Furuta for synthetic assistance.

Registry No. **1**·2HF, 136364-88-0; **1**·2HCl, 136364-87-9; **1**·2HBr, 141411-03-2; **1**·5HF, 141411-04-3; **1**·2H$^+$, 125927-22-2; F$^-$, 16984-48-8.

Supplementary Material Available: Tables of anisotropic thermal parameters for the non-H atoms, positional and isotropic thermal parameters for all atoms, bond lengths and angles, and least-squares planes and a packing diagram (14 pages); a listing of observed and calculated structure factors (24 pages). Ordering information is given on any current masthead page.

Crystal Structures of Two Polymorphic Thallium(I) Salts of the Antibiotic Lasalocid A: A Polymeric Form Involving Metal–Phenyl π-Bonding and a Monomeric Form Involving the "Half-Naked" Metal Ion

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Abstract: The crystal and molecular structures of two polymorphic lasalocid A–thallium(I) salts, which were prepared from lasalocid A sodium salt and thallium nitrate, have been determined by X-ray diffraction. Salt **1**, which was crystallized from aqueous methanol, forms a one-dimensional polymer, $[Tl^+(\text{lasalocid A}^-)]_n$, where the metal ion is coordinated, on one side, to five oxygens of an ionophore molecule and, on the other side, to the phenyl ring of the neighboring molecule, with Tl–O distances of 2.678 (8)–3.363 (10) Å and a Tl–ring (centroid) distance of 3.22 Å. The coordinated oxygens are the hydroxyl O4 and O8, carbonyl O5, and ether O6 and O7. Salt **2**, which was crystallized from aqueous methanol–ethylene glycol, forms a monomer, $Tl^+(\text{lasalocid A}^-)$, where the metal ion is coordinated, on one side, to six oxygens of an anion ligand with Tl–O distances of 2.618 (8)–3.202 (8) Å. The coordinated oxygens involve the carboxylate O2 in addition to the five oxygens in **1**. The other side of the metal ion is completely naked and exposed to a nonpolar environment provided by hydrophobic alkyl groups of neighboring molecules in the crystal structure. This is the first ionophore–metal complex that lacks three-dimensional nonpolar enclosure of the metal ion. In both salts, the conformational rigidity of the lasalocid A anion molecule is preserved: the pseudocyclic conformation is stabilized by "head-to-tail" O1···H–O8 and also by O2···H–O4 hydrogen bonds, with most of the polar oxygens directed inward to capture the metal ion and with all nonpolar groups outward. The formation of two polymorphic structures under similar crystallization conditions indicates that the Tl$^+$–phenyl η^6-bonding in salt **1** is weak. Crystallographic details: for **1**, $Tl^+(C_{34}H_{53}O_8^-)$, space group $P2_12_12_1$, a = 22.851 (2) Å, b = 11.320 (1) Å, c = 13.790 (2) Å, V = 3567.1 (8) Å^3, Z = 4, R_F and R_{wF} of 0.056 and 0.036, respectively, for 2573 reflections with $F_o > 5\sigma(F_o)$; for **2**, $Tl^+(C_{34}H_{53}O_8^-)$, space group $P2_12_12_1$, a = 18.928 (5) Å, b = 18.649 (6) Å, c = 10.054 (1) Å, V = 3549 (1) Å^3, Z = 4, R_F and R_{wF} of 0.048 and 0.028, respectively, for 2041 reflections with $F_o > 5\sigma(F_o)$.

A structural principle of ionophore–metal complexes not only for naturally occurring ionophores[1] but also for synthesized ones[1b] such as crown ethers, cryptands, or podands is that ionophores entrap charged hydrophilic metal ions with the hydrophobic side chains of the ionophore being oriented toward the periphery of the molecule. This provides effective screening of the central cation from solvent interactions and facilitates solubilization of metal ions into nonpolar media in the presence of ionophores. This is the basis of the function of ionophores as complexation and transporting agents for metal ions through lipophilic membranes. Lasalocid A (I), a carboxylic acid-type polyether antibiotic, is one of the first representatives of the naturally occurring ionophores.[2] It is unique in both its structure and its function: it is relatively small and contains an aromatic ring with a salicylic acid moiety, and it possesses the ability to complex and transport mono-, di-, and even trivalent cations through natural and artificial membranes, thus attracting the attention of numerous investigators, resulting in a large body of data on its biology[3a] and chemistry.[3b] Indeed, lasalocid A is one of the ionophores which has most extensively been subjected to X-ray crystallographic studies;[1] these include free acids,[4] amine complexes,[5] and metal salts such as those of Na$^+$,[6a–c] Ag$^+$,[6d–f] Cs$^+$,[6i] and Ba^{2+}.[6g,h] Usually, lasalocid A forms

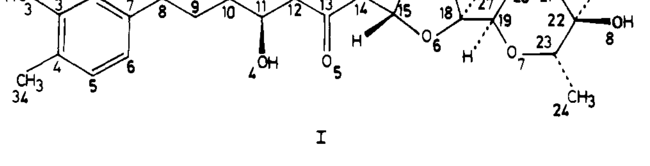

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Table I. Summary of Crystal, Data Collection, and Refinement Parameters for the Polymeric Salt **1** and the Monomeric Salt **2**

compd	Tl^+(lasalocid A^-) (**1**)	Tl^+(lasalocid A^-) (**2**)
formula	$C_{34}H_{53}O_8Tl$	$C_{34}H_{53}O_8Tl$
fw	794.16	794.16
space group	$P2_12_12_1$	$P2_12_12_1$
a (Å)	22.851 (2)	18.928 (5)
b (Å)	11.320 (1)	18.649 (6)
c (Å)	13.790 (2)	10.054 (1)
V (Å^3)	3567.1 (8)	3549 (1)
Z	4	4
d_{calcd} (g/cm^3)	1.479	1.486
$d_{measd}{}^a$ (g/cm^3)	1.48	1.48
F(000)	1608	1608
cryst shape and dimens	plate; {100}, 0.25 mm; {010}, 0.20 mm; {001}, 0.36 mm	columnar; {110}, 0.19 mm; {100}, 0.20 mm; {1,−1,0}, 0.22 mm; {001}, 0.49 mm
radiatn	Mo Kα (λ = 0.71073 Å) from graphite monochromator	
μ(Mo Kα) (cm^{-1})	46.15	46.39
transm coeff^b	0.32–0.44	0.39–0.49
T (K)	294	294
2θ limits (deg)	3.0–55.0	3.0–55.0
scan range (deg)	$1.2 + 0.5 \tan \theta$	$1.2 + 0.5 \tan \theta$
scan speed (deg in 2θ/min)	4.0	4.0
bkg counting (s)	5 at the lower and upper limits of each scan	
scan mode	ω scan for $2\theta \leq 30°$ and ω–2θ scan for $2\theta > 30°$	
no. of unique data measd	4557	4531
no. of unique data used ($F_o > 5\sigma(F_o)$)^c (m)	2573	2041
no. of variable params (n)	388	388
weighting scheme (w)	$1/\sigma^2(F_o)$	$1/\sigma^2(F_o)$
R_F	0.056	0.048
R_{wF}	0.036	0.028
S	2.19	2.11
(shift/error)$_{max}$	0.38	0.24
largest peak (e/Å^3)	2.2 (1.1 Å from Tl)	0.8 (1.2 Å from Tl)

^{a} Measured by flotation in an aqueous zinc chloride solution. ^{b} Calculated by using the Gaussian integration method of Busing and Levy.[8] ^{c} A 5σ cutting criterion was adopted on the basis of $F_o/\sigma(F_o)$ ratios of reflections with $h00$, $0k0$, and $00l$, which should disappear when h, k, or l is odd due to an extinction rule.

monomeric or dimeric structures, the latter[4c,6b–h] being in preference to the former,[4a,b,5a,6a] and the metal ion is bonded through oxygen functional groups. In minor cases, the Cs^+ salt[6i] assumes a polymeric structure and the Ag^+ salt[6d] involves the metal–phenyl η^2(olefin)-bonding. We report here the preparation and the crystal structures of the two polymorphs of the thallium(I) salts of lasalocid A, which show unusual structural features. Salt **1** is doubly rare in that it forms the polymeric structure and contains the metal–phenyl η^6-bonding. The structure of salt **2** is quite novel in that the metal ion is complexed on only one side by the ionophore ligand through the usual oxygen groups, while the other side of the metal is completely naked and exposed directly to the hydrophobic alkyl groups of neighboring ionophores. This suggests the existence of this type of structure as a stable form also in the lipid membranes. The formation of the two polymorphic structures under similar crystallization conditions is of interest and is indicative of the weak polymerization link through the Tl^+–phenyl bonding in salt **1**, consistent with the interatomic distances observed, which essentially fall within the range of van der Waals contacts. Possible roles of the salicylic acid ring moiety of lasalocid A in complexation with metal ions are also suggested.

