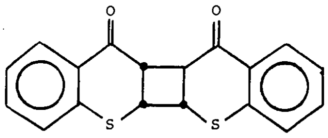
of the cyclobutane mean plane and that to C(4′) lying on the other (Table 7*a*). As can be seen from Table 7(*b*) the heterocyclic rings of dimer (5) have one boat and one chair conformation.



(IV)

The fact that the five independent dimer molecules in these crystals show such differing heterocyclic ring conformations could only be due to their inherent flexibility. The conformations adopted appear to be simply those which minimize intermolecular repulsions. There were no especially short distances found in any of the crystals.

As has been seen, because of disorder, it is not possible to classify dimer (4) as either *HH* or *HT*. The existence of a high-frequency IR carbonyl band at 1700 cm^{-1} would suggest the *HH* conformation.

We are grateful to the Natural Sciences and Engineering Research Council of Canada for financial assistance.

References

Germain, G., Main, P. & Woolfson, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

Grant, D. F. & Gabe, E. J. (1978). *J. Appl. Cryst.* **11**, 114–120.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

Johnson, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

Larson, A. C. & Gabe, E. J. (1978). *Computing in Crystallography*, edited by H. Schenk, R. Olthof-Hazekamp, H. Van Koningsveld & G. C. Bassi, p. 81. Delft Univ. Press.

Still, I. W. J. & Leong, T. S. (1981). *Tetrahedron Lett.* **22**, 1183–1186.

Yuen, P. & Nyburg, S. C. (1979). *J. Appl. Cryst.* **12**, 258.

Acta Cryst. (1986). C**42**, 821–823

Structure of 1-{2-[2-(4-Hydroxyphenyl)ethylthio]ethyl}thymine

By Yoshinori Tsuchiya, Akio Takenaka and Yoshio Sasada

Faculty of Science, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 227, *Japan*

and Minoru Ohki

Research Institute, Wakamoto Pharmaceutical Co Ltd, Kanate, Ohimachi, Ashigara-kamigun, Kanagawa 258, *Japan*

(*Received* 23 *December* 1985; *accepted* 22 *January* 1986)

Abstract. $C_{15}H_{18}N_2O_3S$, $M_r = 306{\cdot}38$, monoclinic, $P2_1/n$, $a = 9{\cdot}993\,(1)$, $b = 8{\cdot}475\,(1)$, $c = 17{\cdot}537\,(1)$ Å, $\beta = 91{\cdot}277\,(6)°$, $V = 1484{\cdot}8\,(2)$ Å^3, $Z = 4$, $D_m = 1{\cdot}361$, $D_x = 1{\cdot}370$ g cm^{-3}, $\lambda(\mathrm{Cu}\,K\alpha) = 1{\cdot}5418$ Å, $\mu = 19{\cdot}8$ cm^{-1}, $F(000) = 648$, $T = 293$ K, $R = 0{\cdot}057$ for 1989 observed reflexions. The molecule takes an extended form. Molecular dimensions of the thymine and phenol moieties are normal. The hydroxyl group of phenol hydrogen bonds with O(4) of the thymine moiety of the molecule at $\frac{1}{2}-x$, $-\frac{3}{2}+y$, $\frac{1}{2}-z$ [OH···O 2·778 (3) Å]. The three infinite chains so formed are assembled to give a triple helix, and the helices are connected side by side at thymine moieties by N(3)H···O(2) hydrogen bonds [2·862 (3) Å] to build up a $(10\bar{1})$ layer structure.

Introduction. As part of a series of studies on elementary binding patterns in protein–nucleic acid interactions, we have determined the structure of the model crystal that contains thymine and tyrosine skeletons. Direct interactions between nucleic acid base and tyrosine have not yet been found in crystal structures so far reported (Ohki, Takenaka, Shimanouchi & Sasada, 1977; Ogawa, Tago, Ishida & Tomita, 1980), although stacking and hydrogen bonding between them were suggested to occur in solution (Lancelot, 1977*a*,*b*; Hélène, Montenay-Garestier & Dimicoli, 1971).

