two benzene rings is 66·5 (5)°, which is in the expected range for molecules with an unsubstituted phenyl ring (Hamor & Martin, 1983).

All intermolecular contact distances correspond to normal van der Waals interactions.

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Stereochemical Aspects of Narcotic Action. II.* 9-(*m*-Hydroxyphenyl)-9α-methoxy-3-methyl-3-azoniabicyclo[3.3.1]nonane *p*-Toluenesulfonate Monohydrate, $C_{16}H_{24}NO_2^+.C_7H_7O_3S^-.H_2O$

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Abstract. $M_r = 451·6$, monoclinic, $P2_1/c$, $a = 10·006$ (3), $b = 28·597$ (5), $c = 8·352$ (2) Å, $\beta = 106·29$ (2)°, $V = 2293·8$ (3) Å^3, $Z = 4$, $D_m = 1·305$ (3), $D_x = 1·307$ (3) Mg m^{-3}, λ(Cu $K\alpha_1$) = 1·5405 Å, $\mu = 1·55$ mm^{-1}, $F(000) = 968$, $T = 293$ K, $R = 0·065$, 2224 reflections. The crystal contains enantiomeric conformations [angles C(5)–C(9)–C(10)–C(11) ±19·5 (6); C(16)–O(1)–C(9)–C(10) ±54·6 (5)°] but not the diastereomeric conformers generated by 180° rotation around the C(9)–C(10) bonds. The chair–chair conformation of the bicyclic nucleus is flattened [N to C(7), 3·080 (7) Å]. Independently calculated, energy-minimized conformations for the non-phenolic analog are consistent with the solid-state conformations.

Introduction. Analogs and diastereoisomers (9α,9β) of (1) are strong narcotic analgetics (Ohki, Oida, Ohashi, Takagi & Iwai, 1970) offering a unique opportunity to determine the relative orientations of the aromatic rings, N atoms and N substituents at the narcotic receptor through a series of linear free-energy correlations (Portoghese, 1965). Before embarking on that study it was necessary to compare the conformations of two representative, diastereomeric analogs, the first of which, the 9α isomer (1), is the subject of this report. The conformation of the bicyclic nucleus and the torsion angle around the C(9)–C(10) bond are of particular interest. These define the distances between the pharmacophoric groups (N, phenyl, OH). In addition, the potencies of some narcotic analgetics have been correlated with the torsion angles of the aromatic rings (Froimowitz, 1982; Portoghese, 1978; Fries, Dodge, Hope & Portoghese, 1982).

* Part I: Tecle & Hite (1976).

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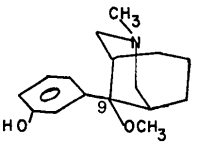

(1)

Experimental. Prisms (0·30 × 0·25 × 0·15 mm) from anhydrous salt (m.p. 465 K) in 1:1 methanol:acetone (0·05% H_2O). D_m by flotation (CCl_4–C_6H_6). Picker FACS-I, Ni-filtered Cu $K\alpha_1$. Lattice parameters from 24 automatically centered reflections ($37° < 2\theta < 56°$), 2438 reflections, 2224 $I > 3\sigma(I)$, $2\theta < 100°$, $\theta/2\theta$ scans. Lorentz, polarization and absorption corrections (North, Phillips & Mathews, 1968) (14·22%, 131). Standards constant [$\pm 2\sigma(I_{avg})$]. Direct methods (*MULTAN*, Declercq, Germain & Woolfson, 1975). Zerovalent scattering factors (*International Tables for X-ray Crystallography*, 1974). Full-matrix least-squares refinement (*ORFLS*, Busing, Martin & Levy, 1962), in blocks (anion–H_2O, cation). $R = 0·087$ minimizing $\sum w(|F_o| - |F_c|)^2$; $w = 1/\sigma^2$; $\sigma = 1·00 - 0·0243|F_o| + 0·0063|F_o|^2$ from counting statistics. All H atoms located in difference maps, assigned isotropic $B = 3·00$ Å^2 (not refined). Refinement converged at $R = 0·065$, $wR = 0·093$. $\Delta/\sigma < 0·5$. Error in observation of unit weight 1·33. No peak greater than 0·34 e Å^{-3} in final difference Fourier synthesis. IBM 370/168 computer. Programs from *XRAY* package (Stewart, Kruger, Ammon, Dickinson & Hall, 1972).

