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Electrophilic Cyclization of *N*-Alkynyl-2-(organochalcogen)imidazoles: An Alternative Access to Imidazo[2,1-*b*]chalcogenazoles

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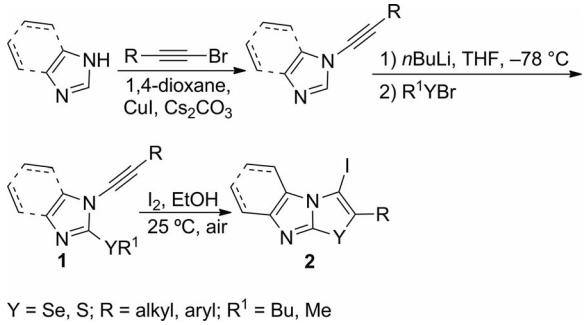
We present here a practical synthesis of multifunctional imidazo[2,1-*b*]chalcogenazoles through electrophilic cyclization of *N*-alkynyl-2-(organochalcogen)imidazoles. The cyclization reaction proceeded cleanly and smoothly under mild reaction conditions in the presence of air. The methodology was highly regioselective: In a competition between the chalcogen and oxygen atoms, only S-, and Se-heterocycles were obtained. The resulting imidazo[2,1-*b*]chalcogenazoles proved to be versatile as precursors for the synthesis of more highly functionalized imidazoselenazoles through copper-catalyzed cross-coupling reactions with arene- and alkanethiols, leading to Ullmann-type products in good yields.

Introduction

Nitrogen-containing heterocycles are known to present a variety of biological and pharmaceutical properties.[1] Among them, imidazole derivatives have attracted much attention, because they are often found in natural and pharmaceutical products and because of their wide-ranging structural variations.[2] In particular, compounds containing a fused imidazo nucleus have been used as antibacterial,[3] antifungal[4] and antitumor[5] agents. They are also important building blocks found in naturally occurring compounds,[6] and are versatile precursors for the synthesis of new fused N-heterocycles. On the basis of these important properties, several methodologies have been described for the preparation of imidazole derivatives.[7] Usually, they are obtained from condensation reactions of halocarbonyl compounds with thioureas or thioamides,[8] amino acids with aldehydes,[9] diazo compounds with amides,[10] or imines with thioamides.[11] The number of imidazoles that could be synthesized by these procedures is limited by the commercial availability of starting materials, low solubility of compounds, difficulty of purification, complex workup, use of toxic metal catalysts, and strongly acidic conditions. Here, we propose an alternative route to prepare imidazochalcogenazoles by electrophilic cyclization of *N*-alkynylimidazole derivatives. In this regard, electrophilic cyclization reactions represent an attractive alternative, because simple substrates can be transformed in more elaborate structures in a stepwise manner.[12] The cyclization reaction of an unsaturated substrate by an electrophilic source is one of the most useful reactions in organic synthesis. Because a halonium intermediate, which is attacked by an internal nucleophilic heteroatom along an *anti* pathway, is involved in these reactions, it becomes a versatile method for the regio- and stereoselective preparation of a wide range of heterocycles, such as indoles, furans, thiophenes, selenophenes, benzo[*b*]furans, benzo[*b*]thiophenes, benzo[*b*]selenophenes and pyrroles.[13] While various substituted heterocycles have thus far been prepared by these methods, the synthesis of imidazochalcogenazoles through the electrophilic cyclization process has not been reported. Therefore, a simple, general, and efficient procedure to prepare functionalized imidazoles, which reduces the dependence on the condensation reactions, is extremely significant. This proposal becomes even more attractive, because this procedure was conducted by using *N*-alkynyl-2-(organochalcogen)imidazole **1** for the preparation of 3-iodoimidazo[2,1-*b*]chalcogenazoles **2**, under mild reaction conditions by employing EtOH as the solvent, at room temperature in the presence of air (Scheme 1).



Scheme 1. General preparation of 3-iodoimidazo[2,1-*b*]chalcogenazoles (**2**).

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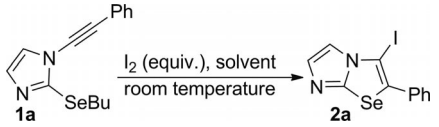
Results and Discussion

