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Molecular aggregation in crystalline 1:1 complexes of hydrophobic D- and L-amino acids. I. The L-isoleucine series

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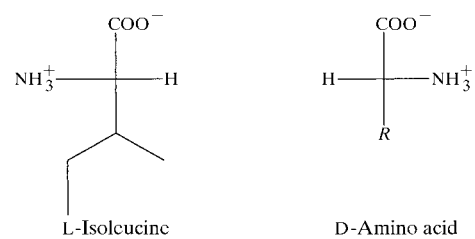
Abstract

The amino acid L-isoleucine has been cocrystallized with seven selected D-amino acids including D-methionine [L-isoleucine–D-methionine (1/1), $C_6H_{13}NO_2.C_5H_{11}NO_2S$, amino-acid side chain $R = -CH_2-CH_2-S-CH_3$] and a homologous series from D-alanine [L-isoleucine–D-alanine (1/1), $C_6H_{13}NO_2.C_3H_7NO_2$, $R = -CH_3$] through D-α-aminobutyric acid [L-isoleucine–D-α-aminobutyric acid (1/1), $C_6H_{13}NO_2.C_4H_9NO_2$, $R = -CH_2-CH_3$] and D-norvaline [L-isoleucine–D-norvaline (1/1), $C_6H_{13}NO_2.C_5H_{11}NO_2$, $R = -CH_2-CH_2-CH_3$] to D-norleucine [L-isoleucine–D-norleucine (1/1), $C_6H_{13}NO_2.C_6H_{13}NO_2$, $R = -CH_2-CH_2-CH_2-CH_3$] with linear side chains, and D-valine [L-isoleucine–D-valine (1/1), $C_6H_{13}NO_2.C_5H_{11}NO_2$, $R = -CH-(CH_3)_2$] and D-leucine [L-isoleucine–D-leucine (1/1), $C_6H_{13}NO_2.C_6H_{13}NO_2$, $R = -CH_2-CH-(CH_3)_2$] with branched side chains. All the crystal structures are divided into distinct hydrophilic and hydrophobic layers. In the five complexes with amino acids with linear side chains the polar parts of the D- and L-amino acids are related by pseudo-glide-plane symmetry, and four of them have remarkably similar molecular arrangements. The D-valine and D-leucine complexes, on the other hand, are structurally quite different with the polar parts of the D- and L-amino acids related by pseudo-inversion. Differences in the hydrogen-bond pattern in the two molecular arrangements are discussed.

1. Introduction

In a series of papers (Dalhus & Görbitz, 1996*a*, and references therein) we have focused on the crystal structures of amino acids with strictly hydrophobic side chains, which are all divided into separate hydrophilic and hydrophobic layers. The layered build-up of the crystals is a consequence of the dual character of these molecules; the charged α-amino and α-carboxylate groups are engaged in hydrogen bonds with each other, while the side chains are distinctly hydrophobic and are involved in van der Waals interactions only. The aims of this project are to acquire accurate geometric information about the hydrogen-bonding network in this class of compounds and to construct a database for multivariate analysis of correlations between hydrogen-bond parameters in identical hydrogen-bonded frameworks.

The layered crystals of hydrophobic amino acids fall within three categories: (i) enantiomeric crystals, (ii) racemic crystals and (iii) complexes of two different hydrophobic amino acids, one with absolute configuration *S* at C^α and one with the opposite chirality. No complex of two different hydrophobic amino acids with the same chirality at C^α has been described so far. In this paper we present the crystal structures of seven 1:1 complexes of category (iii), all with L-isoleucine (L-Ile) as the L enantiomer (Table 1). The structure of L-Ile complexed with D-*allo*-isoleucine (D-*allo*-Ile) will be presented in a forthcoming paper (Dalhus & Görbitz, 1999*a*). L-Phenylalanine:D-valine (Sridhar Prasad & Vijayan, 1991) is the only such complex described previously.



2. Experimental

2.1. *Crystallization*

Aqueous solutions of the complexes were prepared by dissolving equimolar amounts (typically 5–20 mg, depending on the solubility properties) of the two selected amino acids in 1–2 ml water. The various solutions were then mixed with tetramethoxysilane in the ratio 10:1 and each resulting mixture was distributed in 10–12 30 × 5 mm test tubes, sealed with Parafilm, and left for a few minutes to polymerize. The complexes crystallized when methanol, ethanol or 2-propanol diffused into the gel at room temperature.

