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Thallium(I) Derivatives of Some Aminoacids and Other Acidic Ligands. Studies in Solution and the Solid State

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Thallium(I) derivatives of a number of acidic ligands, including some aminoacids, carboxylic acids, phenols and thiols, have been prepared and characterised by mass-, U.V., and I.R. spectroscopy. Interaction between thallium(I) and certain of these ligands in aqueous solution has been studied by U.V. and fluorescence spectroscopy, and formation constants measured in some cases. It is concluded that neither property is of particular utility in characterising the interaction of thallium(I) with biological macromolecules.

Introduction

Thallium(I) is known [1, 2] to be a possible probe for potassium in biological processes, even though the two ions differ somewhat in their chemistry. Thus thallium(I) bears certain resemblances to silver(I), while its tendency to covalency results in parallels with lithium rather than the other alkali metals [3, 4]. We have studied the interaction of Tl(I) with some biologically important ligands both in solution and in the solid state in an attempt to establish the extent of its similarity to potassium. We now report studies on some Tl(I) derivatives of acidic ligands, including aminoacids which do not appear to be much studied. Several related investigations have been published [5–7] including a study of thallium derivatives of β-diketones, phenols and carboxylic acids [5].

Results and Discussion

The compounds were prepared by reacting the ligands with thallium hydroxide or hexafluoroacetylacetonate. Analytical data for these and for some adducts with 1,10-phenanthroline are given in Table I. Several ligands with two acidic groups gave products of stoicheiometry Tl_2L. It is known that dicarboxylic acids can give normal and acid thallium de-

TABLE I. Analytical Data.

Compound	Colour	Found %			Calculated %		
		C	H	N	C	H	N
Tl_2-cysteinate	Green	6.64	1.12	2.43	6.82	0.95	2.65
Tl-N-phenylglycinate	Brown	26.8	2.26	3.98	27.1	2.20	3.90
Tl-*o*-nitrobenzoate	White	23.1	1.80	4.00	22.8	1.10	3.80
Tl_2-*o*-mercaptobenzoate	Yellow	15.5	0.80		15.0	0.71	
Tl-acetylsalicylate[a]	White	28.3	1.97		28.2	1.86	
Tl-(ac.salicylate)·phen	White	43.5	2.45	4.88	44.8	2.67	4.97
Tl-oxamate[b]	White	8.85	1.37	5.28	8.23	0.69	4.90
Tl-*o*-nitrophenolate	Purple	20.9	1.22	3.58	21.0	1.17	4.09
Tl-*m*-nitrophenolate	Brown–red	21.0	1.35	4.97	21.0	1.17	4.09
Tl-(*m*-NO_2phenolate)·phen	Red	40.7	2.54	7.14	41.4	2.30	8.00
Tl(C_2H_5S)	Yellow	8.73	1.78		8.53	1.78	
Tl-2-benzoxazolethiolate	White	23.8	1.39	4.00	23.7	1.13	3.95
Tl-kojate	Yellow	21.5	1.62		20.9	1.45	
Tl-phenanthridonate	Grey	39.6	2.25	4.00	39.2	2.10	3.52
Tl_2-dimethylglyoximate	Yellow	9.33	1.35	5.38	9.33	1.14	5.35

[a]Molecular weight by osmometer: found 395, calculated 383. Thallium: found 54.0%, calculated 53.9%. [b]Thallium: found 69.8%, calculated 69.8%. Phen = 1,10 phenanthroline.

TABLE II. Mass Spectra of Thallium Compounds.[a]

