Crystal structure of a new polymeric thallium-lasalocid complex: lasalocide anion-thallium(I) containing aryl-Tl interactions

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Abstract

The title complex, $[Tl(C_{34}H_{53}O_8)]_n$, forms a pseudo individual monomer complex, in which the anionic oxygen of carboxylate group serves to neutralise the charge of Tl^+, the other five O centres of the first lasalocid anionic ligand (Lasa 1) and in which this ligand is pentadentate O-ligand and bonded to a second Tl centre by using phenyl-metal coordination. A second lasalocid ligand (Lasa 2) is also pentadentate O-ligand and bridges the first Tl centre within the polymer. The monomeric unit is stabilized by strong intramolecular aryl-Tl type-metal half sandwich bonding interactions.

Keywords: Lasalocid, veterinary antibiotic, thallium (I) complex, structure, half sandwich

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

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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 micro-organisms need in their metabolism.[9]

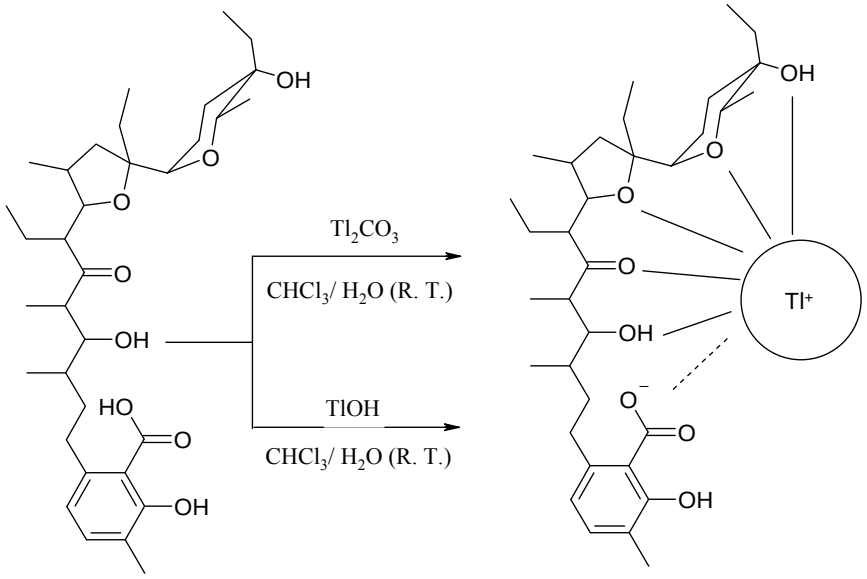
Results and Discussion

We report the synthesis and structure of the first compound of a series of Lasalocid-thallium(I) complexes that is readily prepared as its pure stochioisomer ligand/metal (1/1). This new thallium (I) complex, deriving from lasalocid / thallium coordination, is obtained through two simple and economical synthetic methods (Scheme 1).

The reaction of lasalocid acid (**1**), with thallium salt (Tl_2CO_3 or TlOH) under ordinary atmosphere, with controlling pH (pH>8), provides a stable coordination product (**2**), the thallium-lasalocid, which is characterised by 1H and ^{13}C NMR (Table 2).

The Tl atom can be coordinated by four, five or six neighbouring Oxygen atoms, leading to a variety of geometrical arrangements, such as tetrahedral, square pyramidal or trigonal bipyramidal, and octahedral. [10-11]

So it is difficult to give precise details about the site of coordination on the basis of NMR data (Tables 1 and 2).



(**1**); Lasalocid Acid (**2**): [Thallium(I)-(Lasalocid anion)]

Scheme 1. Synthesis of [thalium(I)-(Lasalocid anion)] complex.

