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(–)-(1*R*,5*R*,9*R*)-2′-Hydroxy-2-methoxyethyl-5,9-dimethyl-6,7-benzomorphan Hydrobromide Monohydrate*†

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Abstract. $C_{17}H_{26}NO_2^+.Br^-.H_2O$, $M_r = 374{\cdot}317$, orthorhombic, $P2_12_12_1$, $a = 8{\cdot}7820\ (4)$, $b = 14{\cdot}3800\ (9)$, $c = 14{\cdot}6860\ (4)$ Å (refinement on θ only), $V = 1854{\cdot}6\ (2)$ Å^3, $Z = 4$, $D_m = 1{\cdot}34\ (2)$, $D_x = 1{\cdot}341$ Mg m^{-3}, $\lambda(\text{Cu } K\alpha) = 1{\cdot}54178$ Å, $\mu(\text{Cu } K\alpha) = 3{\cdot}12$ mm^{-1}, $F(000) = 784$, 291 K, final $R = 0{\cdot}036$ for 2963 observed reflections. The *N*-side-chain torsion angles starting from the asymmetric carbon towards the terminal methyl group are about the global energy minimum in the three-dimensional torsional space: (–)-synclinal, (+)-synclinal and antiperiplanar respectively. An intramolecular (C–)H···O hydrogen bond is present.

Introduction. As part of a structure–activity study on 6,7-benzomorphans the structure of the title compound was determined. On the basis of *in vivo* pharmacological studies in mice it was classified as a morphine-like agonist (Merz & Stockhaus, 1979). The main purpose of this study lies in determining the conformation of the *N*-side chain which is believed to be essential for opioid kappa activity (De Ranter, Verlinde, Blaton & Peeters, 1984). The title compound displays only a marginal partial agonism in the rabbit vas deferens assay (Verlinde & De Ranter, 1988), a preparation containing exclusively the kappa receptor type.

Experimental. Crystals obtained at room temperature from an equimolar ethyl acetate–methanol solution. Density measured by flotation in *n*-heptane/CCl_4, $\sim 0{\cdot}3 \times 0{\cdot}2 \times 0{\cdot}1$ mm, Hilger & Watts computer-controlled four-circle diffractometer, Ni-filtered Cu $K\alpha$ radiation, $\omega/2\theta$ scan technique ($2\theta_{max} = 140°$, $0 \le h \le 11$, $0 \le k \le 18$, $-18 \le l \le 18$), cell dimensions by least-squares refinement of the θ values of 25 reflections with $41 < 2\theta < 50°$, space group $P2_12_12_1$ from systematic absences $h00$ for h odd, $0k0$ for k odd, $00l$ for l odd respectively. Four standard reflections (200, 006, 080, 279) monitored after each 50 reflections deviated from their initial intensity at most by 4%. 3331 independent reflections measured (Friedel's law not obeyed), 2963 observed reflections [with $I > 3\sigma(I)$], Lorentz–polarization corrections, absorption corrections by the method of North, Phillips & Mathews (1968) with values between 0·999 and 0·865, scattering factors from Cromer & Mann (1968), and Stewart, Davidson & Simpson (1965) (for H), anomalous-dispersion correction for Br (*International Tables for X-ray Crystallography*, 1974).

The position of the Br was revealed through a Patterson synthesis and served as input for *DIRDIF* (Beurskens *et al.*, 1981). The resulting *E* map showed the complete molecule, including the water molecule. Refinement with *XRAY*76 (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976) by block-diagonal least squares on *F*, first with isotropic temperature factors and then anisotropically; full-matrix least squares finally executed. H positions from ΔF synthesis included in refinement with fixed isotropic temperature factors of the atoms to which they are attached; final $R = 0{\cdot}036$, $wR = 0{\cdot}047$ and $S = 0{\cdot}06$, $w = (100 + |F_o| + 0{\cdot}1|F_o|^2 + 0{\cdot}005|F_o|^3)^{-1}$; $(\Delta/\sigma)_{ave} = 0{\cdot}2$, $(\Delta/\sigma)_{max} = 1{\cdot}5$, $-0{\cdot}41 \le$ final $\Delta\rho$ excursions $\le 0{\cdot}41$ e Å^{-3}.

