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Direct synthesis of 2-aryl-1,3-benzoselenazoles by reaction of bis(2-aminophenyl) diselenides with aryl aldehydes using sodium metabisulfite

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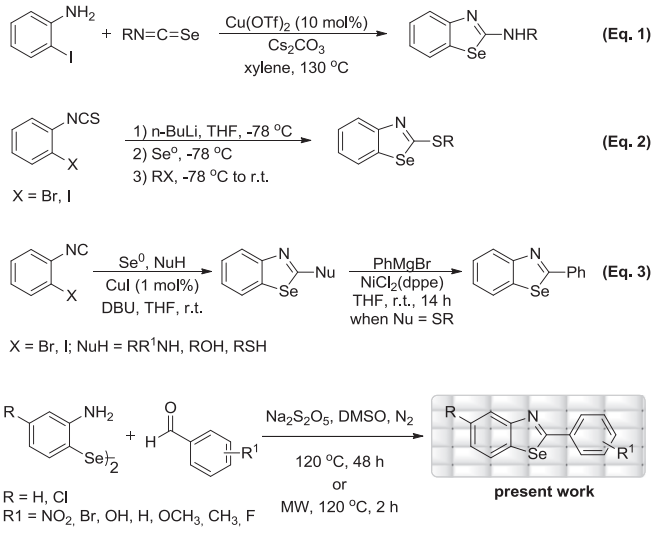
ABSTRACT

We present here a general and easy method for the synthesis of several 2-aryl-1,3-benzoselenazoles from the reaction of bis(2-aminophenyl) diselenides with different aryl aldehydes, promoted by the non-toxic inorganic reducing agent sodium metabisulfite ($Na_2S_2O_5$) in DMSO at 120 °C. This efficient method furnishes in high yields the corresponding 2-aryl substituted 1,3-benzoselenazoles and tolerates a range of substituents at the aryl ring of aldehydes. The use of focused microwave irradiation decreases drastically the reaction time from 48 to 2 h.

1. Introduction

Substituted benzoheteroazole units, particularly benzoxazoles,[1] benzothiazoles[2] and benzimidazoles,[3] are privileged heterocyclic systems because of their great reactivities, notable chemical properties and biological activities. Specially, the synthesis of 2-substituted 1,3-benzothiazoles has attracted much attention not only in synthetic chemistry but also in medicinal and industrial fields.[2] Their different applications range from antitumoral, antidiabetic and antituberculotics agents, to chemiluminescent and photosensitizer agents.[2g,4] Therefore, diverse synthetic methods have been developed for the synthesis of these compounds.[5] However, in the case of selenium analogues,[6] there are few reports on the preparation of the 2-substituted benzoselenazoles and this kind of heterocyclic compounds despite their potential importance.[6c] Interest in the chemistry and application of different selenium-containing compounds as potential pharmaceuticals,[7] new materials,[8] ionic liquids[9] and catalysts[10] has expanded rapidly during the last years. For example, selenium-containing heterocycles, including 1,3-selenazoles[11] have biological activities[7,12] and some 1,3-benzoselenazole derivatives are used as cyanine dyes.[13]

In the context of the synthesis of 1,3-benzoselenazoles, Sashida and co-workers[6d] synthesized 2-amino-1,3-benzoselenazoles by the copper-catalyzed reaction of 2-iodoanilines with isoselenocyanates via the phenylselenourea intermediate (Eq. 1, Scheme 1). More recently, 2-thio-organyl-1,3-benzoselenazoles were prepared in moderated yields from 2-halophenyl isothiocyanates in reactions using firstly *n*-BuLi and elemental selenium, and further alkyl halides (Eq. 2, Scheme 1).[6e]



Scheme 1. Synthesis of 2-substituted-1,3-benzoselenazoles.

