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Synthesis of 2-Substituted 1,3-Benzoselenazoles from Carboxylic Acids Promoted by Tributylphosphine

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We report a general, practical, and simple metal-free method for the synthesis of 2-substituted 1,3-benzoselenazoles by the reaction of bis(2-aminophenyl)diselenide with a wide range of carboxylic acids, promoted by tributylphosphine. This efficient reaction furnishes 2-aryl-1,3-benzoselenazoles in good yields and tolerates a variety of substituents at the aryl moiety of carboxylic acids. For the first time, 2-alkyl-1,3-benzoselenazoles could be obtained from aliphatic carboxylic acids and thiazolidine-4-carboxylic acid in high chemical yields. The use of focused microwave irradiation considerably decreased the reaction time from 48 to 2 h. The experimental data provide insights into the mechanism of the reaction.

Introduction

Research into the use of selenium-containing heterocyclic compounds as potential pharmaceuticals,[1] new materials,[2] and as reagents and catalysts[3] has expanded rapidly in recent years. Recently, selenium-containing compounds have attracted increased attention because of their ability to act as glutathione peroxidase (GPX) mimics, catalytic antioxidants, and cancer-chemopreventive compounds.[4]

Furthermore, substituted benzoheteroazole units, particularly benzoxazoles,[5] benzothiazoles,[6] and benzimidazoles,[7] are privileged heterocyclic systems because of their excellent reactivities, notable chemical properties, and biological activities. Especially, the preparation of 2-substituted 1,3-benzothiazoles has attracted much attention because this is an important class of bicyclic substructure with potent utility as imaging agents for β-amyloid, antitumor agents, calcium channel antagonists, antituberculotics, antiparasitics, chemiluminescent agents, and also as photosensitizers.[8]

However, in the case of selenium analogues, there are few reports on the synthesis of 2-substituted benzoselenazoles and related compounds despite their potential importance.[9,10] In this respect, a copper(I)-catalyzed reaction of 2-halophenyl isocyanides with selenium and heteroatom nucleophiles was disclosed by Kambe and co-workers for the synthesis of 1,3-benzoselenazoles having heteroatom substituent (NRR′, OR and SR) groups at the 2-position,[9c] Sashida and co-workers also focused on the construction of the 1,3-benzoselenazole core;[9d] their approach involved the preparation of benzoselanazoles by a copper-catalyzed one-pot reaction of 2-iodoanilines and isoselenocyanates. Moreover, Kobayashi and co-workers[9e] conducted a study in which 2-thio-organyl-1,3-benzoselenazole derivatives were prepared in moderate yields from 2-halophenyl isothiocyanates in a reaction using *n*BuLi, elemental selenium, and subsequent treatment with several electrophiles. Our group recently reported the direct synthesis of 2-aryl-1,3-benzoselenazoles from the reaction of bis(2-aminophenyl) diselenides with different aryl aldehydes, promoted by the reducing agent sodium metabisulfite ($Na_2S_2O_5$).[9f] This efficient method furnishes the corresponding 2-aryl-substituted 1,3-benzoselenazoles in high yields and tolerates a range of substituents at the aryl ring of the aldehydes. However, the method could not be used to furnish products from alkyl aldehydes. These reactions were conducted under conventional heating as well as under microwave irradiation, because the use of focused microwave irradiation was found to drastically decrease the reaction time.[9f]

In this context, microwave irradiation (MW) is an attractive alternative to conventional heating to supply energy to reactions. In most cases, microwave heating leads to a drastic reduction in reaction times, improves workup procedures, and ultimately increases product yields.[11]

To our knowledge, there are no reports on the synthesis of 2-substituted 1,3-benzoselenazoles from carboxylic acids. Furthermore, until now, 2-alkyl-1,3-benzoselenazoles could

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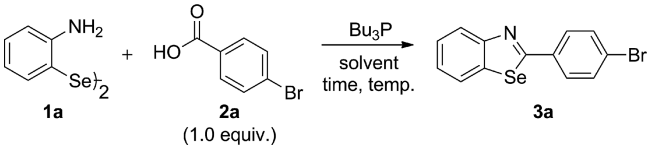
not be achieved by the available synthetic tools. In this context, our interest on the synthesis of organoselenium compounds[9f,12] prompted us to explore a general procedure with which to obtain 2-substituted 1,3-benzoselenazoles from bis(2-aminophenyl) diselenide and carboxylic acids by using tributylphosphine under conventional heating or microwave irradiation.

Results and Discussion

To explore suitable reaction conditions for the synthesis of 2-substituted 1,3-benzoselenazoles from carboxylic acids, a set of experiments were performed by employing bis(2-aminophenyl)diselenide (**1a**),[13] 4-bromobenzoic acid (**2a**), and tributylphosphine as a model system. The reaction was performed under conventional heating (Table 1).

