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# 2′-Hydroxy-5,9-dimethyl-2-(3-methyl-2-butenyl)-6,7-benzomorphan (Pentazocine) Hydrochloride Hydrate

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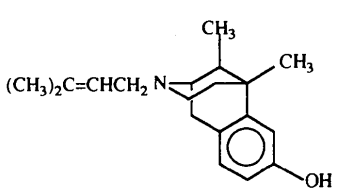
## Abstract

The title compound [1,2,3,4,5,6-hexahydro-6,11-dimethyl-3-(3-methyl-2-butenyl)-2,6-methano-3-benzazocin-8-ol hydrochloride hydrate, $C_{19}H_{28}NO^+.Cl^-.\frac{1}{8}H_2O$, (I)] crystallizes with two molecules per asymmetric unit. A comparison of the bond lengths and torsion angles shows a side-chain orientation similar to that of cyclazocine but unlike that of naloxone. The two molecules are linked through a hydrogen-bond network to the interlayer Cl ions, forming a linear chain extending along the *ac* diagonal of the unit cell.

## Comment

The structure determination of pentazocine hydrochloride (I) was undertaken as part of a larger study designed to map the $\mu$-opioid receptor using the X-ray structures of active molecules. The structure of pentazocine is of interest because it is an opioid known to exhibit mixed agonist–antagonist activity. It has been suggested that this mixed activity might be due to there being two different orientations of the nitrogen side chain, so that at any given time some molecules are in the agonist form and some are not. In this study we were interested in comparing the solid-state structure of the molecule with those of analogs active at the same receptor.




(I)

An *ORTEP*II (Johnson, 1976) view of the two molecular conformations together with the atomic labeling scheme is given in Fig. 1. The unit-cell packing is displayed in Fig. 2. Pentazocine exists as a racemate, presumably of both active and inactive isomers (Archer, Albertson, Harris, Pierson & Bird,

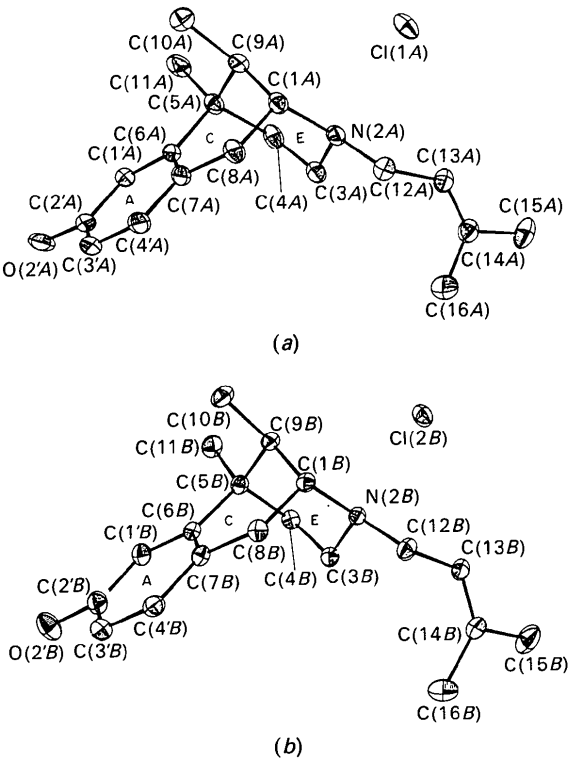



Fig. 1. Perspective view of the two unique pentazocine hydrochloride molecules with non-H atoms represented by 50% probability ellipsoids.

