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# Synthesis of Selenazoles by in Situ Cycloisomerization of Propargyl Selenoamides Using Oxygen−Selenium Exchange Reaction

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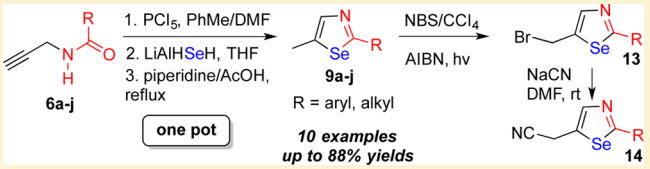
Supporting Information

**ABSTRACT:** Herein, we describe an approach toward selenazole preparation based on the cycloisomerization of propargyl selenoamides. The selenoamides were synthesized in situ using the Ishihara reagent with spontaneous cyclization to form the 2,5-disubstituted selenazoles. Heterocylcles **9a−j** were prepared using readily available starting materials, and yields ranged from moderate to good (20−80%). Methylselenazole **9a** could be transformed into a bromomethyl derivative **13** using NBS. The intermediate **13** would provide a more versatile building block for further derivatizations, e.g., the cyanide **14**.




The interest in organoselenium compounds has been growing during the last decades due to its importance as useful intermediates in synthetic chemistry[1] and as precursors of new materials,[2] but the most outstanding field is related to its biological and medicinal significance.[3] In particular, selenazole heterocycles are being currently studied because of their interesting biological properties; see Figure 1.[4]

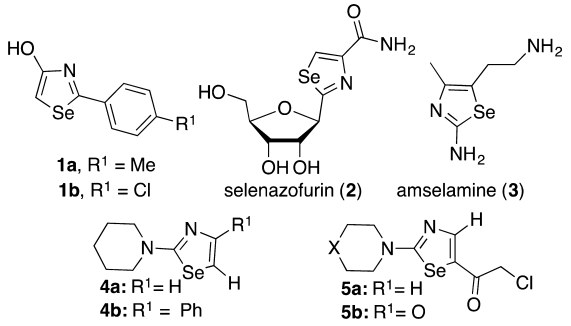



**Figure 1.** Biologically relevant selenazole derivatives.

Selenazole **1a** is able to induce apoptosis in human ovarian cancer (SKOV3) and leukemia HL6 cell lines;[5] selenazole **1b** is useful for prevention of nitric oxide-mediated inflammatory damages;[6] selenazofurin **2** is a potent known antiviral agent;[7] amselamine **3** is a selective histamine $H_2$-agonist;[8] 2-piperidinoselenazole **4a** and 4-phenyl-2-piperidinoselenazole **4b** exhibit superoxide anion-scavenging activity,[9] while 2-piperidino- and 5-(chloroacetyl)-2-morpholinoselenazoles (**5a**,**b**) strongly inhibit LPS-induced nitric oxide release from microglial cells.[10]

The selenazole heterocyclic structure is closely related to its sulfur and oxygen analogue compounds, but their properties often present marked differences. There are few strategies for the synthesis of selenazoles, mainly concerning variations of the Hantzsch procedure used for oxazole and thiazole synthesis. This methodology is based on the condensation of $\alpha$-halo ketone with selenoureas or selenoamides.[11] Selenoureas are inconvenient due to their high cost and low stability to air and light.

As part of our interest in the preparation and biological evaluation of organoselenium compounds,[12] we are interested in a general approach toward the preparation of selenazolyl compounds. We decided to explore the cycloisomerization of propargyl selenoamides to obtain selenazoles. Cycloaddition is a powerful methodology used to prepare aromatic heterocycles like thiazole and oxazole. The cycloisomerization of propargyl amides or thioamides has been reported using different catalysts such as $SiO_2$,[13] Au(I),[14] Ag(I),[15] and *p*-Ts-OH acid,[16] among others. Herein, we report an efficient tandem procedure for the synthesis of 2,5-disubtituted selenazoles by in situ cycloisomerization of propargyl selenoamides.