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



1a **2a** (1.0 equiv.) **3a**

Entry	Solvent	**1a** [equiv.]	Bu_3P [equiv.]	Temp. [°C]	Time [h]	Yield [%][b]
1	CH_2Cl_2	1.0	1.0	r.t.	120	10
2	MeCN	1.0	1.0	82	48	32
3	THF	1.0	1.0	66	48	50
4	DMSO	1.0	1.0	120	48	n.d.
5	*o*-xylene	1.0	1.0	140	48	54
6	toluene	1.0	1.0	110	48	63
7	THF	1.0	1.5	66	48	60
8	toluene	1.0	1.5	110	48	68
9	toluene	1.0	3.0	110	48	75
10	toluene	2.0	3.0	110	48	97
11	THF	2.0	3.0	66	48	83
12	toluene	2.0	3.0	110	24	70

[a] Reactions were conducted with **2a** (0.5 mmol, 1 equiv.) under an N_2 atmosphere. [b] Yield of isolated product.

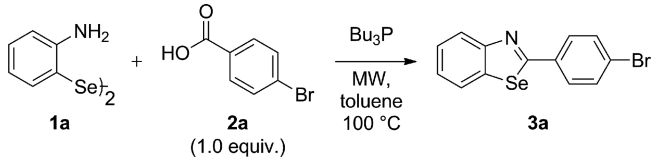
In the first experiment, **1a** (0.5 mmol, 1 equiv.), **2a** (0.5 mmol, 1 equiv.), and tributylphosphine (0.5 mmol, 1 equiv.) were reacted in dichloromethane (5 mL) at room temperature. Unfortunately, under these conditions, even after 120 h, the desired benzoselenazole **3a** was obtained in only 10% yield (Table 1, entry 1). Thus, in an attempt to increase the yield, a series of different solvents including aprotic polar solvents [CH_3CN, tetrahydrofuran (THF) and dimethyl sulfoxide (DMSO)] and non-polar solvents (toluene and *o*-xylene) were evaluated (Table 1, entries 2–6).

Among them, polar aprotic solvents of intermediate polarity gave good results of benzoselenazole **3a**; for example the use of THF as solvent gave a yield of 50% (Table 1, entry 3). When the reaction was performed in polar aprotic solvents of higher polarity, such as acetonitrile and DMSO, the product **3a** was obtained either in lower yields or were not detected, respectively (Table 1, entry 2 and 4). For the reactions using non-polar solvents, the best yield was obtained when toluene was employed (Table 1, entry 6).

Having established THF and toluene to be the best solvents in these first experiments, we next investigated some parameters regarding the stoichiometry of diaryl diselenide **1a** and tributylphosphine. We observed that increasing the amount of tributylphosphine from 1.0 to 1.5 equiv. gave a small increase in yields in both solvents (Table 1, entries 7 and 8). When the reaction was performed using toluene as the solvent and an excess of 3.0 equiv. of tributylphosphine, product **3a** was obtained in 75% yield (Table 1, entry 9). By increasing the amount of diselenide **1a** to 2.0 equiv. and including 3.0 equiv. tributylphosphine, an excellent yield of **3a** was observed in toluene as the solvent (Table 1, entry 10). Finally, we attempted to reduce the reaction time to 24 h, but the yield decreased to 70% (Table 1, entry 12). We observed the same tendency in THF, but with a slight reduction in reaction yield (Table 1, entry 11).

In recent years, it has been shown that the use of focused microwave irradiation (MW) in organic reactions can considerably decrease the reaction time, often accompanied by an increase in product yield.[11,14] Therefore, to reduce the reaction time and the amount of substrate required for the synthesis of benzoselenazole **3a**, we performed experiments using focused microwave irradiation (Table 2).

Table 2. Optimization of the reaction conditions under microwave irradiation.[a]



1a **2a** (1.0 equiv.) **3a**

Entry	**1a** [equiv.]	Bu_3P [equiv.]	Time [h]	Yield [%][b]
1	1.0	3.0	0.5	43
2	1.0	3.0	1.0	54
3	1.0	3.0	1.5	89
4	1.0	3.0	2.0	92
5	0.5	3.0	2.0	67
6	1.0	2.0	2.0	70
7[c]	1.0	3.0	2.0	15
8[d]	1.0	3.0	2.0	n.d.
9[e]	1.0	3.0	2.0	61

[a] Reactions were conducted with **2a** (0.25 mmol, 1 equiv.) under an N_2 atmosphere. [b] Yield of isolated product. [c] Reaction was performed in an air atmosphere. [d] Reaction was performed using DMSO as the solvent at 100 °C. [e] Reaction was performed using THF as the solvent at 50 °C.

Thus, experiments were performed with **1a** (0.25 mmol, 1.0 equiv.), **2a** (0.25 mmol, 1.0 equiv.), and tributylphosphine (0.75 mmol, 3.0 equiv.) in toluene as the solvent. In these processes, **1a** was dissolved in toluene (2 mL), and tributylphosphine was then added and the mixture and stirred at room temperature under an N_2 atmosphere for 5 min.

