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Design of Bioactive Chalcogenobismuth(III) Heterocycles

by

Lisa Lynn Agocs

Submitted in partial fulfillment of the requirements

for the degree of Doctor of Philosophy

at

Dalhousie University

Halifax, Nova Scotia

July 1997

DALHOUSIE UNIVERSITY

FACULTY OF GRADUATE STUDIES

The undersigned hereby certify that they have read and recommend to the Faculty of Graduate Studies for acceptance a thesis entitled "Design of Bioactive Chalcogenobismuth (III) Heterocycles"

by Lisa Lynn Agocs

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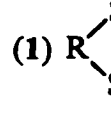
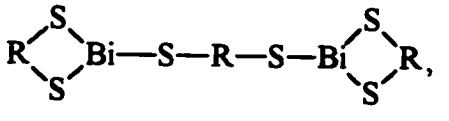
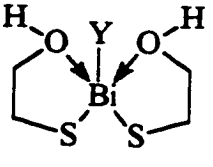
Abstract

Bismuth compounds have demonstrated bioactivity for over two hundred years. The most obvious exploitation is the widespread use of bismuth pharmaceuticals, namely, Pepto-Bismol and De-Nol in the treatment of peptic ulcer disease. However, the mechanism of bioactivity for bismuth compounds remains unknown and enhancement and development of their utility requires a fundamental understanding of the bismuth chemistry involved. An effective approach is the rational synthesis of systematic series of structurally simple bismuth(III) compounds. General, high yield metathesis reactions provide three related and comprehensive series of dithia and oxathiabismuth heterocycles, (**1**), (**2**) and (**3**) (X = Cl, Br, I, SCH CH_2CH_2OH; R = $(CH_2)_{2-4}$, $(CH_2)_2O(CH_2)$, $(CH_2)S(CH_2)_2$, Y = Cl, Br, I, NO_3, CH_3COO). The thermodynamic preference for bismuth to adopt five-membered rings is demonstrated in the structures of dithiabismolane derivatives (X = Cl, Br, I, $S(CH_2)_2OH$) and the bicyclic bis-(2-hydroxylethanethiolato)bismuth compounds. The compounds are characterized by vibrational and mass spectroscopic, and X-ray crystal analysis. The solid state structures of (**3**) show a flexible framework which is attributed to the relative donor capabilities of the anions.

(**1**) 

, (**2**) 

, (**3**) 

List of Abbreviations

APCI	atmospheric pressure chemical ionization
bipy	bipyridyl, $C_{10}H_{10}N_2$
BSS	bismuth subsalicylate
Bu	butyl, C_4H_9
CBS	colloidal bismuth subcitrate
CN	coordination number
cond	conductivity
cyc	cyclohexyl, C_6H_{11}
CyDTPA	*N*-(2-aminoethyl)-*trans*-1,2-diaminocyclohexane-*N,N',N'*-pentaacetic acid, $C_{18}H_{29}N_3O_{10}$
DMF	dimethyl formamide, C_3H_7NO
DMSO	dimethyl sulfoxide, C_2H_6SO
dp	decomposition point
DTPA	diethylenetriaminepentaacetic acid, $C_{14}H_{23}N_3O_{10}$
EA	elemental analysis
EDTA	ethylenediaminetetraacetic acid, $C_{10}H_{16}N_2O_8$
EI	electron impact
Et	ethyl, C_2H_5
FAB	fast atom bombardment
HOMO	highest occupied molecular orbital
Hp	*Helicobacter pylori*

HSAB	hard and soft acid-base
IR	infrared
MAA	mercaptoacetic acid, $HSCH_2CO_2H$
Me	methyl, CH_3
Mes	mesityl, 2,4,6-trimethylphenyl, C_9H_{11}
MIC	minimum inhibitory concentration
mp	melting point
MPA	mercaptopropionic acid, $HS(CH_2)_2CO_2H$
MS	mass spectrometry
NMR	nuclear magnetic resonance
NTA	nitrilotriacetic acid, $C_6H_9NO_6$
Ph	phenyl, C_6H_5
phen	phenanthroline, $C_{12}H_8N_2$
Pr	propyl, C_3H_7
RBC	ranitidine bismuth citrate
RT	room temperature
SC	sampling cone
TMS	tetramethyl silane, $C_4H_{12}Si$
TSA	thiosalicylic acid, $C_6H_4(CO_2H)(SH)$
VSEPR	valence shell electron pair repulsion

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Introduction to The Thesis

The chemistry of bismuth is in its infancy and requires an understanding of the fundamental concepts for enhancement and development of applications such as bioactivity and low-temperature superconducting materials.[1,2,3,4] Inherent insolubility of bismuth compounds, namely bismuth chloride ($BiCl_3$), bismuth oxide (Bi_2O_3) and bismuth citrate ($BiC_6H_5O_7$) is partially responsible for the restricted understanding of the chemistry of bismuth. Since the discovery that the pathogen, *Helicobacter pylori* (*Hp*) which is strongly associated with peptic ulcer disease in a large percentage of the world population, extensive research has determined that bismuth compounds are an essential part of anti-*Hp* regimens, however, undesirable factors such as side effects and high cost give cause for improvements.[5,6,7,8,9,10,11,12,13] Therefore, the establishment of the importance of bismuth to medicine, particularly gastroenterology, has effected a growing interest in systematically developing extensive and diverse series of novel bismuth compounds. Fundamental understanding of bismuth chemistry is necessary before rational developments in synthesis and applications can be made. Our approach is the design and development of novel, systematic, extensive series of simple bismuth compounds which can be quantitatively obtained, comprehensively characterized and then can be altered by rational modifications. Collaborations with microbiologists, pharmacologists and gastroenterologists have been instituted with the common goal to identify relationships between the structural environment of bismuth compounds and their antimicrobial and other bioactivity.[14,15]

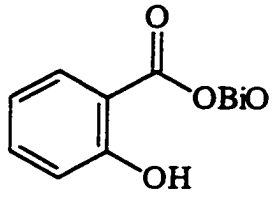
The relevance of bismuth to medicine is rationalized through the development of a chronological history of bismuth pharmaceuticals and their low toxicity in Chapter 1. Understanding the etiology of ulcer disease allows for a foundation for the mechanism of efficacious action of bismuth compounds can be established and an opportunity for the discovery of novel approaches to ulcer-healing may emerge. The chemistry of oxabismuth heterocycles is comprehensively reviewed in Chapter 2 and a preliminary investigation of simple dioxa chelate compounds of bismuth is described. The chemistry of CBS, a complex bismuth citrate salt which is currently used as a pharmaceutical is assessed and an elementary synthetic attempt is presented. A novel series of bicyclic bis-(2-hydroxyethanethiolato)bismuth compounds is introduced and along with other oxathiabismuth heterocycles, some interesting structural trends are observed in Chapter 3. Chapter 4 provides a review of dithiabismuth heterocycles and discusses two novel series of tethered and halodithiabismuth compounds. Chapter 5 connects interpretations and conclusions of Chapters 2, 3 and 4 together through an assessment of the overall state of characterization of chalcogenobismuth compounds. A discussion on the relevance of the stereochemically active lone pair on bismuth(III), trends such as bonding environments and molecular conformations, and a brief summary of the results from bioactivity studies on five examples of dithiabismuth and oxathiabismuth heterocycles is given. A proposal for rational, systematic expansion of the series of chalcogenobismuth heterocycles is presented in Chapter 6.

Chapter 1. Relevance of Bismuth to Medicine

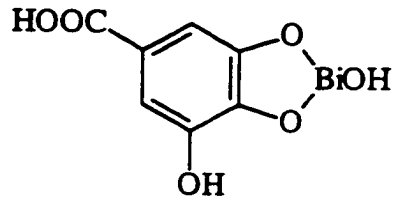
1.1 History of Bismuth in Medicine

The medicinal history of bismuth salts dates back to 1733 when it was documented that a bismuth salt was used topically in salves.[16] In 1786, bismuth subnitrate was the first bismuth compound to be prescribed for internal use for stomach ailments.[11,12] Since then, bismuth salts have been utilized for a variety of medicinal purposes, especially as a principal component of gastrointestinal regimens. For example, the therapeutic potential of bismuth salts in syphilitic patients was recognized by Félix Balzer in 1889 and the first successful treatment occurred 32 years later. In the early 20th century, the pharmaceutical usage of bismuth salts, namely bismuth nitrate ($Bi(NO_3)_3$) and bismuth oxychloride (BiOCl) increased dramatically and its widespread applications included antimicrobial and protective agents; salves for burns; hemorrhoid creams, ointments and suppositories; treatment for hypertension, syphilis and Vincent's angina; controlling stomach acid and colostomy odor; a cure for threadworms; and a contrast media in gastrointestinal radiography.[11,12,17] The costliness of and recognition that bismuth salts were less effective as antacids than other alkaline earth salts, caused a decline in popularity of bismuth salt usage which began in the 1930's. A temporary halt occurred in the mid-1970's because of reports of severe neurological symptoms associated with prolonged intake of bismuth subgallate and subnitrate.[18] A renaissance of interest in bismuth salts occurred after the discovery of the pathogen, *Helicobacter pylori* in 1985.[19] Currently, bismuth subsalicylate (BSS, Pepto-Bismol) (see Figure 1.1) and

bismuth subcitrate (CBS, De-Nol, see Section 2.3) are an integral part of the treatment for gastritis, duodenal ulcer disease associated with *Hp* and distal ulcerative colitis; and are used in treatment and prevention of infectious diarrhea, especially childhood and traveler's diarrhea.[17,20,21,22] Bismuth subgallate (see Figure 1.1), bismuth carbonate ($Bi_2(CO_3)_2$) and bismuth oxyiodide (BiOI) are used in tonsillectomy procedures and ear surgery to assist blood clotting and reduce the operating time; and in hemorrhoid treatments.[23,24,25,26] Antitumour activity has been shown for certain bismuth thiolates.[27] BSS is available in North America whereas both BSS and CBS are used in Europe, Asia and Australia.[20]



Bismuth subsalicylate



Bismuth subgallate

Figure 1.1. Proposed structures and formulae of bismuth compounds used as pharmaceuticals.

The most widely known bismuth-containing pharmaceutical is Pepto-Bismol which has been used for almost a century and the active ingredient is BSS.[16] In 1900, in order to combat a fatal illness called "cholera infantum," a physician designed a liquid preparation which contained BSS, zinc salts and phenyl salicylate. The preparation

known as "Mixture Cholera Infantum" was designed to appeal to children by the addition oil of wintergreen for flavor and a red dye to make it pink. The success of Mixture Cholera Infantum was unprecedented, as it was the only treatment which cured cholera infantum. The name was eventually changed to Pepto-Bismol since its use had expanded to include treatment of acute gastroenteritis, diarrhea, nausea, stomach cramps and vomiting. It has been proposed that the mechanism of anti-diarrheal action of Pepto-Bismol is the inhibition of bacterial invasion in the gastrointestinal tract.[28] Research has confirmed that BSS inhibits growth of a broad spectrum of bacteria *in vitro* including human diarrheal pathogens.[29]

"Colloidal bismuth subcitrate" is an amorphous, complex salt which has been reported as many molecular formulae, (e.g. $Bi_x(OH)_y(C_6H_5O_7)_z$, $K_{5-x}(NH_4)_x[Bi_2(C_6H_4O_7)_2(C_6H_5O_7)](H_2O)_{13}$ and $KBi(C_6H_4O_7)(H_2O)_3$) and is purported to consist of many structural and stoichiometric combinations in the solid state.[30,31,32] The name "colloidal bismuth subcitrate" arises from the idea that the average molecules are large enough that in solution, they are considered colloidal.[30]

The diversity of the therapeutic uses of bismuth salts throughout the history of bismuth in medicine suggest that most of these applications were discovered serendipitously.

1.2 *Helicobacter pylori* and Treatments Involving Bismuth

Helicobacter pylori is a gram-negative spiral bacteria discovered in 1983 by Marshall and Warren in the stomach of patients suffering from chronic gastritis.[19] More specifically, *Hp* is found in gastric mucous on the epithelial surface, among epithelial cells or on mucous glands. *Hp* is strongly associated with peptic ulcer disease and gastritis; it is present in 90 - 100 % of patients diagnosed with duodenal ulcers, 75 % with gastric ulcers and 50 - 60 % with non-ulcer dyspepsia.[12] Studies have also linked *Hp* infection to gastric cancer.[33] The eradication of *Hp* does cure duodenal and gastric ulcers, whereas previously, only a control of ulcers was possible with medications that lower acid production in the stomach. A proposed mechanism of injurious action of *Hp* is the induction of mucosal inflammation and injury in the stomach by the release of a protease enzyme thereby weakening the barrier properties of the mucous lining and allowing stomach acid to come in contact with gastric epithelial cells.[34]

Current research has indicated the importance of bismuth salts as part of a regimen for *Hp* eradication and treatment of peptic ulceration and non-ulcer dyspepsia.[35,36,37,39] Administration of CBS alone improves dyspepsia by eradication of *Hp* and not by any other drug effect in the gastrointestinal tract.[38] The most effective anti-*Hp* regimen is triple therapy which consists of bismuth subsalicylate (2 tablets, four times daily), metronidazole (500 mg three times daily), and either amoxicillin or tetracycline (500 mg three or four times daily, respectively) for one or two weeks and is effective in 73 - 94 % of patients.[39] Ulcer relapse rates are dramatically reduced after *Hp* eradication.[36]

Several mechanisms have been proposed to explain the efficacy of bismuth salts in healing *Hp*-associated duodenal and gastric ulcers.[13,40,50,41,42,43,44] The pharmacological mechanism is presumed to be largely due to mucosal protection since CBS actively binds

mucosal-damaging bile salts and it does not neutralize stomach acid or interfere with acid secretion. A general mechanistic outline is the formation of an insoluble precipitate, bismuth oxychloride at the ulcer site immediately upon contact with the acidic environment of the stomach (pH ~ 1); inhibition of pepsin and prevention of gastric lesions; and promotion of reepithialization by production of a prostaglandin by gastric epithelia. It has been estimated that 90 % of precipitation occurs in the ulcer craters to form a protective coating which prevents further destruction of the gastric epithelial cells. Stimulation of endogenous prostaglandin synthesis implies that there is an additional cellular protective effect. Byproducts such as bismuth sulfide (Bi_2S_3), bismuth subcarbonate ($(BiO)_2CO_3$), bismuth phosphate ($BiPO_4$) and salicylic acid ($C_6H_4CO_2HOH$) are formed along the metabolic pathway.[28] The antibacterial mechanism of BSS and CBS includes reduction of bacterial adherence to the epithelial surface, inhibition of enzymes secreted by *Hp* and disruption of bacterial structural integrity by interference with thiol groups.[28,35,44,45] Oxidative phosphorylation is the only source of energy for an aerobic organism such as *Hp* which causes the bacteria to be susceptible to drugs which interfere with the respiratory chain.[46] Bismuth subgallate and bismuth subsalicylate inhibit the respiratory chain of *Hp in vitro*.

Recently, clinical studies have been carried out with ranitidine bismuth citrate, (RBC) which is an amorphous substance formed by the equimolar reaction of bismuth citrate with the H_2-receptor antagonist ranitidine with intended combinatorial effects of the antibacterial effects of bismuth and the antisecretory effects of ranitidine.[41,47,48] It was found that RBC has acid-suppressive, mucosal protective, *in vitro* and *in vivo* anti-*Hp* properties and in combination with antibiotic clarithromycin, it heals duodenal ulcers and provides symptom relief.[49,52] Both *in vitro* and *in vivo* anti-*Hp* activities of RBC are approximately equivalent to those of CBS, however, ulcer relapse rates remain high at

31%.[49,50] RBC is also effective in protecting gastric and duodenal mucosa from aspirin-induced injury.[51,52]

1.3 Etiology of Ulcer Disease

Peptic ulcer disease encompasses a range of ailments in the upper gastrointestinal tract such as duodenal and gastric ulcers, gastritis, dyspepsia and esophagitis.[12] When discerning the cause of ulcer disease, one considers the imbalance between aggressive and defensive factors.[42] The cause of a duodenal ulcer is an excess of aggressive factors such as acid, pepsin and the presence of *Hp*. However, the extent of weakening of defensive factors is not completely understood. Conversely, the cause of a gastric ulcer is the degradation of gastric defensive factors such as the thickness and quality of the mucous lining, bicarbonate buffering capacity, the integrity of the epithelial cell barrier, microvasculature and the overall epithelial regenerative capacity.[53] The degradation of the mucous lining and epithelial barrier is attributed to *Hp*.[34] Unless *Hp* is eradicated from the gastric mucosa, ulcer relapse rates will remain high, therefore, therapies are primarily aimed at the eradication of *Hp* along with the concurrent reduction of acid secretion.[54] Optimal treatment strategy considerations for *Hp*-associated peptic ulcer disease and gastritis must include high efficacy, simplicity, short treatment duration, minimized side effects and low cost.[55]

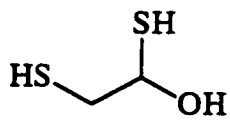
1.4 Toxicity of Bismuth Compounds

The toxic characteristics of arsenic, antimony (like bismuth, also group 15 elements of the periodic table), lead and mercury (periodic neighbours of bismuth) raise obvious concerns when bismuth compounds are being considered as oral medications.[56,57] Bismuth has been used in medicine for a long period of time, however, there is little

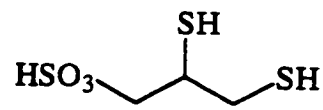
documentation of side effects caused by the metal and its salts. In the 19th century, bismuth salts were contaminated with arsenic which caused great uncertainty in the safety of their ingestion.[11] Adverse effects were not recorded again until the 1970's in France when there were reports of acute encephalopathy with symptoms of cognitive and motor dysfunction, hallucinations and delirium. It was determined that the severe side effects were caused by unsupervised and indiscriminate use of bismuth subnitrate, subcarbonate and/or subgallate. For example, the dosage of bismuth salts ranged from 700 mg to 20 g daily for time periods ranging from 4 weeks to 30 years.[12] A similar situation simultaneously arose in Australia and after an investigation into many sudden reports of bismuth encephalopathy revealed that the cause was prolonged use of high doses of bismuth subgallate.[11,54] Periodic reports of bismuth encephalopathy have occurred since then which are attributed to the abuse of bismuth salts, such as BSS, bismuth nitrate and bismuth subgallate.[26,58,59]

Bismuth poisoning is manifested by toxic effects in humans such as nephropathy (kidneys), encephalopathy (brain), osteoarthropathy (bone), gingivitis (gums), stomatitis (stomach) and colitis (intestines). Mental disorders such as depression, anxiety, irritability, ataxia, impaired motor coordination, tremors, and seizures occur in the preliminary stages of bismuth poisoning.[60,68] Other effects include unpleasant visual and auditory hallucinations and altered taste and smell.[58,59] However, if bismuth intake is extremely prolonged, a permanent tremor and occasionally death may result.[58,59] Severe renal failure was the result of overdoses of CBS and has been deemed a confirmation for bismuth use because of accumulation in the kidney.[61,62] Serious intoxication and death due to salicylate poisoning have occurred following prolonged, large doses of BSS and especially to children when BSS is combined with aspirin.[63,64,65] The most effective treatment of bismuth poisoning is cessation of intake of all bismuth-containing

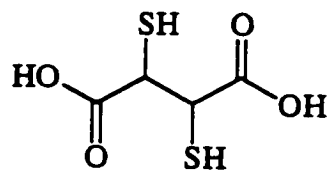
substances.[66] Recovery may be gradual as bismuth is excreted from the body with the symptoms disappearing in reverse order of appearance. The mechanism of bismuth excretion may involve transport of bismuth from the liver to bile and is by formation of bismuth-glutathione complexes.[67] The use of dimercaprol (1,2-dimercaptopropan-3-ol) as a antidote for bismuth poisoning has given both positive and negative results.[68] A systematic *in vivo* study has shown that chelating dithiol ligands such as dimercaprol, 2,3-dimercapto-1-propane-sulfonic acid and *meso*-2,3-dimercaptosuccinic acid (see Figure 1.2) are the best candidates for treating bismuth poisoning.[62] However, it has been suggested that dimercaprol be reserved for patients with life-threatening intoxication or severe bismuth encephalopathy because of its own toxic potential and painful intramuscular administration.



Dimercaprol



2,3-Dimercapto-1-propanesulfonic acid



2,3-Dimercaptosuccinic acid

Figure 1.2. Structures of dithiols used as antidotes for bismuth poisoning.

Currently, the maximum recommended dosage of BSS is 4.2 g daily for 3 - 4 weeks.[16] There have been no reported cases of neurotoxicity or any other toxic effects in North America and very few worldwide for persons taking the recommended dosage for the recommended duration of treatment.[68] Only minor adverse effects have been reported after more than 1.5 million prescriptions for De-Nol have been dispensed.[42] Utilized in recommended dosages, bismuth salts pose no safety hazard. For a complete discussion of the toxicity of bismuth compounds, see reference 57.

Chapter 2. Oxabismuth Heterocycles

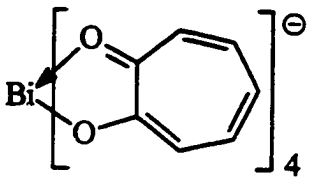
2.1 Introduction

An oxabismuth heterocycle contains at least one ligand which chelates a single bismuth atom to form two Bi-O bonds which are covalent, coordinative or a combination. X-ray crystal structure analysis was the most common characterization technique and reveals similar structural features for the oxabismuth heterocycles. For example, oxabismuth heterocycles are often contain polyfunctional ligands which are multidentate and provide intermolecular coordinations to other bismuth centers to link molecules to form coordination polymers, or encrypt single bismuth atoms restricting intermolecular coordinations. The most common structural feature is the five-membered ring. The compounds which contain a five-membered ring can be categorized into tropolone chelate complexes, multidentate aminoactetatobismuth complexes and other oxabismuth heterocycles. Tropolone chelate complexes comprise the largest section of the oxabismuth heterocycles.

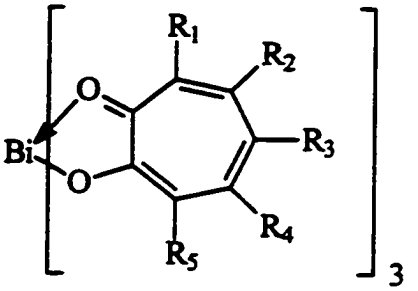
The chemistry of colloidal bismuth subcitrate (CBS) has been extensively studied, primarily for antimicrobial and medicinal purposes. The complexity of the chemistry of CBS renders it unique and therefore, discussions are separated from the other oxabismuth heterocycles.

2.1.1 Tropolonatobismuth Compounds

An extensive series of trisubstituted tropolonatobismuth compounds and their disubstituted chloro, nitrato and phenyl*bis*tropolonatobismuth derivatives has been synthesized and characterized (see Figures 2.1, 2.2 and Tables 2.1, 2.2).[69,70,71,72] The reaction of chloro*bis*tropolonatobismuth (**2.14**) with sodium tropolonate yields (**2.1**) and (**2.2**) (see Figure 2.1 and Table 2.1).[6,70] Compounds (**2.2**) - (**2.14**) were synthesized by the reaction of $Bi(NO_3)_3$ with the appropriate tropolone analogue and were characterized by elemental analysis, ^1H and ^{13}C NMR and IR spectroscopy. ^1H and ^{13}C NMR studies show delocalization of the double bonds in the tropolone ring and partial double bond character for the two Bi-O bonds. Conductivity studies of (**2.2**), (**2.4**), (**2.5**), (**2.8**) - (**2.13**) indicate that they are neutral in polar solutions. X-ray crystal structures were not obtained for any of the *tris*tropolonatobismuth compounds.



(2.1)



(2.2) - (2.13)

Compound	R_1	R_2	R_3	R_4	R_5
(2.2)	H	H	H	H	H
(2.3)	H	Me	H	H	H
(2.4)	H	H	Me	H	H
(2.5)	Me	Me	Me	H	H
(2.6)	H		C_4H_4	H	H
(2.7)	H	H	NO_2	H	H
(2.8)	H	H	CHO	H	H
(2.9)	Br	H	H	H	H
(2.10)	Br	H	H	H	Br
(2.11)	Br	H	Br	H	Br
(2.12)	CH_2OH	H	CH_2OH	H	CH_2OH
(2.13)	$CH_2NC_4H_8O$	H	$CH_2NC_4H_8O$	H	$CH_2NC_4H_8O$

Figure 2.1. Proposed structures for trisubstituted tropolonatobismuth compounds (2.1) - (2.13).

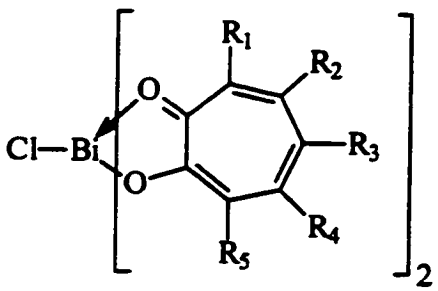
Table 2.1. Analytical data for trisubstituted tropolonatobismuth compounds.

Compound	mp[dp] °C	Yield g, %	EA	NMR	IR	MS	Conductivity	X-ray
[Na](**2.1**)[70]	>400	-	x	-	-	-	-	-
(**2.2**)[6,70,73]	[323-326]	- 1.6, 90	x	^{1}H, ^{13}C	x	x	x	-
(**2.3**)[6]	273	0.8, 41	x	^{1}H, ^{13}C	x	-	-	-
(**2.4**)[6]	[302]	1.8, 95	x	^{1}H, ^{13}C	x	-	x	-
(**2.5**)[6]	275	1.5, 72	x	^{1}H, ^{13}C	x	-	x	-
(**2.6**)[6]	265-266	0.6, 84	x	^{1}H, ^{13}C	x	-	-	-
(**2.7**)[6]	[330]	0.5, 79	x	^{1}H, ^{13}C	x	-	-	-
(**2.8**)[6]	[290]	0.6, 91	x	^{1}H, ^{13}C	x	x	x	-
(**2.9**)[6]	[215]	0.6, 74	x	^{1}H, ^{13}C	x	-	x	-
(**2.10**)[6]	233	0.9, 89	x	^{1}H, ^{13}C	x	-	x	-
(**2.11**)[6]	313	3.7, 96	x	^{1}H, ^{13}C	x	-	x	-
(**2.12**)[6]	[275]	0.5, 63	x	^{1}H, ^{13}C	x	-	x	-
(**2.13**)[6]	183	1.4, 98	x	^{1}H, ^{13}C	x	-	x	-

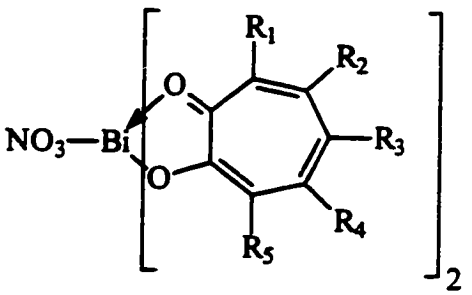
The series of disubstituted tropolonatobismuth compounds are analogous to the trisubstituted tropolonatobismuth series, except that one tropolone ligand is replaced by a Cl, NO_3 or Ph group . The chloro*bis*tropolonatobismuth compounds, (**2.14**) - (**2.19**) were

synthesized by the reaction of $Bi(NO_3)_3$ in concentrated HCl with a three-fold molar excess of the appropriate tropolone derivative (see Figure 2.2 and Table 2.2). The nitrato*bis*tropolonatobismuth compounds (**2.20**) - (**2.23**) were similarly synthesized by the reaction of $Bi(NO_3)_3$ with a two-fold molar excess of the appropriate tropolone derivative (see Figure 2.2 and Table 2.2). Elemental analysis, ^1H, ^{13}C NMR and IR spectroscopy and conductivity measurements were used to characterize the disubstituted compounds (see Table 2.2). The chemical composition of (**2.14**) was confirmed by elemental analysis and a square pyramidal structure was proposed.[69] Conductivity studies show that the phenyl derivative, (**2.24**) is neutral and compounds (**2.19**) - (**2.22**) are 1:1 electrolytes in polar solutions.

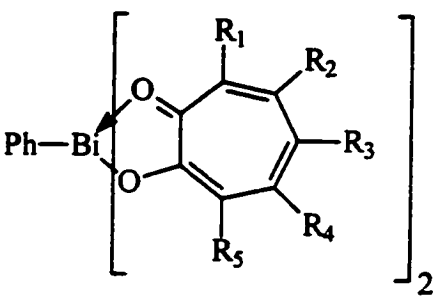
X-ray crystal structures were obtained for compounds (**2.20**) and (**2.22**) which show two bidentate tropolone ligands forming a square planar geometry around the bismuth atom. Compound (**2.20**) has two different molecules in the unit cell which dimerize through intermolecular coordinations from oxygen atoms rendering one bismuth atom six-coordinate and the other, seven-coordinate. Compound (**2.22**) crystallizes as monomers presumably because of the steric bulk of the 4,5-benzotropolone ligand which restricts intermolecular coordinations from oxygen atoms to the bismuth center. The lone pair is described as stereochemically active in both compounds.



(2.14) - (2.19)



(2.20) - (2.23)



(2.24)

Compound	R_1	R_2	R_3	R_4	R_5
(2.14)	H	H	H	H	H
(2.15)	H	Me	H	H	H
(2.16)	H	H	Me	H	H
(2.17)	H	Et	H	H	H
(2.18)	H	Pr^i	H	H	H
(2.19)	Br	H	H	H	H
(2.20)	H	H	H	H	H
(2.21)	Br	H	Me	H	H
(2.22)	Br	H	C_4H_4		H
(2.23)	H	H	C_4H_4		H
(2.24)	H	H	H	H	H

Figure 2.2. Proposed structures of disubstituted tropolonatobismuth compounds (2.14) - (2.24).

Table 2.2. Analytical data for disubstituted tropolonatobismuth compounds.

Compound	mp[dp] °C	Yield g, %	EA	NMR	IR	MS	Conductivity	X-ray
(2.14)[6,69,73]	[311-313]	-	x	^{1}H, ^{13}C	x	x	x	-
		3.9, 98						
		0.4, 90						
(2.15)[6]	285-286	0.3, 60	x	^{1}H, ^{13}C	x	-	-	-
(2.16)[6]	243-245	0.4, 82	x	^{1}H, ^{13}C	x	-	-	-
(2.17)[6]	228-230	0.3, 57	x	^{1}H, ^{13}C	x	-	-	-
(2.18)[6]	285-286	0.2, 36	x	^{1}H, ^{13}C	x	-	-	-
(2.19)[6]	290	0.5, 76	x	^{1}H, ^{13}C	x	-	x	-
(2.20)[6]	271-275	1.4, 55	x	^{1}H, ^{13}C	x	x	x	x
(2.21)[6]	276-279	2.2, 81	x	^{1}H, ^{13}C	x	-	x	-
(2.22)[6]	180	1.1, 57	x	^{1}H, ^{13}C	x	x	x	x
(2.23)[6]	-	-	x	-	-	-	-	-
(2.24)[6]	>330	0.4, 78	x	^{1}H, ^{13}C	x	x	x	-

Compounds **(2.1)** - **(2.3)**, **(2.6)**, **(2.7)**, **(2.14)**, **(2.15)** and **(2.17)** were examined for antimicrobial activity for ten strains of *Helicobacter pylori (Hp)* and MIC (minimum inhibitory concentration) values were reported.[6] Compound **(2.6)** was the only tropolonatobismuth compound which did not display anti-*Hp* activity. These results

indicate that the anti-*Hp* properties of the tropolonatobismuth compounds may be structure and solubility related.

Monosubstituted derivatives are noticeably absent from the extensive series of tropolonatobismuth compounds. Two compounds were characterized by X-ray crystal structure analyses. The solid state structures of the nitrato*bis*tropolonato compounds, (**2.20**) and (**2.22**) are unusually simple and contain few intermolecular donations, unlike the complex polymeric structures commonly found for other oxabismuth heterocycles. However, it is not clear if the crystals were representative of the bulk sample, since the overall yields were reported for the powders and not crystals.

Demonstrated bioactivity and air and water-stability make the tropolonatobismuth compounds appealing candidates for further bioactivity studies and potential pharmaceutical use. However, characterization of the series is not complete and reproducibility is not discussed by the authors. Comprehensive characterization must be completed and reproducibility must be demonstrated. For example, in addition to ^{1}H and ^{13}C NMR spectroscopy, APCI mass spectrometry of each member of a particular series of tropolonatobismuth compounds would be required to show their behaviour in solution.

2.1.2 Multidentate Aminoacetatobismuth Heterocycles

The five-membered ring motif is also prevalent within the series of multidentate aminoacetatobismuth compounds, (**2.25**) - (**2.29**) (see Figure 2.3).[8,74,75] Complex dimeric structures are observed for compounds (**2.25**), (**2.26**) and (**2.27**) which were synthesized by the reaction of $(BiO)_2CO_3$ with the appropriate aqueous aminoacetic acid (see Table

2.3).[8] The nitrilotriacetate ligand is tetradentate in (**2.25**) and the bismuth center is additionally coordinated by two carbonyl oxygen atoms and two water molecules. Compound (**2.26**) contains one monoprotic hexadentate ethylenediaminetetraacetate ligand and two intermolecular donations from neighboring carbonyl oxygens give the bismuth center a bicapped trigonal prismatic coordination geometry. The anion in (**2.27**) can be described as a nine-coordinate ligand-encapsulated bismuth atom with a monocapped square antiprismatic coordination geometry.

Two anionic derivatives of (**2.27**), were synthesized and characterized as (**2.28**) and (**2.29**) by elemental analyses and X-ray crystal structures (see Figure 2.3 and Table 2.3).[74] Compound (**2.28**) is the dianionic conjugate base of (**2.27**) and compound (**2.29**) is a derivative of (**2.27**) by addition of one cyclohexyl unit to the diethyltriamine backbone. Intermolecular donations from carbonyl groups link molecules of (**2.28**) to form a coordination polymer and cause dimerization in (**2.27**). Compound (**2.28**) crystallizes as monomers in which the bismuth atoms are ligand-encapsulated. The bismuth centers in compounds (**2.25**) - (**2.29**) are eight-coordinate (except (**2.27**)) and the lone pair is described as stereochemically inactive. The Bi-$O_{alkoxide}$ bonds are highly irregular and range from 2.253(7) - 2.767(9) Å throughout the aminoacetatobismuth compounds, (**2.25**) - (**2.29**).

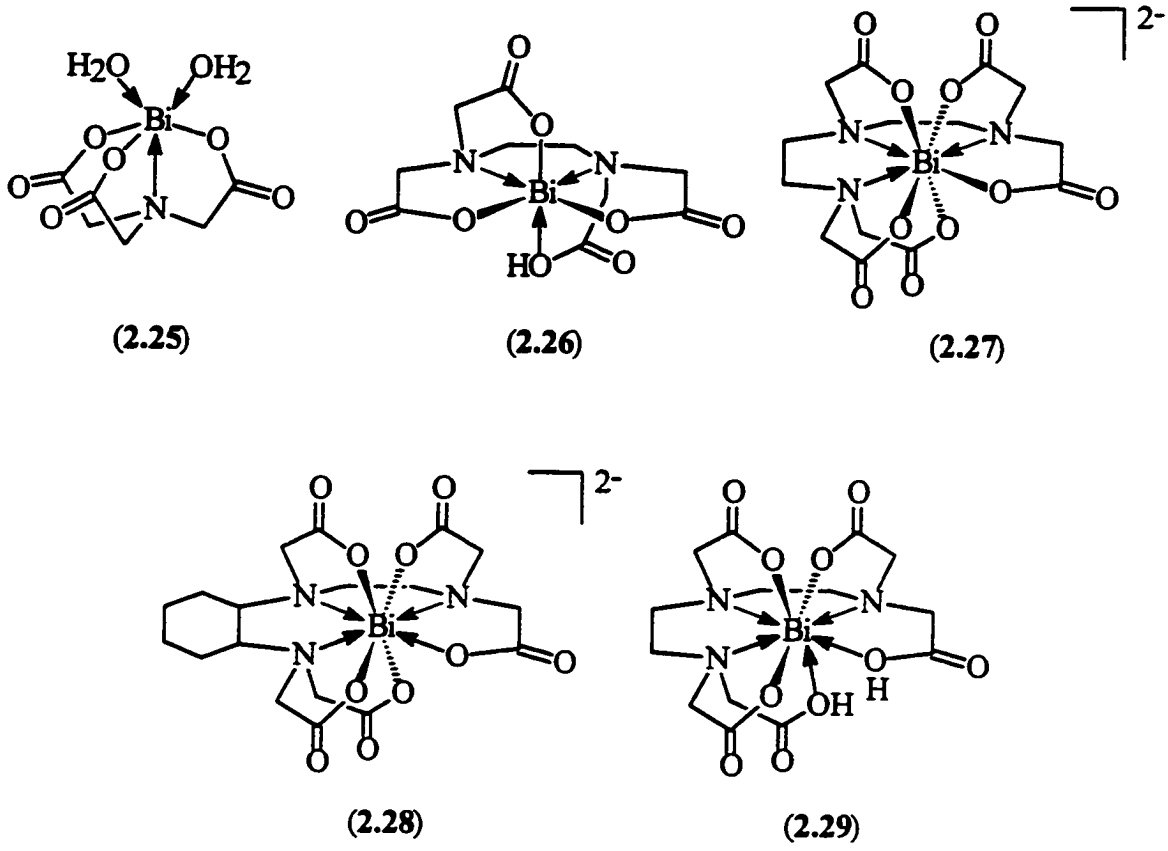


Figure 2.3. Structure of monomeric units of aminoacetatobismuth heterocycles, (**2.25**) - (**2.29**).

Table 2.3. Analytical data for aminoacetatobismuth heterocycles with five-membered rings.

Compound	Reactants	Yield g, %	mp[dp] °C	EA	NMR	MS	X-ray
(2.25)[8]	$(BiO)_2CO_3$, NTA	-	-	x	-	-	x
(2.26)[8]	$(BiO)_2CO_3$, EDTA	-	-	x	-	-	x
(2.27)[8]	$(BiO)_2CO_3$, DTPA, $(C_2H_{12}N_6)CO_3$	-	-	x	-	-	x
(2.28)[74]	$(BiO)_2CO_3$, H_5DTPA	-	-	x	^1H, ^{13}C	x	x
(2.29)[74]	$(BiO)_2CO_3$, CyDTPA, $(C_2H_{12}N_6)CO_3$	0.1, 82	-	x	^1H, ^{13}C	-	x

NTA = nitrilotriacetic acid, $C_6H_9NO_6$

EDTA = ethylenediaminetetraacetic acid, $C_{10}H_{16}N_2O_8$

DTPA = diethylenetriaminepentaacetic acid, $C_{14}H_{23}N_3O_{10}$

CyDTPA = *N*-(2-aminoethyl)-*trans*-1,2-diaminocyclohexane-*N,N'N'*-pentaacetic acid, $C_{18}H_{29}N_3O_{10}$

The synthesis of aminoacetatobismuth heterocycles occurs in water and the completely encapsulated monomeric bismuth complexes precipitate immediately upon formation. This implies that aminoacetate ligands such as DTPA and CyDTPA would be

ideal candidates for water purification studies.[76] The aminoacetatobismuth heterocycles were characterized by elemental analysis, ^{1}H and ^{13}C NMR spectroscopy, however, a yield was reported for one compound only. ^{1}H and ^{13}C NMR spectroscopic studies confirm the presence of the ligands in solutions of (**2.28**) and (**2.29**). X-ray crystal structures reveal multidentate aminoacetate ligands which are bulky and completely surround the bismuth atoms restricting intermolecular coordinations and stereochemical expression of the lone pair on bismuth is expressed.

2.1.3 Other Oxabismuth Five-Membered Heterocycles

Flexible polyethylene glycols are observed to arrange into cyclic crown ether-like structures around Bi^{3+} in the solid state structures of the polyethylene complexes of $Bi(NO_3)_2^+$, (**2.30**) - (**2.33**) (See Figure 2.4).[77] The polyethylene complexes were shown to be dimers bridged by two alkoxide oxygen atoms and each monomer contains five-membered rings formed by neighboring alkoxide chelates. Compound (**2.32**) has a very complex ionic structure in which bismuthate anions form a polymeric chain and the bismuthenium counterions are monomeric. The bismuth atoms are nine-coordinate in (**2.30**) and ten-coordinate in (**2.31**) - (**2.33**). The lone pair is stereochemically active in all of the structures.

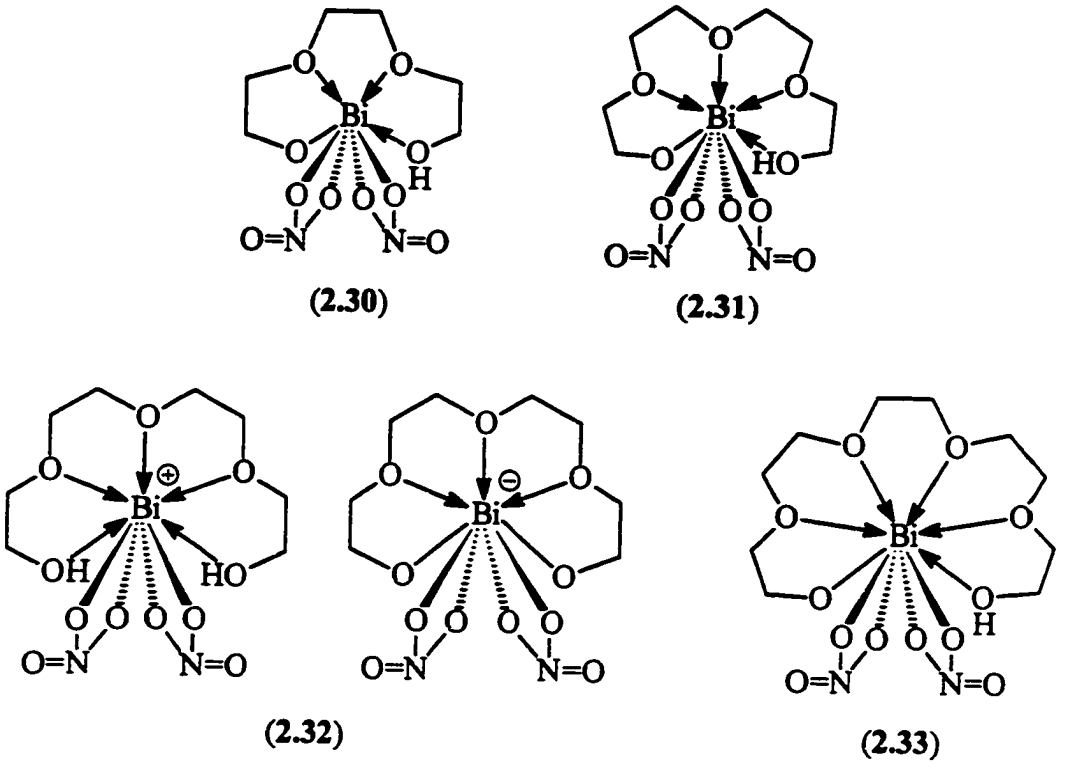


Figure 2.4. Structure of monomeric units of polyethylene glycol complexes, (**2.30**), (**2.31**) and (**2.33**). A monomeric unit is shown for each cation and anion in compound (**2.32**). Intermolecular coordinations are omitted from the structures of (**2.31**) - (**2.33**).