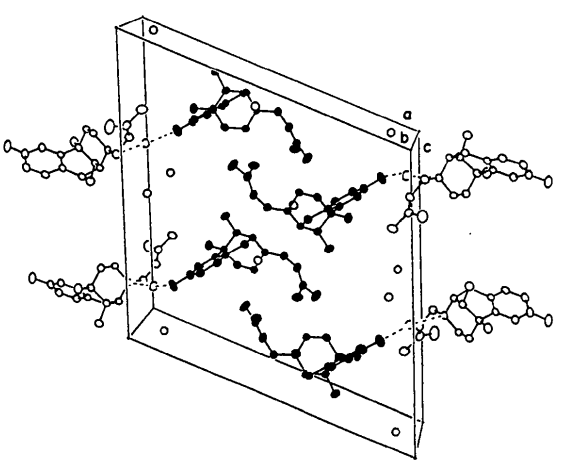



Fig. 2. Packing diagram for pentazocine hydrochloride. Broken lines show the hydrogen-bond interactions between the Cl ion and the N atom. The atoms of molecule *A* are depicted by filled ellipsoids, those of molecule *B* by open ellipsoids.

1964). It has not been established which isomer is pharmacologically active. Each molecule in the cell is hydrogen bonded to an interlayer chloride ion through the H atom on the quaternary N atom. The chloride ion connects molecule *A* to molecule *B* through hydrogen bonding to the hydroxyl O atom.

The hydrogen-bond scheme from the quaternary N atom of molecule *A* through the Cl ion *A* to the hydroxyl O atom of molecule *B* is verified by the distances $N^+\cdots Cl^-$ 3.103 (3) and $Cl\cdots O$ 3.105 (3) Å and the angle $N^+\cdots Cl^-\cdots O$ 168.80 (8)°. This linkage forms a segment of the linear chain that extends along the *ac* diagonal of the unit cell. The other segment that completes this linkage is formed from molecule *B* through the chloride ion *B* to the proton bonded to the hydroxyl O atom of molecule *A* [$N^+\cdots Cl^-$ 3.091 (2), $Cl^-\cdots O$ 3.023 (2) Å, $N^+\cdots Cl^-\cdots O$ 145.93 (7)°].

Pentazocine has four sites for water molecules in the unit cell. Each site has been determined to have a partial occupancy equivalent to 0.25. These water molecules do not appear to be involved in the overall hydrogen-bonding scheme. The closest contact for the O atom of a water molecule to any atom in the pentazocine molecule is 3.159 (8) Å [O*W*···O(2′*B*)] and the closest water-to-chlorine contact is 3.683 (9) Å [O*W*···Cl(1*A*)]. Taking into account the fact that the water molecule is not tightly bound to the links of the linear chain helps to explain the partial occupancy of the four sites.

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å²)

$B_{eq} = (4/3)\Sigma_i\Sigma_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j.$