Discussion. The atomic positional parameters of Table 1* define one of the two chiral conformations of (1) in this crystal. The existence in the solid state of one or both mirror images of molecules which, like (1), lack asymmetric C atoms is not unusual (Lewis, Paul & Curtin, 1980). The chiral conformations of (1) arise by rotations of the aromatic ring and C(16) around the C(9)–C(10) and O(1)–C(9) bonds, respectively. The two enantiomeric conformations of (1) are defined by the C(5)–C(9)–C(10)–C(11) and C(16)–O(1)–C(9)–C(10) torsion angles of ±19·5 (6) and ±54·6 (5)°, respectively. Diastereomers generated by 180° rotation of the aromatic rings around the C(9)–C(10) bonds are absent. Packing forces (Figs. 1–3) appear to be responsible for the diastereomerically specific crystallization. The O(4) and O(5) atoms of the sulfonate anion are hydrogen bonded to H(N). The *N*-methyl group and O(3) of the sulfonate anion are on the same side of the plane defined by S, O(4), O(5) and H(N) (Fig. 2). Molecules of one enantiomer form chains running diagonally up the *c* axis parallel to the *ac* plane. These are linked by hydrogen bonds from O(3) to H2(O6) and O(6) to H(O2) of the neighboring molecule (65401···55501···45601··· *etc.*, Figs. 1 and 2). A neighboring enantiomeric chain is an inversion of the first through $\frac{1}{2}$–y but it is translated one half unit cell along the *c* axis. These chains are crosslinked by hydrogen bonds from H1(O6) to O(5) so that each molecule is hydrogen bonded to its enantiomers in two different chains (55504···55501···55404··· *etc.*, Fig. 2). This arrangement generates layers of chains of one enantiomer and an adjacent layer of chains of the other facing in opposite directions ($\pm b$) forming a polar interface parallel to the *ac* plane and centered at $b/4$. This interface contains the amine cation, the sulfonate anion, water and the phenolic hydroxyl (Fig. 2). A hydrophobic interface centered on the *ac* plane at $b/2$ is formed with an adjacent enantiomeric layer (55503, *etc.*, Fig. 3). Thus, two enantiomeric layers linked by hydrogen bonds are in turn held together by van der Waals attractions with adjacent sets of layers in a pattern that is repeated twice in every translation along the *b* axis. The organization of the polar interface

Table 1. *Atomic positional parameters* (×10⁴) *and equivalent isotropic thermal parameters* (×10³) *derived from refined anisotropic thermal parameters (deposited) corresponding to the form*: $\exp[-2\pi^2 \times (U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)]$; $U = (U_{11}U_{22}U_{33})^{1/3}$

Isotropic thermal parameters (3·00 Å²) for H atoms correspond to the expression: $\exp(-B\sin^2\theta/\lambda^2)$ and were not refined. See Fig. 1 for numbering system. Estimated standard deviations are given in parentheses.

	x	*y*	*z*	U_{eq}(Å²)
S	8249 (1)	1625 (1)	6968 (2)	51
O(1)	11346 (3)	537 (1)	1616 (4)	53
O(2)	13477 (4)	2111 (1)	−887 (5)	75
O(3)	8174 (4)	1975 (1)	8182 (5)	86
O(4)	9603 (4)	1405 (1)	7308 (4)	64
O(5)	7795 (4)	1786 (1)	5240 (5)	67
O(6)	15963 (5)	2450 (1)	8953 (7)	101
C(1)	11565 (5)	942 (2)	4127 (6)	47
C(2)	11687 (5)	1414 (2)	4981 (6)	46
N	10449 (5)	1724 (1)	4268 (6)	45
C(4)	10030 (5)	1734 (2)	2385 (6)	43
C(5)	10008 (5)	1262 (2)	1562 (5)	42
C(6)	8809 (5)	946 (2)	1697 (6)	54
C(7)	8936 (5)	778 (2)	3469 (6)	54
C(8)	10416 (6)	624 (2)	4406 (6)	55
C(9)	11421 (5)	1010 (2)	2252 (5)	42
C(10)	12672 (5)	1253 (2)	1912 (5)	42
C(11)	12534 (5)	1585 (2)	669 (6)	47
C(12)	13706 (5)	1786 (2)	363 (6)	54
C(13)	15009 (6)	1658 (2)	1301 (7)	59
C(14)	15152 (5)	1319 (2)	2492 (7)	60
C(15)	14005 (5)	1118 (2)	2833 (6)	51
C(16)	11314 (5)	492 (2)	−78 (6)	69
C(17)	10726 (5)	2208 (2)	4975 (7)	61
C(18)	7080 (5)	1178 (2)	7155 (5)	46
C(19)	7372 (6)	718 (2)	6955 (6)	58
C(20)	6463 (6)	370 (2)	7098 (7)	62
C(21)	5220 (6)	475 (2)	7459 (6)	54
C(22)	4937 (5)	940 (2)	7656 (6)	59
C(23)	5836 (6)	1287 (2)	7498 (6)	57
C(24)	4215 (7)	98 (2)	7571 (8)	80

