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Heteroatom-Directed Aromatic Lithiation: A Versatile Route to the Synthesis of Organochalcogen (Se, Te) Compounds

GOVINDASAMY MUGESH AND HARKESH B. SINGH*

Department of Chemistry, Indian Institute of Technology, Powai, Bombay 400 076, India

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ABSTRACT

Chiral and achiral organochalcogen compounds bearing a heteroatom in close proximity are easily accessible via the directed aromatic lithiation route. The lithium chalcogenolates prepared by the insertion of selenium or tellurium into the C−Li bond are used to synthesize various chalcogen compounds such as Se/Te, N donor ligands, dichalcogenides, monomeric metal chalcogenolates, and macrocycles. The differences in the stability and reactivity of the organochalcogen compounds derived from various substrates are described in terms of electronic and stereochemical properties of donor atoms.

Introduction

Recent advances in the area of organochalcogen chemistry have been driven by the potential applications of chalcogen compounds in modern organic synthesis, precursors for metal−organic chemical vapor deposition (MOCVD) of semiconducting materials, ligand chemistry, and biochemistry. The use of selenium/tellurium-based synthetic methods is well established in organic synthesis. Organoselenium/tellurium moieties can be incorporated into a variety of substrates for functional group manipulations under mild conditions either as nucleophiles or as electrophiles.[1,2] Asymmetric synthesis using organochalcogen compounds is of current interest and presents a new trend in the field of organometallic chemistry.[3,4] The importance of metal chalcogenide semiconductors such as In_2Se_3, MnSe, MnTe, $MnTe_2$, SnTe, PbSe, PbTe, Ln_2Te_3, ZnSe, CdSe, and CdTe has given rise to much current activity targeted toward the synthesis of new organochalcogenide precursors for these substances.[5,6] The chemistry of selenium and tellurium ligands has yielded many surprising results with respect to structural features, methods of preparation, and degree of aggregation.[7−9] In addition to these applications, much attention has been devoted to the synthesis of organoselenium and tellurium compounds that could be used as enzyme mimics and chemotherapeutic agents.[10−13]

The applications of organochalcogen compounds in the above-mentioned areas have, however, been restricted by difficulties in synthetic methodologies, purification, and the instability of certain derivatives. Two major approaches are being used to overcome these difficulties. In the first approach, the unstable organochalcogen derivatives are stabilized by introducing sterically bulky substituents, and in the second approach, the chalcogen derivatives are stabilized by attaching chelating groups in the close proximity to selenium or tellurium. Recent studies on internally chelated organoselenium and tellurium compounds show that the attractive interactions between chalcogen atom and other heteroatoms such as N or O play an important role not only in the catalytic antioxidant activity of these compounds but also in their application as reagents in synthetic organic chemistry.[14,15] In asymmetric reactions, these interactions play a crucial role in chirality transfer.[3,4] The application of internal chelation has been extended to the synthesis of novel hybrid organoselenium and tellurium ligands containing both "hard" and "soft" donor atoms. More recently, this approach has been used for the isolation of monomeric metal chalcogenolates, in particular, the isolation of group 12 metal (Zn, Cd, Hg) chalcogenolates which generally form polymeric materials through bridging by the chalcogenolate ligands.[5,6]

In this paper we summarize our results on the synthesis of organochalcogen compounds which are stabilized by internal chelation. These compounds are derived from substrates which are capable of undergoing heteroatom-directed aromatic lithiation. The purpose of this Account is to address a few critical points on the synthetic aspects rather than presenting a comprehensive treatise on the structural aspects of organochalcogen compounds.

Synthesis of Organochalcogen Compounds by Directed Lithiation

Heteroatom-directed aromatic lithiation is a key step in many organic transformations.[16] Recently, this strategy has been found to be a promising approach for the synthesis of various organochalcogen compounds. The reaction is generally affected by treatment of the aromatic substrate with an alkyllithium reagent such as *n*-BuLi, followed by the introduction of a selenium/tellurium moiety. Normally, the lithiations of aromatic substrates by lithium−halogen exchange are found to be much more facile and

Govindasamy Mugesh, born in 1970 in Tamilnadu, India, obtained his Ph.D. (1998) at the Department of Chemistry, Indian Institute of Technology, Bombay, India, under the supervision of Prof. Harkesh B. Singh. He subsequently worked in the laboratory of Prof. W.-W. du Mont at the Institute of Inorganic and Analytical Chemistry, Technical University of Braunschweig, Germany, as an Alexander von Humboldt Fellow. Currently, he is working as a Research Associate with the group of Prof. K. C. Nicolaou at the Department of Chemistry, The Scripps Research Institute, San Diego, CA.

Harkesh B. Singh, born in 1956 in UP, India, obtained his Ph.D. (1979) at Lucknow University with Prof. T. N. Srivastava. In 1979, he moved to the U.K. and did a second Ph.D. at Aston University, Birmingham, under the supervision of Prof. W. R. McWhinnie (1979−1983). After a brief stay at the Indian Institute of Technology, Delhi, as Pool Scientist with Prof. B. L. Khandelwal, he joined the Indian Institute of Technology, Bombay, in 1984 as a lecturer and rose through the ranks to become a full professor in 1995. He is a Fellow of the National Academy of Sciences (FNASc), Allahabad, and of the Royal Society of Chemistry (FRSC). He has been a Visiting Scientist at the University of California, Santa Barbara (Prof. Fred Wudl's laboratory), under the BOYS−CAST scheme.

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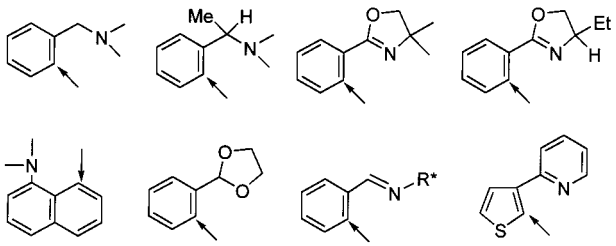
Chart 1



selective than the ortho deprotonation. However, when a heteroatom is properly substituted, the lithiation reactions occur specifically at the ortho position, irrespective of whether the group, as a whole, is electron donating or electron withdrawing. Lithiation also occurs at other positions that are sterically close to the substituents bearing heteroatoms. A few examples of substrates which were used for the synthesis of organochalcogen compounds in our laboratory are shown in Chart 1.

Organochalcogen Compounds Based on N-Substituted Benzylamine

Lithiation of *N*,*N*-dimethylbenzylamine (**1**) is a typical example of heteroatom-directed lithiation, where the electron donor atom is not directly bonded to the aromatic ring. Ortho lithiation of **1** with *n*-BuLi in ether afforded the lithiated compound **2**, which in turn reacted with elemental selenium or tellurium to give the aryllithium selenolate (**3**)[17] or tellurolate (**4**),[18] respectively (Scheme 1). The formation of a six-membered chelate ring in both cases controls the degree of aggregation and increases its solubility in ether. Although the unstable chalcogenolates **3** and **4** could be oxidized to the corresponding dichalcogenides **5** and **6**, the unreacted amine posed a major problem in the purification of **5**. To overcome this problem, it is desirable to use equimolar ratios of the amine, *n*-BuLi, and selenium rather than an excess of either. It is also necessary to deprotonate the areneselenolate **3** by quenching with a saturated solution of $NaHCO_3$ before it is oxidized by the passage of oxygen. In an earlier attempt to synthesize compound **5**, Wilson et al. reported that the oxidative workup of **3** gave a viscous oil that was handled as its hydrochloride salt.[19] The structure of the diselenide **5** was determined by X-ray crystallography. The Se atom has T-shaped three-coordination, with each selenium atom bonded to a selenium, a carbon, and a nitrogen atom.[17]

