Crystal and Molecular Structure of 2-Aminoadamantane-2-carboxylic Acid Hydrobromide*

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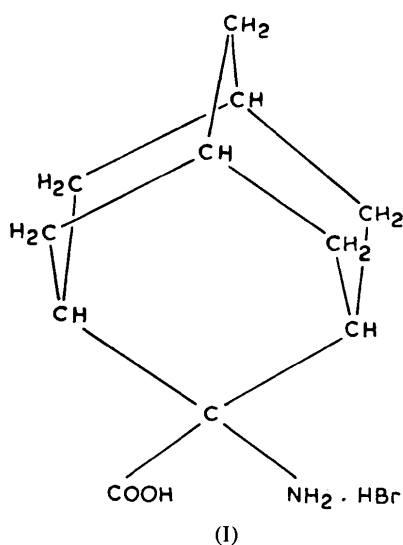
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2-Aminoadamantane-2-carboxylic acid hydrobromide crystallizes in space group $P2_1/c$ with $a = 6\cdot40$, $b = 11\cdot62$ and $c = 15\cdot38$ Å, $\beta = 95\cdot2°$, $Z = 4$. The structure was solved by the heavy-atom method with 1484 visual reflexions and refined to an R of $0\cdot097$. The substitution of the amino and the carboxyl group at C(2) of the adamantane does not significantly affect its highly symmetric cage-like structure. In relation to amino acid structures, a rare occurrence of the C(11)–O(2) double bond *trans* to the nitrogen N about the C(2)–C(11) bond is observed in this structure. The nitrogen atom lies $1\cdot07$ Å out of the plane containing the carboxyl group and C(2).

Introduction

A series of crystal structure determinations of cyclo-alkane compounds, in particular amino carboxylic acid derivatives, has been undertaken in this laboratory (Chandrasekharan, Mallikarjunan, Godavari Chandrasekharan & Zand, 1968; Chacko, Srinivasan & Zand, 1971*a,b*; Mallikarjunan, Chacko & Zand, 1972). Their molecular structures are of interest both from the point of view of the conformational features of the cycloalkane rings and their nature as amino acids. The structural investigation of 2-aminoadamantane-2-carboxylic acid hydrobromide (I) was carried out because of its close similarity to the amino cycloalkane carboxylic acid derivatives.

(I)

The structure of adamantane ($C_{10}H_{16}$) has been reported by Nordman & Schmitkons (1965) both at room and at low temperature. It undergoes a phase transition at $-65°C$, changing from face-centred cubic to a tetragonal low-temperature form. The room temperature form is disordered. The structures of congressane (Karle & Karle, 1965), diadamantane (Alden, Kraut & Taylor, 1968), tetramantane (Schleyer, Osawa & Drew, 1968) and an ethano-bridged diadamantane (Rao & Sundaralingam, 1972) have also been reported.

Experimental

Crystals of 2-aminoadamantane-2-carboxylic acid hydrobromide are fine needles. Rotation, Weissenberg and precession photographs were taken with Cu $K\alpha$ ($\lambda = 1\cdot5418$ Å) radiation. The crystal data are:

Crystal system	Monoclinic
Cell dimensions	$a = 6\cdot40$ (1) Å
	$b = 11\cdot62$ (2)
	$c = 15\cdot38$ (2)
	$\beta = 105\cdot2$ (2)°
Space group	$P2_1/c$ ($0k0$, k odd and $h0l$, l odd absent)
Formula	$C_{11}H_{18}NO_2Br$
F.W.	$276\cdot2$
Z	4
$F(000)$	568
D_m	$1\cdot65$ g cm^{-3} (by flotation)
D_c	$1\cdot644$ g cm^{-3}
μ(Cu $K\alpha$)	$32\cdot4$ cm^{-1}.

