The Structure and Conformation of Tryptophan in the Crystal of the pure Racemic Compound and the Hydrogen Oxalate

ØYSTEIN BAKKE and ARVID MOSTAD

Department of Chemistry, University of Oslo, Oslo 3, Norway

The crystal structure of pure DL-tryptophan has been determined by X-ray crystallographic methods using 522 reflections observed by counter methods. The crystals are monoclinic, space group $P2_1/c$ with unit cell dimensions $a = 18.986(8)$ Å, $b = 5.768(2)$ Å, $c = 9.379(3)$ Å, $\beta = 101.84(3)°$. The structure was refined to a conventional R-factor of 0.085; estimated standard deviations are 0.02 Å in distances and 1.6° in angles when hydrogen atoms are not involved.

The conformation is different from that earlier reported for the tryptophan molecule. The cationic form of tryptophan in the hydrogen oxalate was also studied using 1519 observed reflections. The crystals are orthorhombic, space group $P2_12_12_1$ with unit cell dimensions $a = 5.8773(9)$ Å, $b = 7.722(1)$ Å, $c = 28.302(3)$ Å. The structure was refined to $R = 0.049$; estimated standard deviations are 0.005 Å and 0.4° in interatomic distances and angles, respectively, when hydrogen atoms are not involved. The general geometry of the tryptophan molecule as well as the interactions between the indole moieties in such crystal structures are discussed.

Most of the twenty-odd α-amino acids commonly found in proteins have been studied in pure state by single crystal X-ray methods, but because of the difficulty in growing suitable single crystals [1,2] no such examination has been reported on tryptophan. We recently succeeded in growing single crystals from pure DL-tryptophan and decided to carry out a complete structure determination even if the crystals were not as good as could be wished. For comparison, and to study the tryptophan molecule in different crystal environments, hoping to gain some insight in the mode of crystallization of such compounds, the crystal structure of tryptophan hydrogen oxalate was included in the study.

EXPERIMENTAL

DL-*Tryptophan* was dissolved in hot pyridine and thin plate-formed crystals separated on cooling. The crystals were easily cleaved in thin flakes parallel to the largest crystal face (100). Weissenberg photographs indicated some disorder in most of the crystals. For the general experimental procedure, see below.

D-*Tryptophan hydrogen oxalate* was prepared by dissolving DL-tryptophan in a hot aquatic solution of oxalic acid. Small prismatic needle-formed crystals of the compound separated by slow cooling of the mixed solution. The general experimental conditions are given in Table 1.

The intensities of the standard reflections indicated stable experimental conditions and no corrections were made in the data sets of the two compounds on this basis. The standard deviations in the intensities were calculated by $\sigma(I) = [C_T + (0.02\ C_N)^2]^{\frac{1}{2}}$ where C_T is the total number of counts and C_N is the scan count minus the background count.

The intensity data sets were corrected for Lorentz and polarization effects. Scattering factors used were those of Doyle and Turner [3] for C, N and O, and of Stewart, Davidson and Simpson [4] for H. Cell parameters were determined by a least-squares fit to the diffractometer settings for 15 general reflections. Description of the computer programs used are given in Refs. 5 and 6.

CRYSTAL DATA

DL-*Tryptophan* $C_{11}H_{12}N_2O_2$, monoclinic, space group $P2_1/c$ (No 14) $a = 18.986(8)$ Å, $b = 5.768(2)$ Å, $c = 9.379(3)$ Å, $\beta = 101.84(3)°$, $V = 1005.4$ Å^3, $M = 204.23$, $Z = 4$, $F(000) = 432$, $D_x = 1.349$ gcm^{-3}, $D_m = 1.31$ gcm^{-3}, $T = 291$ K.

D-*Tryptophan hydrogen oxalate* $C_{11}H_{13}N_2O_2^+$-$C_2HO_4^-$, orthorhombic, space group: $P2_12_12_1$ (No 19), $a = 5.8773(9)$ Å, $b = 7.722(1)$ Å, $c = 28.302(3)$ Å, $V = 1284.5$ Å^3, $M = 294.27$, $Z = 4$, $F(000) = 616$, $D_x = 1.521$ gcm^{-3}, $D_m = 1.50$ gcm^{-3}, $T = 121$ K.

Table 1. Experimental conditions.

	DL-Tryptophan	D-Tryptophan hydrogen oxalate
Instrument	SYNTEX P$\bar{1}$	SYNTEX P$\bar{1}$
Radiation	Graphite crystal monochromated MoKα $\lambda = 0.7107$ Å	Graphite crystal monochromated MoKα $\lambda = 0.7107$ Å
Crystal dimension (mm)	$0.30 \times 0.20 \times 0.015$	$0.25 \times 0.15 \times 0.07$
Scanning mode	ω	$\theta/2\theta$
Scan speed (° min^{-1})	1	2
Scan range (°)	1.4	$0.8 < 2\theta\alpha_1, 0.8 > 2\theta\alpha_2$
Background counts at (°)	$1.4 < \omega_{K\alpha 1,2} < 1.4$	at scan limits
Temperature (K)	298	121
2θ range (°)	$2 < 2\theta < 50$	$2 < 2\theta < 65$
Number of refl. meas.	1767	2031
No. of refl. $I > 2.5\sigma(I)$	522	1519
No. of stnd. refl.	3	3
No. of refl. between stnd. refl.	57	57

Table 2. Fractional atomic coordinates and thermal parameters for DL-tryptophan. The anisotropic temperature factor is given by $\exp - 2\pi^2(U_{11}a^{*2}h^2 + \cdots + 2U_{12}a^*b^*hk + \cdots)$. Estimated standard deviations in positional parameters are given in parantheses. The standard deviations in the U values are about 10^{-2}. Data for the hydrogen atoms are excluded because of the large uncertainties.

