

Structure of 6-Amino-5-cinnamoyl-1,3-dimethyluracil

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Abstract. $C_{15}H_{15}N_3O_3$, $M_r = 286$, triclinic, $P\bar{1}$, $a = 15.247$ (3), $b = 11.855$ (2), $c = 7.480$ (2) Å, $\alpha = 95.86$ (5), $\beta = 90.50$ (5), $\gamma = 87.90$ (5)°, $Z = 4$, $V = 1344$ Å³, $D_c = 1.33$ Mg m⁻³. The planar conformation which is stabilized by intramolecular hydrogen bonds and the length of the molecule, $C(112)\cdots H(C105)-C(105) = 9.71$ Å, could account for an extensive stacking interaction between the nucleic bases of DNA, consistent with the anticancer activity of the title compound.

Introduction. The title compound (NSC 290115) is active against the P338 tumor system (J. L. Bernier & J. P. Henichart, unpublished results). The study of the conformation of this molecule may yield information about the mechanism of its biological activity. NMR spectra recorded in Me_2SO-d_6 clearly revealed a planar structure stabilized by the establishment of an intramolecular hydrogen bond involving one proton of the amino group and the O atom of a ketone group. In order to investigate whether the crystalline structure was in accordance with the preferred solution conformation, we have carried out an X-ray diffraction analysis.

Single crystals were transparent parallelepipeds. The data were collected on a Philips PW 1100 diffractometer with graphite-monochromated $Cu K\alpha$ radiation. Intensities for 3004 reflections were measured by the $\theta/2\theta$ scan method. An invariant scan width of 1.4° was used. The data were corrected for Lorentz and polarization effects, but not for absorption or extinction. 2117 reflections with $F > 6\sigma(F)$ were used in the analysis.

The structure was solved by direct methods. 400 reflections with $|E| \geq 1.4$ were used in *MULTAN* (Germain, Main & Woolfson, 1971). A Fourier synthesis based on the solution with the highest Σ_2 consistency revealed the complete structure, which was refined by full-matrix least squares. The H atoms were located from a difference synthesis and included in the

refinement with the isotropic temperature factor of the carrier atom. Fig. 1 shows the atomic numbering.

The refinement converged to $R = 0.051$ for all reflections with $F > 6\sigma(F)$.*

The final atomic parameters are listed in Tables 1 and 2. Scattering factors for the heavy atoms were those of Hanson, Herman, Lea & Skillman (1964), for H those of Stewart, Davidson & Simpson (1965). Unit weights were used throughout. Peaks and troughs in the final difference synthesis did not exceed ± 0.3 e Å⁻³.

Discussion. The bond distances and angles are given in Tables 3 and 4. They are in excellent agreement with values reported for the pyrimidine moiety and for an α,β -unsaturated ketone.

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35207 (24 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

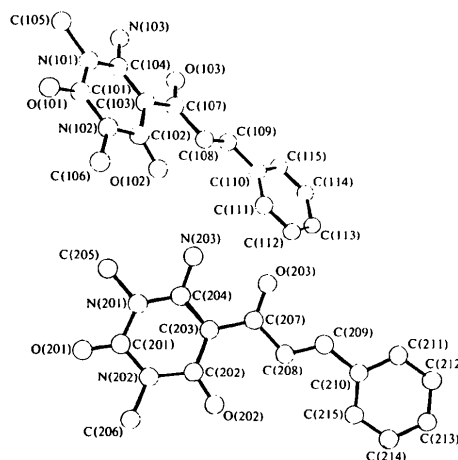


Fig. 1. Perspective views of molecules (1) and (2).