The reaction of $Bi(OH)_3$ and lactic acid yields a complex coordinative polymeric species, (**2.34**).[78] Each monomer in (**2.34**) (see Figure 2.5) contains four lactate ligands which can be described as two bidentate ligands each with one Bi-$O_{alkoxide}$ bond and Bi-$O_{carbonyl}$ coordinative bond; one bidentate ligand with two Bi-O coordinative bonds and one Bi-$O_{alkoxide}$ covalent bond. The bismuth centers are nine-coordinate with no evidence for a stereochemically active lone pair.

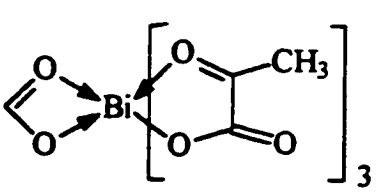
The ethylmaltolate ligand is bidentate to form three five-membered rings in *tris*(ethylmaltolato)bismuth (**2.35**) (see Figure 2.5).[79] The monomeric structure contains a stereochemically active lone pair which occupies an axial position in the pentagonal bipyramidal coordination sphere. An X-ray crystal structure was the only characterization technique reported (see Table 2.4).

The reaction of $Bi(NO_3)_3$ with an aqueous solution of L-(+)-tartaric acid results in the formation of (**2.36**) (see Figure 2.5) as crystals. Elemental analysis confirms the presence of two different tartrate ligands, [L-(+)-tartrate]$^-$ and [L-(+)-tartrate]$^{2-}$.[80] An X-ray crystal structure of (**2.36**) reveals is a coordination polymer in which intermolecular coordinations from oxygen atoms render each bismuth center nine-coordinate with a stereochemically active lone pair.

A nine-coordinate bismuthate anion, (**3.27**) is formed by the reaction of $BiCl_3$ with guanidinium oxalate.[81] The three oxalate ligands chelate the bismuth atom in a monoanionic fashion (see Figure 2.6).

Two unusual examples of an oxabismuth heterocycle are (**2.38**), a bismuth-vanadium heterobimetallic alkoxide and (**2.39**), a bicyclic radical species (see Figure 2.6).

Compound (**2.38**) is the first example of a bismuth-transition metal heterobimetallic alkoxide and the air-sensitive compound crystallizes as dimers connected by strong donations from the vandyl oxygen atoms to the bismuth centers. Each molecule contains a bidentate methoxyethanolate ligand which forms a five-membered ring. The bismuth atoms are seven-coordinate with a capped octahedral coordination geometry.[82] The lone pair on bismuth is stereochemically inactive. ^{1}H and ^{13}C NMR confirm that (**2.38**) maintains its structure in solution. The radical (**2.39**) is proposed based on e.s.r. spectra of the product from the reactions of $BiCl_3$ or $BiPh_3$ with benzo[2,1-*b*;3,4-*b'*]dithiophen-4,5-dione.[83] The proposed structure contains one five-membered ring which formed through the oxygen atoms of the bidentate ligand.



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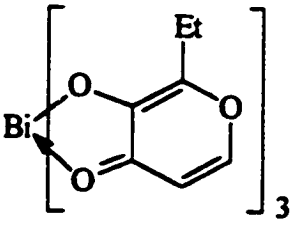

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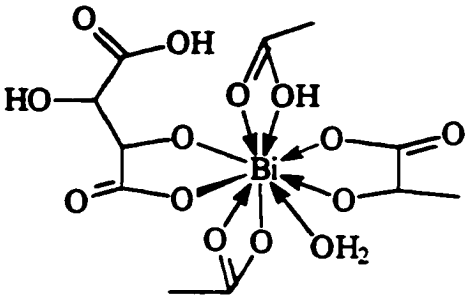

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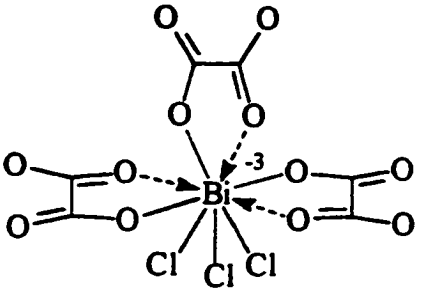
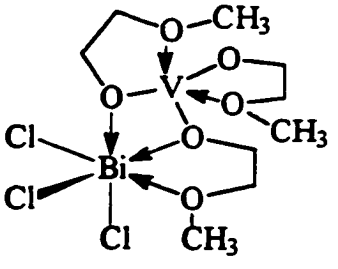


(2.37)

Figure 2.5. Structure of (**2.35**) and one monomeric unit of each compound, (**2.34**), (**2.36**) and (**2.37**).



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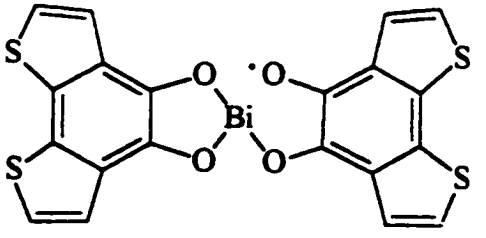


(2.39)

Figure 2.6. Structure of a dimeric unit of (**2.38**) and the proposed structure of (**2.39**).

Table 2.4. Analytical data for other oxabismuth five-membered heterocycles.

Compound	Reactants	Yield g, %	mp[dp] °C	EA	NMR	e.s.r.	MS	X-ray
(2.30)[77]	$Bi(NO_3)_3$, $C_3H_9O_3$	-	>360	x	-	-	-	x
(2.31)[77]	$Bi(NO_3)_3$, $C_4H_{12}O_4$	-	129.5-140	x	-	-	-	x
(2.32)[77]	$Bi(NO_3)_3$, $C_5H_{15}O_5$	-	[189-200]	x	-	-	-	x
(2.33)[77]	$Bi(NO_3)_3$, $C_6H_{18}O_6$	-	113-117.5	x	-	-	-	x
(2.34)[78]	$Bi(OH)_3$, $C_3H_6O_3$	-	-	x	^1H	-	-	x
(2.35)[79]	-	-	-	-	-	-	-	x
(2.36)[80]	$Bi(NO_3)_3$, $C_4H_6O_6$	-	-	x	-	-	-	x
(2.37)[81]	$BiCl_3$, $[CN_3H_6][C_2O_4]$	-	-	-	-	-	-	-
(2.38)[82]	$BiCl_3$, $VO(OPr^i)_3$, $CH_3OC_2H_4OH$	0.3, 63	-	-	^1H, ^{13}C, ^{51}V	-	-	x
(2.39)[83]	$BiCl_3$, $BiPh_3$, $C_8H_4O_2S_2$	-	-	-	-	x	-	-

Characterization of the other five-membered oxabismuth heterocycles was minimal. For example, (**2.35**) was characterized by an X-ray crystal structure and neither a synthetic procedure nor a yield were reported. In fact, a yield was reported for (**2.38**) only. X-ray crystal structures were often the only characterization technique and reveal complex systems for oxabismuth heterocycles with polyfunctional ligands. Coordination polymers were commonly formed by many intermolecular coordinations. When the

ligand was sufficiently bulky, intermolecular coordinations are blocked and the compound is monomeric in the solid state.

2.1.4 Oxabismuth Heterocycles with Unusual Ring Sizes

There are a few examples of oxabismuth heterocycles with ring sizes other than five. This may be reflective of the relative thermodynamic stability of five-membered organometallic and inorganic ring systems.[84] A four-membered dioxabismuth heterocycle is found in the monomeric anion of the salt, $[Me_2NH(CH_2)_2NHMe][Bi(O_2CCF_3)_4Ph]$ (**2.40**) (see Figure 2.7).[85] One four-membered ring is formed by one of the four trifluoroacetate ligands. Strong hydrogen bonding restricts chelation by the remaining three carboxylate groups. The five oxygen atoms bound to bismuth are coplanar and form the base of the pentagonal bipyramid. ^1H NMR spectroscopic studies confirm the presence of the diammonium cation and the phenyl group.

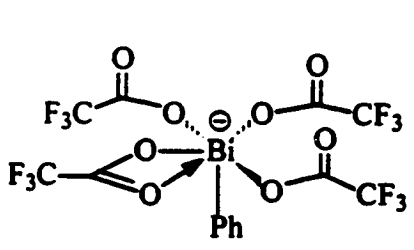
Polymeric bismuth malate monohydrate (**2.41**) is obtained by the reaction of $Bi(NO_3)_3$ with L-(−)-malic acid and characterized by elemental analysis and an X-ray crystal structure (see Figure 2.7 and Table 2.5).[80] The solid state structure of (**2.41**) consists of bismuth atoms connected by chelating malate ligands which form alternating four and six-membered rings. The bismuth centers are nine-coordinate and the lone pair is stereochemically inactive.

Three bidentate tetraphenylimidophosphinate ligands each form a six-membered chelate ring through coordinative Bi-O bonds in (**2.42**) (see Figure 2.7).[86,87] Ligand

chelation is confirmed by ^{31}P NMR spectroscopic studies of the benzene complex, (**2.42**)•C_6H_6. FAB MS demonstrates that (**2.42**) is molecular. An X-ray crystal structure reveals an octahedral coordination sphere for the bismuth atoms and the stereochemically active lone pair occupies a face.

Tridentate disubstituted pyridine-*N*-oxide ligands form coordination complexes of $Bi(NO_3)_3$ to afford (**2.43**) and (**2.44**) in which each ligand is observed to form two six-membered rings (see Figure 2.7).[88] Compounds (**2.43**) and (**2.44**) crystallize as monomers with nine-coordinate bismuth centers. IR and ^1H NMR spectroscopy were reported, however, the authors state that the spectra were not interpreted because they are so complex that "it is inappropriate to assign ... shifts relative to the free ligand."

Reaction of Ph_2BiCl with $HN(SO_2Me)_2$ yields a twelve-membered cyclodimer (**2.45**) (see Figure 2.7).[89] ^1H NMR spectroscopic studies confirm the presence of two methyl groups and a phenyl ring with non-equivalent hydrogen atoms, indicating that the



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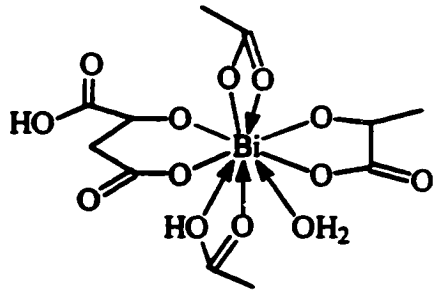

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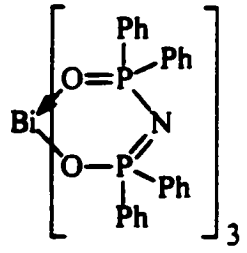

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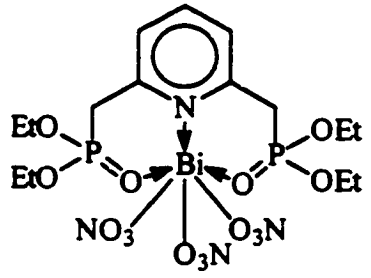

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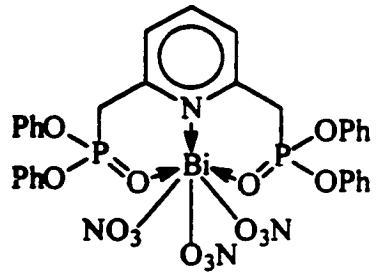

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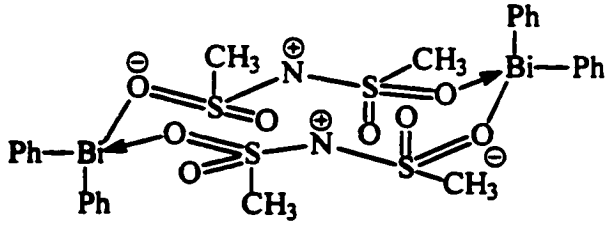


(2.45)

Figure 2.7. Structure of (2.40), (2.42) - (2.45) and the monomeric unit of (2.41). The NO_3^- groups are shown as monocoordinate for clarity but are dicoordinate in the solid state.

ligands are bound to the bismuth atom in solution. The solid state structure confirms dimer formation and shows that each bismuth atom has a trigonal bipyramidal geometry, including the stereochemically active lone pair which occupies an apical position *trans* to the phenyl group.

Table 2.5. Analytical data for oxabismuth heterocycles with ring sizes other than five.

Compound	Reactants	Yield g, %	mp[dp] °C	EA	NMR	IR	MS	X-ray
$[Me_2NH(CH_2)_2NHMe]$	$BiPh_3, C_2HF_3O_2$,	-	-	x	^1H	-	-	x
(2.40)[85]	$(Me_2NCH_2)_2$							
(2.41)[80]	$Bi(NO_3)_3$, $C_4H_6O_5$	-	-	x	-	-	-	x
(2.42)[86]	-	-	[270]	-	-	-	x	x
(2.42)$\bullet C_6H_6$ [87]	$BiCl_3$, $K[(OPPh_2)_2N]$	2.4, 50	271-273	x	^{31}P	-	-	-
(2.43)[88]	$Bi(NO_3)_3$, $((EtO)_2POCH_2)_2C_5H_3NO$	-	-	x	^1H	x	-	x
(2.44)[88]	$Bi(NO_3)_3$, $((EtO)_2POCH_2)_2C_5H_3NO$	-	-	x	^1H	x	-	x
(2.45)[89]	PhBiCl, $HN(SO_2Me)_2$, $AgN(SO_2Me)_2$	-	228-231	x	^1H	-	-	x

X-ray crystal structures were obtained for each of the oxabismuth heterocycles with unusual ring sizes and a variety of analytical techniques were used for compound

characterization, however, a yield was reported for one compound only. In general, the solid state structures of the oxabismuth compounds are comprised of monomers in which the ligands are bulky and resonance stabilized, except for (**2.41**) which is a coordination polymer and (**2.45**) which dimerizes.

2.1.5 Overall Assessment of Oxabismuth Heterocycles

Domination of the five-membered ring motif is expressed throughout the oxabismuth heterocycles. For example, an extensive series of 24 tropolonatobismuth compounds (five-membered rings) has been synthesized. Formation of coordination polymers and complex structures occurs because of multidentate ligands, strong intermolecular coordinations and coordination of water, which also give rise to high coordination numbers and a variety of ring sizes. The $Bi\text{-}O_{dicoordinate}$ bond lengths [2.124(7) - 2.767(9) Å] widely range and relatively elongated $Bi\text{-}O_{tricoordinate}$ bond lengths [2.409(9) - 2.98(1) Å] are observed. ^1H NMR spectroscopy was used to characterize the oxabismuth heterocycles, however, the technique gives little information other than to confirm the presence of the ligand. Often, NMR spectroscopy does not reveal the polymeric nature of the compounds and whether the strong intermolecular coordinations persist in solution.

2.2 Results and Discussion

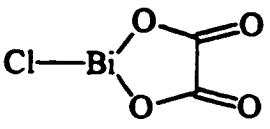
2.2.1 Synthesis of Oxabismuth Heterocycles

On the basis of the antimicrobial success (especially for *Hp*) of the bismuth-containing pharmaceuticals, CBS, BSS and RBC, attempts to discover other biologically active bismuth compounds are described below. As well as for exploitation of the

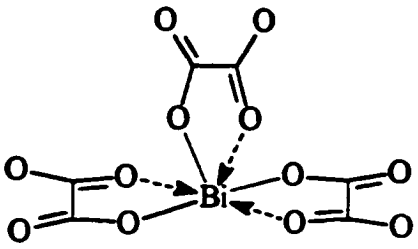
favorability of five-membered ring formation, ligands such as ethylene glycol, catechol and oxalate which are smaller, simpler analogues of those described in Sections 2.1.3 and 2.1.4, were chosen in order to begin a comprehensive, systematic survey of simple dianionic chelate complexes of bismuth targeted as potential bioactive compounds.

Reactions of $BiCl_3$ or $Bi(NO_3)_3$ with ethylene glycol and catechol did not result in the desired metathesis. Further attempts by deprotonation of ethylene glycol using excess molar amounts of NaOH or BuLi before reaction with $BiCl_3$ yielded BiOCl.

Reactions of $BiCl_3$ and $Bi(NO_3)_3$ with $K_2C_2O_4$ afforded amorphous white powders, which were characterized as (**2.46**) and (**2.47**), respectively, based on elemental analysis (see Figure 2.8). Compounds (**2.46**) and (**2.47**) are insoluble in all common organic solvents (e.g. EtOH, THF, DMF, DMSO, pyridine) and characterized by IR and Raman spectroscopy, elemental analysis and a melting point. IR spectroscopy confirmed the presence of the C=O stretch [(**2.46**) ν(C=O) 1660 cm^{-1}, (**2.47**) ν(C=O) 1713 cm^{-1}] of the oxalate ligand. Elemental analysis of (**2.46**) was consistent with the formula, C_2O_4BiCl. The absence of nitrogen was shown by the chemical analysis of (**2.47**) and indicates that the white powdered product may be a complex salt or polymer of bismuth oxalate. The decomposition points of (**2.46**) and (**2.47**) were 225 and 240 °C, respectively (cf. $K_2C_2O_4$, dp > 310 °C).



(2.46)



(2.47)

Figure 2.8. Proposed structures of (**2.46**) and a monomeric unit of (**2.47**).

2.2.2 Conclusions

Formation of Bi-O bonds with ligands containing hydroxyl groups was unsuccessful using conventional synthetic techniques. Product formation was successful with potassium oxalate which is a dianionic chelate, in the synthesis of compounds (**2.46**) and (**2.47**), however, they are insoluble and difficult to characterize. An explanation for the formation of (**2.46**) and (**2.47**) may be immediate precipitation effected by crystal lattice energy stabilization. Electron impact (EI) mass spectrometry can be done on solid materials and may provide confirmation of the presence of the oxalate ligands. APCI MS can be performed on low concentrations of compounds and is a less harsh technique which would increase the likelihood of detecting parent ions or oligomers of a polymeric compound.

Synthetic attempts to obtain molecular oxabismuth heterocycles using the protic ligands, ethylene glycol and catechol afforded starting materials. Although catechol has potential resonance stability, formation of a catecholatobismuth complex is unlikely due to rapid reprotonation by HCl, a byproduct of the reaction of $BiCl_3$ with water. Deprotonation of catechol prior to reaction with BiX_3 (X = Cl, Br, I, CH_3COO, NO_3) as well as rigorous exclusion of water may provide the necessary conditions for formation of a catecholatobismuth complex.

The hard and soft acid-base theory[90] and the poor nucleophilic behavior of alcohols, alkoxides and ethers predict that the probability of the formation of bismuth oxygen covalent bonds is small. It is evident that in order to form Bi-O bonds using conventional synthetic techniques, other driving forces are required for stabilization such as the entropic effects of polyfunctional ligands, ligand resonance stabilization, macrocyclic ligands and insolubility of the resulting products.

2.3 Colloidal Bismuth Subcitrate (CBS)

2.3.1 Introduction

Colloidal bismuth subcitrate, (CBS) is a complex bismuth salt of citric acid and has been the subject of many microbiology and pharmacology studies.[14,43,45,68,91] Synthetic and X-ray structural studies on CBS have been published and varied results have been obtained.[31,32,92,93,94,95,96,97] For instance, there is a discrepancy in the empirical formula of CBS; Asato *et al.*, report the empirical formula of CBS as $K_3(NH_4)_2Bi_6O_3(OH)_5(C_6H_5O_7)_4$[93,94,95,96] and Herrmann *et al.*, report it to be $K_3Bi(C_6H_5O_7)_2$.[92] This discrepancy is also recognized by the Merck index which reports the chemical formula as $K_3(NH_4)_2Bi_6O_3(OH)_5(C_6H_5O_7)_4$ in the 11th edition[98] and has since changed it to "*tripotassium dicitrato bismuthate*" in the most recent 12th edition.[99] In attempts to synthesize and definitively characterize CBS, 16 different compounds have been isolated from either aqueous solutions of CBS or synthesized from aqueous mixtures of CBS starting materials ($K_3C_6H_5O_7$, $C_6H_8O_7$, $BiC_6H_5O_7$, KOH, NH_3) and characterized by elemental analysis and have been proposed to be components of CBS. A sodium analogue of CBS was obtained from reaction mixture of RBC, glutathione (a biologically active tripeptide), D_2O and NaOD.

2.3.2 Synthesis and Characterization of CBS

Elemental analysis and X-ray crystallography have been the primary characterization methods for the components of CBS (see Table 2.6). Reported yields are very low, and the reproducibility of synthetic and crystallization procedures is not discussed.

Table 2.6. Analytical data for components of CBS.

Compound	Reactants	Yield g, %	EA	NMR	DSC	X-ray
$KBi(C_6H_4O_7)\cdot H_2O$(**2.48**)[92]	$[K_3Bi(C_6H_5O_7)_2]$, CBS, $Bi(C_6H_5O_7)$, $K_3C_6H_5O_7$, NH_4OH	-	-	-	-	x
$K_{4.75}(NH_4)_{0.25}[Bi_2(C_6H_4O_7)(C_6H_4O_7)]\cdot 4H_2O$(**2.49**)[31]	$Bi(C_6H_5O_7)$, KOH, $C_6H_8O_7\cdot H_2O$, NH_4OH	3.8, 11	x	^1H,^{13}C	-	x
$K_{2.7}(NH_4)_{0.3}[Bi(C_6H_4O_7]_3\cdot 4H_2O$ (**2.50**)[31]	(**2.49**), H_2O	60-70	x	^1H,^{13}C	-	-
$K_{1.4}(NH_4)_{1.6}[Bi_3(C_6H_4O_7)_3]\cdot 6H_2O$ (**2.51**)[31]	$Bi(C_6H_5O_7)$, KOH $C_6H_8O_7\cdot H_2O$, NH_4OH	1.2, 4	-	^1H,^{13}C	-	-
$K[Bi(C_6H_4O_7)]\cdot H_2O$(**2.52**)[31]	$Bi(C_6H_5O_7)$, KOH $C_6H_8O_7\cdot H_2O$, H_2O	4.8, 27	x	^1H,^{13}C	-	-
$(NH_4)_3[(BiO)_2Bi(C_6H_4O_7)_2]\cdot H_2O$ (**2.53**)[31]	$Bi(C_6H_5O_7)$, NH_4OH, $C_6H_8O_7\cdot H_2O$, CH_3OH	3.2, 11	x	^1H,^{13}C	-	-
$(NH_4)_3[(BiO)_2Bi(C_6H_4O_7)_2]\cdot 3H_2O$ (**2.54**)[31]	$Bi(C_6H_5O_7)$, NH_4OH, $C_6H_8O_7\cdot H_2O$, CH_3OH	4, 14	x	^1H,^{13}C	-	-
$K_{1.4}(NH_4)_{1.6}[(BiO)_2Bi(C_6H_4O_7)_2]\cdot 5H_2O$(**2.55**)[31]	(**2.50**), NH_3, H_2O	-, <10	x	^1H,^{13}C	-	-
$(NH_4)_4[Bi(C_6H_4O_7)(C_6H_5O_7)(H_2O)_2]\cdot H_2O$(**2.56**)[31]	$Bi(C_6H_5O_7)$, NH_4OH, $C_6H_8O_7\cdot H_2O$, CH_3OH	4.2, -	x	^1H,^{13}C	x[94]	x
$[(NH_4)Bi(C_6H_4O_7)]\cdot 2H_2O$(**2.57**)[32]	$C_{24}H_{20}Bi_4O_{28}\cdot 6NH_3$	-	-	-	-	x
$(NH_4)_6[Bi_6O_4(OH)(C_6H_4O_7)(H_2O)_3](C_6H_5O_7)\cdot 2H_2O$(**2.58**)[93]	$Bi(C_6H_5O_7)$, NH_4OH	0.5, *	-	^1H,^{13}C	-	x
$K_{0.8}(NH_4)_{0.2}[Bi(C_6H_4O_7)]\cdot H_2O$(**2.59**)[94]	CBS, H_2O	0.5, *	x	-	-	-
$K_{0.6}(NH_4)_{0.4}[Bi(C_6H_4O_7)]\cdot 2H_2O$ (**2.60**)[94]	CBS, NH_3, H_2O	0.5, *	x	-	-	-
$K_{0.5}(NH_4)_{0.5}[Bi(C_6H_4O_7)]\cdot 3H_2O$ (**2.61**)[94]	$Bi(C_6H_5O_7)$, NH_4OH, KOH	-	x	-	x	x[95]
$K_{0.5}(NH_4)_{0.5}Bi(C_6H_4O_7)\cdot 2H_2O$(**2.62**)[95]	$Bi(C_6H_5O_7)$, NH_4OH, KOH	-	x	-	-	x
$(NH_4)_6Bi_6O_4(C_6H_4O_7)_4\cdot 5H_2O$(**2.63**)[96]	$Bi(C_6H_5O_7)$, NH_4OH	4, 7	x	^1H,^{13}C	-	x
$Na_2[Bi_2(C_6H_4O_7)_2]\cdot 7H_2O$(**2.64**)[97,100]	RBC, glutathione, D_2O, NaOD	-	x	^1H,^{13}C, $^{13}C_{solid}$	-	IR

* % yield was not reported and could not be calculated because the chemical composition of the starting material, CBS is unknown.

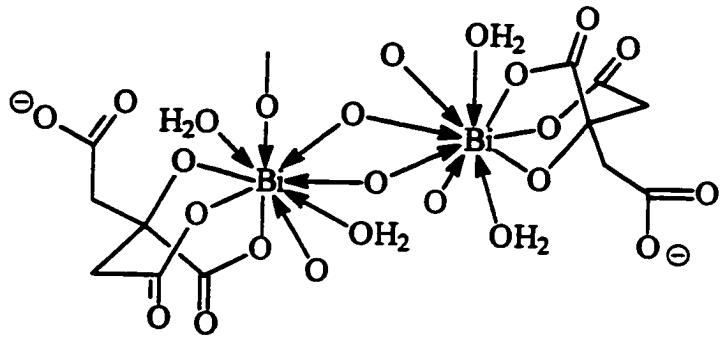
Eight components of CBS were characterized by an X-ray crystal structure analysis. Each compound for which a crystal structure has been determined has a synthetic description and an overview of important structural features is presented below.

Compound (**2.48**) was crystallized from a solution of $K_3Bi(C_6H_5O_7)_2$ kept at 8 °C "for some time."[92] Neutralization with ammonia of an equimolar suspension of $BiC_6H_5O_7$ and $K_3Bi(C_6H_5O_7)_2$ at 60 °C also results in formation of crystals of (**2.48**). The solid state structure of (**2.48**) consists of dimers connected by ionic interactions from citrate ligands and water molecules to the bismuth centers (see Figure 2.9).

White needlelike crystals formed after one week from a cooled solution of $BiC_6H_5O_7$, $C_6H_8O_7$, NH_4OH and KOH.[31] Compound (**2.49**) crystallizes as dimers which are linked by bridging citrate ligands to form tetramers which further aggregate into a polymeric structure (see Figure 2.10). Lattice water is present but not coordinated to bismuth atoms.

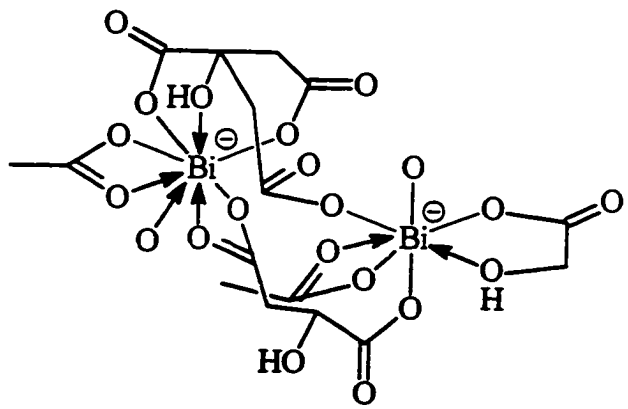
Compound (**2.56**) was synthesized using the same procedure as (**2.49**) with additional KOH.[31] Diffusion of methanol into the reaction mixture precipitated a white powder (uncharacterized) and after subsequent filtration, crystals of (**2.53**) and (**2.56**) formed. The crystals of (**2.53**) were unsuitable for X-ray crystallography. The solid state structure of (**2.56**) is a complex polymer formed by dimers which are linked by bridging citrate ions and water molecules (see Figure 2.11).

The ammonium analogue of (**2.48**) is (**2.57**) which was crystallized from an aqueous solution of $(NH_4)_3Bi(C_6H_5O_7)_2$ at - 4 °C.[32] The citrate ligands are both chelating and bridging to form a linear coordination polymer (See Figure 2.12). A three dimensional anionic network is formed by weak ionic interactions and ammonium ions are embedded in the channels. The potassium analogue, can be synthesized by neutralization with ammonia of an aqueous suspension of equimolar $BiC_6H_5O_7$ and $K_3C_6H_5O_7$ at 60 °C.



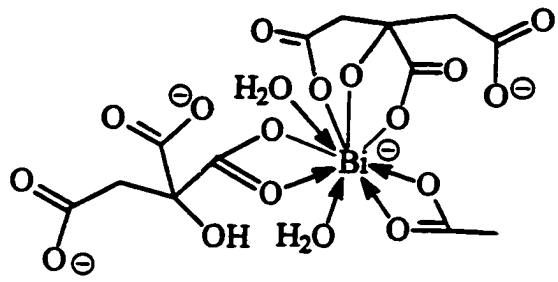
(2.48)

Figure 2.9. Solid state structure of a dimeric unit of compound (**2.48**).



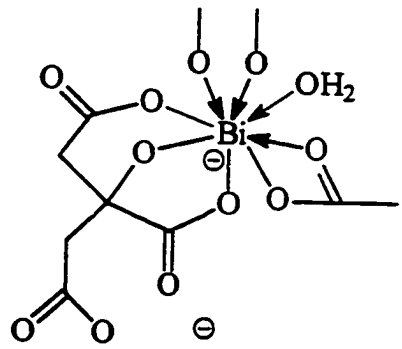
(2.49)

Figure 2.10. Solid state structure of a dimeric unit of compound (**2.49**).



(2.56)

Figure 2.11. Solid state structure of a monomeric unit of compound (2.56).



(2.57)

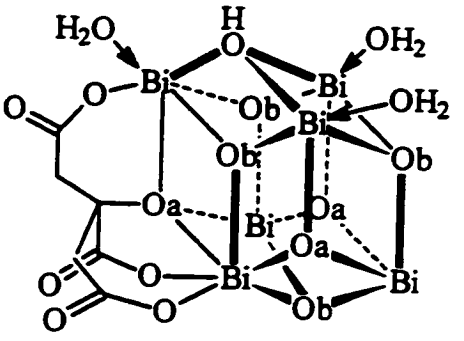
Figure 2.12. Solid state structure of a monomeric unit of compound (2.57).

Crystals of (**2.58**) were obtained from the filtrate of $BiC_6H_5O_7$ and NH_4OH.[93] Elemental analysis of (**2.58**) is consistent with the formula, $(NH_4)_6[Bi_6O_4(OH)_4(C_6H_5O_7)_4]\bullet 2H_2O$. However, an X-ray crystal structure indicates that (**2.58**) contains hexanuclear units with the formula $[Bi_6O_4OH(C_6H_4O_7)_3(H_2O)_3]$ and is a complex polymeric structure consisting of hexanuclear bismuth citrate units linked by polyfunctional citrate ligands, water and ammonium cations (see Figure 2.13).

Two different crystals, (**2.61**) and (**2.62**) were obtained from a solution of $BiC_6H_5O_7$, NH_4OH and KOH upon standing for two months and separated manually.[95] Both (**2.61**) and (**2.62**) (see Figures 2.14 and 2.15) consist of dimers which form tetramers by connections through terminal carboxyl groups which then aggregate to form a complex polymer. The difference between (**2.61**) and (**2.62**) is the contents of asymmetric unit: (**2.61**) contains two bismuth atoms and two citrate ions, one potassium ion, one ammonium ion and six water molecules and (**2.62**) contains one bismuth atom, one citrate anion, one lattice and one coordinated water molecule, one potassium ion and one disordered ammonium ion.

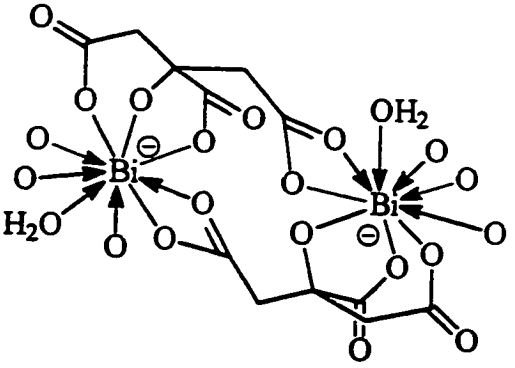
Crystals of (**2.56**) and (**2.63**) can be obtained from a solution of $BiC_6H_5O_7$ and NH_4OH.[96] Compound (**2.63**) is a polymeric compound composed of dodecanuclear citrato-oxo-bismuth clusters, $[Bi_{12}O_8(C_6H_4O_7)]^{12-}$ which can be further subdivided into two hexanuclear units which are connected by three carboxylate bridges (see Figure 2.16). The structure is stabilized by a hydrogen bond network involving $[Bi_{12}O_8(C_6H_4O_7)]^{12-}$ complex anions, ammonium cations and water molecules.

All of the compounds (**2.48**), (**2.49**), (**2.56**) - (**2.58**), (**2.61**) - (**2.63**) are very water soluble due to the ionic bonding in the citrate complexes which contain the potential for extensive hydrogen bonding. In fact, the complex solid state structures are comprised of multinuclear units connected by the polyfunctional citrate ligands and further aggregate to



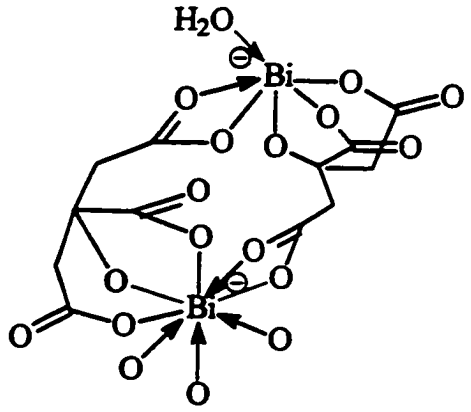
(2.58)

Figure 2.13. Solid state structure of a hexameric unit of compound (**2.58**), Oa = O^- (citrate), Ob = O^{2-}. Only one citrate ligand is drawn for clarity.



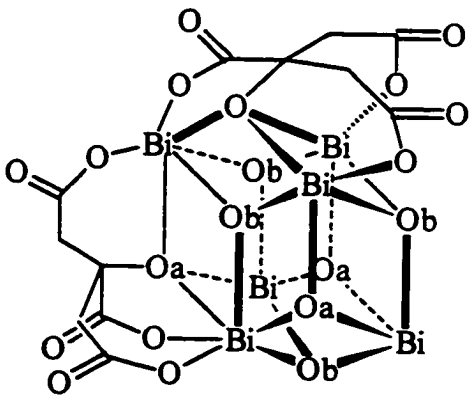
(2.61)

Figure 2.14. Solid state sturcture of a dimeric unit of compound (**2.61**).



(2.62)

Figure 2.15. Solid state structure of a dimeric unit of compound (**2.62**).



(2.63)

Figure 2.16. Solid state structure of a hexameric unit of compound (**2.63**). Oa = O^- (citrate), Ob = O^{2-}. Only two citrate ligands are drawn for clarity.

form polymers or three-dimensional networks by means of ionic interactions and hydrogen bonding. Channels formed within the anionic three-dimensional networks often contain K^+ and NH_4^+ counterions. The bismuth centers have high coordination numbers due to many intermolecular coordinations from bridging citrate, water and oxide ligands which cause a wide range of Bi-O bond lengths [2.07(2) - 3.41(6) Å] and distortion of the coordination geometry.

2.3.3 Interpretation of the Characterization Data Available for CBS

Chemical studies of CBS have been incomplete and in some cases are not scientific, leading to inconclusive results. Synthetic techniques, characterization, reproducibility of results and conclusions are inconsistent and questionable. For example, Asato's paper describes "a bunch of CBS solid ... was dissolved in water (5 ml), a white powder was precipitated."[95] Yields were reported in all cases for uncharacterized powders but not for crystals for which X-ray studies are reported.

Moreover, I have discovered that the two compounds, (**2.57**) and (**2.62**) are isomorphous (see Table 2.7), the only difference being the replacement of one ammonium ion in (**2.62**) by one potassium ion in (**2.57**) in the asymmetric unit. This comparison was not noted by the authors of the paper.[32,95]

Table 2.7. Unit cell parameters of (**2.57**) and (**2.62**).

Compound	Space Group	a (Å)	b (Å)	c (Å)	b (°)	Z
(**2.57**)[32]	C2/c	16.80(2)	12.544(3)	10.401(2)	91.27(2)	8
(**2.62**)[95]	C2/c	16.860(4)	12.395(2)	10.328(3)	91.79(2)	8

X-ray crystallography, elemental analysis and ^{1}H and ^{13}C NMR spectroscopy are methods employed for characterization of the components of CBS. In general, identification of CBS was solely based on single crystal X-ray crystallography in which it is assumed that the best crystal was chosen for diffraction. In one case, two different crystals were separated from one batch, each was different in shape and different elemental analysis are reported.[95] Such observations indicate that the chosen crystals are not representative of the bulk sample.

The chemical structure of CBS in solution is not known; it actually contains a complex mixture of bismuth compounds. All of the components of CBS were synthesized from aqueous solutions of CBS or combinations of the starting materials of CBS ($Bi(C_6H_5O_7)$, $K_3(C_6H_5O_7)$, $C_6H_8O_7$, KOH, NH_3). Two different solid state structures were isolated from powdered CBS using similar techniques of recrystallization. It is evident that reproducibility and complete characterization of CBS have not been achieved. Bismuth compounds targeted for treatment of gastric ailments, especially those associated with *Hp* must be obtained in pure form and be structurally simple (in contrast to CBS), such that they may be completely and comprehensively characterized.

There has been no synthetic, analytical or structural reports on bismuth subsalicylate (BSS) in the literature to date.

2.3.4 Results and Discussion

Development of a synthetic method for obtaining reproducible, high yields and complete characterization of CBS is necessary. A preliminary study of the current synthetic procedure for CBS and characterization techniques and data are included in the

following discussion. A crude model of the behaviour of CBS in the stomach was investigated by determination of the solubility of the CBS precipitates in 1 M HCl.

The compounds $Bi_3C_6H_5O_7$, $K_3C_6H_5O_7$ and KOH were separately dissolved in a minimum amount of distilled water then combined and stirred for 5 minutes at a desired temperature (see Table 7.1 for reaction conditions and stoichiometries). If the reaction mixture did not contain a precipitate, it was reduced to 10 ml by boiling. If the reaction mixture contained a precipitate, a 2:1 v/v solution (20-30 ml) of methanol/acetone was added then the suspension was centrifuged. Precipitates were washed with distilled water and acetone, respectively, then dried by evacuation.

expected stoichiometry: $K_3C_6H_5O_7 + BiC_6H_5O_7 + 2KOH \longrightarrow K_5Bi(OH)_2(C_6H_5O_7)_2$

2.3.5 Characterization of Materials Obtained from Synthetic Attempts of CBS

The precipitates were characterized by melting point and solubility in water, 1 M HCl and 1 M KOH (see Table 7.2). The solubility was determined by dissolving the precipitate (70 mg) in the solvent (5 mL). All precipitates became a colloidal suspension in 1 M KOH.

2.3.6 Conclusions

Changes in reaction conditions cause drastic effects on the product obtained in reactions of KOH with bismuth citrate and potassium citrate. For example, a ten-fold increase in the volume of solvent (water) gave a polymeric white gel. Slight changes in the reaction stoichiometry also had drastic effects on the final product. For example, the addition of one pellet of KOH to the reaction mixture gave a different white precipitate.

The complex behaviour of CBS may be indicative of competing equilibria with many other species in aqueous solutions.

2.4 Ranitidine Bismuth Citrate

The development of ranitidine bismuth citrate (RBC) as a novel therapy for peptic ulcer disease originated from observations that a combination of ranitidine and CBS (complex bismuth citrate salt) were highly efficacious. The ranitidine bismuth citrate salt which is currently on clinical trial as an antiulcer drug, is synthesized by the reaction of ranitidine hydrochloride (*N,N*-dimethyl-5-(3-nitromethylene-7-thia-2,4-diazaoctyl)furan-2-methanamine) and bismuth citrate.[50] Maintenance of the properties of the admixture of ranitidine and CBS has been demonstrated for RBC.

RBC is a highly water-soluble complex bismuth salt which is composed of a ranitidinium cation and a bismuth citrate anion and is mononuclear (cf. CBS and active components of CBS).[48,109] Characterization methods have included elemental analysis, ^{1}H and ^{13}C NMR and IR spectroscopy, polarography and X-ray powder diffraction. In solution, ^{1}H NMR shows that RBC undergoes a structural transition which appears to liberate ranitidine and ranitidine becomes intermolecularly coordinated by hydrogen bonds to polymeric bismuth citrate.[10] IR data confirms the deprotonation of the remaining citrate hydroxyl group upon addition of ranitidine to bismuth citrate.[10] Polarographic measurements of a solution of $Bi(NO_3)_3$, citric acid and ranitidine show the presence of a bismuth citrate ranitidine complex which does not contain an interaction between the NO_2 group of ranitidine and a bismuth atom.[10] It has been proposed that the strongest interaction may involve the formation of a five membered ring by chelation of the bismuth center by NMe_2 and O_{furan} groups of ranitidine (see Figure 2.17).[10] X-ray

powder diffraction confirmed the amorphous nature of RBC by the lack of a characteristic pattern.[48] Raman spectroscopy did not provide any structural information.[48]

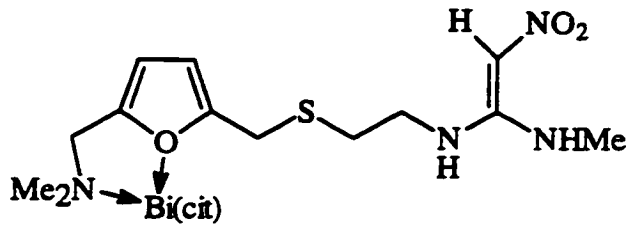


Figure 2.17. Proposed structure of a monomeric unit of RBC.