Atom	X	Y	Z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N1	0.1822(8)	0.7223(24)	0.1580(16)	0.046	0.037	0.047	−0.030	0.010	−0.004
C2	0.2497(11)	0.8069(32)	0.2116(19)	0.069	0.035	0.050	−0.004	0.027	0.021
C3	0.2666(9)	0.9929(28)	0.1461(17)	0.039	0.037	0.031	0.006	0.017	0.001
C4	0.1872(9)	1.2214(29)	−0.0785(17)	0.039	0.041	0.035	0.020	0.007	0.016
C5	0.1188(10)	1.2217(33)	−0.1574(18)	0.053	0.041	0.050	0.021	0.003	0.019
C6	0.0678(9)	1.0464(38)	−0.1511(22)	0.033	0.063	0.072	0.030	0.007	−0.011
C7	0.0838(9)	0.8715(34)	−0.0486(18)	0.033	0.039	0.053	−0.010	0.005	−0.002
C8	0.1535(8)	0.8682(34)	0.0445(16)	0.043	0.061	0.012	−0.015	0.009	−0.012
C9	0.2018(8)	1.0474(27)	0.0275(16)	0.024	0.036	0.023	−0.002	0.024	−0.015
C10	0.3348(8)	1.1361(26)	0.1747(16)	0.038	0.013	0.020	−0.008	0.008	−0.003
C11	0.3818(9)	1.1025(32)	0.0585(17)	0.038	0.012	0.047	0.001	0.006	0.016
C12	0.4155(10)	0.8498(32)	0.0695(18)	0.049	0.038	0.026	0.030	0.019	0.018
O13	0.4808(5)	0.8382(16)	0.1332(10)	0.022	0.022	0.037	0.002	−0.003	0.009
O14	0.3768(6)	0.6928(20)	0.0065(11)	0.043	0.028	0.063	0.008	−0.012	−0.013
N15	0.4386(6)	1.2843(23)	0.0803(13)	0.025	0.014	0.031	−0.012	0.003	0.000

Table 3. Fractional atomic coordinates and thermal parameters for the non-hydrogen atoms in D-tryptophan hydrogen oxalate. The anistropic temperature factor is given by exp-$2\pi^2(U_{11}a^{*2}h^2+\dots+2U_{12}a^*b^*hk^+\dots)$. Standard deviations are given in parantheses.

Atom	X	Y	Z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N1	1.6708(7)	0.8364(5)	0.5474(1)	0.0139(18)	0.0251(20)	0.0251(20)	0.0061(18)	0.0040(17)	0.0015(16)
C2	1.5555(7)	0.9552(6)	0.5747(1)	0.0217(22)	0.0172(21)	0.0147(18)	0.0048(20)	0.0015(18)	0.0026(17)
C3	1.3592(7)	0.8846(5)	0.5913(1)	0.0178(20)	0.0147(19)	0.0131(17)	0.0037(18)	0.0014(16)	0.0013(16)
C4	1.1984(7)	0.5709(5)	0.5784(1)	0.0175(22)	0.0214(21)	0.0129(18)	0.0025(19)	0.0003(18)	0.0030(16)
C5	1.2487(8)	0.4148(5)	0.5573(1)	0.0244(24)	0.0187(21)	0.0166(19)	0.0025(20)	0.0007(18)	0.0006(17)
C6	1.4465(8)	0.3937(6)	0.5302(1)	0.0285(23)	0.0165(21)	0.0166(19)	0.0068(21)	0.0014(19)	0.0029(17)
C7	1.6000(7)	0.5266(6)	0.5240(1)	0.0204(23)	0.0278(24)	0.0123(19)	0.0113(20)	0.0008(17)	0.0017(18)
C8	1.5497(7)	0.6839(5)	0.5461(1)	0.0144(20)	0.0197(20)	0.0124(18)	0.0037(19)	0.0006(18)	0.0013(16)
C9	1.3517(7)	0.7091(5)	0.5734(1)	0.0160(21)	0.0196(20)	0.0095(17)	0.0013(18)	0.0026(17)	0.0013(16)
C10	1.1911(7)	0.9665(5)	0.6238(1)	0.0153(20)	0.0126(18)	0.0153(18)	0.0006(19)	0.0010(17)	0.0034(16)
C11	1.1746(7)	0.8733(5)	0.6711(1)	0.0068(17)	0.0133(18)	0.0148(17)	0.0002(18)	0.0032(15)	0.0004(16)
C12	0.9959(6)	0.9479(5)	0.7039(1)	0.0116(18)	0.0061(16)	0.0203(19)	0.0023(15)	0.0027(16)	0.0020(17)
O13	0.8270(5)	1.0189(3)	0.6877(1)	0.0102(13)	0.0143(14)	0.0301(15)	0.0017(13)	0.0002(13)	0.0044(12)
O14	1.0339(5)	0.9189(4)	0.7487(1)	0.0125(15)	0.0229(16)	0.0183(13)	0.0065(14)	0.0046(12)	0.0007(13)
N15	1.3992(6)	0.8656(5)	0.6954(1)	0.0091(17)	0.0123(18)	0.0179(18)	0.0003(14)	0.0006(14)	0.0023(16)
C16	0.6595(7)	0.4630(5)	0.6636(1)	0.0115(19)	0.0175(19)	0.0142(18)	0.0010(19)	0.0009(16)	0.0031(16)
C17	0.4483(7)	0.3989(5)	0.6921(1)	0.0129(19)	0.0128(19)	0.0129(17)	0.0036(17)	0.0002(17)	0.0007(15)
O18	0.7987(6)	0.3405(4)	0.6487(1)	0.0187(16)	0.0126(15)	0.0291(16)	0.0035(15)	0.0100(15)	0.0054(14)
O19	0.6965(5)	0.6137(3)	0.6554(1)	0.0164(15)	0.0138(13)	0.0233(14)	0.0027(14)	0.0038(13)	0.0033(12)
O20	0.3073(5)	0.5133(3)	0.7038(1)	0.0173(14)	0.0136(13)	0.0271(15)	0.0027(14)	0.0103(13)	0.0047(12)
O21	0.4426(5)	0.2422(3)	0.7019(1)	0.0182(15)	0.0113(14)	0.0371(17)	0.0042(13)	0.0062(15)	0.0051(14)