A crystal of dimensions $0\cdot2 \times 0\cdot25 \times 0\cdot55$ mm was chosen for the collection of data about the needle axis a, and Hkl reflexions (H, 0 through 5) were collected by the multiple-film equi-inclination Weissenberg method. A crystal $0\cdot2 \times 0\cdot3 \times 0\cdot4$ mm was cut and mounted about **b** for cross-axis data and hKl layers,

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(*K*, 0 through 2) were collected. The intensities were measured visually with a calibrated set of intensities taken with the same crystal, and corrected for Lorentz and polarization factors. No absorption correction was applied. The common reflexions measured about the two axes were used to put the data on a common scale by the method of Rollett & Sparks (1960). 1484 independent reflexions were observed.

Structure determination and refinement

An unsharpened Patterson synthesis was used to determine the coordinates of the bromine atom. An initial structure factor calculation gave an *R* of 0·45. A Fourier synthesis phased on Br revealed all the non-hydrogen atoms, which gave an *R* of 0·38. Five cycles of full-matrix least-squares refinement were carried out on a CDC 3600 computer with the program of Gantzel, Sparks & Trueblood (1961). Unit weight was given to individual reflexions and refinement of the positional parameters, individual isotropic temperature parameters and a common scale factor reduced *R* to 0·13. A difference synthesis computed at this stage located all 18 hydrogen atoms. The structure was further refined with an anisotropic temperature factor for the bromine atom and inclusion of the hydrogen atoms parameters, which were not refined. A Hughes (1941) weighting scheme was employed with weights $1/w^2$ where $w = |F_o|$ for $|F_o| \geq 40\cdot0$, and $w = 40\cdot0$ for $|F_o| < 40\cdot0$. After three cycles of refinement *R* dropped to a final value of 0·097. The shifts in the last cycle were less than 1/10th of the standard deviation in parameters.

Atomic scattering factors used for Br, O, N, C and H are those listed in *International Tables for X-ray Crystallography* (1962). Anomalous dispersion corrections were applied to Br⁻ in the form $f = [(f_o +$

Table 1(*a*). *Atomic coordinates and thermal parameters*

	x	*y*	*z*	*B*(Å²)
Br	0·18358 (21)	0·30504 (11)	0·50752 (8)	*
C(1)	0·7352 (18)	0·5613 (10)	0·2352 (7)	2·25
C(2)	0·7420 (17)	0·4611 (9)	0·3012 (7)	1·81
C(3)	0·7679 (19)	0·3463 (10)	0·2519 (7)	2·44
C(4)	0·5860 (21)	0·3306 (11)	0·1832 (8)	3·14
C(5)	0·5809 (21)	0·4297 (11)	0·1158 (8)	3·17
C(6)	0·5510 (20)	0·5442 (11)	0·1625 (8)	2·88
C(7)	0·9378 (20)	0·5651 (10)	0·1900 (8)	2·80
C(8)	0·9741 (19)	0·3497 (10)	0·2089 (7)	2·52
C(9)	0·7911 (22)	0·4303 (12)	0·0728 (9)	3·48
C(10)	0·9685 (19)	0·4490 (10)	0·1419 (7)	2·55
C(11)	0·5508 (19)	0·4539 (10)	0·3530 (7)	2·60
N	0·9211 (15)	0·4796 (8)	0·3689 (6)	2·42
O(1)	0·5826 (17)	0·3806 (9)	0·4176 (7)	4·57
O(2)	0·3876 (15)	0·5020 (8)	0·3360 (6)	3·74

*b_{11}	0·01615	b_{12}	−0·00123
b_{22}	0·00592	b_{13}	0·00313
b_{33}	0·00267	b_{23}	−0·00113

Temperature factor:

$$\exp\left[-(b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + b_{12}hk + b_{13}hl + b_{23}kl)\right].$$