During our initial attempts to synthesize compound **6**, the major problem we encountered was the conversion of this compound to overoxidized species **7**. Similar to the ditelluride, compound **7** also underwent facile halogenolysis with sulfuryl chloride and bromine to give organotellurium(IV) halides. Reduction with hydrazine hydrate yielded the corresponding monohalides **8** and **9** in high yield.[18] Since the oxidation of **6** may be due to the presence of a small amount of peroxides in ether, peroxide-free ether must be used for both the reaction and the purification. During our attempts to isolate pure **6**, we found that the isolation of the product and its subsequent crystallization depends on the ratio of product and the unreacted amine, and less than 10% of amine favors crystallization.[20]

Compound **5** underwent facile reaction with stoichiometric amounts of bromine and iodine to give the arylselenenyl halides **10** and **11**, respectively. In contrast to most of the diaryl diselenides, which form charge-transfer adducts with iodine,[21] diselenide **5** afforded stable **11**, in which the selenium is covalently bonded to iodine. Reaction of **5** with HCl afforded the hydrochloride salt **12**, which has been reported to be a glutathione peroxidase (GPx) mimic.[19] The Se···N interactions in **5**, as proved by X-ray studies, activated the Se−Se bond toward insertion of a sulfur atom (**13**) and a methylene group (**14**). The stability and reactivity of **5** led us to investigate its use in catalytic conversions of olefins to allylic ethers (Table 1). The reactions were performed in acetic acid solution using copper(II) nitrate as the co-oxidant and $Na_2S_2O_8$ as the oxidant. In these reactions, the diselenide bond is expected to be cleaved to form a selenenyl sulfate derivative.[22] Compound **5** also exhibited GPx activity by reducing H_2O_2 to water.[23] The diselenide reacts with 2 equiv of PhSH to produce the selenol, which reduces H_2O_2 to form selenenic acid. This intermediate is converted to selenol through a selenenyl sulfide adduct, as shown in Scheme 2.[24] As proved by Tomoda et al.,[14] the nitrogen base plays an important role in the catalytic process.

We studied the reactivity of the lithiated compound **2** with some selenium and tellurium electrophiles.[20,25] Reaction of **2** with PhTeBr afforded the telluride **15** as a white powder. The reactions of **2** with $E(dtc)_2$ (E = Se, Te; dtc = diethyldithiacarbamate) afforded the corresponding diaryl chalcogenides **18** and **19**.[25] The telluride **19** could also be synthesized from the reaction of **2** with TeI_2.[20] The reactivity of lithium selenolate **3** toward MeI differs considerably from that of the corresponding tellurolate. The addition of MeI to an ethereal solution of **3** afforded the expected methylated derivative **20**. On the other hand, the reaction of **4** with MeI gave the desired methylated telluride **21**, along with two other minor products which were separated by column chromatography and identified as the diaryl telluride **19** and the tellurenyl iodide **22**. The unexpected formation of these two products can be rationalized by the existence of elemental iodine in solution, which upon reaction with **4** affords **22**, and subsequent reaction of this compound with **2** probably leads to the formation of **19**. The single-crystal X-ray structure of **19** showed a V-shaped bond configuration about the Te atom.

We studied the monotellurides **19** and **21** further for their complexation behavior.[20] Stirring an equimolar solution of the tridentate ligand **19** with the monoactivated species $Cr(CO)_5$·THF at room temperature gave complex **24**, which serves as a rare example of compounds containing a Cr−Te bond. The X-ray crystal structure showed that compound **19** acts as a monodenate ligand. Although the reaction of $Cr(CO)_6$ with aryl compounds leads to (η^6-arene)chromium complexes, our attempts to displace

Scheme 1

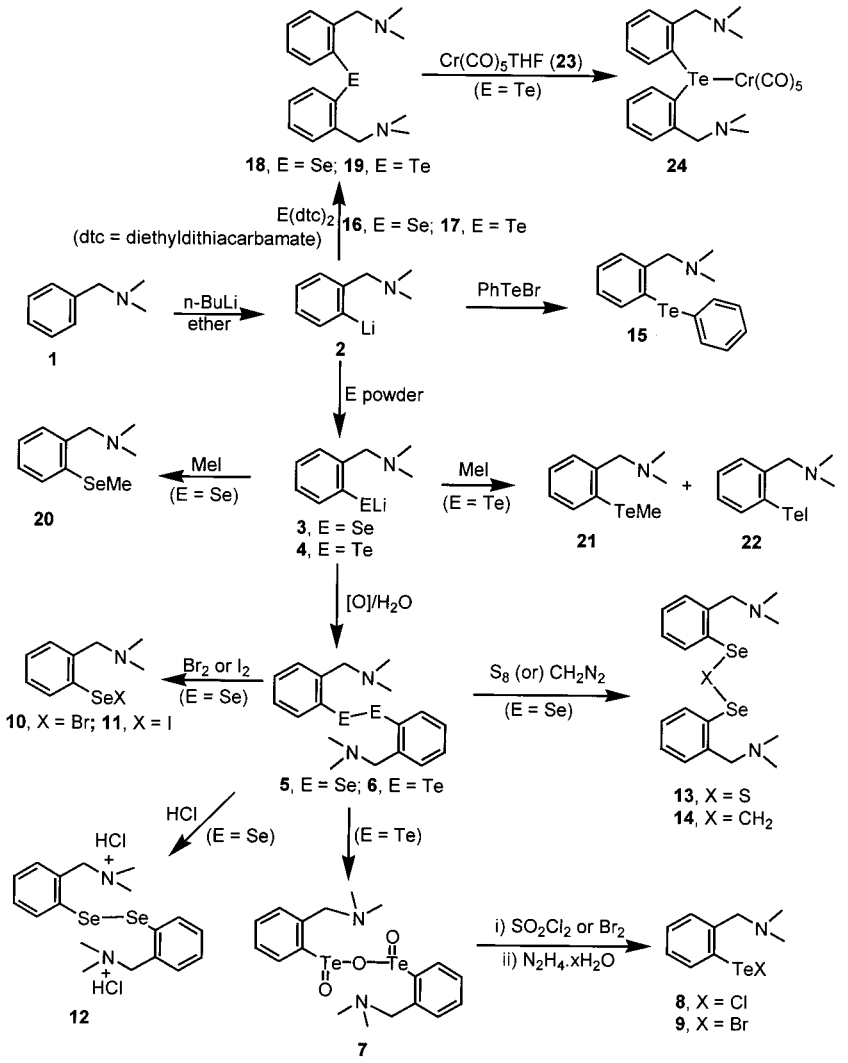
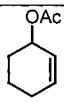
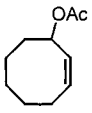
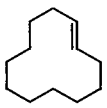
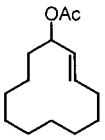
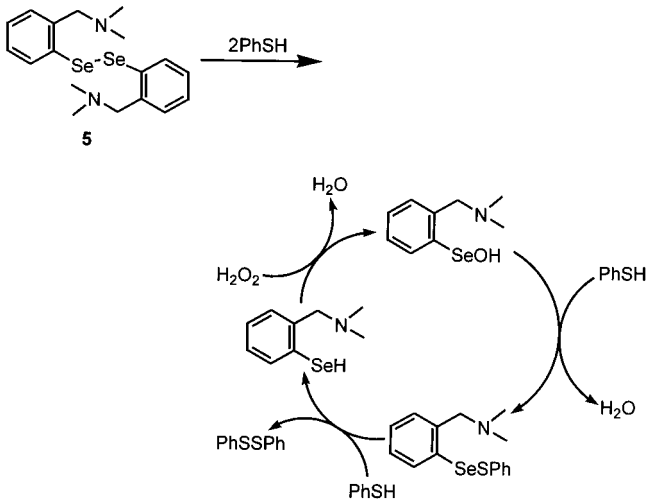


Table 1. Conversion of Alkenes into Allylic Acetates Catalyzed by Compound 5[17]

Substrate	time (h)	Products	isolated yield[a] (%)
	48		72
	72		57
	72		85

[a] Actual yields of allylic acetates considering the amounts of alkenes recovered.

