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X-ray studies on crystalline complexes involving amino acids and peptides. XXXV. Invariance and variability in amino acid aggregation in the complexes of maleic acid with L-histidine and L-lysine

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The crystal structures of complexes of maleic acid with L-histidine and L-lysine have been determined. The two crystallographically independent amino acid molecules in the L-histidine complex have different closed conformations, while the lysine molecule in its complex has the most favourable conformation sterically with an all-*trans* sidechain *trans* to the α-carboxylate group. The maleic acid molecules exist as semi-maleate ions of similar conformation and contain a symmetric O···H···O hydrogen bond. Amino acid cations and semi-maleate anions aggregate into alternate layers in both the structures. The arrangement of molecules in the histidine layer in L-histidine semi-maleate is closer to that in the crystals of the free amino acid than in other L-histidine complexes. On the other hand, the arrangement of lysine molecules in its semi-maleate complex is different from any observed so far. However, the well established characteristic interaction patterns involving amino and carboxylate groups still play a major role in holding the molecules together in the crystal of the complex.

1. Introduction

A major long-range program being pursued in this laboratory is concerned with biomolecular interactions and consists of the preparation and X-ray analysis of crystalline complexes involving amino acids and peptides, among themselves and with other molecules (Vijayan, 1988; Ravishankar *et al.*, 1998). This has led to the generation of a wealth of data, at atomic resolution, on interaction and aggregation patterns of amino acids and peptides, and the effect of chirality on them. The results of this programme have implications for chemical evolution, especially with reference to prebiotic polymerization, chiral discrimination and self assembly, and also to present day biological systems (Vijayan, 1980, 1988). The current focus of the program is on complexes of basic amino acids with carboxylic acids which are believed to have existed in the prebiotic milieu (Miller & Orgel, 1974). Complexes involving succinic acid, acetic acid, formic acid, glycolic acid and oxalic acid have already been analysed (Prasad & Vijayan, 1993*b*; Suresh, Padmanabhan & Vijayan, 1994; Suresh, Prasad & Vijayan, 1994; Suresh & Vijayan, 1995*a*, 1996; Chandra *et al.*, 1998). These studies yielded unexpectedly interesting results on the variability of the ionization state of the component molecules when they are brought together and its effect on stoichiometry and molecular aggregation, in addition to enriching the general results obtained in previous studies. It

appeared that, in addition to their implications in biological interactions and chemical evolution, studies on amino acid–carboxylic acid complexes are of intrinsic interest in relation to molecular interactions and their consequences. Maleic acid is one of the compounds thought to have been in existence on the prebiotic earth. We had earlier reported the crystal structure of L- and DL-arginine complexed to this molecule (Ravishankar *et al.*, 1998). In this paper, we present the maleic acid complexes with L-histidine and L-lysine.

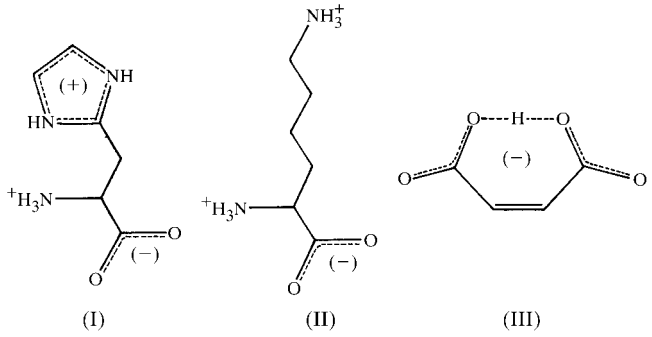
2. Materials and methods

Crystals of the maleic acid complex with L-histidine were prepared by the slow diffusion of acetronitrile or methanol into solutions of equimolar quantities of maleic acid and L-histidine. The complex with L-lysine was crystallized by the slow diffusion of acetonitrile into solutions of maleic acid and L-lysine mixed in a 3:1 molar ratio. Extensive attempts to crystallize the corresponding DL-amino acid complexes were not fruitful. Crystal data, data collection statistics and refinement details are given in Table 1. The structures were solved by direct methods using *SHELXS*86 (Sheldrick, 1985) and refined by full-matrix least-squares using *SHELXL*93 (Sheldrick, 1993). The H atom belonging to the carboxyl group of the semi-maleate ion was refined isotropically, while the other H atoms were assumed to ride on the heavy atoms to which they are attached. Restraints were applied on O—H distances in the semi-maleate ion in the L-lysine complex such that the H atom was almost equidistant from the two hydrogen-bonded O atoms. The non-H atoms were refined anisotropically. The final positional and equivalent isotropic thermal parameters of non-H atoms are listed in Tables 2 and 3.[1]

