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2-Seleno-1-alkylbenzimidazoles and their Diselenides: Synthesis and Structural Characterization of a 2-Seleno-1-methylbenzimidazole Complex of Mercury†

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Abstract

2-Seleno-1-methylbenzimidazole, H(sebenzim^{Me}), can be synthesized from 1-methylbenzimidazole by sequential treatment with (i) BuⁿLi, (ii) elemental selenium and (iii) HCl(aq). This method is also applicable to the synthesis of 2-seleno-1-t-butylbenzimidazole, H(sebenzim^{Bu^t}). Single crystal X-ray diffraction and NMR spectroscopic data demonstrate that H(sebenzim^{Me}) and H(sebenzim^{Bu^t}) exist as the selone rather than the selenol tautomers, which is in accord with the results of density functional theory (B3LYP) calculations. The data also indicate that the selone is best represented as a C⁺–Se[–] zwitterion rather than as a C=Se doubly bonded species. Aerobic oxidation of H(sebenzim^{Me}) and H(sebenzim^{Bu^t}) in the presence of Et₃N yields the diselenides, (sebenzim^{Me})₂ and (sebenzim^{Bu^t})₂. In addition, H(sebenzim^{Me}) reacts with HgCl₂ to give [H(sebenzim^{Me})]₂HgCl₂, the first structurally characterized example of a 2-seleno-1-alkylimidazole mercury complex.

INTRODUCTION

While the toxicological properties of mercury are often associated with its high affinity for sulfur,^{1,2,3} its toxicity has also been attributed to its impact on the biochemical roles of selenium,⁴ which has been described as the most important antioxidant element in the human body.⁵ Specifically, it has been suggested that (i) the interaction between Hg(II) and selenium compounds may reduce the bioavailability of selenium *via* the formation of insoluble mercury selenide species⁶ and (ii) mercury may bind to the active sites of selenoenzymes and thereby inhibit their functions.⁷ Selenium is a well-known component of a variety of enzymes that incorporate the amino acids selenocysteine and selenomethionine (Figure 1), examples of which include glutathione peroxidases, thioredoxin reductases, glycine reductase, formate dehydrogenases, and selenoprotein P.^{4,8} Furthermore, the amino

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*2-Seleno-1-methylbenzimidazole is also referred to in the literature as 1-methylbenzimidazole-2-selone and 1-methyl-2,3-dihydro-1*H*-benzimidazole-2-selone.

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APPENDIX A. Supplementary Data

Tables of computational data for the geometry optimized structures and crystallographic data in CIF format (CCDC #885520–885524). These data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/contents/retrieving.html>, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.poly.xxxxxx.

acid derivative selenoneine (Figure 1), a 2-selenoimidazole analogue of ergothioneine, has been discovered in the blood of bluefin tuna,⁹ while Se-methylselenoneine (Figure 1) has more recently identified in human urine and blood.¹⁰ In view of the proposal that the toxicity of mercury is linked to its impact on the biochemical roles of selenium, it is pertinent to develop further the coordination chemistry of mercury in an environment that features selenium. Therefore, we describe here the synthesis and molecular structure of a mercury complex derived from 2-seleno-1-methylbenzimidazole, a structural analogue of selenoneine.

RESULTS AND DISCUSSION

1. Synthesis and structural characterization of 2-seleno-1-R-benzimidazoles

2-mercapto-1-R-imidazoles (Hmim^R),¹¹ which primarily exist as their thione tautomers (Figure 2),¹² are a well-studied class of molecules, in part because of the fact that the parent methyl derivative, methimazole (tapazole), is a widely used antithyroid drug.¹³ Such molecules may also serve as ligands for both transition metals and main group elements.¹⁴ For example, we have previously demonstrated that 2-mercapto-1-t-butylimidazole can coordinate effectively to mercury.¹⁵ On this basis, we anticipated that the selenium counterparts, H(seim^R), which may be considered mimics of the biomolecule selenoneine, would also bind to mercury. However, by comparison with 1-R-2-mercaptoimidazoles, the chemistry of the selenium analogues, H(seim^R), is virtually unknown, with few H(seim^R) derivatives having been reported.^{16,17,18,19,20} Therefore, we considered it worthwhile to develop further the chemistry of this class of molecules, which has also received attention with respect to potential antithyroid activity.^{16,17,21}

The methyl and mesityl derivatives, H(seim^{Me}) and H(seim^{Mes}), have previously been synthesized *via* deprotonation of the corresponding 1-R-imidazole, followed by reaction with elemental selenium and subsequent protonation.^{16,19} We have now demonstrated that this method can be extended to benzimidazole derivatives, as illustrated in Scheme 1. For example, sequential treatment of 1-methylbenzimidazole with (i) BuⁿLi, (ii) elemental selenium and (iii) HCl(aq), yields 2-seleno-1-methylbenzimidazole, H(sebenzim^{Me}),* as confirmed by X-ray diffraction (Figure 3).† 2-Seleno-1-methylbenzimidazole was originally synthesized *via* treatment of *N*-methyl-*o*-diaminobenzene with CSe₂,²⁰ which has a repulsive stench²² and is not conveniently obtainable. A distinct advantage of the method described here is, therefore, that it avoids the use of CSe₂. Furthermore, another synthetic route to H(sebenzim^{Me}) involves the reaction of sodium hydroselenide with 2-chloro-1-methylbenzimidazole,^{20c} a compound that is not readily available from commercial sources, which is in contrast to the widespread availability of 1-methylbenzimidazole.

