contact between H(3) and N(1′) of length 2·44 (1) Å. In the only reported crystal structure determination of a metal chelate of 2,2′-biquinolyl, $Au(C_{18}H_{12}N_2)Cl_3$, the biquinolyl group is planar but in the *cis* configuration (Charlton, Harris, Patil & Stephenson, 1966).

The C(2)–C(2′) bond length is 1·492 (3) Å, in excellent agreement with the corresponding values of 1·495 (2) Å in 8,8′-biquinolyl (Lenner & Lindgren, 1976), 1·493 (3) Å in biphenyl (Charbonneau & Delugeard, 1977) and also with the value of 1·50 Å observed in 2,2′-bipyridine (Merritt & Schroeder, 1956). Table 2 compares our bond lengths with those in 8,8′-biquinolyl. For comparison we also list the distances corrected for rigid-body thermal motion as well as the calculated distances in quinoline (Dewar & Trinajstic, 1971).

Normal probability plots comparing the bonds after the correction showed a significant improvement.

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Norcocaine Hydrobromide*

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Abstract. $HBr[C_{16}H_{20}BrNO_4]$, (2*βR*-methoxycarbonyl-3*βS*-benzoyloxy-8-azabicyclo[3.2.1]octane), space group $P2_12_12_1$, $a = 11{\cdot}543\ (8)$, $b = 12{\cdot}610\ (9)$, $c = 11{\cdot}474\ (8)$ Å, $Z = 4$, $D_x = 1{\cdot}472$, $D_m = 1{\cdot}45$ g cm^{-3} (flotation: CCl_4–C_6H_6). The structure was solved by the heavy-atom method. Full-matrix least-squares refinements converged to $R = 0{\cdot}072$. The piperidine ring is in the chair conformation. The Br^- is hydrogen bonded to one N proton and lies over the pyrrolidine ring. The carbonyl O of the methoxycarbonyl moiety is intramolecularly hydrogen bonded to the other N proton which also hydrogen bonds intermolecularly with the carbonyl O of the benzoate group.

Introduction. Shen, Ruble & Hite (1975) suggested that the local anesthetic action of cocaine could be rationalized on the basis of the piperidine boat conformation since it superimposes more completely than the chair conformation upon other, more potent (Lokhandwala, Patel, Patel, Merker, Shafi'ee & Hite,

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[*] Stereochemical Aspects of Local Anesthetic Action. III. Part II: Shen, Ruble & Hite (1975).

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1971), local anesthetics in which a benzoate moiety is axial to a piperidine ring (Hite & Craven, 1973). Cocaine methiodide, in which a 1,3-diaxial non-bonded repulsion was introduced to destabilize the chair relative to the boat, was found to differ little in conformation from the HCl salt (Shen, Ruble & Hite, 1975). The boat conformation of cocaine HCl is sterically precluded by the orientation of the N-proton$\cdots$Cl$^-$ hydrogen bond which, like one of the *N*-methyl groups of cocaine methiodide, extends over the piperidine ring and is *cis* to the benzoate moiety. To alleviate this steric impediment to the development of a boat conformation, norcocaine HBr was synthesized in the expectation that the N-proton$\cdots$Br$^-$ hydrogen bond, like the methyl group in cocaine HCl, would be directed over the pyrrolidine ring. This could leave the remaining N proton to interact with the benzoate moiety. This interaction could stabilize the cocaine boat relative to the chair and would support a hypothesis imputing biological significance to the boat conformation of cocaine and to superimposable conformations of related amino ester-type local anesthetics.

Norcocaine, m.p. 82·5–83·5°C [literature value 80–82°C (Schmidt & Werner, 1962)] was prepared by demethylation of (–)-cocaine with the method of Montzka, Matiskella & Partyka (1974). The HBr salt was formed in ether solution with dry HBr gas and was recrystallized from dry acetone, m.p. 164–165°C. A monohydrate is obtained if the solution is exposed to moisture. Space group and lattice parameters for the monohydrate were determined from Weissenberg and precession photographs: $P2_1$, $a = 11{\cdot}70$, $b = 9{\cdot}84$, $c = 16{\cdot}16$ Å, $\beta = 100{\cdot}5°$, $Z = 4$, $D_x = 1{\cdot}410$, $D_m = 1{\cdot}41$ g cm^{-3} (flotation: CCl_4–C_6H_6).

