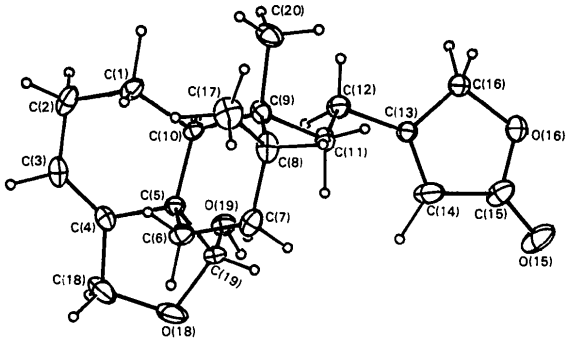

Fig. 1. *ORTEP* drawing of the title compound. Thermal ellipsoids are drawn at the 35% probability level and H atoms as spheres of arbitrary size.

The NMR of (1) was correlated with that of (2); however, the optical rotation was of opposite sign and the configuration shown in Fig. 1 was inferred (Gao & Mabry, 1986). The crystal structures of the *cis*-clerodanes (3) (Bally, Billet, Durgeat & Heitz, 1976) and (4) (Ferguson, Marsh, McCrindle & Nakamura, 1975; Ferguson & Marsh, 1976) have been reported. The angle between the mean planes of the two six-membered rings ranges between 54 and 65° for compounds (1), (3) and (4). Statistically significant differences in angles and distances in the three compounds are associated with variations in fusion of C(5) and C(6). Methyl C(17) lies within 2·999 (7) Å of methyl C(20) and within 3·178 (7) Å of C(6) with a C(17)C(8)C(9)C(20) torsion angle of 44·6 (5)°. There is an intermolecular H bond formed between OH(19) and O(15) (0·5 + x, 1·5 − y, 1 − z), O(19)···O(15) = 2·811 (4) Å, H(19)···O(15) = 1·83 (4) Å and O(19)–H(19)···O(15) = 164 (1)°.

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References

BALLEY, R., BILLET, D., DURGEAT, M. & HEITZ, S. (1976). *Tetrahedron Lett.* pp. 2777–2778.

CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A**24**, 321–324.

FERGUSON, G. & MARSH, W. C. (1976). *Cryst. Struct. Commun.* **5**, 35–38.

FERGUSON, G., MARSH, W. C., MCCRINDLE, R. & NAKAMURA, E. (1975). *J. Chem. Soc. Chem. Commun.* p. 299.

GAO, F. & MABRY, T. J. (1986). *Phytochemistry.* In the press.

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

JOHNSON, C. K. (1971). *ORTEP*II. Report ORNL-3794, revised. Oak Ridge National Laboratory, Tennessee.

MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1978). *MULTAN*78. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

STEWART, J. M., MACHIN, P. A., DICKINSON, C. W., AMMON, H. L., HECK, H. & FLACK, H. (1976). The *XRAY*76 system. Tech. Rep. TR-446. Computer Science Center, Univ. of Maryland, College Park, Maryland.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

Syntex (1976). *XTL/XTLE Structure Determination System.* Syntex Analytical Instruments, Cupertino, California.

TOROMANOFF, E. (1980). *Tetrahedron*, **36**, 2809–2931.

Acta Cryst. (1986). C**42**, 1442–1444

Structure of Methyl(1,5,6-trihydroxy-1,2,3,4-tetrahydro-2-naphthyl)ammonium Bromide

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Abstract. $C_{11}H_{16}NO_3^+.Br^-$, $M_r = 290{\cdot}2$, triclinic, $P\bar{1}$, $a = 7{\cdot}710$ (5), $b = 8{\cdot}762$ (8), $c = 9{\cdot}882$ (2) Å, $\alpha = 104{\cdot}15$ (2), $\beta = 106{\cdot}19$ (4), $\gamma = 95{\cdot}66$ (7)°, $V = 611{\cdot}6$ Å^3, $Z = 2$, $D_m = 1{\cdot}56$ (2), $D_x = 1{\cdot}575$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 32{\cdot}6$ cm^{-1}, $F(000) = 296$, $T = 294$ K, final $R = 0{\cdot}051$ for 1440 reflections. The cyclohexane moiety adopts a half-chair conformation with the hydroxyl and protonated amine groups in diequatorial orientations. The O–C(1)–C(2)–N(1) and C(9)–C(1)–C(2)–N(1) torsion angles are 63 (1) and 172 (1)°, respectively.

