

9-Aminobicyclo[3.3.1]nonane-9-carboxylic Acid Hydrobromide Monohydrate

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Abstract

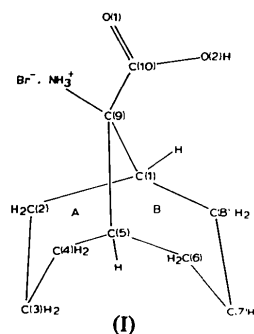
$C_{10}H_{17}NO_2 \cdot HBr \cdot H_2O$, FW = 238.3, monoclinic, $P2_1/c$, $a = 11.247$ (6), $b = 7.172$ (4), $c = 15.040$ (4) Å, $\beta = 90.04$ (2)°, $Z = 4$, D_m (floatation) = 1.44, $D_x = 1.457$ Mg m⁻³, $F(000) = 584$, Cu $K\alpha$ radiation ($\lambda = 1.54178$ Å, $\mu = 4.72$ mm⁻¹). The structure was refined to $R = 0.084$ for 1952 counter reflections. The bicyclo[3.3.1]nonane system exists in a distorted twin-chair conformation. The structure is stabilized by a network of N—H...Br, O—H...Br, N—H...O and O—H...O hydrogen bonds.

Introduction

Structure analyses of several acyclic, heterocyclic and bicyclic amino acid analogues have been reported from this laboratory. Analysis of 2-aminobicyclo[3.2.1]octane-2-carboxylic acid monohydrate (Chacko, Bhattacharjee, Zand & Water, 1978) showed that the asymmetric substitution of the amino acid on the bicyclo[3.2.1]octane nucleus significantly affects its expected mirror symmetry. On the other hand, analysis of 2-aminoadamantane-2-carboxylic acid.HBr (Chacko & Zand, 1973) showed that the substitution of the amino and carboxyl groups at the C(2) position did not disturb its highly symmetric cage-like symmetry. The conformation of the bicyclo[3.3.1]nonane system is of interest to stereochemists, and Eliel (1962) predicted that this bicyclic molecule, which contains two cyclohexane rings, would prefer a boat-chair instead of a twin-chair conformation to relieve the strong repulsion of the axial H atoms on C(3) and C(7).

Crystals of 9-aminobicyclo[3.3.1]nonane-9-carboxylic acid hydrobromide monohydrate (I) are needle-shaped. Cell dimensions were determined by a least-squares method from 2θ values for 30 reflections measured on a Picker diffractometer.

A crystal of cross-section 0.2 × 0.4 mm and length 0.5 mm was mounted on the diffractometer for data collection such that the needle axis b coincided with the



φ axis. The θ - 2θ scan mode was employed with a scan speed of 2° min⁻¹. The scan range was 2° with background measured on either side of the peak for 10 s. There were 1952 reflections with $2\theta \leq 130^\circ$ and $I > 2\sigma(I)$. The data were corrected for Lorentz and polarization factors and initially scaled by Wilson's method.

The Br atom was located on a Patterson map and gave an R of 0.50 for the structure factor calculations. A heavy-atom-phased Fourier synthesis gave the positions of all the non-hydrogen atoms which were refined initially by a block-diagonal least-squares method (Shiono, 1968) to an R of 0.15. A difference synthesis located the H atoms. They were included in further refinement carried out by a full-matrix least-squares procedure (Gantzel, Sparks & Trueblood, 1961) with anisotropic temperature factors for the non-hydrogen atoms, which converged at $R = 0.084$. The function minimized was $\sum w(|F_o| - |F_c|)^2$ where $w = (1/\sigma_F^2)$ based on counting statistics (Stout & Jensen, 1968). Anomalous-dispersion corrections for Br⁻ were from Cromer & Liberman (1970). Scattering factors were from *International Tables for X-ray Crystallography* (1962). Tables 1 and 2 give the atomic parameters.‡

‡ Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34005 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. Positional parameters with their e.s.d.'s

