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Novel chiral organoselenenyl halides stabilized by Se···N nonbonded interactions: synthesis and structural characterization

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Abstract

The first examples of structurally characterized chiral organoselenenyl halides stabilized by Se···N intramolecular interactions are described. The existence of strong nonbonded Se···N interactions in the solid state as well as in solution was unambiguously determined by single-crystal X-ray analysis and ^{77}Se NMR spectroscopy. © 1999 Elsevier Science Ltd. All rights reserved.

1. Introduction

Organoselenium compounds have become standard reagents for organic synthesis.[1] Chiral organoselenenyl halides and related derivatives in particular have attracted much attention recently because of their versatility as chiral electrophilic reagents in asymmetric reactions such as methoxyselenenylation,[2] aminoselenenylation,[3] and selenocyclization.[4] The applications of organoselenenyl halides for the synthesis of natural products such as (+)-samin[5] and (+)-membrine[6] have also been reported. Interestingly, most of the selenium reagents used have an asymmetric moiety with a heteroatom in close proximity to the selenium atom. It has been proposed that there should be a strong Se···N or Se···O interaction which would allow chiral sources on the nitrogen or oxygen atom to come close to the reaction center in the transition state of the reaction.[2f,h,l] The Se···N or Se···O interactions in such cases, therefore, not only dictate the molecular structure of the active selenium reagent so that the reaction proceeds through a relatively confined transition state but also increase the electrophilic reactivity of the selenium compounds.

Although the chemistry of chiral organoselenenyl halides and related derivatives having basic amino groups has led to very promising results, to the best of our knowledge, no chiral organoselenenyl halide has been structurally characterized. In continuation of our work on intramolecularly coordinated

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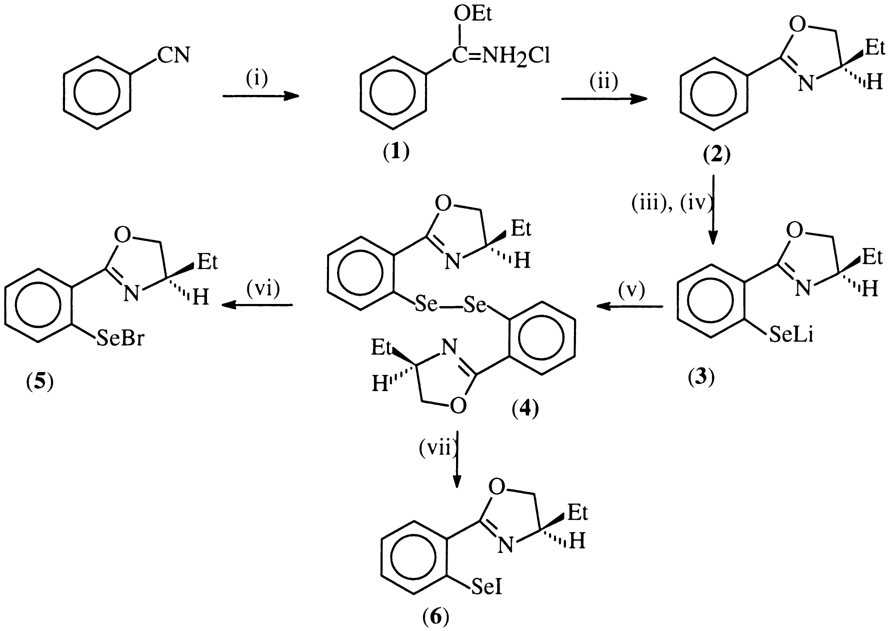
organochalcogens,[7] we report here the synthesis and the first structural characterization of two novel chiral organoselenenyl halides derived from (*R*)-(4-ethyl)-2-phenyloxazoline.

2. Results and discussion

Synthesis of (*R*)-(4-ethyl)-2-phenyloxazoline (**2**) was accomplished by the reaction of benzoyl chloride with (*R*)-(−)-2-amino-1-butanol. Although the oxazoline obtained by this method was pure enough for further reaction, the yield was poor. Alternatively, when the reaction of ethylbenzimidate (**1**) with (*R*)-(−)-2-amino-1-butanol under reflux conditions was carried out, the desired oxazoline was obtained in 80% yield. The diselenide (**4**) was then synthesized by the organolithium route. The lithium areneselenolate, $OxSe^{-}Li^{+}$ (**3**), was easily prepared by the direct low temperature metalation of (*R*)-(4-ethyl)-2-phenyloxazoline (**2**) with *n*-BuLi in ether followed by the addition of selenium powder. Oxidation of this lithium selenolate (**3**) then gave the desired diselenide (**4**)[8] (Scheme 1).