Table 1. ^1H and ^{13}C NMR data of complex (**2**)

	^{13}C NMR (□ ppm)			^1H NMR (□ ppm)			^1H NMR (□ ppm)	
Cx	CD_3OD	$CDCl_3$	Hx	CD_3OD	$CDCl_3$	JHx-Hy	CD_3OD	$CDCl_3$
C1	177.7	175.9	H5	7.06	7.01	H5-H6	7.5	7.5
C2	116.9	116.3	H6	6.58	6.51	H8A-H8B	11.2	12.5
C3	160.0	161.7	H8A	3.39	4.16	H8A-H9A	4.0	2.5
C4	124.1	123.4	H8B	2.33	2.14	H8A-H9B	11.2	12.5
C5	133.1	132.0	H9A	1.61	1.48	H8B-H9A	11.2	12.5
C6	121.6	119.7	H9B	1.61	1.48	H8B-H9B	5.6	5.6
C7	145.0	144.1	H10	1.77	1.66	H9A-H9B	11	12.5
C8	33.8	32.6	H11	4.42	4.41	H9A-H10	7.5	4
C9	38.8	37.6	H12	2.98	2.79	H9B-H10	7.5	2
C10	35.0	33.7	H14	2.75	2.48	H10-H33	6.5	7.0
C11	71.6	70.4	H15	4.15	4.15	H10-H11	1.8	1.2
C12	50.0	48.1	H16	2.35	2.24	H11-H12	10.0	10.0
C13	218.5	217.0	H17A	2.02	1.88	H12-H32	7.0	7.0
C14	57.1	56.4	H17B	1.5	1.38	H14-H30A	10.0	10.0
C15	86.5	84.9	H19	3.9	3.72	H14-H30B	4.0	2.5

Table 2. ^{1}H and ^{13}C NMR data of complex (**2**)

	^{13}C NMR (□ ppm)			^{1}H NMR (□ ppm)			^{1}H NMR (□ ppm)	
Carbon	CD_3OD	$CDCl_3$	H	CD_3OD	$CDCl_3$	JHx-Hy	CD_3OD	$CDCl_3$
C16	36.5	35.0	H20A	2.10	1.96	H14-H15	4.0	2.5
C17	38.8	37.8	H20B	1.63	1.57	H15-H16	10.0	10.4
C18	89.2	87.9	H21A	1.81	1.78	H16-H17A	8.0	5.0
C19	72.1	69.7	H21B	1.81	1.78	H16-H17B	11.0	10.5
C20	20.8	19.8	H23	3.97	3.84	H16-H29	6.5	6.5
C21	30.6	29.4	H24	1.32	1.19	H17A-H17B	12.6	12.6
C22	72.9	71.6	H25A	1.92	1.78	H19-H20A	107.0	11.2
C23	78.0	77.4	H25B	1.5	1.26	H19-H20B	3.2	1.6
C24	14.1	13.6	H26	0.94	0.81	H20A-H20B	14.0	12.6
C25	32.6	31.6	H27A	1.63	1.51	H20A-H21A	11	9.0
C26	6.8	6.5	H27B	1.53	1.40	H20A-H21B	5	3.0
C27	31.7	30.3	H28	1.03	0.97	H20B-H21A	6	4.5
C28	9.8	9.5	H29	1.17	1.03	H20B-H21B	-	-
C29	16.2	16.2	H30A	2.02	1.96	H21A-H21B	12	12.6
C30	17.1	15.8	H30B	1.53	1.30	H23-H24	7.0	7.0
C31	13.1	12.5	H31	0.92	0.8	H25-H26	7.0	7.0
C32	13.7	13.4	H32	1.00	0.93	H25A-H25B	-	14.0
C33	12.8	12.6	H33	0.91	0.84	H27-H28	6.8	7.0
C34	15.8	15.6	H34	2.22	2.21	H27A-H27B	-	14.0

Crystallographic study

The crystallographically complementary coordinating aryl group is located on a second lasalocid (Lasa 2). These two lasalocid ligands (Lasa **1** and Lasa **2**) are not tied together by a three-dimensional hydrogen-bonding network as it was observed previously by Akkurt *et al*. in the case of $[Sr(Lasa)_2(H_2O)]$ as it is reported.[12] These monomeric units are not stacked by any Van der Waals forces between the coordination spheres (Figures 1 and 2).