A crystal (0·65 × 0·4 × 0·4 mm) of the anhydrous, orthorhombic modification was selected to avoid both polar and hydrogen-bonding effects of water. Intensity data were collected with Zr-filtered, Mo $K\alpha$ radiation ($\lambda = 0{\cdot}7107$ Å) at a take-off angle of 4° on an automated Picker FACS-I diffractometer. An ω-step scan (Cohen, 1975) was used with 15 4 s steps 0·05° apart. Three reflections were monitored every 150 reflections to check crystal alignment and deterioration. No significant changes in these reflections were observed during data collection. No absorption correction was applied ($\mu = 26{\cdot}2$ cm^{-1}). Data were collected for 3967 reflections. Equivalent reflections were averaged to yield 2038 unique data over a 2θ range of 3 to 55°. Intensity step data were least-squares fitted to a Gaussian curve to produce integrated intensities which were corrected for Lorentz and polarization effects. Those reflections (318) which had background-corrected intensities (I_o) less than $2\sigma(I_o)$ were considered unobserved and were assigned an intensity of $I_o + 2\sigma(I_o)$ for later comparison with F_c. A Patterson synthesis to locate the Br$^-$ ions was carried out with the XRAY 72 system (Stewart, Kruger, Ammon, Dickinson & Hall, 1972) on an IBM-360/65 computer. The remaining atoms (C,N,O) were located during three cycles of Fourier synthesis and least-squares refine-

Table 1. *Atomic positional parameters*

Positional parameters are given as fractions of the lattice translations (×10^4; for H ×10^3). Isotropic temperature factors (×10^2) are given by the expression $T = \exp(-B \sin^2 \theta/\lambda^2)$. Estimated standard deviations are given in parentheses.

	x	y	z		x	y	z	B (Å^2)
Br$^-$	4624 (1)	−280 (1)	−3584 (1)	H(1)	403	−42	−106	4·7
C(1)	3683	352 (8)	−612 (7)	H(2)	329	0	102	3·5
C(2)	3580 (9)	702 (8)	638 (7)	H(3)	197	178	60	3·7
C(3)	3000 (9)	1787 (8)	691 (7)	H_a(4)	430	285	0	4·5
C(4)	3497 (10)	2605 (9)	−131 (8)	H_e(4)	294	334	−14	4·5
C(5)	3584 (11)	2104 (9)	−1357 (10)	H(5)	405	265	−191	5·0
C(6)	2463 (11)	1560 (11)	−1770 (9)	H*exo*(6)	241	146	−267	4·8
C(7)	2529 (6)	411 (8)	−1245 (8)	*H*endo*(6)	204	229	−125	4·8
C(8)	2542 (9)	2842 (8)	2411 (9)	H*exo*(7)	253	−21	−193	5·1
C(9)	2897 (9)	3072 (7)	3611 (8)	*H*endo*(7)	217	14	−36	5·1
C(10)	2481 (11)	3987 (8)	4123 (9)	H_e(N)	463	94	−209	4·9
C(11)	2852 (10)	4267 (9)	5235 (8)	H_a(N)	513	125	−92	4·9
C(12)	3678 (13)	3642 (9)	5765 (9)	*H(10)	187	448	366	5·0
C(13)	4052 (14)	2732 (11)	5298 (10)	*H(11)	250	496	567	5·2
C(14)	3692 (11)	2442 (9)	4165 (8)	*H(12)	404	390	659	6·1
C(15)	4751 (10)	732 (8)	1239 (7)	*H(13)	462	222	579	7·4
C(16)	5702 (13)	314 (16)	2994 (14)	*H(14)	404	174	374	5·5
N	4398 (7)	1157 (7)	−1250 (7)	H_1(16)	653	0	267	8·4
O(1)	3232 (6)	2129 (6)	1902 (5)	H_2(16)	579	115	319	8·4
O(2)	1729 (7)	3255 (8)	1871 (7)	H_3(16)	594	−12	353	8·4
O(3)	5593 (6)	1208 (7)	881 (7)					
O(4)	4720 (7)	211 (7)	2240 (6)					

* H atoms positioned by geometric constraints with C–H = 1·02 Å.

ment. The last cycle of full-matrix least-squares refinement with anisotropic temperature factors yielded a residual of 0·089, minimizing $\Sigma w(|F_o| - |F_c|)^2$ where $w = \sigma^{-2}(F_o)$.

