

Structure of 1-(2-Carboxyethyl)uracil*†

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Abstract. $C_7H_8N_2O_4$, $P2_1/c$, $a = 8.455(1)$, $b = 14.235(2)$, $c = 6.825(1)$ Å, $\beta = 110.12(1)^\circ$, $D_x = 1.586$, $D_m = 1.58$ g cm $^{-3}$, $Z = 4$; $R = 0.044$ for 1212 diffractometer-measured intensities. The uracil moieties are paired around an inversion centre through N(3)—H...O(4) hydrogen bonds and the carboxyl group is hydrogen-bonded to O(2) of the uracil moiety in the neighbouring molecule. This hydrogen bond may be one of the elementary interaction patterns between the carboxyl group of an acidic amino acid residue and the base-paired uracil.

Introduction. As part of a series of studies on the elementary interaction patterns between amino acid residues and nucleotide bases (Takimoto, Takenaka & Sasada, 1982), we have investigated binary systems involving uracil. Some compounds containing a carboxyl group and a uracil moiety have already been reported: 6-methyluracil-5-acetic acid (1) (Destro & Marsh, 1972), α -S-cysteinylthymine (2) (Berman, Zacharias, Carrell & Varghese, 1976) and 5-nitro-1-(β -D-ribosyluronic acid)uracil monohydrate [1-(5-nitro-2,4-dioxo-1-pyrimidinyl)- β -D-ribofuranic acid monohydrate] (3) (Takusagawa, Koetzle, Srikrishnan & Parthasarathy, 1979). In (1), the carboxyl group is doubly hydrogen-bonded to uracil at N(3)—H and O(4), which participate in Watson—Crick-type base pairing. A similar hydrogen bond, though single, has also been reported in (2) and (3). Such hydrogen bonding might represent one of the interactions between the carboxyl group and unpaired uracil. A new compound blocked at N(1), 1-(2-carboxyethyl)uracil, was synthesized from uracil and β -propiolactone in dimethylformamide (Kondo, Sato & Takemoto, 1973) and separated by cellulose column chromatography. Crystals in the form of colourless plates were obtained by slow evaporation from ethyl acetate:ethanol (40:1) effusion. The space group was assigned from Weissenberg photographs. A crystal 0.5 \times 0.5 \times 0.1 mm was used for data collection on a Rigaku four-circle diffractometer with Ni-filtered Cu $K\alpha$

radiation. Accurate unit-cell dimensions were obtained by the least-squares method with 42 reflexions ($50^\circ < 2\theta < 55^\circ$). The density was measured by flotation in an *n*-hexane and tetrachloromethane mixture.

Intensities were measured in the $\omega/2\theta$ scan mode with a scan width of 1.3° (in ω) and scan speed of $4^\circ(2\theta)$ min $^{-1}$. Five reference reflexions monitored every fifty reflexions showed no significant intensity deterioration. The intensities were corrected for Lorentz and polarization factors but not for absorption effects. Of 1230 independent reflexions within the range $3^\circ < 2\theta < 125^\circ$, 18 weak reflexions below background were considered zero reflexions. The standard deviations were estimated by $\sigma^2(F_o) = \sigma_p^2(F_o) + qF_o^2$ where $\sigma_p(F_o)$ is evaluated by counting statistics and q was estimated to be 1.84×10^{-5} from the variances of the monitored reflexions (McCandlish & Stout, 1975).

The structure was solved by the direct method and its parameters were refined by the block-diagonal least-squares technique. All the H atoms, found on a difference map, were included. The quantity minimized was $\sum w(|F_o| - |F_c|)^2$, where $w = 1/[\sigma(F_o)]^2$. The zero

Table 1. Fractional coordinates and isotropic temperature factors

The B values accompanied by $\langle \rangle$ are the equivalent isotropic temperature factors calculated from the anisotropic thermal parameters: $B = 8\pi^2(U_1 + U_2 + U_3)/3$, where U_1 , U_2 , and U_3 are the principal components of the mean-square-displacement matrix U . Values in $\langle \rangle$ are the anisotropy defined by $[\sum (B - 8\pi^2 U_i)^2/3]^{1/2}$. The e.s.d.'s in parentheses refer to the last decimal places.

