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DL-Norleucine: Redetermination of Structure and Observations with Synchrotron Radiation Laue Diffraction on Heating Towards Transformation

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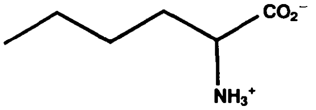
Abstract

Redetermination of the structure of DL-norleucine (2-aminohexanoic acid), $C_6H_{13}NO_2$, has given more accurate geometrical information than the early work of Mathieson [*Acta Cryst.* (1953), **6**, 399–403]. Synchrotron radiation Laue diffraction patterns recorded over a range of temperatures have shown (*a*) the presence of streaks, indicating disorder in the stacking of layers within the crystal at room temperature, (*b*) complete or almost complete disappearance of these streaks when the crystal is heated to *ca* 373 K, indicating annealing of the crystal, and (*c*) loss of single crystal characteristics above 390 K so that it was not possible to record diffraction data for the high-temperature form proposed by Mathieson.

Introduction

Mathieson (1953) reported the structure of α-DL-norleucine, in space group $P2_1/a$.



The structure consists of double layers, parallel to (001). In the centre of the double layers the molecules are tightly linked by hydrogen bonds (Fig. 1) involving the —COO⁻ and —NH_3^+ groups in a fashion typical of amino acids. The 'outer' surfaces are composed of the ends of the aliphatic chains; these form an approximately close-packed array, and stack against those of the next double layer. Mathieson (1952) had previously established the structure of two forms of DL-methionine crystals, α and β, and the DL-norleucine crystals closely resembled the α form [methionine, CH_3—S—$(CH_2)_2CH(NH_2)COOH$, is a close chemical analogue of norleucine]. He also reported that many DL-norleucine crystals showed streaking and/or additional reflections (Mathieson, 1953). By analogy with DL-methionine he proposed that a β form should also exist with identical double layers, and the alternative packing of the aliphatic chain ends in adjacent double layers. The β form should have space group $I2/a$. Crystals of the pure β form have not been observed, but Mathieson accounted for streaks and additional reflections as the result of mixing of the α and β patterns of stacking. Both DL-methionine structures have been redetermined with greater accuracy by Taniguchi, Takaki & Sakura (1980), the β form at room temperature, the α form at a higher temperature of 333 K. The α form was obtained from the β form by heating.

Mnyukh, Panfilova, Petropavlov & Uchvatova (1975) heated crystals of DL-norleucine from room temperature

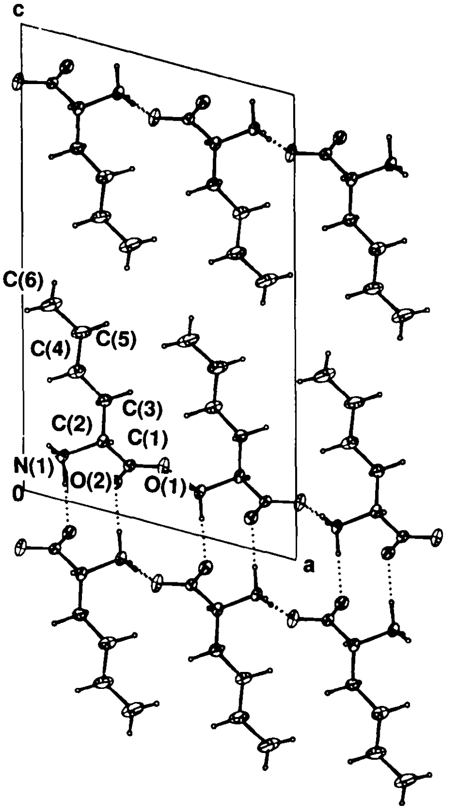


Fig. 1. View of the structure along the *b* axis. Hydrogen bonds between NH_3^+ and COO⁻ groups around $x = 0$ link the molecules in double layers. In the region around $x = \frac{1}{2}$, the packing of the ends of the aliphatic chains depends entirely on van der Waals interactions [drawn using *CAMERON* (Watkin, 1995)].