	<i>x</i>	<i>y</i>	<i>z</i>
Br	0.36045 (6)	0.64258 (10)	0.37079 (4)
C(1)	0.2753 (5)	0.1794 (8)	0.0789 (4)
C(2)	0.1705 (6)	0.0433 (11)	0.0717 (5)
C(3)	0.0505 (6)	0.1180 (10)	0.1058 (5)
C(4)	0.0590 (5)	0.2338 (12)	0.1893 (5)
C(5)	0.1675 (5)	0.3677 (8)	0.1932 (4)
C(6)	0.1540 (5)	0.5290 (10)	0.1257 (4)
C(7)	0.1673 (6)	0.4761 (10)	0.0274 (5)
C(8)	0.2683 (6)	0.3373 (10)	0.0103 (4)
C(9)	0.2830 (5)	0.2643 (9)	0.1729 (4)
C(10)	0.3167 (5)	0.1159 (8)	0.2451 (4)
N	0.3860 (4)	0.3984 (7)	0.1173 (3)
O(1)	0.4039 (5)	0.1363 (7)	0.2904 (4)
O(2)	0.2464 (5)	-0.0227 (9)	0.2540 (4)
OW	0.4239 (4)	0.7281 (8)	0.0781 (3)

Table 2. Parameters of H atoms

Bonded to	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> (Å ²)	
H(1)	C(1)	0.360	0.098	0.067	2.6
H(2)	C(2)	0.161	0.006	0.002	3.2
H(3)	C(2)	0.192	-0.082	0.110	3.2
H(4)	C(3)	0.008	0.195	0.052	3.4
H(5)	C(3)	-0.007	-0.007	0.120	3.4
H(6)	C(4)	-0.021	0.324	0.194	3.6
H(7)	C(4)	0.062	0.145	0.248	3.6
H(8)	C(5)	0.177	0.419	0.216	2.6
H(9)	C(6)	0.067	0.598	0.136	3.4
H(10)	C(6)	0.223	0.637	0.141	3.4
H(11)	C(7)	0.083	0.411	0.003	3.6
H(12)	C(7)	0.182	0.600	-0.016	3.6
H(13)	C(8)	0.253	0.277	-0.055	3.2
H(14)	C(8)	0.350	0.417	0.013	3.2
H(15)	N	0.378	0.502	1.125	2.2
H(16)	N	0.391	0.465	0.242	2.2
H(17)	N	0.468	0.317	0.166	2.2
H(18)	O(2)	0.292	-0.125	0.286	5.5
H(19)	OW	0.467	0.565	0.134	4.0
H(20)	OW	0.383	0.767	0.008	4.0

Discussion

Bond lengths and angles are given in Table 3. A list of torsion angles is given in Table 4. The amino N atom exists as NH₃⁺ and the carboxyl group as COOH. The bond distances and angles of the carboxyl group indicate that it is not ionized. The C(9)–N distance of 1.507 (8) Å is fairly close to the value of 1.487 Å for

Table 3. Bond lengths (Å) and angles (°)

C(1)–C(2)	1.534 (9)	C(9)–C(1)–C(2)	111.0 (5)
C(4)–C(5)	1.538 (9)	C(4)–C(5)–C(9)	110.0 (5)
C(2)–C(3)	1.541 (10)	C(1)–C(2)–C(3)	115.4 (5)
C(3)–C(4)	1.509 (11)	C(3)–C(4)–C(5)	115.2 (5)
C(1)–C(9)	1.542 (8)	C(2)–C(3)–C(4)	114.4 (5)
C(5)–C(9)	1.544 (8)	C(1)–C(9)–C(5)	108.9 (4)
C(1)–C(8)	1.534 (9)	C(9)–C(1)–C(8)	109.2 (4)
C(5)–C(6)	1.545 (9)	C(6)–C(5)–C(9)	107.6 (5)
C(6)–C(7)	1.533 (10)	C(1)–C(8)–C(7)	113.8 (5)
C(7)–C(8)	1.532 (10)	C(5)–C(6)–C(7)	116.1 (5)
C(9)–C(10)	1.566 (8)	C(6)–C(7)–C(8)	113.3 (5)
C(9)–N	1.507 (8)	C(4)–C(5)–C(6)	112.1 (5)
C(10)–O(1)	1.203 (8)	C(2)–C(1)–C(8)	112.5 (5)
C(10)–C(2)	1.277 (9)	C(5)–C(9)–C(10)	113.3 (4)
		C(10)–C(9)–C(1)	112.4 (4)
		C(1)–C(9)–N	109.5 (4)
		C(10)–C(9)–N	102.6 (4)
		C(5)–C(9)–N	110.0 (4)
		C(9)–C(10)–O(1)	120.5 (5)
		C(9)–C(10)–O(2)	116.9 (5)
		O(1)–C(10)–O(2)	122.6 (5)

