Inorg. Chem. **2008**, *47*, 2428−2441

Inorganic Chemistry
Article

# Identification of Bismuth-Thiolate-Carboxylate Clusters by Electrospray Ionization Mass Spectrometry

**Heather A. Phillips and Neil Burford***

*Department of Chemistry, Dalhousie University, Halifax, Nova Scotia B3H 4J3, Canada*

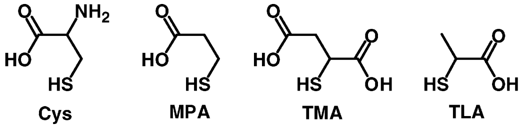
Received August 22, 2007

The known thermal and hydrolytic stability of bismuth−sulfur bonds indicates that biological targets for bismuth likely involve thiol or thiolate functionalities, such as in L-cysteine. Complexes of bismuth with cysteine or other thiol−carboxylic acid ligands have been isolated and characterized providing a preliminary view of the potential participation of these functional groups in the biochemical mechanisms involving bismuth. A broader assessment of bismuth−thiolate interactions has been possible using electrospray ionization mass spectrometry (ESI-MS). A wide range of complexes has been observed containing mercaptosuccinic acid, 2-mercaptopropionic acid, 3-mercaptopropionic acid, and/or 2-amino-3-mercaptopropionic acid (cysteine). The identification of various multibismuth multiligand cluster ions defines new chemistry for bismuth.

## Introduction

Compounds of bismuth have been used to treat a variety of human ailments for over two hundred years.[1,2] Pepto-Bismol, De-Nol, and Pylorid are modern remedies for gastrointestinal ailments, containing bismuth subsalicylate (BSS), colloidal bismuth subcitrate (CBS), and ranitidine bismuth citrate (RBC), respectively. Along with other bismuth compounds, BSS, CBS, and RBC show antimicrobial activity toward the bacterium, *Helicobacter pylori*,[3–5] established as a cause of peptic ulcers.[6] Nevertheless, the biological activity of bismuth is not understood at a molecular level. We have exploited electrospray ionization mass spectrometry (ESI-MS) as a data-rich tool for examining reaction mixtures containing ions of bismuth or other metals (Cd, Hg, Tl, Pb, As, Sb) and biological molecules, such as amino acids[7–9] and peptides.[7,10] Seven different amino acids are known to form complexes with bismuth,[8] and bismuth exhibits a preference for interaction with molecules containing sulfur.[11] Moreover, the presence of a thiol such as L-cysteine promotes the formation of complex ions of bismuth with nonthiol amino acids,[8,9] and solid state structures indicate that bismuth is chelated by thiolate−carboxylate ligands.[12] In this context, a comprehensive ESI-MS study of reaction mixtures containing $Bi(NO_3)_3$ with mercaptosuccinic acid (thiomalic acid, TMA), 2-mercaptopropionic acid (thiolactic acid, TLA), 3-mercaptopropionic acid (MPA), or 2-amino-3-mercaptopropionic acid (L-cysteine, Cys) provides insight into the possible therapeutic chemistry of bismuth compounds. This selection of biologically relevant thiol−carboxylic acids (Chart 1) represents a palette of comple-

**Chart 1.** Structurally Related Thiol−Carboxylic Acids, Cysteine (Cys), 3-Mercaptopriopionic Acid (MPA), Thiomalic Acid (TMA), and Thiolactic Acid (TLA)



---

* To whom correspondence should be addressed. E-mail: neil.burford@dal.ca.

(1) Sadler, P. J.; Li, H.; Sun, H. *Coord. Chem. Rev.* **1999**, *185–186*, 689–709.
(2) Briand, G. G.; Burford, N. *Chem. Rev.* **1999**, *99*, 2601–2657.
(3) Marshall, B. J. *Am. J. Gastroenterol.* **1991**, *86*, 16–25.
(4) McColm, A. A.; McLaren, A.; Klinkert, G.; Francis, M. R.; Connolly, P. C.; Grinham, C. J.; Campbell, C. J.; Selway, S.; Williamson, R. *Aliment. Pharmacol. Ther.* **1996**, *10*, 241–250.
(5) Vondracek, T. G. *Ann. Pharmacother.* **1998**, *32*, 672–679.
(6) Ables, A. Z.; Simon, I.; Melton, E. R. *Am. Fam. Phys.* **2007**, *75*, 351–358.
(7) Burford, N.; Eelman, M. D.; Mahony, D.; Morash, M. *Chem. Commun.* **2003**, 146–147.
(8) Burford, N.; Eelman, M. D.; LeBlanc, W. G. *Can. J. Chem.* **2004**, *82*, 1254–1259.
(9) Phillips, H. A.; Eelman, M. D.; Burford, N. *J. Inorg. Biochem.* **2007**, *101*, 736–739.
(10) Burford, N.; Eelman, M. D.; Groom, K. A. *J. Inorg. Biochem.* **2005**, *99*, 1992–1997.
(11) Briand, G. G.; Burford, N. *Adv. Inorg. Chem.* **2000**, *50*, 285–357.
(12) Briand, G. G.; Burford, N.; Eelman, M. D.; Aumeerally, N.; Chen, L.; Cameron, T. S.; Robertson, K. N. *Inorg. Chem.* **2004**, *43*, 6495–6500.

10.1021/ic701657r CCC: $40.75

**Table 1.** Positive and Negative Ion ESI-MS Data for Reaction Mixtures of $Bi(NO_3)_3$ with MPA in 50:50 Ethanol:Water

| *m*/*z* | relative abundance (%) | positive ion assignment | MS/MS (*m*/*z*) | positive ion fragment assignment |
|---|---|---|---|---|
| 419.0 | 20–32 | $[Bi(MPA)_2 - 2H]^+$ | 312.9 | $[Bi(MPA) - 2H]^+$ |
| | | | 330.9 | $[Bi(SCH_2CH_3)_2]^+$ |
| | | | 358.8 | $[Bi(MPA)_2 - 2H - C_2H_4O_2]^+$ |
| | | | 400.8 | $[Bi(MPA)_2 - 2H - H_2O]^+$ |
| 441.1 | 6–13 | $[BiNa(MPA)_2 - 3H]^+$ | 336.9 | $[BiNa(MPA) - H]^+$ |
| | | | 368.9 | $[BiNa(MPA)(S) - H]^+$ |
| 730.9 | 100 | $[Bi_2(MPA)_3 - 5H]^+$ | 586.9 | $[Bi_2(MPA)(S)_2 - H]^+$ |
| | | | 658.9 | $[Bi_2(MPA)_2(S) - 3H]^+$ |
| 753.0 | 17–42 | $[Bi_2Na(MPA)_3 - 6H]^+$ | 680.9 | $[Bi_2Na(MPA)_2(S) - 4H]^+$ |
| 1042.8 | 34–46 | $[Bi_3(MPA)_4 - 8H]^+$ | 866.9 | $[Bi_3(MPA)_2(O)_2 - 4H]^+$ |
| | | | 882.8 | $[Bi_3(MPA)_2(S)(O) - 4H]^+$ |
| | | | 898.9 | $[Bi_3(MPA)_2(S)_2 - 4H]^+$ |
| | | | 954.8 | $[Bi_3(MPA)_3(O) - 6H]^+$ |
| | | | 970.8 | $[Bi_3(MPA)_3(S) - 6H]^+$ |
| 1460.5 | 1–5 | $[Bi_4(MPA)_6 - 11H]^+$ | | |
| 1482.5 | 2–6 | $[Bi_4Na(MPA)_6 - 12H]^+$ | | |
| 1772.5 | 2–4 | $[Bi_5(MPA)_7 - 14H]^+$ | | |
| *m*/*z* | relative abundance (%) | negative ion assignment | MS/MS (*m*/*z*) | negative ion fragment assignment |
| 344.9 | 20–26 | $[Bi(MPA)(S) - 2H]^-$ | 241.1 | $[Bi(S)]^-$ |
| | | | 273.2 | $[Bi(S)_2]^-$ |
| | | | 300.8 | $[Bi(MPA)(S) - 2H - CO_2]^-$ |
| 416.9 | 100 | $[Bi(MPA)_2 - 4H]^-$ | 312.8 | $[Bi(MPA) - 2H]^-$ |
| | | | 345.0 | $[Bi(MPA)(S) - 2H]^-$ |
| | | | 372.9 | $[Bi(MPA)_2 - 4H - CO_2]^-$ |
| 501.8 | 10–34 | $[BiNa(MPA)_2(NO_3) - 4H]^-$ | 416.9 | $[Bi(MPA)_2 - 4H]^-$ |
| 791.7 | 13–27 | $[Bi_2(MPA)_3(NO_3) - 6H]^-$ | 345.0 | $[Bi(MPA)(S) - 2H]^-$ |
| | | | 416.9 | $[Bi(MPA)_2 - 4H]^-$ |
| | | | 719.8 | $[Bi_2(MPA)_2(S)(NO_3) - 4H]^-$ |
| 1146.7 | 28–35 | $[Bi_3(MPA)_5 - 10H]^-$ | 344.9 | $[Bi(MPA)(S) - 2H]^-$ |
| | | | 416.9 | $[Bi(MPA)_2 - 4H]^-$ |
| | | | 1074.6 | $[Bi_3(MPA)_4(S) - 8H]^-$ |

**Table 2.** Positive and Negative Ion ESI-MS Data for Reaction Mixtures of $Bi(NO_3)_3$ with TLA in 50:50 Ethanol:Water

| *m*/*z* | relative abundance (%) | positive ion assignment | MS/MS (*m*/*z*) | positive ion fragment assignment |
|---|---|---|---|---|
| 312.9 | 8–10 | $[Bi(TLA) - 2H]^+$ | | |
| 419.0 | 74–87 | $[Bi(TLA)_2 - 2H]^+$ | 312.9 | $[Bi(TLA) - 2H]^+$ |
| | | | 372.8 | $[Bi(TLA)_2 - 2H - CH_2O_2]^+$ |
| | | | 400.7 | $[Bi(TLA)_2 - 2H - H_2O]^+$ |
| 730.7 | 95–100 | $[Bi_2(TLA)_3 - 5H]^+$ | | |
| 752.9 | 61–86 | $[Bi_2Na(TLA)_3 - 6H]^+$ | 576.9 | $[Bi_2Na(TLA)(O)_2 - 2H]^+$ |
| | | | 648.8 | $[Bi_2Na(TLA)_2 - 4H]^+$ |
| | | | 664.9 | $[Bi_2Na(TLA)_2(O) - 4H]^+$ |
| | | | 680.9 | $[Bi_2Na(TLA)_2(S) - 4H]^+$ |
| 1042.7 | 76–100 | $[Bi_3(TLA)_4 - 8H]^+$ | 970.9 | $[Bi_3(TLA)_3(S) - 6H]^+$ |
| 1460.4 | 12–18 | $[Bi_4(TLA)_6 - 11H]^+$ | | |
| 1482.4 | 8–14 | $[Bi_4Na(TLA)_6 - 12H]^+$ | 680.8 | $[Bi_2Na(TLA)_2(S) - 4H]^+$ |
| | | | 752.9 | $[Bi_2Na(TLA)_3 - 6H]^+$ |
| 1772.3 | 39–47 | $[Bi_5(TLA)_7 - 14H]^+$ | 1042.7 | $[Bi_3(TLA)_4 - 8H]^+$ |
| *m*/*z* | relative abundance (%) | negative ion assignment | MS/MS (*m*/*z*) | negative ion fragment assignment |
| 312.9 | 19–28 | $[Bi(TLA) - 2H]^-$ | 209.1 | $[Bi]^-$ |
| | | | 268.9 | $[Bi(TLA) - 2H - CO_2]^-$ |
| 416.9 | 100 | $[Bi(TLA)_2 - 4H]^-$ | 312.9 | $[Bi(TLA) - 2H]^-$ |
| 501.7 | 4–10 | $[BiNa(TLA)_2(NO_3) - 4H]^-$ | | |
| 791.7 | 23–28 | $[Bi_2(TLA)_3(NO_3) - 6H]^-$ | | |
| 1146.5 | 58–69 | $[Bi_3(TLA)_5 - 10H]^-$ | | |

mentary ligand frameworks with which to further assess bismuth-thiolate-carboxylate coordination chemistry and has enabled the development of bismuth−thiolate chemistry through the discovery of a series of multibismuth multiligand cluster ions.

## Experimental Section

**General.** Bismuth(III) nitrate pentahydrate, L-cysteine (Cys), 3-mercaptopropionic acid (MPA), thiolactic acid (TLA), and thiomalic acid (TMA) were used as received from Sigma-Aldrich. Ethanol (HPLC reagent grade) was used as received from Fisher. All reactions were performed at room temperature using distilled water.

