4-HYDROXY-2,2,6,6 TETRAMETHYL PIPERIDINE, A PERCURSOR OF THE SPIN LABEL 4-HYDROXY-2,2,6,6 PIPERIDINE-1-OXYL

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ABSTRACT. 4-Hydroxy-2,2,6,6 tetramethyl piperidine, orthorhombic, $C222_1$, $a = 10.144(1)$, $b = 14.157(5)$, $c = 13.382(5)Å$, $V = 1922(2)Å^3$, $Z = 8$, $D_x = 1.091g/cm^3$, $D_{obs} = 1.08g/cm^3$ (measured by the flotation method), $\mu = 4.75cm^{-1}$ (CuKα). The structure was solved by direct methods. A full-matrix least-squares refinement proceeded to 0.047 for 575 reflections measured above background and to 0.081 for all reflections. The molecule is in chair conformation with the hydroxyl group equatorial. The crystal structure consists of parallel sheets of molecules roughly parallel to the (010) in which each nitrogen is hydrogen bonded to the oxygen of two different molecules.

INTRODUCTION

The title compound (I), whose chemical configuration formula is shown in Figure 1 is used in the preparation of the spin label 4-hydroxy-2,2,6,6-tetramethyl-4-piperidine-1-oxyl. This radical (II) is used as a spin-label in structure-function studies of biological molecules [1]. As the structure of (II) is known [2,3], an EPR study was done to obtain information on the dependence of the magnetic parameters of this spin label on the structure of its environment. To do this a small amount of the radical (II) was introduced as impurity in the crystal matrix of (I), single crystals obtained, and the EPR measurements performed [4]. To provide the necessary data for the interpretation of the EPR properties of (II) in that environment the crystal structure determination of (I) was undertaken.

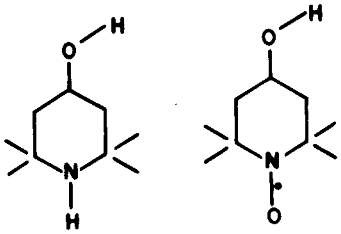
(I) (II)

Figure 1. Chemical configuration formula of 4-hydroxy-2,2,6,6 tetramethyl piperidine and of the spin label 4-hydroxy-2,2,6,6 piperidine-1-oxyl.

This was specially interesting in view of the presence of hydrogen bonds in the crystal that could affect the g-tensor and A-tensor, which are the main EPR parameters giving information on the electron localization in the N-O paramagnetic fragment. From EPR crystal studies the orientation of these tensors relative to the crystal and in some cases relative to the molecular orientation can be obtained [5].

EXPERIMENTAL AND METHODS

The compound I was crystallized by slow evaporation from a mixture of diethyl ether and n-hexane (normally 2:1). The product was obtained from Aldrich Co. and used without further purification. Tabular colorless prismatic crystals were obtained with well developed (100) faces. Unfortunatelly they were quite unstable regarding single crystalinity desintegrating spontaneously into a crystalline powder without change in either cell dimensions or systematic extinctions as could be seen from its diffraction pattern. The desintegration is speeded up when the crystals are exposed to x-rays but can be considerably slowed if the crystals are sealed in a glass capillary tube. For this reason a crystal of approximate dimensions 0.2 x 0.2 x 0.3 mm sealed in a Lyndeman glass capillary was used for the data collection on a Enraf-Nonius CAD-4 single crystal diffractometer. The cell dimensions were refined by least-squares method from the setting angles of 25 reflections. Three-dimensional intensity data was collected using graphite-monochromated CuKα radiation up to $2\theta = 120^{o}$. Three standard reflections, measured every 3600 sec to check on any crystal deterioration, did not show any significant intensity variation. The ω-2θ scanning mode with varying interval was used. Of the 945 recorded independent reflections 575 were observed above background ($I > 3\sigma(I)$, where $\sigma(I)$ was based on counting statistics). The data was reduced to structure factors without absorption correction. The structure was solved by application of MULTAN 78 [6]. All the non-hydrogen atoms were found on the E-map based on the set of phases giving the highest combined figure of merit. Several hydrogen, including the hydroxyl and the amino hydrogens, appeared on a difference Fourier map and the positions of the remainder were calculated. Refinement, by minimization of the function $\Sigma\,\omega(k|Fo|-|Fc|)^2$, was carried out by full-matrix least squares calculations. As in the first stages of refinement it was found a high correlation between position and thermal parameters of C(2) and C(6), C(7), and C(9), C(8) and C(10), probably due to the molecular symmetry, it was necessary to include interatomic distances constraints in the refinement. Least squares refinement done using weights calculated as $\omega_i = 1.0000/(\sigma(F)^2 + 0.0026\ F^2)$ led to a final R of 0.047 . The atomic scattering factors used were those of Cromer & Waber [7].

Lists of structure factors, anisotropic thermal parameters and hydrogen positional and thermal parameters are available by request from Y.P. Mascarenhas.

