Structural Feature and Molecular Interaction of Basic Amino Acid–Picric Acid Complexes by X-Ray Crystal Analyses

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As a part of elucidating the structural features of a host molecule necessary for the recognition of basic amino acids, the crystal structures of the picrates of DL-arginine (1), L-arginine (2), L-lysine (3) and L-ornitine (4) have been determined by X-ray analyses. The molecular packing pattern is found to be common in these crystal structures. The picric acids themselves form layers perpendicular to a crystallographic axis, and respective basic amino acids are packed into these layers, where the amino acids themselves also form singly or doubly arranged layers in a head-to-tail fashion and are stabilized by hydrogen bonds between the α-carboxyl and guanidyl or terminal amino groups. The picric acid interacts with the amino acid by three to seven NH(amino acid) · · · O(picric acid) hydrogen bonds. A notable feature of the molecular interaction commonly found in complexes 1—4 is the simultaneous fixation at three portions of the amino acid (α-amino, α-carboxyl and terminal amino or guanidyl groups) by a hydrogen bond and/or electrostatic interactions. In conclusion, it was shown that both the crystal packing and the molecular interaction modes are important for the complex formation between the basic amino acid and picric acid molecules.

Key words X-ray crystal structure; arginine picrate; lysine picrate; ornitine picrate; molecular interaction

It is known that picric acid (PA) functions not only as an acceptor to form various π-stacking complexes in the interaction with aromatic biomolecules such as tryptophan metabolites,[1] but also as an acidic ligand ($K_d = 4.2 \times 10^{-1}$) to form salts with metal or small cations through specific electrostatic or hydrogen bond interactions. Therefore, the picrates have been used for the identification or quantitative analysis of organic compounds, and their structural features have also been evaluated at the atomic level.[2] On the other hand, there has been no report on the crystal structure of the molecular complex concerning the interaction of PA with basic amino acids. However, it could be thought that the structural analysis of the basic amino acid–PA molecular complex provides useful information about the common structural requisite and/or feature of the host molecule, which is necessary for the recognition of a basic amino acid. Therefore, we have been attempting to prepare and structurally determine a series of basic amino acid–PA complex crystals. The present paper deals with the crystal structures of picrates of DL-arginine (DL-Arg) (**1**), L-arginine (L-Arg) (**2**), L-lysine (L-Lys) (**3**) and L-ornitine (L-Orn) (**4**). The chemical structures of Arg, Lys, Orn and PA, together with their atomic numberings used in this work, are shown in Fig. 1.

Experimental

The complex crystals of **1**—**4** were all prepared from an aqueous solution containing an equimolar amount of basic amino acids and PA by slow evaporation at room temperature (293 K). Crystal density was measured by the floatation method using a benzene–carbon tetrachloride mixture at 293 K. The densities, cell parameters and thermal analyses of the crystals suggested that **1** and **2** consist of 1 : 1 complexes of component molecules without a solvent and with two water molecules, respectively,

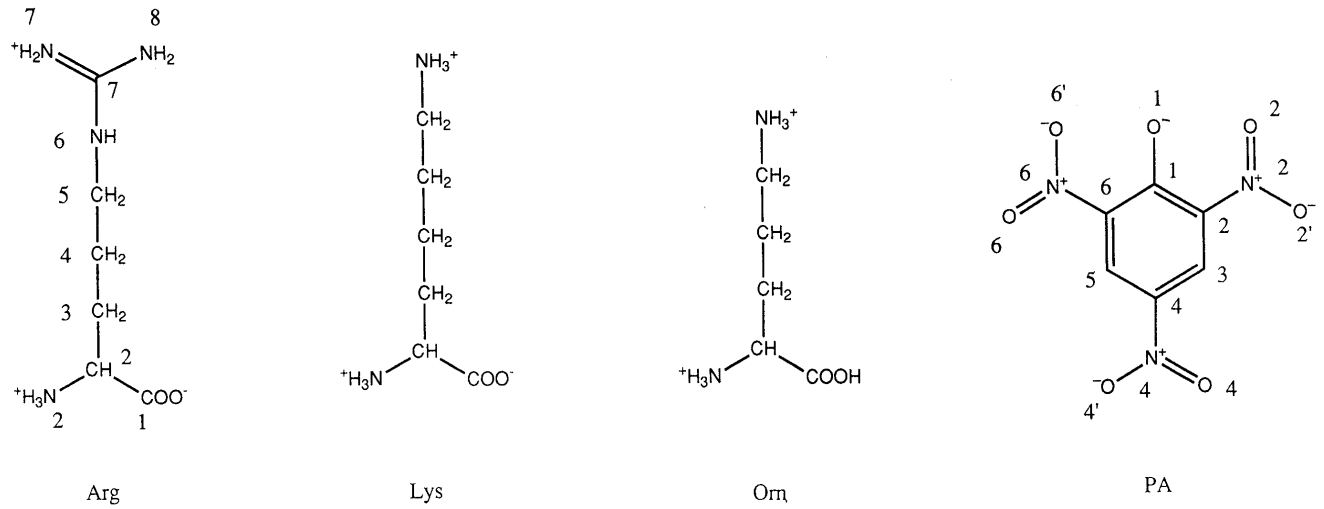

Fig. 1. Chemical Structures of DL-Arg, L-Arg, L-Lys, L-Orn and PA
The atomic numbering used in this work is also given.

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Table 1. Details of Crystal Data, Data Collection and Structure Refinements of Complexes **1**—**4**

	1	**2**	**3**	**4**
Chemical formula	$C_6H_{15}N_4O_2^+ \cdot C_6H_2N_3O_7^-$	$C_6H_{15}N_4O_2^+ \cdot C_6H_2N_3O_7^- \cdot 2H_2O$	$C_6H_{15}N_2O_2^+ \cdot C_6H_2N_3O_7^-$	$C_5H_{14}N_2O_2^{2+} \cdot 2C_6H_2N_3O_7^-$
M_r	403.308	439.338	375.294	590.373
Crystal system	Monoclinic	Monoclinic	Triclinic	Monoclinic
Space group	$P2_1/n$	$P2_1$	$P1$	$P2_1$
Cell constant				
a, Å	32.833 (3)	17.798 (3)	10.367 (3)	11.692 (2)
b, Å	9.989 (1)	5.005 (1)	15.962 (6)	14.058 (3)
c, Å	5.051 (1)	10.732 (2)	5.081 (3)	7.364 (1)
α, °	90	90	99.07 (5)	90
β, °	91.25 (3)	98.32 (3)	99.13 (4)	104.65 (2)
γ, °	90	90	74.70 (3)	90
Volume, Å^3	1656.1 (4)	945.9 (3)	794.8 (6)	1171.1 (4)
Z	4	2	2	2
D_m, g·cm^{-3}	1.604 (3)	1.541 (3)	1.552 (3)	1.669 (3)
D_x, g·cm^{-3}	1.617	1.542	1.567	1.673
μ (CuK_α), cm^{-1}	10.96	10.77	10.63	12.02
$F(000)$	840	460	392	608
No. of unique data measured	2816	1809	2700	2087
No. of data used for refinement $[F_O \geq 3\sigma(F_O)]$	2411	1737	2322	2004
No. of parameters refined	320	271	465	370
R	0.070	0.065	0.064	0.064
R_w	0.077	0.071	0.078	0.066
S	0.9432	0.6356	0.7729	0.7125
$(\Delta/\sigma)_{max}$ for non-H atoms	0.934	0.369	0.481	0.248
$(\Delta\rho)_{max}$, eÅ^{-3}	0.25	0.28	0.33	0.27
$(\Delta\rho)_{min}$, eÅ^{-3}	−0.23	−0.25	−0.29	−0.25

3 contains two crystallographically independent 1:1 complex pairs per asymmetric unit, and the complex **4** consists of a molar ratio of L-Orn : PA = 1 : 2.