For the preparation of the *N*-alkynyl-2-(organochalcogen)imidazole precursor **1**, we chose the known reaction of imidazole with bromoalkyne in 1,4-dioxane, using CuI as the catalyst and Cs_2CO_3 as the base.[14] For the introduction of an organochalcogen group, we first generated the lithium imidazole intermediate by treating *N*-alkynylimidazole with 1 equiv. of *n*BuLi, in THF at –78 °C for 30 min, followed by reaction with an electrophilic chalcogen species (Scheme 1. All details of the preparation of *N*-alkynyl-2-(organochalcogen)imidazoles are found in the Supporting Information. We first examined the cyclization reaction of *N*-alkynyl-2-(butylselenyl)imidazole **1a** in the presence of I_2 (1.1 equiv.) using CH_2Cl_2 as solvent, under argon at room temperature. The desired 3-iodo-2-phenylimidazo[2,1-*b*]-selenazole **2a** was obtained in 81% yield (Table 1, Entry 1). This result was considered satisfactory; however, in order to better understand the reaction behavior with respect to the solvent, temperature, amount of iodine, and atmosphere, we decided to carry out a full reaction parameter screen as summarized in Table 1. The choice of the iodine quantities had a crucial effect on the yield, and 1.1 equiv. was chosen as the best of those used. It should be noted that the increase of iodine quantities to 1.5 and 2.0 equiv. corresponded to a decrease in the yields (Table 1, Entries 2 and 3). This could be explained by a competitive selenium halogenation reaction, a typical reaction for organoselenium compounds with the halogen excess that yields the selenium(IV) species and consumes the substrate in the reaction mixture.[15] With I_2 (1.1 equiv.) as the electrophile source, we screened other solvents as demonstrated in Table 1. No trace of the cyclized product was obtained in the presence of THF or dioxane, while moderate yields were observed when reactions were carried out in acetonitrile or acetone (Table 1, Entries 4–7). Notably, benzene and ethanol were found to be as effective as CH_2Cl_2, affording the product in 81% yield (Table 1, Entries 8 and 9). Due to environmental and health concerns associated with benzene and CH_2Cl_2, we selected ethanol as the best solvent. To make our methodology more attractive from an economic standpoint, we tested the cyclization reaction in the absence of an inert gas by running the reaction in contact with atmosphere using an open tube. By using this reaction system, the selenazole derivative **2a** was obtained in 91% yield (Table 1, Entry 10). Finally, it was found that if the reaction temperature is elevated to 78 °C the reaction yield decreased (Table 1, Entry 11). On the basis of the above investigation, the optimal conditions for this intramolecular cyclization reaction were: *N*-alkynyl-2-(butylselenyl)imidazole **1a** (0.25 mmol), I_2 (1.1 equiv.) as the electrophile source, EtOH (5 mL) as solvent, at room temperature under air.

As summarized in Table 2, the electrophilic cyclization of various *N*-alkynyl-2-(organochalcogen)imidazoles **1** was carried out smoothly to afford the corresponding 3-iodoimidazo[2,1-*b*]chalcogenazoles **2** in moderate to good yields under the optimum reaction conditions. The analysis of these experiments showed that the cyclization process was not significantly influenced by the electronic effects of the substituents on the aromatic rings. Neutral, electron-donating and electron-withdrawing groups bonded to the C_{sp} atom led to the desired 3-iodoimidazo[2,1-*b*]selenazoles **2a**–**h** in good to excellent yields (Table 2, Entries 1–8). On the other hand, the presence of a naphthalene group directly bonded to the triple bond in compound **1i** led to a decrease in the cyclization efficiency, furnishing the corresponding cyclized product **2i** in 54% yield (Table 2, Entry 9). The effect of changing aryl to alkyl substituents directly bonded to the triple bond of the *N*-alkynylimidazole was also investigated (Table 2, Entry 10). We were concerned that the absence of pi (π) bonds next to the triple bond could result in decreased reactivity for the selenium nucleophilic attack. However, this synthetic method was efficient in promoting the cyclization of the substrate **1j**, affording the expected 3-iodo-2-pentylimidazo[2,1-*b*]selenazole **2j** in 78% yield (Table 2, Entry 10). Like nucleophilic selenium groups, thiols showed good reactivity in the present cyclization reaction, and 3-iodo-2-phenylimidazo[2,1-*b*]thiazole **2l** and 3-iodo-2-(2-methoxyphenyl)imidazo[2,1-*b*]thiazole **2m** were efficiently obtained in 85 and 87% yields, respectively (Table 2, Entries 12 and 13). We observed that as well as iodine, PhSeBr was efficient as a cyclizing agent. We found that reaction with PhSeBr, an electrophilic selenium species, promoted the cyclization of *N*-alkynyl-2-(organochalcogen)-imidazole **1a**, producing the highly substituted 3-(phenylselenyl)imidazoselenazole **2n** in 68% yield (Table 2, Entry 14). Although it is known that Br_2, NBS, $CuBr_2$ and BuTeBr can act as efficient electrophile donors to the alkyne triple bond, under our conditions no cyclized products were isolated when we used these electrophile sources. It is important to point out that our cyclization approach was highly regioselective regarding a possible nucleophilic competition between the selenium and oxygen atoms, and

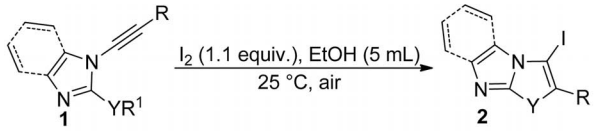
Table 1. Optimization of the cyclization conditions.[a]

