Inorg. Chem. **2004**, *43*, 6495–6500

Identification, Isolation, and Characterization of Cysteinate and Thiolactate Complexes of Bismuth

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Received March 26, 2004

Although bismuth compounds have been used in medicine for over 200 years, chemical characterization of complexes involving biological molecules is minimal and mechanisms of bioactivity are ill-defined. The thiophilic nature of bismuth implicates sulfur centers as likely sites for interaction, and we have exploited this feature to identify, isolate, and characterize complexes of bismuth with thiolate–carboxylate bifunctional ligands including the amino acid L-cysteine. The solid-state structures of potassium dichloro(thiopropionato)bismuth (K[**1d**]), dimethylaminoethanethiolato(thiopropionato)bismuth (**4**), and dinitrato(cysteinato)bismuthphenanthroline [**5**(phen)] are compared with data from electrospray ionization mass spectrometry (ESI-MS). ESI-MS is applied to reactions of $BiCl_3$ or $Bi(NO_3)_3$ with mercaptosuccinic, malic, and succinic acids to illustrate the general observation of 1:1 and 1:2 complexes.

Introduction

Metals and metalloids are increasingly important in the treatment of a variety of diseases and disorders.[1] Bismuth compounds have been used in medicine for over 200 years,[2,3] culminating in the widespread application of the commercially available preparations Pepto-Bismol (bismuth subsalicylate, BSS) and De-Nol (colloidal bismuth subcitrate, CBS) for gastrointestinal disorders. Nevertheless, mechanisms of bioactivity for bismuth are ill-defined as complexes involving biological molecules as ligands have not been confirmed.[4] The thiophilic nature of bismuth[3] highlights thiol-containing biological molecules as potential sites for interaction. In this context, we have prepared complexes with cysteinate and thiolactate ligands, which are characterized by X-ray diffraction and mass spectrometry. The observations demonstrate that bismuth can accommodate both mono- and dianionic thiolate−carboxylate ligands.

Results and Discussion

Extensive medicinal use of BSS and CBS has prompted the structural characterization of bismuth complexes involving conjugate bases of citric,[9−16] lactic,[17] malic,[18] tartaric,[18,19] and salicylic acids.[20] Although the database for solid-state structural features of bismuth with biologically relevant

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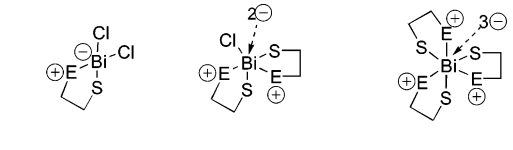
10.1021/ic049594n CCC: $27.50
Published on Web 09/10/2004

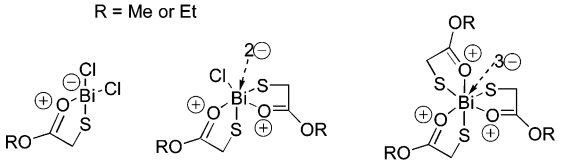
functional groups is developing,[21] there are no definitive conclusions regarding the potential sites for interaction of bismuth within biosystems. Recognizing the pronounced thiophilicity of bismuth,[21] we consider thiol-containing peptides and proteins as probable ligands. In this context, conjugates of thio−carboxylic acids, containing a combination of thiolate and carboxylate functionalities, are key model ligands for bismuth and are suitably represented by thiolactate and cysteinate. For comparison, the heterobifunctional amino−thiolate (**a**),[22] hydroxy−thiolate (**b**),[23,24] and ester−thiolate (**c**)[25,26] ligands are known to form monothiolate (**1**), bisthiolate (**2**), and tristhiolate (**3**) chelate complexes with bismuth. Although the amino, hydroxyl, and ester functionalities are relatively weak Lewis donors, the thiolate functionality behaves as an anchor to bismuth by virtue of the strong Bi−S bond.



