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The Molecular Structure of 1-Phenyl-3-methyl-3-azabicyclo[3.3.1]nonan-9-one Hydrochloride determined by X-Ray Studies

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The conformation and configuration of 1-phenyl-3-methyl-3-azabicyclo[3.3.1]nonan-9-one were examined by X-ray diffraction methods. The 3-azabicyclo[3.3.1]nonane system, like bicyclo[3.3.1]nonane itself, exists in the chair-chair form, in accord with other published reports on related compounds. The title compound, $C_{15}H_{19}NO \cdot HCl \cdot 1/2 H_2O$ crystallizes in space group C2/c with lattice parameters $a=32.263(10)$, $b=7.362(1)$, $c=12.266(6)$ Å, $\beta=99.88(3)°$, and $Z=8$. The intensities of 2510 unique reflections were measured on a Rigaku AFC diffractometer (Cu K_α radiation) and the structure was solved by the direct methods using MULTAN78.

Keywords——X-ray analysis; crystal structure; MULTAN78; 1-phenyl-3-methyl-3-azabicyclo[3.3.1]nonan-9-one; azabicyclo[3.3.1]nonane

The 3-azabicyclo[3.3.1]nonane is of considerable stereochemical interest because of the presence of two fused ring systems free of angular strain. Fig. 1 shows four possible conformations of the 3-azabicyclo[3.3.1]nonan-9-one ring system; one chair-chair, two chair-boat, and one boat-boat. However, the boat-boat form is energetically very unstable compared with the other three forms and hence the possibility of the structure existing in this conformation seems negligible. The conformation of the phenyl group attached to the 3-azabicyclo[3.3.1]nonane ring system is another interesting point, because only a few such examples have been studied by the X-ray diffraction method. The hydrochloride of the title compound recrystallized from methanol contains a half molecule of water, which is considered to occupy a special position in the unit cell.

In this paper, the 3-azabicyclo[3.3.1]nonan-9-one ring system is discussed in detail and compared with the data reported for 3-azabicyclo[3.3.1]nonane hydrobromide(I)[1] and 1,5-dinitro-3-methyl-3-azabicyclo[3.3.1]nonan-7-one(II).[2]

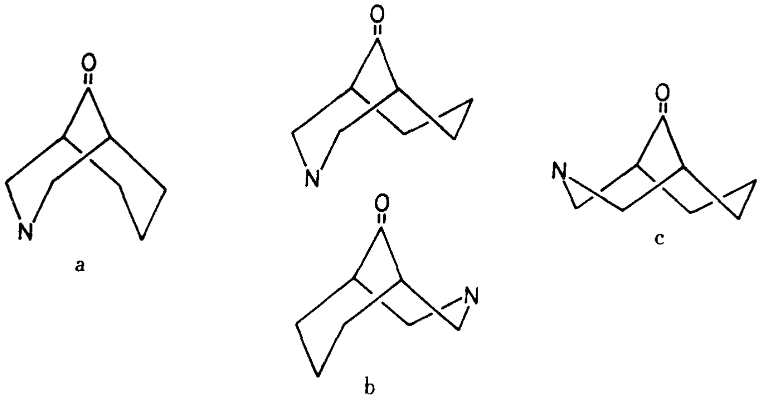

Fig. 1. Possible Conformations of 3-Azabicyclo[3.3.1]nonan-9-one; Chair-chair (a), Chair-boat (b), and Boat-boat (c)

Experimental

Preparation of 1-Phenyl-3-methyl-3-azabicyclo[3.3.1]nonan-9-one Hydrochloride——A mixture of 1.5 g of 2-phenylcyclohexanone in 5 ml of glacial acetic acid and 1.16 g of methylamine hydrochloride in 3.24 g of formalin was refluxed for 2 h, then cooled. After the solvent had been distilled off under reduced pressure, the residue was poured into 15 ml of ice-water. The precipitates were taken up in ether, and the water layer was basified with sodium hydroxide, then extracted three times with 50 ml of ether. The ether extracts were washed with water and dried over anhydrous sodium sulfate. The ethereal solution of the crude product was bubbled through with anhydrous hydrogen chloride gas at 0—5°C for 10 min. The resulting colorless crystals were filtered off and recrystallized from methanol–ethyl acetate (10: 1 v/v). Yield 1.84 g (80%). mp 210°C. Colorless prisms, $C_{15}H_{19}NO \cdot HCl$. Mass spectra (MS) m/z: Calcd 229.1466 (M^+), Found 229.1470 (M^+).