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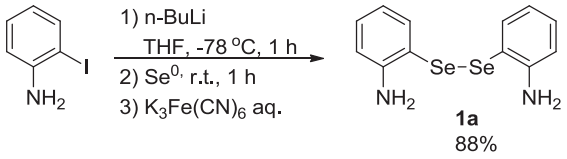
In other study, Kambe and co-workers described the synthesis of 1,3-benzoselenazoles having a heteroatom substituent at the 2-position by the copper-catalyzed reaction of 2-halophenyl isocyanides with elemental selenium and heteroatom nucleophiles (Eq. 3, Scheme 1).[6c] In addition, these authors described the synthesis of 2-phenyl-1,3-benzoselenazoles by nickel-catalyzed cross-coupling reaction of thus-formed 2 arylthio-1,3-benzoselenazole with PhMgBr.[6c] One of the most simple protocol for the synthesis of 2-aryl-1,3-benzoselenazole ring is the reaction of zinc bis(*o*-aminophenylselenolate) with acid chlorides.[6a] Consequently, the development of a simple and direct methodology for the synthesis of 2-aryl-1,3-benzoselenazoles, remains a significant challenge in heterocyclic chemistry.

Recently, a straight approach for the synthesis of 2-aryl-1,3-benzothiazoles was described, where the reaction of substituted bis(2-aminoaryl) disulfides and aryl aldehydes was promoted by sodium metabisulfite ($Na_2S_2O_5$).[14] Besides, this inexpensive and non-toxic inorganic salt can also be used in the synthesis of benzothiazoles,[14] benzimidazoles[15] and in chlorotelluration of terminal alkynes.[16] This fact and according to our continuous interest in the synthesis of organoselenium compounds,[17] prompted us to explore another approach for the synthesis of substituted 2-aryl-1,3-benzoselenazoles from bis(2-aminophenyl) diselenides and aryl aldehydes, using $Na_2S_2O_5$ in DMSO under conventional heating or focused microwave irradiation (Scheme 1).

2. Results and discussion

Our procedure begins with the synthesis of the starting material bis(2-aminophenyl) diselenide **1a**, which was performed according to a procedure recently described by Braga and co-workers. Treating 2-iodoaniline with *n*-BuLi, subsequent trapping of the lithium anion with elemental selenium and potassium ferrocyanide oxidation, affords the corresponding diselenide **1a** in 88% yield[18](Scheme 2).



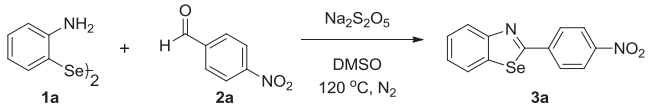
Scheme 2. Synthesis of bis(2-aminophenyl) diselenide **1a**.

Having obtained the diselenide **1a**, we concentrated our efforts on the synthesis of the target molecules. Our initial studies were focused on the development of an optimum set of reaction conditions. The reaction between bis(2-aminophenyl) diselenide **1a** and 4-nitrobenzaldehyde **2a** was selected as a model reaction, using $Na_2S_2O_5$ as the reducing agent and DMSO as solvent.

In a first experiment, bis(2-aminophenyl) diselenide **1a** (0.5 mmol), 4-nitrobenzaldehyde **2a** (1.0 mmol), $Na_2S_2O_5$ (1.0 mmol), were reacted in DMSO (3.0 mL) at room temperature and under these conditions, even after 72 h, no formation of the product was observed (Table 1, entry 1). When the reaction temperature was increased to 120 °C for 24 h the reaction proceeded smoothly, furnishing the desired substituted 2-phenyl-1,3-benzoselenazole **3a** in 64% yield (Table 1, entry 2). To our delight, raising the reaction time to 48 h, afforded the desired product **3a** in excellent yield (Table 1, entry 3). Furthermore, when the reaction was performed in 72 h, no change in the yield was observed (Table 1, entry 4).

Using the best conditions of temperature and time, we next investigated some parameters regarding the stoichiometry. At first we observed that increasing the amount of diselenide **1a** from 0.5 to 1.0 equiv did not alter the yield of the reaction (Table 1, entry 5). On the other hand, when the reaction was performed using 0.5 equiv of $Na_2S_2O_5$, product **3a** was obtained in moderate 69% yield (Table 1, entry 6). Finally, we conducted the reaction under air atmosphere and only 10% yield of product **3a** was obtained confirming that the presence of inert atmosphere is essential for the reaction (Table 1, entries 3 vs 7).

