MOSTAD, A. & RØMMING, C. (1973). *Acta Chem. Scand.* **27**, 471-484.
- CHOTHIA, C. & PAULING, P. (1969). *Proc. Natl. Acad. Sci. U.S.A.* **63**, 1063-1070.
- COTRAIT, M. & BARRANS, Y. (1974). *Acta Cryst.* **B30**, 510-513.
- CRUICKSHANK, D. W. J., BUJOSA, A., LOVELL, F. M. & TRUTER, M. R. (1961). In *Computing Methods and the Phase Problem in X-ray Crystal Analysis*, edited by R. PEPINSKY, J. M. ROBERTSON & J. C. SPEAKMAN, New York: Pergamon Press.
- DALE, D., HODGKIN, D. C. & VENKATESAN, K. (1963). In *Crystallography and Crystal Perfection*, edited by G. N. RAMACHANDRAN, p. 237. London: Academic Press.
- FALKENBERG, G. & CARLSTRÖM, D. (1971). *Acta Cryst.* **B27**, 411-418.
- HAAS, D. J. (1965). *Acta Cryst.* **19**, 860-861.
- International Tables for X-ray Crystallography* (1962). Vol. III. Birmingham: Kynoch Press.
- KANTERS, J. A., KROON, J., PEERDEMAN, A. F. & SCHOONE, J. C. (1967). *Tetrahedron*, **23**, 4027-4033.
- KARLE, I. L., BRITTS, K. & GUM, P. (1964). *Acta Cryst.* **17**, 496-499.
- KARLE, I. L., DRAGONETTE, K. S. & BRENNER, S. A. (1965). *Acta Cryst.* **19**, 713-716.
- MARSH, R. E. & DONOHUE, J. (1967). *Advanc. Protein Chem.* **22**, 235-256.
- PASTERNAK, R. A. (1956). *Acta Cryst.* **9**, 341-349.
- PIERET, A. F., DURANT, F., GRIFFÉ, M., GERMAIN, G. & DEBAERDEMAEKER, T. (1970). *Acta Cryst.* **B26**, 2117-2124.
- RAMACHANDRAN, G. N. & LAKSHMINARAYANAN, A. V. (1966). *Biopolymers*, **4**, 495-497.
- ROLLETT, J. S. & SPARKS, R. A. (1960). *Acta Cryst.* **13**, 273-274.
- SHIONO, R. (1968). *Block Diagonal Least-Squares Program for the IBM-1130*. Department of Crystallography, Univ. of Pittsburgh.
- TAKIGAWA, T., ASHIDA, T., SASADA, Y. & KAKUDO, M. (1966). *Bull. Chem. Soc. Japan*, **39**, 2369-2378.
- THEWALT, U. & BUGG, C. E. (1972). *Acta Cryst.* **B28**, 82-92.
- WAKAHARA, A., FUJIWARA, T. & TOMITA, K. (1973). *Bull. Chem. Soc. Japan*, **46**, 2481-2486.
- WAKAHARA, A., KIDO, M., FUJIWARA, T. & TOMITA, K. (1973). *Bull. Chem. Soc. Japan*, **46**, 2475-2480.