The method illustrated in Scheme 1 is also applicable to the synthesis of 2-seleno-1-t-butylbenzimidazole, H(sebenzim^{Bu^t}), which has been structurally characterized by X-ray diffraction (Figure 4). The hydrogen atom attached to nitrogen was located and refined for both H(sebenzim^{Me}) and H(sebenzim^{Bu^t}), thereby providing excellent evidence that the compounds correspond to the selone‡ rather than the selenol tautomers, in accord with our previous structural characterization of H(seim^{Me}) and H(seim^{Mes}).¹⁹ This observation is also in agreement with density functional theory (B3LYP) calculations, which indicate that the

*2-Seleno-1-methylbenzimidazole is also referred to in the literature as 1-methylbenzimidazole-2-selone and 1-methyl-2,3-dihydro-1*H*-benzimidazole-2-selone.

†The molecular structure of H(sebenzim^{Me}) has been recently reported, but the atomic coordinates of the hydrogen atom attached to nitrogen were not freely refined. See reference 20c.

‡The term “selone” is used in this paper as an abbreviated form of “imidazoleselone” to refer to the terminal [CSe] group and thereby provide a distinction with the selenol tautomer. The term is not intended to convey any distinction between C=Se and zwitterionic C⁺–Se[–] resonance structures.

geometry optimized structures of the selones are more stable than those of the selenol tautomers (Figure 5). A noteworthy feature of $\text{H}(\text{sebenzim}^{\text{Bu}^t})$ is that the two Se–C–N angles are substantially different [$120.7(2)^\circ$ and $132.1(2)^\circ$], which is presumably a consequence of steric interactions between the selenium atom and the t-butyl substituent. This displacement of the selenium atom is also reproduced in the geometry optimized structure (119.6° and 133.9°) illustrated in Figure 5.

The most interesting aspects of the structures of $\text{H}(\text{sebenzim}^{\text{Me}})$ and $\text{H}(\text{sebenzim}^{\text{Bu}^t})$, however, are that they do not exhibit the same type of extended motif that is observed for $\text{H}(\text{seim}^{\text{Me}})$ and $\text{H}(\text{seim}^{\text{Mes}})$. For example, whereas $\text{H}(\text{seim}^{\text{Me}})$ and $\text{H}(\text{seim}^{\text{Mes}})$ exist as centrosymmetric N–H $\cdots$ Se “head-to-head” hydrogen bonded dimers in the solid state (Figure 6), hydrogen bonding within the methyl benzimidazole compound $\text{H}(\text{sebenzim}^{\text{Me}})$ results in a polymeric “head-to-tail” structure (Figure 7). In contrast to these hydrogen-bonded structures, the t-butyl derivative $\text{H}(\text{sebenzim}^{\text{Bu}^t})$ is devoid of N–H $\cdots$ Se hydrogen bonding interactions and forms columns of π -stacked molecules (Figure 8). The closest nonbonding interactions of selenium are with hydrogen atoms of C–H bonds, and are in the range 2.95 – 3.06 Å. The distance between the π -stacked planes is 3.47 Å, with the molecules in adjacent planes being related by an inversion center, such that a 6-membered ring of one molecule overlaps with a 5-membered ring of another molecule, with a centroid-to-centroid distance of 3.66 Å.

In accord with the selone nature of the compound, the C–Se bond lengths in $\text{H}(\text{sebenzim}^{\text{Me}})$ [1.838(2) Å] and $\text{H}(\text{sebenzim}^{\text{Bu}^t})$ [1.845(2) Å] are shorter than the corresponding values for the diselenides, $(\text{sebenzim}^{\text{Me}})_2$ [1.878(6) and 1.903(6) Å for the two crystallographically independent molecules] and $(\text{sebenzim}^{\text{Bu}^t})_2$ [1.907(2) Å], which have been synthesized by aerobic oxidation of $\text{H}(\text{sebenzim}^{\text{R}})$ in the presence of Et_3N^{23} (Scheme 1) and structurally characterized by X-ray diffraction (Figure 9 and Figure 10). However, despite the fact that the C–Se bonds in $\text{H}(\text{sebenzim}^{\text{R}})$ are shorter than in $(\text{sebenzim}^{\text{R}})_2$, the difference (*ca.* 0.05 Å) is less than would be expected (0.2 Å) on the basis of the single and double bond covalent radii of carbon and selenium.²⁴ The C–Se bonds in the selones are, therefore, evidently longer than would be expected for a C=Se double bond, thereby suggesting that the zwitterionic form, with a C⁺–Se[–] dative covalent bond, is an important resonance contributor (Scheme 1). Consistent with this suggestion, examination of the occupied π -symmetry molecular orbitals indicates that there is little π -overlap between the selenium and carbon atoms (Figure 11), which is in accord with our previous studies of $\text{H}(\text{seim}^{\text{Mes}})$.¹⁹