For the complex L-Ile:D-Ala (L1) the crystals were generally of low quality. Only a few crystals extinguished and brightened satisfactorily when rotated in plane-

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Table 1. *Various* D-*amino acids co-crystallized with* L-*isoleucine*

Complex	D-Amino acid	Side-chain group
(B1)	D-Valine (D-Val)	$-CH-(CH_3)_2$
(B2)	D-Leucine (D-Leu)	$-CH_2-CH-(CH_3)_2$
(L1)	D-Alanine (D-Ala)	$-CH_3$
(L2)	D-α-Aminobutyric acid (D-Abu)	$-CH_2-CH_3$
(L3)	D-Norvaline (D-Nva)	$-CH_2-CH_2-CH_3$
(L4)	D-Norleucine (D-Nle)	$-CH_2-CH_2-CH_2-CH_3$
(L5)	D-Methionine (D-Met)	$-CH_2-CH_2-S-CH_3$

polarized light. The best crystals were obtained with methanol as the precipitating alcohol. There is a substantial improvement in crystal quality when D-Ala is replaced by the other amino acids (Table 1). The crystals of the complexes L-Ile:D-Abu (L2) and L-Ile:D-Nle (L4) were obtained using ethanol while those of L-Ile:D-Nva (L3), L-Ile:D-Met (L5), L-Ile:D-Val (B1) and L-Ile:D-Leu (B2) were crystallized using 2-propanol.

2.2. *Structure determination and refinement*

The data collections were carried out using a Siemens SMART CCD area-detector diffractometer and *SMART* and *SAINT* software (Siemens, 1995). They nominally covered over a hemisphere of reciprocal space, by a combination of 5–8 different sets of exposures. *SADABS* (Sheldrick, 1996) was used to correct for absorption. All structures were solved using direct methods followed by full-matrix least-squares refinement (*SHELXTL*; Sheldrick, 1994). Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4).† Further experimental conditions with information on the data reduction and refinement results for the seven complexes are summarized in Table 2.

All non-H atoms were refined anisotropically. Amino-H atoms were refined isotropically, while all the remaining H atoms were kept in idealized positions, refining a single C—H distance for all H atoms connected to the same C atom. A rotating-group refinement was utilized for methyl-H atoms using the *AFIX* card 138 of *SHELXTL*. Isotropic displacement parameters for the H atoms were fixed at $1.5 \times U_{eq}$ (for $-CH_3$) and $1.2 \times U_{eq}$ (for $-CH_2-$ and $-CH-$) of the bonded C atom.

3. Results and discussion

Hydrogen-bond geometries are listed in Table 3. Figs. 1(*a*)–(*g*) illustrate the molecular-packing arrangement in the seven structures and include the atomic numbering. The L-Ile and D-amino-acid molecules are labelled *A* and *B*, respectively, except in the L-Ile:D-Nle crystal where the two L-Ile molecules are labelled *A* and *B* while *C* and *D* designate the two D-Nle molecules.

3.1. *Crystal structures*

In the complexes containing D-amino acids with branched side chains, (B1) and (B2), the L- and D-amino acids crystallize in separate molecular layers, Figs. 1(*a*) and (*b*). In each crystal, the polar moieties and substantial parts of the side chains in the L- and D-molecules are related by pseudo-inversion symmetry. In fact, in (B1) the symmetry is closely obeyed for all atoms but C6*A*. (B1) crystallizes in a monoclinic space group while (B2) is triclinic. However, the molecular-packing arrangement in the monoclinic (B1) crystal can be generated by transforming the ~13.7 Å *c* axis in (B2) into a twofold screw axis corresponding to the ~24.0 Å *b* axis in (B1) (Figs. 1*a* and *b*). Interestingly, an equivalent relationship is found between the triclinic (Dalhus & Görbitz, 1996*b*) and monoclinic (Mallikarjunan & Thyagaraja Rao, 1969) polymorphs of the racemate DL-valine.

The molecular arrangements in the complexes (L1)–(L5) are fundamentally different from (B1) and (B2). The hydrophilic parts of the molecules (and portions of the side chains) of neighbouring L- and D-amino acids along the ~10 Å axes are related by a pseudo glide plane normal to the *b* axis, Figs. 1(*c*)–(*g*). Both amino acids in the complexes are thus present within a single molecular chain along the ~10 Å axis. The pseudocentrosymmetric natures of all seven crystals are also evident in the statistical analysis of *E* values, with mean $|E^2 - 1|$ in the range 0.802–0.896. The theoretical values are 0.968 and 0.736 for centrosymmetric and non-centrosymmetric crystals, respectively.

In the series (L1), (L2), (L3) and (L5) the molecular arrangements are remarkably similar. Substitution of D-Ala in (L1) by D-Abu in (L2) is accompanied by the inclusion of an additional twofold axis in the hydrophobic layer (corresponding to a change from a primitive to a *C*-centred lattice) followed by an ~1° increase in the β angle (Table 2). Further extensions of the D-amino-acid side chain in (L3) and (L5) occur with only small modifications in the hydrophobic layers, moderate increases of the β angles [94.546 (1) (L2) → 101.358 (1) (L3) → 105.914 (1)° (L5)] and small increases of the *a* axes [26.9873 (6) (L2) → 29.0557 (7) (L3) → 31.7681 (3) Å (L5)] (Table 2). Furthermore, the molecular conformation of equivalent parts of the D-amino-acid side chains remains unchanged in the series (L1) → (L2) → (L3) → (L5), Fig. 2.

