Acta Cryst. (1992). C**48**, 1734–1737

Structure and Conformation of *cis*-9a-Methoxy-1,2,3,4,4a,9a-hexahydrofluoren-9-one Oxime

SANDRA IANELLI AND MARIO NARDELLI*

Istituto di Chimica Generale ed Inorganica, Università degli Studi di Parma, Centro di Studio CNR per la Strutturistica Diffrattometrica, Viale delle Scienze 78, I-43100 Parma, Italy

DANIELE BELLETTI

Istituto di Strutturistica Chimica, Università degli Studi di Parma, Centro di Studio CNR per la Strutturistica Diffrattometrica, Viale delle Scienze 78, I-43100 Parma, Italy

BRIGITTE JAMART-GRÉGOIRE AND PAUL CAUBÈRE

Laboratoire de Chimie Organique I, UA CNRS 457, Université de Nancy I, BP 239, 54506 Vandoeuvre-Les-Nancy CEDEX, France

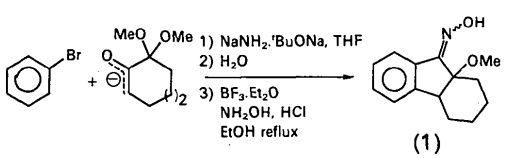
(*Received* 10 *March* 1992; *accepted* 28 *May* 1992)

Abstract

The title compound was prepared as part of a study of β-blocking adrenergic agents. X-ray crystal structure analysis was used to determine the *E* configuration of the oxime group and the chiralities of the C atoms at the junction of the cyclopentene and cyclohexane rings (the chiralities are opposite). Both enantiomers are present in the crystal, the space group being centrosymmetric ($P\bar{1}$). The methoxy group and the H atom at the junction are *cis*. There are two crystallographically independent molecules in the asymmetric unit having different environments. These results are relevant from the chemical point of view and are quite reliable in spite of the poor quality of the diffraction data; this was caused by thermal motion and/or disorder which prevented the accurate determination of the molecular geometry.

Comment

In order to obtain new β-adrenergic agents (Jamart-Grégoire, Caubère, Blanc, Gnassounou & Advenier, 1989), oxime (1) was prepared according to the scheme shown below.

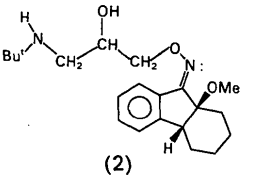


(1)

Transformation of the oxime (1) into the corresponding oxyiminopropanolamine was performed in the usual manner (Amlaiky, Leclerc, Decker & Schwartz, 1983). This produced a series of new compounds which were then tested as β_2-blocking agents. The main problem was to establish the exact stereochemistry of (1) and in particular the *E* or *Z* conformation of the oxime group. As the synthesis of oximes from the corresponding ketones can lead to two isomers, *Z* and *E*, it was important to determine the exact stereochemistry of the oxime obtained since the pharmacological properties are strongly dependent on its structure.

Although ^{1}H and ^{13}C NMR spectra gave some indication of the stereochemistry, it was not possible to ascertain its exact structure. It was therefore decided to use X-ray analysis and this was successful in establishing the *E* nature of this compound

The present paper reports the results of this study, which is made more interesting by the fact that pharmacological results have established that compound (2) has the highest known value (343) of the ratio (β_2 activity)/(β_1 activity).



(2)

From the *ORTEP* drawings showing the two independent molecules of the asymmetric unit (Fig. 1) and the U_{eq} values (Table 1), it appears that some of the atoms are affected by rather high thermal motions and that some of them exhibit exceptionally high anisotropies as indicated by the ratios r_{max}/r_{min} of the principal axes of the displacement ellipsoids. These data suggest that static disorder is probably more important than thermal motion; this is consistent with the fact that the melting point is not particularly low (393 K). This disordered situation is responsible for the poor quality of the diffraction data which prevented an accurate refinement. The bond distances and angles (Table 2) are therefore only suitable for describing the molecular conformation. The conformation is however important from the chemical and pharmacological point of view.