Introduction. The determination of the active conformations of hormones and drugs is important since such information can be used to infer molecular modes of action and in the design of new drugs. However, many active molecules are very flexible and while solid-state and isolated-state geometries can be obtained by crystallographic and theoretical methods,

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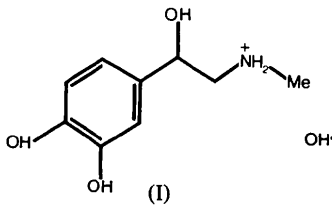
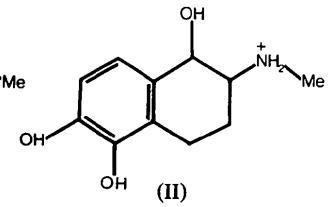
these do not necessarily correspond to the active conformation. Rigid, conformationally constrained analogues of the active compounds can be used to infer the preferred conformation; thus, if the rigid analogue has activity similar to that of the parent drug then the receptor-preferred conformation probably corresponds to that of the analogue (Horn & Rodgers, 1977).

Epinephrine (adrenalin) (I) has a flexible side arm with hydroxyl and amine functions which are believed to be involved in receptor binding (Mathew & Palenik, 1971). We have determined the structure of (II) as the bromide salt, a constrained analogue of epinephrine, which has been shown to have similar β-stimulating activity for tracheal muscle tissue (Nishikawa *et al.*, 1975), in order to establish the active side-arm conformation and geometry.



(I)



(II)

Experimental. D_m by flotation in $CH_2Br_2/CHCl_3$. Data collected using Enraf–Nonius CAD-4 automatic diffractometer, graphite-monochromated Mo $K\alpha$ radiation; 25 independent reflections with $10 \le 2\theta \le 30°$ used for least-squares determination of cell constants. Intensities of three standard reflections monitored, less than 1% decomposition.

Structure solved by heavy-atom method with *SHELX*76 (Sheldrick, 1976), H atoms bonded to O refined with fixed bond lengths (O–H, 0·87 Å), those bonded to N included at calculated sites (N–H, 0·97 Å), and those bonded to C fully refined with isotropic temperature factors, non-H atoms refined anisotropically. Full-matrix least-squares refinement on F converged with shifts $< 0{\cdot}4\sigma$ in parameters of non-H atoms, $< 1{\cdot}2\sigma$ for H. Maximum excursions in a final difference map 1·2 and −1·5 e Å^{-3}.

All calculations performed using *SHELX*76 (Sheldrick, 1976) and figures drawn with *ORTEP* (Johnson, 1965). Scattering factors and anomalous-dispersion terms were taken from *International Tables for X-ray Crystallography* (1974). Data-collection and refinement parameters are presented in Table 1. Final positional parameters are listed in Table 2.*

* Lists of structure factors, anisotropic thermal parameters, H-atom parameters, H-bond distances and details of least-squares-planes calculations have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 43057 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Discussion. A schematic view of (II) showing bond lengths and angles is given in Fig. 1 and a view of the crystal packing is shown in Fig. 2. There are a number of quite strong intermolecular H bonds involving amine, hydroxyl and bromide moieties. There is also a close intramolecular contact between the amine H atom and the adjacent hydroxyl O atom which may correspond to a H bond but these atoms are of course constrained to be close. A least-squares plane through the six atoms of the phenyl moiety reveals no significant deviation from planarity. Of the atoms directly bonded to the phenyl ring, O(2) is distorted most from the plane, lying 0·06 (2) Å below it.