Table 1. Final positional parameters ($\times 10^4$) of the nonhydrogen atoms and their *e.s.d.*'s in parentheses

	<i>x</i>	<i>y</i>	<i>z</i>
C(101)	6196 (4)	8143 (6)	9631 (8)
N(101)	6904 (3)	7450 (4)	8999 (7)
C(102)	5220 (3)	6589 (4)	8579 (8)
C(112)	2703 (4)	2162 (6)	6038 (9)
C(108)	5064 (4)	4182 (6)	6886 (8)
N(102)	5391 (3)	7665 (4)	9459 (6)
C(103)	5980 (3)	5905 (5)	7929 (7)
C(107)	5903 (4)	4773 (5)	7012 (8)
O(102)	4453 (3)	6327 (4)	8423 (6)
O(103)	6561 (3)	4246 (4)	6321 (6)
C(104)	6813 (4)	6393 (5)	8087 (8)
C(109)	5012 (4)	3170 (5)	5974 (8)
O(101)	6297 (3)	9110 (4)	10276 (6)
C(110)	4244 (4)	2473 (6)	5731 (8)
C(111)	3407 (4)	2855 (6)	6322 (9)
N(103)	7534 (3)	5862 (5)	7416 (7)
C(113)	2801 (4)	1080 (6)	5156 (9)
C(114)	3622 (4)	710 (6)	4563 (9)
C(115)	4339 (4)	1386 (6)	4812 (8)
C(105)	7775 (4)	7937 (6)	9265 (9)
C(106)	4639 (4)	8394 (6)	10171 (9)
C(201)	1162 (4)	8215 (6)	6294 (8)
C(202)	205 (3)	6660 (5)	6846 (7)
C(203)	958 (3)	5986 (5)	7266 (7)
C(204)	1794 (4)	6472 (5)	7256 (7)
N(201)	1874 (3)	7540 (4)	6737 (6)
N(202)	358 (3)	7735 (4)	6291 (6)
C(207)	904 (4)	4845 (5)	7822 (8)
C(208)	55 (4)	4260 (5)	7778 (8)
O(202)	-565 (3)	6399 (4)	6903 (6)
O(203)	1566 (3)	4309 (4)	8329 (6)
O(201)	1247 (3)	9178 (4)	5944 (6)
N(203)	2522 (3)	5930 (5)	7732 (7)
C(205)	2742 (4)	8046 (6)	6733 (9)
C(206)	-389 (4)	8442 (6)	5775 (9)
C(209)	20 (4)	3253 (5)	8380 (8)
C(210)	-749 (4)	2548 (5)	8469 (7)
C(211)	-624 (4)	1489 (6)	9130 (9)
C(212)	-1332 (4)	811 (6)	9286 (9)
C(213)	-2162 (4)	1154 (6)	8771 (9)
C(214)	-2284 (4)	2196 (6)	8123 (9)
C(215)	-1585 (4)	2898 (6)	7966 (8)

The least-squares plane calculated through the phenyl ring (*P1*) and the uracil ring (*P2*) (Table 5) indicates that the molecule is almost planar with an extended structure (overall length 9.71 Å).

Intramolecular interactions appear to be stabilizing forces in this conjugated system. The carboxyl group O(103) participates in a relatively strong hydrogen bond with a proton from N(103): H(N103)B...O(103) = 1.876 (10) Å. Also, the distance between H(C108) and O(102), 2.235 (11) Å, is much less than the sum of the van der Waals radii of the atoms involved (2.6 Å). This suggests that this C-H...O contact is a hydrogen-bonding-like interaction. The acidic character of H(C108) possibly results from the polarization of the α,β -unsaturated ketone portion, as demonstrated by NMR spectroscopy.