After this time, a slight decoloration of the solution was observed. At this point, **2a** was added and the reaction was carried out under focused microwave irradiation at 100 °C.

First, the reaction was carried out for 0.5 h under MW irradiation and the desired product **3a** was obtained in 43% yield (Table 2, entry 1). To our satisfaction, when the reactions were performed for 1.0, 1.5 and 2 h, the yields of product **3a** progressively increased (entries 2–4) with an excellent yield of 92% **3a** being obtained under MW irradiation after 2 h (entry 4). This outstanding result gives only 5% difference in yield when compared with reactions under conventional heating (Table 2, entry 4; vs. Table 1, entry 10), while employing a smaller amount of diselenide **1a** (1.0 equiv.) in just 2 h. When the reaction was performed by using 0.5 equiv. **3a**, the yield of product **3a** decreased to 67% (Table 2, entry 5). When the reaction was run with 2.0 equiv. tributylphosphine, the yield of **3a** dropped to 70% (Table 2, entry 6).

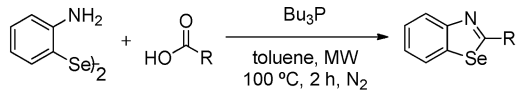
In an additional experiment, all reagents were solubilized in toluene under an air atmosphere. The reaction vial was then tightly sealed and the mixture was irradiated in a microwave reactor for 2 h at 100 °C. By using this procedure, the desired 1,3-benzoselenazole **3a** was obtained in 15% yield, confirming that an N_2 atmosphere is essential for the reaction.

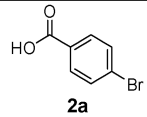
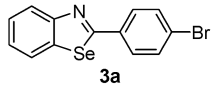
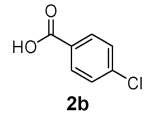
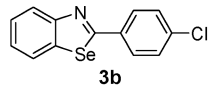
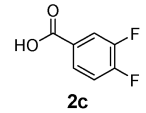
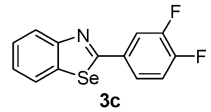
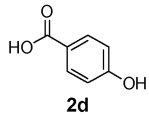
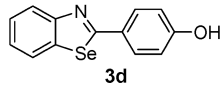
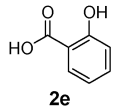
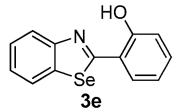
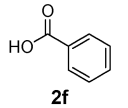
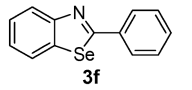
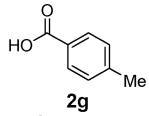
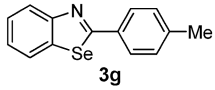
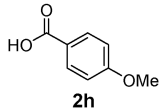
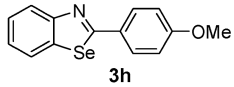
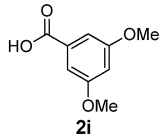
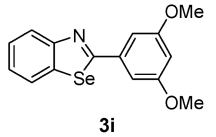
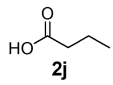
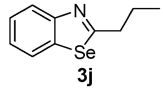
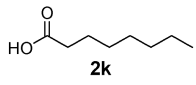
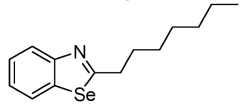
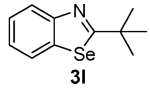
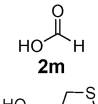
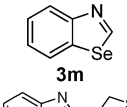
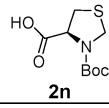
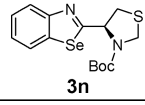
To check the effect of solvent polarity in the reaction under microwave irradiation, the system was carried out with a polar aprotic solvent (DMSO); under these conditions, **3a** was not observed with conventional heating. In this sense, DMSO was again not suitable for the reaction. (Table 2, entry 8). Another study using THF was performed (Table 2, entry 9), but due to the lower boiling point,[15] the reaction was conducted at 50 °C. Even after 2 h reaction, the desired product was obtained in only 61% yield (Table 2, entry 8). These data suggest that the reaction requires solvents of intermediate or low polarity, and also that selenophosphonium salts formed in the reaction environment might result in DMSO deoxygenation.[16]

To explore the scope and limitations of this method, the reactions between **1a** and a variety of carboxylic acids **2a**–**m** were performed, employing the optimal conditions under microwave irradiation; the results are shown in Table 3. Generally, all reactions proceeded smoothly, furnishing the desired products in good yields.

