

## FACILE SYNTHESIS OF 4*H*-1,3-BENZOSELENAZINES BY THE ARYNE REACTION

U. Narasimha Rao, Ramadas Sathunuru, and Edward R. Biehl\*

Department of Chemistry, Southern Methodist University, Dallas, TX 75275

U. S. A. ebiehl@smu.edu.

**Abstract** - Attempts to prepare benzoselenazoles by trapping benzyne with selenoureas failed. These reactions gave instead symmetrically substituted diaryl diselenides. However, when the selenoureas were converted to selenoazadienes, 4*H*-1,3-benzoselenazines were obtained in excellent yields. Furthermore, addition of the selenium atom of the selenoazadienes occurred regioselectively at the position 1 of 3-methoxybenzyne and 3,4-dimethoxybenzyne.

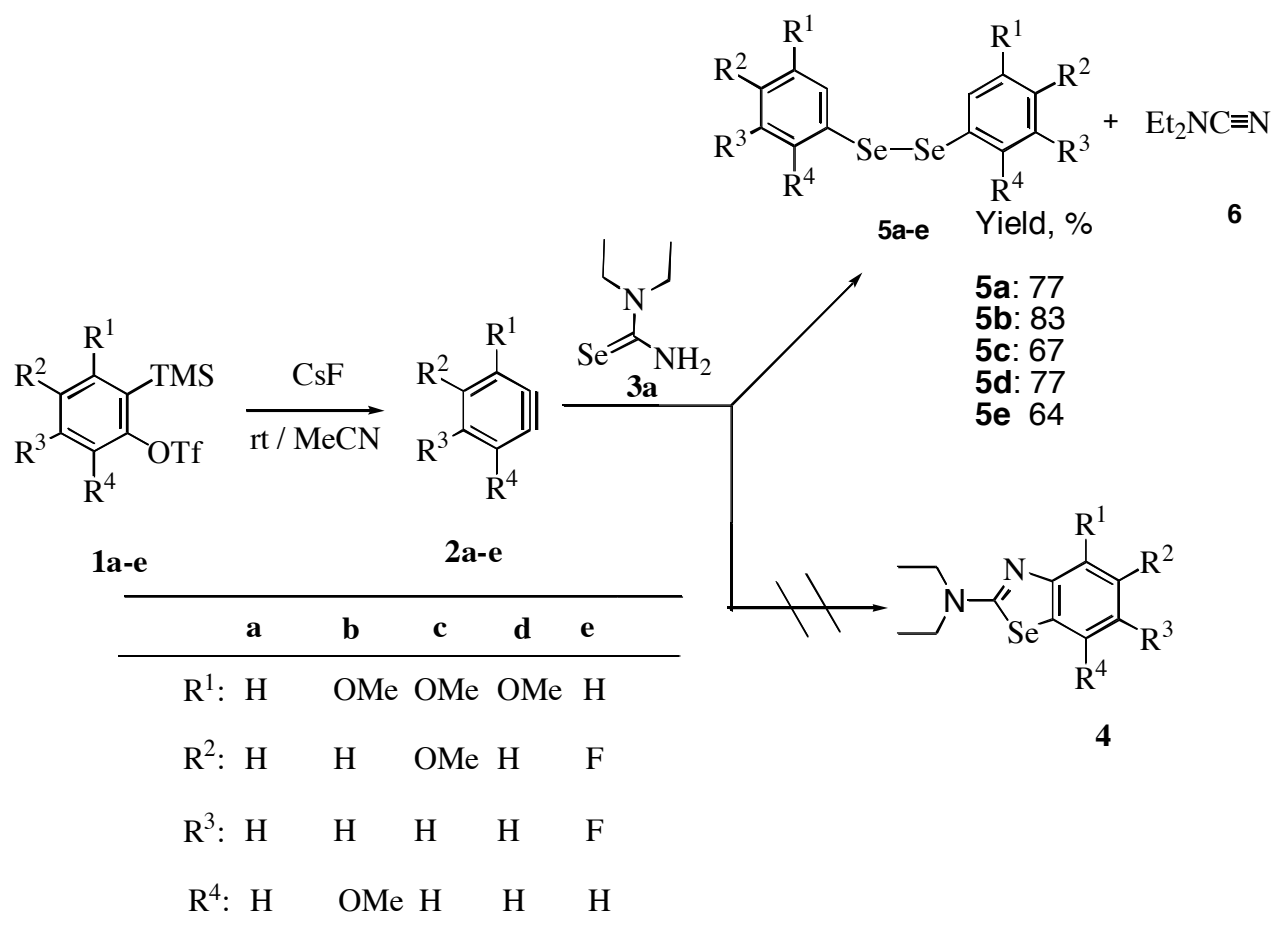
### INTRODUCTION

We recently prepared benzo[4,5]thieno[2,3-*b*]pyridines<sup>1</sup> and benzo[4,5]seleno[2,3-*b*]pyridines<sup>2</sup> by the reaction of various benzyne with the respective sulfur and selenium containing Barton esters. We next turned our attention to preparing benzoselenazoles by trapping benzyne (**2a-e**) generated from the reaction of 2-trimethylsilylphenyl triflates (**1a-e**)<sup>3</sup> with selenourea derivatives (**3a-c**). The derivatives (**3a-c**) were prepared by the reaction of cyanamides with LiAlSeH in the presence of HCl.