No intermolecular distance between C-C, C-O or C-N atoms is < 3.3 Å, except for O(202)...H(N103)

Table 2. Hydrogen-atom positional parameters ($\times 10^3$), isotropic temperature factors and bond distances, with *e.s.d.*'s in parentheses

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> (Å ²)	C,O,N-H (Å)
H(C106)A	413 (4)	803 (5)	998 (7)	3.6 (3)	0.90 (6)
H(C106)B	483 (4)	885 (5)	1102 (7)	3.6 (3)	0.86 (6)
H(C106)C	443 (4)	900 (5)	931 (7)	3.6 (3)	1.05 (6)
H(C105)A	774 (3)	855 (5)	1023 (7)	3.1 (3)	0.98 (6)
H(C105)B	793 (3)	812 (5)	822 (7)	3.1 (3)	0.87 (5)
H(C105)C	816 (3)	737 (5)	972 (7)	3.1 (3)	0.97 (5)
H(N103)A	818 (3)	611 (5)	743 (7)	2.8 (2)	1.04 (5)
H(N103)B	750 (3)	521 (5)	684 (7)	2.8 (2)	0.84 (6)
H(C108)	460 (3)	449 (5)	743 (7)	2.7 (3)	0.86 (5)
H(C109)	558 (3)	282 (5)	551 (7)	2.8 (3)	1.00 (5)
H(C111)	333 (3)	368 (5)	698 (7)	3.0 (3)	1.05 (6)
H(C112)	210 (4)	247 (5)	628 (7)	3.7 (3)	0.99 (6)
H(C115)	494 (3)	110 (5)	447 (7)	3.1 (3)	1.00 (6)
H(C114)	371 (4)	-7 (5)	405 (7)	3.6 (3)	0.98 (6)
H(C113)	226 (4)	61 (5)	485 (7)	3.7 (3)	1.02 (6)
H(C212)	-125 (4)	12 (5)	966 (7)	3.5 (3)	0.89 (6)
H(C213)	-267 (4)	64 (5)	889 (7)	3.6 (3)	1.02 (6)
H(C211)	4 (4)	120 (5)	953 (7)	3.3 (3)	1.11 (6)
H(C214)	-287 (4)	251 (5)	772 (7)	3.5 (3)	1.02 (6)
H(C215)	-173 (3)	368 (5)	765 (7)	2.9 (3)	1.00 (6)
H(C209)	54 (3)	286 (5)	881 (7)	2.9 (3)	0.98 (5)
H(C208)	-46 (3)	468 (5)	736 (7)	2.6 (3)	0.99 (5)
H(N203)A	309 (4)	620 (5)	780 (7)	2.9 (2)	0.94 (6)
H(N203)B	243 (4)	518 (5)	806 (7)	2.9 (2)	0.96 (6)
H(C205)A	312 (4)	760 (5)	616 (7)	3.2 (3)	0.86 (5)
H(C205)B	310 (4)	796 (5)	782 (7)	3.2 (3)	1.00 (5)
H(C205)C	264 (4)	878 (5)	626 (7)	3.2 (3)	0.98 (5)
H(C206)A	-85 (4)	794 (5)	546 (7)	3.4 (3)	0.95 (6)
H(C206)B	-24 (4)	888 (5)	491 (7)	3.4 (3)	0.91 (6)
H(C206)C	-46 (4)	902 (5)	649 (7)	3.4 (3)	0.84 (6)

Table 3. Interatomic distances (Å)

Molecule (1)		Molecule (2)	
N(101)-C(104)	1.376 (8)	N(201)-C(204)	1.371 (8)
N(101)-C(101)	1.388 (8)	N(201)-C(201)	1.384 (7)
N(101)-C(105)	1.472 (7)	N(201)-C(205)	1.473 (7)
C(101)-C(102)	1.370 (7)	C(201)-N(202)	1.370 (7)
C(101)-O(101)	1.213 (8)	C(201)-O(201)	1.209 (8)
N(102)-C(102)	1.407 (8)	N(202)-C(202)	1.407 (8)
N(102)-C(106)	1.479 (8)	N(202)-C(206)	1.463 (8)
C(102)-C(103)	1.448 (8)	C(202)-C(203)	1.426 (8)
C(102)-O(102)	1.222 (7)	C(202)-O(202)	1.230 (6)
C(103)-C(104)	1.413 (8)	C(203)-C(204)	1.419 (8)
C(103)-C(107)	1.452 (9)	C(203)-C(207)	1.460 (9)
C(104)-N(103)	1.323 (7)	C(204)-N(203)	1.326 (7)
C(107)-O(103)	1.250 (7)	C(207)-O(203)	1.249 (7)
C(107)-C(108)	1.479 (8)	C(207)-C(208)	1.490 (8)
C(108)-C(109)	1.323 (9)	C(208)-C(209)	1.321 (9)
C(109)-C(110)	1.456 (8)	C(209)-C(210)	1.472 (8)
C(110)-C(111)	1.399 (8)	C(210)-C(211)	1.402 (9)
C(111)-C(112)	1.377 (9)	C(211)-C(212)	1.382 (9)
C(112)-C(113)	1.385 (10)	C(212)-C(213)	1.379 (10)
C(113)-C(114)	1.373 (9)	C(213)-C(214)	1.379 (9)
C(114)-C(115)	1.379 (9)	C(214)-C(215)	1.389 (9)
C(115)-C(110)	1.401 (9)	C(215)-C(210)	1.387 (9)