The cyclohexane moiety adopts a half-chair conformation with the associated hydroxyl and amine groups both occupying equatorial positions. The β-stimulating activity of (II) suggests that its conformation is similar to the active conformation of epinephrine and related compounds. A comparison of the torsion angles, observed in the solid state, for

Table 1. *Summary of data-collection and processing parameters*

Crystal dimensions	0·10 × 0·10 × 0·10 mm
Data-collection range	$3 < 2\theta < 45°$
Scan width	$(0{\cdot}80 + 0{\cdot}35\tan\theta)°$
Horizontal counter aperture	$(2{\cdot}00 + 0{\cdot}50\tan\theta)$ mm
Scan type	ω–2θ
Absorption correction	
number of sampling points	64
max. correction	1·431
min. correction	1·269
Range of *hkl*	−7→7, −9→9, 0→10
R_{int}	0·011
Total data collected	1719
Data with $I > 2{\cdot}5\sigma(I)$	1440
Total variables	205
R	0·051
wR	0·071
Weighting constants $[w = g/(\sigma^2F_o + kF_o^2)]$	$g = 1{\cdot}0$, $k = 0{\cdot}0062$

Table 2. *Positional* ($\times 10^4$) *and equivalent isotropic thermal parameters*

$B_{eq} = 8\pi^2(U_{11}U_{22}U_{33})^{1/3}$.

	x	y	z	B_{eq}(Å^2)
Br(1)	2208 (1)	1566 (1)	3301 (1)	3·74
O(1)	3539 (5)	8771 (4)	191 (4)	3·38
O(2)	7 (6)	2014 (4)	−2706 (4)	4·24
O(3)	340 (5)	1788 (4)	37 (4)	3·57
N(1)	3977 (6)	8827 (5)	−2576 (5)	3·36
C(1)	3701 (6)	7347 (6)	−810 (5)	2·79
C(2)	2905 (7)	7438 (6)	−2375 (6)	3·00
C(3)	2930 (7)	5908 (6)	−3457 (6)	3·41
C(4)	1587 (9)	4583 (7)	−3333 (6)	3·91
C(5)	1036 (6)	3226 (6)	−1515 (5)	3·05
C(6)	1204 (6)	3152 (6)	−109 (5)	3·02
C(7)	2182 (6)	4433 (6)	1071 (6)	3·21
C(8)	3022 (7)	5773 (6)	819 (6)	3·08
C(9)	2836 (6)	5873 (6)	−566 (5)	2·52
C(10)	1851 (6)	4564 (5)	−1781 (5)	2·88
C(11)	2977 (11)	9442 (10)	−3812 (9)	5·92

Table 3. *Torsion angles* (°) *for* (II) *and some related phenylethylamines*

	(II)	Epinephrine[a]	Epinephrine hydrogen tartrate[b]	Norepinephrine[c]	Isoproterenol[d]
C(7)–C(8)–C(9)–C(1)	178 (1)	175	177	177	179
C(8)–C(9)–C(1)–C(2)	163 (1)	80	97	3	102
C(10)–C(9)–C(1)–C(2)	18 (1)	96	82	179	77
C(8)–C(9)–C(1)–O(1)	39 (1)	38	147	126	19
C(9)–C(1)–C(2)–N(1)	172 (1)	172	176	179	175
C(1)–C(2)–N(1)–C(11)	157 (1)	158	–	173	156
O(1)–C(1)–C(2)–N(1)	63 (1)	65	64	58	62

References: (*a*) Andersen (1975); (*b*) Carlström (1973); (*c*) Carlström & Bergin (1967); (*d*) Mathew & Palenik (1971).

