# Crystal and Molecular Structure of Hexapyrronium Bromide [3-(2-Cyclohexyl-2-hydroxy-2-phenylacetoxy)-1,1-dimethylpyrrolidinium Bromide]

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The structure of the title compound (I) has been determined by single-crystal X-ray diffraction. Crystals are monoclinic with $Z = 4$ in a unit cell of dimensions: $a = 17 \cdot 167(8)$, $b = 9 \cdot 796(4)$, $c = 12 \cdot 185(6)$ Å, $\beta = 101 \cdot 63(2)°$, space group $P2_1/c$. The structure was solved by Patterson and Fourier methods and refined by least-squares to R 0·048 for 1593 observed diffractometer data. All hydrogen atoms were located. The ester bridge is planar: the phenyl group makes an angle of 63° and the mean plane of the cyclohexyl group an angle of 69° with the ester plane. The angle between the phenyl group and mean plane of the cyclohexyl group is 84°. The pyrrolidine ring is in the envelope conformation with the nitrogen atom out of the plane. A hydrogen bond between the bromide ion and the hydroxy oxygen was found.

HEXAPYRRONIUM BROMIDE (I) contains two asymmetric carbon atoms; there are therefore four possible stereoisomers (two pairs of enantiomers). The compound is
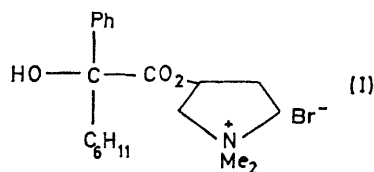
an antimuscarinic drug [1] and as part of a systematic investigation of drugs affecting the cholinergic system, we have determined the crystal structure of one pair of enantiomers by X-ray diffraction.

EXPERIMENTAL

Crystals of hexapyrronium bromide recrystallised from acetone–methanol–ethyl acetate are colourless plates elongated in the b direction and show the forms $\{100\}$, $\{\bar{1}01\}$, $\{111\}$, and $\{\bar{1}11\}$.

Examination of the crystal in convergent plane-polarised light gives a biaxial interference figure with an optic axis almost perpendicular to the plate.

Crystal Data.—$C_{20}H_{30}BrNO_3$, $M = 412 \cdot 4$. Monoclinic, $a = 17 \cdot 167(8)$, $b = 9 \cdot 796(4)$, $c = 12 \cdot 185(6)$ Å, $\beta = 101 \cdot 63(2)°$, $U = 2007$ Å³, $D_m = 1 \cdot 37(1)$ g cm⁻³ (by flotation), $Z = 4$, $D_c = 1 \cdot 36$ g cm⁻³. Systematic absences: $h0l$ for $l = 2n + 1$, $0k0$ for $k = 2n + 1$, spacegroup $P2_1/c$ (C_{2h}^5). Mo-K_α radiation $\lambda = 0 \cdot 7107$ Å; μ(Mo-K_α) $= 22 \cdot 6$ cm⁻¹.

Cell parameters were derived from Weissenberg, oscillation, and precession photographs, and refined parameters

and associated standard deviations determined as described in ref. 2.

Intensity Measurements.—Three-dimensional X-ray diffraction data from a small single crystal ($ca.$ 0·28 × 0·25 × 0·14 mm) were collected on a computer-controlled [2] four-circle diffractometer by use of Mo-K_α radiation with graphite monochromator (002). A coupled θ—2θ step scan with $\Delta 2\theta$ 0·04, a counting time of 6s per step, and a peak-width of 1·6° were used. In the range $2\theta = 5$—45°, 1593 intensities out of a possible 2089 in the quadrant of reciprocal space $(h,k,\pm l)$ had $I \geqslant 3\sigma(I)$. Data were corrected for Lorentz and polarisation effects but not for absorption or extinction.

Structure Solution and Refinement.—The position of the bromine atom in the asymmetric unit was found from an unsharpened Patterson synthesis. [3] A Fourier synthesis using observed data phased with the bromine atom produced a satisfactory trial structure. After successive cycles of full-matrix least-squares refinement [4] of positional and anisotropic thermal parameters a difference electron-density synthesis revealed all the hydrogen atom positions. Hydrogen atoms were included in the calculation of structure factors but not refined. The final refinement of non-hydrogen atoms by full-matrix least-squares was continued until all parameter shifts were $\leqslant 0 \cdot 1\sigma$. The function minimised was $\Sigma w(|F_o| - |F_c|)^2$ with $w = 1$ for all reflections. Atomic scattering factors for neutral carbon, nitrogen, and oxygen, and for the bromide ion were taken from ref. 5 and for hydrogen from ref. 6. The final R was 0·048. Positional and thermal parameters for non-hydrogen atoms for one molecule are listed in Table 1, and

[1] B. V. Franko and C. D. Lunsford, *J. Medicin. Pharmacol. Chem.*, 1960, **2**, 523.