3. Results and discussion

3.1. Ionization state and molecular conformation

Perspective views of the molecules in the structures are given in Fig. 1. The amino acid molecules are zwitterionic and carry a net positive charge each (I, II). The maleic acid molecules in the complexes exist as semi-maleate ions (III)



and carry a net negative charge each. The conformation of the histidine molecule is defined by χ^1 and χ^{21} (IUPAC-IUB Comission on Biochemical Nomenclature, 1970). χ^1 can take values in the neighbourhood of −60, 60 or 180° corresponding to the open conformation (I) (*g*−), closed conformation (*g*+) and open conformation (II) (Bhat & Vijayan, 1978; Suresh & Vijayan, 1995*a*). χ^{21} has preferred values of 90 and −90°. Larger deviations in χ^{21} are seen in crystal structures, often caused by hydrogen bonds involving the imidazole N atoms. One of the amino acid molecules (molecule *A*) in the complex with L-histidine has a conformation defined by χ^1 = 63.6 (5), χ^{21} = −113.6 (2)°, while the other (molecule *B*) has a conformation defined by χ^1 = 55.5 (5), χ^{21} = 63.4 (2)°. Thus, both the histidine molecules in the present structure are in the closed conformation (*g*+). On the other hand, the imidazole ring is differently oriented in them. As in several other structures containing lysine (Suresh & Vijayan, 1995*a*,*b*), the lysine molecule in its complex has sterically the most favourable conformation with a fully extended sidechain *trans* to the α-carboxylate group [χ^1 = −71.4 (5), χ^2 = 176.6 (4), χ^3 = −177.2 (4) and χ^4 = −173.6 (4)°].

Maleic acid, with two carboxyl functions can exist as a neutral molecule, as a single negatively charged semi-maleate ion or as a double negatively charged maleate ion. The semi-maleate ions in the structures are essentially planar. As observed in other structures containing semi-maleate ions (James & Williams, 1974; Town & Small, 1973; Darlow & Cochran, 1961; Barnes & Weakly, 1997; Ravishankar *et al.*, 1998), the two carboxyl groups in each molecule share a

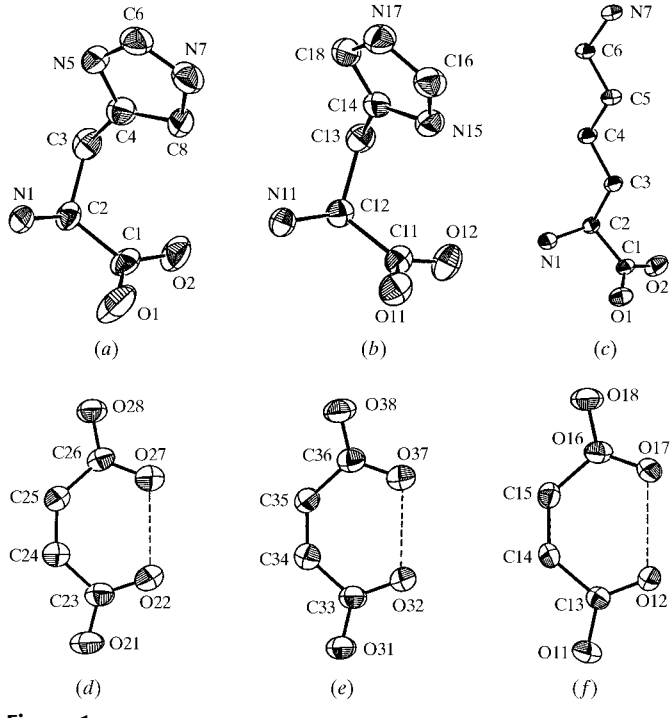


Figure 1
ZORTEP diagrams (Zsolnai, 1994) of histidine molecules (*a*) *A* and (*b*) *B*, and semi-maleate ions (*d*) *A* and (*e*) *B* in the L-histidine complex, and the lysine molecule (*c*) and the semi-maleate ion (*f*) in the lysine complex. The displacement ellipsoids are at the 50% probability level. The numbering scheme is indicated.

[1] Supplementary data for this paper are available from the IUCr electronic archives (Reference: HA0195). Services for accessing these data are described at the back of the journal.

Table 1
Experimental details.