NMR spectroscopic studies provide additional support for the existence of $\text{H}(\text{sebenzim}^{\text{Me}})$ and $\text{H}(\text{sebenzim}^{\text{Bu}^t})$ as the selone rather than the selenol tautomers. For example, the $^1J_{\text{Se-C}}$ coupling constants for $\text{H}(\text{sebenzim}^{\text{Me}})$ and $\text{H}(\text{sebenzim}^{\text{Bu}^t})$ are 230 and 232 Hz, respectively, values that are similar to those for other compounds with C=Se groups (203 – 292 Hz),^{25,26,27} and much larger than those for non-zwitterionic sp^2 hybridized compounds with C–Se single bonds,^{18,25,28} as illustrated by the value of 123 Hz for Ph_2Se_2 .²⁸ Also in accord with the selone description, the ^1H -coupled ^{77}Se NMR spectra of $\text{H}(\text{sebenzim}^{\text{Me}})$ and $\text{H}(\text{sebenzim}^{\text{Bu}^t})$ display singlets, thereby indicating the absence of a Se–H bond. Furthermore, while ^{77}Se NMR chemical shifts of compounds with C=Se moieties span a very large range of *ca.* 2500 to –500 ppm,^{25,29,30} the ^{77}Se NMR chemical shifts of $\text{H}(\text{sebenzim}^{\text{Me}})$ (83 ppm) and $\text{H}(\text{sebenzim}^{\text{Bu}^t})$ (222 ppm) are in the range typically observed for related compounds, such as selenoureas and 1,3-dialkylimidazole-2-selone derivatives (*ca.* 20 – 245 ppm).^{25,26,29}

2. Synthesis and Structural Characterization of a Mercury 2-Seleno-1-methylbenzimidazole Compound

The selenium atom of H(sebenzim^{Me}) is an effective donor for mercury, as illustrated by the formation of [H(sebenzim^{Me})]₂HgCl₂ upon treatment of the selenoimidazole with HgCl₂ (Scheme 2). [H(sebenzim^{Me})]₂HgCl₂ is the first structurally characterized example of a 2-seleno-1-alkylimidazole mercury complex (Figure 12) and its coordination geometry is close to tetrahedral. However, the Se–Hg–Se bond angle [109.080(13)°] is larger than the Cl–Hg–Cl bond angle [103.09(2)°], such that the structure is classified by a τ_4 parameter of 0.94.³¹ An interesting feature of the structure of [H(sebenzim^{Me})]₂HgCl₂ is that the N–H groups of the H(sebenzim^{Me}) ligands participate in N–H...Cl hydrogen bonding interactions, with $d(N\cdots Cl)$ = 3.14 Å and 3.23 Å. A hydrogen bonding motif of this type has also been observed for (N-PrImSe)₂HgCl₂, which features saturated imidazolidine-2-selone ligands.³²

The Hg–Se bond lengths within [H(sebenzim^{Me})]₂HgCl₂ [2.5732(5) Å and 2.6090(5) Å] are shorter than the Hg–Se bond length for the *tris*(2-seleno-1-mesitylimidazolyl)hydroborato complex, [Tse^{Mes}]HgI [2.674 Å],³³ the only other reported mercury compound featuring coordination of imidazoleselone moieties, although the latter are components of a tripodal L₂X ligand.³⁴ The Hg–Se bonds in [H(sebenzim^{Me})]₂HgCl₂ are, nevertheless, distinctly longer than those in compounds such as the phenylselenolate derivative, Hg(SePh)₂ [2.4802(2) Å].³⁵ This difference undoubtedly reflects the fact that H(sebenzim^{Me}) is an L-type donor and coordinates *via* a dative bond, whereas PhSe is an X-type ligand and coordinates *via* a normal covalent bond.³⁴ The distinction between normal covalent and dative covalent bonds has been highlighted by Haaland, with the lengths of dative bonds being very sensitive to the environment of the acceptor atom.³⁶ An illustration of the flexibility of dative Hg←Se interactions is provided by the observation that the Hg–Se bonds within [Hg₂(SePh₂)₄][ClO₄]₂ vary from 2.65 Å to 2.92 Å.³⁷ For further comparison, the mean Hg–Se bond length for compounds listed in the Cambridge Structural Database³⁸ is 2.660 Å, and a selection of such compounds is listed in Table 1.^{39–49}

Coordination of H(sebenzim^{Me}) is accompanied by a relatively small lengthening of the C–Se bond. Thus, the C–Se bond lengths in [H(sebenzim^{Me})]₂HgCl₂ [1.862(3) and 1.864(3) Å] are only *ca.* 0.02 Å longer than that in uncoordinated H(sebenzim^{Me}) [1.838(2) Å]. Despite the fact that the lengthening is small, the ¹³C and ⁷⁷Se NMR chemical shifts of the [CSe] moiety are very sensitive with respect to mercury coordination. Thus, upon coordination, the ¹³C NMR spectroscopic signal shifts upfield by 11 ppm (from δ 162.8 to 151.8), while the ⁷⁷Se NMR spectroscopic signal shifts upfield by 63 ppm (from 83 ppm to 20 ppm). Similar trends have been observed in related systems,^{32,50} including thione counterparts.⁵¹ Also of note, ¹J_{Se-C} is reduced from a value of 230 Hz for H(sebenzim^{Me}) to a value of 204 Hz upon coordination. Thus, it is apparent that both ¹³C and ⁷⁷Se NMR spectroscopy can be used effectively to probe coordination of 2-seleno-1-alkylimidazole ligands. Finally, [H(sebenzim^{Me})]₂HgCl₂ is also characterized by a ¹⁹⁹Hg{¹H} NMR spectroscopic signal at –1026 ppm, which is close to the range observed for *bis*(imidazolidine-2-thione) adducts of HgX₂ (X = Cl, Br, CN).⁵²