* Lists of anisotropic thermal parameters, structure factors and H-atom positional parameters and torsion angles have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39076 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

appears to be the prime reason for diastereomerically specific crystallization. The closest intermolecular neighbors of H(C14) and O(2) are just beyond the sums of van der Waals radii. A dummy O at C(14) simulates one of the two missing diastereomers and encounters severe non-bonded repulsions with H(C7*e*) (2·06 Å), O(5) (2·47 Å) and C(7) (2·71 Å) (55601). It intrudes into the hydrophobic interface and is unable to form hydrogen bonds. While only two of the four theoretically observable chiral conformations of (1) are observed because of diastereomerically specific packing constraints, other derivatives of (1) may exhibit packing schemes specific for one enantiomer, for either diastereomer or for both diastereomers.

Bond distances and angles (Fig. 1) and torsion angles (deposited) are consistent with previous crystallographic reports on a number of bicyclo[3.3.1]nonanes reviewed by Bhattacharjee & Chacko (1979) including 3-azabicyclo[3.3.1]nonane (Dobler & Dunitz, 1964) and on a related 2-azabicyclo[3.3.1]nonane (Cochran, 1974). They are also in excellent agreement with those for an independently calculated, energy-minimized conformation of the non-phenolic analog of (1) (Froimowitz, Salva, Hite, Gianutsos, Suzdak & Heyman, 1984). As in the related chair–chair structures, the cyclohexane and piperidine rings of (1) are distorted from perfect chairs (60° internal torsion angles). This is caused by the close approach of H(N) and H(C7*a*) (2·02 Å). The equilibrium N to C(7) distance is 3·080 (7) Å. This results in a flattening of both rings primarily by reduction of four torsion angles, two in the cyclohexane ring [C(1)–C(8)–C(7)–C(6) = +41·3 (6) and C(5)–C(6)–C(7)–C(8) = −43·0 (5)°] and two in the piperidine ring [C(1)–C(2)–N–C(4) = −46·7 (5) and C(5)–C(4)–N–C(2) = 44·1 (5)°]. Total conformational distortion defined as $\sum|\text{torsion angle}|-60|$ for the twelve internal torsion angles in the cyclohexane and piperidine rings is 97°. The comparable internuclear distance in the 2-azabicyclo[3.3.1]nonane system [C(3) to C(7)] is 3·080 Å (Cochran, 1974) and ring distortion is 104°. There are no statistically significant differences between these values and the average of values (3·08 Å, 103°) found in related chair–chair bicyclo[3.3.1]nonanes (Bhattacharjee & Chacko, 1979). The slightly smaller (6°) ring distortion in (1) may be attributed to the C(9) substituents. Despite the ring strain, non-bonded repulsion between the bowsprit H atoms in the chair–boat conformation of bicyclo[3.3.1]nonanes generates even greater strain. Chair–boat conformations are found only in analogs of (1) containing bulky substituents in the 3- and/or 7-*endo* positions (Bhattacharjee & Chacko, 1979) and in the recently reported 3-benzyl-7-methyl-3,7-diazabicyclo[3.3.1]nonan-9-one (Smith-Verdier, Florencio & García-Blanco, 1983) in which the 3- and 7-substituents are *exo*. Theoretical calculations and experiments show that the chair–chair conformation of bicyclo[3.3.1]nonane is 8 kJ mol^{-1} more stable than the chair–boat conformation (Mastryukov, Popik, Dorofeeva, Golubinskii, Vilkov, Belikova & Allinger, 1979). The stability of the chair–boat conformation of 3-benzyl-7-methyl-3,7-diazabicyclo[3.3.1]-nonan-9-one is attributable to the absence of non-bonded repulsion between bowsprit H atoms and to transannular electrostatic attraction between the positive end of the carbonyl dipole at C(9) and the

O(3)-S-O(5)	114.5(2)	N-C(4)-C(5)	114.9(4)
O(4)-S-C(18)	105.9(2)	H(C4e)-C(4)-H(C4a)	109 (4)
C(2)-N-H(N)	103 (3)	C(4)-C(5)-C(6)	113.9(4)
C(4)-N-C(17)	111.1(4)	C(9)-C(5)-H(C5)	107 (3)
C(2)-C(1)-H(C1)	102 (3)	C(5)-C(6)-C(7)	113.8(4)
C(8)-C(1)-C(9)	111.6(3)	H(C6e)-C(6)-H(C6a)	112 (4)
N-C(2)-H(C2a)	107 (3)	H(C7e)-C(7)-C(6)	110 (3)
C(1)-C(2)-H(C2e)	109 (3)	H(C7a)-C(7)-C(8)	110 (2)
H(C8e)-C(8)-C(1)	111 (3)		
H(C8a)-C(8)-C(7)	108 (3)		
O(1)-C(9)-C(5)	110.6(3)		
C(1)-C(9)-C(10)	113.4(3)		
H2(C17)-C(17)-N	107 (3)		
H1(C17)-C(17)-H3(C17)	110 (4)		
H1(C16)-C(16)-H2(C16)	91 (4)		
O(1)-C(16)-H3(C16)	106 (3)		