Intuitively, (L4) with a normal *n*-alkyl side chain would appear to be a more natural addition to the homologous series (L1), (L2) and (L3) than (L5), discussed above. Rather unexpectedly, (L4) has a

† Supplementary data for this paper are available from the IUCr electronic archives (Reference: OS0011). Services for accessing these data are described at the back of the journal.

somewhat different structural build-up. The hydrophobic layer is formed by the amino-acid side chains from two crystallographically independent molecular layers (one with molecules *A* and *C*, the other with *B* and *D*), and the crystal accommodates two independent hydrophilic layers, Fig. 1(*f*). The molecular conforma-

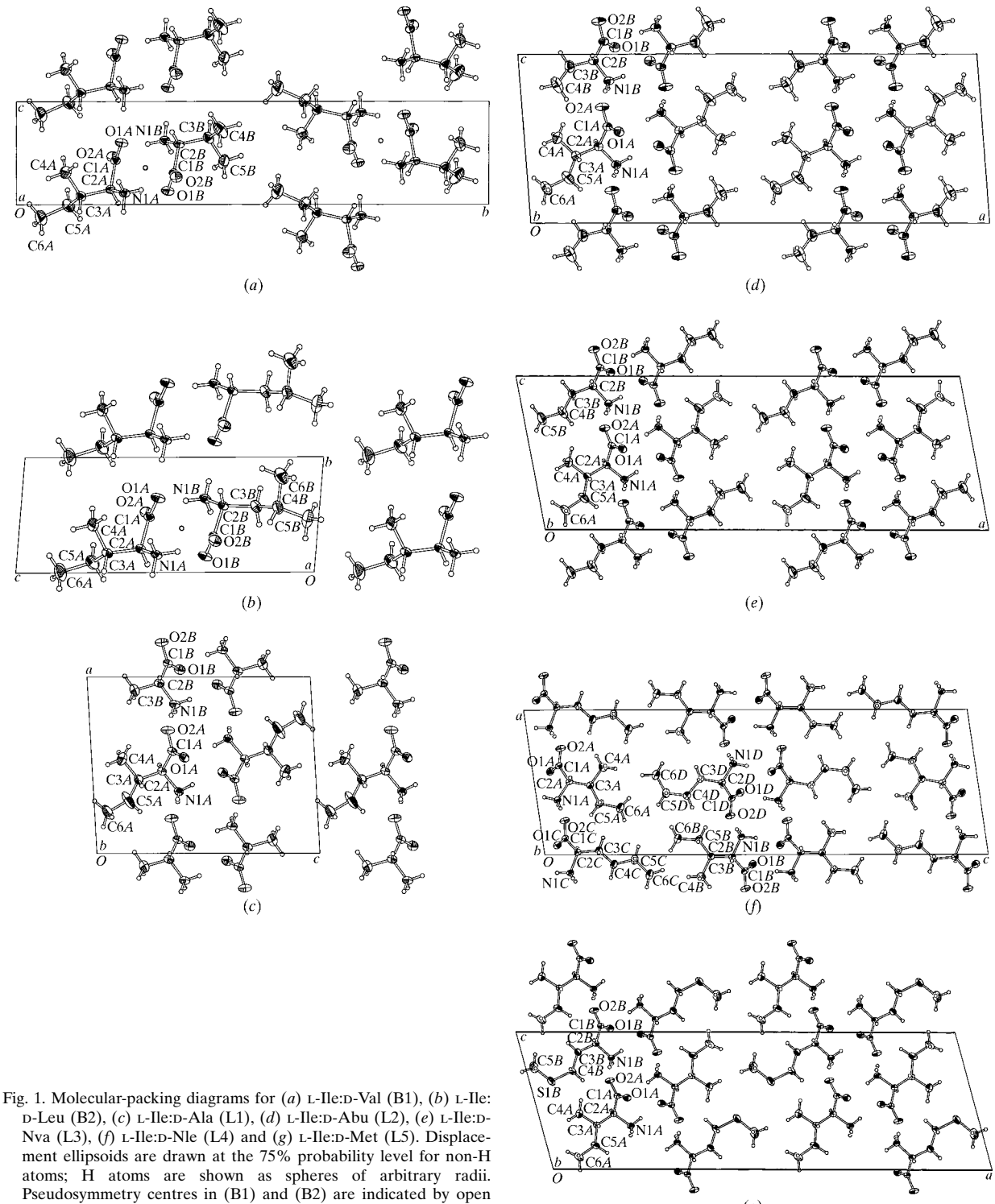

Fig. 1. Molecular-packing diagrams for (*a*) L-Ile:D-Val (B1), (*b*) L-Ile:D-Leu (B2), (*c*) L-Ile:D-Ala (L1), (*d*) L-Ile:D-Abu (L2), (*e*) L-Ile:D-Nva (L3), (*f*) L-Ile:D-Nle (L4) and (*g*) L-Ile:D-Met (L5). Displacement ellipsoids are drawn at the 75% probability level for non-H atoms; H atoms are shown as spheres of arbitrary radii. Pseudosymmetry centres in (B1) and (B2) are indicated by open circles.

Table 2. *Experimental details*

	(L1)	(L2)	(L3)	(L4)
Crystal data				
Chemical formula	$C_6H_{13}NO_2{\cdot}C_3H_7NO_2$	$C_6H_{13}NO_2{\cdot}C_4H_9NO_2$	$C_6H_{13}NO_2{\cdot}$-$C_5H_{11}NO_2$	$C_6H_{13}NO_2{\cdot}$-$C_6H_{13}NO_2$
Chemical formula weight	220.27	234.3	248.32	262.35
Crystal class	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1$	$C2$	$C2$	$P2_1$
a (Å)	9.8944 (2)	26.9873 (6)	29.0557 (7)	10.012 (2)
b (Å)	4.7425 (1)	4.7471 (1)	4.7551 (1)	4.7227 (9)
c (Å)	12.9045 (2)	9.9652 (2)	9.9398 (2)	30.335 (6)
β (°)	93.374 (1)	94.546 (1)	101.358 (1)	98.38 (3)
V (Å^3)	604.48 (2)	1272.64 (5)	1346.41 (5)	1419.1 (5)
Z	2	4	4	4
D_x (Mg m^{-3})	1.210	1.223	1.225	1.228
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073
No. of reflections for cell parameters	6890	8192	8192	8192
