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Selenium compounds in Click Chemistry: copper catalyzed 1,3-dipolar cycloaddition of azidomethyl arylselenides and alkynes

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ABSTRACT

We described herein the use of selenium compounds in Click Chemistry by copper catalyzed 1,3-dipolar cycloaddition of azidomethyl arylselenides with alkynes. The reactions were performed under mild conditions reacting azidomethyl arylselenides with a range of terminal alkynes using catalytic amount of Cu(OAc)₂.H₂O/sodium ascorbate and the corresponding 1-(arylseleno-methyl)-1,2,3-triazoles were obtained in high yields. The reaction time of these reactions could be reduced to a few minutes using microwave irradiation.

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1. Introduction

1,2,3-Triazoles, classic nitrogen heterocyclic compounds, are an important class of molecules, which display a broad spectrum of biological activities.¹ These compounds are also widely employed in various fields of chemistry, such as in the research and modulation of drug candidates,² development of new materials,³ design of new catalysts,⁴ among others.⁵ There is a variety of methods available in the literature for the preparation of 1,2,3-triazoles. The most attractive way to prepare these compounds involves the thermal 1,3-dipolar cycloaddition of azides with alkynes, pioneered by Huisgen.⁶ Independently, Sharpless⁷ and Meldal⁸ not only popularized this reaction but also discovered a copper-catalyzed version for this useful transformation. The development of the copper-catalyzed azide–alkyne cycloaddition (CuAAC) process was a definitive advance in triazole synthesis, and represents the most effective reaction of 'Click Chemistry'.⁹

On the other hand, organoselenium compounds are attractive synthetic targets. They can promote transformations with high levels of selectivity,^{10,11} can be used as ionic liquids,¹² in asymmetric reactions,^{10b,13} exhibit fluorescent properties¹⁴ and are often linked to interesting biological activities.¹⁵ The versatility and applicability of organoselenium compounds in organic chemistry is well described in a great number of reviews¹⁰ and books.¹¹ Among organoselenium compounds, those containing nitrogen atoms in their structure are of

special interest. This class of molecules have been employed in various organic transformations, for instance, in asymmetric synthesis.^{10b,13} Consequently, the search for new and efficient methods for the synthesis of nitrogen-functionalized organoselenium compounds, more specifically organoselenium—triazoles, remains a challenge in organic chemistry. A number of examples for the synthesis of selenium-containing 1,2,3-triazole compounds has been reported,¹⁶ and recently, a CuAAC protocol was published for the synthesis of arylseleno-1,2,3-triazoles in excellent yields under mild reaction conditions, starting from azido arylselenides (Scheme 1).^{16d}



Scheme 1. CuAAC synthesis of arylseleno-1,2,3-triazoles.

However, to the best of our knowledge, methodologies involving CuAAC for the synthesis of organoselenium—triazoles are scarce and have not been well explored. In this sense, and due to our interest correlated to CuAAC protocol for the synthesis





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organoselenium—triazoles, we describe herein the copper catalyzed 1,3-dipolar cycloaddition of azidomethyl arylselenides **1** with terminal alkynes to obtain 1-(arylseleno-methyl)-1,2,3-triazoles **3** (Scheme 2).



Scheme 2. Synthesis of 1-(arylseleno-methyl)-1,2,3-triazoles 3.

2. Results and discussion

Initially, our studies were focused on the synthesis of azidomethyl arylselenides **1**, the starting materials for the synthesis of the selenium-triazoles **3**. Thus, phenylselenolate, generated in situ by the reaction of diphenyl diselenide **4a** with NaBH₄/EtOH, reacted with methylene chloride at reflux, affording chloromethyl phenylselenide **5a** in satisfactory yield (Scheme 3).¹⁷ This compound was easily converted to azidomethyl phenylselenide **1a** in excellent yield after reaction with sodium azide and 18-crown-6 in CH₃CN at room temperature.¹⁸ This protocol was extended to the chloro- and methyl–arylselenide **5b** and **5c**, giving the products **1b** and **1c** in 87% and 92% yield, respectively (Scheme 3).



Scheme 3. Synthesis of azidomethyl arylselenides 1.