Experimental Section

Preparation of the Thallium Salts of Lasalocid A. Salt **1** was prepared by mixing lasalocid A sodium salt (61 mg, 0.1 mmol; Sigma) dissolved in 10 mL of methanol (or acetone) and $TlNO_3$ (27 mg, 0.1 mmol; Wako Pure Chemical Industries) dissolved in 10 mL of water. The mixture was allowed to stand at room temperature, and colorless columnar crystals formed after 1 day. These were filtered off, washed with a little water, and air-dried. Anal. Calcd for $C_{34}H_{53}O_8Tl$: C, 51.42; H, 6.73; Tl, 25.73. Found: C, 51.38; H, 6.73; Tl, 26.35. The same reaction conditions gave, but only occasionally, salt **2** after several weeks.

Salt **2** was prepared more readily by mixing lasalocid A sodium salt (31 mg, 0.05 mmol) dissolved in 10 mL of methanol and $TlNO_3$ (14 mg, 0.05 mmol), followed by the addition of 5 mL of ethylene glycol. The mixture was allowed to stand at room temperature, and colorless columnar crystals formed after 1 day. Anal. Calcd for $C_{34}H_{53}O_8Tl$: C, 51.42; H, 6.73; Tl, 25.73. Found: C, 51.51: H, 6.77; Tl, 25.38.

Collection and Reduction of the X-ray Intensity Data for 1 and 2. Cell constants were determined on a Rigaku automated diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) from 20 high-order reflections for each ($21° < 2\theta < 27°$ for **1** and $22° < 2\theta < 27°$ for **2**). The crystal parameters along with details of the data collection and structure refinement are summarized in Table I. Data collection followed normal procedures.[7] Intensity data were corrected for Lorentz and polarization effects and for absorption.[8]

Solution and Refinement of the Structures. The structures were solved by Patterson and Fourier methods and refined by block-diagonal least-squares methods.[9] The absolute configuration of the lasalocid A molecule was deduced from the known stereochemistry.[10] The function $\sum w(F_o - |F_c|)^2$ was minimized with the weighting factor w equal to $\sigma(F_o)^{-2}$. A total of 43 non-hydrogen atoms were assigned anisotropic thermal parameters; at this stage, the discrepancy factors R_F[11] and R_{wF} were 0.065 and 0.045, respectively, for **1** and 0.056 and 0.038 for **2**. All 50 hydrogen atoms attached to carbon atoms were calculated from the known stereochemistry for **1** and **2**, and a hydroxyl O8 hydrogen for **1** was located from a difference Fourier map; the missing H atoms are two attached to O3 and O4 for **1** and three attached to O3, O4, and O8 for **2**. The H atom positions were not refined but were included in the

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(11) $R_F = \sum||F_o| - |F_c||/\sum F_o$, $R_{wF} = [\sum w(F_0 - |F_c|)^2/\sum wF_o{}^2\}^{1/2}$, and $S = [\sum w(F_o - |F_c|)^2/(m - n)]^{1/2}$.

Table II. Final Atomic Parameters for the Polymeric Tl^+(lasalocid A^-) Salt **1**

atom	x	y	z	$B_{eq}{}^a$ (Å^2)
Tl	0.32557 (3)	0.01441 (5)	0.01752 (4)	4.0
O1	0.1549 (5)	0.1617 (11)	−0.1492 (7)	7.4
O2	0.2480 (5)	0.1535 (10)	−0.1909 (8)	6.5
O3	0.0791 (4)	0.1820 (10)	−0.2690 (8)	6.2
O4	0.3440 (4)	0.2553 (9)	−0.1219 (7)	4.7
O5	0.4386 (4)	0.0564 (8)	−0.1071 (7)	4.9
O6	0.3912 (4)	0.1868 (8)	0.1051 (6)	3.5
O7	0.2824 (4)	0.1227 (8)	0.1845 (6)	3.4
O8	0.2151 (3)	0.0931 (8)	0.0203 (7)	4.5
C1	0.1948 (7)	0.1742 (14)	−0.2088 (11)	5.1
C2	0.1791 (6)	0.2156 (11)	−0.3118 (9)	2.7
C3	0.1188 (6)	0.2159 (12)	−0.3391 (10)	3.2
C4	0.1026 (6)	0.2517 (13)	−0.4305 (11)	4.2
C5	0.1448 (6)	0.2889 (12)	−0.4943 (10)	4.0
C6	0.2008 (6)	0.2908 (13)	−0.4711 (10)	3.8
C7	0.2202 (6)	0.2528 (13)	−0.3850 (10)	3.7
C8	0.2859 (6)	0.2571 (13)	−0.3607 (10)	3.9
C9	0.3046 (6)	0.3641 (13)	−0.3028 (11)	4.2
C10	0.3691 (7)	0.3620 (13)	−0.2685 (12)	4.7
C11	0.3811 (6)	0.2576 (13)	−0.2038 (10)	3.7
C12	0.4461 (6)	0.2546 (12)	−0.1651 (10)	2.9
C13	0.4520 (6)	0.1599 (13)	−0.0906 (10)	3.4
C14	0.4785 (5)	0.1975 (11)	0.0108 (12)	4.2
C15	0.4310 (6)	0.2691 (12)	0.0641 (10)	3.4
C16	0.4547 (6)	0.3393 (12)	0.1478 (11)	4.0
C17	0.3976 (7)	0.3553 (14)	0.2065 (11)	4.5
C18	0.3692 (6)	0.2325 (13)	0.1976 (10)	3.5
C19	0.3007 (5)	0.2459 (12)	0.1850 (10)	2.8
C20	0.2807 (6)	0.3064 (13)	0.0975 (11)	4.1
C21	0.2124 (6)	0.2924 (13)	0.0873 (11)	3.8
C22	0.1923 (6)	0.1635 (12)	0.0966 (9)	3.2
C23	0.2188 (6)	0.1093 (12)	0.1861 (10)	3.7
C24	0.1927 (6)	0.1525 (15)	0.2850 (10)	5.1
C25	0.1235 (6)	0.1588 (14)	0.0945 (10)	3.8
C26	0.1001 (6)	0.0352 (16)	0.1070 (11)	5.3
C27	0.3872 (6)	0.1516 (15)	0.2778 (11)	4.6
C28	0.3646 (8)	0.1789 (18)	0.3740 (12)	7.5
C29	0.4810 (6)	0.4547 (15)	0.1189 (11)	5.8
C30	0.5057 (6)	0.0957 (13)	0.0676 (10)	4.2
C31	0.5601 (6)	0.0424 (12)	0.0200 (12)	5.7
C32	0.4894 (8)	0.2355 (18)	−0.2425 (17)	5.4
C33	0.3837 (7)	0.4798 (17)	−0.2202 (13)	8.2
C34	0.0389 (7)	0.2434 (14)	−0.4579 (13)	6.1

[a] Equivalent temperature factors are of the form $B_{eq} = {}^4/_3\sum_i\sum_j\beta_{ij}\mathbf{a}_i\cdot\mathbf{a}_j$.