Experimental. 1-(2-Mercaptoethyl)thymine synthesized from isothiourea and 1-(2-hydroxyethyl)thymine was condensed with 4-(2-chloroethyl)phenol to give the title compound in the presence of potassium *tert*-butoxide. Plate crystals from aqueous solution. D_m by flotation in mixture of dichloromethane and carbon tetrachloride. Rigaku four-circle diffractometer; graphite-monochromated Cu $K\alpha$ radiation; crystal size $0{\cdot}25 \times 0{\cdot}20 \times 0{\cdot}10$ mm; unit-cell dimensions determined with 40 reflexions ($31 < 2\theta < 42°$); 2368 independent reflexions measured, $2 < 2\theta < 125°$, h 0–20, k 0–9, l −20–20; 379 reflexions with $|F_o| < 3\sigma$ considered unobserved; ω-scan mode, scan rate 4° min^{-1}, scan width 1·5°. Five reference reflexions monitored every 50 reflexions showed no significant intensity deterioration. Corrections for Lorentz and polarization factors, not for absorption because $\mu R < 0{\cdot}5$. Standard deviations $\sigma^2(F_o) = \sigma_P^2(F_o) + qF_o^2$, σ_P evaluated by counting statistics and q estimated to be $3{\cdot}82 \times 10^{-5}$ from measurement of monitored reflexions (McCandlish & Stout, 1975). Structure solved by direct methods, refined by full-matrix least squares; all H atoms found on difference map and refined isotropically; $\sum w(|F_o| - |F_c|)^2$ minimized, $w = 1/\sigma^2(F_o)$; final R value 0·057 for 1989 reflexions with $|F_o| > 3\sigma$ (wR = 0·042, S = 2·06); max. shift of coordinates $0{\cdot}02\sigma$ for non-H atoms, $\Delta\rho$ peak 0·41 e Å^{-3}. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974); programs used: *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), *LSAP*80 (Takenaka & Sasada, 1980), *DCMS*82 (Takenaka & Sasada, 1982) and *LISTUP* (Takenaka & Sasada, 1983). Final atomic parameters are given in Table 1.*

Table 1. *Fractional coordinates and equivalent isotropic temperature factors*

B_{eq} values are calculated from the anisotropic thermal parameters using the equation $B_{eq} = 8\pi^2(U_1 + U_2 + U_3)/3$, where U_1, U_2 and U_3 are the principal components of the mean-square displacement matrix U. Values in ⟨⟩ are anisotropically defined by $[\sum(B_{eq} \times 8\pi^2 U_i)^2/3]^{1/2}$ and those in ( ) are e.s.d.'s; they refer to last decimal places.

	x	y	z	B_{eq}(Å^2)
N(1)	0·2268 (3)	0·2453 (3)	0·0813 (2)	2·9 ⟨10⟩
C(2)	0·1357 (3)	0·3487 (4)	0·0499 (2)	3·0 ⟨6⟩
O(2)	0·0202 (2)	0·3113 (3)	0·0331 (1)	4·1 ⟨21⟩
N(3)	0·1837 (3)	0·4990 (3)	0·0383 (2)	2·9 ⟨9⟩
C(4)	0·3111 (3)	0·5537 (4)	0·0565 (2)	2·9 ⟨4⟩
O(4)	0·3411 (2)	0·6911 (2)	0·0398 (1)	3·5 ⟨9⟩
C(5)	0·3991 (3)	0·4410 (4)	0·0939 (2)	2·7 ⟨4⟩
C(6)	0·3532 (3)	0·2939 (4)	0·1028 (2)	3·0 ⟨7⟩
C(7)	0·5372 (4)	0·4891 (5)	0·1194 (3)	3·7 ⟨10⟩
C(8)	0·1884 (4)	0·0765 (4)	0·0909 (2)	3·3 ⟨8⟩
C(9)	0·1523 (4)	0·0462 (4)	0·1729 (2)	3·7 ⟨7⟩
S	0·11658 (9)	−0·1632 (1)	0·18797 (5)	3·57 ⟨149⟩
C(10)	−0·0575 (4)	−0·1659 (5)	0·1576 (2)	3·9 ⟨14⟩
C(11)	−0·1143 (4)	−0·3329 (5)	0·1581 (2)	4·2 ⟨13⟩
C(12)	−0·1035 (3)	−0·4126 (4)	0·2352 (2)	3·4 ⟨13⟩
C(13)	−0·1837 (4)	−0·3677 (4)	0·2952 (2)	3·7 ⟨14⟩
C(14)	−0·1715 (4)	−0·4374 (4)	0·3663 (2)	3·6 ⟨8⟩
C(15)	−0·0773 (3)	−0·5578 (4)	0·3784 (2)	3·2 ⟨9⟩
O(15)	−0·0718 (3)	−0·6266 (3)	0·4490 (1)	4·2 ⟨9⟩
C(16)	0·0048 (3)	−0·6023 (4)	0·3198 (2)	3·4 ⟨7⟩
C(17)	−0·0090 (4)	−0·5295 (4)	0·2490 (2)	3·6 ⟨7⟩