A-N(103) = 3.03 (6) Å [bond angle 167 (2)°]. The molecules can be considered to be bound by van der Waals contacts. The crystal structure can be described as comprising layers of closely packed molecules parallel to the mean plane (Fig. 2).

Table 4. Bond angles ($^{\circ}$)

Molecule (1)		Molecule (2)	
N(101)–C(101)–N(102)	115.8 (5)	N(201)–C(201)–N(202)	116.3 (5)
N(101)–C(101)–O(101)	121.1 (6)	N(201)–C(201)–O(201)	121.6 (5)
O(101)–C(101)–N(102)	123.1 (6)	O(201)–C(201)–N(202)	122.1 (5)
C(101)–N(102)–C(102)	125.8 (5)	C(201)–N(202)–C(202)	124.8 (5)
C(102)–N(102)–C(106)	118.3 (5)	C(202)–N(202)–C(206)	119.0 (5)
C(101)–N(102)–C(106)	115.8 (5)	C(201)–N(202)–C(206)	116.1 (5)
C(101)–N(101)–C(104)	123.2 (5)	C(201)–N(201)–C(204)	123.0 (5)
C(101)–N(101)–C(105)	116.1 (5)	C(201)–N(201)–C(205)	116.7 (5)
C(104)–N(101)–C(105)	120.7 (5)	C(204)–N(201)–C(205)	120.2 (5)
C(103)–C(102)–N(102)	116.0 (5)	C(203)–C(202)–N(202)	116.8 (5)
C(103)–C(102)–O(102)	126.6 (5)	C(203)–C(202)–O(202)	126.8 (5)
N(102)–C(102)–O(102)	117.4 (5)	N(202)–C(202)–O(202)	116.3 (5)
C(102)–C(103)–C(107)	122.0 (5)	C(202)–C(203)–C(207)	123.1 (5)
C(102)–C(103)–C(104)	118.5 (5)	C(202)–C(203)–C(204)	118.5 (5)
C(104)–C(103)–C(107)	119.4 (5)	C(204)–C(203)–C(207)	118.3 (5)
N(101)–C(104)–C(103)	120.2 (5)	N(201)–C(204)–C(203)	120.2 (5)
N(101)–C(104)–N(103)	117.1 (5)	N(201)–C(204)–N(203)	117.3 (5)
C(103)–C(104)–N(103)	122.7 (5)	C(203)–C(204)–N(203)	122.5 (5)
C(103)–C(107)–C(108)	122.5 (5)	C(203)–C(207)–C(208)	121.2 (5)
C(103)–C(107)–O(103)	120.4 (5)	C(203)–C(207)–O(203)	121.8 (5)
C(108)–C(107)–O(103)	117.1 (5)	C(208)–C(207)–O(203)	117.0 (5)
C(107)–C(108)–C(109)	120.7 (6)	C(207)–C(208)–C(209)	119.7 (6)
C(108)–C(109)–C(110)	127.6 (6)	C(208)–C(209)–C(210)	127.9 (6)
C(109)–C(110)–C(111)	122.9 (6)	C(209)–C(210)–C(211)	117.8 (5)
C(109)–C(110)–C(115)	118.8 (5)	C(209)–C(210)–C(215)	122.9 (5)
C(111)–C(110)–C(115)	118.2 (6)	C(211)–C(210)–C(215)	119.3 (5)
C(110)–C(111)–C(112)	120.4 (6)	C(210)–C(211)–C(212)	119.9 (6)
C(111)–C(112)–C(113)	121.3 (6)	C(211)–C(212)–C(213)	120.9 (6)
C(112)–C(113)–C(114)	118.3 (6)	C(212)–C(213)–C(214)	119.2 (6)
C(113)–C(114)–C(115)	121.9 (6)	C(213)–C(214)–C(215)	121.1 (6)
C(114)–C(115)–C(110)	119.9 (6)	C(214)–C(215)–C(210)	119.5 (6)

