are reported in Table 3. Moreover, in both compounds, the Br atom has a short contact distance with an O atom of the substituted base [(I): Br···O(6) ($-x$, $y-\frac{1}{2}$, $-z$) = 3·285 (5) Å; (II): Br···O(4) ($x-1$, y, z) = 2·993 (7) Å]. The pyrimidine moiety being non-planar due to the substitutions, no base stacking was observed in either compound.

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Structure of 5-Methoxy-2-{[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl}-1*H*-benzimidazole (Omeprazole)

BY HIROFUMI OHISHI, YASUKO IN, TOSHIMASA ISHIDA* AND MASATOSHI INOUE

Osaka University of Pharmaceutical Sciences, 2-10-65 *Kawai, Matsubara, Osaka* 580, *Japan*

AND FUMIO SATO, MITSUHITO OKITSU AND TOMOCHIKA OHNO

Suntory Institute for Biomedical Research, 1-11 *Wakayamadai, Shimamoto-cho, Mishima-gun, Osaka* 618, *Japan*

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Abstract. $C_{17}H_{19}N_3O_3S$, M_r = 345·42, triclinic, $P\bar{1}$, a = 10·686 (5), b = 10·608 (7), c = 9·666 (6) Å, α = 119·75 (5), β = 112·02 (5), γ = 68·33 (4)°, V = 859 (1) Å^3, Z = 2, D_m = 1·332 (2), D_x = 1·335 g cm^{-3}, Cu $K\alpha$, λ = 1·5418 Å, μ = 18·04 cm^{-1}, $F(000)$ = 364, T = 293 K, R = 0·057 for 1962 observed reflections. The methylsulfinyl group, which adopts a *trans* conformation, links the pyridine and benzimidazole rings in an almost coplanar orientation. Thus the molecule, as a whole, adopts a nearly extended form. Two centrosymmetrically related molecules form a cyclic dimer by intermolecular N—H···O hydrogen bonding, and the dimers are held together by van der Waals contacts between the neighboring aromatic rings in the crystal structure.

Introduction. Recently, H^+,K^+-ATPase has been recognized as the acid pump involved in the terminal steps of the gastric acid secretory process, and H^+,K^+-ATPase inhibitors have attracted much attention for peptic ulcer therapy (Sachs, Carlsson, Lindberg & Wallmark, 1988). Omeprazole (1), a potent inhibitor for this enzyme, is presently under extensive clinical evaluation (Clissold & Campoli-

* To whom correspondence should be addressed.

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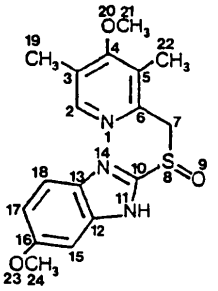
Richards, 1986): the active form is the sulfenamide formed *in vivo* from omeprazole (Lindberg, Brändström & Wallmark, 1987).



(1)

As part of evaluations of the structure–activity relationships of H^+,K^+-ATPase inhibitors, the present paper deals with the crystal structure of omeprazole.

Experimental. Crystals of the title compound were grown as colorless prisms from a chloroform solution. Crystal density by the flotation method using an aqueous KI solution. A well shaped crystal with approximate dimensions of 0·2 × 0·2 × 0·4 mm was mounted on a Rigaku automated four-circle diffractometer with graphite-monochromated Cu $K\alpha$ radiation ($\lambda = 1{\cdot}5418$ Å). Unit-cell dimensions were determined by a least-squares fit of 2θ values of 25 reflections in the 2θ range 30–55°. Intensities were measured by the θ–2θ scan technique with a scan rate of 4° min^{-1} in 2θ and a scan width of $\Delta(2\theta) = (1{\cdot}3 + 0{\cdot}15 \tan\theta)°$. Background intensities were measured for 5 s at each end of a scan. Four standard reflections (400, 050, $\bar{1}04$, $33\bar{3}$) were remeasured after every 100 reflections; the intensity decreased linearly as a function of measuring time (total loss of intensity = 13·5%). 2720 independent reflections were collected with $2\theta_{max} = 130°$ ($\sin\theta/\lambda = 0{\cdot}589$ Å^{-1}) and $h-12$ to 11, $k-12$ to 10, l 0 to 9. Corrections for the linear decrease and for Lorentz and polarization effects were applied to the intensity data; no absorption or extinction corrections were carried out.

