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## Structure of 3 $\alpha$ -Bromotropane Hydrobromide Monohydrate\*

BY T. A. HAMOR AND IN PART N. KINGS†

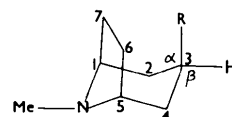
*Department of Chemistry, University of Birmingham, Birmingham B15 2TT, England*

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**Abstract.** C<sub>8</sub>H<sub>15</sub>BrN<sup>+</sup>.Br<sup>-</sup>.H<sub>2</sub>O, *M<sub>r</sub>* = 303.0, orthorhombic, *Pbca*, *a* = 7.01 (1), *b* = 13.51 (1), *c* = 23.64 (2) Å, *U* = 2239 Å<sup>3</sup>, *Z* = 8, *D<sub>c</sub>* = 1.80 Mg m<sup>-3</sup>, *F*(000) = 1200, Mo *K* $\alpha$  radiation,  $\lambda$  = 0.71069 Å,  $\mu$ (Mo *K* $\alpha$ ) = 7.05 mm<sup>-1</sup>. *R* = 7.1% for 401 observed counter amplitudes with anisotropic temperature factors for Br and isotropic for the lighter atoms. The presence of the 3 $\alpha$ -bromo substituent appears to cause a flattening of the piperidinium ring at C(3), so that the C(3)–Br bond is tilted outwards, away from the C(6)–C(7) bridge.

**Introduction.** The 3 $\alpha$ -substituted tropane ring system (I) occurs in a number of alkaloids, such as atropine and scopolamine which are potent anticholinergic agents. Following earlier studies of 3 $\alpha$ -halogenotropanes in solution by dipole-moment and NMR spectroscopic methods (Scheiber, Kraiss & Nádor, 1970) and crystal structure analysis of 3 $\alpha$ -chlorotropane (II) (Vooren, Schenk & MacGillavry, 1970), the structure of the hydrobromide of 3 $\alpha$ -bromotropane (III) has been determined to assess the effect of a large

3 $\alpha$  substituent on the solid-state conformation of the ring system.



- |       |               |      |                               |
|-------|---------------|------|-------------------------------|
| (I)   | <i>R</i> = X  | (IV) | <i>R</i> = OCOPh              |
| (II)  | <i>R</i> = Cl | (V)  | <i>R</i> = OCHPh <sub>2</sub> |
| (III) | <i>R</i> = Br |      |                               |

Thin plate-like crystals were obtained from butanone. Cell dimensions and intensities were measured on a Stoe two-circle computer-controlled diffractometer with graphite-monochromated Mo *K* $\alpha$  radiation. The crystal, 1.0 × 0.4 × 0.05 mm, was mounted about the direction of elongation (*a*). The  $\omega$ -scan technique was employed with a stepping interval of 0.02° and a step time of 1 s. Backgrounds were measured for 30 s at each end of the scan. The intensities of three *Ok**l* reflexions were remeasured after each layer of data collection to monitor the stability of the system. There was some loss of intensity, and appropriate layer scale factors ranging from 1.0 to 1.09 were applied to the intensities.

Reflexions were scanned within the range 0.1 < sin  $\theta/\lambda$  < 0.59 Å<sup>-1</sup> and 401 having *I* > 3 $\sigma$ (*I*) were used

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† Sixth form pupil at King Edward's School, Birmingham, participating in a joint project.

in the analysis. In the conversion of intensities to structure amplitudes, absorption corrections were applied.

The structure was solved by Patterson and Fourier methods. Refinement of the atomic parameters was carried out by least squares, anisotropic temperature factors being adjusted for Br and isotropic for C and N. H atoms were included in the calculations in their theoretical positions, but their coordinates were not refined. An O atom of a molecule of water of crystallization was located from a difference map and was included in the refinement. The positions of the two H atoms bonded to the O atom could not be determined. The refinement was terminated when all the calculated shifts were  $<0.1\sigma$  and  $R$  was 0.071 for the 401 observed structure amplitudes\*. The weighting

\* A list of observed and calculated structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35574 (4 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Fractional atomic coordinates ( $\times 10^4$ ) and thermal parameters ( $\times 10^3$ )