1 **2** **3**

a: E = NR_2; R = H or Me
b: E = OH

R = Me or Et



1c **2c** **3c**

The potential for thiolactate and cysteinate to act as either monoanionic or dianionic conjugate bases for chelation introduces further chemical and structural diversity. For example, the reaction mixture of thiolactic acid, KOH, and $BiCl_3$ gives the potassium salt of **1d**, representing an anionic bismuth complex. The centrosymmetric (both D- and L-enantiomers) solid-state structure of K[**1d**] (Figure 1) confirms the five-membered heterocyclic arrangement imposed by chelate coordination of the thiolate−carboxylate ligand. The potassium ion interacts with centers from five separate anions imposing an eight-coordinate environment including four chlorine centers, two oxygen centers, and two sulfur centers. The carboxylate moiety is also responsible for interanionic chelate interaction with the bismuth center

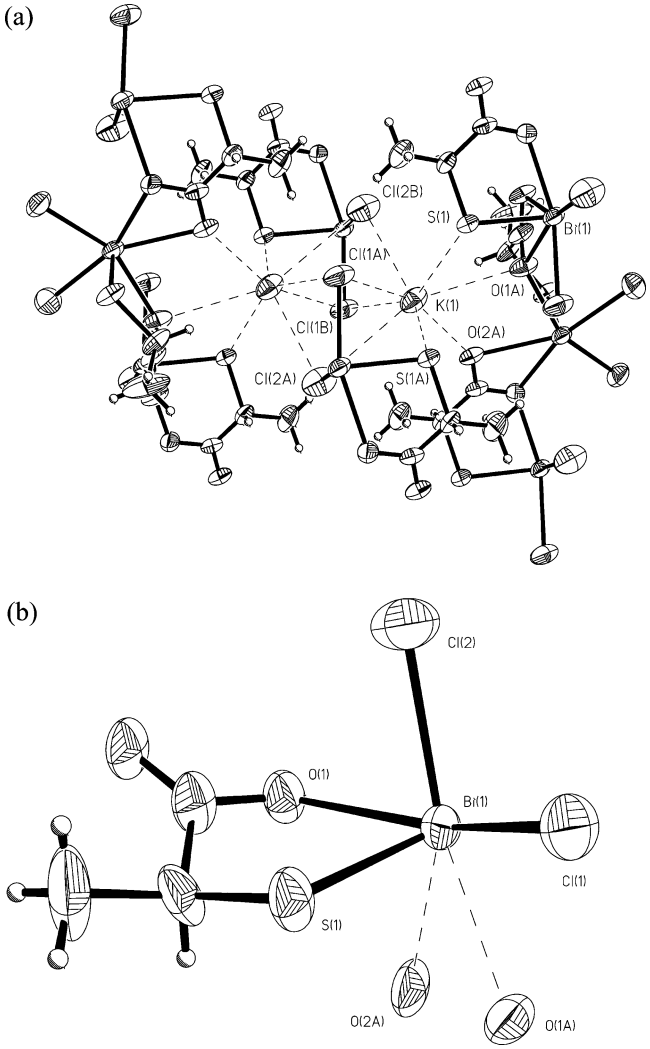
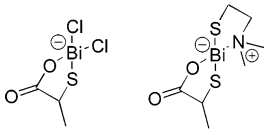


Figure 1. Crystallographic view of K[**1d**] showing eight anionic units surrounding two potassium centers (a) and a view of the formula unit illustrating the hexacoordinate site for bismuth (b). Thermal ellipsoids are shown to 50% probability.

of a neighboring anion, which, in addition to the four interactions illustrated in the line drawing of the anion (**1d**), imposes a six-coordinate environment for bismuth (Figure 1b).



1d **4**

A heteroleptic[27] thiolate complex (**4**) has been isolated as the L-enantiomer from treatment of a racemic mixture of K[**1d**] with 1 equiv of dimethylaminoethanethiol in 95% ethanol and excess KOH. The spirocyclic framework of **4** (Figure 2) represents a neutral bismuth complex composed of a dianionic thiolate−carboxylate ligand and a monoanionic