Table III. Final Atomic Parameters for the Monomeric Tl^+(lasalocid A^-) Salt **2**

atom	x	y	z	$B_{eq}{}^a$ (Å^2)
Tl	0.20472 (3)	0.20071 (3)	0.05487 (7)	5.5
O1	0.1320 (4)	0.4002 (4)	0.1187 (8)	6.9
O2	0.2030 (4)	0.3457 (3)	−0.0268 (11)	5.8
O3	0.0624 (3)	0.5046 (3)	0.0562 (11)	5.8
O4	0.3320 (4)	0.2987 (4)	−0.0211 (8)	4.9
O5	0.3101 (2)	0.1518 (2)	−0.1771 (8)	5.5
O6	0.3353 (4)	0.1349 (4)	0.1505 (9)	4.9
O7	0.2220 (2)	0.1532 (1)	0.3382 (5)	4.7
O8	0.1554 (2)	0.2771 (2)	0.2526 (7)	5.2
C1	0.1627 (5)	0.3973 (6)	0.0095 (13)	4.3
C2	0.1550 (6)	0.4606 (6)	−0.0881 (16)	3.6
C3	0.1016 (6)	0.5105 (6)	−0.0594 (18)	4.2
C4	0.0849 (7)	0.5680 (7)	−0.1437 (15)	4.3
C5	0.1252 (8)	0.5738 (8)	−0.2533 (17)	5.8
C6	0.1792 (7)	0.5264 (6)	−0.2857 (16)	4.2
C7	0.1937 (8)	0.4676 (6)	−0.2063 (14)	3.9
C8	0.2526 (7)	0.4173 (8)	−0.2507 (14)	5.3
C9	0.3213 (7)	0.4297 (7)	−0.1841 (16)	5.3
C10	0.3775 (7)	0.3706 (6)	−0.2102 (15)	5.0
C11	0.3519 (6)	0.2979 (8)	−0.1608 (12)	4.3
C12	0.4048 (7)	0.2349 (6)	−0.1812 (15)	4.0
C13	0.3675 (7)	0.1659 (6)	−0.1374 (14)	4.5
C14	0.4099 (6)	0.1167 (6)	−0.0481 (16)	3.9
C15	0.4041 (6)	0.1497 (6)	0.0976 (13)	3.6
C16	0.4588 (6)	0.1207 (7)	0.1931 (15)	4.8
C17	0.4197 (7)	0.1308 (7)	0.3263 (16)	5.3
C18	0.3424 (8)	0.1188 (8)	0.2935 (16)	5.4
C19	0.2922 (8)	0.1720 (5)	0.3708 (13)	4.6
C20	0.3052 (8)	0.2501 (6)	0.3438 (15)	4.3
C21	0.2475 (6)	0.2963 (8)	0.4122 (13)	4.9
C22	0.1724 (7)	0.2678 (6)	0.3949 (13)	4.9
C23	0.1705 (6)	0.1896 (7)	0.4209 (15)	4.7
C24	0.1739 (6)	0.1652 (6)	0.5631 (16)	5.4
C25	0.1208 (7)	0.3103 (7)	0.4794 (13)	5.3
C26	0.1083 (7)	0.3875 (7)	0.4463 (19)	6.8
C27	0.3204 (8)	0.0415 (7)	0.3077 (18)	7.3
C28	0.3196 (8)	0.0142 (7)	0.4392 (20)	9.7
C29	0.5277 (8)	0.1650 (8)	0.1843 (16)	6.7
C30	0.3836 (7)	0.0400 (6)	−0.0511 (19)	5.7
C31	0.3977 (8)	0.0077 (7)	−0.1900 (17)	6.3
C32	0.4277 (7)	0.2274 (6)	−0.3228 (17)	6.9
C33	0.4480 (7)	0.3915 (8)	−0.1430 (16)	7.1
C34	0.0256 (7)	0.6187 (7)	−0.1057 (17)	6.2

[a] Equivalent temperature factors are of the form $B_{eq} = {}^4/_3\sum_i\sum_j\beta_{ij}\mathbf{a}_i\cdot\mathbf{a}_j$.

structure factor calculations in the final cycles of refinement with isotropic temperature factors of 6 Å^2. The final R_F, R_{wF}, and S[11] values were 0.056, 0.036, and 2.19, respectively, for **1** and 0.048, 0.028, and 2.11 for **2**.

Neutral-atomic scattering factors[12] were used with Tl corrected for anomalous dispersion.[12] The final atomic parameters for the non-hydrogen atoms with the equivalent isotropic temperature factors are listed in Tables II and III. The anisotropic temperature factors for the non-hydrogen atoms and the atomic parameters for hydrogen atoms are available in Tables S1–S4.[13] Lists of final calculated and observed structure amplitudes are collected in Tables S5 and S6.[13]

^{1}H and ^{13}C NMR Measurements. NMR spectra of freshly prepared crystalline samples of salts **1** and **2** dissolved in $CDCl_3$, which was dried by distillation from P_2O_5 before use, were recorded on a JEOL GX-500 or GX-270 instrument. Assignments of ^{1}H and ^{13}C NMR spectra were carried out on the basis of the ^{13}C NMR data[14] reported by Lallemand and Michon, together with the aid of H–H and C–H COSY techniques, which could clarify several ambiguous assignments by Lallemand and Michon. Final assignments are listed in Table S7.[13]

Results

Crystal and Molecular Structure of the Polymeric Lasalocid A–Thallium Salt 1. The complex forms as a polymeric structure with the composition $[Tl^+(\text{lasalocid } A^-)]_n$, a segment of which is shown in Figure 1. The carboxylate group is deprotonated as usual. The Tl^+ ion is complexed, on one side, to five oxygen atoms of an ionophore molecule, with Tl–O distances ranging from 2.678 (8) to 3.363 (10) Å (Table IV); they are the hydroxyl O4[15] and O8, the carbonyl O5,[15] and the ether O6 and O7. The other side of the Tl^+ ion is capped by the phenyl ring of the neighboring molecule, related by $^1/_2 - x, -y, {}^1/_2 + z$, with a Tl-ring (centroid) distance of 3.22 Å,[18,19] thereby producing a one-dimensional zigzag

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(12) *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. IV.

(13) Supplementary material.

(14) Lallemand, J. Y.; Michon, V. *J. Chem. Res., Synop.* **1978**, 162–163; *J. Chem. Res., Miniprint* **1978**, 2081–2090.

(15) Though the Tl–O4(hydroxyl) and the Tl–O5(carbonyl) distances [3.363 (10) and 3.138 (1) Å in **1** and 3.119 (8) and 3.202 (8) Å in **2**] are somewhat longer than the sum of the ionic radius of Tl^+ (1.47[16a] Å) and the van der Waals radii[16b] of >O (1.52 Å) or =O (1.50 Å), we adopted these as coordination distances, since the Tl^+ ion has been known to be usually six- or eight-coordinate in the crystalline state[17] and to be far from being spherical due to the "inert-pair effect".[17]

(16) (a) *CRC Handbook of Chemistry and Physics*; Weast, R. C., Ed.; The Chemical Rubber Co.: Cleveland, OH, 1971; p F-153. (b) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441–451.

(17) (a) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 4th ed.; Interscience Publishers: New York, London, and Sydney, 1980; pp 326–351. (b) Alcock, N. W.; Jenkins, H. D. B. *J. Chem. Soc., Dalton Trans.* **1974**, 1907–1911. We thank a reviewer for directing our attention to these references.

(18) The sum of the ionic radius of Tl^+ and the van der Waals radius of the aromatic ring (1.77[16b] Å) is 3.24 Å.

(19) The displacement of the Tl atom from the least-squares plane of the phenyl ring is also 3.219 (6) Å (Table S8[13]), indicating that the metal atom rides just over the center of the ring.