Table 1
Optimization of the reaction conditions



Entry	Diselenide (equiv)	$Na_2S_2O_5$ (equiv)	Time (h)	Yield (%)[a]
1	0.5	1.0	72[b]	n.d.
2	0.5	1.0	24	64
3	0.5	1.0	48	91
4	0.5	1.0	72	90
5	1.0	1.0	48	92
6	0.5	0.5	48	69
7[c]	0.5	1.0	48	10

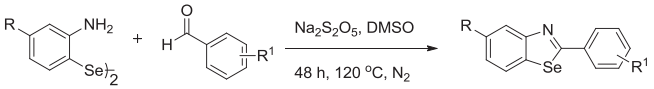
[a] Yields are given for pure isolated products.
[b] Reaction was performed at room temperature.
[c] Reaction was performed on air atmosphere.

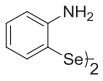
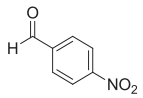
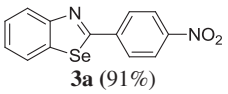
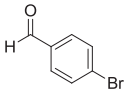
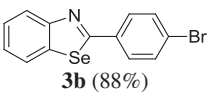
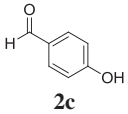
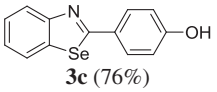
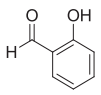
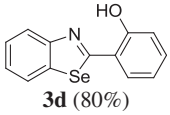
In an optimized reaction, bis(2-aminophenyl) diselenide **1a** (0.5 equiv) was reacted with 4-nitrobenzaldehyde **2a** (1.0 equiv) using $Na_2S_2O_5$ (1.0 equiv) and DMSO (3.0 mL), under nitrogen atmosphere at 120 °C during 48 h, afforded 2-(4-nitrophenyl)-1,3-benzoselenazole **3a** in 91% yield.

After optimization, the reaction of different bis(2-aminoaryl) diselenides **1a**,**b** with a range of aryl aldehydes **2a**–**h** was investigated to check the versatility of the protocol, and the results are summarized in Table 2. In general, all reactions proceeded smoothly furnishing the desired products in good yields.

Several aryl aldehydes were reacted with bis(2-aminophenyl) diselenide **1a** furnishing the corresponding 2-aryl-1,3-benzoselenazoles **3a**–**j** in moderate to excellent yields (Table 2, entries

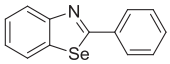
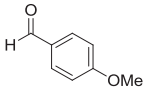
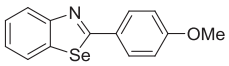
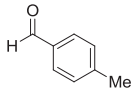
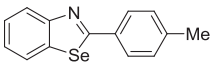
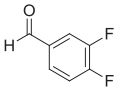
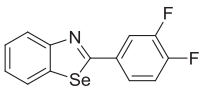
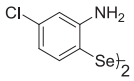
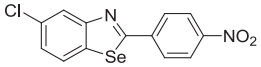
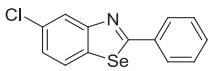
Table 2
Scope of the direct synthesis of 2-aryl-1,3-benzoselenazoles prompted by sodium metabisulfite



Entry	Diselenide	Aldehyde	Product (yield)[a]
1	 **1a**	 **2a**	 **3a** (91%)
2	**1a**	 **2b**	 **3b** (88%)
3	**1a**	 **2c**	 **3c** (76%)
4	**1a**	 **2d**	 **3d** (80%)

(*continued on next page*)

Table 2 (*continued*)

Entry	Diselenide	Aldehyde	Product (yield)[a]
5	**1a**	 **2e**	 **3e** (83%)
6	**1a**	 **2f**	 **3f** (68%)
7	**1a**	 **2g**	 **3g** (62%)
8	**1a**	 **2h**	 **3h** (88%)
9	 **1b**	**2a**	 **3i** (89%)
10	**1b**	**2e**	 **3j** (80%)

[a] Yields are given for pure isolated products.