<sup>4</sup> This improved method, which is superior to most previous ones which invariably used highly toxic materials such as poisonous hydrogen selenides, has led to the facile preparation of selenium-nitrogen and sulfur-nitrogen heterocycles.

### RESULTS AND DISCUSSION

We chose **1a-e** as benzyne precursors since benzyne generation occurs at room temperature under non-basic conditions. We initially studied the reaction of **1a-e** with *N*<sup>l</sup>, *N*<sup>l</sup>-diethylselenourea (**3a**). However, as shown in Scheme 1, these reactions gave no aryne addition products (**4a-e**), but rather produced diaryl

diselenides (**5a-e**) plus *N,N*-diethylcyanamide (**6**). Interestingly **6** was the starting material for the synthesis of **3a**. So the net result of this reaction is the transfer of a selenium atom to benzyne (**2a-e**). A

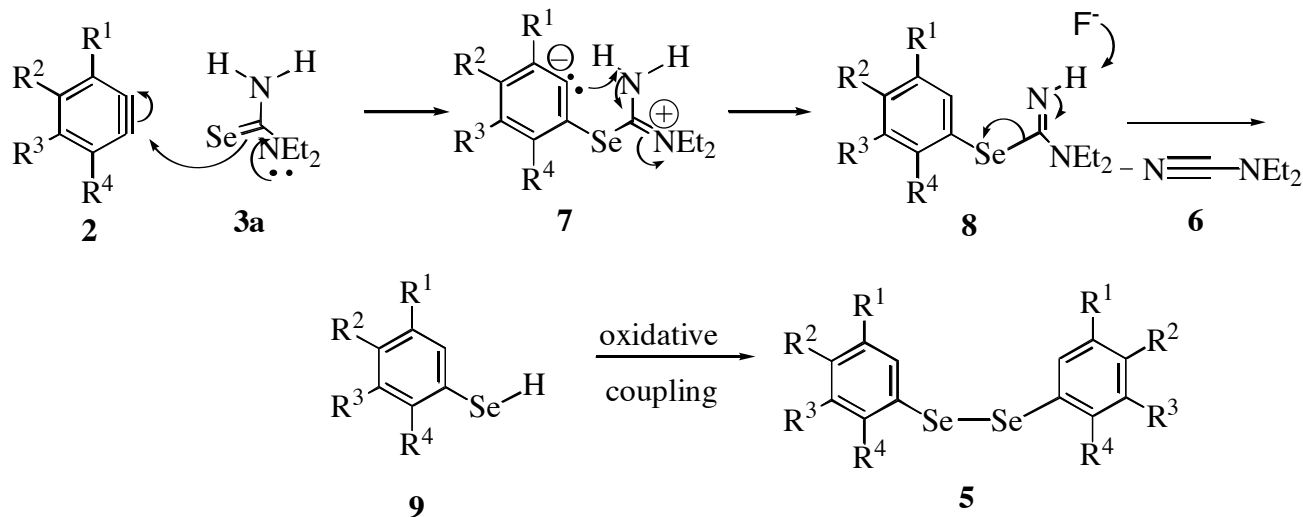


### Scheme 1

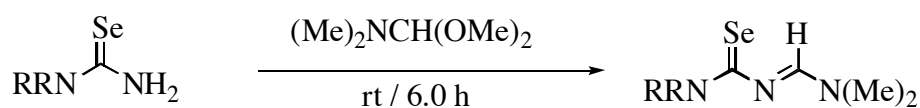
possible mechanism for the synthesis of **5a-e** is shown in Scheme 2. Thus, addition of the Se atom of **3** to benzyne (**2**) gives an adduct (**7**) from which a hydrogen atom from the amino group is transferred to the negatively charged carbon yielding intermediate (**8**). Fluoride ion induced elimination of cyanamide (**6**) from **8** gives ArSeH (**9**) that oxidatively dimerizes to **5**.