| | *x* | *y* | *z* | $B_{eq}$ |
|---|---|---|---|---|
| Cl(1*A*) | −0.02176 (6) | 0.6969 (2) | 0.39731 (6) | 5.64 (3) |
| O(2′*A*) | 0.4617 (1) | 0.4689 (3) | 0.5795 (2) | 5.55 (8) |
| C(1′*A*) | 0.3449 (2) | 0.5470 (4) | 0.5442 (2) | 3.66 (9) |
| C(2′*A*) | 0.3958 (2) | 0.4463 (4) | 0.5781 (2) | 3.95 (9) |
| C(3′*A*) | 0.3791 (2) | 0.3310 (4) | 0.6100 (2) | 4.1 (1) |
| C(4′*A*) | 0.3110 (2) | 0.3160 (4) | 0.6059 (2) | 3.88 (9) |
| C(1*A*) | 0.1304 (2) | 0.5022 (5) | 0.5265 (2) | 3.63 (9) |
| N(2*A*) | 0.0942 (1) | 0.4624 (4) | 0.4502 (1) | 3.57 (7) |
| C(3*A*) | 0.1444 (2) | 0.4601 (5) | 0.4147 (2) | 4.06 (9) |
| C(4*A*) | 0.1832 (2) | 0.6001 (5) | 0.4250 (2) | 4.3 (1) |
| C(5*A*) | 0.2202 (2) | 0.6450 (4) | 0.5022 (2) | 3.66 (9) |
| C(6*A*) | 0.2764 (2) | 0.5343 (4) | 0.5409 (2) | 3.26 (8) |
| C(7*A*) | 0.2586 (2) | 0.4156 (4) | 0.5712 (2) | 3.36 (8) |
| C(8*A*) | 0.1852 (2) | 0.3921 (5) | 0.5690 (2) | 3.95 (9) |
| C(9*A*) | 0.1628 (2) | 0.6495 (4) | 0.5319 (2) | 3.79 (9) |
| C(10*A*) | 0.1883 (2) | 0.7059 (5) | 0.6063 (2) | 5.3 (1) |
| C(11*A*) | 0.2512 (2) | 0.7946 (5) | 0.5044 (2) | 5.2 (1) |
| C(12*A*) | 0.0506 (2) | 0.3276 (5) | 0.4382 (2) | 4.6 (1) |
| C(13*A*) | 0.0006 (2) | 0.3161 (5) | 0.3635 (2) | 4.8 (1) |
| C(14*A*) | −0.0010 (2) | 0.2154 (6) | 0.3200 (2) | 5.4 (1) |
| C(15*A*) | −0.0575 (3) | 0.2157 (7) | 0.2464 (2) | 7.5 (1) |
| C(16*A*) | 0.0476 (3) | 0.0934 (8) | 0.3365 (4) | 10.0 (2) |
| Cl(2*B*) | 0.54807 (5) | 0.2019 (1) | 0.59008 (5) | 4.41 (2) |
| O(2′*B*) | 0.1177 (2) | 0.4603 (3) | 0.1664 (2) | 5.86 (9) |
| C(1′*B*) | 0.1964 (2) | 0.2864 (4) | 0.2438 (2) | 3.51 (8) |
| C(2′*B*) | 0.1789 (2) | 0.4264 (5) | 0.2222 (2) | 4.00 (9) |
| C(3′*B*) | 0.2239 (2) | 0.5367 (4) | 0.2565 (2) | 3.91 (9) |
| C(4′*B*) | 0.2863 (2) | 0.5057 (4) | 0.3120 (2) | 3.40 (8) |
| C(1*B*) | 0.3944 (2) | 0.1832 (4) | 0.4136 (2) | 2.96 (7) |
| N(2*B*) | 0.4347 (1) | 0.1201 (3) | 0.3733 (1) | 2.78 (6) |
| C(3*B*) | 0.3927 (2) | 0.1241 (4) | 0.2965 (2) | 3.00 (7) |
| C(4*B*) | 0.3242 (2) | 0.0450 (4) | 0.2797 (2) | 3.12 (8) |
| C(5*B*) | 0.2810 (2) | 0.0996 (4) | 0.3200 (2) | 3.01 (8) |
| C(6*B*) | 0.2596 (2) | 0.2544 (4) | 0.2993 (2) | 2.89 (7) |
| C(7*B*) | 0.3057 (2) | 0.3652 (4) | 0.3339 (2) | 2.92 (7) |
| C(8*B*) | 0.3749 (2) | 0.3399 (4) | 0.3956 (2) | 3.30 (8) |
| C(9*B*) | 0.3291 (2) | 0.0911 (4) | 0.3986 (2) | 3.14 (8) |
| C(10*B*) | 0.2926 (2) | 0.1377 (5) | 0.4464 (2) | 4.31 (9) |
| C(11*B*) | 0.2178 (2) | −0.0011 (5) | 0.3031 (2) | 4.3 (1) |
| C(12*B*) | 0.5077 (2) | 0.1846 (4) | 0.3944 (2) | 3.59 (8) |
| C(13*B*) | 0.5502 (2) | 0.1023 (4) | 0.3636 (2) | 3.82 (9) |
| C(14*B*) | 0.5727 (2) | 0.1491 (5) | 0.3165 (2) | 3.92 (9) |
| C(15*B*) | 0.6157 (2) | 0.0556 (6) | 0.2900 (3) | 6.6 (1) |
| C(16*B*) | 0.5591 (2) | 0.2968 (5) | 0.2849 (2) | 5.5 (1) |
| O*W* | 0.9161 (6) | 0.491 (1) | −0.0065 (5) | 4.5 (3) |

