

The Structure of DL- and D-Leucine

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It would appear possible by a comparison of the crystal structures of optically active compounds with those of the corresponding racemic forms, to obtain some information about the rôle played by the D- and L-molecules in the latter *e. g.* whether they are distributed at random in solid solution or whether distinct pairs of DL-molecules do exist. For this reason and also in order to see how α -amino acid molecules with relatively large branched carbon chains may be packed together, we have examined the crystal structure of DL-, L- and D-leucine by x-rays. Although we have not been able to determine the complete structure, some results have been obtained which may be of interest.

Oscillation- and Weissenberg photographs were taken of several crystals about different axes with CoK α and CuK α radiation, a Buerger-Weissenberg camera of 57.3 mm diameter being used. The density of the crystals was determined by the flotation method in mixtures of xylene and ethylene chloride.

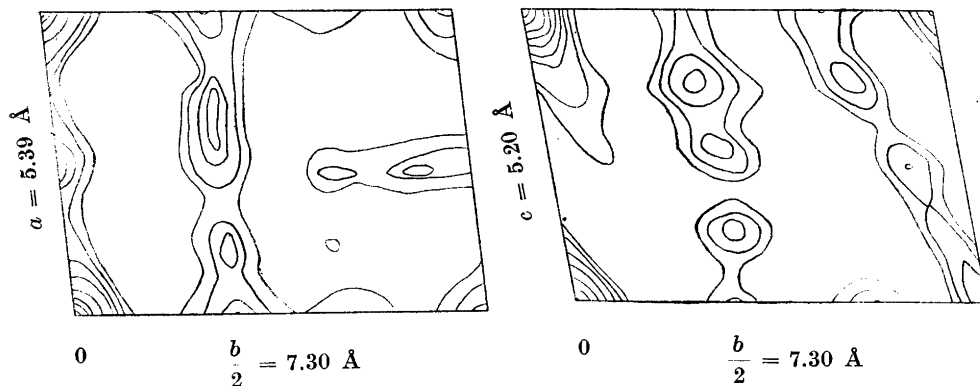
DL-Leucine

Crystals of a preparation from Schering-Kahlbaum were used for the experiments. They were thin tablets with angles of approx. 70 and 110° between the adjacent sides. The extinction directions were respectively parallel and perpendicular to the one of these which was chosen as *a*-axis. The refractive indices parallel and perpendicular to the *a*-axis were measured in natural light by embedding the crystals in mixtures of paraffin and 1-bromonaphthalene. Axial dispersion could be observed.

$$\alpha' \sim n_{|a} : 1.525$$

$$\gamma' \sim n_{|a} : 1.552$$

The crystals were triclinic with a density of 1.18 g/cm³. The unit cell dimensions were: $a = 5.39 \text{ \AA}$, $b = 14.6 \text{ \AA}$, $c = 5.18 \text{ \AA}$ and the angles between the axes: $\alpha = 103^\circ$; $\beta = 111.5^\circ$, $\gamma = 96^\circ$. There are two molecules in the unit



Figs. 1 and 2. The Patterson-function of DL-leucine parallel-projected on the ab - and bc -planes.

cell. Systematic absences of reflections were not observed, and, as the crystals turned out to be piezoelectric according to a test performed by Mr. E. Blomgren, Uppsala, the space group is P 1.

Patterson projections were calculated on the b^*c^* and a^*b^* planes from the visually estimated intensities, but too many maxima appeared and made an interpretation very difficult. Strong maxima, however, corresponding to the distances 2.75 and 2.90 Å at about right angles to each other were present. They probably are the $O_I-(H)-O_{II}$ and $N_IH_2-(H)-O_{II}$ distances, while another set of maxima from 3.60–4.00 Å corresponds to the $C_IH_3-C_{II}H_3$ -distances. The Patterson projections indicate a layer structure with the molecules nearly parallel to the b -axis.

An attempt was made to calculate the electron projection on the b^* -axis from the first eleven orders of the $(0k0)$ -reflections. The signs were obtained by calculations on models based on previous investigations of amino acids^{1, 2}. From the one-dimensional electron projection, mean values of the y -parameters of the atoms in the two molecules could be obtained, and by using Robertson and Woodward's empirical atomic scattering factors³, the $(0k0)$ -intensities were calculated. Smaller displacements of the atoms were tried. The y -parameters giving best agreement between calculated and observed intensities were:

$C'H_3: \pm 0.030$, $C''H_3: \pm 0.110$, $CH: \pm 0.115$, $CH_2: \pm 0.215$, $CH: \pm 0.285$, $C: \pm 0.380$, $NH_2: \pm 0.220$, $O': \pm 0.390$, $O'': \pm 0.430$. — And the relative intensities were:

(0 <i>k</i> 0)	010	020	030	040	050	060	070	080	090	0100	0110
Calculated intensity	72	6	1	46	78	79	1	7	5	19	4
Observed	v.s	w	v.w	s	v.s	s	—	—	w-m	w-m	w

From the optical anisotropy one would expect the COO-groups to be approximately perpendicular to the a -axis.