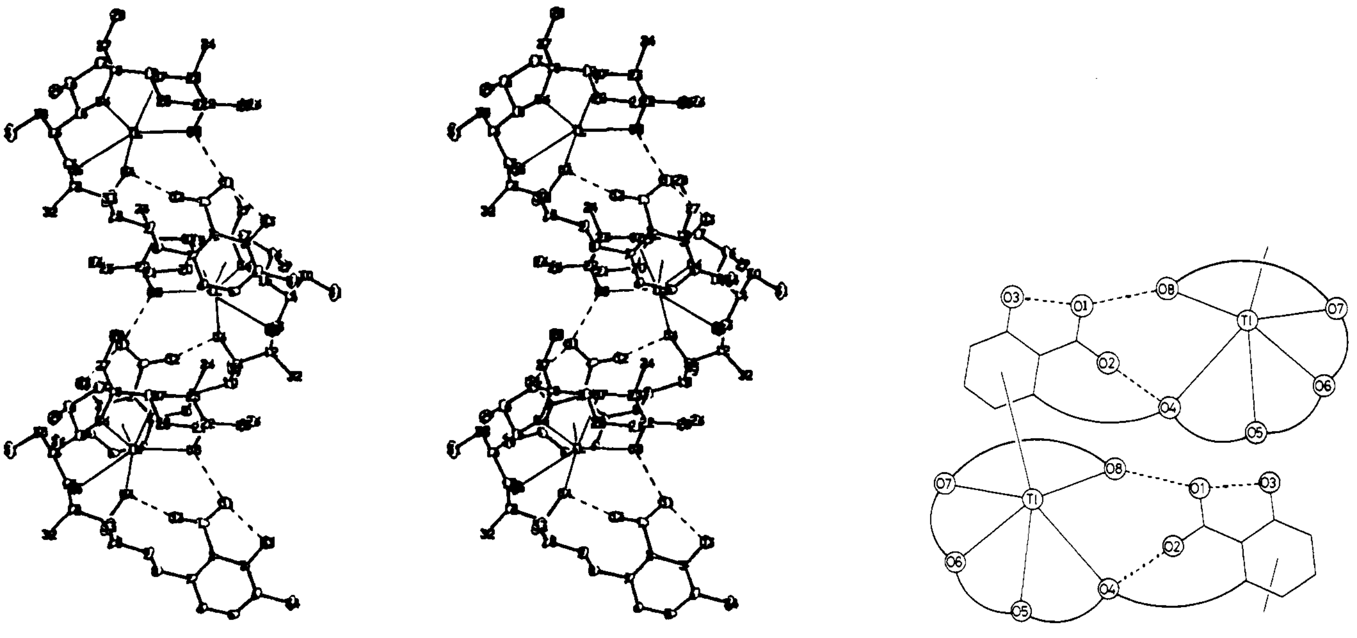

Figure 1. (a, left) Stereoscopic view of the polymeric Tl$^+$(lasalocid A$^-$) salt **1** and (b, right) its schematic representation. Broken lines denote hydrogen bonds.

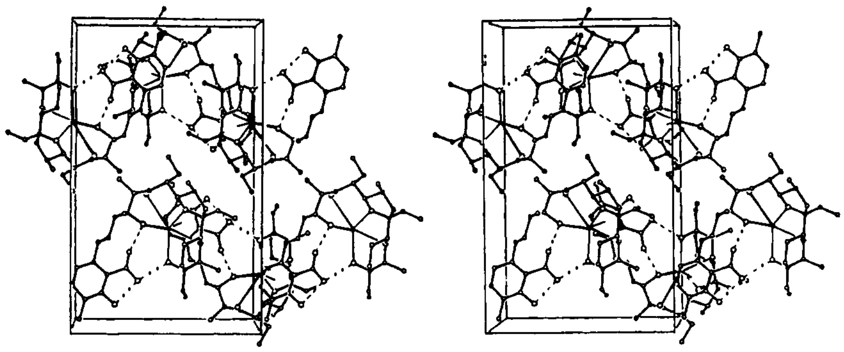

Figure 2. Stereoscopic view of the polymeric Tl$^+$(lasalocid A$^-$) salt **1**, showing the crystal packing, down the *c* axis with the *a* axis horizontal and the *b* axis vertical. Broken lines denote hydrogen bonds.

chain along the *c* axis with a Tl···Tl distance of 7.719 (1) Å and a Tl···Tl···Tl angle of 126.56 (1)°. The Tl$^+$-phenyl distance of 3.22 Å is comparable to that of 3.27 Å in [Tl(PhNNNPh)]$_2$[20] and 3.33 Å in [Tl(TolNNNNNTol)]$_2$,[20] and these values fall essentially within the range of van der Waals distances.[18] The lasalocid A molecule adopts the familiar pseudocyclic conformation, which is stabilized by an intramolecular "head-to-tail" hydrogen bond between the carboxylate oxygen O1 of the "head" phenyl ring and the hydroxyl O8 of the "tail" ether ring [2.82 (1) Å] and is further reinforced by an intramolecular hydrogen bond[21] between the carboxylate O2 and the hydroxyl O4 [2.66 (1) Å] and by a "salicylic acid-type" hydrogen bond between the hydroxyl O3 and the carboxylate O1 [2.40 (2) Å], thus forming an O3–H···O1···H–O8 hydrogen-bonding chain. The polar oxygen groups of the backbone are directed toward the metal ion, and the nonpolar groups toward the exterior of the molecule. Thus Tl$^+$ ions are captured in an infinite double layer composed of lasalocid A molecules with its outer surface being lipophilic. The carboxylate group is nearly coplanar with the phenyl ring, the torsion angle C3-C2-C1-O1 being -12 (2)°. The six-membered tetrahydropyran ring is in the chair conformation and the five-membered tetrahydrofuran ring adopts an envelope conformation with C16 deviating from the plane of the remaining four atoms by 0.66 (2) Å (Table S8[13]) and with the torsion angle C15–O6–C18–C17 being 3 (1)° (0° for the ideal envelope conformation). The ethyl C25–C26 substituent attached to the "tail" ether ring takes the "type A" position (designated by Deusler and Paul[1a]), i.e., bisecting the C23–C22–O8 angle [C23–C22–C25–C26 = -55 (2)°]. The bond distances and angles of the anion molecule are mostly as expected.[5,6b,f-h]

The crystal packing (Figure 2) is mainly dominated by nonpolar van der Waals contacts; the closest contact between columns which are running parallel to each other in the *bc* plane is one between C29 and C34 [3.61 (2) Å], and the closest contact between columns running antiparallel in the *ac* plane is one between O3 and C16 [3.31 (2) Å] (Table V).

Crystal and Molecular Structure of the Monomeric Lasalocid A–Thallium Salt 2. This complex forms as a monomeric structure with the composition Tl$^+$(lasalocid A$^-$), which is shown in Figure 3. The Tl$^+$ ion is coordinated on one side to six oxygen atoms, the carboxylate O2, the hydroxyl O4[15] and O8, the carbonyl O5,[15] and the ether O6 and O7, with Tl–O distances ranging from 2.618 (8) to 3.202 (8) Å (Table IV). The other side of the metal ion is, however, completely naked. The lasalocid A molecule again assumes the pseudocyclic conformation stabilized by a "head-to-head" hydrogen bond[23] [O1···O8 = 2.70 (1) Å], by a "head-to-near-head" hydrogen bond [O2···O4 = 2.59 (1) Å], and by a

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(20) Beck, J.; Strahle, J. *Z. Naturforsch.* **1986**, *41B*, 1381–1386.

(21) The possibility of bifurcated hydrogen bonding of this hydrogen atom to the other carboxylate oxygen O2 [O8···O2 = 3.08 (1) Å and H···O2 = 2.53 Å] may be rejected on the basis of its unfavorable geometry:[22] O8···O2–C1 89.4 (9)° and H···O2–C1 = 73°.

(22) Taylor, R.; Kennard, O.; Versichel, W. *J. Am. Chem. Soc.* **1983**, *105*, 5761–5766.

(23) Though the hydroxyl O8 also makes close contact with the carboxylate O2, the dimensions and geometry [O8···O(2) = 3.22 (1) Å and O8···O2–C1 = 83.3 (7)°], which are similar to those[21] in **1**, may exclude the possibility of its hydrogen bonding to O2 (the O8 hydrogen was not located).

Table IV. Bond Distances (Å) and Angles (deg) for the Polymeric Salt **1** and the Monomeric Salt **2**