Collection and Reduction of Crystallographic Data——The crystal selected for the measurement of lattice parameters and intensity data was a cleaved fragment which had approximate dimensions of $0.20 \times 0.15 \times 0.20$ mm. A preliminary examination of the crystal carried out on a Rigaku AFC diffractometer showed it to be monoclinic. Systematic absences of $h+k=2n+1$ for hkl established the space group to belong to C2/c. The unit cell parameters at 10°C were refined by the least-squares method using the Bragg angles (Mo, $\lambda=0.791069$ Å) of thirty reflections ($20° < 2\theta < 30°$). The unit cell dimensions and other crystal data are listed in Table I. Intensity data were collected at 10°C on the Rigaku diffractometer utilizing nickel-filtered Cu K_α radiation. The $2\theta-\omega$ scans of 1.0° were employed with scan rates which varied from 0 to 8.0° $\min^{-1}$ depending on a direct manner on the number of counts obtained in a rapid preliminary count of the peak. Background counts were taken at both ends of the scan with ω displaced $\pm 3.0°$ from the K_α peak; the time of each measurement was one-third of the scan time. A total of 2510 unique reflections were measured in the range of $0° < 2\theta < 120°$. The intensities of three standard reflections were measured after every 57 reflections; these intensities dropped by an average of a few percent over the period of data collection, but no correction factor was applied because the decrease was not considered significant. No absorption corrections were applied ($\mu=22.1$ cm^{-1}). Lorentz and polarization corrections were applied to convert intensities to structure amplitudes. Standard deviations in the intensities, $\sigma(I)$, and in the structure amplitudes, $\sigma(F_o)$, were derived directly from counting statistics.

TABLE I. Crystal Data

Mol. formula	$C_{15}H_{19}NO \cdot HCl \cdot 1/2\ H_2O$
Mol. wt.	274.82
Space group	C2/c
Cell dimensions	
a, Å	32.263 (10)
b, Å	7.362 (1)
c, Å	12.266 (6)
β, °	99.88 (3)
Unit cell volume, Å^3	2870.2
Z-Value	8
D_c, gcm^{-3}	1.28
μ, cm^{-1}	22.10

Solution and Refinement of the Structure——The structure was solved by direct methods using MULTAN78[3] to calculate phases for the 300 $|E_o|$ values greater than 1.46. The E-map computed from the phases with the largest combined figure of merit (2.86) revealed all non-hydrogen atoms except for one oxygen atom of water molecule. The subsequent difference Fourier map readily gave the remaining oxygen atom.

The 1858 observed reflections for which F_o were greater than 3 $\sigma(F_o)$ were used for the block-diagonal least-squares refinement of the structure. The function minimized was $\sum w(|F_o|-|F_c|)^2$, where w is the wheight calculated as $1/\sigma^2(F_o)$. An initial refinement using individual isotropic temperature factors for the non-hydrogen atoms led to a conventional $R=(\sum||F_o|-|F_c||)/\sum|F_o|$ of 0.115. After the successive refinement with the anisotropic temperature factors, all hydrogen atoms were readily located from the difference Fourier map. Included in the further refinement were isotropic thermal parameters for hydrogen atoms, which were started with those of the carbon atoms to which they are attached. The refinement, after 6 cycles of block-diagonal least-squares calculation, converged to a conventional R of 0.033 and a weighted $R_w=(\sum w(|F_o|-|F_c|)^2/\sum w|F_o|^2)^{1/2}$ of 0.039. An extinction parameter was not refined, because extinction effects were not considered significant.[8]