2.4.1 Interpretation of RBC Literature

RBC is a complex salt which has been comprehensively characterized and the preparation has been shown to be reproducible by a variety of analytical techniques. A single crystal X-ray structure was not obtained because paucity of suitable crystals for X-ray crystal structure analysis. ^{1}H NMR indicates that there are many structural possibilities because of the potential for extensive hydrogen bonding and other intermolecular coordinations. The proposed solid state structure of RBC involves chelation of the bismuth atom by the NMe_2 and O_{furan} groups of ranitidine (see Figure 2.17). Formation of a thermodynamically favored five-membered ring can also occur by chelation of the bismuth atom by O_{furan} and $S_{dicoordinate}$ groups of the ranitidine (see Figure 2.18). This alternative interaction is more likely since $S_{dicoordinate}$ is a better nucleophile and a soft donor in comparison to $O_{dicoordinate}$ which is a poor nucleophile and a hard donor.

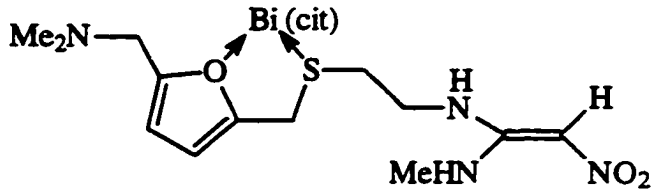


Figure 2.18. Alternate proposed structure of a monomeric unit of RBC.

2.5 Conclusions

Formation of coordination polymers and complex structures due to multidentate ligands, strong intermolecular coordinations and coordination of water give rise to high coordination numbers and a variety of ring sizes in oxabismuth heterocycles. A common observation is the presence of five-membered rings formed by chelating ligands which serve to bridge two or more bismuth centers to form coordination polymers, hexamers or dimers.

CBS and RBC are complex salts which have many structural possibilities because they contain the polyfunctional citrate ligand which has the potential for extensive hydrogen bonding and other intermolecular coordinations. The complex behaviour of CBS indicates that it exists in equilibrium with many other species in aqueous solutions. Comprehensive characterization of CBS would require an understanding of the complex equilibrium and characterization of all the species involved in the equilibrium.

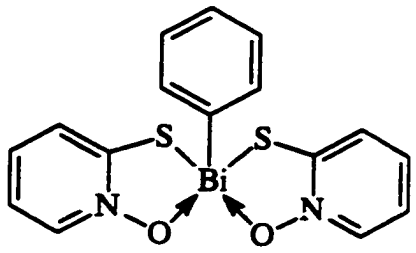
Chemical studies of oxabismuth compounds, especially CBS have been incomplete and in some cases are not scientific, leading to inconclusive results.

Chapter 3. Oxathiabismuth Heterocycles

3.1 Introduction

The chemistry of oxathiabismuth heterocycles is limited to the studies of five and six-membered heterocycles. The number of examples of oxathiabismuth heterocycles is less than for oxabismuth (see Section 2.1) and dithiabismuth (see Section 4.1) heterocycles, however, characterization is significantly more comprehensive. The oxathiabismuth heterocycles are air and water-stable and have been synthesized by conventional techniques.

The reaction of diphenylbismuth acetate with sodium 1-oxopyridine-2-thiolate yields the crystals of (**3.1**) (see Figure 3.1).[101] The X-ray crystal structure reveals a square planar bicyclic structure in which the two oxopyridinethiolate ligands are *cis* and the phenyl ring is perpendicular to the plane. The coordination geometry of the bismuth atom is described as distorted octahedral in which the stereochemically active lone pair occupies the axial position *trans* to the phenyl group.



(3.1)

Figure 3.1. Structure of compound (**3.1**).

Eleven oxathiabismuth heterocycles (**3.2**) - (**3.12**) (see Figure 3.2) are obtained in high yields by the reaction of Ph_3Bi or Me_3Bi with the appropriate mercaptocarboxylic acid (see Table 3.1).[102,103,104] The heterocyclic structures of (**3.2**) - (**3.11**) are confirmed by ^1H NMR and IR spectroscopy and elemental analysis. The anomalous dissolution of compounds (**3.2**) - (**3.11**) in pyridine led to the proposal that they are polymeric in the solid state. Complete metathesis of $Bi(NO_3)$ by thiosalicylate occurs to form an octanuclear bismuth thiosalicylate complex, (**3.12**) which was characterized by an X-ray crystal structure only. Four sets of two crystallographically different bismuth atoms comprise the Bi_8O_{12} cluster core. Each salicylate ligand is bimodally chelating and acts to bridge two bismuth atoms.

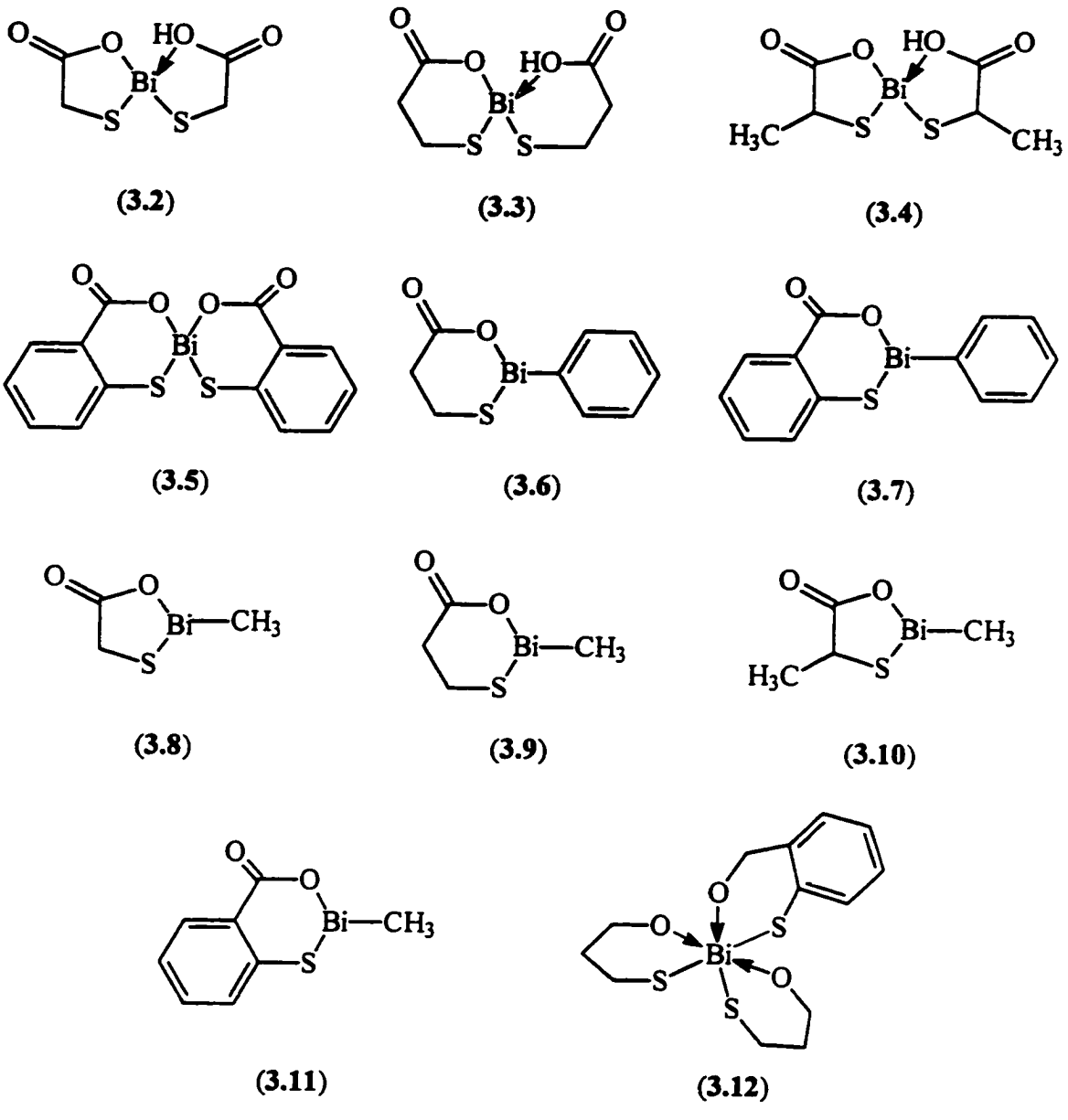
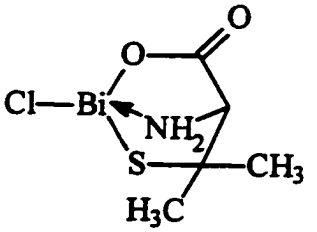


Figure 3.2. Proposed structures of the series of five and six-membered carboxylate-thiolatobismuth heterocycles, (**3.2**) - (**3.11**) and the structure of one of the two crystallographically unique molecules comprising the octanuclear bismuth salicylate complex, (**3.12**). The seven-coordinate molecule is similar and has an additional coordination from a DMF molecule.

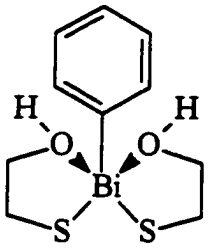
The six-membered oxathiabismuth heterocycle, (**3.13**) is obtained by the reaction of bismuth oxychloride with an aqueous solution of D-(-)-penacillamine.[105] An X-ray crystal structure reveals a six-membered oxathiabismuth ring with cross-ring intramolecular donation from the amine to the bismuth center (see Figure 3.3). ^{1}H and ^{13}C NMR spectroscopy confirm ligand chelation, however, the amine H's were absent from the ^{1}H NMR spectrum. Additional intermolecular coordinations from carbonyl oxygen atoms impose a coordination number of seven on the bismuth centers, including the stereochemically active lone pair and serve to link the molecules to form a polymer in the solid state.

A series of asymmetric thiolate-alcohol chelate complexes of Bi^{3+} were synthesized for assessment as potential chemotherapeutic agents and characterized as (**3.14**) - (**3.18**) (see Figure 3.4 and Table 3.1).[106,107,108] Reaction of diethoxyphenylbismuth with mercaptoethanol yields (**3.14**) as crystals which were characterized by ^{1}H NMR and mass spectra. An equimolar mixture of aqueous bismuth perchlorate and mercaptoethanol affords crystals of the ionic complex, (**3.15**). The reaction of mercaptoethanol with $Bi(NO_3)_3$ forms (**3.16**), and subsequent addition of ammonia immediately precipitates the deprotonated analogue, (**3.17**). The trisubstituted derivative, (**3.18**) can be synthesized by the reaction of mercaptoethanol with (**3.17**) or $Bi(OEt)_3$. Compounds (**3.16**) - (**3.18**) were found to have moderately strong activities against *Helicobacter pylori*. The X-ray crystal structures of compounds (**3.15**), (**3.16**) and (**3.17**) show chelation of the bismuth centers by two hydroxyethanethiolate ligands in a

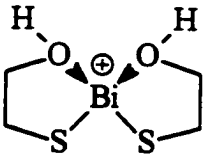


(3.13)

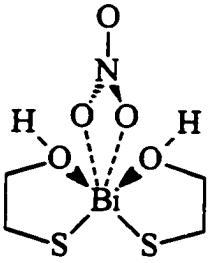
Figure 3.3. Solid state structure of (3.13).



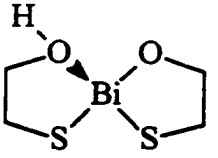
(3.14)



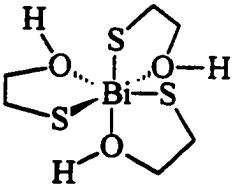
(3.15)



(3.16)



(3.17)



(3.18)

Figure 3.4. Solid state structures of (3.15), (3.16) and (3.17) and the proposed structures of (3.14) and (3.18).

cis fashion. Compounds (**3.15**) and (**3.16**) are ionic and have planar structural conformations, whereas the neutral compound, (**3.17**) has a spirocyclic structure. Intermolecular donations from sulfur atoms of the hydroxyethanethiolate ligands in (**3.15**) and (**3.16**), and from hydroxyl groups in (**3.17**) to the bismuth centers are responsible for coordination polymer formation. ^{1}H NMR spectroscopic studies reveal that (**3.16**) - (**3.18**) dissociate in solution and behave as monomeric species.

Table 3.1. Analytical data for oxathiabismuth heterocycles.

Compound	Reactants	Yield g, %	mp [dp] (°C)	EA	IR	NMR	X-ray
(3.1)[101]	$Ph_2BiCO_2CH_3$, C_5H_4NOSH	-	[215-218]	x	-	-	x
(3.2)[102]	$Bi(OH)_3$, $BiPh_3$, MAA	-, 80	118	x	x	^1H	-
(3.3)[102]	$Bi(OH)_3$, $BiPh_3$, MPA	-, 65	155	x	x	^1H	-
(3.4)[102]	$Bi(OH)_3$, $BiPh_3$, 2MPA	-, 80	126	x	x	^1H	-
(3.5)[102]	$Bi(OH)_3$, $BiPh_3$, TSA	-, 77	274	x	x	^1H	-
(3.6)[102]	$BiPh_3$, MPA	-, 62	209	x	x	-	-
(3.7)[102,103]	$BiPh_3$, TSA	-, 62	302	x	x	-	-
(3.8)[102]	$BiMe_3$, MAA	-, 72	202	x	x	-	-
(3.9)[102]	$BiMe_3$, MPA	-, 43	172	x	x	-	-
(3.10)[102]	$BiMe_3$, 2MPA	-, 70	209	x	x	-	-
(3.11)[102]	$BiMe_3$, TSA	-, 77	290	x	x	-	-
(3.12)[104]	$Bi(NO_3)_3$, TSA, NH_4OH, DMF	0.3, 4	-	-	-	-	x
(3.13)[105]	BiOCl, $HSCMe_2CH(NH_2)CO_2H$	2.5, 96	-	x	-	^1H, ^{13}C	x
(3.14)[108]	$PhBi(OEt)_2$, $HS(CH_2)_2OH$	3.2, 75	57	x	-	^1H	-
(3.15)[106]	Bi_2O_3, $HClO_4$, $HS(CH_2)_2OH$	-	-	x	x	-	x
(3.16)[106]	$Bi(NO_3)_3$, $HS(CH_2)_2OH$	0.3, 41	-	x	-	^1H	x
(3.17)[106]	$Bi(NO_3)_3$, $HS(CH_2)_2OH$, NH_4OH	0.1, 30	-	x	-	^1H	x
(3.18)[106,108]	(3.16), $HS(CH_2)_2OH$	0.1, 33 3.1, 70	77	x	-	^1H	-

MAA = mercaptoacetic acid, $HSCH_2CO_2H$; MPA = 3-mercaptopropionic acid, $HS(CH_2)_2CO_2H$; 2MPA = 2-mercaptopropionic acid, $CH_3CH(SH)CO_2H$; TSA = thiosalicylic acid, $C_6H_4(CO_2H)(SH)$.

3.1.2 Interpretation of Analytical Data Available for Oxathiabismuth Heterocycles

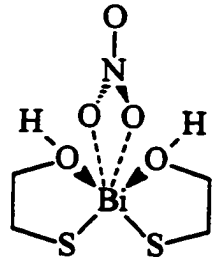
The oxathiabismuth heterocycles were generally synthesized by simple, straightforward methods, in the presence of water and were obtained in high yields, with the exception of (**3.12**) which has a reported yield of 4 % (0.3 g). Characterization techniques such as IR and NMR spectroscopy, elemental and X-ray crystal structure analyses reveal common structural features. Most prominent is the prevalence of the bicyclic framework which is comprised of five or six-membered rings. Three closely related compounds, (**3.15**), (**3.16**) and (**3.17**) have been comprehensively characterized and show that the bicyclic framework has structural flexibility in the solid state. Intermolecular coordinations from thiolate, hydroxyl and carbonyl groups to bismuth atoms give rise to coordination polymers in most of the solid state structures. The maintenance of hydroxyl groups upon ligation of mercaptoacetic acid, mercaptopropionic acid and mercaptoethanol to form compounds, (**3.2**) - (**3.4**), (**3.14**) - (**3.18**) indicates that the bismuth thiolate interaction is quantitatively favoured over the bismuth alkoxide. The lone pair on bismuth was described as stereochemically active. The absence of halogen derivatives is noted.

3.2 Results and Discussion

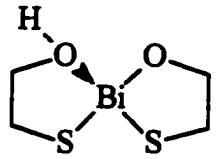
3.2.1 Introduction

The prevalence of the chelate motif is revealed in the complex solid state structures observed for the components of CBS, an established pharmaceutical which also possesses antibiotic properties (see Section 2.3).[6,31,32,92,93,94,95,96,97,105,109] Attempts to systematically develop small chalcogenobismuth heterocycles as alternatives to the complex salt, CBS have been made by metathesis reactions with simple, small oxythio chelating ligands. Reactions of $Bi(NO_3)_3$ and BiX_3 (X = Cl, Br) with the asymmetric diprotic chelate 2-mercaptoethanol generally form the bicyclic bis-(2-hydroxyethanethiolato)bismuth complexes (**3.16**), (**3.19**) and (**3.20**) (see Figure 3.5). Furthermore, the compounds (**3.19**) - (**3.21**) can be obtained by the reaction of NaX (X = Cl, Br, I) with ethanolic solutions of (**3.16**) followed by neutralization to effect precipitation. The acetate salt of (**3.16**), (**3.22**) has also been obtained *via* the conjugate base, (**3.17**). The series of derivatives (**3.16**), (**3.19**) and (**3.22**) show structural flexibility for the bicyclic framework, and the compounds represent simple models for asymmetric monoanionic chelate complexes of bismuth.

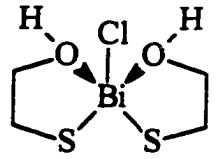
Enhancement of solubility in organic solvents would presumably occur upon substitution of the hydroxyl groups in the bicyclic bis-(2-hydroxyethanethiolato)bismuth compounds for methoxy groups and eliminate competing acid/base equilibria. Preliminary investigations indicate the formation of the methyl derivatives (**3.23**) and (**3.24**) (see Figure 3.6).



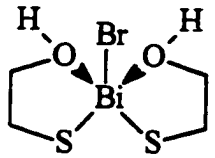
(3.16)



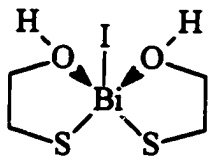
(3.17)



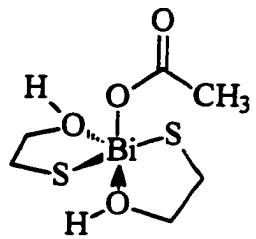
(3.19)



(3.20)

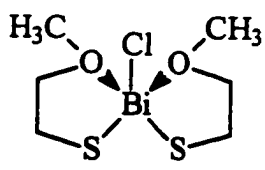


(3.21)

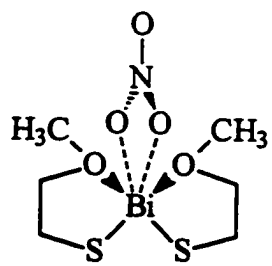


(3.22)

Figure 3.5. Solid state and proposed structures of the series of bicyclic bis-(2-hydroxylethanethiolato)bismuth compounds, (**3.16**), (**3.17**) - (**3.22**) and the proposed structure of the neutral conjugate base, (**3.17**).



(3.23)



(3.24)

Figure 3.6. Proposed structures of the methyl derivatives, (**3.23**) and (**3.24**).

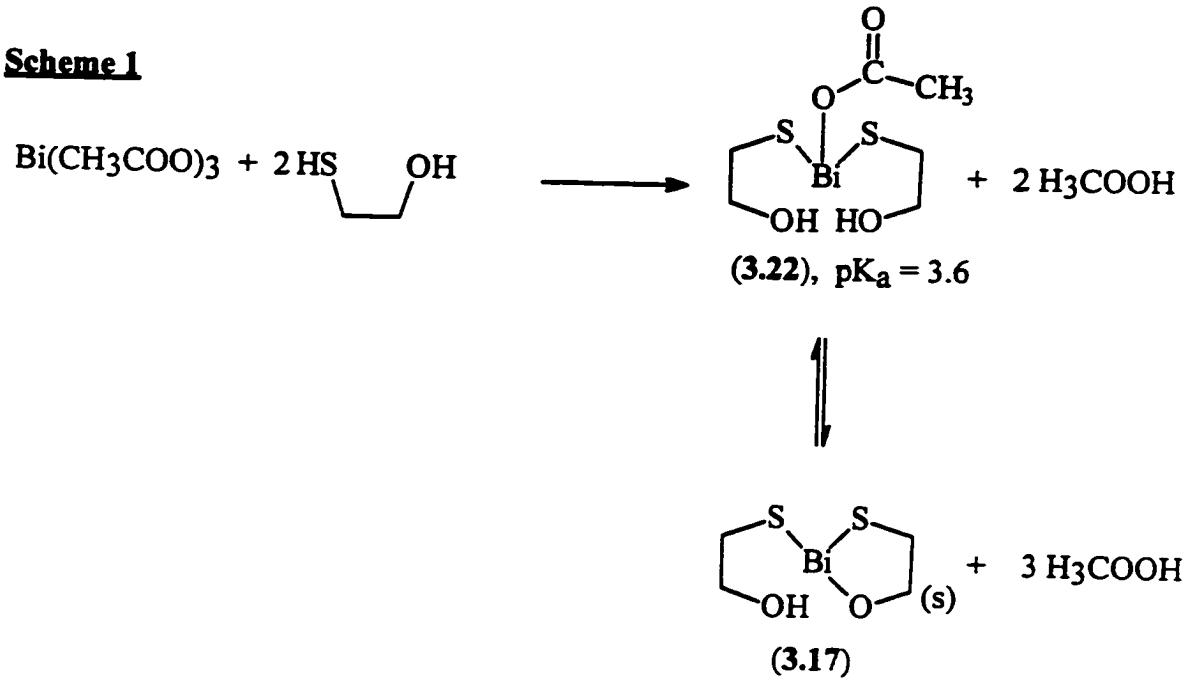
3.2.2 Synthesis and Characterization of Bicyclic Oxathiabismuth Compounds

Reaction of $Bi(NO_3)_3$ with 2-mercaptoethanol in ethanol occurs rapidly to give (**3.16**), in high yield, independent of stoichiometry. Rapid anion exchange effected by the addition of NaX (X = Cl, Br, I) to ethanolic solutions of (**3.16**) (generated *in situ*) to form (**3.19**), (**3.20**) and (**3.21**) as precipitates in high yield after evaporation of the reaction mixtures. Compounds (**3.19**) and (**3.20**) have also been obtained from the reactions of BiX_3 with 2-mercaptoethanol in ethanol. The relative acidity of (**3.16**), (**3.19**) and (**3.21**) ($pK_a = 3.6$) compared to acetic acid ($pK_a = 4.75$) impedes the formation of (**3.22**) from the reaction of $Bi(CH_3COO)_3$ with 2-mercaptoethanol which yields the conjugate base, (**3.17**) (see Scheme 3.1). Nevertheless, compound (**3.22**) can be obtained in high yield as needlelike crystals by the reaction of (**3.17**) with glacial acetic acid.

The hydroxyl characterization has been confirmed by the observation of a characteristically broad singlet in the solution ^1H NMR spectra, distinct broad bands in the 3400 cm^{-1} region of the infrared spectra and relatively low pK_a values (3.6 for (**3.16**), (**3.19**), (**3.21**) and (**3.22**)) (see Table 7.4). The Raman spectra of the series of bicyclic bis-(2-hydroxyethanethiolato)bismuth complexes show an identical fingerprint in the region 0 - 450 cm^{-1} for both (**3.16**) and (**3.22**) and a remarkably similar pattern is observed for (**3.19**), (**3.20**) and (**3.21**) (see Table 7.4). A pKa measurement and a ^1H NMR spectrum were not obtained for (**3.20**) because of low solubility in water, acetone-d_6 and DMSO-d_6.

For compounds (**3.16**), (**3.19**), (**3.21**) and (**3.22**), maintenance of the cyclic structure is demonstrated in the ^1H NMR spectra. The chemical shifts of the hydroxyl

Scheme 1



Scheme 3.1. Acid/base equilibrium showing the formation of (**3.17**) and (**3.22**).

and methylene protons are widely variable which is result of the lability of the hydroxyethanethiolate chelate effected by competition for coordination to the bismuth site with the solvent, DMSO-d_6. In fact, the ^{1}H NMR spectrum of (**3.22**) reveals the loss of one hydroxyl coordination of the ligand to render the molecule monocyclic.

Addition of solid BiX_3 (X = Cl, NO_3) to a methanolic solution of ethylene sulfide and 1 % HX effects rapid precipitation of amorphous yellow powders which were characterized as (**3.23**) and (**3.24**), respectively by elemental analysis (for (**3.23**) only), IR and Raman spectroscopy. The preliminary assignment of the bicyclic structure for (**3.23**) and (**3.24**) is based on comparative IR and Raman spectral data. Inherent low solubility in organic solvents (for e.g., DMSO, acetone, pyridine) has restricted crystal growth and other characterization techniques such as ^{1}H and ^{13}C NMR and has led to the suggestion that compounds (**3.23**) and (**3.24**) are coordinative polymers in the solid state. Electron impact mass spectrometry is an analytical technique suitable for solid materials and may provide additional compositional and structural information necessary for confirmation of the structures proposed for (**3.23**) and (**3.24**).

Reactions of $BiCl_3$ and $Bi(NO_3)_3$ with 2-methylthioethanol yielded BiOCl and $BiONO_3$, respectively, instead of the desired metathesis. Deprotonation of the hydroxyl group of 2-methylthioethanol by reaction with NaOH or BuLi prior to addition to solid $BiCl_3$ or $Bi(NO_3)_3$ was attempted and also resulted in the recovery of BiOCl and $BiONO_3$. The difficulty of the formation of bismuth alkoxide bonds by conventional synthetic methods is perhaps a consequence of the HSAB theory.[90] The author suggests that

reaction of $BiCl_3$ with an excess of $LiO(CH_2)_2SLi$ in addition to rigorous exclusion of water may result in bismuth-alkoxide bond formation.

3.2.3 Structural Features

An X-ray crystallographic study of (**3.16**) (see Figure 3.7) reveals an essentially ionic structure composed of an almost planar bicyclic framework in which two sulfur atoms and two oxygen atoms adopt a square-planar *cis* arrangement around the bismuth center. The NO_3^- anion forms a third weak chelate between the two hydroxyl oxygen centers, with the nitrogen center in the BiO_2S_2 plane and the two donor oxygen centers of the anion above and below the plane. A simultaneous X-ray crystal structure analysis of (**3.16**) was performed by Asato *et al.*, and reported a similar atomic arrangement but in a different space group ($I\bar{4}$) containing crystallographic dimers.[107] This is a result of a refinement in an illegally low symmetry space group and the atomic coordinates of the two crystallographically different molecules in Asato's structure can be transformed into one molecule of (**3.16**) in the space group $I4_1/a$ determined for this report (see Appendix 1, page 174).[110]

X-ray crystallographic studies of (**3.19**) (see Figure 3.8) and (**3.22**) (see Figure 3.9) show that both contain the bicyclic bis-(2-hydroxyethanethiolato)bismuth moiety, with a fifth coordination site at bismuth occupied by the chlorine and carbonyl oxygen center of the acetate, respectively. For (**3.19**), weak intermolecular Bi···Cl [3.488(4) Å] and Bi···S [3.124(4) Å] interactions render the bismuth site formally seven-coordinate and are responsible for a polymeric arrangement. The solid state structure of (**3.22**) involves

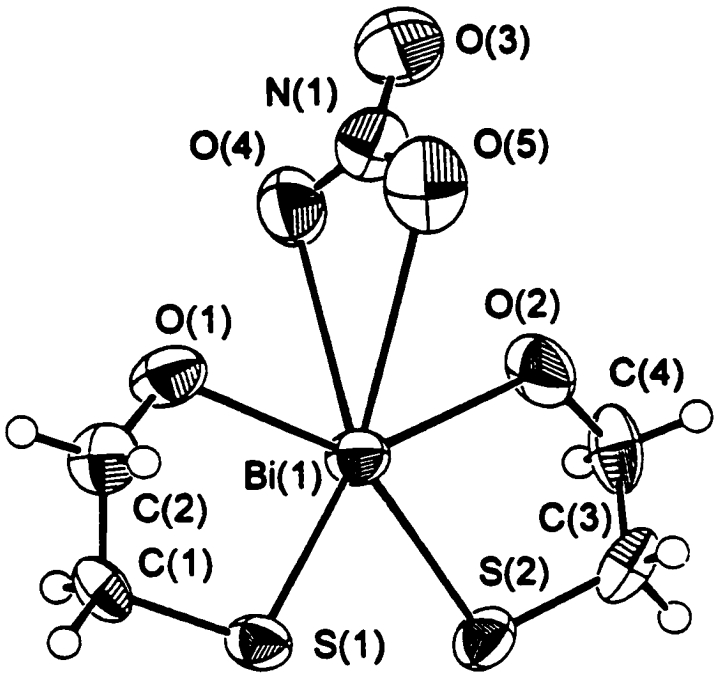


Figure 3.7. Crystallographic view of (**3.16**). The water molecule is omitted for clarity. Important bond lengths (Å) and angles (°): Bi(1)-S(1) 2.639(5), Bi(1)-S(2) 2.655(5), Bi(1)-O(1) 2.63(1), Bi(1)-O(2) 2.63(1), Bi(1)-O(4) 3.01(2), Bi(1)-O(5) 3.17(5), S(1)-Bi(1)-O(1) 72.8(3), S(1)-Bi(1)-S(2) 78.1(1), S(2)-Bi(1)-O(2) 71.4(3), O(1)-Bi(1)-O(2) 138.4(4), S(1)-Bi(1)-O(4) 140.6(3), S(1)-Bi(1)-O(5) 139.5(3).

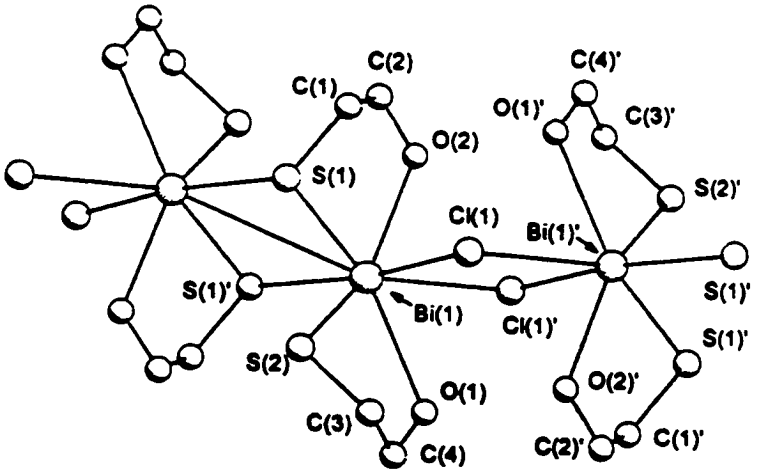


Figure 3.8. Crystallographic view of (**3.19**). Important bond lengths (Å) and angles (°): Bi(1)-S(1) 2.595(3), Bi(1)-S(2) 2.558(4), Bi(1)-O(1) 2.86(1), Bi(1)-O(2) 2.80(1), Bi(1)-Cl(1) 2.589(3), S(1)-Bi(1)-O(1) 154.2(2), S(1)-Bi(1)-S(2) 83.7(1), S(2)-Bi(1)-O(2) 152.3(2), O(1)-Bi(1)-O(2) 132.9(3), S(1)-Bi(1)-Cl(1) 94.0(1).

intermolecular hydrogen bonding between the hydroxyl group of the chelate ring and the carbonyl moiety of the acetate anion [O···O 2.73(3) Å]. The resulting centrosymmetric dimeric arrangment, as well as the weak inter-dimer Bi···S contacts [3.379(8), 3.457(8) Å] are comparable in length to those observed in related compounds [3.134(7) - 3.5910(9) Å].[111]

The bicyclic framework adopts quite different conformations as illustrated in (**3.16**), (**3.19**) and (**3.22**) which may be imposed by the differing donor capabilities of each anion. In (**3.16**), the two oxygen [O(1) -0.24(1) Å; O(2) 0.32(1) Å] and two sulfur atoms [S(1) 0.048(5) Å; S(2) 0.044(5) Å] form a slightly twisted plane which essentially contains both the bismuth center [-0.006 Å] and the nitrogen center [0.106 Å] of the anion. While the same five atom plane can be envisaged for (**3.19**), [O(1) -0.12(1) Å; O(2) 0.15(1) Å; S(1) -0.021(4) Å; S(2) 0.022(4) Å; Bi(1) -0.202 Å] the chlorine center occupies an apical position above this plane, with a typical Bi-Cl bond length.[111] The general conformation of (**3.19**) is similar to that observed for the bismuth aryloxide derivative bis(1-oxopyridine-2-thiolato)phenylbismuth (**3.1**).[101]

In contrast, the cation in (**3.22**) has a severely twisted structure with the chelating ligands essentially *cis* and one hydroxyl oxygen *trans* to the acetate oxygen. The conformation and configuration of the cation in (**3.16**) is significantly different to that in the isoelectronic (**3.25**)[112] (see Figure 3.10) in which the chelate ligands are *trans* and the structure is a folded bicyclic bis-(2-aminoethanethiolato)bismuth cation with the bismuth center in an apparently apical position. The S-Bi-S angles in the bicyclic framework

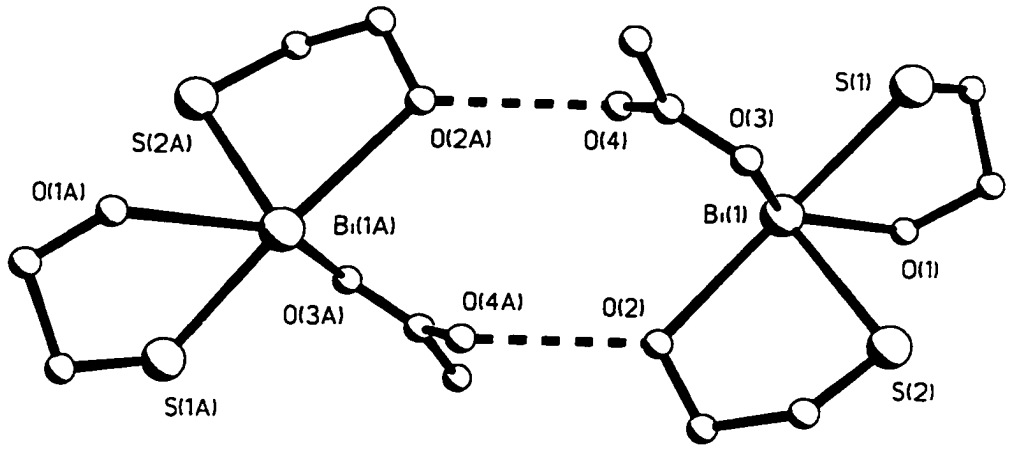
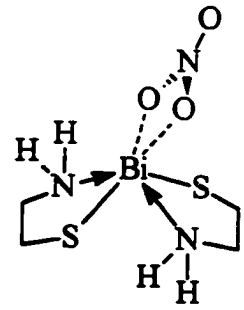


Figure 3.9. Crystallographic view of (**3.22**) illustrating hydrogen bonding between the hydroxyl group of the chelate ring and the carbonyl oxygen of the acetate group. Important bond lengths (Å) and angles (°): Bi(1)-S(1) 2.608(7), Bi(1)-S(2) 2.577(7), Bi(1)-O(1) 2.54(2), Bi(1)-O(2) 2.72(2), Bi(1)-O(3) 2.35(1), S(1)-Bi(1)-O(1) 74.4(5), S(1)-Bi(1)-S(2) 93.7(2), S(2)-Bi(1)-O(2) 71.6(4), O(1)-Bi(1)-O(2) 130.7(6), S(1)-Bi(1)-O(3) 73.9(5).



(**3.25**)

Figure 3.10. Solid state structure of bicyclic bis-(2-aminoethanethiolato)bismuth nitrate (**3.25**).

increase with increasing distortion from planarity around the bismuth center, whereas the opposite trend is evident for the O-Bi-O angles.

The Bi-S bond lengths in (**3.16**), (**3.19**) and (**3.22**) are typical,[111,113,114,115] but are slightly longer in (**3.16**) [2.639(5) and 2.655(5) Å] than in (**3.19**) [2.558(4) and 2.595(3) Å] and (**3.22**) [2.577(7) and 2.608(7) Å]. In contrast, the Bi-O bond lengths are substantially shorter in (**3.19**) than in (**3.16**), but in both cases they are longer than Bi-$O_{dicoordinate}$ bonds [2.08-2.86 Å][6,8,77,79,85,86,88,89,101,109,116,117] and are comparable to those of Bi-$O_{tricoordinate}$ [2.323-3.159 Å],[77,117] which might be considered coordinative.

Although the hydrogen atoms of the hydroxyl moieties could not be located in their respective Fourier maps, the oxygen-oxygen contact distances [O(1) - O(4) 2.72(2) Å] are representative of hydrogen bonded moieties. For (**3.22**), two close intermolecular contacts [O(1)···O(3) 2.67(3) Å and O(1)···O(3) 2.67(3) Å] are responsible for the centrosymmetric dimer arrangement. The closest contact in (**3.19**) is longer [2.80(2) Å] but still within the hydrogen bond range.

Further confirmation of the formulae are provided by APCI mass spectrometry on saturated solutions in acetonitrile at cone voltages of 10V and 30V and assignments for the most intense peaks have been confirmed by MS/MS (see Table 7.3). All spectra show the presence of the molecular cation $[\mathbf{3.26}]^+$ (m/z 363) as a dominant peak at a low cone voltage (10V) and at higher cone voltages, and the dominant peak becomes (m/z 285), which is assigned to the monocyclic oxathiabismolanium cation fragment which results from loss of 2-mercaptomethanol, and is present in all spectra at both cone voltages. The

acetonitrile complex (**3.26**)•MeCN is also observed in all spectra at low cone voltage, but is apparently too labile to exist at the higher cone voltage.

(**3.26**) (**3.26**)·MeCN

Figure 3.11. Proposed structure of the molecular bismuthenium cation, [**3.26**]$^+$ and the acetonitrile complex, (**3.26**)•MeCN which are present in the MS of all of the bicyclic bis-(2-hydroxylethanethiolato)bismuth compounds.

3.2.4 Conclusions

Compounds (**3.16**), (**3.19**) - (**3.22**) are best described as *bis* chelate complexes of Bi^{3+} involving the hydroxyethanethiolate ligand, with two essentially equivalent intramolecular hydroxyl coordinative interactions responsible for the bicyclic framework. The *cis* orientation of the hydroxyl groups in (**3.16**) and (**3.19**) is perhaps imposed by intra-ligand hydrogen bonding in the transition state during complex formation. The twisted cation structures observed in (**3.22**) and (**3.25**) are possibly due to the presence of substantial intermolecular hydrogen bonding. In general, cations (**3.16**) and (**3.25**) can be considered as intramolecularly base-stabilized bismuthenium cations and are related to the previously reported solvent stabilized examples.[77,117,118] The general and quantitative

formation of bicyclic bis-(2-hydroxyethanethiolato)bismuth complexes is a definitive indication of the preference for thiolate ligation of bismuth over bismuth-alkoxide formation, which has its roots in the hard and soft acid-base theory,[90] although there are exceptions.[119]

Chapter 4. Dithiabismuth Heterocycles

4.1 Introduction

4.1.1 Four-Membered Rings

Dithiacarbamatobismuth,[120] xanthatobismuth and dithiaphosphinatobismuth compounds have been extensively surveyed in the literature and the development of synthetic methods has been comprehensive. They have been used as starting materials for metathetical and addition reactions and adduct formations.

A series of *tris*(dialkyldithiocarbamato)bismuth compounds, (**4.1**) - (**4.8**) (see Figure 4.1) was synthesized by reacting $BiCl_3$ with excess amounts of the appropriate dialkylamine and CS_2 (see Table 4.1).[121,122,123,124,125,126,127,128,129,130] Compound (**4.1**) was also synthesized by reacting $BiCl_3$ with sodium diethyldithiacarbamate or diethyldithiacarbamic acid. IR and ^1H NMR spectroscopic studies of (**4.1**) reveal the nonequivalence of the Bi-S bonds and the formation of 1:1 (**4.1**)•C_6H_6 adduct. X-ray crystal structures were obtained for (**4.1**), (**4.4**), (**4.7**) and (**4.8**). Compound (**4.4**) was reported to be characterized by an X-ray crystal structure, however, data and a structural discussion were not presented. Intermolecular coordinations from sulfur render the bismuth centers eight-coordinate and result in dimer formation in the solid state for (**4.1**) and (**4.8**). Compound (**4.7**) is monomeric and has a six-coordinate bismuth site.

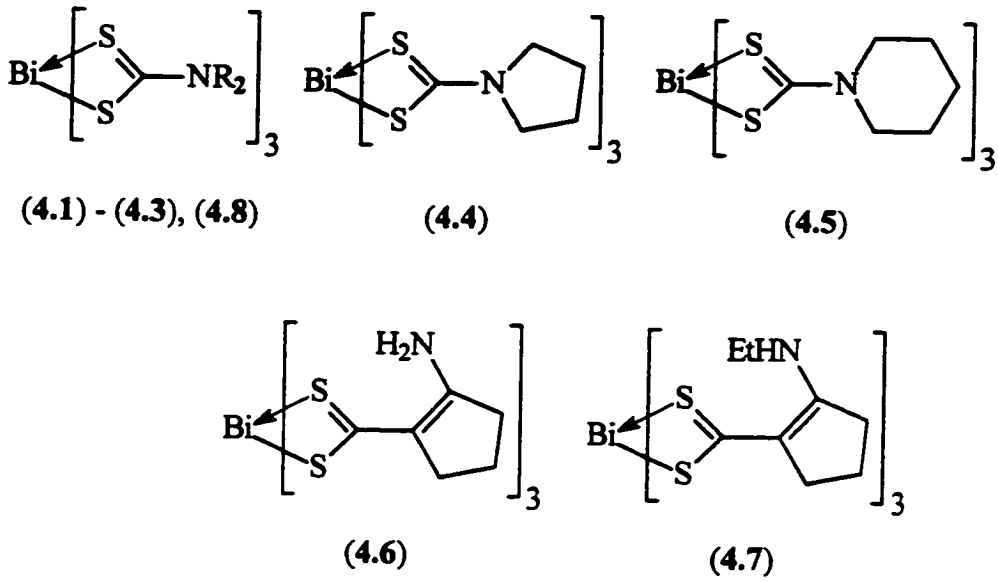


Figure 4.1. Proposed structures of *tris*(dialkyldithiacarbamato)bismuth compounds, (**4.1**) - (**4.8**), R = Et (**4.1**), Bu^i (**4.2**), CH_2Ph (**4.3**), EtOH (**4.8**).

