Crystalline structure of a new strontium-lasalocid complex: aqua bis-(lasalocid)-strontium(II) containing nine-coordinate Sr

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Abstract

The title complex, $[Sr(C_{68}H_{106}O_{16})(H_2O)]$, forms a pseudo-centrosymmetric monomer complex, in which one aquo (or water) ligand bridges three O centres of the first lasalocid anionic ligand (Lasa 2) and in which this ligand is tridentate and bonded to just one Sr atom, and the other lasalocid ligand (Lasa 1) is pentadentate and bridges the Sr centre within the monomer. The monomeric unit is stabilized by intramolecular C—H···O and O—H…O type-hydrogen bonding interactions.

Keywords: Lasalocid, veterinary antibiotic, strontium complex, structure

Introduction

Lasalocid A salt of sodium is one of the most commonly used veterinary antibiotics, where it has found wide spread application as an anticoccidial and to improve feed efficiency. The mechanism of action of lasalocid is clearly attributed to its ionophoric properties, because it has been reported to determine the influx of Na^+ in the cell of Gram positive and anaerobic bacteria, causing swelling, vacuolization, and death. At the origin of these processes, there is the property of forming lipophilic metal complexes, which can penetrate membranes and disrupt cation equilibria.[1,2]

The molecular basis of this action are still debated; more specifically which of the oxygen atoms are directly involved in cation coordination. To date, this problem has been the object of many investigations almost invariably taking advantage of the concerted use of several experimental and computational techniques, which demonstrate both the relevance of the problem and its intrinsic difficulty.[3]

The identity of the various complexes formed according to the nature of the cation, to the solvent, and to the solution composition has been initially faced with optical spectroscopy and circular dichroism (CD), possibly using lanthanides as probes.[4] X-ray diffraction data became available for several cations, among others Na^{+},[5] and Ba^{2+}.[6] Often, it has been observed that aggregates of different stoichiometry can take place, leading to the formation of sandwiches, where the cation occupies a cavity between two ligand molecules.[3] Molecular dynamic calculations have been reported both in vacuo,[7] and in solvent.[8] Finally, there has recently appeared a series of papers on polyoxaalkyllasalocid esters/cation complexes making use of multinuclear NMR, IR, ESI-MS, and semiempirical methods.[9]

It has been proposed that antibacterial and fungicidal activity and also antitumor and anti-HIV-integrase inhibition of antibiotics lie in their ability to chelate the essential metals, which the microorganisms need in their metabolism.[9e-g]

Results and Discussion

We report the synthesis and structure of the first compound of a series of strontium(II) complexes that is readily prepared as its pure stochioisomer ligand/metal (2/1). This new strontium(II) complex, deriving from a lasalocid/ strontium coordination, is obtained through a simple and economical synthetic method. The reaction of lasalocid acid (**1**) (Figure 1), with strontium salt under ordinary atmosphere, with controlling pH (pH>8), provides a stable coordination product (Figure 2), the aquo-strontium-bis-lasalocid, which is characterised by X-ray (Figure 3).

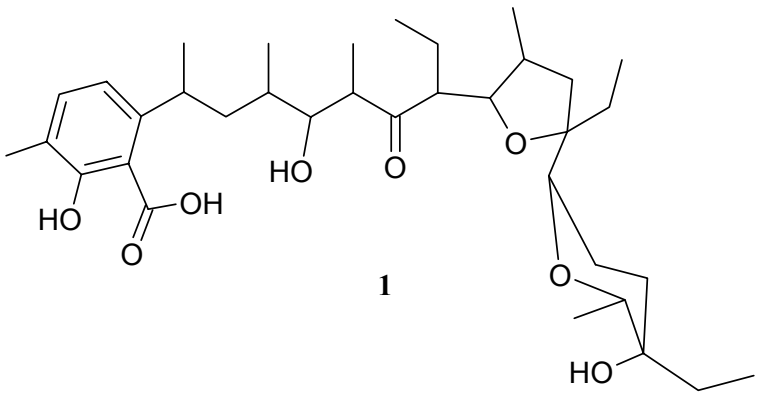

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Figure 1. Structure of lasalocide acid **1**.