	L-Histidine semi-maleate	L-Lysine semi-maleate
Crystal data		
Chemical formula	$C_6H_{10}N_3O_2^+\cdot C_4H_3O_4^-$	$C_6H_{15}N_2O_2^+\cdot C_4H_3O_4^-$
Chemical formula weight	271	262
Cell setting	Triclinic	Monoclinic
Space group	*P*1	$P2_1$
a (Å)	5.3893 (12)	9.854 (4)
b (Å)	9.3851 (13)	7.136 (2)
c (Å)	12.3681 (9)	9.7388 (1)
α (°)	107.054 (9)	90
β (°)	98.569 (12)	115.887 (12)
γ (°)	97.303 (14)	90
V (Å^3)	581.7 (2)	616.1 (3)
Z	2	2
D_x (Mg m^{-3})	1.549	1.414
Radiation type	Cu $K\alpha$	Mo $K\alpha$
Wavelength (Å)	1.5418	0.70930
No. of reflections for cell parameters	25	25
θ range (°)	11.2–69.6	1.1–17.6
μ (mm^{-1})	1.118	0.117
Temperature (K)	293 (2)	293 (2)
Crystal form	Needle	Needle
Crystal size (mm)	0.65 × 0.45 × 0.12	0.49 × 0.25 × 0.10
Crystal colour	Colourless	Colourless
Data collection		
Diffractometer	CAD-4	CAD-4
Data collection method	ω–2θ scans	ω–2θ scans
Absorption correction	ψ scan	ψ scan
T_{min}	0.644	0.965
T_{max}	0.762	0.988
No. of measured reflections	2372	1759
No. of independent reflections	2123	1598
No. of observed reflections	2097	1097
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.019	0.0573
θ_{max} (°)	70.0	27.96
Range of *h*, *k*, *l*	$0 \rightarrow h \rightarrow 6$ $-11 \rightarrow k \rightarrow 11$ $-15 \rightarrow l \rightarrow 14$	$-12 \rightarrow h \rightarrow 11$ $0 \rightarrow k \rightarrow 9$ $0 \rightarrow l \rightarrow 12$
No. of standard reflections	3	3
Frequency of standard reflections	Every 100 reflections	Every 60 min
Intensity decay (%)	5	0
Refinement		
Refinement on	F^2	F^2
$R[F^2>2\sigma(F^2)]$	0.0512	0.0573
$wR(F^2)$	0.1473	0.1351
S	1.047	1.053
No. of reflections used in refinement	2370	1598
No. of parameters used	350	167
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement	H atoms treated by a mixture of independent and constrained refinement
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0905P)^2 + 0.4731P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0823P)^2 + 0.3879P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	−0.014	0.000
$\Delta\rho_{max}$ (e Å^{-3})	0.265	0.343
$\Delta\rho_{min}$ (e Å^{-3})	−0.307	−0.314
Extinction method	*SHELXL*93 (Sheldrick, 1993)	*SHELXL*93 (Sheldrick, 1993)
Extinction coefficient	0.045 (6)	0.012 (8)
Source of atomic scattering factors	*International Tables for Crystalography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)	*International Tables for Crystalography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)
Computer programs		
Data collection	*CAD*-4 (Enraf–Nonius, 1989)	*CAD*-4 (Enraf–Nonius, 1989)
Cell refinement	*CAD*-4 (Enraf–Nonius, 1989)	*CAD*-4 (Enraf–Nonius, 1989)
Data reduction	*CAD*-4 (Enraf–Nonius, 1989)	*CAD*-4 (Enraf–Nonius, 1989)
Structure solution	*SHELXS*86 (Sheldrick, 1985)	*SHELXS*86 (Sheldrick, 1985)
Structure refinement	*SHELXL*93 (Sheldrick, 1993)	*SHELXL*93 (Sheldrick, 1993)
Preparation of material for publication	MS–WORD, Version 6.0	MS–WORD, Version 6.0

proton in a symmetric hydrogen bond with O---O distances of 2.406 (9) Å (O22–O27) in molecule *A*, 2.429 (8) Å (O32–O37) in molecule *B* of the L-histidine complex and 2.427 (6) Å (O12–O17) in the L-lysine complex.

3.2. Molecular aggregation, pseudosymmetry and characteristic interaction patterns

The crystal structures of the complexes are shown in Figs. 2 and 3, while the parameters of the hydrogen bonds that stabilize them are listed in Table 4.

