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## 1:1 Cytidine-*N*-Carbobenzoxyglutamic Acid Dihydrate

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**Abstract.** Monoclinic,  $P2_1$ ,  $a=29.63$  (3),  $b=8.43$  (2),  $c=5.14$  (1) Å,  $\beta=91.2$  (1)°,  $D_m=1.44$ ,  $D_x=1.44$  g cm<sup>-3</sup>,  $Z=2$ . The two components are hydrogen bonded to each other through the imidine group in cytidine and the  $\alpha$ -carboxylic acid group in *N*-carbobenzoxyglutamic acid (*N*-CBZ-glu). This hydrogen-bond scheme may play an important role in some biological processes involving peptide synthesis.

**Introduction.** Intermolecular complex formation involving organic compounds and nucleotide bases or their derivatives can be regarded as a powerful method for demonstrating biochemical interactions at the molecular level. We have been studying a large number of simple organic molecules which can bind with nucleotide bases, and have found that many substances hydrogen bond with one or two bases (Tamura, Sakurai & Sato, 1971). The existence of several complexes in the crystalline state has been demonstrated. In the amino acid series only one complex, cytosine-*N*-benzoylglycine complex monohydrate, has so far been studied (Tamura, Hata, Sato & Sakurai, 1972), while Jain & Sobell (1972) showed that the actinomycine-deoxyguanosine complex demonstrated a specific nucleoside peptide binding scheme. The present work forms part of a series of studies of molecular complex formation.

It was initially difficult to crystallize the complex and we found that complex formation proved to be very dependent on the solvent properties. Thus several organic solvents which were mixed with a 90% aqueous ethanol solution were tested. Hydrocarbons such as ligroin, cyclohexane, furan, acetone, ethyl acetate, xylene, mesitylene, nitrobenzene and chloroform help the formation of the complex whereas some very similar aromatic hydrocarbons, benzene, toluene and acetophenone, do not. Comparatively large single crystals of the complex of both components separated from a chloroform-ethanol-water (50:45:5 v/v%) mixture.

Along the  $c$  axis a small number of very weak reflexions were observable between the layer lines in the lower  $\sin \theta/\lambda$ ; but in the present work, we assumed the crystal to have an average structure whereby these spots could be ignored. 1380 intensities were collected on a Rigaku computer-controlled four-circle diffractometer. Lorentz-polarization corrections were made but the absorption correction was not applied.

The structure was analysed mainly by the program *MULTAN*, originally written by Germain, Main &

Woolfson (1971). Attempts at a modified  $E$ -map calculation were unsuccessful, but finally successive tangent-formula refinement of phases from the partially known structure gave all the atoms of the molecule. Throughout this analysis, mirror images along the  $b$  axis hindered the detection of the true atomic positions. Several cycles of block-diagonal least-squares refinement using all the data reduced  $R$  to 0.10. Owing to the disorder of the atomic positions, the bond

Table 1. *Positional coordinates* ( $\times 10^4$ ) *and isotropic temperature factors* (Å<sup>2</sup>)

E.s.d.'s are in parentheses.				
	$x$	$y$	$z$	$B$
<b>Cytidine</b>				
N(1)	1424 (4)	6522 (16)	495 (22)	1.99
C(2)	1670 (5)	5687 (20)	-1295 (31)	2.46
N(3)	1940 (4)	6521 (16)	-2891 (23)	1.98
C(4)	1985 (5)	8128 (19)	-2786 (31)	2.31
C(5)	1744 (5)	8948 (19)	-814 (28)	2.04
C(6)	1466 (5)	8151 (20)	721 (33)	2.53
O(2)	1629 (3)	4249 (13)	-1497 (19)	2.32
N(4)	2261 (4)	8865 (17)	-4384 (24)	2.70
C(1')	1138 (5)	5565 (21)	2240 (30)	2.37
C(2')	706 (4)	4983 (18)	690 (27)	1.50
C(3')	392 (4)	6409 (20)	985 (27)	2.01
C(4')	503 (4)	6923 (17)	3820 (28)	1.90
C(5')	403 (5)	8701 (21)	4127 (31)	2.74
O(1')	965 (3)	6599 (13)	4181 (19)	2.11
O(2')	545 (3)	3641 (13)	2086 (20)	2.37
O(3')	-65 (3)	6189 (13)	388 (20)	2.46
O(5')	568 (3)	9278 (14)	6583 (20)	2.67
<b><i>N</i>-CBZ-glu</b>				
O(1A)	2362 (3)	4990 (13)	3511 (20)	2.61
O(1B)	2751 (4)	7064 (15)	2125 (22)	3.52
C(1)	2695 (5)	5615 (20)	2418 (29)	2.13
C(2)	3063 (4)	4414 (18)	1564 (27)	1.79
C(3)	2885 (4)	3581 (20)	-922 (31)	2.58
C(4)	3152 (5)	2018 (19)	-1423 (30)	2.47
C(5)	2993 (6)	666 (23)	131 (34)	3.20
O(5A)	2717 (4)	756 (17)	1809 (26)	4.62
O(5B)	3203 (4)	-663 (15)	-341 (22)	3.58
N(2)	3483 (4)	5224 (16)	1071 (24)	2.40
C(1')	3723 (6)	5797 (23)	3088 (23)	3.28
O(1')	4073 (4)	6647 (18)	2321 (25)	4.75
O(2')	3630 (4)	5613 (17)	5353 (24)	4.20
C(3')	4382 (8)	7054 (33)	4447 (48)	6.42
C(4')	4385 (6)	9070 (25)	3715 (35)	4.07
C(5')	4134 (9)	10110 (37)	4762 (53)	7.99
C(6')	4135 (11)	11725 (46)	4065 (64)	10.42
C(7')	4429 (9)	12354 (36)	2293 (51)	7.46
C(8')	4675 (14)	11203 (57)	1200 (76)	13.98
C(9')	4727 (14)	9570 (49)	1989 (72)	12.57
<b>Water</b>				
W(O1)	2002 (4)	2107 (15)	5185 (22)	3.41
W(O2)	1144 (4)	1207 (19)	4267 (26)	5.07