CONCLUSIONS

In summary, the 2-seleno-1-alkylbenzimidazole compounds, H(sebenzim^{Me}) and H(sebenzim^{Bu^t}), which are structurally related to the biomolecule selenoneine, may be conveniently synthesized *via* sequential treatment of 1-methylbenzimidazole or 1-*t*-butylbenzimidazole with (i) BuⁿLi, (ii) elemental selenium and (iii) HCl(aq). Analysis by both X-ray diffraction and NMR spectroscopy provides evidence that the compounds exist as selone rather than selenol tautomers. Together with computational studies, the data indicate that the selone moiety in these compounds is best represented as a C⁺–Se[–]

zwitterion, rather than as a C=Se doubly bonded species. Aerobic oxidation of H(sebenzim^{Me}) and H(sebenzim^{Bu^t}) in the presence of Et₃N yields the diselenides, (sebenzim^{Me})₂ and (sebenzim^{Bu^t})₂. 2-Seleno-1-methylbenzimidazole is effective for coordinating mercury, and treatment of the selone with HgCl₂ gives [H(sebenzim^{Me})₂HgCl₂], the first structurally characterized example of a 2-seleno-1-alkylimidazole mercury complex.

EXPERIMENTAL SECTION

General Considerations

NMR spectra were measured on a Bruker Avance 500 DMX spectrometer. ¹H NMR spectra are reported in ppm relative to SiMe₄ (δ = 0) and were referenced internally with respect to the protio solvent impurity (δ 7.16 for C₆D₅H, 2.50 for Me₂SO-*d*₅ and 5.32 for CDHCl₂).⁵³ ¹³C NMR spectra are reported in ppm relative to SiMe₄ (δ = 0) and were referenced internally with respect to the solvent (δ 128.06 for C₆D₆, 39.52 for Me₂SO-*d*₆, 54.00 for CD₂Cl₂).⁵³ ⁷⁷Se NMR spectra are reported in ppm relative to neat Me₂Se (δ = 0) and were referenced using a solution of Ph₂Se₂ in C₆D₆ (δ = 460) as an external standard.⁵⁴ ¹⁹⁹Hg NMR spectra are reported in ppm relative to neat Me₂Hg (δ = 0) and were referenced using a 1.0 M solution of HgI₂ in Me₂SO-*d*₆ (δ = -3106) as an external standard.⁵⁵ Coupling constants are given in hertz. IR spectra were recorded as KBr pellets on a Nicolet iS10 FT-IR spectrometer (ThermoScientific), and the data are reported in reciprocal centimeters. 1-*tert*-butylbenzene-1,2-diamine was obtained by a literature method⁵⁶ and, with the exception of 1-fluoro-2-nitrobenzene (VWR), all chemicals were purchased from Sigma-Aldrich. **CAUTION: All mercury compounds are toxic and appropriate safety precautions must be taken in handling these compounds.**

X-ray structure determinations

Single crystal X-ray diffraction data were collected on a Bruker Apex II diffractometer and crystal data, data collection and refinement parameters are summarized in Table 2. The structures were solved using direct methods and standard difference map techniques, and were refined by full-matrix least-squares procedures on *F*² with SHELXTL (Version 6.12).⁵⁷

Computational Details

Calculations were carried out using DFT as implemented in the Jaguar 7.5 (release 207) suite of *ab initio* quantum chemistry programs.⁵⁸ Geometry optimizations were performed with the B3LYP density functional⁵⁹ using the 6-31G** (C, H, N) and LAV3P (Se) basis sets.⁶⁰ The energies of the optimized structures were reevaluated by additional single point calculations on each optimized geometry using cc-pVTZ(-f) correlation consistent triple-ζ basis set. Molecular orbital analyses were performed with the aid of JIMP2,⁶¹ which employs Fenske-Hall calculations and visualization using MOPLOT.⁶²

Synthesis of H(sebenzim^{Me})

A solution of 1-methylbenzimidazole (5.0 g, 37.8 mmol) in THF (80 mL) was cooled to -78°C and treated dropwise with BuⁿLi (16.5 mL, 2.5 M solution in hexanes, 41.3 mmol). The mixture was stirred at -78°C for 30 minutes and then slowly allowed to warm to room temperature. The mixture was stirred at room temperature for an additional 30 minutes and the resulting bronze-colored solution was then cooled to -78°C. Selenium pellets (*ca.* 4 mm diameter, 4.5 g, 57.0 mmol) were added and the mixture was allowed to warm up to room temperature with stirring. Over this period, the selenium pellets dissolved, giving a bright green solution that became orange and finally red. The mixture was stirred overnight at