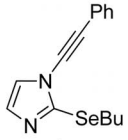
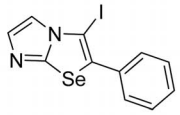
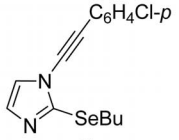
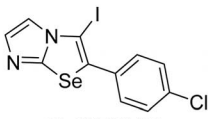
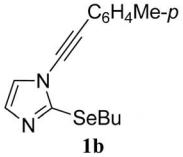
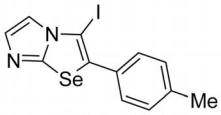
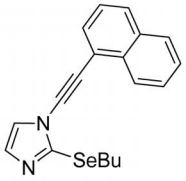
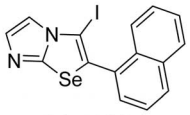
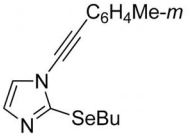
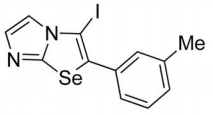
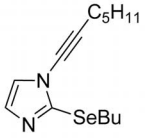
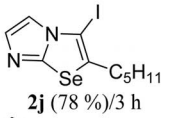
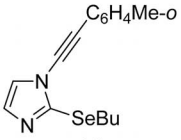
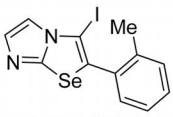
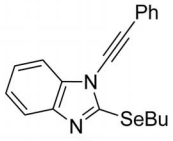
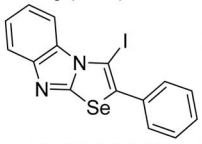
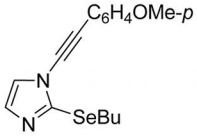
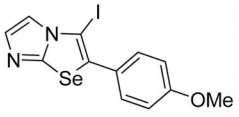
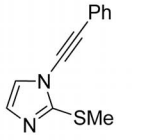
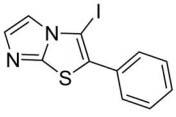
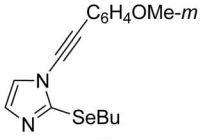
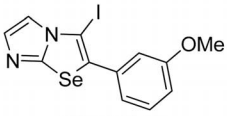
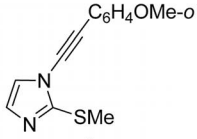
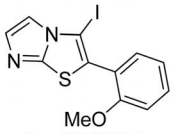
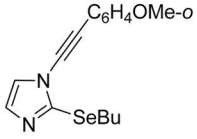
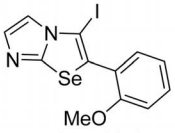
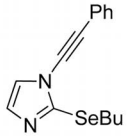
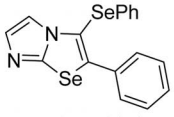


Entry	Electrophile [equiv.]	Solvent	Yield [%][b]
1	I_2 (1.1)	CH_2Cl_2	81
2	I_2 (1.5)	CH_2Cl_2	78
3	I_2 (2.0)	CH_2Cl_2	71
4	I_2 (1.1)	THF	n.r.[c]
5	I_2 (1.1)	dioxane	n.r.[c]
6	I_2 (1.1)	MeCN	59
7	I_2 (1.1)	acetone	64
8	I_2 (1.1)	benzene	81
9	I_2 (1.1)	EtOH	81
10	**I_2 (1.1)**	**EtOH**	**91**[d]
11	I_2 (1.1)	EtOH	77[e]

[a] The reaction was performed in the presence of **1a** (0.25 mmol), solvent (5 mL) under argon at room temperature for 3 h. [b] Yields were measured by GC analysis. [c] **1a** was recovered quantitatively. [d] The reaction was performed in the presence of air (open tube). [e] The reaction was carried out at 78 °C.

Table 2. Scope and generality of the electrophilic cyclization of *N*-alkynyl-2-(organochalcogen)imidazoles **1**.[a]

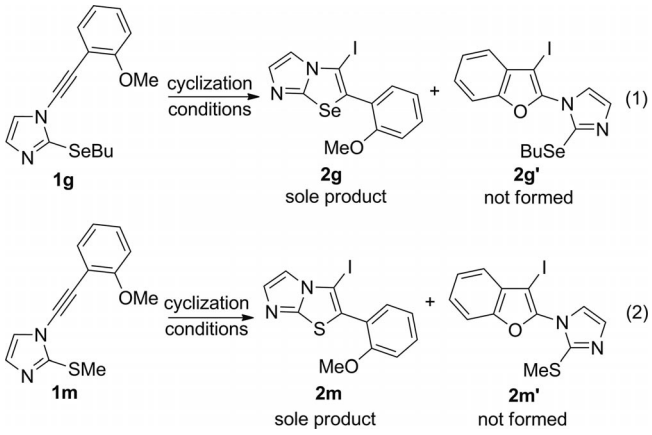


Entry	Substrate	Product (yield)[b]/time	Entry	Substrate	Product (yield)[b]/time
1	 **1a**	 **2a** (86 %)/3 h	8	 **1h**	 **2h** (83 %)/3 h
2	 **1b**	 **2b** (78 %)/3 h	9	 **1i**	 **2i** (54 %)/1 h
3	 **1c**	 **2c** (62 %)/3 h	10	 **1j**	 **2j** (78 %)/3 h
4	 **1d**	 **2d** (71 %)/1 h	11	 **1k**	 **2k** (39 %)/12 h
5	 **1e**	 **2e** (81 %)/3 h	12	 **1l**	 **2l** (85 %)/3 h
6	 **1f**	 **2f** (80 %)/3 h	13	 **1m**	 **2m** (87 %)/3 h
7	 **1g**	 **2g** (69 %)/1 h	14[c]	 **1a**	 **2n** (68 %)/3 h

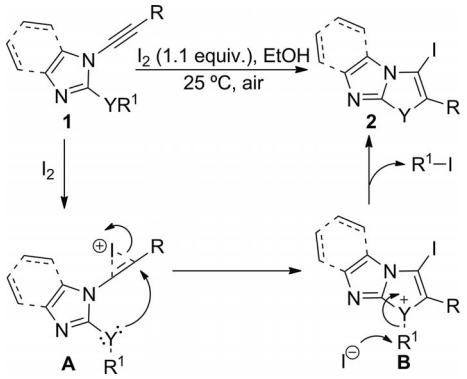
[a] The reaction was carried out in the presence of **1** (0.25 mmol), I_2 (1.1 equiv.), EtOH (5 mL) as solvent, at room temperature in the presence of air (open tube). [b] Isolated yield after column chromatography. [c] PhSeBr was used as electrophile source.