RESULTS AND DISCUSSION

The final atomic parameters are given in Table I. Bond lengths and angles are given in Figure 2 with atomic numbering. The molecular structure of (I) is similar to that of (II) as found by J. Lajzerowicz-Bonneteau [2] and further refined by L.J. Berliner [3]. The piperidine ring has the chair configuration with the hydroxyl group and the hydrogen bonded to the ring nitrogen equatorial. Some torsion angles are: O(1)-C(4)-C(3)-C(2) = 178.9, O(1)-C(4)-C(5)-C(6)=178.2, C(3)-C(2)-N(1)-C(6) = 47.1, C(2)-N(1)-C(6)-C(5) = 50.1, N(1)-C(6)-C(5)-C(4) = 54.9° and N(1)-C(2)-C(3)-C(4) = 50.1. C-N distance and the C2-N-C6 angle are in agreement with similar distance and angle found by M. Cygler et al [8]. for the molecule of 4-ethynyl-2,2,6,6-tetramethylpiperidin-4-ol. The molecular dimensions found in this determination agree with the expected values within their standard deviations.

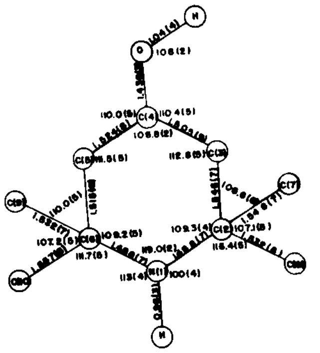

Figure 2. Representation of molecule giving bond lenghts (Å) and angles (°) with standard deviations in parenthesis and atomic numbering.

TABLE I. Atomic coordinates and calculated equivalent isotropic temperature factors with esd's in parenthesis.

For non-H atoms $B_{eq} = \frac{8}{3}\pi^2\Sigma_{ij}\,\vec{a}_i.\vec{a}_j$

For H-atoms the temperature factor is of the form $T = \exp(-B\ sen^2\theta/\lambda^2)$

ATOM	X/A	Y/B	Z/C	B_{eq}
N(1)	0.3318(2)	0.2515(4)	-0.1417(2)	2.63(7)
H(N)	0.336(3)	0.244(5)	-0.213(3)	4.74(0)*
O(1)	0.1169(2)	0.2494(5)	0.1277(1)	3.65(7)
H(O)	0.018(4)	0.231(3)	0.134(3)	5.71(0)*
C(2)	0.2691(5)	0.1602(4)	-0.1145(3)	3.2(2)
C(3)	0.2280(5)	0.1628(5)	-0.0033(4)	3.0(2)
C(4)	0.1503(2)	0.2498(5)	0.0232(2)	2.73(8)
C(5)	0.2329(5)	0.3367(5)	-0.0013(4)	3.0(2)
C(6)	0.2664(5)	0.3411(4)	-0.1115(4)	3.1(2)
C(7)	0.3727(8)	0.0810(4)	-0.1287(6)	5.3(3)
C(8)	0.1470(8)	0.1319(5)	-0.1748(5)	5.6(3)
C(9)	0.3717(7)	0.4167(3)	-0.1300(6)	4.4(2)
C(10)	0.1470(7)	0.3648(5)	-0.1802(6)	5.5(3)

* not refined

An ORTEP stereo representation of the molecular crystal packing is shown in Figure 3. It may be described as two hydrogen bonded parallel sheets of molecules approximately parallel to the (010) crystal face. In Figure 4 it is shown one of these sheets projected along the b axis where it can be seen that the nitrogen atom is hydrogen bonded to the hydroxyl oxygen of two different molecules and each hydroxyl oxygen is hydrogen bonded to two nitrogens of two different molecules. The observed interatomic distances and angles in the hydrogen bond network are shown in Table II.

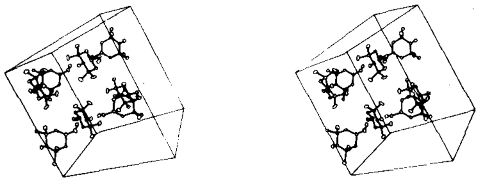

Figure 3. Stereoview of the structure.

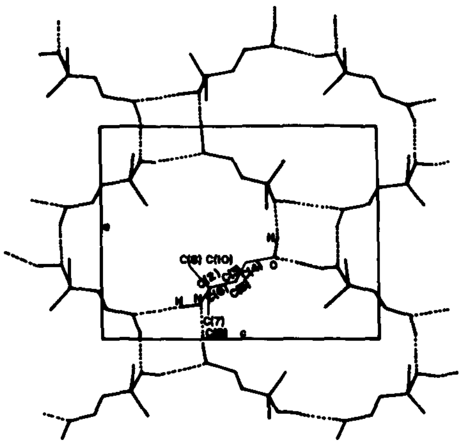

Figure 4. Projection on x,z plane of one sheet of molecules with the hydrogen bond network represented by broken lines.

It is interesting to note that the crystal packing of compound (I) is entirely different from the crystal packing of the nitroxyl radical (II), where the molecules are associated by hydrogen bonds forming chains [9].

TABLE II. Observed interatomic distances and angles in the hydrogen bond network.

A	B	C	D(AB)	D(BC)	ANGLE
O^{ii}	N^{i}	O^{iii}	2.898	3.129	84.1^{o}
O^{ii}	N^{i}	HN^{i}	2.898	0.961	91.8^{o}
O^{iii}	N^{i}	HN^{i}	3.129	0.961	9.3^{o}
N	O^{ii}	HO^{ii}	2.898	1.040	14.3^{o}
N	O^{iii}	HO^{iii}	3.129	1.040	94.6^{o}
N^{i}	HN^{i}	O^{iii}	0.961	2.187	166.6^{o}
N^{i}	HO^{ii}	O^{ii}	1.908	1.040	158.0^{o}

Symmetry code

i 0,5 + x, 0,5 + y, z
ii x, -y, -z
iii -x, -y, 0,5 + z

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