	1	**2**		**1**	**2**
		(a) Coordination Sphere			
		Bond Distances			
Tl–O2		2.826 (7)	Tl–O7	2.789 (9)	3.001 (8)
Tl–O4	3.363 (10)	3.119 (8)	Tl–O8	2.678 (8)	2.618 (8)
Tl–O5	3.138 (10)	3.202 (8)	Tl–C*[a]	3.219	
Tl–O6	2.741 (9)	2.922 (8)			
		Bond Angles			
O2–Tl–O4		51.5 (2)	O5–Tl–O7	132.6 (3)	122.7 (2)
O2–Tl–O5		93.9 (3)	O5–Tl–O8	137.2 (3)	158.5 (2)
O2–Tl–O6		120.5 (2)	O6–Tl–O7	61.1 (3)	58.1 (2)
O2–Tl–O7		124.0 (3)	O6–Tl–O8	105.8 (3)	106.3 (3)
O2–Tl–O8		72.3 (2)	O7–Tl–O8	60.5 (3)	58.6 (2)
O4–Tl–O5	57.4 (2)	60.5 (2)	O4–Tl–C*[a]	159.8	
O4–Tl–O6	66.8 (3)	70.9 (2)	O5–Tl–C*[a]	104.2	
O4–Tl–O7	99.2 (3)	108.7 (2)	O6–Tl–C*[a]	118.1	
O4–Tl–O8	81.8 (3)	98.2 (2)	O7–Tl–C*[a]	100.0	
O5–Tl–O6	71.5 (3)	66.0 (2)	O8–Tl–C*[a]	113.4	
		(b) Lasalocid A Anion			
		Bond Distances			
C1–C2	1.54 (2)	1.54 (2)	C14–C15	1.54 (2)	1.59 (2)
C2–C3	1.43 (2)	1.40 (2)	C14–C30	1.53 (2)	1.51 (2)
C3–C4	1.38 (2)	1.40 (2)	C30–C31	1.53 (2)	1.54 (2)
C4–C5	1.37 (2)	1.34 (2)	C15–C16	1.50 (2)	1.51 (2)
C5–C6	1.32 (2)	1.39 (2)	C16–C17	1.55 (2)	1.54 (2)
C6–C7	1.34 (2)	1.38 (2)	C17–C18	1.54 (2)	1.52 (2)
C7–C2	1.44 (2)	1.40 (2)	C18–O6	1.47 (2)	1.47 (2)
C1–O1	1.23 (2)	1.24 (1)	O6–C15	1.42 (2)	1.43 (1)
C1–O2	1.26 (2)	1.28 (1)	C16–C29	1.49 (2)	1.55 (2)
C3–O3	1.38 (2)	1.38 (2)	C18–C19	1.58 (2)	1.58 (2)
C4–C34	1.51 (2)	1.52 (2)	C18–C27	1.49 (2)	1.51 (2)
C7–C8	1.54 (2)	1.52 (2)	C27–C28	1.46 (2)	1.42 (2)
C8–C9	1.51 (2)	1.48 (2)	C19–C20	1.46 (2)	1.50 (2)
C9–C10	1.55 (2)	1.55 (2)	C20–C21	1.58 (2)	1.55 (2)
C10–C11	1.51 (2)	1.52 (2)	C21–C22	1.54 (2)	1.53 (2)
C10–C33	1.53 (2)	1.55 (2)	C22–C23	1.51 (2)	1.48 (2)
C11–C12	1.58 (2)	1.56 (2)	C23–O7	1.46 (2)	1.45 (1)
C11–O4	1.41 (2)	1.45 (1)	O7–C19	1.46 (2)	1.41 (2)
C12–C13	1.49 (2)	1.53 (2)	C22–O8	1.42 (2)	1.48 (1)
C12–C32	1.47 (3)	1.49 (2)	C22–C25	1.57 (2)	1.52 (2)
C13–C14	1.58 (2)	1.51 (2)	C25–C26	1.51 (2)	1.50 (2)
C13–O5	1.23 (2)	1.19 (1)	C23–C24	1.54 (2)	1.50 (2)
		Bond Angles			
C1–C2–C3	118 (1)	116 (1)	C15–C14–C30	116 (1)	111 (1)
C2–C3–C4	120 (1)	123 (1)	C14–C30–C31	114 (1)	109 (1)
C3–C4–C5	119 (1)	115 (1)	C14–C15–C16	113 (1)	113 (1)
C4–C5–C6	122 (1)	124 (1)	C15–C16–C17	99 (1)	100 (1)
C5–C6–C7	122 (1)	121 (1)	C16–C17–C18	102 (1)	105 (1)
C6–C7–C2	120 (1)	117 (1)	C17–C18–O6	104 (1)	106 (1)
C7–C2–C1	126 (1)	124 (1)	C18–O6–C15	110 (1)	109 (1)
C7–C2–C3	116 (1)	119 (1)	O6–C15–C16	106 (1)	109 (1)
C2–C1–O1	119 (1)	119 (1)	O6–C15–C14	107 (1)	109 (1)
C2–C1–O2	117 (1)	117 (1)	C15–C16–C29	114 (1)	110 (1)
O1–C1–O2	124 (1)	124 (1)	C17–C16–C29	112 (1)	113 (1)
C2–C3–O3	117 (1)	120 (1)	C17–C18–C19	110 (1)	112 (1)
C4–C3–O3	123 (1)	117 (1)	O6–C18–C19	106 (1)	107 (1)
C3–C4–C34	118 (1)	119 (1)	C17–C18–C27	112 (1)	113 (1)
C5–C4–C34	122 (1)	125 (1)	O6–C18–C27	109 (1)	105 (1)
C2–C7–C8	120 (1)	125 (1)	C19–C18–C27	114 (1)	113 (1)
C6–C7–C8	120 (1)	118 (1)	C18–C27–C28	116 (1)	116 (1)
C7–C8–C9	115 (1)	114 (1)	C18–C19–C20	116 (1)	115 (1)
C8–C9–C10	115 (1)	114 (1)	C19–C20–C21	110 (1)	110 (1)
C9–C10–C11	112 (1)	111 (1)	C20–C21–C22	113 (1)	114 (1)
C9–C10–C33	109 (1)	110 (1)	C21–C22–C23	110 (1)	110 (1)
C11–C10–C33	113 (1)	111 (1)	C22–C23–O7	110 (1)	110 (1)
C10–C11–C12	113 (1)	115 (1)	C23–O7–C19	113 (1)	113 (1)
C10–C11–O4	112 (1)	113 (1)	O7–C19–C20	111 (1)	111 (1)
C12–C11–O4	107 (1)	108 (1)	O7–C19–C18	101 (1)	107 (1)
C11–C12–C13	109 (1)	107 (1)	C21–C22–O8	111 (1)	106 (1)
C11–C12–C32	113 (1)	112 (1)	C23–C22–O8	103 (1)	106 (1)
C13–C12–C32	110 (1)	109 (1)	C21–C22–C25	109 (1)	111 (1)
C12–C13–C14	117 (1)	116 (1)	C23–C22–C25	114 (1)	114 (1)
C12–C13–O5	122 (1)	121 (1)	O8–C22–C25	110 (1)	110 (1)
C14–C13–O5	121 (1)	123 (1)	C22–C25–C26	113 (1)	119 (1)
C13–C14–C15	107 (1)	106 (1)	C22–C23–C24	115 (1)	118 (1)
C13–C14–C30	114 (1)	113 (1)	O7–C23–C24	111 (1)	112 (1)

[a] The centroid of the phenyl ring.

Table V. Hydrogen-Bonding Distances (Å) and Angles (deg) and Other Short Contacts (Å) for the Polymeric Salt **1**[a]

Hydrogen Bonding

donor (D)	acceptor (A)	D–H	D···A	H···A	D–H···A
O3–H[b]	O1		2.40 (2)		
O4–H[b]	O2		2.66 (1)		
O8–H[c]	O1	1.1	2.82 (1)	1.86	144

Other Short Contacts (Less Than 3.6 Å)

B	C	B···C	B	C	B···C
		(a) Intramolecular Contacts			
O1	C25	3.44 (2)	O5	C31	3.29 (2)
O2	O8	3.08 (1)	O7	C28	3.28 (2)
O2	C8	2.76 (2)	C1	C9	3.55 (2)
O2	C9	3.12 (2)	C15	C20	3.49 (2)
O4	C8	3.55 (1)	C24	C26	3.48 (2)
O4	C20	3.40 (2)			
		(b) Intermolecular Contacts			
O2	$C23^{i}$	3.51 (2)[d]	O3	$C29^{iii}$	3.42 (2)[e]
O3	$C16^{ii}$	3.31 (2)[e]			

[a] Symmetry codes: (none) x, y, z; (i) $^1/_2 - x, -y, ^1/_2 + z$; (ii) $x - ^1/_2, ^1/_2 - y, 1 - z$; (iii) $x - ^1/_2, ^1/_2 - y, -z$. [b] This hydrogen atom was not located. [c] This hydrogen atom was located from a difference Fourier map. [d] Intrapolymer. [e] Interpolymer.

