

The Crystal Structure of 1,4-Cyclohexadiene-1-glycine

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Abstract: The crystal structure of 1,4-cyclohexadiene-1-glycine was investigated to determine the conformation of the 1,4-cyclohexadiene ring. The crystals are monoclinic, space group $P2_1/c$, with the unit cell parameters $a = 15.864$, $b = 4.810$, $c = 10.022$ Å, $\beta = 98.03^\circ$, and $z = 4$ formula weights per unit cell. The structure was solved by the Karle symbolic addition method and refined to a conventional R of 9.3% for 625 observed reflections. The 1,4-cyclohexadiene ring was found to be planar; extensive intermolecular hydrogen bonding is present, and the molecules are in the zwitterion form.

The conformation of the 1,4-cyclohexadiene ring has been studied by various methods without conclusive results. Infrared² and Raman³ spectroscopic studies of 1,4-cyclohexadiene and the X-ray diffraction study of 9,10-dihydro-1,2:5,6-dibenzanthracene⁴ suggest the ring is planar, although the spectra do not distinguish between the planar and the rapidly inverting boat conformations. The dipole-moment measurement of 1,4-dichloro-1,4-cyclohexadiene,⁵ potential energy calculations,⁶ and the X-ray study of 9,10-dihydroanthracene⁷ predict a nonplanar boat conformation for 1,4-cyclohexadiene. An electron diffraction study of 1,4-cyclohexadiene indicates a planar conformation is the most probable.⁸ Recent nuclear magnetic resonance studies of 1,4-cyclohexadiene have shown the methylene protons to be equivalent. This equivalence is consistent with either the planar or the inverting boat conformation.⁹

1,4-Cyclohexadiene-1-alanine has been observed to be an effective antagonist of phenylalanine in strains of *Escherichia coli*,^{9,10} and this fact suggested the possibility of the planar conformation of the 1,4-cyclohexadiene ring in this compound. Because no X-ray diffraction studies had been made of the 1,4-cyclohexadiene ring except when included in a polycyclic ring system, the X-ray diffraction investigation of 1,4-cyclohexadiene-1-glycine was undertaken.

Experimental Section

A suitable single crystal was obtained by slow evaporation of an aqueous solution of DL-1,4-cyclohexadiene-1-glycine (kindly furnished by R. M. Gipson); the crystal was found to be monoclinic, $P2_1/c$. The following lattice constants were determined by a least-squares fit of two θ values measured on a diffractometer at a 1° take-off angle and with a 0.05° receiving slit: $a = 15.864 \pm 0.005$ Å; $b = 4.810 \pm 0.005$ Å; $c = 10.022 \pm 0.005$ Å; $\beta = 98.03 \pm 0.04^\circ$.

No density measurement was made since there were only four crystals large enough for data collection or density measurement. The volume of the unit cell was found to be approximately one-half

that of D-phenylalanine which has eight molecules per unit cell in space group $P2_12_1$.¹¹ It was therefore assumed that the unit cell of 1,4-cyclohexadiene-1-glycine contains four molecules.

Intensities of 1139 reflections ($d_{\min} = 0.8894$) were measured by the stationary counter, stationary crystal technique with Cu $K\alpha$ radiation and balanced filters; 625 of these with net intensity of more than four counts were considered to be observed reflections. Five standard reflections were measured every 3 hr to monitor any change in the crystal or the equipment, and there was no variation in the intensity of these reflections during the data collection. The intensity data were converted to structure amplitudes by applying Lorentz and polarization factors, correcting for $\alpha_1\alpha_2$ splitting, and approximately correcting absorption as a function of the diffractometer ϕ setting.

Structure Determination. The structure amplitudes were placed on an absolute scale with thermal motion removed by a plot of the $K(s)$ curve,¹² and then normalized structure-factor magnitudes were calculated. The phases of 123 of the large E factors were determined by the Karle symbolic addition procedure.¹³ The origin-determining phases and four symbols were assigned as shown in Table I. It became evident that C and D were equal and that $A = +$. The first E map was calculated with $A = B = +$ and $C = D = -$, but no meaningful peaks were found. The second E map was calculated with $B = -$ and $A = C = D = +$, and the structure of 1,4-cyclohexadiene-1-glycine was revealed except with a single spurious peak as large as the smallest atomic peak. The spurious peak was not within bonding distance of any of the atomic peaks and was eliminated from consideration.