Several aryl carboxylic acids reacted with **1a**, furnishing the corresponding 2-substituted 1,3-benzoselenazoles **3a**–**i** in moderate to excellent yields (Table 3, entries 1–9). As shown in Table 3, electronic effects on the aryl moiety of the carboxylic acid seemed to have an influence on the product yield. For example, carboxylic acids with electron-withdrawing groups at the aromatic ring gave better results than those with electron-donating groups (entries 1–3 vs. 7–9), suggesting that the addition of a nucleophile to the carboxyl group has an important influence on the reaction path. When benzoic acid was used, the desired product 2-phenyl-1,3-benzoselenazole (**3f**) was reached in 75% yield (entry 6). By the use of disubstituted carboxylic acids **2c** and **2i**, the products **3c** and **3i** were obtained in good yields (entries 3

Table 3. Scope of the synthesis of 2-substituted 1,3-benzoselenazoles from carboxylic acids using MW irradiation.



Entry	Carboxylic acid	Product (yield)	Yield (%)[a]
1	 **2a**	 **3a**	92
2	 **2b**	 **3b**	93
3	 **2c**	 **3c**	93
4	 **2d**	 **3d**	70
5	 **2e**	 **3e**	89
6	 **2f**	 **3f**	75
7	 **2g**	 **3g**	69
8	 **2h**	 **3h**	71
9	 **2i**	 **3i**	81
10	 **2j**	 **3j**	90
11	 **2k**	 **3k**	95
12	 **2l**	 **3l**	78
13	 **2m**	 **3m**	63
14	 **2n**	 **3n**	76

[a] Yield of pure isolated product.

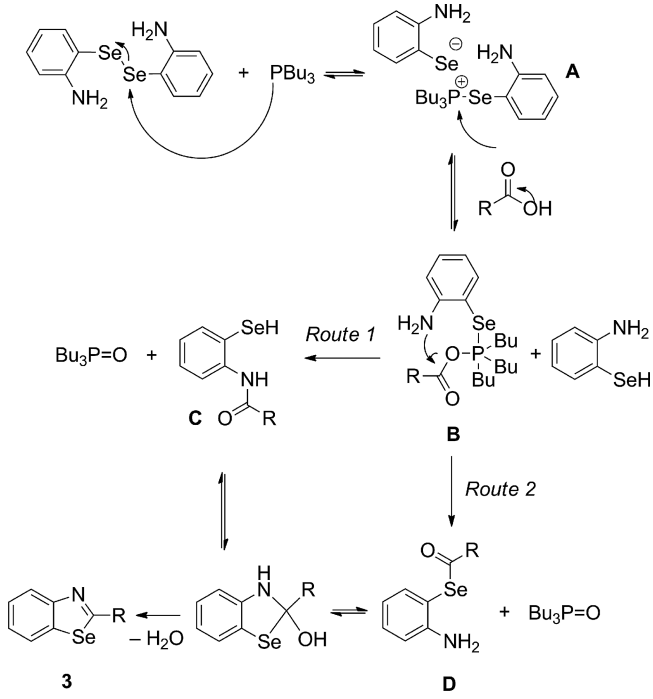
and 9). Additionally, when the reactions were performed by using *para* and *ortho* hydroxybenzoic acid, good yields were obtained in both cases, demonstrating that the sterically demanding *ortho* substituent did not affect the reaction yield (entries 4 and 5). Indeed, substrates with an *ortho* hydroxy group gave a higher yield of the product (**3e**) because the carboxyl group was more reactive due to the inductive effect of oxygen and because of the slightly broken planarity with the aromatic ring, despite the electron-donating behavior.

So far, the synthesis of 2-alkyl-substituted 1,3-benzoselenazoles has not been described.[9] Thus, to expand the synthetic scope of this protocol, we carried out reactions using aliphatic carboxylic acids **2j**–**m**. Interestingly, despite the electron-donating nature of the alkyl group, 2-alkyl-1,3-benzoselenazoles were obtained in moderate to excellent yields (Table 3, entries 10–13). These are important results because the development of a broad, mild, and selective chemical process for the construction of 2-substituted 1,3-benzoselenazoles avoiding radical paths or metal-catalyzed reactions has not been described before.[9,10]

When the reactions were carried out with butyric and caprylic acid, the corresponding 1,3-benzoselenazoles **3j** and **3k** were obtained in 90 and 95% yield, respectively (Table 3, entries 10 and 11). The reaction was also performed with the sterically hindered pivalic acid **2l** and, to our satisfaction, the product was obtained in good yield, demonstrating that sterically demanding substituents have only a small effect on the reaction yield (entry 12). Furthermore, 1,3-benzoselenazole (**3m**) was obtained in 63% yield when the reaction was performed with formic acid **2m** (entry 13).