Table 4.1. Analytical data for *tris*(dialkyldithiacarbamato)bismuth compounds, $Bi(S_2CNR_2)_3$.

Compound	Reactants	Yield g, %	mp (°C)	EA	NMR	IR	UV	X-ray
(4.1)[121,122,123,124,126,127]	$BiCl_3$, HS_2CNEt_2	-	186	x	^1H	x	x	x
	PhBiCl, NaS_2CNEt_2	-						
	$BiCl_3$, CS_2, $HNEt_2$	10, 63						
(4.2)[127]	$BiCl_3$, CS_2, $HNBu_2$	-	-	-	^1H	-	x	-
(4.3)[127]	$BiCl_3$, CS_2, $HNPh_2$	-	-	-	^1H	-	-	-
(4.4)[125]	$BiCl_3$, CS_2, $HN(CH_2)_4$	-	-	-	-	-	-	x
(4.5)[129]	$BiCl_3$, CS_2, $HN(CH_2)_5$	-	-	-	-	-	-	-
(4.6)[130]	$BiCl_3$, ACDA	-, 99	-	-	-	-	-	-
(4.7)[130]	$BiCl_3$, EACDA	-, 98	-	-	-	-	-	x
	BiOCl, EACDA	-						
(4.8)[128]	$BiONO_3$, HCl, CS_2,	-	-	-	-	-	-	x
	$HN(CH_2CH_2OH)$							

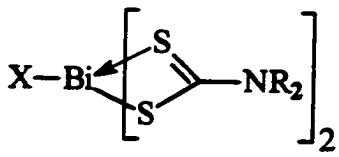
ACDA = 2-aminocyclopent-1-ene-1-dithiocarboxylic acid, $C_6H_9NS_2$

EACDA = 2-(ethylamino)cyclopent-1-ene-1-dithiocarboxylic acid, $C_8H_{13}NS_2$

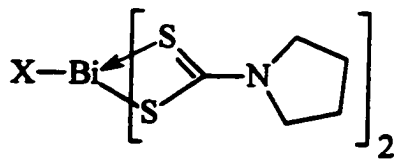
The complete characterization of (**4.1**) is anomalous; identification of compounds (**4.2**) - (**4.8**) was based on an X-ray crystal structure or a ^1H NMR spectrum except for one compound which was characterized by both techniques. The absence of analytical data for (**4.5**) and (**4.5**) indicates that the compounds were characterized by speculation based on the reaction stoichiometry. Yields were reported for three compounds and a

synthetic description is not provided for five compounds. Steric differences prevented intermolecular donations to the bismuth atoms of (**4.7**) and allowed for dimerization of (**4.1**) and (**4.8**).

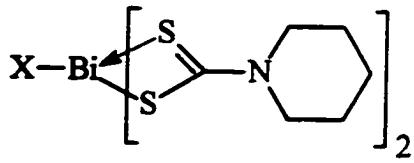
Reactions of five *tris*(dialkyldithiacarbamato)bismuth compounds with equimolar amounts of X_2 (X = Br, I) resulted in high yields of the corresponding monosubstituted compounds (see Figure 4.2 and Table 4.2).[131,132,133,134,135,136] Displacement of a dialkyldithiacarbamate ligand from compounds (**4.1**), (**4.4**) and (**4.5**) by BF_4^- occurred upon reaction with BF_3 to form the tetrafluoroborate salts, (**4.16**), (**4.23**) and (**4.26**) (see Figure 4.2).[137] X-ray crystal structures were obtained for (**4.11**) - (**4.15**). Compound (**4.11**) is a centrosymmetric tetramer in which seven-coordinate bismuth centers are bridged by two and three-coordinate bromine atoms. The polymeric structure of (**4.12**) is propagated by intermolecular donations from iodine atoms to render each bismuth site six-coordinate. Compounds (**4.13**) and (**4.15**) crystallize as centrosymmetric dimers which are linked by coordinating sulfur atoms. Compound (**4.14**) contains monomers in which the coordination sphere around bismuth is pentagonal bipyramidal. The lone pair is described as stereochemically active for compounds (**4.11**) - (**4.15**). Conductance measurements in nitrobenzene indicate that (**4.11**), (**4.17**), (**4.19**), (**4.21**) and (**4.24**) are nonelectrolytes and (**4.16**), (**4.23**) and (**4.26**) are univalent electrolytes.



(4.9) - (4.20)



(4.21) - (4.23)



(4.24) - (4.26)

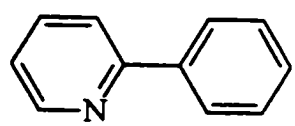
Compound	R	X
(4.9)	Me	Me
(4.10)	Me	Ph
(4.11)	Et	Br
(4.12)	Et	I
(4.13)	Et	Me
(4.14)	Et	Ph
(4.15)	Et	
(4.16)	Et	BF_4
(4.17)	Bu^i	Br
(4.18)	Bu^i	I
(4.19)	CH_2Ph	Br
(4.20)	CH_2Ph	I

Figure 4.2. Proposed structures of disubstituted dialkyldithiacarbamatobismuth compounds, (4.2) - (4.26). X = Br for (4.21), (4.24); I for (4.22), (4.25); BF_4 for (4.23), (26).

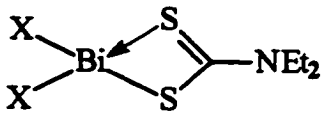
Table 4.2. Analytical data for monosubstituted *bis*(dialkyldithiacarbamato)bismuth compounds, $XBi(S_2CNR_2)_2$.

Compound	Reactants	Yield g, %	mp [dp] (°C)	EA	NMR	IR	MS	UV	X-ray
(4.9)[134]	$MeBiBr_2$, NaS_2CNMe_2	1.3,55	185	x	^1H	-	-	-	-
(4.10)[122.134]	$PhBiCl_2$, NaS_2CNMe_2	-, 98	210-211	x	-	x	-	x	-
	$PhBiBr_2$, NaS_2CNMe_2	1.5,58	219	x	^1H	-	-	-	-
(4.11)[131.133]	$Bi(S_2CNEt_2)_3$, Br_2	-,94	139-141	x	^1H	x	-	x	x
(4.12)[132.133]	$Bi(S_2CNEt_2)_3$, I_2	-, 85	159-160	x	^1H	x	x	x	x
(4.13)[134.135]	$MeBiBr_2$, NaS_2CNEt_2	1.8,76	141	x	^1H	-	-	-	x
(4.14)[122.134.136]	$PhBiBr_2$, NaS_2CNEt_2	-, 38	137	x	^1H	-	-	x	x
	$PhBiCl_2$, NaS_2CNEt_2	1.9,65	131-133	x	-	x	-	x	-
(4.15)[136]	$C_{11}H_8NBiBr_2$, NaS_2CNEt_2	1.4,46	222-224	x	^1H,$^{13}C^1$ ^4N	x	-	x	x
(4.16)[137]	$Bi(S_2CNEt_2)_3$, BF_3	-, ~70	[155]	x	^1H	x	x	x	-
(4.17)[131]	$Bi(S_2CNBu^i_2)_3$, Br_2	-, 86	139-141	x	^1H	x	-	x	-
(4.18)[132]	$Bi(S_2CNBu^i_2)_3$, I_2	-, 80	143-144	x	^1H	x	x	x	-
(4.19)[131]	$Bi(S_2CNCH_2Ph_2)_3$, Br_2	-, 84	[100]	x	^1H	x	-	x	-
(4.20)[132]	$Bi(S_2CNCH_2Ph_2)_3$, I_2	-, 75	[86-105]	x	^1H	x	x	x	-
(4.21)[131]	$Bi(S2CN(CH_2)_4)_3$, Br_2	-, 91	[245]	x	^1H	x	-	x	-
(4.22)[132]	$Bi(S_2CN(CH_2)_4)_3$, I_2	-, 84	[263-265]	x	^1H	x	x	x	-
(4.23)[137]	$Bi(S_2CN(CH_2)_4)_3$, BF_3	-, ~70	[240]	x	^1H	x	x	x	-
(4.24)[131]	$Bi(S2CN(CH_2)_5)_3$, Br_2	-, 95	[246]	x	^1H	x	-	x	-
(4.25)[132]	$Bi(S_2CN(CH_2)_5)_3$, I_2	-, 88	[243-245]	x	^1H	x	x	x	-
(4.26)[137]	$Bi(S_2CN(CH_2)_5)_3$, BF_3	-, ~70	[245]	x	^1H	x	x	x	-

Monosubstituted dialklydithiacarbamatobismuth compounds were obtained in high yields and characterized predominantly by spectroscopic techniques. For the compounds which were characterized by an X-ray crystal structure, intermolecular donations from sulfur and halogen atoms give rise to polymer, tetramer and dimer formation, except for (**4.14**) which is monomeric. The ionicity of compounds (**4.16**), (**4.23**) and (**4.26**) in comparison to the molecular analogues, $XBi(S_2CNR_2)_2$, X = Cl, Br, I may be a result of the relative Lewis acidity of BF_3.

Reaction of BiX_3 (X = Cl, Br, I) with (**4.1**) generates the halogen derivatives, (**4.27**) - (**4.29**), respectively (see Figure 4.3 and Table 4.3).[138,139,140] Successful mono and di-phenylation of (**4.27**) by reaction with one or two equivalents of PhLi, results in the formation of (**4.30**) and (**4.31**) (see Figure 4.3 and Table 4.3), respectively, which are demonstrated to behave as non-electrolytes in solution by conductance studies.[141]

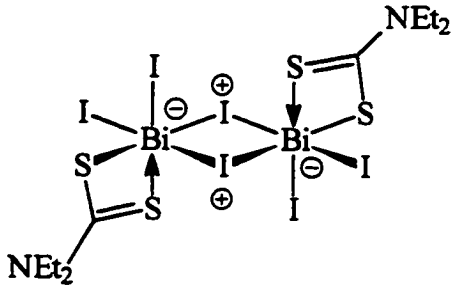
X-ray crystal structures were obtained for Lewis base adducts, (**4.27**)•4pyr and (**4.28**)•4pyr which reveal monomeric pentagonal bipyramidal bismuth centers.[142] Recrystallization of (**4.27**) and (**4.28**) from a DMF/n-butanol mixture results in the formation of a pentanuclear complex, $[Bi_5(S_2CNEt_2)X_2]$•DMF, X = Cl, Br in which a $[BiX_6]^{3-}$ anion bridges four coordinating $[Bi(S_2CNEt_2)_2]^+$ cations.[143] Compound (**4.29**) is a coordination polymer in which capped octahedral bismuth centers are linked by intermolecular coordinations from sulfur and iodine atoms. Reaction of (**4.29**) with NEt_4I yields crystals of (**4.29**)•NEt_4I in which the anion, $[I_2(Et_2NCS_2)BiI_2Bi(S_2CNEt_2)I_2]^-$ is a



(4.27) - (4.31)

Compound	(4.27)	(4.28)	(4.29)	(4.30)	(4.31)
X	Cl	Br	I	Ph	Ph, Cl

Figure 4.3. Proposed structures for the monosubstituted diethyldithiacarbamatobismuth compounds, (**4.27**) - (**4.31**).



(4.29)·NEt_4I

Figure 4.4. Structure of (**4.29**)·NEt_4I showing edge-shared octahedral dimers.

centrosymmetric dimer with a structure described as two edge-shared octahedra (see Figure 4.4).[144] Adducts of (**4.29**) are formed with 2,2'-bipyridyl and 2,2':6',2''-terpyridyl, to yield (**4.29**)•bipy and (**4.29**)•terpy, which crystallize as seven-coordinate dimers and monomers, respectively.[145]

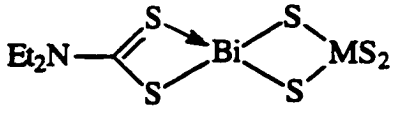
Table 4.3. Analytical data for disubstituted dialkyldithiacarbamatobismuth compounds, $X_2Bi(S_2CNR_2)$.

Compound	Reactants	Yield g, %	mp (°C)	EA	NMR	IR	UV	X-ray
(**4.27**)[138.139.140]	$BiCl_3$, $Bi(S_2CNEt_2)_3$	-	119.5-121	x	^1H	x	-	x
(**4.27**)•4pyr[146]	$Cl_2Bi(S_2CNEt_2)_2$, pyridine	-	-	-	-	-	-	x
(**4.28**)[138.140]	$BiBr_3$, $Bi(S_2CNEt_2)_3$	-	232-233	x	^1H	x	-	x
(**4.28**)•4pyr[146]	$Br_2Bi(S_2CNEt_2)_2$, pyridine	-	-	-	-	-	-	x
(**4.29**)[138.142]	BiI_3, $Bi(S_2CNEt_2)_3$	-	226.5-227.5	x	^1H	x	-	x
(**4.29**)•4pyr[146]	$I_2Bi(S_2CNEt_2)_2$, pyridine	-	-	-	-	-	-	x
(**4.30**)[141]	$Cl_2Bi(S_2CNEt_2)_2$, PhLi	-, 66	-	x	^1H	x	-	-
(**4.31**)[141]	$Cl_2Bi(S_2CNEt_2)_2$, PhLi	-, 52	125-127	x	^1H	x	-	-

In general, characterization was comprehensive for the uncomplexed dithiabismuth compounds, (**4.27**) - (**4.31**), however, yields were rarely reported. The solid state structures reveal complex atomic arrangements which involve multinuclear

clusters bridged by sulfur and halogen atoms imposing high coordination numbers on the bismuth centers.

Binuclear complexes, $(Et_2NCS_2)Bi(MoS_4)$ (**4.32**) and $(Et_2NCS_2)Bi(WS_4)$ (**4.33**) (see Figure 4.5) were obtained in high yield by the reaction of (**4.27**) with $(NH_4)MS_4$ in an inert atmosphere.[146] Characterization by elemental analysis, conductivity measurements and IR, UV and ^1H NMR spectroscopic studies indicate that the tetrathiometallate ligands are bidentate and the complexes are molecular and behave as nonelectrolytes.

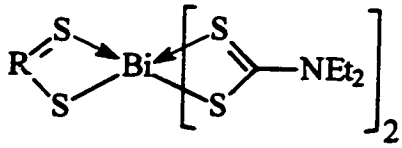


(**4.32**), (**4.33**)

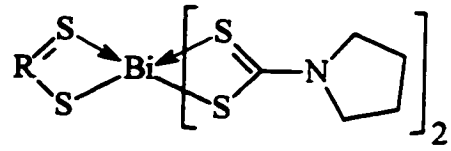
Figure 4.5. Proposed structures of (**4.32**), (M = Mo) and (**4.33**), (M = W).

A series of eight mixed dialkyldithiacarbamatobismuth compounds, (**4.34**) - (**4.41**) (see Figure 4.6 and Table 4.4) was synthesized by the reaction of iodo-bis(dialkyldithiocarbamato)bismuth with either CS_2 and $R'NH_2$ or sodium dialkyldithiacarbamatobismuth.[147] The reaction of potassium O-ethylxanthate with equimolar amounts of (**4.12**) and (**4.25**) yield (**4.42**) and (**4.43**), respectively (see Figure 4.6 and Table 4.4).[147,148] An extensive spectroscopic study confirms the presence of two

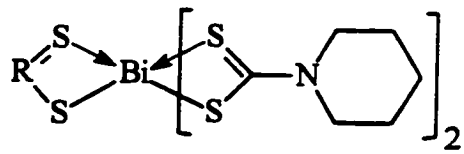
different alkyl groups. Comparative UV spectroscopy reveals that the electronic properties of (**4.34**) - (**4.43**) are not altered by the presence of differing alkyl groups and that alkylxanthate ligands are weaker chelators than their dialkyldithiacarbamate counterparts.



(4.34) - (4.36)



(4.37) - (4.40)



(4.40) - (4.43)

Compound	R
(4.34)	NC_4H_8
(4.35)	NCH_2Ph
(4.36)	OEt
(4.37)	NEt_2
(4.38)	NCH_2Ph
(4.39)	NC_5H_4
(4.40)	OEt
(4.41)	NEt_2
(4.42)	NCH_2Ph
(4.43)	NC_5H_4

Figure 4.6. Proposed structures of disubstituted mixed dialkyldithiacarbamatobismuth compounds, (4.34) - (4.43).

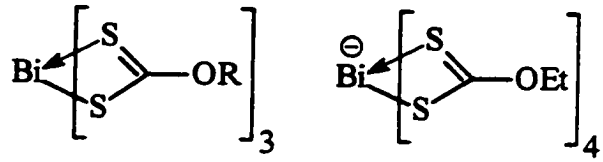
Table 4.4. Analytical data for monosubstituted mixed dialkyldithiacarbamatobismuth complexes, $Bi(S_2CNR_2)_2R'$.

Product	Yield g, %	mp[dp]°C	NMR	IR	UV	MS	X-ray
(4.34)[147]	-, 90	[166]	^1H	x	x	x	-
(4.35)[147]	-, 58	[69]	^1H	x	x	x	-
(4.36)[147,148]	-, 58	102-103	^1H	x	x	x	-
(4.37)[147]	-, 83	[229]	^1H	x	x	x	-
(4.38)[147]	-, 64	[90]	^1H	x	x	x	-
(4.39)[147]	-, 86	214-215	^1H	x	x	x	-
(4.40)[147]	-, 97	[135]	^1H	x	x	x	-
(4.41)[147]	-, 85	[85]	^1H	x	x	x	-
(4.42)[147]	-, 88	[185]	^1H	x	x	x	-
(4.43)[147]	-, 80	[188]	^1H	x	x	x	-

The mixed dialkyldithiacarbamate and alkylxanthatobismuth complexes were obtained in high yields and extensively characterized by spectroscopic studies which provided electronic and structural information such as relative ligand donor strength and molecular composition. X-ray crystal structures were not obtained, although the compounds were described as "yellow crystalline solids."[147]

Reaction of sodium or potassium *p*-methoxyphenylcarbonithionate with bismuth salts results in a characteristic precipitate, however, neither a yield, proposed structure nor characterization data were reported.[149]

A series of alkylxanthatobismuth complexes, (**4.44**) - (**4.50**), (see Figure 4.7 and Table 4.5) was synthesized by the reaction of $Bi(NO_3)_3$ with excess molar amounts of potassium alkylxanthate.[150,151,152,153] Thermogravimetric studies of the series of complexes show that Bi_2S_3 is a common decomposition product. Intraligand and charge-transfer bands are identified in the UV spectra for (**4.45**) and (**4.50**). The solid state structures consist of either dimeric or polymeric units in which the bismuth centers are seven-coordinate with distorted pentagonal bipyramidal and capped trigonal prismatic coordination geometries, respectively. Crystals of the ionic complex, tetraethylammonium *tetrakis*(O-ethylxanthato)bismuthate (**4.50**) were obtained by the reaction of (**4.45**) with an equimolar amount of $[NEt_4][S_2COEt]$ and are comprised of monomeric dodecahedral eight-coordinate bismuth centers.[154] Preliminary observations of the reaction of $BiCl_3$ with potassium salts of methyl xanthate or ethyl xanthate in concentrated HCl consisted of a description of air-stable yellow crystals which decompose in pyridine solutions.[155]



(4.44) - (4.49) **(4.50)**

Compound	(4.44)	(4.45)	(4.46)	(4.47)	(4.48)	(4.49)
R	Me	Et	Pr^i	Bu^n	Cyc	CH_2Ph

Figure 4.7. Proposed structures of *tris*(alkylxanthato)bismuth compounds, (**4.44**) - (**4.49**) and the *tetrakis*(ethylxanthato)bismuthate anion, (**4.50**).

Table 4.5. Analytical data for *tris*(alkylxanthato)bismuth compounds, $Bi(S_2COR)_3$.

Compound	Reactants	Yield g, %	mp (°C)	EA	UV	IR	MS	X-ray
(4.44)[155.150.151.152]	$Bi(NO_3)_3$, KS_2COMe	-	130-131	x	-	x	x	x
(4.45)[150.152]	$Bi(NO_3)_3$, KS_2COEt	-	94-95	x	x	x	x	x
	$BiCl_3$, KS_2COEt							
(4.46)[150]	$Bi(NO_3)_3$, KS_2COPr^i	-	160-162	x	-	x	x	x[156.157]
(4.47)[150]	$Bi(NO_3)_3$, $KS_2CO(n\text{-}Bu)$	-	30	x	-	x	x	-
(4.48)[150.153]	$Bi(NO_3)_3$, KS_2COCyc	-	160-161	x	-	x	x	x
(4.49)[153]	$Bi(NO_3)_3$, KS_2COCH_2Ph	-	-	-	-	x	-	x
$[NEt_4]$**(4.50)**[152]	**(4.45)**, $[NEt_4][S_2COEt]$	-	-	-	x	x	-	x[154]

Cyc = cyclohexyl, C_6H_5

IR spectroscopy and mass spectrometry were reported as characterization techniques for compounds **(4.44)** - **(4.50)**, however, the data and a discussion were not presented. It is inferred that compound characterization was based on elemental analyses and X-ray crystal structures.

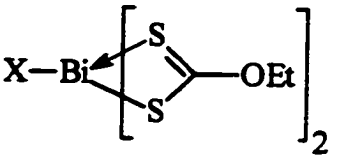
The dialkyldithiacarbamatobismuth compounds and their derivatives exhibit high coordination numbers and geometries in the solid state and a stereochemically active lone pair on bismuth is observed in structures which contain less than three intermolecular coordinations to the bismuth center. Common coordination geometries are pentagonal bipyramidal and capped trigonal prismatic.

Compounds (**4.51**) and (**4.52**) (see Figure 4.8 and Table 4.6) were synthesized by the reaction of (**4.45**) with X_2, CuX_2 (X = Cl, Br) or $BiCl_3$.[158] The crystalline compounds are susceptible to hydrolysis. Mixed xanthates were obtained by reacting (**4.52**) with aqueous solutions of potassium methyl xanthate and sodium diethyldithiacarbamate to afford the compounds, (**4.53**) and (**4.54**), respectively (see Figure 4.8).[152] Comparative IR and ^1H NMR spectroscopy indicate the presence of different alkyl groups and confirm successful substitution.

Table 4.6. Analytical data for disubstituted ethylxanthatobismuth compounds, $XBi(S_2COEt)_2$.

Compound	Reactants	Yield g, %	mp[dp] (°C)	EA	NMR	IR	MS	X-Ray
(**4.51**)[158]	(**4.45**), Cl_2	-	-	x	-	x	-	-
	(**4.45**), $CuCl_2$							
	(**4.45**), $BiCl_3$							
(**4.52**)[158]	(**4.45**), Br_2	-	-	x	-	x	-	-
	(**4.45**), $CuBr_2$							
(**4.53**)[158]	(**4.51**) , KS_2COMe	-	>[80]	-	^1H	x	-	-
(**4.54**)[158]	(**4.51**), NaS_2CNEt_2	-	>[105]	-	^1H	x	-	-

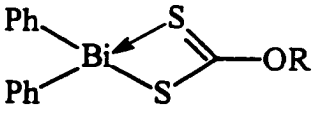
Derivatization of ethylxanthatobismuth (**4.45**) afforded a series of monosubstituted ethylxanthatobismuth compounds which were comprehensively



(4.51) - (4.54)

Compound	(4.51)	(4.52)	(4.53)	(4.54)
X	Cl	Br	S_2COMe	S_2CNEt_2

Figure 4.8. Proposed structures of disubstituted ethylxanthatobismuth compounds, (**4.51**) - (**4.54**).



(4.55) - (4.60)

Compound	(4.55)	(4.56)	(4.57)	(4.58)	(4.59)	(4.60)
R	Me	Et	Pr^n	Pr^i	Bu^n	Bu^t

Figure 4.9. Proposed structures of diphenyl alkylxanthatobismuth compounds, (**4.55**) - (**4.60**).

characterized, however, yields were not reported. Iododiethylxanthatobismuth and other alkyl analogues were not obtained. The solution IR spectra were markedly different from the solid state IR spectra which is attributed to adduct formation in solution with the solvent, CS_2, which is a Lewis base. Although the compounds were crystalline, X-ray crystal structures were not obtained.

An extensive series of diphenyl alkyldithiaxanthatobismuth compounds, (**4.55**) - (**4.61**) (see Figure 4.9 and Table 4.7) were obtained by the reaction of Ph_2BiBr with equimolar amounts of the appropriate sodium alkylxanthate.[159] The polymeric structure of (**4.58**) is unique because the di-*iso*-propylxanthate ligand is monodentate and bridges two bismuth atoms rather than chelating a single bismuth center. The coordination geometry is described as trigonal bipyramidal and the stereochemically active lone pair on bismuth occupying an axial position.

Table 4.7. Analytical data for diphenyl(alkylxanthato)bismuth compounds, $Ph_2Bi(S_2COR)$.

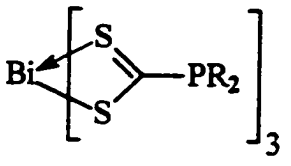
Compound	Yield g, %	mp (°C)	EA	NMR	IR	MS	X-Ray
(**4.55**)[159]	3.8, 93	96	x	^1H	-	-	-
(**4.56**)[159]	3.2, 75	77	x	^1H	-	-	-
(**4.57**)[159]	3.4, 68	86	x	^1H	-	-	-
(**4.58**)[159]	3.1, 72	135	x	^1H	-	-	x
(**4.59**)[159]	2.9, 64	72	x	^1H	-	-	-
(**4.60**)[159]	3.1, 70	90	x	^1H	-	-	-

The diphenylalkylxanthatobismuth compounds were obtained in high yield and characterized by elemental analysis and ^1H NMR spectroscopy. An X-ray crystal structure of (**4.58**) was obtained and reveals a bridging *iso*-propylxanthate ligand which is unexpected since all preceding alkyldithiacarbamate, xanthate and dithiaphosphinate ligands are bidentate (*vide infra*). An explanation offered is that steric bulk and hydrogen bonding (C_{phenyl}-H···O) must be sufficient to overcome thermodynamically favorable ligand chelation.

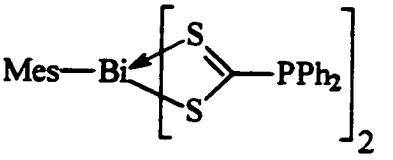
Characterization of alkylxanthatobismuth compounds is incomplete. Most notable is the paucity of reported yields. All compounds were isolated as crystals, however, X-ray crystal structures were obtained for only five compounds. The solid state

structures contain intermolecular coordinations from sulfur atoms to give rise to high coordination numbers and dimer or polymer formation.

An extensive series of *tris*(dialkyldithiaphosphinato)bismuth compounds, (**4.61**) - (**4.66**) was synthesized by the reaction of BiX_3 (X = Cl, NO_3) with the appropriate *O,O'*-dialkyldithiaphosphinate salt (see Figure 4.10 and Table 4.8).[160,161,162,163,164,165,166,167] The reaction of dimesitylbismuth bromide with one molar equivalent of ammonium diphenyldithiophosphinate unexpectedly forms the monosubstituted analogue of (**4.64**), (**4.67**) (see Figure 4.10).[168] X-ray crystal structures of (**4.61**), (**4.62**), (**4.64**) - (**4.67**) in addition to IR and ^{1}H NMR spectroscopy confirm the presence of bidentate dialkylphosphorodithioate ligands. Compounds (**4.61**) and (**4.64**) contain dimers which are connected through short intermolecular Bi···S contacts, whereas, compounds (**4.62**), (**4.64**)•C_6H_6, (**4.65**), (**4.66**) and (**4.67**) are monomeric in the solid state.



(4.61) - (4.66)



(4.67)

Compound	(4.61)	(4.62)	(4.63)	(4.64)	(4.65)	(4.66)
R	Me	Et	Pr^n	Ph	OEt	OPr^i

Figure 4.10. Proposed structures of *tris*(dialkyldithiaphosphinato)bismuth compounds, (**4.61**) - (**4.66**) and the disubstituted (diphenylxanthato)mesitylbismuth compound, (**4.67**).

Table 4.8. Analytical data for *tris*(dialkyldithiaphosphinato)bismuth compounds, $Bi(S_2PR_2)_3$.

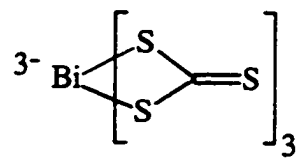
Compound	Reactants	Yield g, %	mp[dp] (°C)	EA	IR	NMR	UV	MS	X-Ray
(4.61)[160]	$BiCl_3$, NaS_2PMe_2	0.9, 62	242	-	x	^1H	-	x	x
(4.62)[161.162]	$BiCl_3$, $NaS_2PEt_2{\cdot}2H_2O$	6.3, 94	94.5	x	-	-	-	-	x
(4.63)[161]	$BiCl_3$, $NaS_2PPr^n_2$	-, 46	201.5	x	-	-	-	-	-
(4.64)[163.165]	$Bi(NO_3)_3$, NaS_2PPh_2	-, 75	-	x	x	-	x	-	x
(4.64)•C_6H_6[166]	(4.65), C_6H_6	-	-	-	-	-	-	-	x
(4.65)[166]	$BiCl_3$, $[NH_4][S_2POEt_2]$	-	-	-	-	-	-	-	x
(4.66)[167]	$BiCl_3$, $NH_4S_2POPr^i_2$	-	-	-	-	-	-	-	x
(4.67)[168]	Mes_2BiBr, $[NH_4][S_2PPh_2]$	0.2, 100	[180]	x	-	^1H	-	-	x

Mes = mesityl, 2,4,6-trimethylphenyl

Compound characterization, in general, was minimal for the dialkyldithiaphosphinatobismuth compounds. For example, elemental analysis was the only analytical technique reported for (**4.63**) and compounds (**4.64**)·C_6H_6, (**4.65**) and (**4.66**) were characterized by an X-ray crystal structure only and yields were not reported. Dimer formation is expected to be hindered by the presence of bulky ligands and, conversely, monomers are expected for compounds containing large bulky ligands. However, (**4.64**) which contains large phenyl groups is observed to be dimeric and

compounds (**4.62**) and (**4.66**) which contain small ligands are observed to be monomeric in the solid state. It is interesting to note that neither spectroscopic characterization nor yields were reported for (**4.64**) - (**4.66**).

Crystals of the ionic trithiocarbonatobismuth complex, $[PPh_4]_3[Bi(CS_3)_3]$ (**4.68**) (see Figure 4.11) were obtained from the reaction of $BiCl_3$ with potassium trithiocarbonate and aqueous tetraphenylphosphonium chloride.[169] Compound (**4.68**) was extensively characterized by elemental analysis, IR and Raman spectroscopy, a magnetic susceptibility measurement, X-ray powder diffraction and a single crystal X-ray structure. Chelation of the trithiocarbonate ligand was confirmed by the presence of characteristic patterns in the IR and Raman spectra of (**4.68**). An X-ray crystal structure confirmed that chelation was asymmetric and that the Bi-S bond lengths widely range from 2.643(7) to 3.029(7) Å in the capped octahedral monomers.



(**4.68**)

Figure 4.11. Structure of the trianion in (**4.68**).

The four-membered dithiabismuth heterocycles are comprised solely of monomeric chelate complexes. The formation of a large number of monoanionic dithia chelate complexes demonstrates a thermodynamic preference. Characterization was

minimal and often completely based on an X-ray crystal structure. Synthetic yields were rarely reported. Large coordination numbers and complex geometries result from intermolecular coordinations form sulfur and halogen atoms. Dimer and polymer formation are commonly observed in the solid state structures, although exceptions occur when the ligand alkyl groups are sterically encumbering.

4.1.2 Five-Membered Dithiabismuth Heterocycles

Preliminary results were obtained by the reactions of sodium bismuth citrate and ammonium bismuth citrate with 2,3-dimercapto-1-propanol to form organobismuth compounds described as therapeutically active.[170,171] The reaction of BiX_3 (X = Cl, Br) with equimolar amounts of 1,2-ethanedithiol in the presence of concentrated HCl yield the air and water-stable compounds, (**4.69**) and (**4.70**) (see Figure 4.12 and Table 4.9).[172] The exclusive solubility of compounds (**4.69**) and (**4.70**) in pyridine, a Lewis base, led to the conclusion that the compounds are coordination polymers in the solid state. In fact, crystalline pyridine coordination complexes, (**4.69**)•2pyr and (**4.70**)•2pyr (see Figure 4.12) were formed, however, X-ray crystal structures were not obtained. IR and Raman spectroscopic studies of liquid and crystalline samples of (**4.69**) and (**4.70**) confirm the *gauche* conformation of the ethanedithiolate ligands.[173] The absence of strong Bi-X stretching vibrations in the IR spectra in addition to the absence of the molecular ion in

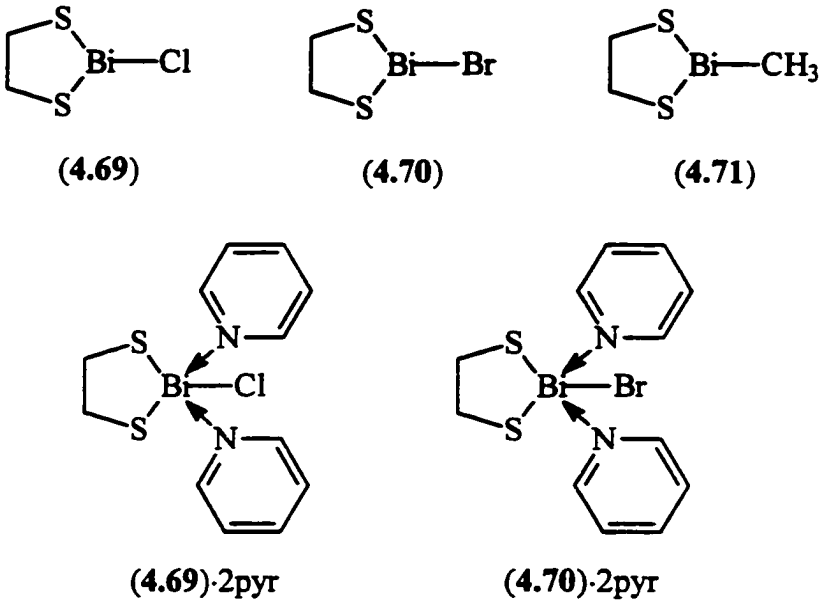


Figure 4.12. Proposed structures of dithiabismolanes, (**4.69**) - (**4.71**) and the pyridine adducts, (**4.69**)•2pyr and (**4.70**)•2pyr.

the mass spectrum of (**4.70**) and the presence dithiabismolanium cation as the most abundant peak indicates that (**4.69**) and (**4.70**) are ionic.[174]

The methyl derivative, (**4.71**) is obtained by the reaction of diethoxymethylbismuth with 1,2-ethanedithiol (see Figure 4.12 and Table 4.9).[175] Characterization by ^{1}H NMR spectroscopy and mass spectrometry confirm the heterocyclic structure. In contrast to the halogen analogues, (**4.69**) and (**4.70**), the molecular ion, $[\mathbf{4.71}]^+$ is observed in the MS as well as the dithiabismolanium cation, $[BiS_2C_2H_4]^+$.

Table 4.9. Analytical data for dithiabismolanes.

Compound	Reactants	Yield g, %	mp [dp] (°C)	EA	NMR	IR	Raman	MS	X-Ray
(**4.69**)[172,173,174]	$BiCl_3$, $HSCH_2CH_2SH$	37, 82	[120]	x	-	x	x	x	-
(**4.69**)•2pyr[172]	(**4.69**), pyridine	-	100-102	x	^{1}H	x	x	x	-
(**4.70**)[172,173]	$BiBr_3$, $HSCH_2CH_2SH$	19, 96	[155]	x	-	-	x	-	-
(**4.70**)•2pyr[172]	(**4.70**), pyridine	-	130-132	x	-	-	-	-	-
(**4.71**)[175]	$CH_3Bi(OEt)_2$, $HSCH_2CH_2SH$	2.5, 78	[100]	x	^{1}H	-	-	x	-

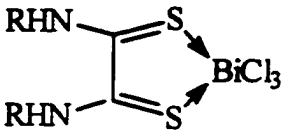
The dithiabismolanes have been synthesized in high yields and extensively characterized although techniques are limited due to inherent low solubility. MS provides additional evidence for the ionicity of the halodithiabismolanes by the absence

of the molecular ion and the simultaneous presence of a dithiabismolanium cation as the most abundant peak.

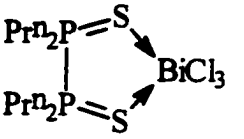
Reaction of $BiCl_3$ with a comprehensive series of dithiooxamides, RNHC(S)C(S)NHR under inert conditions, yields the five-membered dithiabismuth heterocycles, (**4.72**) - (**4.78**) (see Figure 4.13 and Table 4.10).[176] Crystals were obtained for each compound, however, their subsequent decomposition in the presence of air and water prevented single crystal X-ray analysis for all compounds, except for (**4.78**). The IR spectra confirm that the potential N-donor sites are not involved in complexation and that Bi-S bonds are formed by *cis*-S,S' ligand attachment. An X-ray crystal structure of (**4.78**) reveals a halide-bridged dimer in which each bismuth atom is chelated by one bidentate tetra-*n*-propyldiphosphane disulfide ligand.[177]

Table 4.10. Analytical data for coordination complexes of $BiCl_3$ which are dithiabismuth heterocycles.

Compound	Reactants	Yield g, %	mp (°C)	EA	NMR	IR	X-ray
(**4.72**)[176]	$BiCl_3$, $(SCNHMe)_2$	-	-	x	-	x	-
(**4.73**)[176]	$BiCl_3$, $(SCNHEt)_2$	-	-	x	-	x	-
(**4.74**)[176]	$BiCl_3$, $(SCNHPr^i)_2$	-	-	x	-	x	-
(**4.75**)[176]	$BiCl_3$, $(SCNHBu^n)_2$	-	-	x	-	x	-
(**4.76**)[176]	$BiCl_3$, $(SCNH\text{-}c\text{-}C_6H_{11})_2$	-	-	x	-	x	-
(**4.77**)[176]	$BiCl_3$, $(SCNHCH_2Ph)_2$	-	-	x	-	x	-
(**4.78**)[177]	$BiCl_3$, $Pr^n_2P(S)P(S)Pr^n_2$	7.4, 77	136-137	x	^1H, ^{31}P	x	x



(4.72) - (4.77)



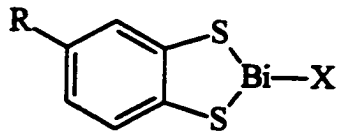
(4.78)

Compound	(4.72)	(4.73)	(4.74)	(4.75)	(4.76)	(4.77)
R	Me	Et	Pr^i	Bu^n	Cyc	CH_2Ph

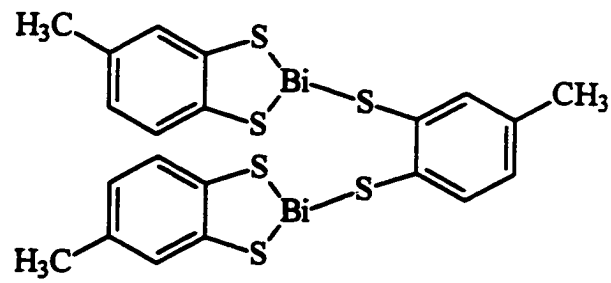
Figure 4.13. Proposed structures of coordination complexes of $BiCl_3$, (**4.72**) - (**4.77**) and monomeric unit of (**4.78**).

Only one five-membered dithiabismuth coordination complex was comprehensively characterized, otherwise, elemental analysis and IR spectroscopy were the only analytical methods used for characterization of compounds for which yields were not reported. Chelation of the bismuth atoms was confirmed by comparative IR spectroscopy. An X-ray crystal structure was obtained for one compound.

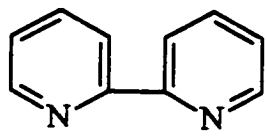
Mononuclear, monocyclic aryldithiabismolanes, (**4.79**) - (**4.82**) were synthesized by the reaction of equimolar amounts of BiX_3 (X = Cl, Br) or diethoxymethylbismuth with the appropriate aryldithiol (see Figure 4.14 and Table 4.11).[172,175,178] However, a bicyclic tethered derivative, (**4.83**) (see Figure 4.14) is obtained by the reaction of $BiCl_3$ with a two molar equivalent of 3,4-dimercaptotoluene.[179] Compounds (**4.80**) and (**4.81**) readily reacted with 2,2'-bipyridyl and with 1,10-phenanthroline to form 1:1 adducts. Molecular ions appear as the most abundant peak in the mass spectra of (**4.79**) and (**4.82**). Conductance and polarographic studies demonstrate (**4.83**) is a weak electrolyte but neither technique confirmed the proposed dimeric structure.



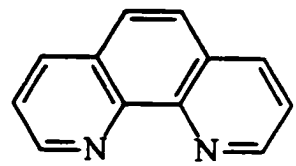
(4.79) - (4.82)



(4.83)



2,2'-bipyridyl



1,10-phenanthroline

Compound	R	X
(4.79)	H	Br
(4.80)	Me	Cl
(4.81)	Me	Br
(4.82)	Me	Me

Figure 4.14. Proposed structures of five-membered aryldithiabismuth heterocycles, (4.79) - (4.83) and structures of 2,2'-bipyridyl (bipy) and 1,10-phenanthroline (phen).

Table 4.11. Analytical data for aryldithiolate complexes of bismuth.