Table 2. *Selected geometric parameters* (Å, °)

| | | | |
|---|---|---|---|
| O(2′*A*)—C(2′*A*) | 1.364 (4) | C(14*A*)—C(16*A*) | 1.466 (6) |
| C(1′*A*)—C(2′*A*) | 1.377 (4) | O(2′*B*)—C(2′*B*) | 1.369 (4) |
| C(1′*A*)—C(6*A*) | 1.391 (4) | C(1′*B*)—C(2′*B*) | 1.384 (4) |
| C(2′*A*)—C(3′*A*) | 1.381 (5) | C(1′*B*)—C(6*B*) | 1.389 (4) |
| C(3′*A*)—C(4′*A*) | 1.380 (4) | C(2′*B*)—C(3′*B*) | 1.381 (4) |
| C(4′*A*)—C(7*A*) | 1.392 (5) | C(3′*B*)—C(4′*B*) | 1.376 (4) |
| C(1*A*)—N(2*A*) | 1.511 (4) | C(4′*B*)—C(7*B*) | 1.396 (5) |
| C(1*A*)—C(8*A*) | 1.526 (4) | C(1*B*)—N(2*B*) | 1.519 (3) |
| C(1*A*)—C(9*A*) | 1.515 (5) | C(1*B*)—C(8*B*) | 1.525 (5) |
| N(2*A*)—C(3*A*) | 1.497 (4) | C(1*B*)—C(9*B*) | 1.522 (4) |
| N(2*A*)—C(12*A*) | 1.509 (4) | N(2*B*)—C(3*B*) | 1.489 (3) |
| C(3*A*)—C(4*A*) | 1.503 (5) | N(2*B*)—C(12*B*) | 1.515 (3) |
| C(4*A*)—C(5*A*) | 1.542 (4) | C(3*B*)—C(4*B*) | 1.508 (4) |
| C(5*A*)—C(6*A*) | 1.523 (4) | C(4*B*)—C(5*B*) | 1.536 (4) |
| C(5*A*)—C(9*A*) | 1.542 (4) | C(5*B*)—C(6*B*) | 1.524 (4) |
| C(14*B*)—C(16*B*) | 1.508 (5) | C(5*B*)—C(9*B*) | 1.544 (4) |
| C(5*A*)—C(11*A*) | 1.530 (5) | C(5*B*)—C(11*B*) | 1.531 (5) |
| C(6*A*)—C(7*A*) | 1.398 (4) | C(6*B*)—C(7*B*) | 1.397 (4) |
| C(7*A*)—C(8*A*) | 1.510 (4) | C(7*B*)—C(8*B*) | 1.512 (4) |
| C(9*A*)—C(10*A*) | 1.521 (4) | C(9*B*)—C(10*B*) | 1.533 (4) |
| C(12*A*)—C(13*A*) | 1.490 (4) | C(12*B*)—C(13*B*) | 1.491 (4) |
| C(13*A*)—C(14*A*) | 1.300 (5) | C(13*B*)—C(14*B*) | 1.320 (4) |
| C(14*A*)—C(15*A*) | 1.512 (5) | C(14*B*)—C(15*B*) | 1.499 (5) |
| C(1*A*)—N(2*A*)—C(3*A*) | 112.2 (2) | C(3′*A*)—C(4′*A*)—C(7*A*) | 121.6 (4) |
| C(1*A*)—N(2*A*)—C(12*A*) | 113.2 (2) | C(1*B*)—N(2*B*)—C(3*B*) | 112.1 (3) |
| C(3*A*)—N(2*A*)—C(12*A*) | 112.9 (3) | C(1*B*)—N(2*B*)—C(12*B*) | 112.6 (2) |
| N(2*A*)—C(1*A*)—C(8*A*) | 112.8 (3) | C(3*B*)—N(2*B*)—C(12*B*) | 112.7 (2) |
| N(2*A*)—C(1*A*)—C(9*A*) | 108.7 (2) | N(2*B*)—C(1*B*)—C(8*B*) | 112.6 (2) |
| C(8*A*)—C(1*A*)—C(9*A*) | 111.7 (3) | N(2*B*)—C(1*B*)—C(9*B*) | 107.6 (2) |
| N(2*A*)—C(3*A*)—C(4*A*) | 110.5 (3) | C(8*B*)—C(1*B*)—C(9*B*) | 111.6 (2) |
| C(3*A*)—C(4*A*)—C(5*A*) | 113.5 (3) | N(2*B*)—C(3*B*)—C(4*B*) | 109.1 (2) |