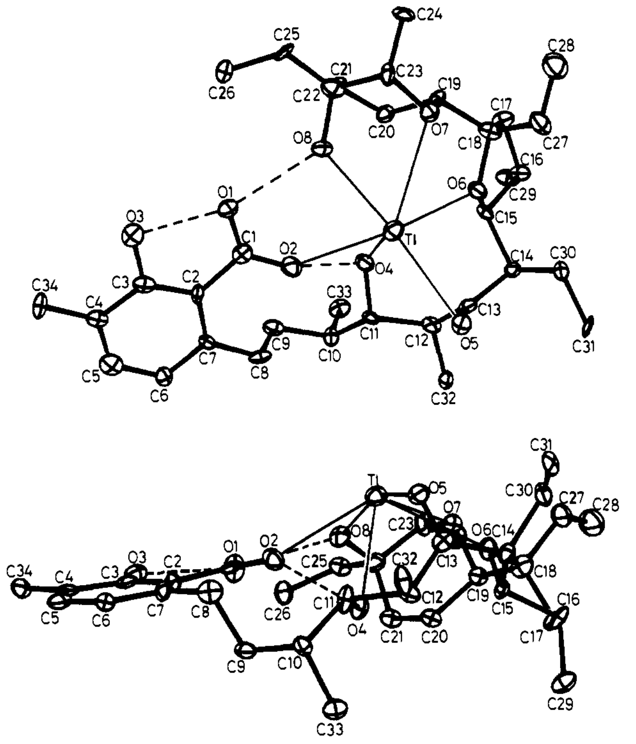

Figure 3. Molecular structure of the monomeric Tl⁺(lasalocid A⁻) salt **2**: (a, top) top view; (b, bottom) side view. Broken lines denote hydrogen bonds.

"salicylic acid-type" hydrogen bond [O1···O3 = 2.43 (1) Å], with the polar oxygen groups directed toward the inside of the molecule and nonpolar groups directed outward. The carboxylate group is nearly coplanar with the phenyl ring, with the torsion angle C3–C2–C1–O1 = −13 (2)°. The tetrahydropyran ring is in the chair conformation and the tetrahydrofuran ring adopts the envelope conformation with C16 deviating 0.52 (2) Å from the other four-atom plane (Table S8[13]) [torsion angle C15–O6–C18–C17 = 4 (1)°], both usual conformations in the lasalocid A structures.[1a] The ethyl substituent C25–C26 bisects the C21–C22–O8 angle [C21–C22–C25–C26 = 66 (2)°] (the "type B" position[1a]). The dimensions of the anion molecule are mostly normal.[5,6b,f–h]

The crystal packing (Figure 4 and Table VI) is largely governed by nonpolar van der Waals contacts, with the closest contact of 3.40 (2) Å between O3 and C31. There is, on the naked side of the metal ion, a relatively large space in a nonpolar environment provided by hydrophobic methyl or ethyl groups of neighboring molecules (see below). The closest distance between Tl⁺ and the neighboring ionophore is 4.20 (1) Å to C28 (at $^1/_2 - x, -y, z - ^1/_2$).

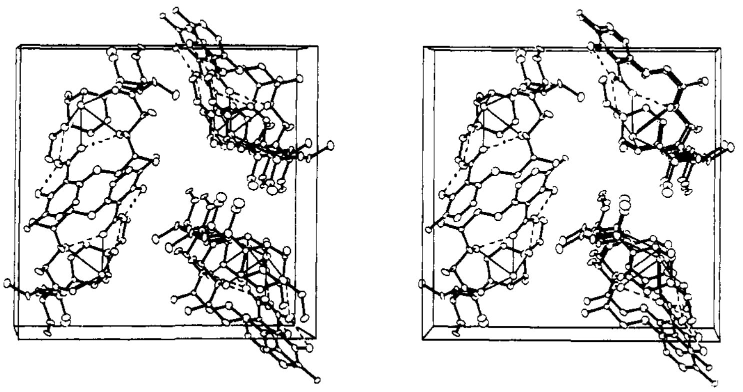

Figure 4. Stereoscopic view of the monomeric Tl^+(lasalocid A^-) salt **2**, showing the crystal packing, down the *c* axis with the *a* axis horizontal and the *b* axis vertical. Broken lines denote hydrogen bonds.

Table VI. Hydrogen-Bonding Distances (Å) and Other Short Contacts (Å) for the Monomeric Salt **2**[a]

Hydrogen Bonding

donor (D)	acceptor (A)	D···A	donor (D)	acceptor (A)	D···A
O3–H[b]	O1	2.43 (1)	O8–H[b]	O1	2.70 (1)
O4–H[b]	O2	2.59 (1)			

Other Short Contacts (Less Than 3.6 Å)

B	C	B···C	B	C	B···C
		(a) Intramolecular Contacts			
O1	C26	3.33 (2)	O4	C8	3.53 (2)
O2	O8	3.22 (1)	O5	C31	3.16 (1)
O2	C8	2.78 (1)	O7	C28	3.34 (1)
O2	C9	3.16 (2)	C32	C33	3.58 (2)
		(b) Intermolecular Contacts			
O3	$C10^{i}$	3.50 (2)	O3	$C31^{ii}$	3.40 (2)
O3	$C33^{i}$	3.60 (2)	C1	$C29^{ii}$	3.42 (2)
O3	$C30^{ii}$	3.49 (1)	C2	$C29^{ii}$	3.50 (2)

[a] Symmetry codes: (none) x, y, z; (i) $^1/_2 - x, 1 - y, ^1/_2 + z$; (ii) $x - ^1/_2, ^1/_2 - y, -z$. [b] Hydrogen atom attached to this atom was not located.

Model Building and NMR Investigations To Examine the Possible Existence of Any Ligand on the Naked Side of the Metal Ion in the Monomeric Salt 2. Because of the unusual structural aspect in salt **2** that the hemisphere of the metal ion is completely naked (see below), we carefully examined the possibile existence of a methanol or a water molecule on the naked side (both water and methanol were used for crystallization of the salt) under the assumption that it was lost during X-ray exposure or extensively disordered,[6d] even though the elementary analysis of the freshly prepared crystalline sample **2** is consistent neither with additional methanol nor water and the final difference Fourier map also showed no residual electron density higher than 0.8 e $Å^3$.

A model-building consideration[24] revealed that the space on the naked side of the metal ion in the crystal lattice is extremely limited and apparently too small for a methanol; however, it is still sufficiently large for a water molecule. This prompted an NMR study to check for the presence of a water ligand, if any, before X-ray exposure.

Lallemand and Michon have carried out a ^{13}C NMR study of the thallium salt of lasalocid A and have assigned almost all the carbon peaks unambiguously.[14] We recorded ^1H–^1H and ^1H–^{13}C COSY spectra on a 500-MHz NMR instrument in order to assign the ^1H NMR peaks. All of the signals were completely consistent with the protons on the lasalocid A framework, apparently excluding the existence of methanol because of the lack of any signal peak around δ 3–4 ppm (Table S7[13]). Similarly, we could not obtain any clear evidence for the existence of coordinated water. Dissolution of **2** in $CDCl_3$ may initiate an exchange of coordinated water with $CDCl_3$; however, no free water peak was observed. Addition of D_2O to the $CDCl_3$ solution of **2** resulted in the disappearance of three broad singlet peaks corresponding to the three OH groups in lasalocid A at δ 5.23, 8.33, and 14.70 ppm, with no change of the spectrum in other regions. This H–D exchange experiment also excludes the existence of water. Additional evidence to exclude coordinated water in **2** was obtained from the comparison of its NMR spectra to those of the polymeric salt **1**: a solution of **1** dissolved in anhydrous $CDCl_3$ afforded the same ^1H NMR spectrum as that of **2**, indicating that the same species may form for **1** and **2** in solution and more importantly that salt **2** may not involve water because salt **1** originally contains no water molecule.

Discussion

Comparison of the Lasalocid A–Thallium Salt Structures 1 and 2 with Free Acid[4] or Other Salt[5,6] Structures. Characteristic common structural features are as follows. First, the pseudocyclic conformation of the ionophore is preserved (Table S10[13]); the cyclic conformation is not due to the metal ligation, since it also holds for free acids, but rather, as well documented,[1] is due to the conformational rigidity of the ionophore molecule itself, presumably arising from steric constraints imposed by methyl or ethyl substituents attached to the backbone. Second, intramolecular hydrogen bonds complete and stabilize the cyclic cavity. These hydrogen bonds include a "head-to-tail" O1 and/or an O2···H–O8 (in the ionized ionophore) or an O2–H···O8 (in the neutral form) hydrogen bond or bonds and a "head-to-tail" O1 and/or an O2···H–O8 (in the ionized ionophore) or an O2–H···O8 (in the neutral form) hydrogen bond or bonds and a "head-to-near-head" O2···H–O4 hydrogen bond (in the ionized form[25]). Third, except for the case of the present monomeric thallium salt **2** (see below), the periphery of the circular molecule of the ionophore or its salt is quite nonpolar, while the majority of the oxygen functional groups are directed toward the interior. These three structural aspects are also common in all the other carboxylic acid-type ionophores. Fourth, the carboxyl or carboxylate group is nearly coplanar with the plane of the phenyl ring. This coplanarity is apparently caused by the formation of the O3–H···O1 hydrogen bond; otherwise the carboxyl group may significantly rotate due to steric hindrance. In the crystal structure of 6-methylaspirin,[26] for example, in which the carboxyl group is flanked by the acetoxy and the methyl substituents but is unable to form any hydrogen bond, it rotates by 44.7 (2)° from the benzene plane. Fifth, usually, oxygens O4, O5, O6, O7, and O8 are involved in the metal ligation (Table S11[13]). The simultaneous involvement of the "tail" oxygen atom O8 and the "head" carboxylate oxygen O2 is rare; this occurs only for large metal ions

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(24) Nonbonded nearest-neighbor contacts between the (assumed) ligating oxygen atom (of a methanol or a water) and the nearest atom in the cell were calculated by generating the Tl–O vector in the whole hemisphere around the metal atom, where the Tl–O distance was assumed to be 2.50 Å (Table S9[13]).