lengths, particularly in the benzene ring, were not plausible. For individual atoms, the isotropic temperature factors were as high as  $13.9 \text{ \AA}^2$ . Thus the standard deviations for the atoms are fairly large, *ca*  $0.05 \text{ \AA}$ . For this reason it was not possible to detect the hydrogen atoms in a difference synthesis.

The atomic parameters are given in Table 1, and the intramolecular bond distances and angles calculated from these parameters are listed in Table 2.\*

**Discussion.** Fig. 1 shows the intermolecular packing in which the two components are bound to each other through the imidine group in cytidine and the carboxylic acid group at the  $\alpha$ -position in *N*-CBZ-glu. The hydrogen-bond distances of 2.60 and 2.78  $\text{\AA}$  are significantly different. It can be assumed from the bond lengths and angles that the proton in the carboxyl group has been transferred to the imidine group to form an anion-cation structure as shown in Fig. 2. This hydrogen-bond scheme is similar to that observed for cytosine-*N*-benzoylglycine monohydrate (Tamura *et al.*, 1972). The other carboxylic acid group at the  $\gamma$ -position is hydrogen bonded to an amino group and a carboxyl group ( $\alpha$ -position) of neighbouring mole-

cules at distances of 2.88 and 2.67  $\text{\AA}$ , respectively. Three hydroxyl groups in the sugar moiety of cytidine and two water molecules are associated with each other at reasonable hydrogen-bond distances. They are  $\text{O}(2')(c) \cdots \text{O}(3')(c)$ , 2.80  $\text{\AA}$ ;  $\text{O}(3')(c) \cdots \text{O}(5')(c)$ , 2.71  $\text{\AA}$ ;  $\text{O}(2)(c) \cdots \text{W}(\text{O}1)$ , 2.73  $\text{\AA}$ ;  $\text{O}(5')(c) \cdots \text{W}(\text{O}2)$ , 2.66  $\text{\AA}$ . There are some other interactions which are

\* (c) stands for cytidine and (g) for *N*-CBZ-glu.

Table 2. Bond distances ( $\text{\AA}$ ) and angles ( $^\circ$ ) with standard deviations

Cytidine		<i>N</i> -CBZ-glu	
N(1)—C(2)	1.378 (20)	O(1A)—C(1)	1.260 (18)
N(1)—C(6)	1.384 (22)	O(1B)—C(1)	1.242 (21)
N(1)—C(1')	1.485 (20)	C(1)—C(2)	1.458 (21)
C(2)—N(3)	1.355 (20)	C(2)—C(3)	1.542 (22)
C(2)—O(2)	1.222 (20)	C(2)—N(2)	1.446 (19)
N(3)—C(4)	1.362 (21)	C(3)—C(4)	1.562 (23)
C(4)—C(5)	1.430 (22)	C(4)—C(5)	1.474 (25)
C(4)—N(4)	1.325 (21)	C(5)—O(5A)	1.306 (23)
C(5)—C(6)	1.335 (23)	C(5)—O(5B)	1.203 (22)
C(1')—C(2')	1.572 (21)	N(2)—C(1')	1.336 (22)
C(1')—O(1')	1.428 (19)	C(1')—O(1')	1.211 (21)
C(2')—C(3')	1.529 (21)	C(1')—O(2')	1.326 (22)
C(2')—O(2')	1.427 (18)	O(2')—C(3')	1.532 (29)
C(3')—C(4')	1.548 (20)	C(3')—C(4')	1.495 (35)
C(3')—O(3')	1.396 (17)	C(4')—C(5')	1.426 (43)
C(4')—C(5')	1.536 (23)	C(4')—C(9')	1.276 (36)
C(4')—O(1')	1.406 (17)	C(5')—C(6')	1.443 (63)
C(5')—O(5')	1.430 (19)	C(6')—C(7')	1.343 (53)
		C(7')—C(8')	1.381 (44)
		C(8')—C(9')	1.408 (49)

