

The Crystal Structure of 9-Chloro-4,5-dihydro-2-ethyl-1-(2,4,6-trichlorophenyl)-1*H*-1,2,4-triazolo[3,2-*d*][1,5]-benzoxazepinium Hexachloroantimonate

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The title compound **4**, *i.e.* 9-chloro-4,5-dihydro-2-ethyl-1-(2,4,6-trichlorophenyl)-1*H*-1,2,4-triazolo[3,2-*d*][1,5]benzoxazepinium hexachloroantimonate, is a novel 6-7-5 tricyclic heterocycle. $C_{18}H_{14}Cl_4N_3O \cdot SbCl_6$, $M = 764.61$, $P2_1/c(\#14)$, $a = 13.457(4)$, $b = 11.583(2)$, $c = 18.992(3)$ Å; $\alpha = 90$, $\beta = 110.11(1)^\circ$, $Z = 4$, $V = 2780(1)$ Å³, $D_c = 1.827$ g/cc, μ (MoK α) = 19.69 cm⁻¹, $F(000) = 1488.00$, $T = 293$ K, $R_{int} = 0.055$ for 3094 independent reflections with $I > 3.00\sigma(I)$. The five-membered heterocyclic ring is nearly planar, with the trichlorophenyl ring at N(2) almost perpendicular to it. However, the seven-membered ring is not planar, but adopts a twist-boat conformation.

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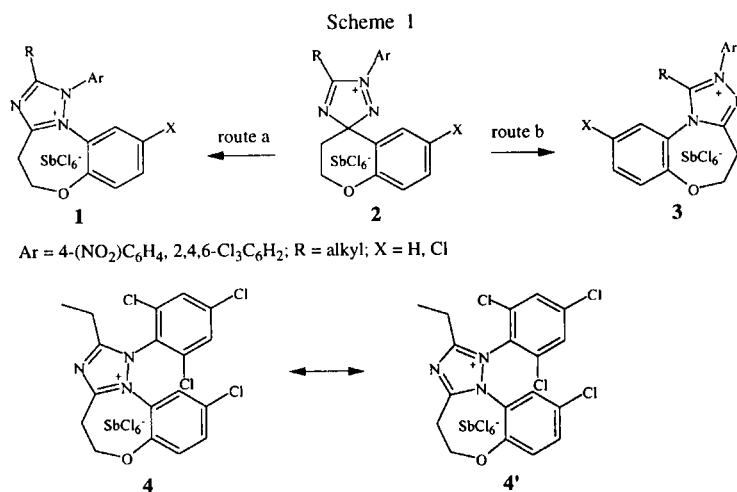
Introduction.

Many tricyclic heterocycles containing a 1,2,4-triazole ring are of interest due to their properties as therapeutic agents, in particular, as psychiatric drugs [1-5]. Generally, the incorporation of a triazole moiety enhances the affinity for benzodiazepine receptors [6,7].

Interestingly, during the past decade derivatives of 1,2,4-triazolobenzoxazepines have been prepared and their biological activities investigated [8-12]. Because they exhibit a range of novel physiological effects, they are among the promising drugs useful as phospholipase A₂ inhibitors [9], interleukin 1 production inhibitors [9] as well as for treatment of osteoporosis [11].

In an ensuing paper [13], we have described an efficient synthesis of [1,2,4]triazolo[3,2-*d*][1,5]benzoxazepinium salts (general formula **1**) *via* cycloaddition of 1-aza-2-azo-

niaallene cations, a kind of positively charged 1,3-dipoles, to the triple bond of nitriles. The structural information for **1** has been obtained principally using spectroscopic methods and microanalysis. However, we found it difficult to distinguish between **1** and their isomer **3**, which can be formed by ring enlargement of the initially formed 3-spiro substituted 3*H*-1,2,4-triazolium salts **2** with the insertion of N(4) into the carbon skeleton (Scheme 1). Also, the site of chlorination on the phenyl ring has been uncertain because of the radical character in the mechanistic process. Therefore, the current crystallographic study on one representative of **1**, namely, 9-chloro-4,5-dihydro-2-ethyl-1-(2,4,6-trichlorophenyl)-1*H*-1,2,4-triazolo[3,2-*d*][1,5]benzoxazepinium hexachloroantimonate (**4**) (**1**, Ar = 2,4,6-Cl₃C₆H₂, R = Et, X = Cl) was undertaken to ascertain the structural assignment unequivocally.