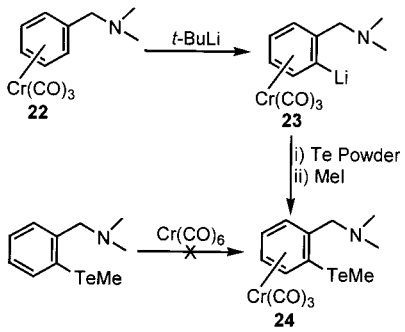
Scheme 2



ligating carbonyls in $Cr(CO)_6$ by the bidentate ligand **21** in THF in a thermal reaction led only to decomposition of the ligand. However, the tricarbonyl (η^6-arene)chromium complex **27** can be obtained by a modified procedure starting from complexed amine **25** via ortho lithiation, as shown in Scheme 3.[26]

Ortho lithiation of an enantiomerically pure (*S*)-*N*,*N*-dimethyl-1-phenylethylamine with *n*-BuLi, followed by treatment with elemental selenium, afforded a mixture of diselenide **30** and triselenide **31** (Scheme 4).[27] Pure chiral diselenide **30** was obtained by bromination of the mixture,

Scheme 3



followed by reduction of the resulting tribromide **32**. Wirth et al. reported that the reduction of di-/triselenide mixture with $NaBH_4$ followed by reoxidation also yields diselenides in pure form.[28] The other enantiomer of **30** was synthesized by ortho lithiation of (*R*)-*N*,*N*-dimethyl-1-phenylethlamine with *t*-BuLi in pentane and used as procatalyst in diethylzinc addition reactions.[29]

The synthesis of the tellurium analogue of **30** was even more difficult compared with that of the achiral analogue.[30] Addition of elemental tellurium to **29** resulted in a facile insertion to yield the corresponding lithium arenetellurolate, which upon oxidative workup afforded a yellowish solid. Characterization of this compound showed the formation of tellurinic anhydride **33** rather than the expected ditelluride. However, compound **33** acted as a normal ditelluride toward reactions with $SOCl_2$ and Br_2 to give the corresponding tellurenyl trihalides **34** and **35**. The monohalides **36** and **37** were obtained by reduction of the trihalides with hydrazine hydrate. We reported similar reactions of the ditelluride derived from 2-(3-thienyl)pyridine (Scheme 5).[31]

The stability of several organoselenium derivatives prompted us to investigate the applicability of internal chelation in the stabilization of monomeric metal selenolates. The salt elimination reactions of lithium selenolate **3** with anhydrous $ZnCl_2$ and $CdCl_2$ afforded insoluble materials which could not be characterized. However, the mercury selenolates **43** and **44** (Chart 2) were prepared by stirring the corresponding diselenides with metallic mercury in methanol. The resulting complexes were monomeric and stable at room temperature.[32]

The formation of a four-membered ring instead of a five- or six-membered ring sometime creates problems in the selenium insertion reactions. For example, in contrast to the 2-lithio derivative of *N*,*N*-dimethylbenzylamine, the lithiated compound derived from *N*,*N*-dimethylaniline failed to react with selenium and tellurium in all common solvents used for chalcogen insertion reactions.[33] The unfavorable coordination of the nitrogen to lithium may allow the formation of higher order aggregates which result in a polymeric compound. This is in agreement with the report that 2,6-dimethoxyphenyllithium, where the formation of a four-membered chelate ring is expected, reacted neither with selenium nor with tellurium due to the less soluble nature of the lithiated derivative in hydrocarbon solvents and etheral solvents.[34] However, this problem has been overcome by the addition of LiCl, which forms soluble double salts with 2,6-dimethoxyphenyllithium to give lithium arenechalcogenolates.

Organochalcogen Compounds Based on 2-Phenyloxazoline

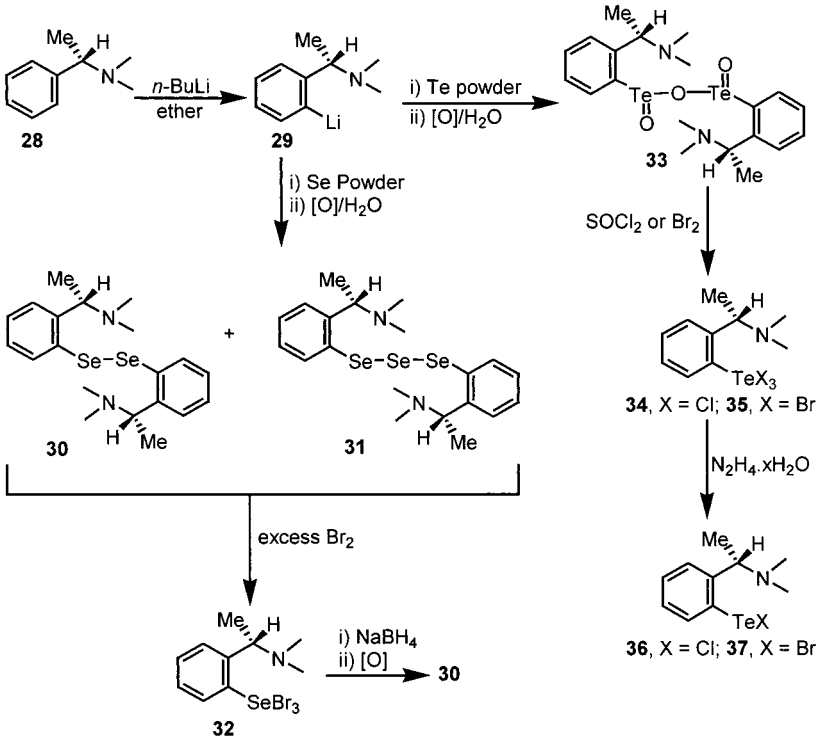
Recently, we utilized 4,4-dimethyl-2-phenyloxazoline extensively for the synthesis of chalcogen compounds due to the ortho-directing ability and rigidity of the oxazoline ring. Although the ortho lithiation and selenium insertion reactions have been reported many years ago,[35] an addition reaction of *n*-BuLi to the imine bond (C═N) of the oxazoline group hampered the early development. We recently found that the pure organochalcogen compounds could be prepared by the direct metalation of **45** with *n*-BuLi in nonpolar solvents such as hexane, followed by chalcogen insertion in etheral solvents.[36]

The lithium arenechalcogenolates **49** and **51** were obtained by the addition of chalcogen powder into the ethereal solution of the lithiated compound.[36,37] Oxidation of the resulting lithium chalcogenolates then afforded the desired diselenide (**52**)[23] and ditelluride (**54**).[37] In contrast to the formation of tellurinic anhydride **7** from *N*,*N*-dimethylbenzylamine, we did not detect any tellurinic anhydride or oxidized species during the synthesis of **54**, indicating higher stability of this compound. Despite its stability, diselenide **52** underwent facile reactions with stoichiometric amounts SO_2Cl_2, Br_2, or I_2 to give the monohalides **55**, **56**, and **58**, respectively. The ^{77}Se NMR chemical shifts of the monohalides were shifted downfield with respect to the diselenide **52**. The intramolecular S···N nonbonding interactions result in a downfield shift of the ^{77}Se NMR peaks.[38]

In contrast to the achiral analogue, lithiation of (*R*)-(4-ethyl)-2-phenyloxazoline (**46**) could not be effected in hexane. However, direct low-temperature metalation of **46** with *n*-BuLi in ether, followed by selenium insertion and oxidation, afforded the expected diselenide **53**.[23] Stable bromo and iodo compounds **57** and **59** were obtained as crystalline solids in good yield by treating the diselenide **53** with a stoichiometric amount of bromine and iodine, respectively.[39] It is worth noting that the halo derivatives are quite stable in solution for a long time and, particularly in the case of **59**, no peaks were detected for the diselenide, indicating much higher stability as a result of the intramolecular Se···N coordination. The Se···N separation of 2.074(6) Å for **59** is much shorter than some of the van der Waals radii (3.5 Å) and results in a T-shaped geometry around Se. Reactions of **47** with $Se(dtc)_2$ and $Te(dtc)_2$ afforded the monoselenide **60** and monotelluride **61**, respectively. The tellurium compound could also be synthesized by reaction of **47** with TeI_2. However, a better yield was obtained when $Te(dtc)_2$ was used as the Te(II) source.[40]