Table 1(*b*). *Coordinates of hydrogen atoms from the difference synthesis*

	x	*y*	*z*	*B*(Å²)	Bonded to
H(1)	1·100	0·495	0·369	2·2	N
H(2)	0·900	0·550	0·400	2·2	N
H(3)	0·944	0·416	0·411	2·2	N
H(4)	0·463	0·356	0·446	4·3	O(1)
H(5)	0·711	0·622	0·275	2·1	C(1)
H(6)	0·789	0·292	0·297	2·2	C(3)
H(7)	0·591	0·250	0·161	3·0	C(4)
H(8)	0·467	0·331	0·219	3·0	C(4)
H(9)	0·450	0·420	0·065	2·9	C(5)
H(10)	0·567	0·625	0·114	2·8	C(6)
H(11)	0·433	0·539	0·200	2·8	C(6)
H(12)	1·056	0·581	0·239	2·4	C(7)
H(13)	0·900	0·625	0·142	2·4	C(7)
H(14)	0·966	0·272	0·178	2·2	C(8)
H(15)	1·100	0·361	0·258	2·2	C(8)
H(16)	0·800	0·497	0·025	3·1	C(9)
H(17)	0·800	0·350	0·033	3·1	C(9)
H(18)	1·133	0·475	0·128	2·2	C(10)

$\Delta f')^2 + \Delta f''^2]^{1/2}$ where $\Delta f'$ and $\Delta f''$ were given values of −0·9 and +1·5 respectively.

Table 1(*a*) gives the final coordinates of the non-hydrogen atoms and Table 1(*b*) the coordinates of the hydrogen atoms obtained from the difference synthesis. Table 2 gives the observed and calculated structure factors.

Description of the structure

The bond lengths and angles are given in Fig. 1 and listed in Table 3. The average standard deviations of the C–C and C–O bonds are 0·017 and 0·016 Å respectively. The average standard deviation of the C–C–C bond angles is 1·2°. The C–C bonds of the adamantane range from 1·499 to 1·562 Å with a mean value of 1·538 Å which is close to the expected value of 1·54 Å. The C(9)–C(10) bond of 1·499 Å has a slightly low value, but lies within 3σ of the expected value. The C–C–C bond angles of the adamantane range from 107·1 to 110·5° with a mean value of 109·46° which is the expected tetrahedral angle. The C(2)–N bond (1·492 Å) is close to the expected value of 1·487 Å (Marsh & Donohue, 1967). The mean values of the C–H, N–H, and O–H bond lengths are 1·05, 1·03, and 0·96 Å respectively.

Molecular conformation

The adamantane part of the molecule consists of 4 cyclohexane rings, and the torsion angles for each of these rings are given in Table 4. These angles suggest that each ring has a nearly perfect chair conformation; the overall mean torsion angle of 59·95° is very close to the expected value of 60° for a perfectly staggered chair conformation of cyclohexane with tetrahedral bond angles. It may be noted that for free cyclohexane the expected torsion angle is ±54·4° with the bond angles not tetrahedral, but having a value of 111·5° (Bixon & Lifson, 1967). This has been found to