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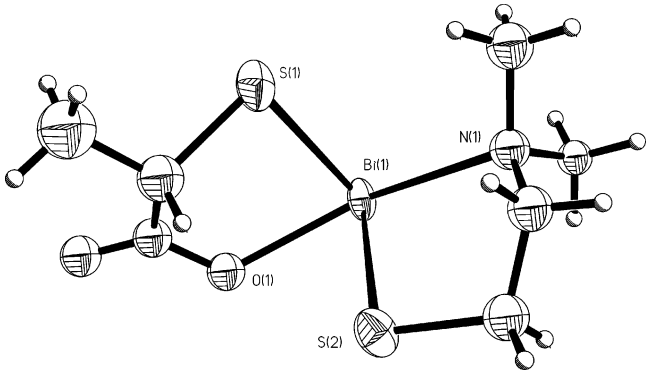


Figure 2. Solid-state molecular structure of **4**. Thermal ellipsoids are shown to 50% probability.

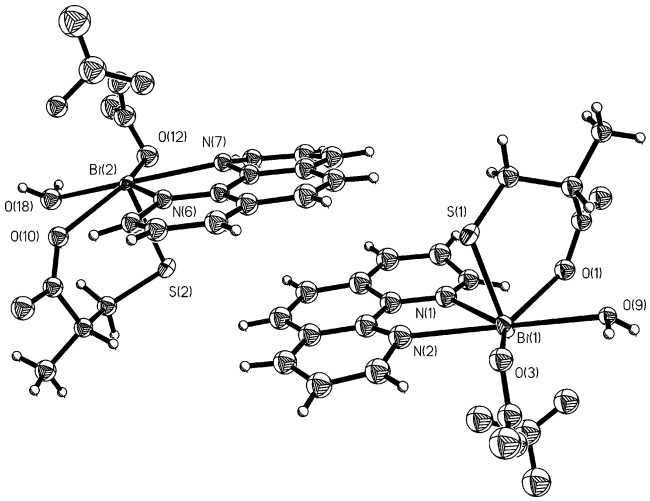


Figure 3. Crystallographic view of the two unique formula units in the asymmetric unit for **5**(phen)·H_2O. Thermal ellipsoids are shown to 50% probability, and hydrogen atoms have been omitted for clarity.

amino−thiolate. The reaction can be viewed as an in situ formation of the potassium aminothiolate enabling KCl metathesis to give the Bi−S bond. Chelation of the formerly pendant amine subsequently displaces the chloride anion to account for elimination of the second equivalent of KCl.

Crystals isolated by slow evaporation of solvent from reaction mixtures containing bismuth(III) nitrate, L-cysteine, and 1,10-phenanthroline (phen) in 50% ethanol have been characterized as the dinitrate salt of bismuth cysteinate with an auxiliary phen ligand [**5**(phen)·H_2O]. The solid-state structure (Figure 3) definitively confirms that both thiolate and carboxylate functionalities of the cysteinate anion are part of a hexacoordinate environment for bismuth, including N,N-chelation from the phen ligand and O-coordination from one nitrate anion and a water molecule. Additional Bi−O contacts are evident with distances greater than 2.5 Å, so that the assignment of a coordination number for bismuth is subjective.

Charge balance for bismuth(III) in **5**(phen)·H_2O requires that the pendant nitrogen center of the monoanionic cysteinate ligand be an ammonium moiety, and the complex is most conveniently represented by **5**, although the solid-state structure defines an ionic nitrate. The isolated six-membered chelate **5** contrasts the five-membered chelate arrangements typically observed for bifunctional thiolate-anchored ligands

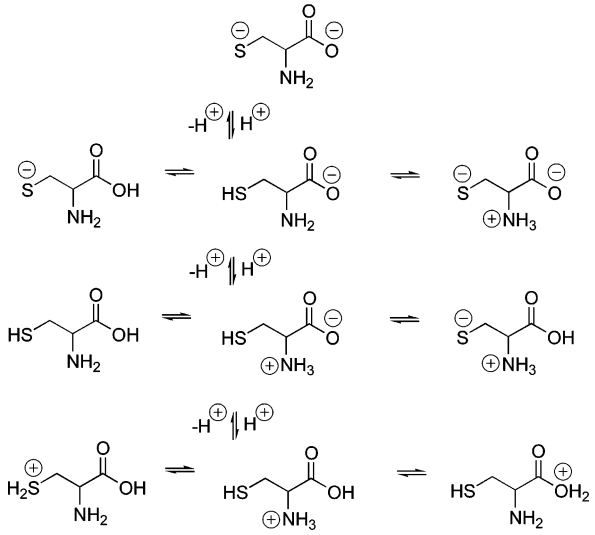
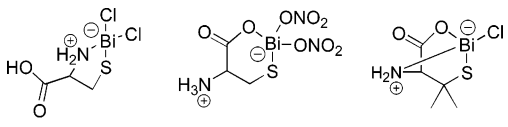