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> (Å ²)
N(1)	0.2038 (2)	0.4016 (1)	0.0532 (2)	2.23 (28)
C(2)	0.2284 (2)	0.4664 (1)	0.2105 (3)	2.16 (55)
O(2)	0.3460 (2)	0.52185 (9)	0.2571 (2)	2.87 (94)
N(3)	0.1113 (2)	0.4650 (1)	0.3080 (3)	2.31 (53)
C(4)	−0.0202 (2)	0.4020 (1)	0.2721 (3)	2.51 (47)
O(4)	−0.1114 (2)	0.4049 (1)	0.3796 (2)	3.76 (186)
C(5)	−0.0393 (2)	0.3374 (1)	0.1047 (3)	2.59 (64)
C(6)	0.0713 (2)	0.3400 (1)	0.0041 (3)	2.50 (55)
C(9)	0.3235 (3)	0.3997 (1)	−0.0616 (3)	2.60 (69)
C(10)	0.4882 (2)	0.3518 (1)	0.0572 (3)	2.51 (66)
C(11)	0.4777 (2)	0.2460 (1)	0.0598 (3)	2.29 (43)
O(12)	0.6278 (2)	0.2070 (1)	0.1445 (3)	3.70 (168)
O(13)	0.3499 (2)	0.20183 (9)	−0.0072 (3)	3.80 (154)

* 3-(2,4-Dioxo-1-pyrimidinyl)propionic acid.

† Elementary Patterns in Protein—Nucleic Acid Interactions. V.

reflexions with $|F_c| > F_{lim}$ were included in the least-squares calculation by assuming $F_o = F_{lim}$ and $w = w(F_{lim})$. The final R value was 0.044 for $F_o > 3\sigma(F_o)$; the maximum shift of parameters was less than 0.03σ in the last cycle of refinement.

Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974). The atomic parameters are listed in Table 1.*

Discussion. Fig. 1 shows the structure of the title compound. The bond distances and angles of the pyrimidine ring (Table 2) are in good agreement with those of 1-methyluracil (Green, Mathews & Rich, 1962). The dimensions of the carboxyl group are typical, as observed in glutamic acid (Lehmann, Koetzle & Hamilton, 1972; Hirayama, Shirahata, Ohashi & Sasada, 1980) and aspartic acid (Derissen, Endeman & Peerdeman, 1968; Rao, 1973). The carboxyl group is in the synplanar conformation (Leiserowitz, 1976), as commonly found in aliphatic carboxylic acids. The pyrimidine ring is planar within 0.023 Å. This plane makes an angle of $66.1(1)^\circ$ with the planar carboxyl group by taking a *gauche* conformation around the C(9)–C(10) bond. The torsion angles C(2)–N(1)–C(9)–C(10), N(1)–C(9)–C(10)–C(11) and C(9)–C(10)–C(11)–O(12) are $77.9(2)$, $75.8(2)$ and $172.8(2)^\circ$, respectively.

Fig. 2 shows the crystal structure viewed along the c axis. The pyrimidine moieties form a dimer around an

Table 2. Bond distances (Å) and angles ($^\circ$)

Standard deviations are given in parentheses.			
N(1)–C(2)	1.376 (3)	N(1)–C(6)	1.370 (3)
N(1)–C(9)	1.478 (3)	C(2)–O(3)	1.223 (2)
C(2)–N(3)	1.370 (3)	N(3)–C(4)	1.383 (3)
C(4)–O(4)	1.235 (3)	C(4)–C(5)	1.431 (3)
C(5)–C(6)	1.338 (3)	C(9)–C(10)	1.512 (3)
C(10)–C(11)	1.508 (3)	C(11)–O(12)	1.323 (3)
C(11)–O(13)	1.197 (3)		
C(2)–N(1)–C(6)	120.8 (2)	C(2)–N(1)–C(9)	118.6 (2)
C(6)–N(1)–C(9)	120.7 (2)	N(1)–C(2)–N(3)	121.8 (2)
N(1)–C(2)–N(3)	115.4 (2)	O(2)–C(2)–N(3)	122.8 (2)
C(2)–N(3)–C(4)	126.5 (2)	N(3)–C(4)–O(4)	120.1 (2)
N(3)–C(4)–C(5)	114.9 (2)	O(4)–C(4)–C(5)	124.9 (2)
C(4)–C(5)–C(6)	119.0 (2)	N(1)–C(6)–C(5)	123.3 (2)
N(1)–C(9)–C(10)	113.4 (2)	C(9)–C(10)–C(11)	114.2 (2)
C(10)–C(11)–O(12)	111.9 (2)	C(10)–C(11)–O(13)	124.7 (2)
O(12)–C(11)–O(13)	123.4 (2)		