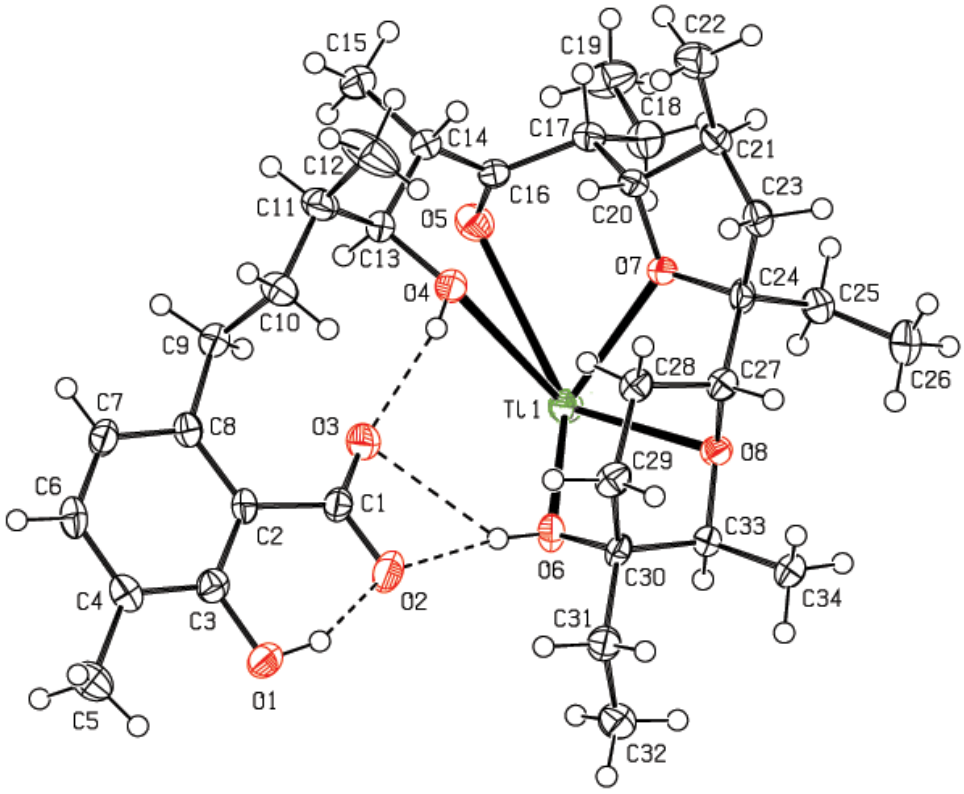


Figure 1. An *ORTEP* view of the title compound, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