Although compounds containing a fused triazole ring such as **3** have been well documented [8], structures of heterocycles featuring 1,2,4-triazolo[3,2-*d*][1,5]benzoxazepine skeleton have not been published. Owing to their obvious structural relationship to the reported tricyclic analogues, heterocycles **1** should be of considerable potential pharmacological interest.

X-Ray Structural Investigation.

Pale yellow prismatic crystals of compound **4**, suitable for X-ray diffraction analysis, were obtained by recrystallization from methanol-acetonitrile (7:2).

The crystallographic data are as follows: $C_{18}H_{14}Cl_{10}N_3OSb$ ($C_{18}H_{14}Cl_4N_3O \cdot SbCl_6$), $M = 764.61$, crystal dimensions $0.20 \times 0.20 \times 0.30$ mm; $a = 13.457(4)$, $b = 11.583(2)$, $c = 18.992(3)$ Å; $\alpha = 90$, $\beta = 110.11(1)$, $\gamma = 90^\circ$; monoclinic, space group $P2_1/c(\#14)$, $Z = 4$, $D_c = 1.827$ g/cc, $V = 2780(1)$ Å³, $F(000) = 1488.00$, $\mu(MoK\alpha) = 19.69$ cm⁻¹.

Cell parameters were calculated using a least-squares procedure involving angle settings of 18 centered reflections ($18.35 < 2\theta < 21.10^\circ$) which were measured on a Rigaku AFC7R diffractometer with Mo-K α radiation (graphite monochromator). The cell measurement temperature was 293 K. The data were corrected for Lorentz and polarization effects. A correction for secondary extinction was applied (coefficient = 5.04241×10^8). A total of 4846 reflections were measured using ω - 2θ scans, with ω -scan angle $(1.63 + 0.30 \tan\theta)^\circ$ and at a speed of $16.0^\circ/\text{min}$ (in ω). Averaging of equivalent reflections gave 3094 independent reflections; $R_{\text{int}} = 0.055$ for observed reflections [$I > 3.00\sigma(I)$]. The partial structure was obtained using direct methods (SHELX86) and the structure was completed using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated but not refined. Refinement of 299 parameters using a least square procedure with weights = $4F_o^2/\sigma^2(F_o)^2$, with a p-factor of 0.03, reached at $R = 0.036$, $R_w = 0.046$. The scattering factors were taken from the literature [14].

The final atomic coordinates and temperature factors for non-hydrogen atoms, bond lengths and bond angles are reported in Tables 1-3. Lists of hydrogen fractional coordinates and anisotropic thermal factors and of the observed and calculated structure factors are available from the authors upon request. A perspective view of the molecule is supplied in Figure 1.

Discussion.

The X-ray crystallographic structure determination reported here confirms the assignment of the structure of **4** which was obtained by spectroscopic analysis.

The five-membered heterocyclic ring is essentially planar ($\chi^2 = 5.0$). The ring contains a significantly long N(2)-N(3) distance of $1.377(5)$ Å characteristic of a single

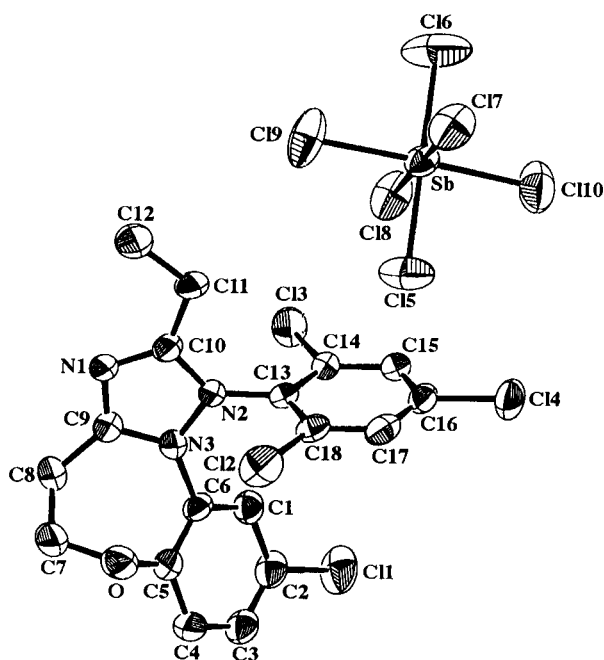


Figure 1. View of the molecule **4** with the atom-labeling scheme.