Table 2. *Observed and calculated structure factors*

Table 3. *Bond lengths and angles with their standard deviations*

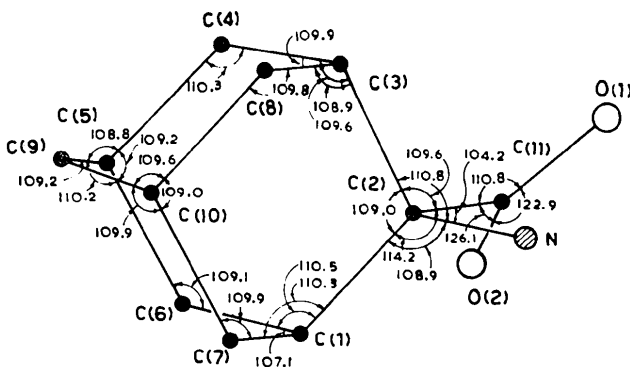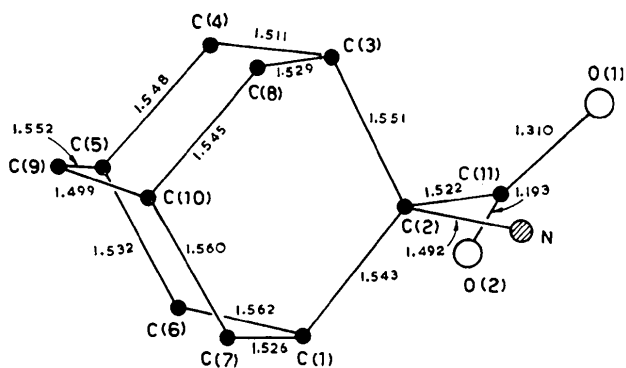| Bond lengths		Bond angles	
C(1)—C(2)	1·543 (15) Å	C(2)—C(1)—C(6)	110·5 (1·1)°
C(1)—C(6)	1·562 (17)	C(2)—C(1)—C(7)	110·3 (1·1)
C(1)—C(7)	1·526 (17)	C(6)—C(1)—C(7)	107·1 (1·1)
C(2)—C(3)	1·551 (16)	C(1)—C(2)—C(3)	109·0 (1·0)
C(3)—C(4)	1·511 (18)	C(2)—C(3)—C(4)	109·6 (1·1)
C(3)—C(8)	1·529 (17)	C(2)—C(3)—C(8)	108·9 (1·1)
C(4)—C(5)	1·548 (19)	C(4)—C(3)—C(8)	109·9 (1·2)
C(5)—C(6)	1·532 (18)	C(3)—C(4)—C(5)	110·3 (1·2)
C(5)—C(9)	1·552 (19)	C(4)—C(5)—C(6)	109·2 (1·3)
C(7)—C(10)	1·560 (17)	C(4)—C(5)—C(9)	108·8 (1·3)
C(8)—C(10)	1·545 (17)	C(6)—C(5)—C(9)	110·2 (1·3)
C(9)—C(10)	1·499 (18)	C(1)—C(6)—C(5)	109·1 (1·2)
C(2)—C(11)	1·522 (17)	C(1)—C(7)—C(10)	109·9 (1·2)
C(2)—N	1·492 (15)	C(3)—C(8)—C(10)	109·8 (1·2)
C(11)-O(1)	1·310 (16)	C(5)—C(9)—C(10)	109·2 (1·3)
C(11)-O(2)	1·193 (15)	C(7)—C(10)—C(8)	109·0 (1·2)
		C(7)—C(10)—C(9)	109·9 (1·2)
		C(8)—C(10)—C(9)	109·6 (1·2)
		C(1)—C(2)—C(11)	114·2 (1·0)
		C(3)—C(2)—C(11)	109·6 (1·1)
		C(1)—C(2)—N	108·9 (1·0)
		C(3)—C(2)—N	110·8 (1·1)
		C(11)-C(2)—N	104·2 (1·1)
		C(2)—C(11)-O(1)	110·8 (1·2)
		C(2)—C(11)-O(2)	126·1 (1·2)
		O(1)—C(11)-O(2)	122·9 (1·3)

Fig. 1. Bond lengths and angles.

be generally true in the case of X-ray structure investigations of cyclohexane compounds (Chacko *et al.*, 1971*b*; Chacko & Srinivasan, 1973).

Table 4. *The torsion angles of the four cyclohexane systems of the adamantane moiety*

(1) Atoms C(1), C(2), C(3), C(4), C(5) and C(6)

Torsion angle about bonds	
1—2—3—4	− 59·5°
2—3—4—5	+ 61·2
3—4—5—6	− 61·3
4—5—6—1	+ 58·9
5—6—1—2	− 58·8
6—1—2—3	+ 58·3

(2) Atoms C(1), C(2), C(3), C(8), C(10) and C(7)

1—2—3—8	+ 60·9
2—3—8—10	− 61·6
3—8—10—7	+ 60·1
8—10—7—1	− 58·3
10—7—1—2	+ 58·9
7—1—2—3	− 60·0

(3) Atoms C(1), C(7), C(10), C(9), C(5) and C(6)