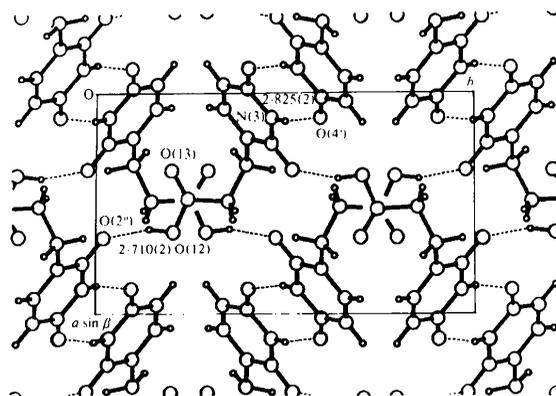


Fig. 2. The crystal structure of the title compound projected along the c axis. (Distances are in Å.)

* Lists of structure factors, anisotropic thermal parameters, H-atom parameters, bond distances and angles involving H atoms, and the least-squares planes for the pyrimidine ring and the carboxyl group have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36967 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

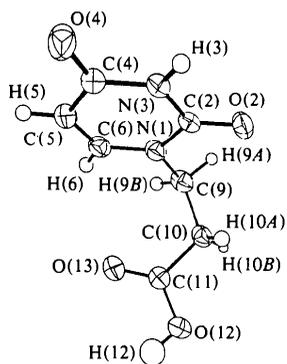


Fig. 1. Molecular structure of the title compound with 50% probability ellipsoids for non-hydrogen atoms. The atomic numbering is also shown.

inversion centre at $x = 0$, $y = \frac{1}{2}$ and $z = \frac{1}{2}$ via N(3)–H···O(4) hydrogen bonds, as shown in Table 3. The carboxyl group is hydrogen-bonded to O(2) of the uracil moiety related by the 2_1 screw axis at $x = \frac{1}{2}$, $z = \frac{1}{4}$. The O(12)···O(2) distance is 2.710(2) Å, the O(12)–H···O(2) angle is $163(3)^\circ$, and the torsion angles N(1)–C(2)–O(2)···O(12), C(2)–O(2)···O(12)–C(11) and O(2)···O(12)–C(11)–C(10) are $138.3(2)$, $166.5(2)$ and $168.4(1)^\circ$, respectively. O(13) does not participate in any hydrogen bonding.

In the present crystal, the functions with which the uracil moieties make a dimer are the same as those for the adenine–uracil complementary base pair. The present O(12)–H···O(2) hydrogen-bonding mode may be one of the possible interaction models for the carboxyl group with base-paired uracil. In order to examine whether the present interaction geometry could be incorporated in the actual macromolecule, model fitting by computer graphics was attempted

Table 3. *Hydrogen-bond distances (Å) and angles (°)*

Standard deviations are given in parentheses.

N(3)···O(4 ⁱ)	2.825 (2)	O(12)···O(2 ⁱⁱ)	2.710 (2)
N(3)—H(3)	0.84 (2)	O(12)—H(12)	0.91 (3)
H(3)···O(4 ⁱ)	2.00 (2)	H(12)···O(2 ⁱⁱ)	1.83 (3)
N(3)—H(3)···O(4 ⁱ)	168 (2)	O(12)—H(12)···O(2 ⁱⁱ)	163 (3)
C(2)—N(3)···O(4 ⁱ)	123.0 (1)	C(11)—O(12)···O(2 ⁱⁱ)	120.1 (1)
C(4)—N(3)···O(4 ⁱ)	110.5 (1)	H(12)···O(2)—C(2 ⁱⁱ)	138 (1)
H(3)···O(4)—C(4 ⁱ)	131.6 (7)	O(12)···O(2)—C(2 ⁱⁱ)	133.0 (1)
N(3)···O(4)—C(4 ⁱ)	129.2 (1)		

Symmetry code: (i) $-x, 1-y, 1-z$; (ii) $1-x, -\frac{1}{2}+y, \frac{1}{2}-z$.

using an RNA model fragment. After some modification with A-form RNA (Arnott & Hukins, 1972), reasonable fitting was successful without abnormal contacts.