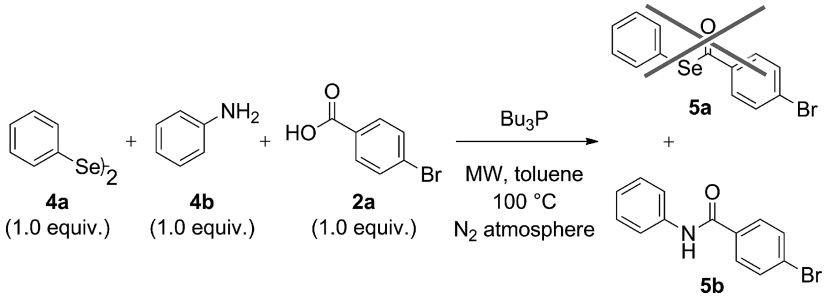
Recently, our research group has described the biological activities of (*R*)-Se-aryl-thiazolidine-4-carboselenoates.[17] Motivated by these results, and to extend the scope of this synthetic protocol, we reacted **1a** with (*S*)-3-(*tert*-butoxycarbonyl)thiazolidine-4-carboxylic acid (**2n**) under the optimized MW conditions. To our delight, the desired 1,3-benzoselenazole **3n** was reached in 76% yield (Table 3, entry 14).

Based on results of disulfide and diselenide bond cleavage by phosphorus nucleophiles,[16b,18] we can propose two reaction pathways (Scheme 1, route **R1** and **R2**). First, the nucleophile Bu_3P attacks the selenium atom in **1a** to produce phosphonium salt **A**. The carboxylic acid could then form the pentacoordinate acyloxyphosphonium intermediate **B** as an activated ester, which, in turn, could generate the 2-substituted 1,3-benzoselenazoles **3** through two routes: (**R1**) direct intramolecular nucleophilic attack of the amine fragment on the carbonyl, producing amide **C** and $Bu_3P{=}O$, followed by intramolecular condensation with a selenolate anion, or (**R2**) intramolecular transfer of a selenium atom to produce selenoester **D** and $Bu_3P{=}O$, with subsequent intramolecular attack of the nitrogen atom through condensation to produce the product **3**.



Scheme 1. Analysis of the reaction mechanisms.

To shed light on this mechanism, an intermolecular competition experiment was performed to determine which path is operative. Under the standard conditions using MW irradiation, diphenyl diselenide **4a** (1.0 equiv.) was added to the reaction flask along with tributylphosphine (3.0 equiv.) and toluene (Scheme 2). The mixture was stirred at room tem-



Scheme 2. Competition experiment.

perature under an N_2 atmosphere for 5 min, then **2a** (1.0 equiv.) and aniline **4b** (1.0 equiv.) were added, and the reaction was carried out under focused microwave irradiation at 100 °C. By following the reaction by using GC–MS analysis, we could not detect selenoester **5a** production at any reaction time point (0.5, 1.0, and 2.0 h), and only amide **5b** was observed. However, under similar conditions for the production of peptides, the first selenoester formation was confirmed in low temperature experiments.[18c] In view of this competition data, and since selenoester production was observed from a intermolecular/intramolecular reaction contest,[18c] we suppose that, in our case, when the reaction occurs by two intramolecular nucleophiles, the attack of the amine group occurs first, with the production of an amide and then intramolecular condensation with a selenolate anion (route **R1**).

Conclusion

We have described an efficient methodology for the synthesis of 2-substituted 1,3-benzoselenazoles in high chemical yields. The reactions of bis(2-aminophenyl)diselenide with a range of carboxylic acids were promoted by tributylphosphine in toluene at 100 °C. Under these reaction conditions, we were able to prepare 2-aryl- and 2-alkyl-1,3-benzoselenazoles from aryl and aliphatic carboxylic acids. Another benefit of the described procedure is that this protocol minimizes energy demands, and the reaction time could be reduced from 48 to only 2 h by using focused MW irradiation.

Experimental Section

General Information: Tributylphosphine was purchased from Aldrich and used without further purifications. Toluene was obtained from Sigma–Aldrich and dried by using standard methods.[19] The reactions were monitored by thin-layer chromatography (TLC) and column chromatography was performed using Merck Silica Gel (230–400 mesh). NMR spectra were obtained with Varian Inova 300 and Bruker 400 spectrometers. Chemical shifts are given in parts per million (δ) and are referenced from tetramethylsilane (TMS) in ^{1}H NMR spectra and from $CDCl_3$ or $(CD_3)_2CO$ in ^{13}C NMR spectra. ATR/FTIR spectra were recorded with a Varian FTIR-640 spectrometer. Low-resolution mass spectra were obtained with a Shimadzu GC–MS-QP5050 mass spectrometer interfaced with a Shimadzu GC-17A gas chromatograph equipped with a DB-17 MS capillary column. Microwave heating was conducted with a CEM Discover, mode operating systems working at 2.45 GHz, with a power programmable from 1 to 300 W.

General Procedure for the Synthesis of 2-Substituted 1,3-Benzoselenazoles under Microwave Irradiation: In a 10 mL glass vial equipped with a small magnetic stirring bar under an inert atmosphere, bis(2-aminophenyl)diselenide **1a** (0.25 mmol) was dissolved in anhydrous toluene (1.5 mL) and *n*-tributylphosphine (0.75 mmol) was added. The mixture was stirred at room temperature for ca. 5 min, then carboxylic acid (0.25 mmol) was added and the mixture was irradiated in a microwave reactor (CEM Explorer) for 2 h at 100 °C (temperature was measured with an IR sensor on the outer surface of the reaction vial), using an irradiation power of 100 W (the ramp temperature rate was 3 min). When the reaction was complete, the reaction mixture was diluted with a saturated solution of Na_2CO_3 (20 mL) and washed with dichloromethane (3 × 20 mL). The organic phase was separated, dried with $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 95:5) to give the product.