STRUCTURE DETERMINATION

Both structures were solved by direct methods using the program assembly MULTAN.[6]

DL-*Tryptophan.* All the hydrogen atoms were introduced from stereochemical considerations and in the final least squares calculations, the positional parameters of all the atoms together with the anisotropic thermal paramters of the non-hydrogen atoms were refined to a final R factor of 0.085 and a goodness of fit: $s = (\Sigma \omega \Delta^2/m - n)^{\frac{1}{2}}$ of 1.8. The thermal parameters of the hydrogen atoms were kept constant at 3.5 Å^2. The final parameters are given in Table 2.

D-*Tryptophan hydrogen oxalate.* The hydrogen atoms except the two belonging to two of the carboxylic groups were localized from a difference map. The last two hydrogen atoms were introduced from considerations of the geometry of the carboxylic groups and the hydrogen bond system. In the final least squares calculations all positional parameters and the anisotropic temperature factors of the non-hydrogen atoms were refined, whereas the temperature factors for the hydrogen atoms were kept constant at 2.5 Å^2. The refinement terminated at an R-factor of 0.049 and a goodness of fit $s = 1.58$. The final parameters are given in Tables 3 and 4.

DESCRIPTION OF THE STRUCTURES

DL-*Tryptophan.* The interatomic distances and bond angles are given in Table 5, the numbering of the atoms being as indicated in Fig. 1. Because of

Table 4. Fractional atomic coordinates for the hydrogen atoms in D-tryptophan hydrogen oxalate. The standard deviations are given in parantheses.

	X	Y	Z
H1	1.780(8)	0.854(6)	0.531(1)
H2	1.624(7)	1.074(6)	0.579(1)
H4	1.073(8)	0.585(6)	0.596(1)
H5	1.139(8)	0.321(5)	0.560(1)
H6	1.489(8)	0.282(6)	0.513(1)
H7	1.742(8)	0.520(6)	0.506(1)
J10a	1.240(8)	1.082(6)	0.628(1)
H10b	1.033(8)	0.959(6)	0.607(1)
H11a	1.132(7)	0.750(5)	0.664(1)
H15b	1.380(8)	0.809(5)	0.726(2)
H15c	1.456(8)	0.951(6)	0.697(2)
H15	1.506(8)	0.791(6)	0.674(2)
H14	0.910(7)	0.940(6)	0.766(1)
H18	0.779(9)	0.259(6)	0.660(2)

the large standard deviations, the bond lengths and angles are of limited interst, but the molecule appears to exist in the zwitterionic form always found for such compounds in their pure crystalline form. The torsional angles C2–C3–C10–C11 and C3–C10–C11–C12 are found to be 107° and –69°, respectively, bringing the amino group in a *trans*, and the carboxylic group in a *gauche* position relative to the aromatic ring system. The distance from one of the oxygen atoms (014) in the carboxylic group to the nearest atom in the ring system (C3) is 3.2 Å, and the angle between the plane of the carboxylic group and that of the indole
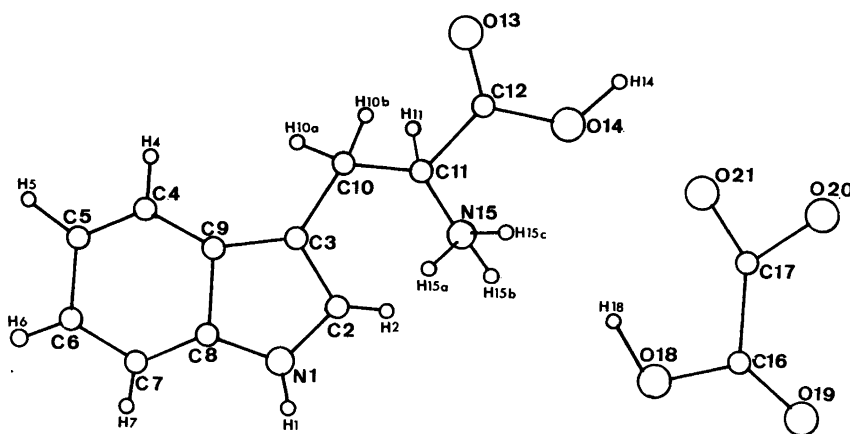

Fig. 1. The numbering of the atoms in the present work.

Table 5. Bond lengths and angles. *A*: DL-tryptophan (estimated standard deviations in bond lengths and angles are 2×10^{-2} Å and 1.6° respectively). *B* D-tryptophan hydrogen oxalate (e.s.d's are 5×10^{-3} Å and and 0.3° for bond lengths and angles not involving hydrogen atoms). *C*: Bond lengths in D-tryptophan hydrogen oxalate corrected for thermal motion.