Azidomethyl arylselenides **1a**–**c** obtained as described above appear to be highly promising substrates for the CuAAC protocol to obtain selenium–triazol derivatives. This class of compounds^{16b,19a} has a large synthetic importance since they combine the well known reactivity of the azido group²⁰ with that of the seleniumcontaining group.^{10,11}

After that, we turned out our attention to the application of the obtained azidomethyl arylselenides **1a**–**c** in the synthesis of 1-(arylseleno-methyl)-1,2,3-triazoles **3**, using a copper-catalyzed 1,3-dipolar cycloaddition reaction. Generally, these reactions require the generation of Cu(I) species in situ starting from $CuSO_4 \cdot 5H_2O$ and sodium ascorbate in aqueous medium.^{7a} In view of this, firstly we studied the reaction of azidomethyl phenylselenide **1a** (0.3 mmol) with phenylacetylene **2a** (0.3 mmol) in the presence of CuSO₄.5H₂O (5 mol %) and sodium ascorbate (10 mol %) in a mixture of different solvents (2 mL) (Table 1).

Checking the Table 1, it is possible to verify that the reaction afforded the selenium-triazole **3a** in good yields using a variety of organic solvents in combination with H₂O. When we used mixtures of MeOH/H₂O, *t*-BuOH/H₂O, CH₂Cl₂/H₂O, Et₂O/H₂O, acetone/H₂O and THF/H₂O, good yields were obtained of the desired product **3a** (Table 1, entries 1–6). Optimal result was achieved using a mixture of THF/H₂O (1:1) as solvent (Table 1, entry 6). A remarkable feature of this reaction was the H₂O dependence in the selenium-triazole synthesis. Reactions using a mixture of THF/H₂O (1:0.5) or just THF, gave poor yields of the desired product **3a** (Table 1, entries 7–8). This may be due to the increased solubility of sodium ascorbate and copper salt in this solvent.^{16d} However, when the reaction was performed only in H₂O, the formation of product **3a**

Table 1

Study of the solvent effect on CuAAC of azidomethyl arylselenide 1a

PhSe N ₃	+ Ph————H CuSO ₄ .5H ₂ O (5 mc Sodium Ascorbate (10 3 h, r.t., air	^{JI%)} Ph SePh N≈ _N SePh N≈ _N 3a
Entry	Solvent (Ratio)	Isolated yield 3a (%)
1	MeOH/H ₂ O (1:1)	80
2	<i>t</i> -BuOH/H ₂ O (1:1)	83
3	$CH_2Cl_2/H_2O/(1:1)$	77
4	Et ₂ O/H ₂ O (1:1)	82
5	acetone/H ₂ O (1:1)	79
6	THF/H ₂ O (1:1)	88
7	THF/H ₂ O (1:0.5)	47
8	THF	Traces
9	H ₂ O	nd
10	THF/H ₂ O (1:1) ^a	86

^a Reaction under argon atmosphere.

was not observed (Table 1, entry 9). It is important to note that the reactions are not air sensitive, allowing the preparation of the respective triazole **3a** in an open atmosphere (Table 1, entry 10).

We observed that the nature of the copper salt and its amount were critical for the success of the reaction. As shown in Table 2, different copper salts, such as $CuSO_4 \cdot 5H_2O$, $CuBr_2$, $Cu(OTf)_2$, $Cu(OAc)_2 \cdot H_2O$, and CuO nanoparticles, exhibited a moderate to good catalytic activity (Table 1, entries 1–5). Among the conditions tested, the best result was obtained using $Cu(OAc)_2 \cdot H_2O$ (5 mol %), which gave the product **3a** in excellent yield (Table 2, entry 5). It is significant to note that when the amount of catalyst was reduced from 5 mol % to 1 mol %, a decrease in the yield was observed (Table 1, entries 5–7). The analysis of the obtained results indicated that the best reaction conditions were found to be use azidomethyl phenylselenide **1a** (0.3 mmol), phenylacetylene **2a** (0.3 mmol) in presence of CuSO₄.5H₂O (1:1, 2 mL) at room temperature under air atmosphere for 8 h.

