X-RAY DIFFRACTION STUDY OF 9-BROMO-3-(TRICHLOROMETHYL)-3,3A,4,5,6,7,8,9-OCTAHYDROCYCLOOCTA[C]ISOXAZOL-3-OL

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***Abstract*—Certain compounds present an analogy with metabolic intermediates of the γ-aminobutyric acid, which suggests that after biological testing, may present some acetylcholinesterase activity modulation. In order to identify new inhibitors, some compounds previously synthesized have some specific physico-chemical properties investigated, such as those obtained by x-ray diffraction. Single crystals were obtained by slow evaporation from methanol and some characteristics of the compound are given below: Crystalline system: Orthorhombic, P 2_1 2_1 2_1, Z=4, a=7.7155(2)Å, b=9.0432(1) Å, c=19.8073(4) Å, R_{int}=0.051. In the compound forming intermolecular bonding, is represented by: O2-H2...N1 = 0.8200(0) Å, H2...N1 = 2.200(0)Å, O2...N1 = 2.977(6)Å, and the angle O2-H2...N1 = 153.00(0)° as shown in Figure. After completion of crystallochemical study sample it is possible propose a chemically consistent structural model and provide data crucial for predicting their properties.**

***Index Terms*— X-ray diffraction; Acetylcholinesterase; Single crystals**

I. INTRODUCTION

Receiving regions of different types of the γ-aminobutyric acid (GABA) were originally defined by its sensitivity to drugs. The GABA A receptors are activated by Muscimol, while the GABA B receptors are activated by Baclofen.

In order to identify new inhibitors of acetylcholinesterase and searching previously synthesized compounds, the verification of its pharmacodynamic and pharmacokinetic properties, as well as their physico-chemical and mechanical characteristics are related to acetylcholinesterase under investigation. Some compounds exhibit metabolic intermediates to GABA analogs, which suggests that the compounds may have some type of modulation of the enzyme activity. The compound presented in this work shows similarity to the GABA agonists for structural similarity, such as Muscimol [1]. For this structural analysis, the X-ray diffraction was used to confirm the proposed structure. Moreover, studies were conducted to elucidate the crystal intermolecular interactions.

II. EXPERIMENTAL

Single crystals of the compound were obtained by slow evaporation from methanol. The crystallographic characteristics and structure refinement statistics are given in Table 1. The structure was determined by direct methods and refined with anisotropic displacement parameters for atoms not hydrogenated and the hydrogen atoms were placed geometrically and refined using a model of equivalence.

A X-ray diffraction analysis of the single crystal was performed on a KAPPA CCD diffractometer Enraf Nonius [2] and X-ray experimental details and selected results for the title compound are given in Table 1. The structure was solved using SHELXS97 [3] and was interpreted and refined with the aid of the SHELX97 software package [3,4]. The hydrogen atoms that are involved in the H-bond formation were determined from the difference electron-density map and isotropically refined. The positions of other hydrogen atoms were calculated from geometric considerations and refined within the riding model. A graphical representation (figure 1) of the molecule was constructed using the ORTEP3 software [5]. The CIF file deposited in the Cambridge Structural Database was obtained using the WinGX software package [6] (CCDC no. 941096).

III. RESULTS AND DISCUSSION

All non-hydrogen atoms were refined anisotropically and hydrogen atoms were positioned geometrically, with d(C–H) =0.970Å. Some chosen distances, bond angles and torsion angles are shown in Table 2 and Table 3.

The molecular structure is shown in Fig. 1 with atom numbering scheme. In the asymmetric unit, there is one molecule. In the compound, the hydrogen atom, of hydroxyl group, form one intermolecular H bond with the N atom:
O2-H2... N1 = 0.8200(0) Å, H2...N1 = 2.200(0) Å, O2...N1 = 2.977(6) Å, and the angle O2-H2...N1 = 153.00(0)°. The symmetric transformation is: 1-x,-1/2+y,1/2-z. The measures of bond lengths and angles formed between atoms that have hydrogen bonding, are within acceptable standards. The formed hydrogen bonding is shown by Figure 2, where it is also possible to observe the crystal packing.