First, we optimized the preparation of selenoamide using different conditions for *O*−*Se* exchange, employing propargyl amide **6a** as a model. The strategies involved the use of the Woollins reagent (WR)[17] or the Ishihara reagent (LiAlHSeH).[18] Attempts to obtain selenoamides using WR failed, leading to the recovery of the starting material (see entry 1, Table 1). The second strategy used LiAlHSeH as reagent, according to the conditions reported by Sureshbabu and coworkers for the preparation of selenopeptides.[19] This methodology uses $PCl_5$ (1 equiv) with a catalytic amount of DMF (0.3 equiv) in PhH for the conversion of peptide amides into iminochloride, followed by the Cl−Se exchange using Ishihara reagent (1 equiv), freshly prepared from $Se^0$ and $LiAlH_4$. Propargyl amide **6a** in the mentioned conditions led to the formation of selenazoline **8a** (72%), probably via selenoamide

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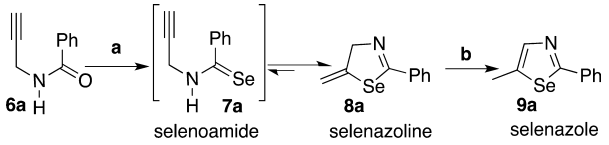
**Table 1. Optimization of the Reaction Conditions for Synthesis of 2-Phenyl-5-methylselenazole**




| entry | conditions a | conditions b | product (ratio),[a] yield[b] (%) |
|---|---|---|---|
| 1 | WR (1.5 equiv), PhMe, reflux 10 h | | **6a**, 70 |
| 2 | (i) $PCl_5$ (3 equiv), DMF (0.3 equiv), PhH, rt; (ii) LiAlHSeH (3 equiv), rt | *p*-TsOH ac, rt | **8a**, 72 |
| 3 | (i) $PCl_5$ (3 equiv), DMF (11 equiv), PhMe, rt; (ii) LiAlHSeH (3 equiv), rt | | **8a** + **9a** (4:6), 10 |
| 4 | (i) $PCl_5$ (3 equiv), DMF (0.3 equiv), PhMe, rt; (ii) LiAlHSeH (3.2 equiv), rt | $Et_3N$ (1 equiv), reflux 9 h | **8a** + **9a** (7:3), 40 |
| 5 | (i) $PCl_5$ (1 equiv), DMF (0.3 equiv), PhMe, rt; (ii) LiAlHSeH (1.2 equiv), rt | PipAcOH (1 equiv) | **8a** + **9a** (3:7), 31 |
| 6 | (i) $PCl_5$ (2 equiv), DMF (0.3 equiv), PhMe, rt; (ii) LiAlHSeH (1.5 equiv), rt | PipAcOH (1 equiv) | **9a**, 74 |

[a]Ratio based on integration of separated $^1$H NMR signals. [b]Isolated yield of the mixture; PipAcOH = piperidinium acetate.

**7a** formation, followed by a spontaneous 5-*exo-dig* cyclization (see entry 2, Table 1). Attempts to isomerize the *exo* double bond to obtain selenazole **9a**, by using *p*-TsOH acid and heat, were unsuccessful (see entry 2, Table 1). An increase in the amount of DMF (11 equiv) led to selenazoline **8a** (4%) and the selenazole **9a** (6%), in low yields (see entry 3, Table 1). In order to promote the complete isomerization of **8a** to **9a**, we used $Et_3N$ (1 equiv) or piperidinium acetate (PipAcOH) (1 equiv) as catalyst (see entries 4 and 5, Table 1, respectively). However, the conversion of **8a** to **9a** was improved when PipAcOH was used but in moderate yield (see entry 5, Table 1). Exploring the effect of the amount of $PCl_5$ and LiAlHSeH (see entries 4 and 5, Table 1, respectively), we found that the best yields were achieved when $PCl_5$ (2 equiv) and LiAlHSeH (1.5 equiv) were used (see entry 6, Table 1). Selenazole **9a**, then, was prepared under these optimized conditions in 74% yield.