N-N bond. However, it is slightly shorter than the N-N single bond value of 1.401 Å reported by Allen [15]. On the other hand, the other four bond lengths in the triazole ring are nearly equal as the value ranges between $1.326(6)$ and $1.353(6)$ Å. These shorter bond lengths have considerable double bond character and compare well with those of other delocalized systems such as 1.338 Å in pyridine [16]. A N=N⁺ double bond in a 1,2,4-triazole salt $1.243(5)$ and for C-N single bonds values of about 1.48 Å have been published by other research groups [17-19]. In addition, 1,4,5-triphenyl-1,2,4-triazole-3-thiolate, a typical mesoionic compound, shows a N-N distance of $1.379(3)$ Å [20] which is similar to our value. More recently, Schantl described a stable five-membered azomethine imine and reported the N-N distance to be $1.303(2)$ Å [21]. These data support our view that hybridization of the two canonical forms **4** and **4'** contribute predominantly to the structure (Scheme 1). It follows that the positive charge is expected to distribute mainly over the N(2) and N(3) atoms.

Due to hindered rotation about the N(2)-C(13) bond, the trichlorophenyl ring at N(2) is nearly perpendicular to the triazole ring. The dihedral angle between these two planes is found to be 93.31° , while the torsion angles of N(3)-N(2)-C(13)-C(14) and C(10)-N(2)-C(13)-C(18) are $97.3(6)^\circ$ and $88.7(6)^\circ$, respectively. This, together with the rather long N(2)-C(13) bond distance [$1.416(6)$ Å] which is indicative of a C(sp²)-N single bond, allows one to conclude that there is no conjugation between the two rings.

The seven-membered ring is not planar, but adopts a twist-boat conformation. This may be described in terms of the torsion angles: O-C(5)-C(6)-N(3) = -4.1(7)°, C(5)-O-C(7)-C(8) = -49.9(7)°, N(3)-C(9)-C(8)-C(7) = 66.6(7)° and O-C(7)-C(8)-C(9) = -34.4(7)°. The bond lengths of C(9)-C(8) and C(8)-C(7) are in good agreement with corresponding values observed in a structurally closely related bicyclic heterocycle, 3,5,6,7,8,9-hexahydro-2-methyl-3-(2,4,6-trichlorophenyl)-1,2,4-triazolo[1,5-*a*]-azepinium hexachloroantimonate [22], while the N(3)-C(6) bond distance [1.428(6) Å] is slightly shortened due to sp² hybridization of the carbon atom. The carbon atom C(8) is situated almost in the plane of the triazole ring as the torsion angle C(8)-C(9)-N(1)-C(10) [179.8(6)°] suggests. Similarly, the oxygen atom is coplanar with the fused benzene nucleus, with the deviation from the least-square plane being only -0.076 Å.

Finally, the fused benzene ring and the triazole ring are not coplanar but form a dihedral angle with value 47.27°, while the dihedral angle between the former ring and the aryl ring at N(2) is 108.29°. Not surprisingly, the hexachloroantimonate anion is arranged in an octahedral unit.

Table 1

Atomic Coordinates and Equivalent Isotropic Thermal Parameters (Å²)

$$\text{Beq} = (8\pi^2/3)(U_{11}(\text{aa}^*)^2 + U_{22}(\text{bb}^*)^2 + U_{33}(\text{cc}^*)^2 + 2U_{12}\text{aa}^*\text{bb}^*\cos\gamma + 2U_{13}\text{aa}^*\text{cc}^*\cos\beta + 2U_{23}\text{bb}^*\text{cc}^*\cos\alpha)$$