μ (mm^{-1})	0.094	0.094	0.092	0.091
Temperature (K)	150 (2)	170 (2)	150 (2)	150 (2)
Crystal form	Plate	Plate	Plate	Plate
Crystal size (mm)	1.05 × 0.25 × 0.05	0.90 × 0.40 × 0.10	0.65 × 0.60 × 0.20	0.55 × 0.30 × 0.15
Crystal colour	Colourless	Colourless	Colourless	Colourless
Data collection				
Data collection method	ω scans	ω scans	ω scans	ω scans
Scan width (°)	0.6	0.6	0.6	0.3
No. of sets of exposures	8	5	5	5
Exposure time per frame (s)	45	30	30	30
Crystal-to-detector distance (cm)	4.99	4.98	5.00	4.99
Absorption correction	Multi-scan	Multi-scan	Multi-scan	Multi-scan
T_{min}	0.906	0.919	0.942	0.951
T_{max}	0.995	0.991	0.982	0.986
No. of measured reflections	15 033	10 909	12 203	25 110
No. of independent reflections	8985	6238	6859	14 651
No. of observed reflections	6393	5817	6684	12 393
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.0618	0.0186	0.0165	0.0250
θ_{max} (°)	49.87	39.06	40.44	40.41
Range of h, k, l	$-21 \rightarrow h \rightarrow 21$ $-9 \rightarrow k \rightarrow 9$ $-20 \rightarrow l \rightarrow 26$	$-47 \rightarrow h \rightarrow 46$ $-8 \rightarrow k \rightarrow 8$ $-17 \rightarrow l \rightarrow 16$	$-52 \rightarrow h \rightarrow 49$ $-8 \rightarrow k \rightarrow 7$ $-17 \rightarrow l \rightarrow 17$	$-18 \rightarrow h \rightarrow 13$ $-8 \rightarrow k \rightarrow 8$ $-54 \rightarrow l \rightarrow 49$
Refinement				
Refinement on	F^2	F^2	F^2	F^2
$R[F^2>2\sigma(F^2)]$	0.0612	0.0385	0.0349	0.0482
$wR(F^2)$	0.1548	0.0995	0.0946	0.1109
S	1.084	1.073	1.079	1.143
No. of reflections used in refinement	8985	6238	6859	14 651
No. of parameters used	164	177	190	399
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0870P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0467P)^2 + 0.3251P]$ where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0480P)^2 + 0.3570P]$ where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0427P)^2 + 0.2719P]$ where $P = (F_o^2 + 2F_c^2)/3$

Table 2 (*cont.*)

