as considerable computing time was saved and we obtained exactly the same values for the bond parameters that were of interest to us.

References

CARLSTRÖM, D. & FALKENBERG, G. (1973). *Acta Chem. Scand.* **27**, 1203–1209.

DOMENICANO, A., VACIAGO, A. & COULSON, C. A. (1975). *Acta Cryst.* B**31**, 1630–1641.

HOSSAIN, M. A., HURSTHOUSE, M. B. & MALIK, K. M. A. (1979). *Acta Cryst.* B**35**, 522–524.

International Tables for X-ray Crystallography (1974). Vol. IV, pp. 99–102. Birmingham: Kynoch Press.

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

KEYES, P. H. & DANIELS, W. B. (1975). *J. Chem. Phys.* **62**, 2000–2001.

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

SHKLOVER, V. E., KALININ, A. E. & GUSEV, A. I. (1973). *Zh. Strukt. Khim.* **14**, 692–699.

SÖDERHOLM, M. & CARLSTRÖM, D. (1977). *Acta Chem. Scand. Ser. B*, **31**, 193–197.

STEINFINK, H., POST, B. & FANKUCHEN, I. (1955). *Acta Cryst.* **8**, 420–424.

VOLINO, F. & DIANOUX, A. J. (1978). *Ann. Phys. (Leipzig)*, **3**, 151–154.

Structure of (±)-N-Methyl-2-(3,4-dihydroxyphenyl)ethylammonium-2-sulfonate Hemihydrate [(±)-Epinine β-Sulfonate Hemihydrate]

BY J. G. HENKEL,* J. B. ANDERSON, M. RAPPOSCH AND G. HITE

Section of Medicinal Chemistry and Pharmacognosy, School of Pharmacy, and Institute of Materials Science, The University of Connecticut, Storrs, Connecticut 06268, USA

Abstract. $C_9H_{13}NO_3S.\frac{1}{2}H_2O$, m.p. 532–533 K (decomposition), *Pbna*, $a = 13.588$ (3), $b = 14.885$ (4), $c = 10.616$ (3) Å, $Z = 8$, $D_x = 1.585$, D_m (C_6H_6–CCl_4) = 1.58 Mg m^{-3}, Mo $K\alpha$ ($\lambda = 0.7093$ Å), 1017 reflections, $2\theta < 40°$, $217 < 3\sigma(F_o)$. The structure was solved by *MULTAN* with magic integers. Full-matrix least-squares refinement converged with $R(F) = 0.040$. This confirms the previous assignment of structure to the racemic degradation product of (−)-epinephrine in the presence of aqueous bisulfite.

Introduction. The degradation of (−)-epinephrine (1) in the presence of aqueous bisulfite or sulfite was first reported by Schroeter, Higuchi & Schuler (1958). They speculated that (±)-epinine β-sulfonate (2) is the reaction product. Although there has been general acceptance of the identity of the product based upon its elemental analysis, melting point, ultraviolet spectrum, pKa and X-ray powder diffraction pattern, there have been occasional reports of confusion in the literature regarding its identity (Kawazu, Inoue, Tomino & Iwao, 1973, and references therein). The kinetics of degradation have been thoroughly studied but fail to unambiguously characterize the mechanism or course of the reaction (Hajratwala, 1975, and references

therein) or the structure of the product. The occurrence of the *o*- or *p*-hydroxybenzyl alcohol structure in this and other molecules appears to favor this type of reactivity (Higuchi & Schroeter, 1959) in which dienones (3) have been implicated (Cohen & Jones,

(1)

(3)

(2)

---
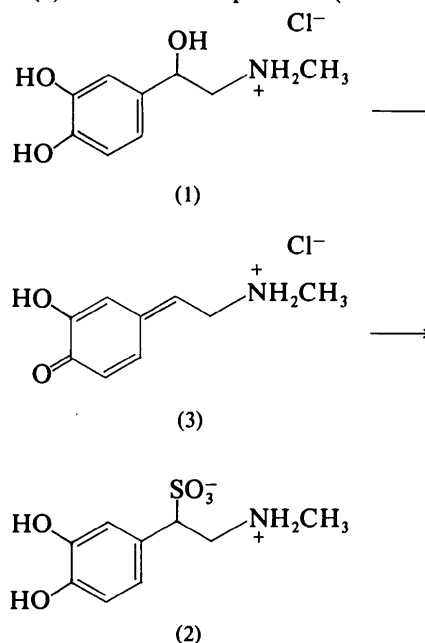
* To whom correspondence should be addressed.

1960). Yet, the intermediacy of a dienone which can be formed from (1) under acidic or basic catalysis has not been considered in kinetic studies and the β-sulfonate (2) is only one of the isomeric structures which could be derived from it by addition of bisulfite. As part of our developing interest in correlating the structures and activities of selected phenethylamines it became necessary to undertake the unambiguous characterization of the title compound (2).