The hydrogen atoms refined normally with the isotropic thermal parameters ranging from 2.00 to 6.98 Å^2. The refinement was completed when the largest shift in any parameters among the non-hydrogen atoms was 0.01σ, while the largest shift for the hydrogen atoms was 0.09σ. The final positional and thermal parameters are given in Table II. The largest peak in the final difference map, 0.2 eÅ^{-3}, was located near the chlorine

Table II. Final Positional and Thermal Parameters of Non-hydrogen and Hydrogen Atoms with Estimated Standard Deviations (B_{ij} are $\times 10^4$)

Atoms	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
CL	0.0578(5)	0.2204(5)	−0.3250(5)	9(1)	198(2)	43(1)	−6(2)	5(1)	11(2)
O1	0.1387(5)	0.2036(5)	0.2142(5)	12(1)	230(6)	42(1)	12(2)	4(1)	−34(5)
O2	0	0.5433(5)	−0.2500	19(1)	193(9)	277(7)	0	43(3)	0
C1	0.1480(5)	0.1102(6)	0.0307(5)	6(1)	126(6)	36(2)	−5(2)	4(1)	−9(5)
C2	0.1159(5)	−0.0136(6)	−0.0445(5)	6(1)	132(6)	45(2)	3(3)	−2(1)	−16(1)
N3	0.0734(5)	0.0669(6)	−0.0875(5)	6(1)	136(5)	48(2)	−5(2)	−1(1)	21(5)
C4	0.0556(6)	0.1768(6)	−0.0030(6)	7(1)	173(7)	63(2)	15(2)	11(1)	28(7)
C5	0.0870(5)	0.3066(6)	0.0622(5)	10(1)	155(7)	56(2)	17(2)	7(1)	−15(7)
C6	0.1017(5)	0.4627(5)	−0.0051(5)	13(1)	119(7)	93(3)	5(3)	0(1)	5(7)
C7	0.1301(5)	0.4020(6)	−0.0855(5)	11(1)	131(7)	70(2)	−16(2)	2(1)	50(7)
C8	0.1642(6)	0.2698(6)	−0.0333(5)	9(1)	159(7)	61(2)	−15(3)	8(1)	31(7)
C9	0.1256(5)	0.2023(6)	0.1157(5)	8(1)	123(6)	45(2)	−5(2)	6(1)	−19(6)
C10	0.1832(6)	−0.0166(7)	0.0835(6)	6(1)	140(6)	42(2)	−2(3)	1(1)	−19(6)
C11	0.1741(6)	−0.1563(6)	0.1521(5)	7(1)	181(7)	47(2)	9(3)	3(1)	24(6)
C12	0.2048(5)	−0.2793(6)	0.1979(5)	10(1)	222(8)	54(2)	29(3)	5(1)	43(7)
C13	0.2456(5)	−0.2633(6)	0.1765(6)	9(1)	247(7)	61(2)	31(2)	−5(1)	−29(7)
C14	0.2550(5)	−0.1250(5)	0.1093(5)	6(1)	231(8)	76(2)	6(3)	2(1)	−64(7)
C15	0.2243(6)	−0.0025(5)	0.0622(5)	6(1)	176(7)	66(2)	−6(3)	6(1)	−31(7)
H21	0.109(3)	−0.129(4)	−0.001(3)	1.9(7)					
H22	0.129(3)	−0.055(3)	−0.110(3)	1.9(7)					
H41	0.044(3)	0.077(4)	0.050(3)	2.9(8)					
H42	0.030(3)	0.251(4)	−0.043(3)	3.0(6)					
H5	0.071(3)	0.365(4)	0.125(3)	2.2(7)					
H61	0.116(3)	0.555(4)	0.051(3)	3.3(8)					
H62	0.076(3)	0.528(4)	−0.041(3)	3.2(8)					
H71	0.113(3)	0.346(4)	−0.155(3)	2.2(8)					
H72	0.144(3)	0.516(4)	−0.112(3)	2.8(8)					
H81	0.180(3)	0.214(4)	−0.092(3)	2.2(8)					
H82	0.186(4)	0.338(4)	0.023(3)	2.5(7)					
H11	0.144(3)	−0.170(4)	0.169(3)	2.3(8)					
H12	0.196(3)	−0.391(4)	0.247(3)	3.3(8)					
H13	0.269(3)	−0.360(4)	0.208(3)	4.0(8)					
H14	0.285(3)	−0.119(4)	0.091(3)	3.4(8)					
H15	0.232(3)	0.101(4)	0.012(3)	2.5(8)					
H161	0.056(4)	−0.152(4)	−0.188(4)	3.1(8)					
H162	0.014(4)	−0.027(4)	−0.160(4)	3.4(8)					
H163	0.039(4)	−0.170(4)	−0.068(4)	3.0(8)					
HCL	0.077(4)	0.141(4)	−0.152(4)	3.5(8)					
HH20	0.020(4)	−0.531(4)	−0.286(4)	7.0(8)					

