C15	0.2197 (7)	1.0246 (11)	0.5274 (5)	0.045 (3)
C16	0.1994 (8)	1.1442 (13)	0.4795 (6)	0.058 (3)
C17	0.2714 (9)	1.2025 (12)	0.4532 (6)	0.059 (3)
C18	0.3580 (10)	1.1464 (15)	0.4768 (6)	0.069 (4)
C19	0.3795 (7)	1.0273 (12)	0.5240 (5)	0.048 (3)
C20	0.1784 (6)	0.6911 (10)	0.4691 (5)	0.037 (2)
C21	0.2619 (6)	0.7059 (10)	0.4373 (5)	0.035 (2)
C22	0.2557 (7)	0.8065 (13)	0.3826 (5)	0.052 (3)
C23	0.3338 (8)	0.8244 (15)	0.3529 (6)	0.064 (3)
C24	0.4116 (8)	0.7345 (16)	0.3752 (6)	0.062 (3)
C25	0.4154 (7)	0.6328 (15)	0.4272 (6)	0.059 (3)
C26	0.3423 (7)	0.6204 (12)	0.4589 (5)	0.048 (3)
C27	0.0872 (7)	0.6856 (10)	0.4147 (5)	0.038 (2)
C28	0.0125 (7)	0.7834 (12)	0.4181 (5)	0.043 (2)
C29	−0.0712 (7)	0.7785 (13)	0.3651 (6)	0.052 (3)
C30	−0.0839 (7)	0.6805 (15)	0.3108 (5)	0.053 (3)
C31	−0.0115 (8)	0.5847 (14)	0.3055 (5)	0.055 (3)
C32	0.0713 (7)	0.5876 (12)	0.3576 (5)	0.045 (3)

Table 4. *Selected geometric parameters for* (I), (II) *and* (III) *(°, Å)*

(I)*		(II)		(III)	
Torsion angles about the central bond					
C6/C5/C5′/C6′	49.2 (2)	C9/C4/C5/C22	48.1 (6)	C7/C4/C6/C20	48.2 (15)
C3/C5/C5′/C3′	50.1 (2)	C2/C4/C5/C6	46.7 (7)	C3/C4/C6/C5	43.1 (12)
Dihedral angle between the overlapping inner phenyl rings					
C13–C18 and C13′–C18′		C16–C21 and C23–C28		C14–C19 and C21–C26	
9.60 (7)		10.5 (1)		14.5 (3)	
Shortest interatomic distance between overlapping inner phenyl rings					
C13···C13′	3.206 (3)	C16···C23	3.118 (5)	C14···C21	3.103 (13)

* The primed atoms are related to the corresponding non-primed atoms by a twofold rotation at $\frac{1}{2}, 0, \frac{1}{4}$.

Compound (I) crystallized as a pure material and provided the most precise structural results. The molecules are located in the crystal on twofold rotational axes of crystallographic symmetry. Somewhat less precise results were obtained for compounds (II) and (III). (II) crystallized as a diethanol solvate. The ethyl residues of the solvate are located in loosely packed regions of the structure and reveal partial disorder. Moreover, the crystals of this compound were slightly 'damaged' by X-rays during the diffraction experiment, most probably due to some polyester-type condensation which occurs in the solid upon prolonged X-ray irradiation. (III) contains two heavy Br atoms. The absorption effects on the diffraction data in this case were initially corrected for by an empirical absorption correction method (Walker & Stuart, 1983). However, since the latter is not acceptable by the journal any longer and the relevant information on the analyzed crystal was lost, the presented results are based on uncorrected data. In spite of the fact that the final electron density maps show somewhat high residual peaks and deep troughs in the vicinity of the two heavy atoms (diffraction ripples), and that there is a slight increase in the e.s.d. values of the refined parameters, the two sets of results (*i.e.* either empirically corrected or uncorrected for absorption effects) are almost the same. Thus, most of the atomic parameters obtained from the two refinements, and the covalent parameters of the resulting structural model, differ by less than 2σ.

For all compounds, data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *CADINT*, local program; program(s) used to solve structures: *SHELXS*86 (Sheldrick, 1985); program(s) used to refine structures: *SHELXL*93 (Sheldrick, 1993); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*93, *PARST* (Nardelli, 1983).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: KA1141). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Allen, F. H. & Kennard, O. (1993). *Chem. Des. Automat. News*, **8**, 31–37.