Species	m/e	I%
LH = *o*-nitrobenzoic acid		
	634	2
Tl_2L^+	576	2
$Tl_2(C_6H_5COO)^+$	530	2
	450	2
	449	20
Tl_2^+	410	2
	355	1.2
	328	3.0
$Tl(C_6H_4NO_2)^+$	327	44.4
$Tl(C_6H_5COO)^+$	326	0.3
	281	2.1
$Tl(O_2C)^+$	249	1.5
	221	1.8
Tl^+	205	100
LH_2 = *o*-mercaptobenzoic acid		
	637	1.0
Tl_2L^+	562	2.7
	550	2.6
$Tl_2(C_6H_4S)^+$	518	1.9
Tl_2^+	410	1.6
$Tl(C_6H_5S)^+$	314	2.0
$Tl(C_6H_5)^+$	282	4.4
$Tl(O_2C)^+$	249	2.6
Tl^+	205	100
LH = acetylsalicylic acid		
$Tl(o\text{-}C_6H_4COO)^+$	546	2.0
	488	1.0
	444	1.0
	343	1.0
	342	6.4
Tl^+	205	100
LH = *m*-nitrophenol		
	548	15.8
	544	3.5
Tl_2L^+	532	0.5
	344	10.6
TlL^+	343	40.3
$Tl(C_6H_4NO_2)^+$	327	17.6
	307	10.6
$Tl(O_2C)^+$	249	21.1
Tl^+	205	100
LH = salicylaldehyde		
Tl_2L^+	531	0.5
	327	24.0
TlL^+	326	49.3
	304	13.3
$Tl(C_6H_5O)^+$	298	5.4
	270	
$Tl(O_2C)^+$	249	
$TlCO^+$	233	
TlO^+	222	
Tl^+	205	100
LH = hexafluoroacetylacetone		
TlL^+	412	4.6
$Tl(CF_3COCH_2CO)^+$	343	1.3
Tl^+	205	100

[a]I = intensity.

rivatives. Mass spectra, infrared and U.V. spectra are listed in Tables II, III and IV. Conductivity measurements in dimethylsulphoxide or acetone solution (when soluble) show the compounds to be non-electrolytes. Thus molar conductivities in the range 0.4–4.7 (acetone) and ~15 (D.M.S.O.) were obtained. A 1:1 electrolyte in D.M.S.O. has a molar conductivity of ~290. Conductivities in methanol were rather higher, but still much lower than that expected for 1:1 electrolytes. Attempts to measure molecular weights by the osmometer were precluded by lack of solubility except for thallium(I) acetylsalicylate, which was shown to be a monomer.

Mass Spectra (Table II)

Several interesting features were observed in the mass spectra (intensities are expressed relative to that of $^{205}Tl^+$). Thallium(I) organocompounds are not well known apart [8] from cyclopentadienylthallium(I), although they have been postulated as intermediates. Lee [5] has tentatively assigned a peak in the mass spectrum of thallium(I) *o*-nitrobenzoate at 327 mass units to $[TlC_6H_4NO_2]^+$ (intensity 2.2% of that for Tl^+), implying the first example of the rearrangement of a Tl(I) derivative to a Tl–C bonded derivative. Our mass spectra were recorded at higher temperatures and decomposition was not so important relative to volatilisation, so we have observed this peak at 44.4% relative intensity, positive confirmation of a Tl(I)–C system. For $Tl(o\text{-}C_6H_4NO_2CO_2)$ we have observed previously unreported fragments of mass numbers 530 and 570 which we assign to $Tl_2(C_6H_4CO_2)^+$ and $Tl_2(o\text{-}C_6H_4NO_2CO_2)^+$, while the mass spectrum of bisthallium mercapto benzoate gave peaks at 518 ($Tl_2C_6H_4S^+$) and 282 ($TlC_6H_5^+$), all further examples of Tl(I)–C systems.

The mass spectrum of thallium(I) acetylsalicylate showed no parent ion, but gave a fragment in which an acetyl group is lost. It is useful to compare the mass spectra of the thallium derivatives of *ortho*- and *meta*-nitrophenol. Lee noted [5] that there was no evidence for the loss of a NO or NO_2 group in the spectrum of the former compound and suggested this

TABLE III. Infrared Spectra.