| C(4*A*)—C(5*A*)—C(6*A*) | 108.9 (3) | C(3*B*)—C(4*B*)—C(5*B*) | 113.8 (2) |
| C(4*A*)—C(5*A*)—C(9*A*) | 106.9 (2) | C(4*B*)—C(5*B*)—C(6*B*) | 109.0 (2) |
| C(4*A*)—C(5*A*)—C(11*A*) | 107.8 (3) | C(4*B*)—C(5*B*)—C(9*B*) | 107.4 (2) |
| C(6*A*)—C(5*A*)—C(9*A*) | 110.4 (2) | C(4*B*)—C(5*B*)—C(11*B*) | 107.1 (2) |
| C(6*A*)—C(5*A*)—C(11*A*) | 112.6 (3) | C(6*B*)—C(5*B*)—C(11*B*) | 113.4 (2) |
| C(9*A*)—C(5*A*)—C11*A*) | 110.0 (3) | C(1′*B*)—C(6*B*)—C(5*B*) | 120.7 (3) |
| C(1′*A*)—C(6*A*)—C(5*A*) | 120.7 (3) | C(1′*B*)—C(6*B*)—C(7*B*) | 119.4 (3) |
| C(1′*A*)—C(6*A*)—C7*A*) | 119.4 (3) | C(5*B*)—C(6*B*)—C(7*B*) | 119.9 (2) |
| C(5*A*)—C(6*A*)—C(7*A*) | 119.9 (3) | C(4′*B*)—C(7*B*)—C(6*B*) | 118.8 (3) |
| C(4′*A*)—C(7*A*)—C(6*A*) | 118.6 (3) | C(4′*B*)—C(7*B*)—C(8*B*) | 118.4 (3) |
| C(4′*A*)—C(7*A*)—C(8*A*) | 118.6 (3) | C(6*B*)—C(7*B*)—C(8*B*) | 122.7 (3) |
| C(6*A*)—C(7*A*)—C(8*A*) | 122.8 (3) | C(1*B*)—C(8*B*)—C(7*B*) | 115.2 (2) |
| C(1*A*)—C(8*A*)—C(7*A*) | 114.8 (3) | C(1*B*)—C(9*B*)—C(5*B*) | 109.3 (2) |
| C(1*A*)—C(9*A*)—C(5*A*) | 109.3 (3) | C(1*B*)—C(9*B*)—C(10*B*) | 109.2 (2) |
| C(1*A*)—C(9*A*)—C(10*A*) | 110.8 (3) | C(5*B*)—C(9*B*)—C(10*B*) | 113.8 (2) |
| C(5*A*)—C(9*A*)—C(10*A*) | 114.4 (3) | N(2*B*)—C(12*B*)—C(13*B*) | 110.8 (2) |
| N(2*A*)—C(12*A*)—C(13*A*) | 110.7 (3) | C(12*B*)—C(13*B*)—C(14*B*) | 126.4 (4) |
| C(12*A*)—C(13*A*)—C(14*A*) | 126.8 (4) | C(13*B*)—C(14*B*)—C(15*B*) | 121.2 (3) |
| C(13*A*)—C(14*A*)—C(15*A*) | 120.3 (5) | C(13*B*)—C(14*B*)—C(16*B*) | 124.8 (3) |
| C(13*A*)—C(14*A*)—C(16*A*) | 125.0 (4) | C(15*B*)—C(14*B*)—C(16*B*) | 114.1 (4) |
| C(15*A*)—C(14*A*)—C(16*A*) | 114.7 (4) | C(2′*B*)—C(1′*B*)—C(6*B*) | 120.8 (3) |
| C(2′*A*)—C(1′*A*)—C(6*A*) | 121.1 (4) | C(1′*B*)—C(2′*B*)—C(3′*B*) | 120.2 (3) |
| C(1′*A*)—C(2′*A*)—C(3′*A*) | 119.8 (3) | C(1′*B*)—C(2′*B*)—O(2′*B*) | 121.9 (3) |
| C(1′*A*)—C(2′*A*)—O(2′*A*) | 117.0 (4) | C(3′*B*)—C(2′*B*)—O(2′*B*) | 117.9 (3) |
| C(3′*A*)—C(2′*A*)—O(2′*A*) | 123.2 (3) | C(2′*B*)—C(3′*B*)—C(4′*B*) | 119.3 (3) |
| C(2′*A*)—C(3′*A*)—C(4′*A*) | 119.5 (3) | C(3′*B*)—C(4′*B*)—C(7*B*) | 121.6 (3) |