2-(4-Bromophenyl)benzo[*d*][1,3]selenazole (3a): Yield 0.078 g (92%); white solid; m.p. 124–126 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01 (d, J = 8.1 Hz, 1 H), 7.84 (d, J = 8.0 Hz, 1 H), 7.78 (d, J = 8.2 Hz, 2 H), 7.52 (d, J = 8.3 Hz, 2 H), 7.41 (t, J = 7.2 Hz, 1 H), 7.24 (t, J = 7.3 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 171.6, 156.3, 139.0, 135.7, 132.9, 130.0, 127.2, 126.2, 126.1, 125.6, 125.5 ppm. IR (KBr): $\tilde{\nu}$ = 1510, 1475, 1432, 1392, 1303, 1216, 1064, 937, 825, 752 cm^{-1}. MS: m/z = 337 [M$^+$]. $C_{13}H_8BrNSe$ (336.90): calcd. C 46.32, H 2.39, N 4.16; found C 46.68, H 2.30, N 5.65.

2-(4-Chlorophenyl)benzo[*d*][1,3]selenazole (3b): Yield 0.068 g (92%); white solid; m.p. 98–100 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09 (d, J = 8.1 Hz, 1 H), 7.96–7.91 (m, 3 H), 7.51–7.42 (m, 3 H), 7.31 (t, J = 7.5 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 170.9, 155.7, 138.4, 137.1, 134.7, 129.3, 129.1, 126.6, 125.5, 124.9, 124.8 ppm. IR (KBr): $\tilde{\nu}$ = 1512, 1479, 1398, 1091, 829, 752 cm^{-1}. MS: m/z = 293 [M$^+$]. HRMS: m/z calcd. for $C_{13}H_8ClNSe$ [M + H]$^+$ 293.9589; found 293.9592.

2-(3,4-Difluorophenyl)benzo[*d*][1,3]selenazole (3c): Yield 0.069 g (93%); yellow solid; m.p. 94–97 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.14 (d, J = 8.0 Hz, 1 H), 7.91–7.98 (m, 2 H), 7.73–7.78 (m, 1 H), 7.54 (t, J = 7.8 Hz, 1 H), 7.30–7.40 (m, 2 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 171.7, 156.1, 154.5 (d, $J_{C,F}$ = 12.9 Hz), 153.0 (d, $J_{C,F}$ = 13.2 Hz), 151.1 (d, $J_{C,F}$ = 12.9 Hz), 149.7 (d, $J_{C,F}$ = 12.9 Hz), 145.2, 139.1, 130.4 (d, $J_{C,F}$ = 77.4 Hz), 126.9 (d, $J_{C,F}$ = 76.6 Hz), 125.6 (d, $J_{C,F}$ = 10.9 Hz), 118.6 (d, $J_{C,F}$ = 18.0 Hz), 117.3 (d, $J_{C,F}$ = 19.0 Hz) ppm. IR (KBr): $\tilde{\nu}$ = 1606, 1500, 1427, 1309, 1268, 1106, 977, 757, 634 cm^{-1}. MS: m/z = 295 [M$^+$]. $C_{13}H_7F_2NSe$ (294.97): calcd. C 53.08, H 2.40, N 4.76; found C 55.07, H 2.48, N 4.13.

4-(Benzo[*d*][1,3]selenazol-2-yl)phenol (3d): Yield 0.048 g (70%); dark-orange solid; m.p. 212–213 °C. ^{1}H NMR [400 MHz, $(CD_3)_2CO$]: δ = 9.04 (s, 1 H), 7.93 (d, J = 8.0 Hz, 1 H), 7.86 (d, J = 8.0 Hz, 1 H), 7.81 (d, J = 8.6 Hz, 2 H), 7.35 (t, J = 7.3 Hz, 1 H), 7.17 (t, J = 7.2 Hz, 1 H), 6.86 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR [100 MHz, $(CD_3)_2CO$]: δ = 172.4, 161.1, 156.7, 138.4, 130.2, 128.6, 126.9, 125.7, 125.5, 124.7, 116.6 ppm. IR (KBr): $\tilde{\nu}$ = 3434, 1604, 1484, 1432, 1292, 1218, 1172, 833, 756 cm^{-1}. MS: m/z = 275 [M$^+$]. $C_{13}H_9NOSe$ (274.98): calcd. C 56.95, H 3.31, N 5.11; found C 56.60, H 2.80, N 5.05.