Compound	Absorption Maxima (cm^{-1})
Tl_2-cysteinate	3430sh, 3350s, 3230sh, 1642m, 1550s, 1538s, 1430m, 1345m, 1290m, 1070m, 1010s, 950s, 885m, 858m, 785m, 665w, 628s.
Tl-*N*-phenylglycinate	3175m, (1595sh), 1570br, 1535m, 1365sh, 1330m, 1178m, 1147m, 1111m, 1098m, 1070w, 1025w, 1002m, 902m, 885m.
Tl_2-mercaptobenzoate	1578m, 1555m, 1505s, 1418m, 1405m, 1382s, 1245m, 1155m, 1053m, 1027w, 972vw, 940w, 835s, 790w, 749m, 735m, 708m, 678s, 650s, 470m, 452m, 390m, 370w.
Tl-*o*-nitrobenzoate	1592m, 1560m, 1540m, 1365m, 1297m, 1074m, 1039w, 962m, 864sp, 838m, 778m.
Tl-acetylsalicylate	1740m, 1600m, 1582m, 1530s, 1505m, 1360s, 1215m, 1186m, 1152m, 1085m, 1028m, 1010m, 960w, 950w, 916m, 874m, 842m, 815sp, 804m, 751m, 708m, 672m, 646m, 495m, 465m, 450m, 435m, 415m, 410m, 370w, 295m, 285m.
Tl-*m*-nitrophenolate	1595s, 1550m, 1500m, 1352s, 1312m, 1282m, 1265s, 1255s, 1161w, 1085m, 1075m, 990m, 932m, 878w, 856m, 815s, 732s, 666s, 652w, 539m.
Tl-oxamate	3420m, 3400m, 3220m, 1730sh, 1670m, br, 1585w, 1355m, 1315m, 1265m, 1238m, 1078m, 1000w, 855s, 816m, 682m, 659m, 582m, 559m, 480m, 460m, 345m, 322m.
Tl-kojate	3220br, 1622m, 1609m, 1572m, 1522m, 1408m, 1328w, 1270m, 1222w, 1205m, 1140m, 1078m, 988m, 942s, 882m, 855m, 780sh, 771s, 760m, 612m, 545m, 436m, 348s, 215m.
Tl-2-benzoxazolethiolate	1592s, 1580s, 1417m, 1404sp, 1373s, 1339m, 1242m, 1222w, 1210w, 1144m, 1112s, 1074s, 999m, 923m, 904m, 887m, 810m, 752sh, sp, 742sh, sp, 735s, 679w, 622sp, 600sp, s, 490m.
Tl_2-dimethylglyoximate	1522m, 1410w, 1351s, 1345s, 1015w, 970s, 905s, 702s, 472m, 372m, 272m, 240m.

TABLE IV. Reflectance Ultraviolet Spectra (nm).

Ligand	Tl Compound	Ligand	Tl Compound	Ligand	Tl Compound
m-Nitrophenol		Acetylsalicylic Acid		Dimethylglyoxime	
233	233		205	233	233
281	255	232	236sh	260	248
	291(?)	280m	250		
		303sh	317	Oxamic Acid	
o-Mercaptobenzoic acid				252	256
	212sh	Phenanthridone			
	235sh	236	237	Kojic Acid	
254	260	257	257	228	227
295sh	310vbr	332	334	260	260
335(?)				298	308
		N-Phenylglycine			
2-Benzoxazole Thiol			233		
264	273		249		
297	297		300		
	336				

Solution Spectra in Dimethylsulphoxide

	o-nitrophenol	*m*-nitrophenol	Kojic Acid
Ligand	267, 341	276, 340	270
Tl Compound	265, 342	268, 337	268

could result from chelation. However, the spectrum of the *meta* derivative (which shows a peak at mass number 327, possibly $TlC_6H_4NO_2^+$) also shows no evidence for fragments without NO or NO_2 groups. As chelation is not possible in this case, Lee's suggestion for the *ortho* product seems less likely to be correct. He also noted that the mass spectra of aromatic aldehydes show prominent peaks corresponding to

loss of the CHO group, and suggested that the failure to observe this for Tl(I) salicylaldehyde suggested chelation. However we have observed a prominent peak at 298 mass number, assignable to $TlC_6H_5O^+$, suggesting that the CHO group is lost. Other peaks and assignments are shown in the Table.

Infrared Spectra (Table III)

A number of differences may be seen between the spectra of the ligands and their thallium derivatives. The ligand absorptions are often well characterised [9]. The spectra of the adducts with 1,10-phenanthroline are very complex and are not presented. The spectra are discussed in terms of the ligand type.

Aminoacid and other carboxylic acids.