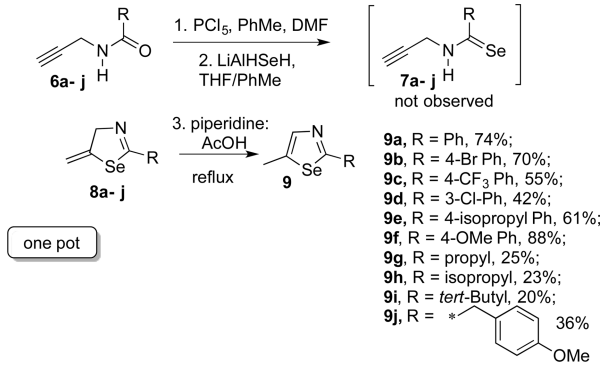
Under optimized conditions, a wide range of aromatic and aliphatic terminal propargyl amides were converted into the desired heterocycles (see Scheme 1). Aromatic propargyl amides **6a**–**f** bearing neutral and both electron-rich and electron-deficient groups gave the cyclized products **9a**–**f** in high and good yields from 88 to 55% (see Scheme 1). In contrast, alkyl propargyl amides **6g**–**j** were converted into their corresponding selenazoles **9g**–**j** in modest yields (20–36%).

In order to explore the scope of the cyclization process we tried to cyclize nonterminal propargyl amides like **10** and **11**, but in all cases the starting material was recovered; see Figure 2.

The proposed mechanism for selenazole formation is similar to those presented for the oxazole synthesis, and it is depicted in Figure 3.[14a] Once the selenoamide **7** is formed, the Se atom promotes a 5-*exo-dig* cyclization, favored according to Baldwin's rules. The electrons of the triple bond take a proton from the media to form selenazoline **8**. The *exo*-double bond isomerizes with PipAcOH toward the aromatic selenazole **9**.

Based on this mechanism, we decided to study the effect of using different electron acceptors to see how electrophiles can compete with the proton uptake within the cyclization reaction process. The product distribution in the presence of NBS or $I_2$ as electrophiles was analyzed; see Scheme 2.

**Scheme 1. Synthesis of 2,5-Disubstituted Selenazoles Using a Tandem Optimized Reaction Sequence[a]**




[a]Percent conversion was 100% in all cases; yields are given as isolated products.

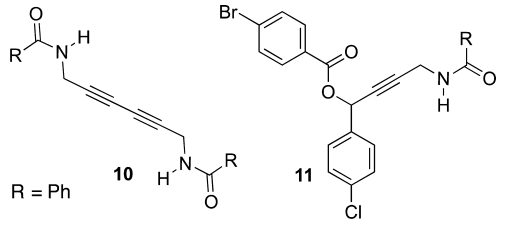



**Figure 2.** Nonterminal propargyl amides **10** and **11**.

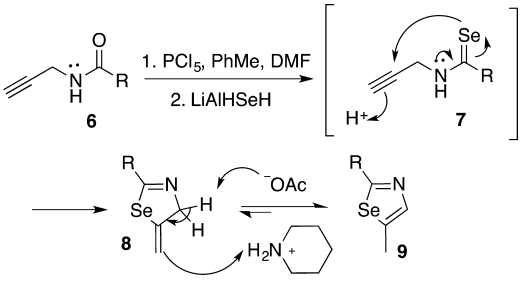
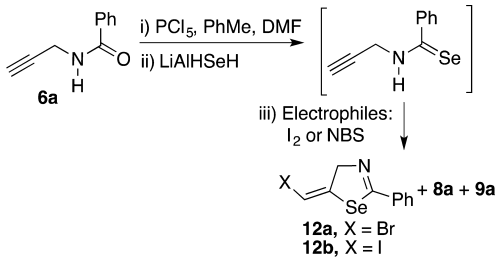



**Figure 3.** Mechanistic proposal for selenazole **9** formation.

**Scheme 2. Synthesis of 5-(Halomethyl)selenazoline 12 Using Different Electrophiles**




The cycloisomerization of propargyl amide **6a** using NBS did not lead to the desired 5-(bromomethyl)selenazole (**12a**); a mixture of compound **8a** and **9a** in a 3:7 ratio and low yield was isolated. When $I_2$ was used as electrophile, a mixture of the desired vinyl iodide **12b** was obtained, together with compounds **8a** and **9a**. The first attempt using the optimized conditions for selenazoline preparation followed by the