atom	x	y	z	Beq
Sb	0.78865(3)	0.24442(3)	0.29633(2)	4.431(10)
Cl(1)	0.6776(2)	-0.1521(2)	0.73618(10)	7.51(5)
Cl(2)	0.5781(1)	-0.2498(2)	0.3810(1)	6.83(4)
Cl(3)	0.9065(1)	-0.0353(1)	0.58127(10)	5.94(4)
Cl(4)	0.5429(1)	0.1899(2)	0.4597(1)	6.82(5)
Cl(5)	0.6492(2)	0.1188(2)	0.2917(1)	8.51(6)
Cl(6)	0.9275(2)	0.3684(3)	0.3017(1)	12.29(9)
Cl(7)	0.7041(2)	0.2899(2)	0.16891(10)	7.90(5)
Cl(8)	0.8729(1)	0.1978(2)	0.42518(9)	7.16(5)
Cl(9)	0.8763(2)	0.0903(2)	0.26086(10)	8.58(6)
Cl(10)	0.6954(2)	0.3949(2)	0.3293(1)	9.10(7)
O	0.6736(3)	-0.5127(3)	0.5191(2)	5.4(1)
N(1)	0.8933(3)	-0.3690(3)	0.4608(2)	4.2(1)
N(2)	0.7974(3)	-0.2304(3)	0.4855(2)	3.48(9)
N(3)	0.7969(3)	-0.3239(3)	0.5301(2)	3.8(1)
C(1)	0.7417(4)	-0.2489(4)	0.6314(3)	4.3(1)
C(2)	0.6789(5)	-0.2637(5)	0.6751(3)	5.0(1)
C(3)	0.6200(5)	-0.3609(6)	0.6699(4)	5.8(2)
C(4)	0.6184(5)	-0.4474(5)	0.6196(4)	5.3(2)
C(5)	0.6791(4)	-0.4321(4)	0.5730(3)	4.1(1)
C(6)	0.7371(4)	-0.3342(4)	0.5790(3)	3.7(1)
C(7)	0.7653(5)	-0.5863(5)	0.5311(4)	5.9(2)
C(8)	0.8682(5)	-0.5198(5)	0.5513(4)	5.6(2)
C(9)	0.8547(4)	-0.4060(4)	0.5127(3)	4.4(1)
C(10)	0.8580(4)	-0.2619(4)	0.4447(3)	4.0(1)
C(11)	0.8765(5)	-0.1817(5)	0.3887(3)	5.0(1)
C(12)	0.9482(6)	-0.2325(5)	0.3521(4)	6.5(2)
C(13)	0.7351(4)	-0.1299(4)	0.4799(3)	3.4(1)
C(14)	0.7773(4)	-0.0329(4)	0.5213(3)	3.7(1)
C(15)	0.7184(4)	0.0667(4)	0.5155(3)	4.1(1)
C(16)	0.6159(4)	0.0658(5)	0.4671(3)	4.5(1)
C(17)	0.5704(4)	-0.0304(5)	0.4252(3)	4.6(1)
C(18)	0.6303(4)	-0.1290(5)	0.4317(3)	3.9(1)

Table 2
Selected Bond Lengths (in Å)

Cl(1)-C(2)	1.740(6)	N(2)-C(10)	1.353(6)
Cl(2)-C(18)	1.706(5)	N(2)-C(13)	1.416(6)
Cl(3)-C(14)	1.721(5)	N(3)-C(6)	1.428(6)
Cl(4)-C(16)	1.719(5)	N(3)-C(9)	1.339(6)
O-C(5)	1.370(6)	C(5)-C(6)	1.359(7)
O-C(7)	1.452(7)	C(7)-C(8)	1.514(9)
N(1)-C(9)	1.334(6)	C(8)-C(9)	1.488(7)
N(1)-C(10)	1.326(6)	C(10)-C(11)	1.497(7)
N(2)-N(3)	1.377(5)	C(11)-C(12)	1.491(8)

Table 3
Selected Bond Angles (°)

O-C(5)-C(6)	120.9(5)	N(1)-C(10)-C(11)	127.6(5)
O-C(5)-C(4)	119.4(5)	C(9)-N(1)-C(10)	105.7(4)
C(4)-C(5)-C(6)	119.6(5)	N(2)-C(10)-C(11)	121.3(4)
N(3)-C(6)-C(1)	120.7(5)	N(3)-N(2)-C(10)	105.8(4)
N(3)-C(6)-C(5)	116.8(4)	C(10)-C(11)-C(12)	112.3(5)
O-C(7)-C(8)	113.2(5)	N(3)-N(2)-C(13)	124.4(4)
C(7)-C(8)-C(9)	112.3(5)	N(2)-C(13)-C(14)	120.7(4)
N(1)-C(9)-N(3)	111.2(5)	C(10)-N(2)-C(13)	129.5(4)
N(1)-C(9)-C(8)	129.5(5)	N(2)-C(13)-C(18)	119.7(4)
N(3)-C(9)-C(8)	119.4(5)	N(2)-N(3)-C(6)	126.1(4)
N(1)-C(10)-N(2)	111.0(4)	N(2)-N(3)-C(9)	106.3(4)
C(5)-O-C(7)	117.3(5)	C(6)-N(3)-C(9)	127.3(4)

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