The C=O stretching vibration of the unionised acid occurs at about 1650 cm^{-1}, while in ionic derivatives two bands are present at 1560–1600 and 1360–1400 cm^{-1}, assigned to antisymmetric and symmetric CO_2^- stretching vibrations. In the spectrum of bis-(thallium(I))cysteinate the loss of the zwitterionic carboxylate group is shown by the absence of the ligand band at 1606 cm^{-1} and the appearance of the ν_{CO} mode at 1642 cm^{-1}. The spectrum of the Tl(I) species shows the presence of NH_2 groups rather than NH_3^+ and the loss of the SH frequency at 2539 cm^{-1}. This implies a structure in which one thallium ion is covalently bound by a (probably) chelating carboxylate group, and the other by the RS^- group. An attempt was made to prepare the 1:1 derivative to see if the thiolate or carboxylate derivative were preferentially formed. However this was not successful, all preparations giving the bis(thallium) product.

The spectrum of N-phenylglycine shows absorptions at 2710 cm^{-1} ($\nu_{NH_2^+}$) and 1570 and 1365 cm^{-1} ($\nu_{CO_2^-\ as,\ s}$). The spectrum of the sodium salt shows a normal ν_{NH} band at 3370 cm^{-1}, but that of the thallium derivative shows this at 3175 cm^{-1}, implying covalent Tl–NH_2 interaction. The $\nu_{NH_2^+}$ band is absent as expected, while the separation between the two carboxylate frequencies is increased to 240 cm^{-1}. This separation is thought [10] to measure the covalency of the metal–oxygen bond in metal carboxylates, and is 183, 210, 214 and 243 cm^{-1} for the ligand and its Ni(II), Co(II) and Cu(II) compounds respectively. Clearly there is appreciable covalency in the thallium compound.

The spectrum of bisthalliummercaptobenzoate shows the absence of –OH and –SH groups, while $\nu_{CO_2^-}$(as, s) may be readily assigned. Similarly the spectra of the thallium derivatives of *o*-nitrobenzoic acid and acetylsalicylic acid show the presence of the Tl–carboxylate group, while in the latter case the shifts in the acetyl carbonyl group indicates the ligand is chelating.

Other ligands

In general the spectra of the thallium compounds show the loss of bands assigned to OH in the ligand, for example in the bis(thallium) derivative of dimethylglyoxime. The spectrum of 2-benzoxazole thiol shows it to exist in the thioketone form; the C=S mode shifts on thallium binding, as does the C=O mode in kojic acid, and the NO_2 modes in *o*- and *m*-nitrophenols, suggesting in each case a chelating ligand.

UV Spectra (Table IV)

The 6*s*–6*p* transition should be sensitive to the nature of the ligands bound to thallium, but in most cases the thallium transition could not be detected in the solid state spectrum. Non-aqueous solution studies were not very successful as the solvent absorbed too strongly in the expected range to allow solution spectra to be utilised. In aqueous solution little variation could be seen from compound to compound, the spectrum being essentially that of the aquated Tl(I) ion. Ligand bands did shift on binding to thallium as discussed by Lee in detail.

Adducts with 1,10-Phenanthroline

Thallium(I) does not readily form complexes in view of the presence of the 6*s* electron pair. Complexes of 1,10-phenanthroline are known with $TlNO_3$ and TlCl [11]. We have prepared 1:1 complexes of 1,10-phenanthroline with thallium acetylsalicylate, thallium oxamate and thallium *m*-nitrophenolate but failed in the other cases.

Studies in Solution

Amongst the properties of the thallium ion which may be utilised to characterise its binding to biological macromolecules are its NMR, UV and fluorescence spectra. The first of these has been successfully exploited, but there is some uncertainty about the usefulness of the other properties. The present solution studies were intended to further check the possibility of using the UV and fluorescence spectra of the thallium ion as probe properties.

The shift of the UV band has been successfully used to measure formation constants for simple ligands [1]. We have similarly determined the formation constants for chloride and iminodiacetate ions. The value for Cl^- agreed well with the literature value [1], while for iminodiacetate at 25 °C, I = 0.15 mol dm^{-3}, logK = 0.22. The results were determined in a straightforward manner and further details will not be presented. However, less success was achieved with other ligands. Shifting of the thallium UV band was not caused by 2-mercaptoethanol, while the thallium band could not always be identified in the presence of more complex ligands as described above. No assignment could be made for thallium(I) bound to the enzyme aldehyde dehydrogenase [12].