The molecule consists of a tricyclic system built up by the fusion of a cyclohexane ring with an indanone oxime. The least-squares planes through the three rings form the dihedral angles $\angle AB$ 9.4(5) in molecule *A*, 6.4(6)° in molecule *B* and $\angle BC$ 60.3(6) in molecule *A*, 55.4(7)° in molecule *B*. The puckering and conformation of the rings, where Q_T is the total puckering amplitude (Cremer & Pople, 1975) and ADP is the minimum asymmetry displacement parameter (Nardelli, 1983*b*) are: ring *B*, molecule *A*, Q_T = 0.318(18), ADP = D_2(C1) = 0.013(6), molecule *B*, Q_T = 0.162(19), ADP = 0.010(6) and ring

0108-2701/92/091734-04$06.00

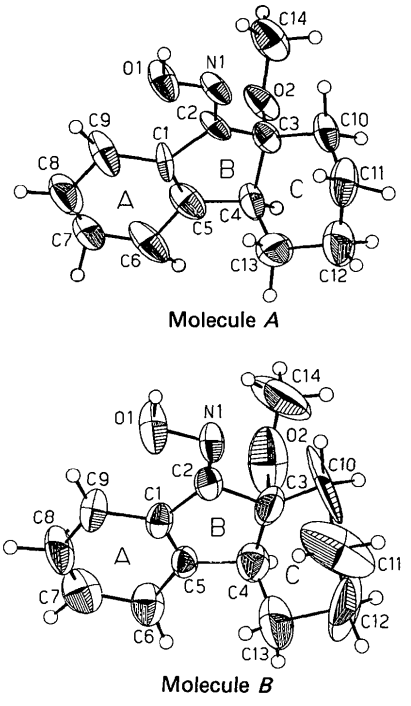


Fig. 1. *ORTEP* drawings of the two independent molecules of compound (1) with ellipsoids at 50% probability.

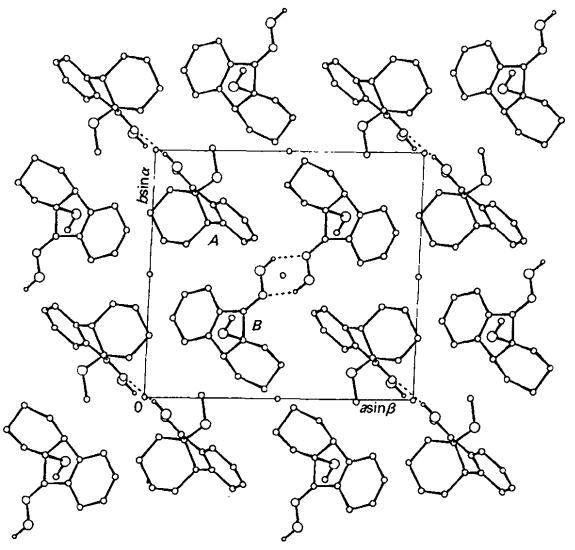


Fig. 2. *PLUTO* drawing of the molecular packing.

C, molecule *A*, Q_T = 0.510(19), ADP = D_2(C3-C4)= 0.029(8), molecule *B*, Q_T = 0.672(32), ADP = 0.048(12); in all cases, the rings adopt a half-chair conformation.

The configuration of the oxime is *E*, and it is possible that the following intramolecular attractive interactions have some influence on it, C9*A*—H9*A* 1.08(4), C9*A*···O1*A* 2.86(2), H9*A*···O1*A* 2.30(3) Å, C9*A*—H9*A*···O1*A* 110 (2)°, C9*B*—H9*B* 1.08(4), C9*B*···O1*B* 2.95(2), H9*B*···O1*B* 2.41(3) Å, C9*B*—H9*B*···O1*B* 109(3)°. Note that in both molecules, the six-membered O1, N1, C2, C1, C9, H9 ring is practically planar; the H9 atoms are 0.33(4) Å (molecule *A*) and 0.21(3) Å (molecule *B*) out of the weighted-least-squares plane through the non-H atoms which themselves show displacements from this plane in the range 0.01(1)-0.11(2) Å.