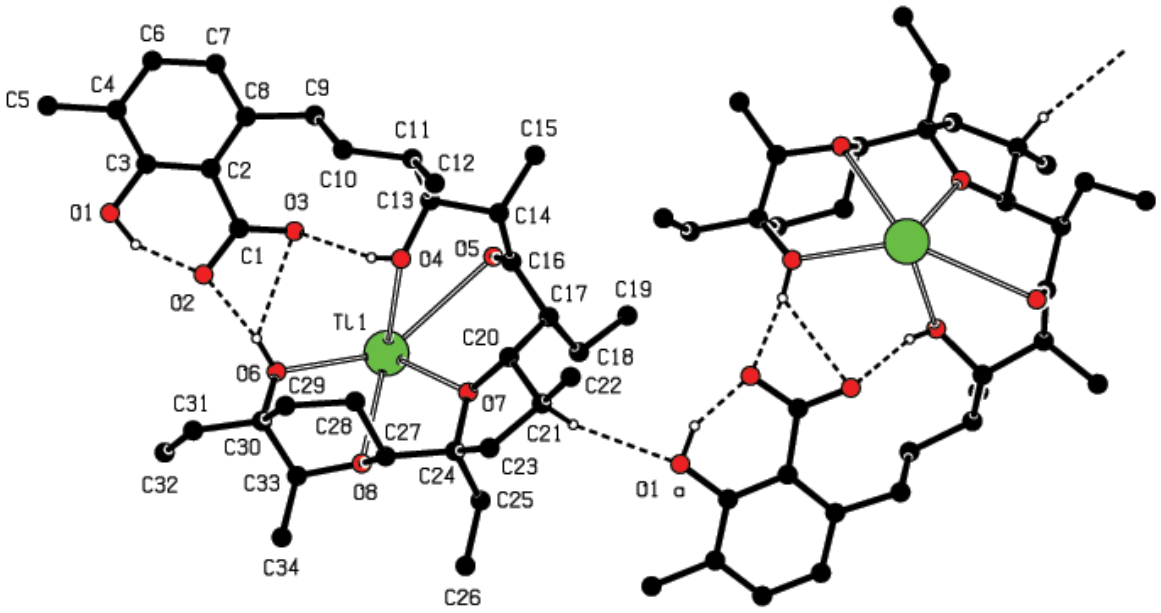
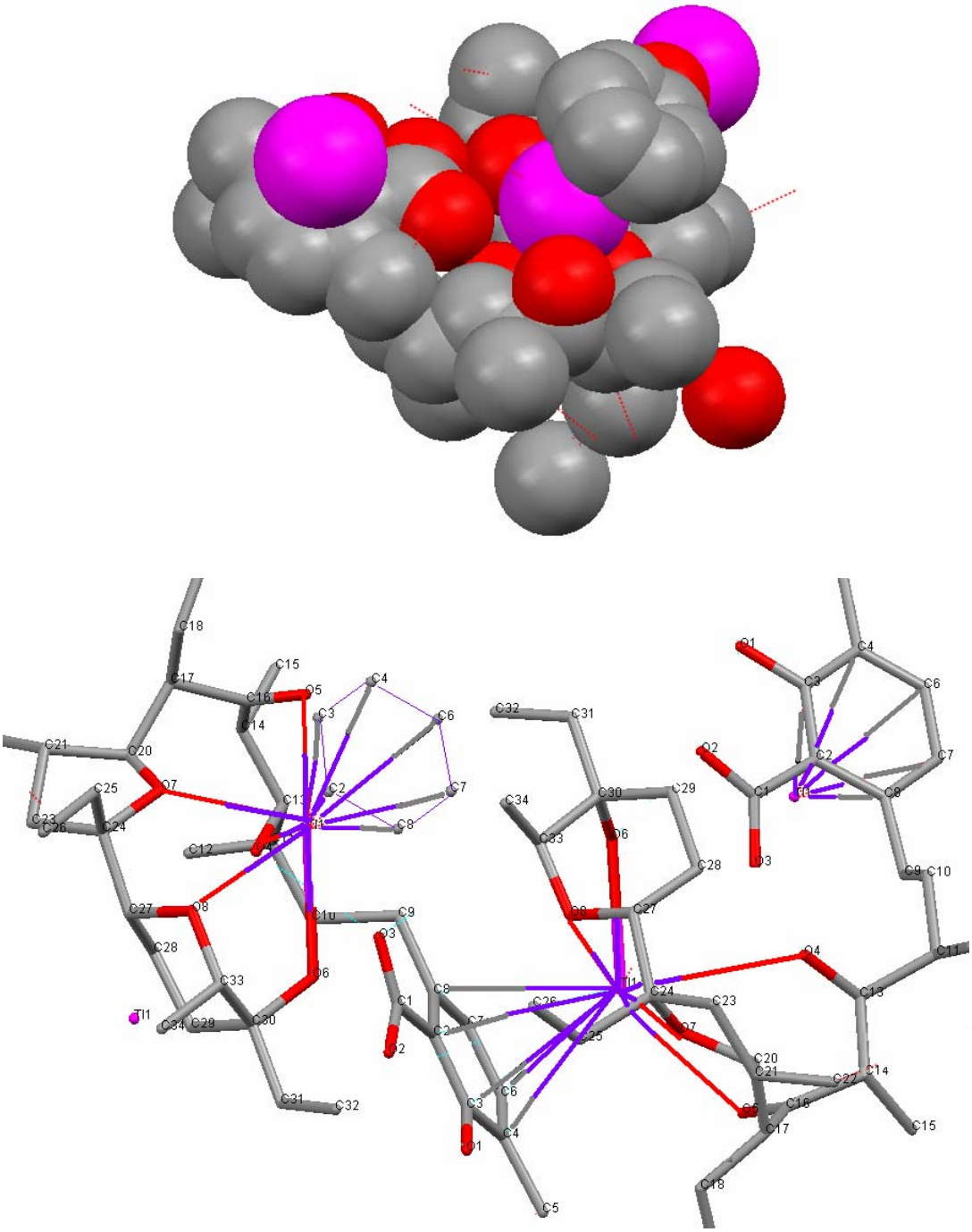