	(L1)	(L2)	(L3)	(L4)
$(\Delta/\sigma)_{max}$	0.002	0.002	0.001	0.008
$\Delta\rho_{max}$ (e Å^{-3})	0.600	0.378	0.587	0.512
$\Delta\rho_{min}$ (e Å^{-3})	−0.466	−0.246	−0.422	−0.262
Extinction method	None	*SHELXTL* (Sheldrick, 1994)	None	None
Extinction coefficient	—	0.0139 (18)	—	—

	(L5)	(B1)	(B2)
Crystal data			
Chemical formula	$C_6H_{13}NO_2$.-$C_5H_{11}NO_2S$	$C_6H_{13}NO_2$.-$C_5H_{11}NO_2$	$C_6H_{13}NO_2$.-$C_6H_{13}NO_2$
Chemical formula weight	280.38	248.32	262.35
Crystal class	Monoclinic	Monoclinic	Triclinic
Space group	*C*2	$P2_1$	*P*1
a (Å)	31.7681 (3)	5.2528 (1)	5.1933 (3)
b (Å)	4.7170 (1)	23.9809 (6)	5.4064 (3)
c (Å)	10.0043 (1)	5.4200 (1)	13.6968 (7)
α (°)	90	90	91.516 (2)
β (°)	105.914 (1)	110.420 (1)	98.603 (2)
γ (°)	90	90	110.376 (2)
V (Å^3)	1441.69 (4)	639.84 (2)	355.16 (3)
Z	4	2	1
D_x (Mg m^{-3})	1.292	1.289	1.227
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
Wavelength (Å)	0.71073	0.71073	0.71073
No. of reflections for cell parameters	8192	6101	1220
μ (mm^{-1})	0.234	0.097	0.091
Temperature (K)	150 (2)	150 (2)	150 (2)
Crystal form	Plate	Plate	Block
Crystal size (mm)	0.70 × 0.25 × 0.10	0.65 × 0.60 × 0.10	0.20 × 0.10 × 0.10
Crystal colour	Colourless	Colourless	Colourless
Data collection			
Data collection method	ω scans	ω scans	ω scans
Scan width (°)	0.6	0.6	1.2
No. of sets of exposures	8	5	5
Exposure time per frame (s)	45	20	120
Crystal-to-detector distance (cm)	4.99	4.98	4.99
Absorption correction	Multi-scan	Multi-scan	Multi-scan
T_{min}	0.849	0.939	0.982
T_{max}	0.977	0.990	0.990
No. of measured reflections	18 678	10 296	5657
No. of independent reflections	10 115	6854	4689
No. of observed reflections	8127	6220	4082
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.0343	0.0213	0.0318
θ_{max} (°)	49.7	40.26	40.58
Range of *h*, *k*, *l*	$-60 \rightarrow h \rightarrow 65$ $-9 \rightarrow k \rightarrow 7$ $-20 \rightarrow l \rightarrow 21$	$-9 \rightarrow h \rightarrow 9$ $-43 \rightarrow k \rightarrow 43$ $-9 \rightarrow l \rightarrow 9$	$-7 \rightarrow h \rightarrow 9$ $-9 \rightarrow k \rightarrow 8$ $-23 \rightarrow l \rightarrow 24$

Table 2 (*cont.*)

	(L5)	(B1)	(B2)
Refinement			
Refinement on	F^2	F^2	F^2
$R[F^2>2\sigma(F^2)]$	0.0419	0.0458	0.0526
$wR(F^2)$	0.0931	0.1066	0.1181
S	1.088	1.145	1.059
No. of reflections used in refinement	10 115	6854	4689
No. of parameters used	199	191	201
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0408P)^2 + 0.0836P]$ where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0390P)^2 + 0.1323P]$ where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0348P)^2 + 0.0860P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	0.002	−0.001	−0.006
$\Delta\rho_{max}$ (e Å^{-3})	0.393	0.373	0.591
$\Delta\rho_{min}$ (e Å^{-3})	−0.407	−0.252	−0.395
Extinction method	None	None	None

tions of D-Met in (L5) and the two D-Nle molecules in (L4) are different, Fig. 2.

The close relationship between the (L1)–(L5) structures is also evident in the covalent bonds in the amino acids. Generally, corresponding bond lengths in the hydrophilic part of both L- and D-amino-acid molecules agree within 0.004 Å between the five structures.†

The side-chain conformation of L-Ile (fully described by the three torsions $\chi^{1,1}$ = N1—C2—C3—C5, $\chi^{1,2}$ = N1—C2—C3—C4 and χ^2 = C2—C3—C5—C6) in the five complexes (L1)–(L5) is identical: $\chi^{1,1}$ = *gauche*$^-$, $\chi^{1,2}$ = *trans* and χ^2 = *trans*. In the three complexes (B1), (B2) and L-Ile:D-*allo*-Ile (Dalhus & Görbitz, 1999*a*) as well as the racemate DL-Ile (Dalhus & Görbitz, 1999*a*) the L-Ile side chain is rotated so that $\chi^{1,1}$ = *trans* and $\chi^{1,2}$ = *gauche*$^+$, again with χ^2 = *trans*.