Scheme 1. Reagents and conditions (i) HCl gas, EtOH; (ii) (*R*)–(−)-2-Amino-1-butanol, $ClCH_2CH_2Cl$, reflux, 24 h; (iii) *n*-BuLi, ether, −5°C, 4 h; (iv) Se powder, −5°C, 2 h; (v) O_2, aq. $NaHCO_3$; (vi) Br_2, CCl_4, 0°C, 0.5 h; (vii) I_2, CCl_4, 0°C, 1 h

The stable bromo compound (**5**) was obtained as a crystalline solid in good yield by reacting the diselenide (**4**) with a stoichiometric amount of bromine. It is known that diorgano diselenides (R_2Se_2) react with iodine to give only charge-transfer adducts ($R_2Se_2 \cdot I_2$) instead of the selenenyl iodides (RSeI).[9] The isolation of the stable binary compounds between iodine and selenium has, however, been difficult due to their similar electronegativities.[10] Du Mont et al. have used a more hindered bis(2,4,6-tri-*tert*-butylphenyl) diselenide to synthesize the stable selenenyl iodide.[11] However, it was later reported by the same authors that the slight reduction in the steric bulk (2,4,6-tri-*iso*-propylphenyl) again leads to the formation of a charge-transfer complex.[12] When the reaction of **4** was carried out with a stoichiometric amount of iodine, the novel monoiodide **6** was obtained. In **6** the intramolecular stabilization leading to the formation of 10-Se-3 selane (10 valence electrons, 3 bound ligands) seems to be responsible for the formation of a covalent Se–I bond rather than a charge-transfer adduct.[13]

The ^{77}Se NMR chemical shifts are quite informative about the Se$\cdots$N nonbonded interactions. The ^{77}Se NMR chemical shift for **4** (456 ppm) is shifted more downfield than the systems having *sp*^{3} nitrogen atoms such as bis[2-(dimethylaminomethyl)-phenyl]diselenide (430 ppm)[7g] and 2,2′-diselenobis(*N*-cyclohexyl-methylbenzylamine) (432 ppm).[14] In the monohalides (**5** and **6**) a large deshielding is observed with respect to the diselenide (**4**) and the magnitude of downfield shift is according to the electronegativity of the atom attached to the selenium. The chemical shift value of **5** (877.7 ppm) is more downfield shifted compared with the achiral analogue, [2-(4,4-dimethyl-2-oxazolinyl)phenyl]selenenyl bromide (849.5 ppm).[15] This is probably due to the stronger Se$\cdots$N interaction (vide infra) in the former case [2.050(9) Å] compared with the latter one [2.063(3) Å]. However, for **6** the ^{77}Se chemical shift value (769.3 ppm) is very close to the value observed for the achiral analogue, [2-(4,4-dimethyl-2-oxazolinyl)phenyl]selenenyl iodide (762.2 ppm).[15] It is worth noting that the halo derivatives are quite stable in solution for a long time, and particularly in the case of **6**, no peaks were detected for the diselenide (**4**), indicating much higher stability as a result of the intramolecular Se$\cdots$N coordination. This is in contrast to a previous report where the authors had observed an equilibrating phenomenon between the diselenide and its iodo derivative.[11]

Optical rotations are given with the analytical data. The enantiomeric purity of the compounds was determined by recording the ^{1}H NMR spectra in the presence of a chiral shift reagent in $CDCl_3$. While compound **2** was found to be 95% enantiomerically pure, the enantiomeric excess of compounds **4**, **5** and **6** was found to be >99%. This suggests that the minor isomer has been removed during the recrystallization process.

The molecular structures of compounds **5** and **6** with significant bond distances and angles are shown in Figs. 1 and 2, respectively.

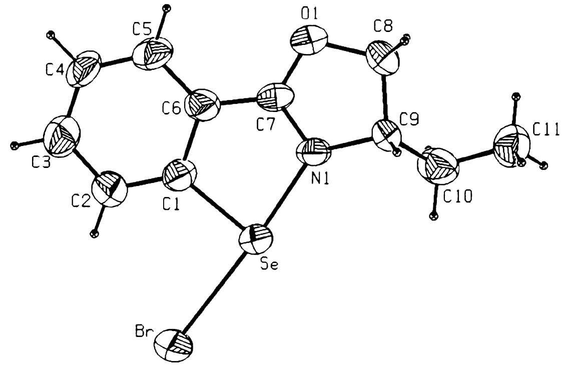


Figure 1. X-Ray structure of **5**. Selected bond distances (Å) and angles (°): Se–N(1): 2.050(9); Se–Br: 2.661(2); Se–C(1): 1.933(9); C(1)–Se–N(1): 82.4(4); C(1)–Se–Br: 93.8(3); N(1)–Se–Br: 175.6(3); C(7)–N(1)–Se: 112.5(8); C(9)–N(1)–Se: 136.5(6); C(2)–C(1)–Se: 127.9(8)