(25) This hydrogen bond is of no significance or is very weak in the neutral form.

(26) Fronczek, F. R.; Merrill, M. L.; Gandour, R. D. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1977**, *B38*, 1337–1339.

such as Ba^{2+},[6g,h] Cs$^+$,[6i] and Tl$^+$ (the present salt **2**). Sixth, there is a strong propensity to form dimeric structures[4c,6b–h] in preference to monomeric structures.[4a,b,5,6a] This is believed[3] to be due to the conformational integrity of the ionophore molecule and its relatively small molecular size, which both make it difficult to provide three-dimensional nonpolar protection for a metal ion in a 1:1 complex.

Therefore, the present thallium salt **1** is doubly rare in lasalocid A structural chemistry in that it forms a polymeric structure and contains metal–phenyl η^6-bonding. This is only the second example of a polymeric structure; the other is the Cs$^+$ salt,[6i] in which the metal ion is complexed on one side by an ionophore and on the other side attaches to the hydroxyl O3 of the next ionophore. This is also the second example involving metal–phenyl π-bonding; the other is the dimeric Ag$^+$ salt,[6d] in which the metal ion binds to the phenyl ring of the pairing ionophore through the C5=C6 double bond. However, Tl$^+$–aromatic ring π-bonding itself is quite common.[20,27]

On the other hand, the structure of thallium salt **2** is quite unusual in that it lacks three-dimensional nonpolar protection of the metal ion. This is the second lasalocid A–metal salt that forms a monomeric structure; of all the ten known lasalocid A–metal complexes,[6] only the Na$^+$ salt[6a] forms a monomeric structure. Importantly, even in the monomeric Na$^+$ salt,[6a] the metal ion is three-dimensionally protected, on one side by an ionophore ligand and on the other side by a capping methanol ligand. Although the reason for the absence of methanol coordination in the Tl$^+$ salt is not clear, it may be due to the nature of the Tl$^+$ ion itself: the Tl$^+$ ion is nonspherical, possibly with its inert pair (6s^2) in some s- and p-hybridized orbital producing an electronic bulge on one side,[17] i.e., on the naked side in the present salt.[28] In fact, the "half-naked" Tl$^+$ ion has been exemplified in the crystal structure of $[(C_5H_5)Co\{C_3B_2(CH_3)_4\}Tl]$[29] or $[PPh_3Me]^+[3,1,2\text{-}TlC_2B_9H_{11}]^-$,[30] with an apical thallium atom η^5-bonded to the C_3B_2 or the C_2B_3 face, respectively,[31] [HB(3-*p*-tolylpyrazolyl)$_3$Tl],[32] or [(malonohydroxamato)Tl].[33] Another important feature of thallium salt **2** is the nonpolar environment around the "half-naked" molecule in the crystal structure, reminiscent of the nonpolar environment in membranes.

Possible Roles of the Salicylic Acid Moiety in Lasalocid A Functions. Since the involvement of the salicylic acid moiety as a constituent is unique in polyether antibiotics, it is of interest to consider its possible roles in lasalocid A functions.

First, we consider the role of the O3 hydroxyl group, which is shown to be essential for the *in vitro* antibacterial activity of lasalocid A.[34] It always forms a hydrogen bond with the carboxyl (or carboxylate) O1, and this apparently forces the carboxyl group to be nearly coplanar with the phenyl ring. Clearly, the orientation of the carboxyl group could affect the formation or the extent of the "head-to-tail" and/or "head-to-near-head" hydrogen bonds that are invariant for all the lasalocid A molecules. In fact, the rotation of the carboxyl group by −45°[35] from the phenyl ring plane brings it into a position in which the O8–H···O1 (or O2–H···O8 for the free acid) and/or the O4–H···O2 hydrogen bond or bonds become nonexistent or extremely weak (Table S12[13]). Thus the carboxyl coplanarity with the phenyl ring may play an important role in the stabilization of the cyclic cavity of the ionophore. Second, the phenyl ring supplies the ionophore with a large hydrophobic environment; the efficient hydrophobicity of the ionophore is a basis of its function. Both these structural "devices", the O3–H···O1 hydrogen bond and the phenyl plane, may be especially effective (or required) for lasalocid A, which has a small molecular size and thus limited conformational flexibility and fewer possibilities for three-dimensional nonpolar protection. This may also hold for the smaller ionophore A23187, which has a bicyclic aromatic ring with the imino group adjacent to the carboxyl group, where the imino nitrogen forms a hydrogen bond with a carboxylate oxygen to fix the carboxylate group nearly coplanar with the benzoxazole ring. It is apparent that this configuration is favorable for the formation of the six-membered chelate ring involving the carboxylate oxygen and the benzoxazole ring nitrogen in the calcium salt.[36] Third, as noted above, the salicylic acid moiety functions as a metal-binding site or sites (Table S11[13]), though this is relatively rare, adding minor or major modifications to the metal–lasalocid A structure. Examples include O2 for Ba^{2+},[6g,h] O2 and O3 for Cs$^+$,[6i] O2 for Tl$^+$ (the present salt **2**), the C5=C6 double bond for Ag$^+$,[6d] and the phenyl ring for Tl$^+$ (salt **1**), where the metal–O2 or the metal–olefin bonding modifies only slightly the circular configuration of the ionophore molecule or the mutual arrangements of the pairing ionophores in the dimeric structure, respectively, while the metal–O3 or the metal–phenyl face bonding produces the distinct polymeric structure. Neither metal–O1 bonding nor the salicylic acid type of metal chelation between the carboxylate and the hydroxyl oxygens has been observed in the solid state, although the latter has often been proposed for lanthanide,[37] alkaline earth,[38] or divalent transition[39] metal ions in solution.

Polymorphic Nature of Lasalocid A–Thallium Salts. Polymorphism is one of the characteristics of lasalocid A–metal salts as well as of the free acids in the solid state (Table S13[13]). Different and even the same[4a] crystallization conditions give different crystal forms, indicating that there are a variety of ways in which a lasalocid A molecule or molecules protect a metal ion or ions or the ionophore or ionophores themselves from solvent interactions. This may again be due to the small molecular size and the structural integrity of the ionophore. The nature of the solvents, polar or nonpolar, affects the structures of the salts; there is a propensity[1a] for a monomer salt to crystallize from polar solvents and for a dimer salt to crystallize from nonpolar ones (Table S13[13]). Thus the Tl$^+$ salt **2** and the Na$^+$ salt[6a] form monomeric structures, both crystals grown from either aqueous methanol (plus ethylene glycol) or methanol solutions. Accordingly, polymorphism of lasalocid A–metal salts is indicative of a variety of structures corresponding to different environments, namely, those corresponding to different stages during metal-transport processes. It has been suggested[1a] that metal uptake and release in polar environments involve monomeric forms, while transport in nonpolar media takes place by means of a lasalocid dimer. Though this monomer–dimer mechanism may hold for most metal ions, the present study suggests an alternative one or ones for certain metal ions, however. For Tl$^+$, for example, a plausible scenario is as follows: (i) metal uptake and release in

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[27] For examples, see: (a) Frasson, E.; Menegus, F.; Panattonic, C. *Nature* **1963**, *199*, 1087–1089. (b) Freeman, M. B.; Sneddon, L. G.; Huffman, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 5194–5196.