\* The table of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30647 (16 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

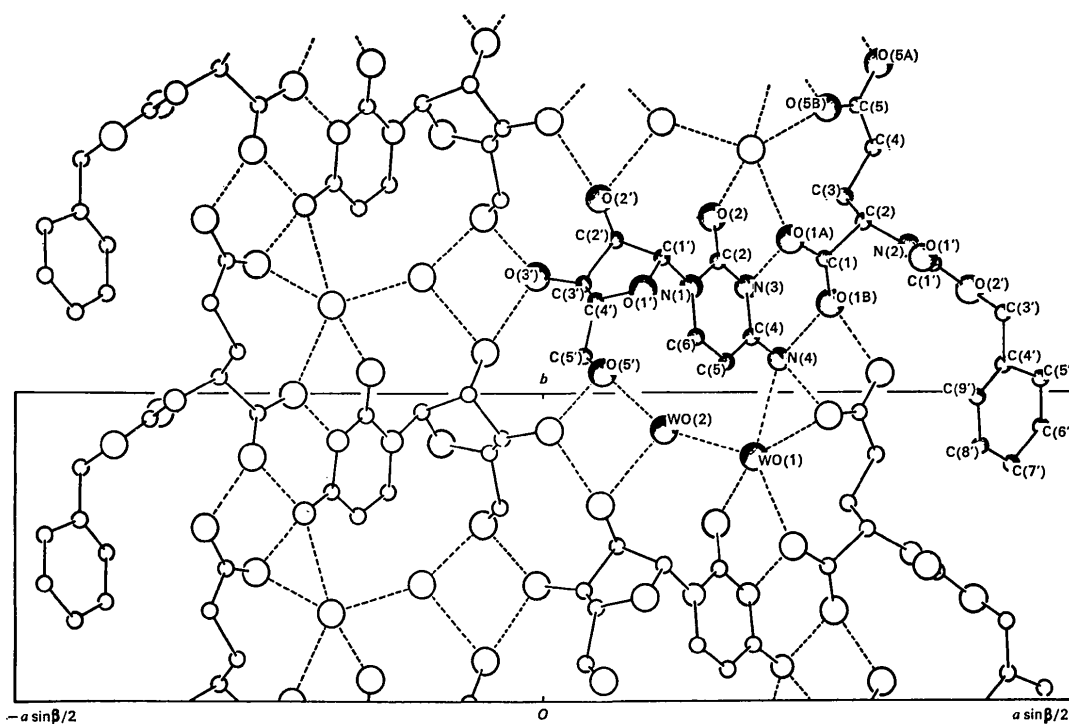
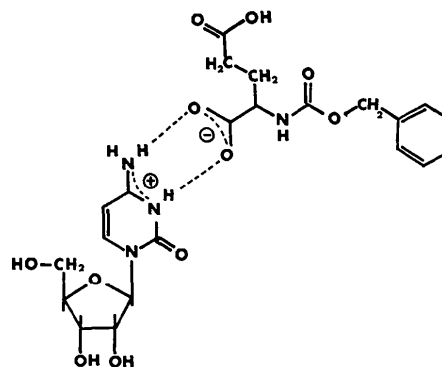


Fig. 1. Packing diagram of the cytidine-*N*-CBZ-glu dihydrate crystal structure viewed down the *c* axis. All short contacts, shown by dashed lines, have values within the range of hydrogen-bond distances.

Table 2 (cont.)