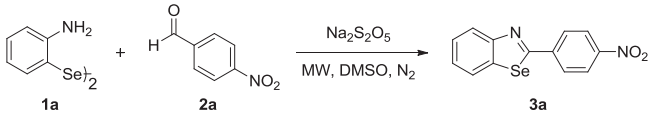
1–8). Upon analysis of Table 2, it can be verified that the electronic effects on the aldehyde moiety seems to have a significant influence on the product yield. For example, aldehydes with electron-withdrawing groups at the aromatic ring gave better results than those with electron-donating groups (Table 2, entries 1, 2 and 8 vs 6–7). This can be explained by the activation of the carbonyl group of the aldehyde by electron-withdrawing groups, facilitating the nucleophilic attack of the nitrogen atom of the amine, to form the intermediate imine (see the plausible reaction mechanism, Fig. 1).

In order to compare the steric effects, reactions were performed with aldehydes containing hydroxyl group in *para* and *ortho* positions and to our satisfaction, good yields were obtained in both cases, demonstrating that sterically demanding *ortho* substituent did not affect the reaction course (Table 2, entries 3, 4). When the benzaldehyde was used, the desired product 2-phenyl-1,3-benzoselenazole **3e** was obtained in 83% yield (Table 2, entry 5).

To expand the synthetic scope of this protocol, we carried out the reactions using bis(2-amino-4-chlorophenyl) diselenide **1b**. Interestingly, despite electron-withdrawing nature of the chloride group in the diselenide **2b**, the yields of 2-aryl-1,3-benzoselenazoles were not greatly reduced and the reactions worked well using aldehydes **2a** and **2e** (Table 2, entries 9, 10).

Over recent years, it has been shown that the organic reactions can be influenced also by microwave irradiation (MW).[19] In all these cases, the authors demonstrated that the use of MW irradiation can considerably decrease the reaction time often accompanied with increase of the product yields.[19,20] Therefore, the synthesis of 2-aryl-1,3-benzoselenazoles from the reaction of bis(2-aminophenyl) diselenide **1a** with aryl aldehydes promoted by $Na_2S_2O_5$ was evaluated also under focused microwave irradiation (Table 3).

Table 3
Optimization of the reaction conditions under microwave irradiation



1a **2a** **3a**

Entry	Temperature (°C)	Time (h)	Yield (%)[a]
1	120	1.0	60
2	180	1.0	60
3	200	1.0	61
4	120	1.5	76
5	120	2.0	90
6	120	2.5	90

[a] Yields are given for pure isolated products.

At first, reaction of diselenide **1a** (0.15 equiv) with aryl aldehyde **2a** (0.3 equiv) using $Na_2S_2O_5$ (0.3 equiv) and DMSO (0.7 mL) as solvent was performed under microwave irradiation at 120 °C and product **3a** was formed in 60% yield after 1.0 h (Table 3, entry

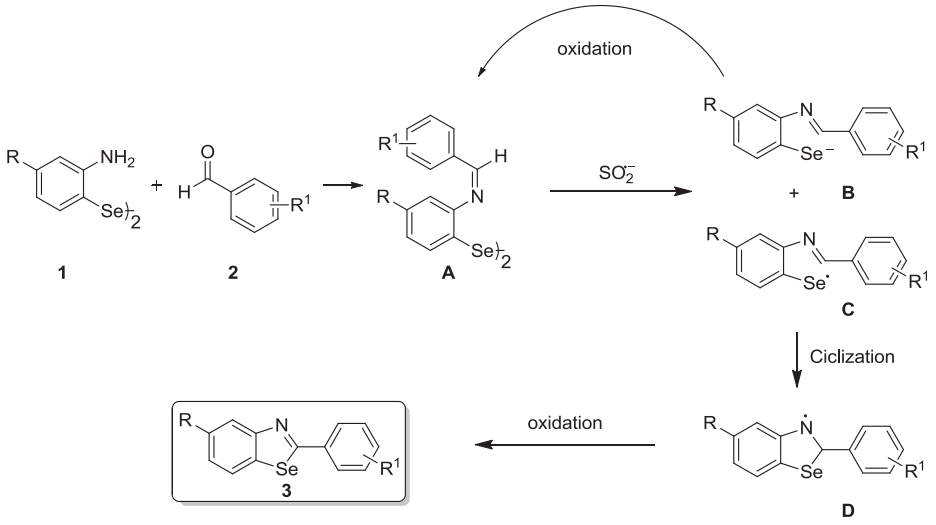
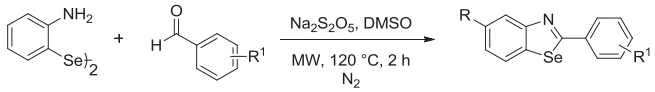