Becker, H.-D., Karlsson, B. & Pilotti, A.-M. (1976). *Chem. Phys. Lett.* **44**, 589–593.

Becker, H.-D., Sandros, K., Karlsson, B. & Pilotti, A.-M. (1978). *Chem. Phys. Lett.* **53**, 232–236.

Burley, S. K. & Petsko, G. A. (1986). *J. Am. Chem. Soc.* **108**, 7995–8001.

Byrn, S. R., Maverick, E., Muscio, O. J., Trueblood, K. N. & Jacobs, T. L. (1971). *J. Am. Chem. Soc.* **93**, 6680–6682.

Enraf–Nonius (1989). *CAD*-4 *Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.

Hart, H., Ward, D. L., Tanaka, K. & Toda., F. (1982). *Tetrahedron Lett.* **23**, 2125–2128.

Iyoda, M., Otani, H., Oda, M., Kai, Y., Baba, Y. & Kasai, N. (1986). *J. Am. Chem. Soc.* **108**, 5371–5372.

Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Klebe, G. & Diederich, F. (1993). *Philos. Trans. R. Soc. London Ser. A*, **345**, 37–48.

Nardelli, M. (1983). *Comput. Chem.* **7**, 95–98.

Sheldrick, G. M. (1985). *SHELXS*86. *Program for the Solution of Crystal Structures*. University of Göttingen, Germany.

Sheldrick, G. M. (1993). *SHELXL*93. *Program for Crystal Structure Refinement*. University of Göttingen, Germany.

Toda, F., Tanaka, K., Stein, Z. & Goldberg, I. (1995). *Acta Cryst.* B**51**, 856–863.

Walker, N. & Stuart, D. (1983). *Acta Cryst.* A**39**, 158–166.

Weber, E., Seichter, W., Goldberg, I., Will, G. & Dasting, H.-J. (1991). *J. Incl. Phenom.* **10**, 267–282.

Acta Cryst. (1996). C**52**, 122–125

A Dihydromorphine-6-*O*-sulfate

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(*Received 6 February 1995; accepted 24 July 1995*)

Abstract

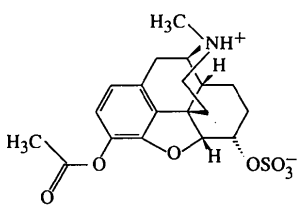
The synthesis of 3-*O*-acetyl-7,8-dihydromorphine-6-*O*-sulfate [IUPAC: (5α,6α)-3-acetoxy-4,5-epoxy-17-methyl-6-morphinaniosulfate], $C_{19}H_{23}NO_7S$, which has important analgesic properties, has been confirmed crystallographically. In the solid state, the zwitterions are linked into chains by N—H···O hydrogen bonds.

Comment

Sulfation at the allylic 6-hydroxy group of morphine yields a sulfate ester with greater analgesic potency than morphine itself (Brown, Roerig, Burger, Cody & Fujimoto, 1985). Morphine-6-*O*-sulfate (M6S) inhibits the specific binding of [^{3}H]-morphine and [^{3}H]-leucine enkephalin to rat membranes (Oguni, Yamada, Shigezane, Hirano & Yoshimura, 1987). Morphine-6-*O*-sulfation has been reported to reduce the binding affinity exhibited by morphine at the μ-receptor, but enhances affinity at the δ-receptor (Oguni, Yamada, Shigezane, Hirano & Yoshimura, 1987).

Acylation of M6S at the phenolic 3-hydroxy group affords analogs with analgesic potencies exceeding that of the parent compound (Crooks, Kottayil, Houdi & Butterfield, 1995). The derivative 3-*O*-acetylmorphine-6-*O*-sulfate (M3A6S) shows greater affinity than morphine for both μ- and κ_3-receptors (Houdi, Kottayil, Crooks & Butterfield, 1995). M3A6S also discriminates better between μ- and δ-receptors in guinea pig brain homogenates than does either morphine or the μ-preferring peptide DAMGO (Houdi, Kottayil, Crooks & Butterfield, 1995).

We have recently synthesized 3-*O*-acetyl-7,8-dihydromorphine-6-*O*-sulfate (DM3A6S), the dihydro analog of M3A6S; the identity of the material was confirmed by the structure determination reported here. DM3A6S exhibits similar *in vivo* analgesic potency to M3A6S in rats when administered subcutaneously, has a much longer duration of action than an equimolar dose of morphine and is relatively more selective for the μ-receptor (Crooks, Kottayil, Houdi & Butterfield, 1995; Kottayil, 1993).



