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X-ray studies of crystalline complexes involving amino acids and peptides. XLIII. Adipic acid complexes of L- and DL-lysine

Alok Sharma, S. Thamotharan, Siddhartha Roy and M. Vijayan*

Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560 012, India
Correspondence e-mail: mv@mbu.iisc.ernet.in

The asymmetric unit of the DL-lysine complex of adipic acid [bis(DL-lysinium) adipate], $2C_6H_{15}N_2O_2^+ \cdot C_6H_8O_4^{2-}$, contains a zwitterionic singly charged lysinium cation and half a doubly charged adipate anion (the complete anion has inversion symmetry). That of the L-lysine complex (lysinium hydrogen adipate), $C_6H_{15}N_2O_2^+ \cdot C_6H_9O_4^-$, consists of a lysinium cation and a singly charged hydrogen adipate anion. In both structures, the lysinium cations organize into layers interconnected by adipate or hydrogen adipate anions. However, the arrangement of the molecular ions in the layer is profoundly different in the DL- and L-lysine complexes. The hydrogen adipate anions in the L-lysine complex form linear arrays in which adjacent ions are interconnected by a symmetric O···H···O hydrogen bond.

Comment

In a long-term programme, we have been investigating the supramolecular association of amino acids and peptides using an approach involving the preparation and X-ray analysis of crystalline complexes of amino acids and peptides among themselves and with other molecules (Vijayan, 1988; Roy *et al.*, 2005). The patterns of association observed in the course of these investigations were found to be of possible relevance to chemical evolution and the origin of life (Vijayan, 1980, 1988). For more than a decade, the focus of the programme has been on complexes of amino acids and peptides, particularly the basic amino acids arginine, lysine and histidine, with carboxylic acids that are believed to have existed in the prebiotic milieu, and with related compounds. The results obtained from the study of complexes involving dicarboxylic acids have been particularly interesting in relation to common features of association, their variability, and the effect of chirality on ionization state, stoichiometry and aggregation patterns. Many of the complexes reported by us have been those of DL- and L-lysine with monocarboxylic acids (Suresh *et*

al., 1994; Suresh & Vijayan, 1983*b*, 1995) and dicarboxylic acids (Prasad & Vijayan, 1991; Venkatraman *et al.*, 1997; Pratap *et al.*, 2000; Saraswathi *et al.*, 2001, 2003) with varying length. They also often exhibit common features of supramolecular association, despite differences in their crystal structures. The effect of reversing the chirality of half the amino acid molecules, as happens when comparing the crystal structures involving DL and L forms of the same amino acid, is manifested in two different ways in amino acid–carboxylic acid complexes. In some instances, the pattern of aggregation remains the same; the effect is absorbed by small alterations. In other instances, the effect is profound and leads to an entirely different pattern. The latter is true in the lysine complexes. Among the lysine complexes studied by us so far, one conspicuous absence was that of complexes involving adipic acid. We report here the crystal structures of the adipic acid complexes of DL-lysine, (I), and L-lysine, (II).

(I)   (II)
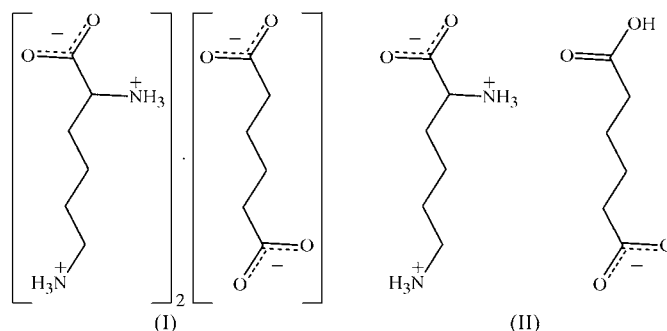
In both complexes, the amino acid exists as a positively charged zwitterion, with protonated amino groups and a deprotonated carboxyl group. Both the carboxyl groups in the adipic acid molecule are deprotonated in the DL-lysine complex, (I). The stoichiometry between the singly charged lysinium cation and the doubly charged adipate anion is 2:1. The lysinium cation occupies a general position, while the adipate ion is located across an inversion centre. In the L-lysine complex, (II), one carboxyl group in the adipic acid molecule is deprotonated and negatively charged while the
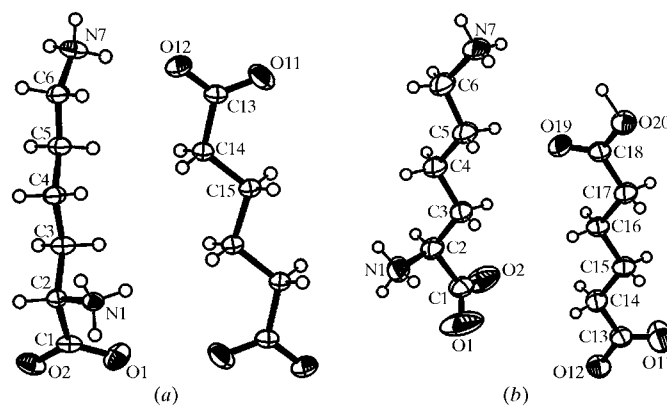