Figure 2. A view of the hydrogen bonding of the title compound. H atoms not involved in hydrogen bonding have been omitted for clarity.

Since the coordination properties of the two neighbour molecules of lasalocid ligands are not different, it is concluded that the two lasalocid ligands are individually but simultaneously coordinated to two Tl atoms (Figures 3).



Figures 3. A view of the aryl-Thallium and Thallium-Oxygen bonding of the title compound. This figure was obtained by displaying packing and short contacts.

To have a clear idea about the coordinative aspect of the lasalocid ligands leading to a polymeric aspect of this complex, the view for the complex $[Tl(Lasa)]_n$ has been added here as shown in Figure 4.

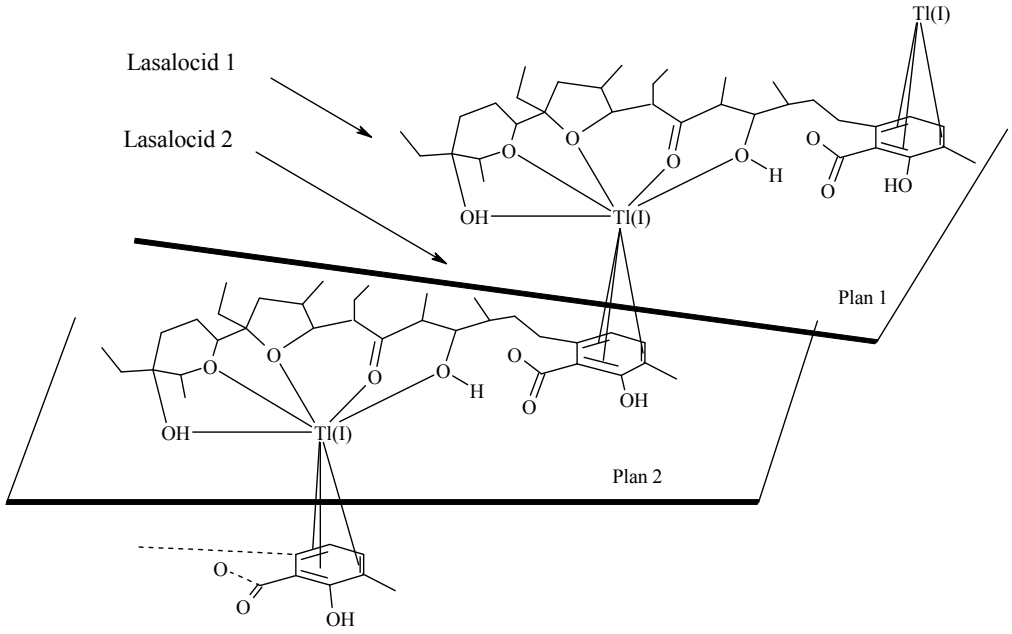


Figure 4. Polymeric aspect of $\{[thallium\text{-}(lasalocid\ anion)]\}_n$ complex.