between sulfur and oxygen atoms. The electrophilic cyclization reaction of **1g** and **1m**, which have methoxy groups, could lead to the formation of undesired benzofuran derivatives [Scheme 2, Equations (1) and (2)]. Gratifyingly, in these two cases, our method afforded the desired imidazochalcogenazole heterocycles **2g** and **2m** as single regioisomers. These results suggest that the higher nucleophilicity of the selenium and sulfur atoms compared with the oxygen atom strongly affects the cyclization mode.[16]

We believe that this cyclization reaction follows a typical electrophilic cyclization pathway.[17] Thus, a plausible mechanism for this process is shown in Scheme 3. The coordination of the electrophile source to the carbon–carbon triple bond generates the iodonium intermediate **A**. Subsequent *anti* nucleophilic attack from the lone pair of the chalcogen atom to the activated carbon–carbon triple bond leads to the cationic species **B**, which affords the cyclized product **2** after facile removal of the alkyl group bonded to



Scheme 2. Regioselectivity of the cyclization reaction.



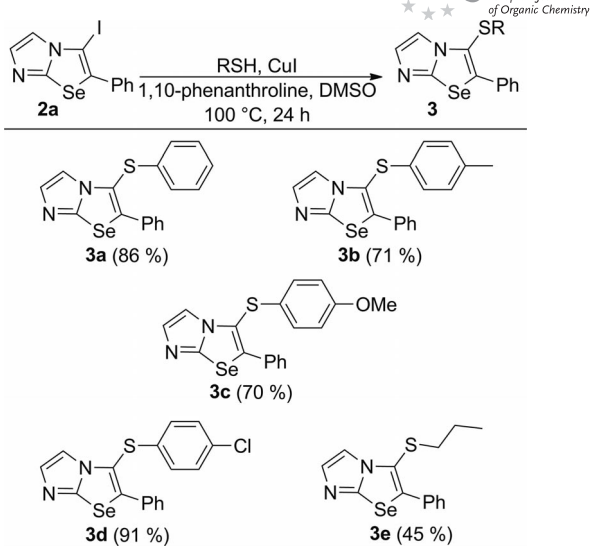
Scheme 3. Plausible electrophilic cyclization mechanism.

the chalcogen atom by S_N2 displacement by the iodide present in the reaction mixture (Scheme 3).

In the context of copper-catalyzed cross coupling reactions, the Ullmann-type reaction is widely known as a classical method for carbon–heteroatom bond formation.[18] Although a great variety of haloheteroaryl compounds have been used as substrates in this reaction, up to now it has not been applied to the 3-iodoimidazoselenazoles. In order to expand the scope of Ullmann cross-coupling and to demonstrate the applicability of 3-iodoimidazo[2,1-*b*]chalcogenazoles, we briefly investigated the reaction of **2a** with arene- and alkanethiols in a copper-catalyzed cross-coupling reaction (Scheme 4). The reaction of 3-iodo-2-phenylimidazoselenazole **2a** (0.25 mmol) with an appropriate thiol (0.75 mmol) in the presence of CuI (0.025 mmol) and 1,10-phenanthroline (0.05 mmol) in DMSO (0.5 mL) gave the 3-(organosulfenyl)imidazoselenazole derivatives in good yields (Scheme 4).

Conclusions

We have described an electrophilic cyclization reaction that provides an efficient tool for the selective synthesis of 3-iodoimidazoselenazoles from *N*-alkynyl-2-(organochalcogen)imidazoles. The main advantages of this methodology are the easy assembly of the starting materials from



Scheme 4. Copper-catalyzed cross-coupling reactions of **2a** with different thiols.

readily available precursors, the incorporation of two different useful functionalities in the structure, and that the reactions were carried out under ambient conditions. Another feature of this protocol is the high regioselectivity with respect to a possible nucleophilic competition between the selenium or sulfur and the oxygen atoms. In our case, only chalcogen heterocycles were obtained. Additionally, the resulting 3-iodoimidazochalcogenazoles proved to be quite versatile as synthetic intermediates for the preparation of more highly functionalized heterocycle units. In this way, the copper-catalyzed Ullmann coupling reactions of the imidazochalcogenazole **2a** with different arene- and alkanethiols furnished the corresponding 3-(organosulfenyl)imidazochalcogenazoles **3** in moderate to excellent yields.

Experimental Section

General Remarks: ^{1}H NMR spectra were obtained at 200 MHz with a DPX-200 NMR spectrometer or at 400 MHz with a DPX-400 NMR spectrometer. Spectra were recorded in $CDCl_3$ solutions. ^{13}C NMR spectra were obtained either at 50 MHz with a DPX-200 NMR spectrometer or at 100 MHz with a DPX-400 NMR spectrometer. Spectra were recorded in $CDCl_3$ solutions. Column chromatography was performed by using Merck Silica Gel (230–400 mesh). Thin layer chromatography (TLC) was performed by using Merck Silica Gel GF254 (0.25 mm thickness). For visualization, TLC plates were either placed under UV light, or stained with iodine vapour or acidic vanillin. Most reactions were monitored by TLC for disappearance of starting material. Mass spectra were recorded with a Shimadzu GC–MS-2010P. Elemental analyses were performed with a Vario EL III elemental analysis instrument. HRMS data were recorded with a Shimadzu LC-MS-IT-TOF spectrometer.