X-Ray data were collected with a Rigaku AFC-5R diffractometer by using the graphite-monochromated CuK_α radiation ($\lambda = 1.5418$ Å) at 293 K. Details for cell parameter determination and the reflectional intensity data collection are summarized in Table 1. Intensity data within $2° \leq 2\theta \leq 130°$ were measured by employing an ω-2θ scan mode. Four standard reflections monitored every 100 reflections showed no significant time-dependence ($< \pm 2\%$).

Each crystal structure was solved by the direct method with the MULTAN87 program.[3] The positional parameters of non-H atoms were refined by full-matrix least-squares with anisotropic temperature parameters using the SHELX76 program.[4] The positions of the H atoms were located on the difference Fourier map for **1** and were included in the subsequent refinements with isotropic temperature parameters, while those of **2**, **3** and **4** were calculated based on their stereochemistry and were included only in the calculations of structure factors but not in the refinements. The atomic scattering factors and terms of anomalous dispersion corrections were taken from International Tables for X-Ray Crystallography.[5] The crystallographic calculations were performed using a CRYSTAN GM soft package.[6] The final atomic coordinates and U_{eq} values for the non-H atoms are given in Table 2.[7]

All numerical calculations were performed on a Micro VAX II computer at the Computation Center, Osaka University of Pharmaceutical Sciences.

Results and Discussion

Molecular Conformations Stereoscopic views of DL-Arg, L-Arg, L-Lys and L-Orn molecular conformations are shown in Fig. 2, where PA in complex **1** is also shown as a representative molecular conformation, because the conformational characteristic of PA is commonly observed among the four different complexes, **1**—**4**. The conformational torsion angles are given in Table 3. The bond lengths and angles of **2** and **3** are not as accurate as usual because of the relatively large standard deviations

Table 2. Atomic Coordinates and Isotropic Temperature Factors of Non-H Atoms with Their e.s.d.'s In Parentheses

Atom	x	y	z	U_{eq}
Complex (**1**)				
Picric acid				
C(1)	0.32882 (9)	0.0197 (3)	−0.0798 (5)	0.025 (1)
O(1)	0.36586 (6)	−0.0088 (2)	−0.0688 (4)	0.032 (1)
C(2)	0.29716 (9)	−0.0425 (3)	0.0735 (6)	0.027 (1)
N(2)	0.30761 (8)	−0.1290 (3)	0.2954 (5)	0.030 (1)
O(2)	0.34335 (8)	−0.1467 (3)	0.3605 (5)	0.043 (1)
O(2′)	0.27964 (9)	−0.1805 (3)	0.4157 (5)	0.052 (2)
C(3)	0.2562 (1)	−0.0219 (3)	0.0251 (6)	0.030 (2)
C(4)	0.24392 (9)	0.0604 (3)	−0.1775 (6)	0.029 (2)
N(4)	0.20149 (8)	0.0795 (3)	−0.2380 (6)	0.039 (2)
O(4)	0.17600 (8)	0.0319 (3)	−0.0893 (7)	0.058 (2)
O(4′)	0.19128 (8)	0.1443 (3)	−0.4354 (6)	0.056 (2)
C(5)	0.2720 (1)	0.1336 (3)	−0.3238 (6)	0.030 (2)
C(6)	0.31226 (9)	0.1180 (3)	−0.2631 (6)	0.026 (1)
N(6)	0.34055 (8)	0.2069 (3)	−0.3981 (5)	0.031 (1)
O(6)	0.33370 (9)	0.2331 (3)	−0.6323 (5)	0.050 (2)
O(6′)	0.36900 (8)	0.2528 (3)	−0.2689 (5)	0.045 (1)
DL-Arginine				
C(1)	0.44408 (9)	−0.2599 (3)	0.2191 (5)	0.022 (1)
O(1)	0.46325 (7)	−0.1890 (2)	0.0646 (4)	0.033 (1)
O(1′)	0.45157 (7)	−0.2721 (2)	0.4645 (4)	0.033 (1)
C(2)	0.40926 (8)	−0.3450 (3)	0.1061 (5)	0.023 (1)
N(2)	0.39348 (8)	−0.2780 (3)	−0.1400 (5)	0.026 (1)
C(3)	0.4234 (1)	−0.4854 (3)	0.0325 (6)	0.029 (2)
C(4)	0.4374 (1)	−0.5712 (3)	0.2664 (6)	0.033 (2)
C(5)	0.4468 (1)	−0.7118 (3)	0.1746 (6)	0.033 (2)
N(6)	0.46573 (8)	−0.7940 (3)	0.3809 (5)	0.030 (1)
C(7)	0.44901 (9)	−0.8975 (3)	0.4990 (5)	0.024 (1)
N(7)	0.41529 (9)	−0.9541 (3)	0.4076 (5)	0.034 (1)
N(8)	0.46690 (9)	−0.9467 (3)	0.7169 (5)	0.030 (1)
Complex (**2**)				
Picric acid				
C(1)	0.1333 (3)	0.5701[a]	0.7846 (3)	0.032 (3)

Table 2. (continued)