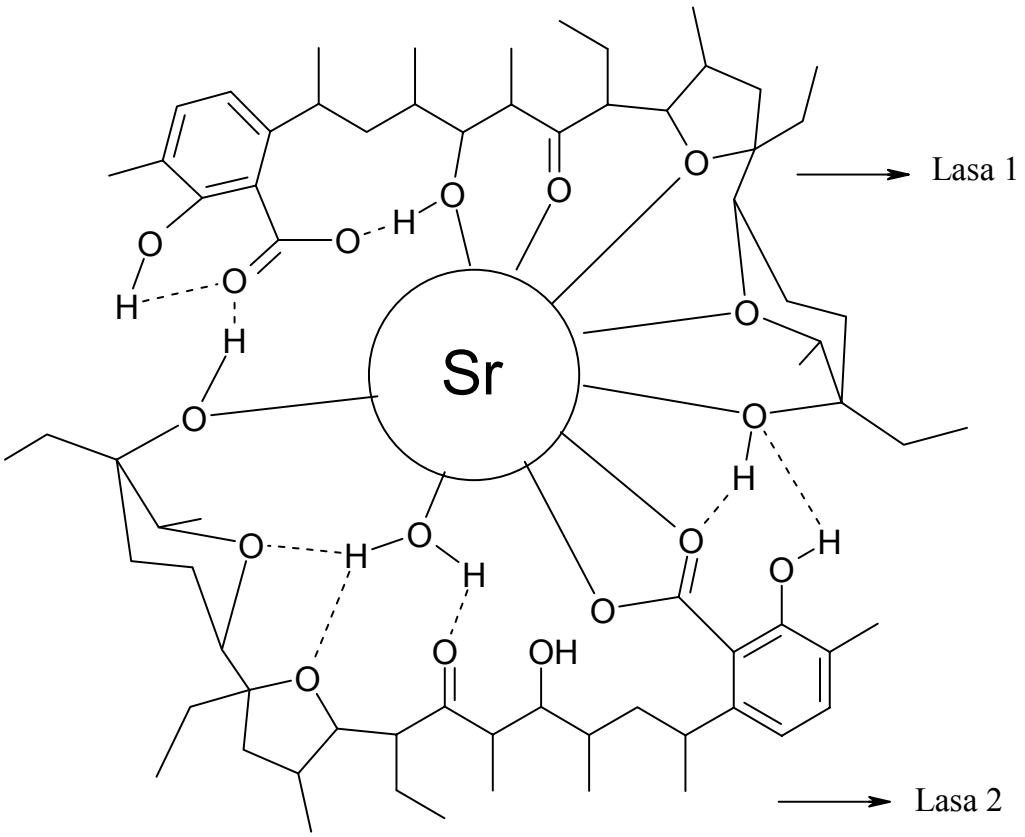

Figure 2. The title complex $[Sr(Lasa)_2(OH_2)]$.

The title complex, $[Sr(C_{68}H_{106}O_{16})(H_2O)]$, crystallizes with nine-coordinated Sr atom three-dimensionally interconnected into a framework structure. The crystallographically dependent water molecule is located on an axial site. These two lasalocid ligands (Lasa 1 and Lasa 2) are tied together by a three-dimensional hydrogen-bonding network. These monomeric units are not stacked by any Van der Waals forces between the coordination spheres.

Since the coordination properties of the two molecules of lasalocid ligands are different, it is concluded that the two lasalocid ligands are not simultaneously coordinated. To have a clear idea about the coordinative aspect of the two ligands, the view for the complex $[Sr(Lasa)_2(OH_2)]$) has been added here as shown in Figure 2.