Table 2

Influence of copper salt in the CuAAC of azidomethyl arylselenide 1a and phenylacetylene 2a

PhSe N ₃ - 1a	Copper Sa + Ph————————————————————————————————————	alt Ph SePh
Entry	Copper salt (mol %)	Isolated yield 3a (%)
1	CuSO ₄ ·5H ₂ O (5%)	88
2	CuBr ₂ (5%)	70
3	Cu(OTf) ₂ (5%)	65
4	CuO·NPs (5%)	75
5	$Cu(OAc)_2 \cdot H_2O(5\%)$	94
6	$Cu(OAc)_2 \cdot H_2O(3\%)^a$	87
7	$Cu(OAc)_2 \cdot H_2O(1\%)^b$	80

^a 6 mol % of sodium ascorbate was used.

^b 2 mol % of sodium ascorbate was used.

To extend the scope of the reaction, a range of terminal alkynes were reacted with azidomethyl phenylselenide **1a** under the optimized reaction conditions. Thus, terminal alkynes with a variety of substituents, including aryl, alkyl, vinyl, alcohol, and ester were successfully employed in these reactions and the corresponding products were obtained in high yields (Table 3, entries 1–11). Good results were achieved when dialkyne **2l** was reacted with two different amounts of azidomethyl phenylselenide **1a**. When we used 0.3 mmol of compound **1a**, the respective alkynyl selenium—triazole **3l** (Table 3, entry 12) was obtained in 68% yield with traces of bis-

Table 3

Scope and variability of CuAAC of azidomethyl arylselenides^a

	A - O -	Cu(OAc) ₂ sodium asco	.H ₂ O (5%) orbate (10%)	
	Arse 1a-	$\sim N_3 + R - H - THF/H_2$	<u>2</u> O (1:1) N≈N .t. air	
	14-		3а-о	
Entry	Selenoazide	Alkyne	Product	Isolated Yield (%) ^c
1	Se N ₃	2а	Se-	94 (93)
	1a	28	3a	
2	1a	<i>n</i> -С ₅ Н ₁₁ ——— Н 2b	$\frac{n-C_5H_{11}}{N\approx_N} Se^{-1}$	80 (94)
3	1a	<i>n</i> -C ₈ H ₁₇ —— Н 2с	$n - C_8 H_{17} $	75
4	1a	<u>></u> н 2d	Se-	87
5	1a	<u>2</u> е	Se-	91 (97)
6	1a	HO H	HO Se Se	85
7	1a	нон	HO N=N 3g	78
8	1a	но 2h	HO Se Se Se Se Se Share Se	77
9	1a	но 2і	HO N=N Se Se 3i	91 (90) (continued on next page)

Table 3	(continued)
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^a Reactions were performed with azidomethyl arylselenides **1** (0.3 mmol), terminal alkynes **2** (0.3 mmol), Cu(OAc)₂· H₂O (5 mol %), sodium ascorbate (10 mol %) in a mixture of THF/H₂O (1:1) (2 mL) at room temperature under air atmosphere for 8 h.

^b Reaction was performed with 0.6 mmol of azidomethyl phenylselenide **1a**.

^c Yields in parenthesis correspond to reactions performed in a microwave reactor at 50 °C for 10 min.

selenium-triazole **3m**. When we used 0.6 mmol of azidomethyl phenylselenide **1a** the corresponding bis-selenium-triazole **3m** was obtained as the sole product (Table 3, entry 13). Additionally, phenylacetylene **2a** reacted smoothly with azidomethyl arylselenides **1b** and **1c** yielding the corresponding products **3n** and **3o** in 91% and 89%, respectively (Table 3, entries 14–15).

In order to obtain an efficient protocol in terms of energy economy, we performed these 1,3-dipolar cycloaddition reactions under microwave irradiation.²¹ Thus, the mixture of azidomethyl phenylselenide **1a** and phenylacetylene **2a** in the presence of CuSO₄.5H₂O (5 mol %) and sodium ascorbate (10 mol %) in a solvent system of THF/H₂O (1:1) was irradiated under stirring and fortunately, after 10 min at 50 °C, selenium–triazole **3a** was obtained in 93% yield (Table 3). To extend the scope of the microwave protocol,

other terminal alkynes were reacted with azidomethyl phenylselenide **1a** under MW irradiation and the desired seleniumtriazoles were obtained in excellent yields in a short reaction time (Table 3, entries 1–2, 5, 9–11).