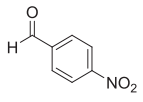
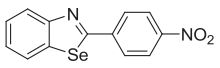
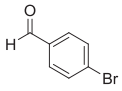
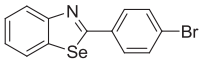
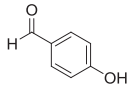
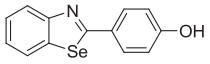
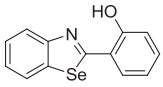
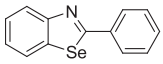
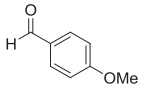
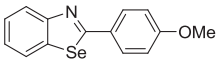
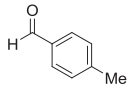
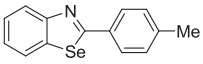
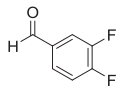
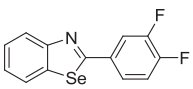
Fig. 1. Plausible reaction mechanism for the formation of 2-aryl-1,3-benzoselenazole **3**.

1). This temperature was measured with an IR sensor on the outer surface of the reaction vial. Encouraged by this result, we decided to explore the benefits of fast heating of the microwave irradiation and performed some experiments under different temperatures. Unfortunately, increasing the temperature to 180 and 200 °C, did not produce significant changes in the yields of desired product **3a** (Table 3, entries 2, 3). After that, we fixed the temperature in 120 °C and investigate if the time could improve the success of the reaction. When the reaction was carried out in 1.5 h the benzoselenazole **1a** was obtained in 76% yield (Table 3, entry 4). To our satisfaction, by increasing the reaction time to 2.0 h we observe a significative improvement, and the desired product was obtained in excellent 90% yield (Table 3, entry 5). Extending the time to 2.5 h did not influence the yield (Table 3, entry 6).

After optimization, the reaction between bis(2-aminophenyl) diselenide **1a** and a set of different aldehydes was investigated to check the versatility of the protocol, and the results are summarized in Table 4.

Table 4
Scope of the direct synthesis of 2-aryl-1,3-benzoselenazoles prompted by sodium metabisulfite using MW Irradiation



Entry	Aldehyde	Product (yield)	Yield (%)[a]
1	 **2a**	 **3a**	90
2	 **2b**	 **3b**	90
3	 **2c**	 **3c**	80
4	 **2d**	 **3d**	84
5	 **2e**	 **3e**	79
6	 **2f**	 **3f**	67
7	 **2g**	 **3g**	60
8	 **2h**	 **3h**	92

[a] Yields are given for pure isolated products.

To demonstrate the generality of MW experiments, we prepared a series of benzoselenazoles **3a**–**h** under microwave irradiation (Table 4). In most cases, the reactions proceeded smoothly to give desired product in good to excellent yields. A structurally diverse range of aryl aldehydes were converted to corresponding benzoselenazoles in good yields (Table 4, entries 1–8). The results depicted in Table 4 show that the use of MW irradiation (Method B) is better than conventional heating (Table 2, Method A), furnishing the corresponding products in comparable yields but in very short reaction time.