Figure 4. Polyprotic equilibria accessible by L-cysteine.

on bismuth (e.g., **1**−**4**).[21] Although there may be only a small energy difference between the thiolate−carboxylate structure **5** and the five-membered heterocyclic amino−thiolate isomer **1a′**, arrangement **5** is isolated with the support of the auxiliary phen ligand. The phen ligand may have a general stabilizing influence on complexes of this type, as indicated by the recent report of salicylate−phen complexes.[20] It is possible that the auxiliary phen ligand inhibits coordination polymer interactions allowing for more soluble molecular complexes.

Notwithstanding the presence of the phen ligand, the dinitrate salt of bismuth cysteinate (**5**) offers an important comparison with the previously reported penicillaminato-bismuth chloride complex **6**,[28] which can be viewed as a conjugate base of **5**. Deprotonation of the ammonium center of **5** would allow for the tridentate chelate structure observed for **6** involving thiolate−bismuth, carboxylate−bismuth, and amine−bismuth interactions. While the difference in pK_a values for ammonium (R−NH_3^+, pK_a 5−10) and thiol (R−SH, pK_a 7−10) functionalities is not large, additional thermodynamic preference for Bi−S bond formation strongly favors the deprotonation of thiol in the presence of bismuth, as observed in **5**.



1a' **5** **6**

The polyprotic nature of cysteine permits access to dianionic, monoanionic, neutral, and cationic species, and tautomeric diversity is imposed by protic equilibria, as illustrated in Figure 4. Consequently, various modes of coordination toward metal centers are accessible. Compound **6**[28] is a complex of the dianionic ligand, which offers the highest Lewis basicity of the species in Figure 4. Compound **5**(phen) represents a complex of the (ammonium) mono-

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Table 1. Crystal Data

	K[**1d**]	**4**	**5**(phen)·H_2O
formula	$C_3H_4BiCl_2KO_2S$	$C_7H_{14}BiNO_2S_2$	$C_{15}H_{16}BiN_5O_9S$
fw	423.11	417.29	651.36
λ (Å)	1.54178	1.54178	0.7107
T (°C)	20(2)	20(2)	−130(2)
a (Å)	7.822(3)	8.847(6)	9.219(2)
b (Å)	14.475(3)	7.434(5)	13.422(4)
c (Å)	8.629(2)	9.510(6)	8.755(2)
α (deg)	90	90	93.39(3)
β (deg)	109.17(2)	111.89(5)	110.01(2)
γ (deg)	90	90	101.34(2)
V (Å^3)	922.8(4)	580.3(7)	988.6(5)
Z	4	2	2
space group	$P2_1/c$	$P2_1$	$P1$
Flack parameter	-	0.03(5)	0.06(3)
D_c (Mg m^{-1})	3.045	2.388	2.188
μ (cm^{-1})	487.27	330.92	90.85
final ρ_{max}/ρ_{min} (e$^-$/Å^3)	2.120/−2.878	1.916/−1.942	4.203/−4.076
R1[a] ($I > 2\sigma$/all data)	0.0597/0.1233	0.0484/0.0497	0.0608/0.1436
wR2[b] ($I > 2\sigma$/all data)	0.1565/0.1923	0.1258/0.1272	0.1528/0.1977

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $wR2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$.