DM3A6S

Zwitterions of DM3A6S related by the translation along **a** are connected by N$^+$—H···O$^-$ bonds [N···O6($x+1$, y, z) 2.704 (7) Å]. The resulting columns of molecules interact with an adjoining column to form a chain of C—H···O interactions that is also parallel to **a** [C19···O3($x-\frac{1}{2}$, $-y-\frac{1}{2}$, $-z$) 3.070 (8) Å] (see Fig. 2). These contacts meet Desiraju's (1991) criteria for C—H···O hydrogen bonds. There are two substantially weaker C—H···O interactions [C9···O3($-x+1$, $y+\frac{1}{2}$, $-z+\frac{1}{2}$) 3.201 (8) and C2···O5($-x$, $y-\frac{1}{2}$, $-z+\frac{1}{2}$) 3.476 (8) Å] that might be considered [see Desiraju (1991)] to link molecules related by the 2_1 axis parallel to **b** (see Fig. 3). Although the intermolecular interactions appear to be strongest along **a**, the crystals are not particularly elongated in that direction. The presence of large {001} faces argues against the suggestion that the chain of C—H···O interactions is structure determining.

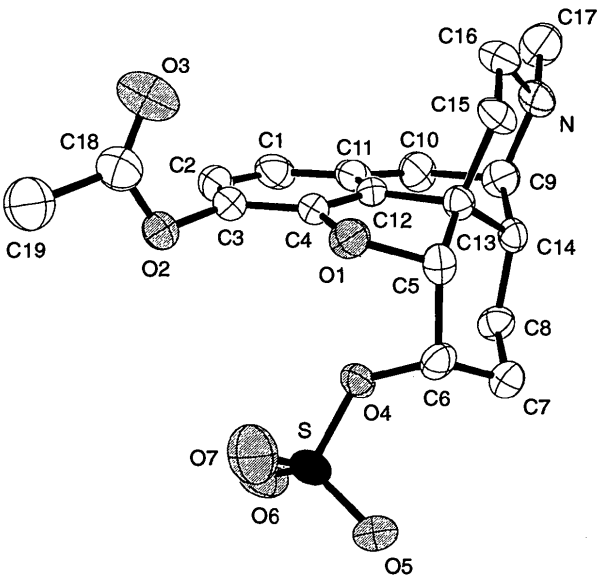


Fig. 1. Perspective drawing of the title molecule showing the atom-numbering scheme. The shapes of the ellipsoids correspond to 50% probability contours of atomic displacement. The H atoms have been omitted for the sake of clarity.

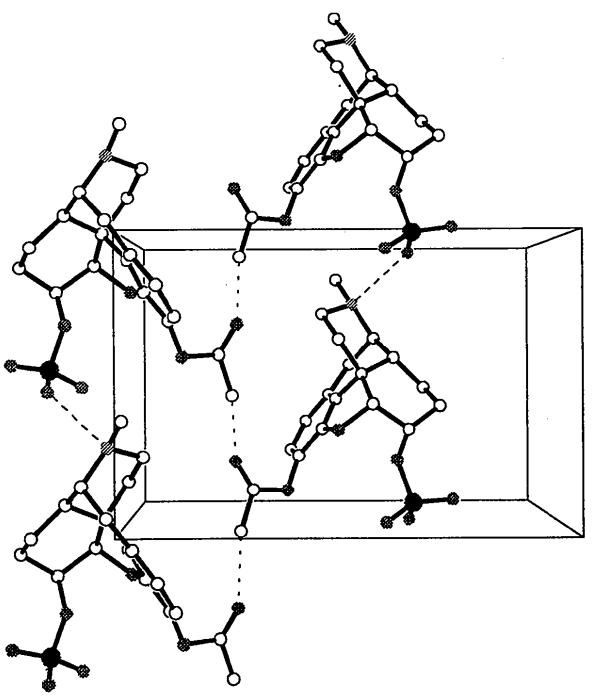


Fig. 2. Drawing of the unit cell showing the columns of molecules related by the **a** translation and connected by N—H···O bonds. The strongest C—H···O interactions, which are between molecules related by the 2_1 axis parallel to **a** and at y = 1/4, z = 1/2, are also marked. The *b* axis points from left to right and the *a* axis points downwards.