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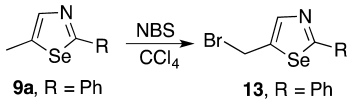
**Table 2. Conditions Assayed for the Synthesis of 5-(Iodomethyl)selenazoles**

| entry | conditions | product (ratio),[a] yield,[b] % |
|---|---|---|
| 1 | (i) $PCl_5$ (2 equiv), DMF (0.3 equiv), PhMe, rt; (ii) LiAlHSeH (1.5 equiv), 0 °C; (iii) $I_2$ (1.5 equiv), 0 °C | **9a** + **12b** (7:3), 19 |
| 2 | (i) $PCl_5$ (2 equiv), $CH_2Cl_2$, −10 °C; (ii) LiAlHSeH (1.5 equiv), −10 °C; (iii) $I_2$ (1.5 equiv), −10 °C | **9a** + **12b** (7:3), 39 |
| 3 | (i) $PCl_5$ (1.5 equiv), $CH_2Cl_2$, 0 °C; (ii) $I_2$ (2 equiv), 0 °C; (iii) LiAlHSeH (1.5 equiv), 0 °C | **9a** + **12b** (7:3), 33 |

[a]Ratio based on integration of separated $^1$H NMR signals. [b]Isolated yield of the mixture.

**Table 3. Optimization of the Bromination Reaction To Obtain 5-(Bromomethyl)selenazole 13**




**9a**, R = Ph **13**, R = Ph

| entry | NBS (eq) | radical initiator (eq) | *hν* time (h) | heating time (h) | conversion[a] (%) | compd **13** yield[b] (%) |
|---|---|---|---|---|---|---|
| 1 | 1.1 | | 1 | rt, overnight | 45 | 20 |
| 2 | 1.8 | | 8 | rt, overnight | 100 | 11 |
| 3 | 1.1 | [PhC(=O)O−]$_2$ (0.02) | | reflux, 4 h | 75 | 21 |
| 4 | 0.9 | [PhC(=O)O−]$_2$ (0.02) | 1 | reflux, 2 h | 78 | 44 |
| 5 | 1.5 | [PhC(=O)O−]$_2$ (0.02) | | reflux, 6 h | 30 | 10 |
| 6 | 1.1 | AIBN (0.1) | 1 | rt, overnight | 100 | 68 |

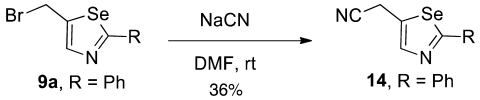
[a]% based on integration of separated $^1$H NMR signals. [b]Isolated yield.

addition of $I_2$ at 0 °C led to a mixture of **9a** and **12b** in a 7:3 ratio (see entry 1, Table 2). We also explored the effect of the solvent influence by replacing with $CH_2Cl_2$, but no change in the product ratio was observed. Furthermore, the order and temperature of $I_2$ addition did not seem to affect the product distribution (see entries 2 and 3, Table 2). Attempts to isomerize the vinyl iodoselenazoline **12b** toward the corresponding 5-(iodomethyl)selenazole using PipAcOH led to decomposition of the starting material.

We then decided to investigate further transformations of the methyl selenazole **9a** and performed a selective bromination of the methyl group present at the 5-position; see Table 3. *N*-Bromosuccinimide (NBS) was used as brominating reagent under different conditions; in all cases, the bromo derivative **13** was selectively obtained (see Table 3). The best conditions were obtained when NBS (1.1 equiv), AIBN (0.1 equiv), *hν* (1 h) in $CCl_4$ at room temperature were used (see entry 6, Table 3).

Compound **13** would provide an easy access to different building blocks for the construction of chemical libraries; e.g., it was readily converted into the cyanide **14** (see Scheme 3).