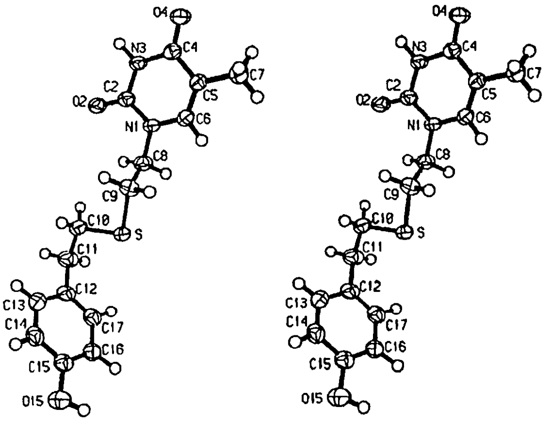


Fig. 1. Stereoview of the 1-{2-[2-(4-hydroxyphenyl)ethylthio]ethyl}thymine molecule (30% probability).

Table 2. *Selected bond distances* (Å) *and angles* (°)

N(1)—C(2)	1·371 (4)	N(1)—C(6)	1·373 (4)
N(1)—C(8)	1·492 (4)	C(2)—O(2)	1·227 (3)
C(2)—N(3)	1·378 (4)	N(3)—C(4)	1·386 (4)
C(4)—O(4)	1·239 (3)	C(4)—C(5)	1·445 (4)
C(5)—C(6)	1·339 (4)	C(5)—C(7)	1·497 (5)
C(8)—C(9)	1·512 (5)	C(9)—S	1·830 (3)
S—C(10)	1·808 (4)	C(10)—C(11)	1·525 (5)
C(11)—C(12)	1·514 (5)	C(12)—C(13)	1·390 (5)
C(12)—C(17)	1·386 (5)	C(13)—C(14)	1·383 (5)
C(14)—C(15)	1·401 (5)	C(15)—O(15)	1·369 (4)
C(15)—C(16)	1·381 (4)	C(16)—C(17)	1·390 (5)
C(2)—N(1)—C(6)	121·1 (2)	C(2)—N(1)—C(8)	119·2 (2)
C(6)—N(1)—C(8)	119·6 (2)	N(1)—C(2)—O(2)	123·0 (2)
N(1)—C(2)—N(3)	114·9 (2)	O(2)—C(2)—N(3)	122·1 (2)
C(2)—N(3)—C(4)	126·6 (2)	N(3)—C(4)—O(4)	119·1 (2)
N(3)—C(4)—C(5)	115·5 (2)	O(4)—C(4)—C(5)	125·5 (2)
C(4)—C(5)—C(6)	117·5 (2)	C(4)—C(5)—C(7)	120·2 (2)
C(6)—C(5)—C(7)	122·3 (3)	N(1)—C(6)—C(5)	124·2 (3)
N(1)—C(8)—C(9)	109·7 (2)	C(8)—C(9)—S	110·7 (2)
C(9)—S—C(10)	99·2 (1)	S—C(10)—C(11)	111·5 (2)
C(10)—C(11)—C(12)	113·5 (3)	C(11)—C(12)—C(13)	121·6 (3)
C(11)—C(12)—C(17)	120·7 (3)	C(13)—C(12)—C(17)	117·7 (3)
C(12)—C(13)—C(14)	121·7 (3)	C(13)—C(14)—C(15)	119·4 (3)
C(14)—C(15)—O(15)	117·4 (3)	C(14)—C(15)—C(16)	119·7 (3)
O(15)—C(15)—C(16)	122·9 (3)	C(15)—C(16)—C(17)	119·6 (3)
C(12)—C(17)—C(16)	121·8 (3)		