On the basis of these results and on previous reports about the use of an oxidizing media,[14] a possible mechanism for the synthesis of 2-aryl-1,3-benzoselenazole can be proposed (Fig. 1). We believe that the amino group of bis(2-aminophenyl) diselenide **1** initially reacts with the aryl aldehyde **2** to form the imine diselenide compound denoted **A**. To confirm our hypothesis we performed a control experiment and this compound **A** could be observed and confirmed by ^{1}H NMR analysis. Next, the Se–Se bond was cleaved by the radical anion $SO_2^{\cdot -}$ generated form $S_2O_5^{2-}$ by heating,[14d] to afford the intermediates **B** and **C**. The intermediate **B** can be reoxidized to starting imine diselenide **A**, and the radical **C** undergoes to the intramolecular cyclocondensation leading to the aminyl radical **D**. Finally, further oxidation of intermediate **D** provides the target product **3**.

3. Conclusion

In conclusion, we have presented here an efficient methodology for the direct synthesis of substituted 2-aryl-1,3-benzoselenazoles in moderated to excellent yields. The condensations of bis(2-aminophenyl) diselenides with a range of substituted aryl aldehydes were promoted by the non-toxic inorganic reducing agent sodium metabisulfite in DMSO at 120 °C. Another benefit of the described procedure is that the protocol minimizes the energy demands and the reaction time could be reduced from 48 to only 2 h using focused MW irradiation. Furthermore, studies of photophysical properties of the synthesized compounds are in progress in our laboratory.

4. Experimental section

4.1. General remarks

The sodium metabisulfite ($Na_2S_2O_5$) was purchased from Reagen® and used without further purifications. Dimethylsulfoxide (DMSO) was obtained from Sigma Aldrich and dried through classical method.[21] The reactions were monitored by thin-layer chromatography (TLC) and column chromatography was performed using Merck silica gel (230–400 mesh). Nuclear magnetic resonance spectra were obtained on Varian Inova 300 and Bruker 400 spectrometer. 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 on 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. The Microwave experiments were conducted using a CEM Discover, mode operating systems working at 2.45 GHz, with a power programmable from 1 to 300 W.

4.2. General procedure for the synthesis of substituted 2-phenylbenzoselenazoles

The appropriate bis(2-aminoaryl) diselenide **1a** or **1b** (0.5 mmol), substituted aryl aldehyde **2a**–**h** (1.0 mmol) and $Na_2S_2O_5$ (1.0 mmol) were dissolved in anhydrous DMSO (3 mL). The resulting reaction

mixture was stirred under nitrogen atmosphere at 120 °C for 48 h. After this time, the mixture was cooled to room temperature, diluted with saturated aq NH_4Cl (20 mL) and washed with ethyl acetate (3×20 mL). The organic phase was separated, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using hexanes/AcOEt (95:5) as eluent to give substituted 2-phenylbenzoselenazoles **3a**–**j**.

*4.2.1. 2-(4-Nitrophenyl)benzo[d][1,3]selenazole (**3a**).* Yield: 0.277 g (91%); yellow solid; mp 147–148 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.27 (d, 2H, J=8.7 Hz); 8.10 (d, 3H, J=8.7 Hz); 7.92 (d, 1H, J=8.0); 7.47 (t, 1H, J=7.5 Hz); 7.32 (t, 1H, J=7.6 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 169.9, 156.2, 149.6, 142.1, 139.6, 129.3, 127.6, 126.9, 126.2, 125.7, 125.0. IR (KBr) ν: 1592, 1521, 1342, 1211, 1141, 943, 854, 769. MS m/z: 304 m/z (M+). Anal. calcd for $C_{13}H_8N_2O_2Se$ (303.98): C 51.50, H 2.66, N 9.24; found: C 51.97; H 2.63; N 9.30.

*4.2.2. 2-(4-Bromophenyl)benzo[d][1,3]selenazole (**3b**).* Yield: 0.296 g (88%); white solid; mp 124–126 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.01 (d, 1H, J=8.1 Hz); 7.84 (d, 1H, J=8.0 Hz); 7.78 (d, 2H, J=8.2 Hz); 7.52 (d, 2H, J=8.3 Hz); 7.41 (t, 1H, J=7.2 Hz); 7.24 (t, 1H, J=7.3 Hz). ^{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. IR (KBr) ν: 1510, 1475, 1432, 1392, 1303, 1216, 1064, 937, 825, 752. MS m/z: 337 m/z (M^+). Anal. calcd for $C_{13}H_8BrNSe$ (336.90): C 46.32, H 2.39, N 4.16; found: C 46.68, H 2.30, N 5.65.