Atom	x	y	z	U_{eq}
O(1)	0.1952 (2)	0.462 (2)	0.7833 (5)	0.055 (3)
C(2)	0.1175 (3)	0.793 (2)	0.8629 (4)	0.029 (3)
N(2)	0.1798 (3)	0.921 (2)	0.9447 (4)	0.033 (3)
O(2)	0.2448 (2)	0.838 (2)	0.9463 (4)	0.056 (3)
O(2′)	0.1650 (3)	1.107 (2)	1.0102 (5)	0.060 (3)
C(3)	0.0455 (3)	0.891 (2)	0.8696 (4)	0.029 (3)
C(4)	−0.0156 (3)	0.778 (2)	0.7953 (4)	0.029 (3)
N(4)	−0.0897 (3)	0.887 (2)	0.7994 (4)	0.034 (3)
O(4)	−0.0968 (3)	1.088 (2)	0.8634 (5)	0.055 (3)
O(4′)	−0.1441 (2)	0.773 (2)	0.7364 (4)	0.053 (3)
C(5)	−0.0073 (3)	0.573 (2)	0.7137 (4)	0.029 (3)
C(6)	0.0643 (3)	0.478 (2)	0.7053 (5)	0.026 (3)
N(6)	0.0693 (3)	0.270 (2)	0.6128 (4)	0.041 (3)
O(6)	0.0143 (4)	0.124 (2)	0.5830 (4)	0.057 (3)
O(6′)	0.1284 (3)	0.256 (2)	0.5649 (6)	0.088 (5)
L-Arginine				
C(1)	0.3746 (3)	−0.160 (2)	0.2164 (5)	0.025 (3)
O(1)	0.4187 (2)	−0.324 (2)	0.1843 (5)	0.049 (3)
O(1′)	0.3876 (2)	0.087 (1)	0.2332 (4)	0.030 (2)
C(2)	0.2972 (2)	−0.260 (2)	0.2419 (5)	0.022 (3)
N(2)	0.2815 (2)	−0.520 (2)	0.1729 (4)	0.034 (2)
C(3)	0.2948 (3)	−0.307 (2)	0.3827 (5)	0.038 (3)
C(4)	0.2975 (3)	−0.048 (2)	0.4586 (5)	0.034 (3)
C(5)	0.2910 (3)	−0.114 (2)	0.5955 (5)	0.044 (3)
N(6)	0.2949 (2)	0.123 (2)	0.6753 (4)	0.036 (3)
C(7)	0.3581 (3)	0.215 (2)	0.7412 (4)	0.026 (3)
N(7)	0.4258 (3)	0.115 (2)	0.7252 (5)	0.046 (3)
N(8)	0.3549 (3)	0.414 (2)	0.8215 (5)	0.041 (3)
Water				
O(1)	0.5003 (2)	0.144 (2)	0.0636 (4)	0.041 (2)
O(2)	0.5032 (3)	0.233 (2)	0.4316 (4)	0.054 (3)
Complex (**3**)				
Picric acid (molecule A)				
C(1)	0.0326[a)]	0.5683[a)]	0.3212[a)]	0.044 (4)
O(1)	0.0632 (6)	0.4891 (3)	0.348 (1)	0.055 (3)
C(2)	−0.0757 (6)	0.6314 (4)	0.452 (1)	0.042 (4)
N(2)	−0.1560 (6)	0.6005 (4)	0.612 (1)	0.051 (4)
O(2)	−0.1080 (6)	0.5358 (4)	0.721 (1)	0.064 (4)
O(2′)	−0.2696 (7)	0.6434 (5)	0.639 (2)	0.088 (6)
C(3)	−0.1107 (6)	0.7185 (4)	0.439 (1)	0.041 (4)
C(4)	−0.0399 (6)	0.7525 (4)	0.288 (1)	0.038 (4)
N(4)	−0.0677 (7)	0.8458 (4)	0.278 (1)	0.050 (4)
O(4)	−0.1499 (8)	0.8937 (4)	0.416 (1)	0.088 (5)
O(4′)	−0.0098 (7)	0.8718 (3)	0.129 (1)	0.075 (4)
C(5)	0.0565 (6)	0.6983 (4)	0.136 (1)	0.041 (4)
C(6)	0.0897 (6)	0.6085 (4)	0.148 (1)	0.039 (4)
N(6)	0.1883 (5)	0.5572 (3)	−0.020 (1)	0.035 (3)
O(6)	0.2286 (6)	0.5939 (3)	−0.170 (1)	0.062 (4)
O(6′)	0.2307 (6)	0.4791 (3)	−0.006 (1)	0.058 (4)
Picric acid (molecule B)				
C(1)	0.3809 (6)	−0.1068 (4)	0.240 (1)	0.038 (4)
O(1)	0.3523 (5)	−0.0271 (3)	0.227 (1)	0.050 (3)
C(2)	0.4866 (7)	−0.1697 (4)	0.103 (1)	0.043 (4)
N(2)	0.5640 (6)	−0.1374 (4)	−0.056 (1)	0.049 (4)
O(2)	0.5036 (7)	−0.0768 (4)	−0.186 (1)	0.073 (5)
O(2′)	0.6789 (7)	−0.1744 (6)	−0.070 (2)	0.094 (6)
C(3)	0.5199 (7)	−0.2581 (4)	0.111 (1)	0.048 (4)
C(4)	0.4486 (7)	−0.2921 (4)	0.259 (1)	0.046 (4)
N(4)	0.4782 (7)	−0.3855 (4)	0.260 (1)	0.055 (4)
O(4)	0.5683 (9)	−0.4324 (4)	0.132 (2)	0.099 (6)
O(4′)	0.4138 (7)	−0.4151 (4)	0.388 (1)	0.087 (5)
C(5)	0.3507 (7)	−0.2390 (5)	0.401 (1)	0.048 (4)
C(6)	0.3181 (7)	−0.1506 (4)	0.394 (1)	0.038 (4)
N(6)	0.2185 (6)	−0.0993 (4)	0.566 (1)	0.047 (4)
O(6)	0.1761 (6)	−0.1363 (4)	0.716 (1)	0.068 (4)
O(6′)	0.1777 (5)	−0.0188 (3)	0.557 (1)	0.057 (4)
L-Lysine (molecule A)				