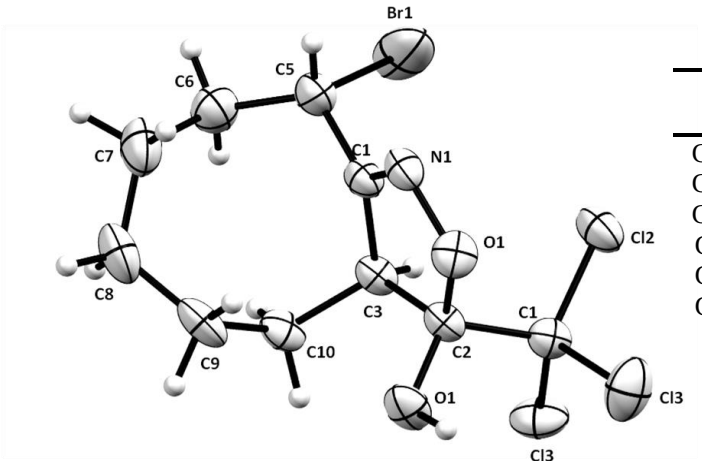

Fig.1. The asymmetric unit of the title compound, represented with displacement ellipsoids drawn at 30% probability level and showing the labeling scheme.

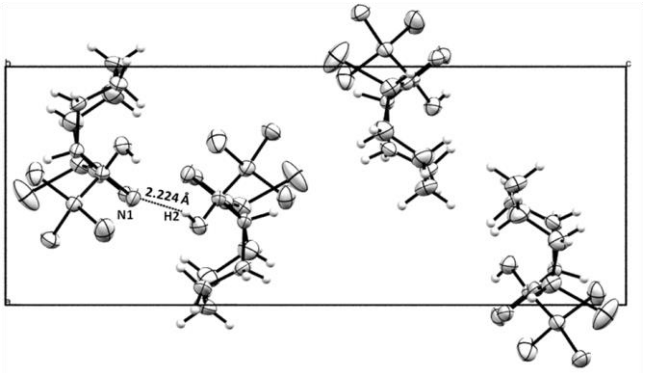

Fig. 2. View of the crystal packing of the title compound.

Table 1. Crystallographic and X ray data, collect and the refinement results for the crystal structure of 9-bromo-3-(trichloromethyl)-3,3a,4,5,6,7,8,9-octahydrocycloocta[c]isoxazol-3-ol.

Molecular weight (g/mol)	365.50
T (K)	293(2)
Crystalline system	Orthorhombic
Space Group, Z	P 2_1 2_1 2_1, 4
a, b, c (Å)	7.7155(2), 9.0432(1), 19.8073(4)
α= β=γ (deg)	90
V (Å^3)	1382.01(0)
λ (Å)	0.71073
d_{calc} (g/cm^3)	1.757
μ (mm^{-1})	3.543
F(000)	728
θ_{max} (deg)	27.88
Number of reflections measured	13809
Number of unique reflections	3288
Number of reflection with I>2σ(I)	2922
Number of parameters refined	154
R1/wR_2 [I>2σ(I)]	0.0562/0.1326
R2/wR_2[all reflections]	0.0651/0.1385
GOF	1.051
Δρmax/Δρmin (e/ Å^3)	1.344/-0.824

Table 2. Selected distances and angles.

Bond	Distance (Å)	Angle (°)	
C(1)-Cl(2)	1.763(5)	C(2)-C(1)-Cl(3)	108.8(3)
C(1)-Cl(3)	1.771(5)	Cl(2)-C(1)-Cl(3)	109.2(2)
C(1)-Cl(1)	1.774(5)	C(2)-C(1)-Cl(1)	108.8(3)
C(2)-O(2)	1.383(6)	Cl(2)-C(1)-Cl(1)	109.8(2)
C(2)-O(1)	1.439(6)	Cl(3)-C(1)-Cl(1)	109.9(2)
C(4)-N(1)	1.279(6)	O(2)-C(2)-C(1)	109.4(4)
		C(4)-C(5)-Br(1)	105.6(3)
		C(4)-N(1)-O(1)	109.4(4)

Table 3. Selected Torsion Angle.

Torsion Angle (°)	
N1-O1-C2-C1	114.9(4)
N1-O1-C2-C3	-3.9(5)
N1-O1-C2-O2	-126.0(4)
O1-N1-C4-C3	2.3(6)
O1-N1-C4-C5	-174.0(4)
Cl3-C1-C2-C3	-61.9(4)
O2-C2-C3-C4	125.1(4)
N1-C4-C5-Br1	106.6(5)
N1-C4-C5-C6	-133.0(5)
C3-C4-C5-Br1	-69.2(6)
Br1-C5-C6-C7	176.9(4)

After analysis of the angles of torsion, isoxizol atoms present in the ring, there is an essentially planar geometry. For the C2-C4-O1-N1 atoms the torsion angles is 1.2°, while for the O1-N1-C3-C4 atoms the torsion angle is 2.3.

IV. Conclusion

The structure determination of the compound under study was performed from the studies by X-ray crystallography. From these studies it was found that conformational changes associated with the replacement of the ligants occurs along the octaisoxazol ring, that repeat with 19 compounds that are characterized and that have similarity structural.

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