Discussion. The atomic numbering scheme is given in Fig. 1 and parameters are listed in Table 1.§ Bond lengths and angles are given in Table 2. *ORTEP* stereopairs (Johnson, 1965) are shown in Fig. 2. A planar aromatic ring connected to a six-membered ring in the half-boat conformation is perpendicular to a piperidine in the chair conformation. The absolute configuration of the three asymmetric carbon atoms was confirmed through comparison of the 24 most

* *Chemical Abstracts* name: (–)-(2*R*,6*R*,11*R*)-1,2,3,4,5,6-hexahydro-3-methoxyethyl-6,11-dimethyl-2,6-methano-3-benzazocin-8-ol hydrobromide monohydrate.

† Structural Studies of Substituted 6,7-Benzomorphan Compounds. X. Part IX: Verlinde, Blaton, Peeters & De Ranter (1988).

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§ Lists of structure factors, anisotropic thermal parameters, H-atom parameters, least-squares-planes data and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51136 (23 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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significant Bijvoet pairs. These were retained according to a selection procedure by Beurskens, Noordik & Beurskens (1980) with $N = 3$ and $N' = 6$. The Bijvoet coefficient proved to be exactly 1·0000. Considering the three torsion angles in the *N*-side chain starting from C(1) towards C(15) its conformation is essentially (−)-synclinal [−59·7 (4)]/(+)-synclinal [81·0 (4)]/antiperiplanar [−178·4 (4)°]. In order to evaluate the influence of packing effects on this conformation a potential-energy grid search of the three-dimensional torsional space of the isolated molecule was executed. For that purpose use was made of the program *EENY* (Motherwell, 1974) which calculates non-bonded van der Waals interactions, with parameters by Giglio (1969). The (−)-synclinal/antiperiplanar/(−)-synclinal conformation appears as the global energy minimum with the crystal structure conformation some 3·8 kJ mol^{-1} above it. However, the intramolecular (C−)H···O hydrogen bond in the crystal structure [C(1)···O(14) 3·038 (5), H(1)···O(14) 2·41 (4) Å, C(1)−H(1)···O(14) 118 (3)°] is not taken into account with this type of calculation. This hydrogen bond is in agreement with its description by Taylor & Kennard (1982): a nearest-neighbour contact of 0·21 Å, and the immediate adjacency of a positively charged N to the proton donor.

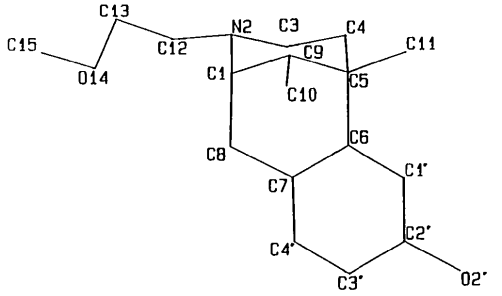

Fig. 1. Atomic numbering scheme.

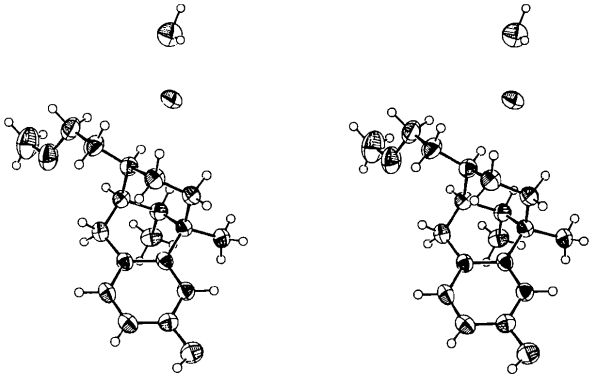

Fig. 2. Stereoscopic view of the title compound with 50% probability anisotropic displacement ellipsoids for the non-hydrogen atoms.