*4.2.3. 4-(Benzo[d][1,3]selenazol-2-yl)phenol (**3c**).* Yield: 0.209 g (76%); dark orange solid; mp 212–213 °C. ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ: 9.04 (s, 1H); 7.93 (d, 1H, J=8.0 Hz); 7.86 (d, 1H, J=8.0 Hz); 7.81 (d, 2H, J=8.6 Hz); 7.35 (t, 1H, J=7.3 Hz); 7.17 (t, 1H, J=7.2 Hz); 6.86 (d, 2H, J=8.6 Hz). ^{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. IR (KBr) ν: 3434, 1604, 1484, 1432, 1292, 1218, 1172, 833, 756. MS m/z: 275 m/z (M^+). Anal. calcd for $C_{13}H_9NOSe$ (274.98): C 56.95, H 3.31, N 5.11; found: C 56.60, H 2.80, N 5.05.

*4.2.4. 2-(Benzo[d][1,3]selenazol-2-yl)phenol (**3d**).* Yield: 0.220 g (80%); white solid; mp 128–130 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 12.57 (s, 1H); 8.01 (d, 1H, J=8.1 Hz); 7.92 (d, 1H, J=8.1 Hz); 7.55 (d, 1H, J=7.8 Hz); 7.49 (t, 1H, J=7.7 Hz); 7.31–7.41 (m, 2H); 7.09 (t, 1H, J=8.3 Hz); 6.95 (t, 1H, J=7.7 Hz). ^{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. IR (KBr) ν: 3448, 1616, 1581, 1483, 1384, 1263, 1201, 798. MS m/z: 275 m/z (M^+). Anal. calcd for $C_{13}H_9NOSe$ (274.98): C 56.95, H 3.31, N 5.11; found: C 54.40, H 3.26, N 5.36.

*4.2.5. 2-Phenylbenzo[d][1,3]selenazole (**3e**).* Yield: 0.215 g (83%); yellow solid; mp 114–116 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.03 (d, 1H, J=8.1 Hz); 7.91–7.94 (m, 2H); 7.84 (d, 1H, J=7.9 Hz); 7.40–7.42 (m, 4H); 7.22 (t, 1H, J=7.5 Hz). ^{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. IR (KBr) ν: 1587, 1552, 1510, 1479, 1430, 1299, 1216, 939, 763. MS m/z: 259 m/z (M^+). Anal. calcd for $C_{13}H_9NSe$ (258.99): C 60.48, H 3.51, N 5.43; found: C 60.09, H 3.07, N 5.35.

*4.2.6. 2-(4-Methoxyphenyl)benzo[d][1,3]selenazole (**3f**).* Yield: 0.196 g (68%); orange solid; mp 122–124 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.97 (d, 1H, J=8.1 Hz); 7.81–7.89 (m, 3H); 7.38 (t, 1H, J=7.3 Hz); 7.19 (t, 1H, J=7.5 Hz); 6.90 (d, 2H, J=8.5 Hz); 3.80 (s, 3H). ^{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. IR (KBr) ν: 1600, 1496, 1434, 1259, 1168, 1024, 831, 765. MS m/z: 289 m/z (M^+). Anal. calcd for $C_{14}H_{11}NOSe$ (289.00): C 58.34, H 3.85, N 4.86; found: C 58.12, H 3.48, N 4.67.

*4.2.7. 2-p-Tolylbenzo[d][1,3]selenazole (**3g**).* Yield: 0.169 g (62%); yellow solid; mp 78–80 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.13 (d, 1H, J=8.1 Hz); 7.93–7.97 (m, 3H); 7.51 (t, 1H, J=7.3 Hz); 7.29-7.35 (m, 3H); 2.44 (s, 3H). ^{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. IR (KBr) ν: 1604, 1490, 1432, 1305, 1220, 937, 815, 754. MS m/z: 273 m/z (M^+). Anal. calcd for $C_{14}H_{11}NSe$ (273.01): C 61.77, H 4.07, N 5.15; found: C 61.64, H 4.00, N 5.06.