the C^α–N distance, and C(9)–C(10), 1.566 Å, is significantly longer than the C^α–C' distance, 1.527 Å, observed in amino acids (Marsh & Donohue, 1967). The C(10)–C(9)–N angle, 102.6°, is significantly smaller than tetrahedral. The two C–C lengths of the one-atom bridgehead involving C(9) have values close to each other with a mean of 1.543 Å. However, the C–C bonds of the three-atom bridgeheads have values lying between a maximum of 1.545 Å [C(5)–C(6)] and a minimum of 1.509 Å [C(3)–C(4)] with an overall mean of 1.527 Å. The C–C–C angle at the one-atom bridgehead is slightly less than tetrahedral [C(5)–C(9)–C(1) = 108.9 (4)°]. The C–C–C angles involving the methine C atoms have values close to tetrahedral while the other C–C–C angles of the three-atom bridgeheads [angles about C(2), C(3), C(4), C(6), C(7) and C(8)] are significantly larger than tetrahedral with a mean of 114.7°. The N atom lies 0.086 Å from the plane of O(1), O(2), C(10) and C(9) (Table 5).

The bicyclo[3.3.1]nonane system takes up a twin-chair conformation contrary to the predicted (Eliel, 1962) boat–chair conformation. In the ideal twin-chair conformation there is an intolerable transannular interaction of ~1 Å between the axial H atoms on C(3) and C(7), and it would appear that the molecule ought to exist in the boat–chair form, even though this still has

Table 4. Torsion angles (°) of the bicyclo[3.3.1]nonane ring system

Ring A		Ring B		Rings A and B	
C(9)–C(1)–C(2)–C(3)	49.5 (7)	C(9)–C(5)–C(6)–C(7)	52.0 (7)	C(3)–C(4)–C(5)–C(6)	69.0 (7)
C(1)–C(2)–C(3)–C(4)	-39.5 (9)	C(5)–C(6)–C(7)–C(8)	-41.9 (8)	C(4)–C(5)–C(6)–C(7)	-70.4 (7)
C(2)–C(3)–C(4)–C(5)	40.2 (9)	C(6)–C(7)–C(8)–C(1)	42.3 (8)	C(7)–C(8)–C(1)–C(2)	69.3 (7)
C(3)–C(4)–C(5)–C(9)	-51.3 (8)	C(7)–C(8)–C(1)–C(8)	-54.4 (7)	C(8)–C(1)–C(2)–C(3)	-73.2 (7)
C(4)–C(5)–C(9)–C(1)	60.0 (6)	C(8)–C(1)–C(9)–C(5)	65.4 (6)		
C(5)–C(9)–C(1)–C(2)	-59.2 (6)	C(1)–C(9)–C(5)–C(6)	-62.9 (6)	Mean (A) = 50.0	
				Mean (B) = 53.2	

