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N-Carboxy-DL-leucine anhydride

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Key indicators

Single-crystal X-ray study
T = 288 K
Mean σ(C–C) = 0.003 Å
R factor = 0.048
wR factor = 0.159
Data-to-parameter ratio = 12.0

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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The structure of 4-isobutyl-1,3-oxazolidine-2,5-dione, $C_7H_{11}NO_3$, has been determined to explain the polymerization of a series of amino acid *N*-carboxy anhydrides in the solid state. A dimer structure is formed between the L- and D-enantiomers around a crystallographic centre of symmetry *via* N—H···O hydrogen bonds. The five-membered rings are arranged in a layer, sandwiched between two layers of isopropyl groups. This structure should be conducive to the polymerization of the compound in the solid state.

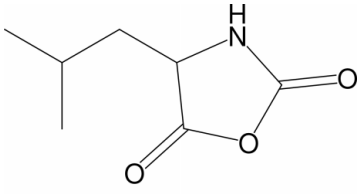
Comment

N-Carboxy anhydrides (NCAs) of amino acids are crystalline compounds and are usually polymerized in solution in the preparation of polypeptides (Bamford *et al.*, 1956). Purified amino acid NCA crystals are generally sensitive to moisture and are polymerized or decomposed by water. When butylamine is added to amino acid NCA crystals suspended in an inert solvent such as hexane or decane, polymerization takes place in the solid state. We have studied this solid-state polymerization and found that the tendency to polymerize is quite different in each amino acid NCA.

The crystal structures of amino acid NCAs were not studied for many years after the very early initial report by Leuchs (1906). We have reported the crystal structures of glycine NCA (Kanazawa *et al.*, 1976*a*) and L-alanine NCA (Kanazawa *et al.*, 1976*b*), and found that the ease of polymerization depended on the crystal structure (Kanazawa & Kawai, 1980). In addition, the crystal structures of γ-benzyl-L-glutamate NCA (Kanazawa *et al.*, 1978*a*), L-leucine NCA (Kanazawa *et al.*, 1978*b*), L-valine NCA (Kanazawa *et al.*, 1984), DL-valine NCA (Takenaka *et al.*, 1994), DL-phenylalanine NCA (Kanazawa *et al.*, 1997), L-phenylalanine NCA (Kanazawa, 2000) and β-benzyl-L-aspartate NCA (Kanazawa & Magoshi, 2003) have also been determined.

We found that L-leucine NCA was the most reactive towards polymerization in the solid state among the amino acid NCAs examined, and the solution polymerization reactivity of L-alanine NCA in acetonitrile seemed to be reater than that in the solid state (Kanazawa *et al.*, 1982; Kanazawa, 1992). However, we recently found that a partial polymerization initiated by moisture is not avoidable for highly purified amino acid NCA crystals under normal experimental conditions. Thus, a normal solution polymerization is affected by the partially polymerized amino acid NCAs dissolved in the solution, and the reactivity may be reported artificially high. In fact, many amino acid NCAs have been observed to be more reactive in the solid state than in the solution state, when the experiments are carried out under cool conditions to avoid moisture.

As the title compound (DL-leucine NCA), (I), is a racemate, it polymerizes slowly in solution. However, we found that the solid-state polymerization of compound (I) was much more facile than its solution polymerization; polymer conversion was 100% in the solid state but only 10% in acetonitrile solution at 313 K under the same conditions (Kanazawa & Hayakawa, 2000). Therefore, it is important to determine its crystal structure. Here, we present the crystal and molecular structure of (I).



(I)

The molecular structure of (I) and the atom-numbering scheme are shown in Fig. 1. In the crystal structure of (I), L- and D-enantiomers form dimeric pairs around a centre of symmetry. They are linked by N1—H1···O1^{i} hydrogen bonds [N1···O1^{i} 2.903 (2) Å, H1···O1^{i} 2.08 Å, and N1—H1···O1^{i} 173°; symmetry code: (i) $1-x$, $2-y$, $1-z$].

As seen in Fig. 2, the five-membered NCA rings in (I) are packed in a layer, with the isobutyl groups packed in another layer which alternates with the first. This sandwich structure is one of the important requirements for high reactivity in the solid state (Kanazawa, 1992, 1998), because the five-membered rings can react with each other within the layer. This structure seems to give a higher reactivity in the solid state than with the solution reaction. Although the hydrogen-bonded dimer structure is not formed in crystalline DL-phenylalanine NCA (Kanazawa *et al.*, 1997), the sandwich structure composed of D and L molecules is found and the crystal is also reactive in the solid state. Therefore, the DL dimer structure in the crystal of (I) is not considered to be an important requirement for high reactivity in the solid state.