References

ARNOTT, S. & HUKINS, D. W. L. (1972). *Biochem. Biophys. Res. Commun.* **47**, 1504–1509.

- BERMAN, H. M., ZACHARIAS, D. E., CARRELL, H. L. & VARGHESE, A. J. (1976). *Biochemistry*, **15**, 463–467.
- DERISSEN, J. L., ENDEMAN, H. J. & PEERDEMAN, A. F. (1968). *Acta Cryst.* **B24**, 1349–1354.
- DESTRO, R. & MARSH, R. E. (1972). *Acta Cryst.* **B28**, 2971–2977.
- GREEN, D. W., MATHEWS, F. S. & RICH, A. (1962). *J. Biol. Chem.* **237**, 3573–3575.
- HIRAYAMA, N., SHIRAHATA, K., OHASHI, Y. & SASADA, Y. (1980). *Bull. Chem. Soc. Jpn.* **53**, 30–35.
- International Tables for X-ray Crystallography* (1974). Vol. IV. Birmingham: Kynoch Press.
- KONDO, K., SATO, T. & TAKEMOTO, K. (1973). *Chem. Lett.* pp. 967–968.
- LEHMANN, M. S., KOETZLE, T. F. & HAMILTON, W. C. (1972). *J. Cryst. Mol. Struct.* **2**, 225–233.
- LEISEROWITZ, L. (1976). *Acta Cryst.* **B32**, 775–802.
- MCCANDLISH, L. E. & STOUT, G. H. (1975). *Acta Cryst.* **A31**, 245–249.
- RAO, S. T. (1973). *Acta Cryst.* **B29**, 1718–1720.
- TAKIMOTO, M., TAKENAKA, A. & SASADA, Y. (1982). *Bull. Chem. Soc. Jpn.* **55**. In the press.
- TAKUSAGAWA, F., KOETZLE, T. F., SRIKRISHNAN, T. & PARTHASARATHY, R. (1979). *Acta Cryst.* **B35**, 1388–1394.

Acta Cryst. (1982). **B38**, 2938–2941

3,4-Dihydro-8-hydroxy-3-(4-hydroxyphenyl)isocoumarin, Hydrangenol

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Abstract. C₁₅H₁₂O₄, monoclinic, $P2_1$, $a = 5.600$ (3), $b = 5.185$ (2), $c = 20.827$ (11) Å, $\beta = 97.52$ (2)° (Mo $K\alpha$ radiation, $T = 293$ K), $V = 599.5$ Å³, $Z = 2$, $M_r = 256.26$, $D_x = 1.419$ Mg m⁻³, $F(000) = 268$, $\mu(\text{Mo } K\alpha) = 0.11$ mm⁻¹; $R_1 = 3.7\%$ for 786 observed reflections. The 4-hydroxyphenyl ring C is equatorially substituted at C(3) of the slightly distorted sofa form of the lactone ring B. The conformation of the molecule is characterized by two planes of ring A and ring C which are approximately perpendicular (78.8°) to each other. The hydroxyl H at O(8) is hydrogen bonded to the C(1) carbonyl group with distances O(8)—H(8) = 0.96 (6) and O(1)···H(8) = 1.82 (12) Å, the angle O(8)—H(8)···O(1) being 138 (4)°. Intermolecular

hydrogen bonds of the type O—H···O form endless chains with alternate molecules along **b**.

Introduction. Many plants are known to cause a cell-mediated type of allergy (contact allergy, allergic contact dermatitis). *Hydrangea (Hydrangea macrophylla* subsp. *macrophylla*) is a member of this class, though cases of allergic reaction to it are not frequently encountered. In addition to the three cases reported by Apted (1973) and Burry (1973), a new case has been discovered recently (Hausen, Bäurle & Schmalte, 1982).

Many of the constituents (Fig. 1) of hydrangea species are stilbene (I) derivatives (Asahina & Asano,