The geometry around Se is T-shaped with strong nonbonded Se$\cdots$N interactions. The Se$\cdots$N separations of 2.050(9) Å for **5** and 2.074(6) Å for **6** are much shorter than the sum of van der Waal's radii (3.5 Å).[16] The Se–Br [2.661(2) Å] and Se–I [2.8616(10) Å] distances are significantly longer than the sum of single-bond covalent radii of Se–Br [2.31 Å] and Se–I [2.50 Å], respectively. The intermolecular distance between Se and Br(A) is 3.856(9) Å which is higher than the sum of single bond covalent radii (2.310 Å), but considerably shorter than the sum of the van der Waal's radii (3.95 Å) indicates weak secondary interactions between the molecules. The iodo compound (**6**) does not show any intermolecular interactions. The N$\cdots$Se–X (X=Br, I) unit is nearly linear due to the Se$\cdots$N interaction. It is observed that the deviation of Se–X (X=Br or I) bond from the phenyl plane is significantly reduced by the Se$\cdots$N interaction, accompanied by an increase in the Se–X bond length. The interaction between the nitrogen

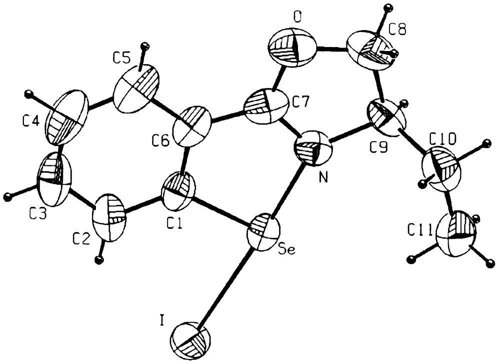


Figure 2. X-Ray structure of **6**. Selected bond distances (Å) and angles (°): Se–N: 2.074(6); Se–I: 2.8616(10); Se–C(1): 1.927(6); C(1)–Se–N: 82.0(3); C(1)–Se–I: 96.5(2); N–Se–I: 176.1(2); C(7)–N–Se: 111.6(6); C(9)–N–Se: 137.1(5); C(2)–C(1)–Se: 126.4(7)

lone pair and the Se–X bond causes a significant charge-transfer from the nitrogen to Se–X bond and weakens the Se–X bond considerably. This elongation of the Se–X bond increases the possibility of nucleophilic attack on the selenium. Refinement of the Flack enantiopole parameter[17] led to a value of approximately zero for **5** and **6**, thus confirming that the crystals of **5** and **6** are enantiomerically very pure.

3. Experimental

3.1. General procedures

All reactions were carried out under nitrogen or argon using standard vacuum-line techniques. Solvents were purified by standard procedures[18] and were freshly distilled prior to use. Melting points were recorded in capillary tubes and are uncorrected. ^{1}H and ^{13}C NMR spectra were obtained at 300 and 75.42 MHz, respectively in $CDCl_3$ on a Varian VXR 300S spectrometer. ^{77}Se NMR spectra were obtained at 95.34 MHz on a Bruker 500 spectrometer. Chemical shifts are cited with respect to $SiMe_4$ as internal (^{1}H and ^{13}C) and Me_2Se (^{77}Se) as external standard. The enantiomeric purity of the compounds was determined by the integration of signals in the ^{1}H NMR spectrum using the chiral shift reagent $Eu(tfc)_3$. Elemental analyses were performed on a Carlo–Erba model 1106 elemental analyzer. IR spectra were recorded as KBr pellets on a Nicolet Impact 400 FTIR spectrometer. Fast atom bombardment (FAB) mass spectra were recorded at room temperature on a JEOL SX 102 DA-6000 mass spectrometer/data system using xenon (6 kV, 10 mV) as the bombarding gas. Optical rotations were measured by a JASCO Model DIP 370 digital polarimeter.