General Procedure for the Preparation of *N*-Alkynyl-2-(organochalcogen)imidazoles 1: To a solution of the appropriate *N*-alkynylimidazole (1 mmol) in THF (10 mL) under argon at –78 °C was added *n*BuLi (2.5 M in hexane, 0.48 mL, 1.2 mmol). The reaction mixture was stirred at this temperature for 30 min. At the same time, in

another reaction vessel, to a solution of $(BuSe)_2$ (0.6 mmol) in THF (5 mL) under argon at 0 °C was added bromine (0.7 mmol) in benzene (3 mL). The reaction mixture was stirred at this temperature for 30 min. After this time, with the assistance of a syringe, this content was added to the first one. The reaction mixture was warmed to room temperature, quenched with a saturated NH_4Cl solution (5 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were dried with $MgSO_4$, concentrated, and subjected to flash chromatography (0–25% EtOAc/hexane).

2-(Butylselenyl)-1-(phenylethynyl)-1*H*-imidazole (1a): Obtained as a yellow oil, yield 0.167 g (55%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.55–4.50 (m, 2 H, =C*H*), 7.40–7.34 (m, 3 H, =C*H*), 7.25 (d, J = 1.6 Hz, 1 H, NC*H*), 7.07 (d, J = 1.5 Hz, 1 H, NC*H*), 3.23 (t, J = 7.4 Hz, 2 H, CH_2), 1.80 (quint, J = 7.8 Hz, 2 H, CH_2), 1.46 (sext, J = 7.5 Hz, 2 H, CH_2), 0.92 (t, J = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 140.7, 131.6, 130.2, 128.8, 128.4, 123.4, 121.2, 102.3, 74.0, 32.2, 28.1, 22.8, 13.5 ppm. MS (EI, 70 eV): *m*/*z* (%) = 303 (11) [M + H]$^+$, 303 (1), 247 (38), 167 (100), 141 (35), 123 (65), 96 (70).

General Procedure for the Preparation of Imidazo[2,1-*b*]chalcogenazoles 2: To a solution of the appropriate *N*-alkynyl-2-chalcogeneimidazole (0.25 mmol) in ethanol (2 mL) was added iodine (0.275 mmol) in ethanol (3 mL). The reaction mixture was stirred at room temperature for 30 min. The reaction mixture was quenched with a saturated $Na_2S_2O_3$ solution (5 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were concentrated and subjected to flash chromatography (0–50% EtOAc/hexane).

3-Iodo-2-phenylimidazo[2,1-*b*][1,3]selenazole (2a): Obtained as a pallid yellow solid, yield 0.080 g (86%); m.p. 197.5–200.5 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.60 (d, J = 1.2 Hz, 1 H, N-C*H*), 7.55 (dd, J = 7.9 Hz, J = 2.0 Hz, 2 H, =C*H*), 7.48-7.41 (m, 3 H, =C*H*), 7.30 (d, J = 1.2 Hz, 1 H, N-C*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.8, 133.6, 132.1, 130.7, 129.7, 129.3, 128.9, 116.9, 65.9. MS (EI, 70 eV): *m*/*z* (%) = 374 [M + 1, (32)], 294 (20), 248 (6), 207 (33), 169 (86), 167 (100), 89 (55), 73 (29), 63 (19). $C_{11}H_7IN_2Se$: calcd. C 35.42, H 1.89, N 7.51; found C 35.59, H 1.94, N 7.57.

3-Iodo-2-(*p*-tolyl)imidazo[2,1-*b*][1,3]selenazole (2b): Obtained as a pale yellow solid, yield 0.075 g (78%); m.p. 195.0–196.8 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.59 (s, 1 H, NC*H*), 7.43 (d, J = 7.9 Hz, 2 H, =C*H*), 7.30–7.25 (m, 3 H, =C*H*, NC*H*), 2.41 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.8, 139.5, 132.0, 130.9, 130.7, 129.6, 129.5, 116.9, 21.3 ppm. MS (EI, 70 eV): *m*/*z* (%) = 388 (81) [M + H]$^+$, 387 (6), 308 (38), 207 (28), 183 (75), 181 (100), 102 (35), 91 (29), 77 (24). HRMS: calcd. for $C_{12}H_9IN_2Se$ [M + H]$^+$ 388.9048; found 388.9010.

3-Iodo-2-(*m*-tolyl)imidazo[2,1-*b*][1,3]selenazole (2c): Obtained as a yellow solid, yield 0.060 g (62%); m.p. 166.3–168.9 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.60 (d, J = 1.1 Hz, 1 H, NC*H*), 7.36–7.26 (m, 5 H, =C*H*, NC*H*), 2.43 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.8, 138.7, 133.4, 181.9, 130.9, 130.2, 130.0, 128.7, 126.7, 116.9, 65.7, 21.3 ppm. MS (EI, 70 eV): *m*/*z* (%) = 388 (7) [M + H]$^+$, 207 (58), 183 (38), 181 (47), 127 (7), 102 (26), 91 (14), 77 (17), 73 (100). HRMS: calcd. for $C_{12}H_9IN_2Se$ [M + Na]$^+$ 410.8868; found 410.8894.

3-Iodo-2-(*o*-tolyl)imidazo[2,1-*b*][1,3]selenazole (2d): Obtained as a yellow solid, yield 0.069 g (71%); m.p. 156.7–158.8 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.56 (d, J = 1.2 Hz, 1 H, NC*H*), 7.38–7.24 (m, 5 H, =C*H*, NC*H*), 2.30 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 144.6, 137.8, 132.9, 132.0, 131.0, 130.5, 130.4, 129.9, 126.1, 116.7, 68.6, 20.2 ppm. MS (EI, 70 eV): *m*/*z* (%) = 388 (23) [M + 1], 207 (67), 181 (45), 154 (17), 127 (28), 115 (40), 102 (34), 73 (100). $C_{12}H_9IN_2Se$ (387.08): calcd. C 37.24, H 2.34, N 7.24; found C 37.39, H 2.39, N 7.31.

