The Crystal and Molecular Structure of 2-Allyl-2′-hydroxy-5,9-dimethyl-6,7-benzomorphan Hydrobromide Monohydrate

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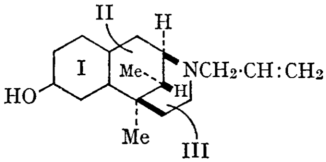
2-ALLYL-2′-HYDROXY-5,9-DIMETHYL-6,7-BENZOMORPHAN (HDAB) is a compound of the 6,7-benzomorphan series and can be considered as a hydronaphthalene containing the *cis*-fused iminoethano-system typical of morphine and 3-hydroxy-*N*-methylmorphinan. HDAB is a potent antagonist[1] of phenazocine, morphine, meperidine, and other analgæsic agents, and has a potency comparable to that of nalorphine. The crystal and molecular structure of the hydrobromide derivative of HDAB has been studied as part of our research programme on the structure and function of analgæsic compounds. This derivative was supplied by the Smith, Kline and French Laboratories (U.S.) and the crystals for single-crystal work were obtained from water by slow cooling.

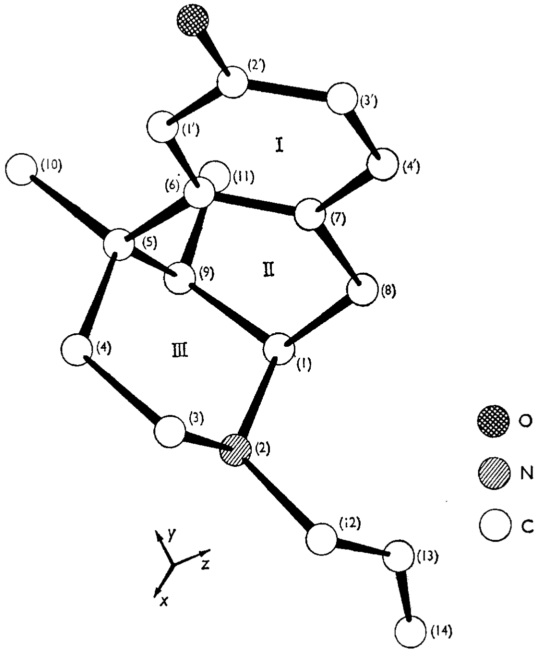
Crystals of 2-allyl-2′-hydroxy-5,9-dimethyl-6,7-benzomorphan hydrobromide monohydrate, $C_{17}H_{23}NO,HBr,H_2O$, are orthorhombic; *space group* $Pca2_1$; $a = 18{\cdot}77$, $b = 10{\cdot}95$, $c = 8{\cdot}64$ Å; $U = 1775{\cdot}79$ Å^3; D_m 1·37 g.cm.$^{-3}$ (by flotation); $Z = 4$; $D_c = 1{\cdot}33$ g.cm.$^{-3}$; $\mu = 35{\cdot}08$ cm.$^{-1}$; $F(000) = 744$. Data from Weissenberg photographs, Cu-K_α ($\lambda = 1{\cdot}5418$ Å) radiation.

The structure was solved by Patterson and Fourier methods,[2] using 1262 independent reflections. Co-ordinates and anisotropic temperature factors were refined by least-squares to the present set of values, corresponding to $R = 0{\cdot}089$ and to an average e.s.d. on bond lengths of 0·02 Å.

The HDAB molecule may be considered essentially as a three-ring segment of the morphine nucleus with the same conformation as the corresponding part of morphine. It is T-shaped and has three asymmetric carbon atoms (at 1, 5, and 9),[3] but, the iminoethano-system being geometrically constrained to a *cis*-fusion, only two enantiomorphic pairs can be constructed without an unacceptable strain. The main plane through the piperidine ring and atoms C-10 and C-11 makes an angle of ∼90° with the main plane (not including C-9) through rings I and II; the conformation about the six single bonds of ring III is staggered and the ring assumes a nearly regular chair form. The allyl group attached to the nitrogen atom, and methyl group C-11 are in equatorial positions with respect to the piperidine ring and so necessarily must be methyl group C-10.[4] The conformation about the C-1–C-8 single bond is intermediate between a staggered and an eclipsed one, and ring II thus has a conformation intermediate between that of a half-chair and a half-boat.



The hydrogen bonding scheme involves four hydrogen atoms: the hydrogen atom of the hydroxyl group at C-2′, two hydrogen atoms of the H_2O molecule and that of the quaternary nitrogen atom. The nitrogen atom has its hydrogen directed outwards towards the bromine atom with a short contact distance $N^+ \cdots Br^-$ of 3·30 Å, as found in similar cases.[5] This bond and the three intramolecular bonds of the nitrogen atom are directed towards the apices of a nearly regular tetrahedron. The water molecule connects the hydroxyl groups of two enantiomorphic molecules of HDAB by hydrogen bonding and it is also linked to the bromine atom by a third hydrogen bond. This results in the formation of a zig-zag chain of oxygen atoms parallel to the *z*-axis, and the molecules of HDAB are packed between this chain and that derived from it by the axial glide plane *a*. There is an almost planar distribution of the three hydrogen bonds around the hydroxyl groups, the water molecule, and the bromine atom.



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[1] M. Gordon, J. J. Lafferty, D. H. Tedeschi, N. B. Eddy, and E. L. May, *Nature*, 1961, **192**, 1089.

[2] The initial singular value of the bromine *x*, *y* co-ordinates (0·125, 0·000) and the arbitrary choice of the origin along the *c*-axis (chosen as the midpoint between the two bromine atoms related by the twofold screw axis) inevitably result in two perpendicular pseudo-mirror planes passing through the same atom, with superposition of the four mirror images of the molecule, in the electron density synthesis computed with bromine phases alone.

[3] Here we use the standard numbering of the positions in the 6,7-benzomorphan series, which is different from that of morphine and morphinan, and also from the crystallographic usage insofar as primed numerals do not indicate a symmetry relationship.

[4] The two optical isomers forming the enantiomorphic pair found in this crystal structure are related by a glide plane. This enantiomorphic pair corresponds to the α-diastereoisomers as defined in N. B. Eddy and E. L. May in "Synthetic Analgesics—Part IIB; 6,7-Benzomorphans", Pergamon Press, Oxford, 1966, p. 126.

[5] J. H. Robertson and C. A. Beevers, *Acta Cryst.*, 1951, **4**, 270; J. Trommel and J. M. Bijvoet, *ibid.*, 1954, **7**, 703; G. A. Sim, *ibid.*, 1955, **8**, 833; G. Kartha, F. R. Ahmed, and W. H. Barnes, *ibid.*, 1961, **14**, 93; M. Brufani, D. Duranti, G. Giacomello, and L. Zambonelli, *Gazzetta*, 1961, **91**, 754; F. R. Ahmed, W. H. Barnes, and L. Di Marco Masironi, *Acta Cryst.*, 1963, **16**, 237.