3. Conclusion

In conclusion, we have demonstrated the use of selenium compounds in Click Chemistry by copper catalyzed 1,3-dipolar cycloaddition of azidomethyl arylselenides with alkynes. The corresponding selenium—triazoles were selectively prepared in high yields under mild conditions via reaction of azidomethyl arylselenides with a range of terminal alkynes. This click protocol minimizes the energy demand, as well the reaction time could be reduced from several hours to few minutes using MW irradiation. This methodology is efficient to synthesize new selenium-containing triazoles with potential application in biological studies.

4. Experimental section

4.1. General remarks

Proton nuclear magnetic resonance spectra (¹H NMR) were obtained at 300 MHz on a Varian Gemini NMR spectrometer. Spectra were recorded in CDCl₃ solutions. Chemical shifts are reported in parts per million, referenced to tetramethylsilane (TMS) as the external reference. Data are reported as follows: chemical shift (δ), multiplicity, coupling constant (*J*) in Hertz and integrated intensity. Carbon-13 nuclear magnetic resonance spectra (¹³C NMR) were obtained at 75 MHz on a Varian Gemini NMR spectrometer. Spectra were recorded in CDCl₃ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of CDCl₃. Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), t (triplet), qua (quartet), qui (quintet), td (triple doublet), bs (broad singlet) and m (multiplet). Mass spectra (MS) were measured on a Shimadzu GC-MS-QP2010 mass spectrometer. High resolution mass spectra were recorded on a Bruker Micro TOF-QII spectrometer. Column chromatography was performed using Merck Silica Gel (230-400 mesh). Thin layer chromatography (TLC) was performed using Merck Silica Gel GF₂₅₄, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or stained with iodine vapor, or acidic vanillin. All solvents were used as purchased unless otherwise noted. Microwave reactions 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 azidomethyl arylselenides 1a–c

To a solution of chloromethyl arylselenide **5** (1 mmol) in CH₃CN (1.5 mL), sodium azide (1.5 mmol) followed by 18-crown-6 (0.20 mmol) were added at room temperature. Then the mixture was stirred at this temperature for 48 h under nitrogen atmosphere. After this time, the solution was diluted with H₂O (10 mL), and washed with CH₂Cl₂ (3×10 mL). The organic layers were combined, dried over MgSO₄, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using hexanes as the eluent. Spectral data of the products prepared are listed below.

4.2.1. Azidomethyl phenylselenide (**1a**). Yield: 0.193 g (91%); yellow oil; ¹H NMR (CDCl₃, 300 MHz) δ =7.64–7.62 (m, 2H); 7.33–7.30 (m, 3H); 4.62 (s, 2H). ¹³C NMR (CDCl₃, 75 MHz) δ =133.97, 129.33, 129.15, 127.69, 48.71. MS (relative intensity) *m*/*z*: 187 (6), 185 (40), 158 (26), 157 (100), 154 (54), 117 (13), 78 (56), 77 (86), 51 (40). HRMS: Calculated mass to C₇H₇N₃Se: 212.9805, found: 212.9807.

4.2.2. Azidomethyl 4-methylphenylselenide (**1b**). Yield: 0.197 g (87%); yellow oil; ¹H NMR (CDCl₃, 300 MHz) δ =7.51 (d, *J*=8.1 Hz, 2H); 7.11(d, *J*=8.1 Hz, 2H); 4.54 (s, 2H); 2.33 (s, 3H). ¹³C NMR (CDCl₃, 75 MHz) δ =138.34, 134.40, 130.11, 124.54, 48.90, 21.10. MS (relative intensity) *m/z*: 199 (24), 171 (49), 169 (31), 92 (18), 91 (100), 89 (18), 77 (6), 65 (16). HRMS: Calculated mass to C₈H₉N₃Se: 226.9962, found: 226.9969.