Table 2. Comparison of Selected Internuclear Distances (Å) Listed in Increasing Order for Derivatives of **1**−**6**

	ref	Bi−S	Bi−S	Bi−S	Bi−N	Bi−N	Bi−N	Bi−O	Bi−O	Bi−O
1a (R = Me)	22	2.530(7)			2.52(2)					
1c (R = Me)	25	3.021(2)						2.562(6)		
K[**1d**]	*a*	2.509(7)						2.45(2)	2.56(2)	2.73(2)
		Bi−S1						Bi−O1	Bi−O1A	Bi−O2A
2a (R = Me)	22	2.569(3)	2.608(3)		2.398(8)	2.528(9)		2.86(1)		
2b (R = Me)	23	2.558(4)	2.595(3)					2.80(1)	2.86(1)	
2c (R = Me)	25	2.849(7)	2.884(6)					2.68(2)	2.77(2)	
3a (R = Me)	22	2.567(5)	2.654(5)	2.748(7)	2.64(2)	2.81(2)	2.83(2)			
3c (R = Me)	25	2.568(2)	2.574(2)	2.608(2)				2.807(5)	2.861(5)	3.071(7)
4	*a*	2.548(7)	2.541(7)		2.55(2)			2.30(2)		
		Bi−S1	Bi−S2		Bi−N1			Bi−O1		
5 (phen)	*a*	2.509(8)			2.50(1)	2.50(1)		2.35(1)	2.59(1)	2.64(1)
		Bi1−S1			Bi1−N2	Bi1−N1		Bi1−O1	Bi1−O3	Bi1−O9
		2.544(8)			2.49(1)	2.50(1)		2.34(1)	2.60(1)	2.66(1)
		Bi2−S2			Bi2−N6	Bi2−N7		Bi2−O10	Bi2−O12	Bi2−O18
6	28	2.527(2)			2.345(6)			2.425(5)		

[a] This work.

anion, which is more viable than the dianion in acidic media and therefore, from a bioactivity perspective, provides a closer model of the potential interaction between bismuth and cysteine in the gastric environment.

Selected internuclear distances for K[**1d**], **4**, and **5**(phen)·H_2O are listed in Table 2 together with related values for **6**[28] and for derivatives of **1**, **2**, and **3**. The Bi−S bonds adopt a relatively narrow range with longer, somewhat exceptional cases for the mono- and bis(ester−thiolate) complexes (**c**). Indeed, bifunctional thiolate ligands involving the weaker donors (hydroxyl and ester) adopt longer Bi−O and Bi−S bonds. The shorter Bi−O distances in **1d**, **4**, **5**, and **6** can be attributed to the formally anionic oxygen donor. Interestingly, the Bi−S distances are indistinguishable in the complexes of a dianionic thiolate−carboxylate ligand (**1d**, **4**, and **6**) and a monoanionic thiolate−carboxylate ligand (**5**) but are generally shorter than those involving other bifunctional thiolate ligands in **1**−**3**.

As ligands, amino acids are multifunctional bases that are expected to engage metals as chelating ligands, but ineffectual NMR spectroscopic features and low success in obtaining crystalline samples have impeded identification and characterization of bismuth complexes. IR and elemental analytical data are available for bismuth complexes involving cysteine[4,29] as well as methionine,[30] and stability constants have been determined for L-lysine complexes[31] and serine complexes.[32] Application of electrospray ionization mass spectrometry (ESI-MS) to the thiolate−carboxylate complexes described here offers supportive characterization data by virtue of definitive m/z values.[33] In addition, ESI-MS studies of reaction mixtures allow for identification of bismuth complexes involving the related malate and succinate ligands. Nevertheless, we note that mass spectrometric data assigned to species in the gas phase do not necessarily correlate with species in solution or in the solid state.

Table 3 summarizes the ESI-MS data for reaction mixtures containing $BiCl_3$ or $Bi(NO_3)_3$ with cysteine, mercaptosuccinic acid, malic acid, or succinic acid in 50% ethanol. The m/z values of prominent peaks corresponding to bismuth contain-

