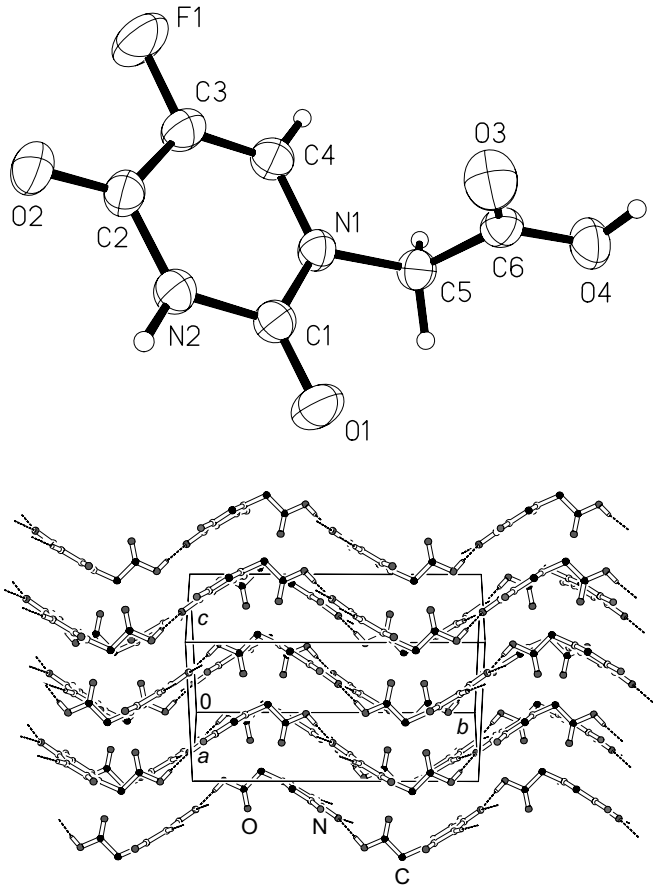
# Crystal structure of 5-fluoro-1-(carboxymethyl)uracil, $C_6H_5FN_2O_4$

L.-J. Zhang[I], J.-C. Ding[II], H.-Y. Wu[II] and M.-C. Liu*,[II]

[I] Wenzhou University, Elementary Educational College, Wenzhou 325027, P. R. China
[II] Wenzhou University, School of Chemistry and Material Science, Wenzhou 325027, P. R. China

Received January 3, 2006, accepted and available on-line February 27, 2006; CCDC no. 1267/1711




**Abstract**

$C_6H_5FN_2O_4$, monoclinic, $P12_1/c1$ (no. 14), $a$ = 4.9363(5) Å, $b$ = 17.056(2) Å, $c$ = 9.4940(8) Å, $\beta$ = 114.466(4)°, $V$ = 727.6 Å$^3$, $Z$ = 4, $R_{gt}(F)$ = 0.044, $wR_{ref}(F^2)$ = 0.109, $T$ = 298 K.

**Source of material**

Bromoacetic acid (45 mmol, 6.25 g) in water (10 ml) was added to a solution of 5-fluoro-uracil (30 mmol, 3.89 g), potassium hydroxide (11.5 mmol, 6.41 g) and water (20 ml) at 313 K. The mixture was cooled after 2 h reaction and the pH value was adjusted to 5.5 using hydrochloric acid. The precipitate was filtered off and the pH of the filtrate was adjusted to 1, again using hydrochloric acid, and the solution was cooled for 6 h in a refrigerator and then filtered. The precipitate was washed with water and dried. Single crystals were obtained by recrystallization from anhydrous ethanol.

* Correspondence author (e-mail: mcl@wznc.zj.cn)

**Discussion**

A great deal of attention has been devoted to the role of nucleobases, since they are responsible for a wide range of biochemical processes, such as complementary base pairings in genetic information storage, transfer and some enzymatic reactions [1]. Consequently, much interest has been focused on nucleobases and their derivatives. 5-Fluorouracil (5FU) is one of the antitumor agents most frequently used for treating solid tumors, such as breast, colorectal, and gastric cancers, in either monotherapy or combination therapy with various cytotoxic drugs [2-3]. Because of its poorly tumor selective and high incidences of toxicity in the bone marrow, gastrointestinal tract, central nervous system and skin, many derivatives of 5FU have been developed to improve its topical delivery and reduce the side effects [4-6]. To our knowledge, the crystal structure of 5-fluoro-1-(carboxymethyl)uracil has never been reported so far.