In the crystal structure of the maleic acid complex with L-histidine, the amino acid molecules aggregate into layers interleaved with layers of semi-maleate ions. In each layer, fragments of the molecules made up of C^{α} and the amino and carboxylate groups attached to it lie in an approximate plane parallel to (001), while the sidechains point to either side of the plane. The distribution of these fragments, along with the C^{β} atoms attached to them, is illustrated in Fig. 4. The prominent feature of aggregation in each layer is a ribbon of histidine molecules running along the [$\bar{1}$10] direction. Along the ribbon, the sidechains of alternating molecules point to the opposite sides of the plane. The molecules in the ribbon are related by a pseudo-2_1 screw axis. If the difference between the carbon and the N atoms in the imidazole ring is ignored, the adjacent molecules in the ribbon are related by a rotation of 178.4° and a translation of 6.39 Å, and they are connected by a N1···O12 (or N11···O2) hydrogen bond. Thus, the ribbon constitutes a Z2 (zigzag) head-to-tail sequence in which the α-amino and α-carboxylate groups are brought into periodic proximity by a pseudo-2_1 screw axis and are connected by a hydrogen bond between the α-N atom of one molecule and the α-carboxylate oxygen *trans* to the amino group of the adjacent molecule (Suresh & Vijayan, 1983; Vijayan, 1988). In the case of molecule *B*, the N11···O12 hydrogen bond and its translational equivalents lead to an S2 (straight) head-to-tail sequence parallel to *a*. Such a sequence,

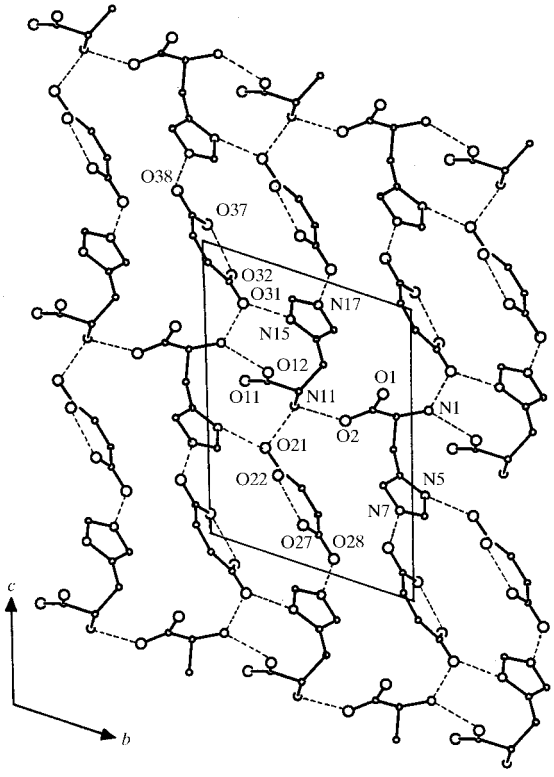


Figure 2
Crystal structure of the L-histidine complex. O, N and C atoms are indicated by circles of decreasing size. Only atoms which make hydrogen bonds are labelled. Hydrogen bonds are indicated by dotted lines. The same convention is used in the subsequent figures also. For clarity, the hydrogen bonds of N11 with O12 and O22 related by an *a* translation to the reference atoms are not shown in this figure. This figure, and also Figs. 3 and 6, were generated using *ORTEP*III (Burnett & Johnson, 1996).

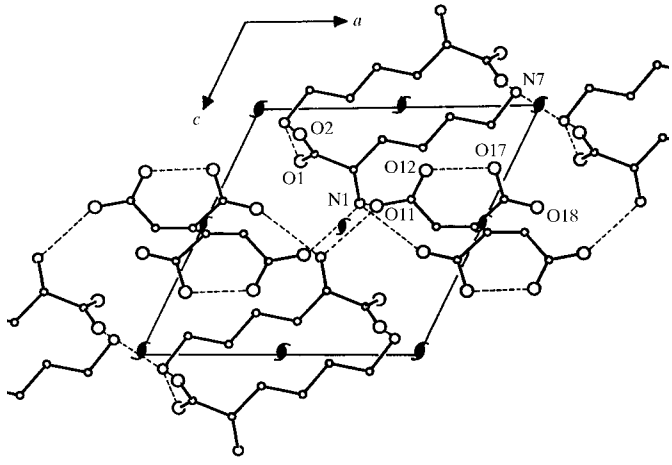


Figure 3
Crystal structure of the L-lysine complex.