atom. The atomic scattering factors for Cl, O, N and C were those of Cromer and Weber;[4] for H, the scattering factors of Stewart, Davidson, and Simpson[5] were used. Mathematical and computational methods are those of the OSAKA UNIKS system developed at Osaka University.[9]

Discussion

The molecular geometry and the respective atom labeling schemes are presented in the ORTEP drawing of Fig. 2. The bond lengths and angles are schematically shown in Fig. 3. The carbonyl group has the normal bond length (1.246(7) Å), which is in good agreement with that of II (1.263 Å).[2] The mean bond length and angle of the phenyl group are normal: 1.39 Å and 120.0°, respectively. The C–C bonds of rings A and B in the azabicyclo[3.3.1]-nonane have average values of 1.543 Å and 1.550 Å, respectively, while the C–N bond of ring A has an average value of 1.520 A.

The characteristic feature in this structure is the chair-chair conformation of the 3-azabicyclo[3.3.1]nonan-9-one system, which is compared with the data reported for the corresponding fragments of compounds I and II in Table III. One interesting point appears in

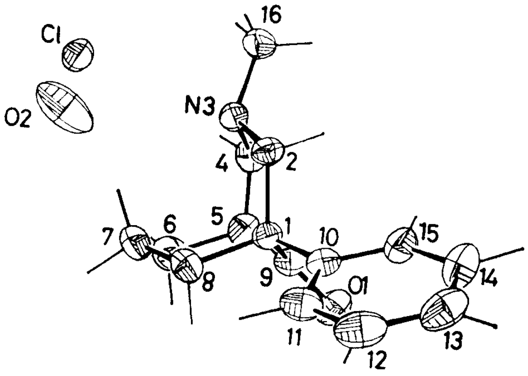

Fig. 2. ORTEP drawing of the Title Compound

Thermal ellipsoids are drawn at the 50% probability level.

the bond lengths listed up in Table III; the distances of C1–C2 and C1–C8 (1.572 (4) and 1.567 (4) Å, respectively) are significantly longer than those of C4–C5 and C5–C6 (1.529 (4) and 1.554 (4) Å, respectively). The significant variations in these C–C bond lengths, which could not be found in I and II, may be due to the bulky substituent of the phenyl group attached to the 1-position. But there are not many examples to be incorporated in Table III for the different groups which would help drawing more meaningful estimates in taking the overall averages of these molecular geometry. Accordingly, the bond lengths and angles of the title compound in Table III are tentatively regarded as representing the normal geometry of the chair-chair form of 3-azabicyclo[3.3.1]nonane. The non-bonded N3–C7 distance (3.071 Å) is almost the same as that of I, 3.02 Å, but significantly different from the N3–C7(=O) distance in II, 2.76 Å, which seems to be due to the special interaction between the lone-pair of nitrogen and the oxygen atom. The bond angles of the three bridgehead atoms (N3, C7 and C9) have values