The methoxy group and the H atom at the junction of the cyclopentene and cyclohexane rings are *cis* with a synclinal conformation; the O2—C3—C4—H4 torsion angles being 35(3) and 32(3)° for molecules *A* and *B* respectively. Molecular-mechanics calculations show that a *Z* configuration for the oxime should cause steric hindrance between the O1 atom and the C10 methylene group.

The configuration at the two chiral centers, C3 and C4, is opposite, being shown as *R* and *S* respectively in Fig 1. The enantiomers are also present in the crystal, the space group being centrosymmetric. The plane of the methoxy group is nearly perpendicular to that of the oxime, the value of the N1—C2—C3—O2 torsion angle being −95(2)° for both independent molecules. The O2—C14 bond is antiperiplanar to the C3—C4 bond and when the methoxy group is rotated about the C3—O2 bond in the free molecule, steric hindrance is encountered between the C14 methyl atom and the C10 methylene, H4 and C5 atoms. This hindrance, together with interactions involving adjacent molecules packed in the crystal, are the factors which determine the orientation of the methoxy group.

The main interactions determining the packing of the molecules in the crystal (Fig. 2) are the hydrogen bonds O1*A*—H1O*A* 0.94(4), O1*A*···N1*A*^{i} 2.82(2), H1O*A*···N1*A*^{i} 2.08(4), O1*A*—H1O*A*···N1*A*^{i} 135(3)° and O1*B*—H1O*B* 0.94(4), O1*B*···N1*B*^{ii} 2.78(2), H1O*B*···N1*B*^{ii} 1.99(4), O1*B*—H1O*B*···N1*B*^{ii} 140(4)° where i = 2 − *x*, −*y*, −*z* and ii = − *x* − 1, −*y* − 1, −*z* − 1.

Experimental

Crystal data

$C_{14}H_{17}NO_2$
M_r = 231.29
Triclinic
$P\bar{1}$
a = 13.474 (2) Å
b = 12.540 (1) Å
c = 7.632 (1) Å
α = 101.78 (1)°
β = 95.02 (1)°
γ = 87.14 (1)°
V = 1256.8 (3) Å^3
Z = 4
D_x = 1.222 Mg m^{-3}
Cu $K\alpha_1$ radiation
λ = 1.540562 Å
Cell parameters from 27 reflections
θ = 11-40°
μ = 0.6178 mm^{-1}
T = 293 (2) K
Needles
0.60 × 0.27 × 0.21 mm
Colourless

Data collection

Siemens-AED diffractometer
θ-2θ scans
4062 measured reflections
h = −13 → 13
k = −12 → 12
l = 0 → 7

1082 observed reflections [$I>3\sigma(I)$]
θ_{max} = 70°
1 standard reflection monitored every 50 reflections
intensity variation: within statistical fluctuation

Refinement

Refinement on F
Final R = 0.0846
wR = 0.0976
S = 2.6728
1082 reflections
307 parameters
H-atom parameters not refined
$w = 0.9552/[\sigma^2(F_o)+0.0005F_o]$
$(\Delta/\sigma)_{max}$ = 0.4
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Tables 2.2A, 2.2C and 2.3.1)

Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å^2)