Isotropic temperature factors are in the form

$$T = \exp[-2\pi^2 U(2 \sin \theta/\lambda)^2].$$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> (Å <sup>2</sup> )
C(1)	1040 (49)	1072 (20)	-1290 (16)	25 (10)
C(2)	2198 (49)	1989 (17)	-1060 (11)	21 (8)
C(3)	3843 (49)	1749 (28)	-709 (13)	41 (9)
C(4)	4855 (51)	857 (23)	-881 (19)	37 (11)
C(5)	3685 (52)	35 (23)	-1149 (16)	36 (11)
C(6)	2218 (51)	-308 (20)	-739 (14)	42 (10)
C(7)	363 (52)	334 (26)	-885 (21)	44 (11)
C(8)	1769 (53)	-228 (23)	-2014 (16)	55 (12)
N	2695 (40)	514 (15)	-1614 (11)	37 (7)
Br	3115 (5)	1679 (3)	113 (2)	†
Br <sup>-</sup>	7598 (6)	3169 (2)	-1661 (1)	†
O(w)	4534 (29)	1809 (14)	-2332 (9)	48 (7)
H(1)	-234	1293	-1514	47
H <sup>1</sup> (2)	1183	2422	-821	46
H <sup>2</sup> (2)	2678	2411	-1421	46
H(3)	4645	2413	-801	61
H <sup>1</sup> (4)	5497	594	-493	53
H <sup>2</sup> (4)	5960	1031	-1183	53
H(5)	4555	-605	-1243	53
H <sup>1</sup> (6)	1899	-1081	-809	48
H <sup>2</sup> (6)	2611	-197	-302	48
H <sup>1</sup> (7)	-153	737	-521	60
H <sup>2</sup> (7)	-777	-111	-1058	60
H <sup>1</sup> (8)	2977	-552	-2229	43
H <sup>2</sup> (8)	862	138	-2319	43
H <sup>3</sup> (8)	971	-802	-1802	43
H(N)	3550	977	-1886	51

† Anisotropic temperature factors in the form

$$T = \exp[-2\pi^2(U_{11}h^2a^{*2} + \dots + 2U_{12}hka^*b^*)]$$

with parameters

	<i>U</i> <sub>11</sub>	<i>U</i> <sub>22</sub>	<i>U</i> <sub>33</sub>	<i>U</i> <sub>23</sub>	<i>U</i> <sub>13</sub>	<i>U</i> <sub>12</sub>
Br	66 (3)	64 (3)	28 (3)	-5 (2)	-4 (2)	0 (2)
Br <sup>-</sup>	56 (2)	41 (2)	40 (3)	-2 (2)	-8 (3)	4 (3)

scheme used in the final cycles was  $w = 1/\sigma^2(F)$  where  $\sigma(F)$  is the standard deviation in the observed amplitudes based on counting statistics.

Final atomic parameters are listed in Table 1. E.s.d.'s are high, averaging 0.03 Å for the coordinates of the C atoms. Contributory causes are the poor quality of the crystals, resulting in a shortage of data, and the high ratio of heavy- to light-atom scattering ( $\sum f_H^2/\sum f_L^2 = 5.9$ ).

Computations were carried out on the Birmingham University ICL 1906A computer with *SHELX* (Sheldrick, 1978).

**Discussion.** The conformation of the cation and the atom numbering are shown in Fig. 1. Table 2 contains molecular dimensions; the results of mean-plane calculations are in Table 3. The piperidinium ring C(1)–C(5),N is in a chair-like conformation which is, however, significantly flattened at C(3). C(1),C(2),C(4),C(5) are coplanar to within  $\pm 0.03$  Å, C(3) and N being displaced by 0.39 and 0.92 Å on opposite sides of this plane. Ring flattening is also indicated by the small ring torsion angles about C(2)–C(3) and C(3)–C(4) of 35 and  $-31^\circ$ . The effect of the ring flattening at C(3) is to swing the Br substituent outwards, away from the C(6)–C(7) bridge, increasing the C...Br distances to 3.41 (3) and 3.55 (3) Å, compared with a separation of *ca* 2.6 Å in

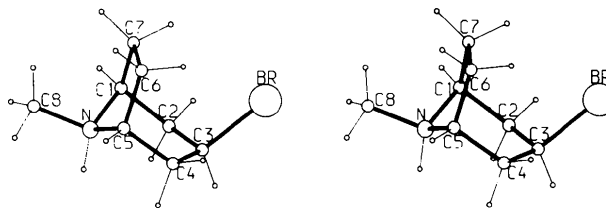


Fig. 1. Stereoscopic view of the cation of (III).

Table 2. Molecular dimensions

(a) Bonded distances (Å)

C(1)–C(2)	1.58 (4)	C(7)–C(1)	1.46 (4)
C(2)–C(3)	1.46 (4)	C(1)–N	1.58 (4)
C(3)–C(4)	1.46 (4)	C(5)–N	1.45 (4)
C(4)–C(5)	1.52 (4)	C(8)–N	1.52 (4)
C(5)–C(6)	1.49 (5)	C(3)–Br	2.01 (3)
C(6)–C(7)	1.60 (4)		

(b) Selected non-bonded distances (Å)

C(6)...Br	3.41 (3)	C(7)...Br	3.55 (3)
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(c) Bond angles ( $^\circ$ )