Difference Fourier syntheses afforded the positions of 13 of the 20 H atoms. The remaining H atoms were placed in geometrically idealized positions. H atoms were assigned isotropic temperature factors equal to those of the atoms to which they are bonded. One further cycle of least-squares refinement of all parameters, except those of the H atoms, gave a final residual of 0·072. Unobserved reflections were omitted from the refinement. Parameter shifts were less than 0·5σ. The absolute configuration was taken from Shen, Ruble & Hite (1975). The final atomic parameters are listed in Table 1.* The atomic scattering factors and anomalous dispersion correction for Br were taken from *International Tables for X-ray Crystallography* (1968).

Discussion. As was expected, Br^- is strongly hydrogen bonded (2·30 Å) to the equatorial proton [H_e(N)] and occupies the same position as the methyl group in cocaine HCl. Model building indicates that if the axial proton [H_a(N)] were hydrogen bonded to either O of the benzoate moiety, the boat conformation of the piperidine ring would be possible. However, since H_a(N) is intramolecularly hydrogen bonded to the methoxycarbonyl carbonyl O [O(3)] (2·14 Å), a similar interaction with either O of the benzoate moiety is precluded and norcocaine HBr, like the HCl and methiodide salts of cocaine, has the piperidine chair conformation. Thus, while the internal tropane torsion angles are normal, the nearly coplanar methoxycarbonyl group is rotated approximately −70° around the C(2)–C(15) bond relative to the orientation seen in the methiodide salt. The driving force for this rotation is the H_a(N)···O(3) hydrogen bond. The nearly coplanar benzoate group is rotated approximately −85° around the C(3)–O(1) bond relative to the orientation seen in the methiodide salt. The impetus for this conformational change is primarily an intermolecular O(2)···H_a(N) interaction (2·23 Å) (Figs. 1 and 2). Three other intermolecular contacts shorter than the sum of the van der Waals radii, Br···H(10) (2·78 Å), Br···H(12) (2·95 Å), and O(2)···H_e(N) (2·63 Å) may also play a role in the benzoate rotation. These interactions are in accord with the smaller O(2)–C(8)–C(9)–C(10) torsion angle in the methiodide salt (8° *vs* 15·7°). The Br^- also appears to be interacting with two bridgehead C atoms, one interaction intramolecular [Br···C(1) (3·67 Å)] and one intermolecular [Br···C(5) (3·89 Å)]. The intramolecular distance to the second bridgehead C atom [C(5)] is 4·12 Å. This skewed orientation of Br^- relative to C(1) and C(5) is also reflected in the torsion angles about the N–H_e(N) bond (Fig. 1). These interactions seem to be governed by electrostatic forces between Br^- and the partial positive character of the bridgehead C atoms contiguous with the cationoid N (Craven & Hite, 1973; Hite & Craven, 1973; Hite & Soares, 1973). The only other intermolecular contacts shorter than or approximating the sum of the van der Waals radii are Br···C(7) (3·72 Å) and Br···C(6) (3·99 Å). No significant differences in bond lengths or bond angles were observed between norcocaine HBr (Fig. 1) and cocaine HCl (Gabe & Barnes, 1963) or cocaine methiodide (Shen, Ruble & Hite, 1975).