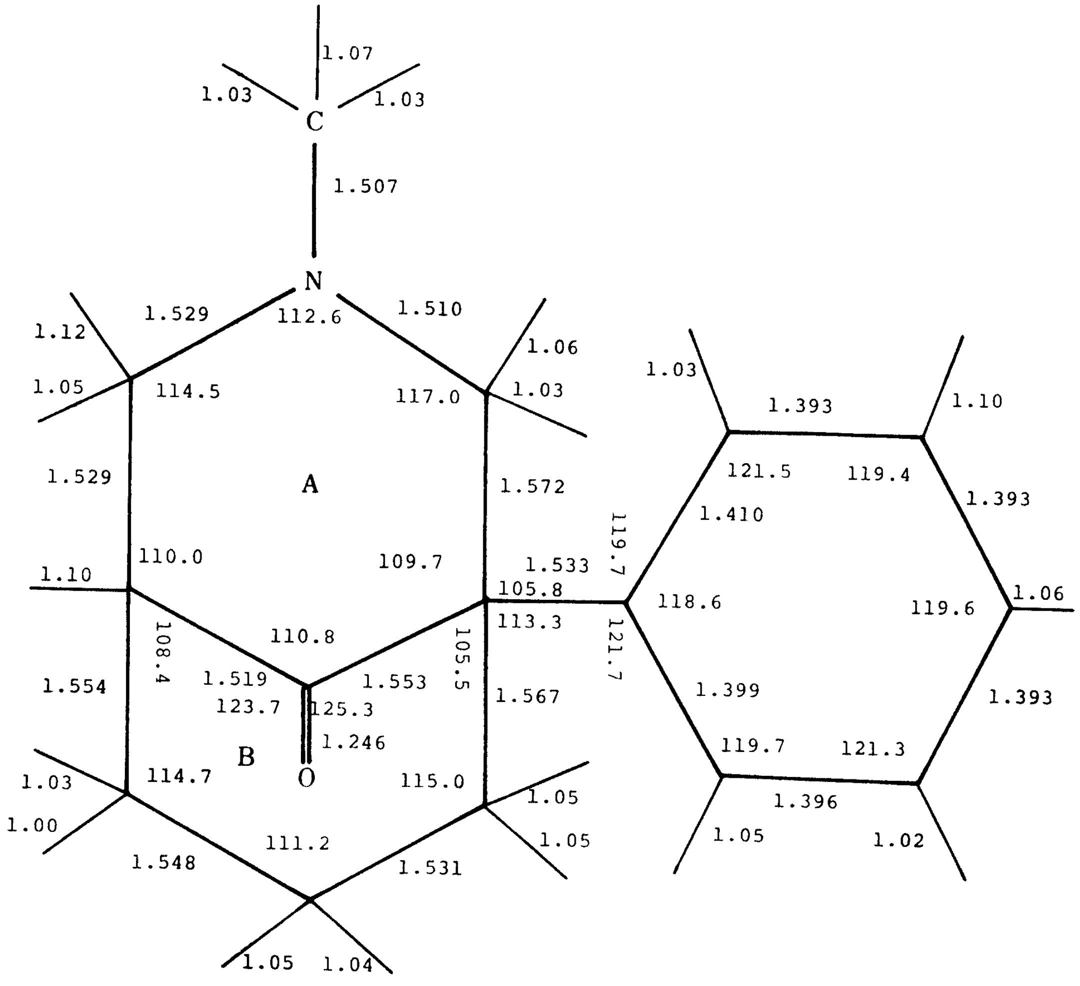

Fig. 3. Bond Lengths (Å) and Angles (Degree)

Standard deviations ranged between 0.007 and 0.009, and 0.4 and 0.7, respectively.

larger than that of an ideal tetrahedron (109.47°) compared to the other bond angles around C1 and C5 atoms in the structure belonging to methylene bridge. On the other hand, the flat parts of the chair form have bond angles between 114° and 117°, which are quite different from normal tetrahedral values. This is due to the considerable distortion of the two cyclohexane rings, which exist in a distorted-chair conformation in the unit cell. Conformational details of ring structures are best understood in terms of torsion angles, which are compared in Table IV for the three structures. The individual values deviate somewhat from the theoretical