[2] W. R. Busing, R. D. Ellison, H. A. Levy, S. P. King, and R. T. Roseberry, U.S. Atomic Energy Commission Report ORNL 143, 1968.

[3] J. Dollimore, A Fourier Program for LUNA, University of London Institute of Computer Science, Circular No. 1.2.

[4] G. Shearing, A Crystallographic SFLS Program in AA, University of Manchester, 1965.

[5] D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1965, **19**, 104.

[6] 'International Tables for X-Ray Crystallography,' vol. III, Kynoch Press, Birmingham, 1962.

TABLE 1

Fractional co-ordinates and thermal motion parameters ($\times 10^4$) * derived from least-squares refinement, with estimated standard deviations in parentheses

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Br(1)	1328(1)	0477(1)	2000(1)	630(00)	598(05)	397(07)	−104(04)	71(05)	−33(03)
N(1)	1037(4)	4256(6)	3556(5)	516(43)	301(44)	339(36)	−8(33)	153(31)	−6(30)
C(2)	0767(5)	4408(9)	2305(6)	502(57)	535(53)	397(43)	−88(50)	127(36)	−124(47)
C(3)	1111(4)	5777(8)	2032(6)	444(57)	442(58)	440(43)	67(38)	208(41)	47(41)
C(4)	1269(6)	6589(9)	3125(7)	845(72)	413(53)	484(51)	109(50)	366(51)	−24(44)
C(5)	0936(5)	5707(9)	3953(6)	587(57)	476(58)	419(43)	46(46)	147(41)	−86(44)
C(6)	1888(5)	3799(9)	3901(7)	387(57)	520(58)	679(58)	100(46)	122(46)	56(47)
C(7)	0511(5)	3260(9)	4008(7)	702(72)	506(58)	541(58)	−150(50)	244(46)	12(47)
O(1)	1884(3)	5633(6)	1713(4)	473(29)	486(34)	411(29)	8(29)	188(25)	−24(30)
C(8)	1868(5)	5282(9)	0626(7)	487(57)	472(58)	433(51)	−50(46)	158(41)	59(44)
O(2)	1253(4)	5076(8)	−0028(5)	530(43)	1240(68)	505(36)	−67(42)	76(31)	−184(39)
C(9)	2692(5)	5208(8)	0350(6)	487(43)	501(53)	274(36)	−17(42)	137(36)	−18(39)
O(3)	2642(3)	4383(6)	−0613(4)	630(29)	510(34)	397(29)	−17(33)	132(25)	−184(30)
C(10)	3297(5)	4532(9)	1299(6)	545(57)	306(44)	448(43)	−138(46)	137(36)	−95(41)
C(11)	4149(5)	4480(10)	1096(7)	387(43)	472(53)	693(58)	−50(50)	153(41)	12(53)
C(12)	4728(5)	3904(9)	2103(8)	459(57)	476(58)	859(72)	79(46)	36(46)	59(53)
C(13)	4477(6)	2469(10)	2407(9)	774(72)	399(58)	902(72)	117(54)	92(61)	136(56)
C(14)	3612(6)	2480(9)	2566(8)	831(72)	335(53)	736(65)	46(54)	208(56)	113(47)
C(15)	3052(5)	3057(8)	1550(7)	545(57)	365(49)	549(58)	−13(46)	158(46)	−15(44)
C(16)	2983(5)	6683(9)	0156(6)	444(57)	457(53)	368(43)	50(42)	142(36)	107(41)
C(17)	2956(5)	7735(9)	0916(7)	745(72)	379(53)	411(51)	−25(50)	158(46)	−30(44)
C(18)	3297(6)	8988(10)	0765(8)	946(86)	428(58)	671(65)	−33(54)	214(61)	−39(50)
C(19)	3680(6)	9200(10)	−0101(9)	831(72)	438(68)	866(72)	−13(54)	208(61)	222(59)
C(20)	3695(6)	8184(11)	−0873(8)	917(86)	549(68)	700(65)	33(63)	397(61)	275(59)
C(21)	3343(5)	6918(10)	−0752(7)	630(57)	549(63)	592(58)	142(50)	275(51)	148(50)

* The Debye–Waller factor is defined as $T = \exp[-2\pi^2 \sum_i \sum_j a_i^* a_j^* h_i h_j U_{ij}]$ with U in Å^2.