C(1)	0.3693 (5)	0.2229 (3)	0.983 (1)	0.031 (3)
O(1)	0.3197 (4)	0.2853 (2)	0.8493 (8)	0.036 (2)
O(1′)	0.3945 (4)	0.2303 (3)	1.2363 (8)	0.044 (3)
C(2)	0.4070 (5)	0.1315 (3)	0.834 (1)	0.028 (3)
N(2)	0.3179 (5)	0.1294 (3)	0.5713 (9)	0.035 (3)
C(3)	0.5526 (6)	0.1080 (4)	0.768 (1)	0.040 (4)
C(4)	0.6590 (6)	0.1063 (4)	1.010 (1)	0.046 (4)
C(5)	0.8016 (6)	0.0790 (4)	0.917 (1)	0.043 (4)
C(6)	0.9106 (6)	0.0759 (4)	1.151 (1)	0.039 (4)
N(7)	1.0441 (5)	0.0476 (3)	1.047 (1)	0.045 (3)
L-Lysine (molecule B)				
C(1)	0.0320 (5)	0.2467 (3)	0.920 (1)	0.030 (3)
O(1)	0.0639 (4)	0.1825 (3)	0.7473 (9)	0.043 (3)
O(1′)	0.0365 (6)	0.2400 (3)	1.1600 (9)	0.061 (4)
C(2)	−0.0261 (6)	0.3370 (4)	0.829 (1)	0.032 (3)
N(2)	0.0570 (5)	0.3486 (3)	0.628 (1)	0.040 (3)
C(3)	−0.1732 (7)	0.3460 (4)	0.693 (2)	0.054 (4)
C(4)	−0.2678 (6)	0.3522 (5)	0.896 (2)	0.049 (5)
C(5)	−0.4062 (8)	0.3399 (6)	0.764 (2)	0.059 (6)
C(6)	−0.4795 (7)	0.4081 (5)	0.599 (2)	0.044 (4)
N(7)	−0.6224 (5)	0.3996 (4)	0.502 (1)	0.047 (3)
Complex (**4**)				
Picric acid (molecule A)				
C(1)	0.1278 (3)	0.5030[a)]	0.7007 (6)	0.028 (2)
O(1)	0.2328 (2)	0.4844 (3)	0.7749 (5)	0.038 (2)
C(2)	0.0316 (3)	0.4367 (3)	0.6897 (5)	0.029 (2)
N(2)	0.0642 (3)	0.3391 (3)	0.7559 (5)	0.031 (2)
O(2)	0.1504 (3)	0.3023 (3)	0.7191 (6)	0.050 (2)
O(2′)	0.0000 (3)	0.2979 (3)	0.8370 (6)	0.057 (2)
C(3)	−0.0853 (4)	0.4562 (4)	0.6333 (6)	0.033 (2)
C(4)	−0.1179 (4)	0.5478 (4)	0.5657 (6)	0.039 (3)
N(4)	−0.2420 (3)	0.5710 (4)	0.5033 (6)	0.042 (3)
O(4)	−0.3130 (4)	0.5094 (5)	0.499 (1)	0.109 (5)
O(4′)	−0.2714 (3)	0.6513 (4)	0.4504 (6)	0.057 (3)
C(5)	−0.0337 (4)	0.6166 (3)	0.5604 (6)	0.035 (2)
C(6)	0.0820 (4)	0.5944 (3)	0.6189 (5)	0.033 (2)
N(6)	0.1654 (3)	0.6683 (3)	0.6002 (5)	0.035 (2)
O(6)	0.1291 (3)	0.7498 (3)	0.5652 (6)	0.050 (2)
O(6′)	0.2703 (3)	0.6478 (3)	0.6212 (5)	0.048 (2)
Picric acid (molecule B)				
C(1)	0.3022 (3)	0.9868 (3)	1.0060 (6)	0.029 (2)
O(1)	0.4112 (2)	0.9855 (3)	1.0692 (4)	0.035 (2)
C(2)	0.2287 (3)	0.9039 (3)	0.9486 (5)	0.032 (2)
N(2)	0.2817 (3)	0.8104 (3)	0.9557 (5)	0.035 (2)
O(2)	0.3828 (3)	0.8033 (3)	0.9389 (5)	0.044 (2)
O(2′)	0.2228 (3)	0.7416 (3)	0.9787 (5)	0.041 (2)
C(3)	0.1071 (4)	0.9053 (4)	0.8879 (5)	0.036 (2)
C(4)	0.0480 (3)	0.9918 (4)	0.8808 (6)	0.036 (2)
N(4)	−0.0775 (3)	0.9930 (4)	0.8143 (7)	0.049 (3)
O(4)	−0.1292 (3)	0.9208 (4)	0.7469 (9)	0.073 (3)
O(4′)	−0.1298 (4)	1.0684 (4)	0.8216 (9)	0.084 (4)
C(5)	0.1111 (4)	1.0759 (4)	0.9364 (6)	0.037 (3)
C(6)	0.2305 (4)	1.0732 (3)	0.9903 (6)	0.031 (3)
N(6)	0.2897 (3)	1.1644 (3)	1.0359 (5)	0.031 (2)
O(6)	0.2493 (4)	1.2208 (3)	1.1252 (7)	0.065 (3)
O(6′)	0.3759 (3)	1.1803 (3)	0.9738 (5)	0.051 (2)
L-Ornitine				
C(1)	0.4727 (4)	0.8007 (3)	0.4605 (6)	0.039 (3)
O(1)	0.3877 (3)	0.8042 (4)	0.3357 (5)	0.063 (3)
O(1′)	0.4780 (3)	0.7558 (3)	0.6184 (5)	0.051 (2)
C(2)	0.5883 (3)	0.8520 (3)	0.4614 (5)	0.035 (2)
N(2)	0.5953 (3)	0.8537 (3)	0.2629 (5)	0.037 (2)
C(3)	0.5864 (3)	0.9547 (3)	0.5290 (6)	0.032 (2)
C(4)	0.5838 (3)	0.9657 (3)	0.7319 (5)	0.035 (2)
C(5)	0.5857 (3)	1.0713 (3)	0.7773 (6)	0.035 (2)
N(6)	0.5911 (3)	1.0877 (3)	0.9780 (5)	0.030 (2)