room temperature and then treated slowly with HCl_{aq} (10%, 10 mL), thereby resulting in the formation of a bright red precipitate. The precipitate was removed by filtration in air and discarded. The filtrate was extracted with dichloromethane (3×50 mL) and the combined extracts were dried with anhydrous sodium sulfate and filtered. The volatile components were removed *in vacuo* at room temperature to give an orange solid that was dissolved in a minimal quantity of dichloromethane (30 mL). Hexanes were added to the solution, thereby resulting in the precipitation of an orange solid that was isolated by filtration and dried *in vacuo*. The orange solid was dissolved in acetone (25 mL) and then treated with distilled water (*ca.* 75 mL). The solution was placed in a refrigerator (*ca.* 5°C), thereby depositing large, white, needle-like crystals overnight. The crystals were isolated by filtration and dried *in vacuo* to give pure $\text{H}(\text{sebenzim}^{\text{Me}})$ (4.3 g, 54% yield). Crystals of $\text{H}(\text{sebenzim}^{\text{Me}})$ suitable for X-ray diffraction were obtained by vapor diffusion of pentane into a benzene solution at room temperature. Anal. calcd for $\text{C}_8\text{H}_8\text{N}_2\text{Se}$: C, 45.5; H, 3.8; N, 13.3. Found: C, 45.0; H, 3.5; N, 12.8. ^1H NMR ($\text{Me}_2\text{SO}-d_6$): δ 3.75 [s, 3H of CH_3], 7.22 [m, 2H of C_6H_4], 7.44 [m, 1H of C_6H_4], 7.45 [m, 1H of C_6H_4], 13.22 [s, 1H of NH]. $^{13}\text{C}\{^1\text{H}\}$ NMR ($\text{Me}_2\text{SO}-d_6$): δ 31.9 [CH_3], 110.0 [CH of C_6H_4], 110.0 [CH of C_6H_4], 122.6 [CH of C_6H_4], 123.3 [CH of C_6H_4], 132.1 [ring junction C of C_6H_4], 133.7 [ring junction C of C_6H_4], 162.8 [CSe, $J_{\text{Se-C}} = 230$]. $^{77}\text{Se}\{^1\text{H}\}$ NMR ($\text{Me}_2\text{SO}-d_6$): δ 83 ppm. IR data (KBr pellet, cm^{-1}): 3137 (m), 3104 (m), 3057 (m), 2984 (w), 2922 (w), 2851 (w), 1926 (w), 1620 (w), 1501 (w), 1459 (s), 1384 (w), 1357 (m), 1333 (s), 1246 (m), 1231 (m), 1182 (w), 1152 (w), 1134 (w), 1093 (m), 1011 (w), 919 (w), 808 (w), 738 (s), 691 (w), 636 (w), 595 (w).

Synthesis of $(\text{sebenzim}^{\text{Me}})_2$

A solution of $\text{H}(\text{sebenzim}^{\text{Me}})$ (212 mg, 1 mmol) in CH_3CN (10 mL) was treated with triethylamine (310 μL , 2.2 mmol) in air. The colorless solution was stirred at room temperature for 1 hour, over which period it became yellow and then orange. The orange solution was stirred overnight, resulting in the precipitation of an amorphous, bright orange powder in a colorless supernatant. The precipitate was isolated by filtration and dried *in vacuo* to give the diselenide $(\text{sebenzim}^{\text{Me}})_2$ (126 mg, 60% yield). Anal. calcd for $\text{C}_{16}\text{H}_{14}\text{N}_4\text{Se}_2$: C, 45.7; H, 3.4; N, 13.3. Found: C, 45.5; H, 3.2; N, 13.2. ^1H NMR (CD_2Cl_2): δ 3.73 [s, 3H of CH_3], 7.27 [t, $^2J_{\text{H-H}} = 8$, 1H of C_6H_4], 7.33 [t, $^2J_{\text{H-H}} = 8$, 1H of C_6H_4], 7.37 [d, $^2J_{\text{H-H}} = 8$, 1H of C_6H_4], 7.70 [d, $^2J_{\text{H-H}} = 8$, 1H of C_6H_4]. $^{13}\text{C}\{^1\text{H}\}$ NMR (CD_2Cl_2): δ 32.7 [CH_3], 110.5 [CH of C_6H_4], 120.4 [CH of C_6H_4], 123.0 [CH of C_6H_4], 124.4 [CH of C_6H_4], 137.3 [ring junction C of C_6H_4], 142.6 [CSe], 144.3 [ring junction C of C_6H_4]. $^{77}\text{Se}\{^1\text{H}\}$ NMR (CD_2Cl_2): δ 404 ppm. IR data (KBr pellet, cm^{-1}): 3048 (w), 2939 (w), 1908 (vw), 1787 (vw), 1687 (vw), 1605 (w), 1478 (w), 1463 (m), 1435 (s), 1327 (s), 1275 (m), 1237 (m), 1154 (w), 1130 (w), 1081 (w), 1002 (w), 939 (vw), 894 (vw), 852 (vw), 803 (m), 756 (s), 722 (m), 659 (vw), 620 (vw), 583 (vw), 528 (vw).

Synthesis of 1-*tert*-butylbenzimidazole hydrochloride

A solution of 1-*tert*-butylbenzene-1,2-diamine (3.175 g, 19.3 mmol) in trimethyl orthoformate (20 mL) was heated at reflux for 90 minutes, after which period the volatile components were removed *in vacuo* (1-*tert*-butylbenzimidazole has been previously synthesized by another method⁶³ and the presence of 1-*tert*-butylbenzimidazole at this point was confirmed by comparison with the literature data⁶⁴).⁶⁵ The resultant black residue was dissolved in dichloromethane (50 mL) and stirred for 15 minutes with HCl_{aq} (50 mL, 3 M). Water (250 mL) was added and the organic layer was separated. The organic layer was extracted with water (2×200 mL), and the combined aqueous layers, including the original HCl_{aq} solution, were evaporated to yield a light red solid. The solid obtained was triturated with a 1:1 mixture of acetone and hexanes (2×50 mL), filtered and then washed with ice-cold acetone (3×50 mL) to give 1-*tert*-butylbenzimidazole hydrochloride as a white solid (2.35 g, 58% yield). Anal. Calcd for $\text{C}_{11}\text{H}_{16}\text{N}_2\text{Cl}$: C, 62.4; H, 7.6; N, 13.2. Found: C, 62.3;