Bond lengths (Å)				Bond angles (°)		
	A	B	C		A	B
N1−C2	1.37	1.378	1.379	N1−C2−C3	115	110.1
N1−C8	1.38	1.376	1.379	N1−C8−C9	112	107.2
C2−C3	1.31	1.361	1.362	C2−N1−C8	105	109.2
C3−C9	1.51	1.448	1.449	C2−C3−C9	106	106.3
C4−C9	1.40	1.404	1.406	C3−C9−C8	102	107.2
C4−C5	1.36	1.378	1.379	C3−C9−C4	133	134.0
C5−C6	1.41	1.402	1.403	C9−C4−C5	115	118.9
C6−C7	1.38	1.379	1.380	C4−C5−C6	124	121.0
C7−C8	1.43	1.400	1.399	C5−C6−C7	120	121.9
C8−C9	1.41	1.411	1.413	C6−C7−C8	119	116.7
C3−C10	1.51	1.490	1.493	C7−C8−C9	118	122.6
C10−C11	1.56	1.524		C8−C9−C4	125	118.8
C11−N15	1.49	1.489		C7−C8−N1	131	130.3
C11−C12	1.59	1.514		C2−C3−C10	130	127.1
C12−O13	1.26	1.223		C9−C3−C10	124	126.5
C12−O14	1.24	1.305		C3−C10−C11	114	112.7
C16−C17		1.561		C10−C11−C12	111	113.8
C16−O18		1.320		C10−C11−N15	109	111.4
C16−O19		1.203		C12−C11−N15	112	110.4
C17−O20		1.255		C11−C12−O13	115	120.3
C17−O21		1.241		C11−C12−O14	117	114.2
N1−H1		0.80		O13−C12−O14	128	125.4
C2−H2		1.01		C16−C17−O20		115.9
C4−H4		0.90		C16−C17−O21		116.4
C5−H5		0.97		O20−C17−O21		127.7
C6−H6		1.02		C17−C16−O18		115.5
C7−H7		0.98		C17−C16−O19		123.3
C10−H101		0.94		O19−C16−O18		121.2
C10−H102		1.05				
C11−H111		1.01				
O14−H14		0.89				
N15−H151		0.98				
N15−H152		0.74				
N15−H153		1.04				
O18−H18		0.71				

Table 6. Suggested hydrogen bond system in the crystals of DL-tryptophan. D: donor, A: acceptor.

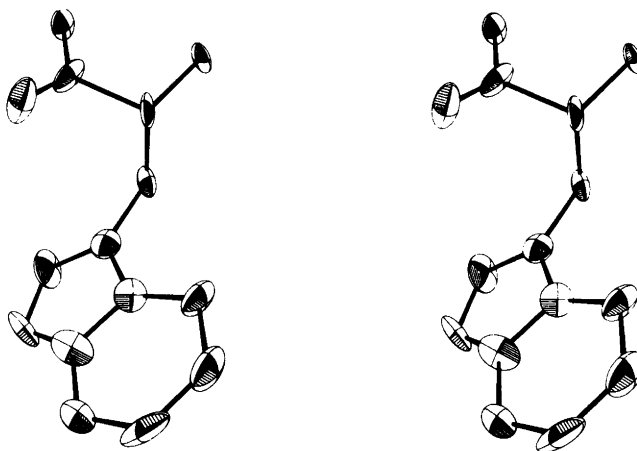| D	A	Equiv. pos.	D−A(Å)	∠C11DA	∠C12AD
N15	O13	$1-x, \frac{1}{2}+y, \frac{1}{2}-z$	2.82	102	138
N15	O13	$1-x, 2-y, -z$	2.85	109	107
N15	O14	$x, 1+y, z$	2.66	143	109

Fig. 2. Stereoscopic drawing of the tryptophan molecule as found in crystals of the pure racemic form.

moiety is 45°. The torsional angle N15−C11−C12 −O13 is +19°. The conformation described above is depicted in a stereoscopic drawing given in Fig. 2.
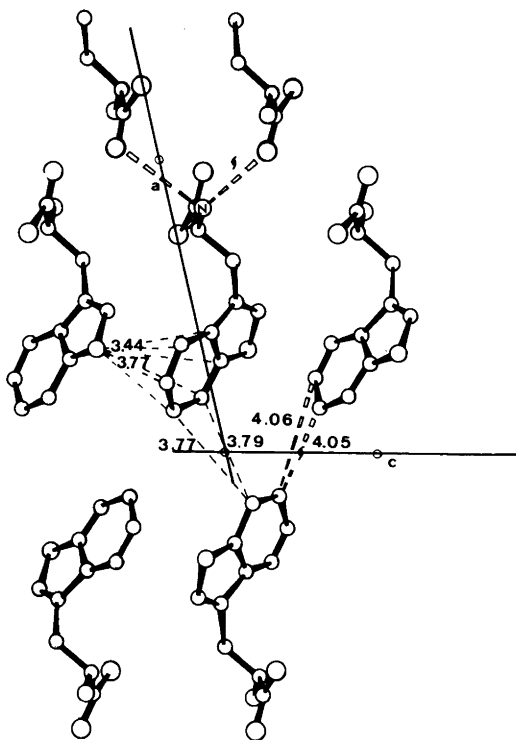

Fig. 3. Packing of molecules in crystals of DL-tryptophan as seen down the *b*-axis.

An illustration of the packing of the molecule is given in Fig. 3, where the intermolecular contacts also are indicated. It is found that the N15 atom is surrounded in a tetrahedral arrangement by three oxygen atoms belonging to carboxylic groups in three different molecules. The geometry of this coordination suggests the hydrogen bond system in the crystal as indicated in Fig. 3, whereas the distances and angles involved are given in Table 6. In this way each molecule will be connected to six neighbour molecules forming a double molecular layer parallel to the (100) plane. Whereas the molecules in these double layers are relatively firmly interconnected through the hydrogen bonds, there appear to be only weak van der Waals forces between the layers. The contacts between molecules in neighbour layers are indicated in Fig. 3.