We thus changed our strategy by converting the selenoureas (**3a-c**) to the corresponding selenoazadienes (**10a-c**) by the method of Koketsu (see Scheme 3).<sup>5</sup> In this way, the interfering reaction of fluoride ion and the N-H postulated in Scheme 2 would be obviated. The initial reactions were quenched with NH<sub>4</sub>Cl and water to yield at least two polar compounds which LC/MS indicated them to be N-oxide derivatives. These compounds could not be separated. However, when the reaction mixture was treated with NaBH<sub>4</sub> and methanol the titled compounds (**11a-o**) were formed in excellent yields. The results are listed in the Table 1. The compounds were identified by <sup>1</sup>H NMR and <sup>13</sup>C NMR spectrum and in the case of compounds (**11d**) by X-Ray crystallographic analysis. The X-Ray structure of **11d** clearly shows that

addition of the Se atom occurs regioselectively to position 1 of 3-methoxybenzyne (**2d**). A possible mechanism for this reaction is shown in Scheme 4 using the reaction of **10a** with **1d** as typical example.



**Scheme 2**

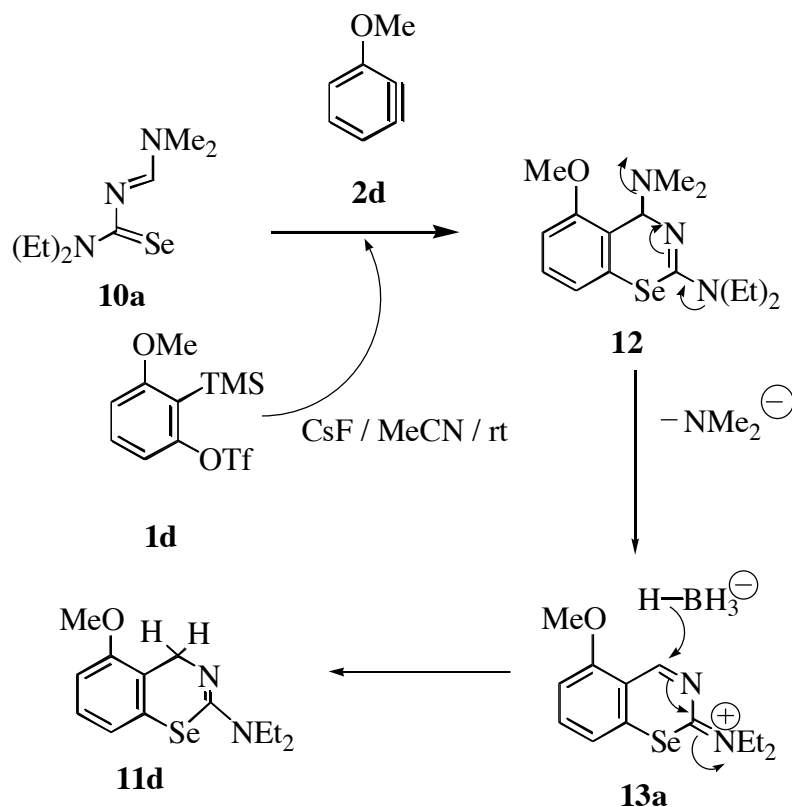


	R	R	Yield (%)
<b>3a</b>	Et	Et	<b>10a</b> 72
<b>3b</b>	$-(CH)_4-$		<b>10b</b> 84
<b>3c</b>	$-(CH_2)_5-$		<b>10c</b> 94