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Table 1. *Experimental details*

Crystal data	
Chemical formula	$C_6H_{13}NO_2$
Chemical formula weight	131.17
Cell setting	Monoclinic
Space group	$P2_1/a$
a (Å)	9.9069 (13)
b (Å)	4.737 (2)
c (Å)	16.382 (2)
α (°)	90.0
β (°)	104.681 (11)
γ (°)	90.0
V (Å^3)	743.8 (3)
Z	4
D_x (Mg m^{-3})	1.171
Radiation type	Mo $K\alpha$
Wavelength (Å)	0.71069
No. of reflections for cell parameters	25
θ range (°)	15–20
μ (mm^{-1})	0.087
Temperature (K)	296 (2)
Crystal form	Thin plates
Crystal size (mm)	0.6 × 0.4 × 0.1
Crystal colour	Colourless
Data collection	
Diffractometer	Rigaku AFC-6*S*
Data collection method	ω–2θ scans
Absorption correction	None
No. of measured reflections	1394
No. of independent reflections	1306
No. of observed reflections	1034
Criterion for observed reflections	$F > 4\sigma(F)$
$R_{\rm int}$	0.0169
$\theta_{\rm max}$ (°)	25
Range of h, k, l	$0 \rightarrow h \rightarrow 11$ $0 \rightarrow k \rightarrow 5$ $-19 \rightarrow l \rightarrow 18$
No. of standard reflections	3
Frequency of standard reflections	150
Intensity decay (%)	Negligible
Refinement	
Refinement on	F^2
$R[F^2 > 2\sigma(F^2)]$	0.0445
$wR(F^2)$	0.1182
S	1.57
No. of reflections used in refinement	1301
No. of parameters used	134
H-atom treatment	*xyz* and *U* refined
Weighting scheme	$w^{-1} = \sigma^2(F_o^2) + 0.23P + 0.458P^2$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max}$	0.027
$\Delta\rho_{\rm max}$ (e Å^{-3})	0.260
$\Delta\rho_{\rm min}$ (e Å^{-3})	−0.173
Extinction method	None
Source of atomic scattering factors	*International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)
Computer programs	
Data collection	*TEXSAN* (Molecular Structure Corporation, 1985)
Cell refinement	*TEXSAN* (Molecular Structure Corporation, 1985)
Data reduction	*TEXSAN* (Molecular Structure Corporation, 1985)
Structure refinement	*SHELXL*93 (Sheldrick, 1993)
Preparation of material for publication	*SHELXL*93 (Sheldrick, 1993)

and observed them under a polarizing microscope. They observed a reversible change, at 390 K, and could also see that macroscopic layers of crystal had been displaced in relation to each other. We have repeated the observations with a polarizing microscope, and used the synchrotron radiation (SR) Laue method and a crystal heating system to record diffraction data on crystals as they are heated up to and through Mynukh's transformation temperature. We had hoped that this would give diffraction data leading to the structure of the high-temperature form, but at no stage did the Laue diffraction pattern above 390 K correspond to that of a good quality single crystal. [Note that the work of Mynukh, Panfilova, Petropavlov & Uchvatova (1975) regards the β form of DL-norleucine (space group $I2/a$) as the phase stable at higher temperatures, the α form ($P2_1/a$) at lower temperatures, whereas Taniguchi, Takaki & Sakura (1980) report having obtained crystals of α-methionine ($P2_1/a$) by heating a crystal of the β form ($I2/a$).]

The synchrotron radiation Laue method has considerable potential for the study of structural changes in single crystals as a function of time (Allinson *et al.*, 1992; Carr, Cheetham, Harding & Rule, 1992). At the SRS, Daresbury, substantial amounts of diffraction data can be recorded for a single crystal with short exposures (*e.g.* 0.1 s) and short time intervals between exposures (1–3 min). With third-generation synchrotron sources and charge-coupled device (c.c.d.) detectors these times are further reduced, *e.g.* to 50 ps exposure time at ESRF. A single Laue diffraction pattern with the crystal in a suitable orientation is sufficient to detect changes in unit-cell axial ratios or angles, and to record 45% of the unique reflections for a monoclinic crystal, or 85% for a tetragonal crystal ($4/mmm$) (see Carr, Dodd & Harding, 1993; Harding, 1991; Helliwell *et al.*, 1989). Thus, the SR Laue method should allow efficient study of a crystal at a series of temperatures. In this case, the results did not justify extensive data processing, but we report our qualitative observations. We also report the recording of four-circle diffractometer data for a crystal at room temperature, and a new refinement of the structure with this data.

Experimental

DL-Norleucine was purchased from Aldrich and crystals were grown by vapour diffusion from aqueous ethanol over a period of several weeks. They are very thin plates with (001) faces, elongated along **a**. Details of the room-temperature structure determination are given in Table 1.