**Preparation of Reaction Mixtures. $Bi(NO_3)_3$ + 1 Thiol−Carboxylic Acid.** $Bi(NO_3)_3 \cdot 5H_2O$ (0.097 g, 0.20 mmol) was stirred for several minutes in 10 mL solvent (50:50 ethanol:water), followed by the addition of MPA (0.017 mL, 0.20 mmol), TLA (0.018 mL, 0.20 mmol), or TMA (0.030 g, 0.20 mmol) and another

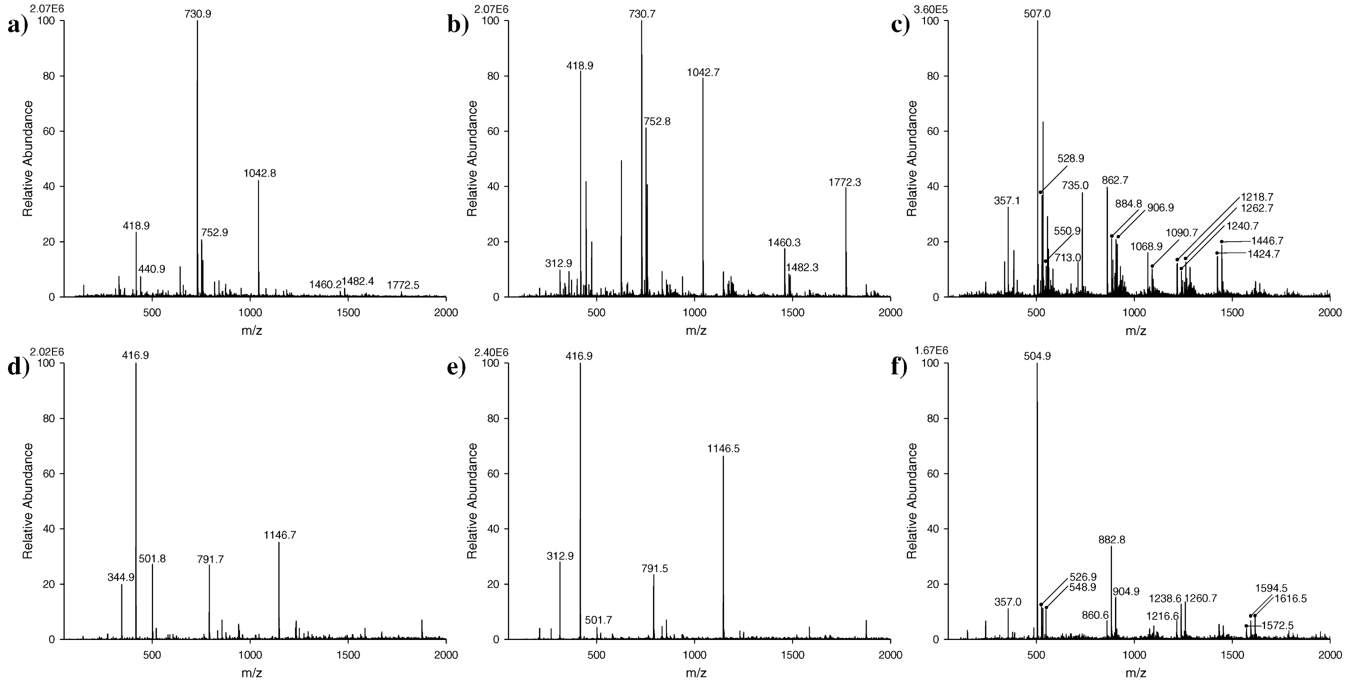


**Figure 1.** Bismuth-thiolate-carboxylate ESI-MS spectra from reaction mixtures containing $Bi(NO_3)_3$ and (a) MPA, (b) TLA, or (c) TMA (positive ion mode) or (d) MPA, (e) TLA, or (f) TMA (negative ion mode), in 50:50 ethanol:water. Denoted peaks are also listed in Tables 1−3.

10 mL of solvent. All reaction mixtures were stirred overnight before suction filtration. Each filtrate was diluted 10-fold to a concentration ca. 0.001 M for analysis by ESI-MS.

**$Bi(NO_3)_3$ + 2 Thiol−Carboxylic Acids.** MPA (0.017 mL, 0.20 mmol), TLA (0.018 mL, 0.20 mmol), TMA (0.030 g, 0.20 mmol), or Cys (0.025 g, 0.20 mmol) was stirred for several minutes in 10 mL solvent (50:50 ethanol:water), followed by the addition of a different thiol−carboxylic acid: MPA (0.017 mL, 0.20 mmol), TLA (0.018 mL, 0.20 mmol), TMA (0.030 g, 0.20 mmol), or Cys (0.024 g, 0.20 mmol). $Bi(NO_3)_3 \cdot 5H_2O$ (0.097 or 0.098 g, 0.20 mmol) and another 10 mL of solvent were added, followed by stirring overnight. The order of addition of reactants did not lead to considerably different ESI mass spectra. All reaction mixtures were filtered by passage through a Nalgene polytetrafluoroethylene (PTFE, Teflon) syringe filter (0.2 μm pore size, 25 mm diameter). Each filtrate solution was diluted 10-fold to a concentration ca. 0.001 M for analysis by way of ESI-MS.

**Electrospray Ionization Mass Spectrometry.** Mass spectra were obtained using a Finnigan LCQ DUO electrospray ionization quadrupole ion trap mass spectrometer. Filtered and diluted reaction mixtures were injected directly into the ESI source in aliquots of 5, 10, or 20 μL. The solvent (50:50 ethanol:water) flow rate was set at 1.2 mL/h, the heated capillary temperature at 200 °C, the sheath gas ($N_{2(g)}$) flow rate at 20 (arbitrary units), and the spray voltage at a magnitude of 4.00 kV for positive ion spectra and 4.00 kV (two-component reaction mixtures) or 4.50 kV (three-component reaction mixtures) for negative ion spectra. Tandem mass spectra were obtained using helium as the collision gas, and applying a collision energy of 12.5−45.0%. In-source collision-induced dissociation (CID) was deactivated during all experiments. All mass spectra were analyzed and processed using software programs, Qual Browser (version 1.2 from Finnigan Corp. 1998–2000) and SigmaPlot (version 10.0 from Systat Software, Inc. 2006), respectively.

## Results and Discussion

**Homoleptic Bismuth-Thiolate-Carboxylate Complexes.** ESI-MS data for reaction mixtures containing $Bi(NO_3)_3$ with MPA, TMA, or TLA are presented in Tables 1−3. Representative positive and negative ion spectra are shown in Figure 1. Relative abundances are listed as ranges over four (TLA, TMA) or ten (MPA) sample injections from two separate samples for each bismuth−ligand combination. In the tables, mass-to-charge ratios (*m*/*z*) are reported to one decimal place (typically varying by 0.0 to −0.2 units). In the text, whole number *m*/*z* values are used. Peaks with relative intensities of less than 5% are not reported unless the identification of these peaks is useful for comparison between spectra.

Peak assignments in Tables 1−3 are presented as generic formulae, $[Bi_vL_w - yH]^z$ (L = MPA, TLA, or TMA; $v = 1$–5; $w = 1$–7; $y = 2$–15; $z = \pm1$), containing one or more bismuth atoms with one or more thiolate−carboxylate ligands. The anionic ligands originate from neutral thiol−carboxylic acids by the loss of $3v - 1$ or $3v + 1$ protons ($v$ = number of bismuth atoms) for monocationic and monoanionic species, respectively. Multiply charged ions have not been observed. In some cases, sodium, nitrate, sulfur or oxygen are involved in the assigned complex ions. The observation of sodiated monocations (e.g., $[Bi_2Na(MPA)_3 - 6H]^+$, *m*/*z* 753 in Table 1 and Figure 1a) indicates that the corresponding neutral, non-sodiated species (e.g., $[Bi_2(MPA)_3 - 6H]$) are present in the initial reaction mixtures. A comparison of experimental and

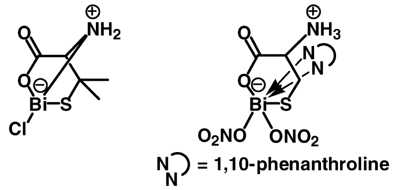
---

(13) Manura, J. J.; Manura, D. J. *Isotope Distribution Calculator and Mass Spec Plotter*; available online at http://www2.sisweb.com/mstools/isotope.htm (accessed July 2007) Scientific Instrument Services, Inc.: Ringoes, NJ, 2003.

**Table 3.** Positive and Negative Ion ESI-MS Data for Reaction Mixtures of $\mathrm{Bi(NO_3)_3}$ with TMA in 50:50 Ethanol:Water

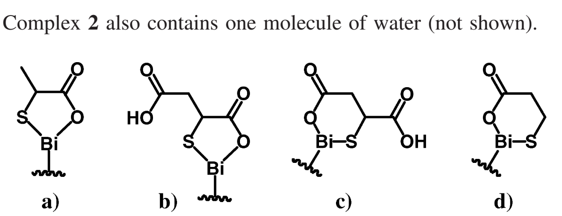
| *m*/*z* | relative abundance (%) | positive ion assignment | MS/MS (*m*/*z*) | positive ion fragment assignment |
|---|---|---|---|---|
| 357.1 | 33–92 | $[\mathrm{Bi(TMA)} - \mathrm{2H}]^+$ | 241.1 | $[\mathrm{Bi(S)}]^+$ |
| | | | 312.9 | $[\mathrm{Bi(TMA)} - \mathrm{2H} - \mathrm{CO_2}]^+$ |
| | | | 338.7 | $[\mathrm{Bi(TMA)} - \mathrm{2H} - \mathrm{H_2O}]^+$ |
| 507.0 | 100 | $[\mathrm{Bi(TMA)_2} - \mathrm{2H}]^+$ | 356.9 | $[\mathrm{Bi(TMA)} - \mathrm{2H}]^+$ |
| | | | 488.9 | $[\mathrm{Bi(TMA)_2} - \mathrm{2H} - \mathrm{H_2O}]^+$ |
| 529.0 | 37–65 | $[\mathrm{BiNa(TMA)_2} - \mathrm{3H}]^+$ | 378.9 | $[\mathrm{BiNa(TMA)} - \mathrm{3H}]^+$ |
| 551.0 | 9–24 | $[\mathrm{BiNa_2(TMA)_2} - \mathrm{4H}]^+$ | | |
| 713.0 | 12–27 | $[\mathrm{Bi_2(TMA)_2} - \mathrm{5H}]^+$ | | |
| 735.0 | 37–74 | $[\mathrm{Bi_2Na(TMA)_2} - \mathrm{6H}]^+$ | 379.1 | $[\mathrm{BiNa(TMA)} - \mathrm{3H}]^+$ |
| 862.9 | 11–42 | $[\mathrm{Bi_2(TMA)_3} - \mathrm{5H}]^+$ | | |
| 884.8 | 13–21 | $[\mathrm{Bi_2Na(TMA)_3} - \mathrm{6H}]^+$ | | |
| 906.9 | 14–21 | $[\mathrm{Bi_2Na_2(TMA)_3} - \mathrm{7H}]^+$ | | |
| 1068.9 | 17–20 | $[\mathrm{Bi_3(TMA)_3} - \mathrm{8H}]^+$ | | |
| 1090.7 | 9–11 | $[\mathrm{Bi_3Na(TMA)_3} - \mathrm{9H}]^+$ | | |
| 1218.9 | 1–11 | $[\mathrm{Bi_3(TMA)_4} - \mathrm{8H}]^+$ | | |
| 1240.7 | 3–11 | $[\mathrm{Bi_3Na(TMA)_4} - \mathrm{9H}]^+$ | | |
| 1262.9 | 8–13 | $[\mathrm{Bi_3Na_2(TMA)_4} - \mathrm{10H}]^+$ | | |
| 1424.9 | 6–15 | $[\mathrm{Bi_4(TMA)_4} - \mathrm{11H}]^+$ | | |
| 1446.9 | 12–20 | $[\mathrm{Bi_4Na(TMA)_4} - \mathrm{12H}]^+$ | 735.0 | $[\mathrm{Bi_2Na(TMA)_2} - \mathrm{6H}]^+$ |
| | | | 1090.6 | $[\mathrm{Bi_3(Na(TMA)_3} - \mathrm{9H}]^+$ |
| ***m*/*z*** | **relative abundance (%)** | **negative ion assignment** | **MS/MS (*m*/*z*)** | **negative ion fragment assignment** |
| 357.1 | 6–13 | $[\mathrm{Bi(TMA)} - \mathrm{2H}]^-$ | 114.9 | $[\mathrm{(TMA)} - \mathrm{3H} - \mathrm{S}]^-$ |
| | | | 241.1 | $[\mathrm{Bi(S)}]^-$ |
| | | | 312.9 | $[\mathrm{Bi(TMA)} - \mathrm{2H} - \mathrm{CO_2}]^-$ |
| | | | 338.7 | $[\mathrm{Bi(TMA)} - \mathrm{2H} - \mathrm{H_2O}]^-$ |
| 505.0 | 100 | $[\mathrm{Bi(TMA)_2} - \mathrm{4H}]^-$ | 149.0 | $[\mathrm{(TMA)} - \mathrm{H}]^-$ |
| | | | 357.1 | $[\mathrm{Bi(TMA)} - \mathrm{2H}]^-$ |
| | | | 389.0 | $[\mathrm{Bi(TMA)(S)} - \mathrm{2H}]^-$ |
| | | | 486.8 | $[\mathrm{Bi(TMA)_2} - \mathrm{4H} - \mathrm{H_2O}]^-$ |
| 526.9 | 5–12 | $[\mathrm{BiNa(TMA)_2} - \mathrm{5H}]^-$ | | |
| 548.9 | 3–11 | $[\mathrm{BiNa_2(TMA)_2} - \mathrm{6H}]^-$ | | |
| 860.6 | 5–13 | $[\mathrm{Bi_2(TMA)_3} - \mathrm{7H}]^-$ | | |
| 882.9 | 26–34 | $[\mathrm{Bi_2Na(TMA)_3} - \mathrm{8H}]^-$ | 526.9 | $[\mathrm{BiNa(TMA)_2} - \mathrm{5H}]^-$ |
| | | | 734.9 | $[\mathrm{Bi_2Na(TMA)_2} - \mathrm{6H}]^-$ |
| | | | 766.9 | $[\mathrm{Bi_2Na(TMA)_2(S)} - \mathrm{6H}]^-$ |
| | | | 864.7 | $[\mathrm{Bi_2Na(TMA)_3} - \mathrm{8H} - \mathrm{H_2O}]^-$ |
| 904.9 | 7–15 | $[\mathrm{Bi_2Na_2(TMA)_3} - \mathrm{9H}]^-$ | | |
| 1216.7 | 5–12 | $[\mathrm{Bi_3(TMA)_4} - \mathrm{10H}]^-$ | | |
| 1238.6 | 11–17 | $[\mathrm{Bi_3Na(TMA)_4} - \mathrm{11H}]^-$ | | |
| 1260.7 | 5–14 | $[\mathrm{Bi_3Na_2(TMA)_4} - \mathrm{12H}]^-$ | 904.8 | $[\mathrm{Bi_2Na_2(TMA)_3} - \mathrm{9H}]^-$ |
| 1572.6 | 3–8 | $[\mathrm{Bi_4(TMA)_5} - \mathrm{13H}]^-$ | | |
| 1594.5 | 6–11 | $[\mathrm{Bi_4Na(TMA)_5} - \mathrm{14H}]^-$ | 882.9 | $[\mathrm{Bi_2Na(TMA)_3} - \mathrm{8H}]^-$ |
| | | | 1238.6 | $[\mathrm{Bi_3Na(TMA)_4} - \mathrm{11H}]^-$ |
| 1616.6 | 3–8 | $[\mathrm{Bi_4Na_2(TMA)_5} - \mathrm{15H}]^-$ | | |