Photographs of a crystal (0·3 × 0·2 × 0·2 mm), from 1 M HCl, revealed orthorhombic symmetry. Systematic absences led to assignment of space group *Pbna*, an alternative setting for *Pbcn* (No. 60). Lattice parameters were refined by least-squares fitting of 12 automatically centered reflections (16° < 2θ < 37°) measured at 298 K. Diffraction intensities were measured with Zr-filtered Mo Kα radiation (λ = 0·7093 Å) on an automated Picker FACS-I diffractometer. Three standard reflections remained constant [±2σ(I_{av})] throughout the data collection. Of 1017 independent reflections (2θ < 40°), 217 were considered unobserved according to the criterion: $|F_o| >$

3·0σ. Integrated intensities were corrected for Lorentz and polarization effects but no absorption correction was applied. The structure was solved using *MULTAN* with magic integers (Declercq, Germain & Woolfson, 1975). Full-matrix least-squares refinement (Busing, Martin & Levy, 1962) with a $1/\sigma^2$ weighting scheme, zerovalent scattering factors, isotropic temperature factors and corrections for secondary extinction was followed by anisotropic refinement and calculation of a difference Fourier map. Peaks corresponding to all H atoms could be discerned. The final cycles of refinement included arbitrarily assigned fixed isotropic thermal parameters of 2·5 Å^2 for H atoms. Refinement converged at $R = 0·040$, $R_w = 0·045$ minimizing $\sum w(|F_o| - |F_c|)^2$. Final parameter shifts were less than 0·5 σ. Final atomic positional parameters are in Table 1.*
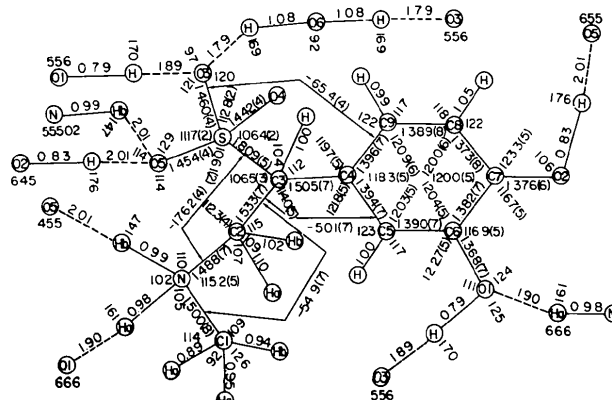
Table 1. *Positional parameters* (× 10⁴ *except hydrogens* × 10³) *given as fractions of the lattice translations*

Estimated standard deviations in the last figures are given in parentheses.

	x	y	z
S	6284 (1)	2235 (1)	2020 (1)
O(1)	6152 (3)	4791 (2)	5986 (4)
O(2)	6675 (3)	6264 (3)	4812 (4)
O(3)	6229 (3)	1934 (2)	3327 (3)
O(4)	5861 (3)	1599 (2)	1149 (3)
O(5)	7273 (3)	2521 (2)	1684 (3)
O(6)	7759 (5)	2500 (*)	5000 (*)
N	3783 (4)	3709 (3)	2364 (5)
C(1)	3730 (6)	4270 (5)	1193 (7)
C(2)	4479 (4)	2938 (4)	2305 (6)
C(3)	5524 (4)	3231 (3)	1945 (5)
C(4)	5912 (4)	4005 (3)	2712 (5)
C(5)	5875 (4)	4004 (4)	4024 (5)
C(6)	6161 (4)	4760 (3)	4699 (5)
C(7)	6460 (4)	5528 (4)	4076 (6)
C(8)	6530 (4)	5530 (4)	2786 (6)
C(9)	6264 (4)	4772 (4)	2105 (6)
H(O1)	615 (5)	430 (4)	627 (7)
H(O2)	697 (5)	662 (4)	435 (6)
H(Na)	389 (5)	414 (4)	305 (6)
H(Nb)	311 (5)	349 (4)	254 (5)
H(C1a)	326 (5)	469 (4)	120 (6)
H(C1b)	353 (5)	391 (4)	52 (6)
H(C1c)	423 (5)	471 (4)	116 (6)
H(C2a)	419 (4)	247 (4)	160 (6)
H(C2b)	442 (4)	266 (4)	318 (6)
H(C3)	549 (4)	338 (4)	103 (6)
H(C5)	559 (4)	350 (4)	451 (5)
H(C8)	682 (4)	608 (4)	229 (6)
H(C9)	630 (4)	482 (4)	117 (7)
H(O6)	721 (4)	280 (4)	561 (5)

* Not refined, O(6) in special position.