**Scheme 3. Synthesis of 5-(Cyanomethyl)selenazole 14**




**9a**, R = Ph **14**, R = Ph

In conclusion, we have developed a catalyst-free pathway for the preparation of 2,5-disubstituted selenazoles directly from terminal propargyl amides. This reaction involves readily available starting materials and tolerates a wide range of aryl and alkyl substituents. Bromination using NBS, under free-radical conditions, was also a useful strategy, providing further transformations into the selenazole moiety.

## EXPERIMENTAL SECTION

**LiAlHSeH 0.1 M Preparation.** To a stirred suspension of selenium powder (0.08 g, 1.0 mmol) in dry THF (9 mL) was added lithium aluminum hydride solution (1 M) in THF (1 mL, 1.0 mmol) at 0 °C under a nitrogen atmosphere. The mixture was stirred for 30 min at 0 °C. The reagent lithium hydrogen selenide (LiAlHSeH) was formed in situ as a gray solution that was directly used in our present studies.

*Synthesis of 5-Methylene-2-phenyl-4,5-dihydro-1,3-selenazole (**8a**).* To a stirred solution of *N*-(prop-2-ynyl)benzamide **6a** (0.70 mmol) in dry PhMe (3.5 mL) were added $PCl_5$ (291 mg, 1.4 mmol) and DMF (0.016 mL, 0.03 mmol) at room temperature and the solution allowed to sit for 30 min. A freshly prepared THF solution of LiAlHSeH (1.0 mmol, 10 mL, 0.1 M) was added at room temperature. The reaction mixture was stirred overnight at room temperature. Then the solvent was removed at reduced pressure until dryness. The residue was poured into water (50 mL), $NaHCO_3$ was added until pH 7, and the mixture was extracted with ethyl acetate (5 × 30 mL). The combined organic layers were dried ($Na_2SO_4$), filtered, and concentrated. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 5:1) to give **8a** (108 mg, 70%) as a yellow oil: $^1$H NMR $\delta$ 5.18 (t, $J$ = 2.7 Hz, 1H), 5.32 (dd, $J$ = 2.8, 4.6 Hz, 1H), 5.60 (dd, $J$ = 2.4, 4.3 Hz, 1H), 7.40 − 7.49 (m, 2H), 7.69 (d, $J$ = 6.8 Hz, 1H); $^{13}$C NMR $\delta$ 75.8, 108.0, 128.7, 128.8, 131.4, 135.5, 149.2, 166.4; HRMS calcd for $C_{10}H_{10}NSe$ $[M + H]^+$ 223.9900, found 223.9930.

**Optimized Procedure for the Synthesis of Selenazoles.** *5-Methyl-2-phenylselenazole (**9a**).* To a stirred solution of *N*-(prop-2-ynyl)benzamide **6a** (0.70 mmol) in dry PhMe (3.5 mL) were added at room temperature $PCl_5$ (291 mg, 1.4 mmol) and DMF (0.016 mL, 0.03 mmol) and the solution allowed to sit for 30 min. A freshly prepared of LiAlHSeH solution in THF (1 mmol, 10 mL, 0.1 M) was added at room temperature. The reaction mixture was stirred at the same temperature for 1 h. Then piperidinium acetate (102 mg, 0.7 mmol) was added, and the reaction was refluxed for 2 h and stirred overnight at room temperature. Then the solvent was removed at reduced pressure until dryness. The residue was poured into water (50 mL), $NaHCO_3$ was added until pH 7, and the mixture was extracted with ethyl acetate (5 × 30 mL). The combined organic layers were dried ($Na_2SO_4$), filtered, and concentrated. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 5:1) to give **9a** (89 mg, 74%) as a yellow oil: $^1$H NMR $\delta$ 2.58 (d, $J$ = 1.4 Hz, 3H), 7.39 − 7.42 (m, 3H), 7.48 (dd, $J$ = 1.4, 2.5 Hz, 1H), 7.83 − 7.85 (m, 2H); $^{13}$C NMR $\delta$ 14.8, 126.8, 129.0, 129.9, 136.6, 141.3, 142.3, 173.9; HRMS calcd for $C_{10}H_{10}NSe$ $[M + H]^+$ 223.9900, found 223.9910.