H, 6.9; N, 13.2. ^1H NMR ($\text{Me}_2\text{SO}-d_6$): δ 1.77 [s, 9H of CH_3], 7.56 [m, 2H of C_6H_4], 7.88 [m, 1H of C_6H_4], 8.22 [m, 1H of C_6H_4], 9.70 [s, 1H of NH]. $^{13}\text{C}\{^1\text{H}\}$ NMR ($\text{Me}_2\text{SO}-d_6$): δ 28.3 [CH_3], 60.2 [CMe_3], 115.0 [CH of C_6H_4], 116.0 [CH of C_6H_4], 125.6 [CH of C_6H_4], 125.9 [CH of C_6H_4], 129.7 [ring junction C of C_6H_4], 132.1 [ring junction C of C_6H_4], 139.8 [$\text{C}=\text{N}$ of imidazole]. IR data (KBR pellet, cm^{-1}): 3188 (w), 3171 (w), 3064 (m), 3033 (w), 2980 (m), 2945 (w), 2885 (m), 2772 (s), 2724 (s), 2666 (s), 2500 (m), 1964 (vw), 1797 (vw), 1727 (w), 1666 (w), 1625 (w), 1603 (w), 1541 (s), 1503 (w), 1480 (w), 1442 (s), 1407 (w), 1382 (w), 1371 (w), 1336 (m), 1290 (m), 1263 (m), 1228 (m), 1198 (s), 1122 (vw), 1052 (w), 1032 (w), 1017 (vw), 933 (vw), 886 (w), 851 (vw), 813 (m), 744 (s), 658 (w), 615 (m), 580 (m), 551 (vw).

Synthesis of $\text{H}(\text{sebenzim}^{\text{Bu}^t})$

A suspension of 1-*tert*-butylbenzimidazole hydrochloride (1.0 g, 3.9 mmol) in diethyl ether (20 mL) was cooled to -78°C and treated dropwise with Bu^nLi (4.2 mL, 2.5 M solution in hexanes, 10.5 mmol) and then slowly allowed to warm to room temperature. The mixture was stirred at room temperature for an additional 30 minutes. The solution was stirred at -78°C for 30 minutes before being slowly warmed up to room temperature and stirred for another 30 minutes. The resulting mixture comprising a yellow solid in an orange solution was then cooled to -78°C and treated with selenium pellets (*ca.* 4mm diameter, 560 mg, 7.1 mmol). The mixture was allowed to warm to room temperature and stirred for 30 minutes, after which THF (10 mL) was added. The resulting yellow solution was stirred overnight, over which period a grey suspension formed. The mixture was cooled to -78°C and treated with HCl (5.5 mL, 1.0 M solution in diethyl ether, 5.5 mmol), resulting in the formation of a light orange solution. The mixture was allowed to warm to room temperature and treated with H_2O (30 mL). The organic layer was separated and washed twice with water and then once with brine and dried over anhydrous sodium sulfate. The volatile components were removed *in vacuo* at room temperature and the solid obtained was dissolved in dichloromethane (20 mL). Pentane (80 mL) was added and the solution was cooled to deposit $\text{H}(\text{sebenzim}^{\text{Bu}^t})$ as tan crystals which were isolated by filtration and dried *in vacuo* (910 mg, 76% yield). The small amount of colored impurity was removed by addition of pentane (80 mL) to a solution of the tan crystals in acetone (20 mL), and storing the solution in a freezer overnight, to give white needles. Crystals of $\text{H}(\text{sebenzim}^{\text{Bu}^t})$ suitable for X-ray diffraction were obtained by vapor diffusion of pentane into a benzene solution at room temperature. Anal. Calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{Se}$: C, 52.2; H, 5.6; N, 11.1. Found: C, 51.7; H, 5.3; N, 10.8. ^1H NMR ($\text{Me}_2\text{SO}-d_6$): δ 2.04 [s, 9H of CH_3], 7.11 [t, $^2J_{\text{H-H}} = 8$, 1H of C_6H_4], 7.15 [t, $^2J_{\text{H-H}} = 8$, 1H of C_6H_4], 7.23 [d, $^2J_{\text{H-H}} = 8$, 1H of C_6H_4], 7.81 [d, $^2J_{\text{H-H}} = 8$, 1H of C_6H_4], 13.13 [s, 1H of NH]. $^{13}\text{C}\{^1\text{H}\}$ NMR ($\text{Me}_2\text{SO}-d_6$): δ 29.9 [CH_3], 62.7 [CMe_3], 109.9 [CH of C_6H_4], 114.4 [CH of C_6H_4], 122.1 [CH of C_6H_4], 122.8 [CH of C_6H_4], 133.0 [ring junction C of C_6H_4], 133.8 [ring junction C of C_6H_4], 160.3 [CSe , $J_{\text{Se-C}} = 232$]. $^{77}\text{Se}\{^1\text{H}\}$ NMR ($\text{Me}_2\text{SO}-d_6$): δ 222 ppm. IR data (KBr pellet, cm^{-1}): 3412 (m), 2989 (w), 2964 (w), 2920 (w), 2866 (w), 1619 (w), 1493 (m), 1474 (w), 1423 (vs), 1399 (m), 1376 (w), 1358 (m), 1337 (m), 1312 (s), 1283 (w), 1230 (m), 1189 (m), 1167 (m), 1156 (m), 1118 (m), 1031 (w), 729 (s), 667 (w), 609 (w), 592 (w), 565 (w), 522 (w).