Conclusions

In conclusion, we describe here what is to our knowledge the first solid-state structure obtained with a strontium-lasalocid complex. The tetra-butyl ammonium salt of lasalocid is able to form a stable 2:1 (ligand : metal) complex with divalent cations such as strontium(II). The structure of this complex is completely different with the respective complexes with other divalent cations

(Mg^{2+} and Ca^{2+}).[15] A preliminary biological activity of the Sr-Lasalocid ester on fungus F. oxysporum was studied *in vitro* at Oujda. It is shown that this compound is biologically active. This result is very important for future agricultural applications and deserves to be extended to a wide series of transition metals [Ru(II), Co(II), Fe(II)].

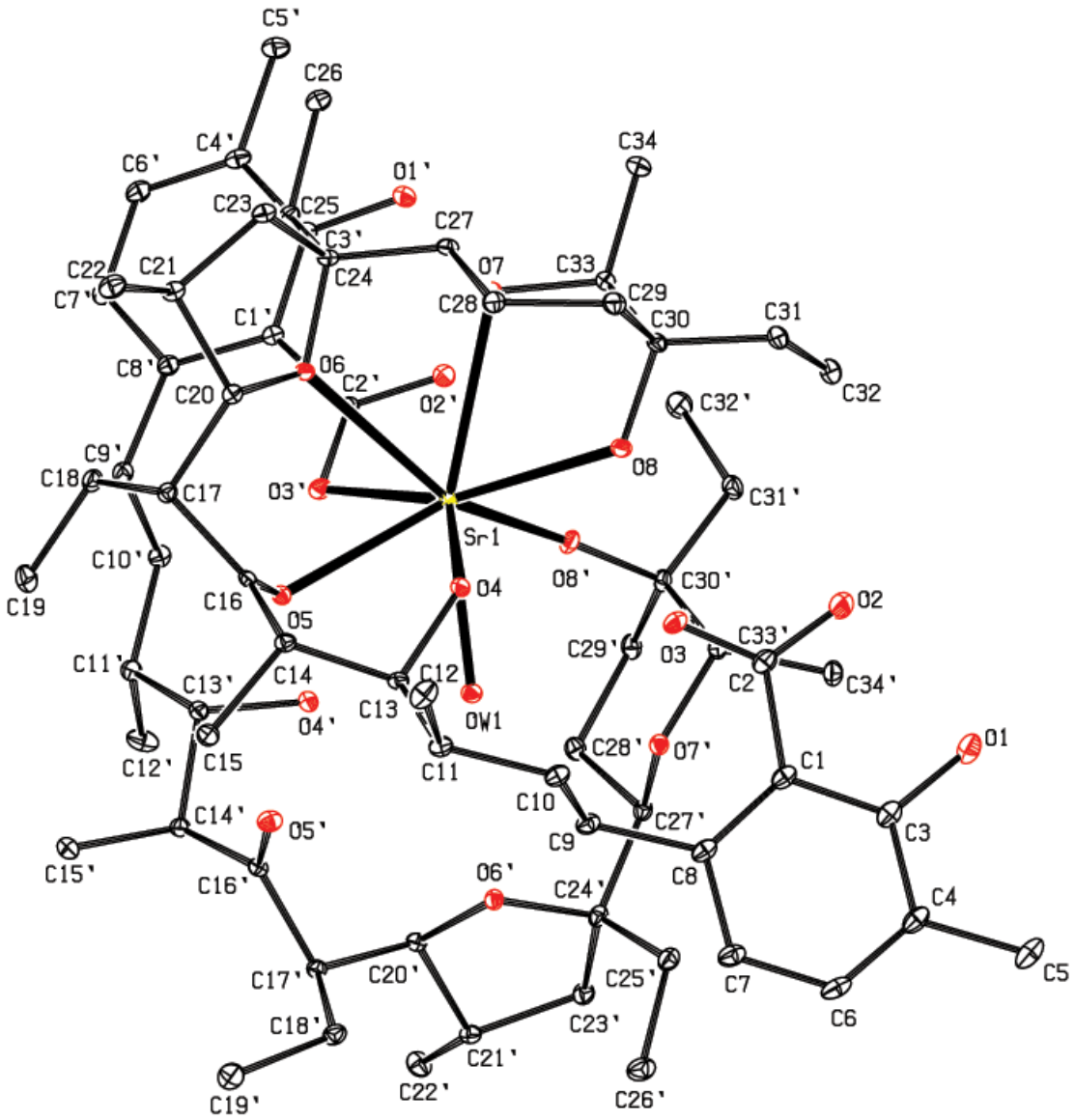

Figure 3. An *ORTEP* view of the title compound, with the atom-numbering scheme and 10% probability displacement ellipsoids. H atoms have been omitted for clarity. Displacement ellipsoids are drawn at the 10% probability level.

Experimental Section

Preparation of complex (I). A solution of tetramethylammonium-lasalocid free salt (6.64 g, 2 mmole, prepared in 20 mL of $CHCl_3$) was stirred with 0.1 M aqueous $SrCl_2$ (0.793g, 1 mmole, prepared in 50 mL of H_2O). The mixture was stirred at 20 °C for 4 h under argon in the dark. The organic layer was then dried over anhydrous Na_2SO_4, filtered and evaporated. The solid residue was dissolved in MeOH and the solvent was left to evaporate at 20 °C for 1 week in the dark. Yellow crystals obtained proved suitable for X-ray analysis (65% Yield).

Crystal structure analysis. The crystal structure of the title compound, $C_{68}H_{108}O_{17}Sr$, has been determined at room temperature. Diffraction data were collected using a Bruker SMART APEX-II CCD diffractometer system, using graphite-monochromated MoK_α radiation.