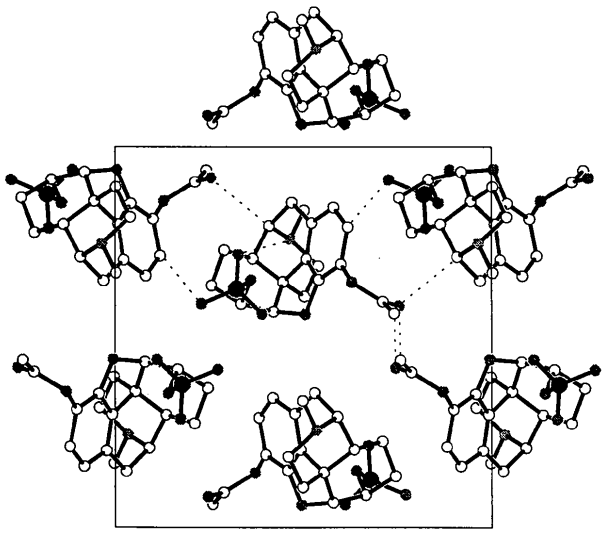


Fig. 3. Projection of the unit cell showing the approximately hexagonal arrangement of the columns of molecules. The C—H···O interactions between the central and surrounding molecules are shown. The *a* axis points out of the plane of the paper, the *b* axis points from right to left and the *c* axis points downwards.

Experimental

The title compound was synthesized in the laboratory of P. A. Crooks. Crystals were grown from water/methanol solution.

Crystal data

$C_{19}H_{23}NO_7S$
$M_r = 409.46$
Orthorhombic
$P2_12_12_1$
$a = 9.3020\,(8)$ Å
$b = 14.0800\,(10)$ Å
$c = 14.1587\,(12)$ Å
$V = 1854.4\,(3)$ Å^3
$Z = 4$
$D_x = 1.467$ Mg m^{-3}
Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 22 reflections
$\theta = 10.6$–$12.8°$
$\mu = 0.21$ mm^{-1}
$T = 296\,(1)$ K
Tablet, short parallel to **c** with major faces {001}, {111} and {012}
$0.25 \times 0.20 \times 0.10$ mm
Colorless

Data collection

Enraf–Nonius CAD-4-VAX diffractometer
$\omega/2\theta$ scans
Absorption correction: none
1869 measured reflections
1869 independent reflections
1078 observed reflections $[I > 2\sigma(I)]$
$\theta_{max} = 25°$
$h = 0 \rightarrow 12$
$k = 0 \rightarrow 18$
$l = 0 \rightarrow 18$
3 standard reflections
frequency: 60 min
intensity decay: 6%

Refinement

Refinement on F^2
$R(F) = 0.0419$
$wR(F^2) = 0.1224$
$S = 1.007$
1851 reflections
254 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F_o^2) + (0.0677P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.065$
$\Delta\rho_{max} = 0.214$ e Å^{-3}
$\Delta\rho_{min} = -0.251$ e Å^{-3}
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)
Absolute configuration: The absolute configuration was chosen to match that expected from the synthetic pathway