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Table 3. ESI-MS Data for Reaction Mixtures Containing $BiCl_3$ or $Bi(NO_3)_3$ with Cysteine, Mercaptosuccinic Acid, Malic Acid, or Succinic Acid in 50% Ethanol[a]

mixture	*m*/*z*	rel int (%)	assignment	MS/MS (*m*/*z*)	assignment
cysteine/$Bi(NO_3)_3$	775.9	5	$[Bi_2(Cys)_3 - 5H]^+$	328.0	$[Bi(Cys) - 2H]^+$
	654.9	20	$[Bi_2(Cys)_2 - 5H]^+$	328.0	$[Bi(Cys) - 2H]^+$
	449.0	45	$[Bi(Cys)_2 - 2H]^+$	328.0	$[Bi(Cys) - 2H]^+$
	328.0	100	$[Bi(Cys) - 2H]^+$	241.0	$[BiS]^+$
				209.0	Bi^+
	241.0	40	$[BiS]^+$	209.0	Bi^+
	209.0	10	Bi^+		
mercaptosuccinic acid/$BiCl_3$	507.0	100	$[Bi(Msuc)_2 - 2H]^+$	357.0	$[Bi(Msuc) - 2H]^+$
				240.8	$[BiS]^+$
				208.8	Bi^+
	393.0	75	$[Bi(Msuc)Cl - H]^+$	357.0	$[Bi(Msuc) - 2H]^+$
				240.8	$[BiS]^+$
				208.8	Bi^+
	374.9	25	$[Bi(Msuc)(H_2O) - 2H]^+$	240.8	$[BiS]^+$
				208.8	Bi^+
	357.0	35	$[Bi(Msuc) - 2H]^+$	240.8	$[BiS]^+$
				208.8	Bi^+
malic acid/$Bi(NO_3)_3$	474.9	15	$[Bi(Mal)_2 - 2H]^+$	340.9	$[Bi(Mal) - 2H]^+$
	340.9	30	$[Bi(Mal) - 2H]^+$	209.0	Bi^+
	135.0	100	$[Mal + H]^+$		
succinic acid/$Bi(NO_3)_3$	766.7	15	$[Bi_2(Suc)_3 - 5H]^+$	442.9	$[Bi(Suc)_2 - 2H]^+$
	560.9	35	$[Bi(Suc)_3 - 2H]^+$	442.9	$[Bi(Suc)_2 - 2H]^+$
	442.9	100	$[Bi(Suc)_2 - 2H]^+$	324.9	$[Bi(Suc) - 2H]^+$
				209.0	Bi^+
	342.9	25	$[Bi(Suc)(H_2O) - 2H]^+$	324.9	$[Bi(Suc) - 2H]^+$

[a] Relative peak intensities (%) are given with respect to the 100% *m*/*z* peak. Assignments of formulas for *m*/*z* peaks are given as $[Bi_nL_m - xH]^+$ (L = carboxylic acid; *n* and *m* = 1, 2, or 3; *x* = 2 or 5) and have been supported by MS/MS.

ing monocations are given together with formula assignments that have been supported by MS/MS experiments. Assignments of formulas are given as $[Bi_nL_m - xH]^+$ (L = carboxylic acid; *n* and *m* = 1 or 2; *x* = 2 or 5; as necessary to balance the charge of Bi^{3+} for a molecular monocation), representing cations with 1:1, 1:2, and 2:2 stoichiometric (*n*:*m*) arrangements. All spectra exhibit *m*/*z* values corresponding to $[BiL - 2H]^+$ and $[BiL_2 - 2H]^+$, which are envisaged as complexes involving dianionic and monoanionic conjugates of the carboxylic acid (L), respectively. ESI mass spectra of reaction mixtures containing $Bi(NO_3)_3$, L-cysteine, and phen in 50% ethanol are similar to those obtained in the absence of phen, notwithstanding the prominent peak with an *m*/*z* value corresponding to the conjugate acid of phen. Although there is no evidence for an *m*/*z* peak corresponding to the dication from **5**, a prominent *m*/*z* peak at 328.0 is assigned to the monocation $[Bi(Cys) - 2H]^+$ and an intense peak at *m*/*z* 449.0 is assigned to $[Bi(Cys)_2 - 2H]^+$, the cysteinate analogue of **2**.

