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# Photocycloadduct of 1-[3-(Imidazol-1-yl)propyl]thymine {Thy[1(CH$_2$)$_3$1′]im*}: 14-Methyl-4,6,10,12-tetraazatetracyclo[8.4.0.0$^{2,6}$.0$^{3,14}$]tetradec-4-ene-11,13-dione, $C_{11}H_{14}N_4O_2$

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**Abstract.** $M_r = 234{\cdot}3$, triclinic, $P\bar{1}$, $a = 5{\cdot}7925$ (8), $b = 9{\cdot}341$ (1), $c = 10{\cdot}902$ (1) Å, $\alpha = 106{\cdot}21$ (1), $\beta = 81{\cdot}11$ (1), $\gamma = 109{\cdot}74$ (1)°, $V = 532{\cdot}0$ (1) Å$^3$, $Z = 2$, $D_x = 1{\cdot}46$ g cm$^{-3}$, $\lambda$(Cu $K\alpha$) = 1·54178 Å, $\mu = 7{\cdot}66$ cm$^{-1}$, $F(000) = 248$, room temperature, $R = 0{\cdot}036$ for 1337 unique observed reflections. The molecule has the *cis–syn* configuration. The conformation of the diazacycloheptane ring is close to a chair. The dihydroimidazole ring is a flattened envelope. The cyclobutane ring is puckered [mean deviation from least-squares plane 0·094 (2) Å] and the dihydrothymine ring is also significantly nonplanar [deviations −0·076 (2)–0·092 (2) Å from best plane].

**Introduction.** Various proteins have been linked covalently to nucleic acids under the influence of UV light (Kornhauser, 1976). The mechanism of this covalent linking is as yet not known. Studies in chemical model systems have shown that pyrimidine bases undergo photochemical reactions with a number of amino acids. Among the latter histidine (α-amino-1*H*-imidazole-4-propanoic acid) has also been shown to combine photochemically with uracil (Smith, 1969). However, no definite conclusion concerning the structure of the photoproduct was given. In connection with this problem the study of the photochemical reaction of thymine in the presence of imidazoles has been undertaken and a photocycloaddition of 4,5-substituted imidazole to thymine has been reported (Wenska, Paszyc & Skalski, 1983). Similarly, irradiation of 1-[3-(imidazol-1-yl)propyl]thymine leads to the cyclobutane product resulting from cycloaddition of imidazole and thymine C=C double bonds (Wenska & Paszyc, 1984). An X-ray structure analysis was carried out to establish the stereochemistry of this cycloadduct.

**Experimental.** Colourless crystal 0·15 × 0·3 × 0·4 mm from methanol–ethyl ether, $D_m$ not determined, Syntex $P2_1$ diffractometer, graphite monochromator, lattice parameters from 15 reflections, profiles measured for 1472 reflections with $2\theta \leq 115°$ ($h$ 0→6, $k$ $\bar{10}$→9, $l$ $\bar{11}$→11), profile analysis according to Lehmann & Larsen (1974), no significant intensity variation for two standard reflections, absorption ignored, 1337 reflections with $I \geq 2\sigma(I)$; structure solved by direct methods with *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980), full-matrix least-squares refinement on $F$ with *SHELX*76 (Sheldrick, 1976), $w = 1/\sigma^2(F)$; final refinement: anisotropic non-H atoms, isotropic H atoms (from $\Delta F$ map) and empirical isotropic extinction parameter $x$ used to correct $F_c$ according to $F_c' = F_c(1 - xF_c^2/\sin\theta)$, $x$ converged at 0·181 (5); $R = 0{\cdot}036$ and $wR = 0{\cdot}051$; in final refinement cycle max. $\Delta/\sigma$ 0·02, largest peak in final $\Delta F$ map 0·18 e Å$^{-3}$, largest hole −0·16 e Å$^{-3}$; atomic scattering factors from *International Tables for X-ray Crystallography* (1974); computer programs: *SHELX*76 (Sheldrick, 1976), local programs (Jaskólski, 1982), *PLUTO* (Motherwell & Clegg, 1978), *ORTEP* (Johnson, 1971).

**Discussion.** Final positional parameters are given in Table 1, molecular dimensions in Table 2.† A view of the molecule with the atom-numbering scheme is shown in Fig. 1.

The product of photocycloaddition of imidazole and thymine C=C double bonds of 1-[3-(imidazol-1-yl)-propyl]thymine, Thy[1(CH$_2$)$_3$1′]im, has a *cis–syn* configuration. The same configuration was found in all

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* The abbreviation is that proposed by Cohn, Leonard & Wang (1974); im stands for imidazole.

