C8—C14—C15 to supply the recognition signal to the glucocorticoid receptor for binding. The testing of compounds (I) and (II) in binding to the glucocorticoid receptor in conjunction with the three-dimensional structure of triamcinolone acetate should resolve this question of the importance of the free access of portions of the α and β faces for glucocorticoid activity.

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X-ray Studies on Crystalline Complexes Involving Amino Acids and Peptides. XXI. Structure of a (1:1) Complex Between L-Phenylalanine and D-Valine

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Abstract. $C_5H_{11}NO_2.C_9H_{11}NO_2$, $M_r = 282{\cdot}3$, $P1$, $a = 5{\cdot}245\ (1)$, $b = 5{\cdot}424\ (1)$, $c = 14{\cdot}414\ (2)$ Å, $\alpha = 97{\cdot}86\ (1)$, $\beta = 93{\cdot}69\ (2)$, $\gamma = 70{\cdot}48\ (2)°$, $V = 356$ Å^3, $Z = 1$, $D_m = 1{\cdot}32\ (2)$, $D_x = 1{\cdot}32$ g cm^{-3}, λ(Mo $K\alpha$) $= 0{\cdot}7107$ Å, $\mu = 5{\cdot}9$ cm^{-1}, $F(000) = 158$, $T = 298$ K, $R = 0{\cdot}035$ for 1518 observed reflections with $I > 2\sigma(I)$. The molecules aggregate in double layers, one layer made up of L-phenylalanine molecules and the other of D-valine molecules. Each double layer is stabilized by interactions involving main-chain atoms of both types of molecules. The interactions include hydrogen bonds which give rise to two head-to-tail sequences. The arrangement of molecules in the complex is almost the same as that in the structure of

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DL-valine (and DL-leucine and DL-isoleucine) except for the change in the side chain of L molecules. The molecules in crystals containing an equal number of L and D hydrophobic amino-acid molecules thus appear to aggregate in a similar fashion, irrespective of the precise details of the side chain.

Introduction. We have been pursuing a programme of X-ray studies on crystalline complexes involving amino acids and peptides in order to elucidate the non-covalent interactions important in the structure and action of proteins (Vijayan, 1983, 1988). The results of these studies have been found to be of considerable relevance to chemical evolution as well (Vijayan, 1980; Suresh & Vijayan, 1985). Recently, the studies on complexes have been extended to include those involving amino acids of mixed chirality to explore the effect of chirality on amino-acid aggregation (Soman & Vijayan, 1988, 1989; Soman, Rao, Radhakrishnan & Vijayan, 1989; Soman, Suresh & Vijayan, 1988; Soman, Vijayan, Ramakrishnan & Guru Row, 1990; Suresh, Ramaswamy & Vijayan, 1986). In the course of the preparation of such complexes, it was found that histidine and aspartic acid of the same chirality form a complex whereas those of opposite chirality do not (Bhat & Vijayan, 1978; Suresh & Vijayan, 1985, 1987). This appeared to point to the possibility, in favourable situations, of chiral separation without the aid of external agencies even in a system containing equal numbers of D and L amino-acid molecules. However, chiral discrimination of the opposite type was indicated by Shiraiwa, Ikawa, Sakaguchi & Kurokawa (1984), who showed that L-phenylalanine preferentially forms complexes with D isomers of amino acids which have aliphatic side chains. The crystal structure of one such complex, namely, that between L-phenylalanine and D-valine, is reported here. It may also be mentioned that this is the first crystalline complex between two neutral amino acids to be analysed by X-rays so far.

Experimental. The crystals were grown by the method described by Shiraiwa, Ikawa, Sakaguchi & Kurokawa (1984). Unit-cell parameters were refined on a CAD-4 computer-controlled diffractometer using Mo $K\alpha$ radiation employing 25 reflections in the range of 6–19°. The density was measured by the flotation method using benzene and carbon tetrachloride. Data were collected to a maximum Bragg angle of 28° using ω–2θ scan and corrected for Lorentz and polarization factors but not for absorption. Additional crystal and experimental data are listed in Table 1.

The structure was solved using direct methods with *MULTAN* (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980) and refined using *SHELX* (Sheldrick, 1976) to $R = 0.035$, $wR = 0.042$ and $S = 0.958$ for 1518 observed reflections with $I > 2\sigma(I)$. The weighting function used was $1.0/[\sigma^2(F_o) + 0.002123(F_o)^2]$. Non-H atoms were refined anisotropically and H atoms isotropically using form factors given in *SHELX*. The chirality was assigned from the known chirality of the component molecules; the coordinates of N(1) were fixed to determine the origin. The coordinates and the equivalent isotropic thermal parameters (Hamilton, 1959) of the non-H atoms are listed in Table 2.*