Discussion. Fig. 1 is a stereoview of the molecule with atomic numbering. The molecule exhibits a rather extended form with respect to the link between the thymine and tyrosine moieties. Torsion angles are 259·0 (3) for C(2)—N(1)—C(8)—C(9), 184·1 (2) for N(1)—C(8)—C(9)—S, 275·3 (3) for C(8)—C(9)—S—C(10), 175·6 (3) for C(9)—S—C(10)—C(11), 57·9 (3) for S—C(10)—C(11)—C(12) and 72·3 (4)° for C(10)—C(11)—C(12)—C(13). Therefore, no direct intramolecular interaction takes place between the nucleic acid base moiety and the tyrosine side group.

Bond distances and angles are listed in Table 2. Molecular dimensions of the thymine and phenol

---

* Lists of structure factors, anisotropic thermal parameters, H-atom parameters, all bond distances and angles involving H and least-squares planes have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42788 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

moieties are in good agreement with those in related compounds, such as thymidine (Young, Tollin & Wilson, 1969) and *N*-acetyl-L-tyrosine (Koszelak & van der Helm, 1981). The thymine ring is planar within 0·025 Å, but exocyclic O(2), O(4), C(7) and C(8) deviate from the ring plane with maximum displacement of 0·100 (3) Å for C(8). Neighbouring exocyclic atoms, O(2) and C(8) or O(4) and C(7), deviate to opposite sides of the plane. The benzene ring shows good planarity with maximum deviation 0·009 (3) Å.

Fig. 2 shows the crystal structures projected along **a** and **b**. The thymine moieties form a dimer around the inversion centre, through a pair of N(3)H···O(2) hydrogen bonds [2·862 (3) Å]. The same type of hydrogen-bonded dimer is found in the 1-thyminylacetic acid–tyramine (1/1) complex (Ogawa *et al.*, 1980) and in 1-(2-hydroxyethyl)uracil (Shibata, Takenaka & Sasada, 1985*b*).

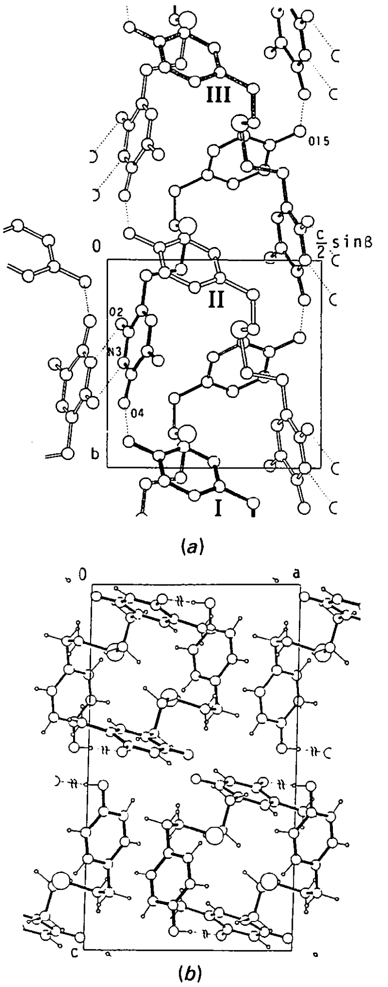


Fig. 2. Crystal structures projected along (*a*) **a** and (*b*) **b**. Three hydrogen-bonded chains along **b** are designated by I, II and III, although they are crystallographically equivalent. Hydrogen bonds are indicated by dotted lines.