[28] However, it was impossible to obtain any indication of the Tl$^+$ "inert-pair" on the naked side of the Tl$^+$ atom from the final difference Fourier map, which showed nine peaks with 0.6–0.8 e Å^{-3} located 1.1–1.2 Å from the Tl$^+$ atom, since they are spherically distributed around the metal center. This was also the case for salt **1** in which six peaks with 0.6–2.2 e Å^3 located 1.1–1.5 Å from the Tl$^+$ atom are spherically distributed.

[29] Stumpf, K.; Pritzkow, H.; Siebert, W. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 71–72.

[30] Colquhoun, H. M.; Greenhough, T. J.; Wallbridge, M. G. H. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1978**, *34*, 2373–2376.

[31] In $[(C_5H_5)Co\{C_3B_2(CH_3)_4\}Tl]$,[29] however, the anionic cyclopentadienyl ring of the neighboring molecule is adjacent to the thallium atom with a distance of 3.65 Å between the Tl$^+$ atom and the center of the cyclopentadienyl ring.

[32] Ferguson, G.; Jennings, M. C.; Lalor, F. J. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1991**, *C47*, 2079–2082.

[33] Huang, S.-H.; Wang, R.-J.; Mak, T. C. W. *J. Chem. Soc., Dalton Trans.* **1991**, 1379–1381.

[34] Westley, J. W.; Oliveto, E. P.; Berger, J.; Evans, R. H., Jr.; Glass, R.; Stempel, A.; Toome, V.; Williams, T. *J. Med. Chem.* **1973**, *16*, 397–403.

[35] This is the case for 6-methylaspirin,[26] which has no ability to form a "salicylic acid-type" hydrogen bond. Usually, except for the Na$^+$ salt[6b] and one of three lasalocid A anions in the $Co(NH_3)_6^{3+}$ salt,[5b] the carboxyl group rotates in the direction opposite to that of the C9 atom to achieve the minimal unfavorable steric interaction between them, i.e., in the minus direction.

[36] Smith, G. D.; Duax, W. L. *J. Am. Chem. Soc.* **1976**, *98*, 1578–1580.

[37] Hanna, D. A.; Yeh, C.; Shaw, J.; Everett, G. W., Jr. *Biochemistry* **1983**, *22*, 5619–5626 and references therein.

[38] Juillard, J.; Tissier, C.; Jeminet, G. *J. Chem. Soc., Faraday Trans. 1* **1988**, *84*, 951–958. (b) Pointud, Y.; Juillard, J. *J. Chem. Soc., Faraday Trans. 1* **1988**, *84*, 959–967.

[39] Pointud, Y.; Juillard, J. *J. Chem. Soc., Faraday Trans. 1* **1990**, *86*, 3395–3398 and references therein.

polar media involve a monomeric form analogous to that in salt **2**, where the "half-naked" side of the metal ion is ligated by a water molecule or molecules, and (ii) water dissociates from the complex in nonpolar membranes to give rise to the "half-naked" monomer or polymer similar to that in salt **1**, with an appropriate degree of polymerization.[40]

Conclusion

Thallium salt **1** contains doubly rare structural aspects, a polymeric structure and metal–phenyl π-bonding, but still obeys a structural principle for ionophore–metal complexes, that is, three-dimensional nonpolar protection of the metal ion. On the other hand, the structure of thallium salt **2** is quite unexpected, the monomeric structure with the metal ion being "half-naked", and thus provides, to our knowledge, the first example that deviates from this rule. Furthermore, the "half-naked" side of the molecule is surrounded by nonpolar groups in the crystal structure, suggesting that the "less-screened" structural form also exists in the lipid membranes, at least for the lasalocid A–thallium(I) system. Clearly, further X-ray studies of metal salts involving different circumstances, possibly crystallization from solvents of different polarities, are necessary to understand the entire mechanism of metal ion capture and release by lasalocid A.[1a]

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Supplementary Material Available: Tables of anisotropic temperature factors (Tables S1 and S2), atomic coordinates for hydrogen atoms (Tables S3 and S4), ^{13}CNMR and ^{1}NMR spectral data for **2** (Table S7), least-squares planes (Table S8), model-building calculations of the nearest-neighbor contacts around the assumed water ligand for **2** (Table S9), torsion angles (Table S10), metal binding sites and distances in various lasalocid A–metal salts (Table S11), model-building estimations of the rotation effects of the carboxyl group of the lasalocid A on the intramolecular hydrogen-bonding formation (Table S12), and polymorphism in the various lasalocid A crystal structures (Table S13) and the structural model for a $[\mathrm{Tl}^+(\text{lasalocid A}^-)]_2$ dimer (Figure S1) (17 pages); listings of observed and calculated structure factors (Tables S5 and S6) (12 pages). Ordering information is given on any current masthead page.

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[40] At the present stage, we cannot exclude a dimer form in nonpolar environments, since there is a preference of dimers over monomers for lasalocid A–metal structures; a model-building consideration supports this (Figure S1[13]). Thus we have now concentrated our efforts on producing a dimer salt in nonpolar solvents.

Polar/π Interactions between Stacked Aryls in 1,8-Diarylnaphthalenes

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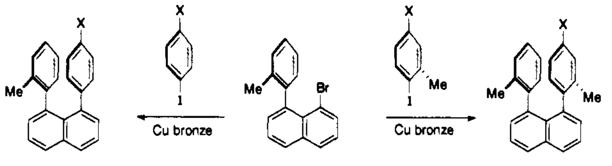
Abstract: A series of substituted 1,8-diarylnaphthalenes, II–X, has been prepared, and the barrier to rotation about the aryl–naphthalene bond has been measured. A monotonic increasing relationship between ΔG^* and σ_{para} values has been found. This is interpreted in terms of a through-space polar interaction between the two aryl units.

The energy for the interaction of two arene units divides roughly into a Coulombic (polar) and a van der Waals (dispersive) term.[2,3] The vdW term depends strongly on the contact surface area whereas the Coulombic term depends on the relative charge distribution. In the case of two benzenes, the surface area, and hence the vdW term, is relatively small; therefore, the Coulombic term dominates the interaction.[4]

A simple picture of the electron distribution in benzene shows an electron-rich central core surrounded by an electron-poor toroidal perifery.[5] Thus, the Coulombic term is repulsive in the parallel-stacked geometry.[3,6] This accounts well for the preference of the herringbone structure of crystalline,[7] liquid,[8] and gaseous[9] benzene.[10]

Scheme I



II - VII 1 VIII - X

II, VIII X = OMe
III X = Me
IV X = H
V, IX X = Cl
VI X = CO$_2$Me
VII, X X = NO$_2$

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[2] Sanders[3a] cites the four-term equation, $E_{\text{total}} = E_{\text{electrostatic}} + E_{\text{induction}} + E_{\text{dispersion}} + E_{\text{repulsion}}$,[3b] to partition the energy of a molecular interaction. Jorgensen[3c] prefers a "Coulomb plus Lennard-Jones format".

[3] (a) Hunter, C. A.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5525. (b) Rigby, M.; Smith, E. B.; Wakeham, W. A.; Maitland, G. C. *The Forces Between Molecules*; Clarendon: Oxford, 1986. (c) Jorgensen, W. L.; Severance, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 4768.

[4] For an assessment of the factors for interacting arenes located in proteins, see: (a) Burley, S. K.; Petsko, G. A. *Science* **1985**, *229*, 23. (b) Hunter, C. A.; Singh, J.; Thornton, J. M. *J. Mol. Biol.* **1991**, *218*, 837–46.

[5] A discussion of the importance of quadrupolar and octupolar terms in the polar profile of benzene has been forwarded by Reisse in the following: (a) Claessens, M.; Palombini, L.; Stein, M.-L.; Reisse, J. *Nouv. J. Chem.* **1982**, *6*, 595. (b) Vrbancich, J.; Ritchie, G. L. D. *J. Chem. Soc., Faraday Trans. 2* **1980**, *76*, 648.

[6] An alternate description, presented by Sanders,[2a] depicts the charge distribution as a sandwich with negative regions at top and bottom and a positive region in between.

[7] (a) Cox, E. G.; Cruickshank, D. W. J.; Smith, J. A. C. *Proc. R. Soc. London, A* **1958**, *A247*, 1. (b) Williams, D. E. *Acta Crystallogr.* **1974**, *A30*, 71. (c) Hall, D.; Williams, D. E. *Acta Crystallogr.* **1975**, *A31*, 56.

[8] Lowden, L. J.; Chandler, D. J. *J. Chem. Phys.* **1974**, *61*, 5228.