*2-(4-Bromophenyl)-5-methylselenazole (**9b**).* Prepared in an analogous route as described for **9a** starting from 4-bromo-*N*-(prop-2-yn-1-yl)benzamide **6b**. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 5:1) to give **9b** (148 mg, 70%) as a yellow solid: mp 82.3−84.1 °C; $^1$H NMR $\delta$ 2.59 (d, $J$ = 1.3 Hz, 3H), 7.46 (d,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$J$ = 1.3 Hz, 1H), 7.53 (d, $J$ = 8.5 Hz, 2H), 7.70 (d, $J$ = 8.5 Hz, 2H); $^{13}$C NMR $\delta$ 14.9, 124.1, 128.2, 132.2, 135.7, 142.0, 142.6, 172.5; HRMS calcd for $C_{10}H_9BrNSe$ $[M + H]^+$ 301.9005, found 301.9030.

*5-Methyl-2-(4-(trifluoromethyl)phenyl)selenazole (**9c**).* Prepared in an analogous route as described for **9a** starting from *N*-(prop-2-yn-1-yl)-4-(trifluoromethyl)benzamide **6c**. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 5:1) to give **9c** (111 mg, 55%) as a yellow solid: mp 109.0−111.6 °C; $^1$H NMR $\delta$ 2.62 (d, $J$ = 1.3 Hz, 3H), 7.53 (d, $J$ = 1.3 Hz, 1H), 7.66 (d, $J$ = 8.2 Hz, 2H), 7.94 (d, $J$ = 8.1 Hz, 2H); $^{13}$C NMR $\delta$ 14.9, 124.1 ($q$, $J_{CF3}$ = 271 Hz), 126.1 ($q$, $J$ = 4 Hz), 127.0, 131.5 ($q$, $J$ = 32 Hz), 139.8, 142.9, 143.0, 171.9; HRMS calcd for $C_{11}H_9F_3NSe$ $[M + H]^+$ 291.9774, found 291.9744.

*2-(3-Chlorophenyl)-5-methylselenazole (**9d**).* Prepared in an analogous route as described for **9a** starting from 3-chloro-*N*-(prop-2-yn-1-yl)benzamide **6d**. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 8:1) to give **9d** (75 mg, 42%) as a yellow oil: $^1$H NMR $\delta$ 2.61 (d, $J$ = 1.3 Hz, 3H), 7.31 − 7.38 (m, 2H), 7.49 (d, $J$ = 1.3 Hz, 1H), 7.69 (dt, $J$ = 7.3, 1.6 Hz, 1H), 7.85 (t, $J$ = 1.6 Hz, 1H); $^{13}$C NMR $\delta$ 14.9, 125.0, 126.6, 129.8, 130.3, 135.1, 138.4, 142.4, 142.7, 172.0; HRMS calcd for $C_{10}H_9ClNSe$ $[M + H]^+$ 257.9510, found 257.9540.

*2-(4-Isopropylphenyl)-5-methylselenazole (**9e**).* Prepared in an analogous route as described for **9a** starting from 4-isopropyl-*N*-(prop-2-yn-1-yl)benzamide **6e**. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 4:1) to give **9e** (112 mg, 61%) as a yellow oil: $^1$H NMR $\delta$ 1.27 (d, $J$ = 7.0 Hz, 6H), 2.58 (d, $J$ = 1.3 Hz, 3H) 2.93 (hept, $J$ = 6.9,Hz, 1H), 7.26 (d, $J$ = 8.3 Hz, 2H), 7.45 (dd, $J$ = 1.3, 2.5 Hz, 1H), 7.76 (d, $J$ = 8.3 Hz, 2H); $^{13}$C NMR $\delta$ 14.8, 23.9, 34.1, 126.8, 127.1, 134.5, 140.6, 142.2, 151.0, 174.0; HRMS calcd for $C_{13}H_{16}NSe$ $[M + H]^+$ 266.0369, found 266.0399.