Using a Linkam HFS91 heating stage and TP92 controller crystals were heated and observed under a polarizing microscope. The observations of Mnyukh and colleagues of a transition at 390 K were confirmed; it was always accompanied by a certain amount of cracking

Table 2. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

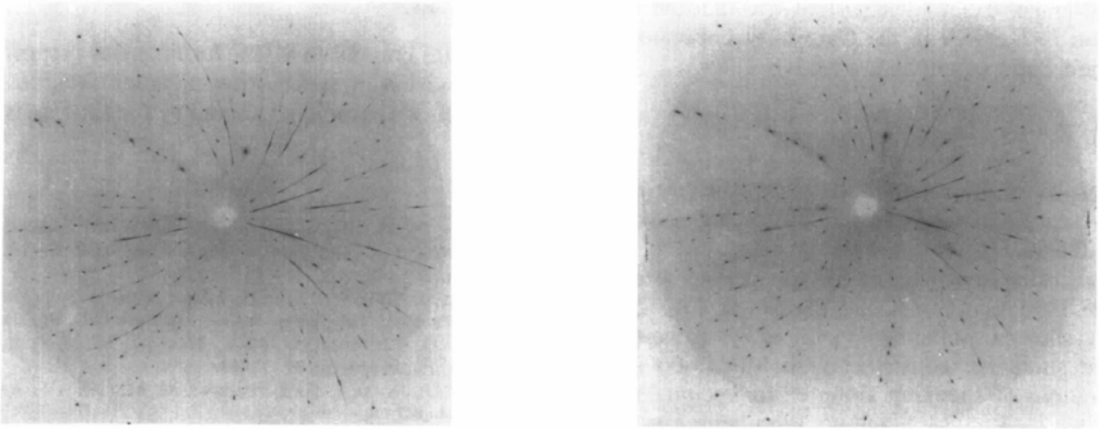
$$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
C(1)	0.3872 (2)	0.1138 (4)	0.1099 (1)	0.026 (1)
C(2)	0.2915 (2)	−0.0601 (4)	0.1496 (1)	0.026 (1)
C(3)	0.2980 (2)	0.0540 (5)	0.2377 (1)	0.036 (1)
C(4)	0.1979 (3)	−0.0759 (6)	0.2832 (2)	0.045 (1)
C(5)	0.2135 (4)	0.0377 (9)	0.3707 (2)	0.063 (1)
C(6)	0.1053 (5)	−0.0686 (11)	0.4135 (2)	0.082 (1)
N(1)	0.1467 (2)	−0.0466 (4)	0.0)950 (1)	0.028 (1)
O(1)	0.5136 (1)	0.0436 (3)	0.1271 (1)	0.040 (1)
O(2)	0.3348 (1)	0.3228 (3)	0.0669 (1)	0.034 (1)

Table 3. *Selected bond lengths* (Å) *and angles* (°) *for* (1)

C(1)—O(2)	1.249 (2)	C(2)—C(3)	1.528 (3)
C(1)—O(1)	1.256 (2)	C(3)—C(4)	1.513 (3)
C(1)—C(2)	1.520 (3)	C(4)—C(5)	1.502 (4)
C(2)—N(1)	1.488 (2)	C(5)—C(6)	1.509 (5)
O(2)—C(1)—O(1)	125.8 (2)	N(1)—C(2)—C(3)	110.9 (2)
O(2)—C(1)—C(2)	117.1 (2)	C(1)—C(2)—C(3)	109.3 (2)
O(1)—C(1)—C(2)	117.0 (2)	C(4)—C(3)—C(2)	116.4 (2)
N(1)—C(2)—C(1)	109.3 (2)	C(5)—C(4)—C(3)	113.7 (2)
		C(4)—C(5)—C(6)	114.3 (3)
N(1)—H···O(2^{i})	2.775 (2)	N(1)—H···O(1^{ii})	2.813 (2)
		N(1)—H···O(1^{iii})	2.837 (2)

Symmetry codes: (i) $\frac{1}{2}-x, -\frac{1}{2}+y, -z$; (ii) $-\frac{1}{2}+x, -\frac{1}{2}-y, z$; (iii) $-\frac{1}{2}+x, \frac{1}{2}-y, z$.