A calculation of the two-dimensional electron projections was attempted, again neglecting the lack of a centre of symmetry. The intensities calculated from the atomic parameters obtained in this way, however, did not agree very well with the experimental ones.

The crystals from Schering-Kahlbaum were exceedingly twinned on the (010)-plane. This was deduced from the fact that all reflections except the (0*k*0)-ones were doubled in such a way that upon constructing the reciprocal lattice, two sets of points resulted, one being obtained from the other by a rotation of 180° about the b^* -axis. A less pronounced twinning about the a -axis, also visible in the reciprocal lattice, sometimes makes the crystals look like irregular hexagons. These twin-formations may be easily understood if one pictures the structure as consisting of double layers of molecules stacked together with the methyl groups from neighbouring layers towards each other at distances of 3.6—4.0 Å, while the polar groups, COO⁻ and NH₃⁺, make strong bonds of length 2.75—2.90 Å between and in the two single layers. — This also explains why the crystals do not wet, since, clearly, the CH₃-groups must stick out.

D-L e u c i n e

Dr. S. E. Darmon, Colloid Science Lab., Cambridge, kindly supplied me with some very good crystals. They too were tablets, but with a shape different from the DL-leucine.

The crystals were orthorhombic in agreement with previous optical investigations ^{4,5}. Cell dimensions were: $a = 5.36$ Å. $b = 14.7$ Å, and $c = 9.65$ Å, with the axes chosen in accordance with those of DL-leucine. From the density of 1.17 g/cm³, we get four molecules per unit cell. (A reference book ⁵ gives the density as 1.29 g/cm³ but this figure leads to the improbable value $z = 4.5$). From systematic absences of reflections, the space group may be P 2₁22₁, but P 2₁22 and P 222 cannot be excluded. It is interesting to note that the a - and b -axes are nearly identical in DL- and L-leucine and the twinning of the DL-leucine crystals makes them simulate the macroscopic symmetry of the D-leucine.. Furthermore, the (0*k*0)-reflections from the two kinds of

crystals have very similar intensities and, in fact, the electron projections on the b^* -axis calculated from these show maxima for practically the same values of y . Hence the D-leucine crystals are also built up of double layers in a similar way to DL-leucine.

Some single crystals of a L-leucine preparation from S. A. Hoffmann-La Roche and Co. were also examined. They, however, gave x-ray-diagrams identical with those of DL-leucine except that reflections due to twin-formation did not appear on the equator diagram and that some extra, relatively weak, reflections accompanied the $(0k0)$ -reflections showing the same variation in intensity as these. These diagrams show that crystals of DL-leucine have been present in the L-leucine preparation and that there are built in $(0k0)$ -layers of orthorhombic L-leucine in them. This is in accordance with the powder photographs of DL- and L-leucine: Nearly all lines on the latter may be indexed on the basis of the orthorhombic unit cell, but some lines, which correspond to the strongest lines on the powder photograph of DL-leucine, still remain. Fractional recrystallization of L-leucine gave, as less soluble product, orthorhombic single crystals with x-ray diagrams similar to those of D-leucine. — The reason that other extra $(hk0)$ -reflections are not easily observed may be that they are weaker and very nearly coincide with the somewhat drawn out $(hk0)$ -reflections from DL-leucine.

In order to ascertain if the triclinic DL-leucine was a true racemic compound, the solubilities were determined.

10 g	aqueous solution	saturated with	DL-leucine	contain	0.104 g	leucine
10 »	»	»	»	»	L- »	» 0.231 » »
10 »	»	»	»	»	L and DL »	» 0.259 » »

The triclinic DL-leucine thus appears to be a true racemic compound with one D- and one L-molecule in the unit cell, arranged in such a way that no centre of symmetry results. This is not in accordance with the assumption, based on previous investigations, that one must be able to bring the molecules of the two antipodes in a true racemic compound to coincide by means of a symmetry operation⁶. It is tempting to regard the twin-formation as a substitute for the desired symmetry operation.

As characteristic features of this amino acid in the solid state may be mentioned the low symmetry of the DL-form, the layer structure along the b -axis, and the ease with which 'mistakes' are introduced into the sequence of the $(0k0)$ -layers.

SUMMARY

X-ray investigation shows that crystals of DL-leucine are triclinic with unit cell dimensions $a = 5.39 \text{ \AA}$, $b = 14.6 \text{ \AA}$, $c = 5.18 \text{ \AA}$, $\alpha = 103^\circ$, $\beta = 111.5^\circ$, $\gamma = 96^\circ$ and 2 molecules per unit cell while those of D-leucine are orthorhombic with $a = 5.36 \text{ \AA}$, $b = 14.7 \text{ \AA}$, $c = 9.65 \text{ \AA}$, and 4 molecules per unit cell. Although it has not been possible to determine the structure completely it is inferred from two-dimensional Patterson- and one-dimensional electron-projections that the crystals in both cases are built up of double-layers consisting of two layers of molecules with the methyl groups pointing outwards. Different kinds of disorder structure have been observed and may be explained by the forces between adjacent double-layers being weak. The symmetry of the DL-form is lower than expected.

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