2-(Benzo[*d*][1,3]selenazol-2-yl)phenol (3e): Yield 0.061 g (89%); white solid; m.p. 128–130 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 12.57 (s, 1 H); 8.01 (d, J = 8.1 Hz, 1 H), 7.92 (d, J = 8.1 Hz, 1 H), 7.55 (d, J = 7.8 Hz, 1 H), 7.49 (t, J = 7.7 Hz, 1 H), 7.31–7.41 (m, 2 H), 7.09 (t, J = 8.3 Hz, 1 H), 6.95 (t, J = 7.7 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 174.7, 157.9, 154.2, 136.4, 133.5, 130.8, 127.4, 126.6, 125.3, 124.4, 120.4, 119.9, 118.4 ppm. IR (KBr): $\tilde{\nu}$ = 3448, 1616, 1581, 1483, 1384, 1263, 1201, 798 cm^{-1}. MS: m/z = 275 [M$^+$]. $C_{13}H_9NOSe$ (274.98): calcd. C 56.95, H 3.31, N 5.11; found C 54.40, H 3.26, N 5.36.

2-Phenylbenzo[*d*][1,3]selenazole (3f): Yield 0.049 g (75%); yellow solid; m.p. 114–116 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03 (d, J = 8.1 Hz, 1 H), 7.91–7.94 (m, 2 H), 7.84 (d, J = 7.9 Hz, 1 H), 7.40–

7.42 (m, 4 H), 7.22 (t, J = 7.5 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 173.2, 165.4, 156.4, 138.9, 136.8, 131.7, 129.7, 128.6, 127.0, 125.9, 125.5 ppm. IR (KBr): $\tilde{\nu}$ = 1587, 1552, 1510, 1479, 1430, 1299, 1216, 939, 763 cm^{-1}. MS: m/z = 259 [M$^+$]. $C_{13}H_9NSe$ (258.99): calcd. C 60.48, H 3.51, N 5.43; found C 60.09, H 3.07, N 5.35.

2-*p*-Tolylbenzo[*d*][1,3]selenazole (3g): Yield 0.047 g (69%); yellow solid; m.p. 78–80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.13 (d, J = 8.1 Hz, 1 H), 7.93–7.97 (m, 3 H), 7.51 (t, J = 7.3 Hz, 1 H), 7.29–7.35 (m, 3 H), 2.44 (s, 3 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 173.2, 156.5, 142.2, 138.8, 134.2, 130.4, 126.9, 125.7, 125.4, 125.3, 128.6, 22.2 ppm. IR (KBr): $\tilde{\nu}$ = 1604, 1490, 1432, 1305, 1220, 937, 815, 754 cm^{-1}. MS: m/z = 273 [M$^+$]. $C_{14}H_{11}NSe$ (273.01): calcd. C 61.77, H 4.07, N 5.15; found C 61.64, H 4.00, N 5.06.

2-(4-Methoxyphenyl)benzo[*d*][1,3]selenazole (3h): Yield 0.051 g (71%); orange solid; m.p. 122–124 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97 (d, J = 8.1 Hz, 1 H), 7.81–7.89 (m, 3 H), 7.38 (t, J = 7.3 Hz, 1 H), 7.19 (t, J = 7.5 Hz, 1 H), 6.90 (d, J = 8.5 Hz, 2 H), 3.80 (s, 3 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 172.7, 162.6, 156.6, 138.7, 130.2, 129.7, 126.9, 125.4, 125.0, 115.0, 56.2 ppm. IR (KBr): $\tilde{\nu}$ = 1600, 1496, 1434, 1259, 1168, 1024, 831, 765 cm^{-1}. MS: m/z = 289 [M$^+$]. $C_{14}H_{11}NOSe$ (289.00): calcd. C 58.34, H 3.85, N 4.86; found C 58.12, H 3.48, N 4.67.

2-(3,5-Dimethoxyphenyl)benzo[*d*][1,3]selenazole (3i): Yield 0.065 g (81%); yellow solid; m.p. 100–101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (d, J = 8.2 Hz, 1 H), 7.92 (d, J = 8.4 Hz, 1 H), 7.48 (t, J = 7.8 Hz, 1 H), 7.31 (t, J = 7.8 Hz, 1 H), 7.17 (d, J = 2.3 Hz, 2 H), 6.59 (t, J = 2.3 Hz, 1 H), 3.88 (s, 6 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 172.3, 160.9, 155.5, 138.2, 137.8, 126.3, 125.3, 124.8, 124.7, 105.8, 103.2, 55.5 ppm. IR (KBr): $\tilde{\nu}$ = 1608, 1593, 1473, 1435, 1321, 1271, 856, 763 cm^{-1}. MS: m/z = 319 [M$^+$]. HRMS: m/z calcd. for $C_{15}H_{13}NO_2Se$ [M + H]$^+$ 320.0190; found 320.0198.