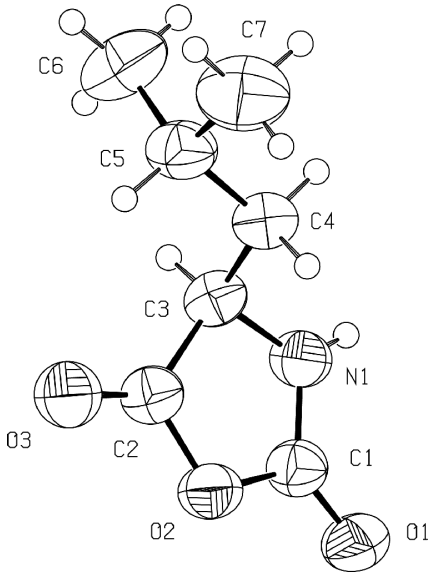


Figure 1
The molecular structure of (I), showing 50% probability displacement ellipsoids with the atom-numbering scheme.

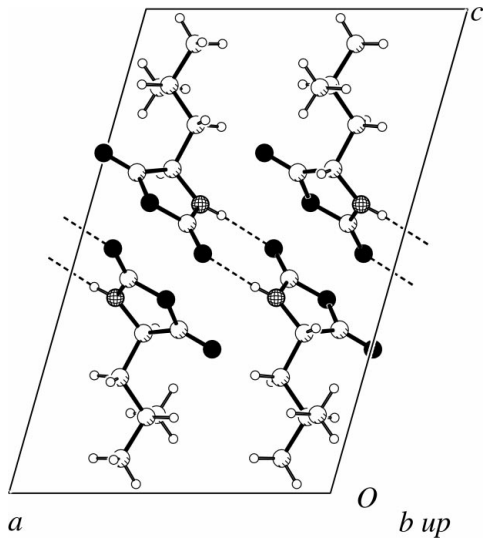


Figure 2
Packing diagram for (I) viewed along the *b* axis. Hydrogen bonds are shown by dashed lines.

Experimental

Compound (I) was obtained by the reaction of DL-leucine with trichloromethyl chloroformate or triphosgene in tetrahydrofuran, as reported previously for other NCAs (Kanazawa, 1992). The reaction product was recrystallized in a mixture of ethyl acetate and hexane (1:1 *v*/*v*), avoiding contamination by moisture.

Crystal data

$C_7H_{11}NO_3$
M_r = 157.17
Monoclinic, $P2_1/a$
a = 9.8780 (9) Å
b = 5.640 (2) Å
c = 15.448 (2) Å
β = 105.844 (3)°
V = 827.9 (3) Å^3
Z = 4
D_x = 1.261 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3 reflections
θ = 2.7–25.0°
μ = 0.10 mm^{-1}
T = 288 (2) K
Plate, colourless
0.55 × 0.40 × 0.15 mm

Data collection

Rigaku R-AXIS IV diffractometer
ω scans
Absorption correction: multi-scan (*ABSCOR*; Higashi, 1995)
T_{min} = 0.938, T_{max} = 0.99
3732 measured reflections
1347 independent reflections
1162 reflections with $I > 2\sigma(I)$
R_{int} = 0.048
θ_{max} = 25°
$h = -11 \rightarrow 11$
$k = -6 \rightarrow 6$
$l = -18 \rightarrow 17$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.048
$wR(F^2)$ = 0.159
S = 1.17
1347 reflections
112 parameters
Only H-atom U's refined
$w = 1/[\sigma^2(F_o^2) + (0.1091P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.099 (17)

Table 1
Selected geometric parameters (Å, °).

O1—C1	1.215 (2)	C2—C3	1.514 (2)
O2—C2	1.376 (2)	C3—C4	1.537 (2)
O2—C1	1.390 (2)	C4—C5	1.534 (2)
O3—C2	1.192 (2)	C5—C6	1.517 (4)
N1—C1	1.329 (2)	C5—C7	1.534 (3)
N1—C3	1.446 (2)		
C2—O2—C1	108.88 (13)	N1—C3—C2	100.09 (12)
C1—N1—C3	113.08 (14)	N1—C3—C4	112.08 (14)
O1—C1—N1	130.53 (18)	C2—C3—C4	112.20 (13)
O1—C1—O2	120.59 (16)	C5—C4—C3	115.96 (15)
N1—C1—O2	108.87 (14)	C6—C5—C4	111.97 (17)
O3—C2—O2	121.86 (16)	C6—C5—C7	111.11 (19)
O3—C2—C3	129.73 (16)	C4—C5—C7	108.54 (18)
O2—C2—C3	108.37 (14)		

As compound (I) crystallizes as thin plates and is very unstable, many crystallization and data-collection attempts were carried out. As the crystal degraded rapidly, only a limited number of oscillation exposures were taken, which covered 120° rotation of the crystal. Thus, the completeness of the reflections up to $2\theta_{max} = 50°$ is relatively low (92%). H atoms were located in a difference Fourier map and they were allowed to ride on the parent atoms, with N—H distances of 0.83 Å and C—H distances in the range 0.94–0.98 Å; their isotropic displacement parameters were refined freely.

Data collection: *PROCESS* (Rigaku, 1996); cell refinement: *PROCESS*; data reduction: *PROCESS*; program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003).

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