Figure 1
The molecular structures in (*a*) the DL-lysine complex, (I), and (*b*) the L-lysine complex, (II). Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

other remains unchanged. The stoichiometry between the components is 1:1. The lysinium cation has the most sterically favourable conformation, with an all-*trans* extended side chain *trans* to the α-carboxylate group in both complexes (Prasad & Vijayan, 1991) (Fig. 1 and Table 1). The adipate and hydrogen adipate anions have nearly fully extended conformations.

The crystal structures of the complexes are illustrated in Figs. 2 and 3, and the parameters of the hydrogen bonds that stabilize them are listed in Tables 2 and 3. The tables include a full description of the three-centred hydrogen bonds, but these are asymmetric and only the shorter branches are given in the figures. Atom N7 in the DL-lysine complex and atoms N1 and N7 in the L-lysine complex are involved in these hydrogen bonds. They are characterized by large deviations of the N—H$\cdots$O angles from $180°$.

In (I), the lysinium cations aggregate into layers parallel to the *ab* plane, as illustrated in Fig. 4. The molecular ions first form hydrogen-bonded dimers across inversion centres, stabilized by a pair of N1$\cdots$O2 hydrogen bonds. These dimers then form ribbons parallel to *a*. Neighbouring dimers, related by translation in the ribbon, are interconnected by a pair of N1$\cdots$O1 hydrogen bonds. We had previously demonstrated, particularly in the context of prebiotic polymerization, that amino acids almost invariably aggregate in head-to-tail sequences of the type $\cdots$NH$_3^+$–CHR–COO$^-\cdots$NH$_3^+$–CHR–COO$^-\cdots$, in which the α-amino and α-carboxylate groups are brought into periodic hydrogen-bonded proximity in a peptide-like arrangement. Adjacent molecules in this
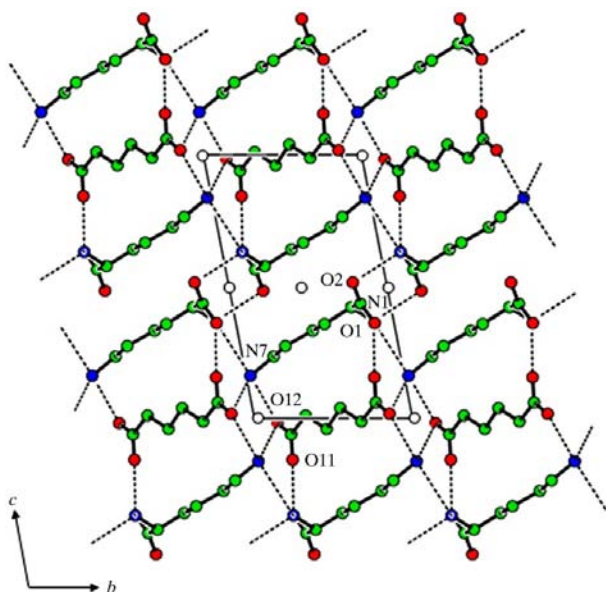