2-Propylbenzo[*d*][1,3]selenazole (3j): Yield 0.051 g (90%); yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.89 (d, J = 8.1 Hz, 1 H), 7.75 (d, J = 8.4 Hz, 1 H), 7.31 (t, J = 7.8 Hz, 1 H), 7.19 (t, J = 7.8 Hz, 1 H), 2.97 (t, J = 7.5 Hz, 2 H), 1.38–1.26 (m, 2 H), 0.95 (t, J = 7.4 Hz, 3 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 177.1, 154.6, 138.4, 125.9, 124.8, 124.7, 123.9, 39.6, 23.6, 13.7 ppm. IR (KBr): $\tilde{\nu}$ = 2958, 2929, 2870, 1701, 1591, 1577, 1450, 758, 721 cm^{-1}. MS: m/z = 225 [M$^+$]. HRMS: m/z calcd. for $C_{10}H_{11}NSe$ [M$^{+\cdot}$] 226.0135; found 226.1659.

2-Heptylbenzo[*d*][1,3]selenazole (3k): Yield 0.067 g (95%); yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99 (d, J = 8.1 Hz, 1 H), 7.85 (d, J = 7.9 Hz, 1 H), 7.41 (t, J = 8.1 Hz, 1 H), 7.24 (t, J = 8.1 Hz, 1 H), 3.09 (t, J = 7.8 Hz, 2 H), 1.89–1.79 (m, 2 H), 1.69–1.52 (m, 2 H), 1.39–1.22 (m, 4 H), 0.96–0.86 (m, 5 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 177.9, 155.1, 138.9, 126.4, 125.3, 125.2, 124.5, 38.2, 32.1, 30.7, 29.6, 29.5, 23.1, 14.6 ppm. IR (KBr): $\tilde{\nu}$ = 2954, 2926, 2854, 1593, 1537, 1450, 1436, 758, 721 cm^{-1}. MS: m/z = 281 [M$^+$]. HRMS: m/z calcd. for $C_{14}H_{19}NSe$ [M + H]$^+$ 282.0761; found 282.0768.

2-*tert*-Butylbenzo[*d*][1,3]selenazole (3l): Yield 0.046 g (78%); yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01 (d, J = 8.2 Hz, 1 H), 7.89 (d, J = 7.9 Hz, 1 H), 7.43 (t, J = 8.1 Hz, 1 H), 7.26 (t, J = 7.9 Hz, 1 H), 1.51 (s, 9 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 187.4, 153.3, 138.0, 126.0, 125.8, 124.1, 30.9, 28.2 ppm. IR (KBr): $\tilde{\nu}$ = 2960, 2927, 2900, 1527, 1436, 1363, 758, 721 cm^{-1}. MS: m/z = 239 [M$^+$]. HRMS: m/z calcd. for $C_{11}H_{13}NSe$ [M + NH_4]$^{+\cdot}$ 257.0557; found 257.0611.

Benzo[*d*][1,3]selenazole (3m): Yield 0.029 g (63%); yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.90 (s, 1 H), 8.18 (d, J = 8.2 Hz, 1 H), 7.99 (d, J = 7.9 Hz, 1 H), 7.50 (t, J = 7.8 Hz, 1 H), 7.36 (t, J = 7.5 Hz, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 158.1, 154.7, 137.1, 126.2, 125.6, 125.2, 125.1 ppm. IR (KBr): $\tilde{\nu}$ = 1693, 1583, 1475, 1427, 852, 752 cm^{-1}. MS: m/z = 283 [M$^+$]. HRMS: m/z calcd. for C_7H_5NSe [M$^{+\cdot}$] 182.9587; found 183.0926.

(*R*)-*tert*-Butyl-4-(benzo[*d*][1,3]selenazol-2-yl)thiazolidine-3-carboxylate (3n): Yield 0.070 g (76%); yellow solid; m.p. 134–135 °C. $[\alpha]_D^{25}$ = –15.9 (c = 0.0034 M, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00 (d, J = 8.1 Hz, 1 H), 7.89 (d, J = 7.9 Hz, 1 H), 7.46 (t, J = 7.8 Hz, 1 H), 7.30 (t, J = 7.7 Hz, 1 H), 5.53 (s, 1 H), 4.73 (d, J = 8.7 Hz, 1 H), 4.56 (s, 1 H), 3.56–3.46 (m, 2 H), 1.38 (s, 9 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 164.9, 154.4, 153.4, 138.0, 126.2, 125.3, 124.9, 124.5, 81.6, 64.2, 49.4, 37.7, 28.2 ppm. IR (KBr): $\tilde{\nu}$ = 1701, 1531, 1436, 1373, 1361, 856, 769 cm^{-1}. MS: m/z = 341. HRMS: m/z calcd. for (-BOC) $C_{10}H_9N_2SSe$ [M$^{+\cdot}$] 269.2288; found (-BOC) 269.2274.

Supporting Information (see footnote on the first page of this article): Experimental details, characterization data, and copies of the ^{1}H and ^{13}C NMR, IR and MS spectra of all compounds.

Acknowledgments

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