The Crystal Structure of the 1-(2-Carboxyethyl)uracil : Phenethylamine (1 : 1) Complex[1)]

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Synopsis. The crystal of the title complex is monoclinic, with a space group of Cc, a=5.678(1), b=33.814(7), c=8.058(2) Å, β=103.42(1)°, and Z=4. The two component molecules are linked to each other by hydrogen bonds between the amino and carboxyl groups. No prominent interaction was observed between benzene and uracil rings.

In effort to obtain information bearing on the nature of the interactions between nucleic acid bases and protein side groups, various studies have been done by using the model systems containing these components. As a result, the stacking interaction, as well as hydrogen bonding, with nucleic-acid bases has been found to be essential for the aromatic amino acids.[2–5)]

As part of the program aimed at exploring, at atomic resolution, the possible geometrical features of the interaction, we prepared the crystals of the 1:1 complex between 1-(2-carboxyethyl)uracil (CEU) and phenethylamine (PEA) as a model for uracil–phenylalanine interaction. The present paper will report its X-ray crystal structure.

Experimental

CEU, synthesized from uracil and acrylonitrile by the Ueda and Fox method[6)] (mp 186—187 °C), was added to a 50% ethanol aqueous solution containing an equimolar amount of PEA.. Transparent platelet crystals were obtained by slow evaporation at room temperature. Although oscillation and Weissenberg photographs showed the space group to be Cc or C2/c, it was assumed to be noncentrosymmetric Cc from the statistical distribution of the normalized structure factors. The crystal data are as follows: a=5.678(1), b=33.814(7), c=8.058(2) Å, β=103.42(1)°, Z=4, D_m=1.344(1), D_x=1.347 g cm^{-3}, $\mu(\text{Cu } K\alpha)$=8.315 cm^{-1}, $F(000)$=648. A total of 1297 independent intensity data were collected on a Rigaku four-circle diffractometer with graphite-monochromated Cu $K\alpha$ radiation using the ω-2θ scan technique ($\sin\theta/\lambda \leqq 0.588$ Å^{-1}) with a scan speed of 4°/min and a scan width of 1.2°; they were corrected for the Lorentz and polarization factors, but not for the absorption effects (crystal size: 0.4×0.3×0.4 mm^3).

The structure was solved by the direct method with the MULTAN program.[7)] All the non-hydrogen atoms appeared clearly in the E-map, while the hydrogen atoms were found on a difference Fourier map. The R value was finally reduced to 0.029 by the block-diagonal least-squares refinement using the HBLS V program,[8)] with anisotropic thermal parameters for non-hydrogen atoms and isotropic ones for hydrogen atoms. The quantity minimized was $\sum w(|F_o|-|F_c|)^2$. In the final refinements, the following weighting scheme was used: w=0.3 for F=0.0, w=1.0 for $0.0<F_o\leqq 22.0$, and $w=1.0/[1.0+0.464(F_o-22.0)]$ for $F_o>22.0$. All the numerical calculations were carried out on an ACOS-900 computer at the Computation Center of Osaka University. The final positional parameters and equivalent isotropic temperature factors for non-hydrogen atoms are listed in Table 1.[9)]

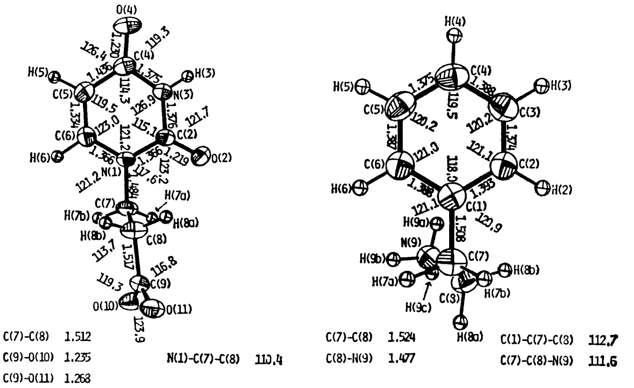

Fig. 1. Atomic numbering of the CEU:PEA complex with the bond lengths (l/Å) and angles (ϕ/°) of non-hydrogen atoms.
E.s.d.'s are 0.003 to 0.004 Å for lengths and 0.2 to 0.3° for angles. This figure also represents the molecular conformations projected onto the uracil and benzene rings.

Results and Discussion

The bond lengths and angles for non-hydrogen atoms are given in Fig. 1. The dimensions of the uracil ring are comparable with the published data.[10)] The ring is almost planar, with a maximum deviation of 0.014(3) Å at C(4), and the atoms attached to the ring except H(3) lie almost on the plane. The bond sequence of N(1)–C(7)–C(8)–C(9)–O(11) forms a fully

Table 1. Fractional coordinates and isotropic temperature factors of non-hydrogen atoms

The B values are the equivalent isotropic temperature factors calculated from the deposited anisotropic thermal parameters(B_{ij}) using this equation: $B_{eq}=4/3(B_{11}a^2+B_{22}b^2+B_{33}c^2+acB_{13}\cos\beta)$.