**Chart 2.** Complexes of Bismuth with Penicillamine and Cysteine[a]



**1** **2**

[a] Complex **2** also contains one molecule of water (not shown).

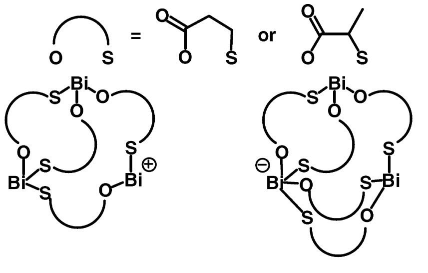


**a)** **b)** **c)** **d)**

**Figure 2.** Chelation of thiolate−carboxylate ligands to bismuth, generating five-membered or six-membered rings: (a) TLA, (b and c) TMA, and (d) MPA.

theoretical[13,14] isotope patterns has been undertaken for all peak assignments in Tables 1−3, and corresponding spectra have been compiled in the Supporting Information. Table 4 provides a summary of the bismuth:ligand (Bi:L) stoichiometric ratios in $[\mathrm{Bi}_v\mathrm{L}_w - y\mathrm{H}]^z$ complex ions (L = MPA, TLA, or TMA) that have been assigned to peaks in positive and negative ion ESI mass spectra.

The numerical value included at the top left corner of each full or tandem mass spectrum is the corresponding normal-



**a)** **b)**

**Figure 3.** Proposed topologies for $[\mathrm{Bi}_v\mathrm{L}_w - y\mathrm{H}]^z$ complex ions (L = TLA or MPA) with Bi:L values of (a) 3:4 and (b) 3:5. Due to exactly eight or ten available sites for deprotonation in the 3:4 cation or 3:5 anion, respectively, a corresponding 3:5 cation or 3:4 anion is not possible.

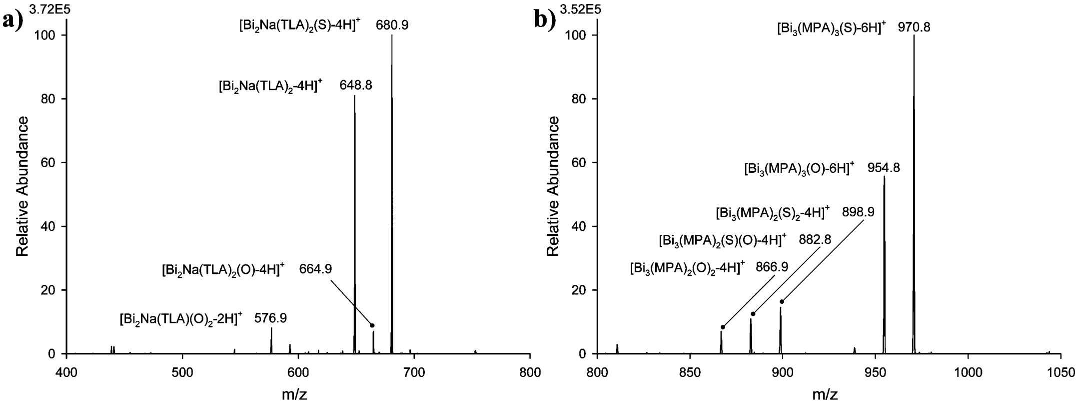


**Figure 4.** CID of (a) $[Bi_2Na(TLA)_3 - 6H]^+$ ions at *m/z* 753 (30% collision energy) and (b) $[Bi_3(MPA)_4 - 8H]^+$ions at *m/z* 1043 (25% collision energy).

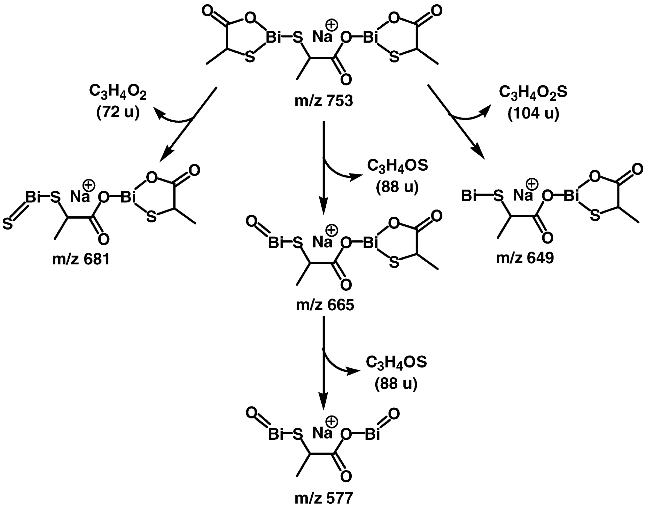


**Figure 5.** Proposed ion fragmentation pathway for $[Bi_2Na(TLA)_3 - 6H]^+$ at *m/z* 753.

**Table 4.** Summary of Bi:L Values in $[Bi_vL_w - yH]^z$ Complexes (L = MPA, TLA, or TMA) Observed in Positive and Negative Ion ESI Mass Spectra

| positive ion mode | | | negative ion mode | | |
|---|---|---|---|---|---|
| Bi:MPA | Bi:TLA | Bi:TMA | Bi:MPA | Bi:TLA | Bi:TMA |
| | 1:1 | 1:1 | 1:1:S | 1:1 | 1:1 |
| 1:2 | 1:2 | 1:2 | 1:2 | 1:2 | 1:2 |
| 1:2:Na | | 1:2:Na | 1:2:Na:$NO_3$ | 1:2:Na:$NO_3$ | 1:2:Na |
| | | 1:2:2Na | | | 1:2:2Na |
| | | 2:2 | | | |
| | | 2:2:Na | | | |
| 2:3 | 2:3 | 2:3 | | | 2:3 |
| 2:3:Na | 2:3:Na | 2:3:Na | 2:3:$NO_3$ | 2:3:$NO_3$ | 2:3:Na |
| | | 2:3:2Na | | | 2:3:2Na |
| | | 3:3 | | | |
| | | 3:3:Na | | | |
| 3:4 | 3:4 | 3:4 | | | 3:4 |
| | | 3:4:Na | | | 3:4:Na |
| | | 3:4:2Na | | | 3:4:2Na |
| | | | 3:5 | 3:5 | |
| | | 4:4 | | | |
| | | 4:4:Na | | | |
| | | | | | 4:5 |
| | | | | | 4:5:Na |
| | | | | | 4:5:2Na |
| 4:6 | 4:6 | | | | |
| 4:6:Na | 4:6:Na | | | | |
| 5:7 | 5:7 | | | | |

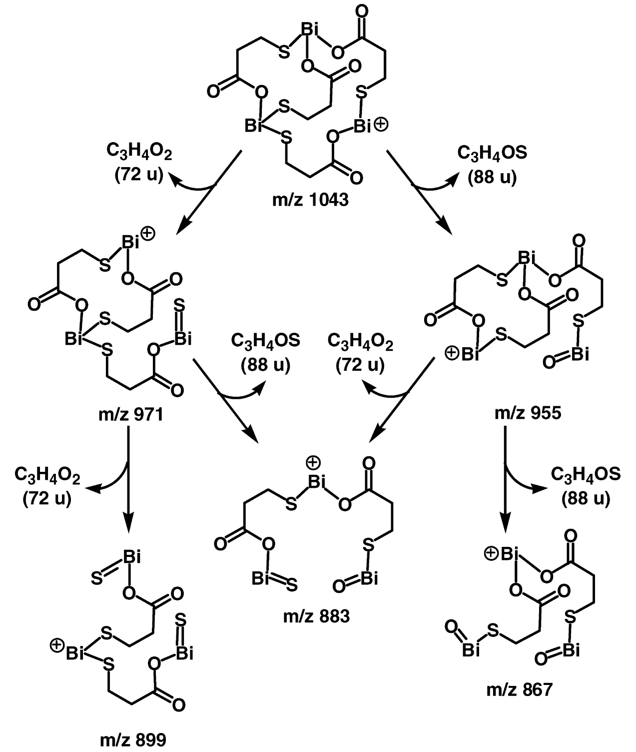


**Figure 6.** Proposed ion fragmentation pathway for $[Bi_3(MPA)_4 - 8H]^+$ at *m/z* 1043.

ized spectral intensity (NL, arbitrary units). Higher NL values indicate that more ions have been detected, increasing the reliability of the spectral results. In our experience, when the NL of MS/MS spectra is relatively low (e.g., $<1 \times 10^4$) there are inconsistencies in the spectral data over time. Therefore, MS/MS peak assignments reported in Tables 1−3 are for spectra with NL $\geq 2 \times 10^4$. Fragment ion formulas are derived from neutral mass losses. Not all fragment ions are listed, and in some cases it was not possible to acquire MS/MS spectra with reliable intensities (NL $\geq 2 \times 10^4$).