3.2. *Hydrogen bonding*

A survey of all crystal structures of amino acids with hydrophobic side chains has identified three major classes of molecular-packing arrangements, each with a unique hydrogen-bond pattern (Dalhus & Görbitz, 1999*b*). The molecular aggregation in the present (L1)–(L5) and (B1)–(B2) complexes fall within class I and II, respectively, while class III includes the structures of enantiomeric amino acids.

In (L1)–(L5) (class I) two of the three amino-H atoms in each independent molecule (H1 and H2 in both the L-Ile and D-amino acid) form chains of hydrogen-bonded pseudo-glide-plane-related L- and D-amino acids, Fig. 3(*a*). Using the graph-set notation introduced by Etter (1990) with the modifications of Bernstein *et al.* (1995), the first-level graph set for atoms H1*A*, H2*A*, H1*B* and H2*B* is *D*, *i.e.* the donor and acceptor are from two independent molecules forming a dimer. In addition, H-atom pairs H1*A*/H2*A* and H1*B*/H2*B* each form a $C_2^1(4)$ chain along the unique *b* axis. Likewise, along the ∼10 Å axis (the *c* axis in Fig. 3*a*), two $C_2^2(10)$ chains are formed by H1*A*/H1*B* and H2*A*/H2*B*, respectively. Both these patterns are second-level graph sets, *i.e.* involving two types of hydrogen bond. Atoms H3*A* and H3*B* form hydrogen bonds across the hydrophilic layer linking symmetry-equivalent molecules with a first-level $C(5)$ chain along **b**. The two crystallographically independent

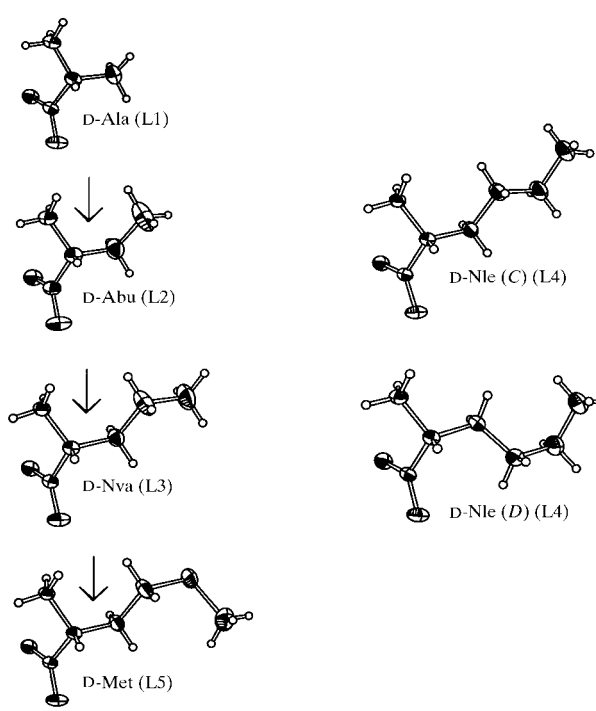

Fig. 2. The molecular conformations for the D-amino acids in complexes (L1)–(L5).