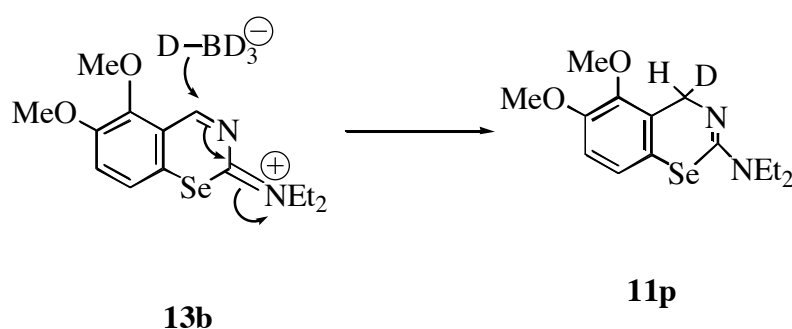
**Scheme 3**

Thus, the azadiene (**10a**) cycloadds to 3-methoxybenzyne (**2d**) via a  $[4n+2]$  process to give adduct (**12**). This intermediate then undergoes loss of the diethylamide group to give cationic species (**13a**) which then is reduced by hydride addition at the C-4 position to give observed products. Support for the last step was obtained by using by carrying out the reaction of 3,4-dimethoxybenzyne (**2c**) and dimethylamino derivative (**10a**) with  $NaBD_4$  and observing the formation of 4-deuterio-2-diethylamino-5,6-dimethoxy-4*H*-1,3-benzoselenazine (**11p**). This intermediate then undergoes loss of the diethylamide group to give cationic species (**13a**) which then is reduced by hydride addition at the C-4 position to give observed products. The observation that 4-deuterio-2-diethylamino-5,6-dimethoxy-4*H*-1,3-benzoselenazine (**11p**) was the product of the reaction of either 3,4-dimethoxybenzyne (**2c**) or the dimethylamino derivative (**10a**) with  $NaBD_4$  lends support for the hydride addition step. This is shown in Scheme 5. To our

knowledge, there has been no report of the elimination of an amide group by a hydride ion. The mechanism shown in Scheme 4 does represent a reasonable sequence of events; however, further work is necessary to establish the mechanism of the reaction.



**Scheme 4**



**Scheme 5**

In conclusion, we have shown that a variety of 4H-1,3-benzoselenazines can be prepared in excellent yields by the reaction of selenoazadienes with arynes.

## EXPERIMENTAL

**General Data:** Melting points were taken on a Mel-Temp capillary apparatus and are uncorrected with respect to stem correction. IR spectra were recorded on a Nicolet Magna-IRTM 550 FTIR spectrophoto-

meter and the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a 400 MHz Bruker AVANCE DRX-400 Multi-nuclear NMR spectrometer. Chemical shifts are reported in reference to TMS as internal standard. The glassware was heated overnight in an oven at 125 °C prior to use. All the benzyne reactions were done under an atmosphere of dry  $\text{O}_2$ -free Ar via balloon.

#### General procedure for the synthesis of diaryl diselenides (**5a-e**)

To a solution containing 179 mg (1 mmol) of  $N^1,N^1$ -diethylselenourea (**3a**) and 1 mmol of the appropriate 2-trimethylsilylphenyl triflate (**1a-e**) in 50 mL of acetonitrile under Ar at rt was added 304 mg (2 mmol) of CsF. After stirring for 6 h, 5 mL of water was added and the resulting solution concentrated. The residue was dissolved in 15 mL of methylene chloride and the resulting solution washed with water (2 X 10 mL), dried ( $\text{Na}_2\text{SO}_4$ ), filtered and evaporated. The residue was purified by column chromatography (silica gel; hexane/ethyl acetate/triethylamine 30:20:1) to isolate diaryl diselenides (**5a-e**). Their physical and spectral properties are given below.

#### Diphenyl diselenide (**5a**)

Yellow needles (hexane), mp: 64 – 65 °C (lit.,<sup>6</sup> 63 – 65 °C).  $^1\text{H}$  NMR (400 MHz, Acetone- $d_6$ ):  $\delta$  7.29-7.35 (m, 6 H), 7.64-7.67 (m, 4 H).

#### Di-(2,5-dimethoxyphenyl) diselenide (**5b**)

Viscous liquid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.80 (s, 6 H), 3.82 (s, 6 H), 6.78 (s, 2 H), 7.20 (s, 2 H). HRMS Calcd for  $\text{C}_{16}\text{H}_{18}\text{O}_4\text{Se}_2$ : 433.95355. Found: 433.95352. Anal. Calcd for  $\text{C}_{16}\text{H}_{18}\text{O}_4\text{Se}_2$ : C, 44.46; H, 4.20. Found: C, 44.58; H, 4.26.

#### Di-(3,4-dimethoxyphenyl) diselenide (**5c**)

Yellow crystals (EtOH), mp: 109-111 °C (lit.,<sup>7</sup> 108-110 °C).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.84 (s, 6 H), 3.89 (s, 6 H), 6.78 (d,  $J = 8.2$  Hz, 2 H), 7.11 (s, 2 H), 7.18 (d,  $J = 8.2$  Hz, 2 H).