Reaction mixtures containing succinic acid exhibit the broadest range of complexes with *m*/*z* values assigned for $[Bi(Suc)_3 - 2H]^+$ and $[Bi_2(Suc)_3 - 5H]^+$. Complexes containing two bismuth centers likely involve at least one bridging ligand, as observed in the solid state for bifunctional ester−thiolates.[25] There is no evidence for complex ions containing bismuth with lactic, tartaric, fumaric, or pyruvic acids in ESI-MS data of respective reaction mixtures.

Conclusions

The solid-state structure of $Bi(Cys)(Phen)(NO_3)_2 \cdot H_2O$ and the supporting mass spectrometric data for **5**(phen) offer the first definitive identification of a bismuth complex containing the amino acid cysteine. Complexes of the thiolactate anion offer useful comparative structural and spectroscopic data. The ESI-MS data of reaction mixtures allow for an assessment of interactions between bismuth and common multifunctional carboxylic acids.

Experimental Methods

General. Bismuth(III) chloride, bismuth(III) nitrate pentahydrate, cysteine (Cys), fumaric acid, mercaptosuccinic acid (Msuc), malic acid (Mal), pyruvic acid, succinic acid (Suc), tartaric acid, thiolactic acid (Tlac), and 1,10-phenanthroline (phen) were used as received from Aldrich. All reactions were performed at room temperature under an atmosphere of nitrogen. Potassium hydroxide was used as received from BDH. All isolated products are air and moisture stable. Melting points were recorded on an Electrothermal melting point apparatus. IR spectra were recorded as Nujol mulls on CsI plates using a Bruker Vector 22 spectrometer and are presented as wavenumber (cm^{-1}) maxima with ranked intensities for each absorption given in parentheses, and the most intense peak is given a ranking of 1. Chemical analyses were determined by Canadian Microanalytical Service Ltd., Delta, British Columbia.

Isolation and Characterization. Potassium Dichloro(thiopropionato)bismuth, K[1d]. A mixture of D,L-thiolactic acid (0.35 g, 3.3 mmol), KOH (0.38 g, 6.9 mmol), and $BiCl_3$ (1.00 g, 3.2 mmol) in 95% ethanol (30 mL) was stirred overnight, and the yellow mixture was filtered through a Whatman glass microfiber filter. Solvent was removed from the filtrate using a rotary evaporator until crystalline material appeared. Continued slow evaporation at room temperature gave yellow crystals: yield 0.42 g, 1.0 mmol, 31%; dp 193 °C. Anal. Calcd for $C_3H_4BiCl_2KO_2S$ (Found): C 8.52 (8.62), H 0.95 (0.95)%. FT-IR: 1576(4), 1564(2), 1447(1), 1373(3), 1357(5), 1341(9), 1270(10), 1188(16), 1076(15), 999(14), 893(8), 786(12), 718(6), 559(7), 383(11), 337(13).

Dimethylaminoethanethiolato(thiopropionato)bismuth, 4. A mixture of K[**1d**] (0.98 g, 2.0 mmol), KOH (0.25 g, 4.5 mmol), and dimethylaminoethanethiol (0.31 g, 2.2 mmol) in 95% ethanol

(30 mL) was stirred for 24 h and filtered. The filtrate was reduced in volume using a rotary evaporator until precipitate began to appear. After 5 days at 4 °C, yellow crystals were filtered and washed with water, ethanol, and diethyl ether: yield 0.30 g, 0.60 mmol, 56%; dp 93−154°C. Anal. Calcd for $C_7H_{14}BiNO_2S_2$ (Found): C 20.1 (19.21), H 3.35 (3.33), N 3.35 (3.18)%. FT-IR: 1461(1), 1414(1), 1377(1), 1284(1), 1257(1), 1242(1) 1171(2), 915(2), 895(2), 886(2), 842(1), 787(2), 723(3), 657(3).