$[Bi_vL_w - yH]^z$ complex ions with Bi:L values of 1:1 were assigned to *m/z* peaks in both positive and negative ion modes for reaction mixtures containing $Bi(NO_3)_3$ and TMA or TLA. Conversely, from reaction mixtures containing $Bi(NO_3)_3$ and MPA, a peak (*m/z* 345) assigned to 1:1:1 Bi:MPA:sulfur was observed only in negative ion mode. Given that MPA is the amine-free structural analogue of Cys (Chart 1) and that a 1:1 Bi:Cys cation at *m/z* 328 is consistently observed,[7−9] the absence of a peak corresponding to a 1:1 Bi:MPA complex ion is somewhat surprising. It is possible that the amine

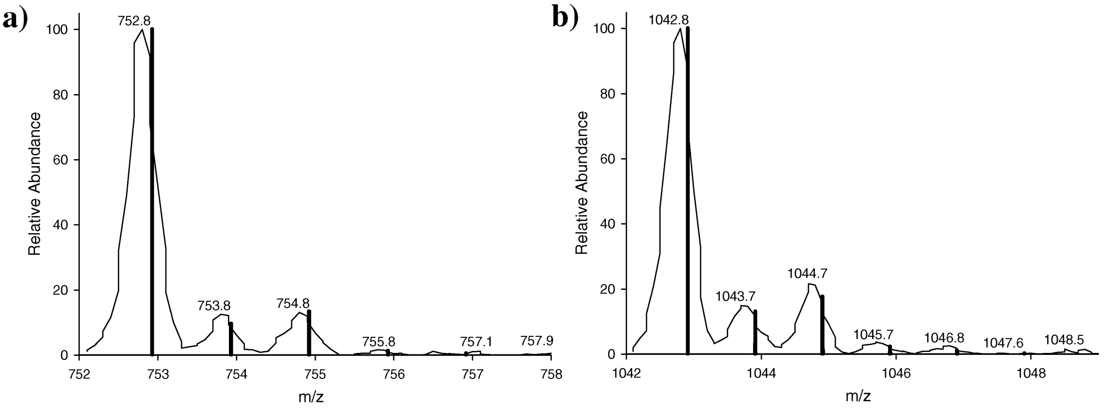
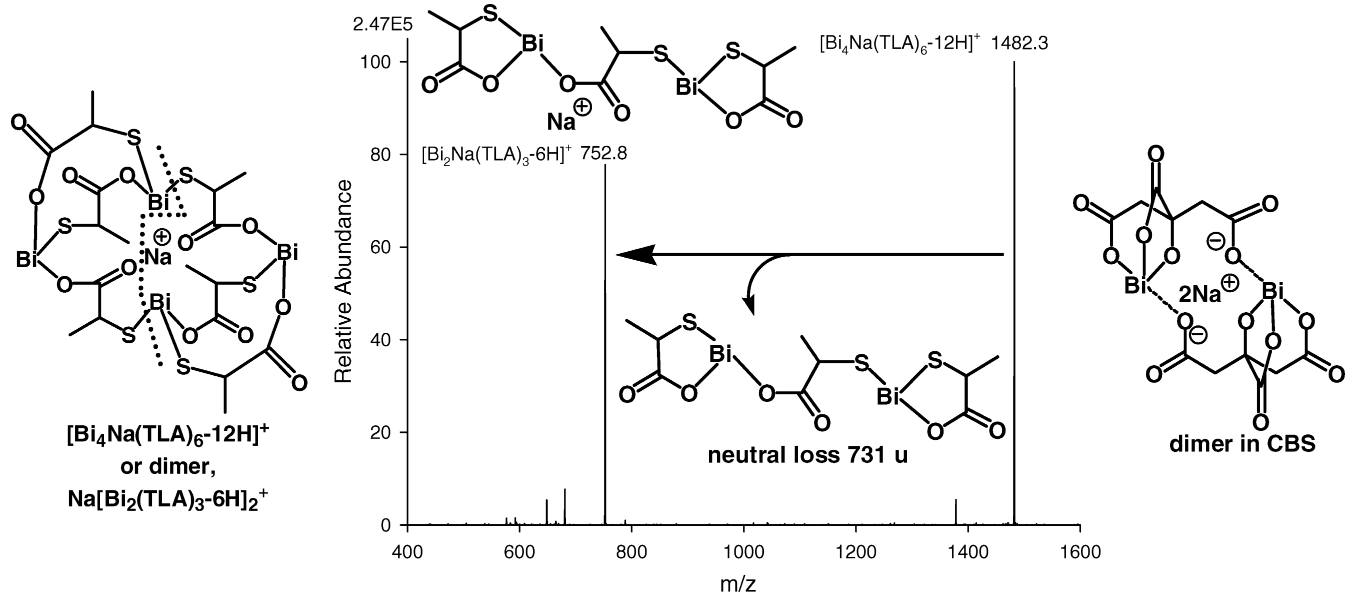


**Figure 7.** Experimental (continuous thin line) and theoretical (vertical bars) isotope patterns are shown for (a) *m/z* 753, assigned as $[Bi_2Na(TLA)_3 - 6H]^+$, and (b) *m/z* 1043, assigned as $[Bi_3(MPA)_4 - 8H]^+$.



a) b) c)

**Figure 8.** CID (at 15% collision energy) of ions at *m/z* 1483, assigned as $[Bi_4Na(TLA)_6 - 12H]^+$. (a) The fragmentation axis (dotted line) through the proposed structure of a 4:6:1 Bi:TLA:Na ion affords (b) a 2:3:1 Bi:TLA:Na product ion (*m/z* 753) and 2:3 Bi:TLA neutral loss (731 u), for which possible structures are shown. The structural drawing in part a can also be considered a sodiated dimer of $[Bi_2(TLA)_3 - 6H]$. (c) For comparison, the 2:2 multibismuth multiligand bismuth:citrate dimer found in many solid state structures of CBS is shown with two counterbalancing sodium cations.

functionality in Cys plays a role in the coordination of bismuth by this ligand. This supposition is supported by the known solid state structure of coordination complex, **1** (Chart 2), involving the interaction of amino, thiolate, and carboxylate functional groups of penicillamine (3,3-dimethylcysteine) with bismuth.[15] In contrast, the known cysteinatobismuth(III) complex, **2**, contains a bidentate monoanionic cysteinate ligand bound to bismuth via the thiolate and carboxylate functionalities only, with support from auxiliary ligand, 1,10-phenanthroline.[12] The molecular drawings throughout this report are provided as Lewis structures (with lone pairs omitted for clarity) with formal charges that should not be considered representative of charge distribution.

While TLA or TMA have the potential to chelate bismuth in a bidentate fashion to generate a five-membered ring (Figures 2a and 2b, respectively), MPA affords a six-membered chelate ring involving bismuth (Figure 2d). Both five[12,16–19] and six-membered[12,16,20] chelate heterocycles are known for thiolate or thiolate−carboxylate ligands coordinated to bismuth, but the five-membered chelate ring is most common.[11] It is possible that the absence of a 1:1 Bi:MPA complex ion in ESI mass spectra is due to the inability of MPA to provide a five-membered chelation environment.

---

(14) Yan, J. *Isotope Pattern Calculator*; v4.0, available online at http://www.geocities.com/junhuayan/pattern.htm (accessed July 2007) Ohio State University: Columbus, OH, 2001.

(15) Herrmann, W. A.; Herdtweck, E.; Pajdla, L. *Chem. Ber.* **1993**, *126*, 895–898.

(16) Agocs, L.; Burford, N.; Cameron, T. S.; Curtis, J. M.; Richardson, J. F.; Robertson, K. N.; Yhard, G. B. *J. Am. Chem. Soc.* **1996**, *118*, 3225–3232.

(17) Agocs, L.; Briand, G. G.; Burford, N.; Cameron, T. S.; Kwiatkowski, W.; Robertson, K. N. *Inorg. Chem.* **1997**, *36*, 2855–2860.

(18) Briand, G. G.; Burford, N.; Cameron, T. S.; Kwiatkowski, W. *J. Am. Chem. Soc.* **1998**, *120*, 11374–11379.

(19) Briand, G. G.; Burford, N.; Eelman, M. D.; Cameron, T. S.; Robertson, K. N. *Inorg. Chem.* **2003**, *42*, 3136–3141.

(20) Burford, N.; Eelman, M. D.; Cameron, T. S. *Chem. Commun.* **2002**, 1402–1403.

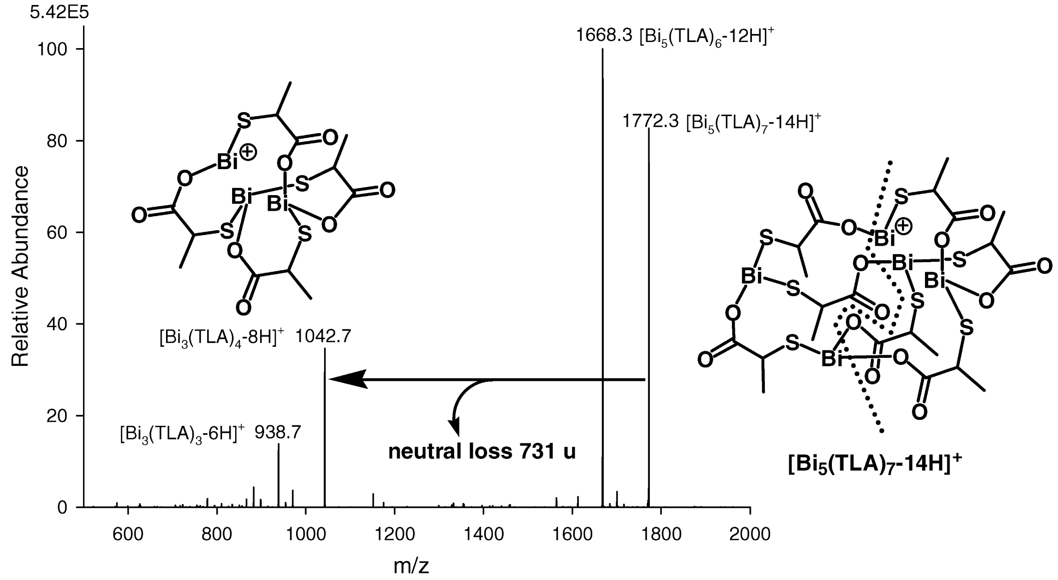


**Figure 9.** Following a neutral loss of 731 u, CID (at 15% collision energy) of ions at *m/z* 1772, assigned as $[Bi_5(TLA)_7 - 14H]^+$ (actual nominal ion mass: 1773 u), yielding $[Bi_3(TLA)_4 - 8H]^+$ at *m/z* 1043.

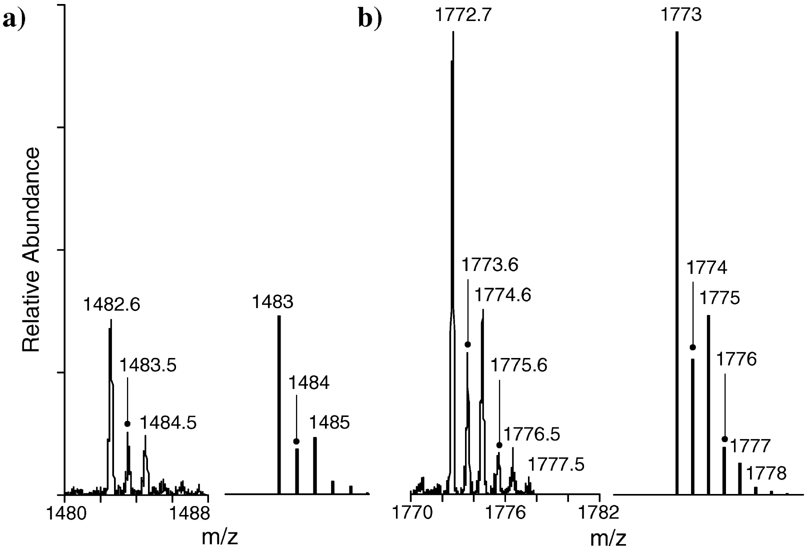


**Figure 10.** Comparison of ZoomScan and theoretical spectra for $[Bi_4Na(TLA)_6 - 12H]^+$ and $[Bi_5(TLA)_7 - 14H]^+$. High resolution (left) and calculated (right) spectra are provided for ions represented by (a) *m/z* 1483 and (b) *m/z* 1773. Correlation between the two types of spectra is observed in both cases.

$[Bi_vL_w - yH]^z$ complex ions with Bi:L (L = MPA, TLA, or TMA) values of 1:2 and 2:3 are assigned to *m/z* peaks in both positive and negative ion modes. A greater number of $[Bi_vL_w - yH]^z$ ions are assigned with L = TMA than for L = MPA or TLA, perhaps due to the coordinate versatility provided by two carboxylic acid groups in TMA and the potential for TMA to adopt either a five-membered (Figure 2b) or six-membered (Figure 2c) chelation framework. Bi:TMA ratios of 2:2, 2:3, 3:3, 3:4, 4:4, and 4:5 have been assigned, along with sodiated analogues. Ions in which there are the same number of bismuth atoms and ligands (Bi:L = 2:2, 3:3, and 4:4) have been assigned to peaks at *m/z* 713, 1069, and 1425, respectively. A 2:2 Bi:Cys complex cation has been previously reported.[7–9] Complex ions $[Bi_3L_4 - 8H]^+$ and $[Bi_3L_5 - 10H]^-$ are assigned for L = MPA or TLA and are rationalized in terms of L as a dianionic ligand (Figure 3), such that the (Bi:L) 3:4 and 3:5 stoichiometric options are limited to those observed in each ion mode.