Figure 2
The crystal structure of the DL-lysine complex, (I). In this and subsequent figures, only atoms involved in the hydrogen-bonding scheme are labelled. For clarity, the inversion centre at $(0, \frac{1}{2}, 0)$ is not indicated.
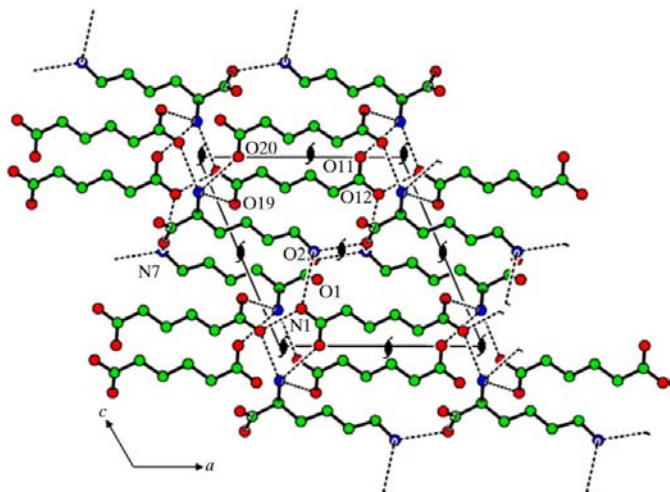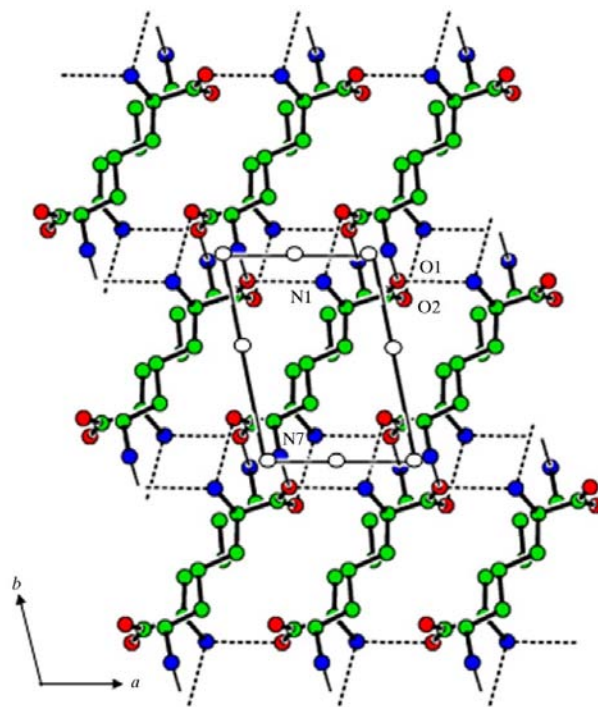

Figure 4
The lysinium layer at a height of $z = \frac{1}{2}$ in the DL-lysine complex, (I). Atoms N7 and O2 of neighbouring ions, which partially overlap, are hydrogen bonded. For clarity, the inversion centre at $a = b = c = \frac{1}{2}$ is not indicated.
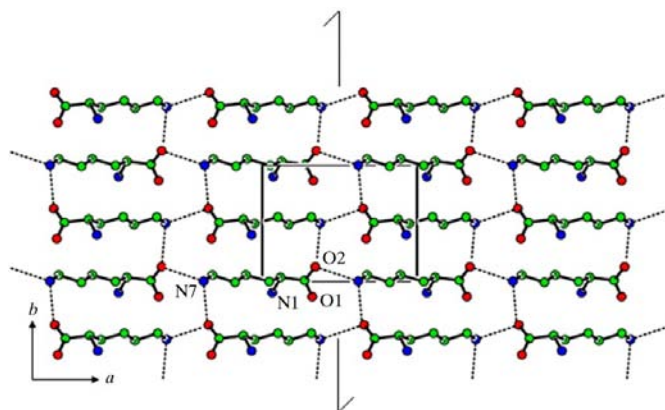

Figure 3
The crystal structure of the L-lysine complex, (II).

Figure 5
The lysinium layer, at a height of $z = \frac{1}{2}$, in the L-lysine complex, (II).