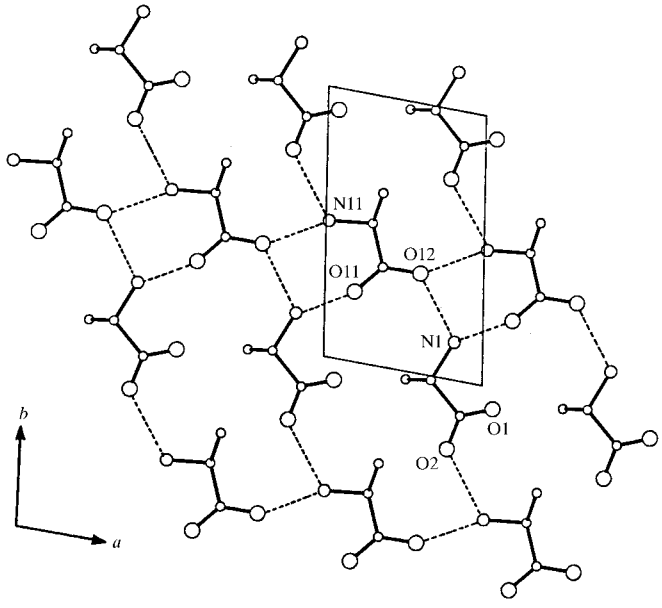


Figure 4
Amino acid fragments made up of C^{α}, α-amino and α-carboxylate groups and C^{β}, in the histidine layer viewed along *c**. This figure and also Fig. 5 were generated using *XPMA* (Zsolnai, 1994).

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

U_{eq} is defined as one third of the trace of the orthogonalized U^C tensor.

	x	y	z	U_{eq}
O1	1.0698 (9)	0.9202 (5)	0.7196 (5)	0.0696 (14)
O2	0.7819 (8)	0.7412 (4)	0.5848 (3)	0.0513 (10)
C1	0.8621 (10)	0.8722 (5)	0.6534 (4)	0.0368 (10)
C2	0.6750 (9)	0.9844 (4)	0.6567 (4)	0.0331 (9)
N1	0.8189 (8)	1.1413 (4)	0.7145 (3)	0.0338 (8)
C3	0.5175 (9)	0.9708 (5)	0.5395 (4)	0.0379 (10)
C4	0.6779 (10)	0.9983 (5)	0.4560 (4)	0.0376 (10)
C8	0.8455 (10)	0.9186 (5)	0.4034 (4)	0.0384 (10)
N7	0.9379 (10)	0.9959 (5)	0.3350 (4)	0.0471 (11)
C6	0.8380 (12)	1.1160 (6)	0.3442 (4)	0.0446 (12)
N5	0.6770 (8)	1.1212 (4)	0.4162 (4)	0.0388 (9)
O11	0.1888 (7)	0.2614 (4)	0.6112 (3)	0.0411 (8)
O12	0.5983 (7)	0.3724 (4)	0.6656 (3)	0.0429 (8)
C11	0.3627 (9)	0.3703 (5)	0.6358 (4)	0.0310 (9)
C12	0.2953 (8)	0.5242 (4)	0.6356 (3)	0.0300 (9)
N11	0.0210 (7)	0.5050 (4)	0.5820 (3)	0.0333 (8)
C13	0.3580 (9)	0.6420 (5)	0.7559 (4)	0.0333 (10)
C14	0.1965 (9)	0.6118 (5)	0.8377 (4)	0.0320 (9)
C18	0.0377 (10)	0.6953 (5)	0.8891 (4)	0.0382 (11)
N17	−0.0663 (9)	0.6240 (5)	0.9586 (4)	0.0408 (9)
C16	0.0280 (11)	0.4991 (6)	0.9494 (4)	0.0425 (12)
N15	0.1878 (8)	0.4882 (4)	0.8769 (3)	0.0370 (9)
O21	0.3955 (9)	0.3564 (5)	0.4009 (3)	0.0573 (11)
O22	0.7140 (10)	0.4150 (6)	0.3198 (5)	0.0698 (13)
C23	0.4928 (12)	0.4260 (6)	0.3431 (4)	0.0456 (12)
C24	0.3482 (12)	0.5335 (6)	0.3037 (5)	0.0485 (13)
C25	0.3918 (11)	0.6090 (6)	0.2295 (5)	0.0456 (12)
C26	0.5947 (11)	0.6097 (6)	0.1616 (4)	0.0425 (12)
O27	0.7763 (10)	0.5345 (7)	0.1759 (5)	0.080 (2)
O28	0.5888 (8)	0.6812 (4)	0.0946 (3)	0.0532 (10)
O31	0.4629 (8)	0.2533 (4)	0.8772 (3)	0.0512 (10)
O32	0.1476 (8)	0.1996 (5)	0.9626 (4)	0.0561 (11)
C33	0.3675 (10)	0.1864 (6)	0.9379 (5)	0.0418 (11)
C34	0.5142 (10)	0.0830 (6)	0.9800 (4)	0.0443 (12)
C35	0.4732 (10)	0.0127 (6)	1.0562 (4)	0.0431 (11)
C36	0.2702 (10)	0.0118 (6)	1.1245 (4)	0.0424 (12)
O37	0.0891 (10)	0.0846 (6)	1.1113 (4)	0.0700 (14)
O38	0.2824 (9)	−0.0571 (5)	1.1950 (3)	0.0559 (11)