Tandem mass spectra have been obtained to support many of the peak assignments in Tables 1−3. In positive ion mode, neutral losses of intact thiol−carboxylic acid ligands or ligand fragments such as water (18 u), carbon dioxide (44 u), $C_3H_4O_2$ (72 u), or $C_3H_4OS$ (88 u) are typically observed. Figures 4−6 show sample tandem mass spectra and proposed fragmentation pathways for the collision-induced dissociation (CID) of cations $[Bi_2Na(TLA)_3 - 6H]^+$ and $[Bi_3(MPA)_4 - 8H]^+$.

The fragmentation spectrum of *m/z* 753 shown in Figure 4a contains four product ion peaks with relative abundances greater than 5%. Three of these peaks, *m/z* 577, 665, and 681, have been assigned as resulting from neutral losses of two units of $C_3H_4OS$, one unit of $C_3H_4OS$, and one unit of $C_3H_4O_2$, respectively. The product ion at *m/z* 649 is thought to be the result of reduction of bismuth with a concurrent

**Table 5.** Positive and Negative Ion ESI-MS Data from Reaction Mixtures Containing Bi($NO_3$)$_3$ with Cys and MPA in 50:50 Ethanol (EtOH):Water

| *m/z* | relative abundance (%) | positive ion assignment | MS/MS (*m/z*) | positive ion fragment assignment |
|---|---|---|---|---|
| 328.1 | 82–100 | $[Bi(Cys) - 2H]^+$ | | |
| 433.9 | 40–53 | $[Bi(Cys)(MPA) - 2H]^+$ | 327.9 | $[Bi(Cys) - 2H]^+$ |
| 455.9 | 9 | $[BiNa(Cys)(MPA) - 3H]^+$ | | |
| 449.0 | 95–100 | $[Bi(Cys)_2 - 2H]^+$ | | |
| 745.7 | 18–19 | $[Bi_2(Cys)(MPA)_2 - 5H]^+$ | | |
| 760.7 | 36–37 | $[Bi_2(Cys)_2(MPA) - 5H]^+$ | | |
| 767.9 | 7–8 | $[Bi_2Na(Cys)(MPA)_2 - 6H]^+$ | | |
| 782.7 | 17–27 | $[Bi_2Na(Cys)_2(MPA) - 6H]^+$ | | |
| 1072.7 | 5–6 | $[Bi_3(Cys)_2(MPA)_2 - 8H]^+$ | | |
| 1087.6 | 13–14 | $[Bi_3(Cys)_3(MPA) - 8H]^+$ | | |
| 1109.5 | 3–6 | $[Bi_3Na(Cys)_3(MPA) - 9H]^+$ | | |

| *m/z* | relative abundance (%) | negative ion assignment | MS/MS (*m/z*) | negative ion fragment assignment |
|---|---|---|---|---|
| 417.0 | 100 | $[Bi(MPA)_2 - 4H]^-$ | | |
| 432.1 | 62–63 | $[Bi(Cys)(MPA) - 4H]^-$ | 344.9 | $[Bi(MPA)(S) - 2H]^-$ |
| 743.8 | 22–32 | $[Bi_2(Cys)(MPA)_2 - 7H]^-$ | | |
| 758.8 | 33–46 | $[Bi_2(Cys)_2(MPA) - 7H]^-$ | | |
| 1070.7 | 8–16 | $[Bi_3(Cys)_2(MPA)_2 - 10H]^-$ | | |
| 1085.7 | 15–27 | $[Bi_3(Cys)_3(MPA) - 10H]^-$ | | |

**Table 6.** Positive and Negative Ion ESI-MS Data from Reaction Mixtures Containing Bi($NO_3$)$_3$ with Cys and TLA in 50:50 Ethanol (EtOH):Water

| *m/z* | relative abundance (%) | positive ion assignment | MS/MS (*m/z*) | positive ion fragment assignment |
|---|---|---|---|---|
| 433.9 | 77–89 | $[Bi(Cys)(TLA) - 2H]^+$ | 327.9 | $[Bi(Cys) - 2H]^+$ |
| 448.9 | 100 | $[Bi(Cys)_2 - 2H]^+$ | | |
| 455.9 | 10–12 | $[BiNa(Cys)(TLA) - 3H]^+$ | 349.8 | $[BiNa(Cys) - 3H]^+$ |
| 461.9 | 16–18 | $[Bi(Cys)(TLA)(EtOH - H_2O) - 2H]^+$ | | |
| 639.9 | 9–14 | $[Bi_2(Cys)(TLA) - 5H]^+$ | | |
| 745.7 | 67–75 | $[Bi_2(Cys)(TLA)_2 - 5H]^+$ | | |
| 760.7 | 60–70 | $[Bi_2(Cys)_2(TLA) - 5H]^+$ | | |
| 767.7 | 22–35 | $[Bi_2Na(Cys)(TLA)_2 - 6H]^+$ | | |
| 782.7 | 25–30 | $[Bi_2Na(Cys)_2(TLA) - 6H]^+$ | | |
| 1057.6 | 16–20 | $[Bi_3(Cys)(TLA)_3 - 8H]^+$ | | |
| 1072.5 | 21–26 | $[Bi_3(Cys)_2(TLA)_2 - 8H]^+$ | | |
| 1087.5 | 13–26 | $[Bi_3(Cys)_3(TLA) - 8H]^+$ | | |
| 1109.5 | 4–5 | $[Bi_3Na(Cys)_3(TLA) - 9H]^+$ | | |

| *m/z* | relative abundance (%) | negative ion assignment | MS/MS (*m/z*) | negative ion fragment assignment |
|---|---|---|---|---|
| 416.9 | 100 | $[Bi(TLA)_2 - 4H]^-$ | | |
| 431.9 | 15–23 | $[Bi(Cys)(TLA) - 4H]^-$ | 344.8 | $[Bi(TLA)(S) - 2H]^-$ |
| 743.6 | 5–10 | $[Bi_2(Cys)(TLA)_2 - 7H]^-$ | | |

neutral loss of 104 u ($C_3H_4O_2S$, possibly a thiolactate diradical), yielding $[Bi_2Na(TLA)_2 - 4H]^+$. The same formula loss may be observed from *m/z* 441 ($[BiNa(MPA)_2 - 3H]^+$, Table 1) to give *m/z* 337, assigned as $[BiNa(MPA) - H]^+$. Similarly, the loss of a lactate ($C_3H_4O_3^{\bullet}$) radical from a Cu(II) cation, $[Cu(LA)_2 - H]^+$ (LA = lactic acid), has been observed to produce a Cu(I) species, $[Cu(LA)]^+$.[21] In general, reduction–oxidation reactions are not uncommon for coordination complexes examined by way of ESI-MS.[22]

As listed in Tables 2 and 3, peaks corresponding to cations of general formula $[Bi(L) - 2H]^+$ (L = TLA, *m/z* 313, or L = TMA, *m/z* 357) are observed at the same *m/z* ratios in the negative ion mode. However, it may be that these anions result from *m/z* 417 ($[Bi(TLA)_2 - 4H]^-$) and *m/z* 505 ($[Bi(TMA)_2 - 4H]^-$), respectively, implicating fragmentation that is reflected in the parent spectrum.

In Figure 4b, we have assigned the neutral losses of mercaptopropionate ligand fragments, $C_3H_4O_2$ (72 u), $C_3H_4OS$ (88 u), $2C_3H_4O_2$ (144 u), $C_3H_4O_2 + C_3H_4OS$ (160 u), and $2C_3H_4OS$ (176 u), to product ion peaks at *m/z* 971, 955, 899, 883, and 867, respectively, from CID of $[Bi_3(MPA)_4 - 8H]^+$ at *m/z* 1043. Fragmentation pathways consistent with the peak designations in Figure 4a and b are provided in Figures 5 and 6, respectively. A possible mechanism for the fragmentation of $[Bi_2Na(TLA)_3 - 6H]^+$ (*m/z* 753) to yield $[Bi_2Na(TLA)_2(S) - 4H]^+$ (*m/z* 681) resembles a reverse gas-phase Meerwein mechanism for the fragmentation of organic 1,3-oxathiolanylium ions using electron ionization mass spectrometry (EI-MS).[23] As shown in Figure 5, the neutral loss of a mass of 72 u is proposed, which may correspond to a functionalized epoxide. We also suggest that a sequential loss of two neutral $C_3H_4O_2$ units (possibly $\beta$-propiolactone) from $[Bi_3(MPA)_4 - 8H]^+$ (*m/z* 1043) is likely to yield fragment cations, $[Bi_3(MPA)_3(S) - 6H]^+$ and $[Bi_3(MPA)_2(S)_2 - 4H]^+$, at *m/z* 971 and 899, respectively (Figure 6).

---

(21) Kumar, M. R.; Prabhakar, S.; Kumar, M. K.; Reddy, T. J.; Vairamani, M. *Rapid Commun. Mass Spectrom.* **2005**, *19*, 113–120.

(22) Henderson, W.; McIndoe, J. S. The ESI MS Behaviour of Coordination Complexes. In *Mass Spectrometry of Inorganic and Organometallic Compounds*; John Wiley & Sons Ltd: Chichester, 2005; pp 127–173..

(23) Moraes, L. A. B.; Eberlin, M. N. *Chem. Eur. J.* **2000**, *6*, 897–905.

**Table 7.** Positive and Negative Ion ESI-MS Data from Reaction Mixtures Containing $Bi(NO_3)_3$ with MPA and TMA in 50:50 Ethanol (EtOH):Water

| *m*/*z* | relative abundance (%) | positive ion assignment | MS/MS (*m*/*z*) | positive ion fragment assignment |
|---|---|---|---|---|
| 462.9 | 54–64 | $[Bi(MPA)(TMA) - 2H]^+$ | 356.9 | $[Bi(TMA) - 2H]^+$ |
| | | | 402.6 | $[Bi(TMA)(EtOH) - 2H]^+$ |
| | | | 444.9 | $[Bi(MPA)(TMA) - 2H - H_2O]^+$ |
| 484.9 | 5–13 | $[BiNa(MPA)(TMA) - 3H]^+$ | 378.8$^a$ | $[BiNa(TMA) - 3H]^+$ |
| 490.9 | 42–46 | $[Bi(MPA)(TMA)(EtOH - H_2O) - 2H]^+$ | 356.9 | $[Bi(TMA) - 2H]^+$ |
| | | | 384.9 | $[Bi(TMA)(EtOH - H_2O) - 2H]^+$ |
| | | | 430.6 | $[Bi(TMA)(EtOH)(EtOH - H_2O) - 2H]^+$ |
| | | | 472.9 | $[Bi(MPA)(TMA)(EtOH - H_2O) - 2H - H_2O]^+$ |
| 513.0 | 5–10 | $[BiNa(MPA)(TMA)(EtOH - H_2O) - 3H]^+$ | | |
| 519.0 | 6–7 | $[Bi(MPA)(TMA)(EtOH - H_2O)_2 - 2H]^+$ | | |
| 534.9 | 100 | $[Bi(TMA)_2(EtOH - H_2O) - 2H]^+$ | | |
| 668.9 | 3–6 | $[Bi_2(MPA)(TMA) - 5H]^+$ | | |
| 774.7 | 5–11 | $[Bi_2(MPA)_2(TMA) - 5H]^+$ | | |
| 802.9 | 13–15 | $[Bi_2(MPA)_2(TMA)(EtOH - H_2O) - 5H]^+$ | | |
| 818.6 | 15–32 | $[Bi_2(MPA)(TMA)_2 - 5H]^+$ | | |
| 846.6 | 6–11 | $[Bi_2(MPA)(TMA)_2(EtOH - H_2O) - 5H]^+$ | | |
| 1096.6 | 10–13 | $[Bi_2Na(MPA)_2(TMA)_3 - 6H]^+$ | | |
| *m*/*z* | relative abundance (%) | negative ion assignment | MS/MS (*m*/*z*) | negative ion fragment assignment |
| 461.0 | 28–45 | $[Bi(MPA)(TMA) - 4H]^-$ | 310.9$^a$ | $[Bi(TMA)(O) - 2H - CO_2 - H_2O]^-$ |
| | | | 312.9$^a$ | $[Bi(MPA) - 2H]^-$ |
| | | | 344.9$^a$ | $[Bi(MPA)(S) - 2H]^-$ |
| | | | 354.7$^a$ | $[Bi(TMA)(O) - 2H - H_2O]^-$ |
| | | | 442.7$^a$ | $[Bi(MPA)(TMA) - 4H - H_2O]^-$ |
| 483.0 | 2–8 | $[BiNa(MPA)(TMA) - 5H]^-$ | | |
| 488.9 | 3–8 | $[Bi(MPA)(TMA)(EtOH - H_2O) - 4H]^-$ | | |
| 505.0 | 100 | $[Bi(TMA)_2 - 4H]^-$ | | |
| 772.9 | 6–18 | $[Bi_2(MPA)_2(TMA) - 7H]^-$ | | |
| 816.7 | 13–14 | $[Bi_2(MPA)(TMA)_2 - 7H]^-$ | | |
| 838.9 | 4–20 | $[Bi_2Na(MPA)(TMA)_2 - 8H]^-$ | | |
| 844.9 | 10–14 | $[Bi_2(MPA)(TMA)_2(EtOH - H_2O) - 7H]^-$ | | |
| 1194.7 | 2–6 | $[Bi_3Na(MPA)(TMA)_3 - 11H]^-$ | | |

[a] NL > 1 × $10^3$.