The failure to synthesize monomeric zinc and cadmium selenolates using the flexible benzylamine ligands led us to further investigate the use of this chelating ligand in the isolation of such unstable species. By using the more

Scheme 4



Scheme 5

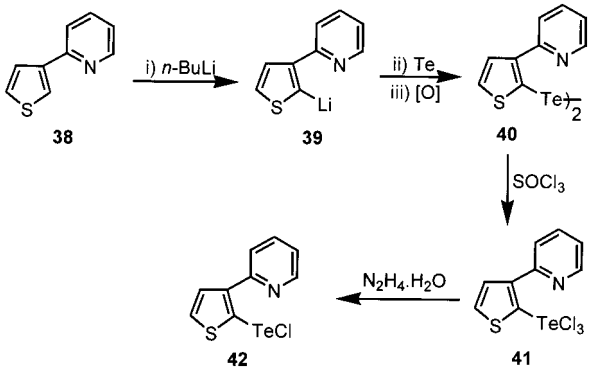
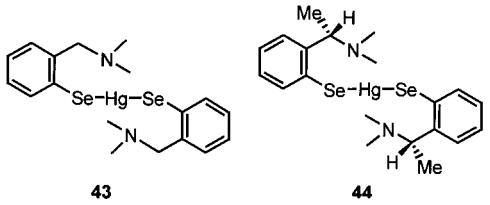


Chart 2



rigid (4,4-dimethyl-2-oxazolinyl)phenyl ligand, we recently succeeded in isolating the selenolato complexes of zinc, cadmium, and mercury (**62**−**64**, Scheme 6).[36] Ortho lithiation and selenium insertion, followed by reaction with anhydrous metal chlorides, afforded the complexes in monomeric form. The mercury complex **64** could be synthesized by treating the corresponding diselenide with metallic mercury in methanol. In all these complexes, the formation of the six-membered chelate ring with metal seems to be an important factor in deciding the molecular nature of these compounds. The strong coordination of the heterocyclic nitrogen to the metal center was clearly seen in the zinc complex, which showed "helical" chirality at the metal center. The complex afforded two types of crystals, plates and needle-shaped crystals, due to spontaneous resolution of the racemate. We used similar synthetic procedures for the isolation of zinc and cadmium tellurolates (**65**, **66**)[37] and a homoleptic bismuth(III) selenolate (**67**)[41] (Scheme 6). All attempts to synthesize the tellurium analogues of the mercury and bismuth complexes were unsuccessful. However, we successfully extended this approach to metal complexes of lighter chalcogens.[42,43] Similar to Se···N/Te···N interactions, some S···N interactions were found in the sulfur derivatives.[42,44] The advantage of having an ortho-chelating group has also been observed in the isolation of the aryl benzylic selenides **68**−**71** (Chart 3), which were synthesized by treating the lithium selenolate **49** with appropriate bromo compounds. The Se···N interactions in the crystal structures of **68** and **70** revealed that these interactions, though they are weaker than the Se···N interactions found in halo derivatives, contribute to the stability of these compounds.[38]

The lithiation and selenium insertion reactions of the oxazoline-based substrates appear to be much faster than that of *N*,*N*-dimethylbenzylamine. This is probably due to the fact that the sp^2 nitrogen in the oxazoline ring may coordinate to lithium much more strongly than the sp^3 nitrogen in benzylamine. Moreover, the orientation of the lone pair of the nitrogen atom and the sterically bulky nature of the oxazoline substituent of the aryl system make its bonding properties completely different from those of the *N*,*N*-dimethylamino substituent. The orientation of the N(sp^2) lone pair and the subsequent strong

Scheme 6

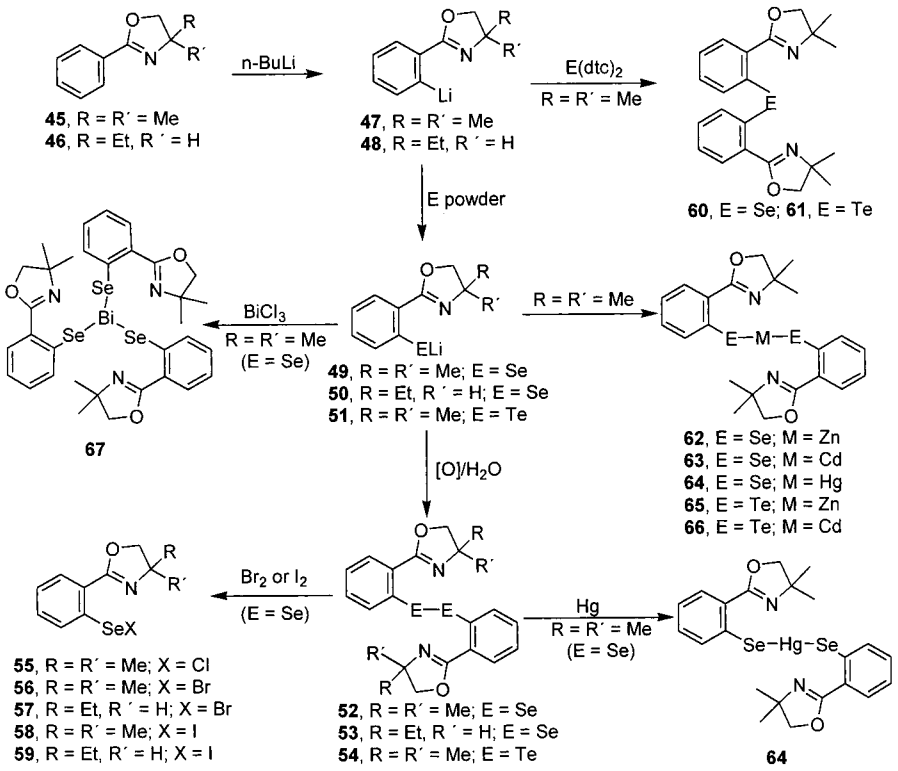
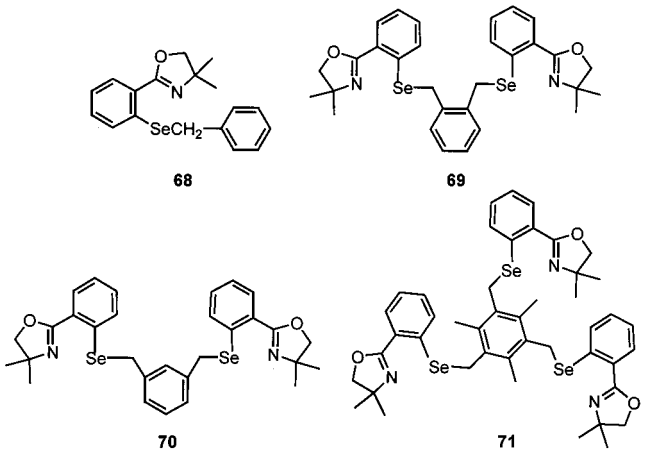