Table 3
Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2).

U_{eq} is defined as one third of the trace of the orthogonalized U^C tensor.

	x	y	z	U_{eq}
N1	0.4769 (4)	0.6481 (8)	0.6095 (4)	0.0317 (9)
O2	0.8134 (4)	0.8491 (6)	0.8937 (5)	0.0416 (10)
O1	0.7635 (4)	0.5686 (5)	0.7829 (4)	0.0378 (9)
C1	0.7268 (5)	0.7245 (7)	0.8118 (5)	0.0255 (10)
C2	0.5583 (5)	0.7681 (7)	0.7471 (5)	0.0235 (9)
C3	0.5067 (5)	0.7232 (8)	0.8699 (5)	0.0278 (11)
C4	0.3476 (5)	0.7882 (8)	0.8356 (5)	0.0292 (12)
C5	0.3054 (5)	0.7259 (8)	0.9607 (5)	0.0284 (10)
C6	0.1456 (5)	0.7790 (10)	0.9276 (6)	0.0390 (15)
N7	0.1119 (4)	0.7364 (7)	1.0587 (4)	0.0298 (9)
O12	0.2976 (4)	0.3213 (6)	0.7425 (4)	0.0417 (10)
O11	0.4121 (4)	0.2541 (7)	0.5990 (4)	0.0431 (10)
C13	0.2992 (5)	0.2478 (8)	0.6247 (5)	0.0290 (10)
C14	0.1628 (5)	0.1499 (9)	0.5124 (5)	0.0332 (11)
C15	0.0280 (6)	0.1241 (8)	0.5115 (6)	0.0324 (11)
C16	−0.0305 (5)	0.1857 (8)	0.6227 (6)	0.0366 (14)
O18	−0.1642 (4)	0.1561 (8)	0.5894 (5)	0.0502 (11)
O17	0.0588 (4)	0.2590 (7)	0.7501 (4)	0.0441 (10)

generated by translational equivalents (Suresh & Vijayan, 1983; Vijayan, 1988), does not exist in the case of molecule *A*. N1 of the amino group of molecule *A* is hydrogen bonded to O11 of molecule *B*, but it does not propagate as a head-to-tail sequence.

As can be seen from Fig. 2, the adjacent layers of amino acid molecules are interconnected through semi-maleate ions. The amino acid molecules do not directly interact across layers. The semi-maleate ions do not interact among themselves; they are interconnected through amino acid molecules. The regions between the planes of interconnected amino acid fragments containing C^{α} and α-amino and α-carboxylate groups are mainly made up of circular features stabilized by hydrogen bonds. Each feature consists of two imidazole rings and two semi-maleate ions. Interestingly, the two sidechains and the two semi-maleate ions in each feature are almost coplanar (Fig. 5), with an r.m.s. (root-mean square) and a maximum displacement of 0.253 and 0.684 Å, respectively, from the mean plane of the 28 atoms involved. The arrangement also contains an approximate inversion centre so that it has a pseudo-2/*m* symmetry. The approximate twofold axis of this arrangement is nearly perpendicular to the pseudo-2_1 screw axis that relates the amino acid molecules in each histidine layer.