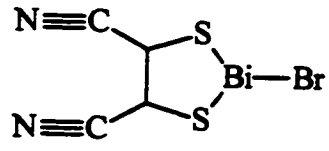
Compound	Reactants	Yield g, %	mp [dp] (°C)	EA	NMR	IR	Cond.	MS	X-Ray
(4.79)[178]	$BiBr_3$, $(HS)_2C_6H_4$	6.4, 43	-	x	^1H	x	-	x	-
(4.80)[172]	$BiCl_3$, $(HS)_2C_6H_3CH_3$	3.4, 86	233-234	x	-	-	-	-	-
(4.80)•2pyr[172]	**(4.80)**, pyridine	-	135-139	x	-	-	-	-	-
(4.80)•2,2'-bipy[172]	**(4.80)**, 2,2'-bipyridyl	0.5, 98	191-192	x	-	-	-	-	-
(4.81)[172]	$BiBr_3$, $(HS)_2C_6H_3CH_3$	-, 87	222-223	x	-	-	-	-	-
(4.81)•2,2'-bipy[172]	**(4.81)**, 2,2'-bipyridyl	-	[198-199]	x	-	-	-	-	-
(4.81)•1,10-phen[172]	**(4.81)**, 1,10-phen	-	-	x	-	-	-	-	-
(4.82)[175]	$CH_3Bi(OEt)_2$, $(HS)_2C_6H_3CH_3$	3.1, 82	185	x	^1H	-	-	x	-
(4.83)[179]	$BiCl_3$, $(HS)_2C_6H_3CH_3$	-	-	x	-	x	x	-	-

phen = 1,10-phenanthroline

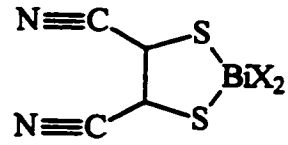
Reaction of $BiCl_3$ with a one molar amount of 3,4-dimercaptotoluene forms **(4.80)** in high yield, and the reaction of $BiCl_3$ with a two molar amount of 3,4-dimercaptotoluene results in the formation of the tethered bicyclic analogue, **(4.83)**.

Furthermore, compound (**4.83**) was not characterized by a yield, melting point or an X-ray crystal structure. Conductivity studies suggest that (**4.83**) is actually the monocyclic chloride compound, (**4.79**). X-ray crystal structures of the aryldithiabismuth compounds were not obtained, however, heterocycle formation was confirmed by MS, ^{1}H NMR and IR spectroscopy for three compounds. Six compounds were characterized by elemental analysis and a melting point only.

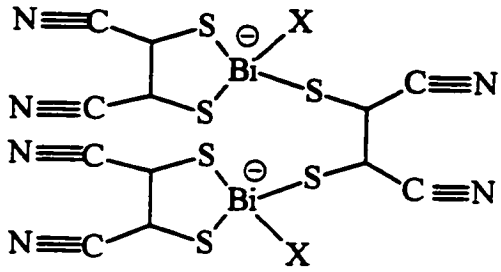
Dicyanoethylene-1,2-dithiabismuth complexes, (**4.84**) - (**4.91**) (see Figure 4.15 and Table 4.12) were synthesized by the reaction of BiX_3 (X = Cl, Br, I) with disodium dicyano-1,2-dithiolate followed by the addition of NEt_4Cl or $AsPh_4Cl$ (except for (**4.86**)) in an inert atomsphere.[178,179,180] Conductance studies in acetonitrile indicate that compounds (**4.84**), (**4.85**), (**4.87**) - (**4.91**) are strong electrolytes, however, dimerization could not be confirmed. Nonetheless, proposed structures are described as dimers in which the bismuth atoms are bridged by two dithiolate ligands. Polarographic studies demonstrate that (**4.84**), (**4.85**), (**4.87**) - (**4.91**) could undergo reversible electron-transfer reactions. The presence of the molecular ion as the most abundant peak in the MS suggests that (**4.86**) is molecular. An X-ray crystal structure of [$AsPh_4$][**4.91**] reveals coordination polymer formation by bridging intermolecular Bi···S contacts. Each bismuth atom has pentagonal bipyramidal coordination geometry in which a stereochemically active lone pair occupies an equatorial position.



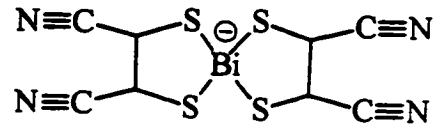
(4.84)



(4.85) - (4.87)



(4.88) - (4.90)



(4.91)

Compound	(4.84)	(4.85)	(4.86)	(4.87)	(4.88)	(4.89)
X	Cl	Br	I	Cl	Br	I

Figure 4.15. Proposed structures of dicyanoethylene-1,2-dithiabismuth complexes, (4.84) - (4.90) and the bicyclic anion in (4.91).

Table 4.12. Analytical data for dicyanoethylene-1,2-dithiabismuth complexes.

Compound	Reactants	Yield g, %	mp (°C)	EA	IR	Cond.	MS	X-Ray
(4.84)[178]	$BiBr_3$, $Na_2S_2C_2(CN)_2$	0.6, 54	-	x	x	-	x	-
$[NEt_4]_2$ **(4.85)**[179]	$BiCl_3$,$Na_2S_2C_2(CN)_2$, NEt_4Cl	-	-	x	x	x	-	-
$[NEt_4]_2$**(4.86)**[179]	$BiBr_3$,$Na_2S_2C_2(CN)_2$, NEt_4Cl	-	-	x	x	x	-	-
$[NEt_4]_2$ **(4.87)**[179]	BiI_3, $Na_2S_2C_2(CN)_2$, NEt_4Cl	-	-	x	x	x	-	-
$[NEt_4]_2$**(4.88)**[179]	$BiCl_3$,$Na_2S_2C_2(CN)_2$, NEt_4Cl	-	-	x	x	x	-	-
$[NEt_4]_2$**(4.89)**[179]	$BiBr_3$,$Na_2S_2C_2(CN)_2$, NEt_4Cl	-	-	x	x	x	-	-
$[NEt_4]_2$**(4.90)**[179]	BiI_3, $Na_2S_2C_2(CN)_2$, NEt_4Cl	-	-	x	x	x	-	-
$[NEt_4]$**(4.91)**[179]	$BiCl_3$,$Na_2S_2C_2(CN)_2$, NEt_4Cl	-	-	x	x	-	-	-
$[AsPh_4]$**(4.91)**[180]	$BiCl_3$,$Na_2S_2C_2(CN)_2$, $AsPh_4Cl$	-	-	-	-	-	-	x

Speculation on structural information for **(4.84)**, **(4.85)**, **(4.87)** - **(4.91)** was extensive, yet elemental analysis and molar conductance studies (the only characterization techniques reported) do not provide conclusive structural evidence. Furthermore, yields

and X-ray crystal structures were not obtained. In contrast to the ionic analogues, (**4.70**) and (**4.81**), (**4.86**) is molecular in solution.

Although, there are many examples of five-membered dithiabismuth heterocycles, X-ray crystal structures were obtained for only four compounds. Examination of the solid state structures reveals high coordination numbers and polymer formation. Monocyclic halogen dithiabismuth heterocycles were found to be ionic, however, there are exceptions. Adduct formation was observed to occur with nitrogenous Lewis bases only which can be rationalized by the hard and soft acid-base theory.[90]

4.1.3 Dithiabismuth Heterocycles with Ring Sizes Greater than Five

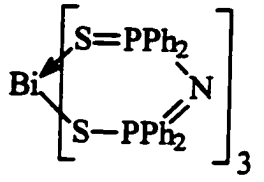
There are few examples of dithiabismuth heterocycles with ring sizes greater than five which is perhaps reflective of the relative thermodynamic stability of five-membered organometallic heterocycles. Synthetic methods are straight-forward and rapid to yield air-stable yellow powders.

Compound (**4.92**) (see Figure 4.16 and Table 4.13) is the only example of a six-membered dithiabismuth heterocycle and is formed by the reaction of $Bi(NO_3)_3$ with $K[SPPh_2NPPh_2S]$.[87] Solution ^{31}P NMR spectroscopic data allowed for the prediction that (**4.92**) is highly symmetric and the lone pair is stereochemically inactive. An X-ray crystal structure reveals a slightly distorted octahedral coordination geometry for the bismuth atoms in the solid state.[181]

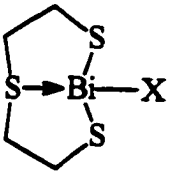
Compound (**4.93**) (see Figure 4.16 and Table 4.13) is a pure bismuth sulfide with a unique tetracyclic tethered structure and is also air and water-stable.[182] An X-ray crystal

structure of $[AsPh_4]_4$[**4.96**] was obtained and reveals an ionic structure in which the $[Bi_2S_{34}]^{4-}$ anion is linked by an S_6^{2-} chain which links two bismuth atoms together which are each chelated by two S_7^{2-} ligands. The coordination geometry around each bismuth atom is described as a distorted square pyramidal and the stereochemically active lone pair on each bismuth center occupies an axial position.

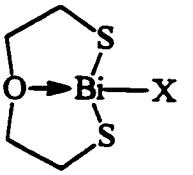
A series of dithiabismocanes (**4.94**) - (**4.99**) (see Figure 4.16 and Table 4.13) was synthesized by reacting $BiCl_3$ or $RBi(OEt)_2$ (R = Me, Ph) with $(HSCH_2CH_2)X$, (X = S, O).[183,184,185] IR spectroscopic and mass spectrometric studies of (**4.95**) - (**4.99**) confirm ligand chelation and indicate that the compounds are molecular. An X-ray crystal structure of (**4.99**) reveals a short intra-ring Bi···O coordination and two long Bi···S intermolecular coordinations which render the bismuth center six-coordinate.



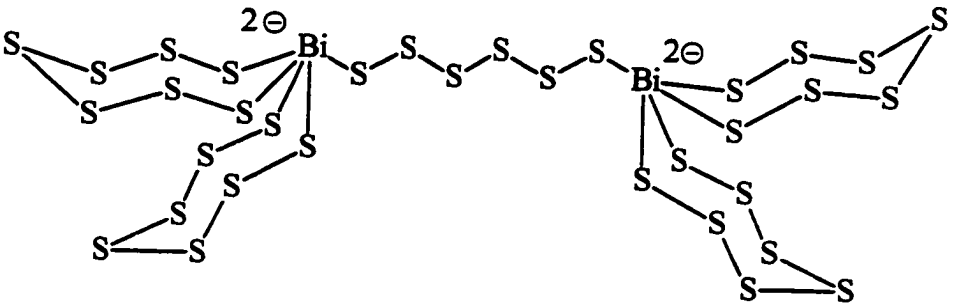
(4.92)



(4.94) - (96)



(4.97) - (4.99)



(4.93)

Compound	(4.94)	(4.95)	(4.96)	(4.97)	(4.98)	(4.99)
X	Cl	Me	Ph	Cl	Me	Ph

Figure 4.16. Proposed structures of dithiabismuth heterocycles with ring sizes greater than five, (4.92) - (4.99).

Table 4.13. Analytical data for dithiabismuth heterocycles with ring sizes greater than five.

Compound	Reactants	Yield g, %	mp[dp] (°C)	EA	NMR	IR	Raman	MS	X-Ray
(4.92)[87]	$Bi(NO_3)_3$, $K[SPPh_2NPPh_2S]$	0.4, 57	235-236	x	^{31}P	-	-	-	x[181]
$[PPh_4]_4$**(4.93)**[182]	$BiCl_3$, H_2S, Ph_4PCl, S_8	-	-	-	-	-	-	-	-
$[AsPh_4]_4$[**(4.93)**[182]	$BiCl_3$, H_2S, Ph_4AsCl, S_8	0.6, ~60	-	-	-	x	x	-	x
(4.94)[183]	$BiCl_3$, $(HSC_2H_4)_2S$	-	[120]	x	-	x	x	x	-
(4.95)[184]	$MeBi(OEt)_2$, $(HSC_2H_4)_2S$	2.8, 80	141	x	^{13}C	x	x	x	-
(4.96)[184]	$PhBi(OEt)_2$, $(HSC_2H_4)_2S$	0.4, 18	125	x	^{13}C	x	x	x	-
(4.97)[185]	$BiCl_3$, $(HSC_2H_4)_2O$	-, ~60	[75]		-				-
(4.98)[184]	$MeBi(OEt)_2$, $(HSC_2H_4)_2O$	2.5, 69	132	x	^{13}C	x	x	x	-
(4.99)[184]	$PhBi(OEt)_2$, $(HSC_2H_4)_2O$	1.7, 79	150	x	^{13}C	x	x	x	x

Compounds **(4.92)** - **(4.99)** were obtained in high yields and are air and water-stable. The solid state structure of **(4.99)** contains long intermolecular coordinations from

sulfur to bismuth atoms, however, the molecules remain monomeric. The cross-ring donation within the eight-membered rings provides structural stabilization and is likely responsible for the five-membered ring fragmentation in the mass spectra of compounds (**4.95**) - (**4.99**).

4.2 Results and Discussion

4.2.1 Introduction

The prevalence and structural simplicity evident for dithiabismuth heterocycles highlight them as ideal candidates for systematic study. Metathesis of BiX_3, X = Cl, Br, I, NO_3, CH_3COO was employed to generate a comprehensive series of monoheterocyclic dithiabismuth halides of varying ring size (**4.69**), (**4.70**), (**4.94**), (**4.97**), (**4.100**) - (**4.104**) (see Figure 4.17), as well as a series of tethered bicyclic systems (**4.105**) - (**4.109**) (see Figure 4.18). Characterization by X-ray crystallography and vibrational spectroscopy establishes the structural simplicity of these compounds. The systematic relationships within the series has allowed for an extensive mass spectrometric study which reveals the prominence of bismuthenium cations.

4.2.2 Synthesis and Characterization of Dithiabismuth Heterocycles

Powell first recognized the rapid, high-yield reaction between BiX_3 (X = Cl, Br) and ethanedithiol, and characterized the products as (**4.69**) and (**4.70**), and their pyridine

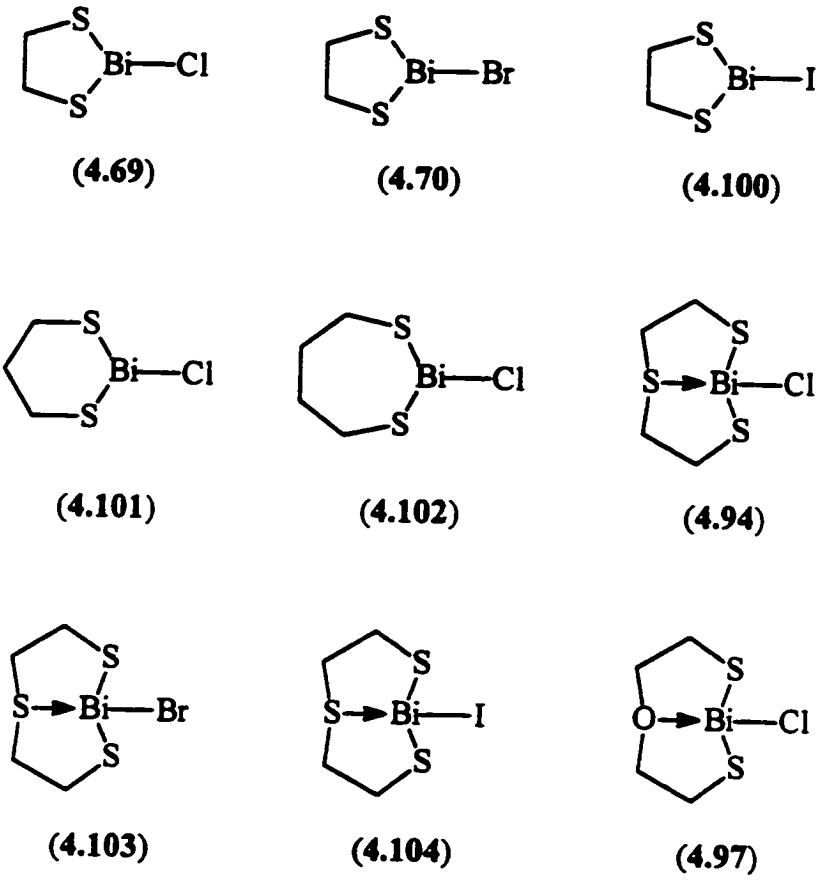
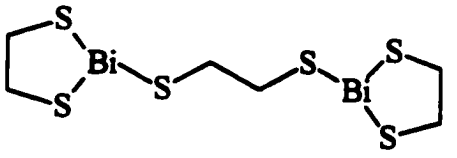
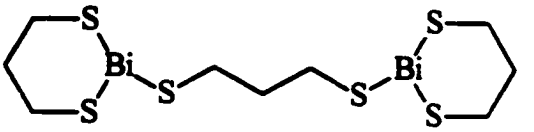


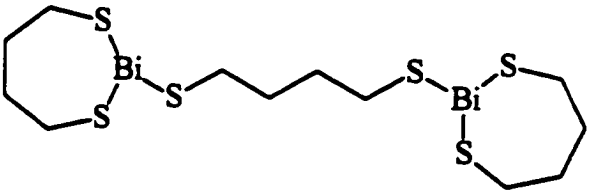
Figure 4.17. Proposed structures of the series of halodithiabismuth heterocycles, (4.69), (4.70), (4.94), (4.97), (4.100) - (4.104).



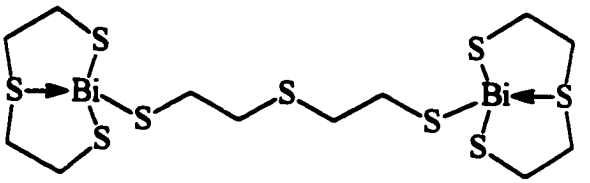
(4.105)



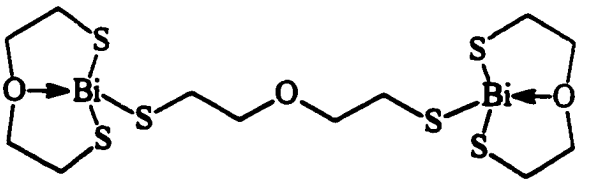
(4.106)



(4.107)



(4.108)

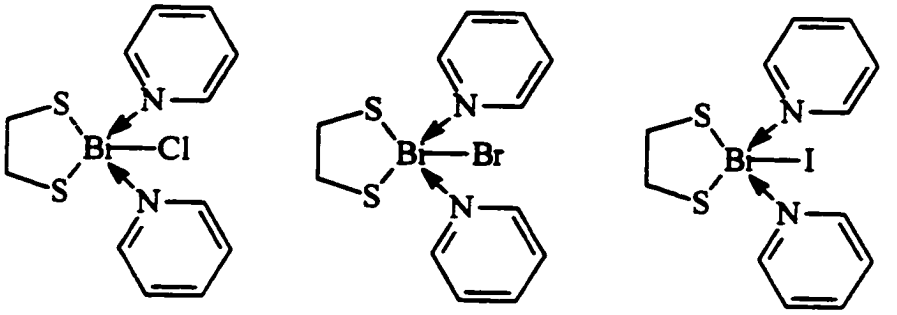


(3.109)

Figure 4.18. Proposed structures of the series of tethered dithiabismuth heterocycles, (4.105) - (4.109).

complexes, (**4.69**)•2pyr and (**4.70**)•2pyr by elemental analysis and IR spectroscopy.[172,173] These observations have been confirmed with a comprehensive characterization of (**4.69**), (**4.70**), (**4.69**)•2pyr and (**4.70**)•2pyr. More importantly, the general quantitative metathesis reaction has been exploited to generate a series of cyclic chloro, bromo and iododithiabismuth compounds (**4.69**), (**4.70**), (**4.94**), (**4.97**), (**4.100**) - (**4.104**) with increasing ring size. As a modification of Powell's procedure, all reactions occur in the absence of acid. Moreover, BiOCl is demonstrated to be the actual reactant by the observation that (**4.69**) is formed in high yield from the reaction of BiOCl with 1,2-ethanedithiol.[186] A formal double metathesis at each bismuth site is inferred in all cases, and the cyclic structures of compounds (**4.69**) and (**4.70**) (as the dipyridyl complexes, (**4.69**)•2pyr and (**4.70**)•2pyr), (**4.94**), (**4.97**), (**4.105**) and (**4.107**) are confirmed by X-ray crystallography. The spectroscopic data for uncomplexed bismolanes (**4.69**), (**4.70**) and (**4.100**); bismane (**4.101**); bismepane (**4.102**); and bismocanes (**4.94**), (**4.97**) and the pyridine complexes, (**4.69**)•2pyr, (**4.70**)•2pyr and (**4.100**)•2pyr (see Figure 4.19) are consistent with the cyclic structure (see Tables 7.6, 7.9 and 7.11). X-ray quality crystals were not obtained for compounds (**4.69**), (**4.70**), (**4.100**), (**4.100**)•2pyr, (**4.101**) - (**4.104**), (**4.106**), (**4.107**) and (**4.109**).

When $Bi(NO_3)_3$ or $Bi(CH_3COO)_3$ are combined with 1,2-ethanedithiol, 1,3-propanedithiol, 1,4-butanedithiol, mercaptoethyl sulfide and mercaptoethyl ether, a complete metathesis is observed to give three Bi-S bonds at each bismuth site, including a cyclic or chelate formation of the analogous compounds, (**4.105**) - (**4.109**), respectively.



(**4.69**)·2pyr (**4.70**)·2pyr (**4.100**)·2pyr

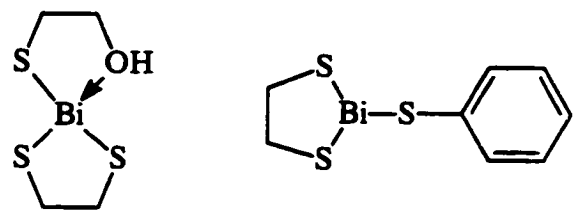
Figure 4.19. Structures of the pyridine complexes, (**4.69**)•2pyr, (**4.70**)•2pyr and (**4.100**)•2pyr.

The compounds are assigned the tethered bicyclic structures (**4.105**) - (**4.109**) on the basis of the X-ray structures of (**4.105**) and (**4.108**), and comparative analytical data for the series of compounds (**4.105**) - (**4.109**) (see Tables 7.6 and 7.11). The formation of all dithiabismuth heterocycles, (**4.69**), (**4.94**), (**4.97**), (**4.100**) - (**4.109**) occurs independent of stoichiometry, illustrating a dominant thermodynamic preference for the Bi-S bond formation and suggesting that the halo-substituted monocyclic derivatives are kinetically stable with respect to the tethered bicyclic analogues in the presence of excess dithiol. Indeed, compound (**4.69**) can been quantitatively tethered to give (**4.105**) by refluxing in ethanedithiol and also upon introduction of sodium nitrate in the presence of ethanedithiol, which presumably facilitates tethering by promoting Bi-Cl heterolytic bond cleavage. This is a general process allowing for tethering of all heterocycles (**4.69**), (**4.94**), (**4.97**), (**4.101**), (**4.102**) to form (**4.105**) - (**4.109**) and the possibility of the tether having a different chain length than the heterocycle. In addition, compound (**4.105**) can be obtained by refluxing the tethered bismane (**4.106**) in ethanedithiol, expressing the thermodynamic preference for five-membered inorganic ring formation.

The utility of heterolytic Bi-Cl bond cleavage facilitated by the addition of sodium nitrate to an aqueous solution of (**4.69**), was exploited to obtain 2-thioethanol-1,3-dithia-2-bismolane (**4.110**) and 2-phenylthiolato-1,3-dithia-2-bismolane (**4.111**) (see Figure 4.20) by the subsequent addition of mercaptoethanol and thiophenol, respectively. Compound (**4.110**) can also be synthesized by addition of an equimolar amount of ethanedithiol to an aqueous solution of bicyclic bis-(2-hydroxyethanethiolato)bismuth nitrate (**3.15**) (generated *in situ* by the reaction of $Bi(NO_3)_3$ and mercaptoethanol). The

bicyclic structure of (**4.110**) was assigned on the basis of an X-ray crystal structure, elemental analysis and comparative spectroscopic data.

Preliminary assignment of 2-phenylthiolato-1,3-dithia-2-bismolane (**4.111**) was made on the basis of comparative spectroscopic data which reveals a heterocyclic structure and the presence of the phenylthiolate ligand. Inherently low solubility of (**4.111**) in common organic solvents such as DMSO, toluene and pyridine restricts crystal growth and many characterization techniques such as solution NMR spectroscopy, APCI MS and X-ray crystal structure analysis. Further characterization may be achieved by EI MS, for chemical composition and structural confirmation of (**4.111**).



(**4.110**) (**4.111**)

Figure 4.20. Proposed structures of derivatives of (**4.69**), (**4.110**) and (**4.111**).

4.2.3 Structural Features

Compounds (**4.69**), (**4.70**), (**4.94**), (**4.97**), (**4.100**) - (**4.110**) have very low solubilities in most solvents, but anomalous is the dissolution of (**4.69**), (**4.70**) and (**4.100**) in pyridine. Needlelike crystals of (**4.69**)•2pyr, (**4.70**)•2pyr and (**4.70**)•2pyr can

be obtained, which slowly release pyridine and lose crystallinity. The X-ray structure of (**4.69**)•2pyr reveals a dipyridyl complex of (**4.69**) with the pyridine ligands in a *trans* orientation with respect to a distorted square plane formed by the S_2C_2 chelate ring and two chlorine atoms (see Figure 4.21). The chlorine centers are dicoordinate with essentially equivalent [3.111(4) and 3.231(5) Å] Bi-Cl bonds, providing an alternating Bi-Cl polymeric backbone which links the heterocycles. The bond lengths are substantially longer than terminal Bi-Cl bonds and are comparable with reported bridging bonds.[105,177,187,188,189] A seventh coordination site is imposed by a contact to a sulfur atom of a neighboring heterocycle. This intermolecular contact is longer [3.443(5) Å] than the two equivalent endocyclic Bi-S bonds [2.545(4) and 2.542(6) Å]. The Bi-N bonds are similar [2.534(8) and 2.592(9) Å] and are typical of N→Bi coordinate bonds.[112,115,189,190,191,192]

Similarly, compound (**4.70**)•2pyr is a dipyridyl complex but can be described as a monomeric base-stabilized bismolanium cation (see Figure 4.22). The two pyridine ligands are *trans* to each other and equivalently coordinated to the bismuth center [2.55(2) Å] and coplanar. The Bi-Br bond [3.264(3) Å] is substantially longer than both terminal and bridging Bi-Br bonds.[193,194] The two endocyclic Bi-S bonds are similar [2.536(5) and 2.550(7) Å] and are comparable to the endocyclic Bi-S bonds in (**4.69**)•2pyr [2.545(4) and 2.542(6) Å]. Three intermolecular contacts from two bromine atoms and one sulfur atom give rise to a pentagonal bipyramidal coordination geometry about the bismuth center, in which the pyridine ligands occupy the axial positions.

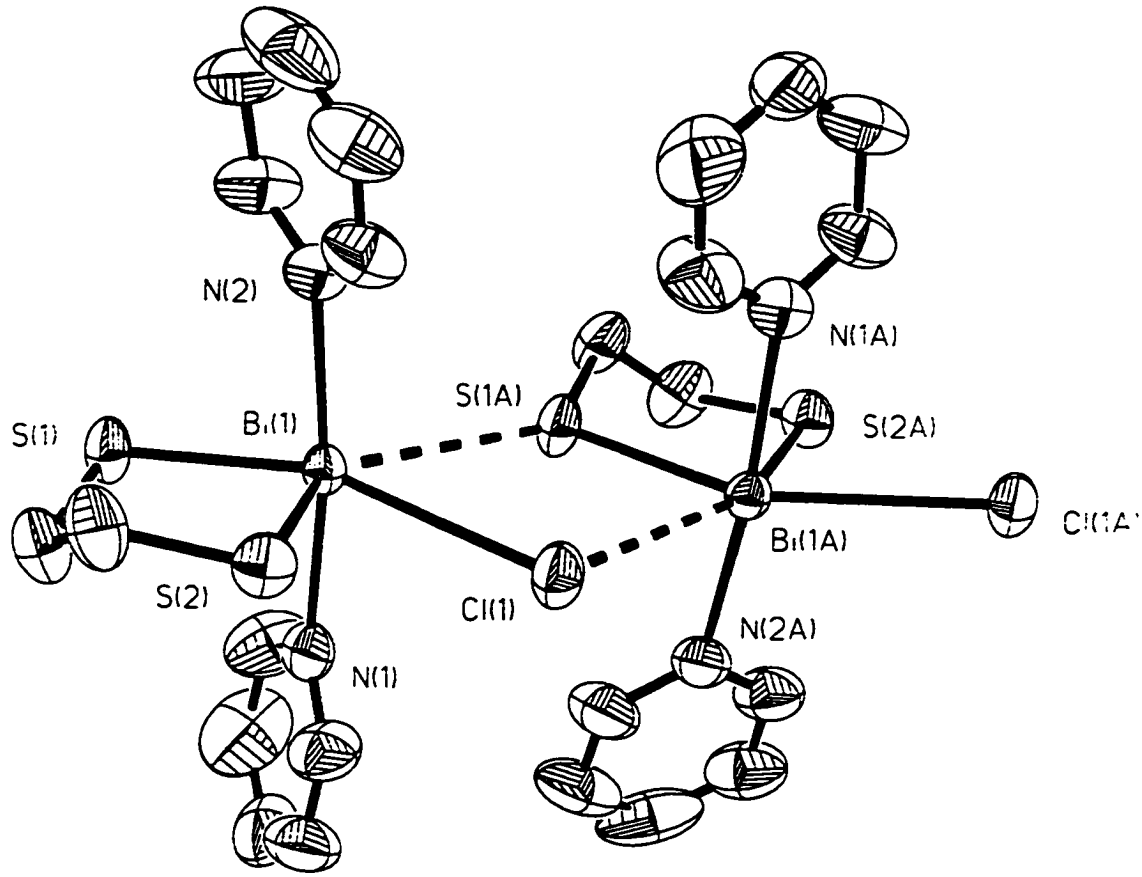


Figure 4.21. Crystallographic view of (**4.69**)•2pyr. Selected bond lengths (Å) and angles (°): Bi(1)-S(1) 2.545(4), Bi(1)-S(2) 2.542(6), Bi(1)-Cl(1) 3.111(4), Bi(1)-N(1) 3.534(8), Bi(1)-N(1) 2.592(9), Bi(1)-S(1a) 3.443(5), Bi(1)-Cl(1a) 3.231(5), S(1)-Bi(1)-S(2) 84.8(2). Cl(1)-Bi(1)-S(1) 157.26(9), Cl(1)-Bi(1)-S(2) 75.3(2), N(1)-Bi(1)-N(2) 173.1(4), Cl(1)-Bi(1)-N(1) 82.8(4), Cl(1)-Bi(1)-N(2) 101.9(3).

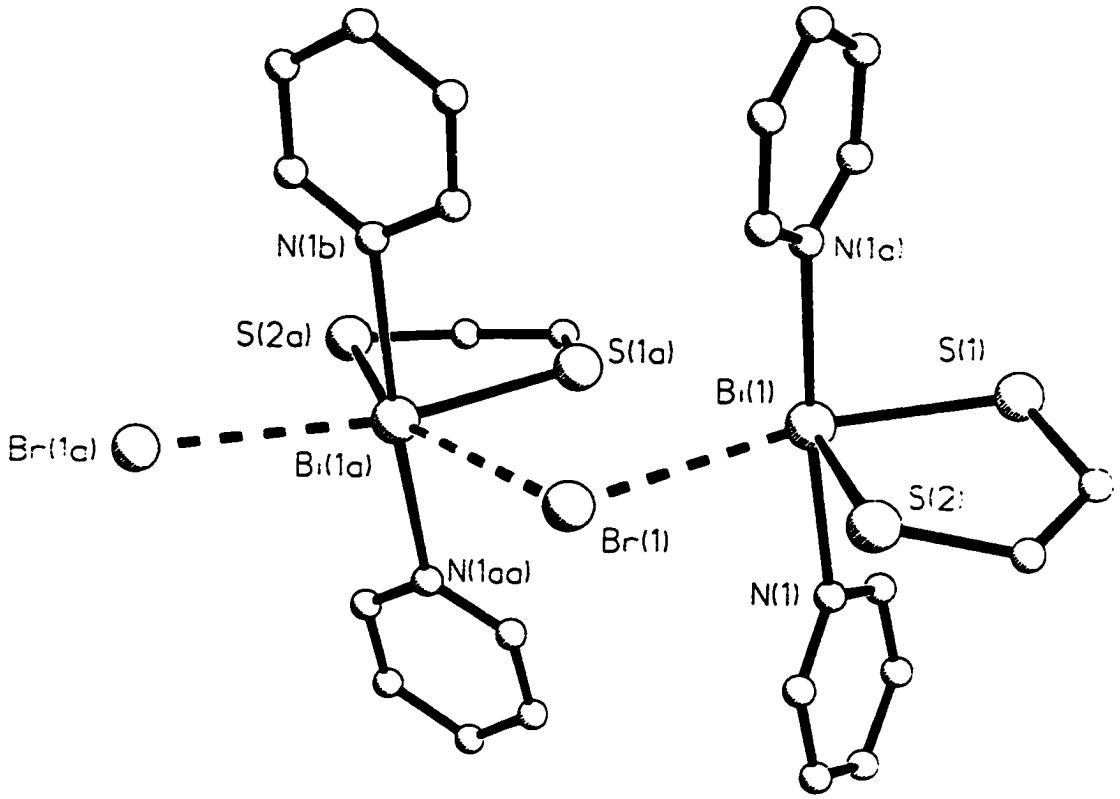


Figure 4.22. Crystallographic view of (**4.70**)•2pyr showing the bromide counterions coordinating to the base-stabilized bismuthenium cations. Selected bond lengths (Å) and angles (°): Bi(1)-S(1) 2.550(7), Bi(1)-S(2) 2.536(5), Bi(1)-Br(1) 3.264(3), Bi(1)-N(1) 2.55(2), Bi(1)-N(1a) 2.55(2), Bi(1)-S(1a) 3.488, Bi(1)-Br(1a) 3.356(5), S(1)-Bi(1)-S(2) 84.5(4), Br(1)-Bi(1)-S(1) 159.8(2), Br(1)-Bi(1)-S(2) 75.3(4), N(1)-Bi(1)-N(1a) 175.4(11), Br(1)-Bi(1)-N(1) 91.5(6), Br(1)-Bi(1)-N(1a) 91.5(6).

Compounds (**4.94**), (**4.97**), (**4.105**) and (**4.108**) have been crystallized free of solvent and show molecular and intermolecular interactions. Compounds (**4.94**) and (**4.97**) (see Figure 4.17) are isostructural and can be viewed as eight-membered heterocycles with a cross-ring 2,6 intramolecular interaction, involving a coordinative donation from sulfur (in (**4.94**), or oxygen in (**4.97**)) to bismuth (see Figure 4.23), which is a well established structural arrangement for many nonmetal elements.[195] Consistent with this bonding model, the two symmetry-related heterocyclic Bi-S bonds [2.541(6) Å] of (**4.94**) are slightly shorter than the cross-ring Bi-S bond [2.849(5) Å], and are comparable to the endocyclic Bi-S bonds in (**4.69**)•2pyr [2.545(4) and 2.542(6) Å] and (**4.70**)•2pyr [2.536(5) and 2.550(7) Å]. Three intermolecular contacts from chlorine and the sulfur centers of a neighboring molecule impose a seven-coordinate environment for bismuth. The structures are fundamentally analogous to those reported for the phenyl derivative of (**4.97**), (**4.99**) and the corresponding arsocane and stibocanes with expected bond length and bond angle distortions.[183,196,197]

Two structurally identical molecules are observed in the asymmetric unit for (**4.105**) (see Figure 4.24), and its tethered bicyclic structure is similar to that of (**4.108**) (see Figure 4.25) in that they both possess essentially equivalent Bi-S bond lengths within the heterocycle [one molecule of (**4.105**), 2.565(7), 2.591(7), 2.552(7), 2.553(7) Å; (**4.108**), 2.597(5), 2.559(4), 2.576(4), 2.599(4) Å] and for the exocyclic tether linkages [(**4.105**), 2.633(7), 2.635(7) Å; (**4.108**), 2.615(4), 2.566(5) Å]. The cross-ring S→Bi contacts observed in the structure of (**4.94**) are also evident in the rings of (**4.108**),

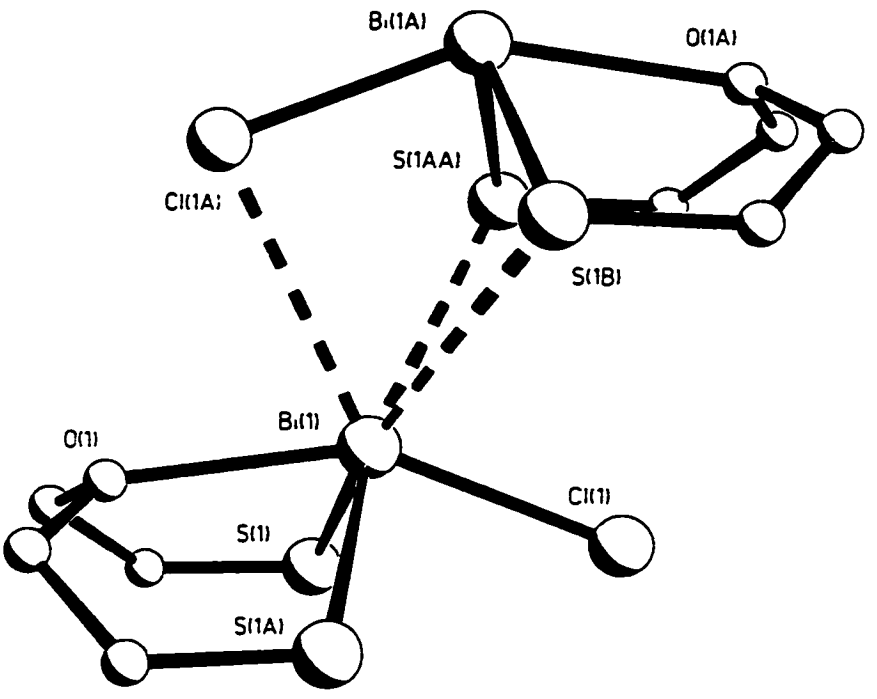


Figure 4.23. Crystallographic view of two molecules of (**4.97**) showing intermolecular coordinations from sulfur and chlorine atoms. Compound (**4.94**) is isostructural. Selected bond lengths (Å) and angles (°) for (**4.94**): Bi(1)-S(1) 2.849(5), Bi(1)-S(2) 2.541(6), Bi(1)-Cl(1) 2.682(5), Bi(1)-S(1b) 3.534(7), Bi(1)-Cl(1a) 3.285(6), S(1)-Bi(1)-S(2) 79.0(1), Cl(1)-Bi(1)-S(1) 155.3(2), Cl(1)-Bi(1)-S(2) 85.2(1), S(1)-Bi(1)-S(1a) 99.4(3); for (**4.97**): Bi(1)-O(1) 2.52(4), Bi(1)-S(1) 2.578(12), Bi(1)-Cl(1) 2.58(2), Bi(1)-S(1b) 3.383(1), Bi(1)-Cl(1a) 3.304(1), O(1)-Bi(1)-S(1) 75.0(7), Cl(1)-Bi(1)-O(1) 149.9(12), Cl(1)-Bi(1)-S(1) 86.1(4), S(1)-Bi(1)-S(1a) 100.6(6).

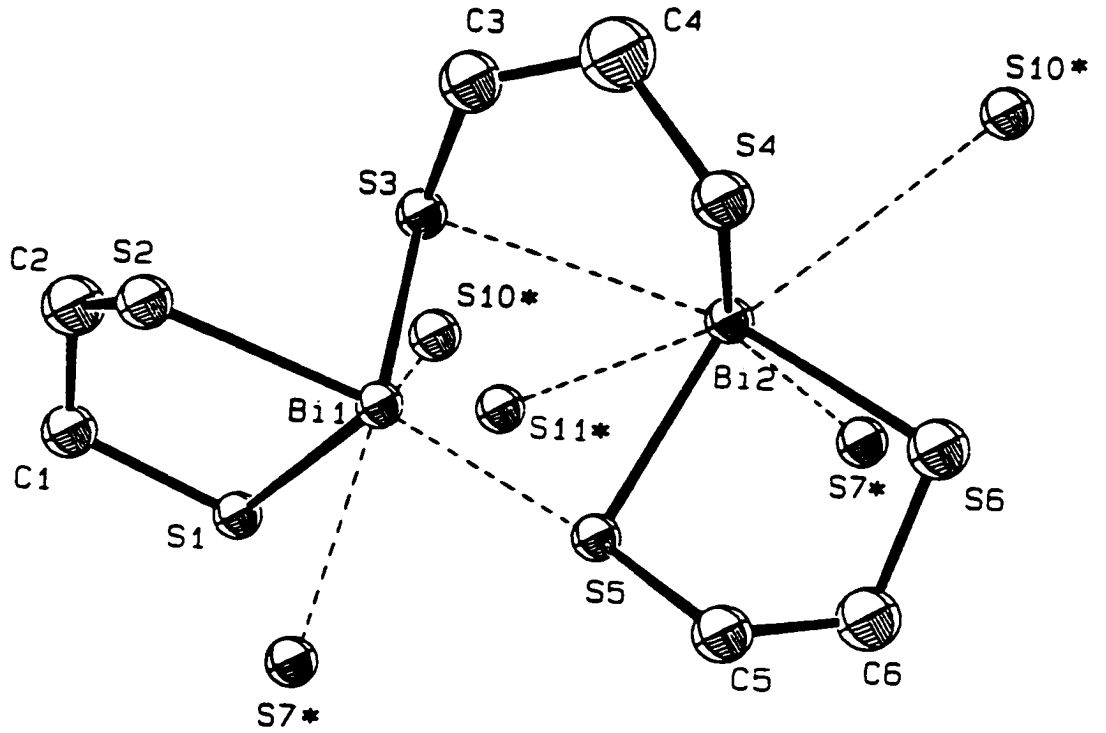


Figure 4.24. Crystallographic view of one of two independent molecules in the unit cell of (**4.105**) showing inter and intramolecular coordinations to the bismuth sites. Selected bond lengths (Å) and angles (°) for one independent molecule in the asymmetric unit: Bi(3)-S(7) 2.580(7), Bi(3)-S(8) 2.540(6), Bi(3)-S(9) 2.665(7), Bi(3)-S(11) 3.2824(9), Bi(4)-S(10) 2.643(6), Bi(4)-S(11) 2.554(7), Bi(4)-S(12) 2.550(7), Bi(4)-S(9) 3.1771(9), S(7)-Bi(3)-S(8) 83.2(2), S(7)-Bi(3)-S(9) 82.6(2), S(8)-Bi(3)-S(9) 94.2(2), S(10)-Bi(4)-S(11) 100.3(2), S(10)-Bi(4)-S(12) 87.1(2), S(11)-Bi(4)-S(12) 85.0(2).