Chart 3



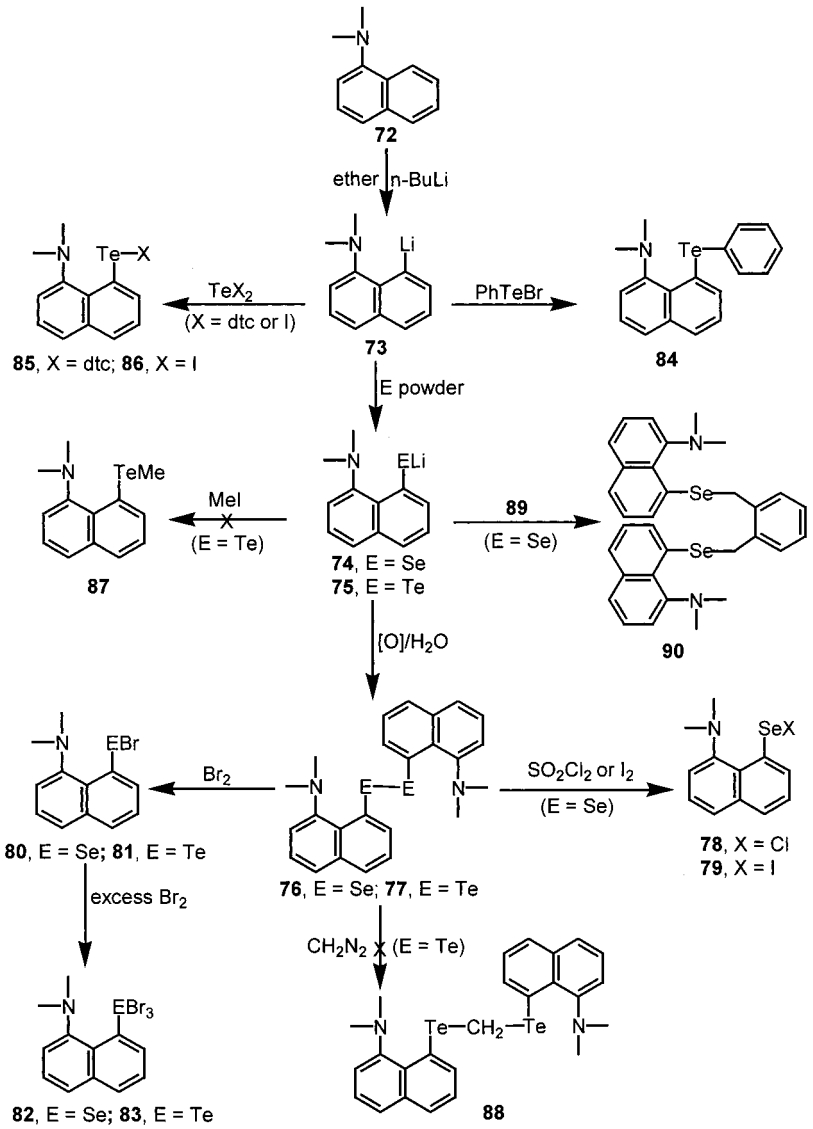
coordination, together with the steric bulk of the oxazoline group, prevents the formation of higher order aggregates and thus increases its solubility.

Organochalcogen Compounds Based on 1-(Dimethylamino)naphthalene

Lithiation of 1-(*N*,*N*-dimethylamino)naphthalene is an interesting example of heteroatom-directed aromatic lithiation where the metalation occurs at a place other than the ortho position. In this case, the lithium can be introduced at the 8-position due to the abstraction of hydrogen, which is sterically close to the substituents. The ligands derived from **72**, generally called "stiff-arm" ligands, are capable of exhibiting hypercoordination in main group chemistry due to the proximity of additional donor sites which are constrained to lie close to or within the primary coordination sphere. The rigidity and planarity of **72** prompted us to investigate the synthesis and isolation of group 16 compounds. Lithiation of **72** with *n*-BuLi in ether and chalcogen insertion reactions occurred selectively at the 8-position (Scheme 7). Aqueous oxidative workup of the unstable chalcogenolates **74** and **75** then afforded the diselenide **76**[23] and ditelluride **77**,[45] respectively, in good yield. The X-ray structures of these two compounds showed the presence of strong Se···N/Te···N interactions. These interactions are much stronger than that of the diselenide derived from *N*,*N*-dimethylbenzylamine. This indicates that the nitrogen lone pair, which is in conjugation with the π-electron system of the aromatic nuclei, is involved in strong coordination to the chalcogen atoms. Owing to the strong interactions, the diselenide and ditelluride crystallized in a chiral space group, and the crystals were enantiomerically pure.

The dichalcogenides synthesized by this method were used for a variety of transformations, as shown in Scheme 7. Reaction of **76** with stoichiometric amounts of sulfuryl chloride and iodine gave the selenenyl chloride **78** and the selenenyl iodide **79**, respectively.[25] Controlled bromination of **76** and **77** afforded the corresponding chalcogenyl(II) bromide (**80**, **81**), and with an excess amount of bromine, the tribromides were obtained.[25,45] While **83** was stable in solution, the selenium analogue **82** dissociated in solution to give the monobromide. As in the case of *N*,*N*-dimethylbezylamine, the phenyl derivative **84** could be synthesized from the lithiated species. The reaction of **73** with $Se(dtc)_2$ led to decomposition, whereas the corresponding reaction with $Te(dtc)_2$ afforded the unex-

Scheme 7



pected dithiacarbamate complex **85**.[26] Surprisingly, reaction of **73** with TeI_2 also afforded the monoaryl derivative **86**, even when less than 0.5 equiv of TeI_2 was used.[45] This indicates that the sterically bulky naphthalene units disfavor the formation of diarylchalcogenides.

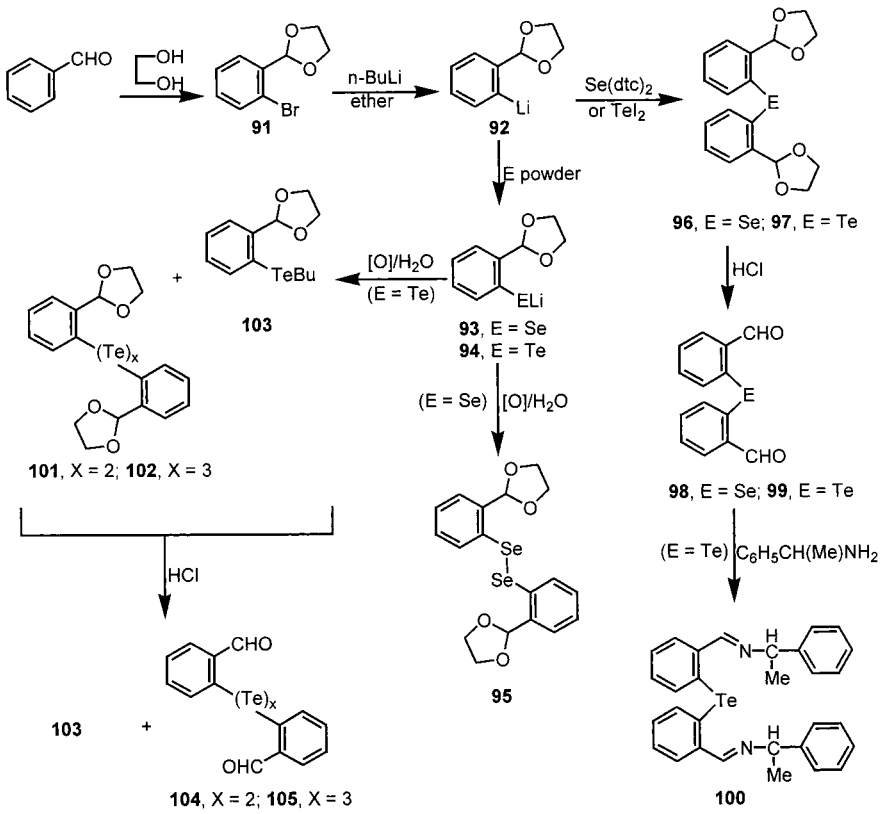
The reactivity of **75** toward MeI also differs from that of **4**. When **75** was treated with MeI, we could not obtain the expected methyl derivative **87**, but the reaction afforded the ditelluride **77**. Reduction of ditelluride with $NaBH_4$, followed by quenching with MeI to get the target compound, was also unsuccessful.[45] The reaction of ditelluride **77** with diazomethane did not give the expected methylene derivative **88**, probably due to the enhanced stability of the ditelluride. In contrast to the lithium tellurolate, which always tends to oxidize to form the ditelluride, the lithium selenolate undergoes some reactions. For example, reaction of **74** with α,α′-dibromo-*o*-xylene (**89**) afforded the tetradentate ligand **90**, which exhibits intramolecular Se···N interaction in solution.[24]

The ^{77}Se and ^{125}Te NMR chemical shifts of the selenium and tellurium compounds derived from *N*,*N*-dimethylnaphthalene appear at downfield positions relative to those of analogous compounds derived from *N*,*N*-dimethylbenzylamine. For example, the chemical shift of **84** appeared at −124.6 ppm, whereas that for **15** appeared at −198 ppm with respect to $Te(dtc)_2$. These differences suggest that the rigidity of the naphthalene skeleton and the high basicity of amino group which is in conjugation with the naphthalene π-electron system impose a close approach of the potential donor nitrogen and acceptor chalcogen atoms. This can be clearly seen from the crystal structures of **76** and **77**, which showed shorter Se···N and Te···N distances compared with those of certain derivatives of *N*,*N*-dimethylbenzylamine.