Table I

h	k	l	E	Sign or symbol
2	4	-7	3.26	+
8	1	-9	3.25	+
13	2	1	2.94	+
7	1	-1	2.75	A
2	1	-9	2.88	B
9	1	5	2.85	C
11	1	3	2.78	D

Refinement of the Structure. After two cycles of isotropic refinement by full-matrix least squares the R value ($\sum(|F_o| - |F_c|)/\sum|F_o|$) was 15.7%. A difference density was calculated, and it showed areas of positive density in the vicinity of probable hydrogen positions. The hydrogen atoms were included in the least squares with constant isotropic thermal parameters of 4.0 Å². Anisotropic refinement with unit weights reduced the R to its final value of 9.3% with the weighted $R(\sqrt{\sum W(|F_o| - |F_c|)^2}/\sqrt{\sum W|F_o|^2})$ equal to 9.8%. With the unobserved reflections included the R value was 16.7% and the weighted R was 14.7%. A difference density was calculated using the refined heavy atom coordinates in the structure-factor calculation and including all reflections. The map

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(2) H. D. Stidham, *Spectrochim. Acta*, **21**, 23 (1965).

(3) B. J. Monostori, *J. Mol. Spectrosc.*, **12**, 129 (1964).

(4) J. Iball, *Acta Crystallogr.*, **11**, 476 (1958).

(5) I. Miyagawa, *Bull. Chem. Soc. Jap.*, **27**, 177 (1954).

(6) F. H. Herbstein, *J. Chem. Soc.*, 2292 (1959).

(7) W. G. Ferrier, *Chem. Ind. (London)*, 1296 (1954).

(8) G. Dallinga and L. H. Toneman, *J. Mol. Structure*, **1**, 117 (1967-1968).

(9) B. A. Shoulders, R. M. Gipson, R. J. Jandacek, S. H. Simonsen, and W. Shive, *J. Amer. Chem. Soc.*, **90**, 2294 (1968).

(10) R. M. Gipson, Dissertation, University of Texas, Austin, Tex., 1965.

(11) J. D. Bernal, *Strukturbericht*, **2**, 876 (1931).

(12) J. Karle and H. Hauptman, *Acta Crystallogr.*, **11**, 757 (1958).

(13) J. Karle and I. Karle, *ibid.*, **21**, 849 (1966).

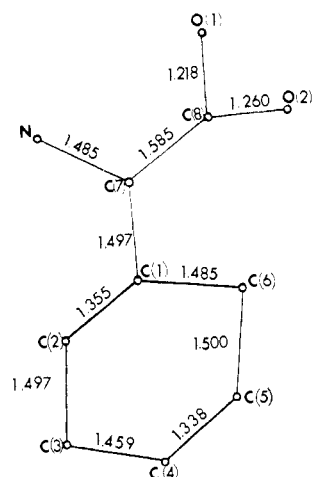


Figure 1. The bond lengths with standard deviations ranging from 0.011 to 0.019 Å with an average of 0.014 Å.

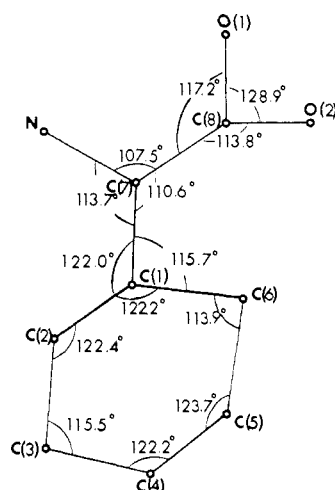


Figure 2. The bond angles with standard deviations ranging from 0.70 to 1.30° with an average of 0.95°.