† Lists of observed and calculated structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42222 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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the photodimers of thymine with the trimethylene bridge between N(1) and N(1′) (Leonard, Golankiewicz, McCredie, Johnson & Paul, 1969; Skrzypczak-Jankun, Małuszyńska, Kałuski & Golankiewicz, 1977; Kozioł & Rajchel, 1982). The *cis* configuration of the molecule gives rise to many short intramolecular contacts, the shortest ones being reported in Table 3. The dihydrothymine ring is significantly nonplanar, the distances of constituent atoms from the best plane ranging from −0·076 (2) to 0·092 (2) Å. The conformation of the diazacycloheptane ring is close to a chair. The dihydroimidazole ring is a flattened envelope with C(5*P*) deviating by −0·245 (2) Å from the best plane through N(1*P*), C(2*P*), N(3*P*) and C(4*P*). The cyclobutane ring is puckered with the mean deviation from the least-squares plane of 0·094 (2) Å.

The molecular packing is shown in Fig. 2. The molecules are joined by a pair of intermolecular N(3)···O(1) hydrogen bonds to form dimers around the centre of symmetry. The geometry of this bond is given in Table 3. There are no other notable short intermolecular contacts.

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Table 1. *Final fractional coordinates and equivalent isotropic thermal parameters* (Å²)

$U_{eq} = (U_{11}U_{22}U_{33})^{1/3}$.

| | $x$ | $y$ | $z$ | $U_{eq}$ |
|---|---|---|---|---|
| N(1) | 0·4064 (3) | 0·2919 (2) | 0·3675 (1) | 0·0307 (6) |
| C(2) | 0·2458 (4) | 0·3721 (2) | 0·4174 (2) | 0·0305 (7) |
| O(1) | 0·0846 (3) | 0·3357 (2) | 0·5011 (1) | 0·0492 (6) |
| N(3) | 0·2682 (3) | 0·5028 (2) | 0·3744 (2) | 0·0335 (6) |
| C(4) | 0·4221 (4) | 0·5548 (2) | 0·2767 (2) | 0·0318 (7) |
| O(2) | 0·4272 (3) | 0·6746 (2) | 0·2513 (1) | 0·0486 (6) |
| C(5) | 0·5774 (4) | 0·4540 (2) | 0·2034 (2) | 0·0296 (7) |
| C(6) | 0·5925 (4) | 0·3268 (2) | 0·2655 (2) | 0·0291 (7) |
| C(7) | 0·8318 (4) | 0·5535 (3) | 0·1648 (2) | 0·0411 (8) |
| N(1*P*) | 0·3122 (3) | 0·0742 (2) | 0·1325 (2) | 0·0357 (6) |
| C(2*P*) | 0·1265 (4) | 0·1304 (3) | 0·1237 (2) | 0·0370 (8) |
| N(3*P*) | 0·1830 (3) | 0·2639 (2) | 0·0974 (2) | 0·0390 (6) |
| C(4*P*) | 0·4553 (4) | 0·3218 (2) | 0·0878 (2) | 0·0325 (7) |
| C(5*P*) | 0·5348 (4) | 0·2046 (2) | 0·1344 (2) | 0·0322 (7) |
| C(8) | 0·3902 (5) | 0·1549 (3) | 0·4143 (2) | 0·0417 (8) |
| C(9) | 0·2117 (5) | 0·0039 (3) | 0·3444 (2) | 0·0465 (9) |
| C(10) | 0·2791 (6) | −0·0457 (3) | 0·2018 (2) | 0·0443 (9) |

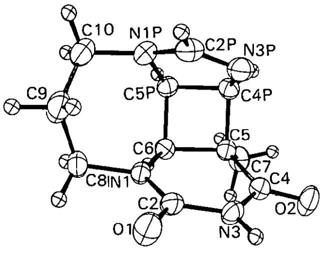

Fig. 1. *ORTEP* (Johnson, 1971) drawing of $Thy[1(CH_2)_31']im$. Thermal ellipsoids are drawn at the 45% probability level.