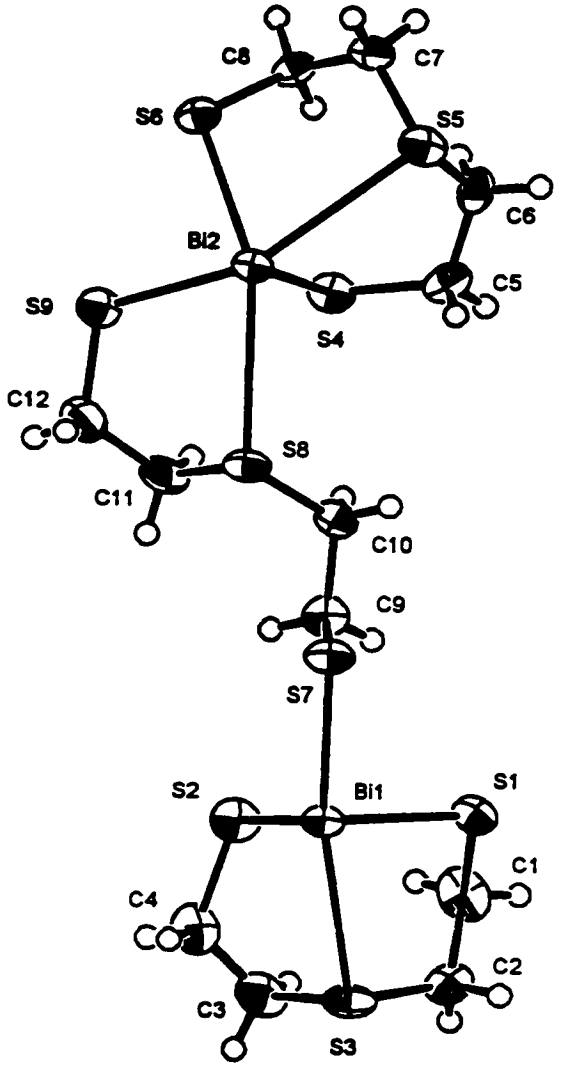


Figure 4.25. Crystallographic view of (**4.108**) showing the cross-ring donation to the bismuth centers. Selected bond lengths (Å) and angles (°): Bi(1)-S(1) 2.597(5), Bi(1)-S(2) 2.559(4), Bi(1)-S(9) 3.017(5), Bi(1)-S(7) 2.615(4), Bi(2)-S(4) 2.576(4), Bi(2)-S(5) 3.197(5), Bi(2)-S(6) 2.599(4), Bi(2)-S(8) 3.192(4), Bi(2)-S(9) 2.566(5), S(1)-Bi(1)-S(2) 94.2(2), S(1)-Bi(1)-S(3) 75.5(1), S(2)-Bi(1)-S(7) 95.6(2), S(4)-Bi(2)-S(6) 93.9(1), S(4)-Bi(2)-S(9) 93.5(2), S(5)-Bi(2)-S(6) 74.2(1), S(6)-Bi(2)-S(9) 81.7(2), S(8)-Bi(2)-S(9) 75.9(1).

although they are slightly longer [(**4.94**), 2.849(5) Å; (**4.108**), 3.071(5), 3.197(4) Å]. In addition, donations from the tether sulfur centers to a bismuth site are observed in both (**4.105**) and (**4.108**), which effect the folding or wrapping of the tether. It is interesting to note the five-membered ring motif that is generated by most of the intramolecular interactions. The presence of the five-membered ring is likely responsible for the onset of five-membered ring fragmentation in the mass spectra. The intermolecular and intramolecular contacts provide for six and seven-coordinate bismuth environments. The observed structure of (**4.105**) is consistent with the previously reported structure of the antimony analogue, and is reminiscent of a diazabismuth derivative.[198,199]

The hydroxyethanethiol derivative, (**4.110**) is bicyclic due to the auxiliary coordination of the hydroxyl group to the bismuth center, and is consistent with the bicyclic framework noted for the series of bicyclic bis-(2-hydroxyethanethiolato)bismuth complexes.[106,107,108,110] The endocyclic Bi-S bonds [2.53(2) and 2.55(2) Å] are equivalent and slightly shorter than the Bi-S and Bi···O bonds [2.63(2) and 2.64(2) Å] in the coordinative hydroxyethanethiolate ligand. Three additional intermolecular contacts from sulfur atoms render the bismuth atom seven-coordinate.

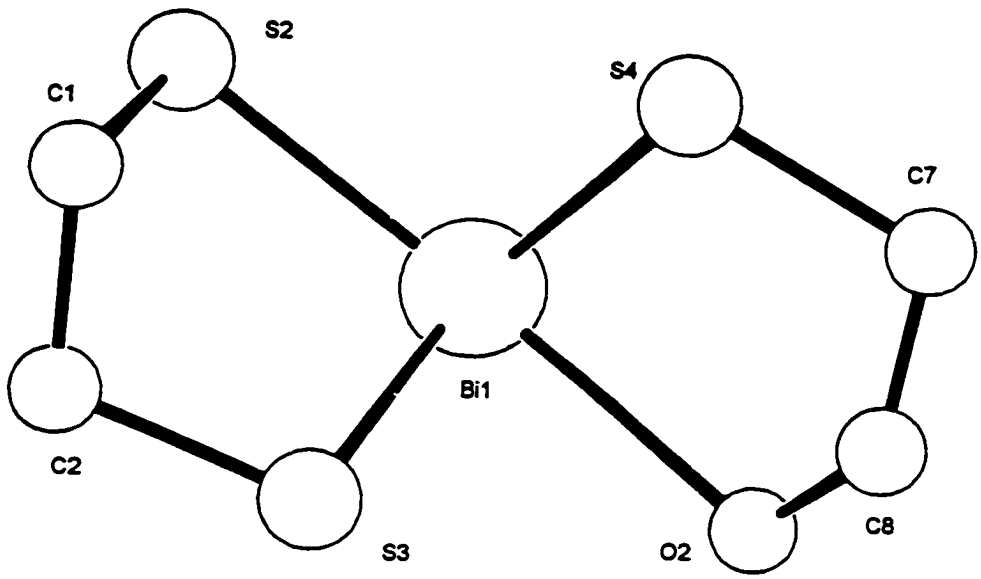


Figure 4.26. Crystallographic view of (**4.110**). Selected bond lengths (Å) and angles (°): Bi(1)-S(1) 2.52(1), Bi(1)-S(2) 2.62(1), Bi(1)-S(3) 2.52(2), Bi(1)-O(1) 2.64(5), Bi(1)-S(3a) 3.50(1), S(1)-Bi(1)-S(2) 85.7(2), S(1)-Bi(1)-S(3) 93.1(4), S(2)-Bi(1)-S(3) 90.7(4), S(1)-Bi(1)-O(1) 74(1), S(2)-Bi(1)-O(2) 154.1(8), S(3)-Bi(1)-O(2) 74(1).

4.2.4 Mass Spectrometric Features

Electron ionization (EI) mass spectra were obtained for compounds (**4.69**), (**4.94**), (**4.97**), (**4.101**), (**4.102**); the data are summarized in Table 7.7. Molecular ions are observed for (**4.69**), (**4.94**) and (**4.97**). The presence of a strong molecular ion $M^{\bullet+}$ for (**4.69**) as well as the major fragment ion $[M - Cl]^+$ have been confirmed by accurate mass measurements ($M^{\bullet+}$, $BiC_2ClH_4S_2$ m/z 335.9237, d = 2.9 ppm; $[M - Cl]^+$, $BiC_2H_4S_2$ measured m/z 300.9550, d = 2.8 ppm). Compound (**4.94**) gives weak $M^{\bullet+}$ ions and major fragment ions at m/z 336 and 301, which are assumed to have the same structure as $M^{\bullet+}$ and $[M - Cl]^+$ ions from (**4.69**). This suggests a thermodynamic preference for the five-membered heterocycle and implies elimination of $S_2C_2H_4$ from $M^{\bullet+}$ and $[M - Cl]^+$ ions of (**4.94**) followed by ring closure, as was proposed earlier for the methyl and phenyl analogues.[184] Similarly, compound (**4.97**) shows a fragment ion (m/z 285) which is the oxa analogue of the $[M - Cl]^+$ ion from (**4.69**). The data for compound (**4.69**) are consistent with those of a previous report; however, previous reports for compounds (**4.94**) and (**4.97**) do not describe the intense peaks for $[M - Cl]^+$ or $[M - Cl - SC_2H_4]^+$.[184]

The EI mass spectra of compounds (**4.101**) and (**4.102**) show ions observed in the spectrum of $BiCl_3$ in addition to the ions corresponding to the organic portion of the molecule, indicative of thermal decomposition. Compounds (**4.105**) - (**4.109**) behave similarly to bismuth sulfide which is polymeric in the solid state and is not sufficiently volatile to give an EI spectrum.

Atmospheric pressure chemical ionization (APCI) mass spectral data for compounds (**4.69**), (**4.94**), (**4.97**) and (**4.101**) in DMSO and compounds (**4.105**), (**4.106**), (**4.108**) and (**4.109**) in acetonitrile with 1 % HCl are summarized in Table 7.8, revealing some general trends. Dominant in all the spectra, are monocyclic cations, which represent $[M - Cl]^+$ for compounds (**4.69**), (**4.94**), (**4.97**) and (**4.101**), and heterolytic Bi-S cleavage of the tether for compounds (**4.105**), (**4.106**), (**4.108**) and (**4.109**). These cations are representative of bismuthenium cations, bismuth analogues of the well-established series of dicoordinate phosphorus and arsenic cations.[200,201] They are also observed in the EI mass spectra of (**4.69**), (**4.94**) and (**4.97**).

Acidified solutions of compounds (**4.105**), (**4.106**), (**4.108**) and (**4.109**) also show bismuthenium cations as the dominant species, and both five-membered (m/z 361 for (**108**); m/z 285 for (**4.109**)) and eight-membered (m/z 361 for (**4.108**); m/z 345 for (**4.109**)) heterocyclic cations are observed in the spectra of (**4.108**) and (**4.109**). A protonated molecular ion was observed for compound (**4.109**) and the MS/MS spectrum of this ion reiterates that the principal fragmentation pathway is the loss of SC_2H_4. Loss of SC_2H_4 or $2SC_2H_4$ from MH^+ may result in a tethered ion with either one of two pendant five-membered heterocycles (at m/z 767 and 706, respectively), each containing an oxygen and a sulfur atom. As was observed for the APCI mass spectrum (Table 7.8), the MS/MS spectrum of $(\mathbf{4.108})H^+$ is dominated by the eight-membered bismuthenium species (m/z 345) plus a minor fragment ion due to loss of SC_2H_4 to give the five-membered species at m/z 285.

Notable in the APCI spectrum of (**4.69**) is the peak at m/z 379 which corresponds to a DMSO complex of the cation and is suggestive of a donor stabilization. Similar complexation is also observed for (**4.94**), (**4.97**) and (**4.101**) in DMSO solution. After a sampling cone (SC) voltage adjustment, single molecule solvent coordination complexes, $[(DMSO)M - Cl]^+$ of (**4.69**), (**4.94**), (**4.97**) and (**4.101**) were observed in the APCI mass spectra. Further SC voltage adjustment resulted in the formation of $[(DMSO)_2M - Cl]^+$ complexes for (**4.69**) and (**4.101**). However, for compounds (**4.94**) and (**4.97**), the cross ring donation from the sulfide and ether, respectively, inhibits complexation of a second solvent molecule. Elimination of SC_2H_4 from (**4.94**) and (**4.97**) in the ion source is observed to occur (confirmed by a precursor ion scan), forming $BiC_2H_4S_2^+$ and $BiC_2H_4OS^+$, respectively, which also form DMSO complexes. The identity of these complex ions is confirmed by MS/MS experiments which show sequential loss of the solvent molecule to yield the dicoordinate bismuthenium cation in each case.

Complex ion formation was also observed in DMSO solutions of compounds (**4.105**), (**4.106**), (**4.108**) and (**4.109**) which is consistent with the spectra of compounds (**4.69**), (**4.94**), (**4.97**) and (**4.101**), whereas in acetonitrile solutions complex ion formation was found to be variable. The ions Bi^+ and BiS^+ are observed in the MS/MS spectra of all compounds.

4.2.5 Conclusions

General, high yield synthesis of two related and comprehensive series of bismuth heterocycles demonstrates a dominant thermodynamic preference for the dianion dithia chelate for bismuth. The halo-substituted monocycles (**4.69**), (**4.70**), (**4.94**), (**4.97**), (**4.100**) - (**4.104**) are kinetically stable with respect to the tethered bicyclic derivatives (**4.105**) - (**4.109**). The preference for five-membered ring formation is expressed by the quantitative metathesis of (**4.106**) by ethanedithiol to form (**4.105**). Base-stabilization of a bismolanium cation was achieved by complexation of (**4.70**) by two pyridine molecules as seen in the X-ray crystal structure. Two bismolane derivatives, (**4.110**) and (**4.111**) provide additional expansion of the array of dithiabismuth heterocycles. Quantitative formation of (**4.110**) contains an intramolecularly coordinating hydroxyl group rather than bismuth-alkoxide bond which may be explained by the hard and soft acid-base theory.[90] Mass spectrometry provides an excellent means of characterization of dithiabismuth heterocycles and reveals monocyclic bismuthenium cations as a general and dominant dissociation product. In addition, the APCI technique exhibits solvent coordination chemistry of the bismuthenium cation.

Chapter 5. Trends in Chalcogenobismuth Chemistry

5.1 General Characterization Trends

The complete communication of scientific facts is perhaps the most important aspect of research and development. A synthetic description should, at minimum, contain a yield reported as a mass and as a percentage relative to a particular starting material. In numerous instances, analytical, spectroscopic and structural data were discussed in detail for chalcogenobismuth heterocycles for which yields were not reported. In fact, 43.0 % of all reported preparations of chalcogenobismuth heterocycles (see Figure 5.1) do not report a yield and an additional 23 % have yields reported as a percentage with no actual yield data. Consequently, only 34 % of all compounds in the literature have properly reported yields.

The importance of reporting yields is to indicate the overall utility of the synthesis in obtaining the targeted product to the reader. As well, it serves to convey the relative thermodynamic and kinetic stability of a product in comparison with competing reactions. A low percent yield may be characteristic of an unrefined synthetic procedure, whereas, a high mass yield decreases the possibility that product formation is an anomaly and may be indicative of thermodynamic favorability. Often, many bismuth compounds are difficult to manipulate and isolate due to their inherent insolubility in common organic solvents which, in turn, hinders synthetic development by conventional means. All of these factors are extremely important in understanding of bismuth chemistry in general and,

therefore, to the advancement of research and development. The author stresses the importance of yield reporting to demonstrate that our systems are potentially transferable to industrial bioactivity-related applications through their reproducibility, single product formation and potential versatility. For example, the simplicity of the "one-pot" synthetic procedure, in which copious amounts of dithiabismuth heterocycles are produced as highly pure single products, outlines an elegant method which is ideal for transfer to large-scale production.

Characterization of the chalcogenobismuth heterocycles, in general, has been poor in the literature. For example, chemical characterization for (**2.35**), (**3.12**) and (**4.8**) was based solely on X-ray crystal structures. Clarification by the authors of whether elemental analyses were performed on the crystals or the initially isolated solid material was not provided. It is unclear if the crystals were representative of the bulk sample, since overall yields were reported for the powders and not the crystals. Emphasis should be placed on comprehensive characterization rather than on structural data collection as a single means of characterization. Systematic studies of structurally similar simple compounds would ideally provide the fundamental information necessary for rational and successful development or enhancement of previous applications of bismuth chemistry.

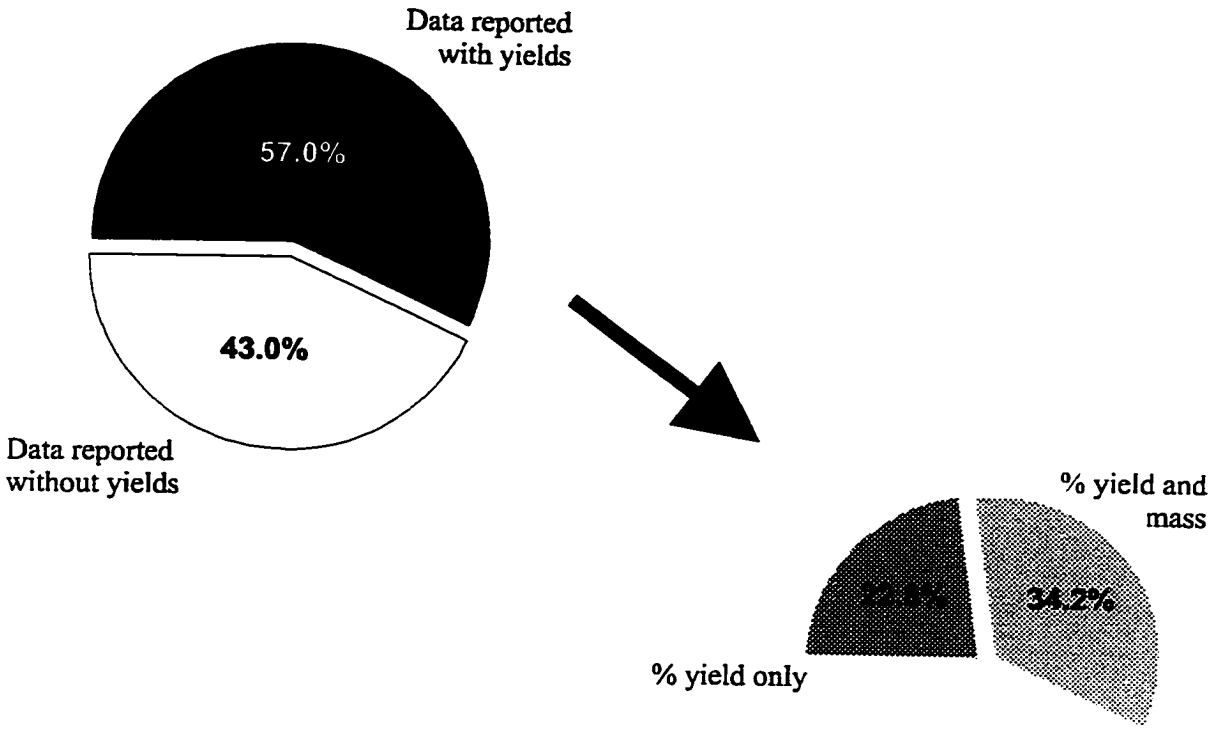


Figure 5.1. Pie chart depicting the percentage of chalcogenobismuth compounds which report data without a yield. The compounds for which a yield was reported can be further subdivided into compounds for which a yield was reported as a percentage only.

5.2 The Significance of the Stereochemically Active Lone Pair on Bismuth(III)

The VSEPR theory predicts the arrangement of atoms within a molecule on basis that electron pairs will be arranged around the central atom such that electron repulsions are minimized. Ligand-ligand repulsions are considered much less significant than electron repulsions and do not have stereochemical consequence.[202] The term "stereochemically active lone pair" arises from the VSEPR model and is used to describe breakdowns in the VSEPR theory. Many exceptions to the VSEPR model occur, especially among compounds containing heavy *p* block atoms and the following explanations are offered: (1) in highly coordinated compounds (CN > 6), ligand-ligand repulsions actually dominate the stereochemical outcome; (2) hard donors such as oxygen and fluorine give rise to a stereochemically active lone pair and conversely, soft donors such as sulfur and iodine suppress the stereoactivity of the lone pair (this explanation arises from the hard and soft acid-base theory[90]);[203] (3) centrosymmetric molecules have an inert lone pair whereas noncentrosymmetric molecules have a stereochemically active lone pair (for group 16);[204] (4) frontier orbital arguments state that the stereochemical activity of the lone pair is governed by the symmetry of the HOMO and that orbital distortion allows for stereochemical activity of the lone pair.[205]

The stereochemical activity of the lone pair on Bi(III) is often an important topic in structural discussions of chalcogenobismuth heterocycles. Evidence for the stereochemically active lone pair is ascertained from coordination geometry observations such as a missing apex of the coordination polygon or angle distortions accompanying bond length extensions of a particular face of the polygon. Usually, the presence of the

stereochemically active lone pair or lack thereof, and its position within the molecular polygon are mentioned without further discussion or speculation as to the chemical significance of their observations. The question remaining is what is the significance of the lone pair and why is it almost invariably a predominate topic in structural discussions and abstracts?

The conditions under which the lone pair is stereochemically active or inactive must be determined before the significance of the lone pair can be addressed. The VSEPR theory is a simple model which assumes *a priori* stereochemical activity of the lone pair. Rationalizations for stereochemical inactivity of the lone pair are provided which are based on the HSAB theory, ligand-ligand repulsions, crystal packing forces and coordination geometry symmetry. The frontier orbital argument oppositely assumes the stereochemical inactivity of the lone pair and provides exceptions for its activity (only for six-coordinate heavy atom main group compounds). However, these rules are not firm and there are exceptions.

Currently, no conclusions can be made as to the significance of the lone pair to bismuth(III) chemistry and that is why the only conclusion drawn by each author is the presence of the stereochemically active lone pair or lack thereof. Nevertheless, in order to come to some conclusions, data regarding the stereochemical activity of the lone pair would be beneficial. Furthermore, specific experiments need to be designed and performed which directly address the significance of the stereochemically active lone pair in terms of effect and consequences in the solid state.

A problematic situation which needs to be addressed is the reliance of all data concerning the stereoactivity of the lone pair on single crystal X-ray crystallography, which in turn relies on crystal quality and the fortuity of crystal growth. The experimentalist should be aware of the possibilities of polymorphism and solvent inclusion which, in combination with the choice of a unique crystal for X-ray analysis may lead to misleading or the incorrect publication of data.

5.3 Structural Trends in Chalcogenobismuth Heterocycles

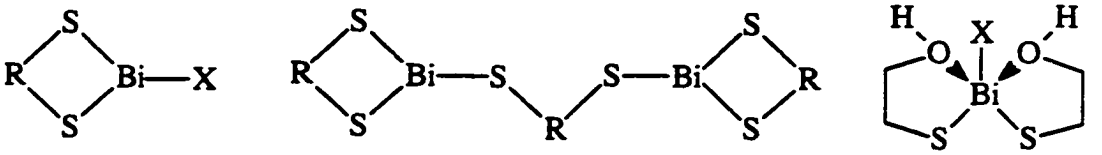
An outstanding trend noticed within the series of chalcogenobismuth heterocycles is the prevalence of five-membered rings formed by monoanionic, dianionic or coordinative chelating ligands. Similar to the thermodynamic stability of six-membered carbon rings, the formation of chalcogenobismuth five-membered rings is favorable because they contain optimal angles for minimizing ring strain.[84]

Solid state structures of chalcogenobismuth heterocycles are observed to have high coordination numbers and complex geometries which result from intra and intermolecular coordinations from neighboring sulfur, oxygen and halogen atoms. Intermolecular coordinations are considered as secondary bonds when they are significantly longer than typical bonds and shorter than the van der Waal's radii (4.5 Å for Bi and S) and are responsible for coordination polymer propagation and geometry distortions.[206] The cause of strong intra and intermolecular coordinations may be attributed to the HSAB theory,[90] in addition to crystal packing consequences. HSAB theory[90] also accounts for the higher incidence of Bi···S coordinations over Bi···O and

Bi···X (X = Cl, Br, I) coordinations. Conversely, thioalcohols are reported to form alkoxide complexes with harder metals such as titanium, consistent with the HSAB theory.[207]

5.4 General Conclusions

The simple, rapid and quantitative synthesis and comprehensive characterization of three series of air and water-stable chalcogenobismuth heterocycles, (**5.1**), (**5.2**) and (**5.3**) (see Figure 5.2) have allowed for some general conclusions which highlight the compounds as ideal candidates for the design and development of bioactive bismuth compounds. A thermodynamic dominance of the five-membered ring is apparent among the chalcogenobismuth heterocycles which is best illustrated by the high yield formation of (**4.105**) by five different synthetic methods (see Figure 5.3). For example, (**4.105**) can be obtained by the reaction of (**4.106**) with 1,2-ethanedithiol.



(**5.1**) (**5.2**) (**5.3**)

Figure 5.2. Chalcogenobismuth heterocycles, (**5.1**), (**5.2**) and (**5.3**).

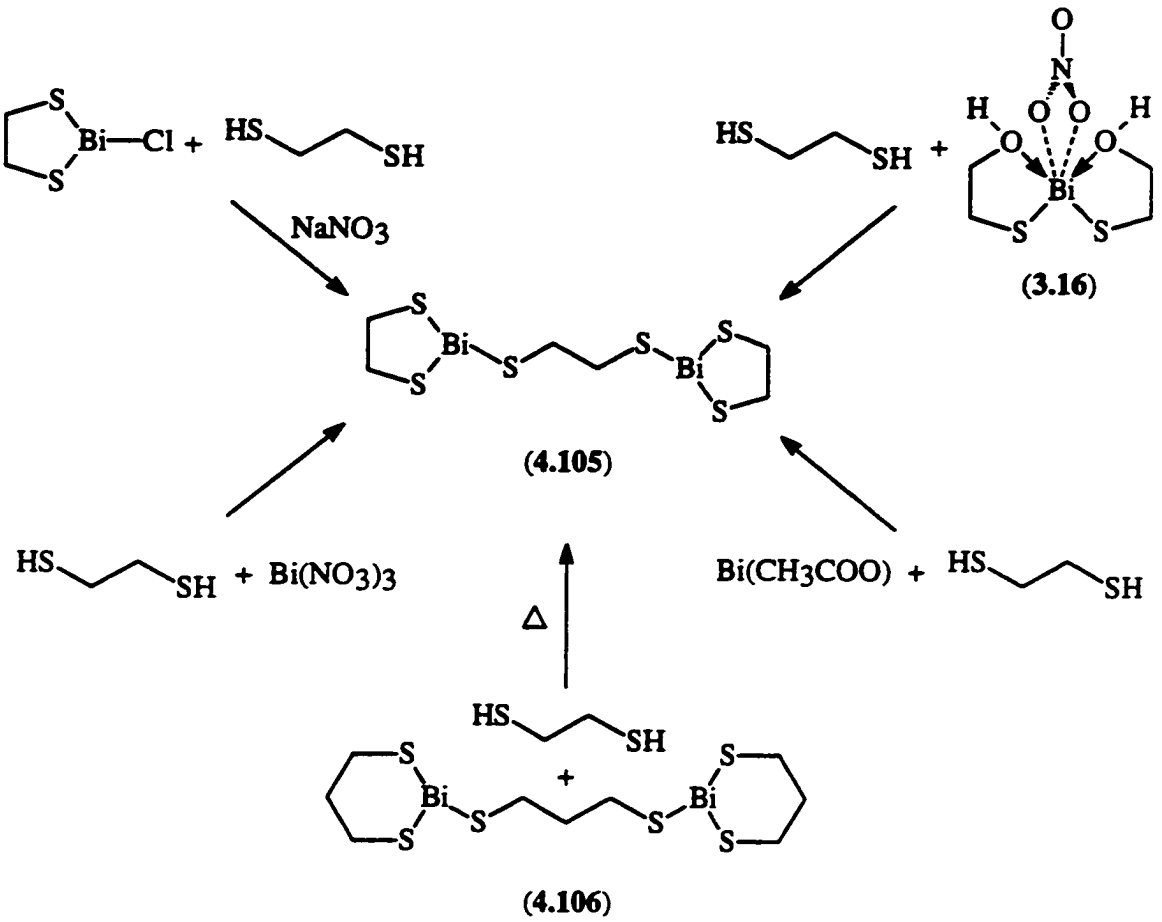


Figure 5.3. Synthetic methods for (**4.105**).

Bismuth-thiolate bond formation prefentially occurs over bismuth-halide and bismuth-alkoxide bond formation. This is demonstrated by the observation that the halodithiabismolanes, (**5.1**) are kinetically stable with respect to the bicyclic tethered analogues, (**5.2**). The bicyclic framework evident for (**5.3**) is comprised of a double hydroxyl-thiolate chelation of bismuth. In addition, bismuth-alkoxide bond formation using conventional synthetic techniques requires other driving forces and stabilization effects, such as immediate precipitation upon compound formation, cryptate ligands and ligand resonance stability.

Air and water-stable, base-stabilized bismuthenium cations occur for compounds of the type, (**5.1**) and (**5.3**) and have been found to persist over a long periods of time. Crystallization is effected upon complexation of (**4.69**), (**4.70**) and (**4.100**) by pyridine to form the respective dipyridyl compounds as crystals. Complexation by pyridine stabilizes the cationic bismuth sites, for compound (**4.16**). Double intramolecular hydroxyl coordination is observed to stabilize and mediate the acidity of the bismuth site. Bismolanium cations and their solvent complexes are dominant fragments in the APCI mass spectra of (**5.1**), (**5.2**) and (**5.3**) and indicate the relative stability of the cyclic five-membered bismuthenium cations.

The synthetic simplicity and thermodynamically stable properties of the chalcogenobismuth heterocycles, (**5.1**), (**5.2**) and (**5.3**) have led to the discovery of an ideal procedure for generating small, structurally simple bismuth compounds for enhancement and development of preferred applications.

5.5 Bioactivity Studies of the Chalcogenobismuth Heterocycles

Collaborations with microbiologists (Drs. P. S. Hoffman and D. E. Mahony), gastroenterologists (Drs. D. L. Leddin and S. J. O. Veldhuyzen van Zanten) and a pharmacologist (Dr. T. C. Peterson) have been established for the purpose of assessing antimicrobial activity, ulcer-healing ability and effect on an ulcerative colitis model of the series of tethered and chlorodithiabismuth heterocycles and bicyclic bis-(2-hydroxyethanethiolato)bismuth compounds.[14,15] A penultimate goal is to design and build molecules which are stable under standard atmospheric conditions, low cost and suitable for *in vivo* activity against harmful microbes and healing of gastrointestinal diseases.

Preliminary studies of the series of tethered and chlorodithiabismuth heterocycles and bicyclic bis-(2-hydroxyethanethiolato)bismuth compounds have demonstrated superior bioactivity against bacterial pathogens such as *Helicobacter pylori, Clostridium diffiicile, Clostridium perfringens, Escherichia coli* and *Pseudomonas aeruginosa* with compounds, (**3.16**), (**3.19**), (**4.69**), (**4.94**) and (**4.108**) (see Figure 5.4) over BSS, CBS and RBC which were considered as controls.[15] A brief investigation of the ulcer-healing properties of three bismuth compounds, (**4.69**), (**4.105**) and CBS which are structurally diverse was performed using a rat model.[14] It was concluded that healing ability, hence bioactivity is structure related. The understanding of the synergistic relationship of the chemistry and bioactivity involved in gastroenterological healing and antimicrobial

activity will allow for development of pharmaceuticals with profound economic implications.

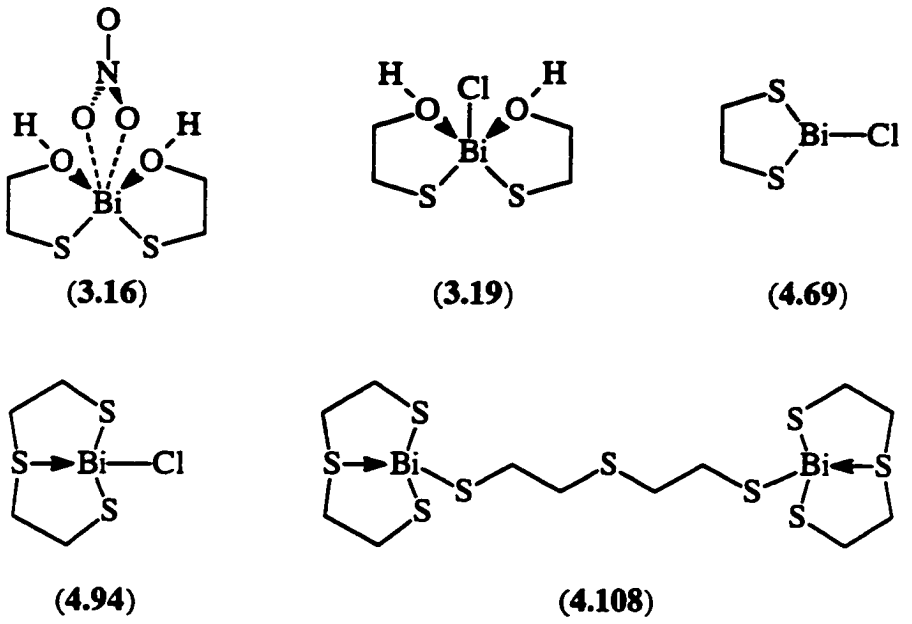


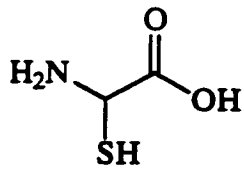
Figure 5.4. Structures of antimicrobial compounds, (**3.16**), (**3.19**), (**4.69**), (**4.94**) and (**4.108**).

Chapter 6. Future Work

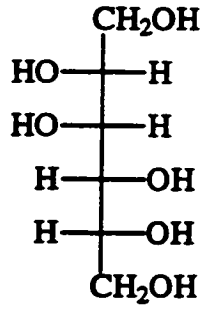
The chemistry of bismuth is in its infancy and requires an understanding of the fundamental concepts for enhancement and development of applications such as bioactivity and low-temperature superconducting materials. Future work should focus on the comprehensive, systematic development of coherent series of bismuth compounds and emphasis should be put on continuing thorough investigations in a scientific manner.

6.1 Bioactive Bismuth Heterocycles

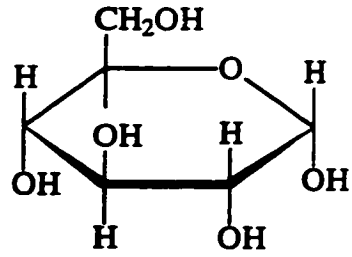
The design and synthesis of molecules which are stable under standard atmospheric conditions and suitable for *in vivo* activity against harmful microbes and healing of gastrointestinal diseases is an obtainable goal. A logical choice for ligation of Bi^{3+} is biological compounds such as amino acids (e.g. cysteine) and sugars (e.g. D-mannitol and D-glucose) which are multifunctional (see Figure 6.1). Complexation of an amino acid or a sugar with BiX_3 offers potential stability by means of the cryptate and chelate effects and perhaps, reduce toxicity concerns.



cysteine



D-mannitol

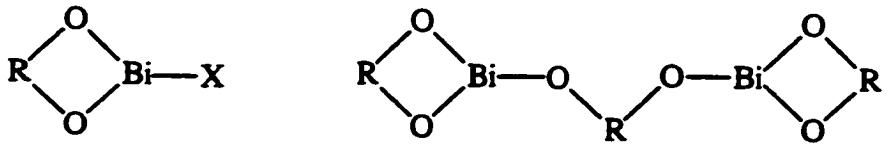


D-glucose

Figure 6.1. Structure of the amino acid, cysteine and the sugars, D-mannitol and D-glucose.

6.2 Small Oxabismuth Heterocycles

Attempts at synthesizing small, simple oxabismuth heterocycles by reaction of BiX_3 with hydroxyl chelates afforded starting materials only. The use of a strong hydrogen abstracting agent, such as butyllithium, in an oxygen and water-free atmosphere may provide suitable conditions for dianionic chelation of BiX_3 by diols to obtain compounds of type (**6.1**) and (**6.2**) (see Figure 6.2) which are direct analogues of the series of dithiabismuth heterocycles, (**4.69**), (**4.70**), (**4.94**), (**4.97**), (**4.100**) - (**4.109**) (see Figures 4.17 and 4.18).



(6.1) (6.2)

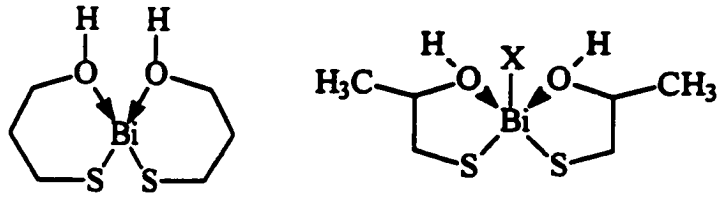
Figure 6.2. Analogues of the dithiabismuth heterocycles with proposed structures, (**6.1**) and (**6.2**), X = Cl, Br, I, R = $(CH)_{2\text{-}4}$, $(CH_2)S(CH_2)_2$, $(CH_2)O(CH_2)_2$.

6.3 Other Bicyclic Oxathiabismuth Compounds

The series of bicyclic bis-(2-hydroxyethanethiolato)bismuth compounds, (**4.16**), (**4.19**) - (**4.22**) (see Figure 3.5) can be extended to include derivatives containing larger ring sizes by reactions of BiX_3 (X = Cl, Br, I, NO_3) with a series of mercaptoalcohols, for example, 3-mercapto-1-propanol and 2-mercapto-1-propanol to give (**6.3**) and (**6.4**), respectively (see Figure 6.3).

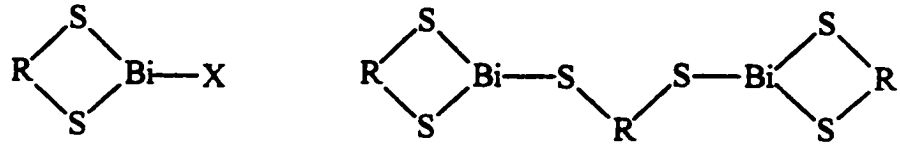
6.4 Bismuth(V) Chalcogen Compounds

A logical expansion of the systematic series of oxathiabismuth(III) and dithiabismuth(III) compounds of types (**6.5**) and (**6.6**) is to include Bi(V) analogues. In order to obtain stable Bi(V) compounds, strongly electronegatively bonding ligands or ligands which possess large group electronegativity such as phenyl or other similar

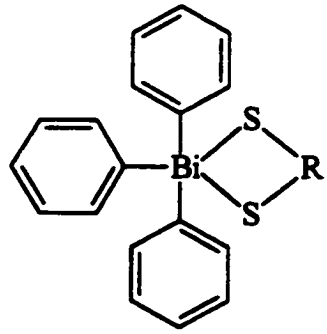


(6.3) (6.4)

Figure 6.3. Structure of proposed oxathiabismuth compounds, (**6.3**) and (**6.4**)



(6.5) (6.6)



(6.7)

Figure 6.4. Dithiabismuth heterocycles, (**6.5**) and (**6.6**) and the proposed triphenyldithiabismuth(V) compound, (**6.7**), R = $(CH)_{2\text{-}4}$, $(CH_2)S(CH_2)_2$, $(CH_2)O(CH_2)_2$.

aromatic groups are required.[208] Dithiols readily metathesize $BiCl_3$ to quantitatively form chlorodithiabismuth heterocycles, (**4.69**), (**4.94**), (**4.97**) (**4.100**) and (**4.101**), and $Bi(NO_3)_3$ and $Bi(CH_3COO)_3$ are metathesized to afford the tethered analogues, (**4.105**) - (**4.109**). Therefore, Ph_3BiX_2 (X = Cl, CH_3COO) and Ph_3BiCO_3 should be amenable to formation of an analogous series of triphenyldithiabismuth(V) compounds, (**6.7**) (see Figure 6.4). Compounds Ph_3BiCl_2 and Ph_3BiCO_3 are commercially available and $Ph_3Bi(CH_3COO)_2$ is obtained by the reaction of Ph_3Bi with acetic acid in the presence of *t*-butylhydroperoxide.[7,209]

Chapter 7. Experimental

7.1 General Procedures

Bismuth(III) acetate, bismuth(III) bromide, bismuth(III) chloride, bismuth(III) iodide, bismuth (III) nitrate pentahydrate, bismuth oxychloride, 1,4-butanedithiol, 1.6 M butyllithium in hexanes, 10.0 M butyllithium in hexanes, 1,2-ethanedithiol, ethylene sulfide, 2-mercaptoethyl ether, 2-mercaptoethyl sulfide, 2-(methylthio)ethanol, 1,3-propanedithiol, potassium citrate and sodium acetate were used as received from Aldrich. Potassium oxalate monohydrate was used as received from Anachemia. 2-Mercaptoethanol was used as received from Eastman. Sodium chloride was used as received from BDH. Anhydrous diethyl ether was used as received from Caledon. Pyridine, sodium bromide and sodium iodide was used as received from Fisher Scientific. Bismuth citrate was used as received from Sigma. Melting points were recorded on a Fisher-Johns melting point apparatus and are uncorrected. IR spectra were recorded as Nujol mulls on CsI plates using a Nicolet 510P spectrometer. Raman spectra were obtained for powdered and crystalline samples in capillary tubes on a Bruker RFS 100 spectrometer. Chemical analyses were performed by Canadian Microanalytical Service Ltd., Delta, British Columbia and MDS Environmental Services Ltd., Halifax, Nova Scotia (Perkin-Elmer Elan 5000 ICPMS). Solution ^{1}H NMR data were recorded on Bruker AMX400 and AC-250 spectrometers by Dr. D. L. Hooper or Dr. M. Lumsden. Chemical shifts are reported in parts per million relative to TMS and are calibrated to the

internal solvent signal. Solid state ^{13}C NMR spectra were measured on a Bruker AMX400 spectrometer by Dr. M. Lumsden. Measurements of pH were recorded using a Fisher Accumet model 620 pH meter. Atmospheric pressure chemical ionization (APCI) mass spectra were obtained by G. G. Briand or G. B. Yhard using a SCIEX API-III triple quadrupole mass spectrometer (SCIEX, Ontario, Canada) controlled by a Macintosh 950 Quadra computer using SCIEX software, or a VG Quattro mass spectrometer (VG Organic, Manchester, U.K.) controlled by a Digital DECpc using Fisons MassLynx software. Solvent flow (1:1 water:acetontrile at 200 mL/min) and sample injection (10-15 mL) used a Hewlett-Packard Series II 1090 liquid chromatograph pump with autoinjector or a Shimadzu LC-6A with a Rheodyne Syringe Loading Sample Injector. MS/MS spectra on either the SCIEX API-III or the VG Quattro used argon collision gas in the second quadrupole resulting in a beam attenuation of approximately 50%.

Electron impact (EI) mass spectra were obtained using either a VG ZAB-EQ double-focusing mass spectrometer (VG Organic, Manchester, U.K.) or a VG 20-250 quadrupole mass spectrometer(VG Organic, Manchester, U.K.). The spectra were obtained at an ionizing electron energy of 70 eV, using a standard solids probe or a direct probe. Accurate mass measurements were made on the ZAB-EQ instrument at a mass resolution of at least 8000 (10% valley definition) with perfluorokerosine (PFK) as reference compound. Data acquisition for the ZAB-EQ was performed using a Digital VAX 4000 model 60 computer running Fisons OPUS software. The 20-250 was controlled using a Fisons 11-250J data system running on a Digital PDP11\73 computer. X-ray data were collected on Rigaku AFC5R and Enraf-Nonius CAD-4 diffractometers

and structures were solved by Dr. T. S. Cameron, Dr. W. Kwiatkowski, Dr. J. F. Richardson or K. N. Robertson.