Table 5. Mean planes

P1: C(109), C(110), C(111), C(112), C(113), C(114), C(115)
P2: N(101), C(101), N(102), C(102), C(103), C(104)
P3: C(209), C(210), C(211), C(212), C(213), C(214), C(215)
P4: N(201), C(201), N(202), C(202), C(203), C(204)

$$P1 \wedge P2 = 5^{\circ} \quad P3 \wedge P4 = 6^{\circ}$$

$$(P_1, P_2) \wedge (P_3, P_4) = 48^{\circ}$$

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3,3',5,5'-Tetraiodothyroformic Acid–*N*-Diethanolamine 1:2 Salt

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Abstract. $C_{13}H_6I_4O_4 \cdot 2C_4H_{11}NO_2$, monoclinic, $P2_1/n$, $Z = 4$, $a = 7.880$ (2), $b = 28.534$ (6), $c = 12.584$ (3) Å, $\beta = 93.16$ (4) $^{\circ}$, $M_r = 944.08$, $D_c = 2.22$ Mg m $^{-3}$, $R = 6.2\%$. Tetraiodothyroformic acid (T_4f) [3,5-diiodo-4-(4-hydroxy-3,5-diiodophenoxy)benzoic acid] forms a 1:2 salt with *N*-diethanolamine (NDEA) via a network of 13 intermolecular hydrogen-bond contacts. T_4f is a dianion with a 4'-phenoxide and 1-carboxylate anion

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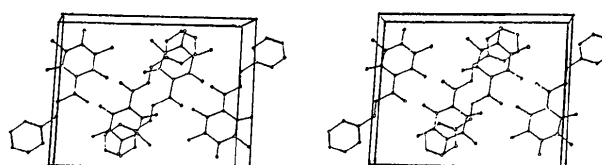


Fig. 2. Stereoview of the packing.

The X-ray analysis unambiguously demonstrates the planar structure of NSC 290115. A wide variety of planar polycyclic molecules with a high degree of activity against leukemia (Kohn, Waring, Glaubiger & Friedman, 1975; Le Pecq, Dat-Xuong, Gosse & Paoletti, 1974) have been shown to interfere with the replication of DNA through intercalation between adjacent partially unwound base pairs (Lerman, 1961). The aromatic groups of NSC 290115 are stabilized in an extended planar structure whose size fits with the base planes of the DNA. This suggests that the antitumor activity may be a consequence of an intercalative process, the affinity for the DNA being enhanced by the presence of a uracil moiety.

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geometry. The conformations of the two NDEA molecules differ; one has the extended conformation usually observed, while the other is folded. This folded NDEA also has a 50% disorder in one of its hydroxyls.

Introduction. The crystal structure determination of 3,3',5,5'-tetraiodothyroformic acid was undertaken as part of a structural study on a series (Cody, Hazel, Langs & Duax, 1977; Cody, Hazel & Osawa, 1978; Cody, 1978) of thyroxine acid metabolites. This study

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