Unlike molecules also aggregate into alternating layers in the structure of the lysine complex (Fig. 3). The arrangement of molecules in the lysine layer is illustrated in Fig. 6. The arrangement is different from any observed thus far in crystals containing this amino acid. The α-amino group is not involved in interactions among lysine molecules. Consequently, the structure is devoid of head-to-tail sequences which bring α-amino and α-carboxylate groups into periodic hydrogen-bonded proximity. Rather than the α-amino group, the ε-amino group interacts with the α-carboxylate group, also in an exclusive manner. The 2_1 screw-related molecules form a ribbon parallel to **b**. The adjacent, fully extended, molecules align in an antiparallel manner and the ribbon is stabilized by two N—H$\cdots$O hydrogen bonds involving ε-amino and α-carboxylate groups and their symmetry equivalents. The ribbons repeat along **a** through cell translation to produce the lysine layer. The α-amino groups project out on either side of the layer and interact with the unprotonated O atoms of the semi-maleate ions. These ions do not interact among themselves; they are interconnected by the amino acid molecules.

It has been noted earlier (*e.g.* Vijayan, 1988) that the amino groups, unlike the guanidyl group in arginine, cannot take part in specific interactions with carboxylate groups. However, they are often involved in characteristic interaction patterns of different types, one consisting of linear arrangements of alternating amino and carboxylate groups and the other of loops made up of these groups (Vijayan, 1988). The interface between ribbons in the lysine layer (Fig. 6) clearly consists of such loop-like characteristic patterns. On the other hand, the interactions among the α-amino groups and the semi-maleate ions (Fig. 3) lead to a linear pattern.

3.3. Comparison with other structures and conclusions

A recurring theme of the work on complexes has been the preservation of some aspects of aggregation patterns across structures in spite of differences in other aspects. Histidine exhibits similar aggregation patterns in different environments to a lesser extent than lysine and arginine. The aggregation of L-amino acids is most often characterized by an S2 head-to-tail sequence running in one direction and a Z2 sequence in another direction. In this S2Z2 arrangement, S2 is usually generated by a cell translation and Z2 by a crystallographic 2_1 screw axis, the favoured space group being $P2_1$ or $P2_12_12_1$ (Vijayan, 1983, 1988). The Z2 sequence is disrupted in the structures of the complexes of L-histidine with aspartic acid (Bhat & Vijayan, 1978; Suresh & Vijayan, 1987) and oxalic acid (Prabu *et al.*, 1996), while the S2 sequence does not exist in its complexes with succinic acid (Prasad & Vijayan, 1993*a*) and 4,5-imidazoledicarboxylic acid (Gorbitz & Husdal, 1998), and the monoclinic form of the complex with acetic acid (Suresh, Padmanabhan & Vijayan, 1994). In another variation, only the Z1 sequence exists in L-histidine formate (Suresh & Vijayan, 1995*a*). L-Histidine glycolate (Suresh & Vijayan, 1996) and the orthorhombic form of L-histidine acetate (Suresh, Prasad & Vijayan, 1994) constitute rare instances where no head-to-tail interactions are seen in structures containing amino acids. The aggregation pattern in the present complex is a close approximation to that (S2Z2) in the crystals of L-histidine (Madden, McGandy & Seeman, 1972; Madden, McGandy, Seeman, Harding & Hoy, 1972), although the complex crystallizes in the triclinic system, unlike L-histidine and its other complexes. All histidine molecules in the structure are involved in Z2 sequences generated by non-crystallographic 2_1 screw axes. Half the molecules take part in S2 sequences also. Thus, L-histidine semi-maleate preserves the aggregation pattern observed in the crystals of the free amino acid more than any other complex.

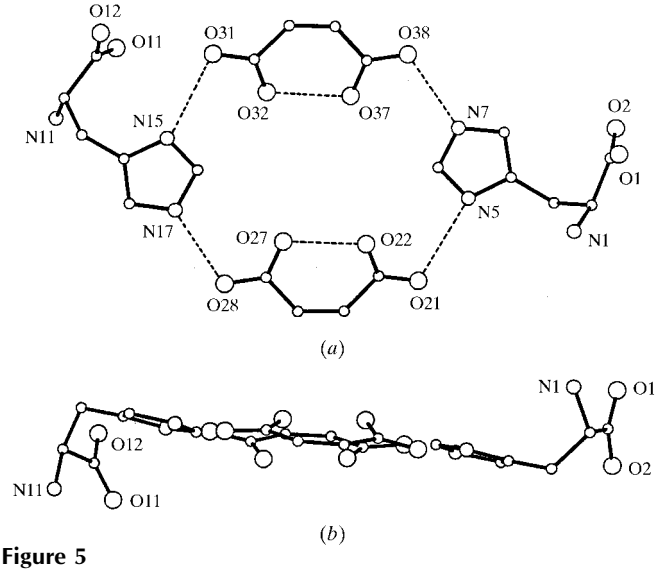


Figure 5
The circular arrangement of molecules viewed (*a*) along the normal to the plane of the two histidine sidechains and semi-maleate ions, and (*b*) perpendicular to it. See text for details.