Table 1. *Atomic coordinates and equivalent isotropic thermal parameters with e.s.d.'s of the refined parameters in parentheses*

$B_{eq} = \frac{4}{3}\sum_i\sum_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	*y*	*z*	B_{eq}(Å^2)
Br	1·01103 (5)	0·32437 (3)	0·38525 (3)	4·79 (1)
C(1′)	0·3092 (4)	0·5653 (2)	0·2912 (2)	3·36 (8)
C(2′)	0·2307 (4)	0·6204 (2)	0·2299 (2)	3·52 (8)
O(2′)	0·1146 (3)	0·6745 (2)	0·2628 (1)	4·73 (7)
C(3′)	0·2666 (4)	0·6167 (2)	0·1379 (2)	3·89 (9)
C(4′)	0·3818 (4)	0·5590 (2)	0·1092 (2)	3·73 (8)
C(1)	0·6795 (4)	0·3886 (2)	0·2035 (2)	3·38 (8)
N(2)	0·8154 (3)	0·4447 (1)	0·2370 (1)	3·43 (7)
C(3)	0·7671 (4)	0·5335 (2)	0·2836 (2)	3·99 (9)
C(4)	0·6594 (4)	0·5109 (2)	0·3607 (2)	3·91 (9)
C(5)	0·5204 (4)	0·4520 (2)	0·3317 (2)	3·40 (7)
C(6)	0·4270 (3)	0·5074 (2)	0·2630 (2)	3·09 (7)
C(7)	0·4636 (3)	0·5033 (2)	0·1698 (2)	3·12 (7)
C(8)	0·5873 (4)	0·4414 (2)	0·1325 (2)	3·70 (8)
C(9)	0·5815 (4)	0·3624 (2)	0·2870 (2)	3·42 (8)
C(10)	0·4581 (4)	0·2933 (2)	0·2586 (2)	4·32 (9)
C(11)	0·4288 (4)	0·4270 (3)	0·4175 (2)	4·51 (10)
C(12)	0·9354 (4)	0·4652 (3)	0·1665 (2)	4·55 (10)
C(13)	1·0070 (5)	0·3805 (2)	0·1242 (2)	5·08 (10)
O(14)	0·9103 (4)	0·3459 (2)	0·0551 (2)	5·94 (9)
C(15)	0·9695 (9)	0·2641 (4)	0·0139 (3)	8·26 (21)
O(16)	1·2517 (4)	0·1483 (2)	0·4370 (2)	6·51 (10)

Table 2. *Bond lengths* (Å) *and bond angles* (°)

C(1′)–C(2′)	1·383 (4)	C(3)–C(4)	1·511 (5)
C(1′)–C(6)	1·392 (4)	C(4)–C(5)	1·545 (5)
C(2′)–O(2′)	1·371 (4)	C(5)–C(6)	1·526 (4)
C(2′)–C(3′)	1·388 (5)	C(5)–C(9)	1·542 (4)
C(3′)–C(4′)	1·374 (5)	C(5)–C(11)	1·538 (4)
C(4′)–C(7)	1·398 (4)	C(6)–C(7)	1·406 (4)
C(1)–N(2)	1·523 (4)	C(7)–C(8)	1·508 (4)
C(1)–C(8)	1·524 (4)	C(9)–C(10)	1·529 (5)
C(1)–C(9)	1·545 (4)	C(12)–C(13)	1·505 (6)
N(2)–C(3)	1·510 (4)	C(13)–O(14)	1·414 (5)
N(2)–C(12)	1·506 (5)	O(14)–C(15)	1·422 (7)

C(2′)–C(1′)–C(6)	121·3 (3)	C(6)–C(5)–C(9)	110·0 (2)
C(1′)–C(2′)–O(2′)	117·8 (3)	C(6)–C(5)–C(11)	112·5 (3)
C(1′)–C(2′)–C(3′)	119·9 (3)	C(9)–C(5)–C(11)	109·6 (2)
O(2′)–C(2′)–C(3′)	122·2 (3)	C(1′)–C(6)–C(5)	121·0 (2)
C(2′)–C(3′)–C(4′)	119·3 (3)	C(1′)–C(6)–C(7)	119·0 (2)
C(3′)–C(4′)–C(7)	121·9 (3)	C(5)–C(6)–C(7)	119·9 (2)
N(2)–C(1)–C(8)	111·9 (2)	C(4′)–C(7)–C(6)	118·6 (2)
N(2)–C(1)–C(9)	108·0 (2)	C(4′)–C(7)–C(8)	118·5 (2)
C(8)–C(1)–C(9)	111·6 (2)	C(6)–C(7)–C(8)	122·9 (2)
C(1)–N(2)–C(3)	112·0 (2)	C(1)–C(8)–C(7)	115·4 (2)
C(1)–N(2)–C(12)	115·5 (2)	C(1)–C(9)–C(5)	109·2 (2)
C(3)–N(2)–C(12)	110·0 (2)	C(1)–C(9)–C(10)	109·6 (2)
N(2)–C(3)–C(4)	109·5 (2)	C(5)–C(9)–C(10)	114·4 (3)
C(3)–C(4)–C(5)	113·9 (2)	N(2)–C(12)–C(13)	114·6 (3)
C(4)–C(5)–C(6)	108·7 (2)	C(12)–C(13)–O(14)	109·3 (3)
C(4)–C(5)–C(9)	107·5 (2)	C(13)–O(14)–C(15)	112·2 (4)
C(4)–C(5)–C(11)	108·4 (2)		