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sequence are often related by a translation (an *S* sequence), a 2_1 screw (*Z*) or a glide plane (*DL*). When the O atom involved in the hydrogen bonds is *cis* to the amino group (conventionally referred to O1), then '1' is added as a suffix to *S*, *Z* or *DL* in the description of the sequence. If the O atom is *trans* to the amino group, then '2' is added (Suresh & Vijayan, 1983*a*). The N1···O1 hydrogen bonds referred to above form part of two *S*1 head-to-tail sequences. Neighbouring ribbons interact through a hydrogen bond between the side-chain terminal amino N atom (N7) from one and a carboxylate O atom (O1) from the other.

The lysinium layers are interconnected by adipate anions. A carboxylate O atom at one end of the adipate anion directly
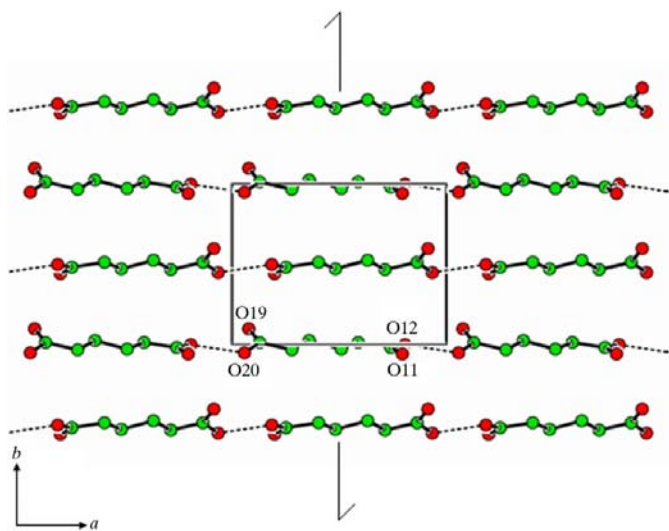

Figure 6
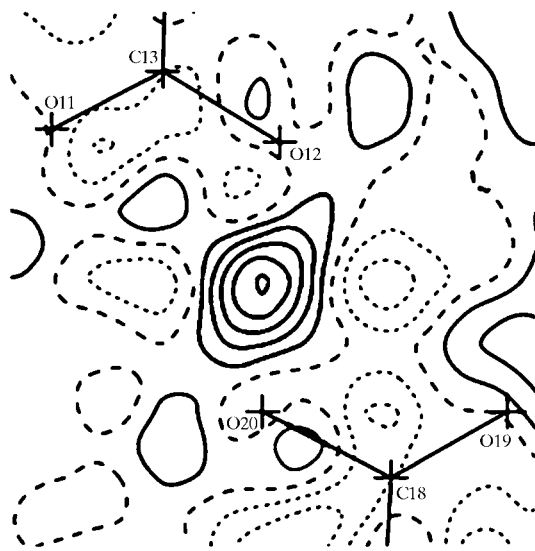The arrangement of hydrogen adipate anions in the L-lysine complex, (II).

Figure 7
Difference density map corresponding to the H atom in the symmetric hydrogen bond in the L-lysine complex, (II).

interacts with atom N1 of a lysinium cation in one layer, while its centrosymmetric equivalent interacts with a centrosymmetrically related atom N1 in the adjacent layer. This O atom also has a weak interaction with a side-chain amino group. The other O atom forms hydrogen bonds with the side-chain amino N atoms of two separate lysinium cations at both ends of the adipate anion. The adipate anions do not interact with each other. They are situated in interstitial spaces between packed lysinium cations.

In the present case, the effect of chirality on molecular aggregation is profound. The crystal structure of the L-lysine complex (Fig. 3) is different from that of the DL-lysine complex, except that in the L-lysine complex the lysinium cations also aggregate in layers. In each layer (Fig. 5), the most prominent feature is linear arrays of lysinium cations stabilized by intermolecular hydrogen bonds between side-chain amino groups and α-carboxylate O atoms. The molecules in the array are related by a translation. Adjacent arrays, related by a 2_1 screw axis, run in opposite directions. They are again interconnected by hydrogen bonds involving the side-chain amino group and carboxylate O atoms. This structure presents a very rare case in which the α-amino group is not involved in intermolecular interactions with the α-carboxylate group. In most cases, such interactions lead to one or more head-to-tail sequences in which the α-amino and α-carboxylate groups are brought into periodic hydrogen-bonded proximity in a peptide-like arrangement (Suresh & Vijayan, 1983*a*).