#### Di-(3-methoxyphenyl) diselenide (**5d**)

Red brown oil, bp: 192 - 194 °C (lit.,<sup>8</sup> 194 °C).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.79 (s, 6 H), 6.78-6.70 (m, 1 H), 7.19-7.23 (m, 4 H), 7.28 (s, 2 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  55.2, 113.1, 116.5, 123.4, 129.8, 131.8, 159.8.

#### Di-(3,4-difluorophenyl) diselenide (**5e**)

Viscous liquid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.05-7.13 (m, 2 H), 7.28-7.36 (m, 2 H), 7.44-7.47 (m, 2 H). HRMS Calcd for  $\text{C}_{12}\text{H}_6\text{F}_4\text{Se}_2$ : 385.87360. Found: 385.87359. Anal. Calcd for  $\text{C}_{12}\text{H}_6\text{F}_4\text{Se}_2$ : C, 37.5; H, 1.57. Found: C, 37.62; H, 1.51.

#### General procedure for the synthesis of 4*H*-1,3-benzoselenazines **11a-o**.

To a solution of 1.1 mmol of 2-trimethylsilylphenyl triflate (**1a-e**) and 1 mmol of  $N$ -(dimethylaminomethylidene)selenourea (**10a-c**) in 50 mL of acetonitrile under Ar at rt was added 304 mg

(2 mmol) of CsF. The mixture was stirred for 12 h then 76 mg (2 mmol) of sodium borohydride was added immediately followed by 5 mL of methanol, and the resulting mixture stirred for 1 h. At this time, 5 mL of water was added and the mixture concentrated under reduced pressure. The residue was dissolved in 15 mL of methylene chloride and the resulting solution washed with water (2 X 10 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and evaporated. The residue was purified by column chromatography (silica gel; hexane/ethylacetate/triethylamine: 30:20:1) to isolate product. Physical and spectral properties are given below.

#### **2-Diethylamino-4*H*-1,3-benzoselenazine (11a)**

Yellow viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 1.18 (t, *J* = 7.1 Hz, 6 H), 3.49 (q, *J* = 7.1 Hz, 4 H), 4.43 (s, 2 H), 7.24-7.34 (m, 4 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 13.7, 43.9, 53.8, 126.3, 126.8, 126.9, 127.1, 131.8, 135.6, 156.0. Anal. Calcd for C<sub>12</sub>H<sub>16</sub>N<sub>2</sub>Se: C, 53.93; H, 6.03; N, 10.48. Found: C, 54.05; H, 5.99; N, 10.57.

#### **2-Diethylamino-5,8-dimethoxy-4*H*-1,3-benzoselenazine (11b)**

Yellow crystals (hexane/CHCl<sub>3</sub>) mp: 68 - 69°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 1.72 (t, *J* = 7.5 Hz, 6 H), 3.49 (q, *J* = 7.5 Hz, 4 H), 3.81 (s, 3 H), 3.51 (s, 3 H), 4.49 (s, 2 H), 6.71 (d, *J* = 8.1 Hz, 1 H), 6.76 (d, *J* = 8.1 Hz, 1 H); (100 MHz, CDCl<sub>3</sub>): <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 13.5, 44.5, 55.8, 61.2, 56.1, 108.1, 109.0, 120.5, 125.0, 150.3, 150.3, 154.5. Anal. Calcd for C<sub>14</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>Se: C, 51.38; H, 6.16; N, 8.56. Found: C, 51.44; H, 6.22; N, 8.60.

#### **2-Diethylamino-5,6-dimethoxy-4*H*-1,3-benzoselenazine (11c)**

Viscous yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 1.25 (t, *J* = 7.1 Hz, 6 H), 3.40 (q, *J* = 7.1 Hz, 4 H), 4.44 (s, 2 H), 3.81 (s, 3 H), 3.83 (s, 3 H), 6.77 (d, *J* = 8.4 Hz, 1 H), 7.53 (d, *J* = 8.4 Hz, 1 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 13.5, 44.5, 50.3, 55.8, 61.2, 111.3, 121.8, 124.7, 129.9, 146.0, 151.8, 155.4. Anal. Calcd for C<sub>14</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>Se: C, 51.38; H, 6.16; N, 8.56. Found: C, 51.44; H, 6.20; N, 8.66.