the hydrogen atom positions derived from the difference Fourier synthesis in Table 2. Bond distances and angles are given in Tables 3 and 4. Observed and calculated structure factors are listed in Supplementary Publication

TABLE 2

Fractional co-ordinates ($\times 10^3$) for hydrogen atoms derived from difference Fourier synthesis

Atom	x	y	z
H(2,1)	016	434	208
H(2,2)	096	360	191
H(3,1)	072	629	143
H(4,1)	101	754	303
H(4,2)	186	679	340
H(5,1)	036	596	395
H(5,2)	122	589	475
H(6,1)	228	450	370
H(6,2)	201	295	349
H(6,3)	199	365	474
H(7,1)	−006	365	384
H(7,2)	052	231	372
H(7,3)	066	330	486
H(03,1)	219	450	−125
H(10,1)	328	517	197
H(11,1)	432	542	088
H(11,2)	416	391	040
H(12,1)	474	452	275
H(12,2)	527	388	195
H(13,1)	486	211	311
H(13,2)	455	179	180
H(14,1)	358	305	324
H(14,2)	344	154	274
H(15,1)	247	304	165
H(15,2)	304	244	087
H(17,1)	268	755	156
H(18,1)	327	971	136
H(19,1)	393	1012	−020
H(20,1)	398	840	−152
H(21,1)	338	615	−134

All hydrogens atoms have U 0·063 Å^2.

TABLE 3

Interatomic distances (Å) and angles (°) for non-hydrogen atoms, with estimated standard deviations in parentheses

(a) Distances

N(1)–C(2)	1·51(1)	C(9)–C(16)	1·56(1)
N(1)–C(5)	1·52(1)	C(10)–C(11)	1·53(1)
N(1)–C(6)	1·51(1)	C(10)–C(15)	1·55(1)
N(1)–C(7)	1·51(1)	C(11)–C(12)	1·52(1)
C(2)–C(3)	1·53(1)	C(12)–C(13)	1·55(1)
C(3)–C(4)	1·53(1)	C(13)–C(14)	1·54(2)
C(3)–O(1)	1·46(1)	C(14)–C(15)	1·52(1)
C(4)–C(5)	1·52(1)	C(16)–C(17)	1·39(1)
O(1)–C(8)	1·36(1)	C(16)–C(21)	1·39(1)
C(8)–O(2)	1·20(1)	C(17)–C(18)	1·39(1)
C(8)–C(9)	1·52(1)	C(18)–C(19)	1·37(2)
C(9)–O(3)	1·41(1)	C(19)–C(20)	1·37(1)
C(9)–C(10)	1·54(1)	C(20)–C(21)	1·40(1)

(b) Angles

C(2)–N(1)–C(5)	101·4(6)	O(3)–C(9)–C(16)	111·8(6)
C(2)–N(1)–C(6)	113·2(6)	C(10)–C(9)–C(16)	108·9(7)
C(2)–N(1)–C(7)	110·3(6)	C(9)–C(10)–C(11)	114·5(7)
C(5)–N(1)–C(6)	110·8(6)	C(9)–C(10)–C(15)	112·4(7)
C(5)–N(1)–C(7)	111·9(6)	C(11)–C(10)–C(15)	107·8(7)
C(6)–N(1)–C(7)	109·0(6)	C(10)–C(11)–C(12)	111·8(7)
N(1)–C(2)–C(3)	104·6(6)	C(11)–C(12)–C(13)	111·4(8)
C(2)–C(3)–C(4)	106·0(6)	C(12)–C(13)–C(14)	110·4(8)
C(2)–C(3)–O(1)	112·6(6)	C(13)–C(14)–C(15)	111·7(7)
C(4)–C(3)–O(1)	105·8(6)	C(14)–C(15)–C(10)	110·8(7)
C(3)–C(4)–C(5)	104·9(7)	C(9)–C(16)–C(17)	121·9(7)
C(4)–C(5)–N(1)	103·7(7)	C(9)–C(16)–C(21)	118·7(7)
O(1)–C(8)–O(2)	122·0(8)	C(17)–C(16)–C(21)	119·1(8)
O(2)–C(8)–O(1)	125·2(8)	C(16)–C(17)–C(18)	119·6(9)
O(1)–C(8)–C(9)	112·9(6)	C(17)–C(18)–C(19)	121·2(9)
C(8)–C(9)–O(3)	107·9(6)	C(18)–C(19)–C(20)	119·8(10)
C(8)–C(9)–C(10)	111·8(7)	C(19)–C(20)–C(21)	120·2(10)
C(8)–C(9)–C(16)	109·3(6)	C(20)–C(21)–C(16)	120·0(9)
O(3)–C(9)–C(10)	107·2(6)		

No. SUP 20834 (6 pp.). All computational work was carried out on the University of London ATLAS computer and University College IBM 360 computer.