4.2.3. Azidomethyl 4-chlorophenylselenide (**1c**). Yield: 0.226 g (92%); yellow oil; ¹H NMR (CDCl₃, 300 MHz) δ =7.54 (d, *J*=8.5 Hz, 2H); 7.28(d, *J*=8.5 Hz, 2H); 4.58 (s, 2H). ¹³C NMR (CDCl₃, 75 MHz) δ =135.41, 134.18, 129.56, 126.51, 48.94. MS (relative intensity) *m/z*: 220 (19), 219 (42), 217 (20), 193 (44), 192 (21), 191 (100), 189 (51),

4.3. General procedure for the synthesis of 1-(arylselanyl-methyl)-1,2,3-triazoles 3a—o

To a solution of azidomethyl arylselenide (0.3 mmol) in THF (1.0 mL), alkyne (0.3 mmol), and distilled water (0.5 mL) were added. Then a fresh solution of sodium ascorbate (0.0012 g, 10 mol %) and Cu(OAc)_2 · H₂O (0.0006 g, 5 mol %) in distilled water (0.5 mL) was added and the mixture was stirred under air for 8 h. Brine solution (3 mL) was added and the mixture was extracted with methylene chloride (3×5 mL). The organic layers were combined, washed with brine (3 mL) and dried with MgSO₄. The solvent was removed under vacuum and the product was isolated by column chromatography using hexane/ethyl acetate as eluent. Spectral data of the products prepared are listed below.

4.3.1. 4-Phenyl-1-(phenylselanylmethyl)-1,2,3-triazole (**3a**). Yield: 0.089 g (94%); white solid; mp 73–74 °C. ¹H NMR (CDCl₃, 300 MHz) δ =7.78–7.75 (m, 2H), 7.64 (s, 1H), 7.52–7.49 (m, 2H), 7.43–7.29 (m, 6H), 5.72 (s, 2H). ¹³C NMR (CDCl₃, 75 MHz) δ =148.09, 134.74, 130.23, 129.52, 128.92, 128.76, 128.19, 127.28, 125.61, 119.28, 44.69. MS (relative intensity) *m*/*z*: 315 (3), 286 (15), 157 (13), 130 (100), 103 (92), 77 (50), 51 (10), 40 (29). Calculated mass to C₁₅H₁₃N₃Se+H⁺: 316.0353, found: 316.0356.

4.3.2. 4-Pentyl-1-(phenylselanylmethyl)-1,2,3-triazole (**3b**). Yield: 0.074 g (80%); white solid; mp 55–56 °C. ¹H NMR (CDCl₃, 300 MHz) δ =7.48–7.45 (m, 2H), 7.35–7.29 (m, 3H), 7.17 (s, 1H), 5.65 (s, 2H), 2.66 (t, *J*=7.7 Hz, 2H), 1.62 (qui, *J*=7.7 Hz, 2H), 1.33–1.30 (m, 4H), 0.89 (t, *J*=7.7 Hz, 3H). ¹³C NMR (CDCl₃, 75 MHz) δ =148.92, 134.68, 129.42, 128.78, 127.38, 120.37, 44.47, 31.23, 28.94, 25.50, 22.33, 13.96. MS (relative intensity) *m/z*: 310 (2), 215 (2), 171 (8), 157 (12), 152 (20), 124 (19), 109 (6), 95 (33), 91 (28), 82 (40), 77 (20), 68 (79), 55 (64), 41 (100). HRMS: Calculated mass to C₁₄H₁₉N₃Se+Na⁺: 332.0642, found: 332.0645.

4.3.3. 4-Octyl-1-(phenylselanylmethyl)-1,2,3-triazole (**3c**). Yield: 0.079 g (75%); white solid; mp 43–44 °C. ¹H NMR (CDCl₃, 300 MHz) δ =7.48–7.45 (m, 2H), 7.35–7.27 (m, 3H), 7.17 (s, 1H), 5.65 (s, 2H), 2.66 (t, *J*=7.7 Hz, 2H), 1.63–1.59 (m, 2H), 1.30–1.26 (m, 10H), 0.88 (t, *J*=7.7 Hz, 3H). ¹³C NMR (CDCl₃, 75 MHz) δ =149.01, 134.71, 129.45, 128.81, 127.44, 120.37, 44.49, 31.85, 29.56, 29.52, 29.29, 29.12, 25.59, 22.64, 14.09. MS (relative intensity) *m/z*: 285 (5), 194 (54), 110 (14), 96 (69), 82 (70), 77 (17), 68 (100). HRMS: Calculated mass to C₁₇H₂₅N₃Se+H⁺: 352.1292, found: 352.1298.