D-*Tryptophan hydrogen oxalate.* The interatomic distances and angles are given in Table 4 as are the corrected[7] bond lengths in the indole moiety. In the crystals of the oxalic acid derivative, the tryptophan molecule exists in the cationic form with a positively charge amino group and an uncharged carboxylic group. The torsional angles C2−C3−C10−C11 and C3−C10−C11−C12 are −115.4 and −176.7°, respectively, and in this case it is the carboxylic group that is in the *trans* position relative to the ring system. The N−C11 −C12−O13 angle is found to be about 150°, and thus it is the protonized oxygen atom that is on the "*cis*-side" relative to N15 (N−C11−C12−OH = −29°).
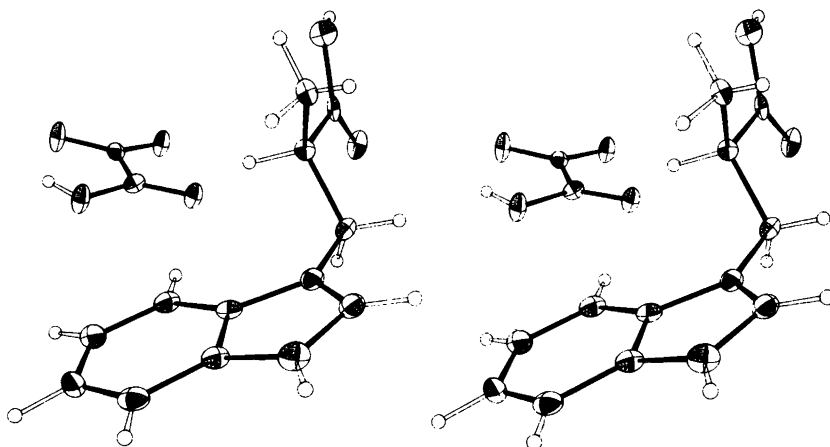
Fig. 4. Stereoscopic drawing of the tryptophan hydrogen oxalate complex.

The plane of the carboxyl group makes an agle of 89.5° with the plane of the indole ring. Least squares planes through the atoms of the six- and five-membered rings, respectively, showed no deviation of more than 0.008 Å from these planes and an angle of 1.6° between the two plane normals. The C10 atom is found to be 0.064 Å out of the five-membered ring plane.

The oxalic acid molecule is found to exist in a mono ionized state in the crystals, and the angle between the planes of the two carboxyl groups is close to 6°. A stereoscopic drawing of the two molecular ions in relative positions as found in the crystals is given in Fig. 4.

The packing of the molecules in the crystal is illustrated in Fig. 5, where the hydrogen bond system and some intermolecular contacts are also indicated, whereas distances and angles are given in Table 7.

It may be seen from this that there is only one possible hydrogen bond directly between two tryptophan molecules (N15−H15b...O13) connecting molecules in a chain along the a axis. However, the hydrogen atom H15b is at about the same distance from O13 as from O21 and the $\angle$DHA is more favourable in the latter case and indicates a more probable bond even if the D−A distance is greater. Also in these crystals the structure may be referred to as being double-layered in the sence that within the layers all molecules are tightly bonded together through hydrogen bonds and ionic forces, whereas there are only van der Waals' forces between molecules in neighbour layers. It is seen from Fig. 5 that the layers are parallel to the (001) plane, and as found in most crystal structures of these types of compounds, the surfaces of the layers are dominated by the aromatic ring systems. The smallest distances between molecules of neighbour layers are found to be 3.40 Å [N1−C7($\frac{1}{2}+x,\frac{3}{2}-y,1-z$)] 3.43 Å [N1−C6($\frac{1}{2}+x,\frac{3}{2}-y,1-z$)] and 3.46 Å [N1−C8($\frac{1}{2}+x,\frac{3}{2}-y,1-z$)].

Table 7. Hydrogen bonds between donor atoms (D) in the molecules given in Table 2 and acceptor atoms (A) in surrounding molecules.