The hydrogen adipate anions are also arranged in linear arrays along *a*. The arrays form corrugated layers parallel to the *ab* plane (Fig. 6). In each array, adjacent hydrogen adipate anions are connected by a symmetric O···H···O hydrogen bond, in which the H atom can be described as being shared by the two anions (Fig. 7). Adjacent arrays in each layer are related by a 2_1 screw parallel to *b*. The arrays in each layer are interconnected by hydrogen bonds involving α-amino groups.

Experimental

In both cases, aqueous solutions of the amino acid (Sigma) and adipic acid in a 1:1 molar ratio were used to grow the crystals of the complexes, employing the liquid diffusion method with acetonitrile as the precipitant.

Table 1
Torsion angles (°) defining the molecular conformations of (I) and (II).

In (I), atoms C16 and C17 correspond to the centrosymmetric equivalents of atoms C15 and C14, respectively.

Torsion	(I)	(II)
N1—C2—C1—O1 (ψ^1)	−36.3 (1)	−16.2 (5)
N1—C2—C3—C4 (χ^1)	−57.2 (1)	−71.3 (4)
C2—C3—C4—C5 (χ^2)	−177.2 (1)	172.4 (3)
C3—C4—C5—C6 (χ^3)	−173.3 (1)	175.7 (4)
C4—C5—C6—N7 (χ^4)	168.8 (1)	−174.8 (3)
O11—C13—C14—C15	14.1 (1)	−6.3 (7)
C13—C14—C15—C16	179.0 (1)	173.6 (4)
C14—C15—C16—C17	180.0 (1)	174.8 (4)
C15—C16—C17—C18		−178.1 (4)
C16—C17—C18—O19		−4.0 (6)

Compound (I)

Crystal data

$2C_6H_{15}N_2O_2{}^+ \cdot C_6H_8O_4{}^{2-}$
$M_r = 438.52$
Triclinic, $P\bar{1}$
$a = 5.4730\ (15)$ Å
$b = 7.773\ (2)$ Å
$c = 13.011\ (4)$ Å
$\alpha = 100.112\ (4)°$
$\beta = 93.292\ (4)°$
$\gamma = 100.744\ (4)°$
$V = 533.0\ (3)$ Å^3

$Z = 1$
$D_x = 1.366$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1582 reflections
$\theta = 1.0–28.0°$
$\mu = 0.11$ mm^{-1}
$T = 298\ (2)$ K
Plate, colourless
$0.69 \times 0.60 \times 0.20$ mm

Data collection

Bruker SMART CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (SADABS; Sheldrick, 1996)
  $T_{min} = 0.912$, $T_{max} = 0.983$
6254 measured reflections
2494 independent reflections

2269 reflections with $I > 2\sigma(I)$
$R_{int} = 0.014$
$\theta_{max} = 28.0°$
$h = -7 \rightarrow 7$
$k = -10 \rightarrow 10$
$l = -16 \rightarrow 17$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.044$
$wR(F^2) = 0.120$
$S = 1.04$
2494 reflections
138 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o{}^2) + (0.0641P)^2 + 0.1692P]$
  where $P = (F_o{}^2 + 2F_c{}^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.45$ e Å^{-3}
$\Delta\rho_{min} = -0.27$ e Å^{-3}

Table 2
Hydrogen-bond geometry (Å, °) for (I).