4.3.4. 1-(*Phenylselanylmethyl*)-4-(*prop*-1-*en*-2-*yl*)-1,2,3-*triazole* (**3d**). Yield: 0.073 g (87%); white solid; mp 67–68 °C. ¹H NMR (CDCl₃, 300 MHz) δ =7.50–7.47 (m, 2H), 7.38–7.27 (m, 4H), 5.70–5.64 (m, 3H), 5.09–5.08 (m, 1H), 2.07–2.06 (m, 3H). ¹³C NMR (CDCl₃, 75 MHz) δ =149.06, 134.71, 133.14, 129.47, 128.85, 127.34, 119.28, 112.68, 44.54, 20.49. MS (relative intensity) *m/z*: 279 (5), 171 (5), 157 (7), 122 (28), 94 (100), 77 (19), 67 (98), 65 (35), 54 (49). HRMS: Calculated mass to C₁₂H₁₃N₃Se+Na⁺: 302.0172, found: 302.0176.

4.3.5. 4-Cyclohexenyl-1-(phenylselanylmethyl)-1,2,3-triazole (**3e**). Yield: 0.087 g (91%); white solid; mp 49–50 °C. ¹H NMR (CDCl₃, 300 MHz) δ =7.49–7.46 (m, 2H), 7.35–7.27 (m, 4H), 6.51–6.47 (m, 1H), 5.65 (s, 2H), 2.33–2.28 (m, 2H), 2.21–2.18 (m, 2H), 1.79–1.64 (m, 4H). ¹³C NMR (CDCl₃, 75 MHz) δ =149.86, 134.61, 129.44, 128.76, 127.49, 126.92, 125.25, 117.90, 44.58, 26.19, 25.17, 22.31, 22.06. MS (relative intensity) *m/z*: 319 (3), 194 (4), 163 (100), 133 (12), 104 (31), 77 (40), 57 (13), 44 (38). HRMS: Calculated mass to $C_{15}H_{17}N_3Se+H^+$: 320.0666, found: 320.6670.

4.3.6. (1-(*Phenylselanylmethyl*)-1,2,3-*triazol*-4-*yl*)*methanol* (**3***f*). Yield: 0.069 g (85%); yellow oil. ¹H NMR (CDCl₃, 300 MHz) δ =7.40–7.37 (m, 3H), 7.24–7.19 (m, 3H), 5.57 (s, 2H), 4.60 (s, 2H), 3.47 (bs, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ =148.34, 134.46, 129.49, 128.78, 127.43, 121.62, 56.09, 44.55. MS (relative intensity) *m/z*: 269 (4), 175 (13), 149 (10), 112 (100), 110 (23), 91 (21), 77 (33), 57 (35), 43 (83), 42 (87). HRMS: Calculated mass to C₁₀H₁₁N₃OSe+Na⁺: 291.9965, found: 291.9970.

4.3.7. (2-(Phenylselanylmethyl)-1,2,3-triazol-4-yl)ethanol (**3g**). Yield: 0.066 g (78%); yellow oil. ¹H NMR (CDCl₃, 300 MHz) δ =7.40–7.37 (m, 2H), 7.27–7.21 (m, 4H), 5.58 (s, 2H), 3.79 (t, J=6.0 Hz, 2H), 3.53 (bs, 1H), 2.81 (t, J=6.0 Hz, 2H). ¹³C NMR (CDCl₃, 75 MHz) δ =145.78, 134.59, 129.46, 128.84, 127.27, 121.61, 61.24, 44.56, 28.56. MS (relative intensity) *m*/*z*: 283 (3), 189 (6), 157 (14), 126 (77), 91 (31), 77 (30), 69 (82), 55 (100). HRMS: Calculated mass to C₁₁H₁₃N₃OSe+Na⁺: 306.0122, found: 306.0124.