a) These atomic positions were fixed to define the origin during the refinement.

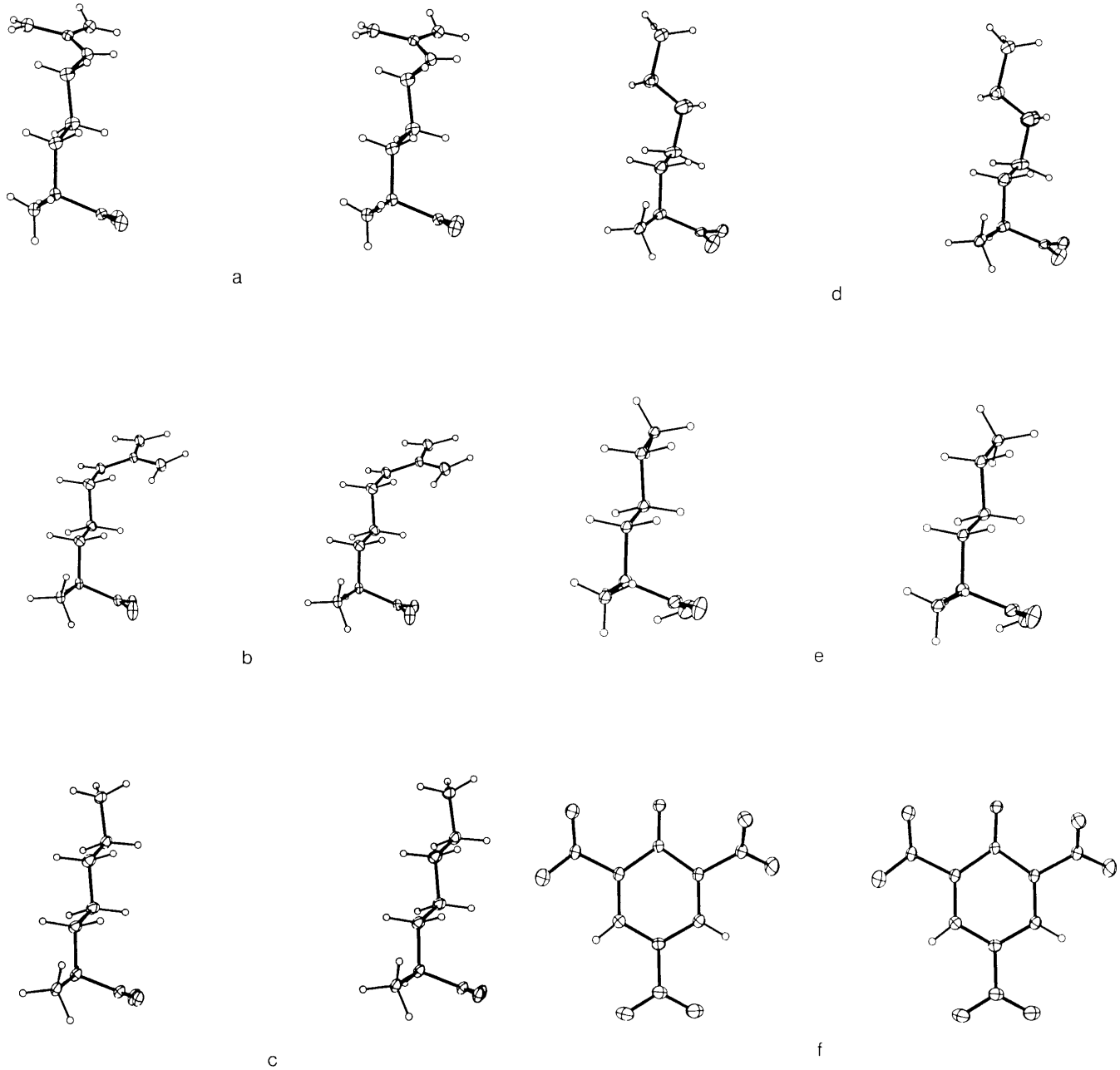

Fig. 2. Stereoscopic Molecular Conformations of DL-Arg (a), L-Arg (b), L-Lys Mol-A (c), Mol-B (d), L-Orn (e) and PA (f)
Among six different PA molecular conformations in **1**—**4** complexes, figure (f) was selected from **1** as a representative molecular conformation.

(0.007—0.01 Å for lengths and 0.3—0.7° for angles). When they are compared with the statistical values of general organic compounds,[8] however, the bonding parameters of **1**—**4** are all within the acceptable region.

Arg is a basic amino acid with a guanidyl side-chain functional group and took a zwitterionic state with α-carboxyl deprotonated and α-amino protonated in **1** and **2**. The molecular conformation of Arg is usually observed in the extended conformation[9,10] with $\Psi = ca. -15°$, $\chi^1 = ca. \pm 60°$, $\chi^2 = ca. 180°$, $\chi^3 = ca. 180°$ and $\chi^4 = ca. \pm 10°$. It can also adopt the conformation with $\chi^1 = \chi^2 = \chi^3 = ca. 180°$.[10] Both Args in **1** and **2** belong to the latter conformation, although their χ^4 values are largely different from each other. The guanidyl groups, which are in a cationic state, show no significant deformation from the planarity, and are almost perpendicular to the plane consisting of a C(2)–C(3)–C(4)–C(5) bond sequence ($\chi^4 = 111.2°$ in **1** and $-93.5°$ in **2**). Lys in **3** is also a basic amino acid characterized by having a cationic amine group at the C^ε atom. There are two crystallographically independent Lys molecules in **3**, and their α-carboxyl and α-amino groups are both in a zwitterionic state. As a simple straight chain, the preferred conformation of Lys[10,11] is known to be fully extended with $\Psi = ca. -20°$, $\chi^1 = ca. -60°$, $\chi^2 = \chi^3 = \chi^4 = ca. 180°$. The two L-Lys's in **3** take on conformations which are slightly deviated from the preferred one; one of them takes a fully extended conformation, and the other is twisted into *gauche* at $\chi^3 (= -64.0°)$. L-Orn in **4**, though not definitive, could be in the electronic state of the neutral α-carboxyl and the cationic α- and ε-amino groups, as judged from its bonding parameters of C(1)–O(1) = 1.172(6) Å, C(1)–O(1′) =

1.311(6) Å, C(2)–N(2) = 1.485(5) Å, C(5)–N(6) = 1.481(5) Å, O(1)–C(1)–O(1′) = 123.8(3)°, C(2)–C(1)–O(1) = 123.8(3)° and C(2)–C(1)–O(1′) = 112.3(3)°. L-Orn takes a fully extended conformation ($\chi^1 = \chi^2 = \chi^3 = ca.\ 180°$).

On the whole, the basic amino acids in **1**—**4** take on an open conformation, respectively, and this would be due to the interaction with the planar PA molecule (discussed later), in addition to their intrinsic conformational preference. Compared with the molecular conformations of Arg and Lys in their uncomplexed crystal structures,[9,11] the present result shows a significant conformational difference at the torsion angle of χ^1. Of the three χ^1 minima ($\pm 60°$, 180°), $\chi^1 = ca.\ \pm 60°$ is most frequently observed at the isolated state.[10] However, $\chi^1 = ca.\ 180°$ was commonly observed in the complexes with the PA molecule.

Concerning the molecular conformation of PA, the nitro groups are all twisted out of the benzene plane ranging from −40° to 42° around the C–N bond (Table 3), and such a notable tilting appears to be a common feature of PA itself; this may result from the effective interaction with the polar atoms of a partner in the complex.

Crystal Structures and Hydrogen Bonds Perspective views of respective crystal structures are shown in Fig. 3. Hydrogen bonding networks formed in the respective crystal structures are schematically depicted in Fig. 4; possible hydrogen bonds and electrostatic short contacts (<3.2 Å) are listed in Table 4.

The DL-Arg and PA molecules in complex **1** are alternatively arranged perpendicular to the *a*-axis. The centrosymmetrically-related D- and L-Args form a dimer

Table 3. Conformational Torsion Angles (°) of DL-Arg, L-Arg, L-Lys, L-Orn and PA Molecules

	DL-Arg	L-Arg	L-Lys		L-Orn
			Mol-A	Mol-B	
O(1)–C(1)–C(2)–C(3)	92.5 (3)	97.7 (6)	89.8 (5)	74.0 (5)	85.2 (4)
O(1′)–C(1)–C(2)–C(3)	−85.3 (2)	−81.0 (5)	−88.2 (5)	−101.2 (5)	−92.0 (4)
O(1)–C(1)–C(2)–N(2):Ψ	−26.3 (2)	−22.2 (5)	−27.4 (4)	−45.0 (4)	−32.1 (3)
O(1′)–C(1)–C(2)–N(2)	156.0 (2)	159.1 (5)	154.6 (5)	139.9 (5)	150.6 (4)
N(2)–C(2)–C(3)–C(4):χ^1	−175.6 (3)	−170.8 (6)	−179.8 (5)	−169.2 (6)	−177.9 (4)
C(1)–C(2)–C(3)–C(4)	65.9 (3)	69.9 (5)	62.2 (5)	71.7 (6)	66.3 (4)
C(2)–C(3)–C(4)–C(5):χ^2	174.6 (3)	177.4 (6)	178.2 (6)	−166.8 (7)	178.4 (4)
C(3)–C(4)–C(5)–N(6):χ^3	172.0 (3)	178.8 (6)			−176.3 (3)
C(3)–C(4)–C(5)–C(6):χ^3			−179.6 (6)	−64.0 (7)	
C(4)–C(5)–N(6)–C(7):χ^4	111.2 (3)	−93.5 (7)			
C(4)–C(5)–C(6)–N(7):χ^4			178.9 (5)	−172.8 (7)	
C(5)–N(6)–C(7)–N(7)	13.0 (3)	9.4 (6)			
C(5)–N(6)–C(7)–N(8)	−167.3 (4)	−172.7 (8)			