C(2)–C(1)–C(7)	119 (3)	C(4)–C(5)–C(6)	109 (3)
C(2)–C(1)–N	99 (2)	C(4)–C(5)–N	104 (3)
C(7)–C(1)–N	103 (3)	C(6)–C(5)–N	108 (3)
C(3)–C(2)–C(1)	115 (3)	C(5)–C(6)–C(7)	105 (3)
C(4)–C(3)–C(2)	114 (3)	C(6)–C(7)–C(1)	104 (3)
C(2)–C(3)–Br	111 (2)	C(5)–N–C(1)	101 (2)
C(4)–C(3)–Br	111 (3)	C(8)–N–C(1)	108 (3)
C(5)–C(4)–C(3)	117 (3)	C(8)–N–C(5)	112 (2)

Table 3. *Mean-plane calculations*

(a) Deviations (Å) of atoms from planes

E.s.d.'s are ca 0.03 Å.

Plane (1): C(1),C(2),C(4),C(5)

C(1) 0.03, C(2) -0.03, C(4) 0.03, C(5) -0.03, C(3) 0.39,  
N -0.92, C(6) 1.32, C(7) 1.28

Plane (2): C(2),C(3),C(4)

C(2) 0.0, C(3) 0.0, C(4) 0.0

Plane (3): C(1),C(5),C(6),C(7)

C(1) 0.04, C(5) -0.03, C(6) 0.05, C(7) -0.05, N -0.63

Plane (4): C(1)-C(5), N

C(1) 0.35, C(2) -0.16, C(3) 0.05, C(4) -0.09, C(5) 0.31,  
N -0.47

(b) Interplanar angle (°)

Plane (1)-Plane (2) 150 (2)

a model of the cation constructed on the basis of standard bond lengths and angles. The experimental C...Br distances are close to the sum of the van der Waals radii of C and Br, 3.55 Å (Bondi, 1964). 3 $\alpha$ -Chlorotropane (Vooren *et al.*, 1970) shows similar\* ring flattening at C(3), whereas this effect is less marked in the hydrochloride of *O*-benzoyltropine (IV) (Hamor, 1976) and in the methanesulphonate of benzotropine (V) (Jones, Kennard & Horn, 1978) which have O as the 3 $\alpha$ -substituent atom.

In the ideal tropane system, based on standard bond lengths and angles, the angle between the planes of C(1),C(2),C(4),C(5) and C(2),C(3),C(4) is about 125°. The corresponding angle in the title compound (III) is 150°, representing a distortion of some 25° from the ideal conformation. This is in excellent agreement with the results obtained by Scheiber *et al.* (1970) from NMR and dipole-moment studies in solution.

The packing in the crystal is illustrated in Fig. 2. A molecule of water of crystallization acts as an acceptor in a hydrogen bond with the protonated N atom of the cation, and as a donor in hydrogen bonds with two symmetry-related Br<sup>-</sup> ions. In this way bromotropane cations, water molecules and Br<sup>-</sup> ions related by the *a* glide plane form hydrogen-bonded columns along the

\* Taking structural parameters at face value, the degree of ring flattening in 3 $\alpha$ -chlorotropane is actually slightly less than in 3 $\alpha$ -bromotropane, paralleling the smaller size of the substituent. However, because of the rather large uncertainties in the measured dimensions in the present study, the differences are not statistically significant.

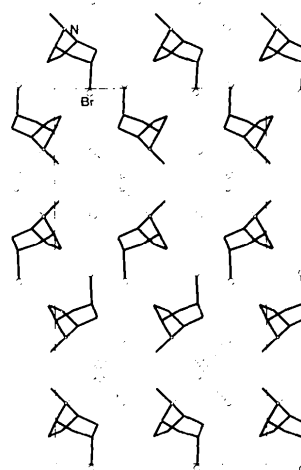


Fig. 2. The crystal structure projected along *x*. The *y* axis points to the right, the *z* axis down the page. Large circles denote Br<sup>-</sup> ions, the smaller circles O atoms of water molecules. Hydrogen bonds are indicated by broken lines.

Table 4. *Hydrogen-bond geometry*

(a) Lengths (Å)

N...O(w)	2.76 (4)	Br <sup>-</sup> ...O(w)	3.30 (3)
H(N)...O(w)	1.69	Br <sup>-1</sup> ...O(w)	3.24 (3)

(b) Angles (°)

H(N)-N...O(w)	6	N...O(w)...Br <sup>-1</sup>	112 (3)
N...O(w)...Br <sup>-</sup>	127 (3)	Br <sup>-</sup> ...O(w)...Br <sup>-1</sup>	108 (3)

Superscript I refers to equivalent position  $-\frac{1}{2} + x, y, -\frac{1}{2} - z$ .

crystallographic *x* axis. Relevant distances and angles are listed in Table 4.

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