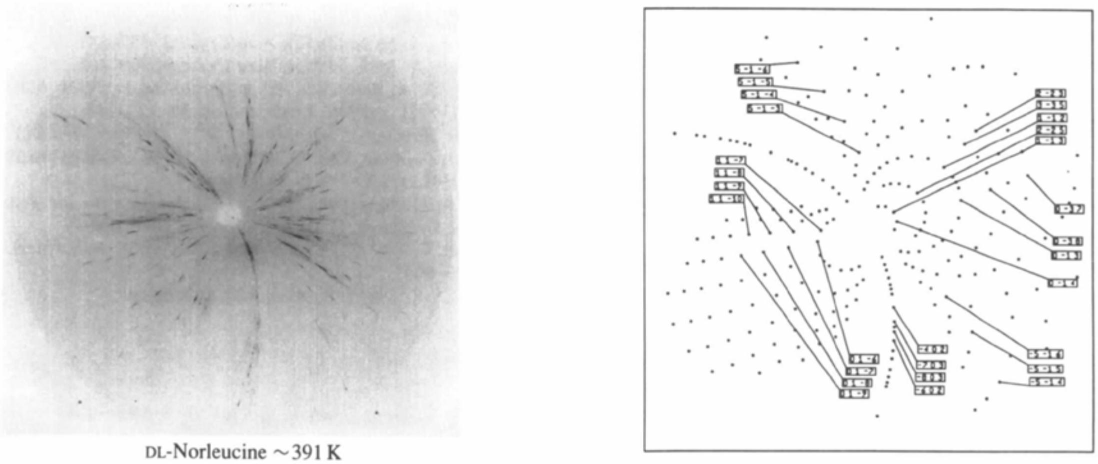


DL-Norleucine ~298 K

(*a*)

DL-Norleucine ~373 K

(*b*)



DL-Norleucine ~391 K

(*c*)

(*d*)

Fig. 2. SR Laue diffraction photographs of a crystal of DL-norleucine at (*a*) room temperature, (*b*) 373 and (*c*) 391 K. The streaking in (*a*) diminishes, but does not disappear in (*b*). The pattern in (*c*) indicates that there is no longer a good quality single crystal. (*d*) Simulation of Laue diffraction pattern, showing indices of selected spots (*LAUEGEN*; Campbell, 1993). For the simulation $d_{\min} = 1.2$, $l_{\min} = 0.25$ and $\lambda_{\max} = 1.5$ Å. Along the lines of spots 117, 118, 119, 1110 and 513, 514, 515, 516 and 402, 703, 803, 602 there are no streaks in Figs. 2(*a*) and (*b*). Along other lines, for which the indices conform to $h + k = 2n + 1$, there are pronounced streaks; they follow reciprocal lattice rows, with changing l.

of the crystal, but the slower the heating rate (*e.g.* 0.2° min^{-1}) the less was the cracking.

At Daresbury Laboratory Laue diffraction patterns were recorded on workstation 9.7 on film or on polaroid film. The usual experimental conditions were SRS at 200–300 mA, 0.2 mm collimator, 0.2 mm Al attenuator in incident beam (to reduce the intensity of the longer wavelength radiation and thus reduce radiation damage), crystal-film distance *ca* 60 mm, exposure time 0.3 s for CEA reflex film, 1 s for polaroid 57 film. Five different crystals were heated with an Enraf–Nonius gas-stream heating system (FR559), which was mounted on the goniometer head. Before the experiments this was calibrated over the range 298–408 K using a separate thermocouple placed exactly at the position the crystal would occupy. (By the end of the series of experiments it was clear that the internal thermocouple in the gas-stream device had moved slightly and the calibration was no longer exact.) The pattern was indexed with the program *LAUEGEN* in the Daresbury Laboratory Laue Software Suite (Campbell, 1993).

Results

The results of the room-temperature structure determination are given in Tables 2 and 3 and the packing illustrated in Fig. 1.

Laue diffraction patterns for one crystal recorded at *ca* 298, 373 and 391 K are shown in Fig. 2. Other crystals showed similar behaviour. At 298 K there is very marked streaking, consistent with Mathieson's (1953) observations of streaking along **c*** for reciprocal lattice rows with $h+k=2n+1$, and not those with $h+k=2n$. It is not simply radial streaking, which in Laue diffraction patterns is an indication of poor crystal quality. With our crystals there was no sign of the additional reflections from which he deduced a supercell. The streaking diminishes greatly as the temperature approaches 373 K. The streaking can be explained as due to a disorder in the stacking of layers as proposed by Mathieson (1953), and so these diffraction patterns show that the stacking becomes more ordered as the temperature increases. Diffraction patterns for a crystal held at 333 K for 35 min were streaked and showed comparatively little change; the annealing appears to occur mainly at temperatures higher than this.

Laue diffraction patterns were also recorded with the crystal held a few degrees below the reported transition temperature and then heated very slowly through it (1° per 5 min from 388 to 398 K). At the transition temperature there is a sharp deterioration (see Fig. 2*c*) in the crystal quality, and above the transition temperature the quality did not improve in any sample.

In summary, in addition to redetermining the structure we have shown that SR Laue diffraction patterns recorded over a range of temperatures can conveniently give information on the annealing of crystals containing stacking disorders or their loss of crystallinity; had there been a transition to a good quality single crystal of the high-temperature form suggested by Mathieson (1953), data adequate for structure determination could have been recorded, but we found no conditions which would lead to such a crystal. The high-temperature form may well have been present, but only as a group of small crystallites.

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