*2-(4-Methoxyphenyl)-5-methylselenazole (**9f**).* Prepared in an analogous route as described for **9a** starting from 4-methoxy-*N*-(prop-2-yn-1-yl)benzamide **6f**. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 6:1) to give **9f** (115 mg, 88%) as a white solid: mp 65.2−66.0 °C; $^1$H NMR $\delta$ 2.57 (d, $J$ = 1.3 Hz, 3H), 3.85 (s, 3H), 6.92 (d, $J$ = 8.9 Hz, 2H), 7.40 (d, $J$ = 1.3 Hz, 1H), 7.77 (d, $J$ = 8.9 Hz, 2H); $^{13}$C NMR $\delta$ 14.9, 55.5, 114.4, 128.2, 129.8, 140.2, 142.1, 161.1, 173.7; HRMS calcd for $C_{11}H_{12}NOSe$ $[M + H]^+$ 254.0006, found 254.0036.

*2-Ethyl-5-methylselenazole (**9g**).* Prepared in an analogous route as described for **9a** starting from *N*-(prop-2-yn-1-yl)propionamide **6g**. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 6:1) to give **9g** (31 mg, 25%) as a yellow oil: $^1$H NMR $\delta$ 1.35 (t, $J$ = 7.6 Hz, 3H), 2.51 (d, $J$ = 1.3 Hz, 3H), 2.96 (q, $J$ = 7.6 Hz, 2H), 7.22 (d, $J$ = 1.3 Hz, 1H); $^{13}$C NMR $\delta$ 14.8, 30.7, 140.1, 140.3, 179.5; HRMS calcd for $C_6H_{10}NSe$ $[M + H]^+$ 175.9900, found 175.9902.

*2-Isopropyl-5-methylselenazole (**9h**).* Prepared in an analogous route as described for **9a** starting from *N*-(prop-2-ynyl)isobutyramide **6h**. The residue was purified by chromatography on $SiO_2$ (*n* hexane/EtOAc 6:1) to give **9h** (31 mg, 23%) as a yellow oil: $^1$H NMR $\delta$ 1.35 (d, $J$ = 6.9 Hz, 6H), 2.51 (d, $J$ = 1.4 Hz, 3H), 3.21 (hept, $J$ = 6.9 Hz, 1H), 7.24 (d, $J$ = 1.4 Hz, 1H); $^{13}$C NMR $\delta$ 14.7, 23.7, 36.6, 139.6, 140.1, 185.2; HRMS calcd for $C_7H_{12}NSe$ $[M + H]^+$ 190.0057, found 190.0035.

*2-(tert-Butyl)-5-methylselenazole (**9i**).* Prepared in an analogous route as described for **9a** starting from *N*-(prop-2-yn-1-yl)pivalamide **6i**. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 10:1) to give **9i** (29 mg, 20%) as a yellow oil: $^1$H NMR $\delta$ 1.40 (s, 9H), 2.51 (d, $J$ = 1.3 Hz, 3H), 7.24 (d, $J$ = 1.3 Hz, 1H); $^{13}$C NMR $\delta$ 14.7, 31.3, 40.5, 139.7, 140.3, 188.4.; HRMS calcd for $C_8H_{13}NSe$ $[M]^+$ 203.0213, found 203.0237.

*2-(4-Methoxybenzyl)-5-methylselenazole (**9j**).* Prepared in an analogous route as described for **9a** starting from 2-(4-methoxyphenyl)-*N*-(prop-2-yn-1-yl)acetamide **6j**. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 5:1) to give **9j** (67 mg, 36%) as a yellow oil: $^1$H NMR $\delta$ 2.47 (d, $J$ = 1.4 Hz, 3H), 3.80 (s, 3H), 4.16 (s, 2H), 6.87 (d, $J$ = 8.7 Hz, 2H), 7.23 (d, $J$ = 8.7 Hz, 2H), 7.27 (dd, $J$ = 1.4, 2.6 Hz, 1H); $^{13}$C NMR $\delta$ 14.7, 42.6, 55.4, 114.3, 130.3, 130.8, 140.7, 141.4, 158.8, 178.1; HRMS calcd for $C_{12}H_{14}NOSe$ $[M + H]^+$ 268.0162, found 268.0175.