TABLE 4

Interatomic distances involving hydrogen atoms; σ for all distances is ca. 0·15 Å

C(2)–H(2,1)	1·02	C(11)–H(11,1)	1·02
C(2)–H(2,2)	1·02	C(11)–H(11,2)	1·03
O(3)–H(03,1)	0·99	C(12)–H(12,1)	0·99
C(3)–H(3,1)	1·02	C(12)–H(12,2)	0·99
C(4)–H(4,1)	1·02	C(13)–H(13,1)	1·03
C(4)–H(4,2)	1·01	C(13)–H(13,2)	1·02
C(5)–H(5,1)	1·02	C(14)–H(14,1)	1·01
C(5)–H(5,2)	1·01	C(14)–H(14,2)	1·00
C(6)–H(6,1)	1·03	C(15)–H(15,1)	1·03
C(6)–H(6,2)	1·02	C(15)–H(15,2)	1·02
C(6)–H(6,3)	1·01	C(17)–H(17,1)	1·01
C(7)–H(7,1)	1·03	C(18)–H(18,1)	1·02
C(7)–H(7,2)	1·00	C(19)–H(19,1)	1·02
C(7)–H(7,3)	1·02	C(20)–H(20,1)	1·03
C(10)–H(10,1)	1·03	C(21)–H(21,1)	1·04

DISCUSSION

Description of the Molecular Structure.—The atom numbering system used is shown in Figure 1. Tables 5
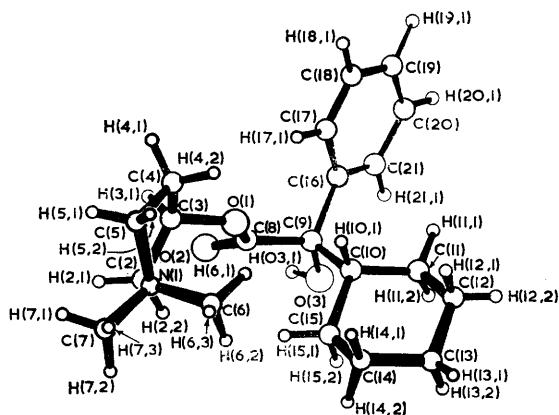

FIGURE 1 Perspective view of molecule and atomic numbering

TABLE 5

Equations * of mean planes with displacements (Å) of relevant atoms in square brackets

Plane (1): O(1), O(2), C(8), C(9), C(3)

$$0·003X + 0·965Y - 0·262Z = 6·082$$

[O(1) − 0·02, O(2) 0·00, C(8) − 0·01, C(3) 0·01, C(9) 0·01]

Plane (2): C(16)—(21)

$$0·769X - 0·323Y + 0·551Z = 9·655$$

[C(16) 0·01, C(17) 0·00, C(18) − 0·02, C(19) 0·02, C(20) 0·00, C(21) − 0·01]

Plane (3): C(10)—(15)

$$- 0·191X + 0·584Y + 0·789Z = 7·427$$

[C(10) 0·26, C(11) − 0·25, C(12) 0·23, C(13) − 0·21, C(14) 0·23, C(15) − 0·26]

Plane (4): C(2)—(5)

$$0·872X - 0·396Y + 0·287Z = 6·559$$

[C(2) 0·02, C(3) − 0·03, C(4) 0·03, C(5) − 0·02, N(1) 0·64]

* Based on orthonormalised co-ordinates: X is parallel to the crystallographic a axis, Y is perpendicular to X in the plane ab, and Z is perpendicular to the plane ab and completes a right-handed set of axes X, Y, Z.

and 6 give the mean plane equations for certain groups of atoms in the molecule and torsion angles for non-hydrogen atoms. From these Tables it can be seen that the ester group formed by atoms O(1), C(3), O(2), C(8), and C(9) is planar. The cyclohexyl group [C(10)—(15)] is in the chair conformation with the substituent atom C(9) in an equatorial position. The mean plane of the cyclohexyl group makes an angle of 69° with the ester plane and 84° with the phenyl group [atoms C(16)—(21)]. The phenyl group is planar and makes an angle of 63° with the ester plane. Interplanar angles may be compared with those in other anticholinergic glycolates.[7]