Dinitrato(cysteinato)bismuthphenanthroline, 5(phen). A mixture of $Bi(NO_3)_3 \cdot 5H_2O$ (0.28 g, 0.57 mmol), L-cysteine (0.07 g, 0.61 mmol), and 1,10-phenanthroline (0.12 g, 0.68 mmol) was stirred overnight in 15 mL of water and 30 mL of ethanol. The reaction mixture was then suction filtered, and the filtrate was allowed to evaporate slowly over 7 days to give yellow crystals: yield 0.11 g, 0.18 mmol, 31%; mp/dp 171−179°C. Anal. Calcd for $C_{15}H_{16}BiN_5O_9S$ (Found): C 27.66 (27.80), H 2.48 (2.48), N 10.79 (10.75)%. FT-IR: 2924(1), 2854(2), 1624(11, sh), 1518(7, sh), 1458(3), 1377(4), 1290(5), 1099(10), 1017(9), 846(8), 773(12), 721(6), 641(13), 523(14), 419(15).

X-ray Crystallography. Data were collected on a Rigaku AFC5R diffractometer equipped with graphite monochromated Mo Kα radiation **5**(phen)·H_2O or Cu Kα radiation (K[**1d**] and **4**) and a 12 kW rotating anode generator. Data collection was carried out at room temperature (K[**1d**] and **4**) or at −130 °C [**5**(phen)·H_2O]. Crystal data and details of the refinements are presented in Table 1. Unit cell parameters were obtained from the setting angles of a minimum of 24 high angle reflections. The choice of space group was based on systematically absent reflections and on chemical considerations (see discussion), and was confirmed in each case by the successful solution and refinement of the structure. During data collection, the intensities of three representative reflections were measured after every 150 reflections; decay corrections were not necessary. The data were corrected for Lorentz and polarization effects, and secondary extinction was refined for K[**1d**]. An empirical absorption correction was applied in each case, ψ-scans[5] for K[**1d**] and **4**, and DIFABS[6] for **5**(phen)·H_2O because of high residual electron density close to the bismuth atoms. The structures were solved by direct methods (SIR-92)[7] and refined by full-matrix least-squares using F^2 data and the program SHELXL-97.[8] A full anisotropic refinement was carried out for K[**1d**], while for the other two structures only the bismuth and sulfur atoms were refined anisotropically. In all three cases, the hydrogen atoms were placed in geometrically calculated positions [with consideration of hydrogen bonding interactions for H(O) and H(N) atoms] and were allowed to ride on the heavy atom to which they were bonded with U_{iso} equal to $1.2U_{eq}$ of the heavy atom [$1.5U_{eq}$ for methyl and H(O) hydrogens]. During refinement, certain bond lengths and angles were restrained to reasonable values, and restraints were placed on the thermal parameters in each structure. Refinement of **5**(phen)·H_2O in the space group *P*1 assumes enantiomeric purity of the L-cysteine but results in a "pseudo" center of symmetry (Figure 3). Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited with the Cambridge Crystallographic Data Centre.

Electrospray Mass Spectrometry. ESI-MS were obtained using a Sciex Qtrap triple quadrupole/ion trap mass spectrometer and/or a Finnigan LCQ Duo ion trap mass spectrometer. Samples were prepared by stirring equimolar amounts of $BiCl_3$ or $Bi(NO_3)_3$ and a carboxylic acid in 50% ethanol at a concentration of 0.02−0.05 M at room temperature for 24 h. The reaction mixtures were filtered, and the filtrate was diluted to a concentration of 0.001 M and injected directly into the electrospray source at a flow rate of 1.2 mL/h. Spectra were obtained with a source temperature of 385 K and a declustering potential of 50 V (Sciex Qtrap triple quadrupole/ion trap mass spectrometer) or a temperature of 473 K with the in-source fragmentation off (Finnigan LCQ Duo ion trap mass spectrometer), respectively. MS/MS spectra were obtained using helium as the collision gas, and the collision energy was optimized for each sample.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada, the Killam Program of the Canada Council for the Arts, the Canada Research Chairs program, the Canada Foundation for Innovation, the Nova Scotia Research and Innovation Trust Fund, and MDS Sciex for funding, the Maritime Mass Spectrometry Laboratories and the National Research Council of Canada, Institute for Marine Biosciences, for use of instrumentation, and Dr. Devanand Pinto for helpful discussion.

Supporting Information Available: Crystallographic data for K[**1d**], **4**, and **5**(phen)·H_2O in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

IC049594N