The structure was solved by direct methods using *MULTAN*87 (Debaerdemaeker, Germain, Main, Tate & Woolfson, 1987). The initial E map gave partial structure around the S atom. Positions of the remaining non-H atoms were located stepwise from the subsequent Fourier syntheses.

The structure was refined by the block-diagonal least-squares procedure. 1962 observed reflections [$|F_o| > 3\sigma(|F_o|)$] were included in the refinement; the function minimized was $\sum w(|F_o| - |F_c|)^2$. Ideal positions of all the H atoms were calculated on the basis of stereochemical considerations, and were verified on the difference Fourier map calculated using the anisotropic non-H atoms. The H-atom parameters were included in subsequent refinement cycles. The weighting scheme used in the final refinement was $w = [\sigma(F_o)^2 + 0{\cdot}14395|F_o| + 0{\cdot}00085|F_o|^2]^{-1}$. The number of observations per refined parameter is 1962/294 = 6·67 and $S = 0{\cdot}70$. The final R and wR values are 0·057 and 0·068, respectively. (Δ/σ) in the final refinement cycle was less than 0·11 and 0·33 for positional and thermal parameters, respectively. The peaks in the final $\Delta\rho$ map were between 0·35 and −0·28 e Å^{-3}. The atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974). For all crystallographic computations, *The Universal Crystallographic Computing System* (1979) was used. The final atomic parameters are listed in Table 1.*

Table 1. *Fractional atomic coordinates and equivalent isotropic temperature factors* (Å^2) *for non-*H *atoms with e.s.d.'s in parentheses*

	x	y	z	B_{eq}*
N(1)	0·1549 (4)	0·5541 (4)	0·9852 (5)	6·5 (2)
C(2)	0·2194 (6)	0·4734 (6)	0·0739 (7)	7·1 (3)
C(3)	0·3401 (5)	0·3692 (6)	1·0539 (7)	6·8 (2)
C(4)	0·3972 (4)	0·3438 (5)	0·9346 (6)	6·2 (2)
C(5)	0·3343 (4)	0·4245 (5)	0·8384 (6)	5·7 (2)
C(6)	0·2131 (5)	0·5300 (5)	0·8731 (6)	5·8 (2)
C(7)	0·1411 (5)	0·6312 (5)	0·7824 (7)	6·8 (2)
S(8)	−0·0444 (1)	0·6751 (1)	0·7611 (2)	5·94 (5)
O(9)	−0·0903 (3)	0·5343 (3)	0·6413 (4)	6·2 (1)
C(10)	−0·0916 (5)	0·7910 (5)	0·6585 (6)	5·9 (2)
N(11)	−0·0656 (4)	0·7435 (4)	0·5106 (5)	5·8 (2)
C(12)	−0·1227 (4)	0·8690 (5)	0·4758 (6)	5·6 (2)
C(13)	−0·1783 (4)	0·9807 (5)	0·6064 (6)	5·6 (2)
N(14)	−0·1591 (4)	0·9295 (4)	0·7203 (5)	6·2 (2)
C(15)	−0·1254 (5)	0·8892 (5)	0·3440 (6)	6·0 (2)
C(16)	−0·1882 (5)	1·0327 (5)	0·3542 (6)	6·2 (2)
C(17)	−0·2437 (5)	1·1469 (5)	0·4831 (7)	6·8 (2)
C(18)	−0·2406 (5)	1·1239 (5)	0·6119 (6)	6·7 (2)
C(19)	0·4135 (7)	0·2880 (9)	1·1666 (9)	10·2 (4)
O(20)	0·5228 (3)	0·2418 (4)	0·9104 (5)	8·2 (2)
C(21)	0·5106 (6)	0·0936 (6)	0·798 (1)	10·3 (3)
C(22)	0·3969 (6)	0·3954 (7)	0·7052 (7)	7·9 (3)
O(23)	−0·1977 (4)	1·0740 (4)	0·2377 (4)	8·2 (2)
C(24)	−0·1520 (8)	0·9590 (7)	0·0972 (7)	8·8 (4)

*$B_{eq} = \frac{4}{3}\sum_i\sum_j \mathbf{a}_i.\mathbf{a}_j\beta_{ij}$.