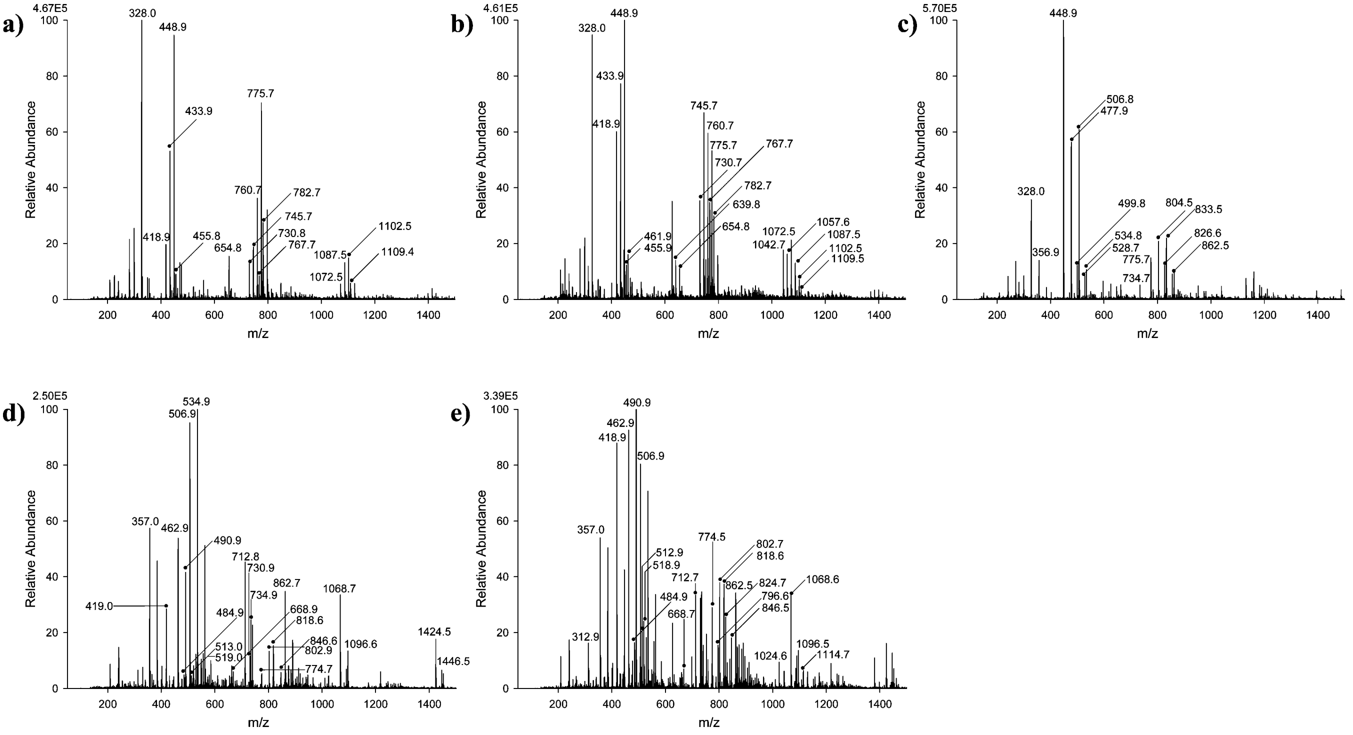


**Figure 11.** Positive ion bismuth-thiolate-carboxylate ESI-MS spectra from reaction mixtures containing $Bi(NO_3)_3$ with (a) Cys and MPA, (b) Cys and TLA, (c) Cys and TMA, (d) MPA and TMA, or (e) TLA and TMA in 50:50 ethanol:water. Denoted peaks are also listed in Tables 5−9.

In general, the experimental isotope patterns for peaks listed in Tables 1−3 have been assigned to chemical formulas that yield matching theoretical isotope patterns. As shown in Figure 7, the experimental isotope distributions of peaks at *m*/*z* 753 and 1043 (expanded from Figure 1b and a, respectively) are consistent with the theoretical distributions

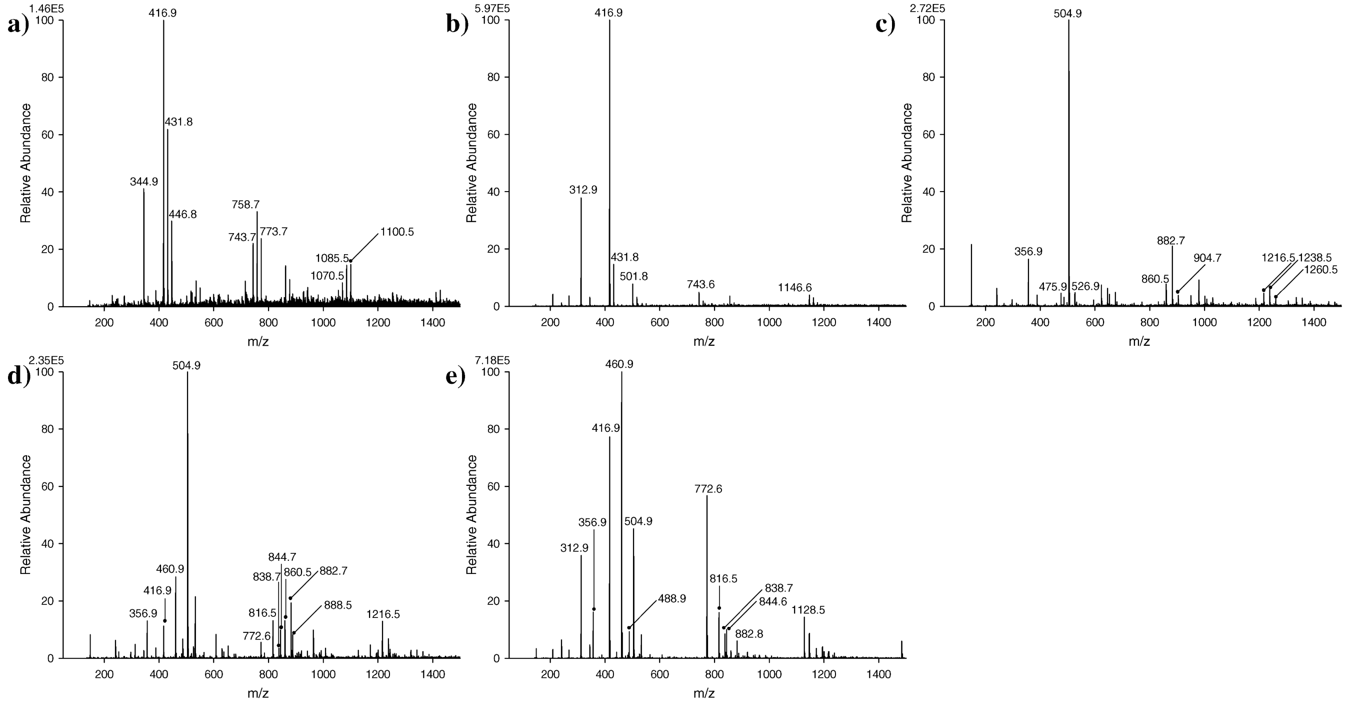


**Figure 12.** Negative ion bismuth-thiolate-carboxylate ESI-MS spectra from reaction mixtures containing Bi(NO$_3$)$_3$ with (a) Cys and MPA, (b) Cys and TLA, (c) Cys and TMA, (d) MPA and TMA, or (e) TLA and TMA in 50:50 ethanol:water. Denoted peaks are also listed in Tables 5−9.

of relative intensities calculated for Bi$_2$NaC$_9$H$_{12}$O$_6$S$_3$ (Figure 7a) and Bi$_3$C$_{12}$H$_{16}$O$_8$S$_4$ (Figure 7b). Given that the abundance of naturally occurring $^{209}$Bi is 100%, *m/z* peaks which represent complex ions containing bismuth do not have a unique bismuth isotope pattern by which efficient identification is possible. However, all of the listed peaks correspond to complex ions featuring both bismuth and sulfur. Therefore, the characteristic isotopic distribution of sulfur — $^{32}$S (95.02%), $^{33}$S (0.75%), $^{34}$S (4.21%), $^{36}$S (0.02%)[24] — can be exploited to support peak assignments. Extended data for empirical and calculated isotope patterns is provided in the Supporting Information.

Multibismuth multiligand complex ions have been discovered with stoichiometric ratios of up to five bismuth centers coordinated by seven thiolate−carboxylate ligands: [Bi$_5$(TLA)$_7$ − 14H]$^+$ (39–47%; see Figure 1b) and [Bi$_5$(MPA)$_7$ − 14H]$^+$ (2–4%; see Figure 1a). Due to the possibility of multibismuth multiligand clusters forming as a result of the ESI process itself, the solution- and gas-phase chemistries of bismuth-thiol-carboxylic acid reaction mixtures cannot be directly correlated. However, we have definitively demonstrated that the formation of gas-phase multibismuth multiligand complexes is possible and can be justifiably compared to known solid state bismuth cluster compounds that have already had an impact on understanding the biologically relevant chemistry of bismuth. For example, [Bi$_2$(TMA)$_2$ − 5H]$^+$ (*m/z* 713 in Figure 1c) along with [Bi$_2$(Cys)$_2$ − 5H]$^+$ and [Bi$_2$(Cit)$_2$ − 5H]$^+$ cations that were previously identified via ESI-MS[8,9] are comparable to the well-known solid state [Bi$_2$(cit)$_2$]$^{2-}$ dimer (cit = tetradepro-

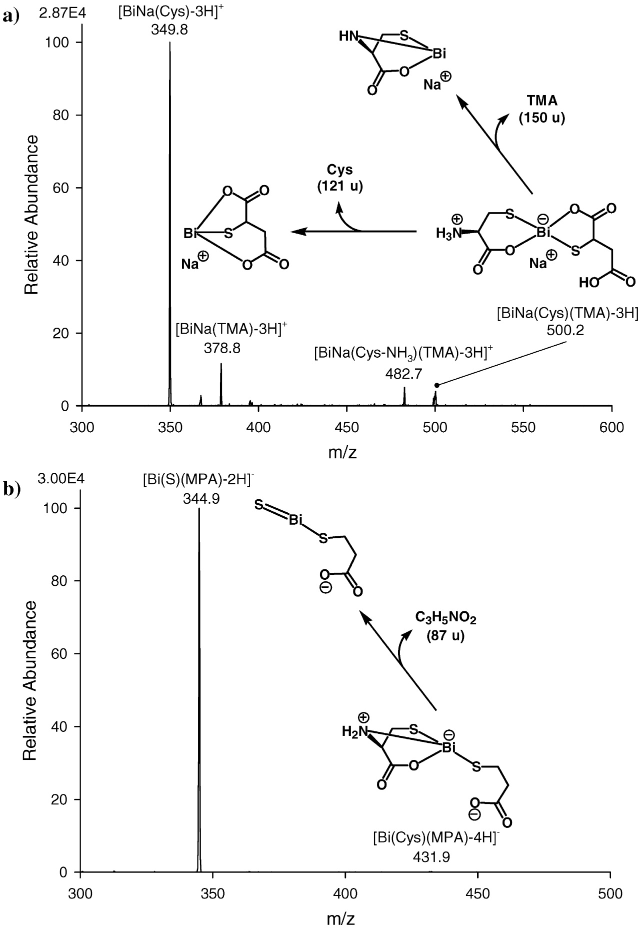


**Figure 13.** Tandem mass spectra for Bi−Cys−TMA and Bi−Cys−MPA ions. (a) [BiNa(Cys)(TMA) − 3H]$^+$ at *m/z* 500 and (b) [Bi(Cys)(MPA) − 4H]$^-$ at *m/z* 432 underwent CID at a collision energy of 20%. Denoted peaks are also listed in Tables 5 and 9. Fragmentation pathways show proposed structures only.