† See deposition footnote on p. 425

Table 3. *Hydrogen-bonding geometry (Å, °)*

N—H···O	*d*(N—H)	*d*(H···O)†	*d*(H···O)‡	*d*(N···O)	*α*(N—H···O)†
L-Ile:D-Ala (L1)					
N1*A*—H1*A*···O2*B*^{i}	0.94 (2)	1.92 (2)	1.832	2.856 (1)	172 (2)
N1*A*—H2*A*···O2*B*^{ii}	0.81 (2)	2.04 (2)	1.829	2.824 (1)	163 (2)
N1*A*—H3*A*···O1*A*^{iii}	0.87 (2)	1.93 (2)	1.772	2.797 (1)	173 (2)
N1*B*—H1*B*···O2*A*	0.87 (2)	1.97 (2)	1.817	2.824 (1)	166 (2)
N1*B*—H2*B*···O2*A*^{iv}	0.94 (2)	1.89 (2)	1.799	2.796 (1)	163 (2)
N1*B*—H3*B*···O1*B*^{v}	0.90 (2)	1.88 (2)	1.748	2.755 (1)	166 (2)
L-Ile:D-Abu (L2)					
N1*A*—H1*A*···O2*B*^{vi}	0.83 (2)	2.02 (2)	1.816	2.838 (1)	172 (1)
N1*A*—H2*A*···O2*B*^{vii}	0.96 (2)	1.88 (2)	1.804	2.812 (1)	166 (2)
N1*A*—H3*A*···O1*A*^{viii}	0.91 (2)	1.88 (2)	1.760	2.788 (1)	176 (1)
N1*B*—H1*B*···O2*A*^{iv}	0.99 (2)	1.88 (2)	1.837	2.854 (1)	169 (1)
N1*B*—H2*B*···O2*A*	0.89 (2)	1.97 (2)	1.840	2.838 (1)	163 (1)
N1*B*—H3*B*···O1*B*^{ix}	0.90 (1)	1.87 (1)	1.737	2.751 (1)	168 (1)
L-Ile:D-Nva (L3)					
N1*A*—H1*A*···O2*B*^{vi}	0.85 (2)	2.00 (2)	1.815	2.838 (1)	172 (1)
N1*A*—H2*A*···O2*B*^{vii}	0.88 (2)	1.95 (2)	1.805	2.805 (1)	164 (1)
N1*A*—H3*A*···O1*A*^{viii}	0.94 (1)	1.85 (1)	1.759	2.788 (1)	178 (1)
N1*B*—H1*B*···O2*A*^{iv}	0.95 (2)	1.92 (2)	1.847	2.854 (1)	165 (1)
N1*B*—H2*B*···O2*A*	0.94 (2)	1.92 (2)	1.837	2.846 (1)	167 (1)
N1*B*—H3*B*···O1*B*^{ix}	0.89 (1)	1.88 (1)	1.744	2.757 (1)	168 (1)
L-Ile:D-Nle (L4)					
N1*A*—H1*A*···O2*C*	0.83 (2)	2.01 (2)	1.811	2.827 (1)	169 (2)
N1*A*—H2*A*···O2*C*^{iv}	0.90 (2)	1.90 (2)	1.780	2.780 (1)	164 (2)
N1*A*—H3*A*···O1*A*^{x}	0.94 (2)	1.84 (2)	1.753	2.780 (1)	176 (2)
N1*B*—H1*B*···O2*D*	0.84 (2)	2.06 (2)	1.876	2.885 (1)	167 (2)
N1*B*—H2*B*···O2*D*^{iv}	0.90 (2)	1.97 (2)	1.834	2.852 (1)	170 (2)
N1*B*—H3*B*···O1*B*^{xi}	1.02 (2)	1.78 (2)	1.765	2.781 (1)	168 (2)
N1*C*—H1*C*···O2*A*^{i}	0.88 (2)	1.99 (2)	1.833	2.853 (1)	170 (2)
N1*C*—H2*C*···O2*A*^{ii}	0.93 (2)	1.96 (2)	1.862	2.855 (1)	162 (2)
N1*C*—H3*C*···O1*C*^{xii}	0.92 (2)	1.87 (2)	1.760	2.751 (1)	161 (1)
N1*D*—H1*D*···O2*B*^{xiii}	0.91 (2)	1.94 (2)	1.816	2.828 (1)	167 (2)
N1*D*—H2*D*···O2*B*^{xiv}	0.92 (2)	1.90 (2)	1.802	2.783 (1)	159 (2)
N1*D*—H3*D*···O1*D*^{iii}	0.95 (2)	1.81 (2)	1.729	2.750 (1)	171 (2)
L-Ile:D-Met (L5)					
N1*A*—H1*A*···O2*B*^{vi}	0.91 (2)	1.94 (2)	1.818	2.835 (1)	169 (2)
N1*A*—H2*A*···O2*B*^{vii}	0.94 (2)	1.88 (2)	1.796	2.790 (1)	162 (1)
N1*A*—H3*A*···O1*A*^{viii}	0.89 (2)	1.91 (2)	1.767	2.790 (1)	172 (2)
N1*B*—H1*B*···O2*A*^{iv}	0.91 (2)	1.96 (2)	1.843	2.852 (1)	166 (1)
N1*B*—H2*B*···O2*A*	0.90 (2)	1.97 (2)	1.848	2.830 (1)	159 (2)
N1*B*—H3*B*···O1*B*^{ix}	0.89 (2)	1.87 (2)	1.725	2.748 (1)	172 (2)
L-Ile:D-Val (B1)					
N1*A*—H1*A*···O2*A*^{xiii}	0.89 (2)	2.02 (2)	1.874	2.890 (1)	169 (2)
N1*A*—H2*A*···O1*A*^{vii}	0.96 (2)	1.80 (2)	1.729	2.757 (1)	176 (2)
N1*A*—H3*A*···O2*B*	0.87 (2)	2.12 (2)	1.970	2.949 (1)	159 (2)
N1*B*—H1*B*···O2*B*^{i}	0.91 (2)	2.00 (2)	1.878	2.890 (1)	167 (2)
N1*B*—H2*B*···O1*B*^{xv}	0.89 (2)	1.86 (2)	1.724	2.753 (1)	177 (2)
N1*B*—H3*B*···O2*A*	0.89 (2)	2.12 (2)	1.987	2.967 (1)	159 (2)
L-Ile:D-Leu (B2)					
N1*A*—H1*A*···O2*A*^{xiii}	0.93 (3)	1.95 (3)	1.850	2.864 (2)	168 (3)
N1*A*—H2*A*···O1*A*^{xvi}	0.96 (4)	1.79 (4)	1.719	2.745 (2)	174 (3)
N1*A*—H3*A*···O2*B*	0.97 (4)	2.03 (4)	1.970	2.929 (2)	154 (4)
N1*B*—H1*B*···O2*B*^{i}	0.95 (3)	1.94 (3)	1.859	2.882 (2)	172 (3)
N1*B*—H2*B*···O1*B*^{iv}	0.81 (3)	1.93 (3)	1.709	2.732 (2)	172 (3)
N1*B*—H3*B*···O2*A*	0.92 (3)	2.02 (3)	1.910	2.923 (2)	168 (3)