	PA1[a]	PA2	PA3		PA4	
			Mol-A	Mol-B	Mol-A	Mol-B
C(1)–C(2)–N(2)–O(2)	2.4 (3)	−0.0 (5)	28.4 (6)	−38.0 (6)	−39.8 (4)	−27.9 (4)
C(1)–C(2)–N(2)–O(2′)	−178.9 (3)	−179.6 (7)	−154.2 (7)	147.5 (8)	143.6 (4)	152.0 (4)
C(3)–C(4)–N(4)–O(4)	7.3 (3)	4.3 (6)	3.3 (6)	1.2 (7)	−5.2 (5)	−7.6 (5)
C(3)–C(4)–N(4)–O(4′)	−173.6 (4)	−176.4 (7)	−175.1 (8)	−179.1 (8)	177.4 (5)	174.7 (6)
C(5)–C(6)–N(6)–O(6)	−39.1 (3)	−26.6 (6)	−4.6 (6)	3.9 (6)	12.7 (4)	42.0 (5)
C(5)–C(6)–N(6)–O(6′)	139.3 (3)	150.6 (7)	174.2 (6)	−175.5 (7)	−168.0 (5)	−135.3 (5)

a) PA1—PA4 represent PAs in complexes (**1**—**4**), respectively.

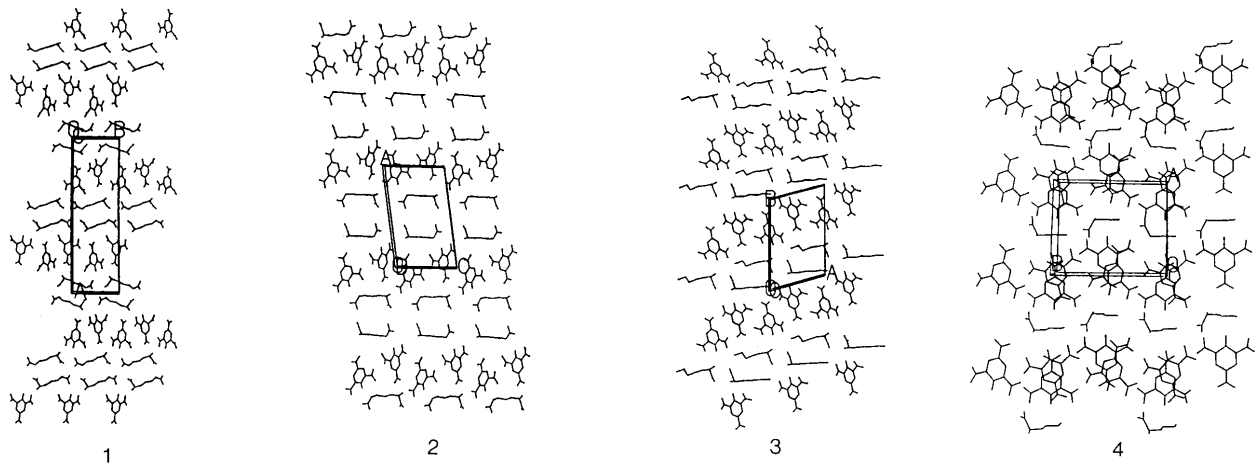

Fig. 3. Molecular Packings in the Complex Crystal Structures of **1**—**4**

Table 4. Possible Hydrogen Bonds and Short Contacts (<3.2 Å)[a]