The hydroxyl group forms a hydrogen bond with O(4) of the thymine at $(\frac{1}{2}-x, -\frac{3}{2}+y, \frac{1}{2}-z)$, O(15)H···O(4) being 2·778 (3) Å. The carbonyl O(4) atom seems to be a good hydrogen-bond acceptor; the same type of hydrogen bonding has been found in 1-(2-hydroxyethyl)thymine monohydrate (Shibata, Takenaka & Sasada, 1985*a*) and thymine monohydrate (Gerdi, 1961). The hydrogen-bond length in the present crystal is somewhat shorter than those in the above-mentioned crystals. The presumed strong OH···O hydrogen bonds link the molecules, in a head-to-tail manner, to form an infinite chain along **b**. Three chains, I, II and III in Fig. 2(*a*), are assembled to form a triple helix, although they are crystallographically equivalent. Close interchain contacts within the helix are 3·666 (5) for C(7)···C($13^{\rm i}$) and 3·650 (5) Å for C(9)···C($16^{\rm i}$) [symmetry code: (i) $\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z$]. The triple helices are connected side by side by the hydrogen bonds in the thymine pair mentioned above to build up a $(10\bar{1})$ layer structure. Close contacts between the layers are 3·152 (4) for C(6)···O($15^{\rm ii}$) and 3·348 (5) Å for C(10)···C($14^{\rm iii}$) [(ii) $\frac{1}{2}+x, -\frac{1}{2}-y, -\frac{1}{2}+z$; (iii) $-\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z$].

The present work was supported in part by a Grant-in-Aid for Scientific Research, No. 59580098, from the Ministry of Education, Science and Culture, to which the authors' thanks are due.

References

GERDI, R. (1961). *Acta Cryst.* **14**, 333–344.

HÉLÈNE, C., MONTENAY-GARESTIER, T. & DIMICOLI, J. L. (1971). *Biochim. Biophys. Acta*, **254**, 349–365.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

KOSZELAK, S. N. & VAN DER HELM, D. (1981). *Acta Cryst.* B**37**, 1122–1124.

LANCELOT, G. (1977*a*). *Biophys. J.* **17**, 243–254.

LANCELOT, G. (1977*b*). *Biochimie*, **59**, 587–596.

MCCANDLISH, L. E. & STOUT, G. H. (1975). *Acta Cryst.* A**31**, 245–249.

MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1978). *MULTAN78. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

OGAWA, K., TAGO, K., ISHIDA, T. & TOMITA, K. (1980). *Acta Cryst.* B**36**, 2095–2099.

OHKI, M., TAKENAKA, A., SHIMANOUCHI, H. & SASADA, Y. (1977). *Acta Cryst.* B**33**, 2956–2958.

SHIBATA, M., TAKENAKA, A. & SASADA, Y. (1985*a*). *Acta Cryst.* C**41**, 1356–1358.

SHIBATA, M., TAKENAKA, A. & SASADA, Y. (1985*b*). *Acta Cryst.* C**41**, 1499–1500.

TAKENAKA, A. & SASADA, Y. (1980). *LSAP80*. Tokyo Institute of Technology, Japan.

TAKENAKA, A. & SASADA, Y. (1982). *DCMS82*. Tokyo Institute of Technology, Japan.

TAKENAKA, A. & SASADA, Y. (1983). *LISTUP*. Tokyo Institute of Technology, Japan.

YOUNG, D. W., TOLLIN, P. & WILSON, H. R. (1969). *Acta Cryst.* B**25**, 1423–1432.