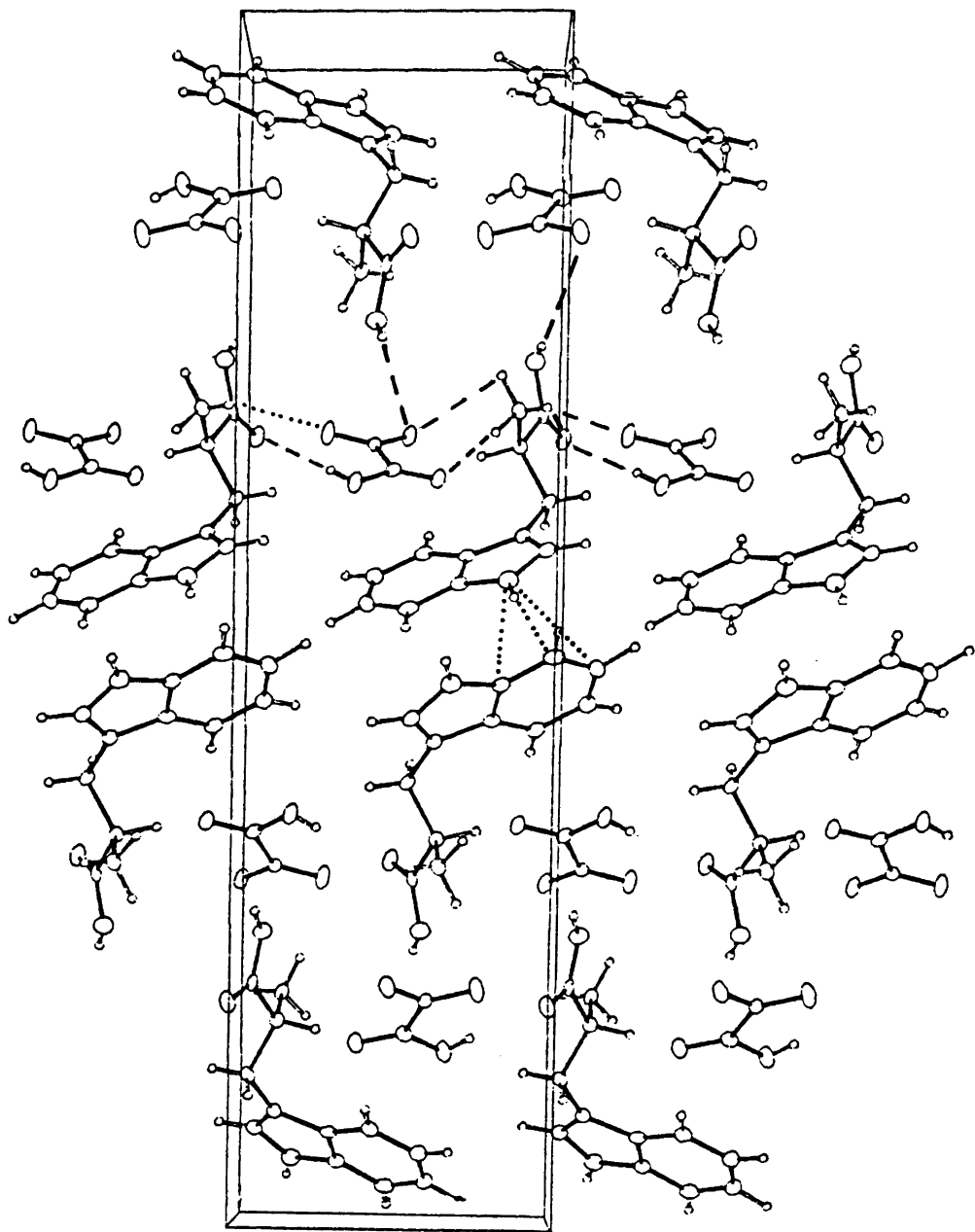| D	A	Equiv. pos.	D−A	H−A	$\angle$DHA
N15	O19	$1+x, y, z$	2.851(4)	1.85(5)	160.7
N15	O20	$1+x, y, z$	2.785(4)	2.40(4)	102.5
N15	O13	$1+x, y, z$	2.787(4)	2.26(5)	129.4
N15	O21	$1+x, 1+y, z$	2.924(4)	2.25(5)	151.4
O18	O13	$x, 1+y, z$	2.722(4)	2.04(4)	162.1
O14	O20	$1-x, \frac{1}{2}+y, \frac{3}{2}-z$	2.525(4)	1.64(4)	170.6

Fig. 5. Packing of the molecules in crystals of D-tryptophan hydrogen oxalate as seen down the *a*-axis.

DISCUSSION

The most interesting result from the study of the crystal structure of DL-tryptophan regards the torsional angle C3 – C10 – C11 – N, which by the IUPAC recommendations [8] is to be denoted χ^1 and found to be 169.0°.

To the best of our knowledge this is the first published example of a conformation of the tryptophan molecule where the amino group is in *trans* position relative to the ring system, even if similar values have been erroneously referred to.[9] A comparison of tortional angles found in some tryptophan derivatives is given in Table 8.

It may be seen from the table that 10 of the 14 structures show a conformation where the carboxyl group is in *trans* position relative to the ring system. In all these structures the amino group is on the *cis* side relative to the C2 atom. Three of the cases presented in the table exist in a conformation where the H11 atom is in the *trans* position and in one of these structures (L-tryptophan.HCl) it is the COOH group which is on the *cis* side to the C2 atom.

In the structure of D-tryptophan the amino group occupies the *trans* position and presents a second example of the carboxyl group being close to the C2 atom.

Furthermore, the torsional angle N15 – C11 – C12 – O13 (ψ) is found to have a rather large positive value (+ 19°) whereas this conformational angle usually is found to exhibit small negative values.[10] This may be explained by the close

intramolecular contact between O14 and C3 (3.2 Å) and possibly an indication that a clockwise rotation (in the D-form) about the C11 – C12 bond is preferable to an increase in the similar rotation about the C3 – C10 bond. Finally it is noted that the crystal structure of DL-tryptophan is strikingly similar to that of 3-indoeacetic acid.[11] Both structures contain the same type of double layers of molecules, and the way these layers are packed together is almost identical. The shortest distances between molecules of neighbour layers are in both structures about 3.8 Å when the molecules are related by a center of symmetry, and just above 4 Å when the molecules are related by a screw axis. These distances explain the easy cleavage along-the (100) planes observed in both types of crystals.