In the title structure, the carboxyl group (C6/O3/O4/H4) and uracil ring (C1-C4/N1/N2) are each almost planar (figure, top). The dihedral angle between the above planes is 82.1(8)°. Moreover, the C—N bond lengths in the uracil ring range from 1.374(2) to 1.380(2) Å, which are shorter than a C—N single bond length of ca 1.443 Å [7], but longer than a typical C=N bond length of ca 1.269 Å, indicating the electron delocalization. Two distinct hydrogen bonds occur in the crystal structure: each pair molecules of the title structure are linked by intermolecular N2–H2···O2$^{i}$ (i: $-x+1,-y+1,-z+1$) hydrogen bond to form a dimer structure, and adjacent dimers are linked by intermolecular O4–H4···O2$^{ii}$ (ii: $-x,y+\frac{1}{2},-z+\frac{1}{2}$) hydrogen bonds, leading to a hydrogen-bonded corrugated layers parallel to the $(10\bar{2})$ plane (figure, bottom).

**Table 1.** Data collection and handling.

| | |
|---|---|
| Crystal: | colorless block, size 0.15 × 0.19 × 0.23 mm |
| Wavelength: | Mo $K_\alpha$ radiation (0.71073 Å) |
| $\mu$: | 1.61 cm$^{-1}$ |
| Diffractometer, scan mode: | Bruker APEX SMART CCD, $\varphi/\omega$ |
| $2\theta_{max}$: | 50.38° |
| $N(hkl)_{measured}$, $N(hkl)_{unique}$: | 3810, 1305 |
| Criterion for $I_{obs}$, $N(hkl)_{gt}$: | $I_{obs} > 2\,\sigma(I_{obs})$, 1190 |
| $N(param)_{refined}$: | 119 |
| Programs: | SHELXS-97 [8], SHELXL-97 [9] |

**Table 2.** Atomic coordinates and displacement parameters (in Å$^2$).

| Atom | Site | $x$ | $y$ | $z$ | $U_{iso}$ |
|---|---|---|---|---|---|
| H(4) | 4*e* | 0.2298 | 0.9294 | 0.1936 | 0.066 |
| H(2) | 4*e* | 0.5836 | 0.5645 | 0.4519 | 0.040 |
| H(4A) | 4*e* | –0.0475 | 0.6739 | 0.0106 | 0.042 |
| H(5A) | 4*e* | 0.3255 | 0.7693 | 0.0338 | 0.036 |
| H(5B) | 4*e* | 0.6254 | 0.7719 | 0.1832 | 0.036 |