Discussion. Bond lengths and angles (Fig. 1) are consistent with known values. Molecules are tightly bound in the lattice by nine hydrogen-bonding interactions (Fig. 1). Of the five non-water oxygens, only O(4) is not hydrogen bonded. Two molecules of the same configuration form head [O(3)] to tail [O(2)–H(O2)] hydrogen-bonded dimers approximately in the

S–C(3)–C(4) = 113 7(4)
C(2)–C(3)–H(C3) = 105
H(C2b)–C(2)–N = 103
C(3)–C(2)–H(C2a) = 110
C(2)–N–H(Na) = 116
C(1)–N–H(Nb) = 107
N–C(1)–H(C1c) = 112

H(C1a)–C(1)–H(C1b) = 102
C(3)–S–O(3) = 105 4(2)
O(5)–S–O(4) = 113 7(2)

N–C(2)–C(3)–C(4) = −49 9(7)
C(2)–C(3)–C(4)–C(9) = 125 8(5)
S–C(3)–C(4)–C(9) = −111 8(5)

Fig. 1. Bond lengths and angles, torsion angles and intra- and intermolecular hydrogen-bonding distances and angles (Å and degrees). Estimated standard deviations (except for hydrogen, of 0·09 Å and 5°) in the last figures are given in parentheses.
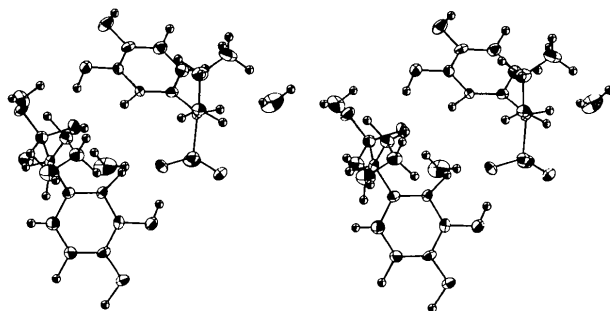
Fig. 2. Stereoprojection down the *x* axis. Atoms are represented by thermal ellipsoids including 50% probability.

yz plane (Fig. 2). Additionally, the water H atoms form two hydrogen bonds by bridging both O(3) atoms of the dimer, and a centrosymmetrically related dimer immediately below the first completes the engagement of water by Coulombic attractions to C(1) and C(2) (Ruble, Hite & Soares, 1976, and previous papers in this series). These features are consistent with the high density and high melting point of this compound.

Several interesting conformational features are present in the molecule when compared to other catecholamines. For one, the protonated nitrogen and the sulfonate are nearly antiperiplanar ($\tau = -176°$), despite the potential for facile intramolecular hydrogen-bonding interaction. Moreover, the conformational characteristics of the ethylammonium side chain in (2) are in many respects more nearly comparable to those of the amino acid precursors of the catecholamines than to those of the catecholamine salts themselves. This is perhaps not unexpected, since (2) is itself an amino acid, albeit of a different type. For all the catecholamine salts reported to date, the ammonium and phenyl substituents on the ethyl chain are essentially antiperiplanar, with τ_2 [C(4)—C(3)—C(2)—N] ranging from 163 to 179° (Carlström, Bergin & Falkenberg, 1973; Giesecke, 1976; Paxton & Hamor, 1977). On the other hand, selected precursors such as phenylalanine.HCl and L-dopa have τ_2 values of −62 and −63° respectively. Epinine β-sulfonate, with $\tau_2 = -49·9°$, is thus

conformationally much closer to these molecules than to the other catecholamines. The existence of both the nitrogen—phenyl synclinal relationship and the nitrogen—sulfonate antiperiplanar relationship makes (2) unique among this class of compounds. The steric interactions that result in this conformation are presumably higher in energy than those occurring in the more commonly encountered fully extended conformations, but these are apparently offset by the high stabilization resulting from the extensive intermolecular hydrogen bonding within the crystal lattice. The conformation of the molecule in solution is currently under investigation.

References

BUSING, W. R., MARTIN, K. O. & LEVY, H. A. (1962). *ORFLS*. Report ORNL-TM-305. Oak Ridge National Laboratory, Tennessee.

CARLSTRÖM, D., BERGIN, R. & FALKENBERG, G. (1973). *Q. Rev. Biophys.* **6**, 257–310.

COHEN, L. A. & JONES, W. M. (1960). *J. Am. Chem. Soc.* **82**, 1907–1911.

DECLERCQ, J. P., GERMAIN, G. & WOOLFSON, M. M. (1975). *Acta Cryst.* A**31**, 367–372.

GIESECKE, J. (1976). *Acta Cryst.* B**32**, 2337–2340.

HAJRATWALA, B. R. (1975). *J. Pharm. Sci.* **64**, 45–48.

HIGUCHI, T. & SCHROETER, L. C. (1959). *J. Am. Pharm. Assoc. Sci. Ed.* **48**, 535–540.

KAWAZU, M., INOUE, H., TOMINO, K. & IWAO, J. (1973). *J. Heterocycl. Chem.* **10**, 1059–1061.

PAXTON, K. & HAMOR, T. A. (1977). *Acta Cryst.* B**33**, 2143–2146.

RUBLE, J. R., HITE, G. & SOARES, J. R. (1976). *Acta Cryst.* B**32**, 136–140.

SCHROETER, L. C., HIGUCHI, T. & SCHULER, E. E. (1958). *J. Am. Pharm. Assoc. Sci. Ed.* **47**, 723–728.