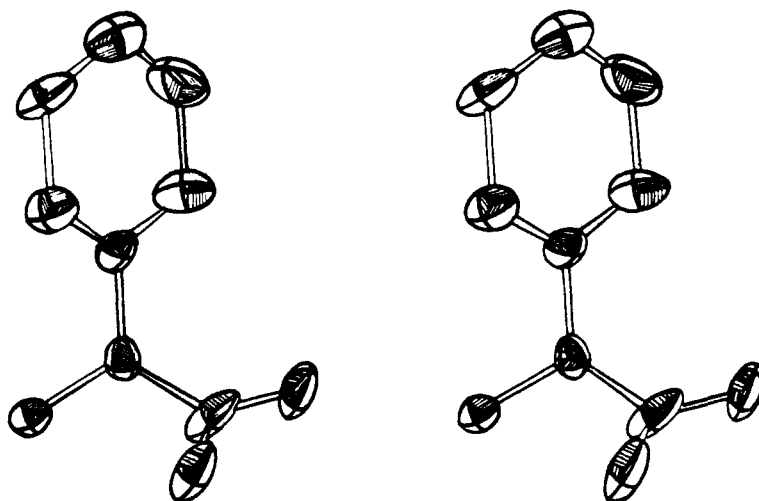


Figure 3. The thermal ellipsoids.

showed all hydrogen atoms with peaks ranging from 0.9 to 1.3 e/Å³. A table of observed and calculated structure amplitudes has been deposited with the ASIS National Publications Service.¹⁴

(14) To procure a copy of this table, order NAPS Document No. 00560 from ASIS National Auxiliary Publications, c/o CCM Information Corp., 909 3rd Ave., New York, N. Y. 10022, remitting \$1.00 for microfilm or \$3.00 for photocopies. Make checks or money orders payable to: ASIS-NAPS.

Discussion of the Structure

Table II lists the atomic fractional coordinates and their standard deviations $\times 10^4$ in parentheses. The

Table II

Atom	X	Y	Z
O(1)	0.0673 (4)	0.8115 (16)	0.3258 (6)
O(2)	0.1209 (4)	0.5262 (15)	0.4922 (6)
N	0.0948 (5)	0.4587 (17)	0.1327 (7)
C(1)	0.2369 (5)	0.4525 (22)	0.2756 (9)
C(2)	0.2699 (6)	0.6289 (27)	0.1912 (10)
C(3)	0.3635 (7)	0.6808 (33)	0.1997 (13)
C(4)	0.4168 (7)	0.5346 (36)	0.3078 (14)
C(5)	0.3843 (7)	0.3627 (33)	0.3924 (14)
C(6)	0.2912 (8)	0.2999 (33)	0.3843 (12)
C(7)	0.1431 (6)	0.4071 (20)	0.2683 (8)
C(8)	0.1046 (6)	0.6038 (22)	0.3713 (10)
H(1)N	0.0295 (7)	0.4879 (26)	0.1142 (10)
H(2)N	0.1089 (7)	0.6607 (28)	0.0756 (11)
H(3)N	0.1035 (7)	0.2792 (26)	0.0632 (11)
HC(2)	0.2227 (7)	0.7593 (25)	0.1102 (10)
H(1)C(3)	0.3671 (7)	0.9325 (28)	0.2036 (11)
H(2)C(3)	0.3834 (7)	0.6801 (25)	0.1279 (10)
HC(4)	0.4837 (8)	0.5717 (27)	0.3376 (12)
HC(5)	0.4341 (7)	0.3477 (26)	0.4641 (11)
H(1)C(6)	0.2734 (7)	0.0577 (28)	0.3641 (12)
H(2)C(6)	0.2903 (8)	0.3949 (29)	0.4506 (13)
HC(7)	0.1404 (7)	0.2085 (27)	0.3170 (11)

hydrogen atoms are labeled corresponding to the atom to which they are bonded (esd $\times 10^3$ in parentheses).

The bond lengths and bond angles are shown in Figure 1 and Figure 2, respectively. The 1.585-Å distance between C(7) and C(8) is 5 esd's longer than the typical 1.527-Å distance (found by averaging the corresponding C-C distances in several amino acids);¹⁵ however, a distance of 1.58 Å has been reported previously in L-arginine hydrochloride.¹⁶ The 0.042-Å difference (nearly 4 esd's) in the C-O distances is also a departure from the

typical amino acid with equal C-O distances.¹⁵ The bond lengths in the ring eliminate the possibility that oxidation of the cyclohexadiene ring to the phenyl group

(15) R. E. Marsh and J. Donohue, *Advan. Protein Chem.*, **22**, 235 (1967).

(16) G. N. Ramachandran, S. K. Mazumdar, K. Venkatesan, and A. V. Lakshminarayanan, *J. Mol. Biol.*, **15**, 232 (1966).

might have occurred. The average double bond in the ring is 1.347 Å, and the single bonds average 1.485 Å, thus showing the ring is the 1,4-cyclohexadiene ring.