All the computations were performed on a MicroVAX II computer at the Computer Center, Osaka University of Pharmaceutical Sciences.

Discussion. The molecular structure of omeprazole drawn by *ORTEP*II (Johnson, 1976) is presented in Fig. 1. Bond distances and angles are presented in Table 2, all of which are normal within their e.s.d.'s in comparison with related compounds.

* Lists of anisotropic temperature factors for non-H atoms, atomic parameters for H atoms and structure factors, together with a stereoscopic view of crystal packing, viewed along the c axis, have been deposited with British Library Document Supply Centre as Supplementary Publication No. SUP 52104 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

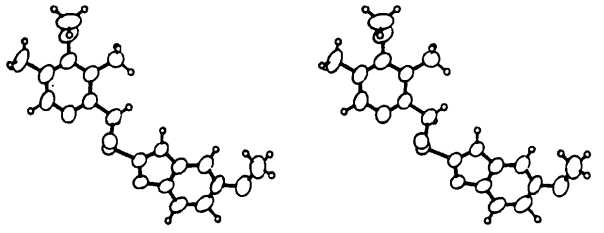
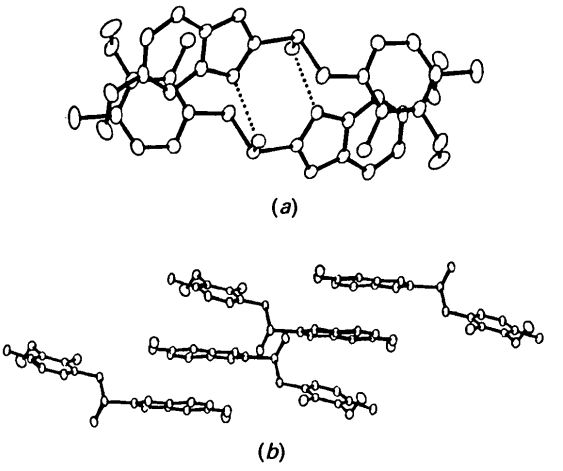


Fig. 1. A stereoscopic view of omeprazole, viewed perpendicular to the pyridine ring.

Table 2. *Bond distances* (Å) *and angles* (°) *for non*-H *atoms with e.s.d.'s in parentheses*