This complex between thallium(I) and antibiotic lasalocid ligand is a polymer. It is based on dimeric, non centrosymmetric $Tl_2(Lasalocid)_2$ units without μ_2-bridging carboxylic groups resulting in Tl···Tl separations of 7.65-7.70 Å. These dimeric units are further linked to form infinite coordination polymers. In bis [(lasalocid anion)-thallium(I)] (**1**) are adjacent units are held together by secondary Tl-(phenyl) p-interactions resulting in a crystal organization which can be described as half sandwich, infinite two-dimensional polymers. Another characteristic structural motif is the tendency of the thallium ion to only use less than one hemisphere to coordinate ligands. This "half-nakedness" is due to the stereochemically active inert pair ($6s^2$), which thus plays a prominent role in controlling the structures of these compounds.[17] The Tl^+ cations are in approximate pyramidal geometries, with five oxygen donor atoms in the basal plane and the stereoactive lone pair occupying the apex position of the pyramid. There are, on the naked side of the metal ions, relatively large spaces in nonpolar environments provided by neighboring phenyl groups. The distances between the planes of the phenyl rings and the Tl^+ cation are in the range 3.43-3.50 Å, indicating that Tl^+-phenyl π^6-interactions are important in the crystal organization.

Conclusions

In conclusion, we describe here what is to our knowledge the first solid-state structure obtained with a thallium-lasalocid complex. The tetra-butyl ammonium salt of lasalocid is able to form a stable 1:1 (ligand:metal) complex with monovalent cations such as thallium(I). The structure of this complex is completely different with the respective complexes with other monovalent cations and divalent cations (Mg^{2+} and Ca^{2+}).[15]

In contrast to Sr-lasalocid complex, the study of *in vitro* biological activity of the Tl-Lasalocid on fungus *F. oxysporum*, at Oujda, shows that this compound is not biologically active. This contrast in this biological antifungal screening for the same ligand containing different metals 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)].

Experimental Section

Preparation of complex (2)

Method (A). A solution of lasalocid free acid (1 mmole, prepared in 20 mL of $CHCl_3$ was stirred with 0.1 M aqueous Tl_2CO_3 (0.7 mmole, prepared in 30 mL of H_2O). The mixture was stirred at 20 °C for 2 hours. 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. White crystals obtained proved suitable for X-ray analysis (83% Yield).

Method (B). A solution of lasalocid free acid (1 mmole, prepared in 20 mL of $CHCl_3$ was stirred with 0.1 M aqueous TlOH (1.2 mmole, prepared in 30 mL of H_2O). The mixture was stirred at 20 °C for 3 hours. 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. White crystals obtained proved suitable for X-ray analysis (85% Yield).

The complex (**2**) is characterised by ^1H and ^{13}C NMR by using Bruker AC 400 MHz spectrometer. The purity of product (**2**) is excellent (99.5%).

Crystal structure analysis. The crystal structure of the title compound, $Tl(C_{34}H_{53}O_8)$, has been determined at room temperature. Diffraction data were collected using a Bruker SMART APEXII CCD diffractometer system, using graphite-monochromated MoKα 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 $Fobs^2$ and by using SHELXL-97 programs. O1, O4 and O6 H atoms were located in a difference Fourier map and refined 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 2; with selected bond lengths, bond and torsion angles angles, and hydrogen-bonding geometry in Tables 2 and 3, respectively.

The title complex, [Tl($C_{34}H_{53}O_8$)], crystallizes with five-coordinated Tl atom three dimensionally interconnected into a polymeric structure. The thallium atom shows a distorted trigonal-pyramidal coordination geometry formed by five O atoms. The mean Tl—O bond lengths 2.9352(3) Å. The geometric parameters of the present structure agree with those previously studied at room temperature but with significantly improved precision.

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.[13] The crystal polymeric structure is stabilized by the metal-aryl Tl(i)---Aryl (Lasa i+1) and Tl(i+1)---Aryl (Lasa i+2) [ring-metal interactions with π-Ph ≤ 4 Å - symmetry code: 1-x, 1/2+y, 1/2-z] type-half sandwich bonding interactions (Table 2).

The molecular and crystal structures are stabilized by the O—H‴O and C—H‴O type-hydrogen bonding interactions (Table 5, Figure 2).

Table 3. Crystal and experimental data.