Table 1. *Crystal and experimental data*

Crystal size (mm)	0·4 × 0·4 × 0·3
Ranges of h, k, l	0–6, −7–7, −17–17
ΔI for standard reflections	0·017
Total number of reflections measured	1923
Number of unique reflections [$I > 2\sigma(I)$]	1518
R_{int}	0·012
$(\Delta/\sigma)_{max}$	0·041
$\Delta\rho_{max}$ (e Å^{-3})	0·22
$\Delta\rho_{min}$ (e Å^{-3})	−0·19

Table 2. *Positional parameters* ($\times 10^4$) *and equivalent isotropic temperature factors of non*-H *atoms, with e.s.d.'s in parentheses*

	x	y	z	B (Å^2)
N(1)	1646	2048	9041	2·0 (1)
O(1)	1632 (6)	6963 (5)	8810 (2)	2·9 (1)
O(2)	6086 (6)	5457 (6)	8578 (2)	2·6 (1)
C(1)	3805 (6)	5179 (6)	8608 (2)	1·8 (1)
C(2)	3669 (7)	2363 (6)	8374 (2)	1·8 (1)
C(3)	2718 (8)	1777 (7)	7294 (3)	2·8 (1)
C(4)	4481 (7)	1959 (7)	6484 (2)	2·7 (1)
C(5)	3686 (12)	4077 (9)	5954 (4)	5·9 (1)
C(6)	5222 (13)	4261 (10)	5169 (4)	6·5 (1)
C(7)	7561 (9)	2287 (9)	4917 (3)	4·4 (1)
C(8)	8409 (9)	187 (11)	5442 (3)	5·4 (1)
C(9)	6868 (9)	5 (10)	6224 (3)	4·5 (1)
N(11)	7782 (5)	7705 (4)	522 (2)	2·0 (1)
O(11)	7623 (6)	2859 (5)	632 (2)	2·5 (1)
O(12)	3208 (6)	4326 (5)	964 (2)	2·4 (1)
C(11)	5441 (6)	4644 (6)	872 (2)	1·7 (1)
C(12)	5523 (7)	7488 (6)	1082 (2)	1·9 (1)
C(13)	5820 (7)	8373 (6)	2213 (2)	2·3 (1)
C(14)	3085 (10)	9402 (10)	2712 (4)	4·7 (1)
C(15)	7795 (9)	6191 (8)	2758 (3)	3·5 (1)

Discussion. *Molecular dimensions.* The bond distances and angles in the structure are normal except for the lengths of four symmetrically disposed bonds in the six-membered ring in the phenylalanine side chain and the two terminal bonds in the valine side chain. The apparent shortening of these six bonds could be readily explained as having resulted from the libration of the concerned groups. The torsion angles that define the conformation of the molecules

* Lists of structure factors, anisotropic thermal parameters, bond lengths and angles, and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54303 (13 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

(IUPAC–IUB Commission on Biochemical Nomenclature, 1970) are as follows:

L-Phe: $\psi^1 = -37{\cdot}1$ (4); $\chi^1 = -177{\cdot}4$ (5); $\chi^{21} = 77{\cdot}8$ (5)°;

D-Val: $\psi^1 = 25{\cdot}8$ (4); $\chi^{21} = 153{\cdot}3$ (3); $\chi^{22} = -82{\cdot}3$ (4)°.

The side chain of the phenylalanine molecule is *trans* to the α-amino group and, as expected (Bhat, Sasisekaran & Vijayan, 1979), the phenyl ring is nearly perpendicular to the plane defined by C^α, C^β and C^γ. A valine molecule can assume three different conformations (Torii & Iitaka, 1970). In two of them, a bulky methyl group is staggered between the α-amino and the α-carboxylate groups whereas an H atom is staggered between them in the third. The first two conformations may be expected to be sterically less favourable than the third. However, surprisingly, one or the other of these less favourable conformations is observed in a majority of the molecules in the structures of DL-valine (Mallikarjunan & Rao, 1969), L-valine (Torii & Iitaka, 1970) and the hydrohalides of L-valine (Lakshminarayan, Sasisekaran & Ramachandran, 1967). The same is true of the D-valine molecule in the present structure.

Hydrogen bonding and crystal structure. The crystal structure of the complex is illustrated in Fig. 1. The hydrogen bonds that stabilize the structure are listed in Table 3. The structure is made up of molecular double layers parallel to the *ab* plane. One layer in each double-layer consists of L-phenylalanine molecules and the other of D-valine molecules. In each layer, the molecules are held together by two sets of N—H···O hydrogen bonds, one set giving rise to head-to-tail sequences of type *S*1 and the other to those of type *S*2 (Suresh & Vijayan, 1983). The two layers are interconnected by two crystallographically

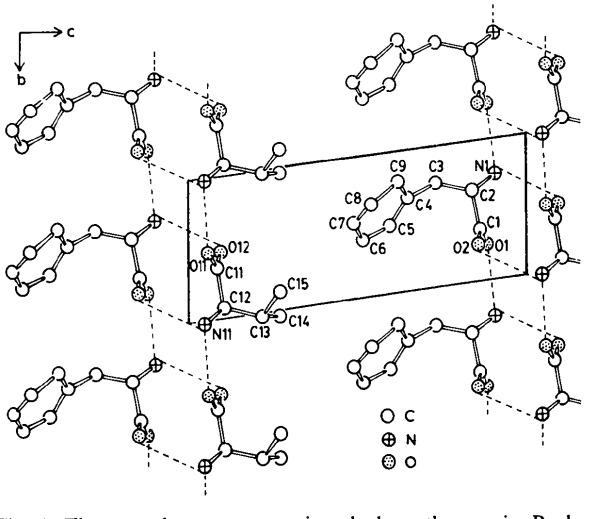

Fig. 1. The crystal structure as viewed along the *a* axis. Broken lines indicate hydrogen bonds. Two hydrogen bonds which connect molecules related by an *a* translation are not shown (see Table 3).