Atom	x	y	z	B_{eq}/Å^2
CEU				
N(1)	0.1547(3)	0.05736(5)	0.1367(2)	2.6
C(2)	0.0277(4)	0.08577(6)	0.0326(3)	2.6
O(2)	0.1016(3)	0.11942(4)	0.0255(2)	3.7
N(3)	−0.1933(4)	0.07383(6)	−0.0645(3)	3.1
C(4)	−0.2980(5)	0.03718(7)	−0.0639(3)	3.6
O(4)	−0.5024(4)	0.03150(6)	−0.1530(3)	5.2
C(5)	−0.1510(5)	0.00898(7)	0.0473(4)	4.2
C(6)	0.0648(5)	0.01999(7)	0.1407(3)	3.7
C(7)	0.3938(4)	0.06855(7)	0.2453(3)	3.0
C(8)	0.3634(4)	0.08753(8)	0.4089(3)	3.3
C(9)	0.5976(4)	0.10321(6)	0.5203(3)	2.6
O(10)	0.7908(3)	0.09612(6)	0.4808(3)	4.0
O(11)	0.5805(3)	0.12337(5)	0.6496(2)	3.0
PEA				
C(1)	0.3822(4)	0.20447(6)	−0.0697(3)	2.9
C(2)	0.2422(5)	0.21917(7)	0.0373(3)	3.3
C(3)	0.3022(5)	0.21176(8)	0.2097(4)	3.7
C(4)	0.5060(5)	0.18946(7)	0.2807(3)	3.8
C(5)	0.6478(5)	0.17502(7)	0.1774(4)	3.7
C(6)	0.5868(4)	0.18259(7)	0.0035(3)	3.3
C(7)	0.3066(5)	0.21043(7)	−0.2600(3)	3.4
C(8)	0.0909(4)	0.18485(7)	−0.3440(3)	3.3
N(9)	0.1377(3)	0.14254(6)	−0.3039(2)	2.9

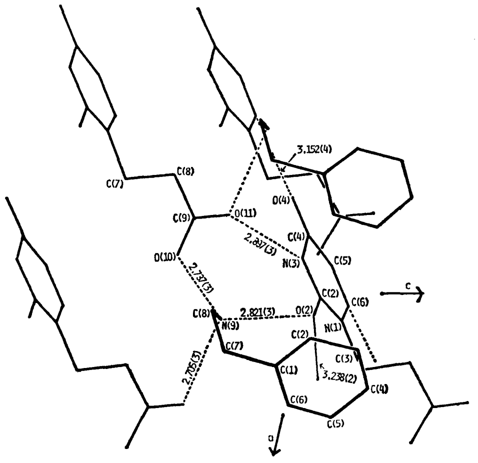

Fig. 2. The molecular arrangement of CEU and PEA in the crystal projected along the b-axis.
The broken lines represent the hydrogen bondings, and the thin line shows the short contact between the O(2) atom of CEU and the benzene ring of PEA.

extended *trans-zigzag* chain, and the torsion angles of C(2)–N(1)–C(7)–C(8), N(1)–C(7)–C(8)–C(9), and C(7)–C(8)–C(9)–O(11) are 84.9(3), −174.8(2), and 172.3(2)° respectively. The carboxyl group makes an angle of 100.6(1)° with the uracil ring. The bond distances and angles of the carboxyl group are in the range of the ionized form.[11]

The bond lengths and angles of PEA are in good agreement with those of phenethylamine[12] and L-phenylalanine.[13] The C–C bond lengths within the benzene ring are in the range of 1.374(4) to 1.393(4) Å (average value of 1.384 Å); this value is slightly shorter than that of the standard aromatic ring (1.395(3) Å).[11] Three hydrogen atoms of H(9a)–H(9c) are tetrahedrally bound to the N(9) atom, indicating the amino group to be in a cationic form. The plane of the aminoethyl group makes an angle of 96.1(1)° with the benzene ring, and the torsion angle of C(1)–C(7)–C(8)–N(9) is −55.3(3)°, in contrast to that of phenethylamine (=−171.1°).

The molecular arrangement projected along the b-axis is shown in Fig. 2. The hydrogen-bond lengths and angles are given in Table 2. In this complex, a salt bridge is formed between the anionic carboxyl group of CEU and the cationic amino group of PEA; the CEU and PEA molecules are linked to each other by three N–H···O hydrogen bonds between the amino nitrogen and carbonyl or carboxyl oxygen atoms [N(9)···O(2), N(9)···O(10) and N(9)···O(11)]. On the other hand, the N(3) of CEU at (*x*,*y*,*z*) is hydrogen-bonded to the O(11) atom of the same molecule translated at (−1+*x*, *y*, −1+*z*), and the O(4) atom is hydrogen-bonded to the C(6) atom translated by the c-glide plane, which forms the *trans-zigzag* connection along the c-axis.

Although the hydrophobic and/or stacking interaction between the aromatic rings was suggested from the solubility study of the phenylalanine–uridine interaction,[14] there was no specific interaction in this crystal; the dihedral angle between the benzene and uracil rings is almost at a right angle [89.1(1)°]. The hydrogen bonds between the acid and amine might be preferable to any specific interaction of the uracil base and the benzene ring.

TABLE 2. HYDROGEN-BOND DISTANCES(l/Å) AND ANGLES (ϕ/°)

Donor (D)	Acceptor (A)	D----A	H---A	D-H---A
N(3) (CEU)^1	O(11) (CEU)^2	2.897(3)	2.00(4)	168(4)
C(6) (CEU)^1	O(4) (CEU)^3	3.152(4)	2.16(4)	156(3)
N(9) (PEA)^1	O(2) (CEU)^1	2.821(3)	1.92(3)	172(3)
N(9) (PEA)^1	O(11) (CEU)^4	2.705(3)	1.77(3)	175(3)
N(9) (PEA)^1	O(10) (CEU)^1	2.787(3)	1.85(4)	177(3)

Symmetry code
1) x, y, z 2) $-1+x, y, -1+z$ 3) $1+x, -y, 1/2+z$ 4) $x, y, -1+z$

However, it is of interest to note that the O(2) atom of CEU points to the center of the benzene ring of PEA, with the distance of 3.238(2) Å, and that the angle of the C(2)–O(2) bond to the ring is 74.0°. Even though this distance is slightly longer than the van der Waals separation (3.1 Å), the possibility of interaction between the polarizable π-electron system and the polar carbonyl oxygen atom cannot be disregarded.

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