C(2)—N(1)—C(6)	121.0 (14)	O(1A)—C(1)—O(1B)	125.0 (15)
C(2)—N(1)—C(1)	116.2 (14)	O(1A)—C(1)—C(2)	114.4 (14)
C(6)—N(1)—C(1)	122.6 (13)	O(1B)—C(1)—C(2)	120.5 (14)
N(1)—C(2)—O(2)	120.7 (15)	C(1)—C(2)—C(3)	107.4 (12)
N(1)—C(2)—N(3)	117.8 (15)	C(1)—C(2)—N(2)	110.7 (13)
C(4)—C(5)—C(6)	120.0 (16)	C(3)—C(2)—N(2)	110.5 (12)
C(5)—C(4)—N(4)	122.4 (15)	C(2)—C(3)—C(4)	110.8 (13)
N(3)—C(4)—N(4)	120.2 (15)	O(5A)—C(5)—O(5B)	121.3 (18)
N(3)—C(4)—C(5)	117.3 (14)	C(4)—C(5)—O(5B)	124.7 (18)
C(2)—N(3)—C(4)	123.4 (14)	C(4)—C(5)—O(5A)	113.8 (15)
N(3)—C(2)—O(2)	121.4 (15)	C(3)—C(4)—C(5)	113.2 (14)
N(1)—C(6)—C(5)	120.3 (15)	C(2)—N(2)—C(1')	118.9 (13)
N(1)—C(1')—C(2')	109.5 (12)	N(2)—C(1')—O(1')	124.8 (17)
N(1)—C(1')—O(1')	107.9 (13)	N(2)—C(1')—O(2')	111.8 (15)
C(2')—C(1')—O(1')	104.2 (12)	O(1')—C(1')—O(2')	123.4 (17)
C(1')—C(2')—C(3')	101.2 (12)	C(1')—O(2')—C(3')	117.2 (15)
C(1')—C(2')—O(2')	105.7 (11)	O(2')—C(3')—C(4')	101.7 (18)
C(4')—C(5')—O(5')	111.1 (12)	C(3')—C(4')—C(5')	116.7 (24)
C(5')—C(4')—O(1')	111.4 (12)	C(3')—C(4')—C(9')	123.6 (22)
C(3')—C(4')—O(1')	104.8 (11)	C(5')—C(4')—C(9')	119.2 (27)
C(3')—C(4')—C(5')	109.4 (12)	C(4')—C(5')—C(6')	112.5 (33)
C(4')—C(3')—O(3')	115.4 (12)	C(7')—C(8')—C(9')	123.0 (31)
C(2')—C(3')—O(3')	117.6 (13)	C(6')—C(7')—C(8')	110.7 (33)
C(2')—C(3')—C(4')	101.4 (11)	C(5')—C(6')—C(7')	128.9 (37)
C(3')—C(2')—O(2')	111.3 (12)	C(4')—C(9')—C(8')	123.5 (27)
C(1')—O(1')—C(4')	112.9 (11)		

Fig. 2. The molecular complex formed by the cytosinyl cation and the *N*-CBZ-glu anion.

within the range of hydrogen-bond distances: N(4)(c)···W(O1), 2.85 Å; O(1A)(g)···W(O1), 2.80 Å; O(2')(c)···W(O2), 2.92 Å; O(5B)(g)···W(O1), 2.99 Å; N(2)(g)···O(1')(g), 3.00 Å. But the number of interactions is greater than the number of protons available for hydrogen bonding. This may be due to a bifurcated hydrogen bond or van der Waals contacts.

The molecular packing is as follows: The sugar moiety in cytidine forms hydrogen bonds along the screw of the *b* axis, while the cytosine moiety binds the two carboxylic acid groups. Also water molecules are hydrogen bonded in the vacancies in the van der Waals packing. The most hydrophobic part of the complex is the carbobenzoxy group in *N*-CBZ-glu which is located along the other screw axis. Although *N*-CBZ-glu binds

with cytidine in two ways using the two-hydrogen-bond scheme, *i.e.*, through the  $\alpha$ - and  $\gamma$ -carboxyl groups, the acidic nature of *N*-CBZ-glu is maintained by binding through the  $\alpha$  position. This is analogous to the acid-base interaction between an organic acid and nucleotide base groups (Tamura, Yoshikawa, Sato & Hata, 1973). It is almost certain that even in solution, both components associate with each other. We feel that there is some biological significance in this type of binding between nucleotide and peptide systems.

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## Copper(I) Tetracetonitrile Perchlorate

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**Abstract.**  $\text{Cu}(\text{CH}_3\text{CN})_4\text{ClO}_4$ , orthorhombic,  $Pn2_1a$ ,  $a = 24.25$  (2),  $b = 20.75$  (2),  $c = 8.42$  (1) Å,  $Z = 12$ ,  $D_x = 1.54$  g cm<sup>-3</sup>. The positional and thermal parameters

of the 54 nonhydrogen atoms of the asymmetric unit were refined *versus* the 1726 most significant reflexions to an  $R$  of 0.077. The copper(I) ions are tetrahedrally