7.2 General Synthetic Procedures.

Colloidal Bismuth Subcitrate. In a typical reaction, bismuth citrate was added to a stirred solution of potassium citrate in distilled water (30 mL) in a 1:1 stoichiometry and the reaction mixture was heated to a specific temperature (see Table 7.1). A solution of potassium hydroxide in a minimal amount of distilled water (~ 10 mL) was added at various stoichiometries (see Table 7.1) and the resulting reaction mixture was cooled to room temperature and stirred for 5 minutes. Clear solutions were heated to 95 °C and evaporated until the overall volume was 10 mL and a slurry was present. A 2:1 mixture of acetone/methanol (~ 20 mL) was added to mixtures containing a precipitate and the resulting slurries were centrifuged. The precipitate was filtered and washed with 5 mL aliquots of distilled water and acetone, respectively, then dried using reduced pressure. A melting point and IR spectrum were obtained for each solid. The solubility was determined by stirring a sample of the solid (0.05 - 0.10 g) in each water, 1M HCl and 1M KOH (see Table 7.2).

Table 7.1. Stoichiometries for the synthesis of colloidal bismuth citrate (CBS) and melting points.

Temperature (°C)	Stoichiometry of KOH (relative to $BiC_6H_5O_7$)	Precipitate Type	mp [dp] (°C)
45	3	P1, P2	[240], [247]
90	20	Bi_2O_3[210]	>300
RT	3	P3	[170]
90	2	P4	*
RT	3	P3	[170]
90	2.1	P5	[184]
RT	2	P6	[230]
45	2	P6	[230]
90	2	P6	[230]

* material was unsuitable for melting point determination

P1 = white precipitate which formed a gel in water, very poor solubility in water

P2 = white precipitate which formed after diffusion of methanol/acetone (2:1) vapor into reaction mixture

P3 = white precipitate which formed upon reduction of aqueous reaction mixture by heating

P4 = solid obtained from a gel

P5 = white precipitate which formed upon addition of excess KOH

P6 = white precipitate which formed upon addition of methanol/acetone (2:1) solution, very poor solubility in water

Table 7.2. Solubilities and melting points of CBS solids.

Precipitate	dp (°C)	Solubility in H_2O	Solubility in 1 M HCl	Solubility in 1 M KOH
P1	240	no	yes	no
P2	247	yes	*	no
P3	170	yes	yes	no
P4	#	yes	yes	no
P5	184	yes	slightly	no
P6	230	no	slightly	no

* insufficient material to determine solubility

material is of unsuitable nature for melting point determination

Reaction of $BiCl_3$ with Potassium Oxalate (2.45). Potassium oxalate monohydrate was added to a stirred aqueous slurry of bismuth trichloride the resulting white slurry was allowed to stir at room temperature overnight. The white precipitate was filtered using a Buchner funnel, rinsed with 10 mL aliquots of distilled water, air dried and characterized by a melting point, elemental analysis, Raman and IR spectroscopy, yield, 3.49 g, 10.5 mmol, 90 %; dp 225 °C; Anal. Calcd. for (**2.45**): C, 7.23; O, 19.25 %; Found: C, 7.20; O, 21.90 %; Raman (cm^{-1}): 516 (s), 397 (w), 200 (s), 145 (vs), 96 (m), 62 (m); IR (cm^{-1}): 3526 (s), 3430 (s sh), 1660 (vs), 1612 (vs), 1351 (m), 1314 (s), 909 (w), 808 (s), 589 (m sh), 520 (s), 488 (s), 391 (m), 333 (s).

Reaction of $Bi(NO_3)_3$ with Potassium Oxalate (2.46). Potassium oxalate monohydrate was added to a stirred aqueous slurry of bismuth nitrate pentahydrate and the resulting white slurry was allowed to stir at room temperature overnight. The white precipitate was filtered using a Buchner funnel, rinsed with 10 mL aliquots of distilled water, air dried and characterized by a melting point, elemental analysis, Raman and IR spectroscopy, yield, 3.13 g; dp 240 °C; Anal. Calcd for (**2.46**): C, 11.32; H, 0; O, 30.18; Found: C, 8.20; H, 0.35; O, 26.62; Raman (cm^{-1}): 581 (w), 513 (m), 500 (s), 467 (m), 440 (s), 315 (w), 242 (m), 196 (s), 158 (m), 98 (s), 60 (m); IR (cm^{-1}): 3500 (m, br), 1713 (s), 1583 (vs), 1352 (s), 1296 (s), 1093 (w), 1081 (m), 796 (s), 517 (s), 457 (m), 394 (m), 249 (m).

Preparation of Bicyclic bis-(2-hydroxyethanethiolato)bismuth(III) nitrate monohydrate (3.16). Addition of $Bi(NO_3)_3$ (4.18 g, 8.61 mmol) to 2-mercaptoethanol

(1.50 g, 19.2 mmol) in a 1:2 molar ratio in 95% ethanol (120 mL) gave a yellow solution, instantaneously. Slow evaporation of the reaction mixture at room temperature yielded yellow, needlelike crystals, which were washed with acetone. A yield, melting point, chemical analysis and mass spectral data are presented in Table 7.3; IR, Raman and ^1H NMR spectral data are presented in Table 7.4 and X-ray data are presented in Table 7.5. Varied stoichiometries [$Bi(NO_3)_3$: 2-mercaptoethanol; 1:1, 1:3, 2:3] provide the same product (confirmed by Raman spectra and melting point) at lower isolated yield, 40, 30, 50 %, respectively.

Table 7.3. Yields, melting points, analyses and mass spectral data for bicyclic bis-(2-hydroxyethanethiolatebismuth compounds, (**3.16**), (**3.19**) - (**3.22**) and the neutral analogue, (**3.17**).

Compd	Yield g (%)	mp[dp] °C	Solubility (ppm Bi)	Elemental Analysis				APCI MS	m/z (rel. int.)
				C_{calc} (C_{found})	H_{calc} (H_{found})	O_{calc} (O_{found})	S_{calc} (S_{found})	10V	30V
(**3.16**)	2.89 (76)	67-70	3100	10.84 (11.03)	2.72 (2.74)	-	-	285(10) 326(33) 363(100)	285(100) 363(8)
(**3.17**)	0.85 (2.34)	180	< 2	13.26 (13.31)	2.50 (2.50)	-	17.70 (18.09)	-	-
(**3.19**)	2.91 (71)	112-114	4.2	12.05 (12.21)	2.53 (2.55)	8.03 (7.95)	16.08 (14.97)	285(9) 321(89) 323(30) 326(22) 362(100) 363(87) 364(42)	285(100)
(**3.20**)	0.41 (19)	185	0.7	10.84 (11.05)	2.27 (2.09)	-	-	285(20) 326(34) 363(100)	285(100) 363(68)
(**3.21**)	2.04 (68)	[140]	2.8	-	-	-	-	285(12) 326(30) 363(10) 413(100) 454(87) 491(3)	285(100) 413(40)
(**3.22**)	0.14 (92)	99-100	220	17.05 (16.90)	3.10 (3.07)	-	15.17 (15.24)	285(7) 326(25) 363(100)	285(100) 363(9)

Table 7.4. Spectroscopic data for the series of bicyclic bis-(2-hydroxyethanethiolatobismuth compounds, (**3.16**), (**3.19**) - (**3.22**) and the neutral analogue, (**3.17**).

Compound	^{1}H NMR (ppm)	IR (cm^{-1})		Raman (cm^{-1})	
(3.16)	4.13	306 (m)	1000 (m)	71 (m)	309 (s)
	(tr, CH_2O)	484 (w)	1048 (m)	93 (m)	489 (w)
	3.91	649 (w)	1161 (w)	136 (s)	654 (m)
	(tr, CH_2S)	825 (m)	1199(w)	212 (vs)	
		935 (w)	1269 (w)		
(3.17)	*	281(s)	844(w)	49(w)	279(vs)
		312(s)	935(m)	83(s)	314(m)
		332(s)	998(s)	119(s)	333(m)
		386(s)	1040(s)	147(m)	389(s)
		481(s)	1053(m)	175(s)	482(w)
		529(s)	1167(m)	236(s)	526(w)
		662(s)	1204(m)	261(s)	663(m)
		823(w)	1276(m)		
(3.19)	5.90	246(s)	936(m)	87(s)	227(vs)
	(br s, OH)	279(m)	1002(m)	101(s)	320(s)
	4.05	303(s)	1045(m)	124(s)	481(w)
	(tr, CH_2O)	324(m)	1217(w)	141(s)	650(w)
	3.77	650(w)	1279(m)		667(m)
	(tr, CH_2S)	667(m)	3264(s)		
		827(m)			
(3.20)	*	269(s)	849(m)	86(s)	255(s)
		308(m)	940(w)	107(m)	304(w)
		413(m)	1006(w)	133(vs)	336(w)
		502(m)	1070(w)	214(m)	409(w)
		520(m)	1173(w)	235(m)	661(w)
		598(s)	1705(br)		
		657(m)	3472(br)		
(3.21)	4.37	268(s)	890(w)	64(s)	
	(br s, OH)	319(m)	936(w)	78(s)	246(m)
	4.09	395(w)	974(m)	114(vs)	278(s)
	(br s, CH_2O)	454(m)	1025(m)	126(vs)	314(m)
	3.59	586(m)	1156(m)	166(s)	487(w)
	(br s, CH_2S)	645(m)	3400(br)	217(s)	648(w)
(3.22)	4.86	267 (vs)	945 (m)	95(s)	272(s)
	(br s, OH)	304 (vs)	1009 (s)	112(vs)	322(s)
	3.72	341 (m)	1047 (s)	133(s)	478(w)
	(tr, CH_{2a}, H_{2b})	412 (s)	1067 (m)	161(m)	658(w)
	3.60	504 (s)	1177 (w)	237(s)	670(w)
	(tr, CH_{2c})	526 (s)	1209 (m)		
	2.78	662 (m)	1274 (s)		
	(tr, CH_{2d})	838 (m)	3365(br)		
	1.86 (s, CH_3)				
	(see Figure 7.1)				

* compound was not soluble enough for a measurement

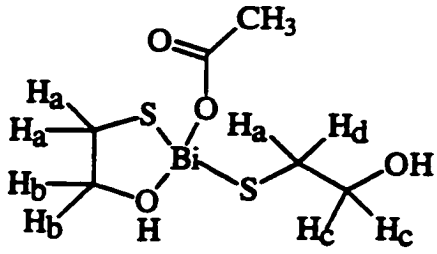


Figure 7.1. Labelled H's of (**3.22**) for the ^{1}H NMR spectrum.

Preparation of 2-Thioethanol-1-oxa-3-thia-2-bismolane (3.17). 2-Mercaptoethanol (1.17 g, 15.3 mmol) was added dropwise to a stirred slurry of bismuth acetate (1.93 g, 5.0 mmol) in acetone (120 mL). The resulting yellow slurry was stirred overnight at room temperature then filtered with a Buchner funnel and washed with 10 mL aliquots of acetone. The light yellow precipitate was air dried and characterized as (**3.17**). The clear, yellow filtrate was allowed to slowly evaporate in a partially covered beaker for 24 hours giving a yellow microcrystalline solid which was also characterized as (**3.17**); yield 0.60 g, 1.67 mmol, 33 %. Total yield, 80 %. A yield, melting point, chemical analysis and mass spectral data are presented in Table 7.3; IR, Raman and ^{1}H NMR spectral data are presented in Table 7.4.

Preparation of (3.17) from (3.16). (**3.16**) (0.05 M) was generated *in situ* by the dropwise addition of two equivalents of 2-mercaptoethanol to a stirred slurry of $Bi(NO_3)_3$ in 95 % ethanol. The resulting yellow solution was stirred for 30 minutes before the addition of $NaCH_3COO$ (3.0 g, 36.6 mmol), followed by stirring for 24 hours.

The yellow slurry was filtered using a Buchner funnel, rinsed with 10 mL aliquots of acetone, air dried and characterized as (**3.17**) by Raman spectroscopy and a melting point; yield 0.98 g, 2.7 mmol, 49 %. The filtrate was allowed to slowly evaporate and gave a yellow microcrystalline solid, which was rinsed with acetone (2 mL) and characterized as (**3.17**) by a melting point and Raman spectroscopy; yield 0.51 g, 1.4 mmol, 25 %. Total yield, 76 %.

Preparation of Bicyclic bis-(2-hydroxyethanethiolato)bismuth(III) Halides. In a typical reaction, (**3.16**) (0.04 - 0.09 M) was generated *in situ* by the dropwise addition of two equivalents of 2-mercaptoethanol to a stirred slurry of $Bi(NO_3)_3$ in 95% ethanol (120 mL). The resulting yellow solution was stirred for 30 minutes before the addition of NaX (X= Cl, Br or I), followed by stirring for 24 hours. The yellow slurry was filtered using a Buchner funnel. The white precipitate ($NaNO_3$, Raman) was rinsed with 10 mL aliquots of acetone and air dried. The clear filtrate was allowed to slowly evaporate in a partially covered beaker. Yields, melting points, chemical analyses and mass spectral data for each compound are presented in Table 7.3; IR, Raman and ^1H NMR spectral data for each compound are presented in Table 7.4 and X-ray crystallographic data is presented in Table 7.5.

The bicyclic bis-(2-hydroxyethanethiolato)bismuth halides were also prepared by a second method. 2-Mercaptoethanol was slowly added to an aqueous slurry of BiX_3 (X = Cl, Br or I). The reaction mixture was stirred at room temperature for one hour and then neutralized with a solution of aqueous Na_2CO_3 (6 M) before being stirred overnight. The

resulting slurry was filtered using a Buchner funnel, rinsed with 10 mL aliquots of distilled water and acetone, respectively, air dried and the precipitate was characterized by Raman spectroscopy and melting point.

Bicyclic bis-(2-hydroxyethanethiolato)bismuth chloride (3.19). Yellow powder was obtained after evaporation of the clear yellow filtrate from the reaction of (**3.19**). (**3.19**) (0.29 g, 0.72 mmol) was recrystallized from boiling acetonitrile producing yellow cubic crystals (0.21 g, 73 % recovery).

Bicyclic bis-(2-hydroxyethanethiolato)bismuth bromide (3.20). The clear, yellow filtrate from the reaction of (**3.20**) was allowed to slowly evaporate in a partially covered beaker for 48 hours giving small yellow needlelike crystals; yield 0.49 g, 1.11 mmol, 22 %. The solubility of (**3.20**) was too low for NMR spectroscopy or pK_a measurement and the crystals were not suitable for X-ray analysis.

Bicyclic bis-(2-hydroxyethanethiolato)bismuth iodide (3.21). The clear, orange filtrate from the reaction of (**3.21**) was allowed to slowly evaporate in a partially covered beaker giving a thick orange oil which could not be characterized.

Table 7.5. X-ray crystallographic data for the bicyclic bis-(2-hydroxyethanethiolatebismuth compounds, (**3.16**), (**3.19**), (**3.22**).

	(**3.16**)	(**3.19**)	(**3.22**)
formula	$C_4H_{10}O_5S_2BiN{\cdot}H_2O$	$C_4H_{10}O_2S_2BiCl$	$C_6H_{13}O_4S_2Bi$
space group	$I4_1/a$	$P2_1/n$	$P2_1/c$
a (Å)	20.337(6)	8.653(2)	8.089(2)
b (Å)	20.337(6)	10.618(3)	16.313(3)
c (Å)	11.303(7)	10.564(2)	8.708(2)
α (°)	90	90	90
β (°)	90	100.51(2)	98.37(3)
γ (°)	90	90	90
V (Å^3)	4674(3)	954.4(4)	1136.8(4)
Z	16	4	4
D_{calc} (g cm^{-3})	2.519	2.774	2.467
μ (cm^{-1})	331.91	426.74	337.79
$100R_w$	4.8	3.6	8.2
Crystallographer	TSC	TSC	TSC

Preparation of Bicyclic bis-(2-hydroxyethanethiolato)bismuth acetate (3.22). (**3.17**) (0.14 g, 0.38 mmol) was dissolved in acetic acid (5 mL), and the solution was slowly evaporated giving yellow needlelike crystals of (**3.22**). Yield, melting point, chemical

analysis and mass spectral data are presented in Table 7.3; IR, Raman and ^{1}H NMR spectral data are presented in Table 7.4 and X-ray crystallographic data is presented in Table 7.5.

Reaction of $BiCl_3$ with $HSCH_2CH_2OMe$ (3.23). A twofold equivalent of ethylene sulfide (2.20 g, 33.6 mmol) was added dropwise to a stirred slurry of $BiCl_3$ (4.27 g, 13.5 mmol) in methanol (100 mL) and conc. HCl (1 mL) and the resulting yellow slurry was stirred at room temperature overnight. The yellow precipitate was filtered using a Buchner funnel and rinsed with 10 mL aliquots of acetone and air dried, yield 4.23 g, 11.4 mmol, 84 %; mp 129 °C; Anal. Calcd for (**3.23**): C, 16.89; H, 3.31; Found: C, 17.08; H, 2.96; Raman (cm^{-1}): 683 (w), 645 (m), 306 (s), 257 (s), 118 (s); IR (cm^{-1}): 1404 (s), 1292 (m), 1263 (s), 1206 (m), 1184 (m), 1173 (w), 1144 (w), 1105 (s), 995 (w), 898 (m), 829 (w), 673 (w), 638 (w), 433 (m), 250 (s). The precipitate is not soluble in common organic solvents such as DMSO, DMF, acetone, water, pyridine and CH_2Cl_2.

Reaction of $Bi(NO_3)_3$ with $HSCH_2CH_2OMe$ (3.24). Ethylene sulfide (1.97 g, 32.7 mmol) was added dropwise to methanol (100 mL) and conc. HNO_3 (1 mL) and stirred at room temperature overnight giving a white precipitate. $Bi(NO_3)_3$ (5.54 g, 11.4 mmol) was added and the resulting yellow slurry was allowed to stir overnight. The yellow precipitate was filtered using a Buchner funnel and rinsed with 10 mL aliquots of acetone and air dried, yield 4.06 g; dp 215 °C; Anal. Calcd for (**3.24**) : C, 15.90; H, 3.11; N, 3.09; Found: C, 16.78; H, 2.90; N, 1.46; Raman (cm^{-1}): 645 (m), 306 (s), 136 (s), 107 (s); IR

(cm^{-1}): 1631 (m), 1428 (s), 1275 (s), 1188 (s), 1145 (m), 1113 (m), 1011 (m), 845 (w), 813 (w), 677 (m), 552 (m), 303 (s). The precipitate is not soluble in common organic solvents such as DMSO, DMF, acetone, water, pyridine and CH_2Cl_2.

Preparation of Halodithiabismuth Heterocycles. In a typical reaction, the dithiol (1,2-ethanedithiol, 1,3-propanedithiol, 1,4-butanedithiol, 2-mercaptoethyl ether or 2-mercaptoethyl sulfide) was added dropwise to a stirred slurry of bismuth trihalide in a 1:1 stoichiometry in 95 % ethanol (100 mL). Yellow precipitate formed immediately, and the reaction mixture was allowed to stir at room temperature overnight. The precipitate was filtered using a Buchner funnel, washed with 20 mL aliquots of distilled water, 95 % ethanol and acetone, respectively, and air dried. Yields, chemical analyses and IR and Raman data for each compound are presented in Table 7.6; mass spectral data are presented in Tables 7.7 and 7.8; and X-ray crystallographic data are presented in Table 7.9. 2-Chloro-1,3-dithia-2-bismolane (**4.60**),[172] 2-bromo-1,3-dithia-2-bismolane (**4.70**),[172] 2-iodo-1,3-dithia-2-bismolane (**4.100**), 2-chloro-1,3-dithia-2-bismane (**4.101**), 2-chloro-1,3-dithia-2,-bismepane (**4.102**), 2-chloro-1,3,6-trithia-2-bismocane (**4.94**),[183] 2-bromo-1,3,6-trithia-2-bismocane (**4.103**), 2-iodo-1,3,6-trithia-2-bismocane (**4.104**) and 2-chloro-1,3-dithia-6-oxa-2-bismocane (**4.97**)[185] were spectroscopically characterized as analytically pure powders. (**4.94**) (0.06 g, 0.15 mmol) was recrystallized from boiling DMSO, yellow needlelike crystals, 0.05 g, 0.13 mmol, 92 % recovery. (**4.97**) (0.08 g, 0.22 mmol) was recrystallized from boiling DMF, yellow cubic crystals, 0.04 g, 0.10 mmol, 43 % recovery. (**4.103**) (0.14 g, 0.31 mmol) was dissolved in hot DMSO (10 mL)

and allowed to slowly evaporate in a partially covered beaker for 24 hours giving a yellow needlelike crystals which were shown to be the same as the powder by a melting point and Raman spectroscopy; yield 0.07 g, 0.16 mmol, 49 % recovery. The crystals were not suitable for X-ray crystallography. (**4.69**) was also formed by the reaction of bismuth oxychloride (2.18 g, 8.4 mmol) in HCl (1 M) with 1,2-ethanedithiol (1.0 g, 10.6 mmol), and was characterized as (**4.69**) by Raman spectroscopy and elemental analysis, yield 2.06 g, 6.1 mmol, 73 %; Anal. Calcd: C, 7.14; H, 1.20; O, 0; S, 19.05; Found: C, 7.98; H, 1.35; O, 0.24; S, 21.07.

Table 7.6. Yields, melting points, analyses and vibrational spectra for halodithiabismuth compounds.

Compd	Yield g (%)	mp [dp]°C	Solubility (ppm Bi)	Elemental Analyses			IR data (cm^{-1})		Raman data (cm^{-1})	
				C_{calc} ($_{found}$)	H_{calc} (H_{found})	S_{calc} (S_{found})				
(4.69)	102.5 (82)	[120]	86	7.14 (7.76)	1.20 (1.25)	19.05 (19.35)	237(s) 330(s) 436(m)	638(m) 665(m)	76(s) 105(s) 126(s) 145(s)	200(s) 279(s) 324(vs) 435(w)
(4.70)	1.03 (92)	[145]	5.1	6.30 (6.74)	1.06 (1.17)	16.83 (20.56)	278(s) 314(m) 432(m) 662(w) 827(s)	907(w) 919(m) 1110(w) 1123(w) 1152(w)	80(s) 110(vs) 126(s) 197(s) 251(m)	277(s) 302(vs) 323(s) 432(m) 635(w)
(4.100)	1.87 (96)	[165]	<0.2	5.57 (5.85)	0.94 (1.00)	*	247(s) 277(s) 293(s) 314(s) 425(s) 634(m) 661(m)	826(s) 916(s) 1022(w) 1111(w) 1153(w) 1161(w) 1248(m)	57(m) 69(m) 83(s) 111(s) 129(m) 166(m) 228(m)	249(m) 277(s) 288(vs) 318(s) 426(w) 550(w) 633(w)
(4.101)	5.95 (95)	110	<0.2	10.24 (10.54)	1.72 (1.72)	14.29 (11.16)	295(vs) 480(w) 528(m)	611(w) 638(w) 669(w)	102(vs) 164(s) 300(vs)	445(w) 480(w) 543(w)
(4.102)	4.59 (97)	[100]	<0.02	13.17 (13.61)	2.21 (2.12)	17.59 (15.12)	286(w) 304(m) 370(w)	388(w) 420(w) 639(w)	68(s) 89(vs) 114(vs) 132(vs) 194(s) 255(vs)	277(vs) 305(vs) 371(m) 461(w) 505(w) 641(m)
(4.94)	15.01 (87)	[170]	140	12.11 (12.34)	2.03 (2.03)	24.25 (23.77)	283(w) 294(s) 332(s) 422(s) 452(w)	463(m) 608(w) 629(w) 660(m) 684(w)	81(s) 120(vs) 163(s) 190(s) 225(s)	294(vs) 331(m) 418(w) 450(w) 610(w)
(4.103)	1.76 (99)	[170]	6.4	10.89 (10.75)	1.83 (1.84)	21.80 (24.16)	226(s) 281(s) 301(s) 416(s) 446(w) 565(w) 669(w)	675(w) 772(w) 836(s) 895(s) 922(s) 969(w) 1110(w)	77(s) 120(vs) 147(s) 174(s) 205(m) 225(m) 298(vs)	318(m) 415(w) 442(w) 624(w) 656(w) 676(w)
(4.104)	2.42 (98)	[140]	<0.2	9.78 (10.13)	1.64 (1.71)	*	278(vs) 304(vs) 415(s) 443(w) 642(w) 674(m)	832(s) 839(s) 900(s) 921(s) 1019(w) 1109(m)	67(m) 117(s) 141(s) 170(m) 203(m) 217(m)	277(m) 295(s) 313(w) 413(w) 439(w) 624(w)
(4.97)	4.78 (92)	[190]	0.3	12.62 (14.64)	2.12 (2.39)	16.80 (20.65)	224(s) 256(s) 293(s) 316(m) 366(w)	471(m) 509(w) 538(w) 666(m)	74(s) 118(vs) 182(s) 237(s) 275(s)	293(s) 318(vs) 361(w) 468(w) 534(w)

Table 7.7. Electron ionization (70 eV) mass spectral data of (**4.69**), (**4.94**), (**4.97**), (**4.101**), (**4.102**).

Compound	m/z	% Abundance	Ion
(**4.69**)	336	25	$M^{\bullet+}$
	301	30	$[M - Cl]^+$
	273	10	$[BiS_2]^+$
	244	18	$[BiCl]^+$
	241	58	$[BiS]^+$
	209	77	Bi^+
	92	100	$[S_2C_2H_4]^+$
(**4.101**)	314	4	$[BiCl_3]^+$
	279	15	$[BiCl_2]^+$
	244	<1	$[BiCl]^+$
	209	8	Bi^+
	106	100	$[S_2C_3H_6]^+$
(**4.102**)	314	35	$[BiCl_3]^+$
	279	100	$[BiCl_2]^+$
	244	19	$[BiCl]^+$
	209	45	Bi^+
	122	3	$[S_2C_4H_8]^+$
(**4.94**)	396	<1	$M^{\bullet+}$
	361	<1	$[M - Cl]^+$
	336	73	$[ClBiS_2C_2H_4]^+$
	301	30	$[BiC_2H_4]^+$
	241	58	$[BiS]^+$
	209	95	Bi^+
	152	100	$[S_3C_4H_8]^+$
(**4.97**)	380	9	$M^{\bullet+}$
	345	8	$[M - Cl]^+$
	285	5	$[BiSC_2H_4O]^+$
	244	9	$[BiCl]^+$
	241	10	$[BiS]^+$
	209	19	Bi^+
	136	100	$[S_2OC_4H_8]^+$

SC = sampling cone

Table 7.8. APCI spectral data for compounds (**4.69**), (**4.194**), (**4.97**) and (**4.101**) in DMSO and (**4.105**), (**4.106**), (**4.108**) and (**4.109**).

Compound	m/z	Relative Abundance		Ion
		SC = 30 V	SC = 10 V	
(**4.69**)	301	100	-	$[M - Cl]^+$
	379	11	100	[M - Cl + DMSO]
	457	-	17	$[M - Cl + 2DMSO]^+$
(**4.101**)	315	100	-	$[M - Cl]^+$
	393	8	100	$[M - Cl + DMSO]^+$
	471	-	23	$[M - Cl + 2DMSO]^+$
(**4.94**)	301	27	-	$[BiS_2C_2H_4]^+$
	361	100	16	$[M - Cl]^+$
	379	4	100	$[BiS_2C_4H_4 + DMSO]^+$
	439	-	55	$[M - Cl + DMSO]^+$
	479	-	18	$[BiS_2C_4H_4 + 2DMSO]^+$
(**4.97**)	285	12	-	$[BiSOC_2H_4]^+$
	345	100	-	$[M - Cl]^+$
	363	10	16	$[BiSOC_2H_4 + DMSO]^+$
	423	-	100	$[M - Cl + DMSO]^+$
(**4.105**)	301	100		$[BiS_2C_2H_4]^+$
(**4.106**)	209	100		Bi^+
	315	86		$[BiS_2C_3H_6]^+$
(**4.108**)	301	16		$[BiS_2C_2H_4]^+$
	361	100		$[BiS_3C_4H_8]^+$
(**4.109**)	209	8		Bi^+
	285	9		$[BiSC_2H_4O]^+$
	345	100		$[BiS_2OC_2H_4]^+$
	827	1		MH^+

Table 7.9. X-ray crystallographic data for the dithiabismuth heterocycles, (**4.69**)·2pyr, (**4.70**)·2pyr, (**4.94**), (**4.97**).

	(**4.69**)•2pyr	(**4.70**)•2pyr	(**4.94**)	(**4.97**)
formula	$C_{12}H_{14}S_2BiClN_2$	$C_{12}H_{14}S_2BiBrN_2$	$C_4H_8S_3BiCl$	$C_4H_8OS_2BiCl$
space group	$P2_1$	$Cmc2_1$	Pnma	Pnma
a (Å)	9.590(3)	16.741(3)	8.1280(9)	7.885(4)
b (Å)	9.206(3)	9.986(2)	12.263(5)	12.307(5)
c (Å)	9.761(2)	9.442(2)	9.2529(9)	9.158(9)
α (°)	90	90	90	90
β (°)	117.1(2)	90	90	90
γ (°)	90	90	90	90
V (Å^3)	767.1(4)	1578.5(5)	922.3(6)	888.7(10)
Z	2	4	4	4
D_{calc} (g cm^{-3})	2.142	2.269	2.857	2.845
μ (cm^{-1})	118.81	272.35	199.7	205.37
$100R_w$	4.7	11.6	3.3	15.8
Crystallographer	TSC	TSC	TSC	TSC

Preparation of 2-Halo-2,2-dipyridyl-1,3-dithia-2-bismolanes, (4.69)•2pyr, (4.70)• 2pyr, (4.100)•2pyr. In a typical reaction, the 2-halo-1,3-dithia-2-bismolane was dissolved in boiling pyridine (30 mL) and the solution slowly cooled to room temperature, giving needlelike crystals which were filtered using a Buchner funnel, washed with cold pyridine (10 mL), air dried for 30 minutes. Yields, IR and Raman spectra are presented in Table 7.10 and X-ray crystal data are presented in Table 7.9 (the crystals of **(4.100)**•2pyr were not suitable for X-ray analysis).

Table 7.10. Yields, melting points, analyses and vibrational data for 2-halo-2,2-dipyridyl-1,3-dithiabismuth compounds.

Compd	Yield g (%)	mp [dp] °C	^{1}H NMR (ppm)	IR (cm^{-1})		Raman (cm^{-1})	
(**4.69**)·2pyr	0.46 (81)	[130]	8.6 (s, 4H) 7.4 (s, 2H) 7.1 (s, 4H) 1.7 (s, 4H)	581(w) 681(m) 837(w) 915(w) 1108(m)	1185(s) 1197(m) 1276(w) 1412(s)	91(s) 195(s) 279(s) 326(vs) 416(w)	439(w) 552(w) 624(w) 647(m) 674(w)
(**4.70**)·2pyr	0.29 (75)	134 - 137	*	281(s) 333(m) 413(m) 443(m) 622(s) 695(s) 759(s) 841(m) 918(m) 1004(m) 1030(m)	1061(m) 1101(m) 1154(m) 1215(m) 1233(w) 1233(w) 1274(w) 1304(w) 1416(w) 1588(m)	87(s) 193(s) 278(s) 326(vs) 414(w)	439(w) 624(w) 646(w) 671(w)
(**4.100**)·2pyr	0.21 (54)	125 - 130	*	279(s) 325(s) 412(m) 439(m) 619(s) 694(s) 753(s) 842(m) 917(w)	998(s) 1034(s) 1061(s) 1105(w) 1144(m) 1208(m) 1275(w) 1591(s)	54(m) 73(s) 101(s) 139(m) 160(m) 198(s) 237(s)	262(s) 281(s) 308(vs) 434(w) 634(w) 656(w)

Preparation of Tethered Bicyclodithiabismuth Heterocycles. In a typical reaction, the dithiol (1,2-ethanedithiol, 1,3-propanedithiol, 1,4-butanedithiol, 2-mercaptoethyl ether or 2-mercaptoethyl sulfide) was added dropwise to a stirred slurry of bismuth nitrate pentahydrate or bismuth acetate in a 2:3 stoichiometry in 95 % ethanol (100 mL). Yellow

precipitate formed immediately, and the reaction mixture was allowed to stir at temperature overnight. The precipitate was filtered using a Buchner funnel, washed with 20 mL aliquots of distilled water, 95 % ethanol and acetone, respectively, and air dried. Yields, chemical analyses, IR and Raman data for each compound are presented in Table 7.11; mass spectral data are presented in Table 7.8 and X-ray crystallographic data are presented in Table 7.12. 1,2-Bis-((1,3-dithia-bismolan-2-yl)thio)ethane (**4.105**), 1,3-bis((1,3-dithia-2-bisman-2-yl)thio)propane (**4.106**), 1,4-bis((1,3-dithia-2-bismepan-2-yl)thio)butane (**4.107**), bis(((1,3,6-trithia-2-bismocan-2-yl)thio)ethyl) sulfide (**4.108**) and bis(((1,3-dithia-6-oxa-2-bismocan-2-yl)thio)ethyl) ether (**4.109**) were spectroscopically characterized as analytically pure powders. (**4.105**) (0.11 g, 0.16 mmol) was recrystallized from boiling DMSO, yellow cubic crystals (0.03 g, 27 % recovery). (**4.108**) (0.26 g, 0.30 mmol) was recrystallized from DMSO, yellow needlelike crystals (0.01 g, 6 % recovery).

Table 7.11. Yields, melting points, analyses and vibrational data for tethered dithiabismuth compounds.

Compd	Yield g (%)	mp [dp]°C	Solubility (ppm Bi)	Elemental Analyses			IR data (cm^{-1})		Raman data (cm^{-1})	
				C_{calc} ($_{found}$)	H_{calc} (H_{found})	S_{calc} (S_{found})				
(4.105)	1.27 (97)	[145]	1.9	10.38 (10.60)	1.74 (1.72)	27.70 (27.65)	255(vs) 269(vs) 302(m) 318(s)	433(s) 634(m) 662(m) 672(w)	71(s) 86(s) 104(s) 132(s) 159(s) 179(s) 196(s)	258(vs) 269(vs) 288(s) 310(vs) 428(m) 633(m) 660(w)
(4.106)	2.06 (92)	[170]	0.6	14.68 (15.11)	2.46 (2.52)	26.12 (22.23)	240(s) 264(s) 297(vs) 307(w) 319(s)	430(m) 636(w) 663(w) 677(m)	86(s) 136(s) 165(s) 181(s) 230(s) 240(s)	278(vs) 430(w) 617(w) 641(w) 658(w) 671(w)
(4.107)	2.58 (98)	[140]	170	18.51 (19.02)	3.11 (3.07)	24.71 (23.62)	256(vs) 266(vs) 319(vs) 350(m) 378(m) 429(s)	526(w) 570(w) 659(m) 669(m) 673(m)	83(vs) 120(vs) 190(s) 203(s) 246(vs) 267(vs)	278(vs) 430(w) 617(w) 641(w) 658(w) 646(m)
(4.108)	1.28 (67)	[180]	48	16.47 (16.78)	2.77 (2.71)	32.99 (32.47)	248(s) 326(m) 467(w)	493(m) 530(w) 669(m)	68(s) 102(s) 126(s) 162(s) 181(s) 242(vs) 271(vs)	294(vs) 332(m) 425(w) 620(m) 656(w) 682(m)
(4.109)	2.06 (99)	177-178	130	17.44 (17.63)	2.93 (2.85)	23.27 (26.65)	283(vs) 294(vs) 301(s) 335(s) 422(s) 453(m)	470(m) 608(w) 629(w) 660(s) 684(m)	92(s) 169(s) 213(s) 242(vs)	271(s) 303(s) 491(w) 666(m)

Table 7.12. X-ray crystallographic data for the tethered dithiabismuth heterocycles, (**4.105**) and (**4.108**).

	(**4.105**)	(**4.108**)	(**4.110**)
formula	$C_6H_{12}S_6Bi_2$	$C_{12}H_{24}S_9Bi$	$C_8H_{17}O_1S_3Bi$
space group	$P2_1/c$	$P\underline{1}$	$P2_1/a$
a (Å)	8.875(4)	9.757(2)	9.158(1)
b (Å)	17.582(12)	16.625(2)	11.872(2)
c (Å)	18.250(9)	37.942(3)	8.037(1)
α (°)	90	90.05(2)	90
β (°)	96.05(4)	107.84(3)	90.09(1)
γ (°)	90	105.81(1)	90
V (Å^3)	2832(3)	1174.9(6)	873.9(2)
Z	8	2	4
D_{calc} (g cm^{-3})	3.260	2.473	2.867
μ (cm^{-1})	256.48	364.17	456.33
$100R_w$	3.5	5.6	6.8
Crystallographer	JFR	TSC	TSC

Formation of (4.105) from (4.69). (**4.69**) (0.58 g, 1.7 mmol) was combined with 1,2-ethanedithiol (0.11 g, 1.1 mmol) in aqueous $NaNO_3$ (0.10 M). The slurry was allowed to stir overnight at room temperature, and the yellow precipitate was filtered using a Buchner funnel, rinsed with 10 mL aliquots of water and acetone, respectively, air dried, and characterized by melting point and Raman spectroscopy, yield 93 %.

Formation of (4.105) from (4.106). (**4.106**) (0.11 g, 0.15 mmol) was dissolved in hot 1,2-ethanedithiol (15 mL) and allowed to slowly evaporate in a partially covered beaker. Cubic yellow crystals formed after 24 hours and were characterized as (**4.105**) by a melting point, Raman and IR spectroscopy, yield 0.057 g, 0.08 mmol, 54 %.

Formation of (4.108) from (4.94). (**4.94**) (1.4 g, 3.6 mmol) was combined with 2-mercaptoethyl sulfide (0.72 g, 4.7 mmol) in aqueous $NaNO_3$ (0.12 M). The slurry was allowed to stir overnight at room temperature, and the yellow preciptiate was filtered using a Buchner funnel, rinsed with 10 mL aliquots of water and acetone, respectively, and characterized as (**4.108**) by a melting point and Raman spectroscopy, yield 97 %.

Preparation of 2-Thioethanol-1,3-dithia-2-bismolane (4.110). 1,2-Ethanedithiol (0.89 g, 9.40 mmol) was added dropwise to an aqueous solution of (**3.16**) which was generated *in situ* by the reaction of 2-mercaptoethanol (1.56 g, 20.0 mmol) with $Bi(NO_3)_3$ (4.59 g, 9.46 mmol). The resulting yellow slurry was allowed to stir overnight and the precipitate was filtered using a Buchner funnel, rinsed with 10 mL aliquots of distilled water, air

dried and characterized as (**4.110**) by Raman and IR spectroscopy and a melting point, yield 3.36 g, 8.89 mmol, 95 %; mp 112 - 114 °C; Raman (cm^{-1}): 667 (w), 644 (w), 482 (w), 433 (w), 321 (vs), 301 (s), 283 (vs), 212 (m), 185 (s), 159 (m), 137 (vs), 123 (s), 100 (s), 79 (m); IR (cm^{-1}): 3222 (s, br), 1413 (s), 1293 (s), 1279 (s), 1236 (m), 1215 (m), 1151 (m), 1118 (m), 1054 (vs), 1012 (m), 988 (vs), 938 (w), 929 (m), 839 (vs), 674 (s), 643 (s), 482 (s), 440 (s), 331 (vs), 305 (s), 272 (vs). Slow evaporation of a hot solution of (**4.110**) (0.29 g, 0.77 mmol) in DMF (7 mL) yielded yellowish-green cubic crystals, 0.18 g, 0.48 mmol, 62 % recovery; Anal: Calcd. C, 12.69; H, 2.40; O, 4.23; S, 25.42 %. Found. C, 12.72; H, 2.38; O, 2.17; S, 26.09 %. X-ray crystallographic data are presented in Table 7.12. (**4.110**) (0.26 g, 0.30 mmol) was recrystallized from DMSO and the yellow needlelike crystals were characterized by Raman, yield 0.01 g, 6 % recovery.

(**4.110**) was also obtained by the dropwise addition of 2-mercaptoethanol (0.60 g, 7.66 mmol) to a stirred slurry of 2-chloro-1,3-dithia-2-bismolane (1.98 g, 5.89 mmol) in an aqueous solution of $NaNO_3$ (0.2 M). The resulting yellow slurry was allowed to stir overnight at room temperature and the yellow precipitate was filtered using a Buchner funnel, rinsed with 10 mL aliquots of distilled water and acetone, respectively, air dried and characterized as (**4.110**) by Raman and IR spectroscopy and melting point analysis, yield 2.12 g, 5.62 mmol, 96 %.

Reaction of 2-Chloro-1,3-dithia-2-bismolane with Thiophenol (4.111). $NaNO_3$ (1.42 g, 16.7 mmol) and 2-thiophenol (0.12 g, 1.1 mmol) were added, respectively, to a slurry

of (**4.69**) (0.29 g, 0.86 mmol) in distilled water (100 mL). The reaction mixture was allowed to stir overnight at room temperature then the orange-yellow precipitate was filtered using a Buchner funnel, rinsed with distilled water and acetone, respectively, air dried, yield 0.56 g; mp 53 °C; Raman (cm^{-1}): 691 (m), 659 (w), 635 (w), 616 (w), 543 (w), 476 (w), 431 (w), 415 (m), 325 (s), 309 (vs), 281 (m), 256 (s), 233 (s), 181 (s), 170 (s), 132 (vs), 108 (vs), 74 (s). IR (cm^{-1}): 1577 (s), 1402 (s), 1300 (w), 1282 (w), 1238 (w), 1151 (w), 1075 (m), 1025 (s), 1000 (w), 913 (m), 896 (w), 838 (m), 737 (vs), 690 (vs), 660 (w), 475 (s), 431 (w), 334 (m), 318 (s), 290 (m), 264 (s). The precipitate was not soluble in common organic solvents such as DMSO, toluene or pyridine.

Appendix A

The atomic coordinates (x_a, y_a, z_a) of the two crystallographically independent molecules of (**3.16**) in the space group I-4 can be transformed into the atomic coordinates (x_b, y_b, z_b) of one molecule in the space group $I4_1/a$ by the following operations.