N(1)—C(2)	1·339 (8)	C(10)—N(11)	1·361 (7)
N(1)—C(6)	1·319 (7)	C(10)—N(14)	1·306 (7)
C(2)—C(3)	1·358 (9)	N(11)—C(12)	1·396 (7)
C(3)—C(4)	1·368 (8)	C(12)—C(13)	1·381 (7)
C(3)—C(19)	1·53 (1)	C(12)—C(15)	1·382 (7)
C(4)—C(5)	1·396 (7)	C(13)—N(14)	1·376 (7)
C(4)—O(20)	1·392 (7)	C(13)—C(18)	1·398 (8)
C(5)—C(6)	1·387 (7)	C(15)—C(16)	1·387 (8)
C(5)—C(22)	1·516 (8)	C(16)—C(17)	1·377 (8)
C(6)—C(7)	1·527 (8)	C(16)—O(23)	1·357 (7)
C(7)—S(8)	1·815 (6)	C(17)—C(18)	1·369 (8)
S(8)—O(9)	1·487 (4)	O(20)—C(21)	1·421 (9)
S(8)—C(10)	1·768 (6)	O(23)—C(24)	1·409 (8)
C(2)—N(1)—C(6)	117·4 (4)	S(8)—C(10)—N(14)	120·7 (2)
N(1)—C(2)—C(3)	123·5 (4)	N(11)—C(10)—N(14)	115·6 (3)
C(2)—C(3)—C(4)	118·0 (4)	C(10)—N(11)—C(12)	104·0 (3)
C(2)—C(3)—C(19)	121·0 (4)	N(11)—C(12)—C(13)	106·1 (3)
C(4)—C(3)—C(19)	120·9 (4)	N(11)—C(21)—C(15)	130·5 (3)
C(3)—C(4)—C(5)	120·9 (4)	C(13)—C(12)—C(15)	123·4 (3)
C(3)—C(4)—O(20)	121·2 (3)	C(12)—C)13)—N(14)	110·8 (3)
C(5)—C(4)—O(20)	117·9 (3)	C(12)—C(13)—C(18)	120·6 (3)
C(4)—C(5)—C(6)	115·6 (3)	N(14)—C(13)—C(18)	128·6 (3)
C(4)—C(5)—C(22)	120·8 (4)	C(10)—N(14)—C(13)	103·6 (3)
C(6)—C(5)—C(22)	123·6 (4)	C(12)—C(15)—C(16)	114·1 (3)
N(1)—C(6)—C(5)	124·5 (3)	C(15)—C(16)—C(17)	124·0 (4)
N(1)—C(6)—C(7)	115·7 (3)	C(15)—C(16)—O(23)	122·4 (3)
C(5)—C(6)—C(7)	119·8 (3)	C(17)—C(16)—O(23)	113·6 (3)
C(6)—C(7)—S(8)	108·7 (2)	C(16)—C(17)—C(18)	120·9 (4)
C(7)—S(8)—O(9)	105·9 (3)	C(13)—C(18)—C)17)	117·0 (3)
C(7)—S(8)—C(10)	96·6 (3)	C(4)—O(20)—C(21)	114·6 (4)
O(9)—S(8)—C(10)	108·0 (2)	C(16)—O(23)—C(24)	116·0 (4)
S(8)—C(10)—N(11)	123·7 (2)		

The molecule takes an extended conformation, in which the pyridine and benzimidazole rings are linked by the methylsulfinyl chain taking a *trans* conformation [C(6)—C(7)—S(8)—C(10) = 179·1 (3)°]; the torsion angles N(1)—C(6)—C(7)—S(8), C(5)—C(6)—C(7)—S(8), C(6)—C(7)—S(8)—C(10) and C(7)—S(8)—C(10)—N(14) are −33·6 (4), 148·3 (5), 60·9 (5) and −121·3 (5)°, respectively, and the dihedral angle between the aromatic rings is 30·0 (2)°. The sulfinyl bond protrudes from the benzimidazole plane. The methoxy group attached to the pyridine ring is almost perpendicular to the ring plane [C(3)—C(4)—O(20)—C(21) = 89·5 (6), C(5)—C(4)—O(20)—C(21) = −93·4 (5)°], while that attached to the benzimidazole ring is almost coplanar with the ring



(*a*)

(*b*)

Fig. 2. (*a*) Cyclic dimer structure formed by N—H···O intermolecular hydrogen bonds represented by dotted lines. (*b*) Overlapping mode among the neighboring aromatic rings.

[C(15)—C(16)—O(23)—C(24) = 6·0 (5), C(17)—C(16)—O(23)—C(24) = −175·4 (6)°].

The molecules are arrayed along the (220) plane corresponding to the strongest intensity among the observed reflections. The two molecules which are related to each other by a center of symmetry form a cyclic dimer with an intermolecular N(11)—H···O(9) hydrogen bond [N(x, y, z)···O($-x$, $1-y$, $1-z$) = 2·744 (6), H···O = 1·78 (7) Å and angle N—H···O = 169 (6)° (see Fig. 2*a*)], and the dimer is stabilized by van der Waals contacts between the pyridine and benzimidazole rings; the average interplanar spacing between the pyridine and benzimidazole rings is 4·13 Å.

On the other hand, the benzimidazole ring in the dimer also forms a stacking interaction with the centrosymmetrically related ring with an average spacing of 3·38 Å (Fig. 2*b*).

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