Table 3. *Hydrogen-bond parameters* (Å, °) *with e.s.d.'s in parentheses*

A—H···*B*	*A*···*B*	H—*A*—*B*
N(1)—H(1)N(1)···O(12^b)	2·892 (4)	11 (3)
N(1)—H(2)N(1)···O(1^a)	2·736 (6)	2 (1)
N(1)—H(3)N(1)···O(2^c)	2·963 (4)	3 (3)
N(11)—H(1)N(11)···O(12^e)	2·897 (4)	11 (3)
N(11)—H(2)N(11)···O(2^f)	2·935 (5)	18 (5)
N(11)—H(3)N(11)···O(11^d)	2·752 (6)	3 (3)

Symmetry code: (*a*) $x, y-1, z$; (*b*) $x, y, z+1$; (*c*) $x-1, y, z$; (*d*) $x, y+1, z$; (*e*) $x+1, y, z$; (*f*) $x, y, z-1$.

independent N—H···O hydrogen bonds. These hydrogen bonds lead to a cyclic arrangement involving the main-chain atoms of the two types of molecules. The two sets of main-chain atoms are related by a pseudo-inversion centre and, hence, the cyclic arrangement is nearly centrosymmetric. The hydrogen-bonded network made up of main-chain atoms at the core of each double layer is flanked by side chains. The double layers are stacked along the largest crystallographic axis to form the crystal. The interactions between adjacent double layers exclusively involve side chains and are of the van der Waals type.

The molecular aggregation in the crystal structure of L-phenylalanine D-valine is very similar to those in the structures of DL-valine (Mallikarjunan & Rao, 1969), DL-leucine (Blasio, Pedone & Sirigu, 1975) and DL-isoleucine (Benedetti, Pedone & Sirigu, 1973) (the crystal structures of DL-phenylalanine and L-phenylalanine are not known). In fact the arrangement of molecules in the double layer of the complex is the same as that in DL-valine (and also in DL-leucine and DL-isoleucine) except for the difference in the side chain of the L layer. Thus the molecules in the crystals consisting of equal number of L and D hydrophobic amino-acid molecules appear to aggregate in a similar fashion, irrespective of the precise details of the side chain. The aggregation pattern in such crystals is, in turn, closely related to those in the crystals of the corresponding L-amino acids (Soman & Vijayan, 1989; Benedetti, Pedone & Sirigu, 1973). The relationship between the aggregation patterns in crystals of the L isomer and the corresponding DL mixture, though present, is weaker in the case of hydrophilic amino acids whose crystal structures are generally made up of single layers (Soman & Vijayan, 1989; Suresh & Vijayan, 1983).

The crystal structures of L-histidine L-aspartate (Bhat & Vijayan, 1978; Suresh & Vijayan, 1987) and L-phenylalanine and D-valine do not offer any ready explanation for the difference in the nature of chiral discrimination in the two systems. However, the higher affinity of a non-polar amino acid of one chirality for another non-polar amino acid with opposite chirality during crystallization could well

have resulted from packing considerations. The fact that the density of the crystals of the DL mixture of a non-polar amino acid is invariably higher than that of the crystals of the corresponding L-isomer, lends support to this conjecture.

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Structure of a Neolignan: $C_{20}H_{28}O_6$

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Abstract. 2-(2*H*-1,3-Benzodioxol-5-yl)-5-ethyl-3a,7a-dimethoxy-3-methyl-2,3,3a,4,5,6,7,7a-octahydro-1-benzofuran-6-ol, $M_r = 336$, monoclinic, $P2_1$, $a = 21{\cdot}198$ (1), $b = 6{\cdot}515$ (4), $c = 7{\cdot}038$ (2) Å, $\beta = 97{\cdot}0$ (5)°, $V = 964{\cdot}73$ Å^3, $Z = 2$, $D_x = 1{\cdot}289$ Mg m^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, $\mu = 0{\cdot}55$ mm^{-1}, $F(000) = 400$, $T = 288$ K, final $R = 0{\cdot}066$ for 1916 observed reflections. The aims of this crystal structure analysis were to determine the spatial configuration and to resolve the ambiguity of the possible positions of the OCH_3 and OH groups in the chemical structure. The cyclohexane ring formed by C(12), C(13), C(18),

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