Symmetry codes: (i) $x-1, y, z$; (ii) $x-1, y-1, z$; (iii) $-x+1, y-\frac{1}{2}, -z+1$; (iv) $x, y+1, z$; (v) $-x+2, y+\frac{1}{2}, -z+1$; (vi) $x, y-1, z-1$; (vii) $x, y, z-1$; (viii) $-x+\frac{1}{2}, y+\frac{1}{2}, -z+1$; (ix) $-x+\frac{1}{2}, y-\frac{1}{2}, -z+2$; (x) $-x+1, y+\frac{1}{2}, -z$; (xi) $-x, y+\frac{1}{2}, -z+1$; (xii) $-x, y-\frac{1}{2}, -z$; (xiii) $x+1, y, z$; (xiv) $x+1, y-1, z$; (xv) $x, y, z+1$; (xvi) $x, y-1, z$. † Experimental N—H distance. ‡ N—H distance normalized to 1.03 Å (Taylor & Kennard, 1983).

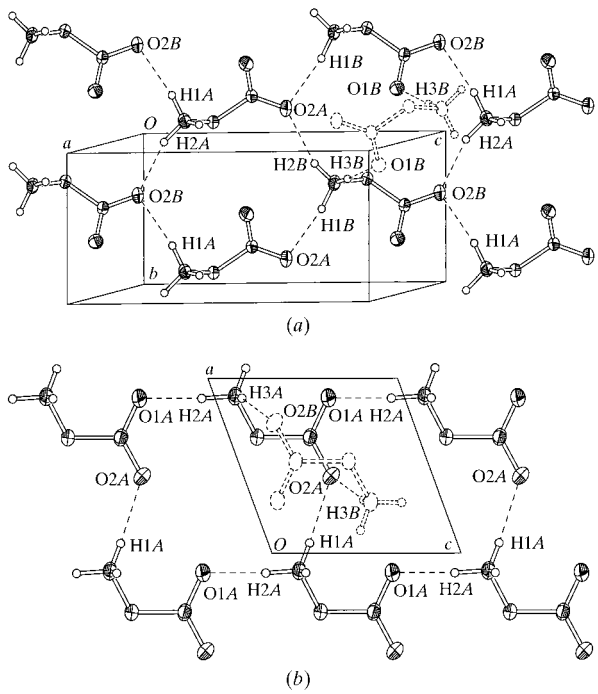

Fig. 3. Hydrogen bonding in (*a*) L-Ile:D-Met (L5) and (*b*) L-Ile:D-Val (B1) illustrating the hydrogen-bond patterns in the (L1)–(L5) and (B1)–(B2) complexes, respectively. Side-chain atoms and H(C^{α}) have been omitted for clarity. Molecules drawn with open ellipsoids and dashed bonds are located in the molecular layer just above the remaining molecules. In (*b*) only an L-Ile layer is shown.

$R_4^3(14)$ rings (Fig. 3*a*) comprise four different hydrogen bonds.

In (B1) and (B2) (class II), on the other hand, H1*A* and H2*A* (as well as H1*B* and H2*B* in the other molecular layer) each form first-level $C(5)$ chains along **a** and **c**. A second-level $R_4^4(16)$ ring also characterizes this class of structures, Fig. 3(*b*). In contrast to the first-level $C(5)$ chains in class I complexes, H3*A* and H3*B* in (B1) and (B2) form hydrogen-bonded dimers of pseudo-inversion-related L- and D-amino acids, giving a second-level $R_2^2(10)$ pattern (Fig. 3*b*).

Experimental and normalized (Taylor & Kennard, 1983) hydrogen-bond geometries for the seven L- and D-amino-acid complexes are listed in Table 3.

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