Donor at x, y, z	Acceptor at symmetry operation		Distance (Å)
Complex **1**			
Hydrogen bonds			
N(2)A	O(1)P	x, y, z	2.863 (3)
N(2)A	O(1′)A	x, y, z−1	2.793 (3)
N(2)A	O(4′)P	1/2−x, y−1/2, −z−1/2	2.921 (4)
N(6)A	O(1′)A	1−x, −y−1, 1−z	2.886 (3)
N(7)A	O(1)P	x, y−1, z	2.924 (3)
N(7)A	O(2)P	x, y−1, z	3.052 (4)
N(8)A	O(1)A	x, y−1, z+1	2.994 (4)
N(8)A	O(1)A	1−x, −y−1, 1−z	2.865 (4)
Short contact			
N(2)A	O(1)A	x, y, z	2.646 (3)
N(7)A	O(1)P	x, y−1, z+1	3.181 (3)
N(7)A	N(6)P	x, y−1, z+1	3.111 (4)
N(7)A	O(6′)P	x, y−1, z+1	3.060 (4)
N(2)P	O(4′)P	1/2−x, y−1/2, −z−1/2	2.905 (4)
N(4)P	O(2′)P	1/2−x, y+1/2, 1/2−z	2.957 (4)
Complex **2**			
Hydrogen bonds			
N(2)A	O(2′)P	x, y−2, z−1	3.129 (8)
N(2)A	O(4′)P	−x, y−3/2, 1−z	2.948 (8)
N(2)A	O(1′)A	x, y−1, z	2.740 (7)
N(6)A	O(1)P	x, y, z	2.823 (8)
N(7)A	O(1)A	1−x, y+1/2, 1−z	2.814 (9)
N(7)A	O(2)W	1−x, y−1/2, 1−z	2.949 (9)
N(8)A	O(1)P	x, y, z	2.823 (9)
N(8)A	O(1)W	1−x, y+1/2, 1−z	2.928 (8)
O(1)W	O(1)A	x, y, z	3.134 (8)
O(1)W	O(1′)A	x, y, z	2.911 (7)
O(1)W	O(1)W	1−x, y−1/2, −z	2.850 (7)
O(2)W	O(1′)A	x, y, z	2.835 (8)
O(2)W	O(2)W	1−x, y−1/2, 1−z	2.912 (8)
Short contacts			
O(1′)A	O(1)A	x, y+1, z	3.058 (8)
N(2)A	O(1)A	x, y, z	2.617 (8)
N(2)A	O(2)P	x, y−1, z−1	3.013 (8)
N(6)A	O(6′)P	x, y, z	3.10 (1)
O(2′)P	O(4′)P	−x, y+1/2, 2−z	2.919 (9)
N(4)P	O(2′)P	−x, y−1/2, 2−z	2.954 (9)
O(4)P	O(2′)P	−x, y−1/2, 2−z	3.094 (9)
N(6)P	O(6)P	−x, y+1/2, 1−z	2.979 (9)
O(6)P	C(4)P	x, y−1, z	2.970 (9)
O(6)P	O(6)P	−x, y−1/2, 1−z	3.071 (9)
Complex **3**			
Hydrogen bonds			
N(2)LA	O(1′)LA	x, y, z−1	2.845 (6)
N(2)LA	O(1)LB	x, y, z	2.789 (6)
N(2)LA	O(1)PB	x, y, z	2.789 (7)
N(7)LA	O(6′)PB	x+1, y, z+1	2.951 (7)
N(7)LA	O(1)LB	x+1, y, z	2.893 (7)
N(7)LA	O(1′)LB	x+1, y, z	3.015 (7)
N(2)LB	O(1)LA	x, y, z	2.764 (6)
N(2)LB	O(1′)LB	x, y, z−1	2.728 (7)
N(2)LB	O(1)PA	x, y, z	2.859 (7)
N(7)LB	O(6′)PA	x−1, y, z+1	3.062 (8)
N(7)LB	O(1′)LA	x−1, y, z−1	2.798 (7)
N(7)LB	O(6′)PA	x−1, y, z	3.057 (8)
Short contacts			
O(1)LA	O(6′)PA	x, y, z+1	2.993 (7)
N(2)LA	O(1)LA	x, y, z	2.664 (6)
N(2)LA	O(6′)PB	x, y, z	3.072 (7)
C(6)LA	O(4′)PA	x+1, y−1, z+1	3.130 (9)
N(7)LA	O(6′)PB	x+1, y, z	2.955 (7)
N(7)LA	O(4′)PA	x+1, y−1, z+1	3.103 (8)
N(7)LA	O(1)PB	x+1, y, z+1	3.142 (7)
O(1)LB	O(6′)PB	x, y, z	3.167 (7)
N(2)LB	O(1)LB	x, y, z	2.791 (7)
N(2)LB	O(2)PA	x, y, z	3.032 (8)
C(6)LB	O(4′)PB	x−1, y+1, z	3.05 (1)
N(7)LB	O(1)LA	x−1, y, z	2.956 (7)
C(1)PA	O(6)PA	x, y, z+1	3.070 (5)
O(2′)PA	O(2′)PB	x−1, y+1, z+1	3.00 (1)
N(4)PA	O(2′)PB	x−1, y+1, z	2.99 (1)
O(4)PA	O(2′)PB	x−1, y+1, z	3.03 (1)
O(4′)PA	N(6)PB	x, y+1, z	3.056 (9)
O(4′)PA	O(6)PB	x, y+1, z−1	3.034 (9)
C(6)PA	O(2)PA	x, y, z−1	3.049 (9)
N(6)PA	O(4′)PB	x, y+1, z	2.946 (9)
C(1)PB	O(2)PB	x, y, z+1	3.007 (9)
N(4)PB	O(2′)PA	x+1, y−1, z	3.08 (1)
C(6)PB	O(2)PB	x, y, z+1	2.96 (1)
Complex **4**			
Hydrogen bonds			
O(1′)O	O(6′)PA	x, y, z	2.868 (5)
O(1′)O	O(2)PB	x, y, z	2.930 (5)
N(2)O	O(1)PA	1−x, y+1/2, 1−z	2.789 (5)
N(2)O	O(1)PB	x, y, z−1	2.924 (5)
N(2)O	O(6′)PB	1−x, y−1/2, 1−z	3.065 (5)
N(6)O	O(1)PA	1−x, y+1/2, 2−z	2.786 (5)
N(6)O	O(1)PB	x, y, z	2.767 (5)
N(6)O	O(6′)PB	x, y, z	2.827 (5)
Short contacts			
O(1)O	N(2)PB	x, y, z−1	2.760 (5)
O(1)O	O(2)PB	x, y, z−1	2.908 (5)
O(1)O	O(2′)PB	x, y, z−1	2.972 (5)
N(2)O	O(1)O	x, y, z	2.706 (5)
N(2)O	O(2)PA	1−x, y+1/2, 1−z	3.030 (5)
N(2)O	O(2)PB	x, y, z−1	3.061 (5)
N(6)O	O(6′)PA	1−x, y+1/2, 2−z	3.103 (5)
N(6)O	O(2)PB	1−x, y+1/2, 2−z	3.092 (5)
N(6)O	O(2′)PB	1−x, y+1/2, 2−z	3.028 (5)
N(2)PA	O(6)PA	−x, y−1/2, 1−z	3.093 (5)
O(2)PA	O(4′)PA	−x, y−1/2, 1−z	2.993 (6)
O(2′)PA	O(6)PA	−x, y−1/2, 1−z	3.040 (6)
O(4′)PA	O(6′)PB	−x, y−1/2, 1−z	3.080 (6)
O(2′)PA	C(3)PB	−x, y−1/2, 2−z	3.040 (6)
N(6)PA	O(2′)PB	x, y, z	2.887 (5)
O(6)PA	N(2)PB	x, y, z	3.096 (5)
O(6)PA	O(2′)PB	x, y, z	2.966 (5)

a) The suffix letters A, P and W in **1** and **2** indicate Arg, PA and water molecules, respectively. The suffix letters of LA, LB, PA and PB in **3** correspond to Lys molecule A, Lys molecule B, PA molecule A and molecule B, and those of O, PA and PB in **4** to Orn, PA molecule A and molecule B, respectively.

by two kinds of NH···O=C hydrogen bonds [N(6)···O(1′) and N(8)···O(1)] in a head-to-tail fashion, and are linked to the neighboring dimer by a N(8)···O(1) hydrogen bond, thus forming an infinite layer along the *b*- and *c*-directions. The DL-Arg and PA molecules are linked with each other by six hydrogen bonds and connect the respective DL-Arg and PA layers. Similar molecular packing is also observed in complex **2** in spite of the different space group, where the respective layers of L-Arg and PA molecules are running perpendicular to the *a*-axis. The head-to-tail interactions among L-Args, translated by diad screw symmetry, are formed by the N(7)···$O(H_2O)$···O(1′) and N(8)···$O(H_2O)$···O(1′) hydrogen bonds, thus forming the columns along the *b*-axis. These columns are linked with the PA layers expanding over the *b*- and *c*-directions by four different NH···O hydrogen bonds; several electrostatic short contacts contribute to the stabilization of crystal packing. Alternative parallel

arrangement of the doubly layered amino acids and the singly layered PAs along a crystallographic axis is also observed in complex **3**, where two structural isomers of L-Lys are arranged head-to-tail with $N\eta H_3^+ \cdots O(\alpha\text{-}COO^-)$ hydrogen bonds, and are further linked with the neighboring ones by $\alpha\text{-}NH_3^+ \cdots O(\alpha\text{-}COO^-)$ hydrogen bonds. PA molecules form a layer expanding perpendicular to the *b*-axis, and interact with the layers of Lys by NH···O hydrogen bonds and short contacts. The crystal **4** consists of a 1:2 complex of L-Orn and PA molecules. Two crystallographically independent PA isomers are stacked on top of each other by extensive electrostatic short contacts and consequently form the columns parallel to the *c*-axis. The layers of L-Orn molecules, which are arranged head-to-tail perpendicular to the *a*-axis, intervene among these PA columns and are linked by NH···O and OH···O hydrogen bonds.

Common Crystal Packing and Molecular Interaction A packing pattern commonly observed in the crystal structures of **1**—**4** is arranged in such a way that the PAs themselves form layers by electrostatic interactions, and the single or double layers of the head-to-tail arranged basic amino acids, which are stabilized by two to four intermolecular NH···O hydrogen bonds, intervene among the PA layers (Fig. 3). The amino or guanidyl group of the basic amino acid side-chain participates not only in forming the head-to-tail molecular arrangement of itself but also in linking with PA by NH···O hydrogen bonds.