Organochalcogen Compounds Derived from *o*-Bromobenzaldehyde

Heteroatom-directed lithiation of benzaldehyde could be achieved by the conversion of the −CHO group to an acetal, followed by the reaction with *n*-BuLi. The reaction of *o*-bromobenzaldehyde with ethylene glycol afforded the

Scheme 8



cyclized product **91**. Ortho lithiation and selenium insertion, followed by oxidative workup, gave a yellowish viscous liquid, from which a pale yellow solid of **95** was obtained upon cooling (Scheme 8).[24] In this case, one of the oxygen atoms present in the five-membered ring is expected to direct the lithiation process. The glutathione peroxidase activity of diselenide **95** was found to be much higher than that of diphenyl diselenide, which indicates that the Se···O nonbonded interactions in compound **95** significantly contribute to the observed enhancement in the activity.[24]

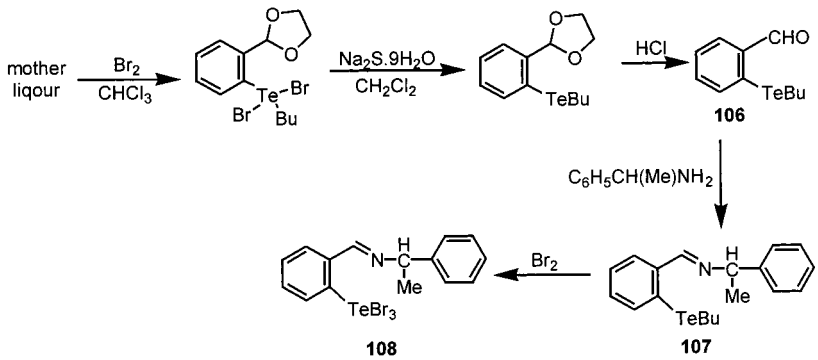
Reactions of the lithiated compound **92** with $Se(dtc)_2$ and TeI_2 afforded the monoselenide **96** and monotelluride **97**, respectively.[46] Cleavage of the heterocycle in **96** and **97** by HCl afforded the aldehyde derivatives **98** and **99**, respectively. These two compounds served as precursors for a variety of compounds. We found that the telluride **99** can be conveniently used for the synthesis of chiral tellurium azomethines such as **100**.[47] This compound was obtained by the condensation of **99** with (*R*)-(+)-(1-phenylethyl)amine.

In contrast to the synthesis of diselenide **95**, synthesis of the corresponding ditelluride was complicated. When we followed the normal route for the synthesis of ditelluride **101** involving lithiation of *o*-bromobenzaldehyde acetal, telluration, and oxidative workup, we obtained the ditelluride acetal **101** and the tritelluride acetal **103**, along with the butyl derivative **103**. The crude acetal, however, on hydrolysis was found to contain the tritelluride **105** and the ditalluride **104**, leaving the butyl derivative in the mother liquor. The butyl derivative **103** was purified by derivatizing with bromine to the Te(IV) derivative, followed by reduction with $Na_2S{\cdot}9H_2O$. Similar to **99**, compound **106** underwent condensation with (*R*)-(+)-(1-phenylethyl)amine to give the azomethine **107**, and further reaction of this azomethine with bromine afforded the tribromo derivative **108** (Scheme 9). The ditelluride **101** could also be separated from the tritelluride by crystallization of the crude product from acetic acid.

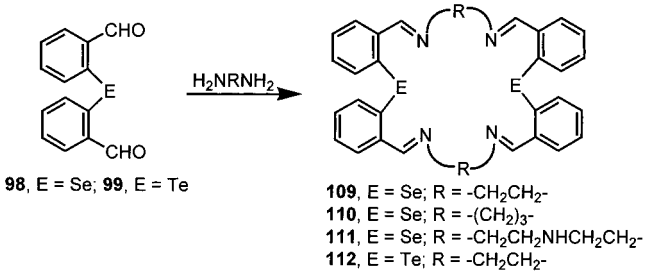
The other important class of compounds that could be obtained from the aldehydes **98** and **99** is the chalcogen-containing macrocycles.[48,49] Our interest in the chemistry of macrocyclic ligands started with the fact that the lower electronegativity of these elements combined with their greater σ electron-donating property should yield metal complexes with interesting structures and redox behavior. The selenium-containing 22-, 24-, and 28-membered macrocyclic Schiff base ligands (**109**−**111**) were synthesized via one-step dipodal condensation of bis(*o*-formylphenyl)selenide and 1,2-diaminoethane, 1,3-diaminopropane, and diethylenetriamine, respectively (Scheme 10).[49] Similarly, the tellurium macrocycle **112** was isolated via condensation reaction of bis(2-formylphenyl)telluride and 1,2-diaminoethane, without recourse to metal ion template or high dilution reaction.[50,51] In the macrocycles, the secondary Se···N and Te···N coordination plays an important role by reducing the unfavorable lone pair−lone pair repulsion between nitrogen atoms in the ring.

As an extension of this work, we studied the complexation behavior of the macrocycles.[50] The complexation of **112** with "soft" Lewis acid, $HgCl_2$, showed a strange behavior. Stirring the ligand at room temperature in

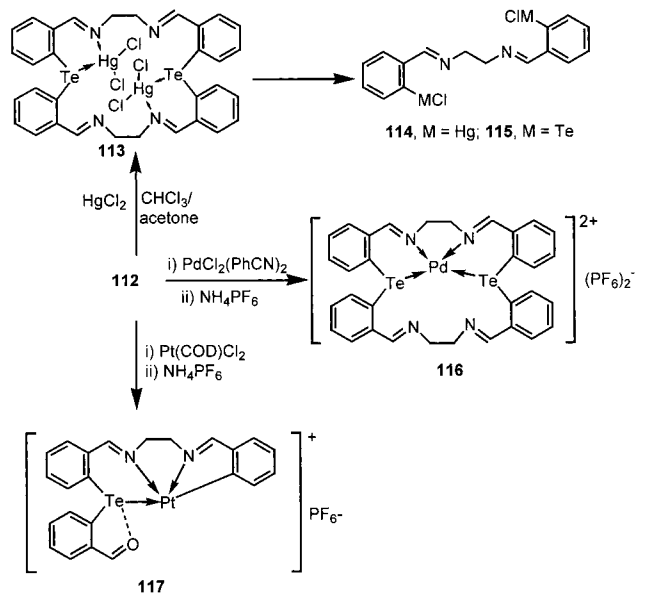
Scheme 9



Scheme 10



Scheme 11



chloroform with 2 equiv of $HgCl_2$ in acetone led to a facile cleavage, affording two products which were characterized as the bis(organomercury) Lewis acid **113** and bis(organotellurenyl chloride) **114**. The interesting dismutation reaction probably proceeds through the formation of a weakly associated addition complex, followed by the migration of groups (Scheme 11).