#### **2-Diethylamino-5-methoxy-4*H*-1,3-benzoselenazine (11d)**

Yellow viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 1.94 (t, *J* = 6.9 Hz, 6H), 3.49 (q, *J* = 6.9 Hz, 4 H), 3.86 (s, 3 H), 4.51 (s, 2 H), 6.81(d, *J* = 7.7 Hz, 1H), 7.10 (d, *J* = 7.0 Hz, 1 H), 7.14-7.18 (m, 1 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 14.2, 45.2, 50.1, 56.0, 109.6, 122.3, 125.0, 128.0, 132.7, 155.1, 156.5.

Anal. Calcd for C<sub>13</sub>H<sub>18</sub>N<sub>2</sub>OSe: C, 52.53; H, 6.10; N, 9.42. Found: C, 52.58; H, 6.21; N, 9.60. X-Ray Crystallographic Data: formula C<sub>13</sub>H<sub>18</sub>N<sub>2</sub>OSe, formula weight 297.26, orthorhombic, space group P2<sub>1</sub>2<sub>1</sub>2, a = 8.2709(5), b = 23.7582(15), c = 6.7579(4) Å, v = 1327.9(1) Å<sup>3</sup>, z = 4, d = 1.547 Mg/m<sup>3</sup>, μ = 2.818 mm<sup>-1</sup>. Data were collected on a Bruker APEX diffractometer at 100 °K, MoKα, 2θ 3.42 – 56.58°. Reflection collected 16212, independent 3229 [R(int) = 0.025]. The structure was solved by direct-methods and subsequent difference Fourier syntheses using SHELXTL program package.<sup>9</sup> Semi-

empirical absorption study was applied. The structure was refined with full-matrix least-squares on  $F^2$ . The final indices  $R_1 [I > 2 \sigma(I)] = 0.021$ ,  $wR_2 [\text{all data}] = 0.049$ . Selected bond lengths (Å) and angles ( $^\circ$ ): Se – C(2) 1.9565(17), Se(1) – C(9) 1.9079(16), C(2) – N(3) 1.273(2), N(3) – C(4) 1.467(2), C(4) – C(10) 1.509(2), C(9) – C(10) 1.391(2); C(2) – Se(1) – C(9) 93.56 (7), Se(1) – C(2) – N(3) 121.86(13), C(2) – N(3) – C(4) 118.74(15), N(3) – C(4) – C(10) 113.56(13), C(4) – C(10) – C(9) 119.06(14), and Se(1) – C(9) – C(10) 117.92 (13).

### **2-Diethylamino-6,7-difluoro-4H-1,3-benzoselenazine (11e)**

Light brown solid (hexane/ $\text{CHCl}_3$ ), mp: 77 - 78 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.63 (t,  $J = 7.0$  Hz, 6 H), 3.47 (q,  $J = 7.0$  Hz, 4 H), 4.30 (s, 2 H), 7.17-7.22 (m, 1 H), 7.29-7.33 (m, 1 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  14.1, 45.4, 57.3, 117.1 (d,  $^2J_{\text{C-8F-7}} = 171$  Hz), 118.6 (d,  $^2J_{\text{C-5F-6}} = 186$  Hz), 125.8 (d,  $^3J = 3.7$  Hz), 133.1 (d,  $^3J = 4.4$  Hz), 149.7 (dd,  $^1J_{\text{CF}} = 244$  Hz,  $^2J_{\text{CF}} = 14.5$  Hz), 150.1 (dd,  $^1J_{\text{CF}} = 250$  Hz,  $^2J_{\text{CF}} = 14.6$  Hz), 156.0. Anal. Calcd for  $\text{C}_{12}\text{H}_{14}\text{N}_2\text{F}_2\text{Se}$ : C, 47.53; H, 4.66; N, 9.24. Found: C, 47.62; H, 4.80; N, 9.31.

### **2-Pyrrolidin-1-yl-4H-1,3-benzoselenazine (11f)**

Yellow crystals (hexane/ $\text{CHCl}_3$ ), mp: 77 – 78°C.  $^1\text{H}$  NMR(400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.91-1.94 (m, 4 H), 3.49 (t,  $J = 6.0$  Hz, 4 H), 4.38 (s, 2 H), 7.20-7.27 (m, 2 H), 7.35 (d  $J = 7.3$  Hz, 1 H), 7.47 (d,  $J = 7.3$  Hz, 1 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  24.8, 25.7, 49.6, 57.5, 126.9, 127.0, 129.6, 130.4, 135.8, 156.7. Anal. Calcd for  $\text{C}_{12}\text{H}_{14}\text{N}_2\text{Se}$ : C, 54.34; H, 5.32; N, 10.56. Found: C, 54.44; H, 5.40; N, 10.66.