1—7—10—9	+ 61·8
7-10—9—5	− 58·6
10—9—5—6	+ 59·2
9—5—6—1	− 60·5
5—6—1—7	+ 61·4
6—1—7-10	− 61·4

(4) Atoms C(3), C(8), C(10), C(9), C(5) and C(4)

3—8—10—9	− 60·4
8-10—9—5	+ 61·2
10—9—5—4	− 60·4
9—5—4—3	+ 59·0
5—4—3—8	− 58·5
4—3—8—10	+ 58·5

The nitrogen is in the NH_3^+ state with the bromine existing as Br^-. A rare feature, as far as amino acid structures are concerned, is that the nitrogen is 1·07 Å out of the plane containing the carboxyl group and C(2). Table 5 gives the equation of the least-squares plane and the corresponding deviation of atoms from this plane. In amino acid structures it is also found that C′=O is *cis* to the amino nitrogen about the C^{α}-C′ bond which results from the electrostatic attraction between the positively charged nitrogen and the negatively charged oxygen atom. In this structure it is found that C′=O is nearly *trans* to the nitrogen. A method of describing the conformation of the carboxyl group has been given (Ramachandran & Lakshminarayanan, 1966). Starting from the C^{α} atom and looking down the C^{α}-C′ bond, a clockwise rotation of the C–O bonds from the position *cis* to C^{α}-N defines the ψ_1 and ψ_2 angles of the carboxyl group. ψ_1 and ψ_2 are expected to be 180 and 0° respectively (Lakshminarayanan, Sasisekharan & Ramachandran, 1967). For this structure, however, the values of ψ_1 and ψ_2 are 309·8 and 133·9°, respectively. The projection down C(2)-C(11) is shown in Fig. 2. There is only one
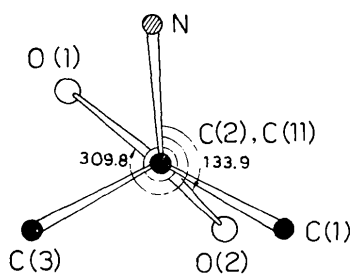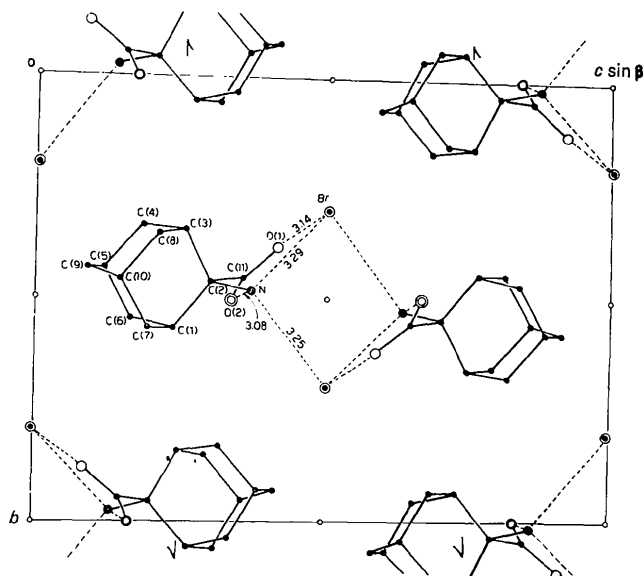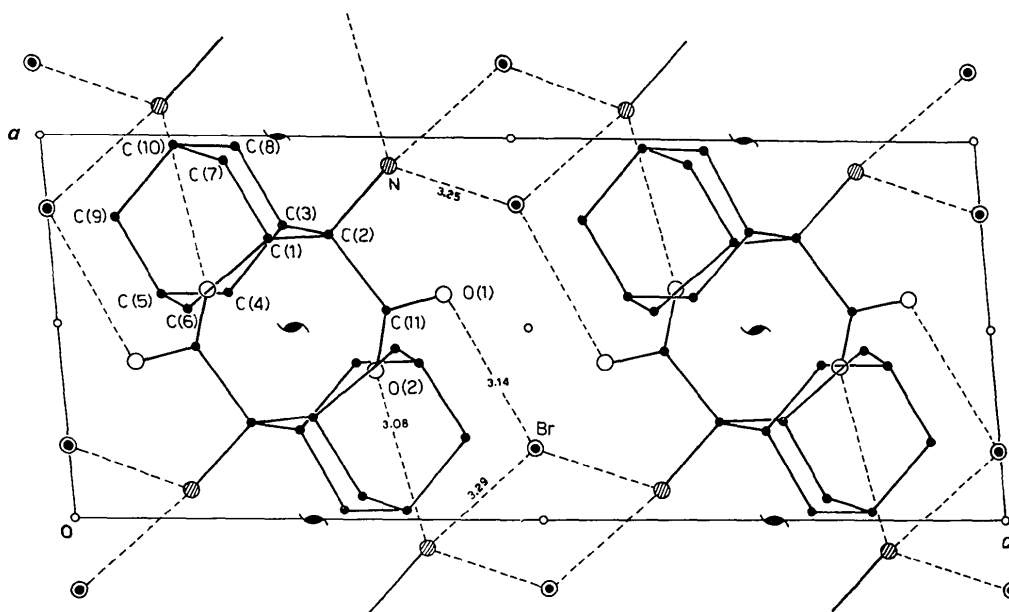
Fig. 2. Projection down the C(2)–C(11) bond.