The crystallographic details are given in Table 1. The structure was solved by direct methods by using SIR-97 program and refined by least-squares on F_{obs}^2 and by using SHELXL-97 programs. O1, O4, O8, O1′, O4′, O8′ and H atoms belonging to the coordinated water molecules were located in a difference Fourier map and refined with mean O-H distances of 0.855(3) Å, freely. All other H atoms were located in calculated positions and treated as riding on their parent atoms, with C—H = 0.96 (CH_3), 0.97 (CH_2) or 0.98 Å (CH), and with $U_{iso}(H) = 1.5U_{eq}(CH_3)$ or $1.2U_{eq}(CH_2, CH)$. A displacement ellipsoid plot with the atomic numbering scheme of the title compound is shown in figure 3; with selected bond lengths and bond angles, and the details of the hydrogen-bonding geometry in Tables 2 and 3, respectively.
The average Sr—O [2.653(2) Å] distance, consistent with usual distances for nine-coordinated Sr^{II} ions [Sr—O 2.564(3) - 2.967(3) Å].[13] Within the ligands, other geometric parameters (C—O and C—C distances, and O—C—O and O—C—C angles) all lie in the expected ranges.[14]
The crystal structure is stabilized by the intramolecular O—H···O and C—H···O type-hydrogen bonding interactions (Table 3).

Table 1. Crystal and experimental data

Formula	$C_{68}H_{108}O_{17}Sr$
Formula weight	1285.17
Crystal system	orthorhombic
Space group	$P2_12_12_1$ (No. 19)
	$Z = 4$
	$a = 17.3910(12)$ Å
	$b = 18.4288(13)$ Å
	$c = 21.3794(15)$ Å
	$V = 6852.0(8)$ Å^3
	$D_x = 1.246$ g.cm^{-3}
	$\mu(MoK_\alpha) = 0.852$ cm^{-1}
	$T = 293$ K
Crystal size	0.48 mm
Radiation	$F(0\ 0\ 0) = 2760$
	0.18 x 0.37 x
	MoK_α
	$R = 0.0323$
	$R_w = 0.0722$
No. of unique data measured	17056
No. of observed data with [$I \geq 2\sigma(I)$]	14341
No. of parameters	807
Goodness-of-fit	1.02
	$(\Delta\rho)_{max} = 0.41$ e.Å^{-3}
	$(\Delta\rho)_{min} = -0.66$ e.Å^{-3} Bruker SMART APEX-II CCD
Measurements	diffractometer [10]
Structure determination	*SIR97* program[11]
Refinement	full matrix least-squares SHELXL-97 program[12]