Table 4
Parameters of intermolecular hydrogen bonds.

D—H···A	D···A (Å)	∠D—H···A (°)
(*a*) L-Histidine complex		
N1—H1N1···O32^{i}	3.162 (5)	172
N1—H3N1···O11^{ii}	2.812 (6)	165
N1—H2N1···O31^{ii}	3.043 (6)	126
N1—H2N1···O12^{ii}	2.773 (5)	140
N7—HN7···O38^{iii}	2.717 (7)	170
N5—HN5···O21^{ii}	2.866 (6)	152
N11—H2N11···O2^{iv}	2.696 (5)	153
N11—H3N11···O12^{iv}	2.923 (5)	157
N11—H1N11···O22^{iv}	3.225 (6)	134
N11—H1N11···O21	3.356 (6)	120
N15—HN15 ···O31	2.809 (6)	157
N17—HN17···O28^{v}	2.688 (6)	168
(b) L-lysine complex		
N1—H1N1···O11^{vi}	2.798 (4)	174
N1—H2N1···O18^{vii}	2.835 (5)	154
N1—H3N1···O11	2.875 (5)	147
N7—H1N7···O2^{iv}	2.784 (4)	153
N7—H2N7···O1^{viii}	2.802 (3)	142
N7—H3N7···O2^{ix}	2.846 (4)	167

Symmetry codes: (i) $x+1, y+1, z$; (ii) $x, y+1, z$; (iii) $x+1, y+1, z-1$; (iv) $x-1, y, z$; (v) $x-1, y, z+1$; (vi) $-x+1, y+\frac{1}{2}, -z+1$; (vii) $-x, y+\frac{1}{2}, -z+1$; (viii) $-x+1, y+\frac{1}{2}, -z+2$; (ix) $-x+1, y-\frac{1}{2}, -z+2$.

In contrast, as indicated earlier, the lysine molecules exhibit a novel aggregation pattern in the present complex. Free lysine has not been crystallized yet. The lysine molecules have the same aggregation pattern involving S1Z2 sequences in the L-lysine complexes with formic, acetic, L-aspartic and D-aspartic acids (Suresh & Vijayan, 1995*a*,*b*). They exhibit different patterns when complexed with succinic acid (Prasad & Vijayan, 1991), picric acid (Nagata *et al.* 1995) and 4,5-imidazoledicarboxylic acid (Gorbitz & Husdal, 1998). However, they also contain head-to-tail sequences. The lysine molecule in the complex with oxalic acid has an unusual ionization state with a neutral carboxyl group and two positively charged amino groups. Presumably, on account of this unusual molecular property, the lysine molecules do not interact among themselves. The lysine molecule in the complex reported here has the usual expected ionization state with a net positive charge as in all complexes other than that with oxalic acid. Yet, the aggregation pattern in the present maleic acid complex is entirely different from those observed

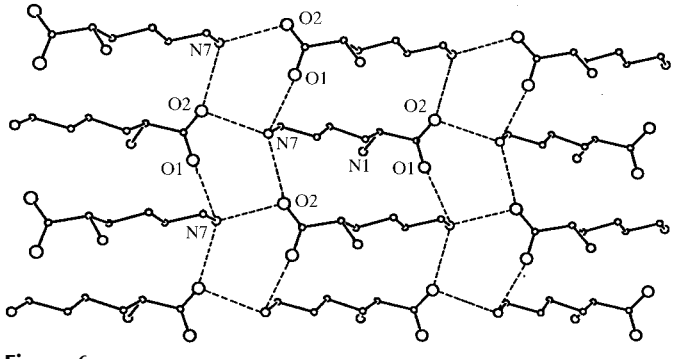


Figure 6
The lysine layer viewed approximately along **c**.

in others. In fact, the pattern is the first one to be observed without a head-to-tail sequence when L-lysine molecules, in the normal ionization state, aggregate.

The unexpectedly different aggregation pattern observed in the L-lysine complex serves as a note of caution and demonstrates how difficult it is to predict crystal structures even though broad generalizations are useful. On the other hand, the histidine complex provides an example of the retention of the basic features of aggregation in different environments and in the presence of different molecules. It is also interesting to note that in spite of the novel aggregation pattern exhibited by the lysine complex, the well established characteristic interaction patterns involving amino and carboxylate groups still play a major role in holding the molecules together.

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