*Synthesis of (E)-5-(iodomethylene)-2-phenyl-4,5-dihydroselenazole (**12b**).* To a stirred solution of *N*-(prop-2-ynyl)benzamide **6a** (0.70 mmol) in dry $CH_2Cl_2$ (3.5 mL) was added crystalline $PCl_5$ (291 mg, 1.4 mmol) at −10 °C. Stirring was continued for 30 min. A freshly prepared THF solution of LiAlHSeH (1.0 mmol) was added, and the reaction mixture was stirred at the same temperature for another 1 h. Then $I_2$ (267 mg, 1.0 mmol) was added, and the reaction was stirred overnight at −10 °C. The solvent was removed at reduced pressure until dryness. The residue was poured into water (50 mL), $NaHCO_3$ was added until pH 7, and the mixture was extracted with ethyl acetate (5 × 30 mL). The combined organic layers were dried ($Na_2SO_4$), filtered, and concentrated. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 5:1) to give **12b** (29 mg, 12%) as yellow oil: $^1$H NMR $\delta$ 5.08 (d, $J$ = 3.1 Hz, 1H), 6.16 (t, $J$ = 3.1 Hz, 1H), 7.41 − 7.49 (m, 3H), 7.65 − 7.68 (m, 2H); $^{13}$C NMR $\delta$ 62.9, 79.7, 128.5, 128.9, 131.7, 135.4, 146.7, 166.0; HRMS calcd for $C_{10}H_8INSe$ 348.8866, $[M]^+$ found 348.8869

*Synthesis of 5-(Bromomethyl)-2-phenylselenazole (**13**).* To a stirred solution of **9a** (600 mg, 2.7 mmol) in $CCl_4$ (45 mL) were added NBS (529 mg, 3.0 mmol) and AIBN (49 mg, 0.3 mmol). Then the solution was irradiated with $h\nu$ for 1 h (200 W, tungsten lamp) using an ice bath to avoid overheating and stirred overnight at room temperature, protected from light. The formed succinimide was filtered off, and the filtrate was concentrated under vacuum. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 3:1) to give **13** (554 mg, 68%) as a white solid: mp 80.6−82.0 °C; $^1$H NMR $\delta$ 4.82 (d, $J$ = 0.8 Hz, 2H), 7.40 − 7.45 (m, 3H), 7.76 (t, $J$ = 0.8 Hz, 1H), 7.86 (dd, $J$ = 1.6, 7.9 Hz, 2H); $^{13}$C NMR $\delta$ 26.6, 127.0, 129.3, 130.8, 136.3, 143.1, 144.2, 177.4; HRMS calcd for $C_{10}H_9NSe$ $[M - Br + H]^+$ 222.9005, found 222.9028.

*Synthesis of 5-(Cyanomethyl)-2-phenylselenazole (**14**).* To a stirred solution of **9a** (150 mg, 0.5 mmol) in DMF (10 mL) was added KCN (39 mg, 0.60 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 2 h, poured into water, and extracted with $Et_2O$. The combined organic layers were dried ($Na_2SO_4$), filtered, and concentrated. The residue was purified by chromatography on $SiO_2$ (*n*-hexane/EtOAc 4:1) to give **14** (38 mg, 36%) as a yellow solid: mp 76.8−78.0 °C; $^1$H NMR $\delta$ 4.02 (d, $J$ = 1.3 Hz, 2H), 7.41 − 7.47 (m, 3H), 7.72 (t, $J$ = 1.3 Hz, 1H), 7.85 (dd, $J$ = 1.7, 7.8 Hz, 2H); $^{13}$C NMR $\delta$ 18.7, 116.7, 127.1, 129.3, 130.9, 132.4, 135.9, 144.2, 176.8; HRMS calcd for $C_{10}H_{10}NSe$ $[M - CN + H]^+$ 223.9900, found 223.9926.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

$^1$H and $^{13}$C spectra for compounds **9a**−**j**, **12b**, **13**, and **14**. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

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