Synthesis of $(\text{sebenzim}^{\text{Bu}^t})_2$

A solution of $\text{H}(\text{sebenzim}^{\text{Bu}^t})$ (25 mg, 0.1 mmol) in CD_3CN (1 mL) was treated with triethylamine (33 μL , 0.24 mmol) in air. The colorless solution was allowed to sit at room temperature 1 hour, during which time it became yellow and then orange. The orange solution was allowed to sit overnight, resulting in the formation of bright red-orange crystals. These crystals were isolated by filtration and dried *in vacuo* to give $(\text{sebenzim}^{\text{Bu}^t})_2$ (10 mg, 40% yield) suitable for X-ray diffraction. Anal. calcd for $\text{C}_{22}\text{H}_{26}\text{N}_4\text{Se}_2$: C, 52.4; H, 5.2; N, 11.1. Found: C, 51.7; H, 4.8; N, 10.8. ^1H NMR (CD_2Cl_2): δ 1.93 [s, 9H of CH_3],

7.16 [m, 2H of C₆H₄], 7.57 [m, 1H of C₆H₄], 7.65 [m, 1H of C₆H₄]. ¹³C{¹H} NMR (CD₂Cl₂): δ 30.7 [CH₃], 59.3 [CMe₃], 114.1 [CH of C₆H₄], 118.8 [CH of C₆H₄], 121.8 [CH of C₆H₄], 121.9 [CH of C₆H₄], 136.8 [ring junction C of C₆H₄], 145.3 [CSe], 145.6 [ring junction C of C₆H₄]. ⁷⁷Se{¹H} NMR (CD₂Cl₂): δ 487 ppm. IR data (KBr pellet, cm⁻¹): 3007 (w), 2974 (m), 2935 (w), 2873 (w), 1604 (vw), 1582 (vw), 1605 (w), 1479 (m), 1458 (m), 1402 (s), 1372 (m), 1306 (s), 1289 (m), 1273 (s), 1228 (w), 1190 (s), 1117 (m), 1051 (w), 1017 (w), 903 (vw), 809 (w), 761 (w), 741 (s), 658 (w), 620 (w), 568 (w), 537 (w).

Synthesis of [H(sebenzim^{Me})]₂HgCl₂

A mixture of H(sebenzim^{Me}) (85 mg, 0.40 mmol) and HgCl₂ (54 mg, 0.20 mmol) were dissolved in CD₃CN (2 mL) in an NMR tube equipped with a J. Young valve and heated overnight at 100°C. Over this period, colorless, X-ray quality crystals of [H(sebenzim^{Me})]₂HgCl₂ (110 mg, 79% yield) were deposited and isolated by decanting the solution. Anal. calcd for C₁₆H₁₆Cl₂HgN₄Se₂: C, 27.7; H, 2.3; N, 8.1. Found: C, 27.8; H, 2.2; N, 8.0. ¹H NMR (Me₂SO-*d*₆): δ 3.86 [s, 6H of CH₃], 7.39 [m, 4H of C₆H₄], 7.46 [m, 2H of C₆H₄], 7.67 [m, 2H of C₆H₄], 14.18 [br, N-H]. ¹³C{¹H} NMR (Me₂SO-*d*₆): δ 33.0 [CH₃], 111.7 [CH of C₆H₄], 111.9 [CH of C₆H₄], 124.3 [CH of C₆H₄], 124.9 [CH of C₆H₄], 131.5 [ring junction C of C₆H₄], 133.4 [ring junction C of C₆H₄], 151.8 [CSe, *J*_{Se-C} = 204]. ⁷⁷Se{¹H} NMR (Me₂SO-*d*₆): δ 20 ppm. ¹⁹⁹Hg{¹H} NMR (Me₂SO-*d*₆): δ -1026 ppm. IR data (KBr pellet, cm⁻¹): 3132 (w), 3088 (m), 3050 (m), 2982 (w), 2926 (w), 2866 (w), 2829 (w), 2747 (w), 1620 (w), 1501 (s), 1449 (s), 1394 (m), 1347 (s), 1334 (m), 1254 (w), 1155 (w), 1132 (w), 1096 (m), 1008 (w), 750 (s), 594 (w), 566 (w).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Selenium-containing derivatives of amino acids.

Figure 2.
Tautomerization of mercapto and selenoimidazoles and abbreviations used.

Figure 3.
Molecular structure of H(sebenzim^{Me}). Hydrogen atoms on carbon are not included.

Figure 4.
Molecular structure of H(sebenzim^{Bu^t}). Hydrogen atoms on carbon are not included.

$$H_{\text{SCF}}^{\text{rel}} = 0.0 \text{ kcal mol}^{-1}$$

$$H_{\text{SCF}}^{\text{rel}} = 16.0 \text{ kcal mol}^{-1}$$

$$H_{\text{SCF}}^{\text{rel}} = 0.0 \text{ kcal mol}^{-1}$$

$$H_{\text{SCF}}^{\text{rel}} = 12.6 \text{ kcal mol}^{-1}$$

Figure 5. Geometry optimized structures of selone and selenol tautomers of H(sebenzim^{Me}) and H(sebenzim^{Bu^t}).

Figure 6.
Hydrogen bonded “head-to-head” dimeric structure of $\text{H}(\text{seim}^{\text{Me}})$ and $\text{H}(\text{seim}^{\text{Mes}})$.

Figure 7.
Hydrogen bonded polymeric “head-to-tail” helical structure of H(sebenzim^{Me}).

Figure 8.
 π -stacked column structure of $\text{H}(\text{sebenzim}^{\text{Bu}^t})$.

Figure 9. Molecular structure of (sebenzim^{Me})₂. Only one of the crystallographically independent molecules is shown.

Figure 10.
Molecular structure of $(\text{sebenzim}^{\text{Bu}^t})_2$.

Figure 11.