As a feature of the molecular interaction commonly found in complexes **1**—**4**, on the other hand, it could be stated that simultaneous fixation occurs at three portions of the amino acid (α-amino, α-carboxyl and terminal amino or guanidyl groups) by a hydrogen bond and/or electrostatic interactions (Fig. 4, Table 4). Since the basic amino acid is characterized by the basic group of the side chain terminal, this kind of fixation at three portions by hydrogen bond or electrostatic interactions would be an elemental stereostructural requisite for the recognition of a basic amino acid by the host molecule. In this definition, it appears interesting to compare the present interactions with those in the crystal structure of the periplasmic lysine/arginine/ornithine-binding protein (LAO) complexed with lysine,[12] where three polar portions of L-Lys are tightly fixed by two to four hydrogen bonds with neighboring polar residues. As is shown in Fig. 5, the spatial orientation of the polar N and O atoms located at the LAO binding pocket is in the distribution range of respective polar atoms interacting with L-Lys in complex

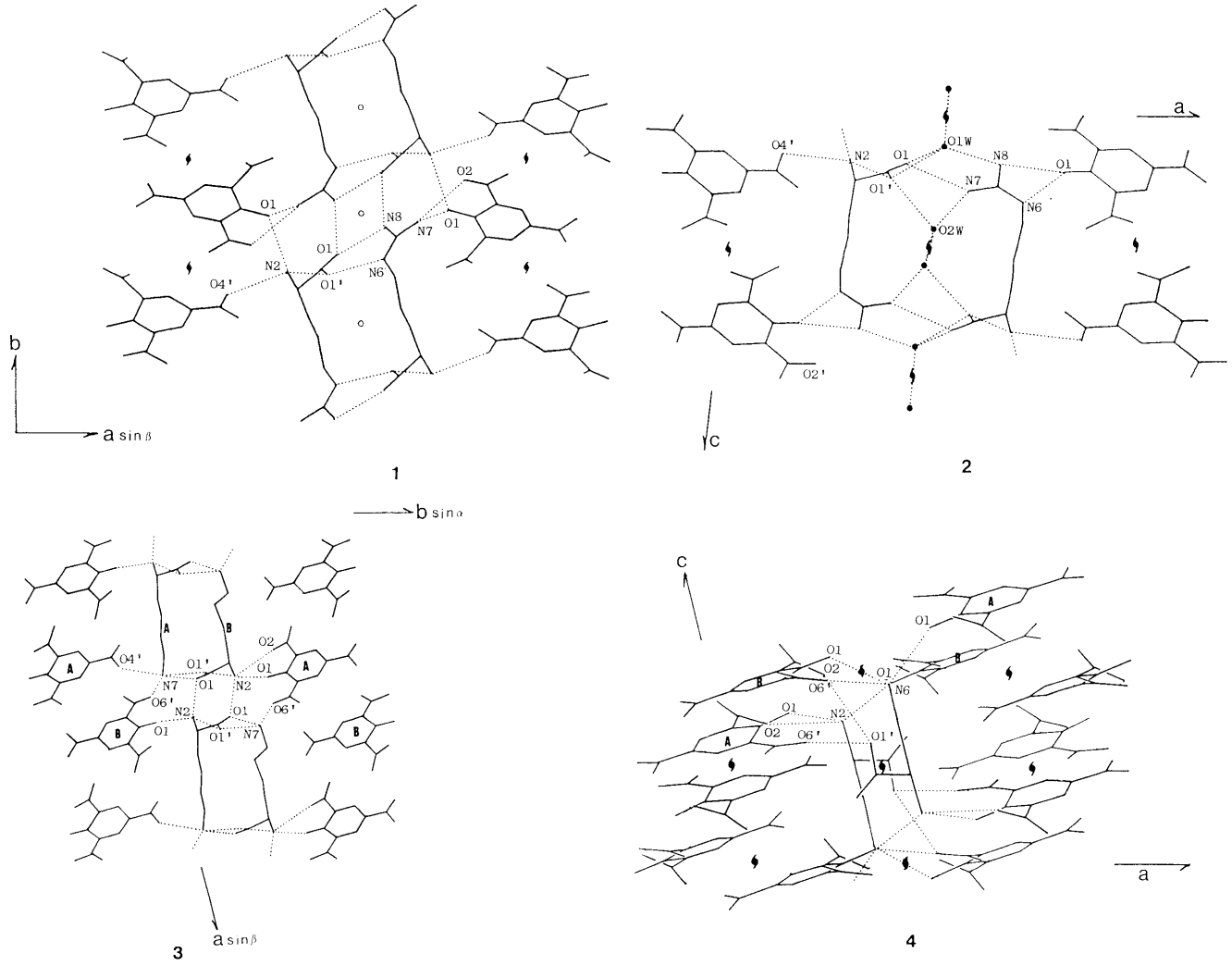

Fig. 4. Hydrogen-Bonding Network Formed in the Complex Crystals of **1**—**4**

The dotted lines represent possible hydrogen bonds.

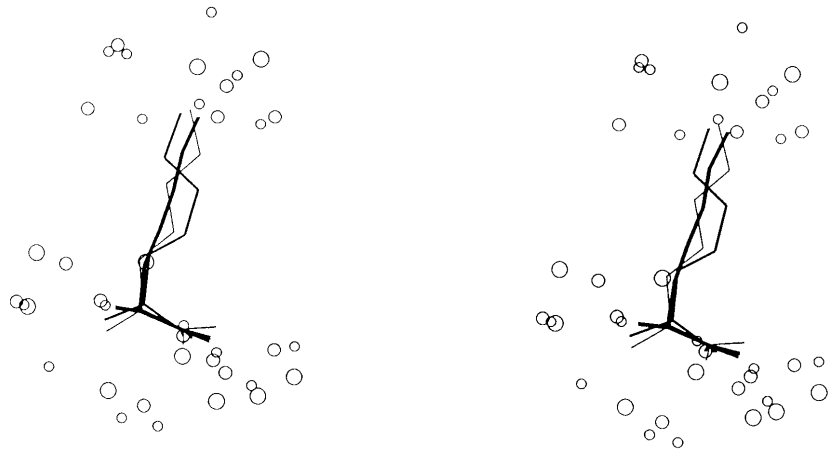

Fig. 5. Stereoscopic Superposition of Polar N or O Atoms Hydrogen-Bonded to L-Lys in LAO and Complex 3

L-Lys's ligated with LAO and of mol-A and mol-B in complex **3** are shown with the thick, thin and middle lines, and the polar N or O atoms interacting with these L-Lys's are shown with the largest, smallest and middle circles, respectively. The N or O polar atoms which interact with L-Lys less than 3.2 Å are also shown for complex **3**.

3. It appears noteworthy that the spatial dispositions of polar atoms around the respective amino acids in complexes **1**, **2** and **4** are also in the same distribution range, and this may be one reason why LAO can recognize Lys, Arg, and Orn each with equal selectivity.

In the L-Lys–LAO complex, the hydrocarbon chain of L-Lys is sandwiched between the aromatic Tyr14 and Phe52 residues and is stabilized by the stacking interactions. In contrast, the hydrocarbon chain of L-Lys in complex **3** is stabilized by the van der Waals contacts with the parallely arranged PA layers. Thus, it may be said that the fundamental requisite for the recognition of L-Lys by LAO protein is to some extent modeled in the present complex.

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