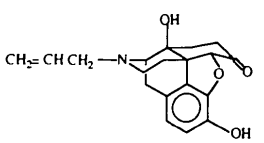
Table 3. *Torsion Angles* (°) *in Pentazocine and Related Compounds*

| | Pentazocine HCl.$\frac{1}{8}H_2O$ Molecule *A* | Pentazocine HCl.$\frac{1}{8}H_2O$ Molecule *B* | Naloxone HCl.2$H_2O$ | Cyclazocine HBr.$H_2O$ | Gemazocine HBr | NCBME* HBr |
|---|---|---|---|---|---|---|
| Ring *A* | | | | | | |
| C(7)—C(6)—C(1′)—C(2′) | 1.4 (5) | −0.5 (5) | −6.7 | 0.7 | 0.9 | 1.4 |
| C(6)—C(1′)—C(2′)—C(3′) | 0.5 (6) | 1.1 (6) | 4.3 | −0.9 | 2.7 | 1.2 |
| C(1′)—C(2′)—C(3′)—C(4′) | −1.8 (6) | −0.5 (6) | −0.9 | −0.6 | −3.9 | −1.6 |
| C(2′)—C(3′)—C(4′)—C(7′) | 1.1 (6) | −0.6 (6) | −0.8 | 2.3 | 1.6 | −0.5 |
| C(3′)—C(4′)—C(7)—C(6) | 0.9 (5) | 1.2 (5) | −1.1 | −2.5 | 2.0 | 3.1 |
| C(4′)—C(7)—C(6)—C(1′) | −2.1 (5) | −0.7 (5) | 4.8 | 0.9 | −3.2 | −3.5 |
| Ring *C* | | | | | | |
| C(8)—C(1)—C(9)—C(5) | −61.8 (4) | −60.9 (4) | −60.4 | −61.8 | −63.2 | −63.0 |
| C(1)—C(9)—C(5)—C(6) | 57.6 (4) | 58.9 (4) | 56.2 | 59.6 | 60.2 | 59.8 |
| C(9)—C(5)—C(6)—C(7) | −28.0 (5) | −31.3 (4) | −32.7 | −28.7 | −30.9 | −32.0 |
| C(5)—C(6)—C(7)—C(8) | 1.4 (5) | 4.6 (5) | 4.4 | −3.0 | 1.9 | 4.4 |
| C(6)—C(7)—C(8)—C(1) | −4.3 (5) | −5.2 (5) | −4.1 | 3.2 | −3.3 | −4.9 |
| C(7)—C(8)—C(1)—C(9) | 34.6 (4) | 33.5 (4) | 33.1 | 30.1 | 34.6 | 34.6 |
| Ring *E* | | | | | | |
| C(9)—C(1)—N(2)—C(3) | −59.7 (4) | −62.6 (3) | −63.3 | −63.5 | −61.9 | −62.3 |
| C(1)—N(2)—C(3)—C(4) | 54.2 (4) | 57.4 (4) | 57.2 | 57.2 | 54.5 | 55.6 |
| N(2)—C(3)—C(4)—C(5) | −53.5 (4) | −54.8 (4) | −51.7 | −56.3 | −52.0 | −53.4 |
| C(3)—C(4)—C(5)—C(9) | 56.5 (4) | 56.1 (4) | 58.2 | 58.5 | 55.0 | 54.7 |
| C(4)—C(5)—C(9)—C(1) | −60.7 (4) | −59.6 (4) | −64.4 | −60.6 | −57.0 | −56.9 |
| C(5)—C(9)—C(1)—N(2) | 63.3 (4) | 63.1 (3) | 64.8 | 64.6 | 61.7 | 61.5 |
| N side chain | | | | | | |
| C(1)—N(2)—C(12)—C(13) | −163.8 (3) | −169.7 (3) | −51.0 | −167.1 | −48.7 | −49.0 |
| C(3)—N(2)—C(12)—C(13) | 67.5 (4) | 62.4 (4) | −179.6 | 66.3 | −177.7 | −176.0 |
| N(2)—C(12)—C(13)—C(14) | −118.6 (5) | −114.3 (4) | −97.9 | −96.1 | −71.1 | −57.0 |