$D-H \cdots A$	H$\cdots A$	$D \cdots A$	$D-H \cdots A$
N1—H1A$\cdots$O11^i	1.94	2.730 (2)	148
N1—H1B$\cdots$O2^{ii}	1.94	2.815 (2)	169
N1—H1C$\cdots$O1^{iii}	1.91	2.762 (2)	160
N7—H7A$\cdots$O12	2.00	2.838 (2)	156
N7—H7B$\cdots$O12^{iv}	1.95	2.764 (2)	152
N7—H7C$\cdots$O1^v	2.33	3.037 (2)	137
N7—H7C$\cdots$O11^{vi}	2.43	3.042 (2)	126

Symmetry codes: (i) $-x+1, -y+1, -z$; (ii) $-x+2, -y+2, -z+1$; (iii) $x-1, y, z$; (iv) $-x, -y, -z$; (v) $x-1, y-1, z$; (vi) $-x+1, -y, -z$.

Compound (II)

Crystal data

$C_6H_{15}N_2O_2{}^+ \cdot C_6H_9O_4{}^-$
$M_r = 292.33$
Monoclinic, $P2_1$
$a = 10.532\ (3)$ Å
$b = 7.2834\ (17)$ Å
$c = 10.599\ (3)$ Å
$\beta = 113.352\ (3)°$
$V = 746.5\ (3)$ Å^3
$Z = 2$
$D_x = 1.301$ Mg m^{-3}

Mo $K\alpha$ radiation
Cell parameters from 2077 reflections
$\theta = 1.0–26.0°$
$\mu = 0.10$ mm^{-1}
$T = 298\ (2)$ K
Prism, colourless
$0.91 \times 0.65 \times 0.17$ mm

Data collection

Bruker SMART CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (SADABS; Sheldrick, 1996)
  $T_{min} = 0.891$, $T_{max} = 0.981$
6202 measured reflections
1481 independent reflections

1329 reflections with $I > 2\sigma(I)$
$R_{int} = 0.017$
$\theta_{max} = 25.3°$
$h = -12 \rightarrow 12$
$k = -8 \rightarrow 8$
$l = -12 \rightarrow 12$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.051$
$wR(F^2) = 0.135$
$S = 1.04$
2701 reflections
187 parameters
H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o{}^2) + (0.0766P)^2 + 0.245P]$
  where $P = (F_o{}^2 + 2F_c{}^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.27$ e Å^{-3}
$\Delta\rho_{min} = -0.21$ e Å^{-3}

Table 3
Hydrogen-bond geometry (Å, °) for (II).

$D-H \cdots A$	H$\cdots A$	$D \cdots A$	$D-H \cdots A$
N1—H1A$\cdots$O19^i	2.31	2.935 (5)	128
N1—H1A$\cdots$O12^{ii}	2.49	3.220 (6)	140
N1—H1B$\cdots$O20^{iii}	2.08	2.796 (4)	137
N1—H1C$\cdots$O11^{iv}	1.89	2.761 (4)	164
N7—H7A$\cdots$O2^i	1.88	2.770 (5)	178
N7—H7B$\cdots$O2^v	2.06	2.918 (4)	163
N7—H7B$\cdots$O1^v	2.37	3.066 (4)	135
N7—H7C$\cdots$O12^v	2.30	3.022 (4)	139
N7—H7C$\cdots$O1^{vi}	2.35	3.037 (7)	134
O20—H20$\cdots$O12^v	1.27 (5)	2.467 (3)	175 (5)

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

The structure of the L-lysine complex was determined using the coordinates of the lysinium cation taken from Saraswathi et al. (2001). For both title complexes, H atoms were located in difference Fourier maps with the aid of geometrical considerations. The amino H atoms were constrained, except for rotation about their respective C—N bonds. All remaining H atoms were treated as riding on their parent atoms. The C—H and N—H distances were constrained at 0.97–0.98 and 0.89 Å, respectively. The lone carboxyl H atom in (II) was refined freely. In the case of (II), Friedel opposite reflections were merged, although the space group is non-centrosymmetric. An absolute configuration consistent with natural L-lysine was assumed.

For both compounds, data collection: SMART (Bruker, 2001); cell refinement: SMART; data reduction: SAINT (Bruker, 2001). Program(s) used to solve structure: SHELXS97 (Sheldrick, 1997) for (I); DIRDIF99 (Beurskens et al., 1999) for (II). For both compounds, program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: ORTEP-3 (Farrugia, 1997); software used to prepare material for publication: PLATON (Spek, 2003).

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