4.3.8. (3-(*Phenylselanylmethyl*)-1,2,3-*triazol*-4-*yl*)*propanol* (**3h**). Yield: 0.069 g (77%); yellow oil. ¹H NMR (CDCl₃, 300 MHz) δ =7.40–7.37 (m, 2H), 7.28–7.22 (m, 3H), 7.16 (s, 1H), 5.57 (s, 2H), 3.58 (t, *J*=6.1 Hz, 2H), 2.70 (t, *J*=6.1 Hz, 2H), 1.80 (t, *J*=6.1 Hz, 2H), 1.18 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ =148.02, 134.67, 130.23, 129.48, 128.86, 127.29, 120.83, 61.69, 44.53, 31.84, 21.87. MS (relative intensity) *m*/*z*: 298 (1), 203 (2), 171 (7), 157 (12), 140 (33), 112 (7), 94 (21), 91 (26), 84 (27), 82 (31), 77 (25), 67 (45), 55 (33), 41 (100). HRMS: Calculated mass to C₁₂H₁₅N₃OSe+Na⁺: 320.0278, found: 320.0282.

4.3.9. (2-(*Phenylselanylmethyl*)-1,2,3-*triazol*-4-*yl*)*propan*-2-*ol* (**3i**). Yield: 0.081 g (91%); yellow oil. ¹H NMR (CDCl₃, 300 MHz) δ =7.40–7.37 (m, 2H), 7.27–7.17 (m, 4H), 5.56 (s, 2H), 1.98 (bs, 1H), 1.49 (s, 6H). ¹³C NMR (CDCl₃, 75 MHz) δ =155.93, 134.72, 129.42, 128.84, 127.22, 119.21, 68.13, 44.50, 30.16. MS (relative intensity) *m*/*z*: 250 (6), 171 (8), 122 (18), 94 (100), 77 (25), 67 (81), 65 (30), 54 (31), 43 (26). HRMS: Calculated mass to C₁₂H₁₅N₃OSe+Na⁺: 320.0278, found: 320.0283.

4.3.10. (1-(Phenylselanylmethyl)-1,2,3-triazol-4-yl)cyclohexanol (**3***j*). Yield: 0.091 g (90%); white solid; mp 45–47 °C. ¹H NMR (CDCl₃, 300 MHz) δ =7.49–7.46 (m, 2H), 7.38–7.27 (m, 4H), 5.65 (s, 2H), 2.66 (bs, 1H), 2.90–1.78 (m, 10H). ¹³C NMR (CDCl₃, 75 MHz) δ =154.62, 134.74, 129.49, 128.88, 127.33, 119.59, 78.75, 44.52, 41.09, 23.49. MS (relative intensity) *m*/*z*: 337 (3), 276 (5), 197 (11), 166 (26), 120 (71), 110 (53), 96 (61), 91 (100), 77 (68), 41 (48). HRMS: Calculated mass to C₁₅H₁₉N₃OSe+Na⁺: 360.0591, found: 360.0593.

4.3.11. Ethyl 1-(phenylselanylmethyl)-1,2,3-triazole-4-carboxylate (**3k**). Yield: 0.079 g (85%); white solid; mp 70–72 °C. ¹H NMR (CDCl₃, 300 MHz) δ =8.00 (s, 1H), 7.48–7.45 (m, 2H), 7.38–7.29 (m, 3H), 5.71 (s, 2H), 4.41 (qua, *J*=7.1 Hz, 2H), 1.40 (t, *J*=7.1 Hz, 3H). ¹³C NMR (CDCl₃, 75 MHz) δ =160.46, 140.58, 134.81, 129.74, 129.27, 127.16, 126.68, 61.37, 44.84, 14.26. MS (relative intensity) *m/z*: 266 (5), 217 (6), 157 (13), 154 (100), 77 (27), 54 (27), 51 (12). HRMS: Calculated mass to C₁₂H₁₃N₃O₂Se+Na⁺: 334.0071, found: 334.0073.

4.3.12. 4-(*Pent-4-ynyl*)-1-(*phenylselanylmethyl*)-1,2,3-*triazole* (**3l**). Yield: 0.062 g (68%); yellow oil. ¹H NMR (CDCl₃, 400 MHz) δ =7.49–7.46 (m, 2H), 7.39–7.27 (m, 3H), 7.23 (s, 1H), 5.66 (s, 1H), 2.81 (t, *J*=7.5 Hz, 2H), 2.20 (td, *J*=6.8; 2.6 Hz, 2H), 1.97 (t, *J*=2.6 Hz, 1H), 1.87 (t, *J*=7.5 Hz, 2H). ¹³C NMR (CDCl₃, 75 MHz) δ =147.46, 134.72, 129.51, 128.89, 127.28, 120.88, 104.66, 83.60, 68.93, 44.56, 27.76, 24.23, 17.65. MS (relative intensity) *m/z*: 224 (6), 196 (4), 157 (9), 118 (19), 91 (97), 80 (65), 77 (100), 65 (29), 41 (39). HRMS: Calculated mass to $C_{14}H_{15}N_3Se+Na^+$: 328.0329, found: 328.0331.