For the first molecule, apply an origin shift by

$[x_a - 0.5 = x_b', y_a - 0.75 = y_b'; z_a - 0.625 = z_b']$

then apply $I4_1/a$ symmetry operation

$[0.5 - x_b' = x_b, -y_b' = y_b; 0.5 + z_b' = z_b]$

For the second molecule, apply the same origin shift by

$[x_a - 0.5 = x_b', y_a - 0.75 = y_b'; z_a - 0.625 = z_b']$

then apply two $I4_1/a$ symmetry operations

$[-x_b' + 0.75 = x_b'', y_b' + 0.75 = y_b''; -(z_b' + 0.75) = z_b'']$

$[0.5 - x_b'' = x_b, -y_b'' = y_b; 0.5 + z_b'' = z_b]$

References

1. Sastry, P. V. P. S. S.; West, A. R. *Physica C* **1995**, *250*, 87-92.

2. Ishibashi, T.; Yoda, O. *J Appl. Phys.* **1995**, *78(3)*, 2120-2122.

3. Matchett, M. A.; Chiang, M.Y.; Buhro, W. E. *Inorg. Chem.* **1990**, *29*, 360-362.

4. Katayana, S.; Sekine, M. *J. Mater. Res.* **1991**, *6(1)*, 36-41.

5. See, for example: Gorbach, S.L. *Gastroenterology* **1990**, *99*, 863-875. Köpf-Maier, P.; Klapötke, T. *Inorg. Chim. Acta* **1988**, *152*, 49-52. Klapötke, T.; Gowik, P. *Z. Naturforsch.* **1987**, *42b*, 940-942. Klapötke, T. *J. Organomet. Chem.* **1987**, *331*, 299-307.

6. Diemer, R.; Keppler, B. K.; Dittes, U.; Nuber, B.; Seifried, V.; Opferkuch, W. *Chem. Ber.* **1995**, *128*, 335-342.

7. Dittes, U.; Keppler, B. K.; Nuber, B. *Angew. Chem. Int. Ed. Engl.* **1996**, *35(1)*, 67-68.

8. Summers, S. P.; Abboud, K. A.; Farrah, S. R.; Palenik, G. J. *Inorg. Chem.* **1994**, *33*, 88-92.

9. Sadler, P. J.; Sun, H.; Li, H. *Chem. Eur. J.* **1996**, *2(6)*, 701-708.

10. Sadler, P. J.; Sun, H. *J. Chem. Soc., Dalton Trans.* **1995**, 1395-1401.

11. Baxter, G. F. *The Pharmaceutical Journal* **1989**, *Dec.*, 805-810.

12. Baxter, G. F. *Chemistry in Britain* **1992**, *May*, 445-448.

13. Sun, H.; Li, H.; Sadler, P. J. *Chem. Ber.* **1997**, *130*, 669-681.

14. Burford, N.; Veldhuyzen van Zanten, S. J. O.; Agocs, L.; Best, L.; Cameron, T. S.; Yhard. G. B.; Curtis, J. M. *Gastroenterology* **1994**, *106*, A59. LeBlanc, R.; Veldhuyzen van Zanten, S. J. O.; Burford, N.; Agocs, L.; Leddin, D. J. *Gastroenterology* **1995**, *106*, A860. Sandha, G. S.; LeBlanc, R.; Veldhuyzen van Zanten, S. J. O.; Agocs, L.; Burford, N.; Leddin, D. J. *Gut* submitted April 1997.

15. Agocs, L.; Best, L.; Bryden, L.; Burford, N.; Hoffman, P. S.; Lim-Morrison, S.; Mahony, D. E. manuscript in progress.

16. Bierer, D. W. *Rev. Infect. Dis.* **1990**, *12(1)*, S3-S8.

17. Cozzi, L. M.; Megerian, C. A.; Dugue, C.; Barcello, M.; Abdul-Karim, F.; Arnold, J. E.; Maniglia, A. J. *Laryngoscope* **1992**, *102*, 597-599.

18. Vanhoe, H.; Versieck, J.; Vanballenberghe, L.; Dams, R. *Clin. Chim. Acta* **1993**, *219*, 79-91.

19. Marshall, B. J.; Warren, J. R. *Lancet.* **1983**, *1*, 1311-1315.

20. Snyder, J. D. *N. Engl. J. Med.* **1993**, *328(23)*, 1705-1706.

21. Veldhuyzen van Zanten, S. J. O.; Sherman, P. M. *Can. Med. Assoc. J.* **1994**, *150(2)*, 177-185.

22. Pullan, R. D.; Ganesh, S.; Mani, V.; Morris, J.; Evans, B. K.; Williams, G. T.; Rhodes, J. *Gut* **1993**, *34*, 676-679.

23. Fenton, J. E.; Blayney, A. W.; O'Dwyer, T. P. *J. Laryngol. Otol.* **1995**, *109*, 203-205.

24. Callanan, V.; Curran, A. J.; Smyth, D. A.; Gormley, P. K. *J. Laryngol. Otol.* **1995**, *109*, 206-208.

25. Wormald, P. J.; Sellars, S. L. *J. Laryngol. Otol.* **1994**, *108*, 761-762.

26. Von Bose, M. J.; Zaudig, M. *Br. J. Psychiatry* **1991**, *158*, 278-280.

27. Köpf-Maier, P. *Eur. J. Clin. Pharmacol.* **1994**, *47*, 1-16.

28. Gump, D. W.; Nadeau, O. W.; Hendricks, G. M.; Meyer, D. H. *Med. Microbiol. Immun.* **1992**, *181*, 131-143.

29. Manhart, M. D. *Rev. Infect. Dis.* **1990**, *12(1)*, S11-S15.

30. Wieriks, J.; Hespe, W.; Jaitly, K. D.; Koekkoek, P. H.; Lavy, U. *Scand. J. Gastroenterol.* **1982**, *17(80)*, 11-16.

31. Asato, E.; Driessen, W. L.; DeGraff, R. A. G.; Hulsbergen, R. B.; Reedjik, J. *Inorg. Chem.* **1991**, *30*, 4210-4218.

32. Herrmann, W. A.; Herdtweck, E.; Pajdla, L. *Z. fur Kristallogr.* **1992**, *198*, 257-264.

33. See, for example: Graham, D. Y. *Gastroenterology* **1989**, *96*, 615-625. Nomura, A.; Stemmerman, G. N.; Chyou, P.-H.; Kato, I.; Perez-Perez, G. I.; Blaser, M. J. *N. Engl. J. Med.* **1988**, *325*, 1132-1136. Parsonnet, J.; Friedman, G. D.; Vandersteen, D. P. *N. Engl. J. Med.* **1991**, *325*, 1127-1131.

34. Ottlecz, A; Romero, J. J.; Hazell, S. L.; Graham, D. Y.; Lichtenberger, L. M. *Dig. Dis. Sci.* **1993**, *38(11)*, 2071-2080.

35. Huesca, M; Gold, B.; Sherman, P.; Lewin, P.; Lingwood, C. *Zbl. Bakt.*, **1993**, *280*, 244-252.

36. Cutler, A. F.; Schubert, T. T. *Am. J. Gastroenterol.* **1993**, *88(4)*, 505-509.

37. Lambert, J. R. *Scand. J. Gastroenterol.* **1991**, *26(S185)*, 13-21.

38. Goh, K. L.; Parasakthi, N.; Peh, S. C.; Wong, N. W.; Lo, Y. L.; Puthucheary, S. D. *Scand. J. Gastroenterol.* **1991**, *26*, 1123-1131.

39. Veldhuyzen van Zanten, S. J. O.; Sherman, P. M. *Can. Med. Assoc. J.* **1994**, *150(2)*, 189-198.

40. Hunter, F. M.; Correa, P.; Fontham, E.; Ruiz, B.; Sobhan, M.; Samloff, M. *Dig. Dis. Sci.* **1993**, *38(11)*, 2081-2086.

41. Abrams, M. J.; Murrer, B. A. *Science* **1993**, *261*, 725-730.

42. Tytgat, G. N. J. *Digestion* **1987**, *37(2)* 31-41.

43. Elder, J. B. *Scand. J. Gastroenterol.* **1986**, *21(S122)*, 14-16.

44. Lee, S. P. *Scand. J. Gastroenterol.* **1991**, *26(S185)*, 1-6.

45. Beil, W.; Bierbaum, S.; Sewing, K.-F. *Pharmacology* **1993**, *47*, 135-140.

46. Baer, W.; Koopman, H.; Wagner, S. *Zbl. Bakt.* **1993**, *280*, 253-258.

47. Prewett, E. J.; Nwokolo, C. U.; Hudson, M.; Sawyerr, A. M.; Fraser, A.; Pounder, R. E. *Aliment. Pharmacol. Ther.* **1991**, *5*, 481-490.

48. 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.

49. Bardhan, K. D.; Dekkers, C. P. M.; Lam, S. K.; Nowak, A.; Schaffalitzky de Muckadell, O. B.; Schutze, K.; Tildesley, G.; Kler, L.; Forster, J. K.; Lacey, L. F.; Roberts, P. M.; Isal, J. P. *Aliment. Pharmacol. Ther.* **1995**, *9*, 497-506.

50. Stables, R.; Campbell, C. J.; Clayton, N. M.; Clitherow, J. W.; Grinham, C. J.; McColm, A. A.; McLaren, A.; Trevethick, M. A. *Aliment. Pharmacol. Ther.* **1993**, *7*, 237-246.

51. Hudson, N.; Murray, F. E.; Cole, A. T.; Turnbull, G. M.; Lettis, S.; Hawkey, C. J. *Aliment. Pharmacol. Ther.* **1995**, *7*, 515-521.

52. Peterson, W. L.; Ciociola, A. A.; Sykes, D. L.; McSorley, D. J.; Webb, D. D. and the RBC *H. pylori* Study Group. *Aliment. Pharmacol. Ther.* **1996**, *10*, 251-261.

53. Tytgat, G. N. J; Rauws, E.; Langenberg, W. *Scand. J. Gastroenterol.* **1986**, *21(S122)*, 22-29.

54. Marshall, B. J. *Am. J. Gastroenterol.* **1991**, *86(1)*, 16-25.

55. de Boer, W. A.; Tytgat, G. N. J. *Am. J. Gastro.* **1995**, *90(9)*, 1381-1382.

56. *Toxicity of Industrial Metals, 2nd Ed.*; Browning, E.; Butterworth & Co. Publishers Ltd. Toronto; 1969. pp 23-60, 87-89, 172-199, 226-242.

57. Slikkerveer, A.; de Wolff, F. A. *Med. Toxicol. Adverse Drug Exp.* **1989**, *4(5)*, 303-323.

58. Jungreis, A. C.; Schaumberg, H. H. *Neurology* **1993**, *43*, 1265.

59. Friedland, R. P.; Lerner, A. J.; Hedera, P.; Brass, E. P. *Clin. Neuropharm.* **1993**, *16(2)*, 173-176.

60. Gordon, M. F.; Abrams, R. I.; Rubin, D. B.; Barr, W. B.; Correa, D. D. *Mov. Dis.* **1995**, *10(2)*, 220-222.

61. Gavey, C. J.; Szeto, M.-L.; Nwokolo, C. U.; Sercombe, J.; Pounder, R. E. *Aliment. Pharmacol. Ther.* **1989**, *3*, 21-28.

62. Slikkerveer, A.; Jong, H. B.; Helmich, R. B.; de Wolff, F. A. *J. Lab. Clin. Med.* **1992**, *119*, 529-537.

63. Levy, G. *Am. J. Dis. Child.* **1993**, *147(12)*, 1281.

64. Sainsbury, S. J. *West. J. Med.* **1991**, *155*, 637-639.

65. Vernace, M. A.; Bellucci, A. G.; Wilkes, B. M. *Am. J. Med.* **1994**, *97*, 308-309.

66. Molina, J. A.; Jiménez- Jiménez, F. J.; Calandre, L. *Lancet* **1994**, *44(3)*, 582.

67. Gyurasics, A.; Koszorus, L.; Varga, F.; Gregus, Z. *Biochem. Pharmacol.* **1992**, *44(7)*, 1275-1281.

68. Lambert, J. R. *Rev. Infect. Dis.* **1991**, *13(8)*, S691-S695.

69. Muetterties, E. L.; Wright, C. M. *J. Am. Chem. Soc.* **1964**, *86*, 5132-5137.

70. Muetterties, E. L.; Roesky, H.; Wright, C. M. *J. Am. Chem. Soc.* **1966**, *88(21)*, 4856-4861.

71. Dittes, U.; Vogel, E.; Keppler, B. K. *Coord. Chem. Rev.* **1997**, in press.

72. Diemer, R.; Keppler, B. K.; Dittes, U.; Nuber, B.; Seifried, V.; Opferkuch, W. *Chem. Ber.* **1995**, *128*, 335-342.

73. Hulett, L. G. and Thornton, D. A. *J. Inorg. Nucl. Chem.* **1973**, *35*, 2661-2668.

74. Brechbiel, M. W.; Gansow, O. A.; Pippin, C. G.; Rogers, R. D.; Planalp, R. P. *Inorg. Chem.* **1996**, *35*, 6343-6348.

75. Brintzinger, H.; Munkelt, S. *Z. Anorg. Allg. Chem.* **1948**, *256*, 65-74.

76. See, for example: Phillips, R. J.; Fritz, J. S. *Anal. Chem.* **1978**, *50(11)*, 1504-1508. Brajter, K.; Dabek-Zlotorzynska, E. *Talanta* **1986**, *33(2)*, 149-154. Isshiki, K.; Tsuji, F.; Kuwamoto, T.; Nakayama, E. *Anal. Chem.* **1987**, *59*, 2491-2495. Daih, B.-J.; Huang, H.-J. *Anal. Chim. Acta* **1992**, *258*, 245-252.

77. Rogers, R. D.; Bond, A. H.; Aguinaga, S. *J. Am. Chem. Soc.* **1992**, *114*, 2960-2967.

78. Kiprof, P.; Scherer, W.; Pajdla, L.; Herdtweck, E.; Herrmann, W. A. *Chem. Ber.* **1992**, *125*, 43-46.

79. Burgess, J.; Fawcett, J.; Parsons, S. A.; Russell, D. R. *Acta Cryst.* **1994**, *C50*, 1911-1913.

80. Herrmann, W. A.; Herdtweck, E.; Scherer, W.; Kiprof, P.; Pajdla, L. *Chem. Ber.* **1993**, *126*, 51-56.

81. Udovenko, A. A.; Volkova, L. M.; Sergienko, S. S.; Davidovich, R. L.; Shevenko, V. Y. *Koord. Khim.* **1983**, *9*, 711.

82. Pell, J. W.; Davis, W. C.; zur Loye, H. C. *Inorg. Chem.* **1996**, *35*, 5754-5755.

83. Alberti, A.; Hudson, A.; Maccioni, A.; Podda, G.; Pedulli, G. F. *J. Chem. Soc., Perkin Trans.* **1981**, 1274-1279.

84. *Inorganic Chemistry, 4th Ed.*; Huheey, J. E.; Keiter, E. A. and Keiter, R. L.; Harper Collins College Pubishers. New York; 1993. 522-524.

85. Breeze, S. R.; Wang, S. *Angew. Chem. Int. Ed. Engl.* **1993**, *32(4)*, 589-591.

86. Garcia-Montalvo, V.; Cea-Olivares, R.; Williams, D. J.; Espinosa-Perez, G. *Inorg. Chem.* **1996**, *35*, 3948-3953.

87. Williams, D. J. *Inorg. Nucl. Chem. Lett.* **1980**, *16*, 189-193.

88. Engelhardt, U.; Rapko, B. M.; Duesler, E. N.; Frutos, D.; Paine, R. T.; Smith, P. H. *Polyhedron* **1995**, *14*, 2361-2369.

89. Weitze, A.; Henschel, D.; Blaschette, A.; Jones, P. G. *Z. Anorg. Allg. Chem.* **1995**, *621*, 1746-1754.

90. See, for example: Pearson, R.G. *J. Am. Chem. Soc.*, **1985**, *107*, 3533-3539. Pearson, R.G. *J. Am. Chem. Soc.* **1985**, *107*, 6801-6806. Politzer, P. *J. Chem. Phys.* **1987**, *86(2)*, 1072-1073.

91. Hespe, W.; Kamsteeg, H.; Harmsen, A. R.; Hall, D. W. R.; De Leede, L. G. J. *Gastroenterol.* **1993**, *104(4)*, 1242-1243.

92. Herrmann, W. A.; Herdtweck, E.; Pajdla, L. *Inorg. Chem.* **1991**, *30*, 2581-2582.

93. Asato, E.; Katsura, K.; Mikuriya, M.; Fujii, T.; Reedjik, J. *Chem. Lett.* **1992**, 1967-1970.

94. Asato, E.; Hol, C. M.; Hulsbergen, F. B.; Klooster, N. T. M.; Reedjik, J. *Inorg. Chim. Acta* **1993**, *214*, 159-167.

95. Asato, E.; Katsura, K.; Mikuriya, M.; Fujii, T.; Reedjik, J. *Inorg. Chem.* **1993**, *32*, 5322-5329.

96. Asato, E.; Katsura, K.; Mikuriya, M.; Turpeinen, U.; Mutakainen, I.; Reedjik, J. *Inorg. Chem.* **1995**, *34*, 2447-2454.

97. 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.

98. *Merck Index* **1989**, *11*, 197.

99. *Merck Index* **1996**, *12*, 421.

100. Sun, H.; Li, H.; Sadler, P. J. *J. Inorg. Biochem.* **1995**, *59*, 190.

101. Curry, J. D.; Jandacek, R. J. *J. Chem. Soc., Dalton Trans.* **1972**, 1120-1123.

102. Praeckel, U.; Huber, F. *Z. Naturforsch.* **1981**, *36B*, 70-73.

103. Gilman, H.; Yale, H. L. *J. Am. Chem. Soc.* **1951**, *73*, 2880-2881.

104. Asato, E.; Katsura, K.; Arakaki, M.; Mikuriya, M.; Kotera, T. *Chem. Lett.* **1994**, 2123-2126.

105. Herrmann, W. A.; Herdtweck, E.; Pajdla, L. *Chem. Ber.* **1993**, *126*, 895-898.

106. Jackson, G. E.; Hancock, R. D. *Polyhedron* **1984**, *3(1)*, 71-73.

107. Asato, E.; Kamamuta, K.; Akamine, Y.; Fukami, T.; Nukada, R.; Mikuriya, M.; Deguchi, S.; Yokota, Y. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 639-648.

108. Wieber, M.; Baudis, U. *Z. Anorg. Allg. Chem.* **1976**, *423*, 40-46.

109. Herrmann, W. A.; Herdtweck, E.; Scherer, W.; Kiprof, P.; Pajdla, L. *Chem. Ber.* **1993**, *126*, 51-56.

110. Agocs, L.; Briand, G. G.; Burford, L.; Cameron, T. S.; Kwiatkowski, W.; Robertson, K. N. *Inorg. Chem.* **1997**, in press.

111. 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.

112. Herrmann, W. A.; Kiprof, P. Scherer, W.; Pajdla, L. *Chem. Ber.* **1992**, *125*, 2657-2660.

113. Edelmann, F. T.; Noltemeyer, M.; Haiduc, I.; Silvestri, C.; Cea-Olivares, R. *Polyhedron* **1994**, *13*, 547-552.

114. Clegg, W.; Elsegood, M. R. J.; Farrugia, L. J.; Lawlor, F. J.; Norman, N. C.; Scott, A. J. *J. Chem. Soc., Dalton Trans.* **1995**, 2129-2135. Farrugia, L. J.; Lawlor, F. J.; Norman, N. C. *J. Chem. Soc., Dalton Trans.* **1995**, 1163-1171. Farrugia, L. J.; Lawlor, F. J.; Norman, N.C. *Polyhedron* **1995**, *14*, 311-314. Atwood, D. A.; Cowley, A. H.; Hernandez, R. D.; Jones, R. A.; Rand, L. L.; Bott, S. G.; Atwood, J. L. *Inorg. Chem.* **1993**, *32*, 2972-2974.

115. See also, Bensch, W.; Reifler, F. A.; Reller, A.; Oswald, H. R. *Z. Kristallogr.* **1989**, *189*, 169-179, and references therein.

116. Yamamoto, Y.; Chen, X.; Kojima, S.; Ohdoi, K.; Kitano, M.; Doi, Y.; Akiba, K. *J. Am. Chem. Soc.* **1995**, *117*, 3922-3932. Drew, M. B. G.; Nicholson, D. G., Sylte, I.;Vasudevan, A. *Inorg. Chim. Acta* **1990**, *171*, 11-15. A.F. Wells. *Structural Inorganic Chemistry, 4th Ed.*, Clarendon Press, Oxford, **1975** pp 889-892.

117. Rogers, R. D.; Bond, A. H.; Aguinaga, S.; Reyes, A. *J. Am. Chem. Soc.* **1992**, *114*, 2967-2977.

118. Carmalt, C. J.; Farrugia, L. J.; Norman, N. C. *J. Chem. Soc., Dalton Trans.* **1996**, 443-454. Clegg, W.; Farrugia, L. J.; McCamley, A.; Norman, N.C.; Orpen, A. G.; Pickett, N. L.; Stratford, S. E. *J. Chem. Soc., Dalton Trans.* **1993**, 2579-2587. Carmalt, C. J.; Norman, N. C; Orpen, A. J.; Stratford, S. E. *J. Organomet. Chem.* **1993**, *460*, C22-C24. Carmalt, C. J.; Farrugia, J. L.; Norman, N. C. *Z. Anorg. Allg. Chem.* **1995**, *621*, 47-56. Schäfer, M.; Frenzen, G.; Neümuller, B.; Dehnicke, K. *Angew. Chem., Int. Ed. Engl.* **1992**, *31(3)*, 334-335. Alcock, N. W.; Ravindran, M.; Willey, G. R. *J. Chem. Soc., Chem. Commun.* **1989**, 1063-1065. Frank, W.; Weber, J.; Fuchs, E. *Angew. Chem. Int. Ed. Engl.* **1987**, *26(1)*, 74-75. Jameson, G. B.; Blaszo, E.; Oswald, H. R. *Acta Crystallogr.* **1984**, *C40*, 350-354. Allman, T.; Goel,

R. G.; Prasad, H. S. *J. Organomet. Chem.* **1979**, *166*, 365-371. Battaglia, L. P.; Bonamartini Corradi, A.; Pelizzi, G.; Vidoni Tani, M. E. *J. Chem. Soc., Dalton Trans.* **1977**, 1141-1144.

119. Crispini, A.; Errington, R.J.; Fisher, G.A.; Funke, F.J.; Norman, N.C.; Orpen, A.G.; Stratford, S.E.; Struve, O. *J. Chem. Soc., Dalton Trans.* **1994**, 1327-1335.

120. Coucouvanis, D. *Prog. Inorg. Chem.* **1970**, *11*, 233-371; Coucouvanis, D. *Prog. Inorg. Chem.* **1979**, *26*, 301-469.

121. Bourgeois, L.; Bolle, J. *Mém. services chim. état (Paris).* **1948**, *34*, 411-413; *Chem. Abstr.* **1949**, *44*, 5814e.

122. Kupchik, E. J.; Thiesen, C. T. *J. Organomet. Chem.* **1968**, *11*, 627-630.

123. Manoussakis, G. E.; Karayannidis, P. *Inorg. Nucl. Chem. Lett.* **1970**, *6*, 71-73.

124. Raston, C. L.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1976**, 791-794.

125. Malissa, H.; Kolbe-Rohde, H. *Talanta* **1961**, *8*, 841-845; *Chem. Abstr.* **1962**, *56*, 9538d.

126. Pilipenko, A. T; Mel'nikova, N. V.; Bankovskii, Y. A. *Anal. Chem.* **1980**, *46(12)*, 1311-1315.

127. Manoussakis, G. E.; Tsipis, C. A. *Z. Anorg. Allg. Chem.* **1973**, *398*, 88-96.

128. Venkatachalam, V; Ramalingam, K.; Casellato, U.; Graziani, R. *Polyhedron* **1997**, *16(7)*, 1211-1221.

129. A synthetic description was not provided but referenced to: Manoussakis, G. E.; Tsipis, C. A. *J. Inorg. Nucl. Chem.* **1973**, *35*, 743-750.

130. Bharadwaj, P. K.; Musker, W. K. *Inorg. Chem.* **1987**, *26*, 1453-1455.

131. Manoussakis, G. E.; Tsipis, C. A.; Hadjikostas, C. C. *Can. J. Chem.* **1975**, *53*, 1530-1535.

132. Tsipis, C. A.; Manoussakis, E. *Inorg. Chim. Acta* **1976**, *18*, 35-45.

133. Raston, C. L.; Rowbottom, G. L.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1981**, 1352-1359.

134. Wieber, M.; Basel, A. *Z. Anorg. Allg. Chem.* **1979**, *448*, 89-92.

135. Burschka, C.; Wieber, M. *Z. Naturforsch.* **1979**, *34b*, 1037-1039.

136. Ali, M.; McWhinnie, W. R., West, A. A.; Hamor, T. A. *J. Chem. Soc., Dalton Trans.* **1990**, 899-905.

137. Manoussakis, G. E.; Lalia-Kantouri, M.; Huff, R. B. *J. Inorg. Nucl. Chem.* **1975**, *37*, 2330-2333.

138. Cras, J. A.; van de Leemput, P. J. H. A. M.; Willemse, J.; Bosman, W. P. *Recl. Trav. Chim. Pays-Bas.* **1977**, *96*, 78-80.

139. Mandal, S.; Mandal, G. C.; Shukla, R.; Bharadwaj, P. K. *Ind. J. Chem.* **1992**, *31A*, 128-130.

140. Bharadwaj, P. K.; Lee, A. M.; Skelton, B. W.; Srinivasan, B. R.; White, A. H. *Aust. J. Chem.* **1994**, *47*, 405-410.

141. Shukla, R.; Bharadwaj, P. K. *Polyhedron* **1993**, *12(9)*, 1079-1081.

142. Raston, C. L.; Rowbottom, G. L.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1981**, 1366-1368.

143. Raston, C. L.; Rowbottom, G. L.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1981**, 1372-1378.

144. Raston, C. L. Rowbottom, G. L.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1981**, 1369-1371.

145. Raston, C. L.; Rowbottom, G. L.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1981**, 1383-1388.

146. Raston, C. L.; Rowbottom, G. L.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1981**, 1379-1382.

147. Kheiri, M.-N.; Tsipis, C. A.; Manoussakis, G. E. *Inorg. Chim. Acta* **1977**, *25*, 223-227.

148. Hoskins, B. F.; Tiekink, E. R. T.; Winter, G. *Inorg. Chim. Acta* **1985**, *105*, 171-176.

149. Hohn, R.; Bloch, I. *J. Prakt. Chem.* **1910**, *82*, 486-511; *Chem. Abstr.* **1911**, *5*, 1266-1267.

150. Khwaja, M. A.; Cardwell, T. J.; Magee, R. J. *Anal. Chim. Acta* **1973**, *64*, 9-17.

151. Snow, M. R.; Tiekink, E. R. T. *Aust. J. Chem.* **1987**, *40*, 743-750.

152. Winter, G. *Aust. J. Chem.* **1976**, *29*, 559-563.

153. Tiekink, E. R. T. *J. Cryst. Spec. Res.* **1992**, *22(2)*, 231-236.

154. Raston, C. L.; White, A. H.; Winter, G. *Aust. J. Chem.* **1978**, *31*, 2207-2212.

155. Dubsky, J. V. *J. Prakt. Chem.*, **1916**, *93*, 142-161; *Chem. Abstr.* **1917**, *11*, 1631-1632.

156. Hoskins, B. F.; Tiekink, E. R. T.; Winter, G. *Inorg. Chim. Acta* **1984**, *81*, L33-L34.

157. Hoskins, B. F.; Tiekink, E. R. T.; Winter, G. *Inorg. Chim. Acta* **1985**, *99*, 177-182.

158. Gable, R. W.; Hoskins, B. F.; Steen, R. J.; Tiekink, E. R. T.; Winter, G. *Inorg. Chim. Acta* **1983**, 15-20.

159. Wieber, M.; Rüdling, H. G.; Burschka, C. Z. *Anorg. Allg. Chem.* **1980**, *470*, 171-176.

160. Edelmann, F. T.; Noltemeyer, M.; Haiduc, I.; Silvestru, C.; Cea-Olivares, R. *Polyhedron* **1994**, *13(4)*, 547-552.

161. Kuchen, W.; Metten, J.; Judat, A. *Chem. Ber.* **1964**, *97*, 2306-2315.

162. Svensson, G.; Albertsson, J. *Acta Chem. Scand.* **1989**, *43*, 511-517.

163. Müller, A.; Krishna Rao, V.; Klinksiek, G. *Chem. Ber.* **1971**, *104*, 1892-1904.

164. Begley, M. J.; Sowerby, D. B.; Haiduc, I. *J. Chem. Soc., Dalton Trans.* **1987**, 145-50.

165. Sowerby, D. B.; Haiduc, I. *J. Chem. Soc., Dalton Trans.* **1987**, 1257-1259.

166. Iglesias, M.; Del Pino, C.; Martinez-Carrera, S. *Polyhedron* **1989**, *8(4)*, 483-489.

167. Lawton, S. L.; Fuhrmeister, C. J.; Haas, R. G.; Jarman, C. S.; Lohmeyer, F. G. *Inorg. Chem.* **1974**, *13(1)*, 135-143.

168. Ebert, K. H.; Schulz, R. E.; Breunig, H. J.; Silvestru, C.; Haiduc, I. *J. Organomet. Chem.* **1994**, *470*, 93-98.

169. Müller, A.; Krickemeyer, E.; El-Katri, F.; Rehder, D.; Stammler, A.; Bögge, H.; Hellweg, R. *Z. Anorg. Allg. Chem.* **1995**, *621*, 1160-1170.

170. Friedheim, E. A. H. *Chem. Abstr.* **1955**, 12530d.

171. Friedheim, E. A. H. *Chem. Abstr.* **1955**, 15946f.

172. Powell, P. *J. Chem. Soc.(A).* **1968**, 2587-2588.

173. Ikram, M.; Powell, D. B. *Spectrochim. Acta* **1972**, *28(A)*, 59-64.

174. Cea-Olivares, R.; Hernandez, A.; Rios, E.; Wingartz, J. Valdes-Martinez, J. *Bol. Soc. Chil. Quím.* **1990**, *35*, 165-168.

175. Wieber, M.; Baudis, U. *Z. Anorg. Allg. Chem.* **1976**, *423*, 40-46.

176. Drew, M. G. B.; Kisenyi, J. M.; Willey, G. R.; Wandiga, S. O. *J. Chem. Soc., Dalton Trans.* **1984**, 1717-1721.

177. Willey, G. R.; Barras, J. R.; Rudd, M. D.; Drew, M. G. B. *J. Chem. Soc., Dalton Trans.* **1994**, 3025-3029.

178. Klapötke, T. *Polyhedron* **1987**, *6(7)*, 1593-1597.

179. Hunter, G. *J. Chem. Soc., Dalton Trans.*, **1972**, 1496-1498.

180. Hunter, G.; Weakley, T. J. R. *J. Chem. Soc., Dalton Trans.* **1983**, 1067-1070.

181. Williams, D. J.; Quicksall, C. O.; Barkigia, K. M. *Inorg. Chem.* **1982**, *21*, 2097-2100.

182. Müller, A.; Zimmerman, M.; Bogge, H. *Angew. Chem., Int. Ed. Engl.* **1986**, *25(3)*, 273.

183. Engler, R. *Z. Anorg. Allg. Chem.* **1974**, *406*, 74-79.

184. Drager, M.; Schmidt, B. M. *J. Organomet. Chem.* **1985**, *290*, 133-145.

185. Engler, R. *Z. Anorg. Allg. Chem.* **1974**, *407*, 35-39.

186. This is expected as $BiCl_3$ is rapidly converted to BiOCl in aqueous media: *Advanced Inorganic Chemistry*, 5th ed.; Cotton, F. A., Wilkinson, G. A., Eds.; J. Wiley & Sons: Toronto, 1988; p 393.

187. See for example: Willey, G. R.; Lakin, M. T.; Alcock, N. W. *J. Chem. Soc., Dalton Trans.* **1992**, 1339-1341. Battaglia, L. P.; Bonamartini Corradi, A.; Pelizzi, G.; Vidoni Tani, M. E. *J. Chem Soc., Dalton Trans.* **1977**, 1141-1144. Battaglia, L. P.; Bonamartini Corradi, A.; Pelizzi, G.; Vidoni Tani, M. E. *Cryst. Struct. Commun.* **1975**, *4*, 399-402. Clegg, W.; Compton, N. A.; Errington, R. J.; Fisher, G. A.; Hockless, D. C. R.; Norman, N. C.; Orpen, A. G.; Stratford. S. E. *J. Chem. Soc., Dalton Trans.* **1992**, 3515-3523.

188. Stizman, H.; Wolmerhäuser, G. *Chem. Ber.* **1994**, *127*, 1335-1342.

189. Battaglia, L. P.; Bonamartini Corradi, A.; Nardelli, M.; Vidoni Tani, M. E. *J. Chem. Soc., Dalton Trans.* **1978**, 583-587.

190. Block, E.; Ofori-Okai, G.; Kang, H.; Wu, J.; Zubieta, J. *Inorg. Chem.* **1991**, *30*, 4784-4788.

191. Crispini, A.; Errington, R. J.; Fisher, G. A.; Funke, F. J.; Norman, N. C.; Orpen, A. G.; Stratford. S. E.; Struve, O. *J. Chem. Soc., Dalton Trans.* **1994**, 1327-1335.

192. See for example: Wullens, H.; Devillers, M.; Tinant, B.; Declerq, J. -P. *J. Chem. Soc., Dalton Trans.* **1996**, 2023-2029. Forster, G. E.; Begley, M. J.; Sowerby, D. B.; Haiduc, I. *J. Chem. Soc., Dalton Trans.* **1995**, 383-387. Bertazzi, N.; Alonzo, G.; Battaglia, L. P.; Bonamartini Corradi, A.; Pelosi, G. *J. Chem Soc., Dalton Trans.* **1990**, 2403-2405. Galdecki, Z.; Glowka, M. L.; Golinski, B. *Acta Crystallogr.* **1976**, *B32*, 2319-2321.

193. See for example: Clegg, W.; Errington, R. J.; Fisher, G. A.; Hockless, D. C. R.; Norman, N. C.; Orpen, A. G.; Stratford, S. E. *J. Chem. Soc., Dalton Trans.* **1992**, 1967-1974. Carmalt, C. J.; Cowley, A. H.; Decken, A.; Norman, N. C. *J. Organomet. Chem.* **1995**, *496*, 59-67. Battaglia, L. P.; Bellito, C.; Cramarossa, M. R.; Vezzosi, I. M. *Inorg. Chem.* **1996**, *35*, 2390-2392. Carmalt, C. J.; Clegg,

W.; Elsegood, M. R. J.; Errington, R. J.; Havelock, J.; Lightfoot, P.; Norman, N. C.; Scott, A. J. *Inorg. Chem.* **1996**, *35*, 3709-3712.

194. Clegg, W.; Elsegood, M. R. J.; Graham, V.; Norman, N. C.; Pickett, N. L.; Tavakkoli, K. *J. Chem. Soc., Dalton Trans.* **1994**, 1743-1751.

195. Cea-Olivares, R.; Lomeli, V.; Hernandez-Ortega, S.; Haiduc, I. *Polyhedron* **1995**, *14(6)*, 747-755. Bräu, E.; Falke, R.; Ellner, A; Beuter, M.; Kolb, U.; Dräger, M. *Polyhedron* **1994**, *13*, 365-374. Kolb, U.; Beuter, M.; Gerner, M.; Dräger, M. *Organometallics* **1994**, *13*, 4413-4425. Kolb, U.; Beuter, M.; Dräger, M. *Inorg. Chem.* **1994**, *33*, 4522-4530.

196. Dräger, M. *Chem. Ber.* **1974**, *107*, 2601-2611.

197. Dräger, M.; Engler, R. Z. *Anorg. Allg. Chem.* **1974**, *405*, 183-192.

198. Hoffmann, H. M.; Dräger, M. *Z. Anorg. Allg. Chem.* **1986**, *41b*, 1455-1460.

199. Veith, M.; Bertsch, B.; Huch, V. *Z. Anorg. Allg. Chem.* **1988**, *559*, 73-88.

200. Sanchez, M.; Mazieres, M. R.; Lamande, L.; Wolf, R. In *Multiple Bonds and Low Coordination in Phosphorus Chemistry*; Regitz, M., Scherer, O. J., Eds.; Georg Thieme Verlag: Stuttgart, 1990; pp 129-148. Burford, N.; Losier, P.; Macdonald, C.; Kyrimis, V.; Bakshi, P. K.; Cameron, T. S. *Inorg. Chem.* **1994**, *33*, 1434-1439.

201. Burford, N.; Parks, T. M.; Royan, B. W.; Borecka, B.; Cameron, T. S.; Richardson, J. F.; Gabe, E. J.; Hynes, R. *J. Am. Chem. Soc.* **1992**, *114*, 8147-8153.

202. Gillespie, R. J. *J. Chem. Ed.* **1970**, *47(1)*, 18-23.

203. Wynne, K. J. *J. Chem. Ed.* **1973**, *50(5)*, 328-330.

204. Knop, O.; Linden, A.; Vincent, B. R.; Choi, B. R.; Cameron, T. S.; Boyd, R. J. *Can. J. Chem.* **1989**, *67*, 1984-2008.

205. Wheeler, R. A.; Kumar, P. N. V. P. *J. Am. Chem. Soc.* **1992**, *114*, 4776-4784.

206. Alcock, N. W. In *Advances in Inorganic Chemistry and Radiochemistry*; Emeleus, H. J., Sharpe, A. G.; Eds.; Academic Press: New York, 1972; pp 1-58.

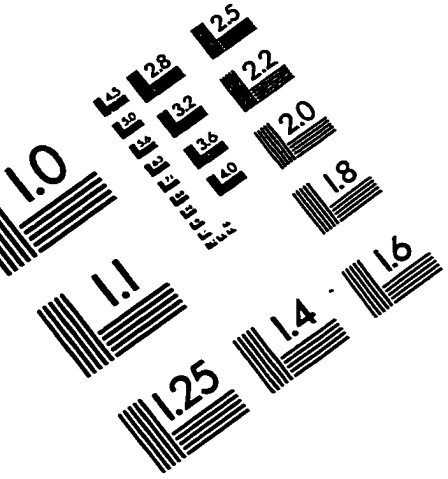
207. Chen, C. -A.; Gau, H. -M. *J. Organomet. Chem.* **1995**, *505*, 17-21. Gau, H.. -M.; Chen, C. -A.; Chang, S. -J.; Shih, W. -E.; Yang, T. -K.; Jong, T. -T.; Chien, M. Y. *Organometallics* **1995**,*12*, 1314-1318.

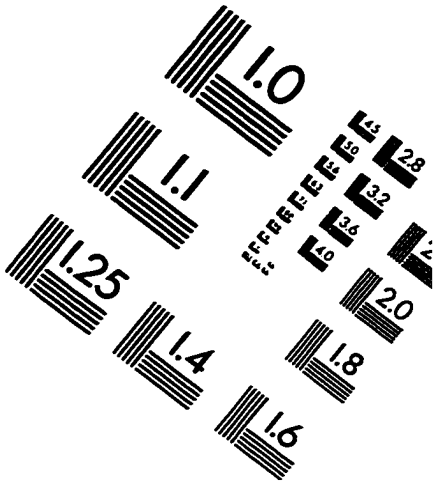
208. Wells, P. R. *Prog. Phys. Org. Chem.* **1968**, *6*, 111.

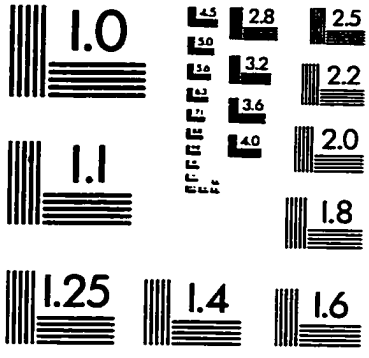
209. Dodonov, V. A.; Zinov'eva, T. I. *Organomet. Chem. USSR* **1992**, *5(6)*, 616-620.

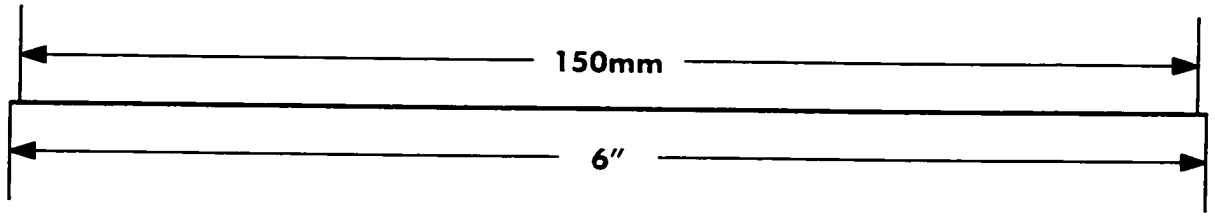
210. Bismuth citrate, $BiC_6H_5O_7$ thermally decomposes to form Bi_2O_3; ref. Srivastava, A.; Gunjikar, V. G.; Sinha, A. P. B. *Thermochim. Acta* **1987**, *117*, 201-217.

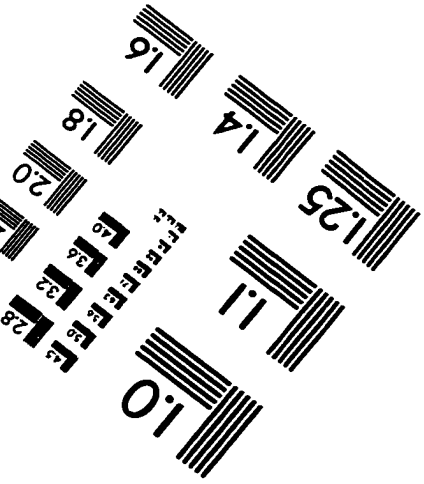
IMAGE EVALUATION TEST TARGET (QA-3)

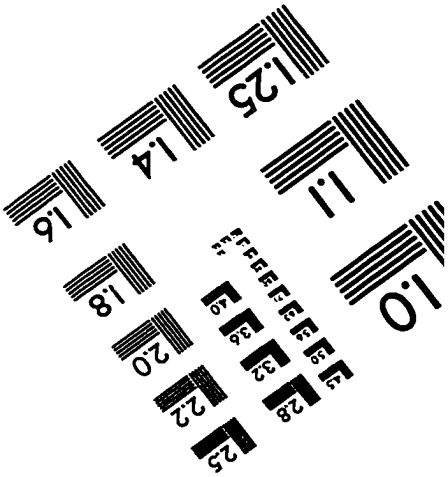












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