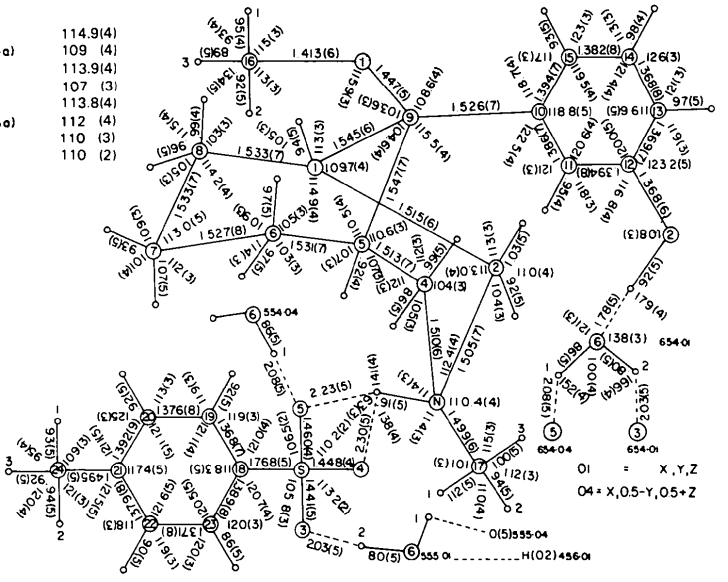

Fig. 1. Bond distances (Å) and angles (°) for (1). Estimated standard deviations are given in parentheses.

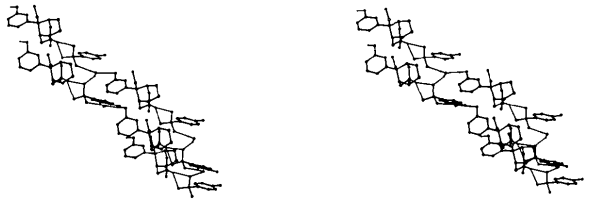

Fig. 2. Stereoprojection (Johnson, 1976) of (1) from the *ac* plane to *b*/2 down the *b* axis. Some molecules have been omitted for clarity, see text.

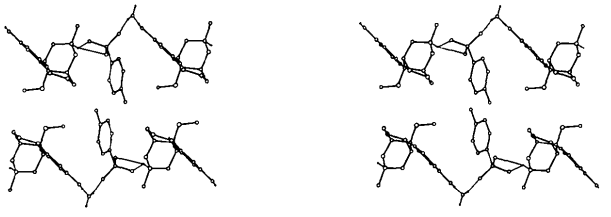

Fig. 3. Stereoprojection (Johnson, 1976) of (1) from *b*/4 to −*b*/4 down the *c* axis. Some molecules have been omitted for clarity, see text.

unshared electron pair on N. It is clear that in the chair–boat conformation of (1) the C(9) substituents would invoke even more severe non-bonded bowsprit repulsions than those encountered in the chair–boat conformation of bicyclo[3.3.1]nonane. Accordingly, (1) conforms to the definition of an effectively rigid chair–chair conformation (Eliel, Allinger, Angyal & Morrison, 1965).

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Methyl 8-Oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate, $C_{13}H_{18}O_3$

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Abstract. $M_r = 222{\cdot}3$, monoclinic, *Cc*. $a = 8{\cdot}399$ (3), $b = 16{\cdot}366$ (3), $c = 9{\cdot}310$ (3) Å, $\beta = 108{\cdot}19$ (2)°, $V = 1215{\cdot}8$ Å^3, $Z = 4$, $D_x = 1{\cdot}21$ g cm^{-3}, λ(Mo $K\alpha_1$) = 0·70926 Å, $\mu = 0{\cdot}79$ cm^{-1}, $F(000) = 480$, $T = 294$ K. Final $R = 0{\cdot}047$ for 891 observed reflections. The five- and six-membered rings are mutually *trans*-disposed about the central four-membered ring. One of the atoms of the six-membered ring is disordered over two sites (0·75:0·25) leading to twist-boat and twist-chair conformations for this ring; the four-membered ring is puckered [torsion angles ±9·4 (3)°] and the five-membered ring has an *endo*-envelope conformation.

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