$U_{eq} = \frac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
O1*A*	0.9161 (7)	0.0664 (8)	−0.1069 (14)	0.0730 (53)
O2*A*	0.7675 (7)	0.1067 (10)	0.3842 (14)	0.0684 (55)
N1*A*	0.9196 (8)	0.0797 (10)	0.0777 (19)	0.0582 (60)
C1*A*	0.7757 (10)	0.2171 (13)	0.0741 (22)	0.0540 (78)
C2*A*	0.8557 (10)	0.1492 (12)	0.1557 (22)	0.0504 (71)
C3*A*	0.8440 (11)	0.1697 (13)	0.3528 (22)	0.0512 (78)
C4*A*	0.7947 (13)	0.2883 (16)	0.3842 (22)	0.0594 (81)
C5*A*	0.7366 (11)	0.2891 (14)	0.2116 (25)	0.0652 (84)
C6*A*	0.6554 (13)	0.3651 (14)	0.1764 (27)	0.087 (11)
C7*A*	0.6186 (13)	0.3485 (16)	−0.0063 (32)	0.082 (12)
C8*A*	0.6561 (14)	0.2779 (17)	−0.1423 (28)	0.092 (11)
C9*A*	0.7387 (12)	0.2020 (15)	−0.1084 (23)	0.0811 (95)
C10*A*	0.9393 (13)	0.1593 (16)	0.4716 (23)	0.0673 (92)
C11*A*	1.0081 (12)	0.2506 (20)	0.5009 (26)	0.087 (10)
C12*A*	0.9550 (14)	0.3637 (19)	0.5680 (25)	0.103 (11)
C13*A*	0.8692 (14)	0.3767 (16)	0.4249 (27)	0.0855 (98)
C14*A*	0.7884 (12)	−0.0099 (15)	0.3564 (25)	0.090 (10)
O1*B*	−0.4083 (7)	−0.5184 (9)	−0.3584 (15)	0.0875 (59)
O2*B*	−0.2824 (10)	−0.2603 (14)	−0.5666 (27)	0.1457 (99)
N1*B*	−0.4221 (9)	−0.4178 (12)	−0.4182 (18)	0.0601 (69)
C1*B*	−0.2662 (11)	−0.3496 (16)	−0.2220 (21)	0.0502 (71)
C2*B*	−0.3553 (11)	−0.3511 (15)	−0.3507 (22)	0.0546 (83)
C3*B*	−0.3576 (15)	−0.2343 (15)	−0.4043 (28)	0.079 (10)
C4*B*	−0.2898 (13)	−0.1692 (16)	−0.2724 (28)	0.0693 (97)
C5*B*	−0.2289 (12)	−0.2507 (16)	−0.1854 (20)	0.0475 (76)
C6*B*	−0.1413 (12)	−0.2256 (14)	−0.0666 (25)	0.0710 (93)
C7*B*	−0.0938 (13)	−0.3221 (21)	−0.0093 (28)	0.083 (12)
C8*B*	−0.1334 (14)	−0.4172 (19)	−0.0472 (28)	0.089 (12)
C9*B*	−0.2193 (13)	−0.4436 (13)	−0.1566 (25)	0.0723 (88)
C10*B*	−0.4389 (21)	−0.2056 (26)	−0.5088 (44)	0.194 (20)
C11*B*	−0.5044 (17)	−0.1360 (30)	−0.3225 (42)	0.185 (23)
C12*B*	−0.4446 (26)	−0.0370 (24)	−0.2287 (42)	0.186 (21)
C13*B*	−0.3457 (18)	−0.0865 (21)	−0.1248 (29)	0.137 (15)
C14*B*	−0.3134 (21)	−0.3243 (25)	−0.7321 (33)	0.178 (18)

Table 2. *Geometric parameters* (Å, °)