The template-free synthesis of Pd and Pt complexes of **112** was achieved by utilizing the Te···N interaction concept.[51] The reaction of **112** with 1 equiv of $PdCl_2(PhCN)_2$, followed by treatment with an excess of NH_4PF_6, gave complex **116**. The spectral data and X-ray crystal structure showed that two of the four nitrogen atoms and two Te atoms are coordinated to the metal center. Interestingly, a similar reaction of **117** with $Pt(COD)Cl_2$ in CH_2Cl_2 afforded an unusual cleaved complex **117**. This complex resulted from a facile C−Te bond cleavage and transmetalation. The facile cleavage of the C−Te bond is due to strong N→Te interactions ($n \rightarrow s^*_{C-Te}$), which activate the trans C−Te bond. The X-ray crystal structure of **117** showed an intramolecular Te···O interaction.

Conclusion

Although heteroatom-directed aromatic lithiation reactions have been used in the synthesis of numerous main group compounds, the application of this versatile route to the synthesis and isolation of organochalcogen derivatives has developed only recently. The heteroatom-directed lithiation methodologies described in this Account lead to several applications, which include (i) the synthesis of hybrid ligands for complexation reactions, (ii) isolation of unstable low-valent organochalcogen derivatives, (iii) synthesis of chiral and achiral reagents/catalysts for organic transformations, (iv) isolation of monomeric metal chalcogenolates with regard to their use as single-source stoichiometric precursors for semiconducting materials, (v) synthesis of novel diselenides as glutathione peroxidase mimics, and (vi) template-free synthesis of chalcogen-containing macrocyclic Schiff base ligands. Further investigations into the synthesis of organochalcogen compounds containing two donor atoms in close proximity are in progress.

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References

(1) *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1986 (Vol. 1), 1987 (Vol. 2).
(2) *Organoselenium Chemistry—A Practical Approach*; Back, T. G., Ed.; Oxford University Press: Oxford, 1999.
(3) Wirth, T. Organoselenium Chemistry in Stereoselective Reactions. *Angew. Chem., Int. Ed.* **2000**, *39*, 3740−3749.

(4) Organoselenium Chemistry: Modern Developments in Organic Synthesis. In *Topics in Current Chemistry*; Wirth, T., Ed.; Springer-Verlag: Berlin, 2000; Vol. 208.

(5) Singh, H. B.; Sudha, N. Organotellurium Precursors for Metal Organic Chemical Vapour Deposition (MOCVD) of Mercury Cadmium Telluride (MCT). *Polyhedron* **1996**, *15*, 745−763.

(6) Bochmann, M. Metal Chalcogenide Materials: Chalcogenolato Complexes as "Single-Source" Precursors. *Chem. Vap. Deposition* **1996**, *2*, 85−96.

(7) Hope E. G.; Levason, W. Recent Developments in the Coordination Chemistry of Selenoether and Telluroether Ligands. *Coord. Chem. Rev.* **1993**, *122*, 109−170.

(8) Arnold, J. The Chemistry of Metal Complexes with Selenolate and Tellurolate Ligands. In *Progress in Inorganic Chemistry*; Karlin, K. D., Ed.; John Wiley & Sons: New York, 1995; Vol. 43, pp 353−417.

(9) Singh, A. K.; Sharma, S. Recent Developments in the Ligand Chemistry of Tellurium. *Coord. Chem. Rev.* **2000**, *209,* 49−98.

(10) Mugesh, G.; Singh, H. B. Synthetic Organoselenium Compounds as Antioxidants: Glutathione Peroxidase Activity. *Chem. Soc. Rev.* **2000**, *29*, 347−357.

(11) Mugesh, G.; Singh, H. B. Biological Activities of Synthetic Organoselenium Compounds: Recent Developments. *Proc. Natl. Acad. Sci., India* **2000**, *70*, 207−220.

(12) Kanda, T.; Engman, L.; Cotgreave, I. A.; Powis, G. Novel Water-Soluble Diorganyl Tellurides with Thiol Peroxidase and Antioxidant Activity. *J. Org. Chem.* **1999**, *64*, 8161−8169.

(13) Mugesh, G.; du Mont, W.-W.; Sies, H. Chemistry of Biologically Important Synthetic Organoselenium Compounds. *Chem. Rev.* **2001**, *101,* 2125−2179 and references therein.

(14) Iwaoka, M.; Tomoda, S. A Model Study on the Effect of an Amino Group on the Antioxidant Activity of Glutathione Peroxidase. *J. Am. Chem. Soc.* **1994**, *116*, 2557−2561.

(15) Sudha, N.; Singh, H. B. Intramolecular Coordination in Tellurium Chemistry. *Coord. Chem. Rev.* **1994**, *135/136*, 469−515.

(16) Schlosser, M. Mechanistic Aspects of Polar Organometallic Chemistry. *Tetrahedron* **1994**, *50*, 5845−6128.

(17) Kaur, R.; Singh, H. B.; Patel, R. P. Synthesis, Characterization and Reaction of Bis[2-(Dimethlyaminomethyl)phenyl]diselenide: Its Structure and that of [2-(Dimethlyaminomethyl)phenyl]selenium Bromide. *J. Chem. Soc., Dalton Trans.* **1996**, 2719−2726.

(18) Singh, H. B.; Sudha, N.; West, A. A.; Hamor, T. A. Orthotellurated Derivatives of *N,N*-Dimethylbenzylamine: Crystal and Molecular Structures of [2-Dimethylaminomethyl)-phenyl] tellurium(IV)Tribromide and [2-(Butyldichlorotelluro)benzyl]dimethylammonium Chloride. *J. Chem. Soc., Dalton Trans.* **1990**, 907−913.

(19) Wilson, S. R.; Zucker, P. A.; Huang, R.-R. C.; Spector, A. Development of Synthetic Compounds with Glutathione Peroxidase Activity. *J. Am. Chem. Soc.* **1989**, *111*, 5936−5939.

(20) Kaur, R.; Singh, H. B.; Butcher, R. J. Syntheses and Characterization of Hybrid Bi- and Multidendate Tellurium Ligands Derived from *N,N*-Dimethlybenzylamine: Coordination Behavior of Bis-[2-((dimethylamino)methly)phenyl]Telluride with Chromium Pentacarbonyl. *Organometallics* **1995**, *14*, 4755−4763.

(21) du Mont, W.-W.; Martents-von Salzen, A.; Ruthe, F.; Seppälä, E.; Mugesh, G.; Devillanova, F.; Lippolis, V.; Kuhn, N. Tunning Selenium−Iodine Contacts: from Secondary Soft−Soft Interactions to Covalent Bonds. *J. Organomet. Chem.* **2001**, *623*, 14−28.

(22) Tiecco, M.; Testaferri, L. O.; Tingoli, M.; Chianelli, D.; Bartoli, D. The Reaction of Diphenyl Diselenide with Peroxydisulphate Ions in Methanol. A Convenient Procedure to Effect the Methoxyselenenylation of Alkenes. *Tetrahedron Lett.* **1989**, *30*, 1417−1420.

(23) Mugesh, G.; Panda, A.; Singh, H. B.; Punekar, N. S.; Butcher, R. J. Diferrocenyl Diselenides: Excellent Thiol Peroxidase-like Antioxidants. *Chem. Commun.* **1998**, 2227−2228.

(24) Mugesh, G.; Panda, A.; Singh, H. B.; Punekar, N. S.; Butcher, R. J. Glutathione Peroxidase-like Antioxidant Activity of Diaryl Diselenides—A Mechanistic Study. *J. Am. Chem. Soc.* **2001**, *123*, 839−850.

(25) Panda, A.; Mugesh, G.; Singh, H. B.; Butcher, R. J. Synthesis, Structure and Reactivity of Organochalcogen (Se, Te) Compounds Derived from 1-(Dimethylamino)naphthalene and *N,N*-Dimethylbenzylamine. *Organometallics* **1999**, *18*, 1986−1993.