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

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

	x	y	z	U_{eq}
S	0.0371 (2)	0.17820 (12)	0.12496 (11)	0.0401 (4)
O1	0.3119 (4)	−0.0051 (3)	0.0593 (3)	0.0384 (10)
O2	0.0829 (4)	−0.1290 (3)	0.1431 (4)	0.0569 (14)
O3	0.1960 (5)	−0.2541 (4)	0.0813 (3)	0.0691 (15)
O4	0.1926 (4)	0.1408 (3)	0.1484 (3)	0.0381 (10)
O5	0.0538 (5)	0.2719 (3)	0.0866 (3)	0.0532 (12)
O6	−0.0346 (5)	0.1733 (4)	0.2154 (3)	0.0651 (13)
O7	−0.0260 (5)	0.1106 (4)	0.0602 (4)	0.075 (2)
N	0.7733 (5)	0.0350 (3)	0.2556 (4)	0.0427 (13)
C1	0.3281 (7)	−0.0812 (5)	0.3397 (5)	0.047 (2)
C2	0.2215 (7)	−0.1188 (5)	0.2880 (6)	0.053 (2)
C3	0.2072 (6)	−0.1004 (4)	0.1906 (5)	0.046 (2)
C4	0.3099 (6)	−0.0419 (4)	0.1496 (4)	0.0332 (14)
C5	0.4058 (6)	0.0792 (4)	0.0662 (4)	0.0335 (14)
C6	0.3114 (6)	0.1663 (4)	0.0861 (4)	0.0339 (13)
C7	0.3953 (6)	0.2450 (4)	0.1346 (4)	0.0393 (14)
C8	0.4611 (6)	0.2105 (4)	0.2266 (4)	0.0350 (14)
C9	0.6448 (6)	0.0906 (4)	0.2908 (4)	0.040 (2)
C10	0.5448 (7)	0.0304 (4)	0.3524 (4)	0.046 (2)
C11	0.4318 (6)	−0.0229 (4)	0.2985 (4)	0.0383 (15)
C12	0.4195 (6)	−0.0081 (4)	0.2037 (4)	0.0298 (13)
C13	0.5144 (5)	0.0542 (3)	0.1438 (4)	0.0291 (13)
C14	0.5733 (5)	0.1354 (4)	0.2045 (4)	0.0306 (13)
C15	0.6431 (6)	−0.0022 (4)	0.1059 (4)	0.0382 (15)
C16	0.7360 (6)	−0.0406 (4)	0.1854 (4)	0.043 (2)
C17	0.8695 (7)	−0.0023 (5)	0.3320 (5)	0.061 (2)
C18	0.0898 (8)	−0.2119 (5)	0.0926 (5)	0.051 (2)
C19	−0.0561 (7)	−0.2415 (5)	0.0618 (6)	0.084 (3)

Table 2. *Selected geometric parameters (Å, °)*

S—O4	1.575 (4)	C3—C4	1.389 (8)
S—O5	1.435 (4)	C4—C12	1.361 (8)
S—O6	1.445 (4)	C5—C6	1.534 (7)
S—O7	1.446 (5)	C5—C13	1.534 (7)
O1—C4	1.381 (6)	C6—C7	1.519 (8)
O1—C5	1.477 (6)	C7—C8	1.519 (7)
O2—C3	1.397 (7)	C8—C14	1.518 (7)
O2—C18	1.370 (8)	C9—C10	1.532 (8)
O3—C18	1.164 (7)	C9—C14	1.529 (7)
O4—C6	1.459 (6)	C10—C11	1.501 (8)
N—C9	1.513 (7)	C11—C12	1.364 (8)
N—C16	1.497 (7)	C12—C13	1.506 (7)
N—C17	1.499 (8)	C13—C14	1.531 (7)
C1—C2	1.341 (9)	C13—C15	1.534 (7)
C1—C11	1.394 (8)	C15—C16	1.520 (8)
C2—C3	1.409 (9)	C18—C19	1.485 (9)
O4—S—O5	106.7 (2)	C6—C7—C8	111.2 (5)
O4—S—O6	102.8 (2)	C7—C8—C14	108.9 (4)
O4—S—O7	106.6 (3)	N—C9—C10	112.4 (5)

O5—S—O6	115.4 (3)	N—C9—C14	107.1 (4)
O5—S—O7	114.2 (3)	C10—C9—C14	114.8 (5)
O6—S—O7	110.1 (3)	C9—C10—C11	114.4 (5)
C4—O1—C5	104.4 (4)	C1—C11—C10	124.5 (6)
C3—O2—C18	117.3 (5)	C1—C11—C12	116.4 (6)
S—O4—C6	119.1 (3)	C10—C11—C12	118.9 (5)
C9—N—C16	113.8 (4)	C4—C12—C11	124.3 (6)
C9—N—C17	114.5 (5)	C4—C12—C13	109.0 (5)
C16—N—C17	111.5 (5)	C11—C12—C13	126.5 (5)
C2—C1—C11	121.0 (6)	C5—C13—C12	98.7 (4)
C1—C2—C3	122.1 (6)	C5—C13—C14	117.8 (4)
O2—C3—C2	119.8 (6)	C5—C13—C15	112.4 (4)
O2—C3—C4	122.6 (6)	C12—C13—C14	109.2 (4)
C2—C3—C4	116.9 (6)	C12—C13—C15	110.7 (4)
O1—C4—C3	128.2 (5)	C14—C13—C15	107.7 (4)
O1—C4—C12	112.3 (5)	C8—C14—C9	114.9 (5)
C3—C4—C12	119.2 (6)	C8—C14—C13	112.9 (4)
O1—C5—C6	108.4 (4)	C9—C14—C13	107.2 (4)
O1—C5—C13	104.6 (4)	C13—C15—C16	111.6 (5)
C6—C5—C13	115.4 (5)	N—C16—C15	111.7 (4)
O4—C6—C5	110.4 (4)	O2—C18—O3	123.1 (6)
O4—C6—C7	107.2 (5)	O2—C18—C19	110.5 (6)
C5—C6—C7	111.8 (4)	O3—C18—C19	126.3 (7)