O1*A*—N1*A*	1.38 (1)	O1*B*—N1*B*	1.42 (1)
O2*A*—C3*A*	1.40 (2)	O2*B*—C3*B*	1.64 (2)
O2*A*—C14*A*	1.45 (2)	O2*B*—C14*B*	1.39 (2)
N1*A*—C2*A*	1.29 (1)	N1*B*—C2*B*	1.26 (2)
C1*A*—C2*A*	1.51 (2)	C1*B*—C2*B*	1.48 (2)
C1*A*—C5*A*	1.36 (2)	C1*B*—C5*B*	1.33 (2)
C1*A*—C9*A*	1.42 (2)	C1*B*—C9*B*	1.47 (2)
C2*A*—C3*A*	1.49 (2)	C2*B*—C3*B*	1.60 (2)
C3*A*—C4*A*	1.58 (2)	C3*B*—C4*B*	1.45 (2)
C3*A*—C10*A*	1.52 (2)	C3*B*—C10*B*	1.38 (3)
C4*A*—C5*A*	1.47 (2)	C4*B*—C5*B*	1.50 (2)
C4*A*—C13*A*	1.50 (2)	C4*B*—C13*B*	1.58 (2)
C5*A*—C6*A*	1.46 (2)	C5*B*—C6*B*	1.43 (2)
C6*A*—C7*A*	1.42 (3)	C6*B*—C7*B*	1.47 (3)
C7*A*—C8*A*	1.34 (2)	C7*B*—C8*B*	1.30 (3)
C8*A*—C9*A*	1.47 (2)	C8*B*—C9*B*	1.38 (2)
C10*A*—C11*A*	1.48 (2)	C10*B*—C11*B*	1.79 (4)
C11*A*—C12*A*	1.57 (3)	C11*B*—C12*B*	1.53 (4)
C12*A*—C13*A*	1.54 (2)	C12*B*—C13*B*	1.65 (4)
C3*A*—O2*A*—C14*A*	116 (1)	C3*B*—O2*B*—C14*B*	120 (2)
O1*A*—N1*A*—C2*A*	116 (1)	O1*B*—N1*B*—C2*B*	113 (1)
C5*A*—C1*A*—C9*A*	125 (1)	C5*B*—C1*B*—C9*B*	124 (2)
C2*A*—C1*A*—C9*A*	127 (1)	C2*B*—C1*B*—C9*B*	126 (1)
C2*A*—C1*A*—C5*A*	107 (1)	C2*B*—C1*B*—C5*B*	109 (2)
N1*A*—C2*A*—C1*A*	129 (1)	N1*B*—C2*B*—C1*B*	136 (2)
C1*A*—C2*A*—C3*A*	107 (1)	C1*B*—C2*B*—C3*B*	104 (1)
N1*A*—C2*A*—C3*A*	123 (1)	N1*B*—C2*B*—C3*B*	120 (1)
O2*A*—C3*A*—C2*A*	109 (1)	O2*B*—C3*B*—C2*B*	100 (1)
C2*A*—C3*A*—C10*A*	116 (1)	C2*B*—C3*B*—C10*B*	118 (2)
C2*A*—C3*A*—C4*A*	101 (1)	C2*B*—C3*B*—C4*B*	106 (2)
O2*A*—C3*A*—C10*A*	113 (1)	O2*B*—C3*B*—C10*B*	95 (2)
O2*A*—C3*A*—C4*A*	103 (1)	O2*B*—C3*B*—C4*B*	97 (1)
C4*A*—C3*A*—C10*A*	114 (1)	C4*B*—C3*B*—C10*B*	132 (2)
C3*A*—C4*A*—C13*A*	113 (1)	C3*B*—C4*B*—C13*B*	113 (2)
C3*A*—C4*A*—C5*A*	102 (1)	C3*B*—C4*B*—C5*B*	105 (2)
C5*A*—C4*A*—C13*A*	111 (1)	C5*B*—C4*B*—C13*B*	109 (2)
C1*A*—C5*A*—C4*A*	112 (1)	C1*B*—C5*B*—C4*B*	114 (2)
C4*A*—C5*A*—C6*A*	127 (2)	C4*B*—C5*B*—C6*B*	124 (2)
C1*A*—C5*A*—C6*A*	121 (2)	C1*B*—C5*B*—C6*B*	122 (2)
C5*A*—C6*A*—C7*A*	113 (2)	C5*B*—C6*B*—C7*B*	113 (2)
C6*A*—C7*A*—C8*A*	126 (2)	C6*B*—C7*B*—C8*B*	123 (2)
C7*A*—C8*A*—C9*A*	121 (2)	C7*B*—C8*B*—C9*B*	126 (2)
C1*A*—C9*A*—C8*A*	114 (2)	C1*B*—C9*B*—C8*B*	112 (2)
C3*A*—C10*A*—C11*A*	116 (2)	C3*B*—C10*B*—C11*B*	95 (2)
C10*A*—C11*A*—C12*A*	113 (1)	C10*B*—C11*B*—C12*B*	108 (2)
C11*A*—C12*A*—C13*A*	107 (2)	C11*B*—C12*B*—C13*B*	106 (2)
C4*A*—C13*A*—C12*A*	116 (2)	C4*B*—C13*B*—C12*B*	107 (2)

The integrated intensities were obtained using a modified version (Belletti, Ugozzoli, Cantoni & Pasquinelli, 1979) of the Lehmann & Larsen (1974) peak-profile analysis procedure. All reflections were corrected for Lorentz and polarization effects. Correction for extinction was carried out according to Zachariasen (1963) [$g = 8.9(6)\times10^{-8}$].