(26) Regini, A.; Kaur, R.; Sudha, N.; Menon, S. C.; Singh, H. B. Orthotellurated Derivatives of Some Arylamines and Imines. *Proc. Indian Acad. Sci. (Chem. Sci.)* **1995**, *107*, 431−442.

(27) Kaur, R.; Singh, H. B. Indian Institute of Technology, Bombay, unpublished results.

(28) Santi, C.; Fragale, G.; Wirth, T. Synthesis of a New Chiral Nitrogen Containing Diselenide as a Precursor for Selenium Electrophiles. *Tetrahedron: Asymmetry* **1998**, *9*, 3625−3628.

(29) Wirth, T. Enantioselective Alkylation of Aldehydes Catalyzed by New Chiral Diselenides. *Tetrahedron Lett.* **1995**, *36*, 7849−7852.

(30) Singh, H. B.; Sudha, N.; Butcher, R. J. Synthesis and Characterization of Novel Chiral Ortho-Tellurated Complexes Derived from [(S)-1-(Dimethylamino)ethyl]benzene: Crystal and Molecular Structure of {2-[(S)-1-(Dimethlyamino)ethyl]phenyl}tellurium Trichloride. *Inorg. Chem.* **1992**, *31*, 1431−1435.

(31) Singh, H. B.; Sudha, N.; Cyclotellurated Derivatives of 2-(3-thienyl)-pyridine. *J. Organomet. Chem.* **1990**, *397*, 153−159.

(32) Kaur, R.; Singh, H. B.; Patel, R. J.; Kulshrestha, S. K. Syntheses, Characterization and Molecular Structures of Monomeric Selenolato Complexes of Mercury with Nitrogen-containing Chelating Ligands. *J. Chem. Soc., Dalton Trans.* **1996**, 461−466.

(33) Mugesh, G.; Singh, H. B. Indian Institute of Technology, Bombay, unpublished results.

(34) Wada, M.; Nobuki, S.-I.; Tenkyuu, Y.; Natsume, S.; Asahara, M.; Erabi T. Bis(2,6-dimethoxyphenyl)sulfide, Selenide and Telluride and their Derivatives. *J. Organomet. Chem.* **1999**, *580*, 282−289.

(35) Christiaens, L.; Luxen, A.; Evers, M.; Thibaut, Ph.; Mbuyi, M.; Welter, A. Synthése d'Alkylchalcogénobenzenes *Ortho*-Substitués par *Ortho*-Lithiation. *Chem. Scr.* **1984**, *24*, 178−184.

(36) Mugesh, G.; Singh, H. B.; Patel, R. P.; Butcher, R. J. Synthesis and Structural Characterization of Monomeric Selenolato Complexes of Zinc, Cadmium and Mercury. *Inorg. Chem.* **1998**, *37*, 2663−2669.

(37) Mugesh, G.; Singh, H. B.; Butcher, R. J. Synthesis and Characterization of Monomeric Tellurolato Complexes of Zinc and Cadmium: Crystal and Molecular Structure of Bis[2-(4,4-dimethyl-2-oxazolinyl)phenyl]ditelluride. *J. Organomet. Chem.* **1999**, *577*, 243−248.

(38) Mugesh, G.; Panda, A.; Singh, H. B.; Butcher, R. J. Intramolecular Se···N Nonbonding Interaction in Low-Valent Organoselenium Derivatives: A Detailed Study by ^{1}H, ^{77}Se NMR Spectroscopy and X-ray Crystallography. *Chem. Eur. J.* **1999**, *5,* 1411−1421.

(39) Mugesh, G.; Singh, H. B.; Butcher, R. J. Novel Chiral Organoselenenyl Halides Stabilized by Se···N Nonbonded Interactions: Synthesis and Structural Characterization. *Tetrahedron: Asymmetry* **1999**, *10*, 237−242.

(40) Apte, S.; Singh, H. B.; Butcher, R. J. Synthesis and Characterization of New Bis[2-(4,4-Dimethyl-2-oxazolinyl)phenyl] chalcogenides; Crystal and Molecular Structure of Bis[2-(4,4-Dimethly-2-oxazolinyl)phenyl)telluride. *J. Chem. Res. (S)* **2000**, 160−161; *J. Chem. Res. (M)* **2000**, 559−569.

(41) Mugesh, G.; Singh, H. B.; Butcher, R. J. The First Example of a Structurally Characterized Monomeric Bismuth Selenolate. *J. Chem. Res. (S)* **1999**, 416−417; *J. Chem. Res. (M)* **1999**, 1801−1810.

(42) Mugesh, G.; Singh, H. B.; Butcher, R. J. Synthesis and Structural Characterization of Monomeric Zinc(II), Cadmium(II) and Mercury-(II) Arenethiolates with a Chelating Oxazoline Ligand. *Eur. J. Inorg. Chem.* **1999**, 1229−1236.

(43) Mugesh, G.; Singh, H. B.; Butcher, R. J. 2-4′,4′-(Dimethyl-3′,4′-dihydrooxazol-2′-yl)phenol: Some First Row Transition Metal Complexes of This Naturally Occurring Binding Group. *Eur. J. Inorg. Chem.* **2001**, 669−678.

(44) Mugesh, G.; Singh, H. B.; Butcher, R. J. Intramolecular S···N Nonbonded Interactions in Organosulfur Derivatives: Crystal and Molecular Structures of [2-(4,4-dimethyl-2-oxazolinyl)phenyl]benzyl sulfide and bis[2-(4,4-dimethyl-2-oxazolinyl)phenyl] sulfide. *J. Chem. Res. (S)* **1999**, 472−473; *J. Chem. Res. (M)* **1999**, 2020−2051.

(45) Menon, S. C.; Singh, H. B.; Jasinski, J. M.; Jasinski, J. P.; Butcher, R. J. Intramolecularly Coordinated Low-Valent Organotellurium Complexes Derived from 1-(Dimethylamino)naphthalene. *Organometallics* **1996**, *15*, 1707−1712.

(46) Panda, A.; Menon, S. C.; Singh, H. B.; Butcher, R. J. Synthesis of Some Macrocycles/bicycles from Bis(o-formylphenyl) Selenide: X-Ray Crystal Structure of Bis(o-formylphenyl) Selenide and the First 28-Membered Selenium Containing Macrocyclic Ligand. *J. Organomet. Chem.* **2001**, *623*, 87−94.

(47) Menon, S. C.; Singh, H. B.; Patel, R. P.; Das, K.; Butcher, R. J. Synthesis and Reactivity of Chiral Tellurium Azomethines: Pseudopolymorphism of [*o*-((((1S,2R)-2-Hxdroxy-2-phenyl-1-methylethyl)-amino)methinyl)phenyl]tellurium(IV)Bromide. *Organometallics* **1997**, *16*, 563−571.

(48) Kaur, R.; Menon, S. C.; Singh, H. B. New Aspects of Intramolecular Coordination in Organochalcogen (Se/Te) Chemistry. *Proc. Indian Acad. Sci. (Chem. Sci.)* **1996**, *108*, 159−164.

(49) Panda, A.; Mugesh, G.; Singh, H. B.; Butcher, R. J. Intramolecularly Coordinated Organoselenium Derivatives: Syntheses, Structure and Reactivity. *Phosphorous, Sulphur Silicon* **2001**, *171*, 187−205.
(50) Menon, S. C.; Singh, H. B.; Patel, R. P.; Kulshreshtha, S. K. Synthesis, Structure and Reactions of the First Tellurium-containing Macrocyclic Schiff Base. *J. Chem. Soc., Dalton Trans.* **1996**, 1203−1207.
(51) Menon, S. C.; Panda, A.; Singh, H. B.; Butcher, R. J. Synthesis and Single-Crystal X-ray Structure of the First Cationic Pd(II) Complex of a Tellurium-containing Polyaza Macrocycle: Contrasting Reactions of Pd(II) and Pt(II) with a 22-Membered Macrocyclic Schiff Base. *Chem. Commun.* **2000**, 143−144.

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