Table 2. *Molecular dimensions*

(*a*) Bond lengths (Å)

| | | | |
|---|---|---|---|
| C(2)–N(1) | 1·345 (3) | C(5*P*)–C(6) | 1·561 (3) |
| C(6)–N(1) | 1·449 (3) | C(2*P*)–N(1*P*) | 1·372 (3) |
| C(8)–N(1) | 1·474 (3) | C(5*P*)–N(1*P*) | 1·442 (2) |
| O(1)–C(2) | 1·231 (2) | C(10)–N(1*P*) | 1·465 (3) |
| N(3)–C(2) | 1·386 (3) | N(3*P*)–C(2*P*) | 1·280 (3) |
| C(4)–N(3) | 1·366 (3) | C(4*P*)–N(3*P*) | 1·482 (3) |
| O(4)–C(4) | 1·216 (2) | C(5)–C(4*P*) | 1·559 (3) |
| C(5)–C(4) | 1·505 (3) | C(5*P*)–C(4*P*) | 1·547 (3) |
| C(6)–C(5) | 1·554 (3) | C(9)–C(8) | 1·516 (4) |
| C(7)–C(5) | 1·521 (3) | C(10)–C(9) | 1·522 (4) |

(*b*) Bond angles (°)

| | | | |
|---|---|---|---|
| C(6)–N(1)–C(2) | 124·3 (2) | C(5*P*)–C(6)–N(1) | 113·6 (2) |
| C(8)–N(1)–C(2) | 119·2 (2) | C(5*P*)–C(6)–C(5) | 88·8 (1) |
| C(8)–N(1)–C(6) | 116·5 (2) | C(5*P*)–N(1*P*)–C(2*P*) | 105·5 (2) |
| O(1)–C(2)–N(1) | 122·5 (2) | C(10)–N(1*P*)–C(2*P*) | 122·9 (2) |
| N(3)–C(2)–N(1) | 118·2 (2) | C(10)–N(1*P*)–C(5*P*) | 122·4 (2) |
| N(3)–C(2)–O(1) | 119·3 (2) | N(3*P*)–C(2*P*)–N(1*P*) | 118·7 (2) |
| C(4)–N(3)–C(2) | 127·8 (2) | C(4*P*)–N(3*P*)–C(2*P*) | 105·3 (2) |
| O(2)–C(4)–N(3) | 120·8 (2) | N(3*P*)–C(4*P*)–C(5) | 115·8 (2) |
| C(5)–C(4)–N(3) | 116·0 (2) | C(5*P*)–C(4*P*)–C(5) | 89·1 (1) |
| C(5)–C(4)–O(2) | 123·2 (2) | C(5*P*)–C(4*P*)–N(3*P*) | 104·9 (2) |
| C(6)–C(5)–C(4) | 116·4 (2) | N(1*P*)–C(5*P*)–C(6) | 116·6 (2) |
| C(7)–C(5)–C(4) | 111·3 (2) | C(4*P*)–C(5*P*)–C(6) | 89·5 (1) |
| C(7)–C(5)–C(6) | 111·4 (2) | C(4*P*)–C(5*P*)–N(1*P*) | 103·1 (2) |
| C(4*P*)–C(5)–C(4) | 115·0 (2) | C(9)–C(8)–N(1) | 113·2 (2) |
| C(4*P*)–C(5)–C(6) | 89·3 (1) | C(10)–C(9)–C(8) | 114·3 (2) |
| C(4*P*)–C(5)–C(7) | 111·8 (2) | C(9)–C(10)–N(1*P*) | 114·1 (2) |
| C(5)–C(6)–N(1) | 115·1 (2) | | |

(*c*) Endocyclic torsion angles (°)

| Ring *A* | | Ring *C* | |
|---|---|---|---|
| N(1)–C(2)–N(3)–C(4) | 6·7 (3) | N(1)–C(6)–C(5*P*)–N(1*P*) | −1·3 (2) |
| C(2)–N(3)–C(4)–C(5) | 3·0 (3) | C(6)–C(5*P*)–N(1*P*)–C(10) | −66·5 (3) |
| N(3)–C(4)–C(5)–C(6) | −14·1 (2) | C(5*P*)–N(1*P*)–C(10)–C(9) | 79·5 (3) |
| C(4)–C(5)–C(6)–N(1) | 15·9 (2) | N(1*P*)–C(10)–C(9)–C(8) | −55·2 (3) |
| C(5)–C(6)–N(1)–C(2) | −7·1 (3) | C(10)–C(9)–C(8)–N(1) | 62·0 (3) |
| C(6)–N(1)–C(2)–N(3) | −4·1 (3) | C(9)–C(8)–N(1)–C(6) | −91·0 (3) |
| | | C(8)–N(1)–C(6)–C(5*P*) | 70·3 (2) |
| Ring *B* | | Ring *D* | |
| N(1*P*)–C(5*P*)–C(4*P*)–N(3*P*) | 14·6 (2) | C(6)–C(5)–C(4*P*)–C(5*P*) | −13·9 (2) |
| C(5*P*)–C(4*P*)–N(3*P*)–C(2*P*) | −8·4 (2) | C(5)–C(4*P*)–C(5*P*)–C(6) | 13·8 (2) |
| C(4*P*)–N(3*P*)–C(2*P*)–N(1*P*) | −1·7 (3) | C(4*P*)–C(5*P*)–C(6)–C(5) | −13·9 (2) |
| N(3*P*)–C(2*P*)–N(1*P*)–C(5*P*) | 11·8 (3) | C(5*P*)–C(6)–C(5)–C(4*P*) | 13·7 (2) |
| C(2*P*)–N(1*P*)–C(5*P*)–C(4*P*) | −15·3 (2) | | |