### **5,8-Dimethoxy-2-pyrrolidin-1-yl-4H-1,3-benzoselenazine (11g)**

Yellow crystals (hexane/ $\text{CHCl}_3$ ), mp: 105 – 106°C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.91-1.93 (m, 4 H), 3.51 (t,  $J = 6.0$  Hz, 4 H), 3.80 (s, 3H), 3.85 (s, 3 H), 4.5 (s, 2 H), 6.70 (d,  $J = 8.8$  Hz, 1 H), 6.76 (d,  $J = 8.8$  Hz, 1 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  25.0, 48.8, 49.3, 56.156.1, 108.2, 109.4, 120.4, 124.5, 150.2, 150.6, 152.8. Anal. Calcd for  $\text{C}_{14}\text{H}_{20}\text{N}_2\text{O}_2\text{Se}$ : C, 51.70; H, 5.58; N, 8.60. Found: C, 51.77; H, 5.64; N, 8.66.

### **5,6-Dimethoxy-2-pyrrolidin-1-yl-4H-1,3-benzoselenazine (11h)**

Viscous oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.66 (m, 4 H), 3.51 (m, 4 H), 3.87 (s, 3 H), 3.87 (s, 3 H), 4.50 (s, 2 H), 6.83 (d,  $J = 8.4$  Hz, 1 H), 7.17 (d,  $J = 8.4$  Hz, 1 H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  25.5, 49.7, 56.5, 61.8, 112.0, 122.2, 130.0, 146.8, 152.5, 154.2. Anal. Calcd for  $\text{C}_{14}\text{H}_{20}\text{N}_2\text{O}_2\text{Se}$ : C, 51.70; H, 5.58; N, 8.61. Found: C, 51.77; H, 5.49; N, 8.68.

### **5-Methoxy-2-pyrrolidin-1-yl-4H-1,3-benzoselenazine (11i)**

Yellow crystals (hexane/ $\text{CHCl}_3$ ), mp: 96 - 97°C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.94 (m, 4H), 3.51 (m, 4 H), 3.85 (s, 3 H), 4.51 (s, 2 H), 6.81(d,  $J = 8.0$  Hz, 1H), 7.08 (d,  $J = 7.2$  Hz, 1 H), 7.14-7.18 (m, 1 H);  $^{13}\text{C}$

NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  25.5, 49.5, 49.9, 56.1, 109.6, 122.2, 124.5, 128.0, 132.4, 153.4, 156.6.

Anal. Calcd for C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>OSe: C, 52.89; H, 5.46; N, 9.49. Found: C, 52.84; H, 5.40; N, 9.54.

#### **6,7-Difluoro-2-pyrrolidin-1-yl-4H-1,3-benzoselenazine (11j)**

Yellow solid (hexane/CHCl<sub>3</sub>), mp: 142 - 143 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 25.5, 49.6, 57.2, 116.2 (d, *J* = 160 Hz), 118.5 (d, *J* = 181 Hz), 125.5 (d, *J* = 34 Hz), 132.5 (d, *J* = 38 Hz), 150.1 (dd, *J* = 250 Hz, 14.3 Hz), 150.3 (dd, *J* = 255 Hz, 15 Hz), 152.7. Anal. Calcd for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>F<sub>2</sub>Se: C, 47.85; H, 4.02; N, 9.30. Found: C, 47.88; H, 3.98; N, 9.38.

**2-Piperidin-1-yl-4H-1,3-benzoselenazine (11k)** Yellow crystals (hexane/CHCl<sub>3</sub>), mp: 72 - 73°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.63 (m, 6 H), 3.52 (m, 4 H), 4.40 (s, 2 H), 7.21 (m, 2 H), 7.36 (d = 7.2 Hz, 1 H), 7.49 (d, *J* = 7.2 Hz, 1 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  24.8, 25.6, 50.0, 57.5, 126.9, 127.0, 129.6, 130.4, 135.8, 156.7. Calcd for C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>Se: C, 55.92; H, 5.78; N, 10.03. Found: C, 55.96; H, 5.88; N, 10.14.