Fig. 3. Molecular packing viewed down a.

other structure where the carboxyl group has such a reversal in its conformation (Dawson, 1967).

Table 5. *Equation of and deviations from the best plane passing through the atoms* C(2), C(11), O(1) *and* O(2)

$$0.2912x + 0.7542y + 0.5885z = 8.0227$$

C(2)	−0.006 Å
C(11)	+0.021
O(1)	−0.006
O(2)	−0.008
N	+1.073

Molecular packing and hydrogen bonding

Projections down **a** and **b** are given in Figs. 3 and 4. The structure is stabilized by a three-dimensional network of strong hydrogen bonds. There are four protons available for hydrogen-bond formation and each is involved in intermolecular hydrogen bonds. Apart from these hydrogen bonds, there are no other short contacts.

The hydrogen-bond distances and angles are given in Table 6. The hydroxyl oxygen atom O(1) forms a strong hydrogen bond of 3·14 Å with the bromide ion. The amino nitrogen (NH$_3^+$) forms a hydrogen bond of length 3·08 Å to the O(2) atom of the molecule translated by one unit along **a**, the remaining two hydrogen bonds of lengths 3·29 and 3·25 Å being to symmetry-related bromide ions. The projection down C(2)–N is given in Fig. 5, showing the three hydrogen-bond directions to be staggered with respect to the bonds covalently linked to C(2). The two hydrogen bonds O(1)···Br (3·14 Å) and N···Br^{ii} (3·25 Å) are strong and are shorter than the lower limit of the respective

Fig. 4. Molecular packing viewed down b.

hydrogen-bond type (Stout & Jensen, 1968). From the hydrogen-bonding scheme it is clear that the carboxyl group has its peculiar twist about the C(2)–C(11) bond in order to satisfy the two hydrogen bonds in which O(1) acts as a donor [O(1)–H(4)$\cdots$Br = 3·14 Å] and O(2) acts as an acceptor [N–H(1)$\cdots$O(2^i) = 3·08 Å]. This would not have been possible if the carboxyl group had the normal conformation.

Table 6. *Hydrogen-bond lengths and angles*

Donor	Acceptor	D$\cdots$A	H$\cdots$A	∠C–D $\cdots$A	∠D–H $\cdots$A
C(11)–O(1)$\cdots$Br		3·14 Å	2·18 Å	116·1°	178°
C(2)—N$\cdots$O(2^i)		3·08	1·95	126·3	164
C(2)—N$\cdots$Br^i		3·29	2·41	132·7	149
C(2)—N$\cdots$Br^{ii}		3·25	2·30	109·5	169

Symmetry code:

(i) 1 + x, y, z
(ii) 1 − x, 1 − y, 1 − z.