3.2. *Synthesis of (*R*)-(−)-[2-(4-ethyl-2-oxazolinyl)phenyl]selenenyl bromide (**5**)*

To a cold solution of diselenide **4** (0.5 g, 1 mmol) in CCl_4 (25 ml) was added a solution of bromine (0.16 g, 1 mmol) in CCl_4. The addition was carried out dropwise over a period of 0.5 h and then allowed to come to room temperature. The solution obtained was concentrated to give yellow crystalline product, **5**. This was recrystallized from chloroform:hexane mixture to give yellow crystals. Yield: 0.61 g (75%), mp 156–158°C. Anal. calcd for $C_{11}H_{12}NOSeBr$: C, 39.65; H, 3.60; N, 4.21. Found: C, 39.18; H, 3.91; N, 3.79; ^{1}H NMR ($CDCl_3$, δ ppm) 1.11 (t, 3H, $-CH_3$, J=7.4 Hz), 1.83–1.92 (m, 1H, –CH–Et), 4.86 (dd, 2H, –CH_2O–, J=8.5 Hz), 4.65–4.75 (m, 2H, –CH_2–Me), 7.42–7.66 (m, 2H, Ar–H), 7.75–8.82 (m, 2H, Ar–H); ^{77}Se NMR ($CDCl_3$, δ ppm): 877.7; IR (KBr, cm^{-1}): 736, 927, 1025, 1420, 1493, 1585, 1618, 2927; m/z: 333 (M^+)(^{80}Se, ^{78}Br)(^{78}Se, ^{81}Br), 252 (100%) (^{78}Se), 199, 181, 155, 116, 54; $[\alpha]_D^{25}$ −22.0 (c 0.5, $CHCl_3$).

*3.3. Synthesis of (*R*)-(−)-[2-(4-ethyl-2-oxazolinyl)phenyl]selenenyl iodide (**6**)*

To a cold solution of diselenide **4** (0.5 g, 1 mmol) in CCl_4 (25 ml) was added a solution of iodine (0.25 g, 1 mmol) in CCl_4. The addition was carried out dropwise over a period of 1 h and then allowed to come to room temperature and the stirring was continued for additional 2 h. The solution obtained was concentrated to give red crystalline product, **6**. This was recrystallized from chloroform:hexane mixture to give brick red crystals of **6**. Yield: 0.64 g (87%), mp 118–120°C. Anal. calcd for $C_{11}H_{12}NOSeI$: C, 34.76; H, 3.16; N, 3.69. Found: C, 34.32; H, 3.08; N, 3.54. ^{1}H NMR ($CDCl_3$, δ ppm) 1.15 (t, 3H, –CH_3, J=7.4 Hz), 1.77–1.86 (m, 1H, –CH–Et), 4.66 (dd, 2H, –CH_2O–, J=8.8 Hz), 4.51–4.61 (m, 2H, –CH_2–Me), 7.39–7.53 (m, 2H, Ar–H), 7.69–8.54 (m, 2H, Ar–H); ^{77}Se NMR ($CDCl_3$, δ ppm): 769.3; IR (KBr, cm^{-1}): 736, 933, 1163, 1420, 1499, 1585, 1618, 2927; m/z: 254 (I_2), 253 (100%), 200, 147, 136, $[\alpha]_D^{25}$ −28.0 (c 0.5, $CHCl_3$).

3.4. Crystallography

(−)-(*R*)-**5**: Monoclinic, space group C2, *a*=16.245(3) Å, *b*=7.028(2) Å, *c*=11.393(3) Å, β=113.508(13)°, Z=4, V=1192.9(5) Å^3, D=1.855 Mg/m^3. Of the 1099 reflections collected, 1009 reflections (F>2σ (F_o)) were used for refinement. The final residuals were R1=4.55%, wR2=9.52%, and GOF=1.077. For (−)-(*R*)-**6**: Orthorhombic, space group $P2_12_12_1$, *a*=6.9470(7) Å, *b*=11.8683(9) Å, *c*=15.5507(13) Å, α, β, γ =90°, Z=4, V=1282.1(2) Å^3, D=1.969 Mg/m^3. All 1677 reflections collected were used for refinement. The final residuals were R1=3.55%, wR2=8.60%, and GOF=1.040. The diffraction measurements for **5** and **6** were performed at room temperature (293 K) on a Siemens R3m/V diffractometer using graphite-monochromated Mo-Kα radiation (λ=0.7170Å). The unit cell was determined from 25 randomly selected reflections using the automatic search index and least-squares routine. The data were corrected for Lorentz, polarization and absorption effects. The data were monitored by measuring two standard reflections every 60 min of X-ray exposure time. The structures for **5** and **6** were solved by routine heavy-atom (using SHELXS 86[19]) and Fourier methods and refined by full-matrix least squares with the non-hydrogen atoms anisotropic and hydrogens with fixed isotropic thermal parameters of 0.07 Å^2 using the SHELXL 93 program.[19] The hydrogens were partially located from difference electron-density maps and the rest were fixed at calculated positions. Scattering factors were from common sources.[20]

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