TABLE III. Bond Lengths and Angles of the Title Compound, Compounds I and II

Atoms	Title compound[a]	I	II
	Length (Å)		
1-2	1.572	1.47	1.530
1-8	1.567	1.56	1.534
1-9	1.553	1.56	1.520
2-3	1.510	1.52	1.464
3-4	1.529	1.44	1.458
4-5	1.529	1.52	1.525
5-6	1.554	1.51	1.508
5-9	1.519	1.56	1.529
6-7	1.548	1.43	1.525
7-8	1.531	1.54	1.477
	Angle (°)		
2-1-9	109.7	109.0	110.5
1-2-3	117.0	112.0	107.6
3-4-5	114.5	114.0	105.9
2-3-4	112.6	111.0	110.5
4-5-9	110.0	107.0	110.5
8-1-9	105.5	114.0	111.6
9-5-6	108.4	112.0	111.5
5-6-7	114.7	118.0	112.4
1-8-7	115.0	112.0	113.0
6-7-8	111.2	112.0	118.0
4-5-6	113.7	115.0	113.1
2-1-8	111.5	115.0	110.9
1-9-5	110.8	101.0	105.2

a) Standard deviations for the bond lengths and the bond angles ranged between 0.007 and 0.009 Å and between 0.4 and 0.7°, respectively.

TABLE IV. Torsion Angles of the Title Compound, Compounds I and II

Atoms	Angle (°)		
	Title compound	I	II
4-5-9-1	61.1	66.8	61.4
5-9-1-2	−55.4	−69.4	−59.4
3-4-5-9	−56.2	−61.9	−64.2
9-1-2-3	46.4	61.9	61.9
1-2-3-4	−41.4	−49.9	−64.9
2-3-4-5	45.7	50.4	65.2
8-1-9-5	64.7	60.9	64.1
1-9-5-6	−63.8	−59.8	−65.3
7-8-1-9	−57.0	−54.7	−50.8
9-5-6-7	53.2	57.6	52.0
5-6-7-8	−45.4	−44.6	−37.4
6-7-8-1	48.2	41.5	36.4
3-4-5-6	65.5	72.6	59.9
4-5-6-7	−69.5	−68.0	−72.4
7-8-1-2	62.0	63.1	72.2
8-1-2-3	−70.0	−64.5	−62.0

TABLE V. Least-squares Planes and Deviations of Atoms from the Planes

Plane 1: a plane defined by the benzene ring.
$-0.1042X-0.6070Y-0.7878Z+1.3441=0$
C10 0.000; C11 −0.004; C12 0.003
C13 0.001; C14 −0.004; C15 0.004
Plane 2: a plane defined by atoms C1, C2, C4 and C5.
$-0.2130X-0.5592Y-0.8012Z+1.1780=0$
C1 0.028; C2 −0.028; C4 0.035; C5 −0.032
Plane 3: a plane defined by atoms C1, C5, C6 and C8.
$-0.4068X-0.3664Y-0.8368Z+2.5495=0$
C1 0.016; C5 −0.015; C6 0.015; C8 −0.016

values of the cyclohexane torsion angles (±56°).[6,7]

A hydrogen bond (3.181 Å) is formed between the chloride anion and nitrogen atom of ring A which forms zigzag chains along the *c*-axis. Another hydrogen bond (3.266 Å) is found between the chloride anion and water molecules which occupy the special position $(0, y, -1/4)$ in the unit cell. In Table V are given the best least-squares planes together with the displacement of atoms from the best planes. The phenyl ring is twisted 22.5° from being parallel to plane 2 (defined by atoms C1–C5–C6–C8), and is 15.6° from being perpendicular to plane 1 (denfined by atoms C1–C2–C4–C5). The dihedral angle between plane 1 and plane 2 is 112.3°.

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