Table 3. *Interatomic contacts*

Intramolecular distances (Å)

| | | | |
|---|---|---|---|
| N(1)···N(1*P*) | 2·788 (3) | C(6)···C(2*P*) | 3·066 (3) |
| C(4)···N(3*P*) | 2·908 (3) | N(1)···C(4*P*) | 3·100 (3) |
| N(1)···C(2*P*) | 3·068 (3) | N(1)···C(10) | 3·068 (3) |
| C(6)···N(3*P*) | 3·022 (3) | N(1*P*)···C(8) | 3·019 (3) |

Hydrogen-bond geometry

| | | | |
|---|---|---|---|
| O(1)···N($3^i$) | 2·894 (2) Å | O(1)···H(3)–N(3) | 178 (2)° |
| O(1)···H($3^i$) | 1·98 (3) | | |

Symmetry code: (i) $-x$, $1-y$, $1-z$.

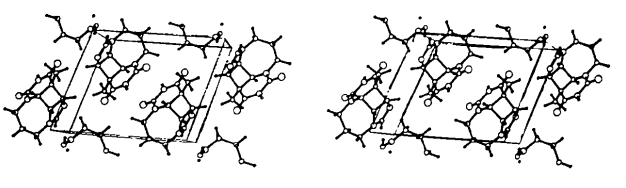

Fig. 2. Stereoview showing the packing in the crystal. The *c* axis is approximately horizontal and the *b* axis approximately vertical.

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# Structural Studies of Colchicine Derivatives. V. The Structure of 6,7-Didehydrocolchiceine, $C_{21}H_{21}NO_6$

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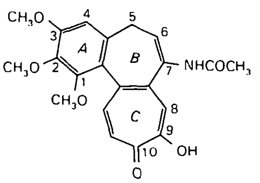
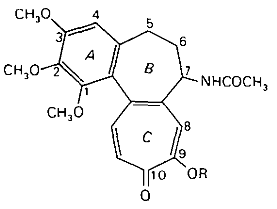
**Abstract.** $M_r = 383\cdot4$, monoclinic, $P2_1/a$, $a = 9\cdot535\,(6)$, $b = 16\cdot660\,(5)$, $c = 12\cdot450\,(4)$ Å, $\beta = 107\cdot89\,(6)^\circ$, $V = 1882\,(1)$ Å$^3$, $Z = 4$, $D_x = 1\cdot353\,(1)$ g cm$^{-3}$, Mo $K\alpha$, $\lambda = 0\cdot71069$ Å, $\mu = 0\cdot93$ cm$^{-1}$, $F(000) = 808$, $T = 294$ K, final $R = 0\cdot040$ for 2016 unique observed reflections. The troponoid ring $C$ presents an arrangement corresponding to an isocolchicine-like structure and shows a skew-boat conformation. The other seven-membered ring $B$ is slightly flattened owing to the double bond and has a boat conformation. Three intramolecular hydrogen bonds influence the overall shape of the molecule.

**Introduction.** The title compound (I) is one of several colchiceine derivatives that has been synthetized and studied to find their conformation in order to correlate it with biological activity (Molins, Rius, Solans, Miravitlles, Bladé-Fonte & Germain, 1985, and references therein). Colchicine and some of its derivatives, which bind well to tubulin, behave as powerful antimitotics and, therefore, have potential antitumour activity.

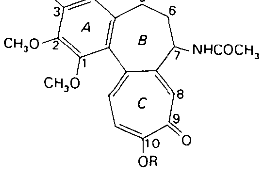
Isocolchicine and its derivatives (II) present considerably less activity, a fact that is strongly related to the



(I)



(II)



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