---

(24) Emsley, J. *The Elements*; Oxford University Press, Inc.: New York, 1998.

(25) Kebarle, P. *J. Mass Spectrom.* **2000**, *35*, 804–817.

**Table 8.** Positive and Negative Ion ESI-MS Data from Reaction Mixtures Containing $Bi(NO_3)_3$ with TLA and TMA in 50:50 Ethanol (EtOH):Water

| *m*/*z* | relative abundance (%) | positive ion assignment | MS/MS (*m*/*z*) | positive ion fragment assignment |
|---|---|---|---|---|
| 462.9 | 67–93 | $[Bi(TLA)(TMA) - 2H]^+$ | 356.8 | $[Bi(TMA) - 2H]^+$ |
| | | | 444.7 | $[Bi(TLA)(TMA) - 2H - H_2O]^+$ |
| 484.9 | 9–16 | $[BiNa(TLA)(TMA) - 3H]^+$ | | |
| 490.9 | 100 | $[Bi(TLA)(TMA)(EtOH - H_2O) - 2H]^+$ | 356.9 | $[Bi(TMA) - 2H]^+$ |
| | | | 384.9 | $[Bi(TMA)(EtOH - H_2O) - 2H]^+$ |
| | | | 402.5 | $[Bi(TMA)(EtOH) - 2H]^+$ |
| | | | 430.6 | $[Bi(TMA)(EtOH)(EtOH - H_2O) - 2H]^+$ |
| | | | 472.8 | $[Bi(TLA)(TMA)(EtOH - H_2O) - 2H - H_2O]^+$ |
| 512.9 | 11–20 | $[BiNa(TLA)(TMA)(EtOH - H_2O) - 3H]^+$ | | |
| 518.9 | 24–32 | $[Bi(TLA)(TMA)(EtOH - H_2O)_2 - 2H]^+$ | | |
| 668.7 | 7–8 | $[Bi_2(TLA)(TMA) - 5H]^+$ | | |
| 774.6 | 12–29 | $[Bi_2(TLA)_2(TMA) - 5H]^+$ | | |
| 796.7 | 9–16 | $[Bi_2Na(TLA)_2(TMA) - 6H]^+$ | | |
| 802.7 | 29–38 | $[Bi_2(TLA)_2(TMA)(EtOH - H_2O) - 5H]^+$ | | |
| 818.6 | 13–37 | $[Bi_2(TLA)(TMA)_2 - 5H]^+$ | 463.1[a] | $[Bi(TLA)(TMA) - 2H]^+$ |
| | | | 774.7[a] | $[Bi_2(TLA)_2(TMA) - 5H]^+$ |
| 824.8 | 26–27 | $[Bi_2Na(TLA)_2(TMA)(EtOH - H_2O) - 6H]^+$ | | |
| 840.7 | 7–11 | $[Bi_2Na(TLA)(TMA)_2 - 6H]^+$ | | |
| 846.5 | 11–18 | $[Bi_2(TLA)(TMA)_2(EtOH - H_2O) - 5H]^+$ | | |
| 868.7 | 4–15 | $[Bi_2Na(TLA)(TMA)_2(EtOH - H_2O) - 6H]^+$ | | |
| 1024.7 | 5–9 | $[Bi_3(TLA)(TMA)_2 - 8H]^+$ | | |
| 1096.5 | 9–14 | $[Bi_2Na(TLA)_2(TMA)_3 - 6H]^+$ | | |
| 1114.7 | 6 | $[Bi_3(TLA)_3(TMA)(EtOH - H_2O) - 8H]^+$ | | |
| *m*/*z* | relative abundance (%) | negative ion assignment | MS/MS (*m*/*z*) | negative ion fragment assignment |
| 416.9 | 77–100 | $[Bi(TLA)_2 - 4H]^-$ | | |
| 460.9 | 77–100 | $[Bi(TLA)(TMA) - 4H]^-$ | 311.0 | $[Bi(TMA)(O) - 2H - CO_2 - H_2O]^-$ |
| | | | 312.9 | $[Bi(TLA) - 2H]^-$ |
| | | | 344.9 | $[Bi(TLA)(S) - 2H]^-$ |
| | | | 356.9 | $[Bi(TMA) - 2H]^-$ |
| | | | 442.7 | $[Bi(TLA)(TMA) - 4H - H_2O]^-$ |
| 488.9 | 8–9 | $[Bi(TLA)(TMA)(EtOH - H_2O) - 4H]^-$ | 312.9[a] | $[Bi(TLA) - 2H]^-$ |
| | | | 344.9[a] | $[Bi(TLA)(S) - 2H]^-$ |
| | | | 442.7[a] | $[Bi(TLA)(TMA) - 4H - H_2O]^-$ |
| 772.7 | 24–57 | $[Bi_2(TLA)_2(TMA) - 7H]^-$ | | |
| 816.6 | 3–16 | $[Bi_2(TLA)(TMA)_2 - 7H]^-$ | | |
| 838.8 | 9–16 | $[Bi_2Na(TLA)(TMA)_2 - 8H]^-$ | | |
| 844.8 | 3–10 | $[Bi_2(TLA)(TMA)_2(EtOH - H_2O) - 7H]^-$ | | |
| 1128.7 | 3–14 | $[Bi_3(TLA)_2(TMA)_2 - 10H]^-$ | | |

[a] NL > 1 × $10^3$.

**Table 9.** Positive and Negative Ion ESI-MS Data from Reaction Mixtures Containing $Bi(NO_3)_3$ with Cys and TMA in 50:50 Ethanol (EtOH):Water

| *m*/*z* | relative abundance (%) | positive ion assignment | MS/MS (*m*/*z*) | positive ion fragment assignment |
|---|---|---|---|---|
| 448.9 | 100 | $[Bi(Cys)_2 - 2H]^+$ | | |
| 477.9 | 48–56 | $[Bi(Cys)(TMA) - 2H]^+$ | 327.9 | $[Bi(Cys) - 2H]^+$ |
| | | | 460.7 | $[Bi(Cys - NH_3)(TMA) - 2H]^+$ |
| 499.9 | 12–16 | $[BiNa(Cys)(TMA) - 3H]^+$ | 349.8 | $[BiNa(Cys) - 3H]^+$ |
| | | | 378.8 | $[BiNa(TMA) - 3H]^+$ |
| | | | 482.7 | $[BiNa(Cys - NH_3)(TMA) - 3H]^+$ |
| 505.9 | 13–20 | $[Bi(Cys)(TMA)(EtOH - H_2O) - 2H]^+$ | | |
| 804.7 | 6–21 | $[Bi_2(Cys)_2(TMA) - 5H]^+$ | | |
| 826.6 | 5–12 | $[Bi_2Na(Cys)_2(TMA) - 6H]^+$ | | |
| 833.6 | 6–22 | $[Bi_2(Cys)(TMA)_2 - 5H]^+$ | | |
| *m*/*z* | relative abundance (%) | negative ion assignment | MS/MS (*m*/*z*) | negative ion fragment assignment |
| 475.9 | 4–5 | $[Bi(Cys)(TMA) - 4H]^-$ | 388.9[a] | $[Bi(TMA)(S) - 2H]^-$ |
| 504.9 | 100 | $[Bi(TMA)_2 - 4H]^-$ | | |

[a] NL > 1 × $10^3$.

tonated citric acid, $C_6H_4O_7^{4-}$), illustrated in Figure 8c.[26–33] Other solid state clusters of bismuth and biologically relevant thiol or carboxylic acid ligands are also known, containing salicylic acid,[34] 2-ethoxybenzoic acid,[35] or 2-mercaptopropanol.[35]

---

(26) Herrmann, W. A.; Herdtweck, E.; Pajdla, L. *Inorg. Chem.* **1991**, *30*, 2579–2581.

(27) Asato, E.; Driessen, W. L.; de Graaff, R. A. G.; Hulsbergen, F. B.; Reedijk, J. *Inorg. Chem.* **1991**, *30*, 4210–4218.

(28) Herrmann, W. A.; Herdtweck, E.; Pajdla, L. *Z. Kristallogr.* **1992**, *198*, 257–264.

(29) Asato, E.; Katsura, K.; Mikuriya, M.; Fujii, T.; Reedijk, J. *Chem. Lett.* **1992**, 1967–1970.

(30) Asato, E.; Katsura, K.; Mikuriya, M.; Fujii, T.; Reedijk, J. *Inorg. Chem.* **1993**, *32*, 5322–5329.

(31) Asato, E.; Katsura, K.; Mikuriya, M.; Turpeinen, U.; Mutikainen, I.; Reedijk, J. *Inorg. Chem.* **1995**, *34*, 2447–2454.

**Table 10.** Summary of Bi:$L_a$:$L_b$ Values in $[Bi_v(L_a)_w(L_b)_x - yH]^z$ Complexes ($L_a$, $L_b$ = Cys, MPA, TLA, or TMA; $L_a \neq L_b$) Observed in Positive and Negative Ion ESI Mass Spectra (Na = Sodium, E = Loss of Water with Concomitant Gain of Ethanol)

| positive ion mode | | | | | negative ion mode | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Bi:Cys:MPA | Bi:Cys:TLA | Bi:Cys:TMA | Bi:MPA:TMA | Bi:TLA:TMA | Bi:Cys:MPA | Bi:Cys:TLA | Bi:Cys:TMA | Bi:MPA:TMA | Bi:TLA:TMA |
| 1:1:1 | 1:1:1 | 1:1:1 | 1:1:1 | 1:1:1 | 1:1:1 | 1:1:1 | 1:1:1 | 1:1:1 | 1:1:1 |
| 1:1:1:Na | 1:1:1:Na | 1:1:1:Na | 1:1:1:Na | 1:1:1:Na | | | | 1:1:1:Na | |
| | 1:1:1:E | 1:1:1:E | 1:1:1:E | 1:1:1:E | | | | 1:1:1:E | 1:1:1:E |
| | | | 1:1:1:Na:E | 1:1:1:Na:E | | | | | |
| | | | 1:1:1:2E | 1:1:1:2E | | | | | |
| | 2:1:1 | | 2:1:1 | 2:1:1 | | | | | |
| 2:1:2 | 2:1:2 | 2:1:2 | 2:1:2 | 2:1:2 | 2:1:2 | 2:1:2 | | 2:1:2 | 2:1:2 |
| 2:1:2:Na | 2:1:2:Na | | | 2:1:2:Na | | | | 2:1:2:Na | 2:1:2:Na |
| | | | 2:1:2:E | 2:1:2:E | | | | 2:1:2:E | 2:1:2:E |
| | | | | 2:1:2:Na:E | | | | | |
| 2:2:1 | 2:2:1 | 2:2:1 | 2:2:1 | 2:2:1 | 2:2:1 | | | 2:2:1 | 2:2:1 |
| 2:2:1:Na | 2:2:1:Na | 2:2:1:Na | | 2:2:1:Na | | | | | |
| | | | 2:2:1:E | 2:2:1:E | | | | | |
| | | | | 2:2:1:Na:E | | | | | |
| | | | 2:2:3:Na | 2:2:3:Na | | | | | |
| | | | | 3:1:2 | | | | | |
| | 3:1:3 | | | | | | | 3:1:3:Na | |
| 3:2:2 | 3:2:2 | | | | 3:2:2 | | | | 3:2:2 |
| 3:3:1 | 3:3:1 | | | | 3:3:1 | | | | |
| 3:3:1:Na | 3:3:1:Na | | | | | | | | |
| | | | | 3:3:1:E | | | | | |

Complex ions containing multiple bismuth centers likely involve at least one bridging ligand, as observed in solid state examples including bismuth−ester−thiolates.[19] With this in mind, we envisage a crownlike complex for $[Bi_4Na(TLA)_6 - 12H]^+$ (Figure 8a), assigned to *m/z* 1482 (see Figure 1b). The result of CID of $[Bi_4Na(TLA)_6 - 12H]^+$ is a product ion assigned as $[Bi_2Na(TLA)_3 - 6H]^+$ at *m/z* 753, which is generated via the loss of neutral $[Bi_2(TLA)_3 - 6H]$ from the original $[Bi_4Na(TLA)_6 - 12H]^+$ cation (Figure 8b). The $[Bi_4Na(TLA)_6 - 12H]^+$ cation can hence be considered a sodiated dimer, $Na[Bi_2(TLA)_3 - 6H]_2{}^+$ which dissociates into one neutral monomer (731 u) and one sodiated monomer (*m/z* 753). Similarly, the spectrum resulting from CID of $[Bi_5(TLA)_7 - 14H]^+$, represented by *m/z* 1772 (see Figure 1b), is shown in Figure 9. A neutral loss of $[Bi_2(TLA)_3 - 6H]$ (731 u) is once again observed, in this case yielding the product ion, $[Bi_3(TLA)_4 - 8H]^+$, at *m/z* 1043.