3-Iodo-2-(4-methoxyphenyl)imidazo[2,1-*b*][1,3]selenazole (2e): Obtained as a pale yellow solid, yield 0.082 g (81%); m.p. 185.5 °C. ^{1}H NMR ([D$_6$]DMSO, 400 MHz): δ = 7.78 (d, J = 1.2 Hz, 1 H, NC*H*), 7.52 (d, J = 8.8 Hz, 2 H, =C*H*), 7.27 (d, J = 1.4 Hz, 1 H, NC*H*), 7.07 (d, J = 8.8 Hz, 2 H, =C*H*), 3.84 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 160.4, 131.9, 131.0, 130.8, 125.8, 116.9, 114.3, 100.0, 65.5, 55.4 ppm. MS (EI, 70 eV): *m*/*z* (%) = 404 (29) [M + H]$^+$, 341 (11), 281 (37), 253 (25), 207 (100), 191 (21), 147 (19), 133 (23), 73 (95). HRMS: calcd. for $C_{12}H_9IN_2OSe$ 403.8925; found 403.8937.

3-Iodo-2-(3-methoxyphenyl)imidazo[2,1-*b*][1,3]selenazole (2f): Obtained as a pale yellow solid, yield 0.081 g (80%); m.p. 162.4–165.2 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.60 (s, 1 H, NC*H*), 7.37 (t, J = 7.9 Hz, 1 H, =C*H*), 7.30 (s, 1 H, NC*H*), 7.13–7.09 (m, 2 H, =C*H*), 6.97 (dd, J = 8.5, 1.7 Hz, 1 H, =C*H*), 3.86 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.7, 134.7, 132.1, 130.6, 130.0, 122.0, 116.9, 115.2, 114.9, 65.9, 55.4 ppm. MS (EI, 70 eV): *m*/*z* (%) = 404 (44) [M + H]$^+$, 403 (2), 324 (16), 281 (40), 253 (25), 207 (100), 191 (20), 156 (29), 147 (19), 133 (23), 73 (92). HRMS: calcd. for $C_{12}H_9IN_2OSe$ 403.8925; found 403.8938.

3-Iodo-2-(2-methoxyphenyl)imidazo[2,1-*b*][1,3]selenazole (2g): Obtained as a pale yellow solid, yield 0.070 g (69%); m.p. 160.5–161.6 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.58 (d, J = 1.5 Hz, 1 H, NC*H*), 7.48–7.39 (m, 2 H, =C*H*), 7.29 (d, J = 1.3 Hz, 1 H, NC*H*), 7.08–6.97 (m, 2 H, =C*H*), 3.86 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.1, 132.2, 132.0, 131.2, 127.4, 122.5, 120.7, 116.7, 111.6, 100.0, 62.8, 55.6 ppm. MS (EI, 70 eV): *m*/*z* (%) = 404 (25) [M + H]$^+$, 281 (24), 253 (22), 207 (69), 197 (22), 135 (23), 118 (37), 91 (55), 73 (100). HRMS: calcd. for $C_{12}H_9IN_2OSe$ 403.8925; found 403.8945.

2-(4-Chlorophenyl)-3-iodoimidazo[2,1-*b*][1,3]selenazole (2h): Obtained as a pale yellow solid, yield 0.085 g (83%); m.p. 172.2 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.60 (d, J = 1.0 Hz, 1 H, NC*H*), 7.46 (d, J = 2.9 Hz, 4 H, =C*H*), 7.31 (s, 3 H, NC*H*) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 143.6, 135.4, 132.1, 132.0, 130.9, 129.3, 129.2, 117.0 ppm. MS (EI, 70 eV): *m*/*z* (%) = 408 (19), 281 (40), 253 (24), 207 (100), 191 (20), 147 (19), 133 (22), 123 (20), 96 (17), 73 (98). $C_{11}H_6ClIN_2Se$ (407.50): calcd. C 32.42, H 1.48, N 6.87; found C 32.59, H 1.53, N 6.94.

3-Iodo-2-(naphthalen-1-yl)imidazo[2,1-*b*][1,3]selenazole (2i): Obtained as a pale yellow solid, yield 0.057 g (54%); m.p. 205.5–208.0 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.99–7.89 (m, 3 H, =C*H*), 7.64 (d, J = 1.5 Hz, 1 H, NC*H*), 7.59–7.51 (m, 4 H, =C*H*), 7.36 (d, J = 1.5 Hz, 1 H, NC*H*) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 144.8, 133.7, 132.2, 131.6, 130.8, 130.3, 129.6, 128.9, 128.5, 127.0, 126.6, 125.5, 125.2, 116.8, 69.7 ppm. MS (EI, 70 eV): *m*/*z* (%) = 424 (17) [M + H]$^+$, 423 (1), 297 (33), 281 (40), 217 (40), 207 (100), 191 (51), 139 (62), 73 (82). $C_{15}H_9IN_2Se$ (423.11): calcd. C 42.58, H 2.14, N 6.62; found C 42.63, H 2.19, N 6.69.