In both structures there also appears to be a specific interaction between the neighbour indole rings within the same layer as indicated in Fig. 3. The relationship and relevant distances between the indole moieties are given in Fig. 6 (a). Moreover, a similar interaction between indole rings at an angle of about 60° to each other appears to be the only interaction responsible for keeping the double molecular layers together in the·crystal structure of D-tryptophan hydrogen oxalate, as may be seen from Fig. 5 and is more specifically illustrated in Fig. 6 (b). In fact, the literature seems to indicate that attractive interaction between indole rings where the ring planes are making an angle of about $60 \pm 30°$ to each other, is fairly common,[2,12–21] and examples of similar interactions between indole moieties and phenyl

Table 8. Torsional angles in some tryptophan derivatives. $\chi^{2.1}$: C2 – C3 – C10 – C11, χ^1: N15 – C11 – C10 – C3, $\chi^{1.2}$: C12 – C11 – C10 – C3. All angles refer to the *R*-configuration at C11, that is; the D-form.

|	$\chi^{2.1}$	χ^1	$\chi^{1.2}$	Ref.
D-Tryptophan	106.6	168.6	– 68.6	–
DL-Tryptophan hydrogen oxalate	– 115.3	57.5	– 176.9	–
DL-Tryptophan formate	– 105.1	53.7	174.6	12
5-OH-DL-Tryptophan	– 110.7	74.7	– 163.6	17
L-Tryptophan.HCl	– 78	– 62.7	57.9	2
L-3-(2-Acetamido-2-ethoxycarbonyl)ethyl indole	– 97.8	68.9	– 167.8	26
Cyclo-glycyl-tryptophan	– 108.0	76.4	– 163.8	15
Glycyl-L-tryptophan dihydrate	– 60.6	65.1	– 170.0	14
DL-Tryptophan ethyl ester. HCl	83.5	– 71.3	51.1	25
DL-Tryptophan picrate methanol compl.	– 99.4	61.1	– 178.8	20
N-Acetyl-DL-tryptophan. N-Methylamide	– 98.7	65.4	– 173.7	9
N-Acetyl-L-tryptophan methylester	– 88.0	64.6	– 172.7	13
N-Acetyl-tryptophan	– 116.5	59.6	– 176.7	16
N-Acetyl-L-tryptophan-1-methyl-3-carbamido pyridin	– 93.1	– 61.4	63.9	27

a

b
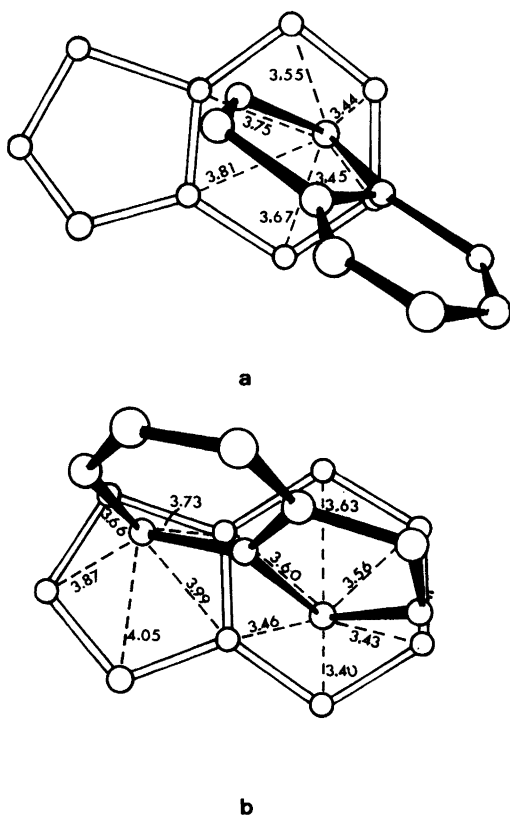
Fig. 6. Interaction between indole moieties in the crystal structure of DL-tryptophan (a) and D-tryptophan hydrogen oxalate (b). The angles between the ring planes are about 70° (a) and 60° (b).

rings are also encountered.[22] Thus, this type of relationship between indole rings, where of course the hydrogen atoms are involved in the interplay, may be worth consideration when interactions between such moieties are discussed.

Bond lengths and angles in the tryptophan molecule as found in the study of the formate[12] as well as in the present study, are compared in Table 9 where the bond lengths involved in the indole part of the molecule are corrected for thermal motion. It appears from the table that there is a good agreement between the bonds and angles in the two structures, except for the angles involving the C12 atom. Thus, the angles C10−C11−C12 and C12−C11−N15 are significantly different in the two structures, and it seems reasonable to explain this by the difference in the torsional angle N15−C11−C12=O, which involves interaction between the N15 atom and one of the oxygen atoms in the carboxylic group. For this reason the mean values of the two angles involving the carboxyl oxygens are not given in Fig. 7, where the weighted mean distances and angles are presented. For similar reasons the mean values of the external angles around the C3 atom are left out, because they are supposed in the present cases to be somewhat dependent on the torsional angle C2 −C3−C10−C11 and the interaction of the NH₃ or the COO group with parts of the ring system.

The bond lengths and angles found for the hydrogen oxalate ion conform well with those earlier reported for this molecule.[23,24] The only deviation from earlier findings is the value of 121.2° for the HO−C−O angle as compared to a mean
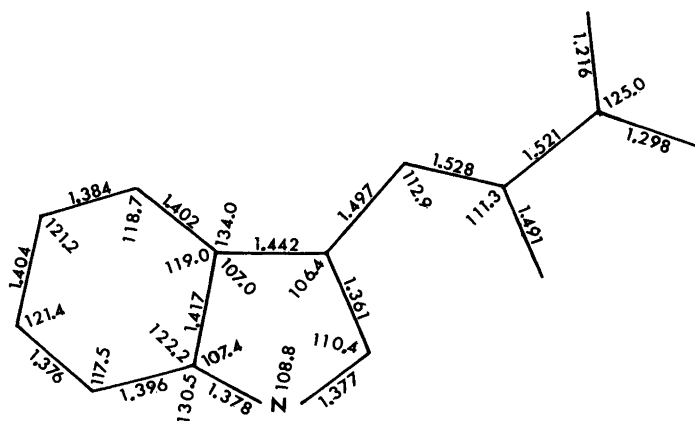

Fig. 7. Weighted average bond lengths and angles in the tryptophan molecule as found in the derivatives of formic and oxalic acids. e.s.d's in bond lengths and angles are 0.0026 Å and 0.13°, respectively.