**Table 3.** Atomic coordinates and displacement parameters (in Å$^2$).

| Atom | Site | *x* | *y* | *z* | $U_{11}$ | $U_{22}$ | $U_{33}$ | $U_{12}$ | $U_{13}$ | $U_{23}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| F(1) | 4*e* | –0.2607(3) | 0.55144(9) | 0.0707(2) | 0.0445(8) | 0.062(1) | 0.0634(9) | –0.0253(7) | –0.0051(7) | 0.0092(7) |
| O(1) | 4*e* | 0.7772(3) | 0.68825(9) | 0.4096(2) | 0.0366(9) | 0.0455(9) | 0.0389(9) | –0.0128(7) | 0.0020(7) | 0.0079(7) |
| O(2) | 4*e* | 0.1259(3) | 0.49076(9) | 0.3512(2) | 0.0428(9) | 0.0326(8) | 0.0507(9) | –0.0073(6) | 0.0151(7) | 0.0092(7) |
| O(3) | 4*e* | 0.1535(4) | 0.81286(9) | 0.2924(2) | 0.060(1) | 0.0445(9) | 0.049(1) | 0.0010(7) | 0.0359(9) | 0.0042(7) |
| O(4) | 4*e* | 0.3316(3) | 0.89748(8) | 0.1724(2) | 0.0482(9) | 0.0293(8) | 0.062(1) | 0.0011(7) | 0.0313(8) | 0.0045(7) |
| N(1) | 4*e* | 0.3514(4) | 0.68637(9) | 0.1883(2) | 0.0318(9) | 0.0263(8) | 0.0297(9) | –0.0014(7) | 0.0115(7) | 0.0022(7) |
| N(2) | 4*e* | 0.4569(4) | 0.58688(9) | 0.3699(2) | 0.0325(9) | 0.0298(9) | 0.0314(9) | –0.0015(7) | 0.0070(7) | 0.0067(7) |
| C(1) | 4*e* | 0.5460(4) | 0.6565(1) | 0.3280(2) | 0.030(1) | 0.030(1) | 0.028(1) | –0.0003(8) | 0.0111(8) | 0.0017(8) |
| C(2) | 4*e* | 0.1895(4) | 0.5494(1) | 0.2957(2) | 0.034(1) | 0.026(1) | 0.039(1) | –0.0021(8) | 0.0174(9) | –0.0013(9) |
| C(3) | 4*e* | 0.0040(5) | 0.5860(1) | 0.1522(3) | 0.032(1) | 0.036(1) | 0.038(1) | –0.0065(8) | 0.0068(9) | –0.0011(9) |
| C(4) | 4*e* | 0.0818(4) | 0.6514(1) | 0.1033(2) | 0.032(1) | 0.036(1) | 0.029(1) | 0.0000(9) | 0.0047(8) | 0.0040(9) |
| C(5) | 4*e* | 0.4121(4) | 0.7644(1) | 0.1456(2) | 0.032(1) | 0.029(1) | 0.031(1) | –0.0007(8) | 0.0140(8) | 0.0061(8) |
| C(6) | 4*e* | 0.2840(4) | 0.8266(1) | 0.2133(2) | 0.028(1) | 0.032(1) | 0.029(1) | –0.0018(8) | 0.0080(8) | 0.0028(8) |

*Acknowledgments.* We acknowledge financial support by the Wenzhou Technology Project Foundation of China (grant no. G2004053), the Zhejiang Provincial Natural Science Foundation of China (grant no. Y405078) and the National Natural Science Foundation of China (grant no. 20571057).

## References

1. Bazzicalupi, C.; Bencini, A.; Berni, E.; Ciattini, S.; Bianchi, A.; Giorgi, C.; Paoletti, P.; Valtancoli, B.: Binding of nucleobases to a dizinc macrocyclic complex. Supramolecular assembling of dinuclear clusters through N–CH···O and C–CH···O hydrogen bonding. Inorg. Chim. Acta **317** (2001) 259-267.
2. Cai Bill, T. W.; Tang, X. P.; Nagorski, J.; Brauschweiger, P. G.; Wang, P. G.: Synthesis and cytotoxicity of 5-fluorouracil/diazeniumdiolate conjugates. Bioorg. Med. Chem. **11** (2003) 4971-4975.
3. Wang, X. Y.; Li, J.; Zhang, X. M.; Liu, Q.; Xu, Q.; Tan, R. X.: 5-Fluorouracil-cisplatin adducts with potential antitumor activity. J. Inorg. Biochem. **94** (2003) 186-192.
4. Hu, M. L.; Zhu, L. W.; Xiao, H. P.: Bis(aqua)bis(benzimidazole-$\kappa N$)-bis(5-fluorouracil-1-acetate-$\kappa O$)cobalt(II). Acta Crystallogr. E**61** (2005) m898-m900.
5. Li, C. Z.; Wang, L. F.; Li, Y. Z.; Xia, C. G.; Dai, R. B.: *trans*-Tetraaquabis(5-fluorouracil-1-acetato-*O*)zinc(II) tetrahydrate. Acta Crystallogr. C**56** (2000) e376-e377.
6. Liu, X. J.; Chen, R. Y.; Liu. Y. Y.: Synthesis and anticancer activities of novel 5-fluorouracil-1-yl phosphonotripeptides. Chem. J. Chin. Univ. **23** (2002) 1299-1303.
7. Jin, Z. M.; Li, L.; Li, M. C.; Hu, M. L.; Shen, L.: Diethyl 3,8-dimethyl-4,7-diazadeca-2,8-dienedioate. Acta Crystallogr. C**60** (2004) o642-o643.
8. Sheldrick, G. M.: SHELXS-97. Program for the Solution of Crystal Structures. University of Göttingen, Germany 1997.
9. Sheldrick, G. M.: SHELXL-97. Program for the Refinement of Crystal Structures. University of Göttingen, Germany 1997.