Table 2. Selected bond lengths (Å) and angles (°)

Sr1 - OW1	2.4758(15)	O1 - C3	1.349(3)
Sr1 - O4	2.8693(13)	O2 - C2	1.259(3)
Sr1 - O5	2.5597(13)	O3 - C2	1.255(3)
Sr1 - O6	2.8012(13)	O4 - C13	1.446(2)
Sr1 - O7	2.7244(13)	O5 - C16	1.219(2)
Sr1 - O8	2.5379(15)	O6 - C20	1.449(2)
Sr1 -O3'	2.5906(14)	O6 - C24	1.475(2)
Sr1 -O8'	2.6652(14)	O7 - C27	1.442(2)
O8 - C30	1.433(2)	O7 - C33	1.449(2)

OW1 - Sr1 - O4	72.04(4)	Sr1 - O4 - C13	116.54(10)
OW1 - Sr1 - O5	69.94(4)	Sr1 - O5 - C16	119.22(11)
OW1 - Sr1 - O6	133.90(4)	Sr1 - O6 - C20	131.52(10)
OW1 - Sr1 - O7	161.43(4)	Sr1 - O6 - C24	115.95(10)
OW1 - Sr1 - O8	101.11(5)	O7 - Sr1 - O8	61.33(4)
Sr1 - O7 - C27	113.61(10)	O6 - Sr1 - O8	101.61(4)
Sr1 - O7 - C33	106.15(10)	O5 - Sr1 - O8	134.97(4)
Sr1 - O8 - C30	126.08(12)	O6 - Sr1 - O7	60.58(4)
O5 - Sr1 - O7	126.13(4)	O5 - Sr1 - O6	65.57(4)
O4 - Sr1 - O7	104.63(4)	O4 - Sr1 - O8	69.87(4)
O4 - Sr1 - O5	65.39(4)	O4 - Sr1 - O6	79.04(4)

Table 3. Hydrogen-bonding geometry (Å, °).

D-H...A	D-H	H...A	D...A	D-H...A
O1 - H1O O2	1.00(3)	1.47(3)	2.438(2)	161(2)
O4 - H4O O3	0.83(2)	2.00(2)	2.802(2)	163(2)
O8 - H8O O3	0.91(3)	1.68(3)	2.551(2)	159(3)
O1' - H1O' . . . O2'	0.87(3)	1.71(3)	2.486(2)	149(3)
O4' - H4O' . . . O3'	0.81(3)	2.13(3)	2.880(2)	154(3)
O8' - H8O' . . . O2'	0.81(2)	2.00(2)	2.666(2)	140(2)
OW1 - HW1 . . O6'	0.84(3)	2.52(3)	2.9648(19)	114(2)
OW1 - HW1 . . O7'	0.84(3)	1.94(3)	2.7652(19)	167(3)
OW1 - HW2 . . O5'	0.77(3)	2.28(3)	3.033(2)	166(3)
C5' - H5'1 . . . . O1'	0.96	2.24	2.723(3)	110
C5 - H5A O1	0.96	2.27	2.743(3)	110
C9' - H9'2 . . . . O3'	0.97	2.25	2.805(2)	115
C9 - H9B O3	0.97	2.36	2.811(3)	107
C10 - H10B . . . O3	0.97	2.40	3.008(3)	120
C10' - H10C . . . O4'	0.97	2.50	2.916(3)	105
C13 - H13 . . . . . OW1	0.98	2.50	3.245(2)	132
C28 - H28A . . . O6	0.97	2.52	2.915(2)	104
C28' - H28C . . . O4'	0.97	2.57	3.494(2)	160
C32' - H32E . . . O2'	0.96	2.51	3.415(3)	157

Note: CCDC 664624 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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