The conformation of the 1,4-cyclohexadiene ring was found to be planar within experimental error. The average distance of a ring atom to the best plane fitted to the ring atoms is 0.007 Å. The individual distances to the plane in Å are as follows: C(1) 0.001; C(2) 0.009; C(3) 0.010; C(4) 0.009; C(5) 0.001; and C(6) 0.010. The equation of the plane for x , y , z in fractional coordinates is $-2.8219x + 3.6586y + 6.4449z = 2.7623$. The anisotropic thermal parameters are listed with their estimated standard deviation in Table III.

Table III. Anisotropic Thermal Parameters $\times 10^4$ ^a

Atom	$\exp -[\beta(11)h^2 + \beta(22)k^2 + \beta(33)l^2 + 2\beta(12)hk + 2\beta(13)hl + 2\beta(23)kl]$					
	$\beta(11)$	$\beta(22)$	$\beta(33)$	$\beta(12)$	$\beta(13)$	$\beta(23)$
O(1)	40 (3)	399 (37)	84 (8)	19 (11)	36 (4)	3 (16)
O(2)	51 (3)	468 (41)	59 (7)	6 (10)	32 (4)	22 (15)
N	20 (3)	329 (45)	63 (9)	-5 (10)	11 (4)	-10 (17)
C(1)	29 (4)	401 (58)	71 (10)	13 (14)	17 (6)	-58 (22)
C(2)	34 (5)	634 (79)	108 (12)	-20 (17)	16 (7)	9 (27)
C(3)	29 (5)	871 (83)	144 (16)	-28 (18)	36 (8)	-43 (35)
C(4)	27 (4)	962 (106)	146 (17)	15 (22)	19 (8)	-22 (40)
C(5)	34 (6)	921 (103)	144 (17)	37 (20)	-10 (8)	-79 (37)
C(6)	32 (5)	764 (93)	109 (17)	18 (20)	7 (8)	-70 (32)
C(7)	29 (4)	293 (50)	52 (10)	22 (12)	8 (5)	16 (19)
C(8)	31 (5)	280 (56)	101 (13)	26 (14)	30 (6)	31 (22)

^a Standard deviations $\times 10^4$ are in parentheses.

The 50% probability ellipsoids are shown in a stereoscopic drawing in Figure 3. Although there is large thermal motion in the ring, it does not appear to suggest ring inversion between the boat conformations.

The nitrogen atom was found to be bonded to three hydrogen atoms thus suggesting the zwitterion form for the compound in the crystal. The intramolecular hydrogen bonding in the crystal is extensive. Each mole-

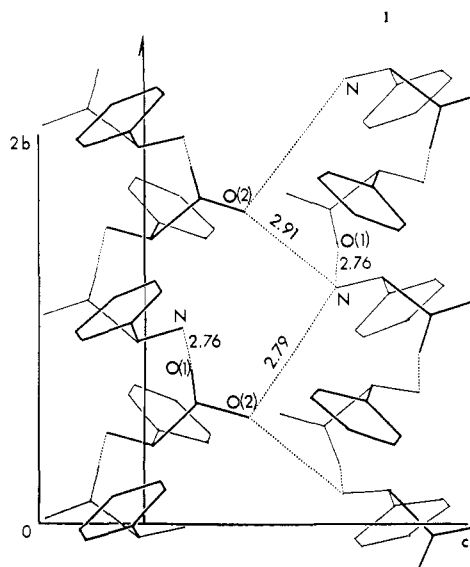


Figure 4. The three types of hydrogen bonds and intermolecular N-O distances.

cule interacts with six other molecules through hydrogen bonding, with all three of the hydrogens bonded to the nitrogen taking part. Table IV summarizes the hydrogen bonding. The type I hydrogen forms a helix around the screw axis, while types II and III bond molecules related by the glide plane (Figure 4).

Table IV

Type of H bond	O-N distance, Å	O-H distance, Å	NHO angle, deg
I	2.76	1.92	134.9
II	2.79	1.67	167.3
III	2.91	1.75	174.8

Acknowledgment. We are indebted to the Robert A. Welch Foundation for financial support of this project.