The structure was determined by direct methods using *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980) and refined by full-matrix least squares on F, using *SHELX*76 (Sheldrick, 1976). The poor quality of the diffraction data, caused by the high thermal motion or disorder in the structure, made structure solution and refinement difficult and prevented a good final R value from being obtained.

The H atoms were placed in calculated positions and not refined while the position of the oxime H atom was found by first assuming a tetrahedral distribution around the O atom and then disregarding the positions giving unacceptably short contacts. *PARST* (Nardelli, 1983*a*) was used for these and all other molecular-geometry calculations.

The correctness of the space group was checked using *TRACER* (Lawton & Jacobson, 1965), *NEWLAT* (Mugnoli, 1985), *LEPAGE* (Spek, 1988) and *MISSYM* (Le Page, 1987). *CAVITY* (Mugnoli, 1990) was then used to make a further check for incorrect holes.

The calculations were carried out on the ENCORE-GOULD-POWERNODE 6040 and ENCORE 91 computers of the 'Centro di Studio per la Strutturistica Diffrattometrica del CNR (Parma)'. In addition to the quoted programs, *LQPARM* (Nardelli & Mangia, 1984), *ORTEP* (Johnson, 1965) and *PLUTO* (Motherwell & Clegg, 1978) were also used.

Following a referee's remark concerning the unfavourable ratio of the number of refined parameters to the number of observations, a new refinement was carried out on F_o^2 using *SHELXL*92.

The results of this refinement are: number of refined parameters p = 315, number of reflections used in the LS refinement n = 4035, wR_2 = 0.2711 for 4035 reflections, $S = [\Sigma w(F_o^2 - F_c^2)/(p - n)]^{1/2}$ = 0.746, $w = 1/[\sigma^2(F_o^2) + (0.1658\ P)^2]$ where $P = 1/3[\max.(F_o^2,0) + 2F_c^2]$, $wR_{2'}$ = 0.2796 for all 4062 reflections (27 reflections with $\Delta/\sigma > 4$ omitted in the refinement), R_1 = 0.0924 for 1267 $F_o > 4\sigma(F_o)$, $R_{1'}$ = 0.2011 for all data, $S = [\Sigma w(F_o - F_c)^2/(p - n)]^{1/2}$ = 0.827 where $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$, $R_1 = \Sigma\ |F_o - F_c|\ /\Sigma F_o$. A comparison of the structural parameters (coordinates, displacement parameters, bond distances, angles, *etc.*) from the two refinements shows that, as a result of the increased number of observations, the e.s.d.'s are much lower (~1/3) for the F_o^2 refinement but that differences between bond distances and angles are not significant, which supports the view that the quality of intensity data is much more important than the amount of data. Half-normal probability plots and a table of the distances and angles obtained from the F_o^2 refinement have been deposited.

The authors gratefully acknowledge financial support from the European Economic Community under grant N.SC1000657. They are also particularly grateful to Professor G. M. Sheldrick of the University of Göttingen who kindly made the *SHELXL92* program available to them at the BETA-TEST checking stage.

Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and complete geometry, together with principal axes of thermal ellipsoids, half-normal probability plots and distances and angles from the F_o^2 refinement, have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55192 (20 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: KA1012]

References

Amlaiky, N., Leclerc, J., Decker, N. & Schwartz, J. (1983). *Eur. J. Med. Chem. Chim. Theor.* **18**, 437-439.
Belletti, D., Ugozzoli, F., Cantoni, A. & Pasquinelli, G. (1979). *Gestione on Line di Diffrattometro a Cristallo Singolo Siemens-AED con Sistema General Automation Jumbo* 220. Internal Report 1-3/79. Centro di Studio per la Strutturistica Diffrattometrica del CNR, Parma, Italy.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354-1358.
Jamart-Grégoire, B., Caubère, P., Blanc, M., Gnassounou, J. P. & Advenier, C. (1989). *J. Med. Chem.* **32**, 315-320.
Johnson, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.
Lawton, S. L. & Jacobson, R. A. (1965). *The Reduced Cell and its Crystallographic Applications*. Ames Laboratory. Available from the Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, US Department of Commerce, Springfield, Virginia, USA.
Lehmann, M. S. & Larsen, F. K. (1974). *Acta Cryst.* A**30**, 580-589.
Le Page, Y. (1987). *J. Appl. Cryst.* A**20**, 264-269.
Main, P., Fiske, S. J., Hull, S. E., Lessinger, L., Germain, G., Declercq, J.-P. & Woolfson, M. M. (1980). *MULTAN80. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
Motherwell, W. D. S. & Clegg, W. (1978). *PLUTO*. Program for plotting molecular and crystal structures. Univ. of Cambridge, England.
Mugnoli, A. (1985). *J. Appl. Cryst.* **18**, 183-184.
Mugnoli, A. (1990). *CAVITY*. Program to locate and measure spherical voids in a crystal structure. Univ. of Genoa, Italy.
Nardelli, M. (1983*a*). *Comput. Chem.* **7**, 95-98.
Nardelli, M. (1983*b*). *Acta Cryst.* C**39**, 1141-1142.
Nardelli, M. & Mangia, A. (1984). *Ann. Chim. (Rome)*, **74**, 163-174.
Sheldrick, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.
Spek, A. L. (1988). *J. Appl. Cryst.* **21**, 578-579.
Zachariasen, W. H. (1963). *Acta Cryst.* **16**, 1139-1144.

Acta Cryst. (1992). C**48**, 1737–1739

Structure of a Novel Carbapenem Antibiotic, Meropenem

KAZUNORI YANAGI

Tsukuba Research Laboratory, Sumitomo Chemical Co. Ltd, 6 Kitahara, Tsukuba, Ibaraki 300-32, Japan

YUTAKA TAKEUCHI AND MAKOTO SUNAGAWA

Research Laboratories, Sumitomo Pharmaceuticals Co. Ltd, 3-1-98 Konohana-ku, Osaka 554, Japan

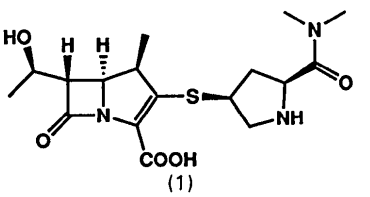
(*Received* 14 *February* 1992; *accepted* 22 *April* 1992)

Abstract

The absolute configuration of the title compound, (4*R*,5*S*,6*S*)-3-[(3*S*,5*S*)-5-dimethylaminocarbonylpyrrolidin-3-ylthio]-6-[(*R*)-1-hydroxyethyl]-4-methyl-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid trihydrate, is confirmed. Meropenem crystallized as a zwitterion with the three molecules of water. The sum of the three bond angles about the N atom of the β-lactam ring is 329.1° and the deviation of the N atom from the plane defined by the three adjacent atoms is 0.457 Å. Short intramolecular contacts are observed between the 1β-methyl group and the β-lactam ring.

Comment

Thienamycin and the related naturally occurring compounds are β-lactam antibiotics possessing potent antibacterial activity (Albers-Schönberg *et al.*, 1978). They are also chemically unstable and easily metabolized by renal dehydropeptidase-I (DHP-I). Meropenem (1) is a new 1β-methylcarbapenem antibiotic possessing excellent antibacterial activity and chemical stability with high stability to DHP-I (Sunagawa, Matsumura, Inoue, Fukasawa & Kato, 1990).



(1)

0108-2701/92/091737-03$06.00