*4.2.8. 2-(3,4-Difluorophenyl)benzo[d][1,3]selenazole (**3h**).* Yield: 0.260 g (88%); yellow solid; mp 94–97 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.14 (d, 1H, J=8.0 Hz); 7.91–7.98 (m, 2H); 7.73–7.78 (m, 1H); 7.54 (t, 1H, J=7.8 Hz); 7.30–7.40 (m, 2H). ^{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). IR (KBr) ν: 1606, 1500, 1427, 1309, 1268, 1106, 977, 757, 634. MS m/z: 295 m/z (M^+). Anal. calcd for $C_{13}H_7F_2NSe$ (294.97): C 53.08, H 2.40, N 4.76; found: C 55.07, H 2.48, N 4.13.

*4.2.9. 5-Chloro-2-(4-nitrophenyl)benzo[d][1,3]selenazole (**3i**).* Yield: 0.301 g (89%); yellow solid; mp 158–160 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.26 (d, 2H, J=8.8 Hz); 8.08 (d, 2H, J=8.3 Hz), 8.06 (s, 1H); 7.81 (d, 1H, J=8.5 Hz); 7.28 (dd, 1H, J=8.4 Hz, J=2.1 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 171.3, 156.7, 149.4, 141.3, 137.2, 133.2, 128.9, 126.8, 125.9, 125.4, 124.6. IR (KBr) ν: 1598, 1515, 1340, 1068, 848, 611. MS m/z: 338 m/z (M^+). Anal. calcd for $C_{13}H_7ClN_2O_2Se$ (337.94): C 46.25, H 2.09, N 8.30; found: C 50.34, H 2.76, N 6.70.

*4.2.10. 5-Chloro-2-phenylbenzo[d][1,3]selenazole (**3j**).* Yield: 0.234 g (80%); yellow solid; mp 138–140 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.09 (d, 1H, J=2.0 Hz); 7.98–8.01 (m, 2H), 7.83 (d, 1H, J=8.4 Hz), 7.45–7.52 (m, 3H), 7.29 (dd, 1H, J=8.4 Hz, J=2.1 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 175.2, 164.4, 157.4, 136.9, 136.5, 133.1, 132.1, 129.8, 128.7, 126.2, 125.3. IR (KBr) ν: 1625, 1477, 1427, 1255, 1062, 883, 759, 686. MS m/z: 293 m/z (M^+). Anal. calcd for $C_{13}H_8ClNSe$ (292.95): C 53.36, H 2.76, N 4.79; found: C 53.22, H 2.19, N 4.80.

4.3. General procedure for the synthesis of substituted 2-phenylbenzoselenazoles under microwave irradiation

In a 10 mL glass vial equipped with a small magnetic stirring bar, the bis(2-aminophenyl) diselenide **1a** (0.15 mmol), substituted aryl aldehyde (0.3 mmol) and $Na_2S_2O_5$ (0.3 mmol) were dissolved in anhydrous DMSO (0.7 mL) and the vial was tightly sealed with an aluminum/Teflon crimp top. The mixture was then irradiated in a microwave reactor (CEM Explorer) for 2.0 h at 120 °C (temperature was measured with an IR sensor on the outer surface of the reaction vial), using an irradiation power of 100 W and pressure of 17.2 bar (the ramp temperature rate was 35 s). After the reaction was complete, the reaction mixture was diluted with saturated aq NH_4Cl (20 mL) and washed with ethyl acetate (3×20 mL). The organic phase was separated, dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using hexane/AcOEt (95:5) as eluent, yielding the products.

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Supplementary data

Electronic Supplementary data (ESI) available: experimental procedures, details ^{1}H and ^{13}C NMR, IR and mass spectra.

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2012.11.091.

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