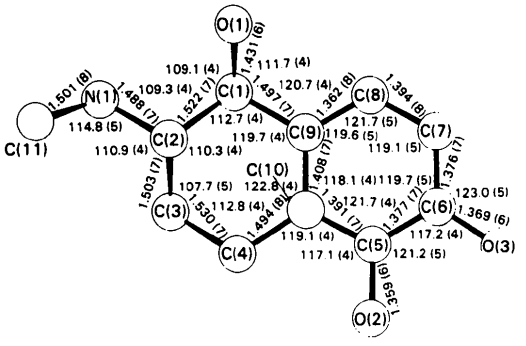


Fig. 1. View of the molecule showing atom labelling, bond lengths (Å) and angles (°).

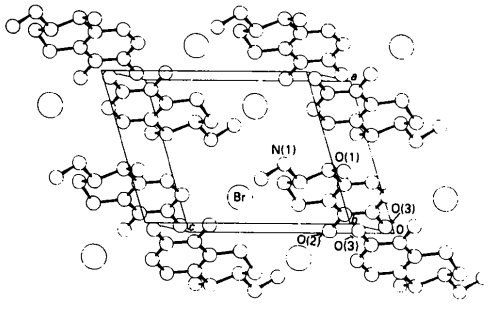


Fig. 2. View of the unit cell of (II).

compound (II), epinephrine, norepinephrine and isoproterenol is given in Table 3. These angles show that the orientation of the side chain relative to the phenyl ring, in the unconstrained molecules, is variable as exemplified by the angles C(8)–C(9)–C(1)–C(2) (τ_1) and C(8)–C(9)–C(1)–O(1), and in no case does it approach the orientation in the constrained molecule (II). However, the conformation of the side chain is remarkably constant and is the same as that of the constrained molecule. Thus, C(9)–C(1)–C(2)–N(1) (τ_2) varies from 171·6 to 179·4° and O(1)–C(1)–C(2)–N(1) from 57·8 to 65·3°. The constancy of these angles may reflect a deep potential-energy minimum or may be due to an intramolecular H bond between the amine and hydroxyl groups. Quantum-mechanical calculations have predicted a potential-energy minimum at $\tau_1 \approx 90°$ and $\tau_2 \approx 180°$ (Caillet, Claverie & Pullman, 1976). The former value is observed in the solid-state structures of epinephrine, isoproterenol sulfate and norepinephrine hydrochloride while the latter is found for all structures in Table 3. However, no potential-energy minimum was found to exist at $\tau_1 \approx 180°$, observed for (II), or $\tau_1 \approx 0°$, observed in epinephrine hydrogen tartrate. It has been suggested that in the latter case this geometry is the result of crystal-packing effects (Caillet *et al.*, 1976). It is possible that other geometries may be stabilized in solution, but the above results suggest that the active conformation of the phenylethylamines does not necessarily have a particular orientation of the side chain relative to the phenyl group. The conformation of the side chain is, however, probably more critical.

References

ANDERSEN, A. M. (1975). *Acta Chem. Scand. Ser. B*, **29**, 239–244.

CAILLET, J., CLAVERIE, P. & PULLMAN, B. (1976). *Acta Cryst.* B**32**, 2740–2745.

CARLSTRÖM, D. (1973). *Acta Cryst.* B**29**, 161–167.

CARLSTRÖM, D. & BERGIN, R. (1967). *Acta Cryst.* **23**, 313–319.

HORN, A. S. & RODGERS, J. R. (1977). *J. Pharm. Pharmacol.* **29**, 257–265.

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.

MATHEW, M. & PALENIK, G. J. (1971). *J. Am. Chem. Soc.* **93**, 497–502.

NISHIKAWA, M., KANNO, M., KURIKI, H., SUGIHARA, H. MOTOHASHI, M., ITOH, K., MIYASHITA, O., OKA, Y. & SANNO, Y. (1975). *Life Sci.* **16**, 305–314.

SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.