The packing of the crystal (Fig. 3) is mainly achieved by hydrogen bonds between piperidinium and bromide, and between bromide and phenol. Thus endless chains along **b** are formed while weak interactions between bromide and the water molecules provide additional packing forces between these chains [N(2)···Br 3·268 (3), H(2)···Br 2·40 (4) Å, N(2)–H(2)···Br

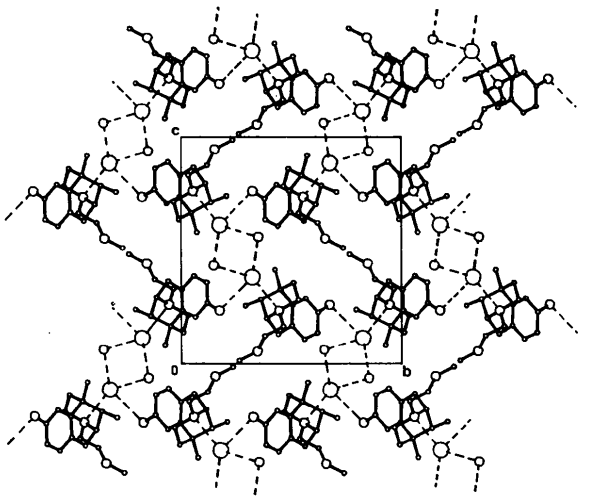

Fig. 3. A view of the crystal along a showing the packing. Hydrogen bonds are indicated by dashed lines.

171 (4)°; O(2′)···Br^{i} 3·254 (3), H(2′)···Br^{i} 2·41 (5) Å, O(2′)—H(2′)···Br^{i} 170 (4)°; O(16)···Br 3·385 (4), H(16*A*)···Br 2·85 (6) Å, O(16)—H(16*A*)···Br 131 (5)°; O(16)···Br^{ii} 3·485 (4), H(16*B*)···Br^{ii} 2·48 (7) Å, O(16)—H(16*B*)···Br^{ii} 152 (6)°; (i) $-x+1$, $y+\frac{1}{2}$, $-z+\frac{1}{2}$; (ii) $x+\frac{1}{2}$, $-y+\frac{1}{2}$, $-z+1$].

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X-ray Studies on Crystalline Complexes Involving Amino Acids and Peptides. XVI.* Structure of L-Ornithine D-Aspartate Monohydrate

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Abstract. $C_5H_{13}N_2O_2^+.C_4H_6NO_4^-.H_2O$, $M_r = 283$, monoclinic, $P2_1$, $a = 5{\cdot}118$ (1), $b = 7{\cdot}881$ (2), $c = 16{\cdot}025$ (2) Å, $\beta = 91{\cdot}78$ (2)°, $V = 646{\cdot}1$ (4) Å^3, $Z = 2$, $D_m = 1{\cdot}46$ (2), $D_x = 1{\cdot}45$ g cm^{-3}, λ(Mo $K\alpha$) = 0·7107 Å, $\mu = 1{\cdot}376$ cm^{-1}, $F(000) = 304$, final $R = 0{\cdot}055$ for 1370 observed reflections. The aggregation pattern in the present structure is entirely different from that in L-ornithine L-aspartate hemihydrate. It is similar to that in L-lysine D-aspartate monohydrate in that the unlike molecules aggregate into separate alternating layers, but is different from that in the other LD amino acid–amino acid complexes analysed so far. An interesting feature of the structure is an internal hydrogen bond between the α-amino group and one of the side-chain carboxyl O atoms in the aspartate ion. The structure contains a closed hydrogen-bonded loop made up of alternating amino and carboxylate groups.

Introduction. X-ray studies of crystalline complexes involving amino acids and peptides being carried out in

* Part XV: Soman, Suresh & Vijayan (1988).

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