4.3.13. 1,3-bis(1-(Phenylselanylmethyl)-1,2,3-triazol-4-yl)propane (**3m**). Yield: 0.121 g (78%); white solid; mp 88–90 °C. ¹H NMR (CDCl₃, 300 MHz) δ =7.48–7.45 (m, 4H), 7.37–7.22 (m, 8H), 5.65 (s, 4H), 2.69 (t, *J*=7.5 Hz, 4H), 1.97 (qui, *J*=7.5 Hz, 4H). ¹³C NMR (CDCl₃, 75 MHz) δ =148.25, 134.96, 129.82, 129.16, 127.70, 121.07, 44.82, 29.12, 25.07. MS (relative intensity) *m/z*: 518 (1), 333 (4), 266 (15), 173 (11), 171 (61), 169 (31), 157 (10), 147 (13), 93 (26), 91 (100), 80 (20), 77 (22), 41 (26). HRMS: Calculated mass to C₂₁H₂₂N₆Se₂+H⁺: 519.0315, found: 519.0320.

4.3.14. 4-Phenyl-1-(4-tolylselanylmethyl)-1,2,3-triazole (**3n**). Yield: 0.090 g (91%); white solid; mp 77–79 °C. ¹H NMR (CDCl₃, 300 MHz) δ =7.76 (d, *J*=7.9 Hz, 2H), 7.63 (s, 1H), 7.41–7.29 (m, 5H), 7.10 (d, *J*=7.9 Hz, 2H), 5.67 (s, 2H), 2.33 (s, 3H). ¹³C NMR (CDCl₃, 75 MHz) δ =148.30, 139.31, 135.11, 130.63, 130.43, 128.82, 128.22, 125.84, 123.88, 119.27, 44.88, 21.13. MS (relative intensity) *m/z*: 329 (7), 300 (16), 130 (100), 103 (76), 91 (22), 77 (35), 57 (39), 43 (30). HRMS: Calculated mass to C₁₆H₁₅N₃Se+H⁺: 330.0509, found: 330.0511.

4.3.15. 4-Phenyl-1-(4-chlorophenylselanylmethyl)-1,2,3-triazole (**30**). Yield: 0.093 g (89%); white solid; mp 82–83 °C. ¹H NMR (CDCl₃, 300 MHz) δ =7.78 (d, *J*=8.0 Hz, 2H), 7.72 (s, 1H), 7.44–7.33 (m, 5H), 7.27 (d, *J*=8.0 Hz, 2H), 5.70 (s, 2H). ¹³C NMR (CDCl₃, 75 MHz) δ =148.39, 136.20, 135.57, 130.12, 129.77, 128.86, 128.37, 125.69, 125.24, 119.19, 44.79. MS (relative intensity) *m/z*: 349 (4), 320 (7), 240 (5), 131 (11), 130 (100), 103 (57), 102 (20), 77 (26), 57 (24), 43 (19). HRMS: Calculated mass to C₁₅H₁₂ClN₃Se+H⁺: 349.9963, found: 349.9968.

4.4. General procedure for the microwave synthesis of 1-(ar-ylselanyl-methyl)-1,2,3-triazoles

In a 10 mL glass vial equipped with a small magnetic stirring bar, containing a solution of azidomethyl phenylselenide **1a** (0.3 mmol) and the appropriate alkyne **2** (0.3 mmol) in THF (1.0 mL), the fresh aforementioned aqueous solution of sodium ascorbate and $Cu(OAc)_2 \cdot H_2O$ was added. The vial was tightly sealed with an aluminum/Teflon crimp top and the mixture was then irradiated in a focused microwaves reactor (CEM) at 50 °C, using an irradiation power of 50 W and pressure of 50 psi. After stirring for 10 min, the products were isolated as described above.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tet.2012.07.019.

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