Despite strong supporting MS/MS evidence for the identities of the ions at *m/z* 1482 and 1772, these rounded whole number *m/z* values are unexpectedly one unit lower than the anticipated nominal masses of 1483 u and 1773 u for $[Bi_4Na(TLA)_6 - 12H]^+$ and $[Bi_5(TLA)_7 - 14H]^+$, respectively. More specifically, in Figure 1b, peaks at *m/z* 1482.3 and 1772.3 are considerably different (0.6 u) from actual monoisotopic ion masses of 1482.9 and 1772.9 u for $[Bi_4Na(TLA)_6 - 12H]^+$ and $[Bi_5(TLA)_7 - 14H]^+$, respectively. For comparison, a peak at *m/z* 1042.7 in the same spectrum is different by only 0.2 u from the expected monoisotopic ion mass of 1042.9 u for a 3:4 Bi:TLA cation. A spectrometer function called ZoomScan can be applied to a small mass range (10 u) to produce a high resolution spectrum within that range.[36] Performing a ZoomScan (Figure 10) on mass ranges of interest for $[Bi_4Na(TLA)_6 - 12H]^+$ and $[Bi_5(TLA)_7 - 14H]^+$ yielded more accurate *m/z* values of 1482.6 and 1772.6, differing from 1482.9 u and 1772.9 u by only 0.3 u, thereby providing further evidence for these peak assignments.

**Heteroleptic Bismuth-Thiolate-Carboxylate Complexes.** In comparison to homoleptic bismuth-thiolate complexes,[16,17,19,20,37,38] few examples of heteroleptic bismuth−thiolate complexes have been previously characterized,[12,18,39] although the complexity of biological systems is expected to provide the opportunity for both types of compounds. Tables 5−9 list ESI-MS data obtained in both positive and negative ion modes for reaction mixtures containing equimolar quantities of $Bi(NO_3)_3$ and two thiol−carboxylic acid ligands (Cys, MPA, TLA, or TMA) in 50:50 ethanol:water. Relative abundances are listed as ranges observed over two sample injections from two independent samples.

Peak assignments are presented as $[Bi_v(L_a)_w(L_b)_x - yH]^z$ ($L_a$, $L_b$ = Cys, MPA, TLA, or TMA; $L_a \neq L_b$; $v$, $w$, $x$ = 1–3; $y$ = 2–11; $z = \pm1$). In general, singly charged complex ions containing between one and three Bi(III) cations and various combinations of two different thiolate−carboxylate ligands have been identified. Many ions have been assigned with sodium as a formula constituent. Some ions have been

---

(32) Barrie, P. J.; Djuran, M. I.; Mazid, M. A.; McPartlin, M.; Sadler, P. J.; Scowen, I. J.; Sun, H. *J. Chem. Soc., Dalton Trans.* **1996**, 2417–2422.

(33) Li, W.; Jin, L.; Zhu, N.; Hou, X.; Deng, F.; Sun, H. *J. Am. Chem. Soc.* **2003**, *125*, 12408–12409.

(34) Andrews, P. C.; Deacon, G. B.; Forsyth, C. M.; Junk, P. C.; Kumar, I.; Maguire, M. *Angew. Chem. Int. Ed.* **2006**, *45*, 5638–5642.

(35) Andrews, P. C.; Deacon, G. B.; Jackson, W. R.; Maguire, M.; Scott, N. M.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Dalton Trans.* **2002**, 4634–4638.

(36) *Finnigan LCQDUO Hardware Manual 97033-97033*; Technical Publications, Thermo Electron Corporation: San Jose, CA, 2003; revision B.

(37) Briand, G. G.; Burford, N.; Cameron, T. S. *Chem. Commun.* **1997**, 2365–2366.

(38) Briand, G. G.; Burford, N.; Cameron, T. S. *Chem. Commun.* **2000**, 13–14.

(39) Agocs, L.; Briand, G. G.; Burford, N.; Eelman, M. D.; Aumeerally, N.; MacKay, D.; Robertson, K. N.; Cameron, T. S. *Can. J. Chem.* **2003**, *81*, 632–637.

tentatively assigned to result from ethanol esterification of the carboxylic acid moiety (denoted as EtOH$-$H$_2$O within tabulated chemical formulas). Table 10 provides a summary of the corresponding Bi:L$_a$:L$_b$ ratios that have been assigned to $[\mathrm{Bi}_v(\mathrm{L}_a)_w(\mathrm{L}_b)_x - y\mathrm{H}]^z$ ions. Because MPA and TLA are structural isomers (Chart 1), it is not possible to distinguish between these ligands using mass spectrometry. Therefore, this pair of ligands was the only combination not examined. Representative mass spectra for each three-component reaction mixture are provided in Figures 11 (positive ion mode) and 12 (negative ion mode).

MS/MS results in Table 5−9 are from selected tandem mass spectra where the NL was $\geq 2 \times 10^4$ unless otherwise noted. The applied collision energy was 20% in each case. Fragment ion formulas represent neutral mass losses, including intact ligands, portions of ligands, and water (18 u). Not all fragment ions are listed, and for reasons not yet elucidated, CID of various ions led to MS/MS spectra with intensities too low to be reliable. Instead peaks can be corroborated by an analysis of experimental and theoretical isotope patterns.

A tandem mass spectrum is shown in Figure 13a, featuring the unambiguous dissociation of $[\mathrm{BiNa(Cys)(TMA)} - 3\mathrm{H}]^+$ (*m/z* 500 in Figure 11c), from which both $[\mathrm{BiNa(Cys)} - 3\mathrm{H}]^+$ (*m/z* 350) and $[\mathrm{BiNa(TMA)} - 3\mathrm{H}]^+$ (*m/z* 379) are liberated. Taken in the context of the overall chronicle of data presented in this report, Figure 13a reflects the self-consistent and definitive nature of the abundance of bismuth-thiolate-carboxylate ESI-MS data that has been compiled.

Although $[\mathrm{Bi(MPA)} - 2\mathrm{H}]^+$ was not detected (see Table 1), complex ions containing bismuth with both MPA and Cys (or TMA) have been confirmed by MS/MS in both ion modes (see Tables 5 and 7). Both $[\mathrm{Bi(Cys)(MPA)} - 4\mathrm{H}]^-$ (*m/z* 432 in Figure 12a) and $[\mathrm{Bi(MPA)(TMA)} - 4\mathrm{H}]^-$ (*m/z* 461 in Figure 12d) were observed to dissociate with the release of $[\mathrm{Bi(MPA)(S)} - 2\mathrm{H}]^-$ (*m/z* 345, see Figure 13b). This anion was previously discussed with respect to Figure 1d, from a reaction of Bi(NO$_3$)$_3$ and MPA only. Although the intricacies of such data have not yet been fully rationalized, the idea that an interaction between bismuth and MPA was observed in the presence of Cys or TMA may imply that MPA coordinates to bismuth but does not chelate to the metal. Instead, it is possible that the coordination of MPA to bismuth through one donor atom only (most likely sulfur) occurs with concurrent tridentate chelation by either Cys or TMA.

For the reaction of Bi(NO$_3$)$_3$ with Cys and TMA (Figure 12c), only one peak (*m/z* 476) was assigned to a three-component complex anion, $[\mathrm{Bi(Cys)(TMA)} - 4\mathrm{H}]^-$. Despite the low relative abundance of this peak (4–5%), employing CID allowed for the identification of a reasonable neutral loss of a cysteine segment ($C_3H_5NO_2$, 87 u), yielding the fragment ion $[\mathrm{Bi(TMA)(S)} - 2\mathrm{H}]^-$ at *m/z* 389. Although the MS/MS NL was relatively low ($2.21 \times 10^3$), in this instance the presence of *m/z* 389 was consistent over a relatively long time frame of 2.45 s. This observation reflects the stability of the *m/z* 389 ions, a peak for which was reproduced in a subsequent tandem mass spectrum from the same sample. In comparison, for spectra reported herein with NL $> 2 \times 10^4$, time ranges of less than 0.5 s were not unusual. With this information in mind, the low intensity MS/MS spectrum containing *m/z* 389—and other spectra acquired by applying similar parameters—is considered to provide reliable data.

Tables 5−9 reveal that all combinations of Bi(NO$_3$)$_3$ with two thiol−carboxylic acids give peaks assigned to cations or anions with equimolar stoichiometries of 1:1:1 Bi:L$_a$:L$_b$ (L$_a$, L$_b$ = Cys, MPA, TLA, or TMA; $\mathrm{L}_a \neq \mathrm{L}_b$). All other three-component complexes that have been identified are multibismuth multiligand cluster complex ions.

Along with the three-component Bi:L$_a$:L$_b$ complexes listed in Tables 5−9, in most cases, there were also two-component Bi:L$_a$ and Bi:L$_b$ ions present, as can be seen from a visual comparison of the corresponding two-component and three-component mass spectra given in Figures 1 and 11 or 12, respectively. It is worth noting that not all of the two-component ions assigned in the Figure 1 spectra can be identified in Figures 11 or 12. For instance, *m/z* 1043, corresponding to $[\mathrm{Bi}_3(\mathrm{MPA})_4 - 8\mathrm{H}]^+$ with a significant relative abundance of 34–46% (Figure 1a), is absent in spectra containing Bi(NO$_3$)$_3$, Cys, and MPA (Figure 11a). Peaks corresponding to Bi:Cys ions were not always observed in negative ion mode. Each spectrum in Figures 11 and 12 otherwise includes some peaks that can be correlated with Bi:Cys, Bi:MPA, Bi:TLA, or Bi:TMA ions, thereby making it difficult to generalize about whether or not there is a preference for coordination to bismuth of thiol−carboxylic acid L$_a$ compared to L$_b$. Rather, it appears that regardless of which two thiol−carboxylic acid ligands interact with bismuth, one or more two-component complex ions are observed along with various heteroleptic bismuth-thiolate-carboxylate ions.

Although the specific binding affinities of various combinations of Cys, MPA, TLA, and TMA to bismuth have not been determined, we conclude from solutions containing 1:1:1 molar ratios of Bi:L$_a$:L$_b$ that there is at least a kinetic preference for the formation of three-component ions containing up to a total of seven bismuth and ligand components: (i.e., 2:2:3:1 Bi:MPA:TMA:Na and Bi:TLA:TMA:Na; 3:2:2 Bi:Cys:MPA, Bi:Cys:TLA, and Bi:TLA:TMA; 3:3:1 Bi:Cys:MPA, Bi:Cys:TLA, and Bi:TLA:TMA). This data is consistent with other three-component spectra that were recently described from reaction mixtures containing equimolar amounts of Bi(NO$_3$)$_3$, Cys, and either citric acid or another amino acid ($\neq$ Cys).[9] Additionally, a 3:3:2 Bi:Cys:Asn cation—containing eight metal and amino acid units—has been documented.[9] Overall, more than forty new three-component bismuth-thiolate-carboxylate complex ions have been identified, along with sodiated analogues, contributing appreciably to a growing collection of known bismuth−biomolecule chemical species.

## Conclusion

As part of a program to develop, expand, and understand the chemistry associated with the bioactivity of bismuth, a comprehensive ESI-MS study has been performed on reaction mixtures containing bismuth nitrate and one or two biologically relevant thiol−carboxylic acids, L-cysteine, thiolactic acid, 3-mercaptopropionic acid, and thiomalic acid. A diverse range of more than seventy (two- and three-component) bismuth-thiolate-carboxylate complex ions have been assigned, enhancing the current body of knowledge available on medicinally relevant bismuth chemistry, and highlighting bismuth−biomolecule clusters as an important feature of the chemistry of this element.

**Acknowledgment.** The authors 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, and the Nova Scotia Research and Innovation Trust Fund for financial support; the Dalhousie Mass Spectrometry Laboratories and Xiao Feng for assistance with instrumentation; Dr. Alan A. Doucette for assistance with spectral interpretation; and Susanne D. Riegel and Cheryl D.L. Saunders for other valuable intellectual input.

**Supporting Information Available:** Experimental and theoretical isotope pattern comparisons for peaks listed in Tables 1−3. This material is available free of charge via the Internet at http://pubs.acs.org.

IC701657R