#### **5,8-Dimethoxy-2-piperidin-1-yl-4H-1,3-benzoselenazine (11l)**

Viscous liquid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.60 (m, 6 H), 3.54 (m, 4 H), 3.81 (s, 3 H), 3.83 (s, 3 H), 4.51 (s, 2 H), 6.71 (d, *J* = 8.8 Hz, 1 H), 6.76 (d, *J* = 8.8 Hz, 1 H); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  24.9, 25.7, 49.6, 56.2, 56.3, 108.3, 109.3, 120.7, 125.0, 150.5, 150.57, 157.3. Anal. Calcd for C<sub>15</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>Se: C, 53.10; H, 5.94; N, 8.26. Found: C, 53.02; H, 6.02; N, 8.25.

#### **5,6-Dimethoxy-2-piperidin-1-yl-4H-1,3-benzoselenazine (11m)**

Viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.61 (m, 6 H), 2.62 (m, 4 H), 3.85 (s, 3 H), 3.87 (s, 3 H), 4.51 (s, 2 H), 6.83 (d, *J* = 8.8 Hz, 1 H), 7.27 (d, *J* = 8.8 Hz, 1 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  26.1, 44.7, 50.1, 50.9, 56.5, 61.9, 112.1, 122.3, 125.4, 130.3, 146.5, 152.5, 158.8. Anal. Calcd for C<sub>15</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>Se: C, 53.10; H, 5.94; N, 8.26. Found: 53.21; H, 6.02; N, 8.30.

#### **5-Methoxy-2-piperidin-1-yl-4H-1,3-benzoselenazine (11n)**

Colorless solid (hexane/CHCl<sub>3</sub>), mp: 101 - 102°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.57 (m, 6H), 3.52 (m, 4 H), 3.86 (s, 3 H), 4.52 (s, 2 H), 6.81 (d, *J* = 7.7 Hz, 1H), 7.10 (d, *J* = 7.0 Hz, 1 H), 7.14-7.18 (m, 1 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  25.4, 26.1, 50.1, 50.2, 56.0, 109.6, 124.9, 128.0, 132.7, 156.6, 157.8. Anal. Calcd for C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>OSe: C, 54.37; H, 5.87; N, 9.06. Found: C, 54.44; H, 5.88; N, 9.13.

#### **6,7-Difluoro-2-piperidin-1-yl-4H-1,3-benzoselenazine (11o)**

Yellow crystals (hexane/CHCl<sub>3</sub>), mp: 103 - 104°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.62 (m, 6H), 3.51 (m, 4 H), 4.32 (s, 2 H), 7.18 (m, 1 H), 7.29 (m, 1 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  25.3, 26.0, 50.3, 57.3, 116.1 (d, <sup>2</sup>*J*<sub>CF</sub> = 171 Hz), 118.6 (d, <sup>2</sup>*J*<sub>C-8,F-7</sub> = 17.1 Hz, <sup>2</sup>*J*<sub>C-6,F-6</sub>), 132.9 (d, <sup>3</sup>*J* = 3.7 Hz), 133.1 (d, <sup>3</sup>*J* = 4.4 Hz), 148.5 (dd, <sup>1</sup>*J*<sub>CF</sub> = 250 Hz, <sup>2</sup>*J*<sub>CF</sub> = 15.3 Hz), 151.0 (dd, <sup>1</sup>*J*<sub>CF</sub> = 248 Hz, <sup>2</sup>*J*<sub>CF</sub> = 14.5 Hz), 156.0. Anal. Calcd for C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>F<sub>2</sub>Se: C, 49.53; H, 4.48; F, 12.05. Found: C, 49.60; H, 4.63; N, 12.16.



### Synthesis of 4-deuterio-2-diethylamino-5,6-dimethoxy-4H-1,3-benzoselenazine (11p)

Compound (11p) was prepared in similar manner as described above and treated with selenazine (10d) with the exception that NaBD<sub>4</sub> was used in place of NaBH<sub>4</sub>. Viscous oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.17 (t, *J* = 7.1 Hz, 6 H), 3.49 (q, *J* = 7.1 Hz, 4 H), 3.86 (s, 3 H), 3.90 (s, 3 H), 4.40 (s, 1 H), 6.82 (d, *J* = 8.4 Hz, 1 H), 7.18 (d, *J* = 8.4 Hz, 1 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 13.7, 44.7, 50.0, 56.0, 61.4, 111.5, 122.0, 124.8, 130.1, 146.2, 152.1, 155.6.

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