Formula: $C_{34}H_{53}O_8Tl$
Formula weight = 794.14
Crystal system: orthorhombic
Space group: $P2_12_12_1$ (No. 19); $Z = 4$
a = 11.211(3) Å
b = 13.684(4) Å
c = 22.690(7) Å
V = 3480.9(17) $Å^3$
D_x = 1.515 g cm^{-3}
μ(MoK_α) = 4.687 cm^{-1}
T = 150 K
F(0 0 0) = 1608
Crystal size = 0.13 x 0.17 x 0.19 mm
Radiation: MoK_α
R = 0.0275
R_w = 0.0557
No. of unique data measured = 10170
No. of observed data with [$I \geq 2\sigma(I)$] = 9327
No. of parameters = 400
Goodness-of-fit = 1.01
$(\Delta\rho)_{max}$ = 0.94 $eÅ^{-3}$

$(\Delta\rho)_{min}$ = -0.54 eÅ^{-3}
Measurements: Bruker SMART APEX-II CCD diffractometer [14]
Structure determination: *SIR97*[15]
Refinement: full matrix least-squares SHELXL-97[16]

Note: CCDC 682527 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.

Table 4. Selected bond lengths (Å), bond and torsion angles (°)

Tl1 - O4	3.320(3)	Tl1 - O7	2.737(2)
Tl1 - O5	3.158(2)	Tl1 - O8	2.825(2)
Tl1 - O6	2.636(2)	O6 - C30	1.433(4)
O1 - C3	1.365(5)	O7 - C20	1.439(4)
O2 - C1	1.277(4)	O7 - C24	1.467(4)
O3 - C1	1.250(4)	O8 - C27	1.439(4)
O4 - C13	1.430(4)	O8 - C33	1.444(4)
O5 - C16	1.205(4)	Tl1 - C6^{i}	3.501(4)
Tl1 - C2^{i}	3.439(3)	Tl1 - C7^{i}	3.482(4)
Tl1 - C3^{i}	3.472(4)	Tl1 -C8^{i}	3.453(3)
Tl1 - C4^{i}	3.491(4)		
O6 - Tl1 - O7	106.82(6)	Tl1 - O7 - C24	117.10(17)
O6 - Tl1 - O8	60.69(6)	C20 - O7 - C24	109.4(2)
O7 - Tl1 - O8	61.55(6)	Tl1 - O8 - C27	106.93(19)
Tl1 - O6 - C30	123.48(16)	Tl1 - O8 - C33	109.28(16)
Tl1 - O7 - C20	129.36(16)	O6 - Tl1 - O8 - C27	-99.89(19)
O7 - Tl1 - O6 - C30	-31.9(2)	O6 - Tl1 - O8 - C33	24.43(17)
O8 - Tl1 - O6 - C30	10.38(19)	O7 - Tl1 - O8 - C27	33.08(17)
O6 - Tl1 - O7 - C20	-110.0(2)	O7 - Tl1 - O8 - C33	157.41(19)
O6 - Tl1 - O7 - C24	44.46(19)	Tl1 - O6 - C30 - C29	77.0(3)
O8 - Tl1 - O7 - C20	-151.8(2)	Tl1 - O6 - C30 -C31	-162.07(18)
O8 - Tl1 - O7 - C24	2.66(17)		

Symmetry Code: i = 1-x,-1/2+y,1/2-z

Table 5. Hydrogen-bonding geometry (Å, °)

D-H···A	D-H	H···A	D...A	D-H···A
O1—HO1...O2	0.89(4)	1.65(4)	2.469(4)	152(4)
O4—HO4...O3	0.67(3)	2.05(3)	2.684(4)	159(4)
O6—HO6...O2	0.89(4)	1.86(4)	2.738(3)	170(3)
O6—HO6...O3	0.89(4)	2.49(4)	3.121(3)	129(3)'
C5—H5A...O1	0.96	2.33	2.794(5)	109
C9—H9B...O3	0.97	2.28	2.802(4)	113
C10—H10B...O4	0.97	2.57	2.935(5)	102
C20—H20...O4	0.98	2.51	3.195(4)	127
C28—H28A...O4	0.97	2.43	3.373(4)	163
C28—H28A...O7	0.97	2.50	2.900(4)	104'
C21—H21...O1^{i}	0.98	2.51	3.321(4)	140

Symmetry Code: i = 3/2-x,1-y,-1/2+z

Acknowledgements

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