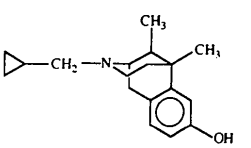
* NCBME = (−)-2-cyclobutylmethyl-5-ethyl-2′-hydroxy-9,9-dimethyl-6,7-benzomorphan.

A comparison of the torsion angles for the two forms (*A* and *B*) of pentazocine (Table 3) shows their conformations to be very similar in all regions. No torsion angle in molecule *A* differs from the equivalent angle in *B* by more than 5°. The only substantial difference between the two molecules is in the orientation of the hydrogen-bonding chain; this makes them crystallographically non-equivalent in the unit cell.

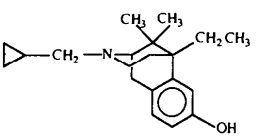
A comparison of the torsion angles of the two forms of pentazocine with a larger set of opioids [naloxone (Karle, 1974), cyclazocine (Karle, Gilardi, Fratini & Karle, 1969), gemazocine (Gelders, De Ranter & Schenk, 1979) and 2-cyclobutylmethyl-5-ethyl-2′-hydroxy-9,9-dimethyl-6,7-benzomorphan (NCBME) (Gelders, De Ranter & Overbeek, 1979)] shows the conformations of all these molecules to be very similar in the region of the fused rings *A*, *C* and *E* (Fig. 1). Here none of the torsion angles differs by more than 6° from the average value for these opioids. A comparison of the side chains of each of the molecules of the title compound, however, showed them to be similar in orientation to that of cyclazocine but different from naloxone, gemazocine and NCBME, all three of which are similar. The molecules group into two sets, as demonstrated by the torsion angles listed in Table 3. It has been suggested that the difference in side-chain orientation plays a role in opioid selectivity and activity.



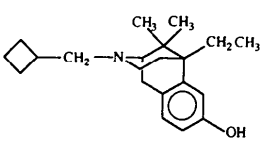

Naloxone




Cyclazocine




Gemazocine




NCBME

## Experimental

*Crystal data*

$C_{19}H_{28}NO^+.Cl^-.\frac{1}{8}H_2O$
$M_r = 324.15$
Monoclinic
$P2_1/c$
$a = 20.614$ (9) Å
$b = 9.349$ (2) Å
$c = 20.888$ (12) Å
$\beta = 113.53$ (7)°
$V = 3690.9$ Å$^3$
$Z = 8$
$D_x = 1.167$ Mg m$^{-3}$
$D_m = 1.166$ (4) Mg m$^{-3}$
$D_m$ measured by flotation