Table 9. Comparison between bond lengths and angles in tryptophan hydrogen-oxalate (A) and tryptophan formate (B). Bond lengths involved in the indol moiety are corrected for thermal motion.

Bond	A (Å)	B (Å)	Bond	A (Å)	B (Å)
N1–C2	1.379	1.376	C7–C8	1.399	1.395
N1–C8	1.379	1.377	C8–C9	1.413	1.418
C2–C3	1.362	1.360	C3–C10	1.493	1.498
C3–C9	1.449	1.440	C10–C11	1.524	1.529
C4–C9	1.406	1.400	C11–C12	1.514	1.523
C4–C5	1.379	1.386	C11–N15	1.489	1.492
C5–C6	1.403	1.404	C12–OH	1.305	1.295
C6–C7	1.380	1.375	C12=O	1.223	1.214

Angle	A (°)	B (°)	Angle	A (°)	B (°)
N1–C2–C3	110.1	110.5	C8–C9–C4	118.8	119.1
N1–C8–C9	107.2	107.4	C7–C8–N1	130.3	130.5
C2–N1–C8	109.3	108.7	C2–C3–C10	127.1	125.8
C2–C3–C9	106.3	106.4	C9–C3–C10	126.5	127.7
C3–C9–C8	107.2	106.7	C3–C10–C11	112.7	112.9
C3–C9–C4	134.0	134.0	C10–C11–C12	113.8	111.1
C9–C4–C5	118.9	118.7	C10–C11–N15	111.4	111.3
C4–C5–C6	121.0	121.2	C12–C11–N15	110.4	108.0
C5–C6–C7	121.9	121.3	C11–C12–OH	114.2	113.2
C6–C7–C8	116.7	117.7	C11–C12=O	120.3	121.8
C7–C8–C9	122.6	122.1	O=C12–OH	125.3	124.9

Torsion angle	A	B	Torsion angle	A	B
C2–C3–C10–C11	−115.4	−105.1	N15–C11–C12=O	150	−4.3
C3–C10–C11–C12	−176.7	−174.6			

value of about 125° for this angle in earlier studied molecules. It seems reasonable to explain this, at least partly, by the fact that the hydrogen atom (H18) in the present case is in *trans* position relative to O19, instead of in *cis* position as most often found. The torsional angle O19–C17–O18–H18 is close to 180°.

REFERENCES

1. Khawas, B. and Krishna Murti, G. S. R. *Acta Crystallogr. B 25* (1969) 1006.
2. Takigawa, T., Ashida, T., Sasada, Y. and Kakuda, M. *Bull. Chem. Soc, Jpn. 39* (1966) 2369.
3. Doyle, P. A. and Turner, P. S. *Acta Crystallogr. A 24* (1968) 390.
4. Stewart, R. F., Davidson, E. R. and Simpson, W. T. *J. Chem, Phys. 42* (1965) 3175.
5. Groth, P. *Acta Chem. Scand. 27* (1973) 1837.
6. Germain, G., Main, P. and Woolfson, M. M. *Acta Crystallogr. A 27* (1971) 368.

7. Schomaker, V. and Trueblood, K. N. *Acta Crystallogr. B 24* (1968) 63.
8. IUPAC *J. Mol. Biol. 52* (1970) 1–17.
9. Harada, Y. and Iitaka, Y. *Acta Crystallogr. B 33* (1977) 244.
10. Marsh, R. E. and Donohue, J. *Adv. Protein Chem. 22* (1967) 235.
11. Karle, I. L., Britts, K. and Gum. P. *Acta Crystallogr. 17* (1964) 496.
12. Bye, E., Mostad, A. and Rømming, C. *Acta Chem. Scand. 27* (1973) 471.
13. Cotrait, M. and Barrans, Y. *Acta Crystallogr. B 30* (1974) 510.
14. Pasternak, R. A. *Acta Crystallogr. 9* (1956) 341.
15. Morris, A. J., Geddes, A. J. and Sheldrick, B. *Cryst. Struct. Commun. 3* (1974) 345.
16. Yamane, T., Andov, T. and Ashida, T. *Acta Crystallogr. B 33* (1977) 1650.
17. Wakahara, A., Fujiwara, T. and Toita, K. *Bull. Chem. Soc. Jpn. 46* (1973) 2481.
18. Falkenberg, G. and Carlström, D. *Acta Crystallogr. B 27* (1971) 411.

19. Falkenberg, G. *Acta Crystallogr. B 28* (1972) 3219.
20. Gartland, G. L., Freeman, G. R. and Bugg, C. E. *Acta Crystallogr. B 30* (1974) 1841.
21. Sakaki, T., Sogo, A., Wakahara, A., Kanai, T., Fusiwara, T. and Tomita, K. *Acta Crystallogr. 832* (1976) 3235.
22. Inoue, M., Sakaki, T., Fujiwara, T. and Tomita, K. *Bull. Chem. Soc. Jpn. 51* (1978) 1123.
23. Thomas, J. O. and Renne, N. *Acta Crystallogr. B 31* (1975) 2161.
24. Amit, A., Mester, L., Klewe, B. and Furberg, S. *Acta Chem. Scand. A 32* (1978) 267.
25. Vijayalakshmi, B. K. and Srinivasan, R. *Acta Crystallogr. B 31* (1975) 999.
26. Vijayalakshmi, B. K. and Srinivasan, R. *J. Cryst. Mol. Struct. 7* (1977) 21.
27. Ash, R. P., Herriott, J. R. and Deranleau, A. D. *J. Am. Chem. Soc. 99* (1977) 4471.