3-Iodo-2-pentylimidazo[2,1-*b*][1,3]selenazole (2j): Obtained as a pale yellow solid, yield 0.081 g (78%); m.p. 77.0–77.3 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.47 (d, J = 1.2 Hz, 1 H, NC*H*), 7.22 (d, J = 1.2 Hz, 1 H, NC*H*), 2.78 (t, J = 7.6 Hz, 2 H, CH_2), 1.67 (quint, J = 7.3 Hz, 2 H, CH_2), 1.44–1.35 (m, 4 H, CH_2), 0.92 (t, J = 7.1 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.0, 133.4, 131.8, 116.3, 65.9, 33.3, 31.0, 30.4, 22.3, 13.8 ppm. MS (EI, 70 eV): *m*/*z* (%) = 368 (56) [M + H]$^+$, 367 (1), 311 (100), 207 (57), 184 (59),

104 (21), 95 (90), 73 (54), 52 (70). $C_{10}H_{13}IN_2Se$ (367.09): calcd. C 32.72, H 3.57, N 7.63; found C 32.90, H 3.61, N 7.70.

3-Iodo-2-phenylbenzo[*d*][1,3]selenazolo[3,2-*a*]imidazole (2k): Obtained as a pale yellow solid, yield 0.041 g (39%); m.p. 203.7–205.8 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.60 (d, J = 8.3 Hz, 1 H, =C*H*), 7.78 (d, J = 8.1 Hz, 1 H, =C*H*), 7.54 (d, J = 6.4 Hz, 2 H, =C*H*), 7.46 (q, J = 5.9 Hz, 3 H, =C*H*), 7.37 (t, J = 7.6 Hz, 1 H, =C*H*), 7.27 (t, J = 8.1 Hz, 1 H, =C*H*) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.6, 147.6, 134.2, 132.9, 130.2, 129.3, 128.9, 127.4, 123.6, 120.7, 119.1, 112.3, 65.3 ppm. MS (EI, 70 eV): *m*/*z* (%) = 424 (25) $[M + H]^+$, 344 (9), 217 (32), 207 (27), 169 (100), 167 (48), 89 (63), 73 (27), 63 (16). $C_{15}H_9IN_2Se$ (423.11): calcd. C 42.58, H 2.14, N 6.62; found C 42.70, H 2.20, N 6.66.

3-Iodo-2-phenylimidazo[2,1-*b*]thiazole (2l): Obtained as a yellow solid, yield 0.069 g (85%); m.p. 195.0–197.9 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.60 (dd, J = 7.3, 1.8 Hz, 2 H, =C*H*), 7.49–7.42 (m, 4 H, =C*H*, N-C*H*), 7.35 (s, 1 H, N-C*H*) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 146.9, 133.0, 131.7, 130.7, 129.5, 128.9, 114.1, 64.6 ppm. MS (EI, 70 eV): *m*/*z* (%) = 326 (39), 199 (10), 172 (10), 121 (100), 89 (16), 77 (19). $C_{11}H_7IN_2S$ (326.15): calcd. C 40.51, H 2.16, N 8.59; found C 40.70, H 2.20, N 8.63.

3-Iodo-2-(2-methoxyphenyl)imidazo[2,1-*b*]thiazole (2m): Obtained as a pale yellow solid, yield 0.077 g (87%); m.p. 160.5–161.6 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.45–7.37 (m, 3 H, =C*H*, NC*H*), 7.33 (d, J = 1.2 Hz, 1 H, NC*H*), 7.05–6.98 (m, 2 H, =C*H*), 3.84 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.2, 147.7, 132.7, 132.4, 131.3, 127.6, 120.6, 120.1, 113.8, 111.4, 67.9, 55.5 ppm. MS (EI, 70 eV): *m*/*z* (%) = 356 (100), 229 (12), 214 (37), 170 (14), 151 (33), 111 (32), 91 (38), 77 (11). HRMS: calcd. for $C_{12}H_9IN_2OS$ $[M + H]^+$ 356.9553; found 356.9521.

2-Phenyl-3-(phenylselenyl)imidazo[2,1-*b*][1,3]selenazole (2n): Obtained as a yellow solid, yield 0.068 g (68%); m.p. 71 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.55–7.52 (m, 2 H, =C*H*), 7.48 (d, J = 1.2 Hz, 1 H, NC*H*), 7.43–7.40 (m, 3 H, =C*H*), 7.22 (s, 5 H, =C*H*), 7.20 (d, J = 1.0 Hz, 1 H, NC*H*) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 138.1, 133.2, 132.5, 129.9, 129.8, 129.7, 129.2, 128.9, 128.6, 127.8, 127.4, 115.5, 111.3 ppm. MS (EI, 70 eV): *m*/*z* (%) = 404 (17) $[M + 2H]^+$, 402 (15), 281 (38), 207 (100), 191 (22), 169 (48), 167 (35), 89 (56), 73 (87), 51 (21). $C_{17}H_{12}N_2Se_2$ (402.22): calcd. C 50.76, H 3.01, N 6.96; found C 50.89, H 3.08, N 7.02.

General Procedure for the Copper-Catalyzed Coupling Reaction of 2a with Different Thiols: A Schlenk flask under argon was charged with 3-iodo-2-phenylimidazo[2,1-*b*][1,3]selenazole (0.25 mmol), CuI (0.025 mmol), 1,10-phenanthroline (0.05 mmol) and the appropriate thiol (0.75 mmol) in DMSO (0.5 mL). The reaction mixture was stirred at room temperature for 10 min, and then was kept at 100 °C for 24 h. The reaction mixture was quenched with a saturated aqueous NH_4Cl solution (5 mL), and the organic phase was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried with $MgSO_4$ and concentrated under vacuum. The residue was purified by flash chromatography (0–50% EtOAc/hexane).