Table 5. Equation of and deviations (Å) from the best plane through C(9), C(10), O(1) and O(2)

$$0.5352x - 0.5073y - 0.6753z = -1.0133$$

C(9)	-0.002	O(2)	-0.003
C(10)	0.008	N	0.086
O(1)	-0.003		

some bad interactions. It is found, however, that the two cyclohexane rings exist as flattened chairs. The strong interaction between the C(3) and C(7) methylene groups is reflected in the increase of the C(3)···C(7) non-bonded separation from the ideal twin-chair value of 2.52 Å (Brown, Martin & Sim, 1965) to 3.12 Å and the concomitant flattening of the rings. The flattening is manifested in the bond angles (Table 3) and torsion angles (Table 4). The two cyclohexane systems, rings *A* and *B*, have mean torsion angles of 50.0 and 53.2° respectively, suggesting that *A* is more flattened than *B*. The theoretical value for a cyclohexane chair conformation is $\pm 54.7^\circ$ while the average C—C bond angle is larger than tetrahedral, 111.5° (Bixon & Lifson, 1967). In general, torsion angles about C—C bonds around the one-atom bridgehead have values close to and in some cases larger than 60° and they gradually reduce to a minimum for the C—C bonds of the three-atom bridgehead involving C(3) and C(7). The torsion angles of bonds involving both *A* and *B* rings have values close to 70°. In 2-

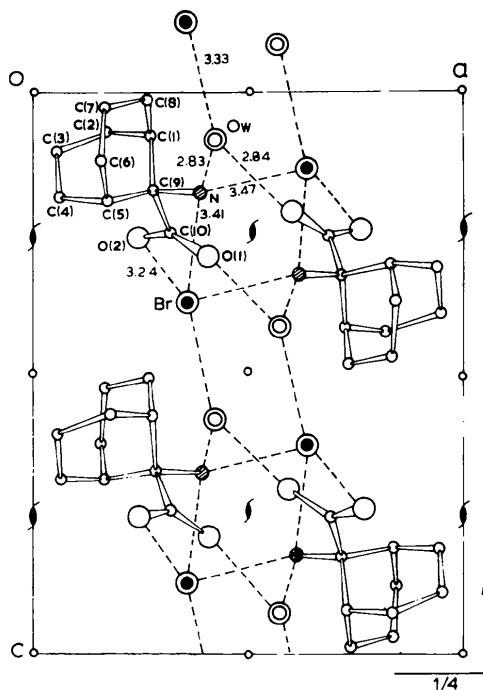
Fig. 1. Projection of the structure down *b*.

Table 6. Hydrogen-bond distances (Å) and angles (°)

D—H···A	D···A	H···A	∠H—D···A
N—H(15)···OW	2.83	1.84	20
N—H(16)···Br	3.41	2.35	9
N—H(17)···Br ⁱ	3.47	2.36	3
O(2)—H(18)···Br ⁱⁱ	3.24	2.24	7
OW—H(19)···O(1 ⁱⁱⁱ)	2.84	1.85	20
OW—H(20)···Br ^{iv}	3.33	2.18	11

Symmetry code

- (i) $1 - x, \frac{1}{2} + y - 1, \frac{1}{2} - z$ (iii) $1 - x, \frac{1}{2} + y, \frac{1}{2} - z$
(ii) $x, y - 1, z$ (iv) $x, \frac{1}{2} - y + 1, \frac{1}{2} + z - 1$

aminoadamantane-2-carboxylic acid.HBr (Chacko & Zand, 1973), the torsion angles of the C—C bonds are all close to $\pm 60^\circ$ and bond angles have values close to tetrahedral due to its highly symmetric and rigid cage-like structure.

A projection of the structure down *b* is given in Fig. 1 with the hydrogen bonds indicated. The N atom is hydrogen bonded to Br, Brⁱ and OW at 3.41, 3.47, 2.83 Å respectively. The hydroxyl O(2) forms an O—H···Br hydrogen bond with Brⁱⁱ, of length 3.24 Å. Water OW enters into hydrogen bonds with Br^{iv} and O(1ⁱⁱⁱ) at 3.33 and 2.84 Å respectively and also acts as an acceptor of a hydrogen bond from N. The hydrogen-bond distances and angles are given in Table 6. The structure is thus stabilized by a network of N—H···Br, N—H···O, O—H···Br and O—H···O hydrogen bonds.

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