Occupied π -symmetry molecular orbitals for H(sebenzim^{Me}), indicating that there is little π -overlap between the selenium 4p orbital and the adjacent carbon atom.

Figure 12. Molecular structure of [H(sebenzim^{Me})]₂HgCl₂, illustrating N–H···Cl hydrogen bonding interactions.

Scheme 1.
Synthesis of selenobenzimidazole derivatives.

Scheme 2.
Synthesis of $[\text{H}(\text{sebenzim}^{\text{Me}})]_2\text{HgCl}_2$.

Table 1

Hg–Se bond lengths for selected compounds.

	$d(\text{Hg-Se})/\text{\AA}$	Reference
$\text{Hg}(\text{Se-2-NC}_5\text{H}_4)_2$	2.458(1)	39
$\text{Hg}[\text{Se}(\text{C}_6\text{F}_5)]_2$	2.459(1) – 2.507(1)	39
$(\text{C}_6\text{H}_2\text{Pr}^i_3)\text{HgMe}$	2.460(3)	40
$\text{Hg}(\text{Se-2-NC}_5\text{H}_3\text{Me})_2$	2.4629(12)	41
$\text{MeHgSeCH}_2\text{CH}(\text{NH}_3)\text{CO}_2$	2.469(4)	42
$[\{(\text{H}_2\text{N})_2\text{CSe}\}\text{HgMe}]\text{NO}_3$	2.477(3)	43
$\text{Hg}(\text{SePh})_2$	2.4802(2)	35
$[\text{Hg}(\text{SePh})_3][\text{NBu}^n_4]$	2.500(1) – 2.600(2)	44
$[\text{Tm}^{\text{Bu}^t}]\text{HgSePh}$	2.5244(4)	45
$[\text{H}(\text{sebenzim}^{\text{Me}})]_2\text{HgCl}_2$	2.5732(5), 2.6090(5)	this work
$(\text{Pr}^i\text{ImSe})_2\text{HgCl}_2$	2.5706(9), 2.5989(8)	32
$[\text{Hg}\{\text{SeC}(\text{O})\text{Tol}\}_3][\text{PPh}_4]$	2.5433(5) – 2.5867(5)	47
$[(\text{MeImSe})_3\text{HgCl}]\text{Cl}$	2.5801(6) – 2.6326(6)	48
$(\text{C}_4\text{H}_8\text{Se})_2\text{HgBr}_2$	2.648(1)	49
$[\text{Tse}^{\text{Mes}}]\text{HgI}$	2.6742(6)	33
$(\text{C}_4\text{H}_8\text{Se})_2\text{HgI}_2$	2.688(1), 2.718(1)	49
$[\text{Hg}_2(\text{SePh}_2)_4][\text{ClO}_4]_2$	2.65 – 2.92	37

Table 2

Crystal, intensity collection and refinement data.

	H(sebenzim^{Me})₂	H(sebenzim^{Bu})₂	(sebenzim^{Me})₂	(sebenzim^{Bu})₂	[H(sebenzim^{Me})₂HgCl₂]
lattice	Monoclinic	Orthorhombic	Monoclinic	Monoclinic	Triclinic
formula	C ₈ H ₈ N ₂ Se	C ₁₁ H ₁₄ N ₂ Se	C ₁₆ H ₁₄ N ₄ Se ₂	C ₂₂ H ₂₆ N ₄ Se ₂	C ₁₆ H ₁₆ Cl ₂ HgN ₄ Se ₂
formula weight	211.12	253.20	420.23	504.39	693.74
space group	<i>P2₁/n</i>	<i>Pnma</i>	<i>P2₁/n</i>	<i>P2₁/c</i>	<i>P</i> $\bar{1}$
<i>a</i> /Å	9.9643(11)	11.635(2)	15.424(3)	9.590(3)	8.9259(15)
<i>b</i> /Å	5.8402(7)	6.9298(13)	6.5867(14)	8.494(2)	8.9631(15)
<i>c</i> /Å	13.7263(16)	12.812(2)	15.432(3)	13.385(4)	14.491(2)
α /°	90	90	90	90	73.484(2)
β /°	95.063(2)	90	108.974(3)	103.296(4)	88.559(2)
γ /°	90	90	90	90	62.319(2)
<i>V</i> /Å ³	795.66(16)	1033.0(3)	1482.6(5)	1061.2(5)	976.5(3)
<i>Z</i>	4	4	4	2	2
temperature (K)	150(2)	150(2)	150(2)	150(2)	150(2)
radiation (λ , Å)	0.71073	0.71073	0.71073	0.71073	0.71073
ρ (calcd.) g cm ⁻³	1.762	1.628	1.883	1.579	2.360
μ (Mo K α), mm ⁻¹	4.648	3.595	4.989	3.500	11.890
θ max, deg.	30.69	30.68	30.03	30.46	30.51
no. of data collected	12410	16065	17436	16434	15802
no. of data	2463	1707	4351	3220	5938
no. of parameters	105	93	202	130	237
<i>R</i> ₁ [<i>I</i> > 2 σ (<i>I</i>)]	0.0309	0.0289	0.0524	0.0339	0.0223
<i>wR</i> ₂ [<i>I</i> > 2 σ (<i>I</i>)]	0.0630	0.0630	0.0944	0.0832	0.0429
<i>R</i> ₁ [all data]	0.0507	0.0443	0.0962	0.0552	0.0290
<i>wR</i> ₂ [all data]	0.0694	0.0682	0.1100	0.0901	0.0449
GOF	1.040	1.111	1.014	1.159	1.002