The H atom attached to the N atom was located in a difference map at a late stage in the refinement. Thereafter the orientation of the N—H vector was fixed, but the N—H distance was allowed to vary [final value 0.96 (6) Å]. Difference maps also revealed disorder of the H atoms attached to C19. Equal occupancy factors and a rotation of 60° between two sets of positions were assumed.

Data collection: *CAD-4 VAX/PC* (Enraf–Nonius, 1988). Cell refinement: *CAD-4 VAX/PC*. Program(s) used to solve structure: *SHELXTL/PC* (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993).

We thank the University of Kentucky Major Research Instrumentation Bond Program for the purchase of equipment used in this study (bond ID No. 7E-8E48-25).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: CR1191). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Brown, E. C., Roerig, S. C., Burger, V. T., Cody, R. B. & Fujimoto, J. M. (1985). *J. Pharm. Sci.* **74**, 821–824.

Crooks, P. A., Kottayil, S., Houdi, A. A. & Butterfield, D. A. (1995). *J. Med. Chem.* Submitted.

Desiraju, G. (1991). *Acc. Chem. Res.* **24**, 290–296.

Enraf–Nonius (1988). *CAD-4 VAX/PC Fortran System. Operator's Guide to the Enraf–Nonius CAD-4 Diffractometer Hardware, its Software and the Operating System.* Enraf–Nonius, Delft, The Netherlands.

Houdi, A. A., Kottayil, S., Crooks, P. A. & Butterfield, D. A. (1995). *Pharmacol. Biochem. Behav.* In the press.

Kottayil, S. (1993). PhD thesis, University of Kentucky, USA.

Oguni, K., Yamada, M. I., Shigezane, J., Hirano, T. & Yoshimura, H. (1987). *Life Sci.* **41**, 1457–1464.

Sheldrick, G. M. (1990). *SHELXTL/PC*. Version 4.1. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures.* University of Göttingen, Germany.

Acta Cryst. (1996). C**52**, 125–127

N,*N*′-Bis(2-hydroxybenzylidene)-2,2-dimethyl-1,3-propanediamine

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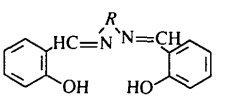
(*Received 14 June 1995; accepted 19 July 1995*)

Abstract

In the title compound, $C_{19}H_{22}N_2O_2$, the average N···O separation of 2.580 (4) Å is indicative of intramolecular hydrogen bonding within each salicylideneimine unit. The two aromatic rings are inclined at an angle of 68.66 (11)° and this results in a conformation which is inappropriate for quadridentate ligand activity.

Comment

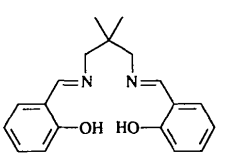
Although the crystal structures of many metal complexes with Schiff base ligands have been reported, very few of the free ligands have been similarly characterized (Calligaris & Randaccio, 1987). For quadridentate ligands of type (I), the solid-state structures have only been reported for (I*a*) (Pahor, Calligaris, Nardin & Randaccio, 1978), (I*b*) (Pahor *et al.*, 1976; Subrahmanyam, Seshasayee & Aravamudan, 1982), (I*c*) (Cimerman, Galesic & Bosner, 1992), (I*d*) (Senn & Nowacki, 1977), and (I*e*) (Elerman, Svoboda & Fuess, 1991). The structure of the title compound, (II), has now been determined so that subsequent changes upon coordination to a metal may be investigated.



(I)

(I*a*) $R = CH_2—CH_2$ (I*b*) $R =$  (I*c*) $R =$ 

(I*d*) $R = CHPh—CHPh$ (I*e*) $R = CH_2—CH_2—CH_2$



(II)

The molecular structure of the title compound, as determined in this work, is represented in Fig. 1. Clearly, the enolimine tautomer is favoured over the ketamine form. This is evident from the observed O1—C1 and