TABLE 6

Torsion angles for non-hydrogen atoms

N(1)–C(2)–C(3)–O(1)	93	C(9)–C(16)–C(17)–C(18)	173
N(1)–C(2)–C(3)–C(4)	−22	C(9)–C(16)–C(21)–C(20)	−172
N(1)–C(5)–C(4)–C(3)	30	C(9)–C(10)–C(11)–C(12)	175
C(2)–C(3)–C(4)–C(5)	−5	C(9)–C(10)–C(15)–C(14)	−174
C(2)–N(1)–C(5)–C(4)	−43	O(3)–C(9)–C(16)–C(17)	169
C(2)–C(3)–O(1)–C(8)	82	O(3)–C(9)–C(16)–C(21)	−16
C(3)–C(2)–N(1)–C(7)*	159	O(3)–C(9)–C(10)–C(11)	64
C(3)–C(2)–N(1)–C(6)*	−79	O(3)–C(9)–C(10)–C(15)	−59
C(3)–C(2)–N(1)–C(5)	40	C(10)–C(9)–C(16)–C(17)	−72
C(3)–O(1)–C(8)–O(2)	−1	C(10)–C(9)–C(16)–C(21)	102
C(3)–O(1)–C(8)–C(9)	178	C(10)–C(11)–C(12)–C(13)	57
C(4)–C(5)–N(1)–C(7)*	−161	C(10)–C(15)–C(14)–C(13)	−58
C(4)–C(5)–N(1)–C(6)*	77	C(11)–C(10)–C(9)–C(16)	−57
C(4)–C(3)–O(1)–C(8)	−163	C(11)–C(10)–C(15)–C(14)	59
C(5)–C(4)–C(3)–O(1)	−125	C(11)–C(12)–C(13)–C(14)	−54
O(1)–C(8)–C(9)–O(3)	159	C(12)–C(11)–C(10)–C(15)	−59
O(1)–C(8)–C(9)–C(16)	−79	C(12)–C(13)–C(14)–C(15)	55
O(1)–C(8)–C(9)–C(10)	41	C(15)–C(10)–C(9)–C(16)	180
C(8)–C(9)–C(16)–C(17)	50	C(16)–C(17)–C(18)–C(19)	−2
C(8)–C(9)–C(16)–C(21)	−136	C(16)–C(21)–C(20)–C(19)	−1
C(8)–C(9)–C(10)–C(11)	−178	C(17)–C(16)–C(21)–C(20)	2
C(8)–C(9)–C(10)–C(15)	59	C(17)–C(18)–C(19)–C(20)	3
O(2)–C(8)–C(9)–O(3)	−22	C(18)–C(17)–C(16)–C(21)	−1
O(2)–C(8)–C(9)–C(16)	100	C(18)–C(19)–C(20)–C(21)	−2
O(2)–C(8)–C(9)–C(10)	−140		

* See text.

The pyrrolidinyl ring is in the envelope conformation with N(1) 0·64 Å out of plane (Table 5). There is an approximate mirror plane through N(1), C(6), and C(7)
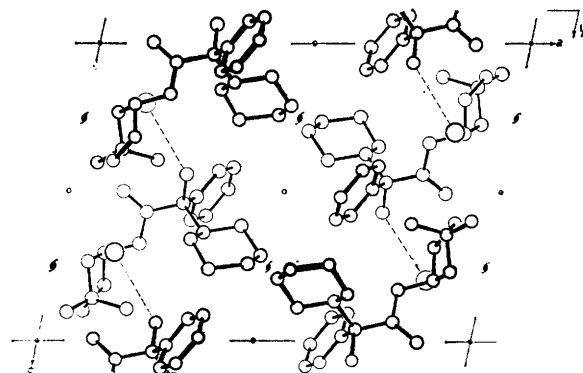
FIGURE 2 Molecular packing viewed down the crystallographic b axis

of the pyrrolidinyl group such that atoms C(3) and C(2) are related to atoms C(4) and C(5). This is illustrated

[7] A. Meyerhöffer, FOA Reports 1972, 6, part 13.

by the relevant torsion angles marked with an asterisk in Table 6.

The hydrogen atoms on the methyl groups are arranged so one hydrogen of each methyl lies approximately on the mirror plane.

Molecular Packing.—Figure 2 shows the contents of one unit cell with the symmetry elements relating the four molecules. There exists a hydrogen bond between the atom O(3) and the bromide ion; O(3) $\cdots$ Br 3·30 Å, Br–H(O3,1) 2·34 Å. There is one molecular contact of non-hydrogen atoms <3.5 Å: C(6) $\cdots$ O(3) at $x,\frac{1}{2} - y,\frac{1}{2} + z$ 3·38 Å.