Mo $K\alpha$ radiation
$\lambda = 0.7107$ Å
Cell parameters from 25 reflections
$\theta = 18$–26°
$\mu = 0.2077$ mm$^{-1}$
$T = 293$ (2) K
Rectangular prism
0.6 × 0.4 × 0.3 mm
Colorless
Crystal source: Sigma Chemical Company

*Data collection*

Enraf–Nonius CAD-4 diffractometer
$\theta$–$2\theta$ scans
Absorption correction: none
7059 measured reflections
6913 independent reflections
4559 observed reflections [$I > 3\sigma(I)$]
$R_{int} = 0.015$
$\theta_{max} = 25°$
$h = -24 \rightarrow 24$
$k = 0 \rightarrow 11$
$l = 0 \rightarrow 24$
3 standard reflections [(5̄00), (004) and (131)]
frequency: 120 min
intensity variation: insignificant

*Refinement*

Refinement on $F$
$R = 0.054$
$wR = 0.059$
$S = 1.71$
4559 reflections
406 parameters
$w = 1/[\sigma^2(F) + (0.04F)^2]$
$(\Delta/\sigma)_{max} < 0.01$
$\Delta\rho_{max} = 0.49$ e Å$^{-3}$
$\Delta\rho_{min} = -0.31$ e Å$^{-3}$
Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

The unit-cell dimensions and systematic absences [(0$k$0) $k = 2n + 1$, ($h$0$l$) $l = 2n + 1$] uniquely determined the space group as $P2_1/c$. Corrections to the intensity measurements and contributions to the e.s.d.'s were calculated from polynomial fits to the observed behavior of the standards (McClandlish, Stout & Andrews, 1975). The structure was solved by direct methods using *MULTAN*11/82 (Main *et al.*, 1982). The initial $E$ map contained 44 non-H-atom peaks corresponding to two molecules per asymmetric unit. Least-squares refinement and subsequent Fourier synthesis resulted in one additional atom identified as the O atom of a water molecule. Least-squares refinement of the occupancy of this site led to a value of 0.25 (1), in agreement with the experimental density. All H atoms except those of the water molecules were placed in calculated positions with C—H 0.95 Å and temperature factors defined as 1.3 × $B$ of the bonded atom. Water H atoms were located on a difference Fourier map. Non-H atoms were refined with anisotropic displacement parameters. H-atom coordinates and temperature factors were held fixed. Comparison of $F_o$ and $F_c$ for the strongest reflections gave no indication of secondary extinction. Corrections were made for anomalous-scattering contributions. The program system used was *SDP* (Frenz, 1978).

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Lists of structure factors, anisotropic displacement parameters and H-atom coordinates have been deposited with the IUCr (Reference: GR1007). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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# *trans*-2-Bromo-5,6-methylenedioxy-1-indanol

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## Abstract

The title compound, $C_{10}H_9BrO_3$, is a key intermediate in the synthesis of some mechanism-based inhibitors of dopamine $\beta$-hydroxylase. The X-ray analysis of the title compound reveals *trans* stereochemistry for the bromo and hydroxyl substituents.

## Comment

*trans*-2-Bromo-5,6-methylenedioxy-1-indanol, (2), which is a key intermediate (Eydoux & Réglier, 1993) in the synthesis of some mechanism-based inhibitors of dopamine $\beta$-hydroxylase (Fitzpatrick & Villafranca, 1987), was quantitatively obtained by hydroxybromination of 5,6-methylenedioxyindene, (1), with *N*-bromosuccinimide (NBS) in aqueous dimethyl sulfoxide (DMSO). The hydroxybromination of olefins is known to proceed by *anti* addition of water molecules to a cyclic $Br^+$ ion (Dalton, Henrickson & Jones, 1966; Hassner, 1971; Mitchell,