References

ALDEN, R. A., KRAUT, J. & TAYLOR, T. G. (1968). *J. Amer. Chem. Soc.* 90, 74–82.

BIXON, M. & LIFSON, S. (1967). *Tetrahedron,* 23, 769–784.

CHACKO, K. K. & SRINIVASAN, R. (1973). To be published.

CHACKO, K. K., SRINIVASAN, R. & ZAND, R. (1971a). *J. Cryst. Mol. Struct.* 1, 213–224.

CHACKO, K. K., SRINIVASAN, R. & ZAND, R. (1971b). *J. Cryst. Mol. Struct.* 1, 261–269.

CHANDRASEKHARAN, R., MALLIKARJUNAN, M., GODAVARI CHANDRASEKHARAN & ZAND, R. (1968). *Curr. Sci.* 37, 91–93.

DAWSON, B. (1967). Private communication to A.V. LAKSHMINARAYANAN, V. SASISEKHARAN & G. N. RAMACHANDRAN, G. N. (1967). In *Conformation of Biopolymers,* edited by G. N. RAMACHANDRAN, p. 61. London: Academic Press.

GANTZEL, P. K., SPARKS, R. A. & TRUEBLOOD, K. N. (1961). *UCLALS*1, Univ. of California Program.

HUGHES, E. W. (1941). *J. Amer. Chem. Soc.* 63, 1737–1752.

International Tables for X-ray Crystallography (1962). Vol. III. Birmingham: Kynoch Press.

KARLE, I. L. & KARLE, J. (1965). *J. Amer. Chem. Soc.* 87, 918–920.

LAKSHMINARAYANAN, A. V., SASISEKHARAN, V. & RAMACHANDRAN, G. N. (1967). In *Conformation of Biopolymers,* edited by G. N. RAMACHANDRAN, p. 61. London: Academic Press.

MALLIKARJUNAN, M., CHACKO, K. K. & ZAND, R. (1972). *J. Cryst. Mol. Struct.* 2, 53–66.

MARSH, R. E. & DONOHUE, J. (1967). *Advanc. Protein Chem.* 22, 235–256.

NORDMAN, C. E. & SCHMITKONS, D. L. (1965). *Acta Cryst.* 18, 764–767.

RAMACHANDRAN, G. N. & LAKSHMINARAYANAN, A. V. (1966). *Biopolymers,* 4, 495–497.

RAO, S. T. & SUNDARALINGAM, M. (1972). *Acta Cryst.* B28, 694–699.

ROLLETT, J. S. & SPARKS, R. A. (1960). *Acta Cryst.* 13, 273–274.

SCHLEYER, P. VON R., OSAWA, E. & DREW, M. G. B. (1968). *J. Amer. Chem. Soc.* 90, 5034–5036.

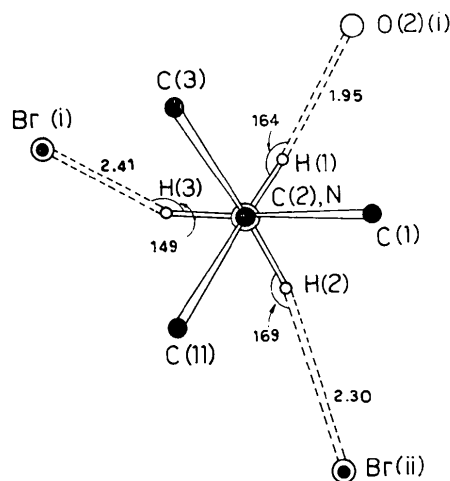STOUT, G. H. & JENSEN, L. H. (1968). *X-ray Structure Determination,* p. 303. New York: Macmillan.

Fig. 5. Projection down the C(2)–N bond.