Of greater potential interest is the fluorescence spectrum of thallium(I). The quenching effect of various ligands on this spectrum through complex formation is often suggested to be of particular value in characterising the binding sites of thallium, for example in membrane systems, so allowing the use of thallium as a probe for K^+-transport. In this connection the stability constants for several Tl^+–ionophore complexes have been measured by exploiting this phenomenon [13]. We have attempted to measure stability constants for thallium complex formation with acetylsalicylate, acetaldehyde, NAD^+, mercaptoethanol, 'tris'buffer and nitrate ion in aqueous solution as well as dibenzo-18-crown-6 in methanol. In all cases other than acetaldehyde the presence of the ligand resulted in a substantial reduction in the intensity of the fluorescence band, but no shift in the band was observed. Such a shift is usually taken as evidence for direct complexation [14]. Furthermore, calculation of the stability constants for these ligand by the method of Cornelius *et al.* [13] using the decrease in intensity as a measure of complex formation, leads to values for the constants that are very much higher than those anticipated or measured by potentiometric titration. This leads to the conclusion that the decrease in Tl^+ fluorescence is not due to direct complexation but to collision quenching in the presence of the ligand molecule [15]. Whether this is so or not it is still quite clear that such quenching occurs so readily with such a wide range of ligands that its possible value as a probe in membranes is very questionable.

Conclusions

The results obtained for the solid thallium(I) compounds show a number of detailed features of some interest, but in general they confirm the tendency towards covalent character in the metal–ligand bond and also the ease with which thallium will form complexes with soft ligands. The results in solution are probably of greater significance in that they show that, despite repeated speculation on the use of the UV and fluorescence spectra of thallium as probes of its environment, the presence of more complicated ligands and certainly macromolecules will render these methods unacceptable. In particular the exploitation of the fluorescence spectrum in the study of metal binding to membranes seems unlikely.

Experimental

Thallium hexafluoroacetylacetonate was prepared by the action of hexafluoroacetylacetone on thallium(I) carbonate, and recrystallised from hot benzene. Thallium hydroxide was obtained by the action of sodium hydroxide on thallium formate using minimum amounts of water. Thallium(I) compounds were prepared by adding a hot ethanolic solution of the ligand in 1:1 molar ratio to either a suspension of thallium(I) hydroxide or a solution of thallium hexafluoroacetylacetonate in ethanol. The product precipitated readily in most cases and was recrystallised from ethanol. Thallium(I) derivatives of mercaptoethanol and cysteine were prepared in aqueous solution by adding sodium hydroxide solution to a mixture of thallium nitrate and the ligand. Adducts with 1,10-phenanthroline were prepared by mixing equimolar amounts of the base and Tl(I) compound in ethanol and cooling. Products were analysed for C, H and N where appropriate and in some cases for thallium by atomic absorption analysis (Hilger and Watts Atomspek).

Infrared spectra were recorded on a Perkin–Elmer 325 spectrometer to 200 cm^{-1} with nujol and hexachlorobutadiene mulls. Mass spectra were obtained on an A.E.I. MS 30 mass spectrometer run at 70eV, 300 μA ionising current and 200 °C source temperature. Ultraviolet spectra were recorded in the solid state by diffuse reflectance and in solution on a Beckmann DK2A spectrometer. Fluorescence spectra were obtained on a Perkin–Elmer 203 spectrofluorimeter with 5×10^{-5} mol dm^{-3} $TlClO_4$ in aqueous solutions. At an excitation wavelength of 225nm Tl^+ gives a characteristic fluorescent spectrum with emission maximum at 368nm. Spectra in the absence and presence of ligand concentrations in the range 5×10^{-5} to 10^{-3} mol dm^{-3} were recorded at 20 °C and I = 10^{-3} mol dm^{-3} made up with sodium perchlorate. Formation constants determined by the UV method were measured using a Unicam SP500 spectrometer.

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