In this crystal structure H_e(N) and H_a(N) are

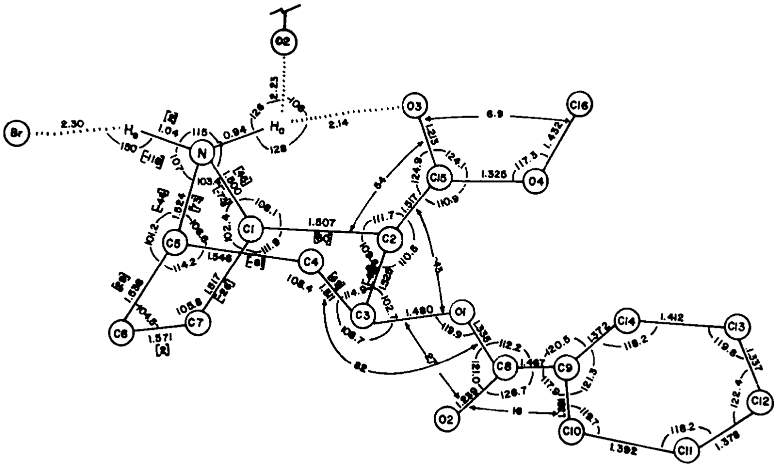

Fig. 1. Bond distances (Å), bond angles (°), and selected torsion angles (°) [tropane internal ring angles in square brackets] for norcocaine hydrobromide. Average standard deviation for bond distances is 0·01 Å and for bond angles is 0·7°.

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32806 (24 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

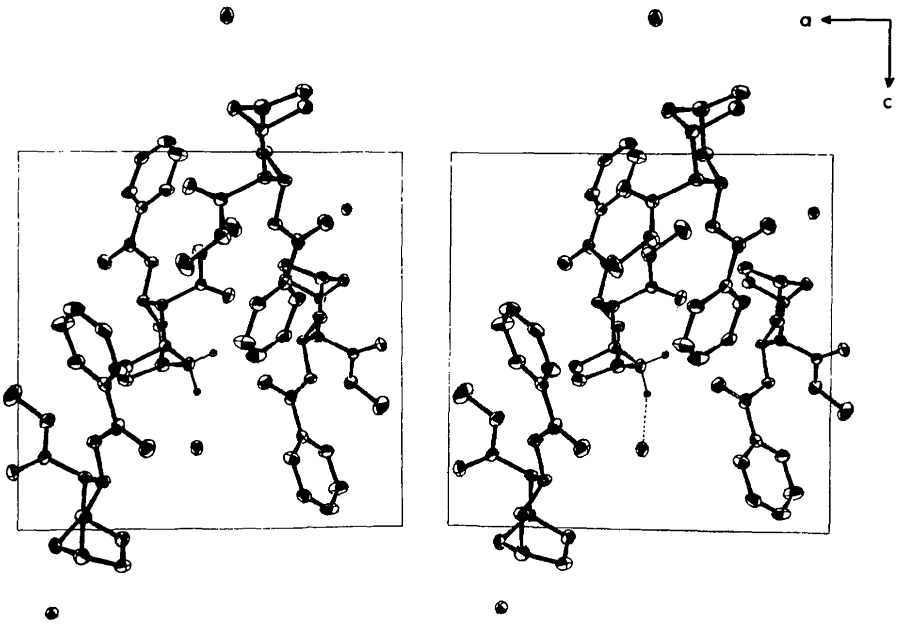

Fig. 2. Projection of the unit cell down $\bar{b}$. The dotted lines indicate the bifurcated hydrogen bond, the dashed line represents the H_e–Br^- bond.

hydrogen bonded to Br^- and to O(3), respectively, yet appear to interact intermolecularly as well with a common *third* ligand [O(2)] at a distance of 2·63 and 2·23 Å respectively. While the latter distance suggests a hydrogen-bonding interaction, the former is too close to the sum of the van der Waals radii to be considered a hydrogen bond. A closer interaction $[O(2)\cdots H_e(N)]$ may be prevented by electrostatic repulsion between O(2) and Br^-. This tricovalency or bifurcated hydrogen bonding of $H_a(N)$ [*cf.* $H_e(N)$] may result from the non-linear nature of the $N{-}H_a(N)\cdots O(3)$ hydrogen bond which leaves $H_a(N)$ more exposed than would be the case if the hydrogen-bond angle were 180°. From the bond angles describing this bifurcated hydrogen bond (Fig. 1), the interacting atoms are coplanar.

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