2-Phenyl-3-(phenylsulfenyl)imidazo[2,1-*b*][1,3]selenazole (3a): Obtained as a pale yellow solid, yield 0.077 g (86%); m.p. 145.5–147.2 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.58 (s, 1 H, NC*H*), 7.55 (s, 1 H, N-C*H*), 7.41–7.30 (m, 5 H, =C*H*), 7.26–7.22 (m, 2 H, =C*H*), 7.16–7.10 (m, 3 H, =C*H*) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 148.7, 141.5, 136.0, 134.1, 132.8, 129.3, 129.1, 128.9, 126.4, 126.3, 126.2, 114.4, 113.9 ppm. MS (EI, 70 eV): *m*/*z* (%) = 356 (31) $[M + H]^+$, 355 (6), 276 (100), 134 (21), 121 (22), 102 (74), 89 (18), 77 (21), 73 (25), 63 (7). $C_{17}H_{12}N_2SSe$ (355.32): calcd. C 57.46, H 3.40, N 7.88; found C 57.62, H 3.48, N 7.93.

2-Phenyl-3-(*p*-tolylsulfenyl)imidazo[2,1-*b*][1,3]selenazole (3b): Obtained as a yellow solid, yield 0.066 g (71%); m.p. 77.0–79.1 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.58 (s, 1 H, NC*H*), 7.53 (s, 1 H, NC*H*), 7.42–7.31 (m, 5 H, =C*H*), 7.07–7.02 (m, 4 H, =C*H*), 2.27 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 148.5, 141.2, 136.4, 134.0, 132.9, 132.2, 130.0, 129.1, 128.9, 126.9, 126.4, 115.1, 113.9, 20.9 ppm. MS (EI, 70 eV): *m*/*z* (%) = 370 (13) $[M + H]^+$, 369 (1), 290 (60), 253 (25), 207 (100), 147 (26), 135 (36), 102 (43), 77 (13), 73 (78). $C_{18}H_{14}N_2SSe$ (369.34): calcd. C 58.53, H 3.82, N 7.58; found C 58.71, H 3.91, N 7.63.

3-(4-Methoxyphenylsulfenyl)-2-phenylimidazo[2,1-*b*][1,3]selenazole (3c): Obtained as a yellow oil, yield 0.068 g (70%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.61 (s, 1 H, NC*H*), 7.51 (s, 1 H, NC*H*), 7.43–7.32 (m, 5 H, =C*H*), 7.16 (d, J = 9.1 Hz, 2 H, =C*H*), 6.81 (d, J = 8.8 Hz, 2 H, =C*H*), 3.75 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 158.9, 140.6, 133.0, 129.4, 129.2, 128.9, 126.5, 126.0, 115.0, 113.9, 55.4 ppm. MS (EI, 70 eV): *m*/*z* (%) = 386 (22) $[M + 2H]^+$, 384 (9), 306 (77), 281 (39), 253 (25), 207 (100), 151 (26), 133 (25), 102 (59), 77 (21), 73 (82). HRMS: calcd. for $C_{18}H_{14}N_2OSSe$ 385.9992; found 386.0017.

3-(4-Chlorophenylsulfenyl)-2-phenylimidazo[2,1-*b*][1,3]selenazole (3d): Obtained as a pale yellow solid, yield 0.089 g (91%); m.p. 118.4–118.8 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.56 (s, 2 H, NC*H*), 7.42–7.33 (m, 5 H, =C*H*), 7.22 (d, J = 8.5 Hz, 2 H, =C*H*), 7.03 (d, J = 8.8 Hz, 2 H, =C*H*) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 141.7, 134.5, 132.7, 132.3, 129.4, 129.2, 129.0, 127.6, 126.5, 113.6 ppm. MS (EI, 70 eV): *m*/*z* (%) = 390 (23) $[M + H]^+$, 389 (4), 310 (84), 281 (39), 253 (25), 207 (100), 133 (31), 102 (94), 89 (32), 77 (13), 73 (82). $C_{17}H_{11}ClN_2SSe$ (389.76): calcd. C 52.39, H 2.84, N 7.19; found C 52.62, H 2.91, N 7.24.

2-Phenyl-3-(propylsulfenyl)imidazo[2,1-*b*][1,3]selenazole (3e): Obtained as a yellow oil, yield 0.036 g (45%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.77 (s, 1 H, NC*H*), 7.49–7.33 (m, 6 H, =C*H*, NC*H*), 2.63 (t, J = 7.3 Hz, 2 H, CH_2), 1.59 (sext, J = 7.3 Hz, 2 H, CH_2), 1.00 (t, J = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.3, 140.1, 133.5, 133.1, 129.2, 128.8, 126.4, 117.6, 114.0, 39.0, 23.0, 12.9 ppm. MS (EI, 70 eV): *m*/*z* (%) = 322 (13) $[M + H]^+$, 281 (42), 275 (3), 253 (22), 207 (100), 135 (17), 133 (22), 102 (61), 77 (5), 73 (76). HRMS: calcd. for $C_{14}H_{14}N_2SSe$ 322.0043; found 322.0065.

Supporting Information (see footnote on the first page of this article): Experimental methods and characterization data, including ^{1}H and ^{13}C NMR spectra.

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